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FORMATION OF AMINO ACIDS FROM ALIPHATIC AMINES BY CONTACT GLOW DISCHARGE ELECTROLYSIS

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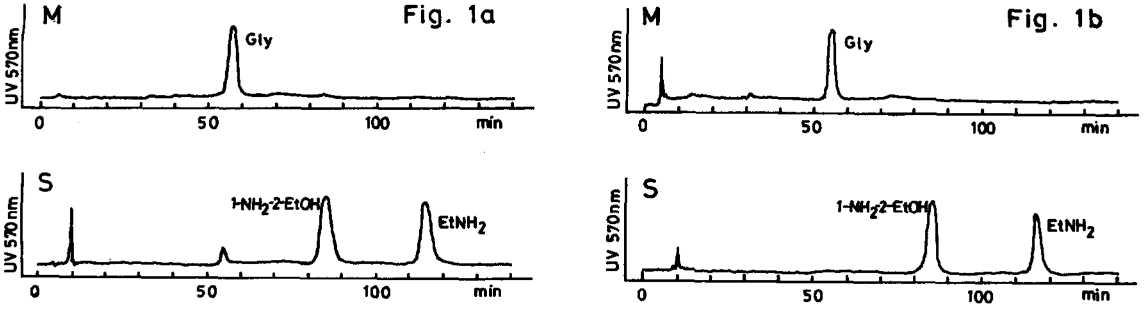
ABSTRACT. Oxidation of aliphatic amines in an aqueous solution by contact glow discharge electrolysis resulted in the formation of several amino acids, which was explained by the oxidative action of a hydroxyl radical generated by the electric discharge process to the aqueous solution.

Contact glow discharge electrolysis (CGDE) is a type of chemical reaction carreid out by means of an electric discharge between an aqueous solution containing a substrate and an electrode in contact with the solution$^{1)}$. Several applications of the CGDE to bioorganic compounds were carried out$^{2-8)}$. In the previous study, a possible reaction pathway of the oxidative degradation of β- and γ-amino acids by CGDE was proposed$^{8)}$. The oxidative degradation of several hydroxy amino acids was also studied$^{7)}$. These results suggest that hydroxyl radicals produced by CGDE are the key oxidizing agent, and that the CGDE could oxidize even methylene groups in the substrate.

In order to further clarify the methyl or methylene group oxidation, aliphatic amines [ethylamine ($EtNH_2$), n-propylamine (n-$PrNH_2$)] in aqueous solution were employed for CGDE. An aqueous solution (20 ml) of an amine (1 mmol) in acidic (pH 2.7-2.8) or basic (pH 12.0-12.1) condition was used for CGDE. The reaction temperature was kept at 10-20 °C by cooling the reaction mixture in a methanol - dry ice bath. The applied electric current was 30 mA at 500-600 V. The reaction mixture was diluted appropriately and the resulting amino acids were analyzed by an amino acid analyzer (Yanagimoto LC-5S). A part of the product was converted to dinitrophenyl (DNP) amino acids by treatment with 2,4-dinitrofluorobenzene. The resulting DNP-amino acids were separated and identified by thin layer chromatography (silica gel) by comparing the R_f values with those of the authentic DNP-amino acids which were prepared separately.

Fig. 1 and 2 show the amino acid analysis of the oxidation product of $EtNH_2$, and the time course of the products by CGDE. In the amino acid analysis, three compounds were found as the major peaks both in acidic (pH 2.8) and in basic (pH 12.1) conditions. These were glycine (Gly), 1-amino-2-ethanol (1-NH_2-2-EtOH), and $EtNH_2$. The yield of Gly and 1-NH_2-2-EtOH in acidic conditions are much higher than those in basic conditions. The finding agree with the results obtained in the carboxylation reaction of aliphatic amines$^{3)}$. In the time course



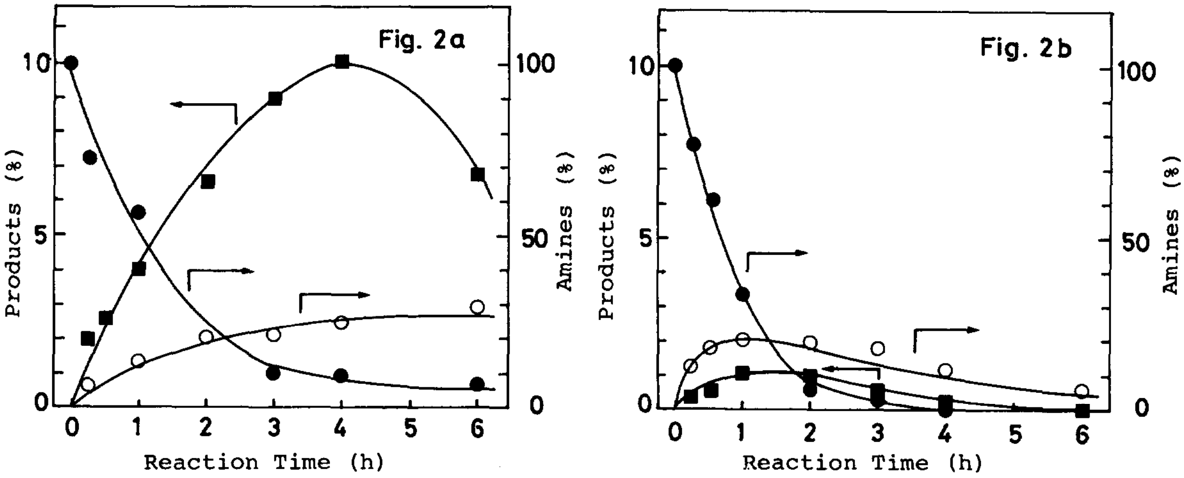
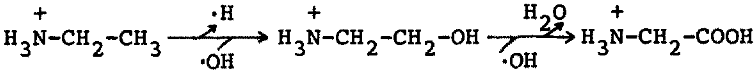


Fig. 1a, 1b. The amino acid analysis of oxidation products of $EtNH_2$ by CGDE at 60 min reaction. Upper chromatogram was analyzed by using the 30 x 0.8 cm^{ϕ} column (M), eluted by pH 3.25 citrate buffer (0-42 min) and pH 4.25 (42-140 min). Lower was analyzed by using 15 x 0.8 cm^{ϕ} column (S), eluted by pH 4.25 citrate buffer.

Fig. 2a, 2b. The time course of the products of $EtNH_2$ by CGDE. 2a : pH 2.8, 2b : pH 12.1, ● $EtNH_2$, ○ 1-NH_2-2-EtOH, ■ Gly.

of the reaction products in acidic conditions, $EtNH_2$ decreased rapidly depending on the reaction time. After 4 h, only 10 % of $EtNH_2$ remained in the reaction mixture and the yield of Gly increased to about 10 %. The yield of 1-NH_2-2-EtOH increased steadily and it reached to about 25 % after 4 h. These results indicate the following stepwise oxidation of $EtNH_2$ to Gly by hydroxyl radical in the aqueous reaction mixture (Scheme 1). On the other hand, in basic conditions (pH 12.1, Fig. 2b), $EtNH_2$ decreased more rapidly than in acidic conditions (pH 2.8, Fig. 2a). The yield of 1-NH_2-2-EtOH and Gly were both low, and the yield of Gly was only about 1 % after 1 h. These results indicate that the amino group and

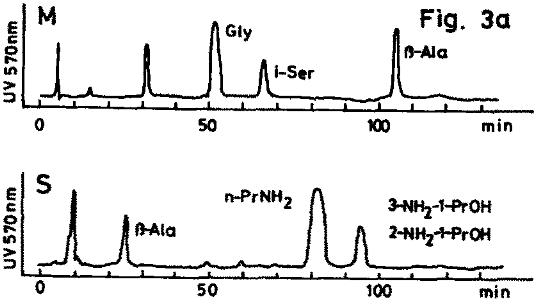


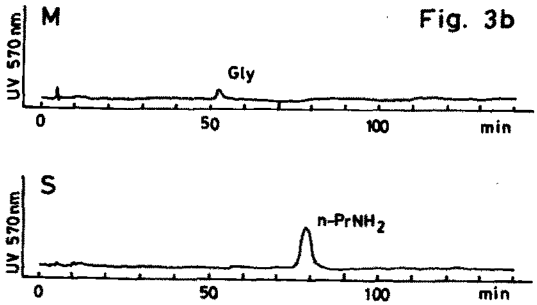
$$H_3\overset{+}{N}-CH_2-CH_3 \xrightarrow[\cdot OH]{\cdot H} H_3\overset{+}{N}-CH_2-CH_2-OH \xrightarrow[\cdot OH]{H_2O} H_3\overset{+}{N}-CH_2-COOH$$

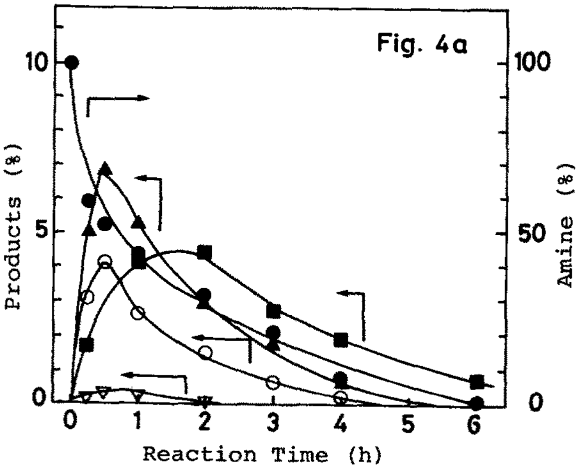
Scheme 1

the α-carbon atom would be oxidized in basic conditions.

Fig. 3a and 3b show the amino acid analysis of the oxidation products of n-propylamine (n-PrNH$_2$), and Fig. 4a and 4b show the time course of the products by CGDE. In the amino acid analysis, three amino acids and three amines were identified in the reaction product in acidic conditions. These are β-alanine (β-Ala), isoserine (i-Ser), Gly, n-PrNH$_2$, 2-NH$_2$-1-PrOH, and 3-NH$_2$-1-PrOH. The peaks of the last two amino alcohols in the amino acid analysis are too close to be separated completely. The time course of the reaction in acidic conditions indicates that the amino alcohols are the primary oxidized products which are further oxidized by CGDE. The formation of i-Ser and Gly could be explained as shown in the







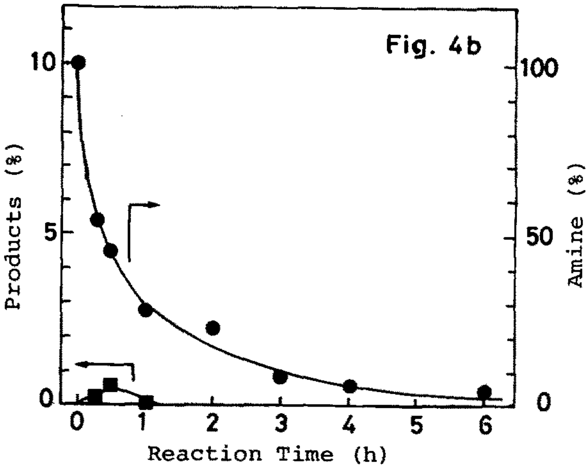
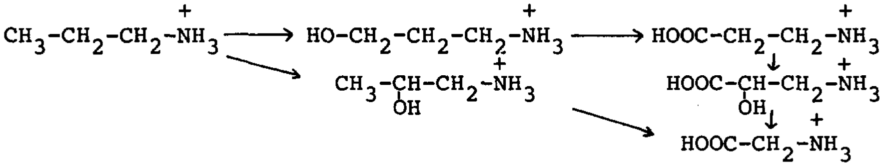


Fig. 3a, 3b. The amino acid analysis of oxidation products of n-PrNH$_2$ by CGDE at 60 min reaction.

Fig. 4a, 4b. The time course of the products of n-PrNH$_2$ by CGDE. 4a : pH 2.7, 4b : pH 12.0, ● n-PrNH$_2$, ○ 2-NH$_2$-1-PrOH + 3-NH$_2$-1-PrOH, ▲ β-Ala, ▽ i-Ser, ■ Gly.

oxidative degradation of β-Ala[8]. The stepwise oxidative process of n-$PrNH_2$ could be shown as in Scheme 2. Most of the major peaks in the amino acid analysis of the reaction products are thus assinged and confirmed. In basic conditions (pH 12.0), n-$PrNH_2$ decreases more rapidly than in acidic conditions. The yield of amino acids in the reaction mixture is low and only less than 1 % of Gly was identified after 30 min, and no other amino acid formation was observed. These results indicate also that amino group and α-carbon atom would be oxidized easily in basic conditions.



Scheme 2

The difference of the two oxidation reactions in acidic and in basic conditions could be explained by the charged and uncharged nitrogen atom of the substrates. In acidic conditions (pH 2.8), the amino group is almost completely protonated, and the charged nitrogen atom attracts electrons strongly. Therefore, the electron density of the α-carbon atom becomes low and the hydroxyl radical, which has electrophilic property, abstracts hydrogen from β- and γ-carbon. The resulting β- and γ-radicals react easily with the hydroxyl radical to form amino alcohols. These amino alcohols are further oxidized stepwise by the hydroxyl radical to form Gly as shown in Scheme 1 and 2. In other words, the amino group and the α-carbon atom of the substrate are protected from oxidation by CGDE because of the charged ammonium ion. On the other hand, in basic conditions, there is no such protecting mechanism and the amino group and the α-carbon atom are both oxidized by CGDE. Therefore, the formation of amino acids by CGDE is considerably smaller in basic conditions.

The oxidative degradation of aliphatic amines by CGDE resulted in the formation of several amino acids, which was explained by the stepwise oxidative process with the hydroxyl radical produced by electric discharge. The study also shows an additional example of a clean and powerful oxidation process by CGDE without using any oxidizing agent.

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