THE STABILITY OF THE KETO ACID FROM METHIONINE[1]

Sir:

The metabolic path of most amino acids seems to be preponderantly through the corresponding keto acids. Hence a thorough knowledge of the behavior of these keto acids is essential for the understanding of amino acid metabolism. In a study of the mechanism of methylation processes in the animal organism we were interested, therefore, in the behavior of the keto acid from methionine. This amino acid is one of the few physiological substances which may yield methyl groups. According to the prevailing view methionine is demethylated to homocysteine during metabolism. We have obtained evidence by studying the behavior of the corresponding keto acid that a second reaction—splitting off of the —SCH_3 group—is also possible.

Since the keto acid from methionine has as yet not been synthesized, we prepared it biologically by the deamination of methionine in the presence of kidney slices according to the technique developed by Krebs.[2] A dinitrophenylhydrazone of the keto acid melting at 149° was obtained in about 20% yield.[3]

Anal. Calcd. for $C_{11}H_{12}O_6N_4S$: C, 40.24; H, 3.68; N, 17.07; S, 9.77. Found: C, 40.40; H, 3.81; N, 16.57; S, 9.80.

Solutions of methionine which had been similarly incubated with kidney slices were deproteinized and the filtrates containing the free keto acid and unchanged methionine were digested with acid and with alkali. Under both conditions methyl mercaptan was produced copiously. The liberated methyl mercaptan was identified by its yellow silver compound and by the melting point and analysis of the mercury mercaptide. In one experiment 400 mg. of *dl*-methionine was metabolized by kidney slices. After deproteinization the keto acid was determined in an aliquot of the solution as the dinitrophenylhydrazone (yield, calculated to the total sample, 210 mg. of the hydrazone). To another aliquot sufficient 10 *N* sodium hydroxide was added to make the solution 2 *N*. The solution was refluxed under nitrogen for one hour and the liberated mercaptan was absorbed in a solution of mercuric cyanide. Most of the methyl mercaptan was liberated during the first twenty minutes. The mercaptan weighed as mercury mercaptide corresponded to 72% of the keto acid in the solution (68 mg. $Hg(SCH_3)_2$). Since the original solution contained negligible amounts of mercaptan and as methionine does not yield mercaptan under these conditions, the reaction is ascribed to the decomposition of the keto acid. This finding may be explained on the basis of the instability of β-keto sulfides investigated by Nicolet.[4]

To establish the possible physiological significance of our findings we are continuing our studies with other sulfur-containing compounds.

(1) This work was made possible through a grant from the Friedsam Fund donated to the Division of Child Neurology, Neurological Institute, New York, N. Y.

(2) Krebs, *Z. physiol. Chem.*, **217**, 216 (1933).

(3) Bernheim, *J. Biol. Chem.*, **114**, 657 (1936), obtained a phenylhydrazone by incubating methionine with a kidney extract.

(4) B. H. Nicolet, THIS JOURNAL, **53**, 3066 (1931).

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RECEIVED JULY 19, 1939

THE VERATRINE ALKALOIDS. VI. THE OXIDATION OF CEVINE

Sir:

In previous work on the degradation of cevine, high temperature pyrolytic procedures (soda lime distillation or selenium dehydrogenation) have been rewarding in the search for degradation products. These, however, have been limited in number and their nature has made them difficult to relate to the parent substance with the exception of those derived from its basic portion. More recently it has been possible, for the first time, to achieve a crystalline oxidation product. Chromic acid in dilute sulfuric acid has given a mixture from which an acid fraction in good yield has been separated. This fraction, still a mixture, could not be directly crystallized. However, when heated to 180° evolution of carbon dioxide occurred, with production in good yield of a crystalline product which was non-nitrogenous (m. p. 273–278°), $[\alpha]^{25}D$ +47.6° (c = 0.925 in pyridine). Analysis indicated a formula $C_{14}H_{14}O_6$. Calculated: C, 60.41; H, 5.07. Found: C, 60.51; H, 5.20.

Diazomethane gave a product which crystallized readily from acetone (m. p. 165–166°). Analysis indicated 2 methoxyl groups. Calcd. for $C_{16}H_{18}O_6$: C, 62.75; H, 5.92; OCH_3, 20.26. Found: C, 62.96; H, 6.07; OCH_3, 19.90. The