On the Oxidation of β-Aminopropionitrile. III

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In the previous papers of this series[1,2], the structure of a resinous oxidation product of β-aminopropionitrile was proposed. β-Aminopropionitrile was oxidized using either air or hydrogen peroxide as an oxidizing agent. In the previous paper[2], it was proposed that in the first step of this oxidation process β-aminopropionitrile was oxidized into β-hydroxylaminopropionitrile which was hydrolyzed to produce an acid amide compound and in the second step, these intermediates reacted to form a compound with azoxy group and -CONH- linkage.

In the present investigation, five different derivatives of β-aminopropionitrile were prepared and the effect of the substituents in the oxidation reaction was studied in addition to the identification of oxidation products of these derivatives and to the investigation of reaction mechanisms. These five derivatives of β-aminopropionitrile are as follows:

α-Methyl-β-aminopropionitrile	(I)
β-Methyl-β-aminopropionitrile	(II)
β-Ethylaminopropionitrile	(III)
β-Dimethylaminopropionitrile	(IV)
β-Methyl-α-aminopropionitrile	(V)

These derivatives did not undergo any change either on standing in the open air or by bubbling air through the materials. On the other hand, these materials were oxidized with hydrogen peroxide and the results are summarized in Table I. Hygroscopic materials were obtained as oxidation products of compounds I and II. These products are quite similar to the oxidation product of β-aminopropionitrile in their hygroscopic properties. The oxidation products of I and II have their softening points at 110°C. Their infrared absorption spectra are shown in Figs. 1 and 2.

As observed in the oxidation product of β-aminopropionitrile, an absorption band at

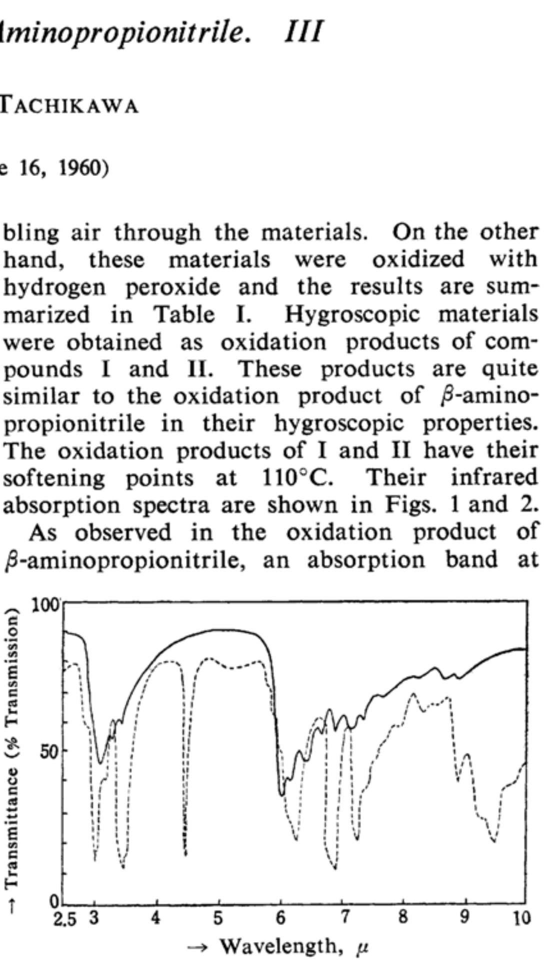

Fig. 1. Infrared absorption spectrum.
---- α-Methyl-β-aminopropionitrile
—— Oxidation product

TABLE I. PRODUCTS BY H_2O_2 OXIDATION

Amino-nitrile	Yield %	Property of the product	Analysis						
			Found			Calcd.			
			C	H	N	C	H	N	
I	45.2	Yellow hygroscopic solid	49.9	7.9	21.2	49.7	7.7	21.8	for $C_{16}H_{30}N_6O_5$
II	47.8	Yellow hygroscopic solid	49.2	7.8	21.0	49.7	7.7	21.8	for $C_{16}H_{30}N_6O_5$
III	No change	—							
IV	46.2	Needle crystal m. p. above 250°C	44.9	9.5	21.0	45.4	9.2	21.2	for $C_5H_{12}N_2O_2$
V	No change	—							

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[1] T. Tachikawa, This Bulletin, 33, 1181 (1960).

[2] T. Tachikawa, ibid., 34, 461 (1961).

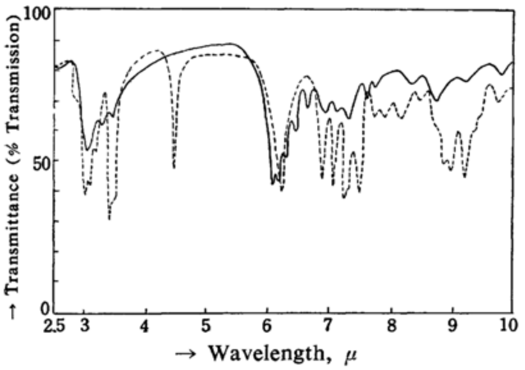
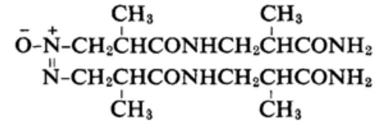


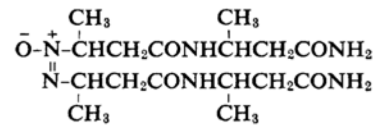
Fig. 2. Infrared absorption spectrum.
---- β-Methyl-β-aminopropionitrile
—— Oxidation product

4.5 μ due to C≡N stretching vibration disappeared and absorption bands at 3.1, 3.3, 3.4 and 6.5 μ which were caused by -CONH- vibrations and at 6.70 μ by the stretching vibration of an azoxy group appeared.

Accordingly, it seems reasonable to propose the following structures for their oxidation products:



$$\begin{array}{l} \overset{-}{\mathrm{O}}\text{-}\overset{+}{\mathrm{N}}\text{-}\mathrm{CH_2\overset{CH_3}{C}HCONHCH_2\overset{CH_3}{C}HCONH_2} \\ \quad\ \| \\ \quad\ \mathrm{N\text{-}CH_2\underset{CH_3}{C}HCONHCH_2\underset{CH_3}{C}HCONH_2} \end{array}$$

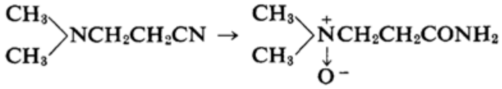


$$\begin{array}{l} \overset{-}{\mathrm{O}}\text{-}\overset{+}{\mathrm{N}}\text{-}\mathrm{\overset{CH_3}{C}HCH_2CONH\overset{CH_3}{C}HCH_2CONH_2} \\ \quad\ \| \\ \quad\ \mathrm{N\text{-}\underset{CH_3}{C}HCH_2CONH\underset{CH_3}{C}HCH_2CONH_2} \end{array}$$

The oxidation reaction of β-aminopropionitrile, proceeded at below 5°C to yield a viscous substance. On the contrary, it was necessary to raise the reaction temperature up to 20°C in the oxidation of compounds I and II. This means presumably that one methyl substituent introduced in β-aminopropionitrile interferes with the oxidation of an amino group.

A tertiary amino compound IV did not yield resinous material, but a crystalline substance in oxidation reaction. Recrystallization of this product from butanol gave a compound with melting point above 250°C and the composition, $C_5H_{12}N_2O_2$, which was obtained from its elemental analysis. The infrared absorption spectrum of this compound does not possess an absorption band at 4.5 μ due to C≡N stretching vibration, while the absorption bands, which correspond to C=O stretching vibration and NH_2 bending vibrations, appeared at 6.0 and 6.15 μ, respectively, as shown in Fig. 3. This result thus indicates the complete hydrolysis of the nitrile to the corresponding acid amide compound.

The strong absorption bands at 7.8 and 10.45 μ present a strong support to the presence of a *N*-oxide group in the molecule. These absorption bands were observed also by Parker[3] and Koelsch[4] to be caused by *N*-oxide vibrations. *N*, *N*-dimethyl-β-alanine was obtained by treating this compound with sodium hydrosulfite and hydrochloric acid. Thus, it is understood from these studies that the compound IV was transformed into β-dimethylaminopropioamide *N*-oxide as shown by the following equation:



$$\begin{matrix}\mathrm{CH_3}\\ \mathrm{CH_3}\end{matrix}\!\!>\mathrm{NCH_2CH_2CN} \rightarrow \begin{matrix}\mathrm{CH_3}\\ \mathrm{CH_3}\end{matrix}\!\!>\underset{\substack{\downarrow\\ \mathrm{O}^-}}{\overset{+}{\mathrm{N}}}\mathrm{CH_2CH_2CONH_2}$$

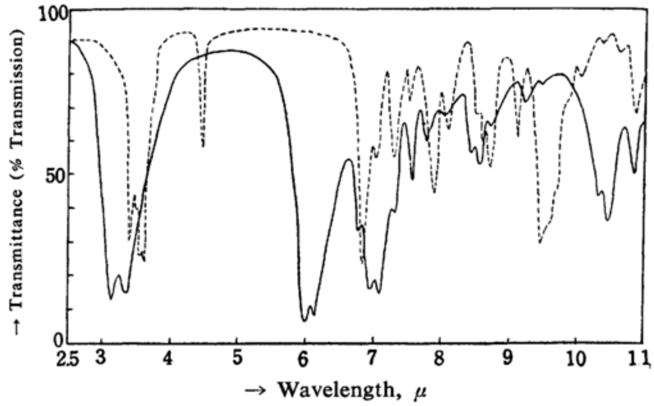


Fig. 3. Infrared absorption spectrum.
---- β-Dimethylaminopropionitrile
—— β-Dimethylaminopropionitrile *N*-oxide

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[3] E. D. Parker and A. Furst, *J. Org. Chem.*, **23**, 201 (1958).

[4] C. F. Koelsch and W. H. Gumprecht, *J. Org. Chem.*, 23, 1603 (1958).

From this fact it is clear that amino groups of these β-aminopropionitrile derivatives are not oxidized to aldehydes or ketones but to hydroxylamino groups.

β-Dimethylaminopropioamide *N*-oxide is comparatively unstable in the air and undergoes a gradual transformation into a reddish substance when it is stored in the air for a prolonged period. As Rogers[5] reported previously, phthalates of the *N*-oxides of β-dimethylaminopropionic esters or nitrile were prepared by the reaction of β-dimethylaminopropionic esters or nitrile with monoperphthalic acids. However, nothing has been reported about the synthesis of an *N*-oxide compound itself. It is very interesting to know that a new *N*-oxide was prepared in the present investigation. This *N*-oxide was prepared by hydrogen peroxide oxidation of the compound IV, a nitrile group which underwent hydrolysis simultaneously to yield an acid amide group. Since the compound V did not yield a resinous substance by the oxidation with hydrogen peroxide, it seems that β-aminonitrile compounds are oxidized with hydrogen peroxide by the mechanism as described in the previous paper[1], but α-aminonitrile compounds are not oxidized by the same mechanism.

Experimental

Preparation of α-Methyl-β-aminopropionitrile[6]. —Thirty-three grams of methacrylonitrile and 110 g. of 28% aqueous ammonia were placed in a Carius-type tube heated for 8 hr. at 70∼75°C. Then, unreacted methacrylonitriles which lay above an aqueous phase were separated. α-Methyl-β-aminopropionitrile, $n_D^{20.2}$ 1.4340, $d_4^{20.2}$ 0.9180, b. p. 76.5∼77.5°C/16.8 mmHg, was obtained from the aqueous phase; yield, 17.5 g.

Found: N, 33.63. Calcd. for $C_4H_8N_2$: N, 33.83%.

Preparation of β-Methyl-β-Aminopropionitrile[7]. —A Carius-type tube containing 41 g. of allyl cyanide and 200 g. of 28% aqueous ammonia was heated for one hour at 70°C. The reaction mixture became homogeneous after this treatment and then distilled in vacuo to give the product, β-methyl-β-aminopropionitrile; yield, 34.5 g., b. p. 84.7∼85.0°C/23 mmHg.

Preparation of β-Dimethylaminopropionitrile[8]. —This was prepared from 60 g. of 50% aqueous dimethylamine and 35 g. of acrylonitrile. Yield, 33.1 g., b. p. 83∼85°C/37 mmHg.

Preparation of β-Ethylaminopropionitrile[8]. — This was prepared from 70% aqueous ethylamine and 45.0 g. of acrylonitrile. Yield, 13.0 g., b. p. 78∼80°C/16 mmHg.

Preparation of α-Methyl-α-aminopropionitrile.— To a mixture containing 110 g. of acetonecyanhydrine and 400 ml. of methanol, ammonia gas was introduced at 15°C with stirring until the solution was saturated with ammonia. After being allowed to stand for 2 days in an ice bath, the reaction mixture was distilled in vacuo to yield α-methyl-α-aminopropionitrile; 35 g., b. p. 48.7∼50.2°C/12 mmHg.

Oxidation Reaction with Hydrogen Peroxide.— Twenty-five per cent hydrogen peroxide was added dropwise to aminonitrile placed in a 100 ml. flask equipped with a thermometer, a dropping funnel and a capillary, keeping the reaction temperature below 5°C. This reaction proceeded under reduced pressure to remove ammonia gas. After the addition of hydrogen peroxide was completed, the reaction temperature was raised gradually up to 50°C, and the ammonia and water were removed. Unreacted aminonitrile was also displaced from the reaction mixture by treating it with anhydrous acetone. When β-dimethylaminopropionitrile was employed as an aminonitrile compound and treated as described above at 50°C, a crystalline product was obtained. Recrystallization of this product from butanol gave glittering needle-like crystals.

Reduction and Hydrolysis of the β-Dimethylaminopropioamide *N*-Oxide. — β-Dimethylaminopropioamide *N*-oxide (13.2 g.) in 50 cc. methanol was boiled with 30% hydrochloric acid (20 g.) for an hour. After cooling and basification with aqueous sodium hydroxide, the reacted solution was stirred with sodium hydrosulfite (25 g.) for 2 hr. at room temperature. The reacted solution was acidified with hydrochloric acid and evaporated at reduced pressure. The residue was extracted with cold ethanol. Evaporation of the ethanol left a crystalline residue which was recrystallized from ethanol and formed leaflets (8.6 g.) m. p. 186.5∼188°C[9]. The melting point was not depressed by admixture with *N*, *N*-dimethyl-β-alanine hydrochloride.

Infrared Absorption Spectrum.—A sample of the oxidation products of the compounds I and II were dissolved in methanol to obtain 3% solution. Then, a piece of thin film was prepared on a cell by evaporating methanol from the solution. The potassium bromide disk method was employed to prepare a sample of the oxidation product of IV.

The Perkin-Elmer model 21 spectrophotometer was used to obtain spectral data.

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5) M. A. T. Rogers, *J. Chem. Soc.*, **1955**, 769.

6) J. B. Dickey, U. S. Pat. 2659739 (1953); *Chem. Abstr.*, **48**, 3036 (1954).

7) B. Bruyland, *Bull. soc. chim. Belg.*, **32**, 257.

8) F. C. Whitmore and H. S. Mosher, *J. Am. Chem. Soc.*, **66**, 725 (1944).

9) T. L. Gresham et al., ibid., **73**, 3168 (1951).