265. *Polycyclic Aromatic Hydrocarbons. Part XXVI.* 1 : 2 : 3 : 4-*Tetramethylphenanthrene.*

By C. L. Hewett and Richard H. Martin.

1 : 2 : 3 : 4-*Tetramethylphenanthrene* has been prepared from 1 : 2 : 3 : 4-tetramethylphenylacetic acid by the Pschorr reaction.

In Part XXII (Hewett, this vol., p. 293) the desirability of obtaining 1 : 2 : 3 : 4-tetramethylphenanthrene (III; R = H) was emphasised because it would constitute a link between the carcinogenic derivatives of 1 : 2-benzanthracene, 3 : 4-benzphenanthrene and chrysene. All of these derivatives contain a phenanthrene system substituted in at least two and often three or four of the 1-, 2-, 3-, and 4-positions, and thus 1 : 2 : 3 : 4-tetramethylphenanthrene can be regarded as the parent of these compounds. The synthesis of this compound has now been achieved, and biological testing is being carried out, the results of which will be published elsewhere.

Two previous attempts to synthesise this compound (Hewett, *loc. cit.*) failed owing in one case to loss of methyl groups from an unsaturated ring during dehydrogenation and in the other case, in which the methyl groups were already present in an aromatic ring, to ring closure to give the alternative anthracene structure. In the present synthesis both

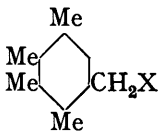
of these difficulties have been overcome by use of the Pschorr method in which the methyl groups are originally present in an aromatic ring and ring closure can give only a phenanthrene structure.

1 : 2 : 3 : 4-Tetramethylbenzene was obtained by the two-stage method of Smith and Cass (*J. Amer. Chem. Soc.*, 1932, **54**, 1614) from a mixture of durene and *iso*durene (Organic Syntheses, Vol. X, p. 32) by means of the sulphonic acid, which was hydrolysed by the " flash method " of Smith and Lux (*J. Amer. Chem. Soc.*, 1929, **51**, 2994). Chloromethylation gave 2 : 3 : 4 : 5-tetramethylbenzyl chloride (I; X = Cl), obtained by Smith and Agre (*ibid.*, 1938, **60**, 648) by means of the aldehyde.

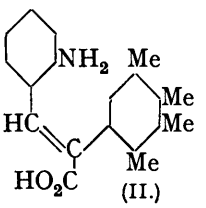
In order to avoid interaction between the reactive chloro-compound and alcohol, acetone was used as the solvent in the preparation of the nitrile (I; X = CN) from the chloromethyl compound; this is preferable to using cuprous cyanide in phenylacetonitrile solution (compare Hewett, *loc. cit.*). Sodium 2 : 3 : 4 : 5-tetramethylphenylacetate (I; X = CO_2Na) underwent the Perkin condensation with *o*-nitrobenzaldehyde to give *o-nitro*-α-2′ : 3′ : 4′ : 5′-*tetramethylphenylcinnamic acid.*

Reduction of the nitro-acid with ferrous sulphate and aqueous ammonia yielded the *amino-acid* (II), which, after diazotisation and treatment with copper powder, gave a mixture of acids from which 1 : 2 : 3 : 4-*tetramethyl*-10-*phenanthroic acid* (III; R = CO_2H) was readily isolated.

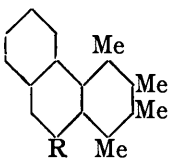
Decarboxylation by means of copper bronze in quinoline solution gave 1 : 2 : 3 : 4-*tetramethylphenanthrene* (III; R = H).



(I.)



(II.)



(III.)

Experimental.

Chloromethylation of 1 : 2 : 3 : 4-*Tetramethylbenzene.*—Paraformaldehyde (2·5 g.) was suspended in glacial acetic acid (70 c.c.), and dry hydrogen chloride passed in to give a clear solution. 1 : 2 : 3 : 4-Tetramethylbenzene (10 g.) was then added, and the solution shaken at room temperature for 24 hours (in larger batches it was found necessary to shake for as long as 60 hours). A white precipitate was filtered off and recrystallised from glacial acetic acid; it formed colourless needles, m. p. 146—147°, and was presumably 2 : 3 : 4 : 5 : 2′ : 3′ : 4′ : 5′-*octamethyldiphenylmethane* (Found: C, 89·8; H, 10·1. $C_{21}H_{28}$ requires C, 89·9; H, 10·1%). The acetic acid filtrate was diluted with water and extracted with benzene. The benzene extract was washed with sodium carbonate solution, dried, and distilled. The chloromethyl compound (I; X = Cl) had b. p. 145—147°/17 mm. and m. p. 43—45° (Smith and Agre, *loc. cit.*, give b. p. 139—140°/15 mm. and m. p. 44—45°). Yield, 95 g. from 112 g. of tetramethylbenzene. The nitrile (I; X = CN) was prepared by adding a solution of potassium cyanide (32 g.) in water (80 c.c.) to a solution of the chloromethyl compound (32 g.) in acetone (350 c.c.). After boiling for 12 hours, the acetone was evaporated, and the nitrile extracted in ether and distilled at 184°/25 mm. Yield, 95%. Hydrolysis of the nitrile (87 g.) in alcohol (350 c.c.) with potassium hydroxide (85 g.) in water (60 c.c.) at the b. p. was complete in 20 hours. The crude acid (I; X = CO_2H) (82 g.), reprecipitated from sodium carbonate solution, had m. p. 158—160° (Smith and Agre, *loc. cit.*, give m. p. 159—160°).

o-*Nitro*-α-2′ : 3′ : 4′ : 5′-*tetramethylphenylcinnamic Acid.*—Sodium 2 : 3 : 4 : 5-tetramethylphenylacetate (35 g., prepared from a solution of the acid in alcohol and the equivalent amount of sodium ethoxide solution), *o*-nitrobenzaldehyde (26 g.), and acetic anhydride (240 c.c.) were heated on a water-bath for 40 hours. After decomposition of the acetic anhydride with water, the resinous product was dissolved in ether and extracted with sodium carbonate solution. The carbonate solution was filtered (charcoal) and acidified, and the *acid* purified through its ammonium salt, which separated in fine yellow needles. The pure acid (12·7 g.) formed light cream needles, m. p. 214—215° after several crystallisations from xylene (Found: C, 70·4; H, 6·0. $C_{19}H_{19}O_4N$ requires C, 70·1; H, 5·9%).

o-*Amino*-α-2′ : 3′ : 4′ : 5′-*tetramethylphenylcinnamic Acid* (II).—The nitro-acid (10 g.) in aqueous ammonia (*d* 0·88; 50 c.c.) was heated on the water-bath with ferrous sulphate (100 g.) in water (250 c.c.) for 2 hours. The black sludge was filtered off and extracted several times with 1% ammonia solution. The combined extracts were filtered (charcoal) and made acid to litmus with acetic acid; the *amino-acid* (7·8 g.) which separated was purified through its sparingly soluble sodium salt and formed bright yellow needles, m. p. 235—236°, after several crystallisations from xylene (Found: C, 77·3; H, 7·3. $C_{19}H_{21}O_2N$ requires C, 77·2; H, 7·2%).

1 : 2 : 3 : 4-*Tetramethyl*-10-*phenanthroic Acid* (III; R = CO_2H).—The amino-acid (18 g.), sodium carbonate (crystalline; 9 g.), and sodium nitrite (4·2 g.) were dissolved in hot water (80 c.c.) and cooled. The paste obtained was added in small amounts, with stirring, to 6N-sulphuric acid (400 c.c.) cooled to 0°, and copper powder added. After being stirred for 1 hour at 0°, the whole was warmed on the water-bath for another hour; the precipitate was filtered off, dissolved in sodium carbonate solution, and filtered. The mixture of acids obtained by acidification was dissolved in methyl alcohol, treated with hydrogen chloride, and boiled for 1 hour. Water was then added, and the oil extracted in ether and shaken with sodium carbonate solution. The sparingly soluble sodium salt of the less easily esterified 1 : 2 : 3 : 4-*tetramethyl*-10-*phenanthroic acid* separated, from which, after washing with ether, the free acid (5 g.) was regenerated. After crystallisation from acetic acid it formed colourless plates, m. p. 226—227° (Found: C, 81·5; H, 6·1. $C_{19}H_{18}O_2$ requires C, 82·0; H, 6·5%).

The ethereal solution was evaporated, the residue distilled from an oil-bath at 220°/0·5 mm., and the distillate crystallised from benzene and, after sublimation at 160—170°/0·5 mm., from xylene. This by-product, *methyl* o-*hydroxy*-α-2′ : 3′ : 4′ : 5′-*tetramethylphenylcinnamate*, formed colourless prisms, m. p. 172—173° (Found: C, 77·4; H, 6·95. $C_{20}H_{22}O_3$ requires C, 77·4; H, 7·15%).

1 : 2 : 3 : 4-*Tetramethylphenanthrene*.—The foregoing acid (4 g.) in quinoline (40 c.c.) was heated at 250—260° with copper bronze (2 g.) for 1 hour. After cooling and dilution with ether, the solution was filtered, washed with dilute hydrochloric acid and sodium carbonate solution, dried, and evaporated. The residue, in benzene, was passed through a column of alumina, and then distilled from an oil-bath at 190—200°/0·5 mm. The distillate was crystallised from acetic acid, 1 : 2 : 3 : 4-*tetramethylphenanthrene* (2·2 g.) separating in colourless plates, m. p. 92—93° (Found: C, 92·55; H, 7·75. $C_{18}H_{18}$ requires C, 92·25; H, 7·75%).

The hydrocarbon gave an unstable picrate, but the s.-*trinitrobenzene complex* separated from alcohol in bright yellow needles, m. p. 161—162° (Found: C, 64·55; H, 4·9. $C_{18}H_{18},C_6H_3O_6N_3$ requires C, 64·4; H, 4·7%).

No pure quinone could be obtained on oxidation, probably on account of the substitution (compare 1 : 2-dimethylchrysene; Hewett, this vol., p. 293). The phenanthrene structure was confirmed by measurement of the absorption spectrum, for which we are indebted to Dr. E. Roe, who will publish the data elsewhere.

We wish to thank the British Empire Cancer Campaign for a grant to the Hospital which has greatly assisted this work. The work forms part of a thesis to be submitted by one of us (R. H. M.) in fulfilment of the requirements for a doctorate in the University of Geneva.

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