52. *A Synthesis of Dihydroindole, Dihydrothionaphthen, and Dihydrobenzofuran.*

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Simple methods are described by which the three heterocyclic substances named in the title may be obtained in good yield from β-phenylethyl alcohol through its *o*-amino-derivative.

Syntheses have been described of 2 : 3-dihydroindole (indoline), 2 : 3-dihydrothionaphthen, and 2 : 3-dihydrobenzofuran (coumaran) by various methods, yet no simple set of analogous syntheses of the three substances appears to have been recorded. Thus v. Braun and his collaborators (*Ber.*, 1925, **58**, 2165) obtained dihydrothionaphthen from *o*-amino-β-chloroethylbenzene and Ferber (*Ber.*, 1929, **62**, 183) converted the same substance into dihydroindole, but the synthesis of dihydrobenzofuran has proceeded from *o*-bromophenyl β-bromoethyl ether (Stoermer and Göhl, *Ber.*, 1903, **36**, 2873) or β-phenoxyethyl alcohol (Rindfusz, *J. Amer. Chem. Soc.*, 1919, **41**, 665; 1920, **42**, 157).

In the course of other work we have found that *o*-amino-β-phenylethyl alcohol can be readily converted into each of these three heterocyclic substances in good yield. Indoline is obtained by heating this base with hydrochloric acid and making alkaline, or directly by the action of benzenesulphonyl chloride on the amine in cold aqueous alkali; a solution of the base, diazotised and neutralised with sodium hydrogen carbonate, yields dihydrobenzofuran; and, finally, if a sulphur atom is introduced by the Leuckhardt process, the product is at once converted into dihydrothionaphthen when warmed with acid.

The great ease of the ring closure in these instances is not only the result of the obvious steric factor : there is also a specially enhanced reactivity of the hydroxyl group, a study of which will be described in another paper.

The ready formation of the indole ring from *o*-amino-β-phenylethyl alcohol and analogous compounds may, as Dr. H. A. Krebs has pointed out to us, indicate the way in which indole is formed from tryptophan by bacterial action, and one of us is studying the matter from this point of view.

Experimental.

Preparation of o-Amino-β-phenylethyl Alcohol.—The crude mixture of isomeric nitro-β-phenylethyl alcohols obtained by the method of Sabetay (*Bull. Soc. chim.*, 1931, **49**, 3; compare Ferber, *loc. cit.*) was freed from solvent, inoculated with the *p*-nitro-alcohol, and kept in the cold. The material which crystallised was filtered off and twice recrystallised from alcohol; it had m. p. 65° (Ferber gives 60—61°). The filtrate was a deep red oil, to which was added any further similar material recovered from the mother-liquors of the recrystallisation of the *p*-isomeride. This oil was separated into two fractions by distillation at low pressure with a spiral glass fractionating column : (I) b. p. 136°/2 mm. and (II) b. p. 136—145°/2 mm. The first distillate (III) obtained on redistillation of (I) was the pure *o*-nitro-β-phenylethyl alcohol, since the refractive index remained constant [$n_D^{25°}$ of crude mixture 1·5682; of (I) 1·5623; of (III) 1·5602, constant to ± 0·0002. Sabetay gives $n_D^{22°}$ 1·5620]. Further quantities of the *o*-isomeride were obtained by freezing out and redistilling the later fractions.

Reduction of the *o*-nitro-alcohol by Sabetay's method was improved by extracting the product from the concentrated solution with ether and then distilling it. The *o*-amino-alcohol is a colourless, viscous oil of b. p. 166—167°/12 mm. or 155° 5 mm. The *N*-acetyl derivative

crystallises from benzene in small prisms with a high double refraction, m. p. 101·5° (Found : C, 66·8; H, 7·2; N, 8·0. Calc. : C, 66·9; H, 7·3; N, 7·8%).

o-*Benzamido-β-phenylethyl alcohol* crystallises from alcohol in nearly rectangular plates with an oblique extinction, m. p. 168° (Found : C, 74·4; H, 5·9; N, 6·0. $C_{15}H_{15}O_2N$ requires C, 74·7; H, 6·2; N, 5·8%).

Synthesis of Indoline.—(a) *o*-Amino-β-phenylethyl alcohol, heated for 4 hours with concentrated hydrochloric acid (5 parts) at 130—140°, gave the hydrochloride of *o*-amino-β-phenylethyl chloride in almost quantitative yield, which crystallised in fine needles, m. p. 174°, from alcohol–ether (Found : C, 50·0; H, 5·7. Calc. : C, 50·0; H, 5·7%). v. Braun and Sobecki (*Ber.*, 1911, **44**, 2158) prepared this substance by the hydrolysis of its *N*-benzoyl derivative (from benzoylindoline by ring fission) but they gave its m. p. as 205°. This is the correct figure for the m. p. of the *p*-isomeride (v. Braun and Gawilow, *Ber.*, 1912, **45**, 1274) and was perhaps due to an error in transcription.

The hydrochloride was made alkaline with sodium hydroxide, the cyclic base distilled in steam and extracted from the distillate with ether, and the solution dried over sodium sulphate or sodium hydroxide and distilled. Indoline was thus obtained as a colourless oil, b. p. 230°, yielding a benzenesulphonyl derivative, m. p. 133° (Ferber gives 132°, *loc. cit.*). The p-*toluenesulphonyl* derivative crystallises from 75% alcohol in prisms with a high double refraction and a straight extinction, m. p. 99° (Found : C, 66·3; H, 5·5; N, 5·5; S, 11·9. $C_{15}H_{15}O_2NS$ requires C, 65·9; H, 5·5; N, 5·1; S, 11·7%). The *acetyl* derivative separates from alcohol in minute white needles with an oblique extinction, m. p. 105° (Found : C, 74·3; H, 6·8; N, 8·8. $C_{10}H_{11}ON$ requires C, 74·5; H, 6·8; N, 8·7%).

(b) *o*-Amino-β-phenylethyl alcohol (3·3 g.), dissolved in aqueous sodium hydroxide (50 c.c., 10%), was shaken for ½ hour with benzenesulphonyl chloride (3·3 c.c.). A trace of solid which separated was benzenesulphonylindoline. The free base in solution was removed in steam and collected from the distillate in ether, and the extract dried and distilled. Indoline was thus obtained in good yield, b. p. 230°, giving the benzenesulphonyl derivative, m. p. 133°.

Synthesis of 2 : 3-*Dihydrothionaphthen.*—*o*-Amino-β-phenylethyl alcohol (24 g.), dissolved in hydrochloric acid (45 c.c. of concentrated acid, 135 c.c. of water), was diazotised at 5° and slowly added to a stirred solution of potassium xanthate (45 g. in 80 c.c. of water) at 65—70°. After the mixture had been heated until evolution of gas had ceased, and cooled, the xanthic ester was removed in ether, and the solution evaporated. This ester was hydrolysed by cautiously adding potassium hydroxide (25 g. in 10 c.c. of water with 40 c.c. of alcohol); when the mixture had cooled, the alcohol was quickly distilled away in a current of nitrogen. The solution was then diluted, extracted once with ether to remove any material insoluble in alkali, acidified with dilute sulphuric acid, and heated on the water-bath for ½ hour. The crude dihydrothionaphthen separated as an oil and was removed in ether and distilled at 105—107°/13·5 mm. (Found : C, 69·1; H, 6·4; S, 23·9. Calc. : C, 70·6; H, 5·9; S, 23·5%). The yield of material, b. p. 233—234°, was almost quantitative. The mercurichloride had m. p. 127—128° (v. Braun gives 128—129°). Heating with an excess of hydrogen peroxide gave the sulphone, m. p. 98° (Found : C, 57·0; H, 4·7. Calc. : C, 57·1; H, 4·7%). When the oil was heated for 2 hours at 200—205° with half its weight of sulphur, and the mixture distilled in steam, thionaphthen was obtained as an oil, oxidised by hydrogen peroxide to the sulphone, m. p. 137—138° (Found : S, 19·1. Calc. : S, 19·3%).

Synthesis of 2 : 3-*Dihydrobenzofuran.*—*o*-Amino-β-phenylethyl alcohol (21 g.) was diazotised in sulphuric acid solution (15 c.c. of concentrated acid in 60 c.c. of water; 11 g. of sodium nitrite) and, when the reaction was complete, sodium hydrogen carbonate added in excess. The mixture was warmed until evolution of nitrogen had ceased; it was then made alkaline with sodium hydroxide, the product taken over in steam, and the distillate extracted with ether. The extract was washed with alkali and with water, dried, and distilled, dihydrobenzofuran being obtained, b. p. 84°/17 mm. or 188°/1 atm. (yield, 50%) (Found : C, 80·1; H, 6·5. Calc. : C, 80·0; H, 6·7%). The substance gave the characteristic violet coloration with ferric chloride and sulphuric acid. With cold saturated alcoholic picric acid it yielded a picrate, m. p. 76°, which lost dihydrobenzofuran on standing in the desiccator.

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