SYNTHESES OF DERIVATIVES OF POLYCYCLIC COMPOUNDS.

T H E S I S

submitted by

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Preface.

The author wishes to express his thanks to his supervisor, Dr. G.M. Badger, and to Professor J.W. Cook, F.R.S. for much valuable advice and encouragement given during the course of the work reported here, and also to Dr. S.T.R.S. Mitchell, under whose direction the work on santonin was carried out.

He is also indebted to Mr. J.M.L. Cameron and Miss R.H. Kennaway, who performed the micro-analyses, and to the University authorities for a maintenance allowance (1 year).

Contents.

Summary.

Part I.

In an attempt to convert β-(9-phenanthryl)-propionic acid to its 9:10-dihydride by high pressure hydrogenation, only β-(9-s-octahydrophenanthryl)propionic acid was obtained. β-(9-Phenanthryl)propionic acid was prepared, by standard reactions, from 9-chloromethyl phenanthrene, which was itself obtained by chloromethylation of phenanthrene. A small amount of 1-chloromethylphenanthrene was also isolated from this reaction.

Cyclisation of β-(1:2:3:4-tetrahydro-9-phenanthryl)-propionic acid has been found to give 3'-keto-9:10-cyclo-penteno-1:2:3:4-tetrahydrophenanthrene.

In another attempt to synthesise 10-methoxy-3:4-benzpyrene, 1-methoxyperinaphthan-7-one was condensed with o-chlorophenylmagnesium bromide to give 1-methoxy-7-(o-chloro-phenyl)perinaphthan-7 ol. Attempted dehydration of this carbinol resulted in demethylation as well, with formation of 4-(o-chlorophenyl)perinaphthan-7-one. The mechanism of this reaction is discussed with regard to bond mobility in the perinaphthene system. 1-Methoxyperinaphthan-7-one was prepared by cyclisation of β-(2-methoxy-1-naphthyl)-propionic acid. The latter compound was obtained from 1-chloromethyl-2-methoxynaphthalene by the malonic ester synthesis.

Part II.

It has been found by other workers in this Department that β-(9-s-octahydroanthranyl)propionic acid undergoes rearrangement and cyclisation in presence of anhydrous hydrofluoric acid to give 1'-keto-9:10-cyclopenteno-s-octahydrophenanthrene. In an investigation of this rearrangement, the behaviour of several derivatives of s-octahydroanthracene when treated with this reagent has been studied. A similar rearrangement has been observed in the case of γ-(9-s-octahydroanthranyl) butyric acid, which is almost quantitatively converted to 4-ketododecahydrotriphenylene when treated with hydrofluoric acid at room temperature. All the other compounds tested were unaffected under these conditions. It seems likely that cyclisation of an acid side chain is concerned in these rearrangements of the octahydroanthracene nucleus, and that they are the first recorded examples of a new type of alkylbenzene isomerisation, brought about by displacement of an alkyl group by cyclisation of an acid chain into that position of the benzene ring.

Several new derivatives of s-octahydroanthracene were prepared. The Friedel-Crafts reaction between s-octahydroanthracene and succinic anhydride, in carbon disulphide, was found to give β-(9-s-octahydrophenanthroyl)propionic acid. In tetrachlorethane, a mixture of this and β-(9-s-octahydroanthranoyl)propionic acid was obtained.

Part III.

Attempts to repeat the synthesis of santonin described by Paranjape, Phalnikar, Bhide and Nargund[77] have been unsuccessful. Treatment of ethyl Δ^2-cyclohexen-1-one-3-methyl malonate and ethyl α-(Δ^2-cyclohexen-1-one-3)propionate with 6N sulphuric acid in 50% aqueous alcohol did not yield the lactone of α-(2-hydroxy-3-ketocyclohexyl)propionic acid as they state. In every case the completely decarboxylated product 3-ethyl-Δ^2-cyclohexene was obtained.

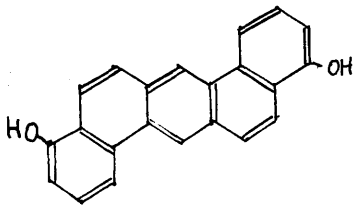
Part I.

Some Attempts to Synthesise 10-Hydroxy-3:4-benzpyrene.

Introduction.

Many compounds of the polycyclic aromatic hydrocarbon series have the property of inducing cancer. The question of the fate of such compounds in the animal body has aroused much attention in recent years. This has been stimulated by a desire to find some relationship between the activity of cancer-producing hydrocarbons and their metabolism. It has been suggested that, in view of their stability and general chemical inertness, these substances may exert their biochemical action as a result of conversion in the body to some active metabolite, rather than by direct action on the cells.

The results of a considerable amount of investigation have shown, however, that there is no essential difference between the metabolism of carcinogenic and related non-carcinogenic hydrocarbons. When polycyclic aromatic hydrocarbons generally are introduced into the animal body phenolic oxidation products are formed. Thus, 1:2:5:6-dibenz-anthracene is converted by rats and mice to the 4':8'-dihydroxy-derivative (I)[1,14], and chrysene gives 3-hydroxy chrysene (II)[2]. There is strong evidence that the 4'-hydroxy-derivatives (III) are formed from 1:2-benzanthracene[3], and 9:10-dimethyl-1:2-benzanthracene[4].



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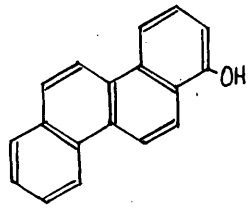

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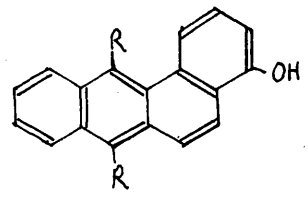
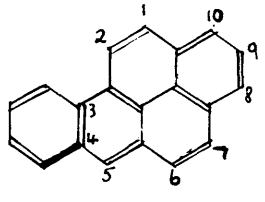


(III) (R=H or Me)

The results of these experiments do not support the view that the activity of the cancer-producing hydrocarbons is due to the formation of an active metabolite. For as far as they have been isolated, these phenolic products have been found to be either non-carcinogenic, or less active than the parent hydrocarbon. The metabolic processes seem rather to represent a means of detoxification and elimination of biologically active material. It is interesting that several methoxy derivatives of the hydrocarbons were found to have strong tumour-inhibitory properties[5].

Included in this systematic investigation of the metabolism of the polycyclic aromatic hydrocarbons, has been a study of the strongly carcinogenic compound 3:4-benzpyrene (IV). Metabolism of this hydrocarbon in rats and rabbits gives rise to two phenolic products, and there is strong evidence that these are the 8- and 10-hydroxy-derivatives[6]. The metabolites were oxidised to the



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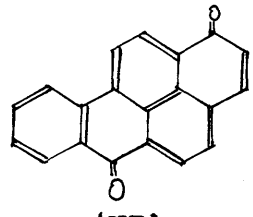

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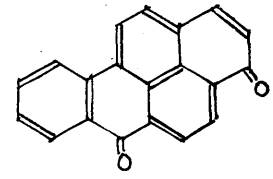


(V)

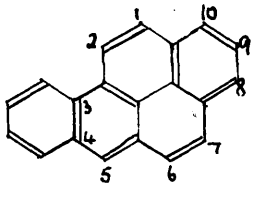
known benzpyrene-5:8- and 5:10-quinones (V and VI). These were converted by reductive methylation to 5:8- and 5:10-dimethoxybenzpyrenes, which were identified by comparison of their fluorescence spectra with those of authentic specimens of these compounds. The quinones (V) and (VI) can be obtained by oxidation of benzpyrene itself[7], and their formation from the metabolites shows that these must be the 5-, 8-, or 10-hydroxy-derivatives, for only compounds with the substituent in these positions could give the same quinones on oxidation. The 5- derivative was excluded, because the fluorescence spectra of the methylated metabolites were both different from that of synthetic 5-methoxy-3:4-benzpyrene, the structure of which is established[13]. This indicated that the metabolites were the 8- and 10-hydroxy-derivatives. Strong support for these structures was found in the identity of the fluorescence and ultra-violet absorption spectra of the methyl ethers, with those of synthetic 8-methoxy- and 10-methoxy-benzpyrenes, prepared by Professor Cook and Dr. Schoental (unpublished).

While this evidence establishes the structures of the benzpyrene metabolites with a good degree of certainty, it does not do so conclusively, for the configurations of the synthetic 8- and 10-methoxy-derivatives

~~is~~ are not absolutely certain. Alternative syntheses of 8- and 10-hydroxy-benzpyrenes, by routes which unequivocally determine the structures of the products, are thus clearly very desirable. Attempts to synthesise the 10-hydroxy-derivative comprised a large part of the present work and are described in the sequel.

An interesting point about the biochemical oxidation of benzpyrene is that it does not take place at the most reactive centre in the molecule, as revealed by ordinary chemical reagents. In this respect the metabolism of benzpyrene conforms to that of other hydrocarbons which are also attacked at less reactive centres. Thus with 1:2-benzanthracene, chemical reaction always takes place at the reactive 9- and 10-positions, but metabolism of the hydrocarbon leads to the 4'-hydroxy-derivative (III)[3]. With 3:4-benzpyrene (IV), whereas metabolic oxidation takes place at positions 8 and 10, chemical substitution almost invariably occurs at position 5. Thus, 5-nitro-[8], 5-chloro-[9] and 5-aldehydo-[10]3:4-benzpyrene can all be obtained directly from the hydrocarbon by nitration, chlorination and reaction with methylformanilide. Coupling with diazonium salts[11] and with sulphur monochloride[12] also takes place at the 5-position, and it is of especial interest in the present connection that the 5-acetoxy compound (VII) is obtained by oxidation with lead tetra-

acetate[10,13]. Only in the Friedel-Crafts condensation with acetyl chloride does reaction take place at some other position. In this case 10-acetyl-3:4-benzpyrene is obtained and possibly a little of the 8-isomer[9,13].



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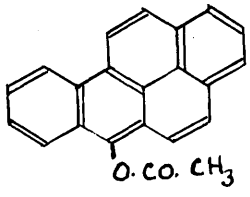

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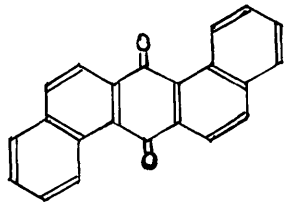
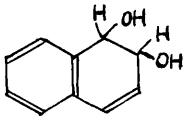


(VIII)

In view of this high reactivity of the 5-position in benzpyrene, it is very surprising that metabolic oxidation does not take place there at all, although the positions which are attacked seem to be those at which chemical reaction takes place when the 5-position is blocked. Thus, nitration of 5-acetoxy-3:4-benzpyrene (VII) takes place at position 10[13], one of the centres attacked in the biochemical oxidation of the hydrocarbon.

This very interesting aspect of the metabolism of polycyclic aromatic hydrocarbons has not yet been adequately explained, although several suggestions have been advanced. It is possible[17] that, in the body, the hydrocarbons are combined with an enzyme or with some other body constituent (such as ascorbic acid[15], or a purine[16]) through the most reactive positions, which are, therefore, protected from attack by the biochemical oxidising agents.

It is probable that formation of the phenolic metabolites takes place through the intermediary of diols - formed by addition of hydroxyl groups to adjacent carbon atoms - which are subsequently converted to phenols by dehydration, either <u>in vivo</u> or during the working up processes. Such diols (VIII and IX) have in fact been isolated from naphthalene[18] and anthracene[19].



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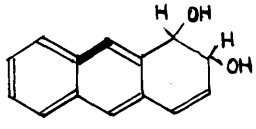
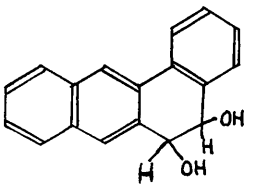


(IX)

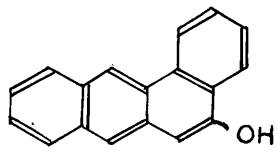
These compounds are readily dehydrated to α-naphthol and α-anthrol respectively, when treated with dilute acids. Diols have not yet been obtained from the metabolism of more complex hydrocarbons, but in view of the great ease with which such compounds are converted to phenols this is not significant. It is probable that metabolic oxidation follows the same course in all cases, and indeed there is spectroscopic evidence that derivatives of diols analogous to (VIII) and (IX) are intermediates in the biochemical oxidation of 3:4-benzpyrene[20].

In this connection the experiments recently described by Cook and Schoental[21], on the oxidation of a number of polycyclic aromatic hydrocarbons with osmium

tetroxide, are of considerable interest. In this case also oxidation takes place at less reactive centres in the molecule, leading first to diols, which are readily converted to phenols by dehydration. Thus from 1:2-benzanthracene, after dehydration of the first formed diol (X), 3-hydroxy-1:2-benzanthracene (XI) is obtained.



(X)

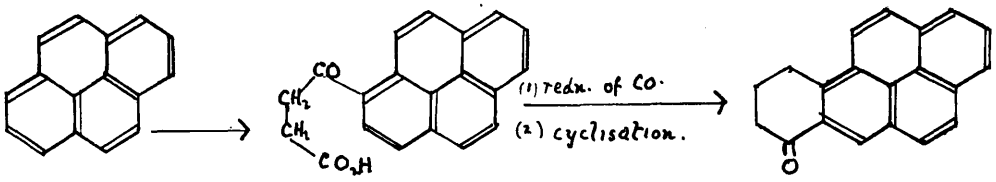


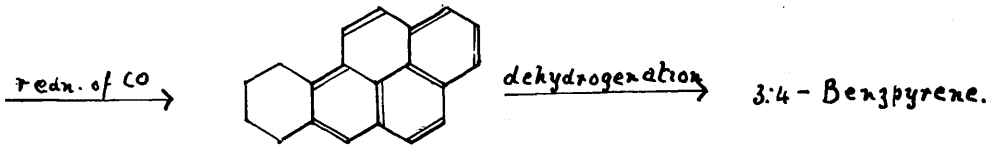
(XI)

Similarly, 3:4-benzpyrene yields a diol which, on dehydration, gives rise to two phenolic products, considered to be the 6- and 7-hydroxy-derivatives. This reaction obviously offers a very close parallel to the biochemical oxidation of the hydrocarbons. Although the positions of attack are not the same, in each case oxidation takes place at less reactive centres in the molecule.

For the synthesis of 10-hydroxy-3:4-benzpyrene, new routes to the benzpyrene nucleus have to be devised. Although a considerable number of derivatives of the hydrocarbon have been prepared since it was first isolated from coal tar in 1933[22], none of the methods employed is very

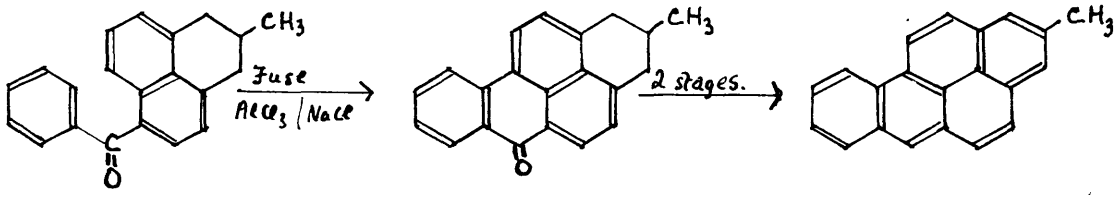
general, and none is suitable for application to the present case. Thus, 3:4-benzpyrene itself was synthesised by Cook and Hewett from pyrene and succinic anhydride, by the steps outlined below[22].





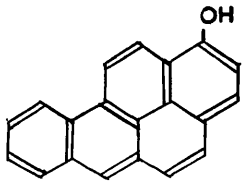
This method has been applied to the synthesis of a few derivatives of the hydrocarbon substituted in the "benz" ring, but is clearly not suitable for the preparation of compounds with a substituent in position 10.

Another route to substituted benzpyrenes, devised by Fieser and Hershberg[23] involves Scholl ring closure of a ketone obtained from a benzoyl chloride and a perinaphthane derivative. It is illustrated by the synthesis of 9-methyl-3:4-benzpyrene shown below[24].

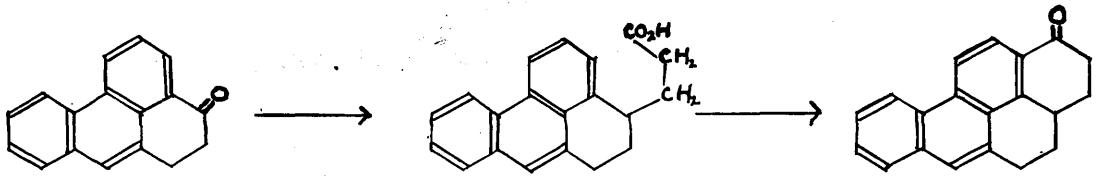


Several derivatives of the parent hydrocarbon have been prepared by this method, but again it is not applicable to the synthesis of the 10-hydroxy compound. Most of the other derivatives of 3:4-benzpyrene which have been obtained were prepared by unique methods, and it seems that no compound with a substituent in position 10 has so far been prepared by a synthetic method, apart from those which can be obtained from the 10-acetyl-derivative. Two general lines of approach to the synthesis of the 10-hydroxy derivative were investigated in the present work. Each of these involved an attempt to build up the benzpyrene nucleus from compounds containing a smaller number of rings.

In the first approach to the synthesis of 10-hydroxy-3:4-benzpyrene (XII) an attempt was made to build up the pentacyclic benzpyrene nucleus by the successive addition of two further rings to the tricyclic phenanthrene nucleus. The scheme envisaged involved the use, as an intermediate, of a ketone of the type (XIII).



(XII)



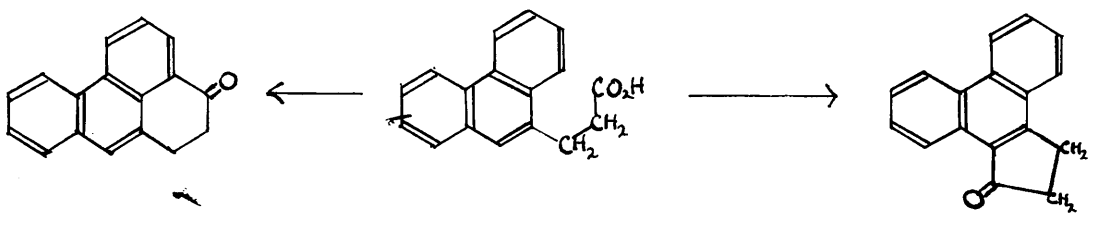
(XIII) (XIV) (XV)

When the synthesis was first projected it was intended to prepare (XII) from (XIII) by introduction of a propionic acid residue at the site of the carbonyl group in (XIII), through the Stobbe condensation with di-ethyl succinate, followed by cyclisation of the acid (XIV) and dehydrogenation of the resulting ketone (XV).

Before the present work was undertaken, however, experiments investigating the possibility of synthesising

the ketone (XIII) by cyclisation of β-(9-phenanthryl) propionic acid (XVI), had been carried out by Mr. P. Pauson in this Department, but without success (unpublished work).

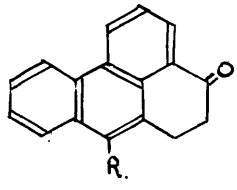
It will be noted that cyclisation of the acid (XVI) can theoretically give rise to the ketones (XIII) and (XVII), by ring closure into the 1- and 9-positions respectively of the phenanthrene nucleus. The well known preference for the formation of six-membered rather than five-membered rings in intramolecular acylations[36], would favour formation of the ketone (XIII) in the present case. On the other hand, the 9-position of the phenanthrene nucleus is much more reactive than the 1-position, as is shown in many substitution reactions of phenanthrene. The tendency for ring closure to take place into the most reactive centre available would thus favour production of the ketone (XVII).



(XIII) (XVI) (XVII)

In the hope of determining conditions which would lead to formation of preponderant amounts of (XIII), Pauson investigated the cyclisation of the acid (XVI) with various cyclising reagents and under a variety of experimental

conditions. In every case, however, mixtures of the two ketones were obtained, from which no pure product could be isolated. These results were in agreement with those of Bachmann and Kloetzel[25], who found that treatment of the acid chloride of (XVI) with aluminium chloride gave inseperable mixtures of (XIII) and (XVII). Weizmann, Bergmann and Berlin[26] obtained only the five-membered ring ketone (XVII) by cyclisation of (XVI) with phosphorus pentoxide. It thus became apparent that the preparation of the ketone (XIII) could not be accomplished by this method. It was still possible, however, that a ketone of a suitable structure could be obtained by blocking the 9-position of the acid (XVI) by introduction of a suitable substituent, and thus forcing cyclisation to take place into the 1-position. This would give rise to a compound (XVIII) which differed from (XIII) only in the presence of a substituent (R) in position 9, and which would undergo the subsequent reactions leading to the benzpyrenol structure in exactly the same manner as (XIII). It was necessary, of course, that the substituent introduced be one which would be easily removed at some later stage in the synthesis.

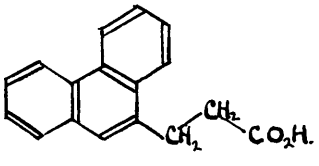


(XVIII)

Pauson had investigated the possibility of blocking the 9-position of (XVI) by means of a bromine atom. The results were not promising, however. Bromination of

(XVI) always gave mixtures of bromo compounds. The method was not further investigated in the present work.

It was considered that hydrogenation of the 9:10-bond in (XVI) would constitute a neat and effective way of attaining the desired object, for cyclisation in the 9:10-dihydro-acid (XIX) could only take place into the 1-position, this being the only aromatic centre available. Further, the hydrogen atoms introduced would not interfere with the subsequent stages of the synthesis, and would be removed during the final dehydrogenation. It was, therefore, considered to be worth while to attempt to prepare the dihydro-acid (XIX).



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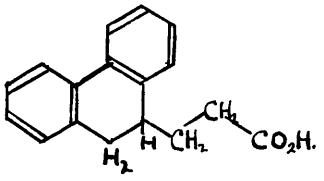

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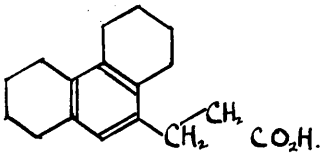
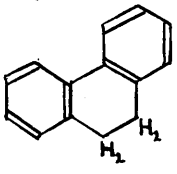


(XXI)



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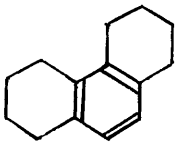


(XXII)

It was anticipated that (XIX) could be obtained by high pressure hydrogenation of (XVI) over copper chromite, for 9:10-dihydrophenanthrene (XX) can be prepared in 90% yield by selective hydrogenation of phenanthrene in this way[27].

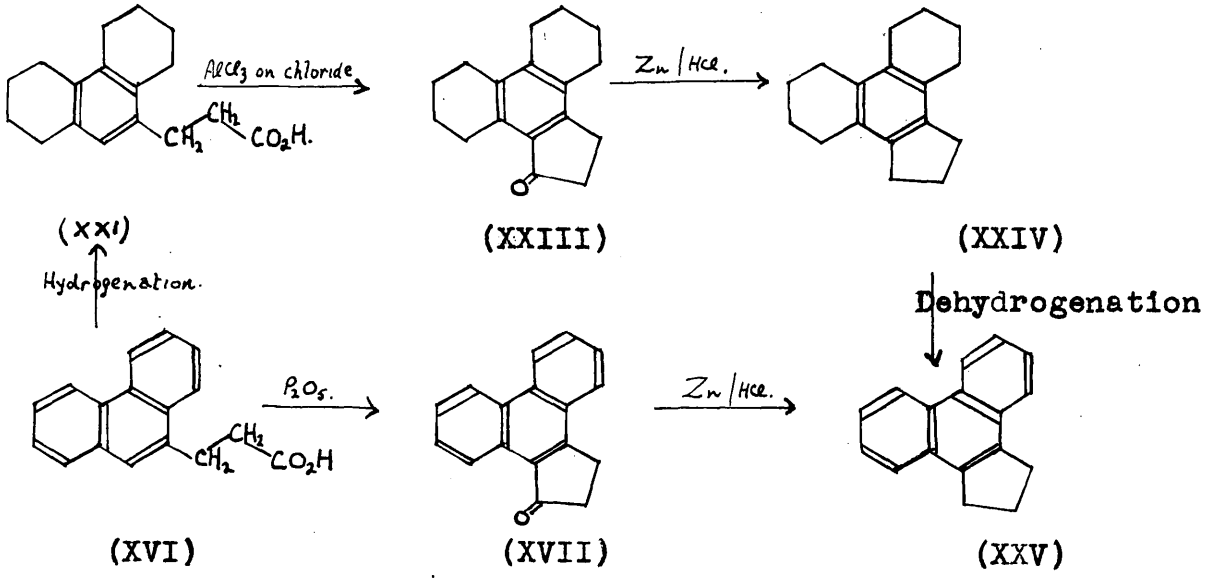
It is surprising therefore, that repeated attempts to prepare the desired dihydro-acid (XIX) by this method were unsuccessful. β-(9-Phenanthryl) propionic acid (XVI) was not attacked under conditions (150°/140 ats.) which had proved sufficient for the conversion of phenanthrene to 9:10-dihydrophenanthrene[27], while at a slightly higher temperature (180-190°) hydrogenation proceeded too far and β-(9-s-octahydrophenanthryl)propionic acid (XXI) was obtained. Under these conditions this acid was formed in good yields and was the only product isolated. The difference between the temperature at which no reduction takes place (150°), and that at which it proceeds right through to the octahydro-compound (190°), is not large. Many attempts were made to stop the reaction at the dihydro-stage by conducting the hydrogenation at temperatures between these two extremes, but in no case was the dihydro-compound (XIX) obtained. Mixtures of acids from which no pure product could be isolated were always produced. It is of some interest in this connection that the production of s-octahydrophenanthrene (XXII) from phenanthrene by high pressure hydrogenation over copper chromite requires a temperature of 220°, only a small amount of the octahydro-compound being produced at 180°[27]. The present case is in striking contrast to this, a temperature of 190° being sufficient for the complete conversion of (XVI) to the octahydro-acid (XXI).

High pressure hydrogenation of (XVI) using a nickel-kieselguhr catalyst also gave mixtures, from which no pure dihydro-acid could be isolated. With this catalyst mixtures containing large amounts of the octahydro-compound (XXI) were produced at a temperature as low as 145-155°. Chemical reduction of (XVI) with Raney-nickel alloy and sodium hydroxide, a reagent described by Papa, Schwenk and Whitman[28], also gave mixtures. This was not unexpected, as chemical reduction of phenanthrene itself is known to give mixtures of hydrophenanthrenes[29]. For this reason no further attempt was made to prepare (XIX) by chemical reduction of (XVI).

In view of the failure to obtain the dihydro-acid (XIX), this attempt to force the acid side chain of (XVI) to cyclise into the 1-position of the nucleus was frustrated. For there is no substituent, other than the two which have been tried, which might be introduced into the 9-position of (XVI) to effect this purpose. This particular approach to the problem of synthesising a ketone of the type (XIII) was therefore abandoned.

The octahydro-acid (XXI) obtained in the above hydrogenations, was readily converted to 1'-keto-9:10-cyclopenteno-8-octahydrophenanthrene (XXIII), when its acid chloride was treated with aluminium chloride in nitrobenzene. The

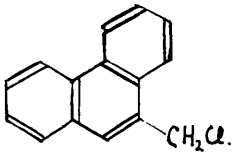
structure of this ketone was confirmed by its reduction by the Clemmensen-Martin procedure to 9:10-cyclopenteno-s-octahydrophenanthrene (XXIV), which was readily dehydrogenated with palladium black to the known 9:10-cyclopentenophenanthrene (XXV)[25,26].



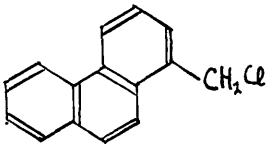
For purposes of comparison, a sample of 9:10-cyclopentenophenanthrene (XXV) was prepared as described by Weizmann, Bergmann and Berlin[26], by Clemmensen reduction of the ketone (XVII) produced by cyclisation of (XVI) with phosphoric oxide.

For the preparation of β-(9-phenanthryl)-propionic acid (XVI) necessary for the above experiments, 9-chloromethylphenanthrene (XXVI) was used as starting material. This resulted in a shorter and more effective synthesis of this acid than that described by Bachmann and

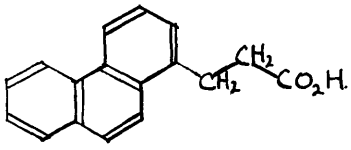
Kloetzel[25], who prepared it by reduction of the corresponding acrylic acid and also from the 9-bromomethyl-compound (prepared by a long process) by means of the malonic ester synthesis.



(XXVI)



(XXVII)

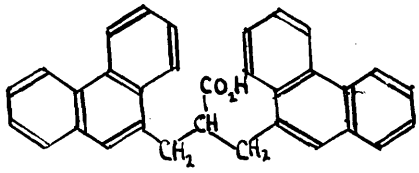


(XXVIII)

The chloromethylation of phenanthrene has already been described by Cook et al.[30] and by Tarbell and Wystrach[31]. It does not take place readily for the phenanthrene nucleus is not a very reactive one. In the present work the best conditions were found to be a modification of those of Tarbell and Wystrach, but even then only poor yields (25%) of the product were obtained. In every case a considerable amount of resinous material was also produced. A small amount of 1-chloromethylphenanthrene (XXVII) was also isolated from the reaction. The structure of this compound was established by reduction to 1-methylphenanthrene with palladium black in acetone. This is a good method for the reduction of chloromethyl compounds. The hydrocarbons are obtained in almost quantitative yield. Chemical methods of reduction, in contrast, are often unsatisfactory owing to the formation of bimolecular products (compare Badger, Cook and

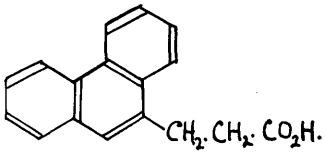
Crosbie[32]). The occurrence of small quantities of the 1-chloromethyl derivative among the products obtained by chloromethylating phenanthrene has been mentioned by von Braun[33], but no description of the compound, or of its method of isolation, was given by him.

9-Chloromethylphenanthrene was condensed with ethyl sodiomalonate to give a malonic ester, which was directly hydrolised without isolation. The resulting malonic acid gave β-(9-phenanthryl)propionic acid (XVI) on decarboxylation. In an early run of this preparation, in which distilled but uncrystallised 9-chloromethylphenanthrene was used, a small amount of another acid was isolated. This was identified as β-(1-phenanthryl)-propionic acid (XXVIII) by comparison of its methyl ester with an authentic specimen kindly supplied by Professor W.E. Bachmann[25]. It has obviously arisen from 1-chloromethylphenanthrene, the presence of which in the crude 9-chloromethyl-compound was hitherto unsuspected. This series of reactions also led to the formation of another acid by-product. The analysis of this compound and of its methyl ester, and a molecular-weight determination, support the conclusion that it is αα'-di-(9-phenanthryl)iso-butyric acid (XXIX), formed by combination of two molecules of 9-chloromethylphenanthrene with one of ethyl malonate.

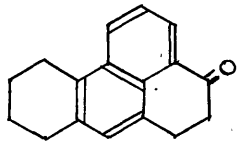


(XXIX)

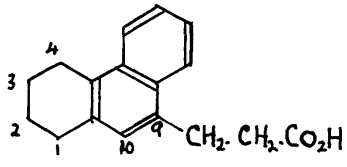
Attention was now turned to consideration of another modification of the structure of (XVI), which, it was considered, might influence the direction of cyclisation of the acid side chain in such a manner that a ketone of a structure suitable for the subsequent stages of the synthesis would be obtained on ring closure. It seemed possible that β-(1:2:3:4-tetrahydro-9-phenanthryl)propionic acid (XXX) would give rise to such a ketone (XXXVI) on cyclisation, and this possibility was investigated.



(XVI)



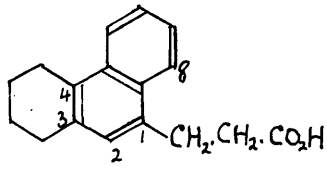
(XXXVI)



(a)

Numbered with respect to phenanthrene

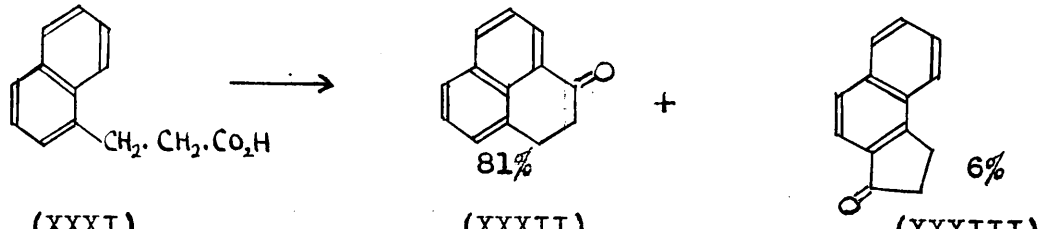
(XXX)



(b)

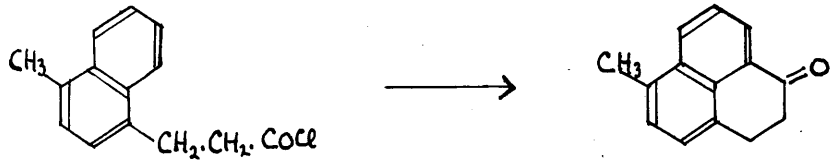
Numbered with respect to naphthalene

The acid (XXX) is a tetrahydro-derivative of (XVI) in which one of the lateral rings is reduced, so that it no longer contains a phenanthrene nucleus in its structure. It can be regarded as a derivative of naphthalene, and is, in effect, a β-1-naphthylpropionic acid with alkyl substituents at positions 3 and 4 (see formula XXXb). Ring-closure of β-1-naphthylpropionic acids can take place theoretically into the 2- or the 8-position, but in the many cyclisations of acids of this type which have been studied, it has been found to occur almost exclusively in the 8-position. For example, Fieser and Gates[34] found that cyclisation of β-1-naphthylpropionic acid itself (XXXI) gave 81% of perinaphthanone (XXXII), formed by cyclisation into the 8-position, and also 6% of the alternative product, 4:5-benzhydrindone (XXXIII).



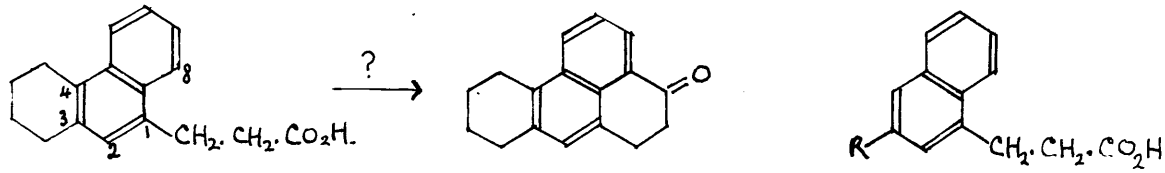
(XXXI) (XXXII) (XXXIII)

Again, Buu, Hoi and Cagnaint[35] showed that treatment of β-(4-methyl-1-naphthyl)propionyl chloride (XXXIV) with aluminium chloride gave 3-methylperinaphthan-7-one (XXXV), none of the other possible product being isolated.



(XXXIV) (XXXV)

These examples (many others are known) serve to indicate the readiness with which cyclisation of β -1-naphthylpropionic acids takes place into position 8. The reason for this is not far to seek. It is favoured both by the well-known preference for the formation of six-membered rather than five-membered rings in intra molecular acylations[36], and by the tendency for cyclisation to take place into the most reactive centre available. Ring closure into position 8 is into the reactive α position of naphthalene, and results in the formation of a six-membered ring ketone. It was, therefore, anticipated that cyclisation of the acid (XXX) (a substituted β -1-naphthylpropionic acid) would also take place into the 8-position, with formation of the ketone (XXXVI), which could be utilised for the succeeding stages of the benzpyrenol synthesis which have been previously outlined.



Numbered with respect to naphthalene (XXX)

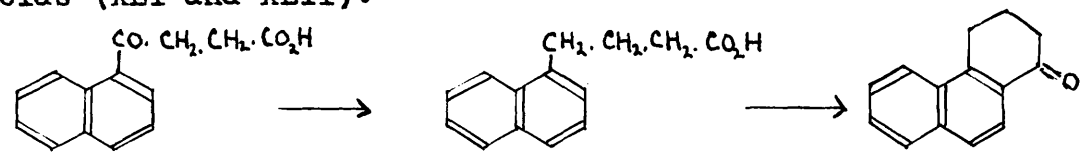
(XXXVI)

(XXXVII) (R = alkyl)

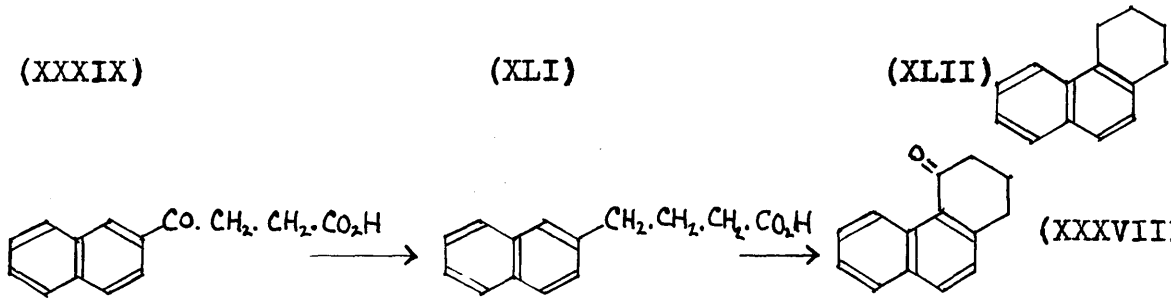
It was recognised that in the acid (XXX) the methylene group (of the reduced ring) at position 3 would activate position 2 to some extent, so that the tendency for cyclisation to take place into this position would be greater than in the examples given above. It is unfortunate, in this connection, that no example is recorded in the literature of cyclisation of an acid of the type (XXXVII), for the products obtained in such a case would have offered a more critical guide than the other examples cited, to the structure of the ketone to be expected by cyclisation of (XXX). It was considered, however, that the preference for cyclisation to take place into position 8, as exhibited in other acids of this type, would lead to formation of preponderant amounts of the desired ketone (XXXVI).

1:2:3:4-Tetrahydrophenanthrene (XXXVIII) cannot be prepared satisfactorily by reduction of phenanthrene, for it is always accompanied by di- and octa-hydrides from which it must be separated[29]. For this reason no attempt was made to prepare the tetrahydro-acid (XXX) by reduction of 3-(9-phenanthryl)propionic acid (XVI). Bachmann and Cronyn[37] have described a synthesis of the tetrahydro-acid using tetrahydrophenanthrene (XXXVIII) as starting material, and this method was adopted in the present work. The starting material was itself obtained by Bachmann and Struves[38]

modification of the original procedure of Haworth[39]. Succinic anhydride and naphthalene were condensed with aluminium chloride in nitrobenzene, giving a mixture of α- and β-naphthoylpropionic acids (XXXIX and XL). These were directly reduced, without separation, by the Clemmensen-Martèn method, to the mixed α- and β-naphthylbutyric acids (XLI and XLII).



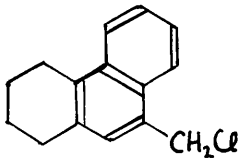
(XXXIX) (XLI) (XLII)



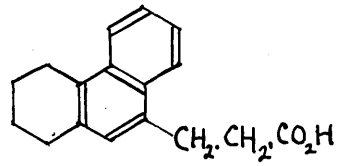
(XL) (XLII) (XLIV) (XXXVIII)

Cyclisation of these mixed acids by treatment of the acid chlorides with stannic chloride gave a mixture of 1'- and 4'-keto-1:2:3:4-tetrahydrophenanthrenes (XLIII and XLIV), from which the hydrocarbon was obtained by Clemmensen reduction.

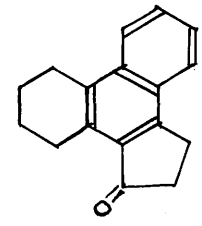
Chloromethylation of this hydrocarbon[37] gave the 9-chloromethyl-compound (XLV), which was condensed with ethyl sodiomalonate. The resulting malonic ester was directly hydrolised to the malonic acid, decarboxylation of which gave the desired β-(1:2:3:4-tetrahydro-9-phenanthryl)-propionic acid (XXX).



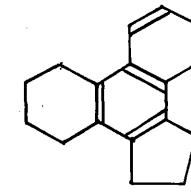
(XLV)



(XXX)



(XLVI)

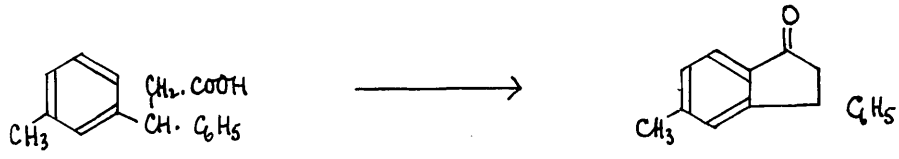


(XLVII)

Cyclisation of this acid was effected by three methods - by treatment of the acid with anhydrous hydrogen fluoride, and by action of stannic chloride and of aluminium chloride on the acid chloride, the former in benzene, the latter in nitrobenzene solution. In each case good yields of ketonic material were obtained. It was with some surprise, however, that this was identified as 3'-keto-9:10-cyclopenteno-1:2:3:4-tetrahydrophenanthrene (XLVI). The structure of this ketone was established by Clemmensen reduction to 9:10-cyclopenteno-1:2:3:4-tetrahydrophenanthrene (XLVII), which was smoothly dehydrogenated with palladium black to the known 9:10-cyclopentenophenanthrene (XXV)[25,26].

The ketone (XLVI) appeared to be the sole product of the reaction in each case, none of the alternative six-membered ring compound (XXVI) being detected. Its formation involves cyclisation of the side chain of (XXX) into the 2-position of the naphthalene nucleus. As already indicated, cyclisation of a β-1-naphthylpropionic acid into position 2 in preference to position 8 is very unusual. This seems to be the first example in which cyclisation into position 2 has

taken place preponderantly. This must be attributed to the activation of position-2 by the methylene group in the adjacent 3-position.

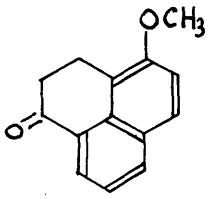


(XLVIII) (IL)

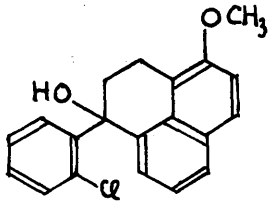
That such alkyl groups do indeed have some effect on the direction of ring closure, has been substantiated[40] in the cyclisation of β -m-tolylhydrocinnamic acid (XLVIII). The product of the reaction consisted solely of 5-methyl-3-phenylhydrindone-1 (IL), arising from acylation <u>para</u> to the methyl group. No material was found which corresponded to cyclisation into the unsubstituted nucleus.

The unexpected formation of the ketone (XLVI) frustrated this attempt to build up the benzpyrene nucleus from the phenanthrene nucleus. This general method was therefore abandoned.

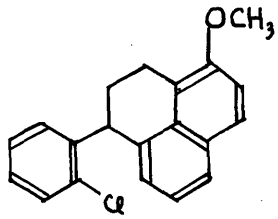
Another attempt was made to synthesise 10-hydroxy-3:4-benzpyrene, in the form of its methyl ether (LIV), from constituents in which the methoxy group was already present.



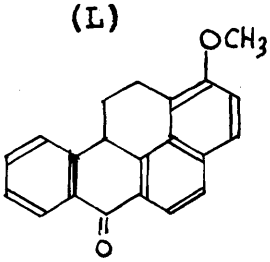
(L)



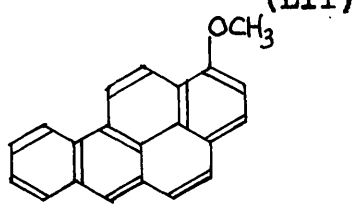
(LI)



(LII)



(LIII)

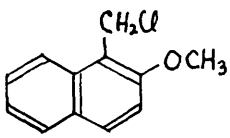


(LIV).

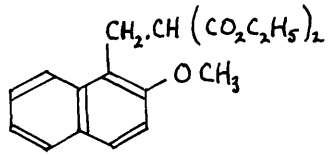
The proposed synthesis involved condensation of the ketone (L) with o-chlorophenylmagnesium bromide to give the carbinol (LI), which was expected to yield (LII) by dehydration followed by reduction. It was anticipated that replacement of chlorine in this compound by carboxyl, through the nitrile, and subsequent ring closure of the acid, would give the ketone (LIII) from which (LIV) could be obtained by reduction and dehydrogenation.

The first step in the scheme was the synthesis of the ketone (L). This was successfully accomplished by cyclisation of β-(2-methoxy-1-naphthyl)propionic acid (LVII). The starting point in the synthesis was 2-methoxynaphthalene. Chloromethylation of this by a modification of the method of Cook, Downer and Hornung[41] gave 1-chloromethyl-2-methoxynaphthalene (LV) readily. This was condensed with ethyl sodiomalonate to give ethyl (2-methoxynaphthyl-1-methyl)-malonate (LVI). On hydrolysis the corresponding malonic

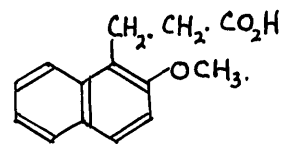
acid was obtained, which was readily decarboxylated to β-(2-methoxy-1-naphthyl)propionic acid (LVII).



(LV)



(LVI)

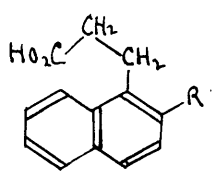


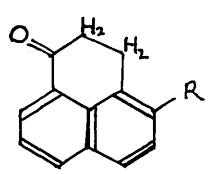
(LVII)

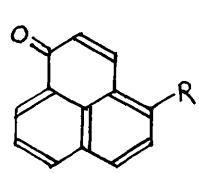
The overall yield from the chloromethyl compound was 80%. This acid has previously been described by Barger and Starling[42], who prepared it, in poor yield, by reduction of the corresponding acrylic acid.

Cyclisation of (LVII) was investigated under three sets of conditions. Following the work of Fieser and Gates[34], who found that treatment of β-1-naphthylpropionic acid (LVIII) with anhydrous hydrogen fluoride gave excellent yields of the colourless perinaphthanone (LIX), it was expected that similar treatment of (LVII) would yield the desired ketone (L). This was indeed found to be the case, 1-methoxyperinaphthan-7-one (L) being obtained in good yield, as a yellow crystalline solid, when the acid (LVII) was left in contact with anhydrous hydrogen fluoride for several hours. The analysis of the well crystalline oxime was in agreement with this structure. The same ketone was obtained in equally good yield, by treatment of the acid chloride of (LVII) with stannic chloride in cold benzene solution. The identity of the ketones was

confirmed by comparison of the oximes. This is of some interest, for it was found by Cook and Hewett[42], and by Fieser and Gates[34], that cyclisation of the acid chloride of the unmethoxylated acid (LVIII) with aluminium chloride, or with stannic chloride, gave not the expected colourless perinaphthanone (LIX), but the yellow compound perinaphthenone (LX), formed by loss of two hydrogen atoms from the initial cyclisation product (LIX). This substance (LX) had marked basic properties and dissolved easily in concentrated hydrochloric acid.







(LVIII) R = H (LIX) R = H (LX) R = H

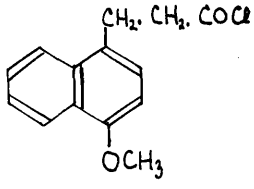
(LVII) R = $-OCH_3$ (L) R = $-OCH_3$ (LXI) R = $-OCH_3$

The fact that the ketone obtained in the present work was yellow in colour suggested that it might be contaminated with some of the corresponding unsaturated compound (LXI). However, attempts to remove the yellow colour from the ketone by repeated extraction of a benzene solution with concentrated hydrochloric acid (in which (LXI) would be soluble, on analogy with (LX)), and also by chromatography on alumina, were unsuccessful. No trace of the unsaturated ketone was isolated from this source. The presence of a methylene group adjacent to the carbonyl group in the yellow ketone was

confirmed by the formation of a benzylidene derivative. There is thus little doubt that the ketone obtained by cyclisation of (LVII) by the methods described has the structure represented by formula (L), and that the yellow colour is not due to the presence of impurity.

It has been reported by Barger and Starling[42] that the ketone (L) is produced, in poor yield, by cyclisation of β-(2-methoxy-1-naphthyl)propionic acid (LVII) with phosphoric oxide. Since the ketone obtained by these authors was plainly different from that isolated in the present work (and designated as (L)), this cyclisation was re-investigated. Reaction as described by these workers gave rise to a complex mixture of products, from which two pure substances were isolated. One of these was evidently identical with that described by Barger and Starling. The analysis of this compound leads to the conclusion that it is the unsaturated 1-methoxyperinaphthen-7-one (LXI) and not the saturated methoxyperinaphthanone (L) as Barger and Starling supposed. The fact that it is readily soluble in concentrated hydrochloric acid is in agreement with this formulation. The other product isolated from this cyclisation was identified as perinaphthenone itself (LX). The formation of this compound involves both dehydrogenation and demethoxylation during cyclisation. A similar loss of a methoxyl group was observed by Mayer and

Sieglitz[44] during cyclisation of β-(4-methoxy-1-naphthyl)propionyl chloride (LXII) with aluminium chloride. In this case perinaphthenone was the only product isolated.

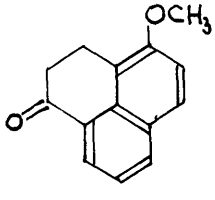


(LXII)

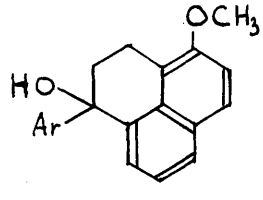
The ketone (L) was now condensed with o-chlorophenylmagnesium bromide in ether-benzene, giving 1-methoxy-7-(o-chlorophenyl)-perinaphthan-7-ol (LI) as a colourless crystalline solid. The presence of the hydroxyl group in this compound could not be proved by the formation of a dinitrobenzoate or an α-naphthylisocyanate, but this is not surprising in view of the well-known resistance of tertiary alcohols to form derivatives of this nature.

The next step in the synthesis was dehydration of the carbinol (LI). To effect this it was treated with a little iodine in boiling light-petroleum. The product, isolated in high yield, was a well-crystalline apparently homogeneous solid. The same compound was obtained in almost quantitative yield by treatment of the carbinol with cold dilute methanolic hydrogen chloride. This substance, however, did not have the properties of the expected dehydration product (LXIII). It did not decolourise bromine water or dilute permanganate, and a Zeisel determination showed the absence of a methoxyl group. The properties of the

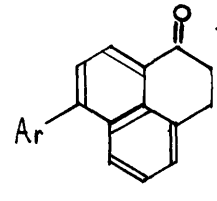
substance lead to the conclusion that it is actually 4-(o-chlorophenyl)-perinaphthan-7-one (LXIV). Its ketonic nature was shown by the preparation of a semicarbazone and a 2:4-dinitrophenylhydrazone, and the presence of a methylene group adjacent to the carbonyl group was demonstrated by the ready formation of a benzylidene derivative. This ketone was the sole product of the reaction. There was no evidence of the formation of the expected dehydration product (LXIII).



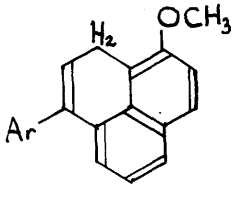
(L)



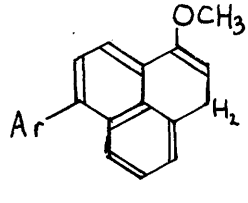
(LI)



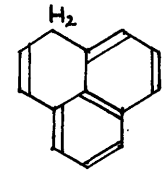
(LXIV)



(LXIII)



(LXV)



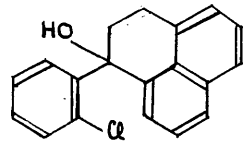
(LXVI)

(Ar = o - C_6H_4Cl)

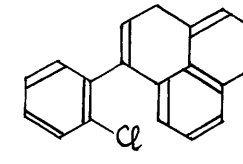
The formation of the ketone (LXIV) from (LI) can be interpreted as taking place by a rearrangement of bonds in the initial "normal" dehydration product (LXIII), with formation of an intermediate compound of structure (LXV). This represents the ether of an enol, and as such, would

readily undergo hydrolysis to give the ketone (LXIV).

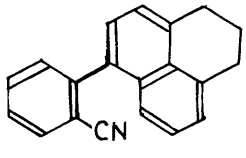
This postulated rearrangement in (LXIII) is not unlikely, since it involves only a redistribution of bonds in a perinaphthene system (LXVI), and this is known to be possible. In 1938, Klyne and Robinson[45] suggested the possibility of tautomerism among six structures in this system, and the double bond mobility inherent in this conception was observed for the first time two years later by Fieser and Gates[34] in an example which is similar to the present one. These authors found that when the carbinol (LXVII) was subjected to a series of reactions involving dehydration, reduction, and replacement of chlorine by cyano, without isolation of intermediates, two products were obtained which were identified as (LXVIII) and (LXIX). The expected product (LXXI) was not encountered.



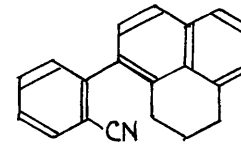
(LXVII)



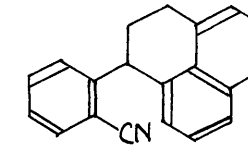
(LXX)



(LXVIII)

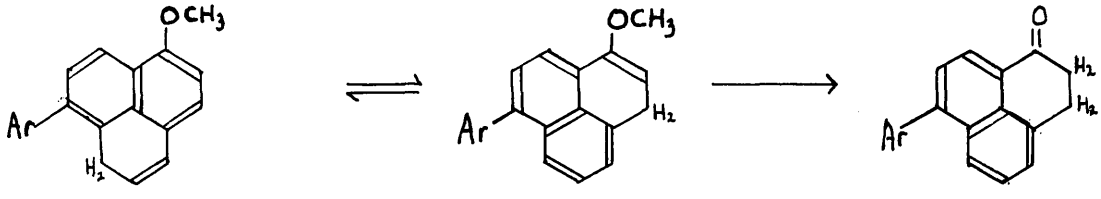


(LXIX)



(LXXI)

The formation of (LXVIII) and (LXIX) can only be explained by a rearrangement of bonds in the initial dehydration product (LXX) - a perinaphthene derivative. It was suggested by Fieser and Gates[34] that the driving force in these rearrangements is the tendency for conjugation between the chlorophenyl group and a naphthalene nucleus. The rearrangement recorded in the present work is analogous to this, and clearly affords a further example of the double bond mobility in the perinaphthene system.



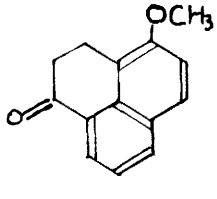
(LXXII) (LXV) (LXIV)

(Ar = o - C_6H_4Cl)

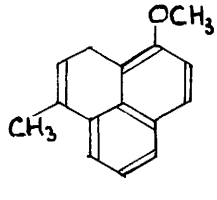
On analogy with the example studied by Fieser and Gates[34], one might expect that two products would be obtained from the carbinol (LI), the ketone (LXIV) and another methoxy compound (LXXII) corresponding to one of the products (LXIX) isolated by Fieser and Gates. It is of considerable interest, therefore, that only the ketone (LXIV) was isolated from the reaction. This is in agreement with the hypothesis of Klyne and Robinson[45] regarding the mobility of bonds in the perinaphthene system.

For if, say, (LXXII) and (LXV) were in tautomeric equilibrium, this would be continually disturbed by the irreversible hydrolysis of (LXV) to the ketone (LXIV), so that ultimately the whole of (LXXII) as well as (LXV) would be converted to the ketone.

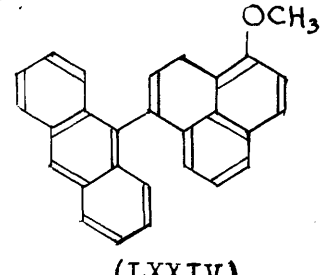
If the explanation suggested by Fieser and Gates[34] regarding the driving force in these bond migrations (see page 34) is the correct one, then it is conceivable that interaction of the ketone (L) with methylmagnesium iodide and with 9-anthranylmagnesium bromide would give rise to carbinols which could undergo dehydration without rearrangement, to give the compounds (LXXIII) and (LXXIV). For in the former case no conjugation is possible, so that there would be no reason for rearrangement taking place. In the latter case it was anticipated that steric inhibition of resonance in the compound (LXXIV) would prevent true conjugation, and hence prevent rearrangement.



(L)



(LXXIII)



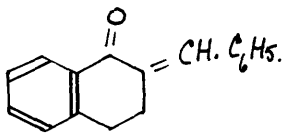
(LXXIV)

Attempts to test this hypothesis, however, were unsuccessful. Methylmagnesium iodide reacted with (L) to give an uncrystallisable oil, and the dehydration product was also an

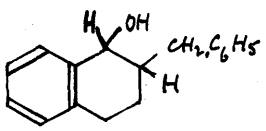
oil. Anthranylmagnesium bromide did not react with (L) even in boiling di-amyl ether (170°). On decomposition of the reaction mixture with acid, only anthracene was obtained. Presumably in this case reaction is prevented by the very steric factor of which it was intended to take advantage.

The ketone (LXIV) cannot be utilised for the further stages of the proposed benzpyrenol synthesis, and its production from the carbinol (LI) thus effectively blocked this method of approach. Some attempts were made to reduce (LI) to the compound (LII) (formula on page 37) by direct reduction with zinc dust and sodium hydrosulphite, but the carbinol was always recovered unchanged. The synthesis was thus abandoned at this stage.

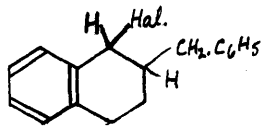
Some preliminary experiments have been carried out in a proposed synthesis of the hexahydro-1:2-benzanthrone (LXXIX). It was intended that this should serve as a model for a similar synthesis of the methoxy-derivative (LXXX), from which it was hoped it would be possible to synthesise 10-methoxy-3:4-benzpyrene (LIV).



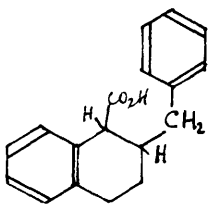
(LXXV)



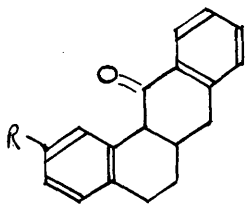
(LXXVI)



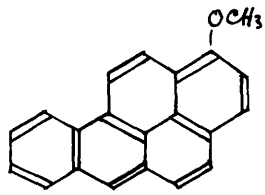
(LXXVII)



(LXXVIII)



(LXXIX) (R = H)
(LXXX) (R = $-OCH_3$)

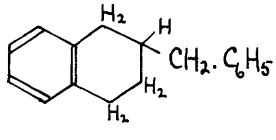


(LIV)

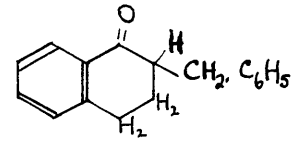
The proposed route to (LXXIX) involved reduction of benzylidenetetralone (LXXV) to the tetralol (LXXVI), conversion of this to the acid (LXXVIII) through the halide (LXXVII), followed by cyclisation of this acid to the hexahydrobenzanthrone (LXXIX).

The starting material, 2-benzylidene-1-tetralone (LXXV), was readily obtained from 1-tetralone and benzaldehyde, as described by Rapson and Shuttleworth[46]. By reduction of this $\alpha\beta$-unsaturated ketone with the specially active Raney nickel recently described by Pavlic and Adkins[47], 1-hydroxy-2-benzyl-1:2:3:4-tetrahydronaphthalene (LXXVI) was obtained in excellent yield. This compound can exist in two geometrically isomeric forms. Both of these were produced in the reaction, and were isolated

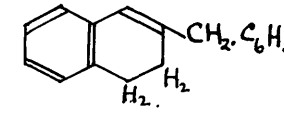
in approximately equal amounts by fractional crystallisation. The higher melting, least soluble isomer is regarded as the trans, and the other as the cis. This alcohol can also be produced from (LXXV) by chemical reduction with sodium and moist ether, but the yield obtained by this method is unsatisfactory, much high boiling material being formed. In this case also, both cis and trans forms were isolated. Hydrogenation of (LXXV) at elevated temperature and pressure over copper chromite, led to complete elimination of oxygen with formation of 2-benzyl-1:2:3:4-tetrahydronaphthalene (LXXXI). This compound was previously prepared by von Braun[48] by reduction of 2-benzyl-1-tetralone (LXXXII), and described by him as an oil. The compound obtained by the present method is a crystalline solid.



(LXXXI)



(LXXXII)

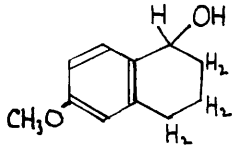


(LXXXIII)

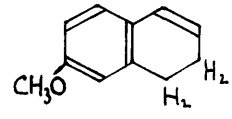
Conversion of the tetralol (LXXVI) to a halide (LXXVII) suitable for transformation to the acid (LXXVIII), either through the nitrile or by the Grignard reaction, proved to be a matter of considerable difficulty, because of the ease with which halogen hydride was lost from the halides with formation of an unsaturated hydrocarbon, probably

2-benzyl-3:4-dihydronaphthalene (LXXXIII). Treatment of either the cis or the trans alcohol with hydrogen bromide in cold benzene[49], or with cold hydrobromic acid, gave an oily product which could not be induced to crystallise. Distillation resulted in complete conversion to (LXXXIII). An attempt to prepare the acid (LXXVIII) directly from the crude oily halide, by treatment with potassium cyanide, followed by boiling with alkali, did not yield any acidic material. Again only the unsaturated hydrocarbon was isolated.

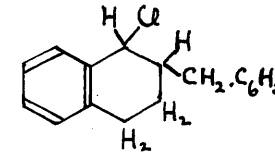
A similar difficulty was encountered by Long and Burger[50], who found that attempts to convert 1-hydroxy-6-methoxy-1:2:3:4-tetrahydronaphthalene (LXXXIV) to the corresponding halide gave only 6-methoxy-3:4-dihydronaphthalene (LXXXVI).



(LXXXIV)



(LXXXV)

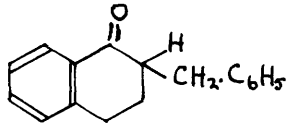


(LXXXVI)

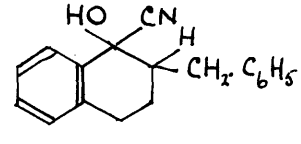
A small amount of 1-chloro-2-benzyl-1:2:3:4-tetrahydronaphthalene (LXXXVI) has been obtained in a pure crystalline condition by treatment of the tetralol (LXXVI), in cold benzene, with dry hydrogen chloride[49]. The yields were not consistent, however, and in many experiments no crystalline material was obtained at all. Most of the

reactions were carried out with the trans alcohol, but in one case the same crystalline chloride was obtained from the cis isomer. If this could be confirmed it would indicate a Walden Inversion during conversion of the alcohol to the chloride. The oil obtained in these attempts to prepare the crystalline chloride was treated as described above for the oily bromide, and the same results were obtained. The unsaturated hydrocarbon (LXXXIII) was formed on distillation, and by treatment with potassium cyanide followed by alkali.

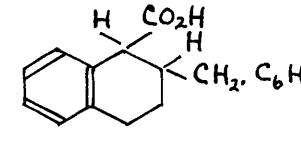
Experiments with the crystalline chloride confirmed the ease with which halogen hydride is lost. Treatment with potassium cyanide in boiling ethyl alcohol resulted in complete conversion to the unsaturated hydrocarbon. A preliminary attempt to prepare the acid (LXXVIII) from the chloride, by the Grignard method, was also unsuccessful. No acidic material was produced, and the oily neutral material which was isolated could not be obtained crystalline.



(LXXXII)



(LXXXVII)



(LXXVIII)

Because of the difficulty encountered in obtaining the pure halide (LXXVII), the possibility of obtaining the

acid (LXXVIII) from the cyanhydrin (LXXXVII) of 2-benzyl-1-tetralone (LXXXII) was investigated. This ketone was prepared by reduction of 2-benzylidene-1-tetralone (LXXV) with palladium black in acetic acid, as described in a patent by Riedel[51]. It was unaffected by hydrogen cyanide, however, repeated attempts to prepare the cyanhydrin being completely unsuccessful. The ketone was recovered unchanged in every case.

Pressure of time has prevented the pushing of this synthesis to a definite conclusion. It is hoped to investigate the Grignard reaction with the chloride further, when a sufficient quantity of crystalline material is available. It is clear that a satisfactory procedure for the preparation of this substance from the tetralol (LXXVI) will require to be worked out, before the further stages of the synthesis are investigated.

Part II.

Isomerisation Reactions with Anhydrous Hydrofluoric Acid.

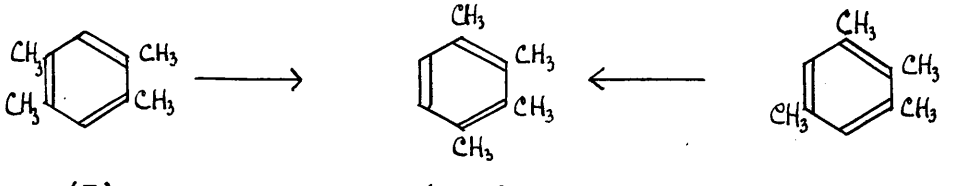
Because of its wide ramifications, isomerisation is one of the most important reactions in all chemistry. It is encountered in organic compounds of many types, but is particularly frequent among hydrocarbons.

Very many examples have been recorded of change of carbon skeleton in hydrocarbons of all classes (aliphatic, alicyclic and aromatic). These include, migration of alkyl groups along the benzene ring, change in ring size of cyclanes, conversion of straight-chain paraffins to their branched-chain isomers, and other types[52]. The last reaction has now assumed great importance in the petroleum industry, where branched-chain aliphatic hydrocarbons (which have better "anti-knock" values) are now prepared on a large scale by this method. Although a vast amount of work has been carried out on isomers and their reactions, no well-grounded theories for alkane, cyclane, or alkylbenzene isomerisations are available. A special theory is required for almost every type of change encountered in hydrocarbon isomerisation.

Isomerisation of hydrocarbons can sometimes be effected by heat alone, but generally a catalyst is employed. Many catalysts have been used for this purpose[52], but outstanding among these are the aluminium halides, which may induce isomerisation under very mild conditions.

These halides are constituents of nearly all the catalysts employed for paraffin isomerisations, and the rearrangement of alkylbenzenes under their influence is well known. (For Review see Nightingale, ref.53). Thus p-xylene is converted to m-xylene in 63% yield when warmed with aluminium chloride at 50° for five hours[54], and many isomerisations of a similar type have been recorded. Complexes of aromatics with aluminium chloride (a large number of which have been described), probably play an important part in such isomersiations[54,55].

Sulphuric acid has also been used to effect isomerisation of certain polyalkylbenzenes. This process, now known as the Jacobsen Reaction[56], is of only limited application however, and seems not to be related to the aluminium chloride catalysed isomerisations. The reaction is observed only in the case of polyalkyl- (and polyhalogeno-) benzenes, and is known to involve the sulphonic acid and not the hydrocarbon[57]. Durene (I) and isodurene (II) are converted to prehnitene (III) when sulphonated in presence of sulphuric acid and subsequently hydrolised[58].



(I) (III) (II)

It is a curious feature of the Jacobsen Reaction that it

always gives rise to products in which the groups occupy vicinal positions.

Hydrofluoric acid is also known to bring about rupture of carbon-carbon linkages under suitable conditions, and is finding increasing application as an isomerising agent in industry. Thus, toluene is prepared on a large scale by treatment of a mixture of xylenes and benzene with hydrofluoric acid at high temperature and pressures[59].

An interesting example of isomerisation in the s-octahydroanthracene nucleus in presence of hydrofluoric acid at ordinary temperatures has been observed in this Department. An investigation of this reaction, described in the sequel, has shown that it has certain unique features, and may be regarded as a new type of isomerisation of polyalkylbenzenes.

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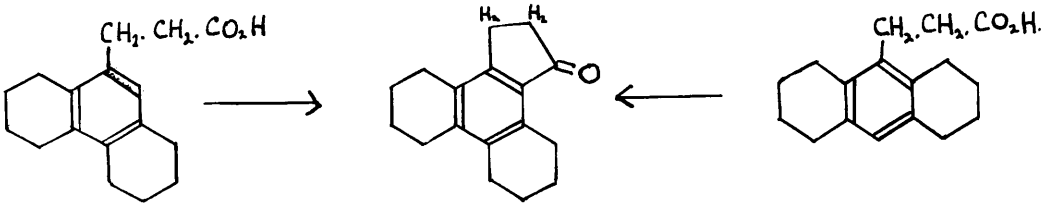
It has already been reported in Part I (page 16) that cyclisation of β-(9-s-octahydrophenanthryl)propionic acid (IV), by treatment of the acid chloride with aluminium chloride, yielded the ketone (V), as expected. The present investigation was initiated by the observation of other workers in this Department[60] that this ketone is obtained also from β-(9-s-octahydroanthranyl)propionic acid (VI) by action of anhydrous hydrofluoric acid.



(IV) (V) (VI)

The formation of (V) from (VI) in these circumstances is very surprising, and clearly involves isomerisation of the octahydroanthracene nucleus of (VI) to an octahydrophenanthrene one at some stage of the reaction.

It seemed of some interest to try to find other examples of similar rearrangements in the octahydroanthracene series, and thus to determine whether isomerisation to octahydrophenanthrene derivatives in presence of hydrofluoric acid is a common property of all derivatives of octahydroanthracene. For this purpose the behaviour of several substituted octahydroanthracenes when treated with hydrofluoric acid was examined. The results are shown in Table I.

The ultimate object of the investigation was to determine the mechanism by which the conversion of (VI) to (V) took place, and the results will therefore be discussed from that viewpoint.

Interconversion of s-octahydroanthracene and s-octahydrophenanthrene is known to take place readily under suitable conditions. Thus, Schroeter observed that treatment of s-octahydroanthracene (VII) with aluminium chloride at

Table I.

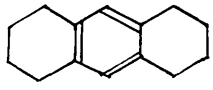
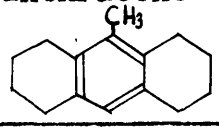
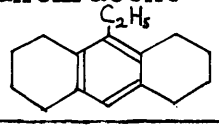
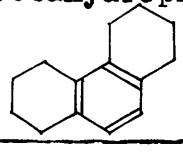
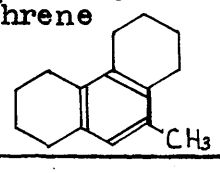
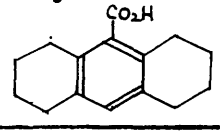
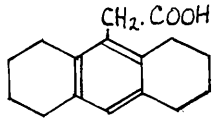
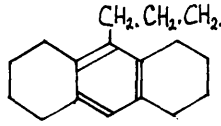
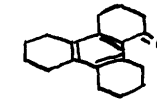
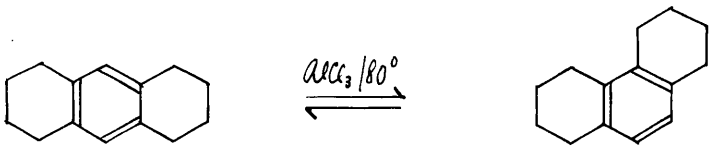
Compound Treated	% Isomerisation	Product
s-octahydroanthracene 	-	-
9-methyl-s-octahydro-anthracene 	-	-
9-ethyl-s-octahydro-anthracene 	-	-
s-octahydrophenanthrene 	-	-
9-methyl-s-octahydro-phenanthrene 	-	-
Octahydroanthracene-9-carboxylic acid 	-	-

Table I (Contd.)

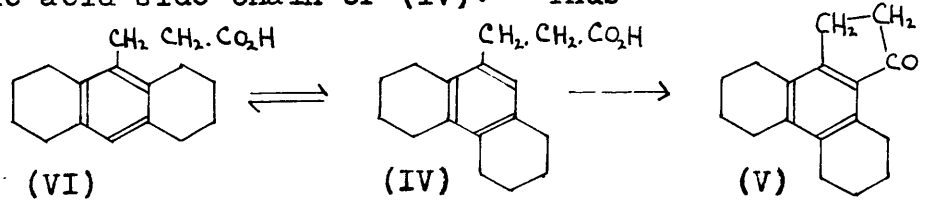
Compound Treated	% Isomerisation	Product
9-s-octahydroanthranyl-acetic acid 	-	-
γ-(9-s-octahydroanthranyl)-butyric acid 	100%	Keto-dodecahydrotriphenylene 

80° gave a complex mixture of products containing about 40% of s-octahydrophenanthrene, as well as 40% of starting material. This reaction was shown to be reversible by the fact that similar treatment of s-octahydrophenanthrene gave a mixture containing nearly the same proportions of these two constituents[61].



(VII) (VIII)

Again, s-octahydroanthracene-9-sulphonic acid was found to rearrange to s-octahydrophenanthrene-9-sulphonic acid, in yields as high as 85%, when heated in presence of sulphuric acid*[62]. Now, as a condensing agent, hydrofluoric acid is related to aluminium chloride and to sulphuric acid. It thus seemed possible that hydrofluoric acid also could bring about interconversion of the two hydrocarbons (VII) and (VIII), and that the formation of the ketone (V) from (VI) in presence of this reagent took place by rearrangement of the octahydroanthracene nucleus of (VI) with consequent formation of (IV), followed by the normal cyclisation of the propionic acid side chain of (IV). Thus



(VI) (IV) (V)

*This is a special case of the Jacobsen rearrangement of polyalkylbenzenes and is not related to the aluminium chloride catalysed rearrangement.

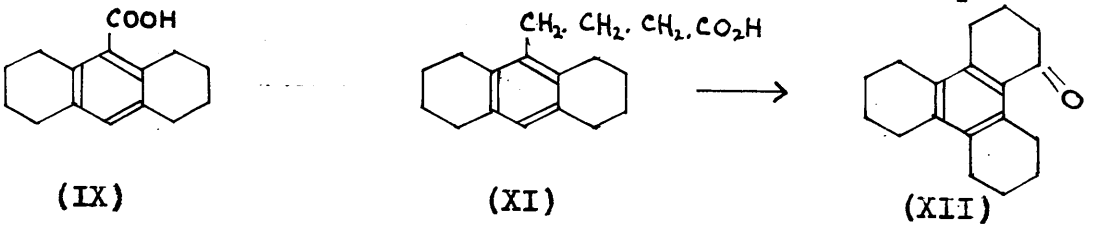
Even the formation of an equilibrium mixture of the two acids containing only a very small proportion of (IV) would be sufficient to bring about the complete conversion of (VI) to (V), for the equilibrium would be continually displaced by removal of (IV) by cyclisation, so that ultimately all of (VI) would be converted to (V).

This view was seen to be untenable however, by the observation that s-octahydroanthracene, 9-methyl-s-octahydroanthracene, and 9-ethyl-s-octahydroanthracene, were completely unchanged when treated with hydrofluoric acid under conditions which had resulted in conversion of (VI) to (V). s-Octahydrophenanthrene and 9-methyl-s-octahydrophenanthrene were also unaffected, thus eliminating any possibility that there was, in fact, an equilibrium between the two sets of derivatives which escaped detection in the previous experiments because it lay far over on the side of the octahydroanthracene compounds. These results show clearly that there is no tendency for interconversion of s-octahydroanthracene and s-octahydrophenanthrene, or their 9-alkyl-derivatives, in presence of hydrofluoric acid. This is in harmony with the findings of Calcott, Tinker and Weinmayr[63] that migration of alkyl groups attached to benzene rings does not occur in presence of hydrofluoric

acid at ordinary temperatures*. The fact that s-octahydroanthracene itself does not rearrange under these conditions makes it extremely unlikely that such a process is the initial step in the conversion of (VI) to (V).

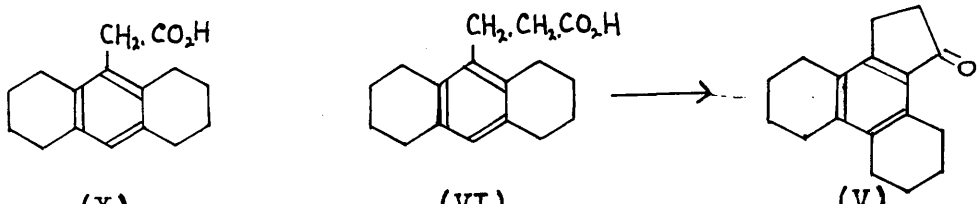
It seemed at this stage that the presence of the propionic acid residue in (VI) must somehow be concerned in the isomerisation of the octahydroanthracene nucleus. A clue to the actual mechanism involved in the rearrangement was obtained when the investigation was extended to derivatives analogous to (VI), but differing from it in the length of the acid side-chain.

s-Octahydroanthracene-9-carboxylic acid (IX) and 9-s-octahydroanthranylacetic acid (X) were both unaffected by hydrofluoric acid, showing that the presence of an acid group in the 9-position of the nucleus was not in itself a sufficient structural condition for isomerisation to take place. Rearrangement was again observed in the case of γ-(9-s-octahydroanthranyl)butyric acid (XI), however. This compound was almost quantitatively converted to the known[76] 4-keto-dodecahydrotriphenylene (XII) when treated with hydrofluoric acid for several hours at room temperature.



(IX) (XI) (XII)

*s-octahydroanthracene can be regarded as a 1:2:4:5-tetraalkylbenzene.

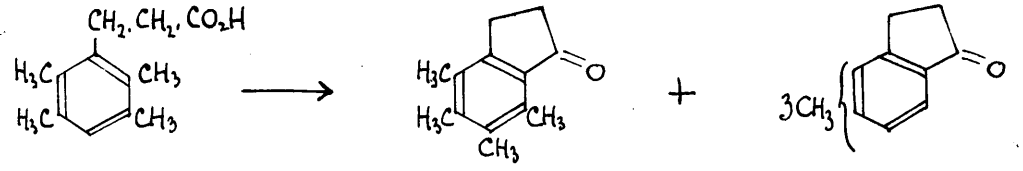


(X) (VI) (V)

This result is significant when considered in conjunction with the conversion of (VI) to (V). It is seen that the only two derivatives of s-octahydroanthracene in which isomerisation has been observed to take place, are characterised by the presence, in the 9-position, of an aliphatic acid residue of such a length that cyclisation into the ortho position gives a stable five- or six-membered-ring ketone. This strongly suggests that cyclisation is an integral part of the rearrangement mechanism in these compounds. The driving force in the rearrangements is the cyclisation of the acid side chains into the ortho position, with consequent displacement of the methylene group already present there. The rearrangement is completed by recombination of the displaced group at the remaining free position in the benzene ring.

One might, therefore, expect that acids derived from (VI) and (XI) by replacement of the reduced rings by alkyl groups would also undergo cyclisation, with displacement of an alkyl group, when treated with hydrofluoric acid. In conformity with this, it has been found by Mr. R.R. Aitken B.Sc. in this Department (private communication) that β-durenylpropionic acid (XIII) gives the indanones (XIV) and (XV)

in presence of this reagent. Durene itself was unaffected under the same conditions.



(XIII) (XIV) (XV)

These three reactions represent the first recorded examples of a new type of alkylbenzene isomerisation*, brought about by the displacement of an alkyl group by cyclisation of an acid side-chain into that position of the benzene ring.

In the absence of any information regarding the mechanism of intramolecular acylations with hydrofluoric acid, it is difficult to understand how displacement of the alkyl groups takes place, and it is not possible to postulate a mechanism for it with any degree of certainty. In Friedel-Crafts acylations with aluminium chloride and the acyl halide R.COCl, the complex $[RCO.]^{+}[AlCl_4]^{-}$ is regarded as an active intermediate(64). It may be that a complex of a similar type is present in acylations with hydrofluoric acid, and that in say, the conversion of (VI) to (V), the cation (XVI) is an intermediate.

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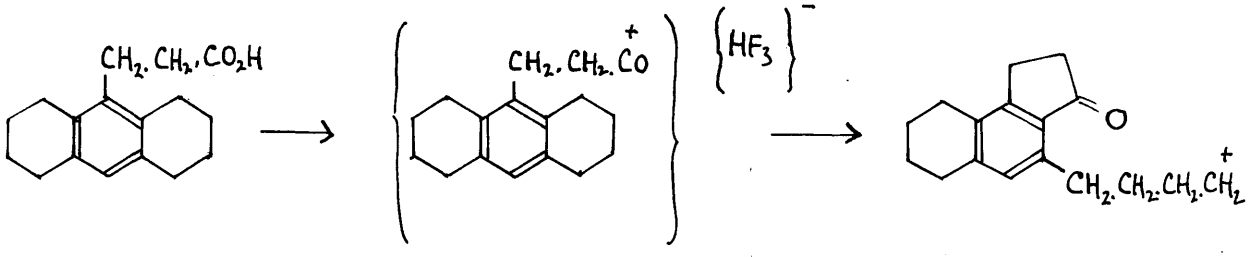
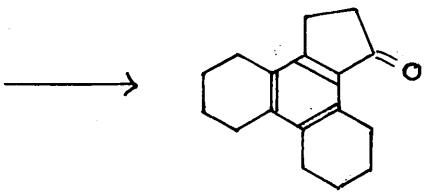
* s-Octahydroanthracene can be regarded as a 1:2:4:5-tetralkylbenzene.



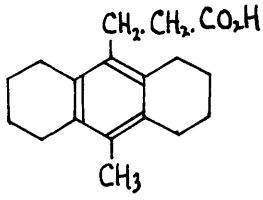
(VI) (XVI) (XVII)



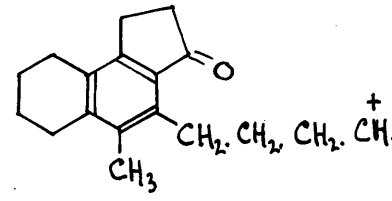
(V)

Rearrangement might then take place by attack of the terminal positively charged carbon atom of (XVI) at the ortho position, with consequent opening of the reduced ring to form the intermediate (XVII), from which (V) would be obtained by cyclisation of the cationic carbon atom into the free position in the benzene ring.

If the carbonium ion (XVII) is indeed produced during conversion of (VI) to (V), then it is conceivable that the ketone (V) might also be obtained from β-(10-methyl-s-octahydro-9-anthranyl)propionic acid (XVIII) on treatment with hydrofluoric acid. One might expect the cationic side chain of the corresponding intermediate (XIX) to cyclise and displace the methyl group to some extent.



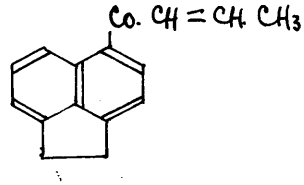
(XVIII)



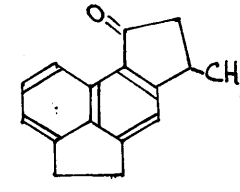
(XIX)

However, on treatment of (XVIII) with hydrofluoric acid under the usual conditions, an oily mixture of ketonic products was obtained, from which no pure constituent could be isolated either as such or in the form of a solid derivative (see Experimental).

Hydrofluoric acid is now widely used in industry as a reagent for alkylation of aromatic hydrocarbons with olefines[63,65], and at least one example has been recorded of its use in bringing about intramolecular alkylation in an aromatic compound with an unsaturated side chain. 3-Crotonyl-acenaphthene (XX) was readily converted to the ketone (XXI) when treated with the reagent at ordinary temperatures[88].



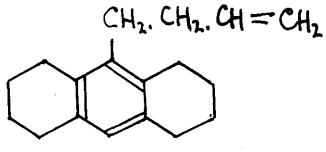
(XX)



(XXI)

It seemed of some interest to determine if the tendency for cyclisation of a suitable unsaturated side chain in the 9-position of s-octahydroanthracene would lead to rearrangement

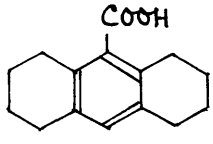
of the nucleus when the compound was treated with hydrofluoric acid. It appears that this is not so, however, for 4-(9-s-octahydroanthranyl)-butene-1 (XXI) was unaffected by the reagent. This is in agreement with the hypothesis that cyclisation of the acid side-chains is concerned in the rearrangements of the octahydroanthracene nucleus noted above.



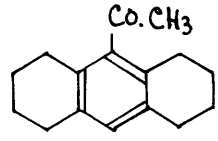
(XXII)

Most of the compounds used in this investigation have not previously been described, and in their preparation from the parent hydrocarbons, several other new derivatives of these were employed as intermediates.

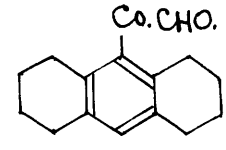
9-Ethyl-s-octahydroanthracene and octahydroanthracene-9-carboxylic acid (IX) were both prepared from the 9-acetyl compound (XXII). This was itself obtained from octahydroanthracene and acetic anhydride, as described by Arnold and Barnes[66].



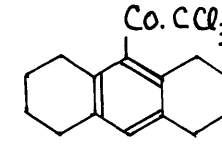
(IX)



(XXIII)



(XXIV)



(XXV)

The 9-carboxylic acid was obtained by the method described by Arnold and Rondesvedt[67]. Oxidation of the acetyl compound with selenium dioxide gave the glyoxal hydrate

(XXIV) which was converted to the required acid (IX) by further oxidation with alkaline hydrogen peroxide. This two stage process must be adopted in the present case, because the usual method of oxidising methylketones to carboxylic acids, with alkaline hypochlorite, leads only to the trichloroketone (XXV) when applied to 9-acetyloctahydroanthracene. Arnold and Barnes[66] have ascribed this to steric hindrance of the 9-position in s-octahydroanthracene. This explanation is supported by the observation in the present work that the acid (IX) cannot be esterified by the Fischer-Speier method, a fact which recalls the behaviour of the hindered 2:6-dimethylbenzoic acid[69]. Further, repeated attempts to prepare the hydrazide of (IX) by action of hydrazine hydrate on the methyl ester* have been completely unsuccessful. An attempt to prepare the acid chloride also resulted in failure, the acid being recovered unchanged after three hours boiling with thionyl chloride. There can thus be little doubt that the 9-position in s-octahydroanthracene is hindered to quite a considerable degree.

Clemmensen reduction of 9-acetyloctahydroanthracene (XXIII) yielded the 9-ethyl compound, the structure of which was confirmed by dehydrogenation to 9-ethylanthracene with

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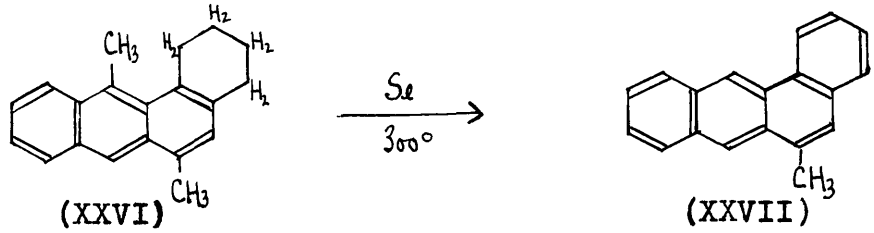
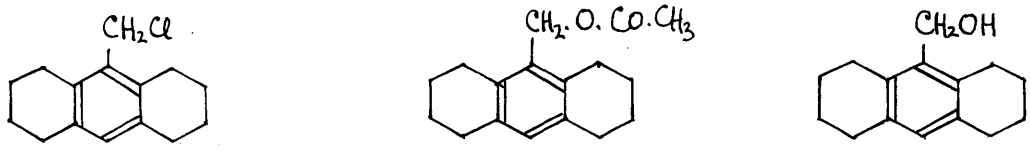
* Arnold and Rondestvedt[67] prepared this by treatment of the acid with diazomethane.

palladium black at 300°. A small amount of anthracene was also produced in this reaction, by loss of the meso alkyl group. Loss of alkyl groups from the meso positions of the anthracene nucleus frequently takes place at high temperatures. For example, Fieser and Jones[70] obtained 4-methyl-1:2-benzanthracene (XXVII) by selenium dehydrogenation of the hydro-compound (XXVI) at 300°.



(XXVI) (XXVII)



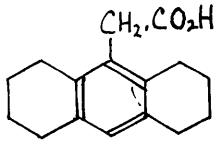
(XXVIII) (XXIX) (XXX)

9-Methyl-s-octahydroanthracene was readily obtained by reduction of the 9-chloromethyl-compound (XXVIII) with palladium black in alcohol. The chloromethyl compound, in turn, was prepared by chloromethylation of s-octahydroanthracene as described by Dr. Schoental[60]. The high reactivity of the chlorine atom in this compound is shown by the fact that an attempt to prepare the corresponding aldehyde from it, by boiling for thirty seconds with hexammine in acetic acid, yielded only 9-acetoxymethyl-s-

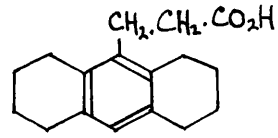
octahydroanthracene (XXIX), identical with the compound obtained from (XXVIII) by reaction with potassium acetate. A similar difficulty was encountered by Badger and Cook[72] in an attempt to convert 10-chloromethyl-1:2-benzanthracene to the corresponding aldehyde, although Hewett[73] has prepared 1-bromo-2-naphthaldehyde from 1-bromo-2-bromomethylnaphthalene by this method. Hydrolysis of the acetoxy-compound gave 9-hydroxymethyl-s-octahydroanthracene (XXX), which was readily converted to the chloromethyl-compound (XXVIII) by action of hydrogen chloride in benzene. The chloromethyl-compound was used as starting material for the preparation of several derivatives of the parent hydrocarbon.

By condensation of allyl bromide with the Grignard reagent from 9-chloromethyl-s-octahydroanthracene, 4-(9-s-octahydroanthranyl)-butene-1 (XXII) was obtained. Treatment of (XXVIII) with aqueous alcoholic potassium cyanide yielded 9-cyanomethyl-s-octahydroanthracene in good yield. Hydrolysis of this with sulphuric acid in acetic acid[74] gave 9-s-octahydroanthranylacetic acid (X). By the malonic ester synthesis, the chloromethyl-compound (XXVIII) was converted to β-(9-s-octahydroanthranyl)propionic acid (VI), as described by Dr. Schoental[60]. Lengthening of the acid side chain of this, by the Arndt-Eistert reaction[75],

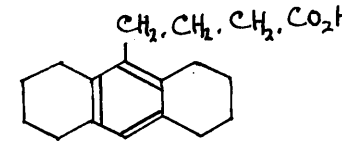
gave γ-(9-s-octahydroanthranyl)butyric acid (XI), in good yield.



(X)



(VI)



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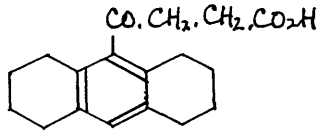
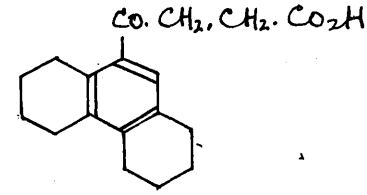
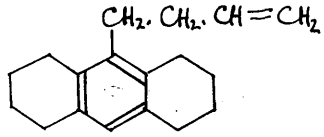


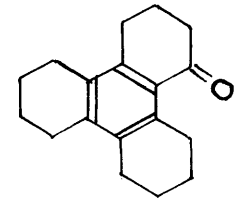
(XXXI)



(XXXII)



(XXII)



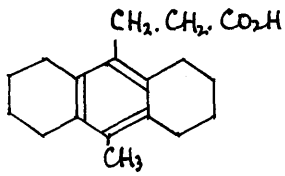
(XII)

A striking example of rearrangement of the s-octahydroanthracene nucleus, in presence of aluminium chloride, was encountered in an attempt to prepare the butyric acid (XI) by way of the keto-acid (XXXI). It was anticipated that this keto-acid could be obtained by Friedel-Crafts condensation of s-octahydroanthracene and succinic anhydride. When the condensation was effected with aluminium chloride in cold carbon disulphide, however, the only product isolated from the reaction was

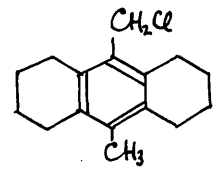
β-(9-s-octahydrophenanthroyl)propionic acid (XXXII), formed by rearrangement of the octahydroanthracene nucleus to an octahydrophenanthrene one. The structure of the product was established by comparison with an authentic specimen of (XXXII), prepared from s-octahydrophenanthrene and succinic anhydride as described by Van de Kamp, Burger and Mossetig[76]. Reduction by the Clemmensen method gave γ-(9-s-octahydrophenanthryl)butyric acid, which was almost quantitatively converted to 4-keto-dodecahydrotriphenylene (XII) by treatment with hydrofluoric acid. Van de Kamp, Burger and Mosettig effected this cyclisation with sulphuric acid[76]. The formation of octahydrophenanthroylpropionic acid (XXXII) from s-octahydroanthracene and succinic anhydride under these conditions, and the apparent absence of octahydroanthranoylpropionic acid from the reaction product, is very surprising. Octahydroanthracene itself gives an equilibrium mixture containing only 40% of octahydrophenanthrene when treated with aluminium chloride at 80°. It is, therefore, in sharp contrast to this that although the present reaction was effected at room temperature, the anthracene system appears to have been completely isomerised. When the condensation was carried out in tetrachlorethane solution, two acids were obtained. These were easily separated by crystallisation. The more

soluble product was identical with the acid obtained in carbon disulphide solution. The other is probably β-(9-s-octahydroanthranoyl)propionic acid (XXXI). The structure of this compound is based on that fact that it is isomeric, but not identical, with (XXXII), the only reasonable alternative. Under these conditions the yield of the octahydroanthranoyl acid (XXXI) was about twice that of the octahydrophenanthroyl acid (XXXII).

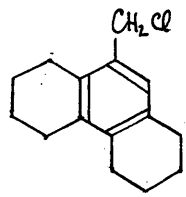
The starting material for the preparation of β-(10-methyl-s-octahydro-9-anthranyl)propionic acid (XVIII) was 9-chloromethyl-10-methyl-s-octahydroanthracene (XXXIII). This was itself obtained by chloromethylation of 9-methyl-s-octahydroanthracene with paraformaldehyde and hydrogen chloride in acetic acid. It was condensed with ethyl sodiomalonate in benzene and the resulting malonic ester hydrolised directly to the malonic acid. Decarboxylation of this gave the desired propionic acid.



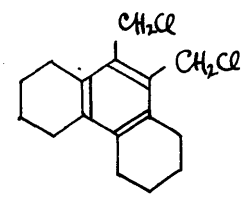
(XVIII)



(XXXIII)



(XXXIV)



(XXXV)

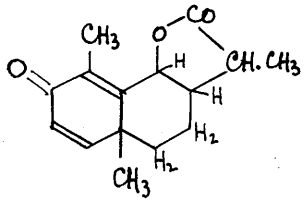
s-Octahydrophenanthrene was prepared by high pressure hydrogenation of phenanthrene over Raney nickel, essentially as described by Durland and Adkins[27]. Chloromethylation of this hydrocarbon with formalin and hydrogen chloride in acetic acid gave 9-chloromethyl-s-octahydrophenanthrene (XXXIV), as well as a small amount of 9:10-dichloromethyl-s-octahydrophenanthrene (XXXV). By catalytic reduction these compounds were converted to 9-methyl-s-octahydrophenanthrene and 9:10-dimethyl-s-octahydrophenanthrene respectively. The structure of the former compound was confirmed by dehydrogenation to 9-methylphenanthrene with palladium black at 280°.

Part III.

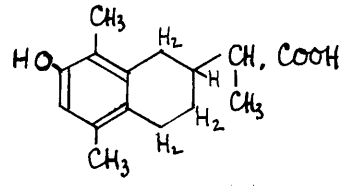
Attempted Synthesis of Santonin.

Santonin occurs in the flower heads of Artemesia maritima, which grows widely in the salt marshes of Russia and elsewhere. These flowers, under the name of "worm-seed", have been used since early times for their anthelmintic action, but have now been replaced by their active principle, santonin, which was first isolated in 1830.

Santonin is a sesqui-terpene-keto-lactone, and the structure (I) was assigned to it by Clemo, Haworth and Walton[68] on the basis of its degradation products. Further evidence for this structure was furnished by these authors by the synthesis of santonous acid[68] (II), a reduction product of santonin, and of dl-desmotroposantonin[71] (III) which is obtained from santonin by the action of mineral acids. The naturally occurring substance is laevo-rotatory.



(I)



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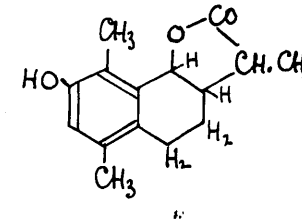


(III)

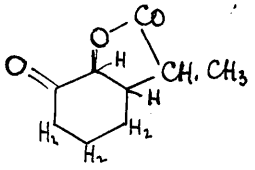
A synthesis of santonin itself was published in 1943 by Paranjape, Phalnikar, Bhide and Nargund[77], and considerable interest was aroused when, in a later paper[78], these authors reported that the product obtained by this

synthetic method was optically active, having a rotation which indicated the presence of 93% of the natural l-form in the synthetic material. If this is true, it represents the first reported achievement of a total asymmetric synthesis, for at no stage of the synthesis was an asymmetric influence present. In the same paper, these authors also claimed to have determined that the optical activity developed during methylation of a formylcyclohexanone derivative, and they even stated that the crude product obtained by them by methylation of optically inactive formylcyclohexanone itself had the large specific rotation of $[\alpha]_D$ = -26.2° in chloroform. This startling claim could not be confirmed, however, either by O'Gorman[79] in America or by Cornforth, Cornforth and Dewar[80] in this country. These authors found that methylation of formylcyclohexanone gave a product which was completely devoid of optical activity. These observations threw considerable doubt on the claim of the Indian workers that their synthetic methylformylcyclohexanone and their synthetic santonin were indeed optically active.

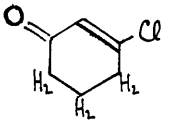
The present work was concerned with an attempt to repeat the santonin synthesis described by the Indian workers. It seemed desirable to try to confirm the claim of these authors that the synthetic material was optically

active, although in view of the findings of O'Gorman and Cornforth et al. outlined above, it was expected that it would show no activity. It was considered that the synthesis might afford a means of obtaining racemic santonin*, a quantity of which was required for another purpose.

An intermediate in the synthesis described by the Indian workers is the lactone of α-(2-hydroxy-3-ketocyclohexyl)-propionic acid (IV). This was obtained by them by condensation of 3-chloro-Δ^2-cyclohexenone (V) with ethyl sodiomethylmalonate, followed by treatment of the crude condensation product (VII or VIII presumably) with 6$\bar{N}$ sulphuric acid in 50% aqueous alcohol, when, it was stated, cyclisation took place to give the desired lactone.



(IV)



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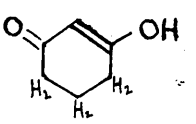

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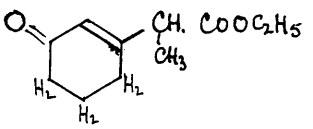

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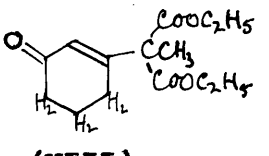

(VIII)

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*It has been found in this Department and elsewhere (unpublished) that racemic santonin cannot be obtained from the naturally occurring laevo-rotatory compound.

The chloro-compound (V) was obtained from dihydroresorcinol (VI) by treatment with phosphorus trichloride, as described by Crossley and Haas[82]. In the present work, (VI) was prepared by catalytic reduction of resorcinol in alkaline solution with Raney nickel, as described by Morrison[83]. Very good yields of a pure product were obtained by this method.

Condensation of the chloro-compound (V) with ethyl sodiomethylmalonate, in benzene, as described by the Indian workers, gave ethyl Δ^2-cyclohexen-1-one-3-methylmalonate* (VIII). This compound was never obtained in a perfectly pure condition, however, because of the formation of difficultly separable mixtures (with presumably (VII)), but it was characterised by means of its well crystalline semicarbazone. Condensation in alcoholic solution gave a different product. In addition to a small amount of dihydroresorcinol (VI), there was obtained ethyl α-(Δ^2-cyclohexen-1-one-3)propionate (VII), formed by loss of a carbethoxyl group. Again, the product could not be obtained in a pure condition, and was shown to consist largely of (VII) by analysis of the semicarbazone.

Elimination of carbethoxyl in this manner from a compound containing a gem dicarbethoxyl group is not unknown.

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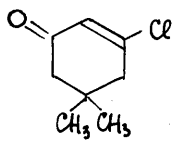
*The Indian workers did not describe the product obtained by them at this stage.

Thus, Crossley and Gilling[84] found that condensation of 5-chloro-1:1-dimethyl- Δ^4-cyclohexen-3-one (IX) with ethyl malonate in alcohol, gave the acetic ester (X), and not the corresponding malonic ester. These examples are in harmony with the finding of Thorpe[85] that esters of the type (XI) react readily with cold alcoholic sodium ethoxide, eliminating ethyl carbonate, with formation of esters of the type (XII)



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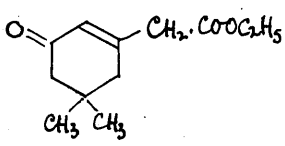

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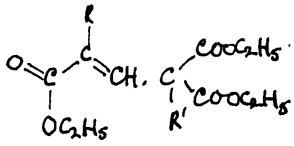

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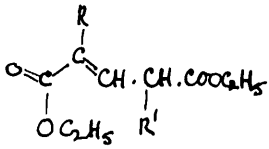

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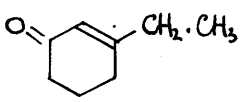

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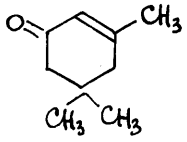


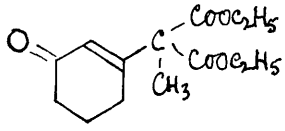
(XIV)

In contrast to the experience of the Indian workers, all attempts in the present work to convert the esters (VII) and (VIII) to the lactone (IV), were unsuccessful. Treatment with hot 6N sulphuric acid in 50% aqueous alcohol as they describe led, not to the lactone, but to the completely decarboxylated product 3-ethyl- Δ^2-cyclohexenone (XIII). Many attempts were made to effect this cyclisation under a variety of other experimental

conditions (cold or hot 20%, 40%, 80% sulphuric acid, hot 80% phosphoric acid), but in no case was there any evidence of the formation of lactonic or acidic material. Decarboxylation always took place to a greater or less extent. The decarboxylated product was even obtained in an attempt to prepare the free acid from (VII) by treatment with cold, dilute potassium hydroxide.

A similar result was observed by Crossley and Gilling[84] during attempted hydrolysis of the analogous ester (X) with dilute alcoholic sodium hydroxide. Only the completely decarboxylated product, isophorone (XIV), was obtained.

It is not surprising that these esters undergo decarboxylation with such ease, for they are, in effect, β-keto-esters. The ethylenic double bond conjugated with



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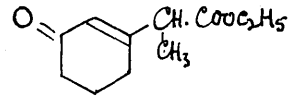

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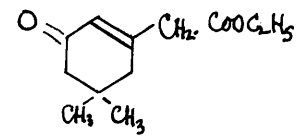


(X)

the keto group in the ring, transfers the effect of this group to the carbon atom in the β position to the carbethoxyl groups. The ready decarboxylation of β-keto esters is well known. Thus benzoylacetic ester (XV) gives acetophenone when treated with dilute acid or alkali, by "ketonic hydrolysis". "Acid hydrolysis" with strong alkali

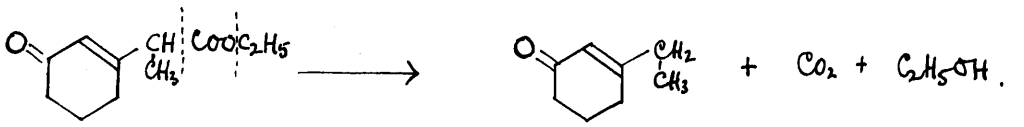
gives benzoic acid. Thus

$$Ph.CO.CH_2|COO|C_2H_5 \xrightarrow{\text{Ketonic hydrolysis}} Ph.COCH_3 + CO_2 + C_2H_5OH$$

(XV)

$$Ph.CO|CH_2.COO|C_2H_5 \xrightarrow{\text{Acid hydrolysis}} Ph.COOH + CH_3COOH + C_2H_5OH$$

Similarly in the present case, "ketonic hydrolysis" of the "acting" β-keto-esters (VII) and (VIII) during treatment with acid, leads to 3-ethyl- Δ^2-cyclohexenone (XIII)



(VII) (XIII)

The formation of dihydroresorcinol during the malonic ester condensation in presence of alcoholic sodium ethoxide can be interpreted as taking place by "acid hydrolysis" of the ester (VII).

While the present work was still in progress, a similar failure to obtain the lactone (IV) by the method described by the Indian workers, was reported by Clemo, Cocker and Hornsby[86]. These authors also obtained the decarboxylated product (XIII) in every case. In view of this, no further attempts were made to prepare the lactone by this method.

Experimental Section.

Experimental to Part I.

Chloromethylation of Phenanthrene.

A rapid stream of hydrogen chloride was passed for twelve hours into a stirred, boiling suspension of powdered phenanthrene (300 g.) in concentrated hydrochloric acid (750 cc.) and formalin (750 cc. of 40%). After cooling, the aqueous layer was decanted and the dark oil washed with water, and then twice with dilute sodium carbonate. The product was then dissolved in ether, filtered from some insoluble material, and thoroughly washed with dilute sodium carbonate, and then water. After drying for 48 hours over anhydrous potassium carbonate, the solvent was removed, and the oil distilled. There was a forerun of unchanged phenanthrene (110 g.), b.p. 170-190°/4 mm., and the main fraction (155 g.) was collected as a yellow oil, b.p. 190-210°/4 mm. On standing, crystals were deposited, which, after crystallisation from benzene/light petroleum and from alcohol, formed colourless needles of 9-chloromethylphenanthrene (XXVI), m.p. 100° (60 g.) (literature m.p. 101-101.5°). Its structure was confirmed by oxidation with sodium dichromate to 9-phenanthroic acid and phenanthraquinone, which were compared with authentic specimens. Hydrogenation of 9-chloromethylphenanthrene, in acetone, over palladium black, proceeded smoothly to give 9-methylphenanthrene,

m.p. 90-91° (literature m.p. 90-91°). The picrate formed orange-red needles from alcohol m.p. 153° (literature, 152-153°).

Evaporation of the benzene-light petroleum mother liquors gave a yellow oil, which was redistilled. The fraction b.p. 210°/4 mm. was collected and dissolved in benzene-light petroleum. After two days, the crystals which had separated were collected, washed with ether, and recrystallised from alcohol. 1-Chloromethylphenanthrene (XXVII) (5 g.) formed colourless lustrous plates, m.p. 89-90°. (Found: C, 79.5; H, 4.8. $C_{15}H_{11}Cl$ requires C, 79.4; H, 4.9%). Its picrate formed fine yellow needles in alcohol, m.p. 110-111°. (Found: C, 55.5; H, 3.0; N, 9.4. $C_{15}H_{11}Cl.C_6H_3O_7N_3$ requires C, 55.3; H, 3.1; N, 9.3%). Reduction of 1-chloromethylphenanthrene with hydrogen and palladium proceeded rapidly to give 1-methylphenanthrene, m.p. 121°. (Found: C, 93.6; H, 6.2. Calc. for $C_{15}H_{12}$, C, 93.8; H, 6.2%) (literature, 123°, corr.). The picrate formed orange yellow needles from alcohol, m.p. 136°. (Found: N, 10.2. Calc. for $C_{15}H_{12}.C_6H_3O_7N_3$, N, 10.0%) (literature m.p. 139°, corr.).

β-(9-Phenanthryl)propionic acid (XVI).

9-Chloromethylphenanthrene (50 g.) was added to a solution prepared from sodium (5.4 g.), ethyl malonate (44 cc.), and ethanol (180 cc.); the mixture was refluxed for two hours. Potassium hydroxide (60 g.) in water (150 cc.) was then added and boiling continued for a further three hours. The acidic product was isolated in the usual way, dried, and decarboxylated by heating at 190°. The residue was extracted with sodium carbonate and on crystallisation of the recovered acid from acetic acid some sparingly soluble material was isolated. This product, evidently αα'-di-(9-phenanthryl)isobutyric acid (XXIX) (6 g.), crystallised from xylene in glistening colourless plates, m.p. 224°. (Found: C, 87.4; H, 5.4; M, Rast method, 430. $C_{32}H_{24}O_2$ requires C, 87.3; H, 5.5; M, 440). The methyl ester, prepared with diazomethane in acetone-ether, crystallised from methanol-ethyl acetate in fluffy colourless needles, m.p. 165-166°. (Found: C, 87.3; H, 6.0. $C_{33}H_{26}O_2$ requires C, 87.2; H, 5.7%). The main bulk of the acidic material, 9-phenanthrylpropionic acid, was crystallised from benzene, and formed colourless needles (40 g.), m.p. 174° (literature, m.p. 173-174°). The methyl ester formed colourless needles, m.p. 71-72° (literature, m.p. 72-73°).

In one run in which crude uncrystallised chloromethylphenanthrene was used, the propionic acid was found to

be impure even after the removal of the sparingly soluble diphenanthrylisobutyric acid. By fractional crystallisation a small quantity of β-(1-phenanthryl)propionic acid (XXVIII) was obtained. It formed colourless crystals, m.p. 186-188°. (Bachmann and Kloetzel[25] give m.p. 189-189.5°). (Found: C, 81.6; H, 5.4. Calc. for $C_{17}H_{14}O_2$, C, 81.7; H, 5.6%). The methyl ester, prepared from the acid with diazomethane, was shown by mixed m.p. to be identical with an authentic specimen kindly supplied by Professor W.E. Bachmann.

β-(9-s-Octahydrophenanthryl)propionic acid (XXI).

The above 9-phenanthrylpropionic acid (6 g.), in dioxan, was reduced by treatment for five hours with hydrogen at 180-190° and 170 atmospheres, in the presence of copper chromite (4 g.). β-(9-s-Octahydrophenanthryl)-propionic acid (5 g.) was crystallised from benzene and from acetic acid, and formed small colourless needles, m.p. 179°. (Found: C, 79.6; H, 8.4. $C_{17}H_{22}O_2$ requires C, 79.2; H, 8.5%). The methyl ester, prepared in ether with diazomethane, formed fine colourless needles, m.p. 40-41° from methanol. (Found: C, 79.8; H, 8.8. $C_{18}H_{24}O_2$ requires C, 79.5; H, 8.8%).

1'-Keto-9:10-cyclopenteno-s-octahydrophenanthrene (XXXIII).

The above octahydrophenanthrylpropionic acid (1 g.) was treated with thionyl chloride (5 c.c.), and warmed gently (50-60°) for one hour, by which time evolution of hydrogen chloride had ceased. The excess thionyl chloride was then removed at 50° under reduced pressure, two small amounts of benzene being added successively and removed in the same way. The solid acid chloride, dissolved in nitrobenzene (3 c.c.), was cooled in ice and added to an ice cold solution of aluminium chloride (1 g.) in nitrobenzene (10 cc.), and the mixture left overnight at room temperature. It was then hydrolised with hydrochloric acid, and nitrobenzene removed in steam. 1'-Keto-9:10-cyclopenteno-s-octahydrophenanthrene formed white needles in alcohol, m.p. 195°. (Found: C, 84.8; H, 8.3. $C_{17}H_{20}O$ requires C, 85.0; H, 8.3%.)

9:10-Cyclopenteno-s-octahydrophenanthrene (XXIV).

The above ketone (0.8 g.) was added to a mixture of amalgamated zinc (8 g.), concentrated hydrochloric acid (40 cc.), glacial acetic acid (10 cc.) and toluene (10 cc.). The mixture was boiled vigorously for 24 hours, a further quantity (10 cc.) of hydrochloric acid being added after 12 hours. The cooled liquid was extracted with benzene, and the extract washed. The solid product (0.7 g.) was sublimed

at 170°/14 mm. and crystallised from ethyl alcohol, from which 9:10-cyclopenteno-s-octahydrophenanthrene separated in long white needles, m.p. 156-158°, after sintering. Repeated crystallisation from various solvents, and passage through a column of alumina did not result in a sharper definition of the m.p. (Found: C, 90.3; H, 9.6. $C_{17}H_{22}$ requires C, 90.3; H, 9.7%).

Dehydrogenation of the above cyclopenteno-octahydrophenanthrene (0.1 g.), with palladium black (0.02 g.) at 290-300° for 30 minutes proceeded smoothly. After sublimation and crystallisation from ethyl alcohol, 9:10-cyclopentenophenanthrene (XXV) formed long white needles m.p. 150° (literature, m.p. 154°; 149-150°); the picrate had m.p. 161° (literature, m.p. 161.5-162°). Both compounds were identified by comparison with authentic specimens prepared as described by Weizmann, Bergmann and Berlin[26].

γ-(1- and 2-Naphthoyl)butyric acids (XLI and XLII)
(After Bachmann and Struve[38]).

To a cold solution of aluminium chloride (410 g.) in dry nitrobenzene (1100 cc.) was added a mixture of naphthalene (300 g.) and succinic anhydride (150 g.). After standing for twelve hours, the dark liquid was

hydrolised by addition of ice and hydrochloric acid, and the nitrobenzene removed in steam. The solid residue was extracted with hot sodium carbonate solution. The recovered acid weighed 280 g. after drying. This mixture of α and β-naphthoylpropionic acids was reduced by refluxing for 24 hours with amalgamated zinc (600 g.), hydrochloric acid (1 l.), acetic acid (50 cc.) and toluene (600 cc.). The toluene layer was separated from the cooled liquid, washed with water, and the dark oil recovered from it distilled. The product was collected as a colourless oil (220 g.), b.p. 210°/3 mm.

1- and 4-Keto-1:2:3:4-tetrahydrophenanthrene (XLIII and XLIV). (After Bachmann and Struve[38]).

The above mixed acids (110 g.), in ether (600 cc.), were treated at room temperature with pyridine (5 c.c.) and thionyl chloride (120 cc.). After one hour ether and excess thionyl chloride were removed at 60° under reduced pressure. The oily acid chloride obtained was dissolved in dry benzene (600 cc.), cooled in ice, and stannic chloride (90 cc.) added to the cold solution. The mixture was left in ice for 15 minutes, then hydrolised with ice and hydrochloric acid. The benzene layer was separated and washed, and the product distilled as a yellow oil (67 g.), b.p. 190°/1 mm.

1:2:3:4-Tetrahydrophenanthrene (XXVIII).

(Bachmann and Struve[38]).

The above mixture of ketotetrahydrophenanthrenes (50 g.), amalgamated zinc (200 g.), hydrochloric acid (300 cc.), acetic acid (300 cc.) and toluene (200 cc.), were refluxed for 24 hours. Additional hydrochloric acid (300 cc. in all) was added during this time. The product was recovered from the separated, washed and dried toluene layer, and distilled as a colourless oil (35 g.), b.p. 136-140°/0.5 mm. It crystallised from alcohol in colourless flat plates, m.p. 30° (literature, 32.5-33.5°). The picrate formed fine yellow needles from alcohol, m.p. 110° (literature, 111°).

9-Chloromethyl-1:2:3:4-tetrahydrophenanthrene (XLV)

(After Bachmann and Cronyn[37]).

1:2:3:4-Tetrahydrophenanthrene (9 g.), paraformaldehyde (2.8 g.), acetic acid (8 cc.), concentrated hydrochloric acid (10 cc.) and phosphoric acid (4 cc.) were stirred vigorously and heated to 80-85° for 6 hours. After cooling, the diluted liquid was extracted with ether. The oil recovered from the washed and dried extract was distilled. There was a forerun of unchanged hydrocarbon, and the chloromethyl-compound was collected as a colourless oil (4.7 g.) at 184°/1 mm. It formed colourless needles in alcohol, m.p. 60° (literature, 60.5-61°).

β-(1:2:3:4-Tetrahydro-9-phenanthryl)propionic acid (XXX)

(Modified Bachmann and Cronyn[37]).

The above chloromethyl compound (11 g.), in benzene (30 cc.), was added to a solution prepared from sodium (1.8 g.), ethyl alcohol (20 cc.), benzene (25 cc.) and ethyl malonate (18 cc.). After the mixture had been refluxed for twelve hours, most of the benzene was removed, and hydrolysis effected with sodium hydroxide (30 g.) in aqueous alcohol. The malonic acid thus obtained was decarboxylated by heating to 190° for a few minutes, yielding β-(1:2:3:4-tetrahydro-9-phenanthryl)propionic acid (10 g.) which formed colourless flat needles in dilute acetic acid, m.p. 165-168° (literature, 168-169°).

Cyclisation of β-(1:2:3:4-tetrahydro-9-phenanthryl)propionic acid.

(a) With hydrofluoric acid. The above propionic acid (0.6 g.) was left in contact with anhydrous hydrofluoric acid for 12 hours at room temperature. The product was dissolved in benzene, and the solution washed with dilute sodium carbonate. No acid was recovered from these washings. The residue remaining on removal of benzene solidified on standing. Crystallisation from ethyl alcohol gave long soft colourless needles of 3'-keto-9:10-cyclopenteno-1:2:3:4-tetrahydrophenanthrene (XLVI) (0.4 g.), m.p. 179°. (Found: C, 86.5; H, 6.9. $C_{17}H_{16}O$ requires C, 86.4; H, 6.8%).

(b) With stannic chloride. The propionic acid (0.5 g.), in dry benzene (10 cc.), was treated with phosphorus pentachloride (0.4 g.). After standing one hour the mixture was warmed on the water bath for five minutes to complete the reaction. The solution of the acid chloride was cooled in ice, and an ice-cold solution of stannic chloride (1 cc.) in benzene (10 cc.) was added. After one hour in ice, the dark red complex was decomposed with ice and hydrochloric acid. The washed (sodium carbonate) and dried benzene solution was concentrated and passed through a column of alumina. Only one product was isolated from the eluate, and this formed colourless needles (0.3 g.) in alcohol, m.p. 177°, not reduced when mixed with the product obtained with hydrofluoric acid.

(c) With aluminium chloride. A mixture of the propionic acid (0.5 g.) and thionyl chloride (2 cc.) in ether, was left at room temperature for 2 hours. Ether and excess thionyl chloride were removed by warming under reduced pressure. The resulting acid chloride in nitrobenzene (5 cc.) was added to an ice-cold suspension of aluminium chloride (1 g.) in nitrobenzene (5 cc.). The mixture was left at room temperature for 24 hours and then worked up in the usual way. The product (0.25 g.) formed colourless needles in alcohol, m.p. and mixed m.p. with the above ketone 177-179°.

9:10-Cyclopenteno-1:2:3:4-tetrahydrophenanthrene (XLVII)

The above keto-cyclopentenotetrahydrophenanthrene (0.7 g.) was refluxed with amalgamated zinc (7 g.), concentrated hydrochloric acid (40 cc.), glacial acetic acid (10 cc.) and toluene (10 cc.) for 24 hours. The toluene was separated, and the product obtained passed through a column of alumina in benzene. A colourless band with blue fluorescence in ultra-violet light was collected, and the solid product recovered from it crystallised from alcohol. 9:10-Cyclopenteno-1:2:3:4-tetrahydrophenanthrene formed colourless needles (0.4 g.), m.p. 65-66°.
(Found: C, 91.9; H, 8.1. $C_{17}H_{18}$ requires C, 91.9; H, 8.1%).

Dehydrogenation of this substance (0.1 g.), with palladium black (0.02 g.) at 290-300° in an atmosphere of carbon dioxide, proceeded smoothly. After sublimation and crystallisation from ethyl alcohol, 9:10-cyclopentenophenanthrene (XXV) formed long white needles, m.p. 149° (literature, 154°; 149-150°). The m.p. was not reduced when the product was mixed with an authentic specimen of 9:10-cyclopentenophenanthrene.

1-Chloromethyl-2-methoxynaphthalene (LV).

The procedure adopted was a slight modification of that of Cook, Downer and Hornung[41].

Hydrogen chloride was passed into an ice-cold suspension of paraformaldehyde (18 g.) in glacial acetic acid (250 cc.) until a clear solution was obtained. A suspension of 2-methoxynaphthalene (45 g.) in glacial acetic acid (400 cc.) was then added, with shaking. Crystalline material soon began to separate and after two hours at room temperature the solid was collected and washed with cold water. Crystallisation from benzene/light-petroleum gave 1-chloromethyl-2-methoxynaphthalene (40 g.) as colourless rhombs, m.p. 117-120° decomp. After further crystallisation it had m.p. 122-123° decomp. (literature, 120° decomp.).

Ethyl (2-methoxynaphthyl-1-methyl) malonate (LVI).

A mixture of dry benzene (50 cc.), absolute alcohol (20 cc.), sodium (1.4 g.) and ethyl malonate (10 g.) was refluxed for one hour, when all the sodium had dissolved. A solution of 1-chloromethyl-2-methoxynaphthalene (10 g.) in benzene (15 cc.) was then added, and refluxing continued for three hours. The pale yellow solution was then diluted with water. The oil recovered from the washed and dried benzene layer was distilled. After removal of excess ethyl malonate, the product was collected as a colourless oil at 200-205°/2-3 mm. (11.9 g.). This solidified readily when chilled and rubbed with methyl alcohol. Crystallisation from ethyl

alcohol gave ethyl (2-methoxynaphthyl-1-methyl) malonate as colourless hexagonal plates, m.p. 56°. (Found: C, 69.3; H, 6.9. $C_{19}H_{22}O_5$ requires C, 69.1; H, 6.9%).

(2-Methoxynaphthyl-1-methyl) malonic acid.

The above ester (11 g.) was hydrolised with 10% aqueous alcoholic potassium hydroxide. The malonic acid (10 g.) was isolated in the usual way, and crystallised from water as white microcrystals, m.p. 174-175° decomp. (Found: C, 65.6; H, 4.6. $C_{15}H_{14}O_5$ requires C, 65.7; H, 5.1%).

β-(2-Methoxy-1-naphthyl)propionic acid (LVII).

The above malonic acid (9.5 g.) was decarboxylated by heating at 190° for a few minutes. The oily residue crystallised from dilute acetic acid (charcoal), and gave β-(2-methoxy-1-naphthyl)propionic acid as colourless flat needles, m.p. 131° (literature, 128°). (Found: C, 73.0; H, 6.0. Calc. for $C_{14}H_{14}O_3$, C, 73.0; H, 6.1%).

The overall yield of the propionic acid from the chloromethyl-compound was 69%. In a large scale run in which the malonic ester was not isolated but was directly hydrolised, the yield was 81%.

Cyclisation of β-(2-methoxy-1-naphthyl)propionic acid.

(a) With hydrofluoric acid. The propionic acid (1.5 g.) was left in contact with anhydrous hydrofluoric acid for

3½ hours at room temperature. The dark red liquid was poured on to ice and the yellow solid obtained extracted with hot sodium carbonate solution. No acid was recovered from this extract. The neutral solid was dissolved in benzene, and the yellow solution repeatedly extracted with portions of concentrated hydrochloric acid. These extracts were orange in colour, but no material was obtained on dilution with water. The benzene solution remained yellow in colour so was concentrated, diluted slightly with hexane, and this solution passed through a column of alumina. On elution with benzene a yellow band passed through and was collected. Evaporation gave a yellow oil which solidified when rubbed with petroleum. 1-Methoxyperinaphthan-7-one (L) crystallised from light petroleum in yellow plates (1.1 g. = 80%), m.p. 65°. (Found: C, 79.4; H, 5.7. $C_{14}H_{12}O_2$ requires C, 79.2; H, 5.7%).

Cyclisation of larger quantities of the acid by this method gave equally good yields of the ketone.

The oxime, prepared by the method of Cook and Lawrence[81] formed pale yellow needles in ethyl alcohol, m.p. 157-159° decomp. (Found: C, 73.8; H, 5.6; N, 6.0. $C_{14}H_{13}O_2N$ requires C, 74.0; H, 5.7; N, 6.1%).

The benzylidene derivative was prepared by treating a mixture of the ketone (0.5 g.) and benzaldehyde (1 g.) in ethyl alcohol (5 cc.) with a solution of potassium hydroxide

(1 g.) in ethyl alcohol (10 cc.). After 24 hours the solution was acidified with acetic acid and diluted with water. A red oil was recovered on extraction with benzene. This deposited solid (0.15 g.) in alcohol. Crystallisation from benzene/light petroleum gave orange red prisms, m.p.172-173°. (Found: C, 84.2; H, 5.7. $C_{21}H_{16}O_2$ requires C, 84.0; H, 5.4%).

(b) Stannic chloride method. A mixture of β-(2-methoxy-1-naphthyl)propionic acid (10 g.) and phosphorus pentachloride (8 g.), in dry sulphur free benzene (100 cc.), was kept at room temperature for one hour, and then heated on the steam bath for five minutes to complete the reaction. The solution was then cooled in ice water and a solution of stannic chloride (10 cc.) in pure dry benzene (100 cc.) added. After standing four hours at room temperature, the complex was hydrolised with ice and hydrochloric acid, and the benzene layer separated. After washing with alkali and concentrated hydrochloric acid (as described in (a) above), the product was obtained as a yellow oil which crystallised in light petroleum, forming yellow plates (8 g.) m.p. 65° both alone and when mixed with the product obtained as in (a). The identity of these products was confirmed by comparison of the oximes.

(c) Phosphoric oxide method. (Compare Barger and Starling[42]) β-(2-Methoxy-1-naphthyl)propionic acid (2 g.), in dry benzene (20 cc.), was treated with phosphoric oxide (10 g.) and the mixture heated on the water bath for two hours. After addition of ice the benzene layer was separated and washed with dilute sodium carbonate. Some starting material (1 g.) was recovered from the carbonate extract. On evaporation of the washed and dried benzene solution a dark oil was obtained, which deposited solid (0.11 g.) in benzene/light petroleum. Crytallisation from ethyl alcohol gave soft yellow needles of 1-methoxyperinaphthen-7-one (LXI), m.p. 142-143° (Barger and Starling[42] reported m.p. 135°). (Found: C, 79.9; H, 4.9. $C_{14}H_{10}O_2$ requires C, 80.0; H, 4.8%).

The oil remaining after removal of solid material was passed through a column of alumina in benzene. On elution with the same solvent several bands were obtained. A pale yellow band with bright yellow fluorescence in ultra-violet light was collected, and on removal of solvent gave perinaphthenone (LX) (10 mgs.). This formed yellow needles in petroleum ether, m.p. 150°. Mixed m.p. with an authentic specimen of perinaphthenone (m.p. 153°) was 150-152°. The substance was readily soluble in concentrated hydrochloric

acid. The other bands of the chromatogram yielded small amounts of uncrystallisable oils, and were not further examined.

1-Methoxy-7-(o-chlorophenyl)-perinaphthan-7-ol (LI).

1-Methoxyperinaphthan-7-one (12 g.) in dry sulphur free benzene (200 cc.) was slowly added, with constant stirring, to a Grignard solution prepared from magnesium (2.3 g.) and o-chlorobromobenzene (18 g.) in absolute ether (200 cc.). A yellow solid gradually separated. The mixture was left overnight and then refluxed for one hour. The complex was decomposed with ammonium chloride solution, and the separated ether-benzene layer washed with dilute sodium hydroxide until the washings were no longer red in colour. The oil remaining on removal of ether was steam distilled, and the ethereal solution of the residue washed, dried and evaporated. The oily residue deposited solid (5 g.) on trituration with petroleum ether. Crystallisation from methyl alcohol and from benzene/light petroleum gave colourless prisms of 1-methoxy-7-(o-chlorophenyl)-perinaphthan-7-ol, m.p. 151-152°. (Found: C, 74.1; H, 5.55; $-OCH_3$, 9.6. $C_{20}H_{17}O_2Cl$ requires C, 73.9; H, 5.24; $-OCH_3$, 9.6%).

4-(o-Chlorophenyl)-perinaphthan-7-one (LXIV).

A solution of the above carbinol (1 g.) and iodine (10 mgs.) in light petroleum (20 cc.) was refluxed for 30 minutes, then cooled and washed with dilute sodium thiosulphate solution and with water. 4-(o-Chlorophenyl)-perinaphthan-7-one was obtained on removal of solvent, and after crystallisation from ethyl alcohol formed pale yellow prisms (0.7 g.), m.p. 109-110°. (Found: C, 77.7; H, 4.5; $-OCH_3$, 0. $C_{19}H_{13}OCl$ requires C, 77.9; H, 4.4; $-OCH_3$, 0.0%). The same ketone was obtained in almost quantitative yield, when the carbinol (0.5 g.), in methanol (5 cc.) and benzene (1 cc.), was treated with a saturated solution of methanolic hydrogen chloride (1 cc.) for 24 hours. The 2:4-dinitrophenylhydrazone was crystallised from glacial acetic acid in soft deep red needles, m.p. 228° decomp. (Found: C, 63.2; H, 3.7. $C_{25}H_{17}O_4N_4Cl$ requires C, 63.5; H, 3.6%). The semicarbazone formed clusters of bright yellow needles in ethyl alcohol, sintering at 220° and melting with decomposition at 236°. (Found: C, 68.9; H, 4.8. $C_{20}H_{16}ON_3Cl$ requires C, 69.2; H, 4.6%).

The benzylidene derivative crystallised out when a mixture of the ketone (0.3 g.), benzaldehyde (1 g.), potassium hydroxide (1 g.) and ethyl alcohol (15 cc.) was left for 24 hours at room temperature. It was collected, washed with water, and crystallised from xylene, in which

it formed bright yellow prisms, m.p. 225°. (Found: C, 81.9; H, 4.7. $C_{26}H_{17}OCl$ requires C, 81.9; H, 4.5%).

2-Benzylidene-1-tetralone (LXXV).

(Compare Rapson and Shuttleworth[46]).

An alcoholic solution of potassium hydroxide (470 cc. of 4%) was added to a mixture of 1-tetralone (68 g.) and benzaldehyde (50 g.). After 2½ hours at room temperature the dark red liquid was acidified with dilute acetic acid, and diluted slightly with water. The crystalline material was collected, washed with water and crystallised from alcohol, when 2-benzylidene-1-tetralone (95 g.) was obtained as pale yellow rhombohedra, m.p. 105-106° (literature, 105-106°).

1-Hydroxy-2-benzyl-1:2:3:4-tetrahydronaphthalene (LXXVI).

(a). Atomised sodium (60 g.) was gradually added to a stirred solution of 2-benzylidene-1-tetralone (LXIV) (15 g.) in ether (450 cc.) containing water (100 cc.). When reaction was complete the solution was acidified with dilute hydrochloric acid, and the ether separated, washed with dilute sodium carbonate and water, and dried. The oil recovered from it was distilled, and the product collected at 180-185°/2 mm. (7 g.). There was a considerable residue which did not distil at 300°/2 mm. The oily product

solidified when rubbed with light petroleum, and after crystallisation from this solvent, fluffy colourless needles of (trans) 1-hydroxy-2-benzyl-1:2:3:4-tetrahydronaphthalene (3.2 g.), m.p. 115-116°, were obtained. (Found: C, 85.7; H, 7.6. $C_{17}H_{18}O$ requires C, 85.7; H, 7.6%). On concentration, the mother liquors deposited crystalline material which, after one more crystallisation from light petroleum, formed silky colourless needles (2 g.) of (cis) 1-hydroxy-2-benzyl-1:2:3:4-tetrahydronaphthalene, m.p. 73-75°. (Found: C, 85.6; H, 7.4. $C_{17}H_{18}O$ requires C, 85.7; H, 7.6%).

(b). 2-Benzylidene-1-tetralone (10 g.) in dioxan (100 cc.) was shaken with Raney nickel catalyst (prepared by the method of Pavlic and Adkins[47]) (5 g.) in an atmosphere of hydrogen, at ordinary temperature and pressure. Hydrogen uptake proceeded very rapidly at first, until one molecule had been absorbed, and then more slowly, and was complete in about 16 hours. Dioxan was removed from the filtered solution under reduced pressure, and the product (9 g.) taken up in light petroleum. Trans 1-hydroxy-2-benzyl-1:2:3:4-tetrahydronaphthalene (4 g.) separated from the solution in long colourless needles, m.p. 115-116° both alone and when mixed with the material prepared as in method (a). Concentration of the mother-liquors gave

cis 1-hydroxy-2-benzyl-1:2:3:4-tetrahydronaphthalene (3.7 g.), which crystallised from light petroleum in long colourless needles, m.p. 73-75°, not reduced on admixture with the more soluble isomer obtained in method (a).

2-Benzyl-1:2:3:4-tetrahydronaphthalene (LXXXI).

This hydrocarbon was obtained when 2-benzylidene-1-tetralone (20 g.) in absolute alcohol (300 cc.) was treated with hydrogen at 130-140 atmospheres and 150-160° for one hour, in presence of copper chromite catalyst (4 g.). The product (19 g.) crystallised from ethyl alcohol in elongated colourless prisms, m.p. 39°. (Found: C, 91.7; H, 8.0. Calc. for $C_{17}H_{18}$, C, 91.9; H, 8.0%).

Von Braun[48] has described this hydrocarbon as an oil, b.p. 194-195°/13 mm.

2-Benzyl-1-tetralone (LXXXII).

(Compare Riedel[51]).

2-Benzylidene-1-tetralone (5 g.) was smoothly reduced with palladium black in acetic acid solution, reduction being complete in about 6 hours. The product was extracted from the diluted solution, and distilled as a yellow oil at 167-170°/1 mm. (4.6 g.). This solidified when rubbed with methanol, and after crystallisation from the same solvent, 2-benzyl-1-tetralone was obtained as long colourless prisms, m.p. 52° (literature 55-56°). (Found: C, 86.1; H, 6.5.

Calc. for $C_{17}H_{16}O$, C, 86.4; H, 6.8%).

1-Chloro-2-benzyl-1:2:3:4-tetrahydronaphthalene (LXXXVI).

Consistent results could not be obtained in this preparation. The following is a description of a successful experiment.

Hydrogen chloride was passed for 30 minutes into a cold solution of (trans) 1-hydroxy-2-benzyl-1:2:3:4-tetrahydronaphthalene (2.5 g.) in dry benzene (10 cc.), containing powdered anhydrous calcium chloride (2.5 g.). After standing at room temperature for 3 - 4 hours, benzene was removed from the filtered solution by heating at 30° under reduced pressure. The oily product crystallised when chilled and rubbed with light petroleum. 1-Chloro-2-benzyl-1:2:3:4-tetrahydronaphthalene formed clusters of colourless needles (1.4 g.) in light petroleum, m.p. 72-73°. (Found: C, 79.2; H, 6.8. $C_{17}H_{17}Cl$ requires C, 79.5; H, 6.6%).

When this chloride (0.2 g.) and potassium cyanide (0.4 g.) in alcohol (10 cc.) and water (1 cc.) were refluxed on the water bath for 4 hours, an oily product was obtained (by extraction of the diluted solution). This could not be induced to crystallise, but was shown to be mainly 2-benzyl-3:4-dihydronaphthalene (LXXXIII) by means of the solid dibromide (see below).

Action of hydrogen bromide on 1-hydroxy-2-benzyl-1:2:3:4-tetrahydronaphthalene (LXXVI).

When either cis or trans hydroxy-benzyl-tetrahydronaphthalene was treated with hydrogen bromide exactly as described above for the chloride, no crystalline material could be obtained from the oily product. Attempted purification by distillation resulted in complete decomposition to 2-benzyl-3:4-dihydronaphthalene (LXXXIII), a colourless oil, b.p. 140° (air bath temperature)/1.5 mm. (Found: C, 92.7; H, 7.4. $C_{17}H_{16}$ requires C, 92.7; H, 7.3%). The same product was obtained by action of pyridine on the crude "bromide" at 100°.

The dibromide was obtained when the hydrocarbon, in acetic acid, was treated dropwise with bromine in acetic acid, until decolourisation no longer took place. It separated when the solution was cooled, and crystallised from light petroleum in colourless needles, m.p. 117-118° decomp. (Found: C, 53.6; H, 4.5. $C_{17}H_{16}Br_2$ requires C, 53.7; H, 4.2%).

Treatment of the crude oily "bromide" (1 g.) with potassium cyanide (2 g.) in alcohol or acetone at reflux temperature for 3 hours gave only 2-benzyl-3:4-dihydronaphthalene, b.p. 155° (air bath temperature)/4 mm., identified through the dibromide. The crude undistilled product of this reaction gave no acidic material when refluxed for 12 hours

with potassium hydroxide solution.

An attempt to convert the tetralol (LXXVI) to the corresponding bromide by treating it (1 g.) with hydrobromic acid (15 cc. of 48%) for several days at room temperature, also gave an oil which could not be induced to crystallise.

Experimental to Part II.

9-Acetyl-s-octahydroanthracene (XXIII).

(By method of Arnold and Barnes[66]).

s-Octahydroanthracene (4.3 g.) was added to a well stirred suspension of powdered aluminium chloride (14 g.) in dry tetrachlorethane (50 cc.). The mixture was cooled in an ice-salt bath, and acetic anhydride (5.7 g.) in tetrachlorethane (10 cc.) added dropwise over a period of one hour. Stirring was continued two hours longer, and the mixture then decomposed with ice and hydrochloric acid, and the solvent removed by steam distillation. The product was obtained from the washed and dried ethereal extract of the residue as an oil (4 g.), which solidified when rubbed with ethyl alcohol. Crystallisation from the same solvent gave colourless needles (2.5 g.) of 9-acetyl-s-octahydroanthracene, m.p. 70° (literature 72-72.5°).

s-Octahydroanthracene-9-glyoxal hydrate (XXIV).

(Arnold and Rondesvedt[67])

The above acetyloctahydroanthracene (2.3 g.) was added to a well-stirred solution of freshly sublimed selenium dioxide (1.2 g.) in dioxan (45 cc.) and water (0.5 cc.), at 50-55°. The temperature was then gradually raised, and the solution refluxed for two hours. The solution was

filtered free of selenium, diluted with water and cooled, when the glyoxal hydrate separated (2 g.), m.p. 98-110° (literature 100-105°). It was not further purified.

s-Octahydroanthracene-9-carboxylic acid (IX).

The above crude glyoxal hydrate (2 g.) in ethyl alcohol (30 cc.) was added to hydrogen peroxide (10 cc. of 30%), and a solution of potassium hydroxide (10%) added gradually until there was no longer vigorous effervescene (~ 60 cc.). The solution was then boiled for 30 minutes, charcoaled, and the acid recovered in the usual way. It crystallised from aqueous alcohol in long silky colourless needles (1.3 g.), sintering at 190° and melting at 218-220° (literature, s, 186°, m.p. 216-219°).

9-Ethyl-s-octahydroanthracene.

9-Acetyl-s-octahydroanthracene (1.5 g.), amalgamated zinc (10 g.), toluene (10 cc.), acetic acid (10 cc.), concentrated hydrochloric acid (50 cc.), were refluxed for 24 hours. The cooled liquid was extracted with benzene, and the oil obtained from the washed and dried extract distilled at 158-162°/2 mm. This could not be induced to crystallise; a portion was redistilled for analysis. 9-Ethyl-s-octahydroanthracene was obtained as a colourless liquid, b.p. 140° (air bath temperature)/2 mm. (Found:

C, 90.1; H, 9.9. $C_{16}H_{22}$ requires C, 89.7; H, 10.3%).

This hydrocarbon (0.16 g.) was dehydrogenated with palladium black at 300° for 30 minutes, in an atmosphere of carbon dioxide. The product was dissolved in alcohol, and a small amount of white solid filtered off. This had m.p. 210° and was identified as anthracene by comparison with an authentic specimen. The alcoholic filtrate ~~solution~~ was treated with picric acid, and the picrate crystallised from alcohol in red-yellow needles, m.p. 120° (literature m.p. for picrate of 9-ethylanthracene is 120°). Decomposition of the pictate on alumina gave 9-ethylanthracene, forming colourless needles in alcohol, m.p. 63-64° (literature, 64°).

Treatment of 9-ethyl-s-octahydroanthracene with anhydrous hydrofluoric acid at room temperature, for 15 hours, gave an oil, which was dehydrogenated as above. Only 9-ethylanthracene was detected in the product.

9-Chloromethyl-s-octahydroanthracene[60] (XXVIII).

A rapid stream of hydrogen chloride was passed into a suspension of paraformaldehyde (3.9 g.) in glacial acetic acid (60 cc.) until a clear solution was obtained. s-Octahydroanthracene (18.6 g.) was then added, and passage of gas continued at 60° for 3-4 hours. The solid which separated

on cooling was filtered, washed with water, and crystallised from alcohol. 9-Chloromethyl-s-octahydroanthracene was obtained as colourless needles, (13g.) m.p. 89-90° (literature, m.p. 91-92°).

9-Acetoxymethyl-s-octahydroanthracene (XXIX) was obtained when the above chloromethyl compound (2.2 g.) and anhydrous potassium acetate (2.2 g.) were heated in boiling glacial acetic acid (100 cc.) for 2 hours. The product (2.4 g.) was recovered when the concentrated solution was diluted with water, and formed colourless glistening thin flat needles in alcohol, m.p. 73°. (Found: C, 78.9; H, 8.6. $C_{17}H_{22}O_2$ requires C, 79.1; H, 8.5%). Hydrolysis of the acetoxy compound (1.5 g.) with alcoholic potassium hydroxide gave 9-hydroxymethyl-s-octahydroanthracene (XXX), which crystallised from ethyl alcohol in colourless prismatic needles (1.2 g.), m.p. 114°. (Found: C, 83.5; H, 9.2. $C_{15}H_{20}O$ requires C, 83.3; H, 9.3%). Passage of hydrogen chloride through a solution of this compound in benzene (containing an equal weight of anhydrous calcium chloride), gave the 9-chloromethyl compound, m.p. 89-90°.

9-Methyl-s-octahydroanthracene.

Reduction of the above chloromethyl-compound with palladium black in alcohol proceeded smoothly, to give 9-methyl-s-octahydroanthracene in almost quantitative yield.

It formed colourless lustrous flat plates in alcohol, m.p. 52°. (Found: C, 90.3; H, 9.8. $C_{15}H_{20}$ requires C, 90.0; H, 10.0%).

This compound could not be satisfactorily dehydrogenated, either with palladium black at 280-300°, or with sulphur at 230-250°. In each case the product was a mixture from which no pure constituent could be isolated.

9-Methyl-s-octahydroanthracene was recovered unchanged after treatment with hydrogen fluoride for 15 hours at room temperature. The product of the reaction was easily crystallised and consisted entirely of starting material. No other product could be detected.

9-Cyanomethyl-s-octahydroanthracene.

9-Chloromethyl-s-octahydroanthracene (1.2 g.) and potassium cyanide (3 g.) in alcohol (15 cc.) and water (5 cc.), were refluxed on the water bath for 2-3 hours. The concentrated solution was diluted with water, and the solid filtered and washed with water. 9-Cyanomethyl-s-octahydroanthracene formed colourless lustrous plates (1 g.) in alcohol, m.p. 108-109°. (Found: C, 85.6; H, 8.3. $C_{16}H_{19}N$ requires C, 85.3; H, 8.4; N, 6.2%).

9-s-Octahydroanthrylacetic acid (X).

The above nitrile (0.9 g.) was heated at 150-160° for 10 hours in a mixture of water, glacial acetic acid and concentrated sulphuric acid (1:1:1, 50 cc.). The product

(0.8 g.) was isolated by pouring the cooled reaction mixture into water. Crystallisation from alcohol gave 9-s-octahydroanthranylacetic acid in colourless plates, m.p. 212-214° decomp. after sintering at 190°. (Found: C, 78.6; H, 8.4. $C_{16}H_{20}O_2$ requires C, 78.7; H, 8.2%).

This acid was completely unchanged when treated with anhydrous hydrofluoric acid under the usual conditions.

β-(9-s-Octahydroanthranyl)propionic acid[60] (VI).

9-Chloromethyl-s-octahydroanthracene (13 g.) in dry benzene (25 cc.) was added to a solution of ethyl sodiomalonate prepared from sodium (2.3 g.), ethyl malonate (15 g.), alcohol (25 cc.) and benzene (25 cc.), and the mixture refluxed for 6 hours. Most of the benzene-alcohol was then distilled off, and the malonic ester hydrolised directly by refluxing for two hours with potassium hydroxide (30 g.) in aqueous alcohol (150 cc. of 50%). The resulting malonic acid was decarboxylated by heating at 190-200° for a few minutes, and the propionic acid (11.5 g.) crystallised from dilute acetic acid in colourless needles, m.p. 166-168° (literature, 167-168°).

γ-(9-s-Octahydroanthranyl)butyric acid (XI).

A mixture of the above propionic acid (2.2 g.), thionyl chloride (25 cc.) and a few drops of pyridine, in

dry benzene (6 cc.) was warmed at 50-60° for 2 hours. Benzene and excess thionyl chloride were then removed by warming under reduced pressure. The acid chloride was obtained as a crystalline solid, and was not further purified.

A solution of the acid chloride in pure dry benzene (10 cc.) was slowly added to a stirred, ice-cold solution of diazomethane (from 7 g. of nitrosomethylurea) in ether (150 cc.). After several hours the ether and excess diazomethane were allowed to evaporate at ordinary temperature. The diazo-ketone thus obtained was a well crystalline, bright yellow solid. To a solution of this in dioxan (15 cc.) was added ammonia solution (15 cc. of 20%) and silver nitrate solution (3 cc. of 10%), and the mixture heated on the steam bath for 2½ hours. The dark coloured mixture was diluted with dioxan (15 cc.) and boiled with charcoal. After filtration and dilution with water, γ-(9-s-octahydroanthranyl)butyramide (1.7 g.) separated. It crystallised from benzene/light petroleum in soft white needles, m.p. 163-164°. (Found: C, 79.9; H, 9.2; N, 5.3. $C_{18}H_{25}ON$ requires C, 79.7; H, 9.2; N, 5.2%). Hydrolysis of the amide (1.15 g.) by refluxing for 12 hours with potassium hydroxide (5 g.) in alcohol (50 cc.) gave γ-(9-s-octahydroanthranyl)butyric acid (1 g.),

which crystallised from alcohol as fine colourless needles, m.p. 152°. (Found: C, 79.5; H, 8.9. $C_{18}H_{24}O_2$ requires C, 79.4; H, 8.8%).

This acid (0.5 g.) was left in contact with anhydrous hydrofluoric acid at room temperature for twelve hours, and the product dissolved in benzene and washed with alkali. No acidic material was recovered from the alkaline extract. The neutral material obtained on removal of benzene crystallised from alcohol in long colourless needles of 4-keto-dodecahydrotriphenylene (XII) (0.39 g.), m.p. 222° (literature 222-222.5°), not reduced when mixed with an authentic sample of this ketone.

Condensation of s-octahydroanthracene and succinic anhydride.

(a). In carbon disulphide solution.

In an ice-cold mixture of s-octahydroanthracene (12.4 g.) and succinic anhydride (8 g.), in carbon disulphide (132 cc.), was added gradually, over half an hour, powdered aluminium chloride (18.4 g.). After standing four hours in ice, the mixture was left overnight at room temperature, and then warmed at 40-50° for 15 minutes. Carbon disulphide was decanted from the cooled mixture, and the gummy residue decomposed with ice and hydrochloric acid. The solid material was collected, extracted with boiling sodium

carbonate, and the acid (14 g.) recovered in the usual way. Crystallisation from acetic acid and from alcohol gave β-(9-s-octahydrophenanthroyl)propionic acid (XXXII) in colourless glistening needles (9.8 g.), m.p. 143-144°, both alone and when mixed with an authentic sample of this acid (m.p. 143-144°), prepared from s-octahydrophenanthrene and succinic anhydride, as described by Van de Kamp, Burger and Mosettig[76]. The same acid was obtained when the reaction was carried out omitting the short period of heating.

Clemmensen reduction of this keto-acid (8.5 g.) by refluxing for 24 hours with amalgamated zinc (30 g.), concentrated hydrochloric acid (100 cc.), acetic acid (20 cc.) and toluene (30 cc.), gave γ-(9-s-octahydrophenanthryl)-butyric acid, distilled at 240°/2 mm. (6 g.), and crystallised from acetic acid and from alcohol in colourless glistening needles, m.p. 128-129° (literature[76], m.p. 128-129°). When this acid (1.5 g.) was treated overnight, at room temperature, with anhydrous hydrofluoric acid, 4-keto-dodecahydrotriphenylene (XII) (1.42 g.) was obtained. It crystallised from alcohol in long colourless needles, m.p. 222° (literature[76], 222-222.5°)

(b). In tetrachlorethane solution.

s-Octahydroanthracene (3.1 g.) was added to a well-stirred suspension of powdered aluminium chloride (10 g.)

in dry tetrachlorethane (30 cc.). This mixture was cooled in an ice-salt bath, and to it was added a slurry of succinic anhydride (3.7 g.) in tetrachlorethane (50 cc.). Stirring and cooling were continued for several hours, and the mixture left overnight. The complex was decomposed with ice and hydrochloric acid, solvent removed with steam, and the residue extracted with boiling sodium carbonate. The acid was recovered in the usual way and dissolved in dilute acetic acid, from which needles separated (2.5 g.). Crystallisation of these from acetic acid and alcohol gave β-(9-s-octahydroanthranoyl)propionic acid (XXXI) in colourless prismatic needles, m.p. 210°. (Found: C, 75.6; H, 7.8. $C_{18}H_{22}O_3$ requires C, 75.5; H, 7.7%). The mother liquors of the initial crystallisation were diluted with water. After standing overnight the crystals were collected (1.4 g.). These had m.p. 143-144° both alone and when mixed with β-(9-s-octahydrophenanthroyl)propionic acid (XXXII).

9-Chloromethyl-10-methyl-s-octahydroanthracene (XXXIII).

Hydrogen chloride was passed into a suspension of paraformaldehyde (1.2 g.) in glacial acetic acid (20 cc.) until a clear solution was obtained. 9-Methyl-s-octahydroanthracene (6 g.) was added and passage of gas continued, the temperature being maintained at 60-70°. After two hours the crystals were filtered off and washed with water. (Yield, 6.7 g.). Crystallisation from benzene/light

petroleum gave 9-chloromethyl-10-methyl-s-octahydroanthracene as colourless plates, m.p. 143-144°. (Found: C, 77.1; H, 8.14. $C_{16}H_{21}Cl$ requires C, 77.3; H, 8.45%).

Attempted crystallisation of this compound from ethyl alcohol led to the formation of 9-ethoxymethyl-10-methyl-s-octahydroanthracene which crystallised from alcohol in fluffy, colourless needles, m.p. 73°. (Found: C, 83.7; H, 9.8. $C_{18}H_{26}O$ requires C, 83.7; H, 10.1%).

The chloromethyl compound was smoothly reduced with palladium black in acetone, giving 9:10-dimethyl-s-octahydroanthracene, crystallising from alcohol in colourless plates, m.p. 146-147°. This was identical with the compound prepared by Dr. Schoental[60] from 9:10-dichloromethyl-s-octahydroanthracene.

β-(10-Methyl-s-octahydro-9-anthranyl)propionic acid (XVIII).

A mixture of atomised sodium (1.1 g.), ethyl malonate (7.5 g.) and dry benzene (25 cc.) was refluxed for 2 hours. To the resulting solution was added 9-chloromethyl-10-methyl-s-octahydroanthracene (5 g.), in dry benzene (35 cc.), and the mixture refluxed for eight hours. The benzene was then removed, and the ester hydrolised by boiling for three hours with a solution of potassium hydroxide (15 g.) in aqueous alcohol (100 cc. of 50%). The resulting malonic acid was decarboxylated by heating at 240° for 15 minutes.

The β-(10-methyl-s-octahydro-9-anthranyl)propionic acid (3.2 g.) thus obtained crystallised from acetic acid in long colourless needles, m.p. 206-208° with previous sintering. (Found: C, 79.4; H, 8.7. $C_{18}H_{24}O_2$ requires C, 79.4; H, 8.8%).

When this acid was treated with hydrofluoric acid under the usual conditions, it was completely converted to neutral ketonic material. This was a yellow gum which could not be induced to crystallise. Attempted distillation led to extensive decomposition, and chromatography resulted in no purification. The substance did form a solid oxime and 2:4-dinitrophenylhydrazone, but these were obviously mixtures and could not be obtained in a pure condition by crystallisation.

4-(9-s-Octahydroanthranyl)-butene-1 (XXII).

9-Chloromethyl-s-octahydroanthracene (XXVIII) (5 g.), in ether (200 cc.), was added to magnesium (1 g.) in absolute ether (80 cc.) and the mixture refluxed for 2 hours. Reaction set in almost immediately and a white precipitate separated. Allyl bromide (15 g.) in ether (30 cc.) was then added dropwise and the mixture refluxed for 12 hours. The complex was decomposed with ammonium chloride solution, and the product isolated in the usual way, as a semi-solid. After washing with light petroleum

and crystallisation from benzene/light petroleum, 4-(9-s-octahydroanthranyl)-butene-1 formed soft colourless needles (0.8 g.), m.p. 178°. (Found: C, 90.3; H, 10.0. $C_{18}H_{24}$ requires C, 90.0; H, 10.0%).

This hydrocarbon was unaffected by hydrofluoric acid under the usual conditions.

s-Octahydrophenanthrene.

(Compare Durland and Adkins[27]).

Pure phenanthrene (25 g.) in cyclohexane (50 cc.) was reduced by treatment with hydrogen at 90-120° and 120 atmospheres pressure, in presence of Raney nickel (5 g.) (prepared by the method of Pavlic and Adkins[47]). When the temperature reached 90° a rapid absorption of hydrogen began, and was complete in ½ hour. The temperature was held at 120° for one hour longer, and the reaction then stopped. The product was fractionally distilled through a column packed with glass helices, and s-octahydrophenanthrene collected at 140°/3 mm. as a colourless oil (12 g.). The refractive index was 1.563 (Durland and Adkins[27] give the refractive index of s-octahydrophenanthrene as 1.564).

The hydrocarbon was unchanged by treatment with hydrofluoric acid under the usual conditions. The oily product was dehydrogenated with palladium black at 280-300° in an atmosphere of carbon dioxide, and gave only phenanthrene; no anthracene was detected.

9-Chloromethyl-s-octahydrophenanthrene (XXXIV).

Hydrogen chloride was passed into a vigorously stirred mixture of s-octahydrophenanthrene (8 g.), formalin solution (8 cc. of 40%), concentrated hydrochloric acid (40 cc.) and acetic acid (5 cc.), at 70° for 5-6 hours. The cooled mixture was extracted with benzene, and the oil recovered from the washed and dried extract distilled. After removal of some unchanged hydrocarbon, a colourless oil (5 g.) was collected at 170-180/1.5 mm. Crystallisation from light petroleum gave 9-chloromethyl-s-octahydrophenanthrene as clusters of colourless prismatic needles, m.p. 56°. (Found: C, 76.8; H, 8.2. $C_{15}H_{19}Cl$ requires C, 76.8; H, 8.1%). The solid residue of the distillation was extracted with light petroleum and gave 9:10-dichloromethyl-s-octahydrophenanthrene (XXXV) (0.8 g.), which crystallised from large quantities of alcohol as colourless needles, m.p. 160°. (Found: C, 67.9; H, 6.9. $C_{16}H_{20}Cl_2$ requires C, 68.1; H, 7.1%).

Reduction of these compounds with palladium black in acetone took place smoothly. 9-Methyl-s-octahydrophenanthrene was obtained as a colourless oil, b.p. 106-110° (air bath temperature)/0.3 mm. (Found: C, 90.0; H, 9.9. $C_{15}H_{20}$ requires C, 90.0; H, 10.0%). Dehydrogenation of this compound with palladium black at 280° for three hours in an

atmosphere of carbon dioxide gave 9-methylphenanthrene.

9:10-Dimethyl-s-octahydrophenanthrene formed colourless glistening plates in alcohol, m.p. 98°: (Found: C, 89.75; H, 10.3. $C_{16}H_{22}$ requires C, 89.72; H, 10.3%).

9-Methyl-s-octahydrophenanthrene was unaffected by hydrofluoric acid under the usual conditions. The structure of the oily product was confirmed by dehydrogenation to 9-methylphenanthrene as above.

Experimental to Part III.

Dihydroresorcinol (VI).

A solution of resorcinol (37 g. = 0.33 mol.) and sodium hydroxide (13 g. = 0.33 mol.) in distilled water (160 cc.) was shaken with Raney nickel (8 g.) in an atmosphere of hydrogen. Reduction proceeded steadily and was complete in about 12 hours. The filtered solution was chilled and acidified by slow addition of concentrated sulphuric acid until acid to Congo Red (p.H. 3). Dihydroresorcinol separated as small glistening white plates either immediately or after a short time. It was dried thoroughly on porous plate, and crystallised from boiling benzene or ethyl acetate, in which it formed colourless prisms (25 g.), m.p. 104-106° (literature, 104-106°).

Ethyl Δ^2-cyclohexen-1-one-3-methylmalonate (VIII).

Ethyl methylmalonate (35 g.) was added to a suspension of atomised sodium (4.6 g.) in dry benzene (100 cc.) and the mixture refluxed until all the sodium had reacted. 3-Chloro- Δ^2-cyclohexen-1-one[82] (V) (24 g.) was slowly added to the resulting solution, with occasional shaking. A brisk reaction took place and heat was evolved. The mixture was refluxed for one hour, cooled, and acidified with hydrochloric acid. The benzene layer was separated,

washed and dried, and the oil recovered from it distilled in two fractions, (a) b.p. 125-140°/1 mm. (10 g.), (b) b.p. 140-145°/1 mm. (19 g.). The fraction (b) was redistilled, when ethyl Δ^2-cyclohexen-1-one-3-methylmalonate was obtained as a colourless oil, b.p. 160°/2.5 mm. (Found: C, 61.7; H, 7.0. $C_{14}H_{20}O_5$ requires C, 62.7; H, 7.5%). Both fractions gave the same semicarbazone when treated with an aqueous alcoholic solution of semicarbazide hydrochloride and potassium acetate. It crystallised from alcohol in stout colourless needles, m.p. 137°. (Found: C, 55.6; H, 7.0; N, 12.8. $C_{15}H_{23}O_5N_3$ requires C, 55.4; H, 7.1; N, 12.9%).

Ethyl α-(Δ^2-Cyclohexen-1-one-3)propionate (VII).

3-Chloro-Δ^2-cyclohexen-1-one[82] (V) (16 g.) was slowly added to a solution prepared from sodium (5.7 g.), ethyl alcohol (70 cc.) and ethyl methylmalonate (42 g.), and the mixture warmed on the water bath for 2 hours. After dilution and acidification with hydrochloric acid, the product was extracted with ether. The oil obtained was steam distilled to remove unchanged starting materials, the residue dissolved in ether, washed, dried, and distilled as a colourless oil, b.p. 160°/16 mm. (9 g.). It could not be induced to crystallise, but readily formed a semicarbazone whose

analysis showed the liquid to be mainly ethyl α-(Δ^2-cyclohexen-1-one-3)propionate. The semicarbazone crystallised from alcohol in colourless needles, m.p. 124°. (Found: C, 57.2; H, 7.3; N, 16.24. $C_{12}H_{19}O_3N_3$ requires C, 56.9; H, 7.5; N, 16.6%). The 2:4-dinitrophenylhydrazone gave small orange prisms in methyl alcohol, m.p. 111-112°. (Found: N, 15.2. $C_{17}H_{20}O_6N_4$ requires N, 14.9%).

After standing several days a small amount of crystalline material separated from the liquid product. This formed colourless prisms in benzene, m.p. 102-104°, both alone and when mixed with authentic dihydroresorcinol.

Attempted formation of the lactone (IV).

(Compare Paranjape, Phalnikar, Bhide and Nargund[77]).

The above esters (VII and VIII) (5 g.) were refluxed for 6 hours with sulphuric acid made 6N with 50% aqueous alcohol (50 g.). The fluorescent green liquid was poured into water and, after cooling, extracted with ether. The oil recovered from the washed extract was boiled for 15 minutes with 0.1N barium hydroxide. The cooled alkaline liquid was extracted with ether, acidified and again extracted. No material was obtained from these last extracts. On removal of ether from the washed and dried extracts of the alkaline liquid, a neutral oil (3.5 g.) was obtained, and was distilled as a colourless oil at 92°/20 mm. A

satisfactory analysis of this liquid could not be obtained, but analysis of its semicarbazone showed it to be 3-ethyl-Δ^2- cyclohexen-1-one (XIII), m.p. 192° decomp. (Found: C, 60.0; H, 8.0. Calc. for $C_9H_{15}ON_3$: C, 59.7; N, 8.3%). (Blaise and Maire[87] have reported that the m.p. of the semicarbazone of 3-ethyl- Δ^2-cyclohexen-1-one is 240° decomp., Clemo, Cocker and Hornsby[84] found that the m.p. was 191-192°, however. The semicarbazone of the lactone (IV) is reported[77] to have m.p. 150°.) The same product was obtained when the esters were left in contact with cold 20%, 40% and 80% sulphuric acid in 50% aqueous alcohol, for several days. A proportion of the starting material was recovered, under these conditions, as also when warm 80% phosphoric acid was employed. Treatment with hot sulphuric acid of the above concentrations led to rapid and complete decarboxylation. The same results were obtained when the crystalline semicarbazones were substituted for the liquid esters.

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