SYNTHESIS AND REACTIONS OF CYCLOHEXENONES.

by

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I should like to express my sincere gratitude to Dr. D. Leaver for his kindness and friendly guidance and assistance throughout the course of this work.

I should also like to take this opportunity of thanking Professor E. L. Hirst, C.B.E., F.R.S., for his interest, and for the provision of laboratory facilities.

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INTRODUCTION.

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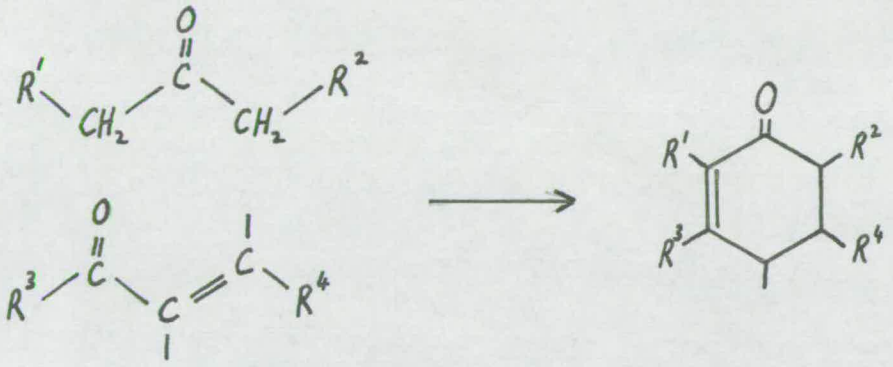
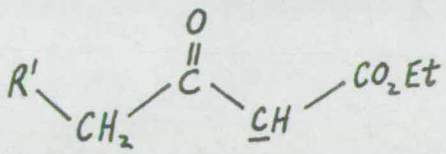
Two methods for the synthesis of cyclohexenones have been widely used in steroid and terpene chemistry. One method is the reaction between an unsaturated ketone and the enolate of a ketone. This process involves a Michael addition followed by aldol condensation and elimination of water.

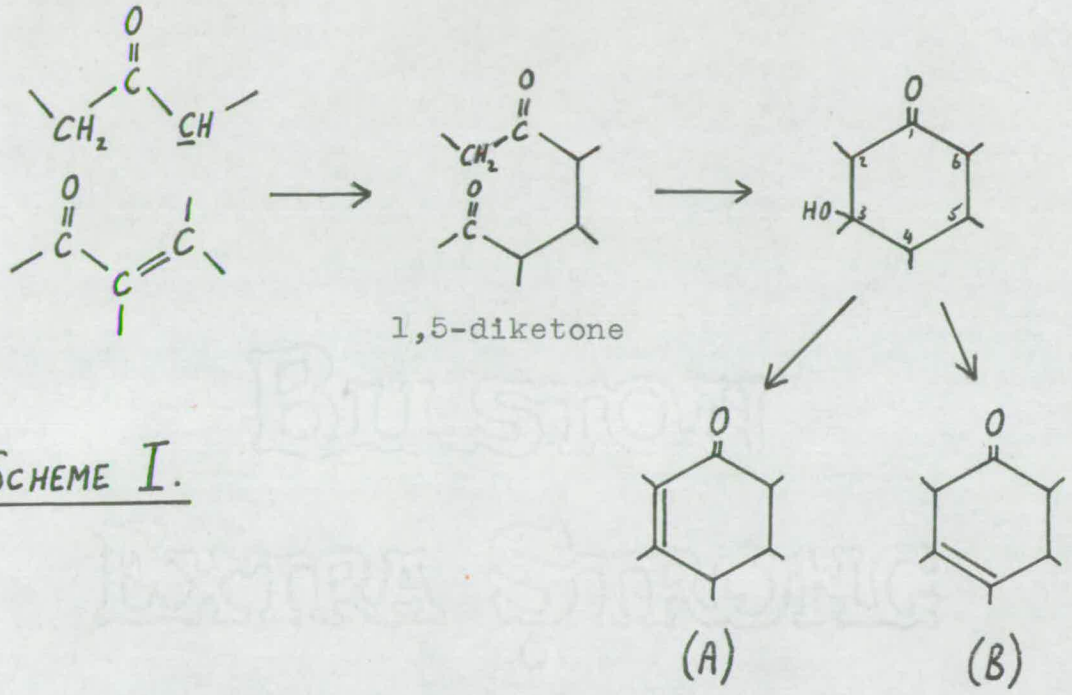


Ethyl acetoacetate (R^1 = H, R^2 = CO_2Et) is frequently used as the ketone component since its methylene group is doubly activated, with the result that the enolate ion is more readily formed, e.g. in sodium ethoxide solution. The enolate ion, which may be represented as



is very reactive and readily undergoes Michael addition. The first product formed is a 1,5-diketone which undergoes ring closure during the aldol condensation. Finally, elimination of a molecule of water produces the double bond in the ring, which, as shown in Scheme I below, may be formed in either the 2,3-position (A) or the 3,4 - position (B),

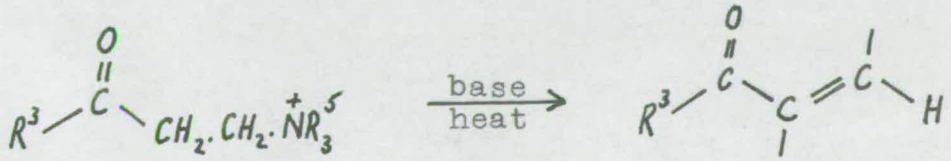
depending upon whether a proton is eliminated from $C_{(2)}$ or from $C_{(4)}$. Under normal circumstances, the conjugated compounds (A) are produced preferentially.



SCHEME I.

Instead of ethyl acetoacetate in sodium ethoxide solution, simple ketones may be used without any other activating groups present if sodamide is used as catalyst, to bring about the formation of the enolate ion.

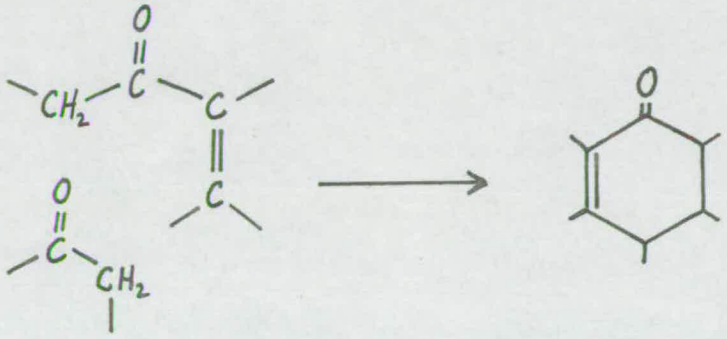
If R^4 = H, a Mannich-Robinson base is used which decomposes on heating in basic solution to give the rather unstable methylene ketone which reacts as it is formed.



The synthetic methods used in the present work had R^1 = H, R^2 = CO_2Et, or Ph, R^4 = Ph or furyl, and the reactions were carried out in sodium ethoxide solution.

The second general method of synthesis of cyclohexenones

involves the reaction of an enolate ion derived from a saturated ketone with an $\alpha\beta$-unsaturated, methyl or methylene ketone.

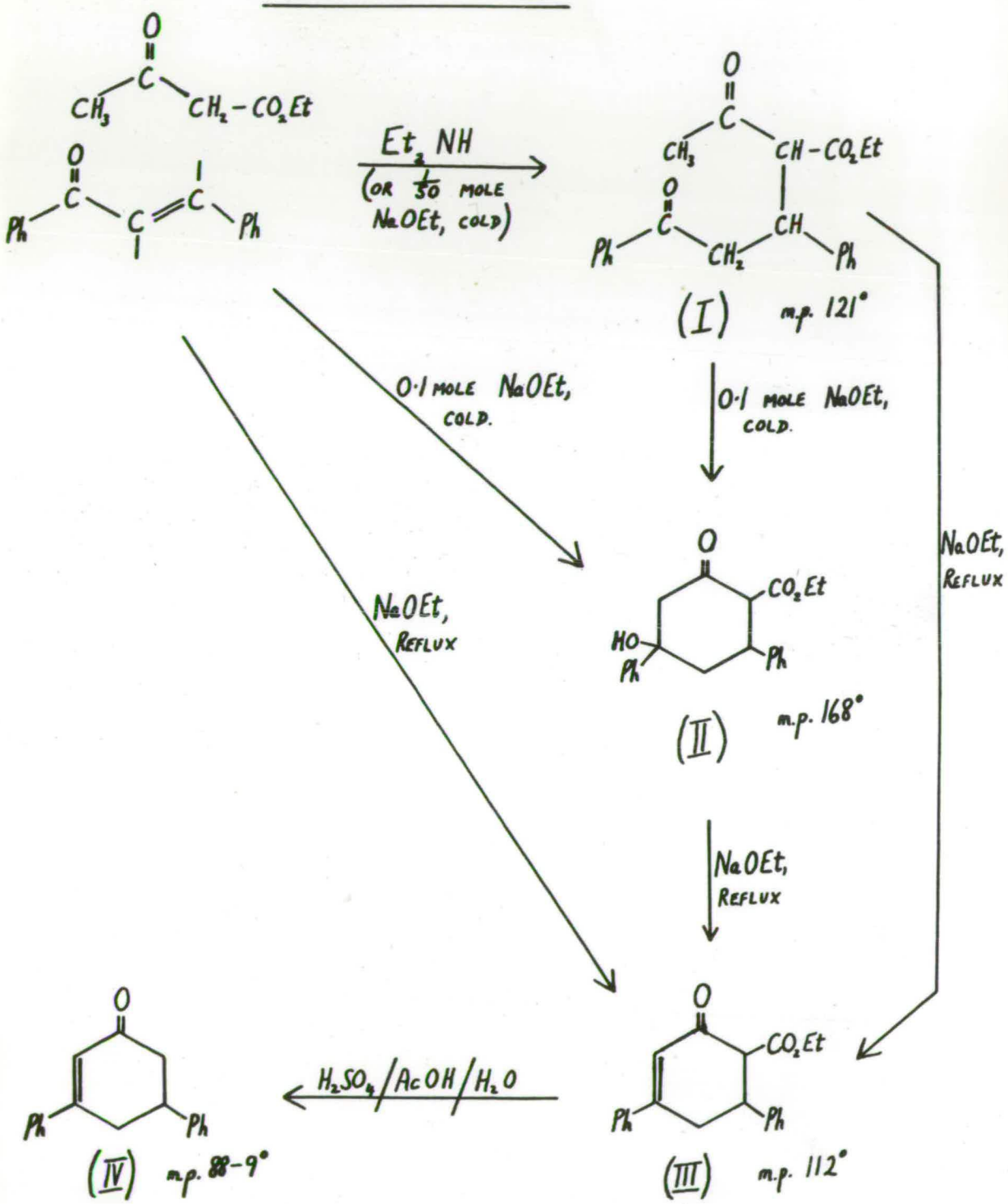


The synthesis of cyclohexenones by means of the Michael addition (or Michael condensation) reaction was first studied in the case of the reaction of benzylideneacetophenone and ethyl acetoacetate in the presence of bases. Knoevenagel and Speyer [1] used diethylamine as base and obtained an adduct, m.p. 120°- 121°. On treatment of this with sodium ethoxide under reflux they obtained a product, m.p. 111°- 112°, which was also obtained by refluxing benzylideneacetophenone and ethyl acetoacetate initially with sodium ethoxide. In this latter case the ethyl acetoacetate-benzylideneacetophenone adduct was considered to be the intermediate product, but could not be isolated because the sodium ethoxide immediately brought about ring closure. Subsequently Kohler [2] used not only diethylamine but also small quantities of sodium ethoxide in the cold to carry out the same reaction. In the former case his product had a m.p. of 121°(thus confirming the results of Knoevenagel and Speyer), but in the latter case Kohler

obtained a product, m.p. 168°. He observed that this substance was evidently closely related to that obtained by using diethylamine, as both gave the same cyclic ester when heated with sodium ethoxide. This ester was a diphenylcarbethoxy-cyclohexenone, m.p. 111°, which was the product also obtained by Knoevenagel on refluxing with sodium ethoxide. Structures were assigned to these compounds by Dieckmann and v. Fischer,[3] and these structures were later confirmed by modern infrared and ultraviolet evidence.[4]

Dieckmann and v. Fischer found that an addition product was obtained by the action of secondary bases on ethyl acetoacetate and benzylideneacetophenone. The use of 0·1 mole sodium ethoxide as condensing agent in the cold gave a product, m.p. 168° - 169°, while condensation with only traces of sodium ethoxide (⅟₅₀ mole) in the cold gave a product, m.p. 120°- 121°, which on further reaction with sodium ethoxide at room temperature was converted into the less soluble isomer, m.p. 168°-169°. These results confirmed those of Knoevenagel and of Kohler. The reaction scheme is shown on the next page, (Scheme II).

SCHEME II

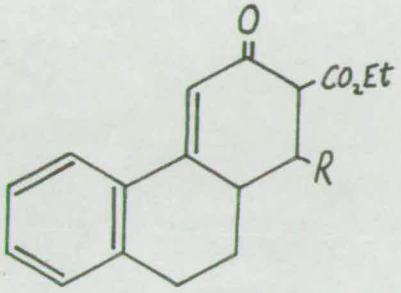

Et₂NH
(OR 1/50 MOLE NaOEt, COLD)
(I) m.p. 121°
0·1 MOLE NaOEt, COLD.
0·1 MOLE NaOEt, COLD.
NaOEt, REFLUX
NaOEt, REFLUX
(II) m.p. 168°
NaOEt, REFLUX
(III) m.p. 112°
H₂SO₄/AcOH/H₂O
(IV) m.p. 88-9°

Dieckmann and v. Fischer stated that the primary addition product was a 1,5-diketone which would be converted to the appropriate hydroxycyclohexanone in such cases as its constitution permitted this condensation to occur. The primary addition products were interpreted as 1,5-diketones, such as (I), and their corresponding cycloisomers, such as (II) (Scheme II). No other formulation for the two isomers appeared possible, since both showed no ferric chloride reaction, so could not be explained as keto-enol isomers. Dieckmann and v. Fischer found that whereas the ethyl 4-hydroxy-2-oxo-4,6-diphenylcyclohexane-1-carboxylate, (II), produced from benzylideneacetophenone and ethyl acetoacetate, was readily converted to ethyl 2-oxo-4,6-diphenylcyclohex-3-ene-1-carboxylate, (III), by heating with a small quantity of sodium ethoxide or piperidine in ethanolic solution, the isomeric ethyl 2-hydroxy-4-oxo-2,6-diphenylcyclohexane-1-carboxylate (from benzylideneacetone and ethyl benzoylacetate) was found to be completely stable to piperidine under the same conditions, and was not converted by the action of sodium ethoxide into the corresponding cyclohexenone carboxylic ester. In general the conversion of the hydroxycyclohexanones into the appropriate cyclohexenone derivatives can be caused by the action of concentrated sulphuric acid which splits off the elements of water by the removal of the hydroxyl group with one of the hydrogen atoms adjacent to the keto-carbonyl group. Dieckmann and v. Fischer observed that all the

1,5-diketo-carboxylic esters which were unable, owing to their constitution, to cyclise to form hydroxycyclohexanones, underwent fission with comparative ease into their original components under the action of alkali. It was in an attempt to determine how readily the compounds of β-keto-carboxylic esters with benzylidene ketones could be split that Dieckmann and v. Fischer came to carry out this work, thereby confirming the results of Knoevenagel and Speyer and of Kohler, and assigning structures to the products obtained (Scheme II). Confirmation of these structures was provided by the infrared and ultraviolet evidence of Anderson, Campbell, Leaver and Stafford [4] in this department. They found that chalkone and ethyl acetoacetate interacted in the presence of bases to give, according to the experimental conditions,[3] a 1,5-diketone (I), the isomeric ethyl 4-hydroxy-2-oxo-4,6-diphenylcyclohexane-1-carboxylate (II), absorbing at 1706 $cm.^{-1}$ (6-membered ring ketone), 1748 $cm.^{-1}$ (non-enolised β-keto-ester), and 3390 $cm.^{-1}$ (OH with bonding), and ethyl 2-oxo-4,6-diphenylcyclohex-3-ene-1-carboxylate, (III), absorbing at 1735 $cm.^{-1}$ (ethoxycarbonyl group), 1663 $cm.^{-1}$ (αβ-unsaturated ketone), and 287 mμ (Ph.CH:CH.CO.CH_2. grouping). Hydrolysis and decarboxylation of the ester (III) gave 3,5-diphenylcyclohex-2-en-1-one, (IV),[2,5,6] shown to be an αβ-unsaturated ketone by absorption at 285 mμ (log ε 4·27) and by an infrared band at 1657 $cm.^{-1}$.

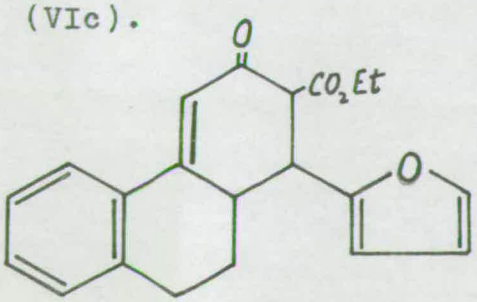
Knoevenagel's synthesis of cyclohexenones from ethyl

acetoacetate and unsaturated ketones can be applied to the synthesis of substances related to the sterols.

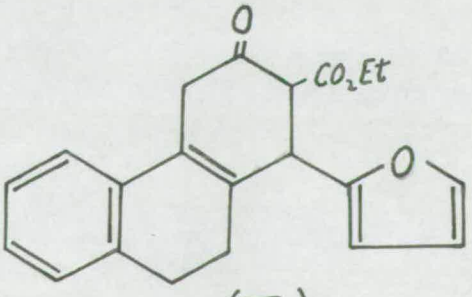


(Ve)

Substances of type (Ve) should be obtainable by one of two alternative methods: (a) by condensation of an alkylidene (or arylidene) -α-tetralone with ethyl acetoacetate, and (b) by the condensation of an α-tetralone with an alkylidene (or arylidene) derivative of ethyl acetoacetate. Robinson and his co-workers [7] obtained (Vc) from ethyl furfurylideneacetoacetate and α-tetralone, and from 2-furfurylidene-α-tetralone and ethyl acetoacetate. In the latter reaction, using sodium ethoxide as catalyst in alcoholic solution, the first product was a bright yellow substance (α-form), which was gradually changed by the action of the reagent into an almost colourless isomer (β-form). The α-form was considered to be an αβ-unsaturated ketone, (Vc), and the β-form was probably (VIc).

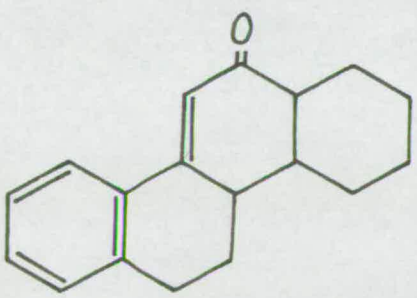


(Vc)

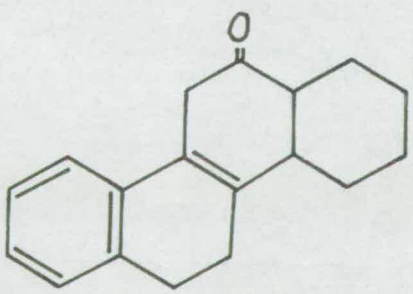


(VIc)

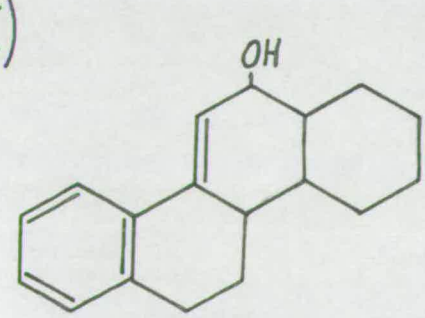
This feature of the migration of the double bond in the cyclohexenone ring was noted in further work by Peak and Robinson[8] on hydrochrysene derivatives. The condensation of sodio-α-tetralone with acetylcyclohexene yielded a ketodecahydrochrysene-(A), (VII), and two isomers, (B) and (C), were isolated from the mother-liquors. Substances (A),(B) and (C) had widely separated melting-points, and mixtures showed large depressions; they were undoubtedly distinct chemical substances. From spectroscopic data, structures were assigned to the three compounds; (A) and (B) showed identical absorption, similar to that characteristic of benzylideneacetone, whereas (C) gave entirely different results indicating that the carbonyl group was no longer conjugated with the unsaturated grouping. Hence structure (VII) was assigned to the stereoisomers (A) and (B), and structure (VIII) to (C).



(VII)

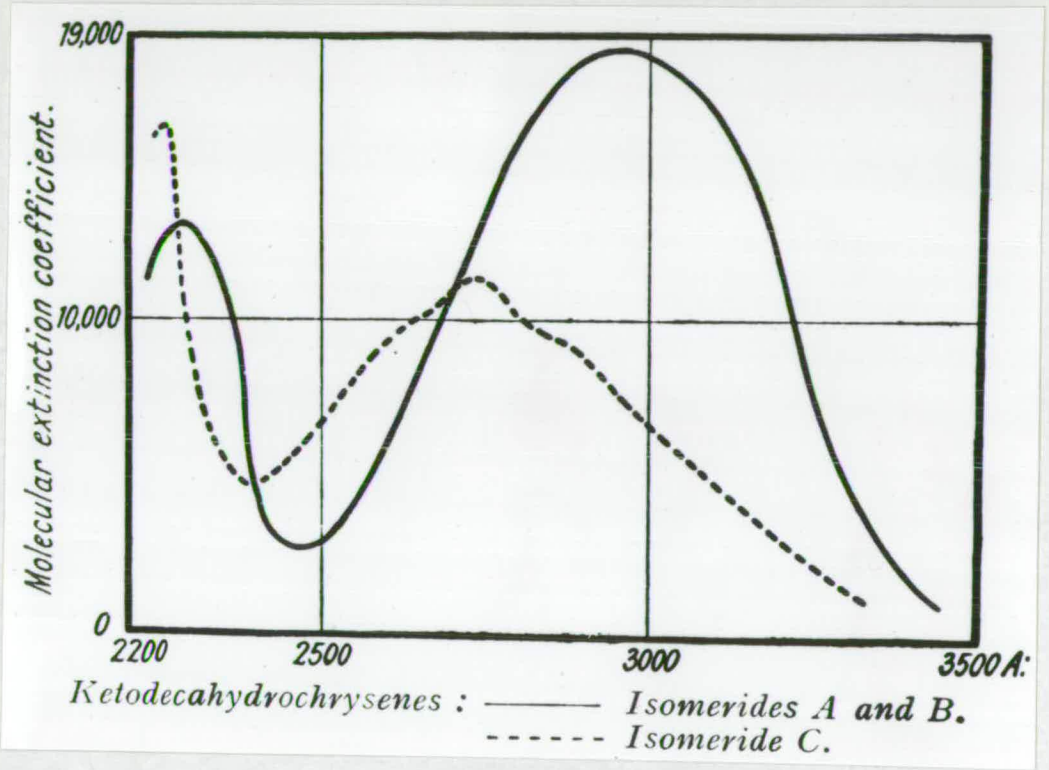


(VIII)

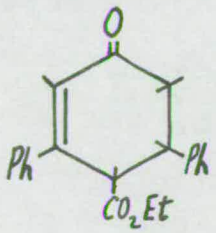


(IX)

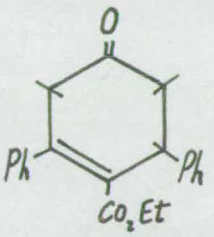
In an attempt to convert (VII) to (VIII) by refluxing the substance with alcoholic sodium ethoxide, the unsaturated alcohol (IX) was obtained.



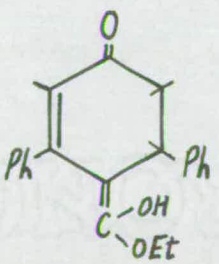
Dieckmann [9] studied the isomerism of ethyl 4-oxo-2,6-diphenylcyclohex-2-ene-1-carboxylate brought about by double bond migration in the cyclohexenone ring, and assigned the structures (X) and (XI) to the possible keto forms, and (Xa), (Xb), (XIa) and (XIb) to the corresponding enol forms. The latter four structures seem inherently improbable and would be worthy of reinvestigation by modern spectroscopic methods.



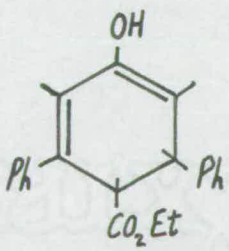
(X)



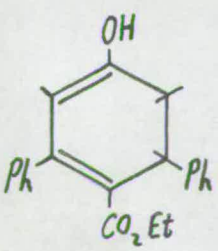
(XI)



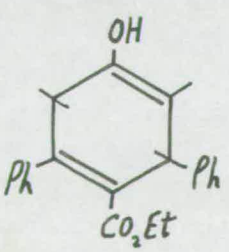
(Xa)



(Xβ)

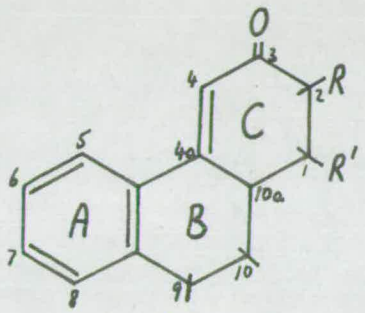


(XIa)



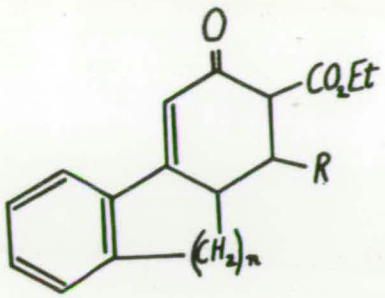
(XIβ)

The study of several cyclohexenones of structures related to those under discussion in this work, was carried out by a number of workers in this department. [4,10,11,12] It has been shown [4] that in a cyclohexenone such as (XII), in which R = CO_2Et, R^1=Ph, or furyl,

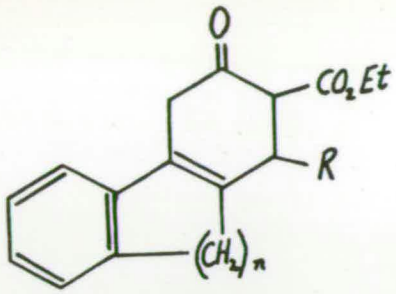


(XII)

under alkaline conditions, the 4,4a double bond may migrate to the 4a,10a position, and that this change is dependent on the stereochemistry of the derived enol. In order to clarify the comparisons and contrasts found in these related series, the following notation has been chosen:



(V)



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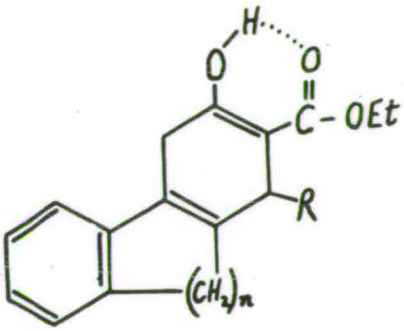
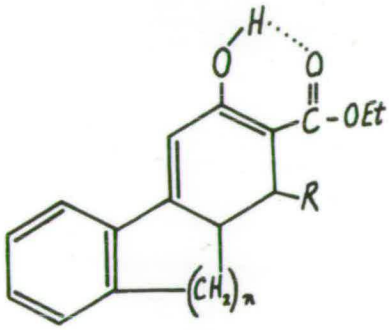
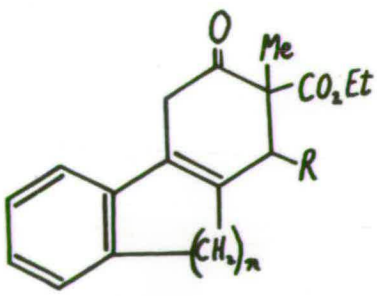


(XIII)



(XIV)



(XV)

a n = 1, R = Ph

b n = 2, R = Ph

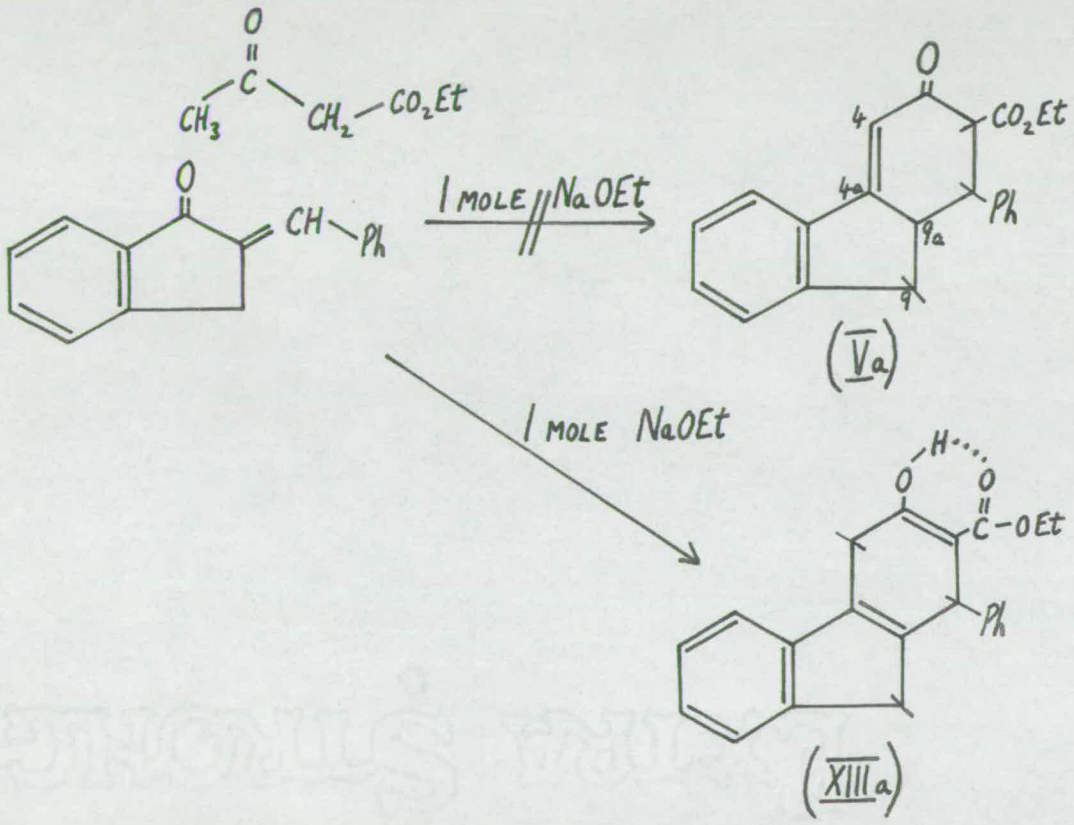
c n = 2, R = 2-Furyl

d n = 1, R = H

e n = 2

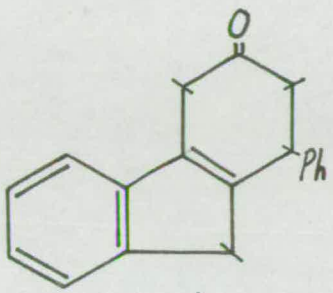
f n = 3, R = Ph

2-benzylideneindan-1-one and ethyl acetoacetate with one mole of sodium ethoxide as catalyst, would be expected to yield ethyl 1,2,3,9a-tetrahydro-3-oxo-1-phenylfluorene-2-carboxylate (Va), but instead gave an ester (XIIIa) in which the 4,4a double bond had migrated to the 4a,9a position.[4,10]

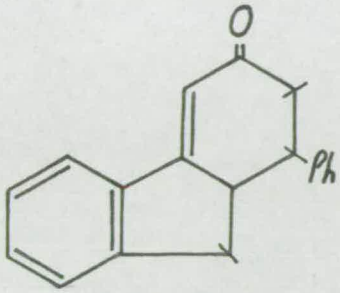


The infrared spectrum showed a single carbonyl absorption band at 1665 cm.$^{-1}$, indicating that only one carbonyl group is present and that this must be that of the ester group which is hydrogen bonded to an enolic hydroxyl group. On heating with sulphuric acid, acetic acid and water, the ester (XIIIa) gave 1,2,3,4-tetrahydro-3-oxo-1-phenylfluorene (XVI), whose structure was confirmed by the similarity shown between its ultraviolet spectrum and those of β-methylstyrene and indene,[13,14], and by the presence

of a single infrared band at 1716 cm.$^{-1}$ denoting an unconjugated carbonyl group.[15]



(XVI)



(XVII)

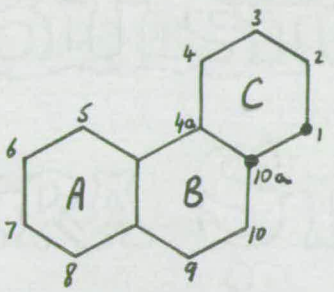
Slightly different conditions but no distillation yielded the isomeric 1,2,3,9a-tetrahydro-3-oxo-1-phenylfluorene, (XVII), whose structure was confirmed by the similarity between its ultraviolet spectrum and that of benzylideneacetone,[7,8] and by infrared bands at 1650 cm.$^{-1}$ and 1622 cm.$^{-1}$, (with a shoulder at 1670 cm.$^{-1}$ which resolved into a peak at 1672 cm.$^{-1}$ by the use of hexachlorobutadiene), attributed to the conjugated carbonyl and ethylenic groups in the fragment CH = CH·CO·.[4] Whereas in many of the cases of isomerism of unsaturated cyclic ketones which have been reported,[7,8,16] double bond migration is brought about by alkali, it was seen that distillation alone was sufficient to convert the $\alpha\beta$-isomer (XVII) partially into the $\beta\gamma$-isomer (XVI). The presence of the double bond in the 4a,9a position of the ester (XIIIa) was shown by methylation to a C-methyl compound, (XVa), having an ultraviolet spectrum similar to that of 1,2,3,4-tetrahydro-3-oxo-1-phenylfluorene (XVI).[4]

The reaction of 2-benzylidenetetral-1-one with ethyl acetoacetate in presence of one mole of sodium ethoxide yielded the ester (XIIIb), (analogous to (XIIIa)). This showed a single carbonyl absorption band in its infrared spectrum at 1672 cm.$^{-1}$, again attributable to a chelated, $\alpha\beta$-unsaturated ester grouping. Both the esters (XIIIa) and (XIIIb) gave a purple colour with ferric chloride, indicating the enolic structure.

Robinson and his co-workers [7] proposed that the similar reaction of 2-furfurylidenetetral-1-one with ethyl acetoacetate yielded the final product (VIc). However, they also reported that their compound gave a purple colour with ferric chloride, which would indicate the enolic structure (XIIIc) as being the more probable form of the compound. The results of a repeat of Robinson's work are reported in section (a) of the discussion following.

The reaction between 2-benzylidenetetral-1-one and ethyl acetoacetate in the presence of only 0.2 mole of sodium ethoxide yielded two isomeric esters,[10] (Vb) and (XIVb). As before, the constitutions of these two esters were determined by a study of their infrared and ultraviolet spectra. The ester (Vb) had an ultraviolet spectrum similar to that of 1,2,3,9,10,10a-hexahydro-3-oxo-1-phenylphenanthrene,[4] and infrared absorptions at 1744 cm.$^{-1}$ (ethoxycarbonyl group) and 1667 cm.$^{-1}$ (conjugated ketone) and gave no colour with ferric chloride. The isomer (XIVb) showed infrared absorption

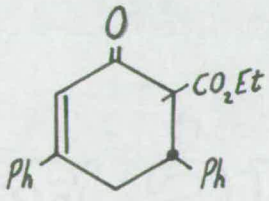
at 1645 cm.$^{-1}$, attributed to the chelated ester group, and gave a green colour with ferric chloride. Anderson and Leaver [10] showed that esters (Vb) and (XIVb) were not tautomeric, but that their respective enolate anions differed sterically. The ester (XIVb) was stable in alkaline solution, but (Vb) was not, and isomerised after several hours to ester (XIIIb).



This was explained by the use of models of the anions which showed that ring C, which had an axial and equatorial arrangement of exocyclic bonds at $C_{(1)}$ and $C_{(10a)}$, must have axial hydrogen at $C_{(10a)}$. The anions, therefore, differed only in the steric arrangement of the phenyl group at $C_{(1)}$. Anderson and Leaver suggested that (Vb) had an equatorial phenyl group since enolisation would then cause the carbethoxy group at $C_{(2)}$ to move closer to the phenyl group, causing steric compression in the molecule, and so rearrangement to (XIIIb) would occur in alkali. The fact that (XIVb) did not rearrange in alkali suggested that the phenyl group was axial in this isomer, so that the steric compression effect did not occur.

Lacey [17] has recently suggested that a steric effect

which inhibited enolisation was the cause of the different proportions of enol tautomers in 2-acetyl-5-methylcyclohexanone (80% enol) and 2-acetyl-3,5-dimethylcyclohexanone (20% enol). The 3-methyl group in the latter compound was thought to inhibit enolisation, but the complication arises in this case that neither of these compounds possesses a rigid conformation, whereas the cyclic β-ketoesters (Vb) and (XIVb) are both of rigid conformation. Ethyl 2-oxo-4,6-diphenylcyclohex-3-ene-1-carboxylate, (III), also possesses a flexible conformation and can be shown, by infrared and ultraviolet absorptions,[4] to exist almost entirely in the keto form, which suggests that the conformation with the 6-phenyl group in the equatorial position is the more stable.

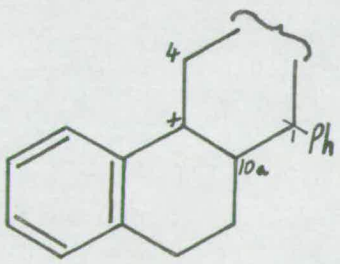


(III)

However, in this case, the enolate anion produced in alkali does not rearrange, and therefore its formation is probably accompanied by a conformational change in the molecule.

Treatment of ester (XIIIb) with concentrated sulphuric acid gave a mixture of esters (Vb) and (XIVb) when the solution was diluted with water. After a short reaction time in sulphuric acid (2 mins.), the product was mainly

ester (XIVb), but an increase in the reaction time in sulphuric acid to 10 mins. gave rise to a greater proportion of the ketoester (Vb), suggesting that this isomer was the more stable in strong acid whereas ester (XIVb) was kinetically favoured. The ester (XIVb) was converted to its isomer (Vb), together with traces of the ester (XIIIb), by boiling in ethanol saturated with dry hydrogen chloride. Anderson and Leaver proposed that these isomeric changes were consistent with the existence, in strong acid, of the diastereomeric species represented by partial formula (XVIII), and formed by protonation of ester (XIIIb) at $C_{(10a)}$ or of its isomers (Vb) and (XIVb) at $C_{(4)}$.

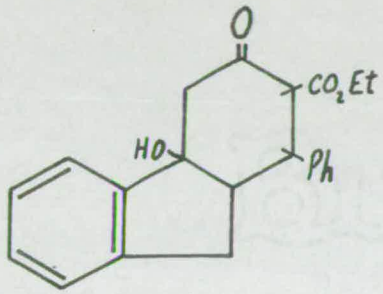


(XVIII)

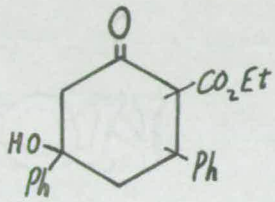
Hydrolysis and decarboxylation in acid or alkali of the three isomers (XIIIb), (Vb) and (XIVb) was found to yield the same compound, 1,2,3,9,10,10a-hexahydro-3-oxo-1-phenylphenanthrene.[4]

The reaction between 2-benzylideneindan-1-one and ethyl acetoacetate, which would not yield the expected ester (Va), as already stated, also failed to yield the ester (XIVa) under any conditions. Progressive reduction of the concentration of sodium ethoxide used as catalyst

in the reaction resulted in the formation of mixtures of the ester (XIIIa) and the hydroxyketoester (XIX), which is analogous to a product, compound (II), from the reaction of chalkone with ethyl acetoacetate. [3,4].



(XIX)



(II)

Reaction of ester (XIIIa) in concentrated sulphuric acid yielded, on dilution of the solution, the isomers (Va) and (XIVa) together with the ester (VIa), the keto-tautomer of (XIIIa). The structure of (VIa) was deduced from the similarity between its ultraviolet spectrum and that of 1,2,3,4-tetrahydro-3-oxo-1-phenylfluorene,[4] and from infrared absorptions at 1748 cm.$^{-1}$ (unconjugated ester) and 1722 cm.$^{-1}$ (unconjugated ketone). The close tautomeric relationship between (VIa) and (XIIIa) was shown by the fact that (XIIIa) gave an immediate purple colour with ferric chloride, whereas (VIa) gave no immediate colouration, but a purple colour developed slowly on standing. On treatment with alkali, (VIa) developed the ultraviolet spectrum characteristic of the enolate anion from (XIIIa), and a neutral solution of (VIa), after standing for several weeks, yielded (XIIIa) on evaporation.

Both hydrofluorene esters (Va) and (XIVa) rearranged in alkaline solution to (XIIIa), with (Va) undergoing rearrangement more rapidly. This is in contrast to the corresponding hydrophenanthrene compounds, in which only (Vb), which had the phenyl group at $C_{(1)}$ in the equatorial position, underwent rearrangement to (XIIIb) in alkali, due to steric compression effects. The additional strain introduced by the five-membered ring is probably the cause of this greater ease of rearrangement in the hydrofluorene series, and, in further agreement with this view, the hydrofluorene ester (Vd), in which the phenyl group at $C_{(1)}$ is absent, rearranged in alkaline solution to the isomer (XIIId). In the preparation of the ester (Vd), the major product of the reaction was found to be its isomer (XIIId), as shown by its ultraviolet and infrared absorption spectra. The ultraviolet and infrared absorptions of the ester (Vd) indicate that it exists largely in the keto-form, (infrared peaks at 1667 $cm.^{-1}$ and 1741 $cm.^{-1}$), but a shoulder in the ultraviolet spectrum at ca.370 mμ. and the reduced intensity of the main ultraviolet maxima, indicate the presence of a small proportion of the enol form (XIVd).

In the present work, one of the problems undertaken was to determine the effects shown by corresponding compounds in which ring B was seven-membered, and to determine how great an effect the relative flexibility of the seven-membered ring had on the absorption spectra of the compounds.

RESULTS
AND
DISCUSSION.

(a). Reaction of 2-furfurylidene-1-tetralone with ethyl acetoacetate.

This section describes work carried out to obtain the α- and β-modifications previously obtained by Robinson and his co-workers,[7] in an attempt to determine whether the colours which the two forms gave with ferric chloride were due to enolic structures, or whether the compounds did in fact exist in the ketonic structures postulated by Robinson.

2-furfurylidene-1-tetralone was prepared by the addition of aqueous sodium hydroxide to a solution of freshly-distilled furfuraldehyde and α-tetralone in ethanol. After the dark green solution thus formed had been left to stand overnight at room temperature, a mass of yellow crystals was filtered off, m.p. 72° and 76°, unaltered by recrystallisation. The substance first melted at 72°, then, after cooling, re-melted at 76°. This was due to the fact that it was a dimorphous substance, existing in two different crystalline forms, needles and prisms, the latter being the more stable form. Robinson had also obtained this dimorphous substance but only quoted one melting-point, 75°-76°.

The condensation of 2-furfurylidene-1-tetralone and ethyl acetoacetate, with sodium ethoxide as catalyst, was not carried out by Robinson's method. He had set up one reaction mixture from which he withdrew specimen samples after various intervals of time, in this way

obtaining firstly the golden-yellow α-modification, followed by mixtures of the α- and β-forms which showed a decrease in colour intensity, and finally the paler yellow β-modification. In this work attempts were made to obtain only the α-modification or the β-modification from any one reaction, by a variation of the reaction conditions.

In the first attempt to prepare the α-modification, 0·4 mole of sodium ethoxide was used as catalyst and after refluxing for 3 hours and working up, the reaction mixture yielded a yellow solid, m.p. 112°- 116° after recrystallisation from ethanol, which gave a greenish-brown colour with ferric chloride, indicating that it was a mixture of the required α- and β-modifications.

More favourable results were obtained by using a higher concentration of sodium ethoxide (2 moles) and a shorter reaction time (30 mins.). Addition of a slight excess of acetic acid, dilution with water and cooling gave a mixture of the two forms which could be partially separated by fractional precipitation with light petroleum from carbon tetrachloride. Working up by addition of a large excess of acetic acid, followed by extraction with ether, yielded only the required α-modification, which gave a pure green colour with ferric chloride.

The β-modification was obtained by refluxing the reaction components in ethanolic sodium ethoxide (2 moles) for 4 hours, and working up. This yielded

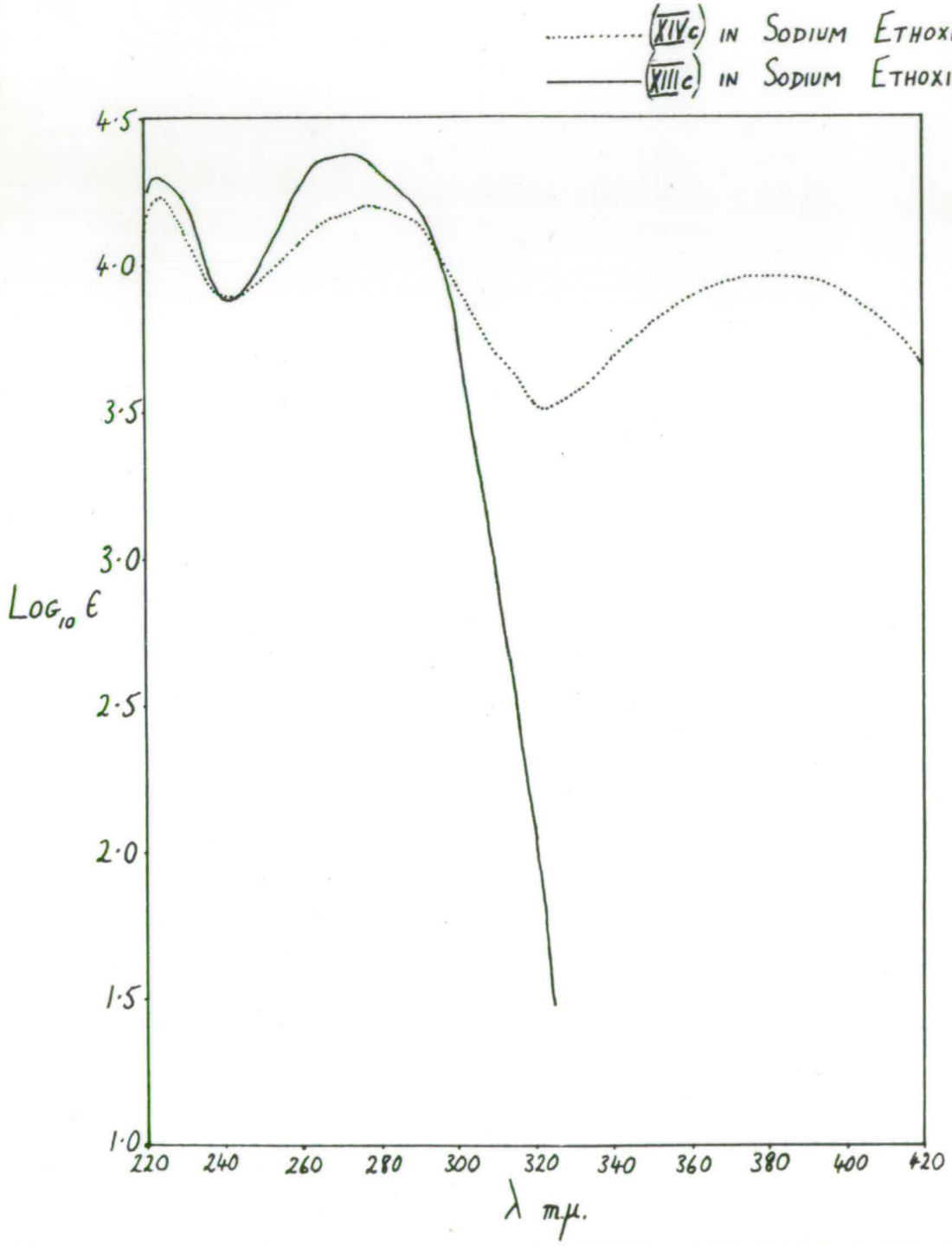
yellow needle-shaped crystals, m.p. 122°-123°. Addition of ferric chloride to an alcoholic solution of this solid gave a violet colour, indicating that it was the β-modification.

Infrared and ultraviolet absorption spectra of the two modifications were measured. The α-modification had a carbonyl absorption band at 1653 $cm.^{-1}$ (chelated ester grouping) and another at 1585 $cm.^{-1}$, due to double bond absorptions. The β-modification showed a carbonyl absorption band at 1684 $cm.^{-1}$ (chelated ester grouping) and two other bands, at 1652 $cm.^{-1}$ and 1635 $cm.^{-1}$, again attributed to double bond absorptions. Compounds possessing the keto structures proposed by Robinson would each show two carbonyl absorptions, one of which would be higher than 1730 $cm.^{-1}$ (unconjugated ester). The ultraviolet absorption maxima of the α- and β-modifications in ethanol and in sodium ethoxide are shown in Table I, as well as those of related compounds with the 2-furyl group replaced by phenyl. A solution of the β-modification in 0·02M ethanolic sodium ethoxide was colourless, and its spectrum is shown in Fig.1, together with the spectrum of the yellow solution of the α-modification in the same solvent. No isomerisation of the α-form occurred in this strength of sodium ethoxide solution, since a second measurement of the spectrum, after the solution had stood for 20 hours, gave peaks at exactly the same wavelengths, and the solution retained its yellow colour. However, in a more

TABLE I.

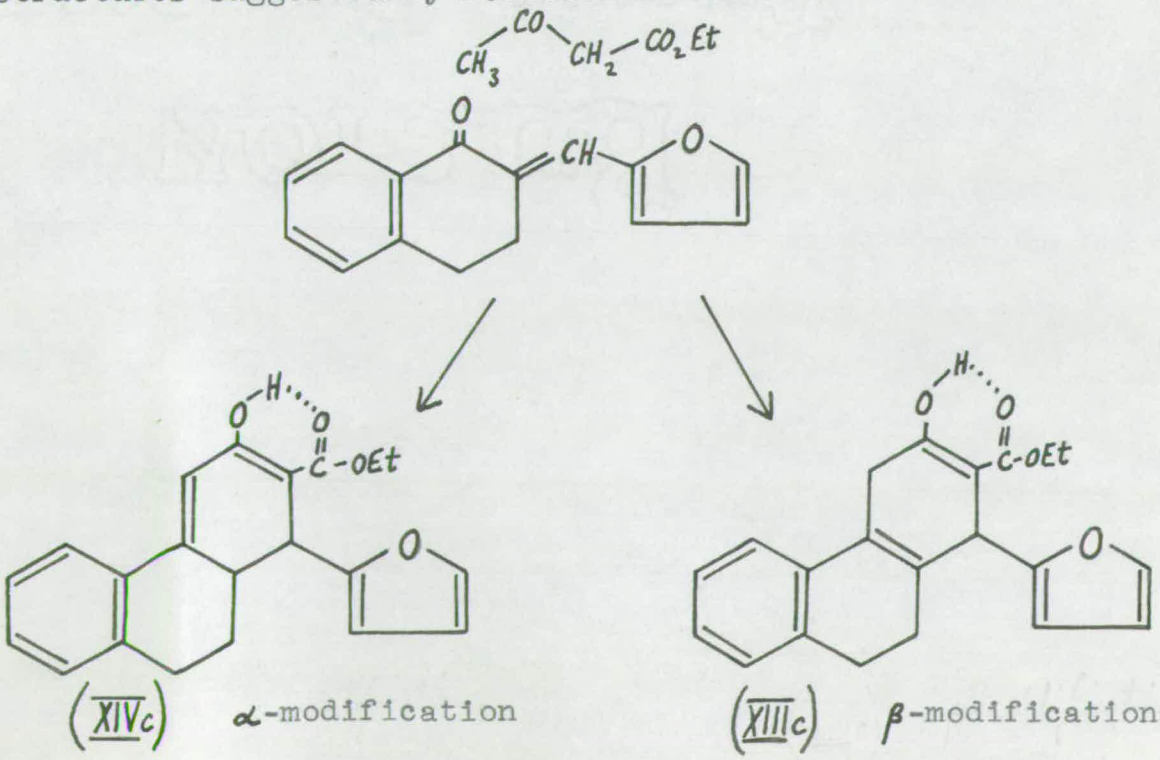
Compound.	$\lambda_{max.}$ mμ.	$\log_{10}\epsilon$	$\lambda_{max.}$ mμ.	$\log_{10}\epsilon$	$\lambda_{max.}$ mμ.	$\log_{10}\epsilon$
(XIIIc) in ethanol. (β-modification).	218 225	4·42 4·36	255	4·22		
(XIIIc) in sodium ethoxide.	223	4·29	273-4	4·37		
(XIVc) in ethanol. (α-modification).	211	4·27	276 287	3·90 3·89	362-3	4·10
(XIVc) in sodium ethoxide.	224	4·23	278	4·20	382	3·96
(XIIIb) in ethanol.	220	4·46	254	4·32		
(XIIIb) in sodium ethoxide.	223	4·38	269 276	4·41 4·41		
(XIVb) in ethanol.			272	4·28	365	3·48
(XIVb) in sodium ethoxide.			271	4·13	387	4·06
(Vc) in ethanol.	214	4·29	300-1	4·35		
(Vc) in sodium ethoxide.	226	4·35	274	4·40		
(Vb) in ethanol.	229	4·01	301	4·34		
(Vb) in sodium ethoxide.	223	4·38	269 276	4·41 4·41		
(XVb) in ethanol.			267 275	4·09 4·10		
(XX) in ethanol.	214	4·29	299	4·33		

FIG. 1


(XIVc) IN SODIUM ETHOXIDE
(XIIIc) IN SODIUM ETHOXIDE
4·5
4·0
3·5
3·0
2·5
2·0
1·5
1·0
Log10 ε
220
240
260
280
300
320
340
360
380
400
420
λ mμ.

concentrated solution of sodium ethoxide, (0·2M), isomerisation of the α-modification to the β-modification began to occur very slowly, as was shown by the appearance of a small additional maximum at 275 mμ. (log ε 4·20), the other maxima remaining at their original wavelengths. The fact that a solution of sodium ethoxide of such relatively high concentration is required to bring about even a slow isomerisation of the α-form is in agreement with the analogous case of (XIVb) (2-furyl group replaced by phenyl) in which no isomerisation occurs in 0·02M alcoholic sodium ethoxide.[10]

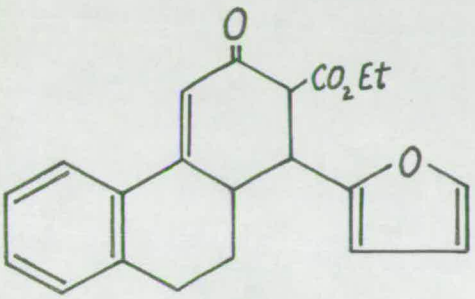
Comparison of the absorption spectra of these two modifications with those of corresponding compounds formed from 2-benzylidenetetralone and ethyl acetoacetate (see Table I) showed conclusively that they possess the enolic structures (XIIIc) and (XIVc) rather than the ketonic structures suggested by Robinson and his co-workers.[7]



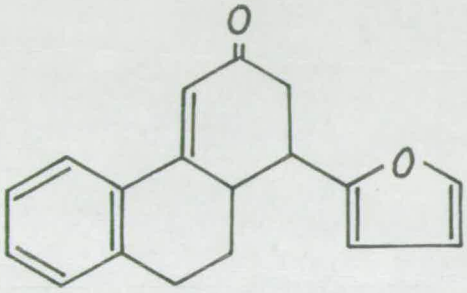
(XIVc) α-modification

(XIIIc) β-modification

Evaporation of the ethanolic filtrate after filtration of the α-modification, followed by chromatography on a deactivated alumina column, yielded two distinct substances, (Vc) and (XX).



(Vc)

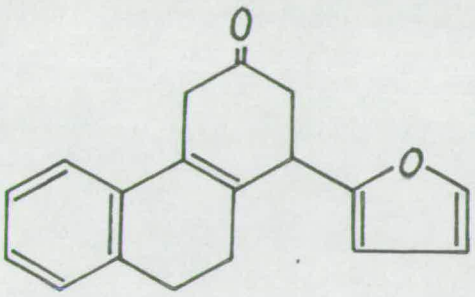


(XX)

Compound (Vc) was colourless, m.p. 111°-113°, with an infrared band at 1733 cm.$^{-1}$, characteristic of an unconjugated ester, as well as a band at 1665 cm.$^{-1}$, attributable, in this instance, to an αβ-unsaturated carbonyl group. The ultraviolet spectrum of compound (Vc) (Table I) was characteristic of a styryl ketone and confirmed the structure assigned. A solution of substance (Vc) in 0·02M ethanolic sodium ethoxide was yellow when first prepared, but the colour faded fairly rapidly and, after 24 hours, the spectrum became the same as that of the β-modification in ethanolic sodium ethoxide. As in the 1-phenyl series, isomerisation to the β-modification (XIIIc) has been proved to be much more rapid in the case of (Vc) than in the case of the α-modification, (XIVc), showing

that the two compounds are $C_{(1)}$-epimers rather than simply keto-enol tautomers. Using the same arguments as in the 1-phenyl series, it may be concluded that the furyl group is equatorial in (Vc) and axial in (XIVc).

The compound (XX) had m.p. 112°-113° and was clearly the ketone (m.p. 113°-114°) to which Robinson and his co-workers assigned the structure (XXA).



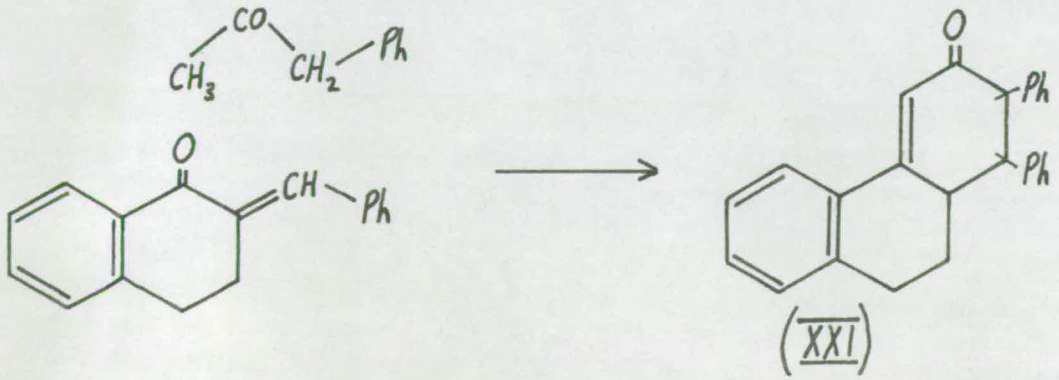
(XXA)

Its ultraviolet spectrum, however, (see Table I), was characteristic of a styryl ketone and, together with an infrared absorption at 1662 cm.$^{-1}$ ($\alpha\beta$-unsaturated ketone) indicated that the structure (XX) is correct.

(b). Reaction of 2-benzylidene-1-tetralone with benzyl methyl ketone.

The work in this section, and in section (c) following, was carried out to investigate the effects of small structural changes on the chemistry of the system which has been studied by Anderson and Leaver,[10] and containing the compounds having the notation shown on p.12 . In this section the structural change involves the replacement of the 2-ethoxycarbonyl group by phenyl.

Equivalent quantities of 2-benzylidene-1-tetralone and benzyl methyl ketone in boiling ethanolic sodium ethoxide yielded a product, m.p. 230°, which from its ultraviolet absorption spectrum in ethanol (Fig.2 and Table II) and its elementary analysis was clearly the required compound 1,2,3,9,10,10a-hexahydro-3-oxo-1,2-diphenylphenanthrene, (XXI), (corresponding to (Vb) in the original notation). The structure was confirmed by the presence of infrared absorption bands at 1650 $cm.^{-1}$ ($\alpha\beta$-unsaturated ketone), 1610 $cm.^{-1}$ and 1597 $cm.^{-1}$ (double bond absorptions), (Fig.4), and by the characteristic styryl ketone absorption in the ultraviolet. (Fig.2).



(XXI)

TABLE II.

Compound.	$\lambda_{max.}$ mμ.	$\log_{10}\epsilon$	$\lambda_{max.}$ mμ.	$\log_{10}\epsilon$	$\lambda_{max.}$ mμ.	$\log_{10}\epsilon$
(XXI) in ethanol.	229	4·05	300	4·35		
(XXI) in sodium ethoxide.			271	4·77		
(XXIII) in ethanol.	222	4·40	278-9	4·28	320-1	4·06
(XXIII) in sodium ethoxide.	225	4·39	256-7	4·41	353	3·91
(Vb) in ethanol.	229	4·01	301	4·34		

FIG. 2

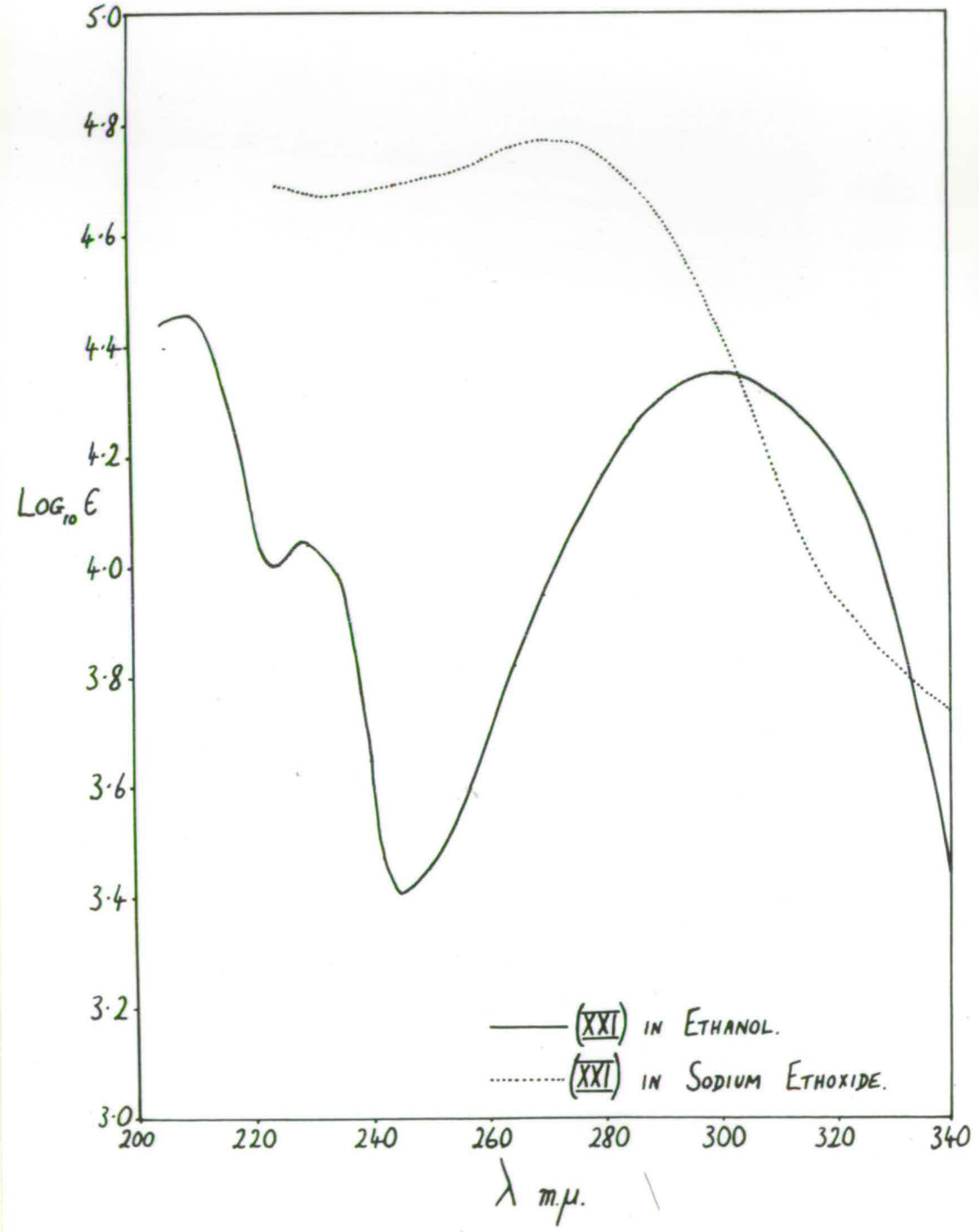

5·0
4·8
4·6
4·4
4·2
4·0
3·8
3·6
3·4
3·2
3·0
Log10 ε
200
220
240
260
280
300
320
340
λ mμ.
(XXI) IN ETHANOL.
(XXI) IN SODIUM ETHOXIDE.

FIG. 3

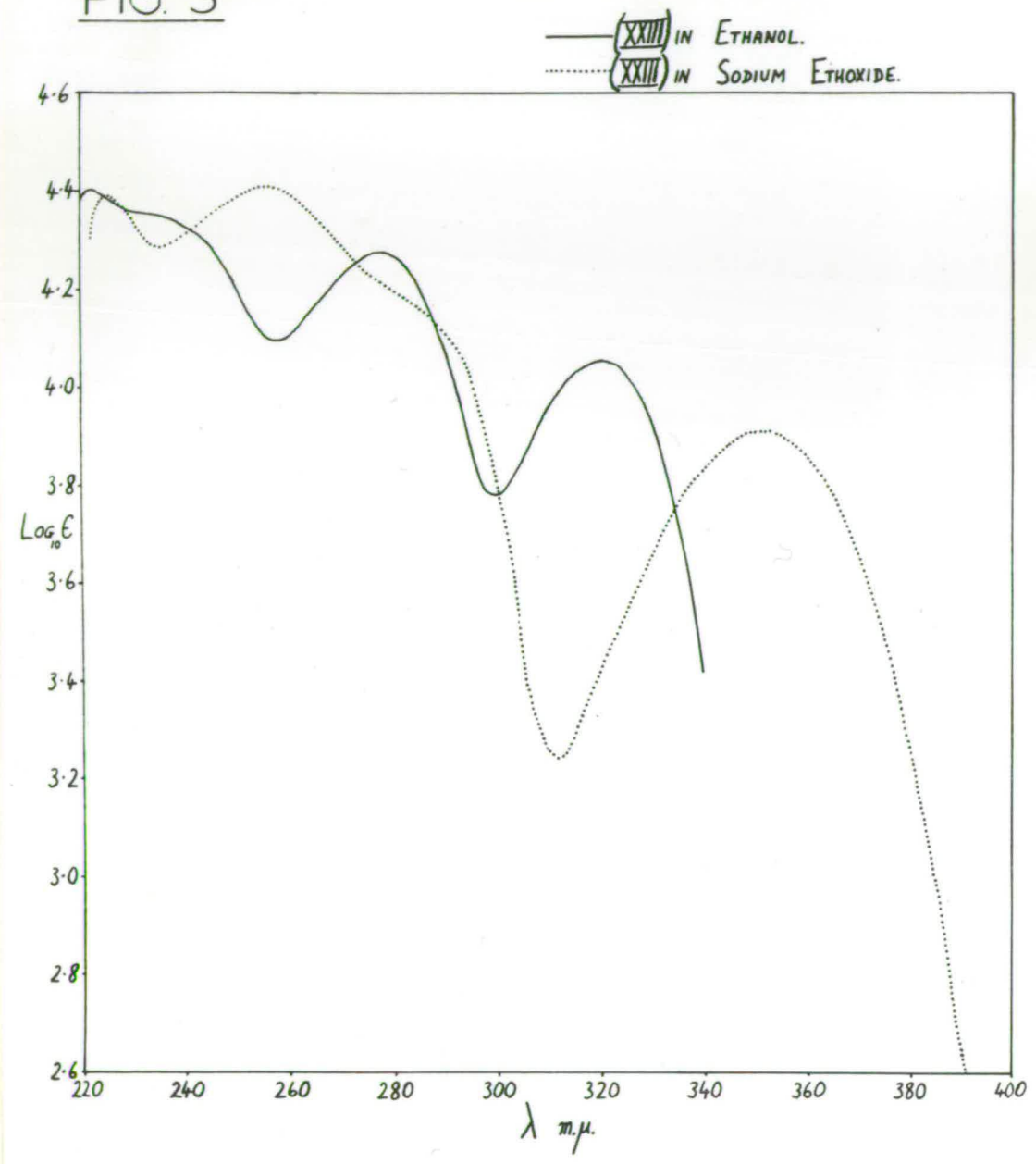

(XXIII) IN ETHANOL.
(XXIII) IN SODIUM ETHOXIDE.
4·6
4·4
4·2
4·0
3·8
Log ε
10
3·6
3·4
3·2
3·0
2·8
2·6
220
240
260
280
300
320
340
360
380
400
λ mμ.

FIG. 4

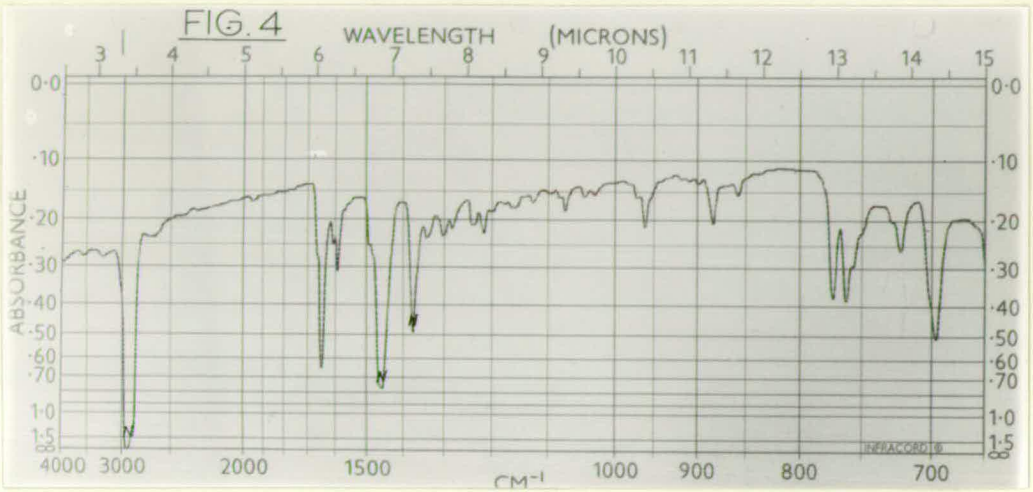
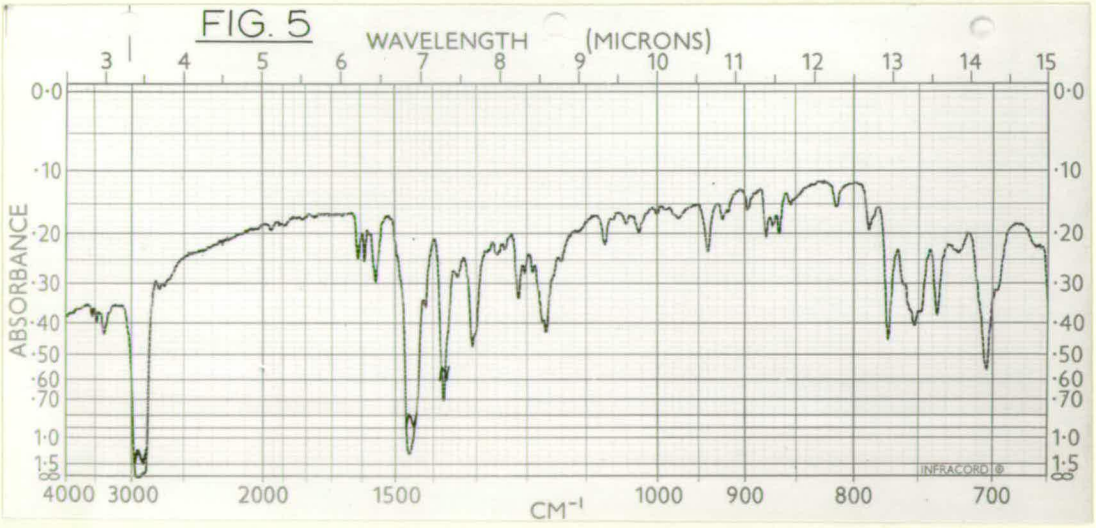
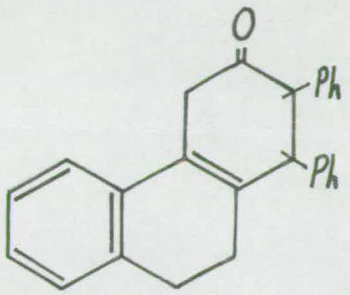

WAVELENGTH (MICRONS)
3 4 5 6 7 8 9 10 11 12 13 14 15
ABSORBANCE
0·0 ·10 ·20 ·30 ·40 ·50 ·60 ·70 1·0 1·5 ∞
4000 3000 2000 1500 1000 900 800 700
CM⁻¹
INFRACORD®

FIG. 5


WAVELENGTH (MICRONS)
3 4 5 6 7 8 9 10 11 12 13 14 15
ABSORBANCE
0·0 ·10 ·20 ·30 ·40 ·50 ·60 ·70 1·0 1·5 ∞
4000 3000 2000 1500 1000 900 800 700
CM⁻¹
INFRACORD®

The ultraviolet absorption spectrum of compound (XXI) in ethanolic sodium ethoxide (see Fig.2 and Table II) slowly changed on standing and ultimately gave rise to a maximum at 271 mμ.. The change was thought to be caused by the expected rearrangement to a βγ-unsaturated ketone 1,2,3,4,9,10-hexahydro-3-oxo-1,2-diphenylphenanthrene, (XXII), (corresponding to (VIb)).

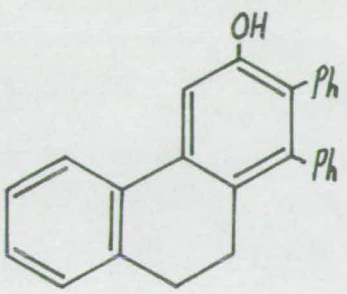


(XXII)

Isolation of the isomeric compound responsible for the change in ultraviolet spectrum was attempted by treatment of (XXI) with ethanolic sodium ethoxide which yielded a light brown solid. Chromatography of this product on a deactivated alumina column followed by recrystallisation from a light petroleum/alcohol mixture produced a white solid, m.p. 158°-159°. The ultraviolet absorption spectra of this product in both neutral solution and sodium ethoxide solution (Fig.3 and Table II) showed that it was not the substance responsible for the change in absorption of (XXI) in ethanolic sodium ethoxide.

Further proof that the substance obtained was not

the expected $\beta\gamma$-unsaturated ketone (XXII), was supplied by its infrared spectrum, which showed the presence of a hydroxyl group at 3390 $cm.^{-1}$ and the absence of a carbonyl group, (Fig.5). This, together with the elementary analysis, indicated that the compound was in fact the phenol, 9,10-dihydro-3-hydroxy-1,2-diphenyl-phenanthrene, (XXIII), probably formed by disproportion-ation under the alkaline conditions.

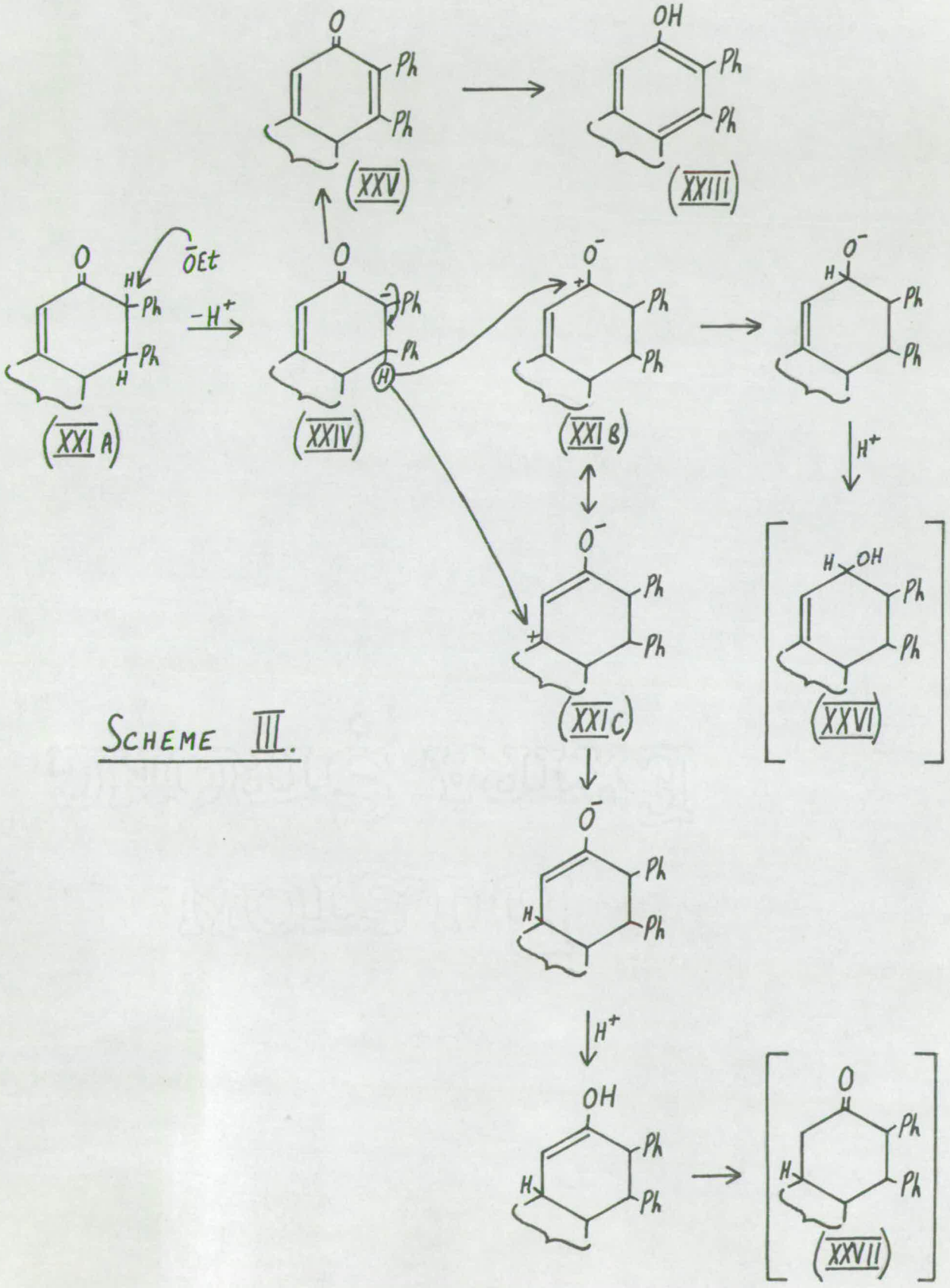


(XXIII)

A reaction, possibly of similar type, in which the product isolated was the unsaturated alcohol (IX) instead of a phenol was reported by Peak and Robinson[8] in their work on hydrochrysene derivatives, discussed in the introduction. (p.8).

It is suggested that the disproportionation reaction may take place by transfer of a hydride ion from the anion (XXIV) derived from (XXI) to the slightly electrophilic 3- or 4a-carbon atom of the un-ionised molecule (XXI), (Scheme III). Thus the chief driving force for the reaction is the presence of an oxygen or carbon anion in the donating molecule. The transference

of a hydride ion is a common type of two-electron oxidation-reduction process.

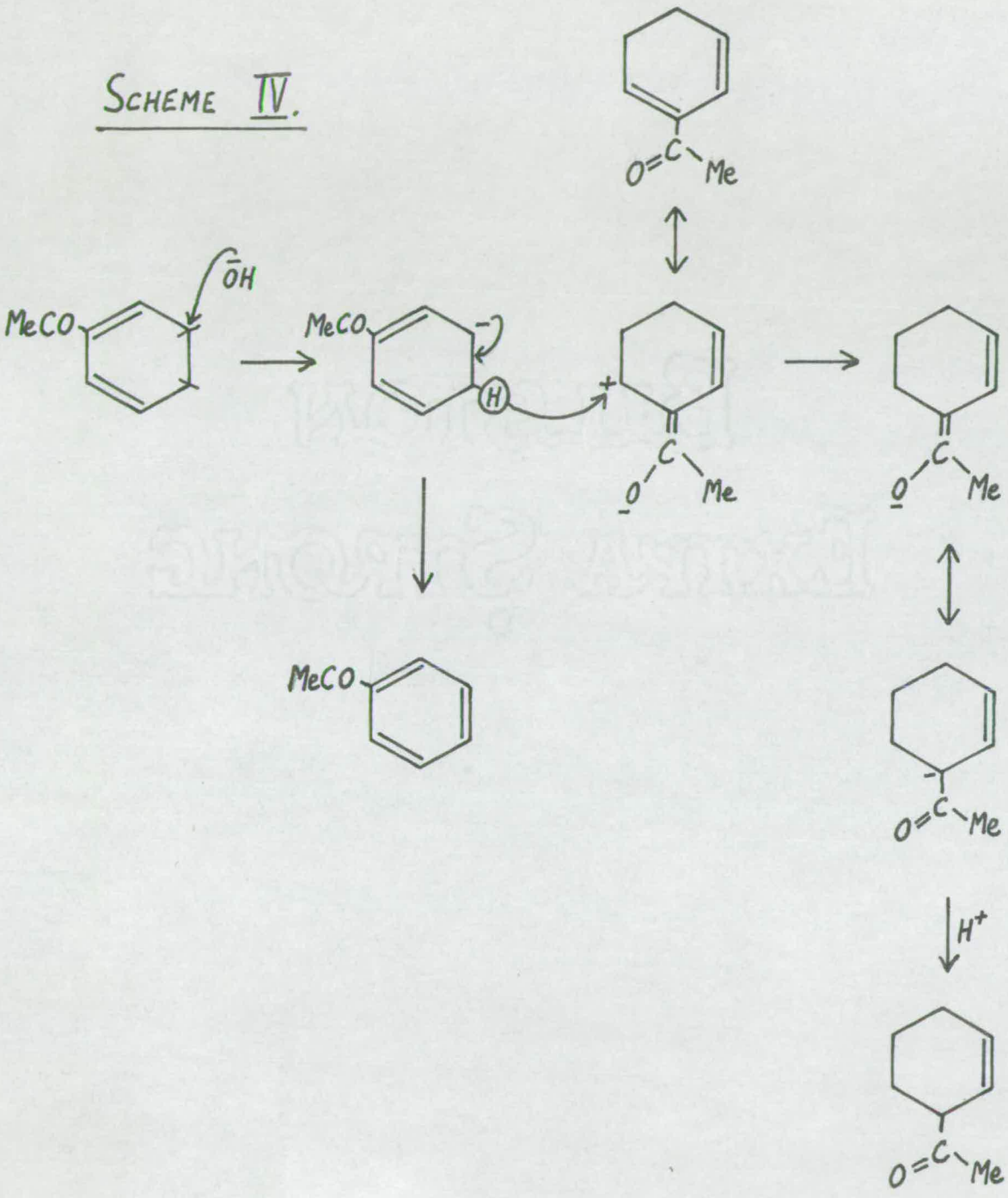


SCHEME III.

The attack of an ethoxide ion on the molecule (XXIA) removes a proton, giving (XXIV), which in turn loses a hydride ion by transfer to another molecule of (XXI), to form a molecule with a second double bond and no charge, (XXV), rearrangement of which produces the compound (XXIII). The hydride ion removed from (XXIV) may attack the original molecule at either of the positions of low electron density, shown, for convenience, in separate canonical forms (XXIB) and (XXIC). An attack on (XXIB), followed by protonation, would result in the formation of (XXVI), which, however, was not isolated. Attack by the hydride ion on (XXIC), followed by protonation and ketonisation of the resultant enol, would yield (XXVII), which again was not isolated.

An analogous disproportionation scheme (Scheme IV) was proposed by Meinwald and Emerman[18] to explain the formation of a mixture of one molecule of acetophenone and one of 1-acetylcyclohexene from two molecules of dihydroacetophenone, produced as an intermediate in the decomposition of ψ-pelletierine methiodide in alkaline solution.

SCHEME IV.

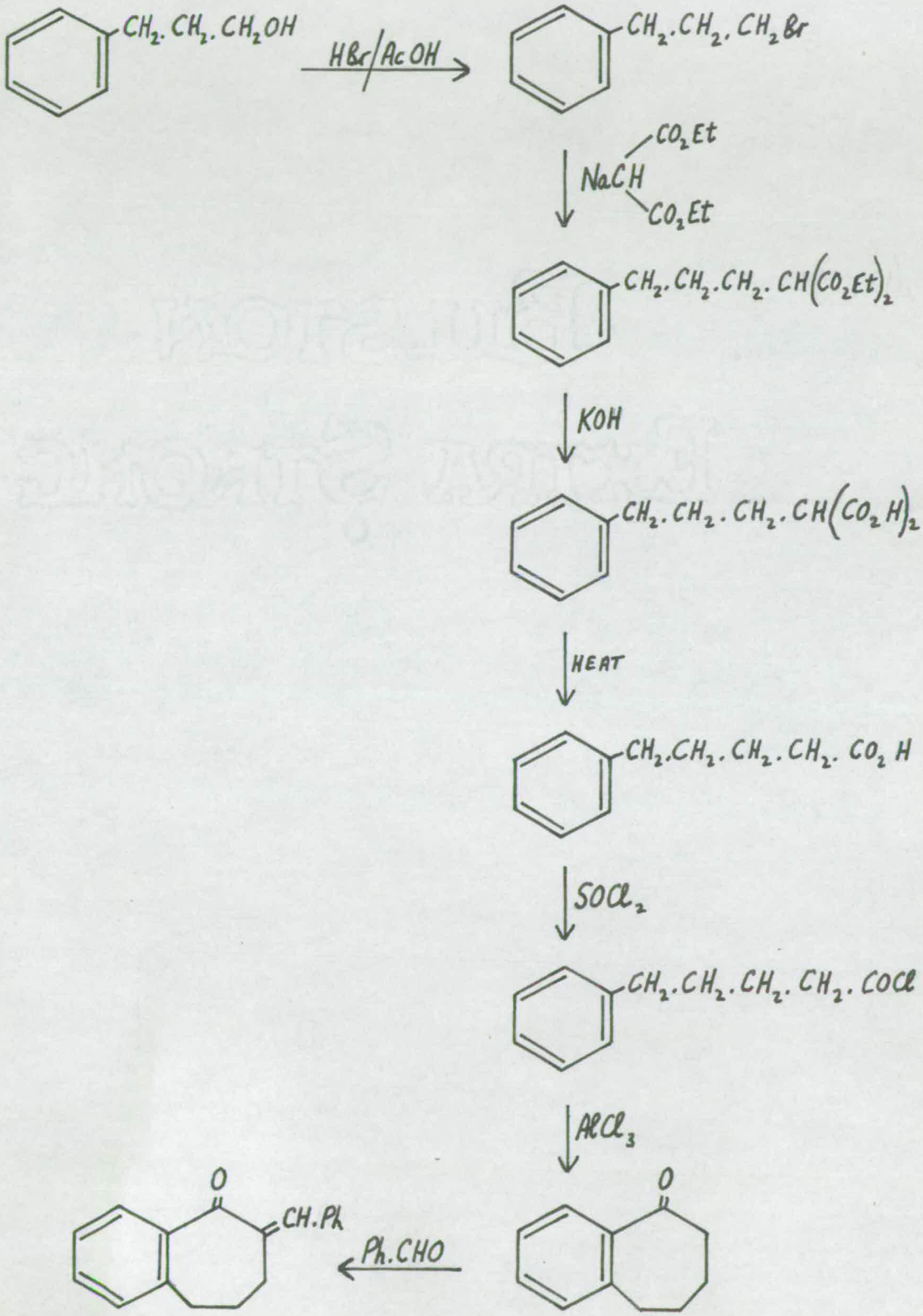


(c) Reaction of 2-benzylidene-6,7-benzocycloheptenone with ethyl acetoacetate.

This work was carried out to determine the effects on the properties, notably the absorption spectra and ease of rearrangement, of the related cyclohexenones shown in the notation scheme on p.12 if ring B is seven-membered. A greater ease of rearrangement has been noted in the hydrofluorene series than in the hydrophenanthrene series,[10] and this is thought to be caused by the strain introduced into the system by the five-membered ring; it is therefore of interest to find the effects brought about by the introduction of a seven-membered ring into the molecule.

The preparation of 2-benzylidene-6,7-benzocycloheptenone from γ-phenylpropyl alcohol is shown in Scheme V. The conversion of the alcohol to the bromide, followed by treatment of the latter with diethyl sodiomalonate, resulted in the formation of diethyl γ-phenylpropylmalonate which was hydrolysed and decarboxylated to form δ-phenylvaleric acid. Treatment of this acid with excess thionyl chloride converted it to the acid chloride which then cyclised in the presence of aluminium chloride to form benzosuberone, and treatment of this with benzaldehyde yielded benzylidenebenzosuberone, or 2-benzylidene-6,7-benzocycloheptenone.

SCHEME V.


CH2.CH2.CH2OH
HBr/AcOH
CH2.CH2.CH2Br
CO2Et
NaCH
CO2Et
CH2.CH2.CH2.CH(CO2Et)2
KOH
CH2.CH2.CH2.CH(CO2H)2
HEAT
CH2.CH2.CH2.CH2.CO2H
SOCl2
CH2.CH2.CH2.CH2.COCl
AlCl3
O
O
CH.Ph
Ph.CHO

In a second preparation of this product, the cyclisation of the δ-phenylvaleric acid was carried out in one stage by the use of polyphosphoric acid.[19,20] This is a cleaner and neater method of formation of many cyclic ketones directly from aryl-substituted acids or their esters as an alternative to conversion to the acid chlorides and ring closure with aluminium chloride.

Equimolar quantities of the benzylidene-compound and ethyl acetoacetate in ethanolic sodium ethoxide (0·2 mole), after refluxing for 3 hours and working up, yielded an oily product. Chromatography of this on a deactivated alumina column gave rise to two substances, X (m.p. 81°) and Y (m.p. 99°). The infrared spectrum of Y (Fig.9) showed a single carbonyl absorption band at 1663 cm.$^{-1}$ ($\alpha\beta$-unsaturated ketone) and a band at 1593 cm.$^{-1}$, attributed to a double bond absorption. The infrared spectrum of X (Fig.10) also showed a single carbonyl absorption band at 1660 cm.$^{-1}$ ($\alpha\beta$-unsaturated ketone) and a band at 1598 cm.$^{-1}$, again attributed to a double bond absorption. These infrared spectra and the elementary analyses of the compounds indicate that they must be the diastereomeric ketones represented by structure (XXVIII), (2,3,4,4a,5,6-hexahydro-2-oxo-4-phenyl-7H-dibenzo[a,c]cycloheptatriene, having asymmetric carbon atoms at $C_{(4)}$ and $C_{(4a)}$), which had evidently been formed by the hydrolysis and

FIG. 6

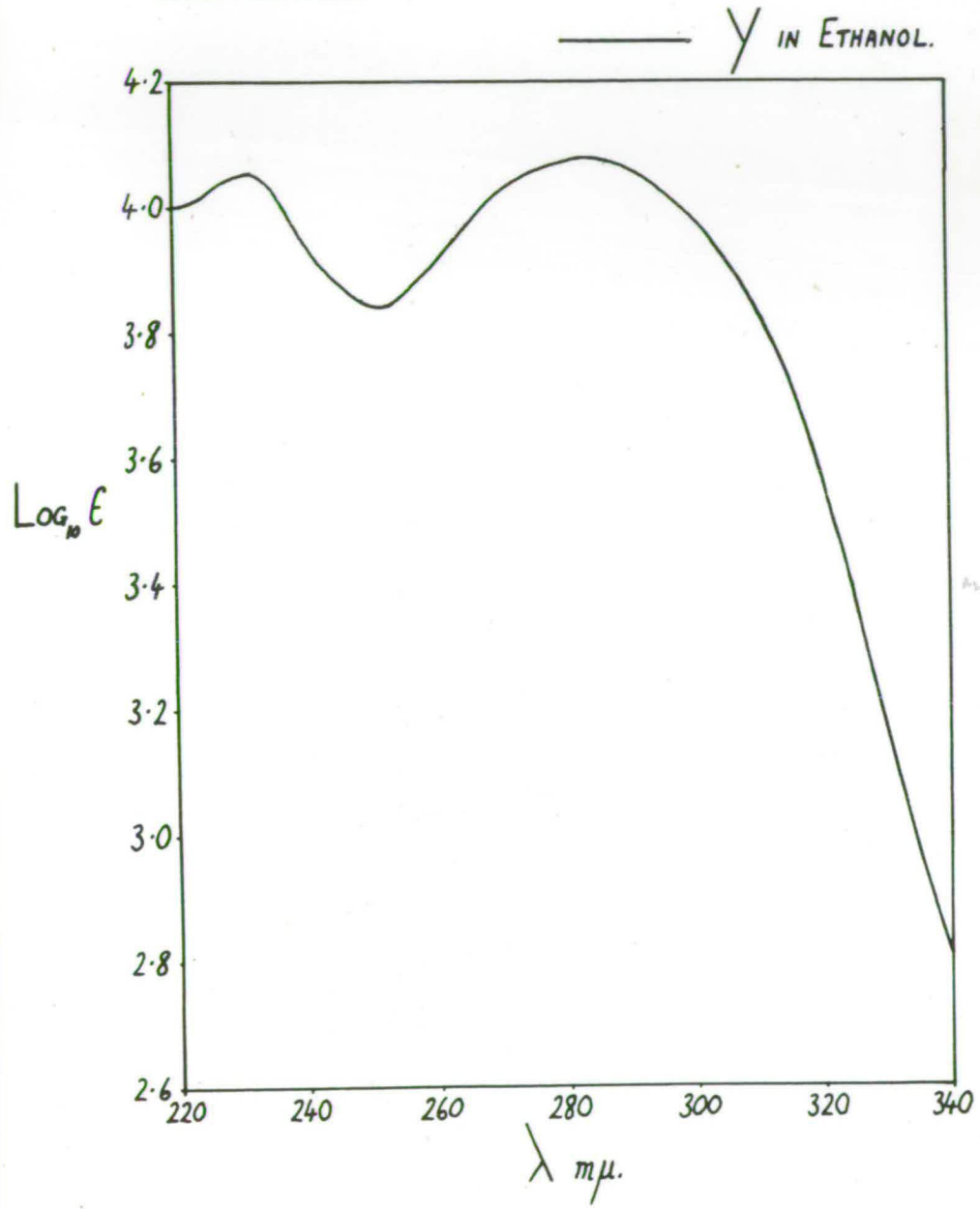

Y IN ETHANOL.
4·2
4·0
3·8
3·6
3·4
3·2
3·0
2·8
2·6
Log10 ε
220
240
260
280
300
320
340
λ mμ.

FIG. 7

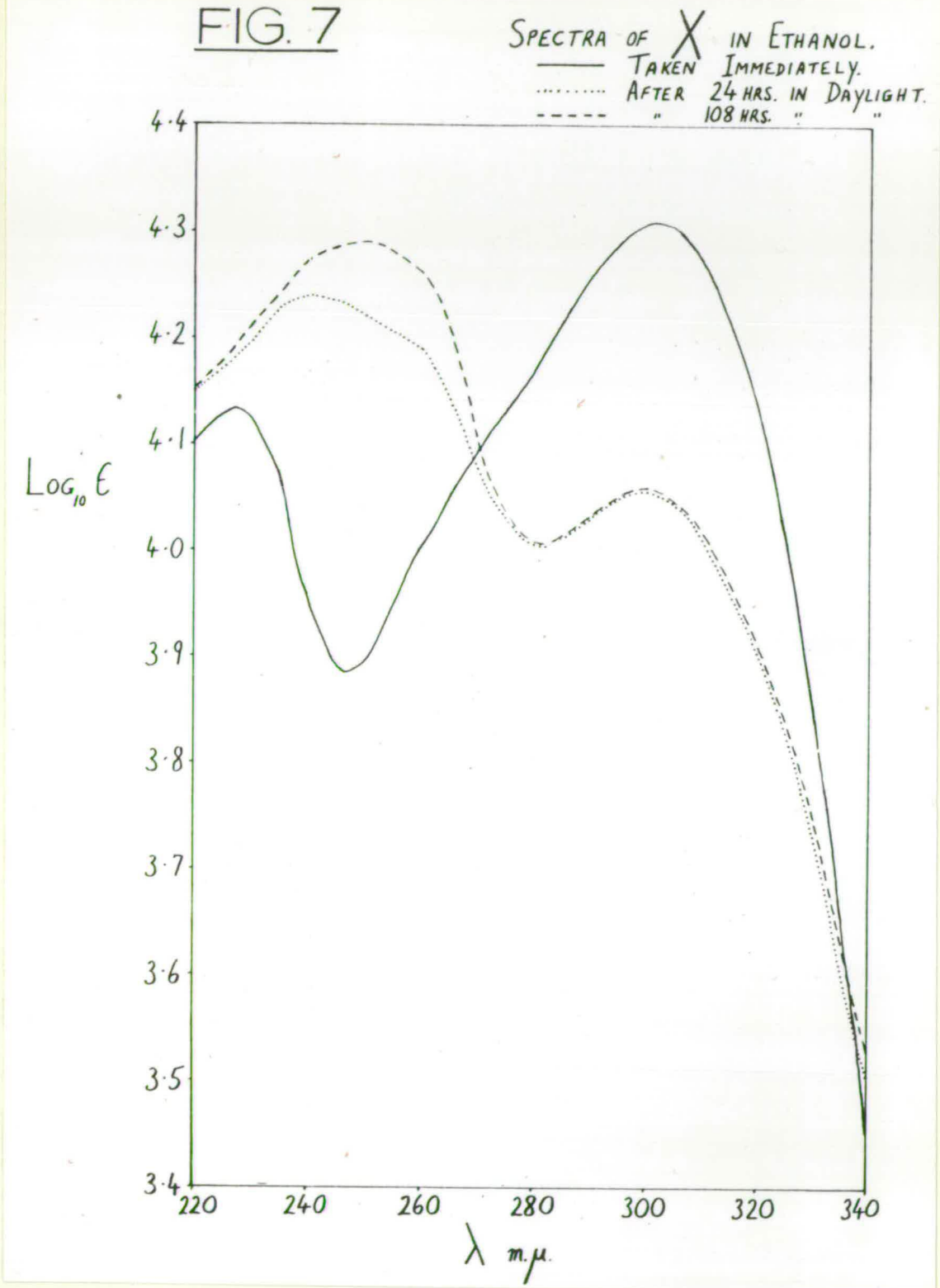

SPECTRA OF X IN ETHANOL.
TAKEN IMMEDIATELY.
AFTER 24 HRS. IN DAYLIGHT.
" 108 HRS. " "
4·4
4·3
4·2
4·1
4·0
3·9
3·8
3·7
3·6
3·5
3·4
Log10 ε
220
240
260
280
300
320
340
λ m.μ.

FIG. 8

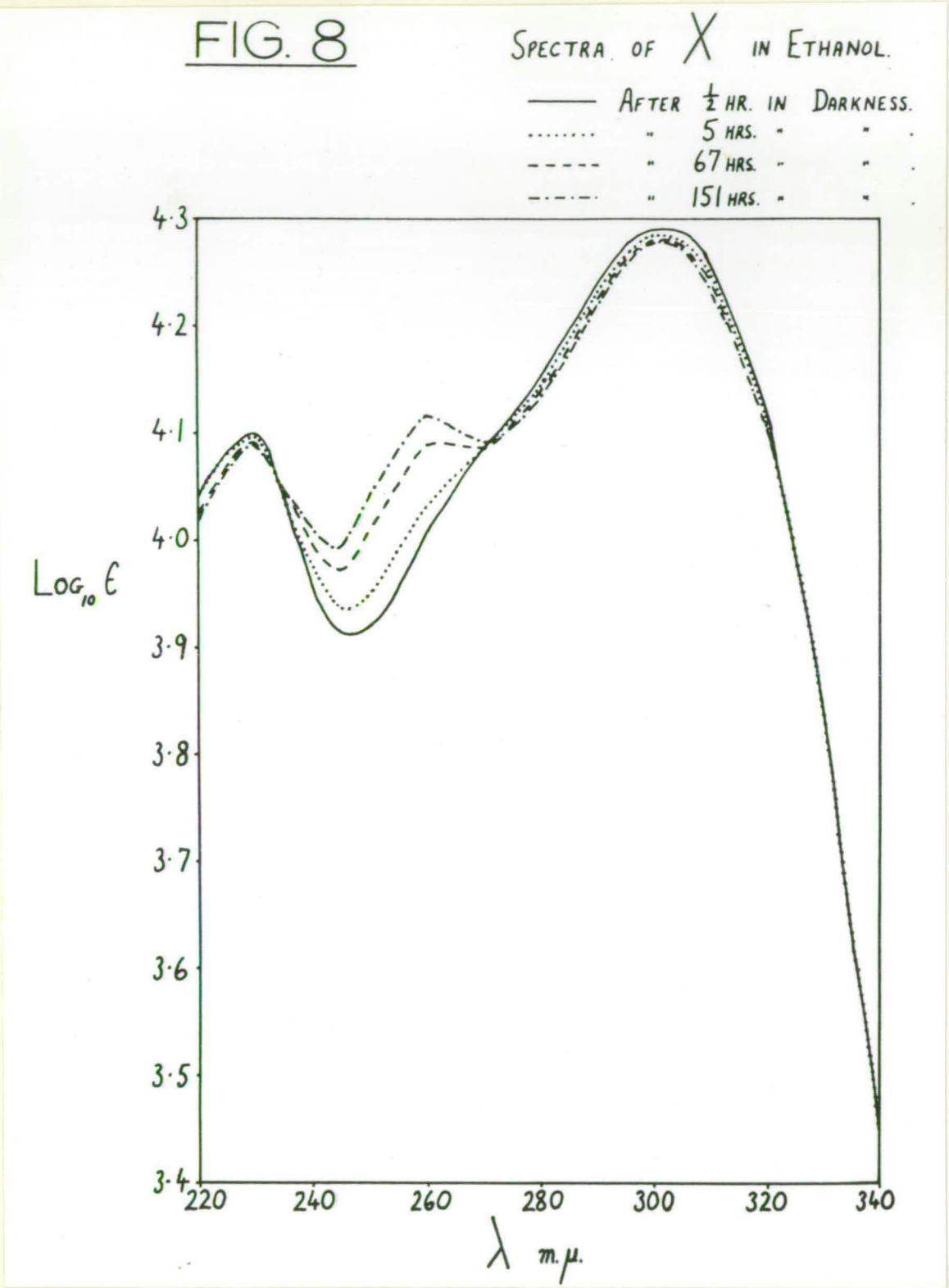

SPECTRA OF X IN ETHANOL.
AFTER ½ HR. IN DARKNESS.
" 5 HRS. " " .
" 67 HRS. " " .
" 151 HRS. " " .
4·3
4·2
4·1
4·0
3·9
3·8
3·7
3·6
3·5
3·4
LOG10 ε
220
240
260
280
300
320
340
λ m.μ.

FIG. 9

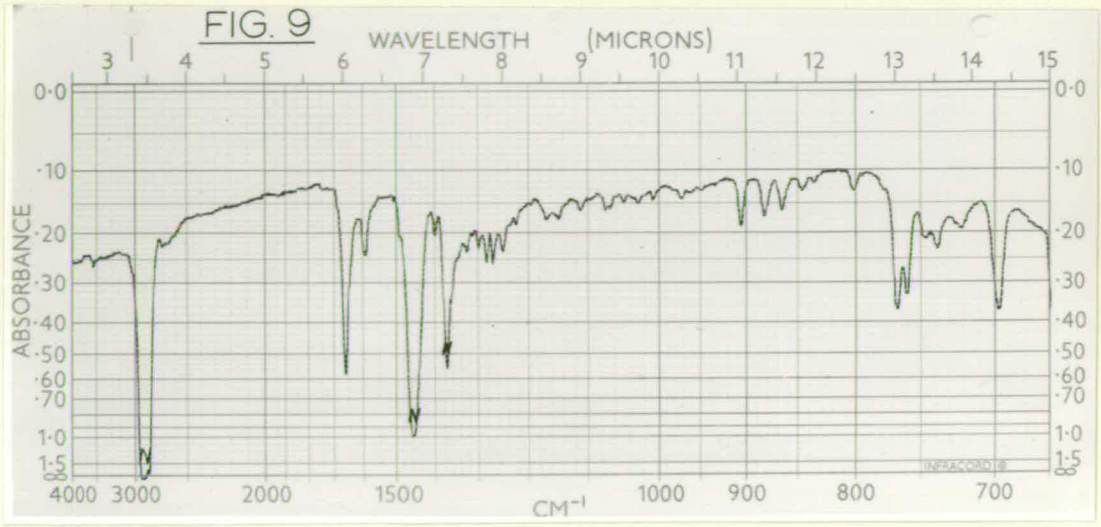

WAVELENGTH (MICRONS)
3 4 5 6 7 8 9 10 11 12 13 14 15
ABSORBANCE
0·0 ·10 ·20 ·30 ·40 ·50 ·60 ·70 1·0 1·5
4000 3000 2000 1500 1000 900 800 700
CM⁻¹
INFRACORD ®

FIG. 10

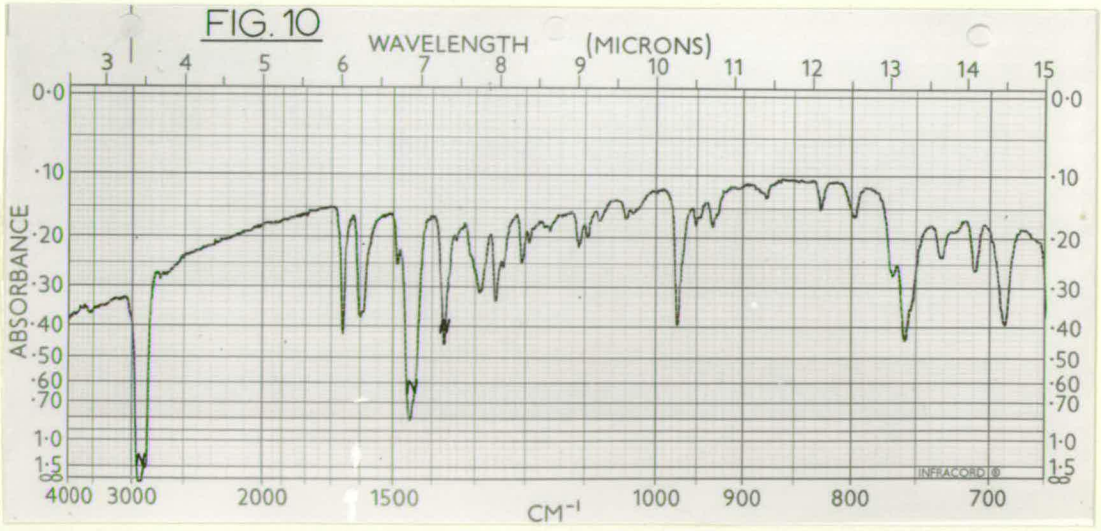

WAVELENGTH (MICRONS)
3 4 5 6 7 8 9 10 11 12 13 14 15
ABSORBANCE
0·0 ·10 ·20 ·30 ·40 ·50 ·60 ·70 1·0 1·5
4000 3000 2000 1500 1000 900 800 700
CM⁻¹
INFRACORD ®

FIG. 11

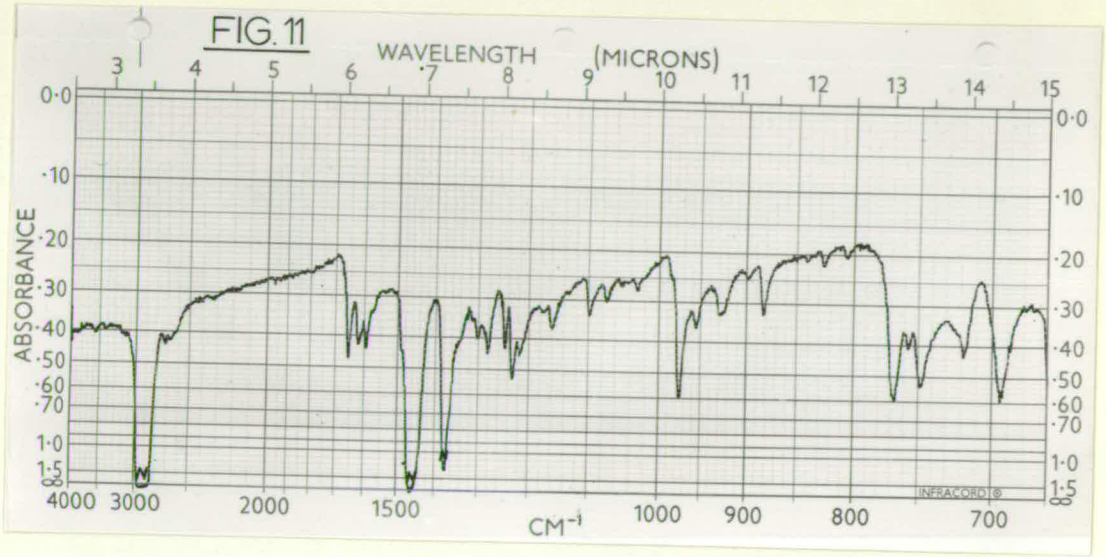
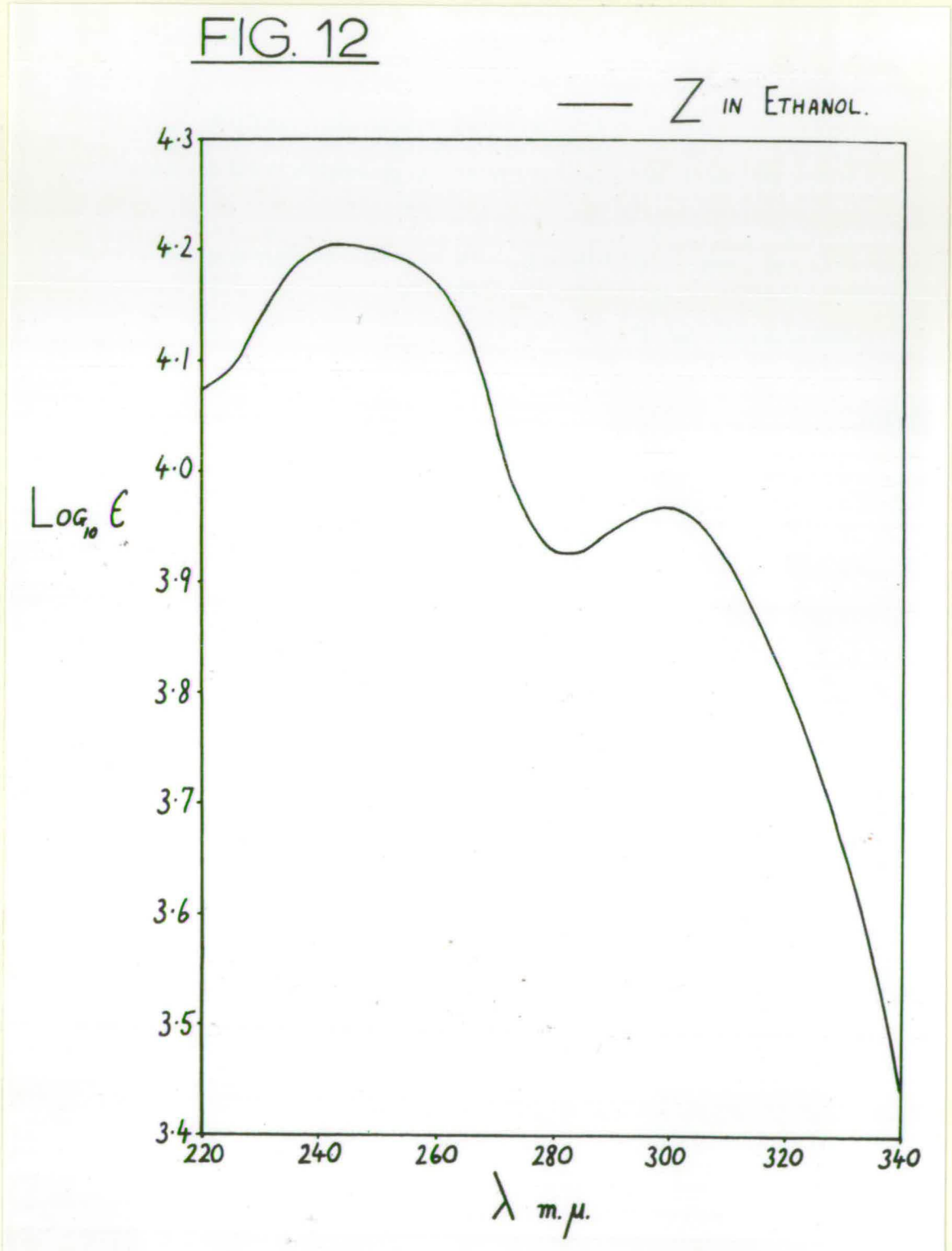
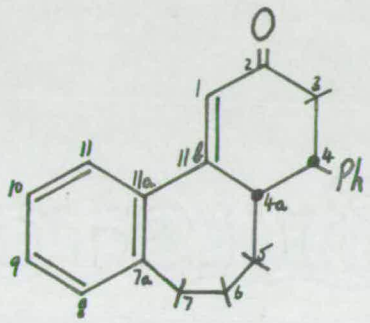

WAVELENGTH (MICRONS)
3
4
5
6
·7
8
9
10
11
12
13
14
15
ABSORBANCE
0·0
·10
·20
·30
·40
·50
·60
·70
1·0
1·5
4000
3000
2000
1500
CM⁻¹
1000
900
800
700
INFRACORD®

FIG. 12


— Z IN ETHANOL.
4·3
4·2
4·1
4·0
3·9
3·8
3·7
3·6
3·5
3·4
LOG10 ε
220
240
260
280
300
320
340
λ m.μ.

decarboxylation of the two isomeric ketoesters (corresponding to (Vf) and (XIVf)), which were the expected products of the reaction.



(XXVIII)

The loss of the carbethoxy group was thought to be due to hydrolysis caused by traces of water present in the ethanol used as reaction medium, but repetition of the reaction using dry ethanol failed to produce the compound with a carbethoxy group on $C_{(3)}$.

The ultraviolet absorption spectra in neutral solution of substances X and Y showed several points of interest, and are given in Table III, and in Figs.6,7 and 8.

TABLE III.

Compound.	Time.	λ max. mμ.	$\log_{10}\epsilon$	λ max. mμ.	$\log_{10}\epsilon$	λ max. mμ.	$\log_{10}$
1,2,3,9,10,10a-hexahydro-3-oxo-1-phenyl-phenanthrene.	Taken at once.	229	4·03			300	4·32
Y.	Taken at once.	231-2	4·05	284	4·08		
Y.	After 24 hrs. in darkness.	232	4·06	284	4·08		
Y.	After 24 hrs. in daylight.	231	4·07	283	4·08		
(Vb) in ethanol.	Taken at once.	229	4·01			301	4·34
X.	Taken at once.	227	4.13			301	4·31
X.	After 5 hrs. in darkness. (Taken at 5 mμ. intervals).	230	4·10			300	4·28
X.	After 151 hrs. in darkness. (Taken at 5 mμ. intervals).	230	4·10	260	4·12	300	4·28
X.	After 24 hrs. in daylight.	241	4·24			299-300	4·06
X.	After 108 hrs. in daylight. (Taken at 5 mμ. intervals).	250	4·29			300	4·06
Z.	Taken at once.	243-4	4·20			299	3·97

The ketone Y, which was formed in larger amount, had a time-independent ultraviolet absorption spectrum, with two absorption bands, at $\lambda_{max.}$ 232 mμ. and 284 mμ., the second of which was of considerably shorter wavelength and intensity than that of the corresponding compound (Vb) in which ring B is six-membered.

Compound X showed an ultraviolet absorption spectrum in ethanol which changed with time. In a freshly-made solution the maxima at 227 mμ. and 301 mμ. were comparable with those of the related compound (Vb) (see Table III). This absorption obviously corresponds to a conformation which is more nearly planar than that of Y. The spectrum of an ethanolic solution of X slowly changed on standing. The absorption maximum at 301 mμ. decreased in intensity and a small peak appeared at 263-4 mμ. which, in its turn, disappeared in time to give a final maximum at approximately 250 mμ. The first hypothesis to account for these spectral changes was that one conformation, with small interplanar angle, might be assumed by the molecule preferentially in the solid state, and another, with a larger interplanar angle, in solution. However, further investigation of the phenomenon revealed that this was not in fact the case. The ultraviolet spectra of solutions kept both in the dark and in daylight are shown in Figs. 7 and 8. A rapid change was produced in daylight, but the solution kept in the dark changed only very slowly, disproving the original theory that the change occurred spontaneously

in solution; it appeared rather to be brought about by light. Since there was no corresponding change in an ethanolic solution of the stereoisomer Y, it appears that the change is dependent on the stereochemistry of the compounds.

In an attempt to isolate the product of the light-induced reaction, it was found that exposure of a concentrated ethanolic solution of X to daylight over a period of 14 weeks was insufficient to bring about a complete transformation, but for a solution of 0·5g. X dissolved in the minimum volume of ethanol, irradiation from a 500 watt projector lamp for 114 hours, followed by ultraviolet irradiation for 24 hours, brought about complete transformation, as was confirmed by measurement of ultraviolet spectra at intervals throughout the irradiation process. (The change was rather slow using the projector lamp alone, but more rapid in ultraviolet light). Evaporation and alumina column chromatography of the irradiated solution yielded a pale yellow crystalline substance, Z, m.p. 86°, the infrared spectrum of which (Fig.11) was definitely not identical with that of X (Fig.10), but did show a very marked similarity. Compound Z (in Nujol) had a carbonyl absorption band at 1658 $cm.^{-1}$ ($\alpha\beta$-unsaturated ketone) and two further bands, at 1620 $cm.^{-1}$ and 1596 $cm.^{-1}$, attributed to double or aromatic bond absorptions. The similarity between the infrared spectra of Z and X

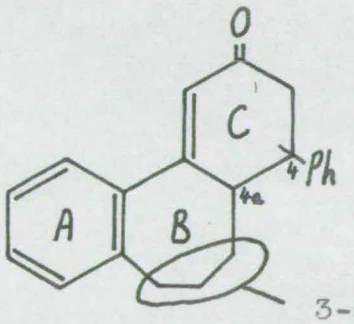
is very striking between 650 and 1100 cm.$^{-1}$. All the peaks in this region can be seen in both spectra with only small shifts in going from one to the other. A strong absorption band at 975 cm.$^{-1}$ in both spectra is particularly noticeable. The pattern of absorptions due to C-H out-of-plane vibrations of aromatic rings between 650 and 800 cm.$^{-1}$ is consistent with the presence of one mono-substituted and one ortho-disubstituted ring in both compounds.[21]

Elementary analysis of Z indicated a percentage composition close to that of X and the compound is considered to be an isomer of X, although molecular weight determinations (Rast) gave rather inconsistent results (222 and 208) which were somewhat lower than the required value for $C_{21}H_{20}O$. The ultraviolet absorption maxima of Z in ethanol are recorded in Table III, and in comparison with those of X, the maximum at ~300 mμ. is retained, but is now much lower in relative intensity, and the lower wavelength maximum at 227 mμ. in the spectrum of X is replaced by a much broader and more intense maximum at 243-4 mμ.. The complete spectrum of Z is shown in Fig.12, and this should be compared with the spectra of X in Fig.7, which show conclusively that Z is indeed the isomeric compound formed when an ethanolic solution of X is exposed to daylight.

To confirm the similarity between the three isomers X, Y and Z, their infrared spectra were measured

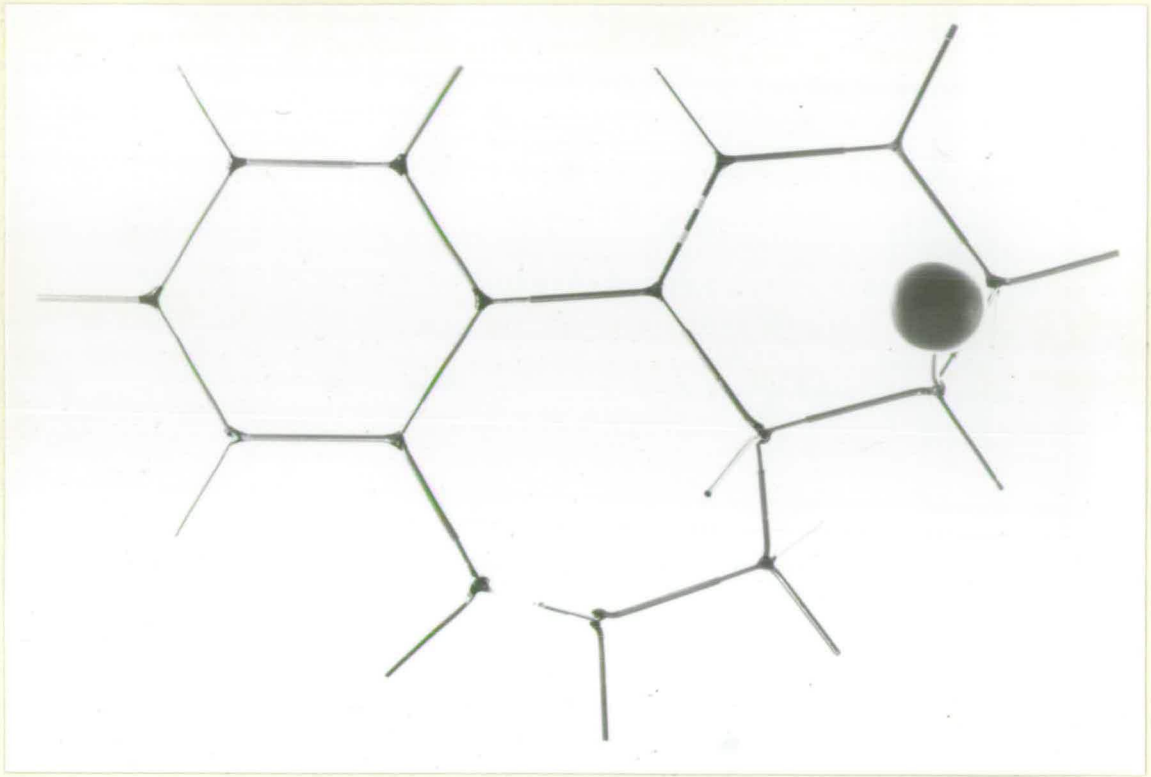
in carbon tetrachloride and showed carbonyl absorption bands at 1675 cm.$^{-1}$, 1674 cm.$^{-1}$ and 1670 cm.$^{-1}$ respectively, all characteristic absorptions of $\alpha\beta$-unsaturated ketones.[15]

The effects of the stereochemistry of these three compounds on their spectra are due to the presence of the 3-carbon bridge between rings A and C which, in order to attain a comparatively strainless conformation, twists the molecule about the single bond joining rings A and C, thus causing changes in interaction between the π-electron systems of these rings.

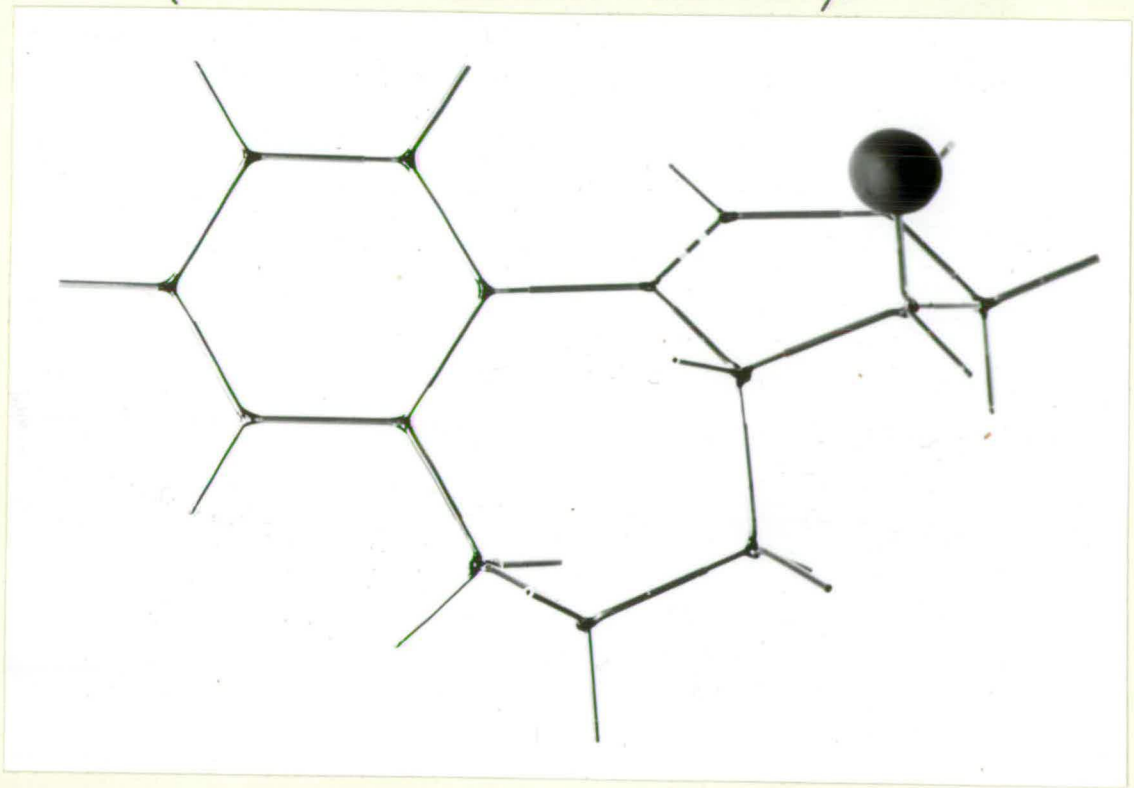


3-carbon bridge.

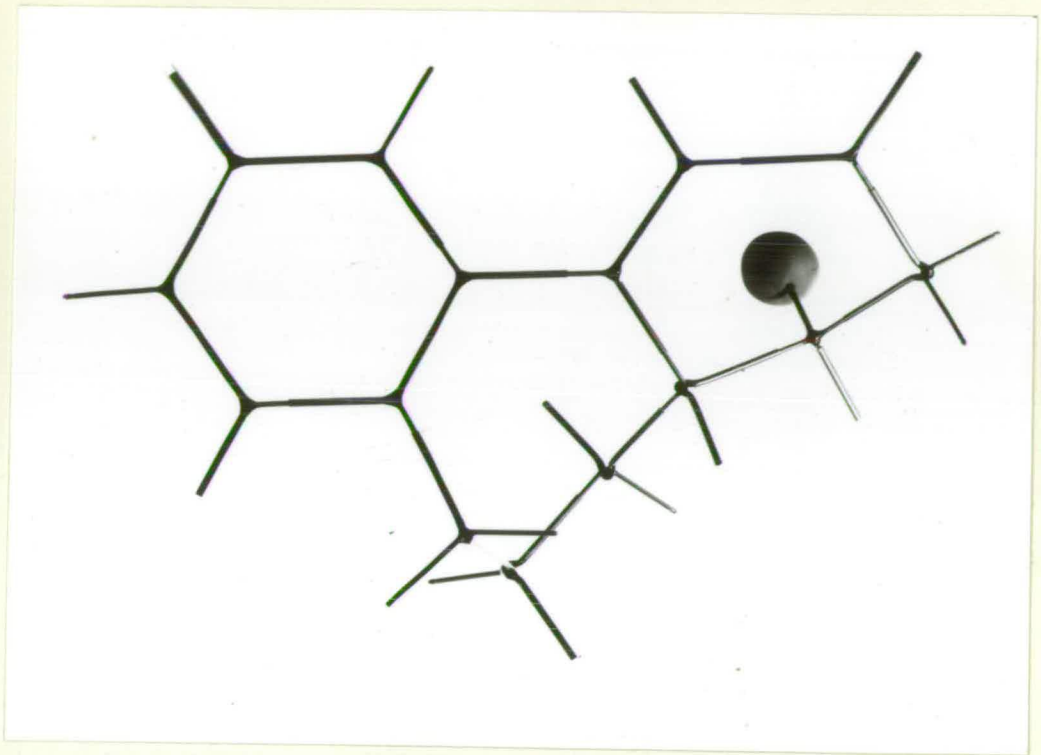
Models of the molecule indicate that great flexibility is possible when ring B is seven-membered, which is not possible in the corresponding series having ring B six-membered, and that, due to the 3-carbon bridge in the seven-membered ring, four principal conformations, relatively free from angle-strain, are possible. In these conformations the angles between the planes of rings A and C are approximately 0°-30° (a flexible conformation), 40°, 55° and 60°. The seven-membered ring exists in a boat[22] form



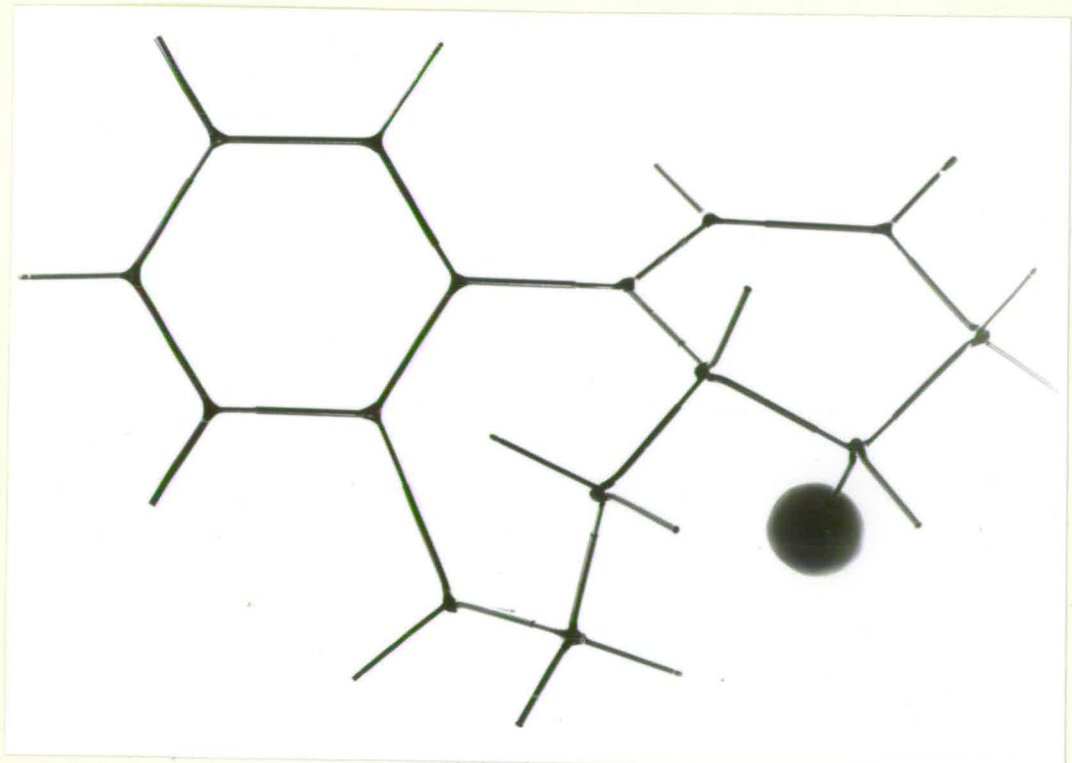
~ 0° – 30° CONFORMATION.
(BLACK BALL REPRESENTS Ph GROUP).



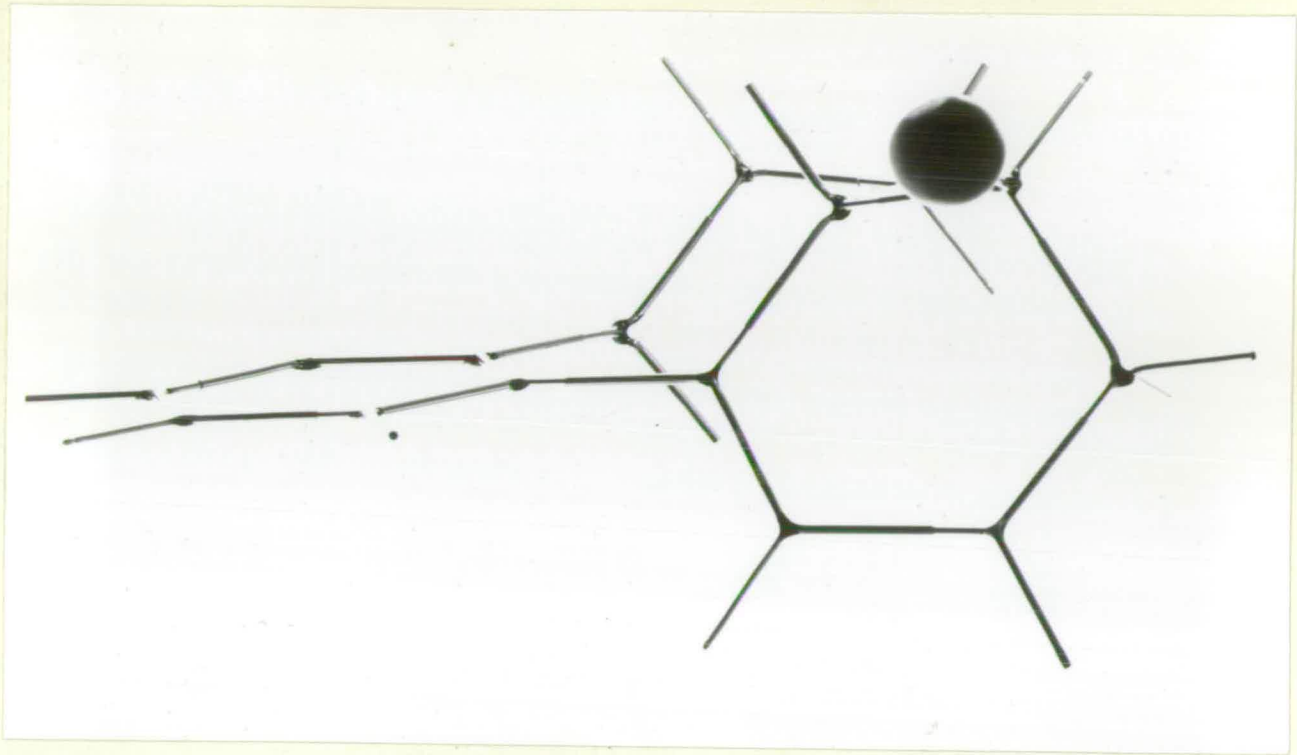
~ 60° CONFORMATION.



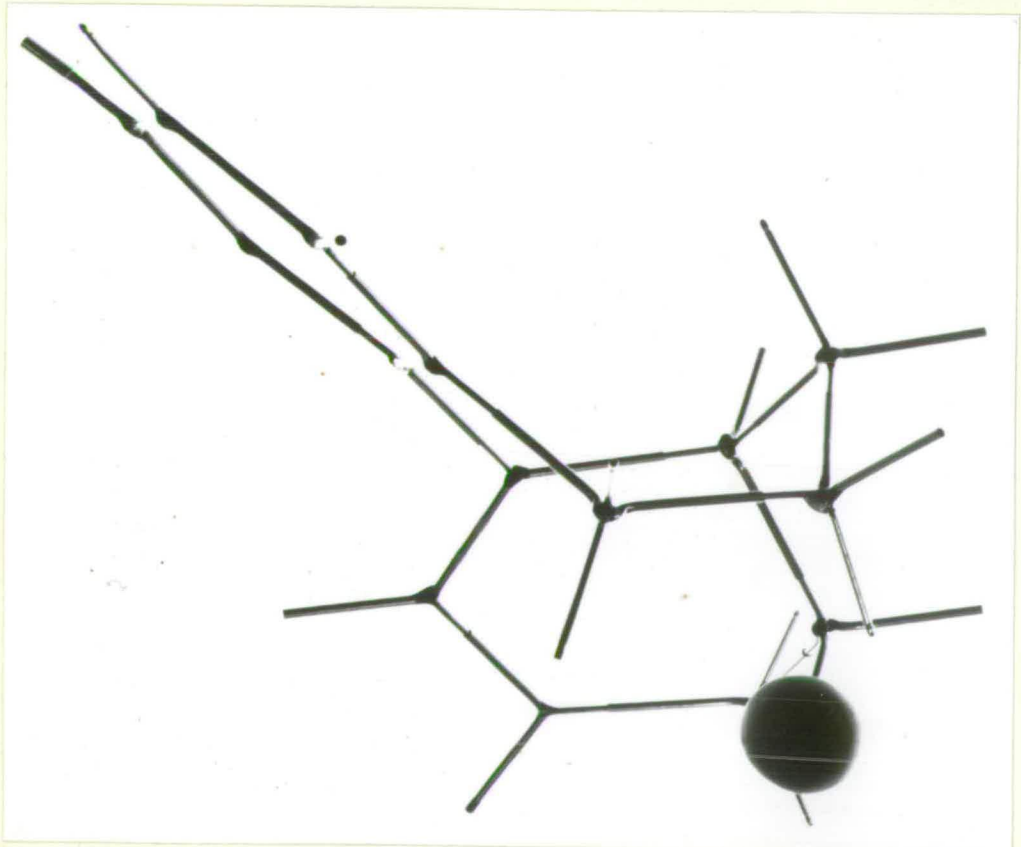
~ 40° CONFORMATION.



~ 55° CONFORMATION.

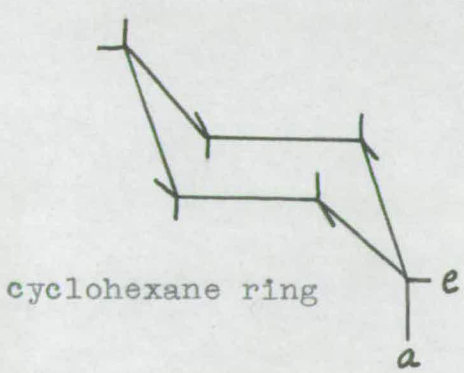


RING B CHAIR FORM.



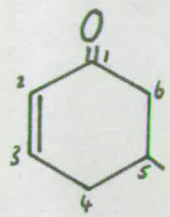
RING B BOAT FORM.

in the first three of these conformations, but in a chair[22] form in the fourth. Measurement of H-H distances (for consideration of H-H interactions) gave no precise indication as to which conformation would be preferred in an unsubstituted molecule having the same cyclic skeleton, but in compounds possessing a 4-phenyl substituent, the stereochemical configuration was clearly of considerable importance in determining the preferred conformations. In a cyclohexane ring a substituent is more stable in an equatorial conformation, because the four repulsive 1,2-interactions which affect such a group are of smaller energy than the two 1,2- and two 1,3-interactions affecting the same group in an axial conformation. For substituents at $C_{(5)}$ in a cyclohexenone ring, however, 1,3-interactions are obviously absent since $C_{(1)}$ and $C_{(3)}$ are both trigonal, so in this case the two repulsive 1,2-interactions affecting an axial substituent are obviously of smaller effect than the four 1,2-interactions affecting the same substituent in an equatorial conformation. It is probable, therefore, that axial conformations of 5-substituents will be preferred.

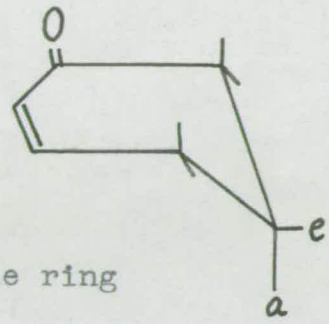


4 x 1,2-interactions

2 x 1,2-interactions
2 x 1,3-interactions



cyclohexenone ring

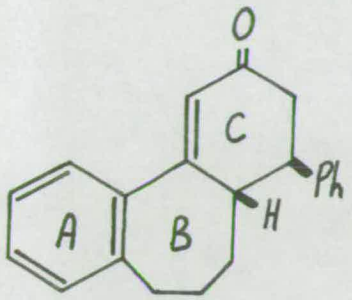


4 x 1,2-interactions

2 x 1,2-interactions

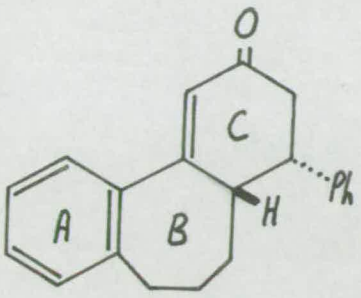
In the compounds in which ring B is five- or six-membered, the hydrogen at $C_{(9a)}$ or $C_{(10a)}$ is fixed in the axial position, the two stereoisomers have axial and equatorial phenyl groups respectively, and it is to be expected that the isomer with axial phenyl will be the more stable. However, owing to the great flexibility of the molecule when ring B is seven-membered, the hydrogen at $C_{(4a)}$ may readily adopt either an axial or an equatorial conformation, so that the phenyl group can remain axial in both stereoisomers which must, therefore, have different preferred conformations with different interplanar angles. The ultraviolet absorption spectrum of X resembles those of 1,2,3,9,10,10a-hexahydro-3-oxo-1-phenylphenanthrene and of the related ester (Vb), (see Table III), which, since both have a very small interplanar angle between rings A and C due to the relatively fixed and rigid six-membered ring B, suggests that compound X also has a small interplanar angle, probably the smallest one possible, (0°-30° conformation).

Since the ultraviolet absorption maximum of Y is at a lower wavelength, compound Y must have a larger interplanar angle, (possibly the 40° conformation). If these conformational assignments are correct, compound X can exist in a second conformation with axial phenyl group, having ring B in the chair form and few repulsive interactions. In this second conformation, however, the interplanar angle is large ($\sim 60^{\circ}$) and the models suggest that a considerable energy barrier exists between the two forms which may be sufficiently great for them to exist separately. It is suggested that Z is this second conformational isomer of X, and that the energy necessary to overcome the barrier to isomerisation $X \rightleftharpoons Z$ is supplied by light. The low wavelength of ultraviolet absorption of Z supports the suggestion that the conjugated system in this isomer deviates considerably from coplanarity. It is similarly possible for compound Y to exist in a second conformation in which the phenyl substituent remains axial, but strong repulsive interactions appear likely to inhibit this form. There appears to be a relatively low energy barrier (apart from the actual difference in energy levels) between the two conformations of Y, which would probably make separate existence of the two conformational isomers impossible.



300 mμ.

X



284 mμ.

Y

hν

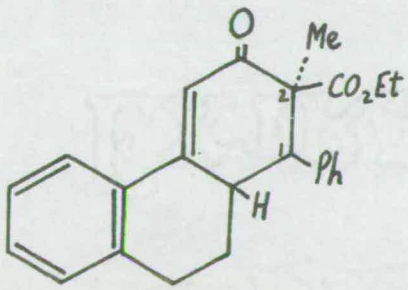
Ring B chair form

Z

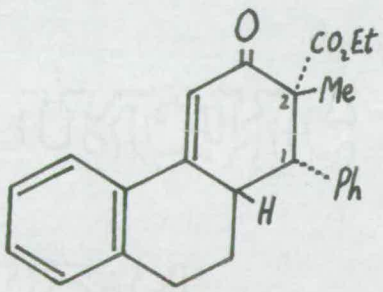
In the suggested conformations for X and Z the hydrogen at $C_{(4a)}$ is equatorial, whereas it is axial in that suggested for Y.

Distillation of Z under reduced pressure at 90°-120° resulted in the recovery of starting-material. After heating at 200° for 30 mins. in an atmosphere of nitrogen, cooling and redistilling, Z was still recovered. A similar experiment with X, heated at 200° for 15 mins. in a stream of nitrogen, cooled, then distilled under reduced pressure, yielded only X. The action of heat often interconverts cis-trans isomers of ethylenic compounds, but failed to interconvert X and Z.

An attempted conversion of X to Y by refluxing X in ethanolic hydrogen chloride, resulted only in recovery of the starting-material. A similar experiment with Y under the same conditions also failed, but in this case the product, as shown by its infrared solution spectrum in carbon tetrachloride, was neither Y nor its isomer X. The object of this experiment was to attempt to confirm the stereochemical relationship between the isomers by comparison with that between two compounds in the hydrophenanthrene series. Anderson and Leaver[10] found that treatment of esters (Vb) and (XIVb) with methyl iodide gave rise to two stereoisomers, (XXIX) and (XXX).



(XXIX)

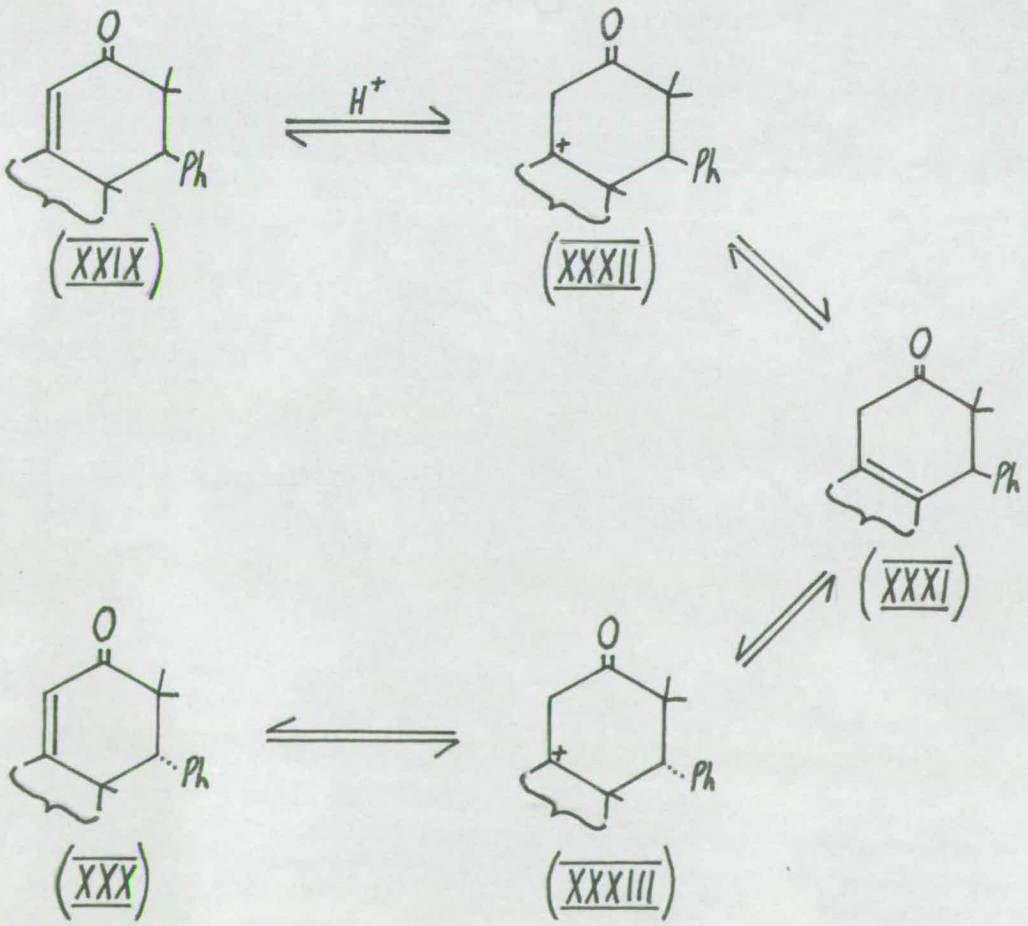


(XXX)

It was further found that treatment of ester (XXX) with ethanolic hydrogen chloride converted it to its stereoisomer (XXIX).[23] Since treatment with acid can only cause inversion at $C_{(10a)}$, (see below), it follows that $C_{(1)}$ bears the same stereochemical relationship

to $C_{(2)}$ in both the above isomers. The asymmetric centre at $C_{(2)}$ can therefore be neglected, thus permitting an analogy with X and Y, where only two asymmetric centres are present in the molecule.

The mechanism of this stereoisomeric conversion depends on the formation, from (XXIX) and (XXX) respectively, in acid solution, of the two cations (XXXII) and (XXXIII) which can be interconverted via the intermediate (XXXI), resulting in the eventual preponderance of the more stable cation. In the hydrophenanthrene series this is evidently (XXXII), corresponding to the isomer (XXIX).



(d). Reaction of 7-benzylideneacenaphthen-8-one with ethyl acetoacetate.

This reaction had been studied by Davison[24] but it seemed probable that some of the structures proposed for the products were incorrect or lacked sufficient evidence.

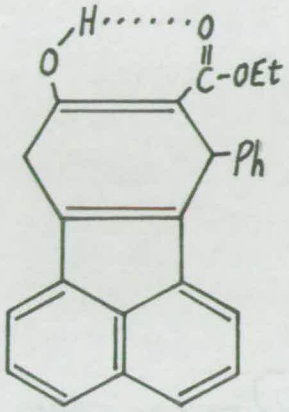
The preparation of acenaphthenone was attempted by two different methods. The first of these involved the polyphosphoric acid cyclisation of 1-naphthylacetic acid, which was carried out in a small-scale experiment first, to determine the optimum time of reaction. This was according to the suggestion of Koo[25] and Uhlig[26] that a study of the colour development might be used as a means of determining optimum reaction conditions. At the optimum point the colour of the reaction mixture reaches maximum intensity, generally a deep red colour but occasionally bright yellow or purple, and the reaction should be terminated at this point. In the preparation of acenaphthenone, use of this method of determining the optimum conditions of reaction gave only a very poor yield of product, 6%. This yield was increased to 26% when the reaction was repeated using the conditions of Green and Hey.[27]

The second method of preparation of acenaphthenone was, that used by Davison,[28] and by Fieser and Cason.[29] This involved the oxidation of acenaphthene to acenaphthenyl-8-acetate, from which acenaphthen-8-ol was formed on

alkaline hydrolysis. Chromic acid oxidation of this resulted in the formation of the required acenaphthen-8-one, which was purified by recrystallisation from acetone, rather than by the lengthier but more efficient method of steam distillation.

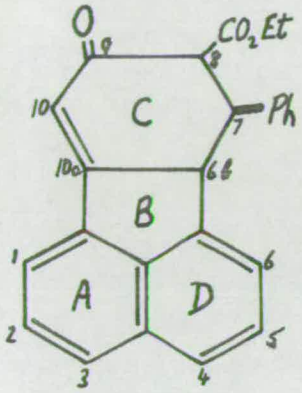
Acenaphthen-8-one (1 mol.) and benzaldehyde (2 mol.) in ethanol reacted in the presence of sodium hydroxide or sodium ethoxide solution to form 7-benzylideneacenaphthen-8-one.

Reaction of 7-benzylideneacenaphthen-8-one and ethyl acetoacetate, with ethanolic sodium ethoxide as catalyst, yielded a bright yellow crystalline product, m.p. 178°-180°, (Davison reported m.p. 180°-$181{\cdot}5^{\circ}$). The compound had an infrared carbonyl absorption band at 1663 $cm.^{-1}$ (chelated ester grouping), and two other bands, at 1618 $cm.^{-1}$ and 1575 $cm.^{-1}$, (with a shoulder at 1594 $cm.^{-1}$), attributed to double bond absorptions; it gave a purple colour with ferric chloride in alcoholic solution, comparable to that given by the β-modification of the compound from 2-furfurylidenetetralone and ethyl acetoacetate (XIIIc), (Section (a)). The compound may therefore be formulated as the enolic ethyl 7,10-dihydro-9-hydroxy-7-phenylfluoranthene-8-carboxylate, (XXXIV), rather than as the keto-tautomer of this compound suggested by Davison. The presence of the acenaphthylene chromophore is clearly shown by the resemblance of its ultraviolet spectrum (reported by Davison) to that of acenaphthylene.

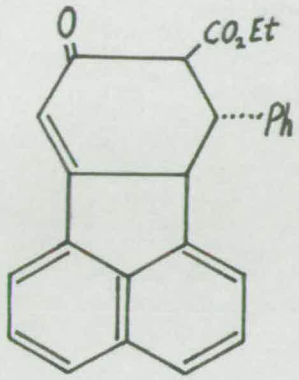


(XXXIV)

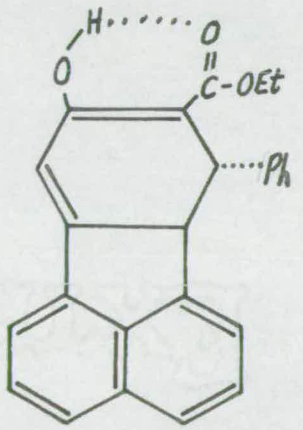
Recovery of material from the mother liquors followed by chromatography on a deactivated alumina column as described by Davison[30] failed to produce the lower-melting pale yellow compound (m.p. 160°-162°) to which the structure (XXXV) [or (XXXVI)] had been assigned.[24] However, analogy with the hydrofluorene and hydrophenanthrene series suggested that treatment of compound (XXXIV) with acid would be expected to give the two stereoisomers, represented by structures (XXXV) and (XXXVI) or (XXXVII), the enolic form of (XXXVI).



(XXXV)



(XXXVI)



(XXXVII)

Treatment of compound (XXXIV) with boiling saturated ethanolic hydrogen chloride resulted only in the recovery of starting-material. It is of interest to compare this result with those of Anderson and Leaver[10] who studied similar compounds which isomerised under these conditions. These workers found that treatment

of ester (XIVb) with ethanol saturated with hydrogen chloride resulted in the formation of a mixture of esters (Vb) and (XIIIb). Similar treatment of the methylated compound from ester (XIIIb) yielded the methylated compound from ester (Vb), and exactly analogous results were found for the hydrofluorene series.

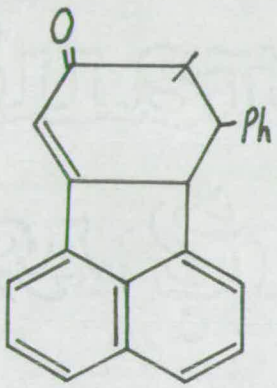
It was found in the hydrophenanthrene series[10] that the reaction of ester (XIIIb) in concentrated sulphuric acid for 2 mins. yielded mainly the isomeric ester (XIVb), and that similar reaction for 10 mins. yielded a mixture of esters (Vb) and (XIVb). In the hydrofluorene series, treatment of ester (XIIIa) in concentrated sulphuric acid for 5 mins. yielded the ester (VIa), together with the isomers (Va) and (XIVa). For comparison with these results, compound (XXXIV) was treated with concentrated sulphuric acid for 5 mins.. The crude material showed, as well as an infrared carbonyl absorption band at 1658 $cm.^{-1}$ ($\alpha\beta$-unsaturated ketone and/or chelated ester), a band at 1737 $cm.^{-1}$ (unconjugated ester), indicating probably that some of the isomeric compound (XXXV), with an equatorial phenyl group, had been produced. However, on recrystallisation of the crude compound, only starting-material was recovered. Attempts to recover the isomer (XXXV) by chromatography of the recrystallisation filtrates were unsuccessful, yielding instead a yellow solid, m.p. 160°-$160{\cdot}5^{\circ}$, which had an infrared carbonyl absorption band at 1655 $cm.^{-1}$ (chelated ester grouping), and another band at 1583 $cm.^{-1}$ attributed

to a double bond absorption [cf. compound (XIVc); ν max. 1653 and 1585 cm.$^{-1}$]. This substance was therefore the enolic isomer (XXXVII) [Ph axial by analogy with (XIVa and b)], and was proved to be the compound (m.p. 160°-162°) obtained by Davison.[24] The confirmation was given by its elementary analysis (although Davison reported rather unsatisfactory figures) and by a comparison of the ultra-violet absorption spectra ($\lambda_{max.}$ 233 mμ. (log ϵ 4·42), 260 (3·93), 269 (3·91), 301 (4·26), 309 (4·26), and 324 (3·93)). With ferric chloride in alcoholic solution the compound gave a transient green colour which rapidly turned yellow.

Compound (XXXV), of which all traces disappeared in recrystallisation, appears to be very unstable. This is readily understandable because, whereas in the previous series studied ring D was absent, in compound (XXXV) the hydrogen atom on $C_{(6)}$ of ring D must interfere considerably with the $C_{(7)}$ phenyl group, if this exists in the equatorial conformation, and probably causes the compound to rearrange very easily, even in absence of alkali, to the isomer (XXXIV). As in the hydrofluorene series, rearrangement of the Ph-axial isomer (XXXVII) evidently occurs fairly readily in alkali since Davison[31] found that the ultraviolet spectra of (XXXIV) and (XXXVII), in ethanolic sodium ethoxide, were almost identical. Presumably ring strain is again a factor leading to greater ease of rearrangement.

Decarbethoxylation of compound (XXXIV) by refluxing with acetic acid, sulphuric acid and water for 15 mins.

and working up, yielded a yellow solid, m.p. 185°-186·5°, which now showed only one infrared absorption band above 1500 cm.$^{-1}$; this was at 1665 cm.$^{-1}$, characteristic of an $\alpha\beta$-unsaturated ketone, thus confirming Davison's[24] assignment of the structure (XXXVIII).



(XXXVIII)

From the work described in this section it appears that the products of the condensation of 7-benzylidene-acenaphthen-8-one with ethyl acetoacetate are isomers, but neither exists in the keto-form as postulated by Davison.

EXPERIMENTAL.

EXPERIMENTAL.

Melting-points were determined in a capillary tube in a butyl phthalate bath,[32] or on a Gallenkamp melting-point apparatus, and are uncorrected. Elementary analyses and molecular weight determinations were carried out by Drs. Weiler and Strauss, Oxford. Infrared and ultraviolet absorption spectra are recorded in the 'Results and Discussion' section. Ultraviolet absorption spectra were measured on a Unicam SP.500 quartz spectrophotometer. Absolute ethanol was purified for spectroscopy by refluxing with sodium (10g. sodium to one Winchester of alcohol) and redistilling. Infrared absorption spectra were measured on a Perkin-Elmer Infracord spectrophotometer. Chromatographic separations were carried out on Peter Spence Type H alumina which had been partially deactivated by addition of aqueous acetic acid. All ether extracts were dried over anhydrous sodium sulphate, and evaporated under reduced pressure. The light petroleum had b.p. 40°-60°, unless otherwise stated.

SECTION (a).

2-Furfurylidene-1-tetralone.[7]

Aqueous sodium hydroxide (2 ml. of 8%) was added to a solution of freshly-distilled furfuraldehyde (11.2g.) and α-tetralone (17g.) in ethanol (50 ml.). The solution immediately turned dark green, and after an hour a mass of needle-shaped crystals had formed. After 18 hours the crystals were filtered off and washed with ethanol. They were pale yellow needles, m.p. 72° and 76°, unaltered by recrystallisation from ethanol. The crystals melted first at 72° and, after cooling, remelted at 76°. Two melting-points are possible since the substance is dimorphous, existing in two different crystalline forms, needles and prisms. Yield = 23·3g. (89·4%).

Condensation of 2-furfurylidene-1-tetralone with ethyl acetoacetate.[cf.7]

(A). Sodium (0·15g.; 0·4 mole) was dissolved in absolute ethanol (25 ml.), ethyl acetoacetate (8·25g.; 4 mols.) and furfurylidenetetralone (3·5g.; 1 mol.) were added, and the solution was made up to 35 ml. with absolute ethanol. After refluxing for 3 hours, the solution was stoppered securely and left at room temperature for 3 days,

during which time it became red in colour, but no crystallisation occurred. The solution was poured into water, acidified with glacial acetic acid, extracted with ether, dried and evaporated, leaving a very viscous brown solution which crystallised slightly on the addition of a few drops of ethanol and light petroleum (b.p. 60°-80°), and completely after a further 24 hours at room temperature. Yellow crystals were filtered off, m.p. 112°-116° from ethanol. They gave a greenish-brown colour with ferric chloride in alcoholic solution, indicating that this product was a mixture of the α- and β-modifications.

(B). Sodium (0·75g.; 2 mols.) was dissolved in absolute ethanol (25 ml.), ethyl acetoacetate (8.25g.; 4 mols.) and furfurylidenetetralone (3·5g.; 1 mol.) were added, and the solution was made up to 35 ml. with absolute ethanol as before. After refluxing for 30 mins. and addition of a large excess of glacial acetic acid, the solution was poured into water, extracted with ether, dried and evaporated. The resulting brown viscous solution crystallised readily on addition of a few drops of ethanol, giving bright yellow crystals, m.p. 120°-121° from ethanol. This substance gave a green colour with ferric chloride in alcoholic solution, and was the α-modification, (XIVc).

(C). The reaction mixture was made up as in (B), and after refluxing for 4 hours the solution was stoppered

and left at room temperature overnight, but no crystallisation occurred. The solution was then poured into water, acidified, extracted with ether, dried and evaporated as in (B). The resulting brown viscous solution crystallised slowly on addition of a few drops of ethanol and light petroleum (b.p. 60°-80°), to yield yellow needles, m.p. 122°-123° from ethanol, which gave a violet colour with ferric chloride in alcoholic solution, and were crystals of the β-modification, (XIIIc).

(D). 1,2,3,9,10,10a-hexahydro-1-2'-furyl-3-oxophenanthrene, (XX).

The ethanolic filtrates from preparation of the α-modification were evaporated, dissolved in benzene and chromatographed on a deactivated alumina column. The alumina had been neutralised and deactivated by shaking up with 5% by weight of water containing 10% glacial acetic acid.[33,34] This preparation of the alumina was in an attempt to isolate the ketone present, which would pass through the column relatively easily, whereas the enolic esters would tend to adhere to the column and be removable only with difficulty. The material was eluted with light petroleum/benzene mixtures; 40% benzene yielded a yellow solid, which became colourless, m.p. 112°-113°, on recrystallisation from ethanol.

(E). Ethyl 1,2,3,9,10,10a-hexahydro-1-furyl-3-oxophenanthrene-2-carboxylate, (Vc).

From the column used in section (D) above, further elution with 50% benzene yielded a pale yellow solid, which became colourless, m.p. 111°-113°, on recrystallisation from ethanol. (Found: C,74·3; H,6·0. $C_{21}H_{20}O_4$ requires C,75·0; H,6·0).

SECTION (b).

2-Benzylidene-1-tetralone.

10% potassium hydroxide in 95% ethanol was added dropwise to a solution of α-tetralone (46·4g.) and freshly-distilled benzaldehyde (33·7g.) in ethanol (135 ml.). The solution darkened, turned green, then purple, and a slight warming of the reaction flask was felt. At this stage the flask was stoppered and left overnight. A mass of large coarse, pale greenish-yellow needles was deposited. After recrystallisation from ethanol, the crystals were very pale yellow, m.p. 105°-106°. Yield = 45·0g. (60·5%).

1,2,3,9,10,10a-hexahydro-3-oxo-1,2-diphenylphenanthrene, (XXI).

Benzylidenetetralone (2·0g.), benzyl methyl ketone (1·15g.) and sodium (0·2g.) were dissolved in 50 ml. ethanol and refluxed for 3 hours. The solution was poured into water, extracted with ether, dried and evaporated. The resultant solid was washed with the minimum amount of light petroleum and dried. The crystals were colourless plates, m.p. 230° from ethanol. (Found: C,88·8; H,6·3. $C_{26}H_{22}O$ requires C,89·2; H,6·3).

In a larger scale preparation, the benzyl methyl ketone (15·0g.) was added first to the benzylidenetetralone (26·2g.), then sodium ethoxide solution (2·6g. sodium in

160 ml. ethanol) was added, and the solution was refluxed for 4 hours, during which time it darkened and deposited a light brown powdery solid. After cooling, the solid was filtered off by suction and the filtrate was refluxed for a further 2 hours. Again a slight deposit of solid formed which was filtered off as before, and the filtrate was refluxed for a further 2 hours. Since little new solid formed, the contents of the reaction flask were poured into water, extracted with ether and dried as before; evaporation of the extract yielded no further solid. The solid product previously filtered off was recrystallised from ethanol, in which it was only sparingly soluble, in a Soxhlet extractor. The product was light brown after washing with light petroleum, but on recrystallisation from an ethanol/benzene mixture, in which it was more readily soluble, colourless needles were obtained, m.p. 227°-228·5°. Yield = 14·7g. (37·5%).

9,10-dihydro-3-hydroxy-1,2-diphenylphenanthrene, (XXIII).

24 ml. of a solution of sodium ethoxide (1g. of sodium in 30 ml. dry ethanol) were added to a suspension of 4g. of 1,2,3,9,10,10a-hexahydro-3-oxo-1,2-diphenyl-phenanthrene, (XXI), in ~25 ml. dry ethanol. A further 200 ml. dry ethanol were added, and the suspension was refluxed for 3 hours, when the solution darkened considerably. Undissolved solid was filtered off, and the remaining

solution was poured into water, extracted with ether, dried and evaporated, leaving a very viscous brown material, (approx. 3g.). After unsuccessful attempts to cause crystallisation, this was dissolved in the minimum amount of benzene and purified by chromatography on an alumina column which had been neutralised and deactivated with 5% by weight of water containing 10% glacial acetic acid. Elution with a light petroleum/benzene mixture containing 40% benzene yielded a pale yellow solid on evaporation. Recrystallisation of the product from a light petroleum (b.p. 60°-80°)/alcohol mixture yielded a white solid, m.p. 158°-159°. (Found: C,89·5; H,5·6. $C_{26}H_{20}O$ requires C,89·7; H,5·7).

SECTION (c).

γ-Phenylpropyl bromide.

γ-Phenylpropyl alcohol (100 ml.) and twice the volume of hydrobromic acid/acetic acid (50%) were refluxed on a water-bath for 3 hours, after which the solution, which had turned dark brown, was diluted with 300 ml. water and separated. The organic layer was washed with water and with sodium carbonate solution containing some hydroxide, to remove free bromine, then was diluted with ether, dried and distilled. The bromide distilled as a colourless liquid, b.p. 114°-115°/13 mm..
Yield = 126·0g. (87·0%).

Diethyl γ-phenylpropylmalonate.[cf.35]

Sodium wire (17·5g.; 1·2 atoms) was added to 1 litre of dry benzene, freshly-distilled malonic ester (121·5g.; 1·2 mols.) was added and the mixture was refluxed. The solution became dark yellow, and an insoluble coating of diethyl sodiomalonate formed on the sodium wire, but on the addition of 20 ml. dimethylformamide a vigorous reaction occurred and the sodium wire dissolved more readily. When all the sodium had dissolved the solution was cooled in ice-water, phenylpropyl bromide (126·0g.; 1 mol.) was added, and the mixture was left to stand overnight at room

temperature. After addition of a further 20 ml. dimethylformamide, the solution was refluxed for 6 hours. The reaction mixture was poured into water, forming two layers. The aqueous layer was extracted with ether and the extract combined with the benzene layer, dried over sodium sulphate, and distilled. After the removal of ether, benzene, and excess malonic ester, the malonate distilled at 134°/0·2 mm.. Yield = 98·2g. (55·8%).

γ-Phenylpropylmalonic acid.[35]

Diethyl γ-phenylpropylmalonate (98·0g.) was warmed and frequently shaken with a two-fold amount by weight of 35% aqueous potassium hydroxide solution and 15-20 ml. ethanol. Saponification was complete after 45 mins. and the solution was cooled, made strongly acid with 20% hydrochloric acid, extracted with ether, dried and evaporated. The resultant yellow oil yielded the white crystalline acid on cooling.

δ-Phenylvaleric acid.[36]

The γ-phenylpropylmalonic acid formed above was decarboxylated by heating under reduced pressure at 140°-180° for 2 hours. On cooling, the dark yellow oily liquid yielded a white crystalline product. Yield = 54·0g. (% yield over the last two stages = 86·1%).

Benzosuberone.

(A). Preparation of δ-phenylvaleryl chloride, and ring closure with aluminium chloride.

δ-Phenylvaleric acid (33·5g.) was refluxed (condenser fitted with calcium chloride tube) with 20% excess thionyl chloride until fumes of hydrogen chloride were no longer evolved (2-3 hours). Addition of 25 ml. dry benzene followed by distillation removed excess thionyl chloride, which distilled off with the benzene, leaving δ-phenylvaleryl chloride. Yield = 28·7g. (77·6%).

δ-Phenylvaleryl chloride (28·7g.) in carbon disulphide (442 ml.)[37] was added dropwise (11 hours) to a stirred refluxing mixture of aluminium chloride (40·5g.) and carbon disulphide (294 ml.), and stirring was continued for a further 12 hours. The carbon disulphide was removed by distillation, and 800g. of ice were added to the reaction flask to decompose the residue. Steam-distillation for 5 hours, followed by extraction of the distillate with ether, drying and evaporation of the extract, yielded benzosuberone which distilled at 135°-136°/12 mm.. Yield = 8·7g. (37·2%).

(B). Polyphosphoric acid cyclisation of δ-phenylvaleric acid.[cf.38]

Polyphosphoric acid was prepared by addition of

phosphorus pentoxide (582g.) to 89% phosphoric acid (280 ml.) in a three-necked flask fitted with condenser and stirrer. The mixture was kept at 120° for 6 hours, i.e. until all the phosphorus pentoxide had dissolved. The polyphosphoric acid was left overnight, then was heated to 80°, and δ-phenylvaleric acid (50g.) was added in small amounts (1-2 hours). The reaction mixture was kept at 100° for 2 hours, then left overnight at room temperature. It was poured into water with cooling, and extracted with benzene. The extract was washed with sodium carbonate solution (5%) and dried over anhydrous sodium sulphate. After distillation of the benzene, the benzosuberone distilled at 130°-132°/10mm.. Yield = 29·0g. (64·6%).

Benzylidenebenzosuberone.

Equivalent quantities of benzosuberone (15·0g.) and freshly-distilled benzaldehyde (9·9g.) were dissolved in ethanol (43 ml.). Sodium ethoxide solution (2·0g. sodium in 40 ml. ethanol) was added dropwise until a slight warming of the reaction flask was felt. The flask was stoppered and left at room temperature overnight. (After standing for 10-15 mins. the pale yellow solution darkened to a light brown and white crystals began to form while the solution was still warm). After filtration, the crystals were washed with the minimum amount of ice-cold ethanol, and then with light petroleum.

M.p. = 81°-82°. Yield = 22·6g. (97·0%).

Condensation of benzylidenebenzosuberone with ethyl acetoacetate.

Benzylidenebenzosuberone (12·0g.) and freshly-distilled ethyl acetoacetate (6·3g.) were added to sodium ethoxide (0·22g. sodium in 80 ml. dry ethanol), and the solution was refluxed for 3 hours, with the condenser fitted with a calcium chloride tube. During refluxing the solution became pale yellow in colour and deposited a small amount of white powdery solid. The solution and solid deposit were poured into water, (200 ml. containing 2 ml. acetic acid), extracted with ether, dried and evaporated. The resultant yellow oily product crystallised slightly on addition of a few drops of light petroleum and ethanol. After filtration and several washings with light petroleum and ethanol, a white solid was obtained, m.p. 95°-96°, (compound Y).

The filtrate was evaporated to remove all solvents, and the residue was dissolved in the minimum amount of benzene for chromatography on an alumina column which had been neutralised and deactivated with 5% by weight of water containing 10% glacial acetic acid. Elution was carried out with benzene/light petroleum mixtures; 30% benzene yielded a white solid, m.p. 81° from ethanol/light petroleum (b.p. 60°-80°), (compound X); 50% benzene yielded colourless needles, m.p. 99° from

ethanol/light petroleum (b.p. 60°-80°), (more of compound Y).

(This experiment was first carried out using an alumina column neutralised and deactivated with 10% by weight of water containing 10% glacial acetic acid, but when analysis of the resultant products indicated that they were ketones and not keto-esters as had been expected, the alumina used for the column was not so deactivated as before (5% by weight of water used), and better separation was achieved. It was also found from the first attempt at this condensation that compound X was light-sensitive in solution, so in the later experiments the bands on the chromatography column were protected from daylight as far as possible).

Approximate yield of X = 1·5g. (Found: C,87·1; H,6·9; and C,87·2; H,6·5. $C_{21}H_{20}O$ requires C,87·5; H,6·9).

Approximate yield of Y = 3·6g. (Found: C,86·9; H,6·9).

Isolation of isomerised product from X.

0·5g. of compound X was dissolved in the minimum amount of spectroscopic ethanol and the solution was left standing in daylight for 2 days. The tip of a glass rod was dipped into the solution to form a fine film of liquid on the end of the rod, and this was then transferred to spectroscopic ethanol in the cell of an

ultraviolet absorption spectrophotometer, and the spectrum was measured. After the solution had stood for a further 14 weeks in daylight, the process was repeated. The spectra obtained showed that the initial maximum at ~300 mμ. was retained but with decreased relative intensity, and a maximum at ~250 mμ. and minimum at ~280 mμ. appeared. Due to the high concentration of compound X in the solution, isomerisation in daylight was still incomplete. Artificial means of irradiation of the solution were found to increase the rate of isomerisation considerably.

0.5g. of compound X was dissolved in the minimum amount of spectroscopic ethanol and this solution was put into the inner tube of a Quickfit condenser held vertically inverted one inch from a 500 watt projector bulb. The cold water circulating through the outer jacket of the condenser prevented evaporation of the solution in the intense heat produced. Irradiation from the projector lamp for 114 hours, followed by ultraviolet irradiation for 24 hours, brought about complete isomerisation, as was confirmed by measurement of ultraviolet spectra at intervals throughout the irradiation process, in the manner described above. (For dilute solutions of X, much shorter periods of irradiation are required to bring about complete isomerisation, and even daylight may be sufficient (see Fig.7)). The irradiated solution was evaporated, dissolved in benzene,

and chromatographed on a column of untreated alumina. Elution was carried out with light petroleum/benzene mixtures; 40% benzene yielded a pale yellow solid, (compound Z), m.p. 85·5°-86° from light petroleum (b.p. 60°-80°)/ethanol. (Found: C,87·3; H,6·4. $C_{21}H_{20}O$ requires C,87·5; H,6·9).

Attempted interconversions of X and Z.

A small amount of compound Z was distilled in a micro-sublimation apparatus at an oil-pump vacuum and from an oil-bath at 90°-120°. A crystalline product formed on the cold finger, but an infrared spectrum showed that this was starting-material which had been recovered. It was thought that the temperature at which the substance distilled may not have been sufficiently high to bring about interconversion of the two isomers, so Z was heated at 200° for 30 mins. in an atmosphere of nitrogen, cooled, then distilled at 100°-120°. Again only starting-material was recovered.

Similarly, compound X was heated at 200° for 15 mins. in a stream of nitrogen, cooled, and distilled in an oil-pump vacuum and from an oil-bath at 120°; starting-material X was recovered.

Attempted interconversions of X and Y.

50-60 mg. of X were added to 5 ml. of ethanol

saturated with dry hydrogen chloride, and the solution was refluxed for 1 hour. Evaporation under reduced pressure yielded a white solid, m.p. 75°-76° after one recrystallisation from ethanol/light petroleum (b.p. 60°-80°). This was substance X which had been recovered.

In a similar experiment, 50-60 mg. of Y were added to 5 ml. of ethanol saturated with dry hydrogen chloride. On addition to the alcoholic solution, Y immediately became bright yellow, then orange, and finally dark red in colour. The dark red colour spread throughout the solution on refluxing. After refluxing for 1 hour, the solution was evaporated under reduced pressure, yielding an oily residue. This was dissolved in benzene and chromatographed on a column of alumina neutralised and deactivated by treatment with 10% by weight of water containing 10% glacial acetic acid. Elution with a light petroleum/benzene solution containing 10% benzene yielded a pale yellow oil on evaporation. This solidified and was recrystallised from ethanol/light petroleum (b.p. 60°-80°). An infrared solution spectrum in carbon tetrachloride of the resultant product showed that it was no longer Y but had not been converted to the isomer X.

SECTION (d).

Acenaphthen-8-one.

(A). Polyphosphoric acid cyclisation of 1-naphthylacetic acid.

Polyphosphoric acid was prepared by the addition of phosphorus pentoxide (232g.) to phosphoric acid (112 ml. of 89%) in a three-necked flask fitted with stirrer and condenser. The mixture was kept at 120° for 4-5 hours (until all the phosphorus pentoxide had dissolved), and was left overnight. A small-scale experiment was carried out to determine the optimum conditions of reaction.[26] 1-Naphthylacetic acid (2g.) was added to 20 ml. stirred polyphosphoric acid at 60°. The temperature was raised slowly to 80°-85°, and the reaction was terminated after 7 mins.. The solution was cooled, poured onto ice, extracted with ether, and the extract was washed first with sodium hydroxide solution, then with water, and was finally dried and evaporated, leaving a bright yellow solid, m.p.(crude) 99°-106°. Yield of crude product = 0·11g. (6·1%).

1-Naphthylacetic acid (9·0g.) was added to stirred polyphosphoric acid (90 ml.) at 60°. The solution was slowly heated to 100° and maintained at that temperature for 30 mins.[27] Ice-water was added to the cooled solution, which was then extracted with ether. The extract

was washed with aqueous sodium hydroxide, and with water, and was then dried and evaporated; the residue was a dark yellow solid. Yield of crude product = 2·11g. (26·0%).

(B). Preparation from acenaphthene.[28,29]

Acenaphthenyl-8-acetate.[39]

Acenaphthene (77g.) was dissolved in Analar glacial acetic acid (550 ml. which had been distilled over 15g. potassium permanganate to free it from aldehydes) in a three-necked flask fitted with stirrer and thermometer. The solution was stirred and heated to 60°, at which point the source of heat was removed, and red lead (410g.) was added in approximately 25g. portions with vigorous stirring over a period of 40-50 mins., enough time being allowed between the additions of red lead for the red colour to disappear. During the addition the temperature was maintained between 60° and 70°, by means of external cooling where necessary. After a further 10 mins. the oxidation was complete. This was shown when a drop of the reaction mixture failed to give any further blue colour (due to the presence of lead tetraacetate) with moist starch-iodide paper. The reddish-yellow slightly viscous solution was poured into 1 litre of water, and the acetate was extracted with 200 ml., 150 ml. and 300 ml. portions of ether. The total extract was washed first with

100 ml. water, then with 300 ml. saturated sodium chloride solution, and was dried and evaporated. Distillation of the residue yielded the acetate, which distilled at 128°-132°/0·3mm. as a yellow oil, which tended to crystallise in the condenser. Yield = 80·6g. (76·0%).

Acenaphthen-8-ol.[39]

Acenaphthenyl-8-acetate (80·6g.) was dissolved in methanol (137 ml.) and a solution of sodium hydroxide (20g. in 200 ml. water) was added. A small amount of crystalline solid separated immediately the alkali was added. The solution and solid were refluxed for 2 hours, then cooled to below 20°. The yellow crystalline acenaphthenol was filtered off, washed well with 750 ml. water, and the crude product was air-dried and recrystallised from 700 ml. benzene. After being washed thoroughly with 250 ml. cold benzene, the acenaphthenol was obtained as colourless needles, m.p. 145·5°-146°. Yield = 56·5g.. A further 3·5g. was recovered from the filtrate. Total yield = 60·0g. (92·9%).

Acenaphthen-8-one.

Acenaphthen-8-ol (60·0g.) was suspended in Analar glacial acetic acid (180 ml.) and stirred. A solution of chromium trioxide (25·8g.) in the minimum amount of

water was diluted with glacial acetic acid (144 ml.), and this solution was added to the acenaphthenol suspension, with constant stirring, over a period of 50 mins., while the temperature of the reactants was carefully maintained between 28° and 32°, by external cooling where necessary. The acenaphthenol dissolved giving a green solution, and after stirring for a further 1 hour at the same temperature, this was poured into 3·6 litres of ice-water, stirred and left to stand overnight. The precipitated ketone was filtered off, washed well with water, and recrystallised from acetone. M.p. = 118°-119°. Yield = 34·6g.. From the recrystallisation filtrate a further amount of crude acenaphthenone was obtained (21·0g.) which would be best purified by steam distillation.

7-Benzylideneacenaphthen-8-one.[28]

From a series of experiments the following conditions were found to give the best results.

Acenaphthen-8-one (15·0g.; 1 mol.) and freshly-distilled benzaldehyde (19·0g.; 2 mol.) were dissolved in ethanol (1 litre), 10-15 ml. of sodium ethoxide solution (2g. sodium in 40 ml. ethanol) were added, and the solution turned red. The red colour lasted for 1-2 mins., and in 5 mins. the solution had turned green. After 2 days at room temperature, the crystalline solid was filtered

off. The crystals were golden plates, m.p. 113·5°-114·5°. Yield = 10·2g. (44·6%).

Ethyl 7,10-dihydro-9-hydroxy-7-phenylfluoranthene-8-carboxylate, (XXXIV).

Two different methods of condensation gave similar yields.

(A). 7-Benzylideneacenaphthen-8-one (5·5g.; 1 mol.) was added to a solution of ethyl acetoacetate (3·35g.; 1·2 mol.) in ethanol (55 ml.) containing dissolved sodium (0·66g.; 1·33 mol.).[30] The mixture was left at room temperature for 20 hours, then unreacted starting-material was filtered off and the filtrate was acidified with dilute hydrochloric acid, giving a yellow crystalline product, m.p. 178°-180° from ethanol/benzene. Yield = 2·6g. (32·9%).

(B). 7-Benzylideneacenaphthen-8-one (10·2g.; 1 mol.) was dissolved in a solution of ethyl acetoacetate (6·2g.; 1·2 mol.) in ethanol (100 ml.) containing dissolved sodium (1·2g.; 1·3 mol.).[40] The mixture was heated for 3 hours on a steam-bath, then was cooled and filtered, and the filtrate was treated with dilute hydrochloric acid (40 ml.). The resultant yellow product had m.p. 178° from benzene/light petroleum (b.p. 60°-80°). Yield = 5·7g. (38·9%).

The mother liquors from preparations (A) and (B) were combined and poured into twice the volume of water.

The solution was extracted with ethyl acetate, and the extract was dried over sodium sulphate, evaporated, and chromatographed on alumina (deactivated with 10% by weight of water containing 10% glacial acetic acid). Elution was carried out with ether and with acetone containing 1% concentrated hydrochloric acid. The eluates were neutralised with ammonia and evaporated, but the residues failed to yield any crystallisable material.

Treatment of ethyl 7,10-dihydro-9-hydroxy-7-phenyl-fluoranthene-8-carboxylate with acid.

(A). Treatment with saturated ethanolic hydrogen chloride.

Compound (XXXIV) (1·0g.) was added to saturated ethanolic hydrogen chloride (150 ml.) and boiled for 2-3 hours. The solution was evaporated, and a yellow residue was left which was recrystallised from ethanol/benzene. Measurement of its infrared spectrum proved that the product was starting-material.

(B). Treatment with concentrated sulphuric acid.

Compound (XXXIV) (2·0g.) in ethanol (2 ml.) was added to concentrated sulphuric acid (20 ml.). The mixture was cooled and left to stand for 5 mins., after which it was poured into 200 ml. water, and left in water for 30 mins. to let the precipitate coagulate. The yellowish-brown precipitate was filtered off, washed

with water and dried. An infrared spectrum of the crude solid indicated the probable presence of the isomeric compound (XXXV). On recrystallisation from ethyl acetate a yellow solid was obtained which was shown, by measurement of its infrared spectrum, to be starting-material. The ethyl acetate filtrates were evaporated, dissolved in benzene and chromatographed on alumina (deactivated with 10% by weight of water containing 10% glacial acetic acid). Elution with a light petroleum/benzene mixture containing 30% benzene yielded a yellow solid, m.p. 160°-160·5° from ethanol/light petroleum (b.p. 60°-80°)/ethyl acetate. This was the enolic isomer (XXXVII), (ethyl 6b,7-dihydro-9-hydroxy-7-phenylfluoranthene-8-carboxylate). (Found: C,81·9; H,5·3. $C_{25}H_{20}O_3$ requires C,81·5; H,5·5).

6b,7,8,9-tetrahydro-9-oxo-7-phenylfluoranthene, (XXXVIII).

Compound (XXXIV) (1·5g.) was added to a solution of glacial acetic acid (5 ml.), concentrated sulphuric acid (2·5 ml.) and water (1·2 ml.), and was refluxed for 15 mins.. The resultant bright red solution was poured into water and extracted with ether. The extract was washed with sodium carbonate, dried and evaporated, to give a yellow solid, m.p. 185°-186·5° from benzene/light petroleum (b.p. 60°-80°).

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