FORMATION OF BIOORGANIC COMPOUNDS IN AQUEOUS SOLUTION INDUCED BY FLAMES

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Abstract: Flames of flammable gases, when blown against a surface of an aqueous solution of organic compounds, were found to induce oxidation as well as other reactions in the solution. This reaction would be regarded as a new model for formation of bioorganic molecules in the primitive hydrosphere exposed to some radical-containing atmosphere.

At the early stage of chemical evolution, oxidative modification of organic molecules would play an important role in the formation of bioorganic molecules, which usually contain many moderately or highly oxidized carbon atoms in a molecule. In model experiments for prebiotic synthesis of biomolecules, oxidation has been effected by electric discharge, ultraviolet rays, radiation, and so forth. We present here a new energy source in liquid-phase reactions. Thus, flames of flammable gases, when blown against a surface of an aqueous solution of organic compounds, were found to induce oxidation as well as other reactions in the solution.

The flames used here were a town gas-, a hydrogen-, an ethylene-, and an acetylene-oxygen flame. Fig. 1 depicts the apparatus for the flame-induced reaction in an aqueous solution. A flame from a burner was kept in contact with the surface of an aqueous solution (ca. 500ml) of a substrate (ca. 5×10^{-4} mol/l) with stirring. The temperature of the solution was kept at 40-50 °C throughout the reaction by circulating it through a glass tube (4.5 m x 5 mmI.D.) in an ice bath. Water was supplied continuously from a resorvoir to the reaction mixture, so as to make up for the solvent lost by evaporation. At regular time-
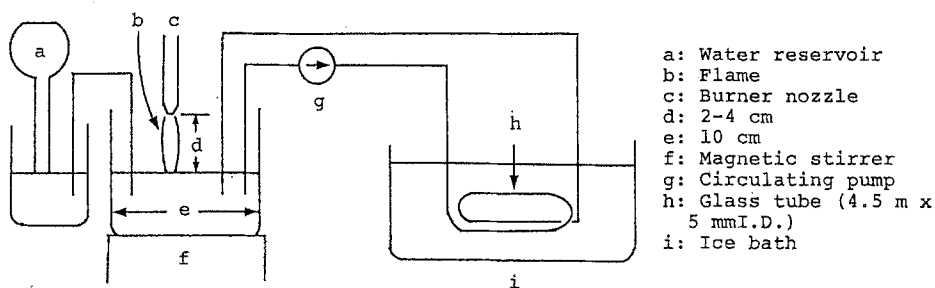
Fig. 1   The apparatus for the flame-induced reaction

intervals, 0.5ml aliquots of the solution were withdrawn and
analyzed with an amino acid analyzer or a liquid chromatograph.

   In the present study, the following reactions were performed
by the use of this method: (A)   oxidation of aliphatic amines
yielding amino acids, (B)   conversion of amino acids into other
amino acids, (C)   carboxylation of saturated and unsaturated
aliphatic amines or amino acids yielding amino acids, and (D)
dehydrogenation of dihydropyrimidines yielding pyrimidines.

   1.   OXIDATION OF ALIPHATIC AMINES
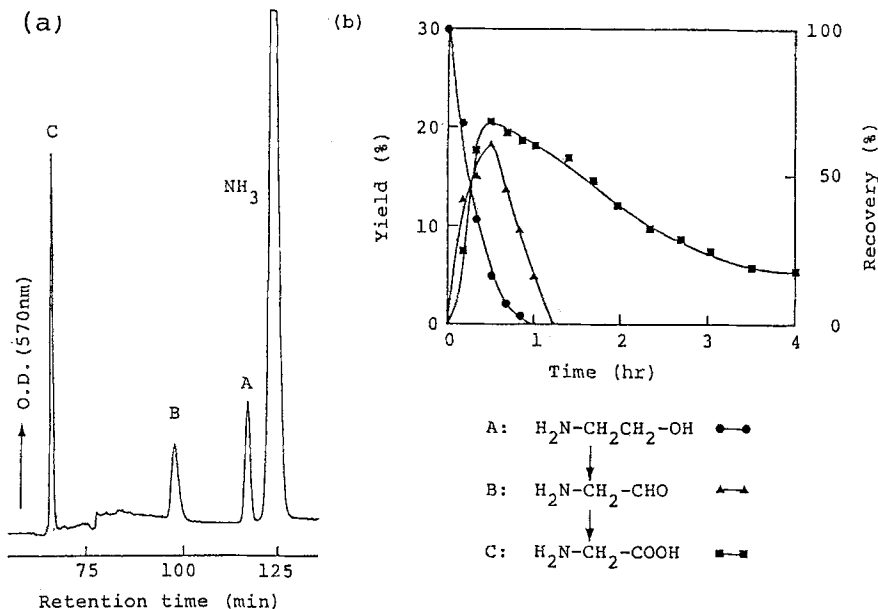

Fig. 2   Oxidation of 1-amino-2-ethanol by a town gas flame
         (a)   The amino acid analysis of products
         (b)   The time course of the yields of products

Fig. 2 shows the results of oxidation of 1-amino-2-ethanol by a town gas-oxygen flame. The substrate was smoothly oxidized and disappeared within 3 hours. The primary product of the oxidation was aminoacetaldehyde, which was further oxidized to afford glycine. The aminomethyl group in the molecule resisted oxidation, since the amino group was protected in the form of an ammonium salt. The yield of glycine also decreased gradually on prolonged reaction, which may indicate that it was decomposed oxidatively to CO_2 and NH_3. There could be two possible reasons why the sum of the yields and the recovery did not reach 100% at any reaction time. First, another oxidation pathway might exist in which oxidation of the aminomethyl group of the substrate precedes that of the hydroxymethyl group, affording products undetectable with an amino acid analyzer. Second, the oxidation reaction would be vigorously proceeding in the vicinity of the solution surface exposed to the flame and therefore part of the substrate might be rapidly and completely decomposed there.

The results of oxidation of several amines by this method are summarized in the Table I. Not only a town gas but an ethylene and a hydrogen flame proved to have the ability to oxidize organic compounds in water. In these reactions, amines or aminoalcohols afforded the corresponding amino acids via aminoaldehydes. The yields of hydroxylated products were generally low, due to their labilities to oxidation. The carbon-carbon bonds were cleaved oxidatively and the final product detected was glycine in all of the reactions.

In contrast to the above-mentioned results, an acetylene-oxygen flame practically failed to oxidize ethylamine under similar conditions. Thus, after exposure to this flame for 3 hours, the starting material did not decrease in the solution and no product was detected. Judging from this fact, the flame-induced reaction reported here could not be due to a thermal decomposition and an air oxidation of the substrates, but would be caused by some reactive species which passes from flame into the solution. Reactive species that exist in flames and oxidize organic compounds in an aqueous solution might be mainly various kinds of radicals, especially OH and OOH radicals. Taking into account the higher reactivity of the former than that of the latter, the OH radical in the flames is considered to oxidize amines in solution. The fact that the acetylene flame lacks the oxidation-inducing ability might indicate that it is poor in OH radicals, possibly because of the lower hydrogen content of acetylene (C_2H_2) than those of the other flammable gases used.

2. CONVERSION OF AMINO ACIDS INTO OTHER AMINO ACIDS

First, α,γ-diaminobutyric acid was subjected to the town gas

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Table I Flame-induced oxidation of aliphatic amines

Substrate	Flame*	Product (Maximum yield, Reaction time**)		
$H_2N-CH_2CH_3$	A	$H_2N-CH_2CH_2-OH$ (3.8%, 15min)	H_2N-CH_2-CHO (7.9%, 30min)	H_2N-CH_2-COOH (21.3%, 60min)
$H_2N-CH_2CH_2-OH$	A	H_2N-CH_2-CHO (18.2%, 30min)	H_2N-CH_2-COOH (20.1%, 30min)	
$H_2N-CH_2CH_2CH_3$	A	$H_2N-CH_2CH_2CH_2-OH$ (8.9%, 15min) H_2N-CH_2-COOH (26.3%, 60min)	$H_2N-CH_2CH_2-CHO$ (7.1%, 15min)	$H_2N-CH_2CH_2-COOH$ (28.7%, 30min)
$H_2N-CH_2CH_2CH_2-OH$	A	$H_2N-CH_2CH_2-CHO$ (3.6%, 20min)	$H_2N-CH_2CH_2-COOH$ (15.1%, 60min)	H_2N-CH_2-COOH (5.3%, 140min)
$\overset{CH_3}{\underset{\mid}{H_2N-CHCH_2-OH}}$	A	$\overset{CH_3}{\underset{\mid}{H_2N-CH-CHO}}$ (18.6%, 30min) H_2N-CH_2-COOH (2.0%, 120min)	$\overset{CH_3}{\underset{\mid}{H_2N-CH-COOH}}$ (14.1%, 60min)	$\overset{CH_2-OH}{\underset{\mid}{H_2N-CH-COOH}}$ (small amount)
$H_2N-CH_2CH_3$	B	$H_2N-CH_2CH_2-OH$ (0.9%, 30min)	H_2N-CH_2-CHO (2.6%, 30min)	H_2N-CH_2-COOH (18.4%, 60min)
$H_2N-CH_2CH_2-OH$	B	H_2N-CH_2-CHO (9.3%, 10min)	H_2N-CH_2-COOH (24.5%, 20min)	
$H_2N-CH_2CH_2CH_3$	B	$H_2N-CH_2CH_2CH_2-OH$ (small amount) H_2N-CH_2-COOH (28.4%, 90min)	$H_2N-CH_2CH_2-CHO$ (5.3%, 10min)	$H_2N-CH_2CH_2-COOH$ (24.9%, 30min)
$H_2N-CH_2CH_2CH_2-OH$	B	$H_2N-CH_2CH_2-CHO$ (18.2%, 10min)	$H_2N-CH_2CH_2-COOH$ (29.0%, 30min)	H_2N-CH_2-COOH (22.9%, 60min)
$\overset{CH_3}{\underset{\mid}{H_2N-CHCH_2-OH}}$	B	$\overset{CH_3}{\underset{\mid}{H_2N-CH-CHO}}$ (15.7%, 20min) H_2N-CH_2COOH (3.7%, 90min)	$\overset{CH_3}{\underset{\mid}{H_2N-CH-COOH}}$ (16.0%, 30min)	$\overset{CH_2-OH}{\underset{\mid}{H_2N-CH-COOH}}$ (2.2%, 60min)
$H_2N-CH_2CH_2-OH$	C	H_2N-CH_2-CHO (16.1%, 10min)	H_2N-CH_2-COOH (34.2%, 45min)	

  * A: town gas-oxygen flame, B: hydrogen-oxygen flame, C: ethylene-oxygen
    flame.
 ** The reaction time taken to reach the maximum yield.

flame-induced reaction (Fig. 3). Although the α-carbon of this amino acid was oxidized to afford β-alanine, oxidation of the γ-carbon, namely conversion of the α-amino acid into the other α-amino acid also took place. The similar oxidative modification of Ala, Glu, Phe, and Met was performed by this method as shown in Fig. 3.

Fig. 3 Oxidative modification of amino acids by a town gas flame

3. CARBOXYLATION OF SATURATED ALIPHATIC AMINES

When saturated aliphatic amines in 20% aqueous formic acid
were exposed to the flames, direct carboxylation took place onto
the alkyl groups to afford amino acids (Table II). The reactive
species of this reaction is considered to be a carboxyl radical
generated from formic acid:

$$-CH_2- \xrightarrow{\cdot COOH \ (or \ \cdot OH)} -CH- \xrightarrow{\cdot COOH} \overset{\displaystyle COOH}{\underset{\displaystyle |}{-CH-}}$$
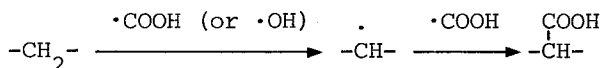
The yields of α-amino acids were lower than those of β- or γ-
amino acids, which is consistent with the lower reactivity of a
methylene adjacent to an ammonium group.

Table II Carboxylation of saturated aliphatic amines
          in 20% HCOOH*

Substrate	Product (Yield, React. Time)	
H_2N-CH_3	H_2N-CH_2-COOH (1.2%, 6hr)	
$H_2N-CH_2CH_3$	$H_2N-\underset{\underset{COOH}{\mid}}{CH}CH_3$ (14.2%, 6hr)	$H_2N-CH_2CH_2-COOH$ (21.5%, 6hr)
$H_2N-CH_2CH_2CH_3$	$H_2N-\underset{\underset{COOH}{\mid}}{CH}CH_2CH_3$ (3.3%, 4hr) $H_2N-CH_2CH_2CH_2-COOH$ (18.2%, 4hr)	$H_2N-CH_2\underset{\underset{COOH}{\mid}}{CH}CH_3$ (16.9%, 4hr)

* H_2-O_2 flame

4. CARBOXYLATION OF UNSATURATED ALIPHATIC AMINES AND AMINO ACIDS

Carboxylation of amines and amino acids containing a carbon-
carbon double bond proved to be more efficient and regeoselective
than that stated in the preceding section (Table III). In this
case, the reaction might proceed through addition of carboxyl
radical to a double bond. N-Acetyl-α,β-dehydroamino acids, which
are readily produced from α-keto acids and acetamide under
rather mild conditions, afforded two types of amino acids, β-
carboxyamino acid and α-carboxyamino acid. On hydrolysis of the
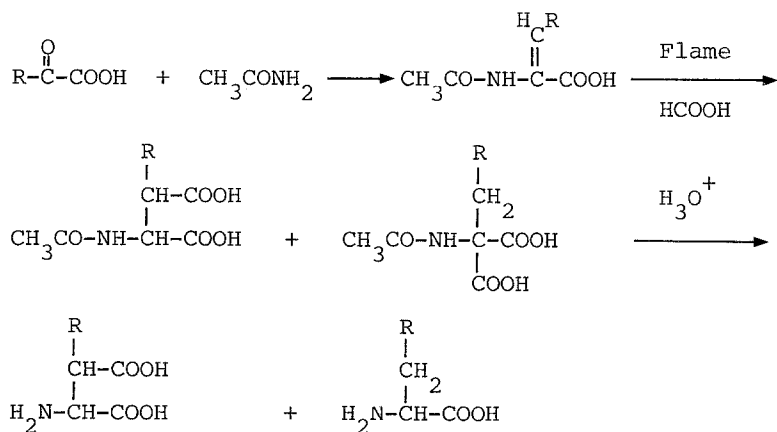products, the latter was converted into a normal amino acid.

Table III Carboxylation of unsaturated amine and amino acids
           in 20% HCOOH*

Substrate	Product (Yield, React. Time)	
$CH_2=C-COOH$ $\quad\ NHCOCH_3$	$CH_3CH-COOH$** $\qquad NH_2$ (28%, 60min)	$COOH$ $CH_2CH-COOH$** $\qquad NH_2$ (20%, 60min)
$CH_3CH=C-COOH$ $\qquad\ NHCOCH_3$	$CH_3CH_2CH-COOH$** $\qquad\quad NH_2$ (11%, 90min)	$COOH$ $CH_3CHCH-COOH$** $\qquad\ NH_2$ (6%, 90min)
$CH_2=CHCH_2CH-COOH$ $\qquad\qquad NH_2$	$COOH$ $CH_3CHCH_2CH-COOH$ $\qquad\qquad NH_2$ (32%, 180min)	$COOH$ $CH_2CH_2CH_2CH-COOH$ $\qquad\qquad NH_2$ (3%, 180min)
$CH_2=CHCH_2-NH_2$	$COOH$ $CH_3CHCH_2-NH_2$ (41%, 180min)	$COOH$ $CH_2CH_2CH_2-NH_2$ (5%, 180min)

* H_2-O_2 flame
** After hydrolysis

Therefore, this reaction provides a new process for a prebiotic
formation of α-amino acids:

$$R-\overset{O}{\overset{\|}{C}}-COOH \ + \ CH_3CONH_2 \longrightarrow CH_3CO-NH-\overset{\overset{H}{\underset{}{\overset{R}{|}}}{C}\ ||}{C}-COOH \xrightarrow[\text{HCOOH}]{\text{Flame}}$$

$$CH_3CO-NH-\overset{\overset{R}{|}}{\underset{}{C}H}-\overset{\overset{\overset{R}{|}}{CH-COOH}}{COOH} \ + \ CH_3CO-NH-\overset{\overset{R}{|}}{\underset{|}{C}}\overset{CH_2}{\underset{COOH}{}}-COOH \xrightarrow{H_3O^+}$$

$$H_2N-\overset{\overset{R}{|}}{\underset{}{C}H}-COOH \ + \ H_2N-\overset{\overset{R}{|}}{\underset{}{C}H}\overset{CH_2}{}-COOH$$

5. DEHYDROGENATION OF DIHYDROPYRIMIDINES

Formation of pyrimidines is reported through dehydrogenation
of dihydropyrimidines by using glow discharge electrolysis (1).
The flames also have the ability to bring about this reaction
(Table IV). The dehydrogenation was induced by an acetylene
flame as well. Since this flame could not introduce a hydroxyl
radical into water phase, the dehydrogenation of dihydro-
pyrimidines is considered to be caused by radicals other than
a hydroxyl radical.

Table IV Dehydrogenation of dihydropyrimidines

Substrate	Flame*	Product (Yield, React. Time)
Dihydrothymine	A	Thymine (2.4%, 60min)
Dihydrouracil	A	Uracil (3.9%, 90min)
Dihydro-6-methyl-uracil	A	6-Methyluracil (6.2%, 60min)
Dihydrothymine	B	Thymine (1.8%, 360min)

* A: H_2-O_2 flame, B: acetylene-O_2 flame

This study provides new experimental evidence of
aqueous phase reactions which are effected by reactive species
in a gas phase. The reaction stated here would be regarded as
a new model for formation of bioorganic molecules in the
primitive hydrosphere exposed to some radical-containing
atmosphere.

REFERENCE

1. K.Harada, J.Terasawa, and S.Suzuki, Naturwiss., 65, 259 (1978)