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ORIENTATION OF CARBOXYLATION REACTION BY CONTACT GLOW DISCHARGE ELECTROLYSIS

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The carboxylation reaction of aliphatic amines and cyclic imines in aqueous formic acid by contact glow discharge electrolysis (CGDE) was studied and the orientation of the carboxylation reaction was investigated. It was found that the orientation of the reaction was controlled by the effect of the charged and uncharged nitrogen atom.

Contact glow discharge electrolysis(CGDE) is a type of chemical reaction carried out by means of an electric discharge between an aqueous solution containing substrates and an electrode in contact with the solution.[1,2] Recently, several applications of CGDE to organic compounds were reported.[3,4,5] Although CGDE is a new type of chemical reaction, no detailed study on the reaction of organic compounds by CGDE have been reported.

In this investigation, the carboxylation of methylamine, ethylamine, propylamine, pyrrolidine and piperidine with formic acid by CGDE in aqueous solutions was carried out in order to clarify the orientation of the carboxylation reaction. The amines were carboxylated under acidic(pH 2.8) and basic(pH 12.5) conditions by CGDE to form corresponding α-, β- and γ-amino acids. In these reactions a small amount of glycine(Gly), serine(Ser) and β-alanine(β-Ala) were formed as the secondary products in addition to the main products. The cyclic imines were also converted to the corresponding α-, β- and γ-imino acids under the same conditions. The formation of small amount of Gly was also observed. The summerized results obtained after 1 hr reaction are shown in Table I and a time course of the yields of amino acids is shown in Fig. 1.

The amino acids formed in CGDE were analyzed by an amino acid analyzer (Yanagimoto LC-5S). A part of the products was treated with 2,4-dinitrofluorobenzene, and the resulting dinitrophenyl(DNP) amino acids were separated by the celite column chromatography.[6] The separated 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. The preparations of α-methyl-β-alanine(α-Me-β-Ala),[7] nipecotic acid[8] and isonipecotic acid[9] were carried out separately to obtain authentic samples of amino acids found in the products of the carboxylation reactions.

Fig. 1 shows the time course of the carboxylation reaction of n-propylamine by CGDE. The results indicate that the yields of amino acids increased proportionally for the first 60 minutes, and the yields of the primary products reached the highest point after 120 minutes and then decreased. The yields of β-Ala and Gly are still increasing after 120 minutes. However, these are secondary products which could be derived from the primary products.10)

In the carboxylation of methylamine, the yield of Gly(4.6%) under basic conditions is higher than that under acidic conditions(0.7%). In the case of ethylamine, the yield of β-Ala(3.1%) is higher than that of alanine(Ala)(1.5%) under acidic conditions; under basic conditions, however, the yield of Ala(3.1%) is higher than that of β-Ala(0.6%). In the case of propylamine, the yields of β- and γ-amino acids(α-Me-β-Ala, 9.8%; γ-aminobutyric acid(GABA), 8.1%) are higher than that of α-aminobutyric acid(α-NH_2BA, 0.9%) under acidic conditions. Under basic conditions, the yield of α-amino acid(1.1%) increased and the yields of β- and γ-amino acids decreased considerably. In the carboxylation of pyrrolidine and piperidine, similar results are obtained in the case of aliphatic amines. The yields of β- and γ-carboxylated imines are higher than those of α-carboxylated imines under acidic conditions; under basic conditions, the yields of α-carboxylated imines are higher than those of β- and γ-carboxylated imines.

It has been known that hydrogen and hydroxyl radicals are the primary products formed by irradiation of aqueous solutions with ionizing radiation.11,12) The formation of hydrogen and hydroxyl radicals in the primary reaction zone in the glow discharge electrolysis(GDE) has been discussed.2) These radicals would abstract hydrogen from the substrates in the aqueous solutions and the resulting radicals would react further with each other to form the several products including amino acids.

The dissociation constants K_b of amines and imines and the pH values of the aqueous reaction mixtures are listed in Table I.13) Under acidic conditions(pH 2.8), the contents of the protonated form of amines and imines are almost 100% and under

$$\mathrm{H_2O} \longrightarrow \mathrm{H\cdot + HO\cdot} \qquad 1$$

$$\mathrm{RH(amine) + HO\cdot} \longrightarrow \mathrm{R\cdot(amine\ radical) + H_2O} \qquad 2$$

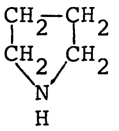
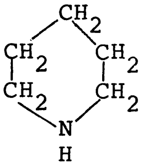
$$\mathrm{HCOOH + HO\cdot} \longrightarrow \mathrm{\cdot COOH + H_2O} \qquad 3$$

$$\mathrm{R\cdot + \cdot COOH} \longrightarrow \mathrm{RCOOH(amino\ acid)} \qquad 4$$

basic conditions(pH 12.4 - 12.8), those are only 2 - 3%. These protonations of amines and imines are considered to be related to the formation of α-, β- or γ-radicals by CGDE. Thus β- and γ-radicals are formed more easily than α-radicals under acidic conditions, and vice versa under basic conditions. The radicals produced by CGDE react with carboxyl radicals to form the corresponding amino and imino acids. This explanation was supported by the fact that radical formation of imines by the electrophilic hydroxyl radical took place more easily at the carbon atom more distant from the protanated positively charged nitrogen.14)

Therefore, the observed orientation in the carboxylation reaction in acidic and basic conditions, could be explained by the orientation in hydrogen abstraction from amines and imines by hydroxyl radicals produced by CGDE. The results obtained in this study showed clearly that the orientation of the carboxylation reaction by CGDE in aqueous solutions was affected by the presence of the charged nitrogen atom.

Table I Orientation of carboxylation reaction by contact glow discharge electrolysis

Starting material[a)] (Dissociation const., Kb)	pH[b)]	$[BH^+]$[c)] %	Yield Carboxylated products, %, (60 min)[d)] α	β	γ	other amino acids	α:β:γ
CH_3NH_2	2.8	100	Gly (0.65)	——	——	——	——
(4.4×10^{-4})	12.4	1.7	Gly (4.6)	——	——	——	——
$CH_3-CH_2-NH_2$	2.8	100	Ala (1.5)	β-Ala (3.1)	——	Gly , Ser (0.1) (0.1)	1.0:2.0 α<β
(5.6×10^{-4})	12.5	1.8	Ala (3.1)	β-Ala (0.6)	——	Gly , Ser (0.3) (1.0)	1.0:0.19 α>β
$CH_3-CH_2-CH_2-NH_2$	2.8	100	α-NH_2BA (0.9)	α-Me-β-Ala (9.8)	GABA (8.1)	Gly , β-Ala (0.2) (3.4)	1.0:10.9:9.0 α<β≈γ
(4.7×10^{-4})	12.4	1.8	α-NH_2BA (1.1)	α-Me-β-Ala (1.2)	GABA (0.42)	Gly , β-Ala (0.28) (0.26)	1.0:1.09:0.38 α≈β>γ
	2.8	100	Pro (1.8)	β-Pro (7.4)	——	Gly (0.1)	1.0:4.1 α<β
(1.3×10^{-3})	12.8	2.1	Pro (2.1)	β-Pro (0.4)	——	Gly (0.1)	1.0:0.19 α>β
	2.8	100	Pipecolic acid (0.8)	Nipecotic acid (2.9)	Isoni-pecotic acid (4.3)	Gly (0.1)	1.0:3.62:5.38 α<β<γ
(1.6×10^{-3})	12.7	3.1	Pipecolic acid (0.5)	Nipecotic acid (0)	Isoni-pecotic acid (0)	Gly (0.1)	1.0:0:0 α>β,γ

a) A solution of amine(imine)(0.005 mole) in 1.5 N HCOOH or HCOONa aqueous solution(20 ml) was applied for CGDE for 1 hr(500-600 V, 45 mA, 10 - 20 °C).

b) The pH of the reaction mixture, low pH(2.8): in HCOOH solution; higher pH(12.4 - 12.8): in HCOONa solution.

c) The percentage of protonated form of amine(imine) was calculated from the pH value and the dissociation constant.

d) The amino acids were identified by an amino acid analyzer and also by column and thin layer chromatography of the DNP-derivatives.

Gly: glycine; Ala: alanine; β-Ala: β-alanine; Ser: serine; α-NH_2BA: α-aminobutyric acid; α-Me-β-Ala: α-methyl-β-alanine; GABA: γ-aminobutyric acid; Pro: proline; β-Pro: β-proline.

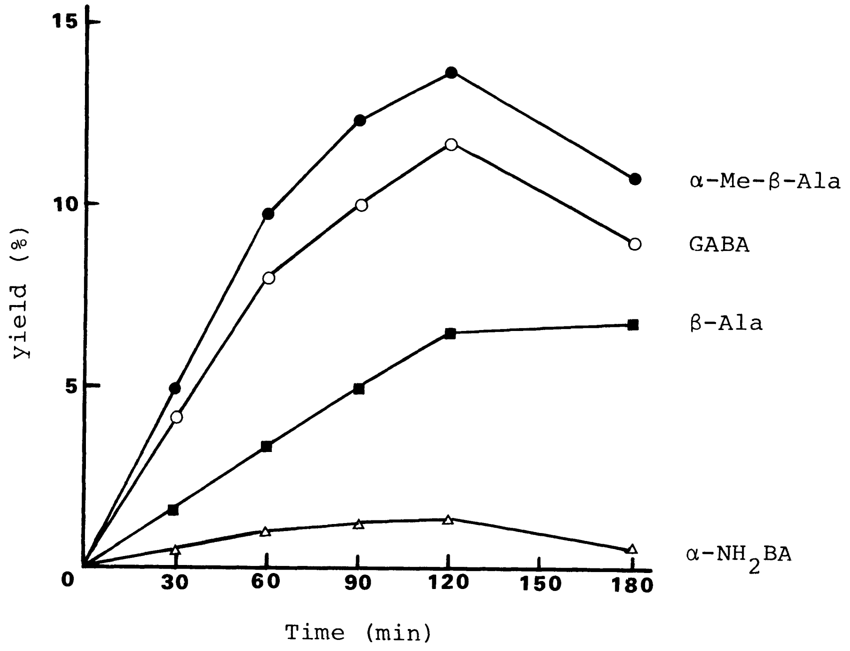


Fig. 1. Time course of amino acid formation from propylamine in 1.5 N formic acid by CGDE. (●) α-Me-β-Ala, α-methyl-β-alanine; (○) GABA, γ-aminobutyric acid; (■) β-Ala, β-alanine; (△) α-NH_2BA, α-aminobutyric acid.

References and Notes

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