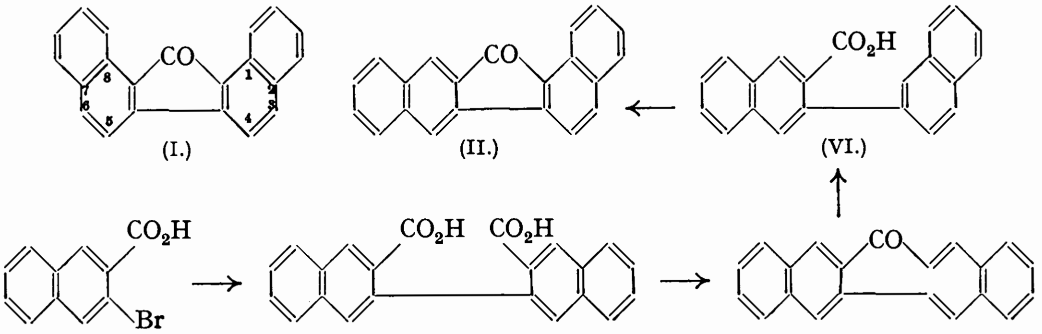
125. *Polycyclic Aromatic Hydrocarbons. Part XXVIII. Dibenzfluorenes.*

By Richard H. Martin.

Confirmation of the molecular structure of a carcinogenic hydrocarbon, 1 : 2 : 7 : 8-dibenzfluorene, has been obtained by its degradation to 2 : 2′-dinaphthyl, and by the synthesis of 2 : 3 : 6 : 7- and 1 : 2 : 6 : 7-*dibenzfluorenones*, different from the ketone formed by oxidation of 1 : 2 : 7 : 8-dibenzfluorene. These three ketones represent all the possible dibenzfluorenones related to 2 : 2′-dinaphthyl. 3 : 4 : 5 : 6-*Dibenzfluorene* has been synthesised from 1-bromo-2-naphthoic acid. The three other dibenzfluorenes which are theoretically possible are all known, and it is concluded that the pentacyclic hydrocarbon formed by dehydration of di-2-naphthylcarbinol is 2 : 3 : 5 : 6-dibenzfluorene.

ABILITY to induce malignant tumours of the skin in mice is shown by 1 : 2 : 5 : 6-dibenzacridine and 1 : 2 : 5 : 6-dibenzcarbazole as well as by the corresponding hydrocarbons 1 : 2 : 5 : 6-dibenzanthracene and 1 : 2 : 5 : 6-dibenzfluorene (Barry *et al.*, *Proc. Roy. Soc.*, 1935, *B*, **117**, 318; Bachmann *et al.*, *ibid.*, 1937, *B*, **123**, 343; Boyland and Brues, *ibid.*, 1937, *B*, **122**, 429). Furthermore, in the case of the heterocyclic compounds this type of biological activity is not confined to the 1 : 2 : 5 : 6-structure but is shown also by the 3 : 4 : 5 : 6-compounds. All these compounds can effect *inhibition* of tumour growth, in which respect 1 : 2 : 5 : 6-dibenzfluorene is especially active (Haddow, 16th Ann. Rept. British Empire Cancer Campaign, 1939, 300; Haddow and Robinson, *Proc. Roy. Soc.*, 1939, *B*, **127**, 277), although it is only weakly carcinogenic. Hence it seemed of interest to extend the study of biological properties to isomeric dibenzfluorenes. Recently it has been found that both 1 : 2 : 3 : 4- and 1 : 2 : 7 : 8-dibenzfluorenes are weakly carcinogenic to the skin of mice, although, like the 1 : 2 : 5 : 6-compound, they have not given sarcomas when injected subcutaneously (Badger, Cook, Hewett, Kennaway, Kennaway, Martin, and Robinson, *Proc. Roy. Soc.*, 1940, *B*, **129**, 439).

The 1 : 2 : 7 : 8-dibenzfluorene used in these experiments was the hydrocarbon, m. p. 234°, obtained by dehydration of di-1-naphthylcarbinol with metaphosphoric acid (Tschitschibabin and Magidson, *J. pr. Chem.*, 1914, **90**, 168; compare Schmidlin and Massini, *Ber.*, 1909, **42**, 2377). However, the red ketone (I), m. p. 270°, obtained by oxidation of this hydrocarbon (Tschitschibabin and Magidson, *loc. cit.*; Schmidlin and Huber, *Ber.*, 1910, **43**, 2824; Wanscheidt, *Ber.*, 1926, **59**, 2092) is clearly different from the orange picylene ketone (m. p. 185°) obtained by Bamberger and Chattaway (*Annalen*, 1895, **284**, 52) by distilling picenequinone with lead oxide or by dehydrating picenic acid. Yet from the available evidence picylene ketone should be 1 : 2 : 7 : 8-dibenzfluorenone (I) or, less probably, 1 : 2 : 6 : 7-dibenzfluorenone (II) (see following paper). Hence it was desirable to secure corroboration of the structure of the hydrocarbon formed from di-1-naphthylcarbinol. In support of the suggested structure it was found that the ketone, m. p. 270°, was converted by fused potash into 2 : 2′-*dinaphthyl*-1-*carboxylic acid*, which gave 2 : 2′-dinaphthyl on decarboxylation and was dehydrated by 80% sulphuric acid to the red ketone whence it was obtained.



(I.) (II.) (VI.)

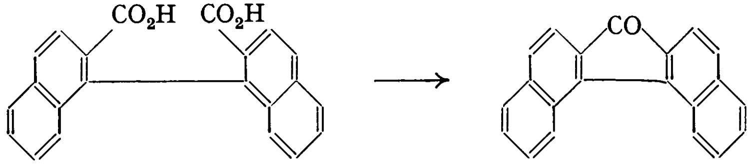
(III.) (IV.) (V.)

This degradation to 2 : 2′-dinaphthyl accords not only with the 1 : 2 : 7 : 8-structure (I) but also with the structures (II) and (V) for the ketone in question. These two alternatives have been excluded by independent synthesis of the 2 : 3 : 6 : 7- and 1 : 2 : 6 : 7-dibenzfluorenones, which differed from the red ketone, m. p. 270°. For this purpose, the methyl ester of 3-bromo-2-naphthoic acid (III) was converted by heated copper bronze into the ester of 2 : 2′-*dinaphthyl*-3 : 3′-*dicarboxylic acid* (IV), which gave 2 : 3 : 6 : 7-

dibenzfluorenone (V) when its lead salt was pyrolysed under reduced pressure. Fusion with potash transformed this ketone into 2 : 2′-*dinaphthyl*-3-*carboxylic acid* (VI), decarboxylated to 2 : 2′-dinaphthyl. Dehydration of the acid (VI) led to ring-closure in the α-position of the uncarboxylated naphthalene ring, so that a new ketone was formed. This was clearly 1 : 2 : 6 : 7-*dibenzfluorenone* (II).

3 : 4 : 5 : 6-*Dibenzfluorenone* (VIII) was synthesised by a similar method to that used for the 2 : 3 : 6 : 7-compound. The *methyl* ester of 1 : 1′-dinaphthyl-2 : 2′-dicarboxylic acid (VII) was prepared by heating methyl 1-bromo-2-naphthoate with copper bronze, and the dicarboxylic acid was transformed into the pentacyclic ketone (VIII). Its structure was confirmed by potash fusion to 1 : 1′-*dinaphthyl*-2-*carboxylic acid*, which was decarboxylated to 1 : 1′-dinaphthyl. Reduction of the ketone (VIII) to 3 : 4 : 5 : 6-*dibenzfluorene* could not be effected by Clemmensen's method, but was successfully accomplished by heating with hydrazine hydrate at 180°. Tests for carcinogenic activity with 3 : 4 : 5 : 6-dibenzfluorene are in progress.

(VII.)

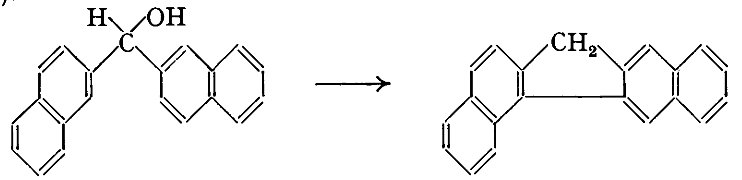


(VIII.)

In view of the biological interest of 1 : 2 : 5 : 6-dibenzfluorene, which was first synthesised by a rather laborious procedure (Cook *et al.*, J., 1935, 1319), a more convenient synthesis was attempted by dehydration of 1 : 2′-dinaphthylcarbinol. The desired hydrocarbon was obtained from this carbinol by heating with metaphosphoric acid, but the yield was too small for the method to be of practical value.

Six dibenzfluorenes have been discussed above. Only one other structure (2 : 3 : 5 : 6) (X) is theoretically possible, and this should therefore represent the hydrocarbon obtained by Schmidlin and Huber (*loc. cit.*) as a by-product in the preparation of di-2-naphthylcarbinol (IX).

(IX.)

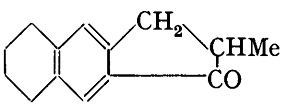


(X.)

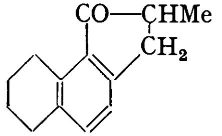
The oxidation product of this hydrocarbon is an orange-red ketone giving a deep blue solution in sulphuric acid, and the m. p.'s of the hydrocarbon (190·5°, corr.) and its ketone (163—165°, corr.) serve to distinguish them from the other six dibenzfluorenes and their ketones.

Although 1 : 2 : 6 : 7-dibenzfluorenone was prepared by cyclisation of the acid (VI), it was not obtained in sufficient quantity for conversion into the corresponding hydrocarbon, and personal circumstances have prevented the completion of this project. During the course of the investigation the synthesis of 1 : 2 : 6 : 7-dibenzfluorene was attempted by a modification of the method used by Cook *et al.* (*loc. cit.*) for the preparation of 1 : 2 : 5 : 6-dibenzfluorene. It was anticipated that chloromethylation of tetralin would take place mainly in the β-position of the aromatic ring, and that by condensation of the chloromethyl-tetralin with ethyl sodiomethylmalonate an acid could be prepared which would undergo cyclisation in the other β-position, leading to the ketone (XI) (see Barbot, *Bull. Soc. chim.*, 1930, **47**, 1314; Darzens and Lévy, *Compt. rend.*, 1935, **201**, 730, 902). Such a ketone, on condensation with β-phenylethylmagnesium chloride, would give a tertiary carbinol which should be capable of dehydration to a hydroaromatic hydrocarbon which would pass into 1 : 2 : 6 : 7-dibenzfluorene on dehydrogenation.

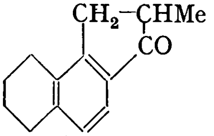
When a ketone was prepared by the method described, there was obtained a liquid product, from which by strong cooling some 10% could be isolated as a pure crystalline *ketone*, m. p. 81°. Both the crystalline ketone and the liquors from which it had been separated were oxidised by dilute nitric acid to mellophanic acid. There was no evidence of the formation of pyromellitic acid, which would arise from (XI). Consequently the crystalline ketone must have structure (XII) or (XIII) and the results indicate that both of these ketones were formed to the exclusion of (XI).



(XI.)



(XII.)



(XIII.)

Experimental.

2 : 3 : 6 : 7-*Dibenzfluorene*.—3-Bromo-2-naphthoic acid (III) was prepared from 3-amino-2-naphthoic acid (kindly presented by Imperial Chemical Industries, Ltd., Dyestuffs Group) by a method which was essentially that of Kenner, Ritchie, and Wain (J., 1937, 1526). The crude bromo-acid was esterified by 10 hours' heating on the water-bath with methyl alcohol (10 parts) saturated with hydrogen chloride. The distilled ester, b. p. 170°/1·5 mm., crystallised immediately. The methyl ester (25 g.) was heated with copper bronze (18 g.) at 190—200°, as described below for the isomeric bromo-ester. The product was extracted with benzene and then distilled in a vacuum. Some unchanged bromo-ester (1·4 g.) was recovered. *Methyl* 2 : 2′-*dinaphthyl*-3 : 3′-*dicarboxylate* (15·8 g.) distilled at 260—270°/0·6 mm. and was recrystallised for analysis from benzene and then alcohol. It had m. p. 173—173·5° (Found : C, 77·6; H, 4·8. $C_{24}H_{18}O_4$ requires C, 77·8; H, 4·9%). Hydrolysis with alcoholic potash gave 2 : 2′-*dinaphthyl*-3 : 3′-*dicarboxylic acid* (IV), which formed colourless needles (from alcohol), m. p. 298—299°, after darkening (bath preheated to 280°) (Found : C, 77·1; H, 4·0. $C_{22}H_{14}O_2$ requires C, 77·2; H, 4·1%).

An attempt to convert this acid into 2 : 3 : 6 : 7-dibenzfluorenone by the procedure used for 3 : 4 : 5 : 6-dibenzfluorenone was unsuccessful, and recourse was had to pyrolysis of the lead salt. This was prepared by addition of lead acetate to an aqueous solution of the sodium salt. The lead salt (5 g.) was heated at 0·2 mm. over a free flame. The distillate was recrystallised from acetic acid and then several times from xylene. 2 : 3 : 6 : 7-*Dibenzfluorenone* (V) (1·5 g.) formed bright yellow needles, m. p. 269—270° (Found : C, 89·8; H, 4·5. $C_{21}H_{12}O$ requires C, 90·0; H, 4·3%). This ketone, which gave a brown solution in concentrated sulphuric acid, depressed the m. p. of 1 : 2 : 7 : 8-dibenzfluorenone. When the pyrolysis was carried out on four times this scale, the product was a mixture of the fluorenone derivative with 2 : 2′-dinaphthyl. Separation was effected by vacuum sublimation, and the more volatile hydrocarbon fraction was purified by chromatographic means (using alumina), followed by preparation of the picrate.

The ketone (V) (1 g.) was reduced by heating for 8 hours in a sealed tube at 205° with hydrazine hydrate (6 c.c.). The resulting 2 : 3 : 6 : 7-*dibenzfluorene*, after sublimation at 210°/0·1 mm. and recrystallisation from benzene, formed colourless plates, m. p. 282·5—283·5° (Found : C, 94·65; H, 5·2. $C_{21}H_{14}$ requires C, 94·7; H, 5·3%).

2 : 2′-*Dinaphthyl*-3-*carboxylic acid* (VI) was formed when 2 : 3 : 6 : 7-dibenzfluorenone (0·5 g.) was heated for ½ hour at 240—250° with potassium hydroxide (3 g.). The acid, precipitated from a filtered extract of the melt, was crystallised from acetic acid and then alcohol. It had m. p. 189—191°, and depressed the m. p. of the acid, m. p. 177—179°, similarly prepared from 1 : 2 : 7 : 8-dibenzfluorenone (Found: C, 84·75; H, 4·8. $C_{21}H_{14}O_2$ requires C, 84·5; H, 4·7%). Decarboxylation of (VI) with copper bronze (0·5 part) in quinoline (10 parts) at 240—250° gave 2 : 2′-dinaphthyl, m. p. 183—184° alone or mixed with an authentic sample. When the acid (VI) was heated on the water-bath for 3 hours with 80% sulphuric acid (50 parts), it was dehydrated to 1 : 2 : 6 : 7-*dibenzfluorenone* (II), which, after crystallisation from acetic acid and then xylene, formed orange plates, m. p. 211°, which gave a carmine-red solution in concentrated sulphuric acid (Found : C, 89·9; H, 4·4. $C_{21}H_{12}O$ requires C, 90·0; H, 4·3%).

3 : 4 : 5 : 6-*Dibenzfluorene*.—1-Bromo-2-naphthylamine, prepared through the bromination of benzylidene-β-naphthylamine (Franzen and Eidis, *J. pr. Chem.*, 1913, **88**, 755), was converted into 1-bromo-2-naphthoic acid as described by Boyes, Grieve, and Rule (J., 1938, 1833). A mixture of methyl 1-bromo-2-naphthoate (19·7 g.) and copper bronze (3 g.) was heated

in an oil-bath to 190°, and more copper bronze (10 g.) was stirred in in portions during ½ hour. The temperature was maintained at 190° for a further 4½ hours, the product extracted with hot benzene, and the benzene removed from the filtered extract. Crystallisation of the residue from *cyclo*hexane and then thrice from methyl alcohol gave *methyl* 1 : 1'-*dinaphthyl*-2 : 2'-*dicarboxylate* (8·5 g.) in small colourless plates, m. p. 156·5—157·5° (Found : C, 77·7; H, 4·9. $C_{24}H_{18}O_4$ requires C, 77·8; H, 4·9%). The acid (VII) obtained by hydrolysis had m. p. 266° in agreement with Kalb (*Ber.*, 1914, **47**, 1724).

For ring-closure to the fluorenone, this acid (17·4 g.) was boiled under reflux for ½ hour with excess of acetic anhydride. This was distilled, and the residue was heated at 280° for 3 hours. The resulting ketone (9·4 g.) was isolated by extraction with hot benzene or by vacuum distillation, followed by recrystallisation from benzene. For analysis, a specimen was sublimed at 0·4 mm. and recrystallised from ethyl acetate. 3 : 4 : 5 : 6-*Dibenzfluorenone* * (VIII) formed dark red, prismatic needles, m. p. 222—222·5°, which gave a carmine-red solution in sulphuric acid (Found ; C, 89·7; H, 4·2. $C_{21}H_{12}O$ requires C, 90·0; H, 4·3%). Its *oxime* crystallised from xylene in small orange-red needles, m. p. 253—254° (Found : C, 85·6; H, 4·3. $C_{21}H_{13}ON$ requires C, 85·4; H, 4·4%).

Reduction of the ketone (2 g.) was effected by heating at 180° for 15 hours in a sealed tube with hydrazine hydrate (12 c.c.). The product was crystallised from acetic acid (charcoal) and then *cyclo*hexane (yield, 1·35 g.; m. p. 151—152°). After sublimation at 180°/0·6 mm. and recrystallisation from benzene, 3 : 4 : 5 : 6-*dibenzfluorene* formed colourless plates, m. p. 152—152·5° (Found : C, 94·8; H, 5·3. $C_{21}H_{14}$ requires C, 94·7; H, 5·3%), and gave a reddish-brown *dipicrate* (from benzene), m. p. 154—155° (Found : C, 54·75; H, 2·8. $C_{21}H_{14},2C_6H_3O_7N_3$ requires C, 54·7; H, 2·8%). When the hydrocarbon (0·2 g.) was heated in a sealed tube at 215° for 2 hours with selenious acid (0·6 g.) and water (0·3 c.c.), the ketone, m. p. 222°, was formed.†

Fission to 1 : 1'-*dinaphthyl*-2-*carboxylic acid* was effected when 3 : 4 : 5 : 6-dibenzfluorenone (0·5 g.) was added during ½ hour to fused potash (2 g.) at 240—250°. The acid, which had m. p. 199—200° (from benzene) (Found : C, 84·6; H, 4·8. $C_{21}H_{14}O_2$ requires C, 84·5; H, 4·7%), was decarboxylated by heating for an hour at 240—250° with quinoline (10 parts) and copper bronze (0·5 part). The resulting 1 : 1'-dinaphthyl had m. p. 156°, alone or mixed with an authentic sample prepared by interaction of 1-naphthylmagnesium bromide with α-tetralone, followed by dehydrogenation with sulphur.

2 : 2'-*Dinaphthyl from* 1 : 2 : 7 : 8-*Dibenzfluorene*.—The hydrocarbon, m. p. 234°, was prepared from 1 : 1'-dinaphthylcarbinol by dehydration with metaphosphoric acid (Tschitschibabin and Magidson, *loc. cit.*) and was purified by vacuum sublimation. The ketone could not be satisfactorily obtained by chromic acid oxidation, which was also the experience of Wanscheidt (*loc. cit.*), who obtained, however, an excellent yield of ketone, m. p. 272° (corr.), by auto-oxidation in boiling methyl-alcoholic potash. The ketone (I) used in the following experiments was prepared by heating 1 : 2 : 7 : 8-dibenzfluorene (1·6 g.) with selenium dioxide (3 g.) and water (3 c.c.) in a sealed tube at 230° for 6 hours. The product was purified by vacuum sublimation and recrystallisation from benzene (yield, 1·2 g.), and then formed dark red needles, m. p. 263—265·5° (uncorr.). This ketone gives a carmine-red solution in sulphuric acid. Fusion with potash at 240—250° gave 2 : 2'-*dinaphthyl*-1-*carboxylic acid*, which, after crystallisation from acetic acid and then benzene, formed colourless prisms, m. p. 177—179° (Found : C, 84·45; H, 4·8. $C_{21}H_{14}O_2$ requires C, 84·5; H, 4·7%). This acid (0·1 g.), on heating for 4 hours at 100° with 80% sulphuric acid (10 c.c.), gave the ketone (45 mg.), m. p. 263°, from which it was obtained. Decarboxylation of the acid with copper-bronze in quinoline gave 2 : 2'-dinaphthyl, m. p. 184—185° alone or mixed with an authentic specimen. Reduction of the red ketone (I) (0·5 g.) with hydrazine hydrate (3 c.c.) (12 hours at 210°) gave the original hydrocarbon, m. p. 234° after purification through its *s*-trinitrobenzene complex.

1 : 2 : 5 : 6-*Dibenzfluorene*.—A mixture of 1-naphthoyl chloride (50 g.), tetralin (36 g.),

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* (Added in proof.) A specimen of 3 : 4 : 5 : 6-dibenzfluorenone was fused with aluminium chloride and sodium chloride, as described by Baddar (this vol., p. 312) for the conversion of 3 : 4-benzfluorenone into 1 : 9-benzanthrone. The product, presumably 1 : 2 : 8 : 9-*dibenzanthrone*, after sublimation at 180°/0·1 mm. and recrystallisation from benzene–alcohol, formed long yellow needles, m. p. 185—186° (Found: C, 89·7; H, 4.3. $C_{21}H_{12}O$ requires C, 90·0; H, 4·3%). This product was identical with a compound synthesised by Swain and Todd (preceding paper).

† This method of oxidation of dibenzfluorenes was developed by Dr. G. M. Badger, and was successfully used by him for the preparation of 1 : 2 : 5 : 6-dibenzfluorenone (this vol., p. 535), which could not be isolated from the products of oxidation of 1 : 2 : 5 : 6-dibenzfluorene with chromic acid.

and carbon disulphide (40 c.c.) was added to an ice-cooled suspension of finely powdered anhydrous aluminium chloride (38 g.) in carbon disulphide (90 c.c.). After 2 hours in the ice-bath the mixture was kept at room temperature for 2½ hours, and was then refluxed for 2½ hours. The aluminium complex was decomposed with ice and hydrochloric acid, the carbon disulphide removed with steam, the product extracted with ether, and the dried extract distilled. The resulting viscous liquid (44 g.) had b. p. 230—235°/0·8 mm., and gave an *oxime*, m. p. 172—172·5° (from benzene) (Found: C, 83·6; H, 6·3. $C_{21}H_{19}ON$ requires C, 83·7; H, 6·3%). Dehydrogenation of the liquid ketone (43 g.) with sulphur (9·7 g.) was effected at 220°, and when complete, copper bronze (1 g.) was added, and the product distilled in a vacuum. After redistillation (b. p. 235°/0·6 mm.) and three crystallisations from benzene–ligroin, pure 1 : 2′-dinaphthyl ketone (20 g.), m. p. 135°, was obtained.

A solution of 1 : 2′-dinaphthyl ketone (5 g.) in boiling amyl alcohol (30 c.c.) was added to a boiling solution of sodium amyloxide (from 10 g. of sodium and 100 c.c. of amyl alcohol). Reduction to the carbinol was completed by boiling for ¾ hour (this method of reduction is due to Diels and Rhodius, *Ber.*, 1909, **42**, 1072). 1 : 2′-Dinaphthylcarbinol (4 g.), isolated from the amyl-alcoholic solution after cautious addition of water, had m. p. 108—109° (from benzene–light petroleum), in agreement with the literature.

For cyclisation, a stirred mixture of 1 : 2′-dinaphthylcarbinol (3 g.) and metaphosphoric acid (6 g.) was heated on the water-bath for 10 minutes and then in an oil-bath to 110°. The temperature was raised during an hour to 175° and maintained there for ½ hour. The cooled mass was extracted with sodium carbonate solution and washed with boiling water until the washings were neutral. The undissolved non-crystalline material was distilled at 0·3 mm. When the bath was at 280°, there distilled a few drops of liquid which crystallised immediately. Recrystallisation from benzene gave 1 : 2 : 5 : 6-dibenzfluorene, m. p. 172° alone or mixed with an authentic specimen. This hydrocarbon was not obtained when dehydration of the carbinol was attempted with (*a*) 1 vol. of concentrated sulphuric acid in 10 vols. of boiling acetic acid, (*b*) hydrogen chloride in acetic acid on the water-bath, (*c*) phthalic anhydride at 190°.

A dibenzfluorene could not be isolated when 2 : 2′-dinaphthylcarbinol was treated with metaphosphoric acid as described above (compare Schmidlin and Huber, *loc. cit.*).

Chloromethylation of Tetralin.—The following procedure is based on that used by Cambron (*Canadian J. Res.*, 1939, **17** *B*, 10) for naphthalene: A mixture of tetralin (50 g.), paraformaldehyde (13 g.), acetic acid (45 c.c.), concentrated hydrochloric acid (50 c.c.), and syrupy phosphoric acid (22 c.c.) was heated on the water-bath for 4½ hours, with mechanical stirring. The product was poured into water (1½ l.) and extracted with benzene. The benzene solution was washed with water and sodium carbonate solution, dried, and distilled. The chloromethyltetralin (22·5 g.), probably a mixture of α- and β-derivatives, had b. p. 148°/20 mm.

Condensation of Chloromethyltetralin with Ethyl Methylmalonate.—The aforesaid chloromethyltetralin (32·9 g.) was added dropwise to the sodio-compound formed from powdered sodium (4·2 g.) and ethyl methylmalonate (31·8 g.) in pure benzene (120 c.c.). The whole was heated for 15 hours on the water-bath, and the product cooled and treated with water. The benzene solution was washed, dried, and distilled. A second distillation gave 29·5 g. of a colourless oil, b. p. 160—161°/0·4 mm. (Found: C, 72·05; H, 8·3. $C_{19}H_{26}O_4$ requires C, 71·65; H, 8·2%). The substituted malonic acid, obtained by hydrolysis of this ester, was heated at 170° until evolution of carbon dioxide ceased. The resulting β-*tetralyl*-α-*methylpropionic acid* (23·8 g.) formed a colourless viscous oil, b. p. 157°/0·1 mm. (Found: C, 76·95; H, 8·4. $C_{14}H_{18}O_2$ requires C, 76·6; H, 8·45%). The chloride was prepared by addition of thionyl chloride (20 c.c.) and quinoline (4 drops) to a solution of the foregoing acid (23 g.) in dry ether (100 c.c.). After ½ hour at room temperature the ether and excess of thionyl chloride were distilled under reduced pressure. The residual acid chloride was dissolved in benzene (200 c.c.) and cyclised by addition of stannic chloride (2 hours at room temperature). The solution was poured on ice, and hydrochloric acid and ether added to accelerate hydrolysis of the tin complex. Distillation of the washed benzene solution gave a mixture of ketones (XII and XIII) (18·5 g.), b. p. 125—135°/0·4 mm. When a solution of this oil (15 g.) in light petroleum (40 c.c.) was kept at − 2° for 8 hours, crystals separated. These were collected, washed, and recrystallised from light petroleum until they melted constantly at 80·5—81·5° (1·4 g.) (Found: C, 83·75; H, 8·05. $C_{14}H_{16}O$ requires C, 84·0; H, 8·05%). The liquid recovered from the liquors was thrice distilled and then formed a viscous yellow oil (12·6 g.), b. p. 123°/0·1 mm. (Found: C, 83·8; H, 8·2%).

For oxidation, the crystalline ketone (1·2 g.) was heated at 175° for 7 hours with nitric acid (*d* 1·4) and water (24 c.c.). The product was evaporated to dryness and neutralised with ammonia, and the solution treated with silver nitrate (4·8 g.). The precipitated silver salt was collected, dried, and refluxed for 24 hours with methyl iodide in benzene. The resulting methyl ester crystallised from methyl alcohol in long white needles, m. p. 130—131° alone or mixed with authentic methyl mellophanate. The same ester was readily obtained pure by similar oxidation of the liquid ketone.

The liquid ketone [presumably a mixture of (XII) and (XIII)] was treated with β-phenylethylmagnesium chloride, and the resulting carbinol dehydrated with potassium hydrogen sulphate (cf. Cook *et al.*, *loc. cit.*). The unsaturated *hydrocarbon* was a viscous oil, b. p. 174°/0·1 mm. (Found: C, 91·45; H, 8·3. $C_{22}H_{24}$ requires C, 91·6; H, 8·4%). Cyclisation with aluminium chloride in ice-cold carbon disulphide gave a saturated *isomeride*, b. p. 176°/0·15 mm. (Found: C, 91·4; H, 8·5%). When this was dehydrogenated with selenium at 305° for 20 hours, it gave a small yield of a crystalline *hydrocarbon* (isolated by chromatographic purification, followed by picrate formation), which crystallised from xylene in colourless plates, m. p. 306—308° (bath preheated to 280°) (Found: C, 94·9; H, 5·4. $C_{21}H_{14}$ requires C, 94·7; H, 5·3%). In view of the heterogeneity of the ketone used in this synthesis, and the small yield of aromatic hydrocarbon formed, no opinion is expressed concerning its structure.

The author thanks Professor J. W. Cook, F.R.S., who suggested this investigation, for his interest in its progress, and the British Empire Cancer Campaign for a grant to this Institute, which has supported this work. A description of the investigation will be incorporated in a thesis to be submitted for a doctorate in the University of Geneva.

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