319. *Polycyclic Aromatic Hydrocarbons. Part XIII. Condensed Fluorene Derivatives.*

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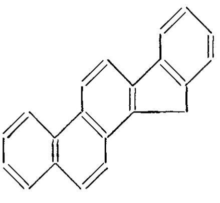
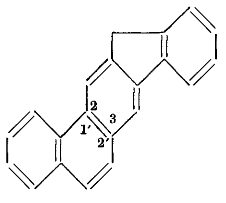
and (Miss) E. Roe.

The pentacyclic aromatic hydrocarbons which are formed by dehydrogenation of sterols and bile acids at 340—360° are probably homologues of 2′ : 1′-naphtha-1 : 2-fluorene (I), although the parent hydrocarbon may be 1′ : 2′-naphtha-2 : 3-fluorene (II). In order to determine whether it is possible to distinguish spectroscopically between these two very similar ring systems we have now synthesised 1′ : 2′-*naphtha*-2 : 3-*fluorene* (II), and compared it with the known 2′ : 1′-naphtha-1 : 2-fluorene (Cook, Hewett, Mayneord, and Roe, J., 1934, 1727).

(I.)

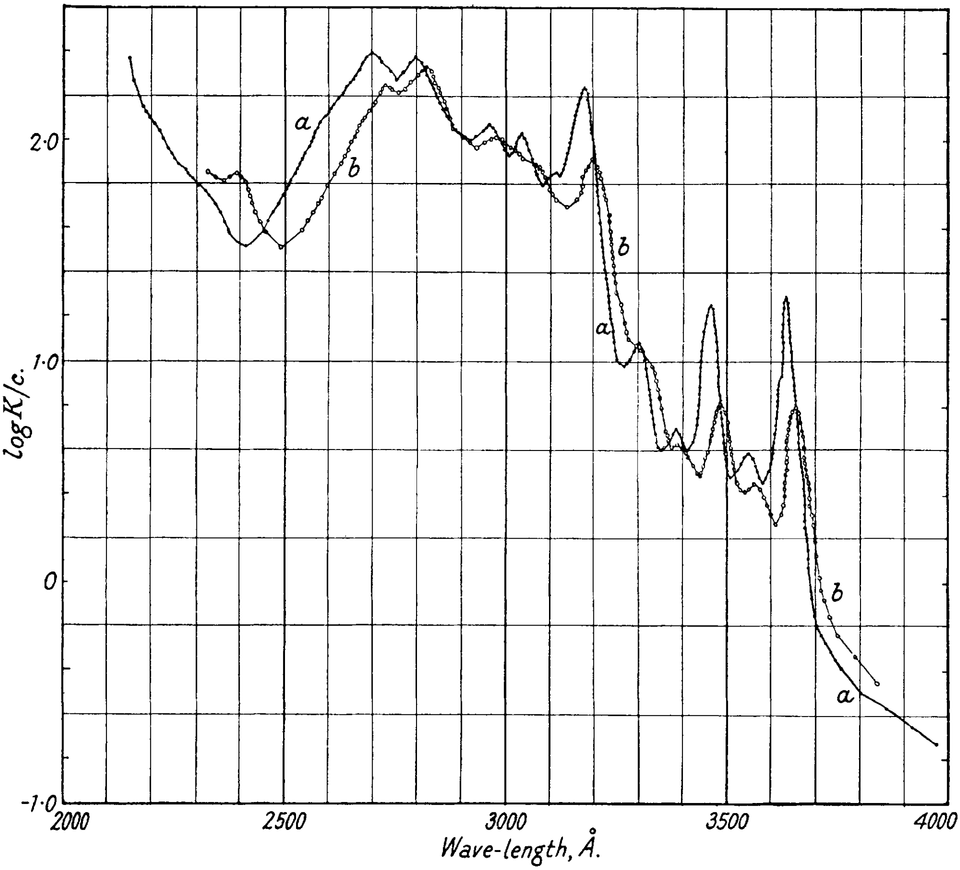




(II.)

The results indicate that (I) rather than (II) is the parent hydrocarbon of the sterol and bile acid dehydrogenation products. The ultra-violet absorption spectra of (I) and (II) have much in common, but there are noteworthy differences in the relative intensities of the bands, and it is clear from examination of the spectra of the two naphthafluorenes, of a methyl*iso*propyl derivative of (I), and of Diels's hydrocarbon, " $C_{25}H_{24}$," from cholesterol (see Fig., and also Figs. 2 and 3 in the paper by Cook, Hewett, Mayneord, and Roe, *loc. cit.*), that the hydrocarbon from cholesterol shows the absorption properties of (I) rather than (II). Moreover, the *ketone* formed by oxidation of (II) gave a magenta colour with concentrated sulphuric acid, whereas the two synthetic ketones containing the ring system of (I), and also the ketone obtained by oxidation of Diels's hydrocarbon, gave intense purple permanganate-like colours.

When this investigation was commenced it appeared likely that the hydrocarbon " $C_{21}H_{16}$ " (m. p. 275°) * obtained from cholic acid by Ruzicka and his collaborators (*Helv. Chim. Acta*, 1933, **16**, 216; 1934, **17**, 200) was the parent hydrocarbon of the group, and as it was not identical with (I) this furnished an additional reason for the synthesis of (II). The synthetic specimen of (II) proved to be different from the cholic acid hydrocarbon. In the meantime, however, accurate molecular-weight determinations carried out by Bernal and Crowfoot (this vol., p. 98) seemed to show that the cholic acid hydrocarbon contains 22 rather than 21 carbon atoms in the molecule. Hence we conclude that this hydrocarbon is probably a methyl derivative of (I), but we reserve discussion of the position of the methyl group or of the mechanism of the dehydrogenation of cholic acid until the completion of experiments designed to give more definite information on these questions.



a = 1′ : 2′-*Naphtha*-2 : 3-*fluorene*. b = *Diels's hydrocarbon* (C_{25}) *from cholesterol.*

The type of method used for the synthesis of (I), namely, cyclisation of an arylethylindene, followed by dehydrogenation, was not well adapted for the production of (II). Before attempting an alternative method of cyclisation of a phenanthrylmethyl*cyclo*hexene it was considered expedient to study a more readily accessible naphthylmethyl compound. For this purpose, β-naphthylmethylmagnesium bromide was condensed with 2-methyl-

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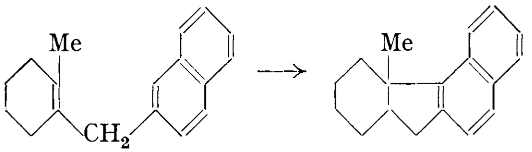
* The spectroscopic data published by Ruzicka show that this hydrocarbon is a prototype of the C_{25} hydrocarbon from cholesterol.

*cyclo*hexanone. The chief product was αβ-di-2-naphthylethane (compare Mayer and Sieglitz, *Ber.*, 1922, **55**, 1854); the smaller carbinol fraction was dehydrated, and the unsaturated hydrocarbon was treated with aluminium chloride, by which means it was anticipated that cyclisation would occur in the following manner :

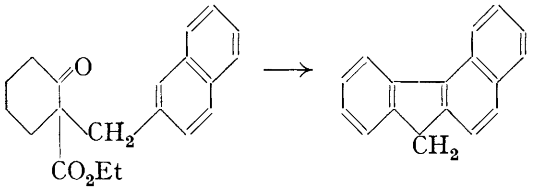


(III.)

The saturated *hydrocarbon* thus formed may have been methylhexahydro-3 : 4-benzfluorene (III), but it was completely unaffected by heating with selenium at 320°, so the method was unsuitable for the synthesis of 3 : 4-benzfluorene.

The synthesis of this hydrocarbon was successfully accomplished by cyclisation and dehydrogenation of *ethyl* 2-β-*naphthylmethyl*cyclo*hexanone*-2-*carboxylate* (IV), formed by condensation of β-naphthylmethyl bromide with ethyl potassio*cyclo*hexanone-2-carboxylate. The structure of the resulting 3 : 4-*benzfluorene* (V) followed from its oxidation to a ketone identical with the known 3 : 4-benzfluorenone (Pfeiffer and Möller, *Ber.*, 1907, **40**, 3839; 1916, **49**, 2425; Schaarschmidt, *Ber.*, 1916, **49**, 1444).

(IV.)



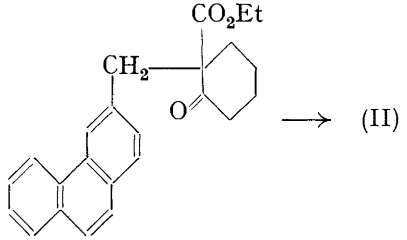
(V.)

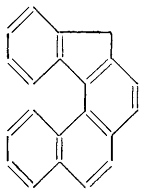
The simpler ethyl 2-benzyl*cyclo*hexanone-2-carboxylate (Cook and Hewett, future communication) could not be cyclised by sulphuric acid of various concentrations; in only one experiment was a minute yield of fluorene obtained. We were likewise unable to synthesise the phenanthrene ring system from ethyl 2-β-phenylethyl*cyclo*hexanone-2-carboxylate, although cyclisations readily occur with the analogous compounds containing naphthyl or acenaphthyl radicals in place of phenyl (compare Ruzicka, Ehmann, Goldberg, and Hösli, *Helv. Chim. Acta*, 1933, **16**, 833; Cook, Haslewood, and Robinson, this vol., p. 667).

The synthesis of 3 : 4-benzfluorene was extended to 1′ : 2′-naphtha-2 : 3-fluorene (II). The 3-phenanthrylmethyl bromide required for this purpose was obtained from 3-phenanthroic acid by essentially the method of Mosettig and van de Kamp (*J. Amer. Chem. Soc.*, 1933, **55**, 2995) with the modification introduced by Bachmann (*ibid.*, 1935, **57**, 559). A preliminary experiment on the chloromethylation of phenanthrene led to 9-*chloromethylphenanthrene*, the orientation of which was shown by oxidation to 9-phenanthroic acid and phenanthraquinone.

3-Phenanthrylmethyl bromide was condensed with ethyl potassio*cyclo*hexanone-2-carboxylate, and the resulting *keto-ester* (VI) cyclised with boiling 65% sulphuric acid. This led to 1′ : 2′-naphtha-2 : 3-fluorene (II), dehydrogenation being completed by heating with selenium.

(VI.)

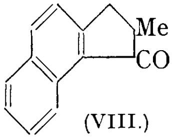




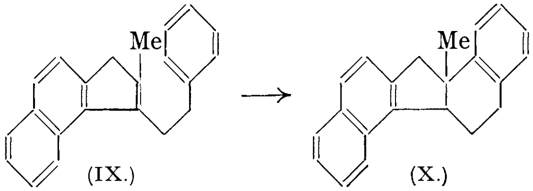
(VII.)

Although there are abundant analogies to justify the assumption that ring closure of (VI) would occur in position 2 rather than position 4 of the phenanthrene system, it was important to exclude decisively the second alternative. This was done by *X*-ray crystallographic examination of the synthetic hydrocarbon, the results of which were in harmony with a long flat molecule (formula II), but could in no way be reconciled with structure (VII). In its cell dimensions, 1′ : 2′-naphtha-2 : 3-fluorene, like 2′ : 1′-naphtha-1 : 2-fluorene, shows considerable similarity to Ruzicka's hydrocarbon "$C_{21}H_{16}$" (compare Bernal and Crowfoot, *loc. cit.*).

As part of our general scheme of investigation of the molecular factors necessary for carcinogenic activity, 1 : 2 : 5 : 6-*dibenzfluorene* was prepared for comparison with the carcinogenic 1 : 2 : 5 : 6-dibenzanthracene. 2-Bromomethylnaphthalene was converted, through *methyl-2-naphthylmethylmalonic acid* and β-2-*naphthyl-α-methylpropionic acid*, into 2-*methyl*-6 : 7-*benzhydrindone* (VIII), from which 3-β-*phenylethyl-2-methyl*-4 : 5-*benzindene* (IX) was obtained by interaction with β-phenylethylmagnesium chloride.



(VIII.)



(IX.) (X.)

The indene (IX) was cyclised by aluminium chloride to *methyltetrahydrodibenzfluorene* (X), which was dehydrogenated by selenium to 1 : 2 : 5 : 6-dibenzfluorene.

EXPERIMENTAL.

* and † denote microanalyses by Dr. A. Schoeller and Dr. G. Weiler, respectively. All other analyses were made by Mr. F. Goulden.

3 : 4-*Benzfluorene*.

*Attempted Synthesis from 2-(2′-Naphthylmethyl)-1-methyl-Δ^1-*cyclo*hexene.*—A mixture of 2-bromomethylnaphthalene (44·2 g.) and anhydrous ether (250 c.c.) was slowly added to magnesium turnings (4·9 g.). After boiling for 2 hours, the product was cooled and treated gradually with 2-methyl*cyclo*hexanone (22·4 g.). The mixture was kept for 3 hours at room temperature, and then decomposed with ice and ammonium chloride. A considerable amount of white crystalline material remained undissolved in the ether. This was collected and identified as αβ-di-2-naphthylethane (10 g.). The ethereal filtrate was washed and dried, and the ether and unchanged ketone removed by distillation. The residual oil (8 g.) was dehydrated with potassium hydrogen sulphate at 160—170° (1 hour). The resulting hydrocarbon (6 g.) had b. p. 178—185°/6 mm., was unsaturated towards bromine, and gave no satisfactory picrate. Cyclisation was effected by aluminium chloride (6 g.) in carbon disulphide (60 c.c.) at 0° (6 hours). The saturated product (2·8 g.) was isolated in the usual way and purified through its picrate, which crystallised from alcohol in orange needles, m. p. 114—118°. The regenerated *hydrocarbon* (III or isomeride) formed a colourless liquid, b. p. 200—205°/7 mm. (Found : C, 91·0; H, 8·6. $C_{18}H_{20}$ requires C, 91·5; H, 8·5%).

This hydrocarbon (0·9 g.) was heated with selenium (2 g.) at 305—320° for 23 hours. After distillation, the product gave a picrate, m. p. 115—118°, not depressed by admixture with the picrate of the original hydrocarbon.

*Ethyl 2-β-Naphthylmethyl*cyclo*hexanone-2-carboxylate* (IV).—Potassium (1·96 g.) was dissolved in ethyl *cyclo*hexanone-2-carboxylate (8 g.) in benzene (50 c.c.), and the cooled solution slowly treated with a benzene solution of 2-bromomethylnaphthalene (11 g.). After boiling for 5 hours, the cooled mixture was treated with ice, the benzene solution washed and dried, and the benzene removed. Distillation of the residue gave the *keto-ester* (IV; 7·9 g.), b. p. 190°/0·7 mm. This formed a viscous liquid which crystallised on standing, and separated from light petroleum in colourless irregular plates, m. p. 69—71° (Found : C, 77·1; H, 7·2. $C_{20}H_{22}O_3$ requires C, 77·3; H, 7·15%).

3 : 4-*Benzfluorene* (V).—This hydrocarbon (0·15 g.) was obtained directly when the aforesaid keto-ester (3 g.) was heated for 16 hours with sulphuric acid (50 c.c.) and water (50 c.c.). Better results were obtained, however, by heating for a shorter time, and then completing the dehydro-

genation by heating with selenium. A suspension of the keto-ester (IV; 18 g.) in sulphuric acid (125 c.c.) and water (125 c.c.) was boiled for 7½ hours, and the product extracted with ether. The extract was washed with dilute sodium carbonate solution and water, and the ether removed. The residue was distilled in a high vacuum and the distillate (8·8 g.) was heated with selenium (5 g.) at 300—320° for 24 hours. The resulting 3 : 4-benzfluorene was purified through its *picrate*, which crystallised from alcohol in brick-red tabular needles, m. p. 130—131° (* Found : C, 61·8; H, 3·4. $C_{17}H_{12},C_6H_3O_7N_3$ requires C, 62·0; H, 3·4%). The regenerated 3 : 4-*benzfluorene* (V; 0·7 g.) separated from alcohol in colourless rectangular plates, m. p. 124—125° († Found : C, 94·0; H, 5·7. $C_{17}H_{12}$ requires C, 94·4; H, 5·6%).

Oxidation of this hydrocarbon (0·5 g.) with sodium dichromate (1 g.) in boiling acetic acid (20 c.c.) for 1¼ hours gave a dark-coloured resin, from which no crystalline product could be obtained directly. The presence of 3 : 4-benzfluorenone was shown, however, in two ways :

(a) A solution of the crude oxidation product in glacial acetic acid (10 c.c.) was boiled for 15 minutes with Girard's ketonic reagent, trimethylaminoacetohydrazide chloride ‡ (1 g.). The cooled solution was treated with ice and water, and most of the acid was neutralised with potassium hydroxide (8·5 g.). Non-ketonic substances were extracted with ether, some unchanged hydrocarbon being isolated from the ethereal extract. The orange aqueous solution was acidified with concentrated hydrochloric acid (20 c.c.), and then warmed on the water-bath for 15 minutes. The resulting brown precipitate was collected and recrystallised from acetic acid, and had m. p. 156—158°, not depressed by a specimen of 3 : 4-benzfluorenone (m. p. 161°) prepared from phenylpropiolic acid (Schaarschmidt, *loc. cit.*).

(b) The crude oxidation product was treated with semicarbazide in boiling aqueous-alcoholic solution. This gave a crystalline substance, from which unchanged hydrocarbon was extracted by boiling alcohol. The insoluble residue had m. p. 230—232° (decomp.), not depressed by the *semicarbazone* prepared from authentic 3 : 4-benzfluorenone. This semicarbazone separated from dioxan in canary-yellow microscopic needles, m. p. 235° (decomp.) († Found : N, 14·55. $C_{18}H_{13}ON_3$ requires N, 14·6%).

1′ : 2′-*Naphtha*-2 : 3-*fluorene*.

9-*Chloromethylphenanthrene*.—Hydrogen chloride was passed for 7 hours into a vigorously stirred suspension of finely powdered phenanthrene (50 g.) in concentrated hydrochloric acid (250 c.c.) and 40% formaldehyde (40 c.c.), the temperature being maintained at 90°. The product was extracted with ether, washed, and fractionally distilled at 0·8 mm. The fraction, b. p. 180—200°, was twice redistilled, giving a fraction, b. p. 185°/0·6 mm. (15 g.). After several recrystallisations from alcohol, the picrate prepared from this fraction had m. p. 99·5—100·5°, and gave 9-*chloromethylphenanthrene*, which crystallised from light petroleum in colourless needles, m. p. 101—101·5° (Found : C, 78·9; H, 5·1. $C_{15}H_{11}Cl$ requires C, 79·4; H, 4·9%). Oxidation of this chloro-compound with 3 parts of sodium dichromate in boiling acetic acid gave a mixture of 9-phenanthroic acid and phenanthraquinone, the latter being converted into the phenazine with *o*-phenylenediamine. All three compounds were identified by direct comparison with authentic specimens.

Ethyl 2-(3′-*Phenanthrylmethyl*)cyclo*hexanone*-2-*carboxylate* (VI).—The chloride of 3-phenanthroic acid (Mosettig and van de Kamp, *J. Amer. Chem. Soc.*, 1930, **52**, 3704) was converted into 3-phenanthraldehyde by the procedure outlined by Bachmann (*loc. cit.*), and the aldehyde hydrogenated to the carbinol by platinum-black in ethyl alcohol. 3-Bromomethylphenanthrene was obtained from this carbinol by the method of Mosettig and van de Kamp (*J. Amer. Chem. Soc.*, 1933, **55**, 2995).

A suspension of powdered potassium (3 g.) in toluene was heated with ethyl *cyclo*hexanone-2-carboxylate (13·2 g.). After all had dissolved, 3-bromomethylphenanthrene (17·5 g.) was added, and the whole boiled for 6 hours. After cooling, water was added, the toluene solution washed and dried, and the toluene removed. Unreacted material was removed by distillation at 0·3 mm. (bath gradually heated to 240°), and the residue was recrystallised from alcohol, yielding 8 g. of the keto-ester, m. p. 97—98°. After two recrystallisations from alcohol (charcoal), *ethyl* 2-(3′-*phenanthrylmethyl*)cyclo*hexanone*-2-*carboxylate* (VI) formed colourless crystals, m. p. 98—98·5° (Found : C, 79·8; H, 6·9. $C_{24}H_{24}O_3$ requires C, 80·0; H, 6·7%).

1′ : 2′-*Naphtha*-2 : 3-*fluorene* (II).—A suspension of the foregoing keto-ester (VI; 6 g.) in sulphuric acid (72 c.c.) and water (72 c.c.) was boiled for 16 hours. The product was extracted with ether, and the extract washed with sodium carbonate solution and water and distilled at 0·4 mm. from an air-bath at 240°. The product, which gave some naphthafluorene on tritur-

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‡ We are indebted to Dr. Girard for a generous supply of this reagent.

ation with alcohol, was completely dehydrogenated by heating with platinum-black at 320° for 24 hours. Crystallisation from alcohol, vacuum sublimation, and then crystallisation from benzene–alcohol gave 0·4 g. of 1′ : *2′-naphtha-*2 : *3-fluorene* (II), which formed colourless leaflets, m. p. 226—226·5° († Found : C, 94·3; H, 5·6; M, Rast method, 297. $C_{21}H_{14}$ requires C, 94·7; H, 5·3%; M, 266).

1′ : *2′-Naphtha-*2 : *3-fluorenone* was obtained when the hydrocarbon (II; 0·2 g.) was oxidised by sodium dichromate (0·6 g.) in boiling glacial acetic acid (15 c.c.) for 15 minutes. The product was sublimed at 200°/0·2 mm. and twice recrystallised from acetic acid, the ketone forming reddish-brown needles, m. p. 214·5—215° (* Found : C, 89·3; H, 4·4. $C_{21}H_{12}O$ requires C, 90·0; H, 4·3%). This ketone gave a magenta solution in concentrated sulphuric acid. The low value for carbon, probably due to contamination with a quinone, was unaffected by recrystallisation, and the amount of material was insufficient for further purification.

Crystal Structure of 1′ : *2′-Naphtha-*2 : *3-fluorene* (by JOHN IBALL).

From X-ray rotation and oscillation photographs the unit cell of crystals of this substance was found to be orthorhombic, with dimensions : $a = 8·66$ Å., $b = 5·71$ Å., $c = 27·3$ Å. The cell contains 4 molecules, and the probable space group is $P2_12_12_1$. The optical sign is negative and α, β, γ are in the directions a, b, c, respectively.

Of the two possible structures (II and VII) which the molecule can possess, only one is consistent with the above data. The molecules must be elongated, and approximately flat. The optical properties show that the length of the molecule is along the c axis and the width approximately along the b axis. Therefore, only structure (II) can be correct.

Assuming the space group $P2_12_12_1$ and allowing for the necessary distance between the molecules, they can be arranged as follows : One molecule lies at each corner of the cell, and the rotated molecule half a translation along the a axis. Then, because of the glide planes, there will be a molecule at the centre of the (100) face. The length of the molecule is along the c axis, but to allow sufficient distance between molecules at each end of the b axis they must be rotated so that their width makes an angle of 30—40° to the b axis. This arrangement brings the plane of the molecule almost into the plane (210), which is the strongest plane observed, two other strong planes being (110) and (200). The (020) plane is very weak.

Ultra-violet Absorption Spectrum of 1′ : *2′-Naphtha-*2 : *3-fluorene* (by W. V. MAYNEORD and E. ROE).

The technique used was that previously described (J., 1934, 1727). The Fig. gives the absorption curve of 1′ : 2′-naphtha-2 : 3-fluorene, as well as that of Diels's hydrocarbon, "$C_{25}H_{24}$," reproduced for comparison. $K = \log (I_0/I)/l$, and has the same significance as ε, the symbol used in our former publication. The more important differences between the two curves are (a) wave-length shifts of the bands throughout, and (b) the much greater intensities of the bands of 1′ : 2′-naphtha-2 : 3-fluorene at 3464 and 3635 Å.

The following are the wave-lengths and extinction coefficients at the maxima of the bands of 1′ : 2′-naphtha-2 : 3-fluorene (c = g./l.) :

λ	3635	3550	3464	3386	3301	3178	3114	3037	2961	2793	2698
$\log (K/c)$......	1·297	0·590	1·255	0·699	1·085	2·239	1·851	2·036	2·069	2·372	2·396

The values for Diels's hydrocarbon are :

λ	3654	3562	3485	3390	3198	2980	2822	2730	2393
$\log (K/c)$......	0·797	0·447	0·806	0·622	1·910	2·009	2·328	2·243	1·854

1 : 2 : 5 : *6-Dibenzfluorene.*

*2-Methyl-*6 : *7-benzhydrindone* (VIII).—2-Bromomethylnaphthalene (44 g.), dissolved in a little benzene, was added to a suspension of the sodio-compound prepared from ethyl methylmalonate (34·8 g.) and sodium (4·5 g.) in benzene (120 c.c.). The whole was boiled for 3 hours, and the new ester was isolated in the usual way. It formed a thick oil (33·5 g.), b. p. 180—190°/0·6 mm. *Methyl-2-naphthylmethylmalonic acid,* obtained by hydrolysis of this ester with boiling alcoholic potassium hydroxide, crystallised from benzene in white, microscopic, slender needles, m. p. 166—168° (Found : C, 69·7; H, 5·4. $C_{15}H_{14}O_4$ requires C, 69·7; H, 5·5%). Heating at 170° decarboxylated this malonic acid to *β-2-naphthyl-α-methylpropionic acid,* which crystallised from ligroin in colourless lath-shaped needles, m. p. 90° (Found: C, 77·9; H, 6·7. $C_{14}H_{14}O_2$ requires C, 78·5; H, 6·6%). For dehydration to *2-methyl-*6 : *7-benzhydrindone* (VIII), a mixture of the propionic acid (13 g.) and anhydrous stannic chloride (20 c.c.) was heated at 120° for 4 hours. The ketone was isolated in the usual way, distilled in a vacuum (b. p. 175°/7 mm.), and recrystallised from light petroleum (yield, 11·5 g.). It formed short colourless prisms, m. p. 51—52° (Found: C, 85·5; H, 6·1. $C_{14}H_{12}O$ requires C, 85·7; H, 6·2%).

3-β-*Phenylethyl*-2-*methyl*-4 : 5-*benzindene* (IX).—2-Methyl-6 : 7-benzhydrindone (11 g.), dissolved in a little ether, was added to a Grignard solution prepared from phenylethyl chloride (8 g.), magnesium turnings (1·4 g.), and anhydrous ether (50 c.c.). After 5 hours at room temperature, ice and ammonium chloride were added, the ethereal solution was washed and dried, and the ether and excess of the hydrindone removed by distillation. The residual crude carbinol (8·9 g.) was dehydrated with potassium hydrogen sulphate, and the indene distilled (b. p. 190—195°/0·4 mm.). The distillate (6·9 g.) was sufficiently pure for the next stage, a sample being purified for analysis by crystallisation of its *dipicrate*, which crystallised from alcoholic picric acid in dark red needles, m. p. 132° (* Found: C, 55·2; H, 3·6. $C_{22}H_{20},2C_6H_3O_7N_3$ requires C, 55·0; H, 3·5%). The regenerated *hydrocarbon* (IX), distilled over sodium in a vacuum, formed a pale yellow, viscous oil, which slowly crystallised (Found: C, 92·5; H, 7·2. $C_{22}H_{20}$ requires C, 92·9; H, 7·1%).

Methyltetrahydro-1 : 2 : 5 : 6-*dibenzfluorene* (X).—Cyclisation of the indene (IX; 6 g.) in carbon disulphide (60 c.c.) with anhydrous aluminium chloride (6 g.) was complete after 4 hours at 0°. The pentacyclic hydrocarbon (X) formed a colourless viscous liquid (3·6 g.), saturated towards bromine, and was characterised by its *picrate*, which crystallised from alcohol in orange needles, m. p. 155° (* Found: C, 65·2; H, 4·5. $C_{22}H_{20},C_6H_3O_7N_3$ requires C, 65·4; H, 4·5%).

1 : 2 : 5 : 6-*Dibenzfluorene*.—The methyltetrahydro-compound (X; 2 g.) was heated with selenium (3 g.) at 310—320° for 20 hours. The product was extracted with benzene, and distilled at 0·3 mm. The resulting 1 : 2 : 5 : 6-*dibenzfluorene* (0·7 g.) crystallised from benzene–alcohol in thin, colourless, rectangular plates, m. p. 171—172° (* Found: C, 94·2; H, 5·3. $C_{21}H_{14}$ requires C, 94·7; H, 5·3%).

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