7), a 10-ml. portion of $0.1N$ sodium hydroxide was added to raise the pH to about 8. An exothermic reaction developed and slight cooling was needed to maintain the temperature at 25–30°. At the end of 3 hr., 95% of the peroxide had been consumed; 0.04 mole of oxygen had been evolved.

After concentration under vacuum at 60° and 5 mm. (final pressure), the residue was diluted with chloroform, chilled, and the crude benzamide (83 g., m.p. 120–125°) collected by filtration. Reconcentration of the filtrate followed by Claisen distillation gave 86 g. of crude pyridine *N*-oxide, b.p. 90–100° (<1 mm.), contaminated with a small amount of benzamide. The latter was removed by dissolving the crude *N*-oxide in water and chilling to precipitate 8 g. The aqueous filtrate was extracted with chloroform, concentrated under vacuum, and Claisen-distilled to give 75 g. (79% yield based on hydrogen peroxide) of purified pyridine *N*-oxide, b.p. 115–120° (5 mm.) [lit.,[16] b.p. 138–140° (15 mm.)]; the product crystallized to a solid white mass.

Anal. Calcd. for C_5H_5NO: C, 63.1; H, 5.3. Found: C, 62.7; H, 5.6.

Oxidation of aniline. To a stirred solution of 18.6 g. (0.20 mole) of freshly distilled aniline and 41 g. (1.0 mole) of acetonitrile in 300 ml. of methanol held at 50° was added 0.60 mole of 50% hydrogen peroxide over a 1-hr. period. The true pH of about 8 was maintained by the addition of $1N$ sodium hydroxide, the meter pH was 9.5. After an additional 3 hr., iodometric titration indicated the presence of 0.26 mole of peroxide. No oxygen was evolved. Palladium on charcoal catalyst was added to decompose the excess peroxide during an overnight stand in the refrigerator. After filtration, followed by concentration under vacuum to a volume of 75 ml., the residue was extracted with ether. The ether extract was washed, dried, and concentrated to a constant weight of 18 g. Recrystallization from a small volume of acetone–petroleum ether (b.p. 30–60°) afforded 12.3 g. (62% yield) of azoxybenzene, m.p. and mixed m.p. 34–35°.

Reaction of benzonitrile with hydrogen peroxide in the absence of added substrate. A solution of 51.6 g. (0.50 mole) of benzonitrile and 34.0 g. (0.50 mole) of 50.1% hydrogen peroxide in 250 ml. of methanol was stirred at 35° ± 2° while $1.09N$ sodium hydroxide was added to maintain a *meter* pH of 9.3–9.5. After 1.5 hr. the reaction was 64% complete by iodometric titration and the pH was then held at 9.7–9.9. At the end of 4 hr. total time, the reaction was 94% complete. After an overnight stand at room temperature without further alkali addition, it was 98% complete. Oxygen evolution, as measured by a calibrated wet test meter, amounted to 0.228 mole. Sodium hydroxide consumption was 32 ml. or 0.035 mole.

In order to recover benzamide quantitatively, the reaction mixture was concentrated under vacuum to a dry residue. This was boiled with chloroform, and insoluble material was removed by filtration. Dilution of the filtrate with excess petroleum ether (b.p. 30–60°) caused 28.5 g. (0.235 mole) of benzamide to precipitate; m.p. 126–127°. The yield of amide based on hydrogen peroxide charged was 94%.

EMERYVILLE, CALIF.

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[16] E. Ochiai, *J. Org. Chem.*, 18, 534 (1953).

[CONTRIBUTION FROM THE SHELL DEVELOPMENT CO.]

Reactions of Hydrogen Peroxide. VIII. Oxidation of Isopropylidenemalononitrile and Ethyl Isopropylidenecyanoacetate

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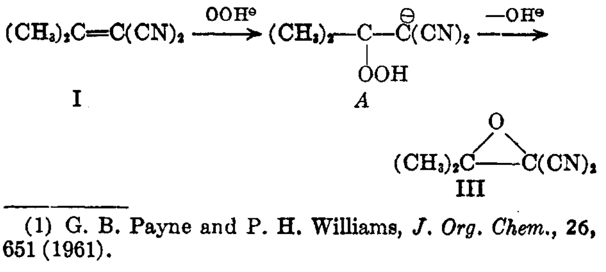
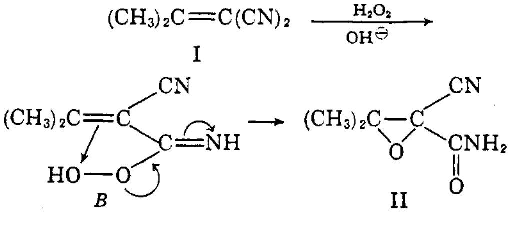
Received April 20, 1960

Isopropylidenemalononitrile and ethyl isopropylidenecyanoacetate were found to react readily with hydrogen peroxide under controlled pH conditions to produce substituted epoxyamides as major products. Also isolated were the corresponding epoxydinitrile and α-cyano epoxy ester. Different reaction mechanisms are proposed to account for the two types of products obtained.

In a continuation of studies concerned with the reactions of hydrogen peroxide under controlled pH conditions, isopropylidenemalononitrile (I) and ethyl isopropylidenecyanoacetate (VIII) were selected as materials considered likely to give products other than epoxyamides.[1] It was originally felt, for example, that I would most likely give the simple epoxide (III) *via* the highly resonance-stabilized carbanion *A:*

Isopropylidenemalononitrile. The reaction of I with hydrogen peroxide was carried out in methanol solution by adding dilute sodium hydroxide at such a rate as to require ice bath cooling of the mixture. This occurred at pH 5–6, and the reaction was complete in about one hour at 25°. In the case where 90% hydrogen peroxide was used as oxidant, peroxide consumption amounted to 1.14 moles per mole of dinitrile. Surprisingly, the major product (69% yield) was again[1] found to be an epoxyamide (II). Epoxydinitrile (III) was also secured, but only in 9% yield.





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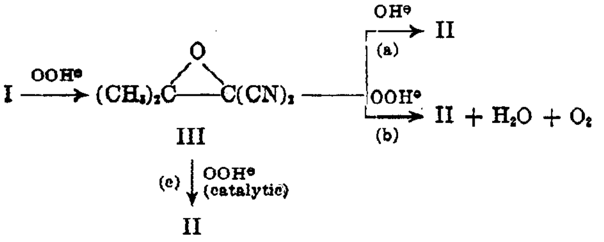
[1] G. B. Payne and P. H. Williams, *J. Org. Chem.*, 26, 651 (1961).

The formation of II from I is considered most likely to proceed *via B*, a substituted peroxyacrylimidic acid. This, of course, is analogous to the intermediate postulated earlier[1] for the conversion of acrylonitrile to glycidamide.

Another possible route to II would be *via* hydrolysis of III:



Since very little oxygen was evolved during the operation, a Radziszewski reaction (b)[2] could not account for the formation of II. Furthermore, the stoichiometry by (b) would be 2:1, hydrogen peroxide to I. An experimental value of nearly 1:1 was already noted.

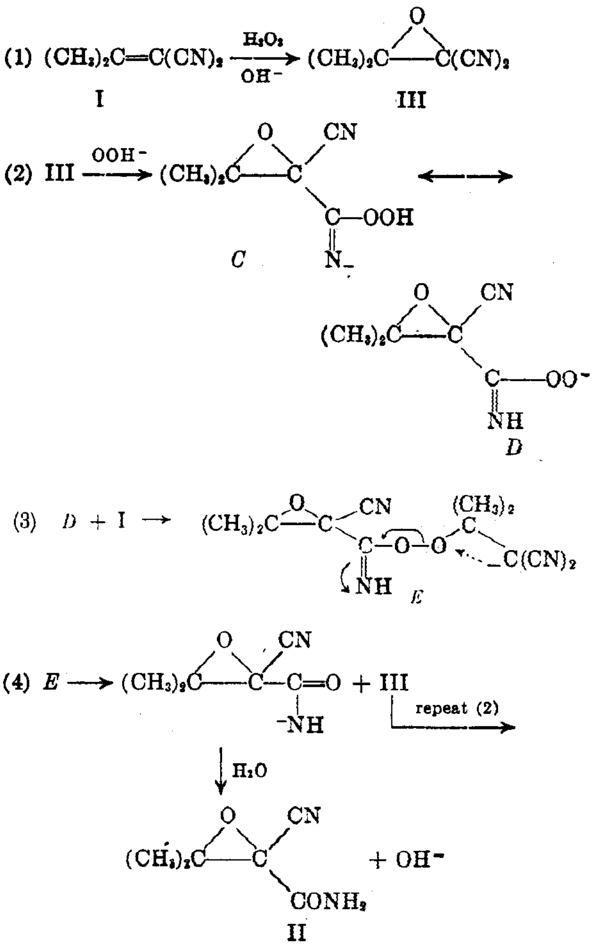
It was conceivable, of course, that III might be particularly prone to hydrolysis and give II by paths (a) or (c) not involving consumption of hydrogen peroxide.

In order to prepare sufficient III for a study of its stability, I was epoxidized by means of alkaline *t*-butyl hydroperoxide.[3] A 59% yield of methyl 3-methyl-2,3-epoxy-2-cyanobutyrimidate (IV) was secured when the reaction was carried out in methanol. With benzene as solvent, however, a 45% yield of III resulted. The imino ester (IV) could also be prepared from III by base-catalyzed reaction with methanol (Fig. 1).

In order to check path (a) as a possible route to II, the epoxydinitrile was subjected to the original reaction conditions, except for the substitution of water for hydrogen peroxide. While no II was isolated, the recovered starting material was contaminated with 30% of IV as determined by a basicity value.

Path (c) was investigated by allowing equimolar amounts of III and hydrogen peroxide to react under the original conditions. The low (20%) yield of crude II obtained indicated that this path was not an important one for the formation of II from I.

It was also considered possible that II might be produced by the following sequence:



The key intermediate is again the epoxydinitrile, III. Once generated (step 1), it might be expected, because of activation by the electron-withdrawing α-oxygen atom, to undergo preferential reaction with the perhydroxyl ion (step 2) to give an anion of the corresponding peroxyimidic acid (*C* and *D*). The latter (*D*) might then undergo nucleophilic attack on the starting material (step 3) to give a reasonance-stabilized intermediate *E*. Breakdown of *E* in the manner indicated would give (step 4) epoxy amide II, along with a molecule of III for recycle to step 2.

Evidence relative to this mechanism was secured by allowing an 80:20 mixture of I and III to react under the conditions used for I alone. If III were, indeed, an important intermediate in the formation of II from I, one might reasonably expect a substantially higher yield of II in the case where III was present initially. Such was not the case. The yield of epoxyamide was actually slightly lower (63% *vs.* 67% in comparable experiments).

When the epoxydinitrile (III) was allowed to react with hydrogen peroxide in the presence of cyclohexene, a significant yield (23%) of cyclohexene oxide was obtained. This indicates that the peroxyimidic acid intermediate produced from III exhibits *electrophilic* character. It seems unlikely

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(2) The reaction of the nitrile with two moles of hydrogen peroxide to give amide, water, and oxygen. *Cf.* B. Radziszewski, Ber., **17**, 1289 (1884). See also K. Wiberg, *J. Am. Chem. Soc.*, **75**, 3961 (1953).

(3) N. C. Yang and R. A. Finnegan, *J. Am. Chem. Soc.*, **80**, 5845 (1958); G. B. Payne, *J. Org. Chem.*, **25**, 275 (1960).

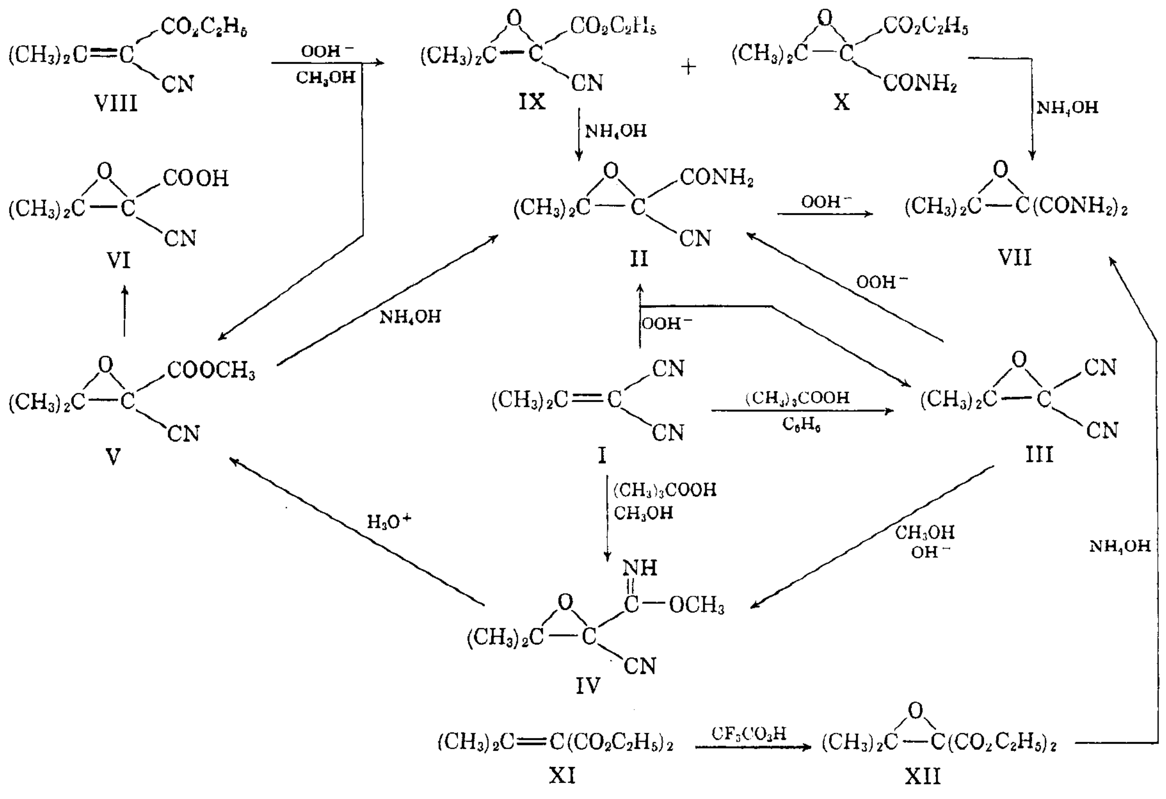

Figure 1

that this same intermediate would also be capable of the *nucleophilic* attack required by step 3.

The foregoing evidence, although admittedly of a negative type, is taken as support for the view that II is formed *via* cyclic intermediate *B*.

Ethyl isopropylidenecyanoacetate. The epoxidation of ethyl isopropylidenecyanoacetate (VIII) proceeded at a somewhat higher *p*H to give the corresponding epoxyamide (X) in 37% yield and the epoxynitrile (IX) in 30% yield. The relatively large amount of latter type of product is explainable on the basis of the greater similarity of VIII to an α, β-unsaturated diester; the latter, of course, gives a simple epoxide.[4]

Analysis of Claisen-distilled IX indicated that about one half of it was the *methyl* ester (V). Careful fractional distillation did not allow a separation, however, and no further attempt was made to secure a homogeneous product. This mixture of esters gave the same epoxy amide (II) on treatment with ammonia.

The formation of methyl ester from ethyl must have resulted from trans-esterification. It has been observed, for example, that ethyl crotonate, on epoxidation by acetonitrile-hydrogen peroxide[5] in methanol solution at *p*H 8, gives mainly the *methyl* ester of 2,3-epoxybutyric acid.[6]

For further confirmation of structure of the products obtained from I and VIII, II and X were both converted to the same epoxydiamide (VII). An alternate synthesis of VII was achieved by first epoxidizing diethyl isopropylidenemalonate (XI) with peroxytrifluoroacetic acid and then treating the resulting epoxy diester (XII) with ammonia.

EXPERIMENTAL[7]

Epoxidation of isopropylidenemalononitrile. A. *In aqueous methanol using 30% hydrogen peroxide.* To a 1-l., five-neck round-bottom flask equipped with stirrer, thermometer, two dropping funnels, condenser, and *p*H electrodes were charged 200 ml. of methanol, 50 ml. of water, and 86.5 g. (0.75 mole) of 29.6% hydrogen peroxide. The meter *p*H was adjusted to 6.5 with *N* sodium hydroxide and maintained at 6.5–6.7 as a solution of 53 g. (0.50 mole) of isopropylidenemalononitrile[8] in 50 ml. of methanol was added dropwise with stirring and cooling at 20–25° over a 25-min. period (*p*H by indicator paper *ca.* 5.5). After an additional 10 min., iodometric titration indicated a consumption of 0.61 mole of peroxide. After another hour, the consumption leveled at 0.71 mole. Alkali utilized in maintaining the desired *p*H was 0.052 equiv; oxygen evolution, as measured by a wet test meter, amounted to 0.023 mole.

The reaction mixture, containing precipitated product was diluted with 300 ml. of water, chilled, and filtered to give 40 g. of essentially pure 3-methyl-2-cyano-2,3-epoxybutyramide (II), m.p. 150.5–151°. Filtrate, after concentration to about 200 ml., gave another 7 g. of product, m.p. 149–150°. The combined yield on the two crops was 67%. A sample was recrystallized from methanol prior to analysis; m.p. 151–151.5°.

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[4] G. B. Payne, *J. Org. Chem.*, **24**, 2048 (1959).

[5] G. B. Payne, P. H. Deming, and P. H. Williams, *J. Org. Chem.*, **26**, 659 (1961).

[6] Unpublished results, Shell Development Company.

[7] All melting and boiling points are uncorrected.

[8] F. S. Prout, *J. Org. Chem.*, **18**, 928 (1953).

Anal. Calcd. for $C_6H_8N_2O_2$: C, 51.4; H, 5.8; N, 20.0. Found: C, 51.5; H, 5.8; N, 19.7.

When the reaction was repeated using a mixture of 0.40 mole of isopropylidenemalononitrile and 0.10 mole of epoxydinitrile (III) (in place of 0.50 mole of unsaturated dinitrile alone) and 0.60 mole of hydrogen peroxide, the two crops weighed 37.8 g. and 6.4 g. (63% yield) and had m.p. 149–151° and 145–148°, respectively.

B. *In methanol using 90% hydrogen peroxide.* The reaction was carried out as above using 400 ml. of methanol as solvent and 22.8 g. (0.60 mole) of 90% hydrogen peroxide as oxidant. A meter *p*H of 7.4–7.6 was maintained by the addition of *N* methanolic sodium hydroxide. Five minutes after the end of dinitrile addition, titration showed 0.04 mole of peroxide remaining; 20 min. later, 0.03 mole remained. Excess peroxide was decomposed by 10% palladium on charcoal catalyst and the mixture was concentrated under vacuum at room temperature. Three successive crops of crystalline epoxyamide were taken: 31.3 g., 8.8 g., and 8.4 g., m.p. 150–151°, 149–151°, and 146–149°, respectively. The yield of combined products amounted to 69% based on unsaturated dinitrile. Filtrate from the third crop was Claisen-distilled at 1 mm. to give only 1 g., b.p. 45–50° and 16 g. of residue.

In a duplicate experiment the work-up was modified. After taking the first large crop of epoxyamide, the filtrate was diluted with 500 ml. of water and extracted with five 100-ml. portions of chloroform. After the usual washing, drying, and concentration, the residue was Claisen-distilled to give 5.5 g. (9% yield) of 3-methyl-2-cyano-2,3-epoxybutyronitrile (III), b.p. 53–54° (5 mm.), n_D^{20} 1.4261. The infrared spectrum of the material was identical with that of the product obtained from the reaction of isopropylidenemalononitrile with alkaline *t*-butyl hydroperoxide.

Methyl 3-methyl-2,3-epoxy-2-cyanobutyrimidate (IV). To a 1-l., round-bottom flask were charged 400 ml. of methanol, 132 g. (1.1 moles) of 75% *t*-butyl hydroperoxide (Lucidol) and 20 ml. of 0.5*N* methanolic sodium hydroxide. A solution of 106 g. (1.0 mole) of isopropylidenemalononitrile[8] in 100 ml. of methanol was added dropwise with stirring at 35–40° over 1.5 hr. In order to maintain *p*H 8 throughout the addition, it was necessary to add two more 10-ml. portions of alkali at 0.5 hr. intervals.

After another 20 min., an iodometric titration indicated the consumption of 1.07 moles of oxidant. The mixture was poured into 1.5 l. of water and extracted with three 200-ml. portions of chloroform. The combined chloroform was washed, dried, concentrated under vacuum, and Claisen-distilled to give 91 g. (59%) of methyl 3-methyl-2,3-epoxy-2-cyanobutyrimidate, b.p. 46–48° (0.4 mm.), n_D^{20} 1.4427.

Anal. Calcd. for $C_7H_{10}N_2O_2$: C, 54.5; H, 6.5; N, 18.2. Found: C, 54.5; H, 6.6; N, 18.0.

Useful bands in the infrared were at 3.00 (—NH), 4.43 (C≡N), 5.94μ (C=NH), as well as at 10.80 and 11.60μ (epoxide).[9]

Methyl 3-methyl-2,3-epoxy-2-cyanobutyrate (V). A 38.5-g. (0.25 mole) sample of imino ester[10] was shaken for 0.5 hr. with a mixture of 50 ml. of water, 50 g. of crushed ice, and 71 ml. of 3.66*N* sulfuric acid (0.26 equiv.). After seeding, the mixture was shaken 5 min. longer, filtered, and the solid product washed well with water. After vacuum drying at room temperature there was secured 36.8 (95%) of methyl 3-methyl-2,3-epoxy-2-cyanobutyrate, m.p. 41–42°. Recrystallization from petroleum ether (b.p. 40–60°) did not affect the melting point.

Anal. Calcd. for $C_7H_9NO_3$: C, 54.2; H, 5.9; sapon. equiv., 155. Found: C, 54.3; H, 5.9; sapon. equiv., 159.[11]

3-Methyl-2,3-epoxy-2-cyanobutyronitrile (III). To a stirred solution of 0.55 mole of 97% *t*-butyl hydroperoxide in 300 ml. of benzene was added 1 ml. of a 35% methanolic solution of benzyl trimethylammonium hydroxide ("Triton B"; Mid-West Laboratories). There was then added dropwise over 0.5 hr. at room temperature 53 g. (0.50 mole) of isopropylidenemalononitrile. Four more 1-ml. portions of catalyst were added at 0.5-hr. intervals and the mixture was allowed to stand overnight. Iodometric titration indicated the reaction to be 94% complete, so the solution was washed, dried, concentrated under vacuum, and Claisen-distilled to give 27.6 g. (45%) of 3-methyl-2,3-epoxy-2-cyanobutyronitrile, b.p. 52–54° (5 mm.), n_D^{20} 1.4238.

Anal. Calcd. for $C_6H_6N_2O$: C, 59.0; H, 5.0; N, 22.9. Found: C, 59.3; H, 5.0; N, 22.8.

Useful bands in the infrared were at 4.42μ (C≡N) and at 10.76 and 11.51μ (epoxide).

Ammonolysis of methyl 3-methyl-2,3-epoxy-2-cyanobutyrate (V). A 3.0-g. portion of epoxy ester was ground to a fine powder and shaken 15 min. with 25 ml. of concd. aqueous ammonia. The solid was observed to dissolve, followed shortly thereafter by precipitation of the product, 3-methyl-2,3-epoxy-2-cyanobutyramide (II), m.p. 150–151°, weight 0.7 g. Another 0.6 g. was secured by concentration and chilling, m.p. 150–151°. A mixed melting point with the product from isopropylidenemalononitrile and hydrogen peroxide was not depressed. A comparison of infrared spectra also showed the materials to be identical.

Saponification of methyl 3-methyl-2,3-epoxy-2-cyanobutyrate (V). A 5.13-g. sample of methyl ester was dissolved in 50 ml. of methanol, treated with 62.5 ml. of 0.52*N* sodium hydroxide (0.032 equivalent), and allowed to stand for 2 days at room temperature. The mixture was then treated with 4.2 ml. of 7.41*N* sulfuric acid (0.031 equivalent) and concentrated *in vacuo* on the water bath. The aqueous concentrate, after saturation with ammonium sulfate, was extracted with two 150-ml. portions of ether. The combined ether was washed with saturated ammonium sulfate, dried, and concentrated to low volume on the steam bath. Recrystallization from ether–petroleum ether (b.p. 40–60°) afforded 1.2 g. of 3-methyl-2,3-epoxy-2-cyanobutyric acid (VI), m.p. 106–108°.

Anal. Calcd. for $C_6H_7NO_3$: C, 51.1; H, 5.0; N, 9.9; neut. equiv., 141. Found: C, 51.3; H, 5.1; N, 9.8; neut. equiv., 142.

Methanolysis of 3-methyl-2,3-epoxy-2-cyanobutyronitrile (III). A solution of 5 ml. of epoxydinitrile in 25 ml. of methanol was treated with 2 drops of 1*N* methanolic sodium hydroxide. The solution warmed from 23° to 39° and the addition of 2 more drops of sodium hydroxide had no further effect on the temperature. After 10 min., 2 drops more were added and the solution was warmed to 50° on the steam bath and allowed to cool to room temperature over 0.5 hr. The mixture was treated with carbon dioxide to neutralize any residual sodium hydroxide and then Claisen-distilled at 1 mm. to give 2.4 g. of pre-cut, b.p. 45–47°, n_D^{20} 1.4374 and 2.1 g. of methyl 3-methyl-2,3-epoxy-2-cyanobutyrimidate (IV), b.p. 47–49°, n_D^{20} 1.4428. The latter was identified on the basis of boiling point, refractive index, infrared spectrum, and by virtue of its hydrolysis with dilute sulfuric acid to methyl 3-methyl-2,3-epoxy-2-cyanobutyrate (V), m.p. 41–42°. A mixed melting point with the product made above was not depressed.

Hydrolysis of 3-methyl-2,3-epoxy-2-cyanobutyramide (II). To a solution of 14.0 g. (0.10 mole) of II in 300 ml. of 50% methanol-water was added 33.2 g. (0.30 mole) of 30% hydrogen peroxide. The mixture was held at 40° while *N* sodium hydroxide was added dropwise with stirring to maintain a true *p*H of 8. After 1.5 hr., 47 ml. of alkali had been utilized, 0.05 mole of oxygen had been evolved, and 0.13 mole of peroxide remained (iodometric titration). After

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[9] J. Bomstein, *Anal. Chem.*, **30**, 544 (1958) reports characteristic epoxide absorption in the region 10.5–12.3μ.

[10] Redistilled through a 0.7 × 50 cm. spiral-packed column; b.p. 63–64° (3 mm.), n_D^{20} 1.4424. When not redistilled, it was difficult to obtain a high yield of crystalline product.

[11] Excess 0.1*N* sodium hydroxide at room temperature for 15 min.

another 1.5 hr., no more alkali had been consumed, but the oxygen evolution amounted to 0.065 mole.

The 8.4 g. (53%) of 3-methyl-2,3-epoxy-2-carbamylbutyramide (VII) which had precipitated was recovered by filtration, washed with water, and dried. It melted at 251–252° dec. after being placed on an aluminum block previously heated to 225°; it turned brown about 240°. A mixed melting point with the product from X and ammonium hydroxide (see below) was not depressed.

Anal. Calcd. for $C_6H_{10}N_2O_3$: C, 45.6; H, 6.4; N, 17.7. Found: C, 45.6; H, 6.4; N, 17.7.

Epoxidation of ethyl isopropylidenecyanoacetate (VIII) To a 1-l., round-bottom flask equipped as in the first experiment were charged 400 ml. of methanol and 0.57 mole of 50% hydrogen peroxide. After adjustment of the meter *p*H to 9.5–10.0 with *N* sodium hydroxide, a solution of 80 g. (0.52 mole) of ethyl isopropylidenecyanoacetate[8] in 50 ml. of methanol was added over 30 min. at 35–40°; ice cooling was needed. After an additional 10 min., iodometric titration indicated that consumption of 1 molar equivalent of peroxide; 30 ml. of sodium hydroxide had been used.

After concentration under vacuum to a volume of 200 ml., the residue was diluted with 200 ml. of water and extracted with three 150-ml. portions of chloroform. After washing with saturated ammonium sulfate solution and drying, the solution was concentrated under vacuum to a constant weight of 72 g. Recrystallization from acetone–petroleum ether (b.p. 40–60°) gave 33 g. of 3-methyl-2,3-epoxy-2-carbethoxybutyramide (X), m.p. 102–103°. A second crop amounted to 3 g., m.p. 101–102° (37% total yield).

Anal. Calcd. for $C_8H_{14}NO_4$: C, 51.1; H, 7.4. Found: C, 51.1; H, 7.0.

Filtrate from the second crop was concentrated on the steam bath and then Claisen-distilled to give 25.6 g. (30%) of product, b.p. 67–68° (2 mm.); n_D^{20} 1.4356. Analysis indicated it to be a mixture of about equal parts of ethyl 3-methyl-2,3-epoxy-2-cyanobutyrate (IX) and the corresponding methyl ester (V). Redistillation through a 0.7 × 50 cm. spiral-packed column did not afford a separation.

Anal. Calcd. for 1:1 mixture of $C_8H_{11}NO_3$ and $C_7H_9NO_3$: C, 55.5; H, 6.2; N, 8.7. Found: C, 55.4; H, 6.2; N, 8.7.

An infrared spectrum of the mixture was found to be essentially identical with that found for pure methyl ester (V) except for the presence of two minor peaks at 9.86 and 11.67μ

Treatment of a small sample of the mixture with concentrated aqueous ammonia gave 3-methyl-2,3-epoxy-2-cyano butyramide (II), m.p. and mixed m.p. 150–151°.

Reaction of a sample of the epoxyamide (X) isolated above with ammonium hydroxide for 1 hr. at room temperature gave 3-methyl-2,3-epoxy-2-carbamylbutyramide (VII), m.p. 251–252° dec. A mixed melting point with the product obtained from II and hydrogen peroxide was not depressed; neither was the mixed melting point with the compound prepared from epoxy diester (XII; see below).

Stability of 3-methyl-2,3-epoxy-2-cyanobutyronitrile (III) *to methanol at pH 6.* A solution of 18.3 g. (0.15 mole) of III in 300 ml. of methanol containing 10 ml. of water was maintained at *p*H 6 for 1 hr. at room temperature by the addition of 0.1*N* methanolic sodium hydroxide. The mixture was diluted with water, extracted with chloroform, and the latter processed in the usual manner. Claisen-distillation gave 16.2 g. b.p. 45–60° (5 mm.), n_D^{20} 1.4308. By interpolation of refractive indices, the product was indicated to be a mixture composed of 69% starting material and 31% epoxy imino ester (IV).

A basicity value was secured by allowing a sample to stand with excess 0.1*N* hydrochloric acid for 20 min. and back titrating with 0.1*N* sodium hydroxide. The value obtained indicated the presence of 30% of IV.

Reaction of 3-methyl-2-cyano-2,3-epoxybutyronitrile (III) *with hydrogen peroxide.* To a solution of 18.3 g. (0.15 mole) of III in 300 ml. of methanol and 10 ml. of water was added dropwise over 0.5 hr. 0.15 mole of 30% hydrogen peroxide The *p*H was maintained at 6 by the addition of 1*N* sodium hydroxide. At the end of the peroxide addition, iodometric titration indicated that 0.07 mole had been consumed; 0.5 hr. later the consumption amounted to 0.09 mole. Only 0.005 mole of oxygen had been evolved and 0.024 mole of alkali consumed.

The reaction mixture was vacuum-flashed to give a residue which was stabilized at 40° and 2 mm. Recrystallization of the 18 g. from methanol-water gave 3.4 g. of 3-methyl-2-cyano-2,3-epoxybutyramide (II), m.p. and mixed m.p. 147–149°.

Since no second crop could be obtained, the solution was diluted with water and extracted with five 100-ml. portions of chloroform. Claisen-distillation of the combined chloroform gave 3.7 g. of product, b.p. 40–55° (2 mm.), n_D^{20} 1.4307, and 2.0 g. of residue which did not crystallize from methanol-water. A basicity value on the distillate indicated the presence of 20% of methyl 3-methyl-2-cyano-2,3-epoxybutyrimidate (IV). The remaining 80% was assumed to be recovered starting material.

The water layer from the chloroform extraction was concentrated under vacuum to an amorphous gummy solid, weighing 9 g. This material was very water-soluble; all of it dissolved in 25 ml. of water. Long chilling gave another 0.9 g. of crude epoxyamide (II), m.p. 142–150°. The total yield of II was therefore 4.3 g., or 0.030 mole; this corresponds to a yield of 20% based on epoxydinitrile charged.

Reaction of III *with hydrogen peroxide in the presence of cyclohexene.* The above eaction was repeated in the presence of 18 g. (0.22 mole) of cyclohexene. At the end of 2 hr. at a meter *p*H of 6.5, 0.03 mole of peroxide remained and consumption was then very slow. No oxygen was evolved, but 0.018 mole of alkali was utilized in maintaining the desired *p*H.

The mixture was vacuum-flashed at room temperature to give an oily residue of 20 g. Volatile material, collected in a trap cooled by Dry Ice–acetone, was titrated for oxirane oxygen; 0.028 mole (23% yield based on peroxide consumed) of cyclohexene oxide was indicated.

Recrystallization of the 20 g. of residue from 25 ml. of methanol gave 4.5 g. (21% yield) of crude 3-methyl-2-cyano-2,3-epoxybutyramide, m.p. 138–147°; mixed m.p. 143–148°. A second crop was obtained by dilution with an equal volume of water followed by chilling; it weighed 0.9 g. (26% total yield) and had m.p. 140–148°.

Epoxidation of diethyl isopropylidenemalonate (XI) The procedure used was that described in the literature for epoxidizing ethyl crotonate.[12] To a 500-ml. round-bottom flask were charged 40 g. (0.20 mole) of diethyl isopropylidenemalonate[13] (b.p. 99–100°/5 mm.; n_D^{20} 1.4494), 200 ml. of methylene chloride and 108 g. of disodium hydrogen phosphate. The mixture was stirred vigorously while 100 ml. of 2.38*M* peroxytrifluoroacetic acid in methylene chloride was added over 40 min. During the addition, the temperature rose from 35° to 44° (gentle reflux). After an additional hour at gentle reflux, the mixture was cooled; an iodometric titration indicated that very little peroxy acid remained. The mixture was shaken with water, washed with dilute sodium bicarbonate, again with water, and dried over magnesium sulfate. After removal of solvent on the steam bath, the residue was distilled very slowly through a 0.7 × 50 cm. glass spiral-packed column at 5 mm. to give 15.8 g. of recovered starting material, b.p. 96–100° (n_D^{20} 1.4470), 6.7 g. of intermediate, b.p. 100–108° (n_D^{20} 1.4392) and 12.4 g. (46% based on unrecovered starting ester) of ethyl 3-methyl-2,3-epoxy-2-carbethoxybutyrate (XII), b.p. 108–110° (n_D^{20} 1.4335).

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(12) W. D. Emmons and A. S. Pagano, *J. Am. Chem. Soc.*, **77**, 89 (1955).

(13) A. C. Cope and E. M. Hancock, *J. Am. Chem. Soc.*, **60**, 2644 (1938).

Anal. Calcd. for $C_{10}H_{16}O_5$: C, 55.5; H, 7.5; sapon. equiv., 108. Found: C, 55.6; H, 7.5; sapon. equiv., 109.

The infrared spectrum showed ester carbonyl absorption at 5.71μ and no unsaturation at 6.07μ (characteristic of the starting material).

A 2-g. sample of epoxy diester was shaken for 1 hr. with 25 ml. of concd. aqueous ammonium hydroxide to give 1.3 g. of 3-methyl-2,3-epoxy-2-carbamylbutyramide (VII), m.p. 250–251° (dec.; placed on block at 225°). Recrystallization from hot water gave material with m.p. 251–252° dec.

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[CONTRIBUTION FROM THE SHELL DEVELOPMENT CO.]

Reactions of Hydrogen Peroxide. IX. Oxidation of Cyanopyridines

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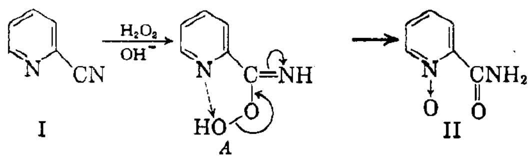
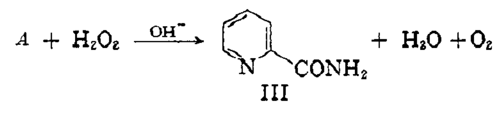
Received April 20, 1960

Reaction of the three isomeric cyanopyridines with hydrogen peroxide was carried out at *p*H 7.5–8. The 2- and 3-isomers gave the corresponding amide 1-oxides in 70 and 44% yields, respectively. The 4-isomer, on the other hand, gave the simple amide as the major product in 45% yield. These results are discussed from the point of view of reaction mechanism.

2- and 4-Cyanopyridines. It was expected, on the basis of the facile oxidation of pyridine by benzonitrile–hydrogen peroxide at *p*H 8,[1] that 2-cyanopyridine (I) might react with hydrogen peroxide under controlled conditions to give 2-picolinamide-1-oxide (II). It was felt that the reaction would probably proceed *via* a cyclic intermediate (*A*) similar to that postulated for the oxidation of acrylonitrile by hydrogen peroxide[2]:

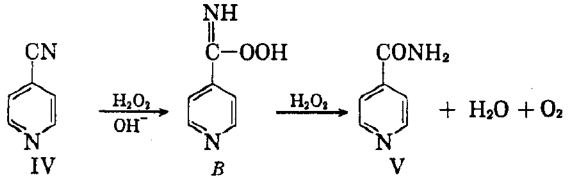


When I was treated with one mole of hydrogen peroxide at *p*H 7.5–8, 96% of the theoretical amount of oxidant was consumed in 2 hours at 35–40°. Only 2 mole % of oxygen was evolved; this indicated that very little of the following type of amide hydrolysis was occurring[3]:



Investigation of the reaction mixture did, indeed, lead to II as the only product isolated (70% yield).

When 4-cyanopyridine (IV) was substituted for the 2-isomer, it was found to react at approximately the same rate.[4] In contrast, however, 1.36 molar equivalents of hydrogen peroxide were consumed and a substantial oxygen evolution indicated a large amount of Radziszewski reaction to be occurring:



From the reaction mixture, V was isolated in 45% yield. Also secured was a 4% yield of the corresponding 1-oxide. The latter undoubtedly was formed by *intermolecular* oxidation-hydration (see below).

This striking difference in the nature of products derived from 2- and 4-cyanopyridines is taken as evidence in support of the intramolecular reaction postulated for the 2-isomer.

3-Cyanopyridine. The reaction of 3-cyanopyridine with strongly alkaline hydrogen peroxide has been studied at some length.[5] There the only product isolated was nicotinamide, in a maximum yield of 19%. This low figure was most likely due to the formation of a substantial amount of the corresponding 1-oxide, but the possibility of isolating the latter product was apparently not realized at that time.

When the 3-isomer (VI) was treated with hydrogen peroxide at *p*H 7.5–8, the reaction proceeded at a slightly slower rate than that found for the other isomers. Nicotinamide 1-oxide (IX) was obtained in 44% yield and no other pure product was isolated. IX was felt to be formed by an inter-

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(1) G. B. Payne, P. H. Deming, and P. H. Williams, *J. Org. Chem.* **26**, 659 (1961).

(2) G. B. Payne and P. H. Williams, *J. Org. Chem.* **26**, 651 (1961).

(3) Nitrile hydrolysis by hydrogen peroxide to give amide, water, and oxygen is called a Radziszewski reaction. *Cf.* B. Radziszewski, *Ber.* **17**, 1289 (1884).

(4) Substituents at the 2- and 4-positions in the pyridine ring usually exhibit similar reactivity. See H. S. Mosher in *Heterocyclic Compounds*, Vol. 1, John Wiley and Sons, Inc., New York, 1950, p. 402.

(5) A. George and P. Bachmann, *Helv. Chim. Acta* **26** 361 (1943).