133. *Polycyclic Aromatic Hydrocarbons. Part XIV. A New Synthesis of* 3 : 4-*Benzphenanthrene.*

By C. L. Hewett.

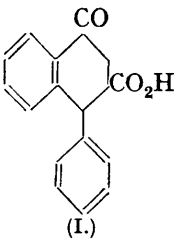
The fact that 3 : 4-benzphenanthrene is one of the few carcinogenic compounds not related to 1 : 2-benzanthracene makes it desirable to extend investigation to a variety of simple derivatives in order to ascertain whether the cancer-producing activity of 3 : 4-benzphenanthrene is fortuitous or whether it is a property commonly associated with this type of molecular structure. In this connexion it is of interest that the three unknown pentacyclic hydrocarbons composed entirely of six-membered benzenoid rings all contain the ring system of 3 : 4-benzphenanthrene (for formulæ, see Barry, Cook, Haslewood, Hewett, Hieger, and Kennaway, *Proc. Roy. Soc.*, 1935, *B*, **117**, 328).

In the method already recorded for the synthesis of 3 : 4-benzphenanthrene (Cook, J., 1931, 2524) the formation of this ring system by a Pschorr reaction is accompanied by considerable cyclisation to the benzanthracene structure in spite of the fact that the latter requires ring closure at a β-position of the naphthalene system of a molecule in which a free α-position is also available for ring closure. This indicates a resistance to formation of the 3 : 4-benzphenanthrene system, which is probably best interpreted as due to steric factors. The present communication describes a new synthetic route to 3 : 4-benzphenanthrene which has the advantage that no alternative mode of cyclisation is possible. Moreover, the new method should be more readily adaptable to the synthesis of benzphenanthrene homologues, one of which is now described, and it is hoped, also, to utilise the same type of method for the synthesis of 1 : 2 : 5 : 6-dibenzphenanthrene.

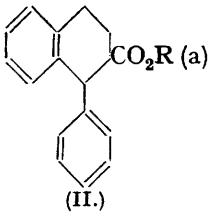
The new method is based on the observation of Haworth and Sheldrick (J., 1935, 637) that diphenylmethylsuccinic acids (obtained by reduction of the diphenylitaconic acids arising from the condensation of benzophenones with ethyl succinate) may be cyclised to phenyltetralone derivatives, whereas Stobbe and Vieweg (*Ber.*, 1902, **35**, 1727) had shown that diphenylitaconic acid is cyclised to an indone derivative. The former authors did not investigate the parent diphenylmethylsuccinic acid, but it has now been found that its anhydride undergoes the expected cyclisation with aluminium chloride to 4-*keto*-1-*phenyl*-1 : 2 : 3 : 4-*tetrahydro*-2-*naphthoic acid* (I). This was reduced by Clemmensen's method to 1-*phenyl*-1 : 2 : 3 : 4-*tetrahydro*-2-*naphthoic acid* (IIa; R = H), the *ethyl* ester of which was reduced by sodium and alcohol to 1-*phenyl*-1 : 2 : 3 : 4-*tetrahydro*-2-*naphthylcarbinol* (IIb).

The Grignard compound of 1-*phenyl*-2-*chloromethyl*-1 : 2 : 3 : 4-*tetrahydronaphthalene* (IIc), obtained from the carbinol (IIb) by means of thionyl chloride and dimethylaniline, reacted with carbon dioxide at − 15° to give a 67% yield of 1-*phenyl*-1 : 2 : 3 : 4-*tetrahydronaphthyl*-2-*acetic acid* (IId; R = H). In this reaction there were obtained as by-products 1-phenyl-2-methyl-1 : 2 : 3 : 4-tetrahydronaphthalene (IIe) and αβ-*bis*-(1-*phenyl*-1 : 2 : 3 : 4-*tetrahydro*-2-*naphthyl*)*ethane*. The acid (IId; R = H) was either sulphonated or un-

affected by treatment at 100° with sulphuric acid of various concentrations, but was converted into 2-*keto*-1 : 2 : 9 : 10 : 11 : 12-*hexahydro*-3 : 4-*benzphenanthrene* (III) by the

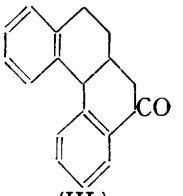


(I.)

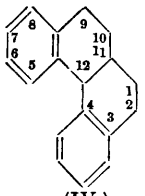


(II.)

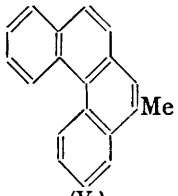
(b) $CH_2 \cdot OH$
(c) CH_2Cl
(d) $CH_2 \cdot CO_2R$
(e) CH_3



(III.)



(IV.)



(V.)

action of aluminium chloride on its chloride. When the reaction was carried out at 0° much acid chloride was unchanged, but complete reaction was effected by heating on the water-bath. This contrasts with the behaviour of 2-phenyl*cyclo*hexylacetic acid (Cook, Hewett, and Lawrence, this vol., p. 77), which is cyclised with the utmost facility, and provides another illustration of the greater difficulty of formation of the 3 : 4-benzphenanthrene system.

The ketone (III) was reduced by the Kishner–Wolff method to 1 : 2 : 9 : 10 : 11 : 12-*hexahydro*-3 : 4-*benzphenanthrene* (IV), which on dehydrogenation with platinum-black gave 3 : 4-benzphenanthrene in 60% yield. Although the stages are somewhat numerous, the yields are good throughout, so that the over-all yield of benzphenanthrene is 7·3% with respect to the diphenylmethylsuccinic acid. It is hoped to determine the configuration of the tetracyclic compounds (III and IV) by *X*-ray crystallographic examination.

The ketone (III) reacted normally with methylmagnesium iodide to give a crude carbinol, which was dehydrated with potassium hydrogen sulphate. The resulting hydrocarbon was dehydrogenated to 2-*methyl*-3 : 4-*benzphenanthrene* (V), the biological testing of which and of the new specimen of 3 : 4-benzphenanthrene will be described elsewhere.

Experimental.

4-*Keto*-1-*phenyl*-1 : 2 : 3 : 4-*tetrahydro*-2-*naphthoic Acid* (I).—Diphenylmethylsuccinic acid (43 g.) (Stobbe, *Annalen*, 1899, **308**, 100) was refluxed with acetyl chloride (45 c.c.) for 2 hours; all the acid had then dissolved. The excess of acetyl chloride and the acetic acid were removed at the pressure of the water-pump and the residue was dissolved in nitrobenzene (50 c.c.) and slowly added to an ice-cold solution of aluminium chloride (43 g.) in nitrobenzene (250 c.c.). After being kept for 20 hours at 0°, the solution was decomposed with ice and hydrochloric acid, the nitrobenzene distilled with steam, and the residue dissolved in dilute sodium carbonate, filtered, and acidified. The *keto-acid* (I) crystallised from acetic acid in almost colourless tablets (29 g.), m. p. 208—209° (Found: C, 76·5; H, 5·35. $C_{17}H_{14}O_3$ requires C, 76·65; H, 5·3%). The *ethyl* ester, prepared by refluxing the acid with five parts of alcoholic hydrogen chloride, crystallised from alcohol in colourless, slender, silky needles, m. p. 122—123° (Found: C, 77·6; H, 6·3. $C_{19}H_{18}O_3$ requires C, 77·5; H, 6·15%).

1-*Phenyl*-1 : 2 : 3 : 4-*tetrahydro*-2-*naphthoic Acid* (IIa; R = H).—This was obtained in poor yield together with much unchanged keto-acid by the ordinary Clemmensen reduction of (I); no better yields were obtained by using the ester. When anisole was used as a solvent and the crude reduced acid was esterified, the yield of distilled ester was 78%. The keto-acid (I) (65 g.), anisole (130 c.c.), water (264 c.c.), concentrated hydrochloric acid (132 c.c.), and amalgamated zinc (200 g.) were boiled under reflux for 5 hours, concentrated hydrochloric acid (33 c.c.) being added at the end of each hour. After cooling, the acid was extracted with ether, separated from

neutral products by solution in dilute sodium carbonate, and converted into the *ethyl* ester by refluxing with alcoholic hydrogen chloride. The ester (IIa; R = Et) (53 g.) distilled at 170—173°/0·8—1·0 mm. and crystallised from alcohol in colourless needles, m. p. 61—62° (Found: C, 81·0; H, 7·2. $C_{19}H_{20}O_2$ requires C, 81·35; H, 7·2%). Hydrolysis with alcoholic potash gave the *acid* (IIa; R = H), b. p. 200°/0·8 mm., which crystallised from *cyclo*hexane in irregular colourless rhombs, m. p. 148—148·5° (Found: C, 80·7; H, 6·3. $C_{17}H_{16}O_2$ requires C, 80·9; H, 6·4%).

1-*Phenyl*-1 : 2 : 3 : 4-*tetrahydro*-2-*naphthylcarbinol* (IIb).—The ester (IIa; R = Et) (55 g.) was dissolved in ethyl alcohol (300 c.c.), and sodium (27 g.) added during ¾—1 hour. After the sodium had dissolved (2—3 hours), most of the alcohol was removed, the residue diluted with water (1 l.), and the precipitated solid extracted four times with ether. The ethereal solution was washed, dried, and distilled; the *carbinol* (IIb) (26 g.), b. p. 175—180°/1 mm., crystallised from aqueous alcohol and then from ligroin in light feathery needles, m. p. 93—94° (yield, 67%) (Found: C, 85·7; H, 7·65. $C_{17}H_{18}O$ requires C, 85·7; H, 7·6%). The aqueous solution on acidification yielded 18 g. of acid, which was re-esterified and again reduced. In this way 60·5 g. of the carbinol and 10 g. of acid were obtained from 94 g. of the ester.

1-*Phenyl*-2-*chloromethyl*-1 : 2 : 3 : 4-*tetrahydronaphthalene* (IIc).—Thionyl chloride (12·5 g.) was slowly added to an ice-cold agitated solution of the alcohol (IIb) (22 g.) in carbon tetrachloride (40 c.c.) and freshly distilled dimethylaniline (14 g.). The mixture was kept for ½ hour in ice and for ¼ hour on the water-bath; ice was added, and the carbon tetrachloride solution washed with dilute hydrochloric acid and dilute sodium carbonate, dried, and distilled. The *chloride* (IIc) (21 g. 90%), b. p. 168°/0·8 mm., crystallised from alcohol in colourless rhombs, m. p. 71—72° (Found: C, 79·5; H, 6·75. $C_{17}H_{17}Cl$ requires C, 79·5; H, 6·7%).

1-*Phenyl*-1 : 2 : 3 : 4-*tetrahydronaphthyl*-2-*acetic Acid* (IId; R = H).—During 4 hours dry carbon dioxide was slowly passed into a Grignard reagent prepared from the aforesaid chloride (16 g.), magnesium (1·6 g.), and ether (70 c.c.), cooled to − 15°. In the preparation of the Grignard solution methylmagnesium iodide was necessary for activation. Ice and hydrochloric acid were then added, the ethereal solution washed with water, and the acid extracted with dilute sodium carbonate. After crystallising from dilute alcohol and then from ligroin, the *acid* (IId; R = H) formed colourless irregular plates (11 g.), m. p. 138—139° after slight previous sintering (Found: C, 81·5; H, 7·0. $C_{18}H_{18}O_2$ requires C, 81·2; H, 6·8%). The neutral fraction, isolated from the ether, was distilled at 150—160°/1 mm. The distillate was dissolved in methyl alcohol and kept at 0° for 2 days; 1-*phenyl*-2-*methyl*-1 : 2 : 3 : 4-*tetrahydronaphthalene* (IIe) was then deposited in stout colourless rhombs (1·1 g.), m. p. 46—47° (Found: C, 91·9; H, 8·0. $C_{17}H_{18}$ requires C, 92·3; H, 7·7%). The residue from the distillation slowly crystallised; after recrystallisation from alcohol and then ligroin it had m. p. 169·5—170·5° and was shown by analysis to be αβ-*bis*-(1-*phenyl*-1 : 2 : 3 : 4-*tetrahydro*-2-*naphthyl*)*ethane* (0·3 g.) [Found: C, 92·2; H, 7·8; *M* (Rast), 359. $C_{34}H_{34}$ requires C, 92·3; H, 7·7%; *M*, 442].

2-*Keto*-1 : 2 : 9 : 10 : 11 : 12-*hexahydro*-3 : 4-*benzphenanthrene* (III).—The acid (14 g.) was boiled with thionyl chloride (70 c.c.) for 1 hour, and the excess of thionyl chloride removed in a vacuum. The residue was dissolved in carbon disulphide (70 c.c.) and cooled in ice, aluminium chloride (14 g.) slowly added, and the mixture kept in ice for 4 hours; ice and hydrochloric acid were then added, together with some benzene to dissolve the sparingly soluble ketone. The benzene–carbon disulphide solution was washed with dilute aqueous sodium carbonate, dried, and evaporated. After crystallising from ethyl alcohol, the *ketone* (5·1 g.) formed almost colourless leaflets, m. p. 154—155° (Found: C, 86·8; H, 6·6. $C_{18}H_{16}O$ requires C, 87·1; H, 6·5%). The mother-liquors of the ketone on distillation gave a solid (7·4 g.), which crystallised from ice-cold methyl alcohol (in which it was easily soluble) in colourless needles, m. p. 55—56° (Found: C, 82·0; H, 7·5. $C_{20}H_{22}O_2$ requires C, 82·3; H, 7·55%). This was the *ethyl* ester (IId; R = Et) formed from some unchanged acid chloride. When ring closure of the acid chloride was effected by heating on the water-bath with aluminium chloride for 4 hours, the yield of ketone was increased to 70% and there was no unchanged acid. The *semicarbazone*, prepared by boiling the ketone with semicarbazide hydrochloride and sodium acetate in aqueous-alcoholic solution for 32 hours, crystallised from aqueous dioxan and had m. p. 235° (Found: N, 13·2. $C_{19}H_{19}ON_3$ requires N, 13·8%). The *oxime*, prepared in anhydrous pyridine, crystallised from alcohol in pale pink tablets, m. p. 191—192° (Found: C, 82·4; H, 6·6. $C_{18}H_{17}ON$ requires C, 82·1; H, 6·5%).

1 : 2 : 9 : 10 : 11 : 12-*Hexahydro*-3 : 4-*benzphenanthrene* (IV).—The semicarbazone of (III) (3 g.) was heated with sodium ethoxide (3 g. of sodium in 45 c.c. of ethyl alcohol) at 175—180° for 9 hours. After cooling, water was added, and the oil extracted with ether. The ethereal

layer was washed, dried, and evaporated, giving a crystalline solid (2·5 g.), which distilled at 148—153°/0·2 mm. After recrystallisation from alcohol, ***hexahydrobenzphenanthrene*** (IV) formed colourless rhombs, m. p. 47·5—48° (Found : C, 92·3; H, 7·8. $C_{18}H_{18}$ requires C, 92·3; H, 7·7%). Dehydrogenation to 3 : 4-benzphenanthrene was effected by heating with platinum-black at 310—320° for 7 hours in an atmosphere of carbon dioxide. Purification was effected through the picrate, m. p. 123—125° (lit., 126—127°), and the regenerated hydrocarbon was distilled (60% yield), and crystallised from alcohol; m. p. 68° (lit., 68°). These m. p.'s were not depressed by specimens prepared by the method of Cook (*loc. cit.*).

2-*Methyl*-3 : 4-*benzphenanthrene* (V).—The Grignard reagent prepared from methyl iodide (2·5 g.; 3 mols.), magnesium (0·5 g.), and ether (15 c.c.) was cooled in ice and treated with finely powdered tetrahydrobenzphenanthrone (III) (1·5 g.). After ½ hour in ice the product was boiled for 1½ hours and cooled, and ice and ammonium chloride added. The ethereal solution, washed, dried, and evaporated, left a gum. Dehydration was effected by heating at 160° for 1 hour with potassium hydrogen sulphate (3 g.), and the non-crystalline hydrocarbon was dehydrogenated with platinum-black at 300—310° for 2 hours in a slow current of carbon dioxide. Distillation at 0·2 mm. from a bath at 210° gave a viscous oil (1·2 g.), of which the vermilion *picrate* crystallised from alcohol in needles, m. p. 132·5—133·5° (Found : C, 64·0; H, 3·5. $C_{19}H_{14},C_6H_3O_7N_3$ requires C, 63·7; H, 3·6%). The m. p. was depressed by 3 : 4-benzphenanthrene picrate. The pure picrate was shaken with ether and ammonia; the ***hydrocarbon*** (V), isolated by evaporation of the ether, crystallised from alcohol in small colourless leaflets, m. p. 69·5—70°, depressed by 3 : 4-benzphenanthrene (Found : C, 94·3; H, 5·75. $C_{19}H_{14}$ requires C, 94·2; H, 5·8%).

The author thanks Prof. J. W. Cook for the interest he has taken in this work.

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[*Received, March 23rd,* 1936.]