"Sulphur Extrusion"

A Thesis for the Degree of Doctor of Philosophy

by

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Part One: Extrusion of Sulphur from Derivatives of Dibenzo[b,f]thiepin.

Part Two: The Interaction of Hydrazoic Acid and Thioxanthenylium Salts.

Part Three: Naphtho[2′:3′-4:5]thiepins.

Addendum: 2-Nitrodibenz[b,f]oxepin-10:11-dicarboxylic Anhydride.

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EXTRUSION OF SULPHUR. PART I. FORMATION OF PHENANTHRENES FROM DIBENZO(b,f)THIEPINS

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758. *Extrusion of Sulphur. Part I. Formation of Phenanthrenes from Dibenzo*[b,f]*thiepins.*

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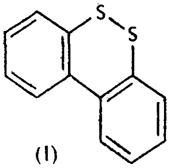
Derivatives of dibenzo[*b,f*]thiepin are prepared from 2-arylthio-5-nitrobenzaldehydes *via* 2-arylthio-5-nitrophenylpyruvic acids and yield phenanthrene derivatives by extrusion of sulphur.

A NUMBER of isolated observations contribute to the view that a thia-atom is fairly readily extruded from a heterocycle if the ring contraction involved leads to an aromatic structure. For example, phenothiazine[1] and several of its benzo-derivatives[2] when heated with copper yield the corresponding carbazoles. The reported similar conversion of phenoxathiin into dibenzofuran[3] has not been confirmed,[4] but thianthren[5] and the cyclic disulphide (I)[6] each yields dibenzothiophen. Thianthrens are thermally stable compounds but *p*-dithiins of type (II; R = H, CHO, or NO_2) are converted by heat or by treatment with phosphorus oxychloride into derivatives of thiophen.[7] A particularly ready extrusion is found for the compound (III) which yields naphthalene-2 : 3-dicarboxylic acid when heated in aqueous methanol.[8] That extrusion is not restricted to the bivalent sulphur atom is shown by the preferential elimination of the oxidised sulphur from *p*-dithiin 1 : 1-dioxides,[7] from thianthren 5-oxide,[9] and from cyclic thiolsulphonates allied to the disulphide (I).[10] Moreover, the *endo*-sulphones which are presumably formed as adducts by the interaction of certain thiophen 1 : 1-dioxides and acetylenic dienophils, decompose *in situ* with elimination of sulphur dioxide and formation of benzene derivatives.[11] To these examples of sulphur extrusion we now add the conversion of certain dibenzo[*b,f*]thiepins into phenanthrenes by the action of heat in presence of copper.



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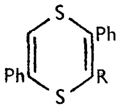

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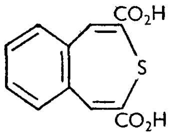

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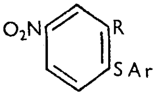

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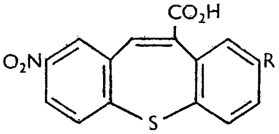

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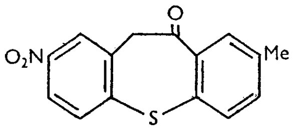

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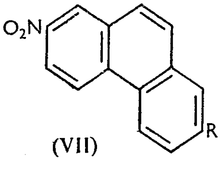

(VII)

Derivatives of dibenzo[*b,f*]thiepin were prepared from 2-arylthio-5-nitrobenzaldehydes (IV; R = CHO) by reactions which closely correspond to those described for the synthesis of dibenz[*b,f*]oxepins.[12] In general the intermediate 2-arylthio-5-nitrophenylpyruvic acids (IV; R = $CH_2{\cdot}CO{\cdot}CO_2H$) were less smoothly cyclised by polyphosphoric acid than were their 2-aryloxy-analogues, and use of hydrobromic acid in acetic acid was sometimes preferred. Satisfactory yields of the carboxylated thiepin, cf. (V), were obtained from the pyruvic acid (IV; R = $CH_2{\cdot}CO{\cdot}CO_2H$) where the aryl group (Ar) was phenyl, *p*-tolyl, or 1-naphthyl, but the reaction failed when the aryl group was *p*-methoxyphenyl or 2-naphthyl. 5-Nitro-2-*p*-tolylthiophenylpyruvic acid was converted, *via* its oxime and the derived benzyl cyanide, into 5-nitro-2-*p*-tolylthiophenylacetic acid which was cyclised to the ketone (VI).

When the thiepin (V; R = Me) was heated with copper in quinoline decarboxylation was accompanied by extrusion of sulphur. That the product was a phenanthrene derivative followed from its oxidation, without loss of carbon, first to a phenanthraquinone and then to a derivative of diphenic acid. It is formulated as 2-methyl-7-nitrophenanthrene (VII; R = Me), other structures conceivably formed by union of the aryl nuclei at centres not originally linked to sulphur being considered unlikely. This is supported by the identification of 2-nitrophenanthrene (VII; R = H) as the product of a similar reaction applied to the thiepin (V; R = H). 2-Nitrophenanthrene was first prepared impure by Schmidt and Heinle[13] and was recently obtained pure by Bavin and Dewar.[14] Our specimen had the m. p. recorded by the latter workers and was further characterised by oxidation to the known 2-nitrophenanthraquinone.[15]

Despite the close homologous relation between the two thiepins (V; R = H) and (V; R = Me) there was an appreciable difference in the ease with which they were converted into phenanthrene derivatives. Treatment of the thiepincarboxylic acid (V; R = H) under various conditions usually afforded 2-nitrodibenzo[*b,f*]thiepin, with varying small amounts of 2-nitrophenanthrene and of 2-nitro-9-phenanthroic acid. The decarboxylated thiepin (V; R = H, H for CO_2H) was likewise convertible into 2-nitrophenanthrene, but again in poor yield. On the other hand the thiepincarboxylic acid (V; R = Me) afforded moderately good yields (*ca.* 50%) of 2-methyl-7-nitrophenanthrene and only traces of 2-methyl-8-nitrodibenzo[*b,f*]thiepin were detected. A similar difference was also found when the methyl esters of (V; R = H) and (V; R = Me) were briefly treated with copper in boiling diethyl phthalate. Thereby methyl 2-nitro-9-phenanthroate and methyl 7-methyl-2-nitro-9-phenanthroate were obtained in 39 and 55% yield respectively and, having regard to reliability and ease of manipulation, this appears at present to be the best pathway from the dibenzothiepin to the phenanthrene series.

EXPERIMENTAL

Throughout petroleum refers to light petroleum (b. p. 60—80°).

5-*Nitro*-2-p-*tolylthiophenylpyruvic Acid*.—5-Nitro-2-*p*-tolylthiobenzaldehyde[16] (1 mol.), aceturic acid (1 mol.), and fused sodium acetate (1 mol.) were heated with acetic anhydride under reflux (1 hr.). The solution was cooled and, after 15 hr., afforded 2-*methyl*-4-(5-*nitro*-2-p-*tolylthiobenzylidene*)-5-*oxazolone*, m. p. 188—189° (from petroleum–benzene; yield 55%) (Found: C, 61·1; H, 4·0. $C_{18}H_{14}O_4N_2S$ requires C, 61·0; H, 3·95%). The pure oxazolone (0·3 g.) was heated (15 hr.) with a mixture of acetic acid (7·5 c.c.), concentrated hydrochloric acid (2 c.c.), and water (4 c.c.) affording 5-*nitro*-2-p-*tolylthiophenylpyruvic acid* as lemon-yellow crystals, m. p. 143° (from benzene–methanol; yield 90%) (Found: C, 57·8; H, 4·0; N, 4·2. $C_{16}H_{13}O_5NS$ requires C, 58·0; H, 3·9; N, 4·2%). The *oxime* had m. p. 169° (decomp.) (from benzene–methanol) (Found: C, 55·6; H, 4·2. $C_{16}H_{14}O_5N_2S$ requires C, 55·5; H, 4·05%).

5-*Nitro*-2-p-*tolylthiophenylacetic Acid*.—The foregoing oxime (3 g.), when heated with acetic anhydride (60 c.c.) for 2 hr. followed by concentration of the solution *in vacuo*, afforded 5-*nitro*-2-p-*tolylthiobenzyl cyanide*, m. p. 80° (from benzene–petroleum; yield 60%) (Found: C, 63·2; H, 4·4. $C_{15}H_{12}O_2N_2S$ requires C, 63·3; H, 4·2%). This (10 g.) was hydrolysed (9 hr.) in hot acetic acid (100 c.c.) and hydrochloric acid (100 c.c.) giving 5-*nitro*-2-p-*tolylthiophenylacetic acid*, m. p. 126° (from benzene–petroleum; yield 70%) (Found: C, 59·5; H, 4·3. $C_{15}H_{13}O_4NS$ requires C, 59·4; H, 4·3%).

2-p-*Tolylthiophenylacetic Acid*.—A solution of the 5-nitro-compound (0·5 g.) in water (60 c.c.) containing potassium carbonate (0·35 g.) was hydrogenated with palladised strontium carbonate as catalyst. Neutralisation of the filtered solution afforded 5-*amino*-2-p-*tolylthiophenylacetic acid*, m. p. 127° (from ethanol–water) (Found: C, 66·2; H, 5·4. $C_{15}H_{15}O_2NS$ requires C, 65·9; H, 5·5%), which formed the *hydrochloride*, m. p. 209° (decomp.), from dilute hydrochloric acid (Found: C, 58·0; H, 5·5. $C_{15}H_{16}O_2NClS$ requires C, 58·1; H, 5·2%). A diazotised solution of the amino-acid in hydrochloric acid was treated with an excess of hypophosphorous acid. After 20 hr. the precipitated 2-p-*tolylthiophenylacetic acid* was collected as straw-coloured needles, m. p. 112° (from benzene–petroleum) (Found: C, 69·9; H, 5·4. $C_{15}H_{14}O_2S$ requires C, 69·8; H, 5·4%).

10 : 11-*Dihydro*-8-*methyl*-2-*nitro*-10-*oxodibenzo*[b,f]*thiepin* (VI) was obtained (yield, 75%) as yellow needles, m. p. 161° (from methanol), by cyclisation of 5-nitro-2-*p*-tolylthiophenylacetic acid by polyphosphoric acid (1½ hr. at 100°) (Found: C, 63·4; H, 4·1. $C_{15}H_{11}O_3NS$ requires C, 63·15; H, 3·9%). Its solution in benzene was colourless. With hydroxylamine hydrochloride in pyridine it afforded the *oxime*, m. p. 191° (from benzene–petroleum) (Found: C, 60·3; H, 4·0. $C_{15}H_{12}O_3N_2S$ requires C, 60·0; H, 4·0%).

8-*Methyl*-2-*nitrodibenzo*[b,f]*thiepin*-10-*carboxylic Acid* (V; R = Me).—(*a*) 5-Nitro-2-*p*-tolylthiophenylpyruvic acid was cyclised in polyphosphoric acid first at 160° (5 min.) and then at 100° (2 hr.). Addition of water to the cooled mixture gave the thiepin, m. p. 268° (from benzene–methanol; yield, 70%). (*b*) A solution of the pyruvic acid (10 g.) in a mixture of hydrobromic acid (48%; 20 c.c.) and acetic acid (35 c.c.) was heated under reflux for 5 hr. After 12 hr. at 18° the resultant greenish-brown needles (8·8 g.; m. p. 269°) were recrystallised (charcoal) from acetic acid affording the *thiepin*, m. p. 276° (Found: C, 61·1; H, 3·5. $C_{16}H_{11}O_4NS$ requires C, 61·3; H, 3·5%). Heated for 12 hr. with methanol (250 c.c.) and concentrated sulphuric acid (2 c.c.) the thiepincarboxylic acid (5 g.) gave the corresponding *methyl ester*, m. p. 183° (from methanol–methyl acetate) (Found: C, 62·6; H, 4·0. $C_{17}H_{13}O_4NS$ requires C, 62·4; H, 4·0%).

2-*Methyl*-7-*nitrophenanthrene* (VII; R = Me).—(*a*) 8-Methyl-2-nitrodibenzothiepin-10-carboxylic acid (2 g.), copper bronze (10 g.), and pure quinoline (50 c.c.) were heated under reflux for 4 hr. The cooled mixture was diluted with benzene and filtered, and the filtrate washed with dilute sulphuric acid, again filtered, and then washed in turn with water, aqueous sodium carbonate, and water. 2-*Methyl*-7-*nitrophenanthrene* was recovered from the solution as pale yellow crystals, m. p. 192° (from benzene–methanol) (Found: C, 75·85; H, 4·6. $C_{15}H_{11}O_2N$ requires C, 75·95; H, 4·6%). A solution of the compound in hot acetic acid was slowly treated with an aqueous solution of chromic acid (in slight excess) affording 2-*methyl*-7-*nitrophenanthraquinone*, m. p. 230° (decomp.) (from benzene–methanol) (Found: C, 67·5; H, 3·5. $C_{15}H_9O_4N$ requires C, 67·4; H, 3·4%). To a suspension of this quinone (0·2 g.) in methanol (2 c.c.) containing hydrogen peroxide (30%; 0·5 c.c.) 4N-sodium hydroxide (1 c.c.) was added, with thorough shaking, and thereafter more hydrogen peroxide (1 c.c.). After 15 hr. the methanol was removed and the residue acidified affording 4-*methyl*-4′-*nitrodiphenic acid*, m. p. 186° (from benzene–methanol) (Found: C, 59·7; H, 4·0. $C_{15}H_{11}O_6N$ requires C, 59·8; H, 3·7%).

(*b*) The thiepincarboxylic acid (V; R = Me) (0·5 g.), copper bronze (0·5 g.), and diethyl phthalate (3 c.c.) were heated (30 min.) at 250° under nitrogen. The mixture was diluted with benzene and filtered through charcoal, and the solvents distilled off *in vacuo*. The resultant dark viscous oil was extracted several times with petroleum, and the combined extracts were chromatographed on alumina and eluted with petroleum. Successive eluates afforded in small quantity (i) 8-*methyl*-2-*nitrodibenzo*[b,f]*thiepin* as yellow needles, m. p. 117° (from methanol) (Found: C, 67·0; H, 3·8; N, 5·1. $C_{15}H_{11}O_2NS$ requires C, 66·9; H, 4·1; N, 5·2%); (ii) a solid mixture which was not resolved by crystallisation; (iii) 2-methyl-7-nitrophenanthrene, m. p. and mixed m. p. 192°.

Methyl 7-*Methyl*-2-*nitro*-9-*phenanthroate*.—The methyl ester (0·5 g.) of compound (V; R = Me), copper bronze (0·5 g.), and diethyl phthalate (3 c.c.) were boiled for 7½ min. under nitrogen. The cold mixture was diluted with benzene, poured on to (alkali-free) alumina and eluted with benzene. Addition of petroleum to the concentrated eluate gave a yellow solid from which, after renewed chromatography, *methyl* 7-*methyl*-2-*nitro*-9-*phenanthroate* was obtained as cream-coloured crystals (0·25 g.), m. p. 188° (from methyl acetate) (Found: C, 69·3; H, 4·5. $C_{17}H_{13}O_4N$ requires C, 69·1; H, 4·4%). It was hydrolysed by boiling acetic–hydrochloric acid to 7-*methyl*-2-*nitro*-9-*phenanthroic acid*, m. p. 291° (from acetonitrile) (Found: C, 68·2; H, 3·8. $C_{16}H_{11}O_4N$ requires C, 68·3; H, 3·9%).

5-*Nitro*-2-*phenylthiobenzaldehyde*.—To a solution of 2-chloro-5-nitrobenzaldehyde (45 g.) and thiophenol (25 g.) in ethanol (500 c.c.) and water (200 c.c.) stirred and maintained at 60°, potassium carbonate was added in portions (18 × 1 g.) during 20 min. and stirring was continued for 40 min. The crystalline product was washed with water affording 5-*nitro*-2-*phenylthiobenzaldehyde*, m. p. 105° (from ethyl acetate; yield, 48 g.) (Found: C, 60·4; H, 3·5. $C_{13}H_9O_3NS$ requires C, 60·2; H, 3·5%).

2-*Nitrodibenzo*[b,f]*thiepin*-10-*carboxylic Acid* (V; R = H).—5-Nitro-2-phenylthiobenzaldehyde and aceturic acid afforded (yield, 55%) 2-*methyl*-4-(5-*nitro*-2-*phenylthiobenzylidene*)-5-*oxazolone*, m. p. 190° (from benzene) (Found: C, 60·0; H, 3·8. $C_{17}H_{12}O_4N_2S$ requires C, 60·0;

H, 3·5%), which was hydrolysed to 5-*nitro*-2-*phenylthiophenylpyruvic acid*, m. p. 146° (from benzene–petroleum; yield, 90%) (Found: C, 56·9; H, 3·55. $C_{15}H_{11}O_5NS$ requires C, 56·8; H, 3·5%). This acid was cyclised by polyphosphoric acid (5 min. at 160°, then 2 hr. at 100°), affording 2-*nitrodibenzo*[b,f]*thiepin*-10-*carboxylic acid*, m. p. 248° (from benzene–methanol; yield, 65%) (Found: C, 60·4; H, 3·3. $C_{15}H_9O_4NS$ requires C, 60·2; H, 3·0%). Cyclisation by procedure (*b*) described for the analogue (V; R = Me), but here prolonged to 12 hr., gave a purer product in 75% yield. Esterification as described for the analogue gave the *methyl ester*, m. p. 156° (from methyl acetate–methanol) (Found: C, 61·5; H, 3·5. $C_{16}H_{11}O_4NS$ requires C, 61·3; H, 3·5%).

Decomposition of 2-*Nitrodibenzo*[b,f]*thiepin*-10-*carboxylic Acid* (V; R = H).—(*a*) When the thiepincarboxylic acid was treated (4 hr.) with copper bronze or cuprous oxide in boiling quinoline, as described under (*a*) for compound (VII; R = Me), 2-*nitrodibenzo*[b,f]*thiepin* was isolated as yellow crystals, m. p. 110° (from methanol; yield, 45—50%) (Found: C, 65·6; H, 3·7. $C_{14}H_9O_2NS$ requires C, 65·9; H, 3·5%).

(*b*) The same thiepin, m. p. and mixed m. p. 110°, was the only crystalline product (yield, 49%) when the acid was treated as described under (*b*) for compound (VII; R = Me).

(*c*) When the reaction time in experiment (*a*), with cuprous oxide, was extended to 9 hr. and the product before chromatography was separated into basic, neutral, and acidic fractions, the neutral fraction afforded a small quantity of yellow needles, m. p. 117° depressed by admixture with 2-nitrodibenzothiepin and unchanged by admixture with 2-nitrophenanthrene, cf. (*d*).

(*d*) The thiepincarboxylic acid (2 g.) was placed under a coil of freshly-reduced copper wire (10 g.) and the whole heated (5 min.) at 300—310° in nitrogen. Products of the vigorous reaction were trapped and washed out in boiling benzene from which, after concentration, a carboxylic acid crystallised, cf. (*f*). The filtrate, purified on alumina and eluted with benzene, afforded 2-nitrophenanthrene (0·07 g.), micro-m. p. 120° (from benzene) (Found: C, 75·5; H, 4·1; N, 6·45. Calc. for $C_{14}H_9O_2N$: C, 75·3; H, 4·1; N, 6·3%). This, on being oxidised with chromic acid in acetic acid, gave 2-nitrophenanthraquinone which was identified by its infrared spectrum and mixed micro-m. p., 265—269°, with an authentic specimen prepared as described by Schmidt and Spoun.[15]

(*e*) The thiepincarboxylic acid (0·5 g.) and copper bronze (0·4 g.) were heated in boiling diethyl phthalate (2 c.c.) for 15 min. The cooled mixture was diluted with benzene, filtered, washed with aqueous sodium carbonate and then with water, and refiltered, hot, through charcoal. The tarry residue, obtained by removing the solvents *in vacuo*, was extracted with boiling methanol from which 2-nitrophenanthrene was recovered and purified by chromatography (0·07 g.; m. p. 120°). When the reaction mixture was heated for only 5 min., 2-nitrodibenzothiepin was obtained.

(*f*) The carboxylic by-product from (*d*), combined with the acidic fraction from (*c*), afforded 2-*nitro*-9-*phenanthroic acid* as pale yellow needles, micro-m. p. 266° (from acetic acid) (Found: C, 67·5; H, 3·3. $C_{15}H_9O_4N$ requires C, 67·4; H, 3·4%). This was identified by oxidation to 2-nitrophenanthraquinone and also by comparison with a sample prepared from the methyl ester (below).

Decomposition of 2-*Nitrodibenzo*[b,f]*thiepin*.—The thiepin (0·25 g.) and copper bronze (0·25 g.) were heated in boiling diethyl phthalate (1·5 c.c.) for 7½ min. under nitrogen. Dilution of the cold mixture with benzene, followed by filtration through charcoal and concentration *in vacuo*, gave a red oil which partially solidified when rubbed with methanol. The solid, purified by chromatography in petroleum on alumina, afforded 2-nitrophenanthrene (0·04 g.), m. p. and mixed m. p. 120°, and some unchanged thiepin.

Methyl 2-*nitro*-9-*phenanthroate*, cream-coloured crystals, m. p. 161° (from methyl acetate), was obtained in 39% yield from methyl 2-nitrodibenzo[*b*,*f*]thiepin-10-carboxylate by the method described for the 7-methyl homologue (Found: C, 68·6; H, 3·8. $C_{16}H_{11}O_4N$ requires C, 68·3; H, 3·9%). The ester was hydrolysed by boiling acetic–hydrochloric acid to 2-nitro-9-phenanthroic acid, m. p. and mixed m. p. 265°.

2-p-*Methoxyphenylthio*-5-*nitrophenylpyruvic Acid*.—2-p-*Methoxyphenylthio*-5-*nitrobenzaldehyde*, m. p. 89° (from aqueous acetic acid), prepared from 2-chloro-5-nitrobenzaldehyde and sodium *p*-methoxyphenyl sulphide (Found: C, 58·1; H, 4·1. $C_{14}H_{11}O_4NS$ requires C, 58·1; H, 3·8%), was converted by reaction with aceturic acid into 2-*methyl*-4-(2-p-*methoxyphenylthio*-5-*nitrobenzylidene*)-5-*oxazolone*, m. p. 206° (from benzene) (Found: C, 58·5; H, 4·0. $C_{18}H_{14}O_5N_2S$ requires C, 58·4; H, 3·8%), and hence into 2-(p-*methoxyphenylthio*)-5-*nitrophenyl*-

pyruvic acid, m. p. 174° (from benzene–methanol) (Found: C, 55·1; H, 3·7. $C_{16}H_{13}O_6NS$ requires C, 55·3; H, 3·7%), which formed an *oxime*, m. p. 167° (decomp.) (from benzene–methanol) (Found: C, 52·9; H, 4·1. $C_{16}H_{14}O_6N_2S$ requires C, 53·0; H, 3·9%), but could not be cyclised by polyphosphoric acid.

2-2′-*Naphthylthio*-5-*nitrophenylpyruvic Acid*.—2-2′-*Naphthylthio*-5-*nitrobenzaldehyde*, m. p. 108° (from acetic acid), prepared from 2-chloro-5-nitrobenzaldehyde and naphthalene-2-thiol (Found: C, 66·25; H, 3·6. $C_{17}H_{11}O_3NS$ requires C, 66·0; H, 3·6%), was converted into 2-*methyl*-4-(2-2′-*naphthylthio*-5-*nitrobenzylidene*)-5-*oxazolone*, m. p. 193° (from benzene–petroleum) (Found: C, 64·65; H, 3·8. $C_{21}H_{14}O_4N_2S$ requires C, 64·6; H, 3·6%), and hence into 2-2′-*naphthylthio*-5-*nitrophenylpyruvic acid*, m. p. 153° (from benzene) (Found: C, 62·35; H, 3·8. $C_{19}H_{13}O_5NS$ requires C, 62·1; H, 3·5%). Attempts to cyclise this acid by polyphosphoric acid failed, starting material being recovered in diminished quantity.

10-*Nitrobenzo*[b]*naphtho*[2,1-f]*thiepin*-7-*carboxylic Acid*.—2-1′-*Naphthylthio*-5-*nitrobenzaldehyde*, m. p. 123° (from acetic acid), prepared from 2-chloro-5-nitrobenzaldehyde and naphthalene-1-thiol (Found: C, 66·2; H, 3·6%), was converted by reaction with aceturic acid into 2-*methyl*-4-(2-1′-*naphthylthio*-5-*nitrobenzylidene*)-5-*oxazolone*, m. p. 195° (from benzene–petroleum) (Found: C, 64·55; H, 3·8%), and hence into 2-1′-*naphthylthio*-5-*nitrophenylpyruvic acid*, m. p. 171° (from benzene–methanol) (Found: C, 62·4; H, 3·7%), which afforded the *oxime*, m. p. 194° (from benzene–methanol) (Found: C, 59·7; H, 3·8. $C_{19}H_{14}O_5N_2S$ requires C, 59·7; H, 3·7%). When the pyruvic acid in polyphosphoric acid was heated first at 230° for a few minutes and then at 100° for 3 hr. it afforded 10-*nitrobenzo*[b]*naphtho*[2,1-f]*thiepin*-7-*carboxylic acid* as yellow needles m. p. 274° (decomp.) (from benzene–methanol) (Found: C, 65·55; H, 3·5. $C_{19}H_{11}O_4NS$ requires C, 65·3; H, 3·2%).

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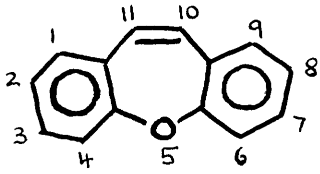
PART ONE

The Extrusion of Sulphur from Derivatives of Dibenzo[b,f]thiepin

Contents



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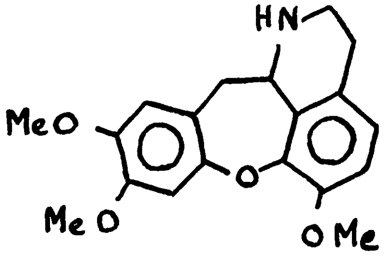

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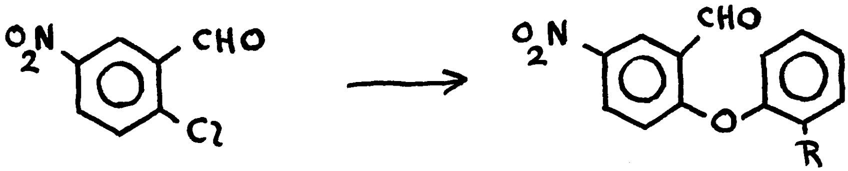

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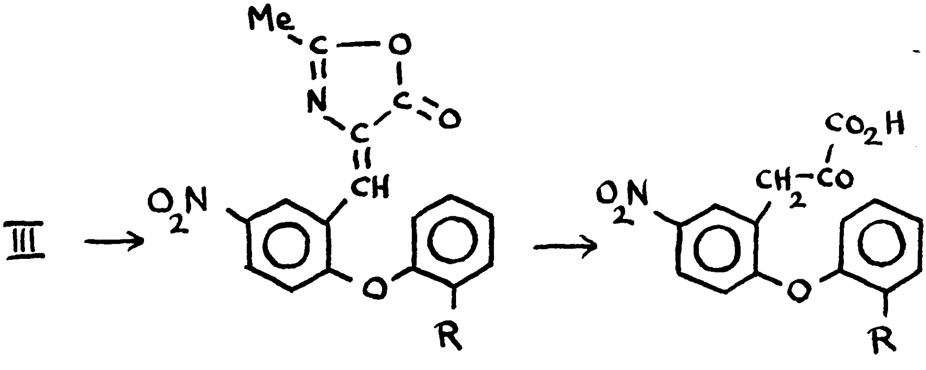

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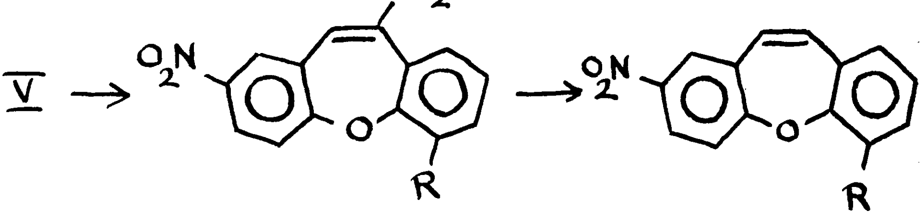


VI

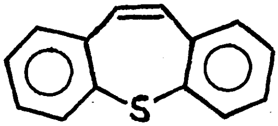
VII

INTRODUCTION

An interest in the dibenz [b,f] oxepin (I) ring system was stimulated by the discovery of a 10:11-dihydrodibenz [b,f] oxepin unit in the substance cularine (II), an alkaloid obtained by Manske[1] from fumariaceous plants.

In this connection Summers[2] developed a synthesis of 2-nitrodibenz [b,f] oxepins (VII, R=H, OMe) which started from 2-chloro-5-nitrobenzaldehyde. Displacement of chloride by a phenoxide ion, to give the ether (III), followed by treatment with aceturic acid under the conditions used by Galat[3] in a modification of Erlenmeyer's classical synthesis, afforded the oxazolone (IV) which was then hydrolysed to the corresponding pyruvic acid (V). The oxepin ring was formed by treatment of the latter substance with polyphosphoric acid. Decarboxylation of the resulting 2-nitrodibenz [b,f] oxepin-10-carboxylic acid (VI) afforded the final product.

The successful preparation of the dibenz [b,f] oxepin ring system by this route invited an attempt to apply a similar method to the synthesis of the thio-analogue viz. the dibenzo[b,f] thiepin (VIII) system.



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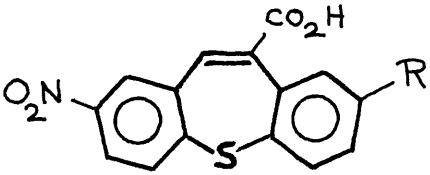
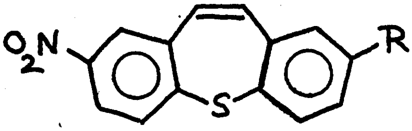


IX

The synthesis of 8-methyl-2-nitrodibenzo [b,f] thiepin-10-carboxylic acid (IX, R=Me) was successfully accomplished in this way, and is discussed in detail in another section. When Summers treated a boiling solution of this substance in quinoline with copper, however, he did not obtain the expected product viz. 8-methyl-2-nitrodibenzo[b,f]-thiepin (X, R=Me).



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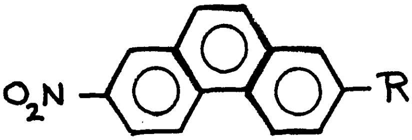
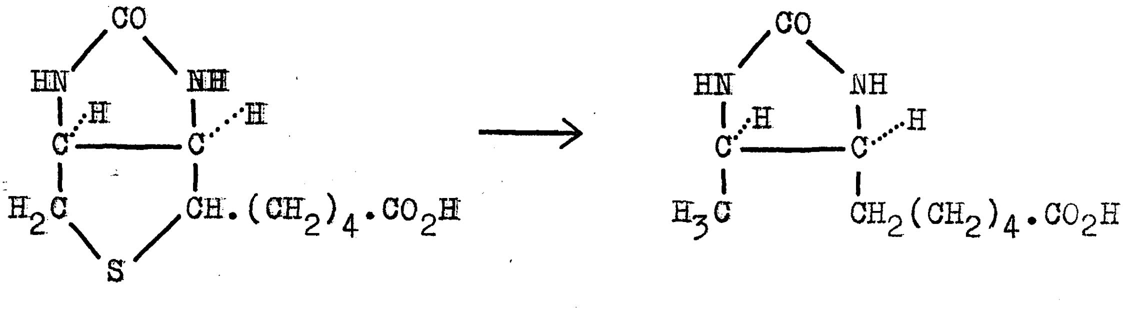


XI

Instead, it was found that extrusion of sulphur had accompanied decarboxylation, and the product (m.p. 187°), of empirical formula $C_{15}H_{11}NO_2$, was given the structure of 7-methyl-2-nitro-phenanthrene (XI, R=Me) after it had been proved to be a phenanthrene by successive oxidations, in the first instance to a phenanthrene-9:10-quinone, from which a diphenic acid was obtained in a second step.

This result was surprising, because the straightforward elimination of a thia atom, accompanied by the direct union of the two atoms to which the latter was attached, does not appear to be a widely-recognised occurrence. For example, Tarbell and Harnish[4], in a quite recent (1951) review article entitled "Cleavage of the Carbon-Sulphur Bond in Divalent Sulphur Compounds," include only four references to such events, although many more were available at the time, as will appear from an inspection of the examples quoted in this thesis. By way of contrast, the hydrogenolytic elimination of sulphur by means of Raney nickel, involving the attachment of a hydrogen atom to each of the atoms from which the sulphur atom has become detached, is well known. This reaction, known after

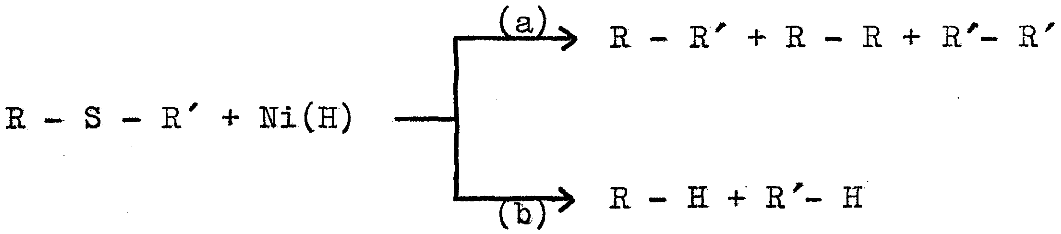
Mozingo, was first used (1942) by du Vigneaud and Mozingo[5] in the investigation of β-biotin:



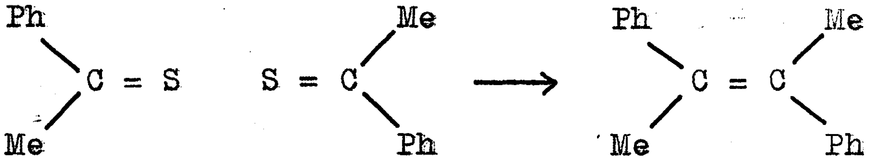
β-Biotin

Desthio-β-biotin

In his original paper (1943) on the hydrogenolysis of sulphur compounds, Mozingo[6] mentions that two possible courses of reaction are open, according to the following scheme:

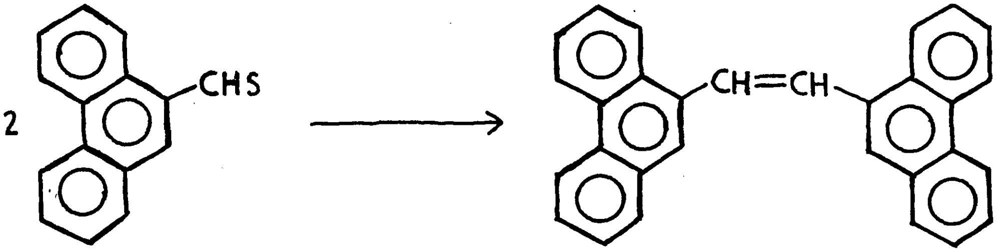


However reaction (a), which he refers to as a Wurtz-type reaction, was not observed by Mozingo. A year later Campaigne[7] discovered a case, which, formally as least, is similar to the Wurtz reaction. A suspension of Raney nickel in boiling xylene brought about the elimination of sulphur



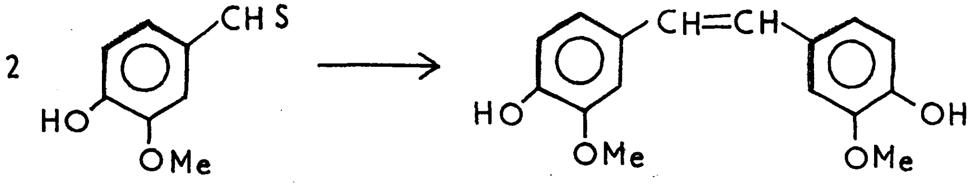
XII

between two molecules of thioacetophenone, with the formation of α:α′-dimethylstilbene (XII). Shortly afterwards Bergmann[8] reported the conversion of 9-thioformylphenanthrene (XIII) to the ethylene (XIV) by treatment with Raney nickel



XIII XIV

There is nothing novel about these transformations. In 1928 Schönberg[9] prepared tetraphenylethylene from thiobenzophenone by treatment with copper bronze in boiling xylene, and in the same year Staudinger[10] reported the spontaneous conversion of thiobenzophenone to tetraphenylethylene at a temperature of 170-180°. There are analogies also for Bergmann's result: for example[11], 4:4′-dihydroxy-3:3′-dimethoxystilbene (XVI) may be distilled from a mixture of copper



XV

XVI

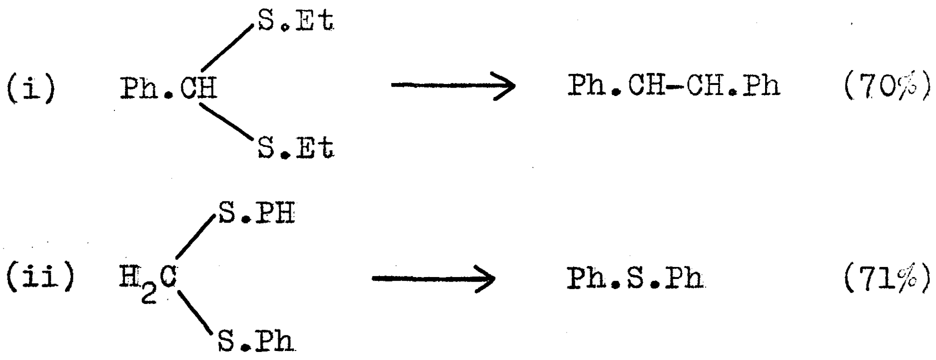
powder and the trimer of 2-methoxy-4-thioformylphenol (XV).

The year 1948 produced the first of a series of papers by Hauptmann[12], in which the desulphurization of representatives from four classes of organic sulphide was described, using a Raney nickel preparation from which most of the adsorbed hydrogen had been driven off by heating under reduced pressure. In all but a few cases the nickel was "de-gassed" at a temperature of 200°. In every case the reaction was carried out at a temperature of 140°, usually by employment of boiling xylene as the solvent. The four classes of sulphide studied were:

A. Mercaptals (i) of benzaldehyde
    (ii) of formaldehyde.
B. Thiol esters of aromatic carboxylic acids.
C. Diphenyl sulphide.
D. Diaryl disulphides.

In view of the reactions of thiocarbonyl compounds recorded above, the response of the diethyl mercaptal of benzaldehyde to this treatment need not cause surprise; an analogy also exists for the conversion of the diphenyl mercaptal of formaldehyde to diphenyl sulphide, because Baumann and Fromm[13] obtained diethyl sulphide, by heating the diethyl mercaptal of acetone at 160-190°.

A.



(i) $Ph.CH\begin{array}{l}S.Et\\S.Et\end{array} \longrightarrow Ph.CH\text{-}CH.Ph$ (70%)

(ii) $H_2C\begin{array}{l}S.PH\\S.Ph\end{array} \longrightarrow Ph.S.Ph$ (71%)

The preparation of diphenyl sulphide in good yield from phenylthiobenzoate (XVII) is much more interesting because there appears to be no analogy

B. $Ph.CO.S.Ph \longrightarrow Ph_2S$ (70%)

XVII

for this reaction. When Raney nickel degassed at 100° (and therefore richer in hydrogen) was used, the result was strikingly different. Under these conditions a moderate yield of diphenyl was obtained:

$Ph.CO.S.Ph \longrightarrow Ph_2$ (40%)

There is an analogy for the latter reaction, albeit a poor one. Anschutz[14] has shown that phenyl cinnamate is decarboxylated

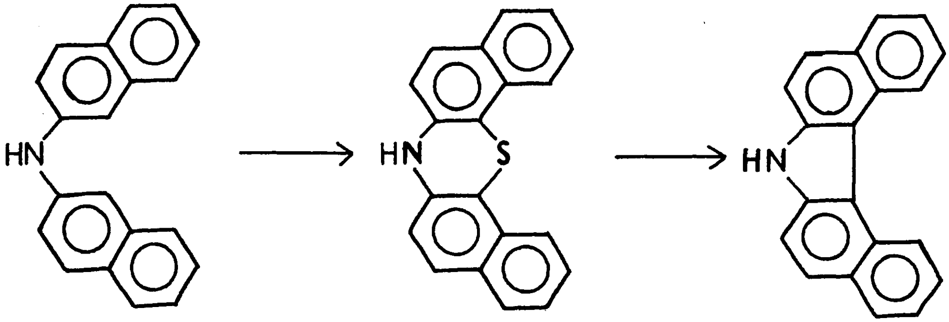
$$PhCH = CH.CO.O.Ph \longrightarrow PhCH = CHPh + CO_2$$

by slow distillation.

Most pertinent of all to the content of this thesis is the effect of the Raney nickel treatment on diphenyl sulphide. Some diphenyl was obtained when nickel which had been degassed at 100° was employed

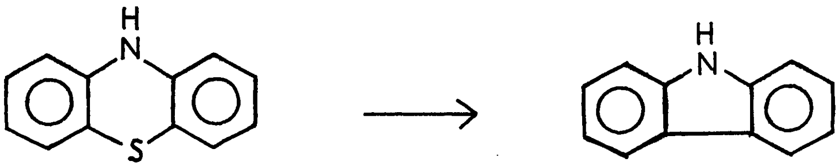
C. $$Ph.S.Ph \longrightarrow Ph_2 \qquad (15\%)$$

but, curiously, there was little reaction with the more thoroughly degassed metal. This is the first true example of the reaction (a) cited as a possibility by Mozingo (see p. 4). Transformations of this kind had however been known long before the days of Raney nickel. The first examples came from the laboratory of Professor Merz (Zurich) and were clearly inspired by him, although his name does not appear at the head of the published articles concerned. Ris (1886)[15] described the desulphurization of a dibenzophenothiazine, which was prepared by heating di-β-naphthylamine with sulphur and probably had the structure (XVIII) by virtue of the greater reactivity of the α-positions in naphthalene.



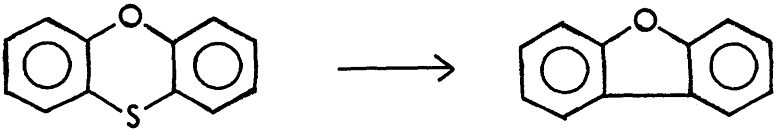
XVIII XIX

The dibenzocarbazole (probably XIX) was obtained by slow distillation under carbon dioxide from a mixture of the dibenzophenothiazine and copper. In the following year Goske[16] described the desulphurization of phenothiazine (XX) itself by boiling with copper for two hours in an atmosphere of coal gas;



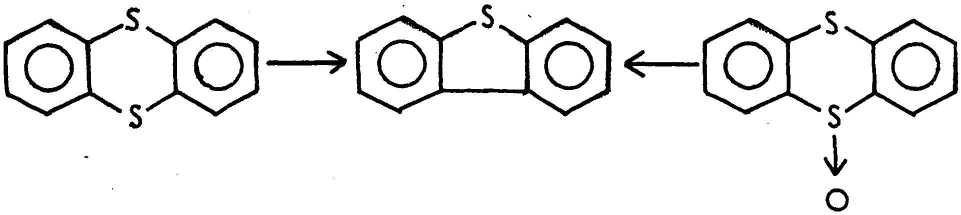
XX

Goske's work was confirmed by Holzmann (1888)[17]. The series was terminated by Kym (1890)[18], who reported the desulphurization of a benzophenothiazine. In 1911 Ferrario[19] reported the formation "avec de très bons rendements" of dibenzofuran from the treatment of phenoxathiin (XXI) with copper at 250°.



XXI

Suter (1936)[20] was unable to confirm this result and Gilman (1940)[21] was likewise unsuccessful in a series of experiments carried out with additives of silver, iron, mercury and zinc as well as copper; Jarrett (1956)[22] recovered phenoxathiin unchanged from its solution in diethyl phthalate after boiling with copper for 140 hr. Cullinane (1937)[23] has described the removal with copper of one atom of sulphur from the molecule of thianthrene (XXII) at its boiling point, and Gilman (1955)[24] has reported a 50% yield of dibenzothiophen from the treatment of thianthrene 5-oxide (XXIII) with butyl lithium at -70°:



XXII XXIII

It is worthy of note that the last of Hauptmann's communications reports the successful deselenization of diphenyl selenide by Raney nickel (degassed at 200°) in boiling benzene.

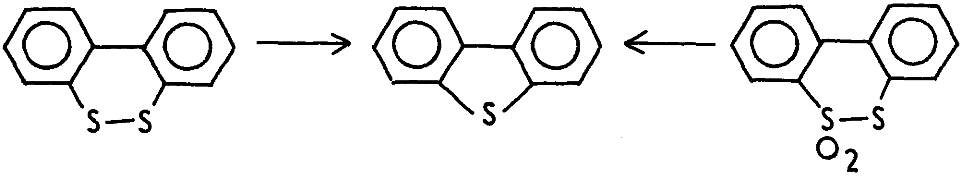
$$Ph.Se.Ph \longrightarrow Ph_2 \quad (77\%)$$

In the same article it is stated that diphenyl is obtained from diphenyl sulphide by treatment with the nickel reagent at 220°, but unfortunately no further details are given.

The results of the Raney nickel treatment of diaryl disulphides are also interesting. Hauptmann obtained an excellent yield of diphenyl sulphide from the corresponding disulphide

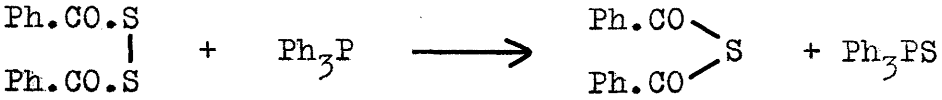
D. Ph.S.S.Ph ⟶ Ph.S.Ph (82%)

under the usual conditions. For this there is considerable precedent. As early as 1874, Graebe[25], attempting to cyclodehydrogenate diphenyl disulphide to dibenzo-o-dithiin (XXIV) by boiling, obtained diphenyl sulphide instead. Later (1928) Barber and Smiles[26] obtained dibenzothiophen by heating a mixture of dibenzo-o-dithiin and copper for two hours at a temperature of 250°. The reaction



XXIV XXV

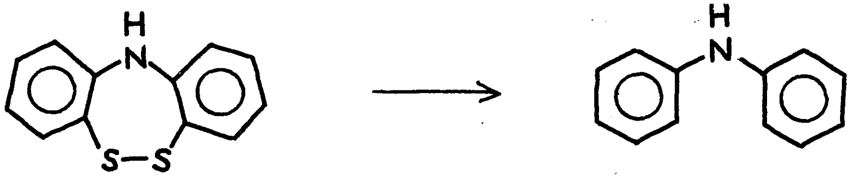
was recently (1956, 1957) extended to various methyl derivatives of dibenzo-o-dithiin by Armarego and Turner[27,28], who have in addition shown that dibenzo-o-dithiin 5:5-dioxide (XXV) loses sulphur dioxide under these conditions. Another example has been provided by Schönberg (1935)^{29}, who showed that triphenylphosphine extruded sulphur from dibenzoyl disulphide (XXVI) with production of dibenzoyl sulphide (XXVII):



$$\begin{array}{l} Ph.CO.S \\ \quad\;\;| \\ Ph.CO.S \end{array} + Ph_3P \longrightarrow \begin{array}{l} Ph.CO \\ Ph.CO \end{array}\!\!>\!S + Ph_3PS$$

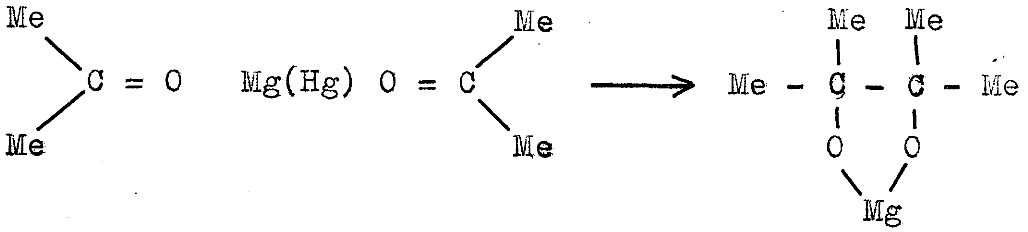
XXVI XXVII

It is interesting that Holzmann (1888)^{17}, in an attempt to make carbazole by heating diphenylamine-2:2′-disulphide (XXVIII) with copper at a temperature of 250°, obtained only diphenylamine:



XXVIII

Since many ketones are reduced to pinacols by metals e.g. the reduction of acetone to pinacol by magnesium amalgam^{30},



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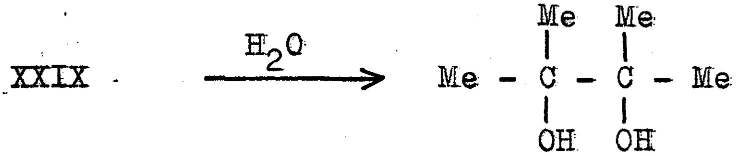
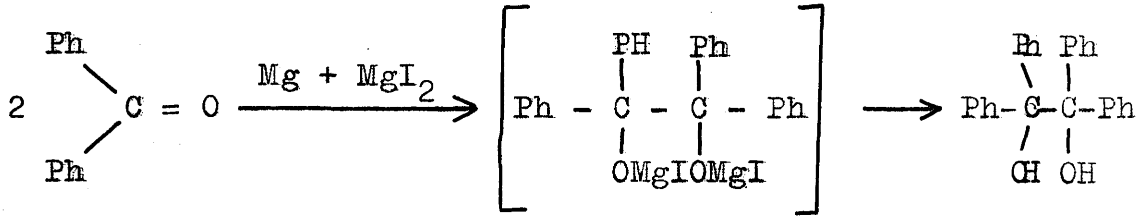
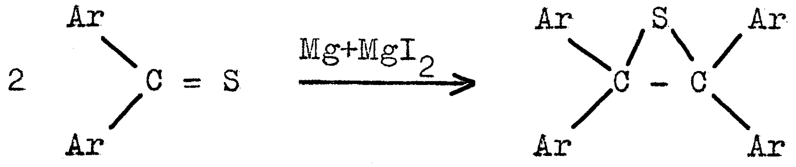


it is quite possible that the previously mentioned conversions of thiocarbonyl compounds into olefins proceed through intermediates analogous to magnesium pinacolate (XXIX). Indeed the magnesium subiodide reagent used by Gomberg and Bachmann[31] to reduce benzophenone to benzopinacol

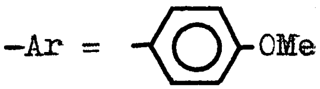


XXX

was found by Schönberg[32] to transform a thiobenzophenone to a tetraphenylethylene sulphide (XXXI):

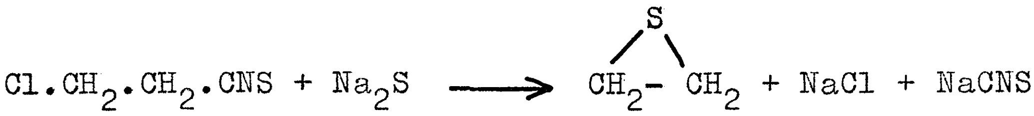


XXXI



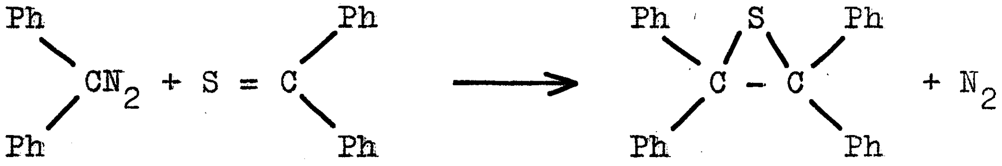
Presumably in this conversion the thio-analogue of the postulated intermediate (XXX) forms the tetraphenylethylene sulphide by elimination of $S(MgI)_2$. Staudinger and Siegwart[33] found that tetraphenylethylene sulphide loses sulphur at a temperature of 175°, giving a quantitative yield of tetraphenylethylene, so that a step by step process of the kind indicated is well supported by the facts available.

The instability of ethylene sulphides has probably much to do with the fact that relatively little study has been made of them; it was not until 1920 that the first 1:2-episulphide was described. In that year Delépine[34] reported the preparation of the parent compound, ethylene sulphide, according to the scheme:



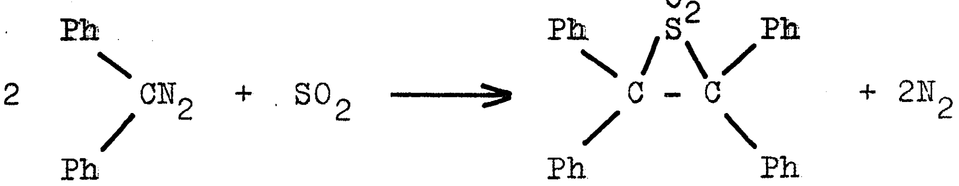
$$Cl.CH_2.CH_2.CNS + Na_2S \longrightarrow CH_2\overset{S}{-}CH_2 + NaCl + NaCNS$$

The product was a colourless liquid which polymerized very readily, but no mention was made of a tendency to form ethylene by loss of sulphur. In the same year Staudinger and Siegwart[33] described the preparation of tetraphenylethylene sulphide from diazodiphenylmethane (XXXII) and thiobenzophenone;



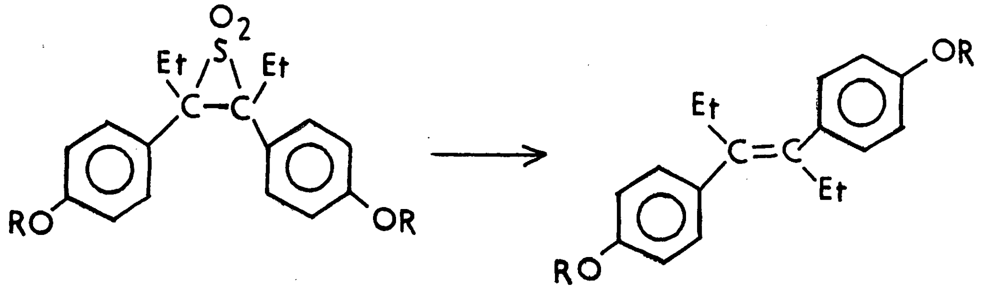
XXXII

The first example of a compound featuring a three-membered ring containing a sulphur atom had however been obtained four years previously. This was tetraphenylethylene sulphone (XXXIII), prepared by Staudinger and Pfenninger[35] from sulphur dioxide and diazodiphenylmethane:



XXXIII

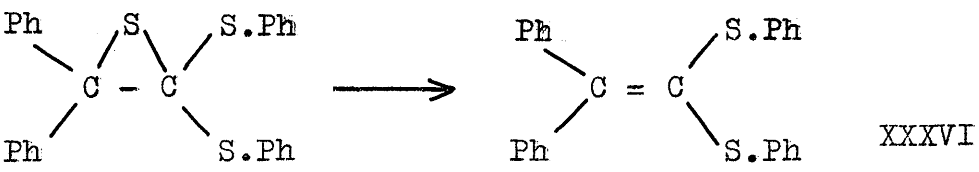
That an ethylene sulphone should be discovered before an ethylene sulphide is interesting, because ethylene sulphones are so very unstable that only one other example is known, the compound (XXXIV, R=Me) employed as an intermediate in their synthesis of



XXXIV XXXV

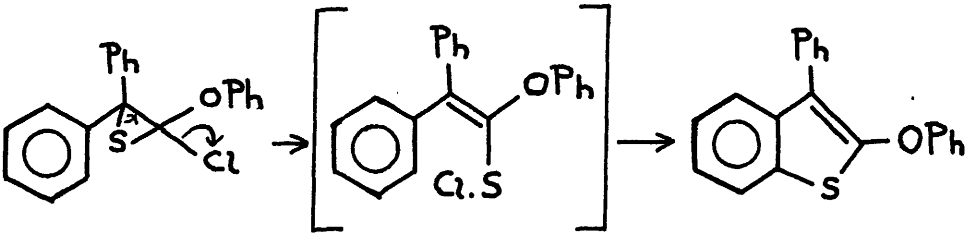
diethylstilboestrol (XXXV, R=H) by v. Vargha and Kovács[36], who prepared it by a process parallel to that of Staudinger. At a temperature of 80-100° both sulphones were smoothly converted by loss of sulphur dioxide to the corresponding olefins. The stability of these sulphones is apparently due to their highly-substituted nature. Attempts to oxidize 1:2-episulphides to the corresponding episulphones have not been successful, not even in the case of tetraphenylethylene sulphide: Staudinger and Siegwart expressly stated that attempts to oxidize the episulphide with nitric acid and potassium permanganate were not successful because the sulphur was too readily extruded.

The pioneer work of Delépine and Staudinger was followed by a lapse of twenty-five years during which ethylene sulphides attracted little attention. Such work as was done in the aliphatic series is reviewed by Culvenor, Davies and Heath[42], and need not concern us here, because purely aliphatic episulphides appear to have little tendency to eliminate the sulphur atom; they are relatively stable to heat and their most outstanding characteristic is a marked tendency to polymerize, more especially when treated with acidic or basic reagents (it is noteworthy that tetraphenylethylene sulphide, which is so thermolabile, has no tendency to polymerize[37]). Of Schönberg's several contributions over this period to the study of aryl-substituted episulphides, two will be mentioned here. The first is included because it illustrates the catalytic action of copper. α-Diphenyl-β-diphenylthioethylene (XXXVI) was obtained by



XXXVI

treatment of its sulphide with copper bronze in boiling benzene; in the absence of copper a temperature of 180-200° was required[38]. The second is chosen because it is the only recorded example of sulphur retention by an aryl-substituted ethylene sulphide during thermal decomposition. When α-chloro-ββ-diphenyl-α-phenoxyethylene sulphide (XXXVII) was



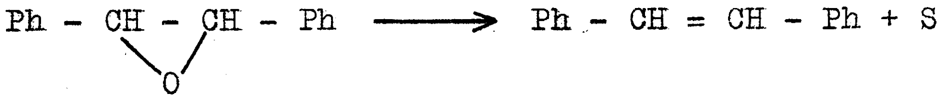
XXXVII

XXXVIII

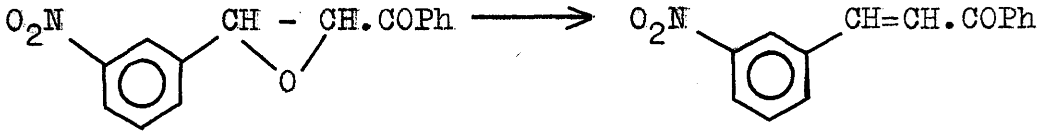
heated at 100°, a rearrangement occurred, hydrogen chloride was eliminated instead of sulphur and a derivative (XXXVIII) of thionaphthen was formed[39].

The chemistry of ethylene sulphides was put on a firmer footing by Culvenor and Davies[40-44], who contributed a series of papers on the subject, the first of which appeared in 1946. These workers prepared their ethylene sulphides by treating the corresponding ethylene oxides with thio-compounds, of which the most favoured was thiourea. For example, treatment of cyclohexene oxide with thiourea in methanol at 60°, for a period of 1-1½ hr., produced a 60% yield of cyclohexene sulphide. This substance can be distilled under reduced pressure (b.p. 68°/16mm.) and no mention is made of any tendency on the part of this episulphide, or on the part of any other purely aliphatic ethylene sulphide, towards extrusion of sulphur under thermal stimulation; tervalent phosphorus compounds did however appropriate the sulphur, but no attempt was made to identify the organic products. Bordwell[45] has shown that good yields of cyclohexene are obtainable by treatment of an ethereal solution of cyclohexene sulphide with butyl lithium or phenylmagnesium bromide.

Treatment of aryl-substituted ethylene oxides with thiourea in ethanol produces the corresponding olefins rather than the ethylene sulphides, which appear to be unstable under these conditions[41]. Thus the treatment of stilbene oxide (XXXIX) with thiourea in ethanol for six days at a temperature of 35° gave an 80% yield of stilbene but no stilbene sulphide; the fact that 65% of the theoretical extruded sulphur was recovered, supports the view that intermediate ethylene sulphides are formed in these reactions. 1-Benzoyl-2-*m*-nitrophenylethylene oxide (XL), treated at the boiling point of ethanol, produced *m*-nitrobenzylideneacetophenone (XLI). Ethyl phenylglycidate (XLII), allowed to react at between 30° and room temperature for sixty hours, gave ethyl cinnamate.

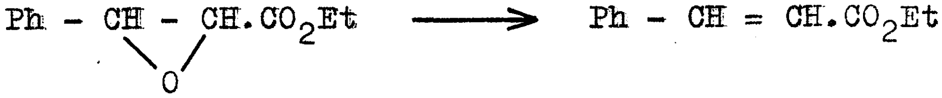


XXXIX



XL

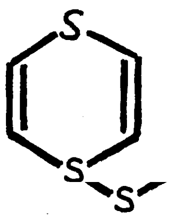
XLI



XLII

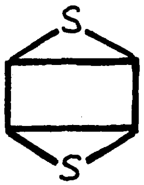
The examples collated above are sufficient to show that the typical reaction of an aryl-substituted ethylene sulphide is its division into sulphur and the corresponding olefin. This fact is the cornerstone of an argument developed in a later part of this thesis, and so the chemistry of ethylene sulphides has been given some prominence.

The recent (1954-1956) interesting work of Parham[46-49] on p-dithiin (XLIII) and its derivatives is important in the same connection. p-Dithiin possesses little aromatic character;



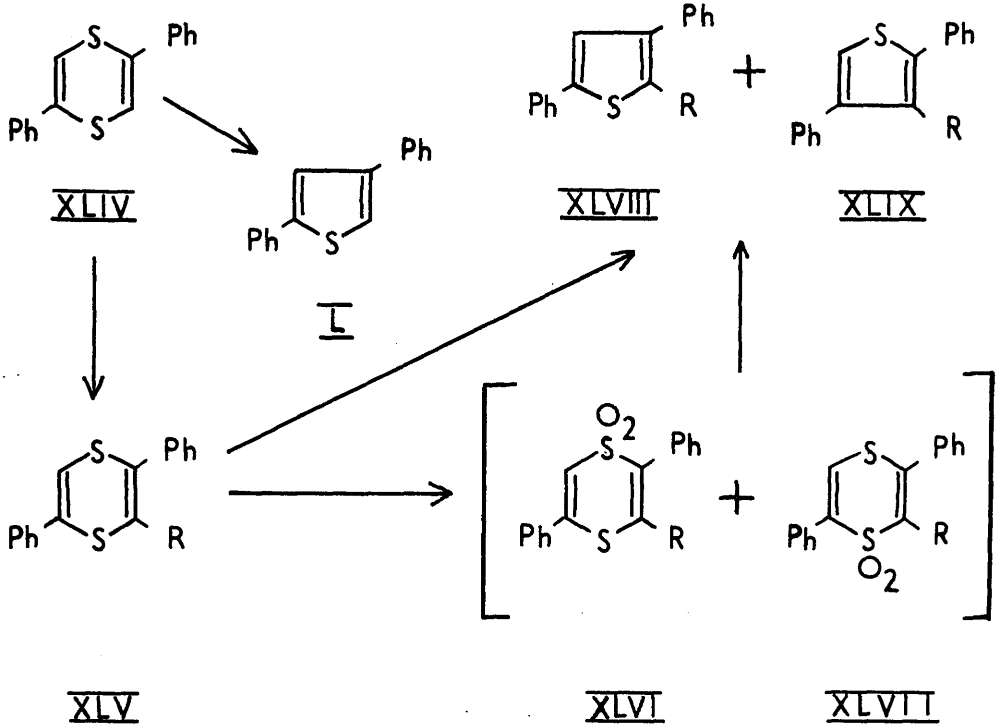
XLIII

XLIII a



XLIII b

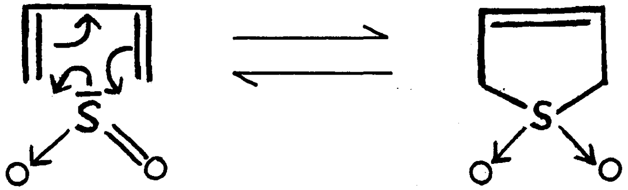
thus it is easily oxidized by peracetic acid to the disulphone, and it is readily polymerized; X-ray studies have shown that the molecule is not planar; but has instead the "boat" form (XLIII a)[46]. The 2:5-diphenyl derivative (XLIV), however, has certain aromatic properties; for example, treatment of the compound (XLIV) with a weak solution of nitric acid in acetic acid and acetic anhydride at room temperature, for five minutes, produced 2:5-diphenyl-3-nitro-p-dithiin (XLV, R=NO_2)[48]; again, brief treatment with



bromine produced 3-bromo-2:5-diphenyl-p-dithiin (XLV, R=Br)[49]. Attempts to oxidize derivatives of 2:5-diphenyl-p-dithiin to the corresponding disulphones have failed: the usual result is the ejection of a sulphur atom and the formation of a derivative of thiophen[47,48,49]. 2:4-Diphenyl-3-nitrothiophen (XLIX, R = NO_2) and 2:4-diphenyl-5-nitrothiophen (XLVIII, R = NO_2) are obtained in 46 and 31% yields, respectively, by the action of peracetic acid on 2:5-diphenyl-3-nitro-p-dithiin (XLV, $R=NO_2$)[48]. Parham at first considered that the reaction took place by preliminary formation of the monosulphones (XLVII and XLVI, $R = NO_2$) followed by elimination of sulphur dioxide, but this scheme had to be dropped when a highly thermostable substance considered to have the structure (XLVI, R=Br) was isolated from the products of the reaction of peracetic acid with 3-bromo-2:5-diphenyl-p-dithiin (XLV, R=Br)[49]. 2:5-Diphenyl-p-dithiin and its derivatives may be converted to thiophen derivatives by heat alone, but the temperatures required are higher than those ($<100°$) at which peracetic acid treatment was successful: thus at 190° 2:5-diphenyl-p-dithiin yields 2:4-diphenylthiophen (L)[47]. The thermal decomposition of 2:5-diphenyl-p-dithiins will be discussed in detail later.

Three striking similarities are exhibited by aryl-substituted p-dithiins and aryl-substituted ethylene sulphides: both groups of substances extrude sulphur, both are less prone to polymerization than the unsubstituted parent compounds, and both are reluctant to form sulphones. This situation may be illustrated by drawing the structure (XLIIIb) for p-dithiin: it is of course very unlikely that such a highly strained structure could make more than a very small contribution to the resonance hybrid.

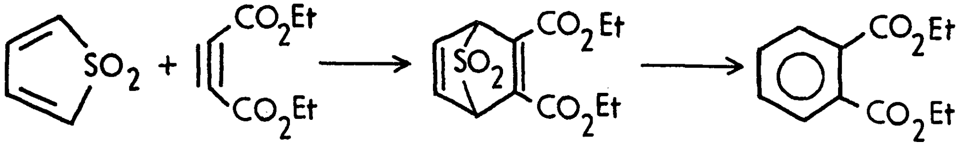
The substance known as butadiene sulphone (2:5-dihydrothiophen S-dioxide; LI) is formed by 1:4-addition of sulphur dioxide to butadiene[50]; the unbonded valency electrons of the sulphur atom play the part of the π-electrons of the dienophil in the Diels-Alder reaction.



LI

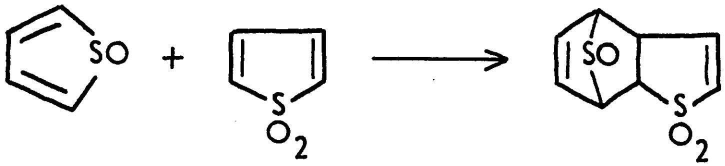
In common with other Diels-Alder reactions, the change is reversible; when the sulphone (LI) is heated at a temperature of 120-130°, sulphur dioxide and butadiene are liberated[50]. It will be observed that butadiene sulphone is a vinylogue of the unknown ethylene sulphone.

Derivatives of butadiene sulphone have figured as unstable intermediates in a recent series of outstandingly interesting researches. The employment of thiophen S-dioxide or one of its derivatives as the diene in Diels-Alder reactions must always lead to the formation of a (bridged) derivative of 2:5-dihydrothiophen S-dioxide as the primary product, but so far only one such intermediate has been isolated. Bailey and Cummins (1954)[53] obtained the example (LIII) from a Diels-Alder condensation of thiophen S-dioxide (LII) and acetylenedicarboxylic ester. The substance melted at 105-106° with evolution of sulphur dioxide, to form diethyl phthalate.



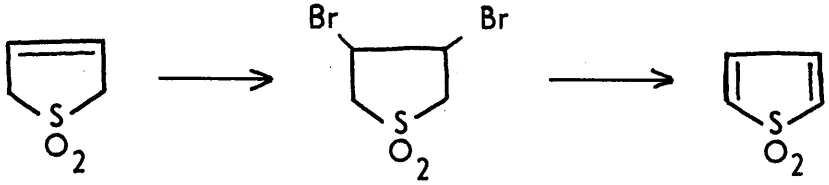
LII LIII

Thiophen S-dioxide is not a stable substance. Indeed, its employment in Diels-Alder reactions is the outcome of the recognition that this substance and its derivatives are prone to undergo self-condensation. Thus Stevens (1940)[54] and Davies (1952)[55] isolated a product of molecular formula $C_8H_8O_3S_2$ from attempts to oxidize thiophen to its dioxide; this substance was considered by both to be the product (LIV) of the condensation of thiophen S-oxide (diene) with thiophen S-dioxide (dienophil):

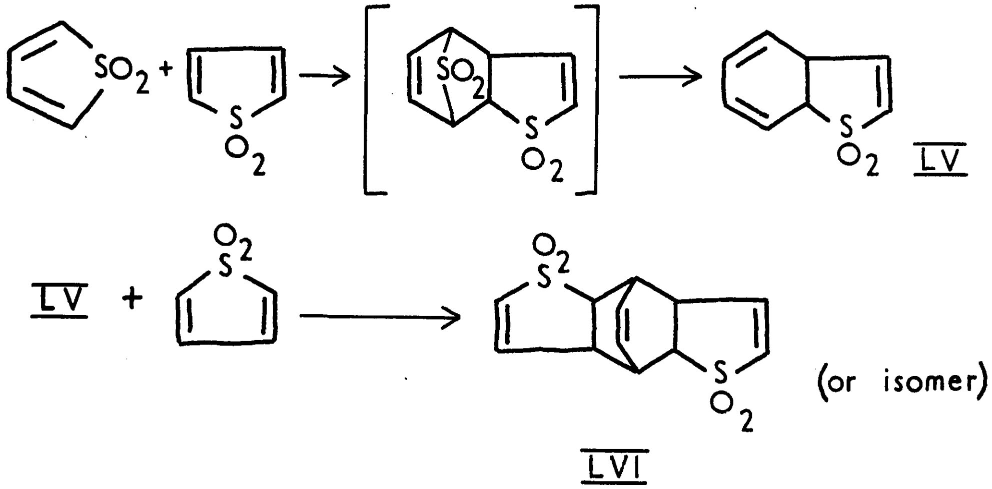


LIV

Backer and Melles (1951)[58] succeeded in preparing a solution of thiophen S-dioxide by bromination of butadiene sulphone followed by dehydrobromination



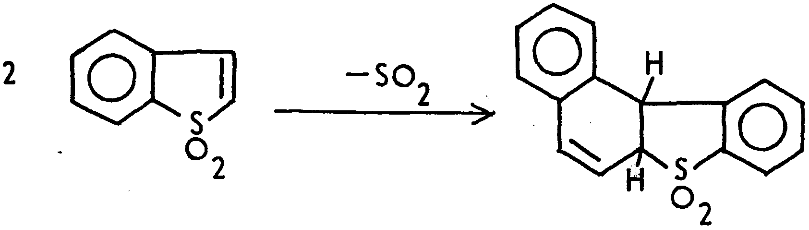
of the product, but after standing for one day the solution afforded a substance which they regarded as the product (LVI) of the Diels-Alder addition of a third molecule of thiophen S-dioxide to the diene (LV) formed by loss of sulphur dioxide from the product of a primary Diels-Alder addition of two molecules of thiophen S-dioxide:



In a more thorough investigation of the self-condensation of thiophen S-dioxide, Bailey and Cummins[52] isolated the compound (LV) and proved its structure by an independent synthesis of the hexahydro derivative.

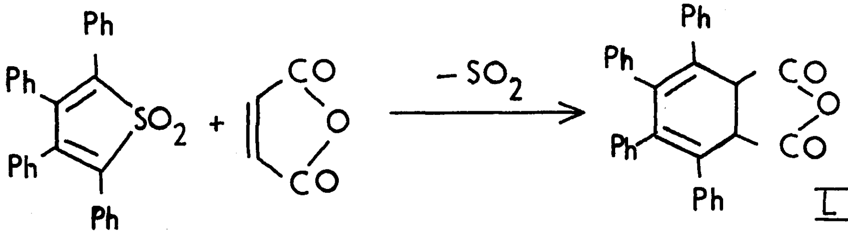
Substituted thiophen S-dioxides are more stable than the parent compound. Melles and Backer[59] have successfully prepared a series of these by oxidation of the corresponding thiophens with organic peracids, and thionaphthen S-dioxide may be prepared readily in the same way. Bordwell (1951)[60] and Davies (1952)[56] have demonstrated that at a high temperature thionaphthen

S-dioxide (LVII) also undergoes self-condensation with formation of the compound (LVIII):

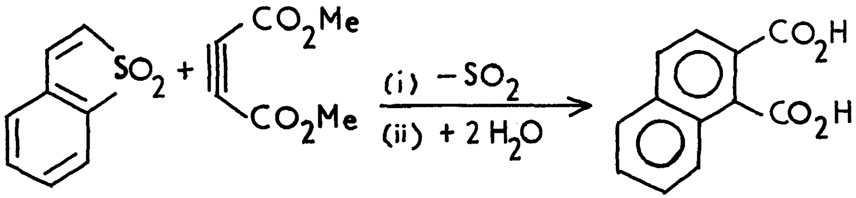


LVII LVIII

Davies[57] has shown that benzothionaphthen S-dioxides behave similarly. It follows from their lesser tendency towards self-condensation that substituted thiophen S-dioxides are less reactive in the Diels-Alder condensation, and the high temperatures necessary have precluded the isolation of the sulphur-containing adducts. A number of interesting condensations have been described both by Melles (1952) and Duck (1955), of which two examples must suffice. Melles[61] has prepared 3:4:5:6-tetraphenyl-1:2-dihydrophthalic anhydride (LIX) by condensation of tetraphenylthiophen S-dioxide with maleic anhydride; naphthalene-1:2-dicarboxylic acid was made by Duck[62] from thionaphthen

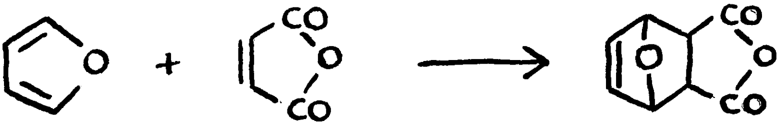


LIX



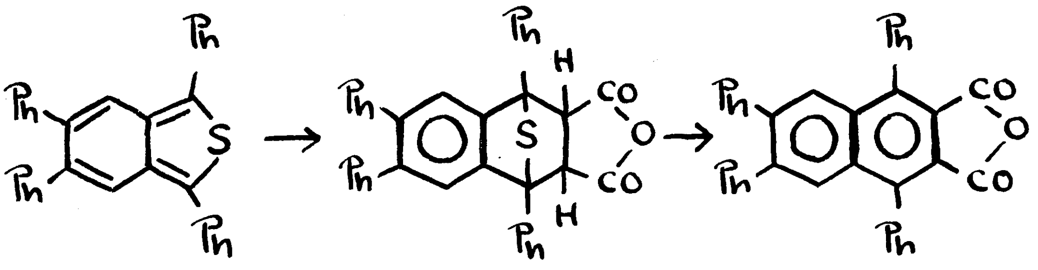
S-dioxide and dimethyl acetylenedicarboxylate.

While thiophen S-dioxide has no aromatic character, due to the lack of the "lone pair" of electrons from the sulphur atom required to make up the aromatic sextet, thiophen has more aromatic character than furan. For this reason it will not play the part of a diene in a Diels-Alder reaction, as furan is well known to do e.g. with maleic anhydride furan forms the adduct (LX)[63]:

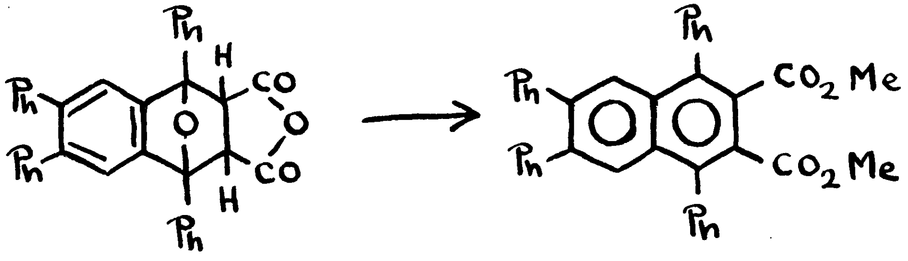


LX

In the case of derivatives of thiophen formed by fusion of the thiophen ring with other systems in such a way that bond localization may be imagined to take place, reaction with a dienophil is possible. Allan and Gates (1943)[64] successfully condensed 1:3:5:6-tetraphenyl<u>iso</u>benzothiophen (LXI) with maleic anhydride to form the adduct (LXII). Treated with hydrogen chloride in boiling xylene, the adduct expelled hydrogen sulphide to form 1:4:6:7-tetraphenylnaphthalene-2:3-dicarboxylic anhydride (LXIII).

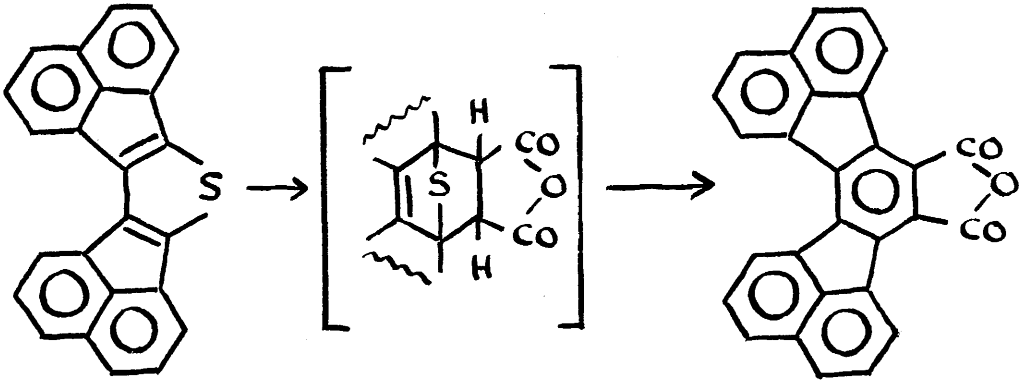


LXI LXII LXIII



LXIV LXV

The analogous adduct (LXIV) obtained from maleic anhydride and 1:3:5:6-tetraphenyl<u>iso</u>benzofuran loses the epoxy oxygen atom by dehydration when treated with hydrogen chloride in methanol, to form the corresponding naphthalene-2:3-dicarboxylic acid dimethyl ester (LXV). Clapp (1939)[65] found that the highly condensed thiophen (LXVI) and maleic anhydride reacted together at a temperature of 225°



LXVI LXVII

with the loss of hydrogen sulphide, to form the corresponding phthalic anhydride (LXVII).

In the cases of sulphur extrusion so far mentioned, the removable sulphur atom was attached either to two carbon atoms or to a carbon atom and another sulphur atom. Sulphur extrusion is more general than this. Mercaptans lose their sulphur to triethyl phosphite[66]

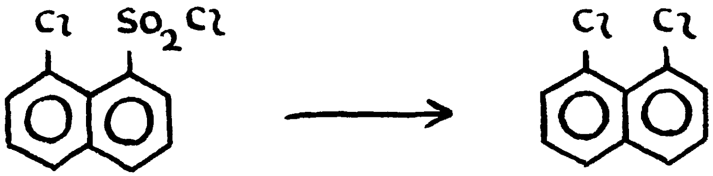
$$RSH + (EtO)_3P \longrightarrow RH + (EtO)_3PS$$

$$R = Me(CH_2)_7 \text{ , } PhCH_2$$

and heat expels sulphur dioxide from some aliphatic and aromatic sulphonyl chlorides e.g. at a temperature of 175-190° camphor-π-sulphonyl chloride (LXVIII) evolves sulphur dioxide with formation of π-chlorocamphor

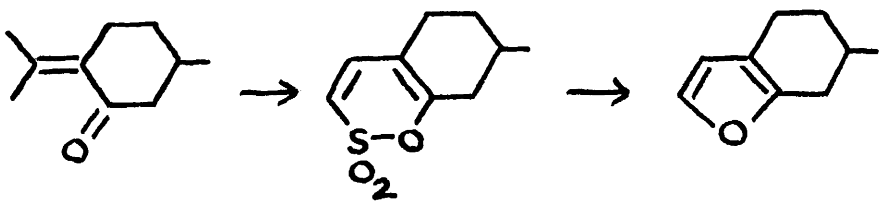
LXVIII LXIX

(LXIX)[67] and at 200-230° sulphur dioxide is evolved from 8-chloronaphthalene-1-sulphonyl chloride (LXX)



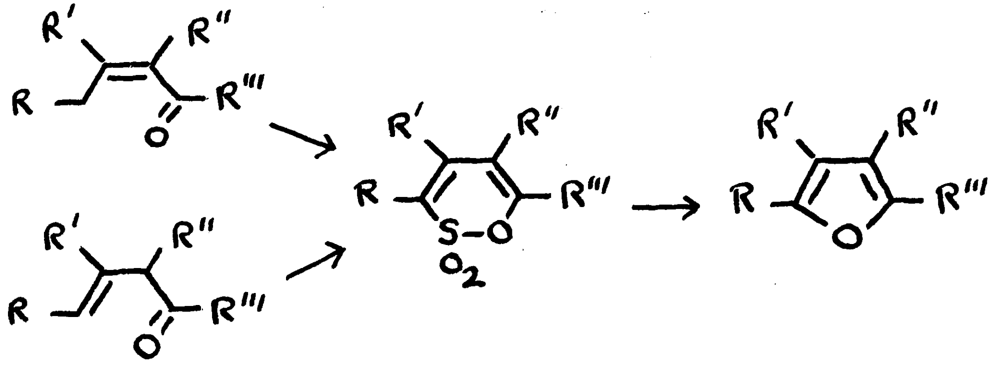
LXX

to give 1:8-dichloronaphthalene in good yield[68]. Sulphur dioxide may also be expelled by heat from the sultone (LXXII), which Treibs (1937)[69] found



LXXI LXXII LXXIII

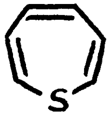
to be the product of treatment of pulegone (LXXI) with Reychler's sulphonating reagent[70] (sulphuric acid in acetic anhydride). In this way menthofuran (LXXIII) is obtained. Morel and Verkade (1948-1951)[71] have applied these reactions to the synthesis of a series of alkyl-substituted furans starting from the corresponding α:β- or β:γ-unsaturated ketones:



This conversion of sultones into furans has its parallel in the more recent work of Armarego and Turner mentioned earlier, whereby dibenz-o-dithiin

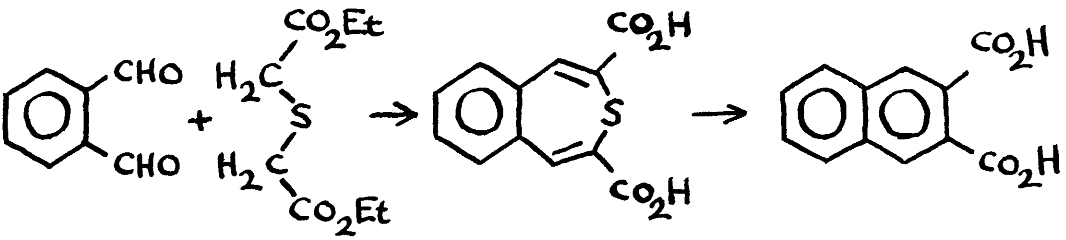
5:5-dioxide (XXV; p. 13) was converted into dibenzothiophen.

Since this thesis is concerned with the desulphurization of derivatives of thiepin (LXXIV) it will be well to draw the present review to a close by mentioning such cognate examples as are known. The parent heterocycle (LXXIV) is unknown.



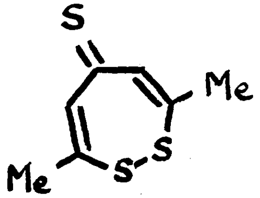
LXXIV

Scott (1953)[72] prepared 4:5-benzothiepin-2:7-dicarboxylic acid (LXXVII) by the condensation of o-phthalaldehyde (LXXV) and diethyl thiodiacetate

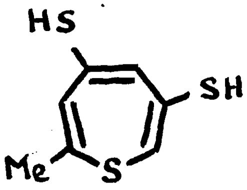


LXXV LXXVI LXXVII LXXVIII

(LXXVI). The thiepin was very labile and was desulphurized to naphthalene-2:3-dicarboxylic acid (LXXVIII) by boiling in aqueous ethanol. Dimroth and Lenke[73] found that the dimethyl ester of the dicarboxylic acid (LXXVII) was more stable, and were able to examine its properties in detail. They found that the ester formed an addition compound with mercuric chloride, that it took up one molecule of bromine to form a dibromo derivative the properties of which were consistent only with the association of the bromine atoms with the sulphur atom, and that it added two molecules of diazomethane. These properties show that the thiepin ring lacks aromatic stability. They are not in accord with the speculations of Arndt[74], who has ascribed the inertness of one of the three sulphur atoms in an isomerization product of the disulphide (LXXIX) to its possession of a structure (LXXX) featuring the thiepin ring.

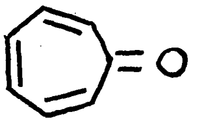


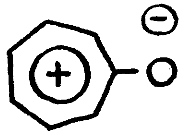
LXXIX

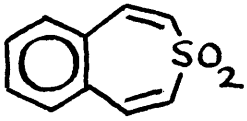


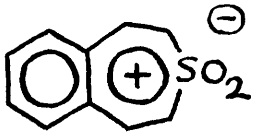
LXXX

The evident unsaturated nature of the sulphur atom in the ester of the acid (LXXVII) suggests that the corresponding sulphone might be preparable by direct oxidation. 4:5-Benzothiepin S-dioxide (LXXXII) and its derivatives are of particular theoretical interest because of their formal relationship to tropone (LXXXI).


LXXXI

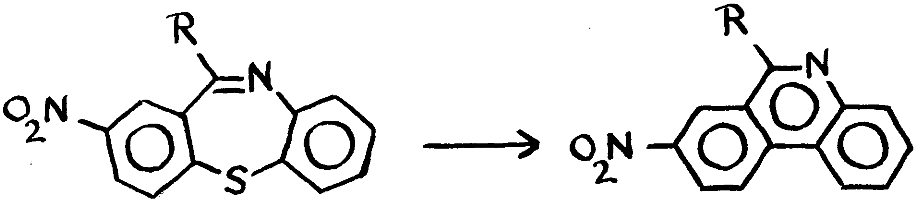

LXXXIa


LXXXII


LXXXIIa

A resonating structure (LXXXIIa) may be written for 4:5-benzothiepin S-dioxide, in the same way as the structure (LXXXIa) which was considered by Doering and Knox[75] to explain the aromaticity of tropone (LXXXI). Apparently Truce and Lotspeich[76], who tackled this problem, were unable to oxidize Scott's acid (LXXVII) to the corresponding sulphone. They did however succeed in making 4:5-benzothiepin S-dioxide by a more roundabout route. The compound was found to be too readily reduced to have significant aromatic character. On heating, 4:5-benzothiepin S-dioxide released sulphur dioxide and formed naphthalene in good yield.

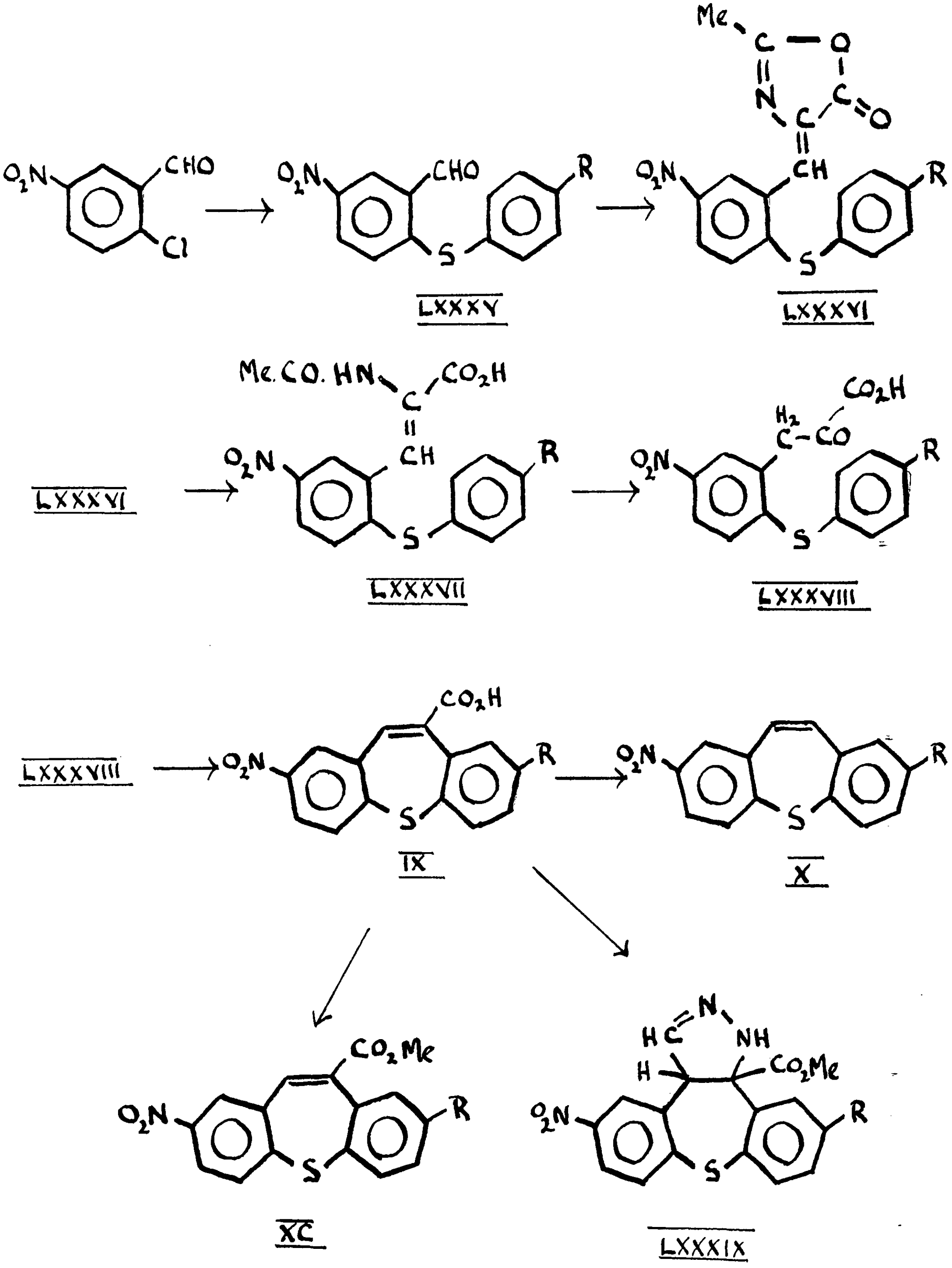
Finally, Jarrett[22] has described the extrusion of sulphur from a number of derivatives of 2-nitrodibenzo [b,f]-1:4-thiazepine (LXXXIII, R=H).



LXXXIII LXXXIV

When heated briefly (5-7 min.) with copper bronze in boiling diethyl phthalate the nitrodibenzothiazepines (LXXXIII, R=H, Me, Ph or m- $NO_2.C_6H_4$) gave good yields of the corresponding phenanthridines (LXXXIV, R=H, etc.).

The experiments described in this chapter are an extension of the work of Summers. The latter, when he attempted to desulphurize 2-nitrodibenzo [b,f] thiepin-10-carboxylic acid (IX, R=H; please refer to p. 2) under the conditions which expelled the sulphur atom from the 8-methyl homologue (IX, R=Me) obtained only 2-nitrodibenzo [b,f] thiepin (X, R=H; p. 2) and (when cuprous oxide was used in place of copper) traces of a straw-yellow material of m.p. 117° which were insufficient for its identification. Further attempts to obtain 2-nitrophenanthrene (XI, R = H; p. 2) by extrusion of sulphur from 2-nitrodibenzo [b,f] thiepin-10-carboxylic acid were desirable, both from the point of view of the extension of the desulphurization reaction and because oxidation of the product to the readily available 2-nitrophenanthraquinone would provide clear-cut confirmation of the nature of the reaction. These, and other experiments which developed from them, are discussed in the next section.



LXXXV

LXXXVI

LXXXVI

LXXXVII

LXXXVIII

LXXXVIII

IX

X

XC

LXXXIX

DISCUSSION

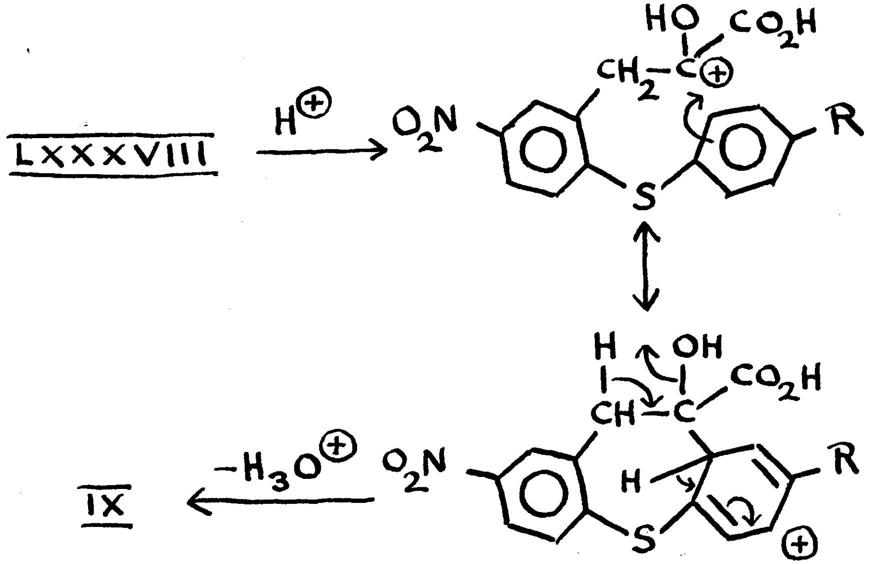
2-Nitrodibenzo[b,f]thiepin-10-carboxylic acids (IX, R=H, Me)

The pathway to 2-nitrodibenzo[b,f]thiepin-10-carboxylic acid (IX, R=H) and its 8-methyl homologue (IX, R=Me) was that followed by Summers[2].

The method of Loudon *et al.*[77], used by Summers for the preparation of 5-nitro-2-*p*-tolylthiobenzaldehyde (LXXXV, R=Me), was modified by the substitution of potassium carbonate for sodium hydroxide. At a temperature of 60° condensation of thio-*p*-cresol with 2-chloro-5-nitrobenzaldehyde took place smoothly, the darkening of colour which occurs with the original method was avoided, and the percentage yield was raised to 82%. A yield of the same order was obtained when the new method was applied to the preparation of 5-nitro-2-phenylthiobenzaldehyde (LXXXV, R=H).

The conversion of the 2-arylthio-5-nitrobenzaldehydes to the corresponding azlactones (LXXXVI, R=H, Me) was the most difficult of the five steps involved in the synthesis. The methods of Herbst and Shemin[78] and of Galat[3] were both used. Results were more easily reproducible when the first method was employed, and the yields were little, if any, lower than the best obtained by the second method. In each case the trouble was due to the presence in the product of impurities, the most annoying of which was a high-melting, bright red material, which could only be removed by fractional crystallization from benzene. Treatment of the benzene solution with charcoal was not satisfactory as a means of removing the more soluble red colours which remained, because these were less strongly adsorbed than the azlactone, which was very readily taken up by charcoal. The azlactones were found to be rapidly hydrolysed to the corresponding α-acetamidocinnamic acids (LXXXVII, R=H, Me) by boiling acetic acid, and, since these substances were not removed from the solution by charcoal to any extent, a product sufficiently pure for use in the next step was most easily obtained by fractional crystallization of the crude azlactone from benzene followed by treatment of an acetic acid solution with charcoal. It was not necessary to isolate the α-acetamidocinnamic acid from the filtrate, since the conditions used by Summers for the hydrolysis of these compounds could be reproduced by addition to the filtrate of the correct proportion of dilute hydrochloric acid.

The 2-arylthio-5-nitrophenylpyruvic acids (LXXXVIII, R=H, Me) were cyclized by a boiling mixture of hydrobromic and acetic acids, in preference to treatment with polyphosphoric acid, the reagent employed by Summers. The treatment with mixed hydrobromic and acetic acids was favoured because it was easier to apply on a moderate scale, was more readily reproduced, and gave a purer product. 5-Nitro-2-p-tolylthiophenylpyruvic acid (LXXXVIII, R=Me) underwent cyclization more smoothly than 5-nitro-2-phenylthiophenylpyruvic acid (LXXXVIII, R=H). 8-Methyl-2-nitrodibenzo[b,f]thiepin-10-carboxylic acid (IX, R=Me) was obtained in 86% yield after a treatment lasting 5 hr., whereas it was necessary to prolong the period of boiling to 12 hr. to secure a 75% yield of 2-nitrodibenzo [b,f]thiepin-10-carboxylic acid (IX, R=H). This result is not surprising, because it is probable that the ring-closure involves an electrophilic attack by the protonated carbonyl group of the pyruvic acid upon the benzene ring to which the group R is attached:



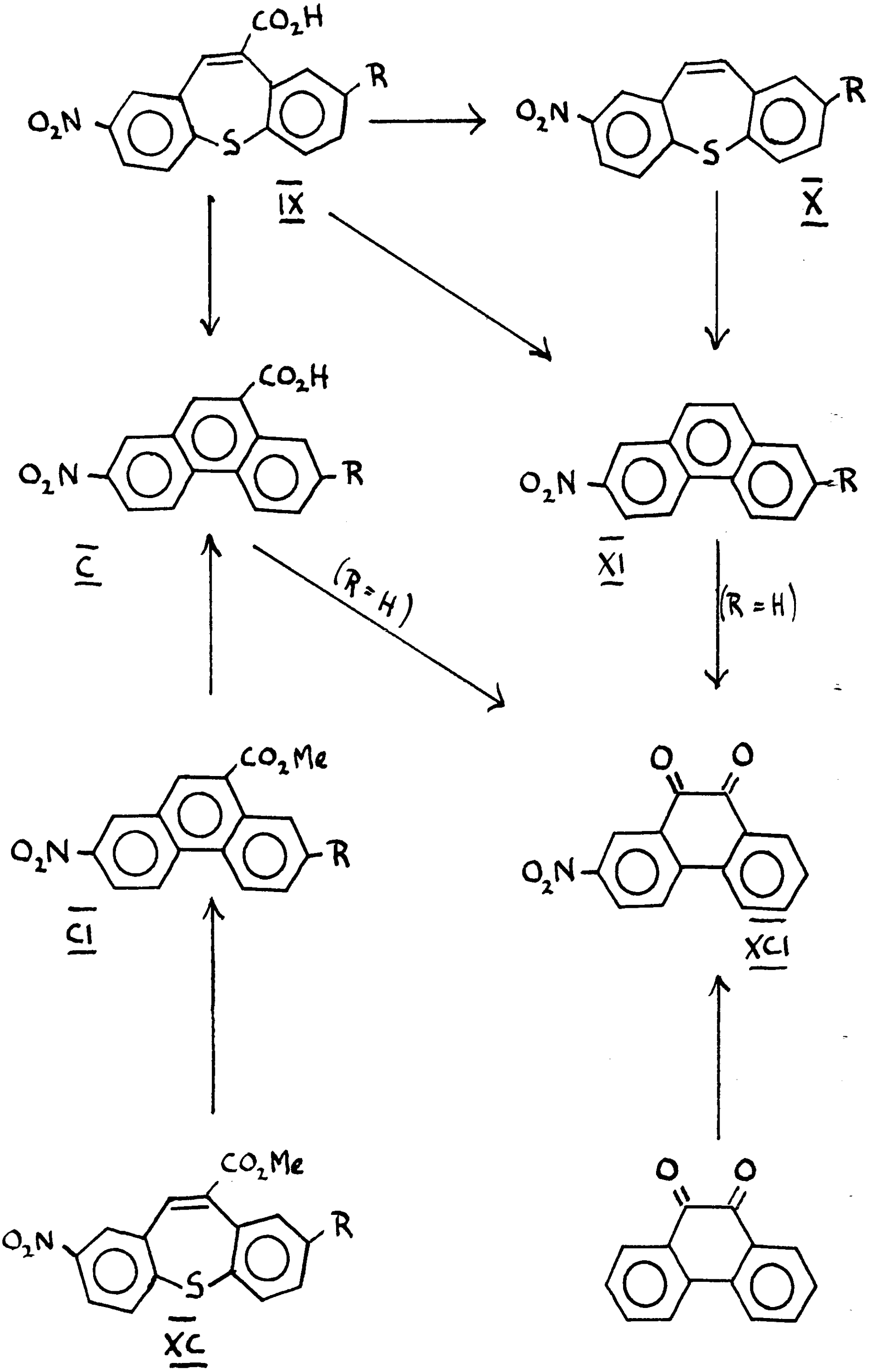
A similar mechanism has been proposed by Bradsher[79] for the formation of aromatic systems by cyclodehydration. If the group R has a tendency to donate electrons to the benzene ring, electrophilic attack of the latter should be promoted. For this reason the pyruvic acid (LXXXVIII, R=Me) would be expected to undergo cyclization more readily than its lower homologue (LXXXVIII, R=H).

Decarboxylation of the 2-Nitrodibenzo[b,f]thiepin-10-carboxylic acids (IX, R=H, Me)

Summers[2] managed to decarboxylate 2-nitrodibenzo[b,f]-thiepin-10-carboxylic acid (IX, R=H) in 45-50% yield by heating with cuprous oxide in quinoline. In the hands of the writer this method gave only traces of 2-nitrodibenzo[b,f]thiepin (X, R=H). Moderate yields (45-50%) were obtained by heating a solution of the acid (IX, R = H) in diethyl phthalate, with copper, on a metal bath at 250°, for 30 min. The product, which was quite soluble in both diethyl phthalate and light petroleum, could not be isolated without distillation of the diethyl phthalate, a circumstance which made the preparation tedious. When 8-methyl-2-nitrodibenzo[b,f]thiepin-10-carboxylic acid (IX, R= Me) was subjected to the same conditions, only a very small quantity of 8-methyl-2-nitrodibenzo[b,f]thiepin (X, R=Me) was secured.

Esterification of the 2-Nitrodibenzo[b,f]thiepin-10-carboxylic acids (IX, R=H, Me)

Treatment of 2-nitrodibenzo[b,f]thiepin-10-carboxylic acid (IX, R=H) with an ethereal solution of diazomethane provided the methyl ester (XC, R=H) in 68% yield. There was also formed a small quantity


IX X C XI CI XCI XC

of a thermolabile compound which contained carbon, hydrogen and nitrogen in the proportions required by the empirical formula $C_{17}H_{13}N_{3}O_{4}S$. This material probably has the structure of methyl pyrazolino-[4′:5′-11:10]-2-nitrodihydrodibenzo[b,f]thiepin-10-carboxylate (LXXXIX).

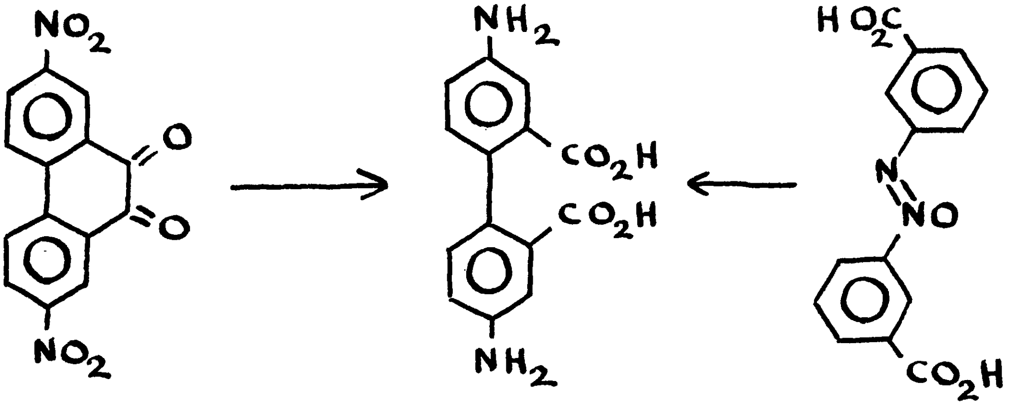
To avoid the complication attendant upon the use of diazomethane as an esterifying agent, resort was made to the method of acid-catalyzed methanolysis. Boiling methanol acidified with sulphuric acid converted the 2-nitrodibenzo[b,f]thiepin-10-carboxylic acids (IX, R=H, Me) to their respective methyl esters (XC, R = H, Me) in yields of 85% and above.

Desulphurization Experiments

(a) Preliminary Work, with a Qualitative Bias.

The Isolation and Characterization of 2-Nitrophenanthrene

The first objective was to establish the nature of the compound of m.p. 117° which was obtained by Summers from 2-nitrodibenzo[b,f]thiepin-10-carboxylic acid (IX, R=H) by treatment with cuprous oxide in boiling quinoline. These conditions had given poor results, and more drastic conditions were used in order to get a sample of pure material for identification. When a mixture of 2-nitrodibenzo[b,f]thiepin-10-carboxylic acid (IX, R=H) and freshly reduced copper wire was heated to 300° under an atmosphere of nitrogen, a reaction of some violence took place, the products being ejected from the reaction vessel in the form of a cloud of yellow smoke, which was trapped in boiling benzene. A pale yellow solid of m.p. 120° and empirical composition $C_{14}H_9NO_2$ was obtained after chromatography of the concentrated benzene solution. Oxidation of this material with chromium trioxide in acetic acid gave a material which comparison (mixed m.p. and infrared absorption spectra) showed to be identical with a sample of 2-nitrophenanthraquinone (XCI) isolated by fractional crystallization from the mixture which is obtained by direct nitration of phenanthraquinone[80]. The position of the nitro group in the comparison sample is not in doubt owing to the work of Strasburger and of Schultz. Strasburger[81] showed that further nitration of the material afforded 2:7-dinitrophenanthraquinone (XCII) the structure of which had been established previously by Schultz after a re-examination of the work of Struve.



XCII XCIII XCIV

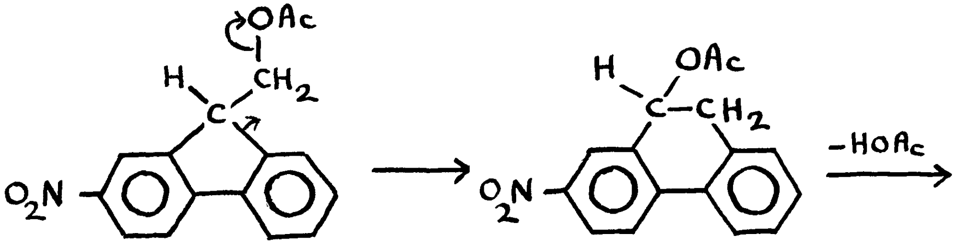
Struve[82] had made a diaminodiphenic acid from the dinitrophenanthraquinone by oxidation to the corresponding dinitrodiphenic acid followed by reduction of the nitro groups, but he considered it to be different from the 4:4′-diamino-2:2′-diphenic acid (XCIII) obtained by Griess[83] from phenylazoxybenzene-3:3′-dicarboxylic acid (XCIV) by reduction with tin and hydrochloric acid. Schultz[84] repeated both preparations and found that the products were identical.

The product of the desulphurization must therefore be 2-nitrophenanthrene (XI, R=H), which was unknown in the pure state at the time when the experiments were performed. Schmidt and Heinle[85], in an examination of the products of the nitration of phenanthrene, had shown 2-nitrophenanthrene to be a component of a mixture of m.p. 99°, by the isolation of 2-nitrophenanthraquinone (XCI) from the products of oxidation of the mixture. Very shortly after the experiments described above had been completed, Bavin and Dewar[86] reported the preparation of 2-nitrophenanthrene by two methods. In one method, the amino group of 2-aminophenanthrene[87] was transformed into a nitro group by the oxidation of the diazonium fluoroborate with a mixture of cuprous oxide, cupric sulphate and sodium nitrite:

$$R\text{-}NH_2 \xrightarrow[HX]{HNO_2} R\text{-}\overset{+}{N}{\equiv}N \Big\} X^- \xrightarrow[\substack{CuSO_4, \\ NaNO_2}]{Cu_2O,} R\text{-}NO_2$$

$R = C_{14}H_9$, $X = BF_4$

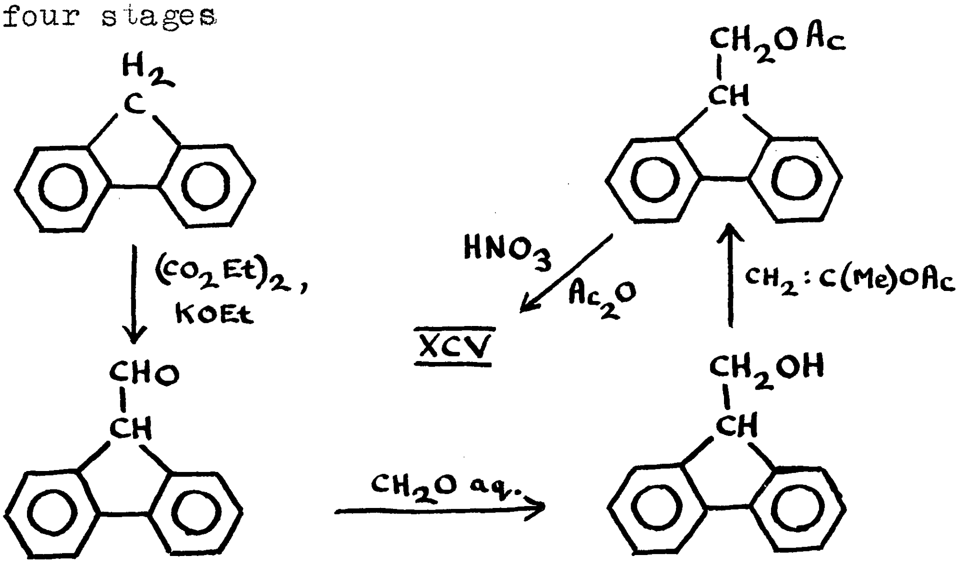
The yields (5–6%) obtained by this method are only slightly better than those (4%) given by the desulphurization reaction described above, but the second method[88], which involves a Wagner-Meerwein rearrangement of 2-nitro-9-fluorenylmethyl acetate (XCV)



XCV

XI
(R= H)

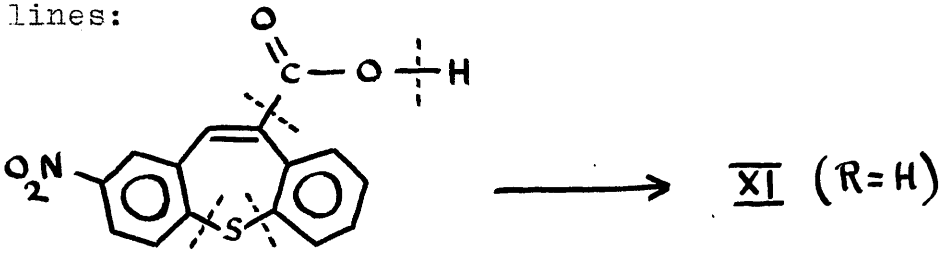
followed by the elimination of a molecule of acetic acid, gives very satisfactory yields (89%). The starting material (XCV) is made from fluorene in the four stages



each of which gives a yield of above 50%, so that this is an excellent route to 2-nitrophenanthrene.

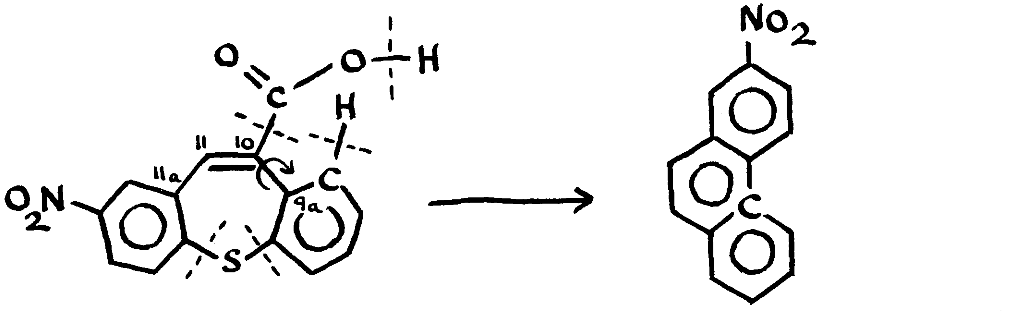
The fact that decarboxylative desulphurization of 2-nitrodibenzo[b,f]thiepin-10-carboxylic acid

(IX, R=H) produces 2-nitrophenanthrene (XI, R=H) suggests that the desulphurization reaction takes the simplest course possible. The transformation demands the breakage of a total of at least four chemical bonds. Decarboxylation requires the cleavage of two bonds and desulphurization requires the cleavage of at least two bonds, as shown by the dotted lines:

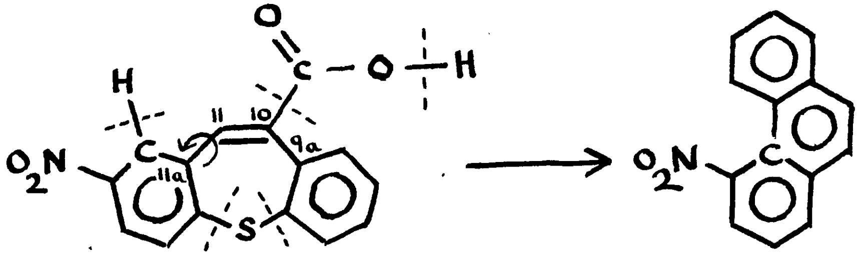


(IX, R=H)

It is conceivable that the course of the reaction may involve, subsequent to the fission of one carbon-sulphur linkage, a rotation about one, or both, of the bonds joining the ethylene group (atoms nos. 10 and 11) to the benzene rings, followed by an <u>intra</u>molecular substitution, which would require the cleavage of a fifth bond.



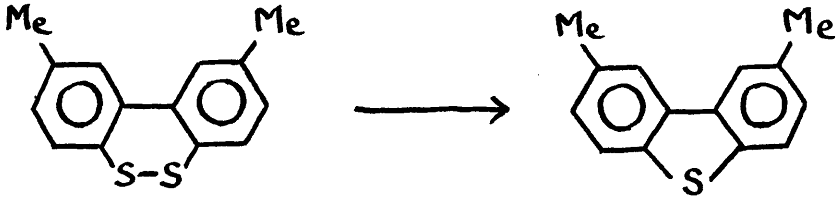
(IX, R=H) (XI, R=H)



(IX, R=H) XCVI

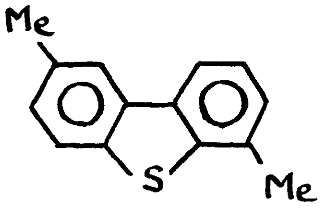
If the rotation is about the bond between atoms Nos. 9a and 10, then the product will be 2-nitrophehanthrene (XI, R=H): but if the rotation is about the bond between atoms Nos. 11 and 11a, the product will be 4-nitrophenanthrene (XCVI). Since 4-nitrophenanthrene does not appear in the reaction products, there can be no rotation about the 11-11a bond, and it therefore seems the less likely that the formation of 2-nitrophenanthrene occurs in the more complicated manner.

To conclusively exclude a re-orientation of the molecule after the fashion indicated, it is necessary to study the desulphurization of a dibenzo[b,f]thiepin with a substituent in each benzene ring, at any position other than the 3- or 7- positions (which are on the axes of possible rotation). The 8-methyl-2-nitrodibenzo[b,f]thiepin-10-carboxylic acid (IX, R=Me) examined by Summers is such a compound, but unfortunately the possible products are not available by other methods. The work of Armarego and Turner[27], who showed that 2:8-dimethyldibenzothiophen (XCVIII) is obtained from



XCVII XCVIII

2:9-dimethyldibenzo-o-dithiin (XCVII) by heating with copper, is of relevance, since the product would have been 2:6-dimethyldibenzothiophen (XCIX) if the loss



XCIX

of a sulphur atom had been accompanied by rotation about the diphenyl axis. Since there is no evidence that the extrusion of sulphur from dibenzo [b,f]-thiepins involves any change more complicated than a union of the carbon atoms to which the sulphur atom was attached, the structures given in this thesis to the products of such desulphurization reactions will embody the assumption that the simplest path is the true one.

The Recognition of 2-Nitrophenanthrene-9-carboxylic acid ($\overline{\mathrm{C}}$, R=H) as a Product of the Desulphurization of 2-Nitrodibenzo[b,f]thiepin-10-carboxylic acid (IX, R=H)

The smoke-cloud which was emitted at the moment of the desulphurization of 2-nitrodibenzo[b,f]thiepin-10-carboxylic acid (IX, R=H), contained, in addition to 2-nitrophenanthrene, a white solid which was much less soluble in benzene than the nitrohydrocarbon. This was regarded at the time as recovered 2-nitrodibenzo [b,f]thiepin-10-carboxylic acid.

A quantity of carboxylic acid which was obtained as a product of an attempt to desulphurize the same material (IX, R=H) with cuprous oxide in boiling quinoline, was put in the same specimen tube, for the same reason. When the mixed material was later examined more minutely, it was found to have a higher melting-point than 2-nitrodibenzo[b,f] thiepin-10-carboxylic acid (IX, R=H) and a quite different ultraviolet absorption spectrum. The percentage of carbon and hydrogen contained by the purified material satisfied the empirical formula $C_{15}H_9NO_4$, and oxidation with sodium dichromate in acetic acid afforded 2-nitrophenanthraquinone (XCI), which was again identified (mixed melting-point and infrared spectra) by comparison with material made by the method of Schmidt and Spoun[80]. The substance was thereby proved to be 2-nitrophenanthrene-9-carboxylic acid (C, R=H). With the isolation of this compound, all three products probable from the treatment of 2-nitrodibenzo[b,f] thiepin-10-carboxylic acid (IX, R=H) with copper have been realized, since the product (X, R=H) of simple decarboxylation unaccompanied by desulphurization, has already been described.

(b) A Search for More Suitable Conditions and Materials

All efforts were now directed to the improvement of the reaction conditions. The 'dry' treatment used hitherto was abandoned in favour of a procedure developed with success by Jarrett[22] for the desulphurization of 2-nitrodibenzo[b,f]-1:4-thiazepine (LXXXIII, R=H, p. 39) and its derivatives, whereby a solution, in diethyl phthalate, of the material to be desulphurized, is boiled with copper bronze in an atmosphere of nitrogen.

When 2-nitrodibenzo[b,f]thiepin-10-carboxylic acid (IX, R=H) was subjected to these conditions for 15 min., 2-nitrophenanthrene (XI, R=H) was obtained in 15% yield. The method suffered from a disadvantage not encountered by Jarrett, who was able to precipitate his products (LXXXIV) by flooding the diethyl phthalate solutions with light petroleum. 2-Nitrophenanthrene is moderately soluble in light petroleum, and its isolation in this simple way is impossible. Instead it was necessary to remove the diethyl phthalate by distillation under reduced pressure, a tedious proceeding which may have incurred losses due to entrainment of product in the vapour.

The appearance of 2-nitrodibenzo[b,f]thiepin (X, R=H), 2-nitrophenanthrene (XI, R=H) and 2-nitrophenanthrene-9-carboxylic acid (C, R=H) after the heating of 2-nitrodibenzo[b,f]thiepin-10-carboxylic acid (IX, R=H) with copper, invites speculation about the relative ease of the reactions

(1) IX $\longrightarrow$ X + CO_2
(2) IX $\longrightarrow$ C + S (as CuS or Cu_2S)
(3) X $\longrightarrow$ XI + S (as CuS or Cu_2S)
(4) C $\longrightarrow$ XI + CO_2

The discovery of 2-nitrophenanthrene-9-carboxylic acid (C, R=H) is rather surprising, since the material has twice escaped decarboxylation (reactions 1 and 4). Its occurrence may be explained by proposing that reaction (2) is faster than reaction (3), that reaction (1) is faster than reaction (4), or that both of these factors are involved. The question of the relative rates of reactions (1) and (4) has no practical relevance, because the total rate of desulphurization is independent of the answer. On the other hand, if reaction (2) is faster than reaction (3), clearly the yield* of desulphurized material will be inversely influenced by the rate of reaction (1).

Since the decarboxylation of esters is unusual, it was hoped that sulphur extrusion from an ester of the acid (IX, R=H) might go more smoothly. It seemed reasonable to assume that replacement of the hydroxyl group of the acid (IX, R=H) by an alkoxy radical would not alter the environment of the sulphur atom sufficiently to hinder its elimination.

A solution of methyl 2-nitrodibenzo[b,f]thiepin-10-carboxylate (XC, R=H) in diethyl phthalate was boiled with copper for various periods, in an atmosphere of nitrogen and under strictly anhydrous conditions (because the boiling-point of dimethyl phthalate is 14° below that of the diethyl ester, the risk of ester interchange was accepted).

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* If the situation were as simple as represented, then the yield could not be affected by reaction velocities; unfortunately, undesirable side-reactions (charring) accounted for the greater part of the starting-material, so it was impossible to prolong the reaction time indefinitely; the yield is therefore dependent on reaction rates.

The highest yields of product were 38.8% and 39.2%, achieved with refluxing periods of 7 and 11 min. respectively. The structure of the product was proved to be that of methyl 2-nitrophenanthrene-9-carboxylate (CI, R=H) by hydrolysis to 2-nitrophenanthrene-9-carboxylic acid ($\overline{\underline{\mathrm{C}}}$, R=H), which was identified by comparison (mixed m.p. and ultraviolet absorption spectra) with the sample already at hand. Methyl 2-nitrophenanthrene-9-carboxylate was found to be insoluble in light petroleum, and was readily precipitated from its solution in diethyl phthalate by addition of light petroleum. This made its isolation from the reaction mixture much easier and more dependable than the isolation of 2-nitrophenanthrene (XI, R=H) after the treatment of 2-nitrodibenzo[b,f] thiepin (X, R=H) with copper in boiling diethyl phthalate. Furthermore, owing to scarcity of material the latter experiment could only be tried once, so that it was not possible to make a fair comparison of the tendencies of the ester (XC, R=H) and of the thiepin (X, R=H) to lose a sulphur atom. The yield of 2-nitrophenanthrene (XI, R=H) obtained from

2-nitrodibenzo[b,f]thiepin was 19%.

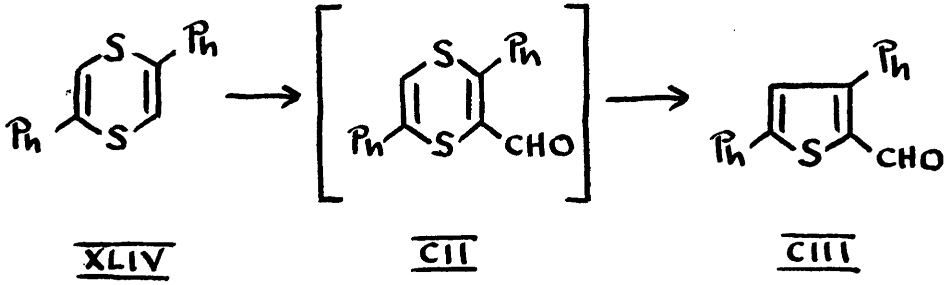
Now that the use of an ester had been shown to be profitable, attention was turned to the desulphurization of methyl 8-methyl-2-nitrodibenzo[b,f]thiepin-10-carboxylate (XC, R=Me), the methyl ester of the acid (IX, R=Me) desulphurized by Summers. The ester, heated under reflux with diethyl phthalate and copper for 7 min., in two successive experiments yielded 53% and 55% of methyl 7-methyl-2-nitrophenanthrene-9-carboxylate (C̅I̅, R = Me), a sample of which was hydrolysed to 7-methyl-2-nitrophenanthrene-9-carboxylic acid (C̅, R=Me).

As described above, the desulphurization, under identical conditions, of methyl 2-nitrodibenzo[b,f]thiepin-10-carboxylate (XC, R=H) and its 8-methyl homologue (XC, R=Me), proceeded in yields of 39% and 54% respectively. This result repeats the trend displayed by the parent acids (IX; R=H, Me), towards easier extrusion of sulphur in the case of the 8-methyl compound.

The difference in the ease of desulphurization of such closely related substances is striking. It was noted previously that 2-p-tolylthio-5-

nitrophenylpyruvic acid (LXXXVIII, R=Me) was more easily cyclized than 2-phenylthio-5-nitrophenylpyruvic acid (LXXXVIII, R=H) and the suggestion was put forward that this was due to the greater susceptibility to electrophilic attack of the p-tolyl group. The fact that the products of this cyclization show a parallel relative tractability in the desulphurization reaction must suggest that the contribution of the methyl group of 8-methyl-2-nitrodibenzo[b,f]thiepin-10-carboxylic acid to the electron density in the benzene ring to which it is conjoined, makes sulphur extrusion easier than in the case of 2-nitrodibenzo[b,f]thiepin-10-carboxylic acid, which lacks an electron-releasing substituent. Support for this view may be found in the literature.

Parham has demonstrated that 2:5-diphenyl-p-dithiin (XLIV) has aromatic properties. Thus it may be nitrated and brominated at the unsubstituted positions in the dithiin ring: the nitro, bromo, dinitro, dibromo and bromonitro derivatives have all been prepared in this way[48,49]. In an attempt to formylate the molecule by treatment with phosphoryl chloride and dimethylformamide at 100°, however, a derivative of thiophen viz. 2:4-diphenyl-5-thenaldehyde (CIII), was obtained instead of the anticipated



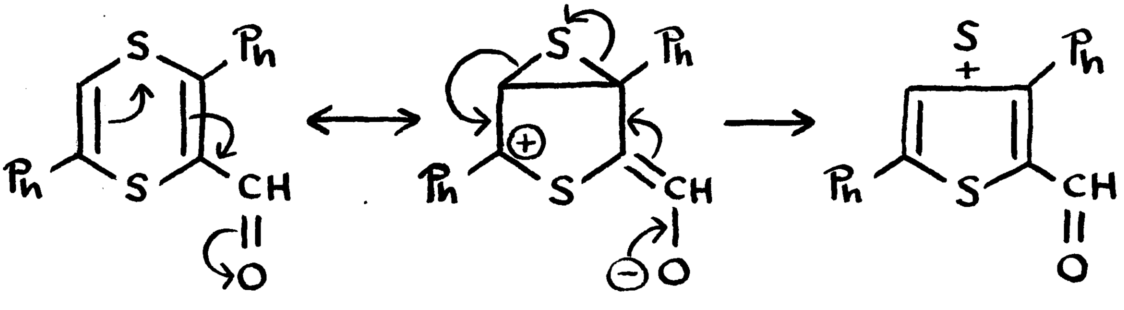
XLIV

CII

CIII

2:5-diphenyl-p-dithiin-3-aldehyde (CII)[47].

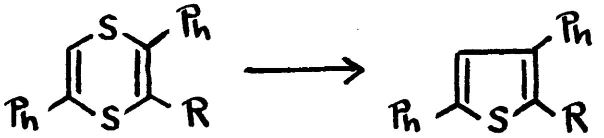
Any endeavour to rationalise this behaviour must above all take account of the fact that the aldehyde group turns up in position 5, and not in position 3, of the product. Parham and Traynelis[47] proposed a mechanism which, written in an abbreviated form, is as follows:



CII a

The postulated intermediate aldehyde (CII) may be written in the canonical form (CII a), which includes a 1:2-episulphide ring; this polarized structure (CII a) may then dissipate its electrical charges by an electron relay movement involving the detachment of the sulphur atom from the episulphide ring. According to this representation, it is the existence in 2:5-diphenyl-p-dithiin-3-aldehyde (CII) of a situation which amounts almost to that present in the conjugated system of an $\alpha:\beta-\gamma:\delta$-dienic aldehyde (e.g. the product CIII) which makes the reaction particularly easy. This kind of "quasi-conjugation" involves only the sulphur in position 1, because imaginary replacement of the other -S- link by a pair of electrons leads to the unconjugated system of a $\beta:\gamma$-unsaturated aldehyde. Hence the episulphide ring, which by this analogy is comparable to a double bond, is preferentially formed round the No. 1 atom, which is then extruded. The mechanism thereby accounts for the position of the aldehyde group in the product.

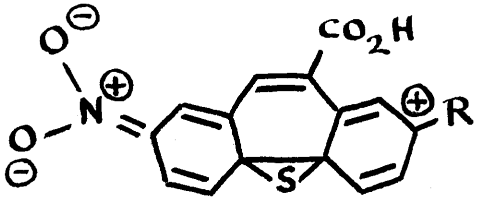
When an attempt was made to formylate 2:5-diphenyl-3-nitro-p-dithiin (XLV, $R=NO_2$) under the same conditions, the compound obtained was 2:4-diphenyl-



XLV XLVIII

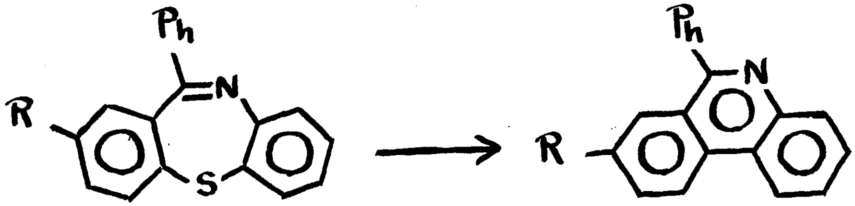
5-nitrothiophen (XLVIII, R=NO_2). The same diphenyl-nitro-p-dithiin, heated alone under nitrogen, underwent decomposition at 135°, also with formation of 2:4-diphenyl-5-nitrothiophen[48]. These results are in accordance with the mechanism, because the nitro group is able, by means of its similar -M effect, to play the part of the formyl group in the postulated intermediate (CII). As we would expect, 2:5-diphenyl-p-dithiin is less thermolabile, because it lacks a substituent with a powerful -M effect. In this instance decomposition does not begin below a temperature of 190°[47].

It will be seen that Parham's mechanism may help to explain the desulphurization of 2-nitrodibenzo[b,f]thiepin-10-carboxylic acid (IX, R=H) and related compounds, because the nitro group is in a position which allows the canonical form (IXa) to be written.



IX a

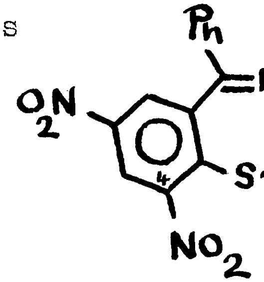
No attempts have been made to desulphurize derivatives of dibenzo[b,f]thiepin which do not possess a nitro group, so it is not possible to assess the influence of the nitro group in this series. In the related dibenzo[b,f] thiazepine series, however, some pertinent results are available.



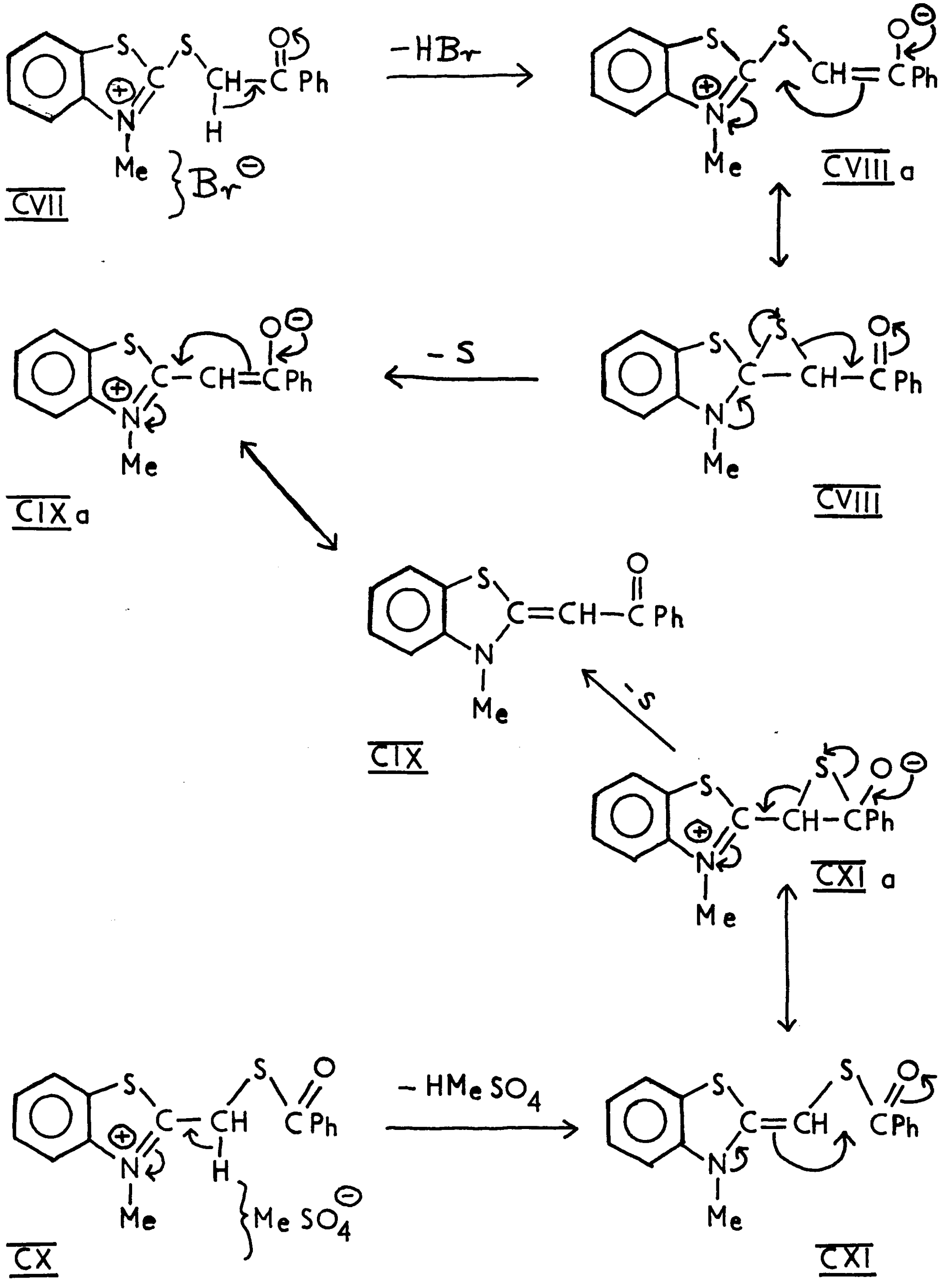
CIV

CV

Jarrett found that treatment of 2-nitro-11-phenyldibenzo[b,f]-1:4-thiazepine (CIV, R=NO_2) with copper bronze in boiling diethyl phthalate for 5-7 min. was sufficient to give a good yield of 7-nitro-9-phenylphenanthridine (CV, R=NO_2). In another chapter of this thesis the desulphurization of 11-phenyldibenzo [b,f]-1:4-thiazepine (CIV, R=H) is described; subjection of this material to the same treatment for 7 min. afforded 9-phenylphenanthridine (CV, R=H) in only 33% yield. The nitro group therefore seems to have an accelerating influence, although the contrary is suggested by another experiment of Jarrett's which showed 2:4-dinitro-11-phenyldibenzo[b,f]-1:4-thiazepine (CVI) to be unresponsive to brief treatment under these conditions. The discrepancy may be due to the fact that the function of the copper has not been taken into account. Donation of a pair of electrons by the sulphur atom to the surface of the copper catalyst could well be a preliminary step, and the presence of a nitro group in position 4 may prevent a sufficiently close approach of the molecule to the metal surface to allow this to happen. Certainly a preliminary step of this nature should assist a desulphurization which operates through a mechanism of the Parham type, because it has been affirmed[42] that a three-membered



CVI


CVII
$Br^{\ominus}$
$-HBr$
CVIII a
CVIII
$-S$
CIX a
CIX
$-S$
CXI a
CX
$MeSO_4^{\ominus}$
$-HMeSO_4$
CXI

ring containing a sulphur atom is unstable when the valency of the sulphur is greater than two; thus the only authentic instances of such compounds are the episulphones of Staudinger and Pfenninger[35] and of Vargha and Kovács[36] (please refer to the Introduction, p. 17); again, Bordwell[89] has published kinetic evidence that the formation of olefins from α-chlorosulphones according to the equation

$$RCH_2.SO_2.CHClR' + 3HO^- \longrightarrow RCH{=}CHR' + Cl^- + SO_3^{=} + 2H_2O$$

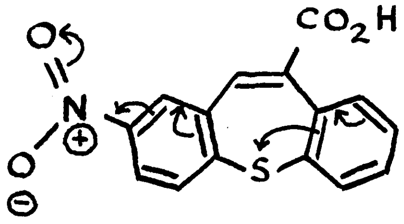
$$(R=R'=H;\quad R=H,\ R'=Ph;\quad R=Ph,\ R'=H)$$

takes place <u>via</u> an intermediary, unstable episulphone.

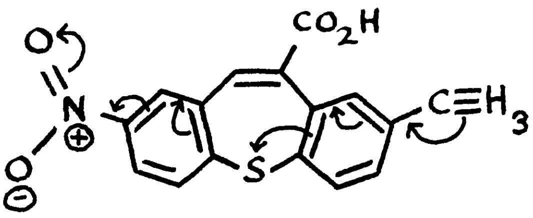
Knott[90] has made some interesting comparative studies of the dequaternization of 3-methyl-2-phenacylthiobenzothiazolium bromide (CVII) and 2-benzoylthiomethyl-3-methylbenzothiazolium methosulphate (CX). Treated with triethylamine at 25°, the first compound became converted, with the loss of hydrogen bromide and a sulphur atom, into 3-methyl-2-phenacylidenebenzothiazoline (CIX). Under the same conditions the second salt is converted into a material which is formulated as 2-benzoylthiomethylene-3-methylbenzothiazoline (CXI), with the loss of methyl hydrogen sulphate. The product (CXI) however, when treated with triethylamine at 80°, is also transformed, with loss of a sulphur atom, into 3-methyl-2-phenacylidenebenzothiazoline (CIX). Knott believes that the elimination of hydrogen bromide from 3-methyl-2-phenacylthiobenzothiazolium bromide (by removal of a proton from the active methylene group) leads to an unstable episulphide (CVIII) which forms the olefin (CIX) by extrusion of the sulphur atom. On the other hand, the structure (CXIa), which also incorporates an episulphide ring, is, because of its polar character, an unimportant contributor to the resonance hybrid of dequaternized 2-benzoylthiomethyl-3-methylbenzothiazolium methosulphate, of which the unpolarized form (CXI) is the typical structure. Thus the dequaternized methosulphate (CX) has little episulphide character, and Knott considers this to be the reason that it is less readily desulphurized than dequaternized 3-methyl-2-phenacylthiobenzothiazolium bromide.

Knott has summed up his results with this very neat generalization: the greater the + M effect of one of the groups attached to the sulphur atom of an organic sulphide, and the greater the -M effect of the other group, the lesser is the stability of the sulphide. Thus, in structure (CVIIIa) the strong -M effect of the quaternary nitrogen atom and the strong +M effect of the enol anion ensure that the form (CVIIIa) has little significance and that the structure (CVIII) is dominant in the resonance hybrid; on the other hand, in the structure (CXI) the -M and +M effects of the carbonyl group and ternary nitrogen atom, respectively, are much weaker because their operation demands the separation of electrical charge, rather than its neutralization, so that the form (CXI) is dominant in the resonance hybrid.

This generalization of Knott's furnishes an explanation of the differing responses of 2-nitrodibenzo[b,f]thiepin-10-carboxylic acid (IX, R=H) and 8-methyl-2-nitrodibenzo[b,f]thiepin-10-carboxylic acid (IX, R=Me) to copper in boiling diethyl phthalate. In the molecule of the acid (IX, R=H) the sulphur atom is joined on one side to a group with a powerful -M effect (the p-nitrophenyl group) and on the other side to a group with a moderate +M effect (the phenyl



(IX, R=H)



(IX, R=Me)

group), while in the molecule of the acid (IX, R=Me) the sulphur atom is joined to the same -M group and to a +M group (the p-tolyl group) fortified by a hyperconjugated methyl group. Polarized canonical forms containing the episulphide ring would therefore be expected to be of more importance in the resonance hybrid of 8-methyl-2-nitrodibenzo[b,f]thiepin-10-carboxylic acid than in the resonance hybrid of its lower homologue, and so the 8-methyl compound should undergo extrusion of sulphur more readily (since in each molecule the carboxyl group is not conjugated with the right-hand benzene ring, there should be little difference in the rates of decarboxylation, and any effects of the kind considered on p. 57 should be equal in both cases).

While the heterolytic mechanism enlarged upon in the foregoing pages may explain the available facts in a qualitatively correct manner, the boiling-point of diethyl phthalate is 296°, and at such a temperature the operation of a homolytic mechanism cannot be ruled out.

Diaryl disulphides are believed to dissociate into free radicals. According to Schönberg, Rupp and Gumlich[91], diphenyl disulphide dissociates into phenylthio radicals

$$\mathrm{Ph - S - S - Ph} \rightleftharpoons \mathrm{2PhS.}$$

at quite low temperatures. Hauptmann _et_ _al_.[12] have shown that treatment of a solution of diphenyl disulphide and di-1-naphthyl disulphide in boiling xylene with de-gassed Raney nickel leads to a mixture of almost equal quantities of diphenyl sulphide, di-1-naphthyl sulphide and 1-naphthyl phenyl sulphide. This is irrefutable evidence that the extrusion of sulphur from diphenyl disulphide with de-gassed Raney nickel is an intermolecular reaction: it is therefore very likely that free radicals are the reactive species. At the present time there appears to be no evidence either to prove or to disprove the participation of free radicals in the extrusion of sulphur from diaryl sulphides.

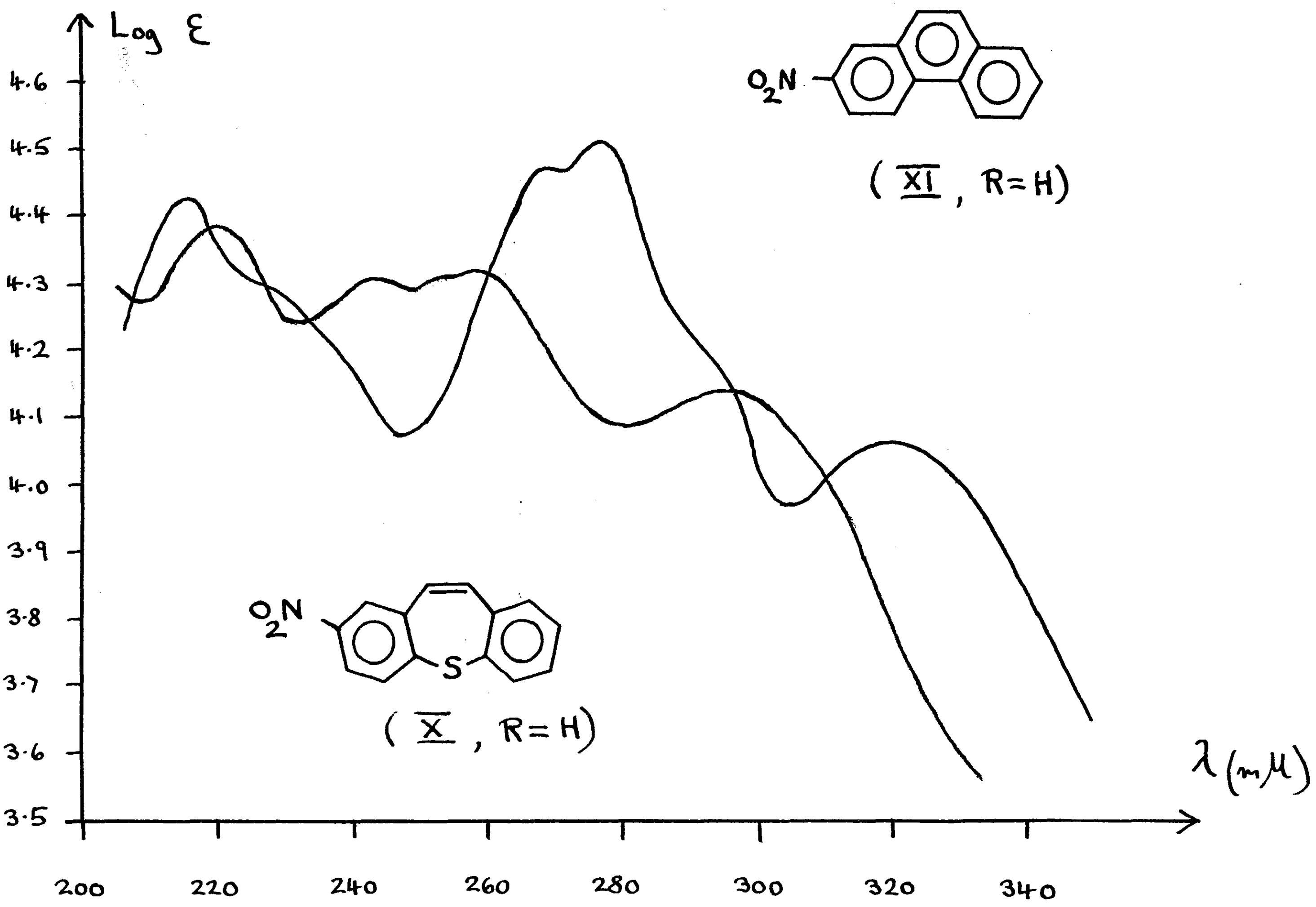
It will be well to conclude this section by summarizing the experimental findings from a strictly practical point of view.

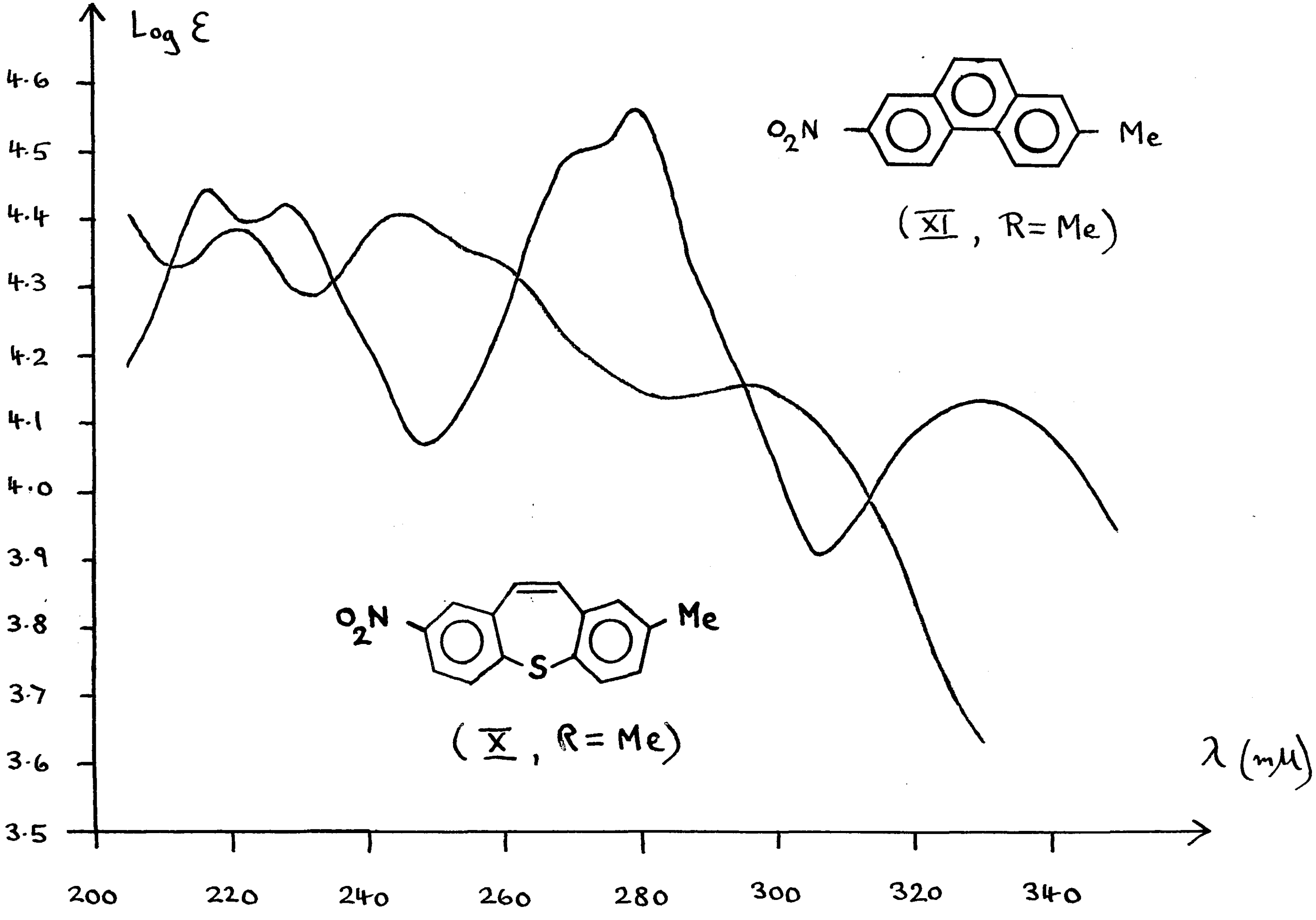
2-Nitrodibenzo[b,f]thiepin (X, R=H), the 2-nitrodibenzo[b,f]thiepin-10-carboxylic acids (IX, R=H, Me) and their methyl esters (XC, R=H, Me) have all been converted to derivatives of phenanthrene by treatment with copper at a moderately high temperature. The first compound was not available in sufficient quantity for a systematic study to be made. The acids may each give as many as three products under these conditions, although Summers succeeded in obtaining a satisfactory yield of 7-methyl-2-nitrophenanthrene (XI, R=Me) from the acid (IX, R=Me). The methyl esters (CI, R=H, Me) of the 2-nitrophenanthrene-9-carboxylic acids (C, R=H, Me) are relatively insoluble substances which may be isolated from a high-boiling solvent without recourse to distillation, so that the use of the thiepin-esters (XC, R=H, Me) is to be preferred from considerations of manipulative ease; the yields are moderate but reproducible. It is however doubtful if the desulphurization of dibenzo[b,f]thiepins has preparative value.

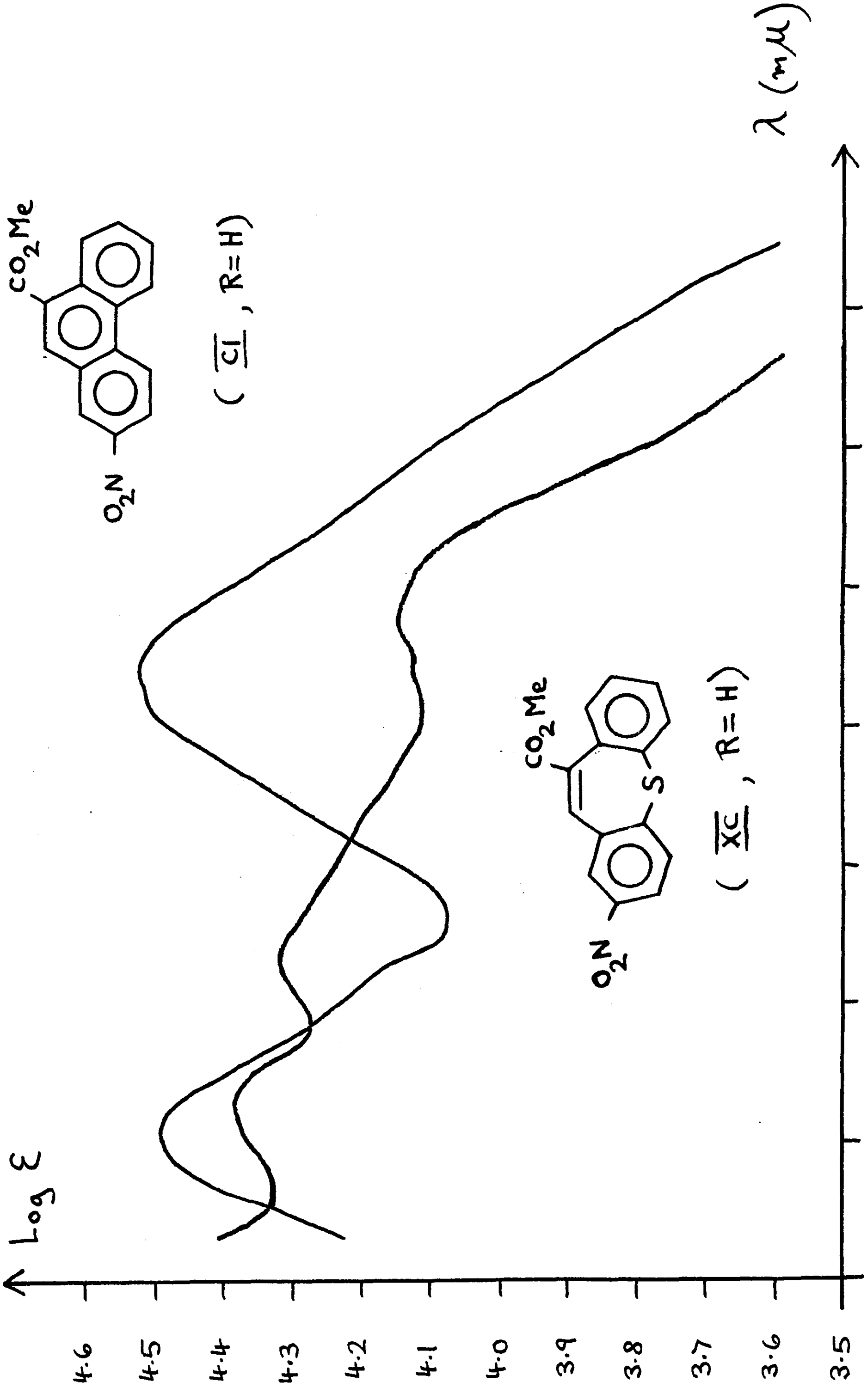
The loss of a sulphur atom from the thiepin derivatives mentioned above is accompanied by a striking change in the shape of the ultraviolet light absorption curves: the presentation of the spectra is arranged to bring out this contrast.

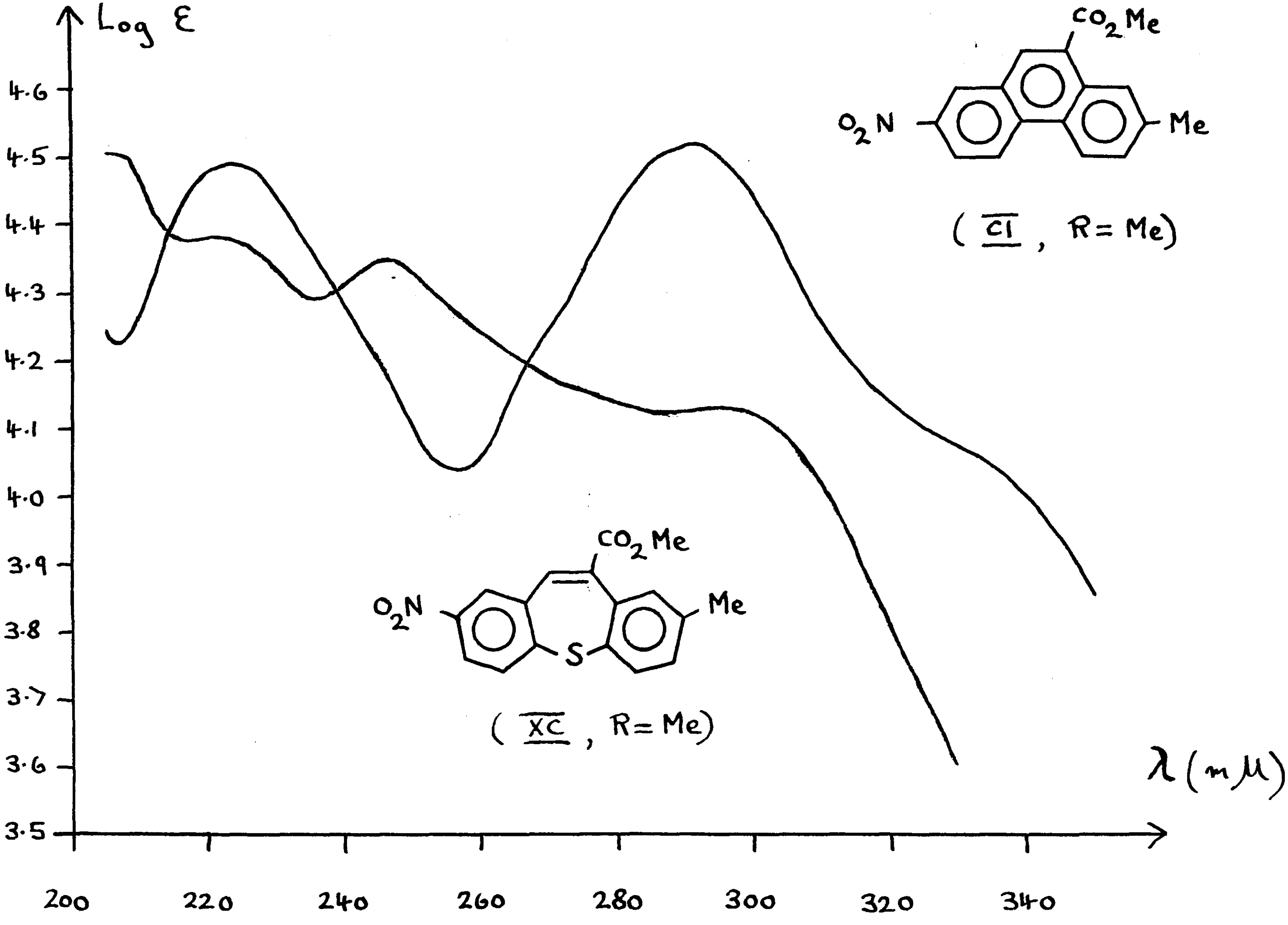
Ultraviolet Absorption Spectra

(measured in 95% ethanol)


Log ε
4.6
4.5
4.4
4.3
4.2
4.1
4.0
3.9
3.8
3.7
3.6
3.5
200
220
240
260
280
300
320
340
λ (mμ)
O_2N
($\overline{XI}$, R=H)
O_2N
S
($\overline{X}$, R=H)


Log ε
4·6
4·5
4·4
4·3
4·2
4·1
4·0
3·9
3·8
3·7
3·6
3·5
200
220
240
260
280
300
320
340
λ (mμ)
O$_2$N
Me
($\underline{\text{XI}}$, R = Me)
O$_2$N
Me
S
($\underline{\text{X}}$, R = Me)


Log ε
λ (mμ)
4.6
4.5
4.4
4.3
4.2
4.1
4.0
3.9
3.8
3.7
3.6
3.5
200
220
240
260
280
300
320
340
CO2Me
O2N
(CI , R=H)
CO2Me
S
O2N
(XC , R=H)


Log ε
4.6
4.5
4.4
4.3
4.2
4.1
4.0
3.9
3.8
3.7
3.6
3.5
200
220
240
260
280
300
320
340
λ (mμ)
CO2Me
O2N
Me
(CI , R= Me)
CO2Me
O2N
Me
S
(XC , R= Me)

EXPERIMENTAL

Melting-points are uncorrected, unless the contrary is stated.

Ultraviolet absorption spectra were measured with a Unicam S.P. 500 spectrophotometer. Corrections were applied for inequality of cell transmission, except where the spectra are described as uncorrected.

Infrared absorption spectra were recorded by a Perkin Elmer spectrophotometer (Model No. 13). The samples were prepared as suspensions, either in pressed discs of potassium chloride or in Nujol; the method used is indicated in each instance. The relative strengths of the bands are sometimes indicated in parentheses after the frequencies, by the symbols vs (very strong), s (strong), m (medium) and w (weak).

The solvent described as "light petroleum" was of boiling-range 60-80°.

The remarks on this page apply also to the experimental work recorded in the other chapters of this thesis.

2-Chloro-5-nitrobenzaldehyde was made according to Erdmann[92].

5-Nitro-2-phenylthiobenzaldehyde (LXXXV, R=H)

2-Chloro-5-nitrobenzaldehyde (45 g.) and thiophenol (25 g.) were dissolved in methylated spirits (500 ml.) by warming the mechanically stirred mixture on a water bath. Warm water (200 ml.) was added and the temperature of the solution was raised to 60°. Potassium carbonate (18 g.) was added in portions over a period of 20 min.; a yellow oil began to separate before the addition had been completed, but this soon crystallized. Stirring at 60° was continued for 40 min., and the preparation was set aside for 12 hr. The 5-nitro-2-phenylthiobenzaldehyde was collected, washed with water, dried over KOH in vacuo and dissolved in ethyl acetate, from which it crystallized in the form of very large, shining yellow prisms (48 g.) m.p. 105°.

5-Nitro-2-p-tolylthiobenzaldehyde (LXXXV, R=Me)

To a solution of 2-chloro-5-nitrobenzaldehyde (45 g.) and thio-p-cresol (30 g.) in methylated spirits (500 ml.) and water (200 ml.), maintained at 60°, potassium carbonate (20 g.) was added in portions over 20 min. and stirring was continued thereafter for 40 min. Crystals of the product began to appear before the addition of the potassium carbonate had been in progress for 3 min. After the preparation had stood for 12 hr., the 5-nitro-2-p-tolylthiobenzaldehyde was collected, washed with water, dried and dissolved in ethyl acetate, from which it formed very large, shining yellow prisms (55 g.) m.p. 156-157°.

5-Nitro-2-phenylthiophenylpyruvic acid (LXXXVIII, R=H)

The recommendations of Galat[3] were incorporated in this preparation.

A mixture of 5-nitro-2-phenylthiobenzaldehyde (LXXXV, R=H; 25 g.), aceturic acid (11.5 g.), potassium bicarbonate (9.8 g.) and acetic anhydride (31 ml.), protected from moisture by a calcium chloride tube, was heated on the steam bath, with occasional stirring, for one hour. After 12 hr. the preparation was filtered and the collected solid was washed with glacial acetic acid (20 ml.), dried at the pump and fractionally recrystallized from benzene: white needles of potassium acetate, the yellow azlactone (LXXXVI, R=H; 18.5 g.) m.p. 183-188°, and an unwanted, bright-red solid of high m.p. appeared in that order. A solution of the azlactone in acetic acid (384 ml.) and water (16 ml.) was boiled under reflux for 20 min., treated with charcoal (4 g.), boiled for a further 10 min. and filtered. If desired, the lemon yellow needles of α-*acetylamino*-β-(5-*nitro*-2-*phenylthiophenyl)acrylic acid* (LXXXVII, R=H; 17.1 g.), m.p. 233° after recrystallization from acetic acid (Found C, 57.23; H, 3.97. $C_{17}H_{14}N_2O_5S$ requires C, 56.96; H, 3.94%), which separated from the filtrate on cooling, were collected, but this was unnecessary: addition of conc. HCl (128 ml.) and water (240 ml.) to the filtrate, followed by boiling for 5 hr. under reflux, effected hydrolysis to pure 5-nitro-2-phenylthiophenylpyruvic acid (LXXXVIII, R=H) m.p. 146°, which crystallized out on cooling. The azlactone (LXXXVI, R=H) and the cinnamic acid (LXXXVII, R=H) both underwent hydrolysis to 5-nitro-2-phenylthiophenylpyruvic acid in quantitative yield.

5-Nitro-2-p-tolylthiophenylpyruvic acid (LXXXVIII, R=Me) The conditions used in the condensation reaction described below were derived from those used by Herbst and Shemin[78].

5-Nitro-2-p-tolylthiobenzaldehyde (LXXXV, R=Me; 20 g.) aceturic acid (9 g.), fused sodium acetate (6.5 g.) and acetic anhydride (25 ml.) were boiled under reflux for one hour. The cold reaction mixture was filtered, the solid residue was washed with acetic acid and water, and dried over $CaCl_2$/KOH *in vacuo*. After two recrystallizations from benzene, the azlactone (LXXXVI, R = Me; 14.3 g.) m.p. 192-195° was dissolved in boiling glacial acetic acid (192 ml.) and water (8 ml.), charcoal (3 g.) was added, the mixture was boiled for 10 min. under reflux and filtered. The filtrate was made up to a weight of 278 g. by addition of acetic acid containing 4% of added water, water (174 ml.) and conc. HCl (94 ml.) were added and the solution was refluxed for 5 hr. Lemon yellow crystals (12.7 g.) m.p. 138° of 5-nitro-2-p-tolylthiophenylpyruvic acid (LXXXVIII, R=Me) separated from the cooling filtrate,

2-Nitrodibenzo[b,f]thiepin-10-carboxylic acid (IX, R=H)

A solution of 5-nitro-2-phenylthiophenylpyruvic acid (LXXXVIII, R=H; 20 g.) in a mixture of 48% hydrobromic acid (40 ml.) and acetic acid (70 ml.) was boiled under reflux for 12 hr. Needles began to separate after about 6½ hr. After the preparation had been laid aside for 12 hr., the crystals were collected, washed with acetic acid (5 ml.) and water, and recrystallized twice from acetic acid, charcoal (2 g.) being employed on the second occasion. The pale yellow crystals m.p. 248° of 2-nitrodibenzo[b,f]thiepin-10-carboxylic acid (IX, R=H) weighed 14.2 g. (75%) after drying over KOH *in vacuo*. Ultraviolet light absorption maxima (in 95% ethanol: 223 (log ε 4.38), 244 (log ε 4.30), and 294.5 mμ (log ε 4.13). (Note: In an earlier experiment a reaction period of 10 hr. produced a yield of 65%).

8-Methyl-2-nitrodibenzo[b,f]thiepin-10-carboxylic acid (IX, R=Me)

A solution of 5-nitro-2-*p*-tolylthiophenylpyruvic acid (LXXXVIII, R=Me; 12.7 g.) in a mixture of 48%

hydrobromic acid (25.4 ml.) and acetic acid (44.5 ml.) was boiled under reflux for 5 hr.; within 30 min. of commencement, needles started to separate. After 12 hr. at room temperature the preparation was filtered and the crystals were washed with water and dried over KOH in vacuo. The greenish-brown product (11.2 g.) m.p. 269° was recrystallized (charcoal, 2 g.) from acetic acid. The pale yellow 8-methyl-2-nitrodibenzo[b,f]thiepin-10-carboxylic acid (IX, R=Me) m.p. 273-276° weighed 10.4 g. (86.5%) after drying over KOH in vacuo. Ultraviolet light absorption maxima (in 95% ethanol): 222 (log ε 4.39), 245 (log ε 4.36) and 292 mμ (log ε 4.14).

Decarboxylation of 2-Nitrodibenzo[b,f]thiepin-10-carboxylic acid (IX, R=H).

The carboxylic acid (0.50 g.), copper bronze (0.5 g.) and diethyl phthalate (3.0 ml.) were heated under nitrogen for 30 min. on a metal-bath at 250-255°. The reaction mixture was diluted with benzene and filtered through a charcoal pad. The benzene and diethyl phthalate were removed from the filtrate by distillation under reduced pressure. At a pressure of 0.2 to 0.3 mm. of mercury, most of the diethyl phthalate distilled from a steam-bath, but a final fraction was taken from an air-bath at 120°. The dark, viscous oil which remained was extracted several times with boiling light petroleum, and the combined extracts were chromatographed on alumina, using light petroleum as eluant. Bright-yellow crystals (0.21 g.) of 2-nitrodibenzo[b,f]thiepin (X, R=H) m.p. 110° (unchanged by admixture with material made by Summers)[2] were obtained by concentration of the eluate. Ultraviolet light absorption maxima (in 95% ethanol): 221 (log ε 4.39), 244 (log ε 4.31), 259 (log ε 4.32) and 295 mμ (log ε 4.14).

8-Methyl-2-nitrodibenzo[b,f]thiepin (X, R=Me)

8-Methyl-2-nitrodibenzo[b,f]thiepin-10-carboxylic acid (IX, R=Me; 0.50 g.), copper bronze (0.5 g.) and diethyl phthalate (3 ml.) were heated under nitrogen for 30 min. on a metal-bath at 250-255°. The reaction mixture was diluted with benzene and filtered through a charcoal pad, and the solvents were removed from the filtrate by distillation under reduced pressure. The residue, including a quantity of yellow crystals which had sublimed onto the upper surfaces of the distillation apparatus, was extracted several times with boiling light petroleum, and the combined extracts were chromatographed on alumina, using light petroleum as eluant. Evaporation of the first eluate fraction to dryness followed by recrystallization of the residue from methanol afforded a small quantity of 8-*methyl*-2-*nitrodibenzo*[b,f]*thiepin* (X, R=Me) Found: C, 66.98; H, 3.76; N, 5.08. $C_{15}H_{11}NO_2S$ requires C, 66.91; H, 4.12; N, 5.20%) in the form of bright yellow needles m.p. 117°. Ultraviolet light absorption maxima (in 95% ethanol): 222 (log ε 4.38), 244 (log ε 4.41) and 296 μu (log ε 4.16).

A mixture was obtained from the second eluate fraction: attempts to resolve this by fractional crystallization from light petroleum and from methanol met with no success. Elution with light petroleum containing 10% (v/v) of benzene afforded a third fraction, from which was obtained a small quantity of 7-methyl-2-nitrophenanthrene (XI, R=Me) m.p. 191-192°, unchanged by admixture with material made by Summers[2]. Ultraviolet light absorption maxima of 7-methyl-2-nitrophenanthrene (in 95% ethanol): 217 (log ε 4.44), 228 (log 4.42), 279 (log ε 4.56) and 330 mμ (log ε 4.14).

The Action of Diazomethane on 2-Nitrodibenzo[b,f]thiepin-10-carboxylic acid (IX, R=H)

A solution of diazomethane (prepared from 2 g. nitrosomethylurea according to the simpler of the two procedures described by Arndt[93]) in ether was added in portions, with shaking, to a suspension of the carboxylic acid (1.50 g.) in ether (20 ml.), and the mixture was laid aside for 12 hr. The ethereal supernatant was decanted from the remaining solid, from which pale yellow crystals (1.06 g.) of methyl 2-nitrodibenzo[b,f]thiepin-10-carboxylate (XC, R=H) (Found: C, 61.53; H, 3.50. $C_{16}H_{11}NO_4S$ requires C, 61.34; H, 3.54%) m.p. 156° were obtained after recrystallization, firstly from acetic acid and finally from a mixture of methyl acetate and methanol. Beautiful colourless prisms of methyl pyrazolino-[4′:5′-11:10]-2-nitrodihydrodibenzo[b,f]thiepin-10-carboxylate (LXXXIX) (Found: C, 57.90; H, 3.63; N, 12.14. $C_{17}H_{13}N_3O_4S$ requires C, 57.46; H, 3.69; N, 11.83%) separated from the decantate on further standing. These evolved nitrogen on heating, but had no definite decomposition point.

Esterification of 2-Nitrodibenzo[b,f]thiepin-10-carboxylic acid (**IX,** R=H) with Methanol and Sulphuric Acid

2-Nitrodibenzo[b,f]thiepin-10-carboxylic acid (5.0 g.), methanol (distilled from magnesium methoxide; 250 ml.) and concentrated sulphuric acid (2 ml.) were heated under reflux and drying ($CaCl_2$) tube on the steam-bath for 10 hr. The crystals formed during overnight standing were filtered off, washed with water, dilute ammonia solution and once more with water, and dried over P_2O_5 *in vacuo*. A further quantity of material was obtained by adding the washing fluids to the filtrate, dividing the collected solid between dilute aqueous sodium carbonate and an organic phase consisting of ether containing a little benzene, drying (Na_2SO_4) the organic layer and evaporating the solvents. The combined solids were dissolved in benzene and chromatographed on a column of neutral alumina, using benzene as eluant. Concentration of the eluate followed by dilution with light petroleum produced beautiful, cream-coloured, shining needles (4.62 g.; 88%) of methyl 2-nitrodibenzo[b,f]thiepin-10-carboxylate (XC, R=H) m.p. 156°, a sample of which was prepared for analysis by recrystallization from methyl acetate/methanol (Found: C, 61.58; H, 3.76; N, 4.96. Calculated for $C_{16}H_{11}NO_4S$: C, 61.34; H, 3.54; N, 4.47%). Ultraviolet light absorption maxima (in 95% ethanol): 225 (log ε 4.38), 247 (log ε 4.32) and 295.5 mμ (log ε 4.14).

Esterification of 8-Methyl-2-nitrodibenzo[b,f]thiepin-10-carboxylic acid (IX, R=Me) with Methanol and Sulphuric Acid

8-Methyl-2-nitrodibenzo[b,f]thiepin-10-carboxylic acid (5.0 g.), methanol (distilled from magnesium methoxide; 250-300 ml.) and concentrated sulphuric acid (2 ml.) were heated under reflux and drying ($CaCl_2$) tube on the steam-bath for 12 hr. The crystals which formed from the solution during standing (48 hr.) were collected, washed with water, dilute ammonia solution and again with water, and dried over P_2O_5 *in vacuo*. A solution of the product in benzene was passed through a column of neutral alumina using benzene as eluant. Concentration of the eluate followed by dilution with light petroleum provided cream-coloured crystals (4.18 g.) of the ester, m.p. 182-184°. The washing fluids were added to the methanol/sulphuric acid filtrate, the precipitate was collected and divided between dilute sodium carbonate solution and benzene, the benzene layer was washed with water, dried (Na_2SO_4), concentrated and diluted with light petroleum. The crystals (0.27 g.; m.p. 182-183°) were twice recrystallized from benzene/light petroleum and once from methyl acetate/methanol, to give a sample m.p. 181-183° of *methyl* 8-*methyl*-2-*nitrodibenzo*[b,f]*thiepin*-10-*carboxylate* (XC, R=Me. Found C, 62.57; H, 4.04. $C_{17}H_{13}NO_4S$ requires C, 62.38; H, 4.00%). Ultraviolet light absorption maxima (in 95% ethanol): 221.5 (log ε 4.38), 246.5 (log ε 4.35) and 295 mμ (log ε 4.13). The total weight of pure ester was 4.45 g. (85%).

Desulphurization Experiments

Treatment of 2-Nitrodibenzo[b,f]thiepin-10-carboxylic Acid (IX, R=H) with Cuprous Oxide in Quinoline: an Attempt to Repeat the Isolation of the Substance of m.p. 117° Reported by Summers

2-Nitrodibenzo[b,f]thiepin-10-carboxylic acid

(0.50 g.) cuprous oxide (previously heated to a temperature of 300° under nitrogen to drive off adsorbed moisture; 1.5 g.) and quinoline (25 ml.) were refluxed with mechanical stirring on a bath of Wood's metal for 9 hr., the mixture was set aside (12 hr.), diluted with benzene and filtered. The opaque filtrate was extracted with dilute sulphuric acid: during this process a dark brown solid appeared, and was removed by filtration. The benzene layer, which was now red in colour and transparent, was washed with water and then with dilute sodium carbonate solution. After a further wash with water, the benzene solution was concentrated, dried and run through a column of alumina, using benzene as eluant. A red intractable oil was obtained by evaporation of the benzene from the eluate.

The sodium carbonate extract deposited a solid on cooling: this was re-dissolved by warming on the steam-bath. The warm solution was acidified by addition of concentrated hydrochloric acid. The cold preparation was filtered and the solid was recrystallized from acetic acid (charcoal). This product will be referred to as "the acid 'A'" under the following heading.

Pyrolysis of 2-Nitrodibenzo[b,f]thiepin-10-carboxylic Acid (IX, R=H) in the Presence of Copper

2-Nitrodibenzo[b,f]thiepin-10-carboxylic acid (2 g.) was distributed about a coil of freshly-reduced copper wire (10 g.) within a small distillation flask fitted with an air-leak and an air condenser, the lower (exit) end of which was connected to a second distillation flask containing benzene: the side-arm of the second flask was directed upwards into the socket of a Liebig condenser, the exit of which was loosely filled with a plug of cotton wool moistened with benzene.

With a stream of nitrogen entering through the air leak and the benzene refluxing vigorously over a water-bath, the flask containing the reactants was introduced into a bath of Wood's metal at a temperature of about 120°. The temperature of the metal bath was raised to 320° as rapidly as possible.

After a short pause a cloud of yellow smoke was projected from the reaction vessel. Most of the yellow colour disappeared from the smoke as it passed through the benzene vapour, the fumes which penetrated as far as the Liebig condenser (where they were finally denied exit by the cotton wool plug) being of a white appearance. The metal-bath was removed 2-3 min. after the "puff" appeared.

The benzene solution was set aside and every piece of the apparatus was thoroughly washed in fresh refluxing benzene. The washings were combined with the benzene solution and the whole was concentrated to small bulk. A nearly colourless solid appeared in the concentrate and was filtered off. This product was combined with the acid 'A' mentioned under the previous heading, and the combination will be dealt with below under the heading "the mixture 'A'." The filtrate was chromatographed on a column of alumina with a benzene eluant. A bright orange band passed down the column, and the eluate (which was almost colourless) was collected and concentrated. The shining, yellow spars which formed on cooling lost their crystalline appearance after collection and drying in a current of air; the amorphous solid (0.069 g.; 3.9%) m.p. 117-120° which remained was twice recrystallized from benzene. The crushed product was dried at 80° over KOH in vacuo (Found: C, 75.47; H, 4.09; N, 6.45. Calculated for $C_{14}H_9NO_2$: C, 75.32; H, 4.06; N, 6.28%) after which it melted at 120°. Ultraviolet light absorption maxima (in 95% ethanol): 216 (log ε 4.44), 277 (log ε 4.51) and 319.5 mμ (log ε 4.07).

The material (0.020 g.) was dissolved in boiling acetic acid (0.2 ml.) and a solution of chromic oxide (0.030 g.) in a small drop of water diluted with acetic acid (0.2 ml.) was added drop by drop over a period of about 10 min. An acetic acid rinse (0.2 ml.) was added and the solution was boiled for a further 2 min.: crystals were precipitated before heating had ceased. The cold reaction mixture was filtered and the solid was washed with a drop of acetic acid and then with water. The air-dried material (0.010 g.; micro- m.p. 267-268°) was recrystallized from acetic acid. The orange-yellow crystals possessed the micro-m.p. 268-269°, which was depressed to 265-266° by admixture with authentic (vide infra) 2-nitrophenanthraquinone (XCI) of micro- m.p. 264-265°; the two samples had identical infrared absorption spectra (KCl disc) which were dominated in the high frequency region by strong peaks at 1680 (C=O), 1590 (benzene ring), 1530 (NO_2), 1345 (NO_2) and 1288 cm^{-1} (C=O) and in the low frequency region by bands at 782 and 747 cm^{-1}.

The authentic sample of 2-nitrophenanthraquinone was obtained by nitration of phenanthraquinone with nitric acid (d 1.4) followed by extraction of the more soluble 4-nitro isomer with boiling ethanol, and recrystallization of the residue from acetic acid, as described by Schmidt and Spoun[80]. After two further recrystallizations from acetic acid the orange crystals melted at 260-262° (S. and S. reported m.p. 258-260°).

The structure of the desulphurization product of m.p. 120° is thereby confirmed as that of 2-nitrophenanthrene (XI, R=H). The material of m.p. 117° obtained by Summers[2] from the treatment of 2-nitrodibenzo[b,f]thiepin-10-carboxylic acid (IX, R=H) with copper in boiling quinoline, was therefore probably impure 2-nitrophenanthrene.

The Mixture 'A'

The mixture was recrystallized (charcoal) from acetic acid. The off-white needles had *micro*-m.p. 260-262° which was depressed to 226-229° by admixture with 2-nitrodibenzo[b,f]thiepin-10-carboxylic acid (IX, R=H) of *micro*-m.p. 248-250°. The material dissolved in warm dilute sodium hydroxide solution, from which it was re-precipitated by acid. The uncorrected ultraviolet light absorption maxima (in 95% ethanol) were as follows (log ε values are calculated assuming a molecular weight of 267): 220 (log ε 4.43), and 285.5 mμ (log ε 4.46). The material is therefore an acid distinct from 2-nitrodibenzo[b,f]thiepin-10-carboxylic acid. A specimen of *micro*-m.p. 265-266° was obtained by a second recrystallization from acetic acid (Found: C, 67.82; H, 3.57. $C_{15}H_9NO_4$ requires C, 67.41; H, 3.39%).

A portion (0.020 g.) of the acid was dissolved in boiling acetic acid, and a solution of sodium dichromate ($Na_2Cr_2O_7.2H_2O$; 0.047 g.) in a drop of water diluted with acetic acid (0.2 ml.) was added over a period of 30 min., followed by an acetic acid rinse (0.2 ml.). Heating was continued for 30 min., some of the acetic acid was allowed to distil off and the solution was permitted to cool. The crystals were collected and divided between chloroform and dilute sodium carbonate solution. A white solid, which was apparently the sodium salt of the organic starting material, appeared during the separation, but remained suspended in the aqueous layer. The sodium carbonate extract was warmed to dissolve the precipitated salt, the solution was acidified and the acid starting material (0.006 g.) was collected. The chloroform solution was washed with water and evaporated to dryness. Orange-yellow crystals micro-m.p. 269-270° were obtained by two recrystallizations of the residue from acetic acid. These were shown to be 2-nitrophenanthraquinone (XCI) by mixed micro-m.p. (263-267°) with authentic (but less pure) 2-nitrophenanthraquinone (micro-m.p. 264-265°) and by comparison of the infrared absorption spectrum with that of the authentic material.

The acid of micro-m.p. 265-266° is therefore 2-nitrophenanthrene-9-carboxylic acid ($\overline{C}$, R=H).

N.B. The preparation of a purer sample of this acid is described on p. 101).

Note: In all experiments described hereafter, the copper bronze employed was taken from a preparation which had been heated at a temperature of 300° in a stream of nitrogen, and the diethyl phthalate required was taken from a batch which had been twice re-distilled in an apparatus isolated from moisture by a drying ($CaCl_2$) tube.

Treatment of 2-Nitrodibenzo[b,f]thiepin-10-carboxylic acid (IX, R=H) with Copper Bronze in Diethyl Phthalate

2-Nitrodibenzo[b,f]thiepin-10-carboxylic acid (0.50 g.), copper bronze (0.40 g.) and diethyl phthalate (2.0ml.) were boiled for 15 min. under reflux in an atmosphere of nitrogen, on a metal-bath maintained at a temperature of 320-325°. The cold reaction mixture was diluted with benzene and filtered, the filtrate was washed with aqueous sodium carbonate and water and re-filtered, hot, through a charcoal pad. The benzene was removed from the filtrate at 100° *in vacuo* and the diethyl phthalate was distilled from an air-bath at 109-111° (bath)/0.65 mm. The residual black tar was extracted with boiling methanol, from which crystals were deposited on cooling. These were dissolved in benzene and the solution was run through a column of alumina by elution with benzene. The concentrated eluate afforded crystals (0.070 g.; 15.7%*) m.p. 118-120° of 2-nitrophenanthrene (XI, R=H) on cooling.

* This figure is lower than it might have been, because some material was lost during concentration of the methanol extracts.

Methyl 2-Nitrophenanthrene-9-carboxylate (CI, R=H)

Methyl 2-nitrodibenzo[b,f]thiepin-10-carboxylate (XC, R=H; 0.50 g.) copper bronze (0.5 g.) and diethyl phthalate (3.0 ml.) were heated under a reflux condenser and drying ($CaCl_2$) tube, in an atmosphere of nitrogen, for 7 min. on a metal-bath maintained at a temperature of 315-335°. The cooled reaction mixture was diluted with benzene, brought to the boil (to ensure solution of any precipitated material), and allowed to cool once more; the mixture was then poured onto a short column of neutral alumina, which was eluted with benzene*. The eluate was concentrated and flooded with light petroleum, the process was repeated twice to remove the last traces of benzene, more light petroleum was added and the preparation was set aside. The yellow needles (0.206 g.; m.p. 153-155°) were collected, re-dissolved in benzene and chromatographed once more on a column of neutral alumina eluted with benzene. Concentration of the eluate and dilution with light petroleum afforded cream-coloured crystals (0.174 g.; 38.8%) m.p. 159-161° of <u>methyl</u> 2-<u>nitrophenanthrene</u>-9-<u>carboxylate</u> ($\overline{\text{CI}}$, R=H) a sample of which was recrystallized from methyl acetate for the purposes of analysis (Found: C, 68.61; H, 3.82.

* This process was more convenient than straightforward filtration for removal of the copper; due to the presence of the diethyl phthalate nothing more than a filtration was achieved.

$C_{16}H_{11}NO_4$ requires C, 68.32; H, 3.94%). Ultraviolet light absorption maxima (in 95% ethanol): 222 (log ε 4.49), and 288 mμ (log ε 4.52).

Note: A subsequent experiment in which the time of heating was prolonged to 11 min. produced 39.2% of the ester; since previous experiments with refluxing periods of 4-5 and 15 min. gave lower yields, it is probable that the optimum period lies between 7 and 11 min.

Hydrolysis of Methyl 2-Nitrophenanthrene-9-carboxylate (CI, R=H)

A solution of the ester (0.34 g.) in a mixture of acetic acid (27 ml.) and 5N-hydrochloric acid (17 ml.) was boiled under reflux for 5 hr.; needles began to separate after 3 hr. The preparation was set aside for 12 hr. and the cream-coloured needles (0.307 g.; 95%) m.p. 258-260° were collected and dried at 100° over KOH in vacuo. A specimen was prepared for analysis by recrystallization from acetonitrile (Found: C, 67.49; H, 3.31. Calculated for $C_{15}H_9NO_4$: C, 67.41; H, 3.39%). The material had micro-m.p. 266°, unchanged by admixture with 2-nitrophenanthrene-9-carboxylic acid (p. 98). Ultraviolet light absorption maxima (in 95% ethanol): 221.5 (log ε 4.48), and 285 mμ (log ε 4.53).

Methyl 7-Methyl-2-nitrophenanthrene-9-carboxylate (CI, R=Me)

Methyl 8-methyl-2-nitrodibenzo[b,f]thiepin-10-carboxylate (XC, R=Me; 0.50 g.), copper bronze (0.5 g.) and diethyl phthalate (3 ml.) were heated under a reflux condenser and drying ($CaCl_2$) tube, in an atmosphere of nitrogen, for 7½ min. on a metal-bath maintained at a temperature of 320-325°. The cooled reaction mixture was diluted with benzene, brought to the boil and allowed to cool once more; the mixture was then poured onto the top of a column of neutral alumina, which was eluted with benzene. The eluate was concentrated and flooded with light petroleum, the process was repeated twice, more light petroleum was added and the preparation was set aside. The yellow solid (0.303 g.; m.p. 179-182°) was collected, washed with light petroleum, re-dissolved in benzene and chromatographed once more on a column of neutral alumina eluted with benzene. Concentration of the eluate and dilution with light petroleum afforded cream-coloured crystals (0.25 g.; 55%) m.p. 186-187° of methyl 7-methyl-2-nitrophenanthrene-9-carboxylate (CI, R=Me) which were recrystallized from methyl acetate to m.p. 187-188° (Found: C, 69.29; H, 4.46. $C_{17}H_{13}NO_4$ requires C, 69.14; H, 4.44%). Ultraviolet light absorption maxima (in 95% ethanol): 224 (log ε 4.49), and 291.5 $m\mu$ (log ε 4.52).

Notes: (i) A previous experiment performed under almost identical conditions provided 53% of the ester; results are therefore reproducible.

(ii) An experiment in which the refluxing time was increased to 15 min., gave only a poor yield of the ester.

7-Methyl-2-nitrophenanthrene-9-carboxylic acid (C, R=Me)

Methyl 7-methyl-2-nitrophenanthrene-9-carboxylate (CI, R=Me; 0.100 g.), acetic acid (8 ml.) and 5N-hydrochloric acid (5 ml.) were boiled under reflux for 4 hr., without complete solution taking place, and the mixture was set aside to cool. The solid was collected, recrystallized from acetic acid and dried at 100° over KOH *in vacuo*. The cream-coloured crystals (0.069 g.; 73%) of 7-*methyl*-2-*nitrophenanthrene*-9-*carboxylic acid* (C, R=Me) melted at 289-291°. A sample was prepared for analysis by recrystallization from acetonitrile (Found: C, 68.23; H, 3.76. $C_{16}H_{11}NO_4$ requires C, 68.32; H, 3.94%). Ultraviolet light absorption maxima (in 95% ethanol): 223 (log ε 4.49), and 287 mμ (log ε 4.52).

Desulphurization of 2-Nitrodibenzo[b,f]thiepin (X, R=H)

2-Nitrodibenzo[b,f]thiepin (0.25 g.), copper bronze (0.25 g.) and diethyl phthalate (1.5 ml.) were boiled for 7½ min. under reflux, in an atmosphere of nitrogen. The reaction mixture was diluted with benzene, warmed, and filtered through a charcoal pad, The solvents were removed from the filtrate by distillation under reduced pressure and the residual oil, together with a sublimate of yellow crystals which had formed on the upper surfaces of the apparatus, was dissolved in benzene, the solution was transferred to a test-tube and the benzene was boiled off over the steam-bath, the removal of the last traces being assisted by addition of light petroleum. The buff solid (0.177 g.; m.p. 86-102°) which was obtained by rubbing the residue under methanol, was extracted with boiling light petroleum and the cold extract was chromatographed on a column of alumina with light petroleum as eluant. A pale greenish-yellow band was collected, and afforded, after removal of the light petroleum and recrystallization of the residue from methanol, yellow crystals (0.042 g.; 19%) m.p. 120°, of 2-nitrophenanthrene (XI, R=H). Concentration of the filtrate afforded a mixture (0.053 g.) which was combined with material (0.012 g.) obtained from a second chromatographic fraction and re-chromatographed on alumina eluted with light petroleum. Patient crystallization from methanol of material from the first fraction of eluate afforded only a small amount of golden-yellow needles (*micro*-m.p. 110°) of starting material.

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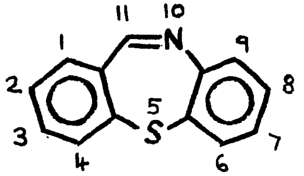
PART TWO

The Interaction of Hydrazoic Acid and Thioxanthenylium Salts as a Route to Dibenzo[b,f]-1:4-thiazepines.

Contents

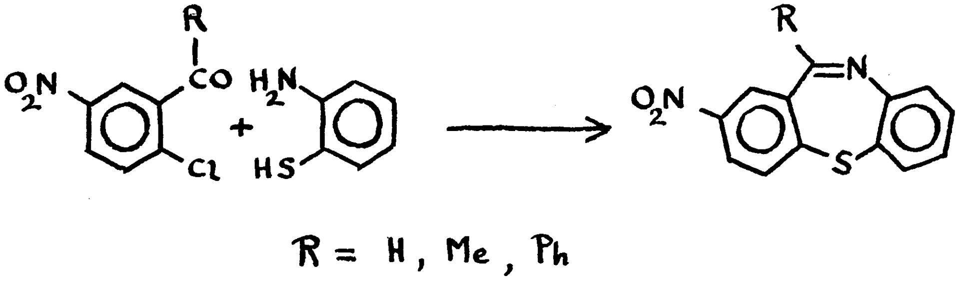
INTRODUCTION

The successful extrusion of sulphur from a number of derivatives of dibenzo[b,f]-1:4-thiazepine (I) by Jarrett[1] made the synthesis of further representatives



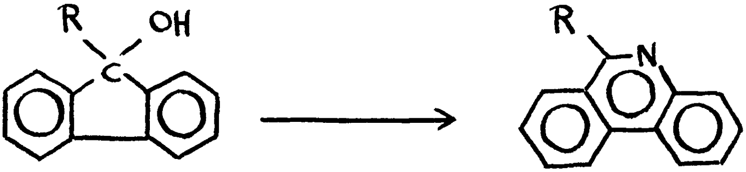
I

of this ring system desirable. Jarrett prepared these compounds by the condensation of o-amino-thiophenol with aromatic aldehydes and ketones containing an activated chlorine atom in the ortho position:



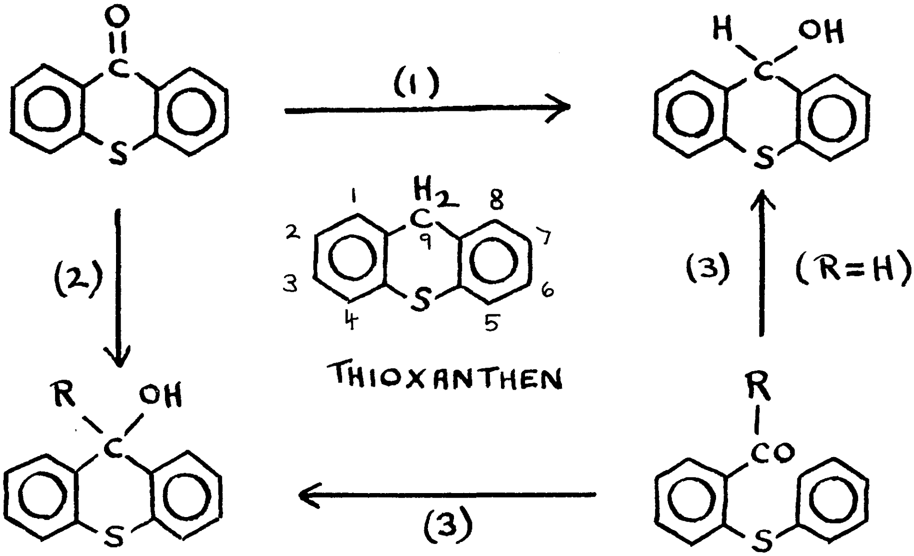
The usefulness of the method is limited by the inaccessibility of derivatives of o-amino-thiophenol.

The recent reports by Arcus et al.[2,3,4] of the conversion of various derivatives of fluoren-9-ol (II, R=H) to phenanthridines (cf. III) by a reaction



II III

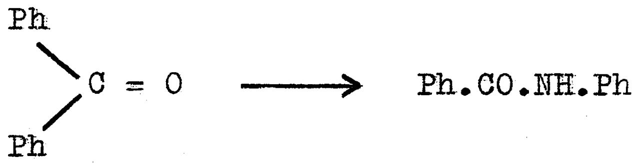
of the Schmidt type, prompted an attempt to prepare dibenzo[b,f]-1:4-thiazepines from derivatives of thioxanthen-9-ol (thioxanthydrol) by a similar procedure. The prospect was attractive, because a variety of thioxanthydrols are made available by three simple methods.



Thioxanthydrols unsubstituted in the 9-position are readily prepared[5] by reduction of thioxanthones (1). Thioxanthydrols substituted in the 9-position by alkyl and aryl groups may be made without difficulty[6,18] by the action of Grignard reagents on thioxanthones (2). Sulphuric acid solutions of thioxanthydrols of both kinds may be made[7] by dissolving o-arylthiobenzaldehydes and benzophenones in sulphuric acid (3); since Schmidt reactions are carried out in a sulphuric acid medium this method promised to be convenient.

DISCUSSION

In 1923 Schmidt found that benzanilide was obtained by the action of a mixture of hydrazoic and sulphuric acids on benzophenone[8]:



The same reagent was found to convert aldehydes to mixtures of nitriles and formamides,

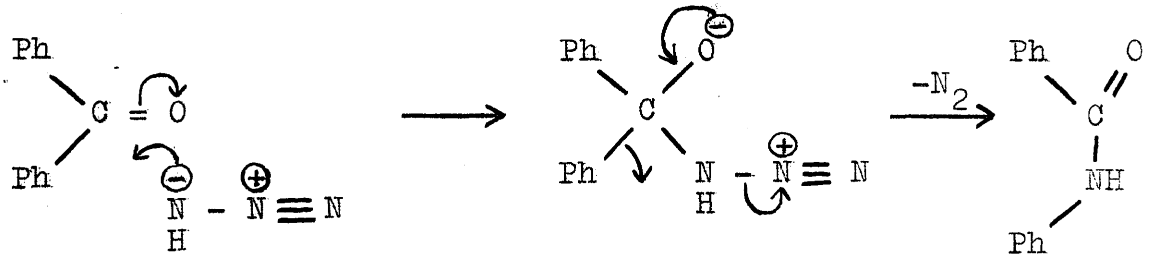
$$R.CHO \longrightarrow R.CN + R.NH.CHO$$

and acted upon carboxylic acids with the formation of amines:

$$R.CO_2H \longrightarrow R.NH_2$$

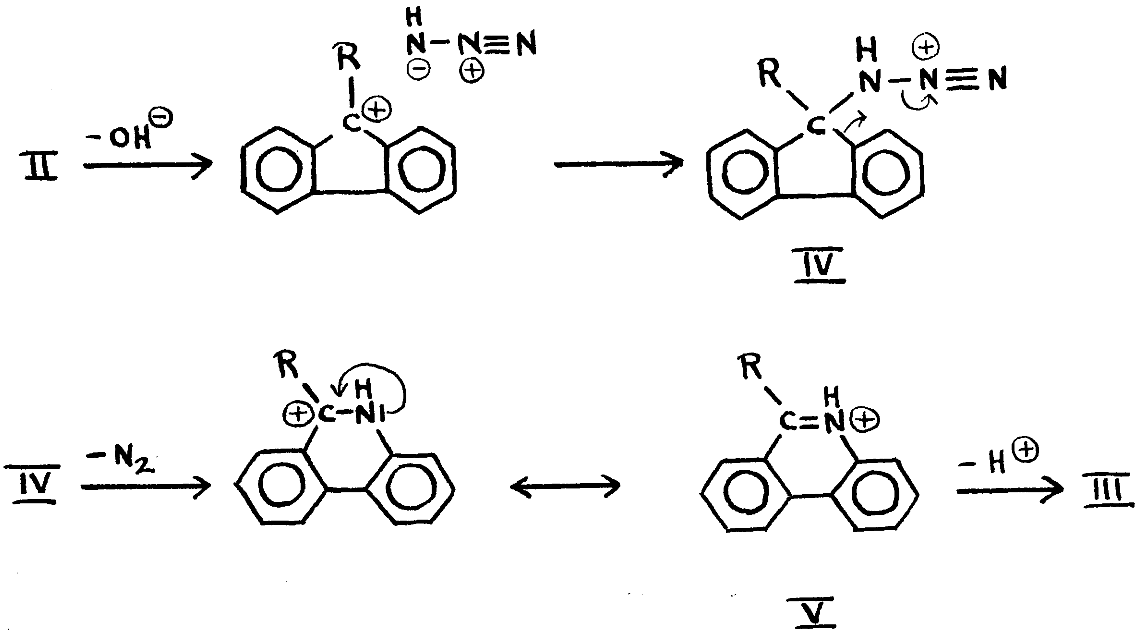
In the words of Wolff[8]: "the reaction between equimolar quantities of hydrazoic acid and carbonyl compounds in the presence of strong mineral acid has become known as the Schmidt reaction."

The most satisfactory mechanism so far proposed for the Schmidt reaction may be written briefly as follows:



An electrophilic attack on the carbonyl group (or more probably its proton-adduct) by the hydrazoic acid species shown, followed by rearrangement with loss of nitrogen, explains the formation of amides from ketones. A similar mechanism accounts satisfactorily for the products obtained from other carbonyl compounds.

The postulation of a first step as shown implies that hydrazoic acid should condense, under the same conditions, with any centre which has a tendency to form a carbonium ion. It was reasoning along these lines that led Arcus[2,3,4] to examine the behaviour of fluoren-9-ols under the conditions of the Schmidt reaction. Since tertiary carbonium ions are so much more stable than secondary carbonium ions, it is in accordance with theory that Arcus obtained the best results from 9-substituted fluoren-9-ols.



The mechanism written out above for the conversion of fluoren-9-ols to phenanthridines is a logical adaptation of the mechanism of the typical Schmidt reaction.

Arcus[2], and later, Newman and Hay[9], observed that azidotriphenylmethane (VI) was the sole product of the treatment of triphenylmethanol with hydrazoic and sulphuric acids. Yet Arcus found that the same conditions converted 9-phenylfluoren-9-ol (II, R=Ph), which is formally so very similar to triphenylmethanol, to 9-phenylphenanthridine (III, R=Ph) in a yield of 94% [3].

It is evident that the driving force for the conversion of the proton-adduct (IV, R=Ph) of 9-azido-9-phenylfluorene to the 9-phenylphenanthridinium cation (V, R=Ph) is the gain in resonance energy achieved by aromatization of the central ring of the fluorene system.

Wieland[10], who first prepared azidotriphenylmethane (VI), noted its extraordinary stability. Lately, Hamer[11] has shown that azidotriphenylmethane, heated to a temperature of 150° in sulphuric acid, reverts to triphenylmethanol.

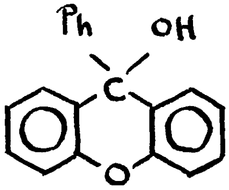
$$Ph_3C^{\oplus} + \overset{\ominus}{N}{=}\overset{\oplus}{N}{=}NH \rightleftharpoons Ph_3C{-}\overset{\oplus}{N}{=}N{=}NH \xrightarrow{-H^{\oplus}} \underset{\underline{\overline{VI}}}{Ph_3CN_3}$$

$$\overset{\ominus}{N}{=}\overset{\oplus}{N}{=}NH \xrightarrow{\Delta} \text{products}$$

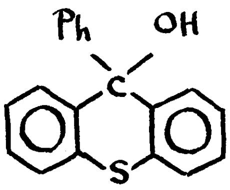
This is easily understood if the condensation of hydrazoic acid with the carbonium ion is considered to be reversible. At high temperatures, in the presence of sulphuric acid, hydrazoic acid decomposes irreversibly to a number of products, so that the equilibrium will be shifted in favour of the reverse reaction. For this reason the Schmidt reaction is always carried out at a temperature of below 50°.

The alacrity with which hydrazoic acid adds to triphenylcarbonium ions led us to choose 9-phenylxanthydrol (VII) for our first experiment; the thio-analogue (VIII) was not at the time available.

As was to be expected, a stable azide was obtained from 9-phenylxanthydrol under the conditions of the Schmidt reaction. In the preliminary experiments the usual conditions were adhered to i.e. the



VII



VIII

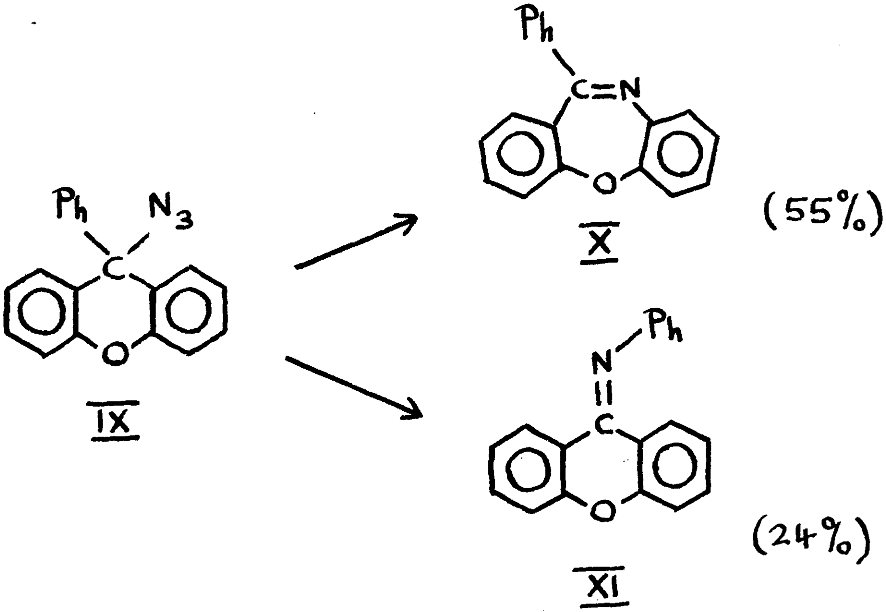
xanthydrol was treated with sodium azide in an environment of sulphuric acid and chloroform. Later the chloroform was omitted. Quantitative yields of 9-azido-9-phenylxanthen (IX) were obtained when an aqueous solution of sodium azide was added (without external cooling) to a solution of 9-phenylxanthydrol in dilute (33% v/v) sulphuric acid. Under these conditions the azide was precipitated immediately.

9-Azido-9-phenylxanthen (IX) is a white crystalline solid of m.p. 109-110°. Gas evolution from the melt was noticeable at 150°, and was brisk at 180°. Heated with ethanol, the azide gave 9-ethoxy-9-phenylxanthen (VII, OEt for OH).

In view of the work of Hamer with azidotriphenylmethane, there was clearly nothing to be gained by heating the sulphuric acid solution of 9-azido-9-phenylxanthen. However, an attempt to pyrolyse the azide seemed worthwhile, because Senior[12] has proved the existence of benzophenone anil in the tar which resulted from pyrolysis of azidotriphenylmethane (VI) in a sealed tube at a temperature of 225°. The anil was not isolated, but after hydrolysis benzophenone and aniline were found, the latter in a yield of 60%:

$$\underset{\textbf{VI}}{Ph_3CN_3} \longrightarrow \left[Ph_2C = NPh\right] \longrightarrow Ph_2CO + HNPh$$

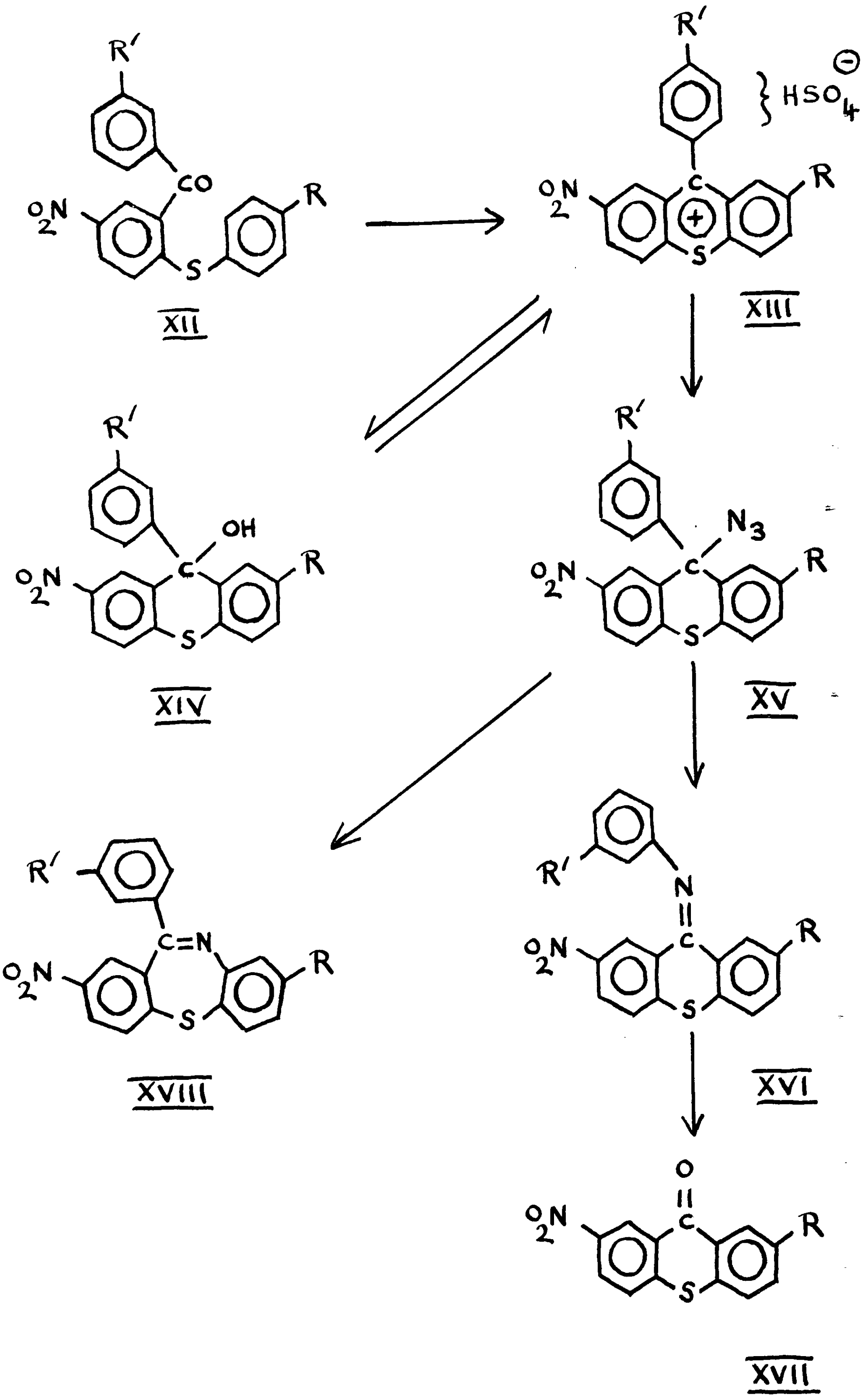
Rearrangement of 9-azido-9-phenylxanthen (IX) along these lines could give two products, because in this molecule the bonds joining the aliphatic carbon atom to the three aryl groups are not all equivalent. The two possible products are 11-phenyldibenz[b,f]-1:4-



oxazepine (X) and the anil (XI) of xanthone.

An early attempt to pyrolyse undiluted 9-azido-9-phenylxanthen was discouraging, and so better results were sought by carrying out the decomposition in a solvent of suitable boiling-point. Only very limited success was obtained by boiling a solution of the azide in xylene for 2½ hr. Cymene was the next solvent tried, but again results left much to be desired. The poor quality of the technical cymene available made it in any case a bad choice. A strictly anhydrous solvent was essential, and so the cymene was treated with sodium: the solvent showed an almost insatiable appetite for the metal, which was not entirely abated even after distillation from sodium.

The use of decalin gave satisfactory results. The total yield (measured on the picrates) of bases of the composition $C_{19}H_{13}NO$, obtained by refluxing a decalin solution of 9-azido-9-phenylxanthen for 22 min., was 79%. Two bases were found in the products, and were readily separated from one another by making use of the very different solubilities of their picrates in benzene. From the higher-melting, less-soluble picrate, a base of m.p. 134½° was obtained: this was proved to be xanthone anil (XI) by direct comparison with a sample made by the method of Schönberg and Asker[13], and by its hydrolysis to xanthone. Chromatography of the second picrate afforded an isomer of m.p. 108-109°, which was by exclusion given the


R′
CO
O2N
R
S
XII
HSO4⊖
C
+
XIII
OH
C
XIV
N3
XV
C=N
XVIII
N
XVI
O
XVII

structure of 11-phenyldibenz[b,f]-1:4-oxazepine (X). The preparation of this oxazepine has been reported by Brodrick *et al.*[14]. In view of the percentage of carbon found by these authors in their product, for which they record m.p. 81°, it is doubtful if their material was pure.

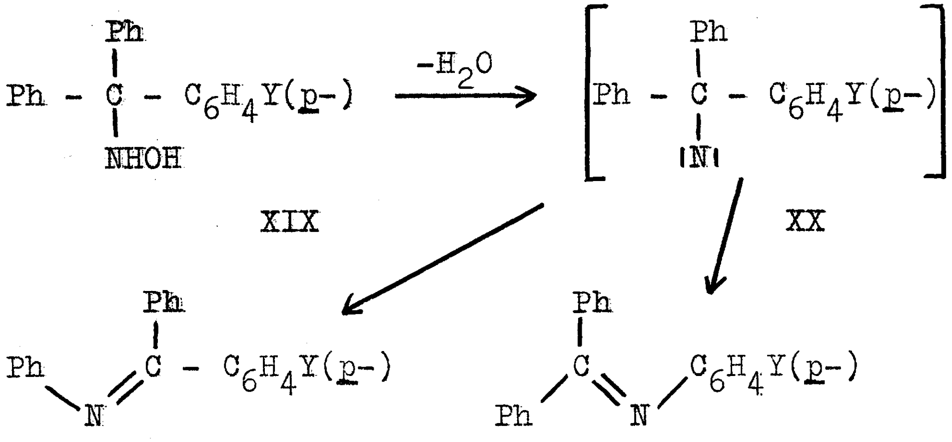
Encouraged by the fact that the desired product (X) was obtained in 55% yield, we now turned with interest to an examination of the behaviour of 9-phenyl-thioxanthydrols (cf. VIII) under similar conditions.

A supply of 5-nitro-2-*p*-tolylthiobenzophenone (XII, R=Me, R′=H) was at hand, and so the effect of hydrazoic acid upon 2-methyl-7-nitro-9-phenyl-thioxanthenylium sulphate (XIII, R=Me, R′=H) was studied forthwith. A solution of the benzophenone in sulphuric acid (*d* 1.84) was allowed to stand for a number of hours in the presence of excess sodium azide. The solubility of 2-methyl-7-nitro-9-phenyl-thioxanthydrol (XIV, R=Me, R′=H) in sulphuric acid was not sufficient to allow dilution of the solution with water. Dilution of the reaction mixture with ice-water precipitated a solid azide (XV, R=Me, R′=H), which was decomposed by heating in decalin. The azide was noticeably less stable at the boiling-point of decalin than was 9-azido-9-phenylxanthen: decomposition was complete after 7 min., whereas in the case of 9-azido-9-phenylxanthen, decomposition was not complete until after about 15 min. (the reaction was followed by measuring the volume of evolved nitrogen). Only one base, of composition $C_{20}H_{14}N_2O_2S$, was isolated from the products. It was proved to be the anil (XVI, R=Me, R′=H) of 2-methyl-7-nitro-thioxanthone (XVII, R=Me) by hydrolysis, and comparison of the product with authentic[7] 2-methyl-7-nitro-thioxanthone. The yield of the anil was 74% of theory.

Likewise, 2-nitro-thioxanthone anil (XVI, R=R′=H) was the only product found after the decomposition of the azide obtained by the treatment of a sulphuric acid solution of 2-nitro-9-phenylthioxanthydrol (XIV, R=R′=H) with sodium azide. The azide (XV, R=R′=H) gave an 86% yield of the anil.

These results were disappointing. It was borne in mind that the presence of a nitro group in one of the benzene rings of the azides (XV, R=H, Me, R′=H) might reduce the potential migratory power of that ring. Facts are available to show that this is probably the case.

Triphenylmethylhydroxylamine (XIX, Y=H) is rearranged (with loss of a molecule of water) to benzophenone anil (XXI or XXII, Y=H) by treatment with phosphorus pentachloride[15]. Newman and Hay[9] have examined the rearrangement of aryldiphenylmethylhydroxylamines, in which the aryl radical is para-substituted phenyl. Diphenyl-p-nitrophenylmethylhydroxylamine (XIX, $Y=NO_2$) was found to give approximately six times as much of the anil (XXI, $Y=NO_2$) as of the p-nitroanil (XXII, $Y=NO_2$): the migratory power of the p-nitrophenyl group is



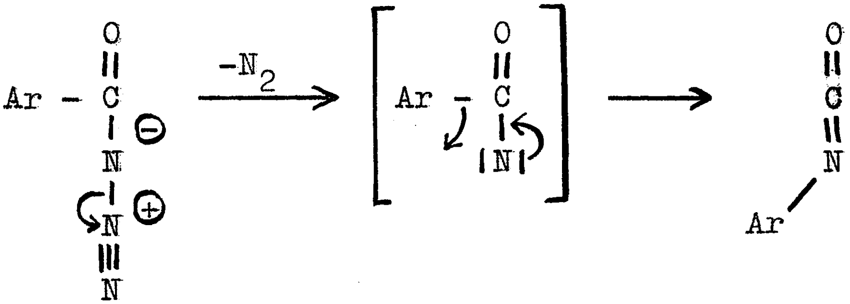
XIX

XX

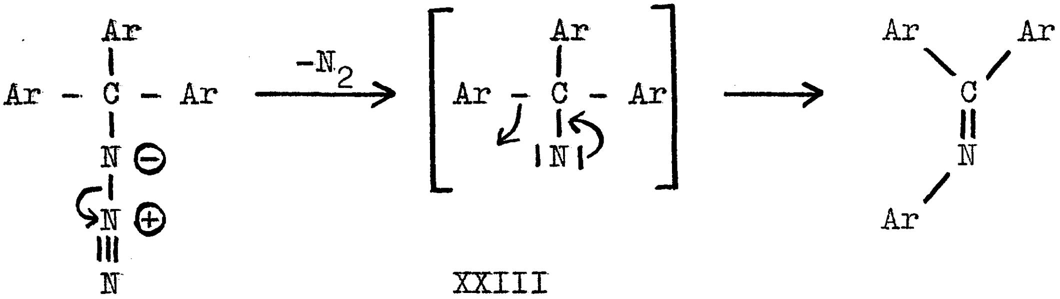
XXI

XXII

therefore about a third of that of the phenyl group. The intermediate (XX) is derived by analogy with those which have been postulated in mechanisms for the Curtius, Hofmann, and related reactions[16]. The mechanism of the Curtius reaction, written for an aroyl azide, has the form:



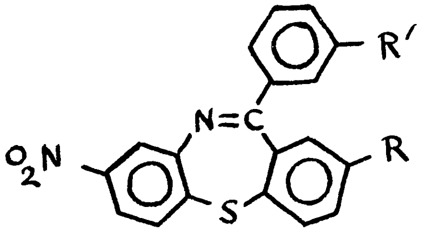
Rewriting this scheme with two aryl groups in place of the carbonyl oxygen atom, we have a mechanism for the



XXIII

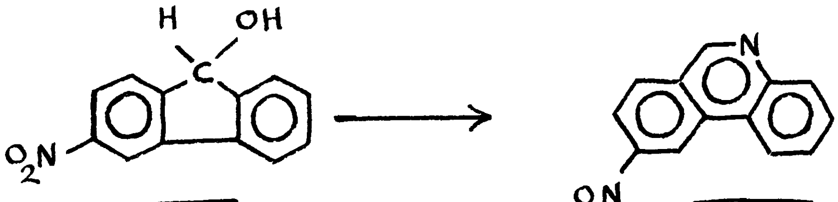
thermal decomposition of azidotriarylmethanes. The intermediate (XXIII) is of exactly the same kind as that (XX, Y=H) considered to be formed by the dehydration of triphenylmethylhydroxylamine, and so it is very probable that the findings of Newman and Hay are of direct relevance to the pyrolysis of 9-azido-2 (or 7)-nitro-9-phenyl-thioxanthens (XV, R=H, Me, R′=H).

In the case of these azides, the nitro group is in the position *meta* to the aliphatic carbon atom, and will be less effective than the *para*-nitro group of Newman and Hay in reducing the electron density about the potentially migratory centre. Since the driving force for any Curtius-type rearrangement is imagined to be the need of the nitrogen atom in the intermediate to augment its sextet of electrons, this means that a *meta*-nitroaryl group is more likely to migrate than a *para*-nitroaryl group. Nevertheless it is to be expected that a *meta*-nitroaryl group will still have much less migratory power than its unsubstituted analogue. It is therefore unlikely that 11-aryl-8-nitrodibenzo[b,f]-1:4-thiazepines (XXIV) will be easily detectable in the decomposition products of 9-aryl-9-azido-2 (or 7)-nitro-thioxanthens (XV).

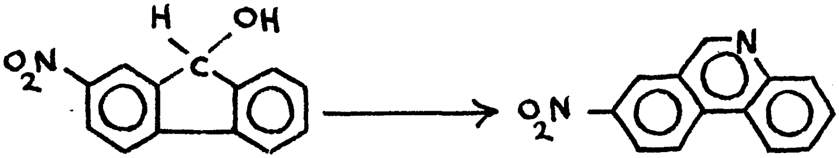


XXIV

There is no essential difference between the mechanism derived above for the pyrolysis of triaryl azides, and the mechanism written earlier (p. 117) for the rearrangement of the proton-adducts (IV) of 9-azidofluorenes. In the latter case an intermediate may be imagined which differs from the intermediate (XXIII) only in the coordination of a proton by the electrons of the nitrogen atom. The resulting positive charge on the nitrogen atom will make migration easier, but should make no difference to the relative migratory powers of the aryl groups. It is therefore in order to invoke the findings of Arcus[3], that, under the conditions of the Schmidt reaction, 3-nitrofluoren-9-ol (XXV) and 2-nitrofluoren-9-ol (XXVI) give mainly 6-nitrophenanthridine (XXVII) and 7-nitrophenanthridine (XXVIII), respectively, as further evidence of the



XXV → XXVII



XXVI → XXVIII

depression of the migratory power of a phenyl group by nitro-substitution.

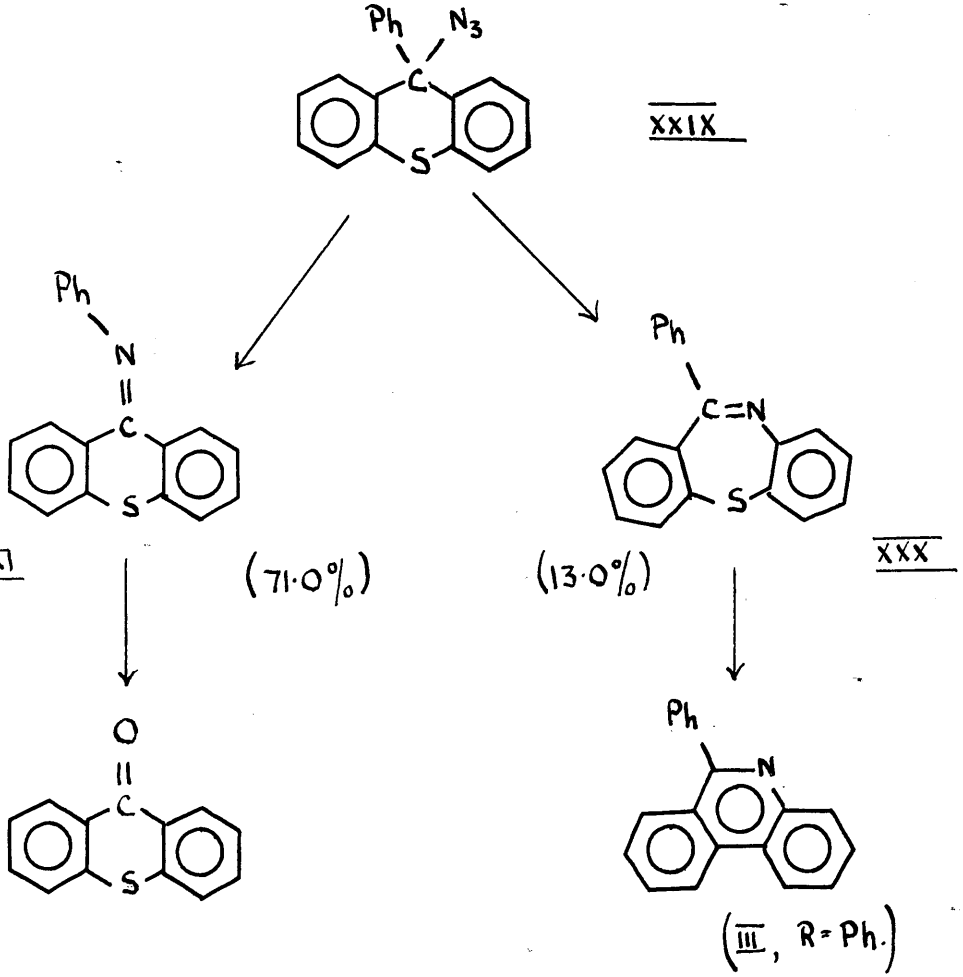
These considerations suggested that the rate of anil formation during the decomposition of 9-aryl-9-azido-2(or7)-nitro-thioxanthens (XV) would be less in a case where the 9-aryl group also possessed a nitro-substituent.

Accordingly, the azide (XV, R=H, R′=NO_2) was made from 5:3′-dinitro-2-phenylthiobenzophenone (XII, R=H, R′=NO_2) by the method already described for the azide (XV, R=Me, R′=H). It was hoped that the additional nitro group would depress anil formation sufficiently to allow a good yield of 2-nitro-11-m-nitrophenyldibenzo[b,f]-1:4-thiazepine (XVIII, R=H, R′=NO_2).

The rate of nitrogen evolution from 9-azido-2-nitro-9-m-nitrophenyl-thioxanthen (XV, R=H, R′=NO_2) in boiling decalin was not noticeably less than that of the azides (XV, R=H, Me, R′=H). The principal product was again an anil of thioxanthone. 2-Nitro-thioxanthone m-nitroanil (XVI, R=H, R′=NO_2), which was obtained in 47% yield, was identified by hydrolysis to 2-nitro-thioxanthone (XVII, R=H). The desired product (XVIII, R=H, R′=NO_2) was also found, but only in very small quantity (3.5%). It was identified by comparison with a sample of 2-nitro-11-m-nitrophenyldibenzo[b,f]-1:4-thiazepine made by Jarrett[1].

It was now clear that the decomposition of 9-azido-9-phenyl-thioxanthens was not a practical route to dibenzo[b,f]-1:4-thiazepines. Nevertheless it was felt that the work would not be complete without a study being made of 9-azido-9-phenyl-thioxanthen (XXIX) itself.

From the treatment of the sulphuric acid solution of 9-phenyl-thioxanthydrol (VIII, p. 119) with sodium azide, an oil was obtained which evolved 95% of the


Ph
N3
C
S
XXIX
Ph
N
C
S
XXXI
(71·0%)
(13·0%)
Ph
C=N
S
XXX
O
C
S
Ph
N
(III, R=Ph.)

theoretical nitrogen after 7 min. at the b.p. of decalin. The rate of decomposition was very little greater than that of any of the nitro-substituted azides (XV, R=H, Me, R′=H, NO_2). As was expected, the major product was the anil (XXXI; m.p. 153°) of thioxanthone, which was identified by hydrolysis to thioxanthone. Thioxanthone anil was isolated in 45.6% yield. The material remaining in the filtrates was heated with hydrochloric acid, when a quantity of thioxanthone corresponding to another 25.4% of the anil was precipitated. Basification of the acid solution then afforded 13% of an isomer of m.p. 117°, which was proved to be 11-phenyldibenzo[b,f]-1:4-thiazepine (XXX) by desulphurization to 9-phenyl-phenanthridine (III, R=Ph).

When a solution of the thiazepine (XXX) in diethyl phthalate was boiled with copper for 65 min., the picrate of the phenanthridine could be isolated in 93.6% yield. The comparison sample of 9-phenyl-phenanthridine was made by the method of Morgan and Walls[17].

To avoid interruption of the above discussion, one or two experiments were not mentioned.

An attempt was made to desulphurize 2-methyl-7-nitro-thioxanthone anil (XVI, R=Me, R′=H) under the conditions used by Jarrett[1] for the desulphurization of the thiazepine (XVIII, R=R′=H): 84% of the base was recovered unchanged.

2-Nitro-9-phenyl-thioxanthydrol (XIV, R=R′=H) and 5:3′-dinitro-2-phenylthiobenzophenone (XII, R=H, R′=NO_2) have not previously been described. These compounds were made according to the methods given by Loudon _et_ _al_.[7] for the preparation of 2-methyl-7-nitro-9-phenyl-thioxanthydrol (XIV, R=Me, R′=H) and 5-nitro-2-_p_-tolylthiobenzophenone (XII, R=Me, R′=H), respectively.

EXPERIMENTAL

Please refer to the remarks on p. 78 .

All experiments involving the use of hydrazoic acid were carried out in a draught cupboard.

9-Phenylxanthydrol (VII)

The undetailed instructions of Bünzly and Decker[18] were applied as follows.

A hot solution of xanthone (10 g.) in benzene (200 ml.) was added rapidly, with mechanical stirring, to a solution of phenylmagnesium bromide in ether (60 ml.), prepared from magnesium (2 g.) and bromobenzene (9 ml.). The mixture was heated under reflux on the steam-bath for 1 hr., with continued stirring. After benzene (100 ml.) had been allowed to distil, the reaction mixture was transferred to a separating funnel, where it was extracted with concentrated hydrochloric acid (total volume from 3 extractions: 200 ml.). The acidity of the combined acid extracts was reduced by addition of aqueous ammonia until it was just sufficient to impart a blue colour to Congo red. White crystals

(12.4 g.; 88.6%) m.p. 157-159° of 9-phenylxanthydrol (VII) were obtained after two recrystallizations (charcoal) of the collected solid from benzene.

9-Azido-9-phenylxanthen (IX)

9-Phenylxanthydrol (VII; 5.00 g.) was dissolved in a mixture of sulphuric acid (d 1.84; 50 ml.) and water (100 ml.) by warming the mechanically-stirred mixture on a water-bath at 55°. The orange solution was allowed to cool to room temperature and a solution of sodium azide (10.0 g.) in water (40 ml.) was run in over a period of 7 min. Stirring was continued for 15 min., the mixture was allowed to stand for a further 15 min. and the white precipitate was collected, washed with water until free from acid and dried over KOH *in vacuo*. The powder (5.32 g.; 99.5%) melted at 108-110°. Colourless crystals (in the form both of needles and tablets) m.p. 109-110° of 9-azido-9-phenylxanthen (IX) were obtained from light petroleum (Found: C, 76.12; H, 4.08; N, 13.88. $C_{19}H_{13}N_3O$ requires C, 76.24; H, 4.38; N, 14.04%).

A solution of the azide in ethanol was heated for a few minutes at the b.p. The cooling solution deposited crystals m.p. 102-103° of 9-ethoxy-9-phenylxanthen (VII, OEt for OH), which did not depress the m.p. of authentic material made by the method of Bünzly and Decker[18].

The Thermal Decomposition of 9-Azido-9-phenylxanthen (IX)

9-Azido-9-phenylxanthen (1.00 g.) and decalin (distilled from sodium; 2.0 ml.) were heated under reflux for 22 min. The displaced air was passed through a tube of calcium chloride and was collected over water by a eudiometer tube: displacement due to thermal expansion was approximately corrected for by subtraction of the volume of air displaced when decalin (2.0 ml.) was heated alone in the same apparatus. The volume of nitrogen evolved was found to be quantitative (98% of theory) after 15 min. at the b.p.

The solution was diluted with benzene and filtered hot through a charcoal pad. A solution of picric acid (0.4 g.) in hot benzene was added to the filtrate (final volume: 15 ml.). An orange-coloured picrate

(0.642 g.) of m.p. 205-208° crystallized out. The mother liquor was evaporated to dryness, the residue was dissolved in methanol (10 ml.) and a solution of picric acid (0.4 g.) in methanol (5 ml.) was added. The discoloured crystals which appeared on standing were collected, a second crop was obtained by concentration of the filtrate, the combined crops were dissolved in benzene and the solution was passed through a column of neutral alumina using benzene as eluant. The yellow eluate was evaporated to dryness, the residue was taken up in methanol (6 ml.), a solution of picric acid (0.4 g.) in methanol (6 ml.) was added and the solution was warmed on the steam-bath. Canary-yellow crystals (0.678 g.) of a picrate m.p. 150-152° appeared almost at once. Recrystallization of the picrate m.p. 205-208° from benzene afforded material (0.393 g.) which melted at 226-227° after insertion in the hot-block at 210°. The mother liquor was evaporated to dryness and hot methanol (3-4 ml.) was added. Canary-yellow crystals (0.153 g.) of m.p. 150-152° were obtained. A further quantity (0.085 g.) of

this picrate was secured by concentration of the filtrate together with the filtrate from the first crop of crystals m.p. 150-152°.
Picrate of m.p. 227° (0.393 g.; 24%).

The picrate (Found: C, 60.34; H, 3.54. $C_{25}H_{16}N_4O_8$ requires C, 60.01; H, 3.22%) is a salt of picric acid and a base $C_{19}H_{13}NO$. The free base was isolated by passing a solution of the picrate in hot benzene through a column of neutral alumina with hot benzene as eluant, evaporating the yellow eluate to dryness and crystallizing the residue from light petroleum. Recrystallization from methanol afforded bright yellow needles of m.p. 134-134½° (Graebe and Röder[19] report m.p. 134.5° for xanthone anil). A sample of xanthone anil (XI) made by the method of Schönberg and Asker[13], after several recrystallizations from methanol, had m.p. 127-129° raised to 129-132½° by admixture with the base of m.p. 134-134½° (Found: C, 83.81; H, 4.82; N, 5.37. Calculated for $C_{19}H_{13}NO$: C, 84.11; H, 4.83; N, 5.16%). The infrared absorption spectra (KCl disc) of the two specimens were identical, with maxima at 1625 (s), 1615 (s), 1595 (s), 1474 (m), 1452 (s), 1336 (s), 1282 (w), 1250 (m), 1210 (m), 1142 (m), 1100 (m), 1072 (w), 1028 (w), 942 (m), 879 (w), 854 (w), 791 (w), 777 (m), 764 (s), 748 (s) and 699 cm.$^{-1}$ (m).

The base of m.p. 134-134½° (0.025 g.) was hydrolysed to xanthone in 85% yield by warming its solution in a mixture (0.25 ml.) of 5N-hydrochloric acid (1 volume) and acetic acid (1 volume) for 1 hr. on the steam-bath; the white needles m.p. 173-174° (0.015 g.) which formed were collected, washed with water and dried over KOH *in vacuo*. The identity of the needles was established by a mixed m.p. determination with an authentic sample (British Drug Houses Ltd.) of xanthone and by a comparison of the infrared absorption spectra (nujol).

The infrared absorption spectrum (nujol) of the picrate was identical with the spectrum of the picrate m.p. 223-224° which was obtained from a sample of xanthone anil prepared according to the directions of Schönberg and Asker.

These facts establish that the picrate of m.p. 227° is the picrate of xanthone anil.

Picrate of m.p. 152° (0.916 g.; 55%).

The picrate was dissolved in benzene and the solution was passed through a column of alumina with benzene as eluant. The pale green eluate was evaporated to dryness and the residue was crystallized from light petroleum. The pale greenish-yellow solid melted at 108-109° (Found: C, 84.39; H, 4.83; N, 5.14. $C_{19}H_{13}NO$ requires C, 84.11; H, 4.83; N, 5.16%) and the mixture with xanthone anil at 90-97°. The material is therefore not xanthone anil, and must have the structure of 11-*phenyldibenz*[b,f]-1:4-*oxazepine* (X).

Brodrick *et al.*[14] claim to have prepared this compound (for which the Editor of J. prefers the name 5-phenyl-2:3-6:7-dibenz-1-oxa-4-aza*cyclo*hepta-2:4:6-triene) and record m.p. 81° for the free base and m.p. 149-150° for its picrate.

5-Nitro-2-p-tolylthiobenzophenone (XII, R=Me, R′=H)

This material was kindly supplied by Dr. J.D. Loudon[7].

2-Methyl-7-nitro-thioxanthone Anil (XVI, R=Me, R′=H)

5-Nitro-2-*p*-tolylthiobenzophenone (XII, R=Me, R′=H 5.0 g.) was dissolved in sulphuric acid (*d* 1.84; 10 ml.), the solution was cooled in ice and sodium azide (5 g.) was added with stirring. The suspension was stirred for a further 10 min. after which it was set aside (12 hr.). The preparation was poured onto ice, and the precipitate (5.3 g.; m.p. *ca*. 80°) was collected, washed well with water and dried over $CaCl_2$ *in vacuo*. The reddish-brown powder was extracted several times with a boiling mixture of benzene and light petroleum (1:3 v/v), the combined extracts were treated with charcoal and the filtrate was concentrated. The azide (XV, R=Me, R′=H) crystallized first, in pale green or pale yellow prisms of undecided m.p. (the colour and m.p. varied with each preparation; the m.p. varied between 90 and 130°, and was always poorly defined) which were readily distinguished from the much smaller crystals (m.p. 203°) of 2-methyl-7-nitro-9-phenyl-thio-xanthydrol (XIV, R=Me, R′=H) which followed. A second recrystallization from the same solvent mixture was sufficient to render the azide free from the thioxanthydrol. A total of 3.92 g. (73%) of the azide was obtained. A sample submitted for analysis was found to contain more than the theoretically required carbon and hydrogen and less than the required nitrogen (Found: C, 67.17; H, 4.26; N, 14.23. $C_{20}H_{14}N_4O_2S$ requires C, 64.17; H, 3.77; N, 14.97%). After crushing and heating (1 hr.) at 50° in vacuo the results were improved (Found: C, 65.29; H, 4.41%) and continued to do so (Found: C, 64.67; H, 3.82%) with further (5 hr.) gentle heating in vacuo.

The azide (1.0 g.) and decalin (5 ml.) were heated under reflux. The volume of nitrogen evolved was measured as described in the account of the thermal decomposition of 9-azido-9-phenylxanthen (IX), and was found to be quantitative after 7 min. at the b.p. The yellow crystals m.p. 198-199° (0.684 g.; 74%) which formed on cooling were collected, washed with a little light petroleum and dried in a current of air. After several recrystallizations from benzene the material (Found: C, 69.68; H, 4.24; N, 8.65. $C_{20}H_{14}N_2O_2S$ requires C, 69.36; H, 4.07; N, 8.09%)

had m.p. 200-202°, depressed to 170-190° by admixture with 2-methyl-7-nitro-9-phenyl-thioxanthydrol (XIV, R=Me, R′=H; m.p. 203°)[7]. Infrared light absorption maxima (KCl disc): 1613 (s), 1603 (s), 1593 (s), 1577 (m), 1520 (s), 1470 (m), 1416 (w), 1340 (vs), 1306 (m), 1256 (m), 1153 (w), 1134 (m), 1107 (w), 1081 (m), 913 (w), 900 (w), 888 (w), 826 (w), 808 (m), 766 (m), 756 (w), 737 (s), 697 (m), and 691 $cm.^{-1}$ (m).

The base $C_{20}H_{14}N_2O_2S$ (0.100 g.) dissolved in a cold mixture of acetic acid (10 ml.) and 5N-hydrochloric acid (5 ml.). When the clear, red solution was warmed material began to precipitate. The reaction was completed by boiling under reflux for 1 hr. The cold mixture was filtered and the solid was washed with water followed by ethanol. After drying over KOH _in vacuo_ the khaki-yellow powder weighed 0.069 g. (88%) and had m.p. 263-264°, unchanged by admixture with a specimen of 2-methyl-7-nitro-thioxanthone (XVII, R=Me) made by the method of Loudon _et al_.[7]; the two samples had identical infrared absorption spectra (nujol).

The base $C_{20}H_{14}N_2O_2S$ of m.p. 200-202° must therefore have the structure of 2-*methyl*-7-*nitrothioxanthone anil* (2-methyl-7-nitro-9-thioxanthenylideneaniline; XVI, R=Me, R′=H).

The overall yield of the anil from 5-nitro-2-*p*-tolylthiobenzophenone was 54% of theory.

Attempted Desulphurization of 2-Methyl-7-nitrothioxanthone Anil (XVI, R=Me, R′=H)

The anil (0.5 g.), copper bronze (0.5 g.) and diethyl phthalate (4 ml.) were heated under reflux for 7-8 min. on a metal-bath maintained at a temperature of 315-320°. The cold reaction mixture was diluted with benzene, warmed and filtered through a charcoal pad. Starting-material (0.42 g.; 84%) m.p. 199-200°, raised 1° by admixture with the pure base (XVI, R=Me, R′=H), was recovered by flooding the filtrate with light petroleum.

2-Nitro-9-phenyl-thioxanhydrol (XIV, R=R′=H)

To a refluxing solution of 2-chloro-5-nitrobenzophenone (1.31 g.) and thiophenol (0.55 g.) in ethanol (17 ml.) and water (5 ml.) a hot solution of sodium hydroxide (0.27 g.) in water (5 ml.) and ethanol (5 ml.) was slowly added, followed by ethanol (10 ml.). The mixture was heated for 1 hr. on the steam-bath and allowed to cool. The aqueous ethanol was decanted from the oil which formed on the bottom of the flask, the oil was washed by decantation with ethanol and dissolved in ether. The ethereal solution was washed with water and dried (Na_2SO_4). Evaporation of the ether left an amber oil which was dissolved in sulphuric acid (d 1.84; 5 ml.). After 12 hr. at 18° the deep red solution was drowned in ice-water; the precipitate was filtered off and washed with water, aqueous sodium carbonate and water. The solid (1.24 g.; 74%; m.p. 144-147°) was dried over KOH *in vacuo*.

After two recrystallizations (charcoal) from a mixture of benzene and light petroleum (1:3 v/v), pale-yellow prisms m.p. 155° of 2-*nitro*-9-*phenylthioxanthydrol* (XIV, R=R′=H) were obtained (Found: C, 68.27; H, 4.08. $C_{19}H_{13}NO_3S$ requires C, 68.06; H, 3.91%).

2-Nitro-thioxanthone Anil (XVI, R=R′=H)

A water-cooled solution of 2-nitro-9-phenylthioxanthydrol (XIV, R=R′=H; 0.50 g.) in sulphuric acid (d 1.84; 1.0 ml.) was treated with sodium azide (0.50 g.). The mixture was stirred occasionally, allowed to stand (12 hr.) and poured onto ice. The green solid was collected, washed with water, dilute sodium carbonate solution, and water, and dried over KOH *in vacuo*. The dry powder (0.53 g.; m.p. 106° after severe pre-softening), which was reddish-brown in colour, was extracted with a boiling mixture of benzene and light petroleum (1:4 v/v) and the hot extract was filtered through a charcoal pad. Concentration of the green filtrate afforded crystals m.p. 112-120° (0.42 g.; 78%) of the azide (XV, R=R′=H).

The azide (0.42 g.) and decalin (distilled from sodium; 1.0 ml.) were refluxed for 7 min. under a tube of $CaCl_2$. The yellow crystals m.p. 199° (0.333 g.; 86%) were collected, washed thoroughly with light petroleum and dried in a current of air. 2-Nitro-thioxanthone anil (XVI, R=R′=H) m.p. 203-205° (Found: C, 68.75; H, 3.46; N, 8.75. $C_{19}H_{12}N_2O_2S$ requires C, 68.67; H, 3.64; N, 8.43%) was obtained by two recrystallizations from benzene and one from methanol.

The structure of the anil was confirmed by hydrolysis. The anil (0.050 g.) was dissolved in a mixture (3-4 ml.) of acetic acid and 5N-hydrochloric acid (2:1 v/v) and the orange-red solution was allowed to stand (12 hr.) at 18°. The light-brown needles m.p. 224-225° (0.039 g; 100%) were collected and dried over KOH in vacuo. The mixture with 2-nitro-thioxanthone[20] (XVII, R=H) of m.p. 226-227° melted at 225-227°; the infrared absorption spectra (nujol) of the two samples were identical.

The overall yield of 2-nitro-thioxanthone anil from 2-nitro-9-phenyl-thioxanthydrol was 67% of theory.

5:3′-Dinitro-2-phenylthiobenzophenone (XII, R=H, R′=NO_2)

A suspension of 2-chloro-5:3′-dinitrobenzophenone (1.0 g.) in ethanol (5 ml.) and water (2½ ml.) was heated on the steam-bath and a solution of thiophenol (0.50 g.) and sodium hydroxide (0.25 g.) in ethanol (3½ ml.) and water (2 ml.) was added in portions every 5 min. over a total period of 65 min. Between additions the suspension was alternately heated to the b.p. and stirred vigorously with a glass rod. Alternate heating and stirring were continued for 15 min. after the addition was complete, and the mixture was set aside for several hours. The yellow solid (1.17 g.; 94%) of m.p. 120-123° was collected, washed with a mixture of ethanol and water (1:1 v/v) and dried over KOH *in vacuo*. Beautiful pale-yellow needles m.p. 123-124° of 5:3′-*dinitro*-2-*phenylthiobenzophenone* (XII, R=H, R′=NO_2) were obtained by recrystallization from ethanol (Found: C, 60.23; H, 3.39. $C_{19}H_{12}N_2O_5S$ requires C, 60.00; H, 3.18%).

2-Nitro-thioxanthone-m-nitroanil (XVI, R=H, R′=NO_2) and *2-Nitro-11-m-nitrophenyldibenzo*[b,f]*-1:4-thiazepine* (XVIII, R=H, R′=NO_2)

To the deep-red, ice-cooled solution of 5:3′-dinitro-2-phenylthiobenzophenone (XII, R=H, R′=NO_2; 0.50 g.) in sulphuric acid (*d* 1.84; 2.0 ml.), sodium azide (0.50 g.) was added, the suspension was stirred occasionally and then allowed to stand (12 hr.). The mixture was poured onto ice, the precipitate was collected, washed with water, dilute sodium carbonate solution, and water, and dried over KOH in vacuo. The reddish-brown powder (0.53 g.) was extracted with boiling benzene, and the extract was heated with charcoal and filtered. The filtrate was concentrated and diluted with light petroleum. The azide (XV, R=H, $R'=NO_2$) was induced to crystallize by scratching the wall of the test-tube with a glass rod. The greenish-yellow material (0.40 g.; 75%) melted at 145-147° with much gas evolution.

The azide (0.40 g.) and decalin (distilled from sodium; 5 ml.) were heated under reflux. The volume of nitrogen evolved was measured as described in the account of the thermal decomposition of 9-azido-9-phenylxanthen (IX), and was quantitative after 7 min. at the b.p. The cooling solution deposited a black oil which solidified after further cooling. The solid was broken up, collected and washed with light petroleum. The brown powder obtained was dissolved in benzene (50 ml.) and the hot solution was filtered through a charcoal pad. The red filtrate was concentrated to a volume of 25 ml. and allowed to crystallize. Yellow needles m.p. 257-258° (0.176 g.; 47%) were obtained. The filtrate was concentrated and seeded with a crystal from the first crop. The heavily-discoloured second crop was filtered off, and the filtrate was chromatographed on neutral alumina with an eluant of benzene. The yellow band which passed first through the column was collected. The green eluate was concentrated and diluted with light petroleum; crystallization proceeded very slowly. Pale-yellow crystals (0.013 g.; 3.5%) of m.p. 247-248° were obtained after several recrystallizations of the product by dilution of its solution in ethyl acetate with ethanol. The mixture with 2-nitro-11-m-nitrophenyldibenzo[b,f]-1:4-thiazepine (XVIII, R=H, R′=NO_2)[1] of identical m.p. melted at the same temperature. The infrared absorption spectrum (KCl disc) with bands at 1603 (m), 1580 (w), 1527 (s), 1452 (m), 1434 (w), 1344 (s), 1310 (m), 1254 (m), 1087 (w), 1063 (w), 1000 (w), 907 (w), 894 (w), 860 (w), 830 (w), 781 (s), 768 (w), 754 (m), 742 (m), 730 (w), 703 (m), and 681 $cm.^{-1}$ (m), was identical with that of the thiazepine (XVIII, R=H, R′=NO_2).

A mixture of the thiazepine (XVIII, R=H, R′=NO_2)

with the more strongly-coloured crystals of m.p. 257-258°, which were isolated before chromatography, melted at 221-229°. The higher-melting material was twice recrystallized from benzene. The bright-yellow needles (Found: C, 60.54; H, 2.89; N, 11.34. $C_{19}H_{11}N_3O_4S$ requires C, 60.48; H, 2.94; N, 11.14%) melted at 258-259° and had infrared light absorption maxima (KCl disc) as follows: 1603 (s), 1577 (m), 1517 (s), 1460 (m), 1434 (m), 1413 (w), 1342 (s), 1302 (m), 1256 (m), 1154 (m), 1135 (w), 1124 (w), 1107 (w), 1071 (m), 1042 (w), 984 (w), 912 (w), 895 (w), 859 (w), 816 (m), 808 (m), 777 (w), 766 (w), 754 (w), 747 (m), 737 (s), 706 (w), and 687 cm.$^{-1}$ (w). Between 1600 and 1250 cm.$^{-1}$ this spectrum closely resembles that of the thiazepine (XVIII, R=H, R′=NO_2) but at lower frequencies the spectra are quite different.

The base $C_{19}H_{11}N_3O_4S$ of m.p. 258-259° was therefore distinct from 2-nitro-11-m-nitrophenyl-dibenzo[b,f]-1:4-thiazepine and was assigned the structure of 2-nitro-thioxanthone m-nitroanil (XVI, R=H, R′=NO_2). This structure was confirmed by hydrolysis.

The anil (0.050 g.), acetic acid (4 ml.) and

5N-hydrochloric acid (2 ml.) were heated on the steam-bath for 30 min. Solution was at no time complete, but the yellow needles were seen to be gradually replaced by colourless needles. After standing (12 hr.) the crystals were collected and dried at 150° over KOH _in vacuo_. The off-white product (0.031 g.; 91%) possessed m.p. 223-225°, raised 2° by admixture with 2-nitro-thioxanthone (XVII, R=H)[20] of m.p. 226-227°. The infrared absorption spectrum (nujol) was identical with that of 2-nitro-thioxanthone.

Thioxanthone

This substance was made according to the directions of Gomberg and Britton[21].

9-Phenyl-thioxanthydrol (VIII)

The rather general instructions of Gomberg and Cone[6] were interpreted as follows.

Thioxanthone (10 g.) was added in portions over 40 min. to a stirred solution of phenylmagnesium bromide in ether (75 ml.) prepared from bromobenzene (10.3 ml.) and magnesium turnings (2.3 g.). The mixture was heated under reflux for 2 hr. and set aside (12 hr.). The preparation was poured onto ice-water; sufficient 5N-hydrochloric acid (theory requires ca. 20 ml.) was added to dissolve the precipitated magnesium hydroxide. The two phases were equilibrated in a separating funnel, and the aqueous layer was drawn off, neutralized by addition of dilute aqueous ammonia, and returned to the separating funnel. After re-equilibration, the ethereal layer was washed with dilute sodium carbonate solution and water. The ether was evaporated, excess bromobenzene was removed by steam-distillation, and the involatile fraction was dissolved in benzene. The benzene solution was dried (K_2CO_3), concentrated, heated with charcoal (2 g.), filtered and diluted with light petroleum. 9-Phenyl-thioxanthydrol (VIII; 11.1 g.; 81%) m.p. 103-106° was obtained by recrystallization of the product from benzene/light petroleum.

Thioxanthone Anil (XXXI) and 11-Phenyldibenzo[b,f]-1:4-thiazepine (XXX)

Sodium azide (4.0 g.) was added with stirring to an ice-cooled solution of 9-phenyl-thioxanthydrol

(VIII; 4.00 g.)in sulphuric acid (d 1.84; 10 ml.). After 12 hr. at 18° the suspension was poured onto crushed ice, and the mixture was extracted with benzene. The benzene extract was washed with water and dilute aqueous sodium carbonate, and dried (K_2CO_3 followed by Na). The benzene was evaporated at 100° *in vacuo* leaving a residue (4.13 g.) of dark-red, viscous oil, which did not crystallize when scratched persistently with a glass rod. The oil was dissolved in decalin (distilled from sodium; 8 ml.) and the solution was heated under reflux. The evolved nitrogen was measured as described in the account of the thermal decomposition of 9-azido-9-phenylxanthen (IX), and was nearly (95%, calculated on the weight of VIII used) quantitative after 7 min. at the b.p., when heating was stopped. The cold solution was scratched with a spatula. The crystals which appeared were collected, washed with light petroleum (15 ml.) and recrystallized twice from ethanol (70 ml.). The dark-brown needles m.p. 147-150° (1.81 g.; 45.6%) were collected, the ethanol was evaporated from the filtrates and the residue was returned to the decalin solution. The latter was combined with the light petroleum used as a washing fluid, and preserved.

The needles were recrystallized (charcoal) from benzene, and a benzene solution of the product was chromatographed on neutral alumina with the same solvent as eluant. The orange eluate was concentrated and diluted with light petroleum. Recrystallization of the precipitated solid from ethanol afforded golden-yellow needles m.p. 153° (Found: C, 79.47; H, 4.94; N, 4.98. $C_{19}H_{13}NS$ requires C, 79.43; H, 4.56; N, 4.88%) which were proved to consist of thioxanthone anil (XXXI) by the following hydrolysis.

The anil (0.025 g.) was dissolved in a mixture (1 ml.) of 5N-hydrochloric acid and acetic acid (1:2 v/v). After 1-2 hr. at 18° no crystals were visible, so the solution was heated on the steam-bath for 30 min. The precipitate of white needles was collected and dried over KOH *in vacuo*. The product (0.016 g.; 86.5%), and a mixture of the product with authentic[21] thioxanthone, both melted at 213-214°. The infrared absorption spectrum (nujol) of the material was identical with that of thioxanthone.

The decalin/light petroleum solution was extracted five times with 5N-hydrochloric acid (total volume: ca. 100 ml.), and the combined acid extracts were heated on the steam-bath for 1 hr. The cold hydrolysate was filtered through a charcoal pad, the dry weight of which was thereby increased by 0.742 g. (corresponding to 1.01 g., or 25.4%, of thioxanthone anil). The clear, red filtrate was evaporated to dryness at 100° in vacuo. Dilute sodium carbonate solution was added and the residue was extracted with benzene. The benzene solution was dried (K_2CO_3), concentrated and chromatographed on alumina with an eluant of benzene. The yellow band was collected. The greenish-yellow eluate was evaporated to dryness and the residual clear oil was rubbed under methanol. The pale-yellow crystals m.p. 116-117° (0.518 g.; 13%) of 11-phenyldibenzo[b,f]-1:4-thiazepine (XXX) were recrystallized from methanol (Found: C, 79.68; H, 4.44; N, 5.02. $C_{19}H_{13}NS$ requires C, 79.43; H, 4.56; N, 4.88%). The mixture with thioxanthone anil foundered at 106-108°. The structure of the base was proved by its desulphurization to 9-phenylphenanthridine (III, R=Ph; vide infra). The base did not form a picrate from benzene or methanol.

The Desulphurization of 11-Phenyldibenz[b,f]-1:4-thiazepine (XXX)

11-Phenyldibenzo[b,f]-1:4-thiazepine (0.150 g.), copper bronze (0.15 g.) and diethyl phthalate (1.0 ml.) were refluxed under nitrogen for 65 min. The reaction mixture was diluted with benzene, warmed on the steam-bath and filtered through a charcoal pad. A solution of picric acid (0.15 g.) in hot benzene was added to the filtrate. The yellow needles which separated were collected, washed with benzene and dried in a current of air. The picrate (0.237 g.; 93.6%) melted at 250-252° after insertion in a hot-block pre-heated to 240° (Arcus and Coombs[3] record m.p. 251° for the picrate of 9-phenylphenanthridine). The picrate was divided between dilute aqueous sodium carbonate and benzene. The benzene layer was dried (K_2CO_3) and the benzene was removed at 100° *in vacuo*. The last traces of benzene were eliminated by several evaporations with light petroleum. The residual pale-yellow oil was crystallized from methanol. White crystals m.p. 104-105° (Found: C, 89.10; H, 5.05; N, 5.58. Calculated for $C_{19}H_{13}N$: C, 89.38; H, 5.13; N, 5.49%) were obtained by recrystallization from ethanol. The material did not depress the m.p. (104-105°; literature 106°) of 9-phenylphenanthridine (III, R=Ph) made by the method of Morgan and Walls[17]. The infrared absorption spectrum (KCl disc) was identical with that of 9-phenylphenanthridine.

Note: The yield of 9-phenylphenanthridine (isolated from the mixture with starting-material by fractional crystallization) was 33% after a reaction time of only 7 min., and an 80% yield of 9-phenylphenanthridine picrate was obtained after a reaction time of 20 min.

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PART THREE

Naphtho[2′:3′-4:5]thiepins

Contents

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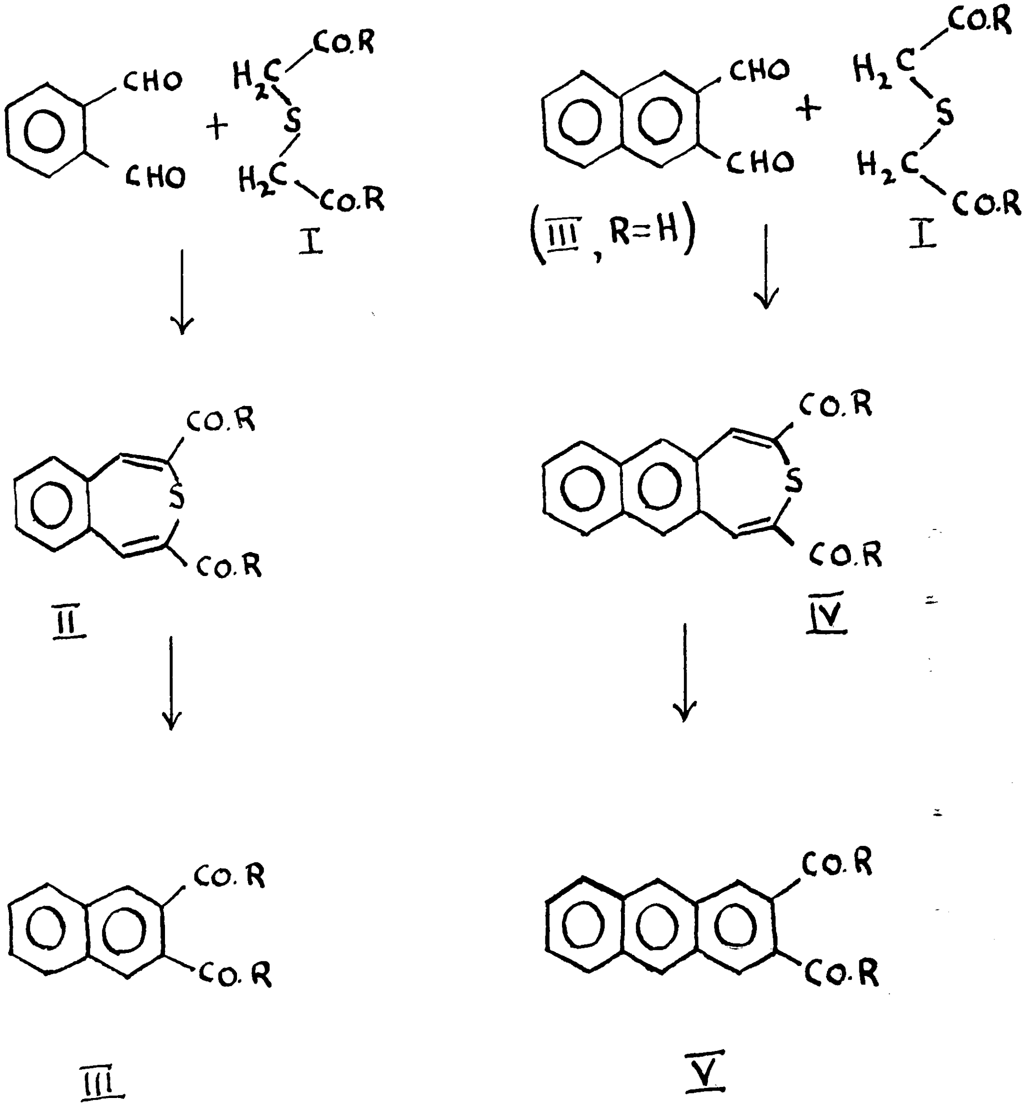
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CHO
+
H_2C
S
H_2C
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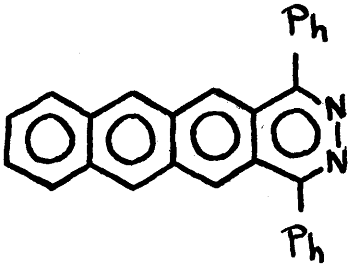
CO.R
I
(III, R=H)
II
III
IV
V

General

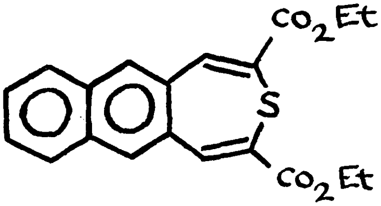
The work of Scott[1] and of Dimroth and Lenke[2] on 4:5-benzothiepin-2:7-dicarboxylic acid (II, R=OH) was mentioned (p. 36) in the introduction to the first chapter of this thesis. The thiepin, which was made by the condensation of diethyl thiodiacetate (I, R=OEt) with <u>o</u>-phthalaldehyde, lost its sulphur atom at the boiling-point of ethanol, with the formation of naphthalene-2:3-dicarboxylic acid (III, R=OH).

A preliminary examination having shown[3] that 2:3-dibenzoylnaphthalene (III, R=Ph) is produced by the alkali-catalysed interaction of <u>o</u>-phthalaldehyde and diphenacyl sulphide (I, R=Ph), the quantitative aspect of this reaction was investigated. Satisfactory yields (55%) of 2:3-dibenzoylnaphthalene were obtained when a solution of o-phthalaldehyde and diphenacyl sulphide in a mixture of methanol and dioxan was treated, at room temperature, with a little sodium hydroxide. A moderate yield (32%) was obtained when the reaction was carried out in a medium of boiling ethanol with potassium carbonate as the condensing agent. The intermediate thiepin (II, R=Ph) was not detected.

The recent report by Ried and Bodem[4] of a relatively convenient route to naphthalene-2:3-dialdehyde (III, R=H) prompted an investigation of its behaviour with diphenacyl sulphide under the same conditions. A 64% yield of 2:7-dibenzoylnaphtho[2′:3′-4:5]thiepin (IV, R=Ph) was obtained. This material was quite stable at 100°, but was readily convertible to 2:3-dibenzoylanthracene (V, R=Ph) and elementary sulphur at temperatures above 180°. The 1:4-diketone (V, R=Ph), heated with hydrazine hydrate in acetic acid, formed the pyridazine (VI).



VI



VII

A study was then made of the condensation of naphthalene-2:3-dialdehyde with diethyl thiodiacetate by the agency of sodium ethoxide, in the hope of making the benzo-analogue (IV, R=OH) of Scott's acid

(II, R=OH). A first experiment afforded small quantities of both the diethyl ester (IV, R=OEt) and the monoethyl ester (VII) of naphtho[2′:3′-4:5]thiepin-2:7-dicarboxylic acid (IV, R=OH). The mono-ester (VII) eliminated sulphur at temperatures of above 180°, with formation of the anhydride of anthracene-2:3-dicarboxylic acid (V, R=OH). The anhydride sublimed without melting as reported by Fairbourne[5] and possessed infrared light absorption bands at frequencies typical of the functional group.

Both the diethyl ester and the monoethyl ester of naphtho[2′:3′-4:5]thiepin-2:7-dicarboxylic acid displayed curious colour changes. The behaviour of the diethyl ester (IV, R=OEt) was particularly puzzling. From its yellow solution in light petroleum this compound formed scarlet needles (*micro*-m.p. 103°) which, on standing under the mother-liquor, were slowly replaced by yellow prisms (*micro*-m.p. 100°). When the yellow crystals were redissolved by warming, and the solution was allowed to cool, the scarlet needles reappeared. Under the microscope the crystals did not appear to melt very sharply, and in consequence a mixed *micro*-m.p.

determination of the yellow and red forms was inconclusive. The two forms did however have identical ultraviolet and infrared absorption spectra, so that their chemical identity is almost certain. Unfortunately it was not possible to obtain sufficient of the yellow form for microanalysis.

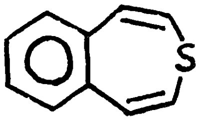
Crystals of an orange-yellow colour were formed when a methanolic solution of the monoethyl ester (VII) was diluted with water. These were converted by heating at 80° to an apparently amorphous, deep-red solid, which contained the proportions of carbon and hydrogen required for the mono- ester. The constitution of the red solid was confirmed by an equivalent-weight determination. The ultraviolet absorption spectra of its solutions in ethanol and in dilute alkali were very similar to the spectrum of an ethanolic solution of the diethyl ester (IV, R = OEt). Insufficiency of material prevented examination of the orange-yellow crystals.

The confusion caused by these colour changes had led to the loss of much material through division of the products into many fractions. The failure to discover naphtho[2′:3′-4:5]thiepin-2:7-dicarboxylic acid in the reaction products therefore did not mean that the free acid was absent. Since Scott, without making any deliberate attempt to hydrolyse the products of the condensation of o-phthalaldehyde and diethyl thiodiacetate, had obtained the dicarboxylic acid (II, R=OH), it seemed only reasonable to suppose that the dicarboxylic acid (IV, R=OH) was the principal product in the present case. This is the product which would be expected if it were assumed that after each aldol condensation a molecule of ethanol is eliminated by lactone formation, as is known to happen in the Stobbe condensation[6]. Although the isolation of the diethyl ester (IV, R=OEt) is evidence that dehydration takes place to some extent, the quantity isolated was scarcely significant.

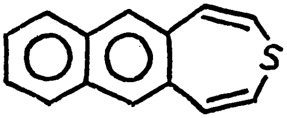
Dimroth and Lenke found it profitable to treat the crude products of the condensation of o-phthalaldehyde and diethyl thiodiacetate with diazomethane, for thereby a 50% yield of the ester (II, R = OMe) was obtained, as compared with the 34% yield of free acid (II, R=OH) obtained by straightforward recrystallization. These authors found that the ester was more stable than the free acid.

When this expedient was tried in the present case, a 28% yield of the dimethyl ester (IV, R=OMe) was obtained. The crystals, which were orange, showed no tendency to change colour. At a temperature of above 180° the dimethyl ester (IV, R=OMe) afforded dimethyl anthracene-2:3-dicarboxylate (V, R=OMe) and elementary sulphur. The structures of the anthracene derivative and of its sulphur-containing precursor were confirmed by conversion of the former through hydrolysis and sublimation to anthracene-2:3-dicarboxylic acid (V, R=OH) anhydride. The ultra-violet absorption spectrum of dimethyl naphtho[2′:3′-4:5]thiepin-2:7-dicarboxylate (IV, R = OMe) was almost identical with that of the diethyl analogue (IV, R=OEt).

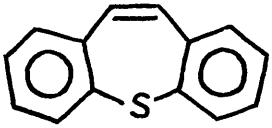
It is fitting to close this chapter, the last dealing with sulphur extrusion, by pointing out that the order of ease of desulphurization of the three known ring systems containing a thiepin ring is that to be expected from thermochemical considerations.



VIII



IX



X

If it is assumed that the fusion of a thiepin ring to an aromatic ring system does not elevate the resonance energy of the latter to any extent, then 4:5-benzothiepin (VIII), naphtho[2′:3′-4:5]thiepin (IX) and dibenzo[b,f]thiepin (X) will have the resonance energies of benzene (36 Kg. cal.), naphthalene (61 Kg. cal.) and two molecules of benzene (72 Kg. cal.) respectively. Since loss of a sulphur atom from these three ring systems leads respectively to naphthalene (resonance energy, 61 Kg. cal.), anthracene (resonance energy, 84 Kg. cal.) and phenanthrene (resonance energy, 92 Kg. cal.), the respective gains of resonance energy will be 25 Kg. cal. (70%), 23 Kg. cal. (38%) and 20 Kg. cal. (28%). The percentage gains of resonance energy given in parentheses indicate the thermochemical driving force available in each instance. The temperatures required for the desulphurization of representatives of the three ring systems (VIII, IX and X) are of the order of 80°, 180° and 300° (in the latter case, with copper present) respectively. The actual order of ease of desulphurization of the three ring systems is therefore in full agreement with the order predicted by the thermochemical argument.

EXPERIMENTAL

Please refer to the remarks on p. 78.

Diphenacyl sulphide (I, R=Ph) was prepared by the method of Fromm and Flaschen[7].

The Condensation of Diphenacyl sulphide with *o*-Phthalaldehyde

An exhaustive examination[3] of the products obtained by the treatment of a hot, ethanolic solution of diphenacyl sulphide and *o*-phthalaldehyde with sodium hydroxide revealed 2:3-dibenzoylnaphthalene (III, R=H), which formed cream-coloured prisms m.p. 143° (Found: C, 85.86; H, 4.82. $C_{24}H_{16}O_2$ requires C, 85.69; H, 4.79%) from acetic acid. The diketone, heated with hydrazine hydrate in acetic acid, formed yellow crystals m.p. 228° of 1:4-diphenylbenzo[g]phthalazine (Found: C, 86.73; H, 5.03; N, 8.55. $C_{24}H_{16}N_2$ requires C, 86.72; H, 4.85; N, 8.43%).

2:3-Dibenzoylnaphthalene was more readily prepared by the methods described below. The first method is included because of its theoretical interest: it was thought noteworthy that the basicity of potassium carbonate was sufficient to effect condensation. The second method is the more useful.

(i) Using potassium carbonate as condensing agent.

A solution of potassium carbonate (0.075 g.) in water (2-3 ml.) was added to a boiling solution of o-phthalaldehyde (0.25 g.) and diphenacyl sulphide (0.50 g.) in ethanol (10 ml.). The whole was heated under reflux for 30 min., and the ethanol was removed at 100° *in vacuo*. The residue was dissolved in a mixture of benzene and water, and the aqueous layer was drawn off in a separating funnel. The benzene solution was washed three times with water, to which it lost most of its deep-red colour. After drying (Na_2SO_4) the benzene solution was concentrated and chromatographed on a column of alumina. The yellow band was collected, the benzene was removed from the eluate and the residue was rubbed under methanol. The pale-yellow crystals (0.236 g.) m.p. 127-144½° were collected, and recrystallized from an acetic acid solution by dilution with ethanol. The cream-coloured prisms (0.203 g.; 32.4%) of 2:3-dibenzoylnaphthalene melted at 144-145½°.

(ii) Using sodium hydroxide as condensing agent.

A small lump (0.065 g.) of sodium hydroxide was added to a solution of o-phthalaldehyde (0.25 g.) and diphenacyl sulphide (0.50 g.) in dioxan (1 ml.) and methanol (1½ ml.), at room temperature. The mixture was shaken for 1 hr. The colour of the liquid steadily deepened over the first 5-10 min., and then it changed very rapidly, with evolution of heat, to an almost opaque green. The preparation was poured into water and allowed to stand for several days. A solid was formed on the bottom of the beaker, but its collection was prevented by the accompanying oily suspension. Acidification with hydrochloric acid produced an easily-worked solid, which was collected. A drop of the basified filtrate did not tarnish a 'silver' coin. A benzene solution of the solid was dried (Na_2SO_4) and chromatographed on a column of alumina. The yellow band was collected and the benzene was removed from the eluate. The residue was dissolved in light petroleum containing the minimum quantity of benzene, and crystallization was induced by scratching with a glass rod. The cream-coloured, microcrystalline powder (0.344 g.; 55%) of 2:3-dibenzoylnaphthalene melted at 143-145°.

Naphthalene-2:3-dialdehyde (III, R=H) was made by the method of Ried and Bodem[4].

2:7-Dibenzoyl-naphtho[2′:3′-4:5]thiepin (IV, R=Ph)

A small lump (0.065 g.) of sodium hydroxide was added to a solution of naphthalene-2:3-dialdehyde (0.34 g.) and diphenacyl sulphide (0.50 g.) in dioxan (4 ml.) and methanol (2 ml.), at room temperature. The preparation was shaken for 30 min.; after 10 min. the colour of the liquid deepened rapidly and heat was evolved. Sometimes a precipitate of yellow crystals formed before shaking had ceased, and at other times it only appeared on standing. After 12 hr. at 18° the solid (0.63 g.; m.p. 166-168°) was collected, washed with water, dilute hydrochloric acid, and water, and dried in a current of air. Addition of the washing fluids to the filtrate precipitated a buff material (0.18 g.) which melted with frothing when inserted in a hot-block at 160°. The benzene solution of this material deposited a small number of crystals on standing. These were combined with the first solid and the whole was recrystallized (charcoal) from benzene. The orange crystals were collected and dried in a current of air, after which they weighed 0.680 g. and melted at 171-172° (sample inserted in hot-block at 160°). When the material was heated for 2-3 hr. at 75° *in vacuo*, it lost its crystalline character, its colour changed to yellow, and its weight was reduced by 0.184 g. (or 2.36 millimoles of benzene) to 0.496 g. (or 1.18 millimoles of the naphthothiepin; 64%); the m.p. was 173-174° (sample inserted in hot-block at 160°). Since decomposition made the m.p. irreversible, the value obtained depended to some extent on the rate of heating. A specimen m.p. 169-170° (sample inserted in 'hot-block at 20°) of 2:7-*dibenzoylnaphtho*[2′:3′-4:5]*thiepin* (IV, R=Ph) was obtained by a second recrystallization from benzene followed by heating for 12 hr. at 100-110° *in vacuo* (Found: C, 80.51; H, 4.29. $C_{28}H_{18}O_2S$ requires C, 80.37;

H, 4.34%). A sample was fused with sodium: a drop of the aqueous extract stained a 'silver' coin, confirming the presence of sulphur.

It is evident from the weights quoted above that in the crystals formed from benzene two molecules of the solvent are associated with each molecule of the naphthothiepin.

2:3-Dibenzoylanthracene (V, R=Ph)

2:7-Dibenzoyl-naphtho[2′:3′-4:5]thiepin (IV, R=Ph; 0.100 g.) was slowly heated from 180° to 250° under a pressure of 0.5 mm. of mercury, in a horizontal subliming tube. The products were allowed to sublime for 40 hr. at the higher temperature. Small, almost colourless crystals of sulphur travelled 7.5 cm. from the source of heat; these had *micro*-m.p. 112°, and were therefore probably rhombic. The anthracene derivative (0.0678 g.; 73.5%) was deposited within 1.5 cm. of the source of heat. The crystals (m.p. 178–180°) were scraped out of the subliming tube, and their solution in benzene was chromatographed on a solumn of alumina. The greenish-yellow band was collected, the benzene was removed from the eluate and the residue was crystallized from acetonitrile. Bright-yellow crystals m.p. 179½-180° of 2:3-dibenzoylanthracene (V, R=Ph) were obtained (Found: C, 87.04; H, 5.09. $C_{28}H_{18}O_2$ requires C, 87.02; H, 4.69%).

Heated with hydrazine hydrate in acetic acid, the diketone formed the pyridazine derivative (VI). This was purified by precipitation from its acetic acid solution with water. 2:3-Diaza-1:4-diphenyltetracene (VI) was thus obtained in the form of a brick-red powder m.p. 256° (Found: C, 87.84; H, 4.82; N, 7.22. $C_{28}H_{18}N_2$ requires C, 87.93; H, 4.74; N, 7.33%).

Diethyl Thiodiacetate (I, R=OEt) was made according to the directions of Overberger *et al*[8].

Diethyl naphtho[2′:3′-4:5]thiepin-2:7-dicarboxylate (IV, R=OEt) and 7-Ethoxycarbonyl-naphtho[2′:3′-4:5] thiepin-2-carboxylic acid (VII)

A solution of sodium (0.05 g.) in ethanol (dried by distillation from sodium ethoxide ; 1 ml.) was added to a warm solution of naphthalene-2:3-dialdehyde

(0.37 g.) and diethyl thiodiacetate (0.41 g.) in dry ethanol (3 ml.). An orange precipitate was at once formed. Addition of ice-water and acidification of the mixture with hydrochloric acid produced a gummy solid, which was taken up in ether. The ethereal solution was washed with aqueous sodium carbonate and water, and dried (Na_2SO_4). The ether was removed and a benzene solution of the residue was chromatographed on neutral alumina. The yellow band was collected, the benzene was removed from the eluate and the residue was dissolved in light petroleum. The yellow solution deposited scarlet needles (0.012 g.) micro-m.p. 101-103° of diethyl naphtho[2′:3′-4:5] thiepin-2:7-dicarboxylate (IV, R=OEt. Found: C, 67.57; H, 4.97. $C_{20}H_{18}O_4S$ requires C, 67.79; H, 5.12%). Ultraviolet light absorption maxima (95% ethanol): 228 (log ε 4.56), 277 (log ε 4.63) and 323 mμ (log ε 4.72). The scarlet needles, allowed to remain under the mother liquor, slowly disappeared and were replaced by yellow prisms micro-m.p. 99-100°. Ultraviolet light absorption maxima (95% ethanol):

228.5 ($\log \varepsilon$ 4.47), 277 ($\log \varepsilon$ 4.56) and 323 mμ ($\log \varepsilon$ 4.65). The intensities of the absorption bands of the scarlet needles are apparently 20% greater than those of the yellow prisms, but in fact they are identical within the experimental error, because the samples (5×10^{-5}g.) were weighed with a balance on which differences of 10^{-5}g. were shown by the fourth significant figure. The red and yellow forms had identical infrared absorption spectra (KCl disc). A mixed *micro*-m.p. determination of the two forms was unsatisfactory as a proof of identity, because the materials did not melt sharply enough for a clear-cut result.

The sodium carbonate extract was cooled in ice and acidified with hydrochloric acid. A solid of m.p. *ca.* 170° was collected. Attempts were made to crystallize this from non-alcoholic solvents, but the products were always red-coloured and amorphous. Crystals were obtained from methanol. Recrystallization from aqueous methanol provided orange-yellow crystals which were converted, by heating at 80° over KOH *in vacuo*, into an amorphous, deep-red coloured solid. Both the red solid and the orange crystals began to form oils at 167° (micro-determination) but with continued heating the oil was gradually replaced by yellow needles. The red solid (Found: C, 65.94; H, 4.55. $C_{18}H_{14}O_4S$ requires C, 66.25; H, 4.32%) was shown to be 7-*ethoxycarbonyl-naphtho*[2′:3′-4:5]*thiepin*-2-*carboxylic acid* (VII) by titration of its solution in ethanol with dilute alkali: 3.33 mg. of the material required 1.02 ml. of 0.01 N-NaOH, so that its equivalent-weight is 327 ($C_{18}H_{14}O_4S$ = 326). Ultraviolet light absorption maxima (95% ethanol): 224 (log ε 4.51), 272 (log ε 4.53), 310 (log ε 4.66) and 322 mμ (log ε 4.78). Maxima in 0.01N-NaOH: 223 (log ε 4.54), 270 (log ε 4.56), 307 (shoulder; log ε 4.61) and 316.5 mμ (log ε 4.67).

A sample of the monoethyl ester (VII) was heated under the conditions used for the desulphurization of the naphthothiepin (IV, R=Ph). A good yield of anthracene-2:3-dicarboxylic acid (V, R=OH) anhydride was obtained. The material was purified by recrystallization from acetonitrile followed by re-sublimation (Found: C, 77.36; H, 3.65. Calculated for $C_{16}H_8O_3$: C, 77.41; H, 3.25%). The infrared absorption spectrum (KCl disc) showed bands at 1820, 1770 and 1222 cm.$^{-1}$, which together are indicative of the anhydride group. Anthracene-2:3-dicarboxylic anhydride, which has been described by Fairbourne[5], sublimes without melting.

Dimethyl naphtho[2′:3′-4:5]thiepin-2:7-dicarboxylate (IV, R=OMe)

Naphthalene-2:3-dialdehyde (0.37 g.) and diethyl thiodiacetate (0.41 g.) were dissolved in ethanol (distilled from sodium ethoxide; 6 ml.) with warming, and the solution was cooled under the tap with shaking, so that a precipitate of small crystals was obtained. The suspension was cooled to 0° and a solution of sodium (0.10 g.) in dry ethanol (2 ml.), also at 0°, was added. The mixture was shaken at 0° for 7 hr. and then set aside (10 hr.) in the refrigerator. The greater part of the ethanol was removed by evaporation at 25° in vacuo. Addition of ice-water to the residue produced a red gum. Rubbed under a mixture of fresh ice-water and ether, the gum dissolved. The aqueous and ethereal fractions were equilibrated in a separating funnel. The ethereal layer was dried (Na_2SO_4) and the ether was evaporated. Chromatography of a benzene solution of the residue on neutral alumina afforded a small quantity of the scarlet needles of the diethyl ester (IV, R=OEt). The aqueous layer was cooled to 10° in an ice-bath, and acidified with 5N-hydrochloric acid. The buff solid (0.37 g.) was collected and dried over KOH in vacuo. Attempts were made to crystallize a little of the material from methanol, but the product was an amorphous powder which was bright-red or pale yellow in colour, depending on the temperature at which it separated.

To a suspension of the crude solid in dry ether (15 ml.), a 2.6% solution of diazomethane (made by the shorter of the two methods described by Arndt[9], and estimated before use; 4.4 ml., or 10% excess assuming the E.W. 149 for the crude acid) was added at 0°. The suspension was shaken at 0° for several hours and allowed to stand at room temperature for 2-3 days. The preparation was filtered and the solid was recrystallized from benzene. The orange-yellow crystals m.p. 178° (with decomposition; the re-solidified melt fused over the range 118-150°) of dimethyl naphtho[2′:3′-4:5]thiepin-2:7-dicarboxylate

(IV, R=OMe) were dried at 90° over KOH <u>in vacuo</u> (Found: C, 66.52; H, 4.33. $C_{18}H_{14}O_4S$ requires C, 66.25; H, 4.32%). Ultraviolet light absorption maxima (in 95% ethanol): 228.5 (log ε 4.45), 277 (log ε 4.52), and 323 mμ (log ε 4.60). The solvents were removed from the combined benzene and ethereal filtrates, and the residue was purified by chromatography of its benzene solution on neutral alumina. The total yield of the dimethyl ester (IV, R=OMe) was 0.185 g. (28.2%).

<u>Dimethyl anthracene-2:3-dicarboxylate</u> (V, R=OMe)

Dimethyl naphtho[2′:3′-4:5]thiepin-2:7-dicarboxylate (IV, R=OMe) was desulphurized in the same way as 2:7-dibenzoyl-naphtho[2′:3′-4:5]thiepin (IV, R=Ph). In the present instance the temperature did not exceed 210° and the sublimation was complete after 10 hr. Recrystallization of the sublimate from methyl acetate/methanol afforded yellow crystals m.p. 150-151½° (Found: C, 73.69; H, 5.03. $C_{18}H_{14}O_4$ requires C, 73.46; H, 4.80%) of <u>dimethyl anthracene</u>-2:3-<u>dicarboxylate</u> (V, R=OMe). Crystals of elementary sulphur were left behind when the subliming tube was rinsed with hot methyl acetate.

The solvents were removed from the mother liquor and the residue was heated on the steam-bath with 5N-sodium hydroxide solution (2-3 ml.) and ethanol, for about 1 hr. After evaporation of most of the ethanol, the solution was acidified with hydrochloric acid. The precipitate was centrifuged and filtered. Anthracene-2:3-dicarboxylic anhydride was sublimed from the filter paper at 200-230°/0.5 mm., and identified by its infrared absorption spectrum (KCl disc), which was the same as that of the sample already at hand.

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   Overberger, Gadea, Smith and Kogon, ibid., 1953, 75, 2075.
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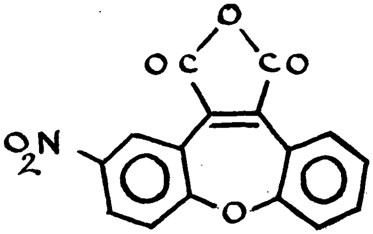
ADDENDUM

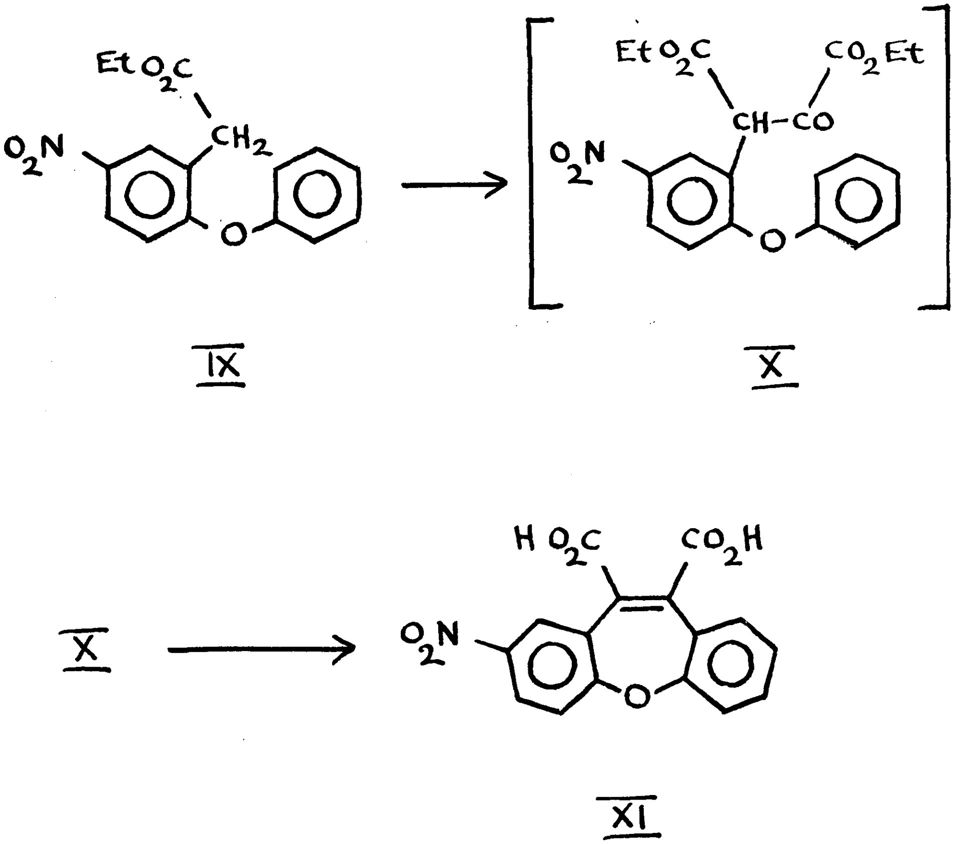
The Synthesis of 2-Nitrodibenz[b,f]oxepin-10:11-dicarboxylic Anhydride (VIII)



VIII

(Note: In the diagram facing p.1 of this thesis there are listed the structural formulae of a number of compounds which will be referred to in the present chapter: to avoid confusion the Roman numerals I to VII assigned to these formulae are retained with their original meaning, but higher numerals belong to a new series. This section is not long enough to justify the repetition of the formulae numbered I to VII, and the indulgence of the reader is requested for referring him to the diagram facing p. 1 when the numeral in question is smaller than VIII).

The preparation by Summers[1] of 2-nitrodibenz[b,f]-oxepin-10-carboxylic acid (VI, R=H) was mentioned in the opening paragraphs of this thesis. The oxepin ring was formed by the cyclodehydration of 5-nitro-2-phenoxyphenylpyruvic acid (V, R=H) with polyphosphoric acid. The purpose of the experiments shortly to be described was the preparation of 2-nitrodibenz[b,f] oxepin-10:11-dicarboxylic acid (XI)



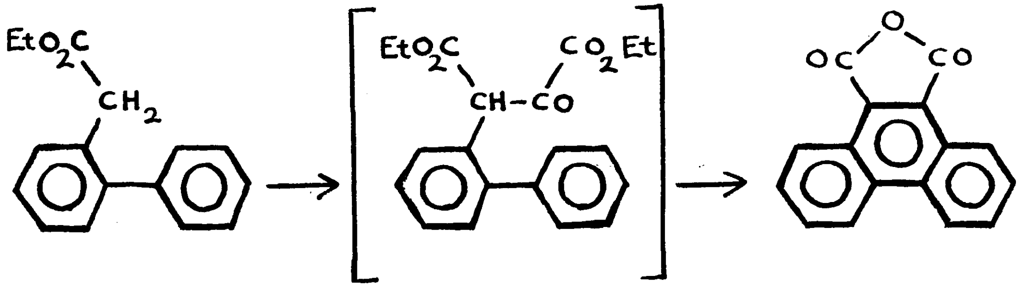
IX

X

XI

by a similar ring-closure of ethyl α-ethoxalyl-5-nitro-2-phenoxyphenylacetate (X). It was proposed to condense ethyl oxalate with ethyl 5-nitro-2-phenoxyphenylacetate (IX) and to cyclize the crude oxaloacetate (X) in situ.

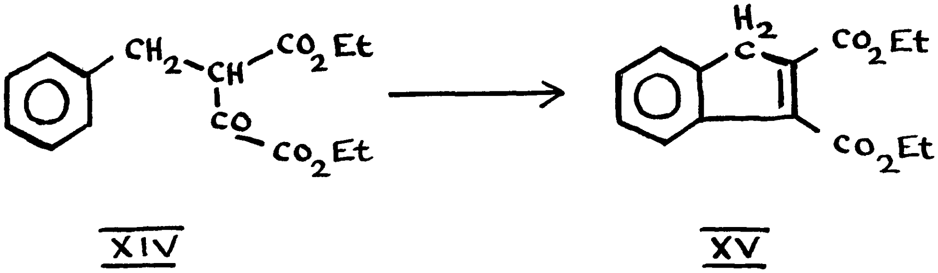
Schönberg and Warren[2] (1939) and Geissman and Tess[3] (1940) have prepared phenanthrene-9:10-dicarboxylic anhydride (XIII) by a similar sequence starting from ethyl ~~diphenyl-2-acetate~~ diphenyl-2-acetate (XII):



XII XIII

Very recently Bradsher et al.[4] have extended this synthesis to the preparation of methoxy derivatives of phenanthrene-9:10-dicarboxylic anhydride.

The original example of an intramolecular condensation of an oxaloacetate group with an aromatic nucleus was provided by Bougault[5], who found that diethyl indene-2:3-dicarboxylate (XV) was the product of treatment of ethyl α-ethoxyalyl-β-phenylpropionate (XIV) with cold, concentrated sulphuric acid:



The reaction has been extended by v. Auwers and Möller[6], and again by Fieser and Hershberg[7].

The cyclodehydrating agents used by the authors mentioned amount to three. These are concentrated sulphuric acid[5,6,7], 80% (w/w) sulphuric acid (at 100°)[2,7] and a mixture of hydrobromic and acetic acids (at the boiling-point)[3,4].

As a first step these reagents were substituted for polyphosphoric acid in the cyclization of 5-nitro-2-phenoxyphenylpyruvic acid (V, R=H) in order to assess their relative usefulness. Only cold concentrated sulphuric acid gave poor results. The purest product was obtained when hot 80% (w/w) sulphuric acid was used, and so these conditions were chosen for the attempted ring-closure of ethyl α-ethoxyalyl-5-nitro-2-phenoxyphenylacetate (X).

Potassium ethoxide was used to condense ethyl 5-nitro-2-phenoxyphenylacetate (IX) and ethyl oxalate, and the crude product was heated with 80% (w/w) sulphuric acid for 4 hr. A small quantity of 2-nitrodibenz[b,f]thiepin-10:11-dicarboxylic anhydride (VIII) was obtained. Its structure was confirmed by elementary analysis and by the presence of bands typical of the anhydride group in the infrared absorption spectrum.

5-Nitro-2-phenoxyphenylpyruvic acid (V, R=H) and 5-nitro-2-phenoxyphenylacetic acid (IX, H for Et) were prepared according to the directions of Summers[1]. The condensation of 2-chloro-5-nitrobenzaldehyde with sodium phenoxide was improved considerably by the use of an excess of sodium phenoxide. 5-Nitro-2-phenoxyphenylacetic acid was esterified with boiling ethanol containing sulphuric acid.

Experimental

Please refer to the remarks on p. 78.

The Condensation of Phenol with 2-Chloro-5-nitrobenzaldehyde

An attempt was made to prepare 5-nitro-2-phenoxybenzaldehyde (III, R=H) under conditions similar to those used by Summers, as follows.

2-Chloro-5-nitrobenzaldehyde (73 g.), phenol (36.5 g.), potassium hydroxide pellets (25.5 g.) and water (182 ml.) were refluxed for 2 hr. and allowed to cool (12 hr.). The oil which formed on the bottom of the flask could not be persuaded to crystallize, even when seeded with a crystal of 5-nitro-2-phenoxybenzaldehyde. Both the oil and the supernatant liquid were extracted with benzene, and the benzene extract was washed with sodium hydroxide solution and water. After drying (Na_2SO_4) the benzene solution was boiled with charcoal and filtered, and the benzene was evaporated from the filtrate under reduced pressure. The residue was a sticky, semi-solid material (55 g.) which could not be crystallized.

Treatment of the gum (1 g.) with acetic anhydride

(1 ml.) containing sulphuric acid ($\frac{1}{5}$th. of 1 drop) at a temperature of 18° for 1 hr., followed by drowning in water, afforded an oil which became sufficiently solid for the purposes of filtration after cooling in the refrigerator. White needles (0.27 g.) of 2-chloro-5-nitro-benzylidene diacetate (Found: C, 46.34; H, 3.37. $C_{11}H_{10}ClNO_6$ requires C, 45.93; H, 3.50%) m.p. 108-109°, unchanged by admixture with material prepared from pure 2-chloro-5-nitrobenzaldehyde, were obtained by three recrystallizations from methanol. The quantity of diacetate isolated indicated that the gum contained at least 17% of starting material: it was considered that the use of an excess of alkali phenoxide might be advantageous, and accordingly a trial was made with sodium phenoxide present in 20% excess.

2-Chloro-5-nitrobenzaldehyde (40 g.), phenol (24 g.) sodium hydroxide (12 g.) and water (400 ml.) were heated under reflux for 5 hr. and allowed to cool (12 hr.). The solid which formed was broken up, filtered off, washed with water and dissolved in benzene. The benzene solution was dried (azeotropic distillation of water/benzene followed by Na_2SO_4) and treated with charcoal (10 g.). Removal of the benzene under reduced pressure left an amber oil (42 g.; 80%) which was poured onto a porcelain tile and allowed to solidify. The solid 5-nitro-2-phenoxybenzaldehyde melted over the range 59-64° (Summers quotes m.p. 66° for the pure material).

5-Nitro-2-phenoxyphenylpyruvic acid (V, R=H)
and
5-Nitro-2-phenoxyphenylacetic acid (IX, H for Et)
were made according to the directions of Summers[1].

Ethyl 5-Nitro-2-phenoxyphenylacetate (IX)

A solution of 5-nitro-2-phenoxyphenylacetic acid (6.0 g.) and sulphuric acid (*d* 1.84; 1.5 ml.) in ethanol (60 ml.) was heated for 5½ hr. under a reflux condenser and $CaCl_2$ tube, on the steam-bath. Ethanol (48 ml.) was distilled off, and the residue was divided between ether (100 ml.) and dilute aqueous sodium carbonate. The ethereal layer was washed with water and dried (Na_2SO_4). The oil which was left after removal of the ether was distilled under reduced pressure from an air-bath. A pale-green oil (6.36 g.; 96%) distilled at 248-250°/15 mm. White crystals began to form in the distillate after 4 hr. at 20°. The solidified ethyl 5-nitro-2-phenoxyphenylacetate (Found: C, 63.78; H, 4.70. $C_{16}H_{15}NO_5$ requires C, 63.78; H, 5.02%) at this stage melted at 33½-34½° but two weeks later was found to have the m.p. 68-69°.

Note: In another experiment the distillation of the product was omitted, purification being by recrystallization from ethanol, from which the crystals of m.p. 68-69° were obtained; the yield was 90.5%.

The Cyclodehydration of 5-Nitro-2-phenoxyphenylpyruvic acid (V, R=H)

A preliminary experiment showed that 5-nitro-2-phenoxyphenylpyruvic acid was not cyclized within the space of a few hours by treatment with 80% (w/w) sulphuric acid at 18°. A second experiment showed that at 18° sulphuric acid (d 1.84) was capable of bringing about the ring closure, but the yield of pure 2-nitrodibenz[b,f]oxepin-10-carboxylic acid (VI, R=H) was poor (40%). The best method was undoubtedly that described under (a) below, in which 80% (w/w) sulphuric acid was employed at a temperature of 100°, but it was closely rivalled by the treatment with a boiling mixture of hydrobromic and acetic acids described under (b); both methods were superior to the use of polyphosphoric acid as described by Summers, which in the writer's hands gave a first product of relatively low purity (m.p. 210-214°) in the apparent yield of 86.5%.

(a) 80% (w/w) Sulphuric Acid at 100°.

The sulphuric acid reagent was prepared by mixing sulphuric acid (d 1.84) and water in the proportions 28:10 by volume.

A suspension of finely-powdered 5-nitro-2-phenoxyphenylpyruvic acid (0.50 g.) in 80% (w/w) sulphuric acid (5 ml.) was stirred at 100° for 3 hr. The cold mixture was drowned in ice-water, allowed to stand (30 min.) and filtered. The greenish solid was washed with water and dried over KOH *in vacuo*, after which it weighed 0.42 g. (89%) and melted at 227-228° [authentic 2-nitrodibenz(b,f)oxepin-10-

carboxylic acid (VI, R=H) prepared by the ~~parentheses~~ method of Summers has m.p. 227-229° after two recrystallizations from acetic acid].

(b) Mixed Hydrobromic and Acetic Acids at the Boiling-Point.

5-Nitro-2-phenoxyphenylpyruvic acid (0.50 g.), 48% hydrobromic acid (1.0 ml.) and acetic acid (1.75 ml.) were heated under reflux for 3 hr. The precipitated buff solid was filtered from the cold mixture, washed with water and dried over KOH *in vacuo*. The material (0.437 g.; 93%) had m.p. 225-227°. Beautiful white needles of 2-nitrodibenz[b,f]oxepin-10-carboxylic acid (VI, R=H) m.p. 227-229° (undepressed by admixture with authentic material) were obtained by recrystallization from acetic acid (charcoal).

2-Nitrodibenz[b,f]oxepin-10:11-dicarboxylic Anhydride (VIII)

Potassium (0.80 g.) was dispersed under xylene, the xylene was decanted, the dispersed metal was washed by decantation with dry ether and was then covered with ether (40 ml.). The suspension was contained in a flask carrying a reflux condenser with attached calcium chloride/soda lime tube. The flask was surrounded by an ice-bath, and ethanol (distilled from sodium ethoxide; 1.25 ml.) was added. When the vigorous reaction had subsided, the ice-bath was replaced by a bath of warm water and the mixture was refluxed for 45 min. Freshly distilled diethyl oxalate (4.1 ml.) was added at 18°, whereupon all the potassium ethoxide dissolved. Ethyl 5-nitro-2-phenoxyphenylacetate (IX; 6.0 g.) was then washed in with ether (10 ml.), whereupon the colour of the liquid immediately deepened from yellow to dark red. The preparation was allowed to stand (12 hr.) at 18°, after which it was heated under reflux for 6 hr., cooled and poured with stirring onto a mixture of ice (20 g.) and 5N-sulphuric acid (20 g.). The ether layer was dried (Na_2SO_4), the ether was evaporated and the oily residue containing the oxaloacetate (X) was stirred vigorously on the steam-bath for 4 hr. with 80% (w/w) sulphuric acid (65 ml.) and allowed to cool. The resulting suspension (of a brown solid in a deep-red coloured liquid) was drowned in ice and the dark brown solid (4.23 g.; m.p. 60-120°) was collected, washed with water and dried in a current of air. The product was crushed under dilute sodium hydroxide solution, charcoal was added and the mixture was warmed on the steam-bath, allowed to cool, and filtered. The filtrate was acidified, allowed to stand several hours in the refrigerator, and the precipitated brown solid (2.52 g.; m.p. 199° after severe pre-softening) was collected, washed with water and dried over KOH *in vacuo*.

A portion (0.50 g.) of the material, after three recrystallizations (charcoal) from acetic acid, afforded beautiful golden needles (0.049 g.) m.p. 205-206° of 2-*nitrodibenz*[b,f]*oxepin*-10:11-*dicarboxylic anhydride* (Found: C, 61.98; H, 2.21; N, 4.71. $C_{16}H_7NO_6$ requires C, 62.14; H, 2.28; N, 4.53%). The infrared absorption spectrum (KCl disc) shows a very strong band at 1770 cm.$^{-1}$ and a moderately strong band at 1835 cm^{-1}: together these bands are characteristic of the anhydride grouping.

The pure material sublimed at 150°/0.6 mm. and a small portion of the crude solid was successfully sublimed, but when it was attempted to sublime the remaining crude material in bulk, only a small sublimate of poor quality was obtained. Extraction of the charred residue with warm dilute alkali and acidification of the filtered solution provided a solid, from which a further quantity (0.084 g.) of the pure anhydride was obtained by recrystallization (charcoal) from acetic acid.

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