TRANSFORMATION OF SOME HYDROXY AMINO ACIDS
TO OTHER AMINO ACIDS

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Abstract. It has been observed that β-hydroxy-α-amino acids are transformed into other amino acids, when heated in dilute solutions with phosphorous acid, phosphoric acid or their ammonium salts. It has been shown that as in the case of previously reported glycine-aldehyde reactions, glycine also reacts with acetone to give β-hydroxyvaline under prebiologically feasible conditions. It is suggested, therefore, that the formation of β-hydroxy-α-amino acids and their transformation to other amino acids may have been a pathway for the synthesis of amino acids under primitive earth conditions.

1. Introduction

The formation of serine and threonine by the reaction of formaldehyde and acetaldehyde respectively with a glycine-copper complex has been described by various authors (Akabori et al., 1959; Otani and Winitz, 1960; Sato et al., 1957; Kutani et al., 1959). Likewise, the synthesis of some other aliphatic β-hydroxy-α-amino acids, by the reaction of appropriate aldehydes and ketones with a glycine-copper complex has been reported by Herman Mix (1962). However, β-phenylserine could be obtained more simply, by the reaction of benzaldehyde with glycine in alkaline solution (Shaw and Fox, 1953). Recently, we have shown that these β-hydroxy-α-amino acids are also formed when glycine and appropriate aldehydes are heated in dilute ammoniacal solutions (Subbaraman et al., 1972). It was observed that if higher temperatures were used, or phosphorous acid, phosphoric acid and their salts were present in the reaction mixture, alanine was formed along with serine. Likewise, with threonine, α-amino-butyric acid was obtained. It was, therefore, likely that in the presence of acids or their salts, reduced or alkyl amino acids were being formed. Since phosphorous acid, phosphoric acid and their salts have prebiotic relevance, these were used in the present studies.

The formation of corresponding alkyl amino acids by heating these β-hydroxy-α-amino acids with phosphorous acid, phosphoric acid or their ammonium salts is reported in this paper. The possible significance of these reactions in chemical evolution is also considered.

2. Materials and Methods

Serine and threonine used in the present work were supplied by Sigma Chemical Co., U.S.A. β-Phenylserine (Shaw and Fox, 1953) and β-hydroxyvaline (Mix, 1962) were prepared by the methods reported in the literature. Phosphoric acid was obtained from Reidel De Halen Ag., and phosphorous acid was prepared according to the
procedure of Voight and Gallais (1953). Diammonium hydrogen phosphate was procured from E. Merck, Germany.

A Beckman Unichrom Amino Acid Analyzer was used for ion exchange chromatography of the amino acids formed in the reactions. Gas chromatography was carried out on Toshniwal Gas Chromatograph Type RL04, supplied by Toshniwal Bros., India. Labelled amino acids (\(-1\text{-}^{14}\text{C}\)) were made available by the Isotope Division of Bhabha Atomic Research Centre. The NMR spectra were recorded on a Varian A60A Spectrometer.

The experimental conditions are summarized in the tables. In a typical experiment, an aqueous solution of the hydroxy amino acid and phosphorous acid, phosphoric acid or the corresponding ammonium salt was heated in a sealed tube at the desired temperature, for an appropriate length of time.

An aliquot of the reaction mixture was taken in citrate buffer and analyzed by ion exchange chromatography (IEC). Another aliquot was examined by two dimensional paper chromatography (descending, Whatman No. 1) using n-butanol-acetic acid-water (100:22:50) and phenol-water-16N NH\(_4\)OH (80:20:1) as the solvent system. For further support of the tentative identifications made by the above procedures, co-chromatography on the analyzer column with standard amino acids was employed. For co-chromatography on paper, the individual spots from a preparative paper chromatogram were eluted with 2\% acetic acid, mixed with the appropriate standard compounds and rechromatographed. The solvent systems used in the two directions were (1) n-propanol-ethanol-water (70:20:10) and (2) pyridine-water (65:35).

For the identification of alanine, valine and phenylalanine, appropriate radioactive amino acid tracers (alanine-\(1\text{-}^{14}\text{C}\), valine-\(1\text{-}^{14}\text{C}\) and phenylalanine-\(1\text{-}^{14}\text{C}\) respectively) were added to the eluted material before rechromatography. The compounds were then identified by the coincidence technique of chromatography-autoradiography (Ponnamperuma et al., 1964; Choughuley and Lemmon, 1966).

Gas chromatography was employed for further characterization of the products. The TAB (N-trifluoroacetyl-n-butyl ester) derivatives of the amino acids from the reaction mixture as well as of individual amino acids of interest were prepared by the method of Roach and Gehrke (1969). The columns used were SE-30 (6' \(\times\) 0.25", 5\% on 80/100 mesh, DMCS treated chromosorb G, glass) and EGS (6' \(\times\) 0.85", 1\% on 80/100 mesh, DMCS treated chromosorb G, stainless steel).

The retention times of the amino acid derivatives from the reaction mixture were the same as those of the expected individual amino acids. Co-chromatography with the derivatives of expected amino acids gave enhanced peaks in each case, thus confirming the homogeneity of the amino acids.

The conversion of the CH\(_2\)OH group of serine or the -CH(OH) group of threonine to corresponding -CH\(_3\) or -CH\(_2\)- groups to give alanine and \(\alpha\)-aminobutyric acid (\(\alpha\)-ABA), respectively, was also confirmed by comparison of the NMR data:

Alanine (experimental as well as standard sample): \(\delta(D_2O)\), 1.48 (d, 3H, -CH-CH\(_3\)), 3.78 (q, 1H, -CH-CH\(_3\)), 4.63 (HDO).