(1) DIBENZCYCLOHEPTATRIENES

(2) A NEW MOLECULAR REARRANGEMENT EFFECTED BY ALUMINIUM CHLORIDE

A THESIS SUBMITTED FOR THE DEGREE OF Ph.D.

BY

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SUMMARY

A : Dibenzcycloheptatrienes.

2:3-Dimethoxy-9-and-10-methylphenanthrenes were synthesised and, by expansion of the central ring in each, were converted into dibenzocycloheptatrienones. Thereby 13:14-dimethoxy-3:4-5:6-dibenzocyclohepta-1:3:5-triene was isolated and fully characterised but the isomeric triene was less well defined and attempted interconversion of the two gave results which were not free of ambiguity.

B : A New Molecular Rearrangement effected by Aluminium Chloride.

It is shown that through being heated with aluminium chloride chromanone is rearranged to 7-hydroxyindanone and dihydrocoumarin to 4-hydroxyindanone. Further applications of this type of rearrangement are described and discussed. In particular it is employed to prepare 6-hydroxyperinaphthen-7-one, the corresponding 8:9-dihydride and 6-hydroxy-perinaphthen-9-one. A comparative study of these three compounds is made to evaluate the chemical effects which are associated with the strong hydrogen-bonding present in the first of them. An improved method for the synthesis of chromanones has been developed.

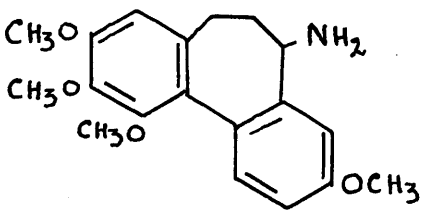
Part I.

Dibenzcycloheptatrienes

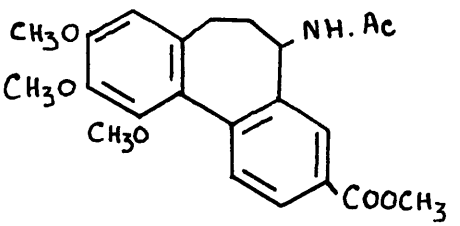
Dibenzcycloheptatrienes

Introduction:-

Nearly all the compounds of this class, except for a few degradative products of colchicine like colchinol methyl ether (I), allocolchicine (II) etc.,



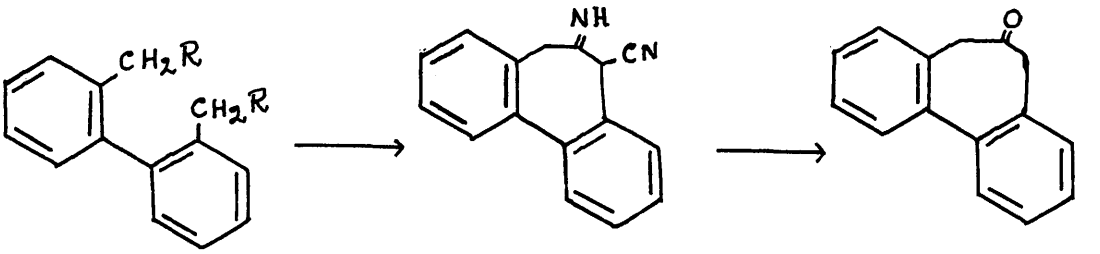
(I)



(II)

are obtained by synthesis. Because of the interest aroused by the chemistry of colchicine and related compounds many new approaches have been made towards their synthesis during the past few years.

Until 1947 compounds of this class have usually been obtained, starting from symmetrically substituted diphenyls of the general formula (III). In 1911 Kenner and Turner[1] reported the synthesis of the ketone (V) by the cyclisation of the dinitrile (III, R = CN) by Thorpe's method, followed by hydrolysis and decarboxylation of the



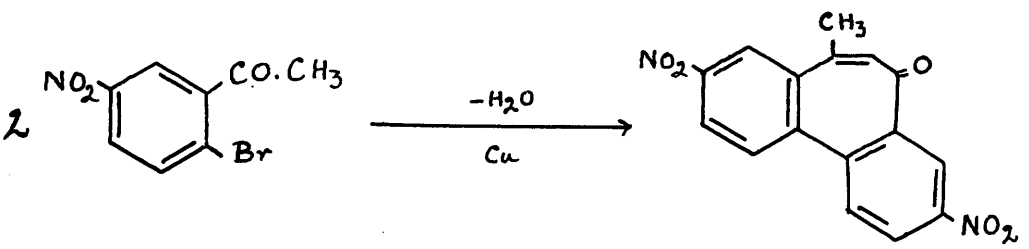
(III) (IV) (V)

ketimine (IV) with hot sulphuric acid. Later Kenner[2] subjected the diester (III, R = CϕϕEt) to the Dieckmann reaction and after hydrolysis of the products obtained the same ketone (V). Similarly the carboxylic acid (VI) was synthesised, starting from ww′-dibromo-oo′-ditolyl (III, R = Br) by condensation with malonic ester followed by hydrolysis and decarboxylation. Using essentially the same method Weitzenböck[3] synthesised the aldehyde (VII) by cyclisation of the bisacetal of diphenyl-oo′-diacet-aldehyde

(VI) (VII)

(III, R = $CH(OEt)_2$) under hydrolytic conditions.

Borsche and Herbert[4] in 1941 claim to have synthesised the ketone (IX) by direct treatment of 2-bromo-5-nitro-acetophenone (VIII) with copper but give no proof of the



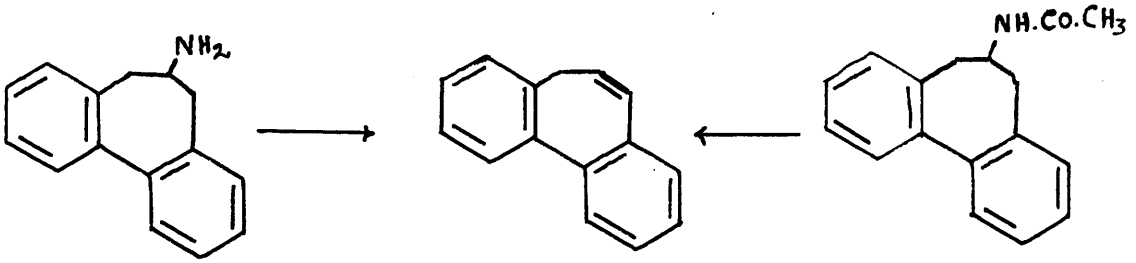
(VIII) (IX)

presence of a seven membered ring.

Kenner (loc cit) converted the carboxylic acid (VI) to the corresponding amine (X) by means of the Curtius reaction but on dry distillation of the hydrochloride of the base, obtained the parent triene (XI) in extremely poor yield. He could not study the properties of dibenz<u>cyclo</u>heptatriene (XI) in detail because of lack of material. Further he pointed out the ease with which such a ring system was formed and compared this with the ease of formation of indene derivatives from xylylene dibromide and suggested an anology between dibenz<u>cyclo</u>-heptatriene and indene series.

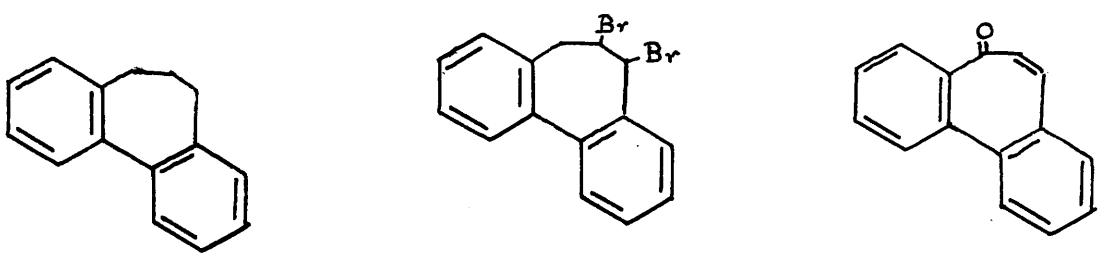
Cook, Dickson and Loudon[5] obtained the pure triene (XI) in 68% yield by the treatment of the acetamido

compound (XII) with phosphoric oxide in boiling xylene,



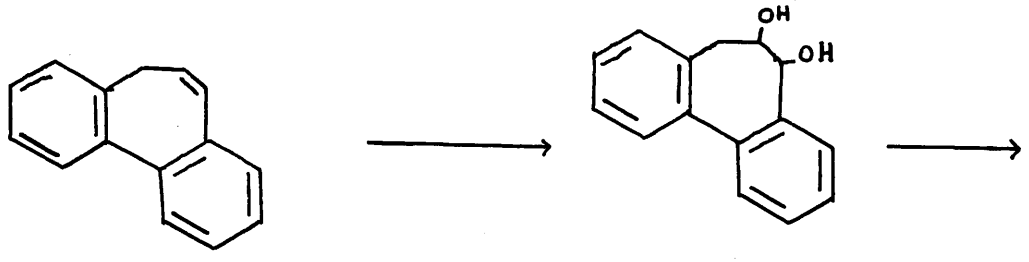
(X) (XI) (XII)

a method discovered by Cook and Graham[6] during investigations on the deamination of colchinol methyl ether (I). The above authors studied the properties of dibenzcyclo-heptatriene and showed that it does not form a picrate as reported by Kenner[2]. It is readily hydrogenated in the presence of palladium in acetic acid, to the dihydride (XIII) and also forms the dibromide (XIV) when treated with bromine in chloroform solution. 9-Methylphenanthrene is produced when the triene is heated with hydroiodic acid then distilled with zinc, and also during the destructive distillation of the hydrochloride of the base (X).

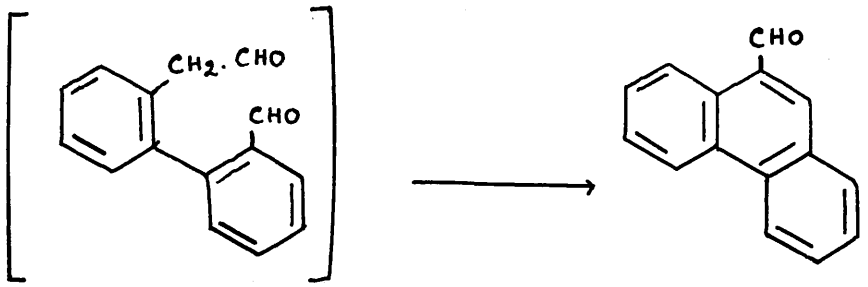


(XIII) (XIV) (XV)

On stepwise oxidation, with osmium tetroxide and lead-tetraacetate, the triene furnished 9-phenanthraldehyde (XVIII) according to the sequence (XVI) → (XVII) → (XVIII).



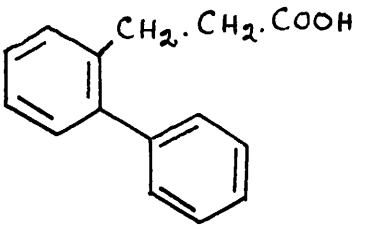
(XVI)



(XVII) (XVIII)

The triene is oxidized to a mixture of phenanthraquinone and the trienone (XV) with sodium dichromate in acetic acid. Oxidation to phenanthraquinone has been observed with the compounds (V), (VII), (XI), (XIII), (XV) and may have some diagnostic value in the series[7].

Another direct approach was made towards the synthesis of dibenzcycloheptatriene by the Friedel-Crafts cyclisation of diphenylpropionic acid (XIX). Although a very small quantity of the required dibenzcycloheptadienone was formed this reaction yielded mainly the expected indanone[8] (XX).



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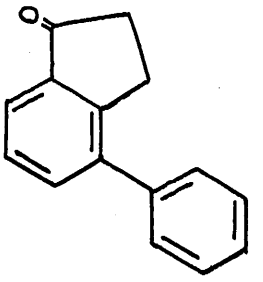
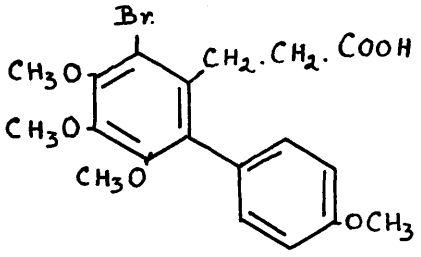
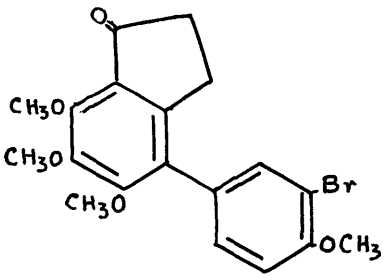


(XX)

In the colchicine field, the acid (XXI) was synthesised by Frank, Fanta and Tarbell[9] by a cross Ullman reaction between the appropriate iodo compounds followed by bromination. Barton, Cook, Loudon and MacMillan[10] also synthesised the same acid (XXI) by a Gomberg-Hey type of reaction between methyl-3:4:5 trimethoxybenzoate and 1-p-methoxy-phenyl-3:3-dimethyltriazen, followed by increase in the acid chain length and finally bromination. Unfortunately, attempted cyclisation of (XXI) always gave a bromo derivative of indanone to which the structure (XXII) has been assigned.

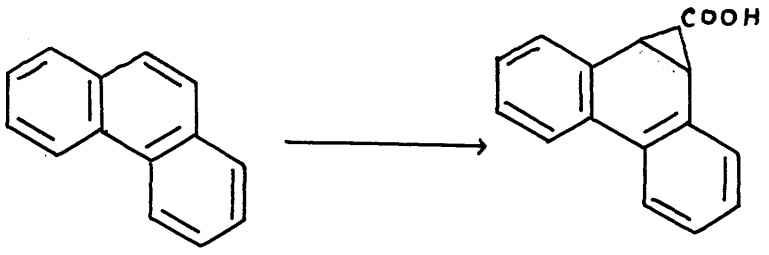


(XXI)



(XXII)

Attempts to synthesise the same ring system by the action of ethyldiazoacetate on phenanthrene was unsuccessful[11,12].

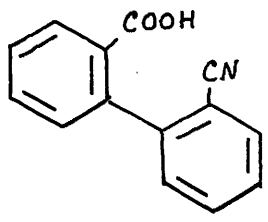


(XXIII)

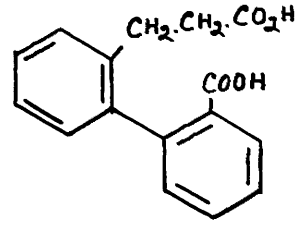
The acid obtained was not dibenzcycloheptatriene carboxylic acid but the alkali stable dibenznorcaradiene carboxylic acid (XXIII).

Rapoport and Williams[13] have succeeded in getting the ketone (XXVI) in 20-30% overall yield from phenanthra-

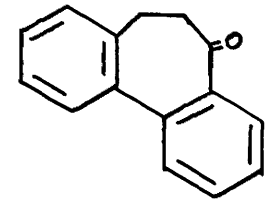
quinone. They obtained the acid (XXIV) by the Beckmann rearrangement of phenanthraquinone monoxime. The carboxyl group in (XXIV) was reduced to -CHO, which on



(XXIV)



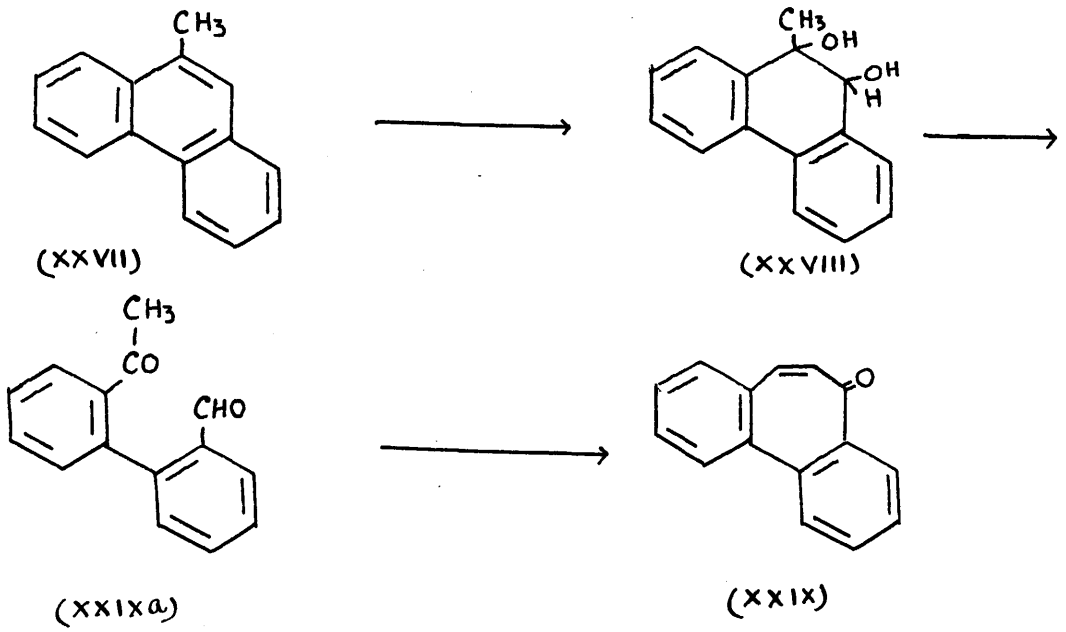
(XXV)



(XXVI)

condensation with malonic acid followed by decarboxylation, hydrogenation and hydrolysis furnished the acid (XXV). The ester of this acid on Dieckmann reaction followed by hydrolysis of the products gave the required ketone (XXVI).

Recently, a synthesis which appears to be general, of dibenzcycloheptatrienones, has been developed by Cook, Jack, Loudon, Buchanan and MacMillan[14] from derivatives of 9-(or 10-) methyl phenanthrenes. The central ring is expanded by the successive steps of hydroxylation by means of osmium tetroxide in benzene/ pyridine, cleavage (lead tetra-acetate) and cyclisation to the corresponding trienone e.g.

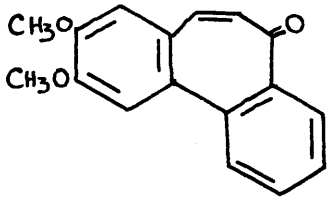


By starting with the appropriate substituted phenanthrene, they have accomplished the synthesis of colchinol methyl ether (I), the most important degradation product of colchicine. This methyl ether has also been synthesised by Rapoport, Williams and Cisney[15], starting from 2:3:4:7 tetramethoxy-10-phenanthroic acid and using essentially the same route as that developed earlier by Rapoport and Williams (loc cit).

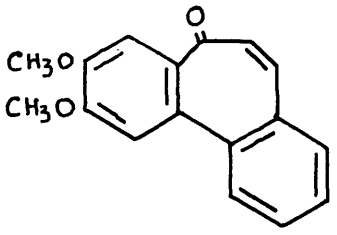
Discussion:-

As pointed out above, the method of Cook and his co-workers[14] for the synthesis of dibenzcycloheptatrienones seems to be the most general in nature. In the present work the same method has now been applied to the synthesis

of the two 13:14-dimethoxy dibenzcycloheptatrienones (XXX) and (XXXI) there by showing the flexibility of the method and establishing its superiority over

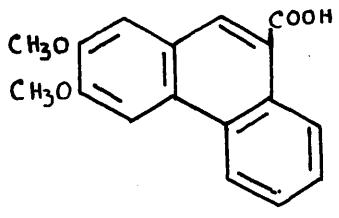


(XXX)

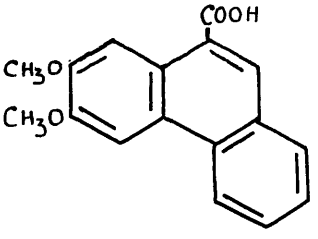


(XXXI)

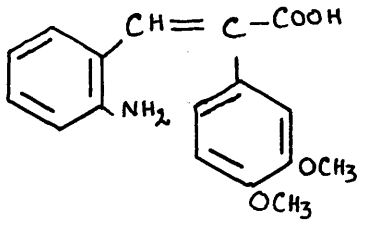
others. Also this study was undertaken with a view to investigating tautomerism in the corresponding dibenzcycloheptatrienes. Their synthesis accordingly requires the two-9- and -10-, 2:3-dimethoxy phenanthroic acids (XXXII) and (XXXIII) as starting materials. These are both already known and have been prepared by



(XXXII)

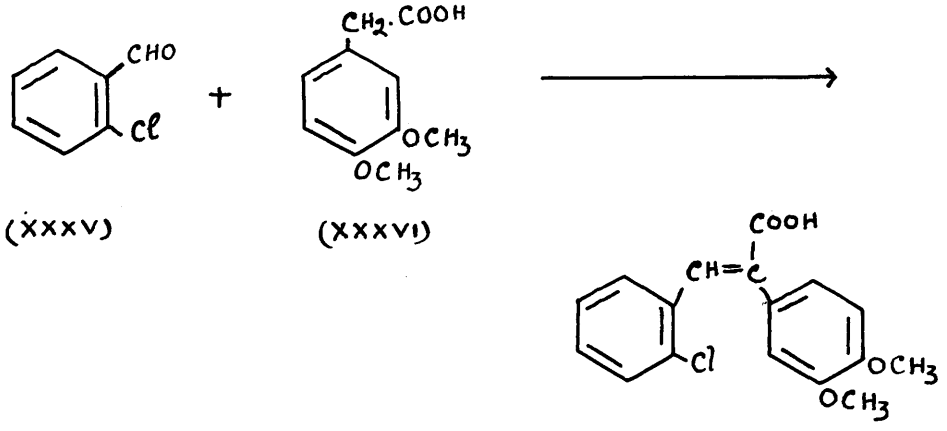


(XXXIII)



(XXXIV)

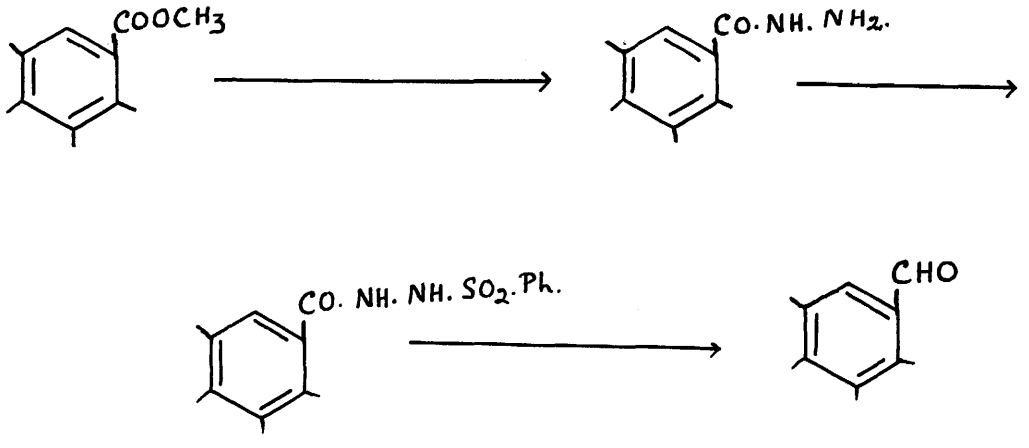
Pschorr and his co-workers[16,17]. The 2:3-dimethoxy-9-phenanthroic acid (XXXII) was easily prepared in large quantities by the method of Pschorr and Buckow[16] with slight modifications (see experimental). However the synthesis of the corresponding 10-acid (XXXIII) gave considerable difficulty, an extremely poor yield of the acid being obtained. A wide variety of conditions were used for the successive stages of diazotisation and decomposition of the corresponding 2-amino, α-(3:4-dimethoxy)-phenyl-cinnamic acid (XXXIV), but in every case a nitrogeneous material, soluble in hot alkali, was obtained. The acid (XXXIII) was eventually synthesised by employing Hewett's technique[18]. O-Chlorobenzaldehyde (XXXV) was condensed with the sodium salt of homoveratric acid (XXXVI) by the Perkin reaction to give the compound (XXXVII).



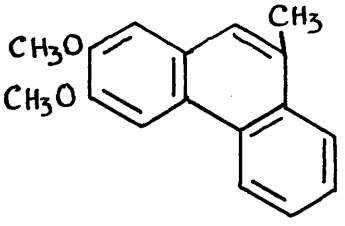
(XXXV) (XXXVI) (XXXVII)

This acid after fusion with potassium hydroxide at 260° and remethylation with dimethyl sulphate in the presence of alkali, furnished the required 2:3-dimethoxy-10-phenanthroic acid (XXXIII). The yield, however, was not very good because of the charring which accompanied the alkali fusion. When attempts were made to effect the ring closure at temperatures lower than 260°, only the starting material was recovered. The 2:3-dimethoxy-10-phenanthroic acid thus prepared crystallised as pale yellow needles from alcohol, and had the same melting point as reported by Pschorr[17].

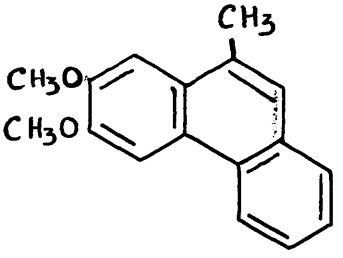
The two phenanthroic acids (XXXII) and (XXXIII) being thus obtained, were then easily converted via their corresponding methyl esters, hydrazides and phenylsulphonhydrazides into 2:3-dimethoxy-9-(and -10-) phenanthraldehydes, in very good yields. A straight forward Wolff-Kishner reduction of these, furnished the required methyl phenanthrenes (XXXVIII) and (XXXIX).



They were obtained in excellent yields and were conveniently purified by passing their solution in



(XXXVIII)

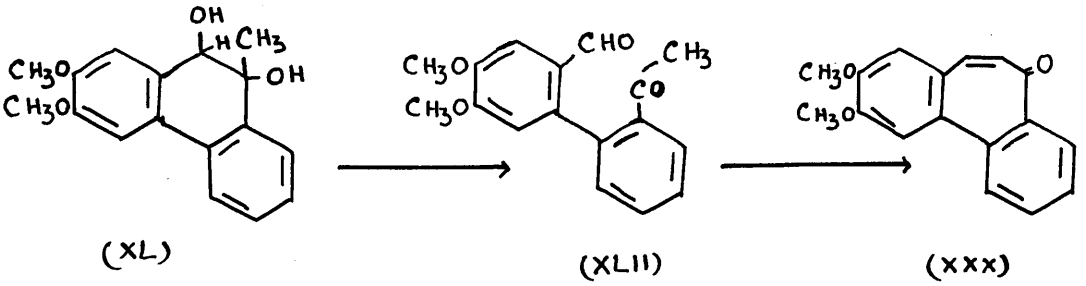


(XXXIX)

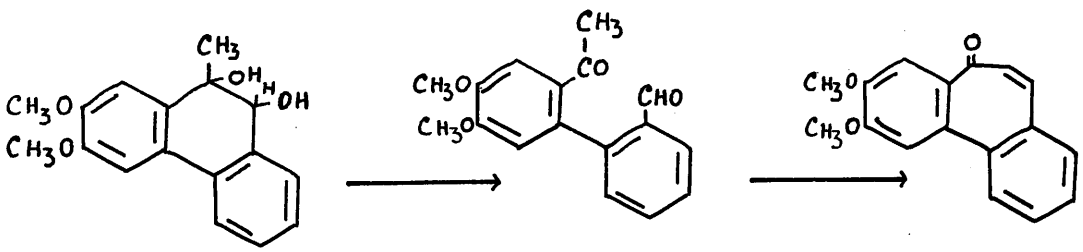
benzene through a column of alumina.

Criegee, Marchand and Wannowius[19] showed for the first time that the 9:10 double bond of phenanthrene could be hydroxylated to the corresponding cis-diol, when treated with osmiumtetroxide in benzene-pyridine solution. This method was extended by Cook and his co-workers[14,20]. to the derivatives of -9-(or 10-) methyl-phenanthrenes, as mentioned before. In the present investigation the two methyl-phenanthrenes (XXXVIII) and (XXXIX) when treated similarly, precipitated the diol as a crystalline complex of the osmic ester with pyridine. This was filtered and its solution in chloroform when shaken with mannitol and alkali, afforded the corresponding cis-diols (XL) and (XLI). The latter was found to be very sensitive to heat, dehydrating, even during crystallisation from

hot methanol to the corresponding methylphenanthrol (XLIV). It was however successfully crystallised



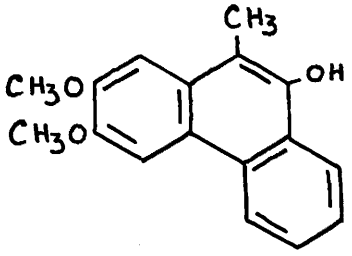
(XL) (XLII) (XXX)



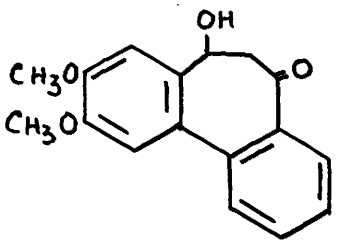
(XLI) (XLIII) (XXXI)

from methanol at room temperature. The scission of these glycols (XL) and (XLI) was accomplished by means of lead tetra-acetate and afforded the corresponding keto-aldehydes (XLII) and (XLIII), [characterised as the dioxime in the case of (XLII)] which, in acetic acid solution and saturated with hydrogenchloride, cyclised to the corresponding trienones (XXX) and (XXXI).

No intermediate of the type (XLV) was isolated. This is yet another example of a series where this type



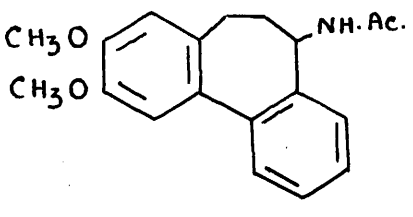
(XLIV)



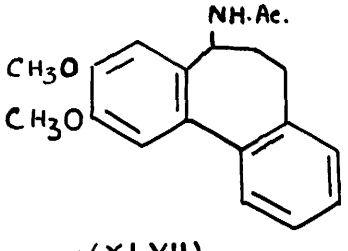
(XLV)

of cyclisation was effected in very good yield by this method. (Compare Cook et al[14]). Both the ketones (XXX) and (XXXI), when oxidized with sodium dichromate and acetic acid, gave the same 2:3-dimethoxyphenanthraquinone thereby showing a bridged diphenyl structure in each case.

The unsaturated ketones (XXX) and (XXXI) were converted into their corresponding oximes (in pyridine) which when hydrogenated in the presence of Adam's' catalyst in acetic anhydride solution, at ordinary room temperature and pressure, afforded the acetamido



(XLVI)

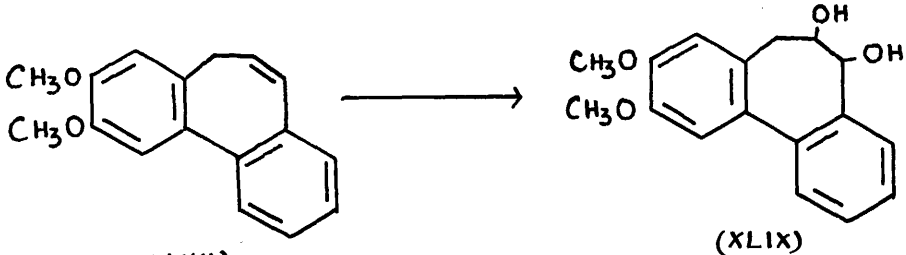


(XLVII)

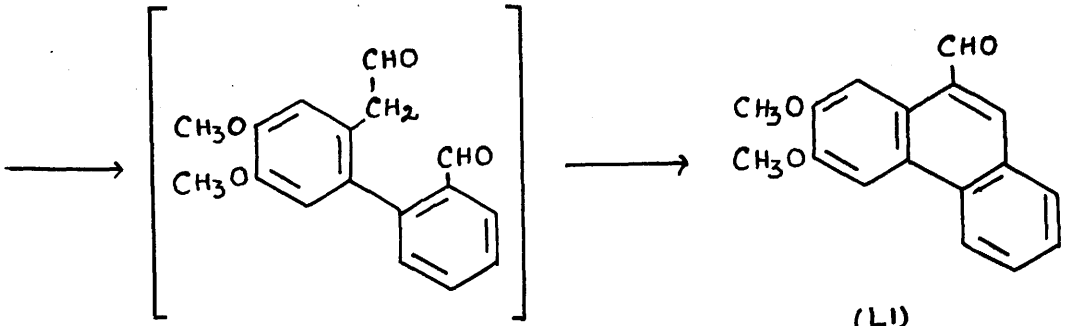
compounds (XLVI) and (XLVII).

Study of the deamination products of the Acetamido compounds (XLVI) and (XLVII):-

The acetamido compound (XLVI) when treated with phosphoric oxide in boiling purified xylene (see experimental part) furnished the triene (XLVIII) m.p. 113-115° (micro). The structure was proved by further degradation through stepwise oxidation with osmium tetroxide in ether[21] to the corresponding glycol (XLIX) followed by lead tetra-acetate fission and recyclisation in the presence of a small trace of alkali to 2:3-

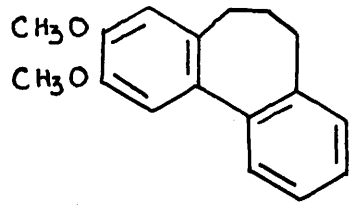


(XLVIII) (XLIX)



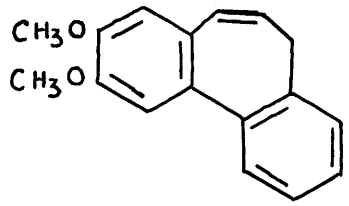
(L) (LI)

dimethoxy-10-phenanthraldehyde (LI). The triene (XLVIII) readily formed a dibromide when its solution in chloroform was treated with a dilute solution of bromine in chloroform. Hydrogenation in the presence of palladium catalyst in acetic acid showed one double bond and gave the dihydride (LII).



(LII)

The other acetamido compound (XLVII) when deaminated under similar conditions furnished a small quantity of a product which after repeated crystallisations from methanol and finally chromatography over alumina had melting point 88-90° (micro). This is in all probability the other triene (LIII) as micro hydrogenation in the presence of palladium catalyst in acetic acid showed



(LIII)

one double bond and gave the same dihydride (LII) in excellent yield. Moreover on one occasion when the deamination was carried out in the presence of ordinary xylene (before it was discovered that xylene needed purification as described in the experimental part) only a gummy liquid was obtained which (a) when oxidized with sodiumdichromate and acetic acid gave the same 2:3-dimethoxyphenanthraquinone and (b), through the same series of reactions as (XLVIII) → (XLIX) → (L) → (LI) gave an impure sample of 2:3-dimethoxy-9-phenanthraldehyde.

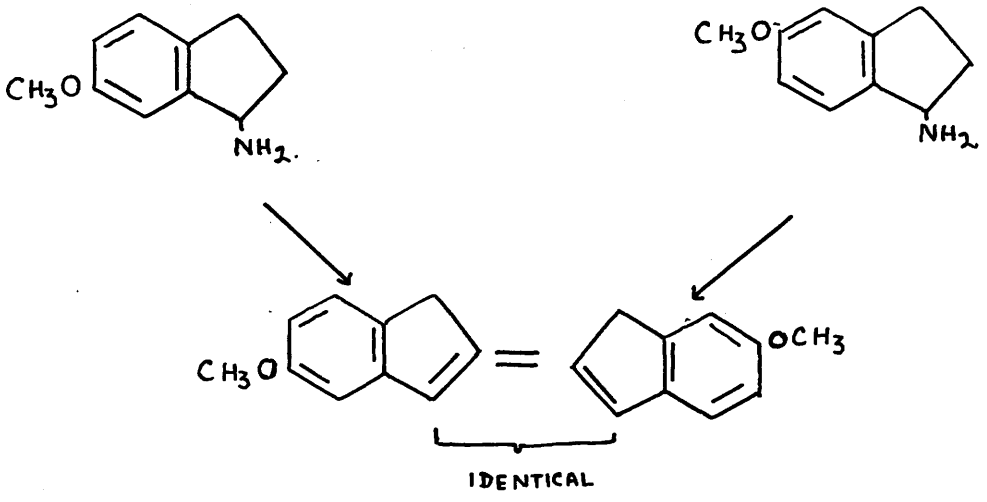
These crystals of m.p. 88-90° were different in appearance (platelets) from the triene (XLVIII) (needles) and it was certainly not a case of polymorphism as all attempts to convert one into the other form by carefully seeding the solution and also the melts (while taking micro melting points), of one with the other, always furnished the original type of crystals with no change in melting point. Unfortunately the mixed melting point of these two compounds was over a range of 86-102° (micro). There was only a slight depression of 2° which is not very significant, although, one could clearly see all the platelets melting first and then the needles.

Many instances are known where the mixed melting point of two closely related compounds is not depressed but is between the two melting points.

The quantity of crystalline material isolated from (XLVII) was too small to be degraded and fully characterised.

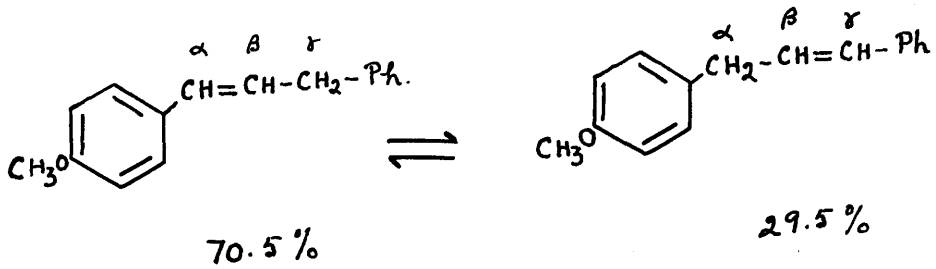
Tautomerism in the triad system in Indene and 1:3Diarylpropenes:-

C. K. Ingold and H.A. Piggott[22] have shown that the triad system in indene is highly mobile. They synthesised the two isomeric 5- and 6- methoxy-1-hydrindamines through unambiguous routes and showed that each isomer, when converted into their salts lose ammonia, yielding the same methoxy indene, thereby



establishing the prototropic mobility of the system[23].

Quite in contrast to this is the reluctant prototropy of 1:3diarylpropenes. Ingold and Piggott[24]



70.5 %

(LIV)

29.5 %

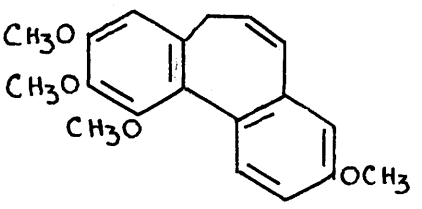
(LV)

found that the two isomers (LIV) and (LV) not only existed as separate static individuals, but also that they showed no tendency whatsoever to undergo interconversion at ordinary conditions[25]. However when treated with 1.45N-ethyl alcoholic sodium ethoxide at 85°, interconversion was readily effected[26], each isomeride giving the same equilibrium mixture having a composition as shown above. To explain the presence of the isomer (LIV) in 70.5% yield, Ingold and Shoppee put forward the suggestion that due to the electron release tendency of the methoxyl group, there is a small accumulation of a negative charge on the para carbon atom of the benzene ring. This negative charge

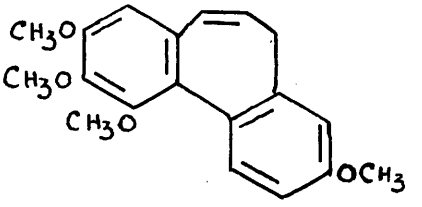
would tend to repel the anionic charge resident on C_α and consequently the more stable ion will be of the form (LIV) as the anionic charge will then be located mainly on the most distant carbon atom C_γ [25].

Tautomerism in Dibenzcycloheptatrienes:-

Barton, Cook and Loudon[27] showed that during the deamination of N-acetyl-colchinol methyl ether, by treatment with phosphoric oxide in boiling xylene, mainly deamino colchinol methyl ether (LVI) is obtained, with always a small quantity of an isomeride, isodeaminocolchinol methyl ether (LVII).



(LVI)



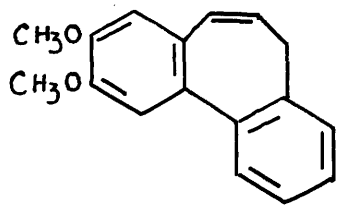
(LVII)

The two were separated by careful fractional crystallisation of the deamination products. The structures assigned to these compounds are firmly established.

This static individual existence of the two isomerides (LVI) and (LVII) suggested that the dibenzcycloheptatriene system would not be very mobile and in that would resemble the diarylpropene system rather than the triad system in indene. The present investigation has also borne this out. However on careful fractional crystallisation of the deamination product obtained from the acetamido compound (XLVI), only about 1-2 mg of a compound as platelets of m.p. 88-94° (micro) were isolated in addition to the fully characterised triene (XLVIII), (needles, micro m.p. 113-115°). It was not possible to purify the platelets further as the quantity was so small and it is therefore difficult to comment on the nature of this compound. It is obvious that no appreciable quantity of another compound could be isolated here, as in the case of the deamination of N-acetyl colchinol methyl ether, (for fractional crystallisation, see experimental part).

On treatment of the triene (XLVIII) under the same conditions as used by Ingold and Shoppee[26] for converting the diaryl propenes to the equilibrium mixture, practically 85-90% of the starting material (XLVIII) was recovered. Also no appreciable change occurred even when the amount of alkali used was doubled. This suggests

that the tendency for interconversion in dibenzcycloheptatrienes is even less pronounced than shown by the diphenylpropene system. But in drawing a conclusion like this, the possibility that we were handling the more stable of the two isomers should not be overlooked. Nevertheless in this connection it should be pointed out that by analogy with the diphenylpropene system and arguing on the same basis as used by Ingold and Shoppee to explain the preponderance of the ion of the form (LIV) in the equilibrium mixture, one would expect this isomer of the triene to be the more stable one. No attempt



could be made to treat similarly the deaminated product from the other series, as the quantity available was very small. This work had to be abandoned at this stage as it was not possible to repeat the whole synthesis with a view to getting more materials for study, because of lack of time. It was therefore not possible to apply the tests as put forward by Ingold and co-workers and thus study, tautomerism in dibenzcycloheptatrienes.

Experimental

Veratric aldehyde:- It was prepared from vanillin according to the method given in Organic Synthesis vol. XVI p. 91.

Nitro-veratric aldehyde:- Best results were obtained by the method of Marr and Bogart[28]; yield 70%, the original method due to Pschorr and Sumuleanu[29] giving only poor yields.

α-Phenyl-6nitro-3:4-dimethoxycinnamic Acid:- Sodium phenyl acetate (75.4g; dried at 120°), nitro-veratric aldehyde (100g) and acetic anhydride (500c.c.) were heated at 100° for 22-24 hours. The solution (dark brown) was added in an equal volume of water with swirling and left overnight after cautious warming to decompose the anhydride. The solid after filteration was ground in a mortar with a small quantity of water, filtered and crystallised from ethanol as yellow needles m.p. 219°.

α-Phenyl-6-amino-3:4-dimethoxycinnamic Acid:- A solution of the nitro acid (50g) in concentrated aqueous ammonia (213c.c.) and water (833 c.c.) was slowly added to a mixture of ferrous sulphate (366g), water (1.15 l)

and concentrated aqueous ammonia (950c.c.) maintained with stirring, at 70°. After 2 hours, the filtrate and washings from the iron hydroxide were acidified with dilute sulphuric acid and the salt of the amino acid filtered, dried and stored as such.

2:3-Dimethoxyphenanthrene-9carboxylic Acid:- A solution of sodium nitrite (13g) in water (100 c.c.) was gradually added at 5° to a suspension of the sulphate of the crude amino acid (as the sulphate salt, 50g) in 1N-sulphuric acid (700c.c.), with stirring. After half an hour water (2 l) was added, and the stirring continued for another 2 hours. The solution was filtered and the resulting diazo-solution was neutralized with sodium carbonate and heated at 50-60° until a coupling test was negative. After cooling the solution was acidified with dilute hydrochloric acid. The precipitated acid (brownish in colour) was filtered, washed, dried and used as such in the next stage. (It was not found desirable to purify the acid at this stage because of the low solubility in ethanol). A sample of the precipitated acid when crystallised repeatedly from ethanol, came as fine small brownish needles m.p. 267° (correct m.p. 270°)[30].

2:3-Dimethoxyphenanthrene-9-carboxylic Acid - methyl ester:-

A suspension of the crude 2:3-dimethoxyphenanthrene-9-carboxylic acid (50g) in methanol (2.2 l) and concentrated sulphuric acid (180c.c.) was heated under reflux for 3 hours. The solution after concentration was thrown in water (4 l) and the resulting solid was filtered, washed with dilute sodium carbonate solution followed by water and dried. The crude ester was purified by repeated crystallizations from methanol (after charcoaling), as colourless cubes m.p. 137° (micro). (Found: C, 72.9; H, 5.2. $C_{18}H_{16}O_4$ requires C, 72.98; H, 5.4 %).

2:3-Dimethoxyphenanthraquinone:- A solution of 2:3-dimethoxy phenanthrene-9-carboxylic acid (obtained as colourless fine needles m.p. 267° by the alkaline hydrolysis of the pure ester; 0.9g) in boiling acetic acid (30c.c.) was treated with a solution of sodium dichromate (1.8g) in water (1c.c.) and acetic acid (5c.c.). After being heated under reflux for 1 hour and then diluted with water (200c.c.), the mixture was extracted with chloroform. The extract was washed with dilute sulphuric acid and then dilute sodium carbonate solution (which removed a small amount of organic acid), dried

and evaporated. The quinone crystallized (from benzene) as red-violet needles, m.p. 301-302°. (Found: C, 71.4; H, 4.6. $C_{16}H_{12}O_4$ requires C, 71.6; H, 4.5 %). A solution of this quinone in hot acetic acid, treated with a warm solution of o-phenylenediamine in hot methanol, gave a diazine which crystallized from methanol in lemon yellow needles m.p. 225-226°. (Found: C,77.66; H, 4.4; N, 8.4. $C_{22}H_{16}N_2O_2$ requires C,77.64; H, 4.7; N, 8.2 %).

2:3-Dimethoxy-9-phenanthraldehyde:- The ester (20g) was heated for 5 hours with 90% hydrazine hydrate (80c.c.) in ethanol (200c.c.), thereby yielding the corresponding hydrazide as colourless needles m.p. 249° (from ethanol) (Found: N, 9.2. $C_{17}H_{16}O_3N_2$ requires N, 9.4 %). A solution of the hydrazide (20g) in pyridine (dried over KOH pellets) (120c.c.) was treated with benzene sulphonyl-chloride (9c.c.) and after 12 hours at room temperature, on being poured into dilute hydrochloric acid at 0°, afforded the phenylsulphonhydrazide m.p. 243° (from acetic acid). (Found: N, 6.55. $C_{23}H_{20}O_5N_2S$ requires N, 6.4 %). A solution of this compound (10g; previously dried at 120°) in ethylene glycol (145 c.c.) at 180° was treated with anhydrous sodium carbonate (6.5g) and after 80 seconds, boiling water (300 c.c.) was added very

carefully with much spurting. The solution was cooled, the dark brownish solid filtered, washed with water and crystallised from methanol (charcoal) as light yellow needles m.p. 135-136°. (Found: C, 76.7; H, 5.7. $C_{17}H_{14}O_3$ requires C, 76.7; H, 5.6 %).

2:3-Dimethoxy-9-methylphenanthrene:- The above aldehyde (1.1g) was heated for 2½ hours with 99% hydrazine hydrate (4 c.c.) in ethanol (40 c.c.). Removal of the solvent afforded a yellow solid, which when intimately mixed with powdered potassium hydroxide (2g) at 125-130° readily gave an effervescent melt. It was maintained at this temperature for 10 minutes and water was added when a greyish coloured solid separated. The solid was filtered and conveniently purified by passing its solution in benzene through a column of alumina. It formed colourless needles (from benzene) m.p. 130-131°. (Found: C, 80.9; H, 6.7. $C_{17}H_{16}O_2$ requires C, 80.9; H, 6.4 %).

cis-9:10-Dihydro-9:10-dihydroxy-2:3-dimethoxy-9-methylphenanthrene:- Pyridine (dried over potassium hydroxide pellets; 12 c.c.) was added to a solution of the above methylphenanthrene (10g) in sodium dried thiophen-free benzene (75 c.c.) and osmium tetroxide (15g). After 9 days the brown precipitate was collected, dissolved in

chloroform (250 c.c.) and shaken for 2½ hours with a solution of mannitol (300g) and potassium hydroxide (12 g) in water (1.5 l). The yellowish brown chloroform layer was washed, dried and on evaporation in vacuo, afforded the glycol as a gum which crystallized from methanol-water as colourless needles (10.2 g) of m.p. 179-180°. (Found: C, 71.1; H, 6.4. $C_{17}H_{18}O_4$ requires C, 71.3; H, 6.3 %).

13:14-Dimethoxy-3:4-5:6-dibenzocyclohepta-3:5:7-trien-2-one:- Lead tetra-acetate (0.42 g) was added to a solution of the diol (0.2 g) in dry benzene (50 c.c.) and the whole mixture shaken for 2½ hours and heated under reflux for ½ hour. The cooled suspension was filtered and the filtrate washed, dried and concentrated in vacuo at 40-50°, affording a colourless gum which crystallized as colourless needles (from methanol-water mixture) of m.p. 88-89°. (Found: C, 71.7; H, 5.6. $C_{17}H_{16}O_4$ requires C, 71.8; H, 5.6 %)., It readily formed a dioxime (in pyridine) of m.p. 182-183°. (Found: N, 8.7. $C_{17}H_{18}N_2O_4$ requires N, 8.9 %). Its solution in glacial acetic acid (7 c.c.) was saturated with dry hydrogen chloride (25 minutes). The solution turned deep red and solid started separating. On leaving it overnight at room temperature,

excess water was added when a white precipitate was obtained. It was filtered, washed free of acetic acid, dried and crystallized from benzene - petroleum ether 40-60° mixture as colourless needles m.p. 119°. (Found: C, 76.7; H, 5.5. $C_{17}H_{14}O_3$ requires C, 76.7; H, 5.3 %). When heated for ½ hour with sodium dichromate in acetic acid it afforded 2:3-dimethoxyphenthraquinone, which was isolated as a neutral extract in chloroform from the diluted reaction mixture and was identified by its melting point and mixed melting point.

13:14-Dimethoxy-2-acetamido-3:4-5:6-dibenzocyclohepta-3:5-diene:- The oxime of the above trienone (0.7 g), colourless needles m.p. 192-193° from methanol. (Found: C, 72.6; H, 5.0; N, 5.2. $C_{17}H_{15}O_3N$ requires C, 72.6; H, 5.3; N, 5.0 %) dissolved in acetic anhydride (30 c.c.) was hydrogenated in presence of Adam's catalyst. Absorption was complete in 3 hours and the acetamido compound obtained by concentration in vacuo formed colourless needles (from methanol-water mixture) of m.p. 260-61°. (Found: C, 73.3; H, 6.2; N, 4.5. $C_{19}H_{20}NO_3$ requires C, 73.5; H, 6.4; N, 4.5 %).

13:14-Dimethoxy-3:4-5:6-dibenzocyclohepta-1:3:5-triene:- Phosphorus pentoxide (0.2g) was added to a solution of the

above acetamido compound (0.1 g) in dry purified xylene (xylene was purified by shaking for 4 hours with 10% of its weight of concentrated sulphuric acid, followed by washing with water, dried and distilled. The distilled xylene was then left over phosphorus pentoxide for a week) and the mixture boiled for 25 minutes. After cooling, the xylene solution was filtered and the residue extracted twice with boiling xylene. The combined filtrate and extract was washed with dilute sodium carbonate solution, then with water, dried and evaporated under reduced pressure. The residual gum was taken up in methanol and on scratching, it solidified. This was conveniently purified by passing through a column of alumina and eluting with benzene when it crystallized as colourless shining needles (from methanol) m.p. 112–115° (micro). (Found: C, 80.75; H, 6.58. $C_{17}H_{16}O_2$ requires C, 80.76; H, 6.4 %). This readily furnished the dibromide when its solution in chloroform was treated with a dilute solution of bromine in chloroform. The dibromide crystallized from methanol as platelets of m.p. 138–142° (micro) and needles m.p. 158–161° (micro). The mixture melted over a range (138–148°, micro). (Found: C, 50.0; H, 3.9. $C_{17}H_{16}O_2Br_2$ requires C, 49.6; H, 3.9 %). Microhydrogenation of the triene

in palladium black/acetic acid showed (0.97) one double bond.

13:14-Dimethoxy-3:4-5:6-dibenzocyclohepta-3:5-diene:- The above triene (50 mg) was hydrogenated by means of palladium black in acetic acid at room temperature and pressure. After the absorption of hydrogen was complete, the solution was filtered and the filtrate on concentration in vacuo furnished the dihydride as colourless plates (from dilute acetic acid) m.p. 73-75° (micro). (Found: C, 80.1; H, 7.5. $C_{17}H_{18}O_2$ requires C, 80.3; H, 7.1 %).

Oxidation of 13:14-dimethoxy-3:4-5:6-dibenzocyclohepta-1:3:5-triene with osmium tetroxide:- A solution of triene (50 mg) in dry ether (5 c.c.) was treated with osmium tetroxide (60 mg) in ether (5 c.c.). After 4 days, the ether was evaporated and the residual black powder heated under reflux for 2½ hours with a solution of hydrated sodium sulphite (0.7 g) in water (10 c.c.) and methanol (15 c.c.). Undissolved solid was collected, extracted twice with boiling methanol, and the combined filtrate and extract boiled with charcoal and evaporated under reduced pressure. The residue was treated with water and the suspension extracted with ether. Evaporation of the ether afforded cis-1:2-dihydroxy-13:14-dimethoxy-3:4-5:6-dibenzocyclohepta-3:5-diene, as colourless needles

(from methanol-water mixture), m.p. 166-167 (micro). (Found: C, 71.4; H, 6.5. $C_{17}H_{18}O_4$ requires C, 71.3; H, 6.3 %).

2:3-Dimethoxy-10-phenanthraldehyde:- Lead tetra-acetate (50 mg) was added portion wise, with shaking and exclusion of moisture to a solution of the above cis-glycol (30 mg) in dry benzene (10 c.c.) maintained at 40°. The mixture was heated to boiling and then set aside for an hour at room temperature. After filteration, the benzene solution was washed with water, dried, and evaporated. A solution of the resulting gum in methanol with a trace of sodium carbonate to the hot solution, caused immediate crystallization of the aldehyde m.p. 171-172°. Mixed m.p. with an authentic sample was undepressed, while with a specimen of 2:3-dimethoxy-9-phenanthraldehyde m.p. 135-136°, was depressed to 116-118°.

Homoveratric Acid:- It was prepared according to the method given in Organic Synthesis Collective volume II, p. 333.

2-Amino-α-(3:4-dimethoxy)phenyl-cinnamic Acid:- This was prepared according to the method of Pschorr[31] as yellow platelets m.p. 173°. (Found: C, 68.35; H, 5.9; N, 5.1. $C_{17}H_{17}NO_4$ requires C, 68.2; H, 5.7; N, 4.7 %).

"Nitrogeneous" Compound:- When the above amino acid was treated in a similar manner as given by Pschorr[31] for the synthesis of the required 2:3-dimethoxyphenanthrene-10-carboxylic acid, only a nitrogeneous substance soluble in hot alkali was isolated as colourless crystals (from methanol) m.p. 180-181°. (Found: C, 67.8; H, 5.5; N, 8.9 %). Various other modifications of the Pschorr synthesis were tried but without any success[32].

2-Chloro-α-(3:4-dimethoxy)phenyl-cinnamic Acid:- Sodium salt of homoveratric acid (5g; dried at 130°), o-chlorobenzaldehyde (2.9g) and acetic anhydride (35 c.c.) were heated at 100-110° for 24 hours. The dark brown solution was added in excess of water and heated cautiously to decompose the acetic anhydride. After 18 hours the solid was filtered and extracted several times with dilute sodium carbonate solution. The combined sodium carbonate extracts on acidification furnished the crude acid, which on treatment with charcoal in acetic acid solution, crystallized as colourless crystals (from acetic acid-water mixture) m.p. 127-128°. (Found: C, 63.81; H, 5.0; $C_{17}H_{15}O_4Cl$ requires C, 63.97; H, 4.7 %).

2:3-Dimethoxyphenanthrene-10-carboxylic Acid:- To fused potassium hydroxide (5g), 2-chloro-α-(3:4-dimethoxy) phenyl-cinnamic acid (1g) was added at 260-65° and stirred for 10 minutes. A vigorous reaction took place and the potassium salt separated as a black oil. After cooling slightly, the still molten potassium hydroxide was poured off from the potassium salt, which was extracted with water. The alkaline solution (dark in colour) was treated with dimethyl sulphate at 60-65° with occasional shaking and left overnight at room temperature. The solution was filtered (the black precipitate was not further examined) and heated to 100° to decompose excess of dimethyl sulphate, cooled (charcoal) and acidified when the crude acid was obtained as a dark brown precipitate. This was once again, precipitated after sodium carbonate extraction and charcoal treatment. A sample of this acid after repeated crystallization came as lemon yellow needles m.p. 252° (from alcohol-water mixture; Pschorr also gives the same m.p.)[31]. (Found: C, 72.2; H, 5.3. $C_{17}H_{14}O_4$ requires C, 72.3; H, 5.0 %).

2:3-Dimethoxyphenenthrene-10-carboxylic Acid-methyl ester:- A suspension of the crude acid (5g) in methanol (220 c.c.) and concentrated sulphuric acid (18 c.c.) was heated under

reflux for 7 hours. The solution after concentration was poured in excess water and extracted with ether. The ether solution was washed with dilute sodium hydroxide solution (on acidification it furnished a dark brown solid which was again methylated with dimethyl sulphate and alkali and esterified in the same way), water and dried. After evaporation of ether in vacuum, the gummy liquid was distilled in 0.1 m.m. vacuum air bath temperature 200°. The distillate, on rubbing with methanol, mostly crystallized. After two crystallizations from methanol (charcoal) the ester crystallized as colourless needles of m.p. 115-116°. (Found: C, 72.8; H, 5.3. $C_{18}H_{16}O_4$ requires C, 72.98; H, 5.4 %).

2:3-Dimethoxy-10-phenanthraldehyde:- The ester (0.5 g) was heated for 2½ hours with 99% hydrazine hydrate (2 c.c.) in ethanol (3 c.c.). The hydrazide started separating as long colourless needles after 1½ hours. The crystals were filtered, washed with cold ethanol and dried. Once crystallized from ethanol as colourless needles m.p. 216-17°. (Found: N, 9.9. $C_{17}H_{16}O_3N_2$ requires N, 9.44 %). A solution of the hydrazide (0.5g) in pure pyridine (6 c.c.) was treated with freshly

distilled benzene sulphonylchloride (0.29c.c.) and after 15 hours at room temperatures on being poured into dilute hydrochloric acid at 0°, afforded the phenylsulphonhydrazide as platelets of m.p. 215-216° (from acetic acid). (Found: N, 6.5. $C_{23}H_{20}O_5N_2S$ requires N, 6.4 %). A solution of this compound (0.6g; previously dried at 120°) in ethyleneglycol (8 c.c.) at 180° was treated with anhydrous sodium carbonate (0.39g) and after 80 seconds boiling water (40 c.c.) was carefully added. The solution was cooled and the yellow solid, filtered, washed and crystallized from methanol-chloroform mixture (charcoal) as light yellow needles m.p. 172°. (Found: C, 76.9; H, 5.7. $C_{17}H_{14}O_3$ requires C, 76.7; H, 5.6%).

2:3-Dimethoxy-10-methylphenanthrene:- The 2:3-dimethoxy-10-phenanthraldehyde (2.6g) was heated for 2 hours with 99% hydrazine hydrate (9 c.c.) in ethanol (90 c.c.). Removal of the solvent afforded a yellowish brown solid, which when intimately mixed with powdered potassium hydroxide (5 g) at 120-125° readily gave an effervescent melt. It was maintained at this temperature for 10 minutes and water was added when a greyish coloured solid separated. The solid was filtered, dried and

chromatographed over a column of alumina. On eluting the fluorescent band in u.v. with benzene, it came as colourless needles (from benzene) m.p. 137-38° (mixed m.p. with a specimen of 2:3-dimethoxy-9-methylphenanthrene m.p. 130-31°, was 112-114°). (Found: C, 80.9; H, 6.1. $C_{17}H_{16}O_2$ requires C, 80.9; H, 6.4 %).

cis-9:10-Dihydro-9:10-dihydroxy-2:3-dimethoxy-10-methylphenanthrene:- Pyridine (dried over potassium hydroxide pellets; 0.8 c.c.) was added to a solution of the above methylphenanthrene (0.7 g) in sodium dried thiophen-free benzene (7 c.c.) and osmium tetroxide (1 g). After 7 days the brown precipitate was collected, washed with cold benzene, dried and dissolved in chloroform (25 c.c.) and shaken for 3 hours with a solution of mannitol (18 c.c.) and potassium hydroxide (0.9g) in water (100 c.c.). The yellowish brown chloroform layer was washed with water, dried and on evaporation in vacuo, afforded the glycol as a gum which slowly solidified on rubbing with methanol. After one crystallization from methanol-water mixture at room temperature it crystallized as colourless needles m.p. 120-121°. (Found: C, 71.3; H, 6.0. $C_{17}H_{18}O_4$ requires C, 71.3; H, 6.3 %). The glycol dehydrated readily on heat treatment. When

crystallized from boiling methanol crystals of m.p. 184-185° were obtained. (Found: C, 75.97; H, 5.8. $C_{17}H_{16}O_3$ requires C, 76.03; H, 6.0 %) which, gave a positive ferric chloride test.

13:14-Dimethoxy-3:4-5:6-dibenzocyclohepta-1:3:5-trien-7-one:- Lead tetra-acetate (0.21g) was added to a solution of the diol (0.1 g) in dry benzene (15 c.c.) and the whole mixture shaken for 2 hours and heated under reflux for ½ hour. The cooled suspension was filtered and the filtrate washed with water, dried and concentrated *in vacuo* at 40-50°, affording a colourless gum which gave a positive test with 2:4-dinitrophenylhydrazine. Its solution in acetic acid (5 c.c.) was saturated with dry hydrogen chloride (25 minutes). After 12 hours at room temperature the orange red solution was diluted with water and extracted with ether. The ethereal extract was washed with sodium bicarbonate solution then with water and was dried and concentrated *in vacuo* affording a pale yellow solid which crystallized from benzene-petroleum ether (40-60°) mixture as colourless needles m.p. 149-150°. (Found: C, 76.8; H, 5.5. $C_{17}H_{14}O_3$ requires C, 76.7; H, 5.3 %). When heated for ½ hour with sodium dichromate in acetic acid it afforded the same 2:3-dimethoxyphenanthraquinone

identified by m.p. and mixed m.p.

13:14-Dimethoxy-7-acetamido-3:4-5:6-dibenzocyclohepta-3:5-diene:- The oxime of the above trienone, (0.12g) colourless needles m.p. 179-180°, (from benzene). (Found: N, 4.9. $C_{17}H_{15}O_3N$ requires N, 5.0 %) dissolved in acetic anhydride (7 c.c.) was hydrogenated in presence of Adam's catalyst. Absorption was complete in 1½ hours and the acetamido compound obtained by concentration in vacuo, solidified slowly on rubbing with dilute ethanol. The solid crystallized from ethanol-water mixture as colourless needles m.p. 162-163°. (Found: C, 73.2; H, 6.5; N, 4.5. $C_{19}H_{20}NO_3$ requires C, 73.5; H, 6.4; N, 4.5 %).

Nature of the product obtained on treatment of the above acetamido compound with phosphorus pentoxide in pure xylene:- Phosphorus pentoxide (0.4g) was added to a solution of the above acetamido compound (0.18g) in dry purified xylene and the mixture boiled for 25 minutes. After cooling the xylene solution was filtered and the residue extracted twice with boiling xylene. The combined filtrate and extract washed with dilute sodium carbonate solution, then with water, dried and evaporated under reduced pressure. The gum left behind solidified on scratching

in methanol. After chromatography on alumina (in benzene) it crystallized in platelets (from methanol) of micro m.p. 88-90° (mixed melting point with a sample of 13:14-dimethoxy-3:4-5:6-dibenzocyclohepta-1:3:5-triene, micro m.p. 112-115°, was over a range 86°-102°). It was not a case of polymorphism as a solution of the above product in methanol and also the melt while taking a micro m.p. when seeded with the compound of m.p. 112-115° afforded the same platelets of m.p. 88-90°. This product of m.p. 88-90° (4 mg) was micro hydrogenated in the presence of palladium black in acetic acid at room temperature and pressure. The absorption was complete in 15 minutes (no. of double bonds 0.94). The solution was taken in large excess of acetic acid, filtered and then evaporated under reduced pressure. The residue was taken in methanol (very soluble) and transferred to a test tube by means of a dropper. The methanol was evaporated off and the substance crystallized from dilute acetic acid. An excellent yield of colourless platelets of micro m.p. 73-75° was obtained. Mixed melting point with an authentic specimen of 13:14-dimethoxy-3:4-5:6-dibenzocyclohepta-3:5-diene was undepressed.

On one occasion, when the above mentioned acetamido compound was treated with phosphorus pentoxide in xylene

(dried over phosphorous pentoxide only and not purified in the manner mentioned before) only a gummy liquid was obtained, which failed to crystallize. This was treated in two ways. (a) Its solution in acetic acid when heated with sodium dichromate (½ hour) afforded the same 2:3-dimethoxyphenthraquinone as identified by m.p. and mixed m.p. (b) The gum (42 mg) was oxidized with osmium tetroxide in ether as described before. No corresponding solid glycol could be obtained. This on further oxidation with lead tetra-acetate and working up in the usual way deposited some crystals (from methanol) of micro m.p. 92-104°. When this substance was mixed with a specimen of 2:3-dimethoxy-9-phenanthraldehyde (m.p. 135°), the m.p. was raised to 120-125°. One individual crystal was selected which had micro m.p. 134-136°. Mixed m.p. with a specimen of the 2:3-dimethoxy-9-phenanthraldehyde showed no depression.

Treatment of 13:14-dimethoxy-3:4-5:6-dibenzocyclohepta-1:3:5-triene with sodium ethoxide in ethanol:- This was done under similar conditions as used by Ingold and Shoppee[26]. The triene (100 mg) was added to a solution of sodium metal (100 mg) in ethanol (4 c.c.) and the solution heated at 85°. After 10 hours the solution

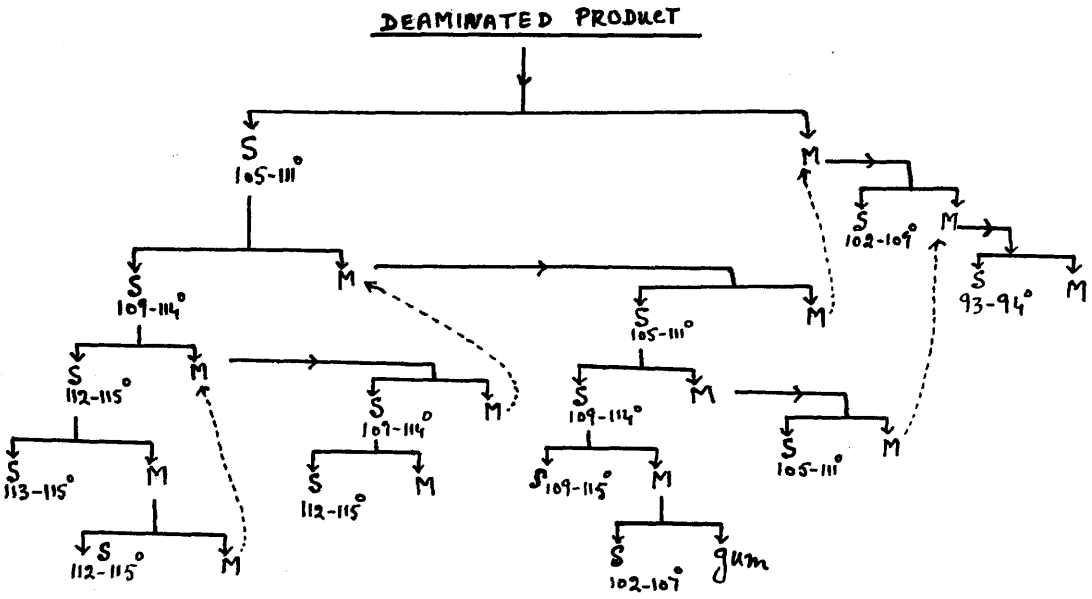
was cooled and the products poured into water and extracted with ether. The ether extract washed with calcium chloride solution, dried and evaporated in vacuo affording a gum which immediately crystallized when taken in methanol, as fine colourless needles (70 mg) m.p. 111-114° (micro). Mixed m.p. with the starting material was undepressed. The mother liquor on concentration furnished another batch (after one crystallization) of the same material (15 mg).

In another experiment the triene (70 mg) was treated with a solution of sodium metal (.14g) in ethanol (3 c.c.) and the whole heated to 85° for 10 hours. Again the starting material was obtained (52 mg) as identified by m.p. and mixed m.p.

Fractional crystallisation of the triene XLVIII in Methanol

S = Solid , M = mother liquor.

The figures indicate the micro m.p. of the solid.

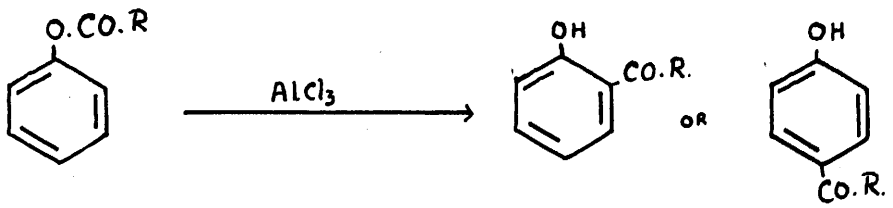

DEAMINATED PRODUCT
S 105-111°
M
S 102-109°
M
S 93-94°
M
S 109-114°
M
S 112-115°
M
S 113-115°
M
S 112-115°
M
S 109-114°
M
S 112-115°
M
S 105-111°
M
S 109-114°
M
S 109-115°
M
S 102-107°
gum
S 105-111°
M

Part II

ATNew Molecular Rearrangement effected by Aluminium Chloride

A New Molecular Rearrangement effected by Aluminium chloride

Various molecular rearrangements are known to have been effected by anhydrous aluminium chloride. The best known of these is the Fries rearrangement where phenolic esters are converted into hydroxy aromatic ketones[33] e.g.

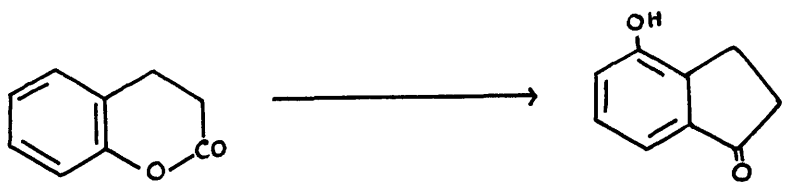


Other rearrangements, less widely studied, include the conversion of alkylphenyl ethers into substituted phenols; sym-acid chlorides of dicarboxylic acids into the lactone form and N-aryl phthalimides into lactams[34].

It has now been found that chromanone (LVIII) on treatment with anhydrous aluminium chloride at 180-190° for 1 hour, is rearranged to the known 7-hydroxy indanone (LIX) in very good yield.

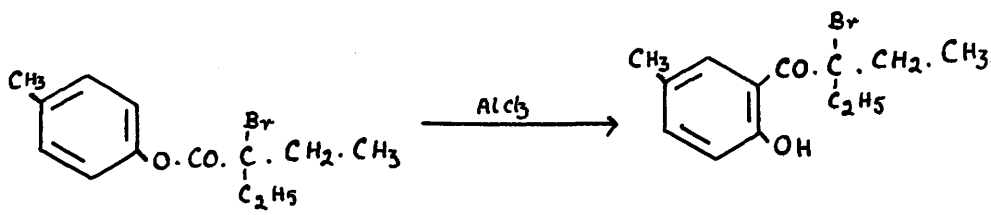
(LVIII) (LIX)

Similarly, dihydrocoumarin (LX) furnished the hitherto unknown, 4-hydroxyindanone (LXI).

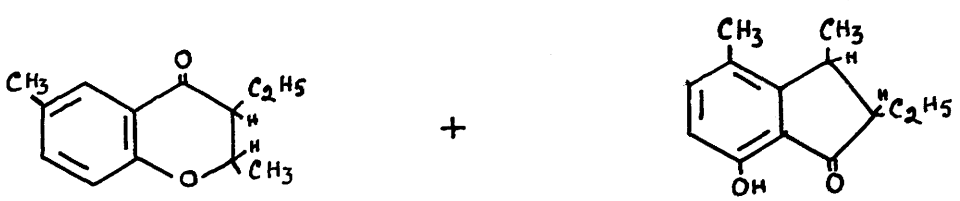


(LX) (LXI)

Although such rearrangements have never before been reported it is possible that the known change of (LXII) to (LXV) proceeds <u>via</u> the chromanone (LXIV) by this



(LXII) (LXIII)



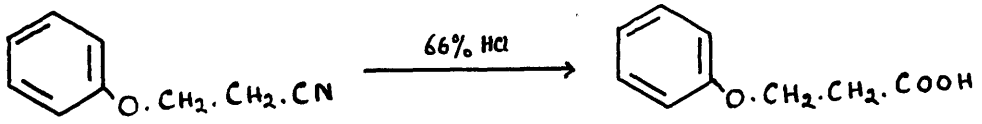
(LXIV) (LXV)

type of rearrangement. On the other hand this interpretation seems a bit unlikely as the conditions used are not the same as those for the conversion of (LVIII) to (LIX)[35].

This new rearrangement offered an attractive route to derivatives of indanone, especially when an improved method was developed for the synthesis of chromanones.

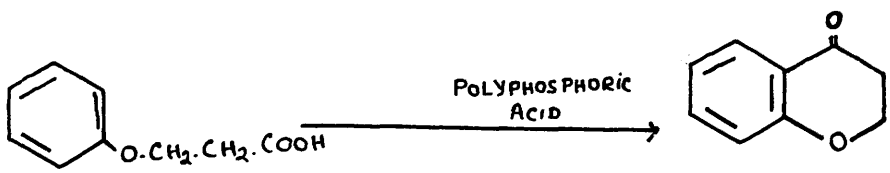
An Improved Synthesis of Chromanones:-

A. H. Cook and Reed[36] showed for the first time that acrylonitrile adds to phenols in the presence of sodium or sodium methoxide to give the corresponding propionitriles. Bachman and Levine[37] improved the yield in this reaction by using Triton B as the condensing agent (in the case of phenol, yield 79%). In the present investigation phenol was condensed with acrylonitrile according to the method of Cook and Reed[36] and the propionitrile (LXVI) on acid hydrolysis (66% hydrochloric acid) furnished the required β-phenoxypropionic acid (LXVII) in excellent yield.



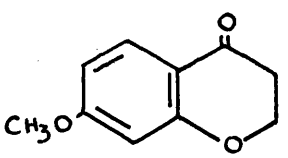
(LXVI) (LXVII)

Hitherto this acid had been obtained in comparatively poor yield either by the condensation of a β-halogeno-propionic acid (usually the β-chloro acid) with the potassium or sodium salt of the phenol[38] or by the oxidation of γ-phenoxypropyl alcohol[39]. β-Phenoxy-propionic acid (LXVII) has been cyclised to the chromanone (LVIII) in various ways e.g. directly on the acid by the action of zinc chloride[40] or phosphorus pentoxide or on the acid chloride with aluminium chloride[41]. So far the most satisfactory had been due to Gottesman[42] who obtained chromanone (LVIII) in 25% yield by using a mixture of sulphuric acid and acetyl chloride. Attempts were made by Bachman and Levine[43] to cyclise the nitrile (LXVI) directly to the chromanone (LVIII) by using 85% sulphuric and phosphoric acids but the yield was extremely poor probably because sulphonation and phosphorylation led to considerable amounts of water soluble-ether in soluble products. However it has now been found that on treatment of the acid (LXVII) with polyphosphoric acid with heating on the water bath, an 85% yield of chromanone (LVIII) is obtained.

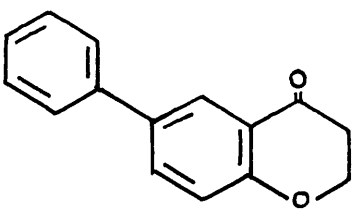


Polyphosphoric acid is becoming an important reagent for effecting cyclisations[43] and it is the case of reaction (with no charring) and high yield of the cyclised product which makes this method of synthesis of chromanone superior to others already known.

It might be mentioned at this stage that by the application of this method the known chromanone (LXVIII) has been obtained in very good yield and a new phenyl chromanone (LXIX) has also been synthesised.



(LXVIII)



(LXIX)

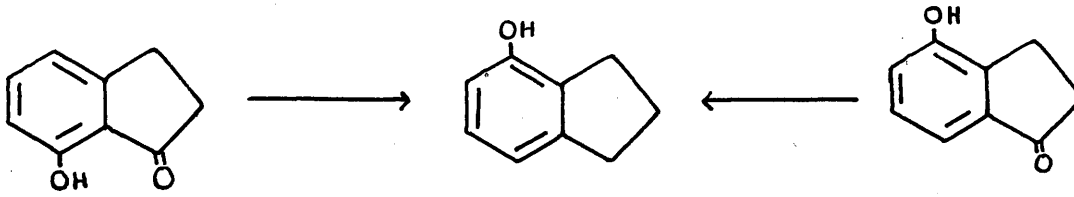
Rearrangement to Hydroxy Indanones:-

As mentioned before, chromanone (LVIII) prepared according to the new method described above was treated with anhydrous aluminium chloride at 180-190° for 1 hour. There was an initial vigorous reaction round about 100° with much evolution of hydrogen chloride.

The dark brown solid mixture thus obtained was decomposed by ice-hydrochloric acid mixture and on steam distillation furnished the known 7-hydroxyindanone (LIX) as identified by its melting point, semicarbazone derivative and the corresponding methoxy compound. 7-Hydroxyindanone gave a deep blue colour with alcoholic ferric chloride solution (the steam volatility and ferric chloride colour both pointing towards the presence of chelation). No trace of any other compound could be found in the non-steam volatile portion. The rearrangement was also effected at 220° but no other compound except the 7-hydroxyindanone (LIX) was isolated.

Similarly when dihydrocoumarin (LX)[44] was treated with anhydrous aluminium chloride at 170-180° for 3 hours and worked up in the same way, an alkali soluble, non-steam volatile, crystalline solid was isolated. It gave a positive 2:4-dinitrophenyl hydrazine test, a reddish brown colour with alcoholic ferric chloride solution and readily furnished the corresponding methoxy compound when treated with methyl iodide in presence of anhydrous potassium carbonate in acetone solution. By analogy with the rearrangement of chromanone (LVIII) to 7-hydroxy-indanone (LIX) and on the basis of its analysis and the

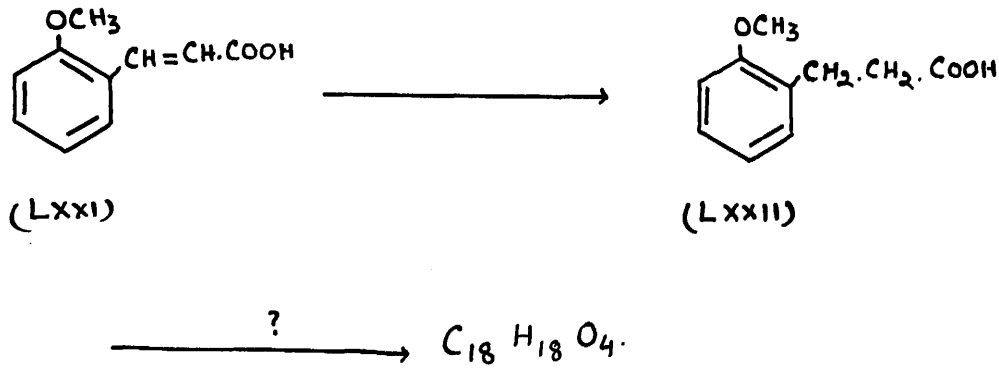
above mentioned properties it has been assigned the structure (LXI). All other hydroxy indanones are already known and the structure is also proved by the fact that both the rearranged products (LIX) and (LXI) furnished the same, known, hydroxyindane (LXX) on Clemmensen reduction.



(LIX) (LXX) (LXI)

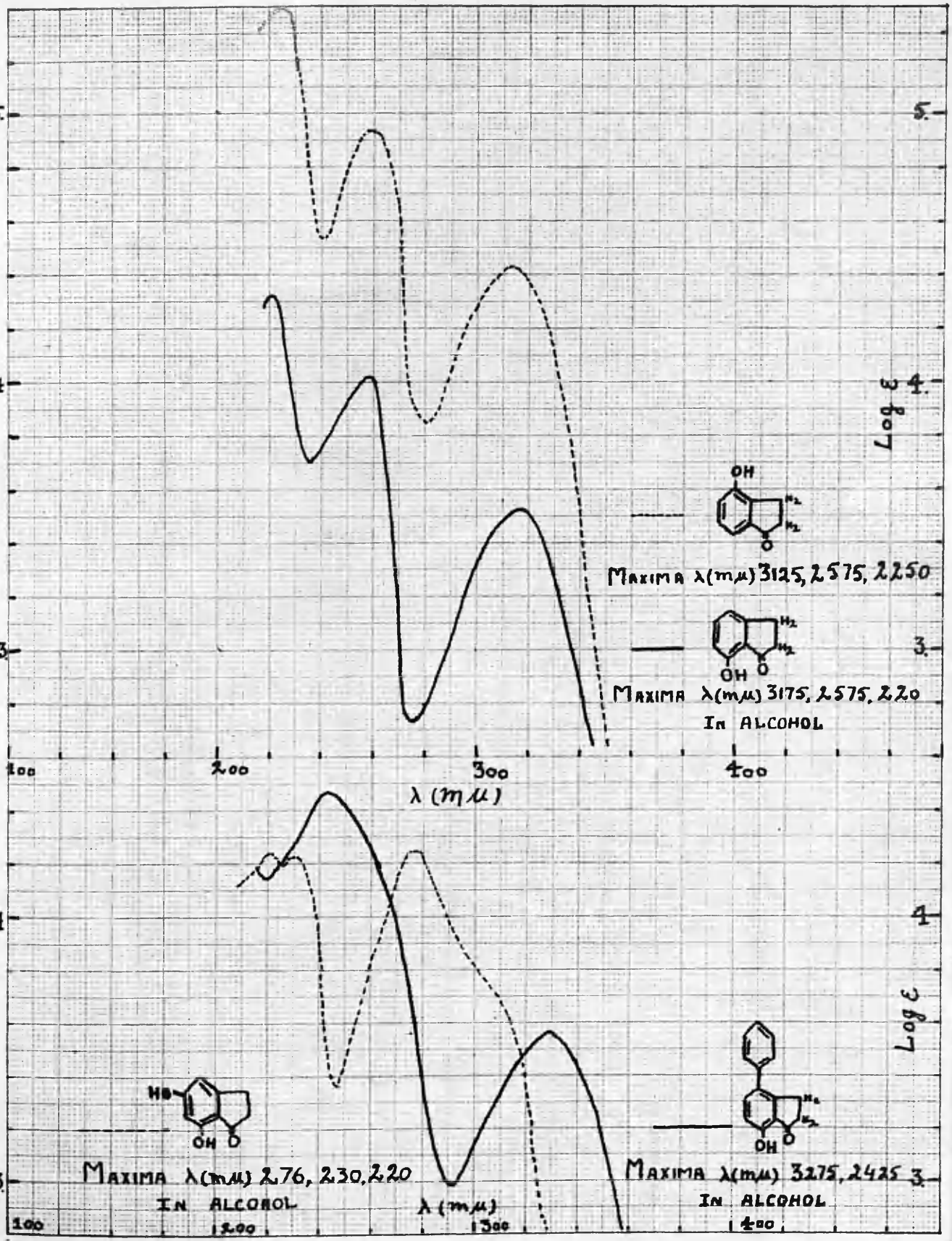
The rearrangement was also effected at 210° for 1 hour and at 230° for 1 hour but in each case only the same non-steam volatile compound (LXI) was isolated with absolutely no trace of any steam volatile product. This search, for another compound, was made with a view to throwing some light on the mechanism of this rearrangement and is discussed more fully later.

An attempt was made to synthesise 4-methoxy indanone by effecting a cyclisation of the known o-methoxydihydro-cinnamic acid. o-Methoxy cinnamic acid (LXXI) was



easily hydrogenated in the presence of palladium black in glacial acetic acid to (LXXII) and on treatment of this with polyphosphoric acid (other methods of cyclisation having already failed to give a crystalline product)[45] a high melting crystalline solid was isolated in poor yield. The analysis and molecular weight data are in good agreement with the molecular formula $C_{18}H_{18}O_4$ for this compound. It is difficult to comment on the nature of this compound but it is definitely not the expected 4-methoxy indanone. Examples are known in the literature where cyclisations do not go in a position - meta to a methoxy group[46].

It is interesting to compare the U.V. Spectra of 7-hydroxyindanone (LIX) and 4-hydroxyindanone (LXI). In shape the curves are very similar which again points to similarity in structure but the maximal


5
4
3
Log ε
100
200
300
400
λ (mμ)
OH
Maxima λ(mμ) 3125, 2575, 2250
OH
Maxima λ(mμ) 3175, 2575, 220
In alcohol
4
3
Log ε
OH
Maxima λ(mμ) 2.76, 230, 220
In alcohol
OH
Maxima λ(mμ) 3275, 2425
In alcohol
100
200
λ (mμ)
300
400

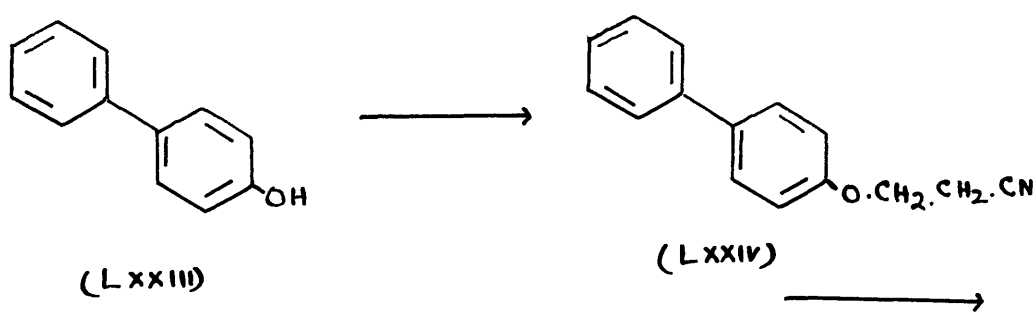
intensity in the case of (LXI) is much more than in that of (LIX). This is in complete agreement with the spectra of salicylaldehyde and parahydroxybenzaldehyde, the intensity in the latter case being more than that of the former[47].

Scope of the Rearrangement:-

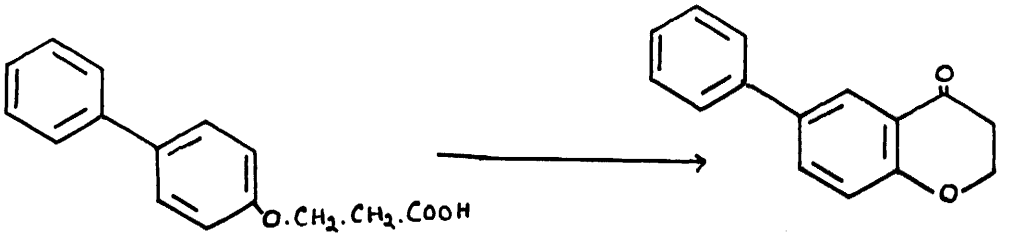
It is obvious that by means of this rearrangement one could get easily to the indanone system and it would be interesting to study the behaviour of various substituted chromanones on similar treatment. As an example of this, and with a specific objective in mind, rearrangement was tried on a new phenyl chromanone.

Phenylhydroxyindanones:-

As mentioned before, by the application of the same method as used for the synthesis of chromanone (LVIII), the synthesis of 6-phenylchromanone (LXIX) has now been accomplished, according to the Scheme shown below.



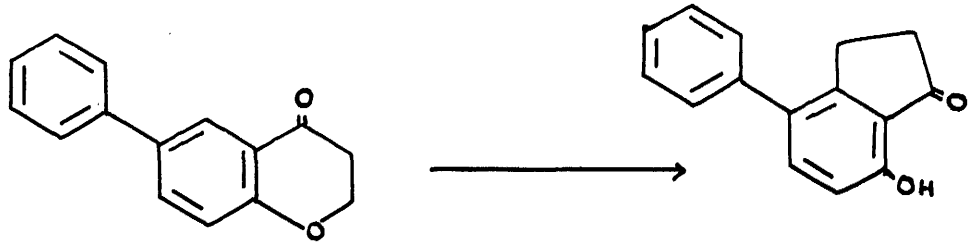
(LXXIII) (LXXIV)



(LXXV) (LXIX)

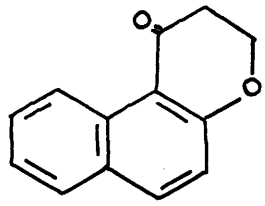
p-Phenylphenol (LXXIII) condensed with acrylonitrile in the presence of sodium methoxide in very good yield when heated in an autoclave at 140-150° for 5 hours. On boiling with 50% sulphuric acid the nitrile (LXXIV) was smoothly hydrolysed to the acid (LXXV), which, on treatment with polyphosphoric acid cyclised to the chromanone (LXIX) in 78% yield. When the chromanone (LXIX) was subjected to the conditions of the rearrangement with anhydrous aluminium chloride only a trace of a phenolic material was isolated. The rearrangement was tried on a whole range of temperatures from 145° to 210° but without any success. Even in nitrobenzene solution the yield of the rearranged material was extremely poor. However on treatment with sodium chloride-aluminium chloride melt, a crystalline product in 66% yield was isolated. It gave an intense blue colour with

alcoholic ferric chloride solution, a positive test with 2:4dinitrophenylhydrazine and formed a sparingly soluble sodium salt which could be crystallised from water as yellow silky needles m.p. 275-77°. The U.V Spectra is very similar to that of 7-hydroxyindanone (LIX) with a shift to the right which is to be expected because of the phenyl substitution in 4-position. It has been assigned the structure (LXXVI).

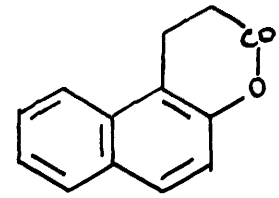


(LXIX) (LXXVI)

Further study was undertaken especially with a view to throwing some light on the mechanism and enlarging the scope of this rearrangement. The easy accessibility of the compounds (LXXVII) and (LXXVIII) at once suggested the possibility of getting to hydroxy-perinaphthenones



(LXXVII)

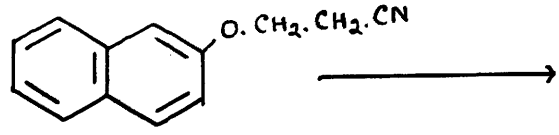


(LXXVIII)

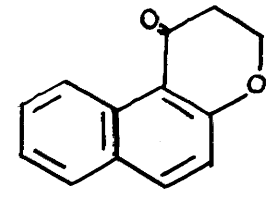
by means of this rearrangement. It has now been found to be so.

Hydroxy-Perinaphthenones:-

The compounds (LXXVII) and (LXXVIII) are both already known. The former was easily prepared from β-naphthol by condensation with acrylonitrile in the presence of triton B followed by cyclisation with 85% sulphuric acid of the nitrile (LXXIX) to the required chromanone[48].

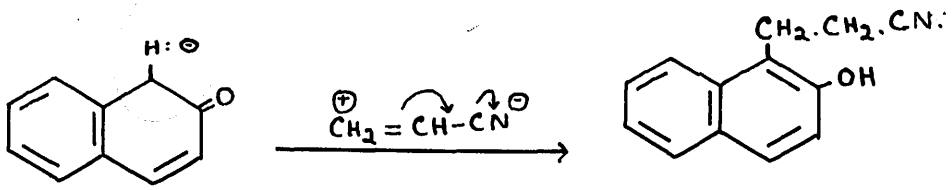


(LXXIX)



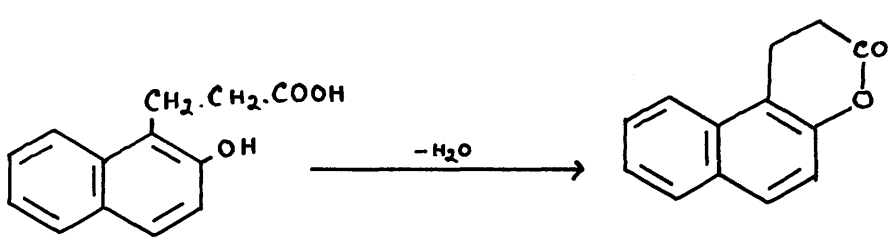
(LXXVII)

However Hardman[49] has shown that when a mixture of β-naphthol, acrylonitrile and benzene is refluxed in the presence of sodium hydroxide pellets, the compound (LXXXI) is formed.



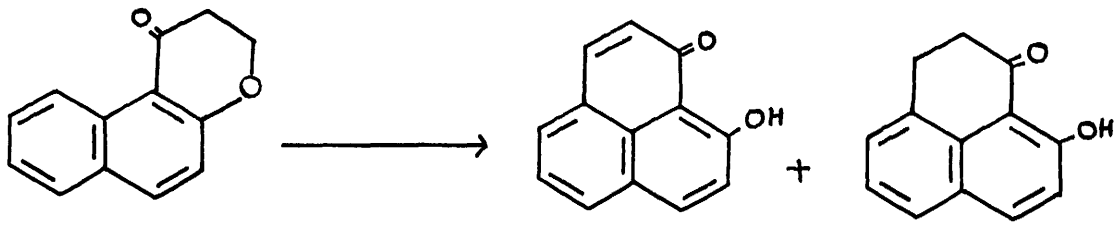
(LXXX) (LXXXI)

Probably β-naphthol reacts in the form (LXXX) in the presence of excess sodium hydroxide (the quantity used is much more than used as a catalyst). On alkaline hydrolysis the corresponding acid (LXXXII) was formed which on distillation furnished the required lactone (LXXVIII).



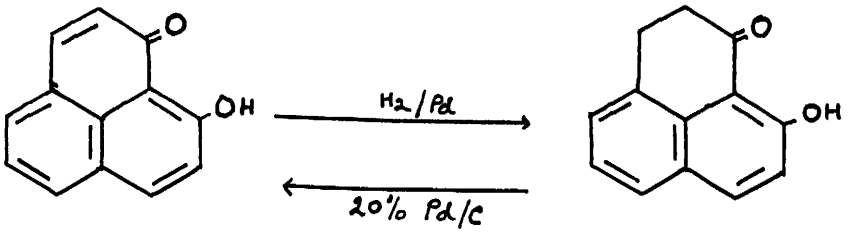
(LXXXII) (LXXVIII)

When the benzo (*f*) chromanone (LXXVII) was treated with anhydrous aluminium chloride at 190-200° for 1 hour and worked up in the usual way, a mixture of 6-hydroxyperinaphthenone-7 (LXXXIII) and the corresponding 8-9-dihydro compound (LXXXIV) was obtained.

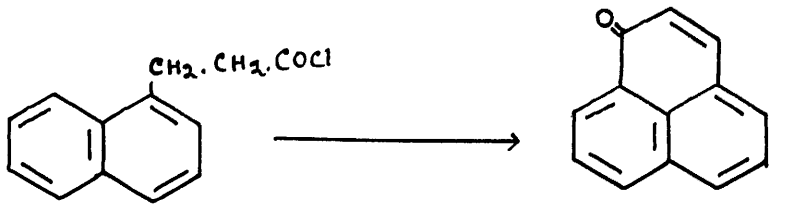


(LXXXIII) (LXXXIV)

The mixture was easily separated into its components by passing dry hydrogen chloride through its benzene solution. The hydrochloride of (LXXXIII) was precipitated and a fraction rich in (LXXXIV) was isolated from the benzene solution. Also, on catalytic hydrogenation in the presence of palladium black in acetic acid solution, 6-hydroxyperinaphthenone-7 (LXXXIII) showed the presence of 1 double bond and gave the same 8:9 dihydro compound (LXXXIV) which in turn on dehydrogenation with 20% palladium charcoal gave the 6-hydroxyperinaphthenone-7 (LXXXIII).



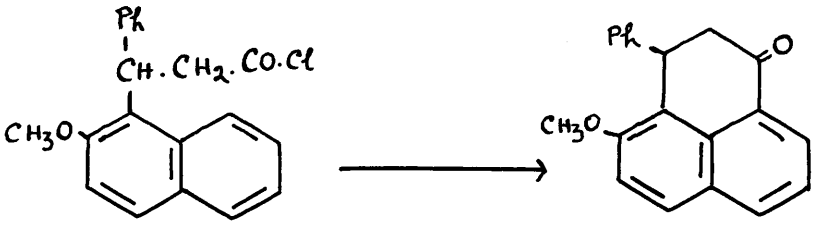
The fact that this rearrangement of benzo (*f*) chromanone (LXXVII) to (LXXXIV) is accompanied with dehydrogenation (formation of LXXXIII) is in complete agreement with the findings of Cook and Hewett[50] who obtained 7-perinaphthenone (LXXXVI) and not the corresponding 8:9-dihydro compound during the cyclisation of



(LXXXV) (LXXXVI)

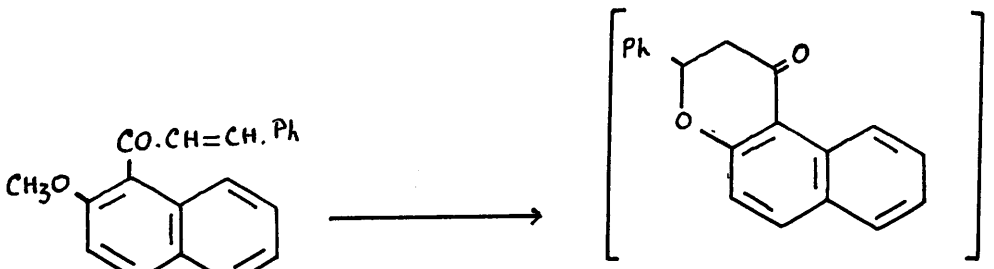
β-(naphthyl-1)-propionyl chloride (LXXXV). It might be mentioned here that Koelesch[51] did succeed in getting

the dihydro compound (LXXXVII) through the cyclisation of the corresponding acid chloride.

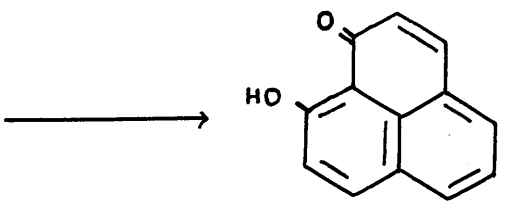


(LXXXVII)

It is interesting to note that the compound (LXXXIII) has already been prepared, albeit in a curious way by Koelsch and Anthes[52]. They found that LXXXVIII was



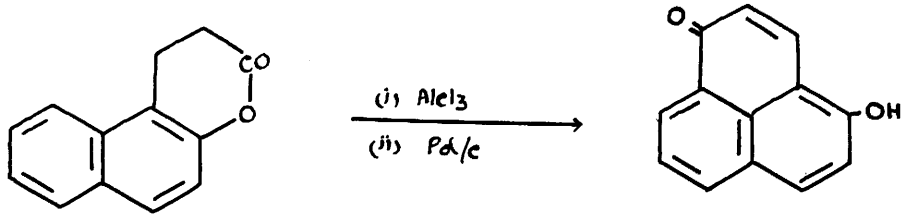
(LXXXVIII) (LXXXIX)



(LXXXIII)

converted through an intermediate of the type (LXXXIX) into 6-hydroxy-perinaphthenone-7 (LXXXIII) with elimination of benzene.

The lactone (LXXVIII) on similar treatment with aluminium chloride at 140-150° for 10 minutes furnished a mixture of gum and crystals which was dehydrogenated in the presence of 20% palladium charcoal in trichlorobenzene when a crystalline product was isolated. It readily gave the corresponding methoxy and acetyl derivatives. On the basis of its derivatives and by analogy with the rearrangement of dihydrocoumarin (LX) it was assigned the structure (XC).

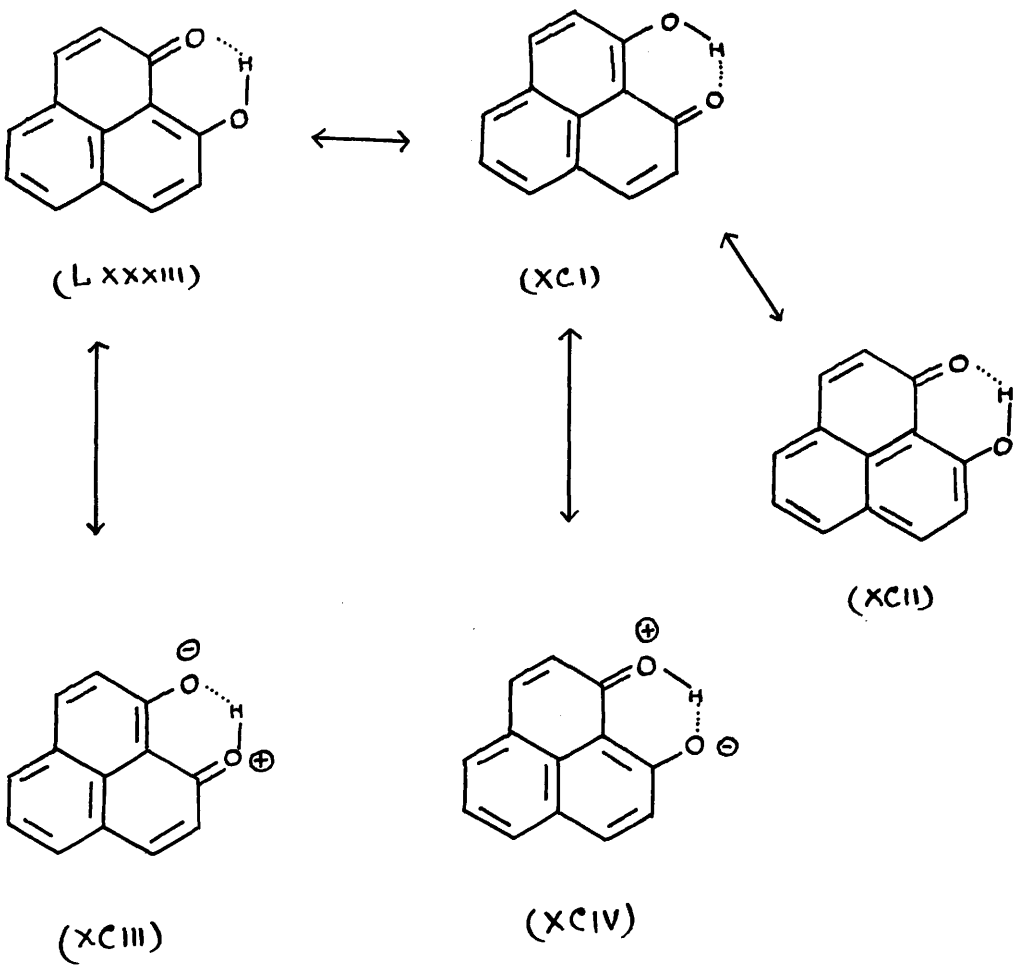


(LXXVIII) (XC)

This structure is also supported by spectroscopic evidence. The shape of the curve is very similar to that of perinaphthenone[63] (LXXXVI) with a shift to longer wavelength which is to be expected due to the presence of the -OH grouping.

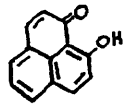
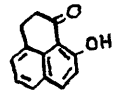
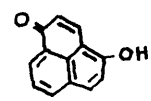
The "Hydrogen Bond":-

Here we have a very interesting series of compounds to study the phenomena of 'hydrogen bonding'. 6-Hydroxy perinaphthenone-7 (LXXXIII) should easily be one of the most strongly hydrogen bonded compounds yet known. The symmetry of the structure makes it possible to resonate in the forms shown below



Moreover the resonance forms (XCIII) and (XCIV) both give a resultant +ve charge to the oxygen atom which donates the proton in hydrogen bond formation and thus increases the ionic character of the O-H bond and the +ve charge of the hydrogen atom. It also gives to the other oxygen atom, the proton acceptor, an increased negative charge. Both these effects and the fact that hydrogen bond formation involves closing a six membered ring, operate to increase the strength of the O-H ... O bond[53].

The difference in physical properties between (LXXXIII) and (XC) also point towards hydrogen bond formation in (LXXXIII) e.g. lower melting point and higher solubility in benzene of (LXXXIII) to that of (XC). A comparative study of the properties of (LXXXIII), (LXXXIV) and (XC) was made and is tabulated below.

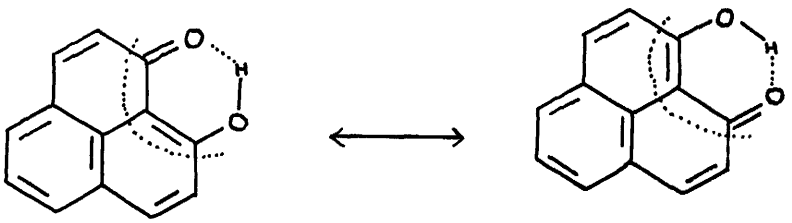
No.	Reagent.			
1.	Alcoholic $FeCl_3$ solution.	brownish-red	reddish-violet changing to green	faint reddish-brown.
2.	2:4Dinitrophenyl hydrazine solution in alcohol	-	"hydrazone"	"hydrazone" (difficulty in isolation).
3.	Acetylation with Ac_2O-H_2SO_4 method	-	"mono-acetate"	"mono-acetate"
4.	CH_3I-K_2CO_3 in Acetone	-	alkali in-soluble gum (could not be crystallised)	"methyl ether"
5.	Diazomethane or Diazomethane-methanol mixture	-	"	
6.	Hydrogenation with Pd black/Ac. acid	1 double bond		1 double bond

It is very interesting to note that whereas the dihydro compound (LXXXIV) and the unchelated compound (XC) give the normal reactions of the groupings present, 6-hydroxyperinaphthenone-7 (LXXXIII) failed to give any derivative when treated under similar conditions. All attempts to methylate (LXXXIII) failed. Koelsch and Anthes[52] also did not succeed in getting any acetyl, benzoyl or methoxy derivative. Also non-ketonic reactivity of (LXXXIII) was shown by the fact that it failed to give an oxime when treated under similar conditions as used by Fieser and Newton[54] for preparing the oxime of perinaphthenone (LXXXVI).

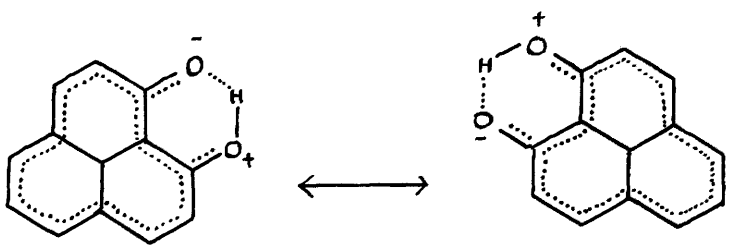
It is known for some time that intramolecular hydrogen bonding affects the vibration of an associated carbonyl group as illustrated by the absorption spectrum of hydroxy anthraquinones[55]. Similarly a comparative study of various aromatic ortho compounds as compared with their meta and para-isomers (e.g. nitrophenols) has shown that phenolic characteristics are to a considerable extent modified as a result of hydrogen bonding[56].

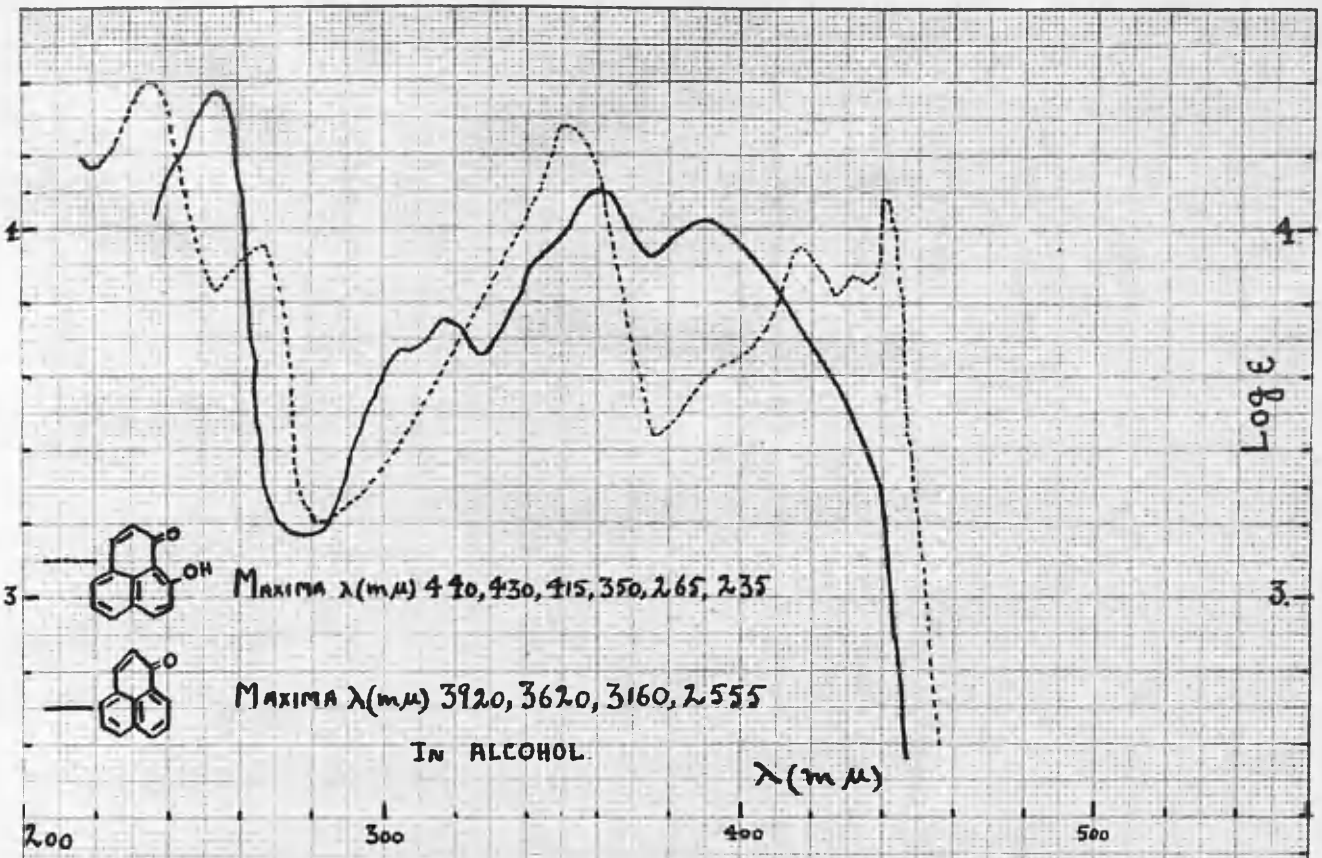
It is now clear from the study of the compounds (LXXXIII), (LXXXIV) and (XC) that the ketonic and phenolic

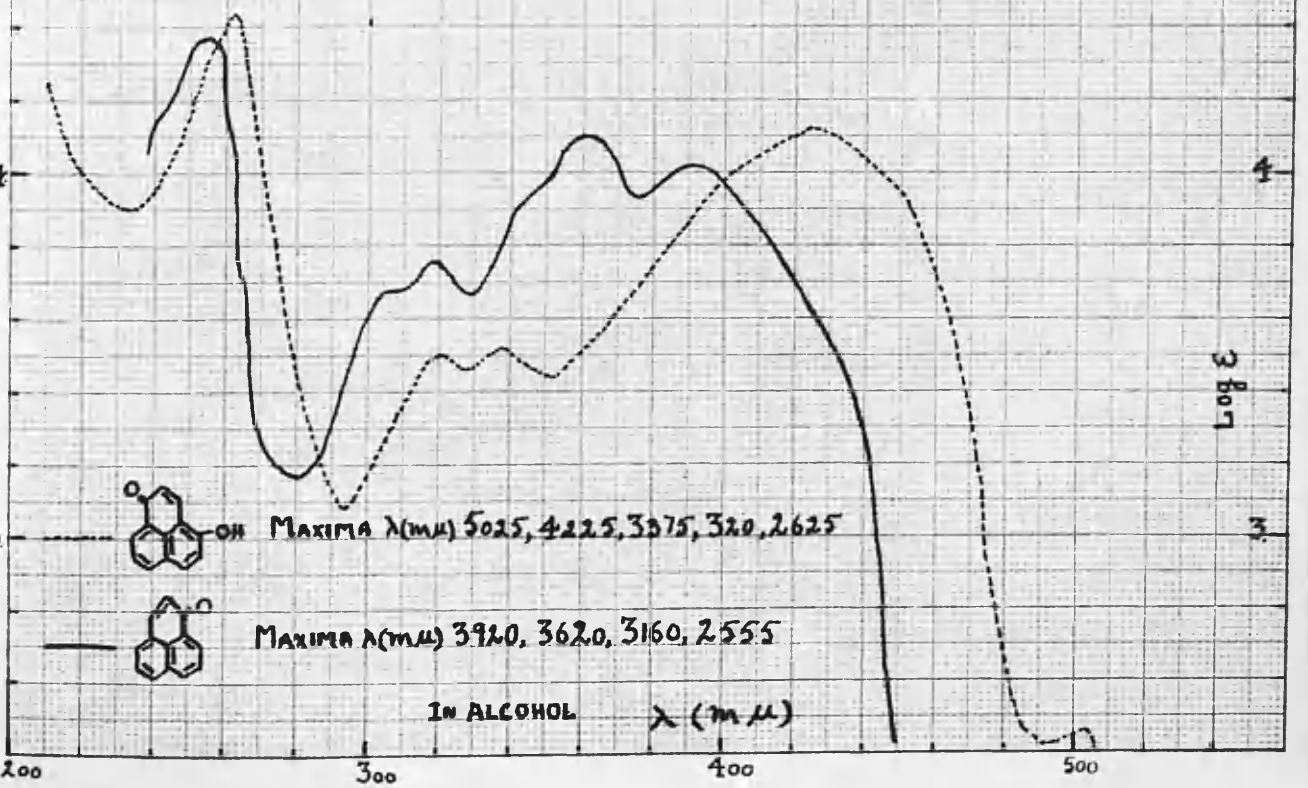
properties are modified only when it is possible to formulate tautomeric or resonating hydrogen-bonded structures as

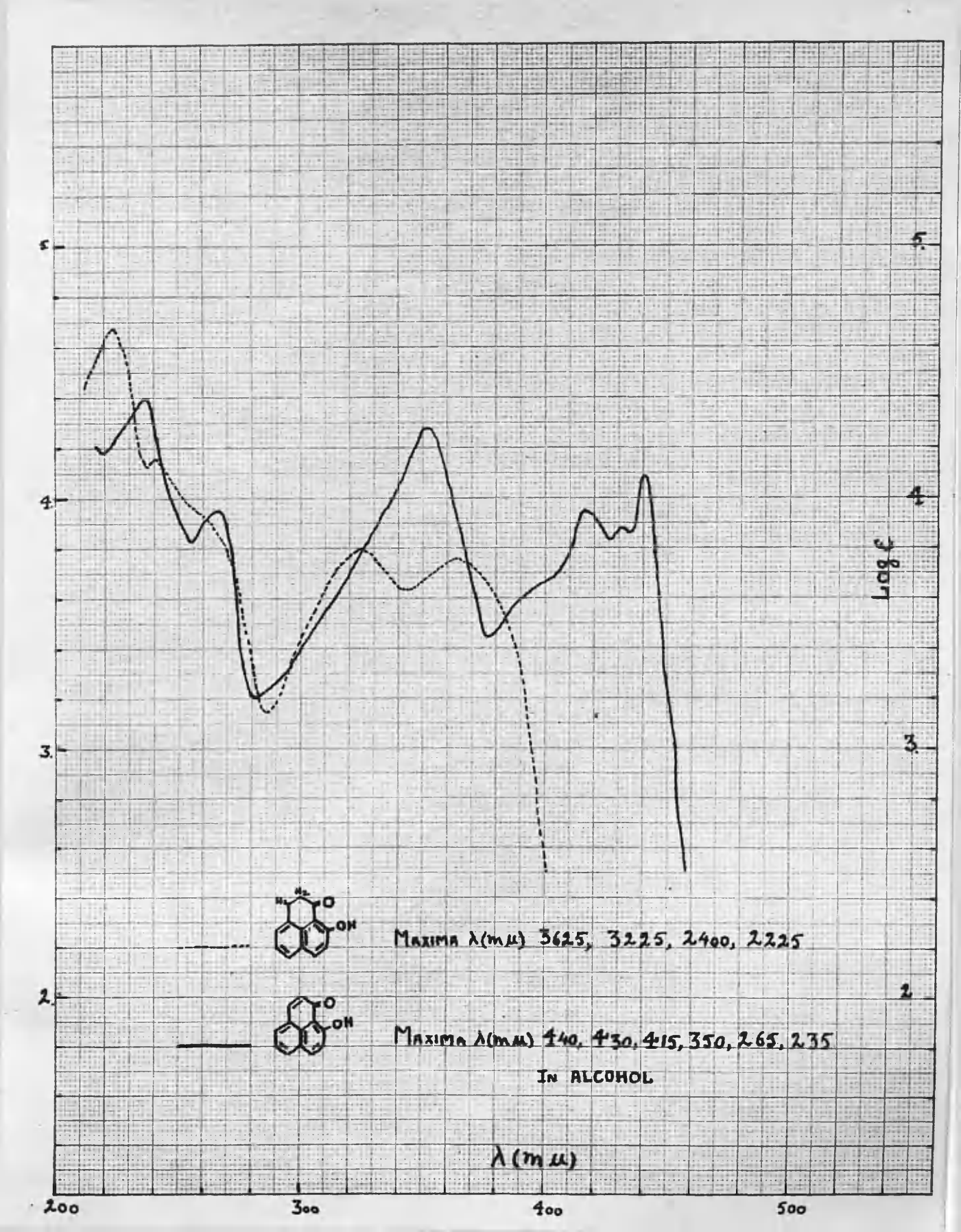


The interesting fact that 6-hydroxy-perinaphthenone-7 (LXXXIII) when hydrogenated in the presence of palladium black in acetic acid gives the corresponding dihydro compound (LXXXIV) shows that the 8.9-double bond retains olefinic character also, thus showing the contribution by structures of the type (LXXXIII). In view of all the properties mentioned above, 6-hydroxy-perinaphthenone-7 (LXXXIII) could be best represented by the following structures



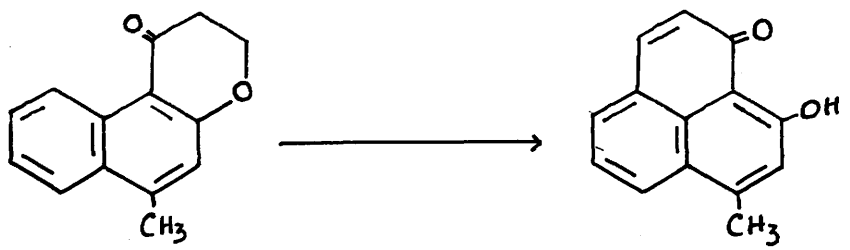

4
3
log ε
3
4
MAXIMA λ(mμ) 440, 430, 415, 350, 265, 235
MAXIMA λ(mμ) 3920, 3620, 3160, 2555
IN ALCOHOL
λ(mμ)
200
300
400
500


4
3
log ε
4
3
MAXIMA λ(mμ) 5025, 4225, 3375, 320, 2625
MAXIMA λ(mμ) 3920, 3620, 3160, 2555
IN ALCOHOL
λ(mμ)
200
300
400
500


5
4
3
2
Log ε
5
4
3
2
O
OH
Maxima λ(mμ) 3625, 3225, 2400, 2225
O
OH
Maxima λ(mμ) 440, 430, 415, 350, 265, 235
In alcohol
λ (mμ)
200
300
400
500

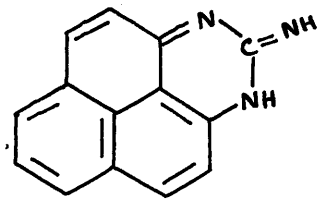
A comparison is made between the U.V. Spectra of 6-hydroxy-perinaphthenone-7 (LXXXIII) and perinaphthenone[63] (LXXXVI). The former is shifted to longer wave lengths (probably due to the -OH group) but with much development of the vibrational fine structure of the bands. On the other hand in the case of the dihydro compound (LXXXIV) the bands are shifted to shorter wave lengths with little fine structure.

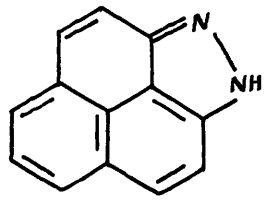
It might be suggested here that similar rearrangement of the compound (XCV) should lead to only one compound (XCVI).



(XCV) (XCVI)

Moreover it should be pointed out that this hydroxy perinaphthenone structure (compound LXXXIII or LXXXIV) has interesting possibilities. Condensation with guanidine or hydrazine hydrate could lead to compounds of the type the chemical behaviour of which would be

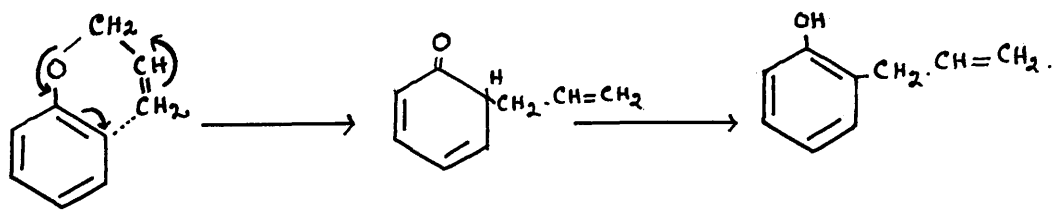




most interesting to study.

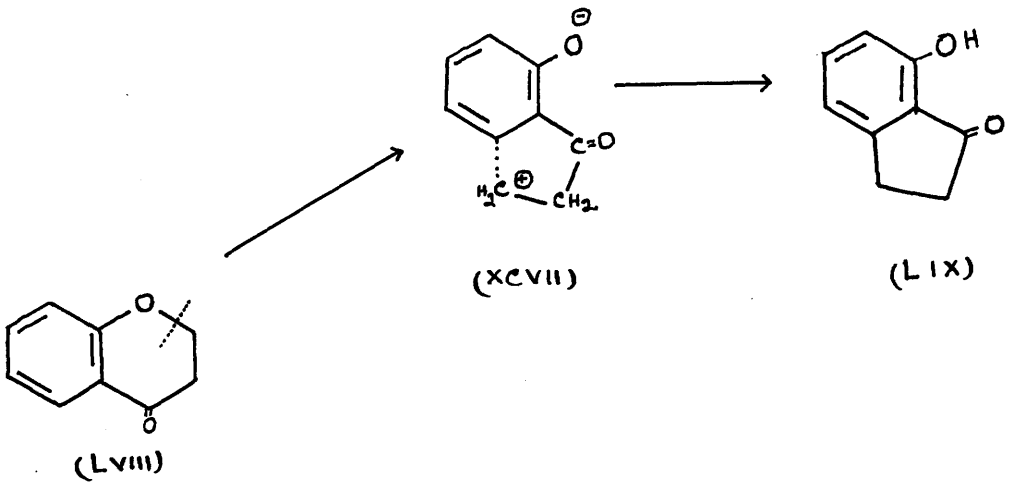
Mechanism of the Rearrangement:-

Very often attempts have been made to put forward mechanisms for various rearrangements on the basis of experimental data e.g. it has been shown that the Fries rearrangement is not an intramolecular reaction whereas the Claisen's rearrangement to the ortho position, is intramolecular since mixtures of ethers do not give cross products as would result from an intermolecular reaction.

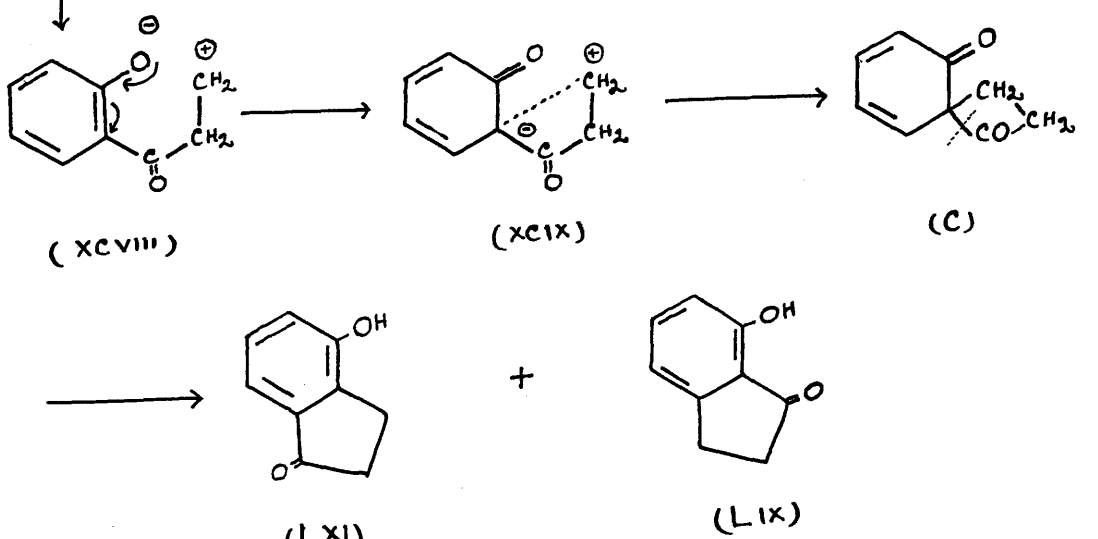


It was therefore thought interesting to find out if this new rearrangement of chromanone (LVIII) to hydroxy indanone was a simple breaking of the ether linkage with a direct, straight forward, linkage to the carbon atom (Scheme a) or it was going through an intermediate of the form (c) (Scheme b). If the

SCHEME a.

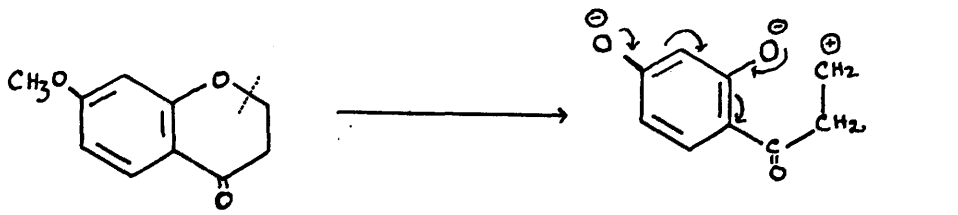


SCHEME b.

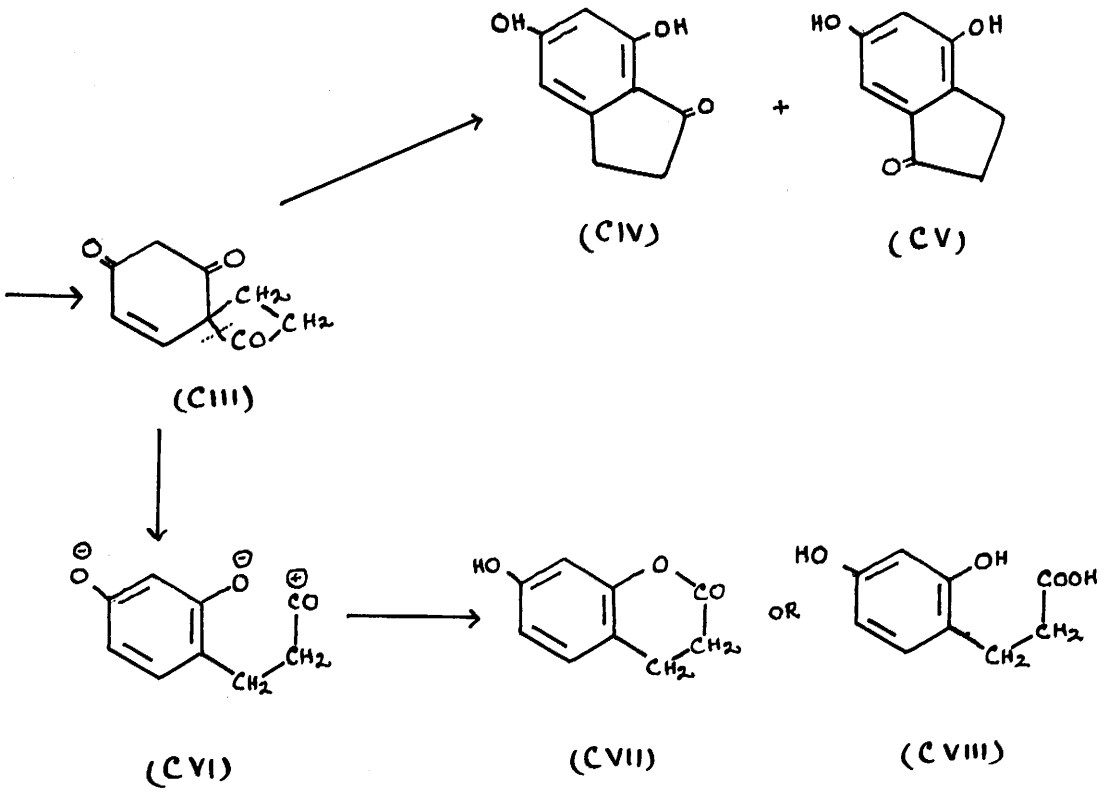


reaction is going through Scheme b then (c) would be expected to give either (LXI) or a mixture of (LXI) and (LIX) as a C-CO-bond should be weaker than a C-CH_2-bond. It was with this idea in view that the rearrangements were effected at various temperatures and a search was made every time to look for a double rearranged product. Since (LIX) is steam volatile and (LXI) is non-steam volatile, it was fairly easily established that only one product was obtained during each rearrangement viz. 7-hydroxyindanone (LIX) from chromanone (LVIII) and 4-hydroxyindanone (LXI) from dihydrocoumarin (LX).

However to throw some further light on the mechanism it was argued that if at all the rearrangement was going according to the Scheme b then in compound (CI)

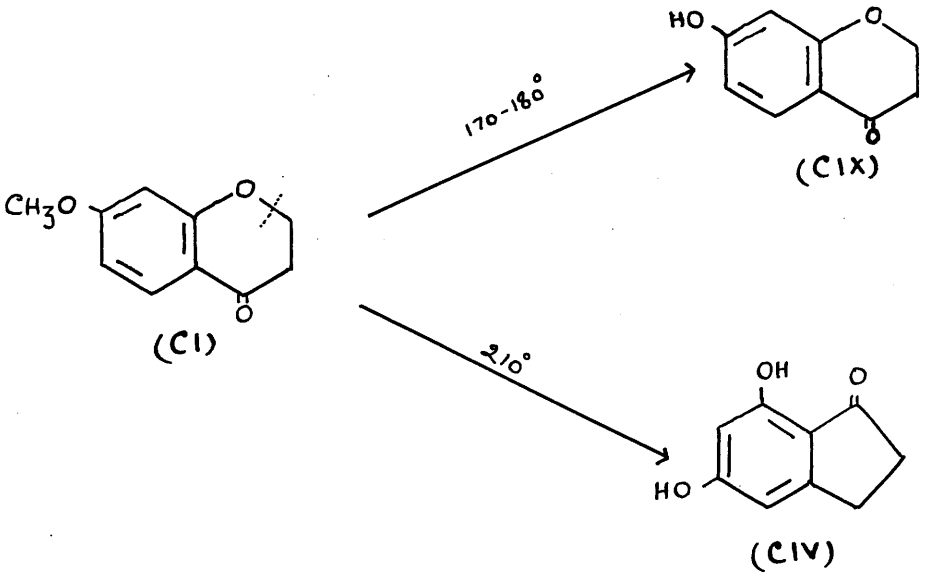


(CI) (CII)



the methoxy group, because of its electron release tendency, would give an increased -ve charge to the p-carbon atom and thus help the formation of the intermediate of the type (CIII) and consequently give either (CV) alone or a mixture of (CV) and (CIV). With this idea in view, rearrangement was tried on 3-methoxy-chromanone (CI). Further, another possibility was considered that the point of cyclisation , because

of the two -OH groups in meta position, might be highly deactivated in which case the lactone (CVII) or the corresponding acid (CVIII) would be expected. When the methoxy chromanone (CI) was subjected to the conditions of the rearrangement as used for chromanone (LVIII), only (CIX) was isolated as a crystalline solid.



However at a higher temperature a very small amount of a phenolic crystalline material was obtained and no acidic material could be isolated. It gave an intense violet colour with alcoholic ferric chloride solution, furnished the corresponding diacetyl derivative when acetylated by the Ac_2O-H_2SO_4 method and gave a positive

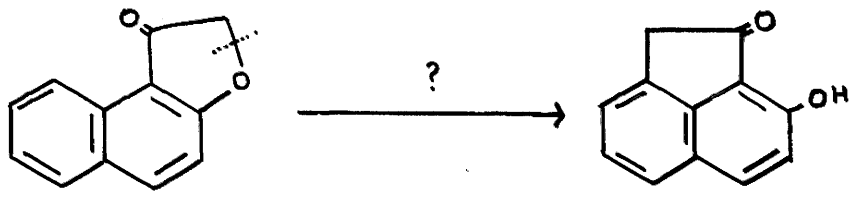
2:4dinitrophenyl hydrazone test. The presence of chelation was shown only by a qualitative colour test (as the quantity of material available was very small) with boroacetic anhydride as used by Dimroth and Faust[64] to differentiate 1-hydroxy from 2-hydroxyanthraquinone. Also, 7 hydroxyindanone (LIX) and 4-phenyl-7-hydroxyindanone (LXXVI) responded to the above test with boroacetic anhydride whereas 4-hydroxyindanone (LXI) did not. In all probability therefore the phenolic material isolated is 7:5-dihydroxyindanone (CIV). Unfortunately the U.V. Spectra could not be of much help in deciding the structure as it is difficult to interpret it especially when no spectra of other dihydroxy indanones is known. The extremely poor yield and the higher temperature required for effecting the rearrangement is probably due to the deactivation of the position of cyclisation as stated before.

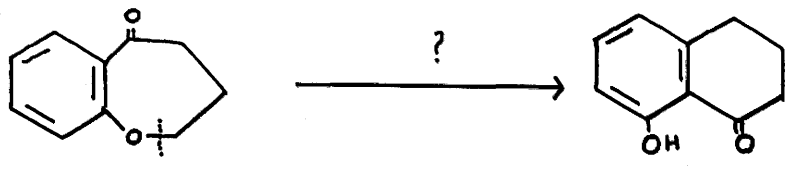
In view of the above discussed facts, it seems most likely that the mechanism of this rearrangement is a straightforward one as shown in Scheme a.

Some Possible applications of this Rearrangement:-

It has already been shown that one could easily get to hydroxy indanones, phenyl hydroxy indanones and hydroxy perinaphthenones by means of this rearrangement.

It would be interesting to see if this would also lead to the acenaphthene and tetralone nucleus as shown below.





The very fact that one could get to such varied types of compounds shows the importance of this rearrangement.

Experimental

Phenoxypropionitrile[36]:-

A mixture of phenol (18.8g), sodium (0.2g) and acrylonitrile (14.0g) was heated in an autoclave for 5 hours at 130-140°. Excess acrylonitrile was removed by distillation under reduced pressure and treated the residue with dilute sodium hydroxide solution to remove unreacted phenol. The solid was washed free of alkali, dried and crystallised from cyclohexane as long colourless needles m.p. 61°.

Phenoxypropionic Acid:-

The above nitrile (1 g) was refluxed with 66% hydrochloric acid (60 c.c.) for 2 hours. At the end of the reaction the oily layer had disappeared and on cooling the acid crystallised out in excellent yield as long needles of m.p. 90-91°. After one crystallisation from water the melting point and the mixed melting point with an authentic specimen (m.p. 96-97°) was 96-97°.

Chromanone:-

Powdered phenoxypropionic acid (0.4g) was slowly added to a mixture of phosphoric oxide (12g) and phosphoric acid (5 c.c; d; 1.7) previously heated on

a steam bath for ½ hour in a 50 c.c. r.b. flask carrying a calcium chloride tube. The colour changed through lemon yellow, orange to deep red-brown. After 2 hours the mixture was poured in excess ice-water mixture. The solution was extracted with benzene (3 x 300 c.c.) after another 2 hours and the benzene extract washed successively with dilute sodium carbonate solution to remove the unreacted acid and then with water. After drying (sodium sulphate) the benzene was removed under reduced pressure. A gum was left behind which on distillation had b.p. 130-132°/15 m.m., crystallised as a solid (from petroleum ether 40-60°) m.p. 38-39°. Semicarbazone (alcohol) m.p. 226-227° yield 85%. (Krollpfeiffer and Schultze[57] report the same m.p.).

Treatment of Chromanone with anhydrous aluminium chloride:-

A mixture of chromanone (1.5g) and anhydrous aluminium chloride (2.7g) was taken in a test tube with a thermometer and heated slowly in a paraffin bath. A vigorous reaction took place between 100-110° with much frothing and evolution of hydrogen chloride. The temperature was then raised to 180-190° and kept there for 20 minutes with occasional stirring when the dark brown mobile liquid started to froth. Finally the

whole mixture was kept at 200° for 15 minutes more, stirring was continued and the liquid turned fairly viscous towards the end. On cooling the dark brownish solid was scraped off the tube, powdered and poured into concentrated hydrochloric acid - ice mixture. A brownish yellow solution was obtained which eventually turned green. This was steam distilled when in the distillate (ca 150 c.c.) a solid, identified as 7-hydroxyindanone was obtained which crystallised as colourless silky needles (from methanol) m.p. 111°. Absorption maxima at 3175, 2575, 220 (log ε 3.52, 4.1, 4.32) in ethanol. It formed a semicarbazone (ethanol) m.p. 242-43° (Auwers and Hillinger[58] report the same melting points) and gave a deep blue colour with alcoholic ferric chloride solution. The non-steam volatile product was extracted with ether. The alkali soluble portion from the ether extract was acidified with dilute hydrochloric acid and extracted with ether. The ether extract was washed, dried (sodium sulphate) and concentrated when only 7-hydroxyindanone (identified by a mixed m.p.) was obtained.

In an other experiment when the rearrangement with aluminium chloride was effected at 220° for 3/4 hours and

working in the same manner as described above, no other compound except 7-hydroxyindanone could be isolated (identified by m.p. and mixed m.p.),

7-Methoxyindanone:-

A mixture of 7-hydroxyindanone (0.3g), potassium carbonate (0.75g), methyl iodide (1 c.c.) and acetone (Analar; 20 c.c.) was heated under reflux. After 4 hours acetone was eveporated in vacuo and water (30 c.c.) was added. This was extracted with benzene and the benzene extract washed with dilute sodium hydroxide solution then with water, dried and on concentration afforded the 7-methoxyindanone as colourless plates m.p. 102-103° from benzene - petroleum ether 40-60° mixture (Found: C, 74.37; H, 6.27. $C_{10}H_{10}O_2$ requires C, 74.04; H, 6.2 %).

Indan-4-ol:-

7-hydroxyindanone (0.2g) was refluxed with a mixture of amalgamated zinc (2g) and dilute hydrochloric acid (30 c.c; 1 vol. of concentrated acid to 2 vol. of water) with occasional addition of dilute hydrochloric acid for 1 hour and then for 2 hours with similar addition of concentrated hydrochloric acid. The solution was cooled, extracted with ether and the ether

extract washed with water, dried and concentrated *in vacuo* when a gum with phenolic odour was left behind. It crystallized as colourless needles (petroleum ether 40-60°) m.p. 48-49°. (lit.[59]. m.p. 49-50°). (Found: C, 80.4; H, 7.3. C_9H_{10} requires C, 80.5; H, 7.5 %).

Dihydrocoumarin[60]:-

Coumarin (21g) was heated under reflux for 2 hours with methanol (160 c.c.) containing sodium methoxide (from 6.9g. of sodium). Water (ca 100 c.c.) was added, most of the methanol was distilled off and the resulting solution was acidified. The collected solid was stirred and shaken with dilute sodium carbonate and the whole extracted with ether to remove coumarin. Acidification of the carbonate solution afforded o-coumaric acid which was crystallised from much boiling water, m.p. 208°.

The above acid (16.7g) was dissolved in 2N sodium hydroxide solution (50 c.c.) and hydrogenated in the presence of palladium charcoal (2 g) at ordinary temperature and pressure. The dihydro acid was recovered in ether and on distillation afforded the dihydrocoumarin with some water. The dihydrocoumarin dried, $CaCl_2$/ in benzene and redistilled at 272-73°/760 m.m.

Treatment of Dihydrocoumarin with Aluminium chloride at 170-180° for 3 hours:-

A mixture of dihydrocoumarin (1.5 g) and aluminium chloride (2.7 g) was treated in a similar manner as described before in the case of chromanone. A vigorous reaction took place at 100° with much evolution of hydrogen chloride. The temperature was then raised to 170-180° and kept there for 3 hours. The dark liquid became slightly viscous towards the end of 3 hours. It was cooled and the powdered brownish-black powder poured into a mixture of ice and hydrochloric acid. A dark brown precipitate in yellowish-brown solution was obtained. After 2 hours this was extracted with ether and the amber coloured ether extract was washed with water, and in turn extracted with dilute sodium carbonate solution (faint turbidity on acidification) and dilute alkali solution. The deep red alkali extract on acidification with dilute hydrochloric acid gave a crystalline compound. This was extracted with ether and the ether extract washed, dried and concentrated when a solid was left behind. After one charcoaling it crystallised as colourless platelets (methanol) m.p. 239-240° (darkens in colour). (Found: C, 72.7; H, 5.6. $C_9H_8O_2$ requires C, 72.9; H, 5.4 %).

Absorption maxima at 3125, 2575, 2250 (log ε , 4.45, 4.94, 5.4) in ethanol. It gave a reddish brown colour with alcoholic ferric chloride solution and furnished the corresponding methyl ether, when refluxed with methyl iodide and potassium carbonate in acetone solution, as silky needles (from methanol) 102-103°. (Found: C, 74.0; H, 6.5. $C_{10}H_{10}O_2$ requires C, 74.04; H, 6.2 %). On Clemmensen reduction, under similar conditions as used for 7-hydroxyindanone, the same Indan-4-ol was isolated as identified by its m.p. and mixed m.p.

Treatment with Aluminium Chloride at 210° for 1 hour:-

The above rearrangement was repeated at a temperature of 210° for 1 hour. Near the end of the reaction the liquid became very viscous and dark in colour. The black powder was decomposed by ice-hydrochloric acid mixture and the amber coloured mixture was steam distilled for ½ hour. No steam volatile product could be detected. Even individual drops of steam distillate when tested with ferric chloride solution, showed no colour change. From non-steam volatile portion only 4-hydroxyindanone was isolated. M.p. and mixed m.p. 239-240°.

Treatment with Aluminium Chloride at 230° for 1 hour:-

No phenolic compound in the steam distillate could be detected only the same non-steam volatile, 4-hydroxy-indanone was isolated, m.p. and mixed m.p. 239-240° in poor yield.

o-Methoxy dihydrocinnamic Acid:-

o-Methoxy cinnamic acid (1 g) was hydrogenated by means of palladium black (100 mg) in glacial acetic acid (50 c.c.) at room temperature and pressure, hydrogen absorption (1 mol) ceasing after 20 minutes. The solvent was distilled under reduced pressure from the filtered solution and the residue crystallized as needles (from petroleum ether 60-80°), m.p. 87° mixed m.p. with an authentic specimen was undepressed yield 95%.

Treatment of o-Methoxydihydrocinnamic Acid with Polyphosphoric Acid:-

o-Methoxydihydrocinnamic acid (1 g) was treated with a mixture of phosphoric oxide (25 g) in phosphoric acid (10 c.c.; d 1.7) as described previously. After heating on the steam bath for 1 hour the deep red mixture was poured in excess ice and worked up in the usual way. The neutral extract crystallised as colourless silky

needles, m.p. 274-75° from chloroform to which a few drops of ethanol had been added. (Found: C, 72.53; H, 6.24; M, 282.. Calculated for $C_{18}H_{16}O_4$. C, 72.5; H, 6.04; M, 298).

p-(phenyl)-Phenoxypropionitrile:-

A mixture of p-hydroxydiphenyl (3 g), sodium methoxide (0.2 g) and acrylonitrile (8 g) was heated in an autoclave at 140-150° for 5 hours. Excess of acrylonitrile was removed in vacuo and the solid treated with a dilute solution of sodium hydroxide. The crystalline solid was filtered, washed several times with water, and crystallized from ethanol, m.p. 124°. (Found: C, 81.1; H, 6.0; N, 6.5. $C_{15}H_{13}NO$ requires C, 80.0; H, 5.8; N, 6.4 %), yield; 88%.

p-(Phenyl)-Phenoxypropionic Acid:-

The above nitrile (1 g) was refluxed with 50% sulphuric acid (20 c.c.) for 1½ hours when solid acid separated in the flask. Cooled, diluted with water (ca 200 c.c.) and filtered. The solid crystallised as colourless plates (ethanol) m.p. 173°. (Found: C, 74.1; H, 6.0. $C_{15}H_{14}O_3$ requires C, 74.3; H, 5.8 %).

6-Phenyl Chromanone:-

The above acid (2 g) was treated with polyphosphoric acid [prepared from phosphoric oxide (25 g) and 85%

phosphoric acid (10 c.c.)] and heated on a steam bath for 3½ hours. The colour changed through lemon yellow, orange to red. The mixture was poured in excess ice and left overnight. It was thoroughly extracted with benzene and the benzene extract in turn washed with dilute sodium carbonate solution and then with water, dried (Na_2SO_4) and evaporated the solvent in vacuo when a crystalline solid was left behind. After charcoaling once, it crystallised as fine needles (from ethanol), m.p. 71-72°. (Found: C, 80.0; H, 5.6. $C_{15}H_{12}O_2$ requires C, 80.3; H, 5.4 %). It gave a positive test with 2:4-dinitrophenylhydrazine solution. Yield; 78 %.

Treatment of 6-Phenyl Chromanone with Aluminium Chloride:-

The phenyl chromanone (0.5 g) was treated with aluminium chloride (0.6 g) in the same way as described before. After treatment at various temperatures as recorded on the following chart, the cooled mass was decomposed by ice-hydrochloric acid mixture and the ether extract separated into carbonate soluble, alkali soluble and neutral products. Each of these were then examined separately in the usual way.

NO.	Rearrangement Temp + Time	Neutral material	Acidic material	Phenolic material
1.	145-50°; ½ hr.	mostly starting material	negligible	v. little
2.	175-180°; ½ hr.	very little starting material	"	"
3.	190-200°; hr.	"	"	"
4.	200-210°; ½ hr.	-	"	"
5.	refluxed 1 hr, in Nitro benzene ;	-	"	"
6.	" ½ hr.	-	"	"

Treatment of 6-PhenylChromanone with Sodium Chloride - Aluminium Chloride melt:-

To a melt of sodium chloride (2.5 g) and aluminium chloride (2 g) was added powdered 6-phenyl chromanone (0.5 g) at 160°. The solution turned reddish-violet and the temperature was kept at 185-190° for 40 minutes. After cooling the solid was powdered and decomposed by ice-hydrochloric acid mixture. This was extracted with

ether and the ether solution was successively extracted with dilute sodium carbonate solution and then with dilute alkali solution. The alkali extract on acidification furnished a crystalline precipitate which was extracted with ether. The ether extract, was washed, dried and concentrated when a yellow solid was left behind. This was conveniently purified by passing its solution in methanol through a short column of charcoal. It crystallized as colourless plates (from methanol) m.p. 123-124°. (Found: C, 80.5; H, 5.7. $C_{15}H_{12}O_2$ requires C, 80.3; H, 5.4 %). It gave an intense blue colour with alcoholic ferric chloride solution and gave a positive test with 2:4dinitrophenyl hydrazine solution. Absorption maxima at 3275, 2425, (log ε 3.55, 4.46) in ethanol.

The sodium salt crystallized from water as pale yellow silky needles m.p. 275-77° (a residue was left behind when heated on a spatula on a flame). Yield; 60 %.

<u>β-(Naphthoxy) propionitrile</u>[48]:-

A mixture of β-naphthol (40 g), acrylonitrile (55 g) and Triton B (4 c.c.) was refluxed for 18 hours. After

cooling for 5 hours the solid was filtered, washed successively with excess 2.5% sodium hydroxide solution and then with water. The crude solid had m.p. 96-98°. After one crystallisation from acetone it had m.p. 105-106°. (Bachman and Levine[48] give the same m.p.).

1-Benzo (*f*) Chromanone:-

The above nitrile (20 g) was poured into a vigorously stirred solution of 85% sulphuric acid (200 c.c.) and the whole stirred for 2 hours. The dark green solution poured on to crushed ice (ca 300 g) and left overnight. The purple coloured solid was filtered, washed with 5% sodium hydroxide solution (100 c.c.) then with water (300 c.c.) and dried. After one charcoaling in benzene it crystallised as colourless cubes (benzene-lèigroin 80-100° mixture) m.p. 47-48° (Bachman and Levine[48] give m.p. 49-50°).

Treatment of 1-Benzo (*f*) Chromanone with Aluminium Chloride:-

1-Benzo (*f*) chromanone (1 g) reacted vigorously with aluminium chloride (1.35g) at 100° when heated in a test tube in a paraffin bath. The temperature was then raised to 190-200° and kept there for 1 hour,

with constant stirring. Towards the end the solution became very viscous. It was cooled, powdered and poured into ice-hydrochloric acid mixture. After 2 hours the solution (yellow brown) was extracted with ether and the ether solution (amber coloured) shaken with dilute alkali. The yellow sodium salt was filtered, acidified with dilute sulphuric acid and extracted with ether. The ether extract was washed, dried (Na_2SO_4) and concentrated when a yellow solid was left behind which was slowly sublimed at 190°/20 m.m. The crystalline yellow solid was dissolved in benzene (20 c.c.) and dry hydrogen chloride was passed for ½ hour. The yellow precipitate was filtered and the filtrate was again saturated with hydrogen chloride when some more precipitate was collected. The combined filtrate and precipitate was treated separately. (a) The yellow solid was dissolved in ethanol (charcoal) and after boiling the solution for some time crystallised as yellow plates m.p. 199-200°. (lit.[52]. m.p. 200°). (Found: C, 79.4; H, 4.2. $C_{13}H_8O_2$ requires C, 79.5; H, 4.1 %). Absorption maxima at 440, 430, 415, 350, 265, 235. (log ε 4.08, 3.87, 3.95, 4.25, 3.95, 4.4) in ethanol.

It gave a deep reddish-brown colour with alcoholic ferric chloride solution. (b) The filtrate was washed with dilute sodium carbonate solution to remove excess of hydrogen chloride, then with water, dried and concentrated in vacuo when a pale yellow solid was left behind. This crystallised as stout needles (from methanol) m.p. 137-138°. (Found: C, 78.7; H, 5.2. $C_{13}H_{10}O_2$ requires C, 78.8; H, 5.1 %). Absorption maxima at 3625, 3225, 240, 2225 (log ε 3.76, 3.8, 4.16, 4.67) in ethanol. When treated with an alcoholic solution of ferric chloride it gave a reddish brown colour changing finally to green. It readily furnished a 2:4dinitrophenylhydrazone crystallising as red needles (from benzene to which a very small amount of ethanol is added) m.p. 265-66°, with decomposition. (Found: C, 60.5; H, 3.5; N, 14.7. $C_{19}H_{14}O_5N_4$ requires C, 60.3; H, 3.7; N, 14.8%).

Hydrogenation of 6-Hydroxyperinaphthenone-7:-

The 6-hydroxyperinaphthenone-7 (0.5 g) was hydrogenated in the presence of palladium black (0.2 g) in acetic acid solution (Analar; 70 c.c.) at ordinary room temperature and pressure. After 4 hours the absorption of hydrogen was complete (1 double bond) and the acetic acid solution (colourless) was filtered free of the catalyst

and evaporated *in vacuo*. The pale yellow solid thus obtained crystallised (charcoaling) from methanol as stout needles m.p. 137-138°. It was identified as the same product as isolated during the previous rearrangement by a mixed m.p. and also as their 2:4dinitrophenyl-hydrazine derivatives.

Dehydrogenation of (LXXXIV) to (LXXXIII)

(a) The dihydro compound (LXXXIV; 100 mg) was refluxed in xylene (20 c.c.) with 5% palladium charcoal (20 mg). After 2 hours the solution was filtered and the solvent evaporated *in vacuo*. Only starting material was recovered as identified by m.p. and mixed m.p.

(b) A mixture of (LXXXIV; 50 mg) and 20% palladium charcoal (20 mg) was heated at 180° for 45 minutes (paraffin bath). It was cooled, extracted with boiling methanol and filtered the solution to remove the catalyst. The yellow solution on concentration afforded the 6-hydroxyperinaphthenone-7, as yellow plates, m.p. and mixed m.p. 200°.

Attempted Acetylation by Acetic anhydride - Sulphuric Acid Method of (LXXXIV) and (LXXXIII)

(a) The dihydro compound LXXXIV

A solution of the dihydro compound (60 mg) in acetic

anhydride (1 c.c.) was treated with two drops of the catalyst (prepared by adding a minute drop of concentrated sulphuric acid to 1 c.c. of acetic anhydride). The solution at once turned brownish-red in colour. It was heated to just about boiling, cooled, and left aside after addition of water (4 c.c.). After 1 hour crystals were deposited on scratching the sides of the test tube. The crystals were filtered and recrystallized (charcoaling) from methanol as pale yellow needles m.p. 104-105°. (Found: C, 74.8; H, 5.1. $C_{15}H_{12}O_3$ requires C, 74.98; H, 5.0 %).

(b) 6-Hydroxyperinaphthenone-7; (LXXXIII).

To (LXXXIII; 30 mg) was added acetic anhydride (1 c.c.) and a drop of the catalyst (prepared as above). The solution at once turned brownish-red in colour and the solid in suspension went into solution. It was worked up in exactly the same way as above when only the starting material (LXXXIII) was isolated (m.p. and mixed m.p. 198-199).

Attempted preparation of the Methyl Ethers of (LXXXIV) and (LXXXIII):-

(a) The Dihydro compound LXXXIV:-

(i) Diazomethane Method:-

A solution of (LXXXIV; 100 mg) in ether (20 c.c.)

was treated with excess of diazomethane (ether solution) in the usual way. After 48 hours the ether was evaporated in vacuo when a gum was left behind. It was dissolved in ether and the ether solution when shaken with dilute alkali, precipitated the sodium salt of LXXXIV (when worked up in the usual way furnished the starting material, m.p. and mixed m.p. 136-137°), and a negligible amount of alkali in soluble product (as a gum) being obtained. The yield of the alkali in soluble gum increased when the above reaction was carried out with diazo methane in methanol - ether mixture (50:50) but no crystalline product could be obtained.

(ii) Treatment of the Sodium Salt of LXXXIV with Dimethyl Sulphate in boiling Toluene:-

A mixture of sodium salt of (LXXXIV; 100 mg), dimethyl sulphate (dried over K_2CO_3, 4 c.c.) and toluene (50 c.c.) was refluxed for 28 hours. The mixture was cooled and the toluene distilled under reduced pressure. Dilute sodium hydroxide solution was added to the residue and warmed on the water bath for 15 minutes to decompose dimethyl sulphate. After acidification with dilute hydrochloric acid the mixture was extracted with ether and the ethereal extract separated into neutral and phenolic material. When worked up in the usual way

the latter furnished pale yellow crystals (from methanol) m.p. 136-137°, (Mixed m.p. with an authentic sample of LXXXIV was undepressed) and the former a very small amount of gummy material which failed to crystallize.

(iii) Methyl Iodide-Potassium carbonate in Acetone, Method:-

A mixture of (LXXXIV; 50 mg), anhydrous potassium carbonate (100 mg) methyl iodide (1 c.c.) and acetone (Analar 10 c.c.) was heated under reflux for 4 hours. On working up in the usual way a neutral gummy material was obtained which failed to crystallise. Even on distillation no crystalline product could be obtained.

(b) 6-Hydroxyperinaphthenone-7 (LXXXIII).

(i) Diazomethane Method:-

By a similar procedure as used for the dihydro compound (LXXXIV), about 90% of the original material (LXXXIII) was recovered. M.p. and mixed m.p. 198-199°.

(ii) Treatment of the Sodium Salt of LXXXIII with Dimethyl Sulphate in boiling Toluene:-

This was carried out exactly in the same manner as described above. Only 6-hydroxyperinaphthenone-7 (LXXXIII) m.p. and mixed m.p. 199-200° was isolated.

(iii) Methyl-toluene-p-Sulphonate, anhydrous Potassium Carbonate in boiling Nitrobenzene:-

To a solution of (LXXXIII; 0.2 g) in nitrobenzene

(Analar; 30 c.c.) was added pure methyl-toluene-p-sulphonate (0.4 g) and anhydrous potassium carbonate (0.6 g, well ground in the form of an emulsion with nitrobenzene 3 c.c.) and the mixture refluxed for 8 hours. Cold water (20 c.c.) was then added and the mixture extracted with ether. The ethereal solution was washed, dried and concentrated. Nitrobenzene was distilled off under reduced pressure (water pump) and the residue (reddish-black tar) extracted with ether. On working up in the usual way mostly a phenolic gum was obtained (deep reddish-black) which gave a positive test with alcoholic ferric chloride solution. No crystalline product could be isolated.

Attempted preparation of the oxime of (LXXXIII)[54]:-

A solution of (LXXXIII; 100 mg) in absolute alcohol (5 c.c.) and hydroxylamine hydrochloride (70 mg) was refluxed for 4 hours. On cooling, yellow plates m.p. 198-199 (mixed m.p. with LXXXIII was undepressed) were obtained (85 mg).

1-β-Cyanoethyl-2naphthol[49].

A mixture of β-naphthol (29 g), acrylonitrile (12 g), sodium hydroxide pellets (9 g) and benzene (50 c.c.) was heated under reflux. After 1½ hours the mixture

separated into two layers. The heating was stopped after 2 hours, cold water (100 c.c.) added and water solution separated from benzene layer and acidified with dilute hydrochloric acid. The crude precipitate was crystallised from ethanol m.p. 142°.

The Lactone (LXXVIII)[49]:-

A mixture of the above nitrile (10g), sodium hydroxide pellets (5 g) and water (50 c.c.) was heated under reflux. After 8 hours the solution was cooled and poured slowly with stirring and scratching the sides of the beaker into dilute hydrochloric acid. A crystalline precipitate was obtained which after one crystallisation from ethanol-water mixture (at room temperature) had m.p. 118-119° (lit.[49]. m.p. 121°).

The acid (5 g) was distilled under vacuum when the lactone came as a colourless viscous liquid at (air bath) 185-190°/0.2 m.m. The liquid solidified to a hard colourless crystalline mass on scratching with a glass rod.

Treatment of the Lactone (LXXVIII) with Aluminium Chloride

A mixture of the lactone (1 g) and anhydrous aluminium chloride (1.35 g) was heated in a test tube in the usual way. There was a vigorous reaction with much evolution of hydrogen chloride between 80-85°. The mass became solid and dark in colour. On raising the

temperature slowly, the solid mass again became mobile at 120-123°. Finally the mixture was kept at 140-145° for 10 minutes with constant stirring. The viscous mass was cooled, powdered and poured into ice-hydrochloric acid mixture. After 2 hours the solution (yellowish-brown) was extracted with ether. The ethereal solution was washed with dilute sodium carbonate solution (a dark green carbonate solution with fluorescence was obtained) and then extracted with dilute alkali. The deep red alkali solution was acidified and again extracted with ether and the ether extract, washed, dried and concentrated in vacuo when a gum was left behind. On leaving the gum, a few crystals were observed but all attempts to separate the two failed. The gum was therefore dissolved in hot trichlorobenzene (20 c.c.) and 20 % palladium charcoal (0.1 g) added and the whole heated under reflux. After 4 hours the solution was cooled, extracted with dilute alkali and the alkali extract washed with ether (to remove trichlorobenzene), and acidified with dilute hydrochloride acid when a yellowish brown precipitate was obtained. The solution was filtered and the precipitate dissolved in hot alcohol (30 c.c.). After charcoaling it crystallised

as orange needles (from ethanol) m.p. 266-267° (sinters at 245°). (Found: C, 79.5; H, 4.1. $C_{13}H_8O_2$ requires C, 79.5; H, 4.18%). Absorption maxima at 5025, 4225, 3375, 320, 2625 (log ε, 2.46, 4.12, 3.52, 3.50, 4.43) in ethanol. It gave a reddish brown colour when treated with alcoholic ferric chloride solution. On catalytic micro hydrogenation in the presence of palladium black in acetic acid it showed the presence of one (0.94) double bond and the corresponding acetyl derivative was readily obtained, when it was treated under the same conditions as used for (LXXXIII) and (LXXXIV), as yellow silky needles (from dilute acetic acid) m.p. 119-120°. (Found: C, 75.4; H, 4.37. $C_{15}H_{10}O_3$ requires (C, 75.58; H, 4.23%). When treated with methyl iodide and anhydrous potassium carbonate in acetone solution the corresponding methoxy compound was obtained as pale yellow silky needles (from alcohol-water mixture) m.p. 52-53°. (Found: C, 79.8; H, 4.8. $C_{14}H_{10}O_2$ requires C, 79.98; H, 4.8 %).

(m-Methoxy)-phenoxypropionitrile[61]:-

A mixture of resorcinol monomethyl ether (b.p. 244°/760 m.m; 77 g), acrylonitrile (330 c.c.) and Triton B (6 c.c.) was refluxed for 20 hours. Ether (1 l.) was added and the ether solution washed 3 times with 5% sodium hydroxide

solution, once with dilute hydrochloric acid (100 c.c.) and then twice with water, dried (Na_2SO_4) and evaporated off the ether when a viscous liquid was left behind. It was left under suction over a steam bath (to remove acrylonitrile) for 15 minutes and then distilled under vacuum when the nitrile came at 124-126°/0.3 m.m. (lit.[61] b.p. 145-146°/3m.m.) as a viscous liquid which solidified on scratching and cooling.

(m-Methoxy)-phenoxypropionic Acid:-

A mixture of the nitrile (15 g), concentrated hydrochloric acid (150 c.c.) and water (75 c.c.) was refluxed for 2½ hours. On cooling and scratching, the oil solidified to a hard mass which was filtered, dissolved in dilute sodium carbonate solution (extracted once with ether to remove a very small amount of oily material) and acidified slowly with concentrated hydrochloric acid. The precipitated colourless acid was crystallised once from much boiling water as colourless plates m.p. 80-81° (lit.[62] m.p. 81°).

7-Methoxy-Chromanone:-

The above acid (2 g) was added to polyphosphoric acid (prepared from 25 g. phosphoric oxide and 10 c.c. of 85% phosphoric acid). The solution at once turned red, kept on the water bath for ½ hour and the deep red solution poured into excess ice-water mixture.

The yellow solution turned greenish on standing and after 2 hours it was extracted with ether and the ether solution washed with dilute carbonate solution, then with water, dried and concentrated in vacuo. The residue was crystallised from petroleum ether 40-60° as colourless stout needles m.p. 52-54° (lit.[61,62] m.p. 52-54°). (Found: C, 67.3; H, 5.6. $C_{10}H_{10}O_3$ requires C, 67.4; H, 5.6 %).

Treatment of Methoxychromanone with Aluminium Chloride at 170-180°:-

Methoxy chromanone (1 g) reacted vigorously with aluminium chloride at 80-90° with much evolution of hydrogen chloride. On continued heating the viscous liquid turned into a yellow solid mass at 130-140°. The temperature was then raised to 170-180° and kept there for 20 minutes. The violet-yellow solid was powdered and decomposed by ice-hydrochloric acid mixture. On working up in the usual way a gummy phenolic material was obtained which slowly crystallized on standing. The solid was repeatedly crystallised from boiling water (charcoal) and finally from ethyl acetate as colourless needles m.p. 140°. (Found: C, 65.8; H, 4.54. $C_9H_8O_3$ requires C, 65.86; H, 4.9%). It readily furnished an acetyl derivative as colourless needles m.p. 94-95° (methanol). (Found: C, 64.3;

H, 4.9. $C_{11}H_{10}O_4$ requires C, 64.1; H, 4.9%) and formed a methoxy derivative (MeI-K_2CO_3 in acetone) as colourless stout needles from petroleum ether 40-60° of m.p. 52-54°. Mixed m.p. with the starting material (CI) was undepressed. The yield of the hydroxychromanone (CIX) was much better when the methoxychromanone (CI) was treated with aluminium chloride at 130-140° for ½ hour.

Treatment with Aluminium Chloride at 210° for ½ hour:-

The above reaction was carried out at 210° for ½ hour. The deep violet solid mass was powdered and worked up in the usual way when a gummy phenolic material was obtained. This was extracted with boiling legroin 80-100° to which a few drops of ethanol had been added. On slow evaporation of the solvent a small quantity (ca 20 mg) of a crystalline material was isolated which crystallised from ethanol as colourless needles m.p. 195-196°. (Found: C, 65-6; H, 4.8. $C_9H_8O_3$ requires C, 65.86; H, 4.9%). Absorption maxima at 278, 230, 220 (log ε 4.24, 4.23, 4.24) in alcohol. Some more of the same material was obtained when the non-legroin soluble fraction was extracted with a small quantity of boiling water and set aside for slow evaporation. When its solution in acetic anhydride was boiled with boroacetic anhydride, a deep yellow colour was obtained. It gave an intense violet colour with alcoholic ferric chloride solution,

furnished the corresponding diacetyl derivative when acetylated by Ac_2O-H_2SO_4 method as colourless needles (from ethanol) m.p. 90-91°. (Found: C, 62.8; H, 4.9. $C_{13}H_{12}O_5$ requires C, 62.9; H, 4.9 %) and gave a positive 2:4dinitrophenyl hydrazine test.

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