

PHENANTHRENE SYNTHESSES WITH 2,3-DIMETHYL-2-CYCLOHEXEN-1-ONE

ERNST BERGMANN AND (MISS) A. WEIZMANN

Received March 21, 1939

The experiments described herein were undertaken originally with the intention of locating by comparison methods the phenolic hydroxyl group in the oestrone molecule. In the intervening time, the synthesis of 7-methoxy-1,2-cyclopentenophenanthrene, the dehydrogenation product of oestrone, has been accomplished by Cohen, Cook, Hewett, and Girard¹, proving the position of the hydroxyl group at C₃ of the oestrone molecule, as suggested previously by Butenandt, Weidlich, and Thompson². Also, the 7-hydroxy-1,2-dimethylphenanthrene obtained by the German authors has been synthesized by Haworth and Sheldrick³. Our method aimed at the synthesis of the latter substance, too, and our results may still be of interest, as they provide a route to the direct preparation of compounds of the 1,2-dimethylphenanthrene type, which are interesting analogs of the corresponding cyclopenteno- or benzophenanthrene derivatives⁴.

The starting material for our synthesis was 2,3-dimethyl-2-cyclohexen-1-one (I)⁵. On reaction with phenethylmagnesium chloride and *m*-methoxyphenethylmagnesium chloride, it gave II and III, respectively. (See p. 267.) It is characteristic of this method, that the position of the double bond created by the Grignard reaction is unambiguous, in spite of the asymmetry of the ketone molecule, since no allene system is capable of existence in a six-membered ring. Therefore the direction of the subsequent cycloisomerisation, which was carried out by means of stannic chloride, is also fixed *a priori*; in addition, the cyclization product (V) is more unsaturated than in the usual syntheses, which facilitates the final dehydrogena-

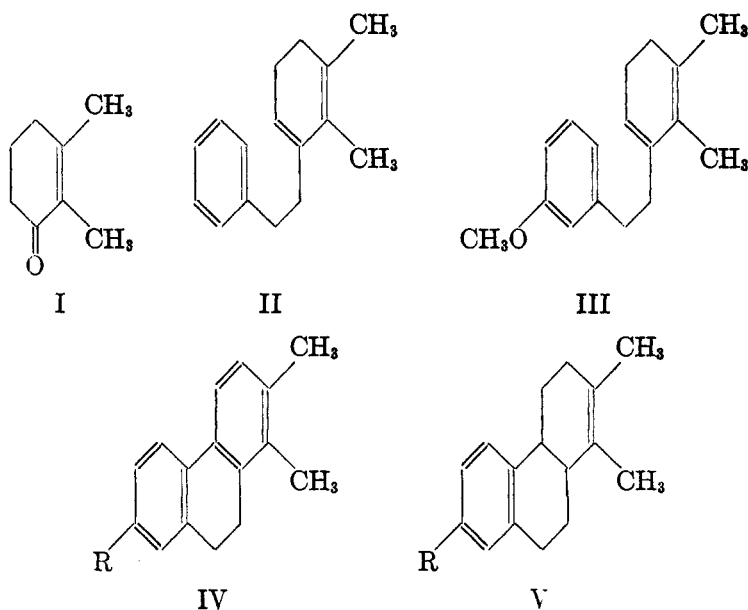
¹ COHEN, COOK, HEWETT, AND GIRARD, *J. Chem. Soc.*, **1934**, 653.

² BUTENANDT, WEIDLICH, AND THOMPSON, *Ber.*, **66**, 601 (1933).

³ HAWORTH AND SHELDRIK, *J. Chem. Soc.*, **1934**, 864.

⁴ 1,2-Dimethylphenanthrene, *e.g.*, gives mixed crystals with the 1,2-cyclopentenocompound. For comparison of carcinogenic properties of such pairs, see, *e.g.*: COOK *et al.*, *Proc. Roy. Soc. London*, **111B**, 455 (1922). FIESER AND NEWMAN, *J. Am. Chem. Soc.*, **58**, 2376 (1936); NEWMAN, *ibid.*, **59**, 1003 (1937); BARRY, COOK *et al.*, *Proc. Roy. Soc. London*, **117B**, 318 (1935).

⁵ KOETZ, AND CO-WORKERS, *Ann.*, **400**, 83 (1913).



tion process. This reaction, however, proved difficult, as along with the desired phenanthrenes, on dehydrogenation, dihydro derivatives, most probably the 9,10-dihydrogenated substances (IV) were obtained. The separation of (IV) and the phenanthrenes was easy, as only the latter form picrates. In this way, 1,2-dimethylphenanthrene, previously described by Haworth, Mavin, and Sheldrick⁶, and 7-methoxy-1,2-dimethylphenanthrene picrate were obtained. The latter compound corresponds to the substance prepared previously by Haworth and Sheldrick³.

EXPERIMENTAL

The necessary *dimethylcyclohexenone* was prepared as follows. The crude condensation product (270 g.) from ethyl acetoacetate (260 g.) and trioxymethylene (30 g.) was heated with a solution of sodium (23 g.) in alcohol (800 cc.) for 2 hours to 85–115°. After removal of the alcohol, the residue, dissolved in water, was treated with acetic acid until the evolution of carbon dioxide ceased, and ethyl 3-methyl-2-cyclohexen-1-one-4-carboxylate was isolated and fractionated; b.p. 160–165°/35 mm., 108°/1 mm.; yield 130 g.

Anal. Calc'd for $C_{10}H_{14}O_3$: C, 65.9; H, 7.7.

Found: C, 65.2; H, 8.3.

This ester (62 g.) was added to a solution of sodium (7.8 g.) in methanol (120 cc.) and methylated with methyl iodide (48.3 g.). After 2 hours' boiling, the solvent was evaporated, water and ether added and the methylation product, ethyl 2,3-dimethyl-2-cyclohexen-1-one-4-carboxylate was isolated; b.p. 158–161°/21 mm.,

⁶ HAWORTH, MAVIN, AND SHELDRIK, *J. Chem. Soc.*, 1934, 454.

104–110°/1 mm.; yield, 39–42 g. It was converted into (I) by heating (20 g.) for 8 hours with 10% alcoholic potash solution (60 cc.). The fraction 53–65°/1.5 mm. was used.

Anal. Calc'd for $C_8H_{10}O$: C, 77.4; H, 9.7.

Found: C, 77.2; H, 10.1.

1,2-Dimethyl-3-phenethyl-1,3-cyclohexadiene (II).—To a Grignard solution, prepared from phenethyl chloride⁷ (14.2 g.) and magnesium (2.3 g.), dimethylcyclohexenone (12.5 g.) was added. The reaction product was isolated as usual; b.p. 155°/6 mm.; yield, 6 g.

Anal. Calc'd for $C_{18}H_{20}$: C, 90.6; H, 9.4.

Found: C, 90.9; H, 9.1.

1,2-Dimethyl-3,4,9,10,11,12-hexahydrophenanthrene (V, R = H)—The solution of the above diene (4 g.) in benzene (60 cc.) was saturated with gaseous hydrogen chloride, and, after addition of stannic chloride (2 cc.), was kept at 0° for several days. The red mass was decomposed with ice and concentrated hydrochloric acid, and the product was isolated by distillation; b.p. 105–107°/0.02 mm., 150–160°/29 mm.; yield, 3.3 g.

Anal. Calc'd for $C_{18}H_{20}$: C, 90.6; H, 9.4.

Found: C, 90.3; H, 9.3.

1,2-Dimethylphenanthrene was obtained by heating the foregoing product with an equal amount of selenium to 330° for 20 hours. The product was isolated by extraction with ether and distillation in a good vacuum. The leaflets obtained were identified by the melting point of a mixture with authentic 1,2-dimethylphenanthrene (m.p. 142–143°). In another experiment, the picrate, m.p. 156°, was isolated. The oily mother liquors were distilled again; they had the boiling point 115–120°/2 mm., and according to the analysis consisted of 2,3-dimethyl-9,10-dihydrophenanthrene (IV, R = H).

Anal. Calc'd for $C_{18}H_{18}$: C, 92.3; H, 7.7.

Found: C, 92.2, 92.2; H, 7.5, 7.8.

m-Methoxyphenethyl alcohol.—*m*-Methoxyphenylmagnesium bromide solution (from 2.4 g. magnesium and 18.7 g. *m*-bromoanisole) reacted violently with ethylene oxide (5.5 g.) at 0°, a yellow precipitate being formed. The reaction was completed by boiling the mixture for 1 hour. The reaction product had the boiling point 105–110°/1 mm.; yield, 7 g.⁸

Anal. Calc'd for $C_9H_{10}O_2$: C, 71.0; H, 7.9.

Found: C, 70.9, 70.9; H, 8.1, 7.9.

m-Methoxyphenethyl chloride.—(a) The alcohol (8 g.) in dimethylaniline (10 g.) reacted violently with thionyl chloride (10 g.) at 0°. After heating for 30 minutes at 100°, the mass was kept at room temperature for 12 hours, was decomposed with cold dilute sulfuric acid, and the chloride was isolated by distillation; b.p. 85–87°/1.5 mm., 128–130°/14 mm.; yield, 6 g.

Anal. Calc'd for $C_9H_{11}OCl$: C, 63.5; H, 6.5.

Found: C, 63.1, 63.0; H, 6.4, 6.7.

The use of pyridine instead of dimethylaniline gave inconstant results.

(b) According to the procedure described by Higginbottom and Hill⁹ the Grignard compound from *m*-bromoanisole (38 g.) and magnesium (4.8 g.) was treated with β -chloroethyl *p*-toluenesulfonate (47 g.). The sluggish reaction, occurring at

⁷ SCHLENK AND BERGMANN, *Ann.*, **479**, 83 (1930).

⁸ HEWETT, *J. Chem. Soc.*, **1936**, 50.

⁹ HIGGINBOTTOM AND HILL, *J. Chem. Soc.*, **1937**, 264.

55°, was completed by 8 hours' boiling, and the *m*-methoxyphenethyl chloride was isolated as usual; b.p. 90–95°/0.7 mm.; yield, 10.5 g.

Anal. Calc'd for $C_9H_{11}OCl$: C, 63.5; H, 6.5.

Found: C, 62.9; H, 6.8.

1,2-Dimethyl-3-(m-methoxyphenethyl)-1,3-cyclohexadiene (III). — (*m*-Methoxyphenethylmagnesium chloride (prepared from 1.55 g. of magnesium and 11 g. of the above chloride) reacted with dimethylcyclohexenone (I) (9.2 g.) as above. The resulting product had the boiling point 145–147°/0.8 mm.; yield, 7.5 g.

Anal. Calc'd for $C_{17}H_{22}$: C, 84.3; H, 9.1.

Found: C, 83.3, 83.6; H, 9.6, 9.8.

Cyclization was carried through as above, yielding *1,2-dimethyl-7-methoxy-3,4,9,10,11,12-hexahydrophenanthrene (V, R = OCH₃)*. It boiled at 135°/0.07 mm.; yield; 3.5 g. (from 7 g. of III).

Anal. Calc'd for $C_{17}H_{22}O$: C, 84.3; H, 9.1.

Found: C, 83.4; H, 9.4.

7-Methoxy-1,2-dimethylphenanthrene.—The hydro derivative (1.5 g.) was heated with selenium (3.5 g.) in a sealed tube at 320° for 24 hours. The dehydrogenation product was isolated by vacuum distillation and treated with picric acid in alcoholic solution. The picrate, after recrystallization from methyl alcohol, had m.p. 149° and analyzed well for the picrate of the desired substance.

Anal. Calc'd for $C_{17}H_{18}O + C_6H_3N_3O_7 = C_{23}H_{19}N_3O_8$: C, 59.4; H, 4.1; OCH₃, 6.7.

Found: C, 59.4, 60.0; H, 3.8, 4.3; OCH₃, 6.9.

From the mother liquor, *2,3-dimethyl-7-methoxy-9,10-dihydrophenanthrene (IV, R = OCH₃)* was isolated by distillation. It boiled at about 150°/1 mm. as a colorless liquid.

Anal. Calc'd for $C_{17}H_{18}O$: C, 85.7; H, 7.6.

Found: C, 85.8; H, 7.9.