13. *The Synthesis of Compounds related to the Sterols, Bile Acids, and Oestrus-producing Hormones. Part IX.*

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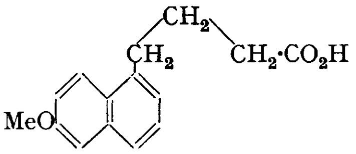
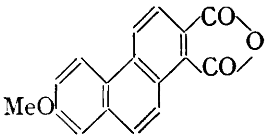
As a preliminary to the synthesis of 7-methoxyphenanthrene-1 : 2-dicarboxylic anhydride, which from its relationship to the degradation products of oestriol methyl ether (MacCorquodale, Levin, Thayer, and Doisy, *J. Biol. Chem.*, 1933, **101**, 753) might be expected to have oestrogenic properties, we intended to study the cyclisation of ethyl α-oxalyl-γ-1-naphthylbutyrate, a reaction analogous to the synthesis of 3 : 4-dihydronaphthalene-1 : 2-dicarboxylic acid by Auwers and Möller (*J. pr. Chem.*, 1925, **109**, 124), to which we directed attention in Part I (J., 1933, 1106). After some unsatisfactory attempts to simplify the preparation of the required type of oxalyl ester by condensation of β-naphthylethyl bromide with ethyl oxalacetate, our experiments were anticipated by Fieser and Hershberg (*J. Amer. Chem. Soc.*, 1935, **57**, 1508), who synthesised 3 : 4-dihydrophenanthrene-1 : 2-dicarboxylic anhydride. In view of the high oestrogenic activity subsequently reported for this compound (*idem, ibid.*, p. 1852) we returned to our original objective and have synthesised 7-*methoxyphenanthrene*-1 : 2-*dicarboxylic anhydride* (II), which we also required for comparison with a sample prepared by one of us by a much simpler method (Cohen, *Nature*, 1935, **136**, 869).

γ-(6-Methoxy-1-naphthyl)butyric acid (I) was obtained by condensing β-(6-methoxy-1-naphthyl)ethyl bromide (Cohen, Cook, and Hewett, J., 1935, 452) with ethyl malonate, with subsequent hydrolysis and decarboxylation.

(I.)





(II.)

The succeeding stages were exactly analogous to those used by Fieser and Hershberg, and require no further comment. The results of tests for oestrogenic activity will be reported elsewhere.

EXPERIMENTAL.

β-(6-*Methoxy*-1-*naphthyl*)*ethylmalonic Acid*.—A solution of β-6-methoxy-1-naphthylethyl bromide (15 g.) in toluene (15 c.c.) was added to the potassio-compound prepared from ethyl malonate (18 g.) and powdered potassium (3·75 g.) in toluene (50 c.c.). The whole was heated at 120—130° for 55—60 hours, and the substituted malonic ester was isolated in the usual manner, b. p. 200—205°/0·3 mm. (13·7 g.). Hydrolysis of this ester with boiling aqueous-alcoholic potash (3 hours) gave β-(6-*methoxy*-1-*naphthyl*)*ethylmalonic acid*, which crystallised from water in lustrous colourless leaflets, m. p. 160° (with gas) (Found: C, 66·9; H, 5·6. $C_{16}H_{16}O_5$ requires C, 66·6; H, 5·6%).

γ-(6-Methoxy-1-naphthyl)butyric acid (I) was obtained by heating the malonic acid at 190° until liberation of carbon dioxide ceased. It crystallised from aqueous alcohol in colourless flat needles, m. p. 150—151° (Found: C, 73·9; H, 6·65; equiv., 240·5. Calc. for $C_{15}H_{16}O_3$: C, 73·7; H, 6·6%; equiv., 244). Butenandt and Schramm (*Ber.*, 1935, **68**, 2089) obtained this acid in poor yield by another method. The *ethyl* ester was prepared with alcoholic hydrogen chloride, and formed a colourless liquid (7·8 g.), b. p. 169°/0·2 mm. (Found: C, 74·8; H, 7·5. $C_{17}H_{20}O_3$ requires C, 74·9; H, 7·4%). When this ester (0·55 g.) was heated on the water-bath for an hour with 80% sulphuric acid (3 c.c.), it gave the 1-keto-7-methoxy-1 : 2 : 3 : 4-tetrahydrophenanthrene described by Butenandt and Schramm (*loc. cit.*) together with a little of the corresponding hydroxy-ketone.

Condensation of Ethyl γ-(6-*Methoxy*-1-*naphthyl*)*butyrate with Ethyl Oxalate*.—Potassium (0·92 g.) was dissolved in a mixture of anhydrous ether (31·5 c.c.) and absolute alcohol (3·5 c.c.), and the suspension was cooled in ice and treated with ethyl oxalate (5 g.), and then, after ½ hour, with ethyl methoxynaphthylbutyrate (6·25 g.). At the end of a further ½ hour, the yellow solution began to deposit crystals of a potassio-compound of the condensation product. After being kept at room temperature over-night, these were collected, washed with anhydrous ether, and decomposed with ice-cold dilute sulphuric acid. The oxalyl ester was dried in ethereal solution, and the ether removed, leaving a yellow viscous liquid (6·25 g.).

7-*Methoxy*-3 : 4-*dihydrophenanthrene*-1 : 2-*dicarboxylic Anhydride*.—The foregoing oxalyl ester (1 g.), warmed on the water-bath for 5 minutes with 80% sulphuric acid (8·5 c.c.), became converted into an orange solid. This was collected, washed, and dried. 7-*Methoxy*-3 : 4-*dihydrophenanthrene*-1 : 2-*dicarboxylic anhydride* crystallised from acetic acid or benzene in orange needles, m. p. 217·5—218·5°; benzene solutions had a strong green fluorescence (Found: C, 73·1; H, 4·3. $C_{17}H_{12}O_4$ requires C, 72·8; H, 4·3%). Demethylation to 7-*hydroxy*-3 : 4-*dihydrophenanthrene*-1 : 2-*dicarboxylic anhydride* was effected by boiling a suspension of the anhydride (1 g.) in acetic acid (25 c.c.) and hydrobromic acid (*d* 1·48; 10 c.c.) for 3 hours (a clear solution was formed after 1½ hours). The solution was concentrated on the water-bath under reduced pressure, and the residue extracted with hot benzene and then recrystallised from acetic acid (0·7 g. of chocolate-brown prisms). After several recrystallisations from dioxan the hydroxy-anhydride formed golden-yellow prismatic needles, m. p. 275—278° after sintering (the colour rapidly changes to red on heating) (Found: C, 71·3; H, 3·5. $C_{16}H_{10}O_4$ requires C, 72·2; H, 3·8%).

7-*Methoxyphenanthrene*-1 : 2-*dicarboxylic Anhydride* (II).—The dihydro-compound (0·1 g.) was heated at 300° for 1½ hours with platinum-black (50 mg.), and the product was sublimed under reduced pressure. The *methoxy-anhydride* (II) crystallised from glacial acetic acid in fine yellow needles, m. p. 253—254° (260—261°, corr.) (Found: C, 73·2; H, 3·7. $C_{17}H_{10}O_4$ requires C, 73·35; H, 3·9%).

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