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β-Substituted α-Cyanoglycidic Esters and Their Reactions

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The reaction of β -alkyl- α -cyanoacrylic esters with hydrogen peroxide was outlined previously as a useful method of synthesizing epoxy nitriles.¹⁾ The applicability of the reaction has now been extended to give β -aryl- α -cyanoglycidic esters from α -cyanocinnamic esters.

$$\begin{array}{c} X- & \longrightarrow \\ CH=C(CN)COOEt \\ & & \swarrow \\ & & \bigcirc \\ & & \bigcirc \\ & & (II) \\ & & X: \ H, \ CI, \ CN, \ NO_{\bullet} \end{array}$$

Ethyl α -cyanocinnamates (I) were prepared by using the conditions developed by Cope.²⁾ The epoxidation of these unsaturated esters with hydrogen peroxide proceeded smoothly at 80—85°C without a catalyst. In an ethanolic solution, ethyl α -cyanocinnamate (I, X=H) gave the corresponding epoxy ester (II, X=H) in a 30% yield after 15 hr. Under similar conditions, ethyl α -cyano- β -(p-nitrophenyl)acrylate (I, X=NO₂) reacted more rapidly with hydrogen peroxide; the epoxy ester (II, X=NO₂) was formed in a 96% yield, with the complete consumption of the olefin, after only 1 hr.

The results shown in Table 1 reveal that the electron-withdrawing p-substituents accelerate the epoxidation of I, whereas the electron-releasing groups have the reverse effect.

The epoxy compounds obtained above gave unknown products upon hydrolysis with acid or alkali. By the reaction with aqueous ammonia, β -phenyl, β -(p-nitrophenyl), and β -(p-chlorophenyl)- α -cyanoglycidic esters (II; X=H, NO₂, Cl) gave the corresponding diol

amides, accompanied by the epoxy ring opening, and the β -(p-cyanophenyl)- α -cyanoglycidic ester (II, X=CN) gave β -(p-cyanophenyl)- α -cyanoglycidamide.

Ethyl α -cyano- β , β -dimethylglycidate (III) had previously been synthesized from ethyl α -cyano- β -methylcrotonate.¹⁾ The conversion of III to α -cyano- β , β -dimethylglycidic acid (IV) was effected by alcoholic alkaline hydrolysis. When IV was kept at 140—150°C in an oil bath, decarboxylation took place and the product was the expected 3-methyl-2-oxobutyronitrile (V), which gave the anilide, VI, upon reaction with aniline. The epoxy ester, III, gave the epoxy amide, VII, on treatment with aqueous ammonia.³⁾ Under similar conditions, the epoxy acid, IV, gave aminohydroxy acid, VIII.

Experimental

Ethyl α -Cyanocinnamates (I). The unsaturated esters (I, X=H, Cl, CN, NO₂, CH₃, CH₃O, OH) were prepared according to the method of Cope.²⁾

Epoxidation of I. A) A mixture of I (0.1 mol), 30% hydrogen peroxide (0.2 mol), and ethanol (30 ml) was refluxed at $80-85^{\circ}$ C on a water bath. To the mixture, water (100 ml) was then added, after which it was extracted with chloroform. After the removal of the solvent, the residual oil was distilled to give the epoxy ester (X=H).

B) The reaction was carried out as above. The solution was cooled, and the resulting precipitate was collected by filtration. Recrystallization from ethanol gave the epoxy ester (X=Cl, CN, NO₂).

 α -Cyano- β , β -dimethylglycidic Acid (IV). To a solution of ethyl α -cyano- β , β -dimethylglycidata (III)¹⁾ in ethanol, ethanolic potassium hydroxide was added at room temperature. A white precipitate formed during the addition. After the mixture had stood overnight, it was separated by filtration,

$$(CH_3)_2C - C(CN)COOEt \xrightarrow{NH_4OH} (CH_3)_2C - C(CN)CONH_2$$

$$(III) \qquad (VII)$$

$$(CH_3)_2C - C(CN)COOH \xrightarrow{NH_4OH} (CH_3)_2C - C(CN)COOH \text{ or } (CH_3)_2C - C(CN)COOH$$

$$O \qquad \qquad H_2N \stackrel{!}{O} OH \qquad HO \stackrel{!}{N} H_2$$

$$(IV) \qquad (VIII)$$

$$\downarrow \qquad \qquad (CH_3)_2CHCOCN \xrightarrow{C_4H_4NH_2} (CH_3)_2CHCONHC_6H_5$$

$$(V) \qquad (VI)$$

¹⁾ M. Igarashi, M. Akano, A. Fujimoto, and H. Midorikawa, This Bulletin, 43, 2138 (1970).

²⁾ A. C. Cope, J. Amer. Chem. Soc., 59, 2327 (1937).

³⁾ G. B. Payne, J. Org. Chem., 26, 663 (1961).

TABLE 1.	PREPARATION OF ETHYL	B-ARYL-X-CYANOGLYCIDATES (TT)	FROM ETHYL α-CYANOCINNAMATES ((\mathbf{I}))

X	Reaction ^{a)} time, hr	Mp, °C (Bp, °C/mmHg)	Yield (%)	Formula	Calcd (%)			Found (%)		
					\mathbf{c}^{-}	Н	N	\mathbf{C}	Н	N
Н	15	(130—133/3)	30	$C_{12}H_{11}O_3N$	66.35	5.10	6.45	65.93	5.31	6.02
NO_2	1	123—124	96	$C_{12}H_{10}O_5N_2$	54.96	3.84	10.68	54.91	3.83	10.65
CN	6	125—127	98	$C_{13}H_{10}O_3N_2$	64.46	4.16	11.57	64.29	4.17	11.57
Cl	15	70	81	$C_{12}H_{10}O_3NCl$	57.27	4.00	5.57	57.22	4.02	5.41
					(0	ી, 14.0	(8)	(C	1, 14.0	01)
CH_3	15	recovery of I								
OCH_3	15	recovery of I								
OH	15	recovery of I								

a) Reaction temp., 80-85°C

washed with ethanol, and dried. The potassium salt was dissolved in water and neutralized with hydrochloric acid at 0—5°C. After the mixture had stood overnight in an ice box, the resulting precipitate was collected by filtration. The yield was 80%. Recrystallization from benzene gave colorless needles of IV; mp 107°C (decomp) (lit,³) mp 106—108°C (decomp). Found: C, 50.71; H, 4.84; N, 9.85%).

Reaction of IV with Ammonia. Epoxy acid, IV (1.4 g), was dissolved in concentrated aqueous ammonia (6 ml) and allowed to stand overnight at room temperature. The solution was then concentrated under a vacuum to dryness. Recrystallization from ethanol afforded colorless needles; mp 193°C (decomp). The yield was 1.4 g (89%). The product had an empirical formula in agreement with that of 3-amino-2-cyano-2-hydroxy-3-methylbutyric acid or its isomer, 2-amino-2-cyano-3-hydroxy-3-methylbutyric acid (VIII).

Found: C, 45.95; H, 6.36; N, 18.06%. Calcd for C_6H_{10} - O_3N_2 : C, 45.56; H, 6.37; N, 17.71%.

Decarboxylation of IV. The epoxy acid, IV, was placed with anhydrous sodium sulfate or liquid paraffin in a Claisen flask and heated in an oil bath at 140—150°C until the decarboxylation had ceased. The product was then distilled directly from the reaction flask. Redistillation gave 3-methyl-2-oxobutyronitrile (V); bp 115—120°C (lit,4) bp 116—118°C) (yield, 45%).

The reaction of a sample of the keto nitrile, V, with aniline gave isobutyranilide (VI); mp 105°C (lit,⁵⁾ mp 106—107°C. Found: C, 73.70; H, 8.81; N, 7.74%).

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⁴⁾ W. Tschelinzeff and W. Schmidt, Ber., 62, 2210 (1929).

⁵⁾ O. Diels and K. Pflaumer, ibid., 48, 223 (1915).