XCVIII.—*The Action of Amines on Semicarbazones.*
Part I. Preparation of an Optically Active
Semicarbazide.

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It has been shown by Borsche and his collaborators (*Ber.*, 1901, **34**, 4299; 1904, **37**, 3177; 1905, **38**, 831) that semicarbazones, such as acetonesemicarbazone, for example, react with aromatic amino-compounds on heating, mainly according to the scheme $\text{CMe}_2\text{N}\cdot\text{NH}\cdot\text{CO}\cdot\text{NH}_2 + \text{R}\cdot\text{NH}_2 = \text{CMe}_2\text{N}\cdot\text{NH}\cdot\text{CO}\cdot\text{NHR} + \text{NH}_3$, this product yielding on hydrolysis the semicarbazide $\text{NH}_2\cdot\text{NH}\cdot\text{CO}\cdot\text{NHR}$. The action of aniline, the toluidines, the naphthylamines, and similar amino-compounds was studied by Borsche, but the action of aliphatic amines or of aromatic amines containing the amino-group in a side chain does not appear to have been investigated.

It has been found that benzylamine reacts with acetonesemicarbazone in the normal manner, yielding *acetone- δ -benzylsemicarbazone*, $\text{CMe}_2\text{N}\cdot\text{NH}\cdot\text{CO}\cdot\text{NH}\cdot\text{CH}_2\text{Ph}$. Hydrolysis of this sub-

stance with dilute hydrochloric acid gave the *hydrochloride* of δ -benzylsemicarbazide, $\text{NH}_2\cdot\text{NH}\cdot\text{CO}\cdot\text{NH}\cdot\text{CH}_2\text{Ph}\cdot\text{HCl}$, from which the free *base* was liberated by means of sodium ethoxide. In aqueous solution, the hydrochloride reacted readily with benzaldehyde, giving *benzaldehyde- δ -benzylsemicarbazone*.

The action of α -phenylethylamine on acetonesemicarbazone was next studied. The racemic base was first employed and was found to react in the normal manner, the *hydrochloride* of racemic δ - α -phenylethylsemicarbazide, $\text{NH}_2\cdot\text{NH}\cdot\text{CO}\cdot\text{NH}\cdot\text{CHMePh}\cdot\text{HCl}$, being ultimately obtained. The reaction was then carried out with *d*- α -phenylethylamine; this with acetonesemicarbazone yielded a *semicarbazone*, $\text{CMe}_2\text{N}\cdot\text{NH}\cdot\text{CO}\cdot\text{NH}\cdot\text{CHMePh}$, which, when polarimetrically examined in alcoholic solution, gave $[\alpha]_D^{20} - 67.3^\circ$. This semicarbazone on hydrolysis with dilute hydrochloric acid gave the *hydrochloride* of an active δ - α -phenylethylsemicarbazide; this salt in aqueous solution gave $[\alpha]_D^{22} + 66.0^\circ$.

It is intended to apply this optically active semicarbazide to the resolution of certain racemic aldehydes and ketones. The only optically active semicarbazide hitherto described appears to be camphoryl- ψ -semicarbazide, which was prepared by Forster and Fierz (T., 1905, 87, 722). It is also hoped to investigate the action of active menthylamine and of esters of amino-acids on semicarbazones.

EXPERIMENTAL.

Action of Benzylamine on Acetonesemicarbazone.

Acetone- δ -benzylsemicarbazone.—When finely powdered acetonesemicarbazone (1 mol.) and benzylamine (slightly more than 1 mol.), heated separately at 180° , were mixed, vigorous reaction ensued and ammonia was evolved. As soon as solution had been effected, the mixture was cooled somewhat, poured into cold water, the viscid mass treated with dilute acetic acid in slight excess to remove unchanged benzylamine, and the product, which quickly solidified, washed with water and extracted with hot alcohol, which dissolved it with the exception of a slight residue of hydrazodicarbonamide. The alcoholic extract, concentrated if necessary and cooled with ice, deposited a small quantity of colourless needles melting at 168° ; these, after recrystallisation from alcohol and washing with carbon tetrachloride, melted at 169° and were identified as *s*-dibenzylcarbamide (m. p. 167°) (Found: N = 11.89 per cent.). The alcoholic extract, on further concentration, yielded long, colourless prisms which, after recrystallisation from alcohol, melted at 113° , were moderately soluble in water, soluble in hot alcohol, and extremely soluble in benzene. This substance

was *acetone- δ -benzylsemicarbazone* (Found : N = 20.35. $C_{11}H_{15}ON_3$ requires N = 20.48 per cent.). It dissolved to a colourless solution in concentrated sulphuric acid.

δ -Benzylsemicarbazide Hydrochloride.—The semicarbazone was heated at 50° with twelve times its weight of *N*-hydrochloric acid until solution was effected. The solution was then extracted with ether, and the aqueous portion evaporated to dryness in a vacuum on the water-bath. The white, flaky residue, consisting of the hydrochloride, recrystallised from alcohol, separated as a thick, felted mass of colourless needles easily soluble in water, soluble in alcohol, insoluble in ether. It melted at $224\text{--}225^\circ$ (Found : Cl = 17.46. $C_8H_{11}ON_3 \cdot HCl$ requires Cl = 17.62 per cent.).

Crude acetone- δ -benzylsemicarbazone containing *s*-dibenzylcarbamide may be conveniently used in this hydrolysis; *s*-dibenzylcarbamide, being sparingly soluble in water, can be easily separated from δ -benzylsemicarbazide hydrochloride.

δ -Benzylsemicarbazide.—To an absolute-alcoholic solution of the hydrochloride an alcoholic solution of sodium ethoxide was added until the solution was alkaline to phenolphthalein. The sodium chloride was filtered off and the filtrate evaporated to dryness at the ordinary temperature by means of a current of dry air free from carbon dioxide. The yellow residue was treated with hot toluene and the filtered extract cooled in ice, when *δ -benzylsemicarbazide* separated as a white powder consisting of small, needle-shaped crystals, which were washed with light petroleum and dried in a vacuum. The substance melted at 111° ; it was soluble in water, ether, or chloroform, very soluble in alcohol, soluble in hot benzene and in hot toluene, and insoluble in light petroleum. The aqueous solution is neutral (Found : N = 25.68, 25.64. $C_8H_{11}ON_3$ requires N = 25.45 per cent.). The *benzylidene* derivative was obtained by shaking an aqueous solution of the hydrochloride with a few drops of benzaldehyde and recrystallising the precipitate from alcohol; it separated in beautiful, large, lustrous prisms melting at 139° (Found : N = 16.77, 16.74. $C_{15}H_{15}ON_3$ requires N = 16.60 per cent.).

Action of α -Phenylethylamine on Acetonesemicarbazone.

The α -phenylethylamine was prepared by the reduction of acetophenoneoxime. It was found that the usual method of preparing this oxime (Janny, *Ber.*, 1882, **15**, 2781) could be very much shortened by adding from time to time potassium hydroxide to neutralise the acidity which appeared during the reaction; the oxime invariably separated as a solid and in practically pure

condition when the reaction mixture was poured into vigorously agitated ice-water.

r-Acetone- δ - α -phenylethylsemicarbazone.—This was prepared, in the same way as the acetone- δ -benzylsemicarbazone previously described, by adding α -phenylethylamine (1.5 mols.) heated at 180° to acetonesemicarbazone (1 mol.) at the same temperature. The mixture was cooled and acidified with dilute acetic acid after the addition of an equal volume of alcohol and a little ice. On diluting with water, a white precipitate appeared, which was collected, washed with water, and dissolved in the minimum quantity of hot alcohol, from which the semicarbazone separated in colourless prisms on cooling in ice. *Acetone- δ - α -phenylethylsemicarbazone* was very soluble in alcohol or benzene, and almost insoluble in light petroleum, and was best recrystallised from a mixture of benzene and light petroleum. It melted at 114° (Found : N = 19.04. $C_{12}H_{17}ON_3$ requires N = 19.17 per cent.).

r- δ - α -Phenylethylsemicarbazide Hydrochloride.—The semicarbazone was heated with about ten times its weight of *N*-hydrochloric acid in a boiling water-bath, and the solution, when cold, was extracted with ether, the aqueous portion being evaporated to dryness on the water-bath. The residue was recrystallised from absolute alcohol, from which the *hydrochloride* separated in small prisms melting at 165° with decomposition (Found : Cl = 16.47. $C_9H_{13}ON_3.HCl$ requires Cl = 16.47 per cent.).

These experiments were then repeated, using *d*- α -phenylethylamine. The base employed gave $[\alpha]_D^{25} + 40.8^\circ$.

Active Acetone- δ - α -phenylethylsemicarbazone.—The reaction was carried out in the same way as in the preparation of the racemic semicarbazone, and a similar plan was adopted in working up the product, which was finally recrystallised from light petroleum; a small, insoluble residue remained. The solution deposited beautiful, rhombic prisms of the semicarbazone, which, after recrystallisation, melted at 84° . Sometimes, after a crop of prisms had continued to grow for some time, the supernatant liquid suddenly became cloudy and a white, apparently amorphous precipitate gradually separated. In such a case, as soon as the cloudiness appeared, the supernatant solution was agitated and decanted, and the prisms were washed with a few c.c. of cold *N*-hydrochloric acid, which readily dissolved the amorphous precipitate. From the solution which had been decanted, the precipitate continued to separate for some time, but afterwards prisms again began to appear. At this stage gentle heat was applied, when the prisms redissolved much more readily than the precipitate, which was then filtered off. In this way a separation

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could be effected. The precipitate, after recrystallisation from benzene, melted with decomposition at 185° . The quantity was too small for investigation; the substance was possibly a derivative from carbamide.

The active *acetone- δ - α -phenylethylsemicarbazone* was extremely soluble in alcohol or benzene, and moderately soluble in light petroleum (Found: N = 19.57, 19.60. $C_{12}H_{17}ON_3$ requires N = 19.17 per cent.). It was lævorotatory in alcoholic solution: 0.7820 gram in 10 c.c. of alcohol gave $\alpha_D^{12} - 5.26^{\circ}$ ($l = 1$), whence $[\alpha]_D^{12} - 67.3^{\circ}$. Both the racemic and the active semicarbazones became bright red on addition of concentrated sulphuric acid and ultimately gave an orange-coloured solution.

Active δ - α -Phenylethylsemicarbazide Hydrochloride.—The active semicarbazone was heated on the water-bath with ten times its weight of *N*-hydrochloric acid, and the solution concentrated until crystals appeared. After cooling, these were collected, washed with a very little water, dried, and thoroughly washed with benzene. The *hydrochloride* formed beautiful, pearly plates melting with decomposition at 189° , was very soluble in water, soluble in alcohol, and insoluble in benzene (Found: Cl = 16.40. $C_9H_{13}ON_3.HCl$ requires Cl = 16.47 per cent.). It was dextro-rotatory in aqueous solution: 0.9766 gram in 10 c.c. of water gave $\alpha_D^{12.2} + 6.56^{\circ}$, whence $[\alpha]_D^{12.2} + 66.0^{\circ}$.

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