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HYDROXYLATION REACTION OF AROMATIC RINGS IN AQUEOUS SOLUTION INDUCED BY HYDROGEN-OXYGEN FLAME

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It was found that direct hydroxylation of aromatic rings proceeded in aqueous solution of phenyl-containing amino acids by using hydrogen-oxygen flame and that the active species of the reaction could be considered as hydroxyl radicals generated in the burning flame.

Much attention has been given to the studies of liquid-phase radical reactions induced by various sources of energy or active species, such as radiations,1) electric discharges,2-4) and plasmas.5-7) Recently, we reported a novel method for inducing radical reactions in aqueous solution of organic compounds.8) When flames of several gases mixed with oxygen were kept in contact with aqueous solutions of aliphatic amines, the alkyl groups of the amines were hydroxylated first and further oxidized to afford amino acids via aminoaldehydes by using hydrogen-, town gas-, and ethylene-oxygen flames. However, such oxidation reactions did not proceed by the action of acetylene-oxygen flame. The results obtained indicate that the flame-induced oxidation could not be due to a thermal decomposition of or an air oxidation of the substrate. The results also indicate that some radicals produced in the flames were directly introduced into the solution to hydroxylate organic compounds in an aqueous solution.

In order to clarify the active species in the flame-induced oxidation reactions, hydroxylation of aromatic rings by using hydrogen-oxygen flame was carried out in aqueous solutions of phenyl-containing amino acids. The apparatus used for the flame-induced reaction was shown in the previous report.8) The substrates used were α-phenylglycine, phenylalanine and homophenylalanine (α-amino-γ-phenylbutyric acid). The flame from a burner was kept in contact with the surface of aqueous solution (500 ml) of the amino acid (2 mmol/l) with stirring. The flow rates of hydrogen and oxygen gases were 1.8 l/min and 0.9 l/min, respectively. The distance from the surface of the aqueous solution to the burner nozzle (1.5 mmI.D) was about 3 cm. The temperature of the solution was kept at about 50 °C throughout the reaction by circulation of the reaction mixture through a glass tube (4.5 m x 5 mmI.D) immersed in an ice bath. The pH of the solution was adjusted to 3.0 with 2 mol dm^{-3} HCl. The products and the substrate in the reaction mixture were analyzed by an amino acid analyzer.

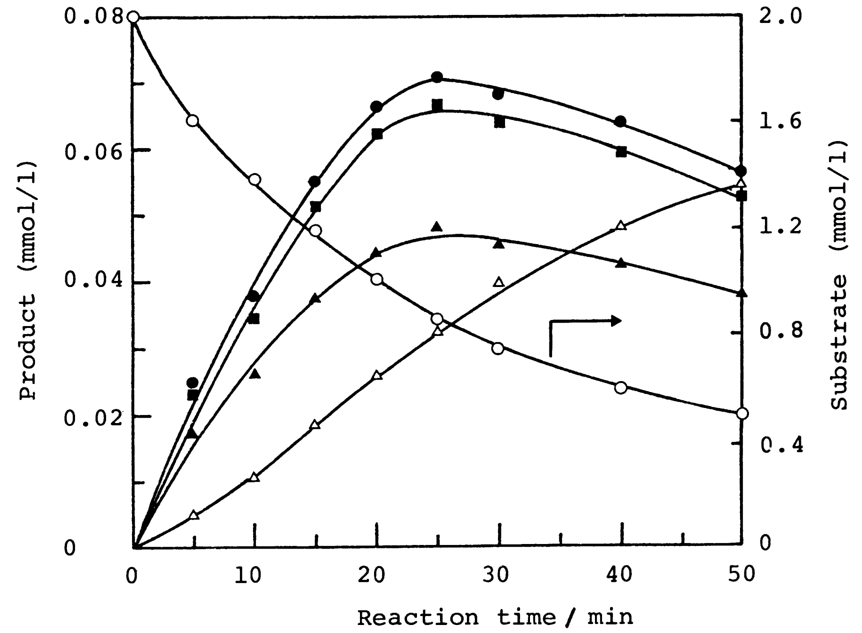

Fig. 1. Hydroxylation reaction of α-phenylglycine in aqueous solution induced by hydrogen-oxygen flame. α-phenylglycine: ○———○ ; o-, m-, and p-hydroxyphenylglycine: ■———■, ●———●, and ▲———▲ ; glycine: △———△ .

As a typical example of the flame induced reaction, the time course of the hydroxylation of α-phenylglycine in an aqueous solution by the use of hydrogen-

Table 1. Hydroxylation reaction of aromatic rings in aqueous solution induced by hydrogen-oxygen flame

Substrate (2 mmol/l)	Reaction time[a] / min	Recovery %	Total yield[b] %	Other products identified [yield[c] / %]
α-Phenylglycine	25	42	9.4	gly(1.3)
Phenylalanine	15	38	11.2	gly(0.8), asp(2.8)
Homophenylalanine[d]	10	39	10.0	gly(6.5), asp(1.0) glu(0.6)

a) Reaction time at maximun yield.
b) Total yield of o-, m-, and p-hydroxyphenyl amino acids based on initial amounts of substrate.
c) Yield based on initial amounts of substrate.
d) Homophenylalanine: α-amino-γ-phenylbutyric acid.

Table 2. Isomer distribution of hydroxylated products from phenyl-containing amino acids

Reaction system	Isomer distribution		
	Products from α-phenylglycine (o : m : p)	Products from phenylalanine (o : m : p)	Products from homophenylalaninea) (o : m : p)
H_2-O_2 flame	36 : 38 : 26	41 : 29 : 30	35 : 33 : 32
Argon plasma jet	36 : 38 : 26b)	42 : 26 : 32b)	-
Fe^{2+}-H_2O_2-EDTA	36 : 39 : 25b)	41 : 29 : 30b)	37 : 33 : 30c)
Fe^{2+}-ascorbic acid-H_2O_2-EDTA	35 : 39 : 26b)	41 : 27 : 32b)	35 : 35 : 30d)
Fe^{2+}-ascorbic acid-O_2-EDTA	32 : 49 : 18b)	40 : 35 : 25b)	38 : 38 : 24e)

a) Homophenylalanine: α-amino-γ-phenylbutyric acid.
b) Isomer distribution taken from Ref. 7.
c) Aqueous hydrogen peroxide solution (0.3%) under nitrogen atmosphere; pH 3 with 2 mol dm^{-3} HCl; $FeSO_4$, 2 mmol/l; EDTA, 10 mmol/l; homophenylalanine, 2 mmol/l.
d) Aqueous hydrogen peroxide solution (0.3%) under nitrogen atmosphere; pH 3 with 2 mol dm^{-3} HCl; $FeSO_4$, 0.2 mmol/l; ascorbic acid, 10 mmol/l; EDTA, 10 mmol/l; homophenylalanine, 2 mmol/l.
e) $FeSO_4$, 0.2 mmol/l; ascorbic acid, 10 mmol/l; EDTA, 10 mmol/l; homophenylalanine, 2 mmol/l; pH 3 with 2 mol dm^{-3} HCl; Air was bubbled through the reaction mixture.

oxygen flame is shown in Fig. 1. The hydroxylation products, o-, m-, and p-hydroxyphenylglycine were formed depending with the decrease of α-phenylglycine. The total yield of o-, m-, and p-hydroxyphenylglycine reached about 10% based on the initial amounts of substrate under the conditions used. The ratio of o- : m- : p-hydroxyphenylglycine was 36 : 38 : 26 at any reaction time. Each hydroxyphenylglycine was further oxidized to afford glycine. No dihydroxylated products were detected.

The results obtained in the hydroxylation reactions by using hydrogen-oxygen flame were summarized in Table 1. In each reaction by the use of hydrogen-oxygen flame, the yields of hydroxyphenyl amino acids were about 10%, which were comparable to those obtained by the oxidation reactions using chemical reagents such as the Fenton reagent,7) and the yields were higher than those of aqueous reactions induced by other high energy species such as argon plasma jet.7)

The isomer distributions of the hydroxyphenyl amino acids in the products were compared with those obtained by using four other hydroxylation methods (Table 2). It has been known that Fe^{2+}-hydrogen peroxide-ethylenediaminetetraacetic acid (EDTA) system and Fe^{2+}-ascorbic acid-hydrogen peroxide-EDTA system apparently involve hydroxyl radicals as the hydroxylating agent of aromatic rings.[9,10] The active species in the argon-plasma induced reaction in aqueous solution could be hydroxyl radicals produced by decomposition of water molecules by the action of argon plasma jet.[7] On the other hand, the active species in the hydroxylation by Fe^{2+}-ascorbic acid-oxygen-EDTA system are not regarded as hydroxyl radicals.[9,10] The ratios of o-, m-, and p-hydroxyphenyl amino acids obtained by the flame induced reactions agreed well with the results obtained by the hydroxylations using the Fe^{2+}-hydrogen peroxide-EDTA system, the Fe^{2+}-ascorbic acid-hydrogen peroxide-EDTA system and argon-plasma induced reaction, but were different from the results obtained by the Fe^{2+}-ascorbic acid-oxygen-EDTA system as shown in Table 2.

Judging from these results, the hydroxylation reaction induced by hydrogen-oxygen flame could be considered to be due to hydroxyl radicals which were produced in the burning flame[12] and these were directly introduced into the aqueous phase to oxidize organic compounds. The hydrogen-oxygen flame offers a novel method of hydroxylation reaction without using any chemical reagent. The clean and powerful oxidation reaction induced by hydrogen-oxygen flame could be applied to various radical reactions in aqueous solutions.

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