

STUDIES ON TROPOLONES

T H E S I S

presented by

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for the Degree of

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P R E F A C E

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The author is indebted to the Department of Scientific and Industrial Research for a Maintenance Allowance during this period, October, 1950 - October, 1953.

PUBLICATIONS

The following papers have been or are about to be published, reprints are enclosed:

- 1) Nitration of Tropolone by J.W. Cook, J.D. Loudon and D.K.V. Steel, published in Chem. & Ind., 1951, 669.
- 2) Pyridotropolone by J.W. Cook, J.D. Loudon and D.K.V. Steel, published in Chem. & Ind., 1952, 562.
- 3) Halogenocycloheptatrienones by B.J. Abadir, J.W. Cook, J.D. Loudon and D.K.V. Steel, published in J.C.S., 1952, 2350.
- 4) Tropolones VII by J.W. Cook, J.D. Loudon and D.K.V. Steel, to be published in J.C.S., 1954.

S U M M A R Y

Nitration of tropolone yields a mixture of α - and γ -mononitrotropolones which are oriented by isomerisation, via their methyl ethers, to o- and p-nitrobenzoic acids respectively. Of the derived amino-tropolones the γ -isomer is also produced by reduction of tropolone coupling-products and is convertible into γ -hydroxy-, γ -halogeno- and γ -cyanotropolone: it also undergoes the Skraup reaction. On the other hand, diazotisation of α -aminotropolone yields much salicylic acid. Nitration of α -bromotropolone yields the γ -nitro-derivative.

γ -Cyanotropolone is used to prepare γ -carboxytropolone and γ -aminomethyltropolone. α -Carboxytropolone is synthesised via a condensate of pimelic and oxalic esters. This condensate is proved by its reactions to be 1:4-dicarbethoxycyclohepta-2:3-dione and on bromination - dehydrobromination, it affords $\alpha\alpha'$ -dibromotropolone.

The conversion of tropolones into chlorotropolones is described and halogen mobility in these compounds and in halogenotropolones is examined with especial reference to mercaptide reagents which, in most cases, can exhaustively replace the halogen substituents. Some incidental rearrangements are noted.

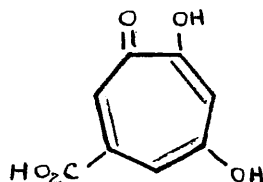
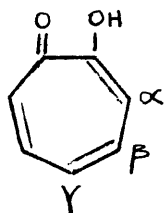
The interaction of ethyl oxalate and di- β -cyanoethyl sulphide - examined in course of preliminary experiments on the synthesis of heterocyclic analogues of tropolone - leads to a sulphur-free compound which is identified, by hydrolysis and degradation, as 3:6-dicyanocatechol.

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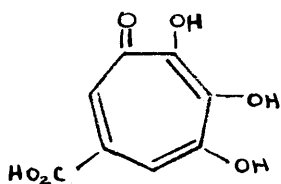
INTRODUCTION

The existence of a new class of natural product has recently been established, in which the common structural feature is the seven-membered carbon ring. The hypothesis of a cycloheptatrienolone (tropolone I) ring system in such compounds was first conceived by Dewar¹ as a basis for interpreting the otherwise perplexing behaviour of the mould metabolite, stipitatic acid II.

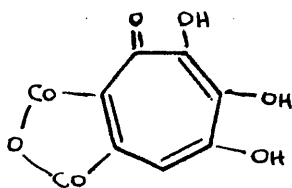


This illuminating proposal has been substantiated^{2,3} by the synthesis of this acid, and many more natural products have been investigated and found to incorporate the tropolone nucleus as a unit of their structure. Two other mould metabolites, puberulic acid III and puberulonic acid IV^{4,5} have been recognised as tropolone derivatives,² whilst the α -, β - and γ -thujaplicins V, obtained from^{6,7,8} the heartwood of Western red cedar, and purpurogallin VI,^{9,10,11} an oxidation product of pyrogallol, are likewise found to contain the tropolone grouping and have been synthesised. The alkaloid colchicine VII¹² isolated from the autumn crocus

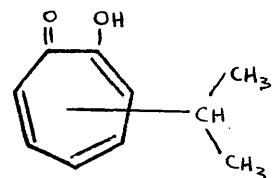
almost certainly possesses the ring system of a tropolone methyl ether.



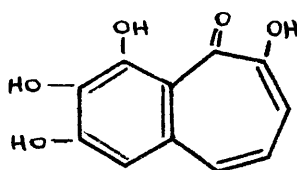
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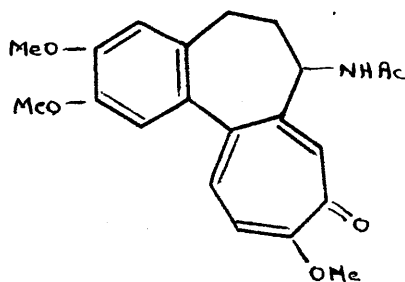
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V



VI

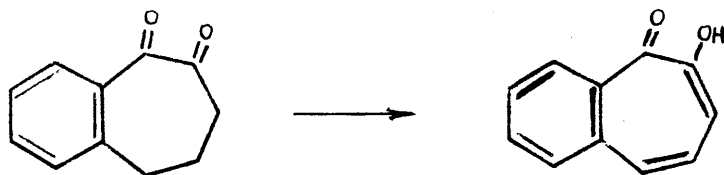


VII

It lies beyond the scope of this monograph to discuss fully the elucidation of structure in these natural products, but an outline of the synthetic approaches to these compounds and an account of their more detailed chemistry are relevant.

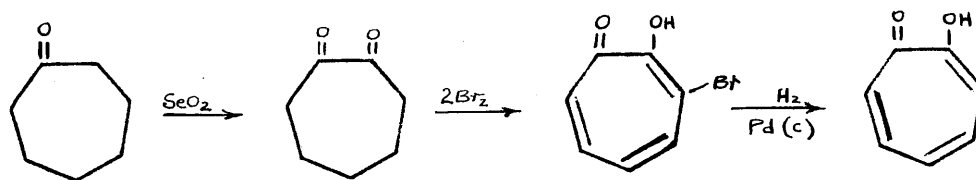
SYNTHETIC TROPOLONES

The first synthesis of a tropolone was reported by Cook & Somerville¹³ in 1949, when they obtained $\alpha\beta$ -benzo-tropolone VIII by dehydrogenation of the appropriate benzocyclohepta-1:2-dione:-



VIII

Their scheme of synthesis was found to be adaptable to the preparation of other tropolones and, in 1950, this research group was successful in synthesising the parent of the series, tropolone¹⁴ itself, from cyclohepta-1:2-dione:-



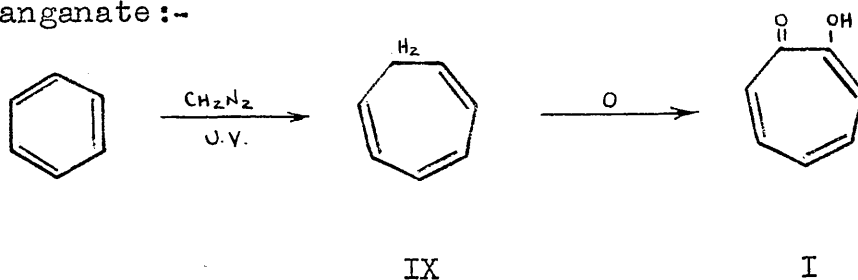
I

This dehydrogenation technique is perhaps the most general for the synthesis of tropolones. The cyclohepta-1:2-diones are obtained by oxidising a reactive methylene group in the appropriate cycloheptanone, particularly by means of selenium dioxide. Successful dehydrogenations have been achieved with 10% palladium charcoal in boiling trichlorobenzene, although the most effective method involves the bromination of the appropriate cyclohepta-1:2-dione and subsequent dehydrobromination. By the same process, Cook, Raphael & Scott⁷ synthesised the three thujaplicins.

The structural characterisation of β -thujaplicin (hinokitiol) including its synthesis has also been reported by a Japanese research team under Nozoe^{15,16} in an extensive chemical study of this natural product. This team evolved the same synthesis as Cook et al. for β -thujaplicin, and concurrently with the latter authors, achieved a similar synthesis of tropolone.¹⁷

Of considerable importance in the tropolone field are the investigations of Doering & Knox in America and Haworth & Hobson in Britain. These groups almost simultaneously with Cook et al. reported the formation of tropolone in two further distinct syntheses.

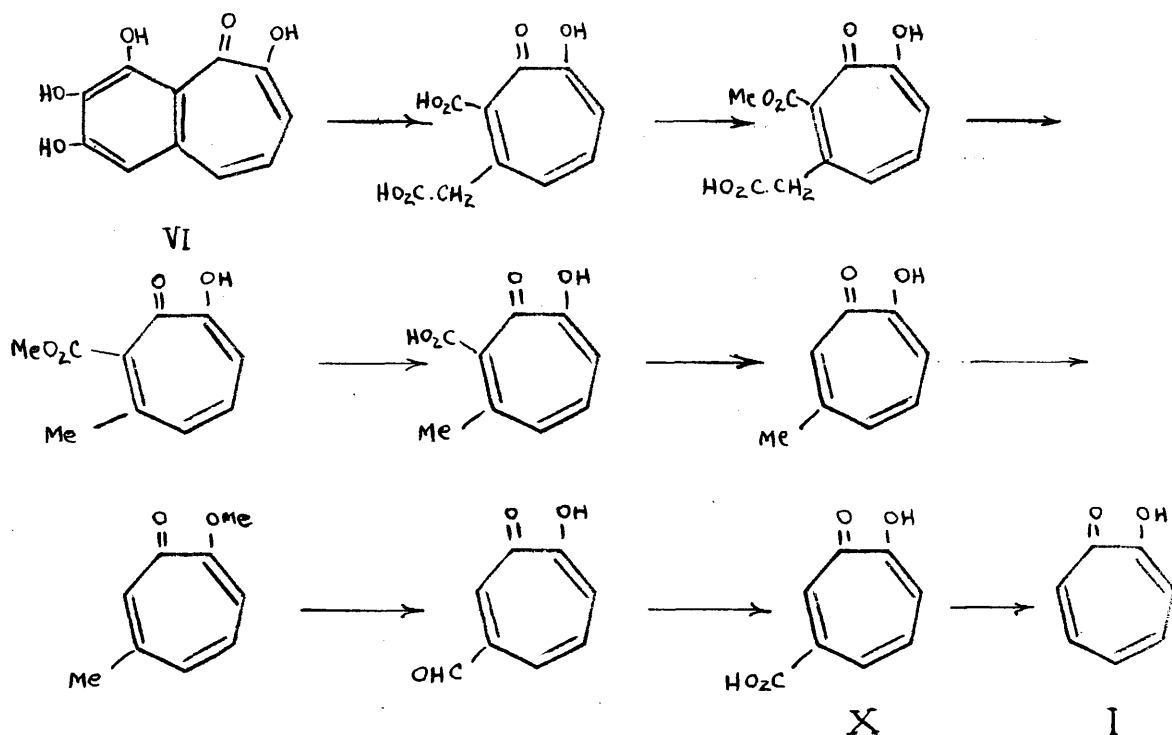
The simple two-step route adopted by Doering & Knox¹⁸ depends on the formation of cycloheptatriene IX by irradiation of a benzene solution of diazomethane with ultraviolet light and the subsequent oxidation of this product with permanganate:-



Although the amount of tropolone isolated is extremely small, 1%, the possibilities are great, as the materials required are relatively inexpensive and easy to obtain. These authors have further progressed with this method

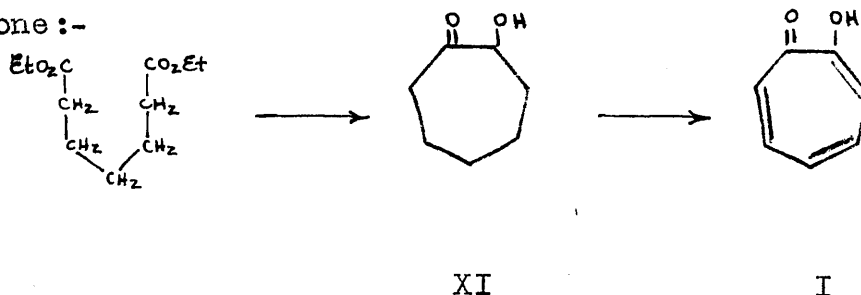
resulting in the recent preparation of a number of γ -alkyltropolones.¹⁹

The method of Haworth & Hobson^{20,21} involves the degradation of purpurogallin, and it is noteworthy that this treatment furnishes a number of difficultly obtainable β -derivatives of tropolone. It consists in the stepwise oxidation of purpurogallin to β -carboxytropolone X and culminates in the decarboxylation of this compound:-

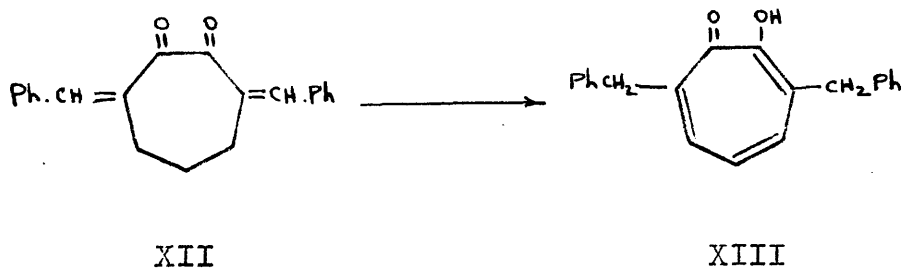


A fifth synthesis of tropolone has been devised by Knight & Cram.²² They investigated the acyloin condensation applied to ethyl pimelate and were successful in isolating the 2-hydroxycycloheptanone XI in ca. 50% yield. Direct

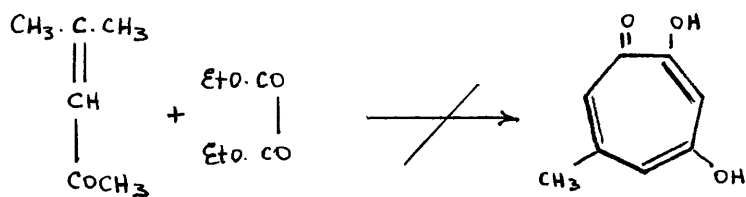
oxidation to the dione could not be realised, but bromination - dehydrobromination resulted in the formation of tropolone:-



Very recently, Leonard & Robinson²³ have reported the isolation of 3:7-dibenzyltropolone XIII from the isomerisation of 3:7-dibenzylidenecyclohepta-1:2-dione XII in hydrogen bromide - acetic acid solution. The dibenzylidene compound was obtained by condensation of cyclohepta-1:2-dione with benzaldehyde in ethanol containing piperidine:-



Many attempts have been made to obtain tropolone and its derivatives by direct synthesis. Dewar¹ described the unsuccessful condensation of mesityl oxide XIV with ethyl oxalate in presence of potassium ethoxide as early as 1945:-

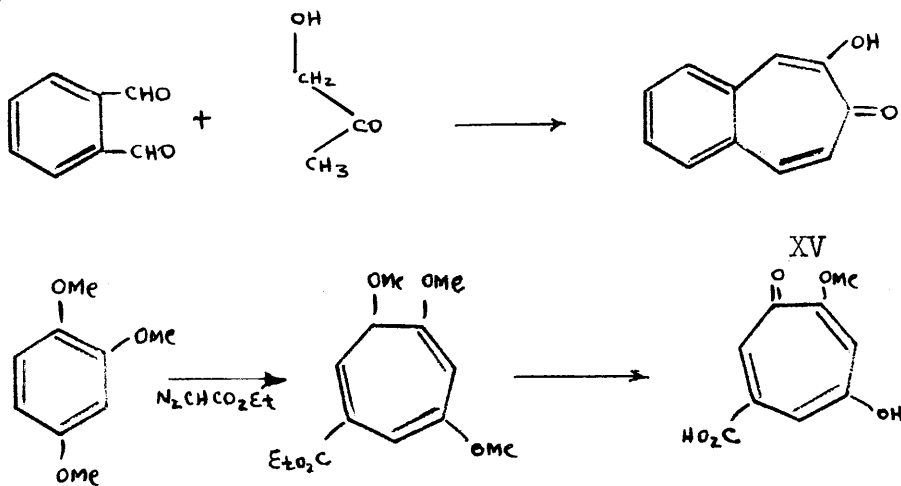


XIV

Other more recent attempts by Cook, Raphael & Scott include the reaction of sodionitromalonyldialdehyde with diacetyl,²⁴ sodionitromalonyldialdehyde with cyclodeca-1:2-dione²⁶ and maleic dialdehyde with hydroxyacetone or methyl ethyl ketone.²⁶ In none of these condensations could any tropolonoid material be isolated.

Not every attempt met with failure, however.

Scott & Tarbell²⁷ synthesised $\beta\gamma$ -benzotropolone XV from *o*-phthalaldehyde and hydroxyacetone, whilst Bartels, Keith & Johnson²⁸ have devised a neat synthesis of stipitatic acid II from 1:2:4-trimethoxybenzene by reaction with diazoacetic ester.



GENERAL PROPERTIES OF TROPOLONES¹²

The tropolones are crystalline solids and can be frequently purified by reason of the ease with which they undergo sublimation. They have an acidic strength intermediate between those of phenol and acetic acid and react, in most cases, with sodium hydrogen carbonate and form coloured salts with alkali which are, generally, insoluble in the alkaline mother liquor.

As enols, the tropolones give an intense colour with ferric chloride solution and form typical coordination complexes with various metals. In particular, formation of a chloroform-soluble copper complex is characteristic of the series.

The tropolones form ethers with various alkylating agents. Methylation of an unsymmetrically substituted tropolone produces, as expected, two isomeric ethers.

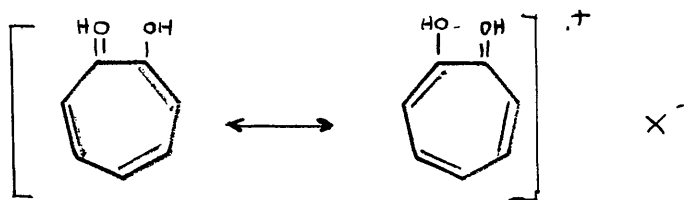
No carbonyl reactivity is apparent in the tropolones and attempts to prepare ketonic derivatives have not, in general, met with success.

The fact that tropolones are fairly resistant to oxidising agents is implicit in two of the methods of preparation, but reaction with alkaline hydrogen peroxide can lead to ring fission and formation of aliphatic dicarboxylic acids. Hydrogenation of the tropolone ring system is

possible, but the resulting product is usually a complex mixture.

Reaction of the tropolones with potassium hydroxide or of their methyl ethers with sodium methoxide can result in their isomerisation to benzenoid compounds. As a means of identifying the position of a group in the tropolones this rearrangement, which is of the benzilic acid type, is of the utmost importance.

The basic character of the tropolones is revealed in their formation of salts with acids. This remarkable property can be explained by assuming that a stable conjugate acid cation XVI is formed, the positive charge being borne by the two oxygen atoms and distributed throughout the ring.



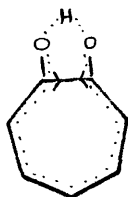
XVI

Substitution by electrophilic reagents rather than addition takes place with the tropolones. According to quantum mechanical calculations made by Dewar, substitution should occur almost exclusively in the γ -position and although this prediction is only approximately fulfilled in the case of nitration and is not in accordance

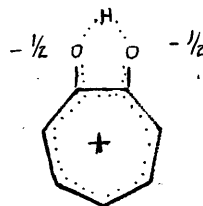
with the results of bromination, yet it appears to hold for diazocoupling.

An X-ray investigation of copper tropolone by Robertson²⁹ has shown that the ring system is a flat regular heptagon with one of the two oxygen atoms more closely bound to the ring than the other.

Finally, the aromaticity of tropolone cannot be explained simply by resonance, involving masking of the ethylenic and carbonyl functions, conveniently represented by XVII, as implied in its chemical formulae. The 1:2-bond of tropolone possesses some double-bond character and is indistinguishable from the other bonds in the ring. A more correct picture of tropolone would be depicted by XVIII.



XVII



XVIII

DISCUSSION.

ORIENTATION AND SUBSTITUTION IN TROPOLONES

The orientation of substituted tropolones has presented its investigators with a frequently difficult problem. It has been recognised that Dewar's prediction 'that substitution of tropolone should occur almost exclusively in the γ -position' is not applicable in every case. This is evinced in the results of bromination, where Cook et al.³⁰ have reported the formation of a scarlet bromine complex with tropolone, which yields a mixture of tropolone, α -bromotropolone and $\alpha\alpha'$ -dibromotropolone on decomposition with alkali. A more practical approach based on isomerisation to benzenoid compounds has not always been possible and it might be that nitro- and aminotropolones would act as key-compounds in orientation. This procedure has been essential in the benzene series and has already been recognised by Haworth & Hobson on β -methyltropolone³¹ and Nozoe et al. on hinokitiol,³² methyltropolone³³ and tropolone.^{34,35}

With this possibility in mind, the nitration and diazocoupling of tropolone was investigated and the position of substitution established by isomerisation of the products to benzenoid compounds of known structure. The investigation was extended to the preparation of some important reference compounds based on the products of nitration.

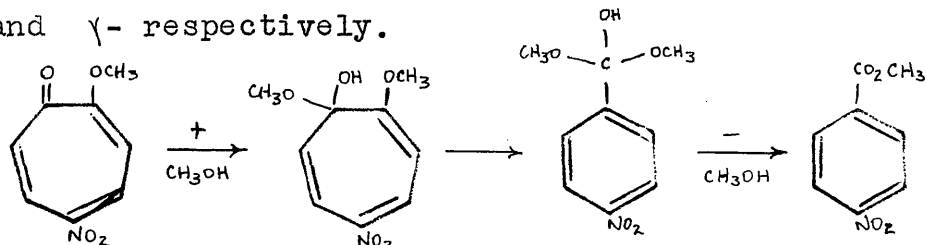
NITRATION OF TROPOLONE

Tropolone in acetic acid was successfully nitrated with nitric acid (S.G. 1.42) in acetic acid, molar quantities of nitric acid being used. Two yellow, crystalline mononitrotropolones were isolated from the reaction mixture. These mononitrotropolones are acidic substances, dissolving with effervescence in aqueous sodium hydrogen carbonate and give a green colour with alcoholic ferric chloride. They were individually separated by fractional crystallisation of their sodium salts from water or of the free acids from benzene.

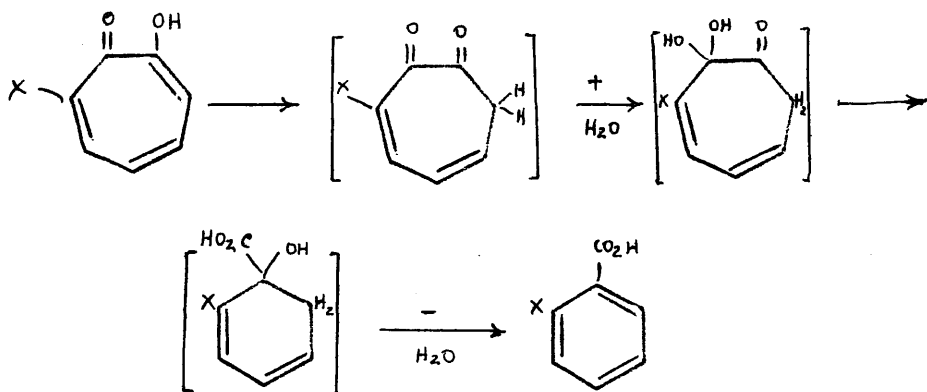
The bulk (40%) of the mononitrotropolone mixture consisted of γ -nitrotropolone, m.p. 194° in sealed tube, which gave a methyl ether, m.p. 224° in sealed tube, on methylation with diazomethane in ether-methanol. α -Nitrotropolone, m.p. 153°, obtained in 10% yield, also afforded a methyl ether, micro-m.p. 127°, on methylation with diazomethane.

In accordance with the methods of Fernholtz & Doering,³⁶ when α -nitrotropolone methyl ether and γ -nitrotropolone methyl ether were heated with sodium methoxide in methanol and subsequently hydrolysed, o- and p-nitrobenzoic acids were formed respectively and were identified by comparison with authentic samples.³⁷ These could only

have been formed by a modified benzilic acid type rearrangement of the mononitrotropolones and consequently the position of the nitro group in the mononitrotropolones must be α - and γ - respectively.



The structure of the α -nitrotropolone was further confirmed by reduction with sodium hydrosulphite to the amino-compound, micro- m.p. 86° , which was diazotised to obtain an α -hydroxytropolone. In accordance with the rearrangement described by Nozoe et al.³⁸ for α -aminohinokitiol, a small quantity of salicylic acid together with some tropolonoid material was obtained. This rearrangement is accounted for as a modified benzilic acid change.



(where X is the amino-group and, in the course of diazotisation and heating, is transformed into the hydroxyl group).

Nitration of tropolone was also effected with nitrogen tetroxide in light petroleum. The procedure adopted was similar to that described by H. Wieland³⁹ for the nitration of phenol and it is interesting to note that in this non-ionic environment, the products formed are the same as in the ionic (nitric-acetic acid reaction), namely, α - and γ -nitrotropolones.

Tropolone in strong acid solution is known to be resistant to substitution, due, presumably, to the formation of a stable conjugate acid cation. In concentrated sulphuric acid, however, tropolone and potassium nitrate were found to react. The reaction, which was carried out at room temperature, was complete in 16 hours and small amounts of α - and γ -nitrotropolones were isolated.

Nitration with dilute nitric acid was not successful, although in one experiment some γ -nitrotropolone was obtained.

Doering & Knox³⁷ have described a mononitrotropolone, m.p. 191° (dec.), formed by the reaction of tropolone with cold dilute nitric acid which is probably identical with the above γ -nitrotropolone. Another investigation on the nitration of tropolone by Nozoe et al.³⁴ has also resulted

in the isolation of a mononitrotropolone from a nitric-acetic mixture in a similar manner to that described above. The latter authors encountered difficulty in orientating the products of nitration. They obtained one mononitrotropolone and originally regarded it as the ortho derivative. This was based on reduction to the amino compound, which by mixed m.p. with an authentic sample of γ -aminotropolone, showed depression. Similarly the amine picrate showed depression of m.p. when fused with an authentic sample of γ -aminotropolone picrate. In a later report,³⁵ however, they identified this mononitrotropolone as the γ -compound by a similar orientation to the one described above for γ -nitrotropolone.

DIAZOCOUPPLING OF TROPOLONE

Coupling of tropolone was carried out with diazotised p-toluidine at different values of pH, the best results being obtained in a 0.25 molar phosphate buffer⁴⁰ at pH ca. 7. At this value, p-tolylazotropolone precipitated as a yellow flocculent mass in 90% yield and formed orange crystals of m.p. 201°, from acetone. The yield and quality of the coupled product deteriorated as the pH of the reaction was raised.

The position of the entrant group was identified by reduction of this azo-compound and of γ -nitrotropolone by

means of sodium hydrosulphite whereby the same amine, namely, γ -aminotropolone, micro-m.p. 173° , was formed.

Nozoe et al.³⁸ and Doering & Knox³⁷ have reported the preparation of such azotropolones, and in each case, substitution has been arrested at the mono-substituted stage.

NITRATION OF α -BROMOTROPOLONE

Nitration of α -bromotropolone has also been carried out, and with a mixture of nitric acid (S.G. 1.42) in acetic acid, a crystalline mononitrobromotropolone, m.p. $138-9^{\circ}$, was obtained. This compound is an acidic substance, dissolving with effervescence in aqueous sodium hydrogen carbonate and giving a greenish-brown colour with alcoholic ferric chloride. It formed a methyl ether, m.p. 196° in sealed tube, on methylation with diazomethane in ether-methanol, which could not be obtained analytically pure either by crystallisation from benzene-light petroleum, methanol or ethanol, or by sublimation in vacuo. The mononitrobromotropolone was identified as γ -nitro- α -bromotropolone by rearrangement of its methyl ether, in a similar manner to that described for γ -nitrotropolone methyl ether, whereby p-nitro-o-bromobenzoic acid was produced.

Nozoe et al.^{34,35} have obtained a mononitrobromotropolone, m.p. $111-112^{\circ}$, in a similar process, which differs greatly

in melting point from the one described above. These authors have orientated their compound by comparison with the mononitrobromotropolone obtained from the bromination of γ -nitrotropolone. As the mixed m.p. of these two compounds showed no depression, it followed that their compound must also be γ -nitro- α -bromotropolone, but direct confirmation is still lacking.

Haworth et al.³¹ have also described the nitration of a substituted tropolone, namely, β -methyltropolone. β -Methyl- γ -nitrotropolone, the α -isomer and the α' -isomer were isolated from this reaction and identified by rearrangement to benzenoid compounds. The γ -isomer was formed in greatest quantity.

γ -AMINOTROPOLONE AND RELATED COMPOUNDS

γ -Aminotropolone was prepared by reduction with sodium hydrosulphite of γ -p-tolylazotropolone or γ -nitrotropolone. It behaves to some extent like aryl amines such as aniline and forms a picrate, an acetyl derivative and gives halogen and hydroxyl compounds via diazonium salts.

Acetylation⁴¹ of γ -aminotropolone in acetic anhydride and crystallisation from water gives a monoacetyl derivative, m.p. 159-162°, which gives a green colour with ferric chloride solution and is therefore the N-acetyl and not the

O-acetyl compound.

$\sqrt{\text{-Aminotropolone}}$ on diazotisation and subsequent heating forms $\sqrt{\text{-hydroxytropolone}}$, m.p. 244° (dec.) in sealed tube, as a stable granular compound from methanol-benzene.¹

Application of the Sandmeyer reaction with cuprous cyanide or better potassium nickelocyanide⁴² on the diazotised material results in an insoluble copper complex being formed from which $\sqrt{\text{-cyanotropolone}}$, m.p. 236° in sealed tube can be obtained, by heating in vacuo at 200° , as a crystallisable sublimate. $\sqrt{\text{-Bromotropolone}}$,³⁸ micro-m.p. and mixed micro-m.p. $186\text{-}188^{\circ}$ with authentic sample, was obtained in a similar manner using cuprous bromide.

Hydrolysis of $\sqrt{\text{-cyanotropolone}}$ was effected either by concentrated acid or alkali yielding $\sqrt{\text{-carboxytropolone}}$, m.p. 288° (dec.) in sealed tube, which gave a crystalline methyl ester methyl ether, micro-m.p. 184° , on methylation with diazomethane. The free acid could not be decar-

boxylated by heating alone or in pyridine, but afforded tropolone on heating in aniline. The action of alkaline hydrogen peroxide⁴³ on $\sqrt{\text{-cyanotropolone}}$ gave an unidentified product of empirical formula $C_5H_5O_5N$, m.p. 269° (dec.).

Catalytic reduction of $\sqrt{\text{-cyanotropolone}}$ in presence of palladium charcoal with 1 molecular proportion of hydrogen chloride gave rise to $\sqrt{\text{-aminomethyltropolone}}$ which was

isolated as its picrate, m.p. 208° (dec.). This procedure was successfully derived by Nozoe et al.⁴⁴ for the hydrogenation of α -cyanotropolone when these authors obtained α -aminomethyltropolone.

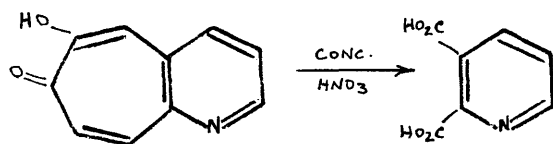
The recognised methods for the preparation of hydrazines from aryl amines by diazotisation and reduction did not, however, yield γ -hydrazinotropolone. Nozoe et al.³⁸ have reported the formation of γ -chloro- and γ -iodo-derivatives of tropolone by a similar process to that described above for γ -bromotropolone and in the elimination of the amino group by diazotisation in ethanol and heating unexpectedly obtained p-ethoxytropolone.

Reaction of γ -aminotropolone with p-toluenesulphonyl chloride in pyridine and dilution with water slowly precipitates a mono-p-toluenesulphonyl derivative, m.p. $178-180^{\circ}$. It produces a faint colour with ferric chloride solution and is probably the N-derivative rather than the O-compound. Nozoe et al.⁴⁵ have described the p-acetylaminobenzenesulphonyl derivative of γ -aminotropolone and report it as the N-compound.

One important reaction of aryl amines is their conversion to quinolines by the Skraup synthesis. This reaction with nitrobenzene, glycerol and 70% sulphuric acid was successfully applied to γ -aminotropolone. The pro-

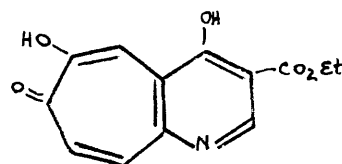
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duct, $\beta:\gamma$ -(3:2-pyrido)tropolone XIX, m.p. 168-9°, which was both basic and enolic, gave a picrate, micro-m.p. 218°, and was shown to contain a pyridine ring by oxidation with nitric acid (S.G. 1.42), whence quinolinic acid XX was identified.

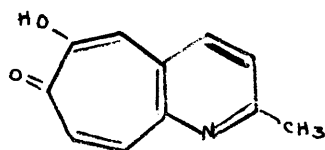


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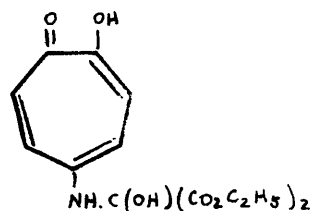
XX



XXI



XXII



XXIII

47

Slack & Attridge have reported the synthesis of two substituted pyridotropolones from γ -aminotropolone by the procedure of Gould & Jacobs and the Doebner-Miller reaction. Thus, the amine and ethoxymethylenemalonic ester at 130° gave γ -($\beta'\beta'$ -dicarbethoxyvinylamino)-tropolone which readily lost ethyl alcohol in boiling Dowerm to yield $\beta:\gamma$ -(3-carbethoxy-4-hydroxy-5:6-pyrido)-tropolone XXI. Similarly, γ -aminotropolone with acetaldehyde in the presence of hydrochloric acid gave $\beta:\gamma$ -(2-

methyl-5:6-pyrido)tropolone XXII.

When cinnamaldehyde and γ -aminotropolone were heated in concentrated sulphuric acid, an insoluble addition product was formed which was hydrolysed by warming with water. Nozoe et al.⁴⁵ have described a similar type of addition product with p-nitrobenzaldehyde and γ -aminotropolone, this being their only success with a number of aldehydes.

A further characteristic of aromatic amines is their condensation with ketomalonic ester to form oxindole-carboxylic acids.⁴⁸ Such a reaction with γ -aminotropolone yielded an addition product, γ -($\alpha\alpha'$ -dicarbethoxy- α' -hydroxymethylamino)tropolone XXIII, m.p. 137-8°. This compound would not cyclise, for when heated in either concentrated sulphuric acid or diphenyl ether, γ -aminotropolone was recovered.

SYNTHETIC TROPOLONES

The concept of an aromatic cycloheptatrienolone (tropolone) ring system has revived the interest in seven-membered carbon ring compounds. There has recently been published a wealth of literature devoted to the synthesis and properties of the tropolones and the search for their direct synthesis is still being continued.

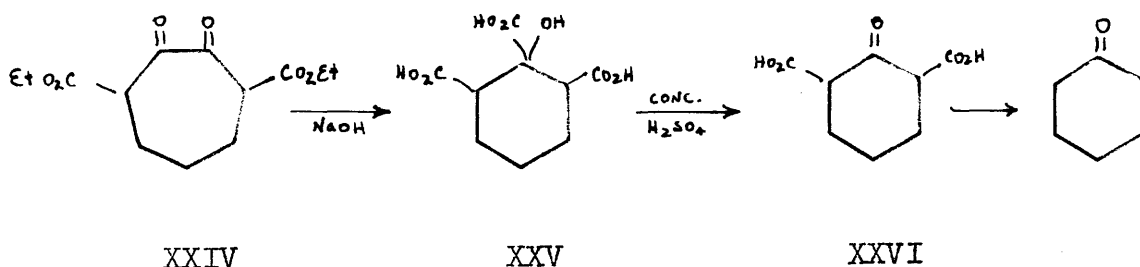
In 1940, S.N. Naumov & A.M. Perminova⁴⁹ described the formation of 1:4-dicarbethoxycyclohepta-2:3-dione XXIV from the condensation of pimelic with oxalic ester. The properties of this dione have been more fully investigated by the present author and, using different methods of dehydrogenation, two substituted tropolones, namely α -carboxytropolone⁵⁰ and $\alpha:\alpha'$ -dibromotropolone³⁰, have been isolated. This is a new synthesis of these substituted tropolones, entailing only two stages, a condensation and a dehydrogenation.

FORMATION AND PROPERTIES OF 1:4-DICARBETHOXYCYCLOHEPTA-2:3-DIONE

Oxalic and pimelic esters were reacted together using two moles of sodium ethoxide as a condensing agent to form a mixture of products from which 1:4-dicarbethoxycyclohepta-2:3-dione has been isolated. Reaction did not occur when the reagents were refluxed in ether, but only took

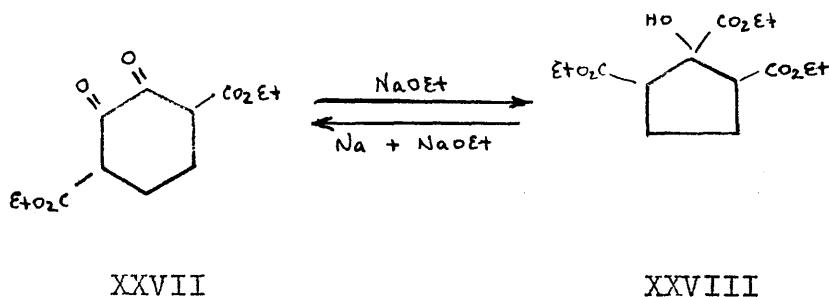
place at a higher temperature, 120-125° under distillation conditions. The dione was separated by means of its ability to form a fairly insoluble yellow sodium salt, which on acidification and crystallisation from ethanol gave an 8% yield of crystalline material.

The structure of the dione was established by alkaline hydrolysis, when a benzilic acid type rearrangement occurred and 1:2:3-tricarboxy-2-hydroxycyclohexane XXV was formed. The product was obtained as a gum which slowly crystallised. It remained unchanged when sublimed in vacuo or when reacted with alkaline hydrogen peroxide and has an equivalent of 79.3. Reaction of this tricarboxy compound with concentrated sulphuric acid afforded 1:3-dicarboxycyclohexan-2-one XXVIst on careful crystallisation from the cooled diluted solution. The degradation was finally completed by warming an ethanolic solution of the 1:3-dicarboxycyclohexan-2-one with 2:4-dinitrophenylhydrazine, when the hydrazone of cyclohexanone was isolated and identified.



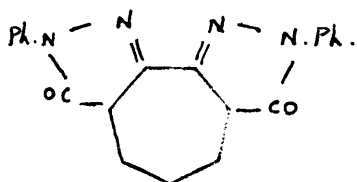
52

Dedusenko has investigated the reversibility of the rearrangement of 1:4-dicarbethoxycyclohexa-2:3-dione XXVII to 1:2:3-tricarbethoxycyclopentan-2-ol XXVIII and established a method for the interchange. The action of sodium ethoxide in ethanol produces the degradation whilst the action of a mixture of sodium and sodium ethoxide in the absence of ethanol brings about enlargement of the ring.

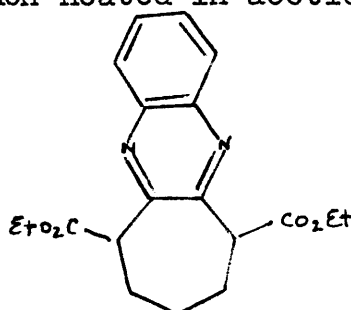


Acid hydrolysis of 1:4-dicarbethoxycyclohepta-2:3-dione was best carried out in acetic acid with 25% sulphuric acid. Addition of an ethanolic solution of 2:4-dinitrophenylhydrazine to the reaction mixture afforded a mixture of hydrazones which were separated on alumina to give two crystalline hydrazones, m.ps. 144° and 198°. The higher melting product was identified as the bis-2:4-dinitrophenyl-⁵³hydrazone of cyclohepta-1:2-dione which crystallises from benzene with 1 molecule of solvent, whilst the other, m.p. 144°, remains unidentified. Consequently, acid hydrolysis of the dione leads simply to decarboxylation.

The presence of two keto groups was shown by reaction with phenylhydrazine, their adjacency being established with *o*-phenylenediamine. Naumov et al.⁴⁹ reported the formation of a phenylhydrazone of 1:4-dicarbethoxycyclohepta-2:3-dione, but experiments carried out here have yielded only the dipyrazolone compound XXIX. A mixture of 1 mole dione with 2 moles phenylhydrazine was refluxed with ethanol and on cooling the colourless dipyrazolone compound crystallised out. Recrystallisation from acetic acid produced a purple form which analysed similarly and showed no depression in the melting point. A 1:1 ratio of dione to phenylhydrazine resulted similarly in the formation of the dipyrazolone compound. When the reactants were mixed in the cold and allowed to stand, the final product on careful evaporation of the ethanol in vacuo was a yellow oil which gave the dipyrazolone compound when heated in acetic acid.



XXIX



XXX

The formation of a quinoxaline derivative XXX, m.p. 142°, of 1:4-dicarbethoxycyclohepta-2:3-dione has been reported

by Naumov et al., but when the dione was refluxed with o-phenylenediamine in ethanol for 1 hour and the reaction liquor carefully diluted with water, two colourless crystalline substances, m.p. 142° and m.p. 82° respectively, were unexpectedly isolated. Neither gave a colour with ferric chloride solution and it is most likely that they are stereoisomers.

α-CARBOXYTROPOLONE

α-Carboxytropolone was isolated in the dehydrogenation of 1:4-dicarbethoxycyclohepta-2:3-dione by the action of a trace of iodine in refluxing nitrobenzene, as described by Treibs⁵⁴ for the preparation of azulene derivatives.

The reaction was carried out by refluxing the dione in nitrobenzene, adding a small crystal of iodine and continuing the heating for a further $\frac{1}{2}$ hour. The nitrobenzene was removed by steam distillation of the alkaline solution and the acidified residual liquor was first extracted with ether and then with methyl ethyl ketone. The methyl ethyl ketone solution afforded on evaporation and sublimation the α-carboxytropolone (0.5%) which was identified by mixed m.p. with an authentic sample.

The bulk of the reaction product was isolated from the ether solution by evaporation and sublimation. This crystalline product is probably 1:3-dicarbethoxy-2-

carboxycyclohexan-2-ol formed from the dione in the moderately alkaline medium. It dissolved in aqueous sodium hydrogen carbonate and warm sulphuric acid with effervescence and has an equivalent of 285.

Further methods of dehydrogenation were tried without success. The dione was refluxed with palladium charcoal in trichlorobenzene⁵⁵ under nitrogen for 8 hours and the products isolated. Most of the material had been transformed into a neutral tar, whilst the small amount of acidic product separated as a brown gum, which possessed little or no tropolonoid character. Dehydrogenation of the dione with chloranil⁵⁷ in refluxing xylene for 28 hours was likewise unproductive.

$\alpha : \alpha'$ -DIBROMOTROPOLONE

^{8,15,16,17,56} Nozoe et al. and ¹² Cook et al. have found the bromination - dehydrobromination of substituted cyclohepta-1:2-diones to yield tropolones satisfactorily. A similar procedure was tried with 1:4-dicarbethoxycyclohepta-2:3-dione with partial success. Bromination with either bromine or N-bromosuccinimide in chloroform was unproductive, but bromination with bromine in acetic acid yielded a moderate quantity of $\alpha : \alpha'$ -dibromotropolone.

Bromination in Chloroform

Bromination was effected by refluxing the dione with two moles bromine in chloroform. After the evolution of hydrogen bromide had ceased, the product was separated into four fractions by washing with sodium hydrogen carbonate, sodium carbonate and finally sodium hydroxide solutions. The bicarbonate and neutral fractions composed nearly the whole of the material and were further investigated.

The bicarbonate fraction was refluxed with dilute caustic soda and an unidentified crystalline material isolated. It gave no colour with ferric chloride solution and the presence of bromine could not be shown by sodium fusion. The neutral fraction gave a strong bromine test on sodium fusion and produced a water soluble gum with no tropolonoid properties on refluxing with caustic soda.

Bromination was also effected with N-bromosuccinimide and the product submitted to thermal dehydrobromination. From the caustic soda fraction was recovered the unchanged dione together with a dark green crystalline material which did not give a colour with ferric chloride solution. No tropolonoid material was isolated from any fraction.

Bromination in Acetic Acid

1:4-Dicarbethoxycyclohepta-2:3-dione in acetic acid was heated under reflux with $2\frac{1}{2}$ moles of bromine until evolution of hydrogen bromide ceased. The reaction mixture was then taken to dryness under reduced pressure and $\alpha:\alpha'$ -dibromotropolone was isolated in 28% yield from the residue. It was separated by reason of its ability to form a fairly insoluble sodium salt and was identified by mixed m.p. with an authentic specimen.

The production of $\alpha:\alpha'$ -dibromotropolone can be most simply explained as the bromination of pre-formed cyclohepta-1:2-dione, a reaction which has been confirmed experimentally. The formation of cyclohepta-1:2-dione from 1:4-dicarbethoxycyclohepta-2:3-dione in acid medium has already been demonstrated in this thesis.

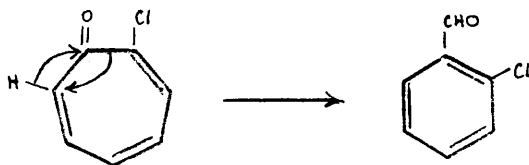
HALOGENOCYCLOHEPTATRIENONES

Exploratory work on the halogenocycloheptatrienones was carried out by researcher B.J. Abadir, whose results have been further investigated by the present author. A completed survey of this work has been published in the Journal of the Chemical Society.⁵⁰

The hydroxyl function of tropolone can be regarded as similar to the hydroxyl of a carboxylic acid in its acidity and etherification with methanolic hydrogen chloride. This comparison is indicative to some extent of the compound's reactivity. Thus Doering & Knox³⁷ in America and Nozoe et al.⁵³ in Japan have reported the formation of 2-aminocycloheptatrienone, a substance corresponding to an acid amide, by heating tropolone methyl ether with methanolic ammonia in a sealed tube.

This parallelism has likewise been supported by the results obtained here on halogenocycloheptatrienones. With thionyl chloride in benzene, tropolone initially forms a white precipitate of tropolone hydrochloride, which dissolves on heating to give 2-chlorotropone XXXI, a compound with some of the properties of an acid chloride. *o*-Chlorobenzaldehyde appears to be a by-product of this reaction. Its singular formation may possibly be interpreted as a rearrangement of 2-chlorotropone in acid environment, and

recalls the production of benzaldehyde⁶³ by treatment of tropolone methyl ether with lithium aluminium hydride.



XXXI

Thionyl chloride also reacts with α -bromotropolone, yielding a dichlorotropolone which has been identified by Nozoe et al.^{59,60,61} as the 2:7-dichloro-compound. The formation of identical 2:7-di-p-tolylthiotropone⁵⁹ from both the dichlorotropolone, prepared by the same method as above and 2-chloro-7-bromotropolone, prepared from 2-hydrazino-7-bromotropolone⁶⁰ established this configuration. 2-Hydrazino-7-bromotropolone has indisputably this structure from its method of preparation from 2-methoxy-7-bromotropolone,⁶¹ a compound whose configuration has been confirmed by X-ray diffraction.

The halogen atom attached to the troponoid nucleus in 2-chlorotropolone is easily substituted and with thio-p-cresol (as the sodium salt) in methanol, p-tolylthiotropolone is formed. Reaction of the 2-chlorotropolone with another anionoid reagent, sodium p-toluenesulphinate, produced an insoluble precipitate which could not be crystallised.

A similar replacement of halogen takes place in 2:7-dichlorotropone. With diethylamine and p-toluidine, mono-replacement occurs even when excess p-toluidine is present, but with thio-p-cresol (as its sodium salt), replacement of both halogen atoms has been achieved. Depending on the molecular proportion used, a mono-p-tolylthio- or a di-p-tolylthio-compound was formed. It is not inconceivable that the 2:7-dichlorotropone might form a quinoxaline compound with o-phenylenediamine, but in conditions suitable for the formation of the p-toluidino-compound the 2:7-dichlorotropone was recovered. When the two reactants were fused together at 100° reaction did indeed occur, but the product is complex.

Acid-catalysed exchange reactions have also been encountered by Doering et al.⁶² in their investigations on halogenotropones. Particular attention was drawn to the replacement of bromine by chlorine, illustrated in their reaction of 3:5:7-tribromotropolone with thionyl chloride in benzene when 2:3:5:7-tetrachlorotropone was formed. Considering that an acid-catalysed exchange had been involved, these authors proceeded to react the 3:5:7-tribromotropolone with concentrated hydrochloric acid at 150°, when the product proved in fact to be 3:5:7-trichlorotropolone.

Neither 2-chlorotropone nor 2:7-dichlorotropone could be caused to react with aromatic hydrocarbons in the presence of aluminium chloride. In both cases, condensation with benzene led to recovery of the chlorotropones but when 2:7-dichlorotropone was reacted with m-xylene as hydrocarbon, there resulted in 70% recovery of the 2:7-dichlorotropone together with a small quantity of unidentified orange prisms.

Catalytic hydrogenation of 2:7-dichlorotropone and chloro-p-tolylthiotropone with Raney nickel did not give homogeneous products but indicated the occurrence of dehalogenation and desulphurisation. Dauben & Ringold⁶³ have prepared 2:4:6-cycloheptatrien-1-one (tropone) by interruption of the hydrogenation of 2:4:7-tribromotropone with palladised barium sulphate, a process which would ultimately give cycloheptanone. It is likely that in the catalytic hydrogenation of the 2:7-dichlorotropone and chloro-p-tolylthiotropone the product is a mixture of tropone, cycloheptanone and partially hydrogenated intermediates.

ANIONOID REPLACEMENT IN SUBSTITUTED TROPOLONES

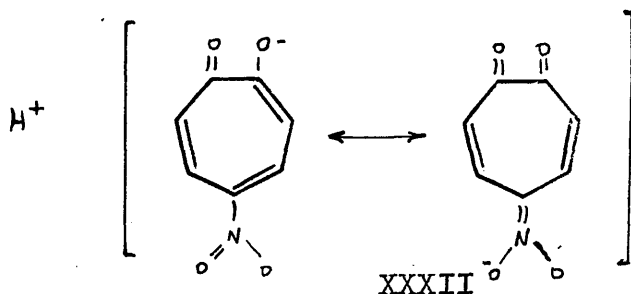
It is well known that *o*-cationoid groups are capable of producing a high degree of mobility in a potential anion attached to a benzene ring. Replacement of a chloro- or nitro-group by the *p*-tolylthio-group has been established for a series of *o*-*p*-disubstituted benzonitriles⁶⁴ and the interaction of *o*/*p*-polyhalogenonitrobenzenes⁶⁵ and the sodium salt of thio-*p*-cresol has yielded complete replacement of halogen.

If a similar type of replacement could be demonstrated in the tropolone nucleus, the problem of orientation of substituted tropolones might well be solved. In experiment, this possibility is not fully realised; there seems to be some resistance to replacement of a χ -bromo-group and under the most vigorous conditions employed, replacement of a χ -nitro-group by the *p*-tolylthio-group could not be effected.

The formation of α -*p*-tolylthiotropolone⁵⁰ from the sodium salt of α -bromotropolone and thio-*p*-cresol in pyridine has already been recognised and the method followed here is essentially the same. $\alpha\alpha'$ -Tribromotropolone was heated with excess thio-*p*-cresol and sodium hydroxide in pyridine and the product isolated. This was

identified as γ -bromo- $\alpha\alpha'$ -di-p-tolylthiotropolone by bromination of $\alpha\alpha'$ -di-p-tolylthiotropolone obtained from $\alpha\alpha'$ -dibromotropolone whereby the same product was formed. The reaction proceeded smoothly without the sodium hydroxide, pyridine providing a suitably basic medium to ensure the presence of thio-p-cresolate ions and to remove liberated hydrogen bromide. Nozoe et al.⁶⁶ have recently carried out a similar reaction in ethanol but besides the above product isolated two other substitution products which our method did not provide. γ -Bromo- $\alpha\alpha'$ -di-p-tolylthiotropolone was further reacted with thio-p-cresol as its sodium salt in ethanol at 150° whence the completely substituted $\alpha\alpha'\gamma$ -tri-p-tolylthiotropolone was produced.

In correspondingly vigorous conditions, γ -nitro-tropolone could not be made to react with thio-p-cresol and was recovered. This would seem to be at variance with the results obtained in the benzene series, but can be explained by the formation of a stable anion due to resonance XXXII.



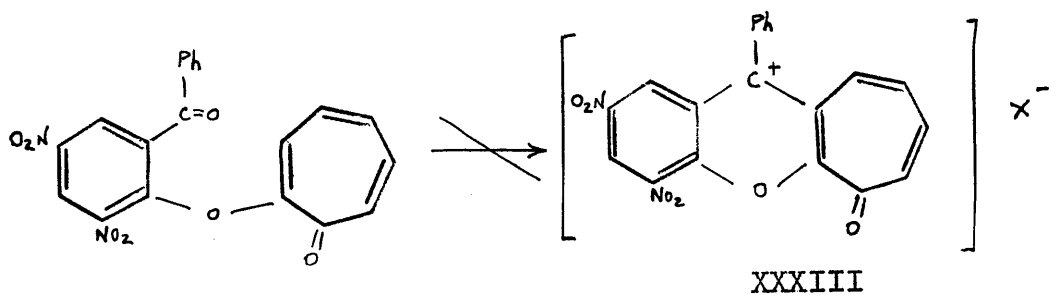
Replacement of halogen in halogenotropones by the p-tolythio-group has already been commented on (cf. halogenotropones), but with 2:3:5:7-tetrachlorotropone,⁶² the alkalinity of the environment produces isomerisation to 2:3:5-trichlorobenzoic acid and the formation of substituted products is not encountered.

As would be expected, tropolone-p-toluenesulphonate⁶² reacts with the sodium salt of thio-p-cresol in ethanol to form α -p-tolythiotropone in 80% yield.

REACTIONS OF THE HYDROXYL GROUP IN TROPOLONE

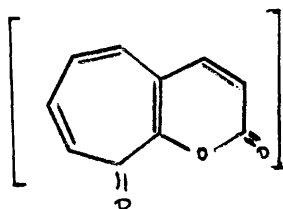
Dewar regards tropolone as an enol of pronounced acidic character, capable of monoalkylation or acylation on either oxygen atom. Our experiments have shown that ethers are formed when 2-chloro-3:5-dinitrobenzophenone is mixed in pyridine with either tropolone or α -bromotropolone. In each case, only one product could be isolated, although there is a possibility of two isomers being formed from the α -bromotropolone.

The method of Loudon, Robertson & Watson⁶⁷ for the orthohydroxylation of phenols now appeared applicable. This reaction depends on the formation of highly coloured xanthylium salts XXXIII in concentrated sulphuric acid and subsequent oxidation and scission. The above ethers gave no characteristic colour in aluminium chloride in ethylene chloride or in concentrated sulphuric acid, even on heating, and the possibility of obtaining xanthylium salts seems rather remote.

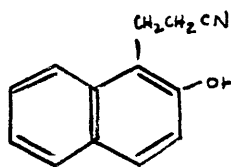


By a similar method, with p-toluenesulphonyl chloride in pyridine, tropolone p-toluenesulphonate was obtained. The same reagent did not form an ether with α -bromotropolone and curiously enough tropolone could not be made to react with 2:4-dinitrochlorobenzene.

Reaction of tropolone with malic acid in hot concentrated sulphuric acid in an attempt to synthesise a coumarin-type compound XXXIV, led to recovery of the tropolone and formation of 6-carboxycoumalin from the malic acid.



XXXIV



XXXV

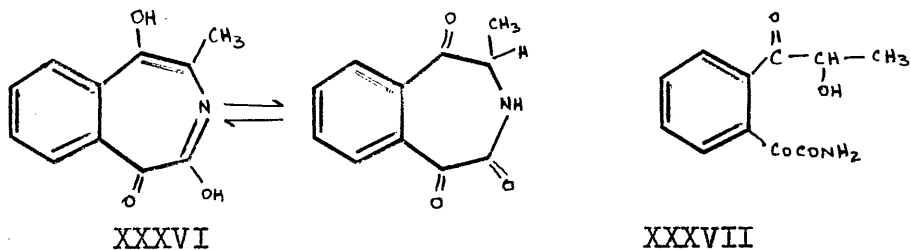
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Various cyanoethyl aryl ethers have been obtained by treating phenols with acrylonitrile in the presence of ca. 1% metallic sodium as catalyst. An unusual reaction of this reagent is represented by the formation of α -(w-cyanoethyl)- β -naphthol⁶⁹ XXXV from β -naphthol and solid caustic soda in boiling benzene. The alkalinity of this reaction favours the formation of a corresponding tropolone derivative (cf. Cook et al. on γ -formyltropolone⁵³ and Nozoe et al. on 3-hydroxymethyltropolone⁷⁰) but nevertheless this procedure led to recovery of the tropolone.

In contrast to the ease with which it is alkylated the hydroxyl group in tropolone is much less readily acylated. C-Acylation is even more difficult and the formation of a C-acetyl derivative of stipitatic acid is perhaps unique. Recently some C-acylation reactions catalysed by strong acids have been investigated by H. Burton & P.F.G. Prail⁷² and with perchloric acid - acetic anhydride mixtures favourable results have been obtained on anisole, etc. A similar reaction applied to tropolone methyl ether or tropolone resulted in the recovery of tropolone. Similarly trifluoroacetic anhydride⁷³ has been shown to promote, under mild conditions, the condensation between suitably activated aromatic compounds and carboxylic acids to give ketones, but a corresponding reaction with tropolone methyl ether or tropolone yielded only unchanged material.

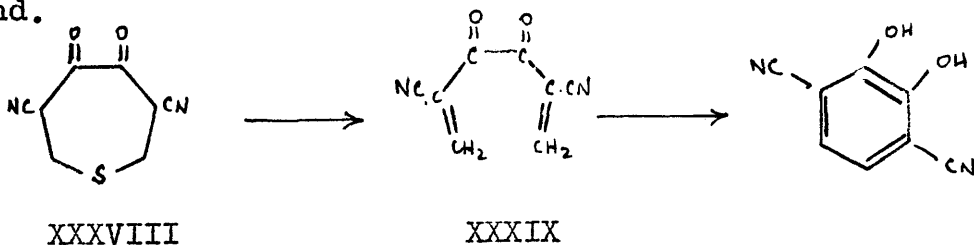
APPENDIX.-HETEROCYCLIC TROPOLONES

The existence of (o-alanylphenyl)glyoxilic acid lactam⁴⁴ XXXVI which might be termed a heterocyclic tropolone is probably unique. The instability of this compound with alkali, ring ruptures on trituration with 10% sodium hydroxide to form (o-lactylphenyl)glyoxalamide XXXVII, has deterred us from preparing this compound and investigating its properties. Nevertheless, it does not exclude the possibility of obtaining a stable heterocyclic tropolone ring and with this idea in mind, a pursuit of such compounds was undertaken.

3:6-DICYANOCATECHOL

The satisfactory preparation of tropolones by condensing oxalic and pimelic esters and subsequent dehydrogenation held promise that this type of reaction could be extended to include heterocyclic tropolones. The condensation of bis-(2-cyanoethyl)sulphide with oxalic ester was first investigated and although the reaction did not produce the expected compound, nevertheless an extremely

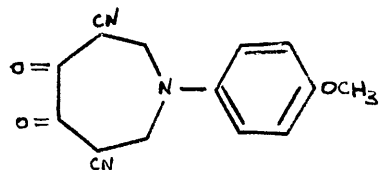
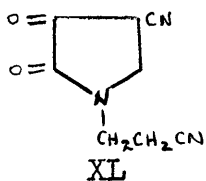
interesting result was obtained. The condensation was effected by heating under reflux the reactants with two moles of sodium ethoxide in ether. A crystalline compound was isolated from the reaction mixture which was identified as the unrecorded 3:6-dicyanocatechol by degradation to catechol. This compound formed a dimethyl ether with diazomethane and was hydrolysed with sodium hydroxide (1:1) to 3:6-dicarboxycatechol, m.p. 288-290° (dec.) (lit. m.p. 290° with gas evolution), which monodecarboxylated to 3-carboxycatechol, m.p. 199-202° in sealed tube (lit. m.p. 204°), on heating at 300°, complete decarboxylation to catechol being achieved by heating under reflux with aniline. The formation of 3:6-dicyanocatechol can possibly be explained by supposing the intermediate formation of 3:6-dicyano-4:5-diketohexamethylenesulphide XXXVIII, elimination of hydrogen sulphide with the formation of 2:5-dicyano-3:4-diketokexa-1,5-diene XXXIX and cyclisation of this compound.



N-(β-CYANOETHYL)-4-CYANO-2:3-DIKETOPYRROLIDINE

Another interesting compound was formed when bis-(2-cyanoethyl)amine and oxalic ester were heated with two

moles of sodium ethoxide in ether. The extremely water soluble product was isolated by passing the alkaline solution through an ion-exchange resin and concentration of the effluent. Part of the residue crystallised and is considered to be *N*-(β -cyanoethyl)-4-cyano-2:3-diketopyrrolidine XL. It gave a red colour with aqueous ferric chloride, dissolved in sodium hydrogen carbonate solution with effervescence, and the presence of one reactive hydrogen was illustrated by the formation of a monomethyl ether with diazomethane. The non-basicity of the ring nitrogen was demonstrated by the failure to isolate a picrate whilst the presence of only one ketonic oxygen was shown by reaction with *o*-phenylenediamine, when only one amino-group reacted.



In order to eliminate participation in this condensation of the hydrogen atom attached to the nitrogen, a suitable derivative of the bis-(2-cyanoethyl)amine was prepared. *p*-Toluenesulphonyl chloride was found to react with the amine in pyridine giving a crystalline derivative. This compound failed to condense with oxalic ester when

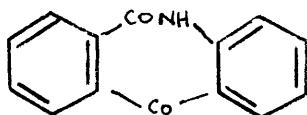
the experiment was conducted under similar conditions to the above. Stronger conditions realised by heating the reactants together under ordinary distillation conditions in the absence of solvent, also failed to produce reaction and a large quantity of the substituted amine was recovered from the melt.

A final effort to synthesise a heterocyclic tropolone by this method was attempted in the condensation of bis-(2-cyanoethyl)anisidine and oxalic ester with two moles of sodium ethoxide in ether. Together with recovered starting material, an amorphous product was obtained. There is very little evidence for suggesting that this compound might be N-p-anisyl-3:6-dicyano-4:5-diketoexamethylenimine XLI, as it dissolves in sodium hydroxide but does not give a colour with ferric chloride and forms only one crystalline derivative, a monophenylhydrazone.

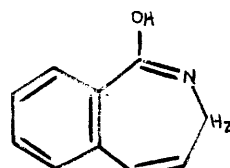
2-(2'-AMINO BENZOYL) BENZOIC ACID LACTAM

We have synthesised 2-(2'-aminobenzoyl)benzoic acid lactam XLII, a compound already known, by a different procedure in a further search for heterocyclic tropolones. Phthalanil rearranged in an aluminium chloride - sodium chloride melt to form the lactam in 40% yield. A similar reaction applied to succinanil in an attempt to prepare 1:5-dihydroxy-3,2-benzazepine, XLIII was not successful.

Under similar conditions to above or under any conditions imposed the product was a mixture of recovered succinanyl and a black amorphous solid which has not been identified.



XLII

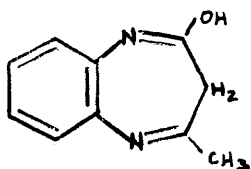


XLIII

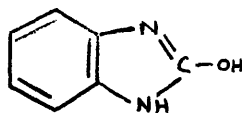
Another unfruitful reaction investigated depended on the straightforward condensation of oxamide and ethyl malonate with two moles of sodium ethoxide in ethanol. The insolubility of the oxamide prevented the formation of any considerable quantity of product but nevertheless reaction did occur. An acidic product, m.p. 240° (Found: C, 45.7; H, 4.4; N, 17.6%) was isolated which did not give a colour with ferric chloride but formed a methylated product, m.p. 116° (Found: C, 50.8; H, 5.5; N, 13.9%) with diazomethane.

A final attempt to prepare a heterocyclic tropolone failed when the oxidation of 2-methyl-4-hydroxybenzazepine XLIV (cf. W.A. Sexton, J.C.S., 1942, 303) was investigated. Selective oxidation of the methylene group was attempted with selenium dioxide, but when the benzazepine was refluxed in either ethanol or acetic acid with 1 mole of selenium dioxide and the precipitated selenium filtered off, the

filtrate afforded a compound which did not depress the m.p. of 2-hydroxybenzimidazole⁷⁸ XLV. Four standard methods⁷⁹ of nitrosation of the reactive methylene group were tried without success on the benzazepine. In each case either starting material was recovered or the compound was hydrolysed to 2-hydroxybenzimidazole. Three methods of condensing benzaldehyde with the benzazepine were tried, also without success. The third method,⁸⁰ involving reaction with sodium acetate and acetic anhydride, produced a new compound which is probably the monoacetate of the benzazepine.



XLIV



XLV

EXPERIMENTAL.

Tropolone was prepared from sodium bromotropolone dihydrate (Cook, Gibb, Raphael & Somerville, J.C.S., 1951, 503-511).

NITRATION OF TROPOLONE

- 1) With nitric-acetic acid mixture
- 2) With nitrogen tetroxide
- 3) With potassium nitrate in conc. sulphuric acid
- 4) With dilute nitric acid.

1). With nitric-acetic acid mixture

Tropolone (0.6 g.) in acetic acid (10 c.c.) was nitrated with nitric acid (0.32 c.c.; S.G. 1.42) in acetic acid (2.9 c.c.), added from a micro-burette in $\frac{1}{4}$ hour. The temperature rose after addition of the first few drops to 27°C where reaction occurred; the rest of the mixture was added slowly maintaining the temperature just below this value. The reaction mixture was allowed to stand for 16 hours at room temperature and the ν -nitrotropolone, which had precipitated as a light yellow solid (0.16 g.), was filtered off. The mother liquor was diluted with water and continuously extracted with benzene. The benzene extract was evaporated to dryness and the product fractionally crystallised from benzene to give a mixture of the more insoluble ν -nitrotropolone (0.16 g.) and α -nitrotropolone (0.08 g.).

γ -Nitrotropolone recrystallised from benzene in yellow needles, m.p. 187° in sealed tube rising to 194° on further crystallisation (Found: C, 50.1; H, 3.0; N, 8.3. $C_7H_5O_4N$ requires C, 50.3; H, 3.0; N, 8.4%). It sublimes at $120^{\circ}/16$ mm., gives a green colour with alcoholic ferric chloride, dissolves in aqueous sodium hydrogen carbonate with effervescence and forms an orange, sparingly soluble sodium salt with alkali.

α -Nitrotropolone recrystallised from benzene in yellow prisms, m.p. 153° (Found: C, 50.5; H, 3.2; N, 8.5. $C_7H_5O_4N$ requires C, 50.3; H, 3.0; N, 8.4%). It gives a green colour with alcoholic ferric chloride, dissolves in aqueous sodium hydrogen carbonate with effervescence and forms a red sparingly soluble sodium salt with alkali.

2). With nitrogen tetroxide

Tropolone (0.5 g.) in 200 c.c. of light petroleum ($60-80^{\circ}$) was nitrated by slow addition of nitrogen tetroxide (0.5 g.) in light petroleum (5 c.c.) at $10-15^{\circ}C$ with mechanical stirring. After leaving under agitation for 3 hours, the light petroleum was decanted off and the product washed with fresh solvent. The gummy residue was successfully worked up by either of the following methods:-

(a) Washing with a little water and filtering yielded 0.36 g. of a mixture of α - and γ -nitrotropolones. Continuous extraction with benzene of the aqueous mother

liquor yielded a little further nitrotropolonic material.

(b) Crystallisation from methanol gave 0.18 g.

γ -nitrotropolone, m.p. in sealed tube 193-194° with
 γ -nitrotropolone obtained in (1). Evaporation of the filtrate and crystallisation from benzene yielded a mixture of α - and γ -nitrotropolones.

3). With potassium nitrate in conc. sulphuric acid

To tropolone (0.05 g.) in conc. sulphuric acid (1 c.c.) was added at 0°C potassium nitrate (0.048 g.) in conc. sulphuric acid (1 c.c.). No reaction occurred till the temperature was raised. After allowing to stand for 16 hours at room temperature, the orange solution was poured on to ice and α - and γ -nitrotropolones isolated as in (1) above, in small yield.

4). With dilute nitric acid

(a) No reaction occurred when nitric acid (0.059 c.c.; S.G. 1.42) in water (0.53 c.c.) was added to tropolone (0.1 g.) in water (1 c.c.) at 0°C. The mixture was allowed to stand at room temperature and then heated on a steam-bath to 95°C, where reaction occurred. Continuous extraction with benzene produced a small amount of γ -nitrotropolone.

(b) In a similar experiment to (a) at a lower temperature (62°C) and with nitric acid (0.059 c.c.) in

water (0.24 c.c.), a more vigorous reaction occurred from which no tropolonic material could be isolated.

γ-NITROTROPOLONE METHYL ETHER

Diazomethane in ether was added to γ-nitrotropolone (0.1 g.) in methanol (10 c.c.) and the solution allowed to stand for 16 hours. Evaporation followed by solution in benzene, washing with dilute aqueous sodium hydrogen carbonate, drying and crystallisation from benzene gave

γ-nitrotropolone methyl ether as bright yellow needles, m.p. 224° in sealed tube (Found: C, 52.8; H, 3.8; N, 7.9. $C_8H_7O_4N$ requires C, 53.0; H, 3.9; N, 7.7%).

REARRANGEMENT OF γ-NITROTROPOLONE METHYL ETHER

γ-Nitrotropolone methyl ether (0.03 g.) was heated under reflux with sodium (0.02 g.) in methanol (5 c.c.) for 3 hours on a steam-bath. After evaporation, 6N caustic soda (2 c.c.) was added and the solution heated for 1 hour on a steam-bath. Acidification, extraction with ether and crystallisation from benzene gave p-nitrobenzoic acid as colourless needles, m.p. and mixed m.p. 238-239° in sealed tube with authentic specimen.

α-NITROTROPOLONE METHYL ETHER

The methyl ether was prepared in a similar manner

to that adopted for the $\sqrt{\text{-nitro-compound}}$ and crystallised from ether in pale yellow feathery crystals, micro-m.p. 127° (Found: C, 53.0; H, 4.1; N, 8.1. $\text{C}_8\text{H}_7\text{O}_4\text{N}$ requires C, 53.0; H, 3.9; N, 7.7%).

REARRANGEMENT OF α -NITROTROPOLONE METHYL ETHER

The rearrangement was carried out in a similar manner to that adopted for $\sqrt{\text{-nitrotropolone methyl ether}}$ and yielded o-nitrobenzoic acid, micro-m.p. and mixed micro-m.p. with authentic sample $136-140^{\circ}$. Mixed m.p. with authentic sample of m-nitrobenzoic acid $97-112^{\circ}$.

REDUCTION OF $\sqrt{\text{-NITROTROPOLONE}}$

A 10% solution of sodium hydrosulphite (10 c.c.) was added to $\sqrt{\text{-nitrotropolone}}$ (0.1 g.) in warm water (10 c.c.). The pale yellow solution was neutralised with ammonia and made faintly acid with acetic acid. Extraction with several portions of methyl ethyl ketone, evaporation and crystallisation from xylene yielded $\sqrt{\text{-aminotropolone}}$ (0.03 g.) as yellow scales, micro-m.p. 173° (Found: C, 61.4; H, 5.4; N, 10.5. $\text{C}_{10}\text{H}_{10}\text{O}_2\text{N}$ requires C, 61.3; H, 5.2; N, 10.2%). It gives a purple colour with alcoholic ferric chloride and dissolves in aqueous sodium hydrogen carbonate with effervescence.

Picrate: Yellow-brown crystals from ethanol,

m.p. 224-6° (dec.).

Acetyl derivative: By heating in acetic anhydride and crystallisation from water, m.p. 159-162° (Found: C, 60.4; H, 5.8. $C_9H_9O_3N$ requires C, 60.3; H, 5.1%).

p-Toluenesulphonyl derivative: γ -Aminotropolone (0.02 g.) and p-toluenesulphonyl chloride (0.03 g.) were left in pyridine (1 c.c.) overnight. Dilution with water produced an opaque solution from which the product slowly crystallised. Recrystallisation from water gave the p-toluenesulphonyl derivative as yellow needles, m.p. 178-180° (Found: C, 56.1; H, 4.8; N, 5.5. $C_{14}H_{13}O_4NS$ requires C, 57.7; H, 4.5; N, 4.8%). It gave a faint colour with ferric chloride in ethanol.

Using twice the quantity of p-toluenesulphonyl chloride and similar treatment to above, a 60% recovery of p-toluenesulphonyl chloride was obtained.

REDUCTION OF α -NITROTROPOLONE

From a similar process to the above, α -aminotropolone was obtained as yellow needles from light petroleum (60-80°), micro-m.p. 86° (Found: C, 61.5; H, 5.2. $C_7H_7O_2N$ requires C, 61.3; H, 5.2%).

REACTION OF TROPOLONE WITH p-TOLUENEDIAZONIUM CHLORIDE

Coupling was carried out at different values of pH, the best results being obtained with a 0.25 molar phosphate

buffer, containing potassium dihydrogen phosphate (2.72 g.) and sodium hydrogen phosphate duodecahydrate (6.92 g.) in water (100 c.c.), which gives a pH in the region of 6.9.

Tropolone (0.5 g.) in the buffer solution (60 c.c.) was coupled with 0.1 molar p-toluenediazonium chloride in 0.06N hydrochloric acid. The yellow flocculent precipitate (0.9 g.), $\sqrt{-p\text{-tolylazotropolone}}$, was filtered, dried and crystallised from acetone. Orange crystals (0.6 g.), m.p. 201° (Found: C, 70.1; H, 5.2; N, 11.8. $C_{14}H_{12}O_2N_2$ requires C, 69.95; H, 5.0; N, 11.7%). It gave a deep-red colour with ferric chloride in ether and forms an insoluble red sodium salt with alkali.

REDUCTION OF $\sqrt{-p\text{-TOLYLAZOTROPOLONE}}$

Reduction of the above compound (0.2 g.) in 30 c.c. acetone-water (2:1) similar to the reduction of $\sqrt{-nitrotropolone}$ yielded $\sqrt{-aminotropolone}$ (0.14 g.), m.p. and mixed m.p. $173\text{-}175^{\circ}$ with $\sqrt{-aminotropolone}$ obtained by reduction of $\sqrt{-nitrotropolone}$.

$\sqrt{-HYDROXYTROPOLONE}$

$\sqrt{-Aminotropolone}$ (0.13 g.) in sulphuric acid (8 c.c. of 0.36N) was cooled in ice and sodium nitrite (1 c.c. of 7%) added and the mixture heated under reflux for 2 hours. Extraction with ether, followed by sublimation at $150^{\circ}/1\text{ m.m.}$

and subsequent crystallisation from methanol-benzene yielded ψ-hydroxytropolone as pale yellow granular crystals, m.p. in sealed tube 244° (dec.) (Found: C, 61.1; H, 4.7. $C_7H_6O_3$ requires C, 60.9; H, 4.4%). It gave a deep blue colour with alcoholic ferric chloride and dissolved in aqueous sodium hydrogen carbonate with effervescence.

ψ-BROMOTROPOLONE

ψ-Aminotropolone (0.14 g.) in sulphuric acid (10 c.c. of 0.36N) was diazotised by addition of sodium nitrite (1 c.c. of 7%) at 0°C. This solution was added to 2 c.c. cuprous bromide solution, allowed to stand for 1 hour and then heated on a steam-bath for 1 hour. An insoluble brown copper complex was formed from which ψ-bromotropolone was obtained by sublimation at 240-260°/1 m.m., crystallising from methanol in needles, micro-m.p. and mixed micro-m.p. with authentic sample of ψ-bromotropolone 186-188°.

ψ-CYANOTROPOLONE

ψ-Aminotropolone (0.32 g.) in sulphuric acid (10 c.c. of 0.72N) was diazotised at 0° with sodium nitrite (8 c.c. of 2%). The cold diazo solution was run into 12 c.c. of a solution of potassium nickelocyanide and sodium carbonate as prepared by Storrie, with stirring.

On standing overnight, the dark red solution was filtered, the filtrate acidified and the yellow flocculent precipitate collected. This insoluble nickel complex afforded √-cyanotropolone (0.13 g.) when heated up to 200° at 0.2 m.m. Extraction of the aqueous solution with chloroform yielded a little further √-cyanotropolone, pale yellow needles from water, m.p. 236° in sealed tube (Found: C, 65.5; H, 3.4; N, 9.7. $C_8H_5O_2N$ requires C, 65.3; H, 3.4; N, 9.5%). It gives a greenish-brown colour with alcoholic ferric chloride. √-cyanotropolone was prepared with cuprous cyanide by a similar procedure.

√-CARBOXYTROPOLONE

1) √-Cyanotropolone (0.08 g.) was added to a 3% solution of hydrogen peroxide (1.5 c.c.) at room temperature, the solution made just alkaline with caustic soda and left overnight. Oxygen was evolved and on acidification a white unidentified precipitate formed which was filtered off and crystallised from water. Yellow prisms (0.05 g.), m.p. 269° (dec.) (Found: C, 38.1; H, 3.1; N, 8.9. $C_5H_5O_5N$ requires C, 37.8; H, 3.2; N, 8.8%).

2) √-Cyanotropolone (0.2 g.) was heated under reflux with 50% potassium hydroxide (5 c.c.) for 25 minutes. Cooling, diluting and acidification yielded a greenish solid, √-carboxytropolone (0.1 g.), which was filtered off

and crystallised from acetic acid. Small yellow crystals m.p. in sealed tube 288° (dec.) (Found: C, 57.7; H, 3.7. $C_8H_6O_4$ requires C, 57.8; H, 3.6%). It gives a greenish-brown colour with alcoholic ferric chloride.

3) $\sqrt{-}$ Cyanotropolone (0.05 g.) was heated under reflux with conc. hydrochloric acid (3 c.c.) for 1 hour. A white product crystallised out on cooling and three crystallisations from acetic acid yielded $\sqrt{-}$ -carboxytropolone (0.02 g.) as yellow crystals, m.p. and mixed m.p. with above in sealed tube $286-7^{\circ}$ (dec.).

METHYL ESTER METHYL ETHER OF $\sqrt{-}$ -CARBOXYTROPOLONE

$\sqrt{-}$ -Carboxytropolone (0.02 g.) was suspended in ether (5 c.c.) and diazomethane in ether added and the mixture left to stand for 16 hours. The methyl ester methyl ether crystallised out and was recrystallised from benzene-light petroleum ($60-80^{\circ}$) as colourless needles, micro-m.p. 184° (Found: C, 62.1; H, 5.1. $C_{10}H_{10}O_4$ requires C, 61.9; H, 5.2%).

DECARBOXYLATION OF $\sqrt{-}$ -CARBOXYTROPOLONE

1) $\sqrt{-}$ -Carboxytropolone was heated under sublimation conditions at atmospheric pressure and the sublimate identified as unchanged starting material.

2) $\sqrt{-}$ -Carboxytropolone (0.02 g.) was heated under reflux in pyridine (3 c.c.) for 1 hour and the cooled

solution added to dilute hydrochloric acid. The crystalline precipitate which formed was identified as unchanged γ -carboxytropolone.

3) γ -Carboxytropolone (0.02 g.) was heated under reflux in aniline (3 c.c.) for 1 hour and the cooled solution poured into dilute hydrochloric acid. The acid solution was extracted with ether and the extract dried and concentrated. The residue was sublimed at $100^{\circ}/20$ m.m. and the sublimate identified as tropolone, m.p. and mixed m.p. with authentic sample $48-49^{\circ}$.

γ -AMINOMETHYLTROPOLONE

γ -Cyanotropolone (0.05 g.) in ethanol (20 c.c.) containing 1 molecular proportion of hydrogen chloride was hydrogenated in the presence of palladium charcoal (0.025 g.). The uptake of hydrogen was complete in 3 hours and the filtered solution was concentrated. The brown gum which remained formed a picrate from ethanol which recrystallised from water as brown needles, m.p. 208° (dec.) (Found: C, 44.3; H, 3.55. $C_{14}H_{12}O_9N_4$ requires C, 44.2; H, 3.2%).

α -HYDROXYTROPOLONE

α -Aminotropolone (0.009 g.) in sulphuric acid (1 c.c. of 0.36N) was diazotised at 0° with sodium nitrite (1 c.c. of 0.005%). The orange solution was heated on a steam-bath

for $\frac{1}{2}$ hour, a deep red replacing the now pale yellow colour. Extraction with ether, evaporation, charcoaling in benzene and finally crystallisation from light petroleum (60-80°) gave two products (a) and (b).

(a) The more soluble product crystallised in colourless needles, micro-m.p. and mixed micro-m.p. with authentic sample of salicylic acid 152-155°. It gave a violet colour with ferric chloride.

(b) The more insoluble product gave granular crystals, having a red-brown colour with ferric chloride, micro-m.p. showing sublimation at 190°.

ATTEMPTED PREPARATION OF $\sqrt{\text{-HYDRAZINOTROPOLONE}}$

a) $\sqrt{\text{-Aminotropolone}}$ (0.1 g.) was diazotised (see $\sqrt{\text{-hydroxytropolone}}$), and the cooled solution run into a solution containing sodium carbonate (0.1 g.) and sodium sulphite (0.5 g.) in water (2 c.c.), with stirring. After 10 mins. the orange solution was warmed to 30° and saturated with sulphur dioxide, then further heated to 70°. The solution was cooled, made alkaline with ammonia, faintly acid with acetic acid and continuously extracted with ether to give $\sqrt{\text{-aminotropolone}}$, m.p. and mixed m.p. 170-174° with authentic specimen of $\sqrt{\text{-aminotropolone}}$.

b) $\sqrt{\text{-Aminotropolone}}$ (0.1 g.) was diazotised (see

γ -hydroxytropolone), and the cooled solution added to stannous chloride (0.3 g.) in conc. hydrochloric acid (0.5 c.c.; 10N). A brown-red precipitate formed which did not sublime and contained both organic and inorganic material.

SKRAUP REACTION ON γ -AMINOTROPOLONE

γ -Aminotropolone (0.3 g.), nitrobenzene (0.35 c.c.), glycerol (0.38 c.c.) and 70% sulphuric acid (2.16 c.c.) were warmed together slowly to 160° and heated for $\frac{1}{4}$ hour at this temperature; Duration of heating $\frac{1}{2}$ hour. After cooling and diluting with water, the solution was made alkaline with caustic soda and the nitrobenzene extracted with ether. The aqueous solution was made acid with dilute hydrochloric acid, neutralised with ammonia and made faintly acid with acetic acid. Extraction with several portions of methyl ethyl ketone and subsequent evaporation and crystallisation from benzene yielded β : γ -(3:2-pyrido)tropolone as pale yellow needles (0.09 g.), m.p. 168-9° (Found: C, 69.5; H, 4.3; N, 8.3. $C_{10}H_7O_2N$ requires C, 69.4; H, 4.1; N, 8.1%).

Picrate: from water, yellow needles, micro-m.p. 218° (Found: C, 49.8; H, 2.8. $C_{16}H_{10}O_8N_4$ requires C, 49.8; H, 2.6%).

OXIDATION OF β -V-(3:2-PYRIDO)TROPOLONE

β -V-(3:2-Pyrido)tropolone (0.01 g.) was heated under reflux with conc. nitric acid till no brown fumes could be detected. Evaporation and washing with ether, followed by crystallisation from ethanol - light petroleum (60-80°) gave colourless crystals, micro-m.p. and mixed m.p. with authentic sample of quinolinic acid showing decomposition at 190-195° with sublimation of a crystalline product from 210-220°.

Sublimation at 180-190°/0.2 m.m. yielded a colourless product, m.p. and mixed m.p. in sealed tube with authentic sample of nicotinic acid 232-4°.

CONDENSATION OF V-AMINOTROPOLONE WITH CINNAMALDEHYDE

V-Aminotropolone (0.1 g.) and cinnamaldehyde (0.11 g.) were heated to 100° for 1 minute with 1 c.c. of conc. sulphuric acid. Diluting with water, precipitated a red-brown insoluble mass which was uncrystallisable. Warming this product in water produced solution and decomposition into cinnamaldehyde and V-aminotropolone, isolated as its picrate.

CONDENSATION OF V-AMINOTROPOLONE WITH KETOMALONIC ESTER

Liquid nitrogen tetroxide (20 g.) was slowly added to ethyl malonate (20 g.) cooled to 0°. After leaving overnight, the product was distilled, the fraction distilling

at 98-110°/13 m.m. being ketomalonic ester.

γ-Aminotropolone (0.1 g.) and ketomalonic ester (0.15 g.) were heated in benzene (10 c.c.) on a steam-bath for 3 hours. γ-(αα'-Dicarbethoxy-α'-hydroxy)-methylaminotropolone crystallised out on concentrating as bright yellow needles, m.p. 137-8° (Found: C, 53.9; H, 5.4. C₁₄H₁₇O₇N requires C, 54.0; H, 5.5%).

Attempted Cyclisation

a) The above product (0.1 g.) was heated in conc. sulphuric acid (3 c.c.) to 100° for 3 minutes, cooled and poured into water and the product isolated as for γ-aminotropolone. γ-Aminotropolone, m.p. and mixed m.p. 174-177°, was identified in the gummy residue.

b) The above product (0.1 g.) when refluxed with diphenyl ether for 5 minutes gave, after evaporation and crystallisation from xylene, γ-aminotropolone, m.p. and mixed m.p. 170-173°.

Oxidation

Oxidation of the above product with conc. nitric acid, evaporation and crystallisation from ether - light petroleum (60-80°) gave oxalic acid, m.p. and mixed m.p. in sealed tube with authentic sample of oxalic acid 100-102°.

NITRATION OF α -BROMOTROPOLONE

α -Bromotropolone (0.5 g.) in acetic acid (10 c.c.) was nitrated with nitric acid (0.165 c.c.; S.G. 1.42) in acetic acid (1.5 c.c.). The temperature of the reaction was kept at 15-17°C by surrounding the solution with a bath of cold water. After dilution with water and continuous extraction with benzene, the product α -bromo- γ -nitrotropolone was crystallised from benzene - light petroleum (60-80°) as yellow crystals (0.2 g.), m.p. 138-9° (Found: C, 34.3; H, 1.8; N, 5.9. $C_7H_4O_4NBr$ requires C, 34.2; H, 1.6; N, 5.7%). It gives a greenish-brown colour with alcoholic ferric chloride and dissolves in aqueous sodium hydrogen carbonate with effervescence.

α -BROMO- γ -NITROTROPOLONE METHYL ETHER

An ethereal solution of diazomethane was added to α -bromo- γ -nitrotropolone (0.1 g.) in methanol (5 c.c.) and left to stand overnight. Evaporation and crystallisation from ethanol gave the methyl ether as yellow needles, m.p. 196° in sealed tube.

The methyl ether could not be obtained analytically pure and gave the following analyses:-

	C	H
$C_8H_6O_4NBr$ requires	36.95%	2.33%
Sublimed at $190^\circ/20$ m.m.	38.02%	2.93%
Crystallised from Methanol	38.00%	2.60%
" " Ethanol	38.5%	3.45%
" " Bz.-Pet.Ether	37.54%	2.93%

REARRANGEMENT OF α -BROMO- γ -NITROTROPOLONE METHYL ETHER

The methyl ether (0.052 g.) was heated under reflux in methanol (5 c.c.) containing sodium (0.045 g.) for 3 hours on a steam-bath. After evaporation 6N caustic soda (2 c.c.) was added and the solution heated for 1 hour on a steam-bath. Acidification, extraction with ether and crystallisation of the product from benzene-light petroleum ($60-80^\circ$) gave o-bromo-p-nitrobenzoic acid as colourless crystals, recrystallising from water in prisms, m.p. and mixed m.p. in sealed tube with authentic specimen $159-162^\circ$.

The benzene-light petroleum mother liquors were evaporated to dryness and the residue crystallised from light petroleum ($60-80^\circ$) as needles, m.p. $120-2^\circ$. This product dissolves in sodium hydrogen carbonate solution with effervescence and contains bromine. It crystallises from water as needles and gives no colour with aqueous ferric chloride.

1:4-DICARBETHOXYCYCLOHEPTA-2:3-DIONE

Sodium (2.18 g.) and dry ethanol (4.36 g.) were reacted to form sodium ethoxide in ether. Oxalic ester (7 g.) was added to this solution with cooling and finally pinelic ester (10.3 g.) added slowly. The resultant solution was heated under reflux for 1 hour and then the ether was distilled off. The residue was heated at 120-125° for 3 hours under ordinary distillation conditions and the dark red-brown mass cooled. The solid mass was dissolved in water (sodium salt comes out but redissolves), acidified with dilute sulphuric acid and extracted with ether.

The ether solution was washed with sodium carbonate solution until the extract was only faintly yellow and then with sodium hydroxide (8N), when a bright yellow sodium salt precipitated. This was filtered off, acidified with dilute sulphuric acid and the solution extracted with ether. Evaporation and crystallisation from ethanol gave the 1:4-dicarbethoxycyclohepta-2:3-dione as colourless prisms, m.p. 70°. Yield, 1.8 g. of pure material.

ALKALINE REARRANGEMENT OF 1:4-DICARBETHOXYCYCLOHEPTA-2:3-DIONE

The dione (0.1 g.) was heated under reflux with 6N sodium hydroxide (5 c.c.) for $\frac{1}{4}$ hour. The initial sodium salt whitened and finally dissolved. The solution was acidified with dilute sulphuric acid and extracted with

ether to give a colourless viscous gum (0.08 g.). This material slowly crystallised from ethyl acetate to give 1:2:3-tricarboxycyclohexan-2-ol as colourless crystals, m.p. in sealed tube 215-16° (dec.) (Found: C, 46.0; H, 4.8. $C_9H_{12}O_7$ requires C, 46.55; H, 5.2%). The product gave no colour with ferric chloride.

REACTIONS OF 1:2:3-TRICARBOXYCYCLOHEXAN-2-OL

1) Molecular weight determination by titration

The tricarboxy compound (0.0516 g.) was dissolved in water (2 c.c.) and titrated with 0.0997N sodium hydroxide solution with 1 drop phenolphthalein as indicated. The titre was 6.49 c.c., giving the equivalent of the tricarboxy compound as 79.7 (requires 77.3).

2) Reaction with peroxide

The tricarboxy compound (0.05 g.) was added to water (2 c.c.) and made just alkaline with dilute sodium hydroxide solution. Hydrogen peroxide (3 c.c.) in excess was added and the solution allowed to stand overnight. Acidification, extraction with ether and crystallisation from ethyl acetate gave the unchanged tricarboxy compound as crystals, m.p. and mixed m.p. in sealed tube 211-15° with authentic sample.

3) Sublimation

The tricarboxy compound (0.05 g.) sublimed as a gum at 200-10°/20 m.m. The product gave the unchanged tri-

carboxy compound as crystals from ethyl acetate, m.p. and mixed m.p. in sealed tube 208-12° with authentic sample.

4) Reaction in conc. sulphuric acid

The tricarboxy compound (0.1 g.) was added to conc. sulphuric acid (2 c.c.). Effervescence occurred and the solution was allowed to stand for 12 hours. Addition of ice to the well-cooled solution gave a solid precipitate of 1:3-dicarboxycyclohexan-2-one, which recrystallised from water in needles (left overnight in refrigerator), melting with decomposition from 120-140° (Found: C, 51.8; H, 5.6. $C_8H_{10}O_5$ requires C, 51.6; H, 5.4%).

1:3-Dicarboxycyclohexan-2-one when warmed with an ethanolic solution of 2:4-dinitrophenylhydrazine gave a yellow precipitate which crystallised from ethanol in plates, m.p. 158°. This was identified as the 2:4-dinitrophenylhydrazone of cyclohexanone by mixed m.p. 156-8° with authentic sample of m.p. 154°.

ACID HYDROLYSIS OF 1:4-DICARBETHOXYCYCLOHEPTA-2:3-DIONE

The dione was recovered unchanged when heated under reflux with 25% sulphuric acid for 1 hour. When the dione (0.1 g.) was heated under reflux for 2 hours with 25% sulphuric acid (4 c.c.) and acetic acid (4 c.c.), the solution turned brown and addition of 2:4-dinitrophenylhydrazine in ethanol gave a precipitate. This was filtered

off, taken up in benzene and chromatographed on alumina with the same solvent. Two compounds were isolated, a more easily eluted pale yellow solid and a dark red less soluble compound. The latter crystallised from benzene in red crystals, m.p. 198-200° (Found: C, 53.6; H, 5.0; N, 20.1. Calc. for $C_{19}H_{18}O_2N_4 \cdot C_6H_6$: C, 53.2; H, 4.3; N, 19.85%). This was identified as the bis-2:4-dinitrophenylhydrazone of cyclohepta-1:2-dione which crystallises from benzene with 1 molecule of solvent.

The first eluted compound crystallises in yellow needles from ethanol, m.p. 142-4° (Found: C, 51.3; H, 4.8; N, 17.3%) and has not been identified.

REACTION OF 1:4-DICARBETHOXYCYCLOHEPTA-2:3-DIONE WITH PHENYLHYDRAZINE

1) The dione (0.125 g.) was heated under reflux with phenylhydrazine (0.15 g.) in ethanol (10 c.c.) for 1½ hours. A white solid (0.13 g.) crystallised out, m.p. 309-11° (dec.) (Found: C, 70.4; H, 5.1. $C_{21}H_{18}O_2N_4$ requires C, 70.4; H, 5.1%).

When recrystallised from acetic acid, a purple crystalline product was obtained, m.p. 310-12° (dec.) (Found: C, 70.2; H, 5.0. $C_{21}H_{18}O_2N_4$ requires C, 70.4; H, 5.1%).

2) The dione (0.27 g.) was heated under reflux with phenylhydrazine (0.1 g.) for $1\frac{1}{2}$ hours in ethanol (3 c.c.). A white crystalline product (0.025 g.) was obtained, m.p. 310° . This recrystallised from acetic acid in purple prisms, m.p. and mixed m.p. with purple compound from 1) above $310-12^{\circ}$.

3) The dione (0.125 g.) was allowed to stand with phenylhydrazine (0.15 g.) in ethanol (15 c.c.) for 24 hours. The colourless solution became bright yellow and no precipitate formed. The ethanol was evaporated off in vacuo giving a yellow oil which gave the purple crystalline material, above, when heated in acetic acid.

REACTION OF 1:4-DICARBETHOXYCYCLOHEPTA-2:3-DIONE WITH
O-PHENYLENEDIAMINE

The dione (0.25 g.) and diamine (0.11 g.) in ethanol (2 c.c.) were heated under reflux for 1 hour and the stoppered solution allowed to stand for 12 hours. No crystals deposited but cautious dilution of the reaction liquor with water produced three crops of crystals. Each was recrystallised from ethanol water mixtures.

Crop I:- Colourless needles (0.06 g.), m.p. $140-2^{\circ}$ (Found: C, 66.3; H, 6.35; N, 8.1. $C_{19}H_{22}O_4N_2$ requires C, 66.7; H, 6.4; N, 8.2%).

Crop II:- Colourless prisms (0.10 g.), m.p. $80-2^{\circ}$ (Found: C, 66.7; H, 6.3; N, 8.7. $C_{19}H_{22}O_4N_2$ requires C, 66.7; H, 6.4; N, 8.2%).

Crop III:- Colourless crystals (0.02 g.), m.p. $78-80^{\circ}$.
Mixed m.p. with sample of crystals (m.p. $80-2^{\circ}$) showed no depression.

DEHYDROGENATION OF 1:4-DICARBETHOXYCYCLOHEPTA-2:3-DIONE

1) α -Carboxytropolone

The dione (1 g.) was refluxed in nitrobenzene (5 c.c.) and one crystal of iodine added. After further heating for $\frac{1}{2}$ hour, the mixture was cooled, made slightly alkaline and the nitrobenzene etc. steam distilled off. The residual liquor was acidified with dilute sulphuric acid and extracted with ether and then methyl ethyl ketone.

a) The ether solution was evaporated to dryness and the brown mass sublimed up to $160^{\circ}/_{20}$ m.m.

The unidentified crystalline sublimate recrystallised from benzene - light petroleum ($60-80^{\circ}$) in colourless needles (0.5 g.), m.p. $128-130^{\circ}$ (Found: C, 54.0; H, 6.6. $C_{13}H_{20}O_7$ requires C, 54.15; H, 7.0%). This product dissolved with effervescence in both aqueous sodium hydrogen carbonate and warm concentrated sulphuric acid and did not produce colouration with ferric chloride solution. 0.02 g. of this acid, dissolved in water (1 c.c.) was titrated with

sodium hydroxide solution (0.2N) with 1 drop phenolphthalein as indicator. The titre was 0.35 c.c., corresponding to an equivalent for the acid of 285 (requires 288).

b) The methyl ethyl ketone solution was evaporated to dryness and the yellow mass sublimed at $100-120^{\circ}/_2$ m.m.. The sublimate, α -carboxytropolone, crystallised from chloroform - light petroleum ($60-80^{\circ}$) as yellow needles (0.01 g.), m.p. $200-202^{\circ}$ (dec.) (Found: C, 57.65; H, 4.0. Calc. for $C_8H_6O_4$: C, 57.8; H, 3.6%). Mixed m.p. with authentic sample of α -carboxytropolone produced no depression.

2) The dione (0.27 g.) was refluxed with palladium charcoal (0.1 g.) in trichlorobenzene (10 c.c.) for 8 hours under nitrogen. The solution was taken up in ether and extracted with dilute sodium hydroxide. The extract was acidified with dilute sulphuric acid then extracted with ether and the solution dried. The ether was evaporated off and the brown gummy residue (0.03 g.) sublimed at $160-200^{\circ}/_2$ m.m.. The product was a yellow gum which gave a faint purple colour with alcoholic ferric chloride and showed no tendency to crystallise from solvents.

3) The dione (0.27 g.) was refluxed with chloranil (0.49 g.; 2 mols.) for 28 hours in 5 c.c. freshly distilled xylene. When a drop of this solution was tested for unchanged chloranil by heating with dilute sodium hydroxide solution, a positive red colouration was produced. The

xylene solution was taken up in ether and extracted with sodium hydroxide solution. The alkaline extract was then concentrated and the brown gum sublimed up to $200^{\circ}/_{20}$ m.m. The solid sublimate crystallised from ethanol-water in cream flakes and was identified as 3:6-dichloro-2:5-dihydroquinone, m.p. and mixed m.p. $275-280^{\circ}$ with authentic specimen.

BROMINATION OF 1:4-DICARBETHOXYCYCLOHEPTA-2:3-DIONE

1). BROMINE IN CHLOROFORM

Bromine (2.4 g.) in chloroform (15 c.c.) was added to the dione (2 g.) in chloroform (15 c.c.) and the solution allowed to stand for $\frac{1}{2}$ hour, then heated under reflux for $1\frac{1}{2}$ hours till evolution of hydrogen bromide gas ceased. The chloroform was evaporated off and the residue taken up in ether. The ether solution was washed with sodium hydrogen carbonate, sodium carbonate and sodium hydroxide solutions in that order, to give four fractions on acidification and extraction with ether.

Sodium hydrogen carbonate fraction: Brown gum (0.6 g.) which gave a purple colour with ferric chloride solution and on fusion with sodium gave a positive bromine test.

a) The gum sublimed at $150-160/_{20}$ m.m. to give a colourless oil, insoluble in sodium hydroxide. The sub-

limate afforded some crystals on long standing from light petroleum (60-80°), micro-m.p. 110-118°. This material did not give a colour with alcoholic ferric chloride.

b) The gum (0.4 g.) was heated under reflux for 1 hour with 6N sodium hydroxide solution. The solution was acidified and extracted with ether. The ether extract was evaporated to dryness to give an oil, soluble in sodium hydroxide solution, which crystallised from chloroform in colourless crystals, m.p. 134-5° with effervescence in sealed tube (Found: C, 47.5; H, 5.2%). This compound gave no colour with alcoholic ferric chloride.

Sodium carbonate fraction: Brown gum (0.1 g.) which gave a purple colour with ferric chloride solution and a positive bromine test on fusion with sodium.

Sodium hydroxide fraction: Brown gum (0.05 g.) which gave a purple colour with alcoholic ferric chloride and a negative bromine test on fusion with sodium.

Neutral fraction: Brown gum (0.7 g.) which gave a positive bromine test on fusion with sodium.

a) The gum sublimed at 150-170°/20 m.m. to give an oil insoluble in sodium hydroxide solution.

b) The gum was heated under reflux with sodium hydroxide solution for 1 hour and the acidified solution extracted with ether. The concentrated ether extract afforded a colourless oil, extremely soluble in water, with

no ferric chloride colouration.

2). N-BROMOSUCCINIMIDE IN CHLOROFORM

The dione (1 g.) was heated under reflux in chloroform (10 c.c.) with freshly prepared N-bromosuccinimide (1.4 g.) for 3 hours. The solution was cooled in the refrigerator and the succinimide filtered off. The chloroform was evaporated off and the residue heated under ordinary distillation conditions at 120-130° for 1 hour. The residue was taken up in ether and washed with sodium hydrogen carbonate, sodium carbonate and sodium hydroxide solutions, in that order, to give four fractions on acidification and extraction with ether.

The sodium hydrogen carbonate, carbonate and neutral fractions afforded small amounts of impure yellow-brown gums, all of which gave a brownish colour with alcoholic ferric chloride.

The sodium hydroxide fraction contained the bulk of the products and was isolated as a green-brown gum with purple colour in alcoholic ferric chloride. A dark green crystalline material, micro-m.p. 85-93°, slowly precipitated out from the gum in ethanol. It did not give a colour with alcoholic ferric chloride. The ethanol mother liquors when concentrated afforded unchanged 1:4-dicarbethoxycyclohepta-2:3-dione as colourless crystals, m.p. and mixed m.p. 66-80° with authentic sample.

A similar experiment was carried out except that the materials were heated at 140-50° for 1 hour, with similar results.

3). BROMINE IN ACETIC ACID

The dione (1.4 g.) was refluxed in acetic acid (20 c.c.) with bromine (2.0 g.) for 5 hours. The acetic acid was evaporated off, in vacuo, and the residue submitted to steam distillation - no material was steam distilled. The residue was taken up in ether and shaken gently with conc. alkali. A yellow precipitate formed which when taken up in water and acidified, yielded a flocculent precipitate of α : α' -dibromotropolone (0.4 g.). Colourless needles from methanol, m.p. and mixed m.p. 156° with authentic specimen.

The alkaline mother liquor was separated and acidified. Extraction with ether and concentration yielded an unidentified greenish gum.

2-CHLOROTROPONE

Tropolone (1 g.), benzene (10 c.c.) and thionyl chloride (10 c.c.) were heated under reflux for 3 hours. The white precipitate of tropolone hydrochloride, m.p. 119-125°, which was initially formed, gradually redissolved. After concentration in vacuo, addition of benzene and renewed concentration, the residual gum was distilled at 90° (bath)/₂ m.m. A solution of the distillate in

benzene was shaken with saturated aqueous sodium bisulphite and the resulting solid (A) was collected. The washed, dried and concentrated benzene solution afforded 2-chloro-tropone as colourless needles, m.p. 63-64° from light petroleum (60-80°). The bisulphite compound (A) was treated with aqueous sodium carbonate and the mixture was extracted with benzene. The recovered oil was oxidised by potassium permanganate to o-chlorobenzoic acid, m.p. and mixed m.p. 143-144°, and afforded a 2:4-dinitrophenylhydrazine, m.p. 205° (Found: C, 48.6; H, 3.2. Calc. for $C_{13}H_9O_4N_4Cl$: C, 48.7; H, 2.8%) and a semicarbazone m.p. 239-240°, which were identified by mixed m.p. with authentic samples prepared from o-chlorobenzaldehyde.

2:7-DICHLOROTROPONE

α -Bromotropone (1 g.) and thionyl chloride (10 c.c.) in benzene (10 c.c.) were heated under reflux for 5 hours. After volatile liquids had been removed in vacuo, the residual gum was sublimed at 80°/2 m.m. and afforded 2:7-dichlorotropone as colourless needles, m.p. 129-130° from light petroleum (60-80°) (Found: C, 47.8; H, 2.2. $C_7H_4O Cl_2$ requires C, 48.0; H, 2.3%).

REACTIONS OF 2-CHLOROCYCLOHEPTATRIENONE

(1) Ethanol solutions (2 c.c. each) of 2-chlorocycloheptatrienone (0.1 g.) and of thio-p-cresol (0.09 g.) with

sodium hydroxide (0.03 g.) were mixed and heated to the b.p. The bright yellow precipitate, which was produced on cooling and dilution with water, afforded 2-p-tolylthiocycloheptatrienone as yellow needles, micro-m.p. 148° , from benzene-light petroleum ($60-80^{\circ}$) (Found: C, 73.7; H, 5.3. $C_{14}H_{12}OS$ requires C, 73.6; H, 5.3%).

(2) A solution of the 2-chloro-compound (0.11 g.) in benzene (2 c.c.) was added to a suspension of aluminium chloride (0.2 g.) in benzene (2 c.c.). In separate experiments the mixture was kept below 10° for 16 hours or was heated under reflux for 1 hour. In each case 2-chlorocycloheptatrienone, m.p. and mixed m.p. $62-63^{\circ}$, was recovered from the washed and dried benzene solution.

(3) 2-chlorocycloheptatrienone (0.02 g.), sodium p-toluenesulphinate (0.026 g.) were heated under reflux in ethanol (3 c.c.) for 1 hour. The solution darkened and an insoluble brown precipitate formed (0.023 g.). This material does not melt below 360° and could not be crystallised.

REACTIONS OF 2:7-DICHLOROCYCLOHEPTATRIENONE

(1) The dichloro-compound (0.3 g.), diethylamine (1 c.c.), and benzene (3 c.c.) were heated under reflux for 2 hours. The benzene solution, after being washed with dilute acid and then with water, was dried and con-

centrated, affording an orange-yellow residue. This, when heated in a sublimation tube at $80^{\circ}/2$ m.m. gave a sublimate which afforded 2-chloro-7-diethylaminocycloheptatrienone as orange prisms, micro-m.p. 56° , from light petroleum (60- 80°) (Found: C, 62.3; H, 6.7. $C_{11}H_{14}ONCl$ requires C, 62.4; H, 6.7%).

(2) The dichloro-compound (0.1 g.), p-toluidine (0.5g.) and xylene (10 c.c.) were heated under reflux for 30 minutes. The cooled solution, after being washed with dilute acid, was dried and evaporated and gave 2-chloro-7-p-toluidinocycloheptatrienone as yellow needles, micro-m.p. 121° from benzene (Found: C, 68.3; H, 4.8; N, 5.8. $C_{14}H_{12}ONCl$ requires C, 68.4; H, 4.9; N, 5.6%).

(3) Ethanol solutions (2 c.c. each) of the dichloro compound (0.1 g.) and thio-p-cresol (0.08 g.) with sodium hydroxide (0.02 g.) were mixed and heated to the b.p. The orange precipitate, which was produced on cooling and dilution with water, afforded 2-chloro-7-p-tolylthiocycloheptatrienone as yellow needles, micro-m.p. 165° , from benzene-light petroleum (60- 80°) (Found: C, 64.1; H, 4.2. $C_{14}H_{11}OSCl$ requires C, 64.0; H, 4.2%).

(4) Experiment (3) was repeated with twice the quantities of thio-p-cresol and sodium hydroxide. 2:7-Di-p-tolylthiocycloheptatrienone was thereby obtained as dark yellow crystals, m.p. 266° , from benzene (Found: C, 71.7;

H, 5.4. $C_{21}H_{18}OS_2$ requires C, 72.0; H, 5.2%).

(5) Attempted condensation of the dichloro-compound with benzene in presence of aluminium chloride (as described for the 2-chloro-compound) led to recovery of the dichloro-compound. Likewise, under reflux conditions, with m-xylene as hydrocarbon, there resulted 70% recovery of the dichlorocycloheptatrienone, but in this case chromatography on alumina afforded also a small quantity of unidentified orange-coloured prisms, m.p. $279-281^\circ$, from light petroleum ($40-60^\circ$).

(6) Attempted reaction with o-phenylenediamine

The dichloro-compound (0.1 g.) and o-phenylenediamine (0.06 g.) were fused at 100° . Reaction occurred and heating was continued for 2-3 mins.; cooling and washing with dilute hydrochloric acid produced a brown solid which gave several multicoloured bands on alumina from benzene. When the two reactants were heated under reflux in xylene for 1 hour, the dichlorotropone was recovered, m.p. and mixed m.p. with authentic sample $128-130^\circ$.

Hydrogenolysis

(1) A solution of the dichloro-compound (0.1 g.) in ethanol (5 c.c.) containing Raney Nickel (0.5 g.) in suspension was heated under reflux for 2 hours. The colourless oil, which was obtained on filtration and concentration, distilled at $70-80^\circ/2$ m.m. (Found: C, 72.6; H, 10.4%).

(ii) Similar treatment of the chloro-p-tolythio-tropone (m.p. 165°) gave a colourless oil, b.p. $50-60^{\circ}/_2$ m.m. (Found: C, 80.7; H, 7.2%).

ANIONOID REPLACEMENT IN SUBSTITUTED TROPOLONES

1) $\alpha\alpha'$ -Tribromotropolone

a) Preparation: The tribromotropolone was prepared by heating under reflux α -bromotropolone (1 g.) and bromine (2 g.) in acetic acid (5 c.c.) for 2 hours and separated out on cooling as yellow needles (0.5 g.), m.p. $122-3^{\circ}$. Addition of water to the mother liquor precipitated a colourless product (0.7 g.) as needles, m.p. 112° (dec.) (Found: C, 18.0; H, 1.1%). This material afforded a further quantity of the tribromotropolone when warmed with alkali and then acidified.

b) γ -Bromo- $\alpha\alpha'$ -di-p-tolythiotropolone

$\alpha\alpha'$ -Tribromotropolone (0.2 g.), sodium hydroxide (0.067 g.) and thio-p-cresol (3 mols.: 0.21 g.) were heated under reflux in pyridine (5 c.c.) for $1\frac{1}{2}$ hours. The cooled solution was added to dilute sulphuric acid and the precipitate collected. Crystallisation from acetic acid afforded γ -bromo- $\alpha\alpha'$ -di-p-tolythiotropolone (0.22 g.) as yellow prisms, m.p. 216° (Found: C, 56.2; H, 3.9. $C_{21}H_{17}O_2BrS_2$ requires C, 56.6; H, 3.85%).

The same product in similar yield was isolated when the sodium hydroxide was omitted in the above experiment.

c) Structural identification of γ -bromo- $\alpha\alpha'$ -di-p-tolylthiotropolone

$\alpha\alpha'$ -Dibromotropolone was prepared according to the method of Cook et al. from α -bromotropolone.

The $\alpha\alpha'$ -dibromotropolone (0.34 g.), thio-p-cresol (0.33 g.) and sodium hydroxide (0.106 g.) in ethanol (5 c.c.) were heated at 150° in a sealed tube for 12 hours. $\alpha\alpha'$ -Di-p-tolylthiotropolone crystallised out on cooling and recrystallised from ethanol as yellow needles, m.p. 159° .

Bromination of $\alpha\alpha'$ -di-p-tolylthiotropolone was effected by heating under reflux the tropolone (0.05 g.) in glacial acetic acid (2 c.c.) with bromine (0.025 g.) for 1 hour. On cooling, the γ -bromo- $\alpha\alpha'$ -di-p-tolylthiotropolone crystallised out and when recrystallised from acetic acid had m.p. 214° . Mixed m.p. with γ -bromo- $\alpha\alpha'$ -di-p-tolylthiotropolone obtained from (b) showed no depression.

d) $\alpha\alpha'\gamma$ -Tri-p-tolylthiotropolone

γ -Bromo- $\alpha\alpha'$ -di-p-tolylthiotropolone (0.26 g.), thio-p-cresol (0.06 g.) and sodium hydroxide (0.026 g.) in ethanol (5 c.c.) were heated at 150° in a sealed tube for 12 hours. The concentrated ethanol solution was added to dilute sulphuric acid and the precipitate filtered off.

The dried residue was crystallised from acetic acid and afforded $\alpha\alpha'$ -tri-p-tolythiotropolone as yellow needles, m.p. 182° (Found: C, 69.1; H, 5.0. $C_{28}H_{24}O_2S_3$ requires C, 68.8; H, 4.95%).

2) λ -Nitrotropolone

a) The sodium salt of λ -nitrotropolone (0.09 g.) was heated under reflux with thio-p-cresol (0.09 g.) in pyridine (3 c.c.) for 2 hours. The cooled solution was added to dilute sulphuric acid and the precipitate filtered off. Crystallisation from methanol afforded λ -nitrotropolone as yellow needles (0.03 g.), m.p. and mixed m.p. $188-190^{\circ}$.

b) λ -Nitrotropolone (0.034 g.), sodium hydroxide (2 mols.: 0.017 g.) and thio-p-cresol (0.037 g.) were heated under reflux in pyridine (5 c.c.) for 2 hours. The cooled solution was added to dilute sulphuric acid and extracted with ether. Evaporation and crystallisation of the residue from methanol afforded λ -nitrotropolone (0.022 g.), m.p. and mixed m.p. $187-190^{\circ}$.

c) The sodium salt of λ -nitrotropolone (0.09 g.) and thio-p-cresol (0.13 g.) in ethanol (5 c.c.) were heated in a sealed tube for 12 hours at 150° . The ethanolic solution was concentrated and added to dilute sulphuric acid. The precipitate was collected and crystallised from methanol-water in colourless needles, m.p. and mixed m.p. 48° with an authentic specimen of p-tolyldisulphide. The orange

coloured filtrate was extracted with chloroform and the extract dried. The residue from the concentrated extract crystallised from methanol in yellow needles (0.01 g.), m.p. and mixed m.p. 192-194° with authentic specimen of γ -nitrotropolone.

3) 2:3:5:7-Tetrachlorotropone

The tetrachlorotropone was prepared according to the method of Doering & Knox by heating under reflux α - γ -tribromotropolone (0.3 g.), thionyl chloride (1 c.c.) and benzene (5 c.c.) for 2 hours. The solvents were evaporated off in vacuo and the residue sublimed at 120°/20 m.m. Crystallisation of the product from cyclohexane afforded 2:3:5:7-tetrachlorotropone as yellowish crystals m.p. 115°.

2:3:5:7-Tetrachlorotropone (0.1 g.), sodium hydroxide (0.066 g.) and thio-p-cresol (0.205 g.) were heated under reflux in ethanol (10 c.c.) for 1 hour. The ethanol was evaporated off in vacuo and the residue taken up in a small amount of water and acidified with dilute sulphuric acid. The solution was extracted with ether, dried, evaporated and the residue crystallised from cyclohexane to give 2:3:5-trichlorobenzoic acid as colourless needles, m.p. and mixed m.p. 165-6° with authentic specimen.

4) Tropolone p-toluenesulphonate

Tropolone p-toluenesulphonate (0.09 g.) and thio-p-cresol (0.04 g.) were heated with sodium hydroxide (0.013 g.) in ethanol (6 c.c.) on a steam-bath for 1 hour. Concentration, diluting with water and filtration of the product afforded 2-p-tolythiotropone (0.05 g.), m.p. and mixed m.p. 147-8°.

SOME ETHERS OF TROPOLONE AND α -BROMOTROPOLONE

1) 3:5-Dinitrobenzophenone ether

Tropolone (0.1 g.) and 2-chloro-3:5-dinitrobenzophenone (0.25 g.) were left in pyridine (2 c.c.) overnight. After adding to dilute hydrochloric acid, acidifying and filtering, the product was crystallised from ethanol. Light brown prisms, m.p. 159° (Found: C, 61.3; H, 3.1. $C_{20}H_{12}O_7N_2$ requires C, 61.2; H, 3.1%). Similarly α -bromotropolone gave light brown crystals from ethanol, m.p. 188-9° (Found: C, 60.0; H, 2.8. $C_{20}H_{11}O_7NBr$ requires C, 60.0; H, 2.4%).

2) Tropolone p-toluenesulphonate

In a similar manner to 1) above tropolone formed with p-toluenesulphonyl chloride colourless needles, m.p. 162° (Found: C, 60.8; H, 4.6. $C_{14}H_{12}O_4S$ requires C, 60.9; H, 4.4%).

α -Bromotropolone did not form an ether with this reagent in a similar manner to tropolone, but was recovered. α -Bromotropolone was also recovered when its sodium salt (0.22 g.) was refluxed in pyridine (5 c.c.) with p-toluenesulphonyl chloride (0.2 g.) for 2 hours.

3) 2:4-Dinitrophenyl ether

Tropolone did not react with 2:4-dinitrochlorobenzene in a similar manner to 1) above, even on heating the mixture

under reflux for $\frac{1}{2}$ hour. A pyridinium salt of 2:4-dinitrochlorobenzene was produced which did not appear to dissolve in boiling pyridine.

REACTION OF THE 2:4-DINITRO-5-CHLOROBENZOPHENONE DERIVATIVE OF TROPOLONE WITH, 1) ALUMINIUM CHLORIDE, 2) CONC. SULPHURIC ACID

1) The ether (0.08 g.) of m.p. 159° was brushed into a suspension of aluminium chloride (0.03 g.) in ethylene chloride (2 c.c.). The solution was allowed to stand for 16 hours and was then diluted with water and the ethylene chloride layer separated, washed with water and dried. The evaporated extract gave a gum which crystallised from benzene and was identified as starting material, m.p. and mixed m.p. $156-7^{\circ}$.

2) The ether (0.05 g.) was dissolved in conc. sulphuric acid (2 c.c.) and heated to 70° for a few minutes: only slight browning of the solution colour occurred. When cooled and poured into water, a solid precipitated which crystallised from benzene and was identified as starting material m.p. and mixed m.p. $155-7^{\circ}$.

ATTEMPTED REACTION OF TROPOLONE WITH MALIC ACID

Tropolone (0.01 g.) and malic acid (0.11 g.) in conc. sulphuric acid (2 c.c.) were heated for 5 mins. at 100° ,

when effervescence occurred with darkening of solution. Diluting with water and extraction with chloroform yielded tropolone m.p. and mixed m.p. 46-48° and an acidic product identified as 6-carboxycoumalin m.p. and mixed m.p. 226-227° with authentic sample.

ATTEMPTED REACTION OF TROPOLONE WITH ACRYLONITRILE

Tropolone (0.244 g.), acrylonitrile (0.12 g.) and sodium hydroxide (0.09 g.) were heated under reflux in benzene (0.5 c.c.) for 8 hours. The benzene solution was decanted and the residue washed once with fresh benzene. The product was taken up in water, acidified with dilute sulphuric acid and extracted with ether. The ether extract afforded tropolone (0.2 g.) m.p. and mixed m.p. 47-48° with authentic specimen.

ATTEMPTED ACYLATION OF, 1) TROPOLONE, 2) TROPOLONE METHYL ETHER WITH A MIXTURE OF PERCHLORIC ACID AND ACETIC ANHYDRIDE

1) TROPOLONE

a) Monoacylation with 0.25 mol. perchloric acid

Acetic anhydride (0.157 g.) was added to a mixture of nitromethane (0.53 g.) and perchloric acid (0.035 g. of 72%) at 0-5°. Tropolone (0.122 g.) was added to this solution at 0-5° in 3 minutes and the mixture left to stand for 18 hours. The solution was poured on to ice and extracted with ether. The ether extract was washed with

ammonia solution (2N) till washings became colourless then with water twice and dried over sodium sulphate. The ether solution when evaporated failed to yield any organic material.

The ammonia extracts were acidified and extracted with ether. The dried ether extract was evaporated to dryness and the residue crystallised from light petroleum (40-60°). Cream needles (0.04 g.) were formed and were identified as unchanged tropolone m.p. and mixed m.p. 46-47° with authentic specimen.

b) Diacylation with 0.25 mol. perchloric acid.

A similar experiment was carried out with tropolone (0.24 g.), perchloric acid (0.07 g. of 72%), nitromethane (2 g.) and twice the above quantity of acetic anhydride (0.518 g.). Tropolone was again recovered in a similar process to above.

c) Diacylation with 1 mol. perchloric acid

Acetic anhydride (0.85 g.) was added to a mixture of nitromethane (2.4 g.) and perchloric acid (0.28 g. of 72%) at 0-5°. Tropolone (0.244 g.) was added slowly to this solution at 0-5°, and the mixture left to stand for 18 hours. When this solution was cooled in the refrigerator for a further 18 hours, crystals m.p. 170° slowly deposited. These contain chlorine, explode on heating and are probably the perchlorate of tropolone.

2) TROPOLONE METHYL ETHER

T.M.E. was prepared from tropolone by adding an ethereal solution of diazomethane to an ether solution of tropolone, evaporating off the ether and crystallising the residue from ether by leaving in refrigerator, needles, m.p. 37-38°

a) Acylation with 0.25 mol. perchloric acid

Acetic anhydride (0.073 g.) was added to a mixture of nitromethane (0.15 g.) and perchloric acid (0.012 g. of 72%) at 0-5°. Tropolone methyl ether (0.05 g.) was added slowly to this solution at 0-5°, and the mixture left to stand for 18 hours. The solution was poured on to ice and extracted with ether. The ether solution failed to give any organic material.

The aqueous liquor was made 2N with dilute sulphuric acid and heated on a steam bath for 45 mins., then extracted with ether. The ether extract on concentration and crystallisation from light petroleum (40-60°) afforded tropolone (0.03 g.) m.p. and mixed m.p. 49° with authentic specimen.

b) Acylation with 1 mol. perchloric acid

Tropolone methyl ether (0.21 g.), perchloric acid (0.203 g.), nitromethane (1 g.) and acetic anhydride (0.55g.) were reacted as in a) above and the solution worked up in a similar manner.

From the dilute sulphuric acid hydrolysed portion there was isolated besides tropolone (0.12 g.), some tropolone perchlorate, m.p. and mixed m.p. 172° with authentic sample, by crystallisation from ethyl acetate.

ATTEMPTED ACYLATION OF, 1) TROPOLONE, 2) TROPOLONE METHYL ETHER WITH ACETIC ACID AND TRIFLUOROACETIC ANHYDRIDE

Trifluoroacetic anhydride was prepared by distilling trifluoroacetic acid over phosphoric oxide, as recommended by Swarts (Bull.Acad.roy.Belg., Classe sci., 1922, 8, 343).

1) TROPOLONE

a) Heat was generated when trifluoroacetic anhydride (0.55 c.c.) was added to a mixture of tropolone (0.122 g.) and glacial acetic acid (0.18 c.c.). The reaction mixture was allowed to stand for 12 hours and then poured into cold dilute sodium carbonate solution and extracted with ether. The ether extract gave no residue on evaporation.

Acidification of the sodium carbonate mother liquor, extraction with ether and evaporation afforded unchanged tropolone (0.07 g.) from light petroleum ($40-60^{\circ}$), m.p. and mixed m.p. with authentic specimen $46-47^{\circ}$.

b) In a similar experiment, the reaction mixture was kept at 60° for 15 mins. and the product worked up with the recovery of unchanged tropolone.

2) TROPOLONE METHYL ETHER

Tropolone methyl ether hemihydrate (0.05 g.) was added to a mixture of acetic acid (0.03 c.c.) and trifluoroacetic anhydride (0.1 c.c.), and the mixture kept at room temperature for 12 hours. The solution was neutralised with aqueous sodium bicarbonate and exhaustively extracted with chloroform. The chloroform extract was evaporated to dryness, the product crystallised from ether and identified as unchanged tropolone methyl ether hemihydrate, m.p. and mixed m.p. 35° .

CONDENSATION OF BIS-(2-CYANOETHYL)SULPHIDE WITH OXALIC ESTER

Sodium (1.64 g.) and dry ethanol (4.15 c.c.) were reacted together in ether to form sodium ethoxide. Oxalic ester (5.2 g.) was added to this solution with cooling and finally bis-(2-cyanoethyl)sulphide (5 g.) added slowly. The resultant solution was refluxed for $\frac{1}{4}$ hour and then the ether distilled off. The residue was heated at $105-120^{\circ}$ for 2 hours under ordinary distillation conditions and the red mass cooled. The solid mass was dissolved in water and unchanged starting materials extracted with ether. The aqueous liquor was acidified with dilute sulphuric acid, when a semi-solid material precipitated, and the whole solution continuously extracted with ether. After 48 hours,

an insoluble precipitate still remained unextracted and was considered to be a polymer of vinyl cyanide.

The ether extract was dried and evaporated to dryness. Part of the residue slowly crystallised from water in colourless needles, m.p. over 330° (Found: C, 60.2; H, 2.8; N, 17.5. $C_8H_4O_2N_2$ requires C, 60.0; H, 2.5; N, 17.5%). This compound was later identified as 3:6-dicyanocatechol by degradation to catechol. It gives a bright green colour with aqueous ferric chloride and dissolves in alkali with pale yellow colour, the solution having a weak yellow-green fluorescence in U.V. light. The aqueous solution of this compound exhibits a feeble blue fluorescence in U.V. light which changes to violet on addition of acids.

If the experiment was carried out with the same quantities as before but the refluxing in ether carried on for 10 hours, without the heating at high temperatures, the products were a 20% yield of 3:6-dicyanocatechol and an unidentified liquid. The liquid gave a red-brown colour with aqueous ferric chloride and when refluxed with alkali (1:1), ammonia was given off and oxalic acid identified in the products, m.p. and mixed m.p. $96-98^{\circ}$ in sealed tube.

3:6-DICYANOCATECHOL DIMETHYL ETHER

3:6-Dicyanocatechol (0.1 g.) was brushed into an ethereal solution of diazomethane. Effervescence occurred

and a crystalline precipitate formed, which on standing 12 hours redissolved. Evaporation and crystallisation from light petroleum (60-80°) gave white needles, m.p. 109-110° (Found: C, 64.1; H, 4.2; N, 15.05.

$C_{10}H_8O_2N_2$ requires C, 64.0; H, 4.3; N, 14.9%).

3:6-DICARBOXYCATECHOL

3:6-Dicyanocatechol (0.1 g.) was refluxed with 4 g. of sodium hydroxide solution (1:1) for 10 mins. The yellow sodium salt dissolved and ammonia was given off. The cooled solution was diluted and acidified with dilute sulphuric acid. The white precipitate which formed was filtered off and crystallised from water, crystals, m.p. 288-290° (dec.) (Found: C, 44.38; H, 3.8. Calc. for $C_8H_8O_7$: C, 44.45; H, 3.7%). It gave a blue-purple colour with aqueous ferric chloride.

3-CARBOXYCATECHOL

- a) The dicarboxy compound sublimed at 210-220°/20 m.m.
- b) The dicarboxy compound was heated at 240-260°/-760 m.m. with final raising of the temperature up to 300° and the sublimate crystallised from toluene, colourless crystals, m.p. 199-202°, in sealed tube. It gave a blue colour with aqueous ferric chloride.

CATECHOL FROM 3-CARBOXYCATECHOL

1) 3-Carboxycatechol sublimed unchanged when heated alone or with pumice or when plunged into a preheated bath at 400°.

2) 3-Carboxycatechol (0.1 g.) was heated under reflux in aniline (3 c.c.) for 1 hour. The acidified solution was extracted with ether and the ether extract dried and concentrated. The residue crystallised from benzene and was identified as catechol, micro-m.p. and mixed micro-m.p. 98-100°.

CONDENSATION OF BIS-(2-CYANOETHYL)AMINE WITH OXALIC ESTER

Sodium (1.64 g.) and dry ethanol (4.15 c.c.) were reacted in ether to form sodium ethoxide. Oxalic ester (5.2 g.) was added to this solution with cooling and finally bis-(2-cyanoethyl)amine (4.4 g.) added slowly. The resultant mixture was refluxed for 1 hour. The cooled solution was filtered and the yellow sodium salt (7.4 g.) which separated dissolved in water. As acidification of this aqueous solution produced a non-ether extractable substance, the alkaline solution was passed through an ion-exchange resin (IR - 120H) in column form. The aqueous acidic liquor which emerged from the column was concentrated under reduced pressure on a steam-bath to give a brown gum (4.5 g.). The gum partially crystallised from water in cream crystals

(1.0 g.), m.p. 175-177° (Found: C, 49.6; H, 4.7; N, 21.5. $C_8H_7O_2N_3 \cdot H_2O$ requires C, 49.2; H, 4.65; N, 21.5%). It gave a red colour with aqueous ferric chloride, dissolved with effervescence in sodium hydrogen carbonate solution and failed to form a picrate from either water or alcohol. It is considered to be N-(β -cyanoethyl)-4-cyano-2:3-diketopyrrolidine.

N-(β -CYANOETHYL)-4-CYANO-2:3-DIKETOPYRROLIDINE METHYL ETHER

The pyrrolidine (0.1 g.) was dissolved in methanol (3 c.c.) and an ether solution of diazomethane added. After standing for 12 hours the solution was taken to dryness and crystallised from methanol. Charcoaling once and re-crystallisation from methanol gave greenish crystals, m.p. 160-162° (Found: C, 56.4; H, 4.7; N, 21.7. $C_9H_9N_3O_2$ requires C, 65.5; H, 4.75; N, 22.0%).

REACTION OF N-(β -CYANOETHYL)-4-CYANO-2:3-DIKETOPYRROLIDINE WITH O-PHENYLENEDIAMINE

The pyrrolidine (0.15 g.) was heated under reflux in ethanol (2 c.c.) for 1 hour with o-phenylenediamine (0.86 g.). The ethanol was evaporated off and the residue taken up in water. On standing a black precipitate was deposited which formed a hydrochloride with dilute hydrochloric acid. The hydrochloride crystallised from methanol in red-purple plates,

m.p. 310-312^o (dec.) (Found: C, 55.3; H, 4.8.

C₁₄H₁₄ON₅Cl requires C, 55.4; H, 4.65%).

ACETYLATION OF N-(β -CYANOETHYL)-4-CYANO-2:3-DIKETOPYRROLIDINE

The pyrrolidine (0.1 g.) was heated under reflux with acetic anhydride (3 c.c.) for 5 mins. The acetic anhydride was evaporated off in vacuo and the residue washed with light petroleum (60-80^o). The gummy mass slowly crystallised, but a suitable solvent for crystallisation could not be found. A small amount crystallised from ether in cream crystals, m.p. 88^o, which did not give a colour with aqueous ferric chloride.

ALKALINE HYDROLYSIS OF N-(β -CYANOETHYL)-4-CYANO-2:3-DIKETOPYRROLIDINE

The pyrrolidine (0.5 g.) was heated under reflux for $\frac{1}{4}$ hour with 10 c.c. of sodium hydroxide solution (1:1). Vigorous frothing ensued and ammonia was given off. A white sodium salt precipitated and was separated and passed through an ion exchange resin (IR - 120H). The emerging liquor was evaporated to dryness and the white residue crystallised from ether-light petroleum (60-80^o). It was identified as oxalic acid, m.p. and mixed m.p. in sealed tubes, 98-101^o.

N-Bis-(2-cyanoethyl)-p-toluenesulphonamide

Bis-(2-cyanoethyl)amine (4 g.) was dissolved in pure pyridine (20 c.c.) and p-toluenesulphonyl chloride (2.5 g.) brushed in with cooling. The reaction mixture was left for 24 hours and then poured into cold dilute hydrochloric acid and the white precipitate (5.2 g.) filtered off. Extraction of the aqueous mother liquor with ether produced a further quantity of product (0.5 g.). The N-bis-(2-cyanoethyl)-p-toluenesulphonamide crystallised from ethanol in colourless needles, m.p. 102° (Found: C, 56.7; H, 5.0. $C_{13}H_{15}O_2N_3S$ requires C, 56.3; H, 5.45%).

CONDENSATION OF N-BIS-(2-CYANOETHYL)-p-TOLUENESULPHONAMIDE WITH OXALIC ESTER

Sodium (0.78 g.) and dry ethanol (1.94 c.c.) were reacted in ether to form sodium ethoxide. Oxalic ester (2.44 g.) was added to this solution with cooling and finally the sulphonamide (4 g.) added slowly. The resultant mixture was refluxed for $3\frac{1}{2}$ hours. A portion of the solution was then removed and found to contain unreacted starting material, m.p. and mixed m.p. with authentic specimen $99-100^{\circ}$.

The ether was evaporated off and the residue heated under distillation conditions for 2 hours, bath temperature

160-180°. No ethanol distilled over and the residue was treated with water and the insoluble solid filtered and identified as unchanged starting material, m.p. and mixed m.p. 99-100° with N-bis-(2-cyanoethyl)-p-toluenesulphonamide.

CONDENSATION OF BIS-(2-CYANOETHYL)ANISIDINE WITH OXALIC ESTER

Bis-(2-cyanoethyl)anisidine was prepared from vinyl cyanide and p-anisidine according to the method of J.T. Braunholtz & F.G. Mam, J.C.S., 1952, 3046.

Sodium (1 g.) and dry ethanol (2.53 c.c.) were reacted in ether to form sodium ethoxide. Oxalic ester (3.18 g.) was added to this solution with cooling and finally the amine (5.0 g.) added slowly. The resultant mixture was refluxed for 5 hours. The ether was evaporated off and the residue treated with water. The insoluble material was filtered off and after crystallisation from ethanol was identified as unchanged bis-(2-cyanoethyl)amine, m.p. and mixed m.p. 97-99° with authentic specimen.

The aqueous mother liquor was acidified with dilute sulphuric acid and the orange-brown solid (2.5 g.) filtered off. This amorphous solid is probably N-p-anisyl-3:6-dicyano-4:5-diketohexamethylenimine and dissolves in caustic soda, gives no colour with ferric chloride and does not form a picrate.

A similar experiment was carried out without the solvent (ether), the reaction mixture being heated at 140° under ordinary distillation conditions. Ethanol distilled over, and similar fractions to the above were obtained.

REACTIONS OF N-p-ANISYL-3:6-DICYANO-4:5-DI-KETOHEXAMETHYLEN-
IMINE

1) The dione (0.15 g.) was refluxed in acetic acid (3 c.c.) with phenylhydrazine (0.12 g.) for 1 hour. A crystalline brown solid precipitated which recrystallised from water after charcoaling as colourless prisms, m.p. 128-129° (Found: C, 63.9; H, 5.9; N, 17.5.

$C_{21}H_{19}N_5O_2 \cdot H_2O$ requires C, 64.4; H, 5.4; N, 17.9%).

2) The dione (0.15 g.) was refluxed in acetic acid (2 c.c.) with o-phenylenediamine (0.12 g.) for 1 hour. The cooled solution was poured into water and the black precipitate filtered off. This precipitate could not be crystallised and did not form a hydrochloride with dilute or conc. hydrochloric acid.

3) On warming the dione (0.1 g.) with caustic soda (1:1), ammonia gas was evolved.

ACTION OF ALUMINIUM CHLORIDE ON PHTHALANIL

a) A mixture of phthalanil (1 g.), sodium chloride (1 g.) and powdered aluminium chloride (5 g.) was heated at 230-240° for 15 minutes. The cooled mass was treated with water and the insoluble product filtered off and crystallised from acetic acid. This proved to be unchanged phthalanil, m.p. and mixed m.p. 203° with authentic specimen.

b) A mixture of phthalanil (1 g.), sodium chloride (1 g.) and powdered aluminium chloride (5 g.) was heated at 290-300° for 15 mins. The cooled mass was treated with water and the insoluble product filtered off and crystallised from acetic acid. This is probably the lactam of 2-(2'-aminobenzoyl)benzoic acid, colourless needles, m.p. 245° (Found: C, 75.4; H, 4.0; N, 6.1. Calc. for $C_{14}H_9O_2N$: C, 75.3; H, 4.1; N, 6.3%).

ACTION OF ALUMINIUM CHLORIDE ON SUCCINANIL

a) A mixture of succinanil (1 g.), aluminium chloride (0.77 g.) and ethylene chloride (5 c.c.) was left for 48 hours at room temperature. Washing with water, concentration, and crystallisation from water yielded unchanged succinanil, m.p. and mixed m.p. 156° with authentic specimen.

A similar experiment with twice the quantity of aluminium chloride (1.55 g.) gave a similar result.

b) A mixture of succinanyl (1 g.) and aluminium chloride (0.77 g.) was heated to 140° for 15 mins. The cooled product was treated with water and the hot filtered solution allowed to cool slowly. Unchanged succinanyl (0.8 g.) crystallised out and was identified by m.p. and mixed m.p. $154-156^{\circ}$ with authentic sample.

A similar experiment with twice the quantity of aluminium chloride (1.55 g.) conducted at a higher temperature, 280° , gave a similar result.

c) A mixture of succinanyl (3 g.), sodium chloride (3 g.) and aluminium chloride (15 g.) was heated at 200° for 30 mins. The cooled product was treated with water and succinanyl (2.4 g.) recovered as in b) above.

A similar series of experiments was carried out at higher temperatures ranging from 240 to 310° . The cooled product was treated with water and the hot filtered solution yielded, in every case, unchanged succinanyl, m.p. and mixed m.p. 156° with authentic specimen. The dark insoluble residue, which remains, was extracted with chloroform and yielded on concentration a black solid. This compound does not melt and could not be crystallised. It formed a 2:4-dinitrophenylhydrazone when treated with the phenylhydrazine in ethanolic solution. Red crystals from n-butanol, m.p. $199-200^{\circ}$ (Found: C, 51.9; H, 4.8; N, 21.9%).

CONDENSATION OF OXAMIDE WITH DIETHYL MALONATE

Sodium (1.3 g.) and dry ethanol (50 c.c.) were reacted to form an ethanolic solution of sodium ethoxide. Diethyl malonate (9.05 g.) and oxamide (5 g.) were added to this solution and the mixture refluxed for 6 hours. The cooled solution was poured into water and unchanged oxamide removed. The filtrate was passed through an ion exchange resin (IR-120H) and the effluent concentrated. The gum partly crystallised from water, colourless needles, m.p. 240° (Found: C, 45.7; H, 4.4; N, 17.6%). It dissolves in sodium hydroxide, slowly with no effervescence in sodium carbonate, and does not give a colour with aqueous ferric chloride. It formed a green methylated compound with diazomethane which recrystallised from light petroleum ($60-80^{\circ}$) as prisms, m.p. 116° (Found: C, 50.8; H, 5.5; N, 13.9%).

The remaining part of the concentrated effluent was a red gum, which gave a red colour with aqueous ferric chloride.

ATTEMPTED OXIDATION OF THE METHYLENE GROUP IN 2-METHYL-4-HYDROXYBENZAZEPINE WITH SELENIUM DIOXIDE

2-Methyl-4-hydroxybenzazepine, m.p. 121° , was prepared from o-phenylenediamine and acetoacetic ester according to the method of W.A. Sexton, J.C.S., 1942, 303.

a) The benzazepine (0.5 g.) and selenium dioxide

(0.32 g.) were refluxed in ethanol (4 c.c.) for 6 hours and the precipitated selenium (0.223 g.) filtered off. The ethanol solution was evaporated to dryness in vacuo and the residue dissolved in ether. The ether extract was concentrated and the product crystallised from n-butanol or ethanol, giving crystals, m.p. and mixed m.p. 310° with an authentic sample of 2-hydroxybenzimidazole.

b) The same quantities as in a) were refluxed in acetic acid (4 c.c.) for 5 hours and the precipitated selenium (0.147 g.) filtered off. The filtrate was evaporated to dryness in vacuo and the residue treated with water and filtered. The insoluble material (0.36 g.) was filtered off and crystallised from ethanol as crystals, m.p. and mixed m.p. 312° with authentic sample of 2-hydroxybenzimidazole.

In both a) and b) the crystalline product was not identical with 2-hydroxybenzimidazole in that the pure compound crystallised much more readily. After sublimation or after passage of hydrogen sulphide into its dioxan solution, the product yielded a more easily crystallised form.

ATTEMPTED NITROSATION OF THE METHYLENE GROUP IN 2-METHYL-4-HYDROXYBENZAZEPINE

1) The benzazepine (1 g.) was dissolved in dry ether (10 c.c.) and n-amyl nitrite (1.35 g.) in dry ether (10 c.c.) added dropwise at 0°C. Dry hydrogen chloride was passed in simultaneously and the operation completed in 30 minutes. The crystalline precipitate was filtered off and decomposed by adding slowly to cold water. It crystallised from ethanol, crystals, m.p. and mixed m.p. 310° with authentic specimen of 2-hydroxybenzimidazole.

2) The benzazepine (1.0 g.) was added to sodium (0.132 g.) in dry ethanol (4 c.c.) at 0°. n-Amyl nitrite (0.68 g.) was added dropwise to this solution and the mixture left for 48 hours. Acidification gave unchanged starting material, m.p. and mixed m.p. 118-121°.

3) Concentrated sulphuric acid (0.56 g.) in water (5 c.c.) was added to a mixture of the azepine (0.5 g.), caustic soda (0.13 g.) and sodium nitrite (0.24 g.) in water (10 c.c.) at 0°C. The solution was allowed to stand overnight and when worked up, afforded unchanged starting material, m.p. and mixed m.p. 119-120°.

4) Sodium nitrite (0.2 g.) was added to a mixture of the azepine (0.2 g.) and acetic acid (3 c.c.) at 0°C. The solution was left overnight and then poured into water and extracted with ether. The ether extract on evaporation

gave a gum which slowly crystallised from ethanol-water and was identified by mixed m.p. 310° as 2-hydroxybenzimidazole.

ATTEMPTED CONDENSATION OF BENZALDEHYDE WITH 2-METHYL-4-HYDROXYBENZAZEPINE

1) A mixture of the benzazepine (0.1 g.), benzaldehyde (0.062 g.), caustic soda (0.001 g.) and ethanol (4 c.c.) was left for 24 hours. Acidification and crystallisation of the precipitate from ethanol gave unchanged starting material, m.p. and mixed m.p. $120-121^{\circ}$.

2) The benzazepine (0.2 g.) and benzaldehyde (0.125 g.) were heated in pyridine (3 c.c.) for 2 hours. The mixture was poured into dilute sulphuric acid and the solution extracted with ether. The ether extract on concentration and crystallisation of the residue from ethanol gave 2-hydroxybenzimidazole, m.p. and mixed m.p. 310° .

3) The benzazepine (0.2 g.), benzaldehyde (0.122 g.), sodium acetate (0.094 g.) and acetic anhydride (0.35 g.) were heated on a steam-bath for 1 hour. The solution was poured into water and left for 12 hours. Extraction with ether and removal of the excess benzaldehyde with bisulphite solution followed by steam distillation and crystallisation of the distillate from ethanol-water gave colourless needles, m.p. 101° (Found: C, 66.6; H, 5.0. $C_{12}H_{12}O_2N_2$ requires C, 66.5; H, 5.6%).

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