CCLXXI.—*Polycyclic Aromatic Hydrocarbons. Part V. Preliminary Studies in the Synthesis of Chrysene Homologues.*

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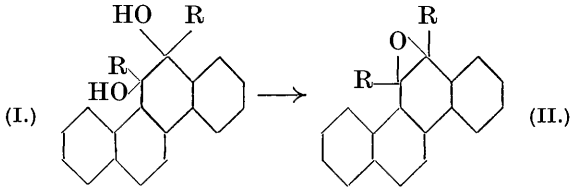
It has been shown in these laboratories that 1 : 2-benzanthracene has latent cancer-producing properties, which are developed by suitable substitution in the molecule. The observation of Twort

and Fulton (*J. Path. Bact.*, 1930, **33**, 119), that chrysene yielded cancers in a small proportion of the mice treated with this compound, has therefore suggested the examination of chrysene homologues. Furthermore, chrysene is very wide-spread as a constituent of cancer-producing tars and oils, and it may be that the active substances are chrysene homologues. Endeavours to devise general methods for the synthesis of chrysene derivatives, while less successful than was hoped, have nevertheless yielded results of some interest.

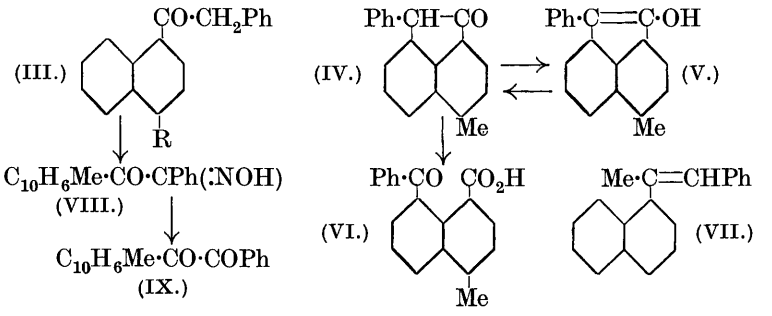
1 : 2-Chrysenequinone reacted normally with Grignard compounds yielding *diols* (I) from which α-pinacolins (II) were formed by dehydration.



(R = Ph or CH_2Ph.)

The *diphenyl* pinacolin (II; R = Ph) was reduced by hydriodic acid and phosphorus to 1 : 2-*diphenylchrysene*, but when the *dibenzyl* compound (I; R = CH_2Ph) was reduced, the benzyl groups were eliminated so that chrysene was the only compound isolated.

The pyrolysis of ketones of type (III) was next examined, for in the absence of any precise knowledge of the mechanism of the Elbs dehydration of *o*-methylbenzophenone derivatives, it was conceivable that chrysene derivatives might be obtained from (III) by dehydration. When 1-phenylacetylnaphthalene (III; R = H) was boiled gently for 3 hours it underwent intramolecular change, with the production of 2-*phenylacetylnaphthalene*, from which 2-naphthoic acid was obtained by oxidation. With 1-*phenylacetyl*-4-*methyl*-



naphthalene (III; R = Me), however, the pyrolysis took a different course, and resulted in dehydrogenation to 7-*phenyl*-3-*methyl*-

8-*acenaphthenone* (IV), which still contained the group $-CO-CH<$ as it yielded a colourless *oxime* and an orange *acetate* (derived from V).

The structure of (IV) follows from its oxidation to 8-*benzoyl*-4-*methyl*-1-*naphthoic acid* (VI), which was converted by fused potassium hydroxide into a mixture of benzoic and 4-methyl-1-naphthoic acids. 1-Phenylacetylnaphthalene and methylmagnesium iodide yielded a carbinol which was easily dehydrated to the corresponding ethylenic hydrocarbon (VII).

Scholl and Schwarzer (*Ber.*, 1922, **55**, 324) obtained phenanthraquinone from benzil in 25% yield by means of aluminium chloride, and this method has recently been extended to substituted benzils by Brass and his collaborators (*Ber.*, 1930, **63**, 2613, 2617, 2621). It thus seemed feasible that chrysenequinone derivatives might be formed from diketones of type (IX).

A substance of this structure was readily obtained from 1-phenylacetyl-4-methylnaphthalene (III; R = Me) through the intermediate iso*nitroso*-compound (VIII). Unfortunately, attempted dehydrogenation with aluminium chloride gave only a microscopic yield of a substance having the properties of a chrysenequinone derivative.

Experimental.

Compounds prepared from 1 : 2-*Chrysenequinone.*

1 : 2-*Dihydroxy*-1 : 2-*diphenyl*-1 : 2-*dihydrochrysene* (I; R = Ph).—A Grignard solution was prepared from bromobenzene (16 c.c.) and magnesium turnings (3·6 g.), the ether removed on the water-bath, and the residue dissolved in benzene (75 c.c.). To the ice-cold solution was gradually added finely powdered chrysenequinone (7·8 g.), and the whole boiled for an hour, and then decomposed with ice and hydrochloric acid. The washed benzene solution was evaporated to small bulk and alcohol added. The resulting crystals were extracted with alkaline hydrosulphite to remove unchanged quinone, and recrystallised from ethyl acetate–alcohol (yield, 4·8 g.). For analysis, a sample of the *diol* was obtained from benzene–light petroleum as a colourless crystalline powder, m. p. 219—220° (Found: C, 86·4; H, 5·35. $C_{30}H_{22}O_2$ requires C, 86·9; H, 5·4%).

1 : 2-*Diphenyl*-1 : 2-*dihydro*-α-*chrysapinacolin* (II; R = Ph).—A solution of the above diol (0·5 g.) in glacial acetic acid (15 c.c.) and concentrated hydrochloric acid (3 c.c.) was boiled for ½ hour. After cooling, the yellowish needles were collected, and recrystallised from benzene–light petroleum (Found: C, 90·6; H, 5·2. $C_{30}H_{20}O$ requires C, 90·9; H, 5·05%). This α-*pinacolin* had m. p. 218·5—219·5°, depressed by the diol, and was not appreciably reduced by zinc powder and hydrochloric acid in acetic acid, by formic acid

and sodium formate, or by hydriodic acid in boiling glacial acetic acid.

1 : 2-*Diphenylchrysene*.—The foregoing α-pinacolin (1·1 g.) was heated at 190—200° for 6 hours with hydriodic acid (*d* 1·9; 10 c.c.) and red phosphorus (0·6 g.). The product was extracted with benzene, and the concentrated extract treated with light petroleum. The resulting solid, recrystallised from benzene, formed a colourless microcrystalline powder, m. p. 208—209° (Found: C, 94·5; H, 5·3. $C_{30}H_{20}$ requires C, 94·7; H, 5·3%).

1 : 2-*Dihydroxy*-1 : 2-*dibenzyl*-1 : 2-*dihydrochrysene* (I; R = CH_2Ph). —Powdered chrysenequinone (7·8 g.) was added to an ice-cold Grignard solution prepared from benzyl chloride (14 c.c.), magnesium turnings (3 g.), and anhydrous ether (75 c.c.). The whole was then boiled for 4½ hours, during which a thick oil separated. The product was decomposed with ice and ammonium chloride, unchanged quinone removed by filtration, and the ethereal solution evaporated. The residual oil was treated with 2—3 volumes of alcohol, and the crystals which slowly separated (3 g.) were recrystallised from alcohol and then *cyclo*hexane. The *diol* formed colourless needles, m. p. 184—185°, and yielded a cherry-red solution in concentrated sulphuric acid (Found: C, 86·8; H, 5·8. $C_{32}H_{26}O_2$ requires C, 86·9; H, 5·9%).

This diol was not changed by boiling acetic acid containing hydrochloric acid or by 2 hours' boiling with zinc powder and acetic acid. Hydriodic acid in acetic acid yielded no pure substance, but when the diol (1·5 g.) was heated at 170—180° for 7 hours with hydriodic acid (*d* 1·9; 12·5 c.c.) and red phosphorus (0·8 g.), chrysene was isolated from the reduction products by crystallisation from benzene.

1 : 2-*Dibenzyl*-1 : 2-*dihydro*-α-*chrysapinacolin* (II; R = CH_2Ph). —A suspension of the diol (I; R = CH_2Ph; 0·8 g.) in 80% sulphuric acid (10 c.c.) was heated on the water-bath for 2 hours. The *product* crystallised from alcohol and then from benzene–*cyclo*hexane as a colourless crystalline powder, m. p. 162—163° (Found: C, 90·3; H, 5·6. $C_{32}H_{24}O$ requires C, 90·5; H, 5·7%).

No crystalline compound could be isolated from the resinous products of the action of methylmagnesium iodide on 1 : 2-chrysenequinone.

Pyrolytic Experiments.

2-*Phenylacetylnaphthalene*.—25 G. of 1-phenylacetylnaphthalene (III; R = H; Graebe and Bungener, *Ber.*, 1879, **12**, 1078) were boiled gently for 3 hours, and the product distilled. By treatment of the viscous oily distillate with light petroleum, a solid was produced which, after two recrystallisations from *cyclo*hexane, formed colourless leaflets, m. p. 99—100° (yield, 2·9 g.). This *ketone* gave

a yellow solution in alcoholic potassium hydroxide (Found : C, 87·7; H, 5·3. $C_{18}H_{14}O$ requires C, 87·8; H, 5·7%). It was oxidised by sodium dichromate in acetic acid at 100° to 2-naphthoic acid (identified by mixed m. p.).

ω-1-*Naphthyl*-ω-*methylstyrene* (VII).—A Grignard solution prepared from methyl iodide (4·6 c.c.) and magnesium turnings (1·8 g.) was added gradually to a water-cooled solution of 1-phenylacetylnaphthalene (12·3 g.) in anhydrous ether (50 c.c.). After 5 hours at room temperature, the product was decomposed with ice and ammonium chloride, the ethereal solution washed, dried with sodium sulphate, and the ether removed. The residual carbinol, which did not crystallise, was dehydrated by heating on the water-bath for 10 minutes with acetic acid (120 c.c.) containing hydrochloric acid (5 c.c.). The crystals which separated on cooling (2·9 g.) were recrystallised from benzene–alcohol, separating as large colourless plates, m. p. 139° (Found : C, 93·1; H, 6·4. $C_{19}H_{16}$ requires C, 93·4; H, 6·6%). This *hydrocarbon* was converted by 2 hours' boiling into an uncrystallisable resin.

1-*Phenylacetyl*-4-*methylnaphthalene* (III; R = Me).—Anhydrous aluminium chloride (35 g.) was added gradually to an ice-cold mixture of 1-methylnaphthalene (28·4 g.), phenylacetyl chloride (30·8 g.), and carbon disulphide (200 c.c.). After standing in ice for 6 hours, the product was decomposed with ice and hydrochloric acid, steam-volatile substances removed, and the residue dried in ethereal solution and distilled. The fraction, b. p. 220—225°/4—5 mm., solidified on cooling (yield, 22 g.), and recrystallisation from light petroleum and then from methyl alcohol gave 1-*phenylacetyl*-4-*methylnaphthalene* (Found : C, 87·5; H, 6·1. $C_{19}H_{16}O$ requires C, 87·7; H, 6·15%), colourless rhombs, m. p. 59—61°.

7-*Phenyl*-3-*methyl*-8-*acenaphthenone* (IV).—1-Phenylacetyl-4-methylnaphthalene (15 g.) was boiled gently for 3 hours, and the product distilled. The distillate was triturated with light petroleum, and the solid (4 g.) recrystallised from *cyclo*hexane and then from alcohol. The new *ketone* formed colourless leaflets, m. p. 162—163°, and gave a purple solution in alcoholic potassium hydroxide [Found : C, 88·35; H, 5·5; *M* (cryoscopic in ethylene dibromide), 255. $C_{19}H_{14}O$ requires C, 88·4; H, 5·4%; *M*, 258]. Reduction experiments with this ketone led to no pure substance.

An *oxime* was formed when 7-phenyl-3-methyl-8-acenaphthenone (IV; 1 g.) in alcohol (50 c.c.) was heated on the water-bath for 2 hours with a solution of hydroxylamine hydrochloride (1·5 g.) and sodium acetate (3 g.) in water (15 c.c.). It formed a colourless crystalline powder (from alcohol), m. p. 195—197° (decomp.) (Found : C, 83·6; H, 5·4. $C_{19}H_{15}ON$ requires C, 83·5; H, 5·5%).

By acetylation of 7-phenyl-3-methyl-8-acenaphthenone (1 g.) with acetic anhydride (1·5 c.c.) in pyridine (5 c.c.) at 100° there was formed an *acetate* of the enolic form (V), which separated from alcohol in deep orange plates, m. p. 113° (Found: C, 83·9; H, 5·2. $C_{21}H_{16}O_2$ requires C, 84·0; H, 5·3%).

8-*Benzoyl*-4-*methyl*-1-*naphthoic Acid* (VI).—A mixture of 7-phenyl-3-methyl-8-acenaphthenone (3 g.), sodium dichromate (3 g.), and glacial acetic acid (50 c.c.) was heated on the water-bath for 2 hours, and the solution cooled and diluted with water. The precipitate was extracted with warm dilute sodium carbonate solution, and the filtered solution acidified with hydrochloric acid. The resulting precipitate was recrystallised from aqueous alcohol (yield, 1·9 g.), methyl alcohol, and finally benzene. The *keto-acid* (VI) formed colourless needles, m. p. 194°, soluble in sulphuric acid with an orange colour (Found: C, 78·7; H, 4·9. $C_{19}H_{14}O_3$ requires C, 78·6; H, 4·8%). Its structure was confirmed by adding it (0·5 g.) to potassium hydroxide (3 g.) at 260°. The melt was kept at 260—280° for 10 minutes, cooled, extracted with water, and acidified. The precipitate, after recrystallisation from aqueous alcohol and benzene, melted at 175—176° alone or mixed with 4-methyl-1-naphthoic acid prepared synthetically from 1-methylnaphthalene. The aqueous liquors were extracted with ether and yielded pure benzoic acid.

Attempted Synthesis of 8-*Methyl*-1 : 2-*chrysenequinone*.

(With R. A. E. Galley.)

α-*Phenyl*-β-(4-*methyl*-1-*naphthyl*)*glyoxal* α-*Monoxime* (VIII).—To an ice-cold solution of sodium (2·4 g.) in absolute alcohol (60 c.c.) was added 1-phenylacetyl-4-methylnaphthalene (III; R = Me; 30 g.) and then amyl nitrite (12 g.), drop by drop. The whole was kept at room temperature for 40 hours, and then treated with dilute alkali and extracted with ether. There remained an insoluble yellow compound (10 g.), which was recrystallised twice from xylene and then formed a lemon-yellow crystalline powder, m. p. 258—259° (decomp.). Analysis showed that this product was probably an *anil* formed by condensation between the original 1-phenylacetyl-4-methylnaphthalene (III) and its iso*nitroso*-derivative (VIII) (Found: C, 85·9; H, 5·6; N, 2·6. $C_{38}H_{29}O_2N$ requires C, 85·9; H, 5·5; N, 2·6%). The aqueous alkaline solution was acidified and extracted with ether, and the ethereal solution washed, dried with anhydrous sodium sulphate, and the ether removed. The residual solid (12 g.) was recrystallised from dilute alcohol and then from benzene (Found: C, 79·0; H, 5·5. $C_{19}H_{15}O_2N$ requires C, 78·9; H, 5·2%). α-*Phenyl*-β-(4-*methyl*-1-*naphthyl*)*glyoxal* α-*monoxime* formed pale yellow crystals, m. p. 160—161°.

α-*Phenyl*-β-(4-*methyl*-1-*naphthyl*)*glyoxal* (IX).—To a solution of the monoxime (5 g.) in a mixture of glacial acetic acid (35 c.c.) and concentrated sulphuric acid (5 c.c.) was added 35% formaldehyde (10 c.c.), the whole warmed on the water-bath for a few minutes, and the clear solution cooled. The crystals which separated were collected after some hours (yield, 4 g.) and recrystallised from *cyclo*hexane. The nitrogen-free *diketone* (IX) formed yellowish plates, m. p. 111·5—112·5° (Found : C, 83·1; H, 5·2. $C_{19}H_{14}O_2$ requires C, 83·2; H, 5·1%).

2-*Phenyl*-3-(4′-*methyl*-1′-*naphthyl*)*quinoxaline*.—This was formed from the diketone (IX; 1·5 g.) and *o*-phenylenediamine (0·75 g.) in acetic acid (10 c.c.) at 100°. It crystallised from *cyclo*hexane as a colourless powder, m. p. 132—133° (Found : N, 8·2. $C_{25}H_{18}N_2$ requires N, 8·1%).

When the diketone (IX) was heated with anhydrous aluminium chloride it was either recovered unchanged or converted into resinous products, according to the conditions. In one experiment, in which the reactants were heated at 150° for 10 minutes, a very small amount of material was extracted from the product by warming with alcohol and aqueous sodium bisulphite. The diluted filtered solution gave a precipitate when boiled with sulphuric acid, which after recrystallisation from acetic acid formed bright red needles, m. p. 217—218°. The yield was only about 0·1%.

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