

**951.** 1 : 7 : 10- and 1 : 6 : 10-Trimethylphenanthrene.

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The compounds named in the title have been synthesised by standard methods.

DURING degradative studies concerning the constitution of the fungal diterpene rosolactone,<sup>1</sup> 1 : 7 : 10- and 1 : 6 : 10-trimethylphenanthrene have been synthesised as reference compounds, by standard methods.

Condensation of 1 : 8-dimethylnaphthalene with methylsuccinic anhydride by the Friedel-Crafts method furnished a mixture of acids (I; R = H, R' = Me, and *vice versa*). Reduction of the keto-acid (I; R = H, R' = Me) by the Huang-Minlon<sup>2</sup> modification of the Wolff-Kishner method gave  $\gamma$ -(4 : 5-dimethyl-1-naphthyl)- $\alpha$ -methylbutyric acid (II; R = H, R' = Me), the acid chloride of which was cyclised to 1 : 2 : 3 : 4-tetrahydro-2 : 8 : 9-trimethyl-1-oxophenanthrene (III; R = H, R' = Me). Reduction of this cyclic ketone by a second application of the Huang-Minlon process yielded 1 : 2 : 3 : 4-tetrahydro-2 : 8 : 9-trimethylphenanthrene (IV; R = H, R' = Me) which furnished 1 : 7 : 10-trimethylphenanthrene on dehydrogenation.

Similarly 1 : 6 : 10-trimethylphenanthrene was prepared from the acid (I; R = Me, R' = H) by the stages (II), (III), and (IV; R = Me, R' = H).

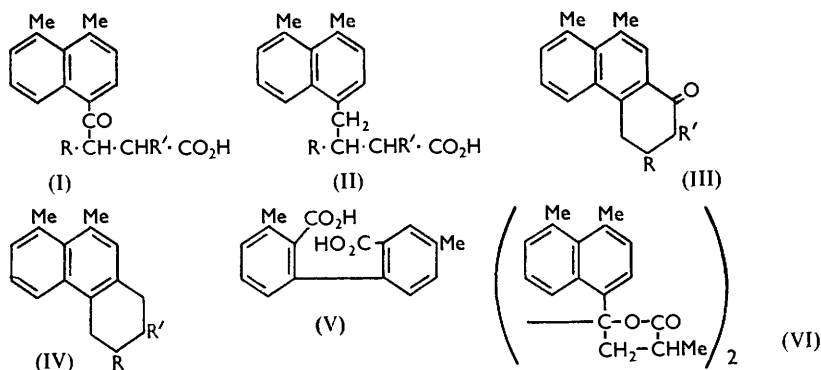
Reduction of  $\beta$ -(4 : 5-dimethyl-1-naphthoyl)- $\alpha$ -methylpropionic acid (I; R = H, R' = Me) by the Clemmensen method furnished a product which, in agreement with the analytical data and infrared absorption at 1783 cm.<sup>-1</sup>, is formulated as the pinacol-di- $\gamma$ -lactone (VI) (cf. Huang-Minlon<sup>2</sup>).

In accordance with general principles the condensation of 1 : 8-dimethylnaphthalene with methylsuccinic anhydride could furnish either the 2- or the 4-naphthoylpropionic acid. Since the ultraviolet absorption spectra show conclusively that the final tricyclic hydrocarbons are phenanthrenes and not anthracenes, it follows that the condensation

<sup>1</sup> Harris, Robertson, and Whalley, *J.*, 1958, 1807; and unpublished work from these laboratories.

<sup>2</sup> Huang-Minlon, *J. Amer. Chem. Soc.*, 1946, **68**, 2487.

furnishes the 4-naphthoylpropionic acids (I), as expected. Exclusive production of 4-substituted naphthalenes has been observed in analogous Friedel-Crafts condensations between succinic anhydride and 1-methylnaphthalene<sup>3</sup> and acenaphthene.<sup>4</sup> The orientation of the two trimethylphenanthrenes and hence of the cognate derivatives follows from the structures of the isomeric cyclic ketones (III; R = H, R' = Me and *vice versa*). The comparatively slow rate of reduction of one ketone (IIIA) in the Wolff-Kishner reaction together with its reluctance to form a 2:4-dinitrophenylhydrazone, in contrast to the isomer (B) which furnishes a derivative immediately and is more rapidly reduced by the Wolff-Kishner method, indicate steric hindrance in the isomer (A) which may thus be formulated as 1:2:3:4-tetrahydro-2:8:9-trimethyl-1-oxophenanthrene (III; R = H, R' = Me). Rates of formation of ketonic derivatives have been used<sup>5</sup> to distinguish between 2(or 8)-methyl- and 2:8-dimethyl-1-tetralones. Collateral evidence for the assignments is that the cyclic ketone formulated as (III; R = H, R' = Me) does not furnish a piperonylidene derivative, whilst the isomer (III; R = Me, R' = H) does.



Attempts to oxidise the two trimethylphenanthrenes to dimethyl-2:2'-diphenic acids with hydrogen peroxide-acetic acid gave intractable products, although 1:7-dimethylphenanthrene readily furnished 3:4'-dimethyl-2:2'-diphenic acid (V), the expected oxidation product from 1:7:10-trimethylphenanthrene.

Improvements in the synthesis of 9-methoxy-1:7-dimethylphenanthrene are recorded below.

#### EXPERIMENTAL

1:8-Dimethylnaphthalene.—Finely divided naphthalic anhydride (10 g.) was reduced when extracted from a Soxhlet thimble by a refluxing suspension of lithium aluminium hydride (5 g.) in ether (500 ml.) during 100 hr. Excess of reagent was destroyed by ethyl acetate, and the reaction complex decomposed with 2N-sulphuric acid (400 ml.). Evaporation of the washed ethereal extract furnished 1:8-di(hydroxymethyl)naphthalene which separated from benzene in needles (6 g.), m. p. 158°. Ghilardi and Kalopissis<sup>6</sup> record m. p. 154—155°.

Concentration of the benzene mother-liquors furnished a product which on chromatography from benzene on aluminium oxide gave 8-hydroxymethyl-1-naphthoic lactone (ca. 0.5 g.) which separated from benzene-light petroleum (b. p. 80—100°) in plates, m. p. 157° (Found: C, 78.4; H, 4.5. C<sub>12</sub>H<sub>8</sub>O<sub>2</sub> requires C, 78.3; H, 4.4%),  $\nu_{\max}$ . 1727 cm.<sup>-1</sup> (lactone). The mixed m. p. with naphthoic anhydride or 1:8-di(hydroxymethyl)naphthalene was depressed. This lactone was insoluble in cold 2N-aqueous sodium hydroxide but dissolved in hot aqueous-alcoholic 2N-sodium hydroxide to furnish a solution which remained clear on dilution and from which the parent lactone was precipitated by acid. Reduction of this lactone with lithium aluminium

<sup>3</sup> Haworth and Mavin, *J.*, 1932, 2720.

<sup>4</sup> Fieser and Peters, *J. Amer. Chem. Soc.*, 1932, **54**, 4347.

<sup>5</sup> Cocker, Fateen, and Lipman, *J.*, 1951, 926.

<sup>6</sup> Ghilardi and Kalopissis, *Bull. Soc. chim. France*, 1952, 217.

hydride gave 1 : 8-di(hydroxymethyl)naphthalene, m. p. 62°, by the method of Ghilardi and Kalopissis,<sup>6</sup> who record no yield.

1 : 7 : 10-Trimethylphenanthrene.—Aluminium chloride (8.3 g.), dissolved in nitrobenzene (15 ml.), was added slowly to a stirred solution of 1 : 8-dimethylnaphthalene (5 g.) and methylsuccinic anhydride (3.7 g.) in nitrobenzene (15 ml.) at 0°, and 5 days later the mixture was decomposed by ice and excess of hydrochloric acid and extracted with ether. Distillation of the ether, followed by removal of the nitrobenzene in a current of steam, furnished a resinous, acid which was esterified by boiling 10% alcoholic sulphuric acid for 4 hr. Isolated in the usual manner followed by distillation, the mixed esters (5.3 g.) had b. p. 185—195°/0.2 mm., and were saponified by refluxing them for 1 hr. with potassium hydroxide (1 g.) in water (50 ml.) and alcohol (50 ml.). Isolation with ether from the cooled, acidified hydrolysate, followed by purification from benzene–light petroleum (b. p. 80—100°), gave  $\gamma$ -(4 : 5-dimethyl-1-naphthyl)- $\alpha$ -methyl- $\gamma$ -oxobutyric acid (2.7 g.) as plates, m. p. 139—141°, unchanged by further crystallisation or by chromatography on silica–Celite (Found: C, 75.3; H, 6.8.  $C_{17}H_{18}O_3$  requires C, 75.5; H, 6.7%). The mother-liquor from this acid slowly deposited a semi-crystalline acid (1.5 g.) which on repeated purification from benzene–light petroleum (b. p. 60—80°) gave  $\gamma$ -(4 : 5-dimethyl-1-naphthyl)- $\beta$ -methyl- $\gamma$ -oxobutyric acid in pale yellow needles, m. p. 137—138° (Found: C, 75.6; H, 6.8%). Occasionally the acids separated in the reverse order during purification from benzene–light petroleum (b. p. 60—80°).

Fractional distillation of the methylated mixture did not achieve a more satisfactory separation of these two acids since hydrolysis of each fraction furnished a crystalline acid, m. p. 139—141°, together with the semi-crystalline butyric acid. The mixed m. p. of these acids was undepressed.

A mixture of the above  $\alpha$ -methylpropionic acid (2 g.), 100% hydrazine hydrate (0.6 ml.), potassium hydroxide (1.3 g.), and diethylene glycol (25 ml.) was refluxed at 170—180° for 2 hr., then excess of hydrazine and water were removed by distillation until the reaction temperature, which was maintained for a further 3 hr., was 220°. Isolated with ether from the cooled, acidified reaction mixture, the product was purified by chromatography (silica) from chloroform–light petroleum (b. p. 60—80°) (1 : 10), to give  $\gamma$ -(4 : 5-dimethylnaphthyl)- $\alpha$ -methylbutyric acid which separated from light petroleum (b. p. 80—100°) in prisms (1.2 g.), m. p. 92° (Found: C, 79.5; H, 7.8.  $C_{17}H_{20}O_2$  requires C, 79.7; H, 7.9%).

The acid (I; R = H; R' = Me) (0.5 g.) was esterified with diazomethane, and the oily ester reduced by refluxing it for 36 hr. with 25% hydrochloric acid (7 ml.), toluene (3 ml.), zinc amalgam (1 g.), and acetic acid (0.5 ml.): additional quantities (1.5 ml.) of concentrated hydrochloric acid were added at six-hourly intervals. Isolated with ether, the *di*- $\gamma$ -lactone (VI) of 4 : 5-bis-(4 : 5-dimethyl-1-naphthyl)-4 : 5-dihydroxy-2 : 7-dimethyloctane-1 : 8-dioic acid separated from benzene–light petroleum (b. p. 60—80°) in needles (0.05 g.), m. p. 282° [Found: C, 80.3; H, 7.0%; *M* (Rast), 467.  $C_{34}H_{38}O_4$  requires C, 80.6; H, 6.8%; *M*, 507]. This substance was insoluble in 2*N*-sodium hydrogen carbonate but readily dissolved in warm aqueous-alcoholic sodium hydroxide to furnish a solution which remained clear on dilution and from which acid precipitated the parent lactone.

A solution of  $\gamma$ -(4 : 5-dimethyl-1-naphthyl)- $\alpha$ -methylbutyryl chloride [prepared from the acid (1 g.) and phosphorus pentachloride (0.9 g.)] in tetrachloroethane (10 ml.) was added slowly to a stirred suspension of aluminium chloride (0.7 g.) in tetrachloroethane (10 ml.) at 0°. 24 Hr. later the mixture was decomposed by ice and excess of 2*N*-hydrochloric acid, the tetrachloroethane removed by distillation with steam, the residue extracted with ether, and the extract washed with 2*N*-hydrochloric acid, water, 2*N*-sodium hydrogen carbonate, dried, and evaporated to yield a semi-crystalline solid which was purified by chromatography from light petroleum (b. p. 60—80°) on aluminium oxide. Purification of the eluate from light petroleum (b. p. 40—60°) furnished 1 : 2 : 3 : 4-tetrahydro-2 : 8 : 9-trimethyl-1-oxophenanthrene in prisms (0.6 g.), m. p. 84°,  $\lambda_{max}$ . 216, 256, 281, 291, 351, ( $\log \epsilon$  5.34, 5.74, 4.83, 4.90, 4.29 respectively) (Found: C, 85.4; H, 7.9.  $C_{17}H_{18}O$  requires C, 85.7; H, 7.6%).

This ketone in alcohol did not give a derivative with alcoholic 2 : 4-dinitrophenylhydrazine sulphate during 24 hr. at room temperature. However the derivative separated when the mixture was heated on the steam-bath for 20 min. Purification from benzene–ethanol gave the 2 : 4-dinitrophenylhydrazone in scarlet needles, m. p. 242 (Found: C, 66.3; H, 5.3; N, 13.2.  $C_{23}H_{22}O_4N_4$  requires C, 66.0; H, 5.3; N, 13.4%). When a solution of the ketone (0.05 g.) and piperonaldehyde (0.03 g.) in alcohol (1 ml.) containing 1% alcoholic sodium ethoxide (1 ml.)

was heated on the steam-bath during 3 hr., no piperonylidene derivative was obtained but unchanged ketone (0.04 g.), m. p. and mixed m. p. 82—83°, was recovered.

Reduction of the foregoing ketone (0.7 g.) with hydrazine hydrate (0.25 ml.), potassium hydroxide (0.4 g.), and diethylene glycol (12 ml.) was carried out at 140° for 2 hr. and then at 200° for 4 hr. after removal of excess of hydrazine. Isolated with ether the product was separated by chromatography from light petroleum (b. p. 60—80°) on activated aluminium oxide into unchanged starting material (0.3 g.) and 1 : 2 : 3 : 4-tetrahydro-2 : 8 : 9-trimethylphenanthrene (0.3 g.), b. p. 170—180°/0.1 mm., m. p. 38—40° (Found: C, 90.6; H, 9.0. C<sub>17</sub>H<sub>20</sub> requires C, 91.0; H, 9.0%).

A mixture of this tetrahydrophenanthrene (1.2 g.), and 30% palladium-charcoal (0.1 g.) was heated under reflux at 300° for 2 hr. and then at 350° for ½ hr. The cooled mixture was extracted with benzene, and the crude product purified by chromatography from the same solvent on activated aluminium oxide, to give 1 : 7 : 10-trimethylphenanthrene which separated from light petroleum (b. p. 40—60°) in plates (1 g.), m. p. 93°, λ<sub>max</sub>. 224, 258, 280, 290, 302, 318, 327, 334, 351 (log ε 4.28, 4.74, 4.07, 3.97, 4.05, 2.56, 2.40, 2.52, and 2.23 respectively) (Found: C, 92.0; H, 7.6. C<sub>17</sub>H<sub>17</sub>, requires C, 92.7; H, 7.3%). The *picrate* separated from alcohol in orange needles, m. p. 149° (Found: C, 61.7; H, 4.1; N, 9.3. C<sub>23</sub>H<sub>19</sub>O<sub>7</sub>N<sub>3</sub> requires C, 61.5; H, 4.3; N, 9.4%).

1 : 6 : 10-Trimethylphenanthrene.—The Wolff-Kishner reduction of γ-(4 : 5-dimethyl-1-naphthyl)-β-methyl-γ-oxobutyric acid (1.3 g.) by the method used for the isomer furnished γ-(4 : 5-dimethyl-1-naphthyl)-β-methylbutyric acid which separated from light petroleum (b. p. 80—100°) in prisms (0.4 g.), m. p. 87°. The mixed m. p. with the isomeric acid was undepressed.

Cyclisation of the acid chloride (0.4 g.) of this acid in tetrachloroethane (5 ml.) containing aluminium chloride (0.3 g.) at 0° furnished 1 : 2 : 3 : 4-tetrahydro-3 : 8 : 9-trimethyl-1-oxophenanthrene which separated from light petroleum (b. p. 40—60°) in needles (0.2 g.), m. p. 94°, λ<sub>max</sub>. 218, 260, 286, 295, 306, 360 (log ε 5.30, 5.68, 4.85, 4.92, 4.77, and 4.51 respectively) (Found: C, 85.9; H, 7.5%). The mixed m. p. with the isomeric 1 : 2 : 3 : 4-tetrahydro-2 : 8 : 9-trimethyl-oxophenanthrene was depressed. When a solution of alcoholic 2 : 4-dinitrophenylhydrazine sulphate was added to a cold solution in alcohol of this ketone the 2 : 4-dinitrophenylhydrazone separated rapidly and was purified from benzene-ethyl acetate, forming red needles, m. p. 305° (decomp.) (Found: C, 65.7; H, 5.1; N, 13.2%). Prepared from this ketone (0.1 g.) and piperonaldehyde (0.1 g.) in alcohol (3 ml.) containing 1% alcoholic sodium ethoxide (1 ml.) on the steam-bath during 3 hr., the difficultly purifiable piperonylidene derivative separated from benzene-acetone in pale yellow needles, m. p. 226°; insufficient material was obtained for analysis. No unchanged ketone was recovered.

Reduction of this ketone (1.9 g.) with 100% hydrazine hydrate (0.75 ml.), potassium hydroxide (1.35 g.), and diethylene glycol (25 ml.) proceeded completely during 2 hr. at 140° followed by 4 hr. at 200°, to furnish 1 : 2 : 3 : 4-tetrahydro-3 : 8 : 9-trimethylphenanthrene in needles (1.6 g.), m. p. 63° [from light petroleum (b. p. 40—60°)] (Found: C, 90.8; H, 8.9%).

Dehydrogenation of this tetrahydrophenanthrene (1.1 g.) with 30% palladium-charcoal (0.1 g.) as before furnished 1 : 6 : 10-trimethylphenanthrene, needles (1 g.) [from methanol or light petroleum (b. p. 40—60°)], m. p. 83°, λ<sub>max</sub>. 216, 260, 283, 292, 305, 325, 340, 357 (log ε, 4.52, 4.82, 4.15, 4.04, 4.07, 2.68, 2.87, and 2.70 respectively) (Found: C, 92.4; H, 7.1%). The mixed m. p. with the isomeric phenanthrene was depressed. The *picrate* separated from alcohol in orange needles, m. p. 140° (Found: C, 61.6; H, 4.1; N, 9.0%) (the mixed m. p. with the isomeric *picrate* was depressed).

3 : 4'-Dimethyl-2 : 2'-diphenic Acid.—Hydrogen peroxide (1.7 ml. of 30%) was added gradually to a solution of 1 : 7-dimethylphenanthrene (0.5 g.) in acetic acid (6 ml.) at 80°. After 3 hr. at this temperature the acetic acid was removed by distillation, and a solution in benzene of the residual oil was washed with 2N-sodium hydrogen carbonate. Acidification of the alkaline extract furnished a solid which, after purification by chromatography from chloroform on silica, gave 3 : 4'-dimethyl-2 : 2'-diphenic acid which separated from benzene-light petroleum (b. p. 60—80°) in needles (0.2 g.), m. p. 205° (decomp.) (Found: C, 71.1; H, 5.3. C<sub>16</sub>H<sub>14</sub>O<sub>4</sub> requires C, 71.1; H, 5.2%).

1 : 7-Dimethyl-9-methoxyphenanthrene.—The following improvements were effected in the synthesis recorded by Ruzicka and Waldmann.<sup>7</sup>

Dehydrogenation of 7-methyl-1-tetralone<sup>7</sup> (10.1 g.) with 30% palladium-charcoal (0.5 g.)

<sup>7</sup> Ruzicka and Waldmann, *Helv. Chim. Acta*, 1932, 15, 907.

was effected at 320° for 3 hr., then the cooled reaction mixture was extracted with ether and the extract washed with 2*N*-sodium hydroxide. Acidification of this furnished 7-methyl-1-naphthol which separated from light petroleum (b. p. 80—100°) in needles (6.1 g.), m. p. 111°. Ruzicka and Waldmann<sup>7</sup> record m. p. 110—111°. The neutral fraction from the dehydrogenation gave 2-methylnaphthalene (3 g.), m. p. and mixed m. p. 34°.

Reduction of  $\gamma$ -(4-methoxy-6-methyl-1-naphthyl)- $\gamma$ -oxobutyric acid<sup>7</sup> (5 g.) with 100% hydrazine hydrate (1.4 g.), potassium hydroxide (3.1 g.), and diethylene glycol (60 ml.) was achieved under reflux for 1 hr. at 180—190° and then for 4 hr. at 205—225°. The cooled mixture was diluted with water and extracted with ether. The ethereal extract was washed with 2*N*-sodium hydrogen carbonate, and the washings were acidified. Methylation of the dried precipitate with methyl sulphate-potassium carbonate in boiling acetone during 6 hr. furnished methyl  $\gamma$ -(4-methoxy-6-methyl-1-naphthyl)butyrate which was purified by chromatography from benzene, followed by elution with benzene-light petroleum (b. p. 60—80°) on neutralised aluminium oxide. Saponification of this ester gave  $\gamma$ -(4-methoxy-6-methyl-1-naphthyl)butyric acid (2.6 g.) in needles, m. p. 144° (from methanol). Ruzicka and Waldmann<sup>7</sup> record m. p. 142°.

Cyclisation of this acid followed by interaction of the resultant ketone with methylmagnesium iodide according to the method of Ruzicka and Waldmann<sup>7</sup> furnished 1 : 2 : 3 : 4-tetrahydro-1-hydroxy-9-methoxy-1 : 7-dimethylphenanthrene which separated from light petroleum (b. p. 60—80°) in needles, m. p. 111°, with infrared absorption at 3393 cm.<sup>-1</sup> (Found: C, 79.1; H, 7.7. C<sub>17</sub>H<sub>20</sub>O<sub>2</sub> requires C, 79.7; H, 7.9%).

9-Methoxy-1 : 7-dimethylphenanthrene, purified by chromatography from light petroleum (b. p. 40—60°) on activated aluminium oxide, separated from the same solvent in plates, m. p. 131° (Found: C, 85.9; H, 7.0; OMe, 12.8. Calc. for C<sub>16</sub>H<sub>13</sub>OMe: C, 86.4; H, 6.8; OMe, 13.1%). Ruzicka and Waldmann<sup>7</sup> record m. p. 126—127°.

The analyses were by Mr. A. S. Inglis, M.Sc., and his associates of this Department. The ultraviolet spectra were determined in alcohol with a Unicam S.P. 500 spectrophotometer, and the infrared spectral data were obtained in Nujol by means of a Grubb-Parsons S3 spectrophotometer. One of us (J. A. C.) is indebted to D.S.I.R. for a Maintenance Grant.