Synthetic Studies Starting from β-Cyanopropionaldehyde. I. The Synthesis of Adipic Dialdehyde

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β-Cyanopropionaldehyde (I) is an interesting compound which has two reactive functional groups. Although several procedures for the synthesis of this compound have hitherto been available, all of them are rather cumbersome as methods of preparation. In recent years, however, an improved technique for the oxo reaction of acrylonitrile to form I in a high yield has been developed by the members of the Ajinomoto Co., Ltd.,[1,2] and this cyanoaldehyde is now being used as an intermediate in the manufacturing of glutamic acid.

The purpose of our work is to extend synthetic studies, starting with β-cyanopropionaldehyde. In this paper the synthesis of adipic dialdehyde by Kolbe's electrolytic reaction is presented.

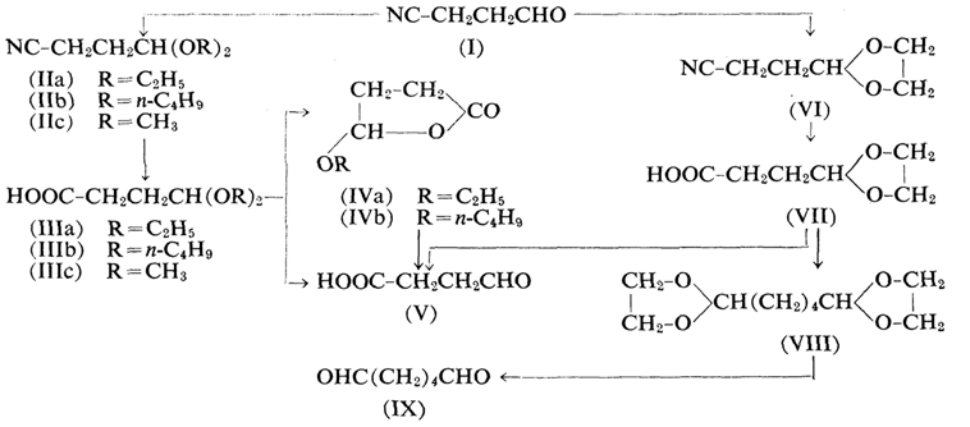
It is expected that the hydrolysis of the nitrile group will lead to β-formylpropionic acid (V), to which Kolbe's reaction is applicable. Although the procedure proposed has already been investigated with diethyl acetal of I (IIa) by Wohl,[3] little attention has been paid to the yield of each step of the reaction and to the isolation of the intermediate, β-formylpropionic acid diethyl acetal (IIIa). Therefore, our experiments will be described in detail in the present communication.

First the authors reinvestigated Wohl's procedure and purified the crude oily product (IIIa) by distillation under reduced pressure. A colorless liquid was obtained in a fairly good yield, but its analytical values were different from those of IIIa. It was a neutral substance, which was insoluble in water and which was hydrolyzed with dilute acid to V. Analytical values were very close to those of 5-ethoxy-γ-butyrolactone (IVa), and the infrared spectrum exhibited characteristic strong peaks at 1790 cm^{-1}, corresponding to that of the γ-lacton linkage. On the basis of these data, it has been concluded that the product is IVa formed by the loss of one molecule of ethanol from IIIa. In addition, it was also found that β-formylpropionic acid dibutyl acetal

1) J. Kato, H. Wakamatsu, R. Iwanaga and T. Yoshida, *J. Chem. Soc. Japan, Ind. Chem. Sec.* (*Kogyo Kagaku Zasshi*), **64**, 2139 (1961).

2) J. Kato, H. Wakamatsu, R. Iwanaga and T. Yoshida, ibid., **64**, 2142 (1961).

3) A. Wohl and H. Schweizer, *Ber.*, **39**, 890 (1906).



(IIIb) was decomposed in a fashion similar to 5-butoxy-γ-butyrolactone (IVb) by distillation, whereas methyl acetal (IIIc) was readily hydrolyzed to V during the course of the isolation.

As an attempt to isolate the acetal acid III of monohydric alcohol was unsuccessful, hydrolysis with the more stable cyclic ethylene acetal VI was examined. In this case, the reaction product was an acidic viscous liquid which was hydrolyzed with dilute acid to V. The analytical values and neutralization equivalent were in harmony with those of the expected acetal acid VII. Therefore, it was identified as β-formylpropionic acid ethylene acetal (VII).

The electrolysis of VII proceeded as usual, and the diethylene acetal of adipic dialdehyde (VIII) was obtained in about a 40%, yield with a small amount of by-product.

Experimental

Material. — β-Cyanopropionaldehyde (β-C.P.A.) (I) was obtained by the hydrolysis of its methyl acetal, supplied by the Ajinomoto Co., Ltd. It was used at once after distillation; b. p. 85°C/3 mmHg.

β-C.P.A.diethyl (IIa) and Dibutyl Acetals (IIb). —These acetals are prepared directly by the oxo reaction of acrylonitrile in the corresponding alcohols.[2] In our experiment, these were obtained by the acetalization of β-C.P.A. with the corresponding alcohols in the presence of hydrochloric acid as a catalyst; diethyl acetal, b. p. 84°C/5 mmHg; dibutyl acetal, b. p. 122°C/3 mmHg.

5-Ethoxy-γ-butyrolactone (IVa). — According to Wohl's method,[3] a crude potassium salt of β-formylpropionic acid diethyl acetal (IIIa) was obtained by the alkaline hydrolysis of β-C.P.A. diethyl acetal (IIa). This potassium salt was dissolved in as little water as possible, and the solution was acidified with dilute hydrochloric acid. Then the acetal acid was separated as a brown oil, which was extracted with ether and dried with anhydrous sodium sulfate. Distillation gave 14.1 g. of 5-ethoxy-γ-butyrolactone (b. p. 85°C/6 mmHg) from 31.4 g. of β-C.P.A. diethyl acetal. It was a neutral substance, insoluble in water, and its infrared spectra exhibited a strong absorption peak at 1790 cm^{-1} (characteristic of γ-lactone). Analysis gave the following results:

Found: C, 55.06; H, 8.01. Calcd. for $C_6H_{10}O_3$: C, 55.36; H, 7.75%.

To 5 g. of 5-ethoxy-γ-butyrolactone, 5 g. of 3% hydrochloric acid were added, and the mixture was refluxed for one hour. After cooling to room temperature, the resulting product was extracted with ether and dried with anhydrous sodium sulfate. Distillation gave 2.1 g. of β-formylpropionic acid (V) (b. p. 130~135°C/14 mmHg) forming a 2,4-dinitrophenylhydrazone, (m. p. 199°C), which showed no depression on admixture with an authentic specimen.

5-Butoxy-γ-butyrolactone (IVb).—Similarly, the hydrolysis of β-C.P.A. dibutyl acetal (IIb) gave 5-butoxy-γ-butyrolactone (b. p. 107°C/6 mmHg).

Found: C, 60.48; H, 9.08. Calcd. for $C_8H_{14}O_3$: C, 60.74; H, 8.92%.

β-Formylpropionic Acid (V). — A Similar treatment of β-C.P.A. dimethyl acetal (IIc) gave β-formylpropionic acid (V), identified as its 2,4-dinitrophenylhydrazone. In this case, no oil was separated after the acidification of the aqueous solution of the potassium salt of IIIc.

β-C.P.A.ethylene Acetal (VI). — A mixture of 1 mol. of β-C.P.A.dimethyl acetal, 1.5 mol. of ethylene glycol and 0.5 g. of *p*-toluenesulfonic acid was heated at 100~130°C in a distillation flask. The methanol formed in the reaction was immediately distilled off. The residue was poured into water, and the oil was extracted with ether. The fractional distillation of the extract gave 92.4 g. of β-C.P.A.ethylene acetal; b. p. 82°C/3 mmHg, yield 72.7%.

Found: N, 11.18. Calcd. for $C_6H_9O_2N$: N, 11.02%.

β-Formylpropionic Acid Ethylene Acetal (VII). —β-C.P.A. ethylene acetal (VI) was hydrolyzed by a method similar to Wohl's procedure. The aqueous solution of the potassium salt of VII was acidified to pH 3 with dilute hydrochloric acid. Since no oil was separated, the solution was extracted with ether repeatedly. The extract was then distilled, and the fraction boiling at 124~126°C/3 mmHg was collected. When this fraction was distilled two more times, 39.1 g. of pure β-formylpropionic acid ethylene acetal was given from 127 g.

of β-C.P.A.ethylene acetal (b. p. 114°C/1 mmHg). The yield was 26.8% of the theoretical amount. The acetal acid was a hygroscopic colorless liquid which solidified on standing at room temperature; m. p. 36°C.

Found: C, 49.07; H, 7.16. Calcd. for $C_6H_{10}O_4$: C, 49.31; H, 6.90%.

Neutralization equivalent. Found: 143.62. Calcd.: 146.14.

Adipic Dialdehyde Diethylene Acetal (VIII).—Forty-five grams (0.31 mol.) of β-formylpropionic acid ethylene acetal (VII) was electrolyzed in 130 ml. of methanol to which 1.7 g. (0.031 mol.) of potassium hydroxide had been added to neutralize about 10% of the total amount of acid used. The solution was placed in a cell consisting of a tall, flat-bottomed cylindrical, glass vessel fitted with a spiral-tube condenser, thermometer, and two parallel electrodes (platinum plate) (4×2.5 cm.), placed about 1~2 mm. apart. The cell was cooled by immersion in an ice-bath (internal temperature of cell, about 25~30°C), and a current of 5 amp. was passed through until the electrolyte became slightly alkaline. This usually required about 20% longer than the calculated time. At the end of the electrolysis, the solvent was removed and the residue diluted with 50 g. of water; the product was separated as an oil, which was extracted with ether and dried with anhydrous sodium sulfate. Distillation gave 12.1 g. of adipic dialdehyde diethylene acetal (b. p. 101~103°C/3 mmHg, yield 38.4%), which solidified upon being cooled in an refrigerator. Plates, m. p. 25~25.5°C.

Found: C, 59.11; H, 9.17. Calcd. for $C_{10}H_{18}O_4$: C, 59.39; H, 8.97%.

Besides, 4.1 g. of a colorless liquid was obtained as an unidentified by-product; b. p. 58~67°C/3 mmHg. VIII was mixed with the same amount of 3% hydrochloric acid and refluxed for one hour. After hydrolysis, the organic layer was extracted with ether and dried with anhydrous sodium sulfate. By distillation, adipic dialdehyde (IX) was obtained at a b. p. of 92~94°C/9 mmHg; yield ca. 95%. Bis-2,4-dinitrophenylhydrazone: m. p. 172~172.5°C (lit. m. p. 170°C).

Summary

A detailed study has been made of the synthesis of adipic dialdehyde starting from β-cyanopropionaldehyde. The hydrolysis of the acetal of this cyanoaldehyde gave β-formylpropionic acid acetal, to which Kolbe's electrolytic reaction was applied. The intermediate acetal acid has been successfully isolated in the case of ethylene acetal, whereas ethyl or butyl acetal decomposed by distillation into ethoxy- or butoxy-γ-butyrolactone, the structure of which has been established by analysis, infrared spectra and conversion to β-formylpropionic acid. Methyl acetal was also readily hydrolyzed to free aldehydic acid during the course of the isolation. Electrolysis of the ethylene acetal of β-formylpropionic acid in methanol gave adipic dialdehyde as its diethylene acetal.

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