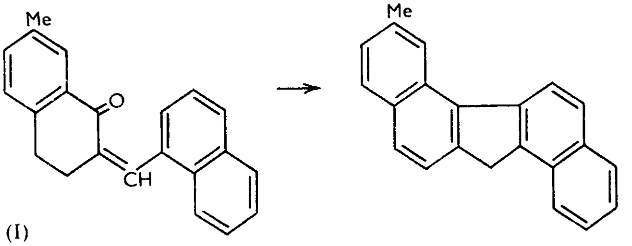
364. *Some New Polycyclic Derivatives of Fluorene and Carbazole.*

By G. Saint-Ruf, Ng. Ph. Buu-Hoï, and P. Jacquignon.

For biological assay as potential carcinogens or tumour-inhibitors, new condensed hydrocarbons derived from fluorene were synthesised by cyclodehydration of the appropriate arylidene-1-tetralones, and new polycyclic derivatives of carbazole were prepared *via* the phenylhydrazones of the appropriate tetralones.

Condensed polycyclic derivatives of fluorene, such as 1 : 2-5 : 6-dibenzofluorene,[1] and of carbazole, such as the mono-[2] and di-benzocarbazoles,[3] are of biological interest as carcinogens and as inhibitors of tumour growth. In order to determine the effect of methyl groups or further rings on these properties, various new compounds in both series have been synthesised.

No homologue of 1 : 2-5 : 6-dibenzofluorene was hitherto known, and the 2″-methyl derivative (II) has now been prepared by cyclodehydration of 1 : 2 : 3 : 4-tetrahydro-7-methyl-2-1′-naphthylidene-1-oxonaphthalene (I) with phosphoric oxide.[4] Like 1 : 2-5 : 6-dibenzofluorene, compound (II) gave a dipicrate. Among more highly condensed hydrocarbons, the compound (IV) was obtained by cyclodehydration of ketone (III), prepared by condensation of acenaphthene-5-aldehyde with 1 : 2 : 3 : 4-tetrahydro-1-oxophenanthrene. Another heptacyclic hydrocarbon (VI), isomeric with (IV) but having an anthracene arrangement, was obtained from ketone (V), itself prepared by condensing 1-naphthaldehyde with 7 : 8 : 9 : 10-tetrahydro-7-oxoaceanthrene.[5] It is interesting that this hydrocarbon can also be considered as a naphtho-derivative of the carcinogenic 7 : 8-*cyclo*pentadienoaceanthrene;[6] the presence of the aceanthrene group was apparent from the yellow colour of the hydrocarbon and the dark colour of its dipicrate [the isomer (IV) gave a monopicrate].



(I) (II)

In the carbazole group,[4] acenaphtheno(4′ : 3′-1 : 2)carbazole (VIII) was obtained by chloranil dehydrogenation [7] of the corresponding dihydro-derivative (VII), prepared by Fischer indolisation of the phenylhydrazone of 7 : 8 : 9 : 10-tetrahydro-10-oxoaceanthrene; similarly, pyreno(4′ : 3′-1 : 2)carbazole (X) was prepared from the dihydro-derivative

---

[1] Badger, Cook, Hewett, Kennaway, Kennaway, Martin, and Robinson, *Proc. Roy. Soc.*, 1940, *B*, **129**, 439; Badger, Elson, Haddow, Hewett, and Robinson, *ibid.*, 1942, *B*, **130**, 255.

[2] Lacassagne, Buu-Hoï, Royer, and Zajdela, *Compt. rend. Soc. Biol.*, 1947, **141**, 635; Schürch and Winterstein, *Z. physiol. Chem.*, 1935, **236**, 79.

[3] Boyland and Brues, *Proc. Roy. Soc.*, 1937, *B*, **122**, 429.

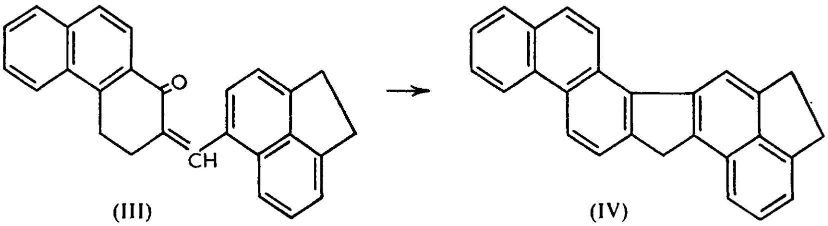
[4] Cf. Buu-Hoï and Cagniant, *Rev. sci.*, 1942, **80**, 319, 384, 436; *ibid.*, 1943, **81**, 30; Buu-Hoï and Saint-Ruf, *J.*, 1957, 3806.

[5] Fieser and Peters, *J. Amer. Chem. Soc.*, 1932, **54**, 4373.

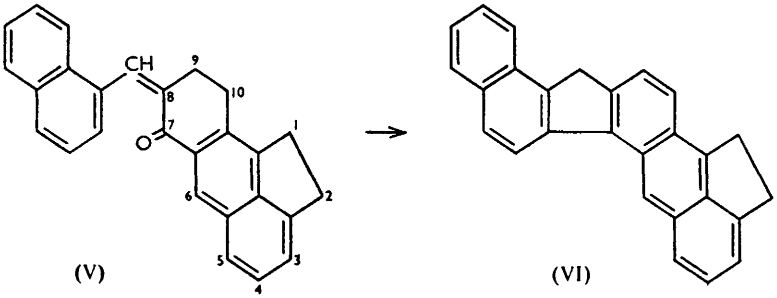
[6] Shear and Leiter, *J. Nat. Cancer Inst.*, 1951, **2**, 99.

[7] Cf. Barclay and Campbell, *J.*, 1945, 530; Buu-Hoï *et al.*, *J. Org. Chem.*, 1949, **14**, 492, 802; 1950, **15**, 131, 511, 957.

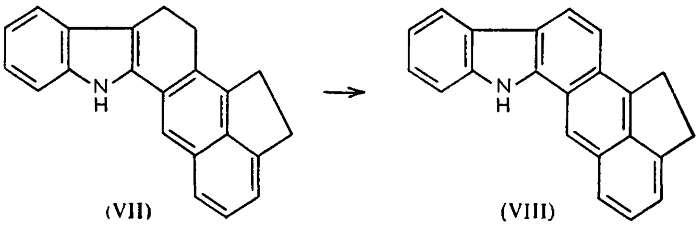
(IX), obtained from the phenylhydrazone of 1′ : 2′ : 3′ : 4′-tetrahydro-4′-oxo-3 : 4-benzopyrene. This last carbazole carries the molecular arrangement of the highly carcinogenic 3 : 4-benzopyrene, which accounts for its intense yellow colour; both the condensed carbazoles (VIII) and (X) share with carbazole itself the property of forming stable, deeply coloured molecular complexes with tetrachlorophthalic anhydride.[8]



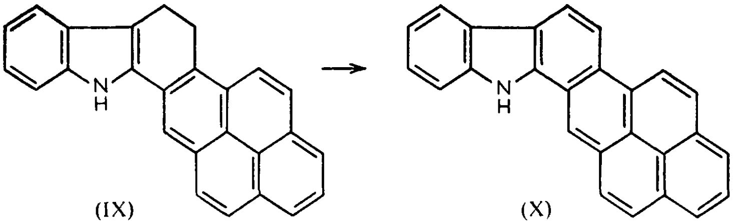
(III) (IV)



(V) (VI)



(VII) (VIII)



(IX) (X)

All the new compounds reported are undergoing tests in this Institute for carcinogenic and tumour-inhibitory effects.

EXPERIMENTAL

1 : 2 : 3 : *4-Tetrahydro-7-methyl-2-1′-naphthylidene-1-oxonaphthalene* (I).—1 : 2 : 3 : 4-Tetrahydro-7-methyl-1-oxonaphthalene [9] (10 g.) and freshly redistilled 1-naphthaldehyde (11 g.) were shaken, at room temperature, with 4% ethanolic potassium hydroxide (50 c.c.) and left overnight. The bulky precipitate formed was filtered off, washed with dilute aqueous acetic acid, then with water, and recrystallised twice from ethanol, giving the *product* as leaflets (18 g.),

---

[8] Buu-Hoï and Jacquignon, *Compt. rend.*, 1952, **234**, 1056; *Bull. Soc. chim. France*, 1957, 488; *Experientia*, 1957, **13**, 375.

[9] Ruzicka and Mörgeli, *Helv. Chim. Acta*, 1936, **19**, 377; Fieser and Dunn, *J. Amer. Chem. Soc.*, 1936, **58**, 572.

m. p. 139°, dissolving in sulphuric acid with a cherry-red halochromy (Found: C, 88·8; H, 5·8. $C_{22}H_{18}O$ requires C, 88·6; H, 6·1%).

*2''-Methyl-*1 : 2-5 : 6-*dibenzofluorene* (II).—A solution of the foregoing ketone (15 g.) in dry xylene (75 c.c.) was refluxed with finely powdered phosphoric oxide (14 g.) for 24 hr. After cooling, ice was added, the xylene layer washed with dilute aqueous sodium hydroxide, then with water, and dried (Na_2SO_4), the solvent removed, and the residue fractionated *in vacuo*. The portion, b. p. 255—265°/1 mm., solidified on trituration with ethanol, and recrystallised from ethanol–benzene as needles (2·5 g.), m. p. 179° (Found: C, 94·2; H, 5·6. $C_{22}H_{16}$ requires C, 94·3; H, 5·7%). This *hydrocarbon* gave a *dipicrate*, brick-red prisms, m. p. 157°, from ethanol (Found: N, 11·9. $C_{34}H_{22}O_{14}N_6$ requires N, 11·4%).

2-*Acenaphthen-5'-ylidene-*1 : 2 : 3 : 4-*tetrahydro-*1-*oxophenanthrene* (III).—A mixture of 1 : 2 : 3 : 4-tetrahydro-1-oxophenanthrene [10] (4·2 g.) and acenaphthene-5-aldehyde (4 g.; prepared by the dimethylformamide technique [11]) was treated with 4% ethanolic potassium hydroxide (50 c.c.) as above; the condensation *product* formed yellow needles (5 g.), m. p. 196°, from ethanol–benzene, giving a violet-red halochromy with sulphuric acid (Found: C, 89·7; H, 5·5. $C_{27}H_{20}O$ requires C, 90·0; H, 5·6%).

1 : 2-*Benzo-*3 : 4'-cyclo*pentenonaphtho*(2'' : 1''-5 : 6)*fluorene* (IV).—The cyclisation *product*, b. p. 262—267°/0·1 mm., obtained by 30 hours' refluxing of the foregoing ketone (4 g.) in xylene (50 c.c.) with phosphoric oxide (3·2 g.), crystallised as colourless leaflets (1·5 g.), m. p. 251°, from benzene (Found: C, 94·6; H, 5·8. $C_{27}H_{18}$ requires C, 94·7; H, 5·3%). The *picrate* formed brownish needles, m. p. 230°, from benzene (Found: N, 7·6. $C_{33}H_{21}O_7N_3$ requires N, 7·4%).

7 : 8 : 9 : 10-*Tetrahydro-*7-*oxoaceanthrene*.—This ketone, m. p. 145°, was prepared by heating a solution of γ-3-acenaphthenylbutyric acid [5] (9 g.) in dry benzene (150 c.c.) with thionyl chloride (6 g.) for 1 hr. on the water-bath, evaporating the solvent *in vacuo*, and cyclising the crude acid chloride with aluminium chloride (6 g.) in nitrobenzene (100 c.c.) at room temperature.

7 : 8 : 9 : 10-*Tetrahydro-*8-1'-*naphthylidene-*7-*oxoaceanthrene* (V).—Prepared from the foregoing ketone (2 g.), 1-naphthaldehyde (1·5 g.), and 4% ethanolic potassium hydroxide (50 c.c.), this *ketone* (3·2 g.) crystallised as pale yellow prisms, m. p. 212°, from ethanol–benzene, giving a deep violet halochromy with sulphuric acid (Found: C, 89·8; H, 5·8. $C_{27}H_{20}O$ requires C, 90·0; H, 5·6%).

7 : 8-*Benzoacenaphtheno*(3' : 4'-3 : 4)*fluorene* (VI).—Prepared from the foregoing ketone (3 g.) and phosphoric oxide (2·4 g.) in xylene (75 c.c.), this *hydrocarbon* (1 g.) crystallised as bright yellow leaflets, m. p. 265°, from ethanol–benzene (Found: C, 94·5; H, 5·3. $C_{27}H_{18}$ requires C, 94·7; H, 5·3%). The *dipicrate* formed almost black needles, m. p. 178°, from benzene (Found: N, 10·8. $C_{39}H_{24}O_{14}N_6$ requires N, 10·5%).

3 : 4-*Dihydroacenaphtheno*(4' : 3'-1 : 2)*carbazole* (VII).—A mixture of 7 : 8 : 9 : 10 tetrahydro-7-oxoaceanthrene (1 g.) and phenylhydrazine (1 g.) was heated at 120° until steam ceased to be evolved, and the crude phenylhydrazone thus obtained was treated with a boiling solution of hydrogen chloride in glacial acetic acid (10 c.c.). After dilution with water, the cyclisation product which was precipitated was washed with water, dried, and recrystallised twice from *cyclo*hexane, giving almost colourless prisms (1 g.), m. p. 206°; the solution in benzene showed a strong violet fluorescence (Found: C, 99·2; H, 5·8. $C_{22}H_{17}N$ requires C, 89·5; H, 5·8%). This *carbazole* gave with an equimolar amount of tetrachlorophthalic anhydride in acetic acid, an addition compound as red needles, m. p. 224° (decomp.).

Acenaphtheno(4' : 3'-1 : 2)*carbazole* (VIII).—The foregoing dihydro-compound (0·7 g.) and chloranil (2·5 g.) in dry xylene (50 c.c.) were refluxed for 2 hr.; after cooling, the precipitated tetrachloroquinol was filtered off, the xylene solution washed several times with aqueous sodium hydroxide, then with water, and dried (Na_2SO_4), and the solvent distilled *in vacuo*. Crystallisation of the solid residue from benzene gave the *carbazole* as pale yellow prisms (0·5 g.), m. p. >340° (brown-violet halochromy with sulphuric acid) (Found: N, 4·8. $C_{22}H_{15}N$ requires N, 4·8%). The molecular complex with tetrachlorophthalic anhydride formed brown needles, decomp. >230°. This carbazole is isomeric with the known acenaphtheno(4' : 5'-1 : 2)-carbazole.[12]

3 : 4-*Dihydropyreno*(4' : 3'-1 : 2)*carbazole* (IX).—The crude phenylhydrazone made from

---

[10] Haworth, *J.*, 1932, 1125.

[11] Cf. Saint-Ruf, Buu-Hoï, and Jacquignon, *J.*, 1958, 48.

[12] Buu-Hoï, Khôi, and Xuong, *J. Org. Chem.*, 1951, **16**, 315.

1′ : 2′ : 3′ : 4′-tetrahydro-4′-oxo-3 : 4-benzopyrene[11] (1·5 g.) and phenylhydrazine (1·5 g.) gave with hydrogen chloride in acetic acid (20 c.c.) in the usual way the *dihydro-compound* which crystallised as yellowish prisms (2 g.), m. p. 158°, from acetic acid (mauve halochromy with sulphuric acid) (Found: C, 90·6; H, 5·2; N, 4·2. $C_{26}H_{17}N$ requires C, 90·9; H, 5·0; N, 4·1%). The picrate formed violet needles, m. p. 172°, from benzene.

Pyreno(4′ : 3′-1 : 2)*carbazole* (X).—Prepared from the above dihydro-compound (0·8 g.) and chloranil (2 g.) in xylene (50 c.c.), this *carbazole* formed deep yellow needles, which showed no definite m. p. below 285° and charred above that temperature (Found: C, 91·1; H, 4·5; N, 4·2. $C_{26}H_{15}N$ requires C, 91·5; H, 4·4; N, 4·1%); the halochromy with sulphuric acid was deep violet, and the addition compound with tetrachlorophthalic anhydride was orange.

This investigation was supported in part by a research grant from the National Cancer Institute of the National Institutes of Health, U.S. Public Health Service; the authors thank the authorities concerned.

THE RADIUM INSTITUTE, THE UNIVERSITY OF PARIS. [*Received, December* 23*rd*, 1957.]