Syntheses of Polycyclic Structures.

A Thesis

submitted by

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in the

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She is also indebted to Mr. J.M.L. Cameron and Miss Kennaway, who carried out the micro-analyses.

Summary.

Part 1.

An attempt to synthesise s-hexahydrochrysene (XlV) using the inactive αβ-diphenylglutaric acid (XX) of higher m.p. as staring material, is described. Cycli--sation of the anhydride of this acid produced α-phenyl--1-indanone-3-acetic acid (XXXV) instead of the expected derivative of tetralone, (XXl). A stereoisomer of (XXXV) was prepared by esterification and hydrolysis. Clemmensen reduction and chain lengthening by the Arndt-Eistert procedure, of both these isomers produced two forms of β-phenyl-β-1-indanepropionic acid (LlX). Cyclisation and reduction of the two homo-acids gave two hydrocarbons, 1-phenyl-1:2:3:9-tetrahydroacenaphthene, (LXl), the structure of which was shown by dehydrog--enation and oxidation of the product to 2-phenyl-1:8--naphthalic anhydride (LXVlll).

Part ll.

dl-αβ-Di-1-naphthylsuccinic acid (1) has been synth--sised from naphthalene as follows:- Chloromethyl-naphthalene (lX) was prepared and converted into naphthyl-acetic acid via the nitrile. The sodium derivative of the ester of this acid underwent self-condensation by means of iodine to give the racemic and meso forms of ethyl-αβ-dinaphthylsuccinate (Xll), both of which were

hydrolysed to the corresponding racemic acid (l). In the hope of obtaining a hexacyclicdihydric phenol (ll), several attempts have been made to cyclise the anhydride of (l). Aluminium chloride in a variety of solvents was used, and anhydrous hydrofluoric acid, but all these attempts were unsuccessful and the line was abandoned.

Part lll.

An attempt has been made to prepare the as yet unknown 4:5-dimethylphenanthrene (lV), from pyrene (l) by the use of two different reactions. Treatment with osmium tetroxide gave a diol (ll) which was oxidised to a substance believed to be phenanthrene-4:5-dialdehyde (XVll). This compound could not be reduced to the required hydrocarbon (lV). Ozonisation of pyrene gave phenanthrene-4-aldehyde-5-carboxylic acid (lll). The aldehyde group of this acid could not be reduced in a straightforward manner. The methyl ester, however, was reduced using lithium aluminium hydride to 4:5-dihyd--roxymethylphenanthrene (XXVl), which did not yield the expected dichloromethyl compound on treatment with hydrochloric acid but instead produced a cyclic ether through loss of water. This work is still in progress.

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Theoretical and Discussion.

PART 1.

Attempted Synthesis of Chrysene Derivatives.

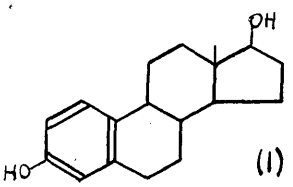
The biological effects of the Sex Hormones have been known for many years. By biological methods it was established that the growth and physiological functioning of the reproductive organs proceeds under the influence of certain chemical compounds with characteristic biological tests, and these have come to be known as the sex hormones. The chemistry of these substances is, however, a modern problem, although the sterols and the bile acids, which have a related constitution, have been studied since the earliest days of science. Recent chemical research has eluci-dated the structure of these hormones and has shown them to consist of three types, viz.:

(a) the oestrogenic hormones, e.g. oestradiol (1), which is partially converted in the body to oestrone (11). (Reference 1)

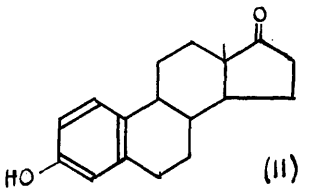
(b) the androgenic hormones, e.g. androsterone (111).

(c) the progestational group of hormones, e.g. progesterone (1V).

Even before the structure of oestrone (the first



(I)



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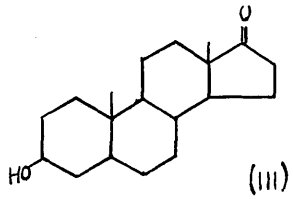

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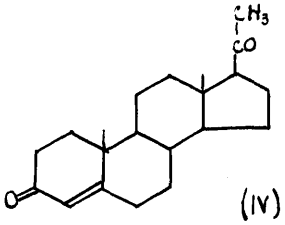
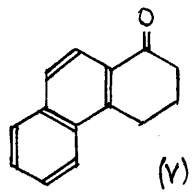


(IV)

oestrogenic hormone to be isolated) had been com--pletely elucidated, Cook, Dodds and Hewett (2) attempted to synthesis the natural hormone. These workers found that their starting material, 1-keto--1:2:3:4-tetrahydrophenanthrene (V) had, itself, definite if feeble oestrogenic activity, and this result indicated that the structural conditions in the molecule which are necessary for a substance to show this type of activity were not highly specific.

Since that time, systematic attempts have been made to prepare oestrogenic compounds, either by suitable adjustment in the molecule of the natural hormone, or, by the synthesis of compounds which resemble oestradiol in the distance between the hydrox--yl groups and in the general size and shape of the

molecule. (3)



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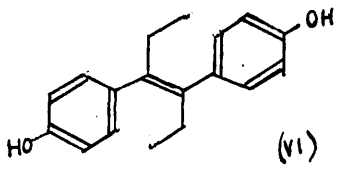

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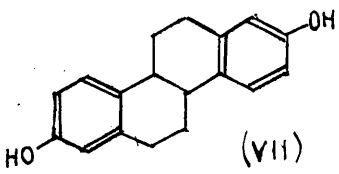

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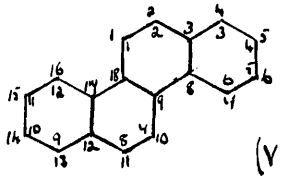
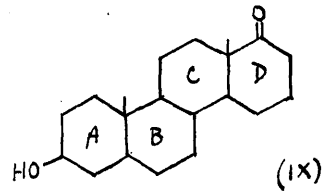


(VIII)

e.g. Stilboestrol (VI), which is a synthetic compound, is as active as oestradiol itself. The <u>trans</u> isomer of 4:10-dihydroxyhexahydrochrysene (VII) was also found to be active although only in fairly large doses. (Chrysene is numbered as shown in formula (VIII). The numbers inside the rings are used for derivatives of chrysene itself. The numbers outside are used for derivatives of hydrogenated chrysenes.)

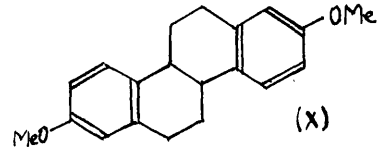
Oestrone was hydrogenated to a non-crystalline product which was not identical with the male sex hormone, androsterone (III), but which possessed the same type of physiological activity. (4) Also a five-membered ring D is not essential for activity of this nature, since D-homoandrosterone (IX) with a reduced chrysene structure, has about the same potency as androsterone itself. (5) This suggests that re--duction of 4:10-dihydroxyhexahydrochrysene (VII)

would produce a compound with androgenic activity.



(IX)

The object of the present work was the synthesis of hexahydrochrysene by a convenient and preparative method which would be applicable to the introduction of methoxyl groups at the desired positions giving 4:10-dimethoxyhexahydrochrysene (X). Demethylation to 4:10-dihydroxyhexahydrochrysene has already been accomplished. (6)

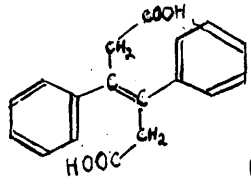


(X)

It was intended to test this substance (VII) and its derivatives for oestrogenic activity, and to reduce these compounds to perhydrochrysene derivatives which could then be tested for androgenic and progestational activity.

Chrysene was first synthesised by Beschke in 1911. (7) A Reformatsky reaction on benzil and its derivatives led to acids of the type (XI), and the essential stage was the double ring closure of these compounds. A similar synthesis was that of von Braun and Irmisch (8) who prepared the saturated ββ'-diphenyl--adipic acids (XII). Cyclisation of the cis and

trans isomers of this acid gave cis and trans-diketo-hexahydrochrysenes (XIII) which were reduced to the two isomers of the desired hydrocarbon (XIV).



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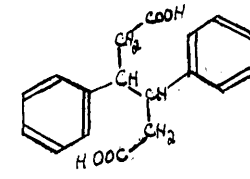

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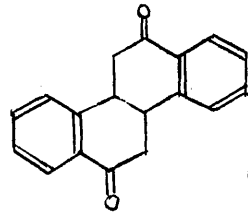

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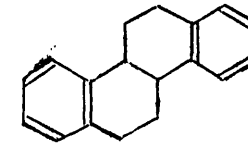
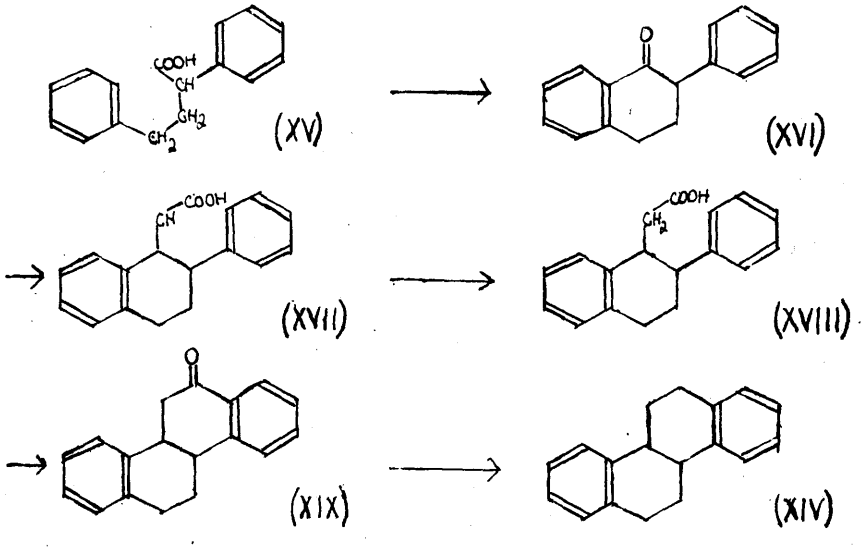


(XIV)

This method enables both cis and trans-hexahydrochrysene to be obtained readily but the preparation of the required $\beta\beta'$-diaryladipic acids is only accomplished in poor yield. The details of this synthesis were improved by Ramage and Robinson (9) and a combination of the syntheses, giving improvements in yield in the preparation of the acids (XII) was carried out by Badger. (10)

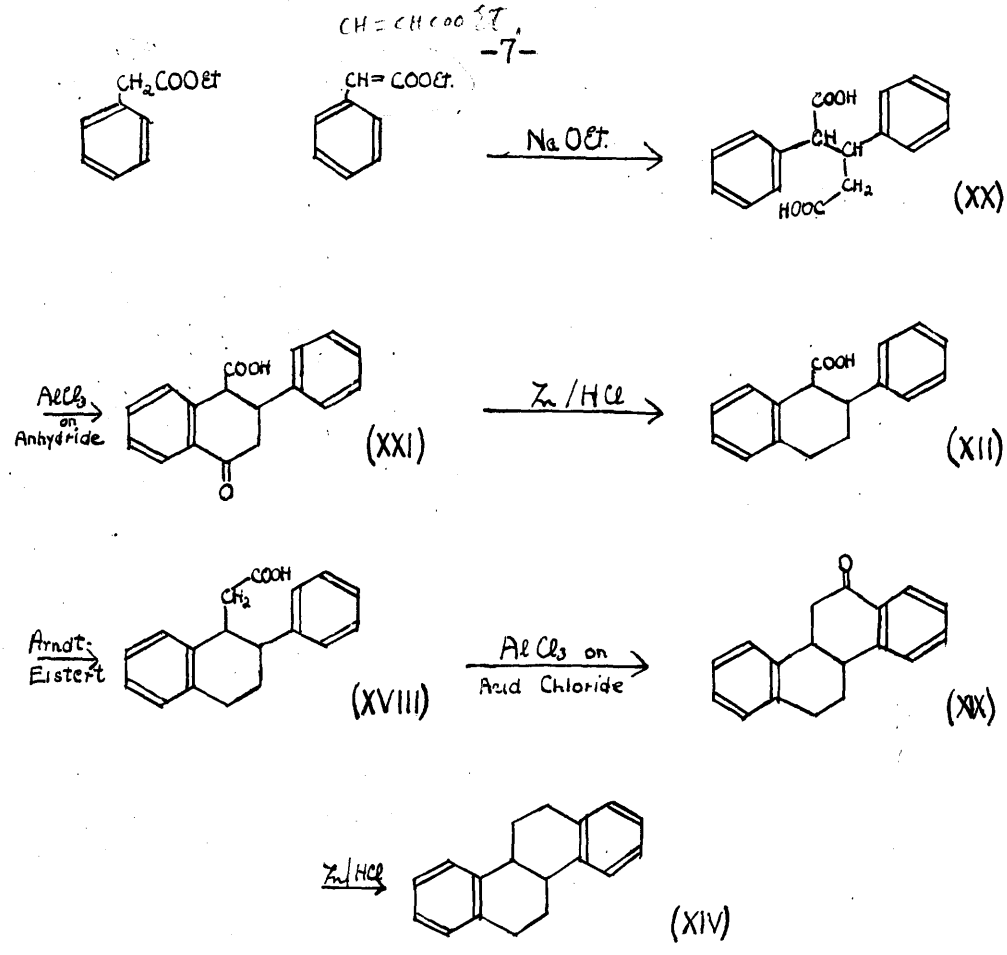
The synthesis of Newman (11) is of interest in the present case. $\alpha\gamma$-Diphenylbutyric acid (XV) was prepared from benzalacetophenone. On cyclisation 2-phenyltetralone (XVI) was obtained and a Reformatsky reaction, followed by dehydration and hydrolysis produced (XVII). Reduction gave 2-phenyl-1:2:3:4-

-tetrahydronaphthalene-1-acetic acid (XVIII) which was cyclised to 2-keto-hexahydrochrysene (XIX) and reduced to cis-hexahydrochrysene (XV). Production of this cis hydrocarbon indicated that the acid (XVIII) was also of cis configuration. This synthesis is suitable for the introduction of alkyl groups at various positions but not for the introduction of methoxyl groups, because of the difficulty of preparing suitable starting materials.



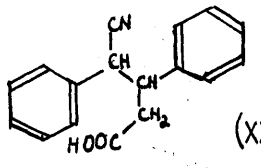
The prefixes cis and trans refer here to the disposition of groups about the fused ring positions of the central hexahydronaphthalene nucleus.(9)

In the proposed synthesis of hexahydrochrysene suitable for extension to methoxylated derivatives αβ-diphenylglutaric acid was used as starting material and the subsequent stages are outlined below.

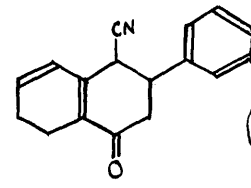


It was hoped that cyclisation of (XX) would yield the keto-acid (XXI), from which a ketohexahydrochrysene (XIX) would be obtained on reduction, chain lengthen--ing, and further cyclisation. The ketone on reduction would then yield the desired hexahydrochrysene (XIV).

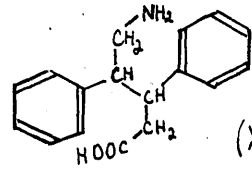
In a preliminary attempt to obtain chrysene deriv-atives by a similar route, W. Barr in this University prepared βγ-diphenyl-γ-cyanobutyric acid (XXIII) by a Michael condensation between benzyl cyanide and ethyl cinnamate.(12)



(XXIII)



(XXIV)



(XXV)

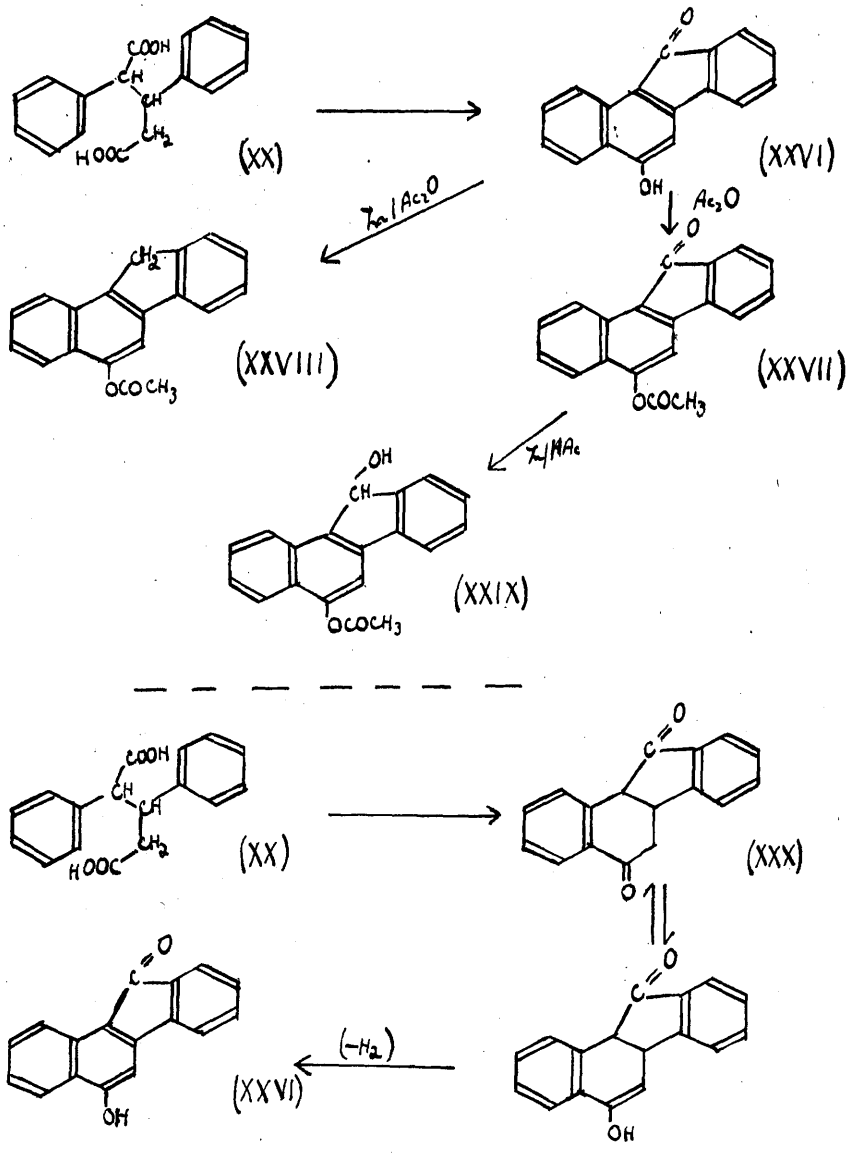
Attempts to cyclise the cyano-acid (XXIII), in order to obtain the cyano-ketone (XXIV) were not promising, nor was it found possible to reduce the cyano group to an amino-methyl group in the hope that this procedure would enable the cyclisation to take place more readily. Moreover, hydrolysis of (XXIII) to αβ-diphenylglutaric acid (XX) could only be brought by heating in a sealed tube with hydrochloric acid.

However, αβ-diphenylglutaric acid is readily prepared by the Michael condensation of ethyl phenyl--acetate and ethyl cinnamate followed by ~~(piece of)~~sis, (13) and this was the method adopted for this ~~(piece of)~~ work. This acid (XX) contains two dissimilar assymetric carbon atoms, and all four optically forms are known. The two racemates have m.p.s 231° and 208°. The acid obtained from the above Michael reaction was the higher melting racemate but the anhydride produced from this acid by refluxing with acetic

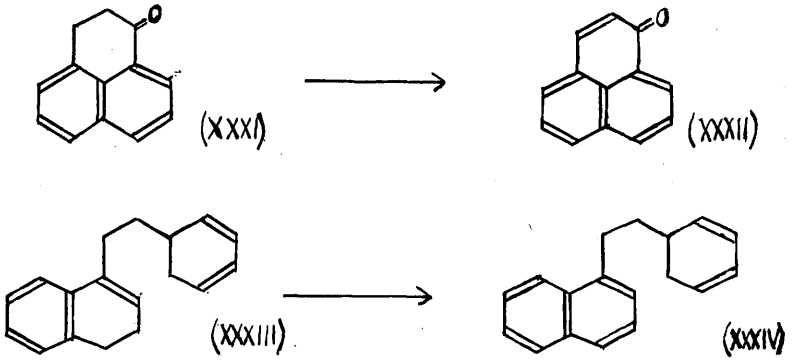
anhydride was that of the lower melting compound. This is shown by its hydrolysis to form the acid of m.p.208°, and its reaction to form the lower melting ester and not that corresponding to the acid from which it was prepared. (14)

Treatment of this anhydride with anhydrous alumin--ium chloride in nitrobenzene solution gave a keto--acid as expected. If, however, the experiment was conducted without ice cooling, there was also obtained a small amount of a bright red compound, which was shown to be 3-hydroxy-1:2-benzfluorenone (XXVI). (15) Treament with acetic anhydride gave 3-acetoxy-1:2-benzfluorenone (XXVII) and reductive acetylation with zinc in acetic anhydride produced 3-acetoxy-1:2-benzfluorene (XXVIII). Both acetyl compounds were identified by comparison with authentic samples. The reduction of the fluorenone (XXVI) to the fluorene(XXVIII) is curious, for Cook and Preston (15) found that the fluorenone (XXVII) was reduced by zinc and acetic acid only as far as the hydroxyl compound 3-acetoxy-1:2-benzfluorenol (XXIX).

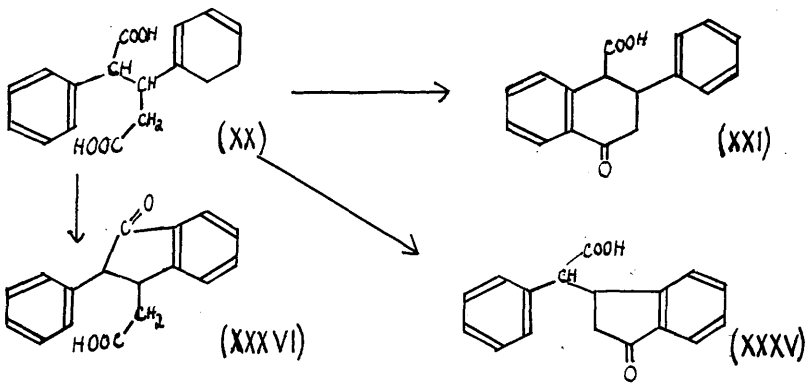
The formation of this hydroxybenzfluorenone has apparently arisen through a double ring closure to a compound (XXX) followed by enolisation and dehydrog--enation.



Dehydrogenation has been noted in many Friedel and Craft reactions; e.g. Cyclisation of β-1-naphthyl--propionyl chloride yielded (XXXII) instead of (XXXI) and treatment of (XXXIII) produced (XXXIV) and no cyclisation product. (16)

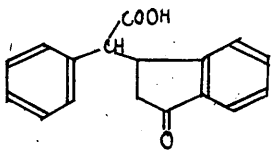


The keto-acid, the main product obtained by monocyclisation of the anhydride of αβ-diphenylglu--taric acid (XX) could, theoretically, have one of the following three structures:

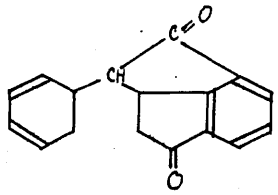


From the work of von Braun and others,(17) who showed that, under similar conditions, six-membered rings are formed in preference to five-membered rings, it was expected that the desired product, 2-phenyl-4-keto--1-carboxy-1:2:3:4-tetrahydronaphthalene (XXI), would be obtained. The formation of 3-hydroxy-1:2-benz--fluorenone provides some evidence in favour of this view. However, the keto-acid was converted to its

acid chloride and treated with a further quantity of aluminium chloride. No cyclisation took place and the keto-acid itself was unaffected by anhydrous hydrofluoric acid. This suggested that the original cyclisation had given rise to one of the indanone derivatives (XXXV) or (XXXVl) instead of the expected tetralone (XXl). Structure (XXXVl) is excluded, however, for the keto-acid gave a benzylidene derivative. The keto-acid must therefore have the structure represented by (XXXV) or (XXl). Further cyclisation of the tetralone (XXl) should give rise to (XXVl) fairly easily as already stated, whereas cyclisation of the indanone (XXXV) would necessitate the formation of a compound (XXXVll).



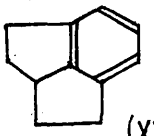
(XXXV)



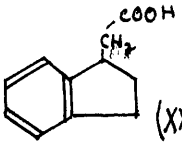
(XXXVll)

This compound contains a strained system of rings, i.e. two five-membered rings mutually fused to a benzene nucleus as in the parent structure (XXXVlll), and until recently, such a structure was unknown. e.g. hydrindenylacetic acid (XXXlX) could not be cyclised and all attempts to bring about ring closure of (XL) and (XLl) resulted in the formation of intermolecular condensation products. (18) Not long ago

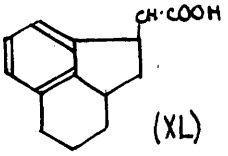
however, Hund and Mold (19) claimed to have prepared 1:9-cyclohexylenefluorene (XLll) but this claim has not yet been substantiated.



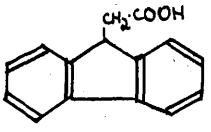
(XXXVIII)



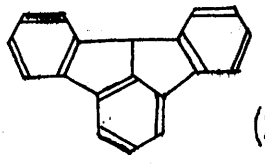
(XXXIX)



(XL)



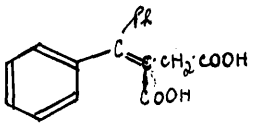
(XLI)



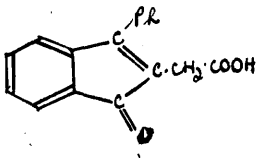
(XLII)

It will therefore be assumed, for the sake of argument, that (XXXV) is the correct structure for the keto-adid, and further proof will be given later.

Intramolecular acylation may lead to a five-membered ring when a six-membered ring is also possible, if there are activating substituents in the aromatic ring concerned in the process. Also, if the carbon chain, which will form the ring, is unsaturated, then five-membered ring formation is favoured by cyclisation. e.g. α-diphenylitaconic acid (XLlll), when treated with cold concentrated sulphuric acid, yields $\underline{\alpha}$-phenyl-$\underline{\gamma}$--indene-one-$\underline{3}$-acetic acid (XLlV).(20)

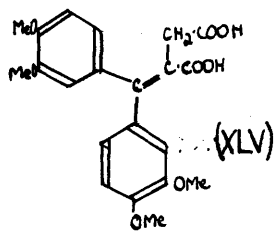


(XLIII)

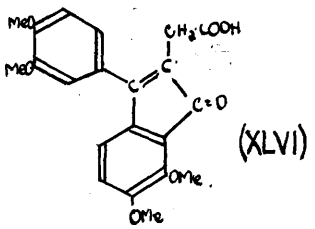


(XLIV)

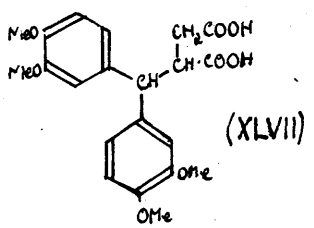
This does not apply to acids with a saturated side chain, however, for although γγ-di-(3:4-dimethoxyphenyl)--itaconic acid (XLV) yields 1-keto-5:6-dimethoxy-3--(3:4'-dimethoxyphenyl)-indene-2-acetic acid (XLVI), with a newly formed five-membered ring, the saturated acid bis-(3:4-dimethoxyphenyl)-methylsuccinic acid (XLVII), gave 4-keto-6:7-dimethoxy-1-(3':4'-dimethoxy--phenyl)1:2:3:4-tetrahydronaphthalenecarboxylic acid (XLVIII), with a newly formed six-membered ring. (21)



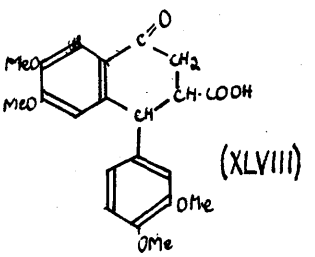
(XLV)



(XLVI)

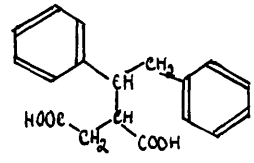


(XLVII)



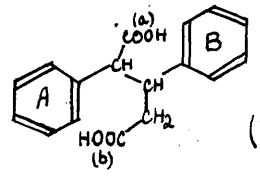
(XLVIII)

Also, cyclisation of γ-phenyl-γ-benzylpyrotartaric acid (XLIX) gave several different ring compounds all containing six-membered rings but there was no evidence of five-membered ring formation. (22)



(XLIX)

There is, moreover, no apparent reason why the cyclisation of carboxyl group (b) in (XX) should be inhibited on steric grounds, and it seems probable that the main factor in promoting theeformation of (XXXV) in preference to (XXI) is the deactivation of ring A) by the carboxyl group (a).

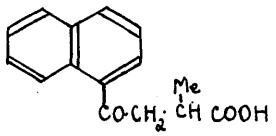


(XX)

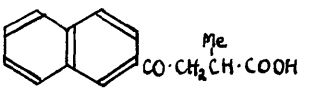
It is interesting that this deactivation completely outweighs that of both carboxyl groups on ring (B). This is consistent with the fact that the induction effect of a group is rapidly dampened on passing along a carbon chain, for both carboxyl groups are removed from ring (B) by two carbon atoms, whereas the effect of carboxyl group (a) on ring (A) requires to be transmitted through on carbon atom only.

The fact that, of the two indanone derivatives

(XXXVI) and (XXXV), only (XXXV) is formed, is also of interest, cyclisation having taken place through a the carboxyl group (b) adjacent to a secondary carbon atom, and not through carboxyl group (a) which is adjacent to a tertiary carbon atom. This is in agree--ment with the results of other workers for Haworth (23) found that in the Friedel and Craft reaction between naphthalene and methylsuccinic anhydride in nitrobenzene solution, two compounds, (L) and (LI), were formed in both of which the carbonyl group nearest the secondary carbon atom became attached to the aromatic nucleus.

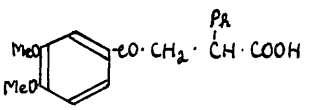


(L)



(LI)

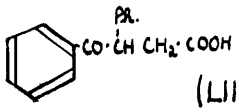
Similarly Robinson and Young (24) obtained the compound (LII) by the condensation of phenylsuccinic anhydride and vetravole also in nitrobenzene solutiom.



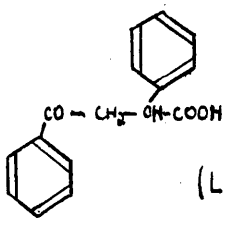
(LII)

These results might be considered as an illustration of the similarity between methyl and phenyl groups as far as orienting influence is concerned, (25) but other results show that this is not always the case. Thus

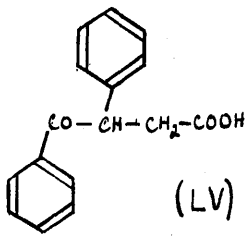
phenylsuccinic anhydride reacts with benzene at the carboxyl group adjacent to the tertiary carbon atom, producing (LIII) (26) and, in the condensation of 2:4-dimethoxyphenylsuccinic anhydride and resorcinol dimethylether approximately equal amounts of the two isomeric ketones (LIV) and (LV) were obtained. (27)



(LIII)

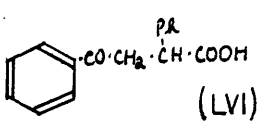


(LIV)

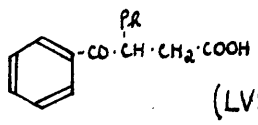


(LV)

In the last two illustrations the solvent was not nitrobenzene and it seems that this may have some bear--ing on the reaction under discussion. e.g. it has been shown that, whereas treatment of phenylsuccinic anhydride and toluene with aluminium chloride in toluene solution produced five times as much (LVI) as (LVII) the pro--portions were reversed in nitrobenzene solution. (28) i.e. although in toluene solution the carboxyl group attached to the least alkylated carbon atom is the more reactive this is not the case in nitrobenzene solution.



(LVI)

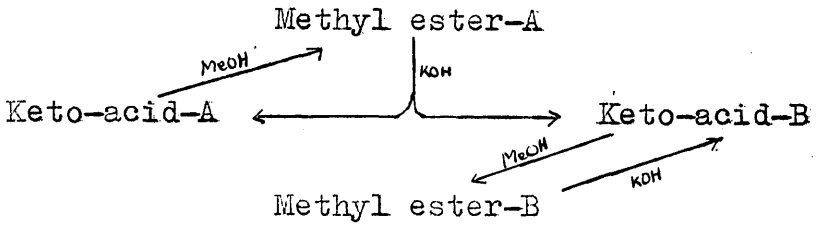


(LVII)

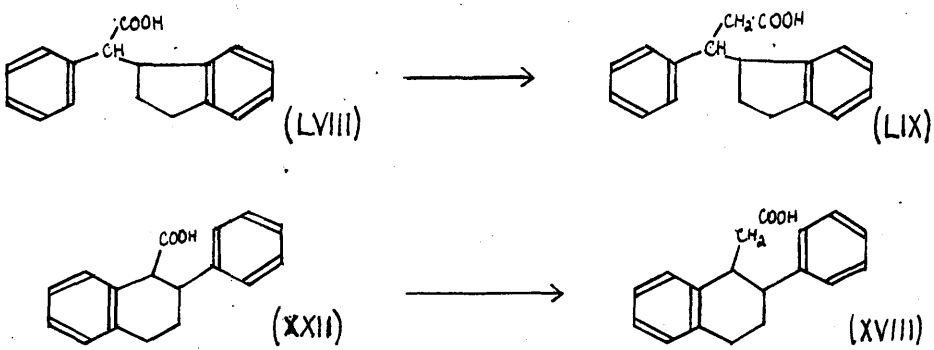
The structure of the cyclisation product as α-phenyl-1-indanone-3-acetic acid (XXXV) was established by further transformations. This keto-acid (now designated as isomeride-A) was dimorphic. Crystals deposited from benzene, acetic acid or methanol had m.p. 154-5°, but those from ethyl acetate had m.p. 170-1°. The lower melting form could be converted into the higher melting form by heating for several hours in the steam oven and the reverse process could be brought about by two or three crystallisations from methanol.

In an early attempt to purify the keto-acid the methyl ester was prepared and had m.p. 99-100°. Hydrolysis of this ester, however, gave a mixture of two acids. The more soluble portion was the original keto-acid-A but there was also obtained a much less soluble substance which, after recrystallisation from methanol had m.p. 225-6°. This acid had the same analysis as the original acid-A and still contained a carbonyl group. It was therefore, evidently a stereoisomer of this acid, viz.: α-phenyl-1-indanone-3-acetic acid-B. Hydrolysis of the methyl ester (m.p. 138-9°) gave only the higher melting isomeride-B in crystalline form but there may have been some of the A isomer in the non-crystalline acidic residues. Partial conversion of the A to the

B isomer could also be brought about by refluxing keto-acid -A for different periods of time with alcoholic alkali.



Clemmensen reduction of these two acids (XXXV) pro--duced α-phenyl-1-indaneacetic acid-A and α-phenyl-1--indaneacetic acid-B (both represented by formula LVlll), and chain lengthening by the Arndt-Eistert procedure (29) gave β-phenyl-β-1-indanepropionic acid-A, obtained through its amide, and β-phenyl-β-1-indanepropionic acid-B, ob--tained through its methyl ester. (Acids, formula LlX)



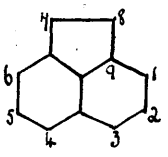
The A isomers of these two acids, (LVlll) and (LlX), could not be dehydrogenated with sulphur, selenium or palladium black. No crystalline material could be

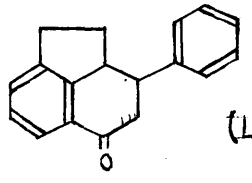
isolated and this is in accordance with the indane structure, for it has been shown that hydrindane, on treatment with palladium black at 300°, gave indane but no indene. Structures such as (XXll) and (XVlll), on the other hand would be expected to dehydrogenate smooth--ly to naphthalene derivatives. (29)

Attempts to cyclise the acid chloride of (LVlll) were also unsuccessful, and no fluorenone, which would be formed readily from (XXll), was obtained. (See page 12)

It is interesting that the two isomers of (LlX) were not interconvertible like those of (XXXV), either by boiling with alcoholic alkali alone or by preparation of the methyl ester pollowed by hydrolysis.

The two homo-acids were cyclised with anhydrous hydrofluoric acid to 3-keto-1-phenyl-1:2:3:9-tetrahydro--acenaphthene, (LX-A and B). (The numbering used for the acenaphthene molecule is shown below.)



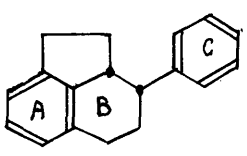


(LX)

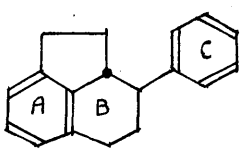
The cyclisation of the acid chloride of the A isomer was also accomplished using aluminium chloride or stannic chloride, although treatment of the same acid with 95% sulphuric acid apparently led to sulphonation.

Ketone-A (LX), on reduction by the Clemmensen-Martin procedure (30), gave a poor yield of a hydrocarbon-X. On reduction using the Huang-Minlon (31) modification of the Wolff-Kishner reaction, however, two substances were obtained, namely, the same hydrocarbon-X, m.p. and mixed m.p. 71-72°, and also another hydrocarbon-Y, m.p. 59-60°, mixed m.p. 40-45°. Since these two hydro--carbons X and Y differed appreciably in crystalline form, they could be separated fairly readily by hand. The ketone-B, when reduced by the modified Wolff-Kishner process, yielded only the hydrocarbon-Y.

The most straightforward explanation of this rather surprising formation of two hydrocarbons from ketone-A is that they represent the cis and trans isomers of 1-phenyl-1:2:3:9-tetrahydroacenaphthene (LXI).



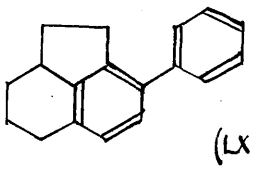
(LXI) cis



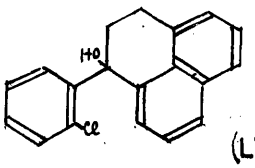
(LXI) trans.

However it is difficult to understand why reduction of the carbonyl group at position 3 should affect the con--figuration of the groups about the bond joining positions 1 and 9. Another possibility is that the electrons forming the double bonds in ring A might migrate to ring B thus allowing the two aromatic rings B and C to become conjugated as in (LXII). i.e. X and Y may be

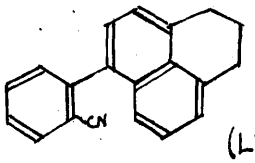
structural and not stereo-isomers. A somewhat similar case was encountered by Fieser and Gates (32), who found that when the carbinol (LXlll) was successively dehydrated, reduced and the chlorine atom replaced by the cyano group, two products were isolated. These were identified as (LXlV) and (LXV) and could only have been produced by a migration of bonds in the expected dehydration product (LXVl). It will be seen that in the two products obtained the two aromatic centres in the molecule have become conjugated.



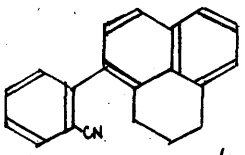
(LXII)



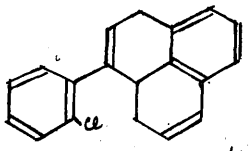
(LXIII)



(LXIV)

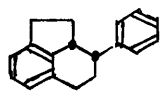
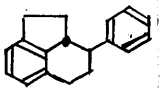
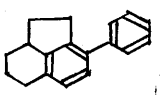


(LXV)



(LXVI)

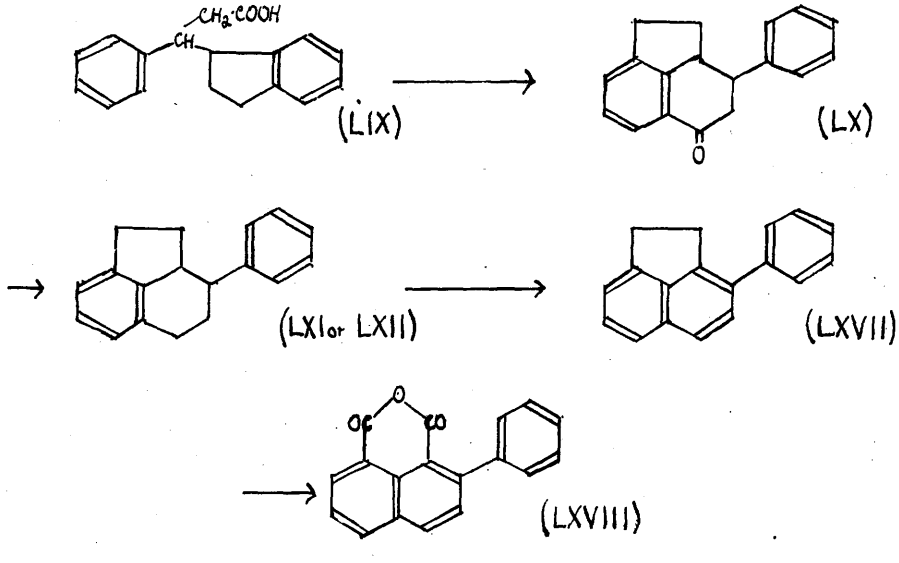
There are no analogous compounds upon which to base the true configuration of the two sets of isomers but if, for the sake of argument, the ketone-A is assumed to have the cis configuration, then there are several possibilities for the products obtained on reduction of the ketones A and B, and these are shown in the table

	Reduction of ketone-A.		Reduction of ketone B.	Changes involved.
	Clemmensen and Wolff-Kishner methods.	Wolff Kishner method.	Wolff Kishner Method.	(C=Clemmensen W.K.=Wolff Kishner.)
1	 (LXI)cis	 (LXI)trans	(LXI)trans	Partial isomerisation during W.K. on ketone-A
2	(LXI)trans	(LXI)cis	(LXI)cis	Complete change in configuration during C. on A and partial change during W.K. on A. Complete isomerisation during W.K. on B.
3	(LXI) cis	 (LXII)	(LXII)	Bond migration in both W.K. reactions.
4	(LXI)trans	(LXII)	(LXII)	Isomerisation during C. on A. Bond migration in W.K. reactions.
5	(LXII)	(LXI)cis	(LXI) cis	Bond migration during C. on A and partially during W.K. on A. Isomerisation during W.K. on B.
6	(LXII)	(LXI)trans	(LXI)trans	Migration during C. on A and partially during W.K. on A.

The alternatives 1) and 3) seem to be the only probable solutions to the problem. It is quite possible that at the high temperature of the Wolff-Kishner reaction

an inversion of configuration takes place and that the trans compound is formed from the cis. This may then retain its structure as in the possibility 1) or, if the bonds migrate, be converted to the structural isomer (LXII) as in 3).

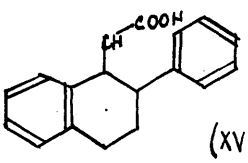
On dehydrogenation, both hydrocarbons X and Y yielded 1-phenylacenaphthene (LXVII) and this could have been produced from either (LXI) or (LXII). Oxidation gave 2-phenyl-1:8-naphthalic anhydride (LXVIII) which is known (33), and the series of reactions is outlined below.



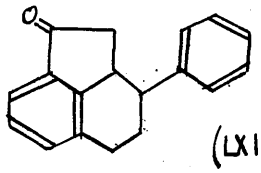
The formation of these two sets of isomers provides fairly conclusive evidence in favour of structure (XXXV) as the correct one for the keto-acid obtained on cyclis-ation of the anhydride of αβ-diphenylglutaric acid (XX). If the keto-acid had the structure (XXI), reduction

followed by chain lengthening would produce the homo--acid (XVlll). From the synthesis of Ramage and Robinson (9) it would be expected that the cyclisation o the trans form of (XVlll) would produce the unknown trans-2-ketohexahydrochrysene, but the possibility that a five-membered ring would be formed instead of a six-membered ring was also considered. If this were the case the ketone (LXlX) would be produced and this would then yield the same hydrocarbon (LXl) (or LXll) on reduction.

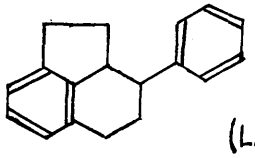
The isolation of two acids of formula $C_{18}H_{18}O_2$ (now designated as LX) removes this possibility, for, if (XVlll) were the structure of these homo-acids, then one of the isomers would have to be the cis-2--phenyl-1:2:3:4-tetrahydronaphthalene-1-acetic acid prepared by Newman, (11) (see page 5) and comparison of the m.p.s of the products now obtained with those of Newman makes this impossible.



(XVlll)

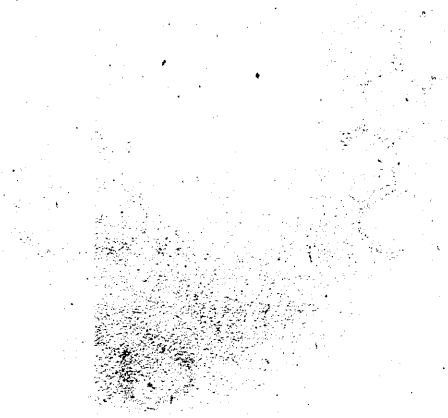


(LXIX)



(LXI)

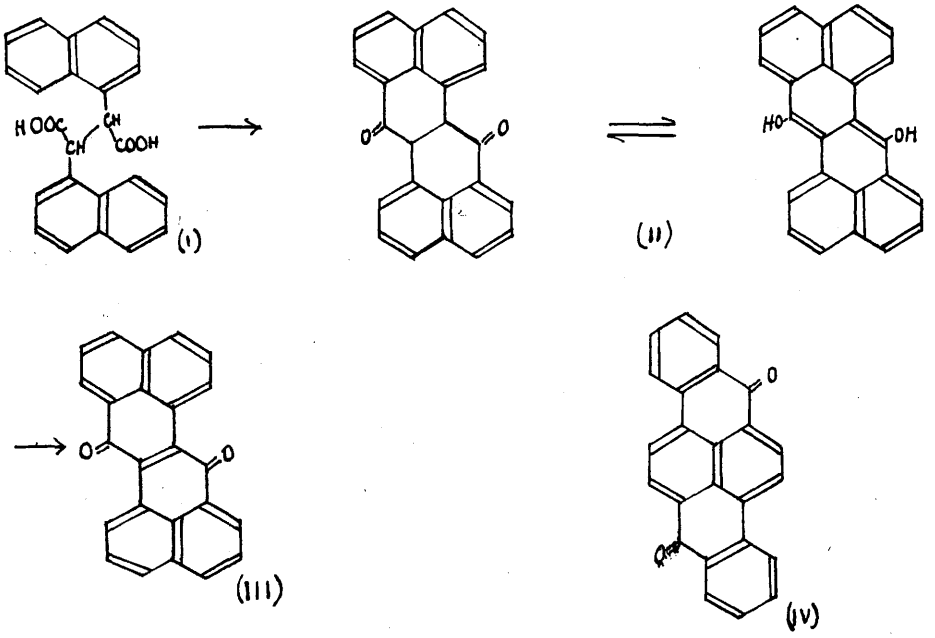
	Present work.	Newman's synthesis.
Homo-acids (XVIII) or (LX)	A-m.p. 123-5°	cis compound m.p. 170-1°
Ketones obtd. on cyclisation.	B-m.p. 103-4°	cis ketone m.p. 76-77°
	A-m.p.101-2°	
	B-m.p. 139-40°	
Hydrocarbons	X-m.p. 71-72°	cis-hexahydro-chrysene-m.p. 76° (trans-m.p. 115°)
	Y-m.p. 59-60°	



PART II.

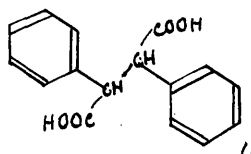
Experiments with αβ-Dinaphthylsuccinic Anhydride.

F. E. King and T. Henshall (34) prepared the meso and racemic forms of αβ-dinaphthylsuccinic acid (I), but were unable to bring about cyclisation of either isomer under the methods investigated. It was hoped that cyclisation would yield the hexacyclicdihydric phenol (II) which could then be oxidised to a possible isomer (III) of the dibenzpyrenequinone dyes. (e.g. IV).

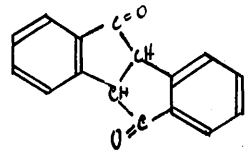


The corresponding isomers of diphenylsuccinic acid (V) had previously been found to cyclise readily (35) under the influence of concentrated sulphuric acid to diphenyl-

-succindone (V1).

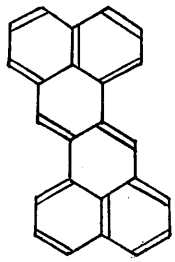


(V)

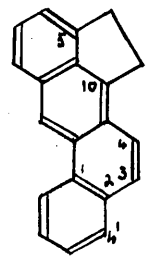


(V1)

It is just possible that, if the hydrocarbon (V11) corresponding to (11) could be prepared, it would possess carcinogenic activity.



(V11)



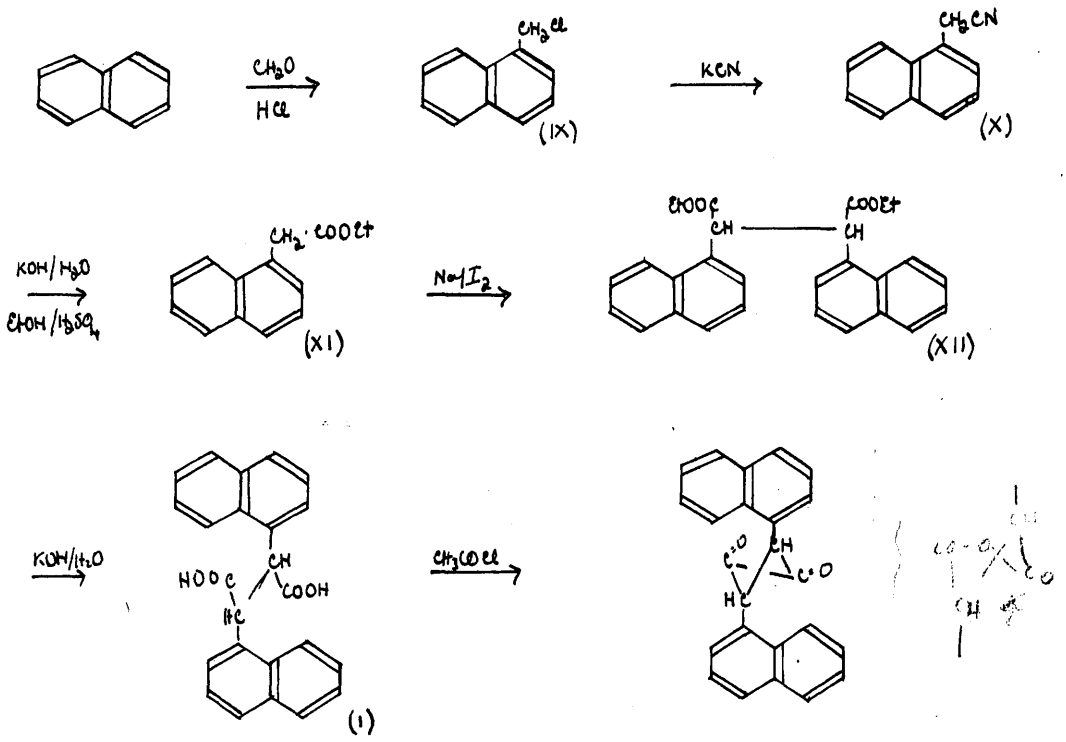
(V111)

It contains the 1:2-benzanthracene ring structure with one benzene ring introduced at positions 5 and 10 and another at positions 3 and 4'. The first of these corresponds to the five-membered ring in the active carcinogenic compound cholanthrene (V111) and, although the second ring across positions 3 and 4' would tend to destroy this activity, it is still possible that some might remain. (36)

The object of the present work was to prepare αβ-dinaphthylsuccinic acid by a similar synthesis to that used by King and Henshall and to attempt to cyclise

the anhydride of the dl-acid using methods known to be satisfactory in most cases of intramolecular acylation.

The synthesis of the acid is outlined below:



Naphthalene was converted to 1-chloromethylnaphthalene (IX) and this into 1-acetonitrile (X) using potassium cyanide in alcohol. The nitrile was hydrolysed with potassium hydroxide solution and the 1-naphthylacetic acid obtained was esterified in the usual manner to give ethyl α-naphthylacetate (XI).

The self-condensation of this ester proved to be a matter of considerable difficulty. The solid sodium

ethoxide used as condensing agent had to be completely free from alcohol or the yield was diminished and even when all possible precautions were taken to exclude moisture and alcohol, small amounts of naphthylacetic acid and unchanged starting ester were always obtained. Several different methods of preparing the condensing agent were tried but these resulted in no improvement in the yield of product which was never greater than 30%. From this condensation both racemic and meso forms of the desired ethyl-$\alpha\beta$-dinaphthylsuccinate (XII) were obtained but the quantity of the more soluble racemic ester was very small.

Both racemic and meso forms of this ester (XII), on hydrolysis with alcoholic potassium hydroxide yield the racemic acid. From the construction of models there seems to be no difference in the ease with which the two forms should cyclise, but King and Henshall discovered that the racemic form was the more reactive one and consequently, this isomer was prepared first.

This racemic acid has not yet been resolved because of the insolubility of the strychnine and brucine salts, (34) but the configuration is based on that of the closely analogous racemic-diphenylsuccinic acid and seems to be definitely established.

King and Henshall had attempted the preparation of the hexacyclic phenol (11) by the use of various re--agents. As has been stated sulphuric acid gave

a water soluble product when added to the meso ester; treatment of the same ester with phosphoryl chloride gave a mixture of tarry products; phosphorus pentoxide on the racemic acid gave the racemic anhydride and thionyl chloride had no effect on this acid.

In the present work $\alpha\beta$-dinaphthylsuccinic anhydride was prepared by the action of acetyl chloride on the racemic acid. This anhydride was treated with aluminium chloride in dry nitrobenzene and left for two days. After working up in the usual manner only unchanged starting material was obtained, and a repeat experiment in which the mixture was heated produced the same result. When carbondisulphide was used as solvent the material was again unchanged. In tetrachloroethane solution black carbonaceous material was produced, but in solution in alcohol this gave no evidence of carbonyl activity. The racemic acid itself and its anhydride were both unaffected by treament with anhydrous hydro--fluoric acid. Finally, the anhydride was added to a melt of sodium chloride and aluminium chloride and the mixture heated for some time. After working up the product was treated with alkali as usual. . Some insol--uble material was left as a residue but this had no carbonyl activity . The alkaline solution yielded a little unchanged starting acid.

Having obtained these results with the more reactive

isomer of (1) no attempt was made to prepare the meso acid and, at this point, the project was abandoned in view of the surprising resistance to cyclisation shown by the acid.

PART III.

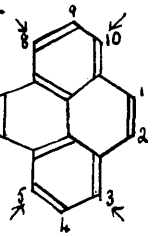
Attempted Synthesis of 4:5-Dimethylphenanthrene.

A systematic investigation of the chemistry of pyrene (1) was carried out by Vollman, Becker, Correll, and Streeck. (37) As a result of investigating a large number of derivatives, these workers found that pyrene displayed some peculiarities as far as substitution reactions are concerned. The molecule of pyrene is symmetrical and three degrees of reactivity are shown by three sets of equivalent positions:-

a) 3, 5, 8, and 10.

b) 1, 2, 6, and 7.

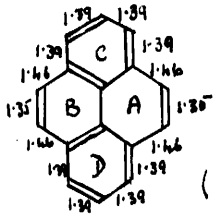
c) 4 and 9.



(I)

The positions 3, 5, 8, and 10 are the most reactive ones, direct monosubstitution invariably occurring at position 3. Direct substitution also gives 3:8 and 3:10-disub--stitution products, 3:8:10-trisubstitution products, and 3:5:8:10-tetrasubstitution products. Chlorine will attack the 1, 2, 6, and 7 positions if the 3, 5, 8, and 10 positions are already occupied and finally the 4 and 9 positions are substituted.

Since substituents enter the molecule of pyrene most easily at those positions which are separated by one

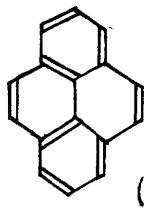


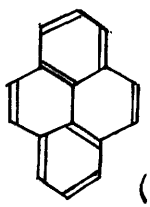
(I)

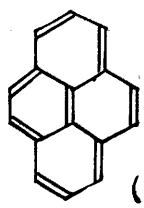
carbon atom, (i.e. meta positions) it seems that some special influence, which makes these hydrogen atoms more easily replaced than the others, must prevail. This influence outweighs any other effects which may be acting where an ortho or para directing group (e.g. -OH, or $-NHCOCH_3$) is present in the 3 or 8 positions, for even in these circumstances there is no ortho but only meta sub--stitution.

Vollman and his coworkers considered pyrene to be essentially a diphenyl derivative in which the ortho pos--itions are substituted by two 'ethenyl' groups and that the presence of these groups in the typical benzene rings C and D causes the 3, 5, 8, and 10 positions to be act--ivated.

If this is the case then of the three possible struc-tures a), b), or c), for pyrene a) and b) are the more


(Ia)


(Ib)

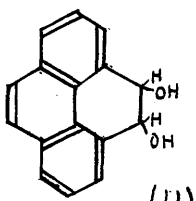

(Ic)

likely, although structure c) possibly contributes a little to the actual state of the molecule.

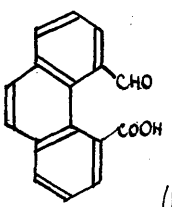
This idea is supported by the fact that ozone, alone of the reagents investigated by Vollman, attacks the molecule at positions 1 and 2 and then at positions 6 and 7. Also X-ray investigation (38) has shown that, although all the outer bonds in pyrene have approximately the same length, those joining the 1, 2 and 6, 7 positions are short bonds between two much longer bonds and are those most likely to be attacked by ozone.

Recently osmium tetroxide has also been shown to attakk the 1:2 bond with the production of 1:2-dihydro--1:2-dihydroxypyrene. (39) (11)

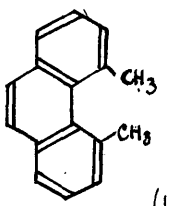
These two reactions, ozonisation which produces as the first product phenanthrene-4-aldehyde-5-carboxylic acid (111), and treatment with osmium tetroxide with the form--ation of a diol, have been employed in an attempt to prepare 4:5-dimethylphenanthrene.(1V)



(11)



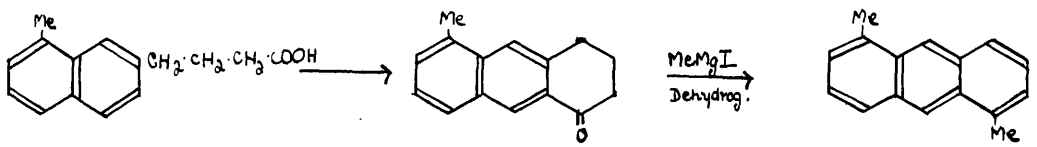
(111)



(IV)

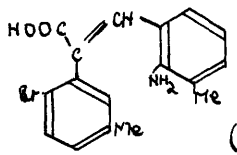
4:5-Dimethylphenanthrene is still unknown although many unsuccessful attempts have been made to synthesise it.e.g. Cyclisation of γ-(8-methyl-2-naphthyl)-butyric

acid (V) gave an anthracene structure instead of the desired phenanthrene derivative. Treatment with methyl--magnesium iodide followed by dehydrogenation produced 1:5-dimethylanthracene (Vl). (40)



(V) (VI)

Also α-(2'-bromo-5'-methylphenyl)-2-amino-3-methyl--cinnamic acid (Vll) could not be induced to undergo the Pshorr ring closure reaction. (41)



(VII)

Unsuccessful attempts have also been made to synthe--sise the closely analogous 1:9-dimethyl-1:2-benzanthra--cene (Vlll) and at one time it was considered that structures of this type could not exist. (42) However, in 1940 Newman (43) succeeded in synthesising 6:7-di--methylchrysene (lX) and discussed the possible struc--ture of these related compounds. The difficulty in preparation lies in the fact that if a model of 4:5-di--methylphenanthrene or a substance in which the methyl groups are similarly situated, is constructed so that the rings are all in one plane and the methyl groups

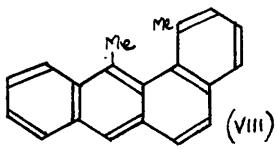
occupy the same volume as in toluene, then the methyl groups are found to interfere with each other to a large extent. There are therefore three possible structures, viz.:

a) the methyl groups lie bent away from each other but in the same plane as the benzene rings,

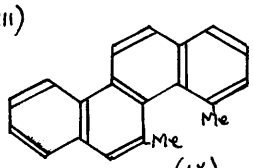
b) the aromatic rings are distorted in same way,

c) the methyl groups are bent out of the plane of the benzene rings.

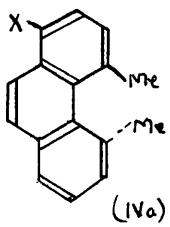
The last of these possibilities was considered by Newman to be the most likely and if this is the case then suitable derivatives of 4:5-dimethylphenanthrene should be capable of resolution into the two enantiomorphs shown below.



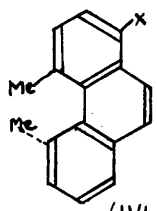
(VIII)



(IX)



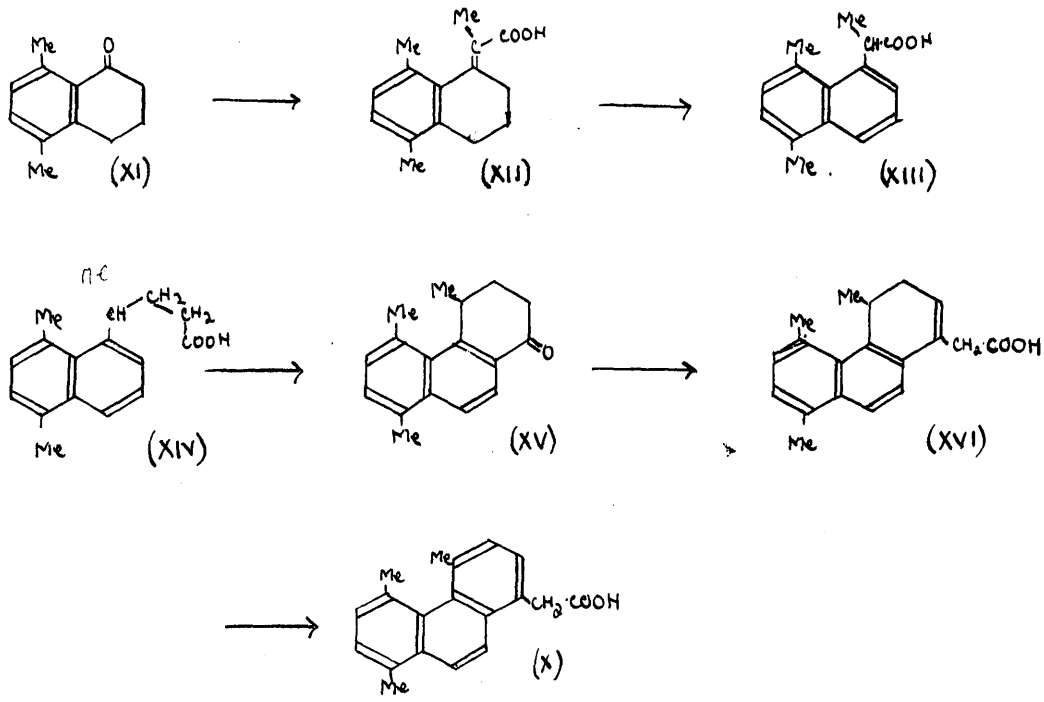
(IVa)



(IVb)

This was indeed shown to be the case for Newman him-self succeeded in preparing and resolving 4:5:8-tri-methylphenanthrene-1-acetic acid. (X) (44) A Reform-atsky reaction on 1:4-dimethyltetralone (X1) gave (X11) which was dehydrogenated and hydrolysed to the acid (X111). The Arndt-Eistert reaction was then carried out twice and the γ-methyl-γ-(5:8-dimethylnaphthyl-1-)-butyric acid (X1V) obtained cyclised to a ketone (XV). A second

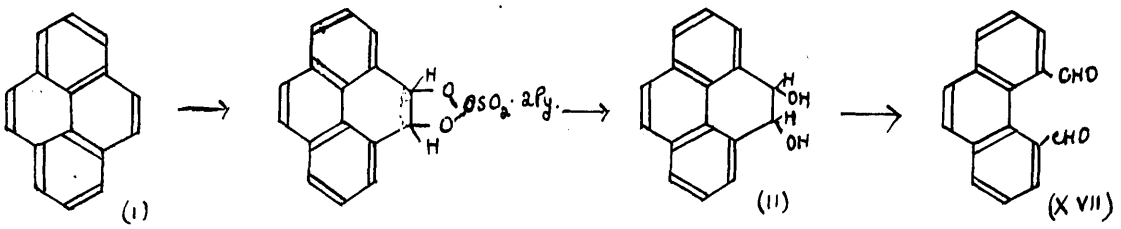
Reformatsky reaction followed by dehydrogenation and hydrolysis gave the required product.(X)



It can be seen, therefore, that although there is considerable resistance to the formation of compounds of this type, under suitable conditions they can be prepared.

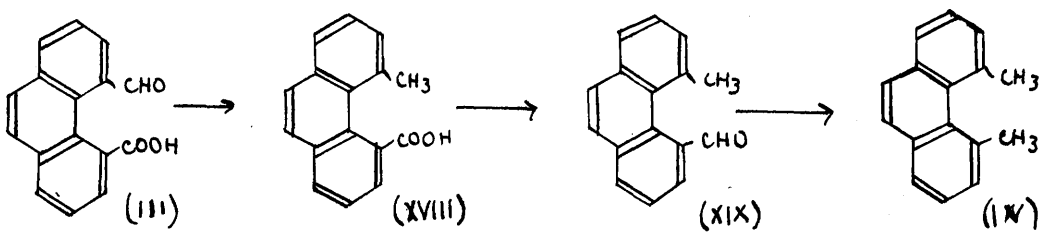
In the present work the first attempt at the preparation of 4:5-dimethylphenanthrene involved the treatment of pyrene with osmium tetroxide and pyridine. The brown complex which formed was hydrolysed to 1:2--dihydro-1:2-dihydroxypyrene (11). Oxidation with lead tetraacetate (45) produced a compound believed to be phenanthrene-4:5-dialdehyde. This was a poorly crystalline substance and both its 2:4-dinitrophenylhydrazone and its oxime readily decomposed. This compound was subjected to

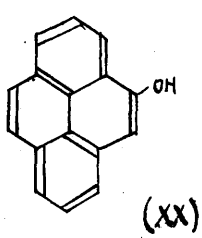
Huang Minlon modification of the Wolff Kishner (31) reaction but the non-crystalline residue yielded only a few crystals of pyrene on distillation. Clemmensen reduction was no more successful for in this case no dist--illate was obtained.

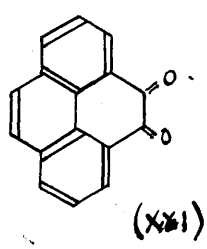


An alternative procedure was therefore adopted. As has been stated, ozonisation of pyrene produces phenan--threne-4-aldehyde-5-carboxylic acid as the first product. Fieser and Novello (46) also studied this reaction and, in an attempt to prepare phenanthrene-4:5-dialdehyde, decom--posed the ozonide by hydrogenation. They used different solvents and temperatures but in all cases obtained the same aldehyde-acid (111) as Vollman and his coworkers had obtained when they decomposed the ozonide by treat--ment with sodium hydroxide solution and hypochlorite solution. It was thought possible that the aldehyde group of (111) might be reduced separately to a methyl group giving (XV111) and that the carboxylic acid group then converted first to an aldehyde group (X1X) and finally to the second methyl group.

Attempts to reduce the aldehyde group met with no success. Vollman had heated the aldehyde-acid (111) with hydrazine hydrate in acetic acid and obtained 1-hydroxypyrene (XX). It appears therefore, that this compound very easily reverts to the pyrene structure. Treatment with alcoholic potassium hydroxide solution e.g. gives pyrene-1:2-quinone. (XXI) (47)



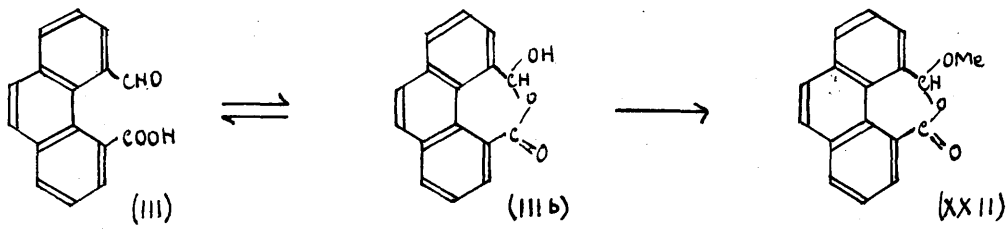


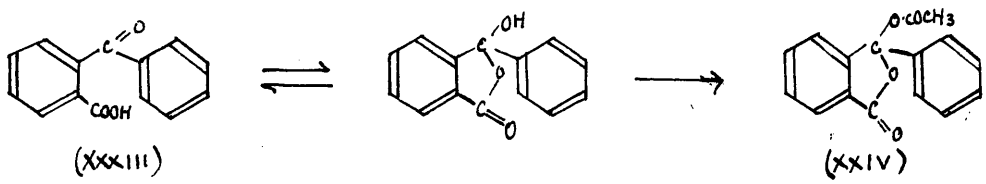


In the present case a Wolff Kishner reduction in diethylene glycol was carried out but a mixture of alkali insoluble products resulted. Clemmensen reduction gave a small amount of 1-hydroxypyrene (XX) (identified by means of a mixed m.p. of the methoxy derivative with an authentic sample), and a complicated mixture of alkali

insoluble products from which no pure substance could be isolated.

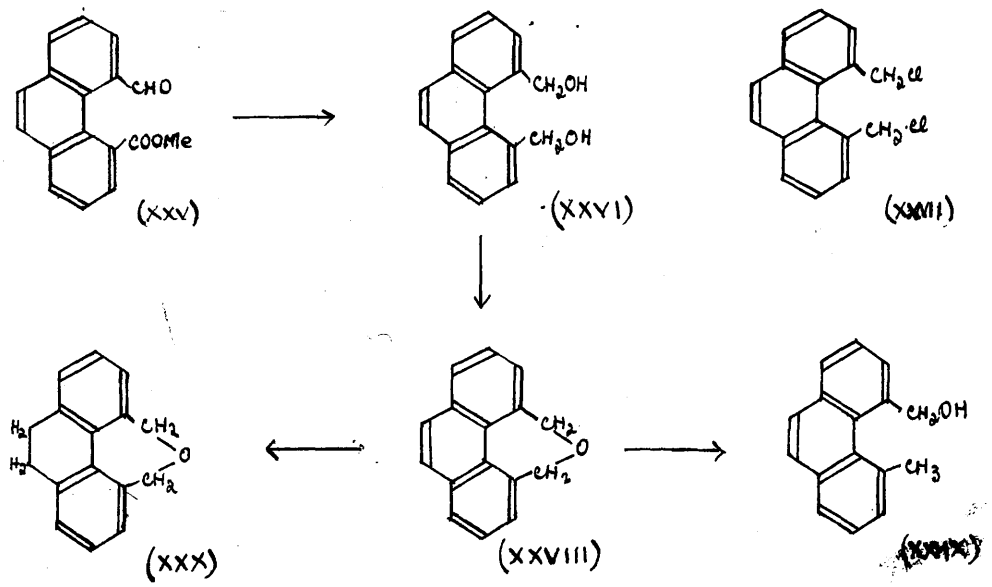
A new approach was sought and in an attempt to pre--pare the methyl ester the aldehyde-acid was treated with methyl alcohol and hydrochloric acid producing a com--pound with m.p. 176-7°. Treatment with diazo-methane in ether, however, produced a substance m.p. 113-4°. Since these two derivatives had the same analysis it was assumed that in the treatment with methyl alcohol and hydrochloric acid, the acid had reacted in its enolic form (111 b) to give the methoxy derivative (XX11). This corresponds to the well known formation of acetoxy-lactones from β-keto-acids, e.g. o-benzoylbenzoic acid (XX111 and XX1V).





The product from the reaction with diazomethane is

assumed to be the normal methyl ester (XXV). Treatment of this ester with lithium aluminium hydride (48) gave a well crystalline compound which analysed correctly for 4:5-dihydroxymethylphenanthrene (XXVI). It was hoped to convert this to the dichloromethyl compound (XXVII), when hydrogenation would be expected to yield the desired hydrocarbon (IV). When (XXVI) was treated with hydrochloric acid in benzene solution, however, analyses results indicated that loss of water had taken place and that a cyclic ether (XXVIII) had been produced.



Hydrogenation of this ether over palladium gave a com-pound which had apparently taken up one molecule of hydrogen. Since (XXVIII) bears some resemblance to a

benzyl ether and these undergo cleavage more readily than other ethers, (see e.g. 49) it is possible that hydrogenation of (XXVIII) would give rise to the mono-hydroxy compound (XXIX). This would be expected to form a chloromethyl compound very readily and then be hydro--genated to 4:5-dimethylphenanthrene. Treatment of the the first reduction product with hydrochloric acid and a further hydrogenation gave a compound which still contained oxygen, and from the evidence it seems more likely that the first hydrogenation of (XXVIII) had reduced the 9:10 bond of the phenanthrene nucleus giving (XXX). This has yet to be proved and the structure of these last products is still being worked out. It is possible that a more satisfactory method of cleaving the ether may be found(e.g. boiling in acetic acid with hydrobromic acid) which may lead to the desired compound

Although, then, 4:5-dimethylphenanthrene has not yet been obtained, this last set of reactions offers the most promising approach to the successful conclusion to the synthesis.

Experimental.

PART 1.

αβ-Diphenylglutaric acid. (cf. 13)

Ethyl phenylacetate (100 g.) was mixed with ethyl cinnamate (100 g.) and the mixture refluxed for 2-3 hours with sodium (4 g.) in dry ethanol (60 cc.). Next day the solid was ground with dilute hydrochloric acid, filtered, and recrystallised from spirit. Yield of higher melting ester -140 g. This ester was refluxed with potassium hydroxide solution (175 g. in 2340 cc. of 50% alcohol) for nine hours. After acidification with dilute hydrochloric acid, trans-αβ-diphenylglutaric acid was obtained. (Yield 110 g. m.p. 230-1°)

αβ-Diphenylglutaric anhydride.

αβ-Diphenylglutaric acid (100 g.) was refluxed for eight hours with acetic anhydride (500 cc.). After re--moving the solvent under reduced pressure αβ-diphenyl--glutaric anhydride was obtained from the residue on crystallisation from chloroform diluted with light pet--roleum, (60-80°) yield - 90% m.p. 125-6°. Avery and Maclay (14), who prepared the anhydride from the same acid by heating under pressure with acetyl chloride, give m.p. 126-7°.

α-Phenyl-1-indanone-3-acetic acid-A.

This experiment was carried out several times with slight differences in experimental conditions (e.g. volume of solvent, absence of freezing mixture etc.) and the procedure which gave the largest quantity of pure material was as follows:

αβ-Diphenylglutaric anhydride (35 g.) was dissolved in dry nitrobenzene (400 cc.) in a three-necked flask and powdered aluminium chloride (40 g.) added gradually. The aluminium chloride was added by means of a device which prevented moisture from entering the flask. (50) During the addition the flask was cooled in a freezing mixture and its contents stirred. Stirring was con--tinued throughout the next day the flask being left altogether for sixty hours. The contents were then poured into ice and hydrochloric acid, and the nitrobenzene removed in steam. Recrystallisation of the residue, which cooled to a gummy solid, yielded 20 g. of pure α-phenyl-1-indanone-3-acetic acid, needles m.p. (of crystals just out of solution) 154-5°.

(Found: C, 76.37; H, 5.14. $C_{17}H_{14}O_3$ requires C, 76.65; H, 5.3%).

In an attempt to purify a sample of the acid, it was crystallised from ethyl acetate. It was found that the m.p. had risen to 166-9°. Further purification gave crystals melting at 170-1°. It was also found that

prolonged heating of crystals with m.p. 154-5° in the steam oven gave crystals with m.p. 170-1°, and if a specimen which melted at 154-5 was allowed to cool it remelted at 170-1°. Three crystallisations of the higher melting form from methanol gave the lower melting form. This change in m.p. took place after crystallisation from different solvents, and after the rise in m.p. the crys--tals had lost their lustrous appearance.

(Analysis of specimen with m.p. 170-1°

Found: C, 76.97; H, 5.6. $C_{17}H_{14}O_3$ requires C, 76.65; H, 5.3%.)

If the cyclisation experiment was carried out without cooling the nitrobenzene solution during the addition of the aluminium chloride, subsequent recrystallisation of the oily residue left a red solid (0.5 g. obtained com--pared with 50 g. of above keto-acid). This substance was almost insoluble in benzene, acetone, and methanol, but was recrystallised from a large quantity of acetic acid, from which it was deposited in shining blood-red needles. Vacuum sublimation (200-220°/0.5 mm.) and further crystallisation gave needles, m.p. 304-10°(D.). The substance was soluble in sodium hydroxide with pro--duction of a violet-red solution and addition of acid reprecipitated the material. It gave a green solution in concentrated sulphuric acid.

Found C, 82.9; H, 4.2. Calc. for $C_{17}H_{10}O_2$, C, 82.9

H, 4.1%.)

The red compound was thus shown to be 3-hydroxy-1:2--benzfluorenone. (15)

After boiling for one hour in acetic anhydride and pour--ing into water a yellow substance was produced, which on recrystallisation from acetic acid gave dark yellow needles of 3-acetoxy-1:2-benzfluorenone, m.p. 185-6°. (Mixed m.p. with an authentic specimen showed no depress--ion.)

3-Hydroxy-1:2-benzfluorenone (0.5 g.) was boiled for two hours with acetic anhydride (2 cc.) and zinc (0.5 g.). After filtering and washing with acetic acid the 3-acetoxy--1:2-benzfluorenone obtained on addition of water was crystallised from ethanol and had m.p. and mixed m.p. 157-8°.

(Found: C, 83.1; H, 5.1. Calc. for $C_{19}H_{14}O_2$, C, 83.2; H, 5.1%.)

The 2:4-dinitrophenylhydrazone of α-phenyl-1-indanone--3-acetic acid-A formed orange-red needles from acetic acid, m.p. 260-1°(D).

(Found: C, 62.0; H, 4.1. $C_{23}H_{18}O_6N_4$ requires C, 61.9; H, 4.1%.)

Treatment of the keto-acid with benzaldehyde and aqueous alcoholic potassium hydroxide solution gave 2-benzylidene-α-phenyl-1-indanone-3-acetic acid-A which crystallised from acetic acid in pale yellow prisms, m.p. 185-6°.

(Found: C, 81.1; H, 5.3. $C_{24}H_{18}O_3$ requires C, 81.4; H, 5.1%.)

Methyl-α-phenyl-1-indanone-3-acetate-A.

One g. of pure keto-acid-A was dissolved in dry methanol (40 cc.) and dry hydrochloric acid gas bubbled into the mixture until the solution was saturated. After refluxing for two hours the mixture was worked up in the usual way, and on removing the solvent the residue was distilled in vacuo (190-200°/2mm.). Crystallisation of the thick oily distillate from methanol produced colourless needles, m.p. 99-100°.

(Found: C, 76.; H, 5.5. $C_{18}H_{16}O_3$ requires C, 77.1; H, 5.8%.)

The ester (1 g.) was hydrolysed by refluxing for one hour with potassium hydroxide (2 g.) in alcohol (15 cc.) and water (5 cc.). The solution developed a bright colour becoming on different occasions dark red, blue or green. A small amount of the original keto-acid-A was obtained on recrystallisation of the oily residue which was precipitated from the solution on addition of dilute hydrochloric acid. A more insoluble substance was also isolated which, on further recrystallisation from methanol formed colourless needles, m.p. 225-6°. Analysis showed it to be an isomer of the above acid, viz.: α-phenyl-1-indanone-3-acetic acid-B. The total yield of

both acids was never more than 50% of the starting acid, the remainder being an uncrystallisable gum. The yield of the higher melting acid varied between 10 and 30%.

Analysis of keto-acid-B.

Found C, 76.8; H, 5.2. $C_{17}H_{14}O_3$ requires C, 76.65; H, 5.3%.)

The 2:4-dinitrophenylhydrazone of α-phenyl-1-indanone--3-acetic acid-B formed orange needles from nitrobenzene, m.p. 284-5°(D).

(Found: C, 61.7; H, 3.9 . $C_{23}H_{18}O_6N_4$ requires C, 61.9; H, 4.1%.)

In order to determine whether it was necessary to prepare the ester to obtain the higher melting acid, keto-acid-A was refluxed in different concentrations of potassium hydroxide in aqueous alcohol for different periods of time. Small amounts of keto-acid-B were obtained but the yield was very low and the material highly impure.

Methyl-α-phenyl-1-indanone-3-acetate-B, was prepared from keto-acid-B in the same way as the ester of keto--acid-A. It formed colourless prisms from methanol, m.p. 138-9°.

(Found: C, 77.2; H, 5.8. $C_{18}H_{16}O_3$ requires C, 77.1; H, 5.8%.)

Hydrolysis of this ester gave only keto-acid-B in cryst--alline form but the oily acidic residue may have con-

-tained traces of keto-acid-A.

Attempts at further cyclisation.

α-Phenyl-1-indanone-3-acetic acid-A (1 g.) was diss--olved in benzene (10 cc.) and treated with an excess of thionyl chloride (5 cc.). After warming for a short time the benzene and excess thionyl chloride were removed on the water pump. The residue was dissolved in dry nitro--benzene (11 cc.) and aluminium chloride (1.2 g.) added with shaking. The flask was then warmed gently for an hour and left overnight. Next day the mixture was poured into hydrochloric acid and the nitrobenzene removed in steam. The oily residue was recrystallised from methanol. The solid obtained was highly impure but repeated cryst--allisation from benzene and methanol gave a specimen of the original keto-acid-A (m.p. and mixed m.p. 154-5°). The residue was also completely soluble in sodium carbonate solution and gave a precipitate with 2:4-dinitrophenyl--hydrazine solution.

Keto-acid-A (0.5 g.) was added to a platinum crucible three quarters full of anhydrous hydrofluoric acid, the mixture stirred and then left overnight. The residue was the original keto-acid-A unchanged.

α-Phenyl-1-indaneacetic acid-A.(cf. 30)

Granulated zinc (25 g.), mercuric chloride (2.5 g.), concentrated hydrochloric acid (1.25 cc.), and water

(37.5 cc.) were shaken together for five minutes. The liquid was decanted off and reagents added as follows: water (18 cc.), concentrated hydrochloric acid (44 cc.), toluene (25 cc.), α-phenyl-1-indanone-3-acetic acid-A (12.5 g.) and acetic acid (5 cc.). The mixture was re--fluxed vigorously for 24 hours (adding 12.5 cc. portions of concentrated hydrochloric acid at intervals of six hours). The product crystallised out on cooling, and, together with small amounts, obtained from the liquors and benzene extracts of the aqueous layer, amounted to 10 g.. The α-phenyl-indaneacetic acid-A crystallised from benzene diluted with light petroleum in colourless needles, m.p. 141-2°.

(Found: C, 81.0; H, 6.3. $C_{17}H_{16}O_2$ requires C, 81.0; H, 6.4%.)

α-Phenyl-1-indaneacetic acid-B.

The keto-acid-B was reduced in the same way as the A isomer but, since the starting material was very in--soluble in toluene, anisole was used for the organic layer. The product, α-phenyl-1-indaneacetic acid-B crystallised from benzene in large colourless prisms, m.p. 153-4°.

(Found: C, 81.1; H, 6.1. $C_{17}H_{16}O_2$ requires C, 81.0; H, 6.4%.)

Attempts at cyclisation.

a) α-Phenyl-1-indaneacetic acid-A (0.5 g.) was converted to its acid chloride using phosphorus penta--chloride in benzene solution. After evaporation of the solvent the residue was treated with aluminium chloride in nitrobenzene solution as for keto-acid-A. The black gummy material obtained was soluble in alkali and could not be induced to crystallise.

b) The acid chloride of reduced acid-A (0.3 g.), prepared either by means of thionyl chloride or phosphorus pentachloride, was dissolved in light petroleum b.p. 60--80°cc. (10 cc.). Aluminium chloride (0.3 g.) was then added while the mixture was cooled. After evolution of hydrochloric acid ceased, the solution was refluxed for 10 minutes, cooled, and poured into ice and hydro--chloric acid. The petroleum layer and benzene extracts of the aqueous layer gave on evaporation a product which could not be crystallised and was again soluble in alkali.

Arndt-Eistert reaction on α-phenyl-1-indaneacetic acids-A and B. (29)

Ice cold dry benzene (8 cc.), 2 drops of pyridine, thionyl chloride (5 cc.) and α-phenyl-1-indaneacetic acid-A (1.25 g.) were placed in a Claisen flask and the mixture left at room temperature for half an hour. It was then warmed to about 40° for half an hour, and the benzene and

excess thionyl chloride evaporated under reduced pressure. The residual acid chloride was dissolved in benzene leaving the solid pyridine hydrochloride behind.

An ethereal solution of diazomethane was prepared from nitrosomethylurea (3 g.) (51)

This solution, after drying over potassium hydroxide pellets, was decanted into a 500 cc. three necked flask and the benzene solution of the acid chloride added gradually through a dropping funnel. During the addition the flask was cooled in a freezing mixture and the con--tents stirred mechanically. The solution was stirred for a further half hour after addition was complete and left overnight. The solution was then poured into an evaporating basin and the solvent allowed to evaporate spontaneously. The bright yellow oily residue was diss--olved in dioxan (15 cc.) and heated on a water bath with 20% ammonium hydroxide solution (20 cc.) and 10% silver nitrate solution (10 cc.) until evolution of nitrogen was complete. A silver mirror or a black deposit of silver formed on the sides of the flask. The mixture was then boiled with charcoal and filtered. The β-phenyl-β-1-indanepropionamide (0.9 g.) formed colourless needles from alcohol, m.p. 151-2°.

(Found: C, 81.5; H, 7.1; N, 5.5. $C_{18}H_{19}ON$ requires C, 81.5; H, 7.2; N, 5.3%.)

β-Phenyl-β-1-indanepropionic acid-A.

The above amide (1 g.) was refluxed for twelve hours with potassium hydroxide (2 g.) in alcohol (25 cc.) and water (2 cc.). Dilute hydrochloric acid was added to the solution and the β-phenyl-β-1-indanepropionic acid-A, which was precipitated, crystallised from dilute acetic acid in colourless prisms, m.p. 123-5°.

(Found: C, 81.3; H, 6.7. $C_{18}H_{18}O_2$ requires C, 81.2; H. 6.8%.)

β-Phenyl-β

β-Phenyl-β-1-indanepropionic acid-B.

α-Phenyl-1-indaneacetic acid-B was converted into its acid chloride as described for the A isomer. After adding this acid chloride to a solution of diazomethane in ether, as before, the diazoketone, obtained by evap-oration of the solvent, was a solid and a specimen, recrystallised for analysis from benzene, formed yellow needles, m.p. 126-8°(D).

(Found: N, 10.2. $C_{18}H_{16}ON_2$ requires N, 10.2%.)

Attempts to prepare the amide from this ketone as before, gave an oily product which could not be cryst-allised, and an effort to prepare the ester or the next higher acid directly met with no success. It was found, however that a pure acid could be obtained from a crude ester and the following procedure was adopted. The diazoketone (0.5 g.) was dissolved in methyl alcohol

(18 cc.). The silver oxide obtained from 2 g. silver nitrate was made into a slurry with methyl alcohol (approx. 10 cc.) and this mixture added in portions to the diazo--ketone solution. After all the silver oxide had been added and the effervescence abated, the mixture was refluxed for one hour, boiled with charcoal and filtered, leaving an almost colourless solution. The filtrate was concentrated to about 15 cc. and potassium hydroxide (1.25 g.) and water (2 cc.) added. After refluxing for one hour, the solution was cooled, acidified with dilute hydrochloric acid, and extracted with ether. The solution was dried and the solvent removed. The oily residue was dissolved in petroleum 60-80° containing a very little chloroform and β-phenyl-β-1-indanepropionic acid-B (0.2 g.) cryst--allised out. A specimen for analysis formed small colourless prisms from petroleum and had m.p. 104-5°. (Found: C, 81.2; H, 6.6. $C_{18}H_{18}O_2$ requires C, 81.2; H, 6.8%.)

β-Phenyl-β-1-indanepropionic acid-A (1 g.) was dissolved in methyl alcohol and converted into its methyl ester as described for α-phenyl-1-indanone-3-acetic acid-A. After working up the ester was left for one night in the refrig--erator but did not solidify. It was accordingly diss--olved in methyl alcohol (20 cc.) and refluxed with potassium hydroxide (2.5 g.) and water (10 cc.) for one and a half hours. On acidification the starting mater-

-ial was recovered unchanged (m.p. and mixed m.p. 123-5°).

Dehydrogenation experiments.

a) α-Phenyl-1-indaneacetic acid-A (1 g.) and sulphur (0.254 g.) were heated together at 200-230° for half an hour. Hydrogensulphide was evolved. When the reaction showed signs of subsiding the temperature was raised to 250 for five minutes. The mixture was then cooled, dissolved in benzene, the benzene shaken with mercury to to remove sulphur and extracted with alkali. The neutral layer gave a black oily residue from which no distillate was obtained at 220°/1 mm.. The alkaline layer gave a small oily precipitate on acidification and this was sublimed in vacuum at 200-220°/1 mm.. Crystallisation of this material from acetic acid yielded a substance which melted at 110-114°. Further crystallisation proved this to be a mixture and no pure compound could be isolated.

b) The same acid (0.5 g.) was heated with palladium black (0.05 g.) in an atmosphere of carbondioxide. (cf.52) The temperature was maintained between 290 and 300° by means of a metal bath. About 10 cc. of gas were given off and increase in the temperature produced no further evolution of gas. The residue was insoluble in alkali and was dissolved in ether. After removing the solvent the residue was distilled under reduced pressure. A

small amount of a pale yellow oil was obtained which was extremely soluble in all common solvents and could not be crystallised. The substance itself could not be ob--tained solid even after long standing in the refriger--ator and did not yield a picrate. (cf. the properties of 2-phenylnaphthalene and 2-phenyl-1-naphthoic acid, 53)

c) β-Phenyl-β-1-indanepropionic acid-A (0.5 g.) was treated with sulphur (0.13 g.) and heated at 200-225° for 90 minutes. (cf. 11) The residue was dissolved in benz--ene as before and extracted with alkali. The neutral layer gave a residue on evaporation which could not be crystallised and acidification of the alkaline layer gave only a small amount of starting acid.

d) Treatment of the same acid with palladium black yielded an alkali insoluble product very similar to that obtained from α-phenyl-1-indaneacetic acid-A. It could not be induced to crystallise and yielded no picrate.

3-Keto-1-phenyl-1:2:3:9-tetrahydroacenaphthene-A.

a) β-Phenyl-β-1-indanepropionic acid-A (1 g.) was converted into its acid chloride as described for α-phenyl--1-indaneacetic acid-A. The acid was dissolved in benzene (16 cc.) and aluminium chloride (0.6 g.) added in portions. The reaction mixture was heated to 30° and the temperature maintained between 30° and 50° for three hours. After pouring into dilute hydrochloric acid, the benzene layer was washed successively with dilute hydrochloric

acid, sodium hydroxide and water. The benzene was removed and the residue was dissolved in a little ethanol from which 3-keto-1-phenyl-1:2:3:9-tetrahydroacenaphthene--A crystallised in large colourless prisms, m.p. 101-2°. (0.6 g.)

(Found: C, 87.0; H, 6.2. $C_{18}H_{16}O$ requires C, 87.1; H, 6.5%.)

Cis-6-keto-5:6:11:12:13:14-hexahydrochrysene has m.p. 75.5-76.5°. (11)

The 2:4-dinitrophenylhydrazone of the above keto-ace--naphthene crystallised in small scarlet prisms from chloroform and had m.p. 249-50°.

(Found: C, 67.4; H, 4.5. $C_{24}H_{20}O_4N_4$ requires C, 67.3; H, 4.7%.)

b) The same homo-acid-A (1 g.) was allowed to stand overnight in contact with anhydrous hydrofluoric acid contained in a platinum crucible. The next day, by which time the excess of hydrofluoric acid had evaporated, the residue obtained was washed with sodium carbonate and dissolved in benzene. After removing the solvent and crystallising the residue from ethanol the same ketone was obtained, (0.75 g.), m.p. and mixed m.p. 101-2°.

c) β-Phenyl-β-1-indanepropionic acid-A (0.25 g.) was heated with 85% sulphuric acid (2 cc.) on the steam bath. The substance began to dissolve very slowly, but on adding 1 cc. of concentrated sulphuric and heating for

a further nine hours, the solution became dark and clear. On pouring into water no precipitate was obtained and extraction of the solution with ether gave no residue on evaporation.

d) The propionic acid-A (0.5 g.) was dissolved in dry benzene (5 cc.) and phosphorus pentachloride (0.45 g.) added with shaking and cooling. After standing at room temperature for an hour nearly all the acid and phosphorus pentachloride were in solution. To complete the reaction the mixture was warmed on the steam bath for five minutes and then cooled in ice. Stannic chloride (0.5 cc.) in benzene (0.5 cc.) was added to the acid chloride and the mixture shaken. After a short time an orange complex separated. It was then poured into ice and concentrated hydrochloric acid (1.5 cc.) and extracted with ether. The combined ether and benzene layer was washed with 5% hydrochloric acid, 5% sodium hydroxide and water. After removing the solvent the residue crystallised from ethanol yielding the same ketone as before. (m.p. and mixed m.p. 101-2°.)

3-Keto-1-phenyl-1:2:3:9-tetrahydroacenaphthene-B.

Indanepropionic acid-B (136 mg.) was treated with hydrofluoric acid as for the A isomer. The residue was worked up as before and 3-keto-1-phenyl-1:2:3:9-tetra-hydroacenaphthene-B crystallised from alcohol, m.p. 139-40°.

(Found: C, 86.9; H, 6.3. $C_{18}H_{16}O$ requires C, 87.1; H, 6.5%.)

The 2:4-dinitrophenylhydrazone of this ketone-B formed scarlet prisms from chloroform diluted with methyl alcohol, m.p. 238-9°.

(Found: C, 67.3; H, 4.7. $C_{24}H_{20}O_4N_4$ requires C, 67.3; H, 4.7%.)

1-Phenyl-1:2:3:9-tetrahydroacenaphthene-X and Y.

a)The ketone-A (0.5 g.) was treated with granulated zinc and hydrochloric acid as described for the reduction of α-phenyl-1-indanone-3-acetic acid. The toluene layer and benzene extracts of the aqueous layer were dried and the solvent evaporated. Attempts to crystallise the residue were unsuccessful. Accordingly the oily material was dissolved in a mixture of light petroleum, b.p. 60-80° and benzene (ratio 3:1), and the solution passed through a column of alumina. The column was eluted with pure benzene and the combined solutions evaporated. The addition of a drop of ethanol to the residue gave a solid product but this was still oily and was sublimed in a vacuum. The sublimate was dissolved in ethanol and gave a few crystals of a substance with m.p. 68-70°. Mixed m.p. of this material and an authentic specimen of cis-hexa--hydrochrysene (m.p. 73-4°) had m.p. 40-5°.

b) Wolff-Kishner reduction. (31)

To a solution of sodium (0.25 g.) in ethylene glycol (10 cc.) there was added the ketone-A (1 g.) and hydrazine hydrate (0.5 cc). After refluxing for one hour the condenser was removed and the mixture heated until the temperature had reached 195-200° when refluxing was continued for another three hours. The mixture was cooled, acidified, and extracted with benzene. Evaporation of the solvent and crystallisation of the product from ethanol gave a first crop of crystals (long colourless needles) with m.p. 57-9°. A specimen for analysis had m.p. 59-60°.

(Found: C, 92.2; H, 8.0. $C_{18}H_{18}$ requires C, 92.3; H, 7.7%.)

A second crop of crystals was a mixture of prisms and needles. These were separated by hand with the aid of a lens. The needles were identical with those obtained from the first fraction, (m.p. and mixed m.p. 59-60°), while the prisms, which were hexagonal in shape, had m.p. 68-70°. (A mixture of both products had m.p. 38-42°)

On recrystallisation from methyl alcohol a specimen of this higher melting substance had m.p. 71-2°.

(Found: C, 92.3; H, 7.5. $C_{18}H_{18}$ requires C, 92.3; H, 7.7%.)

A mixture of this hydrocarbon and that obtained by the Clemmensen reduction melted at 68-70°, and this substance is therefore named 1-phenyl-1:2:3:9-tetrahydroacenaphthene-X

and that melting at 59-60 1-phenyl-1:2:3:9-tetrahydro-acenaphthene-Y. (but see discussion page 21)

c) The ketone-B (0.2 g.) was treated with sodium in ethylene glycol and hydrazine hydrate as above. On working up the product and crystallising from ethanol the hydro-carbon-Y was obtained (m.p. and mixed m.p. 57-9°). The solvent was allowed to evaporate completely but the re--sidue was homogeneous and no trace of the hydrocarbon-X m.p. 71-2° was obtained.

1-Phenylacenaphthene.

1-Phenyl-1:2:3:9-tetrahydroacenaphthene-Y (0.34 g.) was dehydrogenated with palladium black (0.05 g.) in an atmosphere of carbon dioxide at a temperature of 290-300°. (cf. 52) When the evolution of hydrogen became very slow, any solid which had sublimed was scraped back into the flask and a further small quantity of palladium (0.01 g.) added. The mixture was heated again and the temperature finally raised to 320° but no more hydrogen was evolved. After removing the benzene an orange crystalline mass remained. This was dissolved in ethanol and treated with charcoal when the solution became pale yellow. 1-Phenyl-acenaphthene (0.2 g.) crystallised out in small leaflets which were coloured faintly pink. A specimen for anal--ysis was colourless and had m.p. 105-6°.

(Found: C, 93.8; H, 6.0. $C_{18}H_{14}$ requires C, 93.9; H, 6.1%.)

A similar dehydrogenation, carried out on 1-phenyl--1:2:3:9-tetrahydroacenaphthene-X, produced the same hydrocarbon, m.p. and mixed m.p. 105-6°.

2-Phenyl-1:8-naphthalic anhydride.

1-Phenylacenaphthene (0.2 g.) was dissolved in acetic acid (3.5 cc.) and sodium dichromate (1.4 g.) added slowly with shaking. The mixture was refluxed for two hours and then poured into warm water, cooled, and filtered. The precipitate was boiled with sodium carbonate containing a little sodium hydroxide and again filtered. A small orange residue (30 mg.) remained and this crystallised from acetic acid with m.p. 238-9°. Acidification of the alkaline solution produced a pale yellow precipitate. On sublimation a substance which was still yellow in colour was obtained and this had m.p. 238-9°. A mixture of the two products also had m.p. 238-9°, the orange colour of the residue being due, presumably, to traces of quinone. After long boiling the orange residue also completely dissolved in alkali. The m.p. of the product agrees with that found for 2-phenyl-1:8-naphthalic anhydride by Koelsch and Rosenwald. (33)

(Found: C, 79.1; H, 3.6. Calc. for $C_{18}H_{10}O_3$ C, 78.8; H, 3.7%.)

PART II.

Naphthyl-1-acetic acid.

1-Chloromethylnaphthalene was prepared according to the method of Organic Syntheses. (54) Treatment with potassium cyanide in alcohol gave 1-naphthaleneaceto--nitrile, and this was converted to naphthyl-1-acetic acid as described by Olivier and Wit (55) for the treatment of 1-bromomethylnaphthalene. The acid crystallised from benzene in colourless needles, m.p. 131-2°.

Ethyl naphthyl-1-acetate.

Concentrated sulphuric acid (6 g.) was added to absol--ute alcohol (156 cc.) and naphthylacetic acid (66 g.) added. The solution was refluxed for two hours, the excess alcohol then distilled off and the residue poured into water. The oily liquid which separated was dissolved in ether and washed with sodium carbonate solution. After removing the solvent the ester distilled at 183°/17 mm.

Ethyl meso- and dl-$\alpha\beta$-di-(1-naphthyl)-succinate.

The ethyl alcohol used throughout was dried by standing over quick lime for several days, decanting the solution, and then distilling from barium oxide.

The ether was dried by standing over caustic soda pellets followed by distillation from phosphorus pentoxide.

a) Potassium (5.1 g.) was dissolved in tertiary butyl alcohol (110 cc.) (dried by crystallisation from itself followed by distillation from potassium hydroxide), and some ether added the whole being contained in a three--necked flask. Ethyl naphthylacetate (20 g.) was added through a dropping funnel, whereupon the whole mixture solidified and had to be stirred mechanically. Iodine (15 g.) in ether (100 cc.) was then added keeping the mixture at 0^{o}. After stirring for several hours at room temperature the contents of the flask were shaken with aqueous sodium thiosulphate to remove excess iodine. As there was no precipitate in the organic layer as expected (34), the ethereal layer was separated and dried. Con--centration did not produce any crystals, so the mixture was distilled in vacuo. Some starting material was ob--tained and a tarry residue which on treatment with acetone yielded a very small of an impure solid.

b) Sodium wire (3 g.) was placed under anhydrous ether in a three-necked flask fitted with condenser, dropping funnel, and stirrer. A very little more than the theor--etical quantity of absolute alcohol was added through the funnel and the flask allowed to stand overnight. After the sodium had dissolved the treatment was similar to the previous experiment. The ester in ether, followed by iodine in ether, was added and after standing the mixture was treated with aqueous thiosulphate. Some impure

racemic ester was obtained on evaporation of the ether layer, but in negligible yield.

c) In order to determine whether or not the ester had actually given a sodium derivative, sodium wire was placed under ether and the ester added directly. After refluxing for two days the ester dissolving, but there was a considerable amount of tarry product. Addition of iodine in ether, followed by aqueous thiosulphate solution gave no precipitate. Evaporation of the ether layer gave a tarry residue which could not be induced to crystallise.

The experiment was repeated in dry benzene with the same result.

d) An experiment similar to b) was carried out using solid potassium tertiary butoxide, but on addition of iodine the mixture darkened and evaporation of the ether layer gave a tarry product which solidified on stirring with alcohol. The yield was very small and the product impure.

e) Instead of sodium wire an experiment was carried out using atomised sodium (56), but there was no improvement in yield.

f) As these methods were useless from a preparative point of view, it was decided to concentrate on the method of King and Henshall (34), and collect a sufficient stock of material to carry out the rest of the synthesis. Accordingly, sodium (0.6 g.) was dissolved in absolute

alcohol and the alcohol evaporated. The residue was then heated under reduced pressure on an oil-bath, the temper--ature of which was maintained between 110 and 115°, to re--move last traces of alcohol. Great care had to be taken to prevent charring. The residue was immediately covered with a solution of ethyl naphthylacetate (5 g.) in ether (30 cc.). The solid lump of sodium ethoxide was broken up by stirring and then iodine in ether added. The mixture was allowed to stand in the usual way and on addition of sodium thiosulphate a solid separated. This was about 1.5 g. (30%) of ethyl meso-__-di-(1-naphthyl)-succinate. Small additional amounts of solid were obtained from the ether liquors, but these were mixtures of dl and meso forms.

In all experiments acidification of the aqueous layer produced naphthylacetic acid in greater or lesser amount. In some cases as much as 50% was obtained in spite of all possible precautions to exclude moisture.

dl-αβ-Di-(1-naphthyl)-succinic acid. (34)

Ethyl dinaphthylsuccinate (meso or racemic or both)(2 g.) was refluxed with a solution of potassium hydroxide (1.1 g) in water (2 cc.) and alcohol (23 cc.). Within ten minutes the ester had dissolved and after twenty minutes the solu--tion was diluted with water (25 cc.), neutralised with concentrated hydrochloric acid (2.5 cc.) and the alcohol evaporated at 100°. Next day the acid was treated with

acetic acid to remove traces of insoluble meso acid and the solution diluted with hot water (30-40 cc.). The dl-dinaphthylsuccinic acid (1.6 g.) separated and was crystallised from aqueous acetic acid or alcohol- colour--less needles, m.p. 243-5°.

dl-αβ-Di-(1-naphthyl)-succinic anhydride.

The racemic acid (1 g.) was heated under reflux with acetyl chloride (30 cc.). After a short time the acid began to pass into solution. Excess acetyl chloride was evaporated in vacuo leaving a crystalline product which on recrystallisation from dry benzene diluted with a little light petroleum formed colourless needles, m.p.161-2°.

Attempted cyclisation of dl-αβ-di-(1-naphthyl)-succinic anhydride.

a) The above anhydride (0.5 g.) was dissolved in dry nitrobenzene (10 cc.) and powdered aluminium chloride (0.45 g.) added with shaking. After standing for two days the mixture was poured into dilute hydrochloric acid and and the nitrobenzene removed by distillation in steam. The residue was recrystallised from benzene and melted about 240°. It was soluble in hot sodium carbonate solu--tion and a mixed m.p. with dl-dinaphthylsuccinic acid showed no depression.

b) The above conditions were repeated except that the mixture was heated on the steam bath for eight hours and

the quantity of aluminium chloride was doubled (0.9 g. for 0.5 g. anhydride). The racemic acid was again obtained unchanged.

c) The anhydride (0.5 g.), aluminium chloride (0.9 g.), and carbon disulphide (100 cc.) were refluxed for nine hours on a water bath. After adding the mixture to dilute acid and distilling the solvent in steam, the residue was found to be unchanged acid as before.

d) Similar quantities of anhydride and aluminium chloride were dissolved in tetrachlorethane and the mixture warmed. It began to darken immediately and hydrochloric acid was given off, but on working up a dark coloured product was obtained. This was treated with sodium carb--onate solution, giving some racemic acid on acidification and the insoluble residue boiled with alcohol. This solution was tested with 2:4-dinitrophenylhydrazine solu--tion, but there was no precipitate nor did the colour of the solution darken.

e) A platinum crucible was three-quarters filled with anhydrous hydrofluoric acid and dl-dinaphthylsuccinic acid (0.5 g.) sprinkled on to it. The crucible was allowed to stand in a waxed container fitted with a calcium chloride tube until all the hydrofluoric acid had evaporated. The acid was found to be unchanged.

f) A similar experiment was carried out on the an-hydride, but once again the residue was completely soluble

in boiling sodium carbonate solution and proved to be dl-dinaphthylsuccinic acid.

g) Sodium chloride (0.4 g.) and aluminium chloride (1.2 g.) were mixed together and heated to about 130°in a round bottomed flask over a sand bath. The anhydride (0.2 g) was added and the mixture kept at a temperature of about 130°, with frequent stirring for two hours. Hot hydrochloric acid was added and the residue treated with sodium carbonate solution. On acidification of this alkaline solution some dl-dinaphthylsuccinic acid was obtained. The insoluble residue was extracted with alcohol but gave no evidence of containing a carbonyl group when tested with 2:4-dinitrophenylhydrazine solution.

PART III.

1:2-Dihydro-1:2-dihydroxypyrene. (39)

Pyrene (0.79 g.) was dissolved in pure benzene (10 cc.) and osmium tetroxide (1 g.) and pyridine (0.5 cc.) added. The solution, which immediately became brown in colour, was allowed to stand in a stoppered bottle in the dark for a week. The benzene was then decanted from the dark brown crystalline mass which adhered to the walls of the bottle. After washing with benzene, the complex was dissolved in methylene chloride (25 cc.) and trans--ferred to a 350 cc. conical flask. Potassium hydroxide (1 g.) and mannitol (10 g.) were dissolved in water (100 cc.) and this aqueous solution added to the methylene chlor--ide solution. The mixture was saturated with nitrogen (to prevent oxidation to pyrene-1:2-quinone), closed with a rubber stopper and shaken mechanically for one hour. The aqueous solution (pinkish brown in colour) was decanted off and a further 100 cc. of a similar solution added. After saturating with nitrogen and shaking for another hour the combined solutions were filtered. 1:2-dihydro-1:2-dihydroxypyrene (0.2 g.) remained as a white amorphous solid which on crystall--isation from benzene diluted with light petroleum b.p. 60-80° had m.p. 180-4° (D).

Phenanthrene-4:5-dialdehyde. (45)

The above diol (0.175 g.) was dissolved in benzene (50 cc.) and lead tetraacetate (0.5 g.) added with shaking while the solution was warmed. An immediate precipitate of lead dioxide was formed and shortly afterwards a precipitate of lead diacetate. After standing for one hour the mixture was filtered and washed with benzene. The solution was shaken with water, dried and the solvent evaporated. The residue solidified to a brown mass, which was dissolved in benzene and boiled with animal charcoal. The light brown micro-crystalline solid which was deposited from the filtrate and is believed to be phenanthrene-4:5-dialdehyde, had m.p. 152-4°.

The 2:4-dinitrophenylhydrazone formed dark red needles from acetic acid, m.p. 306-8° (D).

The aldehyde also yielded an oxime which was pale greenish-yellow in colour and melted over a large range. It turned brown in alcohol and could not be purified.

Phenanthrene-4-aldehyde-5-carboxylic acid. (cf. 37)

Pyrene (10 g.) was suspended in acetic acid (100 cc.) and ozone (obtained from a transformer through which oxygen was passed by means of a fine gauge at 5lbs/sq.in. bubbled through the mixture for two hours. The contents of the flask which were dark brown were poured into water (300 cc.) and then warmed. The yellowish brown solid

became a brown oil which solidified again on cooling and adding more water. After filtering the residue was washed with water and boiled twice with a solution of sodium hydroxide (2.5 g.) in water (150 cc.) and filtered again. A residue of pyrene remained and the dark brown filtrate was warmed with bleaching powder (12 g.) until the supernatant liquid became very pale yellow. The mixture was filtered and on adding 40 cc. of sodium hydroxide (50%) the sodium salt of the aldehyde-acid precipitated out. The next day the solid was filtered, washed with concentrated sodium chloride solution and warmed with dilute hydrochloric acid to liberate the free acid. Phenanthrene-4-aldehyde-5-carboxylic acid (1.3 g.) crystallised from acetic acid in long shining needles, m.p. 271-2°.

The aldehyde acid (1 g.) was suspended in methyl alcohol (40 cc.) and hydrochloric acid gas passed into the mixture until it was saturated. After refluxing for two hours the solid had still not dissolved. The alcohol was then removed and water and sodium carbonate added. The residue did not go into solution and the solid was filtered and dissolved in a large quantity of methyl alcohol from which it crystallised in shining needles, m.p. 176-7°.

(Found: C, 77.0; H, 4.6. $C_{17}H_{12}O_3$ requires C, 76.9; H, 4.6%.)

Clemmensen reduction.

The aldehyde-acid (0.5 g.) was boiled for twenty four hours with zinc, concentrated hydrochloric acid, water and toluene. (30) The toluene layer and benzene extracts of the aqueous layer were shaken with sodium hydroxide solution. Acidification of the alkaline extract gave a precipitate which was redissolved in sodium hydroxide solution and converted to its methyl ether with dimethyl-sulphate. The small amount of crystalline product melted at 120-3° but showed no depression in m.p. when mixed with an authentic specimen of 1-methoxypyrene, m.p. 126-8°.

The neutral organic solution gave a residue on evapor--ation of the solvent. This was treated with picric acid, the product crystallised, and the pictrate passed through a column of alumina. The product obtained was still a complex mixture and could not be purified.

Wolff Kishner reduction (31) also gave a mixture of alkali insoluble products.

Methyl-phenanthrene-4aldehyde-5-carboxylate.

The aldehyde-acid was suspended in acetone and mixed with a solution of diazomethane in ether. The mixture was shaken thoroughly and then left overnight in the refrigerator. The excess diazomethane was destroyed with acetic acid and after evaporating the solvent the residue

of methyl phenanthrene-4-aldehyde-5-carboxylate cryst--allised from methyl alcohol in needles, m.p. 113-4°. (Found: C, 77.1; H, 4.8. $C_{17}H_{12}O_3$ requires C, 76.9; H, 4.6%.)

4:5-Dihydroxymethylphenanthrene. (48)

Lithium aluminium hydride (8 g.) was added to anhyd--rous ether (200 cc.) in a three-necked flask fitted with condenser, dropping funnel, and mercury seal stirrer. A solution of the above methyl ester (2.5 g.) in ether (200 cc.) was added through the dropping funnel gradually and the mixture then refluxed for half an hour. Water was added very cautiously cooling the flask in ice. When effervescence ceased the contents of the flask were poured into ice water and 10% sulphuric acid (400 cc.) added. The liquid was extracted with ether and after evaporation of the solvent the residue (2.25 g.) of 4:5-dihydroxymethylphenanthrene crystallised from alcohol in shining prisms, m.p. 171-2°. A first analysis indic--ated that the substance had crystallised with alcohol of crystallisation but a new specimen was prepared using benzene as solvent.

(Found: C, 80.6; H, 5.9. $C_{16}H_{14}O_2$ requires C, 80.6; H, 5.9%.)

Treatment of this hydroxy-compound in benzene solution containing a little calcium chloride, with hydrochloric

acid gas produced a substance which formed shining plates from petroleum ether b.p. 60-80 , m.p.77-8°. This was presumably the cyclic ether formed by loss of water from the dihydroxy compound.

(Found: C, 87.8; H, 5.4. $C_{16}H_{12}O$ requires C, 87.3; H, 5.5%.)

A second analysis is being carried out but this is sufficient to exclude the possibility that the dichloromethyl compound has been formed for this has a carbon value of 69.8%.

The above ether was dissolved in acetone and shaken with palladium black and hydrogen. The residue obtained on filtration and evaporation of the solvent crystallised from alcohol in colourless prisms, m.p. 85-87°

(Found: C, 86.8; H, 6.0. $C_{16}H_{14}O$ requires C, 86.5; H, 6.4%.)

The reduced product was distilled in a vacuum and dissolved in benzene. This solution was treated with hydrochloric acid, the benzene evaporated and last traces of solvent removed under reduced pressure. The residue was dissolved in in acetone and shaken with hydrogen and palladium . After filtering the solution and evaporating the solvent the solid residue was dissolved in alcohol from which it crystallised in thick needles, m.p. 94-6°.

(Found: C, 86.1; H, 6.7. $C_{16}H_{14}O$ requires C, 86.5; H, 6.4%.)

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