Liberation of an Amino Acid Derivative from its Copper Complex by means of Hydrogen Sulphide Generated *in situ* from Thioacetamide

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Thioacetamide, CH_3CSNH_2, may be smoothly hydrolysed to produce hydrogen sulphide[1], and generally allows easy domination of problems caused by the objectionable properties of the gas.

The use of thioacetamide for the detection of certain heavy metals was reported [2] in 1934, and during the last decade the reagent has been extensively used in inorganic analysis [3]. Compared with hydrogen sulphide [4], thioacetamide usually provides sulphide precipitates of superior coagulative properties.

When amino acids and derivatives are prepared or isolated *via* heavy metal compounds, the metal has hitherto been removed by means of hydrogen sulphide [5,6]. Heating is often necessary, and even in strongly acidic solution the reaction may take several hours, and frequently results in precipitates difficult to filter. It therefore appeared attractive to try thioacetamide in this field. The copper complex [7] of ε-benzoxycarbonyl-L-lysine was chosen as an example. In boiling water containing a little acetic acid, the precipitation of copper sulphide by means of thioacetamide was completed in a few minutes, and the precipitate was easily removed by filtration, with no visible colloidal sulphide passing the filter. The use of thioacetamide in similar cases is therefore indicated.

Experimental. Pulverized copper complex [7] (15.0 g) of ε-benzoxycarbonyl-L-lysine, prepared from 0.05 mole of L-lysine monohydrochloride with $[\alpha]_D^{25}$ + 24.5° ± 1.0° (6 N HCl, *c* 2, calc. as free base, *l* 1), was suspended in 350 ml of boiling water, and 20 ml of acetic acid added, immediately followed by 7.5 g (0.10 mole) of thioacetamide. The lysine derivative dissolved completely, and copper sulphide began to precipitate. After boiling 5 min the precipitate was filtered off on a hot Büchner funnel. ε-Benzoxycarbonyl-L-lysine crystallized immediately from the filtrate. After some hours at +4°, the crystals were collected, washed with a little cold water and dried *in vacuo* over potassium hydroxide. Yield 10.2 g (73 % calc. from L-lysine monohydrochloride), m.p. 252–254° (decomp.); $[\alpha]_D^{20}$ + 6.4° (2 N NaOH, *c* 6.6 *l* 1); reported [8] m.p. near 255°. (Found: N 9.8. Calc. for $C_{14}H_{20}O_4N_2$ (280.3): N 10.0).

To test the optical purity of the compound, 1.4 g (5 mmoles) were debenzoxycarbonylated in 5 ml of 12 N HCl (steam bath, 5 min.). Benzyl chloride separated, and when the reaction mixture had attained room temperature, 25 ml of ethanol and 50 ml of ether were added, causing 0.90 g (91 %) of L-lysine dihydrochloride to crystallize; $[\alpha]_D^{20}$ + 25.9° ± 1.5° (6 N HCl, *c* 1.3 calc. as free base, *l* 1). (Found: N 12.7. Calc. for $C_6H_{14}O_2N_2$, 2 HCl (219.1): N 12.8). Racemization is therefore not apparent.

The use of thiourea [9] or ethylenediaminotetraacetic acid (EDTA) for the removal of copper from the above complex has also been tried, with good preliminary results.

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