REACTION OF CYANOHYDRINS WITH POLYENIC AND ENYNIC ALDEHYDES IN THE PRESENCE OF TRIETHYLAMINE

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We have shown [1] that α,β-unsaturated aldehydes carrying electron-acceptor groups in the β-position react with cyanohydrins in the presence of tertiary amines to give rise to saturated esters of the cyanohydrins in accordance with the scheme

$$\mathrm{RCH{=}CR'CHO} \xrightarrow[(\mathrm{C_2H_5})_3\mathrm{N}]{\mathrm{R''R'''C(OH)CN}} \mathrm{RCH_2CHR'COOCR''R'''CN}$$

An analogous reaction was observed also in the case of phenylpropargyl aldehyde [2], which gave rise to a mixture of esters of cis- and trans-cinnamic acids.

In a further study of these interesting transformations we have now investigated the reaction between acetone cyanohydrin and certain conjugated dienic, trienic, and vinylacetylenic aldehydes in the presence of triethylamine; the reactions were carried out either in the absence of a solvent or in alcoholic solution. Sorbic aldehyde (I) reacts smoothly with acetone cyanohydrin in the presence of triethylamine (molar ratio 1 : 2 : 2) to give rise to a mixture of the acetone cyanohydrin ester (II) and the 1-cyanohexa-2,4-dien-1-yl ester (III) of 3-penten-1-carboxylic acid

$$\underset{\mathrm{I}}{\mathrm{CH_3CH = CHCH = CHCHO}} + \mathrm{(CH_3)_2C(OH)CN} \rightarrow \underset{\mathrm{II}}{\mathrm{CH_3CH = CHCH_2CH_2COOC(CH_3)_2CN}}$$
$$+ \underset{\mathrm{III}}{\mathrm{CH_3CH = CHCH_2CH_2COOCH(CN)CH = CHCH = CHCH_3}}$$

The structure of these products was established by elementary analysis, and by IR, UV, and mass spectroscopy. Formation of the ester (III) confirms that in this case the reaction proceeds in part normally with the formation of the cyanohydrin of the α,β-unsaturated aldehyde. In the cases of 5-phenyl (IVa) and 5-carbethoxy-2,4-pentadien-1-al (IVb) the reaction likewise proceeds unequivocally, and the action of acetone cyanohydrin on these aldehydes furnishes, in the absence of a solvent, the acetone cyanohydrin esters (Va and b; R' = $(CH_3)_2{\cdot}CCN$) of the corresponding γ,δ-unsaturated acids; on the other hand, when the reaction is carried out in alcoholic solution, the ethyl esters (Va and b; R' = C_2H_5) of the same acids are produced instead

$$\underset{\mathrm{(IV)}}{\mathrm{RCH{=}CHCH{=}CHCHO}} \xrightarrow[\mathrm{R'OH}]{\mathrm{(CH_3)_2C(OH)CN}} \underset{\mathrm{(V)}}{\mathrm{RCH{=}CHCH_2CH_2COOR'}}$$

$$\mathrm{a\ R{=}C_6H_5;\ b\ C_2H_5O_2C;\ R'{=}C_2H_5;\ (CH_3)_2C(CN)}$$

The structure of the resulting esters was established by elementary analysis, and by IR, UV, and mass spectroscopy. Trienic aldehydes, such as 2,4,6-octatrien-1-al (VIa) and 7-phenyl-2,4,6-heptatrien-1-al (VIb), react with acetone cyanohydrin in alcoholic solution equally smoothly with the formation of the ethyl esters of the γ,δ-unsaturated acids (VIIa and b respectively)

$$\underset{\mathrm{(VI)}}{\mathrm{R{-}(CH{=}CH)_3\,CHO}} \xrightarrow[\substack{(\mathrm{C_2H_5})_3\mathrm{N} \\ \mathrm{C_2H_5OH}}]{\mathrm{(CH_3)_2C(OH)CN}} \underset{\mathrm{(VII)}}{\mathrm{R{-}(CH{=}CH)_2\,CH_2CH_2COOC_2H_5}}$$

$$\mathrm{a\ R{=}CH_3;\ b\ R{=}C_6H_5}$$

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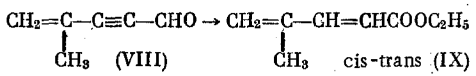
The structure of all the esters described in this paper was established by spectroscopic means and was, in addition, confirmed by saponification to the corresponding γ,δ-unsaturated acids.

The aldehyde, 4-methylpent-4-en-2-yn-1-al (VIII), reacts with acetone cyanohydrin in alcoholic solution and is converted in 20% yield to a mixture of the ethyl esters of 2,3-cis- and 2,3-trans-4-methyl-2,4-pentadienoic acid (IX), as shown by the IR spectrum



$$\underset{CH_3}{CH_2{=}C}{-}C{\equiv}C{-}CHO \;(VIII) \rightarrow \underset{CH_3}{CH_2{=}C}{-}CH{=}CHCOOC_2H_5 \;\text{cis-trans (IX)}$$

This shows that in vinylacetylenic aldehydes the only multiple bond to take part in the reaction is the one immediately adjacent to the aldehyde group.

The reactions investigated in this paper provide a novel method of passing from polyenic aldehydes to γ,δ-unsaturated acids and afford therefore a new synthesis of these compounds, hitherto accessible only with difficulty.

EXPERIMENTAL

Reaction of Sorbic Aldehyde (I) with Acetone Cyanohydrin. To a mixture of sorbic aldehyde (I) (4.8 g) and acetone cyanohydrin (8.5 g) was added triethylamine (10 g). Readily volatile products were driven off during 1 h, whereupon distillation of the reaction mixture afforded the acetone cyanohydrin ester of 3-penten-1-carboxylic acid (II) (4.8 g; 53%), bp 80-82°C (0.4 mm), n_D^{20} 1.4417. Found %: C 65.83; H 8.43; mol. wt. 191.* $C_{10}H_{15}NO_2$. Calculated %: C 66.27; H 8.34. IR spectrum (thin layer): $\nu = 1755\ cm^{-1}$ (CO). Also obtained: the 1-cyanohexa-2,4-1-yl ester of 3-penten-1-carboxylic acid (III) (0.6 g; 21%), bp 98-100°C (0.4 mm), n_D^{20} 1.4840. Found %: C 70.98; H 7.98; N 6.48; mol. wt. 219. $C_{13}H_{17}NO_2$. Calculated %: C 71.20; H 7.82; N 6.39. IR spectrum (thin layer): $\nu = 1752\ cm^{-1}$ (CO); $1660\ cm^{-1}$, $1626\ cm^{-1}$, and $982\ cm^{-1}$ (CH = CH); λ_{max} (in alcohol) 232 nm ($\varepsilon = 20{,}000$).

A mixture of (II) (2.4 g) and 5 N KOH (3 ml) was stirred until it became homogeneous; it was then extracted with ether, the aqueous layer acidified with conc. HCl, and again extracted with ether. This latter extract, after drying over Na_2SO_4, was evaporated down. The residue on distillation gave 3-penten-1-carboxylic acid (0.8 g; 70%), bp 115° (30 mm), n_D^{20} 1.4360, in agreement with the literature data [3]. Found %: C 62.68; H 8.58. $C_6H_{10}O_2$. Calculated %: C 63.13; H 8.83. IR spectrum (thin layer): $\nu = 1730\ cm^{-1}$ (CO).

Reaction of 5-Phenyl-2,4-pentadien-1-al (IVa) with Acetone Cyanohydrin. The aldehyde, (IVa), (7.4 g) was dissolved in benzene (20 ml) and acetone cyanohydrin (8.5 g) and triethylamine (10 g) were added. When the exothermic reaction had subsided, the solution was passed through a column of activated charcoal and the benzene was distilled off. The residue, after recrystallization from petroleum ether, gave the acetone cyanohydrin ester of 3-styrylpropionic acid (Va; $R' = (CH_3)_2CCN$) (1.2 g; 11%), mp 35.5-36.5°. Found %: C 74.03; H 7.16; mol. wt. 243. $C_{15}H_{17}NO_2$. Calculated %: C 74.05; H 7.04. IR spectrum (thin layer): $\nu = 1750\ cm^{-1}$ (CO); $2250\ cm^{-1}$ (CN very weak), λ_{max} (in alcohol) 250 nm ($\varepsilon = 18{,}100$).

A solution of 5-phenyl-2,4-pentadien-1-al (IVa) (5 g) in alcohol (30 ml) was treated with acetone cyanohydrin (5 g) and triethylamine (5 g). After 1 h the alcohol and readily volatile products were driven off. The residue gave on distillation the ethyl ester of 3-styrylpropionic acid (Va; $R' = C_2H_5$) (3.5 g; 55%), bp 103-105° (0.7 mm), n_D^{20} 1.5373. Found %: C 76.07; H 7.91; mol. wt. 204. $C_{13}H_{16}O_2$. Calculated %: C 76.44; H 7.90. IR spectrum (in CCl_4): $\nu = 1740\ cm^{-1}$ (CO); λ_{max} (in alcohol) 250 nm ($\varepsilon = 12{,}250$).

Saponification of (Va) (0.8g) in a manner analogous to that previously used gave 3-styrylpropionic acid (0.5 g; 86%), mp 87.5-89° (from hexane), in agreement with the literature [4]. Found %: C 74.37; H 6.73. $C_{11}H_{12}O_2$. Calculated %: C 74.97; H 6.86. Addition of a molecule of bromine leads to 4,5-dibromo-5-phenylpentanoic acid, mp 158-160.5° (from hexane), consistent with [4].

Reaction of 5-Carbethoxy-2,4-pentadien-1-al (IVb) with Acetone Cyanohydrin. By a method analogous to that previously described, (IVb) (1.2 g), acetone cyanohydrin (1.3 g), and triethylamine (1.5 g) in alcohol (10 ml) gave the diethyl ester of Δ^2-dihydromuconic acid (Vb; $R' = C_2H_5$) (0.8 g; 56%), bp 88-89° (0.5 mm), n_D^{20} 1.4457. Found %: C 59.58; H 7.96; mol. wt. 250. $C_{10}H_{16}O_4$. Calculated %: C 59.97; H 8.05. IR spectrum (thin layer) $\nu = 1740\ cm^{-1}$ (CO); λ_{max} (in alcohol) 250 nm ($\varepsilon = 247$).

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*All molecular weights were determined by mass spectroscopy.

Hydrolysis of the Diethyl Ester of Δ^2-Dihydromuconic Acid (Vb). By a method analogous to that previously described, (Vb; $R' = C_2H_5$) (0.2 g) gave Δ^2-dihydromuconic acid (0.12 g; 83%), mp 167.5-168.5° (from water), in agreement with the values given in [5].

Reaction of 2,4,6-Octatrien-1-al (VIa) with Acetone Cyanohydrin. From 2,4,6-octatrien-1-al (1.4 g), acetone cyanohydrin (1.7 g), and triethylamine (2 g) in alcohol (10 ml) there resulted, as previously, the ethyl ester of 4,6-octadienoic acid (VIIa) (0.7 g; 41%), bp 90-91° (0.85 mm), n_D^{20} 1.4800. IR spectrum (thin layer): $\nu = 1740$ cm^{-1} (CO); λ_{max} (in alcohol) 230 nm ($\varepsilon = 22{,}900$). Found %: C 71.57; H 9.60; mol. wt. 168 (by mass spectroscopy). $C_{10}H_{16}O_2$. Calculated %: C 71.39; H 9.59.

Reaction of 7-Phenyl-2,4,6-heptatrien-1-al (VIb) with Acetone Cyanohydrin. The aldehyde, 7-phenyl-2,4,6-heptatrien-1-al (VIb), (0.4 g), acetone cyanohydrin (0.43 g), and triethylamine (1 g) in alcohol (10 ml) similarly gave the ethyl ester of 7-phenyl-4,6-heptadienoic acid (VIIb) (0.2 g; 40%), bp 130-135° (0.04 mm). Found %: C 78.03; H 7.95; mol. wt. 230. $C_{15}H_{18}O_2$. Calculated %: C 78.23; H 7.88. IR spectrum (in CCl_4): $\nu = 1740$ cm^{-1}.

Reaction of 4-Methylpent-4-en-2-yn-1-al with Acetone Cyanohydrin. As before, 4-methylpent-4-en-2-yn-1-al (0.4 g), acetone cyanohydrin (0.5 g), and triethylamine (1 g) in alcohol (3 ml) gave a mixture (0.14 g; 20%) of the ethyl esters of 2,3-cis- and 2,3-trans-4-methyl-2,4-pentadien-1-oic acid, bp 68-70° (17 mm), n_D^{20} 1.4710. Found %: C 68.56; H 8.83. $C_8H_{12}O_2$. Calculated %: C 68.54; H 8.63. IR spectrum (thin layer): $\nu = 1720$ cm^{-1} (CO), and 770, 980 cm^{-1} (CH = CH).

CONCLUSIONS

1. Conjugated polyenic aldehydes react with acetone cyanohydrin in the presence of triethylamine to give esters of γ,δ-unsaturated acids.

2. The aldehyde 4-methylpent-4-en-2-yn-1-al reacts with acetone cyanohydrin, in the presence of triethylamine and in alcoholic solution, to give a mixture of the ethyl esters of 2,3-cis- and 2,3-trans-4-methyl-2,4-pentadienoic acid.

3. The elucidation of the reactions described in this paper affords a new method for the synthesis of γ,δ-unsaturated esters and acids, hitherto accessible only with difficulty.

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