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OXIDATIVE DEGRADATION OF HYDROXY AMINO ACIDS BY CONTACT GLOW DISCHARGE ELECTROLYSIS

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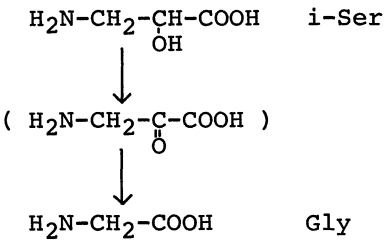
Oxidative degradation of several hydroxy amino acids was carried out in order to confirm the reaction pathway of the oxidative degradation of β- and γ-amino acids by contact glow discharge electrolysis. The results indicate that the reaction products from hydroxy amino acids support the hypothesis that the oxidative degradation of β- and γ-amino acids pass through hydroxy amino acids.

Contact glow discharge electrolysis (CGDE) is a type of chemical reaction carried 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[2-9]. In the previous study, the carboxylation reaction of protonated aliphatic amines by CGDE results in the formation of β- and γ-carboxylated products[8]. This indicates that the radical formation takes place at β- and γ-positions. Therefore, the formation of β- and γ-hydroxy aliphatic amines would be expected, when the CGDE was applied in an aqueous solution. In the oxidative degradation of β- and γ-amino acids by CGDE, the formation of several hydroxy amino acids was observed and all of the degradation products were explained by the oxidative degradation of the hydroxylated products[9].

In order to further clarify the reaction pathway of the oxidative degradation of β- and γ-amino acids, several hydroxy amino acids in aqueous solutions were employed for CGDE. Some representative results are shown below. The hydroxy amino acids used are isoserine (i-Ser), γ-amino-β-hydroxybutyric acid (γ-NH_2-β-OH-BA), serine (Ser), β-amino-α-hydroxyisobutyric acid (β-NH_2-α-OH-IBA), β-amino-α-hydroxybutyric acid (β-NH_2-α-OH-BA), γ-amino-α-hydroxybutyric acid (γ-NH_2-α-OH-BA), and homoserine (h-Ser). An aqueous solution (20 ml) of an amino acid (1 mmol) was applied to 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 50 - 60 mA at 500 - 600 V. The amino acids formed by CGDE were analyzed by an amino acid analyzer (Yanagimoto LC-5S) after the reaction mixture was diluted appropriately. A part of the product was treated with 2,4-dinitrofluorobenzene, and the resulting dinitrophenyl (DNP) amino acids were separated by Celite column chromatography. The DNP-amino acids were further identified by thin layer chromatography (silica gel) by comparing the R_f values with those of the authentic DNP-amino acids. All of the amino acids found in the products were prepared separately and the chromatographic properties (retention time in amino acid analyzer, R_f value

of DNP-amino acid) were compared with those of the amino acids in the products.

Fig. 1 shows the time course of the oxidative degradation of i-Ser. The sole degradation product of the amino acid is glycine (Gly). The yield of Gly increases steadily and reaches to a maximum (about 50%) after 1.5 h. The high yield of Gly formation suggests the formation of the intermediately oxidized β-amino pyruvic acid and the compound could be further oxidized to form Gly.



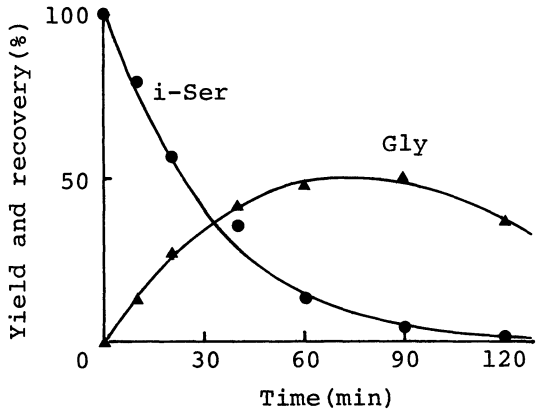
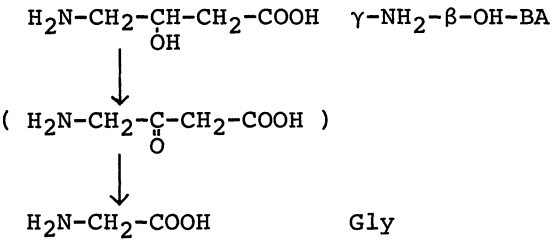


Fig. 1. Oxidation of i-Ser by CGDE

Fig. 2 shows the time course of the oxidative degradation of γ-NH_2-β-OH-BA. The only product of the amino acid is Gly. The formation of Gly was also explained by the oxidation of the β-carbon atom of γ-NH_2-β-OH-BA to form γ-amino-β-keto acid, and the compound could be further oxidized to form Gly.



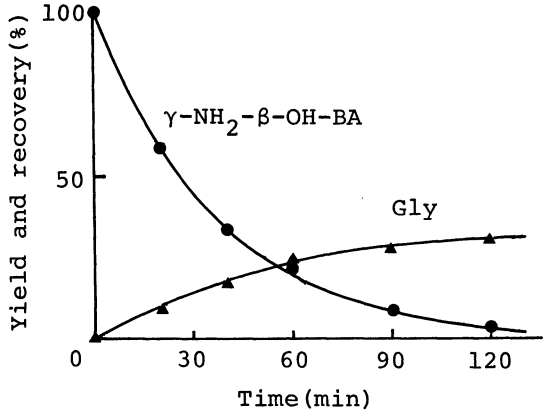
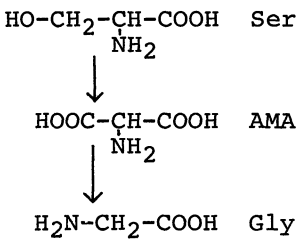


Fig. 2. Oxidation of γ-NH_2-β-OH-BA by CGDE

Fig. 3 shows the time course of the oxidative degradation of Ser. The time course shows that amino malonic acid (AMA) is the primary oxidation product and the AMA was converted to Gly by CGDE.



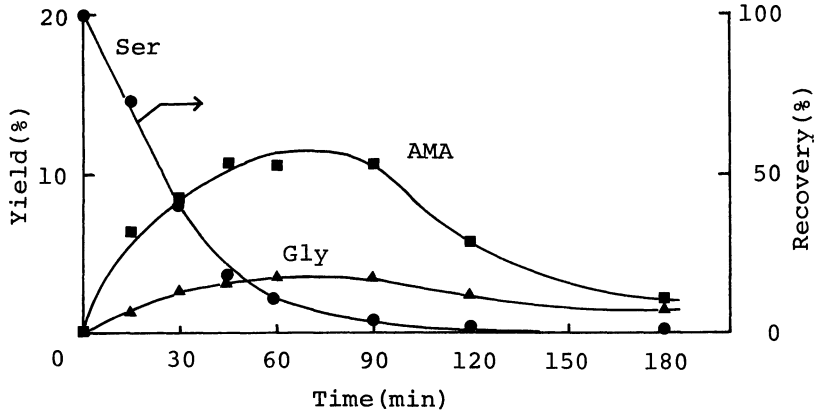


Fig. 3. Oxidation of Ser by CGDE

Fig. 4 shows the time course of the oxidation reaction of β-NH_2-α-OH-IBA. In the reaction, Gly is also the major oxidation product. In the previous study, it was found that the oxidation of α-methyl-β-alanine (α-Me-β-Ala) resulted in the formation of Gly in a 14% yield. During the course of the oxidation reaction of α-Me-β-Ala, β-NH_2-α-OH-IBA would be formed as an intermediate. The results of the oxidation of β-NH_2-α-OH-IBA support the possible route of the oxidation reaction of α-Me-β-Ala.

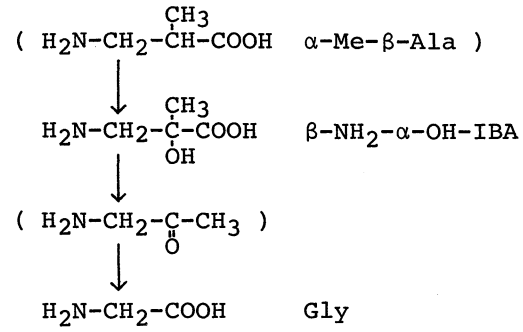


Fig. 4. Oxidation of β-NH_2-α-OH-IBA by CGDE

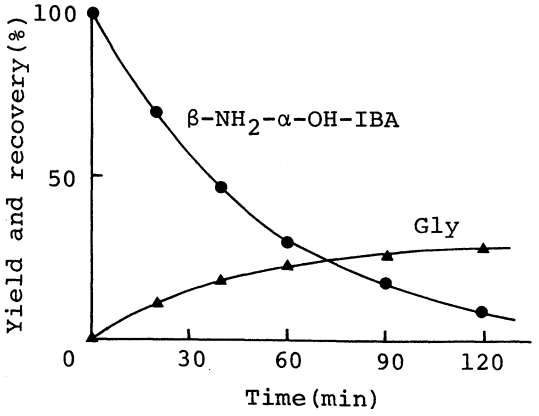


Fig. 5 shows the time course of the oxidative degradation of β-NH_2-α-OH-BA by CGDE. The primary oxidized product is Ala, and a small amount of Ser formation by further oxidation was observed.

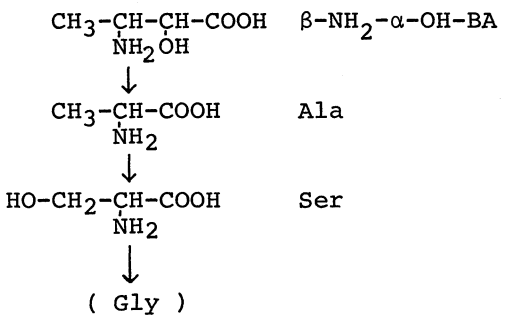


Fig. 5. Oxidation of β-NH_2-α-OH-BA by CGDE

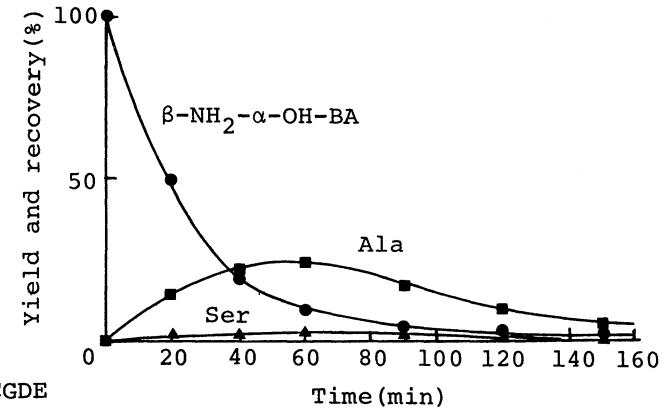


Fig. 6 shows the time course of the oxidation of γ-NH_2-α-OH-BA by CGDE. The time course shows that the primary product is β-Ala and the β-Ala is oxidized stepwise to i-Ser and then to Gly as reported earlier[9].

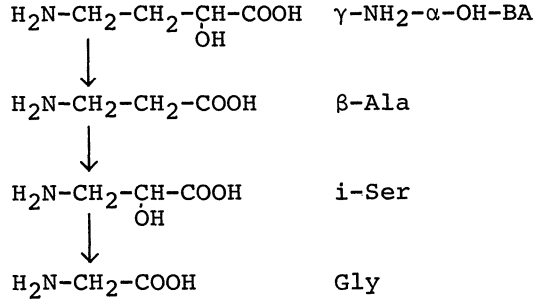


Fig. 6. Oxidation of γ-NH_2-α-OH-BA by CGDE

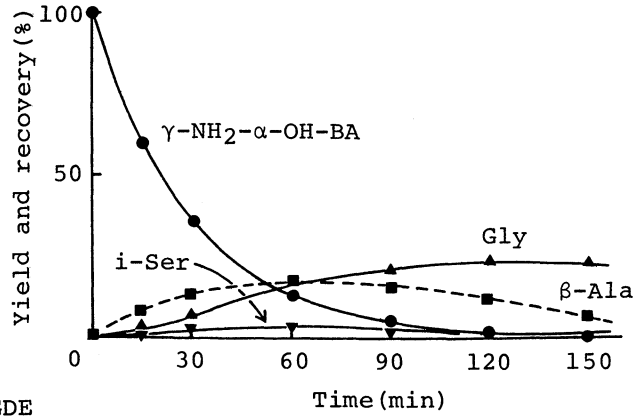


Fig. 7 shows the time course of the oxidative degradation of h-Ser. The primary product of oxidation is aspartic acid (Asp). The Asp is oxidized to hydroxy aspartic acid (OH-Asp) and the OH-Asp is further oxidized to AMA and then to Gly. The time course of the oxidative degradation of h-Ser clearly shows the stepwise oxidative degradation of h-Ser to Gly.

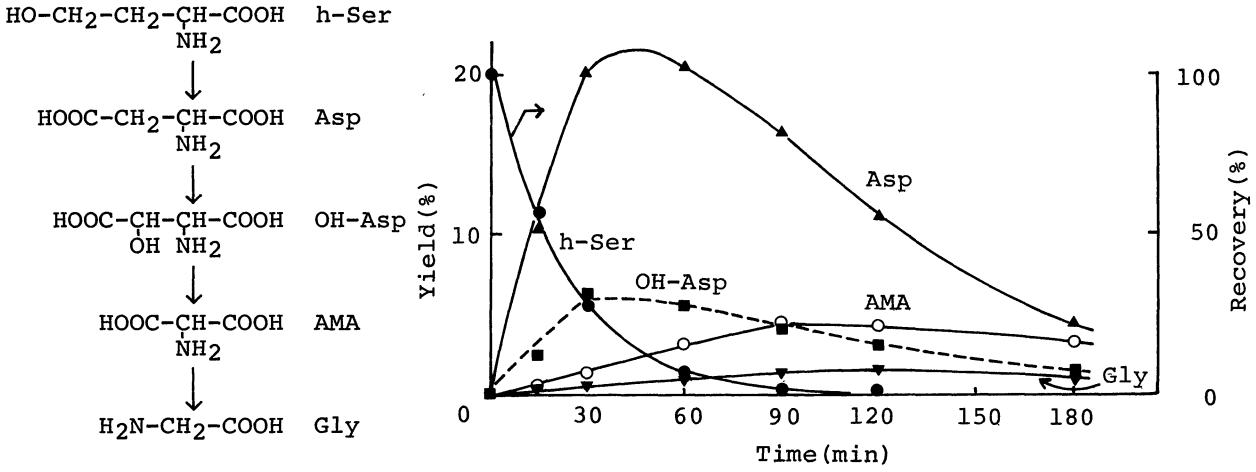
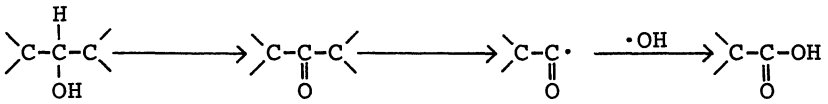


Fig. 7. Oxidation of h-Ser by CGDE

The oxidative degradation of several hydroxy amino acids by CGDE indicates that the oxidation reaction takes place at the carbon atom combined with the hydroxyl group. The oxidative degradation takes place stepwise as shown below.



The carbon-carbon bond is cleaved and hydroxy amino acids are converted to the final amino acid Gly. These results agree well with the hypothesis proposed and with the results reported in the previous paper[9]. The study also explains why Gly is always in the reaction mixture of the amino acid related CGDE reaction. This study shows an additional example of clean and powerful oxidation of bio-organic compounds by CGDE without using any oxidizing agent.

References

1) A.Hickling, in "Modern Aspects of Electrochemistry", ed. by J.O.Bockris, B.E. Conway, Plenum Press, New York (1971), Vol 6, p.329.
2) K.Harada and T.Iwasaki, Nature (London), 250, 426 (1974).
3) K.Harada and T.Iwasaki, Chem. Lett., 1975, 185.
4) K.Harada and S.Suzuki, Nature (London), 266, 275 (1977).
5) K.Harada and S.Suzuki, Naturwissenschaften, 64, 484 (1977).
6) K.Harada, J.Terasawa, and S.Suzuki, Naturwissenschaften, 65, 259 (1978).
7) S.Suzuki, M.Tamura, J.Terasawa, and K.Harada, Bioorg. Chem., 7, 111 (1978).
8) J.Terasawa and K.Harada, Chem. Lett., 1980, 73.
9) K.Harada and J.Terasawa, Chem. Lett., 1980, 441.

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