

341. *Experiments on the Synthesis of Substances Related to the Sterols.
Part V. The Condensation of Phenylsuccinic Anhydride with Veratrole under the Influence of Aluminium Chloride.*

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THE application of the Friedel-Crafts reaction to phenylsuccinic anhydride and veratrole might give either (I) or (II), and it was important to ascertain the course taken by the reaction, in order to select suitable further stages of an attempted synthesis of 5:6-dimethoxyhexahydrochrysenes, which is feasible in either case (I or II). A similar



problem has been studied by Anschütz, Hahn, and Walter (*Annalen*, 1907, **354**, 150), who found that phenylsuccinic anhydride, benzene, and aluminium chloride afforded

desylacetic acid, $\text{Ph}\cdot\text{CO}\cdot\text{CHPh}\cdot\text{CH}_2\cdot\text{CO}_2\text{H}$ (analogous to I); we expected a similar result when veratrole was used instead of benzene.

The condensation was effected in nitrobenzene solution and gave an excellent yield of a homogeneous product which proved to be (II), because its characteristic *methyl ester* was also obtained by the action of aluminium chloride on a mixture of veratrole and β -carbomethoxy- β -phenylpropionyl chloride, $\text{Ph}\cdot\text{CH}(\text{CO}_2\text{Me})\cdot\text{CH}_2\cdot\text{COCl}$. Similarly treated, β -carbomethoxy- α -phenylpropionyl chloride, $\text{Ph}\cdot\text{CH}(\text{COCl})\cdot\text{CH}_2\cdot\text{CO}_2\text{Me}$, gave an uncrystallisable oil. The constitutions of these isomeric ester-chlorides have been established by Anschütz, Hahn, and Walter (*loc. cit.*). It may be noted in this connection that Rice (*J. Amer. Chem. Soc.*, 1931, **53**, 3159) obtained about equal amounts of isomeric acids as the result of the Friedel-Crafts reaction applied to resorcinol dimethyl ether and 2 : 4-dimethoxyphenylsuccinic anhydride. It is curious that only one of the isomerides was formed in the condensation of resorcinol dimethyl ether with maleic anhydride.

The acid (II) has been reduced by Clemmensen's method to α -phenyl- γ -veratrylbutyric acid, which may be dehydrated to a *ketodimethoxyphenyltetrahydronaphthalene* (III). A



Reformatsky reaction with ethyl bromoacetate then affords an unsaturated *ester* of the probable constitution (IV), but the conditions for the final stage of ring-closure to a chrysene derivative have not yet been found.

EXPERIMENTAL.

Phenylsuccinic Anhydride.—In the preparation of α -cyano- β -phenylacrylic acid ("Organic Syntheses," VII, 20 or I—IX, 175) by Lapworth and McRae's method (J., 1922, **121**, 1699) the yield (from 100 g. of benzaldehyde) was found to be 134 g. instead of the 105—110 g. claimed. The amount of sodium hydroxide employed in the condensation was increased. The dehydration of phenylsuccinic acid by means of boiling acetic anhydride does not proceed satisfactorily, but a quantitative yield was obtained when the acid (22 g.) was refluxed for 1.5 hours with acetyl chloride (80 c.c.); b. p. $161^\circ/8$ mm., m. p. 54° (from ether).

β -Veratroyl- α -phenylpropionic Acid (II).—A mixture of phenylsuccinic anhydride (4 g.) and veratrole (6 g.; nearly 2 mols.) was added to a cooled solution of aluminium chloride (7.5 g.) in pure nitrobenzene (15 c.c.), and the whole kept in a stoppered vessel for 48 hours. After addition of ice and hydrochloric acid the solvent and unchanged veratrole were removed in a current of steam; the residual oil solidified on cooling. The acid was purified by solution in aqueous sodium hydrogen carbonate, and recovery after washing with ether to remove neutral impurities; the amorphous precipitate was collected, washed with boiling water, and dried (6.0 g. or 84%). It crystallised from benzene in colourless quadrilateral leaflets, m. p. 134 — 135° , raised to 142 — 143° (constant) by several recrystallisations (Found in material dried at 110° in a high vacuum: C, 68.7; H, 5.7. $\text{C}_{18}\text{H}_{18}\text{O}_5$ requires C, 68.8; H, 5.7%). The acid is readily soluble in most organic solvents, but sparingly in carbon disulphide, light petroleum, and hot water.

Its *mononitro*-derivative, formed by the action of nitric acid (*d* 1.42) in the cold, crystallised from alcohol in pale yellow needles, m. p. 176 — 179° (Found: N, 3.9. $\text{C}_{18}\text{H}_{17}\text{O}_7\text{N}$ requires N, 3.9%). The substance contains the 6-nitroveratroyl group, because, after vigorous reduction (Clemmensen), the ferric reaction characteristic of 4-aminoveratroles was observed.

The Methyl Ester.—(A) The acid (4 g.) was refluxed for 6.5 hours with 5% methyl-alcoholic hydrogen chloride (120 g.). The derivative crystallised from methyl alcohol in colourless prisms or hexagonal plates, m. p. 100 — 100.5° (Found: C, 69.3; H, 6.1. $\text{C}_{18}\text{H}_{20}\text{O}_5$ requires C, 69.5; H, 6.1%).

(B) β -Carbomethoxy- β -phenylpropionyl chloride (from 1.1 g. of the acid) (Anschütz, Hahn, and Walter, *loc. cit.*) and veratrole (1 g.) were gradually treated in boiling carbon disulphide solution with powdered anhydrous aluminium chloride (1.8 g.) and then refluxed for 1 hour. The neutral oil isolated after decomposition with ice and hydrochloric acid was freed from last

traces of solvent and veratrole by washing with boiling light petroleum (b. p. 40—60°). The substance was eventually crystallised from methyl alcohol and was identified with the ester obtained as in (A) by m. p., undepressed mixed m. p., and by a comparison of crystal form.

When a mixture with piperonal and sodium hydroxide was refluxed in alcoholic solution, the liquid became brownish-yellow and on dilution and acidification a gummy, pale yellow acid was precipitated. This could not be crystallised; it dissolved in sulphuric acid to an intense blue solution (dichroic-red), which became magenta and then colourless on the addition of water. Evidently a piperonylidene derivative was formed and this confirms our view of the course of the main reaction considered.

1-Keto-6:7-dimethoxy-2-phenyl-1:2:3:4-tetrahydronaphthalene (III).—A mixture of β -veratroyl- α -phenylpropionic acid (5 g.), amalgamated zinc (60 g.), and concentrated hydrochloric acid (20 c.c.) was heated under reflux for 15.5 hours, and occasionally replenished by the addition of a few c.c. of hydrochloric acid. The acidic substance formed was isolated as an oil (4.35 g.), that later crystallised; a small quantity of a neutral compound was also obtained and found to consist of phenyldimethoxytetralone (below). The *phenylveratrylbutyric acid* was dissolved in a little anhydrous ether, a large volume of *n*-pentane added, and the solution concentrated to a small volume and seeded; on keeping in the ice-chest, a colourless crystalline crust and some flocculent needles separated, m. p. 83° (Found: C, 71.9; H, 6.7. $C_{18}H_{20}O_4$ requires C, 72.0; H, 6.7%).

Crude α -phenyl- γ -veratrylbutyric acid (4.2 g.) was directly heated with 80% sulphuric acid (20 c.c.) for 30 minutes. After dilution of the reaction mixture with water the solid was collected, triturated with warm dilute aqueous sodium hydroxide, washed, dried, and dissolved in hot methyl alcohol (70 c.c.). Colourless prisms (1.75 g.) separated on cooling, and the mother-liquor afforded 1.1 g. of the same substance, m. p. 140—141° (Found: C, 76.4; H, 6.3. $C_{18}H_{18}O_3$ requires C, 76.6; H, 6.4%), moderately readily soluble in the common organic solvents except light petroleum.

In agreement with our view of the constitution of this substance, it does not form a piperonylidene derivative under the usual conditions, nor does it condense with *o*-hydroxybenzaldehydes and hydrogen chloride to pyrylium salts.

Ethyl 6:7-Dimethoxy-2-phenyl-3:4-dihydronaphthyl-1-acetate (IV).—A mixture of the foregoing ketone (0.8 g.), ethyl bromoacetate (0.8 g.), zinc wool (0.4 g., previously heated in iodine vapour), and benzene (*ca.* 10 c.c.) was refluxed for 23 hours. The reaction product was washed with dilute sulphuric acid, isolated by means of ether, and dried in a vacuum at 100° (0.3 g.). It crystallised when rubbed with a little fresh ether and was recrystallised from acetone (0.18 g., m. p. 152—161°) and from acetone-methyl alcohol; flat prisms (0.1 g.), m. p. 159—161.5° (Found: C, 75.2; H, 6.8. $C_{22}H_{24}O_4$ requires C, 75.0; H, 6.8%). On hydrolysis by means of aqueous methyl-alcoholic potassium hydroxide, the related solid acid was obtained. A solution of this in aqueous sodium carbonate gave no cloudiness or precipitate on the addition of bromine water. Hence it is probably a $\beta\gamma$ - and not an $\alpha\beta$ -unsaturated acid.

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[Received, August 1st, 1935.]