"SULPHUR EXTRUSION"

Thesis

Submitted to Glasgow University

for the Degree of

Doctor of Philosophy

by

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October, 1958.

Acknowledgements

The author thanks Dr. J.D. Loudon for expert supervision and encouragement during the last three years, and also Professor D.H.R. Barton, who supervised the work described in the addendum.

Mr. J.M.L. Cameron and his assistants are thanked for speedy and accurate microanalysis.

Thanks is due also to Mr. G. Milmine for assistance in preparing some starting materials.

The author is indebted to the Department of Scientific and Industrial Research for a three-year maintenance grant.

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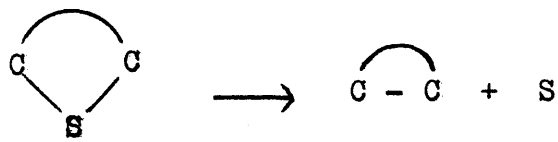
PART 1

Effect of Substituents on Extrusion of Sulphur from 11-Phenydibenzo[b,f]-1:4-thiazepines

CONTENTS

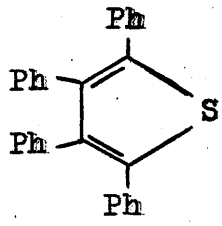
INTRODUCTION

The extrusion of a thia atom linked to two carbon atoms in a cyclic system with the concomitant formation of a bond between the two carbon atoms is not a common occurrence in organic chemistry



Only four references to such a reaction are made by Tarbel and Harnish[1] in a fairly recent review of the "cleavage of the carbon-sulphur bond in divalent sulphur compounds." As will be seen however, several more examples were extant although dispersed throughout the literature.

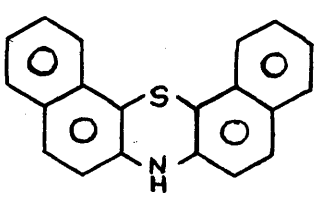
The reaction is not to be confused with the hydrogenolytic removal of sulphur by means of, for example, Raney-nickel, which is well known. An interesting illustration of the latter is recorded by Badger et al[2] who prepared 1:2:3:4-tetraphenylbutane (II) from 2:3:4:5-tetraphenylthiophen (I) by the action of Raney-nickel in boiling mesitylene. In this type of reaction, reduction always accompanies removal of sulphur.



$\longrightarrow$ $PhCH_2.CHPh.CHPh.CH_2Ph$

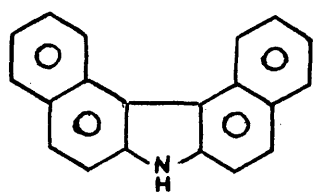
I II

Most of the earlier instances of "bona fide" extrusion describe the elimination of a sulphur atom from a six-membered heterocyclic ring. Thus Ris[3], in 1886, prepared a dibenzocarbazole (probably IV) by slow distillation of a dibenzophenothiazine in a carbon dioxide atmosphere. The latter compound was prepared by heating di-β-naphthylamine with sulphur and almost certainly had the structure (III)



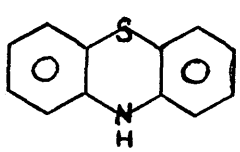
III

$\longrightarrow$



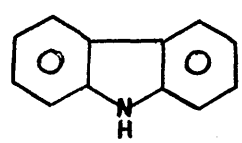
IV

A year later, Goske[4] isolated carbazole itself after boiling phenothiazine (V) with copper for two hours.



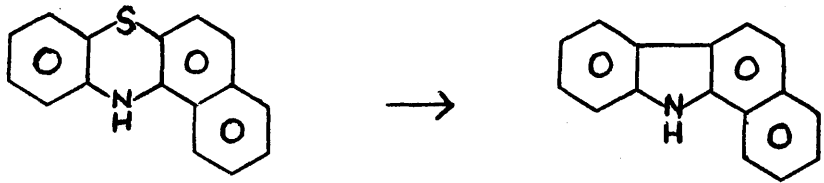
V

$\longrightarrow$



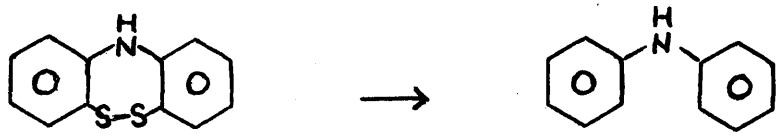
VI

In 1890, Kym[5] completed the series by preparing 1:2-benzcarbazole (VIII) from 1:2-benzophenothiazine (VII).



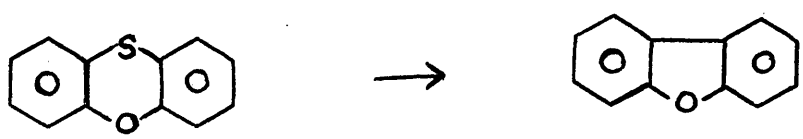
VII VIII

It is an interesting anomaly that, Holtzmann[6], attempting to obtain carbazole by decomposition of diphenylamine-2:2′-disulphide (IX) with copper at 250°C, could only isolate diphenylamine (X).



IX X

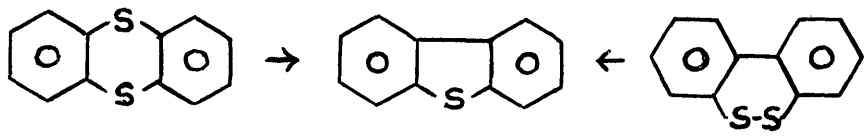
In 1911, Ferrario[7] reported the desulphurisation of phenoxathiin (XI) to dibenzofuran (XII) but later workers[8,9,10] were unable to repeat this experiment, even by varying the reaction conditions.



XI XII

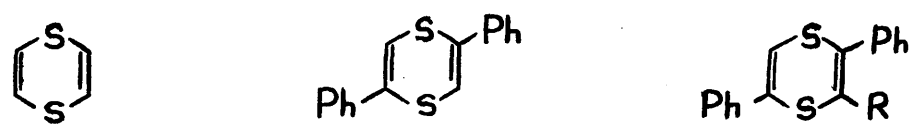
However, Ferrario's claim has some analogy in the

conversion of thianthrene (XIII) to dibenzothiophen (XIV)[11], a reaction which is well authenticated. Dibenzothiophen was also preparable by treatment of dibenzo-o-dithiin (XV) with copper at 250°C for two hours[12].



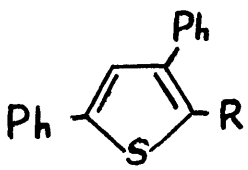
XIII XIV XV

Perhaps the most interesting discoveries, as far as the contents of part 1 of this thesis are concerned, were those of Parham et al.,[13,14,15,16] working on p-dithiins. p-Dithiin (XVI) itself is not very aromatic but its 2:5-diphenyl derivative (XVII) shows some aromatic character; thus, when treated in acetic anhydride with a weak solution of nitric acid in acetic acid, 3-nitro-2:5-diphenyl-p-dithiin (XVIII; R = NO_2) was obtained; and brief treatment with bromine gave the corresponding 3-bromo derivative (XVIII ; R = Br)

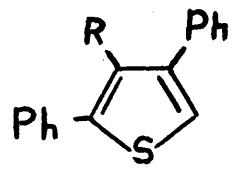


XVI XVII XVIII

When (XVII) was treated with dimethylformamide and phosphoryl chloride, extrusion of sulphur accompanied formylation, the product being 5-aldehyde-2:4-diphenylthiophen (XIX ; R = CHO), the structure of which was established by independent synthesis. Decomposition to 2:4-diphenylthiophen (XIX ; R = H) resulted when (XVII) was heated in an inert atmosphere at 190°C. To effect a similar decomposition on (XVIII ; R = NO_2), however, a temperature of only 135° was required. The main product was 5-nitro-2:4-diphenylthiophen (XIX ; R = NO_2), the structure once again being confirmed by synthesis. 3-Nitro-2:4-diphenylthiophen (XX ; R = NO_2) was not detected

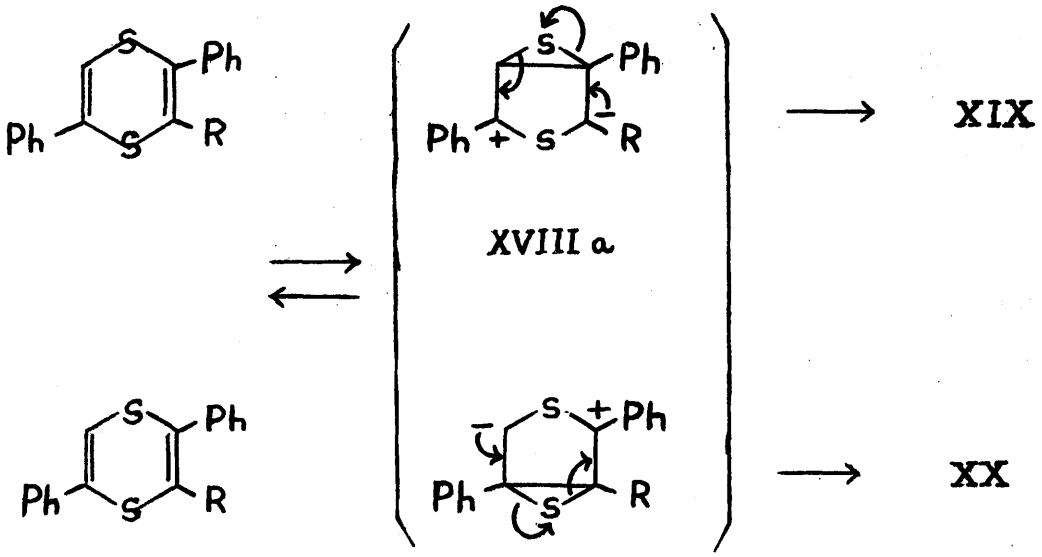


XIX



XX

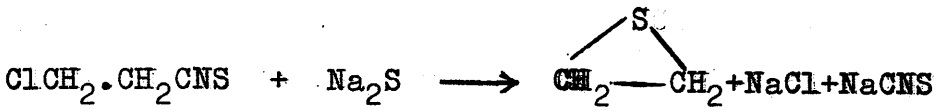
To interpret the experimental facts, Parham forwarded the following mechanism involving extrusion of sulphur from the episulphide structures (XVIIIa and XVIIIb) which he considered resonance hybrids of XVIII.



XVIII XVIIIb

The formation of (XIX ; R = NO_2, CHO) in preference to (XX; R = NO_2,CHO) was explained by examination of the possible resonance hybrids of (XVIII ; R = NO_2,CHO). The contribution of structure (XVIIIa), where the negative charge may be delocalised by the nitro- or aldehydo-group should be greater than the contribution of (XVIIIb). This mechanism, which also explains why (XVIII ; R = NO_2) loses sulphur more readily than (XVII), is all the more reasonable in view of the fact that episulphide rings are very labile. This instability is probably the reason why comparatively little is known of them.

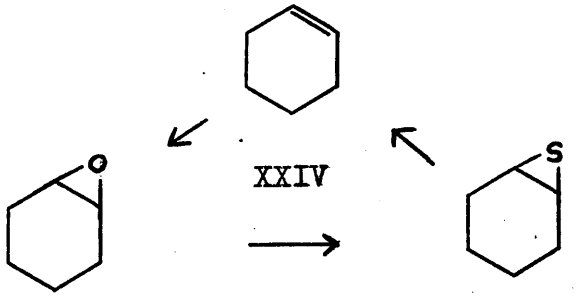
Delépine[17], however, has reported the preparation of the parent compound, ethylene sulphide (XXI) by the action of sodium sulphide on β-chloroethylthiocyanate.



XXI

The product was a colourless liquid which polymerised readily but no mention was made of its tendency to extrude sulphur.

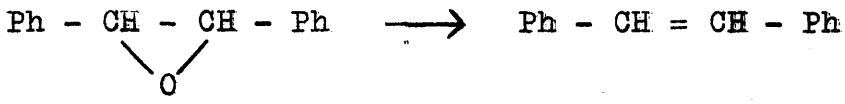
A convenient method of preparation of episulphides was discovered by Culvenor, Davies et al.,[18,19,20,21,22] who heated the corresponding epoxides with thio-compounds, of which the most commonly used was thiourea. Thus, treatment of cyclohexene oxide (XXII) with thiourea in methanol at 60°C for just over an hour gave cyclohexene sulphide (XXIII) in good yield. The product was distilled without decomposition. More recently, however, Bordwell et al.[23] have prepared cyclohexene (XXIV) from this episulphide by the action of butyl lithium or phenyl magnesium bromide in ether.



XXII XXIV XXIII

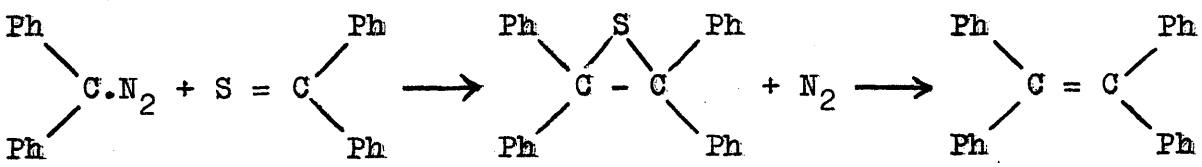
Aryl-substituted episulphides show little tendency to

polymerise but readily split out sulphur to form olefins. When stilbene oxide (XXV) was treated with thiourea in ethanol for six days, stilbene (XXVI) was obtained in 80% yield[19]. No episulphide was detected but the high recovery of sulphur (65% of the theoretical amount) supported the view that an intermediate sulphide had been formed.



XXV XXVI

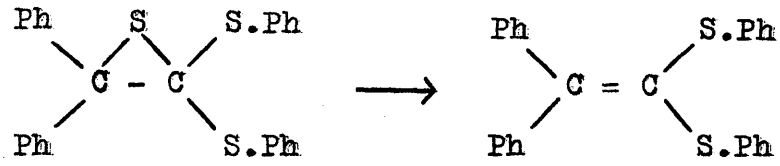
By reaction between diazodiphenylmethane and thiobenzophenone, Staudinger and Siegwart[24] isolated tetraphenylethylene sulphide (XXVII) which lost sulphur when heated at 175°, producing tetraphenylethylene (XXVIII)



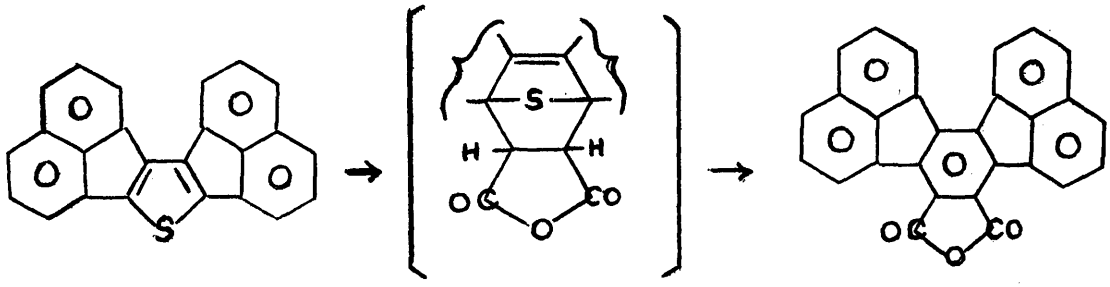
XXVII XXVIII

The catalytic effect of copper on extrusion of sulphur was illustrated by Schönberg[25] in his experiments on the decomposition of the episulphide (XXIX), which when treated with copper bronze in boiling benzene, gave α-diphenyl-β-

dithiophenylethylene (XXX). In the absence of copper, a temperature of 180-200° was required.



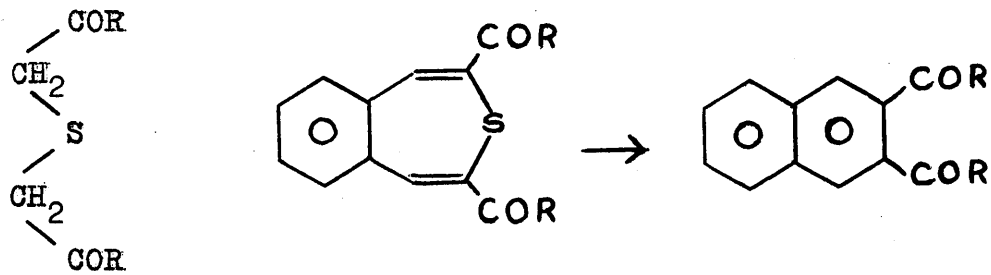
An interesting example of sulphur removal (as distinct from extrusion) from a five-membered heterocyclic ring emerged from a Diels-Alder type of reaction between the highly-condensed thiophen (XXXI) and maleic anhydride[26]. Hydrogen sulphide was evolved - presumably from the adduct (XXXII) which was not isolated - and the final product was the phthalic anhydride (XXXIII)



XXXI XXXII XXXIII

Instances of sulphur extrusion from seven-membered heterocyclic rings are of more recent origin. Condensation of o-phthalaldehyde with diethyl thiodiacetate (XXXIV ; R = OEt) afforded 4:5-benzothiepin-2:7-dicarboxylic acid

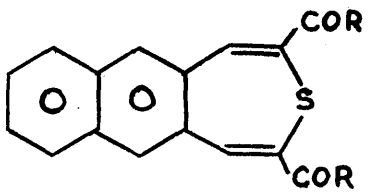
(XXXV ; R = OH), which proved particularly labile sulphur being eliminated in boiling aqueous ethanol, giving naphthalene-2:3-dicarboxylic acid (XXXVI ; R = OH)[27,28].



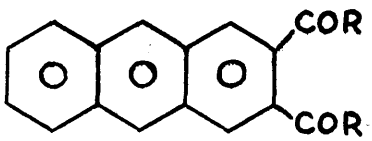
XXXIV XXXV XXXVI

In a further investigation of this reaction, Sloan[29] found that condensation between phthalaldehyde and diphenacyl sulphide (XXXIV ; R = Ph) in alkali, gave 2:3-dibenzoyl-naphthalene, no intermediate thiepin being isolated. However, a similar experiment, this time with naphthalene-2:3-dialdehyde, furnished a good yield of 2:7-dibenzoyl-naphtho[2′:3′-4:5]thiepin (XXXVII ; R = Ph), which decomposed to 2:3-dibenzoylanthracene (XXXVIII; R = Ph) at 180°C. The interaction of this aldehyde and diethyl thiodiacetate proved to be more complicated, a mixture of the mono and diethylesters of the thiepin (XXXVII ; R = OH) being obtained. The former ester eliminated sulphur at 180°C, producing the anhydride of anthracene-

2:3-dicarboxylic acid (XXXVIII ; R = OH)

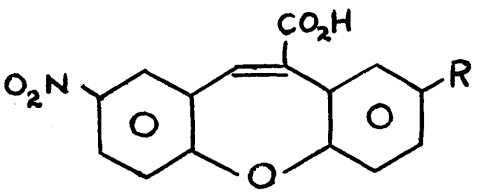


XXXVII

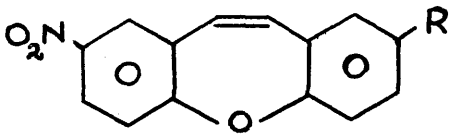


XXXVIII

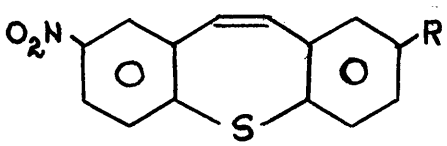
Summers[30] prepared the dibenzo[b,f]oxepins (XXXIX ; R = H, CH_3) by decarboxylation of the 10-carboxy-2-nitro-dibenzo[b,f]oxepins (XL ; R = H,CH_3) with copper in boiling quinoline. Attempting to synthesise the corresponding dibenzo[b,f]thiepins (XLI ; R = H,CH_3) by an analogous route, he found that desulphurisation accompanied decarboxylation and the products were the 7-nitrophenanthrenes (XLII ; R = H, CH_3)



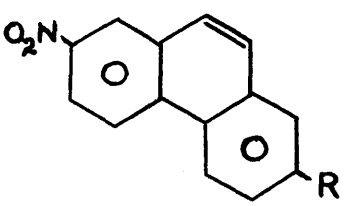
XL



XXXIX

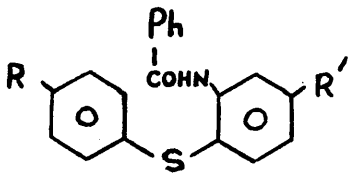


XLI

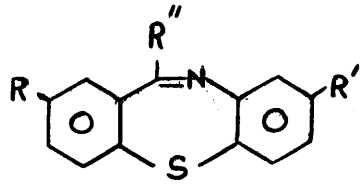


XLII

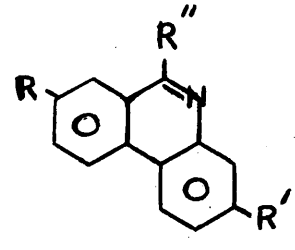
Substituted 11-phenyldibenzo[b,f]-1:4-thiazepines (XLIII) were preparable via a Bischler-Napieralski type of ring closure of 2-acylaminodiaryl sulphides (XLIV)[31], a reaction which finds considerable application in this thesis. Treatment of (XLIII ; R = R′ = Br, CN, R′′ = Ph) with cuprous salts in boiling quinoline produced small amounts of the corresponding phenanthridines (XLV ; R = R′ = Br, CN, R′′ = Ph). Recently, Jarrett and Loudon[32] considerably improved the yields from this type of decomposition, by treatment of the thiazepines (XLIII ; R = NO_2, R′ = H, R′′ = CH_3,Ph) with copper bronze in boiling diethyl phthalate for 5-7 minutes. Similar reaction conditions, with the time of heating extended to one hour, gave a high yield of 9-phenylphenanthridine (XLV ; R = R′ = H, R′′ = Ph) from 11-phenyldibenzo[b,f]-1:4-thiazepine (XLIII ; R = R′ = H, R′′ = Ph)[33]



XLIV



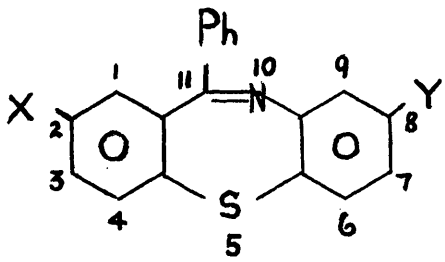
XLIII



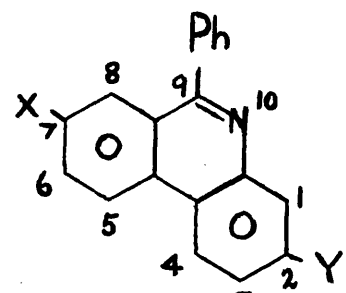
XLV

DISCUSSION

2-Nitro-11-phenyldibenzo[b,f]-1:4-thiazepine (I ; X = NO_2, Y = H) gives a much higher yield of 7-nitro-9-phenylphenanthridine (II ; X = NO_2, Y = H) than 11-phenyldibenzo[b,f]-1:4-thiazepine (I ; X = Y = H) does of 9-phenylphenanthridine (II ; X = Y = H) when heated for the same time with copper bronze and diethyl phthalate[32,33].



I



II

In order to study more carefully the effect of ring substituents on the ease of extrusion of a thia atom, a series of compounds was synthesised, possessing the 11-phenyldibenzo[b,f]-1:4-thiazepine skeleton with various substituents at X and Y, the 2- and 8- positions respectively (cf. I). Attention was restricted to this particular substitution pattern, since substituents <u>para</u> to the sulphur atom were likely to be the most significant and to be free from steric complications. The compounds

examined are listed below:-

I ; X = H : Y = H, CH_3, Cl, OCH_3, OH and NO_2.

Y = H : X = CH_3, Cl, OCH_3, OH and NO_2.

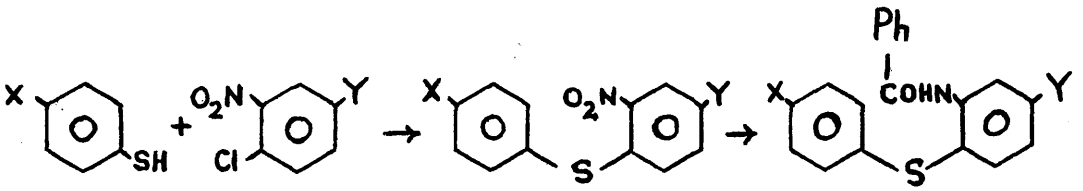
X = CH_3: Y = Cl and NO_2

X = Cl, Y = Cl

X = OCH_3, Y = NO_2.

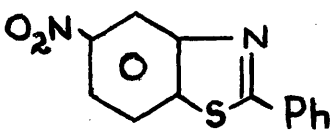
X = NO_2, Y = CH_3

Three methods of synthesis were employed. Compounds (I ; X = H, Y = H, CH_3, Cl, OCH_3 : Y = H, X = CH_3, Cl, OCH_3 : X = Cl, Y = Cl : X = CH_3, Y = Cl) were prepared by the method of Brodrick, Nicholson and Short[31] who applied a Bischler-Napieralski type of ring closure to 2-benzamido-diaryl sulphides (III). The latter were obtained from the corresponding 2-nitrodiaryl sulphides (II) by reduction of the nitro group with iron filings and water in presence of a trace of ferric chloride[34], followed by benzoylation of the resultant aniline.



II III

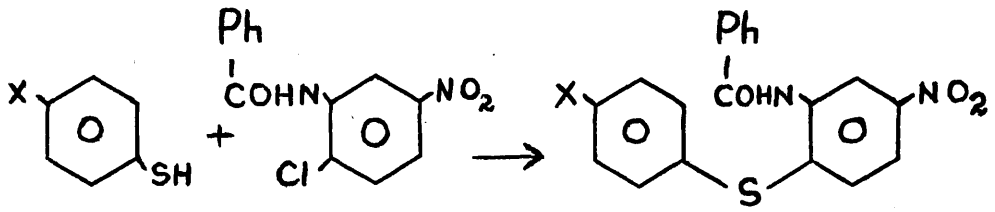
With the exception of two cases, the cyclisation step, using phosphoryl chloride in nitrobenzene, was effected without complication and in yields of 70 to 80%. In one of the exceptional cases, ring closure of (III ; X = OCH_3, Y = NO_2) afforded only a 41% yield of thiazepine together with a small quantity of 5-nitro-2-phenylbenzthiazole (IV) which was identified by melting point[35] and analysis.



IV

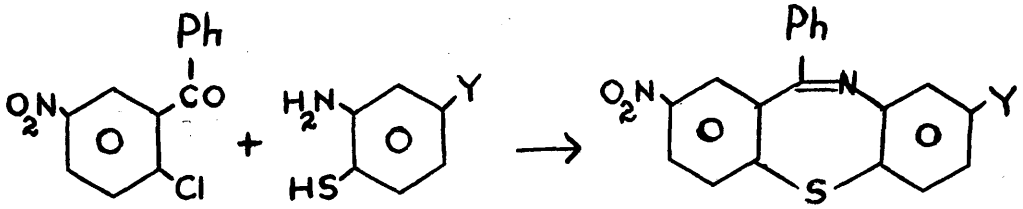
The second anomaly arose in the cyclisation of (III ; X = H, Y = OCH_3) when, apart from the expected thiazepine (I ; X = H, Y = OCH_3), there was isolated 2-methoxy-9-phenylphenanthridine in 43% yield. Extrusion of sulphur in these low temperature conditions was an encouraging sign at this stage, indicating as it did that a significant range of reactivity would be found. Demethylation of (I ; X = H, Y = OCH_3) and of (I ; X = OCH_3, Y = H) with 50% aqueous hydrobromic acid and acetic acid produced (I ; X = H, Y = OH) and (I ; X = OH, Y = H) respectively.

The thiazepines (I ; X = H, CH_3, OCH_3, Y = NO_2) were prepared by the condensation of 2-chloro-5-nitrobenzanilide with thiophenol, p-thiocresol and p-methoxythiophenol respectively and the so-formed 2-benzamidodiaryl sulphides (V) were cyclised as in the first method. This is a new and convenient method of preparation of thiazepines of this type.



V

In the third synthetic route, condensation between 2-chloro-5-nitrobenzophenone and o-aminothiophenol by the method of Garrett and Loudon[32] afforded (I ; X = NO_2, Y = H) in a single stage.



A similar reaction this time using p-methyl-o-aminothiophenol gave (I ; X = NO_2, Y = CH_3). p-Methyl-o-aminothio-

phenol was prepared by reductive cleavage of 2:2′-dinitro-4:4′-dimethyldiphenyl disulphide[36].

It seems probable that the extrusion could be followed by physical methods. The ultraviolet absorption spectra of 11-phenyldibenzo[b,f]-1:4-thiazepines and 9-phenyl-phenanthridines are sufficiently different[10] so that the percentage conversion of one to the other could be calculated from the relative intensities of suitable maxima. The minimum energy necessary for extrusion of the sulphur atom can also be measured by mass spectrometry, for when the thiazepine (I ; X = Y = H) was bombarded with a beam of about twelve electron volts, two distinct peaks were obtained corresponding to the molecular weights of the thiazepine and phenanthridine. It was decided, however, to study the reaction, firstly, by purely chemical methods, involving the isolation and characterisation of the various products.

Each of the synthesised thiazepines was heated for ten, fifteen and thirty minutes under carefully standardised conditions with copper bronze and boiling diethyl phthalate, a medium which was known to give high yields of desulphurisation products from compounds of this type. When heated for sixty-five minutes, for example, 11-phenyldibenzo[b,f]-1:4-thiazepine (I ; X = Y = H) gave a yield of over 90%

of 9-phenylphenanthridine[33]. It was hoped that the yields of phenanthridines produced during the different times of heating would give a measure of the rate of decomposition and also that, in a few favourable cases, desulphurisation would be complete in ten minutes.

The apparatus was of simple construction, but was so designed that all reactions could be conducted in a moisture-free atmosphere of nitrogen. The phenanthridines produced were conveniently isolated as their picrates and, unless when otherwise indicated, the yields recorded are based on the weights of picrates formed. Control experiments revealed, however, that for the phenanthridines (I ; X = NO_2, Y = H, CH_3 : X = H, CH_3, OCH_3, Y = NO_2: X = OH, Y = H), precipitation of picrates was slow and incomplete. In these cases modified techniques were adopted (see Experimental). The results are shown in Table 1.

It should be noted here, that, although three systems of numbering the phenanthridine (benzo[C]quinoline) nucleus have been advanced, the literature, until quite recently has adopted almost exclusively that of Beilstien's Handbuch (cf. formula II). This system is adopted here and accordingly the X and Y substituents occupy the 7- and 2-positions respectively in phenanthridines.

Table 1

X	Y	% Yield (Time) 10 minutes	15	30
H	H	57	73	86
H	CH_3	80	-	86
CH_3	H	51	-	83
H	Cl	61	73	81
Cl	H	56	71	84
H	OCH_3	82	-	82
OCH_3	H	77	85	88
H	OH	75	-	-
OH	H	52^{+}	-	-
H	NO_2	nil^{x}	-	15^{x}
NO_2	H	79	-	-
Cl	Cl	66	77	83
CH_3	Cl	61	79	89
CH_3	NO_2	nil^{x}	-	20^{x}
NO_2	CH_3	88	-	-
OCH_3	NO_2	60^{x}	-	-

Notes: + anomalous picrate formation (see later).

x high recovery of thiazepine.

Although these results show definite trends, the general rapidity of the reaction in diethyl phthalate tends to obscure significant detail. Consequently, a further series of experiments was conducted in which selected thiazepines were heated for one hour with copper bronze in boiling quinoline. For this series, the methods of isolation varied considerably (see Experimental) because of the difference in properties of the phenanthridines formed and also because of the basic reaction medium. The results, however, proved to be repeatable with fair accuracy ($\pm$ 10% variation) and are listed in Table II.

Table II

X	Y	% yield of phenanthridine in 60 minutes	Recovery of thiazepine
H	H	nil	0.116g. from 0.145g.
H	CH_3	38	0.050g. " 0.150g.
H	OCH_3	79	-
OCH_3	H	10	0.104g. from 0.158g.
H	OH	76	-
OH	H	nil	0.113g. from 0.151g.
NO_2	H	30	0.040g. " 0.166g.
NO_2	CH_3	60	-
OCH_3	NO_2	9	0.115g. from 0.181g.

It is clear that, in diethyl phthalate, thiazepines possessing an electron-donating substituent in the Y position (I ; X = H, Y = CH_3, OH, OCH_3) or an electron-attracting substituent in the X position (I ; X = NO_2, Y = H) or a combination of these two (I ; X = NO_2, Y = CH_3) react much more rapidly than the parent compound (I ; X = Y = H).

An electron-attracting group in the Y position (I ; X = H, CH_3, Y = NO_2) considerably retards the reaction, only meagre yields of phenanthridine being obtained from these thiazepines even after heating for thirty minutes. However, when the molecule possesses a powerful electron donor in the X position as well as an electron acceptor at Y (I ; X = OCH_3, Y = NO_2), the reaction is markedly accelerated.

A weak electron-donating substituent in the X position (I ; X = CH_3, Y = H) has little effect on the reaction rate, whereas when this group is a powerful donor (I ; X = OCH_3, Y = H), there is a significant increase in rate. The thiazepine (I ; X = OH, Y = H) which might have been expected to resemble (I ; X = OCH_3, Y = H) behaved anomalously in respect of picrate formation. On addition of picric acid to a benzene solution of this phenolic product after completion of the extrusion reaction, there

was a colour change from yellow to red and crystallisation of picrate began only after some hours. Concentration of the solution afforded further crops of picrate with progressively lower melting points and, for this reason, accurate assessment was difficult. The figure in Table I which represents the yield of pure picrate is almost certainly a minimal value.

The difference in reaction rate between the halogen-substituted thiazepines (I ; X = H, CH_3, Cl, Y = Cl : X = Cl, Y = H) and the parent compound is almost negligible.

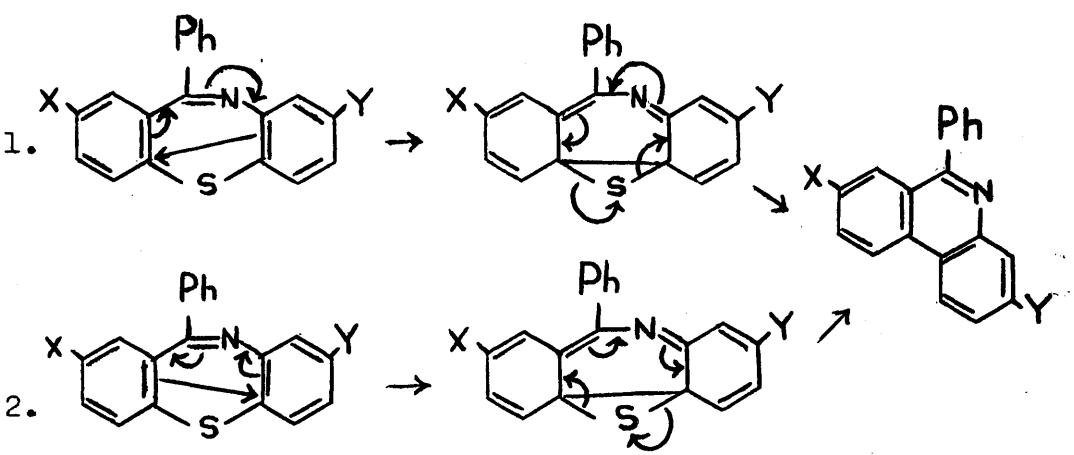
The results obtained in the quinoline medium (Table II) provide a more detailed picture of the reaction and, in many ways, support those of Table I. The parent compound (I ; X = Y = H) was recovered unchanged under these conditions, a fact which supports a previous similar finding by Brodrick et al[31]. Once again, an electron donor in the Y position promotes the reaction but, in this medium, the rate is seen to depend on the nature of this donor (i.e. whether weak or strong), a differentiation which is not apparent in the higher-temperature reactions (cf. I ; X = H, Y = CH_3 and I ; X = H, Y = OH, OCH_3).

An electron-attracting substituent in the X position also promotes the reaction (I ; X = NO_2, Y = H, CH_3) but the effect of the methyl group in the latter is emphasised

at this temperature. A powerful electron donor in the X position (I ; X = OCH_3, OH, Y = H) does not promote the reaction, however, little or no yield of phenanthridine being obtained. The thiazepine (I ; X = OCH_3, Y = NO_2) is similarly inert. Unless of particular interest, those thiazepines which gave less than a 70% yield of phenanthridine in diethyl phthalate, were not subjected to the lower-temperature conditions. There is little doubt that the yields of desulphurisation would be small for Brodrick et al[31]., who used cuprous salts as catalysts, report only meagre yields of phenanthridines from the thiazepines (I ; X = Y = Br) and (I ; X = Y = CN) after heating them in boiling quinoline for three hours.

The mechanism of this reaction must be such that two carbon atoms, previously indirectly linked through a sulphur atom, become directly linked. There is no direct evidence to indicate whether this takes place before or after the thia atom has been extruded. However, if it precedes extrusion, the picture more clearly explains the absence of isomers in the products and the extrusion of sulphur from an episulphide intermediate (VI) can then be collated with other examples of the same kind. On the basis that(VI)is truly an intermediate - and is neither the actual nor a contributory structure of the thiazepine itself - two mechanisms,1 and 2, can account for its

formation from the thiazepine and two complementary mechanisms account for its decomposition to the phenanthridine. The well-known ready decomposition of episulphide rings lends support to the view that (VI) will be a relatively unstable structure. Its formation, therefore, rather than its decomposition will be the rate-determining process in the overall reaction. Accordingly in interpreting the experimental results the effect of substituents is here considered as relating to the processes by which the episulphide intermediate is formed.



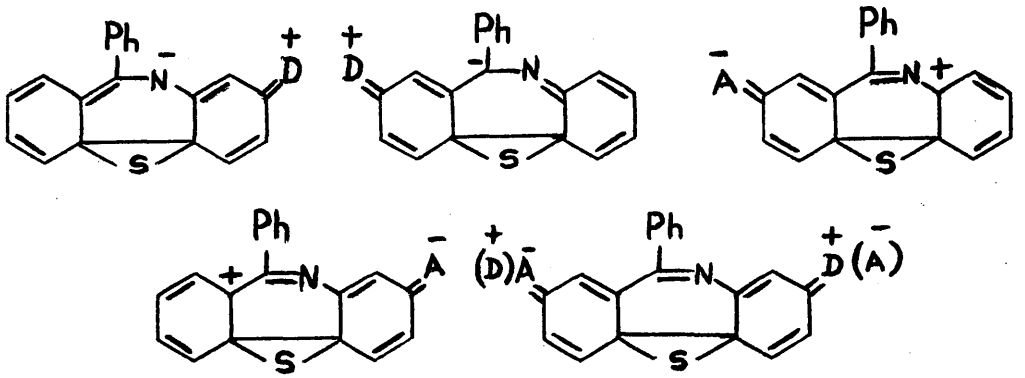
VI

With some notable exceptions, the results obtained in diethyl phthalate conform with the expectations of process 1. Of the two benzene nuclei present in a dibenzothiazepine the one attached to nitrogen (in an anil form) should be more

nucleophilic than the other. Accordingly the pre-determined electron flow should be from the former to the latter. Increased nucleophilicity provided by a donor group in the Y position (I ; X = H, Y = CH_3, OH, OCH_3) should and does increase the rate of reaction, whereas an electron-attracting group at Y (I ; X = H, CH_3, Y = NO_2) should, as it does, retard the reaction. In the other benzene nucleus the reaction-promoting effect of an acceptor group at X (I ; X = NO_2, Y = H, CH_3) is also at once explicable. However, there are clear indications that this simple interpretation is insufficient. Thus a methoxyl group at X (I ; X = OCH_3, Y = H) is also seen to promote the reaction and this can hardly be due to the electron restraint attributable to the inductive effect of methoxyl since a chloro-substituent at X (I ; X = Cl, Y = H) does not have the same effect. It is also difficult to explain the high yield of phenanthridine from the thiazepine (I ; X = OCH_3, Y = NO_2) on the basis of mechanism 1 alone, for the effect of a nitro group in the Y position in the thiazepines (I ; X = H, CH_3, Y = NO_2) is to bring the reaction almost completely to a stop. It seems necessary therefore to invoke the mechanism, 2, as a subsidiary process in which the roles of the two benzene nuclei are reversed and a powerful electron-donor at X promotes the reaction.

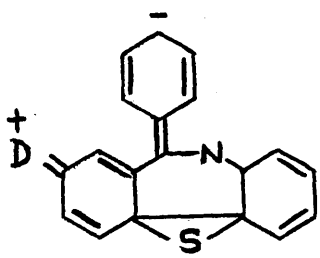
The results in Table II are interpreted satisfactorily by employing similar arguments. From the low yields of phenanthridines obtained from the thiazepines (I ; X = OH, OCH_3, Y = H), it is clear that there is little or no contribution from the less favourable mechanism 2 at the lower temperature. However, the 9% yield of phenanthridine from the thiazepine (I ; X = OCH_3, Y = NO_2) provides further evidence for the introduction of subsidiary mechanism, 2; considering the retarding effect of a nitro group in the Y position (I ; X = H, Y = NO_2) at the high temperature, it seems unlikely that mechanism 1 alone can operate for this compound in boiling quinoline.

It is possible that further pathways to desulphurisation are opened up by conjugation between the substituents <u>para</u> to the thia atom. Such pathways would involve intermediates of the following types (VII) where D and A represent an electron donor and acceptor respectively.

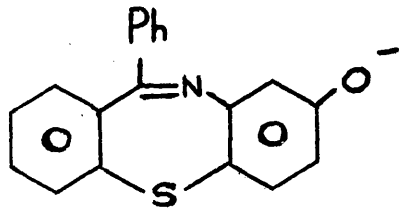


VII

Intermediates of the type (VIII) may also be involved in this reaction and it might be interesting to compare the relative ease of desulphurisation of, for example, (I ; X = CH_3, Y = H) and 2-methyl-11-p-nitrophenyldibenzo [b,f]-1:4-thiazepine. However the available evidence does not warrant elaboration along these lines at present.



VIII



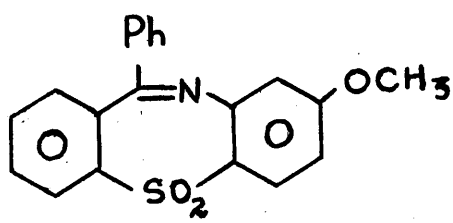
IX

In quinoline, the thiazepine (I ; X = H, Y = OH) will exist to some extent in the ionic form (IX), a favourable structure for promoting mechanism 1. However, attempts to extrude the sulphur atom by boiling with 2N sodium hydroxide were unsuccessful as were attempts to desulphurise the parent compound with phosphoric acid or the thiazepine (I ; X = CH_3, Y = Cl) with 6N hydrochloric acid.

The hydroxyphenanthridines (II ; X = H, Y = OH and X = OH, Y = H) had infra-red spectra similar to 2-hydroxy and 7-hydroxyphenanthridine respectively showing a broad absorption band between 2450 and 2950 cm^{-1} due to hydrogen bonding and not the normal sharp hydroxyl peak[37]. The

corresponding hydroxythiazepines (I) also showed considerable hydrogen bonding in this region.

When the thiazepine (I; X = H, Y = OCH_3) was refluxed for an hour with 30% aqueous hydrogen peroxide and glacial acetic acid and the product chromatographed over alumina in benzene, a colourless gum was obtained. After several days, trituration with methanol gave the sulphone (X) in 33% yield, the only product to be isolated. Shortage of time prevented further investigation into this reaction, which, as previous examples have shown, is a very interesting one. Treatment of 11-aryldibenzothiazepines with this reagent has in one case oxidised the thiazepine to the sulphone as above[31]; in another case, has broken the heterocyclic ring as in the formation of 2-benzoyl-2′:4-dinitrodiphenylsulphone from the thiazepine (I ; X = NO_2, Y = H)[32]; and, in a third case, has brought about extrusion of sulphur[33].



X

Although the figures in the thirty minute column

of Table 1 are not necessarily the best attainable, this reaction is certainly a useful synthetic route to phenanthridines of this substitution pattern, some of which are of interest therapeutically as potential trypanocides[38].

EXPERIMENTAL

Light petroleum refers to the fraction of b.p. 60-80°.

2-Nitrodiaryl sulphides (Table III)

The o-chloronitrobenzene derivative (1 mol.) was dissolved in ethanol (500 c.c.) containing the thiophenol (1.1 mol.). An aqueous solution of sodium hydroxide (30% ; 1.1 mol.) was then added dropwise and the mixture refluxed for thirty minutes. The solution was diluted, the solid filtered, washed with water, and crystallised from a suitable solvent. Yields 60-80%.

Table III

X	Y	m.p.	Formula	Solvent	Found	Required
H	H^{34}	79°	$C_{12}H_9O_2NS$	light petroleum	-	-
H	Cl^{39}	86°	$C_{12}H_8O_2NSCl$	ethanol	-	-
Cl	H	97°	"	"	C, 54.11; H, 3.23 ; N, 5.68 .	C, 54.24; H, 3.01; N, 5.28%.
H	CH_3	72°	$C_{13}H_{11}O_2NS$	methanol	C, 63.74; H, 4.25; N, 5.83;	C, 63,67; H, 4.52; N, 5.71%.

Table III (Contd.)

X	Y	m.p.	Formula	Solvent	Found	Required
CH_3	H^{40}	89°	$C_{13}H_{11}O_2NS$	methanol	-	-
Cl	Cl^{39}	158°	$C_{12}H_7O_2NSCl_2$	acetic acid	-	-
CH_3	Cl^{41}	121°	$C_{13}H_{10}O_2NSCl$	"	-	-
H	OCH_3	oil*	-	-	-	-
OCH_3	H	94°	$C_{13}H_{11}O_3NS$	ethanol	C, 59.53; H, 3.86; N, 5.60.	C, 59.77; H, 4.24; N, 5.30%.

* The oil was used as such and was characterised by oxidation with aqueous hydrogen peroxide (30%) in acetic acid to the corresponding sulphone. m.p. 105° (from methanol) (Found: C, 53.33; H, 3.77; N, 4.80. $C_{13}H_{11}O_5NS$ requires C, 53.24; H, 3.78; N, 4.78).

2-Benzamidodiaryl sulphides (Table IV)

(a) The 2-nitrodiaryl sulphides were reduced by the method of Roberts and Turner[34] using iron filings and water in presence of a trace of ferric chloride. Without purification, the dried amine hydrochloride (1 mol.) was dissolved in pure pyridine (7 mol.) and treated slowly with benzoyl chloride (1.5 mol.) at room temperature. After two hours, water was added and the mixture was extracted with ether. The ether layer was washed with dilute sulphuric acid, water, dilute sodium hydroxide (until there was no precipitation of benzoic acid on acidification) and finally with water again. Removal of solvent gave the product. Yields 50-70%.

(b) 2-Chloro-5-nitrobenzanilide (1 mol.) was suspended in ethanol (500 c.c.) containing the thiophenol (1.1 mol.). An aqueous solution of sodium hydroxide (1.1 mol. 30%) was added dropwise and the mixture refluxed on the steam-bath for thirty minutes. The method of work-up was as that for 2-nitrodiaryl sulphides. Yields 70-90%.

Table IV

X	Y	m.p.	Formula	Solvent	Found	Required
H	H[31]	67°	$C_{19}H_{15}ONS$	-	-	-
H	Cl	81°	$C_{19}H_{14}ONSCl$	light petroleum	C, 67.08; H, 4.50; N, 4.30;	C, 67.16; H, 4.12; H, 4.12%.
Cl	H	102°	"	methanol	C, 67.05; H, 4.75; N, 4.20.	"
H	CH_3	91°	$C_{20}H_{17}ONS$	"	C, 74.89; H, 5.53; N, 4.53;	C, 75.22; H, 5.37; N, 4.39%.
CH_3	H	94°	"	"	C, 75.15; H, 5.05; N, 4.20.	"
Cl	Cl	110°	$C_{19}H_{13}ONSCl_2$	ethanol	C, 61.24; H, 3.66; N, 4.04;	C, 60.96; H, 3.46; N, 3.74%.
CH_3	Cl	85°	$C_{20}H_{16}ONSCl$	"	C, 67.53; H, 4.55; N, 4.04;	C, 67.89; H, 4.53; N, 3.96%.

Table IV (Contd.)

X	Y	m.p.	Formula	Solvent	Found	Required
H	OCH_3	61°	$C_{20}H_{17}O_2NS$	methanol	C, 71.91 H, 5.29; N, 4.17.	C, 71.63; H, 5.11; N, 4.18%.
OCH_3	H	78°	"	"	C, 71.34; H, 4.87; N, 4.10.	"
H	NO_2	115°	$C_{19}H_{14}O_3N_2S$	ethanol	C, 65.24; H, 3.98; N, 8.30.	C, 65.14; H, 4.03; N, 8.00%.
CH_3	NO_2	125°	$C_{20}H_{16}O_3N_2S$	"	C, 65.63; H, 4.26; N, 7.90.	C, 65.93; H, 4.43; N, 7.69%.
OCH_3	NO_2	142°	$C_{20}H_{16}O_4N_2S$	"	C, 63.20; H, 4.12; N, 7.56.	C, 63.15; H, 4.24; N, 7.37%.

11-Phenyldibenzo[b,f]-1:4-thiazepines (Table V)

(a) A mixture of the 2-benzamidodiaryl sulphide (1 mol.), phosphoryl chloride (4 mol.) and pure nitrobenzene (13 mol.)

was heated under reflux for four hours. The phosphoryl chloride and nitrobenzene were distilled off in vacuo (0.1 mm.), and, after trituration of the residue with dilute sodium hydroxide, the thiazepine was recovered in benzene. Yields 60-80% (Two exceptions - see below).

(b) An aqueous solution of sodium hydroxide (30% ; 2.2. mol.) was added dropwise to a hot solution of 2-chloro-5-nitrobenzophenone (1 mol.) and the o-aminothiophenol hydrochloride (1.1 mol.) in ethanol (3 l.). The mixture was warmed for fifteen minutes when water was added. After standing, the aqueous layer was decanted from the gummy-solid, which crystallised from acetic acid.

Exceptions

(1) When procedure (a) was applied to 2-benzamido-4-nitro-4′-methoxydiphenyl sulphide (18 g.), the benzene extract gave firstly colourless needles (0.4 g.) m.p. 193° (from ethanol) (Found: C, 61.07; H, 2.89; N, 10.62. $C_{13}H_8O_2N_2S$ - 5-nitro-2-phenylbenzthiazole[35] - requires C, 60.94; H, 3.15; N, 10.93%). The remainder was chromatographed over alumina in benzene whereupon the thiazepine was obtained as yellow needles (7 g.) m.p. 138° (from ethanol).

(2) When procedure (a) was applied to 2-benzamido-4-methoxydiphenyl sulphide (15 g.), trituration with dilute sodium hydroxide, followed by extraction with boiling benzene, left a considerable quantity of an amorphous

yellow solid undissolved. The benzene extract contained a mixture of crystals (4.5 g.) m.p. 145-155°, which after chromatography over alumina in benzene, gave the pure thiazepine (4 g.) m.p. 157-9° (from ethanol). Treatment of the yellow solid with hot dilute sodium hydroxide, followed by extraction with boiling benzene gave the phenanthridine (II ; X = H, Y = OCH_3) as colourless plates (5.5 g.) m.p. 115° (from ethanol). Moreover, a portion of the yellow solid dissolved in hot dilute sulphuric acid. On cooling, yellow needles separated m.p. 283° (decomp.) (Found: C, 62.47; H, 4.25; N, 3.84. $C_{20}H_{16}ON.HSO_4$ requires C, 62.66; H, 4.47; N, 3.65).

2-Hydroxy-11-phenyldibenzo[b,f]-1:4-thiazepine (I ; X = OH, Y = H)

An aqueous solution of hydrobromic acid (50% ; 100 c.c.) was added to 2-methoxy-11-phenyldibenzo[b,f]-1:4-thiazepine (4 g.) in glacial acetic acid (100 c.c.) and the mixture heated under reflux for three hours. Concentration of the solution to small bulk gave a yellow amorphous solid which was filtered (m.p. 265-275°). Repeated crystallisation from ethanol, with charcoaling, produced the phenol as pale yellow prisms (2.45 g.) m.p. 300-4° (decomp.).

8-Hydroxy-11-phenyldibenzo[b,f]-1:4-thiazepine (I ; X = H, Y = OH)

The thiazepine (I ; X = H, Y = OCH_3) (1.5 g.) was treated as in the previous experiment. Concentration of the solution,

in this case, gave an ill-defined product. Treatment of this with hot dilute sodium hydroxide gave a homogeneous solution which was extracted with boiling benzene (to remove any starting material). The aqueous alkaline fraction was acidified carefully with glacial acetic acid and the solid filtered. Crystallisation from benzene, with charcoaling, gave the phenol as cream-coloured needles (0.6 g.) m.p. 254-256°. The benzene extract gave a further crop (0.3 g.).

Table V

X	Y	M.p.	Formula	Solvent	Found	Required
H	H^{31}	118°	$C_{19}H_{13}NS$	-	-	-
H	Cl	150°	$C_{19}H_{12}NSCl$	ethanol	C, 71.08; H, 4.00; N, 4.31	C, 70.92; H, 3.73; N, 4.36%.
Cl	H	134°	"	"	C, 71.19; H, 3.51; N, 4.61.	"
H	CH_3	127°	$C_{20}H_{15}NS$	"	C, 79.80; H, 4.56; N, 4.49.	C, 79.71; H, 5.02; N, 4.65%.
CH_3	H	164°	"	acetic acid	C, 79.56; H, 4.71; N, 4.56.	"

Table V (Contd.)

X	Y	m.p.	Formula	Solvent	Found	Required
Cl	Cl	152°	$C_{19}H_{11}NSCl_2$	ethanol	C, 64.27; H, 3.40; N, 3.96;	C, 64.05; H, 3.09; N, 3.93%.
CH_3	Cl	147°	$C_{20}H_{14}NSCl$	acetic acid	C, 71.49; H, 4.19; N, 4.20;	C, 71.54; H, 4.17; N, 4.17%.
H	OCH_3	159°	$C_{20}H_{15}ONS$	ethanol	C, 75.41; H, 4.58; N, 4.04.	C, 75.69; H, 4.76; N, 4.41%.
OCH_3	H	140°	"	"	C, 75.77; H, 4.91; N, 4.49.	"
H	OH	255°	$C_{19}H_{13}ONS$	methanol	C, 75.23; H, 4.12.	C, 75.24; H, 4.32%
OH	H	304°	"	ethanol	C, 75.08; H, 4.40.	"

Table V (Contd.)

X	Y	m.p.	Formula	Solvent	Found	Required
H	NO_2	187°	$C_{19}H_{12}O_2N_2S$	acetic acid	C, 68.48; H, 3.82; N, 8.56;	C, 68.67; H, 3.64; N, 8.43%.
CH_3	NO_2	185°	$C_{20}H_{14}O_2N_2S$	"	C, 69.18; H, 3.82; N, 8.02	C, 69.36; H, 4.07; N, 8.09%.
OCH_3	NO_2	138°	$C_{20}H_{14}O_3N_2S$	ethanol	C, 66.48; H, 3.93; N, 7.80.	C, 66.29; H, 3.89; N, 7.73%.
NO_2	H^{32}	159°	$C_{19}H_{12}O_2N_2S$	"	-	-
NO_2	CH_3	177°	$C_{20}H_{14}O_2N_2S$	acetic acid	C, 69.50; H, 4.16; N, 8.10.	

9-Phenylphenanthridines and picrates (Table VI)

(a) The thiazepine (.001 mol.) copper bronze (.4 g.) and diethylphthalate (3 c.c.) were mixed together in a small pear-shaped flask, fitted with a drying tube and a nitrogen inlet. The flask was then plunged into a Wood's metal bath, previously set at a steady temperature of 315°C. In each experiment the temperature of the bath fell to about 300°C and then began to rise slowly, so that at no time did it fall below the boiling point of the solvent (298°C). Heating was continued for ten, fifteen or thirty minutes as required. After cooling, the mixture was diluted with benzene, transferred to a larger flask, boiled, then filtered through a charcoal pad. The solution was then concentrated to 25 c.c. and a saturated solution of picric acid in benzene (4 c.c.) added. For all phenanthridines except those possessing nitro-substituents and the particular one (II ; X = OH, Y = H) precipitation of picrate was immediate. After thirty minutes, the picrate was filtered, washed with a little benzene and dried in air. From the weights of dry picrates, the yields listed in Table I were calculated. The corresponding phenanthridines were obtained by decomposition of their picrates, suspended in benzene, with dilute aqueous sodium hydroxide.

When a saturated solution of picric acid in benzene (4 ml.) was added to a solution of a nitrosubstituted

phenanthridine or to a solution of (II ; X = OH, Y = H) in benzene (25 ml.), picrate formation was slow and incomplete. In these cases the solution, after addition of picric acid, was allowed to stand overnight. A first crop of picrate was then filtered off, and subsequent crops were obtained by repeated concentration of the solution. Alternatively, the solvents were removed (120°; 0.1 mm.) from the original benzene filtrate and the resultant bases were fractionally crystallised from ethanol.

(b) Reactions in quinoline were conducted in a similar manner, the bath temperature being adjusted to 255°C prior to each experiment. The solution was filtered through charcoal as before, and then the benzene and quinoline were removed in vacuo. The residue was dissolved in benzene and washed with 10% acetic acid. Phenanthridines, except for the cases (I ; X = NO_2 Y = H, CH_3 : X = OCH_3, Y = NO_2) - where the free bases were fractionally crystallised - were precipitated as picrates and, thereafter, unchanged thiazepines were recovered from the alkali-washed benzene mother liquor.

Table VI

X	Y	m.p.	Formula	Solvent	Found	Required	m.p. of picrate
H	H[31]	105°	$C_{19}H_{13}N$	methanol	-	-	251°
H	Cl	134°	$C_{19}H_{12}NCl$	"	C, 79.09; H, 4.33; N, 4.75.	C, 78.74; H, 4.15; N, 4.84%.	245°
Cl	H[42]	120°	"	"	-	-	262°
H	CH_3[43]	119°	$C_{20}H_{15}N$	"	-	-	240-5°
CH_3	H	90°	"	"	C, 89.32; H, 5.42 -	C, 89.19; H, 5.61% -	280°
Cl	Cl	195°	$C_{19}H_{11}NCl_2$	ethanol	C, 79.08; H, 3.92; N, 4.61.	C, 79.29; H, 3.40; N, 4.57%.	213°
CH_3	Cl	179°	$C_{20}H_{14}NCl$	methanol	C, 70.41; H, 4.61; N, 4.45.	C, 70.37; H, 4.56; N, 4.32%.	231°
H	OCH_3	116°	$C_{20}H_{15}ON$	"	C, 84.10; H, 5.52; N, 5.13.	C, 84.18; H, 5.30; N, 4.91%.	259°

Table VI (Contd.)

X	Y	m.p.	Formula	Solvent	Found	Required	m.p. of picrate
OCH_3	H[38]	liquid	-	-	-	-	270°
H	OH	290°	$C_{19}H_{13}ON$	ethanol	C, 83.92; H, 5.05; N, 5.05;	C, 84.11; H, 4.83; N, 5.16%.	295°
OH	H	265°	$C_{19}H_{13}ON$	ethanol	C, 83.78; H, 4.73; N, 5.20.	"	245°
H	NO_2	223°	$C_{19}H_{12}O_2N_2$	benzene/ light petroleum	C, 76.33; H, 3.81; N, 9.32.	C, 76.00; H, 4.00; N, 9.33%.	215°
CH_3	NO_2	228°	$C_{20}H_{14}O_2N_2$	ethanol	C, 76.78; H, 4.90; N, 8.91.	C, 76.42; H, 4.49; N, 8.91%.	209°
OCH_3	NO_2	213°	$C_{20}H_{14}O_3N_2$	acetic acid	C, 72.66; H, 3.96; N, 8.62.	C, 72.72; H, 4.27; N, 8.48%.	230°
NO_2	H[32]	236°	$C_{19}H_{12}O_2N_2$	ethanol	-	-	246°
NO_2	CH_3	229°	$C_{20}H_{14}O_2N_2$	"	C, 76.30; H, 4.70; N, 9.04.		207°

Picrate Analysis

(II; X = H, Y = OCH_3) (Found: C, 60.50; H, 3.70. $C_{26}H_{18}O_8N_4$ requires C, 60.70; H, 3.53%).
(II; X = OH, Y = H) (Found: C, 59.40; H, 3.12. $C_{25}H_{16}O_8N_4$ requires C, 60.00; H, 3.22%).

p-Methyl-o-aminothiophenol hydrochloride

2:2′-Dinitro-4:4′-dimethyldiphenyl disulphide was prepared as described in Organic Synthesis[36]. Finely-ground sulphur (4.8 g.) was added to a boiling solution of crystalline sodium sulphide (36 g.) in ethanol (95% ; 150 c.c.). When all had dissolved, the cooled solution was added slowly to a solution of 4-chloro-3-nitrotoluene (34 g.) in ethanol (95% ; 200 c.c.). After refluxing for one hour, the solution was cooled, the solid collected and washed thoroughly with warm water. This was then dissolved in an excess of boiling glacial acetic acid. Thereafter, keeping the solution just under the boiling point, concentrated hydrochloric acid (a few c.c.'s) and zinc dust (about 1 g.) were added repeatedly in that order allowing each zinc addition to complete its reaction before the next was made. When the solution was clear and colourless, it was filtered hot and added to twice its volume of water containing enough sodium acetate to compensate for the hydrochloric

acid used. The zinc salt was collected, washed with water, then ether, air-dried and converted to the amine hydrochloride by treatment with hot concentrated hydrochloric acid. The amine hydrochloride was recrystallised from hot concentrated hydrochloric acid and washed with ethanol, then ether. m.p. 189° (decomp.) (Found: C, 47.64; H, 5.52; N, 7.80. $C_7H_{10}NSCl$ requires C, 47.86; H, 5.69; N, 7.98%).

8-Methoxy-11-phenyldibenzo[b,f]-1:4-thiazepine-S-dioxide (X)

The thiazepine (I ; X = H, Y = OCH_3) (0.14 g.) was refluxed for one hour with aqueous hydrogen peroxide (30% ; 0.5 c.c.) in glacial acetic acid (25 c.c.). Neutralisation of the cooled solution with dilute sodium hydroxide afforded a gummy solid which was carefully filtered off, dried, dissolved in benzene and chromatographed on alumina. The main fraction yielded an uncrystallisable gum. After several days however, trituration of this gum with methanol gave the sulphone (.05 g.) m.p. 198° (from methanol) (Found: C, 68.36; H, 4.00. $C_{20}H_{15}O_3NS$ requires C, 68.76; H, 4.30%).

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Contents

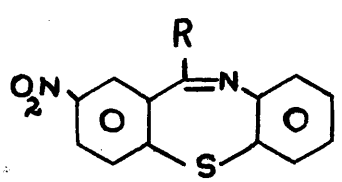
Part 2

Extrusion of Sulphur from Some Polycyclic 1:4-Thiazepines

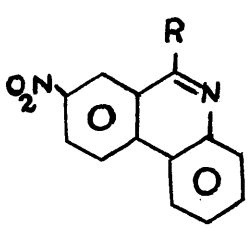
Contents

INTRODUCTION

Many of the examples quoted in the introduction to Part 1 support the view that a thia atom is fairly readily extruded from a heterocycle when the ring-contraction involved leads to an aromatic structure. This extrusion reaction is also useful synthetically, particularly in the preparation of compounds which could not be prepared easily by more conventional methods. Mention was made of the synthetic route to 2-nitrodibenzo [b,f]thiazepines (I ; R = CH_3,Ph) taken by Jarrett and Loudon[1], who condensed o-aminothiophenol with reactive o-chlorophenyl-aldehydes or-ketones. The thiazepines were readily converted to the corresponding 7-nitrophen-anthridines (II ; R = CH_3, Ph), compounds which might not be prepared easily by ring closure of 2-acylamino-4′-nitrodiphenyls (III ; R = CH_3,Ph), due to the deactivation effect of the nitro-group.



I



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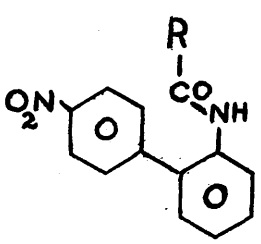
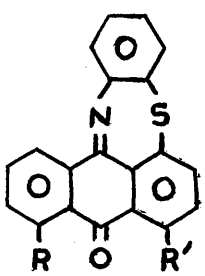


III

The method of Jarrett and Loudon, although limited to some extent by the inaccessibility of o-aminothiophenol derivatives, has in this section, been successfully extended to include reagents of the chloroanthraquinone type.

DISCUSSION

o-Aminothiophenol was condensed with 1-chloroanthraquinone in the presence of alkali. The product of the reaction was a red coloured solid, presumably 1-(o-aminophenylthio)-anthraquinone, which proved to be susceptible to dehydration. Without characterisation, it was converted into the thiazepine (I ; R = R′= H) by boiling with glacial acetic acid. By a similar reaction, 1:5-dichloroanthraquinone produced the compound (I ; R = Cl, R′= H) and, either thence or directly, with a further mol. of o-aminothiophenol afforded the bisthiazepine (II). By the same method, 1-chloro-4-nitroanthraquinone gave in the first instance the chloro-thiazepine (I ; R = H, R′= Cl) and then the bisthiazepine (III). It was rather surprising that the nitro-group was replaced in preference to the chloro-substituent.



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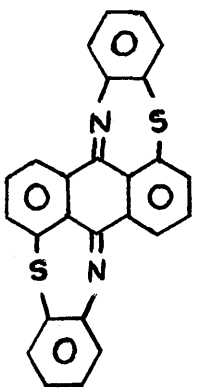

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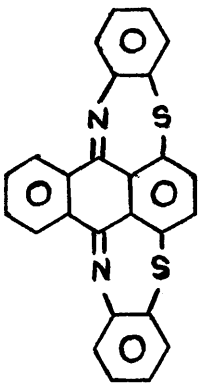
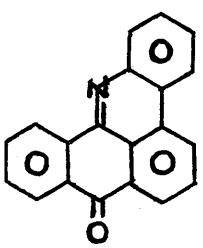


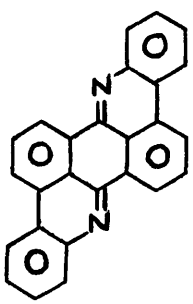
III

When the thiazepine (I ; R = R′= H) was treated with copper bronze and boiling diethyl phthalate for 5-7 minutes,

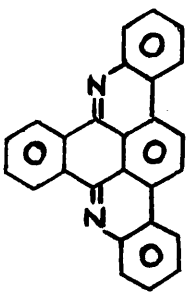
ready extrusion of the sulphur atom took place and 8-oxodibenzo[c, mn] acridine (IV) was obtained in high yield. Similarly, the bisthiazepines (II and III) gave the polycyclic diaza compounds, 8:16-diazadibenzo[b,k,] perylene (V) and 11:16-diazatribenzo[a,e,i]pyrene (VI) respectively. With similar treatment, however, the chloro-compounds (I; R = H, R′= Cl) and (I ; R′= Cl, R = H) gave ill-defined products, from which, even after chromatography, no pure compound was isolated.



IV

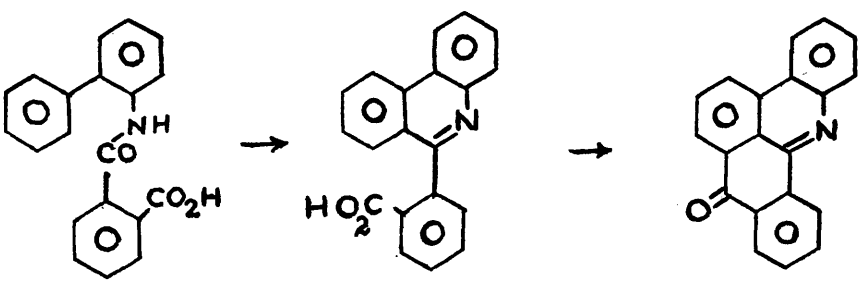


V



VI

The dibenzacridine (IV) had the properties recorded by Koelsch[2] who prepared it in the following manner, during his study of the chemistry of the vat dye, flavanthrene.



More recently, Braude and Fawcett[3] synthesised this compound and also 8:16 diazadibenzo[b,k]perylene (V) via the adducts of o-nitrophenylbutadiene with naphthaquinone and benzoquinone respectively. The ultraviolet absorption spectrum of the hitherto unknown 11:16-diazatribenzo[a,e,i]pyrene (VI) resembles that of its carbocyclic analogue[4](see p. 59).

It was interesting that the thiazepine (I ; R = R′= H) gave the acridine (IV) in 71% yield when heated in boiling diethyl phthalate alone. This was increased to 75% and 83% in the presence of hydrogen-free Raney nickel and copper bronze respectively. It appears, therefore, that in favourable cases at least, extrusion of sulphur from these thiazepines in boiling diethyl phthalate is largely a thermal decomposition, only slightly better yields being obtained in presence of metal catalysts. The Raney nickel catalyst in boiling xylene[5] was ineffective as was simple heating in phosphoryl chloride, in phosphoryl chloride-dimethylformamide[6], or in acetic acid. When the thiazepine (I ; R = R′= H) was heated in acetic acid with 30% hydrogen peroxide, the acridine was obtained in 67% yield. When refluxed for the same time with acetic acid alone, the thiazepinewas recovered unchanged. The effect of this

reagent on 11-aryldibenzothiazepines has already been discussed in the previous section; this particular example has an analogy in the ring-contraction to thiophenes accompanying similar oxidation of p-dithiins[6]. During the oxidation, the evolution of hydrogen sulphide was detected. It is suggested that this is produced by the elimination of sulphur monoxide from an intermediate thiazepine-S-monoxide, followed by the disproportionation :

$$3\ SO + H_2O \longrightarrow 2SO_2 + H_2S.$$

EXPERIMENTAL

9-Oxoanthra[9,1-ef]benzo[b]thiazepine (I ; R = R′= H)

To a solution of 1-chloroanthraquinone (0.22 g.) in peroxide-free dioxan (4 c.c.) were added o-aminothiophenol hydrochloride (0.18 g.) and then, dropwise, a solution of sodium hydroxide (0.1 g.) in ethanol-water (1 : 1 ; 2 c.c.). The mixture was heated at 100°C for 30 minutes, then cooled and water added. An acetic acid solution of the resultant red solid was heated under reflux for one hour, affording the thiazepine (I; R = R′= H) as yellow needles (0.2g.), m.p. 218°C (from acetic acid) (Found: C, 76.35; H, 4.05. $C_{20}H_{11}ONS$ requires C, 76.7 ; H, 3.55%).

10-Chloro-9-oxoanthra [9,1-ef]benzo[b]thiazepine (I ; R = Cl, R′= H)

1:5-Dichloroanthraquinone (0.35 g.) in dioxan (8 c.c.) was treated as for the 1-chloro-compound with sodium o-aminophenyl sulphide (1 mol.) generated as before, the reaction time being extended to three hours. The immediate product, after being heated for two hours in glacial acetic acid, gave an insoluble yellow solid (0.05 g., m. pt. > 360°; cf. below) and the more soluble thiazepine (I ; R = Cl, R′= H) as orange-red needles (0.29 g.) m. pt. 239° (from acetic acid) (Found: C, 68.7; H, 2.85; N, 4.4. $C_{20}H_{10}ONSCl$ requires C, 69.1 ; H, 2.7; N, 4.0%).

Anthra[9,1-ef, 10,5-e′f′]bisbenzo[b]thiazepine (II)

When two mols. of sodium o-aminophenyl sulphide were used in the preceeding reaction, or when the thiazepine (I, R = Cl, R′= H) was treated with one mol. of this reagent, the procedure described gave the yellow solid mentioned previously (m.p. > 360°C) in about 75% yield. On crystallisation from ethylene glycol, this compound afforded the bisthiazepine (II) as yellow needles (Found: C, 74.3 ; H, 3.7; N, 6.8. $C_{26}H_{14}N_2S_2$ requires C, 74.6 ; H, 3.4 ; N, 6.7%).

8-Chloro-9-oxoanthra[9,1-ef]benzo[b]thiazepine (I; R = H, R′= Cl) and Anthra[9,1-ef, 10,4-e′f′]bisbenzo[b]thiazepine (III)

By procedures similar to those described above 1-chloro-4-nitroanthraquinone was converted into the monothiazepine (I ; R = H, R′= Cl), m.p. 229° (from acetic acid) in 50% yield (Found: C, 68.9; H, 3.0; N, 4.6%), and the bisthiazepine (III), m.p. 262° (from acetic acid), in 51% yield. (Found: C, 74.4; H, 3.2; N, 6.9%).

8-Oxodibenzo[c,mn]acridine (IV)

(a) A solution of the thiazepine (I ; R = R′= H) (0.3 g.) in diethyl phthalate (4 c.c.) was boiled under nitrogen in the presence of copper bronze (0.3 g.) for 5-7 minutes. The cooled mixture was diluted with benzene, heated with charcoal, filtered and concentrated, thus affording the acridine (IV), (0.22 g.), m.p. 224° (from acetic

acid; $\lambda_{max.}$ 263 (shoulder), 303, 382 mu (log ε 4.465, 4.19 and 4.15) in chloroform. (Found: C, 85.1 ; H, 3.9; N, 5.3. $C_{20}H_{11}ON$ requires C, 85.4; H, 3.9; N, 5.0%).

(b) A solution of the thiazepine (0.2 g.) in acetic acid (25 c.c.) containing aqueous hydrogen peroxide (30% ; 0.6 c.c.) was heated under reflux for forty-five minutes, during which hydrogen sulphide was evolved. The solution was concentrated, the residue treated with water, and the resultant solid chromatographed over alumina in benzene-light petroleum (2:1) affording the acridine in 67% yield.

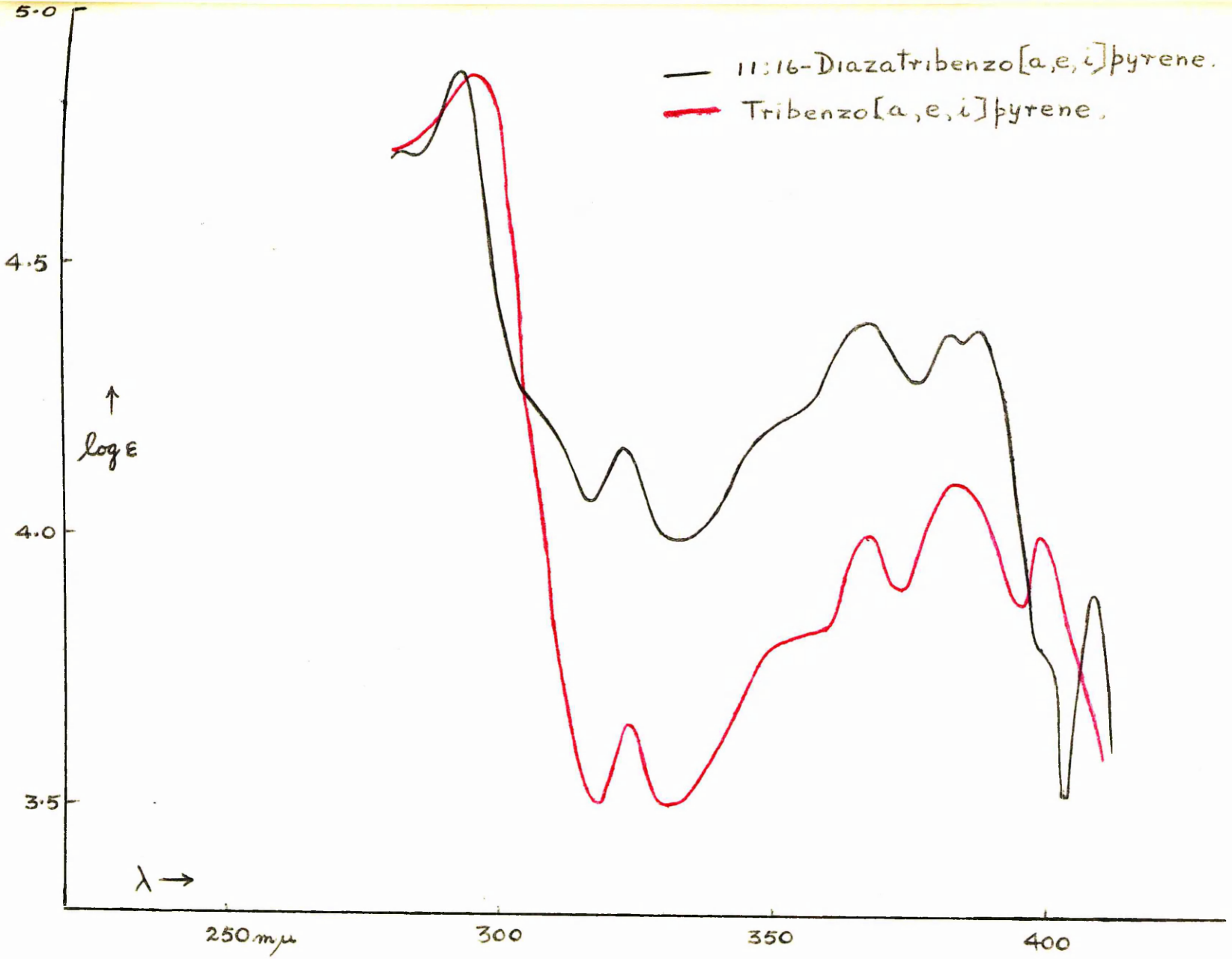
8:16-Diazadibenzo[b,k]perylene (V)

This compound m.p. ~ 370°, was obtained when procedure (a) was applied to the bisthiazepine (II) and the desulphurised solid product was recovered in chloroform from a soxhlet thimble. (Found: C, 88.2; H, 3.9; N, 7.95. $C_{26}H_{14}N_2$ requires C, 88.1 ; H, 4.0 ; N, 7.9%); $\lambda_{max.}$ 258 (shoulder), 282, 294, 370, 390, 410, and 435 mu (log ε 4.38, 4.47, 4.57, 4.68, 4.15, 4.33, 4.59, and 4.65) in dioxan.

11:16-Diazatribenzo[a,e,i]pyrene (VI)

This compound, m.p. 311° (from xylene), was similarly obtained in 76% yield from the bisthiazepine (III)

(Found: C, 87.9; H, 3.7; N, 7.9); $\lambda_{max.}$ 267, 283, 292, 323, 368, 382, 388, and 408 mu (log ϵ 4.67, 4.71, 4.86, 4.17, 4.39, 4.37, 4.38, and 3.90) in dioxan.


11:16-Diazatribenzo[a,e,i]pyrene.
Tribenzo[a,e,i]pyrene.
5·0
4·5
4·0
3·5
log ε
λ →
250mμ
300
350
400

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1. Jarrett and Loudon, J., 1957, 3818.
2. Koelsch, J.A.C.S., 1936, 58, 1325.
3. Braude and Fawcett, J., 1951, 3118.
4. Clar, J., 1949, 2168.
5. Hauptmann and Wladislaw, J.A.C.S., 1950, 72, 707, 711.
6. Parham and Traynelis, ibid., 1954, 76, 4960.

Part III

Studies in Sultones and Sultams.

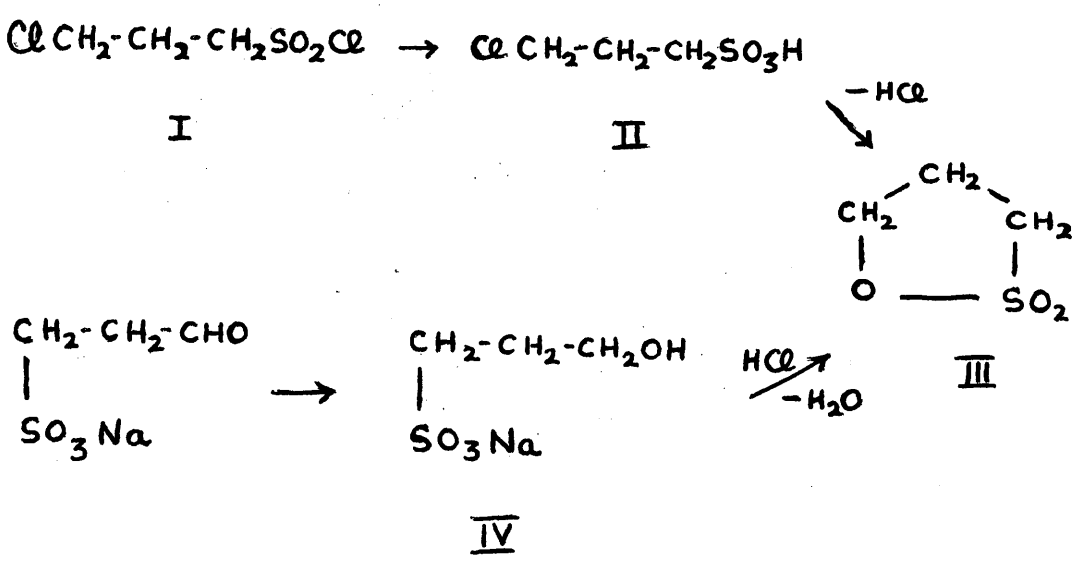
CONTENTS

INTRODUCTION

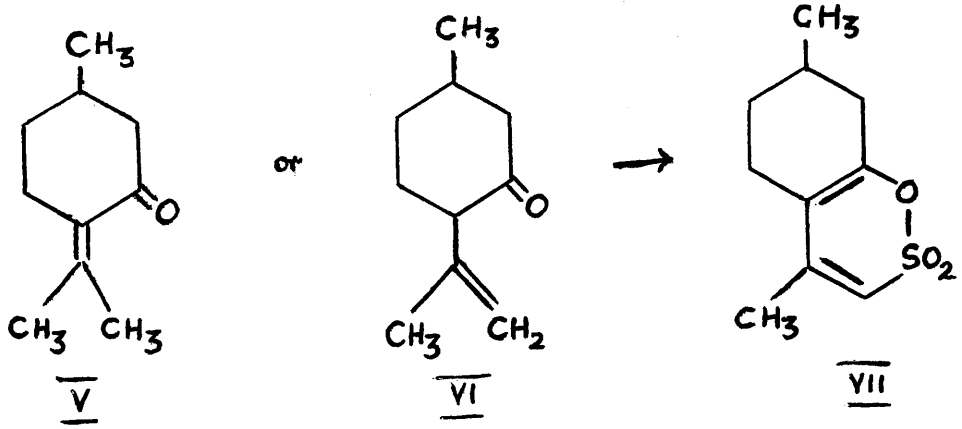
Sultones are the cyclic esters of hydroxysulphonic acids just as lactones are cyclic esters of hydroxy-carboxylic acids. Sultone rings are usually 5- or 6-membered and may be saturated or unsaturated. Similarly, sultams are the analogues of γ-and δ-lactams. β-Sultones or β-sultams have not yet been synthesised.

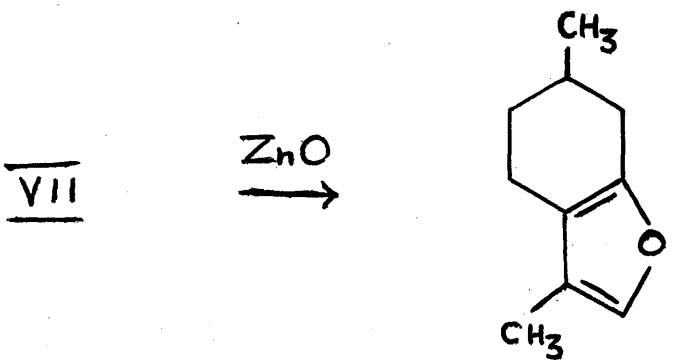
Sultones are preparable from a variety of organic compounds but generally the final stage involves the elimination of the elements of water from the corresponding hydroxysulphonic acid.

Aliphatic sultones are formed by irradiation of alkyl halides in an atmosphere of sulphur dioxide and chlorine[1]. By this procedure, γ-propanesultone (III) is produced from 1-chloropropane via the intermediates, γ-chloropropanesulphonyl chloride (I) and γ-chloropropane-sulphonic acid (II). Treatment of acrolein with sodium bisulphite, followed by reduction with Raney-nickel, hydrolysis of the sodium salt (IV) and heating is another route to this sultone (III)[2].



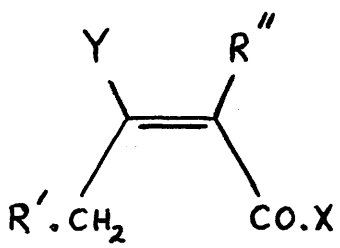
Interest in the synthesis of sultones from α:β- or β:γ- unsaturated ketones was stimulated by the work of Treibs[3] who prepared the δ-sultone (VII) by the action of concentrated sulphuric acid in acetic anhydride on either pulegone (V) or isopulegone (VI) at 0°C. Pyrolysis of (VII) in the presence of zinc oxide causes elimination of sulphur dioxide and the corresponding furan (VIII) is produced





VIII

Using the same reaction conditions, Morel and Verkade[4,5,6] prepared the δ-sultones (XI to XIV) from the $\alpha:\beta$- and $\beta:\gamma$-unsaturated ketones (IX and X, in which R′, R″, X and Y represent hydrocarbon residues). On pyrolysis these sultones yield sulphur dioxide and the substituted furans (XV to XVIII)



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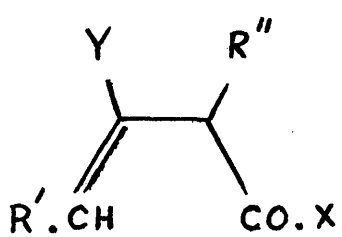

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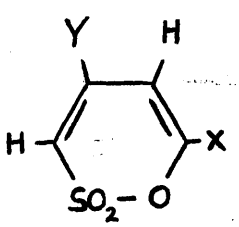

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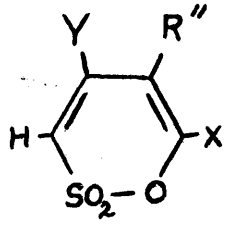

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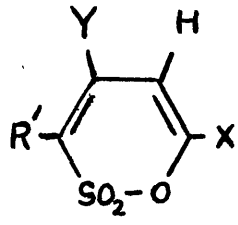

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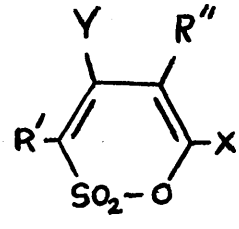

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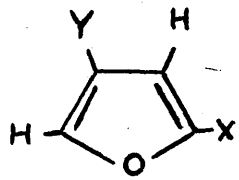

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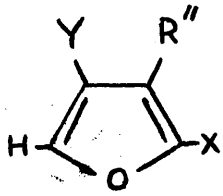

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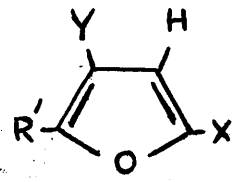
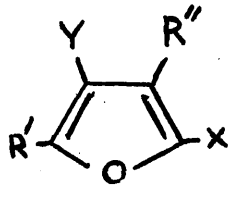
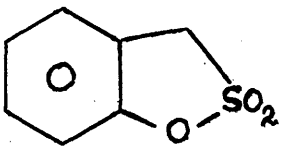


XVII



XVIII

Aromatic sultones have been prepared most frequently by boiling a diazotised solution of an o- or peri-aminoarylsulphonic acid. Thus, when a diazotised solution of 2-aminobenzylsulphonic acid is heated with dilute sulphuric acid on the steam bath, the product is the sultone of 2-hydroxybenzylsulphonic acid, "benzylsultone" (XIX). Similarly naphthosultone (XX) is obtained from 8-aminonaphthalene-1-sulphonic acid[8].



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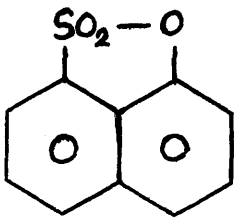
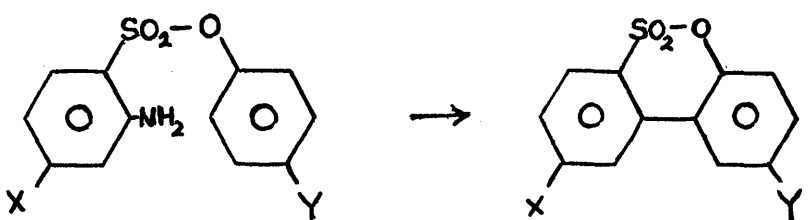


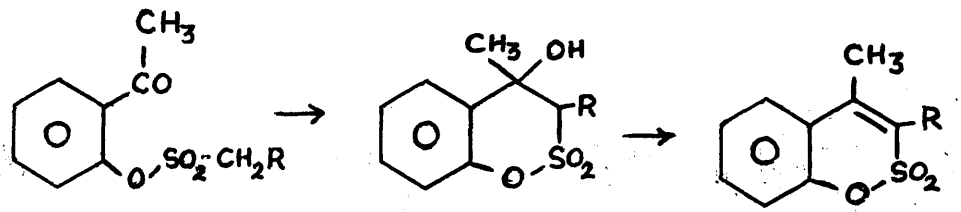
XX

Sultones of the type (XXII) are prepared by treatment of the diazotised solutions of aryl esters of o-aminoaryl-sulphonic acids (XXI) firstly with sodium acetate and then with copper powder[9].



XXI XXII

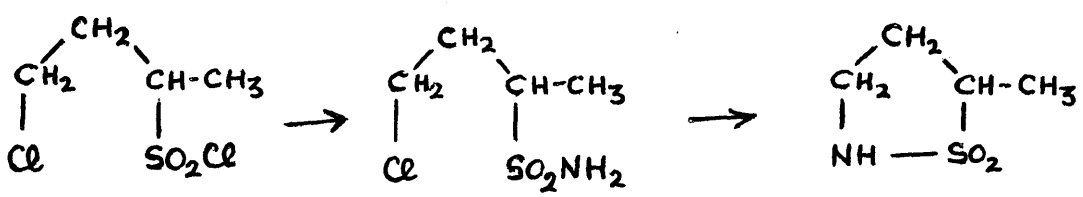
Recently Wheeler et al.[10] described the preparation of 2-o-hydroxyphenylprop-1-ene-1-sulphonic acid sultones (XXV ; R = H, Ph) from o-hydroxyacetophenone by the synthetic route (XXIII ⟶ XXV)



XXIII XXIV XXV

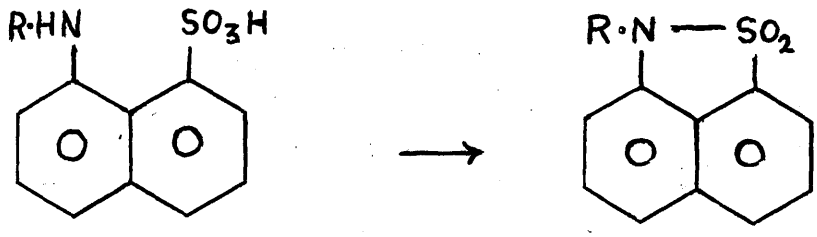
The formation of δ-sultones in this way recalls the production of coumarins by the Kostanecki-Robinson method from o-acetylaryl acetates[11].

The few aliphatic sultams which are known (cf. XXVIII) were made by treating chloroalkylsulphonyl chlorides of the type (XXVI) with ammonia, followed by heating the resultant chloroalkylsulphonamide (cf. XXVII) at 200°[1].



XXVI XXVII XXVIII

1:8-Naphthosultam and its derivatives (XXX ; R = H, alkyl, or aryl) are the best known of the aromatic sultams and are prepared by treatment of the sodium and potassium salts of 8-aminonaphthalene-1-sulphonic acid and its derivatives (XXIX) with phosphoryl chloride.[12,13] The parent compound (XXX ; R = H) is also obtained from 8-nitronaphthalene-1-sulphonic acid by the action of sodium sulphide in sodium carbonate[14].



XXIX XXX

Diphenylene sultam (XXXII), analogous to the sultone (XXII ; X = Y = H), is prepared similarly, by warming a diazotised solution of o-aminobenzenesulphonanilide (XXXI) on the steam bath[15]. Reference will be made to this particular sultam and its N-methyl derivative later in this section.

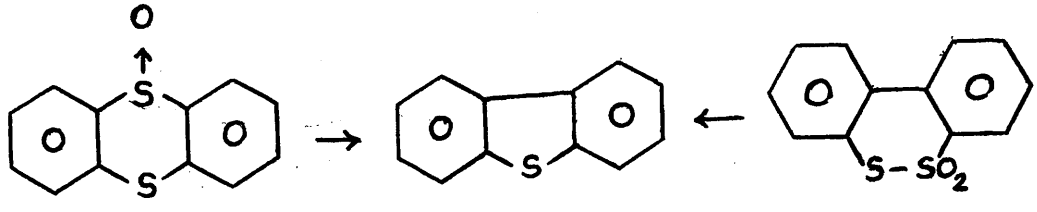
XXXI XXXII

The properties of sultones and sultams are discussed briefly in a fairly recent review by Mustafa[16], and it appears that only naphthosultone and naphthosultam have received close study. Mustafa and Ali have made a more detailed investigation of the properties of the latter compound, with particular reference to bromination and chloromethylation[17].

It is noteworthy that treatment with hot alkali opens sultone and sultam rings forming the corresponding alkali salt of the hydroxy- or amino-sulphonic acid.

The extrusion of sulphur dioxide from sultones is a subject which has received little attention and there is no instance of such an occurrence in sultam chemistry. However, there is evidence to support the view that sulphur bearing one or two oxygen atoms is readily extruded (even more readily than sulphur itself) from heterocycles especially when the ring contraction involved leads to an aromatic structure.

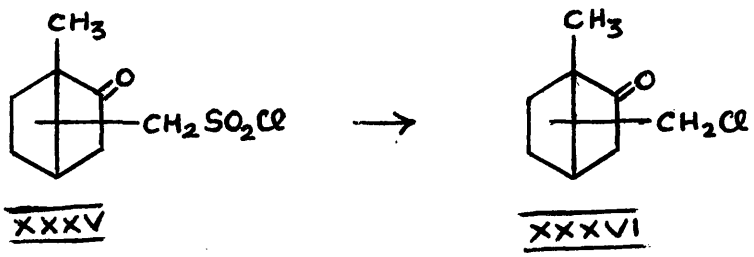
Gilman[18] found that dibenzothiophen is the product when thianthrene-S-monoxide (XXXIII) is treated with butyl lithium at -70°. Dibenzothiophen is also obtained when dibenzo-o-dithiin-5:5-dioxide (XXXIV) is heated at 250° for two hours in the presence of copper[19].



XXXIII XXXIV

Two examples of expulsion of sulphur dioxide from an aliphatic and an aromatic sulphonyl chloride are worthy of mention here for they are exceptional in the sense that the reaction is not motivated by the greater aromaticity of the product.

Camphor-π-sulphonyl chloride (XXXV) evolves sulphur dioxide to give π-chlorocamphor[20] (XXXVI) and 8-chloronaphthalene-1-sulphonyl chloride (XXXVII) decomposes at 230°C, furnishing 1:8-dichloronaphthalene (XXXVIII)[21].

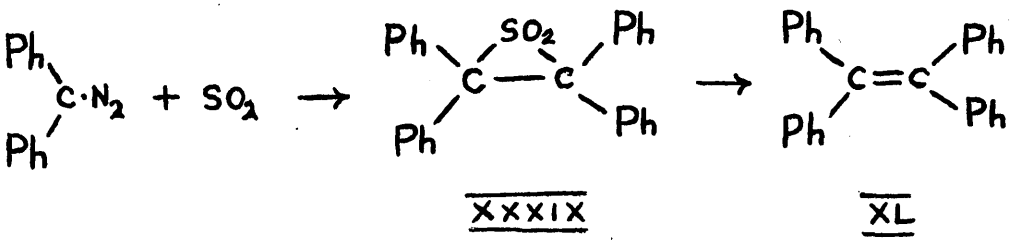


XXXV XXXVI

XXXVII XXXVIII

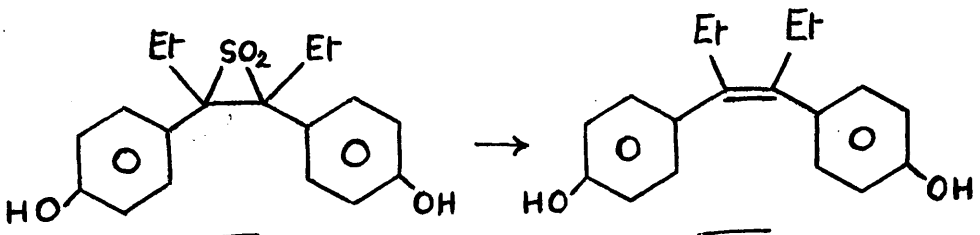
In Part 1, mention was made of the instability of ethylene sulphides (episulphides). Ethylene sulphones are equally unstable; only a few are known. The first of these, tetraphenylethylene sulphone (XXXIX) was prepared by Staudinger and Pfenninger[22] by interaction of diazodiphenylmethane and sulphur dioxide, and is readily converted to

tetraphenylethylene (XL)



XXXIX XL

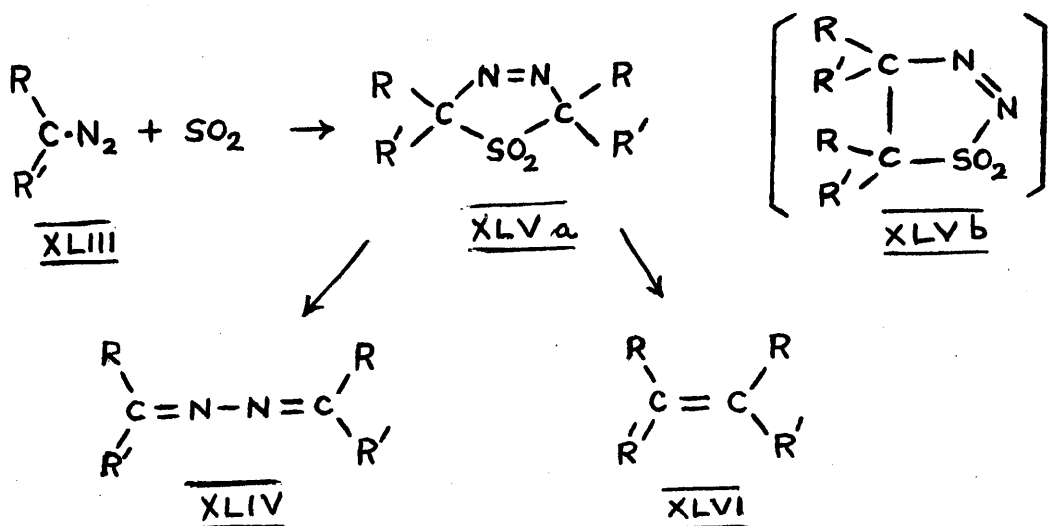
In a similar experiment this time starting from diazophenylethylmethane, the intermediate sulphone could not be isolated. However, in the synthesis of diethylstilboestrol (XLII) by this procedure, Vargha and Kovács[23] did manage to isolate the precursory ethylene sulphone (XLI) which eliminates sulphur dioxide at 100°.



XLI XLII

Recently Hesse and Reichold[24] have re-investigated this type of reaction. On treatment of diazodyclohexylethylmethane (XLIII ; R = C_2H_5, R′= C_6H_{11}) with sulphur dioxide, two stereoisomers of empirical formula, $C_{18}H_{32}O_2N_2S$, are

obtained. When either isomer in petroleum ether is passed through neutral alumina, the katazine (XLIV ; $R = C_2H_5$, $R' = C_6H_{11}$) is produced; at 200°, both decompose giving 1:2-diethyl-1:2-dicyclohexylethylene (XLVI; $R = C_2H_5$, $R' = C_6H_{11}$). On account of the facile loss of sulphur dioxide, the authors prefer the structures (XLVa ; $R=C_2H_5$, $R'=C_6H_{11}$. cis and trans) for the isomers; Staudinger[22] had previously suggested the structure (XLV b; R = R′=Ph) as an intermediate in a related reaction.



In contrast to arylsubstituted diazosulphones, diazosulphones having alkyl or alicyclic substituents appear to be relatively stable compounds; when decomposition does occur, sulphur dioxide is evolved before nitrogen. Hesse and

Reichold[25] also report the isolation of the parent compound, ethylene sulphone. When sulphur dioxide reacted with excess diazomethane at -45°C, only 3% of the theoretical amount of ethylene (see equation) was collected.

$$2\ CH_2{\cdot}N_2 \ + \ SO_2 \longrightarrow \ CH_2{=}CH_2 \ + 2N_2 + \ SO_2$$

The main product (50% of theory) was a sulphur-containing intermediate which was a colourless, odourless, mobile liquid at room temperature. On cooling, it solidified and could be crystallised from methanol (m.p. 19°). On the basis of a good analysis and cryoscopic estimation of the molecular weight, the structure (XLVII) is suggested. Thermal decomposition to ethylene and sulphur dioxide was further evidence for this structure.

$$2\ CH_2N_2 + \ SO_2 \longrightarrow \ \begin{matrix} & SO_2 & \\ CH_2 & & CH_2 \end{matrix} \longrightarrow \ CH_2{=}CH_2 + \ SO_2$$

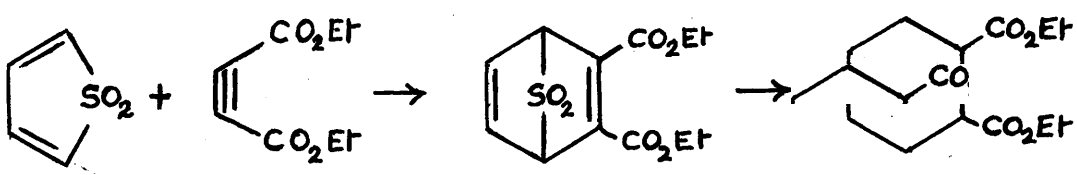
XLVII

Attempts to prepare ethylene sulphone by oxidation of ethylene sulphide with per-acids gave only polymeric products.

Butadiene sulphone (2:5-dihydrothiophen-S-dioxide) (XLVIII), a vinylogue of ethylene sulphone is formed by the 1:4-addition of sulphur dioxide to butadiene[26]. In common with other Diels-Alder reactions, the change is reversible .

XLVIII

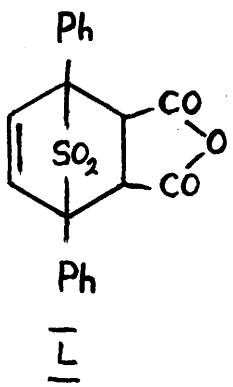
Derivatives of butadiene sulphone have participated in a number of interesting Diels-Alder type of reactions. Thus thiophen-S-dioxide condenses with acetylene diethylcarboxylate giving the adduct (IL), which evolves sulphur dioxide at its melting point (106°) to yield diethyl phthalate[27].



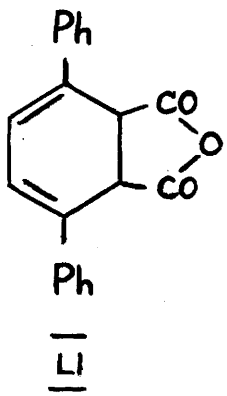
IL

Thiophen-S-dioxide itself proved to be rather unstable and reactions involving its use have often been complicated

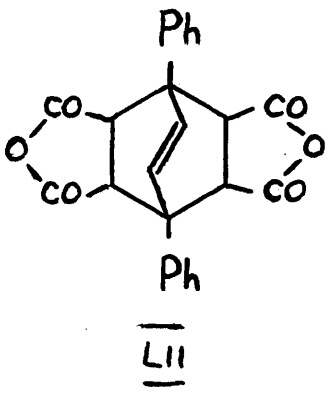
by self-condensations[28,29,30,31]. Substituted thiophen-S-dioxides, however, generally prepared by oxidation of the corresponding thiophen, are more stable compounds. They do not dimerise like the related cyclopentadieneones, and react with maleic anhydride only at elevated temperatures, making the isolation of intermediate sulphur-containing adducts virtually impossible. Melles and Duck describe some interesting condensations of which only brief mention can be made. Melles[32] found that when equimolecular quantities of 2:5-diphenylthiophen-S-dioxide and maleic anhydride are heated together at 200°, the product is not the dihydrophthalic anhydride (LI) but the bicyclic tetracarboxylic anhydride (LII). Two mols. of maleic anhydride are added, the second more rapidly than the first for a considerable amount of the sulphone is recovered unchanged. Under the influence of such a high temperature, sulphur dioxide is split out immediately - presumably from the intermediate (L)



L

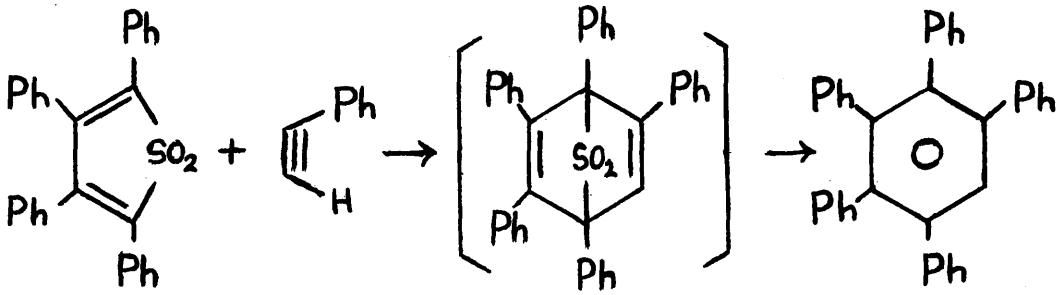


LI



LII

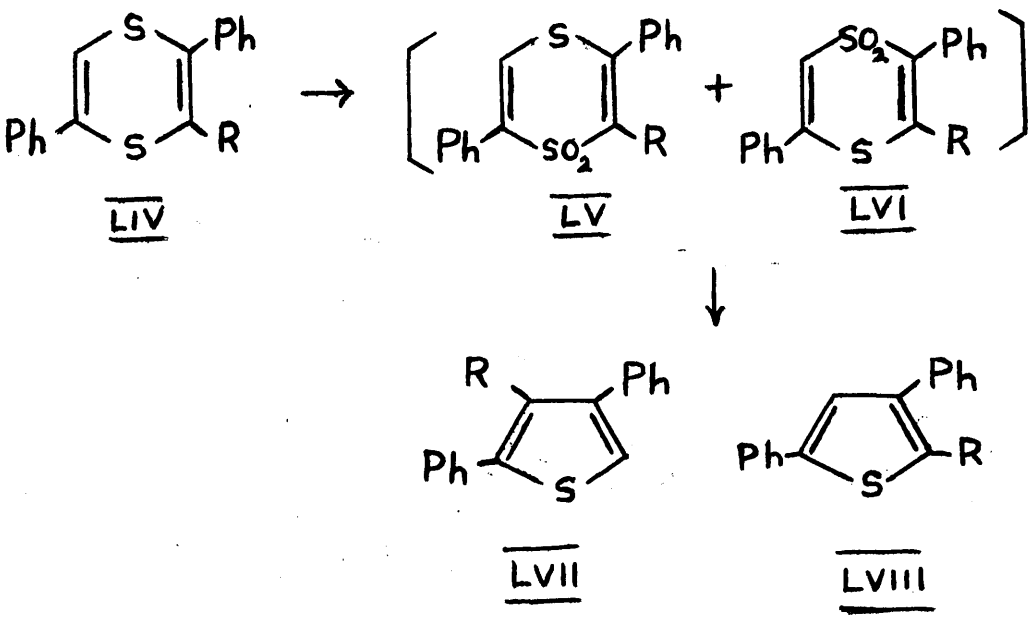
Duck[33] prepared pentaphenylbenzene by interaction between 2:3:4:5-tetraphenylthiophen-S-dioxide (LIII) and phenylacetylene at 180°.



LIII

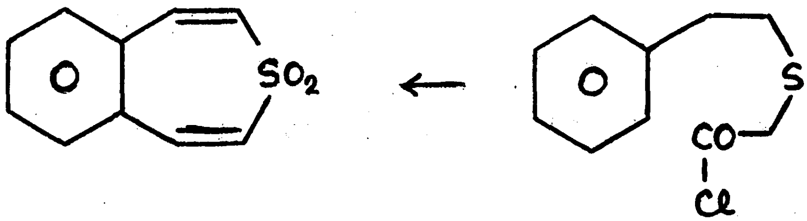
Parham's work on p-dithiins is discussed in Part 1. His attempts to oxidise derivatives of 2:5-diphenyl-p-dithiin to the corresponding disulphones were unsuccessful. In most cases, extrusion of sulphur accompanies oxidation with the formation of thiophen derivatives. 2:4-Diphenyl-3-nitrothiophen (LVII ; R = NO_2) and 2:4-diphenyl-5-nitrothiophen (LVIII ; R = NO_2) are obtained in 46 and 31% yields respectively when 2:5-diphenyl-3-nitro-p-dithiin (LIV ; R = NO_2) is treated with peracetic acid[34]. Parham postulated that the initial products of the reaction were the monosulphones (LV and LVI ; R = NO_2) which then eliminated sulphur dioxide, but this theory was put in some doubt by the isolation of a highly thermostable compound

considered to have the structure (LVI ; R = Br) from the products of the reaction between 3-bromo-2:5-diphenyl-p-dithiin (LIV ; R = Br) and peracetic acid[35].



Truce and Lotspeich[36] prepared 4:5-benzothiepin-S-dioxide (LIX) from S-(β-phenylethyl)-mercaptoacetyl chloride (LX), after several more obvious routes had been unfruitful. Since the sulphone grouping, like the carbonyl group is capable of conjugation by electron attraction, (LIX) could be considered as a conjugated unsaturated system having six π-electrons, and might possess some aromatic character. As part of the evidence for the structure of

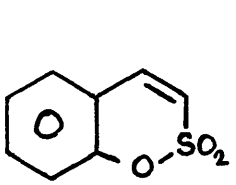
(LIX), the authors report a high yield of naphthalene on pyrolysis. (LIX) shows little aromatic character.



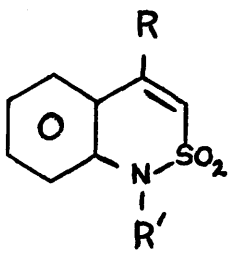
LIX LX

DISCUSSION

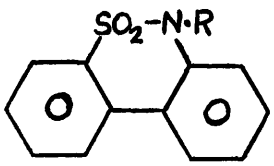
Some sultones and sultams of the types (I, II and III; R and R′= H or methyl) were prepared for the primary purpose of investigating their tendency to extrude sulphur dioxide to form benzofuran, indole and carbazole derivatives respectively. Since some of these compounds were novel in type, the general aspects of their chemistry were also of interest



I



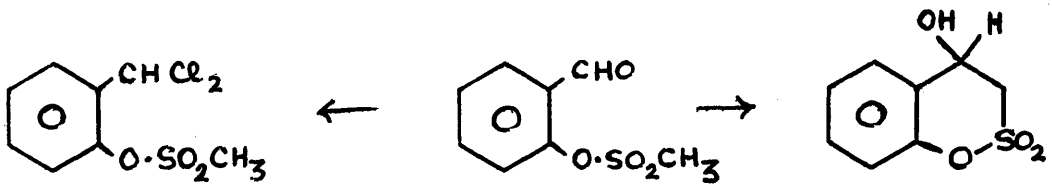
II



III

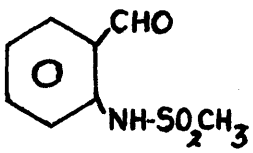
Wheeler et al.[10] have previously prepared compounds similar to (I) and their methods were employed frequently in the synthesis of types (I) and (II). Methanesulphonyl chloride reacted rapidly with salicylaldehyde in pyridine at room temperature producing the methanesulphonate (V), which, when shaken in pyridine with powdered potassium hydroxide for thirty hours, cyclised to the aldol (VI). Dehydration of (VI) with phosphoryl chloride gave 2-o-hydroxyphenylethylene-1-sulphonic sultone (I). Attempts to effect cyclisation of (V) in acid media were unsuccessful.

Treatment with phosphoryl chloride produced not unexpectedly, the chloral (IV), the structure of which was proved by decomposition with sulphuric acid followed by treatment with ethanolic 2:4-dinitrophenylhydrazine. The 2:4-dinitrophenylhydrazone formed was identical with that of (V).

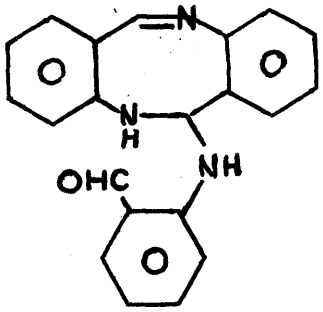


IV V VI

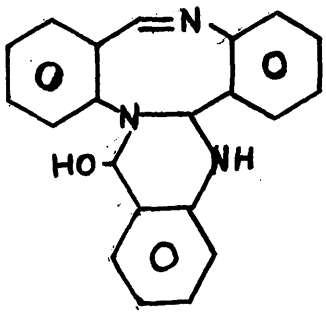
When o-aminobenzaldehyde in pyridine was treated with methanesulphonyl chloride, the simple sulphonamide (VII) was not the product. When stored for long periods or under the influence of alkali, o-aminobenzaldehyde trimerises to give anhydro-tris-o-aminobenzaldehyde, $C_{21}H_{17}ON_3$ [37]. With little supporting experimental evidence, Bamberger suggested structure (VIII) for this trimer which breaks down with mineral acids to regenerate the monomeric o-aminobenzaldehyde.



VII

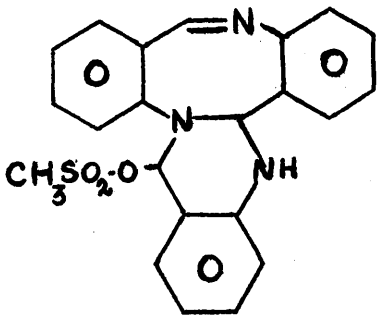


VIII

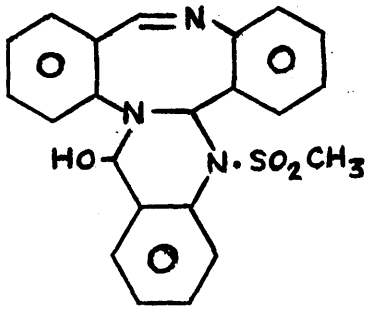


IX

The product from the above reaction had the empirical formula, $C_{22}H_{19}O_3N_3S$, and was probably a methanesulphonyl derivative of (VIII). In the infra-red spectrum, this compound showed absorption in the OH, NH region but not in the carbonyl region; yet it formed a 2:4-dinitrophenyl-hydrazone (m.p. 272-4°). Assuming Bamberger's structure to be correct and probably existing in the carbinolamine form (IX), there are two possible structures (X and XI) for the sulphonyl derivative. The 2:4-dinitrophenyl-hydrazone was found to contain sulphur which suggested that structure (XI) was the correct one.



X

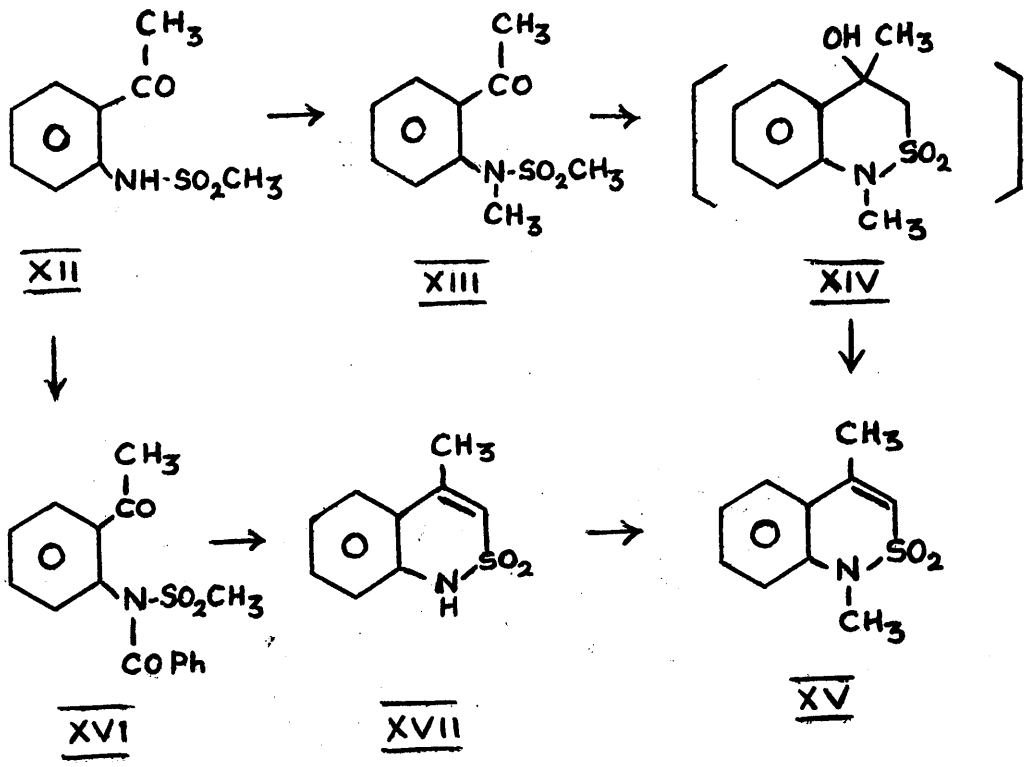


XI

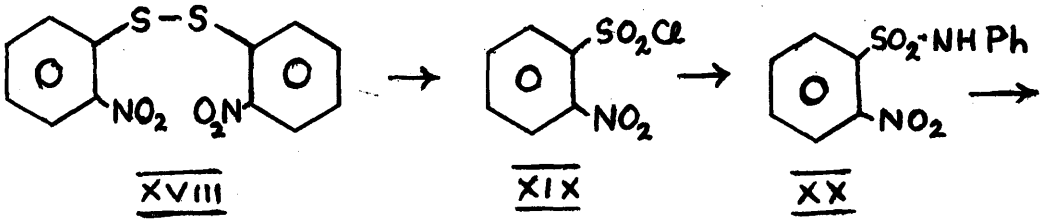
(XI) was again the product when the aldehyde was brushed into methansulphonyl chloride in pyridine and also when the two reagents were mixed together in ether - without pyridine - and allowed to stand overnight.

With o-aminoacetophenone as starting material, the mesylation was effected smoothly. To increase the chances of cyclisation, the resultant sulphonamide (XII) was then N-methylated (XIII) by the method of Pachter and Kloetzel[38] using methyl iodide and powdered potassium hydroxide in acetone. Under the influence of pyridine-potassium hydroxide, (XIII) gave 2-o-methylaminophenylprop-1-ene-1-sulphonic sultam (XV). The intermediate aldol (XIV) was not detected. A Schotten-Baumann type of reaction on (XII) afforded the N-benzoyl derivative (XVI), which by

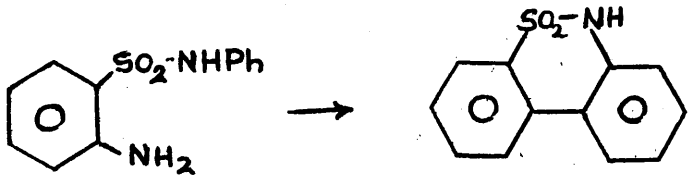
the action of pyridine-potassium hydroxide, underwent cyclisation, dehydration and hydrolysis *in situ*, giving 2-o-aminophenylprop-1-ene-1-sulphonic sultam (XVII). N-methylation of (XVII) by the procedure already mentioned[38] produced (XV)



Diphenylene sultam (XXII) was prepared by the method of Gross and Ullmann[15], *via* the intermediates (XVIII → XX).



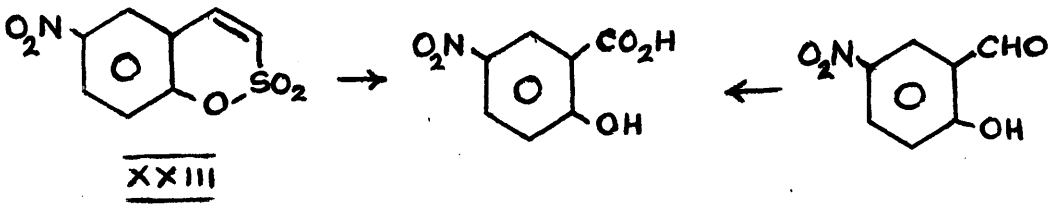
XVIII XIX XX



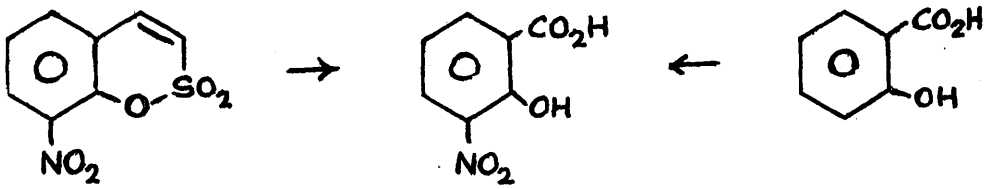
XXI XXII

Methylation as before[38] gave N-methyldiphenylenesultam (III ; R = CH_3).

Some chemical properties of the sultone (I) and its derivatives were then investigated. Treatment of (I) with fuming nitric acid at room temperature gave mainly a sparingly soluble (ethanol) mononitroderivative (A), m.p. 186°, together with a small amount of a more soluble isomer (B), m.p. 116°. Oxidation of these nitrosultones, (A) and (B), with alkaline potassium permanganate produced 5-nitro and 3-nitro-salicyclic acid respectively, which were identified by comparison with authentic specimens. The products of the nitration were therefore 2-(2-hydroxy-5-nitrophenyl)ethylene-1-sulphonic sultone (XXIII) (A) and 2-(2-hydroxy-3-nitrophenyl)ethylene-1-sulphonic sultone (XXIV) (B).



XXIII



XXIV

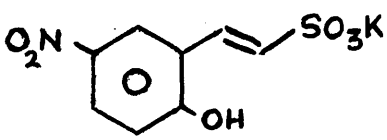
In this respect, the sultone resembles coumarin, which, on nitration, gives a mixture of the 6- and 8-nitro derivatives[39].

An attempt to prepare (XXIII) by cyclisation of the methanesulphonyl derivatives of 5-nitrosalicylaldehyde was unsuccessful.

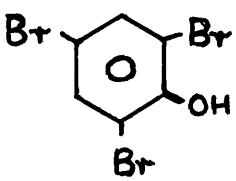
The nitrosultone (XXIII) was stable to oxidation by alkaline peroxide. Treatment with a very concentrated solution of potassium hydroxide then hydrogen peroxide, furnished a sulphur-containing compound which was soluble in sodium carbonate solution, gave a potassium flame test, decomposed at about 250° and gave a violet colour with ferric chloride solution. It analysed for the empirical

formula, $C_8H_8O_7NSK$, and was probably the monohydrate of (XXV). The course of this reaction was unchanged by the absence of peroxide.

When the sultone (I) was heated with potassium hydroxide and a little water, a dark red solution was obtained. Dilution with water, acidification, followed by treatment with excess bromine, gave 2:4:6-tribromophenol (XXVI)[40].



XXV

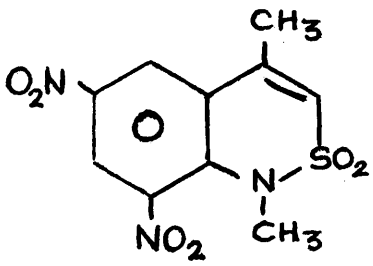


XXVI

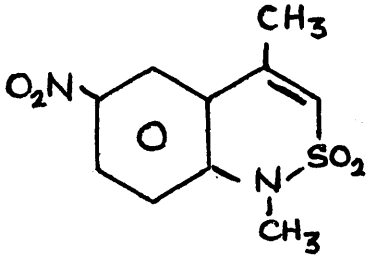
Attempts to extrude sulphur dioxide from the sultone (I) by dry distillation or by heating at 270° with anhydrous quicklime in the presence of a little quinoline met with no success. The inability to detect benzofuran in this reaction was rather surprising in view of the work of Treibs[3] and of Morel and Verkade[6].

The sultam (XV) reacted more vigorously than the sultone (I) with fuming nitric acid, a dinitrosultam

being obtained. With concentrated nitric acid as reagent, a mononitrosultam was produced. By analogy with the sultone experiments, the structures (XXVII) and (XXVIII) are suggested for these compounds.



XXVII



XXVIII

Treatment of (XV) with quicklime-quinoline at 270° as above gave a 5% yield of N-methylskatole (as picrate), which was identified by mixed melting-point with an authentic specimen and by comparison of infra-red spectra. Under similar conditions but with the temperature raised to 350°, N-methyldiphenylene sultam afforded an 11% yield of N-methylcarbazole, which was isolated and characterised in the same manner as N-methylskatole.

With similar treatment, the sultam (XVII) showed no sign of decomposition and diphenylene sultam gave only a trace of picrate, micro m.p. 175-180° (m.p. of picrate of carbazole - 182°). The greater stability of these last two sultams in this medium may be associated with the

formation of a stable calcium salt for both possess a free acidic hydrogen atom on the nitrogen.

If the yields from such decompositions were improved, the reaction could be of considerable use synthetically. However, the indication is that sultones and sultams - at least the types studied in this section - do not readily evolve sulphur dioxide. The particular stability of the sultone (I), in relation to the sultones of Morel and Verkade, may be due to the feebler aromaticity of the heterocycle in benzofuran.

EXPERIMENTAL

Salicylaldehyde-O-methanesulphonate (V)

Methanesulphonyl chloride (1.4 c.c.) was added dropwise to salicyaldehyde (1.7 c.c.) in pure pyridine (10 c.c.) at room temperature. After an hour, chloroform was added and the solution was washed with acid, alkali and water. Evaporation of solvent gave a yellow oil which soon crystallised. m.p. 51-2° (from ether) (Found: C, 48.17; H, 4.29. $C_8H_8O_4S$ requires C, 48.01; H, 4.03%).

2-Hydroxy-2-o-hydroxyphenylethane-1-sulphonic Sultone (VI)

The sulphonate (V) (0.7 g.), powdered potassium hydroxide (0.15 g.) and pure pyridine (9 c.c.) were shaken for thirty hours at room temperature. A little water was added then the solution acidified and extracted with ether. The ether was washed with dilute acid and then the solvent removed giving(VI). m.p. 97-8° (from benzene) (Found: C, 48.24; H, 4.33. $C_8H_8O_4S$ requires C, 48.01; H, 4.03%).

2-o-Hydroxyphenylethylene-1-sulphonic Sultone (I)

The sultone (VI) (1.7 g.) was refluxed with phosphoryl chloride (20 c.c.) for two hours. The solution was carefully added to water, extracted with ether and the ether layer washed with carbonate then evaporated. m.p. 81-3° (from benzene-petroleum ether) (Found: C, 52.57; H, 3.18. C H O S requires C, 52.73; H, 3.32%).

Cyclisation Attempts on the Sulphonate (V) in Acid Media

(1) After standing overnight in concentrated sulphuric acid, the sulphonate was recovered unchanged.

(2) (V)(1 g.) was refluxed with phosphoryl chloride (20 c.c.) for two hours and the reaction mixture worked up as in the previous experiment. The product (1 g.) after chromatography over alumina in benzene, had a m.p. 79-80° and depressed both (V) and (I). (Found: C, 38.05; H, 3.90. $C_8H_8O_3SCl_2$ requires C, 37.70; H, 3.14%).

That this was the chloral (IV) was verified by warming a portion with two mols. of concentrated sulphuric acid, diluting and treating with ethanolic 2:4-dinitrophenylhydrazine. The 2:4-dinitrophenylhydrazone obtained was identical to that of (V).

Methanesulphonyl Derivative of Anhydro-tris-o-aminobenzaldehyde (probably XI)

Methanesulphonyl chloride (0.6 c.c.) was added dropwise to o-aminobenzaldehyde (0.6 g.) in pyridine (5 c.c.), and the reaction worked up as in the preparation of (V). m.p. 218-9° (from ethanol) (Found: C, 65.27; H, 4.80; N, 10.34. $C_{22}H_{19}O_3N_3S$ requires C, 65.18; H, 4.72; N, 10.37%).

2:4-Dinitrophenylhydrazone m.p. 272-4° (contained S).

N-Methanesulphonyl-o-aminoacetophenone (XII)

Methanesulphonyl chloride (.65 c.c.) was added dropwise to o-aminoacetophenone (0.9 g.) in pyridine (5 c.c.). The colour darkened and crystals separated. After an hour, the reaction mixture was poured into dilute sulphuric acid, and the product filtered, washed and dried. m.p. 105-6° (from benzene-petroleum ether). (Found: C, 50.86; H, 5.28; N, 6.62. $C_9H_{11}O_3NS$ requires C, 50.70; H, 5.20; N, 6.57%).

N-Methyl-N-methanesulphonyl-o-aminoacetophenone (XIII)

Powdered potassium hydroxide (0.4 g.) was mixed with the sulphonamide (XII) (0.3 g.) in pure acetone (20 c.c.), then methyl iodide (0.5 c.c.) in acetone (5 c.c.) added to the refluxing solution. Heating was continued for a further fifteen minutes. Filtration of the solution, followed by dilution with water, concentration and cooling gave (XIII) m.p. 102-4° (from methanol) (Found: C, 52.68; H, 6.35; N, 6.21. $C_{10}H_{13}O_3NS$ requires C, 52.86; H, 5.77; N, 6.17%).

5-Nitrosalicylaldehyde-O-methanesulphonate

As in the preparation of (V), using 5-nitrosalicylaldehyde m.p. 98-99° (from ethylacetate-petroleum ether) (Found: C, 39.08; H, 3.08; N, 5.85. $C_8H_7O_6NS$ requires C, 39.19; H, 2.86; N, 5.71).

2-o-Methylaminophenylprop-1-ene-1-sulphonic Sultam (XV)

(1) As in the preparation of (VI). m.p. 92 (from ethyl acetate - petroleum ether) (Found: C, 57.47; H, 5.09; N, 6.40. $C_{10}H_{11}O_2NS$ requires C, 57.41; H, 5.30; N, 6.70%). $\lambda_{max.}$ (ethanol) 226, 266 and 318 mu. log ϵ : 4.49, 3.93 and 3.49.

(2) By N-methylation of (XVII) using the method of Pachter and Kloetzel[38].

N-Benzoyl-N-methanesulphonyl-o-aminoacetophenone (XVI)

The sulphonamide (XII) (0.5 g.), benzoyl chloride (0.5 c.c.) and pure pyridine (1.2 c.c.) were heated on the steam-bath for thirty minutes. Cooling and addition of methanol gave a good yield of (XVI) m.p. 146-7° (from ethanol) (Found: C, 60.63; H, 4.63; N, 4.82. $C_{16}H_{15}O_4NS$ requires C, 60.56; H, 4.77; N, 4.41%).

2-o-Aminophenylprop-1-ene-1-sulphonic Sultam (XVII)

The N-benzoylsulphonamide (XVI) (0.4 g.), powdered potassium hydroxide (0.13 g.) and pyridine (7 c.c.) were shaken together for three days. The isolation was similar to that for other cyclisations of this type.

m.p. 171-3° (from benzene) (Found: C, 55.97; H, 4.35; N, 7.06. $C_9H_9O_2NS$ requires C, 55.40; H, 4.65; N, 7.18%).

Diphenylene Sultam and N-methyldiphenylene Sultam

These were prepared by the method of Gross and Ullmann[15].

2-(2-Hydroxy-5-nitrophenyl)ethylene-1-sulphonic Sultone (XXIII) and 2-(2-Hydroxy-3-nitrophenyl)ethylene-1-sulphonic Sultone (XXIV)

The sultone (I) (9 g.) was brushed into fuming nitric acid (30 c.c.) at room temperature. After an hour, the solution was poured into water and the solid filtered. Careful crystallisation from ethanol afforded a sparingly soluble isomer (XXIII) (8 g.) m.p. 184-6° (Found: C, 42.37; H, 2.23; N, 6.13. $C_8H_5O_5NS$ requires C, 42.30; H, 2.20; N, 6.17%), and a readily soluble one (XXIV) (0.7 g.) m.p. 114-6°. (Found: C, 62.49; H, 2.32; N, 6.03%).

Identification of the Nitrosultones

A potassium permanganate solution was added slowly to the nitrosultone (XXIII) suspended in 3 c.c. of 2N sodium hydroxide until the pink colour persisted after shaking. After the excess permanganate had been destroyed, the solution was filtered and acidified m.p. 226-9° (from acetic acid). Mixed m.p. with 5-nitrosalicyclic acid 227-9°. The nitrosultone (XXIV) was oxidised in the same manner, m.p. and mixed m.p. with 3-nitrosalicyclic acid, 143-6°.

Potassium Salt of 2-(2-hydroxy-5-nitrophenyl)ethylene-1-sulphonic Acid (XXV)

The nitrosultone (XXIII) (0.5 g.) was heated for a few minutes with potassium hydroxide (1 g.) in presence of a little water. A dark-red homogeneous solution resulted which solidified on cooling. This was dissolved in the minimum amount of water, acidified and the yellow solid filtered. It crystallised from water in yellow needles. m.p. ~ 250° (decomp.) (Found: C, 32.29; H, 2.33; N, 4.83. $C_8H_8O_7NSK$ requires C, 31.90; H, 2.66; N, 4.65%).

2:4:6-Tribromophenol (XXVI)

The sultone (I) (0.2 g.), potassium hydroxide (0.3 g.) and water (0.5 c.c.) were heated together until the solution was homogeneous. The solution was diluted with a little water and neutralised with dilute sulphuric acid. Excess bromine was added and soon a yellow solid precipitated (0.27 g.) m.p. 88-91 (aqueous methanol); mixed m.p. with 2:4:6-tribromophenol, 89-92°.

Nitration of the Sultam (XV)

(1) Nitration and isolation by the method described for the sultone (I) gave a dinitrosultam, m.p. 150-2° (from methanol) (Found: C, 40.06; H, 2.83; N, 13.99. $C_{10}H_9O_6N_3S$ requires C, 40.14; H, 3.03; N, 14.05), which was probably 2-(2-methylamino-3:5-dinitrophenylprop-1-ene-1-sulphonic sultam (XXVII).

(2) The sultam (.4 g.) was brushed into concentrated nitric acid at 5°C. The temperature was allowed to rise for fifteen minutes, when the solution was poured into water and the solid collected. m.p. 145-6° (from ethanol) (Found: C, 47.43; H, 3.93; N, 10.99. $C_{10}H_{10}O_4N_2S$ requires C, 47.25; H, 3.97; N, 11.02%). This was probably 2-(2-methylamino-5-nitrophenyl)prop-1-ene-1-sulphonic sultam (XXVIII).

N-Methylskatole

The sultam (XV) (0.8 g.), freshly ignited quicklime (0.8 g.) and pure quinoline (0.15 c.c.) were heated together in a micro-distillation apparatus for thirty minutes at ~270°C. The mixture was then slowly heated in an air-bath to about 230° (0.5 mm.). The distillate in ether was washed four times with dilute hydrochloric acid (1 N), then with water and the solvent removed. An ethanolic picric acid solution was added to the residue. The colour changed from yellow to deep red and red needles separated (0.06 g.) m.p. 140-2° (from ethanol) (Found: C, 51-18; H, 3.79. $C_{16}H_{14}O_7N_4$ requires C, 51.34; H, 3.77%). Mixed m.p. with authentic specimen of picrate of N-methylskatole, 139-142°.

Carbazole (XXII)

Diphenylene sultam (0.4 g.) was treated as above for five hours at 350°. On addition of picric acid to the product,

only a few needles of picrate were obtained. m.p. 175-180°. Mixed m.p. with authentic specimen of picrate of carbazole, 176-182°.

N-Methylcarbazole

N-Methyldiphenylene sultam (III; R = CH_3) (0.15 g.), quicklime (0.15 g.) and quinoline were heated together at 350° for five hours. The product was isolated as in the previous experiments (0.027 g.) m.p. 143-4°. Mixed m.p. with authentic specimen of picrate of N-methylcarbazole, 143-5°. (Found: C, 55.32; H, 3.29; N, 13.62. $C_{19}H_{14}O_7N_4$ requires C, 55.61; H, 3.44; N, 13.66%).

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CONTENTS

ADDENDUM

An Attempted Synthesis of Glauconin, a Degradation Product of Glauconic Acid.

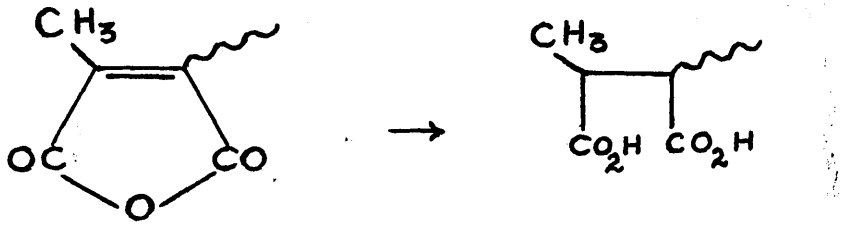
CONTENTS

INTRODUCTION

Glauconic acid, a metabolite from "Aspergillus Flavus" has the empirical formula, $C_{18}H_{20}O_7$. Its structure is unknown, but when heated above its melting-point, it decomposes to give a volatile product, $C_7H_{12}O$, identified as α:β-diethylacrolein and a non-volatile product, $C_{11}H_8O_6$, which was called glauconin.

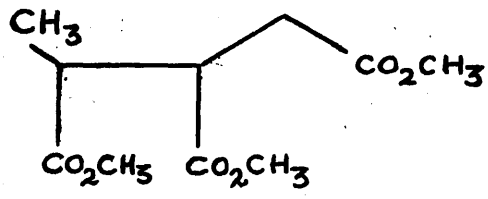
The structures of glauconic acid and glauconin have been the subject of much experimental work, related in a series of papers between the years 1931-7[1,2,3,4,5,6]. Glauconin, m.p. 171°, is optically inactive, has no active hydrogen atoms, contains two C-methyl groups and possesses a masked tetra-acid character when titrated with base. Glauconin is unresponsive to ferric chloride, bromine, tetranitromethane and perbenzoic acid but forms an ozonide or, more likely, a di-ozonide from which, by catalytic reduction, one mol. upwards of pyruvic acid is obtained as the 2:4-dinitrophenylhydrazone. The high yield of pyruvic acid suggests an origin from two centres in glauconin. From the ozonisation, oxalacetic acid, which might be a precursor of part of the pyruvic acid, oxalic acid and formic acid were also isolated.

With alkaline dimethysulphate, glauconin forms a dimethyl ester, $C_{13}H_{14}O_7$, in which the elements of water have been added. Glauconin is partially reduced when treated with red phosphorus and hydrogen iodide, one mol. of both hydrogen and water being added. The product, $C_{11}H_{12}O_7$, has a higher titre than glauconin in cold alkali and about the same titre as glauconin in warm alkali. By analogy with known behaviour, reduction and opening of a maleic anhydride grouping is inferred and (I) is tentatively suggested as part of the glauconin molecule.



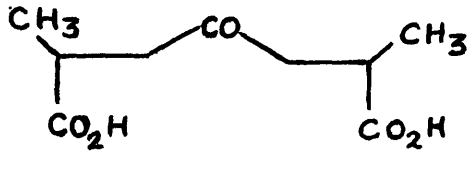
I II

This was substantiated by ozonisation of the completely methylated derivative of the acid (II), which itself is incompletely attacked by ozone. Reductive scission of the ozonide, followed by re-methylation of the product gives a trimethyl ester, $C_{10}H_{16}O_6$, which was identified as (III) by synthesis.

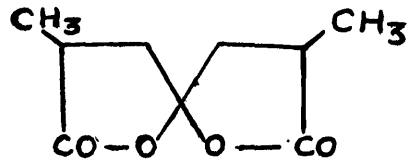


III

With hydrochloric acid at 200°C, glauconin loses two mols. of carbon dioxide and yields a mixture of products identified and confirmed by synthesis as the two acids (IV ; meso and racemic) and the three derived dilactones (V)



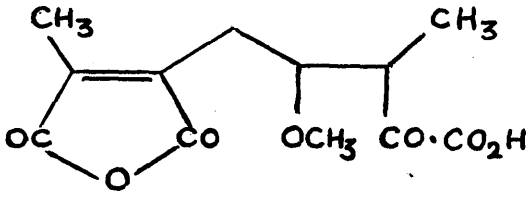
IV



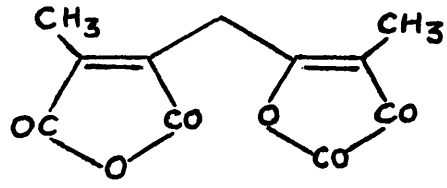
V

Glauconin, itself resists hydrogenation, but with platinum oxide at 100°C and 150 atmospheres, it yields an acidic oil which, after methylation and distillation, produces a liquid ester (2 OCH_3). Hydrolysis of this ester with excess decinormal alkali, followed by back titration, suggested that the acid formed (not isolated)

was tri-basic. On similar treatment with platinum oxide, glauconin dimethyl ester, which is readily hydrogenated at ordinary temperature and pressure, takes up about one mol. of hydrogen giving a liquid product, titrating, after hydrolysis, as a tri-acid. This acid turns ferric chloride solution red-brown. From the hydrogenation behaviour, Kraft[6] suggests the structures (VI) and (VII) for this acid and for glauconin respectively, inferring the presence of an enol-lactone grouping, opened on esterification and then readily subject to reduction.



VI

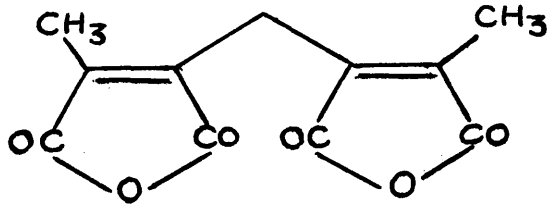


VII

The hydrogenation experiments, however are rather difficult to assess due to the absence in many instances of C and H analyses or due to their ambiguity when reported. The evidence for structure (VI) is not convincing and attempts to measure carbon monoxide evolution on heating with

sulphuric acid, gave very poor results. Moreover, it is difficult to explain the formation of compounds (IV) and (V) on the basis of structure (VII) for glauconin.

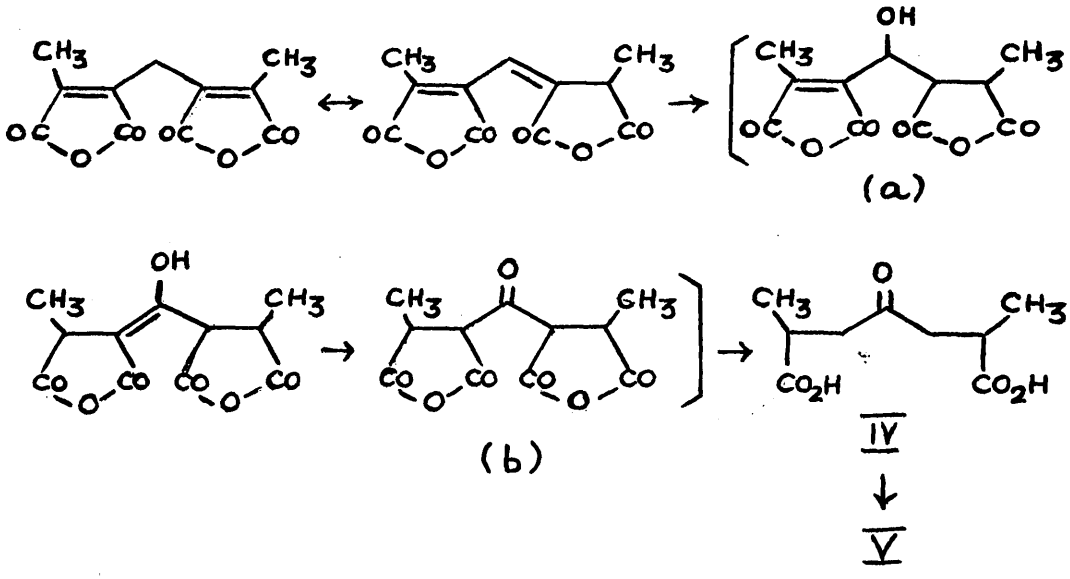
Mention is made of the possibility of structure (VIII) for glauconin but this is rejected in view of the hydrogenation data and is said to be irreconcilable with absorption spectra.



VIII

DISCUSSION

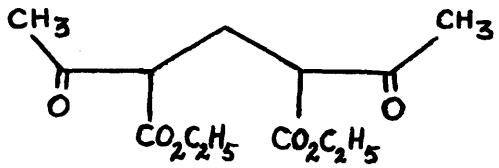
The double anhydride structure (VIII) was preferred for glauconin and by postulating mobility of the double bonds, all the experimental data can be explained satisfactorily. The compounds (IV) and (V), for example, might be formed thus:-



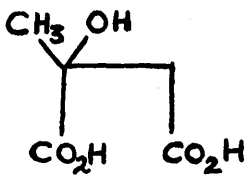
Although the allylic alcohol (a) may be the more stable structure, only a slight isomerisation to structure (b) is required to start the reaction which is then rendered irreversible by decarboxylation.

Synthetic routes to structure (VIII) were then considered. Formation of the dicyanhydrin of methylene-bis-acetoacetic-ester (IX) with subsequent hydrolysis and dehydration appeared to be the simplest method of approach.

The preparation of citraconic anhydride by dehydration of the hydroxydicarboxylic acid (X), obtained by hydrolysis of the cyanhydrin of acetoacetic ester, made this idea all the more conceivable[7,8].



IX

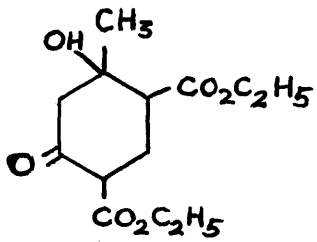


X

The ester (IX) was reported to be rather unstable[9] and purification by distillation was not recommended. For this reason, preliminary experiments in this field were carried out with the crude ester. Later, however, a pure sample was prepared by rapid distillation under strongly reduced pressure.

The crude ester in ether was treated with excess potassium cyanide and concentrated hydrochloric acid, then allowed to stand for fourteen days with occasional shaking. The product, after hydrolysis, was a red viscous syrup admixed with a little crystalline material.

Chromatography over silica gel gave a partial separation. The unknown compound, "X," was crystallised repeatedly from ethyl acetate/petroleum ether and then several times from water until its melting point could not be raised above 165°C. It had the empirical formula, $C_9H_{12}O_5$, and dissolved in sodium bicarbonate solution with effervescence. "X" contained two C-methyl groups, thus eliminating structure (XI) (from head to tail condensation of IX) as a precursor[9]

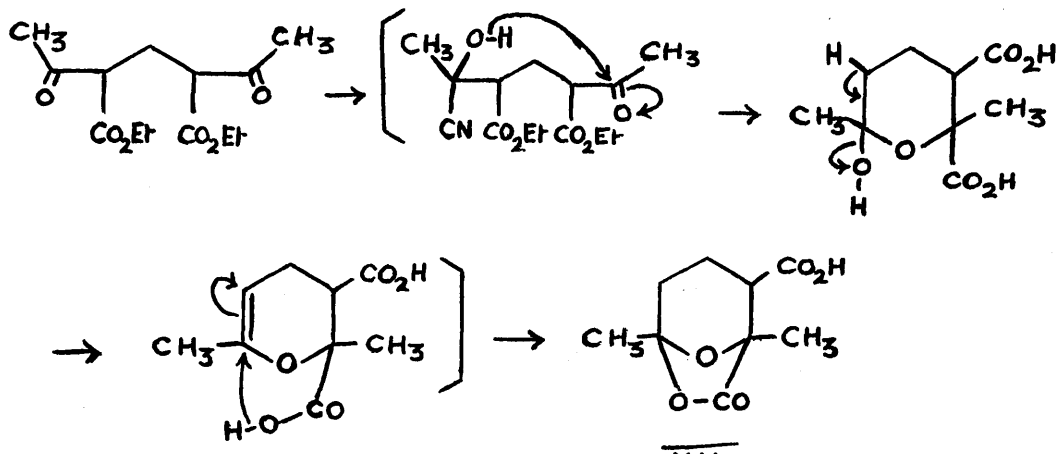


XI

"X" gave a negative iodoform test and had infra-red absorption bands at 1790 and 1735 $cm.^{-1}$, probably due to a γ-lactone and carboxyl grouping respectively. The ultraviolet spectrum showed only general absorption. "X" formed a monoanilide, $C_{15}H_{17}O_4N$, and with diazomethane gave a monomethyl ester, $C_{10}H_{14}O_5$, which like "X" itself, had infra-red bands at 1795 and 1735 $cm.^{-1}$, due to a γ-lactone and ester carbonyl group respectively. Titration against cold $^N/_{50}$ sodium hydroxide gave equivalent values of

about two hundred, whereas back titration in warm alkali gave a figure of about one hundred, inferring the opening of a lactone ring. "X" did not contain a hydroxyl group and did not react with carbonyl reagents under normal conditions. When treated more vigorously with 2:4-dinitrophenylhydrazine, a small amount of a red microcrystalline compound, $C_{15}H_{18}O_8N_4$, was isolated. In this compound the infra-red peak at 1790 $cm.^{-1}$ was absent and it is suggested that this compound is a hydrazide.

Assuming that the fifth oxygen atom is contained in an ether linkage, the structure (XII) is suggested for "X", formed presumably through the following mechanism:-



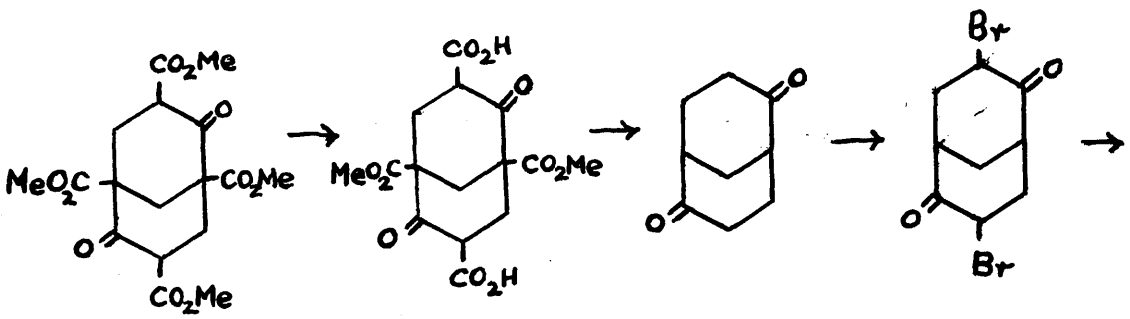
XII

Attempts to distil the red syrup, the major product of the reaction, resulted in much decomposition and no

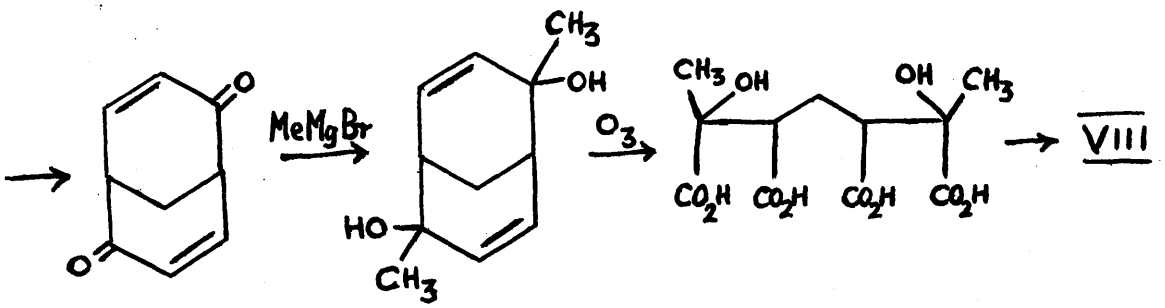
constant boiling fraction could be obtained. Sublimation produced similar results although small amounts of "X" were isolated from the sublimates. Dehydration was essayed in boiling acetyl chloride but no crystallisable product could be extracted.

When an ethereal solution of a freshly distilled analytically pure sample of (IX) was treated with a large excess of potassium cyanide and concentrated hydrochloric acid and the mixture shaken automatically for fourteen days, the result was much as before. The major product, after hydrolysis, was once again a red syrup with which little could be done. The lactonic acid, "X," was obtained in slightly higher yield. The course of the reaction was unaltered when anhydrous liquid hydrocyanic acid in presence of a trace of potassium cyanide was used as reagent.

The synthetic scheme (XIII ⟶ XIX) was next considered as a possible route to glauconin.



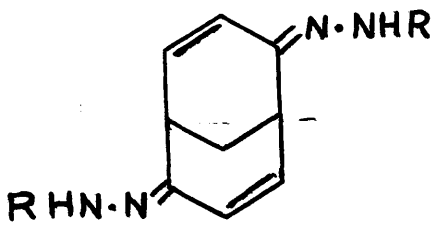
XIII XIV XV XVI



XVII XVIII XIX

Methyl bicyclo[3:3:1]nona-2:6-dione-1:3:5:7-tetracarboxylate (XIII) was readily prepared by condensation between a mixture of methyl methylenemalonate and methyl methylene-dimalonate (2:1) in the presence of sodium methoxide[10]. This reaction gave surprisingly low yields when the ethyl esters were used. The tetra ester (XIII) was hydrolysed with barytra to the dicarboxylic acid (XIV) which was smoothly converted to bicyclo[3:3:1]nona-2:6-dione (XV) when heated with water in a sealed tube[10]. Treatment of (XV) with bromine gave a dibromide, $C_9H_{10}O_2Br_2$, which almost certainly had the structure (XVI). Attempts to dehydrobrominate this compound by the standard methods were unsuccessful. It did however undergo a Mattox-

Kendall[11,12] reaction with 2:4-dinitrophenylhydrazine to give a bis-α:β-unsaturated 2:4-dinitrophenylhydrazone, $C_{21}H_{16}O_8N_8$ (XX ; R = $C_6H_3O_4N_2$), the ultraviolet absorption spectrum of which showed the expected maximum at 287 mu



XX

The corresponding bis-α:β-unsaturated semicarbazone (XX ; R = CO. NH_2) could not be obtained crystalline and attempts to generate the diketone (XVII) by cleavage of either with pyruvic acid were unsuccessful.

EXPERIMENTAL

Methylene-bis-acetoaceticester

This was prepared from formaldehyde and acetoacetic ester without any basic condensing agent[9]. b.p. 190-210° (20 mm.), 135-140° (0.5 mm.) $^{24}n = 1.4550$. (Found: C, 57.12; H, 7.29. $C_{13}H_{20}O_6$ requires C, 57.34; H, 7.40%).

Reaction of Methylene-bis-acetoaceticester with CN^-

(a) To methylene-bis-acetoaceticester (10 g.) in dry ether (30 c.c.) was added potassium cyanide (10 g.) and then, dropwise, concentrated hydrochloric acid (16 c.c.). The mixture was stood at room temperature for fourteen days with occasional shaking. The dark-coloured supernatant liquor was decanted from the inorganic residue, the solvent removed and the residue refluxed with 5N hydrochloric acid for six hours. The solution was concentrated to small bulk and exhaustively extracted with ether. The product was a red syrup admixed with a small quantity of crystalline material. Chromatography over silica gel in benzene effected partial separation. The crystalline compound produced, "X" was recrystallised three times from ethyl acetate/petroleum ether and then twice from water, m.p.

164-5° (Found: C, 53.70, 53.94; H, 5.80, 6.10. $C_9H_{12}O_5$ requires C, 54.00; H, 6.05%).
Equivalent (in cold alkali) - 196, 207, 206;
Equivalent (back titration with hot alkali) - 97, 102.

Methyl Ester of "X"

"X" (0.18 g.) was brushed into an excess of diazomethane in ether at room temperature. The ester (0.17 g.) was distilled *in vacuo* using an air-bath. b.p. 70-75° (0.06 mm.) (Bath temperature). (Found: C, 56.22; H, 6.53. $C_{10}H_{14}O_5$ requires C, 56.10 ; H, 6.60%).

Monoanilide of "X"

"X" (0.1 g.) was refluxed with thionyl chloride (3 c.c.) for two hours. The thionyl chloride was removed *in vacuo* and the residue in ether treated with aniline. m.p. 228-9° (from ethanol) (Found: C, 64.90; H, 6.62; N, 5.40. $C_{15}H_{17}O_4N$ requires C, 65.44; H, 6.22; N, 5.10%).

Derivative with 2:4-dinitrophenylhydrazine

"X" (0.1 g.) in ethanol (10 c.c.) was refluxed with 2:4-dinitrophenylhydrazine sulphate for three hours. Dilution with water and cooling afforded a small quantity of an orange-red solid, m.p. 166-9°. (Found: C, 47.14; H, 4.42. $C_{15}H_{18}O_8N_4$ requires C, 47.12; H, 4.75%).

(b) The course of the reaction was not changed extensively when pure methylene-bis-acetoaceticester was used or

when anhydrous liquid hydrocyanic acid in presence of a trace of potassium cyanide was employed as reagent.

Ethyl Bicyclo[3:3:1]nona-2:6-dione-1:3:5:7-tetracarboxylate

The method was the same as that for the corresponding tetramethyl ester[10] (XIII). The yield was only 5% of the theoretical amount. m.p. 108-110° (from methanol) (Found: C, 57.40; H, 6.45. $C_{21}H_{28}O_{10}$ requires C, 57.26; H, 6.41%).

Bicyclo[3:3:1]nona-2:6-dione-1:3:5:7-tetracarboxylic Acid 1:5-Diethyl Ester

The above tetraethyl ester was hydrolysed with barytra as in the methyl ester series (cf. XIV). m.p. 210-211° (from aqueous methanol) (Found: C, 53.24; H, 5.57. $C_{17}H_{20}O_{10}$ requires C, 53.12; H, 5.25%).

Bicyclo[3:3:1]nona-2:6-dione-3:7-dibromide (XVI)

Bromine (0.22 c.c.) in glacial acetic acid (1 c.c.) was added dropwise to the diketone (XV) (0.3 g.) in glacial acetic acid (3 c.c.) at room temperature. Crystals separated overnight and a second crop was obtained by dilution of the filtrate. m.p. 163-4° (from benzene-petroleum ether) (Found: C, 35.00; H, 3.52. $C_9H_{10}O_2Br_2$ requires C, 34.84; H, 3.23).

Bis-2:4-dinitrophenylhydrazone of Bicyclo[3:3:1]nona-2:6-dione-3:7-diene (XX; R = $C_6H_3O_4N_2$)

To the dibromodiketone (XVI) (0.017 g.) in glacial acetic acid (1 c.c.) was added 2:4-dinitrophenylhydrazine (0.025 g.) in glacial acetic acid (2 c.c.). The mixture was refluxed for five minutes. Cooling gave the 2:4-dinitrophenylhydrazone (XX; R = $C_6H_3O_4N_2$) (0.019 g.) m.p. 270° (decomp.) (Found: C, 48.92; H, 3.13; N, 21.72. $C_{21}H_{16}O_8N_8$ requires C, 49.60; H, 3.15; N, 22.00%). $\lambda_{max.}$ (chloroform) 287 mu. log ε = 4.706.

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