STUDIES ON AROMATIC STRUCTURE

A Thesis for the Degree of Ph.D.

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Part I:

The Reactivity of Aromatic Double Bonds.

A : The Reactivity of Aromatic Double Bonds.

Summary.

Diazoacetic ester has been reacted with anthracene, benzanthracene and pyrene. In each case an acid has been obtained by hydrolytic treatment of the reaction mixture. The acid from anthracene has been assigned the structure naphthonorcaradienecarboxylic acid XXV on the basis of hydrogenation experiments and ultra-violet light absorption data. Oxidative degradation has proved the acid from benzanthracene to be benznaphthonorcaradienecarboxylic acid XXXIV, while the product from pyrene is apparently tribenznorcaradienecarboxylic acid XXXVII.

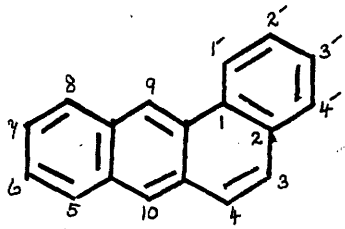
Attention is drawn to the remarkable stability shown by these condensed cyclopropane acids towards attempted rearrangement. An explanation for this is proposed on the grounds of the ability of the cyclopropane ring to conjugate with aromatic centres.

Contents.

There are certain chemical reagents which, as a rule, do not attack carbon centres, but react preferentially with carbon-carbon double bonds. Examples of these so-called double bond reagents are osmium tetroxide-pyridine reagent, ozone, and many peracids such as perbenzoic acid. Such reactions frequently give excellent yields, indeed perbenzoic acid can be used to estimate unsaturated hydrocarbons (1). These reagents are, generally speaking, less reactive towards aromatic bonds, and their behaviour towards complex aromatic systems is of special interest. When benzanthracene I, for example, is drawn in any of the theoretically possible canonical structures, the 9- and 10-positions which are the points of attack in orthodox addition, substitution and oxidation reactions, form parts of sterically hindered double bonds. Furthermore, a molecular orbital treatment shows that positions 9 and 10 possess the highest free valence values while the 3:4-bond can be assigned the highest bond order (2). Similar considerations apply to many other polycyclic hydrocarbons (2), (3).

In such cases osmium tetroxide-pyridine, alone of the reagents mentioned, has been proved to attack double bonds exclusively and consistently (4). The products are osmic ester complexes which can be hydrolysed to diols. For example, anthracene, which is generally attacked at the 9- and 10-positions, gives finally II, (5). With benzanthra-

cene the product is III (6). Pyrene IV is attacked at the



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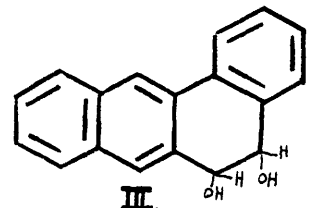

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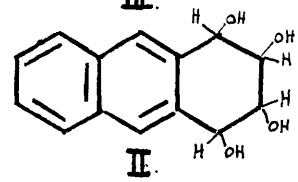

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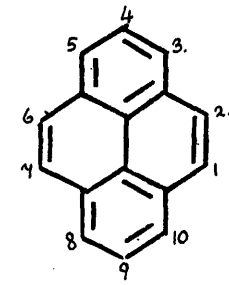


IV.

1:2-bond by this reagent, while halogenation (7), (8), (9), nitration (7),(10), Friedel Crafts condensation (11),(12), etc., occur at one or more of the equivalent 3-, 5-, 8- and 10-positions. Oxidation gives a mixture of 3:8- and 3:10-quinones (7).

Ozone is a more vigorous reagent than osmium tetroxide, as it reacts even with benzene, to form glyoxal, via an explosive triozonide. It also attacks the 1:2-bond of pyrene, and this ozonide is decomposed to phenanthrene-4-aldehyde-5-carboxylic acid V, (13). On the other hand, anthraquinone has been obtained as the sole reaction product by treatment of anthracene with ozone (14).

Pyrene reacts with two mols. of perbenzoic acid, but no attempt has been made to isolate the product (70). Both peracetic acid (15),(16),(44) and perbenzoic acid (14) are known to give the usual 9:10-quinone with anthracene. The analogous 9:10-benzanthraquinone is obtained by reacting

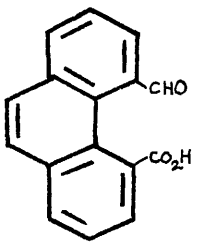
perbenzoic acid with benzanthracene (14).

In this connection, the biological oxidation in vivo of polycyclic hydrocarbons should be mentioned. Here again, the centres attacked are usually not those susceptible to normal reagents. However as they often differ from the positions attacked by osmium tetroxide-pyridine, and indeed are dependent to some extent on the species of animal employed, it is not possible to draw any clear analogy (17).

It is well known that diazoacetic ester, in ~~connection~~ common with many other aliphatic diazo compounds, can attack aliphatic carbon-carbon double bonds. The primary products are substituted pyrazolines which often decompose, especially on heating, with the formation of cyclopropane derivatives. This reaction has been used for the synthesis of such compounds (18),(19),(20),(21).

Diazoacetic ester is much less reactive towards aromatic bonds: higher temperatures are required and the yields are generally poor. The action of this reagent on benzene and its methyl derivatives was investigated over a considerable number of years by Buchner and coworkers (22)-(34). They demonstrated that the primary reaction product is the ester of a norcaradienecarboxylic acid. It forms a tetrabromide by addition as expected, and in the case of the

product from benzene itself, the presence of the three-membered ring was proved by the formation of 1:2:3-cyclopropanetricarboxylic acid on permanganate oxidation. The primary products of type VI were also shown to undergo a variety of rearrangements, especially at moderately high temperatures, leading to derivatives of cycloheptatrienecarboxylic acid VII, phenylacetic acid VIII and, with the presence of a methyl substituent, hydrocinnamic acid IX.



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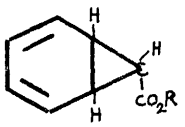

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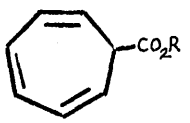

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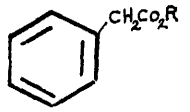

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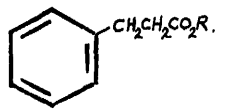


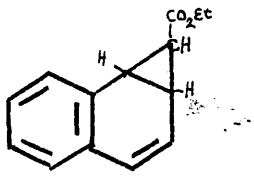
IX.

In the di- and poly-methyl benzenes, the least sterically hindered double bond is apparently attacked. Where the molecule has no bond with two unsubstituted hydrogens, as in mesitylene (34), durene (35), and prehnitene (36), only products of types VII, VIII, and IX could be isolated. It should be mentioned however that diazoacetic ester does form cyclopropane derivatives by reaction with a sterically hindered double bond which is aliphatic, although conditions more drastic than usual are required (37).

Diazoacetic ester was also shown to react with naphthalene, giving ethyl benznorcaradienecarboxylate X(38). Its structure was proved by oxidation of the free acid to

1-(2'-carboxyphenyl)2:3-cyclopropanedicarboxylic acid XI, and finally to 1:2:3-cyclopropanetricarboxylic acid.

More recently, Drake and Sweeney (39) have obtained dibenznorcaradienecarboxylic acid XII by reacting diazoacetic ester with phenanthrene, then hydrolysis. Oxidative degradation to XI, identical with the compound obtained by similar treatment of benznorcaradienecarboxylic acid, established the structure of this compound. Both X and XII were stable to all attempts at rearrangement.



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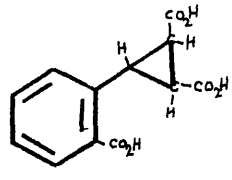

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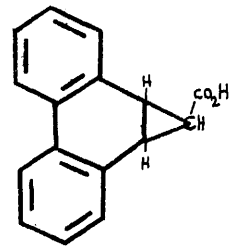
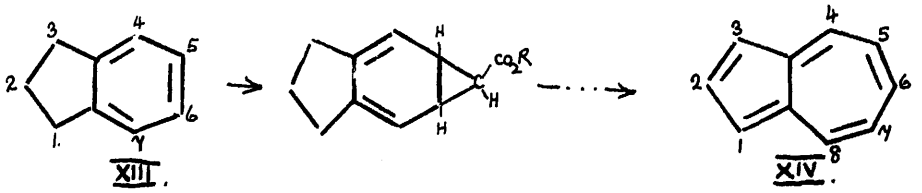


XII.

It is interesting to compare the behaviour of other double bond reagents towards naphthalene and phenanthrene. No reaction has so far been described between naphthalene and osmium tetroxide-pyridine; with phenanthrene an osmic ester complex forms at the 9:10-bond (40). With ozone, naphthalene forms a diozonide, which decomposes to o-phthalaldehyde and (probably) glyoxal (41). The more reactive 2:3-dimethyl-naphthalene gives penta-ozonides which decompose to glyoxal and diacetyl (42). Kooyman has pointed out (43) that these results are reasonable if we assume primary attack at the 1:2-bond of the molecule. Surprisingly, a diozonide was

also obtained from phenanthrene, but none of the decomposition products could be identified (41). Phthalic acid was obtained by Henderson and Boyd (44) through the action of peracetic acid on naphthalene; later workers claim to have obtained a good yield of o-carboxy-allocinnamic acid (45). Peracetic acid oxidises phenanthrene to the 9:10-quinone (44).

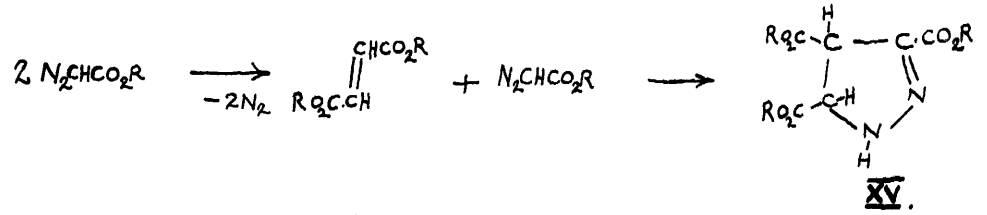
From 1939 onwards (46), diazoacetic ester has been used mainly by Plattner and coworkers in Switzerland, and by Arnold, Wagner-Jawegg and others in Germany, to prepare a large number of the alkylated azulenes XIV, starting from the corresponding substituted indane XIII.



XIII. XIV.

In the standard procedure of these workers, the intermediate products are not examined or characterised, but merely saponified, then dehydrogenated and decarboxylated by heating with palladium/charcoal. Azulene esters are obtained when the hydrolysis step is omitted. In this way, benzazulene has been obtained from fluorene, a reaction studied by three separate goups of workers (47),(48),(49),(50),(51).

Rather little is known of the mechanism of the addition of diazoacetic ester to an aromatic bond. Darapsky (52) showed the action of heat on the reagent alone was as follows:



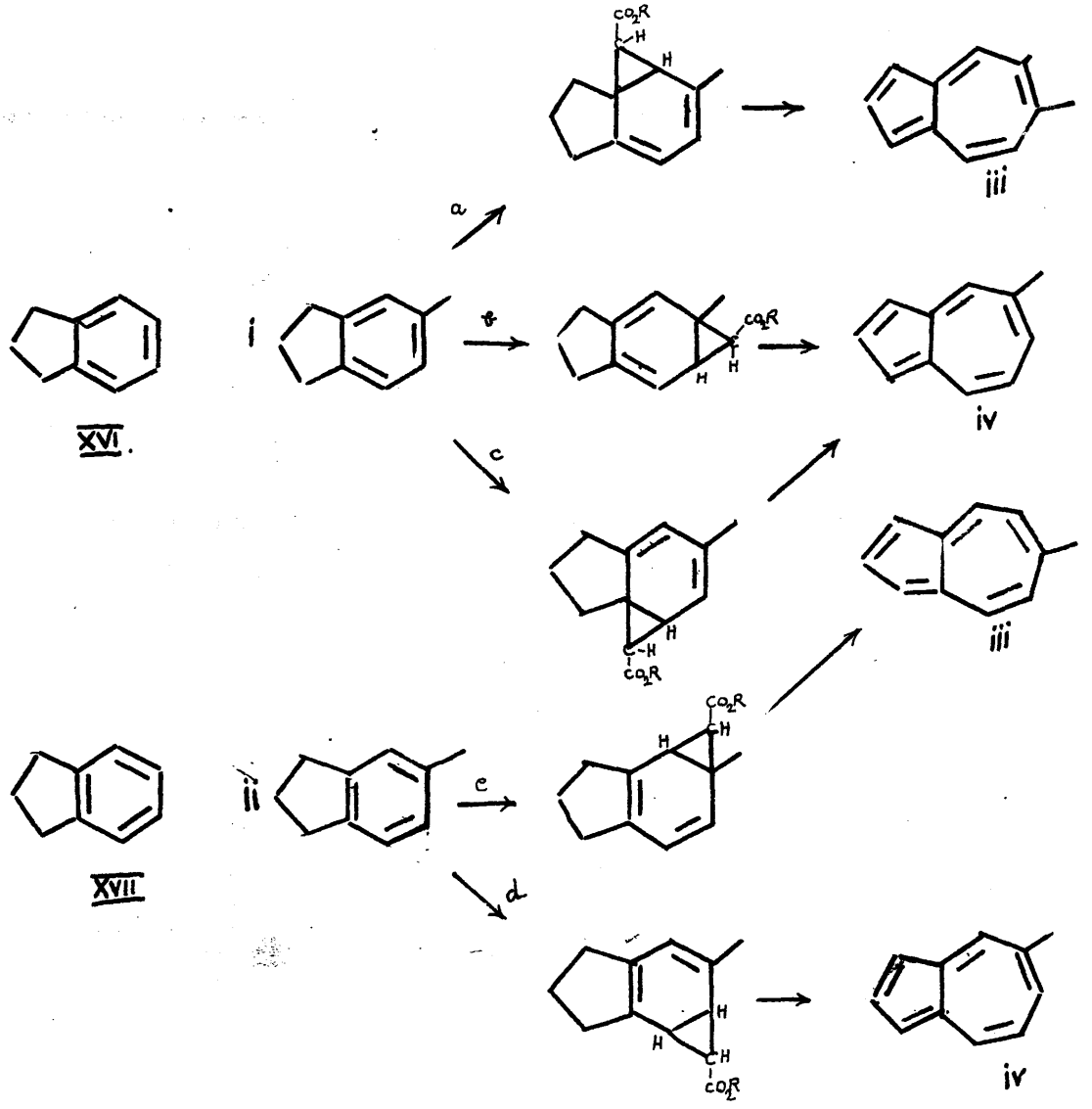
XV.

At an elevated temperature, XV decomposes to cyclopropane-tricarboxylic ester. With platinum, mercury or aluminium in petrol at 100°C, diazoacetic ester yields pyrazoline-tricarboxylic ester XV. With copper bronze the reagent yields a mixture of fumaric and maleic esters, under similar conditions (53). Copper bronze has found some limited use as a catalyst in diazoacetic ester condensations, mainly in the aliphatic series (37),(20).

A search of the literature reveals no evidence for the formation of pyrazoline derivatives as intermediates in the reaction of diazoacetic ester with aromatic bonds, and indeed it seems likely that they do not occur. Auwers (98) found that pyrazolinemonocarboxylic esters tend to decompose to ethylenic and not to cyclopropyl derivatives, and Dyakonov has pointed out that we should then expect Buchner's reaction to give phenylacetic ester or cycloheptatrienecarboxylic ester and not norcaradienecarboxylic ester, if the condensation proceeded via a pyrazoline intermediate. He therefore put forward the idea that reaction comes about by direct attack of a "diradical" $\rangle CHCO_2Et$ (56). Such a mechanism has also been suggested or implied by other authors (38),(53). It was mentioned earlier that in the reaction with the polymethyl

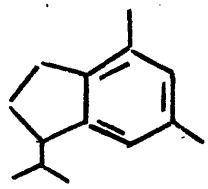
benzenes possessing no unsubstituted adjacent positions, only products of the three types VII, VIII, and IX could be isolated. It is interesting to consider whether this might come about by direct attack at one aromatic centre, or by decomposition of a first-formed norcaradiene derivative. The reaction with polymethyl indanes offers a suitable field for such an inquiry.

The azulene workers assume norcaradienes as intermediates in their syntheses, and they use them in the reaction routes drawn up for the orientation of their products. In drawing up these reaction routes, they are guided by two assumptions: (a) the least sterically hindered double bond is attacked: (b) the indane molecule reacts as if it possessed the structure favoured by the theory of Mills & Nixon, who suggested that the alicyclic five-membered ring in the indane molecule would lead to stabilisation of one form XVI rather than the other XVII, (59),(60). In recent years a considerable body of evidence has been found which is at variance with Mills and Nixon's ideas (61),(62),(75). This orientation method can be illustrated by the following example (76), with 5-methylindane.

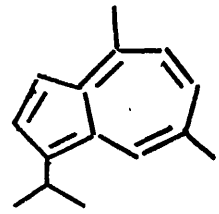


Route (d) is most favoured by steric effects, (b) by the Mills-Nixon effect: it was therefore concluded that the product, which was different from the known 6-methylazulene, was iv. The following year, Arnold (63) prepared 5-methylazulene by an unambiguous route and proved it identical with this compound. Using this same orientation method, Wagner-Jauregg, Arnold and Huter (64) concluded that their

product obtained from XVIII was XIX. The spectral evidence was found to be in good agreement with this proposed formula.

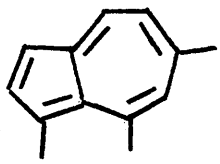


XVIII.

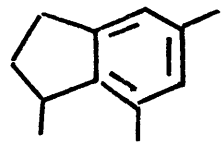


XIX.

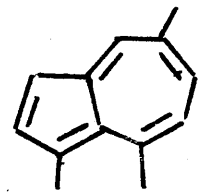
In one case however, results were obtained in apparent contradiction to this line of reasoning, the indane XX giving XXI instead of XXII (65):



XXI

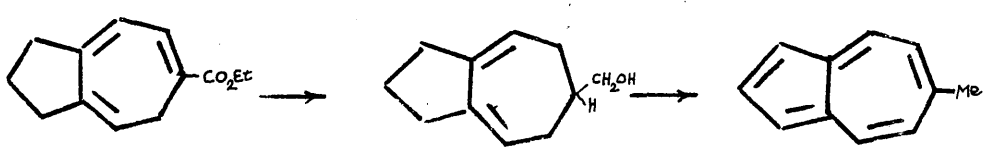


XX.



XXII.

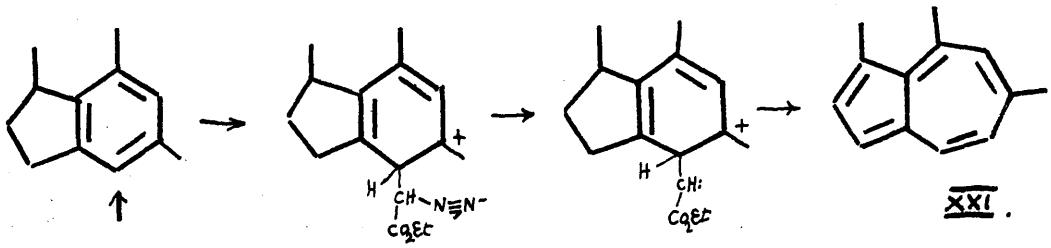
The effect of possible bond fixation of the Mills-Nixon type in this reaction has been examined by Arnold (66). He reacted diazoacetic ester with indane, isomerised the product, reduced the acid by the Beaveault-Blanc method and dehydrogenated to the azulene. Assuming that indane reacted in the form XVI, we would expect the reaction to be as follows:



XXIII.

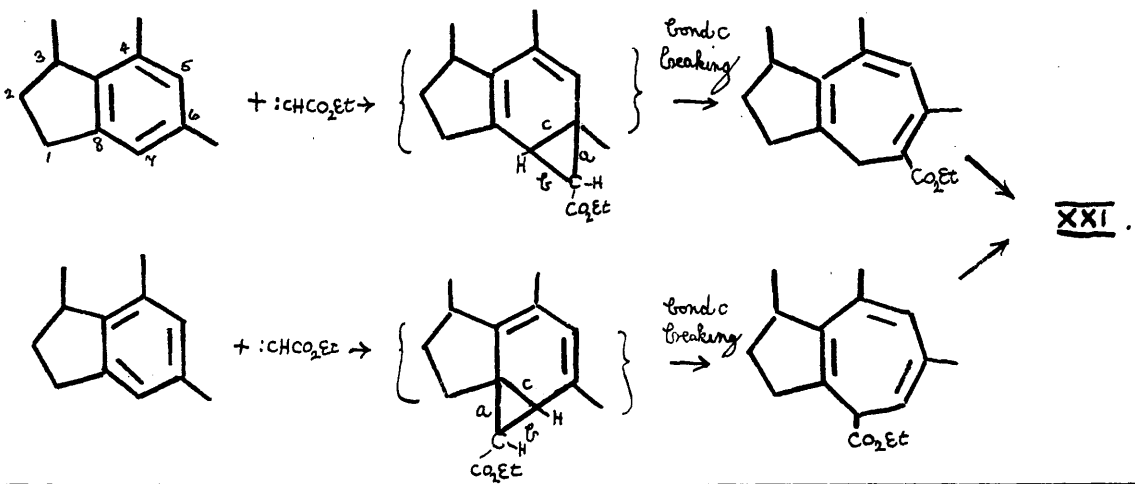
and 6-methylazulene XXIII to be the product. Actually Arnold isolated only 5-methylazulene and concluded that indane reacts in the alternative form XVII. The evidence however is not conclusive. On a simple statistical basis, there is twice the chance that indane will react in the form XVII, assuming that the 4:5-, 5:6-, and the 6:7-bonds be equally reactive, because the 4:5- and the 6:7-bonds are equivalent. The reaction conditions and yields do not rule out the possibility that two products were formed but only one isolated. Arnold (67) obtained 6-methyl-1-isopropyl-azulene from 1-isopropylindane in the same way, work that seemed to cast doubt on his interpretation of his previous result. It can be demonstrated by a model however, that the 1-isopropyl group offers considerable steric hindrance at the 6:7-bond. As previously mentioned, other investigations have cast doubt on the practical value of the Mills-Nixon theory, and it must be emphasised that the yields and purity of products in this type of reaction are not such as to engender confidence in such attempts to demonstrate double bond distribution.

The above facts could be explained if we assumed that in the indanes with sterically hindered double bonds, the reagent attacks the most reactive centre, and that the adjacent bond is then ruptured and reformed to give the seven-membered ring, by some such mechanism as:



XXI.

It very simply explains the formation of XXI instead of XXII. In the case of 1-isopropyl-4:6-dimethylindane, the isopropyl group offers considerable steric hindrance to the 7-position, hence attack would be at position 5, and the product 1-isopropyl-4:7-dimethylazulene as obtained. But an alternative, slight modification of the above mechanism, may also be considered. If a molecule possesses a number of carbon centres of different reactivity, which form the "poles" of different double bonds, and if all the bonds are sterically hindered to approximately the same extent, we should expect those bonds to be attacked which have the most reactive centre as one of their "poles". Thus if position 7 is the most active centre, the linkages 6:7 and 7:8 would be the most active bonds:

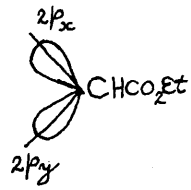


Bonds (a) and (c) joined to a tertiary carbon atom would be more likely to rupture than bond (b). (The cycloheptatriene products could, of course, have an isomeric arrangement of bonds without the argument being affected.)

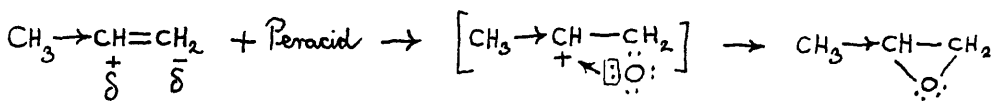
Either mechanism accounts equally well for the products formed. It is unlikely however that the intermediates, as actually isolated, in the standard azulene synthesis, are norcaradienes. The drastic reaction conditions probably bring about rearrangement to the cycloheptatriene system. As the two systems VI and VII give different colour reactions with concentrated sulphuric acid, it should be possible to obtain some evidence on this point. The study of their absorption spectra might also be helpful.

Allusion was made earlier to a paper by Dyakonov (56). In this he makes reference to Pearson's work on free methylene (55), and suggests that the hypothetical carboxymethylene "diradical" has actually the structure of a "molecule" with the electronic state ($1s^2$, $2s^2$, $2p^2$), i.e., containing divalent carbon. The alternative would of course by ($1s^2$, $2s^2$, $2p_x 2p_y$), the two unshared electrons having parallel spins (77). Hund's Rule of Maximum Multiplicity states that such an arrangement occurs in atoms with incompletely filled orbitals, but there is no evidence for the extension of such an idea to compound radicals. However, if carboxymethylene possessed such a structure, the two electrons would be

"splayed out:"



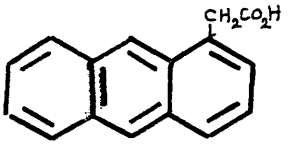
When such a radical approaches say, a benzene ring, it is unlikely that both these electrons should come within bonding distance of the same ring carbon atom. This might perhaps explain the formation of the three-membered ring. Swern has pointed out that the results of peracid oxidation are explicable if we assume that, "in the peracid molecule, the peroxide oxygen is electrophilic and is readily released from the peracid in the presence of a nucleophilic group such as the double bond. The reaction of an olefin such as propylene, with a peracid may be represented in the following way:



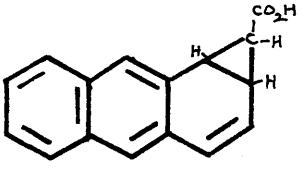
The oxirane compound may or may not be the final product, depending upon its stability, the reaction conditions, the peracid employed, etc." (68). However, peracids are not only electrophilic but actually electron deficient. If attack on a double bond was by an oxygen radical ($1s^2$, $2s^2$,$2p_x^2 2p_y 2p_z$) we could explain the formation of the oxirane compound in the manner described above with carboxymethylene. These must of course be considered merely tentative suggestions.

The aim of the present work was to extend this reaction of diazoacetic ester to anthracene 1:2-benzanthracene and pyrene, and to compare the position of attack of the reagent with that of osmium tetroxide-pyridine reagent. It was hoped in this way to obtain further evidence concerning the fine structure of these polycyclic hydrocarbons.

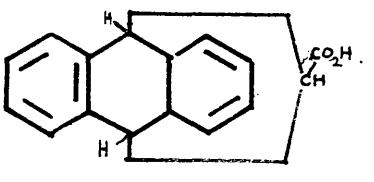
The isolation of a product in poor yield by the action of diazoacetic ester on anthracene has already been reported briefly by Clar (54). He suggested for it either of the structures XXIV or XXV, and mentioned that in its absorption spectrum it resembled phenanthrene rather than anthracene



XXIV.



XXV.



XXVI.

In this present research, reactions were carried out in a solvent, decalin, suitable by reason of its inertness and high boiling point. The conditions giving most satisfactory results were found to be similar to those used by Buchner and Hediger (38), and followed by subsequent workers. In each of the cases now described a solid product was isolated by hydrolysis of the crude reaction mixture and finally, acidification.

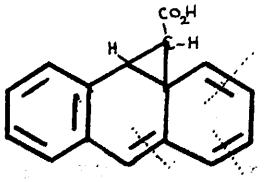
Anthracene:

By the action of diazoacetic ester on anthracene there was obtained a stable colourless acid, $C_{16}H_{12}O_2$, m.p. 282-284°C (dec.), in about 10% yield. In the presence of a platinum catalyst, its methyl ester absorbed three moles of hydrogen, giving a hexahydro compound, $C_{17}H_{20}O_2$, m.p. 69-70°C.

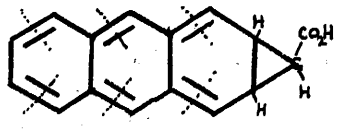
If the product were an anthraceneacetic acid such as XXIV, complete hydrogenation would be expected to produce an octahydroanthracene derivative with uptake of four moles of hydrogen, the central ring being left intact (cf. (57),(58)), and the unreduced compound should have an absorption spectrum rather similar to anthracene itself (p.48 H). Actually, the spectrum is entirely different (p.46 , F). A similar argument rules out XXVI, involving a 9:10-bridge, which by comparison with the maleic anhydride adduct of anthracene XXVII, would probably have a benzene-type of spectrum (69).

Formulae such as XXVIII, XXIX and XXX, involve a number of "non-aromatic" double bonds, i.e., bonds not involved in resonating canonical structures. Such molecules might be expected to have a higher general reactivity than our product actually displays. Of these three formulae only one XXVIII could reasonably give a fully saturated hexa-

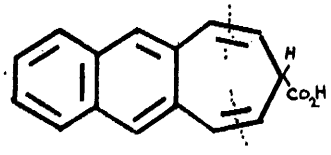
hydroderivative, but as mentioned earlier, compounds, where the carboxymethylene group has attacked a highly hindered aromatic bond, are never obtained in this reaction. There remains formula XXV. This structure contains the stable naphthalene nucleus, and could give a saturated hexahydro compound, analogous to octahydroanthracene. We therefore propose this formula XXV, naphthonorcaradienecarboxylic acid, for our product. The reduction product is accordingly XXXI. Its absorption spectrum (p.44, C), is very like that of octahydroanthracene (99) (see later).



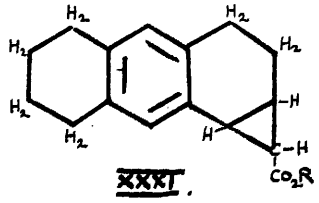
XXVIII.



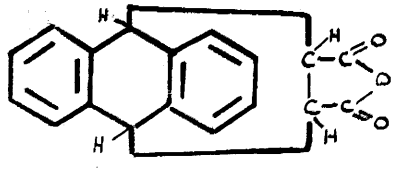
XXIX.



XXX.



XXXI.



XXVII.

The 3:4-bond in XXV is conjugated with an aromatic system, but is not involved in resonance among the unexcited canonical structures we can draw for this molecule. This bond proved, however, to be surprisingly inert. No reaction occurred between the methyl ester of XXV and osmium tetroxide-pyridine reagent. Conditions which brought about reaction in the case of anthracene (5),(6), gave a product which analysed accurately for $OSO_4 \cdot 1Py$, and some unchanged ester. Similarly this ester apparently did not react with perbenzoic acid in dilute chloroform solution (cf. (70), (14)). Chromium trioxide oxidation of XXV gave in poor yield an inseparable mixture of acids. This produced a melting point depression with XI, which would be an expected product of oxidation if our acid had formula XXVIII instead of XXV. The oxidation mixture contained a higher percentage of oxygen than that calculated for 1-(3'-carboxy-2'-naphthyl)-2:3-cyclopropanedicarboxylic acid, the hypothetical benzologue of XI. The acid XXV absorbed one mole of bromine rather slowly, and the product lost hydrogen bromide readily, to give a stable monobromide, characterised as its methyl ester, probably XXXII. A dibromide of appreciable stability is formed from benznorcaradienecarboxylic acid (38). Comparison

experiments showed that bromination in this case is more rapid than with XXV, but not instantaneous (augenblicklich) as is stated by Buchner and Hediger. In XXV, the 3:4-bond is conjugated with a larger aromatic system than the 3:4-bond in X, i.e., it is part of a larger conjugated system, and this might account for its lower reactivity. (Compare the analogous effect in the diphenylpolyenes). This bond is perhaps even less reactive than the 1:2-bond in anthracene, but of course, whatever the effect of the cyclopropane ring, the carboxyl grouping could exert a deactivating influence through the inductive effect alone.

Benzanthracene:

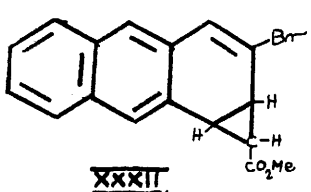
In the same way, a colourless stable acid was obtained from benzanthracene in about 7% yield, $C_{20}H_{14}O_2$, m.p. 290-1°C (dec.). It absorbed 1.1 mols. of hydrogen on microhydrogenation.

In many of its properties, this acid resembled the parent hydrocarbon, benzanthracene. It was oxidised to a yellow acid $C_{20}H_{12}O_4$, which gave Liebermann's anthraquinone reaction (intense red colour with zinc dust and alkali). Prolonged shaking of the methyl ester of the parent acid with powdered sodium in ether/benzene produced an intense scarlet solution. This reaction, which is shown by a number of polycyclic hydrocarbons (71),(72),(97), involves addition of the metal, probably in this case to a pair of meso-positions. Decolorisation of such a solution with ethanol should have resulted in the formation of a 9:10-dihydro-derivative. In actual fact a gum was produced which tarred with acid and alkali, and it has since been realised that Claisen condensation of the ester grouping was a possibility under the conditions used.

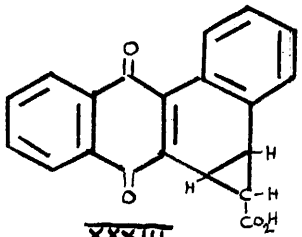
These results seemed to suggest that our product was a benzanthraceneacetic acid, the side chain being attached at some point other than the 9:10-positions. The fact that the absorption spectrum of our acid bears a superficial resemblance to that of benzanthracene lent some colour to this view

(P47, E, G.)

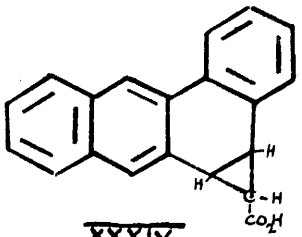
The acid $C_{20}H_{12}O_4$ was now further oxidised with alkaline hydrogen peroxide, and gave 1-(2'-carboxyphenyl)-2:3-cyclopropanedicarboxylic acid XI. This at once ruled out the previous hypothesis and established XXXIII as the most probable formula for this quinone acid. On this basis the original acid is thus XXXIV, benzaaphthonorcaradiene-carboxylic acid. This is rigid proof of the presence of a



XXXII.



XXXIII.



XXXIV.

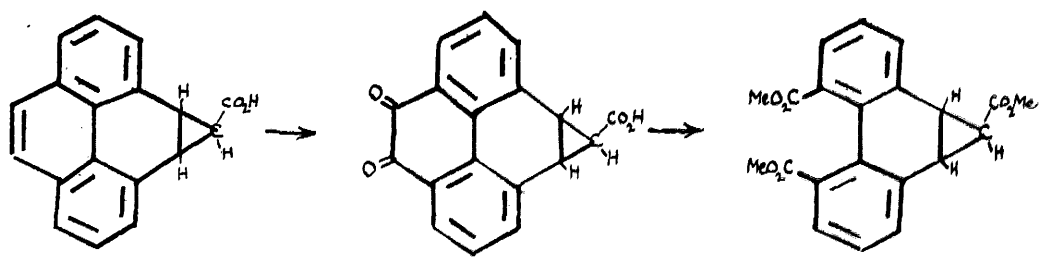
cyclopropane ring in the molecule. Microhydrogenation most likely occurred at the 9:10-positions. Benzanthracene itself, with a platinum catalyst, hydrogenates to the 5:6:7:8-tetrahydro compound.

Pyrene:

The reaction of diazoacetic ester with pyrene gave a mixture of at least two components, from which was isolated an acid $C_{18}H_{12}O_2$, m.p. 267-8°C (dec.), in 5% yield. It absorbed 1 mol. of hydrogen on microhydrogenation.

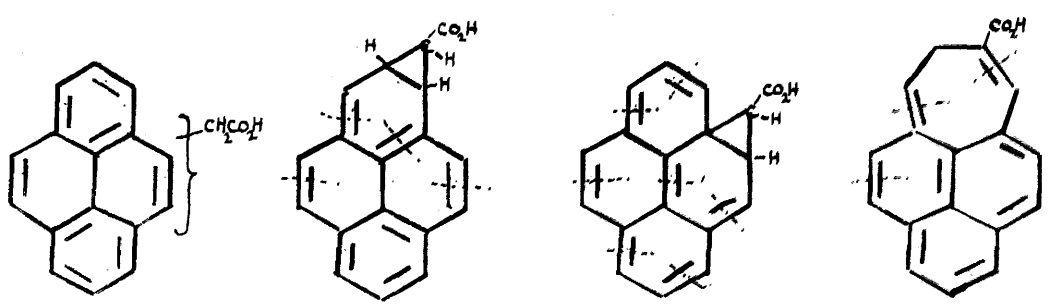
Chromium trioxide oxidation of this compound gave in

poor yield, a deep red acid with the properties of an ortho-quinone (condensed with o-phenylene diamine, colourless solution with bisulphite). This acid could not be obtained free from inorganic contaminant, and attempts to prepare crystalline derivatives were frustrated because reagents (diazomethane, methyl alcohol/hydrogen chloride, o-phenylene diamine) reacted indiscriminately with both the o-quinone and carboxyl groupings. This o-quinone acid was therefore further oxidised with alkaline hydrogen peroxide, and gave an excellent yield of a tricarboxylic acid, characterised as the trimethyl ester $C_{21}H_{18}O_6$. This is the empirical formula of XXXV. The o-quinone is then possibly XXXVI, and the parent acid XXXVII, tribenz<u>nor</u>caradienecarboxylic acid.



XXXVII. XXXVI. XXXV.

Other possible formulae are listed below:



XXXVIII. XXXIX. XL. XLI.

XXXVIII with a pyrene nucleus might be expected to oxidise to a 3:8- or a 3:10-quinone. XXXIX-XLI would probably undergo extensive oxidative degradation. XXXVII is the only structure likely to oxidise in the steps described above.

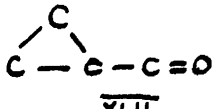
This tribenznorcaradienecarboxylic acid formula XXXVII incorporates a phenanthrene skeleton, and indeed its absorption spectrum distinctly resembles that of phenanthrene (p. 49, K/L ; p. 50, K/M). The microhydrogenation occurred most probably at the 6:7-bond: phenanthrene itself gives a 9:10-dihydroderivative (73), a 1:2:3:4-tetrahydroderivative (74), and the 1:2:3:4:5:6:7:8-octahydro compound (74) with different catalysts and experimental conditions.

None of these three polycyclic norcaradiene acids from the three different hydrocarbons could be induced to isomerise on drastic treatment with alkali.

An intensely yellow, highly stable methyl ester was also isolated from the reaction with pyrene in about 0.5% yield. It has the same empirical formula as tribenznorcaradienecarboxylic ester, but it has not been found possible to assign any structure to it.

Evidence gathered over a number of years seems to indicate that the classical picture of a highly strained cyclopropane ring of three tetrahedral carbon atoms is quite inadequate. The evident stability of our compounds supports

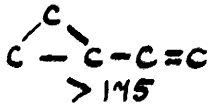
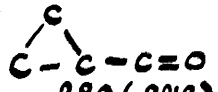
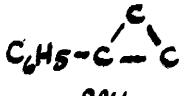
this view. As early as 1916 Robinson (78) postulated the conjugation of cyclopropane with the ethylene linkage in certain terpenes, and a year later Kohler and Conant pointed out similarities between the systems XLII and XLIII in many of their reactions (79). Since then the study of absorption spectra has provided evidence for conjugation between the cyclopropane ring and various chromophores, such as the carbonyl bond (80),(81),(82), a double bond (83), the benzene ring (84), and the pyridine ring (85). Its effect seems to be intermediate between that of a single and a double bond.



XLII.

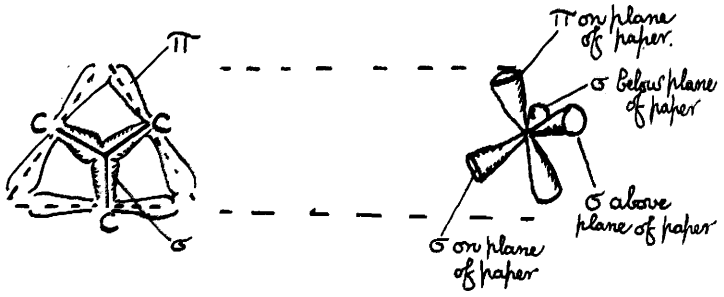
XLIII.

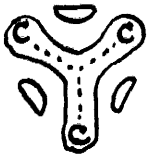
Ferguson (86) has illustrated this point with a table, part of which is reproduced below, which ascribes a wavelength maximum to each system:

λ, mμ.	C=C	C=C−C=C	
	145	217	>145
	C=O	C=C−C=O	
	280	310-330	290 (243)
	C_6H_5-R	C_6H_5-C=C	
	259	290	244

To account for the anomalous properties of the cyclopropane ring, Walsh has proposed the following theory

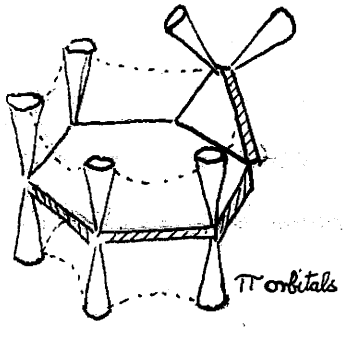
(87),(88),(89),(90),(91),(92). The carbon atoms in the ring are in a trigonal, not a tetrahedral state, and the - orbitals are non-localised, the π -electrons being shared equally between the three carbon atoms as illustrated below.





XLIV.

As a result, the central plane of the ring is a region of high electron density (XLIV). From this theory it is possible to visualise interaction between a three-membered ring and a conjugated system, if the ring (as is quite reasonable) lay at some angle approaching 90° to the plane of the double bonds:



(This theory does not necessarily contradict the mechanism proposed for the reaction of the carboxymethylene radical with a double bond (p.13), as transition to the structure XLIV would only involve a "reshuffle" of electrons). Further, the carboxylic group in the norcaradiene acids would now be conjugated with the rest of the molecule and could exert a deactivating influence not only, as mentioned earlier, by the inductive effect, but also by the mesomeric effect.

In light of these observations, it is interesting to consider the absorption spectra of these norcaradiene acids in more detail. In the series of compounds benzene, n-propylbenzene, phenylcyclopropane and styrene, there can be observed a gradual transition in the shape of the absorption curves and the position and intensity of the maxima (84), (p.45, 1,2,3,4). This illustrates the chromphoric effect of the cyclopropyl group. As was remarked our hexahydronorcaradienecarboxylic ester has an absorption spectrum very similar indeed to that of octahydroanthracene (99). It appears then that in this case, the cyclopropane ring makes a negligible contribution to the total effect caused by the methylene rings (p.44, C). (See the table below).

We can visualise the spectra of the benznorcaradiene- and dibenznorcaradienecarboxylic acids as an extension of the benzene-styrene series mentioned above. The spectra of

these two acids are rather similar to each other (p.44 , A,B), and also similar to the spectrum of fluorene (p.45, D). The latter compound shows more intense absorption however, and the curve is shifted towards the ultraviolet. Replacement of the methylene group in fluorene by a double bond gives the molecule of phenanthrene, with its highly characteristic absorption spectrum (p.49 ,L.). Replacement of the methylene by carboxycyclopropylene gives of course, dibenznorcaradienecarboxylic acid. As there is no large difference between the spectra of this compound and fluorene, the conjugation effect of the cyclopropane ring must again in this case be negligible.

Linearly anellated polycyclic hydrocarbons such as anthracene, which tend to react exclusively at para- (meso-) positions have a very characteristic absorption curve (e.g., p.48 , H). Angularly anellated hydrocarbons, such as phenanthrene, also possess a characteristic curve, different from the first (p.49 , L) (94). We could perhaps interpret the spectrum of benzanthracene by saying that it is intermediate between these two types (p.47, G). The spectra of naphthonorcaradienecarboxylic ester and benznaphthonorcaradienecarboxylic acid (p.46, E and F) have a general similarity to each other, and also a vague similarity to the curve for benzanthracene. In the case of naphthonorcaradienecarboxylic ester this is probably connected with the undoubted shift of

some of the reactivity from the 9:10-positions to the 3:4-bond, when the compound is prepared from anthracene.

As mentioned earlier, the spectrum of tribenznorcaradienecarboxylic acid shows the presence of the phenanthrene skeleton (p.49, K, L) . If the cyclopropane ring has a chromophoric effect comparable to that of a double bond, the spectra of our three condensation products should be very similar to those of the parent hydrocarbons. As this is not so, we must again conclude that the absorption effect of such a ring is slight, when condensed with a large aromatic nucleus.

We can see that no simple clear-cut picture emerges from our examination of these spectra. It does however, in one case at least, give support to the structure proposed from chemical evidence (tribenznorcaradienecarboxylic acid). In the case of the other two acids, while the spectra give us no clear clue to the structure, they do not contradict the formula we have proposed.

Benznorcaradiene-carboxylic acid	220	4.5	305	3.17
Dibenznorcaradiene-carboxylic acid	220	4.6-4.65	309	3.74
~~Dihydrobenznorcaradiene-carboxylic acid~~	~~220~~	~~3.95-4.0~~	~~268~~	~~2.51~~
Hexahydronaphthonorcaradiene-carboxylic ester	236	4.04	287	3.13
Phenylcyclopropane (84)	220	3.92	274	2.45
2-cyclopropylpyridine (85)	220	?	270	3.60
2-vinylpyridine (85)	236	4.05	278	3.70
Styrene (95)	245	4.20	290	2.74
Ethylbenzene (84)	206	4.51	259	2.23
2-n-propylpyridine (85)	220	?	262	3.60
Fluorene (93)	220	?	300	4.0
Octahydroanthracene (99)	?	?	286	3.32.

Experimental.

Technical decalin was shaken with portions of concentrated sulphuric acid till a sample decolourised bromine water only on shaking and long standing. It was then washed with water and sodium carbonate solution, dried and distilled. This was the solvent used as mentioned in the condensation reactions.

Condensation of diazoacetic ester with anthracene: 59 g. pure anthracene in 300 c.c. decalin was maintained at 140-145°C, while 9.5 g. diazoacetic ester was added over a period of 4 hours, with efficient stirring. The temperature was gradually raised to 160°C over one hour and maintained there for one hour. The cold solution was filtered and decalin was steam distilled from the filtrate till about 50-80 c.c. sticky residue remained. This was combined with the anthracene residue from the filtration, the whole was suspended in 500 c.c. alcoholic sodium hydroxide and refluxed for 3 hours. After removal by distillation, of about 350 c.c. alcohol, the suspension was diluted with water and treated with steam till alcohol and practically all decalin was removed, and anthracene started to come over. The solution in the flask (circa 800 c.c.) was filtered at boiling point. About 54-55 g. anthracene was recovered, suitable for further condensations. The

cooled filtrate was acidified and after standing 2 hours, the sticky brown solid was collected, dried on the filter by suction, washed with 20 c.c. benzene, triturated with 5 c.c. ethanol and again dried by suction. 2.2 g. was obtained of almost colourless naphthonorcaradienecarboxylic acid XXV. It was purified by crystallisation from glacial acetic acid, and obtained as a poorly crystalline, violet-fluorescing, white powder, which started to decompose above 240°C, and finally melted 282-284°C. It gave a slight green colour with conc. sulphuric acid, and then dissolved to give a colourless solution. It was recovered completely unchanged after heating with a large excess of sodium hydroxide in ethylene glycol at 160°C for 5 hours. It was soluble in hot ethanol and acetic acid, sparingly soluble in benzene, carbon disulphide, petroleum ether, etc.
Analysis: Found: C, 81.08; H, 5.33. $C_{16}H_{12}O_2$ requires C, 81.33; H, 5.12%. On microhydrogenation over a palladium/-charcoal catalyst, it absorbed 3.1 mols. of hydrogen.

Methyl naphthonorcaradienecarboxylate - was prepared by treatment of the acid with ethereal diazomethane, and crystallised from methanol as lustrous plates, m.p. 123-124°C.
Analysis: Found: C, 81.55; H, 5.75. $C_{17}H_{14}O_2$ requires C, 81.58; H, 5.75%.

Methyl hexahydronaphthonorcaradienecarboxylate, XXXI. The acid did not hydrogenate in the presence of Raney Nickel at normal temperature and pressure. In the presence of a palladium/asbestos catalyst, the acid or its ester in dioxane or acetic acid gave mixtures - largely unchanged starting material. 0.27 g. methyl ester was shaken in 10 c.c. acetic acid solution in the presence of Adam's platinum catalyst (0.09 g.). When the slow absorption had ceased, the filtered solution was taken to small bulk under vacuum. Addition of water precipitated a gum which, after treatment with a little ethereal diazomethane to counteract hydrolysis, crystallised from methanol as soft polyhedra, m.p. 79-80°C, mixed with original ester 50-58°C. Yield: 50%. Analysis: Found: C, 79.82; H, 7.73. $C_{17}H_{20}O_2$ requires C, 79.68; H, 7.87%. The ester (60 mgs.) was left 24 hours in a cold solution of potassium hydroxide (0.2 g.) in 50% methanol (10 c.c.). The solution was warmed with steam for 2 hours, concentrated under vacuum, diluted with water and acidified, whereupon a colourless solid (45 mgs.) precipitated. Hexahydronaphthonorcaradienecarboxylic acid crystallised from petrol (b.p. 100-120°) in lustrous plates, m.p. 192-193°C. Analysis: Found: C, 79.57; H, 7.47. $C_{16}H_{18}O_2$ requires C, 79.31; H, 7.50%.

Bromination: 0.1 g. Methyl naphthonorcaradienecarboxylate in carbon disulphide was treated with 1.1 mol. bromine in carbon disulphide and stood till the solution was practically colourless - ½ hour. The carbon disulphide was removed and the product was obtained as a yellow powder from methanol decomposing 145°C. It was a mild skin irritant.

Analysis: Found: C, 54.68; H, 4.34. $C_{17}H_{14}O_2Br_2$ requires C, 48.27; H, 3.54%. (See p. 31a)

0.1 g. of the original free acid was treated with 1.1 mol. bromine in glacial acetic acid. When the solution was almost colourless (30 mins.), it was refluxed for 15 mins., (hydrogen bromide evolved), concentrated under vacuum, and the product precipitated with water. The dry compound on treatment with ethereal diazomethane gave the ester XXXII crystallised in needles from petroleum ether, m.p. 202-204°C. (not dec.).

Analysis: Found: C, 62.17; H, 4.12. $C_{17}H_{13}O_2.Br$ requires C, 62.03; H, 3.98%.

Oxidation reaction: 1.0 g. naphthonorcaradienecarboxylic acid in 50 c.c. glacial acetic acid was warmed to 60°C and treated with 4 g. sodium dichromate in 5 c.c. 80% acetic acid over one hour. After standing over night, the solution was taken to small bulk under vacuum, diluted with water and again concentrated under vacuum (temperature $\not>$ 50°C). No

solid separated. The diluted solution was subjected to liquid/liquid extraction with ether. The extraction was taken to dryness and the resulting orange solid was separated by crystallisation from dilute acetic acid into a white powder (0.23 g.) and an orange acidic gum (20 mgs.). The gum, which could not be obtained crystalline, was treated with zinc dust/ammonia, when it dissolved with a deep brown colour. On warming an intense indigo-coloured tar separated which was insoluble in alkali. The white powder after repeated crystallisations from dilute acetic acid decomposed 230-307°C, and still gave a fluorescein colour on resorcinol/sulphuric acid treatment.

Analysis: Found: C, 59.94; H, 4.3: $C_{16}H_{12}O_6$ requires C, 64.0; H, 4.03%. (SEE P.IVa)

Condensation with benzanthracene: 26 g. pure benzanthracene in 40 c.c. decalin was treated with 4 g. diazoacetic ester in the same way as described for anthracene. The cold mass was suspended in 50 c.c. alcoholic sodium hydroxide and refluxed for 3 hours. Decalin was removed and the acid isolated as in the case of anthracene. The resulting brown solid was dissolved in 8 c.c. glacial acetic acid and left for 10 days with occasional scraping of the containing vessel. Yield, 0.8 g. benznaphthonorcaradienecarboxylic acid XXXIV. It was obtained pure by recrystallisations from glacial acetic acid m.p. 290-1°C (dec.).

Analysis: Found: C, 83.69; H, 5.1. $C_{20}H_{14}O_2$ requires C, 83.89; H, 4.93%.

It reacted slightly on long standing with permanganate in acetone and bromine in acetic acid. Heating in ethylene glycol for 5 hours with a large excess of sodium hydroxide produced only slight charring of the original product. It dissolved in conc. sulphuric acid with charring. 1.1 mol. of hydrogen was absorbed in presence of palladium charcoal on the micro-scale. About 23 g. benzanthracene was recovered from the reaction.

Methyl naphthobenznorcaradienecarboxylate was obtained by treatment of the acid with ethereal diazomethane, and crystallised from methanol. M.p. 149-150°C.

Analysis: Found: C, 83.91; H, 5.36. $C_{21}H_{16}O_2$ requires C, 83.98; H, 5.37%.

The methyl ester 0.1 g. was dissolved in 50 c.c. of benzene/-dry ether (1:1) with 0.5 g. "atomised" sodium and some glass beads. Solution gradually turned dark brown, then after 7-12 hours an intense red colour. It was decolourised with a drop of methanol, filtered through cotton wool and concentrated. The product was a gum as described in the text.

Oxidation: 0.4 g. naphthobenznorcaradienecarboxylic acid in 20 c.c. glacial acetic acid was treated gradually with 1.6 g. sodium dichromate in 10 c.c. 80% acetic acid at simmering

point. After refluxing for ½ hour, the solution was concentrated under vacuum, diluted with water, and the yellow flocculent precipitate collected, yield 0.35 g. The product was contaminated with tar, and was best purified by recrystallisation from benzene. Micropolyhedra, m.p. 278-80°C (dec.) XXXIII.

Analysis: Found: C, 76.14; H, 3.89. $C_{20}H_{12}O_4$ requires C, 75.94; H, 3.82%.

It gave an intense red colour with zinc dust and dilute ammonia. With zinc dust and ammonia/sodium hydroxide (boiling), an intense indigo-blue, alkali-insoluble tar was formed (cf. oxidation of naphthonorcaradienecarboxylic acid, above).

Oxidation of the quinone acid to 1-(2'-carboxyphenyl)-2:3-cyclopropanedicarboxylic acid XI. 100 mgs. of the quinone acid was dissolved in 5 c.c. of water containing 70 mgs. sodium hydroxide. Dilute hydrogen peroxide was added at intervals, with warming, over 1 hour or so, till the solution was practically colourless. It was then boiled briskly for 10 minutes, acidified with dilute sulphuric acid, cooled, saturated with salt, and extracted with ether and ethyl acetate. By taking the combined extracts to dryness a yellowish powder was obtained, m.p. 200-240°C (dec.), which gave a strong fluorescein test. This was sublimed in two fractions (a) subliming below 240°C/5 m.m., melting 100-

250°C, and (b) subliming at 240-280°C/5 m.m. Fraction (b) was resublimed to a colourless powder, m.p. 272-4°C (slight dec.), mixed with authentic XI, melted 274-6°C (slight dec.).

Reaction of diazoacetic ester with pyrene: Tribenznorcaradienecarboxylic acid. XXXVII. Pure pyrene (40 g.) in decalin (40 c.c.) was treated with 7.5 g. diazoacetic ester and the mixture worked up exactly as described in the case of benzanthracene. In this way a dark brown powder was obtained and about 37 g. pyrene was recovered, suitable for recycling. The powder was refluxed 20 mins. with 150 c.c. ether, then the solution filtered. The filtrate was taken to dryness, left at 0°C for 2 hours, then triturated with 5-10 c.c. ethanol, and separated by filtration. 0.7 g. pale yellow powder were thus obtained, which, recrystallised from glacial acetic acid, gave tribenznorcaradienecarboxylic acid as colourless violet-fluorescent needles, m.p. 267-268°C (dec.).

Analysis: Found: C, 83.34; H, 4.87. $C_{18}H_{12}O_2$ requires C, 83.06; H, 4.65%.

The acid was recovered unchanged after heating 5 hours in an ethylene glycol solution containing much sodium hydroxide, but was charred in conc. sulphuric acid solution. It absorbed 1 mol. hydrogen on microhydrogenation.

Methyl tribenznorcaradienecarboxylate. This was prepared by ethereal diazomethane treatment of the acid. It crystallised in needles from methanol, m.p. 142-3°C.
Analysis: Found: C, 83.22; H, 5.16. $C_{19}H_{14}O_2$ requires C, 83.18; H, 5.16%.

The dark brown residue from the ether extraction mentioned above, was practically insoluble in all solvents. This powder from four different condensation experiments was suspended in excess ethereal diazomethane and left over night. This process was repeated. The residue on removal of the ether was taken up in 300 c.c. toluene (boiling), and the cold solution passed down a column of alumina. Fine, intensely yellow, yellow-fluorescing crystals were obtained from the eluate. This product was recrystallised from toluene, yield, 150 mgs., m.p. 280-282°C.
Analysis: Found: C, 83.45; H, 4.73. $C_{19}H_{14}O$ requires C, 83.18; H, 5.1%.
It was sparingly soluble or insoluble in most solvents, slightly soluble in dioxane and toluene, absorbed no hydrogen on microhydrogenation, and was so insoluble that carbomethoxyl determination failed. It did not decolourise bromine in acetic acid nor permanganate in acetone. After heating 5 hours in ethylene glycol/sodium hydroxide, it had only partially dissolved, and that part decomposed. On prolonged refluxing with excess alcoholic sodium hydroxide, hydrolysis

took place. On acidification, a yellow acid was obtained which decomposed above 340°C, and dissolved in no solvent except boiling nitrobenzene, and then with decomposition. Its sodium salt was semi-colloidal, and showed good frothing power.

Oxidation of tribenznorcaradienecarboxylic acid.

The acid (0.4 g.) in 15 c.c. glacial acetic acid at simmering point was treated with 1.6 g. chromic anhydride in 5 c.c. 80% acetic acid over 1 hour. The solution was then refluxed ½ hour, concentrated to half bulk, diluted with water, then left over night. 95 mgs. deep red micro-needles were obtained on filtration XXXVI, m.p. 300-320°C (dec.). It was sparingly soluble in most solvents and ignited to an inorganic residue even after recrystallisation from toluene. Samples with ethereal diazomethane, and alcoholic hydrogen chloride, gave colourless products which were not further investigated. When heated in dioxane with 1 mol. o-phenylene diamine, it gave a yellow amorphous product, which was neutral and sparingly soluble in most solvents, m.p. 340-350°C (dec.). This gave an intense magenta coloured solution with conc. sulphuric acid, and a pale green colour when suspended in boiling acetic acid/methyl ethyl ketone. An alkaline solution of the o-quinone turned pale yellow when saturated with sulphur dioxide, the red o-quinone being reprecipitated on adding dilute acid and boiling. No purification could be effected by this method.

Further Oxidation of o-quinone. 50 mgs. o-quinone was dissolved in 5 c.c. sodium carbonate solution. This was warmed with the periodic addition of dilute hydrogen peroxide, till colourless. The solution was boiled for ten minutes, cooled and acidified. Yield, 45 mgs., m.p. 274-278°C., gives a 30°C depression with acid XI. The trimethyl ester was prepared by treatment with ethereal diazomethane, and crystallised from 80/100 petroleum ether in straw-coloured polyhedra XXXV, m.p. 175-176°C.

Analysis: Found: C, 68.90; H, 5.28. $C_{21}H_{18}O_6$ requires C, 68.82; H, 4.95%. Carbomethoxyl determination (as methoxyl): Found: 25.16% methoxyl. $C_{21}H_{18}O_6$ requires 25.40% methoxyl.

Benznorcaradienecarboxylic acid was prepared, largely as described by Buchner and Hediger, m.p. 162-164°C (lit. 165-166°C). It was brominated to the dibromide, m.p. 163-165°C (slight dec.) - lit. 169°C (complete dec.). Bromination took about ½ hour on the 0.4 g. scale. Benznorcaradienecarboxylic acid was also oxidised with alkaline permanganate to 1-(2'-carboxyphenyl)-2:3-cyclopropanedicarboxylic acid, which was crystallised from dilute ethanol, and sublimed 240°C/4 m.m., m.p. 281-2°C (slight dec.). Buchner and Hediger, 273-5°C (slight dec.), Drake and Sweeney, 281-2°C.

Dibenznorcaradienecarboxylic acid was prepared as described by Drake and Sweeney, m.p. 256-258°C (dec.). Lit. 257.5-8°C.

Light Absorption Data. The spectra were determined using a Hilger "Spekker" Quartz Spectrophotometer, slit width 0.03 m.m., with a hydrogen discharge lamp as light source. The position and extinction of peaks were checked with a Unicam Spectrometer. Curves designated with reference numbers were adapted from the literature, and the original papers should be consulted for further details.

References.

(1) Nametkin & Brüssoff: J.pr.Chem., 1926, 112, 169.

(2) Berthier, Coulson, Greenwood & Pullman: Compt.rend., 1948, 226, 1906.

(3) Buu-Hoi, Daudel & Vroelant: Bull.Soc.chim., 1949, 16, 211.

(4) Schoental; Biochemical Society Symposia No.5: "Oxidation of Aromatic Rings by purely chemical means", p.6.

(5) Cook & Schoental: Nature, 1948, 161, 237.

(6) Cook & Schoental: J.C.S., 1948, 172.

(7) Vollmann, Becker, Corell & Streeck: Ann., 1937, 531, 1.

(8) Lock: Ber., 1937, 70, 926.

(9) Buu-Hoi & Lecocq: Compt.rend., 1948, 226, 87.

(10) Goldschmeidt: Monatsh., 2, 580.

(11) Cook & Hewett: J.C.S., 1933, 398.

(12) Scholl & Seer: Ann., 1912, 394, 160.

(13) Vollmann, Becker, Corell & Streeck: Ann., 1937, 531, 65.

(14) Roitt & Waters: J.C.S., 1949, 3060.

(15) Charrier & Moggi: Gazzetta, 1927, 57, 736.

(16) Greenspan: Ind.Eng.Chem., 1947, 39, 847.

(17) Young : Biochemical Society Symposia No.5., p.27.

(18) Buchner: Ber., 1888, 21, 2637.

(19) Buchner & Witter: Ann., 1895, 284, 219.

(20) Dyakonov: J.Gen.Chem.Russ., 1949, 19, 1891.

(21) Hancox: J.Aust.Chem.Inst., 1949, 16, 282.

(22) Buchner & Curtius: Ber., 1885, 18, 2377.

(23) Buchner: Ber., 1896, 29, 106.

(24) Buchner: Ber., 1897, 30, 632.

(25) Buchner: Ber., 1898, 31, 2241.

(26) Buchner & Lingg: Ber., 1898, 31, 402.

(27) Buchner & Lingg: Ber., 1898, 31, 2247.

(28) Braren & Buchner: Ber., 1900, 33, 684.

(29) Braren & Buchner: Ber., 1901, 34, 982.

(30) Buchner & Kurtz: Ber., 1896, 29, 106.

(31) Buchner & Feldmann: Ber., 1903, 36, 3509.

(32) Buchner & Delbrück: Ann., 1908, 358, 1.

(33) Buchner & Schulze: Ann., 1910, 377, 259.

(34) Buchner & Schottenhammer: Ber., 1920, 53, 865.

(35) Smith & Tauney: J.A.C.S., 1934, 56, 2167.

(36) Smith & Agre: J.A.C.S., 1938, 60, 648.

(37) Buchner & Rehorst: Ber., 1913, 46, 2680.

(38) Buchner & Hediger: Ber., 1903, 36, 3502.

(39) Drake & Sweeney: J.Org.Chem., 1946, 11, 67.

(40) Criegee, Marchand & Wannowius: Ann., 1942, 550, 116.

(41) Harries: Ann., 1905, 343, 372.

(42) Wilbaut & van Dŷk: Rec.trav.chim., 1946, 65, 413.

(43) Kooyman: Rec.trav.chim., 1947, 66, 201.

(44) Henderson & Boyd: J.C.S., 1910, 1659.

(45) Böeseken & Sloof: Rec.trav.chim., 1930, 49, 100.

(46) St.Pfau & Plattner: Helv.Chim.Acta., 1939, 22, 202.

(47) Treibs: Naturwiss., 1946, 33, 371.

(48) Treibs: Ber., 1948, 81, 38.

(49) Plattner, Furst, Chopin & Winteler: Helv.Chim.Acta., 1948, 31, 501.

(50) Horn, Nunn & Rapson: Nature, 1947, 160, 829.

(51) Nunn & Rapson: J.C.S., 1949, 825.

(52) Darapsky: Ber., 1910, 43, 1112.

(53) Loose: J.pr.Chem., 1909, 79, 505.

(54) Clar: Reichsamt Wirtschaftsausbau, Chem.Ber.Prüf - Nr 015 (PB 52017) 859-878, 1942.

(55) Pearson, Pursell & Saigh: J.C.S., 1938, 409.

(56) Dyakonov: J.Gen.Chem.Russ., 1949, 19, 1734.

(57) Fries & Schilling: Ber., 1932, 65, 1494.

(58) Brown, Durand and Marvel: J.A.C.S., 1936, 58, 1594.

(59) Mills & Nixon: J.C.S., 1930, 2510.

(60) "Organic Chemistry, an advanced treatise": Fieser, p.136.

(61) Campbell: Annual Reports, 1947, 126.

(62) Newlan, Slavin & Wheeler: J.C.S., 1950, 340.

(63) Arnold: Ber., 1943, 76, 777.

(64) Wagner-Jauregg, Arnold & Huter: Ber., 1942, 75, 1293.

(65) Wagner-Jauregg, Friess, Hippchen & Prier: Ber., 1943, 76, 1157.

(66) Arnold: Ber., 1947, 80, 123.

(67) Arnold: Ber., 1947, 80, 172.

(68) Swern: J.A.C.S., 1947, 69, 1692.

(69) Clar: Ber., 1932, 65, 503.

(70) Eckhardt: Ber., 1940, 73, 13.

(71) Schlenk & Bergmann: Ber., 1914, 47, 473.

(72) Schlenk & Bergmann: Ann., 1928, 463, 134.

(73) Fieser & Johnson: J.A.C.S., 1939, 61, 168.

(74) Schroeter, Müller & Huang: Ber., 1929, 62, 645.

(75) Badger: Quarterly Reviews, 1951, 5, 147.

(76) Plattner & Roniger: Helv.Chim.Acta, 1942, 25, 590.

(77) Coulson: Quarterly Reviews, 1947, 144.

(78) Robinson: J.C.S., 1916, 109, 1042.

(79) Kohler & Conant: J.A.C.S., 1917, 39, 1404.

(80) Carr & Burt: J.A.C.S., 1918, 40, 1590.

(81) Rogers & Roberts: J.A.C.S., 1946, 68, 843.

(82) Klotz: J.A.C.S., 1944, 66, 88.

(83) Volkenburgh, Greenlee, Derfer & Boord: J.A.C.S., 1949, 71, 3595.

(84) Rogers: J.A.C.S., 1947, 69, 2544.

(85) Mariella, Lowell, Peterson & Ferris: J.A.C.S., 1948, 70, 1494.

(86) Ferguson: Chem.Revs., 1948, 43, 358.

(87) Walsh: Nature, 1947, 159, 165.

(88) Walsh: Nature, 1947, 159, 712.

(89) Walsh: Trans.Farad.Soc., 1949, 45, 179.

(90) McDowell: Nature, 1947, 159, 508.

(91) Robinson: Nature, 1947, 159, 400.

(92) Skinner: Nature, 1947, 160, 4078.

(93) Ramart-Lucas & Hoch: Bull.Soc.Chim., 1935, 5, 1376.

(94) Clar: "Aromatische Kohlenwasserstoffe".

(95) Pestemer & Wiligut: Monatsh., 1935, 66, 119.

(96) Badger: Aust.Chem.Inst.J. & Proc., 1950, 17, 14.

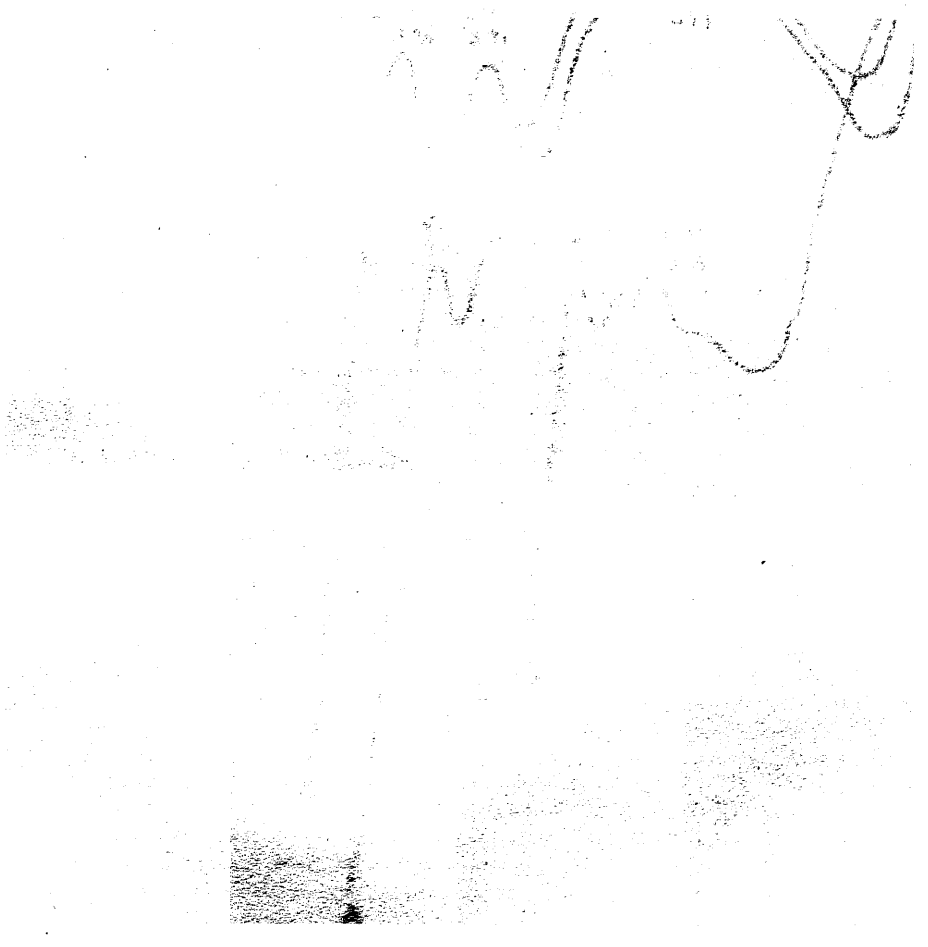
(97) Bachmann: J.Org.Chem., 1937, 1, 347.

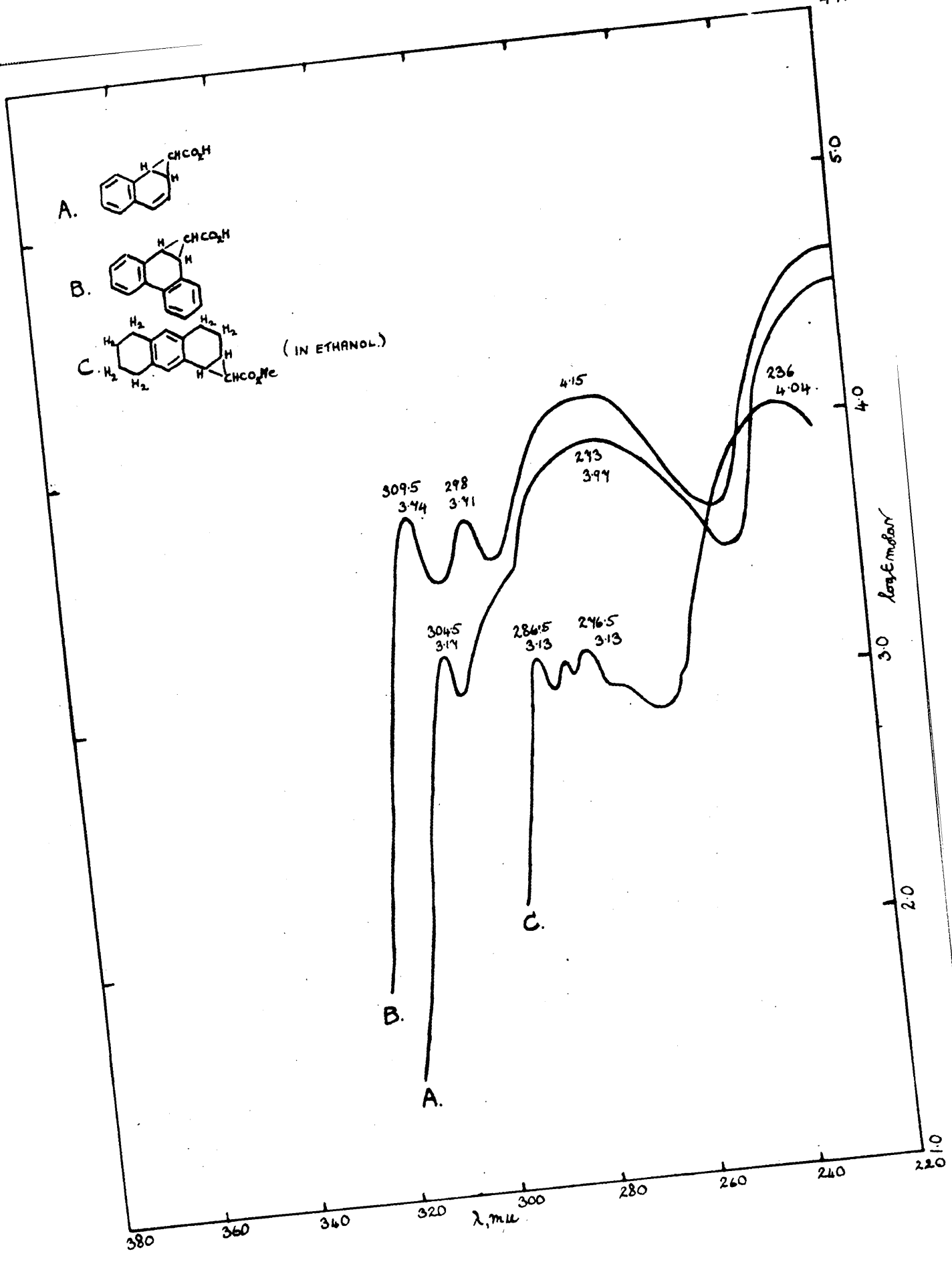
(98) Auwers & König: Ann., 1932, 496, 252.

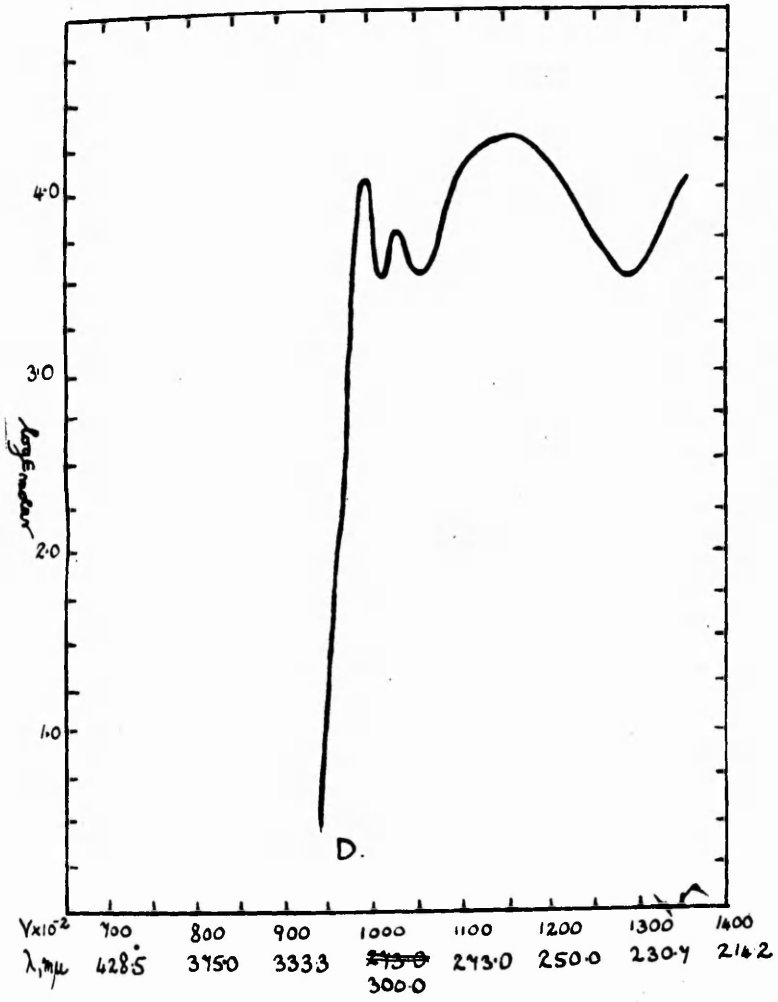
(99) Heerjes & Waterman: Bull.Soc.chim., 1940, 7, 188.

(100) Clar & Lombardi : Ber., 1932, 65, 1422.

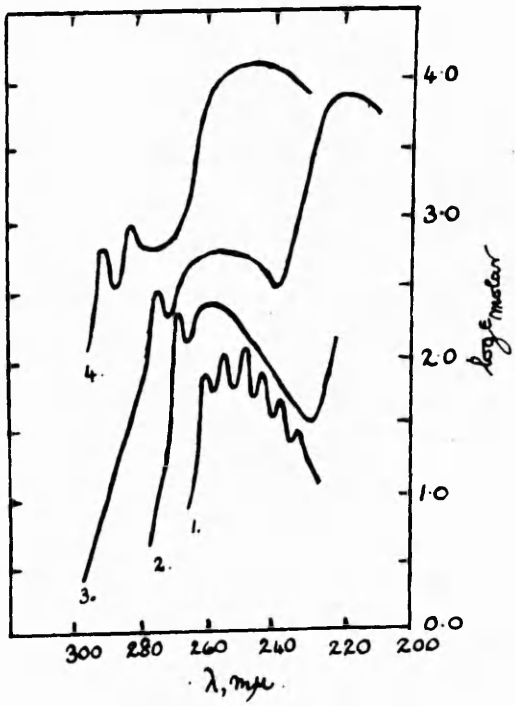
(101) Clar : Ber., 1936, 69, 1674.



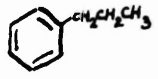

A.
B.
C.
(IN ETHANOL.)
309·5
3·44
298
3·41
304·5
3·19
293
3·99
4·15
286·5
3·13
296·5
3·13
236
4·04
B.
A.
C.
5·0
4·0
3·0
2·0
1·0
log ε molar
380
360
340
320
300
280
260
240
220
λ, mμ


4·0
3·0
2·0
1·0
log ε molar
D.
Y x10⁻²
700
800
900
1000
1100
1200
1300
1400
λ, mμ
4285
3950
3333
~~2750~~
3000
2930
2500
2307
2142

D.  (93)


4·0
3·0
2·0
1·0
0·0
log ε molar
4.
3.
2.
1.
300
280
260
240
220
200
λ, mμ

1. 

2. 
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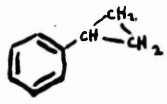
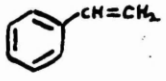
3. 
CH₂
CH
CH₂

4. 
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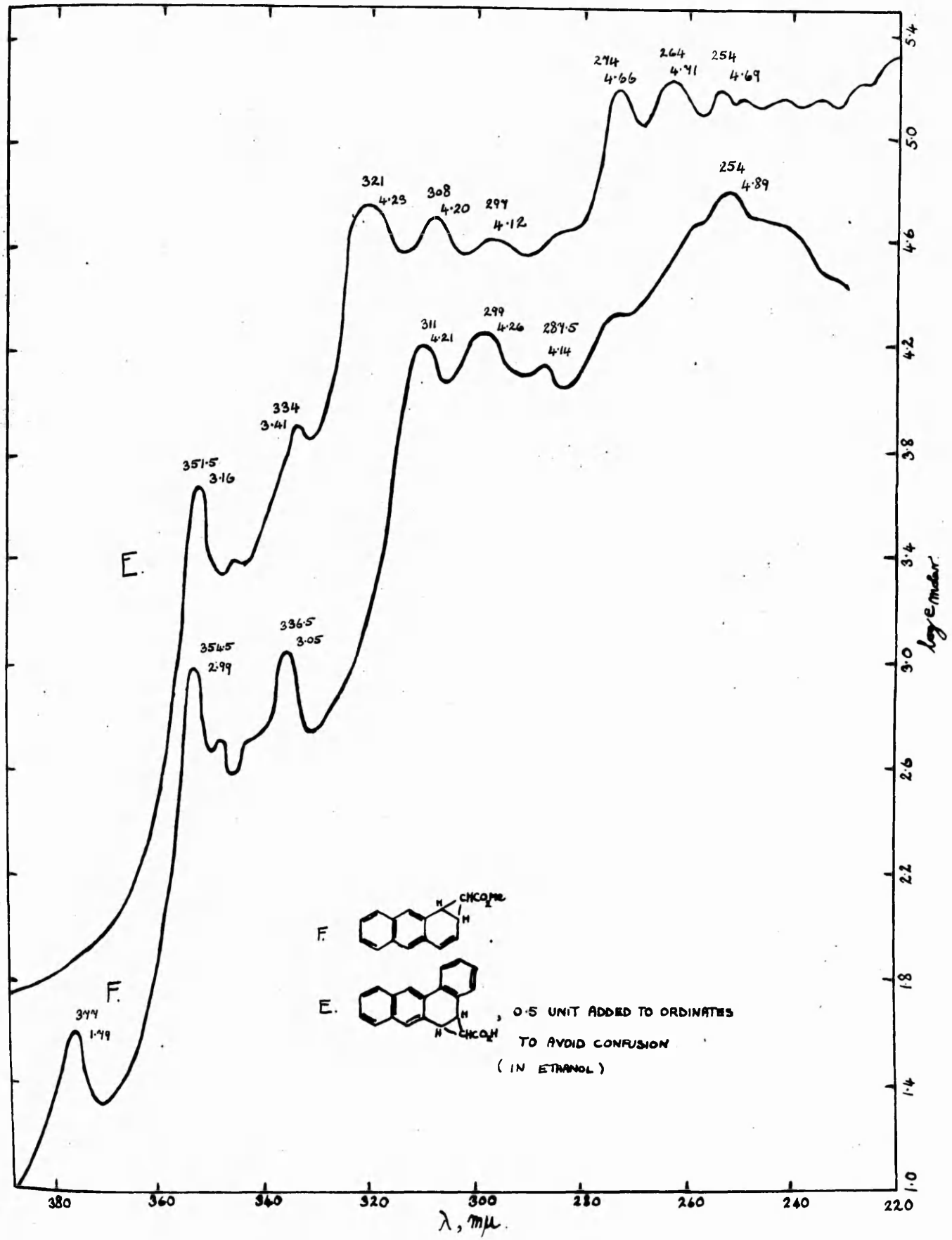
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264
4·41
254
4·69
321
4·23
308
4·20
299
4·12
254
4·89
311
4·21
299
4·26
289·5
4·14
334
3·41
351·5
3·16
354·5
2·99
336·5
3·05
344
1·49
E.
F.
F
E.
CHCOMe
CHCO₂H
0·5 UNIT ADDED TO ORDINATES
TO AVOID CONFUSION
(IN ETHANOL)
log ε molar
λ, mμ
380
360
340
320
300
280
260
240
220
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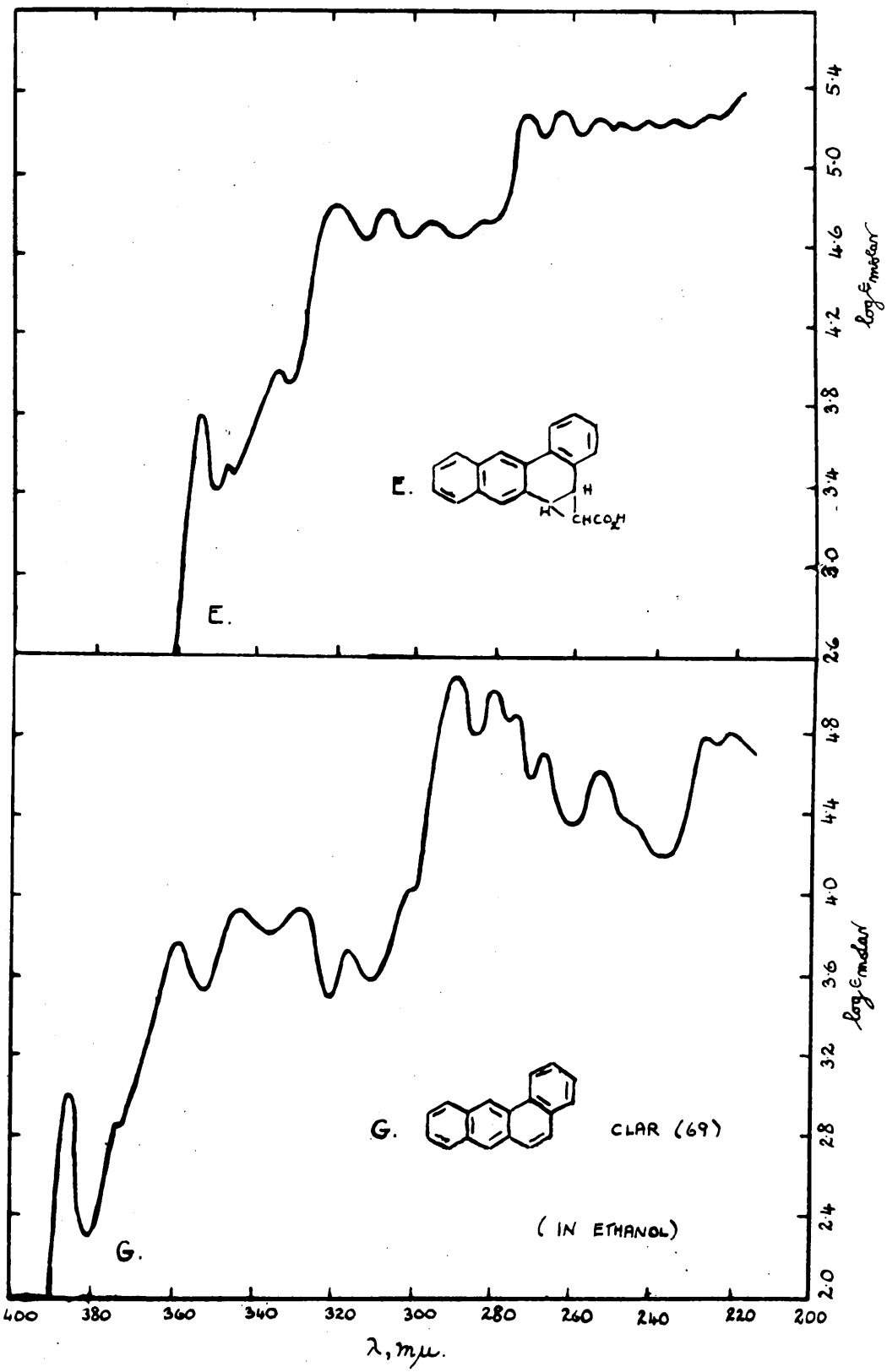
5·0
4·6
4·2
3·8
3·4
3·0
2·6
2·2
1·8
1·4
1·0


E.
H
H
CHCO₂H
E.
log ε molar
5·4
5·0
4·6
4·2
3·8
3·4
3·0
2·6
G.
CLAR (69)
(IN ETHANOL)
G.
log ε molar
4·8
4·4
4·0
3·6
3·2
2·8
2·4
2·0
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340
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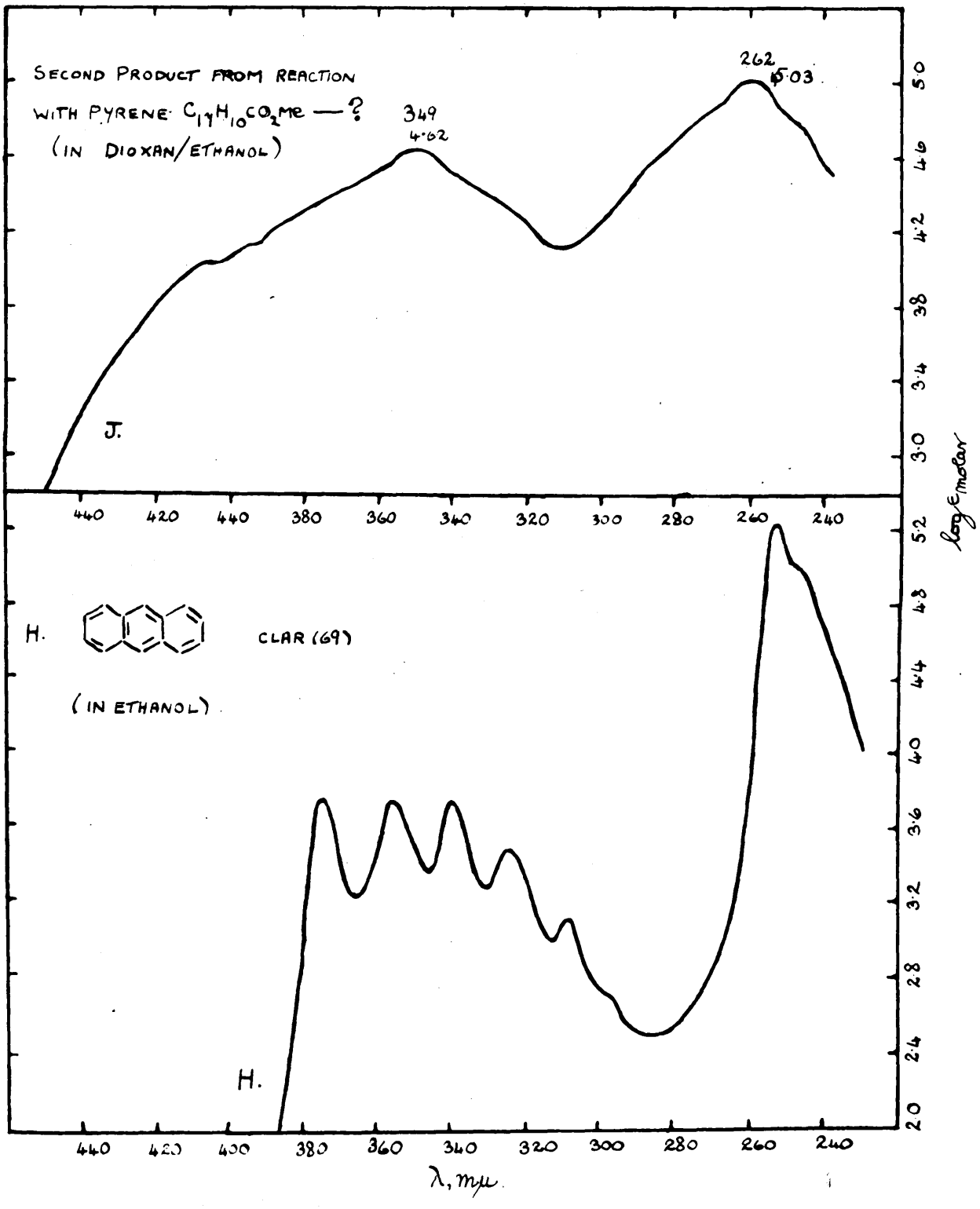
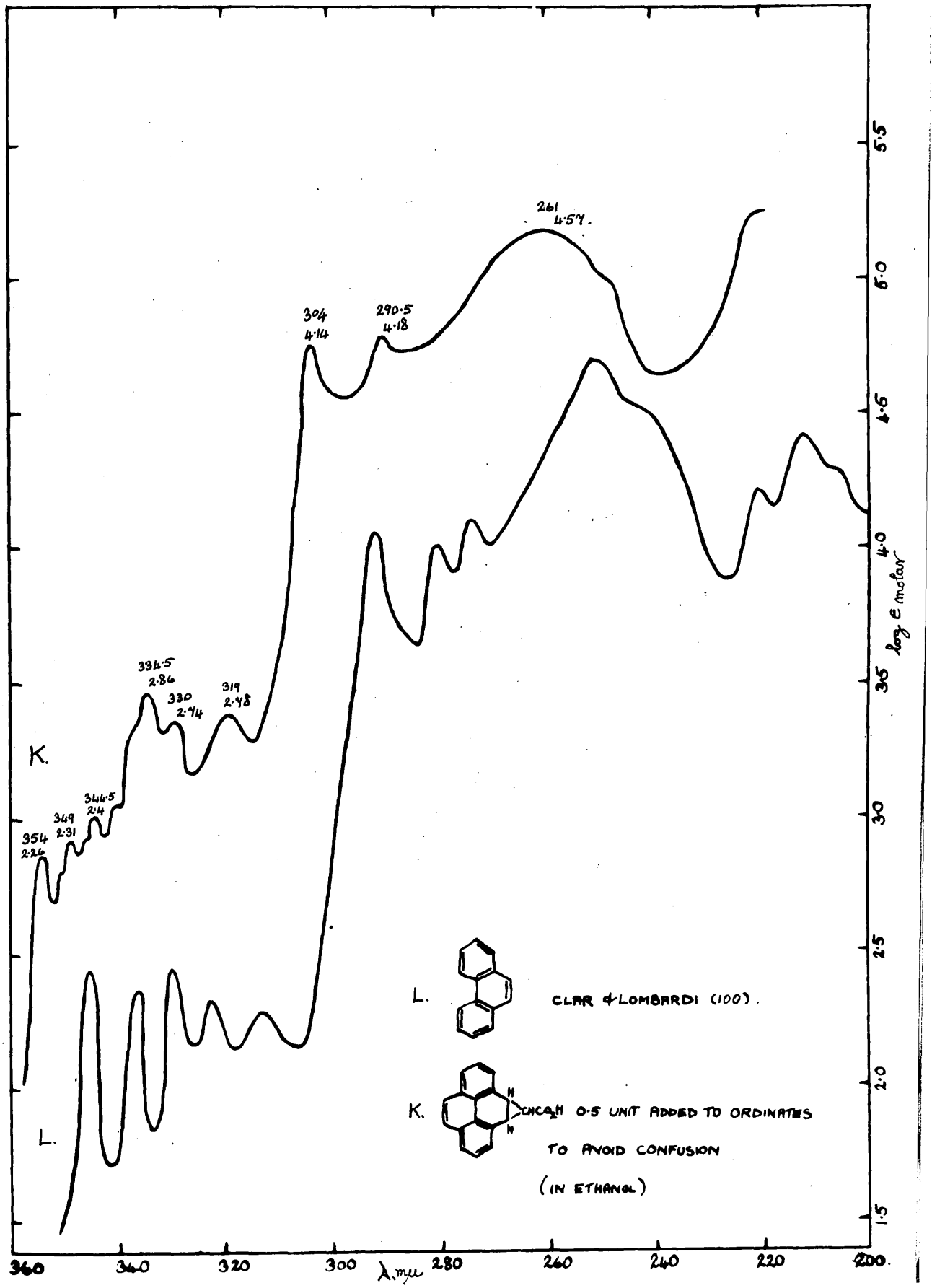
300
280
260
240
220
200
λ, mμ.


SECOND PRODUCT FROM REACTION
WITH PYRENE $C_{17}H_{10}CO_2Me$ — ?
(IN DIOXAN/ETHANOL)
349
4·62
262
5·03
J.
440 420 440 380 360 340 320 300 280 260 240
5·0 4·6 4·2 3·8 3·4 3·0
H.
CLAR (69)
(IN ETHANOL)
H.
440 420 400 380 360 340 320 300 280 260 240
λ, mμ.
5·2 4·8 4·4 4·0 3·6 3·2 2·8 2·4 2·0
log ε molar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4·14
290·5
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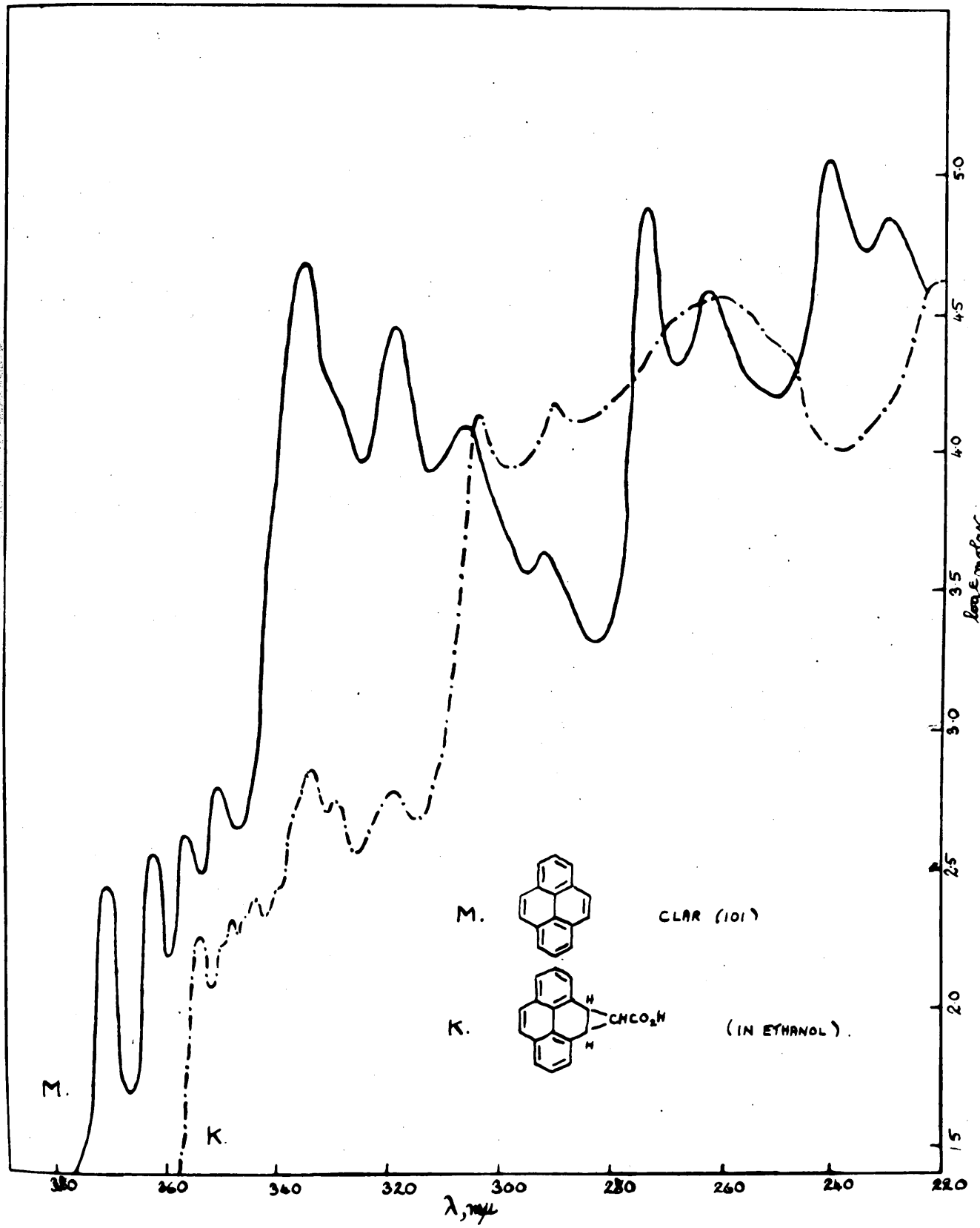
334·5
2·86
330
2·74
319
2·98
344·5
2·4
349
2·31
354
2·26
K.
L.
L. CLAR & LOMBARDI (100).
K. CH₂CO₂H
0·5 UNIT ADDED TO ORDINATES
TO AVOID CONFUSION
(IN ETHANOL)
360
340
320
300
λ mμ
280
260
240
220
200
5·5
5·0
4·5
4·0
3·5
3·0
2·5
2·0
1·5
log ε molar


M.
K.
M.
CLAR (101)
K.
H
CHCO₂H
H
(IN ETHANOL).
380
360
340
320
300
280
260
240
220
λ, mμ
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
log ε molar

Part II.

T r o p o l o n e s.

B : Tropolones.

S u m m a r y.

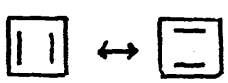
By the reaction of suberandione with different proportions of bromine, followed by thermal dehydrobromination and treatment with alkali, tropolone itself has been prepared, also the mono-, di-, and trisubstituted bromotropolones. The orientation of these bromotropolones has been proved by isomerisation to bromobenzoic acid derivatives, and their interrelationship verified by further bromination experiments. Tropolone has also been prepared more conveniently by the catalytic hydrogenolysis of the α-bromo derivative. The reactions of tropolone have been studied, and a number of derivatives prepared.

Bromination of benzsuberandione and catalytic hydrogenolysis of the bromobenzotropolone thus obtained have given an improved yield of the known α/β-benzotropolone. Studies on this compound have been extended.

The results of these investigations are discussed with reference to the light thrown by them on the structure and stability of tropolone derivatives.

Contents

The possibility of aromatic properties in a closed system of conjugated double bonds has frequently been recognised before a compound containing such a system has been isolated or synthesised. Cyclobutadiene, which might theoretically occur as a resonance hybrid I, has evaded synthesis since the first unsuccessful attempts in 1905 (1). Possibly the high angular strain in such a molecule would prevent its existence, although the synthesis of various "diphenylene" derivatives II has been claimed from time to time (2),(3),(4). Pentalene III was postulated as a possible aromatic system in 1922 (5), but neither it nor heptalene IV, has yet been synthesised (4),(6),(7)



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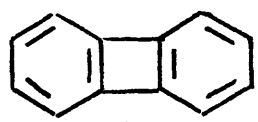
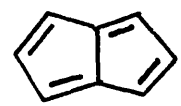
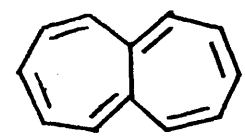


II.

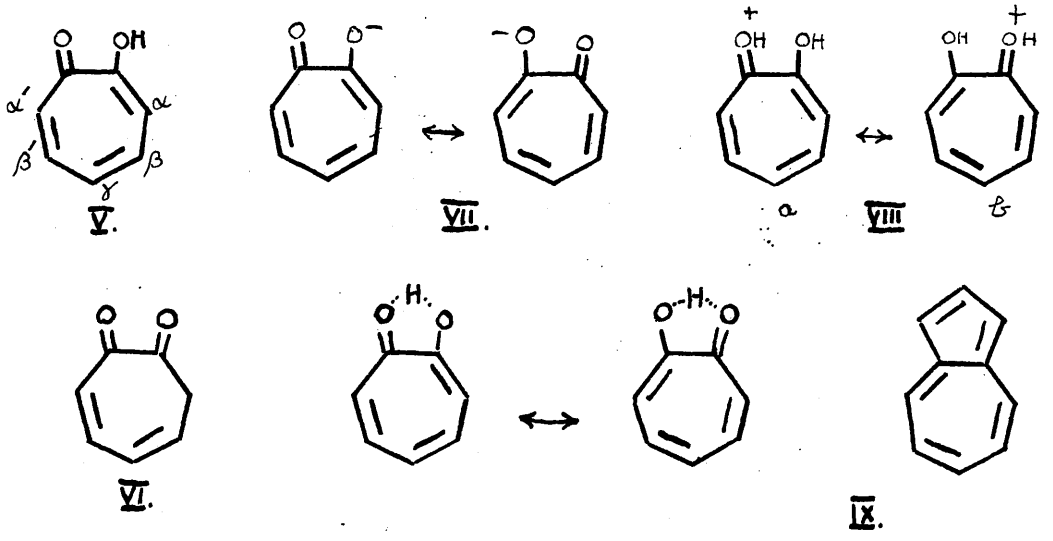


III.



IV.

It was in 1945 that Dewar (8) first pointed out the unique possibilities of the cycloheptatrienolone ring system. This structure may be regarded as the mono-enol form V of an unsaturated o-diketone VI, which on ionisation of the hydroxyl hydrogen can give rise to an anionic resonance hybrid VII; on addition of a proton, a cationic resonance hybrid becomes possible VIII:



V. VII. VIII. IX.

From another viewpoint, the system may be regarded as the divinylogue of a carboxylic acid (9). Dewar coined the name "tropolone" for this system, and suggested that it occurred in the mould metabolites stipitatic acid and puberulic acid, and the alkaloid colchicine.

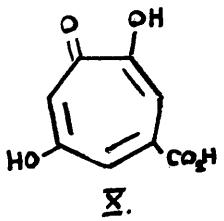
As originally set out, Dewar's theory envisaged resonance in the unionised molecule, the system being somewhat analogous to azulene IX. A subsequent calculation of the inter-oxygen distance proved such a state of affairs highly improbable, and led Dewar to withdraw this idea (10), but on all other points his original hypothesis has received extensive experimental confirmation.

The elegance of this idea attracted the attention of many chemists in different parts of the world, and since 1945 a considerable and continuously growing mass of literature has been published on naturally occurring and synthetic tropolone derivatives. This has led to the production of

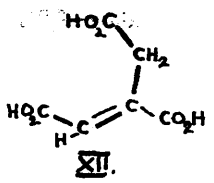
two reviews (11),(12) which between them give a detailed coverage of this field up till Spring, 1951. It is therefore proposed to refer only briefly to the various synthetic and natural tropolones examined by other workers.

The Natural Tropolones.

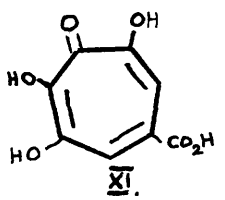
Three tropolones occur as mould metabolites: stipitatic acid X, puberulic acid XI and puberulonic acid. The first two compounds can be converted by mild oxidation to aconitic acid XII. This, and much other chemical evidence, has rigidly established their structures (13),(14),(15),(16),(17),(18),(19). Puberulonic acid differs from puberulic acid only in possessing a readily eliminated carboxyl group masked in a lactone or an anhydride structure. Evidence seemed in favour of one of the three formulae XIII, XIV, XV, but a recent examination of this compound's light absorption in the ultraviolet and infrared regions points overwhelmingly to formula XVI (20),(21),(22).



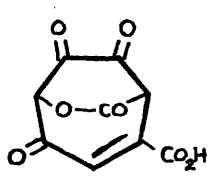
X.



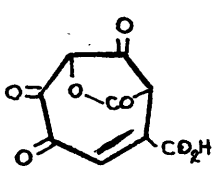
XII.



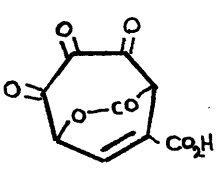
XI.



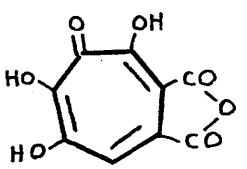
XIII.



XIV.



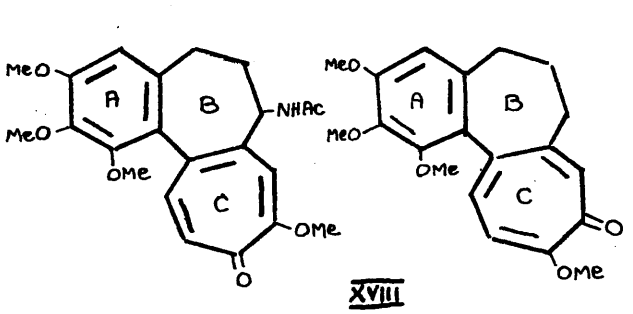
XV.



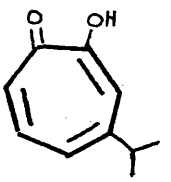
XVI.

The three theoretically possible monoisopropyltropolones, the so-called thujaplicins, are found naturally as a fungicical constituent of red cedar heartwood from Swedish and American sources. Their tropolone structures have been proved by isomerisation to the known isopropylbenzoic acids and by oxidation and reduction experiments, the work being carried out by Erdtman and his collaborators (23),(24),(25), (26). β -Thujaplicin (hinokitiol) XVII obtained from local sources was also extensively examined by a Japanese research team (27),(28).

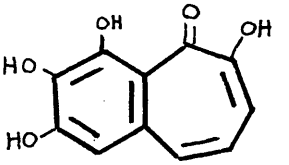
The alkaloid colchicine has attracted wide interest because of its interference with the process of mitosis during cell division. The structure of rings A and B of this tricyclic compound are well established (12),(29),(30), (31), and it is now fairly certain that ring C has the structure of a tropolone methyl ether. Colchicine can be converted through the free tropolone to its isomer isocolchicine, but which formula represents which isomer is not yet established XVIII.



XVIII



XVII.



XIX.

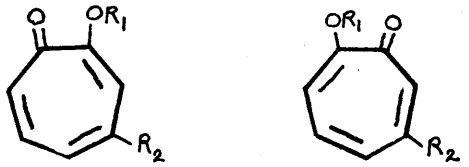
The tropolone ring is incorporated in the skeleton of yet another natural product, namely, purpurogallin XIX (32),(33),(34),(35). This occurs as a red diglucoside in various galls and is also readily obtainable in the laboratory by the oxidation of pyrogallol (11),(36). It shows many of the typical tropolone properties.

From the experimental data available on these naturally occurring derivatives, it is possible to build up a fairly complete picture of the characteristic properties to be expected in a tropolone derivative. Not all the tropolones mentioned above undergo each of the reactions now to be listed, and indeed, in this respect information is incomplete, for as far as is known, every compound has not been thoroughly examined. In any case, the presence of substituents might well be expected to affect considerably the fundamental properties of the ring, just as, for example, some of the characteristic properties of a phenol are altered or suppressed by various substituents. However, with these limitations in mind, a list of properties and reactions typical of tropolones may be drawn up.

1. Tropolones possess a cyclohepta- Δ 3:5:7-1-ol-2-one ring in which carbonyl reactivity is completely suppressed.
2. The hydroxyl group adjacent to the carbonyl is acidic, more so, apparently, than the hydroxyl in an analogous

phenol. It can usually be methylated with diazomethane or methanol/hydrogen chloride, and the ether is readily hydrolysed with acid or alkali.

3. The hydrogen of the ortho-hydroxyl migrates back and forth between the two oxygens too rapidly for isomers of the type XX (R_1 = H) to be detected.



XX.

(When R_2 is in the α-position the possibility exists that steric hindrance causes the molecule to exist in one form only. Where R_2 is in the γ-position, the two isomers are, of course, equivalent.)

4. When R_1 = Me etc. XX, two isomers <u>can</u> be isolated.

5. Solution in alkali is accompanied by a bathochromic shift in the absorption spectrum.

6. Tropolones are soluble in strong acids, being reprecipitated on dilution.

7. They form chloroform soluble, covalent complexes with certain transition metals especially copper.

8. They give intense colours with ferric chloride, irrespective of any ferric complex which might be formed.

9. They form azo-compounds with diazotized arylamines.

10. Tropolones undergo substitution rather than addition reactions.

11. They can be rearranged to benzoic acid derivatives by fusion with alkali.

12. By heating with sodium methoxide/methanol the methyl ethers are sometimes converted to methyl benzoate derivatives.

13. Treatment with iodine/alkali sometimes gives an iodophenol.

14. The ring is opened and partially degraded by alkaline peroxide and other mild oxidising agents.

15. The ring can be hydrogenated in the presence of platinum or palladium.

Researches on tropolones in these laboratories and elsewhere shed further light on the reactions listed above, but further comment will be postponed to a later section of this thesis.

Synthetic Tropolones.

Many tropolones, including most of the natural derivatives, have now been synthesised. The parent compound, tropolone itself, has been prepared by no less than three different independent research teams in the Western Hemisphere all using different synthetic routes, published within a very short time of each other (37),(38),(39). The recently resumed exchange of scientific information with the Far East has brought to our attention yet another independent synthesis of tropolone, very similar to our own, and again published

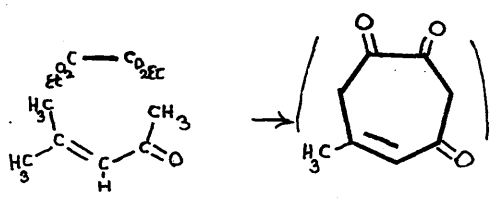
contemporaneously (40).

A Japanese research team under Nozoe had been studying the natural product hinokitiol (see above) since about 1936 and on the basis of their investigations had finally decided on the formula XVII. These conclusions they published in 1944, but it was not until the cessation of hostilities that they made contact with Western chemists and till then, it appears, were unaware that European workers were investigating related compounds and had come to similar conclusions (81). Nozoe and coworkers have now prepared a considerable number of tropolone derivatives by substitution reactions with hinokitiol, using various reagents. They have also more recently carried out some synthetic work (41). However, at the moment, complete information on these researches is not available.

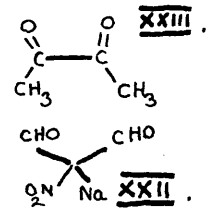
A wide variety of reactions have been employed in the synthesis of tropolones and these preparative methods can be classified under the following headings:

(A). Perhaps the most obviously attractive type of reaction is a one- or two-stage condensation to give straightway the complete tropolone ring. This line of attack has not however, proved generally fruitful. Dewar condensed ethyl oxalate with mesityloxide, in the hope of obtaining XXI (presumably), but could only isolate "the isomeric benzene derivative" (8). Similarly an attempted condensation of

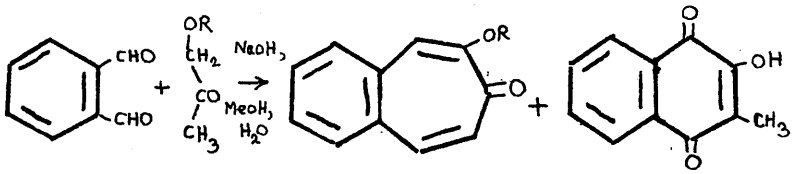
sodio-nitro-malondialdehyde XXII with diacetyl XXIII has given only tars (42).



XXI.



XXIII. XXII.



XXIV, R = H

XXV, R = C_6H_5

XXVI, R = p-$C_6H_4NO_2$.

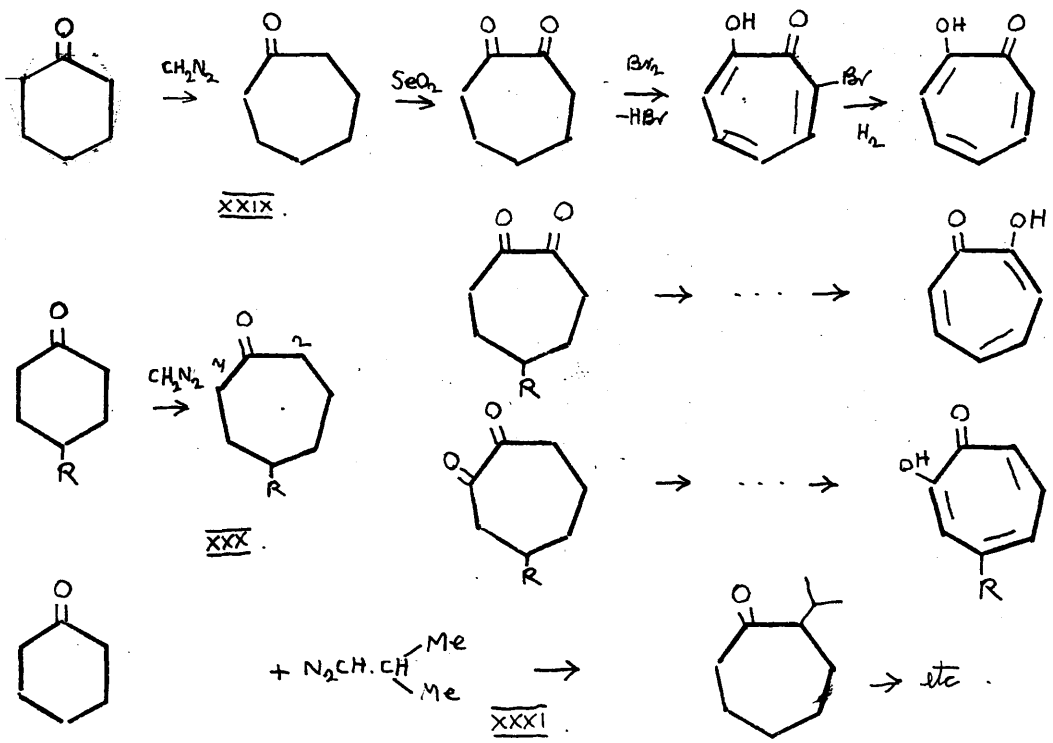
XXVII.

The preparation by Tarbell et al of $\beta\gamma$-benzotropolone, XXIV, is the one example in this field of a synthesis by a condensation reaction (43). As indicated, some phthiocol XXVII was also isolated, and the free benzotropolone was obtained in less than 10% yield. Rather better yields were obtained in the case of the two aryl ethers XXV, XXVI. These, however, were apparently not converted to the free benzotropolone. A large number of permutations may be envisaged for the possible components for this type of reaction. Success, it would appear, depends largely in choosing by trial and error the most suitable conditions and reactants.

(B). A substituted cyclohexanone is subjected to ring enlargement by means of an aliphatic diazo compound, the resulting cycloheptanone is oxidised to a dione, which in

turn is dehydrogenated to the tropolone. The final stage is most conveniently accomplished by bromination-dehydrobromination processes. Thus, cyclohexanone itself was ring enlarged with diazomethane to suberone, and this in turn was oxidised with selenium dioxide to suberandione. Bromination followed by thermal dehydrobromination gave bromotropolone which was readily converted to tropolone by catalytic hydrogenation (37),(44) XXIX. In the synthesis by Nozoe et al., the dione was brominated with N-bromosuccinimide in chloroform, then thermally dehydrobrominated to unsubstituted tropolone (40).

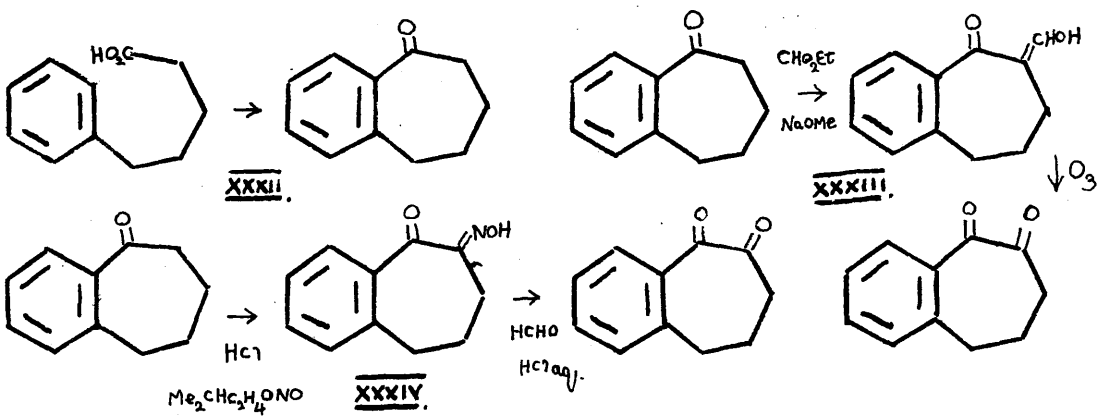
Starting from a para-substituted cyclohexanone a mixture of the β - and γ -substituted tropolones is obtained, since the 2 and 7 positions in XXX are not equivalent.



β - and γ-thujaplicin (45),(46),(47), and the methyl (β- and γ-) (48), ethyl (β-) (48) and tert.-butyl (β- and γ-) (49) substituted tropolones have all been synthesised, with the corresponding p-alkyl cyclohexanone as starting material.

α-Substituted tropolones, uncontaminated by position isomers, are now made accessible through an elegant modification of this synthesis, whereby ring enlargement is carried out using a higher diazoalkane. α-Thujaplicin was synthesised by this route (42), (50) XXXI.

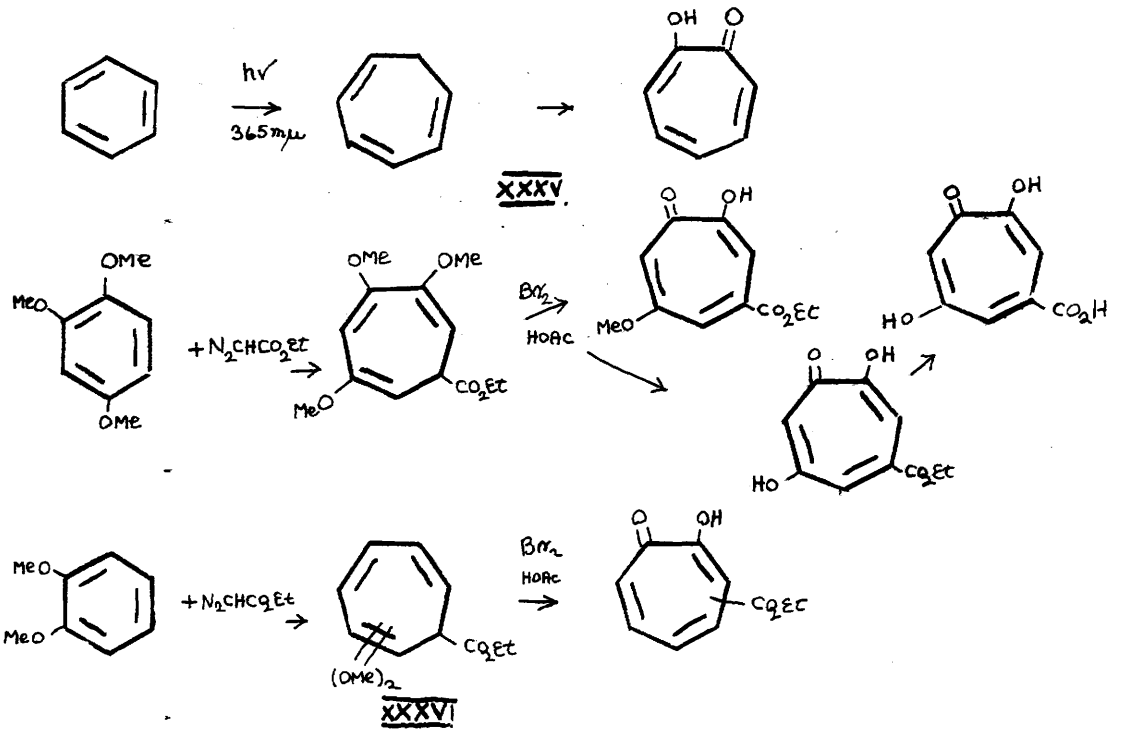
(C). Ring closure of a γ-aryl-(phenyl-) butyric acid gives a benzosuberone XXXII; this may be converted to the benzotropolone in the same steps as under (B) (51). The sometimes troublesome selenium dioxide oxidation can be avoided, either by preparing the α-hydroxymethyleneketone followed by ozonolysis XXXII (35),(52), or by hydrolysis of the α-oximinoketone with hydrochloric acid/formaldehyde (35),(53) XXXIV.



Into this group fall the syntheses of αβ-benzotropolone (51) and of the ar-polyhydroxy (or ar-polymethoxy-) benzotropolones including purpurogallin (35),(52). Till now in all cases final dehydrogenation of the diones has been accomplished catalytically in the presence of palladium/charcoal. As shown later, the bromination/dehydrobromination procedure has been found much more convenient in the preparation of the parent benzotropolone, and it may also be suitable in the case of the methoxy derivatives. Of course, the enhanced reactivity of the aryl nucleus might prove a complicating factor with such compounds.

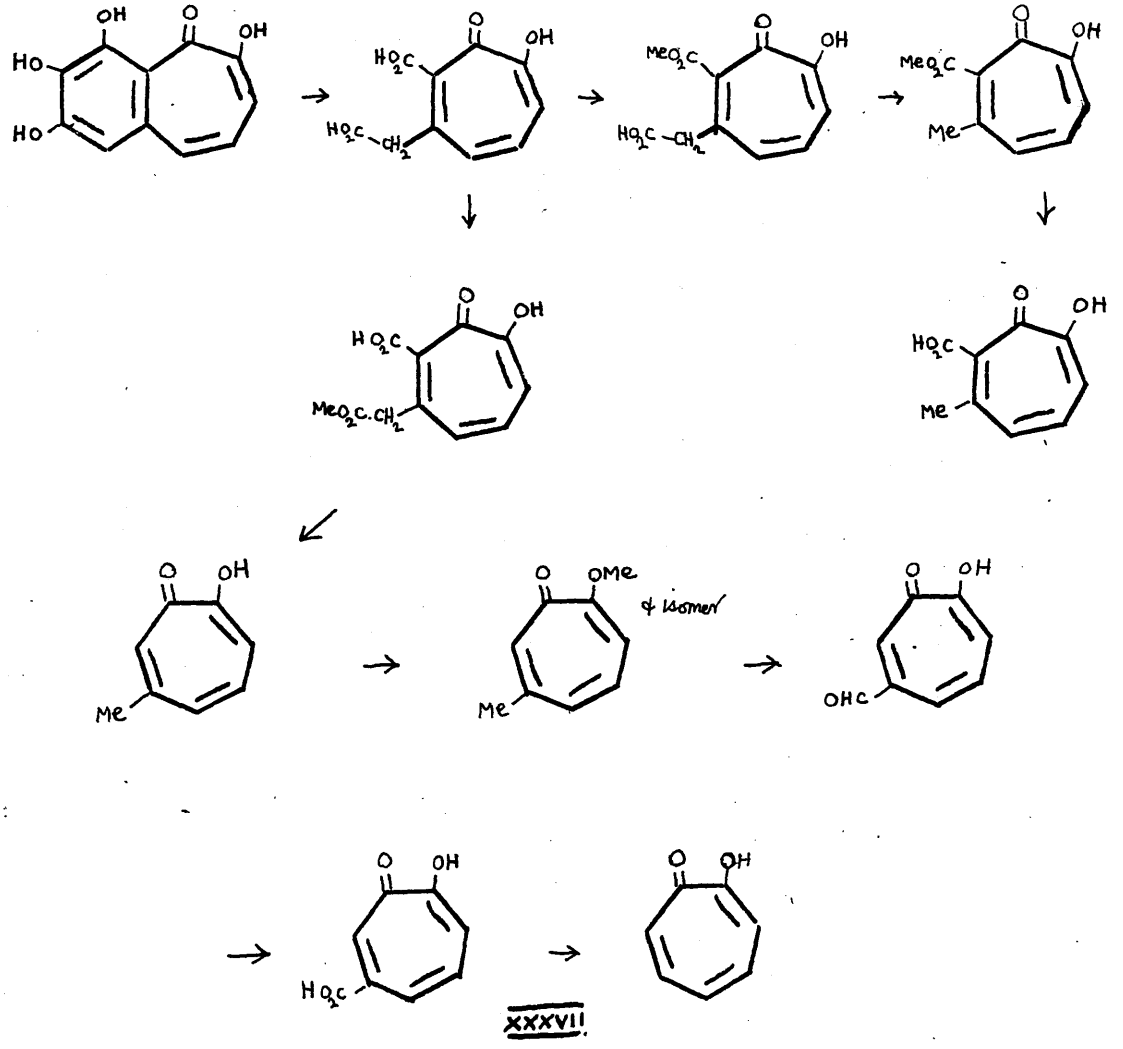
(D). A substituted benzene derivative, or benzene itself, is condensed with an aliphatic diazo compound, and the cycloheptatriene derivative obtained is oxidised to a tropolone. This is the general type of reaction of which the diazoacetic ester condensation, reviewed in the first part of this thesis, is a particular example. Doering and Knox used this route in their novel synthesis of tropolone (39),(54) XXXV. Diazomethane in benzene solution irradiated with ultraviolet light gave cycloheptatriene (yield unspecified) which in turn was oxidised with alkaline per-

manganate to tropolone in 6.3% yield. Bartels-Keith et al. have applied Buchner's diazoacetic ester reaction to certain methoxy-benzenes. They found that bromine in acetic acid converted their cycloheptatriene products to tropolones by simultaneous demethylation and dehydrogenation, and in this way they have synthesised stipitatic acid (55) and a tropolone carboxylic ester (56), XXXVI.



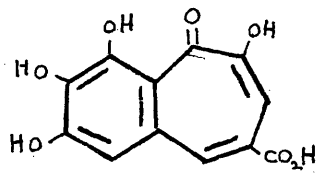
This last condensation suggests a possible modification of Doering's synthesis. If diazomethane were reacted with veratrole and the product treated with bromine as above, tropolone might be obtained with the avoidance of the wasteful oxidation stage.

(E). A naturally occurring tropolone is degraded to a simpler derivative. Purpurogallin, as mentioned previously, is readily available in quantity by the oxidation of pyrogallol. The benzene ring in this tropolone derivative may be oxidatively degraded under mild conditions to a tropolone dicarboxylic acid in 30% yield. Further reactions lead to less complicated derivatives, including tropolone itself (38), as the accompanying diagram illustrates XXXVII.

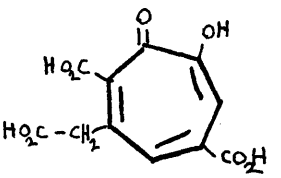


XXXVII

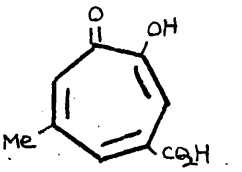
Purpurogallin carboxylic acid XXXVIII is obtained by oxidation of a mixture of pyrogallol and pyrogallic acid (58), and degradation of this product makes available two further tropolone carboxylic acids, IXL, XL.



XXXVIII



IXL.



XL.

Researches carried out in these laboratories by Cook & Somerville have already culminated in a synthesis of $\alpha\beta$-benzotropolone and of a bromine substitution product of tropolone itself. This was the first published synthesis of tropolone compounds (51). As will be shown, these studies have now been supplemented and extended.

Synthesis of Tropolone.

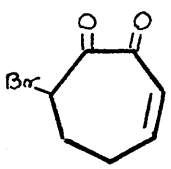
Cook & Somerville prepared their bromotropolone by bromination of suberandione, followed by thermal dehydrobromination (51),(59). This reaction has now been studied in greater detail with special reference to the effects of variation in the bromine concentration.

Bromination of suberandione with one mole of bromine.

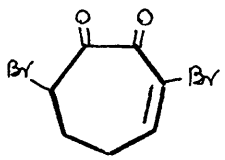
On heating the reaction mixture hydrogen bromide was evolved, much tar was formed, and a dark pungent oil could be isolated, probably XLI. This dissolved in sodium hydroxide with loss of a second molecule of hydrogen bromide, and a poor yield of tropolone was isolated on acidification. As isolation of the product and intermediate was troublesome and tedious, this route was not used for the general preparation of tropolone.

Bromination with two moles. This was the proportion of bromine used by Cook & Somerville. Here again thermal dehydrobromination was accompanied by much tarring if carried

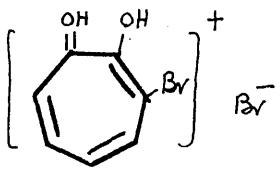
to completion, and a mixture of two monobromotropolones was isolated. Much the larger proportion was Cook & Somerville's bromo compound melting point 103-106°, but a little of an isomer melting 188° (sublimation) was also isolated. It was actually found much more convenient to interrupt the heating process whenever hydrogen bromide evolution showed slight signs of slackening, and then to isolate the sparingly soluble intermediate, $C_7H_5O_2Br_2$ m.p. 168-172° (dec.) which crystallised out on cooling, XLII a or XLII b? . This compound was not a tropolone, but it readily lost hydrogen bromide when dissolved in hydroxylic solvents or better, in hot sodium hydroxide solution, whereby sodium monobromotropolonate dihydrate was isolated as lustrous yellow plates in an overall yield of 26% from the dione. Acidification gave the bromotropolone, m.p. 103-106°.



XLI.



XLIIa



XLIIb

Bromination with three moles. In this case no intermediate could be isolated. When gas evolution had ceased, the solution was concentrated, and a highly crystalline dibromotropolone m.p. 157-158° separated out.

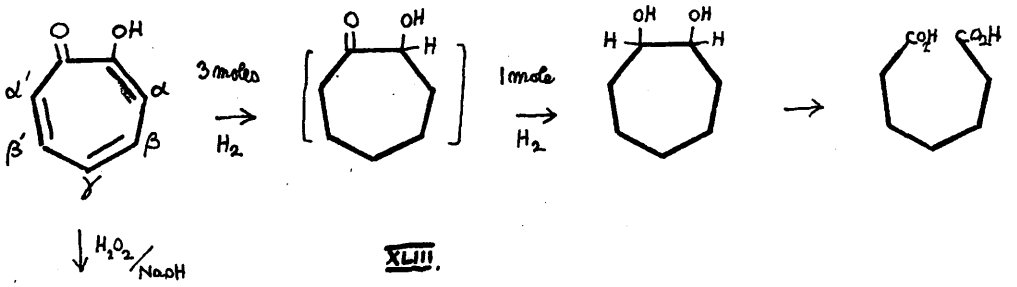
Bromination with four moles of Bromine. This again gave very complex results. When the unheated reaction mixture

was poured into water an oily semisolid precipitated which crystallised from acetic acid m.p. 82-84°. A tetrabromosuberandione was indicated by its analysis and chemical reactions. If however the original mixture was heated with steam in the usual way, much acid vapour and free bromine was evolved, but the resulting dark red syrup was not amenable to crystallisation attempts and was not further dehydrobrominated by alkali treatment. Elevation of its temperature to 130° did however result in the evolution of more hydrogen bromide, and by solution of the residue in alkali, then acidification a tribromotropolone m.p. 122-123° was obtained in poor yield.

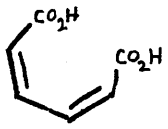
The bromotropolone m.p. 103-106° was available in quantity and attempts were now made to replace the bromine atom by hydrogen catalytically. Success was obtained, but only under rather specific conditions. An alcoholic solution of sodium monobromotropolonate dihydrate absorbed one mole of hydrogen rapidly and smoothly in the presence of palladium charcoal, sodium bromide was formed, and tropolone was readily isolated in 78% yield. Using the free bromotropolone or a distinctly alkaline solution of the sodium salt resulted only in an extremely slow uptake of hydrogen. Tropolone was also obtained by the hydrogenation of sodium dibromotropolonate; reduction in this case was less specific and the final yield was poor.

Tropolone crystallised from petrol in large colourless prisms, m.p. 49-50°: it was apparently stable to strong acids and alkali, but tended to decompose in air at room temperatures. It underwent many reactions characteristic of this class of compound (see p. 6), and several typical derivatives were prepared: a 3:5-dinitrobenzoate, a methyl ether hemihydrate readily soluble in water, a methyl ether picrate, a p-tolylazo derivative, a chloroform soluble copper complex $(tropolone)_2Cu$, a similar red ferric complex $(tropolone)_3Fe$, etc. Tropolone was a weak acid (pK 7.0) and also a weak base, as it formed a crystalline hydrochloride and hydrobromide unstable to hydroxylic solvents. It existed as a monomer in solution, and also apparently in the solid state as it sublimed with the greatest of ease.

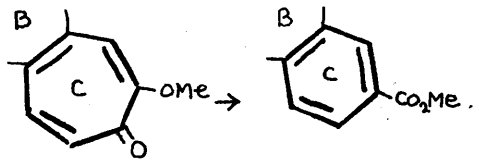
Tropolone absorbed three moles of hydrogen smoothly in the presence of platinum, then a fourth mole more slowly (α-thujaplicin behaved similarly (25)). The waxy mixture of cis- and trans-diols obtained in this way was oxidised to pimelic acid, thus providing rigid proof that the compound possesses a seven membered carbon ring XLIII. Alkaline hydrogen peroxide oxidised tropolone to cis-cis-muconic acid XLIV (cf. the oxidation of stipitatic acid and puberulic acid to itaconic acid).



XLIII.



XLIV.

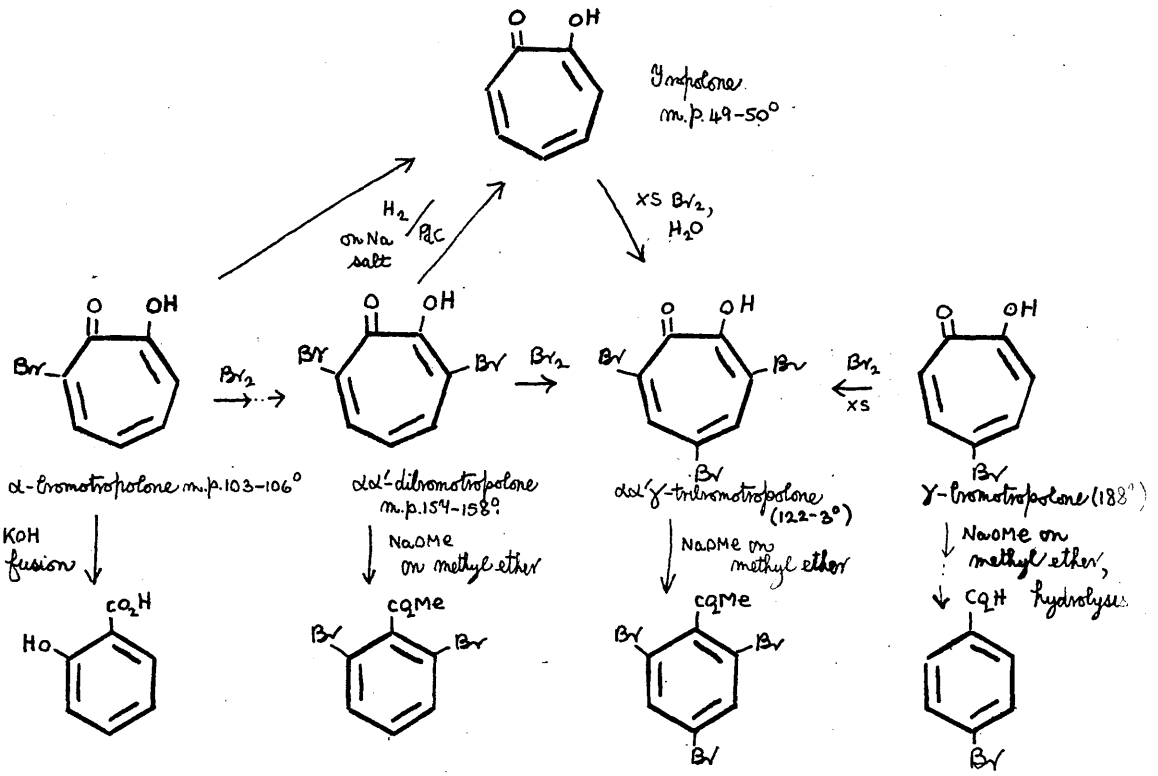


XLV.

The orientation of the four bromotropolones was carried out by rearrangement to the corresponding benzoic acid derivatives. Their interrelation was established and their structures confirmed by further bromination experiments. Tribromotropolone methyl ether isomerised, on heating with methanolic sodium methoxide, to methyl 2:4:6-tribromobenzoate. This reaction, which establishes the structure of the compound as $\alpha\alpha'\gamma$-tribromotropolone, was first described by Santavý (60) who converted colchicine to allocolchichine XLV.

Similarly dibromotropolone was shown to be the $\alpha\alpha'$-disubstitution compound by conversion of its methyl ether to methyl 2:6-dibromobenzoate. Isolation of 4-bromobenzoic acid by hydrolysis of the product from the methyl ether of monobromotropolone m.p. 188° proved this isomer to be sub-

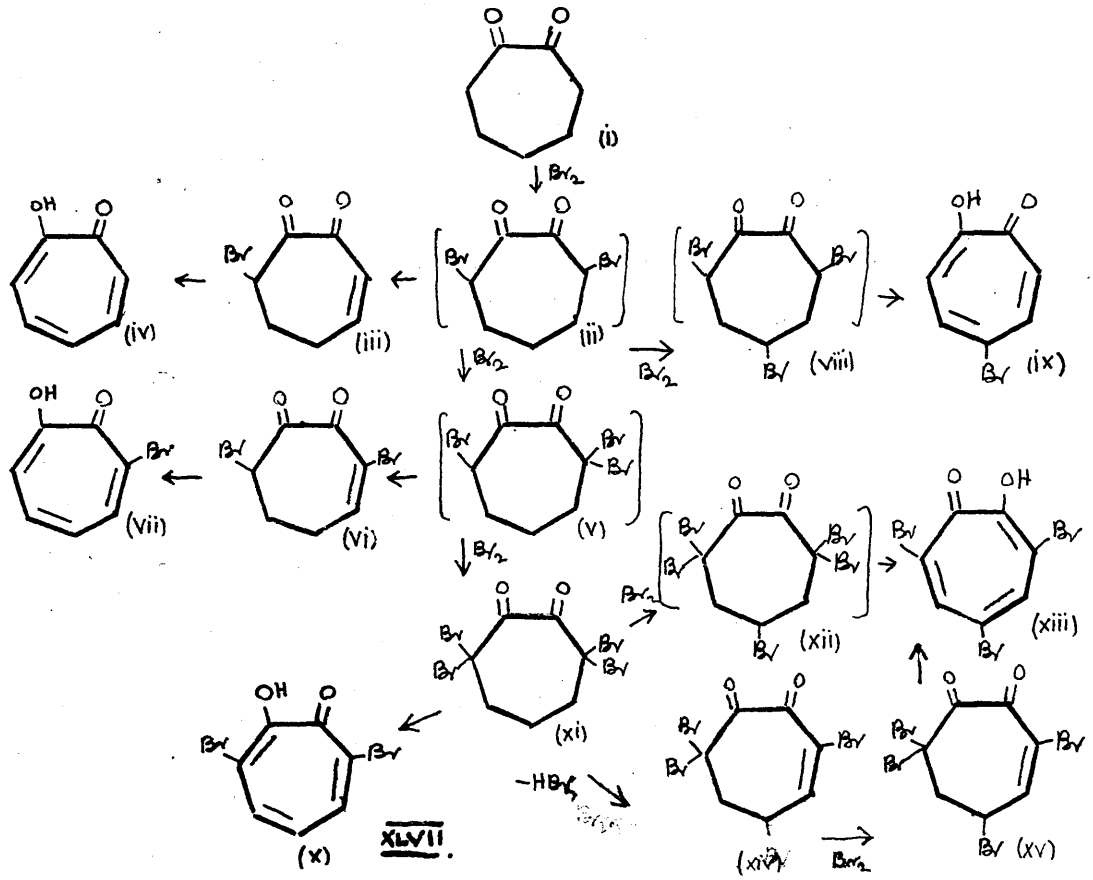
stituted in the γ-position. Successful results were not obtained by sodium methoxide treatment of the other monobromotropolone methyl ether. A little salicylic acid has however been obtained (61) by alkali fusion of the unmethylated compound, and this indicates its structure to be α-bromotropolone. The results of these rearrangements and the further brominations carried out, are summarised in the accompanying diagram XLVI.



XLVI.

These bromotropolones were stronger acids than tropolone itself; they stained the skin yellow, gave bright yellow sparingly soluble sodium and potassium salts, and even showed slight reactivity with soft glass surfaces. They were all stable compounds and the bromine atoms were completely inert to the usual reagents (alkali, silver nitrate, etc.). The results of these investigations on tropolone and the bromotropolones are in good agreement with the findings of other workers (38),(57),(39),(54),(40),(61),(62).

As the orientation of the bromotropolones had been established, it was now attempted to interpret the bromination of suberandione. The following scheme was drawn up:

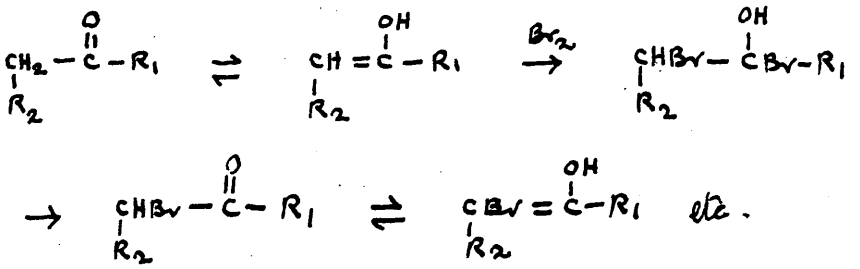


This scheme accounts for the formation of tropolone (reaction with one mole of bromine) (i) → (ii) → (iii) → (iv), α-bromotropolone (i) → (ii) → (v) → (vi) → (vii) and γ-bromotropolone (i) → (ii) → (viii) → (ix) (reaction with two moles of bromine). The formation of αα′-dibromotropolone could come about either by direct bromination of first formed α-bromotropolone, which would certainly give (x) (see p. 21), or by the steps (i) → (ii) → (v) → (xi) → (x). The latter route seems the more reasonable, as, for the steps (v) → (vi) → (vii) to occur in the presence of excess bromine, would require that the free α-position in (v) should be much less reactive than the two unoccupied vic-positions in (ii). In the reaction with four moles of bromine there are again two possible routes: (a) (i) ..... (xi) → (xii) → (xiii). The tetrabromosuberandione m.p. 84° is accordingly (xi). It should therefore be possible to isolate this compound from the reaction with three moles of bromine, and it should decompose to (x). This requires experimental confirmation. (b) Alternatively, (xi) undergoes dehydrobromination to (xiv), which reacts in the allyl position with the excess bromine present, giving (xv), and this decomposes at an elevated temperature to (xiii).

It will have been observed that the product in each case is more highly brominated than the stoichiometric equation would lead us to expect. It must be borne in mind, however, that suberandione is rather unstable to strong acids

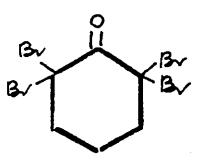
and its available concentration is probably lowered by the formation of tarry byproducts.

According to Bodroux & Taboury (63),(64), bromine reacts with cyclohexanone in carbon tetrachloride to give a tetrabromo compound, which at 125° decomposes to 2:6-dibromophenol. In acetic acid as solvent some 2:4:6-tribromophenol can be isolated from this reaction. These findings bear some resemblance to our results with suberandione. The bromination of ketones is usually assumed to occur by addition to the enol double bond then dehydrobromination:

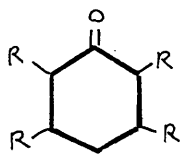


The most reasonable formula for tetrabromocyclohexanone is then XLVIII, which is analogous to (xi). Hassel & Lunde (65) have recently carried out an electron diffraction investigation on tetrachlorocyclohexanone, a compound which they claim to be closely similar to the tetrabromo derivative. Their preliminary results seem to indicate that it possesses the structure XLIX (R = Cl). Even if further evidence is found which confirms this formula for both the tetrachloro and the tetrabromo compound, it would be rash to assume then that tetrabromosuberandione is L. Substitution of hydrogen

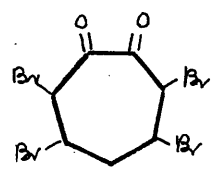
by the second pair of bromines (assuming α and α' to be the first positions attacked) to give L. and (xi) respectively would come about by two different mechanisms, in the first case, by direct substitution and in the second, by addition of bromine to an enol double bond. Thus two ketones of the type LI, which exist in the enol form to very different extents, might give rise to different products on further bromination. The possible effect of the smaller ring size in cyclohexanone must also be considered. It may be that in this case a vic-dibromo structure is favoured rather than a gem-structure, by steric factors which do not arise in the larger suberandione ring. Such an interpretation is consistent with recent ideas on the conformation of the cyclohexane ring (86).



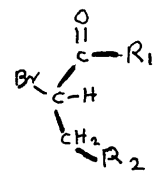
XLVIII.



XLIX.



L.



LI.

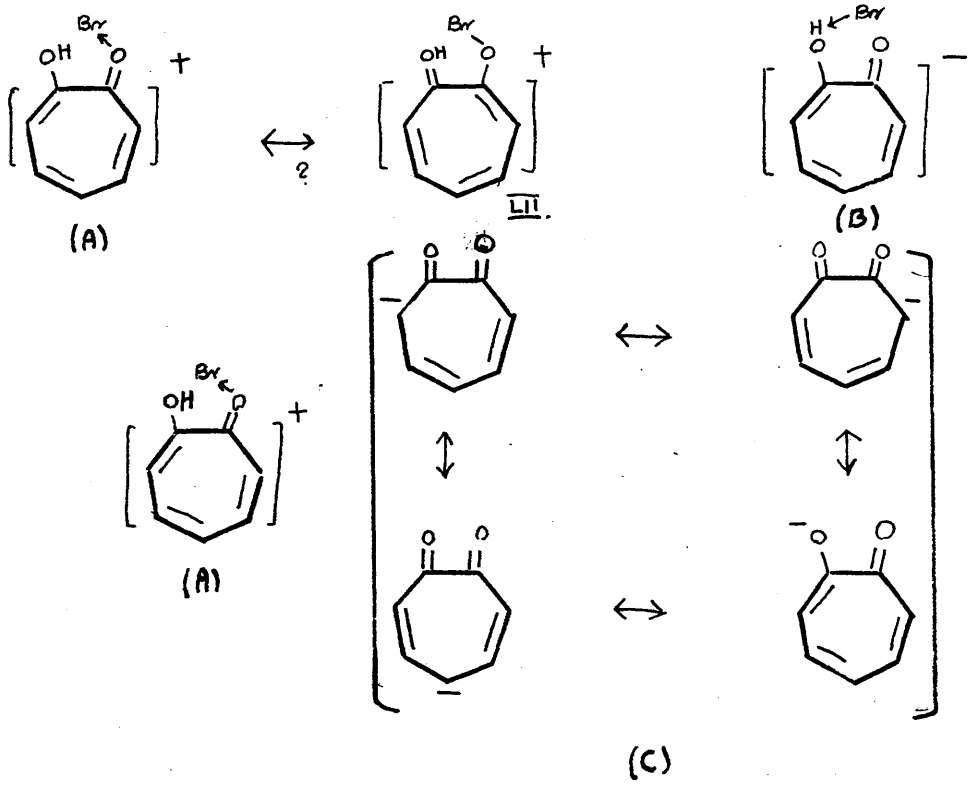
An alternative interpretation of the reaction between bromine and suberandione is one which involves primary formation of tropolone then further bromination by substitution. The requirement of alkali to bring about the stage (iii) (iv) is evidence against such a mechanism, and indeed it has been proved unsatisfactory by bromination experiments on tropolone itself.

Addition of bromine to tropolone in dry acetic acid brought about the immediate precipitation of a bright scarlet complex, which analysed for $(C_7H_6O_2)_2Br_2$. At temperatures above 110°, one mole of hydrogen bromide was evolved and a residue obtained consisting of a mixture of tropolone, α-bromotropolone, $\alpha\alpha'$-dibromotropolone and (probably) γ-bromotropolone. Solution of the complex in hydrolytic solvents gave a similar mixture of products.

These results have been explained in the following manner. Bromine reacts with two molecules of tropolone to form the ionic complex (A)(B). The cation (A) is regarded as being formed by the donation of the carbonyl oxygen lone pair to the unoccupied 4p orbital of a bromonium cation. It should be compared with the tropolonium cation VIII postulated to account for the solubility of this class of compound in strong acid. (A) may be stabilised by resonance LII, but necessarily to a less extent than in the case of VIII, because of the difference in electronegativity between hydrogen and bromine. In the anion (B) hydrogen bonding is conceived to occur between the hydroxylic hydrogen and the bromide ion, giving a structure analogous to the well-established hydrofluoride ion (F - H F$^-$). Thermal treatment is assumed to result in conversion of (B) to the mesomeric anion (C) with loss of hydrogen bromide. Decomposition of (A) regenerates free tropolone, and bromonium cation which reacts

with anion (C) at the nucleophilic α - and γ -positions. In hydroxylic solvents the ease of formation of hydroxonium ion by interaction of anion (B) with a water molecule would be the driving force for the same decomposition route and could give rise to the same products.

The formation of highly coloured complexes with halogens has been observed with a number of polycyclic aromatic compounds (66). Analyses of some of these complexes suggest a structure comparable to that suggested in the case of tropolone. The ability of many such polycyclic compounds also to form oxonium salts is indicated by solubility in strong mineral acids such as sulphuric acid, the resultant solutions frequently being coloured.



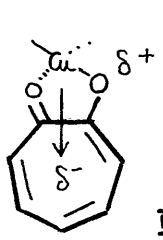
From molecular orbital calculations, Dewar (67) has predicted that electrophilic substitution of the tropolone molecule should occur almost exclusively in the γ-position. As, in general, electrophilic substitution is believed to occur through interaction of a molecule with a cation formed by heterolytic fission, the interpretation given above is not confined to bromination reactions. Even if no complex is isolated during a substitution reaction, we cannot be sure that it did not have a transitory existence and took part in the reaction mechanism. Most substitution reactions of tropolone could thus be reaction between a cation X^+ and an anion (C), and from them we could make no true assessment of the predictions of Dewar.

The bromination of cupric tropolone in non-hydroxylic solvents should follow the equation:

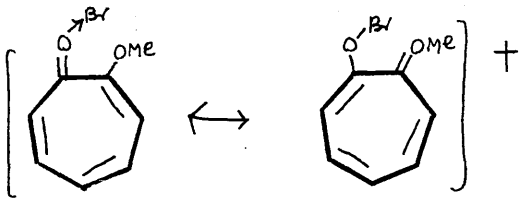
$$(C_7H_5O_2)Cu + 2Br_2 \rightarrow CuBr_2 + 2C_7H_5O_2Br$$

The structure of the molecule might be expected to preclude complex formation of the type (A)(C) and we could envisage reaction in the following steps: (1) heterolytic fission of the bromine molecule and attack on the ring by bromonium cation Br^+, leading to (2) formation of a hydrogen ion H^+ which combines with Br^-. (3) Hydrogen bromide reacts with the cupric copper, cupric bromide should then precipitate leaving the brominated tropolone in solution. The actual

substitution should thus follow the normal course assumed by Dewar. However, we are not necessarily dealing with the same ring as in the tropolone molecule; as copper forms positive ions with the loss of electrons, the copper atom might be expected to activate the two rings by the inductive and mesomeric effects LIII. The mesomeric effect would enhance the intrinsic reactivity of the ring carbon atoms but would not effect their relative reactivity as compared with the carbon atoms in free tropolone. The mesomeric effect on the other hand falls off with distance and should preferentially enhance the reactivity of the α-positions. (See also p. 46).



LIII.



LIV.

Addition of two moles of bromine to cupric tropolone in chloroform produced a light black precipitate (probably anhydrous cupric bromide (69)), which on addition of water gave a blue aqueous layer. This in turn rapidly reacted with the bromotropolones formed by ring substitution:

$$(C_7H_5O_2)_2Cu + 2Br_2 \rightarrow 2\,C_7H_5O_2Br + CuBr_2$$

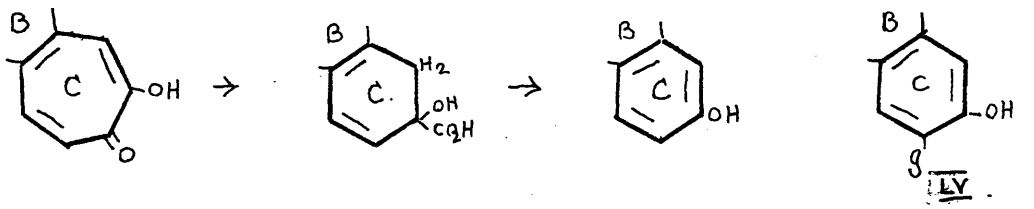
$$\text{Addition of water;} \rightarrow (C_7H_4O_2Br)_2Cu + 2H_3O^+ + 2Br^-.$$

The bromotropolone material, liberated by hydrogen sulphide, proved to be a mixture of the γ- and α-isomers in the very approximate ratio of 2:1. This experiment does then give some support to Dewar's contention that the γ-position should be the most reactive, if the possible modification caused by the presence of the copper atom is borne in mind.

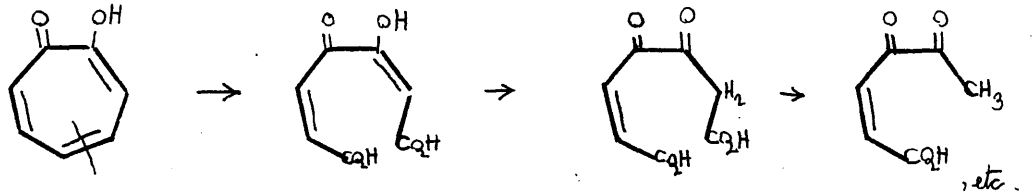
In the hope of obtaining the pure γ-monobromo derivative in larger quantity and relatively uncontaminated by position isomers, the bromination of tropolone methyl ether hemihydrate was now examined, but in this case also a complex was obtained. The yellow oil which immediately separated underwent thermal dehydrobromination to a mixture of free bromotropolones and (probably) methyl ethers in which the presence of the α- and γ-isomers was established. Bromination of anhydrous tropolone methyl ether gave a different complex, a scarlet oil, but no homogeneous product could be isolated on thermal dehydrobromination. Replacement of the tropolone hydroxyl by methoxyl does not prevent the possible formation of a cation LIV corresponding to (A); however, a methyl ether anion similar to (B) would seem highly improbable as this would require a hydrogen bond from a methyl hydrogen. In any case as no analyses were possible with these unstable oils, it would be rash to propose structures for them. In the case of the hemihydrate at least, the actual substitution is accompanied by partial or complete

hydrolysis of the methoxyl group, which is a further complicating factor.

A black, crystalline complex, $(C_7H_6O_2)_2I_2$, apparently analogous to (A)(B) was readily prepared by treatment of aqueous tropolone with iodine/potassium iodide solution. As the reaction conditions imply, it was stable to water and hydroxylic solvents. However, it dissociated into its components readily on sublimation and slowly even under atmospheric conditions. Further experiments proved tropolone very resistant to iodination by substitution. With excess iodine in alkaline solution (i.e., hypoiodite) degradative reaction took place, and 2:4:6-triiodophenol was finally isolated (cf. (54)). Reference to page 7 will indicate that this rather curious reaction is known to occur with at least one other tropolone derivative, namely colchiceine, which is converted to N-acetyl-iodocolchinol LV by cold iodine/alkali (70),(11).



From this reaction with tropolone, iodoform was also isolated. Its yield varied with the experimental conditions, and it was possibly formed by a side reaction, perhaps some such mechanism as LVI:

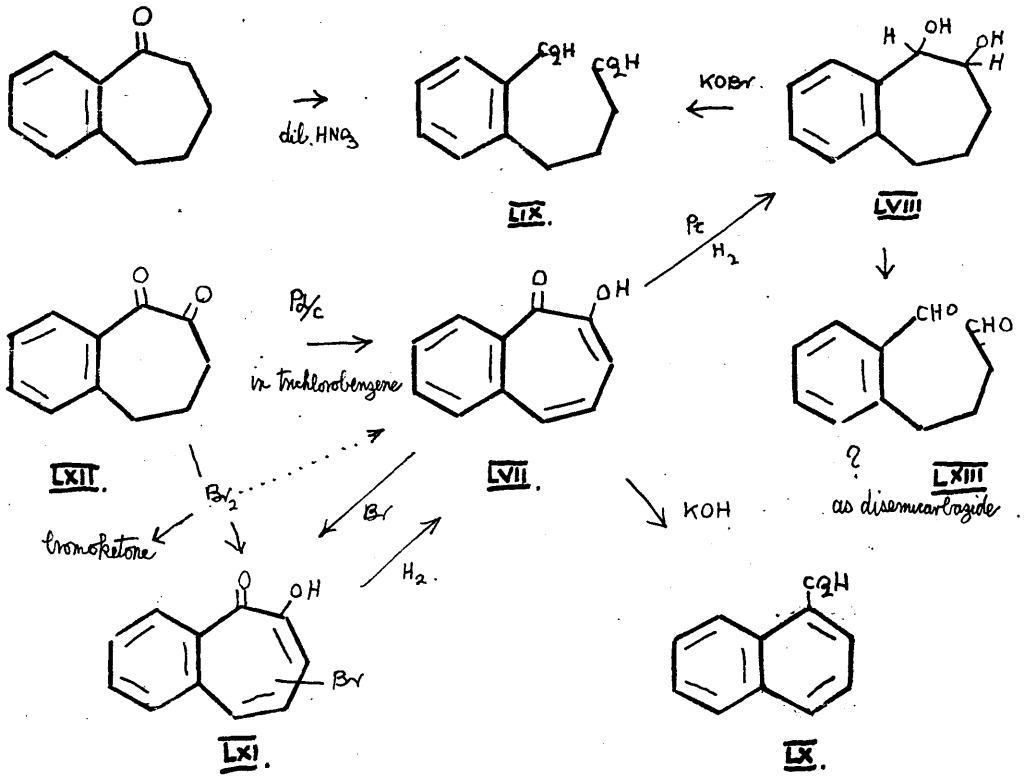


LVI.

According to Birkinshaw et al. (13) stipitatic acid also was found to give an iodoform reaction, and recently Booth & Saunders have reported other compounds which do not contain the acetyl group yet give this diagnostic reaction (71). In these cases primary oxidation to an acetyl or acetoacetic acid intermediate, as in LVIII, can be visualised.

Cook & Somerville supplemented their synthesis of αβ-benzotropolone LVII (51),(p.12.) with investigations on the properties and reactions of this compound. Its structure was proved by hydrogenation to the diol LVIII, followed by oxidation with hypobromite to the known γ-2-carboxyphenyl-butyric acid LIX. Alkali fusion brought about rearrangement to α-naphthoic acid LX. αβ-Benzotropolone was a typical tropolone and gave a red ferric chloride colour, a yellow sodium salt, a green crystalline copper complex, and coupled with diazotized arylamines. No carbonyl reactivity could be detected. A product, m.p. 142-144°, possibly a monobromobenzotropolone, was obtained by reaction with one mole of bromine LXI. By catalytic hydrogenation it was partially converted back to LVII. Some of this same bromo compound, together with a bromo-ketone and sometimes a little

LVII, could also be obtained by treatment of suberandione with one mole of bromine.



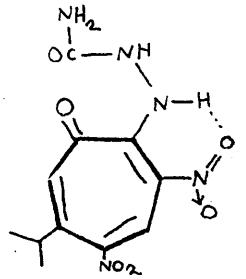
It was felt that this work might profitably be extended, and the successful results obtained from the bromination of suberandione encouraged us to examine further this reaction with the higher benzologue. A repetition of Somerville's work (59) on the bromination of benzsuberandione with one mole of bromine gave no solid material and the skin irritant properties of the reaction mixture discouraged a rigorous examination. With two moles of bromine, slow evolution of hydrogen bromide occurred even in the cold, and

a large mass of yellow prisms gradually deposited. This product melted at 143° and appeared to be identical with LXI. Its analysis and chemical properties proved it to be a monobromobenzotropolone. Trial experiments showed the best conditions for the hydrogenolysis step LXI → LVII to be in ethanol solution with excess triethylamine in the presence of palladised charcoal. By this method αβ-benzotropolone was obtained in an overall yield 26.8% from benzsuberone. Thus, this route doubles the yield previously obtained from benzsuberone (12.8%) and also avoids the tedious catalytic dehydrogenation in trichlorobenzene (LXII → LVII).

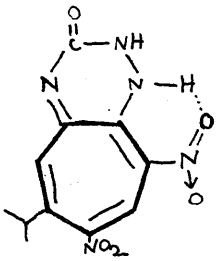
αβ-Benzotropolone melted 85-86°, and showed the tropolone reactions as previously described. It gave an orange, crystalline picrate $(C_{11}H_8O_2)_2C_6H_3O_7N_3$, and a 3:5-dinitrobenzoate. Its acetate was an oil, which hydrolysed rapidly with acid or alkali. No solid hydrochloride was obtained with dry ether/hydrogen chloride: evaporation of the yellow solution left an orange oil from which benzotropolone was recovered by application of vacuum. Yellow solutions were also obtained in concentrated mineral acid, the free benzotropolone being recovered on dilution. These latter reactions, and even the acid-precipitation of the compound from its alkali salts, were generally accompanied by some slight tar formation. Thus, in general, benzotropolone appeared to be rather less stable to acids and possibly also to alkali, than tro-

polone itself. It did not react with ethereal diazomethane, but a liquid methyl ether was obtained by treatment with methyl p-toluenesulphonate/alkali.

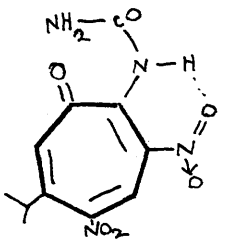
Tarbell et al. (43) have obtained a 2:4-dinitrophenylhydrazone from βγ-benzotropolonephenyl ether XXV. This is the only case so far reported of true carbonyl reactivity shown by a tropolone derivative. The Japanese workers claim (81) that dinitrohinokitiol reacts with semicarbazide to form a heterocyclic compound LXIV via a rather unstable intermediate LXV. With urea they obtain a product LXVI similar to LXV and reaction also occurs with o-phenylenediamine giving LXVII. As the first step in these reactions is really amide formation, followed in the case of LXIV and LXVII by ring-closure to a six-membered ring, these cannot be classed as straightforward reactions with a carbonyl bond. αβ-Benzotropolone methyl ether has been found to react slowly with hot 2:4-dinitrophenylhydrazine/sulphate in alcohol to give a deep red micro-crystalline product m.p. 242-3°. This might be the orthodox 2:4-dinitrophenylhydrazone LXVIII, the hydrazo compound LXIX formed by replacement of the methoxyl (cf. LXIV and LXV), or the azo compound LXX, the oxidation product of LXIX.



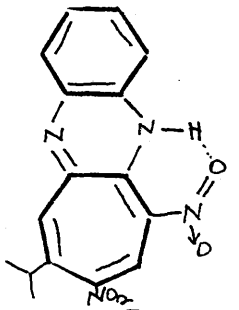
LXV.



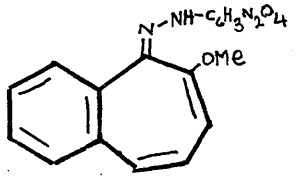
LXIV.



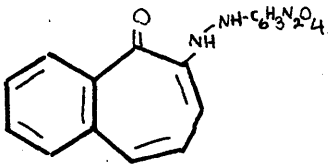
LXVI.



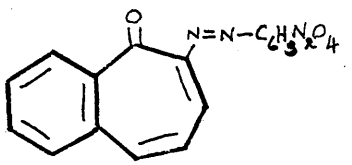
LXVII.



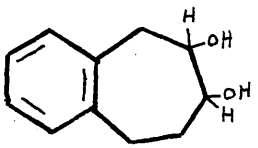
LXVIII.



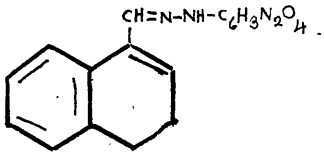
LXIX.



LXX.



LXXI.



LXXII.

This compound has been analysed, but the percentage compositions of LXVIII → LXX are rather similar, so that it is not possible to make a clear decision on its structure from this evidence alone. However, an examination of its visible absorption spectrum and a methoxyl determination should solve this problem.

Somerville oxidised benzsuberandiol with periodate and succeeded in preparing a semicarbazide from the reaction mixture, which analysed approximately for the disemicarbazide of LXIII. Tarbell et al. obtained a compound by a similar oxidation of their isomeric diol LXXI, followed by 2:4-

dinitrophenylhydrazine reagent treatment, to which they have assigned the structure LXXII, on the basis of a nitrogen determination. The ring closure of a dialdehyde to a cyclic unsaturated mono-aldehyde, which this formulation implies, is known to occur with butane-1:4-dialdehyde (87), the medium, however, being alkaline. As repetition of the hydrogenation steps LXII → LVIII and LVII → LVIII has not so far given a clearcut reduction to the mixture of solid cis- and trans-diols obtained by Somerville, no further evidence has been obtained on the structure of the periodate oxidation product.

αβ-Benzotropolone underwent bromination via the mono-bromo compound LXI to a dibromobenzotropolone. The positions of the bromine atoms in these two compounds are not as yet known, but they are probably the α′- and αγ-substituted derivatives. With hydrogen peroxide in alkali slow oxidation occurred giving o-carboxycinnamic acid, the reaction corresponding exactly to the conversion of tropolone to cis-cis-muconic acid.

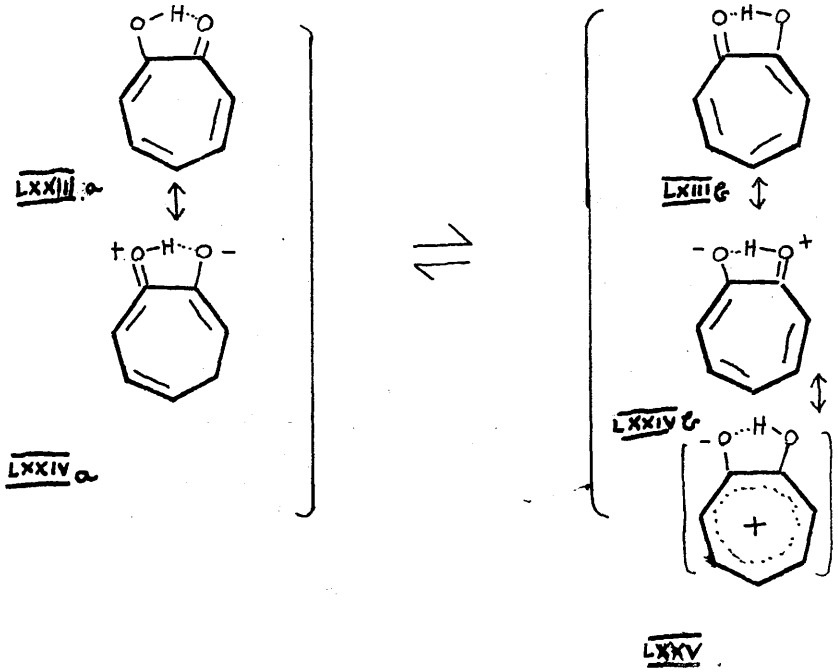
As far as can be gathered from the brief description of its properties (43), βγ-benzotropolone appears to be not dissimilar to our isomer. In the following table, tropolone and αβ-benzotropolone are compared.

	Tropolone	αβ-Benzotropolone
m.p.	49-50°	85-86°
pK (30% Ethanol)	7.3	9.5
Stability to alkali fusion	Rearranges 230-5° (54)	Rearranges 180-5° (59)
Behaviour with strong mineral acids	Dissolves: colourless solution	Dissolves: yellow solution
Treatment with ether/hydrogen halide	colourless solid	yellow oil
Reactivity with ethereal diazomethane	Brisk	Negligible
Copper salt	Highly stable	Slowly decomposes above 80°.
Arylazo compounds	Reasonably stable	Decompose readily above 60°.

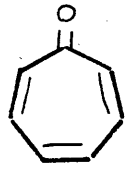
Nozoe et al. (92) have recently repeated the synthesis of αβ-benzotropolone using Cook & Somerville's method. They obtained a monobromo compound, but surprisingly no dibromo derivative, even with excess bromine. From benzotropolone they claim to have isolated a methyl ether m.p. 82.5-83.5° by ethereal diazomethane treatment (melting point depression with starting material, no ferric chloride colour). By the same method we obtained a product m.p. 78-80°, but the negative results of a methoxyl determination, and subsequent mixed melting point determinations with benzotropolone itself, proved that no methylation had occurred in this case.

These investigations have now given a fuller picture of tropolone chemistry, and together with recent work published in the literature make feasible some interpretation of the properties shown by this interesting group of compounds.

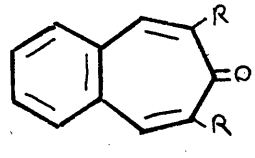
The stability of tropolone. Quite soon after Dewar first suggested the tropolone structure, his further calculations proved resonance of the type LXXIIIa ↔ LXXIIIb to be improbable (10), and subsequent infrared measurements (84) give a picture of the tropolone molecule in which the hydrogen atom oscillates rapidly between the oxygens, but with ionised structures such as LXXIVa and LXXIVb, making important contributions. We can also draw other feasible structures with the positive charge on the ring LXXV



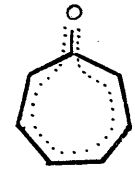
Two independent syntheses of cycloheptatrienone or tropone LXXVI (72),(73) have now been published. These seem to indicate that many of the properties characteristic of tropolones are really intrinsic to the simple hydroxyl-free ring. Thus tropone forms a crystalline hydrochloride, pircylsulphonate and picrate, shows no carbonyl reactivity, forms bromo-substitution products via unstable addition compounds, and couples with diazotized arylamines. The $\gamma\gamma$-benzocycloheptatrienones ("benzocycloheptadienones") (LXXVII, R = H, -Me, Et, $-CO_2H$, -Ph) have been known since 1909 (74), (75), and these compounds also show no carbonyl reactivity. Little is known concerning their other properties, except that the parent compound (R = H) forms a dibromide (m.p. 204°) by addition in carbon disulphide solution. This was reported to give a potassium bromide precipitate with alcoholic potash but no details of the product were given. Another compound (m.p. 124°, not examined further) was also obtained from the bromination (75). Dibenzcycloheptatrienone (82) on the other hand, does show some carbonyl reactivity.



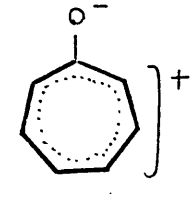
LXXVI



LXXVII.

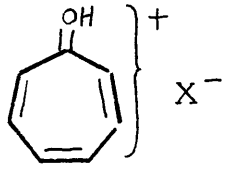


LXXVIII.

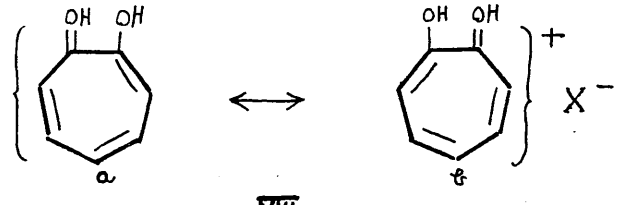


LXXIX.

The stability of tropolone in different media can be ascribed to different factors. In neutral media it is largely the intrinsic stability of the tropone ring, which has aromatic properties probably because the π -electrons of the ring carbon atoms and the carbonyl bond form a closed conjugated system LXXVIII. Excited structures LXXIX can also be drawn, corresponding to LXXV. The stability in acid media (e.g., oxonium salt formation) is also a property of the fundamental tropone nucleus LXXX, although the tropolonium ion probably acquires additional stability by resonating between the two structures VIIIa-b. It is only in alkaline ~~stable~~ media that the hydroxyl function of tropolone, which permits the formation of the tropolonate ion VII, has special significance.



LXXX.

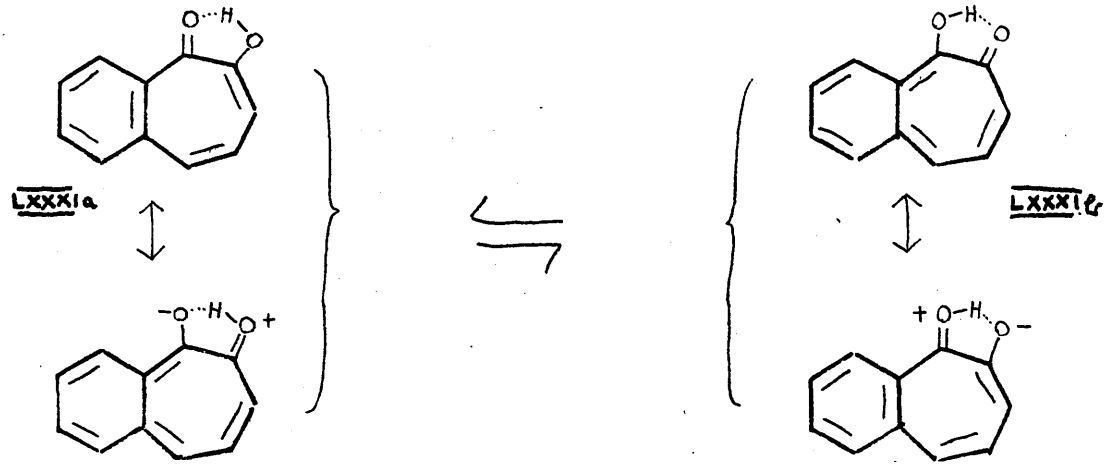


VIII.

The acidity of tropolones. $\alpha\beta$-Benzotropolone is a distinctly weaker acid than tropolone itself. An examination of the following table of pK values would seem to suggest that the larger size of the aryl nucleus should have little effect on the acidity:

Substance	Solvent	Temperature	pK	Reference
Acetic acid	water	18°	4.8	(76), etc.
tropolone	water	20°	7.0	(44)
	30% ethanol	20°	7.3	
αβ-benzotropolone	30% ethanol	20°	9.6	
phenol	water	20°	10.0	(77)
α-naphthol	water	20°	9.8	(79)
	50% ethanol	25°	11.0	(78)
β-naphthol	water	20°	9.9	(79)
	50% ethanol	25°	11.0	(78)
α-anthrol	water	20°	9.9	(79)
β-anthrol	water	20°	9.9	(79)

A comparison between the structures of tropolone and the αβ-benzologue reveals a significant difference. We can draw tautomeric forms of benzotropolone corresponding to LXXIII,a ⇌ b ↔ LXXIV,a ⇌ b. However, the benzene



ring in formulae LXXXIIa and LXXXIb has an o-quinoid structure in which it cannot resonate between two kekule forms. These formulae should therefore make a smaller contribution to the structure of the molecule. (In the extreme case, where the acid hydrogen is replaced by an alkyl group, the molecule can exist in only one unexcited form, as in the isomer corresponding to LXXXIb the o-quinoid structure would be "fixed".) This effect may in some way be responsible for the lower acidity of benzotropolone.

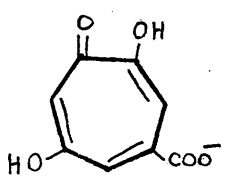
According to Aulin-Erdtman (85), the three pK values of stipitatic acid are 3.5 or lower, 5.8 and 9.7. An examination of the ultraviolet absorption at the three different equivalence points has revealed that the typical spectrum of the tropolonate ion (cf. p. 49) is shown only by the most alkaline solution (i.e., on neutralisation of the third acidic hydrogen). This leads to the conclusion that the order of acidity is carboxyl > ring hydroxyl > tropolone hydroxyl. This result is rather unexpected as it has been customary to consider the acidity of tropolones to be due especially to the unique properties of the olone system, rather than to the aromatic nature of the ring. This, of course, infers that hydroxyl groups in β - or γ -positions should be less acidic than the tropolone hydroxyl.

Accepting this evidence from light absorption, the spectrum at the first equivalence point is that of LXXXIII,

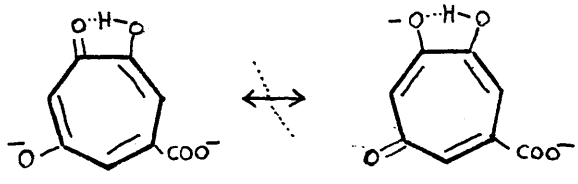
and the second, of LXXXIVa. As these two curves are similar in type, resonance LXXXIVa ↔ b cannot occur. It is surprising that LXXXIV should be more stable than the resonating anion LXXXV.

A similar examination of the spectra and pK values with puberulic acid (85) has shown that here also the tropolonate spectrum is not developed until the final acidic hydrogen is neutralised. This case is further complicated by the possibility of four tautomerides LXXXVI, so that the position of the -olone system cannot be fixed with certainty.

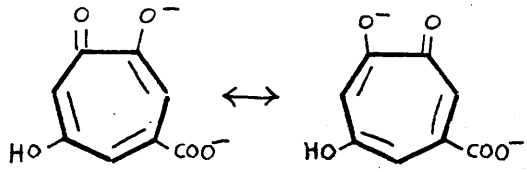
These discoveries lead to a consideration of the three possible iso-tropolones LXXXVII. These structures present as many intriguing possibilities as tropolone itself, for tautomerism, which could not occur in the solid state, becomes possible on solution in an ionising solvent, e.g., LXXXVIII, and we can draw resonating anions and cations, e.g., IXC, corresponding to VII and VIII (but c.f., LXXXIVa, b).



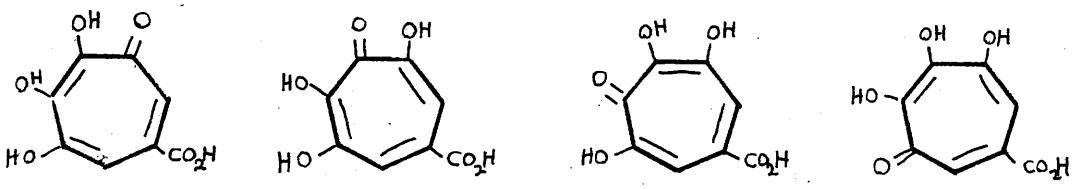
LXXXIII.



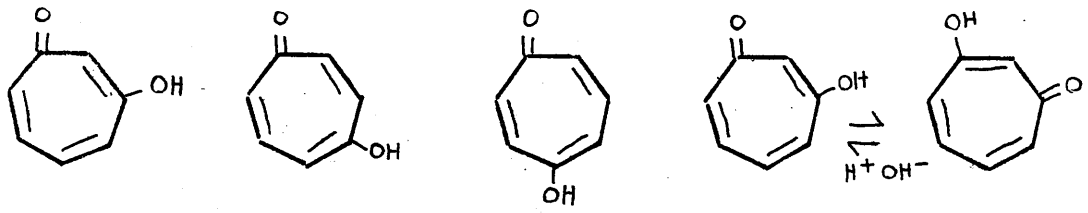
LXXXIVa ↔ LXXXIVb



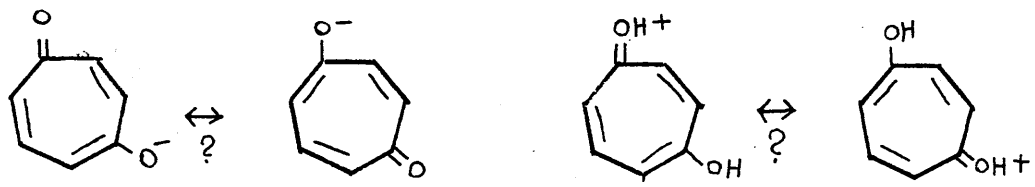
LXXXV.



LXXXVI.



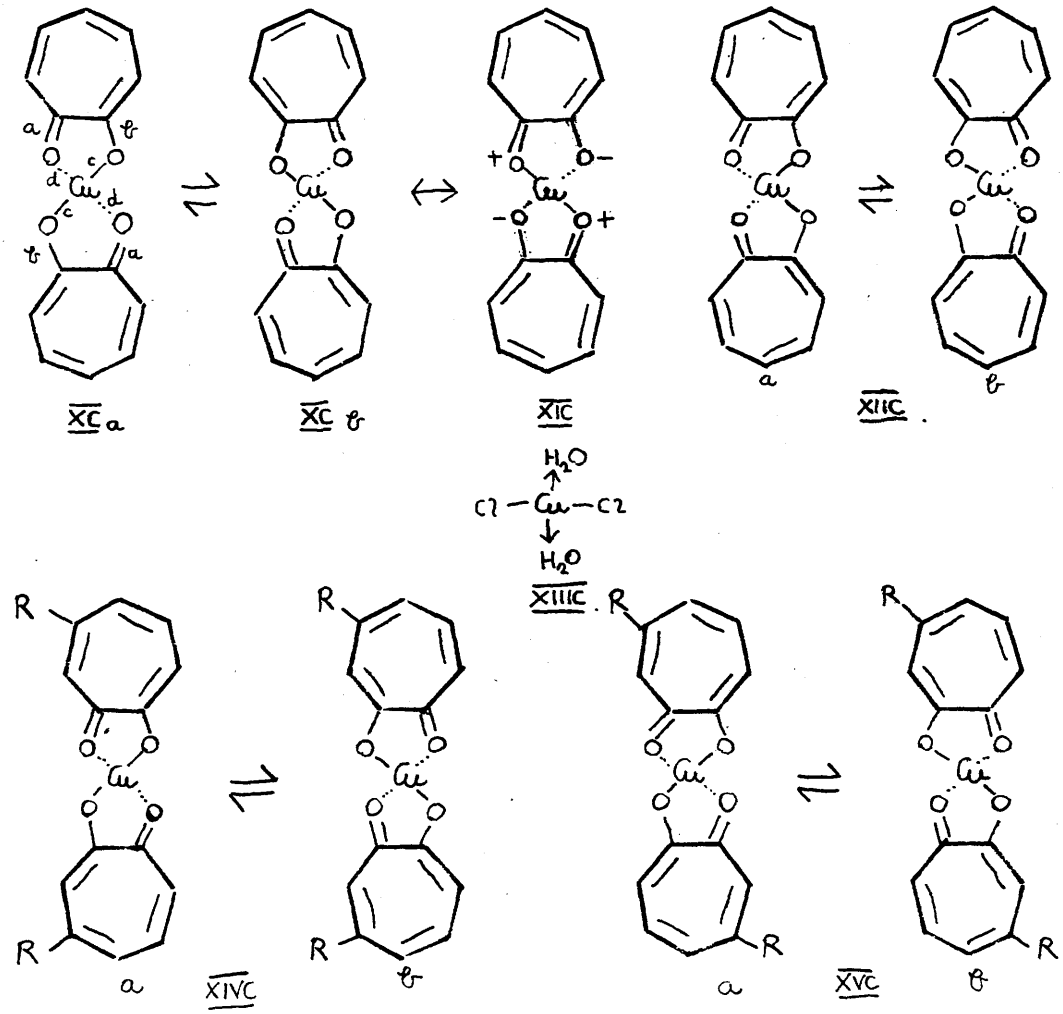
LXXXVII. LXXXVIII.



IXC.

Chelated complexes of tropolones. An X-ray crystallographic examination of cupric tropolone (68) shows it to have the structure XCa. Bond lengths a and b are different as also are bond lengths c and d. This would suggest that

resonance between XCa and XCb could not occur, as the change from one form to the other involves displacement of the oxygen atoms. Tautomerism between these two forms is, however, possible, and we can also postulate resonance structures such as XIC (cf., LXXIVa, b) which would enhance the stability of the molecule. Existence of tautomerides XIICa, b seems unlikely as planar complexes of quadricovalent copper and such compounds as $Cu.Cl_2.2H_2O$, XIIIC, occur in the trans configuration(99).



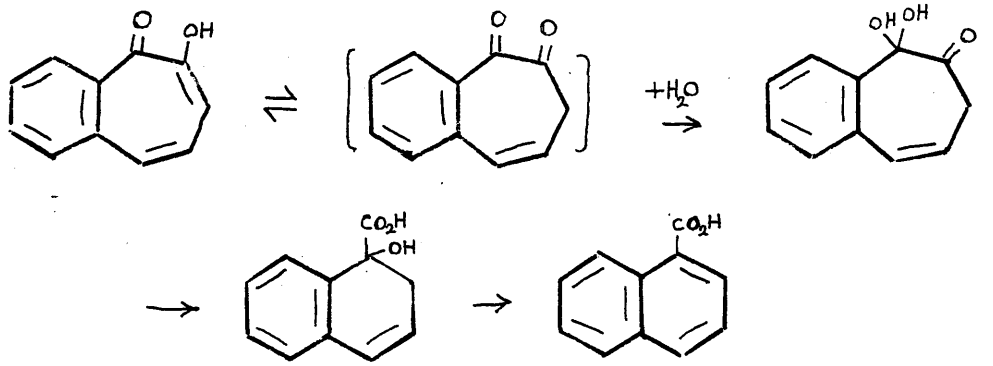
In the case of an unsymmetrically substituted tropolone, there is the possibility of two cis-substituted tautomerides XIVC a,b (equivalent) and two trans-substituted XVC a,b (non-equivalent). However in the latter case, the influence of R and also intermolecular forces, might lead to the detection of only one trans tautomeride in the crystalline state. With α/β-benzotropolone we should expect only a trans isomer, as the cis molecule involves either cis double bonds (cf., XIIC a,b) or occurrence of one benzotropolone group in the "improbable" structure LXXXI b. In tropolones with a large α-group steric factors might permit the existence of only a trans isomer.

According to Nozoe (80),(81) hinokitiol XVII "formed neutral inner complex salts of formula $(C_{10}H_{11}{=}O{\rightarrow}O{-})_3M^{III}$ or $(C_{10}H_{11}{=}O{\rightarrow}O{-})_2M^{II}$ with trivalent metals such as Fe, Cr and Co, as well as with divalent metals such as Cu, Ni, Mn, Cd, Zn and Mg. The majority of these complex salts give sharp melting points, are soluble in organic solvents and insoluble in water. Divalent metal salts further combine with pyridine, quinoline and aniline and give crystalline compounds of formula $(C_{10}H_{11}{=}O{\rightarrow}O{-})_2M^{II}{\leftarrow}B$ ".

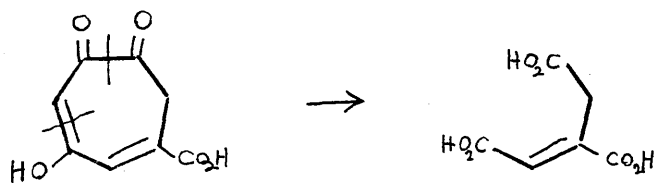
Rearrangement of tropolones to benzene derivatives.

The already mentioned conversion of tropolones by hypoiodite to iodophenols has been interpreted as a benzilic acid re-

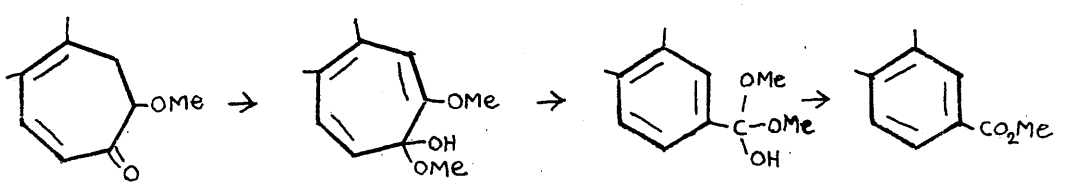
arrangement followed by oxidation and halogenation (11) (but cf., (54)). Benzilic acid rearrangement, which is a general reaction of α-diketones and the related diosphenols, also explains the conversion to benzoic acid derivatives by strong alkali (8)



It is interesting that this reaction can be interpreted by attack on the diketone form of the molecule. The mild oxidation of the mould tropolones is also more easily represented by attack on such a structure, e.g.,



A slightly modified reaction mechanism explains the rearrangement of the methyl ethers by sodium methoxide (11) (cf. also (81)).



The absorption spectra of tropolones (pages 91-94)

The spectrum of tropolone in water or ethanol shows a region of strong absorption circa 240 mμ, a deep trough at 270 mμ and a broad weaker band between 310 and 370 mμ. Fine structure is revealed in this last region when an examination is carried out in cyclohexane solution. The spectra of most substituted tropolones so far examined have a broad similarity to that of the parent compound (e.g., (21),(85)).

Distinct changes appear when the spectrum of tropolone is measured in alkaline solution. The broad region between 310 and 370 mu is now split into two distinct bands, and there is some slight structure developed in the higher band. Dewar predicted such effects in the tropolone spectrum from molecular orbital calculations (67).

The spectra of the methyl ethers are similar to the free acids, indicating no profound structural differences between the two. (The loss of fine structure in the spectrum of dibromotropolone methyl ether is perhaps connected with the steric effect of the two α-bromine atoms.)

Experimental.

Ethyl N-methylcarbamate was prepared from ethyl chloroformate as described in Organic Syntheses (88). It was found convenient to work on $2\frac{1}{2}$ times the quantities recommended. The product was obtained in about 90% yield, and was converted to nitrosomethylurethane (89). After removal of solvent it was sufficiently pure for use in the following reaction, without vacuum distillation. Yield, 70-80%.

Cycloheptanone was prepared by the method of Kohler, Tishler, Potter & Thomson (90). To 170 c.c. dry cyclohexanone in 170 c.c. methanol, containing 0.6 g. anhydrous sodium carbonate, was added all at once, about 5 c.c. nitrosomethylurethane. After an induction period of 2 minutes, there was a rise in temperature and evolution of nitrogen. The temperature was kept at 20-25°C by occasional additions of ice to a surrounding water bath, while the remainder of 204 g. nitrosomethylurethane was dropped in slowly, over about 2 hours. Efficient stirring was maintained throughout the whole of the reaction, and continued for 30 mins. after addition had been completed. After standing overnight, the sodium carbonate was filtered off, and the solution distilled. When a temperature of 140°C had been reached, the solution was allowed to cool, then distilled through a column under vacuum, 72-77°C/23 m.m. Yield, 60%.

This was now oxidised to suberandione (91). To 100 g. cycloheptanone in 208 c.c. absolute alcohol at refluxing temperature, was added over 1 hour a solution of 99 g. selenium dioxide in a mixture of 600 c.c. of absolute alcohol and 24 c.c. water. This was refluxed 6 hours, left overnight, filtered, and about 300 c.c. alcohol distilled off the filtrate. After filtering again, distillation was continued under vacuum. A small quantity of pale yellow, mobile liquid came over at 60-100°C/17 m.m. Cycloheptandione (suberandione) was obtained in 80-90% yield, boiling 107-9°C/17 m.m.

Bromination of suberandione with two moles of bromine: α-Bromotropolone. To a cooled solution (0°) of 20 g. suberandione in 20 c.c. glacial acetic acid, was added 52 g. bromine in 30 c.c. glacial acetic acid over 1 hour. Hydrogen bromide was evolved. The deep orange syrup was allowed to stand 1 hour, then heated for exactly 20 minutes on the water bath, during which time a mass of brown crystals separated. The cold mixture was filtered, washed with a little acetic acid then petrol, and finally dried by suction. Yield, 14 g. This product lost hydrogen bromide very readily, and merely by dissolving in warm, aqueous methanol was converted to impure α-bromotropolone. It was rather sparingly soluble in non-hydroxylic solvents. A portion was re-

crystallised rapidly from glacial acetic acid, m.p. 168-172°C (dec.). Analysis: Found: Br, 53.69. $C_7H_6O_2Br_2$ requires Br, 56.69% (XLII). The remainder was dissolved in warm sodium hydroxide solution. On cooling, the yellow sodium salt of bromotropolone crystallised out in lustrous plates. Yield, 10.7 g. (30%). Recrystallised from aqueous ethanol and dried at 100°C under vacuum, it melted 307-308°C (dec.). Analysis: Found: C, 36.70; H, 1.60. $C_7H_4O_2.Br.Na$ requires C, 37.71; H, 1.81%. A second specimen crystallised from water and not dried under vacuum showed sintering below 100°C. Analysis: Found: C, 32.63; H, 2.9. $C_7H_4O_2.Br.Na.2H_2O$ requires C, 32.71; H, 3.11%. By treatment with dilute acid, free α-bromotropolone was obtained. It was sparingly soluble in cold water, and crystallised from hot water in colourless plates, but was best obtained pure by recrystallisation from cyclohexane. It came out of this solvent first as creamy needles; on leaving overnight this form was replaced by pale yellow-green polyhedra. Both forms melted 103-106°C. Analysis: Found: C, 41.74; H, 2.60; Br, 39.89. $C_7H_5O_2.Br$ requires C, 41.82; H, 2.51; Br, 39.75%. It gave a yellow colour with sodium hydrogen carbonate solution and an intense greenish-black colour with ferric chloride, from which chloroform extracted a blood-red colour. On boiling with alcoholic silver nitrate it gave a bright yellow silver salt which could

be recrystallised from aqueous ethanol and decomposed vigorously 176-178°C. When boiled in water this silver salt gave a reddish precipitate. α-Bromotropolone could be recovered unchanged on boiling with strong alcoholic potassium hydroxide and showed no reaction with thiourea in acetone. Neither a p-nitrobenzyl ether nor a 2:4-dinitrophenyl ether was formed under conditions described as suitable for phenols, and it did not form a 2:4-dinitrophenylhydrazone. On warming with 3:5-dinitrobenzoyl chloride in a loosely stoppered tube, a 3:5-dinitrobenzoate was formed, which crystallised in colourless, stout needles from benzene/petrol, m.p. 105-106°C. Analysis: Found: C, 42.81; H, 2.13. $C_{13}H_7O_7N_2Br$ requires C, 42.55; H, 1.79%. α-Bromotropolone reacted with S-benzylisothiouronium chloride, but the product decomposed on attempted recrystallisation.

Copper salt. An aqueous solution of sodium bromotropolonate with excess copper/ammonia solution gave a dense, light green amorphous precipitate, which was insoluble or sparingly soluble in water and most organic solvents, but which could be crystallised from tetrachloroethane, as an amorphous powder. Analysis: Found: C, 36.42; H, 1.74. $C_{14}H_8O_4Br_2Cu$ requires C, 36.42; H, 1.74%.

α-Bromotropolone methyl ether. Bromotropolone reacted briskly with ethereal diazomethane, to form a methyl ether. It was recrystallised from petrol (b.p. 80-100°) in which it

was sparingly soluble, giving needles m.p. 89-90°C. Analysis: Found: C, 44.70; H, 3.51; OMe, 14.0. $C_8H_7O_2Br$ requires C, 44.7; H, 3.29; OMe, 14.4%.

Reaction with ~~one~~ Two moles of bromine: alternative procedure. This was carried out as previously described, except that heating of the brominated solution was continued for 90 mins., till evolution of hydrogen bromide was slight. Sometimes very impure bromotropolone crystallised out at this stage. The diluted solution was now steam distilled, and the distillate (ca. 1,500 c.c.) filtered and extracted with ether. This extract gave 1.9 g. pale yellow solid. The tar remaining in the flask was extracted with hot alkali solution and gave 4.5 g. impure sodium α-bromotropolonate. The solid obtained by steam distillation was fractionated in ethanol. In this way there was isolated a less soluble bromo-compound (160 mgs.), γ-bromotropolone, yellow needles, m.p. 188° (vigorous sublimation). (Found: C, 41.9; H, 2.7. $C_7H_5O_2Br$ requires C, 41.8; H, 2.5%). From the mother liquors, the main portion of the product was isolated and identified as α-bromotropolone, by mixed melting point determinations with an authentic specimen.

The methyl ether of γ-bromotropolone was obtained on ethereal diazomethane treatment, in the usual way. It crystallised from petrol (b.p. 60-80°) in needles, m.p. 135-137°, with a change in crystal form below the melting point.

(Found: C, 44.9; H, 3.3. $C_8H_7O_2Br$ requires C, 44.7; H, 3.3%).

Attempted debromination of α-bromotropolone with sodium in liquid ammonia. 0.55 g. sodium α-bromotropolonate was dissolved in liquid ammonia and treated with 0.15 g. sodium. The solution was allowed to stand for 3 minutes, was treated with ammonium chloride, then left overnight. The reddish residue was taken up in water and dilute acid, and subjected to liquid/liquid extraction with ether. About 140 mgs. slightly impure bromotropolone was recovered, and a small quantity of red tar obtained which did not sublime under vacuum.

Debromination of α-bromotropolone: Synthesis of tropolone. Sodium α-bromotropolonate (5 g.) was suspended in 40 c.c. ethanol in which it is rather sparingly soluble, and hydrogenated in presence of 10% palladium/charcoal (0.5 g.). It absorbed 1 mol. of hydrogen smoothly and rapidly then absorption practically ceased. The cherry-pink solution was filtered free of catalyst and the solvent removed under vacuum (temperature $\nmid$ 40°C). The residual red gum was extracted with portions of hot petrol (b.p. 40-60°) and the combined and concentrated extracts cooled at -15°C. Colourless needles m.p. 49-50°C., yield 2 g. Analysis: Found: C, 68.73; H, 4.81. $C_7H_6O_2$ requires C, 68.84; H, 4.95%.

Calc'd. mol. wt., 122.12. Found from titration curve 125.7. Tropolone was rather soluble in water and most organic solvents, and sublimed at 40-60°C/4 m.m. At room temperature it gradually turned brown and became sticky, and it kept best at 0°C in a hard glass tube. Its alkaline solutions were faintly straw coloured: it gave no precipitate with lead acetate, and under the conditions prescribed for reaction with phenols, chloroacetic acid/sodium hydroxide did not react with it. In benzene solution it formed a heavy yellow precipitate with benzylamine (100), which however, decomposed with the smell of the free base on attempted crystallisation. A 3:5-dinitrobenzoate was formed with 3:5-dinitrobenzoyl chloride in pyridine, but only in very poor yield. Crystallised from 100-120° petrol/toluene, it melted 169-171°C. Analysis: Found: C, 53.60; H, 2.74. $C_{13}H_8O_7N_2$ requires C, 53.16; H, 2.56%.

Ferric Salt. Tropolone with a little ferric chloride solution gave an intense red precipitate, then on further addition, a greenish-black colour. This solution was filtered, and extracted with chloroform. The combined material from filtration and extraction was crystallised from chloroform/carbon tetrachloride as lustrous intensely red needles, which did not melt or decompose below 360°C. Analysis:

Found: C, 60.1; H, 3.7. $C_{21}H_{15}O_6Fe$ requires C, 60.15; H, 3.6%.

Copper salt. When treated with a slight excess of cuprammonium sulphate solution, tropolone formed a pale green precipitate. This was readily soluble in chloroform, crystallising in narrow plates which effloresced on removal from the solvent. Slightly soluble in other organic solvents, it was best crystallised from ethanol. Pale green lustrous needles m.p. 240-300°C (dec.). Analysis: Found: C, 55.50; H, 3.26. $C_{14}H_{10}O_4Cu$ requires C, 54.98; H, 3.30. With ethereal diazomethane tropolone gave a yellow oil which rapidly crystallised on cooling, and exposure to moist air. This solid was a hemihydrate. Application of vacuum regenerated the oil, but a few moments' exposure to the atmosphere once more converted it to the solid. It crystallised from moist ether or carbon tetrachloride in colourless needles, m.p. 37-38°C. (Found: C, 66.5; H, 6.1; OMe, 21.8. $C_8H_8O_2,0.5H_2O$ requires C, 66.2; H, 6.25; OMe, 21.4%). This methyl ether was rapidly hydrolysed to tropolone on warming with dilute sulphuric acid. The picrate of the methyl ether crystallised from methanol in yellow needles m.p. 119-120°C. (Found: C, 45.8; H, 3.25. $C_8H_8O_2,C_6H_3O_7N_3$ requires C, 46.05; H, 3.05%).

Azo compound. Tropolone in alkali with excess p-toluenediazonium chloride solution gave p-tolylazotropolone, which crystallised from ethanol as a light brown microcrystalline powder m.p. 190-193°, with much sintering below this temperature. It gave a green colour with alcoholic ferric chloride, and a deep green copper salt with copper sulphate solution. (Found: N, 12.0. $C_{14}H_{12}O_2N_2$ requires N, 11.65%).

Bromination of suberandione with one mole of bromine. 10 g. suberandione in 10 c.c. glacial acetic acid was cooled to 0°C and 12.8 g. bromine in 10 c.c. acetic acid was added over 15 mins. with stirring. Hydrogen bromide was evolved and a deep amber solution resulted. After 1 hour the solution was heated with steam till evolution of hydrogen bromide had practically ceased (circa 1 hour). The solution was now very dark and did not deposit solid on cooling in ice, scratching with a glass rod, etc. It was therefore treated with steam and the distillate (800 c.c.) so obtained was made alkaline with sodium carbonate and extracted with ether. The alkaline solution was concentrated under vacuum to about 150 c.c., then acidified and extracted again with ether till the aqueous layer gave practically no ferric chloride test. Tropolone was precipitated from these vacuum-concentrated extracts as its copper salt. The alkaline extracts were now concentrated and a brown oil separated.

This reacted with 20% sodium hydroxide to give the sodium salt of tropolone. This proved too soluble for ready manipulation, so was acidified and the free tropolone isolated by ether extraction. The material remaining in the flask from the steam distillation was also treated with hot alkali, filtered and ether extracted free of tar, acidified, and again extracted with ether. These two acidic ether extracts were combined, taken to dryness and the resulting gum sublimed under vacuum. A total yield of 1.4 g. impure tropolone was obtained.

Bromination of suberandione with three moles of bromine. (This reaction was carried out by Mr. G. Buchanan). 20 g. suberandione in 20 c.c. glacial acetic acid was cooled in an ice bath while 78 g. bromine in 80 c.c. glacial acetic acid was added, over about 20 mins., with stirring. After standing for 2 hours, the dark solution was warmed on the water bath till evolution of hydrogen bromide was very slight. The solution was then concentrated under vacuum and allowed to crystallise. 13.5 g. light brown product was isolated, which recrystallised from ethanol, then toluene as colourless needles m.p. 157-8°C. αα'-dibromotropolone.

Analysis: Found: C, 30.21; H, 1.46; Br, 57.61.

$C_7H_4O_2Br_2$ requires C, 30.00; H, 1.44; Br, 57.10%. It gave

a typical greenish-black ferric chloride test. With sodium carbonate, it formed a bright yellow sodium salt, which crystallised from hot water as yellow needles m.p. 294-6°C. (dec.). Analysis: Found: C, 28.03; H, 1.13. $C_7H_3O_2Br_2.Na$ requires C, 27.86; H, 1.00%.

αα'-Dibromotropolone methyl ether. Dibromotropolone reacted vigorously with ethereal diazomethane giving its methyl ether, crystallised from toluene/100-120° petrol as colourless needles, m.p. 130-1°C. Analysis: Found: C, 33.01; H, 2.15. $C_8H_6O_2Br_2$ requires C, 32.7; H, 2.06. Methoxyl determination: Found: 10.85%. $C_8H_6O_2Br_2$ requires 10.55% methoxyl.

Reduction of αα'-dibromotropolone to tropolone. 1 g. sodium salt was suspended in 50 c.c. ethanol in which it was very sparingly soluble, and hydrogenated in presence of 0.2 g. 10% palladium/charcoal. Absorption was very slow. When 1 mole of hydrogen had been absorbed, 1 mole N sodium hydroxide solution was added then more catalyst. When 2 mols. hydrogen had been absorbed, the reaction was stopped. The solution was still yellow and still contained a little suspended sodium salt. It was now filtered, treated with a drop of acetic acid and concentrated under vacuum (temperature $\not>$ 40°C). The resulting red gum was extracted with

hot petrol (b.p. 40-60°), which gave 360 mgs. tropolone m.p. 44-48°C, no depression on admixture with an authentic specimen. The filtered material (catalyst) was suspended in a little alcohol/acetic acid, and refiltered. About 100 mgs. dibromotropolone was recovered from this solution. Yield (allowing for recovery), 50%. If the reduction was stopped after absorption of 1 mol., a mixture of $\alpha\alpha'$-dibromotropolone and tropolone was obtained, but no α-monobromotropolone.

Bromination of suberandione with four moles of bromine (A): Tribromotropolone. To suberandione (10 g.) in glacial acetic acid (10 c.c.) was added with stirring during 30 mins., bromine (54 g.) in glacial acetic acid (20 c.c.). After standing one hour, it was heated with steam till evolution of hydrogen bromide had practically ceased, and the concentrated under vacuum, when a viscous red gum was obtained, which resinified with alkali and gave no colour with ferric chloride. On heating the red gum to 130°, hydrogen bromide was again briskly evolved. The product remaining was now soluble in hot sodium hydroxide, and a bright yellow sodium salt separated on cooling (1.7 g.). $\alpha\alpha\gamma$-Tribromotropolone was obtained on acidification. It crystallised from ethanol as pale yellow needles m.p. 122-123°. (Found: C, 23.7; H, 1.1; Br, 66.5. $C_7H_3O_2Br_3$ requires C, 23.45; H, 0.85; Br, 66.8%).

It gave a deep green colour with ferric chloride in ethanol. Tribromotropolone methyl ether was obtained by treatment with ethereal diazomethane. It crystallised from petrol (b.p. 40-60°) in yellow nodules m.p. 123-124° (strongly depressed on admixture with starting material). Found: C, 26.05; H, 1.5. $C_8H_5O_2Br_3$ requires C, 25.8; H, 1.35%.

Bromination with four moles (B) Tetrabromosuberandione.

The dione was treated with bromine as above, and allowed to stand. The mixture was poured into water, whereupon an oil separated and partially solidified. From acetic acid and then benzene/petrol (b.p. 60-80°) colourless plates of tetrabromosuberandione were obtained, m.p. 82-84°C. Found: C, 18.5; H, 1.75; Br, 72.2. $C_7H_6O_2Br_4$ requires C, 19.0; H, 1.35; Br, 72.4%. It gave no ferric chloride colour.

Hydrogenation of tropolone. Tropolone (160 mgs.) in alcohol (25 c.c.) was stirred under hydrogen in the presence of 100 mgs. pre-reduced Adam's catalyst. Three moles of hydrogen were absorbed smoothly, then a fourth mole more slowly, and a waxy solid was isolated on removal of catalyst and solvent. This wax was oxidised in the cold with alkaline permanganate. The product obtained on acidification and ether extraction (125 mgs.) crystallised from benzene in small needles m.p. 99-101°. Its melting point was undepressed in admixture with authentic pimelic acid, m.p. 103-4°C.

Oxidation with conc. nitric acid also gave pimelic acid, but in poorer yield.

Oxidation of tropolone (By Dr. R.A. Raphael).

A solution of tropolone (244 mg.) in sodium hydroxide solution (5 c.c. of N) was treated with hydrogen peroxide (1 c.c.; 30%) and set aside in the dark for 48 hours. No colour change from the original yellow took place. The solution was acidified (2N-sulphuric acid) to Congo-red and extracted with ether. The oily residue obtained by drying and evaporation was extracted with cyclohexane; the extract on cooling deposited needles of unchanged tropolone (180 mg.). The hydrocarbon-insoluble residue (ca. 10 mg.) consisted of an acidic solid which was purified by dissolution in sodium carbonate and precipitation by acid; it then melted at 182-184° undepressed on admixture with authentic cis:cis-muconic acid cf. (95).

When the oxidation was carried out in the presence of light the fission product had m.p. 154-162°. A similar m.p. range for cis:cis-muconic acid prepared in the light has been noted by Grundmann (96).

Bromination of tropolone (By Dr. R.A. Raphael).

(a) To a cold solution of tropolone (56.1 mg.) in dry carbon tetrachloride (3 c.c.) contained in a weighed filter beaker was added a solution of bromine in carbon tetrachloride (0.34 c.c. of a solution containing 110 mg./c.c. of bromine;

0.5 mol.). The orange-red precipitate immediately formed was filtered, washed with a little carbon tetrachloride, dried *in vacuo* and weighed (68.4 mg.; 74%). The yields obtained with 1 mol. (85%) and 2 mols. (81%) of bromine were similar, but that produced by 0.25 mol. (31%) was approximately halved. The complex dissolved in hot glacial acetic acid to give a yellow solution from which it crystallised on cooling as a mass of scarlet needles; accurate analysis was difficult owing to its ready reaction with atmospheric moisture. Found: C, 39.9; H, 3.5; Br, 40.3. $(C_7H_6O_2)_2 \cdot Br_2$ requires C, 41.6; H, 3.0; Br, 39.6%. On being heated to 110° the substance sintered and rapidly decolourised to form a white, crystalline mass which melted unsharply to a clear liquid at 152-163°. On careful heating at $70^\circ/10^{-5}$ m.m. the complex slowly sublimed with only slight decomposition. A sample of the complex (84.2 mg.) was heated to 140° for 45 minutes in a slow stream of nitrogen, the issuing gases being bubbled through caustic soda solution (5 c.c. of N). The latter was treated with excess nitric acid and silver nitrate and the precipitated silver bromide was coagulated by boiling, filtered off, washed, dried and weighed. (Found: 32.3 mg. AgBr. Calc. for the production of one mol. of HBr from $(C_7H_6O_2)_2 \cdot Br_2$, 39.2 mg.).

The complex (127 mg.) was heated in an oil bath to 110° at atmospheric pressure in sublimation apparatus until decolourisation was complete. The bath was then cooled to 60° and the apparatus evacuated to 20 m.m.; the crystalline sublimate thus obtained (6 mg.) had m.p. 48-50° undepressed on admixture with tropolone. The bath temperature was then raised to 120° and the pale yellow sublimate formed (42 mg.) m.p. 83-94°, was purified by repeated crystallisation from cyclohexane to yield pure α-bromotropolone m.p. 105-107° (17 mg.) undepressed on admixture with an authentic specimen. From the number of crystallisations required to attain purity it is probable that the product contained a little of the higher-melting γ-bromotropolone. The residue remaining in the sublimation apparatus was dissolved in a small quantity of warm glacial acetic acid. On being cooled, the solution deposited small rosettes of needles m.p. 154-157° (11 mg.) undepressed on admixture with dibromotropolone (m.p. 157-158°). Evaporation of the acetic acid mother liquors to dryness under reduced pressure left a white crystalline mass (38 mg.) insoluble in hydrocarbon solvents but crystallising from a small volume of methanol or methyl ethyl ketone in long needles m.p. 130-132° (Kofler block) resolidifying slowly on further heating to a mass of needles which did not melt below 250°. This compound was found to be tropolone hydrobromide identical with an authentic sample

prepared by passing hydrogen bromide into a benzene solution of tropolone. (Found: Br, 38.6. $C_7H_7O_2Br$ requires Br, 39.35%). On being heated under reflux with a small volume of ethyl acetate the hydrobromide slowly dissolved; evaporation to dryness gave tropolone (18 mgs.), crystallising from petrol (b.p. 40-60°) in needles m.p. 49-50° undepressed on admixture with an authentic specimen.

(b) To a cold solution of tropolone (57 mg.) in water (5 c.c.) was rapidly added a solution of bromine (290 mg.; 3.5 moles) in potassium bromide solution. The yellow precipitate formed was filtered off, washed with water and crystallised from methanol, from which solvent it formed yellow needles (116 mg.) m.p. 123° undepressed on admixture with tribromotropolone.

Bromination of Copper Tropolone.

To a cold solution of copper tropolone (176 mg.) in chloroform (20 c.c.) was rapidly added a solution of bromine in chloroform (1.51 c.c. of a solution containing 1.35 g./c.c. of bromine; 2 moles); a black, powdery precipitate was formed. After standing overnight at room temperature an equal volume of water was added, whereupon the black precipitate disappeared to be replaced by a pale green suspension. The mixture was treated with hydrogen sulphide, and extracted with ether. The dried extracts yielded a dark gum on evaporation, which sublimed 110-120°/0.5 m.m. to a pale

yellow solid (196 mg.) melting 85-110°. By crystallisation from petrol (b.p. 60-80°), this was divided into two main concentrates: (a) m.p. 96-103°, not improved by further crystallisation (28 mg.) was identified as α-bromotropolone by mixed melting point determination; (b) m.p. 176-180°, recrystallised from ethanol m.p. 188° (sublimation) (46 mg.). It gave no melting point depression in admixture with authentic γ-bromotropolone.

Bromination of Tropolone Methyl Ether.

To tropolone methyl ether hemihydrate (100 mg.) in carbon tetrachloride (30 c.c.) was added bromine (100 mgs.) in carbon tetrachloride (0.5 c.c.). A yellow oil immediately separated, but redissolved with evolution of hydrogen bromide on refluxing the solution for thirty mins. Removal of solvent left a yellow semisolid melting range 30-80°, which reacted with cold dilute alkali to give a mixture of yellow sodium salts. Extensive darkening and decomposition resulted on heating a portion of this alkaline suspension. Acidification of the larger part gave back the yellow semisolid apparently unchanged. After being crystallised from cyclohexane it melted 70-80° (40-50 mgs.). Further crystallisations from ethanol gave γ-bromotropolone (10 mg.) m.p. 174-178° identified by mixed melting point determinations. The material remaining in the mother liquors had a melting

range 80-90° not improved by further crystallisations but not depressed in admixture with α-bromotropolone.

Bromination of the dry oily tropolone methyl ether with 1 mole of bromine in dry carbon tetrachloride resulted in the immediate deposition of a bright scarlet oil which did not solidify at -15°, but redissolved to a colourless solution, with evolution of hydrogen bromine, on refluxing thirty mins. The mixture obtained on removal of solvent was apparently even more complex than with the hemihydrate and no definite, sharp melting products could be isolated from it.

Bromination of α-Bromotropolone.

α-Bromotropolone (200 mg.) in glacial acetic acid (3 c.c.) was treated with 160 mg. (1 mole) of bromine. A yellow crystalline precipitate (210 mg.) separated in a few minutes and was filtered off. Evaporation of the filtrate to dryness gave 60 mg. dibromotropolone, crystallised from methanol m.p. 156-157°. The yellow precipitate melted at 80-85° with loss of hydrogen bromide, rapidly resolidifying and remelting at 145-153°. It was found to be identical with dibromotropolone hydrobromide obtained by treatment of the parent compound with acetic acid/hydrogen bromide, and gave pure αα'-dibromotropolone m.p. 157-158° (118 mg.) on solution in warm methanol.

Bromination of γ-Bromotropolone.

γ-Bromotropolone (40 mg.) refluxed in glacial acetic acid with excess bromine (2.5 moles) gave αα'γ-tribromotropolone in almost quantitative yield, m.p. and mixed m.p. 123°.

Bromination of αα' -dibromotropolone.

A solution of dibromotropolone (47 mg.) in glacial acetic acid (2 c.c.) was treated with bromine 40 mg.; 1.5 moles) in acetic acid. On heating under gentle reflux for 30 mins., the bromine colour was slowly discharged, and evaporation to dryness under vacuum gave αα'γ-tribromotropolone (42 mg.) recrystallised from methanol m.p. 123°, undepressed on admixture with an authentic specimen.

Rearrangement of Bromotropolone Methyl Ethers.

γ-Bromotropolone methyl ether,

(108 mg.) was dissolved in dry methanol (3 c.c.) and treated with 150 mgs. sodium dissolved in methanol (5 c.c.). The solution was refluxed for 18 hours, taken to dryness in vacuo, treated with 5 c.c. 2N sodium hydroxide and refluxed for a further hour. The cold solution was freed from neutral impurities by ether extraction, acidified with dilute sulphuric acid, and again extracted with ether. The dried acid extracts were evaporated and the resulting brown residue sublimed (140°/0.5 mm.). The sublimate (33 mg.) crystallised

from benzene as tiny needles m.p. 245-247° with rapid sublimation - p-bromobenzoic acid. Its melting point was undepressed in admixture with an authentic specimen (m.p. 248-250°).

Dibromotropolone methyl ether. (By Dr. R.A. Raphael).

The methyl ether of dibromotropolone (46 g.) was treated with sodium dissolved in methanol as above and refluxed 30 mins. The solvent was removed under reduced pressure and water and ether added to the residue. The separated and dried ether layer furnished 32 mgs. of a product, which crystallised from aqueous ethanol in platelets m.p. 61-62°, undepressed on admixture with authentic methyl 2:6-dibromobenzoate (m.p. 61-62°). (Found: C, 32.6; H, 2.3. $C_8H_6O_2Br_2$ requires C, 32.7; H, 2.05%). The ester was prepared by the action of ethereal diazomethane on 2:6-dibromobenzoic acid obtained by the method of Olivier (94). On the two previous occasions that this ester has been mentioned in the literature the melting point has been recorded as 83° (97) and 78° (98); in these cases the compound was prepared by reaction of the acid chloride with methanol or sodium methoxide. Dimorphism seems to be the most likely explanation of this discrepancy; the melting point of our ester was not changed by repeated crystallisation from various solvents or by melting and resolidification.

Tribromotropolone methyl ether. (By Dr. R.A. Raphael).

Tribromotropolone methyl ether was treated in a manner analogous to above. The product was an oil which rapidly solidified. Crystallisation from aqueous ethanol gave methyl 2:4:6-tribromobenzoate (26 mg.) as plates m.p. 69-70° undepressed on admixture with an authentic specimen (m.p. 69-70°)

Iodination of Tropolone.

(a). To a solution of tropolone (100 mg.) in water (15 c.c.) was added a solution of iodine (150 mg.) in potassium iodide solution (5 c.c. of 10%). The black precipitate immediately formed (160 mg.) was filtered off, dried on porous tile and crystallised from chloroform in black lustrous needles decomposing ca. 140°. The complex slowly lost iodine even at room temperature which made accurate analysis difficult. (Found: I, 49.5. $(C_7H_6O_2)_2 \cdot I_2$ requires I, 50.9%). The complex was slightly soluble in water and soluble in organic solvents, in each case the solution assumed the colour possessed by free iodine in that solvent, i.e., brown in ether, water, etc., red in carbon tetrachloride. The colour of a chloroform solution was discharged on shaking with aqueous sodium thiosulphate, and free tropolone was recovered from the organic solvent layer on evaporation. Attempted sublimation under vacuum resulted in complete disproportionation into iodine and tropolone.

(b). Tropolone (100 mg.) and iodine (210 mg.: 1 mole) were refluxed in 30 c.c. carbon tetrachloride for 72 hours without reaction. The solution was placed in a glass tube which was evacuated and sealed. Heating at 100° for 45 mins. resulted in a partial loss of the iodine colour, formation of a slight white floc, and separation of some tarry material. The contents of the tube were treated with water whereupon the white floc immediately disappeared (tropolone hydriodide?). Excess iodine was destroyed with a little sodium bisulphite, and ether extraction of the solution isolated 20 mg. tropolone identified by mixed melting point determination. A similar carbon tetrachloride solution gave only tar after heating for three hours in an evacuated sealed tube at 150°. Iodination was also attempted in carbon tetrachloride solution in the presence of mercuric oxide, to remove any hydrogen iodide formed. Some reaction did occur, but the tropolone mixture formed stable yellow complexes with mercuric iodide, soluble in organic solvents and subliming under vacuum with only partial disproportionation.

(c). To a cold solution of tropolone (200 mg.) in sodium hydroxide (30 c.c.; N) was rapidly added a solution of iodine (3 g.) in potassium iodide solution. The yellow crystalline precipitate immediately formed (140 mg.) was filtered off and crystallised from ethanol to give yellow plates m.p. 119-120° undepressed in admixture with iodoform

(m.p. 119-120°). The filtrate was allowed to stand overnight, acidified, decolourised with a little sodium bisulphite. The solid product thus obtained was crystallised from glacial acetic acid forming needles (260 mg.) m.p. 153-155° undepressed on admixture with 2:4:6-triiodophenol (m.p. 155-156°).

When the aqueous iodine/potassium iodide was dropped into the solution very slowly, no iodoform was isolated. If this solution was now warmed, subsequent treatment as above gave much tar, a mixture of lower iodophenols which could be converted to triiodophenol with more iodine/iodide, and a few milligrams of a white compound m.p. 80-85° from petrol (b.p. 40-60°). The latter product gave a 20° depression in admixture with triiodophenol; it gave a green ferric chloride colour and may have been a mixture of tropolone and lower iodophenols.

$\alpha\beta$-Benzotropolone.

δ-Phenylvaleric acid (59). Cinnamaldehyde (100 g.), malonic acid (80 g.) and quinoline (98 g.) were warmed together on the water bath to a clear solution, then treated with a few drops of piperidine. After standing 4 days in the cold the mixture was warmed 2 hours on the water bath, dissolved in sodium hydroxide solution (270 g. in 2 l. water) and the quinoline removed by ether extraction. The solution, freed from dissolved ether by distillation, was raised to boiling point and Raney nickel/aluminium alloy (160°) added during 45 mins. with vigorous stirring. Stirring was continued a further 30 mins. at 90°, then the suspension was filtered, and the hot filtrate was siphoned slowly into hot sulphuric acid (600 c.c. conc. in 1 l. water) with brisk stirring. The precipitated oil was separated from the cold solution, then freed from aluminium salts by dissolving in ether and shaking with water. The dried and evaporated organic layer was heated under vacuum (16-20 m.m.) in the presence of copper powder for 2 hours at 140-180°. The soft, sticky phenylvaleric acid thus obtained was crystallised from light petroleum, m.p. 58-60°. (Yield: 110 g.).

2:3-Benzosuberone (59),(93). Phenylvaleric acid (19.6 g.) was warmed on a water bath with thionyl chloride (20 c.c.) till hydrogen chloride evolution commenced, and the

reaction allowed to proceed to completion without heat. The mixture was now heated 10 mins. with steam and the excess thionyl chloride removed under vacuum. The resultant pale yellow oil was dissolved in 1.1. carbon disulphide (dried and distilled over aluminium chloride) and dropped gradually over three days into a stirred suspension of aluminium chloride (28 g.) in carbon disulphide (500 c.c.) at simmering point. Stirring was continued 2 hours after addition was complete, then most of the carbon disulphide was distilled off and the residue treated with crushed ice (750 g.). This was then exhaustively steam distilled and the distillate (2.5 l.) saturated with salt and extracted with ether. The oil obtained on removal of solvent was distilled $78^{\circ}/0.2$ m.m. Yield, 15 g.

Benzsuberandione (59). Selenium dioxide (10.5 g.) in ethanol (80 c.c.) was added dropwise over 4 hours to a boiling solution of benzosuberone (15 g.) in ethanol (30 c.c.), and refluxing was continued a further 2 hours. The cold solution was filtered, ethanol was distilled off and the remaining oil distilled in two fractions:

(a) b.p. $80\text{-}110^{\circ}/0.4$ m.m. Mobile, pale yellow (0.6 g.)

(b) benzsuberandione b.p. $128\text{-}132^{\circ}/0.4$ m.m. A viscous deep yellow oil. (Yield, 13 g.).

On standing 6 weeks at 0°, benzsuberandione solidified to

sticky yellow prisms. A sample, pressed on porous tile, melted 45-49°, but did not recrystallise from dilute methanol even after 6 months at -15°.

Reaction of benzsuberandione with one mole of bromine: Benzsuberandione (2 g.) in acetic acid (5 c.c.) was treated with bromine (2 g.: 1 mole) in acetic acid (5 c.c.) over 30 mins. After standing 1 hour the solution was warmed, whereupon it darkened extensively. No tropolone material was isolated on further heating or on alkali treatment, and as the solution was a painful skin irritant, it was not examined further.

Reaction with two moles of bromine : Bromobenzotropolone: To benzsuberandione (10 g.) in acetic acid (10 c.c.) was added slowly and with stirring 19.8 g. (2 moles) bromine in glacial acetic acid (20 c.c.). The solution was allowed to stand at room temperature for four days during which time it darkened and deposited a mass of large yellow-brown prisms. These were filtered off, the solution was diluted with 10 c.c. acetic acid, and warmed to 60° for 3 hours, after which a further small quantity of crystals separated. Total yield: 7 g. of bromobenzotropolone. It crystallised almost quantitatively from glacial acetic acid in stout yellow prisms, m.p. 143-144°. Analysis: Found: C, 52.37; 52.22; H, 3.26, 3.11; Br, 31.85. $C_{11}H_7O_2Br$ requires C, 52.6; H, 2.81; Br, 31.82. Bromobenzotropolone in chloroform solution was

treated with aqueous alcoholic solutions of the following inorganic salts, and the colour of the organic layer noted:

A. Ferric chloride
deep red

B. Cuprammonium sulphate
yellow green, amorphous precipitate

C. Manganese sulphate
very pale brown

D. Nickel sulphate
yellow

E. Cobalt nitrate
pale yellow.

With alcoholic silver nitrate solution bromobenzotropolone gave a yellow silver salt which decomposed on boiling. The bright yellow sparingly soluble sodium salt was also unstable to boiling water, and a little free bromobenzotropolone (m.p. and mixed m.p.) contaminated with much tar could be recovered by ether extraction of the cooled suspension. It did not react with 2:4-dinitrophenylhydrazine in acetic acid or alcohol/sulphuric acid, and was recovered unchanged (m.p. and mixed m.p. 140-2°) from an acetic acid solution of picric acid. Warming with diphenyl diazomethane in petrol solution, or refluxing with 3:5-dinitrobenzoyl chloride in pyridine gave only tars. Treatment of bromobenzotropolone in alkali (0°) with diazotized p-toluidine resulted in a maroon precipitate which immediately decomposed to a tar with nitrogen evolution. Bromobenzotropolone was dissolved in alcohol and treated with a large excess of 50% potassium hydroxide. The solution was concentrated under vacuum, then the temperature of the resultant paste gradually

raised. The mix darkened slightly then at 169° decomposed suddenly and briskly with formation of tar and gas evolution. No solid product could be obtained. Bromobenzotropolone when suspended in ether then treated with ethereal diazomethane gradually dissolved to be replaced by a colourless floc. On addition of a little methanol, the floc disappeared, the solution turned deep orange, then gradually faded to pale yellow with brisk nitrogen evolution. The resulting product crystallised from light petrol/carbon tetrachloride in tiny colourless prisms. Bromobenzotropolone methyl ether m.p. 84-85°C. (Found: C, 54.28; H, 3.42. $C_{12}H_8O_2Br$ requires C, 54.36; H, 3.42%). It was not hydrolysed by hot 1N sodium hydroxide.

No further bromobenzotropolone could be isolated by alkaline extraction of the vacuum-concentrated mother liquors of the bromination reaction. Instead a neutral oil was obtained (yield: circa 2.5 g.) which partially resinified at temperatures above 130°. It was freed from tar by passing down a column of alumina. It gave an orange precipitate with 2:4-dinitrophenylhydrazine, a brown ferric chloride colour, and was not converted to a tropolone by boiling alkali. As it was a painful skin irritant it was not examined further.

α/β-Benztropolone (A): Hydrogenation of sodium bromobenzotropolonate, as described in the preparation of

tropolone from the α-bromo compound, gave unsatisfactory results due to the extremely low solubility of this sodium salt. The following method was found satisfactory. Bromobenzotropolone (5.8 g.) was dissolved in a mixture of ethanol (50 c.c.) and triethylamine (6 c.c.), and the clear yellow solution treated with hydrogen in the presence of 10% palladised charcoal (1 g.). Absorption slackened considerably after the smooth uptake of 600 c.c. (theoretical volume for 1 mole at room temperature and pressure: 570 c.c.) and the flask was disconnected. The solution was filtered hot, concentrated in vacuo, diluted with water, made distinctly acid with 2N sulphuric acid, then filtered. The filtrate gave a precipitate with silver nitrate solution. The solid residue sublimed above 60°/0.18 m.m. to pale yellow prisms of αβ-benzotropolone, which when recrystallised from cyclohexane/petrol (b.p. 60-80°) melted 85-86°. Yield: 2.75 g. (68%). Overall yield from benzosuberone: 26.8%. (Found: C, 76.50; H, 4.65. $C_{11}H_8O_2$ requires C, 76.73; H, 4.68%).

αβ-Benzotropolone (B). To bromobenzotropolone (0.5 g.) in pyridine (10 c.c.) and acetic acid (0.5 c.c.) at 40° was added zinc dust (1 g.). The temperature rose spontaneously to 60° and the solution darkened. After 2 mins., the solution was filtered, cooled, poured into excess acid and

extracted with ether. The dark brown gum obtained on removal of ether was sublimed 60-80°/0.2 m.m., and gave a yellow solid m.p. 60-65°; recrystallised from cyclohexane m.p. 78-82°, undepressed in admixture with authentic α3-benzotropolone. Yield: 40 mg.

α/β -Benzotropolone was sparingly soluble in water, readily soluble in benzene and hydroxylic solvents, moderately soluble in hydrocarbon solvents. The compound dissolved in chloroform was shaken with inorganic salts A → E (p. 44 and the colour of the organic layer noted. A. Deep red, B. green, depositing yellow-green needles, C. very pale brown, D. practically colourless, E. yellow. It did not form a 2:4-dinitrophenylhydrazone and was weakly acidic (P_K, 9·5), the alkali salts being bright yellow. A solution of its triethylamine salt (0°) gave a red-brown amorphous precipitate with diazotized aniline, but this azocompound decomposed to tars on attempted crystallisations. Standard treatment of benzotropolone with 3:5-dinitrobenzoyl chloride in pyridine gave much red tar and a poor yield of benztropolone 3:5-dinitrobenzoate, colourless plates from ethanol or benzene/petrol m.p. 174-5°. (Found: C, 59.05; H, 3.00. $C_{18}H_{10}O_7N_2$ requires C, 59.02; H, 2.75%). It was crystallised unchanged from 2:4-dinitrophenylhydrazine sulphate/alcohol. Benzotropolone was dissolved in a saturated

solution of picric acid. After 5 days large orange prisms crystallised out of benztropolone picrate m.p. 63-64°. (Found: C, 58.71; H, 3.55; N, 7.33. $(C_{11}H_8O_2)_2 \cdot C_6H_3O_7N_3$ requires C, 58.64; H, 3.32; N, 7.33%). Benztropolone dissolved in conc. sulphuric acid or hydrochloric acid to give a bright yellow solution from which it was reprecipitated on dilution with water. Its solution in dry ether turned bright yellow on treatment with hydrogen chloride. Removal of solvent by warming to 60° left a bright orange oil, not solidified at -15°, and application of vacuum regenerated benzotropolone contaminated with a little tarry material (identified by melting point and mixed melting point determinations).

Benzotropolone (50 mgs.) in pyridine (2.5 c.c.) and acetic anhydride (0.75 c.c.) was left at room temperature 24 hrs., then heated with steam 1 hour, poured into 3% hydrochloric acid, and the solution was extracted with ether. (cf. (43)). Removal of solvent left a pale yellow oil, benztropolone acetate slightly soluble in petrol but not solidified even at -15°. It was hydrolysed immediately by cold 1N sodium hydroxide and on 30 seconds' warming with ethanolic hydrochloric acid/ferric chloride. It showed no reaction with trinitrobenzene in ethanol. After standing for 14 days with trinitrofluorenone in ethanol/acetic acid, a red product

was obtained which however was contaminated with straw coloured crystals of unchanged trinitrofluorenone.

No identifiable product was obtained by the treatment of benzotropolone with warm diphenyldiazomethane in petrol solution. With ethereal diazomethane, a slight yellow floc deposited; this redissolved on addition of a little methanol. The resultant pale orange solution lightened on standing but practically no nitrogen was evolved, and unchanged benzotropolone was recovered 24 hours later. To benzotropolone (0.2 g.) in 1N sodium hydroxide (1.16 c.c.; 1 mole) was added methyl p-toluenesulphonate (0.2 g.; 1 mole) and the mixture was warmed with steam till colourless. The oily suspension was extracted with ether, and the ether in turn extracted with dilute sodium carbonate solution (colourless extract). Evaporation of the ether left a yellowish oil which crystallised from petrol (b.p. 40-60°) at -15° in rosettes of colourless prisms - benzotropolone methyl ether. It remelted at room temperature. The colour of a warm ethanolic picric acid solution deepened slightly after addition of this oil, but only yellow crystals of slightly impure picric acid (m.p. and mixed m.p.) were obtained on standing. The oil was dissolved in 2:4-dinitrophenylhydrazine sulphate/ethanol and the solution heated to boiling, whereupon it turned red. On cooling tiny red prisms

separated, which when recrystallised from ethyl acetate melted 242-243°. (Found: C, 58.36; H, 3.71; N, 15.29. $C_{17}H_{10}O_5N_4$ LXX requires C, 58.28; H, 2.88; N, 16.00. $C_{17}H_{12}O_5N_2$ LXIX requires C, 57.95; H, 3.43; N, 15.91. $C_{18}H_{14}O_5N_4$ LXVIII requires C, 59.02; H, 3.85; N, 15.30%).

Oxidation of benzotropolone: Benzotropolone (200 mgs.) was dissolved in 0.5N sodium hydroxide and the cold suspension treated with circa 5 drops 30% hydrogen peroxide. The yellow sodium salt disappeared to a colourless solution over 36 hours. This was acidified, warmed, then saturated with salt and extracted with ether. Evaporation gave a colourless solid m.p. 176-180°. It gave a fluorescein test with resorcinol/sulphuric acid. Recrystallised from aqueous acetic acid it melted 186-188°. On being allowed to solidify, it remelted 146-148°. (Yield: 60 mg.). o-Carboxy-cinnamic acid, prepared by the oxidation of β-naphthol with acetic acid/hydrogen peroxide (83), crystallised from acetic acid m.p. 196-7°. On cooling and reheating melted, 150-1°. (Conversion to the lactone of β-hydroxy-β-(2-carboxyphenyl)-propionic acid.) Mixed with the oxidation product from benzotropolone it melted 187-9°, and after cooling remelted 147-149°.

Bromination reactions: Benzotropolone (100 mg.) in glacial acetic acid (5 c.c.) was treated dropwise with bromine

(100 mg.; 1.1 mole) in acetic acid (0.5 c.c.). A yellow oil separated, but redissolved with hydrogen bromide evolution and slight darkening, on refluxing the solution. The product obtained on vacuum concentration was recrystallised from acetic acid, m.p. 140-2°, alone and in admixture with authentic bromobenzotropolone. Yield: 90 mg.

Bromobenzotropolone (100 mg.) in glacial acetic acid (10 c.c.) was treated dropwise with bromine (200 mg.; excess) in acetic acid (0.5 c.c.) and the solution refluxed 30 mins. Concentration in vacuo gave silky yellow needles, recrystallised from acetic acid, m.p. 119-121°.

Dibromobenzotropolone. Yield: 120 mg. (Found: C, 40.02; H, 1.97. $C_{11}H_6O_2Br_2$ requires C, 40.03; H, 1.83%). The compound in chloroform solution was treated with solutions A → E (page 77) exactly as described previously. A. Red precipitate, B. yellow-green precipitate, C. red brown solution, D. bright yellow solution, E. orange solution. It gave a bright yellow, sparingly soluble sodium salt with sodium hydroxide and a similar yellow silver salt with hot alcoholic silver nitrate. Dibromobenzotropolone was also obtained in excellent yield by refluxing benzotropolone (100 mg.) in acetic acid (5 c.c.) with bromine (300 mg; excess of two moles) in acetic acid (1 c.c.), or better,

merely by mixing the two solutions and leaving to stand 14 days in the cold, whereupon the product crystallised out, identified by melting points and mixed melting points.

Ultra-violet light absorption measurements were carried out on the Unicam Spectrometer, except in the case of the spectrum of tropolone in cyclohexane, for which the Hilger "Spekker" Spectrophotometer was used (slit width 0.03 m.m.).

References.

(1). Willstätter: Ber., 1905, 38, 1992.

(2). Lothrop: J.A.C.S., 1941, 63, 1187.

(3). Lothrop: J.A.C.S., 1942, 64, 1698.

(4). Baker: J.C.S., 1945, 258.

(5). Armit & Robinson: J.C.S., 1922, 121; 828.

(6). Baker: Scientific J.Roy.Coll.Sci., 1948, 27, 54.

(7). Horn & Rapson: J.C.S., 1949, 2421.

(8). Dewar: Nature, 1945, 155, 50.

(9). Erdman & Gripenberg: Acta Chem.Scand., 1948, 2, 625.

(10). Dewar: Nature, 1945, 155, 479.

(11). Cook & Loudon: Quarterly Reviews, 1951, 99.

(12). Loudon: Annual Reports, 1948, 187.

(13). Birkinshaw, Chambers & Raistrick: Biochem.J., 1942, 36, 242.

(14). Corbett, Hassall, Johnson & Todd: Chem. & Ind., 1949, 626.

(15). Corbett, Johnson & Todd: J.C.S., 1950, 148.

(16). Birkinshaw & Raistrick: Biochem.J., 1932, 26, 441.

(17). Barger & Dorrer: Biochem.J., 1934, 28, 11.

(18). Corbett, Hassall, Johnson & Todd: J.C.S., 1950, 1.

(19). Corbett, Johnson & Todd: J.C.S., 1950, 6.

(20). Aulin-Erdtman: Chem. & Ind., 1951, 12, 28.

(21). Aulin-Erdtman: Acta Chem.Scand., 1950, 4, 1490.

(22). Johnson, Sheppard & Todd: J.C.S., 1951, 1139.

(23). Erdtman & Gripenberg: Nature, 1948, 161, 719.

(24). Erdtman & Gripenberg: Acta Chem.Scand., 1948, 2, 625.

(25). Gripenberg: Acta Chem.Scand., 1948, 2, 639.

(26). Anderson & Gripenberg: Acta Chem.Scand., 1948, 2, 644.

(27). Nozoe: Bull.Chem.Soc.Japan, 1936, 11, 295.

(28). Nozoe & Katsura: J.Pharm.Soc.Japan, 1944, 64, 181.

(29). Cook, Jack & Loudon: Chem. & Ind., 1950, 650.

(30). Cook, Jack, Loudon, Buchanan & Macmillan: J.C.S., 1951, 1397.

(31). Rapoport, Williams & Cisney: J.A.C.S., 1951, 73, 1414.

(32). Barltop & Nicholson: J.C.S., 1948, 116.

(33). Haworth, Moore & Pauson: J.C S., 1948, 1045.

(34). Haworth, Moore & Pauson: J.C.S., 1949, 3271.

(35). Caunt, Crow, Haworth & Vodoz: J.C.S., 1950, 1631.

(36). Critchlow, Haworth & Pauson: J.C.S., 1951, 1318.

(37). Cook, Gibb, Raphael & Somerville: Chem. & Ind., 1950, 35, 427.

(38). Haworth & Hobson: Chem. & Ind., 1950, 35, 441.

(39). Doering & Knox: J.A.C.S., 1950, 72, 2305.

(40). Nozoe, Seto, Kitahara, Kunori & Nakayama: Proc.Japan Acad., 1950, 26, 38.

(41). Nozoe: Nature, 1951, 167, 1055.

(42). Cook, Raphael & Scott: Personal communication.

(43). Tarbell, Scott & Kemp: J.A.C.S., 1950, 72, 379.

(44). Cook, Gibb, Raphael & Somerville: J.C.S., 1951, 503.

(45). Cook, Raphael & Scott: J.C.S., 1951, 695.

(46). Nozoe, Seto, Kikuchi, Mukai, Matsumoto & Murase: Proc.Japan Acad., 1950, 26, 43.

(47). Nozoe, Seto, Kikuchi & Takeda: Proc.Japan Acad., 1951, 27, 146.

(48). Nozoe et al.: Proc.Japan Acad., 1951, 27, 110.

(49) Nozoe, Kishi & Yoshikoshi: Proc.Japan Acad., 1951, 27, 149.

(50). Nozoe, Kitahara & Ito: Proc.Japan Acad., 1950, 26, 47.

(51). Cook & Somerville: Nature, 1949, 163, 410.

(52). Caunt, Crow & Haworth: J.C.S., 1951, 1313.

(53). Barltrop, Johnson & Meakins: J.C.S., 1951, 182.

(54). Doering & Knox: J.A.C.S., 1951, 73, 828.

(55). Bartels-Keith, Johnson & Taylor: Chem. & Ind., 1951, 537.

(56). Bartels-Keith & Johnson: Chem. & Ind., 1950, 677.

(57). Haworth & Hobson: J.C.S., 1951, 561.

(58). Crow & Haworth: J.C.S., 1951, 1325.

(59). Somerville: Ph.D. thesis.

(60). Santavý: Helv.Chim.Acta, 1948, 31, 821.

(61). Nozoe, Seto, Ikemi & Arai: Proc.Japan Acad., 1951, 27, 102

(62). Nozoe, Kitahara, Yamare & Yoshikoshi: Proc.Japan Acad., 1951, 27, 18.

(63). Bodroux & Taboury: Compt.rend., 1912, 154, 1509.

(64). Bodroux & Taboury: Bull.soc.chim., 1912, 11, 658.

(65). Hasell & Lunde: Acta Chem.Scand., 1950, 4, 200.

(66). Cook: Annual Reports, 1942, 39, 167.

(67). Dewar: Nature, 1950, 166, 790.

(68). Robertson: J.C.S., 1951, 1222.

(69). Mellor: "Comprehensive Treatise on Inorganic and Theoretical Chemistry, 1923, Vol.III, p.192.

(70). Windaus: Sitzungsber.Heidelberger Akad.Wiss., Math.-Nat.Kl., A, 1914, 18 Abh.; 1919, 16 Abh.

(71). Booth & Saunders: Chem. & Ind., 1950, 824.

(72). Dauben & Ringold: J.A.C.S., 1951, 73 , 876.

(73). Doering & Detert: J.A.C.S., 1951, 73 , 876.

(74). Thiele & Schneider: Ann., 1909, 369, 287.

(75). Thiele & Weitz: Ann., 1910, 377, 1.

(76). Britton & German: J.C.S., 1930, 1249.

(77). Hahn & Klockmann: Zeitzchr.physik.Chem. (A), 1930, 146, 389.

(78). Arnold & Sprung: J.A.C.S., 1938, 60, 1163.

(79). Lauer: Ber., 1937, 70, 1288.

(80). Nozoe: Bull.Chem.Soc.Japan, 1936, 11, 295.

(81). Nozoe: Science Reports of the Tôhuku University, 1950, Series I, vol.34, no.4.

(82). Cook, Dickson & Loudon: J.C.S., 1946, 746.

(83). Bigiavi & Cerchiai: R.C.Atti Accad.Lincei, (5), 31 II, 28.

(84). Koch: J.C.S., 1951, 512.

(85). Aulin-Erdtman: Acta Chem.Scand., 1951, 5, 301.

(86). Barton: Experientia, 1950,7, 316.

(87). Brown, Henbest & Jones: J.C.S., 1950, 3639.

(88). Hartman & Brethren: Organic Synth., Coll.Vol.II, 278.

(89). Hartman & Phillips: Organic Synth., Coll.Vol.II, 464.

(90). Kohler, Tishler, Potter & Thomson: J.A.C.S., 1939, 61, 1057.

(91). Vander Haar, Voter & Banks: J.Org.Chem., 1949, 14, 836.

(92). Nozoe, Kitahara & Andô: Proc.Japan Acad., 1951, 27, 107.

(93). Plattner: Helv.Chim.Acta, 1944, 27, 801.

(94). Olivier: Rec.Trav.Chim., 1924, 43, 875.

(95). Elvidge, Linstead, Sims & Orkin: J.C.S., 1950, 2235.

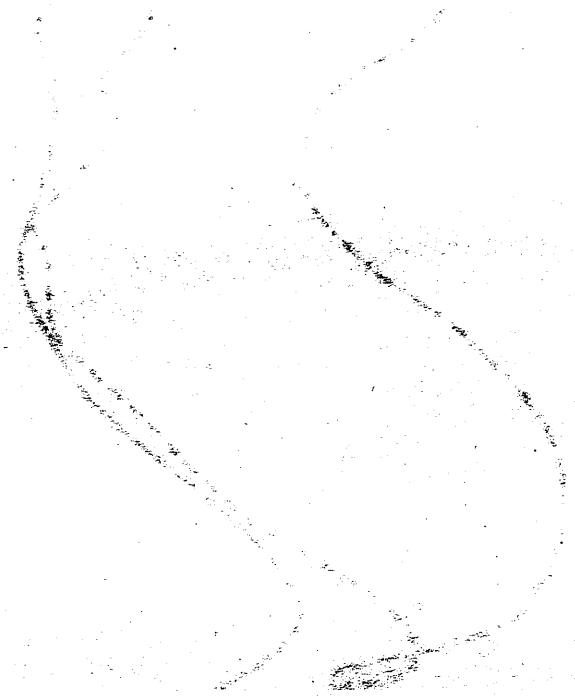
(96). Grundmann: Ber., 1936, 69, 1755.

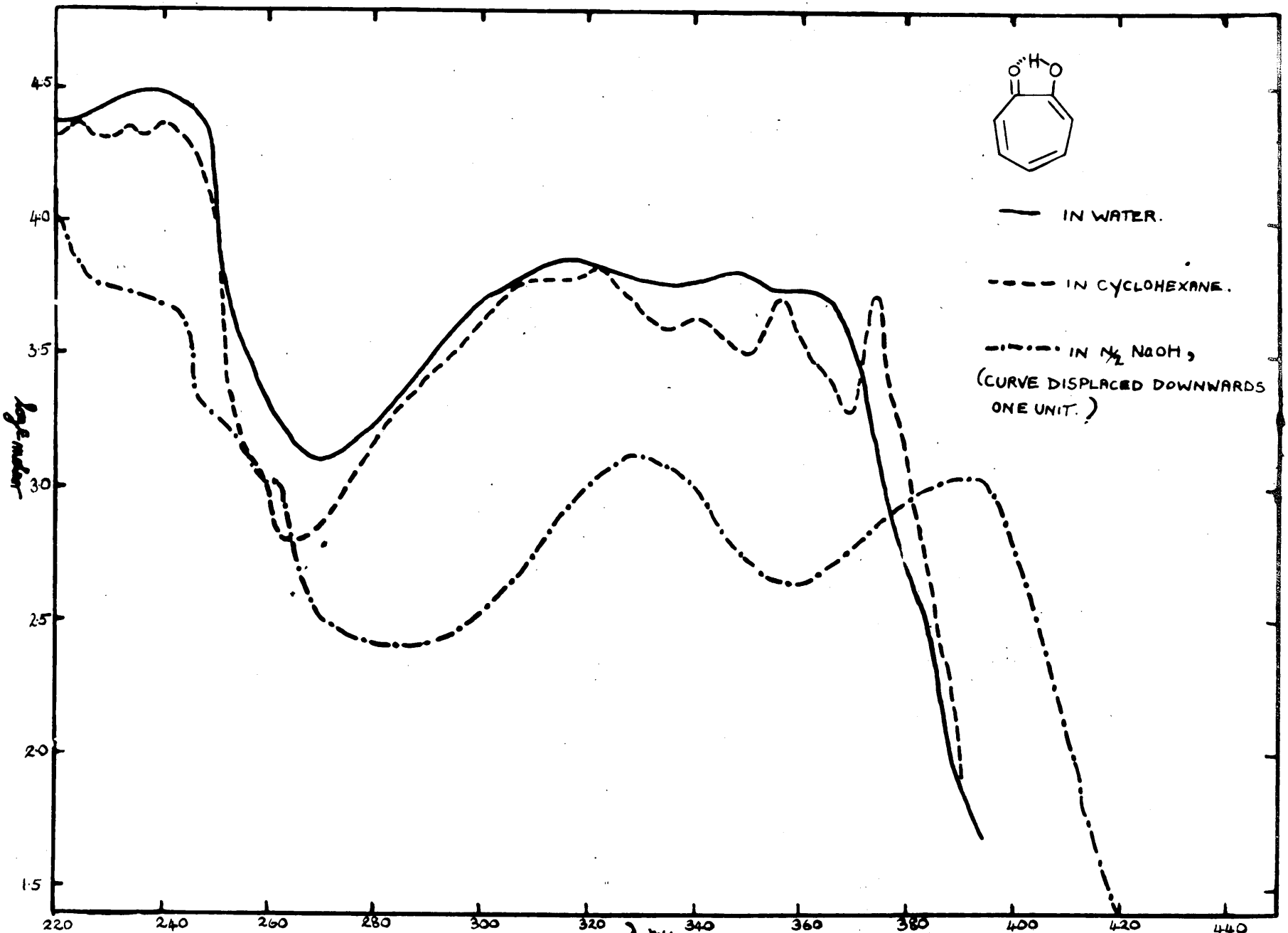
(97). Buning: Rec.Trav.Chim., 1921, 40, 350.

(98). Sudborough: J.C.S., 1895, 67, 595.

(99) Pauling : "Nature of the Chemical Bond", 1945, P.105

(100) Boudet : Bull. Soc. chim., 1948, 15, 390

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IN N/2 NaOH,
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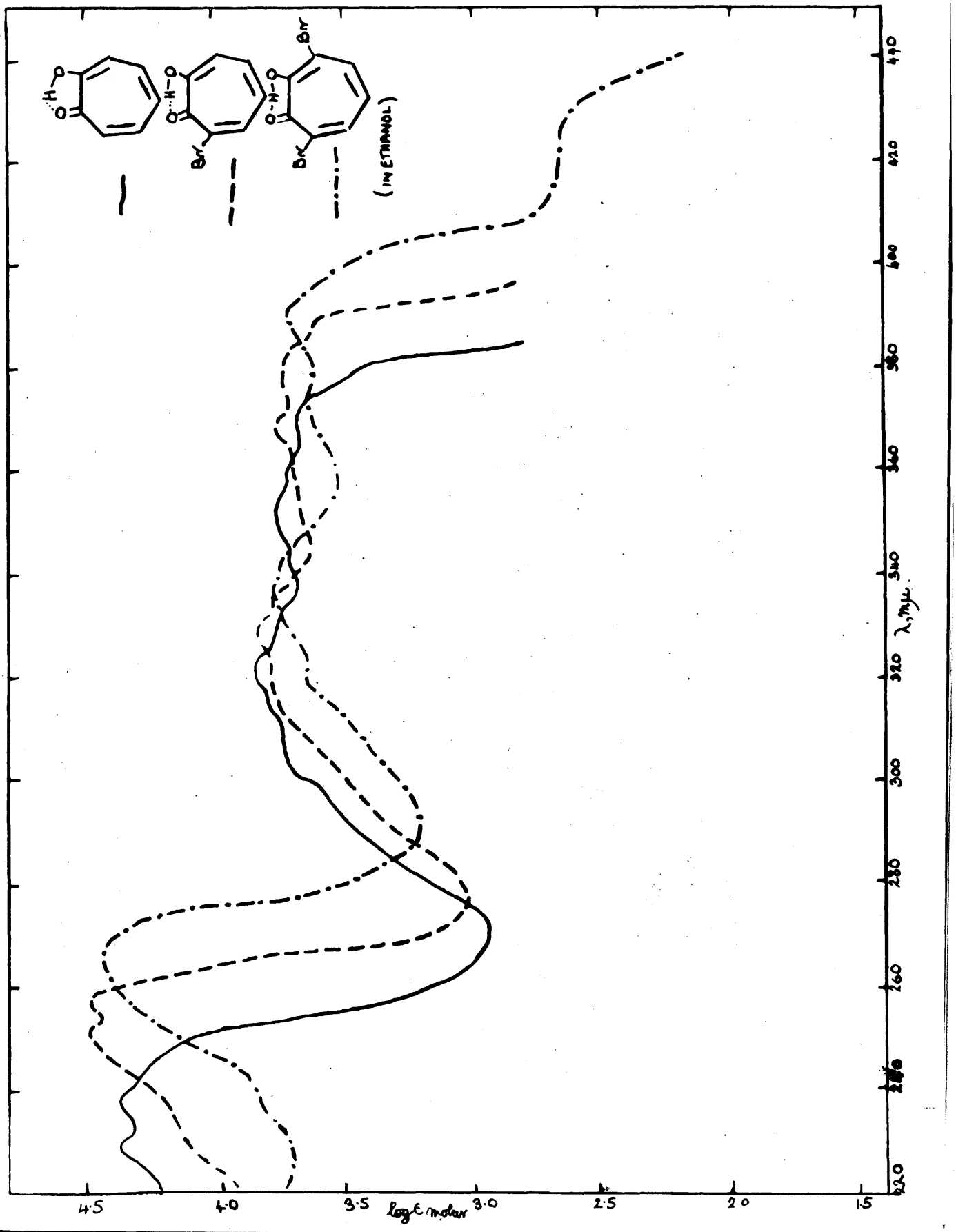
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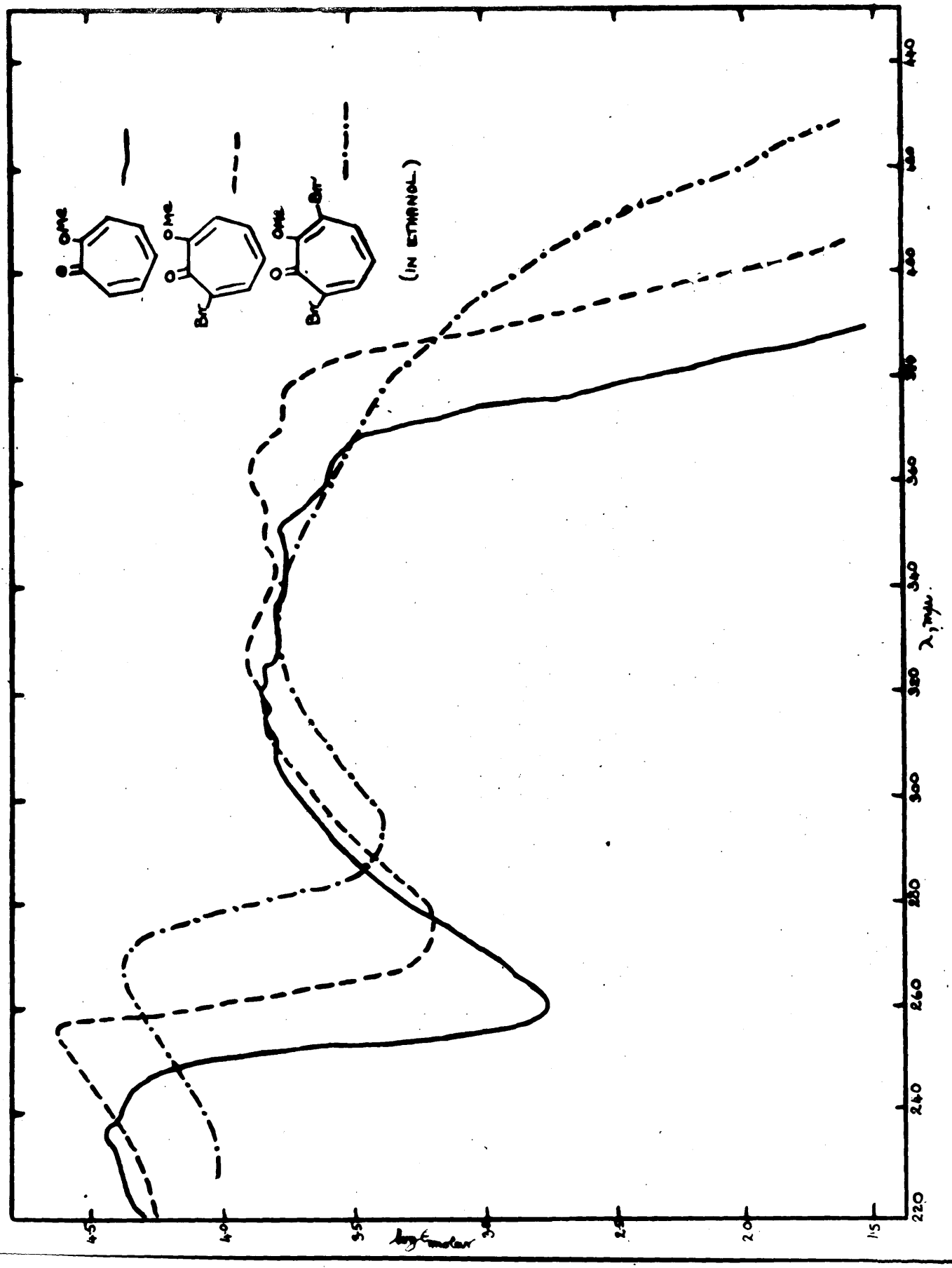
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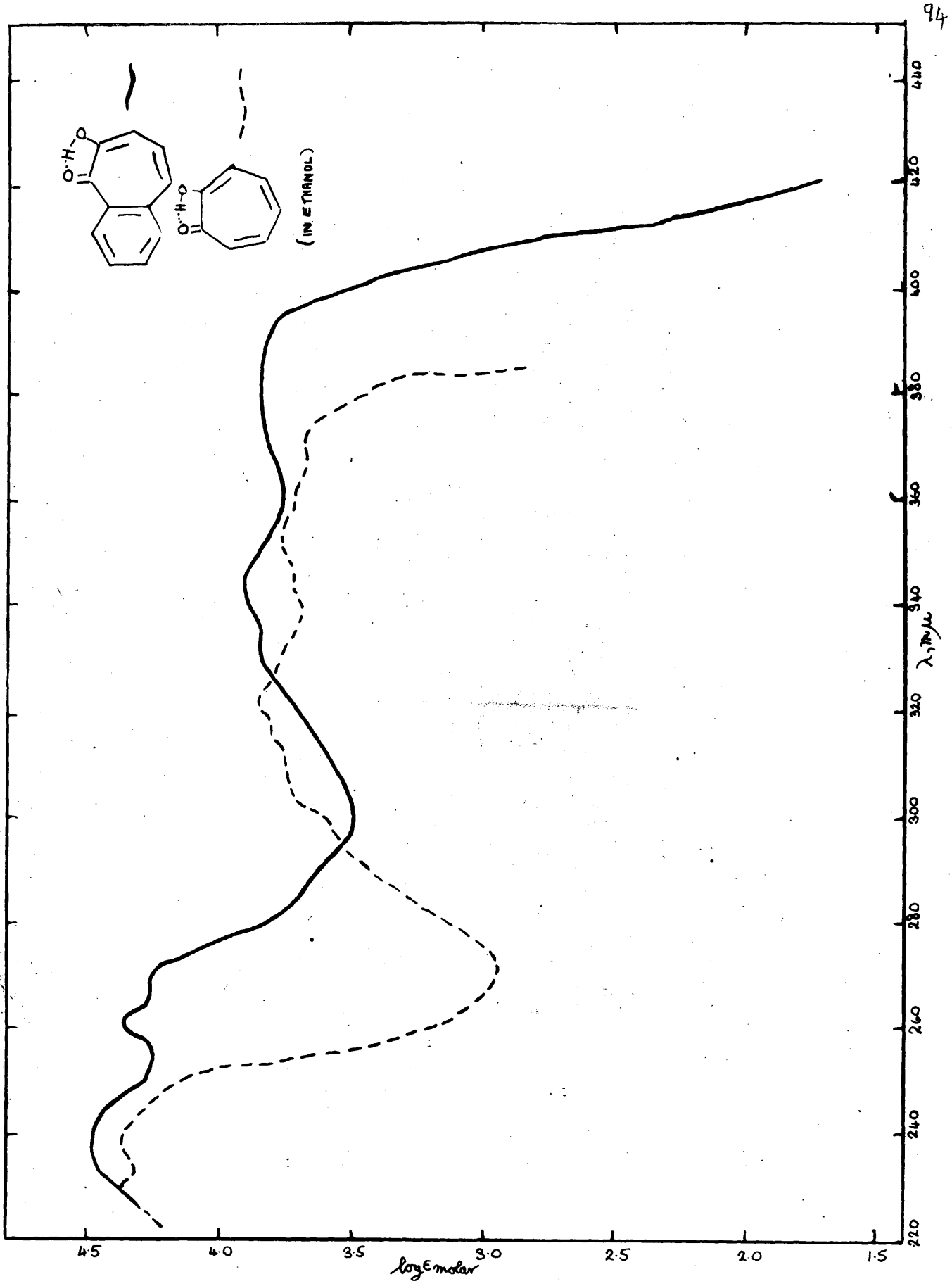
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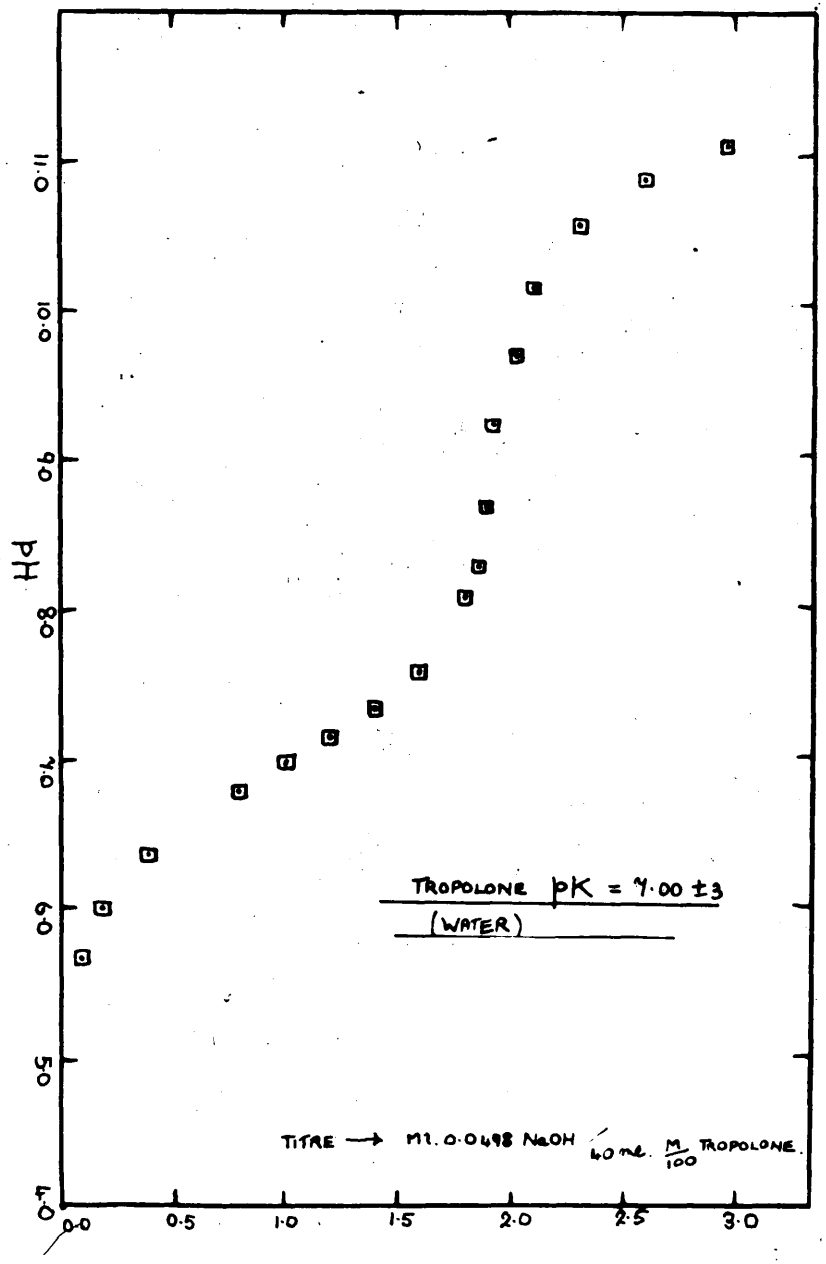
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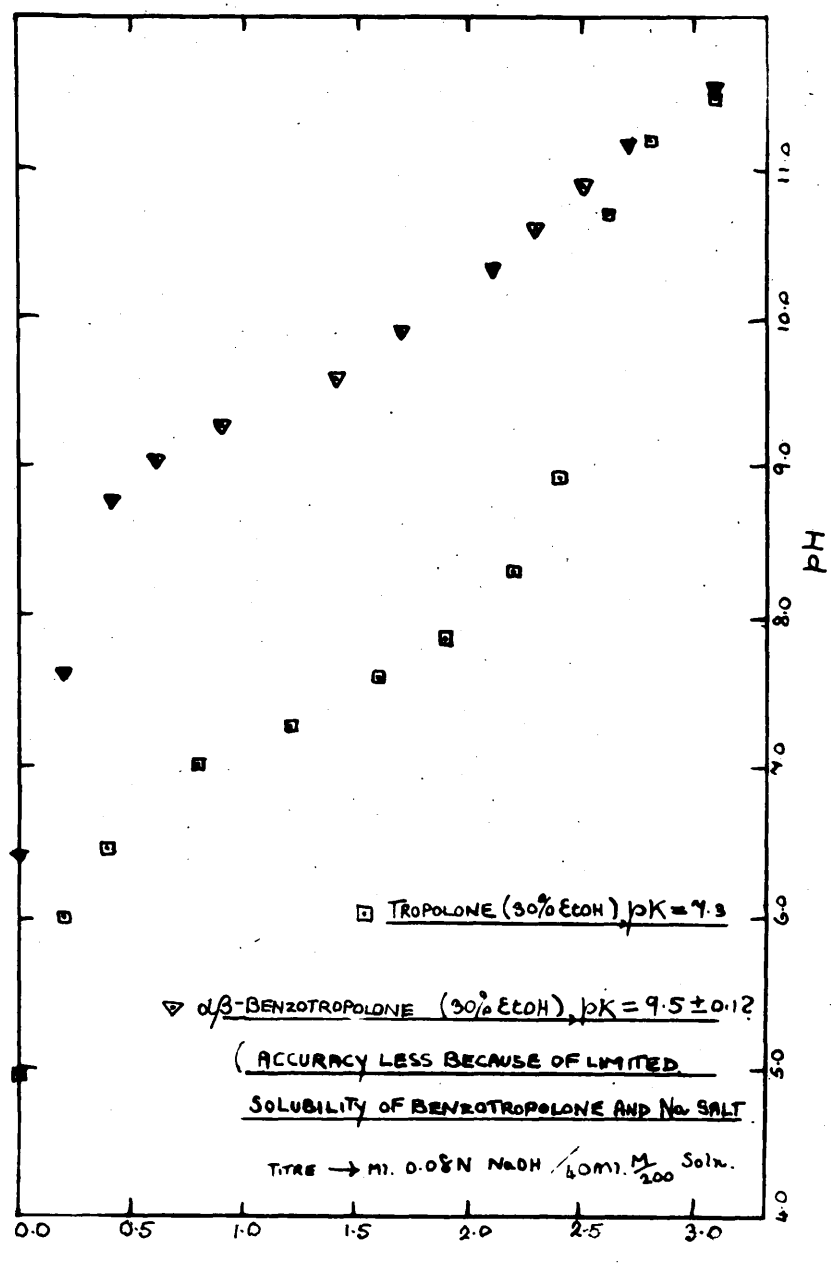
(WATER)
TITRE → Ml. 0·0498 N NaOH / 40 ml. M/100 TROPOLONE.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2·5
3·0
TROPOLONE (30% EtOH) pK = 7·3
α/β-BENZOTROPOLONE (30% EtOH) pK = 9·5 ± 0·1?
(ACCURACY LESS BECAUSE OF LIMITED
SOLUBILITY OF BENZOTROPOLONE AND Na SALT
TITRE → Ml. 0·08N NaOH / 40 Ml. M/200 Soln.