

CHEMOTHERAPY OF BACTERIAL INFECTIONS

Part VIII. Synthesis of Carboxylic Acid Derivatives of 2-Sulphanilamidothiazole

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IN Part V of this series,¹ many alkyl derivatives of 2-sulphanilamidothiazole were described. In continuation of this, herein is reported the synthesis of some typical carboxylic acid derivatives with the acid grouping attached directly or through alkyl radicals to the thiazole ring in the positions 4 or 5. The synthesis of such acid derivatives has another object also. The exhaustive studies carried out hitherto with the various sulphanilamide derivatives have led to a novel application of these drugs for purposes wherein only their *in vitro* bacteriostatic and bactericidal effects are of prime importance. For one of such purposes are required solutions of these drugs in concentrations of the order of 1 to 30% at about 0° C. with the pH of the solution being as near as possible to 7.4. In the cases of 2-sulphanilamidopyridine and 2-sulphanilamidothiazole, such concentrations are possible only with their sodium salts and the pH of these solutions is about 10 to 11. We anticipate the sodium salts of the acid derivatives described here to satisfy our requirements.

The sulphanilamido derivatives herein reported were all synthesised by the usual method of condensing the 2-aminothiazole derivative with acet-sulfanilylchloride and hydrolysing the resulting product. The hydrolysis was carried out in alcoholic hydrochloric acid or sodium hydroxide. When the conditions were more drastic, decarboxylation was also effected. For example, the hydrolysis of 2-acetsulphanilamido-4-methyl-5-carbethoxythiazole or 2-acetsulphanilamido-4-carbethoxymethylthiazole with about 5 N hydrochloric acid, yielded 2-sulphanilamido-4-methylthiazole. Similarly, 2-acetsulphanilamido-4-methyl-5-carbethoxymethylthiazole furnished 2-sulphanilamido-4:5-dimethylthiazole. We are adopting this method to synthesise some alkyl and other derivatives of 2-sulphanilamidothiazole, the preparation of which by the usual methods are more involved.

The starting aminothiazole derivatives are all known excepting ethyl 2-aminothiazole-5-carboxylate and ethyl α -(2-aminothiazolyl)caproate. The