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Amination of Carboxylic Acids by Reductive Fixation of Molecular Nitrogen by Glow Discharge Against Aqueous Solution

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Amination of several carboxylic acids by reductive fixation of molecular nitrogen was achieved by glow discharge against aqueous solution of these carboxylic acids. The yield of the aminated product is the highest in the case of maleic acid among carboxylic acids used. The addition of hydrochloric acid to the reaction mixture enhances the yields of aminated products. This may be caused by the fact that chloride anion is oxidized by hydroxyl radicals to chlorate ion, and the fixation of molecular nitrogen proceeds under relatively reducing conditions.

Numerous experimental studies on the formation of bioorganic compounds under possible prebiotic conditions have been reported in the past three decades.1) Most of the studies were carried out under reducing conditions, using hydrocarbon, ammonia, hydrogen, and carbon monoxide etc. However, if the temperature on the primitive earth was high (1000 °C), the chemical equilibrium of the atmosphere would have shifted to the non-reducing side as shown in Eq. 1. The resulting hydrogen gas would have escaped from the gravitational field of the earth, and the primitive atmosphere would be a mixture of nitrogen, carbon dioxide and water. This is an extreme case of the non-reducing atmosphere of the primitive earth.

$$\begin{aligned}&H_2 + 1/2O_2 \longrightarrow H_2O\\&CO + 1/2O_2 \longrightarrow CO_2\\&CH_4 + 2H_2O \longrightarrow CO_2 + 4H_2\\&2NH_3 \longrightarrow N_2 + 3H_2\end{aligned}\qquad(1)$$

Ammonia is one of the important starting materials for the formation of nitrogen-containing bioorganic compounds under prebiotic conditions. If ammonia did not exist on the primitive earth, abiotic formation of nitrogen-containing bioorganic compounds would strongly restricted. The formation of ammonia from molecular nitrogen is thermodynamically favored when hydrogen is present at relatively low temperature (Harber-Bosch methods). However ammonia is difficult to be produced without hydrogen. And ammonia is unstable both thermally and photochemically.

Molecular nitrogen is one of the most inert diatomic molecules, and the reductive fixation of molecular nitrogen with water is thermodynamically difficult because of the large positive ΔG° value as shown in Eq. 2.

$$\begin{aligned}&4/5N_2 + 9/5H_2O \longrightarrow NH_3 + 3/5HNO_3\\&\Delta G^\circ = +86.2\ \mathrm{kcal\,mol^{-1}}\end{aligned}\qquad(2)$$

Photochemical conversion of molecular nitrogen in the presence of catalyst2,3) and hydrolysis of nitrogen-metal complexes4) are known as reductive fixation of molecular nitrogen, while little study has been carried out on the molecular fixation of notrogen in the absence of a catalyst.5,6)

In our previous investigation, we reported that direct amination of carboxylic acids in aqueous ammoniacal solution by using glow discharge.5) It was found that the reductive fixation of molecular nitrogen with water by using glow discharge yields ammonia and nitrate ion.6) When aqueous acetic acid was added to this system, it was found that aminated product (glycine) was identified.7)

In this paper, details of the experimental results of the amination reactions of various carboxylic acids using molecular nitrogen and water induced by glow discharge are described. And some of the additive effects on the reductive fixation of nitrogen gas was studied. Under these reactions it was found that a) ammonia and nitrate

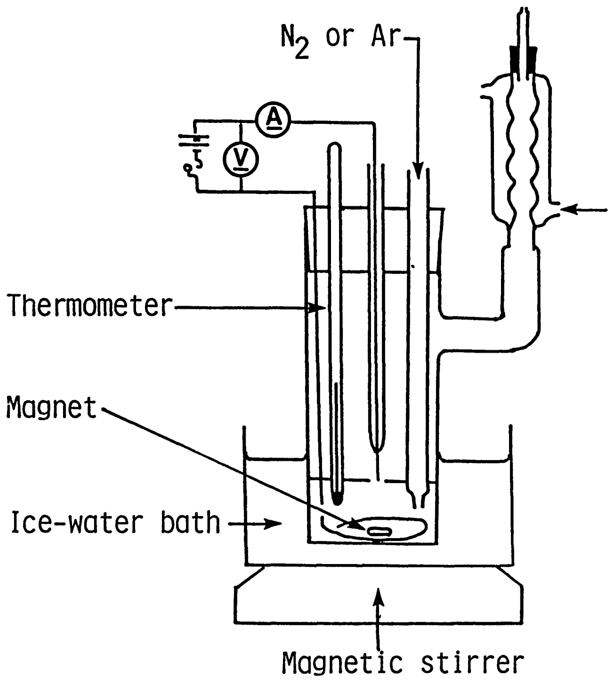

Fig. 1. Apparatus for nitrogen fixation by CGDE.

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ions were simultaneously formed in the aqueous solution, and that b) various amino acids and aminated degradation products were formed. Formation of amino acid was chosen because of the ease of identification and also as a model for the formation of the bioorganic compounds under non-reducing conditions.

Experimental

Glow discharge was applied on the surface of water (20 ml) containing a small amount of sulfuric acid (0.025 mmol) under nitrogen atmosphere. The applied electric current was 20—50 mA at 500—600 V. The reaction temperature was kept at 25—40 °C by cooling the reaction mixture in an ice-water bath. The reaction tube for the glow discharge reaction is shown in Fig. 1. A small amount of reaction mixture was withdrawn at intervals and each sample was analyzed with an amino acid analyzer for amino acid and ammonia, and also by ion chromatography for nitrate and nitrite ions.

Results and Discussion

The experimental results of reductive fixation of molecular nitrogen are summarized in Figs. 2 and 3. As shown in Fig. 2, the amount of ammonia and nitrate ion found in the reaction mixture increased as the reaction proceeded and the concentrations of ammonia and nitrate ion were 0.45 mmol/20 ml and 0.38 mmol/20 ml, respectively, after 24 h. As a control reaction, the glow discharge was carried out in a similar way under argon atmosphere. Neither ammonia nor nitrate ion was found in the reaction mixture (Fig. 3). This whole process was also carried out without glow discharge, and ammonia or nitrate ion was not detected. Nitrite ion was not found in the reaction mixture, probably because of the rapid oxidation to nitrate ion. A possible pathway for the formation of ammonia and nitrate ion could be shown as follows:

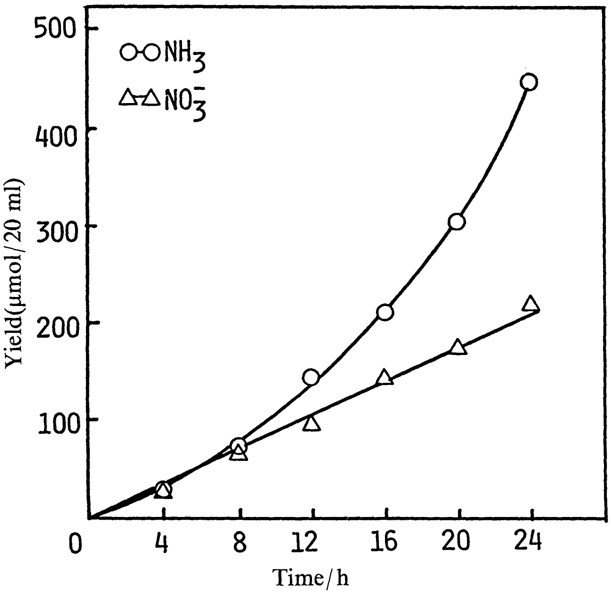

Fig. 2. Formation of NH_3 and NO_3^- from N_2 and H_2O by CGDE.
Reaction conditions: 520—600 V, 50 mA, 35—45 °C.
Substrate: H_2SO_4 0.025 mmol/20 ml H_2O-N_2.

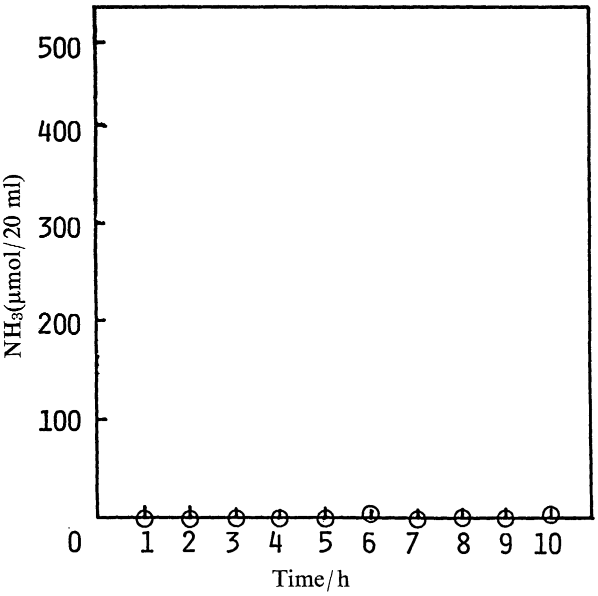

Fig. 3. Ammonia found in the reaction mixture of H_2O-Ar system by CGDE.
Reaction conditions: 720—800 V, 50—60 mA, 40—50 °C.
Substrate: H_2SO_4 0.1 mmol/20 ml H_2O-Ar.

$$N_2 \longrightarrow 2N$$
$$H_2O \longrightarrow OH + H$$
$$N + H_2O \longrightarrow N + H + OH$$
$$N + nH \longrightarrow NH \longrightarrow NH_2 \longrightarrow NH_3$$
$$N + OH \longrightarrow NO_2^- \longrightarrow NO_3^-$$
$$N_2 + H_2O \longrightarrow NH_3 + NO_3^- \qquad (3)$$

The nitrogen atom generated under high energy conditions is reduced with hydrogen to form NH and NH_2 radicals, and finally NH_3. Therefore, if some suitable organic amino acceptor is present in the reaction mixture, the glow discharge reaction could result in the formation of several amino compounds. In this study, several aliphatic carboxylic acids were used and the time course of the resulting amino compounds was shown in Figs. 4—9. Carboxylic acids used were acetic acid, propionic acid, succinic acid, acrylic acid and maleic acid in the glow discharge reaction using molecular nitrogen and water. The effect of added sodium chloride and hydrochloric acid on the reductive amination of molecular nitrogen was also studied (Figs. 10—12).

Figure 4 shows the time course of the amination reaction of aqueous acetic acid (10%, 20 ml) by glow discharge under nitrogen atmosphere. The aminated product, glycine, and the aminated degradation product, methylamine, were confirmed. The yields of these aminated products are smaller than those from the reaction of other carboxylic acids.

Figure 5 shows the time course of the amination

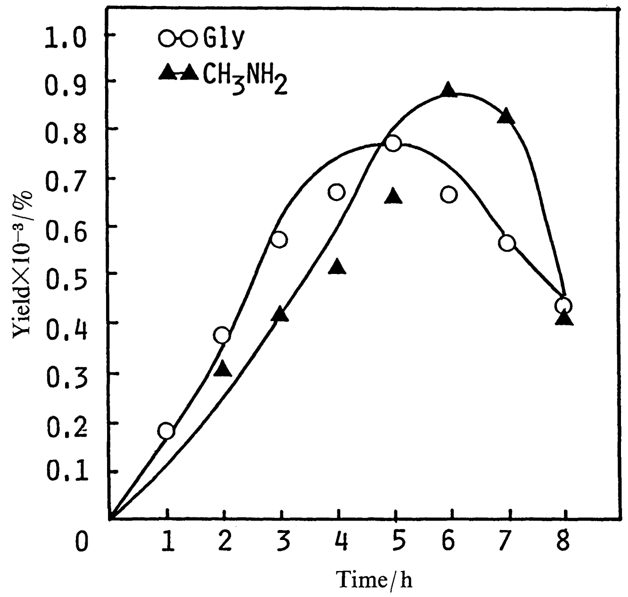

Fig. 4. The amination of acetic acid by CGDE.
Reaction conditions: 540—640 V, 40—50 mA, 30—40 °C.
Substrate: acetic acid 33 mmol/ H_2O(total 20 ml) $-N_2$.

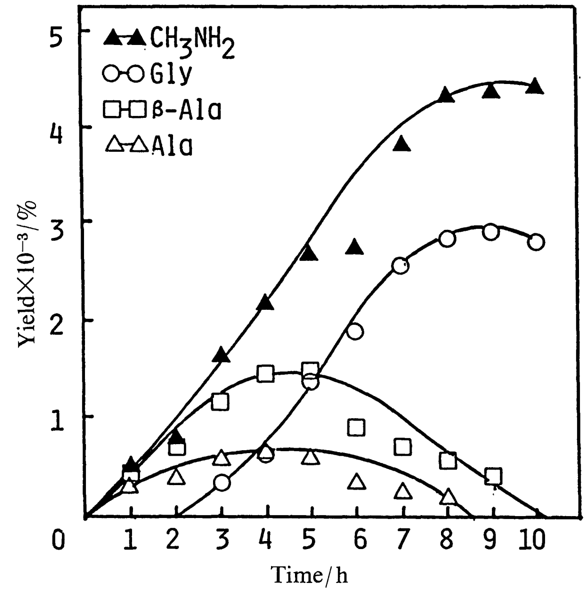

Fig. 5. The amination of propionic acid by CGDE.
Reaction conditions: 560—680 V, 40—60 mA, 35—45 °C.
Substrate: propionic acid 27 mmol/ H_2O(total 20 ml) $-N_2$.

reaction of propionic acid (10%, 20 ml). β-Alanine and alanine were confirmed as aminated products. The ratio of β-ala : ala after 1 h was roughly 1.5 : 1. Methylamine and glycine, which are the aminated degradation products, were also confirmed. This indicates that the C–C bond could easily be cleaved under the conditions used.

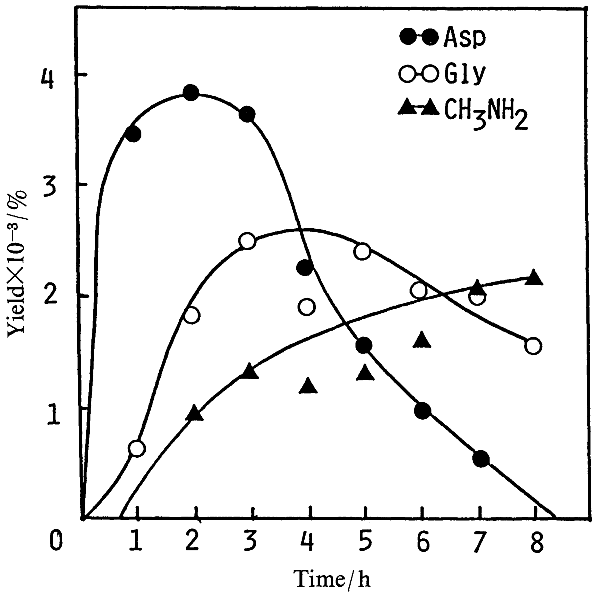

Fig. 6. The amination of succinic acid by CGDE.
Reaction conditions: 560—620 V, 50 mA, 35—45 °C.
Substrate: succinic acid 10 mmol/ H_2O(total 20 ml) $-N_2$.

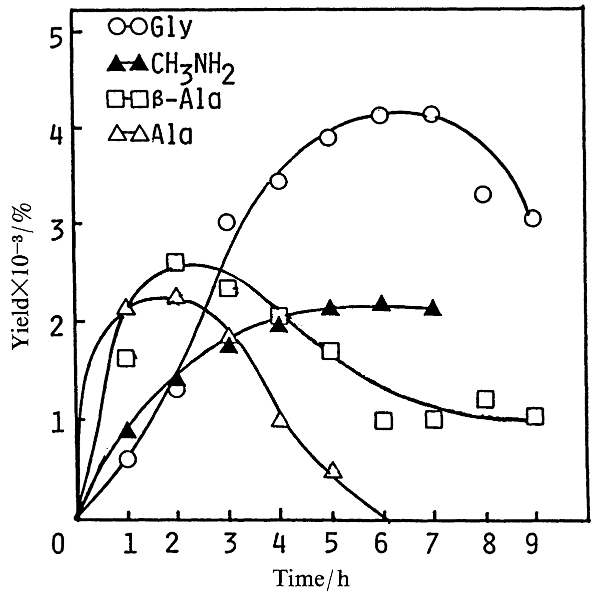

Fig. 7. The amination of acrylic acid by CGDE.
Reaction conditions: 560—600 V, 40—60 mA, 35—45 °C.
Substrate: acrylic acid 8.3 mmol, H_2O(total 20 ml) $-N_2$.

Figure 6 shows the amination of succinic acid (10 mmol/ 20 ml). The directly aminated product, aspartic acid, formed first, and the aminated degradation products, glycine and methylamine, increased with time. The yields were similar to the case of propionic acid.

Figure 7 shows the time course of amination of acrylic acid (3%, 20 ml) with nitrogen. In this case the concentration of acrylic acid was reduced in order to avoid radical polymerization of the unsaturated carboxylic acid. The direct amination product, β-alanine and alanine, were formed first and the yields of aminated degradation products, glycine and methylamine, increased with the reaction time. The yield of alanine reached almost zero after 6 h in the reaction, while the yield of β-alanine remained at the higher level at that time. This suggests that β-alanine might be formed from the degradation products, for example, by the coupling of methylamine and acetic acid.

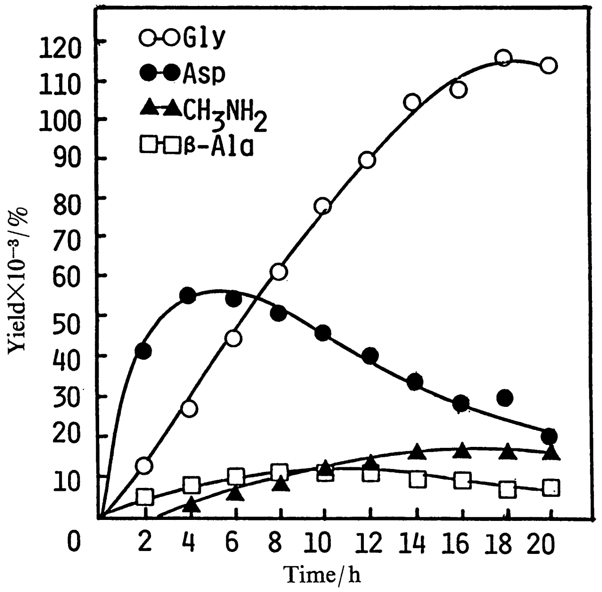

Fig. 8. The amination of maleic acid by CGDE. Reaction conditions: 460—500 V, 20 mA, 10—20 °C. Substrate: maleic acid 10 mmol/H_2O(total 20 ml) -N_2.

Figure 8 shows the amination of maleic acid by glow discharge under nitrogen atmosphere. Direct amination product, aspartic acid, was synthesized first, and the aminated degradation products, glycine, methylamine, and β-alanine, were formed with the reaction proceeded. The yields of aminated products in this reaction were much higher (>50×) than those of the other carboxylic acids.

As was described earlier, the direct amination of aliphatic carboxylic acids by using electric discharge was possible in relatively high concentration of aqueous ammonia.[5] In this reductive fixation of nitrogen by using electric discharge, a small amount of ammonia was formed in aqueous solution. Therefore, it is worthwhile to investigate whether the direct amination of carboxylic acid in such a low ammonia concentration proceeds or not under the high energy conditions. When glow discharge was applied to the N_2-H_2O system for 24 h, 450 mol/20 ml of ammonia was produced. The concentration of ammonia is equivalent to about 0.03% aqueous ammonia. Therefore, glow discharge was applied to 10% acetic acid (20 ml) containing 0.03% ammonia. The time course of the reaction is shown in Fig. 9. The highest yield of glycine and methylamine reach 3×10^{-3} and 2×10^{-3}%, and the formation of β-alanine and aspartic acid was confirmed. The yields are higher than those obtained by using molecular nitrogen.

In the following investigation, the effect of additives

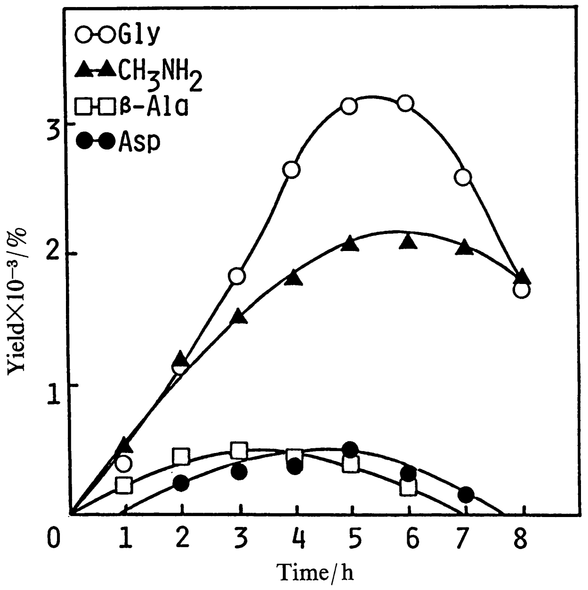

Fig. 9. The amination of acetic acid by CGDE. Reaction conditions: 540—640 V, 40—60 mA, 35—45 °C. Substrate: ammonia 17 mmol+acetic acid 33 mmol/H_2O(total 20 ml) -N_2.

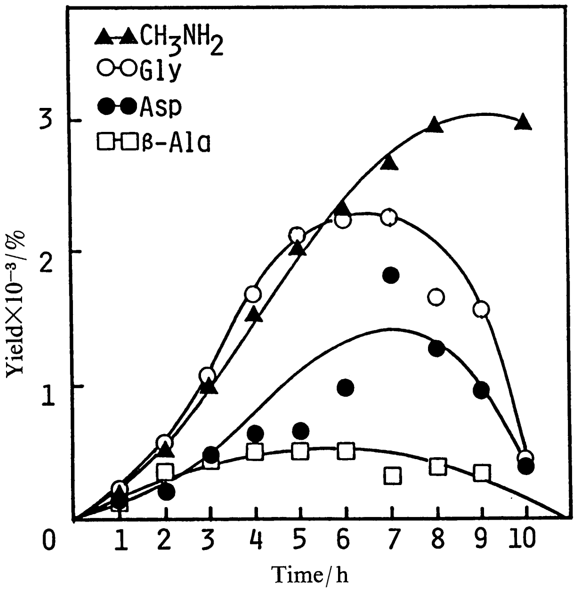

Fig. 10. The amination of acetic acid by CGDE in the presence of NaCl. Reaction conditions: 520—560 V, 20—40 mA, 20—30 °C. Substrate: acetic acid 33 mmol, 0.09M-NaCl/H_2O(total 20 ml) -N_2.

(NaCl and HCl) in the reductive amination of carboxylic acids is described. Because chloride anion could be oxidized under the reaction conditions, this might enhance the yields in the reductive amination of nitrogen molecule. The effect of sodium chloride in the amination reaction of acetic acid is shown in Fig. 10. The yield of glycine increased about three times compared with that of reactions without sodium chloride. The yields of other aminated secondary products, methylamine, glycine, β-alanine, and aspartic acid, were also higher than the case without sodium chloride.

The effect of hydrogen chloride addition was investigated in the reaction with acetic acid. The time course of the formation of aminated products using 0.1 M HCl (1 M=1 mol dm^{-3}) is shown in Fig. 11. In addition to the direct amination product, glycine, aminated secondary products, methylamine, β-alanine, and aspartic acid, were synthesized in higher yields. The yield of glycine is much higher (×30) compared with the yields without hydrogen chloride. When the concentration of hydrogen chloride was reduced to 0.01 M, the yield of glycine decreased, but, the yield was still four times higher than that without hydrogen chloride (Fig. 12). Therefore, the effect of hydrogen chloride in the reductive amination by glow discharge in aqueous solution is significant. Similarly, the effect of hydrogen chloride in the reductive amination of maleic acid is shown in Fig. 13. When the concentration of hydrochloric acid was 0.01 M, the yield of aspartic acid is similar to that obtained without hydrochloric acid. However, when the concentration of HCl was increased to 0.1 M, the yields of aspartic acid and glycine increased roughly twice. The formation of chlorate ion (ClO_3^-) was confirmed in the reaction mixture by ion chromatography. This indicates that chloride ion (Cl^-) was oxidized to chlorate ion by hydroxyl radicals ($Cl^- \rightarrow [ClO^-]$

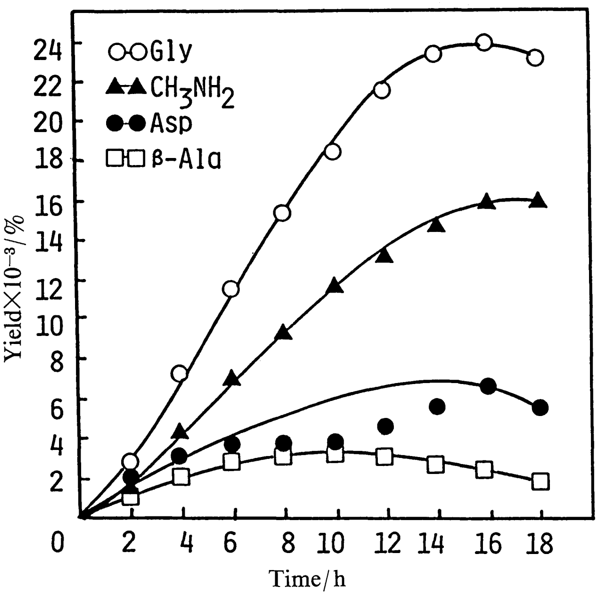

Fig. 11. The amination of acetic acid by CGDE in the presence of HCl.
Reaction conditions: 480—500 V, 20 mA, 10—20 °C.
Substrate: acetic acid 33 mmol, 0.09M-HCl/H_2O(total 20 ml) -N_2.

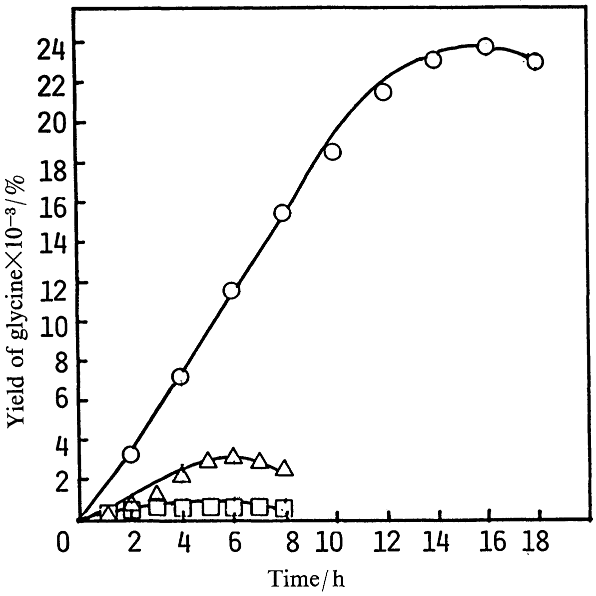

Fig. 12. The amination of acetic acid by CGDE in the presence of HCl.
Reaction conditions: ○—○ 480—500 V, 20 mA, 10—20 °C. △—△ 520—600 V, 40 mA, 30—40 °C. □—□ 540—640 V, 40—50 mA, 35—45 °C.
Substrate: ○—○ acetic acid 33 mmol, 0.09 M-HCl(total 20 ml)-N_2; △—△ acetic acid 33 mmol, 0.009 M-HCl(total 20 ml)-N_2; □—□ acetic acid, H_2O(total 20 ml)-N_2.

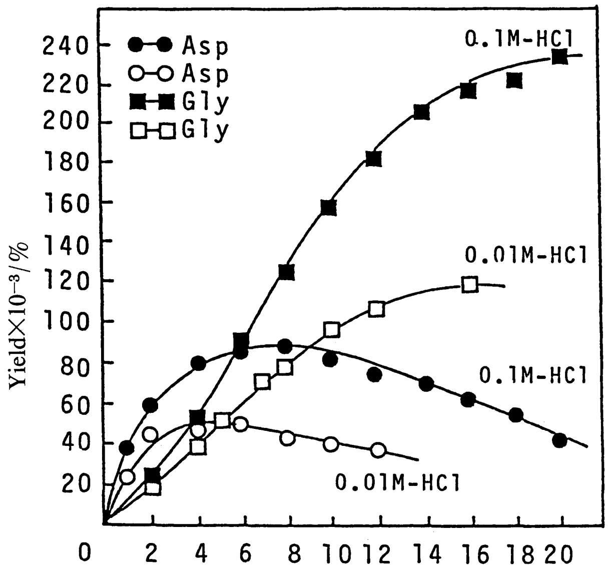

Fig. 13. The amination of maleic acid by CGDE in the presence of HCl.
Reaction conditions: 440—460 V, 20 mA, 10—20 °C.
Substrate: △—△, ○—○ maleic acid 10 mmol/0.01M-HCl(total 20 ml)-N_2; ■—■, ●—● maleic acid 10 mmol/0.1M-HCl(total 20 ml)-N_2.

$\rightarrow ClO_3^-$). When the Cl^- concentration decreased to 55% of the initial concentration of hydrogen chloride (0.1 M), the yield of ClO_3^- reached 45% after glow discharge for 12 h. This suggests that Cl^- serves as a scavenger for hydroxyl radicals, therefore forming relatively reducing reaction conditions, and increasing the yields of reductive amination products.

The formation of ammonia and nitrate ion from molecular nitrogen and water is a new type of chemical reaction that could be regarded as a disproportionation reaction under high energy conditions. The reaction is not controlled thermodynamically. The simultaneous formation of reduced (ammonia) and oxidized (nitrate ion) compounds could be explained by the decomposition of nitrogen and water molecules under high energy conditions and the recombination of the resulting radicals. The active species in the ammination reaction could be NH or NH_2 radicals formed by the coupling reaction of nitrogen and hydrogen atoms generated by glow discharge. The ratio of ala : β-ala produced from propionic acid (1 : 1.5) was similar to that obtained in NH radical reaction to propionic acid (1 : 1.6).[7,8] This indicates that the amination of carboxylic acid by reductive fixation of molecular nitrogen under high energy conditions may proceed via a radical mechanism.

The reductive fixation reaction of molecular nitrogen with water is not only interesting chemically, but also interesting from the point of view of chemical evolution. This type of reaction could be regarded as a model experiment to examine the effect of lightning struck on the hydrosphere in a non-reducing atmosphere (composed mainly of H_2O, N_2, and CO_2) on the primitive earth. The lightning may induce various chemical reactions under aqueous conditions, which could produce various bioorganic compounds that cannot arise thermodynamically.

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