"SYNTHESIS OF AROMATIC COMPOUNDS".

A Thesis for the Degree of

Doctor of Philosophy.

by

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Part One:-   A New Synthesis of Chrysene.

Part Two:-   A New Synthesis of Phenanthridines.

Addendum:-   Cyclisation of Diazoketones.

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CONTENTS.

Part One:- A New Synthesis of Chrysene.

CONTENTS.

INTRODUCTION.

The work to be described originated in a seemingly anomolous intramolecular acylation reaction reported by Badger, Campbell and Cook[1]. Thus, contrary to the rule proposed by v. Braun and his co-workers,[2] cyclisation of $\alpha\beta$-diphenylglutaric acid (I) was found to yield the <u>cyclo</u>pentane derivative (II) and not the expected <u>cyclohexane</u> compound (III). This unusual reaction course led to the abandonment of a projected synthesis of chrysene (and its derivatives) <u>via</u> the hexahydrochrysene (IV).
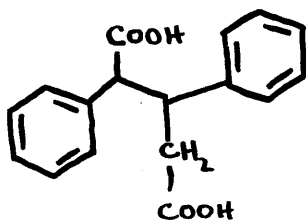
I
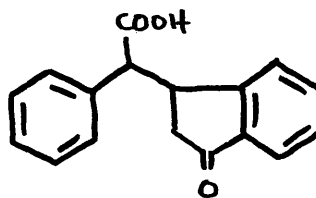
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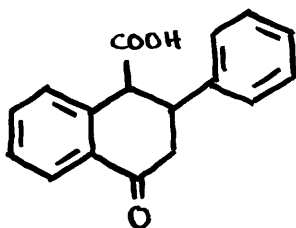
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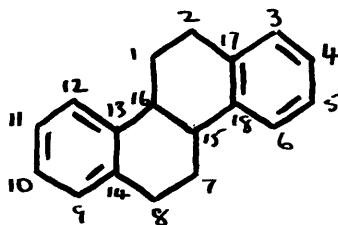
IV

The numbering system for hydrogenated chrysenes is shown in formula $\overline{IV}$. This hexahydrochrysene is known to exist in two forms [3], designated by the prefixes cis and trans , which refer to the disposition of groups at C_{15} and C_{16}.

Earlier synthetic work included that of Beschke[4], whose synthesis is based on a Reformatsky reaction with benzil or its derivatives, followed by double ring closure of dibasic carboxylic acids of type $\overline{V}$.
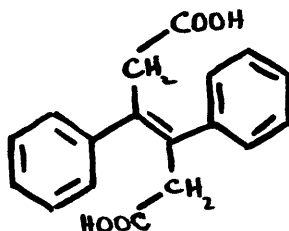
$$\overline{V}$$

A more convenient method was that of v. Braun and Irmische [5], who use the same principle as Beschke but employ $\beta\gamma$ -diphenyladipic acid (VI) for cyclisation.

$\underline{VI}$ $\underline{VII}$
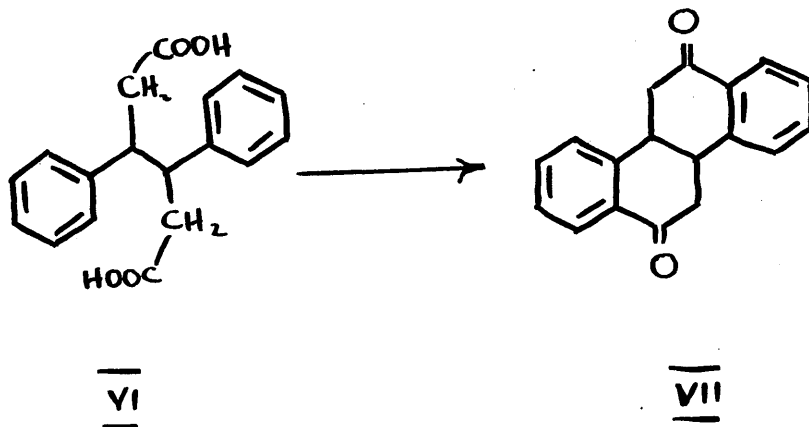
$\beta\gamma$ -Diphenyladipic acid is obtained in two

isomeric forms [6] meso-$\beta\gamma$-diphenyladipic acid and

r-$\beta\gamma$-diphenyladipic acid ("r" ≡ optically resolvable).

Each isomer was converted into its acid chloride, by

v. Braun and Irmische, and submitted to the action of aluminium

chloride, thus providing the "meso-" and "r-" diketohexahydro-

chrysenes (VII).   These compounds were then reduced to the

hexahydrochrysenes (IV).

Following this, Ramage and Robinson [3] became

interested in this synthesis with a view to obtaining perhydro-

chrysene, and such of its derivatives as might be significant

for the chemistry of sterols, bile acids, etc.   These workers

repeated the work of v. Braun and Irmische, but used hot

sulphuric acid as condensing agent. They reported good results, synthesising trans-isomers from the meso-acid and cis-isomers from the r-acid. However, the physical constants of these compounds were not found to tally with those reported previously [5]. Ramage and Robinson report the cis-hexahydrochrysene, m.p. 75°, and the trans-isomer, m.p. 115° obtained by Clemmensen reduction of the corresponding dicarbonyl compounds. Each of these homogeneous products gave chrysene on heating with selenium. Because this route suffers from the disadvantage of poor yields, especially in the formation of the intermediate $\beta\beta'$-diaryladipic acids. Badger et al attempted the synthesis from $\beta\gamma$-diarylglutaric acids via substituted phenylnaphthoic acid intermediates (III). As previously stated the preponderant course of Friedel-Craft cyclisation was that to the indanone derivative (II) — α-phenyl-α-(3-oxoindanyl)acetic acid. An indication that cyclisation to a tetralone is not completely excluded is furnished by the isolation of some 3-hydroxy-1:2-benzofluorenone (VIII), undoubtedly the product of further cyclisation of the tetralone acid (III) and subsequent dehydrogenation.
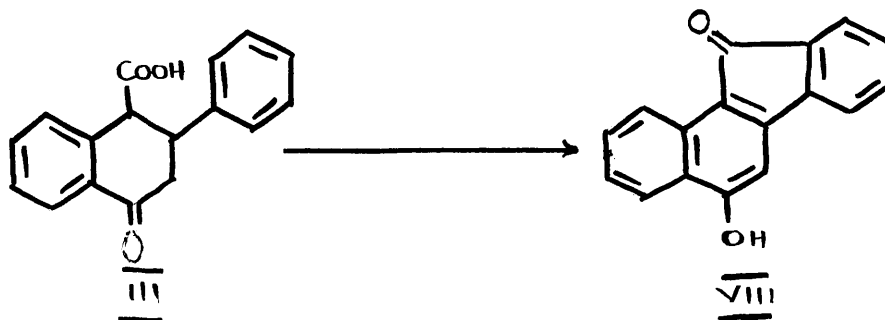
Two stereoisomers of the indanone (II) were isolated and their structures proved by parallel conversions into two isomeric 1-phenyl-1:2:3:9-tetrahydroacenaphthenes (XII), each of which, on dehydrogenation, gave the same compound —— 1-phenylacenaphthene (XIII).
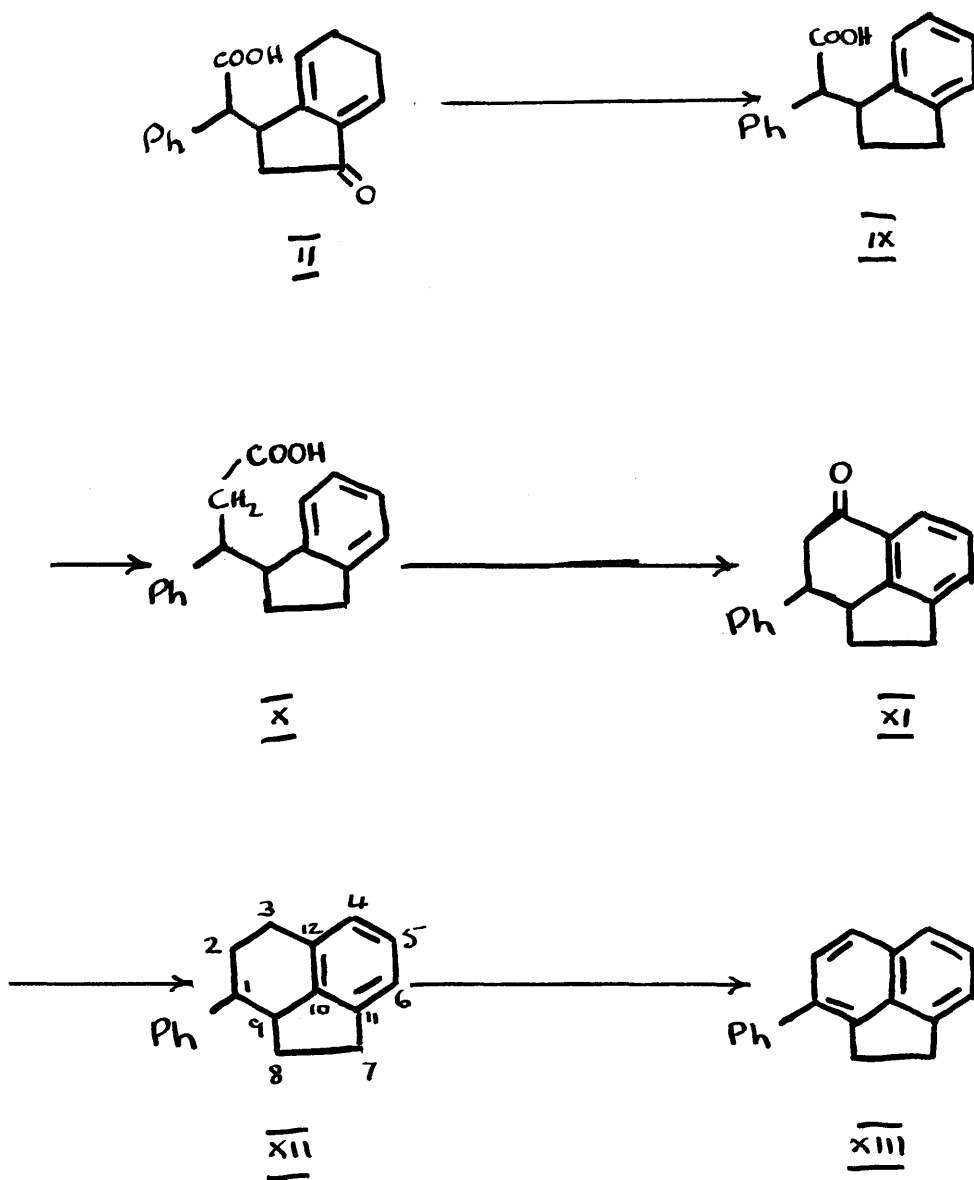
A synthesis of the <u>cis</u>-hexahydrochrysene is reported by Newman [7], who uses an extension of the phenanthrene synthesis of Cook [8]. This consists of cyclisation of αγ,β-diphenylbutyric acid (XIV) to the 2-phenyltetrahydronaphthone (XV), followed by a Reformatsky reaction, subsequent dehydration and reduction to the 2-phenyltetrahydronaphthylacetic acid (XVII). The corresponding acid chloride underwent an intramolecular Friedel-Craft acylation and the resulting ketone (XVIII) was reduced by a modified Clemmensen reaction to the desired product (IV).
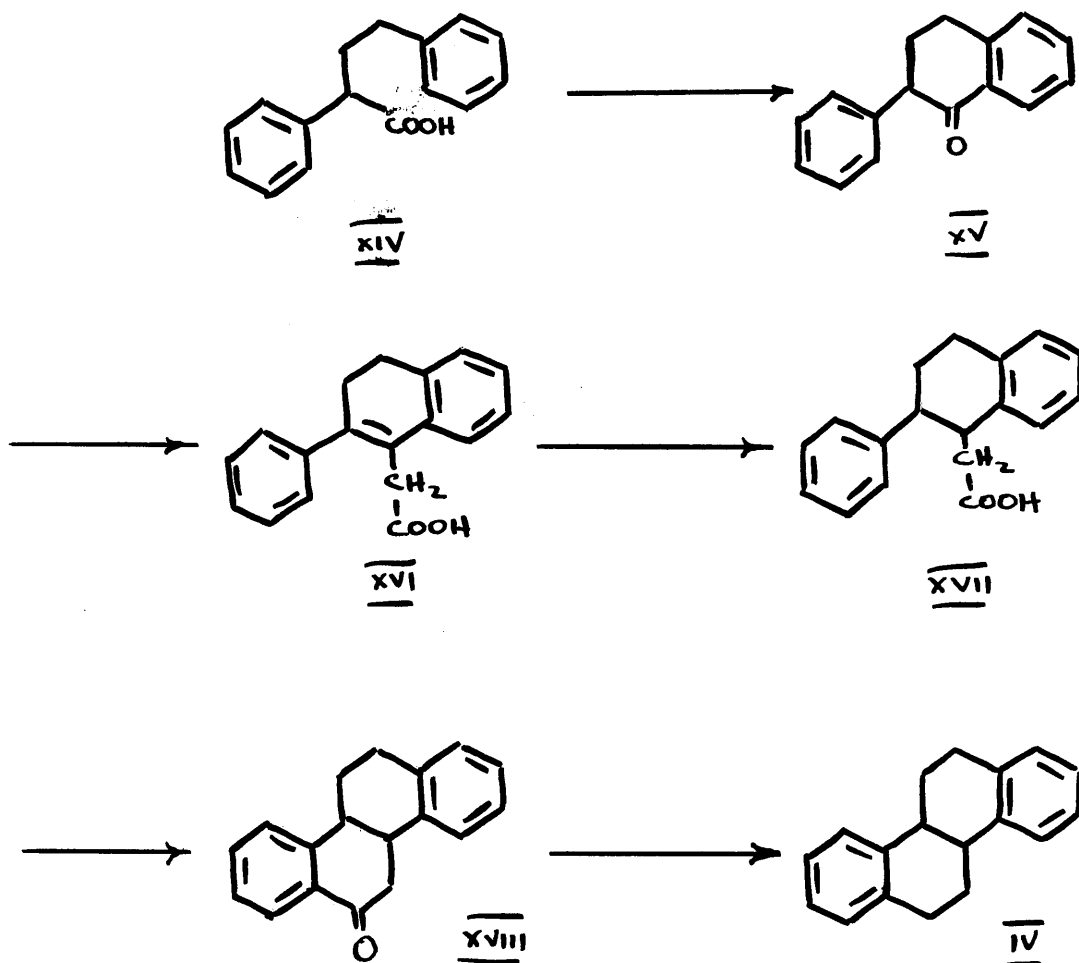
It is pointed out by Badger et al that the
possibility of ring closure of the phenyltetralinacetic acid
(XVII) to the oxophenyltetrahydroacenaphthalene (XI) in the
series above, is excluded. This statement is based on a
comparison of the melting point of Newman's cis-hexahydrochrysene
with that of either isomer of 1-phenyltetrahydroacenaphthalene
(XII). As these three compounds are obviously all different,
the possibility of the cyclisation product being an acenaphthalene
derivative is dismissed.

Hence, from the work of Ramage and Robinson it was
expected that the trans-acid (XVII), obtained from a normal
ring closure of the glutaric acid (I) and subsequent
Arndt-Eistert reaction, would give the previously unknown
trans-ketone (XVIII).

$$\underline{I}$$
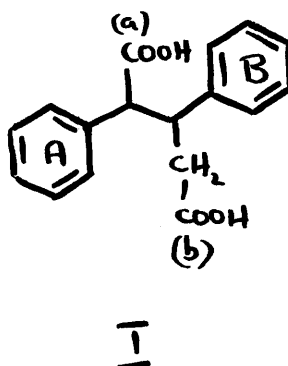
The cause of the preferential cyclisation, involving

carboxyl group (b) with ring B in formula $\overline{\text{I}}$ is said to be the deactivation of ring A by the proximate carboxyl group (a). This is consistent with the known rapid diminution of an inductive effect along a saturated carbon chain. Hence it is possible for the deactivating effect of group (a) on ring A, passing through one saturated carbon atom to be greater than the combined deactivation of both group (a) and group (b) on ring B, each effect being transmitted through two saturated carbon atoms.

Similar retarding effects have been reported by Ansell and Hey [9] in cyclisation of α -phenylglutaric acid (XIX). The yield of product was very low (17%) compared with the corresponding yield of cyclised material obtained from α -(2-phenylethyl)glutaric acid (XX).
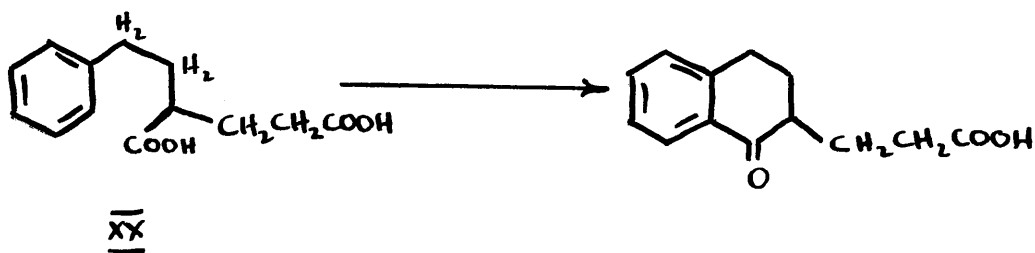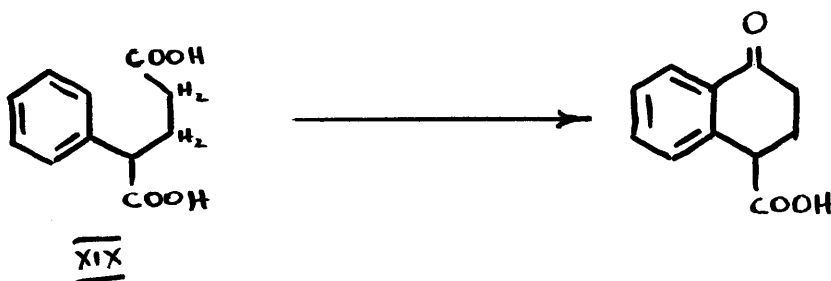
During cyclisation studies on methoxyphenylglutaric acids, Hey and Nagdy [10] found that a methoxyl group para to the position of acylation produces activation greatly outweighing the deactivation of a neighbouring carboxyl group.
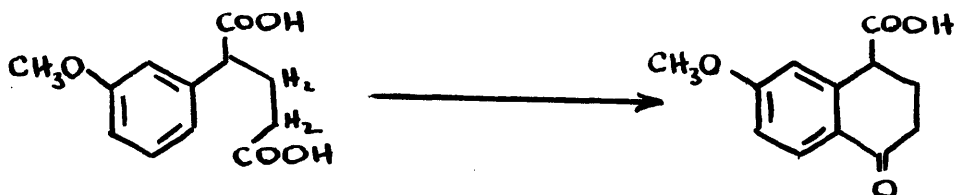
On the other hand, cyclisation was prevented, even with methoxyl groups in other ring positions.

The same workers later showed [11] that, in contrast with the known [12] [13] ready cyclisation of γ -phenylpimelic acid (XXI, R = H) to β -(1:2:3:4-tetrahydro-4-oxo-1-naphthyl)propionic acid (XXII, R = H), the corresponding γ -carboxypimelic acid (XXI, R = COOH) gives a low yield of β -(1-carboxy-1:2:3:4-tetrahydro-4-oxo-1-naphthyl)propionic acid (XXII, R = COOH).   This is another case of deactivation by a proximate carboxyl-group.
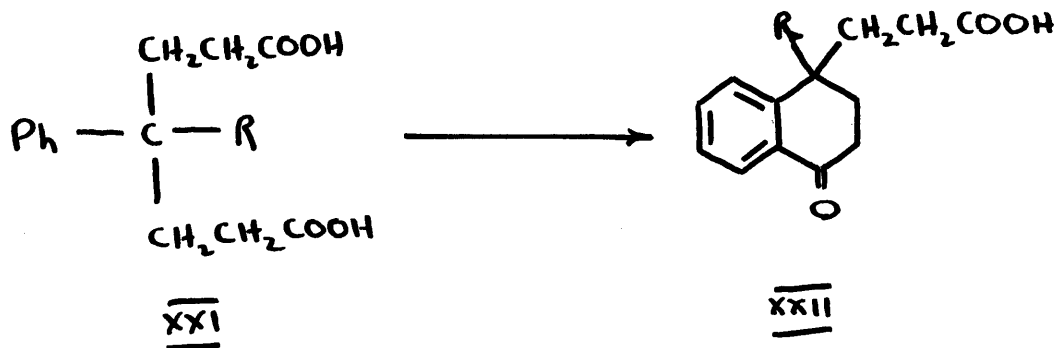
On the other hand, χ -cyana- χ -phenylpimelic acid (XXI, R = CN) readily gives a good yield of cyclic ketone (XXII, R = CN) suggesting that exchange of the carboxyl-grou p for a cyano-group removes the deactivation and thus facilitates the acylation.   Since a cyano-group normally exerts a more powerful deactivating influence than a carboxyl-group it is postulated that the latter, (R - COOH) is converted into the charged entity (R-CO) in the cyclising environment whereas no comparable change occurs with the nitrile.

From such considerations it is apparent that the undesired cyclisation of Badger, Campbell and Cook's projected synthesis may be avoided by modification of the starting point (I) through replacement of carboxyl-group (a) by -CN.

DISCUSSION.

Experiments with αβ –diphenylglutaric acid and its anhydride.

In preliminary work αβ –diphenylglutaric acid was prepared by the method of Badger et al[1] using a Michael condensation between ethyl phenylacetate and ethyl cinnamate. This gave a theoretical yield of the mixed racemic esters. The higher melting isomeride, which constituted 80% of the yield, was hydrolysed by heating with ethanolic potassium hydroxide solution, giving (±)–αβ –diphenylglutaric acid, m.p. 231°; this is the higher melting acid racemate, the other melting at 208° [26]. From this acid the anhydride of the lower melting acid was prepared by heating under reflux with acetic anhydride. The experiment of Badger, viz treatment of the above anhydride with aluminium chloride in nitrobenzene, was repeated exactly, thus furnishing authentic samples of α –phenyl–α –indan–3–on–1–ylacetic acid – A (II) and 3–hydroxy–1:2–benzofluorenone (VIII).

Cyclisation under other conditions was examined, but it was found that both the diphenylglutaric acid and its anhydride resisted reaction with anhydrous hydrogen fluoride, showing no sign of dissolution nor the usual colour development. However, treatment of the acid with polyphosphoric acid gave a considerable amount of decomposition and a small yield of α –phenyl–α –indan–3–on–1–ylacetic acid – A; no 3–hydroxy–1:2–benzofluorenone, nor any

other crystalline material was isolated.   These conditions,

applied to the anhydride, gave hydrolysis to the acid,

probably during the working up process.

Experiments with βγ-diphenyl- γ -cyanobutyric acid (XXIII).

As described by Helmkamp and his co-workers [15],

two isomers of ethyl βγ -diphenyl- γ -cyanobutyrate were

prepared by a Michael condensation between benzyl cyanide and

ethyl cinnamate.   Each of these isomeric racemates was

hydrolysed with ethanolic potash solution [16] to give the

same cyanobutyric acid (XXIII) of m.p. 163–165°.   This acid

is the more stable racemate and is thought to have <u>trans</u>   ?

configuration
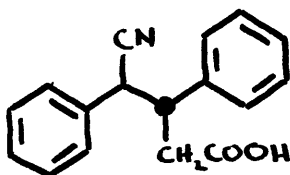
This acid also resisted cyclisation by hydrogen

fluoride, showing the same reluctance to dissolve and lack

of colour development as did the glutaric acid.   On the

other hand, treatment with polyphosphoric acid yielded a

mixture of wholly non-carboxylic products.

By careful fractional crystallisation, two crystalline compounds were isolated. The higher melting compound, which was the more insoluble in the solvent, acetic acid, was found to be weakly acidic, and by extracting it from the mixture with sodium hydroxide solution, a complete separation was effected.

The lower melting compound, shown to be neutral, was the main product being obtained in 60% yield. It was characterised as a ketone by its 2:4-dinitrophenylhydrazone. Analyses showed the ketone to be isomeric with the starting acid – $C_{17}H_{15}NO_2$. This was readily explained as cyclodehydration of the carboxyl-group and hydrolysis of the cyanide to an acid amide, a reaction course in harmony with the findings of Snyder and Elston[17] that this type of nitrile hydrolysis is common in polyphosphoric acid. The ketone could have the structure XXIV or XXIV(a)
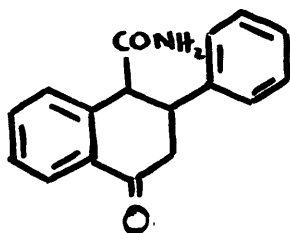
XXIV
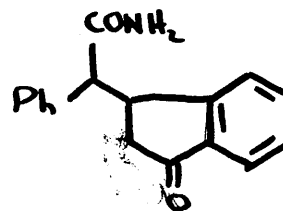
XXIV(a)

From the work of Hey and Nagdy[11], it was
expected that the tetralone (XXIV) would be formed.   This
was proved to be correct by ethanolic alkaline hydrolysis of
the amide to the ketocarboxylic acid (XXV) and further ring-
closure with polyphosphoric acid to give a dione (XXVI).

This rules out system XXIV(a), since the dione,
formed by the second intramolecular acylation, would then have
the extremely strained system of two five-membered rings and a
six-membered ring fused together:-
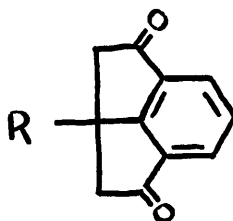
Further proof for structure XXIV was furnished
by the facile dehydrogenation of the dione to 3-hydroxy-1:2-
benzofluorenone (VIII), identified by mixed m.p. with an
authentic sample and by comparison of infrared absorption
spectra.   The dione (XXVI is therefore 3:4:10:11-tetrahydro-
3-oxo-1:2-benzofluorenone (XXVI), and the acid and amide are
the required tetralone derivatives, XXIV and III
respectively.

XXIV → III

XXVI → VIII
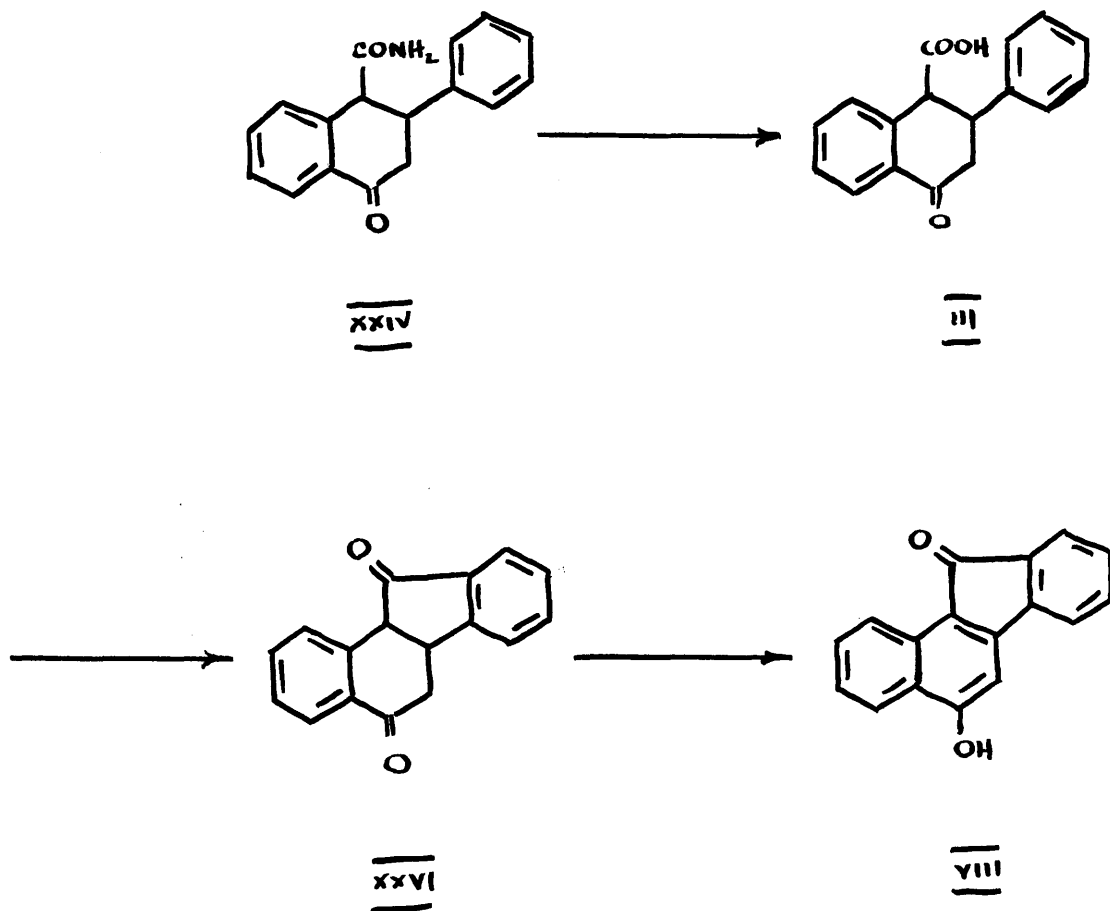
    The alkali–soluble cyclisation product from

βγ –diphenyl– γ –cyanobutyric acid was found to be isomeric

with the neutral product and the starting acid.   The

infrared absorption spectrum showed bands suggesting a

system containing an imide (-CO.NH.CO-) group.   A possible

structure, containing this group and having the required

molecular formula is $\alpha\beta$ -diphenylglutarimide (XXVIII).
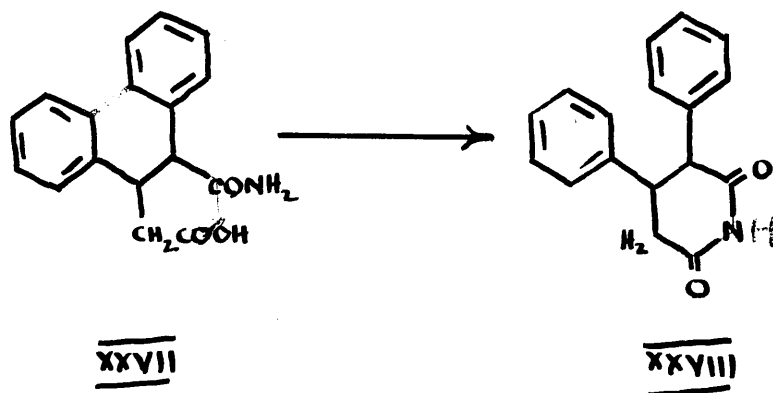
A sample of $\alpha\beta$ -diphenylglutarimide was synthesised

by bubbling ammonia gas through liquid $\alpha\beta$ -diphenylglutaric

anhydride, following a method by Trivedi and his collaborators[18].

This sample proved to be identical in all respects with the

acidic product of cyclisation.   Barr and Cook [19] have

reported the m.p. of this compound to be 222-223°, compared

with 226-227° found by both methods described here.   They

prepared the imide by heating $\beta\gamma$ -diphenyl- γ -monamidoglutaric

acid (XXVII) above its melting point.

It is found that cyclisation of $\beta\gamma$ -diphenyl- γ -

monamidoglutaric acid gave the same products in approximately

the same proportions as the cyano-acid did under identical

conditions.

The availability of the carboxyphenyltetralone (III) opened the way to the synthesis of Robinson's[3] trans-hexahydrochrysene and its derivatives.

The tetralone carboxylic acid was reduced to a tetralin derivative by the Martin modification[19] of the Clemmensen reduction. The ketone had resisted reduction by the Huang-Minlon variation [23] of the Wolff-Kishner reduction and also by conventional Clemmensen reaction. However, following the introduction of an organic solvent, the reaction went to completion in 50 hours..

During one Martin reduction experiment, the mixture was inadvertently boiled dry after 36 hours of heating under reflux. The dry residue was heated for 3 - 4 hours at ca. 250-300°, and from the charred mass, a hydrocarbon, with the empirical formula C_8H_6 was extracted with benzene. After careful purification by chromatography, sublimation and re-crystallisation the m.p. was constant at 100-101° and this, together with spectral evidence suggested that the hydrocarbon was 2-phenylnaphthalene. Identity was proved in all respects with an authentic sample, kindly supplied by Dr. Neil Campbell. The isolation of 2-phenylnaphthalene gives satisfactory proof for the suggested carbon skeleton of III.

It is of interest that, during the unsuccessful Huang-Minlon reaction the tetralone hydrazone intermediate (XXIX) underwent decarboxylation rather than the expected decomposition of the hydrazine group.
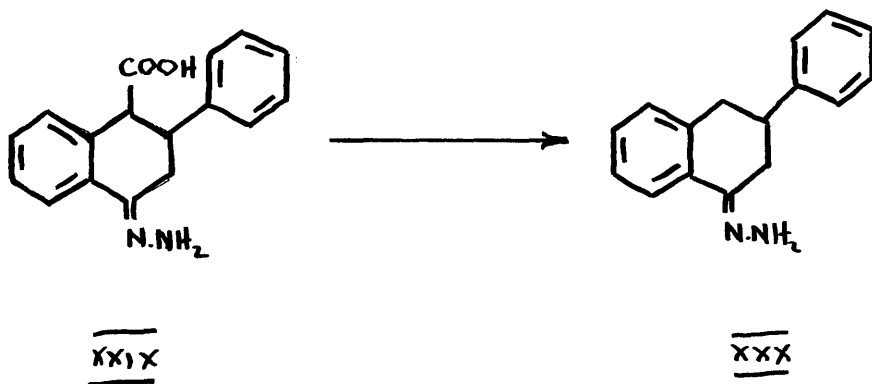
The structure of XXX was assumed from analysis, but since decarboxylation had rendered the compound useless for the required synthesis, no further attempts were made to prove this assumption or to decompose the hydrazone by prolonging the heating with alkali.

The conversion of the acid (XXV) into the homo acid, 1:2:3:4-tetrahydro-2-phenyl-1-naphthylacetic acid (XVII) proved more difficult than expected.   The starting acid was converted into its acid chloride by treatment with thionyl chloride, and this was characterised as the crystalline amide,

but the subsequent Arndt-Eistert reaction[20] gave very

poor yields.

The diazoketone was prepared by treatment of the acid

chloride with an ethereal solution of diazomethane.   This

diazoketone was treated in dioxan solution with silver oxide,

sodium bicarbonate and sodium thiosulphate after the manner

of Arndt and Eistert [21], but the 10% yields of homo-acid

was too low for this method to be practicable.   Preparation

of the homo-acid via the amide or ester by using ammonium

hydroxide or methanol as solvent proved equally unsuccessful.

However, a modification of the reaction by Newman and Beal [24]

was tried and found to be more satisfactory.   In this method

a solution of silver benzoate in triethylamine is used to

decompose the diazoketone in methanol solution, thus

affording the methyl ester of the required acid.   The ester

obtained was not purified, but was hydrolysed by aqueous

alkali to the acid.   The overall yield of the homo-acid

(based on the naphthoic acid) averaged 60%.   The crystalline

product formed colourless prisms of m.p. 134-136°, which

differs widely from ~~Newland's~~ Newman's description of cis-1:2:3:4-

tetrahydro-2-phenyl-1-naphthylacetic acid as "white needles

melting at 172.0-172.8°C".

This gives the first indication of the trans

configuration of the Arndt-Eistert product.

The substituted acetic acid (XVII) was cyclised in good yield to 1:2:7:8:15:16-hexahydro-2-oxochrysene (XVIII) by polyphosphoric acid.   The product was characterised by its analysis and that of its semicarbazone.   The m.ps. of this ketone and its derivative were 118° and 237-239° (decomp.) respectively, which again differ widely from those of Newman's corresponding cis isomeric compounds. (76-77° and 255-258°).

The carbonyl group of this hydrogenated oxochrysene was reduced by the modified Clemmensen method.   The reaction was complete after 24 hours, giving a good yield of very pale yellow needles, m.p. 112-114°.

Ramage and Robinson [3] note the m.p. of the trans-hexahydrochrysene as 115°, and that of the cis-isomer as 75°. The light absorption in ethanol showed maxima at 266 and 274 mμ this is in close agreement with results recorded by Askew[25] for the Ramage and Robinson sample of trans-compound (maxima at 263 and 272 mμ).   The selenium dehydrogenation of the hexahydrochrysene to chrysene achieved by Ramage and Robinson was repeated successfully and the product identified with an authentic sample.

From the evidence presented it is obvious that the phenyltetralinacetic acid and the subsequent products have

trans-configuration at the positions shown below.
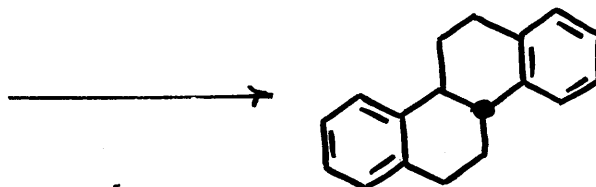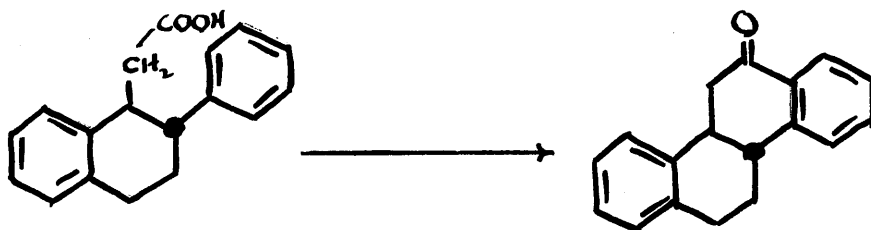
EXPERIMENTAL.

Light petroleum refers to the fraction with b.p. 60–80°, unless otherwise stated.

$\alpha\beta$ –Diphenylglutaric acid was prepared by condensation of ethyl phenylacetate (100g.) and ethyl cinnamate(100g.), isolation of the higher-melting product and hydrolysis with alkali. This is the method employed by Badger et al [1].

Yield   112g.   M.p. 230–231°

Cyclisation of $\alpha\beta$ –diphenylglutaric acid.

a).   Dry, finely powdered acid (3g.) was dusted into anhydrous hydrogen fluoride (50ml.) contained in a "Polythene" beaker. No change or reaction appeared to take place. The mixture was covered and left standing for 48 hours, then the bulk of the reagent was allowed to evaporate off and the remainder neutralised with sodium acetate solution. The solid product was shown to be starting material by melting and mixed melting points. Recovery, 95%.

b).   Phosphoric anhydride (5g.) and syrupy phosphoric acid (2ml.) were intimately mixed. Into this mixture was stirred dry, powdered acid (400mg.) and the whole heated at 100°

for 2 - 3 hours. On cooling, water (200ml.) was added to the dark brown mass, and the resultant solid was filtered, washed with water and recrystallised from methanol forming colourless needles, m.p. 153-154°.   Mixed m.p. with α-phenyl-α-indan-3-on-1-yl-acetic acid 153-155°.   Y ield - very low.

$\beta\gamma$-Diphenyl- γ-cyanobutyric acid (XXIII).

Two isomers of ethyl-$\beta\gamma$-diphenyl-γ-cyanobutyrate were prepared by the Michael Condensation of benzyl cyanide (45ml.) and ethyl cinnamate (64ml.) as described by Helmkamp, Tanghe and Plati[15].

Yield 39g. of isomer with m.p. 98-100° and

10g.   "   "   "   "   58-60°

Each isomer was hydrolysed by the method of Avery[16], with 95% ethanolic potash solution.

Yield 90% of theoretical ,   m.p. 163-165°.

Cyclisation of $\beta\gamma$-diphenyl- γ-cyanobutyric acid.

a).   The method, described before, using anhydrous hydrogen fluoride was tried, but in a similar matter a good recovery of starting material was the only result.

b).   Finely powdered acid was mixed with polyphosphoric acid from phosphoric anhydride (25g.) and syrupy phosphoric acid (10ml.)   and heated at 100° for 2$\frac{1}{2}$ hours.   The mixture,

dark brown in colour with a green-yellow fluorescence, was cooled and decomposed with crushed ice giving a precipitate which was filtered, washed with dilute sodium carbonate solution and then with water. The residue was rubbed with $5\overline{N}$ aqueous sodium hydroxide solution and the remaining solid was filtered off. This was washed with water, dried and recrystallised from methanol giving white plates m.p. 200-201°.

Found: C, 76.99 ; H, 6.04 ; N, 5.32 %

$C_{17}H_{15}NO_2$ requires   C, 76.95 ; H, 5.70 ; N, 5.28 %

Light absorption in ethanol, maxima at 248 and 291 mμ.

(log ε 4.05 and 3.23 respectively).

2:4-Dinitrophenylhydrozone - orange plates, m.p. 277-279° (decomp.)

(from acetic acid).

Found: C, 62.33 ; H, 4.50 ; N, 15.60 %

$C_{23}H_{17}N_5O_4$ requires   C, 62.03 ; H, 4.30 ; N, 15.72%

The alkaline filtrate was acidified with dilute mineral acid and the white solid precipitate was washed with water, dried and recrystallised from ethanol to white needles, m.p. 226-227°.

Found: C, 76.84 ; H, 5.66 ; N, 5.44 %

$C_{17}H_{15}NO_2$ requires   C, 76.95 ; H, 5.70 ; N, 5.28 %

$\alpha\beta$ –Diphenylglutarimide (XXVIII).

$\alpha\beta$-Diphenylglutaric acid (55g.) was heated under reflux with acetic anhydride (25ml.) for 8 hours [1]. The excess of anhydride reagent was removed under reduced pressure and the residue was crystallised from chloroform–light petroleum giving colourless needles, m.p. 125-126°. Yield – 3.4g. This glutaric anhydride was heated to 220° and ammonia gas was bubbled through the liquid until it had all solidified at that temperature, this took 4 – 5 minutes. The solid was recrystallised from ethanol giving white needles, m.p. 228°. Yield 2.9g.

Mixed m.p. with cyclisation product 226-228°.

1:2:3:4-Tetrahydro-4-oxo-2-phenyl-1-naphthoic acid (III).

1:2:3:4-Tetrahydro-4-oxo-2-phenyl-1-naphthamide (2g.) was heated under reflux with $5\overline{N}$ aqueous sodium hydroxide solution (25ml.) and ethanol (5ml.) for 3 hours. After cooling, the solution was carefully acidified with dilute hydrochloric acid and the precipitated solid was purified by solution in sodium carbonate solution and reprecipitation. Recrystallisation from acetic acid gave pale yellow needles, m.p. 147-150°. A sample was further purified by boiling with charcoal and recrystallisation from light petroleum giving colourless needles melting at 152°.

Found: C, 76.69 ; H, 5.64 %

$C_{17}H_{14}O_3$ requires   C, 76.68 ; H, 5.31 %

2:4-Dinitrophenylhydrazone – orange needles from ethanol,

m.p. 240-242° (decomp.)

Found: C, 61.67 ; H, 3.85 ; N, 12.82 %

$C_{23}H_{18}N_4O_6$ requires   C, 61.88 ; H, 4.03 ; N, 12.55 %

3:4:10:11-Tetrahydro-3-oxo-1:2-benzofluorenone (XXVI).

1:2:3:4-Tetrahydro-4-oxo-2-phenyl-1-naphthoic acid

(800mg.) was treated with polyphosphoric acid (10g. phosphoric

anhydride and 4ml.. syrupy phosphoric acid) for 40 minutes at

100°.   A dark red colour developed, but by cooling and the

addition of crushed ice a straw-coloured solid was precipitated.

This was washed with dilute sodium carbonate solution, then

with water, dried and recrystallised from methanol giving

pale buff needles, m.p. 148-150°.

Found: C, 82.00 ; H, 5.17 %

$C_{17}H_{12}O_2$ requires   C, 82.24 ; H, 4.85 %

3-Hydroxy-1:2-benzofluorenone (VIII).

3:4:10:11-Tetrahydro-3-oxo-1:2-benzofluorenone (50mg.)

was heated under reflux in nitrobenzene (5ml.) containing a

small crystal of iodine.   After 5 minutes, the iodine was

removed by distillation with the bulk of the solvent.   The

remaining nitrobenzene was removed in a high vacuum and the dark-coloured residue was sublimed in vacuo. The sublimate recrystallised from glacial acetic acid as bright red needles, m.p. 303-307° (decomp.)

1:2:3:4-Tetrahydro-2-phenyl-1-naphthoic acid (XXV).

The keto-acid III (2g.), amalgamated zinc (5g.), water (3ml.), concentrated hydrochloric acid (7ml.) and toluene (4ml.) were heated briskly under reflux for 50 hours, concentrated hydrochloric acid (2ml.) was added every 10 hours. The separated organic layer and the ethereal extract of the aqueous layer were mixed, washed with water and dried. After recovery of the solvents, by distillation under reduced pressure, the colourless residue was recrystallised from aqueous acetic acid giving needles, m.p. 143-144°.

Found: C, 80.97 ; H, 6.29 %

$C_{17}H_{16}O_2$ requires C, 80.93 ; H, 6.39 %

2-Phenyl naphthalene.

During one of the above reductions, the mixture was boiled dry after 36 hour heating. Heating was continued for 3-4 hours at 250° and the cooled mass was extracted with benzene. Purification with charcoal, chromatography in benzene on alumina, sublimation and recrystallisation from light petroleum gave

colourless needles of 2-phenylnaphthalene, m.p. 100-101°.
Light absorption in ethanol.

Maxima at 253 and 287 **mμ** (log ϵ 4.66 and 3.98 respectively).

1:2:3:4-Tetrahydro-2-phenyl-1-naphthylacetic acid XVII).

The acid, XXV, (4g.) was dissolved in anhydrous
benzene (10ml.) and heated under reflux with excess of thionyl
chloride (5ml.) for 3 hours.   The excess of reagent and the
solvent were removed by distillation under reduced pressure.
The residual acid chloride was sufficiently pure for the next
preparation and was not purified further.   A sample was stoppered
with concentrated ammonium hydroxide solution (sp.gr. 0.88)
overnight.   The amide formed was washed with water and
recrystallised from benzene giving colourless needles with m.p.
183-184°.

Found: C, 81.05 ; H, 6.92 %

$C_{17}H_{17}NO$ requires C, 81.22 ; H, 6.81 %

The acid chloride was dissolved in ether (10ml.) and
slowly added to a stirred dry ethereal solution of diazomethane[27]
(3 mols.) at -10°.   The mixture was allowed to heat up to room
temperature and left standing overnight, after which the ether
and excess diazomethane were removed at reduced pressure.   The
residue was dissolved in anhydrous methanol (55ml.) at room

temperature and a few drops of a solution of silverbenzoate

(1g.) in triethylamide (1.1g.) were added.   Reaction occurred

and during two hours more of the solution (3.8ml.) was added.

The mixture was warmed on a water bath for a further two hours,

then boiled with charcoal and filtered.   After recovery of solvent

the residual gum was covered with 5$\overline{\mathrm{N}}$ potassium hydroxide solution

(25ml.), ethanol (1ml.) was added and the mixture heated under

reflux for 30 minutes.   The cooled solution was acidified with

dilute mineral acid giving colourless prisms, m.p. 134-136°,

from benzene-light petroleum.   Recrystallisation from

acetonitrile raised the m.p. to 136-137°.

Found:	C, 80.90 ; H, 6.64 %
$C_{18}H_{18}O_2$ requires	C, 80.87 ; H, 6.78 %

1:2:7:8:15:6-Hexahydro-2-oxochrysene (XVIII).

The homo-acid (XVII) (800 mg.) was intimately mixed

with polyphosphoric acid (10g. phosphoric anhydride and 4ml.

syrupy phosphoric acid) and heated on an oilbath at 120-130°

for 3 - 4 hours.   Water (100ml) was added to the cooled

mixture and the organic material was extracted with benzene.

The benzene layer was washed with dilute sodium carbonate solution,

then with water, dried, boiled with charcoal and filtered.

The solvent was recovered and the solid residue recrystallised

from light petroleum giving colourless rhombs, m.p. 118°.

Found: C, 86.92 ; H, 6.27 %

$C_{18}H_{16}O$ requires   C, 87.07 ; H, 6.50 %

Light absorption in ethanol.   Maxima at 253 and 294 mμ

(log ε 4.12 and 3.34 respectively).

Semicarbazone – colourless needles, m.p. 237–239° (decomp.)

from acetic acid

Found: C, 74.65 ; H, 6.07 ; N, 13.46 %

$C_{19}H_{19}N_3O$ requires   C, 74.71 ; H, 6.27 ; N, 13.76 %

Trans–1:2:7:8:15:16–hexahydrochrysene (IV).

The oxochrysene (1g.) prepared above, amalgamated zinc
(3g.), water (2ml.), concentrated hydrochloric acid (4ml.),
toluene (3ml.) and acetic acid (2 drops) were heated together
under reflux for 24 hours; concentrated hydrochloric acid (1ml.)
was added every 4 hours.   The product was purified by boiling
with charcoal in benzene, and chromatography in light petroleum
on alumina giving very pale yellow needles from petroleum ether
(40–60°), m.p. 112–114°.

Found: C, 92.25 ; H, 7.41 %

$C_{18}H_{18}$ requires   C, 92.26 ; H, 7.74 %

Light absorption in ethanol.   Maxima at 266 and 274 mμ

(log ε 3.19 and 3.01 respectively).

Chrysene

The <u>trans</u>-hexahydrochrysene (IV) was dehydrogenated by heating with selenium, following the method of Ramage and Robinson[3].

Huang-Minlon Reduction.

The keto acid (III, 250mg.) was dissolved in redistilled diethylene glycol (15ml.), 90% hydrazine hydrate (1ml.) was added and the mixture was heated at 100° for 90 minutes. Solvent (2-3ml.) was distilled off and the remaining solution was heated at 200° for 4 hours with sodium hydroxide (200mg.). The cooled mixture was poured into water (30ml.) giving a milky suspension from which a white crystalline precipitate deposited. Recrystallisation from aqueous ethanol gave needles, m.p. $119-120^{\circ}$.

Found:	C, 80.86 ; H, 6.69 ; N, 12.61 %
$C_{16}H_{16}N_2$ requires	C, 81.32 ; H, 6.83 ; N, 11.86 %

2:4-Dinitrophenylhydrazone - orange-red needles, m.p. $238-239^{\circ}$ from benzene.

Found:	C, 65.64 ; H, 4.73 ; N, 13.80 %
$C_{22}H_{18}N_4O_4$ requires	C, 65.66 ; H, 4.51 ; N, 13.93 %

SUMMARY.

A new synthesis of chrysene is described.   This starts from ɣ -cyano-βɣ -diphenylbutyric acid and proceeds by standard methods through 1:2:3:4-tetrahydro-4-oxo-2-phenyl-1-naphthoic acid and 1:2:3:4-tetrahydro-2-phenyl-1-naphthylacetic acid, to trans-derivatives of hexahydrochrysene and hence to chrysene itself.

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Part Two:-   A New Synthesis of Phenanthridines.


CONTENTS.

<u>INTRODUCTION</u>.

The chemistry of the seven-membered heterocyclic ring systems containing one nitrogen and one sulphur atom has not as yet been the subject of much attention.   Indeed, the parent thiazepines, of which there could be three structural isomers (I, II and III), have not been described.
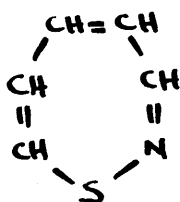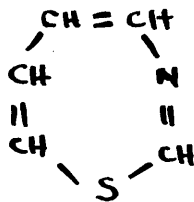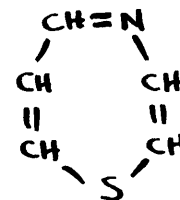

I II III

A few isolated examples of sulphur-containing seven membered cyclic lactams, which could be classed as derivatives of II or III, have been reported [1, 2, 3, 4], and a benzothiazepine derivative (IV) has been reported by Mayer and Horst [5].
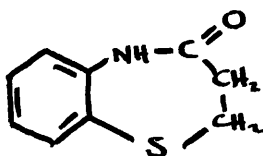
IV

Summers [6] describes the synthesis of dibenzo(b,f)-

oxepin (V), some of its derivatives and, – of more interest

here – representatives of the corresponding thia-system, dibenzo

(b,f)thiapin (VI).
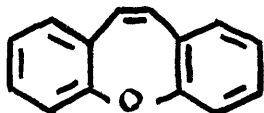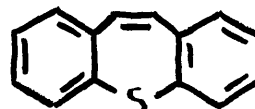
$$\underline{V} \qquad\qquad \underline{VI}$$

He reports the extrusion of the thia-atom when a substituted

dibenzothiepin was heated to a relatively high temperature

with copper.   This occurred during attempted decarboxylation

of the dibenzothiepin carboxylic acid (VII) by heating with

copper in quinoline.   The product was 7-methyl-2-nitro-

phenanthrene (IX), and not the expected dibenzothiepin (VIII).

$$\underline{VII} \qquad\qquad \underline{IX}$$
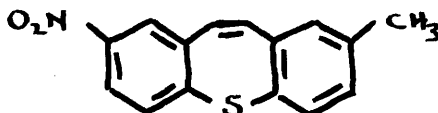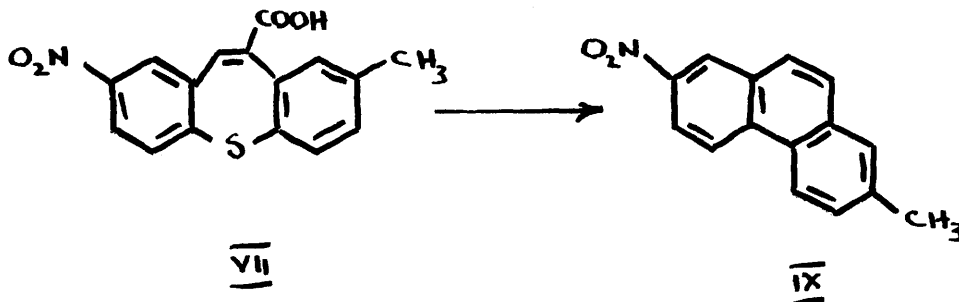
$$\underline{VIII}$$

Examples of a similar extrusion of sulphur from a cyclic sulphide have been reported.

$$C-S-C \qquad C-C$$

It was claimed by Ferrario [7], that dibenzofuran (XI) is formed by heating phenoxthin (X) with copper metal at 250°. However, later workers [8, 9] have been unable to repeat this work, despite the extension of temperature range and the use of metals other than copper. However, Ferrario's claim has some analogy in the conversion of thianthrene (XII) into dibenzothiophene (XIII), a reaction which is well substantiated (10, 11).
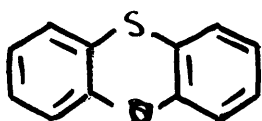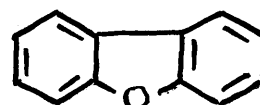
$$\overline{X} \qquad\qquad \overline{XI}$$
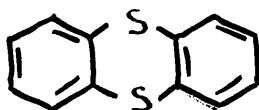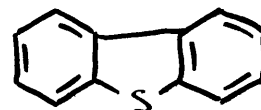
$$\overline{XII} \qquad\qquad \overline{XIII}$$

The original example of sulphur extrusion effected
by copper is provided by Ris [12]. He prepared
3:4:5:6-dibenzocarbazole (XV) from the corresponding
dibenzophenothiazine (XIV). This was followed by the preparation
[13] of the parent carbazole (XVII) from phenothiazine (XVI)
and of 1:2-benzocarbazole (XIX) [14] from the heterocycle (XVIII).
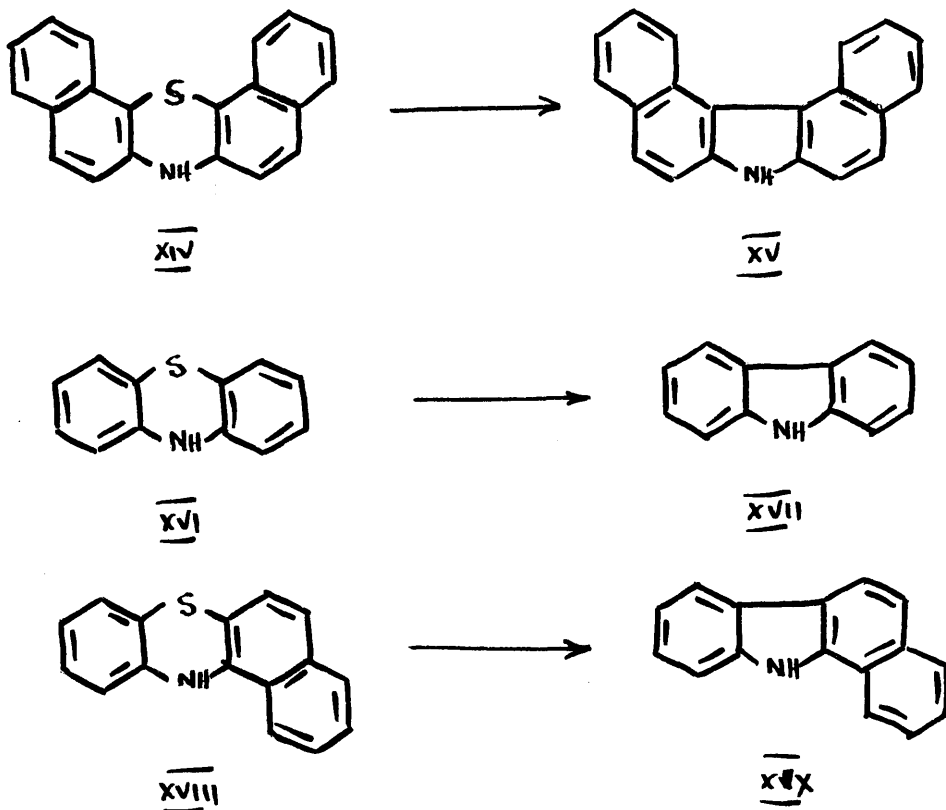
Since this early work relatively little information
on the topic has accrued. Certainly, this type of reaction
has not been the subject of systematic inquiry. However, a

few isolated examples give an indication of the potentialities

of sulphur extrusion as a synthetic tool.

For instance Groth [15] describes the removal of

both sulphur atoms from the disulphide (XX) giving the

dibenzoylated hydrocarbon (XXI).

$$PhCOCH_2S$$
$$|$$
$$PhCOCH_2S$$

$$PhCOCH_2$$
$$|$$
$$PhCOCH_2$$

$$\overline{XX}$$

$$\overline{XXI}$$
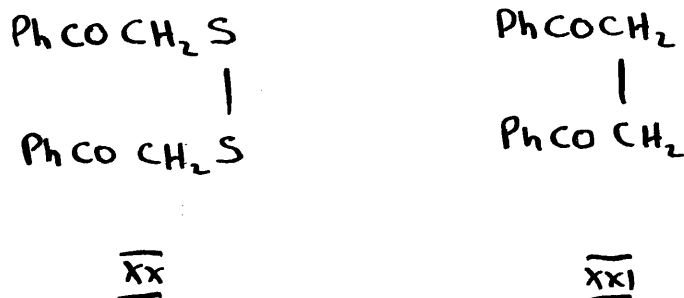
Schonberg and Vargha [16] found that gentle heating

of an episulphide (XXII) afforded the substituted ethylene

(XXIII).   In this reaction, it is said that the presence of

copper facilitates thia-extrusion.

$$\begin{array}{c} Ar \\ \diagdown \\ \diagup \\ Ar \end{array} C = S \longrightarrow \left[\begin{array}{cc} Ar \diagdown & \diagup Ar \\ C & \!\!\!\!-\!\!\!\! C \\ Ar \diagup | & | \diagdown Ar \\ SH & SH \end{array} \right]$$

$$\longrightarrow Ar_2C - CAr_2 \longrightarrow Ar_2C = CAr_2$$
$$\diagdown S \diagup$$

$$\overline{XXII}$$

$$\overline{XXIII}$$
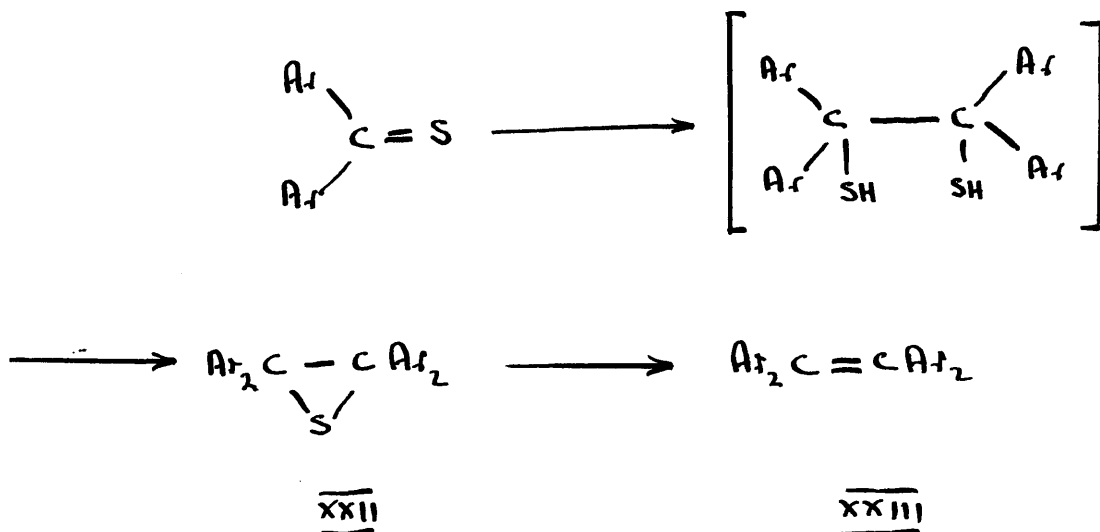
More recently Parham and Traynelis [17, 18] have
shown that it is possible to convert 2:5-diphenyl-1:4-dithiin
(XXIV) into 2:4-diphenylthiophene (XXV) by heating it to 190°.
In this reaction elemental sulphur is produced and the workers
postulate the formation of an episulphide intermediate.
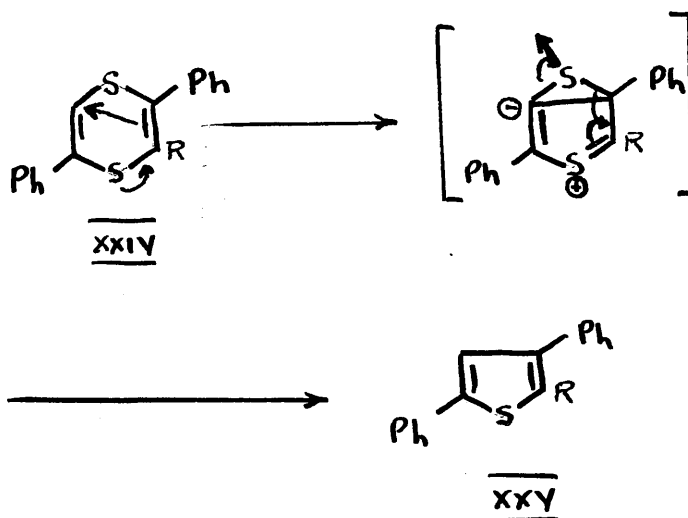
It was found that R = NO_2 or R = CHO facilitated the
extrusion.   In this case copper was not required.

Bordwell and various collaborators have carried out
work involving the removal of sulphur.   With Andersen and Pitt[19]
he prepared thiophenols using aryl lithium compounds in reactions
of the type shown below.

$$ArLi + CH_2{-}CHCH_3 \longrightarrow ArSLi + CH_2{=}CHCH_3$$
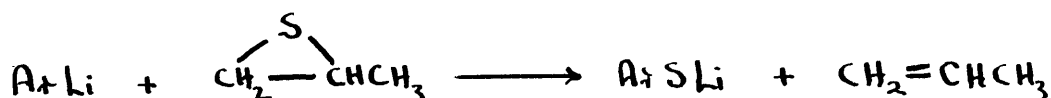
The same worker, with Cooper [20] had previously shown that the group $-SO_2-$ was removable from a cyclic sulphone. This was illustrated by the preparation of n-but-2-ene (XXVI) as shown.

$$\begin{array}{ccc}
\overset{\displaystyle CH_3}{\underset{\displaystyle CH_2\ SO_2}{|}} \quad \overset{\displaystyle CH_3}{\underset{\displaystyle CH}{|}} & \longrightarrow & \overset{\displaystyle CH_3}{\underset{\displaystyle CH}{|}} - \overset{\displaystyle CH_3}{\underset{\displaystyle CH}{|}} \\
& & \diagdown SO_2 \diagup
\end{array} \longrightarrow \quad \overset{\displaystyle CH_3}{\underset{\displaystyle CH}{|}} = \overset{\displaystyle CH_3}{\underset{\displaystyle CH}{|}}$$
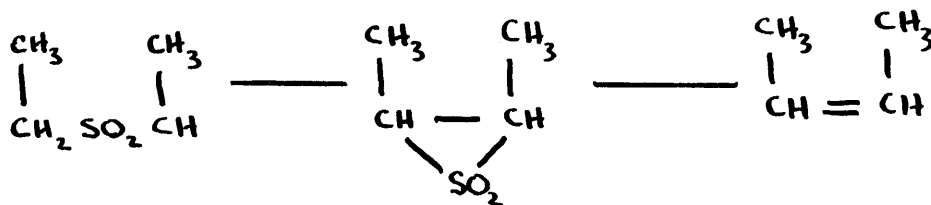
A further example of sulphur removal involving an episulphide intermediate is given by Knott [21] in the following proposed reaction scheme.
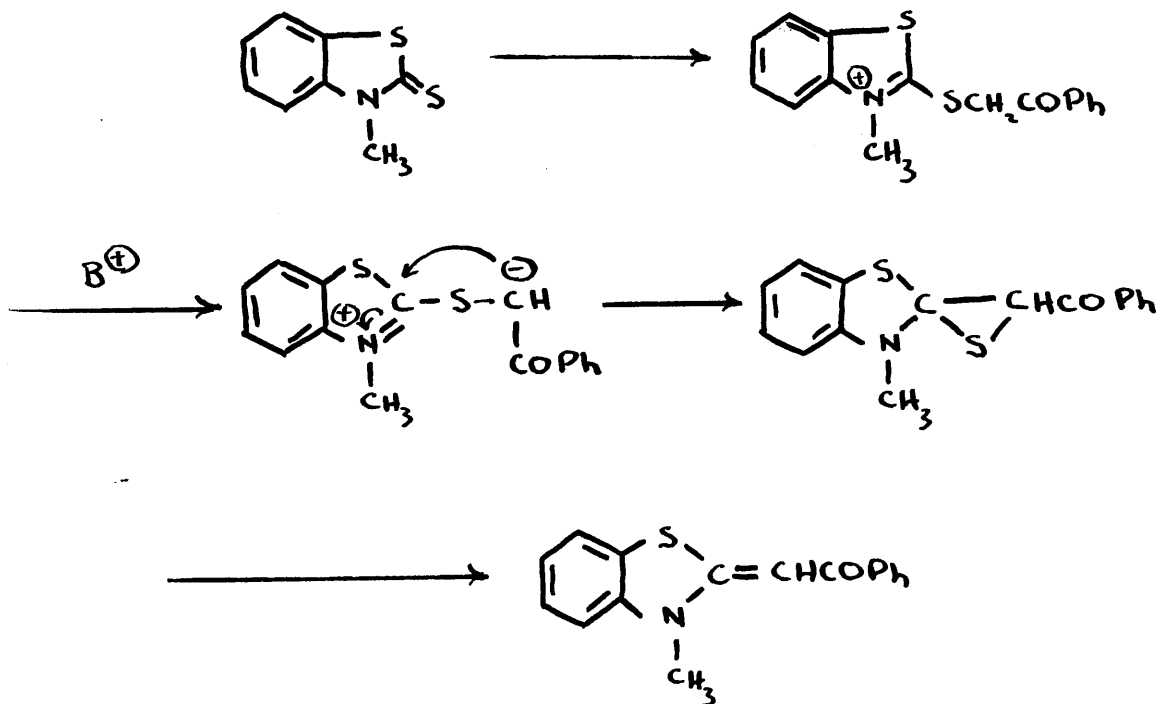
It was inferred from the phenanthrene synthesis of Summers [6] that removal of the sulphur-atom from a dibenzo(b,f)(1,4)thiazepine (XXVII) might provide a synthetic route to phenanthridines (XXVIII), a class of rather inaccessible compounds.
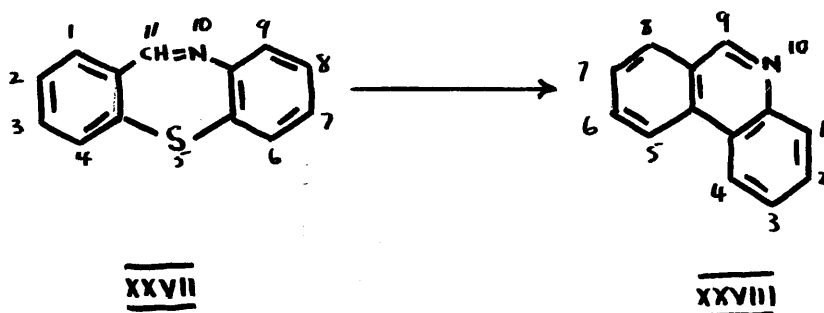
XXVII   **XXVIII**

Whilst the main object of the work to be described is the preparation of compounds of type (XXVII and XXVIII) desulphurisation of a few miscellaneous thia-heterocyclic systems will be examined.

DISCUSSION.

All dibenzothiazepines discussed in this work
are dibenzo(b,f)(1,4)thiazepines, hereafter named simply
"dibenzothiazepines".

Preparation of dibenzothiazepines.

Compounds of this class were unknown but proved
to be preparable through condensation of sodium o-aminothiophenate
with 2-halogeno-5-nitrophenyl ketones or aldehydes.   Thus,
2-chloro-5-nitrobenzophenone (XXIX) was condensed with the
thiophenate yielding 2-nitro-11-phenyldibenzothiazepine (XXX).
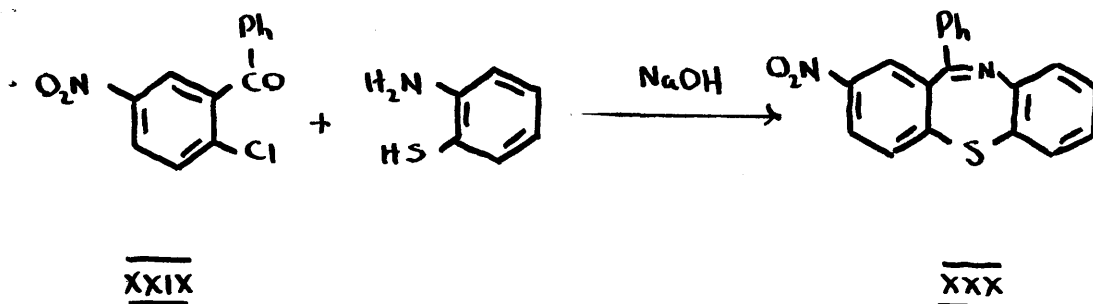
This was the ultimate condensation product, but a considerable
amount of an intermediate 2-(o-aminothiophenoxy)-5-nitrobenzo-
phenone (XXXI) was also formed.   Fortunately, this intermediate
was readily cyclised, affording compound (XXX), when dissolved in

hot acetic acid or heated in alcohol with a trace of alkali.
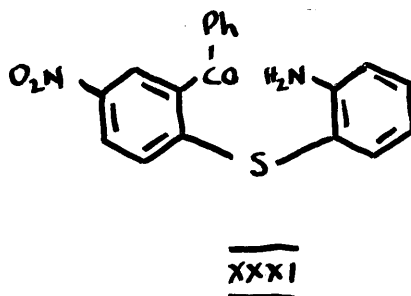
$$\underline{\textbf{XXXI}}$$

<u>o</u>-Aminothiophenol was condensed with 2-chloro-3:5-dinitrobenzophenone (XXXII), with 2-bromo-5-nitroacetophenone (XXXIV), with 2-chloro-3':5-dinitrobenzophenone (XXXVI), and with 2-chloro-5-nitrobenzaldehyde (XXXVIII) affording respectively 2:4-dinitro-11-phenyldibenzothiazepine (XXXIII), 2-nitro-11-methyldibenzo-thiazepine (XXXV), 2-nitro-11-(<u>m</u>-nitrophenyl)-dibenzothiazepine (XXXVII), and 2-nitrodibenzothiazepine (XXXIX) as shown.

XXXVI + H₂N ⟶ XXXVII

XXXVIII + ⟶ XXXIX
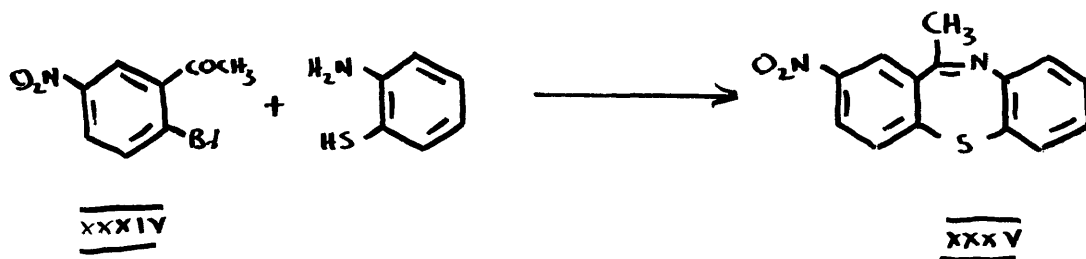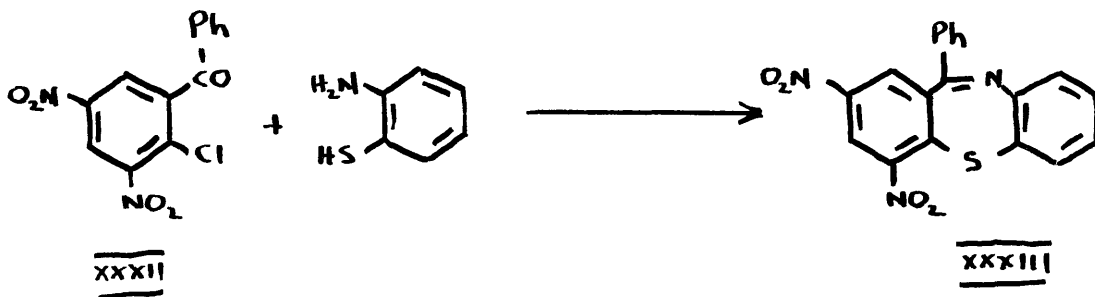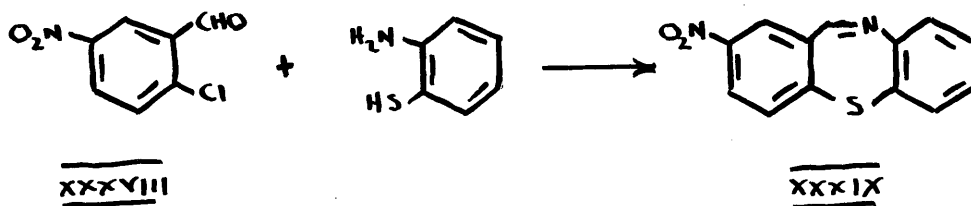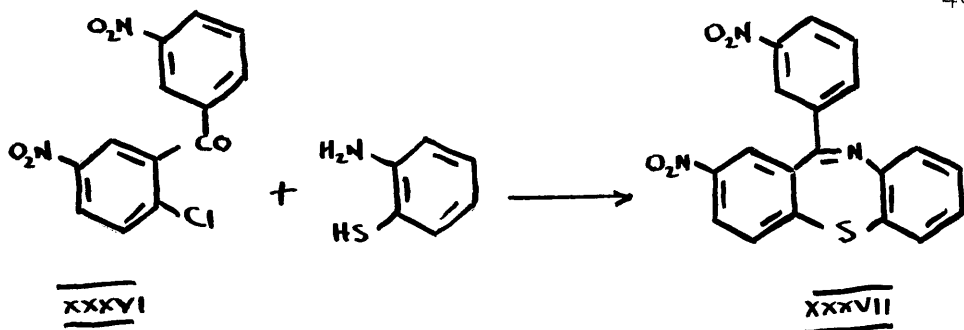
In no instance was the intermediate sulphide
(c.f. XXXI) isolated by design.   However, 2-bromo-5-nitro-
acetophenone gave a sulphide (XL) as a remarkably stable
condensation product.   This sulphide resisted cyclisation
under the influence of boiling acetic anhydride, being
acetylated thereby.   Formation of the dibenzothiazepine
(XXXV) required treatment of the amino-sulphide (XL) with
hot polyphosphoric acid

XL
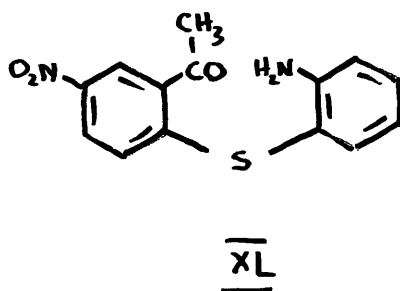
In all but one case the dibenzothiazepine was the only final product.   The exception was found in the condensation of 2-chloro-3:5-dinitrobenzophenone (XXXII), which yielded two products.   This will be discussed later, (p. 49).

The effect of using a sulphonate in place of the reactive halogen substituent in (XXXVIII)was examined. 5-Nitrosalicylaldehyde (XLI) was converted into its toluene-p-sulphonic ester (XLII), and this in turn into the corresponding pyridinium salt (XLIII) as described by Allan and Loudon [22]. This salt was condensed with o-aminothiophenol in pyridine affording the previously prepared 2-nitrodibenzothiazepine (XXXIX).   It was also shown, using the same quaternary salt that other thiophenols would condense in the same way, e.g. the known 2-formyl-4-nitro-4'-methyldiphenyl sulphide (XLIV) was formed from thio-p-cresol in reaction with the quaternary salt.

3:5-Dinitrosalicylaldehyde (XLV) gave a moderate yield of 2:4-dinitrodibenzothiazepine (XLVI) under the same reaction.conditions.   In this condensation a second compound was formed but was not crystalline.

XLI → XLII

XLIII

XXXIX

XLIV

XLV → XLVI
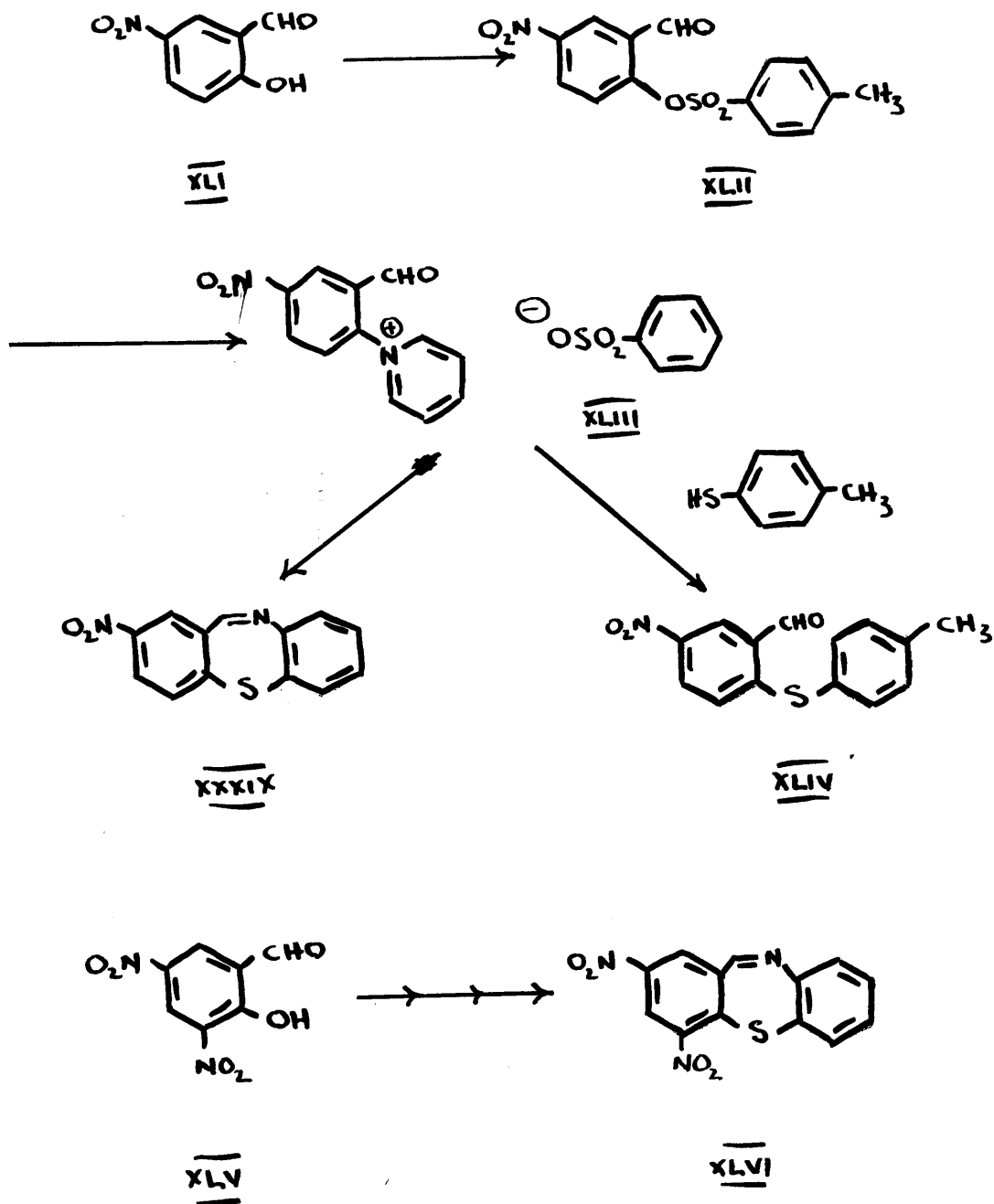
However, 3-nitrosalicylaldehyde (XLVII) did not give

the expected 4-nitrodibenzothiazepine (XLVIII). The aldehyde

was treated with toluene-p-sulphonyl chloride in pyridine in the

same manner as with the 5-nitro isomer, but formation of the

pyridinium quaternary salt from the tosyl-ester required

heating at 100° for an hour, before a test drop remained clear

on being added to water, thus indicating salt formation.

Treatment of the quaternary salt with o-aminothiophenol

in pyridine yielded a crystalline product, with constant

analyses, to which, however, no likely empirical formula could

be fitted. The lack of definition in the ultraviolet

absorption spectrum of this product suggests that it may

not be a single compound.
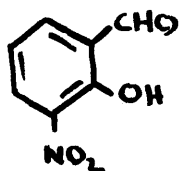
XLVII
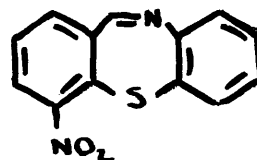
XLVIII

It was noted previously that condensation of

2-chloro-3:5-dinitrobenzophenone (XXXII) with o-aminothiophenol

gave two products. One was the dibenzothiazepine, the other,

a bright red crystalline solid, which was shown to contain a

single nitro-group. It is known that a mercapto-group in a

suitable environment can displace a nitro-group, with

elimination of nitrous acid.   An example of this is seen

in the formation of 1:3-dinitrophenothiazine (XLIX) from

picryl chloride and o-aminothiophenol.   The intermediate in

this reaction is probably a diphenyl sulphide (L), which

undergoes a Smiles rearrangement in alkaline solution,

followed by condensation with elimination of nitrous acid.

L

XLIX
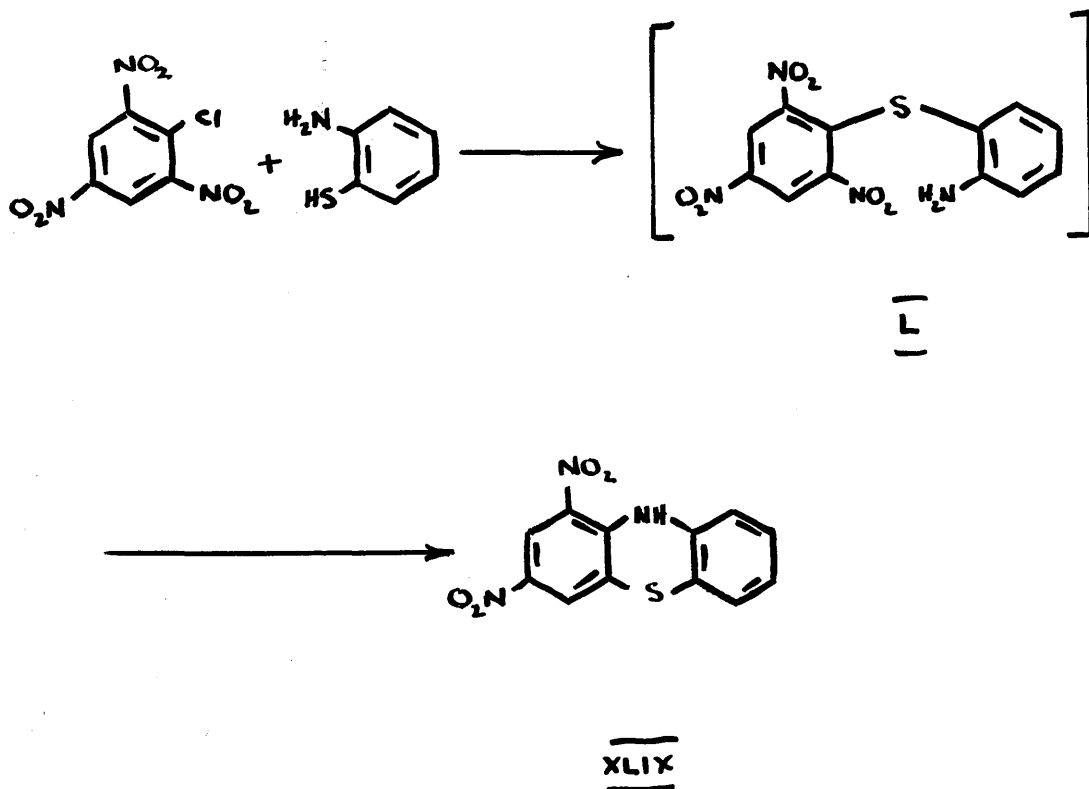
Oxidation of this compound by hydrogen peroxide in

acetic acid gave the S-dioxide derivative (LII).   By

analogy, the red product obtained from 2-chloro-3:5-dinitro-

benzophenone (XXXII) is considered to be 1-benzoyl-3-nitro-

phenothiazine (LI).
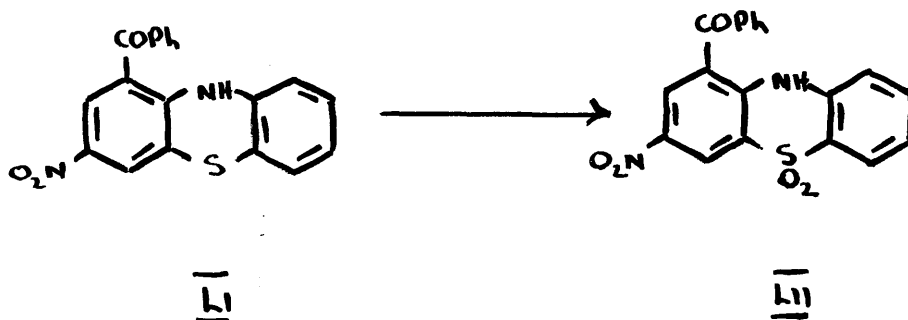
The possible displacement of a nitro-group in

2:4-dinitrobenzaldehyde by a mercaptide suggested a further

probable synthesis of dibenzothiazepines.   Hence 2:4-dinitro-

benzaldehyde was treated with o-aminothiophenol in alkaline

solution.   However, the crystalline product, formed in good

yield, did not have the expected empirical formula.   Instead, it

was thought to be the anil (LIII).   This anil, a red solid

which afforded a yellow solution in benzene or ethanol, was

readily acetylated with acetic anhydride and was oxidised to

the benzothiazole (LIV) by warming with excess ferric chloride

or sodium hydroxide in alcoholic solution, or by dissolution

in hot pyridine .   This is in agreement with the work of

Lankelma and Sharnhoff[23, 24] who prepared benzothiazoles

by condensation of thiophenols with aldehydes or ketones
in pyridine. Oxidation of the anil by an aqueous alcoholic
solution of iodine/potassium iodide gave the disulphide (LV).
This was identified by comparison of m.ps. and infrared
absorption spectra with those of a sample prepared by
condensing 2:4-dinitrobenzaldehyde with 2:2'-diamino diphenyl
disulphide.

The benzothiazole (LIV) was also prepared by the
reaction of 2:4-dinitrobenzaldehyde with the zinc salt of
o-aminothiophenol in glacial acetic acid and passing hydrogen
sulphide, using the method of Bogert and Stull [25] for the
preparation of 2-phenylbenzothiazole (LVI). Bogert and
Stull's product was prepared for a spectral comparison with
its dinitro-derivative (LIV). Since this last benzothiazole
preparation is so similar to the original reaction, it was
decided to use the benzothiazole synthesis of Bogert and
Snell [26] from acid chlorides in reaction with the zinc salt
of o-aminothiophenol. This was carried out using 2:4-dinitro-
benzoyl chloride and afforded the same product (LIV).
Identification was established by direct comparison of m.p.,
mixed m.p. and infrared absorption spectra. The infrared
absorption spectrum of 2-phenylbenzothiazole (LVI) exhibits
points of similarity to that of its dinitro derivative.

LIII
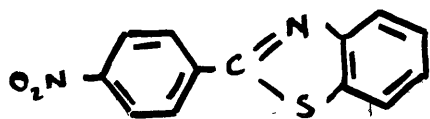
LIV
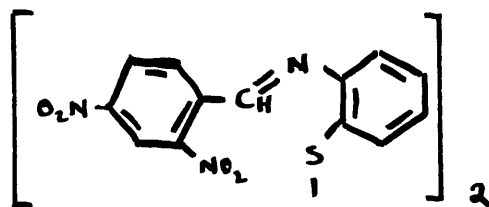
LV
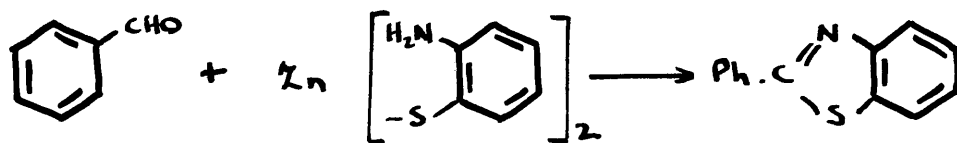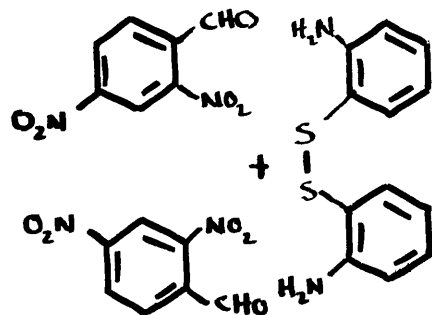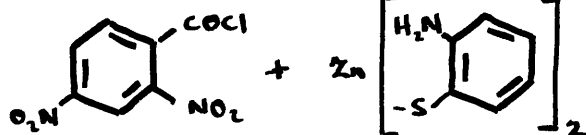
LVI

Reactions of Dibenzothiazepines.

The most important reaction of dibenzothiazepines which was investigated was that involving desulphurisation with copper to give the aromatic phenanthridine nucleus.

2-Nitro-11-phenyldibenzothiazepine (XXX) was mixed with dry copper bronze and heated in an atmosphere of nitrogen. It was found that at the high temperature of 280-290° reaction took place, releasing a cloud of finely powdered sublimate. This was shown to be 7-nitro-9-phenylphenanthridine (LVII), but the yield was very poor. Several variations of this method were tried using precipitated copper or copper bronze. Distillation or sublimation through copper gauze was also tried. All the variants were unsatisfactory in that the only tractable products were in the initial cloud of sublimate, no crystalline material being isolated from the residual charred mass, which

was always formed. To prevent this charring a solvent was introduced. The choice of solvent was limited by the requirements of inertness and stability at the high temperature necessary for the reaction. A solvent which satisfies these conditions is diethyl phthalate.

By heating a solution of a dibenzothiazepine in diethyl phthalate under reflux with copper bronze for a short period (4 - 7 minutes) high yields of the corresponding phenanthridine were obtained. By this means the following compounds were prepared:- 7-nitrophenanthridine (LVIII) from 2-nitrodibenzothiazepine (XXXIX), 7-nitro-9-(m-nitrophenyl) phenanthridine (LIX) from 2-nitro-11-(m-nitrophenyl)dibenzo-thiazepine (XXXVII) and 7-nitro-9-methylphenanthridine (LX), from 2-nitro-11-methyldibenzothiazepine (XXXV).

By direct comparison (of m.ps. and infrared absorption spectra)with authentic specimens, which were kindly supplied by Dr. Walls, the identities of the compounds (LIX and LX) were completely established.

Only the phenanthridines (LVII and LVIII) had been obtained by heating with dry copper bronze, and then in very poor yield, but using a solvent, they were all obtained in moderate or good yields.

It may be significant that neither 2:4-dinitro-dibenzothiazepine (XLIX) nor 2:4-dinitro-11-phenyldibenzothiazepine (XXXIII) yielded a phenanthridine by this method;   However, insufficient work has been carried out to warrant the proposal of any theory or reason for this.
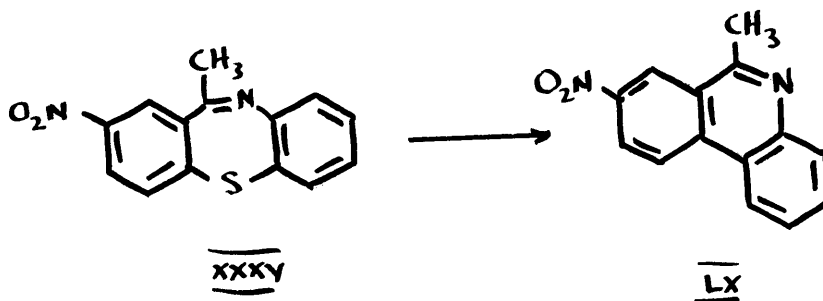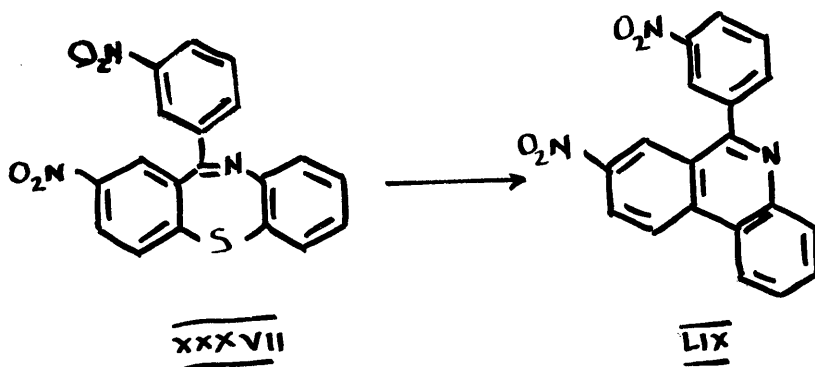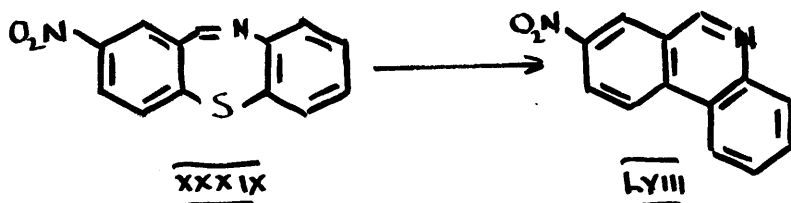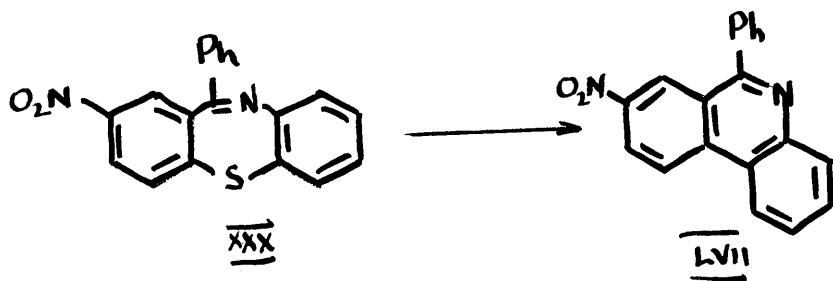
2-Nitro-11-phenyldibenzothiazepine (XXX) was
oxidised by hydrogen peroxide in acetic acid to a crystalline
product, which was distinct from the starting material, but
which was still desulphurised almost quantitatively to
2-nitro-11-phenylphenanthridine when heated with copper
in diethyl phthalate.   Analyses suggest that the new compound
is either the S-oxide or the N-oxide of the dibenzothiazepine.
From spectroscopic evidence it is considered to be the amine-oxide
(LXI).   This hypothesis is supported by the oxidation of
7-nitro-9-phenylphenanthridine (LVII) to its N-oxide by
hydrogen peroxide in acetic acid;   and subsequent regeneration
of the phenanthridine, by heating the oxide with copper in
diethyl phthalate.

Further oxidation of the thiazepine oxide, or longer
oxidation of the dibenzothiazepine (XXX) gave 2-benzoyl-4:2'-
dinitrodiphenyl sulphone (LXII).   The identity of this unexpected
product was indicated by analysis and by cleavage of the compound
with piperidine to the known 2-piperidino-5-nitrobenzophenone
(LXIII) and o-nitrobenzene sulphinic acid (LXIV).   This
acid was identified after conversion into the more easily
recognised o-nitrobenzene sulphonamide (LXV).   Final confirmation
of the structure (LXII) was obtained by mixed m.p. and spectral
comparison with a sample synthesised by oxidation of the sulphide
(LXVI) which in turn was prepared from o-nitrothiophenol and

2-chloro-5-nitrobenzophenone.
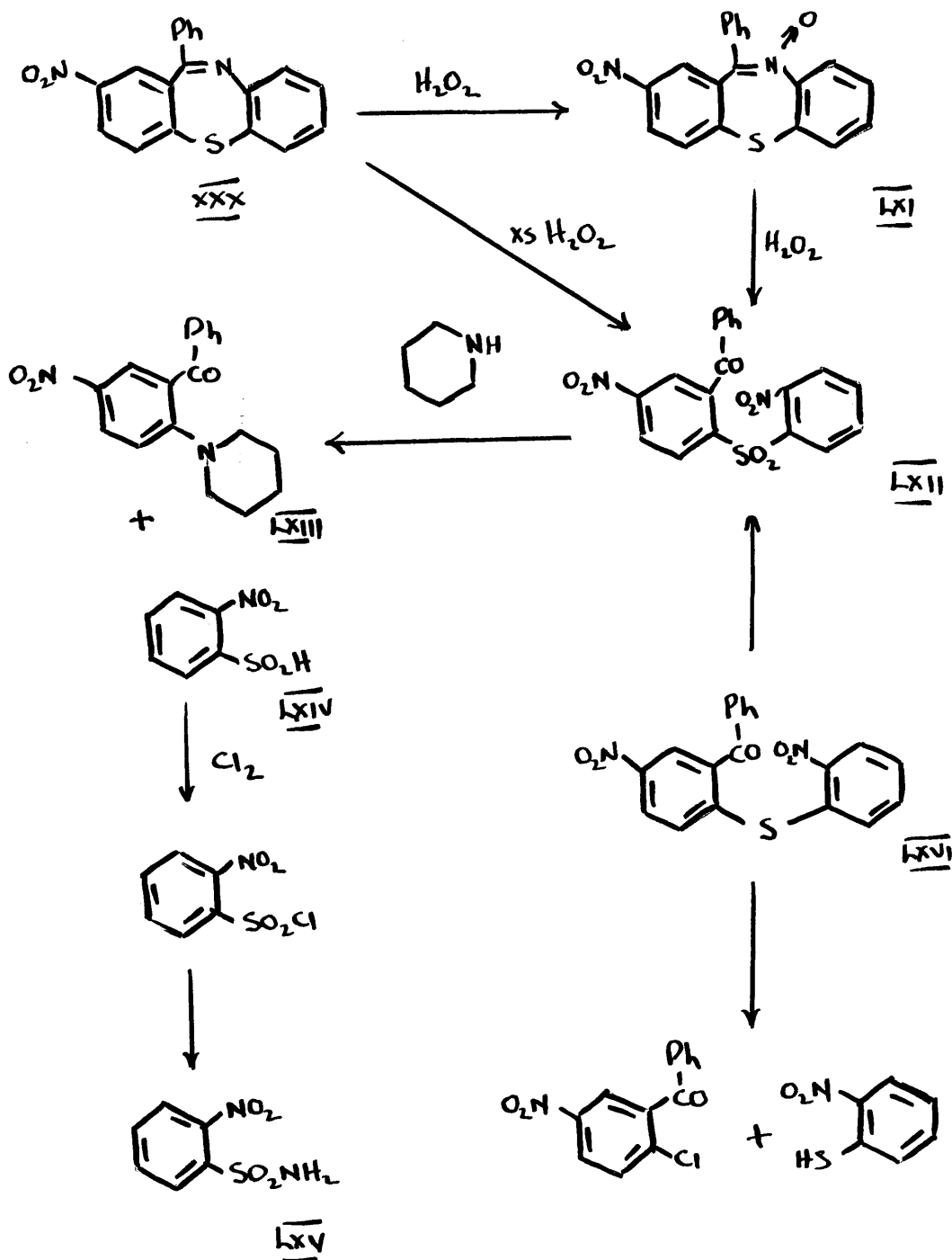
This oxidation of the thiazepine ring, although unusual, may be compared with the findings of Kosuge and Miyashita [27], who oxidised quinoline to o-nitrobenzoic acid via the amine-oxide.
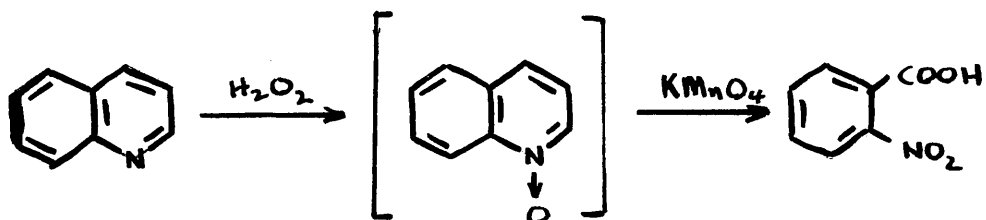
7-Nitro-9-methylphenanthridine (LX) was oxidised by sodium dichromate in acetic acid to give 7-nitrophenanthridone (LXVII).
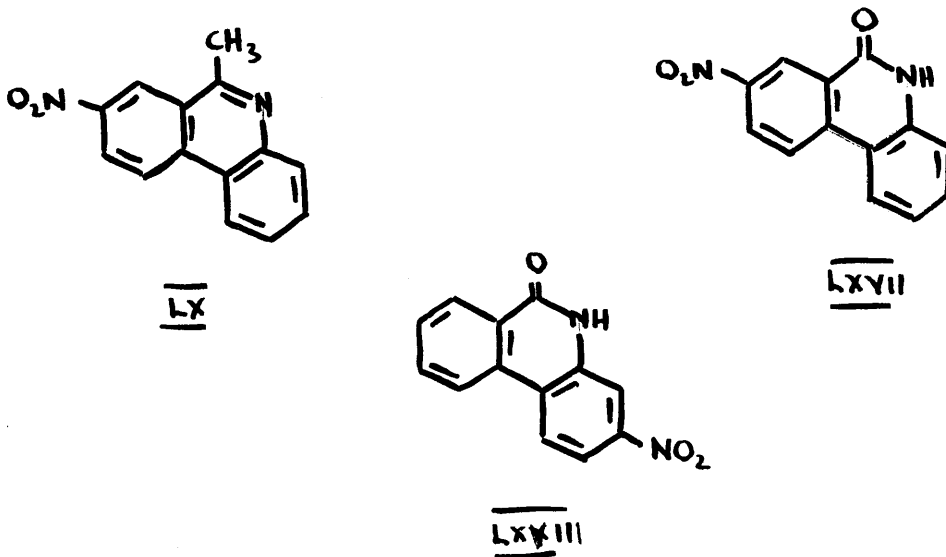
7-Nitrophenanthridine and its 9-methyl derivative,
when oxidised by sodium dichromate in acetic acid, each
afforded the same product, 7-nitrophenanthridone (LXVII).
Further oxidation of the phenanthridone yielded 4-nitrophthalic
acid and/or oxalic acid, but no phthalic acid.   These results
are consistent with the structures assigned ~~(LXXIII)~~ (LX) and
(LXVII), but until recently characterisation of the phenanthridone
(LXVII) was the subject of error.   The present product had
m.p. 324-326° in good agreement with recent values and in
contrast to the value (m.p. 284-287°) reported for the compound
by Moore and Huntress.   These authors considered that they had
prepared a homogeneous specimen of the phenanthridone by
Beckmann rearrangement of 2-nitrofluorenone oxime.   Nunn
Scholfield and Theobald [28], however, conclude that the
material, m.p. 284-287°, is really a mixture (or complex)
of 2- and 7-nitrophenanthridones (LXVII + LXVIII)   Confirmation of this was
obtained in the present work by oxidising material prepared as
described by Moore and Huntress [30]:   phthalic and
4-nitrophthalic acids were identified in the products.   A
quantitative method for identifying these acids, in small
quantities and in admixture with each other or with oxalic acid,
is described in the Experimental Section (p. 80).

Miscellaneous Sulphur Compounds.

In order to testdesulphurisation by means of

copper in a wider field, certain preliminary experiments were

carried out with various sulphur containing heterocyclic

compounds.

Phenoxthin (X) was heated with copper in diethyl

phthalate under reflux for periods up to a week, but in all

cases only starting material was recovered.

The red phenothiazine (LI), prepared by the method

described earlier, was heated with copper in diethyl phthalate,

but once again the only crystalline product was returned

starting material.

Following this 2-nitrophenothiazine (LXX) and

2:4-dinitrophenothiazine (XLIX) were prepared by the

condensation of o-aminothiophenol with 2:6-dinitrochlorobenzene

(LXIX) and picryl chloride respectively. These compounds were

also recovered unchanged after being heated with copper in

diethyl phthalate.

The substituted thioxanthone (LXXI, R = OCH_3) and

thioxanthen (LXXII, R = OCH_3) were prepared by the method of

Campbell, Dick, Ferguson and Loudon [31] for the preparation

of corresponding compounds (R = CH_3).

Recovery of starting material when either of these compounds (LXXI and LXXII, R = OCH_3) was heated with copper in diethyl phthalate served to confirm the findings of Lockhart[32] who failed to extrude the thia-atom from the products of Campbell et al.

X

LI

LXX

XLIX

LXXI

LXXII

LOG ε

WAVELENGTH (mμ)
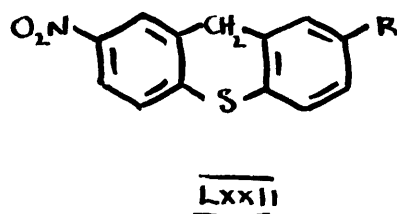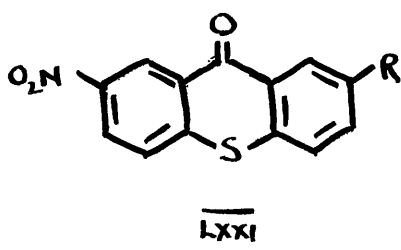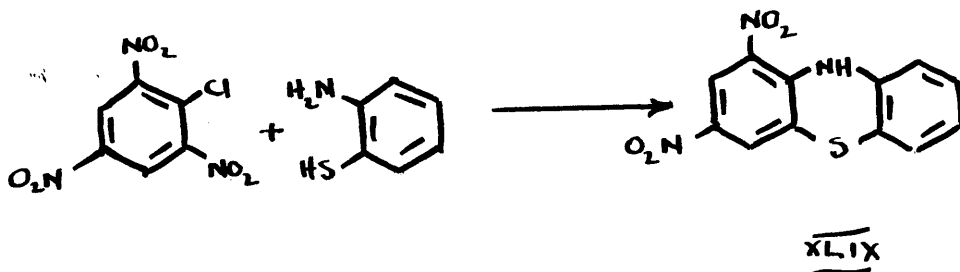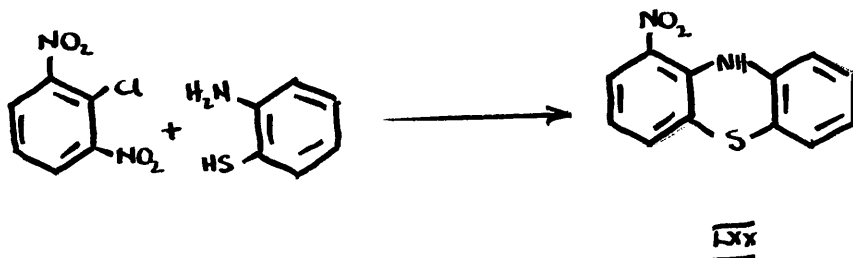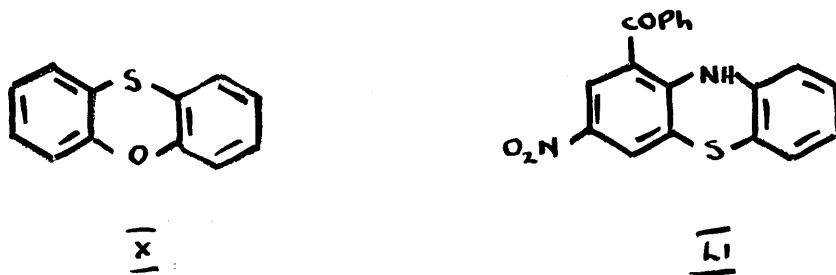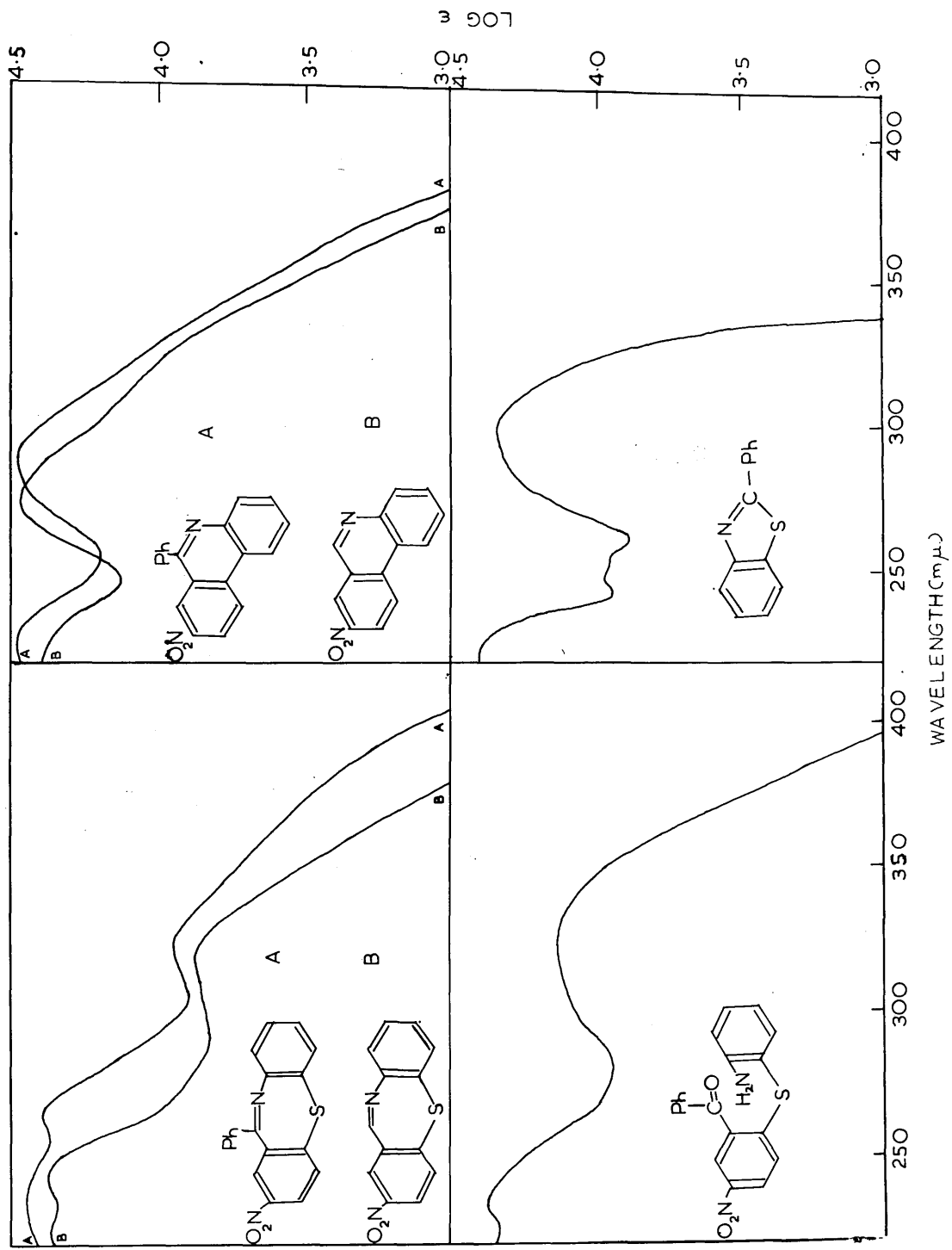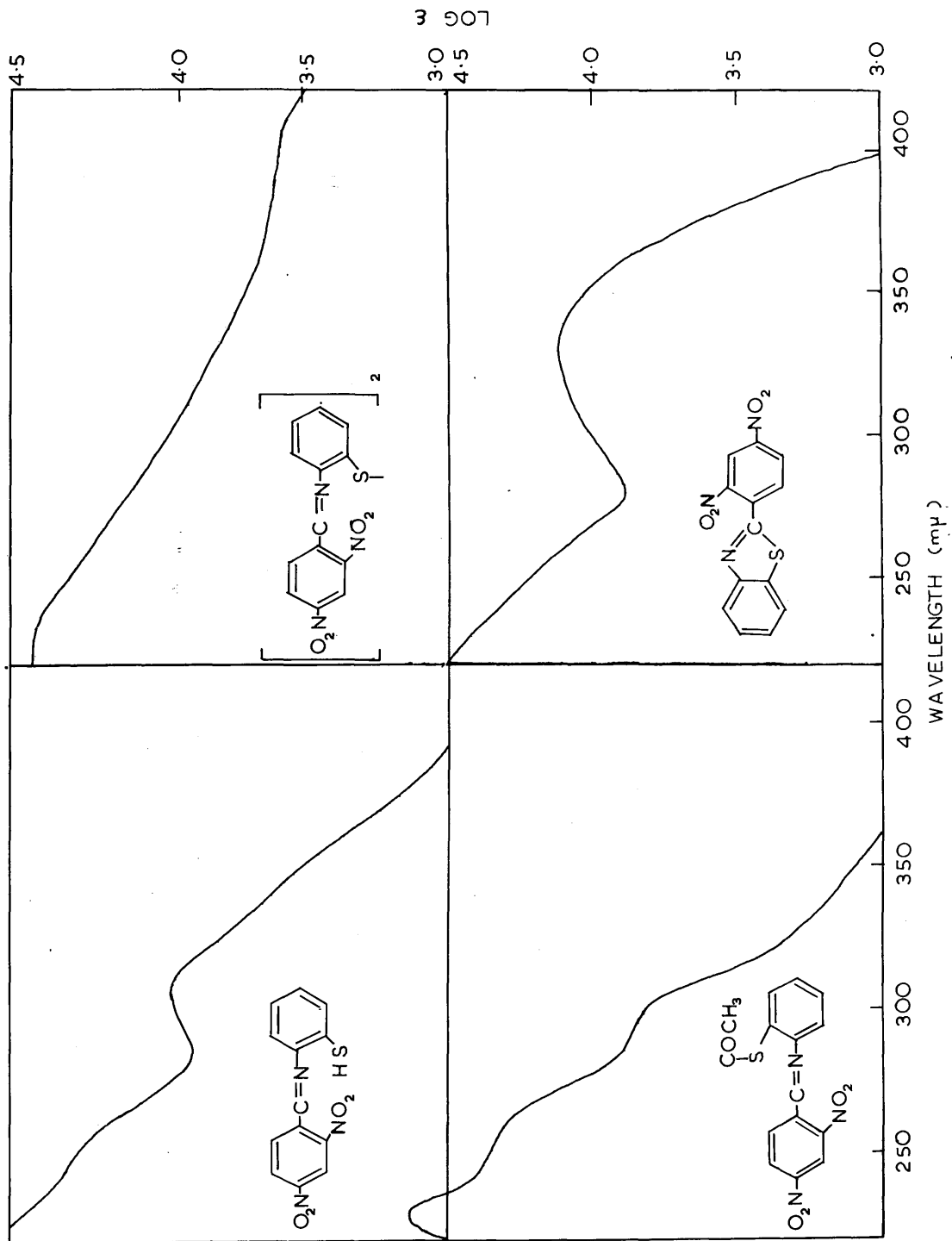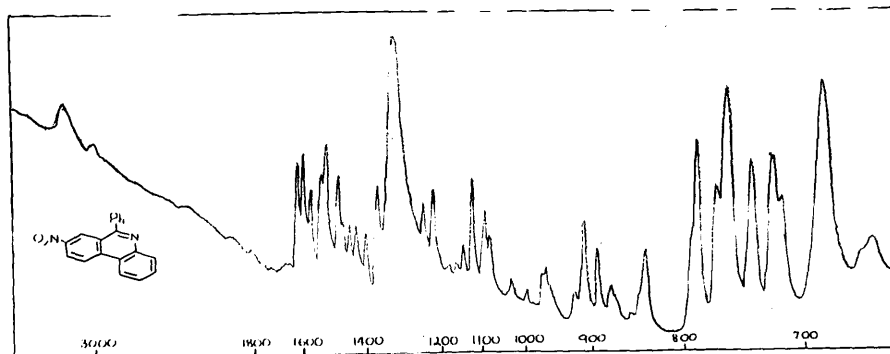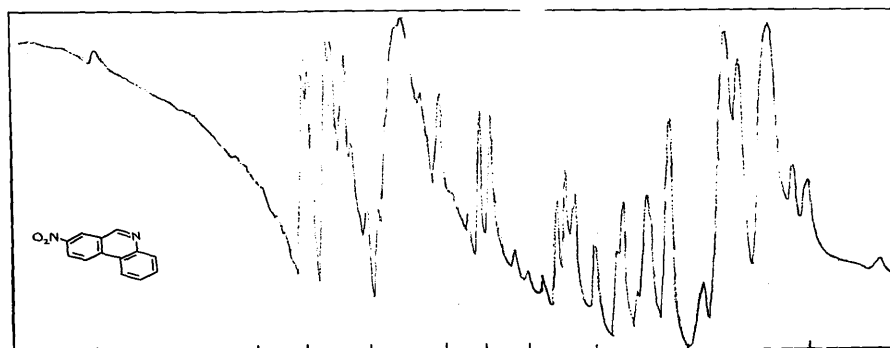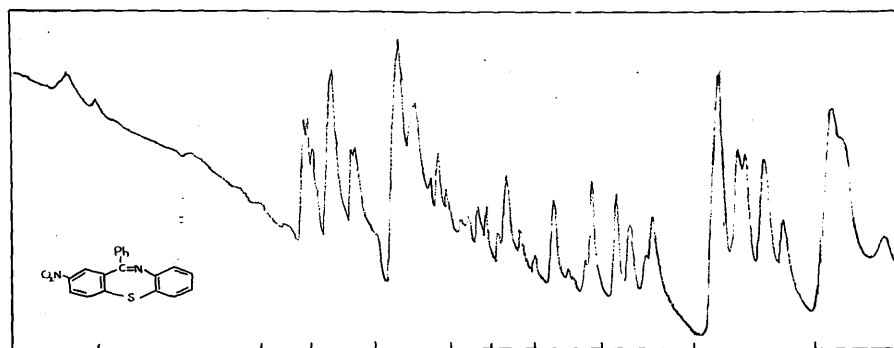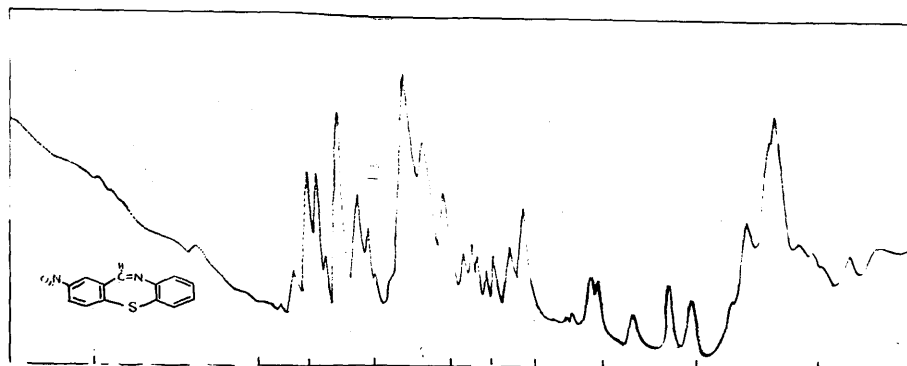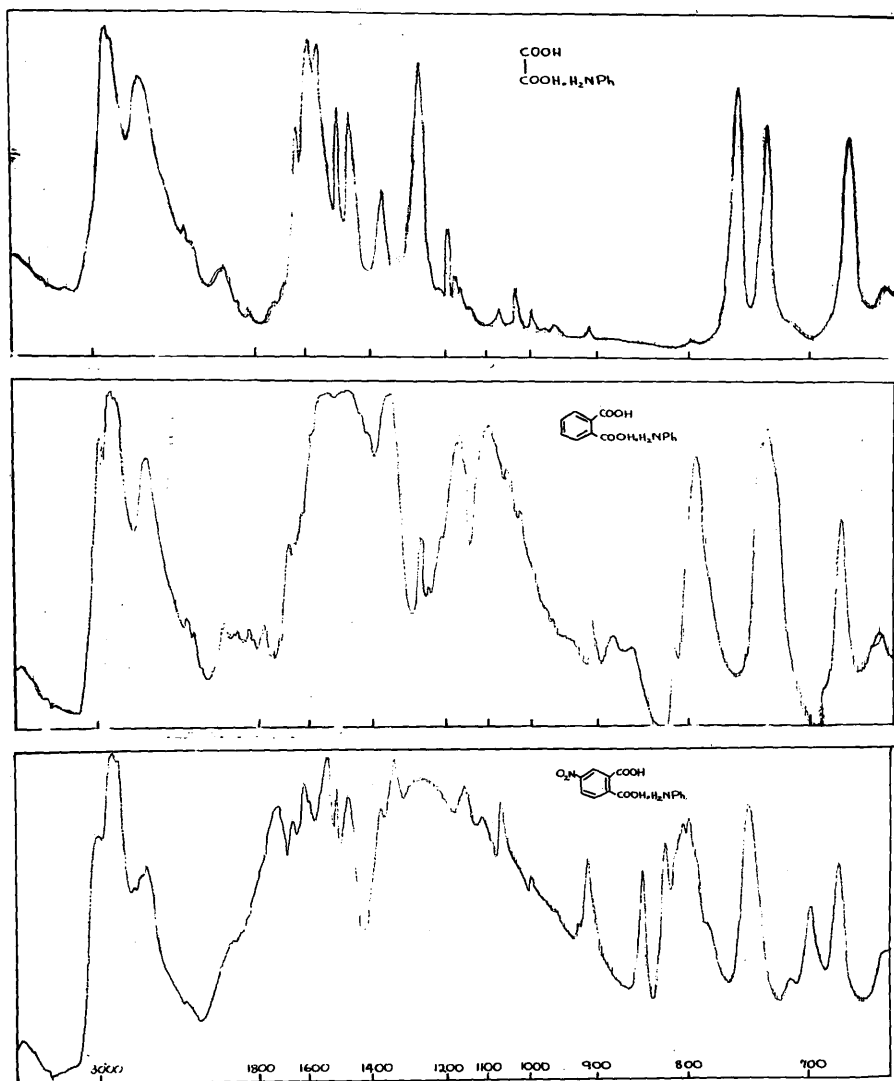
EXPERIMENTAL.

All light absorption data reported in this section were measured in rectified spirits.

o-Aminothiophenol Hydrochloride.

Di-(o-nitrophenyl) disulphide was prepared by the method of Bogert and Stull [33]. This disulphide (300g.) was suspended in glacial acetic acid (1500ml). To this stirred suspension portions of zinc (5g) and concentrated hydrochloric acid (10-12ml.) were added alternately so that the acetic acid never quite boiled, external cooling was used when required. In all, 500g. zinc and ca. 1000ml. hydrochloric acid were added giving a milky solution, which was poured into a solution of sodium acetate (600g.) in water (10l.). After 2 hours, the solid zinc o-aminothiophenate was filtered, washed with water (2 x 500ml.), alcohol (100ml.) and dried. Yield, 290g. This reduction is the method of Metzger [34]. The zinc salt (8.5g) was dissolved in hot concentrated hydrochloric acid (75ml.). On cooling, solid o-aminothiophenol hydrochloride precipitated out. Yield (recrystallised from concentrated hydrochloric acid), 80%. M.p. 217°.

2-Chloro-5-nitrobenzophenone (XXIX).

2-Chloro-5-nitrobenzoic acid was prepared by nitration of o-chlorobenzoic acid using the method of Rupe [35]. This

nitro-acid was used in a Friedel-Craft reaction described
by Fries [36] affording 2-chloro-5-nitrobenzophenone.

2-Benzoyl-4-nitro-2'-aminodiphenyl Sulphide (XXXI).

A warm solution of 2-chloro-5-nitrobenzophenone
(1.5g., 1 mol.) in 80% aqueous ethanol (20ml.) was added
slowly with stirring to a warm solution of o-aminothiophenol
hydrochloride (1g., 1 mol.) in the same solvent (10ml.)
containing dissolved sodium hydroxide (0.5g., 2 mols).   On
standing brown-orange prisms were deposited, these recrystallised
from ethanol as brownish-yellow prisms, m.p. 136-138°.
Yield 1.8g. (85%).

Found: C, 65.52 ; H, 3.81 ; N, 8.17 %

$C_{19}H_{14}N_2O_3S$ requires   C, 65.15 ; H, 4.03 ; N, 8.00 %

Light absorption: Maxima at 241 and 332 mμ.

(log ε 4.366 and 4.125 respectively).

2-Nitro-11-phenyldibenzothiazepine (XXX).

The sulphide (XXXI) described above underwent a
change when rubbed with a little glacial acetic acid.   The
product crystallised as fine, pale yellow needles, m.p. 159.5-160°,
from ethanol.   A small amount of this material was found in
the alkaline mother-liquors of the sulphide preparation. Yield 82%.

Found: C, 68.67 ; H, 3.96 ; N, 8.66 %

$C_{19}H_{12}N_2O_2S$ requires   C, 68.67 ; H, 3.65 ; N, 8.46 %

Light absorption: Maxima at 238, 266 and 323 mμ.

(log ε 4.44, 4.38, 3.93 respectively).

2-Nitro-11-(m-nitrophenyl)dibenzothiazepine (XXXVII).

2-Chloro-3':5-dinitrobenzophenone (1.9g.) was

suspended in hot 80% aqueous ethanol (25ml.) and treated

with a solution of o-aminothiophenol hydrochloride (1g.) in

the same solvent (15ml.) which contained sodium hydroxide (0.5g.)

The suspended solid dissolved during the addition, but on

cooling a crystalline material deposited.   This recrystallised

from acetic acid as yellow prisms, m.p. 245-246°.   Yield, 76%.

Found: C, 60.66 ; H, 3.32 ; N, 11.31 %

$C_{19}H_{11}N_3O_4S$
    requires   C, 60.47 ; H, 2.94 ; N, 11.14 %.

2:4-Dinitro-11-phenyldibenzothiazepine (XXXIII).

2-Chloro-3:5-dinitrobenzophenone was condensed with

o-aminothiophenol hydrochloride in the same way as its isomer

(XXXVII).   The product, a reddish solid, was dissolved in

benzene and chromatographed on alumina, in benzene-light

petroleum (1:1).   The first fraction was a bright yellow

solution yielding glistening yellow prisms from ethanol, m.p.

199-200°.   Yield, 50%.

Found: C, 60.87 ; H, 3.15 ; N,10.97%

$C_{19}H_{11}N_3O_4S$ requires   C, 60.47 ; H, 2.94 ; N,11.14%

Light absorption: Maxima at 233 and 320 mμ.
                  (log ε 4.46 and 3.86 respectively).
                  Shoulder at 265 mμ (log ε 4.29).

1-Benzoyl-3-nitrophenothiazine (LI).

The second fraction from the above chromatogram was eluted with benzene (+ 1% ethanol) yielding bright red needles from the resulting red solution.

M.p. 178-179° from ethanol.   Yield, 20%.

Found: C, 64.77 ; H, 3.26 ; N, 7.99 %

$C_{19}H_{12}N_2O_3S$ requires   C, 65.52 ; H, 3.47 ; N, 8.04 %

Light absorption: Maxima at 242, 301 and 462 mμ.
               (log ε 4.7, 4.45 and 3.205 respectively).

This condensation, with pyridine (20ml.) as solvent, afforded only the phenothiazine in 58% yield.

1-Benzoyl-3-nitrophenothiazine-5-dioxide (LII).

The above phenothiazine (LI) (100mg.) was dissolved in hot glacial acetic acid (10ml.).   Hydrogen peroxide (0.5ml. 30%) was added changing the solution colour from intense red to bright yellow.   Two further equal additions of peroxide were made at 30 minute intervals, the temperature being maintained at 100°.   On cooling, fine yellow needles crystallised from the solution.   These recrystallised from acetic acid, m.p. 257-258°.

Found: C, 59.84 ; H, 3.40 ; N, 7.73 %

$C_{19}H_{12}N_2O_5S$ requires   C, 60.00 ; H, 3.18 ; N, 7.37 %

2-Bromo-5-nitroacetophenone (XXXIV).

Acetophenone was nitrated by the method of
Simpson et al [38], followed by reduction to o-aminoacetophenone
with tin/hydrochloric acid, acetylation, nitration, diazatisation
and conversion into 2-bromo-5-nitroacetophenone by the method
of Meisenheimer [39].

2-Acetyl-4-nitro-2'-diphenyl Sulphide.

2-Bromo-5-nitroacetophenone (1.5g., 1 mol.) was
dissolved in hot 80% aqueous ethanol and added to a solution of
o-aminothiophenol (1g., 1mol.) in the same solvent (10ml.).
To this mixture was added sodium hydroxide solution (0.5g. in
2ml. water). The solution turned brown and turbid, affording
a yellow solid, which crystallised as yellow prisms from
benzene-light petroleum, m.p. 160-162°. Yield 78%.

Found: C, 58.53 ; H, 4.01 ; N, 9.77 %

$C_{14}H_{12}N_2O_3S$ requires C, 58.32 ; H, 4.19 ; N, 9.70 %

$\overline{N}$-Acetyl derivative:- prepared by heating the sulphide
in acetic anhydride for 2 hours. Yellow prisms from
benzene-light petroleum, m.p. 148°.

Found: C, 58.41 ; H, 4.23 ; N, 8.75 %

$C_{16}H_{14}N_2O_4S$ requires C, 58.18 ; H, 4.27 ; N, 8.48 %

2-Nitro-11-methyldibenzothiazepine (XXXV).

The above sulphide resisted cyclisation by (i) acetic acid/sulphuric acid (1:1), and (ii) polyphosphoric acid at 100° for $2\frac{1}{2}$ hours.   A 90% recovery of starting material was obtained in each case.

The sulphide (800mg.) was mixed with polyphosphoric acid (10g. phosphorous anhydride and 4ml. syrupy phosphoric acid).   The mixture turned dark brown when heated at 140° for 30 minutes.   Decomposition with water (75ml.) afforded a pale yellow solid, which recrystallised as yellow prisms from methanol.   m.p. $138-139^{\circ}$.   Yield, 82%.

Found: C, 62.35 ; H, 3.76 ; N, 10.36 %

$C_{14}H_{10}N_2O_2S$ requires   C, 62.22 ; H, 3.73 ; N, 10.37 %

Light absorption: Maxima at 226, 298 and 309 mμ.

(log ε , 4.36, 3.85 and 3.85 respectively).

2-Nitrodibenzothiazepine (XXXIX).

a).   2-Chloro-5-nitrobenzaldehyde was prepared by the method of Erdmann [37].   This compound was condensed with o-aminothiophenol hydrochloride by the same method as was the benzophenone (XXIX), but at room temperature affording pale yellow needles, m.p. $177-178^{\circ}$, from ethanol.   Yield, 45%.

Found: C, 61.05%.; H, 3.46 ; N, 11.33%

$C_{13}H_8N_2O_2S$ requires   C, 60.93 ; H, 3.15 ; N, 10.93%

Light absorption: Maxima at 224 and 317 mμ.

                      (log ϵ , 4.36 and 3.86 respectively).

b).   (4-Nitro-2-formylphenyl)pyridinium toluene-p-sulphonate (XLIII) was prepared by the method of Allan and Loudon [22]. This salt (400mg.) was suspended in anhydrous pyridine (3ml.) and treated with o-aminothiophenol hydrochloride (161mg., 1 mol.). After one hour, the deep red solution was poured into dilute hydrochloric acid/ice and left overnight. The yellow solid which precipitated was chromatographed on alumina in benzene affording 2-nitrodibenzothiazepine.

5-Nitro-2-(p-tolylthio)benzaldehyde. (XLIV)

      The quaternary salt (XLIII, 400mg.) was suspended in anhydrous pyridine (3ml.) and treated with thio-p-cresol (130mg., 1 mol.). After standing for one hour, the dark solution produced was poured into ice/hydrochloric acid. The yellow solid thus obtained recrystallised as yellow prisms, m.p. 195-196°, from acetic acid. M.p. and mm.p. with an authentic sample, 195-196°.

2:4-Dinitrodibenzothiazepine (XLVI).

      3:5-Dinitrosalicylaldehyde (XLV, 500mg.) was

suspended in anhydrous pyridine (4ml.).   Toluene-p-sulphonyl

chloride (445mg.) was added and the mixture was stoppered and

set aside for one hour.   Then o-aminothiophenol hydrochloride

(376mg.) was brushed in, giving a deep red solution which, after

standing for 50 minutes was poured into ice/hydrochloric acid,

yielding a brown-red solid.   This was chromatographed in

benzene on alumina, affording bright yellow prisms, m.p. 232-234°

from chloroform.   Yield, 65%.

Found:	C, 51.96 ; H, 2.64 ; N, 14.24 %
$C_{13}H_7N_3O_4S$ requires	C, 51.83 ; H, 2.34 ; N, 13.95 %

Light absorption: Maxima at 234 and 317 mμ.

(log ε , 4.45 and 3.82 respectively.)

Reaction on 3-Nitrosalicylaldehyde (XLVII).

3-Nitrosalicylaldehyde was treated in the same

manner as its nitrated derivative (XLV) except that heating

at 100° for one hour was required to form the quaternary salt.

The resultant brown solid was chromatographed in benzene on

alumina affording pale yellow needles, m.p. 189-191°,

recrystallised from ethanol.   This product gave the average

analysis.

Found: C, 57.8 ; H, 3.3 ; N, 10.8 %

but no empirical formula could be assigned for this.

The material is basic, has a flat, peakless ultraviolet absorption spectrum, sublimes (165-170°/0.5mm.) and does not form a picrate.

7-Nitro-9-phenylphenanthridine (LVII).

a). 2-Nitro-11-phenyldibenzothiazepine (XXX, 300mg.) was heated with copper bronze (300mg.) in an atmosphere of nitrogen. At the bath temperature 280-290°, a reaction ensued releasing a cloud of yellow sublimate. This crystallised as pale yellow needles, m.p. 235-236° (decomp.), from ethanol. No crystalline material was recovered from the copper. Yield, 8-10mg.

b). The thiazepine (300mg.) was heated under reflux with copper bronze (300mg.) in diethyl phthalate (3ml.) in an atmosphere of nitrogen. Heating was continued for 5 - 7 minutes (temperature, 298°), after which the formation of a black precipitate of copper sulphide turned the yellow solution opaque. The product was isolated by extracting the mixture with hot benzene (2 x 15ml.), boiling with charcoal, filtering, recovering the benzene and adding light petroleum. This afforded a pale yellow solid which recrystallised as in (a) above. Yield, 82%.

Found: C, 76.41 ; H, 3.94 ; N, 9.53 %
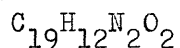
Calculated for
$C_{19}H_{12}N_2O_2$ C, 76.00 ; H, 4.03 ; N, 9.32 %

Light absorption: Maxima at 226 and 290 mμ.

(log ε 4.49 and 4.48 respectively).

Walls [40] describes this compound as "fine yellow silky

needles, m.p. 237°, from pyridine".

7-Nitro-9-phenylphenanthridine Oxide (LXI).

7-Nitro-9-phenylphenanthridine (100mg.) was dissolved

in glacial acetic acid (5ml.) and treated with hydrogen

peroxide (1ml., 30%).   This mixture was refluxed for 2 hours,

further additions of peroxide were made at 30 minute intervals.

Cooling and dilution afforded a yellow solid, which crystallised

as yellow needles, m.p. 255-259°, from ethanol.

Found: N, 8.94 %

$C_{19}H_{12}N_2O_3$ requires N, 8.86 %

Heating this oxide with an equal weight of copper bronze in

diethyl phthalate at 290-300° for 5 minutes afforded a good

yield of the phenanthridine.

7-Nitrophenanthridine (LVIII).

2-Nitrodibenzothiazepine (XXXIX) was desulphurised as

described for (XXX).   Yield - with copper alone - very low.

- with diethyl phthalate, 63%.

The product crystallised as pale yellow prisms, m.p.

173-174°, from ethyl acetate.

Found: C, 69.76 ; H, 3.65 ; N, 12.40 %

   Calculated for $C_{12}H_8N_2O_2$ C, 69.64 ; H, 3.60 ; N, 12.49 %

Light absorption: Maximum at 274 mμ.   (log ε , 4.46)

                                Shoulder at 224 mμ.   (log ε , 4.38)

Ritchie[41] reports the m.p. 178°, while Arcus and Coombs [29]

report 180°.

7-Nitro-9-(m-nitrophenyl)phenanthridine (LIX).

2-Nitro-11-(m-nitrophenyl)dibenzothiazepine (XXXVII)

was desulphurised by heating with copper in diethyl phthalate

as described before.   Yield, 70%.   The product crystallised

from benzene-ethanol as fine, pale yellow needles, m.p. 263-264°.

   Found: C, 66.07 ; H, 3.04 ; N, 12.19 %

   Calculated for $C_{19}H_{11}N_3O_4$ C, 66.08 ; H, 3.21 ; N, 12.17 %

Walls [40] reports m.p. 269°. M.m.p. with sample from Dr.Walls, 264°

Infrared absorption spectra are   identical.

2:4-Dinitro-11-phenyldibenzothiazepine (XXXIII) and 2:4-dinitrobenzothiazepine (XLVI) with Copper.

These thiazepines gave no sublimate or any other

product when heated with copper bronze at 300° in an atmosphere

of nitrogen.   On heating either of them under reflux with

copper in diethyl phthalate,the solution went turbid and brown.

After 11 minutes heating an 80% yield of starting material was

recovered, but after 45 minutes no crystalline material was isolated.

7-Nitro-9-methylphenanthridine (LVII).

2-Nitro-11-methyldibenzothiazepine (XXXV) was heated with copper by the methods described previously. However, no product was obtained by heating the "dry" mixture with copper bronze, and by heating with diethyl phthalate a clean solution was not obtained on boiling with charcoal and filtering, as in previous desulphurisation experiments. The yield of product was also lower, 48-55%.

Buff-coloured needles, m.p. 242-243°, from benzene.

Found: C, 70.71 ; H, 4.09 ; N, 11.75 %

Calculated for $C_{14}H_{10}N_2O_2$ C, 70.58 ; H, 4.23 ; N, 11.75 %

Light absorption: Maximum at 275 mμ. (log ϵ , 4.45)

Shoulder at 228 mμ. (log ϵ , 4.40)

Morgan and Walls [42] report buff needles, m.p. 243-245°.

Nunn, Schofield and Theobald [28] give the m.p. as 242-243°.

M.m.p. with sample from Dr. Walls, 242-243°.

Infrared absorption spectra are identical.

7-Amino-9-methylphenanthridine.

Attempts to reduce 7-nitro-9-methylphenanthridine (LX) catalytically using palladium black proved unsuccessful.

The nitro-phenanthridine (1g) was treated with iron filings (1g) in hot acidulated, following the reduction method described by Morgan and Walls [42]. The black aggregate produced was extracted with chloroform in a Soxhlet extractor. The solvent was removed and the residue recrystallised from a large volume of ethanol as almost white needles, m.p. 232-233°. Walls [43] reports m.p. 232°. M.m.p. with sample from Dr. Walls, 232°.

7-Nitrophenanthridone (LXVII).

a). 7-Nitrophenanthridine was oxidised by acid permanganate solution using the method described by Arcus and Coombs [29]. The phenanthridone produced crystallised from acetic acid as pale yellow needles, m.p. 324-326°.
Reported m.ps. 325-328° [28], 326-327° [29].

b). 7-Nitro-9-methylphenanthridine was oxidised by sodium dichromate in glacial acetic acid by the method used by Walls [43] for the oxidation of 9-methylphenanthridine. This reaction afforded a 72% yield of 7-nitrophenanthridone as pale yellow needles, m.p. 320-325°.

Found:	C, 65.44 ; H, 3.32 ; N, 11.82 %
Calculated for $C_{13}H_8N_2O_3$	C, 65.00 ; H, 3.33 ; N, 11.66 %

Oxidation of 7-nitrophenanthridone.

7-Nitrophenanthridone was heated under reflux with alkaline permanganate solution using the conditions employed by Moore and Huntress [30]. Extraction of the acidified filtrate in a constant ether extraction apparatus yielded a small amount of semi-solid. This residue was dissolved in a little ethanol and a drop of aniline was added. After a few minutes a crystalline salt wa deposited. The salt produced had m.p. :-

a). Product after 4 hour oxidation, 162-163° (decomp.)

b). Product after 15 minutes oxidation, 181-182°(decomp.)

By comparison of infrared absorption spectra with authentically prepared samples (a) was shown to be oxalic acid aniline salt, and (b) 4-nitrophthalic acid aniline salt. The reported m.ps. of these compounds are 163° [45] and 181-182° [46] respectively.

2-Nitro- and 7-Nitrophenanthridone Mixture.

A sample of this mixture was prepared exactly as by Moore and Huntress [30]. M.p. 284-287°. The infrared absorption spectrum of this mixture is closely allied to that of pure 7-nitrophenanthridone but shown broader bands and less definition. Oxidation of this mixture with alkaline permanganate as described by the same workers gave a sample

of phthalic acid in the first ethereal extract.   This

was identified by formation of phthalic acid aniline salt,

m.p. 158-159° (decomp.).

Grae $^{(47)}$ reports m.p. 156° for this compound.

More thorough ethereal extraction of the acidified

filtrate afforded a little oxalic acid, which was identified

as before.

2-(2'-Aminothiophenoxy)-5-nitrobenzoic Acid.

2-Chloro-5-nitrobenzoic acid (1.2g.) was dissolved

in 80% aqueous ethanol (20ml.) and treated at 30-35° with a

solution of o-aminothiophenol hydrochloride (1g.) in the same

solvent (10ml.) containing dissolved sodium hydroxide

(0.75g., 3 mols).   The mixture was heated at 80° for 30 minutes,

cooled, diluted with water (30ml.) and carefully neutralised with

dilute hydrochloric acid.   The precipitated solid recrystallised

from aqueous ethanol as brown-yellow needles, m.p. 212-215°

(decomp.).   Yield 36%.

Found: C, 53.97 ; H, 3.60 ; N, 9.83 %

$C_{13}H_{10}N_2O_4S$ requires   C, 53.80 ; H, 3.47 ; N, 9.65 %

This acid hasresisted attempts to effect a cyclodehydration

using polyphosphoric acid.

2-Benzoyl-2':5-dinitrodiphenyl Sulphone (LXII).

a).   2-Nitro-11-phenyldibenzothiazepine (XXX, 2g.) was

dissolved in glacial acetic acid (20ml.).   Hydrogen peroxide

(2ml. 30%) was added turning the pale yellow solution dark

brown.   After 30 minutes heating under reflux, the solution,

on cooling, afforded a straw-coloured solid.   This product,

thought to be the $\overline{N}$-oxide, crystallised as pale yellow

needles from acetic acid, m.p. 175-177° (decomp.).

Found: C, 66.27 ; H, 3.63 ; N, 8.17 %

$C_{19}H_{12}N_2O_3S$ requires   C, 65.52 ; H, 3.47 ; N, 8.04 %

Heated with copper bronze in diethyl phthalate for 2 minutes

at ca. 300°, this oxide affords 7-nitro-9-phenylphenanthridine

in almost theoretical yield.   If the initial heating under

reflux is continued for 6 hours, with addition of hydrogen

peroxide (1ml.) at 30 minute intervals, dilution with water

and cooling affords a pale yellow solid, which crystallises

as pale yellow needles, m.p. 215-217°, from ethanol.

Found: C, 55.68 ; H, 3.32 ; N, 6.98 %

$C_{19}H_{12}N_2O_7S$ requires   C, 55.35 ; H, 2.93 ; N, 6.80 %

b.) 2-Nitrothiophenol was prepared by reduction of 2:2'-dinitro-

diphenyl disulphide using the method of Claasz [48].   This

was condensed with 2-chloro-5-nitrobenzophenone by the

addition of an alkaline solution to the ketone dissolved in

ethanol.   The product formed, 2-benzoyl-2':4-dinitrodiphenyl

sulphide (LXVI), crystallised from ethanol-benzene as yellow plates, m.p. 137-139°.

Found: C, 60.25 ; H, 3.31 ; N, 7.46 %

$C_{19}H_{12}N_2O_5S$ requires C, 60.00 ; H, 3.18 ; N, 7.37 %

This sulphide(100mg) was readily oxidised by heating with hydrogen peroxide (2.5ml., 30%) in acetic acid for one hour affording 2-benzoyl-2':4-dinitrodiphenyl sulphone, m.p. 215-217°.

2-Piperidino-5-nitrobenzophenone (LXIII).

The above sulphone (LXII, 400mg.) was dissolved in piperidine (2ml.) and gently warmed giving a brown solution. After cooling, and acidification with bench hydrochloric acid, the mixture was extracted with ether. The ethereal extract was washed with a minimum of water, potassium carbonate solution, and again with water. Removal of the ether afforded a yellow solid, which was chromatographed in benzene on alumina. The product crystallised from methanol, m.p. 100-102°. Reported m.p. 102° [31].

o-Nitrobenzene Sulphonamide (LXV).

The carbonate wash from the reaction above was treated with gaseous chlorine for a few minutes. The liquid was decanted from the gum produced, which was further washed with water by decantation. Concentrated ammonium hydroxide

solution (sp. gr. 0.88) was added and the mixture allowed to

stand overnight.   The resultant brittle solid recrystallised

from methanol as glistening plates, m.p. 189-191°.

Limpricht [49] reports m.p. 188°.

o-(2:4-Dinitrobenzylidine)aminothiophenol (LIII).

2:4-Dinitrobenzaldehyde (500mg.) dissolved in 80% aqueous

ethanol (4ml.) at 0° was slowly added to a solution of

o-aminothiophenol hydrochloride (500mg.) in the same solvent

containing dissolved sodium hydroxide (250mg., 2 mol.).

On standing, red prismatic crystals were deposited.   These

crystallised from ethanol, m.p. 130-131°.

Found: C, 51.33 ; H, 3.40 ; N, 13.85 %

$C_{13}H_9N_3O_4S$ requires   C, 51.49 ; H, 2.99 ; N, 13.86 %

This condensation is obtained in theoretical yield

when no alkali is present.

Light absorption: Maximum at 318 mμ. (log ε , 3.94).

Acetyl derivative - prepared by heating the anil under

reflux with acetic anhydride affording glittering yellow

needles, m.p. 139-141° from methanol.

Found: C, 52.55 ; H, 3.22 ; N, 12.26 %

$C_{15}H_{11}N_3O_5S$ requires   C, 52.18 ; H, 3.21 ; N, 12.17 %

Light absorption: Maximum at 230 mμ (log ε , 4.63).

Shoulders at 255 and 297 mμ.
(log ε , 4.35 and 3.84 respectively).

Disulphide - (a) An ethanolic solution of the anil was treated with an ethanolic solution of iodine/potassium iodide. The solution became turbid and afforded yellow needles on standihg. Recrystallised from acetic acid, m.p. 200-201°.

(b) Di-(o-aminophenyl)disulphide was condensed with 2:4-dinitrobenzaldehyde in alcohol containing a drop of concentrated hydrochloric acid. M.p. and m.m.p. with sample from (a) 201°.

Light absorption: As shown.

2-(2:4-Dinitrophenyl)benzothiazole (LIV).

(a). This was prepared from 2:4-dinitrobenzaldehyde using the method of Bogert and Naiman [50] for the preparation of 2-phenylbenzothiazole.

(b). The above anil (LIII) was oxidised by the addition of ethanolic ferric chloride solution or by dissolution in pyridine.

(c). 2:4-Dinitrobenzoic acid was prepared from 2:4-dinitrobenzaldehyde via the oxime, and the nitrile [51]. This was converted into the acid chloride by treatment with excess thionyl chloride in dry benzene. The acid chloride, which was not purified, was slowly added to an equimoleoular amount of zinc o-aminothiophenate. This mixture was heated

at 100° for 5 minutes and worked up by the method of Bogert and Snell [26] affording yellow prisms, m.p. 160-162° from ethanol.

Found: C, 52.00 ; H, 2.72 ; N, 13.69 %

$C_{13}H_7N_3O_4S$ requires C, 51.83 ; H, 2.35 ; N, 13.95 %

Light absorption: Maximum at 330 mμ (log ε , 4.115).

2-Phenylbenzothiazole (LVI).

Benzaldehyde was condensed with the zinc salt of o-aminothiophenol by the method of Bogert and Naiman [50].

Light absorption: Maxima at 248 and 300 mμ.

(log ε 3.97 and 4.324 respectively).

1-Nitrophenothiazine (LXX).

2:6-Dinitrochlorobenzene (LXIX, 1mol.) was condensed with o-aminothiophenol hydrochloride in alkaline ethanol. The initial product was 2:6-dinitro-2'-aminodiphenyl sulphide (yellow prisms, m.p. 133-134° from ethanol), which was heated in pyridine solution affording 1-nitrophenothiazine as violet black leaflets, m.p. 110° from sublimation. Kehrmann and Nossenko [54] report m.p. 111°.

This compound was recovered unchanged after heating with coppe r in diethylphthalate.

1:3-Dinitrophenothiazine (XLIX).

Picryl chloride (1mol) was condensed with

o-aminothiophenol hydrochloride (1mol) in aqueous ethanol with sodium hydroxide (2mols).   The deep red solution was heated to 100°.   Dilution of the blue violet product afforded an almost quantitative yield of 1:3-dinitrophenothiazine, m.p. 188°.   Wight and Smiles[52] report the same m.p. This compound was unchanged by heating with copper in diethyl phthalate.

6-Nitro-2-methoxythioxanthone (LXXI) and -thioxanthen (LXXII).

5-Nitro-2-(p-anisylthio)benzaldehyde, prepared by condensation of 2-chloro-5-nitrobenzaldehyde with p-methoxythiophenol, was disproportionately cyclised using the method described for the tolyl analogue.

The products isolated were:-

i).   6-nitro-2-methoxythioxanthone as pale yellow prisms, m.p. 242-243°, from acetic acid.

Found: C, 58.66 ; H, 3.14 ; N, 4.97 %

$C_{14}H_9NO_4S$ requires   C, 58.51 ; H, 3.16 ; N, 4.88 %

ii)   6-nitro-2-methoxythioxanthen as yellow needles, m.p. 127°, from ethyl acetate.

Found: C, 61.34 ; H, 4.01 ; N, 5.28 %

$C_{14}H_{11}NO_5S$ requires   C, 61.52 ; H, 4.06 ; N, 5.13 %

Both these compounds were recovered in good yield after heating with copper in diethyl phthalate.

Phenoxthin. (X).

Phenoxthin, prepared from diphenyl ether by the method of Suter and Maxwell,[53] was heated to 300° with copper bronze in an atmosphere of nitrogen. Starting material was recovered by sublimation at this temperature. Phenoxthin was recovered unchanged after heating with copper bronze in diethyl phthalate at 300° for 140 hours in an atmosphere of nitrogen.

SUMMARY.

2-Nitrodibenzo(b,f)(1,4)thiazepine and various derivatives are prepared by condensing o-aminothiophenol with 2-chloro-5-nitrobenzaldehyde, with 2-chloro-5-nitrobenzophenone or with derivatives of these. Toluene-p-sulphonic ester of nitrosalicylaldehydes are also used in similar condensations. In most cases, the dibenzothiazepine when heated with copper in diethyl phthalate solution, affords the corresponding phenanthridine by extrusion of the thia-atom.

2-Chloro-3:5-dinitrobenzophenone condenses with o-aminothiophenol to yield a phenothiazine, alone or together with the expected dibenzothiazepine. This and other known phenothiazines when heated in diethyl phthalate solution with copper did not undergo change. Various other cyclic sulphides were prepared and examined for sulphur extrusion.

2:4-Dinitrobenzaldehyde condenses with o-aminothiophenol to a product, from which, among other compounds, 2-(2:4-dinitrophenyl)benzothiazole is obtained.

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A D D E N D U M.

The work to be described in this section is a brief
preliminary survey designed to test the scope of a reaction
first reported by Cook and Schoental [1].

This reaction involves conversion of suitable
diazoketones into cyclic ketones by treatment with a solution
of sulphuric acid in acetic acid.   By this means Cook and
Schoental synthesised 2-chrysenol (III) from ∝ -chrysenic acid
(I) via the diazoketone (II).
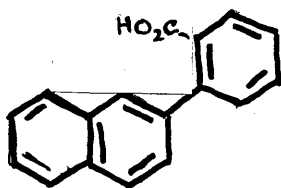
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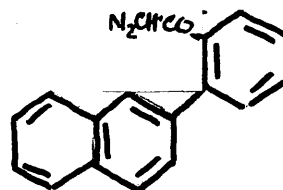
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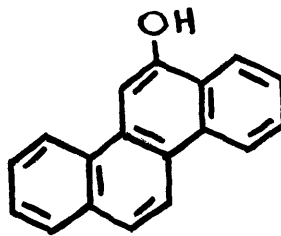
III

Newman, Eglinton and Grotta[2] used this reaction in
the preparation of 2-methyl-3-oxo-1:2:3:4-tetrahydro-1:2-cyclopentano-
naphthalene (V) from 1-methyl-2-phenylcyclopentanecarboxylic acid (IV)

$$\overline{IV} \qquad \overline{V}$$
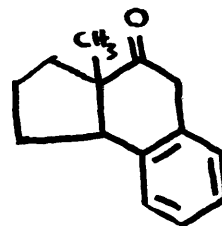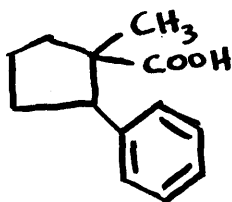
In both of these cases it is to be noted that the reaction leads to the formation of a six membered ring, not necessarily aromatic.

Cook and Schoental suggest that a hydroxymethyl ketone, or its ester, is an intermediate in the reaction. Indeed, Langenbeck and Baehren[3] report the synthesis of hydroxymethyl-β - naphthylketone acetate by the following route.
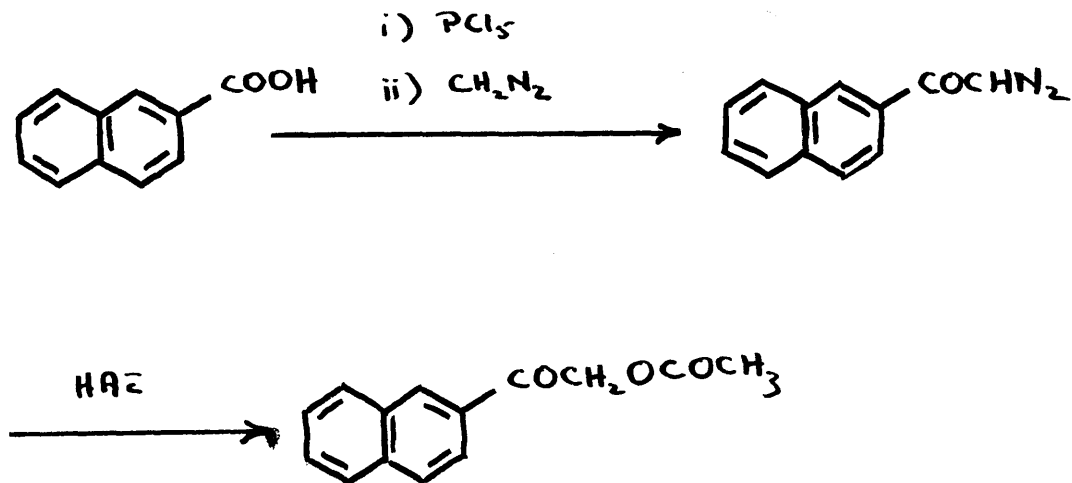
The applicability of the reaction to the simple case of preparing β-tetralone from β-phenylpropionic acid was first examined.
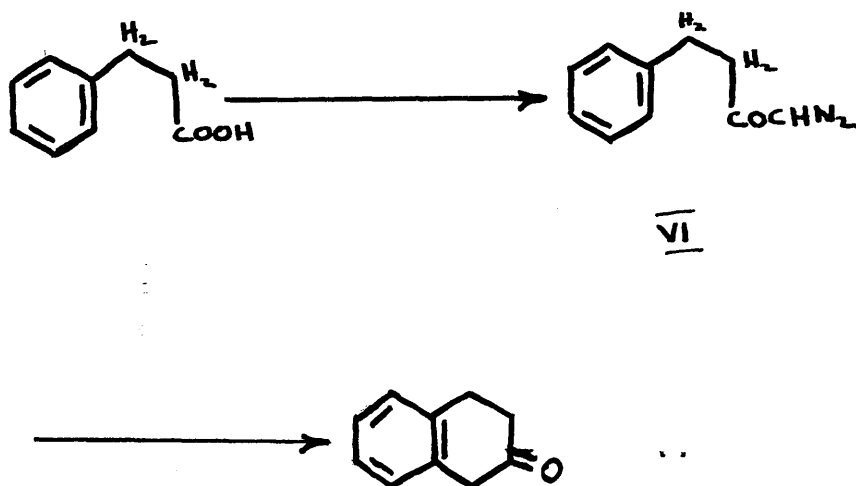
The diazoketone (VI), prepared from β-phenylpropionyl chloride and an excess of diazomethane, was added to a sulphuric acetic acid mixture. This was gently heated and the reaction mixture was poured into water. The precipitated oil was distilled under reduced pressure giving a pale yellow oil, which solidified to colourless crystals. These were shown to consist of the acetate (VII) of the uncyclised hydroxymethyl ketone (VIII). This compound forms an osazone (IX) with

2:4-dinitrophenylhydrazine in acid conditions.
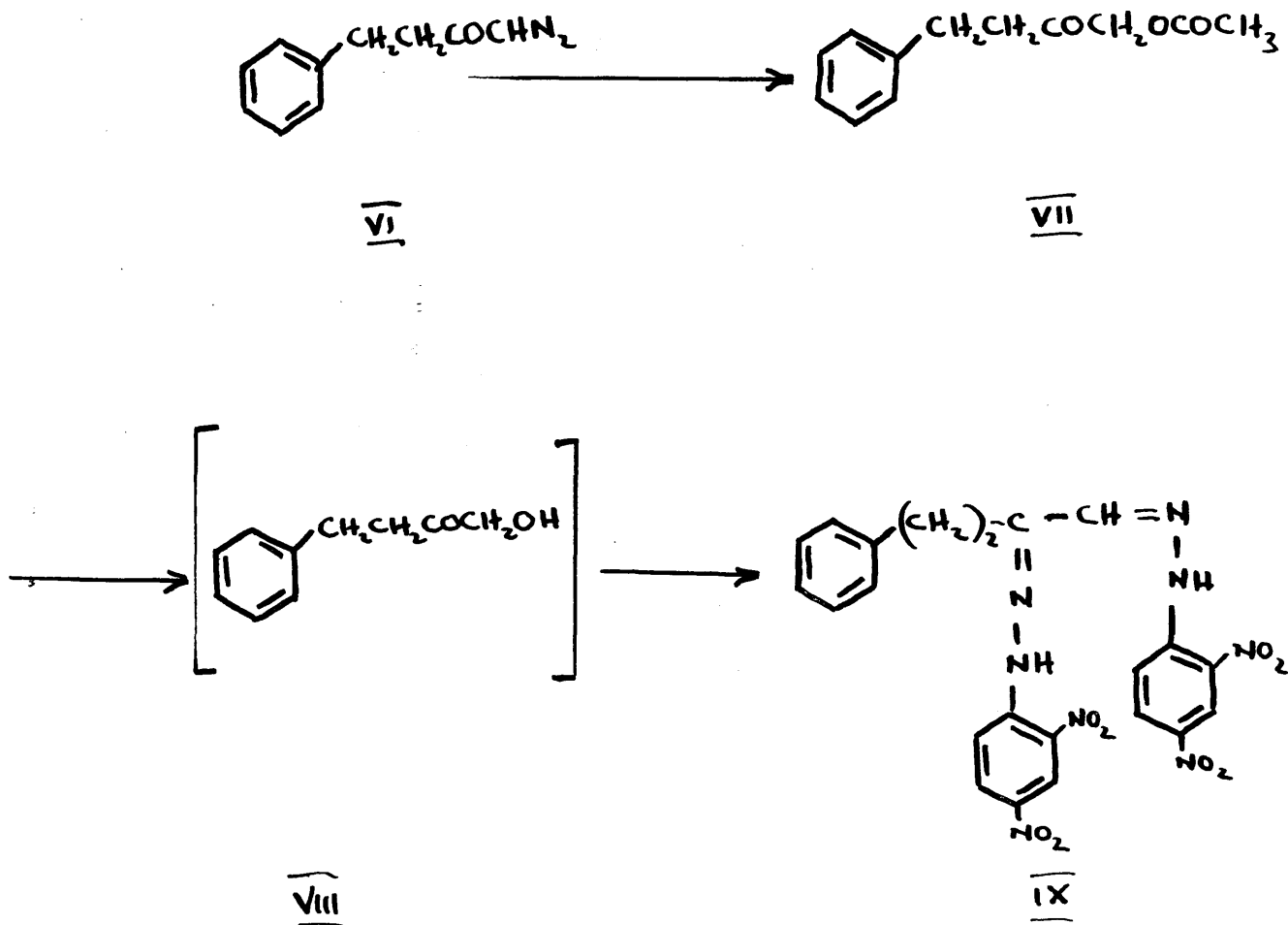
Chromatography of the solid, obtained by similar treatment of the undistilled oil with 2:4-dinitrophenylhydrazine,

afforded a little benzalacetone-2:4-dinitrophenylhydrazone (X),

which was identified by comparison with an authentic specimen.

$$\overline{\underline{X}}.$$
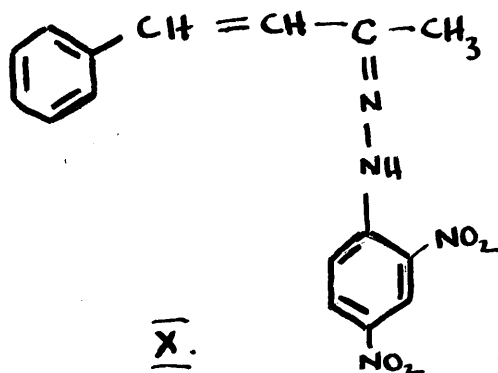
N o evidence of any cyclised material was found,

in particular the reaction mixture appeared to contain no

β -tetralone.   Moreover, an attempt to cyclise the product

(VII) by polyphosphoric acid was unsuccessful.

The behaviour of the diazoketone from phenylacetic

acid was next examined, but in this case the product isolated

was the sulphuric acid ester (XI).   This sulphate also gave an

osazone and resisted cyclisation by polyphosphoric acid.

$$\overline{\underline{XI}}$$
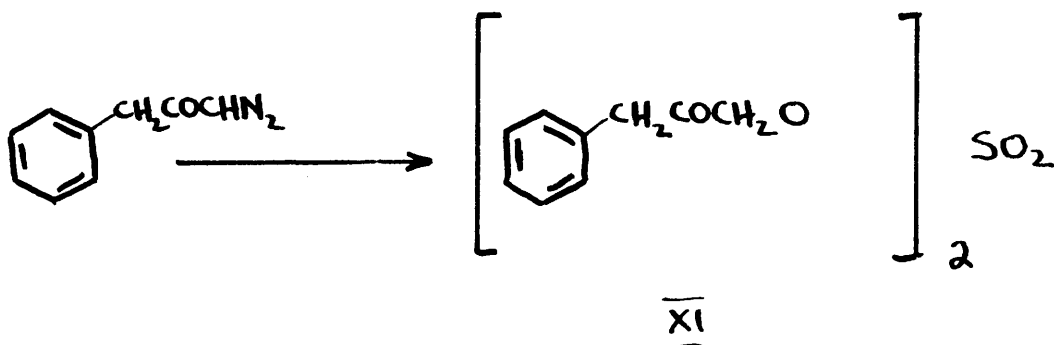
Subsequently, it has been found by Buchanan and Sutherland [4] that similar attempts to fuse a seven-membered ring with a benzene ring also failed.   They prepared the diazoketone from γ -phenylbutyric acid in an attempt to synthesise 4-oxobenzocycloheptene.   However, varying conditions gave the monocyclic hydroxymethyl ketone, its acetate or sulphate.   2-Phenoxy-5-nitrobenzoic acid was prepared by a standard route and converted into the corresponding diazoketone (XII), which was treated with the sulphuric-acetic acid solution.   However, the product was again the sulphuric ester (XIII) of the corresponding hydroxymethyl ketone.
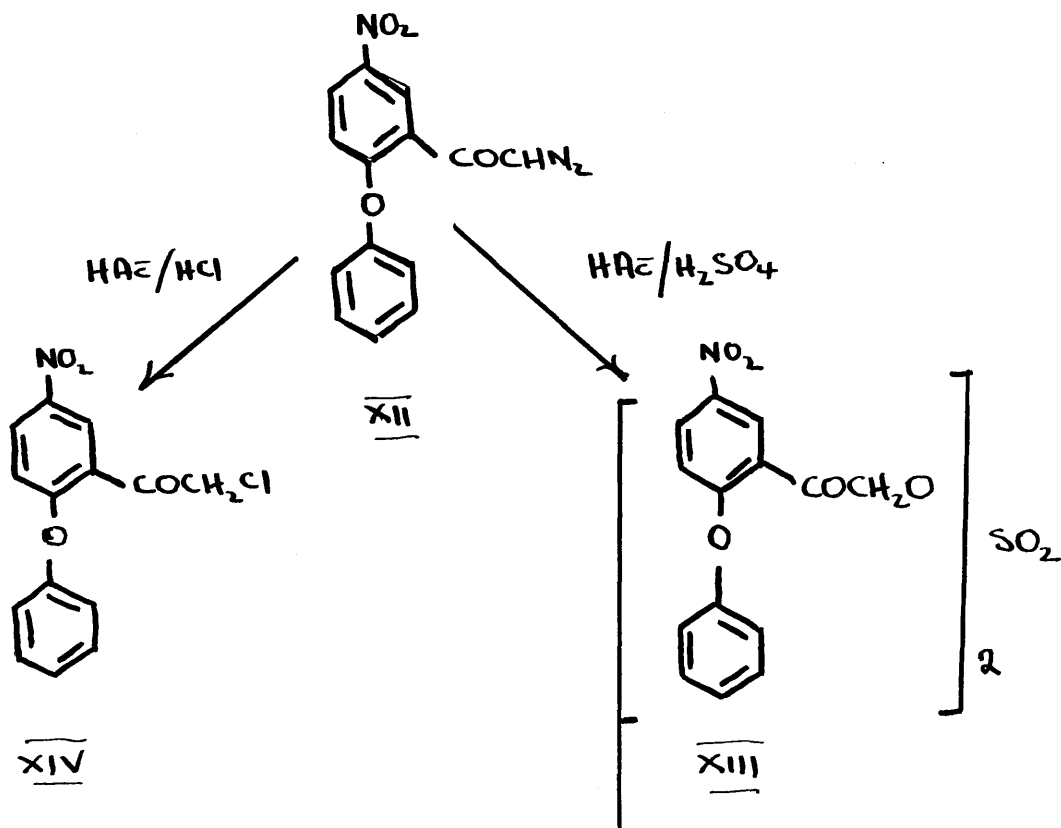
The chloromethyl ketone (XIV) was prepared by
adding the diazoketone (XII) to acetic acid saturated with dry
hydrogen chloride.   Using this chlorocompound, a Friedel-Craft
cyclisation was attempted by Baddeley's method[5] using
aluminium chloride in ethylenedichloride.   However, the only
product was an intractable gum.

Following these failures to effect cyclisation, the
reaction was applied to a compound closely allied in structure
to that successfully cyclised by Cook and Schoental [1].
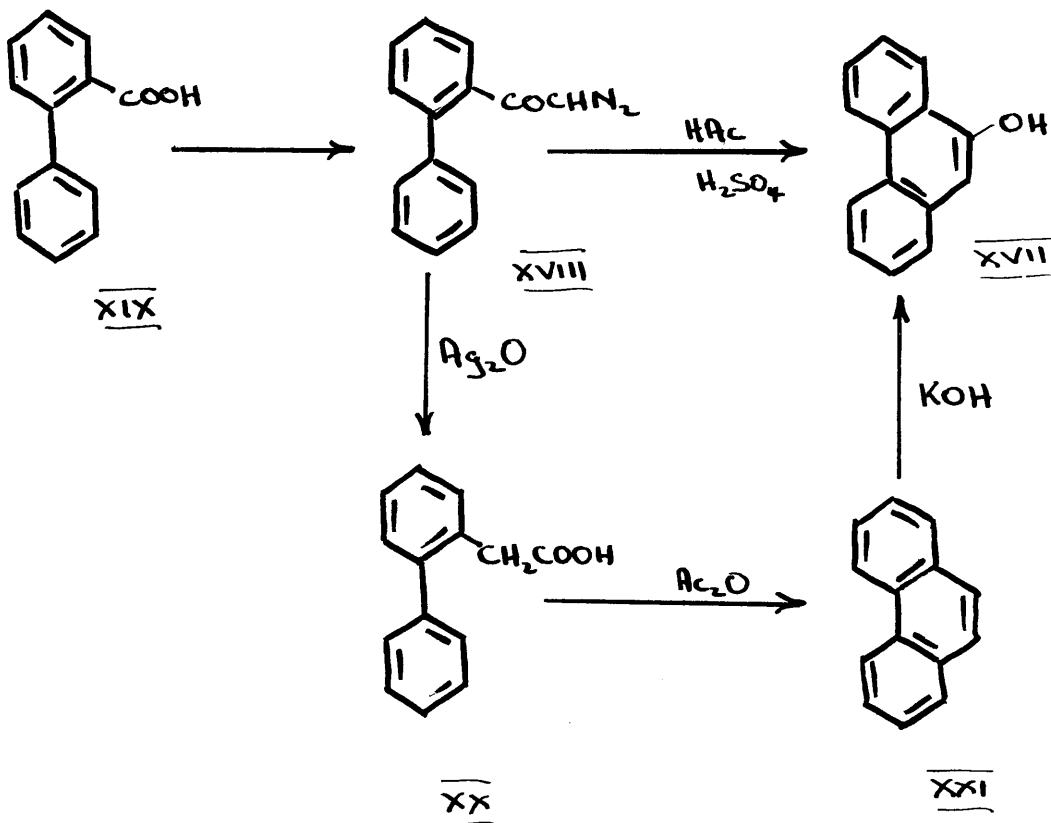
ω –Diazo-o-phenylacetophenone (XVIII) was prepared by the standard method from diphenyl-2-carboxylic acid (XIX). The acid itself was prepared from fluorenone by the method of Graebe and Rateanu [6] and was converted into the acid chloride by treatment with oxalyl chloride at 30°, in order to minimise intramolecular acylation. Treated with sulphuric acid/acetic acid, the diazoketone (XVIII) gave a moderate yield of 9-phenanthrol (XVII), the only crystalline product. This was identified by direct comparison with an authentic sample [7], prepared via diphenyl-2-acetic acid (XX) and 9-phenanthrylacetate (XXI).

Using these two methods of phenanthrol synthesis it should be possible to prepare two structurally isomeric phenanthrols e.g. (XXIII and XXIV) from a given unsymmetrically substituted acid (XXII). Accordingly, a sample of 2:5-dimethoxydiphenyl-2'-carboxylic acid [8] (XXII, R' = OCH_3 R = COOH), was converted into the corresponding diazoketone. By a standard Arndt-Eistert reaction, a sample of this diazoketone was converted into 2:5-dimethoxydiphenyl-2'-acetic acid (XXII R' = OCH_3 R = CH_2COOH). However, this homo-acid did not undergo cyclisation by Schonberg and Warren's method, nor by treatment with polyphosphoric acid. A further sample of the diazoketone treated with sulphuric acid in acetic acid gave only a black amorphous solid, from which no

crystalline material was obtained.

XXII

XXIII

XXIV
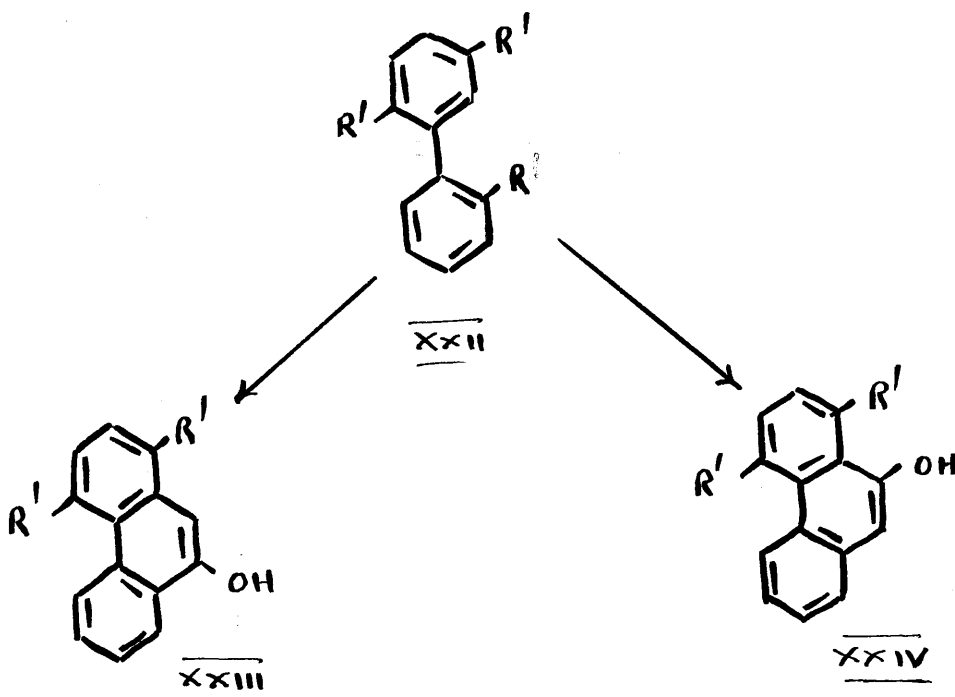
Although this brief survey is too restricted to permit of definite conclusions, it indicates that the Cook-Schoental method of cyclisation is likely to be limited in its application.

EXPERIMENTAL

Diazomethane.

Diazomethane was prepared and used in ethereal solution. It was prepared from nitrosomethylurea by the method of Arndt [9].

General Preparation of Diazoketones.

The method used was that reported by Arndt and Eistert [10]. It involves the slow addition of a cooled ethereal solution of the acid chloride to an efficiently stirred ethereal solution of diazomethane (3 mols.) at $-10°$. The mixture is allowed to revert to room temperature, stoppered and left overnight. The excess of diazomethane and the solvent is removed under slightly reduced pressure. The solid or oily residue is usually pure enough for use in the next stage.

Reaction of diazoketones with sulphuric-acetic acid solution.

A solution of sulphuric acid (10g.) in glacial acetic acid (90g.) is made up. The diazoketone (2g.) is added to the solution (20ml.) at room temperature. After the first evolution of nitrogen has subsided, the dark brown mixture is gently warmed on a steam bath for 10 minutes. The cooled mixture is then poured into water (50 - 100ml.), and the oily product is worked up by the procedures later described in individual cases.

β -Phenylpropionic Acid (VI).

Cinnamic acid (55g.) was catalytically hydrogenated using glacial acetic acid (200ml.) as solvent and palladium black (100mg.) as catalyst. The catalyst was filtered off and the solvent removed by distillation under reduced pressure. Distillation of the residue gave a colourless crystalline solid. Yield, 52g. (94%).   B.p. 190° – 193°/12mm.   M.p. 48°.

β -Phenylpropionyl chloride.

β -Phenylpropionic acid (22g.) was dissolved in anhydrous benzene (30ml.). The mixture was heated under reflux for 2 hours, with thionyl chloride (20ml.). The excess of reagent and the solvent were removed under reduced pressure and the product distilled, b.p. 105°/10mm. Yield 14.3g. (64%).

1-Acetoxy-2-oxo-4-phenylbutane (VIII).

β -Phenylpropionyl chloride (2g.) was converted into its diazoketone and treated with a 10% solution of sulphuric acid in acetic acid (20ml.) as described previously. The resulting oil was extracted with ether. The ethereal layer was washed with sodium carbonate solution, then with water, dried and the solvent distilled off. The residue was distilled under reduced pressure. The main fraction, distilling at 90-94°/0.3mm. solidified as colourless crystalline plates, m.p. 42°.

Found: C,69.68 ; H, 6.57%

$C_{12}H_{14}O_3$ requires   C,69.87 ; H, 6.80%

Treatment of this fraction with 2:4-dinitrophenyl-hydrazine sulphate in ethanol gave the osazone (IX) as red needles, m.p. 262-263°, from acetic acid.

Found: C, 50.55 ; H, 3.69 ; N, 20.84%

$C_{22}H_{18}N_8O_8$ requires C, 50.57 ; H, 3.45 ; N, 21.07 %

Similar treatment of the crude undistilled oil, followed by chromatography of the solid product in benzene on alumina, gave a small first fraction, shown to be benzalacetone-2:4-dinitrophenylhydrazone (X) by m.p. and mixed m.p. with an authentic sample, 213-215° [11].

Found: C, 58.67 ; H, 4.75 %

Calc. for $C_{16}H_{14}N_4O_4$ C, 58.89 ; H, 4.33 %

Bis-(2-oxo-3-phenylpropan-1-ol) Sulphate (XI).

This was prepared from phenylacetic acid in the same way as described for the preceding compound (VIII).   In this case, distillation of the product was followed by recrystallisation from benzene-light petroleum, giving white needles, m.p. 87°. (decomp.)

Found: C, 59.86 ; H, 5.15 %

$C_{18}H_{18}O_6S$ requires   C, 59.65 ; H, 5.01 %

Osazone — orange, yellow needles, m.p. 239-240°, from aqueous

acetic acid.

Found: C, 49.52 ; H, 2.66 ; N, 21.94 %

$C_{21}H_{16}N_8O_8$ requires   C, 49.60 ; H, 3.15 ; N, 22.04 %

2-Phenoxy-5-nitrobenzoic Acid.

2-Chloro-5-nitrobenzoic acid (5g.), prepared by

nitration of o-chlorobenzoic acid, was dissolved in molten

phenol (15g.).   Anhydrous potassium carbonate (5g.) was

dusted into the liquid in small portions.   The mixture was

then heated at 140° for 3 hours, poured into water, acidified

with dilute mineral acid, and steam-distilled to remove the

excess phenol.   After cooling, the solid residue was filtered

off and recrystallised from aqueous acetic acid and then from

toluene giving white micro-crystals, m.p. 164-167°.   The

purity of this acid was doubted.   This doubt was removed by

formation of the methyl ester by diazomethane treatment.   This

ester (3.5g.), white needles m.p. 80.5° from methanol, was

hydrolysed with N̄ potassium hydroxide solution (60ml.), to give

the pure acid, m.p. 168-169°.   Reported m.p. [12] 171°.

2-Phenoxy-5-nitrobenzoyl Chloride.

2-Phenoxybenzoic acid (2.4g.) was dissolved in

anhydrous benzene (24ml.).   Thionyl chloride (2.5ml.) was added

and the mixture heated under reflux for 90 minutes.   The

excess of reagent and solvent were removed by distillation

under reduced pressure leaving a gum which solidified after the

addition of petroleum ether (40-60°) from which solvent it

recrystallised.as white needles, m.p. 67-68°.

Found: C, 56.48 ; H, 2.97 ; N, 5.20 %

$C_{13}H_8NO_4Cl$ requires   C, 56.25 ; H, 2.90 ; N, 5.04 %

Amide – white plates from benzene – light petroleum, m.p.
195-196°.

Found: C, 60.63 ; H, 4.02 ; N, 10.70 %

$C_{13}H_{10}O_4N_2$ requires   C, 60.45 ; H, 3.81 ; N, 10.80 %

ω -Hydroxy-2-phenoxy-5-nitroacetophenone Sulphate (XIII).

2-Phenoxy-5-nitro-benzoyl chloride was converted into

its diazoketone (XII), a pale yellow viscous oil, which was

treated by sulphuric acid/acetic acid.   Distillation was

not necessary in this case.   The product recrystallised from

aqueous acetic acid as white plates, m.p. 141-142°.

Found: C, 55.45 ; H, 3.46 ; N, 4.67 %

$C_{28}H_{20}N_2O_{12}S$ requires   C, 55.27 ; H, 3.47 ; N, 4.61 %

⍵ -Chloro-2-phenoxy-5-nitroacetophenone (XIV).

The above diazoketone (XII) (5g.) was dissolved in glacial acetic acid (20ml.), which had been saturated with dry hydrogen chloride. A vigorous reaction ensued, after which, addition of water precipitated a solid. This recrystallised from aqueous acetic acid as almost colourless plates, m.p. 105°.

Found: C, 57.95 ; H, 3.74 ; N, 4.85 %

$C_{14}H_{10}NO_4Cl$ requires   C, 57.65 ; H, 3.46 ; N ,4.80 %

The chloracetophenone (1 mol.) was dissolved in ethylene dichloride. The solution was slowly added, at room temperature or at 0°, to a solution of aluminium chloride (1 mol.) in the same solvent. The mixture was left overnight, then poured onto crushed ice. The organic layer was washed with dilute hydrochloric acid and then with water. After drying the solution, the solvent was removed under reduced pressure leaving a gum, from which no crystalline material or derivative could be obtained.

⍵ -Diazo-2-phenylacetophenone (XVIII).

Water (1ml.) was added to potassium hydroxide (30g.) and the mixture heated to 180°. Fluorenone (10g.) was dusted in and the whole heated with efficient stirring at that temperature for one hour. Acidification with dilute mineral acid gave an oil which was isolated and distilled,

giving diphenyl-2-carboxylic acid (XIX) as colourless prisms,

m.p. 111°.   To this acid (10g.), dissolved in anhydrous

benzene (20ml.), was added oxalyl chloride (10g.).   This

mixture was maintained at a temperature of 30° for one hour,

by which time evolution of gas had ceased.   The solvent

and the excess of reagent were removed under reduced pressure.

The residue was shown to be pure enough for the next stage by

quantitative conversion of a sample into the acid amide, pale

yellow needles from ethanol, m.p. 106°.

Treatment of the acid chloride with diazomethane gave

a solid diazoketone (XVIII).

9-Phenanthrol (XVII).

a). ω -Diazo-2-phenylacetophenone (XVIII) underwent

the Arndt-Eistert reaction to afford diphenyl-2-acetic acid (XX).

By the method of Schonberg and Warren [7], this acid was cyclised

to 9-phenanthrol via 9-phenanthryl acetate (XXI) by treatment

with acetic anhydride and zinc chloride, followed by subsequent

alkaline hydrolysis.

b). The diazoketone (XVIII) was treated with the 10%

solution of sulphuric acid/acetic acid in the normal manner. The

product, precipitated by water, was purified by reprecipitation

from dilute alkali solution and recrystallisation from
benzene, giving pinkish brown needles, m.p. 154°.

Mixed m.p. with product from (a), 153-154°.

These compounds also give the same picrate, m.p. 185°.

o-(2:5-Dimethoxyphenyl)benzoyl chloride (XXII, R'' = OCH$_3$ R = COCl).

A sample of 2:5-dimethoxydiphenyl-2'-carboxylic acid
(XXII R' = OCH$_3$ R = COOH) was recrystallised from methanol
to a constant m.p., 155°.

Treatment with oxalyl chloride at 30° for one hour
afforded a fairly pure sample of the acid chloride, pale yellow
needles, m.p. 62-63°, which was characterised as the acid amide,
m.p. 138-139°, white platelets from benzene-light petroleum.

Found: C, 70.11 ; H, 5.58 ; N, 5.25 %

C$_{15}$H$_{15}$NO$_3$ requires   C, 70.09 ; H, 5.88 ; N, 5.44 %

2:5-Dimethoxydiphenyl-2'-acetic acid (XXII, R' = OCH$_3$ R= CH$_2$COOH).

The acid chloride (XXII, R' = OCH$_3$ R = COCl) was
converted into the diazoketone (XXII, R' = OCH$_3$ R = COCHN$_2$) by
the standard method.   This was rearranged by the same Arndt-
Eistert reaction as was the non-methoxylated compound, to give
the substituted acetic acid which crystallised as colourless
needles, m.p. 129° from benzene-light petroleum.   Yield 66%.

Found: C, 70.33 ; H, 6.03 %

C$_{16}$H$_{16}$O$_4$ requires   C, 70.50 ; H, 5.92 %

This acid was treated with oxalyl chloride to give an oily acid chloride (XII, R = CH_2COCl) which gave an acid amide, as white needles, m.p. 98°, from benzene–light petroleum.

Found: C, 70.87 ; H, 6.50 ; N, 5.16 %

$C_{16}H_{17}NO_3$ requires   C, 70.83 ; H, 6.13 ; N, 5.16 %

Unsuccessful attempts to ring–close the acid or the acid chloride included treatment of the acid (i) with polyphosphoric acid, (ii) by the Schonberg and Warren method, and (iii) treatment of the acid chloride with aluminium chloride in ethylene dichloride.

The diazoketone (1g.) was treated with a 10% solution of sulphuric acid in acetic acid (5ml.), but only a black amorphous solid resulted.

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