Stereochemistry of Perhydrophenanthrene Derivatives.

THESIS

presented by

Alexander Crawford Ritchie, B.Sc.,

for the Degree of

Doctor of Philosophy

in the Faculty of Science of the

University of Glasgow.

September, 1950.

Preface.

The author would like to place on record his appreciation of the unfailing assistance, advice and encouragement received from his supervisor, Dr. C. Buchanan, throughout this work.

He is also indebted to Professor J.W. Cook, F.R.S. for his interest; to the Department of Scientific and Industrial Research for a maintenance grant during the tenure of which part of the present work was conducted; and to Mr. J.M.L. Cameron and Miss R.H. Kennaway who performed the micro-analyses.

INDEX.

Theoretical:

Summary.

The stereochemistry of the adduct between 1-phenyl-1:3-butadiene and acrolein has been studied. The reaction has been proved to produce a cis-configuration, and conflicting claims by earlier workers have been shown to be due to inversion on the carbon atom α to the aldehyde group. Hydrolysis of the aldehyde bisulphite compound with acid or alkali gives a similar cis-trans isomerisation, but the use of formalin leads to retention of configuration. The existence of both a cis and trans series of 2-phenyl-cyclo-hexyl compounds derived from this has been demonstrated, and their relationship to a hexahydrofluorene and hexahydrofluorenone established. Interconversion between the cis- and trans forms has been achieved in some cases.

A new synthesis of cis-9-keto-as-octohydrophenanthrene is described in which 3-bromo-2-phenyl-cyclo-hexene is condensed with diethyl malonate followed by hydrolysis, decarboxylation, hydrogenation, and cyclisation.

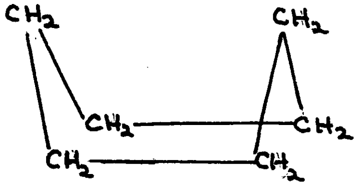
The reduction of trans-9-keto-as-octohydrophenanthrene has been shown to give mainly elimination of oxygen and the formation of a perhydrophenanthrene. A little cis-anti-trans-perhydro-9-phenanthrol is formed at the same time

A synthesis of *trans*-*anti*-*trans*-9-keto-perhydrophenanthrene from the corresponding perhydrodiphenic acid has been accomplished, but attempts to extend the scope of the method to produce other isomers were unsuccessful.

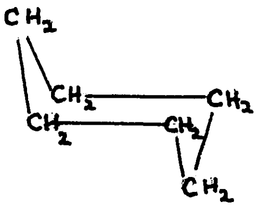
The perhydrophenanthrene derivative obtained by a Diels-Alder reaction between di-Δ-1:1'-*cyclo*-hexene and maleic anhydride, with subsequent hydrolysis, esterification and catalytic hydrogenation over Raney nickel, has been shown to possess the *cis*-*anti*-*trans* configuration. The conversion of this and the product obtained by hydrogenation of the corresponding acrolein adduct, into a *cis*-*anti*-*trans*-9-keto-perhydrophenanthrene, could not, however, be effected.

Introduction and Historical.

It was early realised(1) that, for a ring of six fully saturated carbon atoms, such as *cyclo*-hexane, to exist in a planar configuration would involve a considerable molecular strain, and that, in order to achieve a "strainless" structure, a non-planar character was essential. Sachse, therefore, suggested that this could be accomplished in two different ways and formulated the hypothesis of the "boat" (I) and "chair" (II) forms of the *cyclo*-hexane ring.



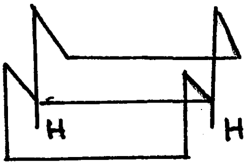
(I)



(II)

Such an arrangement, however, necessitates the existence of a large number of isomers for even a simple mono-substituted *cyclo*-hexane derivative, and examples of these have not, so far, been isolated. Thus it seems probable that there is an equilibrium between forms (I) and (II) and that the two structures vibrate so rapidly from one to the other that the net result is a planar molecule.

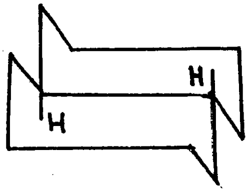
When polynuclear systems are examined, however, a different aspect arises, since now, the ring fusion exerts a stabilising influence. Mohr(2) pointed out that two strainless models could be constructed for the decahydro naphthalene molecule and the existence of a pair of stereoisomers of this and several related compounds was later demonstrated by Hückel(3). These were formulated as:-



"meso"

(IIIa)

"cis"

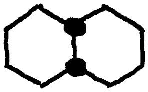


"meso"

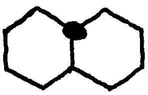
(IVa)

"trans"

It will be seen that, in the "boat" form (IIIa) both the hydrogen atoms attached to the carbon atoms involved in the ring fusion are on the same side of the plane of the rings, while in the "chair" structure (IVa), they are opposite. These modifications are designated "*cis*", and "*trans*" respectively and if we use the convention due to Linstead(5) in which a hydrogen atom above the plane is represented by a black dot, we may write (IIIa) and (IVa) as:-



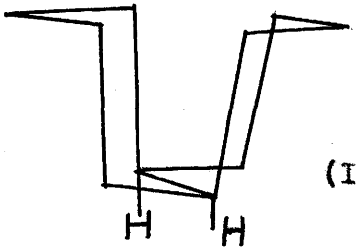
and



"cis"

"trans"

Recently(4), however, results of electron diffraction experiments suggested that, while the structure assigned by Mohr to the "trans" decalin was probably correct, the "cis" isomer arose also from fusion of two "chair" forms (IIIb).



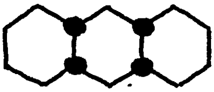
(IIIb)

"cis"

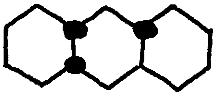
racemic.

If this is so, then since the only element of symmetry present is a two-fold axis, the molecule should exist in optically active forms. On the basis of the Mohr theory both molecules would be optically inactive, since, in addition, they possess at least one plane of symmetry.

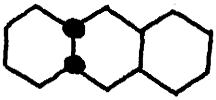
The fusion of more than two rings greatly increases the number of possible <u>cis-trans</u> isomers and gives rise to great difficulties both of isolation and identification. In the case of the perhydro-anthracenes five stereochemical modifications are possible (V - IX), three of which are known$^{(6)}$ (V, VI, VIII).



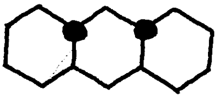
(V)



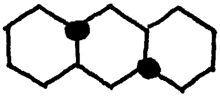
(VI)



(VII)



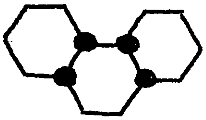
(VIII)



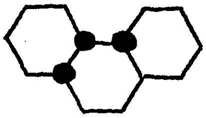
(IX)

When we have a tricyclic system involving an angular fusion, then the number of possible stereoisomers is increased to six because of the stereochemical relationships possible across the backbone of the molecule(7). Thus, if we designate two hydrogen atoms on the same side of the backbone as syn, and those on opposite sides of the plane as anti, we obtain:-

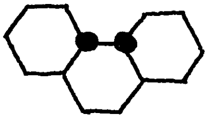
syn: series



cis-syn-cis (X)

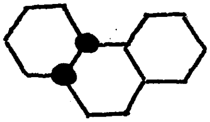


cis-syn-trans (XI)

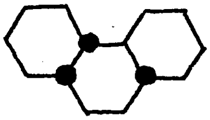


trans-syn-trans (XII)

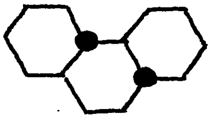
anti: series



cis-anti-cis (XIII)



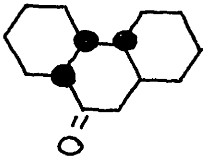
cis-anti-trans (XIV)



trans-anti-trans (XV)

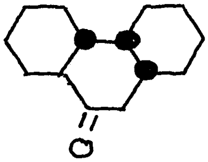
The first perhydrophenanthrene to be isolated was prepared by Ipatiew(8) by reduction of phenanthrene over a nickel oxide catalyst and is probably identical with those subsequently obtained in a somewhat similar manner by Marvel(9), and Adkins(55). What is probably a different isomer was produced by the reduction of 7-hydroxy-9-keto-cis-as-octohydrophenanthrene over a platinum catalyst(10), but in none of these cases could the stereochemical nature of these substances be determined.

A systematic attempt to elucidate the problems involved in the study of the perhydrophenanthrene ring system was undertaken by Linstead and his co-workers(11). Owing to the difficulties, both of working with mixtures of the liquid perhydrophenanthrenes themselves, and of subsequently assigning configurations, suitably substituted derivatives were employed which, on perhydrogenation, gave rise to products capable of easier separation, and which, at the same time, provided a point of attack on the molecule enabling it to be degraded to compounds of known stereochemical structure. It was pointed out that, if a substituent e.g., a carbonyl group, is introduced into, say, the 9-position, then the number of possible stereo-isomers is increased to eight, since, in addition to the six forms corresponding to (X) to (XV), two more are required as the carbonyl group in (XI) and (XIV) may be adjacent to either a <u>cis</u> or a <u>trans</u> linkage, thus:-



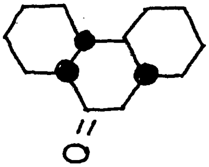
(XVI)

cis-syn-trans



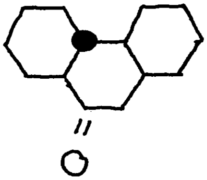
(XVII)

trans-syn-cis



(XVIII)

cis-anti-trans



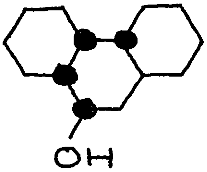
(XIX)

trans-anti-cis

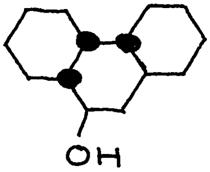
On oxidation the 9-keto-perhydrophenanthrenes give rise to the corresponding perhydrodiphenic acids, the configurations of which have been completely established(12).

When the present work was undertaken three of the eight forms were known, viz., *cis-syn-cis*-9-keto perhydrophenanthrene(11), *trans-syn-cis*-9-keto-perhydrophenanthrene(11,13) and *trans-anti-trans*-9-keto-perhydrophenanthrene(7,14). Recently(15) *cis-syn-trans*-9-keto-perhydrophenanthrene and *cis-anti-trans*-9-keto-perhydrophenanthrene have been described, so that of the six possible stereoisomeric forms of the perhydrophenanthrene nucleus, four have so far been characterized.

All the ketones are capable of existence in enantiomorphic forms and since each, on reduction, may give rise to two epimeric alcohols, e.g., (XX) and (XXI) from (XVI), sixteen racemic modifications of mono-hydroxy-perhydrophenanthrene are possible.



(XX)



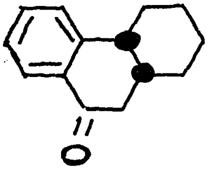
(XXI)

The most important class of naturally occurring compounds containing a perhydrophenanthrene nucleus are the steroids which are assigned a *trans-anti-trans* configuration in the androstane, 5-*allo*-pregnane, 5-*allo*-cholane, and cholestane series, and the *cis-anti-trans* form in the aetiocholane, pregnane, cholane, and coprostane series, although their stereochemistry is immensely complicated by the number of substituents present(16). Derivatives of many of the resin acids and related diterpenoids also contain a hydrogenated phenanthrene nucleus of this type and now that the structures of these substances have been elucidated, investigations of their stereochemistry are being commenced(58), and their relationship to the pentacyclic triterpenes of the amyrin type (hydrogenated picene derivatives) being studied, although little is yet known of the configuration of these fused ring systems(59).

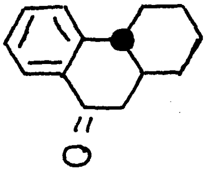
Theoretical.

During the course of their studies of the stereochemistry of catalytic hydrogenation and the configuration of the perhydrodiphenic acids, Linstead and his co-workers(12) demonstrated that, in hydrogenation involving the use of a platinum catalyst, the integrity of the established configuration in the *cis* and *trans*-hexahydrodiphenic acids was preserved, subsequent addition of hydrogen in a *syn* and *cis* manner leading to the formation of the *cis*-*syn*-*cis*- and *cis*-*syn*-*trans*-perhydrodiphenic acids. Later investigations(11) of the hydrogenation of *cis*-9-keto-1,2,3,4,9,10,11,12-octohydrophenanthrene (XXII) indicated that this stereochemical selectivity was again evident, as *cis*-*syn*-*cis*-9-hydroxy-perhydrophenanthrene was the major product of the reaction. Oxidation of the latter with chromic acid in the cold gave rise to *cis*-*syn*-*cis*-9-keto-perhydrophenanthrene, but, when performed on the water bath, inversion of configuration occurred and *trans*-*syn*-*cis*-9-keto-perhydrophenanthrene (XVII) was produced, identical with that obtained by Marvel(13). Perhydrogenation of 9-phenanthrol with platinum catalysts followed a similar course, resulting, again, in the formation of *cis*-*syn*-*cis*-9-hydroxy-perhydrophenanthrene.

In view of this *syn*- and *cis* reduction it seemed desirable to investigate the perhydrogenation of the corresponding *trans*-9-keto-1,2,3,4,9,10,11,12-octohydrophenanthrene (XXIII) since this might, theoretically at least, result in the production of a *cis*-*syn*-*trans*-9-hydroxy-perhydrophenanthrene, oxidation of which would possibly yield the unknown *cis*-*syn*-*trans*-9-keto-perhydrophenanthrene (XVI) in the cold, or, by inversion on the water bath, the *trans*-*syn*-*trans*-9-keto-perhydrophenanthrene, a hitherto undescribed modification of the perhydrophenanthrene ring.



(XXII)

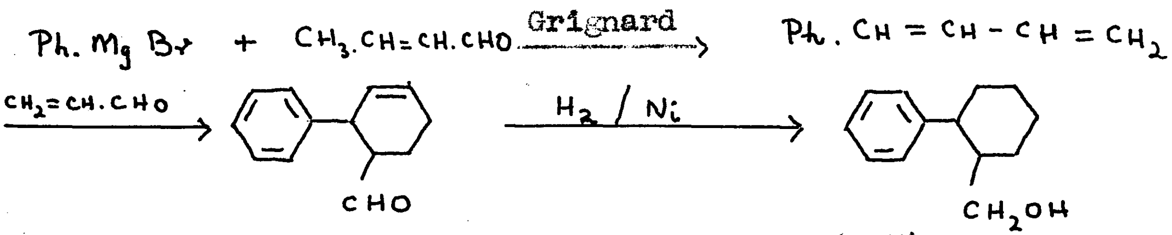


(XXIII).

From earlier work by Cook and his co-workers(6,17), a synthesis of the *cis*-*as*-octohydrophenanthrone (XXII) was known, from which the desired *trans*-isomer (XXIII) could be obtained by inversion with aluminium chloride, but all other attempts at a direct synthesis of the *trans*-compound have resolved into efforts to prepare *trans*-2-phenyl-*cyclo*-hexane acetic acid (XXVII) prior to cyclisation.

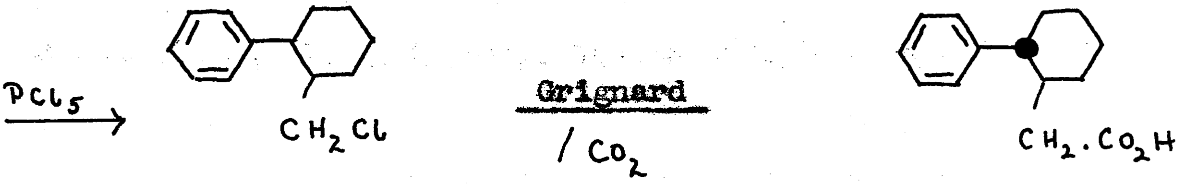
Poor yields of this acid have been obtained from a stereoisomeric mixture with the *cis* compound, by treatment of 2-phenyl-*cyclo*-hexyl bromide with diethyl malonate, with subsequent hydrolysis and decarboxylation(17), and also by a hydrogenation process which will be considered later(11). More recently(18,19), two syntheses have been announced in which it is claimed that the <u>trans</u> modification is produced exclusively. Both of these claims have been re-investigated, and, in one, radical alterations in experimental technique and a readjustment of views on the stereochemistry of various intermediates have been found necessary.

In the synthesis due to Blumenfeld(18), 1-phenyl-1:3-butadiene was condensed in a Diels-Alder reaction with acrolein to give 2-phenyl- Δ3-tetrahydrobenzaldehyde (XXIV), from which 2-phenyl-hexahydrobenzyl alcohol (XXV) was obtained by catalytic reduction over Raney nickel. Subsequent treatment of (XXV) with phosphorus pentachloride resulted in the formation of the corresponding 2-phenyl-hexahydrobenzyl chloride (XXVI), the Grignard complex of which, on carbonation, gave rise solely to the required <u>trans</u>-2-phenyl-<u>cyclo</u>-hexane acetic acid (XXVII). Cyclisation with sulphuric acid formed the <u>trans</u>-9-keto-<u>as</u>-octohydrophenanthrene (XXIII).



(XXIV)

(XXV)



(XXVI) (XXVII)

$\longrightarrow$ (XXIII).

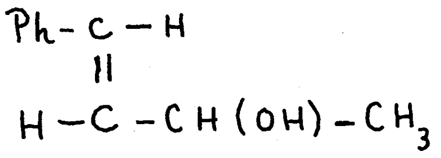
The preparation of 1-phenyl-1:3-butadiene in good and consistent yield by most of the known methods presented unexpected and considerable difficulty - a difficulty later confirmed by several authors(20,21) - and much time was spent on an endeavour to achieve an improvement.

Initial experiments followed the technique due to Blumenfeld in which the Grignard complex between phenyl magnesium bromide and crotonaldehyde was decomposed by pouring into 30% sulphuric acid without cooling and leaving overnight in contact with the acid, when the product was isolated in the usual way. Although this reaction was performed several times with rigid adherence to the exact experimental conditions specified, the optimum yield of the diene was only about 5%. This was always accompanied by some diphenyl, but the major product was a dark-brown glassy polymer. A series of control experiments were carried out involving variation of the significant, contributory factors such as the proportion of reactants, the concentration of the sulphuric acid, the rate of decomposition of the complex, and the time of contact of the ethereal solution with the acid, but the maximum yield was of the order of 10% as opposed to the 40% claimed. The contamination with diphenyl could be eliminated by the use of the theoretical quantities of reactants instead of the 20% excess of bromobenzene employed by Blumenfeld.

Isolation of the intermediate carbinol and subsequent dehydration appeared to offer the best solution to the problem, and the two stages were effected separately. The α-phenyl-γ-methyl allyl alcohol was readily prepared(22) and dehydration attempted with sulphuric acid of varying concentration, potassium bisulphate, oxalic acid, iodine, and phthalic anhydride. Of these, the best results were obtained by the use of potassium bisulphate, although, even here, yields were rarely in excess of 15-20%. These conclusions anticipate those later published by Coyner and Ropp(20) whose investigations of the dehydration of the various carbinols possible in the preparation of 1-phenyl-1:3-butadiene, showed inter alia that the optimum yield from α-phenyl-γ-methyl allyl alcohol and dilute sulphuric acid was only about 6% while much polymeric residue was formed.

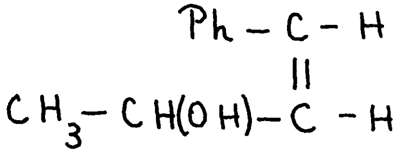
An older but more promising method appeared to be the dehydration of methyl styryl carbinol (XXVIII) from cinnamic aldehyde and methyl magnesium iodide(23,24).

$$Ph.CH=CH-CH(OH).-CH_3 \qquad \text{(XXVIII)}$$



$$\begin{array}{l} Ph-C-H \\ \quad\;\; \| \\ H-C-CH(OH)-CH_3 \end{array}$$

(A)



$$\begin{array}{r} Ph-C-H \\ \| \quad\; \\ CH_3-CH(OH)-C-H \end{array}$$

(B)

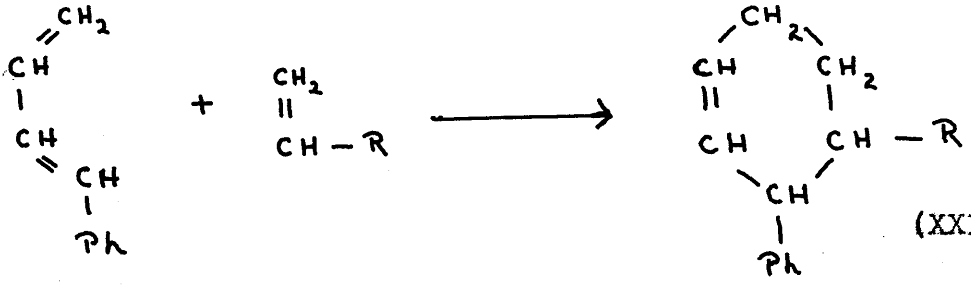
According to whether the dilute acid employed in the hydrolysis of the Grignard complex is completely eliminated or not, two stereoisomeric carbinols may arise. If the ethereal layer arising from the decomposition was washed only twice with water and then dried over anhydrous sodium sulphate so that a trace of dilute acid was still present, then the main product of the reaction was the <u>cis</u>-methyl-styryl carbinol (XXVIII B) characterised by the readiness with which it split off the elements of water. Distillation of this <u>cis</u> carbinol with a small quantity of potassium bisulphate in vacuo was found to produce the desired <u>cis</u>-1-phenyl-1:3-butadiene in overall average yields of 50%.

Complete removal of the acid, on the other hand, by thorough washing and subsequent drying over anhydrous potassium carbonate resulted in the formation of the <u>trans</u> methyl styryl carbinol (XXVIII A), which resisted dehydration in a marked degree. Elimination of the elements of water by converting the carbinol into the corresponding chloride with hydrochloric acid and dehydrohalogenation by heating with pyridine, was, however, readily effected and led to the production of trans-1-phenyl-1:3-butadiene in 55-60% yield. This method is capable of being performed on a large scale, in high yield, and with a lower tendency to the polymerisation which inevitably accompanies the formation of the cis diene. A similar technique was later employed by Alder(26) in extensive work on the stereochemistry of the condensation products of the diene with asymmetric dienophiles which will be discussed presently. The 1-phenyl-1:3-butadiene was characterised by its addition product with maleic anhydride(25).

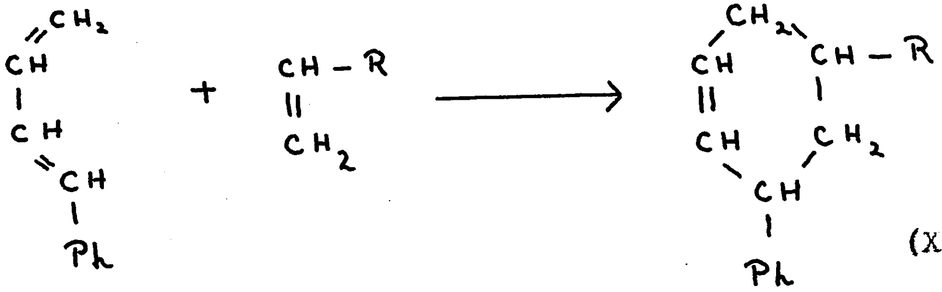
When this work had been concluded, further evidence of the difficulties encountered was afforded by Crummitt and Becker(21). These authors refer to the time and trouble expended in efforts to obtain the diene successfully and state that, "Although phenyl butadiene has been made by several different reactions the synthesis of this hydrocarbon in good yield proved to be difficult", and that, " .... adequate directions for preparing 1-phenyl-1:3-butadiene are not in the literature." Their final method, claimed to give the diene in 60% yield, involved the reaction of methyl magnesium bromide with cinnamic aldehyde in an inert atmosphere, with subsequent decomposition by pouring into dilute sulphuric acid under very stringent conditions, and in the presence of phenyl-β-naphthylamine as an anti polymerising agent. Repetition of this procedure confirmed the published results.

It is interesting to note that, in a comparative study of the efficiencies of various substances as inhibitors of polymerisation, Crummitt and Becker demonstrated that the latter process took place as rapidly in the presence of hydroquinone (the inhibitor used by Blumenfeld) as in the absence of any preservative.

The reaction between 1-phenyl-1:3-butadiene and acrolein, together with the closely related one involving acrylic acid, was first observed by Lehmann(27), who pointed out that the product might possess one of two constitutions according to the molecular arrangement at the moment of combination (XXIX ; XXX ; R = -CHO ; - COOH)

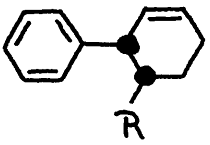


(XXIX)

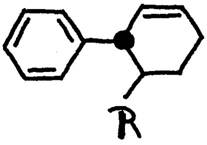


(XXX)

Conversion of the adduct with acrylic acid into a fluorenone derivative indicated that it belonged to the ortho type (XXIX : R = -COOH), and when it was found that oxidation of the acrolein adduct gave rise to a different carboxylic acid, then, merely on this basis, it was assumed that this latter condensation must be of the meta type (XXX : R = -CHO). The validity of this hypothesis was later doubted by Cook(28), and finally disproved by Blumenfeld(18) who showed that the structural course of both reactions was identical (of the ortho type) and that the differences arose from stereochemical factors resulting in the formation of cis-trans isomers (XXXI, XXXII ; R = -CHO, COOH).



(XXXI)

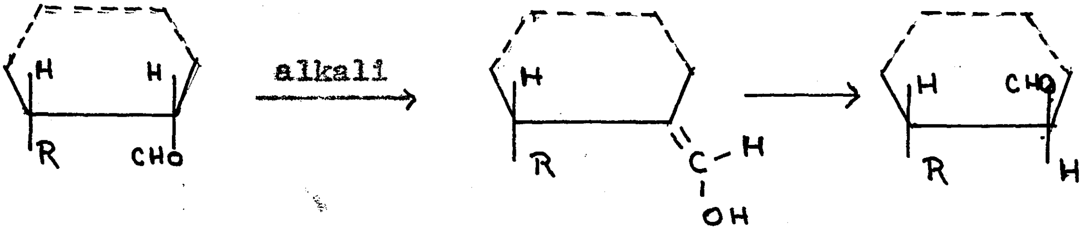


(XXXII)

The question of which adducts represented the cis configuration and which the trans was, however, left open, although it seems since to have been tacitly assumed that, as the Blumenfeld synthesis gives rise exclusively to the trans-9-keto-as-octohydrophenanthrene (XXIII), the initial 2-phenyl-Δ_3-tetra-hydro benzaldehyde must belong to the same series (XXXII : R = -CHO).

A good yield of 2-phenyl-Δ_3-tetra-hydro benzaldehyde (XXIV) was obtained from acrolein and 1-phenyl-1:3-butadiene in boiling benzene, but the conditions employed for hydrogenation to 2-phenyl-hexahydro-benzyl alcohol (XXV) (100 atmospheres hydrogen pressure, 150-160°, with Raney nickel for 3 hours[(18)]) appeared rather drastic and, in fact, were found to lead to the formation of 2-*cyclo*-hexyl-hexahydrobenzyl alcohol (XXXIII). When milder conditions of temperature ($< 90^{\circ}$) were applied, however, reduction of the double bond and aldehyde functions proceeded very smoothly in a short time, while the benzene nucleus remained untouched. Even at atmospheric pressure and room temperature hydrogenation to the required product was fairly rapid. To ensure that subsequent operations would be performed on a stereochemically pure form, the 2-phenyl-hexahydrobenzyl hydrogen phthalate was crystallised until homogeneous and of sharp melting point. Alkaline hydrolysis then regenerated the pure 2-phenyl-hexahydrobenzyl alcohol (XXXIV), m.p. 67-68°, in overall yields of about 70%. Since oxidation of this alcohol with chromic acid and acetic acid in the cold gave a 70% conversion into an acid whose melting point, and that of its S-benzyl-thiouronium derivative, corresponded with those of *cis*-2-phenyl-hexahydrobenzoic acid (XXXV)(29), it is apparent that the adduct from the condensation of acrolein with 1-phenyl-1:3-butadiene must possess, almost exclusively, the *cis* configuration, in spite of what may be inferred from the earlier literature.

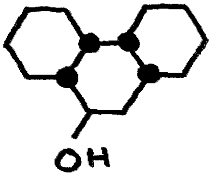
It is well known(36) that, in compounds of this type, in which a carbonyl or carboxylic group is α to a hydrogen atom involved in the stereochemical configuration, conversion of a cis to the more stable trans isomer can be effected via an enolic form and is promoted inter alia by the presence of alkali, e.g.,



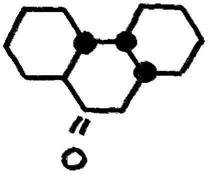
On this basis conversion of the cis-2-phenyl-Δ_3-tetrahydrobenzaldehyde into the corresponding trans form (XXXII ; R = -CHO) seemed feasible by a similar means. A dilute alcoholic solution of the cis-aldehyde (XXXI ; R = -CHO) was therefore treated with a small amount of dilute sodium hydroxide solution and allowed to stand at room temperature for 2-3 days. The recovered aldehyde did not appear to differ much in physical properties (boiling point etc.) from the starting material but hydrogenation to a 2-phenyl-hexahydrobenzyl alcohol as previously described yielded a substance which did not solidify so readily and had a melting point of 39-46°. As oxidation of this with chromic acid and acetic acid in the cold gave a good yield of an acid whose melting point and that of its S-benzyl-thiouronium derivative corresponded to those of trans-2-phenyl-hexahydrobenzoic acid(29) (XXXVII), either alone or when mixed with authentic specimens, both the 2-phenyl-hexahydrobenzyl alcohol (XXXVI) and the 2-phenyl- Δ_3-tetrahydrobenzaldehyde (XXXII ; R = -CHO) must also possess the *trans* configuration and *cis-trans* inversion must therefore have occurred.

When this work had been performed several papers appeared on the stereochemistry of the adducts from 1-phenyl-1:3-butadiene with acrolein and acrylic acid(30,31), which proved that the 2-phenyl- Δ_3-tetrahydrobenzoic acid (XL) from the acrylic acid belonged to the *cis* series. Since this could be isomerised with alkali into the corresponding *trans*-acid (XLI) identical with that obtained by Lehmann and Blumenfeld by oxidation of the acrolein adduct with hot chromic acid and acetic acid, the theory that the acrolein adduct represented the *trans* configuration appeared to acquire some justification.

Meek(30) rightly pointed out that, because of the low yield ($< 30\%$) obtained in the oxidation, this method of assigning configuration is very unsatisfactory, but omitted to mention, however, the possibility that the use of the hot chromic and acetic acids could cause inversion of the *cis* to the *trans* form (compare the preparation of (XXXIX) from (XXXVIII)) - a possibility which has, in fact, been shown to occur.



(XXXVIII)



(xxxix)

Oxidation of the aldehyde adduct was therefore effected by the use of a mixture of silver nitrate and sodium hydroxide over a period of 2-3 days when a 90% yield of the *trans*-2-phenyl-Δ_3-tetrahydrobenzoic acid was formed, and, solely on this basis, the authors assign a *trans* configuration to the adduct, stating that the method does not involve conditions likely to lead to inversion. In view however of the fact that the reaction required the use of a fair excess of sodium hydroxide, which we have shown to cause inversion of the *cis* aldehyde, this procedure appeared to be very unsatisfactory and, when the oxidation was performed under these conditions a large amount of inversion did, in fact take place with the production of almost equal quantities of the *cis*-2-phenyl-Δ_3-tetrahydrobenzoic acid (XL) and the corresponding *trans* structure (XLI).

Thus it was concluded that the reaction between 1-phenyl-1:3-butadiene and acrolein proceeded not only along the same structural lines as with acrylic acid, but pursued the same sterical course. This is what we might expect as, with two such similar dienophiles, it is difficult to account for formation of the *cis* configuration in one case and the trans in the other.

When this work had been completed, Alder$^{(26)}$ produced evidence to support the view that the acrolein adduct belonged to the cis series and that previous workers had obtained trans derivatives from this by inversion. He claimed, however, that this inversion resulted from the formation of the bisulphite compound of the aldehyde, to substantiate which theory it was demonstrated that oxidation before formation of the bisulphite compound gave rise to the cis-2-phenyl-Δ_3-tetrahydrobenzoic acid, whereas, afterwards the corresponding trans modification ensued. In view, however, of the fact that his procedure involved a modified treatment with silver nitrate and sodium hydroxide, which we have shown might be expected to lead to some inversion, and that the yields of acids obtained are not quoted, it was decided to investigate the phenomenon.

Since no indication was given either by Alder or any previous workers on the method of decomposition of the bisulphite compound of the aldehyde, various reagents were employed and the general procedure involved hydrogenation of the regenerated aldehyde, followed by identification of the stereoisomeric form produced by means of the melting point of the 3:5-dinitrobenzoate of the 2-phenyl-hexahydrobenzyl alcohol. This process gave excellent yields and, as has been shown, could not give rise to inversion. When the decomposition was effected by heating for a few minutes with dilute hydrochloric acid or for some time with dilute sodium carbonate solution, subsequent treatment, as above, resulted in the identification of trans-2-phenyl-hexahydrobenzyl alcohol showing inversion to have taken place. When, on the other hand, heating with dilute sodium carbonate for a shorter time, or, better, heating with formalin was employed, then the cis-2-phenyl-hexahydrobenzyl alcohol was recovered, indicating that the original cis configuration of the 2-phenyl- Δ_3-tetrahydrobenzaldehyde had been retained, and that it is not, as Alder supposes, formation of the bisulphite compound which causes inversion but its method of decomposition.

The stereochemical relationships between these substances and others which will be discussed presently is given in Table A.

While inversion of configuration via the bisulphite compound was probably at least one factor in the work of Lehmann(27), Meek(30), and Coyner(31), the case of Blumenfeld(18) is not so obvious, although Alder(26) attributes it to the same cause. In spite of the fact that full experimental details are quoted by Blumenfeld, no mention is made of the use of a bisulphite compound as an intermediate, and, moreover, a small scale hydrogenation with Raney nickel at

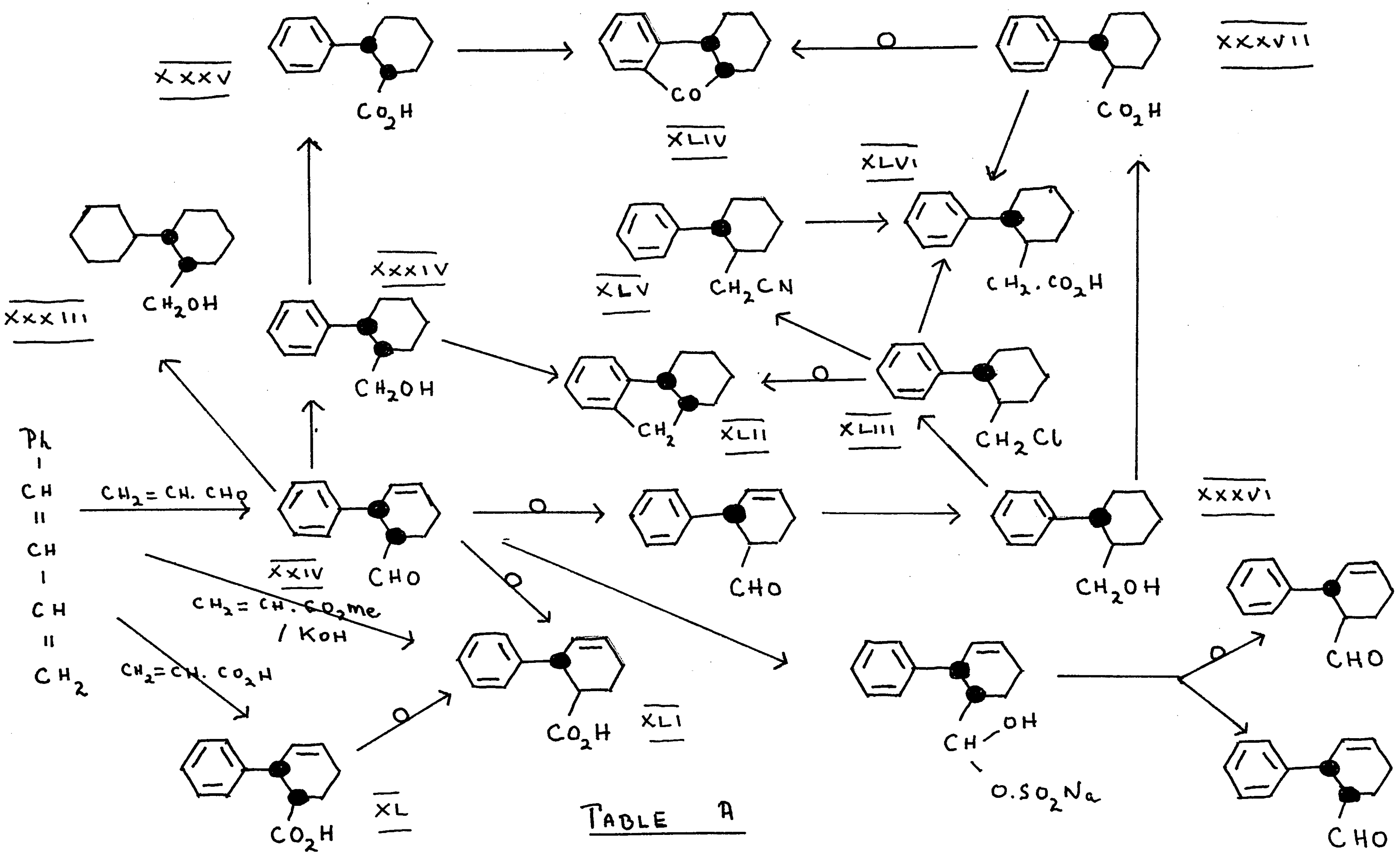
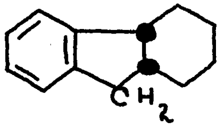
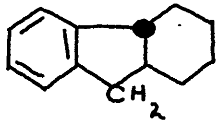

XXXV
CO_2H
CO
XLIV
O
CO_2H
XXXVII
XLVI
XXXIII
CH_2OH
XXXIV
CH_2OH
XLV
CH_2CN
$CH_2.CO_2H$
CH_2
XLII
O
XLIII
CH_2Cl
Ph
CH
CH
CH
CH_2
$CH_2=CH.CHO$
XXIV
CHO
O
CHO
CH_2OH
XXXVI
$CH_2=CH.CO_2me$
/ KOH
$CH_2=CH.CO_2H$
O
O
CO_2H
XLI
CH
OH
$O.SO_2Na$
O
CHO
CHO
CO_2H
XL

TABLE A

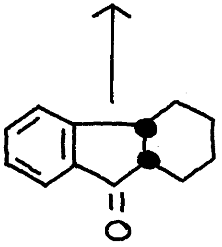
atmospheric pressure and room temperature resulted in the formation of a 2-phenyl-hexahydrobenzyl alcohol whose 3:5-dinitrobenzoate possessed a melting point of 101°. Since the melting point of the cis-3:5-dinitrobenzoate has been shown to be 108° while that of the corresponding trans isomer is 81-82°, it is clear that the bulk of the alcohol, and therefore of the original aldehyde, must have possessed a cis configuration. The inversion in the Blumenfeld synthesis must occur during or before the formation of the 2-phenyl-hexahydrobenzyl alcohol, as subsequent reactions have no effect on any of the configurational centres involved in the stereochemistry of the molecule. Since this has not taken place in the formation of the 2-phenyl-Δ_3-tetrahydrobenzaldehyde, it must have done so in the succeeding stage in which the bulk of the aldehyde was heated to 180° with hydrogen over Raney nickel, and, unfortunately no 3:5-dinitrobenzoate is recorded for the alcohol derived from this experiment. As already indicated, these conditions of reduction were found to give rise to 2-cyclo-hexyl hexahydrobenzyl alcohol, thus demonstrating that the catalyst employed by Blumenfeld must have been singularly inactive, and attempts to invert the aldehyde by hydrogenation with Raney nickel to which alkali had been added were unsuccessful, as the reaction with our catalyst achieved completion very rapidly before this could occur. Heating the cis-2-phenyl-hexahydrobenzyl alcohol with Raney nickel or with alkali had, as would be expected, no effect and it seems most probable, therefore, that with the extremely poor catalyst employed by Blumenfeld, heating to a high temperature with Raney nickel brought about a configurational inversion of the aldehyde before the hydrogenation occurred. In support of this hypothesis may be adduced the fact(30) that, when an aqueous solution of cis-2-phenyl- Δ_3-tetrahydrobenzoic acid is heated for two hours with Raney nickel, then trans-2-phenyl-hexahydrobenzoic acid is quantitatively produced. It might be expected that enolisation (and therefore inversion) would occur even more readily in the case of the corresponding aldehyde.

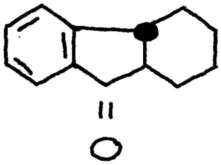
Several interesting observations arose when attempts to prepare the cis-2-phenyl-hexahydrobenzyl chloride were made. When the cis-2-phenyl-hexahydrobenzyl alcohol was treated with phosphorus pentachloride and chloroform, after the manner of Blumenfeld, a rapid reaction and vigorous evolution of hydrochloric acid gas took place but no halogen-containing compound could be isolated from the reaction mixture. Instead, the sole product was a hydrocarbon whose analysis corresponded to 1,2,3,4,10,11-hexahydrofluorene (XLII) and whose structure was confirmed by dehydrogenation with Adams' catalyst to fluorene. In view of its spontaneous formation from the cis alcohol under mild conditions, its ready dehydrogenation, and its relationship to a 1,2,3,4,10,11-hexahydrofluorenone which will be considered presently, the hydrocarbon has been assigned the cis configuration (XLII (a)), which is in keeping with the steric juxtaposition of the chlorine and phenyl groupings facilitating cyclisation.





(XLII) (a) "cis" (b) "trans"





(XLIV) (a) "cis"

A similar procedure on the trans-2-phenyl-hexahydrobenzyl alcohol yielded anomalous results. The initial product of the reaction obtained by distillation in vacuo, after removal of the solvent and the phosphorus oxychloride, although possessing the same boiling point as that quoted by Blumenfeld for the trans-2-phenyl-hexahydrobenzyl chloride, became blue or violet after a few seconds, and on redistillation, after washing with dilute sodium carbonate solution, had a boiling point almost 20° lower than previously.

Halogen was absent and the physical properties (boiling point and refractive index) were identical with those of the hexahydrofluorene previously obtained from the *cis*-alcohol. Identity was established by the formation of fluorene under the same conditions of dehydrogenation as in the latter case.

Since the high colour of the intermediates in the decomposition of the chloride to the hydrocarbon was probably due to phosphorus complexes, the reaction mixture was worked up by first removing all these by automatic shaking, for some time, with an excess of sodium hydroxide solution. Under these conditions the *trans*-2-phenyl-hexahydrobenzyl chloride (XLIII) was obtained in good yield on distillation.

The fact that both the *cis* and *trans*-2-phenyl-hexahydrobenzyl alcohols give rise to the same 1,2,3,4,10,11-hexahydrofluorene signifies that, in one case, inversion must have occurred. For the previous reasons and since the intermediate *trans* chloride could be isolated and subsequently converted to the hydrocarbon by distillation with phosphorus pentachloride, it seemed most probable that the latter was the reaction giving rise to inversion and that the 1,2,3,4,10,11-hexahydrofluorene has the *cis* configuration (XLIV).

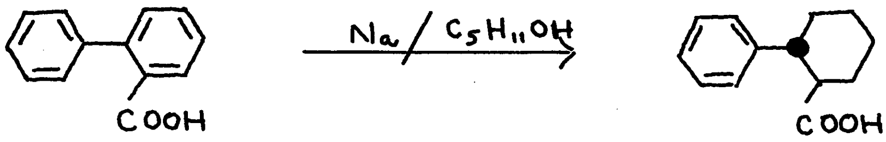
In a similar manner the acid chlorides of both the *cis* and *trans*-2-phenyl-hexahydrobenzoic acids were cyclised in a Friedel-Crafts reaction to the same 1,2,3,4,10,11-hexahydrofluorenone (an observation later confirmed by Alder(26)) demonstrating that again an inversion must have taken place. From analogy with the 1,2,3,4,10,11-hexahydrofluorene it might be expected that the ketone, too, would possess a cis structure, and that inversion of the trans acid chloride had taken place. This hypothesis is supported by the fact that repeated efforts to cyclise the trans-2-phenyl-hexahydrobenzoic acid (XXXVII) with anhydrous hydrogen fluoride were unsuccessful, the starting material being recovered unchanged, while similar treatment of the cis acid (XXV) gave rise to a ketone identical with that obtained from the Friedel-Crafts cyclisation of both acids. Ring closure of the cis acid again was readily effected with concentrated sulphuric acid whereas no neutral or acidic product could be obtained from the trans isomer, sulphonation having presumably occurred. Dilution of the concentrated sulphuric acid with acetic acid led to similar results until, in the case of the trans acid, a little starting material began to be recovered after a certain critical value was reached. Still no neutral material was observed and further dilution with acetic acid resulted in the complete recovery of the unchanged trans acid. These results afford confirmation that it is indeed the cis-1,2,3,4,10,11-hexahydro-9-fluorenone which is formed (XLIV). That the hexahydrofluorene and the hexahydrofluoranone belong to the same stereochemical series is also evidenced by the fact that Clemmensen reduction of the latter gives rise to a hexahydrofluorene whose physical properties correspond exactly with those of the former(28).

The *trans*-2-phenyl-hexahydrobenzyl chloride (XLIII) was converted into the corresponding *trans*-2-phenyl-*cyclo*-hexyl acetic acid (XLVI) both via the 2-phenyl-hexahydrobenzyl nitrile (XLV) and subsequent hydrolysis, and by carbonation of the Grignard complex with carbon dioxide at the boiling point as described by Blumenfeld.

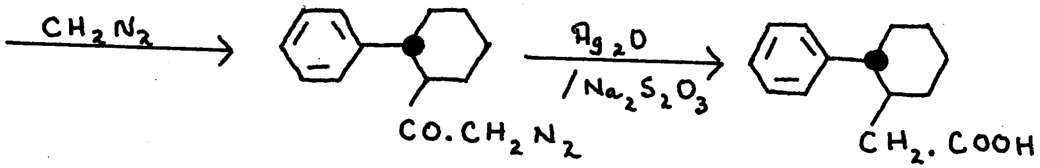
Ring closure of the *trans*-2-phenyl-*cyclo*-hexyl acetic acid to the required *trans*-9-keto-1,2,3,4,9,10,11,12-octohydrophenanthrene (XXIII) was achieved by means of concentrated sulphuric acid and also of anhydrous hydrofluoric acid.

A second synthesis which, it is claimed, gives rise solely to the *trans*-2-phenyl-*cyclo*-hexyl acetic acid is due to Gutsche and Johnson(19).

Phenyl-o-benzoic acid (XLVII) was reduced by means of sodium and amyl alcohol to the stereochemically homogeneous *trans*-2-phenyl-hexahydrobenzoic acid (XLVIII) the acid chloride of which underwent an Arndt-Eistert reaction via the intermediate *trans*-ω-diaza-2-phenyl-hexahydro-acetophenone to the *trans*:-2-phenyl-*cyclo*-hexyl acetic acid (XLVI).



(XLVII) (XLVIII)



(XLVI)

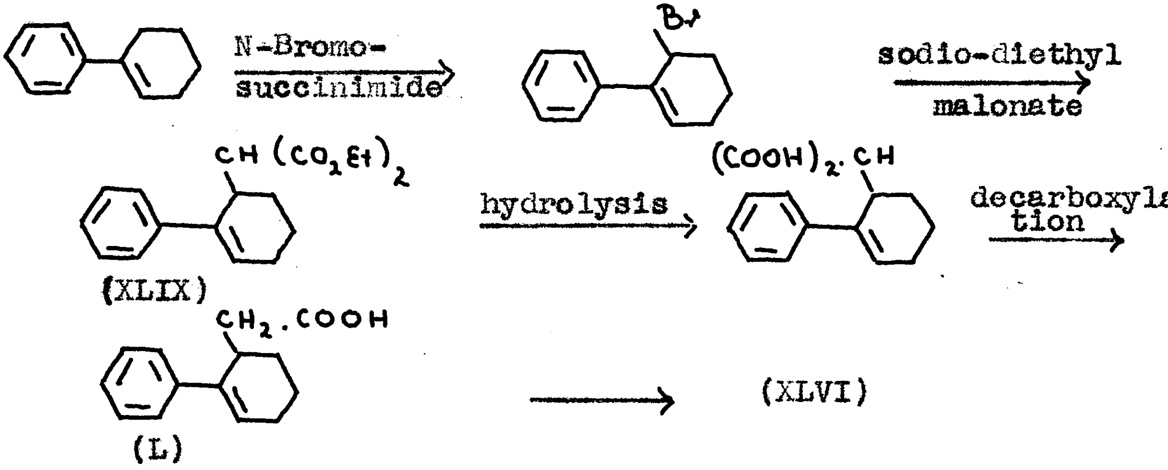
The claims of these authors have been re-investigated and confirmed. Hydrogenation of (XLVII) took place readily and the acid chloride reacted smoothly with diazo methane with the formation of the *ω*-diazoketone. The isolation of the acid (XLVI) by their procedure proved rather difficult and much better results were obtained if the decomposition of the diazoketone was allowed to proceed via the amide or ester, with subsequent hydrolysis.

Attempts to perform the Arndt-Eistert reaction on a scale larger than about 5 g. of material proved unsatisfactory and this represents the chief limiting factor of the method.

Ring closure gave the required *trans*-ketone (XXIII). Several procedures have been described for the preparation of the required *trans*-2-phenyl-*cyclo*-hexyl acetic acid, involving the condensation of phenyl *cyclo*-hexyl derivatives with, e.g., diethyl malonate$^{(17)}$, or ethyl bromacetate$^{(11)}$, but these for the most part have resulted in the formation of very low yields of even the mixed *cis*-*trans* isomers.

Linstead(11) showed that hydrogenation of the β-γ unsaturated acid obtained by dehydration of 2-phenyl-*cyclo*-hexanol acetic acid gave almost exclusively the *cis*-2-phenyl-*cyclo*-hexane acetic acid. When, however, the dehydration was performed with acetic or n-butyric anhydride a 30% yield of the isomeric α/β unsaturated acid (2-phenyl-*cyclo*-hexylidene acetic acid) was produced, and, although hydrogenation proceeded in a *cis* manner under most conditions, the use of palladium in benzene solution resulted in the formation of about 33% of the *trans*-2-phenyl-*cyclo*-hexane acetic acid.

It was thought that a feasible synthesis of (XLVI) might be achieved by the following series of steps in which 1-phenyl-*cyclo*-hexene is brominated with N-bromo-succinimide to 3-bromo-2-phenyl *cyclo*-hexene (LI), followed by condensation with diethyl malonate to 3 (2-phenyl-*cyclo*-hexenyl) malonic ester (XLIX). Subsequent hydrolysis and decarboxylation should yield 3 (2-phenyl-*cyclo*-hexenyl) acetic acid which might be converted into the *trans*-2-phenyl-*cyclo*-hexyl acetic acid on suitable hydrogenation



1-Phenyl-cyclo-hexene was reacted with N-bromo-succinimide, a reagent which causes the bromination of unsaturated hydrocarbons in the allyl position(32,33). Since, in the present case, there are two distinct allyl positions, two structural isomers (LI (a) or (b)) are possible, of which, it was considered that (LI (a)) would be the most probable product.

(LI) (a) (b)

In the presence of carbon tetrachloride as an inert diluent there was a smooth and rapid reaction but attempts to isolate the pure bromo compound by distillation were unsuccessful, due to the ease with which decomposition of the latter occurred on heating, even in vacuo, with the elimination of hydrobromic acid and the formation of diphenyl. When the reactants were mixed together at room temperature, a spontaneous and violent reaction took place, hydrobromic acid was copiously evolved and diphenyl was obtained in 50% yield.

This use of N-bromo-succinimide as a dehydrogenating and aromatising agent was later suggested by Barnes(34) and employed on substances of a similar nature.

Condensation of the crude bromo compound with sodio-diethyl malonate took place readily to give the pure

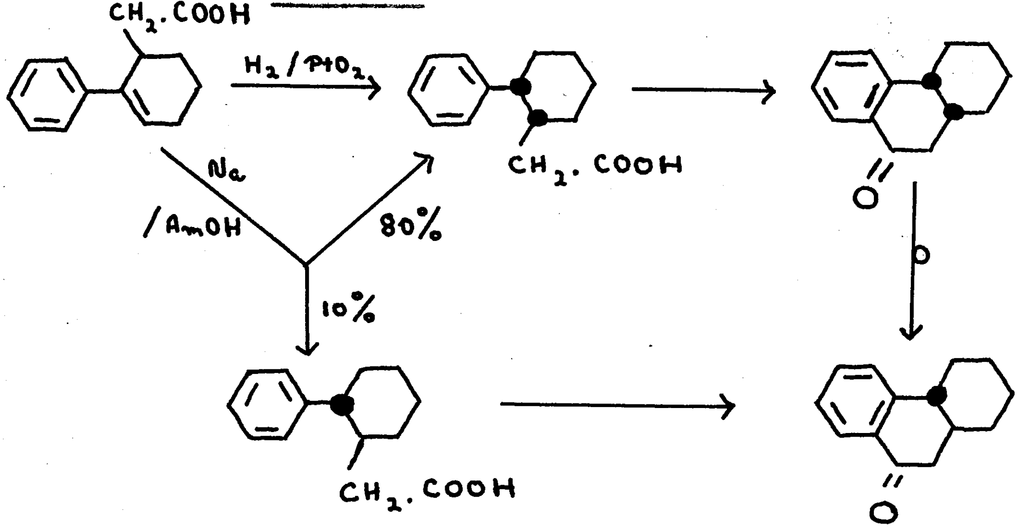
3 (2-phenyl-cyclo-hexenyl) malonic ester (XLIX) in good yield. 3 (2-phenyl-cyclo-hexenyl) malonic acid, obtained from the latter by hydrolysis could be decarboxylated by heating above its melting point, with the formation of 3 (2-phenyl-cyclo-hexenyl) acetic acid (L).

Hydrogenation of the double bond proved somewhat difficult as it was unaffected by the use of a platinic oxide or palladium black catalyst in ethanol. Although the unsaturated isomeric acids obtained by Linstead(11) were fairly readily reduced over platinum or palladium in benzene, the closely related 2 (3-methyl-3-phenyl-cyclo-hexenyl) acetic acid(35) was completely resistant to hydrogenation with platinic oxide even in acetic acid.

(L) was reduced with hydrogen over Adam's catalyst in acetic acid to give an acid, whose melting point and those of its derivatives corresponded to those of cis-2-phenyl-cyclohexyl acetic acid, and the structure of which was confirmed by cyclisation to a ketone whose oxime was identical with that of cis-9-keto-as-octohydrophenanthrene. This indicates that the initial bromination had followed the structural course expected and had formed (LI (a)) almost exclusively. An alternative procedure offering a route to a trans configuration was to effect the reduction with sodium and amylalcohol. Since the double bond is not isolated it should be susceptible to reduction by chemical means and the hydrogen, being in atomic form, has an equal chance of adding cis or trans across the double bond, a state of affairs which is unlikely, on the basis of Linstead's theory of Catalyst Hindrance, with the use of molecular hydrogen and a platinum catalyst. Application of this technique, however, while giving rise to a small amount (10%) of the trans-2-phenyl-cyclo-hexyl acetic acid, yielded mainly the cis isomer (80%), thus demonstrating that there was a preferential addition of a hydrogen atom trans to the acetic acid side chain, and the question of how the other hydrogen atom adds is, of course, irrelevant to the stereochemistry of the molecule as a whole. In the present case, too, the use of an alkaline reduction medium cannot cause cis-trans inversion in the usual way by enolisation as the hydrogen atoms on the carbon α to the carboxyl group are not concerned in the stereochemical configuration.

The stereochemical relationships of these substances are shown in Table B. Although it is mainly the cis acid and hence the cis ketone which is obtained by this method, the trans ketone can, of course, be obtained by inversion with aluminium chloride, and since the yields in this synthesis are good, it represents a convenient method of preparing either ketone.

Table B.



Hydrogenation of trans-9-keto-1,2,3,4,9,10,11,12-octohydrophenanthrene.

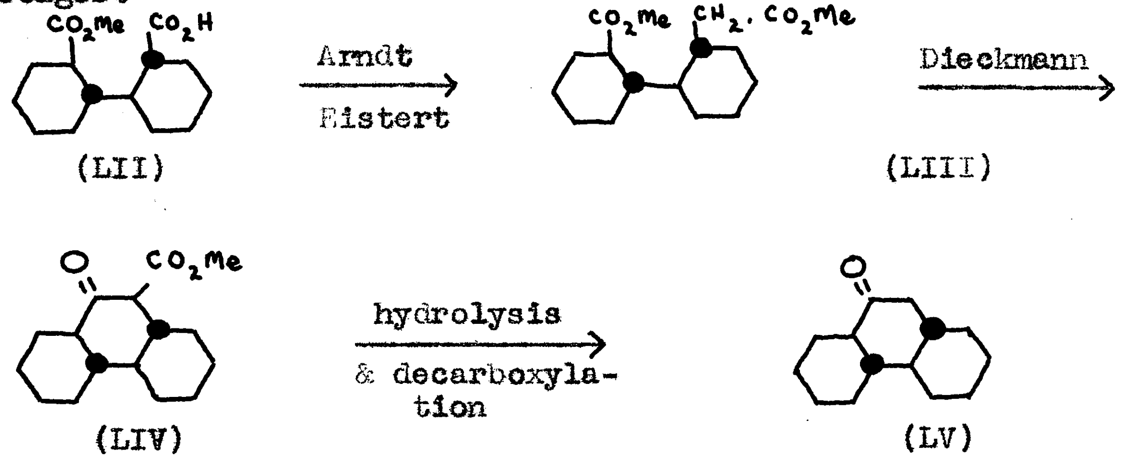
Hydrogenation of the *trans* ketone (XXIII) would be expected to follow the same general lines as that of the *cis* ketone(11) although the rate of reaction would be much slower. Thus, in the latter case, Linstead has shown that hydrogenation with platinum catalysts in acetic acid solution leads to the elimination of oxygen and formation of a hydrocarbon, while, in a similar manner, it is known that 7-hydroxy-9-keto-*cis*-*as*-octohydrophenanthrene gives rise mainly to a perhydrophenanthrene(10). With platinic oxide in ethanolic solution the *cis* ketone yielded *cis*-*syn*-*cis*-9-hydroxyphenanthrene, but the addition of even a little acetic acid resulted in loss of the oxygen atom. When a sample of the trans ketone was treated in alcoholic solution with hydrogen and platinic oxide, addition of one mole of hydrogen occurred in about 4 hours instead of the 19 quoted by Linstead and the product was 9-hydroxy-trans-as-octohydrophenanthrene, m.p. 89-91°. If reduction was allowed to go to completion about 4 moles of hydrogen were absorbed in 4 days, but this resulted mainly in the formation of a liquid hydrocarbon corresponding to a perhydrophenanthrene, which was probably a mixture of the cis-syn-trans and cis-anti-trans modifications(15), together with a few crystals of a cis-anti-trans-9-hydroxy-perhydrophenanthrene, m.p. 132-133°. The rate of reaction was surprisingly rapid as Linstead has shown that, under the same conditions, the cis ketone required 4 days to absorb 3.4 moles of hydrogen. In an attempt to slow down reduction therefore and prevent elimination of the oxygen, the reaction was carried out in more dilute solution, with a much smaller proportion of catalyst, and under these conditions an alcohol, m.p. 105-106° was obtained, together with the liquid perhydrophenanthrene. The former, however, corresponded to an octohydro-rather than a perhydrophenanthrene structure and, as oxidation with cold chromic acid gave back the trans-9-keto-as-octohydrophenanthrene, it was therefore an epimeric modification of the alcohol, m.p. 89-91° and probably identical with the 9-hydroxy-trans-as-octohydrophenanthrene, m.p. 101°, described by Linstead.

During the course of these experiments it became known that work of an exactly similar nature had been accomplished by Linstead and accepted for publication. In view of this, further investigations on the hydrogenation of the trans ketone were discontinued.

Note: Linstead and Whetstone(15) were unable to effect any reduction of the trans-9-keto-as-octohydrophenanthrene beyond the corresponding phenanthrol by use of Adam's catalyst in ethanol. In the presence of a little acetic acid hydrogenation took place with the formation of a mixture of two perhydro-9-phenanthrols and a small amount of hydrocarbon, separation of which, and oxidation with cold chromic acid gave about equal amounts of the cis-syn-trans- (XVI) and cis-anti-trans- (XVIII) 9-keto-perhydrophenanthrenes. Attempts to convert the cis-syn-trans-perhydro-9-phenanthrol into the trans-syn-trans-9-keto-perhydro phenanthrene by inversion with hot chromic acid were unsuccessful. Thus (XVIII) represents a fourth form of the perhydrophenanthrene ring, while (XVI) is the second of the structural isomers of the cis-syn-trans ketone, corresponding to a ring form which was previously known.

9-keto-perhydrophenanthrenes from perhydro diphenic acids.

All the methods so far described for the preparation of perhydrophenanthrene derivatives have consisted either in the building up of partly hydrogenated phenanthrene skeletons or in the use of a suitably substituted phenanthrene derivative followed, in both events, by complete catalytic reduction and investigation of the products. An alternative route was sought involving the use of a starting material possessing a known configuration of the perhydrophenanthrene type, which could be converted into a 9-keto-perhydrophenanthrene in which the stereochemical structure was retained, by the following stages:-



(LII) (LIII) (LIV) (LV)

Perhydro-methyl-hydrogen diphenate is converted via an Arndt-Eistert reaction to a 2-carbomethoxy-2' carbomethoxymethyl-perhydro-diphenyl (LIII) which is subjected to a Dickmann reaction with the production of a 9-keto-10-carbomethoxy-perhydrophenanthrene (LIV). Being a β -keto-ester this should undergo simultaneous hydrolysis and decarboxylation to the 9-keto-perhydrophenanthrene (LV).

Since all of the six possible perhydrodiphenic acids are known(36) this synthesis might be capable of yielding all the possible stereoisomeric modifications of the perhydrophenanthrene nucleus, as the conditions throughout seem unlikely to cause inversion except in the case of the Dieckmann reaction.

Trans-*anti*-*trans*-perhydrodimethyl diphenate, from hydrogenation of dimethyl diphenate over Raney nickel at high temperature and pressure, was hydrolysed to the corresponding acid, and thence to the *trans*-*anti*-*trans*-perhydrodiphenic anhydride by treatment with acetic anhydride. This was readily converted to the *trans*-*anti*-*trans*-2-carboxy-2'-carbomethoxy-perhydrodiphenyl (LII) with sodium methoxide, and afterwards to the acid chloride with thionyl chloride. The reaction of the latter with diazo methane was smooth and rapid, and decomposition of the intermediate diazo ketone in the usual way readily gave rise to *trans*-*anti*-*trans*-2-carbomethoxy-2'-carbomethoxy methyl perhydrodiphenyl (LIII). A Dieckmann reaction with sodium in benzene formed the *trans*-*anti*-*trans*-9-keto-10-carbomethoxy-perhydrophenanthrene (LIV) which underwent simultaneous hydrolysis and decarboxylation to the desired *trans*-*anti*-*trans*-9-keto-perhydrophenanthrene (LV), identified by its oxime and by oxidation to *trans*-*anti*-*trans*-perhydrodiphenic acid.

The other modifications of the perhydrodiphenic acids are obtained either as by-products in the hydrogenation of diphenic acid with Adam's catalyst in acetic acid, or by controlled inversion of the cis-syn-cis isomer which is the main product of the reaction. The exact conditions specified by Linstead (60 lbs./sq.inch hydrogen pressure and 25°C) were, however, not obtainable on the apparatus available and repeated attempts at reduction of the acid and its dimethyl ester were made under other conditions including:-

(a) Atmospheric pressure and room temperature with platinic oxide in acetic acid or ethanol plus a trace of hydrogen chloride(37),

(b) catalyst as in (a) in a high pressure hydrogenation bomb.

All these, however, failed to give any observed hydrogenation. To eliminate the possibility of catalyst poisoning, the diphenic acid was obtained from several sources:-

(1) Diazotisation of anthranilic acid and treatment with ammoniacal cuprous hydroxide(38).

(2) Oxidation of phenanthraquinone with hydrogen peroxide in sodium hydroxide.

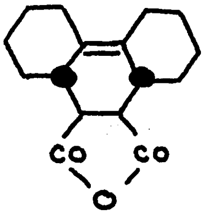
(3) Ullmann reaction on o-iodo-methyl-benzoate and subsequent hydrolysis(52).

In each case the acid was purified by the technique of Linstead, and the activity of the catalyst tested by the rate of its reduction of benzoic acid. Finally, almost pure phenanthrene was treated for several hours with molten sodium(39), and the diphenic acid obtained by oxidation heated for some time with Raney nickel. When no reaction was observed using this material the scheme was abandoned.

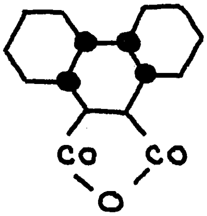
The failure may be due to the fact that sufficiently drastic conditions could not be employed on the apparatus available, or, when they could be approximated in a high pressure hydrogenation bomb, the vigorous mechanical agitation of the Parr apparatus could not be reproduced.

Perhydrophenanthrene derivatives from Di- Δ 1:1'-*cyclo*-hexene.

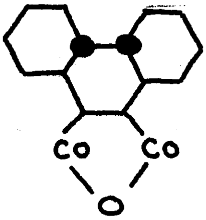
A method of preparation of partially hydrogenated phenanthrene derivatives possessing substituents in the 9 and 10 positions, consists of a Diels-Alder reaction between di- Δ 1:1'-*cyclo*-hexene and a suitable dienophile such as maleic anhydride(40). In the latter case Δ 12:13-dodecahydrophenanthrene-9:10-dicarboxylic acid anhydride (LVI) results, a substance which seemed suitable for conversion into a perhydrophenanthrene derivative whose configuration could be established. The problem resolved itself into two parts, (a) preparation of the substituted perhydrophenanthrene and elucidation of its stereochemical structure, and (b) conversion into the corresponding 9-keto-perhydrophenanthrene.



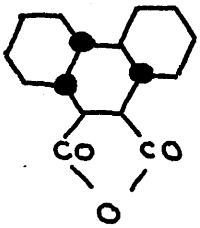
(LVI)



(LVII)



(LVIII)



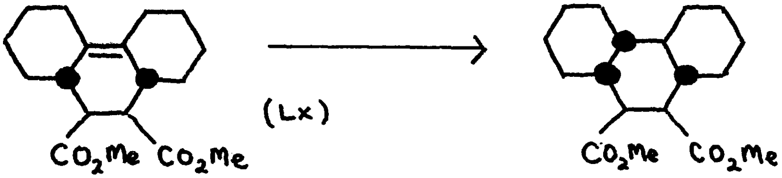
(LIX)

On the basis of the Alder Rules concerning the stereochemical configuration of the adducts in the Diels-Alder reaction we should expect that the hydrogen atoms on C_{11} and C_{14} would be *cis* to each other (LVI). It will readily be seen, therefore, that subsequent saturation of the molecule could, theoretically, give rise to three of the six possible isomers of the perhydrophenanthrene system. Thus *cis* addition of hydrogen across the double bond could produce either the *cis*-*syn*-*cis* (LVII) or *trans*-*syn*-*trans* forms (LVIII) although the latter, according to the theory of Catalyst Hindrance, would be unlikely. *Trans* addition, on the other hand, could result only in the formation of the *cis*-*anti*-*trans* modification. When this work was undertaken the only corresponding 9-keto perhydrophenanthrene known was the *cis*-*syn*-*cis* form, although one of the *cis*-*anti*-*trans* species has recently been described(15).

Attempts to bring about cis hydrogenation by employing a palladium or platinum catalyst in glacial acetic acid or in ethanol were unsuccessful. This marked resistance to reduction and the unreactivity of the double bond are not surprising, in view of the fact that we are dealing with a tetra-substituted ethylene having the double bond between two rings. Thus Adkins(41) has shown that the closely analogous Δ 11:12-dodecahydrophenanthrene required to be heated with hydrogen over Raney nickel to 250° under high pressure before saturation was effected.

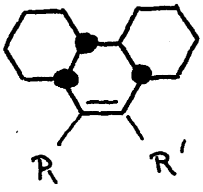
An indirect route to ensure trans-hydrogenation, viz. addition of bromine (which takes place in a trans fashion) followed by catalytic hydrogenation with palladised strontium carbonate also failed because of this lack of olefinic activity, as no reaction appeared to take place on allowing the anhydride to stand for some time with bromine.

Finally, this lack of reactivity had to be overcome by reduction over Raney nickel at elevated temperature and pressure, a procedure which we should expect to give rise to trans addition and therefore production of a cis-anti-trans configuration. (Note: In order to avoid confusion it will be assumed that subsequent assignment of configuration has been experimentally justified.) Since these conditions would also afford reduction of one of the carbonyl groupings with the production of a type of phthalide, the experiment was performed on the dimethyl ester of the free acid (LX) when *cis*-*anti*-*trans*-9:10-dicarbomethoxy perhydrophenanthrene (LXI) was obtained.

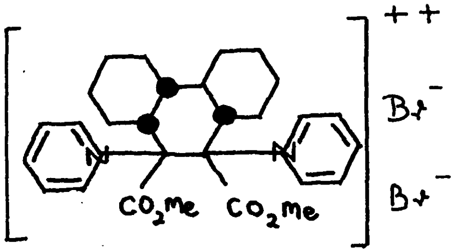


(LXI)

Determination of the stereochemical structure by the normal method of conversion to the corresponding perhydrodiphenic acid requires the presence in the molecule of some readily oxidisable centre in the 9 or 10 positions, for which purpose an olefinic link appeared admirable (LXII; R = R' = CO_2H). It is well known that, when we have a system of the type $R\cdot CH_2\cdot CH_2\cdot R'$ in which two methylene groups are attached to activating centres (R,R' may be unsaturated linkages, carbonyl groups, esters, or aromatic nuclei), then oxidation with selenium dioxide may give rise to $R\cdot CH = CH\cdot R'$[42] with the removal of two atoms of hydrogen. In a similar manner it was hoped that (LXII; R = R' = CO_2Me) might arise from (LXI) but on heating with selenium dioxide in a sealed tube to a high temperature, (LXI) was invariably recovered and no oxidation occurred.

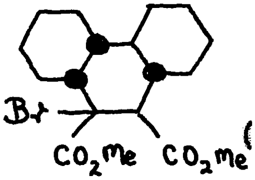


(LXII)

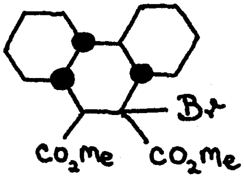


(LXII

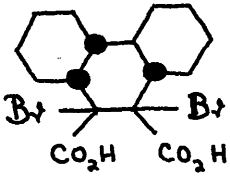
An alternative procedure appeared to consist of α-monobromination of the ester or acid with subsequent elimination of hydrogen bromide, but results by this method proved disappointing. No reaction was observed on prolonged treatment of (LXI) with bromine in carbon disulphide or chloroform(43) and the presence of halogen carriers, e.g., iodine, or irradiation with strong sunlight had little effect, although, when a little pyridine was employed an orange solid was produced, which was soluble in warm water, neutral, and contained a bromide anion, to which the formula of the quaternary pyridinium salt, *cis*-*anti*-*trans*-9:10-dicarbomethoxy-perhydrophenanthrene-9:10-dipyridinium dibromide (LXIII) was assigned. The pyridine however did not promote the reaction in the direction hoped for, and, while the yield of the di-pyridinium salt varied with the quantity of pyridine used, in no case was any simple bromination observed. Extended heating of (LXI) in carbon disulphide with one mole of bromine and a trace of iodine as catalyst gave a poor yield of the required *cis*-*anti*-*trans*-9-bromo-9:10-dicarbomethoxy-perhydrophenanthrene (LXIV or LXV) which, on simultaneous dehydrobromination and hydrolysis with alcoholic potassium hydroxide, afforded the *cis*-*anti*-*trans*-Δ 9:10-dodecahydrophenanthrene-9:10-dicarboxylic acid (LXII; $R = R' = CO_2H$).



(LXIV)



(LXV)

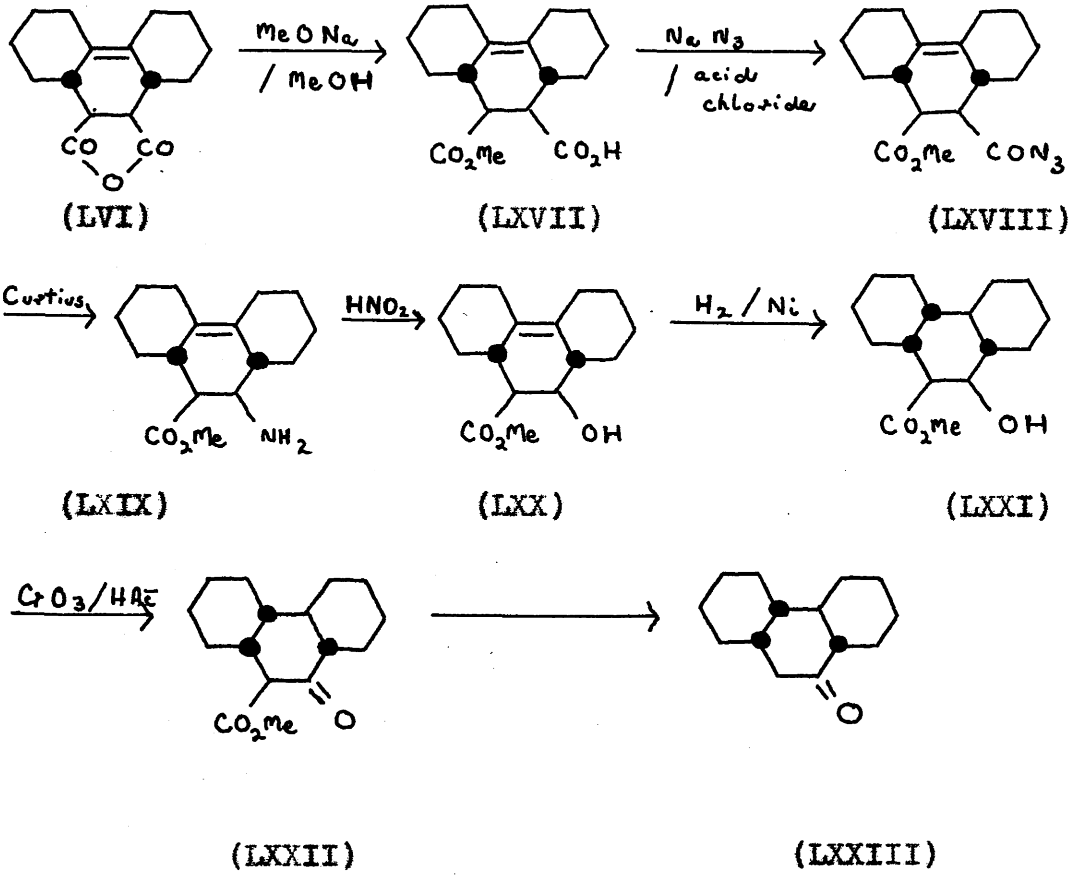


(LXVI)

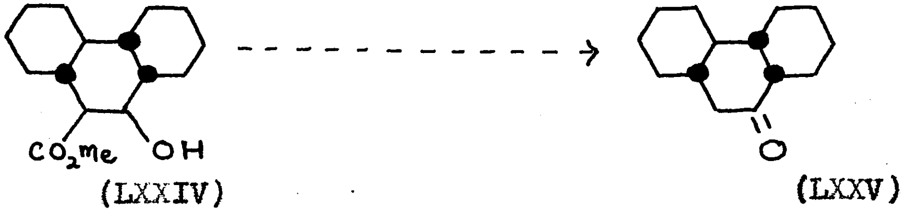
Dibromination of *cis*-*anti*-*trans*-perhydrophenanthrene-9:10-dicarboxylic acid by a modification of the Hell-Volhard-Zelinsky reaction(44) with thionyl chloride and bromine led to the formation of *cis*-*anti*-*trans*-9:10-dibromo-perhydrophenanthrene-9:10-dicarboxylic acid (LXVI), treatment of which with sodium iodide in acetone brought about the elimination of iodine from the unstable, intermediate di-iodo compound, and the production of the desired *cis*-*anti*-*trans*-Δ-9:10-dodecahydrophenanthrene-9:10-dicarboxylic acid (LXII; R = R' = COOH).

Oxidation of the latter with fuming nitric acid resulted in the isolation of *cis*-*anti*-*trans*-perhydrodiphenic acid, showing that (LXI - LXVI) all possess the *cis*-*anti*-*trans* configuration.

Conversion of the anhydride (LVI) into a 9-keto-perhydrophenanthrene appeared to be possible by a series of reactions such as the following scheme suggests:-



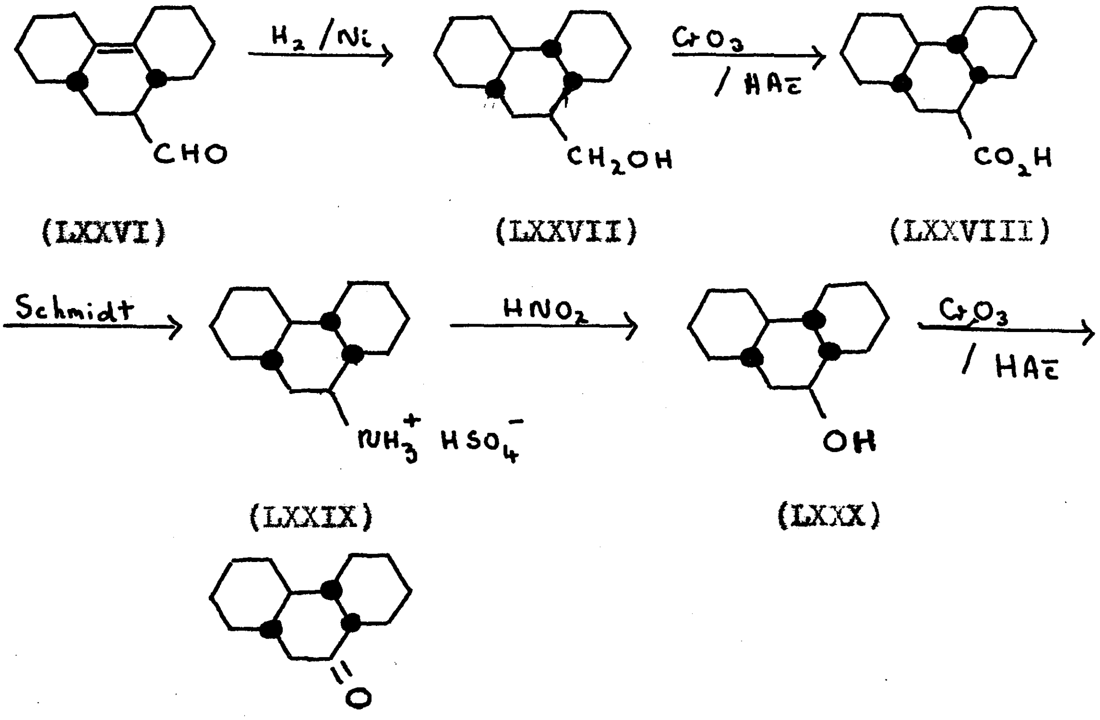
The final product might be expected to consist of a mixture of both the possible ketones corresponding to the *cis-anti-trans* form of the perhydrophenanthrene ring, viz., (LXXIII) and (LXXV), the latter of which would arise from the reduction over Raney nickel affording (LXXIV) rather than (LXXI)



The anhydride exhibited a remarkable resistance to the action of methanol from which it could be recrystallised, after prolonged refluxing, without the occurrence of any chemical change. On treatment with sodium methoxide, however, a quantitative yield of the Δ 12:13-dodecahydro-9-carbomethoxyphenanthrene-10-carboxylic acid (LXVII) was obtained. Attempts to convert the carboxyl into an amino grouping, however, met with little success. Although the acid ester reacted readily with thionyl chloride and the resulting acid chloride combined with sodium azide in the wet modification of the Curtius reaction(56) with the formation of Δ 12:13-dodecahydro-9-carbomethoxy-phenanthrene-10-carboxylic acid azide (LXVIII), the succeeding stage of heating with mineral acid to bring about rearrangement to the isocyanate and subsequent hydrolysis to the amine resulted almost entirely in the formation of an intractable gum. The latter, which would not solidify or distil, exhibited neither basic nor acidic properties, and is considered to represent a high-molecular weight polymer. A very small yield of the anticipated Δ 12:13-dodecahydro-9-amino-10-carbomethoxy-phenanthrene (LXIX) was obtained, but the quantity precluded the procedure as a feasible experimental method. Application of the one-stage Schmidt reaction(57) to the acid ester by heating with sodium azide and strong mineral acid again afforded a gum possessing properties similar to those of the Curtius product.

Since no homogeneous product could be obtained and tests for a primary amino group proved negative, the scheme had to be discarded and an alternative method sought.

A somewhat similar route had as its basis △ 12:13-dodecahydro-9-phenanthraldehyde (LXXVI), obtained from di-△ 1:1'-*cyclo*-hexene and acrolein. This might be treated as follows:-



(LXXVI) (LXXVII) (LXXVIII)

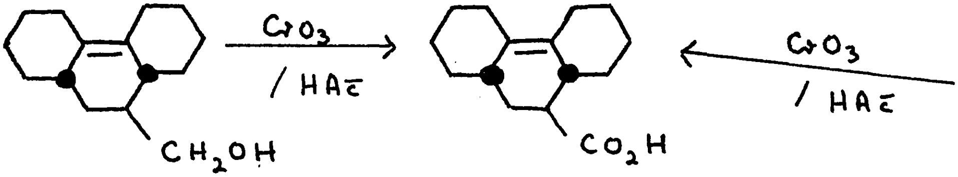
(LXXIX) (LXXX)

(LXXV)

This again should give rise to a mixture of ketones (LXXV) and (LXXIII) due to the formation of (LXXXI) rather than (LXXVII) on hydrogenation.

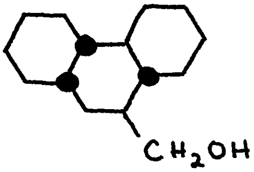
The initial disadvantage of this series of reactions as compared with the use of the anhydride, viz. the low yield

(20%) of the acrolein adduct claimed in the literature(40), was overcome, and up to 60% of the aldehyde (LXXVI) obtained. On catalytic hydrogenation over Raney nickel at high temperature and pressure, it was found possible to isolate three alcohols according to the activity of the catalyst employed. One of these, a solid m.p. 82-83°, was a Δ 12:13-dodecahydro-9-hydroxy methyl-phenanthrene (LXXXII), as was demonstrated by oxidation to the corresponding acid, identical with that obtained by oxidation of (LXXVI)

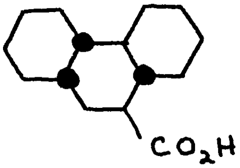


(LXXVI)

(LXXXII)



(LXXXI)



(LXXXII)

The other two afforded 3:5-dinitrobenzoates m.p. 139-140° and 149-150° respectively, the analysis results for which indicated that they were both derived from the 9-hydroxy methyl-perhydro-phenanthrene series. The production of two isomeric alcohols and the analogy of the hydrogenation of the Δ 12:13-dodecahydro-9:10-dicarbomethoxy-phenanthrene already described, render it extremely probable that reduction has given rise to a <u>cis-anti-trans</u> configuration (LXXVII ; LXXXI). Oxidation of these alcohols with chromic and acetic acids produced two carboxylic acids m.p. 193-195° and 162-164° respectively, which are tentatively formulated as *cis*-*anti*-*trans*-perhydrophenanthrene-9-carboxylic acids (LXXVIII LXXXII) since analytical results are not yet available. Application of the Schmidt reaction to the 195° isomer gave an amine sulphate which is considered to be one of the *cis*-*anti*-*trans*-9-amino-perhydrophenanthrene sulphates (e.g., LXXIX). Preliminary investigations of the replacement of the amino by a hydroxyl grouping suggest that treatment with nitrous acid does not bring about simple substitution under the conditions employed, as oxidation with chromic acid of the product yields a neutral material, showing ketonic activity, but having a melting point of 160-162°. This is far above that of the *cis*-*anti*-*trans*-9-keto-perhydrophenanthrene (m.p. 72°) described by Linstead(15), or, indeed, of any known 9-keto-perhydrophenanthrene. Oxidation of the ketone with fuming and concentrated nitric acids resulted in the isolation of a low melting solid which was not identified but which was clearly not a perhydrodiphenic acid. Lack of time, however, precluded the fuller investigation of the phenomenon.

Experimental.

Syntheses of trans-9-keto-1,2,3,4,9,10,11,12-octohydrophenanthrene.

1-Phenyl-1:3:-butadiene:

(a) From phenyl magnesium bromide and crotonaldehyde.

Phenyl magnesium bromide, made in the usual way from magnesium turnings (20 g.), bromobenzene (105 c.c.), anhydrous ether (334 cc.) and a crystal of iodine, was cooled to 0°C in an ice bath and a solution of crotonaldehyde (68 g.) in dry ether (210 cc.) added over a period of 2 hours with vigorous stirring. After standing, with stirring, at 0°C for a further four hours, decomposition of the Grignard complex was effected by pouring into 30% sulphuric acid (1.67 kg.) with frequent shaking without cooling, and the product, after addition of hydroquinone, was left overnight at room temperature. The sulphuric acid layer was separated, the ethereal solution washed with water till the washings were neutral to litmus, and the ether removed. When the residue was heated for an hour on the water bath more water was split off and the remaining oil was extracted with ether, separated, and the ethereal layer dried over anhydrous sodium sulphate. Fractionation of the residue in vacuo, after evaporation of the solvent, yielded impure 1-phenyl-1:3-butadiene (7 g.) b.p. 93-104°/13 mm. A second fraction b.p. 121-126°/13 mm., m.p. 70° was diphenyl (8.1 g.) while the remainder which would not distil, solidified on cooling to a hard, dark, glassy polymer.

<u>Note:</u> In the above and all subsequent distillations of 1-phenyl-1:3-butadiene, a trace of hydroquinone was added as an anti-polymerising agent. It is possible that better yields would be obtained if phenyl-β-naphthylamine were substituted.

If the Grignard complex from the above reaction was decomposed by pouring into ice and ammonium chloride, the ethereal layer separated, washed with water, and dried over anhydrous sodium sulphate, then removal of the ether and distillation of the residue yielded 1-phenyl-3-methyl allyl alcohol, b.p. 118-122°/12 mm. Yield = 84 g. (58%).

In a series of experiments 1-phenyl-3-methyl-allyl alcohol (10 g.) was slowly distilled in vacuo with various dehydrating agents (1 g.) and a little hydroquinone. The distillate was extracted with ether, dried over sodium sulphate, and the solvent evaporated. By fractionation of the residue, the 1-phenyl-1:3-butadiene could be isolated, b.p. 95-100°/14 mm.

Dehydrating Agent.	% Yield of diene
30% sulphuric acid	5.1
anhydrous oxalic acid	3.8
iodine	3.2
potassium bisulphate	23.2
phthalic anhydride	0.76.

(b) From methyl magnesium iodide and cinnamic aldehyde:

Methyl magnesium iodide from magnesium (5 g.), methyl iodide (30 g.) and dry ether (50 cc.) was cooled to 0°C in a freezing mixture and a solution of cinnamic aldehyde (20 g.) in ether (60 cc.) added over two hours with mechanical stirring. The mixture was allowed to stand at 0°C for one hour and was then decomposed by either of the following experimental procedures:-

(1). By pouring into water (200 cc.), concentrated sulphuric acid (12 cc.) and crushed ice. The ethereal extract was washed with sulphurous acid, twice with water, and dried over anhydrous sodium sulphate. After removal of the solvent the residue was distilled, the fraction coming over between 100° and 140° under 12 mm. pressure being collected. Slow redistillation of the latter with potassium bisulphate (0.5 g.), and subsequent treatment of the distillate in the usual manner gave rise to the cis-1-phenyl-1:3-butadiene, b.p. 90-95°/10 mm. Yield = 10 g. (50%). As in all cases where the cis-diene was produced, a considerable amount of resinification occurred.

(2). By gradual addition to a mixture of crushed ice and ammonium chloride solution. The ethereal layer was separated, washed copiously with water, and dried overnight with anhydrous potassium carbonate. After the ether had been distilled, the residual trans-methyl styryl carbinol came over at 132-133°/14 mm. Yield = 16 g. (73%).

The trans-carbinol (16 g.) was dissolved in anhydrous ether and dry hydrochloric acid gas was passed in till the solution was saturated, the mixture being immersed in an ice bath. When the reaction was complete, the ethereal solution was washed with dilute sodium hydroxide solution, then with water until neutral, and dried over anhydrous sodium sulphate. 1-methyl-3-phenyl allyl chloride (b.p. 120-130°/18 mm.) was obtained in almost quantitative yield on removal of the ether and subsequent distillation. After the chloride had been refluxed for five hours with anhydrous pyridine (50 cc.), the reaction mixture was taken up in ether, washed with dilute hydrochloric acid, then with water till neutral, and dried over sodium sulphate. Distillation of the ether, and fractionation of the residue in vacuo gave the trans-1-phenyl-1:3-butadiene, b.p. 78-83°/12 mm. Yield = 12.2 g. (60%). Very little polymerisation took place.

cis-2-phenyl- Δ 3-tetrahydrobenzaldehyde.

1-Phenyl-1:3-butadiene (58 g.) was treated with acrolein (24.3 g.) in dry benzene (75 cc.) with a little hydroquinone, and the solution refluxed on the water bath for eight hours. Cis-2-phenyl- Δ 3-tetrahydrobenzaldehyde was isolated as a colourless oil by distillation of the benzene and fractionation in vacuo. b.p. 152-154°/13 mm. Yield = 45.3 g. (55%).

cis-2-cyclo-hexyl-hexahydro-benzyl alcohol.

cis-2-phenyl- Δ 3-tetrahydrobenzaldehyde (7 g.) in ethanol (60 cc.) was heated with Raney nickel (~ 1 g.) to a temperature of 150-160° for 3 hours under an initial hydrogen pressure of 100 atmospheres. After filtration of the catalyst and removal of the ethanol, cis-2-cyclo-hexyl-hexahydrobenzyl alcohol came over as a colourless, viscous oil, b.p. 156-160°/10 mm., which slowly solidified to a crystalline mass of long needles, m.p. 62-63.5°. Yield = 4.7 g. (66%).

The 3:5-dinitrobenzoate recrystallised from ethanol m.p. 145-146°.

Found:		$C_{20}H_{26}O_6N_2$	
	C = 61.22%		C = 61.53%
	H = 6.35%.	requires	H = 6.66%.

The hydrogen phthalate recrystallised from benzene, m.p. 132-133°.

Found:		$C_{21}H_{28}O_4$	
	C = 72.87%		C = 72.96%
	H = 8.11%	requires	H = 8.14%.

cis-2-phenyl-hexahydrobenzyl alcohol.

cis-2-phenyl- Δ 3-tetrahydrobenzaldehyde (45 g.) in ethanol (400 cc.) under an initial hydrogen pressure of 100 atmospheres was heated with Raney nickel (~ 4 g.) to 90°

over a period of 1 hour. The catalyst was filtered, the ethanol removed, and the cis-2-phenyl-hexahydrobenzyl alcohol isolated by distillation in vacuo as a colourless, viscous liquid b.p. 160-162°/12 mm., which slowly solidified to a white, greasy, crystalline mass m.p. 58-63°. Yield = 35.4 g. (75%).

Preparation of phthalic anhydride derivative:

The cis-2-phenyl-hexahydrobenzyl alcohol (23.2 g.) was treated with phthalic anhydride (18.4 g.) in purified pyridine (13 cc.) and heated on the water bath for about 3 hours. After cooling, the reaction mixture was taken up in chloroform and washed successively with dilute hydrochloric acid, and with dilute sodium hydroxide solution to remove the excess of phthalic anhydride. (Note: In the presence of other sodium salts, the sodium derivative of the hydrogen phthalate is more soluble in chloroform or benzene than in alkali.) The chloroform solution was washed several times with water, and the combined aqueous extracts acidified with dilute hydrochloric acid, when the precipitated hydrogen phthalate was taken up in benzene. When the benzene solution had been washed several times with water and dried over anhydrous sodium sulphate, the solvent was removed and the pale yellow solid which remained was recrystallised from aqueous ethanol or benzene as small colourless needles, m.p. 145-146°.

Found: C = 74.35% $C_{21}H_{22}O_4$ C = 74.56%
H = 6.59% requires H = 6.51%.

Hydrolysis of the hydrogen phthalate was achieved by heating with a slight excess of 10% aqueous potassium hydroxide for 2 hours on the water bath. The regenerated cis-2-phenylhexahydrobenzyl alcohol was extracted from the mixture with ether, and the ethereal extract washed with water and dried over sodium sulphate. Removal of the solvent, followed by distillation in vacuo gave the pure cis alcohol, b.p. 162-163°/13 mm., which rapidly solidified to a white solid. Yield = 18.5 g. (80%).

The latter crystallised from light petroleum (b.p. 60-80°) as colourless prisms, m.p. 67-68°.

Found: C = 82.09% $C_{13}H_{18}O$ C = 82.11%
H = 9.40% requires H = 9.40%.

3:5 dinitrobenzoate.

To the cis-2-phenyl-hexahydrobenzyl alcohol (0.8 g.) was added purified 3:5-dinitrobenzoyl chloride (1 g.) in anhydrous benzene (10 cc.), and anhydrous pyridine (2 cc.), when a white solid was produced, and the mixture refluxed for 1 hour. The cooled product was taken up in ether and the solution washed successively with dilute hydrochloric acid, dilute sodium hydroxide solution and several times with water. After drying over anhydrous sodium sulphate and evaporation of the ether, the solid residue was crystallised from ethanol as long colourless needles, m.p. 108-109°.

Found:	C = 62.21%	$C_{20}H_{20}O_6N_2$	C = 62.30%
	H = 5.40%	requires	H = 5.21%
	N = 7.42%		N = 7.30%.

cis-2-phenyl-hexahydrobenzoic acid.

cis-2-phenyl-hexahydrobenzyl alcohol (2 g.) in glacial acetic acid (6 cc.) was cooled to 0° in an ice bath and chromic acid (1.6 g.) dissolved in glacial acetic acid (5 cc.) and water (2 cc.) added slowly with shaking. When addition was complete the mixture was allowed to stand at 0° for 30 minutes and then overnight at room temperature. The solution was then poured into excess water and the product extracted several times with ether. After washing with water, the ethereal solution was shaken repeatedly with dilute sodium hydroxide solution (10 cc. portions) until a test sample of the latter gave no precipitate with dilute acid. Acidification of the combined alkaline extracts with dilute hydrochloric acid gave a white solid which was filtered, washed with water and dried. Recrystallisation from light petroleum (b.p. 60-80°) produced small, white needles of *cis*-2-phenyl hexahydrobenzoic acid, m.p. 76-77° (lit. 76-77°).
Yield = 1.5 g. (70%).

S-benzyl-thiouronium salt m.p. 152-153° (lit. 152°).

trans-2-phenyl- Δ 3-tetrahydrobenzaldehyde.

cis-2-phenyl- Δ 3-tetrahydrobenzaldehyde (5 g.) was dissolved in ethanol (20 cc.) and a 10% solution of aqueous sodium hydroxide (1 cc.) added, a drop at a time, with constant shaking. Initially the mixture acquired a pale green colouration which gradually turned to a brownish-red. After standing for 2½ days at room temperature the product was poured into an excess of water, extracted with ether, and the ethereal solution washed several times with water. Drying over anhydrous sodium sulphate and removal of the solvent left an oil from which trans-2-phenyl- Δ 3-tetrahydrobenzaldehyde was obtained as a colourless mobile liquid by distillation in vacuo, b.p. 148-150°/10 mm. Yield = 4 g. (80%).

trans-2-phenyl-hexahydrobenzyl alcohol.

trans-2-phenyl- Δ 3-tetrahydrobenzaldehyde (4 g.) in ethanol (100 cc.) was heated for 1 hour at 90° with hydrogen at a pressure of 100 atmospheres, over a Raney nickel catalyst ($\sim$ 1 g.). When the nickel had been filtered and the ethanol distilled off, fractionation of the residue gave trans-2-phenyl-hexahydrobenzyl alcohol which came over as a colourless mobile oil, b.p. 155-160°/12 mm. Yield = 2.9 g. (70%).

On standing for some time the latter solidified to a greasy crystalline mass from which a white solid, m.p. 46-48° was isolated by pressing on a porous plate.

The hydrogen phthalate of the *trans*-alcohol was prepared in exactly analogous fashion to the *cis*-isomer and afforded clumps of small white needles from a mixture of benzene and light petroleum (b.p. 60-80°), m.p. 114-116°.

Found: C = 74.97% $C_{21}H_{22}O_4$ C = 74.56%
H = 6.60%   requires H = 6.51%.

3:5-Dinitrobenzoate:

Treatment of the *trans*-2-phenyl-hexahydrobenzyl alcohol with 3:5-dinitrobenzoyl chloride, in a similar manner as for the *cis* isomer, afforded a yellow oil which, on cooling and scratching, formed a hard, white solid. Repeated crystallisation of this from ethanol gave small, granular crystals of the 3:5-dinitrobenzoate, m.p. 81-83° with slight previous softening.

Found: C = 62.07% $C_{20}H_{20}O_6N_2$ C = 62.30%
H = 4.96%   requires H = 5.21%
N = 7.61%   N = 7.30%.

Hydrogenation of *cis*-2-phenyl- Δ 3-tetrahydrobenzaldehyde (5 g.) as previously described but with the addition of sodium hydroxide (0.25 g.), in an attempt to prepare the *trans*-2-phenyl-hexahydrobenzyl alcohol directly, gave rise, after working up in the usual way, to an alcohol, the 3:5-dinitrobenzoate of which had m.p. 108-109° either alone or when mixed with an authentic specimen of the 3:5-dinitrobenzoate of cis-2-phenyl-hexahydrobenzyl alcohol.

When the cis alcohol was heated to 150-160° with Raney nickel (~ 1 g.), no inversion occurred and the substance was recovered unchanged.

trans-2-phenyl-hexahydrobenzoic acid.

trans-2-phenyl-hexahydrobenzyl alcohol (0.5 g.) dissolved in glacial acetic acid (5 cc.) was cooled to 0° in a freezing mixture and a solution of chromic acid (0.4 g.) in a mixture of glacial acetic acid (5 cc.) and water (2 cc.) was added slowly with shaking. The solution was allowed to stand at room temperature overnight and then poured into excess water. The resulting mixture was extracted with ether and the ethereal solution washed first with water and then with several portions of dilute sodium hydroxide solution until no more acid was taken up. Acidification of the combined alkaline extracts with dilute hydrochloric acid solution gave a milky solution from which a powdery white solid slowly separated. This recrystallised from light petroleum (b.p. 60-80°) as colourless plates, m.p. 105-106° either alone or when mixed with an authentic specimen of trans-2-phenyl-hexahydrobenzoic acid. Yield = 0.37 g. (69%).

S-benzyl-thiouronium salt, m.p. 124-126° either alone or when mixed with the corresponding trans-2-phenyl-hexahydrobenzoic acid derivative.

trans-2-phenyl- Δ 3-tetrahydrobenzoic acid.

(a). Oxidation of cis-2-phenyl- Δ 3-tetrahydrobenzaldehyde with chromic acid.

cis-2-phenyl- Δ 3-tetrahydrobenzaldehyde (5 g.) dissolved in glacial acetic acid (25 cc.), was mixed with chromic acid (2 g.) in glacial acetic acid (10 cc.) and water (4 cc.). Heat was generated, and the reactants were warmed on the water bath for 30 minutes. After cooling, the solution was poured into water and taken up with ether. The ethereal layer was washed successively with water, and then three 15 cc. portions of dilute sodium hydroxide solution, when the alkaline extract was carefully acidified with dilute hydrochloric acid. The trans-2-phenyl- Δ 3-tetrahydrobenzoic acid was extracted from the solution with ether, washed several times with water, and the ethereal layer finally dried over anhydrous sodium sulphate. Removal of the solvent gave the acid as a pale oil which solidified, on cooling and scratching, to a colourless solid, and which deposited colourless needles from light petroleum (b.p. 60-80°) m.p. 99-102° (lit. m.p. 100-102°). Yield = 1.0 g. (19%).

(b). Oxidation of *cis*-2-phenyl-Δ3-tetrahydrobenzaldehyde with silver nitrate and sodium hydroxide.

cis-2-phenyl-Δ3-tetrahydrobenzaldehyde (5 g.) was added to a suspension of silver nitrate (5 g.) in 75% ethanol (12 cc.) and cooled to 0° in an ice bath. A solution of 10% aqueous sodium hydroxide (30 cc.) was slowly run in, with mechanical stirring, over a period of 2 hours, ensuring that the temperature did not rise above 5°C. When the addition was complete, the mixture was stirred for a further 15 minutes and then allowed to stand at room temperature for 2½ days. The mixed precipitate of silver and silver oxide was filtered off, washed with a little ethanol, and the filtrate extracted several times with ether.

After the ethereal solution had been washed with water, dried over anhydrous sodium sulphate, and the ether removed, *trans*-2-phenyl-Δ3-tetrahydrobenzaldehyde (0.7 g.) was obtained, the identity of which was established by hydrogenation and formation of the 3:5-dinitrobenzoate of the alcohol produced. The latter crystallised from ethanol as colourless granular rosettes, m.p. 80-81° either alone or when mixed with an authentic specimen of the 3:5-dinitrobenzoate of *trans*-2-phenyl-hexahydrobenzyl alcohol.

The aqueous layer from the ethereal extraction was cooled in ice and carefully acidified with dilute hydrochloric acid, constant stirring being maintained during the addition. A dark oil separated which, after long scratching, copious washing by decantation, and standing overnight in the refrigerator, gave a hard brown solid which was filtered and dried. This consisted of the crude *cis* and *trans*-2-phenyl- Δ3-tetrahydrobenzoic acids (4.5 g.).

Fractional crystallisation from light petroleum (b.p. 60-80°) with charcoal gave the pure *trans*-2-phenyl- Δ3-tetrahydrobenzoic acid (2.1 g.) m.p. 102-103° (lit. 100-102°) and the *cis*-2-phenyl- Δ3-tetrahydrobenzoic acid (1.8 g.) m.p. 120-121° (lit. m.p. 122°).

Isomerisation reactions of *cis*-2-phenyl- Δ3-tetrahydro benzaldehyde after formation of the bisulphite compound.

The bisulphite compound was formed in the usual way as a white, bulky solid from *cis*-2-phenyl- Δ3-tetrahydrobenzaldehyde, and portions decomposed as follows:-

Sodium carbonate:

The bisulphite compound (5 g.) was heated to boiling with a 10% solution of aqueous sodium carbonate (40 cc.) for 2 hours and, after cooling, the liberated aldehyde extracted with ether. After the ethereal layer had been washed with water, dried over sodium sulphate and the solvent removed, the aldehyde came over as a colourless, mobile liquid on fractionation in vacuo. b.p. 158-163°/14 mm. Yield = 2.2 g. (75%).

Hydrogenation, in the manner described, over Raney nickel, gave the corresponding trans-2-phenyl-hexahydrobenzyl alcohol. b.p. 160-165°/18 mm. Yield = 1.5 g. The 3:5-dinitrobenzoate had m.p. 78-80° which was not depressed on admixture of an authentic specimen of the corresponding trans-2-phenyl-hexahydrobenzyl alcohol derivative.

When the bisulphite compound (41 g.) was refluxed with a 10% solution of aqueous sodium carbonate for only 45 minutes and then worked up as above, 19 g. (72%) of the aldehyde was regenerated, b.p. 150-155°/14 mm.

Reduction over Raney nickel led to the formation of cis-2-phenyl-hexahydrobenzyl alcohol (18.5 g.) b.p. 158-160°/10 mm.; 3:5-dinitrobenzoate m.p. 100-104°.

Hydrochloric acid.

Warming the bisulphite compound (5 g.) for 10 minutes with dilute hydrochloric acid (30 cc.), and extraction of the regenerated aldehyde as described above, afforded a mobile liquid b.p. 164-168°/18 mm. Yield = 2.5 g. Hydrogenation of this material (2 g.) resulted in the isolation of trans-2-phenyl-hexahydrobenzyl alcohol, b.p. 158-162°/10 mm. Yield = 1.5 g. 3:5-dinitrobenzoate, m.p. 79-82°.

Formalin.

Repetition of the preceding process, in which formalin (20 cc.) was substituted for the dilute hydrochloric acid, gave an aldehyde, b.p. 152-156°/14 mm. (2.3 g.) which on subsequent reduction was converted into cis-2-phenyl-hexahydrobenzyl alcohol (1.6 g.). b.p. 160-162°/12 mm. 3:5-dinitrobenzoate, m.p. 108-109°.

cis-1,2,3,4,10,11-hexahydrofluorene-9-one.

(a) Cyclisation of cis-2-phenyl-hexahydrobenzoic acid with anhydrous hydrogen fluoride.

cis-2-phenyl-hexahydrobenzoic acid (0.5 g.) was treated with an excess of liquid hydrogen fluoride in a platinum crucible and left overnight at room temperature. After the excess of hydrogen fluoride had been evaporated, the residue was taken up in ether, washed several times with water, dilute sodium carbonate solution, and water again, and finally dried over anhydrous sodium sulphate. When the ether had been removed by distillation, a yellow-brown oil was left which formed a semicarbazone (0.6 g.) m.p. 204° either alone or when mixed with an authentic specimen of the semicarbazone of 1,2,3,4,10,11-hexahydrofluorene-9-one.

Similar treatment of the trans-2-phenyl-hexahydrobenzoic acid (0.5 g.) resulted in the recovery of the unchanged starting material.

(b). Cyclisation with concentrated sulphuric acid.

cis-2-phenyl-hexahydrobenzoic acid was ring closed to the cis-1,2,3,4,10,11-hexahydrofluorene-9-one, by heating for a few seconds with concentrated sulphuric acid on the water bath(18). (I.)

cis-2-phenyl-hexahydrobenzoic acid (0.25 g.) was heated with concentrated sulphuric acid (3 c.c.) and glacial acetic acid (1 cc.) for 15 minutes, then diluted with water and made alkaline with sodium hydroxide solution. A neutral fraction was obtained which was extracted with ether and which formed the semicarbazone, m.p. 205°. (II.)

When the trans-2-phenyl-hexahydrobenzoic acid (1 g.) was subjected to treatment under the conditions of (I) or (II) no neutral product was obtained and no acid was recovered.

The use of concentrated sulphuric acid (2 cc.) and glacial acetic acid (2 cc.) again gave no neutral fraction but the trans acid (0.05 g.) was recovered. Further dilution of the concentrated sulphuric acid by glacial acetic acid gave complete recovery of the trans-2-phenyl-hexahydrobenzoic acid.

(c). Cyclisation via the Friedel-Crafts reaction.

cis-2-phenyl-hexahydrobenzoic acid (1 g.) was heated to reflux with thionyl chloride until the evolution of hydrogen chloride had ceased. The excess thionyl chloride was removed by distillation in vacuo, followed by evaporation with several successive portions of benzene, and the residue dissolved in dry carbon disulphide (25 cc.) This solution was added dropwise to a mixture of anhydrous aluminium chloride (1 g.) in dry carbon disulphide (25 cc.) and cooled in a freezing mixture to 0°C. Evolution of hydrogen chloride set in immediately and, when addition was complete, the reactants were allowed to stand overnight at room temperature, then poured carefully on to a mixture of crushed ice and hydrochloric acid. The carbon disulphide layer was separated, washed first with dilute sodium carbonate solution, then with water, and dried over anhydrous sodium sulphate. Removal of the solvent yielded a dark oil which, on heating with semicarbazide hydrochloride and pyridine in methanol, gave the semicarbazone of cis-1,2,3,4,10,11-hexahydrofluorene-9-one as yellow powdery crystals from ethanol, m.p. 205-206°. Yield = 1.05 g.

Similar treatment of the trans-2-phenyl-hexahydrobenzoic acid afforded the identical semicarbazone, m.p. 204-206°

cis-1,2,3,4,10,11-hexahydrofluorene.

(a). From cis-2-phenyl-hexahydrobenzyl alcohol.

A suspension of phosphorous pentachloride (14.8 g.) in purified chloroform (30 cc.) was treated a little at a time, with constant shaking, with a solution of cis-2-phenyl-hexahydrobenzyl alcohol (11.4 g.) in chloroform (20 cc.). A vigorous reaction occurred which was completed by refluxing the mixture on the water bath for 2 hours. When the chloroform and phosphorus oxychloride had been removed in vacuo a pale yellow, mobile liquid came over, b.p. 120-130°/13 mm. Shaking with dilute sodium carbonate solution, and redistillation in vacuo after the usual treatment gave cis-1,2,3,4,10,11-hexahydrofluorene as a pale oil, b.p. 120-123°/11 mm. Yield = 7 g. (67%). $n_D^{18.5} = 1.5547$.

Found:	C = 90.42%	Calculated for	C = 90.61%
	H = 9.20%	$C_{13}H_{16}$	H = 9.39%

(b). From trans-2-phenyl-hexahydrobenzyl alcohol.

trans-2-phenyl-hexahydrobenzyl alcohol (1 g.) in dry chloroform was slowly added, as above, to phosphorus pentachloride (1.3 g.) in dry chloroform (2.5 cc.) and the reaction carried out as already described for the cis-alcohol. The first few drops of distillate, after removal of the solvent and phosphorus oxychloride had b.p. 140-150°/12 mm., but the residue in the flask and the succeeding distillate darkened rapidly to a deep-violet colour. Redistillation, after shaking with dilute sodium carbonate solution, gave the pale, mobile hydrocarbon, b.p. 122-125°/13 mm.; $n_D^{18.5} = 1.5541$. Yield = 0.5 g. (55%).

The same hydrocarbon was obtained when trans-2-phenyl-hexahydrobenzyl chloride (1 g.) was slowly distilled in vacuo with phosphorus pentachloride, and the distillate redistilled after shaking with dilute sodium carbonate solution.
Yield = 0.5 g. (60%).

Dehydrogenation of hydrocarbons from (a) and (b).

Platinic oxide (0.1 g.)(45) was reduced with hydrogen in an alcoholic suspension to the metallic platinum and an alcoholic solution of the hydrocarbon (0.5 g.) added. The alcohol was removed and the apparatus swept out with a current of carbon dioxide. The mixture was heated in a metal bath to a temperature of 260° for 2 hours and the hydrogen evolved was measured. (Theoretical volume of gas = 195 cc. at N.T.P.; Actual volume = 185 cc. at N.T.P.). The residue was cooled, extracted with boiling ethanol, and filtered. On cooling, colourless crystals of fluorene were obtained, m.p. 112-113° either alone or when mixed with an authentic specimen.

trans-2-phenyl-hexahydrobenzyl chloride.

trans-2-phenyl-hexahydrobenzyl alcohol (5.0 g.) dissolved in dry chloroform (25 cc.) was added slowly, with shaking, to a suspension of phosphorus pentachloride (6.5 g.) in dry chloroform (13 cc.). Reaction was completed by heating for two hours, when the solid had all gone into solution and the evolution of gas had ceased. The chloroform and most of the phosphorus oxychloride were removed on the water bath, in vacuo, and the residue vigorously shaken automatically with an excess of dilute sodium hydroxide solution, for two hours. After dilution with water, the mixture was taken up with ether, washed with water, dried over anhydrous sodium sulphate, and the ether removed by distillation. Fractionation of the residue in vacuo gave trans-2-phenyl-hexahydrobenzyl chloride as a pale, mobile oil, b.p. 145-146°/12 mm. Yield = 4.3 g. (78%).

Found:		Calculated for	
	C = 74.47%		C = 74.76%
	H = 8.03%	$C_{13}H_{17}Cl$	H = 8.21%

trans-2-phenyl-hexahydrobenzyl cyanide.

trans-2-phenyl-hexahydrobenzyl chloride (4 g.), dissolved in an equal volume of ethanol, was added slowly, with shaking, to a solution of sodium cyanide (1.2 g.) in water (3 cc.) and the mixture heated to reflux on the water bath. A very dark colour gradually developed and solid began to separate out, on to the sides of the flask. After three hours' boiling, the alcohol was distilled off and the residue diluted with water. The product was extracted with ether, washed with water, dried over anhydrous sodium sulphate, and the solvent evaporated. trans-2-phenyl-hexahydrobenzyl cyanide came over as a mobile, yellow oil on fractionation of the residue. b.p. 152-156°/13 mm. : Yield = 2.5 g. (48%).

Found:		$C_{14}H_{17}N$	
	C = 84.16%		C = 84.37%
	H = 8.72%	requires	H = 8.60%
	N = 7.05%		N = 7.03%.

trans-2-phenyl-*cyclo*-hexyl-acetic acid.

(a). Hydrolysis of *trans*-2-phenyl-hexahydrobenzyl cyanide.

trans-2-phenyl-hexahydrobenzyl cyanide (5 g.) was treated with a solution of sodium hydroxide (1.4 g.) in water (1.8 cc.) and ethanol (5 cc.), and the mixture refluxed on the water bath till the evolution of ammonia had ceased (about 24 hours). The ethanol was distilled off, the solution diluted with water, and any unchanged cyanide removed by extraction with ether. Careful acidification of the aqueous layer with dilute hydrochloric acid resulted in the separation of a dark oil which rapidly solidified and could be crystallised from light petroleum (b.p. 60-80°) as colourless plates of *trans*-2-phenyl-*cyclo*-hexyl-acetic acid m.p. 111-112°, either alone or when mixed with an authentic specimen. Yield = 4.3 g. (79%).

(b). Grignard reaction on *trans*-2-phenyl-hexahydrobenzyl chloride.

trans-2-phenyl-hexahydrobenzyl chloride (3.65 g.) in ether (12 cc.) was treated with magnesium turnings (0.6 g.) which had been previously heated with iodine. Reaction commenced on addition of a drop of methyl iodide and was completed by refluxing the mixture for about 8 hours, after which a rapid stream of carbon dioxide was bubbled through the refluxing solution for a further 2 hours, when a brown oil separated. The reaction mixture was poured on to ice and dilute hydrochloric acid, and the separated ethereal layer, after washing with water, shaken with several portions of dilute sodium carbonate solution. The combined alkaline extracts were carefully acidified with dilute hydrochloric acid and the oil which was initially deposited soon solidified. Subsequent filtration, drying and recrystallisation from light petroleum (b.p. 60-80°) gave a white crystalline solid, m.p. 110-112° not depressed on admixture with authentic trans-2-phenyl-cyclo-hexyl acetic acid. Yield = 3.1 g. (82%).

trans-9-keto-1,2,3,4,9,10,11,12-octohydrophenanthrene.

trans-2-phenyl-cyclo-hexyl-acetic acid (2 g.) was cyclised with concentrated sulphuric acid (10 cc.) by the method of Blumenfeld(18), when the trans-9-keto-as-octohydrophenanthrene obtained was recrystallised from methanol as colourless plates, m.p. 96° (lit. 96°). Yield = 1.5 g.

Fluorenone was prepared by the oxidation of fluorene with chromic acid and acetic acid(46).

2-phenyl-benzoic acid.

Potassium hydroxide (150 g.) and water (3 cc.) were heated in a nickel basin in an oil bath to about 180°, and fluorenone (50 g.) was carefully added through a slot in the crucible lid, in small portions, with an automatic nickel stirrer, so that the temperature of the melt did not rise above 200°. The almost black mixture was dissolved in about 4 litres of hot water and the dark, oily solution nearly acidified with concentrated hydrochloric acid. Filtration of the mixture through a pad of animal charcoal gave a clear, pale-yellow, solution which was carefully acidified with concentrated hydrochloric acid, using the minimum amount of stirring necessary to ensure mixing. A white, opalescent solution was obtained which, on standing overnight, gave a white powdery deposit of 2-phenyl-benzoic acid (38 g.), m.p. 109-112°.

By the Fischer-Speir method the acid (35 g.) gave the corresponding methyl ester, b.p. 163°/12 mm.
Yield = 28 g.

Hydrolysis of the ester in the usual way, with aqueous alcoholic potassium hydroxide, gave the pure 2-phenyl-benzoic acid (25 g.), m.p. 114-115°.

trans-2-phenyl-hexahydrobenzoic acid.

2-phenyl benzoic acid (10 g.) was dissolved in amyl alcohol (600 cc.) and heated to reflux with automatic stirring. Sodium (60 g.) was added as rapidly as possible to the hot solution and, when this had dissolved, heating and stirring were continued for another 15 minutes. The colourless solution was allowed to cool until a yellow colour became apparent and then, when still warm, hot water (600 cc.) was cautiously added down the condenser. The amyl alcohol was removed by steam distillation, the residue acidified with dilute hydrochloric acid, and volatile impurities steam-distilled off. On cooling the crude trans -2-phenyl-hexahydrobenzoic acid solidified, m.p. 91-96°. Yield = 8 g.

Recrystallisation from light petroleum (b.p. 60-80°) gave colourless prisms, m.p. 104° (lit. 105°).

trans-2-phenyl-cyclo-hexyl acetic acid.

trans-2-phenyl-benzoic acid (2.4 g.) by the method of Gutsche and Johnson(19) gave the trans-2-phenyl-benzoyl chloride, m.p. 80-82° (lit. m.p. 80-83°). Yield = 2.4 g.

A mixture of the acid chloride in dry ether (10 cc.) was treated with a solution of diazo methane (from N-nitroso-methyl urea (7 g.)(47)). After standing overnight at room temperature the ether and excess diazo methane were removed and the yellow ω -diaza-trans-2-phenyl-hexahydro-aceto-phenone (m.p. 99-101° (d)) was obtained as an amorphous solid.

The diazo ketone was dissolved in methanol (30 cc.) and a slurry of silver oxide (from 8.1 cc. of 10% silver nitrate) in methanol (10 cc.) was added slowly with constant stirring to the refluxing solution. A vigorous evolution of nitrogen occurred and addition was complete after about half an hour, when the mixture was heated for a further hour, then filtered, and the methanol removed by distillation.

The residue was refluxed with a solution of potassium hydroxide (3 g.) in water (20 cc.) for 3 hours. On cooling, the homogeneous solution solidified, and acidification with dilute hydrochloric acid yielded a white sticky gum which gradually hardened to a yellow mass after freezing and scratching (m.p. 95-105°). Recrystallisation from light petroleum (b.p. 60-80°) gave colourless plates of *trans*-2-phenyl-*cyclo*-hexyl-acetic acid m.p. 110-111° (lit. m.p. 112°). Yield = 2 g. (77%).

trans-9-keto-*as*-octohydrophenanthrene.

The *trans*-2-phenyl-*cyclo*-hexyl acetic acid (2 g.) was cyclised by treatment with anhydrous hydrogen fluoride in the usual way and the ketone crystallised from methanol. Yield = 1.6 g., m.p. 96° (lit. 96°).

N-bromo-succinimide was obtained from succinimide(50) by the action of bromine in alkali(32).

1-phenyl-*cyclo*-hexanol was prepared from *cyclo*-hexanone (49.2 g.) and phenyl magnesium bromide(48).

Dehydration of this with anhydrous oxalic acid(49) gave 1-phenyl-cyclo-hexene (37 g.).

3-Bromo-2-phenyl-cyclo-hexa-1-ene.

N-Bromo-succinimide (34 g.) was suspended in purified carbon tetrachloride (100 cc.) and 1-phenyl-cyclo-hexene (30.2 g.) was added slowly with shaking. The mixture was warmed gently till a vigorous reaction set in, when the flame was removed. After the initial reaction had subsided, a gentle reflux was maintained for a further 2 hours, protecting the reactants from moisture with a calcium chloride tube, when the product was cooled and left overnight in the refrigerator. The succinimide was filtered off and the last traces removed by washing the filtrate several times with ice-cold dilute sodium hydroxide and then with water. After drying over anhydrous sodium sulphate, the carbon tetrachloride was removed and the residue fractionated in vacuo.

A pale, mobile oil b.p. 120°/12 mm. was mostly 1-phenyl-cyclo-hexene (13 g.) which slowly deposited crystals of diphenyl (1.5 g.) m.p. 70°, but any attempt to distil the residue resulted in decomposition and the evolution of hydrogen bromide, even on the high vacuum pump.

N-Bromo-succinimide as a dehydrogenating agent.

When 1-phenyl-cyclo-hexene (20 g.) was mixed with N-bromo-succinimide (11.9 g.) and allowed to stand for a few minutes, a spontaneous and violent reaction occurred with a copious evolution of hydrogen bromide.

Distillation of the mixture, after heating on the water bath for an hour to complete the reaction, yielded a pale mobile oil b.p. 120-125°/13 mm. which solidified to a greasy crystalline mass. When this was pressed on a porous plate diphenyl (10 g.) was isolated, m.p. 70-71°.

3 (2-phenyl-*cyclo*-hexenyl) malonic ester.

The residue (14. 5 g.) from the bromination of 1-phenyl *cyclo*-hexene as above was warmed with a suspension of sodio-diethyl malonate, made in the usual way by shaking diethyl malonate (2.78 g.) with a solution of sodium (1.41 g.) in ethanol (19.6 cc.) until a thick curd was formed. A vigorous reaction took place and a light brown solid separated. After the mixture had been refluxed on the water bath for a further 2½ hours most of the ethanol was removed, water (50 cc.) was added to dissolve the sodium bromide, and the dark oil which separated was extracted with ether. When the ethereal solution had been washed with water, dried over anhydrous sodium sulphate, and the solvent removed, the residue was distilled in vacuo. A small, initial fraction was unchanged diethyl malonate, which was followed by a pale yellow, viscous liquid with a slight fluorescence. The latter was the desired 3 (2-phenyl-*cyclo*-hexenyl) malonic ester. b.p. 158-160°/0.3 mm. Yield = 10 g. (52% on crude starting material).

Found: C = 71.65% $C_{19}H_{24}O_4$ C = 71.90%
H = 8.06% requires H = 7.94%

3 (2-phenyl-*cyclo*-hexenyl) malonic acid.

3 (2-phenyl-*cyclo*-hexenyl)malonic ester (5 g.) was refluxed for 4 hours with potassium hydroxide (2 g.) in water (2 cc.) and ethanol (10 cc.). The ethanol was removed by distillation and the residue, after dilution with water (25 cc.), taken up in ether. Careful acidification of the aqueous solution at 0°C with dilute hydrochloric acid and constant stirring gave rise to a sticky brown precipitate, which, on prolonged washing with cold water was converted into a cream-coloured solid (m.p. 135-145° ( )). Several re-crystallisations with charcoal from aqueous ethanol afforded 3 (2-phenyl-*cyclo*-hexenyl) malonic acid as white, powdery plates, m.p. 157-159° (d.). Yield = 2.88 g. (68%).

Found: C = 68.75% $C_{15}H_{16}O_4$ C = 68.94%
H = 6.51% requires H = 6.56%

3 (2-phenyl-*cyclo*-hexenyl) acetic acid.

3 (2-phenyl-*cyclo*-hexenyl) malonic acid (1.5 g.) was heated in an oil bath at 160° for 30 minutes, until the evolution of gas, which was, at first, very vigorous, had ceased. The flask was cooled and the residual gum triturated with light petroleum (b.p. 60-80°), when a light brown solid

was obtained. The latter formed clumps of small needles from light petroleum (b.p. 60-80°), which, after several recrystallisations, had m.p. 116-118° with slight previous softening. Yield = 0.9 g. (71%).

Found:	C = 77.31%	$C_{14}H_{16}O_2$	C = 77.60%
	H = 7.30%	requires	H = 7.41%.

Hydrogenation.

(a). With platinic oxide catalyst.

3 (2-phenyl-*cyclo*-hexenyl) acetic acid (0.2 g.) was dissolved in purified glacial acetic acid (20 cc.) and platinic oxide (0.01 g.) was added. The mixture was shaken for three hours with hydrogen at room temperature and atmospheric pressure, when one mole of hydrogen was absorbed. When the catalyst had been filtered off, and the solvent evaporated, the gummy residue was triturated with light petroleum (b.p. 60-80°) and a white solid, m.p. 160-165° was produced. Recrystallisation from benzene gave the colourless *cis*-2-phenyl-*cyclo*-hexyl-acetic acid m.p. 168-169° (lit. 168-170°). Yield = 0.18 g.

Cyclisation with concentrated sulphuric acid by the method of Cook(17) gave a liquid ketone. This latter (36 mg.) was dissolved in pyridine (2 cc.), a solution of semicarbazide hydrochloride (0.02 g.) added, and the mixture heated on the water bath for 1 hour. The solid obtained on cooling was recrystallised from ethanol, m.p. 194-196°. (Semi-carbazone of cis-9-keto-as-octohydrophenanthrene has m.p. 194-196°).

When the acetic acid in the hydrogenation was replaced by ethanol (20 cc.) no reduction was observed and the starting material was recovered unchanged.

(b). With sodium in amyl alcohol.

3 (2-phenyl-cyclo-hexenyl) acetic acid (0.48 g.) was dissolved in dry amyl alcohol (30 cc.) and the solution heated to boiling. Sodium (2 g.) was added in thin slices over a period of about 15 minutes so that a vigorous reflux was maintained. Heating was continued for another 30 minutes, when water (30 cc.) was cautiously added, and the amyl alcohol removed by steam distillation. Acidification of the cooled solution with dilute hydrochloric acid produced a white opalescence and, on standing overnight, the suspension precipitated a creamy-brown solid (0.45 g.). When this was fractionally crystallised from benzene and light petroleum (b.p. 60-80°) cis-2-phenyl-cyclo-hexyl-acetic acid (8 parts) m.p. 168-169°, and trans-2-phenyl-cyclo-hexyl-acetic acid (1 part), m.p. 109-110°, were produced.

Ring closure of the trans- acid in the usual way gave trans-9-keto-as-octohydrophenanthrene, m.p. 95-96°, which was also obtained from the corresponding cis-ketone by isomerisation with aluminium chloride(6).

Hydrogenation of trans-9-keto-as-octohydrophenanthrene-9-hydroxy-trans-as-octohydrophenanthrene (m.p. 89-91°).

trans-9-keto-1,2,3,4,9,10,11,12-octohydrophenanthrene (0.5 g.) in purified ethanol (30 cc.) was treated with platinic oxide (0.1 g.) and hydrogen at atmospheric pressure and 15°C. After shaking for 3-4 hours the theoretical quantity (one mole) of hydrogen was absorbed. The catalyst was filtered, the solvent removed, and the resulting oily residue solidified by cooling and scratching, when a hard, white mass was obtained. Two recrystallisations from n-hexane gave 9-hydroxy-trans-1,2,3,4,9,10,11,12-octohydrophenanthrene, m.p. 89-91° (0.32 g.) as colourless short needles, together with a small amount of the stereoisomer m.p. 105-106°.

Stereoisomer, m.p. 105-106°.

trans-9-keto-as-octohydrophenanthrene (0.5 g.) was shaken in purified ethanol (50 cc.) with hydrogen over a platinic oxide catalyst (0.01 g.) at atmospheric pressure and 18°C for 23 hours. Filtration of the catalyst and evaporation of the ethanol gave a solid residue which was recrystallised from n-hexane, m.p. 105-106°, and was stereoisomeric with the alcohol obtained above.

Found:	C = 83.02%	Calculated for	C = 83.12%
	H = 8.86%	$C_{14}H_{18}O$	H = 8.97%

Oxidation.

9-hydroxy-trans-as-octohydrophenanthrene (m.p. 105-106°) (0.17 g.) was dissolved in glacial acetic acid (2.2 cc.) and cooled in an ice bath. To this was slowly added a mixture of chromic acid (0.07 g.) in 80% acetic acid (0.5 cc.) and the mixture allowed to stand overnight at room temperature. On pouring into water a white solid separated which was filtered, washed and dried. Recrystallisation from methanol gave a white solid, m.p. 96°, which was not depressed by admixture of an authentic specimen of trans-9-keto-as-octohydrophenanthrene.

Perhydrogenation of trans-9-keto-as-octohydrophenanthrene.

Trans-9-keto-as-octohydrophenanthrene (2 g.) was dissolved in purified ethanol (50 cc.) and platinic oxide (0.1 g.) added. When the mixture was shaken with hydrogen at room temperature and atmospheric pressure, initial reduction was rapid, but soon became slow and further portions of catalyst were added over four days, by which time the total amount present was 0.5 g., and the hydrogen uptake was 3.95 moles. Filtration of the catalyst and removal of the solvent, in the usual way, resulted in the production of a colourless, mobile oil which did not solidify and which, on distillation in vacuo, came over almost quantitatively as a clear liquid, b.p. 160-163°/11 mm. This was probably either *cis*-*syn*-*trans*-perhydrophenanthrene or a mixture of the latter with the *cis*-*anti*-*trans* form.

Found: C = 87.60% $C_{14}H_{24}$ C = 87.43%
H = 12.42% requires H = 12.58%.

The residue, after distillation, solidified and recrystallisation from n-hexane gave a few colourless needles m.p. 131-132° which are probably identical with one of the stereoisomeric *cis*-*anti*-*trans*-perhydro-9-phenanthrols (m.p. 133°) isolated by Linstead(15).

---

o-Iodobenzoic acid was prepared by diazotisation of anthranilic acid and decomposition of the diazonium salt with potassium iodide(51). Light brown needles from glacial acetic acid, m.p. 160-161°.

Esterification by the Fischer-Speir process with methanol gave the o-iodomethyl benzoate, b.p. 146°/15 mm., as a pale yellow oil.

Dimethyl diphenate was obtained from o-iodomethyl benzoate by a slight modification of the method due to Ullmann(52), as white crystals, m.p. 74-75°, from methanol.

Esterification of diphenic acid.

Diphenic acid (1 g.) was dissolved in 100% sulphuric acid and added, all at once, to a large excess of methanol cooled in ice. When the initial violent reaction was over most of the methanol was removed and the residue taken up in ether. After washing the ethereal solution successively with water, dilute sodium hydroxide solution, and again with water, the solvent was removed and the solid residue crystallised from methanol, m.p. 75°. Yield = 0.6 g.

trans-*anti*-*trans*-perhydrodimethyldiphenate.

Dimethyl diphenate (34.5 g.) in a suspension of *cyclo*-hexane (400 cc.) was heated with Raney nickel (~ 4 g.) and hydrogen to 230° and 180 atmospheres pressure for 3 hours. The catalyst was filtered, the solvent removed and the residue fractionated in vacuo, when *trans*-*anti*-*trans*-perhydrodimethyl diphenate was collected as a colourless, mobile oil, b.p. 155-158°/2 mm. Yield = 29 g.

Hydrolysis.

Trans-*anti*-*trans*-perhydrodimethyl diphenate (29 g.) was refluxed for 15 hours with potassium hydroxide (15 g.) in methanol (100 cc.) and water (20 cc.). The methanol was removed and the residue, after dilution with water (100 cc.), taken up in ether. Careful acidification of the aqueous layer with dilute hydrochloric acid gave a white precipitate of trans-anti-trans-perhydro diphenic acid, which was recrystallised from light petroleum (b.p. 60-80°), m.p. 245° (lit. 247°). Yield = 22 g.

Trans-anti-trans-2-carboxy-2'-carbomethoxy-perhydro diphenyl.

Trans-anti-trans-perhydrodiphenic acid (10 g.) was refluxed for 20 hours with purified acetic anhydride (100 cc.). Removal of the excess anhydride in vacuo left a viscous gum which would not crystallise probably owing to the difficulty of removing the last traces of solvent. This residue was heated for 2 hours with a solution of sodium (3.14 g.) and methanol (150 cc.) and then left overnight at room temperature. On distillation of the methanol, a solid was left which was treated with water, filtered, and the aqueous solution acidified with dilute hydrochloric acid. The crude half-ester separated as a gum which trituration with benzene converted into a light brown solid, m.p. 130-138°. Recrystallisation from aqueous acetic acid gave small colourless needles of trans-anti-trans-2-carboxy-2'-carbomethoxy perhydro diphenyl, m.p. 152-154°. Yield = 8.5 g. (81%).

Found: C = 67.30% $C_{15}H_{24}O_4$ C = 67.10%
H = 8.86% requires H = 8.95%.

trans-anti-trans-2-carbomethoxy-2'-carbomethoxymethyl-perhydrodiphenyl.

trans-anti-trans-2-carboxy-2'-carbomethoxy perhydrodiphenyl (2 g.) dissolved in dry benzene (8 cc.) was treated with thionyl chloride (4 cc.). A vigorous evolution of hydrogen chloride commenced in the cold and the reaction was completed by warming on the water bath for 2 hours. The benzene and thionyl chloride were removed in vacuo and the last traces of the latter excluded by two further evaporations with small quantities of benzene.

A solution of the gummy residue in anhydrous ether (15 cc.) was slowly added, over a period of about half an hour, to an ethereal solution of diazomethane (from 10 g. of N-nitrosomethyl urea(47)) at 0°, and the mixture left first for 30 minutes in the ice bath, then overnight at room temperature. Removal of the ether and excess diazomethane by evaporation at room temperature under reduced pressure afforded a pale yellow, sticky solid, which decomposed with evolution of a gas on heating above 25°C.

This crude diazoketone was dissolved in methanol (20 cc.) and a slurry of silver oxide (from 2 cc. of 10% silver nitrate) in methanol (10 cc.) was added slowly with automatic stirring. As the temperature was gradually raised, a vigorous reaction, shown by the copious evolution of nitrogen, took place and was completed by refluxing for 2 hours on the water bath. The silver and silver oxide precipitates were filtered off and the excess methanol removed by distillation. On distillation of the residue, trans-anti-trans-2-carbomethoxy-2'-carbomethoxy methyl-perhydrodiphenyl came over as a pale, rather viscous liquid, b.p. 155-157°/0.8 mm. Yield = 1.8 g. (82%).

Found:		Calculated for	
C = 68.71%		$C_{17}H_{28}O_4$	C = 68.90%
H = 9.40%			H = 9.46%

trans-anti-trans-9-keto-perhydrophenanthrene (see (14)).

trans-anti-trans-2-carbomethoxy-2'-carbomethoxy methyl-perhydrodiphenyl (1.8 g.) was refluxed with atomised sodium (0.3 g.) in dry benzene (25 cc.) until all the sodium had gone into solution (about 10 hours). The reaction mixture was cautiously poured on to crushed ice and very dilute hydrochloric acid and the product extracted with further quantities of benzene. Drying of the benzene extract over anhydrous sodium sulphate and removal of the solvent left a brown, mobile oil which gave a pale purple colour with a drop of ferric chloride solution.

This residue was refluxed with 60% sulphuric acid (10 cc.) for 10 hours, cooled, and extracted with ether. When the ethereal solution had been washed with water, dried, and the solvent distilled off, the residual oil was fraction-

ated in vacuo and collected, b.p. 128-131°/2.8 mm.
Yield = 0.7 g.

Preparation of the oxime in pyridine and ethanol gave colourless needles from ethanol, m.p. 225-227° (lit. 226-227°).

Oxidation of the ketone (0.3 g.) with a mixture of concentrated and fuming nitric acids(11) gave trans-anti-trans-perhydrodiphenic acid (30 mg.), m.p. 244-246° (lit. 247°) from aqueous acetic acid.

Attempted Hydrogenation of Diphenic Acid.

Catalyst	Solvent	Pressure (atm.)	Temp.	Time
PtO_2	Acetic acid	1	17	4 days
*PtO_2	Acetic acid	10	30	2 days
PtO_2	Ethanol + 1% HCl	1	17	5 days
*PtO_2	Ethanol + 1% HCl	25	30	2 days.

*Performed in high pressure steel bomb.

No reduction was observed in any of the above cases, or when similar experiments were performed on the dimethyl ester.

1:1'-Dihydroxy- Δ 1:1'-di-cyclo-hexene was prepared by pinacolic reduction of cyclo-hexanone (364 cc.)(40). Yield = 80 g., white needles from light petroleum (b.p. 100-120°), m.p. 128-130°. Dehydration with 10% sulphuric acid(40) gave di- Δ 1:1'-cyclo-hexene as a pale oil. Yield = 62.4 g. b.p. 85-87°/0.8 mm.

Δ12:13-Dodecahydrophenanthrene-9:10-dicarboxylic acid anhydride.

Di- Δ1:1'-*cyclo*-hexene (30 g.) and maleic anhydride (18 g.) were refluxed with benzene (60 cc.) for 2 hours. After the mixture had been allowed to stand overnight, the solvent was removed and an oily, crystalline mass left behind. This was washed several times with light petroleum (b.p. 100-120°) and crystallised from methanol as colourless needles, m.p. 119-120° (lit. 112.5-123.5°). Yield = 22 g. (46%).

Found:		Calculated for	
	C = 73.66%		C = 73.70%
	H = 7.79%	$C_{16}H_{20}O_3$	H = 7.69%

The anhydride was recovered unchanged after it had been refluxed for 3 hours with excess methanol and crystallised twice from the same solvent.

Attempted Hydrogenation.

The anhydride (2 g.) was dissolved in the solvent (20 cc.) and the catalyst (0.1 g.) was added. The mixture was shaken with hydrogen at 18°C and atmospheric pressure.

Catalysts and solvents used included:- platinic oxide in acetic acid or ethanol, and palladium black in ethanol. No reduction was observed in any of these cases or when similar experiments were performed on the free Δ12:13-dodecahydrophenanthrene-9:10-dicarboxylic acid.

Δ 12:13-Dodecahydro-9:10-dicarbomethoxy-phenanthrene.

A mixture of Δ 12:13-dodecahydrophenanthrene-9:10-dicarboxylic acid anhydride (22 g.) and 5% sodium hydroxide solution (250 cc.) was heated till the anhydride dissolved. The solution was filtered, cooled to 0°C in an ice bath, carefully acidified with dilute hydrochloric acid, and the semi-solid gummy precipitate which separated recrystallised from glacial acetic acid as colourless prisms, m.p. 240-241° (lit. 242°). Yield = 15 g.

This acid was dissolved in dry ether (100 cc.) and treated, a few c.c. at a time, with stirring, with an ethereal solution of diazo methane (from 30 g. of N-nitroso-methyl urea) until the solution was no longer decolourised. The product was allowed to stand for 2 hours, the ether and excess diazo methane evaporated, and the white, solid residue recrystallised from methanol as colourless needles, m.p. 110-111°. Yield = 16 g.

Found:	C = 70.76%	$C_{18}H_{26}O_4$	C = 70.60%
	H = 8.66%	requires	H = 8.56%.

cis-anti-trans-9:10-dicarbomethoxy-perhydrophenanthrene.

Δ 12:13-Dodecahydro-9:10-dicarbomethoxy-phenanthrene (12 g.) in *cyclo*-hexane (80 cc.) was heated with hydrogen over Raney nickel (~ 2 g.) to 190° and 140 atmospheres pressure for 2 hours. Filtration of the catalyst and removal of the solvent gave a colourless solid which was recrystallised several times from methanol as short needles, m.p. 119-120°. Yield = 9 g. (74%).

Found: C = 70.1% $C_{18}H_{28}O_4$ C = 70.06%
H = 9.15% requires H = 9.12%.

Attempted oxidation with selenium dioxide.

cis-*anti*-*trans*-9:10-dicarbomethoxy-perhydrophenanthrene (0.5 g.) was mixed with resublimed selenium dioxide (0.18 g.) and heated in a sealed tube at 200° for 10 hours. The dark product was taken up in ether and the insoluble material filtered off. Evaporation of the ethereal solution and crystallisation of the solid residue from methanol yielded a pale solid m.p. 116-118° either alone or on admixture with the starting material.

cis-*anti*-*trans*-9-bromo-9:10-dicarbomethoxy-perhydrophenanthrene

cis-*anti*-*trans*-9:10-dicarbomethoxy-perhydrophenanthrene (0.36 g.) in dry carbon disulphide (10 cc.) was treated with bromine (0.19 g. = 1 mole) in dry carbon disulphide (1 cc.). A crystal of iodine was added and the whole refluxed for 2 days. The solvent was evaporated and the sticky gum which was left, triturated with light petroleum (b.p. 60-80°), when a pale amorphous solid was obtained. Recrystallisation from aqueous ethanol gave a granular solid, m.p. 99-101° with previous softening. Yield = 0.14 g. (31%).

cis-anti-trans-9:10-dicarbomethoxy-perhydrophenanthrene-9:10-dipyridinium dibromide.

cis-anti-trans-9:10-dicarbomethoxy-perhydrophenanthrene (147 mg.) dissolved in chloroform (1.8 cc.) was treated dropwise, at room temperature, with a solution of bromine (77 mg.) in chloroform (1 cc.), and two drops of pyridine added. The mixture was heated gently for a few minutes and then allowed to stand overnight at room temperature, when long orange-red needles were deposited (70 mg.) (A). Filtration and removal of the chloroform gave a pale yellow solid (100 mg.) (B).

(A) recrystallised from ethyl acetate as pale, orange needles, m.p. 101-103°. These were soluble in warm water to give a neutral solution and, when treated with nitric acid and silver nitrate, a pale yellow precipitate of silver bromide was obtained. Hence (A) was formulated as cis-anti-trans-9:10-dicarbomethoxy-perhydrophenanthrene-9:10-dipyridinium dibromide.

Found: N = 4.79%. $C_{28}H_{36}O_4N_2$ requires: N = 4.59%.

When the solid (B) was recrystallised from ethanol colourless needles were obtained, m.p. 121-122° either alone or on admixture of the starting material.

If the ester (228 mg.) in dry chloroform (2 cc.) was treated as above with an excess of bromine (224 mg.) in chloroform (2 cc.) and an excess of pyridine (0.4 cc.) an almost quantitative yield of the red dibromide was obtained.

Omission of the pyridine from the above experiments resulted in the recovery, without loss, of the unchanged *cis*-*anti*-*trans*-9:10-dicarbomethoxy-perhydrophenanthrene.

cis-*anti*-*trans*- Δ 9:10-Dodecahydrophenanthrene-9:10-dicarboxylic acid.

cis-*anti*-*trans*-9-bromo-9:10-dicarbomethoxy perhydrophenanthrene (0.14 g.) was treated with a solution of potassium hydroxide (0.1 g.) in ethanol (5 cc.) and water (1 cc.), and the mixture refluxed on the water bath for 4 hours. The ethanol was removed by distillation, the residue taken up in water, and the solution filtered. Cautious acidification of the filtrate with dilute hydrochloric acid gave a brownish solid which was recrystallised from light petroleum (b.p. 60-80°) as colourless flaky crystals, m.p. 167-168° either alone or when mixed with a specimen of *cis*-*anti*-*trans*- Δ 9:10-dodecahydrophenanthrene-9:10-dicarboxylic acid obtained by an independent synthesis.
Yield = 50 mg. (45%).

cis-*anti*-*trans*-9:10-dibromoperhydrophenanthrene-9:10-dicarboxylic acid.

cis-*anti*-*trans*-9:10-dicarbomethoxy-perhydrophenanthrene (1.14 g.) was refluxed for 12 hours with a solution of potassium hydroxide (0.7 g.) in water (1 cc.) and methanol

(10 cc.). The excess methanol was distilled off on the water bath and the dark, solid residue dissolved in hot water and filtered. On cooling the filtrate a grey crystalline precipitate of the sodium salt of the corresponding dicarboxylic acid separated out, which was filtered and rendered acid with an excess of dilute hydrochloric acid solution. The white precipitate so obtained was recrystallised from a mixture of benzene and light petroleum (b.p. 60-80°) as colourless needles, m.p. 164-166°. Yield = Theoretical.

Found:	C = 68.31:	$C_{16}H_{24}O_4$	C = 68.57%
	H = 8.76%	requires	H = 8.57%.

This acid (320 mg.) was treated with a large excess (3 cc.) of purified thionyl chloride and heated on the water bath for about 2 hours until the evolution of hydrogen chloride had ceased. An excess (0.3 cc.) of bromine was added and the mixture refluxed for a further 3 hours, during which an evolution of hydrogen bromide occurred. After the solution had been left overnight at room temperature, the excess thionyl chloride and bromine were distilled off, finally in vacuo, water (10 cc.) added to the dark residue, and the whole boiled for 2 hours. The dark brown granular solid, obtained on cooling, was filtered off, dried, and crystallised from aqueous methanol, when pale prisms of <u>cis</u>-<u>anti</u>-<u>trans</u>-9:10-dibromo-perhydrophenanthrene-9:10-dicarboxylic acid, m.p. 188-192° (d) were produced. Yield = 360 mg. (72%).

Found: C = 43.61% $C_{16}H_{22}O_4Br_2$ C = 43.80%
H = 5.32% requires H = 5.02%.

Finkelstein Reaction.

cis-*anti*-*trans*-9:10-dibromo-perhydrophenanthrene-9:10-dicarboxylic acid (210 mg.), dissolved in analar acetone (12 cc.), was mixed with sodium iodide (210 mg.) and refluxed for 2 hours, when a deep reddish-black solution was produced. This was cooled, poured into water, and the dark gum which separated extracted from the aqueous solution with ether. The ethereal extract was washed with water, dried over anhydrous sodium sulphate, and the solvent removed. Trituration of the dark gum with a little methanol gave a pale yellow amorphous solid, free of halogen, which crystallised from light petroleum (b.p. 60-80°) as colourless flakes, m.p. 167-168°, either alone or when mixed with a specimen of *cis*-*anti*-*trans*- Δ 9:10-dodecahydrophenanthrene-9:10-dicarboxylic acid obtained from an independent synthesis. Yield = 60 mg. (45%).

Oxidation of *cis*-*anti*-*trans*-perhydrodiphenic acid.

The latter acid (125 mg.) was heated on the water bath for 5 hours with 3 cc. of a mixture of concentrated nitric acid (3 cc.) and fuming nitric acid (6 cc.). After cooling, the solution was poured on to crushed ice, when a white flocculent solid separated which was filtered, washed with water, and dried. Recrystallisation from light petroleum (b.p. 60-80°) gave colourless prisms, m.p. 202-203° (lit. 206°). Yield = 7 mg.

Δ12:13-dodecahydro-9-carbomethoxyphenanthrene-10-carboxylic acid.

Δ12:13-dodecahydrophenanthrene-9:10-dicarboxylic acid anhydride (2 g.) was treated with a solution of sodium methoxide (0.415 g.) in methanol (10 cc.) and refluxed for 3 hours. After the methanol had been removed, the pale yellow sticky oil which was left was acidified with an excess of dilute hydrochloric acid, when a gummy solid was produced which slowly solidified on cooling and scratching to a hard, white mass. This was recrystallised from aqueous acetic acid as colourless needles, m.p. 136-137°. Yield = Theoretical.

Found: C = 69.83% $C_{17}H_{24}O_4$ C = 69.82%
H = 8.41% requires H = 8.27%.

Δ12:13-dodecahydro-9-carbomethoxyphenanthrene-10-carboxylic acid azide.

Δ12:13-dodecahydro-9-carbomethoxy-phenanthrene-10-carboxylic acid (2.2 g.) was dissolved in dry benzene (10 cc.) and purified thionyl chloride (7 cc.) added. The reaction commenced in the cold and was completed by refluxing on the water bath for 4 hours. Excess thionyl chloride and benzene were removed by distillation, the last traces of the former being eliminated by successive addition and removal in vacuo of 5 cc. portions of benzene and light petroleum (b.p. 60-80°). The pure acid chloride was left as a viscous red gum.

A solution of the latter in dried analar acetone (25 cc.) was cooled in an ice bath and a mixture of sodium azide (1 g.) in water (3 cc.) was added, drop by drop, with mechanical stirring, over a period of 30 minutes. The resulting dark suspension was stirred in the freezing mixture for a further 15 minutes and water (50 cc.) added dropwise from a burette. A sticky, dark brown gum separated which solidified, on standing overnight in the refrigerator, to a pale brown mass. This was filtered, washed and dried. Decomposes at 80-83° with evolution of a gas. Yield = 1.83 g.

Azide (0.0915 g.) gives off 64.2 cc. nitrogen at N.T.P. $C_{17}H_{23}O_3N_3$ requires 64.6 cc. nitrogen at N.T.P.

Curtius Reaction on the azide.

The acid azide (1.6 g.) in dry toluene (6 cc.) was heated on the water bath for 2 hours until the vigorous evolution of nitrogen had ceased. To the solution was added, all at once, concentrated hydrochloric acid (6 cc.) and heating continued for a further two hours, when water (15 cc.) was added, and the benzene layer separated, washed with water, and dried over sodium sulphate. Evaporation of the solvent yielded a dark, sticky gum (1.3 g.) insoluble in acid or alkali, which would not solidify or distil.

The aqueous acid layer was neutralised with dilute sodium hydroxide solution, taken up in ether, and the ethereal extract washed with water, dried over anhydrous sodium sulphate, and the solvent removed. A sticky, orange residue was left which, on trituration with light petroleum (b.p. 60-80°), yielded a pale yellow solid (30 mg.). This recrystallised from ethyl acetate as colourless needles of Δ 12:13-dodecahydro-9-amino-10-carbomethoxy-phenanthrene, m.p. 149-150°

Found:	C = 72.61%	$C_{16}H_{25}O_2N$	C = 72.95%
	H = 9.23%	requires	H = 9.56%.

Schmidt Reaction.

Δ 12:13-dodecahydro-9-carbomethoxy phenanthrene-10-carboxylic acid (2 g.) was dissolved in dry chloroform (15 cc.) and concentrated sulphuric acid (6 cc.) was added. The mixture was heated on the water bath to 45°C and sodium azide (1.54 g. = 3 moles) was introduced, a little at a time, so that the temperature remained constant. A brisk evolution of nitrogen occurred and vigorous mechanical stirring was maintained during addition and for a further 30 minutes. Water (25 cc.) was added, and the mixture carefully neutralised with ammonia solution (S.G. = 0.88). When the organic layer had been washed with water, dried and the chloroform distilled, a light-brown, sticky residue was obtained, possessing properties similar to those of the material obtained previously in the Curtius reaction, and from which no homogeneous product could be isolated.

Δ 12:13-Dodecahydro-9-phenanthraldehyde.

Di- Δ 1:1'-*cyclo*-hexene (46.5 g.), acrolein (30 g.), and dry benzene (40 cc.) were mixed together with a little hydroquinone and refluxed on an oil bath for 64 hours. Removal of the solvent and fractionation of the residue gave unchanged di- Δ 1:1'-*cyclo*-hexene (20 g.), b.p. 85-100°/0.8 mm and Δ 12:13-dodecahydro-9-phenanthraldehyde, b.p. 129-131°/0.8 mm. as a colourless mobile liquid.

Yield = 34 g. (55%).

cis-anti-trans (?)-9-hydroxymethyl-perhydrophenanthrene.

Δ 12:13-dodecahydro-9-phenanthraldehyde (25 g.) in ethanol (250 cc.) was heated over Raney nickel (~ 5 g.) to 190° for 3 hours, with hydrogen at a pressure of 190 atmospheres. The catalyst was filtered, the solvent removed, and the residue distilled in vacuo. A small, initial fraction (A) of a colourless mobile oil was collected, b.p. 95-105°/0.2 mm. (3.2 g.) which was followed by a viscous liquid which hardened to a sticky glass, b.p. 125-135°/0.2 mm. (B).

Yield = 18.3 g.

(B) afforded a 3:5-dinitrobenzoate as pale, short needles from ethanol, m.p. 138-140°.

Found: C = 63.53% $C_{22}H_{28}O_6N_2$ C = 63.46%
H = 6.64% requires H = 6.73%.

(A) rapidly solidified to a greasy solid which was pressed on a porous plate. Recrystallisation from light petroleum (b.p. 60-80°) gave Δ 12:13-dodecahydro-9-hydroxymethyl phenanthrene as small, colourless needles, m.p. 82-83°.

3:5-dinitrobenzoate formed white prisms from methanol, m.p. 106-107°.

When the above process was repeated using a much more active Raney nickel catalyst, the adduct (6.4 g.), gave a very viscous oil, b.p. 133-135°/0.3 mm. Yield = 5.6 g.

3:5-dinitrobenzoate gave small, colourless, flocculent needles from a large volume of ethanol, m.p. 149-150°.

Found: C = 63.44% $C_{22}H_{28}O_6N_2$ C = 63.46%
H = 6.43% requires H = 6.73%.

cis-anti-trans (?) perhydrophenanthrene-9-carboxylic acid.

cis-anti-trans (?)-9-hydroxymethyl perhydrophenanthrene (15.6 g.) in glacial acetic acid (100 cc.) was treated a little at a time with a solution of chromic acid (12 g.) in glacial acetic acid (100 cc.) and water (15 cc.), shaking between each addition. Heat was developed and the mixture allowed to stand overnight at room temperature. The solution was poured into water, extracted with ether, and the ethereal layer washed successively with water, and then several portions of dilute sodium hydroxide solution. Acidification of the alkaline extract gave the crude acid. When the alcohol whose 3:5-dinitrobenzoate had m.p. 138-140° was employed, the acid obtained was recrystallised from a large volume of light petroleum (b.p. 60-80°) as colourless prisms, m.p. 193-195°. Yield = 9.5 g.

When the isomeric alcohol was employed, the acid produced was readily soluble in cold light petroleum (b.p. 60-80°) but could be crystallised from aqueous acetic acid m.p. 158-164°.

Analyses Results not available.

Schmidt reaction on 195° isomer.

The acid (7.0 g.) was dissolved in dry chloroform (53 cc.), concentrated sulphuric acid (25 cc.) added, and the mixture heated on the water bath to 50°C. Sodium azide (5.3 g.) was slowly added, with automatic stirring, while the temperature was maintained at 50°C. When addition was about two thirds complete, an evolution of gas commenced, which soon became vigorous, and stirring was continued at 50°C until this had died down (about 4 hours). The mixture was carefully diluted and the chloroform layer separated. On cooling, a pale, granular solid separated from the latter, which was filtered and recrystallised from the same solvent, m.p. 114-116°. Yield = 5.5 g. (60%).

Analysis results for this compound are not available, but in view of the fact that it contains nitrogen and sulphur, is soluble in warm water to give an acidic solution, and gives a positive carbylamine and sulphate anion test, it is formulated as a cis-anti-trans (?)-9-amino-perhydrophenanthrene sulphate.

Attempted replacement of the amino- by the hydroxyl group.

The amine sulphate (3.5 g.) was dissolved in warm water (50 cc.) to which dilute sulphuric acid (5 cc.) had been added, and the clear solution treated with sodium nitrite (4 g.) in water (10 cc.), a little at a time, with shaking between each addition. A vigorous effervescence occurred and a pale brown oil separated, which, after standing overnight at room temperature, became a sticky solid. Trituration with light petroleum (b.p. 60-80°) yielded a pale brown solid (1.7 g.).

Oxidation of the latter with chromic acid (0.8 g.) in glacial acetic acid in the usual way at 0°C afforded a neutral liquid (0.6 g.), which gave an orange-red precipitate with 2:4-dinitrophenylhydrazine, and which, on trituration with light petroleum (b.p. 60-80°), produced a colourless solid. This was recrystallised from light petroleum (b.p. 60-80°), m.p. 160-162°.

The ketone (0.25 g.), hydroxylamine hydrochloride (0.09 g.), methanol (3 cc.), and pyridine (3 cc.) were kept at room temperature for 18 hours and then poured into water. The oily precipitate which separated was extracted with ether, the solution washed with water, dried over sodium sulphate, and the solvent removed. Trituration of the oily residue with methanol gave a white solid, m.p. 203-205° with previous softening.

Attempted formation of a perhydrodiphenic acid.

The ketone (0.25 g.) was heated on the water bath for 30 minutes, with a mixture of fuming nitric acid (2 cc.) and concentrated nitric acid (2 cc.). A vigorous effervescence occurred, and the solution, after standing overnight at room temperature, was poured into water, and the pale-yellow solid precipitate filtered, washed and dried. Yield = 72 mg. This softened over a wide range and finally decomposed at about 80°C.

Δ12:13-dodecahydrophenanthrene-9-carboxylic acid.

This was obtained in the usual way by oxidation of either Δ12:13-dodecahydro-9-phenanthraldehyde or the corresponding alcohol, with chromic acid in glacial acetic acid at 0°C. It formed colourless needles from light petroleum (b.p. 60-80°), m.p. 178-180°.

Bibliography.

(1). Sachse, Ber., 1890, 23, 1363.

(2). Mohr, J.pr.chim., 1918 II , 98, 315,
Ber., 1922, 55, 230.

(3). Hückel, Ann., 1927, 451, 109,
ibid, 1933, 502, 99.

(4). Bastiansen and Hassel, Nature, 1946, 765.

(5). Linstead, Chem. & Ind., 1937, 56, 510.

(6). Cook, McGinnis & Mitchell, J.Chem.Soc., 1944, 286.

(7). Linstead & Walpole, J.Chem Soc., 1939, 842.

(8). Ipatiew, Jakowlew & Rakitin, Ber., 1908, 41, 996.

(9).Pinkney, Nesty, Wiley & Marvel, J.Amer.Chem.Soc., 1936, 58, 972.

(10). Cook, Hewett & Robinson, J.Chem.Soc., 1939, 168.

(11). Linstead, Whetstone & Levine, J.Amer.Chem.Soc., 1942, 64, 2014.

(12). Linstead & Davis, J.Amer.Chem.Soc., 1942, 64, 2006.

(13). Marvel & White, J.Amer.Chem.Soc., 1940, 62, 2739.

(14). Bhattacharyya, J.Ind.Chem.Soc., 1945, 22, 85.

(15). Linstead & Whetstone, J.Chem.Soc., 1950, 1428.

(16). Shoppee, Ann.Rep., 1946, XLIII, 200.

(17). Cook, Hewett & Lawrence, J.Chem.Soc., 1936, 71.

(18). Blumenfeld, Ber., 1941, 74, 524.

(19). Gutsche & Johnson, J.Amer.Chem.Soc., 1946, 68, 2239

(20). Coyner & Ropp, J.Amer.Chem.Soc., 1947, 69, 2231.

(21). Crummitt & Becker, J.Amer.Chem.Soc., 1948, 70, 149.

(22). Burton, J.Chem.Soc., 1929, 455.

(23). Klages, Ber., 1904, 37, 2301.

(24). Muskat & Herrman, J.Amer.Chem.Soc., 1931, 53, 252.

(25). Diels & Alder, Ber., 1929, 62, 2085.

(26). Alder, Vagt & Vogt, Ann., 1949, 565, 135.

(27). Lehmann & Paashe, Ber., 1935, 68, 1146.

(28). Cook & Hewett, J.Chem.Soc., 1936, 62.

(29). Gutsche, J.Amer.Chem.Soc., 1948, 70, 4150.

(30). Meek, Lorenzi & Cristol, Ibid, 1949, 71, 1830.

(31). Ropp & Coyner, Ibid, 1949, 71, 1832.

(32). Ziegler, Späth, Schaf, Schumann & Winklemann,
Ann., 1942, 551, 80.

(33). Djerassi, Chem.Rev., 1948, 43, 271.

(34). Barnes, J.Amer.Chem.Soc., 1948, 70, 145.

(35). Newman & Farbman, Ibid, 1944, 66, 1550.

(36). Linstead & Doering, Ibid, 1942, 64, 1991.

(37). Adams & Marshall, Ibid, 1928, 50, 1970.

(38). Organic Syntheses, Vol.7, p.30.

(39). Fieser & Johnson, J.Amer.Chem.Soc., 1939, 61, 168.

(40). Gruber & Adams, Ibid, 1935, 57, 2555.

(41). Durland & Adkins, Ibid, 1938, 60, 1501.

(42). Astin, Newman & Riley, J.Chem.Soc., 1933, 391.

(43). Fieser & Dunn, J.Amer.Chem.Soc., 1936, 58, 572.

(44). Schwenk & Papa, Ibid, 1948, 70, 3626.

(45). Adams, Org.Syn., Coll.Vol.I, 463.

(46). Huntress, Hershberg & Cliff, J.Amer.Chem.Soc., 1931, 53, 2720.

(47). Bachmann & Struve, "Organic Reactions", Vol.I, 50.

(48). Auwers, Ber., 1915, 48, 1207.

(49). Le Brazidec, Bull.soc.chim., 1915, 4 , 17, 101.

(50). Organic Syntheses, Coll.Vol.II, 562.

(51). Cohen & Raper, J.Chem.Soc., 1904, 85, 1272.

(52). Ullmann, Ann., 1904, 332, 70.

(53). Vocke, Ibid, 1934, 508, 1.

(54). Fieser, "Experiments in Organic Chemistry", p.232.

(55). Durland & Adkins, J.Amer.Chem.Soc., 1937, 59, 135.

(56). Smith, "Organic Reactions", Vol.III, p.373.

(57). Wolff, Ibid, p.307.

(58). Harper, Ann.Rep., 1948, XLV, 182.

(59). Barton, Quarterly Reviews, 1949, III, 60.