129. *Syntheses of* 1-*Phenylnaphthalenes.*

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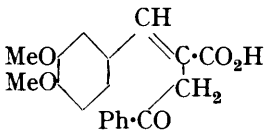
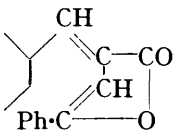
THE work described in this paper was undertaken as a continuation of a synthetical contribution to the structure of podophyllotoxin and its degradation products (J., **1933**, 83), but when it became known to us that a similar investigation, having the same objective, had reached a more advanced stage in Dr. R. D. Haworth's laboratory (private communication) we decided to abandon our project (compare Haworth and co-workers, J., **1935**, 1576). When our experiments were initiated in 1934 it appeared from the literature that little attention had been devoted to the synthesis of 1-phenylnaphthalenes. 1-Phenyl- and 1-*p*-tolyl-naphthalene had been obtained by dehydrogenation of the corresponding dihydro-derivatives prepared by the interaction of α-tetralone with phenyl- and tolylmagnesium bromide respectively (Weiss and Woidich, *Monatsh.*, 1925, **46**, 453; Braun and Anton, *Ber.*, **1934**, **67**, 1051), but for the preparation of polymethoxy-derivatives having a skeleton of the podophyllotoxin type this method has obvious limitations. Nevertheless it was decided to utilise this procedure for the preparation of reference compounds which would serve as a check on the products obtained by other methods. As an example, decarboxylation of the acid (III, R = CO_2H), formed by cyclisation of the *keto-acid* (I) or its *lactone* (II), gives rise to the *naphthalene* (III, R = H), identical with the product obtained by the dehydrogenation of the *dihydro*-derivative (IV). The last compound was prepared by the interaction of phenylmagnesium bromide and the appropriate tetralone.



(I.)



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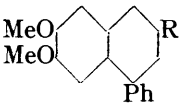

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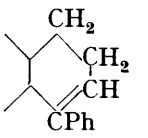

(IV.)

EXPERIMENTAL.

4'-Methoxy-1-phenylnaphthalene.—α-Tetralone (26 g.) in ether (100 c.c.) was gradually added to a solution of *p*-anisylmagnesium bromide (from 7·4 g. of metal and 57 g. of *p*-bromoanisole in 75 c.c. of ether) and 12 hours later the mixture was refluxed for 2 hours. The product was hydrolysed in the usual manner, the ether and unchanged tetralone removed with steam, and *4'-methoxy-1-phenyl-3 : 4-dihydronaphthalene* (22 g.), b. p. 198—200°/12 mm., isolated from the residual product by fractional distillation in a vacuum, forming colourless diamond-shaped plates, m. p. 76°, from alcohol, easily soluble in the usual organic solvents except alcohol (Found : C, 86·4; H, 6·9; OMe, 12·6. $C_{16}H_{13}$·OMe requires C, 86·4; H, 6·8; OMe, 13·1%).

Dehydrogenation of the dihydro-compound (2 g.) with powdered selenium (2 g.) at 280—300° for 24 hours gave a product (1·5 g.) from which *4'-methoxy-1-phenylnaphthalene* was isolated by repeated crystallisation from 70% alcohol, being finally obtained in colourless needles, m. p. 116·5°, easily soluble in acetic acid or benzene (Found : C, 87·2; H, 6·0. $C_{17}H_{14}O$ requires C, 87·2; H, 6·0%). Nitration of this substance (0·8 g.) in acetic acid (5 c.c.) with nitric acid (1·2 c.c., *d* 1·4) at room temperature in the course of 4 hours gave a *mononitro*-derivative, which separated from alcohol in long yellow needles (0·6 g.), m. p. 129° (Found in material dried at 80° in a high vacuum : N, 5·1. $C_{17}H_{13}O_3N$ requires N, 5·0%).

6 : 7-Dihydroxy-1-phenylnaphthalene.—*6 : 7-Dimethoxy-1-phenyl-3 : 4-dihydronaphthalene* was prepared from 6 : 7-dimethoxy-α-tetralone (17 g.) and phenylmagnesium bromide (from 26·4 g. of bromobenzene) in ether (300 c.c.) and purified by distillation in a vacuum and then by crystallisation from 95% alcohol, forming colourless hexagonal plates (16·8 g.), b. p. 215—217°/14 mm., m. p. 88·5°, readily soluble in benzene or light petroleum and moderately easily soluble in

acetic acid [Found : C, 81·3; H, 6·8; OMe, 23·0. $C_{16}H_{12}(OMe)_2$ requires C, 81·2; H, 6·8; OMe, 23·3%]. Dehydrogenation of this compound (2 g.) with selenium (2 g.) at 280—300° for 24 hours gave an ether-soluble product (1·4 g.), from which 6 : 7-*dimethoxy*-1-*phenylnaphthalene* was isolated by repeated crystallisation, from alcohol, forming colourless needles, m. p. 110°, having solubilities almost identical with those of the dihydro-derivative (Found : C, 81·8; H, 6·1. $C_{18}H_{16}O_2$ requires C, 81·8; H, 6·1%).

Demethylation of the dimethyl ether (1·75 g.) by heating with a mixture of hydriodic acid (50 c.c., *d* 1·7) and acetic anhydride (30 c.c.) at 140—145° for 50 minutes gave rise to the *dihydroxy*-compound (1·4 g.), which separated from warm water and then light petroleum (b. p. 60—80°) in colourless needles, m. p. 167—168°, easily soluble in benzene or alcohol (Found : C, 81·7; H, 5·2. $C_{16}H_{12}O_2$ requires C, 81·4; H, 5·1%). This compound gives a royal-blue ferric chloride reaction and a deep red coloration with concentrated sulphuric acid.

7-*Methoxy*-1-*phenylnaphthalene*.—Prepared from 7-methoxy-α-tetralone by the Grignard reaction, 7-*methoxy*-1-*phenyl*-3 : 4-*dihydronaphthalene* was purified by distillation in a vacuum and then by crystallisation from 95% alcohol, forming elongated hexagonal plates, m. p. 42·5—43·5°, easily soluble in benzene, light petroleum, or chloroform (Found : C, 86·7; H, 6·9; OMe, 13·1. $C_{16}H_{13}$·OMe requires C, 86·4; H, 6·8; OMe, 13·1%). Dehydrogenation of this substance with selenium at 280—300° gave a product, b. p. 210—222°/19 mm., from which 7-*methoxy*-1-*phenylnaphthalene* was isolated by fractional distillation over sodium in a vacuum, being finally obtained as a colourless oil, b. p. 214—215°/19 mm., with a faint blue fluorescence, which solidified in the course of 6 months; m. p. 48—50° (Found : C, 87·3; H, 6·2. $C_{17}H_{14}O$ requires C, 87·2; H, 6·0%).

4′-*Methoxy*-1-*phenyl*-2-*methylnaphthalene*.—Prepared by the Grignard method, the 3 : 4-*dihydro*-derivative was contaminated with *pp*′-dianisyl, from which it was separated by fractional crystallisation from light petroleum (b. p. 60—80°), forming diamond-shaped plates, m. p. 91—92° (Found : C, 86·0; H, 7·4; OMe, 12·5. $C_{17}H_{15}$·OMe requires C, 86·4; H, 7·2; OMe, 12·4%). On dehydrogenation this compound gave the *naphthalene*, which crystallised from 50% alcohol in hexagonal plates and from dilute acetic acid in needles, m. p. 108° (Found : C, 87·3; H, 6·6. $C_{18}H_{16}O$ requires C, 87·1; H, 6·5%).

β-*Benzoyl*-α-*veratrylidenepropionic Acid* (I).—Condensation of sodium β-benzoylpropionate (16·2 g.) and veratraldehyde (25 g.) by means of acetic anhydride (50 c.c.) at 100° during 12 hours (method of Borsche, *Ber.*, 1914, **47**, 1108) gave rise to the *γ-lactone* of the acid (15·5 g.), which crystallised from warm (not boiling) methyl alcohol in golden-yellow plates, m. p. 131°, easily soluble in benzene or chloroform and sparingly soluble in cold acetic acid (Found : C, 74·1; H, 5·3. $C_{19}H_{16}O_4$ requires C, 74·0; H, 5·2%). On being boiled with methyl alcohol for 5 minutes, the lactone was converted into the *methyl* ester of the acid, which separated from the cooled solution in colourless needles, m. p. 96° after recrystallisation (Found : C, 70·5; H, 5·9. $C_{20}H_{20}O_5$ requires C, 70·6; H, 5·9%).

Treatment of the lactone (5 g.) with cold alcoholic sodium methoxide (from 0·35 g. of sodium and 50 c.c. of methyl alcohol) gave rise to a mixture of the ester (2·5 g.) and the *acid*. The latter substance formed colourless plates (1·5 g.), m. p. 168°, from dilute acetic acid, easily soluble in chloroform or methyl alcohol (Found : C, 69·8; H, 5·8. $C_{19}H_{18}O_5$ requires C, 69·9; H, 5·5%).

6 : 7-*Dimethoxy*-1-*phenylnaphthalene*-3-*carboxylic acid* (III, R = CO_2H) separated from a solution of the foregoing lactone (1·7 g.) in chloroform (20 c.c.) containing iodine (1·7 g.) in the course of 5 days at room temperature. Crystallised from dilute methyl alcohol, the compound formed colourless stout rods (0·7 g.), m. p. 265° (Found : C, 74·4; H, 5·4. $C_{19}H_{16}O_4$ requires C, 74·0; H, 5·2%). A further quantity (0·6 g.) was obtained from the chloroform liquor.

On being heated with methyl alcohol saturated with hydrogen chloride for 4 hours β-benzoyl-α-veratrylidenepropionic acid or its methyl ester gave rise to the methyl ester of (III, R = CO_2H), forming clusters of colourless needles, m. p. 124°, from methyl alcohol, which on hydrolysis with boiling 6% aqueous-alcoholic potassium hydroxide for 2 hours yielded the naphthalene-3-carboxylic acid, m. p. and mixed m. p. 265°, after purification.

Decarboxylation of this acid (0·23 g.) by boiling with quinoline (3 c.c.) in the presence of copper bronze (0·2 g.) for 2 hours furnished 6 : 7-dimethoxynaphthalene (III, R = H), forming long needles, m. p. 110°, from 50% aqueous alcohol, identical with an authentic specimen prepared from 6 : 7-dimethoxy-α-tetralone.

β-p-*Anisoyl*-α-*benzylidenepropionic Acid*.—Condensation of sodium β-*p*-anisoylpropionate (35 g.) and benzaldehyde (32 g.) with acetic anhydride (64 c.c.) at 100° for 12 hours yielded the *γ-lactone* of the acid, which separated from benzene in greenish-yellow needles (25 g.), m. p. 174° (Found : C, 77·6; H, 4·9. $C_{18}H_{14}O_3$ requires C, 77·7; H, 5·0%). The lactone (2 g.) gradually

dissolved in methyl alcohol (20 c.c.) containing sodium methoxide (from 0·17 g. of sodium). Addition of water to the solution precipitated the *methyl* ester, which formed colourless needles, m. p. 74—75°, from methyl alcohol (Found : C, 73·4; H, 5·8. $C_{19}H_{18}O_4$ requires C, 73·5; H, 5·8%).

The *acid* was isolated from the concentrated alkaline liquor and on crystallisation from benzene formed colourless needles, m. p. 170°, containing solvent of crystallisation (Found : C, 75·0; H, 5·7. $C_{18}H_{16}O_4,0{\cdot}5C_6H_6$ requires C, 75·2; H, 5·7%. Found in material dried at 80° in a high vacuum : C, 73·4; H, 5·3. $C_{18}H_{16}O_4$ requires C, 73·0; H, 5·4%).

Attempts to effect cyclisation of this acid (or its ester) with alcoholic hydrogen chloride or sulphuric acid were unsuccessful. In the case of the lactone negative results were also obtained with iodine and chloroform.

ω-Chloro-3 : 4 : 5-trimethoxyacetophenone (7 g.) was prepared by treating ω-diazo-3 : 4 : 5-trimethoxyacetophenone (Robinson and co-workers, J., 1933, 374) (8 g.) with excess of hydrogen chloride in ether (500 c.c.) at 0°. Crystallised from ether–light petroleum (b. p. 60—80°), the compound formed rhombic prisms, m. p. 86—87° (Found : C, 54·5; H, 5·5. $C_{11}H_{13}O_4Cl$ requires C, 54·0; H, 5·3). A solution of this substance (1 g.) in alcohol (20 c.c.) containing potassium acetate (1 g.) and a crystal of sodium iodide was refluxed for 1 hour, cooled, and diluted with water. Crystallisation of the resulting solid (1 g.) from alcohol gave *ω-acetoxy-3 : 4 : 5-trimethoxyacetophenone* in colourless needles, m. p. 85—86° (Found : C, 58·2; H, 6·1. $C_{13}H_{16}O_6$ requires C, 58·2; H, 6·0%).

β-(3 : 4 : 5-Trimethoxybenzoyl)propionic Acid.—Interaction between the foregoing chloro-compound (12·5 g.) and ethyl sodiomalonate (from 7·5 g. of ester and 1·15 g. of sodium) in boiling benzene was complete in 2 hours. The product was hydrolysed with boiling 30% alcohol (50 c.c.) containing potassium hydroxide (10 g.) for 3 hours; the resulting *malonic acid* (6 g.) crystallised from ethyl acetate–light petroleum (b. p. 60—80°) in plates, m. p. 167—168° (decomp.) (Found : C, 54·2; H, 5·3. $C_{14}H_{16}O_8$ requires C, 53·8; H, 5·1%). On being kept at 160° for ½ hour, this compound was converted into the propionic acid, separating from water in needles which melted at 116° and then on solidification changed into the form, m. p. 122° (Found : C, 58·3; H, 6·1. Calc. for $C_{13}H_{16}O_6$: C, 58·2; H, 6·0%) (compare Haworth and co-workers, *loc. cit.*, who give m. p. 121—122°).

Condensation of the sodium salt of this acid (2·6 g.) with veratraldehyde (3·3 g.) in the usual manner furnished the *γ-lactone* of β-(3 : 4 : 5-trimethoxybenzoyl)-α-veratrylidenepropionic acid, forming golden needles, m. p. 172—173°, from benzene–light petroleum (b. p. 60—80°) (Found : C, 66·3; H, 5·7. $C_{22}H_{22}O_7$ requires C, 66·3; H, 5·6%).

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