

99. *A Synthesis of Dihydrocarbostyryl and Homodihydrocarbostyryl by Ring Enlargement and a Synthesis of Tetrahydroquinoline.*

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SCHMIDT (*Ber.*, 1924, **57**, 704) has found that the action of hydrazoic acid on cyclohexanone in the presence of concentrated sulphuric acid yields ϵ -leucine lactam by the introduction of an imino-group next to the carbonyl group with consequent ring enlargement. The reaction has now been extended to cyclic ketones attached to the benzene nucleus, *viz.*, α -hydrindone and α -tetralone. The former gives dihydrocarbostyryl, m. p. 163°, in 68% yield, but none of the isomeric dihydroisocarbostyryl, m. p. 71°. 5:6-Methylenedioxy-1-hydrindone, however, failed to react with hydrazoic acid in the presence of concentrated sulphuric acid, syrupy phosphoric acid or acetic anhydride, owing doubtless to the decreased carbonyl activity produced by electromeric effect of the methylenedioxy-group. α -Tetralone likewise yielded homodihydrocarbostyryl, m. p. 141°, in 70% yield. Schroeter and co-workers (*Ber.*, 1930, **63**, 1308) obtained homodihydrocarbostyryl also from α -tetralone by a Beckmann transformation of the oxime, using *p*-toluenesulphonyl chloride. By hydrolysis of homodihydrocarbostyryl, γ -*o*-aminophenylbutyric acid was obtained, which by further treatment with hydrazoic acid and concentrated sulphuric acid gave γ -*o*-aminophenylpropylamine in 44% yield. The hydrochloride of the latter on dry distillation at atmospheric pressure gave a 50% yield of tetrahydroquinoline (*cf.* Ladenburg, *Ber.*, 1885, **18**, 3100; Helfer, *Helv. Chim. Acta*, 1923, **6**, 785).

In conformity with the position of the entering imino-group into α -hydrindone and α -tetralone, acetophenone on treatment with hydrazoic acid and concentrated sulphuric acid produces a 77% yield of acetanilide, no benzomethylamide being isolated.

EXPERIMENTAL.

Dihydrocarbostyryl.—A mixture of α -hydrindone (2 g.; 1 mol.) in benzene (20 c.c.) and concentrated sulphuric acid (4 c.c.) was stirred at 40°, and a 5% solution of hydrazoic acid (1.5 mols.) in benzene gradually added. When reaction had ceased, the sulphuric acid layer was poured into water, precipitating a whitish solid, the quantity of which was increased by neutralisation of the acid with ammonia; yield, 1.52 g. (68%). By a single crystallisation from alcohol (charcoal) pure dihydrocarbostyryl was obtained, m. p. 163°; Kipping (*J.*, 1894, **65**, 480) records m. p. 163°. From the benzene layer a very small amount of dihydrocarbostyryl was obtained but no dihydroisocarbostyryl.

Homodihydrocarbostyryl.—A solution of α -tetralone (20 g.; 1 mol.) and hydrazoic acid (1.25 mols.) in chloroform (140 c.c.) was stirred at 40°, and concentrated sulphuric acid (36 c.c.; 5 mols.) gradually added (1 hour). The acid layer was poured into water (900 c.c.), and the creamy solid, homodihydrocarbostyryl, crystallised from a large volume of hot water; m. p. 141°, yield 15.5 g. (70%). Von Braun (*Ber.*, 1907, **40**, 1843) and Schroeter and co-workers (*loc. cit.*) record m. p. 139–140°. The acid filtrate on neutralisation yielded a further small quantity of the same product.

Homodihydrocarbostyryl (14 g.) was hydrolysed almost quantitatively into the hydrochloride of γ -*o*-aminophenylbutyric acid, m. p. 201° (von Braun, *loc. cit.*), by heating with concentrated hydrochloric acid (175 c.c.). The free acid, m. p. 125°, was obtained (91% yield) by treating a solution of the hydrochloride in the minimum amount of water with a saturated aqueous solution of sodium acetate. Schroeter *et al.* (*loc. cit.*) give m. p. 125–126°.

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γ -o-Aminophenylpropylamine.—To a solution of γ -o-aminophenylbutyric acid (15 g.; 1 mol.) and hydrazoic acid (1.25 mols.) in chloroform (110 c.c.) at 40° was gradually added concentrated sulphuric acid (24 c.c.; 5 mols.). Reaction was less vigorous than in the previous cases and a further amount of concentrated sulphuric acid (10 c.c.; 2 mols.) was added, and the reaction allowed to proceed for 3.5 hours. The acid layer was poured into water (450 c.c.) and neutralised with concentrated sodium hydroxide solution. The mixture gave to ether a light yellow oil, b. p. 139–140°/19 mm., in 44% yield. Although the b. p. does not agree with that of γ -o-aminophenylpropylamine recorded by Kanevska, 165°/16 mm. (*J. pr. Chem.*, 1929, 124, 33), the m. p.'s of the dibenzoyl derivative, m. p. 157–158° (from alcohol), and the dihydrochloride, m. p. 231–232°, prepared in dry ethereal solution by passage of hydrogen chloride, show good agreement with those of Kanevska's preparations, m. p. 158–159° and m. p. 228–230° respectively.

Since γ -phenylpropylamine belongs to the type of sympathomimetic amines (cf. Barger and Dale, *J. Physiol.*, 1910, 41, 19; Hartung and Munch, *J. Amer. Chem. Soc.*, 1931, 53, 1875), a sample of the hydrochloride was submitted for physiological tests. We are indebted for these tests to Dr. M. Bell, Otago University, who has reported that small doses, injected intravenously, produce a slight rise, followed rapidly by a slight temporary fall, of blood pressure.

Tetrahydroquinoline.— γ -o-Aminophenylpropylamine dihydrochloride (3.5 g.) was rapidly heated in a small retort. White fumes (ammonium chloride), a brown oil, and a reddish-brown solid were the products of distillation. The distillate was boiled with sodium hydroxide solution to remove ammonia and cooled. The residue gave to ether a colourless oil, b. p. 139–141°/35 mm., in 50% yield, identified as tetrahydroquinoline by means of the benzoyl derivative, m. p. 74–75° (lit. m. p. 75°), and the hydrochloride, prepared as in the previous case, m. p. 180° (lit. m. p. 180–181°).

Acetanilide.—Acetophenone (5 g.), treated similarly to α -hydrindone above, gave 4.3 g. (77% yield) of acetanilide.

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