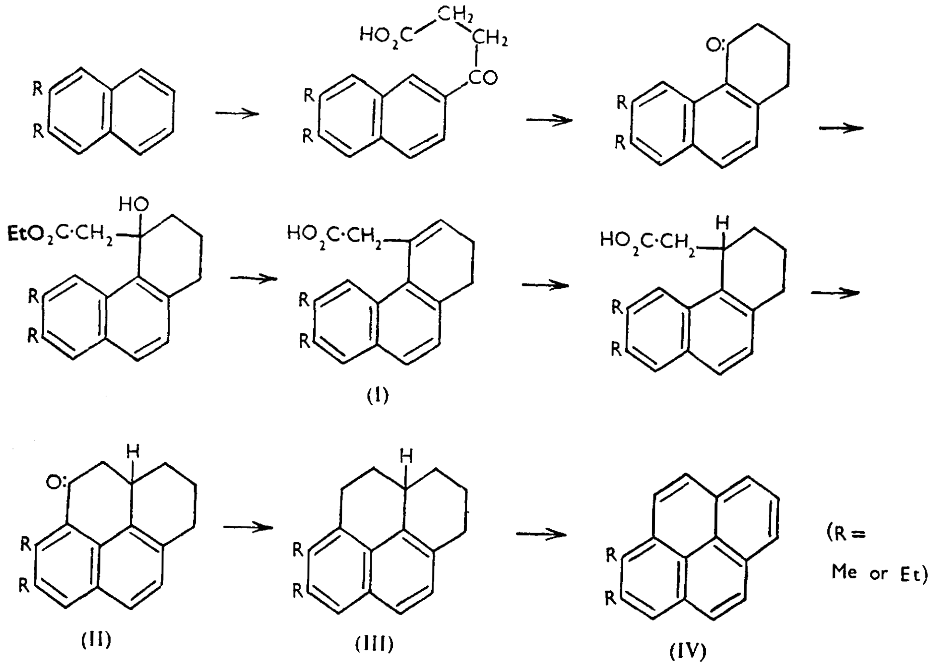
220. *Syntheses of Hydrocarbons possibly related to Carcinogenic Factors in City Smoke.*

By G. R. Clemo and N. D. Ghatge.

3 : 4-Dimethyl- and 3 : 4-diethyl-pyrene and 7 : 9-dimethylaceanthrene have been synthesised from disubstituted naphthalenes.

One of us [1] described the isolation, from a fraction of city smoke, of a hydrocarbon X since shown [2] to be carcinogenic to mice. Its analysis, ultraviolet spectrum, and other properties resembled those of a substituted pyrene, so it was decided to synthesise certain alkylpyrenes for comparison. Since in the benzanthracene series two methyl groups in a terminal ring accentuate the carcinogenic activity and since 3 : 4-benzopyrene is a well-known carcinogen, the first syntheses were those of the hitherto undescribed 3 : 4-dimethyl- and 3 : 4-diethyl-pyrene.



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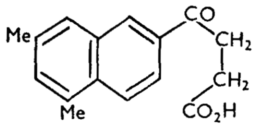
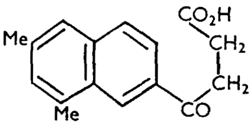




(VI)

The synthetical route shown in the annexed scheme was explored by Bograchove [3] as far as (II; R = Me) but the acid then formulated as (I) melts 23° lower than our acid. This difference could clearly be due to a different position of the double bond. Clemmensen reduction of the ketone (II; R = Me) has now given the hexahydrodimethylpyrene (III; R = Me) which on dehydrogenation by palladium–charcoal gave 3 : 4-dimethylpyrene

[1] Clemo, Presidential Address, British Assoc., Sect. B, 1953.
[2] Clemo and Miller, *Chem. and Ind.*, 1955, 38.
[3] Bograchove, *J. Amer. Chem. Soc.*, 1944, **66**, 1613.

(IV; R = Me). Similarly, by starting from 2 : 3-diethylnaphthalene, 3 : 4-diethylpyrene was obtained. Neither compound however corresponds to the hydrocarbon X : the ultraviolet spectra of the three compounds are given in Fig. 1.

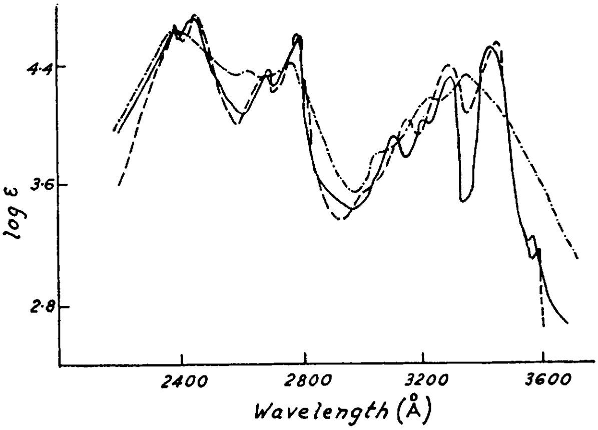


FIG. 1. *Absorption spectra of* (——) 3 : 4-*dimethylpyrene,* (– – –) 3 : 4-*diethylpyrene, and* (— · —) *substance* X *in ethyl alcohol.*

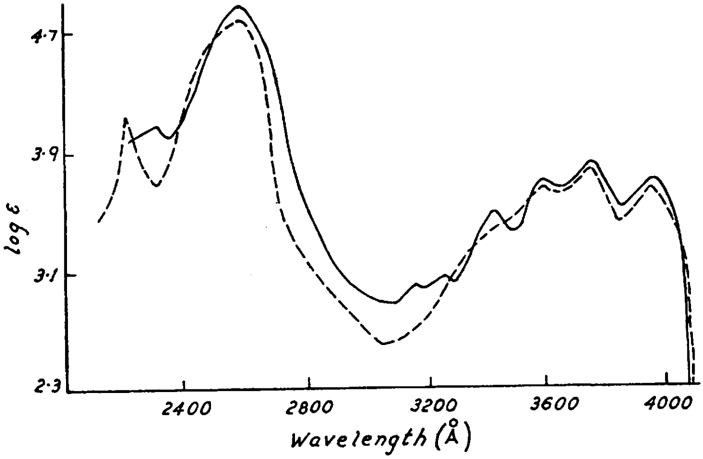
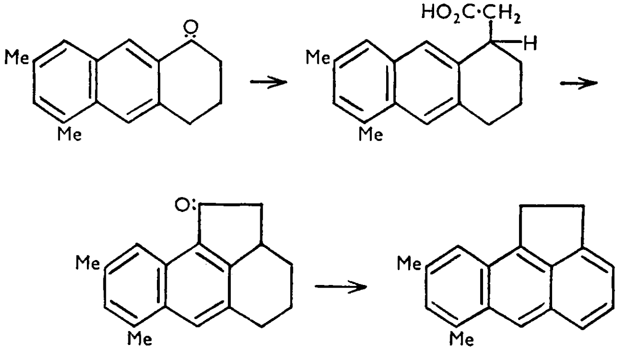


FIG. 2. *Absorption spectra of* (——) 7 : 9- *and* (– – –) 7 : 8-*dimethylaceanthrene in ethyl alcohol.*

Continuing, we attempted to prepare other dialkylated pyrenes, such as 3 : 5-dimethylpyrene. Succinoylation of 1 : 3-dimethylnaphthalene in a β-position could give either keto-acid (V) or (VI) or a mixture, but only one pure acid was actually obtained. If this were (V), it should lead, by the reactions described above for 3 : 4-dimethylpyrene, to



the 3 : 5-dimethyl analogue. The ultraviolet spectrum (Fig. 2) of the compound obtained is, however, different from that of authentic pyrenes, pointing to our acid's being (VI); on Clemmensen reduction this would give β-(6 : 8-dimethyl-2-naphthyl)butyric acid and, by analogy,[4] steric hindrance would be expected to lead to its cyclisation to 1 : 2 : 3 : 4-tetrahydro-5 : 7-dimethyl-1-oxoanthracene. The correctness of this view has been proved by conversion of this product into the known 1 : 3-dimethylanthracene.

The further reactions described from 1 : 2 : 3 : 4-tetrahydro-5 : 7-dimethyl-1-oxoanthracene would almost certainly proceed as shown, giving 7 : 9-dimethylaceanthrene. The ultraviolet spectra (Fig. 2) of this hydrocarbon and of 7 : 8-dimethylaceanthrene (very kindly supplied by Professor L. Fieser) leave no doubt as to the correctness of the formulation.

EXPERIMENTAL

1 : 2-*Dihydro*-6 : 7-*dimethyl*-4-*phenanthrylacetic Acid*.—To a solution of 1 : 2 : 3 : 4-tetrahydro-6 : 7-dimethyl-1-oxophenanthrene (6 g.) in benzene (25 c.c.), ethyl bromoacetate (5·4 c.c.), zinc wool (1·9 g.), and a crystal of iodine were added and the mixture was warmed for 4 hr. on the water-bath. Dilute sulphuric acid was then added, the benzene layer separated and dried, and the hydroxy-ester dehydrated (in the benzene) with phosphoric oxide. After removal of the solvent, the crude dehydrated ester was hydrolysed by refluxing ethanolic potassium hydroxide (20%). The resulting acid, after crystallisation from acetic acid (charcoal), gave colourless needles, m. p. 209° (lit., m. p. 186°) (Found: C, 80·9; H, 6·8. Calc. for $C_{18}H_{18}O_2$: C, 81·2; H, 6·8%).

1 : 2 : 2a : 3 : 4 : 5-*Hexahydro*-9 : 10-*dimethyl*-1-*oxopyrene*.—The foregoing acid was reduced catalytically (platinum oxide) to 1 : 2 : 3 : 4-tetrahydro-6 : 7-dimethyl-4-phenanthrylacetic acid (m. p. 167—168°) which, when heated on the water-bath with 80% sulphuric acid, gave 1 : 2 : 2a : 3 : 4 : 5-hexahydro-9 : 10-dimethyl-1-oxopyrene, m. p. 161—162° (lit., m. p. 160°) (Found: C, 86·7; H, 7·5. Calc. for $C_{18}H_{18}O$: C, 86·4; H, 7·2%).

1 : 2 : 2a : 3 : 4 : 5-*Hexahydro*-9 : 10-*dimethylpyrene*.—The ketone (0·5 g.), benzene–methanol (20 c.c.; 1 : 1), amalgamated zinc (2 g.), and concentrated hydrochloric acid (10 c.c.) were refluxed for 4 hr. Amalgamated zinc (2 g.) and concentrated hydrochloric acid (10 c.c.) were then added and the refluxing was continued a further 4 hr. After cooling, the benzene layer was separated, washed with water, and evaporated. The residue distilled at 190—200°/0·1 mm., giving a *hydrocarbon* which formed needles, m. p. 127° (0·3 g.), from light petroleum (b. p. 40—60°) (Found: C, 91·4; H, 8·8. $C_{18}H_{20}$ requires C, 91·5; H, 8·5%). Its *trinitrobenzene derivative* formed orange needles (from alcohol), m. p. 163° (Found: C, 64·5; H, 5·5. $C_{24}H_{23}O_6N_3$ requires C, 64·2; H, 5·1%).

3 : 4-*Dimethylpyrene*.—The foregoing hexahydro-pyrene (0·2 g.), mixed with palladised charcoal (10 mg.), was heated for ½ hr. at 260—270°, then extracted with ether, the ether was removed, and the *product* distilled at 0·1 mm. and crystallised from light petroleum (b. p. 40—60°), giving needles, m. p. 103° (Found: C, 93·7; H, 6·0. $C_{18}H_{14}$ requires C, 93·9; H, 6·1%). Its *trinitrobenzene derivative* formed orange needles (from alcohol), m. p. 217—218° (Found: C, 65·0; H, 4·3. $C_{24}H_{17}O_6N_3$ requires C, 65·0; H, 3·8%).

β-(6 : 7-*Diethyl*-2-*naphthoyl*)*propionic Acid*.—To 2 : 3-diethylnaphthalene (10 g.) and succinic anhydride (5·4 g.) in tetrachloroethane (75 c.c.), powdered aluminium chloride (16 g.) was added, the temperature being kept below 35°. The mixture was kept at room temperature for 6 hr., then decomposed with ice and hydrochloric acid. Tetrachloroethane was removed in steam. The resulting greenish solid was collected, washed with water, and extracted with sodium carbonate solution. The solution was filtered and acidified with dilute hydrochloric acid. The *acid* crystallised from toluene in white needles, m. p. 155° (8·5 g.) (Found: C, 76·0; H, 7·3. $C_{18}H_{20}O_3$ requires C, 76·0; H, 7·0%).

6 : 7-*Diethyl*-1 : 2 : 3 : 4-*tetrahydro*-4-*oxophenanthrene*.—The above acid was reduced by Clemmensen's method, but this gave unsatisfactory analyses. The crude product (5 g.) was heated on the water-bath with 80% sulphuric acid (25 c.c.) for 1 hr. The *ketone* thus obtained was passed down an alumina column and then recrystallised from light petroleum (b. p. 40—60°), forming needles, m. p. 64° (3·6 g.) (Found: C, 85·9; H, 8·3. $C_{18}H_{20}O$ requires C, 85·7; H, 7·9%). It gave a reddish 2 : 4-*dinitrophenylhydrazone*, m. p. 236—237° (Found: C, 66·2; H, 5·5. $C_{24}H_{24}O_4N_4$ requires C, 66·6; H, 5·5%).

Ethyl 6 : 7-*Diethyl*-1 : 2 : 3 : 4-*tetrahydro*-4-*hydroxy*-4-*phenanthrylacetate*.—The foregoing

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[4] Haworth, *J.*, 1934, 1950.

ketone (3 g.) in benzene (25 c.c.) was treated with ethyl bromoacetate (2·9 c.c.), zinc wool (0·85 g.), and a crystal of iodine. The mixture was warmed on the water-bath for 4 hr., dilute sulphuric acid added, the benzene layer separated and dried (Na_2SO_4), and the benzene removed. The residual ester, when kept in light petroleum (b. p. 40—60°) at 0°, afforded needles which, recrystallised from this solvent, melted at 72—73° (1·2 g.) (Found: C, 77·4; H, 8·5. $C_{22}H_{28}O_3$ requires C, 77·6; H, 8·2%).

6 : 7-*Diethyl*-1 : 2-*dihydro*-4-*phenanthrylacetic Acid*.—A solution of 6 : 7-diethyl-1 : 2 : 3 : 4-tetrahydro-4-hydroxy-4-phenanthrylacetic acid (1 g.) and phosphoric oxide (0·5 g.) in benzene (20 c.c.) was refluxed for 1·5 hr. The crude unsaturated ester was hydrolysed with alcoholic potassium hydroxide (20%); the resulting *acid*, after crystallisation from alcohol (charcoal), formed needles, m. p. 194—195° (0·6 g.) (Found: C, 81·7; H, 7·7. $C_{20}H_{22}O_2$ requires C, 81·6; H, 7·5%).

6 : 7-*Diethyl*-1 : 2 : 3 : 4-*tetrahydro*-4-*phenanthrylacetic Acid*.—The dihydro-acid (0·6 g.) was catalytically reduced (platinum oxide), and the *product* (0·6 g.) recrystallised from light petroleum (b. p. 40—60°) in needles, m. p. 163° (Found: C, 81·5; H, 8·0. $C_{20}H_{24}O_2$ requires C, 81·1; H, 8·1%).

9 : 10-*Diethyl*-1 : 2 : 2a : 3 : 4 : 5-*hexahydro*-1-*oxopyrene*.—The tetrahydro-acid (0·5 g.) was heated on the water-bath for ½ hr. with 80% sulphuric acid (2·5 c.c.). The resulting *ketone* was passed down a column of alumina and recrystallised from light petroleum (b. p. 40—60°) in yellowish needles, m. p. 105° (0·33 g.) (Found: C, 86·5; H, 8·3. $C_{20}H_{22}O$ requires C, 86·3; H, 7·9%).

9 : 10-*Diethyl*-1 : 2 : 2a : 3 : 4 : 5-*hexahydropyrene*.—The hexahydropyrene (0·3 g.) was reduced as described for the dimethyl analogue. The *hydrocarbon* obtained recrystallised from light petroleum as needles, m. p. 70° (0·2 g.) (Found: C, 91·1; H, 9·4. $C_{20}H_{24}$ requires C, 90·9; H, 9·1%).

3 : 4-*Diethylpyrene*.—The diethylhexahydropyrene (0·1 g.) was heated with palladised charcoal (50 mg.) for ½ hr. at 260—270°. The organic matter was extracted with ether, the ether removed, and the *product* distilled at 0·1 mm. and crystallised from light petroleum (b. p. 40—60°), giving plates, which fluoresced in ultraviolet light and had m. p. 84° (Found: C, 92·6; H, 7·5. $C_{20}H_{18}$ requires C, 93·0; H, 7·0%). Its *trinitrobenzene derivative* formed orange needles (from alcohol), m. p. 173—174° (Found: C, 66·2; H, 4·4. $C_{26}H_{21}O_6N_3$ requires C, 66·2; H, 4·5%).

β-(6 : 8-*Dimethyl*-2-*naphthoyl*)*propionic Acid*.—To 1 : 3-dimethylnaphthalene[5] (10 g.) and succinic anhydride (6·4 g.) in tetrachloroethane (75 c.c.), powdered aluminium chloride (19 g.) was added at <35°. After 6 hr. at room temperature, the complex was decomposed with ice and hydrochloric acid, and the tetrachloroethane removed in steam. The resultant mass was separated and extracted with sodium carbonate solution. The solution was filtered and acidified with dilute hydrochloric acid. The *acid*, filtered off and recrystallised from toluene, had m. p. 184° (9·2 g.) (Found: C, 74·7; H, 6·2. $C_{16}H_{16}O_3$ requires C, 75·0; H, 6·3%).

γ-(6 : 8-*Dimethyl*-2-*naphthyl*)*butyric Acid*.—The foregoing acid (9 g.), toluene (50 c.c.), amalgamated zinc (27 g.), and concentrated hydrochloric acid (50 c.c.) were refluxed for 8 hr., with the addition of further acid (2 × 20 c.c.) at intervals of 3 hr. The toluene layer was separated, washed with water, dried (Na_2SO_4), and distilled. The residual *acid*, recrystallised from light petroleum, had m. p. 146° (5·2 g.) (Found: C, 79·2; H, 7·5. $C_{16}H_{18}O_2$ requires C, 79·3; H, 7·4%).

1 : 2 : 3 : 4-*Tetrahydro*-5 : 7-*dimethyl*-1-*oxoanthracene*.—The preceding butyric acid (7 g.) was heated on the water-bath for 1·5 hr. with 80% sulphuric acid (35 c.c.), then poured on ice. The organic matter was extracted with ether, and the solution washed with a solution of sodium carbonate, then with water, dried (Na_2SO_4), and evaporated. The residual *ketone*, crystallised from light petroleum, had m. p. 110° (Found: C, 85·9; H, 7·4. $C_{16}H_{16}O$ requires C, 85·7; H, 7·2%).

1 : 3-*Dimethylanthracene*. The oxoanthracene (0·2 g.) was reduced by Clemmensen's method to 1 : 2 : 3 : 4-*tetrahydro*-5 : 7-*dimethylanthracene*, b. p. 120—125°/mm., m. p. 35°, which could not be crystallised easily (Found: C, 91·3; H, 8·7. $C_{16}H_{18}$ requires C, 91·4; H, 8·6%). On dehydrogenation with palladised charcoal this gave a product which distilled at 140—145°/2 mm. and solidified. On recrystallisation from light petroleum it melted at 78° (lit., m. p. 78—79°), and gave a reddish picrate, m. p. 132° (lit., m. p. 132—133°). Its ultraviolet spectrum is similar to that of anthracene.

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[5] Barnett and Sanders, *J.*, 1933, 434.

3 : 4-*Dihydro*-5 : 7-*dimethyl*-1-*anthrylacetic Acid.*—To a solution of 1 : 2 : 3 : 4-tetrahydro-5 : 7-dimethyl-1-oxoanthracene (4 g.) in benzene (25 c.c.), ethyl bromoacetate (3 c.c.), zinc wool (1·3 g.), and a crystal of iodine were added and the mixture warmed for 4 hr. Dilute sulphuric acid was then added, the benzene layer separated and dried (Na_2SO_4), and the hydroxy-ester dehydrated in the benzene with phosphoric oxide. After removal of the solvent, the crude dehydrated ester was hydrolysed by refluxing ethanolic potassium hydroxide (20%). The resulting *acid* formed needles, m. p. 182° (3 g.), from light petroleum (Found : C, 81·2; H, 6·8. $C_{18}H_{18}O_2$ requires C, 81·2; H, 6·8%).

1 : 2 : 3 : 4-*Tetrahydro*-5 : 7-*dimethyl*-1-*anthrylacetic Acid.*—The dihydro-acid (1 g.) was reduced over platinum oxide in quantitative yield. The *tetrahydro-acid*, crystallised from light petroleum, had m. p. 125° (0·99 g.) (Found : C, 80·2; H, 7·1. $C_{18}H_{20}O_2$ requires C, 80·6; H, 7·4%).

2a : 3 : 4 : 5-*Tetrahydro*-7 : 9-*dimethylaceanthrene.*—Heating the preceding acid (0·7 g.) on the water-bath ½ hr. with 80% sulphuric acid (3·5 c.c.) gave a ketone, which, purified by passage through alumina and crystallisation from light petroleum, had m. p. 116° (0·42 g.) (Found : C, 86·7; H, 7·6. $C_{18}H_{18}O$ requires C, 86·4; H, 7·2%). This 2a : 3 : 4 : 5-*tetrahydro*-7 : 9-*dimethyl*-1-*oxoaceanthrene* (0·4 g.) was reduced by Clemmensen's method, as described for the preparation of the hexahydrodimethylpyrene. The *hydrocarbon* obtained, when crystallised from light petroleum, had m. p. 50° (0·3 g.) (Found : 91·3; H, 8·7. $C_{18}H_{20}$ requires C, 91·5; H, 8·5%). Its *trinitrobenzene derivative* (from alcohol) melted at 165° (Found : C, 64·1; H, 5·3. $C_{24}H_{23}O_6N_3$ requires C, 64·1; H, 5·1%).

7 : 9-*Dimethylaceanthrene.*—The tetrahydroaceanthrene (0·2 g.) was heated with palladised charcoal for ½ hr. at 260—270°. The aromatic *hydrocarbon* then extracted with ether sublimed at 2 mm. and crystallised from alcohol in yellowish needles, m. p. 134° (0·11 g.) (Found : C, 92·8; H, 7·1. $C_{18}H_{16}$ requires C, 93·1; H, 6·9%). It gave a reddish *trinitrobenzene derivative*, m. p. 176° (Found : C, 64·5; H, 4·5. $C_{24}H_{19}O_6N_3$ requires C, 64·7; H, 4·3%).

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