3. *Polycyclic Aromatic Hydrocarbons. Part XXI.*

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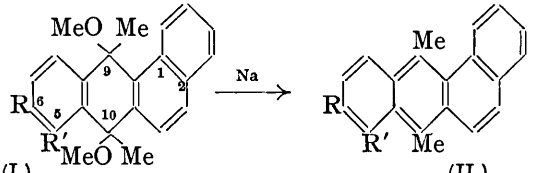
The 6 : 9 : 10-trimethyl and the 5 : 6 : 9 : 10-tetramethyl derivative of 1 : 2-benzanthracene have been synthesised for biological comparison with other hydrocarbons of similar structure.

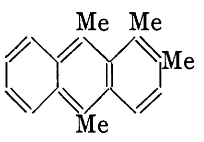
THE strikingly rapid production of tumours of the skin of mice with 9 : 10-dimethyl- and 5 : 9 : 10-trimethyl-1 : 2-benzanthracene (Bachmann and E. L. and N. M. Kennaway, *Yale J. Biol. Med.*, 1938, **11**, 97) is in contrast to the almost complete carcinogenic inactivity of 9 : 10-dimethyl-1 : 2 : 5 : 6-dibenzanthracene (Cook, *Proc. Roy. Soc.*, 1932, *B*, **111**, 494) and suggested the examination of further hydrocarbons of this class. We now record the synthesis of 6 : 9 : 10-*trimethyl*- and 5 : 6 : 9 : 10-*tetramethyl*-1 : 2-*benzanthracene.* Reports of tests for carcinogenic and growth-inhibitory activity will be published elsewhere. As a condensed aromatic ring in the molecule of a carcinogenic hydrocarbon may sometimes be contracted to a five-membered ring or to two methyl groups without appreciable modification of carcinogenic activity, it seemed of interest also to examine 1 : 2 : 9 : 10-tetramethylanthracene. This we were unable to obtain by the general procedure employed.

The method adopted consisted in the action of methylmagnesium iodide on the appropriate derivatives of 9 : 10-anthraquinone, conversion of the resulting *diols* into their *dimethyl* ethers (Type I), followed by treatment of these with metallic sodium, which gave the 9 : 10-dimethyl hydrocarbons (Type II) :



(I.) (II.)

(R, R' = H or Me.)



(III.)

This demethoxylation reaction is due to Bachmann and Chemerda (*J. Amer. Chem. Soc.*, 1938, **60**, 1023), who have recently (*ibid.*, 1939, **61**, 2358) studied its mechanism. Analogous conversion of 9 : 10-*dimethoxy*-1 : 2 : 9 : 10-*tetramethyl*-9 : 10-*dihydroanthracene* into 1 : 2 : 9 : 10-tetramethylanthracene (III) could not be effected, although 9 : 10-dimethylanthracene was obtained in good yield from the corresponding dimethoxy-compound.

EXPERIMENTAL.

9 : 10-*Dimethoxy*-6 : 9 : 10-*trimethyl*-9 : 10-*dihydro*-1 : 2-*benzanthracene* (I; R = Me, R′ = H).—A suspension of 6-methyl-1 : 2-benzanthraquinone (Dziewoński and Ritt, *Bull. Acad. Polonaise*, 1927, *A*, 181) (7·1 g.) in pure dry benzene (30 c.c.) was added to methylmagnesium iodide (from 6·6 c.c. of methyl iodide, 2·4 g. of magnesium, and 40 c.c. of ether). After 2 hours, ice and ammonium chloride were added, the benzene–ether solution shaken with ammonium chloride solution, and the solvents removed. A few drops of methyl-alcoholic hydrogen chloride were added to a methyl-alcoholic solution of the residual gum-like crude diol. The resulting 9 : 10-*dimethoxy*-6 : 9 : 10-*trimethyl*-9 : 10-*dihydro*-1 : 2-*benzanthracene* (2·35 g.) crystallised from benzene–methyl alcohol in colourless rectangular plates, m. p. 232—233·5° (Found : C, 82·85; H, 7·15. $C_{23}H_{24}O_2$ requires C, 83·1; H, 7·3%). In another experiment the crude diol was obtained solid by trituration with benzene–*cyclo*hexane. This tended to separate with solvent of crystallisation and was somewhat thermolabile. Recrystallisation from benzene, followed by drying in a vacuum at 60°, gave 9 : 10-*dihydroxy*-6 : 9 : 10-*trimethyl*-9 : 10-*dihydro*-1 : 2-*benzanthracene* as a colourless microcrystalline powder, m. p. 151—152° (Found : C, 83·2; H, 6·9. $C_{21}H_{20}O_2$ requires C, 82·8; H, 6·6%).

6 : 9 : 10-*Trimethyl*-1 : 2-*benzanthracene* (II; R = Me, R′ = H).—A suspension of the aforesaid methyl ether (2 g.) in anhydrous ether (50 c.c.) was shaken with powdered sodium (0·28 g.) for 24 hours. Some of the resulting hydrocarbon (1 g.) was separated from the deep mauve solution, and a further quantity (0·5 g.) was obtained from the ethereal solution by concentration, after washing with dilute hydrochloric acid. The hydrocarbon was purified through its *picrate*, which crystallised from benzene in lustrous purplish-brown plates, m. p. 145—146° (Found: C, 65·0; H, 4·9. $C_{21}H_{18},C_6H_3O_7N_3$ requires C, 64·9; H, 4·2%). The regenerated 6 : 9 : 10-*trimethyl*-1 : 2-*benzanthracene* formed yellowish plates (from benzene–alcohol), m. p. 157—158° (Found : C, 93·3; H, 6·75. $C_{21}H_{18}$ requires C, 93·3; H, 6·7%).

3-*Bromo*-o-*xylene*.—*o*-3-Xylidine was isolated from technical *o*-xylidine through its crystalline formyl compound (Hodgkinson and Limpach, J., 1900, **77**, 65). Technical *o*-xylidine (from British Drug Houses) (100 g.) was heated on the water-bath for 2 hours with formic acid (37·5 g.) and water (115 c.c.). The formyl compound crystallised on cooling and was collected, well pressed, and recrystallised from aqueous alcohol. Hydrolysis of the formyl compound (m. p. 102°) with sodium hydroxide (19 g.) in boiling alcoholic solution gave 50 g. of pure *o*-3-xylidine

o-3-Xylidine (25 g.) in 40% hydrobromic acid (120 c.c.) was diazotised by gradual addition of finely powdered sodium nitrite (15·6 g.) at such a rate that the temperature of the reactants, cooled in a freezing mixture, was maintained between 5° and 10°. Freshly precipitated copper powder was then slowly added, after which gentle warming caused a vigorous reaction to set in. After ½ hour this was completed by ½ hour's heating on the water-bath. The resulting 3-bromo-*o*-xylene (17·3 g.; b. p. 210—213°) was isolated by steam-distillation, first from the mixture and then in presence of alkali, followed by distillation.

2-(2′ : 3′-*Dimethylbenzoyl*)-1-*naphthoic Acid*.—A Grignard solution prepared from 3-bromo-*o*-xylene (30 g.), magnesium turnings (3·9 g.), and anhydrous ether (120 c.c.) was added dropwise to a boiling solution of 1 : 2-naphthalic anhydride (Fieser and Hershberg, *J. Amer. Chem. Soc.*, 1935, **57**, 1853) (29·7 g.) in anhydrous benzene (270 c.c.). A thick yellow precipitate was formed. After 2 hours' boiling, the cooled suspension was decomposed with ice and dilute sulphuric acid, and the benzene–ether solution extracted with dilute sodium carbonate solution. Acidification precipitated the crude acidic product, which became solid after a time. This was recrystallised from toluene and from acetic acid. Further purification of the keto-acid (yield, 10·8 g.) was effected through its *acetoxy-lactone*, formed by heating on the water-bath for 2 hours with acetic anhydride (18 c.c.) in pyridine (60 c.c.). This separated from xylene as a colourless microcrystalline powder, m. p. 189—191° (Found : C, 76·6; H, 5·4. $C_{22}H_{18}O_4$ requires C, 76·3; H, 5·2%), and was hydrolysed by alcoholic potash to 2-(2′ : 3′-*dimethylbenzoyl*)-1-*naphthoic acid*, which formed small colourless needles (from toluene), m. p. 168—169° (Found : C, 79·1; H, 5·4. $C_{20}H_{16}O_3$ requires C, 78·9; H, 5·3%).

5 : 6-*Dimethyl*-1 : 2-*benzanthraquinone*.—A mixture of 2-(2′ : 3′-dimethylbenzoyl)-1-naphthoic acid (5 g.) and benzoyl chloride (5 c.c.) was treated with a few drops of concentrated sulphuric acid and heated for an hour in an oil-bath at 130°. Evolution of hydrogen chloride had then ceased, and the hot solution was poured into 6N-sodium hydroxide. After warming to complete hydrolysis of the benzoyl chloride the 5 : 6-dimethyl-1 : 2-benzanthraquinone (95% yield) was collected, washed, and recrystallised from acetic acid. It was identified by direct comparison with an authentic sample (Cook and Haslewood, J., 1934, 433), and for the preparation of this quinone in quantity the present method is preferable to the former one.

9 : 10-*Dihydroxy*-5 : 6 : 9 : 10-*tetramethyl*-9 : 10-*dihydro*-1 : 2-*benzanthracene*.—This *diol* (2·2 g.) was obtained from 5 : 6-dimethyl-1 : 2-benzanthraquinone (5 g.) and methylmagnesium iodide (from 5 c.c. of methyl iodide and 1·8 g. of magnesium) by 2 hours' boiling in benzene–ether (compare the above described reaction with the 6-methyl quinone). It separated from benzene in clumps of microscopic colourless crystals, m. p. 217—219° (Found : C, 82·8; H, 6·9. $C_{22}H_{22}O_2$ requires C, 83·0; H, 7·0%). On treatment for 1 hour at room temperature with methyl alcohol containing one drop of concentrated hydrochloric acid, this diol (5·6 g.) gave 9 : 10-*dimethoxy*-5 : 6 : 9 : 10-*tetramethyl*-9 : 10-*dihydro*-1 : 2-*benzanthracene* (I; R = R′ = Me) (4·6 g.), which crystallised from benzene–methyl alcohol in colourless rectangular prisms, m. p. 229—230° (Found : C, 83·1; H, 7·4. $C_{24}H_{26}O_2$ requires C, 83·2; H, 7·6%).

5 : 6 : 9 : 10-*Tetramethyl*-1 : 2-*benzanthracene* (II; R = R′ = Me).—A suspension of the aforesaid dimethyl ether (4·6 g.) and powdered sodium (0·6 g.) in ether (150 c.c.) was shaken for 48 hours. The purple solution was treated with a few drops of methyl alcohol and washed with dilute hydrochloric acid. The hydrocarbon obtained on evaporation was recrystallised from alcohol (yield, 3·7 g.) and purified through its purplish-brown crystalline *picrate*, m. p. 120—121° (Found : C, 65·8; H, 4·75. $C_{22}H_{20},C_6H_3O_7N_3$ requires C, 65·5; H, 4·5%). Dissociation of the picrate was effected by passing its benzene solution through a tower of alumina, and the resulting 5 : 6 : 9 : 10-*tetramethyl*-1 : 2-*benzanthracene* (3·1 g.) formed pale yellow needles, m. p. 132—133° (Found : C, 92·6; H, 7·1. $C_{22}H_{20}$ requires C, 92·9; H, 7·1%).

The ready isolation of peroxides by photo-oxidation of this tetramethylbenzanthracene and of 6 : 9 : 10-trimethylbenzanthracene has been reported elsewhere (Cook, Martin, and Roe, *Nature*, 1939, **143**, 1020).

2-(2′ : 3′-*Dimethylbenzoyl*)*benzoic Acid*.—A Grignard solution prepared from 3-bromo-*o*-xylene (above) (30 g.), magnesium turnings (4 g.), and anhydrous ether (100 c.c.) was added dropwise during ½ hour to a boiling solution of phthalic anhydride (21 g.) in pure benzene (200 c.c.) (compare Weizmann and E. and F. Bergmann, J., 1935, 1367). After 2 hours' boiling, the suspension was cooled and decomposed with ice and dilute sulphuric acid, and the 2-(2′ : 3′-*dimethylbenzoyl*)*benzoic acid* (25 g.) isolated by means of sodium carbonate solution and recrystallised from benzene–light petroleum. It formed colourless prisms, m. p. 126—127° (Found : C, 75·5; H, 5·5. $C_{16}H_{14}O_3$ requires C, 75·6; H, 5·5%).

1 : 2-Dimethylanthraquinone was obtained in 80% yield when this keto-acid (10 g.) was heated for 1½ hours at 130° with benzoyl chloride (10 c.c.) and a few drops of concentrated sulphuric acid. The quinone formed pale yellow needles (from acetone), m. p. 154·5—155·5°. Fairbourne (J., 1921, **119**, 1573), who isolated this quinone from a mixture consisting chiefly of 2 : 3-dimethylanthraquinone, gives m. p. 150°.

1 : 2-*Dimethylanthracene*.—1 : 2-Dimethylanthraquinone was reduced in two stages to the hydrocarbon, the procedure being that described by Badger and Cook (J., 1939, 804) for the reduction of 1 : 2-benzanthraquinone. The resulting 1 : 2-*dimethylanthracene* was distilled at 180°/0·4 mm. (86% yield) and formed colourless transparent plates (from acetic acid), m. p. 85·5—86° (Found : C, 92·95; H, 7·0. $C_{16}H_{14}$ requires C, 93·15; H, 6·85%).

9 : 10-*Dihydroxy*-1 : 2 : 9 : 10-*tetramethyl*-9 : 10-*dihydroanthracene*.—A suspension of 1 : 2-dimethylanthraquinone (7·1 g.) in dry benzene (35 c.c.) was added with constant stirring to a Grignard solution prepared from methyl iodide (8·4 c.c.), magnesium turnings (3·3 g.), and anhydrous ether (50 c.c.). The mixture was kept at room temperature overnight and then decomposed with ice and ammonium chloride. The *diol*, obtained in variable yield (up to 3·2 g.), was isolated by evaporation of the benzene–ether solution as an oil, which solidified on trituration with light petroleum. It crystallised from benzene in colourless lustrous plates, m. p. 162—163° (Found : C, 80·3; H, 7·5. $C_{18}H_{20}O_2$ requires C, 80·6; H, 7·5%). By treatment for several hours with cold methyl alcohol containing a trace of hydrochloric acid this was converted into 9 : 10-*dimethoxy*-1 : 2 : 9 : 10-*tetramethyl*-9 : 10-*dihydroanthracene* (50% yield), which crystallised from benzene–methyl alcohol in colourless transparent plates, m. p. 140—141·5° (Found : C, 80·8; H, 8·25. $C_{20}H_{24}O_2$ requires C, 81·0; H, 8·2%).

This dimethoxy-compound was recovered unchanged after being shaken for 6 days with sodium powder in ether.

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