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The Chemistry of Acrylonitrile. V. Cyanoethylation of Aldehydes

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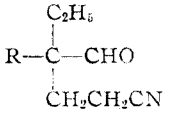
Acrylonitrile reacts with aldehydes in the presence of alkaline catalysts to yield condensation products which in general are more complex than those obtained by the action of acrylonitrile upon ketones.[1]

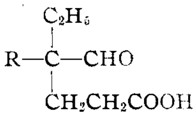
The direct cyanoethylation reaction so characteristic of ketones, is shown most clearly by those aldehydes which do not readily aldolize, oxidize, or resinify under the influence of the alkaline catalyst used. Typical of such amenable aldehydes are the dialkyl acetaldehydes, particularly those which are higher in the series than isobutyraldehyde. Of these, the commercially available diethylacetaldehyde and 2-ethylhexanal are eminently suitable. These aldehydes react smoothly with acrylonitrile in the presence of a little concentrated aqueous potassium hydroxide solution as a catalyst to form the corresponding cyanoethylation products (I) and (II) in good yields (75–80%).



$$R{-}\overset{C_2H_5}{\underset{CH_2CH_2CN}{C}}{-}CHO$$

I (R = Ethyl)
II (R = Butyl)

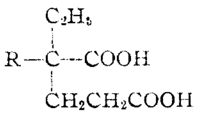
From these aldehydo-nitriles, the corresponding aldehydo-acids (III) and (IV) were obtained by hydrolysis with aqueous sodium hydroxide solution; the tertiary aldehyde groups being hardly affected by the alkali.



$$R{-}\overset{C_2H_5}{\underset{CH_2CH_2COOH}{C}}{-}CHO$$

III (R = Ethyl)
IV (R = Butyl)

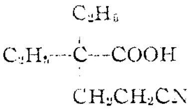
Upon oxidation with air, hydrogen peroxide, or potassium permanganate, the aldehydo-acids (III) and (IV) yielded the corresponding α,α-dialkylglutaric acids (V) and (VI), respectively, in crystalline form.



$$R{-}\overset{C_2H_5}{\underset{CH_2CH_2COOH}{C}}{-}COOH$$

V (R = Ethyl)
VI (R = Butyl)

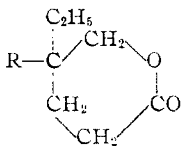
Although the aldehydo-nitriles (I) and (II) are not readily affected by dilute alkalies, they do rapidly autoxidize in the air to the corresponding cyano-acids. From (I), the cyano-acid (VII) separates in crystalline form upon exposure of a thin layer of the cyano-aldehyde to the air, whereas (II) remains oily.



$$C_2H_5{-}\overset{C_2H_5}{\underset{CH_2CH_2CN}{C}}{-}COOH$$

(VII)

Upon catalytic hydrogenation of the sodium salts of the aldehydo-acids (III) and (IV) in water by means of nickel, the sodium salts of the respective δ-hydroxy acids are formed, which upon acidification yield the corresponding δ-lactones (VIII) and (IX).

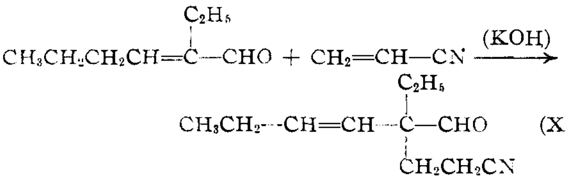


VIII (R = Ethyl)
IX (R = Butyl)

On the other hand, isobutyraldehyde and acetaldehyde are so strongly aldolized that they condense with acrylonitrile in the presence of potassium hydroxide to form a complex mixture of higher cyanoethylation products. The same holds true for propionaldehyde, *n*-butyraldehyde and heptaldehyde. Crotonaldehyde as well as acetaldol likewise form more complex nitrogeneous condensation products with acrylonitrile.

Since it appeared probable that dehydration products of the aldols involved in these reactions, also took part in the condensation with acrylonitrile, it was thought that α-ethyl-β-propylacrolein which is easily formed by the action of alkali on *n*-butyraldehyde through dehydration of the butyraldol[2] might yield a clue concerning the nature of some of the more complex cyanoethylation products encountered.

When equimolecular proportions of α-ethyl-β-propylacrolein and acrylonitrile were mixed in the presence of concentrated aqueous or methanolic potassium hydroxide solution as a catalyst, reaction occurred to form a 50% yield of a *mono*-cyanoethylation product *even though an α-hydrogen atom is lacking in the aldehyde used.* This *mono*-cyanoethylation product (X) is formed in accordance with the following equation



$$CH_3CH_2CH_2CH{=}\overset{C_2H_5}{C}{-}CHO + CH_2{=}CH{-}CN \xrightarrow{(KOH)} CH_3CH_2{-}CH{=}CH{-}\overset{C_2H_5}{\underset{CH_2CH_2CN}{C}}{-}CHO$$

(X)

Under the influence of the alkali, the α-ethyl-β-propylacrolein apparently undergoes a hydrogen shift and the migrating hydrogen atom becomes stabilized by the powerful acceptor action of the acrylonitrile to yield compound (X). In this respect, the reaction is quite analogous to the behavior of other α,β-unsaturated compounds such as mesityl oxide, crotonamide and

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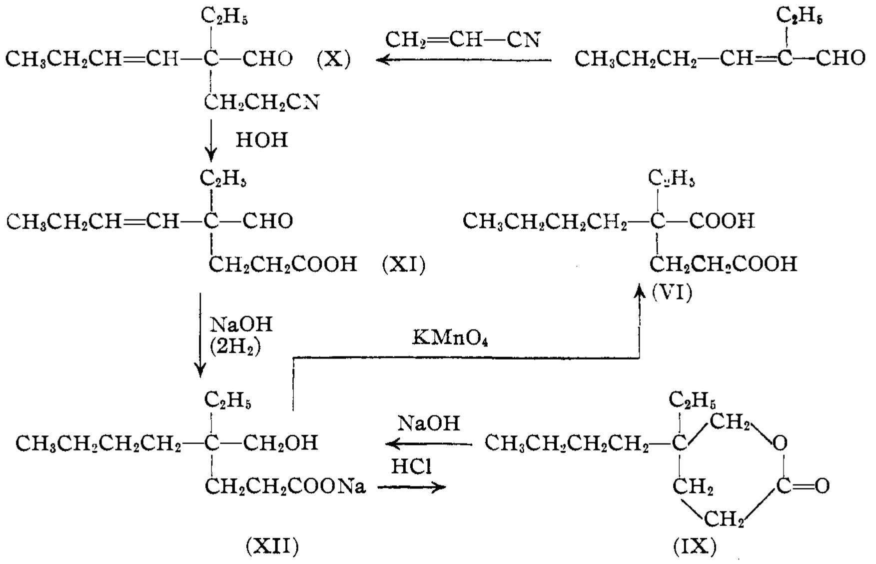
[1] Bruson and Riener, THIS JOURNAL, 64, 2850 (1942).

[2] Weizmann and Garrand, *J. Chem. Soc.*, 329 (1920).

crotononitrile toward acrylonitrile as described previously.[3]

That the cyanoethyl group is in fact *alpha* to the aldehydo group in (X) was shown by hydrolyzing (X) to the unsaturated aldehydo-acid (XI) by means of aqueous sodium hydroxide solution. The pure aldehydo-acid was isolated, converted to its sodium salt and the aqueous solution of the latter was subjected to catalytic hydrogenation in the presence of Raney nickel. The sodium salt of the saturated hydroxy acid formed (XII) was acidified to yield a liquid lactone (IX) which was found to be identical with γ-ethyl-γ-butyl-δ-valero-lactone obtained previously from 2-ethylhexanal through compounds II and IV. Furthermore a portion of this lactone was oxidized in alkaline solution by means of potassium permanganate to α-ethyl-α-butylglutaric acid identical with (VI) derived from 2-ethylhexanal.

The sequence of reactions described above is shown more clearly in the appended equations.



Experimental

(I) **2-(β-Cyanoethyl)-2-ethylbutyraldehyde.**—To a stirred solution of 700 g. of freshly distilled 2-ethylbutyraldehyde (7 moles) and 20 g. of aqueous 50% potassium hydroxide solution, there was added dropwise 408 g. of acrylonitrile (7.7 moles) during the course of two hours while maintaining the reaction temperature at 55–58° by occasional cooling. After all had been added, the mixture was stirred for an additional ninety minutes until the exothermal reaction had ceased, and finally heated for one hour at 55° to complete the reaction. The product was acidified to congo red with dilute hydrochloric acid, washed twice with water, dried under reduced pressure and the residual oil (1018 g.) distilled in vacuum while nitrogen was admitted through the capillary tube to prevent oxidation. The crude product distilled at 115 to 125° at 4–6 mm. as a colorless oil; yield 821 g. or 76.6%. Upon redistillation in nitrogen under vacuum the analytical sample boiled at 128° at 4 mm. *Anal.* Calcd. for $C_9H_{15}ON$: C, 70.53; H, 9.87; N, 9.14. Found: C, 69.98; H, 9.91; N, 9.24; $n^{25}D$ 1.4500; $d^{25}{}_4$ 0.9528.

(II) **2-(β-Cyanoethyl)-2-ethylhexanal.**—The procedure above was applied to a mixture of 384 g. 2-ethylhexanal, 10 g. 50% potassium hydroxide solution and 175 g. of acrylonitrile. The product distilled at 130–135° at 4 mm. as a colorless oil; yield 432 g. or 79.5%. Upon redistillation in nitrogen the analytical sample boiled at 140–142° (5 mm.). *Anal.* Calcd. for $C_{11}H_{19}ON$: C, 72.87; H 10.57; N, 7.73. Found: C, 73.00; H, 10.61; N, 7.82; $n^{25}D$ 1.4515; $d^{25}{}_4$ 0.9269.

(III) **2-(β-Carboxyethyl)-2-ethylbutyraldehyde.**—A mixture of 153 g. of compound (I), 50 g. of sodium hydroxide and 500 cc. of water was stirred and boiled under reflux for one and one-half hours until the oil had disappeared. The solution was cooled, acidified with hydrochloric acid, and the precipitated oil separated, washed with water and dried in vacuum. The residual oil (152 g.) was distilled *in vacuo* in a stream of nitrogen. The product (122 g.) came over at 145–150° (5 mm.) as a colorless oil; acid no. 335 (calcd., 326). The analytical sample obtained by redistillation in vacuum in an atmosphere of nitrogen, boiled at 142° (3 mm.). *Anal.* Calcd. for $C_9H_{16}O_3$: C, 62.74; H, 9.37. Found: C, 62.40; H, 9.46; $n^{25}D$ 1.4550; $d^{25}{}_4$ 1.0338.

(IV) **2-(β-Carboxyethyl)-2-ethylhexanal.**—The procedure described above was applied to a mixture of 30 g. of compound (II), 10 g. of sodium hydroxide and 100 g. of water except that the boiling was continued for five hours. The crude yield of aldehydo-acid boiling at 160–165° (4 mm.) was 24.5 g. The analytical sample obtained by redistillation *in vacuo* was a colorless oil boiling at 157° (4 mm.). *Anal.* Calcd. for $C_{11}H_{20}O_3$: C, 65.94; H, 10.07. Found: C, 65.90; H, 10.12; $n^{25}D$ 1.4564; $d^{25}{}_4$ 1.0325.

(V) **α,α-Diethylglutaric Acid.**—To a stirred solution of 41.6 g. of compound (III), 25 g. of potassium hydroxide and 250 g. of water, a suspension of 57 g. of potassium permanganate in 500 g. of warm water was added gradually during the course of fifteen minutes while maintaining the reaction temperature at 30–40° by occasional cooling. The mixture was stirred for three hours and allowed to stand eighteen hours. The product was filtered, the precipitate washed, and the combined washings and filtrate acidified with hydrochloric acid. The turbid solution obtained was evaporated to dryness *in vacuo* on a steam-bath and the crystalline residue extracted several times with acetone. The acetone extract upon evaporation of the acetone deposited 26 g. of colorless crystals which after recrystallization from nitromethane formed colorless needles, m. p. 84° (uncor.). *Anal.* Calcd. for $C_9H_{16}O_4$: C, 57.40; H, 8.57. Found: C, 57.20; H, 8.70.

(VI) **α-Ethyl-α-butylglutaric Acid.**—A suspension of 57 g. of potassium permanganate in 500 cc. of water was added gradually to a solution of 60 g. of compound (IV), 250 cc. of water and 25 g. of potassium hydroxide at 45–50°. The mixture was stirred thereafter at room temperature for eighteen hours, filtered, and the filtrate acidified with concentrated hydrochloric acid. The product precipitated as a viscous oil. It was taken up in toluene, washed once with water and dried to yield 53 g. of crude acid. This was dissolved in hot nitromethane from which it separated on cooling in colorless crystals; yield 39 g. After several recrystallizations from nitromethane the melting point remained constant at 81–82°. *Anal.* Calcd. for $C_{11}H_{20}O_4$: C, 61.07; H, 9.28. Found: C, 60.70; H, 9.25.

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[3] Bruson and Riener, This Journal, **65**, 18 (1943).

(VII) **2-(β-Cyanoethyl)-2-ethylbutyric Acid.**—A small quantity of 2-(β-cyanoethyl)-2-ethylbutyraldehyde (I) was spread out on a watch glass and exposed to the air for about a week. The crystalline crust which formed was separated and recrystallized from diisobutylene or petroleum ether (90–100°). The product separated in colorless needles, m.p. 88° (uncor.). *Anal.* Calcd. for $C_9H_{15}O_2N$: C, 63.86; H, 8.94; N, 8.28. Found: C, 63.80; H, 8.88; N, 8.29.

(VIII) **γ,γ-Diethyl-δ-valerolactone.**—Eighty-six grams of 2-(β-carboxyethyl)-2-ethylbutyraldehyde (III) was made faintly alkaline with a solution of about 20 g. of sodium hydroxide in 115 g. of water. This solution was shaken in an autoclave with 10 g. of Raney nickel catalyst and hydrogen under an initial pressure of 100 atmospheres, for seven hours at 120–140°. At the end of this time the pressure had fallen to about 40 atmospheres. The mixture was filtered free from catalyst and the clear filtrate acidified with concentrated hydrochloric acid. The thick oil which separated was dissolved in toluene, washed with water and evaporated to dryness *in vacuo* on a steam-bath. The residual oil was distilled under reduced pressure. The lactone came over between 112 and 118° at 4–5 mm. as a colorless oil; yield 63 g. The analytical sample obtained by redistillation boiled at 101° (2.5 mm.); n^{25}_D 1.4634; d^{25}_4 1.0064. *Anal.* Calcd. for $C_9H_{16}O_2$: C, 69.17; H, 10.33. Found: C, 68.78; H, 10.40.

(IX) **γ-Ethyl-γ-butyl-δ-valerolactone.**—The procedure described in (VIII) above was applied to 80 g. of 2-(β-carboxyethyl)-2-ethylhexanal (IV), 16 g. sodium hydroxide and 100 g. of water, using 10 g. of Raney nickel catalyst. After three hours at 125° the hydrogenation was complete. The acidification of the product yielded a colorless oil (IX) boiling at 124° (3.5 mm.); yield 44 g.; n^{25}_D 1.4635; d^{25}_4 0.9747. *Anal.* Calcd. for $C_{11}H_{20}O_2$: C, 71.68; H, 10.95. Found: C, 71.30; H, 11.19.

(X) **2-(β-Cyanoethyl)-2-ethyl-3-hexenal.**—The procedure described for (I) was applied to a mixture of 252 g. freshly distilled α-ethyl-β-propylacrolein, 10 g. of 50% potassium hydroxide solution, and 110 g. of acrylonitrile, except that the condensation was made at 45–55°. The product distilled at 126–135° at 4–5 mm. as a pale yellow oil; yield 175 g. or 49%. The analytical sample boiled at 138–140° at 6 mm. *Anal.* Calcd. for $C_{11}H_{17}ON$: C, 73.68; H, 9.57; N, 7.82. Found: C, 73.14; H, 9.43; N, 7.63; n^{25}_D 1.4640; d^{25}_4 0.9375.

(XI) **2-(β-Carboxyethyl)-2-ethyl-3-hexenal.**—A mixture of 55 g. (X), 20 g. sodium hydroxide and 200 g. of water was stirred and boiled under reflux for five hours, cooled, acidified, and worked up as described in the case of compound (III). The crude aldehydo-acid distilled at 160–170° at 5 mm. as a pale yellow oil; yield 40 g. The analytical sample boiled at 154° at 4 mm. *Anal.* Calcd. for $C_{11}H_{18}O_3$: C, 66.62; H, 9.15. Found: C, 66.60; H, 9.35; n^{25}_D 1.4695; d^{25}_4 1.0112.

Hydrogenation of (XI).—Sixty-three grams of 2-(β-carboxyethyl)-2-ethyl-3-hexenal (XI) was made faintly alkaline with an aqueous 20% sodium hydroxide solution and shaken in an autoclave with 10 g. of Raney nickel catalyst for five hours at 130–135° with hydrogen at an initial pressure of 110 atmospheres. The filtered product (XII) was acidified with concentrated hydrochloric acid and the heavy oil taken up in toluene, washed, and evaporated to dryness *in vacuo* on a steam-bath. The residual oil was distilled under reduced pressure. The product (45 g.) came over at 121–123° at 3 mm. as a colorless oil. The redistilled analytical sample boiled at 120° (3 mm.) and possessed the following constants: n^{25}_D 1.4632; d^{25}_4 0.9736. *Anal.* Calcd. for $C_{11}H_{20}O_2$: C, 71.68; H, 10.95 Found: C, 71.24; H, 10.96. Its constants and analysis show it to be identical with γ-ethyl-γ-butyl-δ-valerolactone (IX).

Oxidation of γ-Ethyl-γ-butyl-δ-valerolactone.—Part of the above lactone (18.4 g.) obtained from the hydrogenation of the unsaturated aldehydo-acid (XI) was oxidized by dissolving it in a solution of 11.2 g. of potassium hydroxide and 200 g. of water. To this solution there was added while stirring, a suspension of 47.4 g. of potassium permanganate in 400 g. of water at 35–40°. The mixture was then heated for eight and one-half hours at 55–60°, filtered and the filtrate acidified with concentrated hydrochloric acid. The oil which separated solidified after several hours at 5°; yield 17 g. After recrystallization from nitromethane it formed colorless needles, m. p. 81° (uncor.). A mixed melting point with (VI) showed no depression. The product was therefore α-ethyl-α-butylglutaric acid.

Acknowledgment.—The analyses of the above products were performed by Mr. C. W. Nash of these Laboratories.

Summary

1. Acrylonitrile condenses in the presence of strong bases, notably aqueous 50% potassium hydroxide as a catalyst, with α-hydrogen-bearing aldehydes that do not readily aldolize, particularly with dialkyl acetaldehydes higher than isobutyraldehyde, to cyanoethylate the α-carbon atom thereof.

2. α,β-Unsaturated aldehydes of the type of α-ethyl-β-propylacrolein, which lack an α-hydrogen atom undergo a 1,3-hydrogen shift to likewise yield the α-cyanoethylated derivatives.

3. The 2-(β-cyanoethyl)-dialkyl acetaldehydes formed are convertible to the corresponding (β-cyanoethyl)-dialkyl acetic acids by autoxidation or into the (β-carboxyethyl)-dialkyl acetaldehydes by hydrolysis. The latter upon reduction yielded γ,γ-dialkyl-δ-valerolactones, and upon oxidation α,α-dialkyl glutaric acids.

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