

56. *Experiments on the Synthesis of Rotenone and its Derivatives.*
Part XI. Tetrahydrotubanol.

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ALTHOUGH the synthesis of tetrahydrotubanol (Haller, *J. Amer. Chem. Soc.*, 1933, **55**, 3032; Robertson, Part IV, J., 1933, 1164) serves to establish its constitution, the procedure is somewhat tedious and consequently we have investigated other possible, more convenient, routes to this compound. The following constitutes an improvement upon the older method. Application of the Fries reaction to the isovalerate of 7-hydroxy-4-methylcoumarin gave the isomeric 7-hydroxy-8-isovaleryl-4-methylcoumarin, which on scission according to Baker's procedure (J., 1935, 631) furnished 2 : 6-dihydroxyisovalerophenone, the orientation of which follows from its conversion into tetrahydrotubanol by reduction according to Clemmensen's method.

7-Hydroxy-8-isovaleryl-4-methylcoumarin.—Interaction of 7-hydroxy-4-methylcoumarin (8 g.) and isovaleryl chloride (6.5 g.) in pyridine (20 c.c.) during $\frac{1}{2}$ hour gave rise to the isovaleric ester of 7-hydroxy-4-methylcoumarin, which separated from alcohol in colourless prisms (8.5 g.), m. p. 63—64°.

For the preparation of the keto-coumarin the following directions must be strictly adhered to. A flask containing an intimate mixture of the ester (10 g.) and well-powdered aluminium chloride (25 g.), protected from atmospheric moisture (calcium chloride tube), was placed in an oil-bath at 80° and heated to 85° in the course of 15 minutes. When the mild reaction (evolution of hydrogen chloride) had almost subsided (5 minutes later), the oil-bath was heated to 150° in the course of $\frac{3}{4}$ hour; temperature after $\frac{1}{2}$ hour, 130°. After cooling, the product (3.3 g.) was isolated with the aid of ice and dilute hydrochloric acid in the usual manner; it crystallised from 50% alcohol in colourless, elongated, flat prisms, m. p. 109—110°, which give a bright purple coloration with alcoholic ferric chloride (Found: C, 69.5; H, 6.5. $C_{15}H_{16}O_4$ requires C, 69.2; H, 6.2%). Prepared according to the directions of Sun and Sah (*Amer. Chem. Abs.*, 1935, **29**, 466), the *o*-chlorobenzoylhydrazone separated from aqueous alcohol in colourless needles, m. p. 128—130° (decomp.) (Found: N, 7.0. $C_{22}H_{21}O_4N_2Cl$ requires N, 6.8%). The highly insoluble semicarbazone could not be purified.

Although Rây and co-workers (J., 1935, 814) report indications of the formation of 7-hydroxy-6-acetyl-4-methylcoumarin from 7-acetoxy-4-methylcoumarin, we have not been able to isolate an isomeric keto-coumarin in the present instance. Attempts to improve the yield of the keto-compound were unsuccessful.

2 : 6-Dihydroxyisovalerophenone.—The foregoing coumarin (8 g.) was refluxed with 20% aqueous sodium hydroxide (56 c.c.) in nitrogen for 3 hours and the mixture was cooled, acidified with hydrochloric acid, and extracted several times with ether. The combined extracts were washed with aqueous sodium bicarbonate to remove acidic material, dried, and evaporated, leaving the ketone, which separated from benzene-light petroleum (b. p. 60—80°) in pale yellow plates (4.5 g.), m. p. 67—68° (Found: C, 68.2; H, 7.2. $C_{11}H_{14}O_3$ requires C, 68.0; H, 7.2%). With alcoholic ferric chloride this compound gives a bluish-green coloration.

2 : 6-Dihydroxyisoamylbenzene (Tetrahydrotubanol).—Reduction of the foregoing ketone (4 g.) was effected by zinc amalgam in a boiling mixture of concentrated hydrochloric acid (25 c.c.), acetic acid (2 c.c.), and water (5 c.c.) in the course of 5 hours. On isolation with ether

the resulting tetrahydrotubanol (2.7 g.) was purified by distillation in a vacuum, b. p. 155—160°/22 mm., and then by recrystallisation from light petroleum (b. p. 60—80°), forming colourless needles, m. p. 83—84°, undepressed by admixture with an authentic specimen (Found : C, 73.4; H, 8.9. Calc. for $C_{11}H_{16}O_2$: C, 73.3; H, 8.9%).

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