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Synthetic Studies Starting from β-Cyanopropionaldehyde. IV. Reactions of β-Cyanoacrolein

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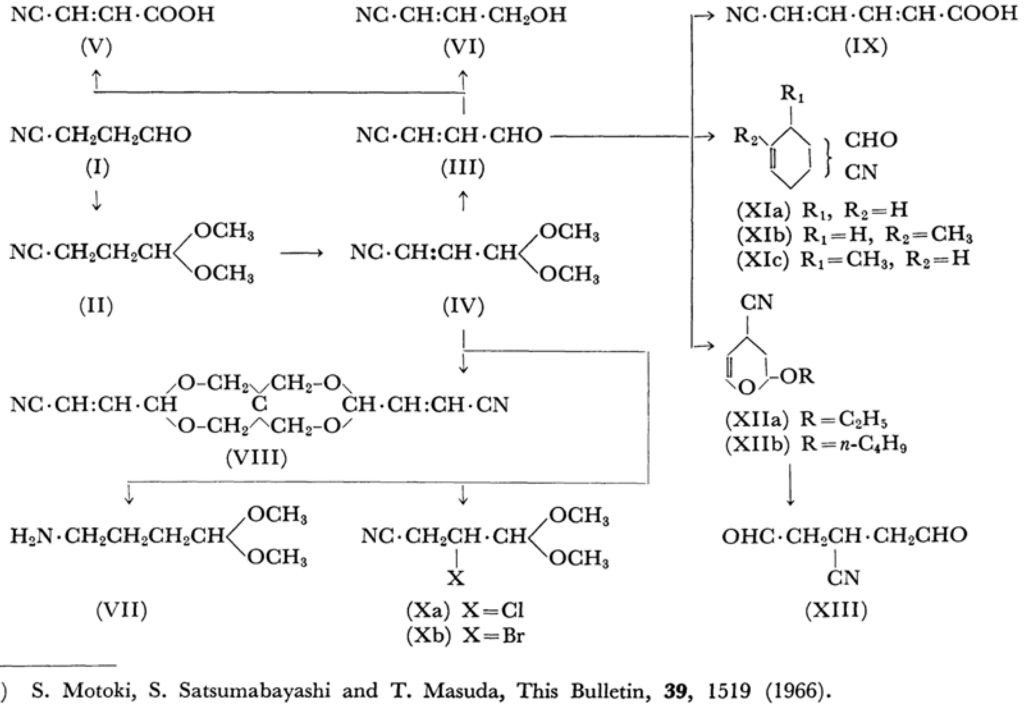
The reactions of β-cyanoacrolein or its dimethyl acetal were investigated. Various new compounds were prepared by the application of several basic reactions, namely, oxidation, reduction, addition, and others. Moreover, β-cyanoacrolein was found to react as a dienophile or as a diene in Diels-Alder reactions. In the reaction with butadiene, isoprene, and 1, 3-pentadiene, cyanotetrahydrobenzaldehyde derivatives were obtained. When ethyl vinyl ether or butyl vinyl ether was used as a dienophile, dihydropyran derivatives were prepared; this pyran was hydrolyzed with dilute hydrochloric acid to 2-cyanoglutaraldehyde.

In a previous paper of this series,[1] the synthesis of β-cyanoacrolein (III) starting from β-cyanopropionaldehyde (β-CPA) (I) was reported. β-Cyanoacrolein is expected to be useful for some synthetic reactions because it has two functional groups and a carbon-carbon double bond which is conjugated with both of these groups. Therefore, various reactions of III were examined in the present experiments. Almost all of the reaction products prepared were new substances and are hard to derive from other materials.

β-Cyanoacrolein was readily oxidized by sodium dichromate to β-cyanoacrylic acid (V), the double bond being preserved. Similarly, the selective reduction of the aldehyde group of III was carried out with sodium borohydride; γ-cyanoallyl alcohol (VI) was thus obtained. When the reduction of dimethyl acetal of III (IV) was carried out by the use of lithium aluminum hydride in dry ether, both the nitrile group and the double bond were attacked and γ-aminobutyraldehyde dimethyl acetal (VII) was obtained.

The treatment of IV with pentaerythritol in the presence of 2% sulfuric acid yielded 3, 9-bis-(2-cyanovinyl)-2, 4, 8, 10-tetraoxaspiro[5, 5]undecane (VIII). The condensation of III with malonic acid by Doebner's method gave 5-cyano-2, 4-pentadienoic acid (IX).



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[1] S. Motoki, S. Satsumabayashi and T. Masuda, This Bulletin, **39**, 1519 (1966).

Dimethyl acetal of III readily absorbed hydrogen chloride or hydrogen bromide to give chloro-β-cyanopropionaldehyde dimethyl acetal or bromo-β-cyanopropionaldehyde dimethyl acetal respectively. By means of a study of the NMR spectra, the bromo acetal thus obtained was found to be identical with that obtained by the bromination of β-CPA dimethyl acetal;1) that is, the bromine was introduced into the α-position of the aldehyde group (Xb). Although the chlorination of β-CPA acetal gave no single product, as has been stated in the previous paper,1) α-chloro acetal (Xa) can be readily isolated by this addition reaction.

In the Diels-Alder reaction, III can serve as a dienophile or a diene analog. For example, the reaction of III with butadiene gave 2-cyano-1, 2, 3, 6-tetrahydrobenzaldehyde (XIa) in a 63.7 % yield. When isoprene or 1, 3-pentadiene was used as a diene component, XIb or XIc was obtained. However, the position of the methyl group in the products was not determined. The reactions of III and cyclopentadiene or furane gave no product, and the starting materials were recovered. The addition of III to ethyl vinyl ether in the presence of a small amount of hydroquinone gave a dihydro-1, 2-pyran in a 72% yield. The NMR spectrum*1 was consistent with the structure XIIa: 6.32 (doublet, 1H) and 5.05 (triplet, 1H) for the olefinic protons, and 4.78 (triplet, 1H) for the methine proton adjacent to the two oxygen functions. Similarly, *n*-butyl vinyl ether condensed with III to give 2-*n*-butoxy-4-cyano-3, 4-dihydro-1, 2-pyran (XIIb). XIIa was hydrolyzed with dilute hydrochloric acid to 2-cyanoglutaraldehyde (XIII). This dialdehyde was an unstable substance and was identified as its 2, 4-dinitrophenylhydrazone.

Experimental

Materials. β-Cyanoacrolein (III) and β-cyanoacrolein dimethyl acetal (IV) were prepared as has been reported in the previous paper.1)

β-Cyanoacrylic Acid (V). A solution of 22.5 g of sodium dichromate, 30 g of concentrated sulfuric acid, and 100 m*l* of water was added to a solution of 12.2 g (0.15 mol) of III and 50 m*l* of water, with the temperature kept between 0 and −5°C. After the solution had been stirred for 2 hr at room temperature, the reaction mixture was extracted with ether and dried over anhydrous sodium sulfate. Ether was then removed, and the crude product was recrystallized from benzene to give 7.1 g of pure V; mp 98.0°C, yield 48.6%. IR: 3250(OH), 2275(CN), 1735(CO), 1645(C : C) cm^{-1}.

Found: C, 49.48; H, 3.34; N, 14.45%. Calcd for $C_4H_3O_2N$: C, 49.47; H, 3.12; N, 14.43%. Neutralization equivalent. Found: 98.4. Calcd: 97.1.

γ-Cyanoallyl Alcohol (VI). To a solution of 1.9 g (0.05 mol) of sodium borohydride and 24 m*l* of water containing one drop of 10% sodium hydroxide, 8.1 g (0.1 mol) of III were added at room temperature. After 3 hours' stirring, the solution was acidified with 20% sulfuric acid, extracted with ether, and dried. The distillation of the ether solution gave 2.5 g of V; bp 119—120°C/15 mmHg (lit.2) bp 119°C/15 mmHg), yield 30.1%. IR: 3380(OH), 2190(CN), 1640(C:C) cm^{-1}.

Found: C, 57.66; H, 6.30; N, 16.88%. Calcd for C_4H_5ON: C, 57.82; H, 6.07; N, 16.86%.

γ-Aminobutyraldehyde Dimethyl Acetal (VII). The reduction of the dimethyl acetal of III (IV) was carried out with lithium aluminum hydride in the usual manner. From 12.7 g of IV, 6.9 g of VII were obtained; bp 90—92°C/30 mmHg, yield 52.1%.

Found: C, 53.92; H, 11.48; N, 10.71%. Calcd for $C_6H_{15}O_2N$: C, 54.10; H, 11.35; N, 10.52%.

3, 9-Bis-(2-cyanovinyl)-2, 4, 8, 10-tetraoxaspiro-[5, 5]undecane (VIII). To a solution of 27 g (0.2 mol) of pentaerythritol in 50 m*l* of 2% sulfuric acid, 38.1 g (0.3 mol) of IV were added over a one-hour period at about 70°C. After another hour's stirring, the reaction mixture was cooled with ice. The crude product thus precipitated was collected and recrystallized from ethanol to give 18.1 g of VIII; mp 169—170°C, yield 46.2%.

Found: C, 59.53; H, 5.34; N, 10.57%. Calcd for $C_{13}H_{14}O_4N_2$: C, 59.53; H, 5.38; N, 10.68%.

5-Cyano-2, 4-pentadienoic Acid (IX). Into a solution of 31.2 g (0.3 mol) of malonic acid in 30 m*l* of pyridine, 24.3 g (0.3 mol) of III were slowly added at about 40°C with good agitation. After the evolution of carbon dioxide had ceased, the reaction mixture was heated on a steam bath for two hours, then cooled, neutralized with 50% sulfuric acid, and extracted with ether. After the removal of ether, a residual white solid was recrystallized from benzene and 10.8 g of IX were obtained; yield 29.2%, mp 173—174°C.

Found: C, 58.28; H, 4.27; N, 11.59%. Calcd for $C_6H_5O_2N$: C, 58.53; H, 4.09; N, 11.38%. Neutralization equivalent.

Found: 125.5. Calcd: 123.1.

α-Chloro-β-cyanopropionaldehyde Dimethyl Acetal (Xa). Into a four-necked, 300-m*l* flask, fitted with a stirrer, a dropping funnel, and an inlet tube, there were placed 100 g of absolute alcohol. The flask was then cooled with an ice-salt bath, and the alcohol was saturated with dry hydrogen chloride at about 0°C. Into the alcoholic hydrogen chloride solution, 38.1 g (0.3 mol) of IV were then stirred, drop by drop, at about 0°C. After the solution had stood overnight, the methanol was distilled off under reduced pressure. The residue was extracted with carbon tetrachloride, washed with water several times, and dried with anhydrous sodium sulfate. By distillation, 22.6 g of Xa were obtained at a bp of 88°C/4 mmHg: yield 46.3%.

Found: C, 43.76; H, 6.44; N, 8.68; Cl, 22.05%. Calcd for $C_6H_{10}O_2NCl$: C, 44.05; H, 6.16; N, 8.56; Cl, 21.67%.

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*1 Measured on a carbon tetrachloride solution at 60 Mc/sec. Chemical shifts are given in ppm units, using tetramethylsilane as an internal standard.

2) R. Vessiere, *Compt. rend.*, **245**, 699 (1957).

α-Bromo-β-cyanopropionaldehyde Dimethyl Acetal (Xb). This experiment was carried out like that described for Xa. From 38.1 g (0.3 mol) of IV, 34.3 g of Xb were obtained; bp 104—105°C/5 mmHg, yield 55.0%.

Found: C, 34.38; H, 5.10; N, 6.81; Br, 38.52%. Calcd for $C_6H_{10}O_2NBr$: C, 34.63; H, 4.87; N, 6.73; Br, 38.40%.

2-Cyano-1, 2, 3, 6-tetrahydrobenzaldehyde (XIa). A solution of 8.1 g (0.15 mol) of butadiene in 50 m*l* of benzene was added to 8.1 g (0.1 mol) of III. The mixture was then heated in an autoclave at about 100°C for 3 hr and cooled. By the distillation of the contents, 8.6 g of XIa were obtained; bp 105—106°C/5 mmHg, 63.7%. IR: 2239(CN), 1732(CO), 1657 (C:C) cm^{-1}.

Found: C, 70.77; H, 7.01; N, 10.28%. Calcd for C_8H_9ON: C, 71.09; H, 6.71; N, 10.36%.

4- or 5-Methyl-2-cyanotetrahydrobenzaldehyde (XIb). A mixture of 8.1 g (0.1 mol) of III and 10.2 g (0.15 mol) of isoprene was treated in the same manner as XIa. The yield of the product was 10.6 g; bp 112—113°C/5 mmHg, yield 71.2%. IR: 2262(CN), 1735 (CO), 1690(C:C) cm^{-1}.

Found: C, 72.13; H, 7.39; N, 9.28%. Calcd for $C_9H_{11}ON$: C, 72.45; H, 7.43; N, 9.39%.

3- or 6-Methyl-2-cyanotetrahydrobenzaldehyde (XIc). As in the preceding experiment, 8.8 g of XIc were obtained from 8.1 g (0.1 mol) of III and 10.2 g (0.15 mol) of 1, 3-pentadiene; bp 106—108°C/4 mmHg, yield 58.9%. IR: 2262(CN), 1735(CO), 1660(C:C) cm^{-1}.

Found: C, 72.15; H, 7.24; N, 9.39%. Calcd for $C_9H_{11}ON$: C 72.45; H, 7.43; N, 9.39%.

2-Ethoxy-4-cyano-3, 4-dihydro-1, 2-pyran (XIIa). A mixture of 8.1 g (0.1 mol) of III, 8.6 g (0.12 mol) of ethyl vinyl ether, and 0.1 g of hydroquinone was heated at 190°C for 3 hr in an autoclave. The mixture was then cooled and distilled to give 11.0 g of XIIa; bp 98—99°C/6 mmHg, yield 72.0%. IR: 2220(CN), 1642(C:C), 1230 and 1029(=C–O–C) cm^{-1}.

Found: C, 62.45; H, 7.48; N, 9.18%. Calcd for $C_8H_{11}O_2N$: C, 62.72; H, 7.24; N, 9.14%.

2-*n*-Butoxy-4-cyano-3, 4-dihydro-1, 2-pyran (XIIb). Similarly, 11.7 g of XIIb were obtained from 8.1 g (0.1 mol) of III and 12.0 g (0.12 mol) of *n*-butyl vinyl ether; bp 118—119°C/7 mmHg, Yield 64.6%. IR: 2224(CN), 1645(C : C), 1231 and 1033(=C–O–C) cm^{-1}.

Found: C, 66.25; H, 8.45; N, 8.02%. Calcd for $C_{10}H_{15}O_2N$: C, 66.27; H, 8.34; N, 7.73%.

2-Cyanoglutaraldehyde (XIII). A mixture of 7.7 g (0.05 mol) of XIIa and 20 g of 2% hydrochloric acid was refluxed for 8 hr. The reaction mixture was then extracted with ether. By distillation, 2.1 g of XIII were obtained at a bp of 135—137°C/4 mmHg, yield 36.8%.

The dialdehyde thus obtained was an unstable compound; it turned to resin immediately after distillation. Therefore, it was identified as 2, 4-dinitrophenylhydrazone, mp 153—155°C (dec.).

Found: C, 44.17; H, 3.38; N, 25.71%. Calcd for $C_{18}H_{15}O_8N_9$: C, 44.54; H, 3.12; N, 25.97%.

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