STRUCTURE OF A NEW AMINO ACID ISOLATED FROM THE URINE OF HYPERCHOLESTEROLEMIC PATIENTS

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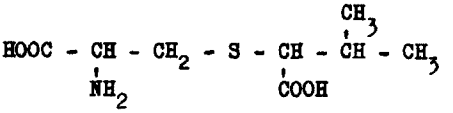
A new amino acid, which was isolated from the urine of hypercholesterolemic patients such as atherosclerosis and myxoedema, contained a cysteine residue and had the following molecular formula : $C_8H_{15}O_4NS$ (Mizuhara, et al., 1959; Mizuhara and Oomori, 1960).

The chemical structure of this new amino acid has now been established to be S-(isopropyl-carboxymethyl)-cysteine by synthesis.



This amino acid is now named "Isovalthine".

The synthesis was carried out as follows. α-Bromoisovaleric acid was prepared by a method described in Organic Synthesis (Coll. Vol., 3, 1955). A three-neck flask was immersed in a bath of dry ice-acetone. Under mechanical stirring, 3g. of cystine were added into the flask containing about 100ml. of liquid ammonia and 0.4g. of sodium was introduced in small portions. α-Bromoisovaleric acid (2.8g.) was then added into the flask drop by drop. After twenty minutes stirring the ammonia was allowed to evaporate. The residue was taken up in water and treated successively with columns of Amberlite CG-45 and Diaion SK-1 (cation exchanger, Mitsubishi

Kasei Co. Ltd.). The ammonia effluent from Diaion SK-1 was evaporated to dryness under vacuum. The residue was repeatedly recrystallized from 50% ethanol and about 1.5g. of rhombic plate were obtained.

In the mixed melting point test, the samples (synthetic, mixed and natural) in three capillaries decomposed at 213°C at the same time.

Anal. Calcd. for $C_8H_{15}O_4NS$: C, 43.43; H, 6.78.

Found : C, 43.79; H, 7.10.

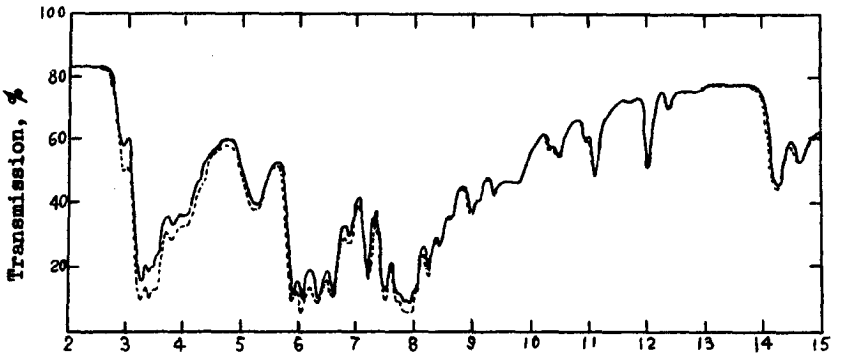
The synthetic compound ran on paper exactly as did the natural compound in the following solvent systems: But-Ac-H_2O (4 : 1 : 4 v/v) and Phenol-H_2O (4 : 1 v/v).

The infrared spectrum definitely shows the identity of the synthetic compound with the natural (Fig. 1).

Fig. 1. Infrared Spectrum of Isovalthine

——— Isolated Compound from Urine

- - - - - - - - - - - - Synthetic Compound



Several analogues including S-(1,1-dimethyl-2-carboxyethyl)-cysteine, etc. were synthesized but they were not identical with the natural compound in some respects such as Rf values and infrared spectra.

A more detailed report of this work will be published elsewhere.

We are obliged to Dr. T. Matsukawa, Takeda Res. Lab., for the elemental and infrared analyses.

References

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