

CCCLVI.—*The Optically Active Diphenylhydroxyethylamines and isoHydrobenzoinis. Part V. β -Hydroxy- β -phenylethylamine and Some Derivatives.*

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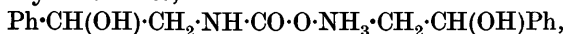
KOLSHORN (*Ber.*, 1904, **37**, 2483) showed that β -hydroxy- β -phenylethylamine was formed on reducing isonitrosoacetophenone, and more recently it has been obtained by Read and Reid (*J.*, 1928, 1487) in the course of an examination of the action of bromine water on styrene. From the work detailed below, it is evident that the latter reaction offers a convenient method for the preparation of the substance in quantity. Among the crystalline derivatives now described are the *d*-methylenecamphor derivative and the *d*-camphor-10-sulphonate, both of which are well-defined, partly racemic compounds. The *d*-base, obtained from the *dl*-base by fractionally crystallising the normal *d*-tartrate, reacts with methyl iodide to form a characteristic dextrorotatory quaternary ammonium iodide, m. p. 223—224°; this, in turn, reacts with silver oxide and water to yield a dextrorotatory oil, which appears to consist mainly of *d*-phenylethylene oxide, $\text{Ph}\cdot\underset{\text{O}}{\text{C}}\cdot\text{CH}\cdot\text{CH}_2$, or a polymeride thereof. The molecule of this substance is interesting as an example of a very simple cyclic structure containing a formally asymmetric carbon atom; the observed rotatory power, $[\alpha]_D + 28.9^\circ$ (alcohol), is less than one-tenth that of *trans*- $\alpha\beta$ -diphenylethylene oxide (this vol., p. 2383). Acetophenone was also formed in this reaction, and possibly some phenylethylene glycol; so that the smooth and almost quantitative conversion into the substituted ethylene oxide shown by the diphenylhydroxyethyltrimethylammonium iodides (*loc. cit.*) does not obtain in this instance. The action of nitrous acid on the *d*-base has not been examined.

EXPERIMENTAL.

dl- β -Hydroxy- β -phenylethylamine.—Styrene (40 g.) freshly prepared from cinnamic acid ("Organic Syntheses," 1928, **8**, 84) was converted into crude β -hydroxy- β -phenylethyl bromide (78.5 g.) by treatment with bromine water at about 90° (Read and Reid, *J.*, 1928, 1488). When shaken with concentrated aqueous ammonia (*loc. cit.*),* material (200 g.; $n_D^{17} 1.5800$) obtained in this way

* From the oily by-product formed in this reaction (Read and Reid, *loc. cit.*) we isolated, by partial distillation under diminished pressure, small amounts of crystalline styrene dibromide (m. p. 75°) and an unidentified base. These substances occurred in the residue, and the latter crystallised from alcohol in pale yellow, iridescent leaflets, m. p. 191—193° (Found: C, 82.2; H, 5.4;

yielded a syrupy base (35 g.); after remaining for several days in a desiccator, the syrup deposited long transparent needles, m. p. 44—45°, which appeared to consist of a mixture of *dl*- β -hydroxy- β -phenylethylcarbamate,



and the free base [Found: C, 65.5; H, 8.2. $\text{C}_{17}\text{H}_{22}\text{O}_4\text{N}_2$ requires C, 64.1; H, 7.0%. $\text{C}_8\text{H}_{11}\text{ON}$ requires C, 70.0; H, 8.1%. $(\text{C}_8\text{H}_{11}\text{ON})_2\cdot\text{H}_2\text{CO}_3$ requires C, 61.1; H, 7.1%]. The crystals gradually became opaque when exposed to the air, and after a week the melting point had risen to 115°. Carbon dioxide was liberated when acid was added to the crystalline preparations, vigorous effervescence occurring with specimens which had been left open to the air for several days. The hydrochloride (compare Beilstein's "Handbuch der organischen Chemie," 4th edn., XIII, 629), prepared from crystalline material of this kind, separated from acetone-ethyl acetate in needles, m. p. 213° (decomp.) (Found, by titration: Cl, 20.3. Calc. for $\text{C}_8\text{H}_{11}\text{ON}\cdot\text{HCl}$: Cl, 20.4%). The benzoyl derivative crystallised from alcohol in glistening leaflets, m. p. 148° (compare *Ber.*, 1904, 37, 2483; *J.*, 1928, 1489) (Found: C, 74.2; H, 6.2. Calc.: C, 74.6; H, 6.3%). The *benzylidene* derivative was deposited from alcohol in fine needles, m. p. 111—112° (Found: C, 79.5; H, 6.6. $\text{C}_{15}\text{H}_{15}\text{ON}$ requires C, 80.0; H, 6.7%).

dl- β -Hydroxy- β -phenylethylamino-*d*-methylenecamphor, when prepared and purified in the usual way, separated from ether-light petroleum in colourless needles, m. p. 106—108°, $\alpha_D + 4.85^\circ$, $[\alpha]_D + 230^\circ$ (*c* 1.0550, absolute alcohol)*; the rotatory power remained unaltered after six successive recrystallisations of the substance (Found: C, 76.0; H, 8.5. $\text{C}_{19}\text{H}_{25}\text{O}_2\text{N}$ requires C, 76.3; H, 8.3%). When dissolved in rectified spirit and treated with bromine, it reacted normally, yielding bromo-oxymethylenecamphor and the hydrobromide of the base; the latter was syrupy and optically inactive in aqueous solution.

dl- β -Hydroxy- β -phenylethylamine *d*-camphor-10-sulphonate crystallised from ethyl acetate in colourless needles, m. p. 125—126°, $\alpha_D + 0.29^\circ$, $[\alpha]_D + 14.3^\circ$, $[M]_D + 52.8^\circ$ (*c* 1.0090, water). The ro-

N, 11.8. $\text{C}_8\text{H}_7\text{N}$ requires C, 82.0; H, 6.0; N, 12.0%). A similar oily by-product from a specimen of styrene containing cinnamyl alcohol yielded another unidentified basic substance; this was insoluble in ether, and it separated from water in small colourless needles, m. p. 192° (Found: C, 59.7; H, 6.6; N, 15.2. $\text{C}_9\text{H}_{12}\text{O}_2\text{N}_2$ requires C, 60.0; H, 6.7; N, 15.6%). It may be noted here that the specimen of styrene used by Read and Reid, *b. p.* 80—83°, was distilled at 70 mm., and not at atmospheric pressure, as might be inferred from the footnote on p. 1488 (*loc. cit.*).

* In all these observations, *l* = 2, *c* = grams dissolved in 100 c.c. of solution, *t* = 15°, approximately.

tatory power of this salt remained unaltered throughout six fractional recrystallisations, and the base regenerated from the final fraction was optically inactive; the salt is therefore partly racemic (Found: C, 58.4; H, 7.4. $C_{18}H_{27}O_5NS$ requires C, 58.5; H, 7.4%).

Optical Resolution of dl- β -Hydroxy- β -phenylethylamine.—The hydrogen *d*-tartrate formed a thick syrup, which could not be induced to crystallise. Upon mixing hot alcoholic solutions of the syrupy *dl*-base (40 g.; 2 mols.) and *d*-tartaric acid (21.6 g.), a crystalline fraction of the normal *d*-tartrate (34.5 g.) was readily obtained, having $[\alpha]_D + 24.6^\circ$ (*c* 1.0, water). Four recrystallisations of this fraction from aqueous acetone yielded pure *d*- β -hydroxy- β -phenylethylamine *d*-tartrate in long silky needles, m. p. 210° , $\alpha_D + 0.89^\circ$, $[\alpha]_D + 46.1^\circ$, $[M]_D + 195^\circ$ (*c* 0.9650, water) (Found: C, 56.6; H, 6.6. $C_{20}H_{28}O_8N_2$ requires C, 56.6; H, 6.7%).

The *d*-base was liberated by adding strong aqueous potassium hydroxide to a concentrated aqueous solution of the above salt. The chloroform extract crystallised slowly after removal of the solvent, and the resulting long needles, after drying upon porous plate over potassium hydroxide in a vacuum desiccator, had m. p. 67° , $\alpha_D + 1.00^\circ$, $[\alpha]_D + 28.3^\circ$ (*c* 1.7655, absolute alcohol); analysis indicated that these crystals, like those of the *dl*-base (*vide supra*), consisted of carbamate mixed with the free base (Found: C, 65.4; H, 8.3%). The yield of *d*-base obtained from 120 g. of the syrupy *dl*-base was 12.2 g.

d- β -Hydroxy- β -phenylethyltrimethylammonium Iodide.—A solution of the above *d*-base (10 g.) in a little dry methyl alcohol was treated with methyl iodide and sodium methoxide in the manner described in an earlier paper (this vol., p. 2679). The quaternary ammonium iodide (80% yield) crystallised from hot water in long colourless needles, m. p. 223 – 224° , $\alpha_D + 0.15^\circ$, $[\alpha]_D + 4.5^\circ$ (*c* 1.6725, methyl alcohol) (Found, by titration: I, 41.1. $C_{11}H_{18}ONI$ requires I, 41.3%). When steam-distilled with freshly prepared silver oxide (20 g.), the iodide (15 g.) yielded only a small quantity (0.6 g.) of a volatile oil; since this had $n_D^{17.5} 1.5295$ and gave a semicarbazone, m. p. 193° , it contained acetophenone (*Ber.*, 1901, **34**, 1797; 1907, **40**, 482). The residual non-volatile oil was distilled from a bath at 200° under a pressure of 0.5–1.0 mm.; the distillate (3 g.) consisted of a brownish-yellow oil, with $n_D^{17.5} 1.5687$ and $[\alpha]_D + 24.9^\circ$ (*c* 2.5, absolute alcohol). Redistillation under similar conditions yielded a pale yellow, limpid oil (2 g.) with $n_D^{17.5} 1.5572$, $\alpha_D + 1.61^\circ$, $[\alpha]_D + 28.9^\circ$ (*c* 2.7790, absolute alcohol), and $\alpha_D + 2.32^\circ$, $[\alpha]_D + 36.4^\circ$ (*c* 3.1815, benzene) (Found: C, 77.2; H, 6.9. C_8H_8O requires C, 80.0; H, 6.7%. $C_8H_{10}O_2$ requires C, 69.5; H, 7.3%). The oil had a pronounced aromatic odour, and it was practically unaffected by

prolonged treatment with a hot concentrated solution of sodium bisulphite; thus, it appeared to consist mainly of *d*-phenylethylene oxide, or a polymeric form of this substance, possibly mixed with a little phenylethylene glycol (Found: *M*, by Rast's method, 182, 191. C_8H_8O requires *M*, 120. $C_8H_{10}O_2$ requires *M*, 138).

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