## 10. *The Synthesis of Some Hexa-, Hepta-, and Octa-cyclic Hydrocarbons Derived from Fluorene.*

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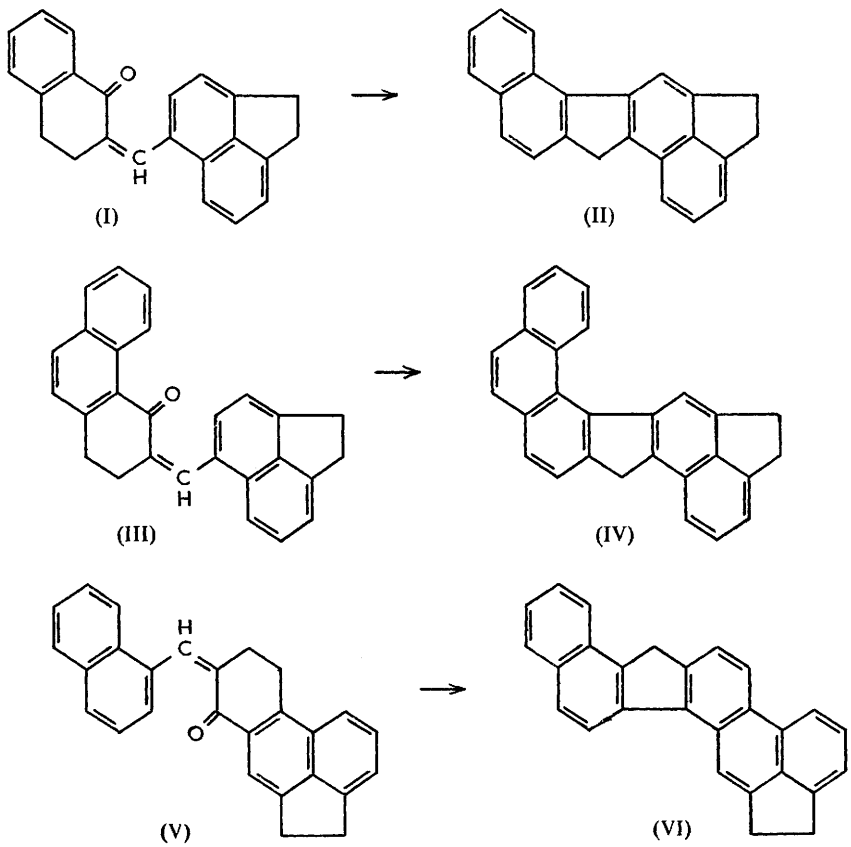
Condensed polycyclic hydrocarbons containing fluorene and acenaphthene or pyrene nuclei have been prepared by cyclodehydration of the appropriate polycyclic arylidene-α-tetralones.

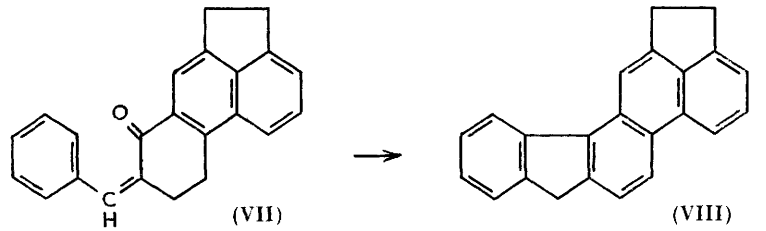
1 : 2-5 : 6-Dibenzofluorene is known to act as a biological antagonist of carcinogenic hydrocarbons such as 20-methylcholanthrene,[1] an effect which has been attributed to competitive fixation on cell proteins.[2] 1 : 2-5 : 6-Dibenzofluorene also exhibits strong inhibitory effects on the growth of grafted tumours in mice,[3] whilst its tumour-producing activity is of a very low order.[4] As part of a general study of the inhibition of



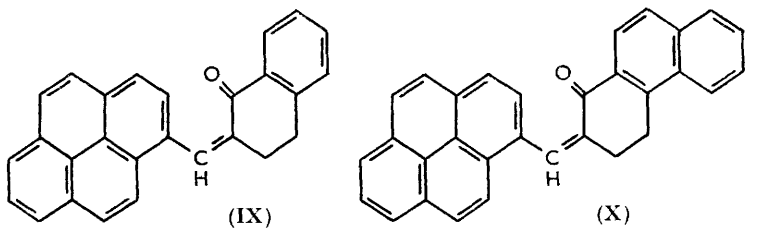

carcinogenesis, further polycyclic hydrocarbons of the same type were investigated, and this paper reports the synthesis of a number of hexa-, hepta-, and octa-cyclic fluorene derivatives containing also an acenaphthene or a pyrene ring.

[1] Lacassagne, Buu-Hoï, and Cagniant, *Compt. rend. Soc. biol.*, 1944, **138**, 16.
[2] Lacassagne, Buu-Hoï, and Rudali, *Brit. J. Expt. Path.*, 1945, **26**, 5; Buu-Hoï, *Arzneimittel-Forschung*, 1954, **4**, 531.
[3] Badger, Elson, Haddow, Hewett, and Robinson, *Proc. Roy. Soc.*, 1942, **130**, *B*, 255.
[4] Cf. Badger, Cook, Hewett, Kennaway, Kennaway, Martin, and Robinson, *Proc. Roy. Soc.*, 1940, **129**, *B*, 439.

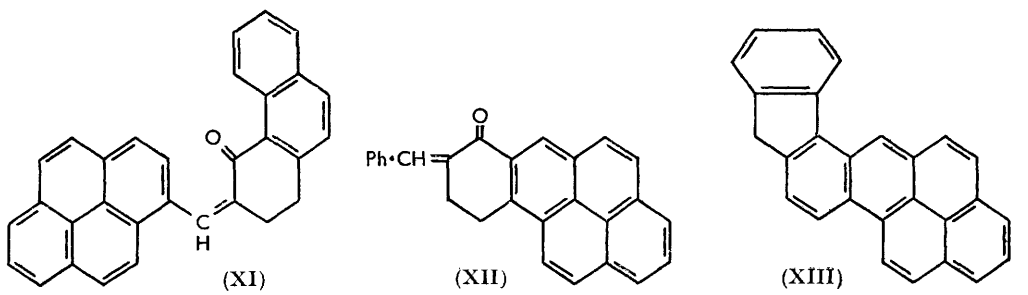
Rapson and Shuttleworth showed that 2-benzylidene-1 : 2 : 3 : 4-tetrahydro-1-oxonaphthalene undergoes cyclodehydration to 3 : 4-benzofluorene,[5] and the mechanism of this reaction was elucidated later by Buu-Hoï and Cagniant,[6] who extended the method to the synthesis of a number of more condensed fluorenes.[7] This reaction has now been applied to 2-(3-acenaphthenylmethylene)-1 : 2 : 3 : 4-tetrahydro-1-oxonaphthalene (I)



(VII) (VIII)

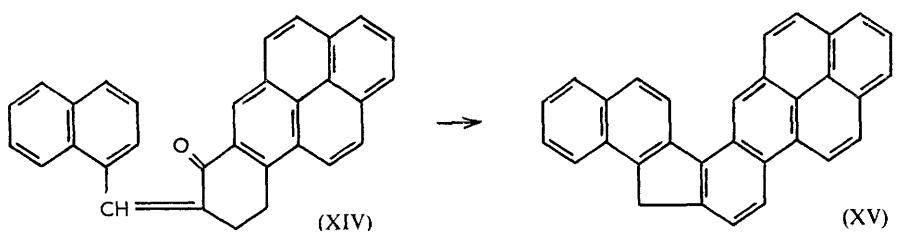


(IX) (X)




(XI) (XII) (XIII)

(prepared by condensation of acenaphthene-3-aldehyde with α-tetralone), which furnished in good yield, the hexacyclic compound (II); similarly, 3-(3-acenaphthenylmethylene)-1 : 2 : 3 : 4-tetrahydro-4-oxophenanthrene (III) gave the heptacyclic hydrocarbon (IV),



(XIV) (XV)

which has the surprisingly low m. p. of 138°, compared with that (228°) of its simpler analogue (II). Isomeric with the hydrocarbon (IV) is the compound (VI) obtained by cyclodehydration of the ketone (V), itself prepared by condensation of 1-naphthaldehyde with 1 : 2 : 3 : 4-tetrahydro-1-oxoacephenanthrene; the similar but simpler compound (VIII) was formed analogously in lower yield.

[5] Rapson and Shuttleworth, *J.*, 1940, 636.
[6] Buu-Hoï and Cagniant, *Rev. sci.*, 1943, **81**, 30.
[7] Buu-Hoï and Cagniant, *ibid.*, 1942, **80**, 319, 384, 436.

In the pyrene series, the ketones (IX), (X), and (XI) did not undergo cyclodehydration, but the reaction was successful with compounds (XII) and (XIV), which gave respectively the heptacyclic (XIII) and octacyclic (XV). These last two, yellow hydrocarbons are of especial interest, since they can be considered as substitution products of the highly carcinogenic 3 : 4-benzopyrene.

Results of tests for carcinogenic and/or tumour inhibitory effects will be reported elsewhere.

## Experimental

2-(3-*Acenaphthenylmethylene*)-1 : 2 : 3 : 4-*tetrahydro*-1-*oxonaphthalene* (I).—The recorded method [8] for the preparation of acenaphthene-3-aldehyde was modified as follows: A solution of acenaphthene (50 g.) and dimethylformamide (27 g.) in dry xylene (100 c.c.) was heated on a water-bath for 6 hr. with phosphorus oxychloride (55 g.), a concentrated aqueous solution of sodium acetate in excess was added, and the mixture refluxed for 30 min. After cooling, the aldehyde was taken up in benzene, washed with water, and dried ($Na_2SO_4$), the solvent removed, and the residue fractionated *in vacuo*, giving 30% of aldehyde, b. p. 207—208°/15 mm., m. p. 88°. A mixture of this aldehyde (5 g.), α-tetralone (4 g.), and 4% ethanolic potassium hydroxide (50 c.c.) was shaken for 30 min., and left for 36 hr. at room temperature; the precipitated crystalline mass was collected, washed with dilute aqueous acetic acid, then with water, dried, and recrystallised from ethanol–benzene, giving the *product* as yellow leaflets (5 g.), m. p. 166°, dissolving in sulphuric acid with a deep violet colour (Found: C, 89·0; H, 5·9. $C_{23}H_{18}O$ requires C, 89·0; H, 5·8%).

3 : 3′-*Dimethylene*-1 : 2-5 : 6-*dibenzofluorene* (II).—A solution of the foregoing ketone (4·3 g.) in dry xylene (50 c.c.) was refluxed with phosphoric oxide (4 g.) for 30 hr.; after cooling, water was added, the organic layer washed with dilute aqueous sodium hydroxide, then with water, and dried ($Na_2SO_4$), the xylene distilled off, and the residue fractionated *in vacuo*. Crystallisation of the portion, b. p. >250°/1 mm., from ethanol–benzene yielded the colourless *hydrocarbon* as needles (1 g.), m. p. 228° (Found: C, 94·3; H, 5·7. $C_{23}H_{16}$ requires C, 94·5; H, 5·5%), giving a *dipicrate*, prisms, m. p. 199° (from benzene) (Found: N, 11·5. $C_{35}H_{22}O_{14}N_6$ requires N, 11·2%).

3 : 3′-*Dimethylene*-1 : 2-*benzonaphtho*(1″ : 2″-5 : 6)*fluorene* (IV).—A mixture of 1 : 2 : 3 : 4-tetrahydro-4-oxophenanthrene [9] (3·5 g.), acenaphthene-5-aldehyde (3·3 g.), and 4% ethanolic potassium hydroxide (50 c.c.) was treated as above, giving a red amorphous resin. The ethanol was distilled off, dilute aqueous acetic acid added, and the crude ketone (III) taken up in benzene; the benzene solution was washed with water and dried ($Na_2SO_4$), the solvent removed, and the residue dissolved in xylene (40 c.c.). The xylene solution was then refluxed for 30 hr. with phosphoric oxide (4 g.), and the product worked up as for (II). The portion of b. p. >260°/0·5 mm. was treated in benzene with picric acid, giving a *dipicrate*, brick red prisms, m. p. 195—196° (Found: N, 10·4. $C_{39}H_{24}O_{14}N_6$ requires N, 10·5%). Treatment with aqueous ammonia yielded a *hydrocarbon*, crystallising as yellowish prisms, m. p. 138°, from ethanol–benzene (no halochromy in sulphuric acid) (Found: C, 94·4; H, 5·4. $C_{27}H_{18}$ requires C, 94·7; H, 5·3%).

7 : 8 : 9 : 10-*Tetrahydro*-8-(1-*naphthylmethylene*)-7-*oxoacephenanthrene* (V).—7 : 8 : 9 : 10-Tetrahydro-7-oxoacephenanthrene was synthesised from succinic anhydride and acenaphthene by Fieser and Peters's method,[10] except that reduction of the keto-acid (m. p. 214°, instead of m. p. 208°) was performed by the Huang-Minlon modification of the Wolff–Kishner reaction; [11] the ketone, b. p. 250—256°/16 mm., m. p. 148° (lit., 147°), gave an orange-yellow halochromy in sulphuric acid. Treatment of this ketone (3·5 g.) with 1-naphthaldehyde (2·8 g.) in the usual way, afforded immediately a crystalline *product*, which formed pale yellow leaflets (3·5 g.), m. p. 220° (ethanol–benzene), giving a deep violet halochromy in sulphuric acid (Found: C, 90·3; H, 5·6. $C_{27}H_{20}O$ requires C, 90·0; H, 5·6%).

1 : 2-*Benzoacenaphtheno*(2′ : 3′-5 : 6)*fluorene* (VI).—A solution of the foregoing ketone (3 g.) in

[8] Cf. Fieser and Herschberg, *J. Amer. Chem. Soc.*, 1938, **60**, 2542.
[9] Buu-Hoï and Saint-Ruf, *J.*, 1957, 3806.
[10] Fieser and Peters, *J. Amer. Chem. Soc.*, 1932, **54**, 4347.
[11] Huang-Minlon, *ibid.*, 1946, **68**, 2487.

xylene (50 c.c.) was refluxed with phosphoric oxide (2·4 g.) for 30 hr.; the mixture, worked up in the usual way, afforded a *hydrocarbon*, yellowish needles (1·2 g.), m. p. 231° (from ethanol–benzene) (Found: C, 94·4; H, 5·5. $C_{27}H_{18}$ requires C, 94·7; H, 5·3%). The *picrate* crystallised as red leaflets, m. p. 211—212° (decomp. >180°), from benzene (Found: N, 7·0. $C_{33}H_{21}O_7N_3$ requires N, 7·4%).

8-*Benzylidene*-7 : 8 : 9 : 10-*tetrahydro*-7-*oxoacephenanthrene* (VII).—This *product*, prepared from 7 : 8 : 9 : 10-tetrahydro-7-oxoacephenanthrene (3·5 g.), benzaldehyde (1·7 g.), and 4% ethanolic potassium hydroxide (50 c.c.), crystallised as pale yellow leaflets (3·5 g.), m. p. 169°, from ethanol, giving a blood-red halochromy with sulphuric acid (Found: C, 88·8; H, 6·2. $C_{23}H_{18}O$ requires C, 89·0; H, 5·9%).

*Acenaphtheno*(3′ : 2′-3 : 4)*fluorene* (VIII).—This *hydrocarbon*, prepared from the foregoing ketone (2·5 g.), formed colourless prisms (0·8 g.), m. p. 209°, from ethanol–benzene, giving no colour in cold sulphuric acid (Found: C, 94·2; H, 5·5. $C_{23}H_{16}$ requires C, 94·5; H, 5·5%).

1-(1 : 2 : 3 : 4-*Tetrahydro*-1-*oxo*-2-*naphthylidenemethyl*)*pyrene* (IX).—Pyrene-1-aldehyde (m. p. 127°, b. p. 287°/17 mm.) was prepared by formylation of pyrene with dimethylformamide, at variance with the literature.[12] Treatment of this aldehyde (4 g.) with α-tetralone (2·5 g.) in the presence of ethanolic potassium hydroxide afforded the *product* as deep yellow leaflets (5·2 g.), m. p. 200°, from ethanol–benzene (dark violet halochromy in sulphuric acid) (Found: C, 90·1; H, 5·1. $C_{27}H_{18}O$ requires C, 90·5; H, 5·1%). Cyclodehydration of this yielded no definite hydrocarbon, the only product which could be identified being pyrene (m. p. 149°; picrate, m. p. 222°) in small amounts.

1-(1 : 2 : 3 : 4-*Tetrahydro*-1-*oxo*-2-*phenanthrylidenemethyl*)*pyrene* (X).—This *ketone* was prepared from 1 : 2 : 3 : 4-tetrahydro-1-oxophenanthrene (2·6 g.) and pyrene-1-aldehyde (3 g.) in 4% ethanolic potassium hydroxide (100 c.c.). Crystallisation from ethanol–benzene afforded deep yellow leaflets (3 g.), m. p. 258—260° (dark violet halochromy in sulphuric acid) (Found: C, 91·0; H, 4·6. $C_{31}H_{20}O$ requires C, 91·2; H, 4·9%). The isomeric 1-(1 : 2 : 3 : 4-*tetrahydro*-4-*oxo*-3-*phenanthrylidenemethyl*)*pyrene* (XI), prepared similarly, crystallised as yellow prisms, m. p. 220° from ethanol–benzene (violet halochromy in sulphuric acid) (Found: C, 90·9; H, 5·0%). Attempts to cyclodehydrate these ketones resulted only in the separation of some pyrene.

2′-*Benzylidene*-1′ : 2′ : 3′ : 4′-*tetrahydro*-1′-*oxo*-1 : 2-*benzopyrene* (XII).—1′ : 2′ : 3′ : 4′-Tetrahydro-4′-oxo-3 : 4-benzopyrene (m. p. 178°) was prepared from pyrene and succinic anhydride as described,[13] except that the keto-acid was reduced by hydrazine hydrate and potassium hydroxide. Condensation of it (3 g.) with benzaldehyde (1·2 g.) furnished the *ketone* (XII) which formed yellow needles (3·2 g.), m. p. 194°, from ethanol–benzene (violet-red halochromy in sulphuric acid) (Found: C, 90·8; H, 5·1%).

*Fluoreno*(3′ : 4′-1 : 2)*pyrene* (XIII).—Cyclodehydration of the foregoing ketone (3 g.) with phosphoric oxide (2 g.) afforded a *hydrocarbon*, crystallising as yellow leaflets (0·8 g.), m. p. 235°, from ethanol–benzene (Found: C, 95·0; H, 4·9. $C_{27}H_{16}$ requires C, 95·3; H, 4·7%).

1′ : 2′ : 3′ : 4′-*Tetrahydro*-2′-(1-*naphthylmethylene*)-3′-*oxo*-1 : 2-*benzopyrene* (XIV).—This *ketone*, prepared as above from 1-naphthaldehyde, formed deep yellow needles, m. p. 235°, from benzene (deep violet halochromy in sulphuric acid) (Found: C, 90·9; H, 5·0%).

7′ : 8′-*Benzofluoreno*(3′ : 4′-1 : 2)*pyrene* (XV).—Cyclodehydration of the foregoing ketone (2 g.) yielded, on distillation *in vacuo*, a portion, b. p. >300°/1 mm., which on crystallisation from *cyclo*hexane, gave the *hydrocarbon* as golden leaflets (0·7 g.), m. p. 286—287° (decomp. >250° if heated in the air) (violet halochromy in sulphuric acid) (Found: C, 95·1; H, 4·4. $C_{31}H_{18}$ requires C, 95·4; H, 4·6%).

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[12] Vollmann, Becker, Corell, and Streeck, *Annalen*, 1937, **531**, 35.
[13] Cook, Hewett, and Hieger, *J.*, 1933, 395.