187. *Synthesis of Alkylphenanthrenes. Part VII. 7-Hydroxy-*1 : 2-*dimethylphenanthrene.*

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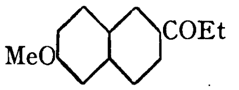
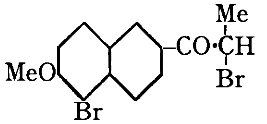
EARLIER work in this series (J., 1932, 1784, 2248) has shown that 2-methylnaphthalene is substituted in position 6 when it is subjected to the Friedel–Crafts reaction in nitrobenzene solution with succinic anhydride or propionyl chloride. Sulphonation also occurs in position 6 (Dziewoński, Schoenówna, and Waldmann, *Ber.*, 1925, **58**, 1212), but other reactions, such as nitration and halogenation, lead to substitution in position 1. The parallelism between sulphonation and the Friedel–Crafts reactions led us to examine the latter reaction on 2-methoxynaphthalene, which has been shown to be sulphonated in position 6 (Lapworth, P., 1895, 49). Gattermann, Ehrhardt, and Maisch (*Ber.*, 1890, **23**, 1208), Witt and Braun (*Ber.*, 1914, **47**, 3216), Fries (*Ber.*, 1921, **54**, 709) and Fries and Schimmelschmidt (*Ber.*, 1925, **58**, 2835) have shown that in benzene or carbon disulphide solution 2-methoxynaphthalene and acetyl chloride react in the presence of aluminium chloride to yield 2-methoxy-1-naphthyl methyl ketone, but it has now been found that 70% yields of 6-methoxy-2-naphthyl methyl ketone are obtained when the reaction is carried out in nitrobenzene solution. The constitution of the ketone was established by oxidation with sodium hypochlorite to 6-methoxy-2-naphthoic acid, identical with a specimen prepared by the method of Fries and Schimmelschmidt (*loc. cit.*).

This observation appears to provide a route to the synthesis of some important phenanthrene derivatives and the present paper describes one of these synthetical researches.

6-*Methoxy*-2-*naphthyl ethyl ketone* (I) was obtained similarly from 2-methoxynaphthalene and propionyl chloride, and its structure confirmed by oxidation to 6-methoxy-2-naphthoic acid. A monobromo-derivative being unobtainable, the ketone (I) was converted into a dibromo-derivative, probably 5-*bromo*-6-*methoxy*-2-*naphthyl α-bromoethyl ketone* (II), which was oxidised to 5-*bromo*-6-*methoxy*-2-*naphthoic acid* by Kröhnke's method (*Ber.*, 1933, **66**, 604). The dibromo-compound (II) was condensed with ethyl sodiomalonate, and converted in the usual manner into β-(5-*bromo*-6-*methoxy*-2-*naphthoyl*)*butyric acid* (III), the *methyl* ester of which reacted with methylmagnesium iodide to give γ-(5-*bromo*-6-*methoxy*-2-*naphthyl*)-β-*methyl*-Δ^{β}-*pentenoic acid* (IV). This acid was reduced with hydrogen in the presence of a palladium–calcium carbonate catalyst in boiling alcoholic solution to *γ-(6-methoxy-2-naphthyl)-β-methylvaleric acid* (V). The conversion of the acid (V) into

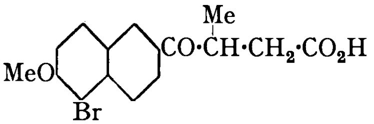
(I.)

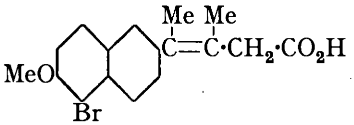




(II.)

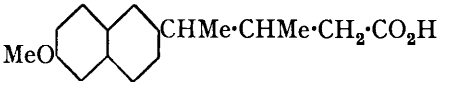
(III.)



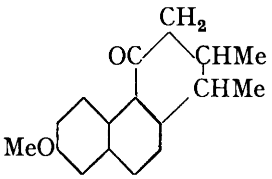


(IV.)

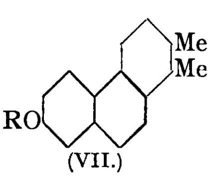
*7-methoxy-4-keto-*1 : 2-*dimethyl-*1 : 2 : 3 : 4-*tetrahydrophenanthrene* (VI) could not be brought about with 80% sulphuric acid, as sulphonation and demethylation occurred. The action



(V.)



(VI.)



(VII.)

of aluminium chloride on a tetrachloroethane solution of the chloride of acid (V) led to 30% yields of the cyclic ketone (VI), but the best results were obtained by the action of stannic chloride on the acid (V). The cyclic ketone (VI), which has not been obtained crystalline, was reduced by Clemmensen's method, and the product on dehydrogenation with selenium was converted into *7-methoxy-*1 : 2-*dimethylphenanthrene* (VII; R = Me), m. p. 153—154°. This ether was demethylated with hydrobromic acid, and *7-hydroxy-*1 : 2-*dimethylphenanthrene* (VII; R = H), m. p. 197—198°, obtained. The *benzoyl* derivative of this phenol melted at 211—212°.

By degradation of oestriol, Butenandt, Weidlich, and Thompson (*Ber.*, 1933, **66**, 601) obtained a 1 : 2-dimethylphenanthrol, m. p. 190—191°, from which a methyl ether, m. p. 153°, and a benzoyl derivative, m. p. 210°, were prepared. Although a direct comparison of the synthetic and the degradation products has not yet been made, the melting points suggest that the products are identical, in which case the synthesis establishes the position of the phenolic hydroxyl group and the aromatic nucleus in oestriol. The slight discrepancy in the melting points of the phenol is probably insignificant in view of the small amounts of material which Butenandt, Weidlich, and Thompson had at their disposal.

(*Added in Proof.*)—Specimens of the phenol, its methyl ether and benzoyl derivative have been submitted to Professor A. Butenandt, who very kindly made a comparison, and reports that the synthetic products are identical with those obtained from oestriol. When the melting points were determined in his apparatus, no discrepancy between the synthetic and the degradation products was observed. Although no specimen of his phenol was available, no depression in melting point was shown in mixtures of his methyl ether and benzoyl derivative with our products.

EXPERIMENTAL.

6-Methoxy-2-naphthyl Methyl Ketone.—Powdered aluminium chloride (8·5 g.) was added gradually, with stirring, to an ice-cold solution of 2-methoxynaphthalene (5 g.) and acetyl chloride (2·5 g.) in nitrobenzene (20 c.c.). After 24 hours, ice and dilute hydrochloric acid were added, the nitrobenzene was removed in steam, and the product extracted with chloroform, dried, and distilled in a vacuum. 6-Methoxy-2-naphthyl methyl ketone, b. p. 195—200°/10 mm., crystallised from light petroleum (b. p. 60—80°) in colourless plates (4·5 g.), m. p. 104—105°. Fries and Schimmelschmidt (*loc. cit.*) give 105°. This ketone (0·25 g.) was boiled for 1 hour with a solution of sodium hypochlorite, prepared by passing chlorine (from 0·3 g. of potassium permanganate) into *N*-sodium hydroxide (20 c.c.). The liquid was filtered and acidified, and the acid collected and crystallised from alcohol; colourless needles, m. p. 209—210°, were obtained, which gave no depression in melting point when mixed with 6-methoxy-2-naphthoic acid prepared by Fries and Schimmelschmidt's method.

6-*Methoxy*-2-*naphthyl ethyl ketone* (I), b. p. 180—185°/0·3 mm., obtained similarly in 80% yield, crystallised from light petroleum (b. p. 60—80°) in colourless plates, m. p. 109° (Found : C, 78·2; H, 6·4. $C_{14}H_{14}O_2$ requires C, 78·5; H, 6·5%). This ketone was oxidised to 6-methoxy-2-naphthoic acid, m. p. 208—209°.

5-*Bromo*-6-*methoxy*-2-*naphthyl α-bromoethyl ketone* (II) was prepared in 80% yield by the gradual addition of bromine (80 g.) in chloroform (250 c.c.) to a solution of the ketone (I) (50 g.) in chloroform (250 c.c.). After 3 hours, the hydrogen bromide was removed in a stream of dry air, and the solvent under diminished pressure; the residue crystallised from light petroleum (b. p. 60—80°)–chloroform in colourless plates, m. p. 162° (Found : C, 45·3; H, 3·4; Br, 42·9. $C_{14}H_{12}O_2Br_2$ requires C, 45·2; H, 3·2; Br, 43·0%). This bromide reacted rapidly with pyridine; the pyridinium bromide which separated was collected, washed with ether, dissolved in aqueous alcohol, and treated with sodium hydroxide as described by Kröhnke (*loc. cit.*). 5-*Bromo*-6-*methoxy*-2-*naphthoic acid* crystallised from alcohol in colourless needles, m. p. 290—291° (Found : equiv., 279. $C_{12}H_9O_3Br$ requires equiv., 281). The *methyl* ester prepared by the action of methyl-alcoholic hydrogen chloride, separated from methyl alcohol in either colourless nodules or slender needles, the latter form being obtained from dilute solutions. Both forms melted at 162—163°, either alone or mixed (Found : C, 53·0; H, 3·9. $C_{13}H_{11}O_3Br$ requires C, 52·9; H, 3·7%).

β-(5-*Bromo*-6-*methoxy*-2-*naphthoyl*)*butyric Acid* (III).—The bromide (II) (14 g.) in benzene (100 c.c.) was added to a suspension of ethyl sodiomalonate (from 1·4 g. of sodium and 9 g. of ethyl malonate) in benzene (80 c.c.). After boiling for 12 hours, the mixture was acidified, the benzene layer dried, and the solvent removed. The residue was hydrolysed by boiling with methyl-alcoholic potassium hydroxide for 1 hour. The alcohol was removed, and the residue extracted several times with boiling water. The extract was acidified and the product, isolated with ethyl acetate, was heated at 180° for 3 hours. The residue was dissolved in hot sodium carbonate solution, filtered with carbon, the filtrate acidified, and the crude acid (III) collected and esterified by boiling for 3 hours with methyl-alcoholic hydrogen chloride. The ester was extracted with ether, washed with water and sodium carbonate solution, and dried, and the ether removed. The residual *ester* was distilled in a high vacuum, preferably in quantities not exceeding 5 g. It boiled at 240—244°/0·2 mm., and crystallised from methyl alcohol in colourless nodules (5·5 g.), m. p. 105—106° (Found : C, 55·9; H, 4·7; Br, 22·1. $C_{17}H_{17}O_4Br$ requires C, 55·9; H, 4·7; Br, 21·9%). The *acid* (III), obtained by hydrolysis of the above ester with methyl-alcoholic potassium hydroxide, crystallised from methyl alcohol in colourless nodules, m. p. 160° (Found : equiv., 347. $C_{16}H_{15}O_4Br$ requires equiv., 351).

γ-(5-*Bromo*-6-*methoxy*-2-*naphthyl*)-β-*methyl*-Δ^{β}-*pentenoic Acid* (IV).—Considerable difficulty was experienced in the preparation of this acid, and the following conditions must be adhered to rigidly if reproducible results are desired. An ethereal solution of methylmagnesium iodide (from magnesium, 0·4 g., methyl iodide, 4·5 g., in ether, 15 c.c.) was added rapidly with cooling and shaking to a solution of the methyl ester of (III) (3·6 g.) in benzene (120 c.c.). The mixture was boiled for 1 hour and acidified, and the benzene layer extracted several times with dilute sodium carbonate solution. Acidification of the carbonate solution precipitated the crude *pentenoic acid* (IV), which was isolated with ether and crystallised from methyl alcohol; colourless needles (1·85 g.), m. p. 159—160°, were obtained (Found : C, 58·2; H, 4·9. $C_{17}H_{17}O_3Br$ requires C, 58·5; H, 4·9%). The sodium, potassium, and ammonium salts were sparingly soluble in water and separated from hot solution as gelatinous precipitates. A solution of the acid in aqueous sodium carbonate was rapidly oxidised by cold potassium permanganate.

γ-(6-*Methoxy*-2-*naphthyl*)-β-*methylvaleric Acid* (V).—A stream of hydrogen was passed through a suspension of palladium–calcium carbonate (from palladium chloride, 0·8 g., and calcium carbonate, 3·2 g.) in a solution of the pentenoic acid (IV) (9·5 g.) in boiling alcohol (120 c.c.) for 3 hours. The mixture was evaporated to dryness, and the residue digested with sodium carbonate solution. The *acid* (V) was liberated by addition of hydrochloric acid to the filtered extract, isolated with ether, and crystallised from light petroleum (b. p. 60—80°); colourless needles (6·6 g.), m. p. 89—90°, were obtained (Found : C, 75·3; H, 7·3. $C_{17}H_{20}O_3$ requires C, 75·0; H, 7·3%). The alkali salts of this acid were readily soluble in water and were stable towards cold potassium permanganate.

7-*Methoxy*-4-*keto*-1 : 2-*dimethyl*-1 : 2 : 3 : 4-*tetrahydrophenanthrene* (VI).—The acid (V) (1·5 g.)

was heated at 100° for 1 hour with stannic chloride (3 c.c.), and after addition of dilute hydrochloric acid, the cyclic *ketone* (VI) was extracted with ether, washed with water and dilute sodium hydroxide solution, and distilled in a vacuum, being obtained as a pale yellow, viscous oil (1 g.), b. p. 205—210°/0·3 mm. (Found : C, 80·1; H, 7·3. $C_{17}H_{18}O_2$ requires C, 80·3; H, 7·1%). The semicarbazone separated from methyl alcohol in small crystals, m. p. 238—240° (decomp.).

7-*Methoxy*-1 : 2-*dimethylphenanthrene* (VII; R = Me).—The cyclic ketone (2·5 g.) was reduced by boiling for 5 hours with amalgamated zinc (12 g.) and concentrated hydrochloric acid (12 c.c.). The product was isolated with ether, washed with sodium hydroxide solution, and distilled. The tetrahydrophenanthrene derivative (1·3 g.), b. p. 185—190°/0·1 mm., was obtained as a colourless oil, which was heated with selenium (2·6 g.) at 300° for 12 hours. 7-*Methoxy*-1 : 2-*dimethylphenanthrene* (1 g.) was isolated with chloroform and distilled over sodium in a vacuum; it boiled at 210—215°/18 mm., and crystallised from methyl alcohol in colourless prisms, m. p. 154—155°, unchanged by further crystallisation (Found : C, 86·4; H, 6·8. $C_{17}H_{16}O$ requires C, 86·4; H, 6·8%).

7-*Hydroxy*-1 : 2-*dimethylphenanthrene* (VII; R = H).—The methoxy-derivative (0·2 g.) was gently boiled for 3 hours with a mixture of acetic acid (9 c.c.) and hydrobromic acid (9 c.c.; *d* 1·49). The mixture was evaporated to dryness in a vacuum, the residue dissolved in hot dilute aqueous sodium hydroxide, and the filtered solution acidified; the precipitate was taken up in ether and dried, and the solvent removed. The residual *phenol* crystallised from ether–light petroleum (b. p. 60—80°) or, better, from a little benzene in small colourless needles (0·16 g.), m. p. 197—198° (Found : C, 86·3; H, 6·2. $C_{16}H_{14}O$ requires C, 86·5; H, 6·3%). The *benzoyl* derivative, prepared by either the Schotten–Baumann or the Einhorn method, crystallised from glacial acetic acid in colourless plates, m. p. 211—212° (Found : C, 84·5; H, 5·6. $C_{23}H_{18}O_2$ requires C, 84·7; H, 5·5%).

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