The Direct Derivations of Some Amino Acids from Glycine

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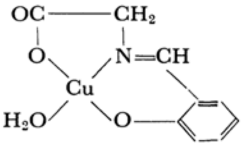
Akabori and his co-workers have synthesized threonine[1] from bis(glycinato)copper(II) and acetaldehyde in the presence of sodium carbonate, and have reasoned that the amino group would be protected by coordination, and sufficient activation of the methylene group would result from the polarizing effect of the metal atom. However, this method is not widely applicable for the derivation of many amino acids other than the β-hydroxy-α-amino acids, perhaps because of incomplete protection of the amino group or incomplete activation of the methylene group in the bis(glycinato)-copper(II).

Recently, we have succeeded in improving the above reaction by employing N-salicylideneglycinatoaquocopper(II)[2] (I) instead of bis(glycinato)-copper(II). The improvement of the reaction has also been made in solvent and activator by employing dimethylformamide and potassium hydroxide, respectively. Thus the reaction of the chelate I with methyl iodide has yielded α-alanine and, in the same way, the reaction of I with benzyl bromide has yielded phenylalanine. Valine, leucine, isolecuine and aspartic acid have also been prepared by the same method as described above. These are summarized in Table 1.



I. N-Salicylideneglycinatoaquocopper(II)

The identification and yield of the produced amino acids was successfully achieved by the use of an amino acid analyzer, for which sample solutions had been prepared by precipitating copper-(II) as copper(II) sulfide from the reaction systems. In case of phenylalanine, the isolation of its pure crystal was also attained; the infrared spectrum of the synthesized phenylalanine showed good agreement with that of the standard phenylalanine.

Though the present investigation is not sufficient to establish a new method of syntheses of amino acids, it would suggest a considerable possibility of deriving most of the amino acids from glycine; hence it might be useful in speculating the process of the build-up of the "*fore-protein*" in the so-called primitive age.[3,4]

TABLE 1. REACTIONS OF THE CHELATE I WITH HALIDES AT 65°C FOR THREE HOURS IN DIMETHYLFORMAMIDE

Halide	Ratio of I : halide : KOH	Amino acid obtained	Ratio of derived amino acid to unreacted glycine*
CH_3I	1 : 94 : 22	α-Alanine	1.13
$\begin{matrix}CH_3\\CH_3\end{matrix}\!>\!CH\text{-}Br$	1 : 124 : 29	Valine	0.11
$\begin{matrix}CH_3\\CH_3\end{matrix}\!>\!CH\text{-}CH_2\text{-}I$	1 : 102 : 31	Leucine	0.09
$\begin{matrix}CH_3\\CH_3\text{-}CH_2\end{matrix}\!>\!CH\text{-}Br$	1 : 100 : 30	Isoleucine	trace
$C_6H_5\text{-}CH_2Br$	1 : 98 : 6	Phenylalanine	0.75
$Br\text{-}CH_2\text{-}COOH$	1 : 10 : 51	Aspartic acid	0.41

* Determined by the use of a Yanagimoto LC-5 Amino Acid Analyzer according to the usual direction.

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1) M. Sato, K. Okawa and S. Akabori, This Bulletin, **30**, 937 (1957).

2) A. Nakahara, *ibid.*, **32**, 1195 (1959).

3) S. Akabori, K. Okawa and M. Sato, *ibid.*, **29**, 608 (1956).

4) S. Akabori, The Proceedings of the 16th General Assembly of the Japan Medical Congress, April 1963, Osaka.