PART I. SYNTHESIS OF POLYMETHYLNAPHTHALENES.

PART II. SYNTHESIS OF SOME POLYMETHYLPHENANTHRENES.

A

THESIS

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DOCTOR OF PHILOSOPHY

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BY

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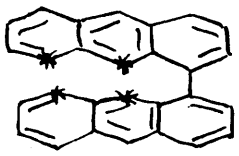
INTRODUCTION.

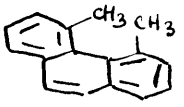
Aromatic hydrocarbons generally tend to adopt a planar configuration [1], but in recent years an increasingly large number of cases has come to light in which coplanarity is prevented by the steric requirements of the molecule. In principle this is not a new phenomenon, for, in the case of derivatives of diphenyl [1a], it has been known for many years. An interesting example of a hydrocarbon of this type, which is nonplanar and has been obtained in optically active forms, is 1:1' dianthryl [3] (I).



I.

If this structure was planar, as drawn above, it is clear that the closest approach between certain non-bonded atoms (designated by *) would be much smaller than the usual Van der Waals gap of about 3.4 Å. This "Intramolecular Overcrowding" has been the subject of much careful chemical investigation, [4],[5] and a few examples of the various types of compounds, which have been studied, will now be given.

From a study of molecular models, it was suggested that 4:5- dimethyl phenanthrene II,



II

would be unable to adopt a planar configuration due to the large overlap of the methyl groups on each other. According to Newman [6] there are three possible spacial conformations for 4:5- dimethyl phenanthrene (II). They are as follows:-

(a) The methyl groups may be bent away from each other but in the same plane as the aromatic rings.

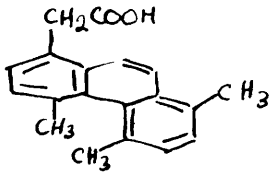
(b) The aromatic rings may be distorted in some way from a planar configuration due to the steric hindrance imposed upon the molecule by the methyl groups.

(c) The methyl groups may lie bent out of the plane of the aromatic rings.

If this latter suggestion (c) is correct then the molecule should exhibit optical activity.

In view of the interest aroused by its stereochemistry several [7] attempts were made to prepare it; some difficulty was experienced in achieving this synthesis due to steric hindrance.

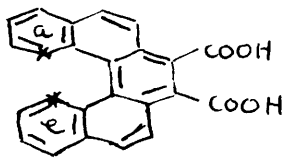
It was finally synthesised both here [7a] and in America [7b]. That compounds of this type could exist in enantiomorphous forms was shown by Newman and Hussey, who succeeded in resolving 4:5:8-trimethyl-1-phenanthryl - acetic acid [8] III.



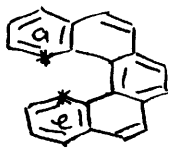
III.

This compound must owe its asymmetry to the fact that the methyl groups in the 4- and 5- positions, due to steric hindrance have been forced to lie bent out of the plane of the aromatic rings.

Bell and Waring [9] have succeeded in resolving 3:4-5:6- dibenzphenanthrene -9:10- dicarboxylic acid (IV), and Robertson etal [10] have shown by x-ray crystallography, that in the parent compound, 3:4-5:6-dibenzphenanthrene (V),



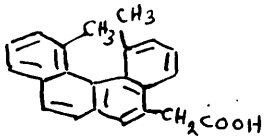
(IV).



(V).

the molecule departs greatly from a coplanar configuration and exists in a spiral form due to the intramolecular overcrowding at positions designated by "*" in rings "a" and "e".

Newman etal have resolved 1:12- dimethylbenzo (c) phenanthrene - 5 - acetic acid (VI)[4] and suggested from a study of a molecular model of the parent compound benzo (c) phenanthrene (VII), that the ring system must be distorted in order to relieve the strain.

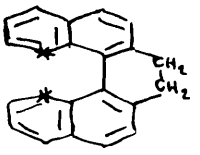


(VI)

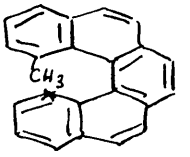
(VII)

This suggestion has been confirmed by Schmidt and Herbstein [11] who have shown by x-ray crystallography that the rings are bent along the axes indicated by the dotted lines in the parent compound (VII).

Yet other interesting examples of compounds exhibiting non-planarity due to intramolecular overcrowding are 9:10 - dihydro - 3:4-5:6- dibenzphenanthrene (VIII) [12], and 1-methyl-benzo (C) phenanthrene (IX) [12a].

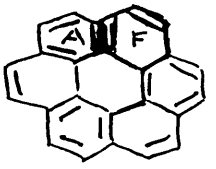


(VIII)



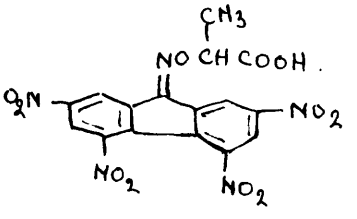
(IX)

A most remarkable hydrocarbon, phenanthro-3:4-C phenanthrene (X) has recently been prepared and resolved by Newman etal [13].



(X)

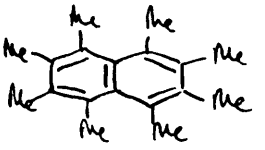
From a study of a molecular model it may be seen that it is impossible for the molecule to adopt a planar configuration but must exist in a spiral form in which rings A and F are overlapped on each other. Resolution of this hydrocarbon was achieved interestingly by complex formation with 2-(2:4:5:7-tetranitro-9-fluorenylideneamino-oxy) - propionic acid (XI).



(XI)

The laevo form of the hydrocarbon (X) had an optical rotation of $[\alpha]_D^{24}$ -3640°, and exhibited remarkable stability, racemisation being incomplete even at its melting point.

Another interesting example is octamethyl naphthalene (XII) which was recently synthesised by Abadir, Cook and Gibson [14]. An x-ray analysis of this compound, carried out by Donaldson and Robertson [15] has shown that the α-methyl groups are displaced from the mean plane by about 0.73 Å, and the β-methyl groups, in an opposite direction, by about 0.25-0.40 Å. It is also stated by these authors that the naphthalene nucleus itself may be distorted in a similar way but to a smaller extent.

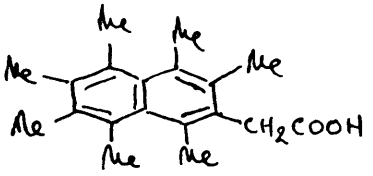


(XII).

It was thought that the hydrocarbon (XII) would probably still be asymmetric in solution as well as in the crystalline state. Asymmetry in solution could be confirmed by the preparation and resolution of a suitable derivative, or by the resolution of the hydro-

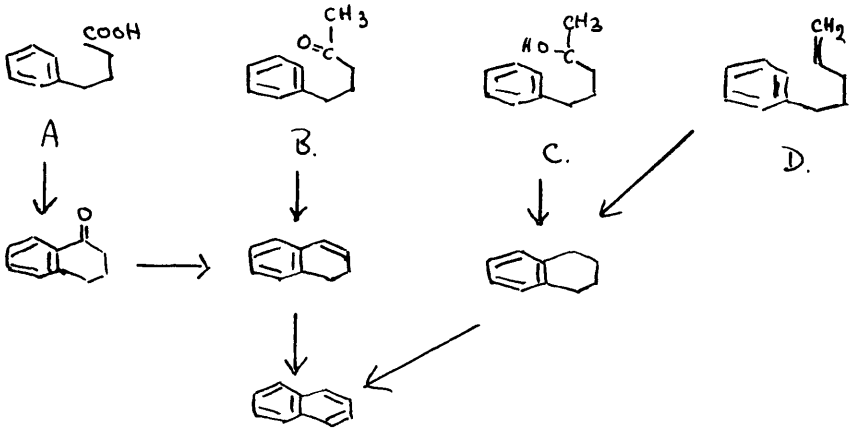
carbon itself by Newman's method. (13)

The derivative chosen was 2-(1:3:4:5:6:7:8-heptamethyl naphthyl) - acetic acid (XIII).



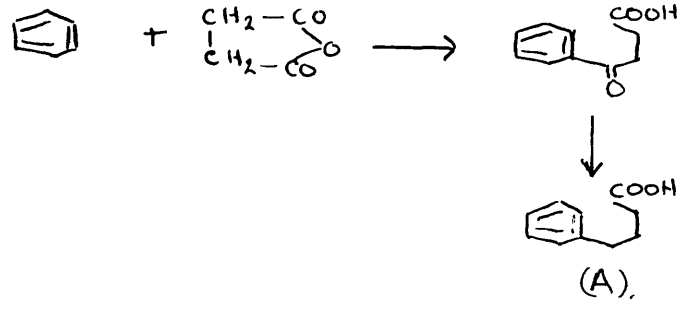
(XIII).

It would be both interesting and useful to give a brief outline of the main methods used to synthesise methyl-derivatives of naphthalene. Many and varied synthesis have been employed, to prepare methyl-naphthalenes (mono-, di-, tri-, tetra-, penta-, hexa-, hepta-, and octa-)(14),(16),(17),(18),(19),(20), but in most of them the first objective was to synthesise one of the four basic units, A or B or C or D - namely, a benzene nucleus with a side chain capable of intramolecular cyclisation.



After cyclisation the product obtained, from each of the types respectively, may be converted to the fully aromatic naphthalene hydrocarbon by standard methods.

A great variety of methods exists for synthesis of γ-aryl butyric acids of the above type (A). The most important one is, however, the "Succinic Anhydride". synthesis illustrated below (Note:- Benzene will be used where possible to illustrate the syntheses).

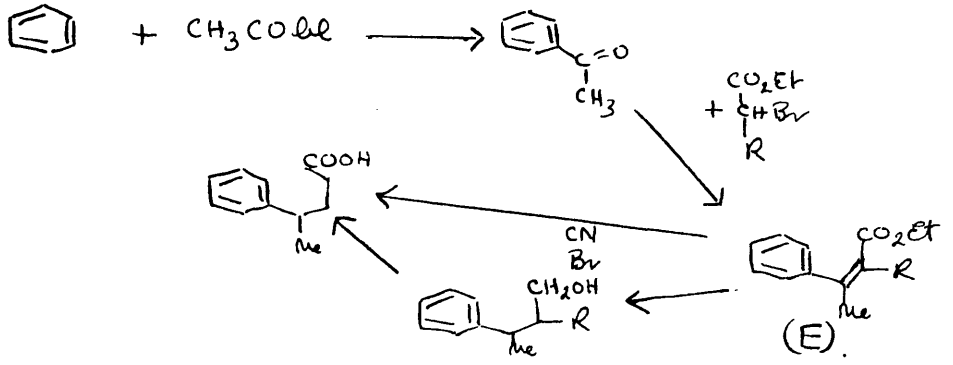


(A).

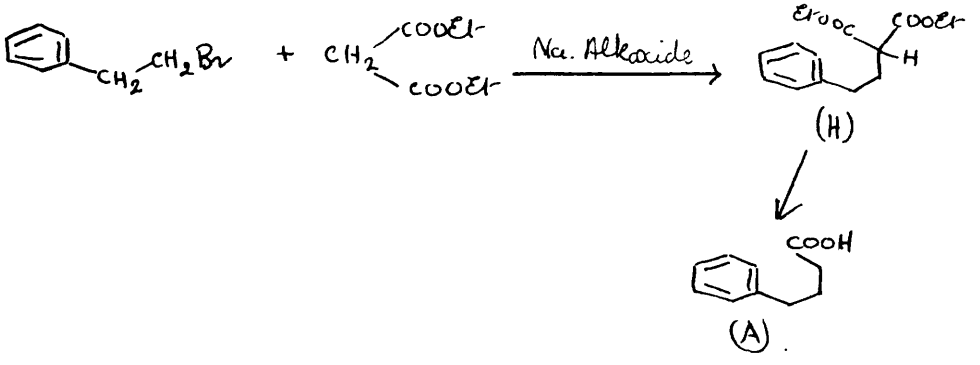
Benzene is condensed with succinic anhydride in the presence of aluminium chloride, in a suitable solvent, (e.g. nitrobenzene, s-tetrachloroethane, methylene chloride), to yield the corresponding γ-aryl - γ keto - butyric acid. On reduction of the keto group, by the Clemmensen or Huang-Minlon procedure, the desired γ-aryl butyric acid (A) is obtained.

Another longer route to γ-aryl butyric acids proceeds from an acyl benzene, followed by a Reformatsky reaction with an α-halogen ester, as illustrated below, to yield the ester (E). This ester (E)

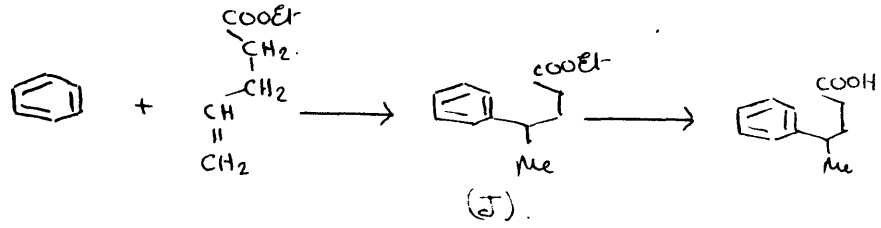
may be converted to the aryl butyric acid of type (A) either by an Arndt-Eistert reaction or by the older method of reduction to the alcohol, replacement of the alcoholic group by bromine, further replacement of bromine by cyano, in the usual way, followed by hydrolysis.



Yet another variant is the condensation of a malonic ester and a β-aryl ethyl bromide, followed by hydrolysis and decarboxylation of the condensation product (H) as illustrated below.



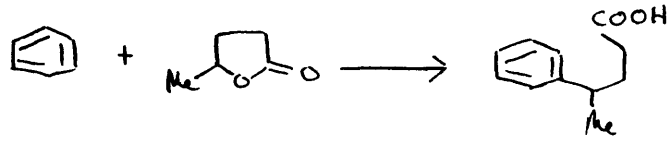
Two recent useful additions, to the methods available for synthesising γ-aryl butyric acids, are those of Colonge [18] and Mosby [17].



(J).

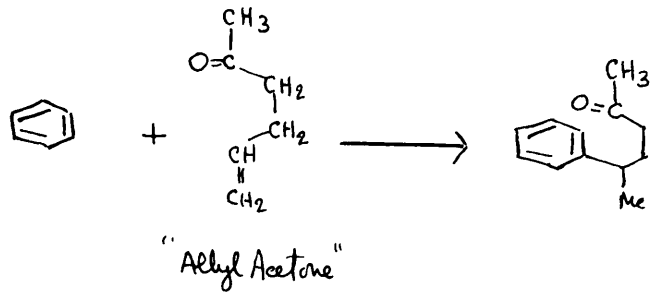
In the first, benzene is condensed with allyl acetic ester in the presence of aluminium chloride yielding the ester (J), which, on hydrolysis, furnishes the desired γ-aryl butyric acid.

In the second, γ-valerolactone on condensation with benzene in the presence of aluminium chloride produces the desired γ-aryl butyric acid as illustrated below.

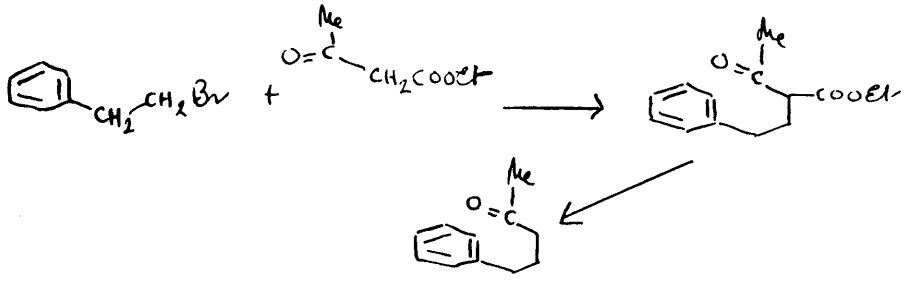


The methods available for the synthesis of the basic unit of the ketones of type (B) are very similar to those used for γ-aryl butyric acids of type (A) and, indeed, the ketones may be built from the acids by the use of cadmium alkyls [20a] and other methods.

Colonge [19] condensed benzene with allyl acetone in the presence of aluminium chloride and obtained the desired ketone of the required type (B).

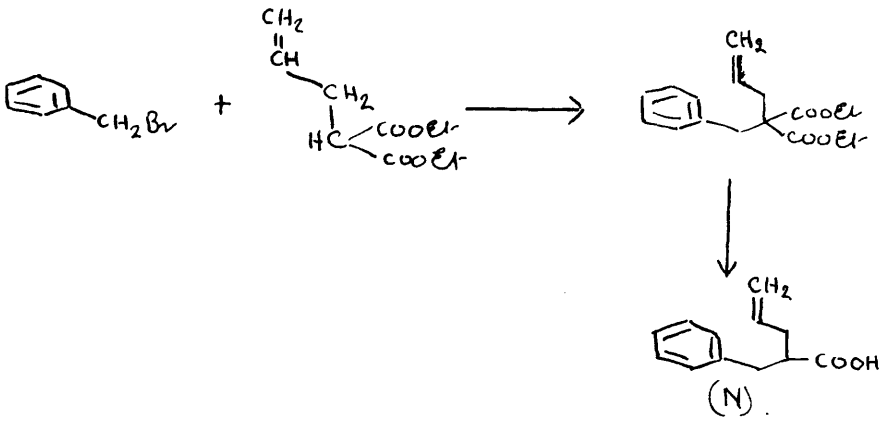


Ketones of the type (B) may also be synthesised by the condensation of a β-aryl ethyl bromide and acetoacetic ester, followed by hydrolysis and decarboxylation as shown below.



In a variant of this method the keto-group is reduced to the alcohol before cyclisation. In this case a tetralin is obtained and not a dihydro-naphthalene.

To synthesise the final type of basic unit (D) benzyl bromide is condensed with allyl malonic ester followed by hydrolysis and decarboxylation. The acid (N) which is obtained is of the requiredtype (D)

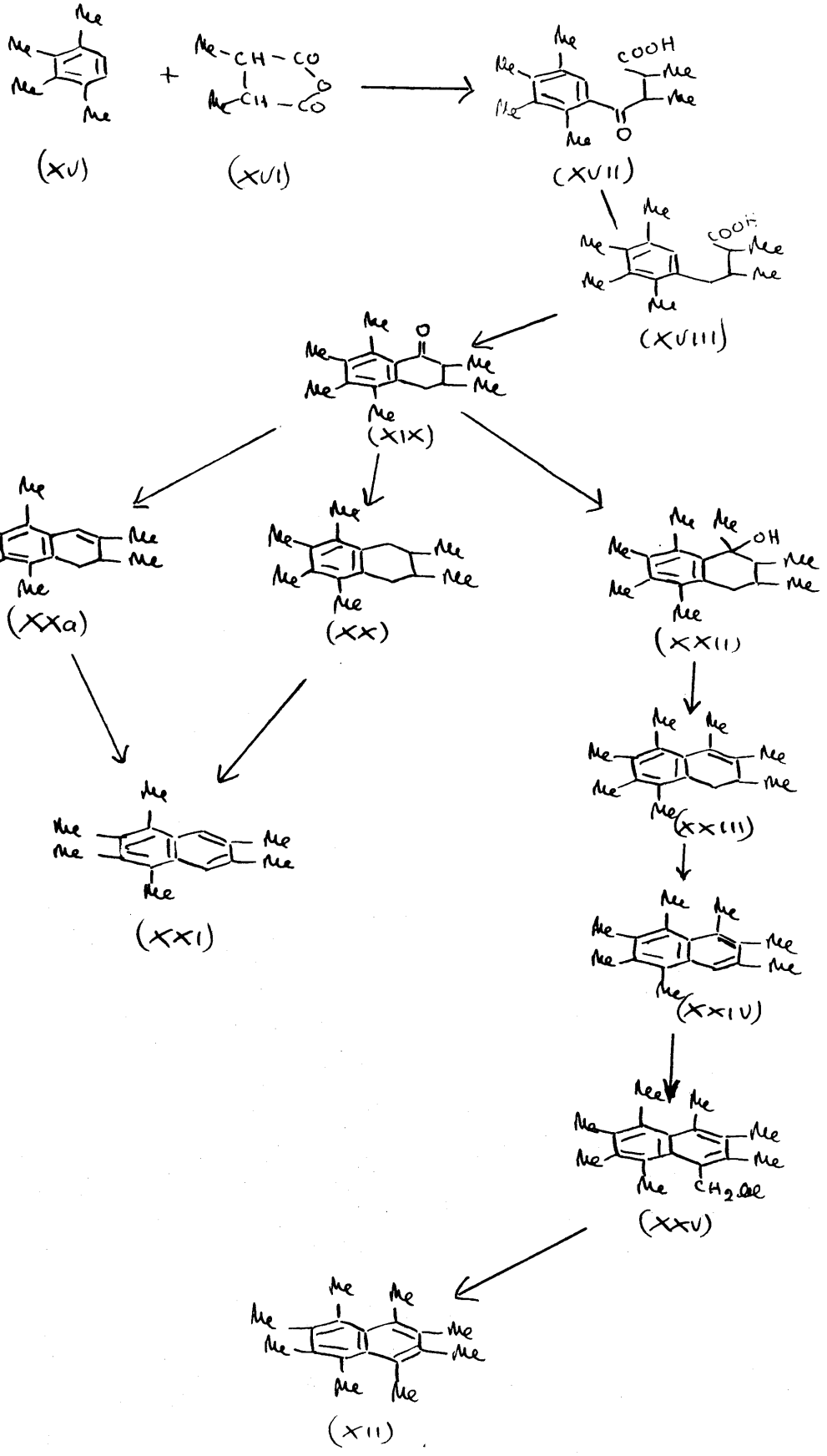


The above schemes have been modified in the literature to yield a large number of naphthalene derivatives.

Abadir, Cook and Gibson [14] synthesised several polymethyl naphthalenes using the "Succinic Anhydride" synthesis. The scheme of work carried out by these authors will now be given in some detail, since results obtained in the present investigation invalidate the orientation assigned by them to a number of their products and it will be necessary to refer to their work later.

The route adopted by them for the synthesis of some of their polymethyl naphthalenes is shown schematically on the following page.

Prehnitene (XV) was condensed with $\alpha\beta$-dimethyl succinic anydride (XV1), in the presence of anydrous aluminium chloride in s-tetrachloroethane solution, to give γ-keto-$\alpha\beta$-dimethyl-γ-prehnityl butyric acid (XVII). Hydrogenation of the sodium salt of this


(XV)
(XVI)
(XVII)
(XVIII)
(XIX)
(XXa)
(XX)
(XXI)
(XXII)
(XXIII)
(XXIV)
(XXV)
(XII)

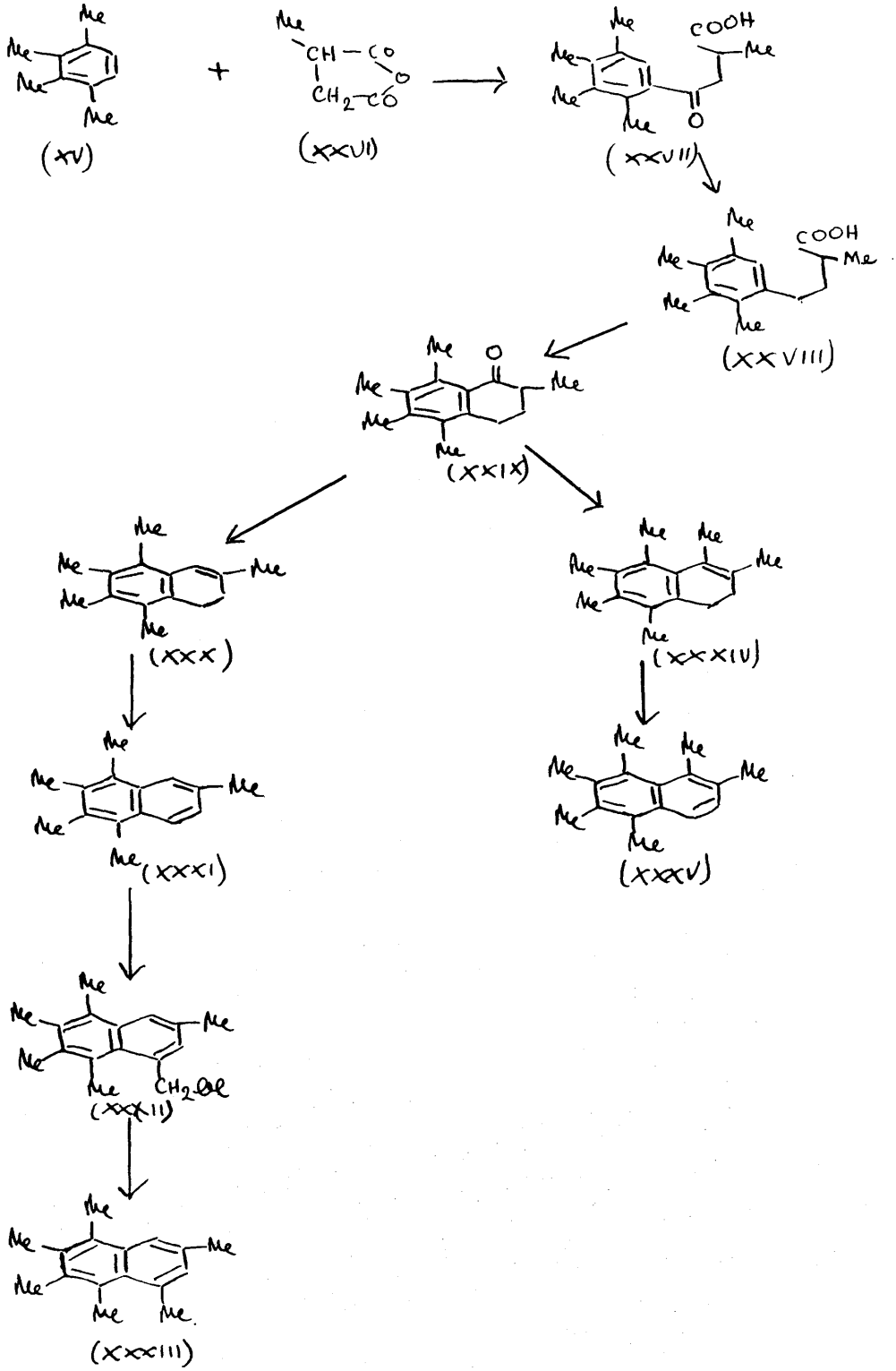
butyric acid (XVII), over copper chromite catalyst, yielded $\alpha\beta$-dimethyl- γ - prehnityl butyric acid (XVIII). This was cyclised by hydrogen fluoride to 1:2:3:4 - tetrahydro-1-keto-2:3:5:6:7:8 - hexamethyl-naphthalene (XIX).

Reduction of this hexamethyl-tetralone (XIX), by the Clemmensen or Huang Minlon procedure, gave, in poor yeild, the corresponding tetrahydro-hexamethyl-naphthalene (XX), but catalytic hydrogenation of the tetralone (XIX), followed by dehydration, gave a good yield of the corresponding dihydro-hexamethylnaphthalene (XXa). On dehydrogenation both these hydrocarbons(XX) and (XXa), afforded 1:2:3:4:6:7 - hexamethylnaphalene (XXl).

The tetralone (XIX) reacted with methyl magnesium iodide with difficulty, yielding the alcohol (XXII), which, on dehydration and dehydrogenation, gave 1:2:3:4-5:6:7 - heptamethylnaphthalene (XXIV).

On chloromethylation, the heptamethylnaphthalene (XXIV) gave the chloromethyl compound (XXV), which on reduction yielded octamethylnaphthalene (XII).

In another series of reactions,(see chart following page) prehnitene (XV) was condensed with methylsuccinic anhydride (XXVI), in the presence of anhydrous aluminium chloride in s-tetrachloroethane


(XV)
(XXVI)
(XXVII)
(XXVIII)
(XXIX)
(XXX)
(XXXI)
(XXXII)
(XXXIII)
(XXXIV)
(XXXV)

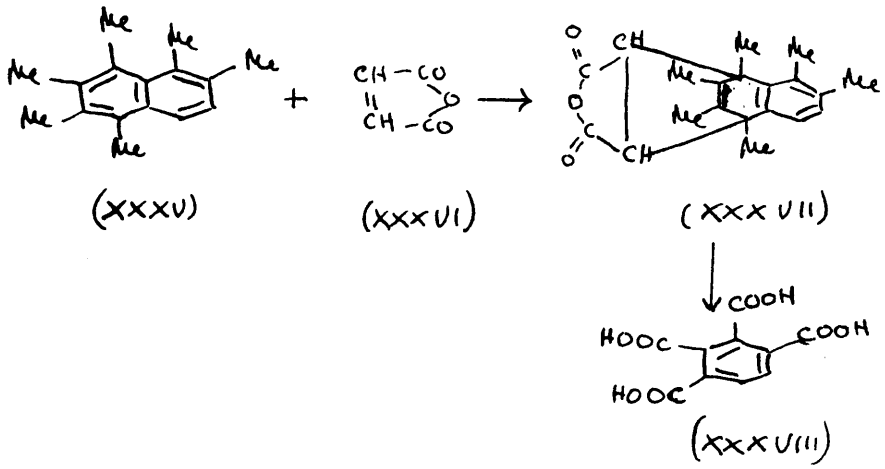
solution, to give in good yield an acid regarded as γ-keto-α-methyl - γ- prehnityl-butyric acid (XXVII) as the only isolable product. This, they stated, readily gave a 2:4 - dinitrophenylhydrazone and was easily reduced by Clemmensen's method to α -methyl-γ - prehnityl butyric acid (XXVIII). In both these respects the behaviour of the keto-acid (XXVII) was in contrast to that of its homologue (XVII), and thus was regarded as supporting their view, that the methyl succinic anhydride had reacted to give the α-methyl keto acid (XXVII) and not the β-methyl acid.

The α -methyl-γ-prehnityl butyric acid (XXVIII) was converted, by a standard series of reactions, (see chart), to 1:2:3:4:6- pentamethylnaphthalene (XXXI).

In another standard series of reactions (see chart) the α- methyl- γ-prehnityl butyric acid (XXVIII) was converted to a hexamethylnaphthalene, which, on the basis of the structure assigned to the acid, was considered to be 1:2:3:4:5:6- hexamethylnaphthalene (XXXV).

On chloromethylation of 1:2:3:4:6- pentamethyl-naphthalene (XXXI), and on reduction of the chloromethyl compound (XXXII) formed, a hydrocarbon was obtained, which was distinct from 1:2:3:4:5:6- and 1:2:3:4:6:7- hexamethylnaphthalenes, and was thus considered to be 1:2:3:4:5:7- hexamethylnaphthalene (XXXIII).

Abadir, Cook and Gibson now reacted 1:2:3:4:5:6-hexamethyl naphthalene (XXXV) with maleic anhydride (XXXVI) and obtained the adduct (XXXVII), which, on

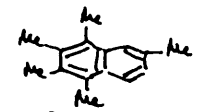
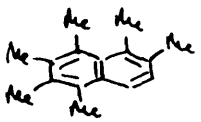
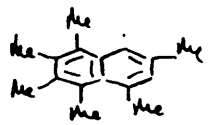
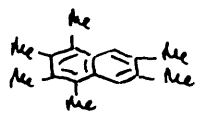
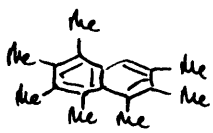
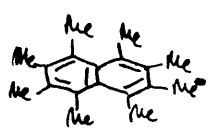


(XXXV) (XXXVI) (XXXVII)

(XXXVIII)

oxidation with alkaline potassium permanganate, yielded benzene - 1:2:3:4-tetracarboxylic acid (XXXVIII). This confirmed the structures assigned by them to the hexamethylnaphthalene (XXXV) and to the keto-acid (XXVII), because, if the isomeric β-methyl γ-keto-γ-prehnityl butyric acid had been obtained initially, it would have led to 1:2:3:4:5:7-hexamethylnaphthalene, the maleic anhydride adduct of which would have been oxidised to benzene - 1:2:3:5- tetracarboxylic acid or to mellitic acid.

Table of Constants of hydrocarbons obtained by Abadir, Cook and Gibson.

Hydrocarbon	m.pt.	Picrate m.pt.	S-T.N.B. m.pt.	2:4:7-T.N.F. m.pt.
 1:2:3:4:6-Pentamethylnaphthalene (XXXI)	85°C	176°C	187°C	174°C.
 1:2:3:4:5:6-Hexamethylnaphthalene (XXXV).	81·5°C	167-168°C	186°C	181°C.
 1:2:3:4:5:7-Hexamethylnaphthalene (XXXIII)	140°C	188°C	207°C	199°C
 1:2:3:4:6:7-Hexamethylnaphthalene (XXI)	145°C	190·5°C	215°C	210°C.
 1:2:3:4:5:6:7-Heptamethylnaphthalene (XXIII)	134°C	184·5°C	210°C	212°C
 Octamethylnaphthalene (XII).	174°C	193°C	192-193°C	209°C.

NOTE:- S-T.N.B ≡ S-Trinitrobenzene Complex.
2:4:7-T.N.F ≡ 2:4:7-Trinitrofluorenone Complex.

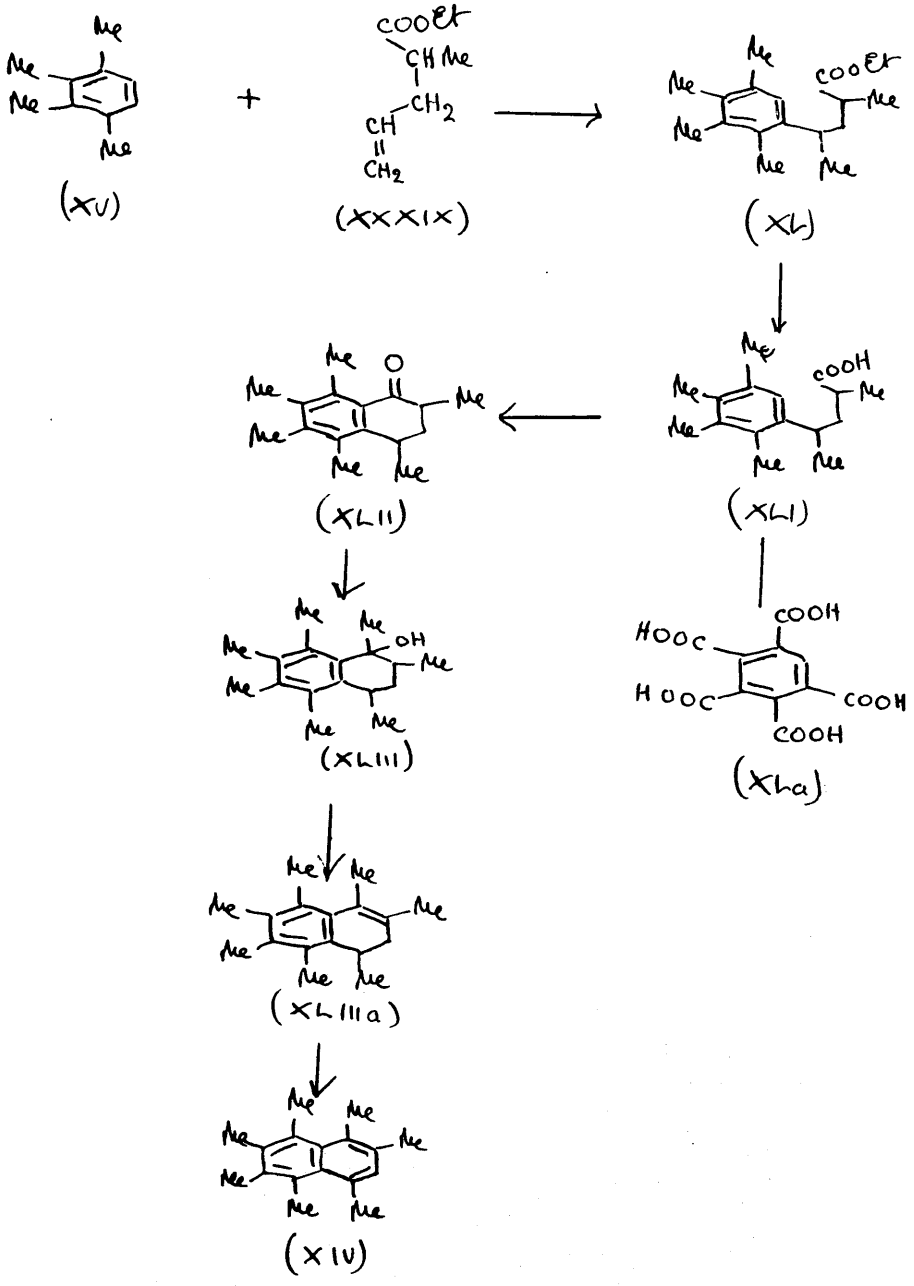
Discussion.

The first main objective, in the synthesis of 2 - (1:3:4:5:6:7:8-heptamethyl-naphthyl)-acetic acid (XIII), referred to earlier in the introduction (p.7), was the preparation of 1:2:3:4:5:6:8-heptamethylnaphthalene (XIV). It was intended to prepare the desired acid (XIII) from this hydrocarbon (XIV) by chloromethylation in the only vacant position, replacement of the chlorine by cyano, followed by hydrolysis. It was also intended to prepare some octamethylnaphthalene (XII) by reduction of the chloromethyl compound of 1:2:3:4:5:6:8-heptamethyl-naphthalene by a similar procedure to that used by Abadir Cook and Gibson [14] (p. 13a) for the 1:2:3:4:5:6:7-isomer.

Our projected route to this hydrocarbon is shown on the following page.

Prehnitene (XV)[21],[22] was condensed with α -methyl-α -allyl acetate (XXXIX) [18], in the presence of anhydrous aluminium chloride yielding ethyl α -methyl-γ-prehnityl valerate (XL) in good yield. The ester (XL) was hydrolysed with aqueous alcoholic caustic potash giving the corresponding acid (XLI) in excellent yield.

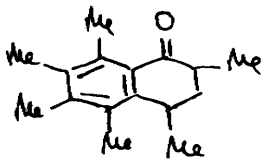
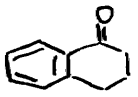
A sample of the acid (XLI) was oxidised to benzene pentacarboxylic acid, characterised as its methyl ester, which thus confirmed the orientation assigned to the acid (XLI).


(XV)
(XXXIX)
(XL)
(XLI)
(XLa)
(XLII)
(XLIII)
(XLIIIa)
(XIV)

There was also isolated at this stage a little of a neutral by-product. Analysis indicated the empirical formula $C_{16}H_{22}O$. Although there was a peak in the ultra-violet absorption spectrum at 270 mu, log E-267, which is similar to that of β-tetralone, it showed no ketonic reactions, nor was there a carbonyl maximum in the infra-red absorption spectrum. No further experimental work was carried out on this compound.

Cyclisation of the acid (XL1) was effected, in excellent yield of 90% of the theoretical by treating the acid chloride [23] with stannic chloride in benzene at $0^{o}C$. The yield of 2:4:5:6:7:8-hexamethyl-tetralone-1 (XL11) isolated, was an improvement on the yields of Colonge and Grimand,[18] who by the use of various cyclising agents obtained yields of from 12% to 85% of the theoretical for various related compounds.

The tetralone (XLII) formed a 2:4-dinitrophenyl-hydrazone only with difficulty, but did not form a semi-carbazone. The presence of the ketonic group was confirmed, by the infra-red spectrum, which exhibited a carbonyl maximum at 1673 cm^{-1}, corresponding to a carbonyl group in conjugation with a benzene ring, and also by the ultra violet absorption spectrum, which was typical for an α-tetralone (see table on following page).

	λ_{max} mμ.	log ε.
 (XLII)	220	4·37
	267·5	4·07
	305	3·37.
 α-Tetralone.	210	4·1
	250	4·07
	300	3·2.

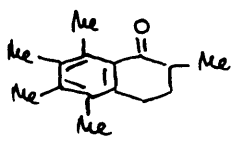
The sluggish reaction with chemical reagents is presumably due to the highly hindered nature of the carbonyl group in the molecule.

The next step in the synthesis involved the reaction of the tetralone (XLII) with methyl magnesium iodide. In spite of many attempts, however, this reaction could not be effected. The reaction failed to take place even in boiling benzene for 40 hours; the tetralone was recovered quantitatively.

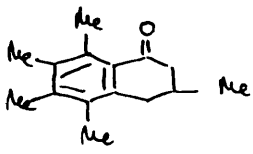
It was thought that it ought to be possible to react the ketone (XLII) with methyl lithium. Various attempts were made but no success was entertained, even when the reaction was carried out in xylene or di-n-butyl ether, by refluxing for periods up to 40 hours, in a nitrogen atmosphere.

The entire failure of the ketone (XLII) to react with either methyl magnesium iodide or methyl lithium appears to be in conformity with its sluggish reaction towards 2:4 dinitrophenylhydrazine and semi-carbazide, but is still very surprising in view of the fact, that analogous compounds (see below) have been made to react under milder conditions than were employed in the above attempted reactions.

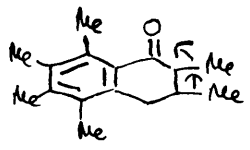
It is worthy of note, that the ketone (XL11) appeared to react towards methyl magnesium iodide and methyl lithium, and it may have been, that an enolisation reaction was occurring. It is known that enolate formation [24] is competitive with normal addition, and that the latter is subject to marked steric hindrance while the former, in general, is not.



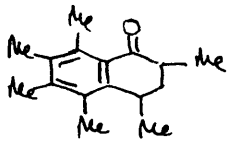
(XLIV)



(XLV)



(XIX)



(XLII).

The behaviour of the above four tetralones, (XLIV), (XLV), (XIX), and (XLII), towards methyl magnesium iodide and methyl lithium is most interesting.

The 2:5:6:7:8-pentamethyl-tetralone-1 (XLIV) reacts smoothly with methyl magnesium iodide or methyl lithium in benzene solution giving the normal addition product

(see p.26a)28)

The 3:5:6:7:8-pentamethyl-tetralone-1 (XLV) also showed reactivity towards methyl magnesium iodide, the normal addition product being obtained (p.36).

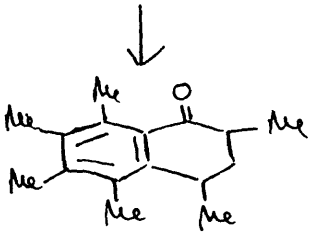
The 2:3:5:6:7:8-hexamethyl tetralone-1 [14] (XIX) reacted with methyl magnesium iodide with difficulty, after prolonged refluxing in benzene solution, yielding the normal addition product. (see p. 13a)

In the present work 2:4:5:6:7:8-hexamethyl tetralone-1 failed to react with either methyl magnesium iodide or methyl lithium, even under more drastic conditions than either of the other three tetralones.

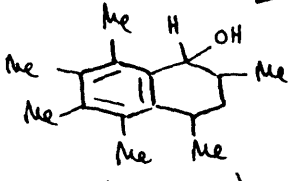
Professor Barton [24a] has suggested that this is an example of the "Buttressing Effect" [25],[26]. The direction of the effect is shown by the arrows in the case of the tetralones (XIX) and (XLII). In the tetralone (XLII) the "Buttressing Effect" of the methyl group in position 4 is apparently great enough to force the methyl groups in positions 5, 6, 7, and 8 to bend, towards the keto-group in position 1, sufficient to block the normal addition reaction. This is in contrast to that of the methyl group, in position 3 of the tetralone (XIX), whose Buttressing Effect is not great enough to prevent the normal addition reaction.

The failure of the tetralone (XLII) to undergo reaction with methyl magnesium iodide or methyl lithium rendered the suggested route (p. 18a) abortive as a means of preparing 1:2:3:4:5:6:8-heptamethylnaphthalene.

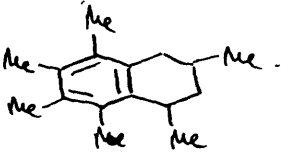
See chart p. 18a.



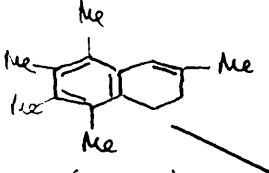
(XLII)



(XLVIII)

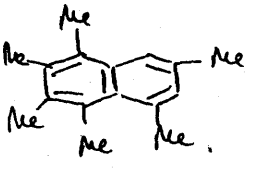


(XLVI)



(XLIX)

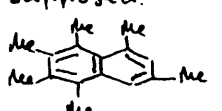
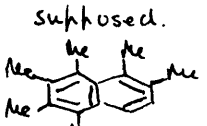
$C_{16}H_{20}$ ≡



(XLVII)

It was thought that conversion of the tetralone (XLII) to 1:2:3:4:5:7-hexamethylnaphthalene would confirm the structure of the ketone and also afford another route to 1:2:3:4:5:7-hexamethylnaphthalene [14] (p. 14a).

The 2:4:5:6:7:8-hexamethyl-tetralone-1 (XLII) (see chart) was reduced by the Clemmensen method [27] to 2:4:5:6:7:8-hexamethyl-1:2:3:4-tetrahydronaphthalene (XLVI) and this on dehydrogenation with palladium charcoal (30%) at 320-330°C yielded a hexamethyl naphthalene with a typical naphthalene spectrum in the ultra violet. From the method of preparation this was assigned the structure 1:2:3:4:5:7-hexamethylnaphthalene (XLVII). Surprisingly however the physical constants (shown below) of our hydrocarbon (XLVII) and its derivatives and those of the supposed 1:2:3:4:5:7-hexamethylnaphthalene and its derivatives prepared by Abadir, Cook, and Gibson [14] (p. 14) were not in agreement.

Hydrocarbon.	m.pt.	Picrate. m.pt.	2:4:7-T.N.F. m.pt.
Hydrocarbon. $C_{16}H_{20}$ (XLVII)	78-80°C (micro-melt)	169-170°C	181-182°C.
Supposed.  (XXXIII) (see p. 14a)	140°C	188°C	199°C.
Supposed.  (XXXV) (see p. 14a).	81.5°C	167-168°C	181°C.

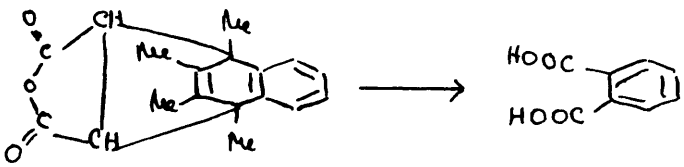
As may be seen from the table, however, the physical constants of our hydrocarbon (XLVII) and those of Abadir's 1:2:3:4:5:6-hexamethylnaphthalene (XXXV) are very similar, and in fact mixed melting point determinations, of our hydrocarbon (XLVII) and its molecular complexes with Abadir's hexamethylnaphthalene (XXXV) and its derivatives respectively, showed no depression.

The method used by Abadir, Cook and Gibson [14] in the preparation of their hexamethylnaphthalene (p.14a) seemed at first sight to be unambiguous and it was thought initially that, in the present work, a methyl migration [28], [29], had occurred, in the "overcrowded" molecule (XLVI) during the high temperature dehydrogenation, with production of the 1:2:3:4:5:6- isomer.

However the same hydrocarbon (XLVII) was obtained by reducing the ketone (XLII) with lithium aluminium hydride, dehydrating the resulting alcohol (XLVIII) to the dihydro-naphthalene (XLIX), and dehydrogenating this latter compound with palladium-charcoal (30%) in boiling 1:2:4 trichlorobenzene at a temperature of 213°C. Methyl migration during dehydrogenation was thought unlikely to occur at such a low temperature as 213°C.

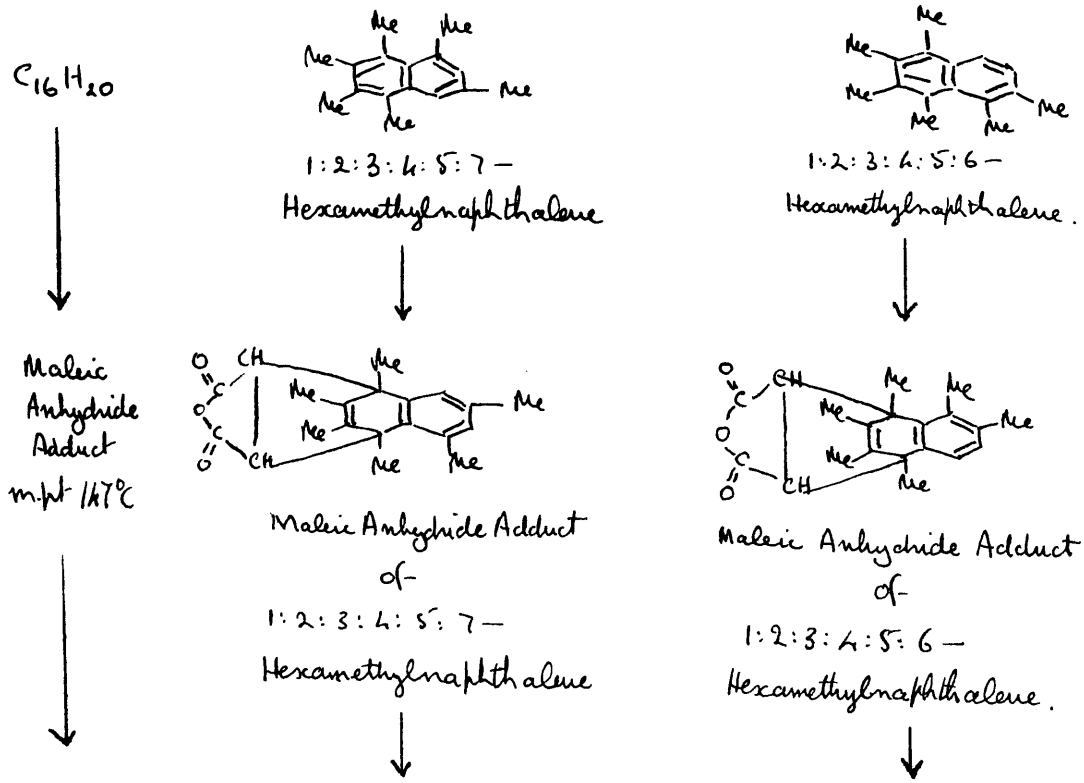
Another series of reactions was carried out with our hydrocarbon (XLVII) in an attempt to establish the correct orientation of the methyl groups in the naphthalene nucleus.

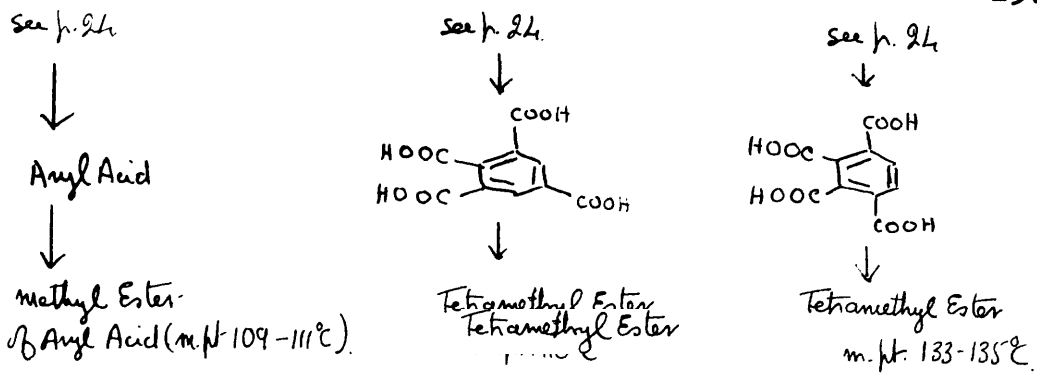
Kloetzel etal [27a] have demonstrated a Diels-Alder type reaction, between maleic anhydride and some methyl naphthalenes, with the formation of adducts of type "O". On oxidation with alkaline permanganate these adducts yielded benzene-carboxylicacids.



Type "O"

It was established by Kloetzel [27a] and also by Abadir, Cook and Gibson [14] that the maleic anhydride adds on to the ring with the most methyl groups and, that it is this ring which is destroyed in the oxidation.

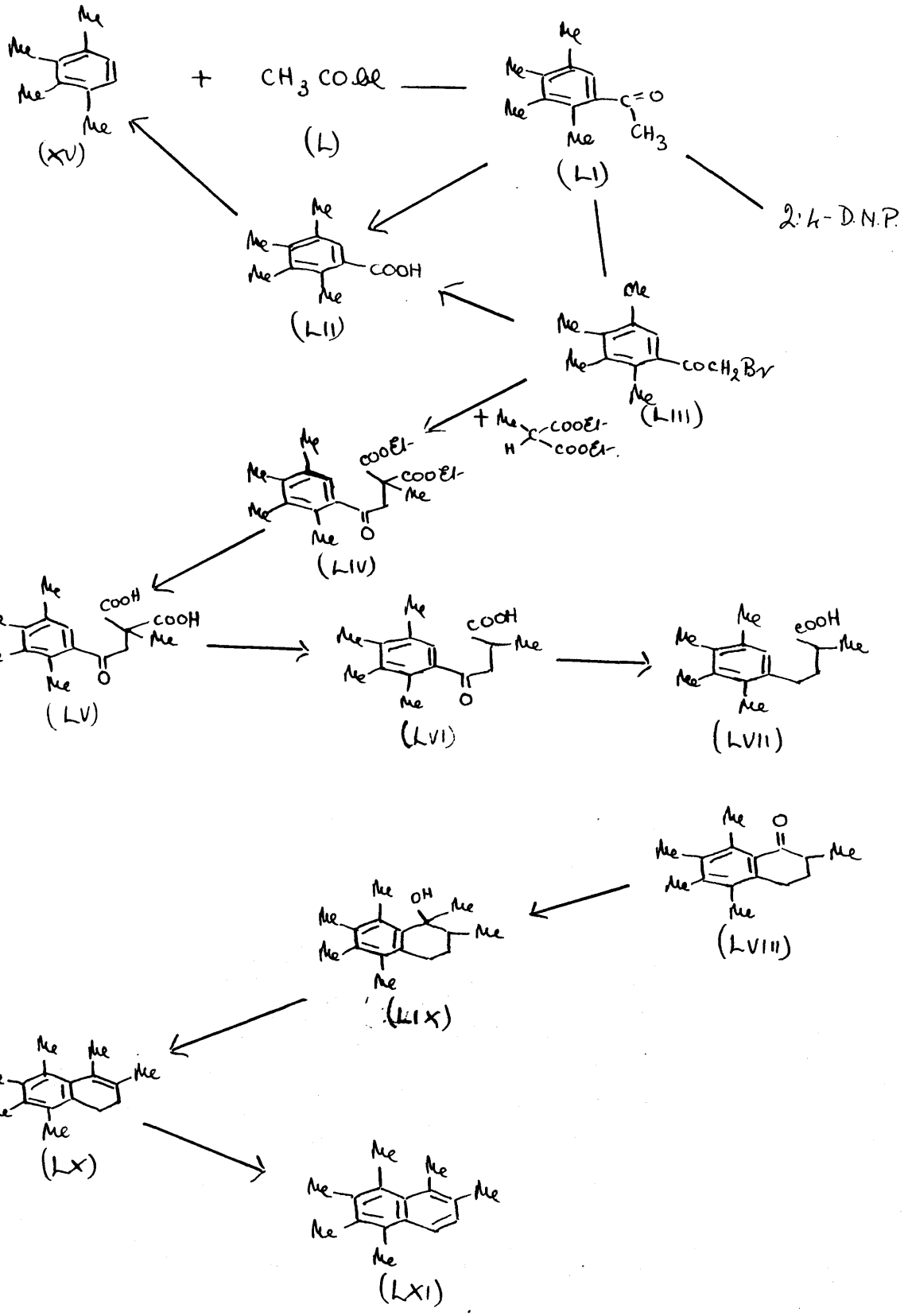




Our hydrocarbon (XLVII) reacted with maleic anhydride to form an adduct (m.pt.147°C), and this on oxidation with alkaline permanganate yielded an aryl acid, whose methyl ester melted at 109-111°C. A mixed melting point of this ester and an authentic specimen of the tetramethyl ester of benzene-1:2:3:5- carboxylic acid (m.pt.110°C) showed no depression.

As is shown schematically, above, 1:2:3:4:5:7-hexamethylnaphthalene would be expected to yield benzene - 1:2:3:5- tetra-carboxylic acid, by this sequence of reactions. While 1:2:3:4:5:6 -hexamethylnaphthalene should give benzene-1:2:3:4-tetracarboxylic acid. The evidence thus obtained by the above sequence of reactions appeared to confirm that our hydrocarbon (XLVII) was indeed 1:2:3:4:5:7-hexamethylnaphthalene.

However Abadir, Cook and Gibson [14] had characterised their 1:2:3:4:5:6-hexamethylnaphthalene (XXXV), - which appeared to be identical with our hydrocarbon(XLVII) -, by a similar sequence of reactions and had obtained benzene-1:2:3:4- tetracarboxylic acid, whose melting point was undepressed on admixture with an authentic specimen prepared by the oxidation of prehnitene.


(XV)
+ CH3COCl
(L)
(LI)
2:4-D.N.P.
(LII)
(LIII)
(LIV)
(LV)
(LVI)
(LVII)
(LVIII)
(LIX)
(LX)
(LXI)

It seemed therefore that an unambiguous route to 1:2:3:4:5:6- and 1:2:3:4:5:7- hexamethylnaphthalenes was desirable. The scheme envisaged is set out on the previous page.

Prehnitene (XV) was condensed with acetyl chloride[30] in the presence of aluminium chloride in methylene chloride solution giving acetyl prehnitene (LI) in good yield. This was an oil whose 2:4 dinitrophenylhydrazone melted at 178-179°C, and its semicarbazone at 210°C-211°C (Lit.209°C). A preparation of acetyl chloride has previously been given by Claus and Föhlisch [31], who used carbon disulphide as the solvent in the Friedel Crafts reaction. Abadir, Cook and Gibson [14] employed this latter method to prepare acetyl prehnitene, but the melting point of the 2:4-dinitrophenylhydrazone of their product was 155-156°C, and that of the semicarbazone was 203°C (Lit. 209°C). The structure of the acetyl prehnitene (LI) obtained in the present synthesis was confirmed by oxidation with sodium hypoiodite [32] to prehnitic acid (LII) (m.pt. 165-169°C; Lit.165°C, 169°C). Claus oxidised the acetyl prehnitene obtained by him to, what he supposed was, prehnitic acid, m.pt.150°C. The low melting point confirms the fact that his acetyl prehnitene was a mixture of isomers. The structure of the product (LI) was further confirmed by decarboxylation of the acid (LII) with soda-lime to prehnitene (XV), characterised by its infra-red spectrum.

Bromo-acetyl prehnitene (LIII) was obtained by brominating acetyl prehnitene (LI) in carbon tetrachloride solution. On oxidation of bromo-acetyl prehnitene, by sodium hypobromite (33), prehnitic acid (LII) was obtained, thus establishing that the bromine was in the designated position in the acetyl side chain.

On condensation of bromo-acetyl prehnitene (LIII) with methyl malonic ester, using sodium ethoxide as condensing agent, the diester (LIV), was obtained. This was hydrolysed with strong aqueous caustic potash to the dicarboxylic acid (LV), which was decraboxylated, affording the monocarboxylic acid, α-methyl-γ-keto-γ-prehnityl butyric acid (LVI) (m.pt.129-130°C). This keto-acid did not form a 2:4-dinitrophenylhydrazone and its ethyl ester was a liquid.

Reduction of the keto-acid was achieved by the Huang-Minlon (34) Procedure; α-methyl-γ-prehnityl butyric acid (LVII) (m.pt.77-78°C) was obtained. Cyclisation of the butyric acid (LVII) was effected by treating the acid chloride with stannic chloride in benzene at 0°C, yielding 2:5:6:7:8- pentamethyl-tetralone-1 (LVIII) (m.pt.57-58°C). This exhibited a carbonyl maximum in the infra-red at 1677 cm^{-1}, which is typical for a keto-group in conjugation with a benzene ring.

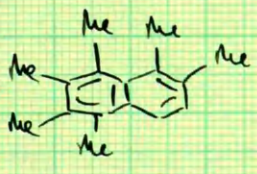
Methyl lithium (35) was prepared in the usual manner and the tetralone (LVIII) was added in ether solution and

refluxed for 6 hours, after which most of the ether was distilled off and benzene (dry) added and the refluxing continued for 3 hours. This method was adopted because of the expected hindered nature of the carbonyl function in the tetralone (LVIII). The product obtained, from the reaction, was 3:5:6:7:8-pentamethyl-1:2-dihydro-naphthalene (LX) (m.pt.89-90°C), the intermediate tertiary alcohol (LIX) having been dehydrated by the hydrochloric acid used to decompose the lithium complex formed in the reaction.

It was attempted to dehydrogenate the dihydro-naphthalene (LX) by heating it with palladium charcoal (30%) in a stream of carbon dioxide. Evolution of hydrogen started smoothly at 280-285°C, but ceased before the half of the theoretical amount had been evolved. On raising the temperature to 325-330°C dehydrogenation recommenced but only very slowly. A mixture was obtained from the experiment which could not be separated but was thought to contain, 1:2:3:4:6- pentamethylnaphthalene and 1:2:3:4:5:6-hexamethylnaphthalene, by the fact that the melting point of the mixture (m.pt.60-70°C) was raised on admixture with a pure sample of 1:2:3:4:6- pentamethyl-naphthalene (m.pt.85°C).

Dehydrogenation of the dihydro-naphthalene (LX) was finally accomplished by refluxing with palladium-charcoal in 1:2:4-trichlorobenzene (b.pt.213°C) in a stream of

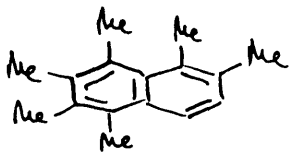
p. 29a.



U.V. spec carried out in Rectified Spirits Solution.

λmax mμ	log ε
337 (small peak)	2·76
301	3·68
241	4·82

carbon dioxide for 17 hours; about half of the theoretical amount of hydrogen was evolved. 1:2:3:4:5:6-hexamethylnaphthalene (LXI) was isolated, from the reaction mixture through its s-trinitrobenzene complex, but did not crystallise well so it was further purified by distillation. The yield was about 50% of the theoretical. The physical constants of this hydrocarbon (LXI) are shown in the table. It exhibited a typical naphthalene spectrum in the ultra-violet (shown opposite).



(LXI) (see p.26a.)

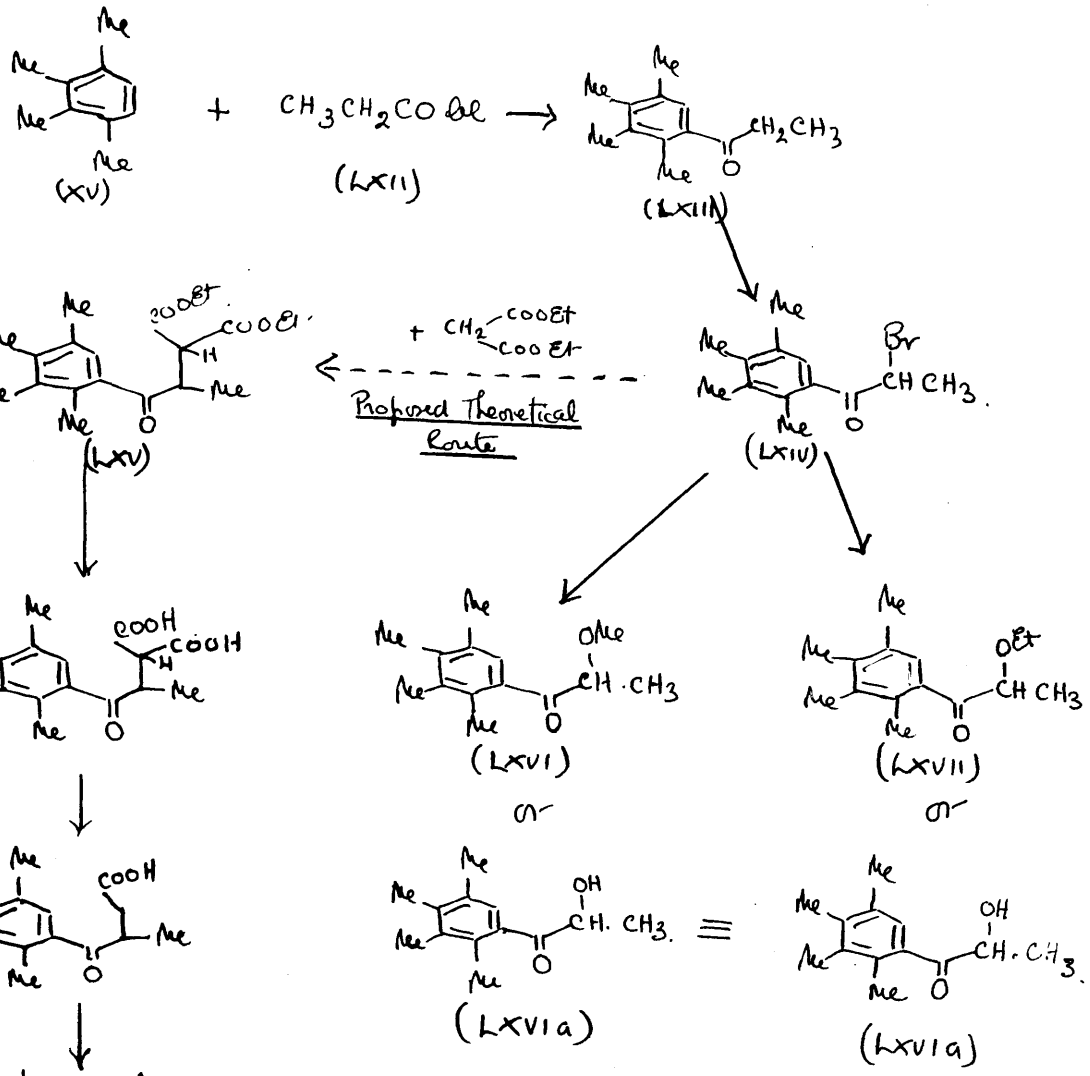
m.pt.	Picrate m.pt.	S-T.N.B. m.pt.	2:4:7-T.N.F. m.pt.
48-50°C	155-157°C Unstable.	186-189°C	186-187°C.

1:2:3:4:5:6-
hexamethylnaphthalene.

Note:- S-T.N.B. ≡ s-trinitrobenzene complex.
2:4:7-T.N.F. ≡ 2:4:7-trinitrofluorenone complex.

The palladium charcoal method of dehydrogenation was chosen since it required less purification of the product than the method using sulphur or selenium, in spite of the fact that disproportionation[36] occurs with the former thus lowering the yield. Mosby [37] found that the more methyl groups present in the dihydronaphthalene, the greater was the difficulty in dehydrogenating it to the corresponding naphthalene. Abadir, Cook and Gibson[14] do not appear to have encountered

30a


(XV)
+ CH_3CH_2COCl
(LXII)
(LXIIA)
(LXIV)
+ $CH_2(COOEt)_2$
Proposed Theoretical Route
(LXV)
(LXVI)
or
(LXVII)
or
(LXVIa)
≡
(LXVIa)
etc., as for
1:2:3:4:5:6 — isomer.
(see p. 26a.)

any such difficulty. The safest method is, however, to carry out the dehydrogenation in boiling 1:2:4-trichlorobenzene (b.pt.213°C), using palladium-charcoal as catalyst since prolonged heating at 213°C is unlikely to cause any migration or elimination of methyl groups in overcrowded molecules.

The success of the above synthesis of 1:2:3:4:5:6-hexamethylnaphthalene encouraged us to attempt the synthesis of the 1:2:3:4:5:7-isomer by a similar oute, shown opposite.

Prehnitene (XV) was condensed with propionyl chloride (LXII), in the presence of aluminium chloride in methylene chloride solution[30], to give propionyl prehnitene (LXIII). Propionyl prehnitene (LXIII) was brominated by the same method as had been used for acetyl prehnitene (p.27); α-bromo-propionyl prehnitene (LXIV) was obtained.

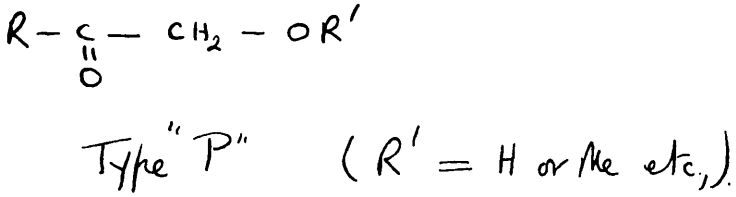
On attempted condensation of α-bromo-propionyl prehnitene and malonic ester, using sodium methoxide as condensing agent, the expected diester (LXV) was not obtained. The liquid product on hydrolysis with aqueous alcoholic caustic potash gave prehnitic acid (m.pt.165-169°C), undepressed on admixture with an authentic specimen.

The condensation was attempted again, using sodium ethoxide as condensing agent, but a similar liquid product was obtained which gave rise to prehnitic acid on hydrolysis.

The α-bromo-propionyl prehnitene was recovered unchanged on attempting to condense it with sodiomalonic ester in benzene solution. This suggests that the reaction has failed due to steric hindrance.

From the available evidence, it is suggested, that the liquid product, from the experiment using sodium methoxide, is α-methoxy propionyl prehnitene (LXVI) or α-hydroxy propionyl prehnitene (LXVIa) and from the experiment using sodium ethoxide is α-ethoxy propionyl prehnitene (LXVII) or α-hydroxy propionyl prehnitene (LXVIa).

It is known that α-hydroxy carbonyl compounds undergo re-arrangement and cleavage [38] with strong alkali similar to that observed in the case of compounds (LXVI) and (LXVII). Moreover, Stevens [38] observed that on addition of alkali to an alcoholic solution of an α-hydroxy carbonyl compound an orange colouration was produced immediately; this was also observed in the case of the compounds obtained here. The structures suggested for these compounds are further supported by the fact that both reduce Fehling's solution and this is characteristic of compounds of type "P" [38a],[38b]

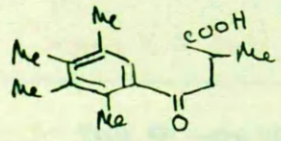


Type "P" (R' = H or Me etc.)

Both compounds exhibit a carbonyl maximum in the

infra-red at 1723 cm^{-1}, which corresponds to a saturated ketone and not to a carbonyl group in conjugation with a benzene nucleus, which exhibits a maximum at about 1680 cm^{-1}. This abnormal carbonyl frequency may be due to some steric factor interrupting resonance of the keto-group and the benzene nucleus, causing the keto group to absorb in the infra-red as a saturated one. Correct analysis for $C_{14}H_{20}O_2$ (LXVI), and $C_{15}H_{22}O_2$ (LXVII) or $C_{13}H_{18}O_2$ (LXVIa) were not obtained but this was probably due to traces of impurities in both liquids.

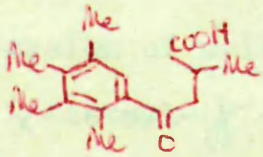
The results obtained in this present synthesis will now be compared with those of Abadir, Cook and Gibson [14].



(LVI) (see p. 26a)

m.pt. 129-130°C

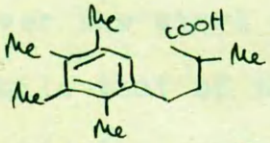
Ethyl Ester. Liquid



(xxvii) (see p. 11ha)

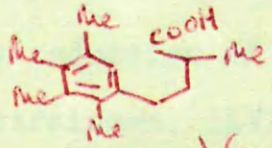
130-131°C

68·5°C m.pt.



(LVII) (see p. 26a)

m.pt. 77-78°C.

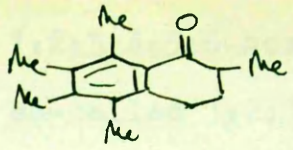


(xxviii) (see p. 11ha)

106-107°C.

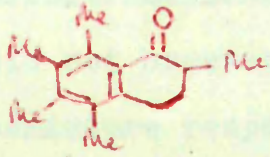
Note:- Our Compounds are in BLACK INK.

ABADIR'S compounds are in RED INK.



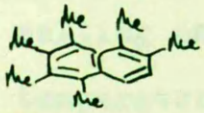
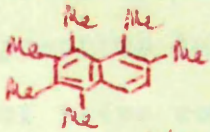
m.pt.
57-58°C.

(LVIII) (see p. 26a).



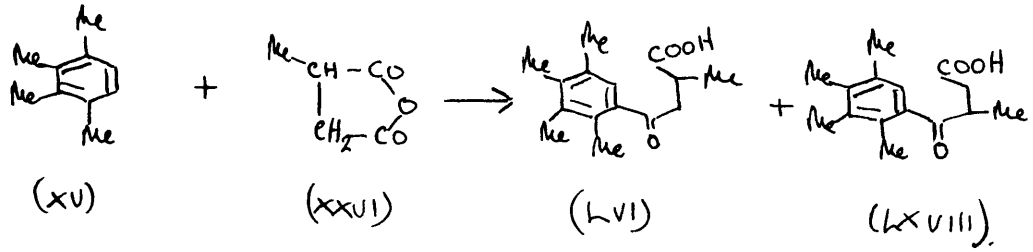
78·5°C

(XXIX) (see p. 14a)

	m.pt.	Picrate m.pt.	S-T.N.B. m.pt.	2:4:7-T.N.F. m.pt.
 (LXI) (see p. 26a)	48-50°C.	155-157°C Unstable.	186-189°C	186-187°C.
 (XXXV) (p. 14a)	81·5°C	167-168°C	186°C	181°C.

The α-methyl-β-keto-γ-prehnityl butyric acid (LVI) obtained by our route (p 26a) did not show a depression of melting point on admixture with the so-called α-methyl-β-keto-γ-prehnityl butyric acid (XXVII) obtained by Abadir, Cook and Gibson [14] (p. 14a). However the ethyl ester of the keto-acid (LVI) was a liquid while that of the keto-acid (XXVII) was a crystalline solid (see chart). Non-identity was confirmed by comparison of the butyric acids (LVII) and (XXVIII) obtained by reduction of the corresponding keto acids. The tetralones, (LVIII) and (XXIX), also depressed the melting points of each other. A mixed melting point of our

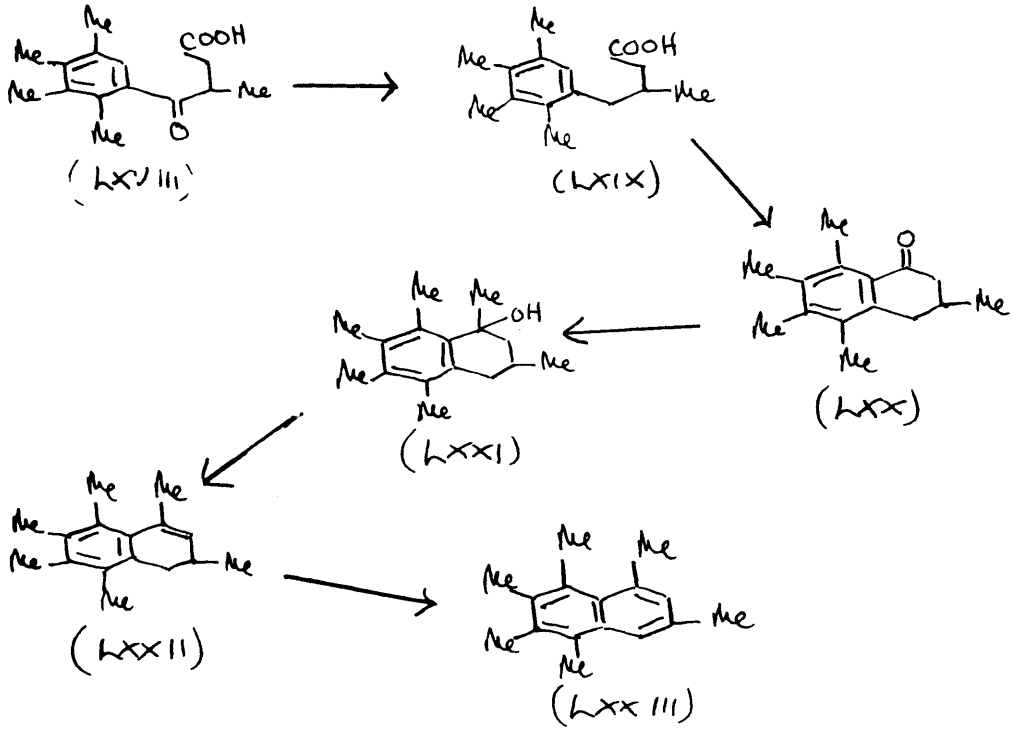
1:2:3:4:5:6-hexamethylnaphthalene (LXI) with Abadir's so-called 1:2:3:4:5:6-isomer (XXXV) showed a depression, this confirmed that they were not identical. The s-trinitrobenzene and 2:4:7-trinitrofluorenone complexes did not however show a depression of melting point on admixture respectively. It has been observed, however, in this present work that polymethyl naphthalenes as well as their derivatives do not always depress the melting point of each other if they melt about the same temperature (p.43). The question now arises concerning the correct structures of Abadir's compounds shown on previous table. On considering the method of synthesis of these compounds it was evident that the initial Friedel Crafts reaction (p.14a) was not unambiguous and could give rise to two possible products (39), namely, α-methyl-γ-keto-γ-prehnityl butyric acid (LVI) and β-methyl-γ-keto-γ-prehnityl butyric acid (LXVIII) as shown below.



(XV) (XXVI) (LVI) (LXVIII).

Since it has been shown unambiguously, that the α-methyl isomer was not identical with the acid obtained by Abadir, Cook and Gibson, the latter must have been the

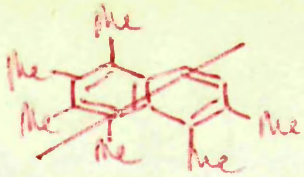
β-methyl isomer (LXVIII). The sequence of reactions shown below applied by Abadir, Cook and Gibson [14] to this acid would of course lead to 1:2:3:4:5:7-hexamethylnaphthalene (LXXIII) and not to 1:2:3:4:5:6-hexamethylnaphthalene which they supposed, they had obtained, and this was confirmed by the fact that their hydrocarbon was apparently identical with 1:2:3:4:5:7-hexamethylnaphthalene prepared by our route (p.22a).



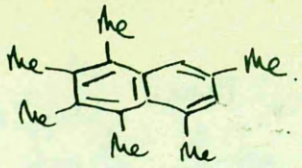
It must be concluded that Abadir [14] has made an error in his oxidation experiments which related his supposed 1:2:3:4:5:6-hexamethylnaphthalene (now shown to be the 1:2:3:4:5:7-isomer) to prehnitic acid (i.e. benzene-1:2:3:4-tetracarboxylic acid)

From the foregoing evidence it must be concluded that,

(1)



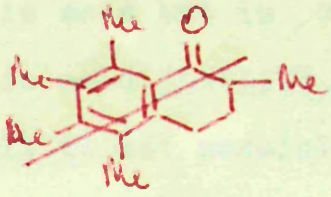
(XXXV)
Wrong.



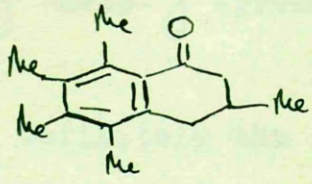
(XXXV) ≡ (LXXIII)
Correct.

the supposed 1:2:3:4:5:6- hexamethylnaphthalene (XXXV) (p. 14a) obtained by Abadir, Cook and Gibson[14] is 1:2:3:4:5:7-hexamethylnaphthalene (LXXIII), (p.35);

(2)



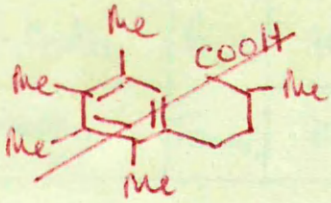
(XXIX)
Wrong



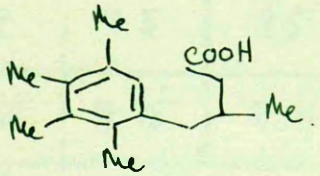
(XXIX) ≡ (LXX)
Correct.

the compound (XXIX) (p. 14a.) obtained by Abadir, Cook and Gibson[14] is not 1:2:3:4-tetrahydro-1-keto-2:5:6:7:8-pentamethylnaphthalene but is 1:2:3:4-tetrahydro-1-keto-3:5:6:7:8-pentamethylnaphalene (LXX), (p.35);

(3)



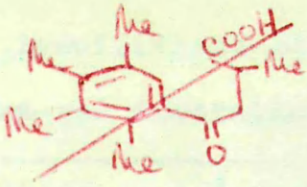
(XXVIII)
Wrong



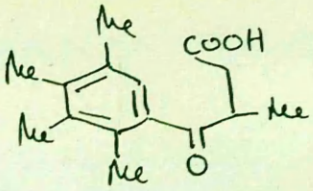
(XXVIII) ≡ (LXIX)
Correct.

the butyric acid (XXXVIII) (p. 14a) obtained by Abadir, Cook and Gibson [14] is not α-methyl - β-prehnityl butyric acid but is β-methyl- β-prehnityl butyric acid (p.35) (LXIX);

(4)



(XXVII)
Wrong.



(XXVII) ≡ (LXVIII)
Correct.

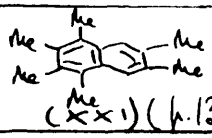
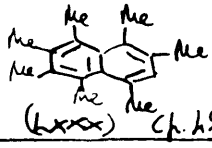
the keto-acid (XXVII)(p. 14a) obtained by Abadir, Cook and Gibson is not α-methyl- γ-keto- γ-prehnityl butyric acid but is β-methyl- γ-keto- γ-prehnityl butyric acid (LXVIII), (p. 35).

It is not possible to state definitely the structure of the compound (XXXIII) (p. 14a.) which Abadir, Cook and Gibson[14] regarded as the 1:2:3:4:5:7-isomer. Neither is it possible to decide from the analysis (shown below) whether it is a hexa - or a heptamethylnaphthalene.

Hydrocarbon		C %	H %	Picrate N%	S-T.N.B. N%	2:4:7-T.N.F. N%
Hexa- $C_{16}H_{20}$	Reqd.	90·5	9·5	9·8	9·9	8·01
Hepta- $C_{17}H_{22}$	Reqd.	90·2	9·8	9·5	9·5	7·75
Hydrocarbon (XXXIII)	Found.	90·45	9·45	9·75	9·91	7·85

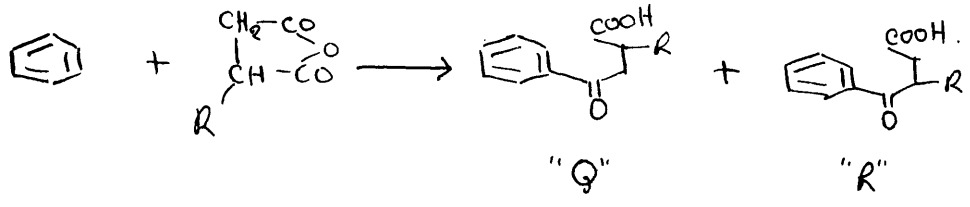
Abadir, Cook and Gibson[14] claim that the 1:2:3:4:6:7- hexamethylnaphthalene (XXI)(p. 13a) and this hydrocarbon depress the melting point of each other but a repeat of this was carried with their samples, which were to hand, and no depression was observed. This does not,

however, allow any positive conclusion to be deduced as to the identity or non-identity of the compounds. There was insufficient of this hydrocarbon (XXXIII) to do an infra-red determination.

	m.pt.	Picrate m.pt.	S-T.N.B m.pt.	2:4:7-T.N.F m.pt.
Hydrocarbon (XXXIII)	140°C	188°C	207°C	199°C
 (XXXI) (p.13a)	145°C	190.5°C	215°C	210°C
 (XXXX) (p.12a)	143°C	194-195°C	217-218°C	208.5°C — 206.5°C.

It is suggested from a comparison of the physical constants (see table) of this hydrocarbon (XXXIII) with those of the 1:2:3:4:6:7-hexamethylnaphthalene and the 1:2:3:4:5:6:8-heptamethyl-isomer, that the hydrocarbon (XXXIII) is either impure 1:2:3:4:6:7-hexamethylnaphthalene or 1:2:3:4:5:6:8:-heptamethylnaphthalene or a mixture of both.

The effect of solvents in Friedel Crafts reaction is a most interesting and important phenomenon. Friedel Crafts reactions with mono-substituted succinic anhydrides and aromatic hydrocarbons generally result in the formation of two isomeric acids[39] of the types shown below "Q" and "R". The amount of each of the acids obtained



is determined largely by the solvent in which the reaction is performed. Some of the usual solvents are nitrobenzene, s-tetrachloroethane, ethylene chloride and methylene chloride. It has been established by numerous examples in the literature[40],[41],[42], that, with nitrobenzene as solvent, the isomer which predominates is invariably the one of type "Q", i.e. the α-R-isomer.

On using s-tetrachloroethane as solvent, however, the amount of the β-R-isomer is usually greatly increased (i.e. type "R"). Baddar etal [42] have carried out experiments with methyl succinic anhydride and various hydrocarbons, to ascertain the ratio by weight of each isomer obtained when using nitrobenzene and s-tetrachloroethane as solvent respectively. They state that their results, some of which are shown below, show that the amount of the β-methyl isomer increases as the dielectric constant of the medium decreases.

Solvent	Ratio α : β
Fluorene + Methyl Succinic Anhydride	
Nitrobenzene	5 : 1
s-Tetrachloroethane	3 : 1
Anisole + Methyl Succinic Anhydride.	
Nitrobenzene	13 : 1
s-Tetrachloroethane.	3 : 1

Note:- Dielectric Constant of Nitrobenzene is greater than Dielectric Constant of s-Tetrachloroethane.

Several theories and mechanisms [42],[43] have been advanced to explain the experimental results but it is doubtful if sufficient is known, not only concerning the effect of the solvent, but also of the hydrocarbon, which likewise affects the ratio of α-isomer to β-isomer, as may be seen from the foregoing results of Baddar etal, to justify the advancement of any of these meantime.

Abadir, Cook and Gibson[14] condensed prehnitene with methyl succinic anhydride in the presence of anhydrous aluminium chloride with s-tetrachloroethane as solvent and obtained in 85% yield a homogeneous acid, which has been shown previously (p.37) to be the β-methyl-γ-keto-γ-prehnityl butyric acid. Since it was unique to obtain only one product from such an experiment it was decided to repeat the experiment using (a) nitrobenzene and (b) s-tetrachloroethane as solvent.

(a) A mixture was obtained with nitrobenzene as solvent, from which α-methyl-γ-keto-γ-prehnityl butyric acid was isolated in 30% yield of the theoretical.

(b) Only one acid was obtained, with s-tetrachloroethane as solvent, which melted at 96.5-99°C and afforded an ethyl ester m.pt.66-67°C, and the latter melting point was undepressed on admixture with an authentic specimen of the ethyl ester of β-methyl-γ-keto-γ-prehnityl butyric acid. On hydrolysis of the ethyl ester, the keto-acid melted at 112°C. A

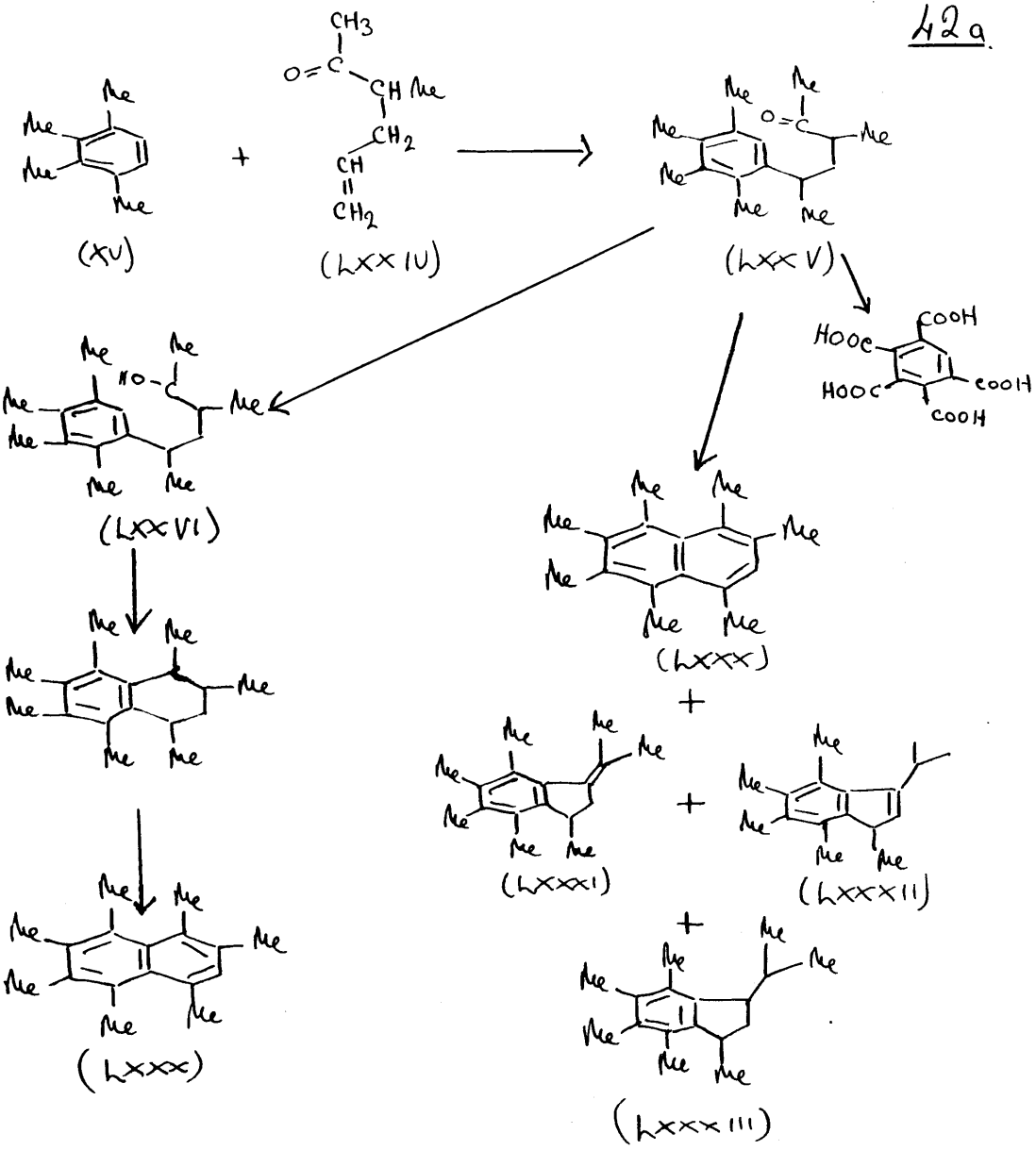
mixed melting point determination with authentic β-methyl-γ-keto-γ-prehnityl butyric acid (m.pt. 130-131°C, p.) melted from 112-130°C.

The keto acid (m.pt.96.5-99°C) gave a sharp melting butyric acid (m.pt.106-107°C), on reduction by the Clemmensen procedure, and the melting point of the latter was undepressed on admixture with an authentic specimen of β-methyl-γ prehnityl butyric acid (p.37). It would thus appear that the keto-acid (m.pt.96.5-99°C) is a homogeneous β-methyl-γ-keto-γ prehnityl butyric acid. The disparity in melting points of the various samples leads to the conclusion that the melting point of the keto-acid is not reliable.

This is a unique example of a Friedal Crafts reaction with methyl succinic anhydride and an aromatic hydrocarbon with s-tetrachloroethane as solvent, yielding only one product and that product being the β-methyl isomer. (Compare Baddar's results p.39).

Since the attempt to prepare 1:2:3:4:5:6:8-hepta-methylnaphthalene by the route shown on page 18a was unsuccessful, the preparation was attempted by a different approach [19] shown on the following page.

Prehnitene (XV) was condensed with α-methyl-α-allyl acetone [19] (LXX1V) in the presence of aluminium chloride, at 30-35°C, yielding 3-methyl-5-prehnityl-hexan-2-one(LXXV).

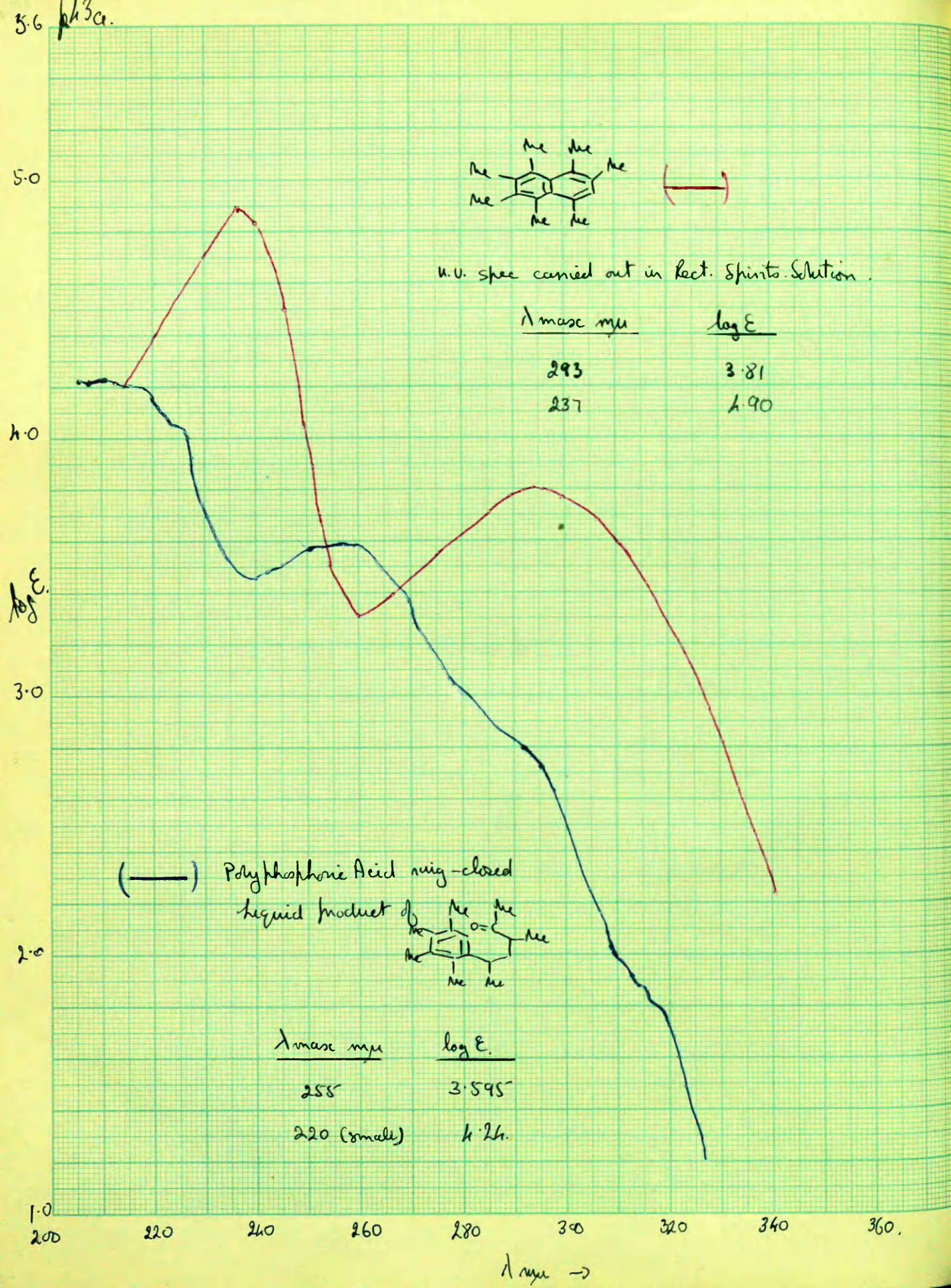

(XV)
(LXXIV)
(LXXV)
(LXXVI)
(LXXX)
(LXXXI)
(LXXXII)
(LXXXIII)

The infra-red absorption spectrum of the ketone (LXXV) exhibited a carbonyl maximum at 1710 cm^{-1}, typical of a saturated ketonic group, and its structure was further confirmed by oxidation to benzene pentacarboxylic acid, characterised as its methyl ester.

The ketone (LXXV) was smoothly reduced, with lithium aluminium hydride to the corresponding alcohol (LXXVI), and this exhibited a hydroxyl maximum in the infra-red at 3360 cm^{-1}.

Attempted cyclisation of the alcohol, by the method of Colonge and Pichat[19] using concentrated sulphuric acid, yielded an oily product which exhibited no hydroxyl maximum in the infra-red. Numerous attempts were made to dehydrogenate the oil using palladium-charcoal, sulphur and selenium but all were fruitless. Oxidation of the oil gave an acid product which on treatment with diazomethane yielded an uncrystallisable semi-solid gum. This confirmed that the oil was a mixture presumably containing ring closed and open chain compounds. The failure to dehydrogenate the oil suggests that it contains five-membered ring compounds.

Cyclisation of the ketone, 3-methyl-5-prehnityl-hexan-2-one (LXXV) was effected with polyphosphoric acid (44),(45),(46). A mixture was obtained from which 1:2:3:4:5:6:8-heptamethylnaphthalene (LXXX) was isolated by crystallisation from benzene-petroleum/ ether (b.pt. 40-60°). The physical constants of this hydrocarbon and



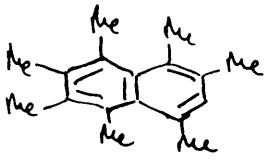
U.V. spec carried out in Rect. Spirits. Solution.

λ max mμ	log ε
293	3·81
237	4·90

(——) Polyphosphoric Acid ring-closed liquid product of

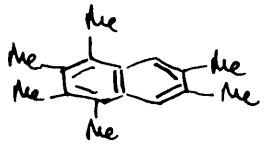
λ max mμ	log ε.
255	3·595
220 (small)	4·24.

its derivatives are shown below and its ultra-violet absorption spectrum is shown opposite.



(LXXX)

	m.pt.	Picrate m.pt.	s-T.N.B m.pt.	2:4:7-T.N.F. m.pt.
1:2:3:4:5:6:8-Heptamethylnaphthalene.	143-144°C	194-195°C	217-218°C	208·5°C-206·5°C.
1:2:3:4:6:7-Hexamethylnaphthalene.	145°C	190·5°C	215°C	210°C.



The infra-red and ultra-violet absorption spectra of the above two hydrocarbons (LXXX) and (XXI) [14] although similar, were not identical thus establishing that they were different compounds. Neither the hydrocarbons nor their derivatives respectively depressed the melting point of each other; this however does not establish identity or non-identity (see p. 34).

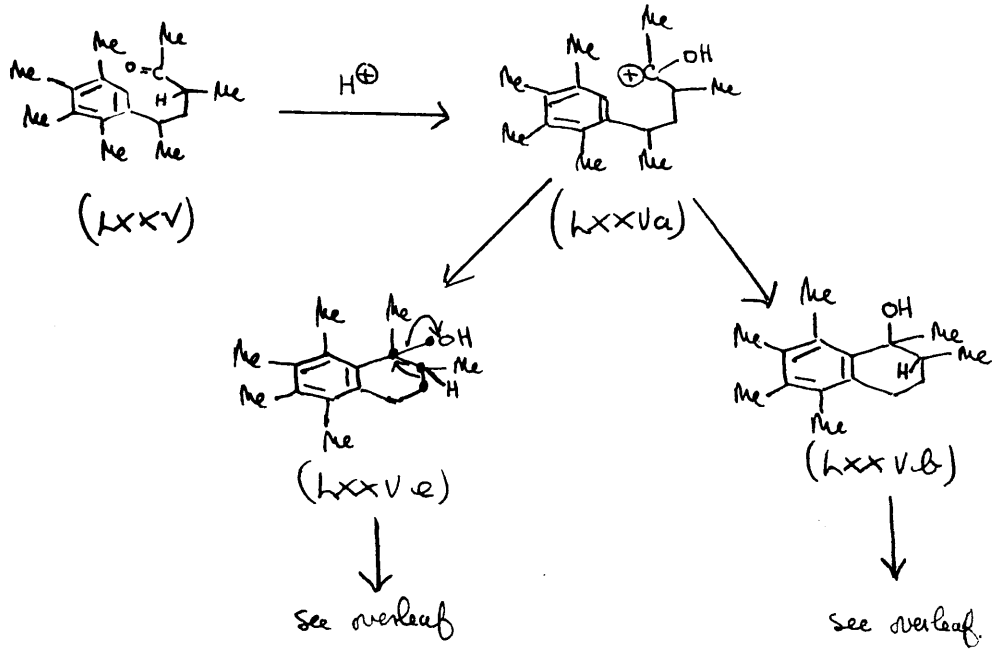
The oily residue from the polyphosporic acid cyclisation was distilled. The ultra-violet absorption spectrum (shown opposite) of the oily distillate was very similar to that of indene [47] and methyl indene [48]. The presence of a compound containing a double bond in the distillate was further confirmed by the following tests,

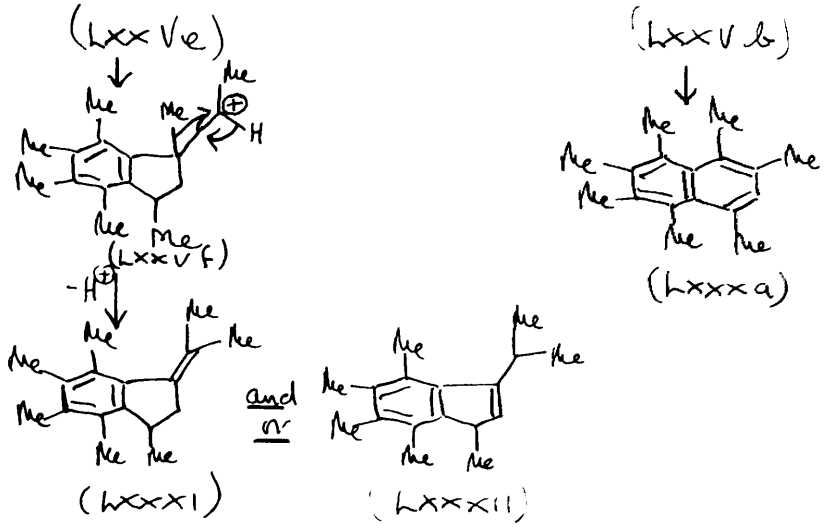
(a) it decolorised bromine water
(b) it decolorised potassium permanganate solution.
(c) a colour was produced with tetramitromethane solution.

The oil analysed for $C_{17}H_{26}$ and not $C_{17}H_{24}$; this latter would be required for a compound containing a double bond with either of the structures (LXXXI) or (LXXXII), (p. 42a).

Numerous attempts were made to dehydrogenate the oil with palladium-charcoal, sulphur and with selenium at 310 and 360°C but no success was entertained. Oxidation of the oil yielded mellitic acid (benzene-hexacarboxylic acid), characterised as its methyl ester, and this confirmed the fact that the oil contained no open chain compounds.

It is suggested from the above evidence that the oil is a mixture of the indane (LXXXIII) and one or both of the indenes (LXXXI) and (LXXXII), (p. 42a), which could be envisaged as being formed in the reaction in the following manner.





The carbonium ion (LXXVa) can cyclise in two ways to produce the alcohols (LXXVb) and (LXXVe) in which the hydroxyl group is axial and equatorial respectively.

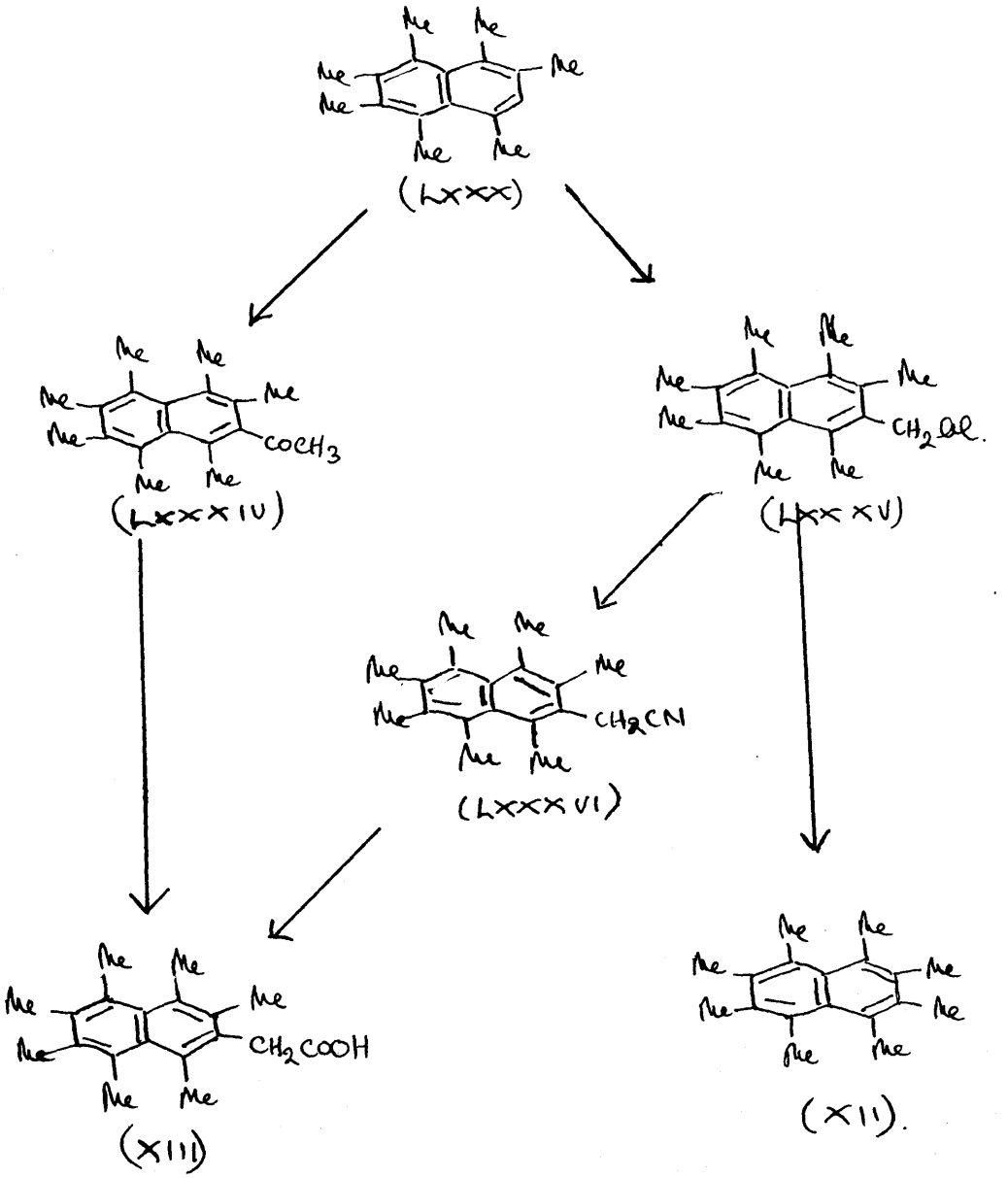
In the alcohol (LXXVb), in which the hydroxyl group is axial, trans elimination [49],[50] of water can take place in the usual manner to yield the corresponding dihydro-naphthalene (LXXXa).

If, however, the hydroxyl group is equatorial as in the alcohol (LXXVe) then trans elimination of water cannot take place. The four centres, designated by ".", in structure (LXXVe), lie in one plane and a 1:2 shift [49],[50] can take place accompanied by ring contraction producing the carbonium ion (LXXVf). The latter can stabilise itself by the expulsion of a proton and the migration of a methyl group, as shown; the indene (LXXXI) or, by migration of the double bond into the ring, the indene (LXXXII) or a mixture of both is produced.

The 1:2:3:4:5:6:8-heptamethylnaphthalene (LXXX) and the indane (LXXXIII) (p.129) can be formed from the mixture of the dihydro-naphthalene (LXXXa) and one or both of the indenes (LXXXI) and (LXXXII) by a hydrogen transfer reaction from the dihydro-naphthalene to the indenes.

The first main objective, namely, the synthesis of 1:2:3:4:5:6:8- heptamethylnaphthalene, having been achieved, the field was now set for the attempted synthesis of 2-(1:3:4:5:6:7:8-heptamethyl naphthyl)-acetic acid (XIII) and of octamethylnaphthalene (XII) (p.17). The projected route to these compounds is shown on the following chart.

1:2:3:4:5:6:7-heptamethylnaphthalene has been chloromethylated in the only vacant position, namely α, by Abadir, Cook and Gibson [14]. Numerous attempts were made to chloromethylate 1:2:3:4:5:6:8-heptamethylnaphthalene (LXXX) in the only vacant position, namely β, by the method used by these authors, but the starting material was recovered unchanged. The reaction conditions were varied but even when hydrogenchloride gas was passed continually through the solution for three hours duration, at intervals of about 17 hours, for periods up to 100 hours, no chloromethyl compound was formed. The temperature was also varied but no success was entertained; the starting material was recovered unchanged or a gummy


(LXXX)
(LXXXIV)
(LXXXV)
(LXXXVI)
(XIII)
(XII).

material was formed which yielded no aromatic hydrocarbon on shaking it in cyclohexane solution with palladium-charcoal in an atmosphere of hydrogen. Although the β-position of 1:2:3:4:5:6:8-heptamethylnaphthalene (LXXX) is not so sterically hindered as the α-position of 1:2:3:4:5:6:7-heptamethylnaphthalene (XXIV) it is not so reactive. The greater reactivity of the α-position must have accounted for the success of Abadir, Cook and Gibson [14] in preparing the chloromethyl compound of the 1:2:3:4:5:6:7- isomer.

The failure to chloromethylate the heptamethylnaphthalene (LXXX) now blocked the proposed route to the octamethylnaphthalene (XII) and to the naphthyl-acetic acid.(XIII)

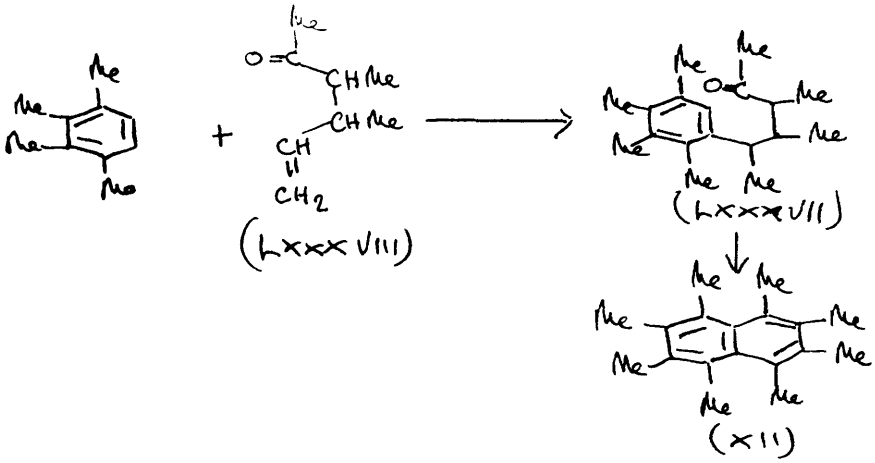
An attempt was made to prepare the desired ~~(XIII)~~-naphthyl-acetic acid (XIII) through the acetyl compound (LXXXIV) by means of a Willgerodt reaction[53], but the heptamethylnaphthalene (LXXX) proved to be too highly hindered to be acetylated[39] even under various experimental conditions.

Since the methyl groups in octamethylnaphthalene[15] lie trans to each other alternatively above and below the plane of the naphthalene nucleus, it may be possible to resolve this by the method of Newman [13].

Because of the difficulties encountered in introducing a further substituent into the heptamethylnaphthalene (LXXX), the possibility of obtaining octamethyl-

naphthalene itself, by the method employed to prepare the heptamethyl compound, was investigated.

The projected route to octamethylnaphthalene is set out below.



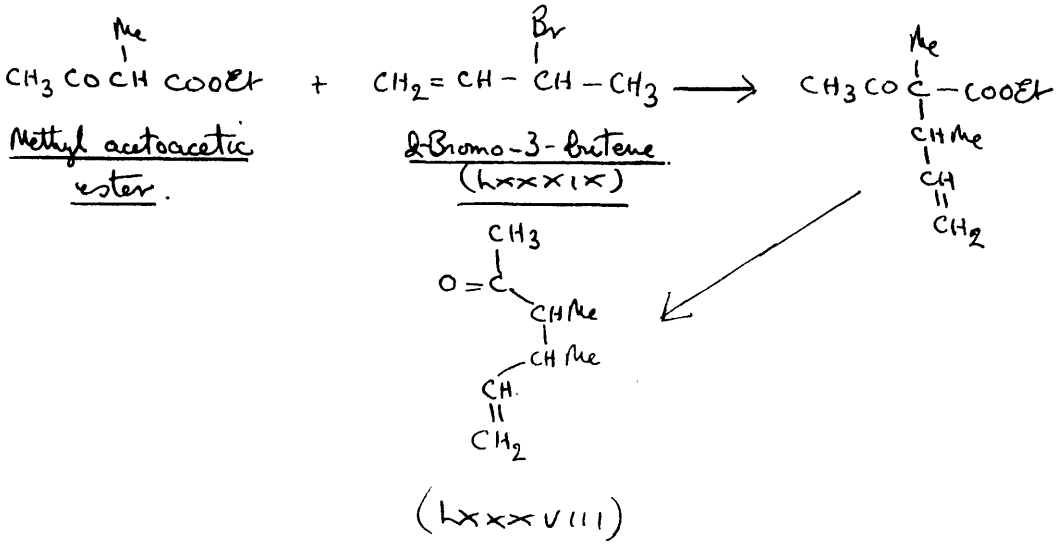
(LXXXVIII)

(LXXXVII)

(XII)

(compare with route to heptamethyl isomer p.42a).

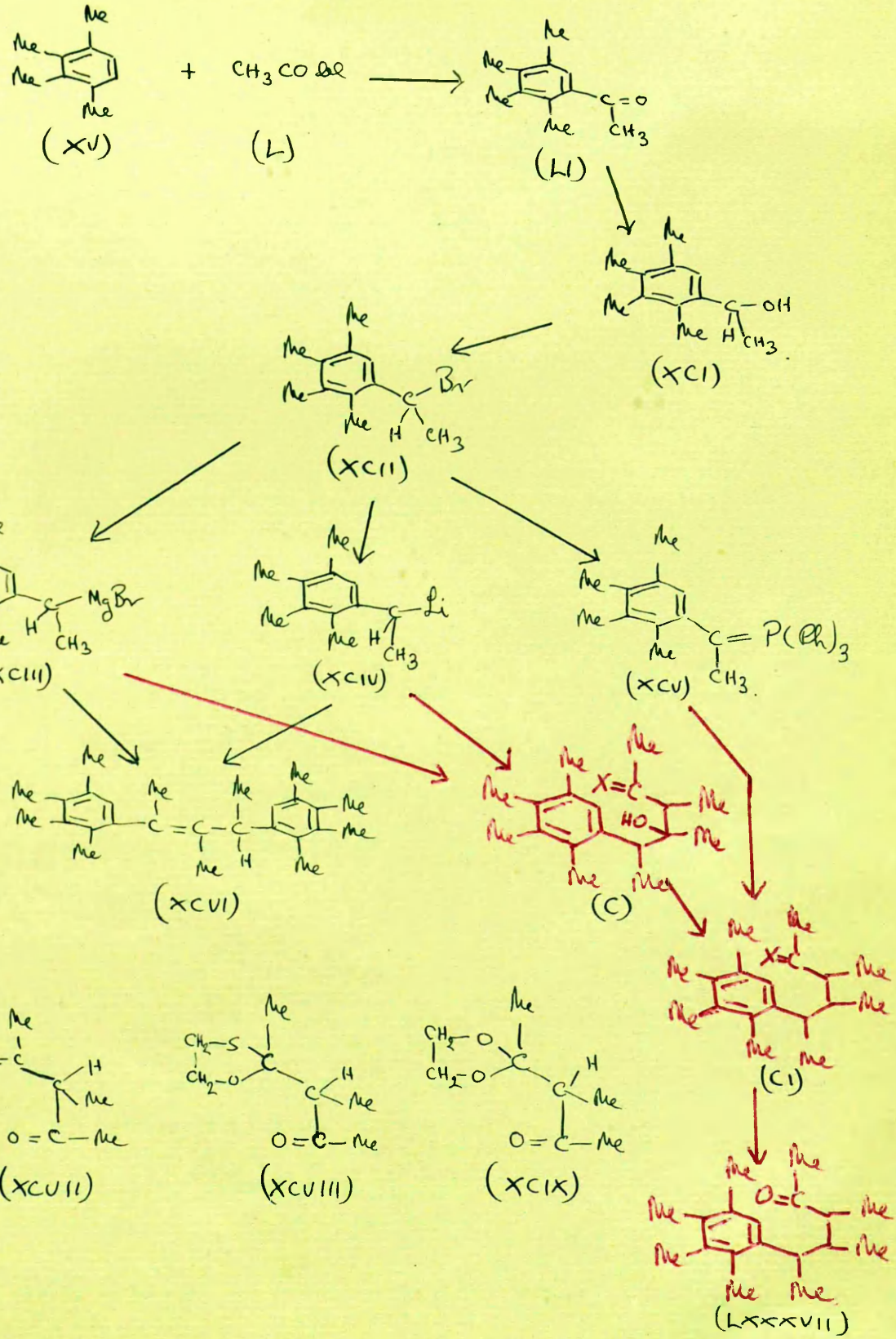
It was intended to prepare the allyl ketone (LXXXVIII) by a similar method to that used for α-methyl α-allyl acetone (p.87-89). Methyl acetoacetic ester on condensation with 2-bromo-butxene, followed by hydrolysis and decarboxylation in the usual way, should give the desired allyl ketone (LXXXVIII) as is shown below.



Methyl acetoacetic ester.

2-Bromo-3-butene (LXXXIX)

(LXXXVIII)


(XV)
(L)
(LI)
(XCI)
(XCII)
(XCIII)
(XCIV)
(XCV)
(XCVI)
(C)
(CI)
(XCVII)
(XCVIII)
(XCIX)
(LXXXVII)
(→ Proposed Theoretical Route)

Theoretically 2-bromo-3-butene (LXXXIX) could be prepared from the corresponding alcohol, 3-buten-2-ol, which is available commercially, but from the literature (54,(55) it was found that this method of preparation in practice requires specialised low temperature apparatus. This is due to the fact that thermal rearrangement of the 2-bromo-3-butene (LXXXIX) occurs at room temperature with the production of 1-bromo-2-butene (XC), an equilibrium being produced.

$$CH_2=CH-\underset{Br}{CH}-CH_3 \rightleftharpoons CH_3-CH=CH-CH_2Br$$

(LXXXIX) (XC)

Owing to the difficulty of preparing 2-bromo-3-butene (LXXXIX) the proposed route was abandoned.

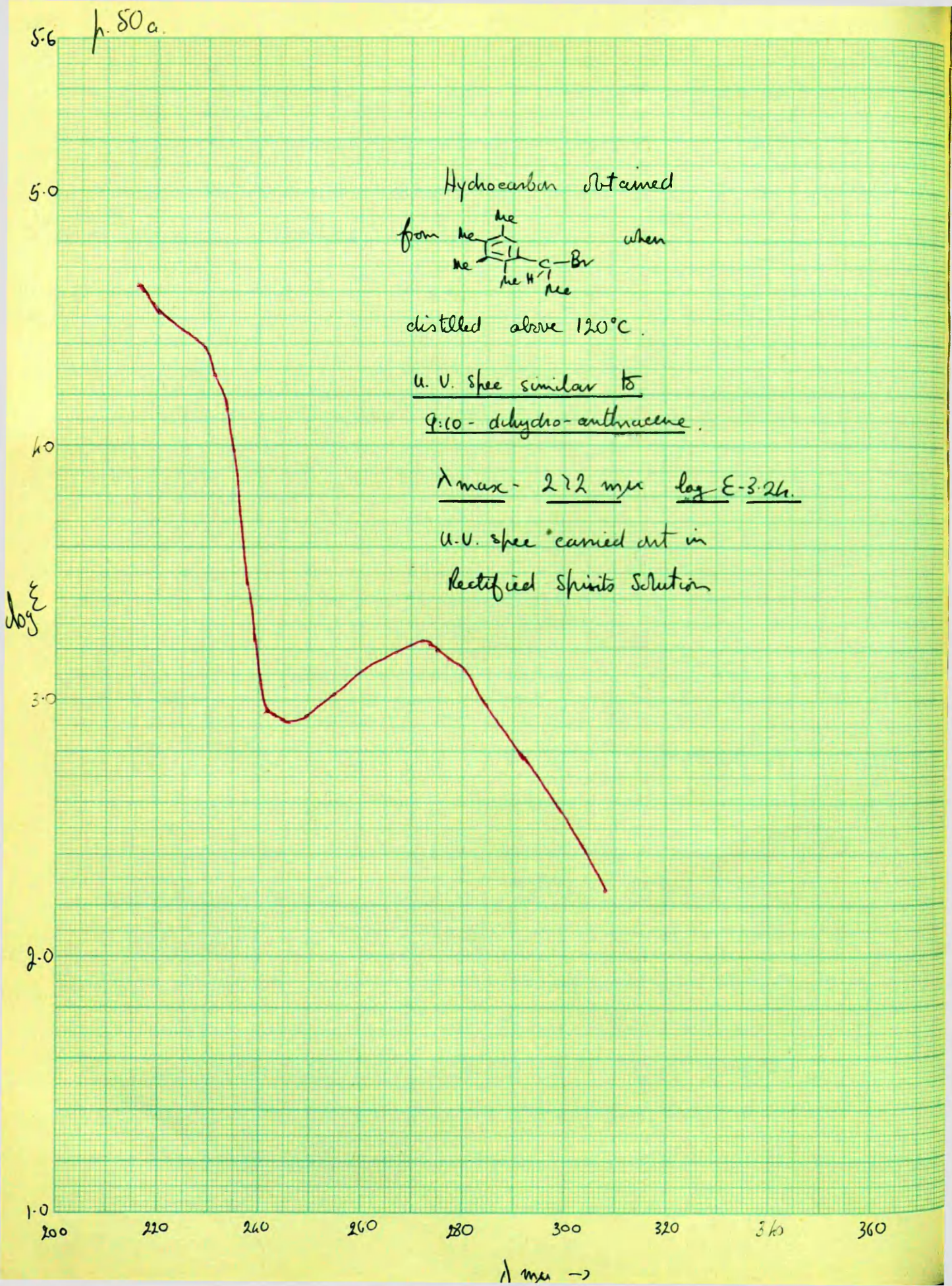
The preparation of the 3:4-dimethyl-5-prehnityl hexan-2-one (LXXXVII) (p. 48) was now attempted by another route, which is outlined on the opposite page.

Acetyl prehnitene (LI) was prepared by the method described on page 73 . It was reduced with lithium aluminium hydride to the corresponding alcohol (XCI) which was brominated with phosphorus tribromide, giving α-bromo-ethyl prehnitene (XCII) in good yield. This latter compound was thermally unstable and if it was distilled above 120°C hydrogen bromide was evolved and a hydrocarbon was obtained with empirical formula C_3H_4.

The ultra-violet absorption spectrum of this hydrocarbon

(shown overleaf)

p. 80a.



Hydrocarbon obtained from when distilled above 120°C.

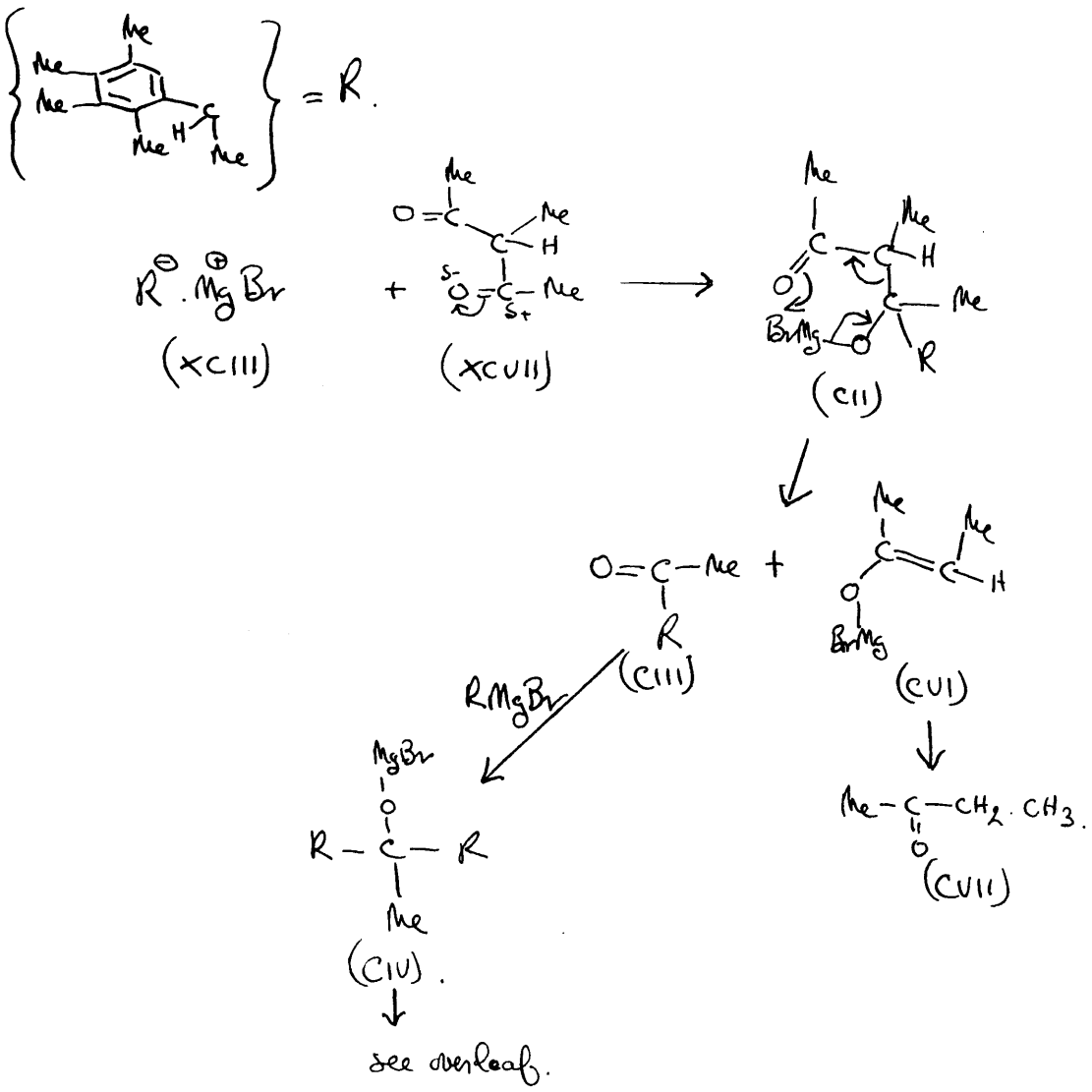
U. V. spec similar to 9:10 - dihydro-anthracene.

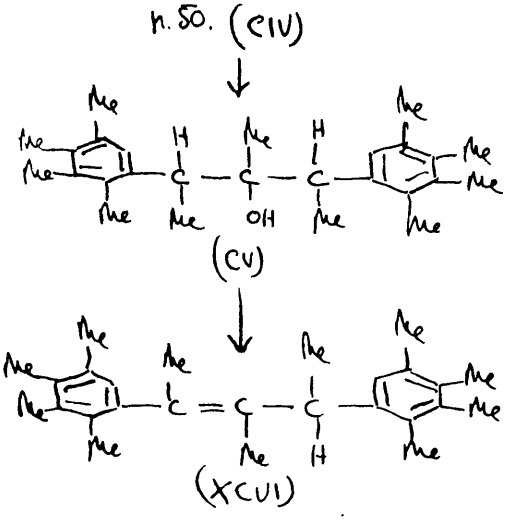
λmax - 272 mμ log ε - 3·24.

U.V. spec carried out in Rectified Spirits Solution

was very similar to that of 9-10 dihydro-anthracene[56], but all attempts to dehydrogenate it to an anthracene failed, even with selenium at 360°C.

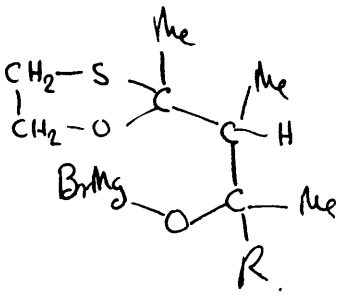
An attempt was now made to react the bromide with methylacetylacetone ((XCVII) through the magnesium compound (XCIII). None of the desired product (C) (X=O) was obtained but a hydrocarbon, 2:4-diprehnityl-3-methyl-pent-2-ene (XCVI) was isolated from the reaction mixture. This could be regarded as being formed in the reaction in the following manner.





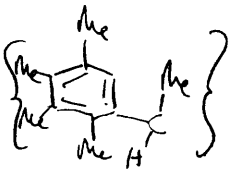
The magnesium complex (XCIII) can react with one molecule of methylacetylacetone (XCVII) in the normal manner with the formation of the magnesium derivative (CII) (see chart). This latter can cleave by the movement of electrons in the direction shown by the arrows with the production of the ketone (CIII) and the magnesium derivative (CVI). The ketone (CIII) can then react with another molecule of the magnesium complex (XCIII) and this produces the hydrocarbon (XCVI) in the manner shown. The production of this hydrocarbon was not entirely unexpected since Kohler and Erickson (59) have shown that mono-substitution products of simple β -diketones cleave in the above manner. They found however that the magnesium complex of type (CII) could sometimes be stabilised by working at low temperatures. In this present work the experiment was carried out at $-80^{\circ}C$ but the hydrocarbon (XCVI) was produced and none of the desired product (C) (X=O).

It was thought that if the mono-hemi-thioketal of methylacetylacetone (XCVIII) was used instead of methylacetylacetone that the magnesium derivative (CVIII) (see below) formed initially would be unable to cleave by the method shown above for the magnesium derivative (CII). The Inverse Grignard was carried out at -80°C but, surprisingly, the same hydrocarbon (XCVI) was obtained, and none of the desired compound (C) (X=$\begin{matrix}CH_2-S\\CH_2-O\end{matrix}$>)



(CVIII)

R=

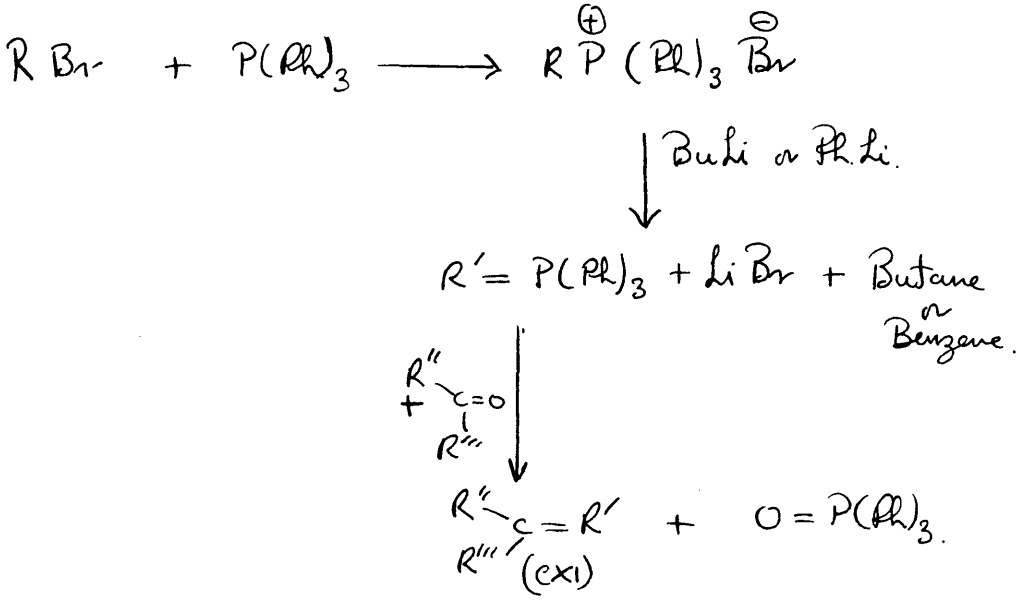


Presumably the magnesium derivative has been unstable and immediate cleavage has occurred similar to the previous case with methylacetylacetone.

The same hydrocarbon (XCVI) was also obtained when the mono-ketal (XCIX) was employed in the Inverse Grignard reaction.

The reaction was also attempted with the Lithium complex (XCIV) and the mono-ketal (XCIX); again however the hydrocarbon (XCVI) was obtained.

Recently Wittig etal[57] have condensed methyl bromide (CIX, R= CH_3) with a ketone through the formation of the phosphorus complex (CX, $R'=CH_2$). The bromide forms a salt with Wittig's Reagent[58] (triphenyl phosphine), and the salt on treatment with butyl lithium or phenyl lithium gives the desired complex (CX, $R'=CH_2$), as shown below.



The phosphorus complex (CX) reacts with ketones with the formation of triphenyl phosphonium oxide and compounds of type (CXI).

An attempt was made to react the bromide (XCII) with the mono-ketal (XCIX) through the phosphorus complex (XCV) ($X=\begin{matrix}CH_2-O\\CH_2-O\end{matrix}$) but none of the desired compound (CI) (p.49a) was obtained.

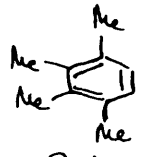
It may be concluded that this method of approach to the synthesis of 3:4-dimethyl-5- prehnityl-hexan-2-one (LXXXVII) (p.49a) is not practicable.

Some interesting work has been published on the

comparison of naphthalenes with the corresponding benzenes in the infra-red [51,(52)].

Werner etal[52] have studied naphthalene substitution in relation to the infra-red spectrum and have stated that the rules based on benzene substitution are generally valid for groups of two or three or four hydrogen atoms in the naphthalene nucleus, although substituents which tend to interact with the ring tend to widen the limits within which a band may be expected to fall. In the case of a single hydrogen atom the relevant bands are often weak and their position variable.

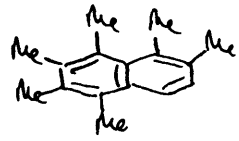
The strong peaks due to the C-H bending vibrations in the region 600-900 cm^{-1} in the infra-red spectra of some polymethylnaphthalenes are shown below, along with those of the corresponding polymethylbenzenes.



Prehnitene

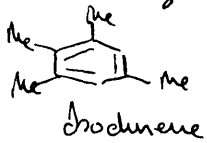
Peaks

804 cm^{-1} ... 2 ortho-hydrogens



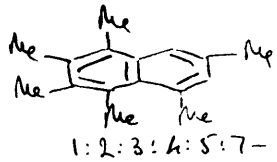
1:2:3:4:5:6-Hexamethylnaphthalene.

806.4 cm^{-1} ... 2 ortho-hydrogens



Isodurene

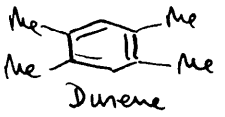
848 cm^{-1} .... 2 meta-hydrogens



1:2:3:4:5:7-Hexamethylnaphthalene.

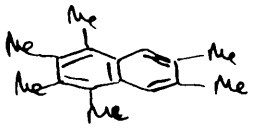
845.4 cm^{-1} .... 2 meta-hydrogens

Peaks



Durene

866 cm^{-1} ... 2 para-hydrogens



1:2:3:4:6:7-Hexamethylnaphthalene.

859·6 cm^{-1} - - 2 para-hydrogens.

It is quite evident that there is a relationship between each of the naphthalenes and the corresponding benzenes and that the rules for the benzenoid compounds apply to the naphthalenes. Thus, prehnitene and 1:2:3:4:5:6-hexamethyl-naphthalene (LXI) show a band about the same position due to the pair of ortho-hydrogens in each compound (see table).

Similarly isodurene and 1:2:3:4:5:7-hexamethylnaphthalene (XXXI) exhibit a maximum about the same position due to the pair of meta-hydrogens in each compound.

Also durene and 1:2:3:4:6:7-hexamethylnaphthalene (XXI) exhibit a maximum about the same position due to the two para-hydrogens in each compound. This peak is not however as characteristic as the peaks due to meta- and ortho-hydrogens, since the para-hydrogens vibrate as single hydrogens and not as a pair. It is thus not possible to distinguish between single and parahydrogens by this peak in the infra-red, but it does show that the compound (XXI) does not contain meta- or ortho-hydrogens.

This data further confirms the structures of the above polymethylnaphthalenes.

Summary.

1:2:3:4:5:6- Hexamethylnaphthalene and 1:2:3:4:5:6:8-heptamethylnaphthalene have been prepared and characterised for the first time.

The compound regarded by Abadir, Cook and Gibson[14] as 1:2:3:4:5:6- hexamethylnaphthalene has been shown to be 1:2:3:4:5:7-hexamethylnaphthalene.

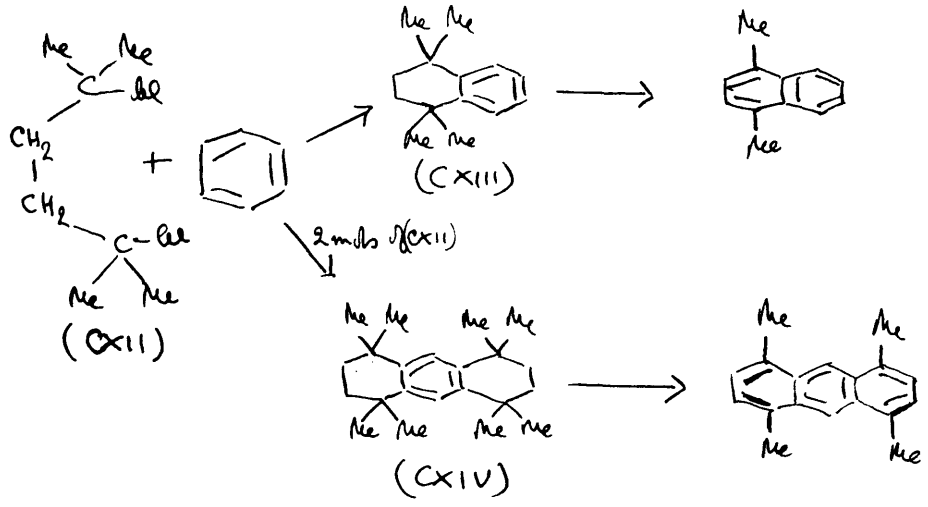
It is suggested that the compound regarded by Abadir, Cook and Gibson [14] as 1:2:3:4:5:7-hexamethylnaphthalene is probably impure 1:2:3:4:6:7-hexa or impure 1:2:3:4:5:6:8-heptamethylnaphthalene or a mixture of both.

Several attempts have been made to prepare octamethylnaphthalene by a different route from that used by Abadir, Cook, and Gibson[14].

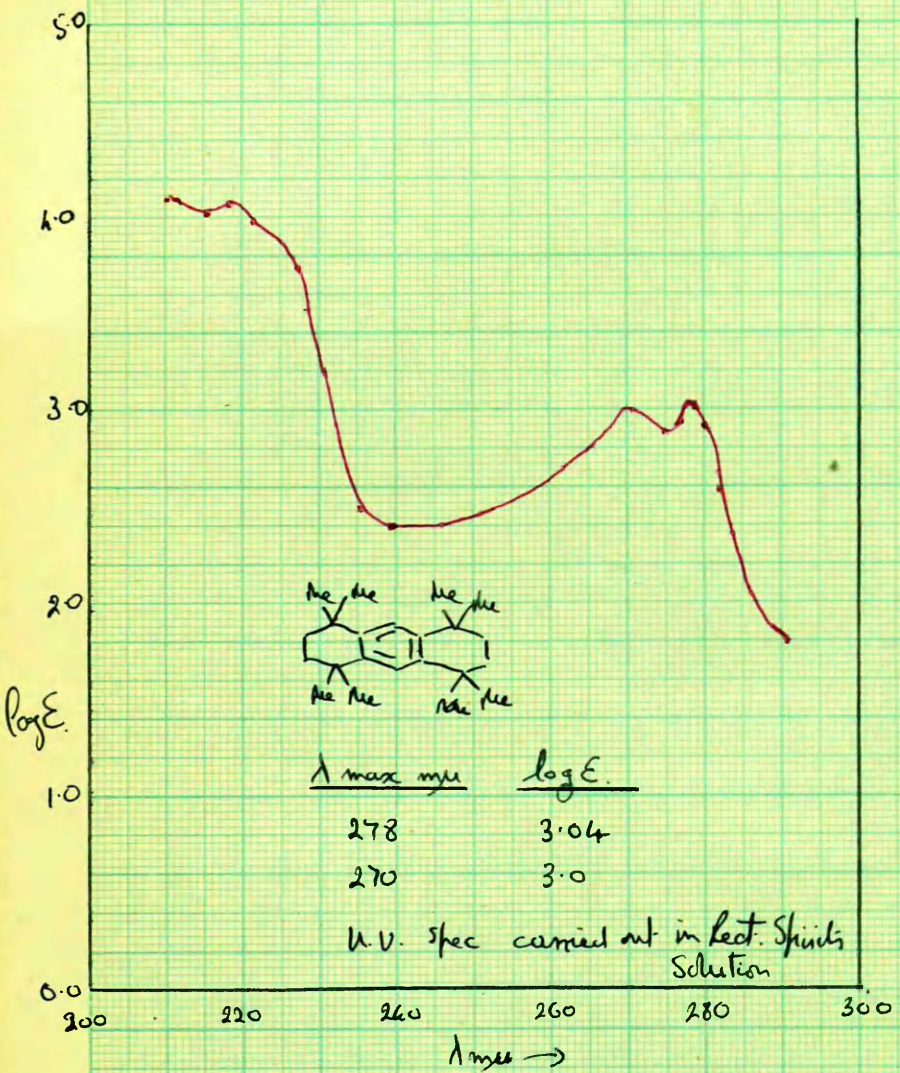
---oOo---

Appendix.

The following reaction was investigated as a possible route to polymethylnaphthalenes.



Bruson and Kroeger[60] condensed 2:5-dichloro-2:5-dimethyl-hexane (CXII) (1g) with benzene (2•16 gms) in the presence of aluminium chloride (0.445gm) and obtained a liquid which by analysis they concluded to be 1:1,4:4-tetramethyl (-1:2:3:4-tetrahydronaphthalene (CXIII) They obtained a solid hydrocarbon however when only a catalytic amount of aluminium chloride (.0278gm) was used which they concluded by analysis to be the dicondensation product 1:1,4:4,5:5,8:8-octamethyl-1:2:3:4:5:6:7:8-octahydroanthracene (CXIV). It was thought that if it was possible to dehydrogenate these two compounds (CXIII) and (CXIV) the above reaction might provide a suitable route to polymethyl naphthalenes and anthracenes as well as establishing definitely the structures of compounds (CXIII) and (CXIV)



λ max mμ	log ε.
278	3·04
270	3·0

U.V. spec carried out in Rect. Spirits Solution

2:5-dichloro-2:5-dimethyl hexane was prepared from 2:5-dimethyl-3-hexyn-2:5-diol which was kindly given to us by I.C.I. Billingham Division.

The compounds (CXIII) and (CXIV) were prepared by the method of Bruson and Kroeger[60]. Several attempts were made to dehydrogenate them, but even with selenium, at 400°C for 100 hours in a sealed tube, they were recovered unchanged.

The presence of gem-dimethyl groups was confirmed in both compounds by the presence of the following characteristic peaks in the infra-red absorption spectra,

compound (CXIII) 1386 cm^{-1}, 1364 cm^{-1}.

compound (CXIV) 1400 cm^{-1}, 1380 cm^{-1}.

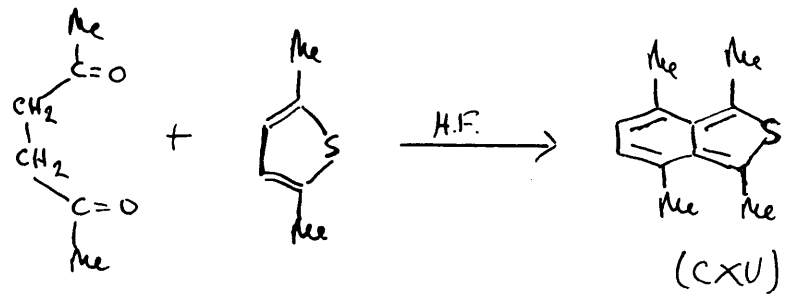
The ultra-violet absorption spectrum of compound (CXIV) (shown opposite) was similar to that of octahydroanthracene[61].

It would thus appear from the evidence obtained that the compounds (CXIII) and (CXIV) have the structures assigned to them by Bruson and Kroeger. Further work was abandoned on the publication of a paper by Barclay and Betts [62], who obtained the hydrocarbon (CXIV) by alkylation of 1:3:5-tri-t-butyl benzene with t-butyl chloride. They record that great difficulty was experienced in attempting to dehydrogenate ~~the~~ it to the corresponding anthracene. With palladium-asbestos at 420°C in a sealed tube they obtained a little of a compound which exhibited an anthracene spectrum in the ultra-violet.

An attempted novel synthesis of 1:2:3:4:5:8-hexamethyl naphthalene.

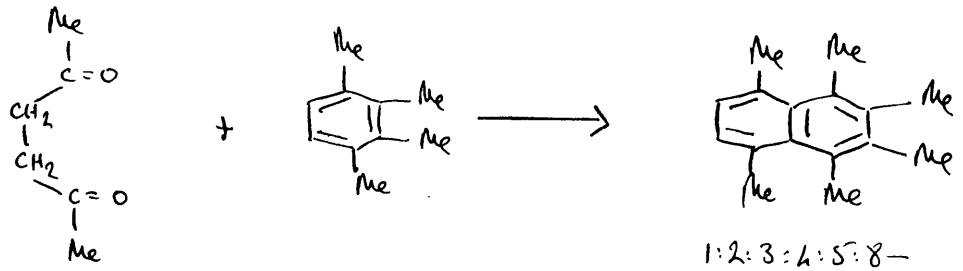
The preparation of 1:2:3:4:5:8-hexamethylnaphthalene (CXV)[17] was attempted by the following method with a view to extending the latter to the synthesis of other polymethylnaphthalenes.

Dann, Kokonudz and Gropper[63] had condensed acetonyl-acetone with 2:5-dimethylthiophen, in presence of anhydrous hydrogen fluoride in a bomb at 100°C for three hours, giving 1:4-dimethyl-2:3-(1':4'-dimethyl-)-benz thiophen (CXV).



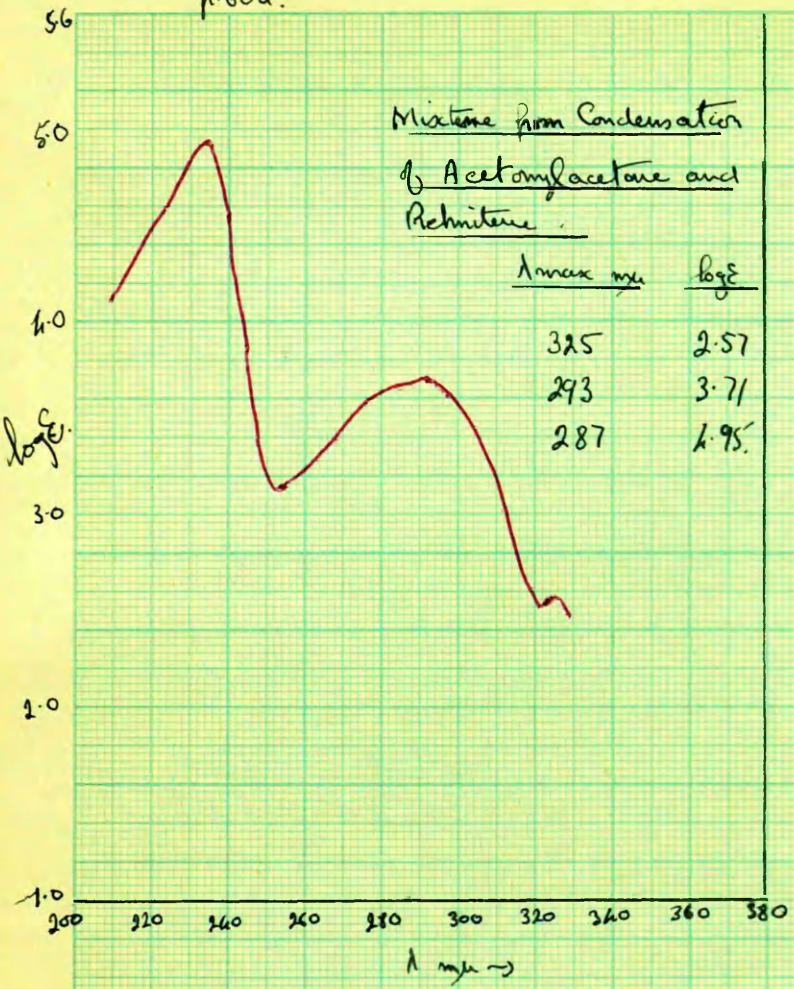
(CXV)

The reaction was attempted under similar conditions with acetonyl acetone and prehnitene (XV). A mixture was obtained from which no pure product could be isolated.



1:2:3:4:5:8-Hexamethylnaphthalene.

p.60a.



Mixture from Condensation of Acetonylacetone and Pelmitone.

λ max mμ	log ε
325	2.57
293	3.71
287	4.95

Two main fractions were separated by distillation leaving a residue of tars.

The first fraction melted over a range of 55-90°C and formed an orange-brown picrate (long needles, m.pt. 158-165°C). The ultra-violet spectrum did not yield any definite evidence as to the molecular structure of any of the components of this mixture.

The second fraction formed a picrate (m.pt.194-195°C) which analysed correctly for a hexamethyl naphthalene. The hydrocarbon recovered from the picrate melted over a range of 145-160°C, and was evidently a mixture. It also formed a styphnate (m.pt.194-195°C) but again on recovering the hydrocarbon it melted over the same range 145-160°C. The second mixtureexhibited a typical naphthalene spectrum in the ultra-violet (shown opposite).

The experiment was not pursued any further although experimental conditions probably could be varied to give a pure product.

We have to thank Mr. Kühn and Mr. Schulz-Kiesow who arranged for this reaction to be carried out at the factory of Rutgers-Werke A.G.

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PART I.

Experimental

Preparation of Ethyloxalylpropionate.

Ref.Org.Syn., 17, 54.

Ether (600ccs.) (dry) was added to powdered sodium (41 gms.), followed by the dropwise addition of absolute ethanol (80.5 gms., dry) to the stirred mixture. Thereafter the whole was stirred and refluxed for several hours till all the sodium had completely reacted. The mixture was now immersed in an ice-water bath and a mixture of ethyl,propionate (199 ccs.) and ethyl oxalate (236 ccs) was added slowly so that the ether did not reflux. The ether and the alcohol, formed in the reaction, were removed by heating the mixture on a steam bath, the distillation being stopped when a yellow scum began to be formed on the surface of the liquid. The mixture was allowed to stand with acetic acid (350 ccs., 33%) for several hours, with occasional shaking, in order to decompose the sodium derivative which had crystallised. The whole was extracted with ether and the ether extract washed with water, and sodium bicarbonate solution and water and dried. On removal of the ether, ethyl oxalylpropionate (157.3 gms.) was obtained on distillation of the residue at 140°C/ 22mm. The yield was 45% of the theoretical.

Preparation of Ethyl methylmalonate.

Ref. Org.Syn. 17, 56.

Ethyl oxalylpropionate (157.3 gms.) was heated to 160°C when a vigorous evolution of carbon monoxide commenced. The temperature of the liquid was gradually raised to 190°C as the gas evolution diminished and refluxed till no more gas was evolved. On distillation ethyl methylmalonate (126 gms.) was obtained at 190°C/ 744-747 mm. The yield was 93.2% of the theoretical.

Preparation of Ethyl methylallylmalonate.

Ref. Paul; Ann. Chim., 1932, 18, 331

Colonge, Grimand; Bull.Soc.Chim.,1951, 439.

Dry ethyl methylmalonate (126 gms.) was introduced, with cooling to sodium ethoxide, prepared by dissolving sodium (18.1 gms.) in alcohol (dry, 202 gms.). The stirred mixture was then heated by an easily removable water bath to 60°C and allyl bromide (96.2 gms) was added in small portions. The solution was then heated on the steam bath to remove the alcohol as completely as possible and the residual liquid treated with water and extracted with ether. The ether extract was washed with water and dried. On evaporation of the ether and distillation of the residual liquid the ethyl methylallylmalonate (136.7 gms.) was obtained at 122°C/ 35 mm. The yield was 88.2% of the theoretical.

Preparation of Methylallylacetic acid.

Ref. (see previous experiment).

Ethyl methylallylmalonate (136.7gms.) was added slowly to a fresh very concentrated solution of potassium hydroxide (76.5 gms.) in a round bottomed flask, which was heated on the steam bath to initiate the reaction. A compound, the mono-potassium salt crystallised, but went into solution again as more of the ester was added and as the reaction proceeded.

The mixture was heated gently for about two hours on the steam bath. The alcohol was distilled, whereupon the di-potassium salt crystallised on cooling. Concentrated hydrochloric acid was added till the solution was acid to litmus, the mixture filtered free from precipitated potassium chloride and the filtrate was extracted with ether.

The ether extract was washed with water and dried and the ether evaporated. Methylallylacetic acid (61.3 gms.) was obtained on distillation at 180-190°C. The yield was 84.2% of the theoretical.

Preparation of Ethyl methylallylacetate.

Methylallylacetic acid (61.3 gms.) was dissolved in benzene (dry, 55 ccs.) and mixed with a previously cooled solution of concentrated sulphuric acid (17 gms.) in ethanol (95%, 42 ccs). The whole was mechanically stirred for ninety hours. The benzene layer was separated and washed with water and sodium bicarbonate solution

and water and dried. On evaporation of the benzene ethyl methylallylacetate (52.5 gms.) was obtained at 153-155°C. The yield was 69% of the theoretical.

Preparation of Pentamethyl Benzene.

Ref. Smith, Org.Syn., 1930, 10, 32.
Abadir, Ph.D.Thesis, Glasgow Univ.1951, p.78.

Freshly pulverised aluminium chloride (350 gms.) was added to a mixture of mesitylene (350 gms.) and m-xylene (800 gms.). The mixture was heated on the steam bath and methyl chloride gas was bubbled through it for 35½ hours under a slight pressure(10 cm. of mercury). The reaction mixture was decomposed with ice and concentrated hydrochloric acid, and the organic material extracted with benzene, and benzene extract washed with water and dried in the usual manner. Pentamethyl benzene (1157gms.) was obtained on distillation of the crude product, distilling at 230°C-235°C. Some hexamethyl benzene was also obtained.

Preparation of Prehnitene.

Ref. Smith Lux, J.A.C.S.,1929,51,2994.

Pentamethyl benzene (389 gms.) was heated to 65°C and to the resulting oil was added with vigorous stirring cold concentrated sulphuric acid (1050 ccs.). The mixture was allowed to stand at room temperature for 36 hours. It was then further cooled to 0°C by means of an ice salt bath and crushed ice added with stirring, and the mixture

filtered at 0°C. The filter cake was leached out thoroughly with cold water and the resulting suspension filtered. The precipitate consisted mainly of hexamethyl benzene and by-productswhile the combined filtrates consisted of a water solution of prehnitic sulphonic acid and sulphuric acid.

The sulphonic acid was converted to its calcium salt by the addition of calcium carbonate till effervescence ceased. The calcium sulphate which precipitated was filtered, washed thoroughly and discarded. The calcium salt was converted to the sodium salt by the addition of sodium carbonate solution to the combined filtrates till the precipitation of calcium carbonate was complete. The calcium carbonate was filtered, washed with water and discarded. On evaporation of the combined filtrates to dryness sodium prehnitene sulphonate was obtained.

Sodium prehnitene sulphonate was hydrolysed to prehnitene by the method of flash hydrolysis. A 1 litre, 3 necked round bottomed flask was fitted with a dropping funnel, thermometer, inlet for superheated steam and outlet for distillation. The flask was charged with water (100ccs) and immersed in an oil bath at about 200°C. Superheated steam was passed through and concentrated sulphuric acid was added till the temperature of the dilute acid in the flask reached 150°C-160°C. A saturated water solution of sodium prehnitene sulphonate was added at such a rate that

the temperature of the acid mixture remained between 140°C-150°C. The hydrolysis took place rapidly and the hydrocarbon was distilled out immediately in the current of steam. Prehnitene (63.5 gms.) was obtained as a light yellow oil.

Condensation of Prehnitene (XV) and Ethyl methylallylacetate (XX XIX)

Ref.Colonge,Grimand,Bull.Soc.Chim.1951,439.

Ethyl methylallylacetate (45.3 gms.) was added dropwise to a stirred mixture of prehnitene (45.6 gms.) and powdered anhydrous aluminium chloride (64.5 gms) at about 35°C. After four hours the complex was decomposed with ice and hydrochloric acid and the organic layer extracted with ether. The ether extract was washed with dilute hydrochloric acid and sodium bicarbonate solution and water and dried. Ethyl α-methyl-γ-prehnityl valerate (XL) (77.55 gams) was obtained, distilling at 198-200°C/ 23 mm. The yield was 88% of the theoretical and the product analysed correctly for $C_{18}H_{28}O_2$. (Found C78.4%; H10.03% Requires C-78.21%; H-10.21%).

Preparation of α-methyl-γ-prehnityl valeric acid (XLI) by hydrolysis of the ethyl ester (XL).

The above ester (77.55 gms.) was hydrolysed by refluxing with aqueous alcoholic potassium hydroxide (20 gms., 20%) for five hours. A neutral fraction (4 gms.) was isolated, melting at 47-48°C, having an empirical formula of $C_{16}H_{22}O$ (Found C83.24%; H9.35%; Requires C-83.43% H9.63%).

The acid, α-methyl-γ-prehnityl valeric acid (70 gms.) was isolated in the usual way, melting at 76-90°C (Found C77.17%; H.9.82%; Requires for $C_{16}H_{24}O_2$ C-77.37%; H-9.74%). The yield was 92% of the theoretical.

The structure of the acid was confirmed by oxidation (64) to benzene pentacarboxylic acid. α-methyl-γ-prehnityl valeric acid (0.2 gm) was heated to 175-180°C in a sealed tube for 6 hours with concentrated nitric acid (1.5 ccs.) and water (3 ccs.). On evaporation of the water the residue was treated with excess ethereal diazo-methane solution, yielding the pentamethyl ester of benzene pentacarboxylic acid which crystallised from methanol, m.pt.143.4-146°C, undepressed on admixture with authentic specimen.

<u>Cyclisation of α-methyl-γ-prehnityl valeric acid (XLI) to 2:4:5:6:7:8-hexamethyl-tetralone-1.(XLII)</u>

Ref. Organic Reactions, <u>Vol.II,</u> 136.

Wilds,J.A.C.S., 1942, <u>64,</u> 1421.

Phosphorus pentachloride (47.7 gms.) was added in portions to a stirred solution of the acid, α-methyl-γ-prehnityl valeric acid (53 gms.) in dry benzene (220 ccs.), in a flask, protected from moisture by a calcium chloride tube, and immersed in an ice-water bath. After the addition of all the phosphorus pentachloride the solution was allowed to stand at room temperature for 1 hour and then heated on a steam bath for five minutes to ensure completeness of reaction.

Stannic Chloride (anhydrous, 52.4 ccs.) in benzene (dry, 52.4 ccs) was added dropwise to the stirred mixture at 0°C. The mixture was stirred for 45 minutes at 0°C and then decomposed with ice and hydrochloric acid. After separation of the organic layer, by extraction with benzene, it was washed with several portions of hydrochloric acid (5%) and sodium hydroxide (5%), and water and dried. The crude product was distilled, 2:4:5:6:7:8-hexamethyl-tetralone-1(39 gms.) being obtained (b.pt.212°C/ 26mm.). On crystallisation from methanol it melted at 62-63°C.(Found C-83.4%; H-9.5%; $C_{16}H_{22}O$ required, C-83.43%; H-9.63%). The yield was 80% of the theoretical. The 2:4-dinitrophenyl-hydrazone derivative melted at 167-168°C. (Found, N-13.90%; $C_{22}H_{26}O_4N_4$ requires N-13.65%).

Attempted preparation of 1:3:4:5:6:7:8-Heptamethyl-1:2-dihydro-naphthalene (XLIIIa).

Ref. Abadir, Cook, Gibson, J., 1953, 8.

(a) The above tetralone (XLII) (1 gm.) was added in ether solution to a Grignard solution prepared from methyl iodide (2.6 gms.) and magnesium turnings (0.445 gm.) and ether (40 ccs.) The ether was removed and replaced by pure benzene and the mixture refluxed for 40 hours. The tetralone was recovered unchanged from the reaction mixture.

(b) The above tetralone (1 gm.) was added in ether solution to a solution of methyl lithium, prepared from methyl-iodide (1.42 gms.) and lithium (.14 gm), in ether and the whole refluxed for 4 hours in a nitrogen atmosphere.

Again the tetralone was recovered unchanged from the reaction mixture.

(c) A similar experiment to (b) was carried out but after the addition of the tetralone the ether was distilled off and pure dry xylene (30 ccs) added and refluxing was continued for 40 hours in a nitrogen atmosphere. Once again the tetralone was recovered unchanged.

(d) This experiment was identical to (C) but di-n-butyl ether (b.pt.140°C) was added instead of xylene. However, no success was entertained, the tetralone being recovered unchanged.

Clemmensen Reduction of 2:4:5:6:7:8-hexamethyl-tetralone-1 (XLII)

Ref.Martin, J.A.C.S., 1936, 58, 1438.

The above tetralone (0.32 gm.) was added to a mixture of amalgamated zinc (1 gm.), water (.75 ccs), concentrated hydrochloric acid (1.75 ccs.), and toluene (1cc). The mixture was refluxed vigorously for 24-hours, three portions of concentrated hydro-chloric acid (0.5cc) being added at intervals of about 6 hours. The cooled liquid was extracted with benzene and the extract washed. On evaporation of the benzene 2:4:5:6:7:8-hexamethyl-1:2:3:4-tetrahydronaphthalene (XLVI) (.239 gm) was obtained.

Dehydrogenation of 2:4:5:6:7:8-hexamethyl-1:2:3:4-tetrahydronaphthalene (XLVI).

The above crude tetrahydronaphthalene (.239 gm) was dehydrogenated by heating with palladium-charcoal (30%),

prepared by the method of Linstead and Thomas (65), in a stream of carbon dioxide at 325°C approximately. The resulting 1:2:3:4:5:7- hexamethyl-naphthalene (XLVII) (.12 gm) purified through its picrate, crystallised from cyclohexane (m.pt.78-80°C, micro-melt.) (Found C-90.44%; H-9.53%; $C_{16}H_{20}$ requires, C-90.5%; H-9.5%). Its picrate had m.pt.169-170°C (Found N-9.42%, $C_{16}H_{20}C_6H_3O_7N_3$ requires N-9.5%); and its 2:4:7 trinitrofluorenone complex had m.pt. 181-182°C. The yield of hexamethyl-naphthalene was 50% of the theoretical.

Reduction of 2:4:5:6:7:8-hexamethyl-tetralone-1 (XLII) with Lithium Aluminium Hydride.

Ref., Org.Reactions, Vol.6, 469,

Nystrom, Brown, J.A.C.S.1947, 69, 1197.

The tetralone (1 gm.) was added dropwise to a slurry of lithium aluminium hydride (0.17 gm.) in ether (dry) so that the ether gently refluxed. The mixture was refluxed for two hours after the addition of the ketone, and allowed to stand overnight. Excess lithium aluminium hydride was destroyed by the dropwise addition of ethyl acetate. The mixture was poured into ice and hydrochloric acid and the ether layer separated. The ether extract was washed, dried and the ether evaporated yielding the crude alcohol (0.93 gm.).

The crude alcohol (0.93 gm.) was dehydrated by heating with fused potassium bisulphate (0.093 gm.) to 160°C for ten minutes and the product distilled. The 2:4:5:6:7:8-

hexamethyl-1:2-dihydronaphthalene (0.743 gm.) (m.pt.38-39°C) was obtained.

Dehydrogenation of 2:4:5:6:7:8-hexamethyl-1:2-dihydronaphthalene (XLIX).

The above dihydro-naphthalene (0.325 gm.) was dehydrogenated by heating with palladium-charcoal [65] in boiling 1:2:4-trichlorobenzene in an atmosphere of carbon dioxide for 5 hours. 1:2:3:4:5:7-Hexamethylnaphthalene (XLVII) (0.19 gm.) (m.pt.78-80°C) was obtained identical with the specimen prepared by reduction of 2:4:5:6:7:8-hexamethyl-tetralone-1 (XLII) by the Clemmensen Reduction (p.69). The yield of hydrocarbon in this experiment was 60% of the theoretical.

Preparation of the Maleic Anhydride Adduct of 1:2:3:4:5:7- Hexamethylnaphthalene.

Ref. Abadir, Cook, Gibson, J., 1953, 8.

The above hexamethylnaphthalene (1.58 gm.) and freshly distilled maleic anhydride (24 gms., ca.30 mols) in benzene (dry) (32 ccs.) were refluxed for 48 hours. On removal of the benzene under reduced pressure, the residue was shaken with water to dissolve the excess maleic anhydride, and the mixture extracted with ether. On evaporation of the ether the residue was boiled with potassium hydroxide (5%) for fifteen minutes and the unchanged hydrocarbon extracted with ether. The aqueous alkaline solution was acidified andthe precipitated acid extracted with ether, and the ether extract washed and

dried. The crude acid, obtained by evaporation of the ether, was refluxed in ethyl acetate solution, containing a few drops of acetic anhydride, for 15 minutes to convert it to the anhydride which crystallised on cooling, (m.pt. 147°C). (Found C-77.47%; H-6.82%; $C_{20}H_{22}O_3$ requiries C-77.4%; H-7.15%). The yield of adduct (1.62 gms.) was 70% of the theoretical.

Oxidation of the above Maleic anhydride adduct with alkaline Potassium Permanganate.

Ref. Abadir, Cook, Gibson, J., 1953, 8

Excess of a solution of potassium permanganate (8%) was added slowly to a solution of the adduct (1.6 gm.) in water (100 ccs.) and sodium hydroxide (1.07 gms.). The mixture was stirred and heated on the steam bath for 16 hours. Methanol (25 ccs.) was added to the cooled mixture which was then heated on the steam bath till the solution was decolourised. The solution was filtered and the filter cake leached out thoroughly with warm water and the resulting suspension filtered. The combined filtrates were evaporated to about 150 cc volume, and acidified. The acid was extracted with ether using a constant-extraction apparatus. On treatment of the crude acid with diazomethane the tetramethyl ester of benzene-1:2:3:5-tetracarboxylic acid was obtained, which after recrystallisation from methanol melted at 109-111°C. A mixed melting point determination with an authentic specimen (m.pt.110°C) showed no depression.

Preparation of 1:2:3:4:5:6- Hexamethylnaphthalene (LXI) by unambiguous synthesis.

Preparation of Acetyl Prehnitene (LI) Ref.

Ref: Baddeley, J, 1949, (Sup.I), 99.

Acetyl chloride (6.28 gms.) and aluminium chloride (anhydrous, 10.14 gms.) in methylene chloride solution (20ccs) were added dropwise to a stirred solution of prehnitene (XV) (10 gms.) in methylene chloride at 0°C. After the addition of the above solution was complete the mixture was stirred at room temperature for 1 hour and then decomposed with ice and hydrochloric acid. The organic material was extracted with ether, washed, dried and the ether and methylene chloride evaporated. The crude product was distilled yielding acetyl prehnitene (9.5 gms.) (b.pt. 135°C/ 5mm; $\mu^{19°C}$ = 1.5437). (Found C-81.69%; H.8.82%; $C_{12}H_{16}O$ requires C-81.77%; H-9.15%). The yield was 84% of the theoretical. The 2:4-dinitrophenylhydrazone derivative of acetyl prehnitene melted at 178-179°C. (Found C-61.1%; H-5.71%; $C_{18}H_{20}O_4N_4$ requires C-60.7%; H-5.71%).

The semicarbazone derivative melted at 210-211°C (Lit 209°C).

Oxidation of Acetyl Prehnitene to Prehnitic Acid (LII).

Ref. Fuson,Tulloch, J.A.C.S., 1934, 56, 1658.

Dioxane (20 ccs.) was added to acetyl prehnitene (0.5 ccs.) and the mixture thoroughly shaken, and sodium hydroxide (5 ccs.,10%) was introduced. Iodine-potassium

iodide* solution was added dropwise to the stirred mixture till a definite dark colour appeared, corresponding to a slight excess of iodine-iodide solution, and which did not disappear on standing for 5 minutes. The mixture was now heated to 60°C for 2 minutes, and the colour which faded on heating was restored by addition of more iodine-iodide solution. A few drops of sodium hydroxide (10%) was added to destroy the excess iodine and the mixture was poured into water. The iodoform was filtered, the filtrate acidified and the precipitated acid isolated in the usual way. Prehnitic acid was obtained which on recrystallisation from cyclohexane melted at 165-169°C (Lit- 165°C; 169°C). (Found C-74.35%; H-8.00%; $C_{11}H_{14}O_2$ requires C-74.13%; H-7.92%).

* The iodine-potassium iodide solution was prepared by adding potassium iodide (20 gms.) and iodine (10 gms.) to distilledwater (80 ccs.) and stirring till solution was complete.

Decarboxylation of Prehnitic Acid.

Prehnitic acid (0.1 gm.) was heated with soda-lime; a liquid hydrocarbon distilled out of the reaction mixture. After further purification by distillation the infra-red absorption spectrum confirmed that this liquid hydrocarbon was prehnitene (XV),(The infra-red spectrum being identical with that of Prehnitene contained in A.P.I. Series).

Preparation of Bromo-acetyl prehnitene (LIII).

Bromine (8.6 gms.) in carbon tetrachloride solution

(30 ccs) was added dropwise to a stirred solution of acetyl prehnitene (9.5 gms.) in carbon tetrachloride (20 ccs.) at room temperature. There was a latent period of about 1 minute after the addition of the first few drops of bromine solution before the commencement of the reaction. It was allowed to stand for ¼ hour and was then washed thoroughly with water, dilute sodium carbonate solution, water and dried. On evaporation of the carbon tetrachloride, bromo-acetyl prehnitene (13 gms.) was obtained by distillation of the residue (b.pt.148-150°C/ 1.5 mm, $\mu^{20°C}$ = 1.5830). It solidified on standing and after recrystallisation from petroleum-ether (40-60°C,b.pt) melted at 54.5°C-55.5°C. (Found C-56.76%; H.5.93%). The yield was 94.5% of the theoretical.

Oxidation of bromo-acetyl prehnitene to Prehnitic Acid(LII)

Ref. Levine, J.A.C.S., 1950, 72, 1642.

Bromo-acetyl prehnitene (0.3 gm.) was oxidised with sodium hypobromite solution to prehnitic acid (m.pt.170°C) (Lit.165°C; 169°C). The melting point was undepressed on admixture with prehnitic acid obtained previously by the oxidation of acetyl prehnitene with sodium hypoiodite solution. This established that the bromine was in the designated position in the acetyl side chain.

Condensation of Bromo-acetyl prehnitene with Methyl-malonic ester.

Dry ethyl methyl malonate (8.9 gms.) was introduced, with cooling, to sodium ethoxide, prepared by dissolving

sodium (1.3 gms.) in ethyl alcohol (dry, 20 ccs.). The stirred mixture was then heated by an easily removable water bath to 60°C and bromo-acetyl prehnitene (13 gms.) was added in small portions in ethyl alcohol solution (13 ccs.). The solution was then heated on the steam bath to remove the alcohol as completely as possible and the residual mixture treated with water and the whole extracted with ether. The ether extract was washed with water and dried. On evaporation of the ether and distillation of the residual liquid the diester (LIV) (9.1 gms.) was obtained (b.pt.172°C/0.3 mm.). The yield was 51% of the theoretical.

Hydrolysis of the diester (LIV).

The diester (9.1 gms.) was added slowly to a fresh very concentrated solution of potassium hydroxide (5.1 gms) in a round bottomed flask, which was heated on the steam bath to initiate the reaction. After the addition the mixture was heated gently for about 2 hours on the steam bath. The alcohol was distilled off whereupon the di-potassium salt crystallised on cooling. Concentrated hydrochloric acid was added till the solution was acid to litmus, the mixture filtered free from precipitated potassium chloride and the filtrate extracted with ether. The ether extract was washed and dried and the ether evaporated giving the crude dicarboxylic acid (LV).

Decarboxylation of the above dicarboxylic acid (LV) to α-methyl-γ- prehnityl-γ-keto-butyric acid (LVI).

The above crude dicarboxylic acid (LV) was heated to 180°C and maintained at this temperature till evolution of carbon dioxide ceased.

On distillation of the crude product, α-methyl-β-prehnityl-γ-keto-butyric acid (4.2 gms.) was obtained, which on recrystallisation from benzene-petroleum/ether (40-60°C b.pt.) melted at 129-130°C. (Found C-72.57%; H-7.95%; $C_{15}H_{20}O_3$ requires C-72.55%; H-8.1%).

The ethyl ester of the above keto acid was prepared by refluxing, the keto acid (0.113 gm.) in ethanol (dry, 1.5 ccs.) containing a few drops of sulphuric acid, on the steam bath for 2 hours. A clear liquid was obtained which could not be induced to crystallise.

Preparation of α-methyl-β-prehnityl butyric acid (LVII)

Ref. Huang-Minlon, J.A.C.S., 1946, 68, 2488.

The above keto-acid (1.5 gms.), sodium hydroxide (0.86 gm.) hydrazine hydrate (0.86 cc, 90%) and diethylene glycol were refluxed for ¾ hour. The condenser was removed and the temperature allowed to rise to approximately 200°C, whereupon the condenser was replaced and refluxing continued for 4 hours. The mixture was cooled, acidified and extracted with ethyl acetate. The ethyl acetate extract was washed, dried and the ethyl acetate evaporated. On distillation of the residue, α-methyl-β-prehnityl butyric acid (1.2 gm.) was obtained which on recrystallisation from petroleum/ether (b.pt.40-60°C) melted at 77-78°C. (Found C-77.11%; H-9.24%; $C_{15}H_{22}O_2$ requires C-76.88%; H-9.46%).

The yield was 86% of the theoretical.

Cyclisation of α-methyl-γ-prehnityl butyric acid (LVII)

Ref. Organic Reactions, Vol.II, 136

Wilds,J.A.C.S., 1942, 64, 1421.

Phosphorus pentachloride (0.835 gm.) was added in portions to a stirred solution of the above butyric acid (0.9 gm.) in dry benzene (4 ccs.) at 0°C. After the addition of all the phosphorus pentachloride the mixture was allowed to stand at room temperature for 1 hour and then heated on the steam bath for five minutes to ensure completeness of reaction.

Stannic chloride (anhydrous, 0.9 cc) in dry benzene (0.9 cc) was added dropwise to the stirred mixture at 0°C. The mixture was stirred for 15 minutes and the complex hydrolysed with ice and hydrochloric acid.

The 2:5:6:7:8-pentamethyl-tetralone (LVIII) (0.56 gm) was isolated as is given on page 67→68, and on recrystallisation from petroleum/ether (b.pt.40-60°C) melted at 57-58°C. (Found C-83.5%; H-9.16%; $C_{15}H_{20}O$ requires C-83.28%; H-9.32%). The yield was 71% of the theoretical.

Preparation of 3:4:5:6:7:8-hexamethyl-1:2-dihydronaphthalene (LX)

Ref.Gilman,Moore,Baine,J.A.C.S.1941, 63,2479.

A solution of the above 2:5:6:7:8-pentamethyl-tetralone-1 (0.56 gm.) in dry ether (5 ccs.) was added to a stirred solution of methyl lithium, prepared from methyl iodide (7 gms.) and lithium (0.7 gm.), in ether in an atmosphere of nitrogen and the mixture refluxed for 6 hours.

Most of the ether was now distilled and benzene (dry) (20 ccs) added and the mixture refluxed for a further 3 hours. The cooled mixture was poured into ice and hydrochloric acid and the product isolated in the usual way. 3:4:5:6:7:8-hexamethyl-1:2-dihydro-naphthalene (0.46 gm.) was obtained (m.pt.89-90°C, on recrystallisation from ethanol). (Found, C-89.5%; H-10.37%; $C_{16}H_{22}$ requires C-89.65%; H-10.35%). The yield was 82% of the theoretical.

Preparation of 1:2:3:4:5:6-Hexamethyl-naphthalene (LXI)

Ref. Abadir, Cook, Gibson, J., 1953, 8.

The above dihydro compound (0.11 gm.) was dehydrogenated by refluxing in 1:2:4-trichlorobenzene solution with palladium-charcoal (30%)(0.6 gm.) in an atmosphere of carbon dioxide. Hydrogen had ceased to be evolved after 17 hours refluxing, 6.5 ccs. had been collected (Theor. amount - 11 ccs.). Benzene was added to the cooled mixture and the whole filtered free from palladium-charcoal. On distillation of the benzene and trichlorobenzene the hydrocarbon, 1:2:3:4:5:6-hexamethylnaphthalene was isolated through its picrate and further purified by distillation owing to its failure to crystallise well from any of the common solvents. (Found C-90.21%; H-9.38%; $C_{16}H_{20}$ requires C-90.5%; H-9.5%). The yield of hydrocarbon was 60 mgs. which is 55% of the theoretical. It crystallised as a fine powder from methanol in an acetone-CO_2bath, m.pt.48-50°C. Its picrate was unstable and

difficult to crystallise (m.pt.155-157°C). Its 2:4:7-trinitrofluorenone complex melted at 186-187°C. Its s-trinitrobenzene complex melted at 186-189°C. (Found C-62.39%; H-5.26%; $C_{16}H_3O_6N_3$ requires C-62.16%; H-5.45%).

Preparation of Propionyl Prehnitene (LXIII)

Ref. Baddeley, J, 1949, (Sup. I), 99.

Propionyl chloride (3.45 gm.) and anhydrous aluminium chloride (5 gms.) in methylene chloride solution (20 ccs) were added dropwise to a stirred solution of prehnitene (5 gms.) in carbon tetrachloride (10 ccs.) at 0°C. After the addition was complete, the mixture was stirred at room temperature for 1 hour and the product isolated as for acetyl prehnitene (p. 73). Propionyl prehnitene was a liquid (b.pt.104/0.2 mm., $\mu^{23°C}$ = 1.5345). (Found C-82.06%; H-9.21%; $C_{13}H_{18}O$ requires C-82.06%; H-9.54%). The yield was 7 gms., which is 90% of the theoretical.

Preparation of α-bromo-propionyl prehnitene (LXIV).

Bromine (5.4 gms) in carbon tetrachloride solution (20 ccs) was added dropwise to a stirred solution of propionyl prehnitene (6.4 gms) in carbon tetrachloride (30 ccs) at room temperature.

The α-bromo-propionyl prehnitene (7.7 gms) was isolated by the method used for the isolation of bromo-acetyl prehnitene (page 75). On crystallisation from benzene-petroleum/ether (b.pt.40-60°C) it melted at 36.5°C-37.5°C. (Found C-57.88% H-6.57%; $C_{13}H_{17}O$ Br. requires C-58.02% H-6.37%). On oxidation of α-bromo-propionyl

prehnitene (0.5 ccs.) by the method used to oxidise acetyl prehnitene (p.73), prehnitic acid was obtained, m.pt.165-169°C. A mixed melting point determination with prehnitic acid (m.pt. 165-169°C) obtained from oxidation of acetyl prehnitene did not show a depression. This confirmed that the bromine was in the propionyl side chain.

Attempted condensation of α-Bromo-propionyl prehnitene and malonic ester.

(a) Dry ethyl malonate (6.2 gms) was introduced, with cooling, to sodium methoxide, prepared by dissolving sodium (0.891 gm.) in methanol (dry, 15 ccs.). The stirred mixture was then heated by an easily removable water bath to 60°C and α-bromo-propionyl prehnitene (10.4 gms) was added in small portions in methanol solution (10 ccs.). The remainder of the experimental details is the same as was given for the condensation of bromo-acetyl prehnitene and methyl malonic ester (p.75). A liquid product (6.4 gms.) was obtained, (b.pt.104-110°C/ 0.1 mm., $\mu^{19°C}$ = 1.5268). (Found, C-73.7%; H-8.7%; the diester (LXV), $C_{20}H_{28}O_5$ requires C-68.94%; H-8.1%). The analysis thus indicated that the expected diester (LXV) had not been obtained. Moreover the diester (LXV), by comparison with the diester (LIV) obtained from condensation of bromo-acetyl prehnitene and methyl malonic ester, would be expected to distil about 135°C/0.1 mm.

On hydrolysis of the above liquid product (2 gms) with aqueous alcoholic caustic potash (6 gms., 20%) an acid was obtained, m.pt. 165-169°C. It was noted that on addition of the alkali solution to the alcoholic solution of the liquid product an orange colour was produced which gradually changed to deep red. A mixed melting point determination of this acid (m.pt.165-169°C) with a previously prepared specimen of prehnitic acid (p.74) showed no depression.

The above liquid product obtained from the condensation also reduced Fehling's solution. On the basis of these results it was assigned the structure (LXVI), α -methoxy-propionyl prehnitene or α-hydroxy-propionyl prehnitene (LXVIa) (p.30a). It was not possible to decide definitely from the analysis which of the two structures was correct. (Found C-73.7%, H-8.7%; α -methoxy-, $C_{14}H_{20}O_2$ requires C-76.32%; H-9.15%; α-hydroxy-$C_{13}H_{18}O_2$ requires C-75.69%, H-8.80%). It would appear from the analysis that the above liquid product must have contained some impurity, causing the analysis to be inaccurate.

It was thought that this peculiar condensation, of sodium methoxide and the α-bromo-propionyl prehnitene, could be overcome by using sodium ethoxide as condensing agent which was used previously for the condensation of bromo-acetyl prehnitene and methyl malonic ester.

(b) Dry ethyl malonate (4.6 gms.) was introduced, with cooling, to sodium ethoxide, prepared by dissolving sodium (0.662 gm.) in ethanol (dry, 15 ccs.). The stirred mixture was heated to 60°C by an easily removable water bath and α-bromo propionyl prehnitene (7.7 gms.) added in small portions in ethyl alcohol solution (10 ccs.). The product was isolatedin the usual manner (p.62). An oil was obtained, (b.pt. 104-110°C/0.1 mm., $\mu^{19°C}$ = 1.5160).

On hydrolysis of this oil (1 gm.) with aqueous alcoholic potassium hydroxide (3 gms., 20%) in the usual manner, an acid was obtained m.pt.165-169°C. This melting point was undepressed on admixture with a sample of prehnitic acid prepared previously (p.74). It was also observed that an orange colour, changing to deep red on standing, was produced immediately the alkali solution was added to the alcoholic solution of the oil.

This oil, obtained from above condensation also reduced Fehling's solution.

On the basis of the above experiments it was assigned the structure (LXVII), α-ethoxy-propionyl prehnitene or α-hydroxy-propionyl prehnitene (38b) (LXVIa). It was not possible to decide definitely from the analysis which was the correct structure. (Found - C-76.19%; H-8.87%; ethoxy-, $C_{15}H_{22}O_2$ requires C-76.88%, H-9.46%; hydroxy- $C_{13}H_{18}O_2$ requires C-75.69%, H-8.80%).

(c) Owing to the failure of the above attempted condensations to yield the desired ester, it was attempted to condense sodiomalonic ester with α-bromo-propionyl prehnitene in benzene.

Malonic ester (dry, 4.6 gms) was added dropwise to a well stirred suspension of powdered sodium (0.662 gm) in benzene (dry, 30 ccs). The mixture was refluxed for 5 hours to ensure completeness of reaction. It was then cooled to 60°C and α-bromo-propionyl prehnitene added in small portions. It did not however appear to react so the whole was refluxed for 3 hours.

Unchanged bromide was recovered quantitatively from the reaction mixture.

The failure of the α-bromo-propionyl prehnitene to react with the malonic ester must be due to steric effects.

Condensation of Prehnitene and methyl succinic anhydride.

Haworth, Bolam, J., 1932, 2248

Dev, Guha, J.Ind.Chem. Soc., 1948, 25, 13.

Baddar, Fahim, Fleifel, J., 1955, 2199

(a) Methyl succinic anhydride (4.3 gms.) and anhydrous aluminium chloride (10 gms.) in nitrobenzene solution (30 ccs) were added dropwise to a stirred solution of prehnitene (5 gms) in nitrobenzene (5 ccs) at 0°C. After the addition was complete the mixture was stirred at room temperature for 1 hour. Ice and hydrochloric acid were added to hydrolyse the complex, the nitrobenzene steam distilled, and the product isolated in the usual way (p.73).

A mixture of acids was obtained. The α-methyl-γ-prehnityl-γ-keto- butyric acid (2 gms) was isolated from the mixture, by crystallisation from methanol and a recrystallisation from benzene-petroleum/ether (40-60°C b.pt). It melted at 130-131°C and the melting point was not depressed on admixture with an authentic specimen (p.76).

No other acid could be isolated pure from the residual mixture. The yield of pure α-methyl-γ-prehnityl-γ-keto-butyric acid was 22% of the theoretical.

(b) Ref. Abadir, Cook, Gibson, J., 1953, 8

Prehnitene (6 gms.) was slowly added to a stirred ice-cold suspension of anhydrous aluminium chloride (20.25 gms) and methyl succinic anhydride (5 gms.) in tetrachloroethane (50 ccs). Stirring at 0°C was continued for 5 hours; the reaction mixturewas treated with ice and hydrochloric acid and the solvent removed in steam.

The residue was extracted with sodium carbonate solution and the filtered solution acidified. The precipitated acid was extracted with ethyl acetate and the ethyl acetate extract washed and dried. On evaporation of the ethyl acetate the crude product (15.8 gms) was obtained. It was recrystallised twice from benzene, once from cyclohexane and again from benzene-petroleum/ether (40-60°C b.pt.) yielding an acid (9.6 gms) m.pt.96.5°C-99°C. (Found C-72.69% H-7.81%; $C_{15}H_{20}O_3$ requires C-72.55%; H-8.1%). The yield of acid was 85% of the theoretical.

The ethyl ester of the above keto-acid was prepared

by refluxing, the keto acid (0.45 gm) in ethanol (dry, 6.0 ccs.) containing a few drops of concentrated sulphuric acid, on the steam bath for 2 hours. The ester was isolated in the usual way and after one crystallisation from ethanol melted at 66-67°C. The melting point was undepressed on admixture with a specimen of Abadir's [14] so-called ethyl ester of δ-keto-α-methyl-δ-prehnityl butyric acid, which has been shown to be the ethyl ester of the β-methyl isomer (p.32,37).

Thus the ethyl ester of the keto-acid obtained in this experiment is ethyl β-methyl-δ-prehnityl-δ-keto-butyrate and therefore the acid isolated in the above condensation is β-methyl-δ-keto-δ-prehnityl butyric acid.

On hydrolysis of the above ethyl ester, the keto-acid obtained melted at 112°C on recrystallisation from benzene-petroleum ether (40-60 b.pt.) A mixed melting point with Abadir's specimen (m.pt.130-131°C) melted from 112°C to 130°C.

Reduction of the above β-methyl-δ-keto-δ-prehnityl butyric acid by the Clemmensen method.

Ref. Martin, J.A.C.S., 1936, 58, 1438.

Clean granulated zinc (3 gms) was shaken with a mixture of water (4.5 ccs), concentrated hydrochloric acid (1.5 ccs), and mercuric chloride (.3 gm). After 5 minutes the aqueous solution was decanted and the reactants added in the following order, water (2.25 ccs), concentrated

hydrochloric acid (5.25 ccs.), toluene (3 ccs), and the above keto-acid (1.5 gms).

The mixture was refluxed briskly for 50 hours, three 1.5-cc portions of concentrated hydrochloric acid were added at intervals of about 6 hours.

The mixture was cooled, diluted with water and the whole extracted with ether. After suitable washing and drying the ether was evaporated and the crude product crystallised from benzene-petroleum/ether (b.pt.40-60°C). The melting point was 106-107°C, undepressed on admixture with Abadir's [14] so-called α-methyl-β-prehnityl butyric acid (m.pt.106-107°C), -this latter acid has been shown to be the β-methyl isomer (p.36).

Preparation of α-methyl-acetoacetic ester.

Ref. Conrad, Limpach, Annalen, 192, 153;
Michael Ber, 1905, 38, 2091, 2095

Dry acetoacetic ester (338 gms.) was introduced, with cooling to sodium ethoxide, prepared by dissolving sodium (59.3 gms) in alcohol (dry 925 ccs). Methyl iodide (380 gms) was added dropwise to the stirred mixture and the whole refluxed for 5 hours; the reaction mixture was now neutral. The alcohol was distilled off, and the residue diluted with water and extracted with ether. The ether extract was washed 5 times with dilute ammonia, and once with water and dried. The ether was evaporated and the product fractionally distilled. A little acetoacetic ester distilled at 175°C/760 mm. and the desired α-methyl

acetoacetic ester (217 gms.) distilled at 181.5°C-182.5°C/760 mm.

Preparation of α-methyl-α-allyl-acetoacetic ester.

The α-methyl-acetoacetic ester (142 gms.) was added dropwise to a stirred suspension of powdered sodium (22.7 gms.) in benzene (dry, 500 ccs) so as to keep the benzene gently refluxing. The sludge was stirred and refluxed for 8 hours to ensure that all the sodium had reacted. The stirred mixture was cooled to 60°C and the allyl bromide (131 gms.) added dropwise. After the addition was complete the mixture was stirred and refluxed for a further 8 hours to ensure completeness of reaction. The mixture was cooled and diluted with water and the benzene layer separated, washed and dried. The benzene was evaporated and the residue fractionally distilled. The α-methyl-α-allyl-acetoacetic ester (108 gms.) distilled at 211-212°C/760 mm. (Lit.209-211°C/760 mm) and did not give a colouration with Ferric Chloride*. The starting material α-methyl-acetoacetic ester gave a blue colouration with Ferric Chloride.

*The ferric chloride solution was a 1% aqueous solution without addition of hydrochloric acid. One drop of ester was added to one drop of ferric chloride solution and the mixture shaken. If there is an enolisable hydrogen in the β-keto-ester a colouration should develop more or less immediately.

The yield of α-methyl-α-allyl-acetoacetic ester

was 60% of the theoretical.

Hydrolysis of above ester to α-methyl-α-allylacetone (LXXIV)

Ref. Rouve, Stoll, Helv. Chim.Acta,1947,30, 2219.

Jacobi, Merling, Annalen, 278, 11.

A filtered solution of barium hydroxide octahydrate (82 gms.) in water (675 ccs) was added in several portions to a solution of the above ester (40 gms.) in ethanol (215 ccs). The mixture was stirred and heated to reflux on an oil bath at 115°C for 20 hours. It was cooled and hydrochloric acid (142 ccs containing 145 gms. per litre) was added, and the whole extracted with ether. The ether extract was washed with water, dilute sodium bicarbonate, water and dried, and the ether evaporated. The residue was distilled and the desired ketone (12.5 gms.) was obtained, (b.pt.143-145°C, Lit-140°C) ($\mu^{21°C}$ = 1.4230). The yield was 50% of the theoretical.

Condensation of Prehnitene (XV) and α-methyl-α-allyl-acetone (LXXIV).

Ref. Colonge,Pichat,Bull.Soc. Chim.,1949,853,855.

The α-methyl-α-allyl-acetone (7.27 gms.) was added dropwise to a stirred mixture of prehnitene (8.2 gms) and powdered anhydrous aluminium chloride (12.8 gms.) at about 35°C. After 4 hours the complex was decomposed with ice and hydrochloric acid and the organic layer extracted with ether. The ether extract was washed and dried (see p. 66) and the ether evaporated. The residue

was distilled and the 3-methyl-5-prehnityl-hexan-2-one ((LXXV) (11.2 gms) was obtained, (b.pt. 159°C/3 mm., $\mu^{19°C}$ = 1.5188). (Found C-82.85%, H-10.33%; $C_{17}H_{26}O$ requires C-82.87%, H-10.64%). The yield was 75% of the theoretical. The semi-carbazone derivative melted at 183-184°C (Found C-71.34%, H-9.45%; $C_{17}H_{26}CH_3ON_3$ requires C-71.3%, H-9.64%).

Oxidation of the above ketone with nitric acid.

The above ketone (0.5 gm.) was heated to 175-180°C in a sealed tube for 6 hours with concentrated nitric acid [64] (3.75 ccs) and water (7.5 ccs). On evaporation of the water the residue was treated with excess etheral diazomethane, the pentamethyl ester of benzene penta-carboxylic acid was obtained which crystallised from methanol, m.pt.144-146°C, undepressed on admixture with an authentic specimen.

This confirmed the structure of the above ketone (LXXV).

Reduction of above ketone (LXXV) to the corresponding alcohol (LXXVI) (see p. 70).

Ref. Org.Reactions, Vol 6, 469

Nystrom,Brown,J.A.C.S.,1947, 69, 1197.

The ketone (2 gms.) was added dropwise in ether (dry) solution to a slurry of lithium aluminium hydride (0.31 gm) in ether (dry) so that the ether gently refluxed. The mixture was refluxed for 2 hours after the addition of the ketone and allowed to stand overnight. Excess lithium aluminium hydride was destroyed by the dropwise addition

of ethyl acetate. The mixture was then poured into ice and hydrochloric acid and the organic material extracted with ether. After suitable washing and drying the ether was evaporated and the residue distilled. The desired alcohol (LXXVI) (1.7 gms) was obtained (b.pt.112°C/0.07 mm., $\mu^{19°C}$ = 1.52.8). (Found C-82.5%, H-11.01%, $C_{17}H_{28}O$ requires C-82.2%, H-11.36%). The yield was 84% of the theoretical.

Attempted ring closure of the above alcohol (LXXVI) with sulphuric acid.

Ref:Colonge, Pichat, Bull.Soc.Chim., 1949,853,855.

The alcohol (LXVI) (1.5 gms) was added dropwise with vigorous stirring to concentrated sulphuric acid (2 gms) at 10°C. The mixture was now stirred at room temperature for 3 hours. Ice water was added and the organic material extracted in the usual way with ether, and the ether extract washed and dried. The ether was evaporated and the residue distilled, an oil (0.8 gm.) was obtained, (b.pt.122-123°C, $\mu^{19°C}$ = 1.5447) (Found C-88.42%, H-9.8%; $C_{17}H_{26}$ requires C-88.68%, H-11.37%).

Oxidation of this oil (0.2 gm) with nitric acid in the usual way (p.67) gave an acid product. This latter on treatment with ethereal diazo-methane solution gave an uncrystallisable gum. This confirmed that the attempted cyclisation of the alcohol (LXXVI) with sulphuric acid had given a mixture presumably of ring closed and open chain compounds.

All attempts to dehydrogenate the oil from the above cyclisation failed. The compound was returned unchanged when heating with selenium at 310° C in a sealed tube, and at 360°C charring occurred, but no aromatic hydrocarbon was isolated from any of the experiments.

This suggests that the oil contains five-membered ring-closed compounds.

Cyclisation of 3-methyl-5-prehnityl-hexan-2-one (LXXV) with polyphosphoric acid.

Ref. Jarrett, Loudon, J., 1955, 4052,
KOO, Chem and Ind., 1955, April, 445;
J.A.C.S., 1953, 75, 1891.

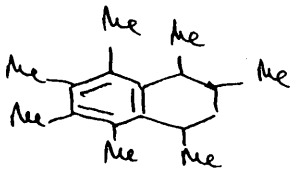
The polyphosphoric acid was made by dissolving phosphorus pentoxide (125 gms) in concentrated phosphoric acid (50 ccs). The syrupy mixture was stirred occasionally and heated on the steam bath for 2 hours.

The ketone (LXXV) (11.2 gms) was added dropwise to the above syrupy polyphosphoric acid at room temperature with stirring. The mixture was then stirred occasionally and heated in an oil bath at 125-130°C for 5 hours. The mixture was cooled and decomposed with ice and the organic material extracted with ether, and the ether extract washed with water and dried. The ether was evaporated and the residue distilled. An oil (4.2 gms) was obtained, b.pt. 100-103°C/0.07 m, and a solid (3.2 gms) b.pt.125-130°C/ 0.07

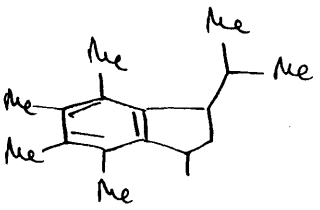
The solid on recrystallisation from benzene-petroleum/ether (b.pt.40-60°C) melted at 143-144°C and exhibited a typical naphthalene spectrum. It analysed correctly for a heptamethylnaphthalene and was thus concluded to be 1:2:3:4:5:6:8-heptamethylnaphthalene. (Found C-90.38%, H-9.51%, $C_{17}H_{22}$ requires C-90.2%, H-9.8%). Its picrate had m.pt. 194-195°C (Found C-60.36%, H-5.68%, $C_{17}H_{22}\cdot C_6H_3O_7N_3$ requires C-60.6%, H-5.54%), its s-trinitrobenzene complex, m.pt. 217-218°C (Found C-63.13%, H-5.59%, $C_{17}H_{22}\cdot C_6H_3O_6N_3$ requires C-62.87%, H-5.74%), and its 2:4:7-trinitrofluorenone complex, m.pt. 205.5°C-206.5°C (Found C-66.43%, H-4.73%, $C_{17}H_{22}\cdot C_{13}H_5O_7N_3$ requires C-66.55%, H-5.03%).

The yield of 1:2:3:4:5:6:8-heptamethylnaphthalene was 30% of the theoretical.

The oil from the above cyclisation with polyphosphoric acid was re-distilled, (b.pt.140°C/0.8 mm, $\mu^{22°C} = 1.5441$). (Found C-88.7%, H-11.00%, $C_{17}H_{26}$ requires C-88.6%, H-11.38%; $C_{17}H_{24}$ requires C-89.41%, H-10.60%). The oil decolorised, bromine water and potassium permanganate solution, and a colouration was produced with tetranitromethane solution. This confirms the presence of an olefinic double-bond. However, the analysis corresponds more closely with the tetralin "Z" or the indane "Y" shown below than with the corresponding dihydro-naphthalene or indene (see p.42a(.



Tetralin "Z"



Indane "Y"

The oil (0.3 gm) was oxidised with nitric acid in the usual way (p. 67). Benzene-hexacarboxylic acid was obtained, m.pt. 185-187°C (Lit. 187°C). This established that the oil contained only ring-closed material.

It was attempted to dehydrogenate the oil with palladium-charcoal (30%) (p. 69)., sulphur and selenium, but no success was entertained. It was heated with selenium at 310°C in a sealed tube for 100 hours, but was recovered unchanged. On heating with selenium at 360°C for 70 hours in a sealed tube charring occurred.

The failure to dehydrogenate the oil suggests that it does not contain any of above tetralin "Z".

It is suggested that the oil is a mixture of the indane "Y" and corresponding indene (p. 42a).

The above cyclisation with polyphosphoric acid was attempted firstly at room temperature and then at 100°C but in both cases the ketone (LXXV) was returned unchanged.

Attempted Chloromethylation of 1:2:3:4:5:6:8-Heptamethylnaphthalene (LXXX) (p. 47a).

An attempt was made to chloromethylate the hydrocarbon (LXXX) by the method described by Abadir, Cook and Gibson [14]. Hydrogen chloride was passed into a

suspension of para-formaldehyde (0.1 gm) in acetic acid (3 cc) until dissolution was complete. The heptamethylnaphthalene was then added and the suspension shaken for 24 hours. More hydrogen chloride was led in for ten minutes and shaking continued for a further 24 hours. Ice was added and the product extracted with ether. The ether extract was washed with sodium bicarbonate solution and dried and the ether distilled off. The heptamethylnaphthalene was recovered quantitatively.

Another attempt was made with the same quantities as above, but this time hydrogen chloride was passed through the reaction mixture for ½ hour after 4 hours and again for the same time after 24 hours. The mixture was shaken for a further 24 hours but once again the starting material was recovered unchanged along with a little of a dark oily residue.

In another attempt with the same quantities as above, the reaction mixture was shaken at room temperature for 13 hours. It was then heated to 70-75°C and maintained at this temperature for 5 hours. On working up in the usual manner, a dark tarry gum was obtained. A very little semi-solid was isolated from this after charcoaling twice, which formed an s-trinitrobenzene complex m.pt.207-215°C. This was concluded to be impure s-T.N.B. of starting material. (s-T.N.B. of heptamethylnaphthalene -m.p.t. 217-218°C).

The experiment was again repeated as above at 45-50°C

but a gummy oil was obtained which yielded no aromatic hydrocarbon on shaking it in cyclohexane solution with palladium charcoal in an atmosphere of hydrogen.

A final attempt was made with the hydrocarbon (0.1 gm), puraformaldehyde (0.39 gm) and acetic acid (1.5 cc). Hydrogen chloride was passed for 3 hours duration at intervals of 16 hours for a period of 100 hours, at room temperature. Some starting material was recovered unchanged along with a little of a dark oily residue which yielded no aromatic hydrocarbon on attempted reduction as described in preceding attempt.

Attempted Acetylation of 1:2:3:4:5:6:8-Heptamethylnaphthalene (LXXV)

Ref: Baddeley, J., 1949, (Sup.I), 99.

Acetyl chloride (0.035 gm) and aluminium chloride (anhydrous, 0.06 gm.) in ethylene chloride solution were added dropwise to a stirred solution of the heptamethylnaphthalene (0.1 gm) in ethylene chloride at 0°C.

After the addition of the above solution was complete the mixture was stirred at room temperature for ½ hour and then decomposed with ice and hydrochloric acid. On working up in the usual way, the heptamethylnaphthalene was recovered unchanged.

The experiment was repeated as above but the temperature during the addition of the acetyl chloride - aluminium chloride solution to the hydrocarbon was 35-40°C. The mixture was stirred at this temperature for 6 hours. The

heptamethylnaphthalene was again recovered unchanged.

The experiment was again repeated with the reactants in the following ratios, 1 mol Hydrocarbon: 2 mols Acetyl Chloride: 2 mols Aluminium Chloride. The temperature was maintained at 45-50°C for 8 hours. A gummy residue was obtained from which a little of the heptamethylnaphthalene was recovered but none of the desired acetyl compound was obtained.

Preparation of 3-Methyl-2:4-pentanedione (XCVII)

Ref. Claisen, vgl Perkin J., 1892, 61, 848.

Conrad, Limpach, Annalen, 1878, 192, 153

Acetyl acetone (100 gms.) was added dropwise over 1 hour to sodium methoxide solution, prepared from sodium (23 gms.) in methanol (300 ccs) at 10-15°C. The mixture was stirred until room temperature was attained. It was again cooled to 10-15°C and methyl iodide (142 gms.) was added dropwise over 1 hour. The mixture was stirred at room temperature for several hours and allowed to stand overnight. It was refluxed on the steam bath for 4 hours and then most of the methanol was distilled off. Water was added and surprisingly methylacetylacetone was miscible and had to be extracted by constant-ether-extraction. It would have been better to have added ether and filtered the precipitated sodium iodide, and evaporated the ether to obtain the crude product. The crude product was fractionally distilled, a little unreacted acetylacetone was obtained, b.pt.35-40oC/25 mm, and the desired product,

methylacetylacetone (XCVII) (60 gms) at 60-65°C/25 mm. The yield was 60% of the theoretical; some of the product was probably not recovered in the constant-ether-extraction.

Acetyl prehnitene was prepared by the method given on page 73.

Reduction of acetyl prehnitene to the corresponding alcohol (XCI).

The acetyl prehnitene (18.5 gms.) was added dropwise to a slurry of lithium aluminium hydride (4 gms.) in dry ether, so that the ether gently refluxed. The mixture was then refluxed on the steam bath for 3 hours. Excess lithium aluminium hydride was destroyed by the dropwise addition of ethyl acetate and the mixture was poured into ice and hydrochloric acid and the ether layer separated. On evaporation of the ether the crude product was distilled, and the desired alcohol (14 gms) obtained, b.pt.121°C/1 mm. It was recrystallised from petroleum/ether (40-60°C b.pt.) and melted at 53-54°C. (Found C-81.19%, H-10.02%, $C_{12}H_{18}O$ requires C-80.85%, H-10.18%). The yield was 75% of the theoretical.

Preparation of α-bromo-ethyl prehnitene (XCII).

Ref. Forge etal, J.A.C.S., 1948, 70, 3707.

Phosphorus tribromide (3.15 gms) in dry ether solution (250 ccs) was added dropwise to a stirred solution of the above alcohol (5 gms) and pyridine (0.5 gm) in dry ether (250 ccs) at -25°C to -30°C; this temperature

was maintained by means of an acetone-solid carbon dioxide bath. A white cloudy substance precipitated on the addition of the phosphorus tribromide. The mixture was stirred at -25°C, after the addition of the phosphorus tribromide, for ½ hour. It was left overnight to regain room temperature gradually. Most of the cloudy precipitate went into solution but there was a little of a white liquid clinging to the sides of the reaction vessel. The reaction mixture was poured into ice water and the ether layer separated. It was washed thoroughly with water, dilute sodium bicarbonate and another twice with water, dried and the ether evaporated. The desired bromide (XCII) (4.8 gms) was obtained by distillation, (b.pt. 90°C-air bath- approx., 0.05 mm). It was recrystallised from petroleum/ether (40-60°C b.pt.) using an acetone/CO_2 bath, m.pt. 48-48.5°C. (Found C-60.08%, H-7.17%; $C_{12}H_{17}Br$ requires C-59.79%, H-7.11%). The yield was 71% of the theoretical.

In a similar experiment to that described above, in which 10.6 gms. of alcohol (XCI) were brominated, the crude bromide was distilled at 120°C/0.15 mm., but only 1.8 gms. was obtained. Hydrogen bromide was evolved at this temperature and a high boiling product (6.8 gms.) distilled at about 200° C/0.15 mm. This product crystallised from benzene, m.pt.169-170°C. (Found C-90.2%, H-9.51%).

The analysis confirmed this was a hydrocarbon and presumably was formed by the self condensation of the

bromide during the distillation. This hydrocarbon exhibited ultra-violet absorption spectrum (page 50a) similar to that of 9:10-dihydro-anthracene, and it was thought that it might be decamethyl-9:10 dihydro-anthracene. This latter compound, $C_{24}H_{32}$, requires C-89.94%, H.10.06%, and could be formed by the condensation of two molecules of bromide (XCII) with the elimination of two molecules of hydrogen bromide.

It was attempted to dehydrogenate it to an anthracene but without success. It was heated with selenium at 340°C in a sealed tube for 50 hours but the product was charred; with selenium at 310°C it was recovered unchanged.

Attempted preparation of the alcohol (C, x=0) (p.49a).

The above bromide (XCII) (0.49 gm) was added to an ether (dry) suspension of magnesium (0.05 gm, activated by subliming iodine through it previously). The mixture was refluxed for several hours till most of the magnesium had reacted. It was cooled to room temperature and added dropwise to a solution of methyl acetylacetone (0.25 gm.) in ether at -80°C; this temperature was maintained by means of an acetone/CO_2 bath.

The reaction took place immediately and a complex precipitated. After the addition it was stirred at -80°C for ¼ hour and then added dropwise to a well stirred suspension of ice and ammonium chloride at -20-to-25°C. The mixture was allowed to regain room temperature and

the ether layer separated. On working up as usual none of the desired product (C, x=O) was obtained. A hydrocarbon, 2-4-diprehnityl-3-methyl-pent-2-ene (XCVI), (0.25 gm), was isolated which crystallised from benzene, m.pt. 220-223°C. (Found C-89.97%, H-10.17%; $C_{26}H_{36}$ requires C-89.59%, H-10.41%).

Preparation of mono-hemithio-ketal of methylacetylacetone (XCVIII)

Ref. Jaeger, Smith, J., 1955, 160.

A mixture of methylacetylacetone (XCVII) (21 gms), 2-mercaptoethanol (16 gms), toluene-para-sulphonic acid (103 gms) and benzene (dry, 420ccs) was refluxed in an inert atmosphere for 20 hours till no more water separated in the Dean Stark head. The mixture was cooled and the benzene layer separated, washed with water, sodium bicarbonate solution, water and dried. On evaporation of the benzene, the residue was distilled. The desired hemithioketal (XCVIII) (17.3 gms) was obtained (b.pt.56°C/0.1 mm, $\mu^{23°C}$ = 1.4860). (Found C-55.54%, H-8.42%, $C_8H_{14}O_2S$ requires C-55.2%, H-8.10%). The yield was 60% of the theoretical.

Attempted preparation of the alcohol (C , x=CH_2-S / CH_2-O) (p.199)

Another attempt was made to prepare the desired alcohol by a similar experiment to that described on page , but instead of the methylacetylacetone the above prepared mono-hemithio-ketal (XCVIII) was used.

Surprisingly however the same hydrocarbon, 2:4-diprehnityl-3-methyl-pent-2-ene (XCVI), was obtained and

none of the desired product.

Preparation of the monoethylene-ketal of methylacetylacetone (XCIX)

Ref. Cronyn, Goodrich, J.A.C.S., 1952, 74,3331.

A mixture of methylacetylacetone (32 gms) and ethylene glycol (18.5 gms) para-toluenesulphonic acid (100 mgs) and benzene (dry, 400 ccs) was refluxed for 20 hours till no more water separated in the Dean Stark head. The crude product was isolated similar to the hemi-thio-ketal (p.101) The monoethylene-ketal(XCIX) (25.6 gms.) was obtained on distillation of the crude product, (b.pt. 60°C/0.1 mm, $\mu^{20°C}$ = 1.4411) (Found C-60.3%,H-9.02%, $C_8H_{14}O_3$ requires C-60.74%, H-8.92%). The yield was 58% of the theoretical.

Attempted preparation of the alcohol (C , x=$\begin{matrix}CH_2-O\\CH_2-O\end{matrix}$>) (p.49a).

Yet another attempt was made to prepare the desired alcohol (C) by a similar experiment to that described on page 100, but instead of methylacetylacetone the monethylene-ketal, prepared above, was used.

Another experiment was carried out with the above monoethylene ketal and the organo-lithium compound (XCIV) instead of the corresponding magnesium compound (XCIII). No success was entertained, the hydrocarbon (XCIV) being obtained once more.

Attempted preparation of the olefin (CI) (p.49a).(x= $\begin{matrix}CH_2-O\\CH_2-O\end{matrix}$>)

REF. Wittig etal, Annalen, 1956, 598, 85, 93.

Bohlmann etal, Ber, 1956, 89, 1276

Triphenyl phosphine (2.6 gms) was added to a solution of the Bromide (XCIII) (3.92 gms) in ether (3 ccs) and the

mixture shaken till the triphenyl phosphine dissolved. It was allowed to stand at room temperature for 24 hours; during this time a white semi-solid salt precipitated.

An ether solution of butyl lithium (0.83 gm) was prepared from butyl bromide (2.24 gms) and lithium (0.224 gm) in ether in the usual way [35].

The butyl lithium in ether solution was added dropwise to the suspension of the above salt in ether. No colour was generated. The mixture was heated to reflux but still no colour was generated. It was cooled and added to a solution of the above monoethylene ketal (XCIX) in ether and the whole refluxed for 6 hours. On working up in the same way as for a Grignard reaction, a small amount of a liquid was obtained which was not the desired compound. (Found C-86.18%, H-10.14%, $C_{20}H_{30}O_2$ requires C-79.42%, H-10.0%). The analysis did not correspond to any other probable structure.

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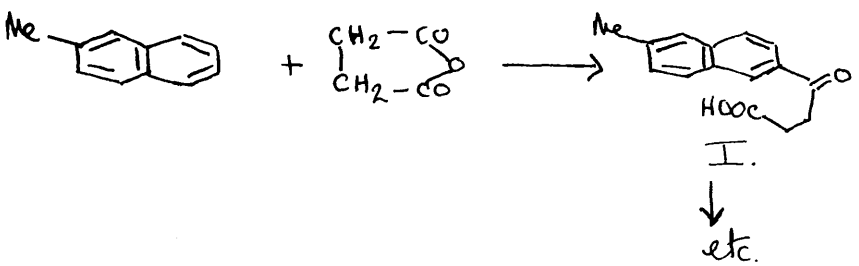
PART II.

SYNTHESIS OF SOME POLYMETHYLPHENANTHRENES.

INTRODUCTION.

It was thought that it would be of interest to prepare some polymethylphenanthrenes, from 2:3:6-trimethylnaphthalene which was available, since relatively few polymethylphenanthrenes[1] were known. Haworth etal [2] [3] have prepared several polymethylphenanthrenes from 2-methylnaphthalene and 2:3-dimethylnaphthalene by routes which involved initially the condensation of succinic anhydride, or a substituted succinic anhydride with the naphthalene derivative.



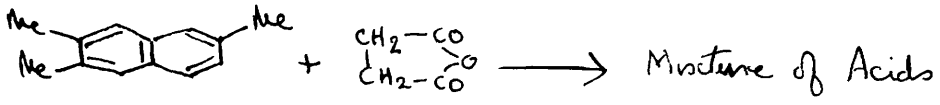
They found that, on condensing 2-methylnaphthalene with succinic anhydride, the acid isolated most easily and in the highest yield was β-(6 methyl-2-naphthoyl)-propionic acid (I). Likewise 2:3-dimethylnaphthalene on condensation with succinic anhydride yielded the corresponding β- (6:7-dimethyl-2-naphthoyl)-propionic acid in good yield.

β-methyl derivatives of naphthalene thus apparently activate the diagonally opposite β-position in the

naphthalene nucleus. It was thought that 2:3:6-trimethylnaphthalene on condensation with succinic anhydride would yield mostly β-(3:6:7-trimethyl-2-naphthoyl)- propionic acid. Thereafter this latter acid could be converted to polymethylphenanthrenes by standard methods.

DISCUSSION.

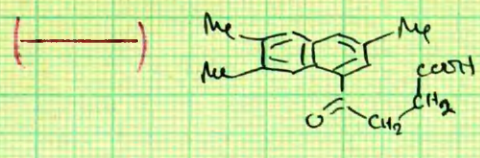
The 2:3:6-trimethylnaphthalene on condensation with succinic anhydride [2] in the presence of aluminium chloride in nitrobenzene yielded a mixture of acids. An α-naphthoyl propionic acid was isolated in 8% yield and on conversion of the residual mixture of acids to their methyl esters a β-naphthoyl propionic ester was isolated in about the same yield. No other acid could be isolated pure from the bulk of the residual mixture.



The observations of Haworth etal[2] do not appear to hold in this case, since an α-naphthoyl propionic acid was most easily isolated and not a β-naphthoyl isomer. Almost equal proportions of the two isomers, α- and β-, were obtained whereas Haworth etal [2] found that the β-isomer usually predominated.

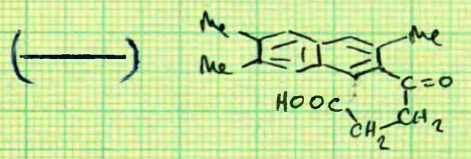
The α-naphthoyl and β-naphthoyl acids were distinguished by means of their ultra-violet absorption spectra. Dannenberg and Dannenberg-von Dresler[4] found that α-and β-acyl naphthalenes have distinct ultra-violet absorption spectra.

λ. IIIa.



λmax mμ	log ε
220 mμ	5.0
217 mμ	3.96.

5.6
5.0
4.0
log ε
3.0
2.0
1.0



λ max mμ	log ε
215 (smale)	4.5
255	4.75
240	4.04
340	3.172.

Both spectra carried out in Rect. spirits Solution.

200 220 240 260 280 300 320 340 360 380

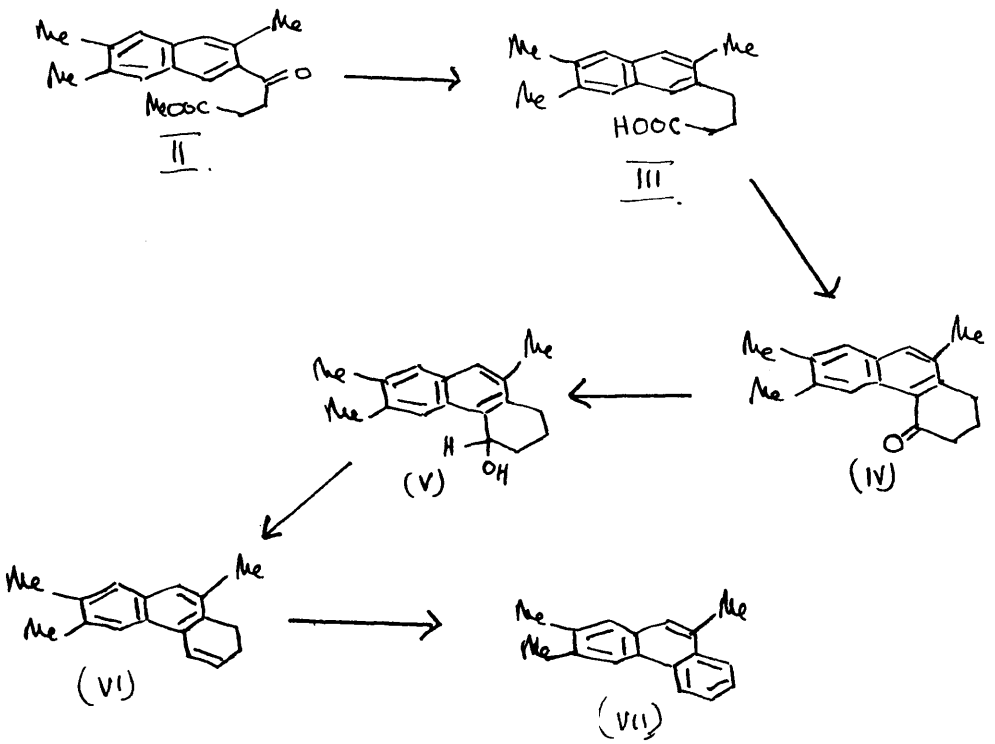
λ mμ →

In α-acyl naphthalenes there is a decided bathochromic shift of the para band while the position of the α-band in relation to the para band does not change so much. The intensity of the α-band is increased by substitution of a strong chromophoric group in the α-position of the naphthalene nucleus, so that there is a merging of the α-band and the p.-band (i.e.para band) and a corresponding loss of fine structure. Thus in α-acylnaphthalenes there are only two bands, one being very broad due to the merging of the α-and p-bands.

In β-acyl naphthalenes there is a bathocromic shift of the α-band, while the p-band both in regard to position (other than pure substitution effects) and also proportionally in regard to intensity changes little. Thus in β-acyl naphthalenes there is no loss of fine structure andthe α-, β-, p-bands are all well defined and distinct from each other.

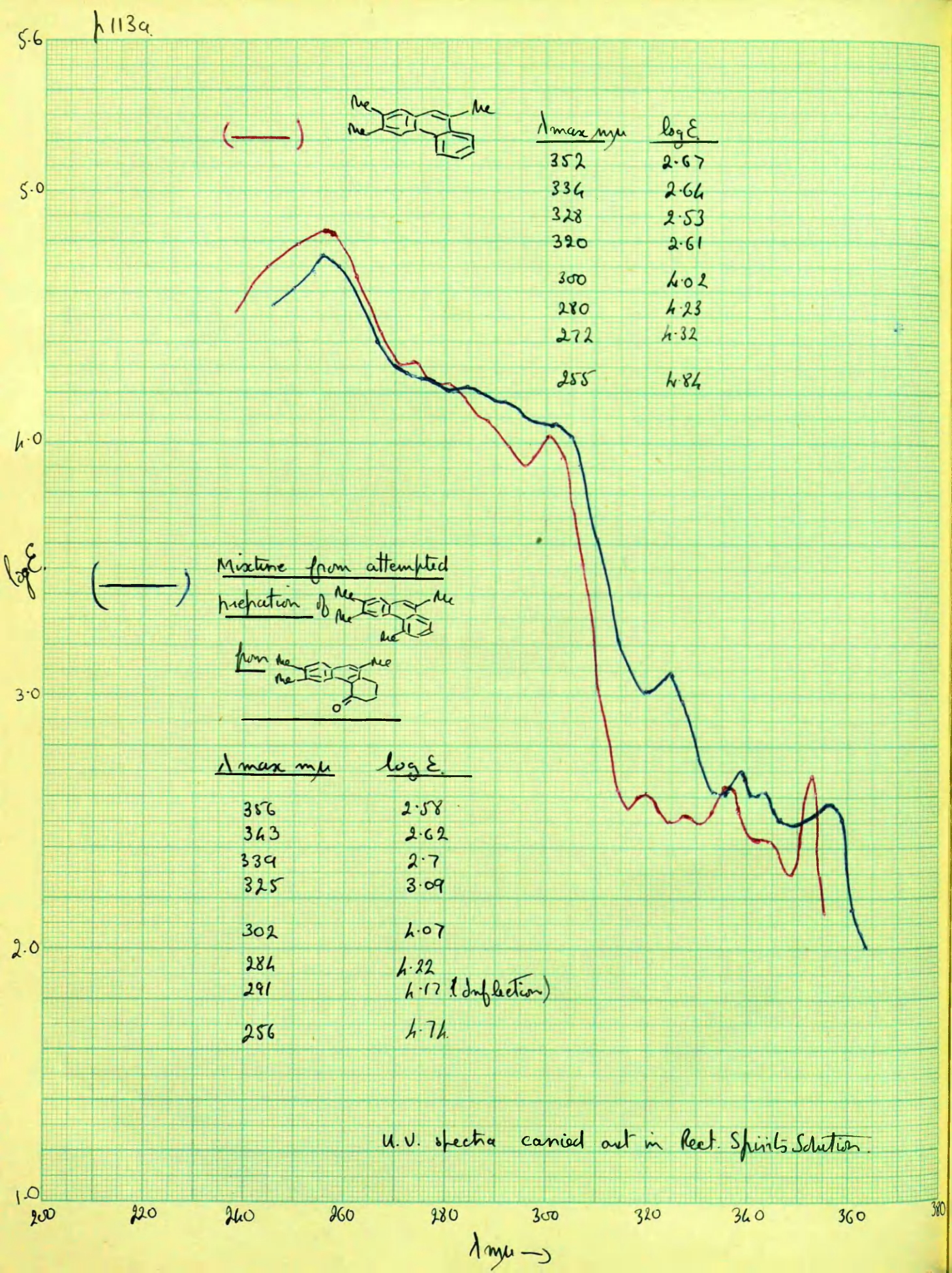
The ultra-violet absorption spectra of the two acids (shown opposite) isolated here agreee with these findings of Dannenberg etal.

The β-naphthoyl isomer isolated must be β-(3:6:7-trimethyl-2-naphthoyl)-propionic acid since there is only one vacant β-position in the nucleus of 2:3:6-trimethyl-naphthalene. There are however four vacant α-positions in this latter compound so that it is not possible as yet to state definitely which one it is.



The 2-naphthoyl propionic ester (II) was reduced by a Huang-Minlon [5] reaction to γ-(3:6:7-trimethyl-2-naphthoyl)-butyric acid (III). Cyclisation of the butyric acid (III) was effected by treating the acid chloride with stannic chloride in benzene solution; the 6:7:10-trimethyl-4-keto-1:2:3:4-tetrahydro-phenanthrene (IV) was obtained. The latter was reduced smoothly with lithium aluminium hydride to the corresponding alcohol (V) which was dehydrated by heating with fused potassium bisulphate yielding the dihydro-phenanthrene (VI). On dehydrogenation of this latter compound (VI) with palladium-charcoal at 240°C, 2:3:9-trimethylphenanthrene was obtained and characterised.

h113a



(——)

λmax mμ	log ε
352	2·67
334	2·64
328	2·53
320	2·61
300	4·02
280	4·23
272	4·32
255	4·84

(——) Mixture from attempted preparation of

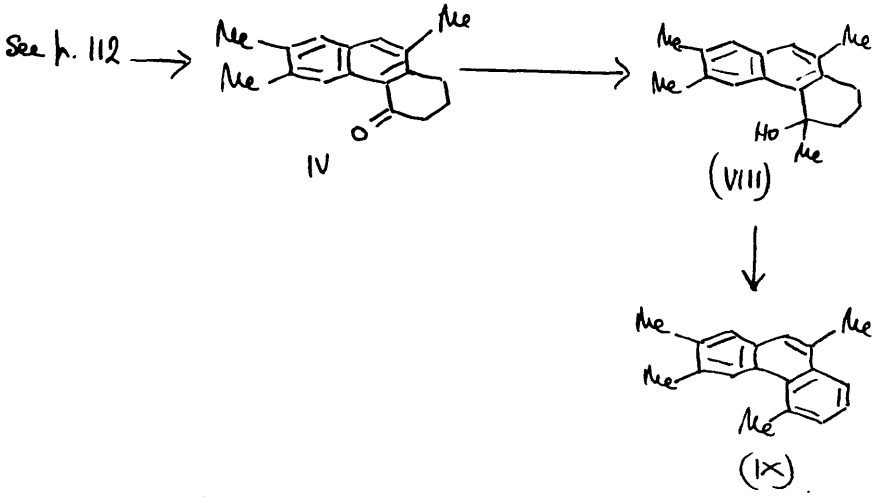
from

λmax mμ	log ε
356	2·58
343	2·62
339	2·7
325	3·09
302	4·07
284	4·22
291	4·17 (Inflection)
256	4·74

U.V. spectra carried out in Rect. Spirits Solution.

The ultra-violet absorption spectrum is shown opposite.

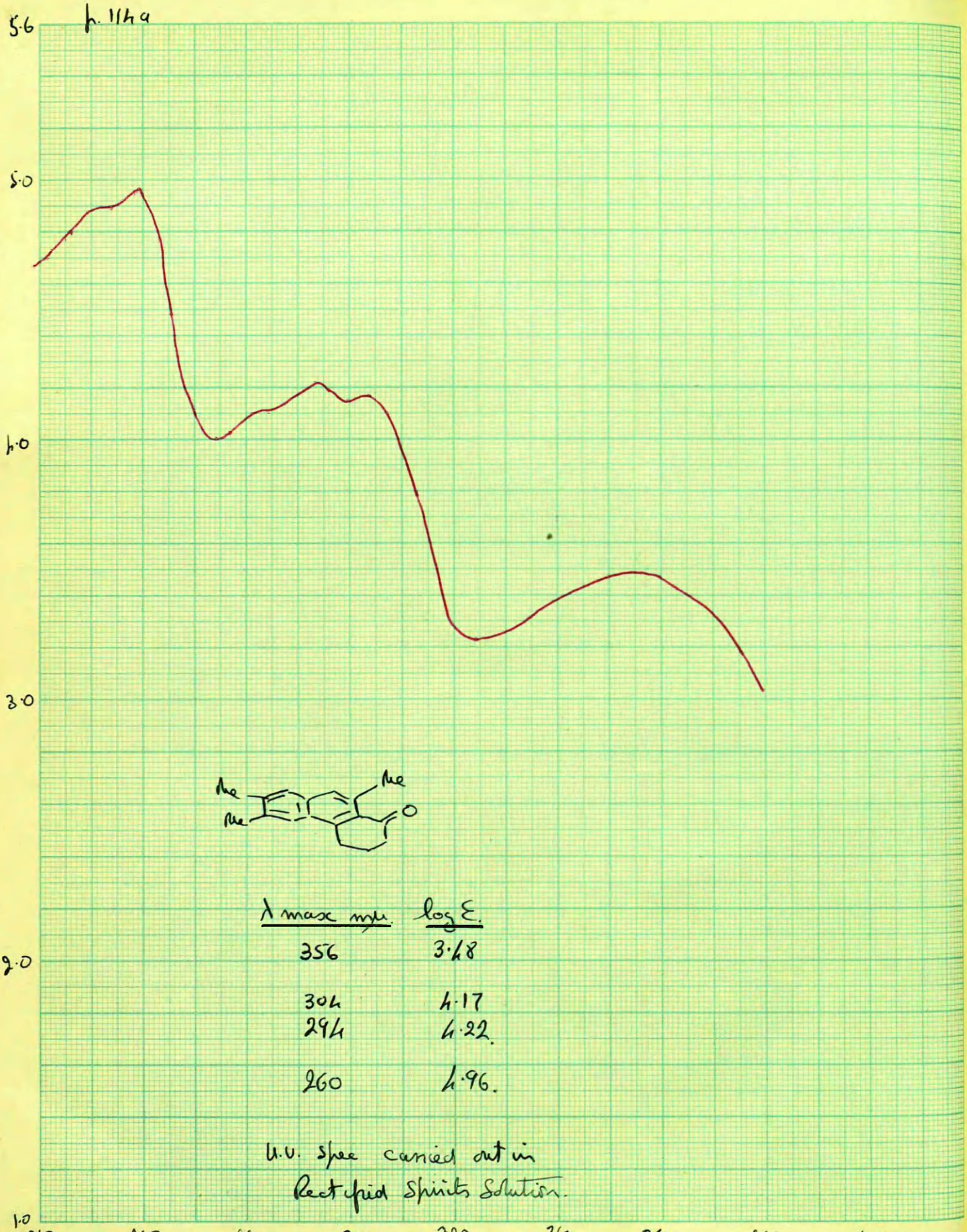
In another series of experiments the tetrahydro-keto-phenanthrene (IV) was treated with methyl magnesium iodide in the usual manner. The crude alcohol (VIII) which was obtained was dehydrated and dehydrogenated simultaneously by heating with palladium-charcoal [65] at 240-250°C in the usual manner, in an atmosphere of carbon dioxide.



A mixture was obtained from which no pure product could be isolated. The ultra-violet absorption spectra (shown opposite) appeared to be of the phenanthrene type although there appeared to be an extreme loss of fine structure in the region 265 mμ to 305 mμ .

It is not uncommon to obtain mixtures from a series of experiments similar to that just described which involve the introduction of an alkyl group into the sterically hindered 4- or 5- positions [7],[8] of the phenanthrene nucleus. It is probable that migration or

h. 1149

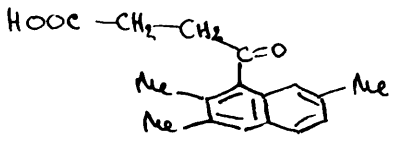


λ max mμ.	log ε.
356	3·48
304	4·17
294	4·22.
260	4·96.

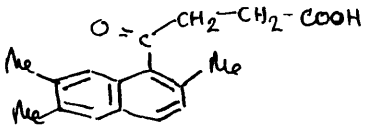
U.V. spec carried out in Rectified Spirits Solution.

loss of a methyl group occurs during dehydrogenation.

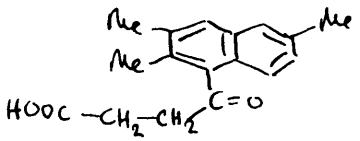
The α-naphthoyl propionic acid, isolated from the mixture of acids obtained from the condensation of 2:3:6-trimethylnaphthalene and succinic anhydride, must be one of the four compounds (X), (XI), (XII) and (XIII) shown below.



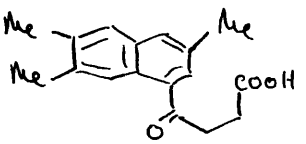
(X)



(XI)



(XII)

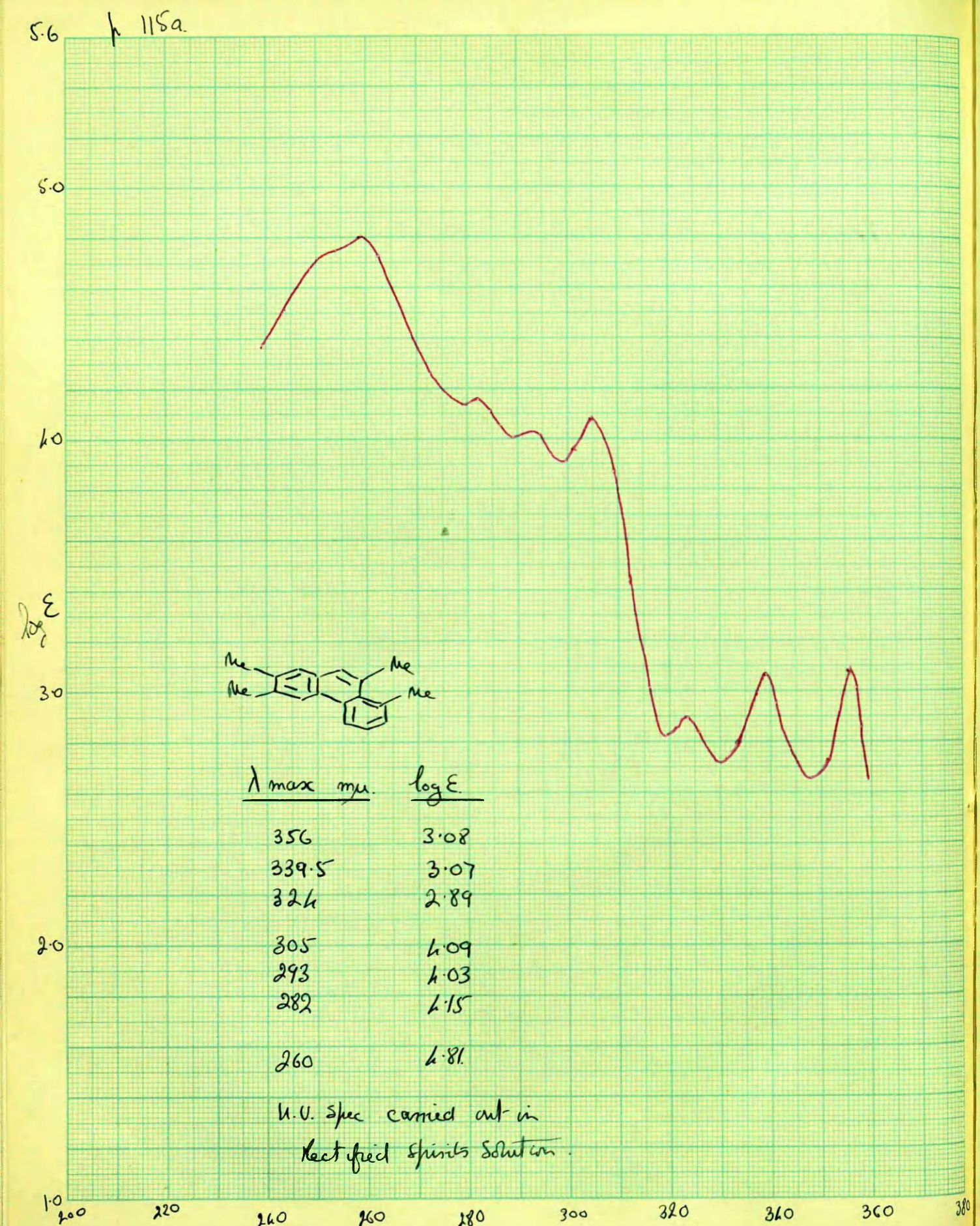


(XIII)

Only one of these acids, namely β-(3:6:7-trimethyl-1-naphthoyl)-propionic acid (XIII) can cyclise into a β-position to yield, after the usual sequence of reactions, a phenanthrene derivative.

The α-naphthoyl acid isolated in this synthesis was reduced by the Huang-Minlon [5] reactions to the corresponding butyric acid. Cyclisation of the butyric acid was effected by treating the acid chloride with stannic chloride [6] in benzene solution, yielding a cyclic ketone. The ultra-violet absorption spectrum (shown opposite) confirmed that the latter was a β-acyl-naphthalene; this

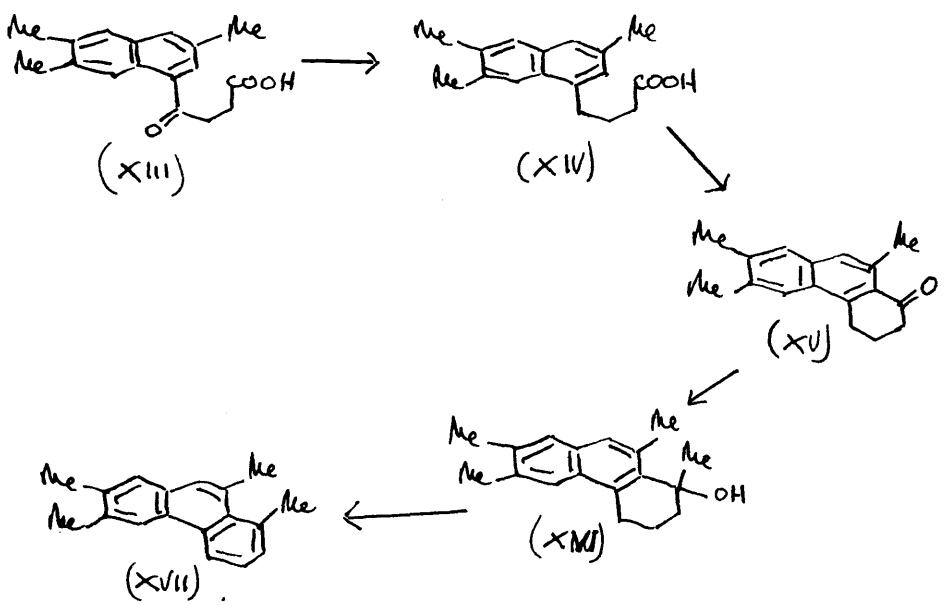
h 115a.



λ max mμ.	log ε.
356	3·08
339·5	3·07
324	2·89
305	4·09
293	4·03
282	4·15
260	4·81

U.V. spec carried out in Rectified Spirits Solution.

established that the acid had cyclised into a β-position of the naphthalene nucleus. Since there is only one vacant position in 2:3:6-trimethylnaphthalene this confirms that the structure of the cyclic ketone is 6:7:10-trimethyl-1-keto-1:2:3:4-tetrahydrophenanthrene (XV), and of the preceding butyric acid is γ-(3:6:7-trimethyl-1-naphthyl-) butyric acid (XIV), and of the preceding α-naphthoyl acid is β-(3:6:7-trimethyl-1-naphthoyl-) propionic acid (XIII).

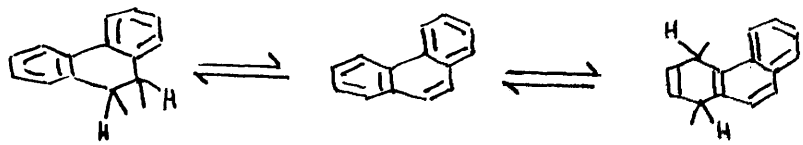


The ketone (XV) on treatment with methyl magnesium iodide in the usual manner afforded the corresponding tertiary alcohol (XVI) which on simultaneous dehydration and dehydrogenation with palladium-charcoal at 280°C yielded the desired 2:3:8:9-tetramethylphenanthrene. The ultra-violet absorption spectrum is shown opposite.

Askew [9] in his studies on the ultra-violet spectram of alkyl phenanthrenes concludes that as the number of alkyl groups increases there is a general shift of the maxima towards the longer wave lengths, and the distinctness of maxima and minima tend to become less marked, many of the maxima in simpler compounds tending to merge into inflexions. This is borne out by the two phenanthrenes prepared here, (XVII) and (VII), in which, in the wave-length region 270-305 mμ , there is a general loss of fine structure. In compounds with substituents in the 9- or 10- position the loss of fine structure in the ultra-violet tends to be greater in this wave-length region 270-305 mμ [10].

It is also interesting to note that in 2:3:8:9-tetramethyl phenanthrene there are only 3 bands in the wave-length region 356-320 mμ , whereas in simpler compounds there are 5 bands. In the ultra-violet absorption spectrum of 2:3:9-trimethyl phenanthrene (given previously) the 2nd, and 4th, bands in this region 356-320 mμ are tending to merge into inflections.

The greatest variation in the heights of the maxima takes place in the wave length region 300-356 mμ . The bands in this region according to Clar [11] are due to the "diyl" states of the molecule and the 1st, 3rd, and 5th, bands depend on the 9-10 diyl state, while the 2nd, and 4th, bands are related to the 1:4-diyl state.



"9:10 diyl state" Phenanthrene "1:4-diyl state"

Askew [9] has shown from the study of various compounds that when there is a substituent in the 9- or 10-position the intensity is usually increased for the 1st, 3rd., and 5th, maxima. In the 2:3:8:9-tetramethyl phenanthrene these latter bands have increased in intensity, i.e. the bands at 356 mμ , 339.5 mμ , and 324 mμ . This increase does not however appear to depend entirely on the substituent in the 9- position since in this case the introduction of the methyl group in position 8 has increased the intensity compared with 2:3:9-trimethyl-phenanthrene (see U.V. Spectrum previous).

Summary.

The 2:3:9-trimethylphenanthrene and the 2:3:8:9-tetramethylphenanthrene have been prepared and characterised for the first time.

An attempt was made to prepare 2:3:5:9-tetramethyl-phenanthrene but an inseparable mixture was obtained.

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PART II

EXPERIMENTAL

Condensation of 2:3:6- Trimethylnaphthalene with Succinic Anhydride.

Ref. Haworth etal, J., 1932, 1784,2248, J.,1934,454.

The 2:3:6-Trimethylnaphthalene (10 gms.), succinic anhydride (5.9 gms.) were added to a solution of aluminium chloride (15.3 gms.) in nitrobenzene (60 ccs) at 0°C. The mixture was stirred at room temperature for 3 hours, decomposed with ice and hydrochloric acid and the nitrobenzene steam distilled. The residual mixture was cooled andextracted with ether and the ether extract was extracted with sodium carbonate. This latter extract was acidified and the precipitated acid extracted with ether. After suitable washing and drying of the ether extract, the ether was evaporated and the crude product obtained.

Fractional crystallisation from methanol three times yielded an acid (1.32 gms) m.pt.183-188°C (softens 180°C) (Found, C-75.78%, H-6.79%; $C_{17}H_{18}O_3$ requires C-75.51%, H.6.72%). Its methyl ester melted at 86-86.5°C (Found, C-75.77%, H-7.31%; $C_{18}H_{20}O_3$ requires C-76.05%, H-7.1%). The ultra-violet absorption spectrum of the acid showed that it was an α-naphthoyl propionic acid, and was established by conversion to 2:3:8:9-tetramethylphenanthrene (see discussion page 115) to be β-(3:6:7-trimethyl-1-naphthoyl-) propionic acid (XIII). The yield of this

acid was about 8.5%.

The crude residual mixture obtained from the mother liquors was treated with ethereal diazo-methane to convert the acids to their methyl esters. On fractional crystallisation of the crude esters 3 times from methanol a pure ester (1.30 gms) was obtained m.pt. 93-94°C. (Found C-75.74%, H-6.96%; $C_{18}H_{20}O_3$ requires C-76.05%, H-7.1%). The acid obtained from the ester by hydrolysis melted at 165-172°C. (Found C-75.36%, H-6.61%; $C_{17}H_{18}O_3$ requires C-75.51%, H-6.72%).

The ultra-violet absorption spectrum confirmed that this was a β-naphthoyl acid, and since there is only one possible β-isomer it must be β-(3:6:7-trimethyl-2-naphthoyl-) propionic acid. The yield of this acid was 7.8% of the theoretical.

Preparation of γ-(3:6:7-trimethyl-2-naphthyl-) butyric acid (III).

Ref. Huang-Minlon, J.A.C.S., 1946, 68, 2488.

The above methyl ester, methyl β-(3:6:7-trimethyl-2-naphthoyl-) ~~butyrate~~ propionate (m.pt. 93-94°C) (1 gm), sodium hydroxide (0.5 gm.), diethylene glycol (8 ccs) and hydrazine hydrate (90%, 0.5 cc) were refluxed for 1 hour. The reflux condenser was then removed and the temperature allowed to rise to 195-200°C. The condenser was replaced and the mixture refluxed at this temperature for 3 hours. It was then cooled, acidified and extracted with ethyl acetate, and the acid (0.7 gm) isolated in the usual way.

On recrystallisation of the acid from benzene-petroleum/ether (40-60°C b.pt.) it melted at 159-164°C. (Found C-79.46%, H-7.54%, $C_{17}H_{20}O_2$ requires C-79.65%, H-7.86%). Its methyl ester, prepared by treating the acid with diazo-methane in the usual way, on crystallisation from methanol melted at 90-91.5°C. The yield was 78% of the theoretical.

Preparation of 6:7;10-trimethyl-4-keto-1:2:3:4-tetrahydrophenanthrene (IV)

Ref. Wilds, J.A.C.S., 1942, 64, 1421. Org. Reactions Vol. II, 136.

Phosphorus pentachloride (0.4 gm) was added to the above butyric acid (III) (0.4 gm) in benzene solution (15 ccs) at 0°C. The mixture was shaken occasionally and allowed to stand at room temperature for 1 hour. It was then heated gently on the steam bath for 5 minutes to ensure completeness of reaction, and afterwards cooled to 0°C. Stannic chloride (0.4 cc) in dry benzene (0.4 cc) was added to the stirred chilled solution of the acid chloride. It was stirred for 15 minutes at 0°C and the complex hydrolysed with ice and hydrochloric acid. The mixture was extracted with benzene and the benzene extract was washed with water, sodium carbonate solution, water and dried. On removal of the benzene the ketone (IV) (0.33 gm) crystallised from cyclohexane, m.pt. 163-164°C. (Found C-85.83%, H-7.88%, $C_{17}H_{18}O$ requires C-85.67%, H-7.61%). The yield was 90% of the theoretical.

Reduction of the above ketone (IV) to the corresponding alcohol (V).

The above ketone (IV) (0.15 gm) was added dropwise in ether (dry) solution to a slurry of lithium aluminium hydride (0.24 gm) in ether (dry) solution. The mixture was refluxed for 3 hours. It was cooled and the excess lithium aluminium hydride decomposed by the dropwise addition of ethyl acetate. The mixture was then poured into ice and hydrochloric acid and the ether layer separated. After suitable washing and drying the ether was evaporated and the crude alcohol (0.15 gm) crystallised from benzene, m.pt. 175-177°C. (Found C-85.17%, H-8.50%; $C_{17}H_{20}O$ requires C-84.95%, H-8.39%).

Preparation of 2:3:9-Trimethylphenanthrene.

The above alcohol (V) (0.15 gm) was dehydrated by heating with fused potassium bisulphate (0.015 gm) to 180°C for ten minutes, and the dihydro-phenanthrene (VI) distilled.

The dihydro-phenanthrne (VI) was dehydrogenated by heating with palladium-charcoal (30%) [65] in an atmosphere of carbondioxide in the usual way (p. 69). The phenanthrene (VII) sublimed out of the catalyst gradually as dehydrogenation proceeded at 240°C, It crystallised from methanol as plates, m.pt. 107-108°C. (Found C-92.91%, H-7.18%, $C_{17}H_{16}$ requires C-92.68%, H-7.32%). Its picrate had m.pt. 179-181°C (Found C-61.23%. H-4.31%;

$C_{17}H_{16}, C_6H_3O_7N_3$ requires C-61.47%, H-4.26%), its s-trinitrobenzene complex had m.pt. 193-194°C (softens prior to melting).

Attempted preparation of 2:3:5:9- Tetramethylphenanthrene(IX)

The ketone (IV) was reacted with methyl magnesium iodide under the normal experimental conditions. The crude product was dehydrated and dehydrogenated simultaneously by heating with palladium-charcoal (30%) (65) at 240-250°C. The product of the dehydrogenation sublimed out of the catalyst gradually.

It was chromatographed on activated aluminia with petroleum/ether (40-60°C b.pt.) - 40% benzene as eluent. On crystallisation from methanol it melted at 138-143°C. (Found C-91.11%, H-9.01%). 2:3:5:9-Tetramethylphenanthrene, $C_{18}H_{18}$ requires C-92.26%, H-7.74%. Its s-Trinitrobenzene complex melted from 155°C to 180°C. The ultra-violet absorption spectrum (p.113a) is of the phenanthrene type.

The analysis suggested that it probably was a mixture of phenanthrene (IX) and the corresponding tetrahydro compound. ($C_{18}H_{22}$ requires C- 90·7 %; H - 9·3%) It was again heated with palladium-charcoal in an atmosphere of carbon dioxide. The product sublimed out slowly at 240°C. On recrystallisation from methanol it still melted at same temperature.

Yet another attempt was made to obtain a pure phenanthrene by subliming the mixture slowly through palladium-

charcoal at 300°C. No pure product was isolated. It was concluded that an inseparable mixture had been obtained.

Preparation of γ-(3:6:7-trimethyl-1-naphthyl-) butyric acid (XIV).

Ref. Huang-Minlon, J.A.C.S., 1946, 68, 2488.

The keto-acid (XIII) (1.2 gm.), sodium hydroxide (0.6 gm), diethylene glycol (15 ccs) and hydrazine hydrate (90%, 0.6 ccs) were refluxed for 1 hour. The condenser was removed and the temperature allowed to rise to 195-200°C. The condenser was replaced and the mixture refluxed for 3 hours. The product was isolated in the usual way (p.77). The desired butyric acid (0.92 gm) was isolated, and on crystallisation from benzene melted at 155-159°C, sinters prior to melting at 150°C. (Found C-79.98%, H-7.98%, $C_{17}H_{20}O_2$ requires C-79.65%, H-7.86%). The yield was 90% of the theoretical.

Preparation of 6:7:10-trimethyl-1-keto-1:2:3:4-tetrahydrophenanthrene (XV).

Phosphorus pentachloride (1 gm) was added to the above butyric acid (0.9 gm) in benzene solution at 0°C. The mixture was shaken occasionally and allowed to stand for 1 hour at room temperature. It was then heated on the steam bath gently for 5 minutes to ensure completeness of reaction and afterwards cooled to 0°C. Stannic chloride (0.98 cc) in dry benzene (0.8 cc) was now added to the

stirred solution. The product was isolated by a similar method to that given on page 67-68. The ketone (XV) (0.9 gm) crystallised in short prismatic crystals from benzene-petroleum/ether (40-60° b.pt.), m.pt. 129-130°C. (Found C-85.60%, H-7.91%, $C_{17}H_{18}O$ requires C-85.67%, H-7.61%).

Preparation of 2:3:8:9-Tetramethylphenanthrene (XVII).

The above ketone (0.9 gm) was added in benzene solution to an ether solution of methyl magnesium iodide prepared from methyl iodide (6 gms) and magnesium turnings (1.01 gms) so that the ether gently refluxed. Most of the ether was distilled off and the mixture refluxed in benzene solution for 3 hours. The crude product was isolated in the usual way (p. 79). It was dehydrated, and dehydrogenated simultaneously by heating with palladium-charcoal (30%) [65] at 280-290°C in an atmosphere of carbon dioxide (p. 69). The crude product isolated in the usual manner was chromatographed on alumina with petroleum/ether (60-80°C b.pt.) - 10% benzene as eluent. The 2:3:8:9-tetramethylphenanthrene crystallised from methanol, m.pt. 106-107°C. (Found C-92.55%, H-7.72%, $C_{18}H_{18}$ requires C-92.26%, H-7.74%). Its picrate had m.pt. 167-169°C. (Found C-62.45%, H-4.76%, $C_{18}H_{18}$, $C_6H_3O_7N_3$ requires C-62.2%, H-4.57%), and its s-trinitrobenzene complex had m.pt. 181-183°C (Found C-64.68%, H-4.70%, $C_{18}H_{18}.C_6H_3O_6N_3$ requires C-64.42%, H-4.76%). The ultra-violet absorption spectrum is shown on page 115a.

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