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THE AMINATION OF FATTY ACIDS USING Cu(II)-AMMINE COMPLEX

Tsutomu KAMIYAMA, Masami INOUE, and Saburo ENOMOTO
Faculty of Pharmaceutical Sciences, University of Toyama,
Gofuku, Toyama 930

Fatty acids were coupled with ammonia to amino acids in the presence of Cu(II)-ammine complex. In aqueous solution, using ammonium acetate, the yield of glycine reached the maximum value of 15.8% after 3 hr at 140°C. The yield and the distribution of amino acids varied with fatty acids used.

One of the well known synthetical methods for amino acids is the dehalogenative amination of halogensubstituted fatty acids in the presence of ammonia.[1)]

From the biochemical interest, the transamination between α-amino acids and α-keto acids in the presence of Cu(II) is reported by Mix.[2)] However, the amination to fatty acids with ammonia by one step has not yet been reported. Authors have found that an oxidative dehydrogenation takes place between fatty acids and ammonia in the presence of certain metal salts. Especially Cu(II) shows a high activity for the formation of amino acids. The reaction is considered to proceed as follows.

$$RCH_2COOH + NH_3 \xrightarrow{Cu(II)} \underset{\displaystyle NH_2}{RCHCOOH} + H_2$$

In the typical experiment, an aqueous solution (25ml) of $[Cu(NH_3)_4]SO_4 \cdot H_2O$ (12.8g, 0.05mol) and ammonium acetate (3.9g, 0.05mol) were added in an autoclave (100ml) and then heated for 3 hr at 140°C in the presence of oxygen. Amino acids produced were analyzed by the dinitrophenylation method of paper chromatography.[3)]

Then the yield of glycine based on acetic acid reached 15.8%. The dependence of the yield on the reaction time is shown in Fig.1. No other amino acids was detected even after 10 hr. The yield of glycine reached the maximum value after 3 hr, and then the amino acid decomposes successively.

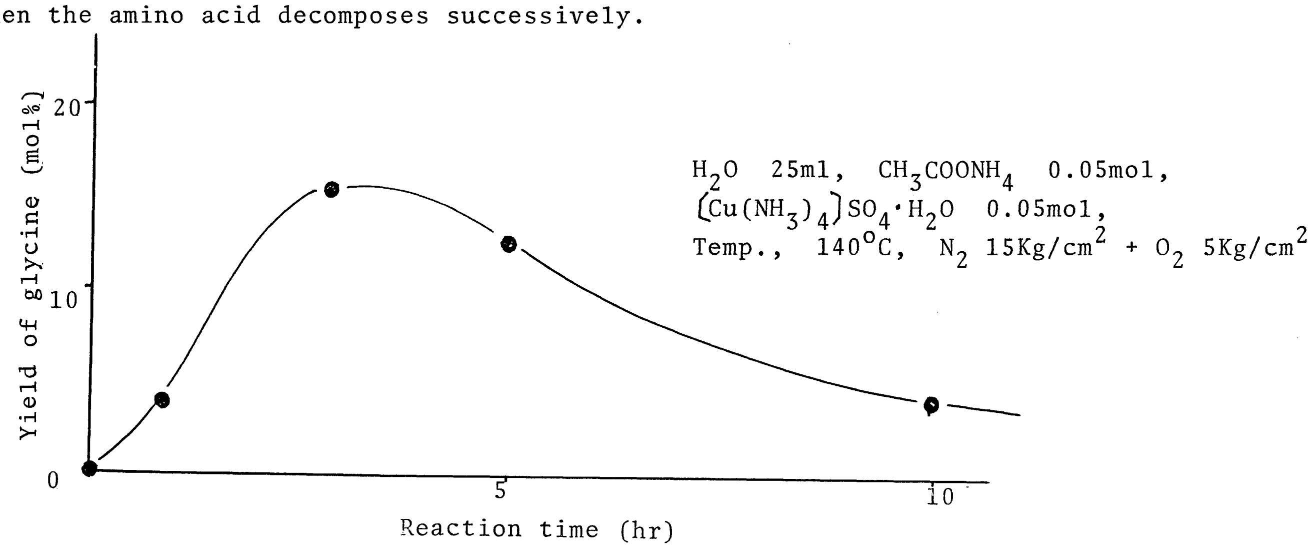

Fig. 1. The dependence of the yield on the reaction time.

In the similar manner, fatty acids such as propionic, n-butyric, 3-indolepropionic, 3-mercaptopropionic and succinic acids were also aminated as shown in Table 1.

Propionic acid produced alanine, β-aminopropionic acid and glycine, a decomposed by-product. From succinic acid, aspartic and β-aminopropionic acids were produced, where β-aminopropionic acid is considered to be formed by the decarboxylation of succinic acid since no β-aminopropionic acid was obtained on decomposition of aspartic acid.

In the amination of 3-mercaptopropionic acid, cysteine could not be obtained. It was noticed that elimination of substituted group took place.

Table 1. The amination of the various fatty acids using Cu(II)-ammine complex in aqueous solution

Fatty acids	Time (hr)	Temp. (^{o}C)	Cu/RCOOH (mol%)	Yield (mol%)	Distribution of Amino Acids (mol%)						
					Gly[a]	Ala[b]	APA[c]	Val[d]	ABA[e]	Asp[f]	Trp[g]
* CH_3COOH	3	140	100	15.8	100	0	0	0	0	0	0
C_2H_5COOH	3	140	50	6.0	8.4	60.5	31.1	0	0	0	0
n-C_3H_7COOH	3	180	50	3.5	8.0	0	5.1	0	86.9	0	0
iso-C_4H_9COOH	3	200	50	1.5	22.7	43.9	0	33.4	0	0	0
* $HSCH_2CH_2COOH$	12	120	50	25.7	0	0	93.8	0	0	6.2	0
*  CH_2CH_2COOH	3	180	50	6.4	0	12.5	21.1	0	0	0	66.4
* $HOOC(CH_2)_2COOH$	3	140	50	11.3	0	0	67.8	0	0	32.1	0

H_2O 25ml, RCH_2COONH_4 0.05mol, $[Cu(NH_3)_4]SO_4 \cdot H_2O$ 0.05mol, O_2 10Kg/cm^2.

* N_2 15Kg/cm^2 + O_2 5Kg/cm^2.

a) glycine b) alanine c) β-aminopropionic acid d) valine

e) α-aminobutyric acid f) aspartic acid g) tryptophan

Under a nitrogen atmosphere, Cu(II) was reduced to Cu metal and a poor yield was obtained. In contrast, when oxygen was charged, the reduction of Cu(II) was inhibited and the yield was improved. Furthermore, Cu(I) showed a negative result for the amination under a nitrogen atmosphere. So, Cu(II) is indispensable for this reaction.

When piperidine, a stronger base than ammonia, was added to the reaction system, the formation of amino acid was disturbed. On the basis of these facts, it is considered that fatty acids are aminated by the ammonia bound to copper.

References

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2) H.Mix, Z. Physiol. Chem., 315, 1 (1959).
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