

Synthetic studies starting from
-cyanopropionaldehyde(9) : Reactions of
-cyanomethylacrolein

その他(別言語等) のタイトル	-シアノプロピオンアルデヒドよりの合成研究(第 9報) : -シアノメチルアクロレインの反応
著者(英語)	Sadayoshi Satsumabayashi, Shichiro Ito, Tadao Sato
journal or publication title	Bulletin of Nippon Dental University. General education
volume	6
page range	69-77
year	1977-03-25
URL	http://doi.org/10.14983/00000147



Synthetic Studies Starting from β -Cyanopropionaldehyde. IX.
Reactions of α -Cyanomethylacrolein

Sadayoshi SATSUMABAYASHI and Shichiro ITO

Nippon Dental University, Tokyo 1-chome, Fujimi, Chiyoda-ku, Tokyo

Tadao SATOH

Daito Chemical Industry Tochidaomiya 352, Tsurumi-ku, Osaka

(Received October 15, 1976)

β -シアノプロピオンアルデヒドよりの
合成研究 第 IX 報

α -シアノメチルアクロレインの反応

歯 学 部 薩摩林 貞 美
伊 藤 七 郎
大東化学工業研究課 佐 藤 忠 生

概 要

α -シアノメチルアクロレイ (2) は上記著者等の一人によりすでに合成発表された化合物で、分子内にアルデヒド基、シアノ基および炭素炭素二重結合をもつ反応性に富んだ特異的化合物である。したがって、化合物 2 は合成有機化学的見地からみると、出発原料である β -シアノプロピオンアルデヒド (1) よりさらに興味深い化合物であると考えられる。本研究では、この新しい合成中間体 2 に対し種々の反応を適用し、いくつかの文献未知の化合物を得たので、 β -シアノプロピオンアルデヒドの利用研究シリーズの 1 つとしてここに報告する。

化合物 2 は、クロム酸ナトリウムの低温酸化により、アルデヒド基のみ酸化され、アクリル酸誘導体 (3) を与えた。一方、ナトリウムボロハイドライドを作用させると、アルデヒド基のみ還元され、二重結合、ニトリル基をもったアルコール (4) が得られたが、リチウムナトリウムハイドライドをもちいると、共役系すべてが攻撃をうけ、化合物 5 が得られた。

ブリーデ等はペンタエリスリトールと脂肪族飽和アルデヒドとの反応によりスピラン環を含む新しい型の接着剤原料を開発した。本研究の原料 2 は先に述べたような特異的構造をもつアルデヒド故、同様な反応をおこなえば、さらに広い利用面が期待される化合物が得られると考えられる。そこで、化合物 2 とペンタエリスリトールとの間で脱水、縮合をおこない、いくつかの官能基を有するスピロアセタール (6) を得た。また、2 と活性メチ

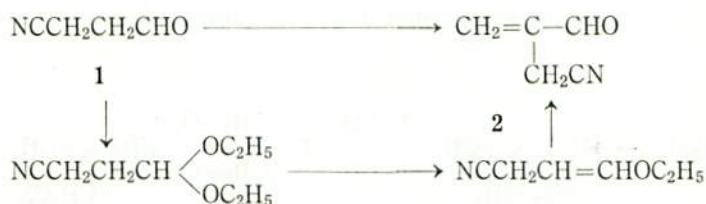
レン基をもつ化合物との反応もおこない、不飽和シアノケトエステル (7a)、不飽和シアノジケトン (7b) を得た。

ジールスアルダー反応は有機合成化学における最も有用な反応の1つであり、アクロレインやその他 α, β -不飽和カルボニル化合物の熱二量化も、1分子がジエンとして、1分子がジエノファイルとして反応していると考えれば、ジールスアルダー反応の1種とみなされる。化合物2もジエン、ジエノファイルの両方にもちいられることになる故、他のジエノファイル、ジエンとの反応をおこなった。ビニルエーテルとの付加反応では1, 2-ピラン誘導体 (8a, 8b) が、ブタジエン、イソプレンとの付加反応では置換シクロヘキセン (10a, 10b) が高収率で得られた。8a, 8b は加水分解によりグルタルアルデヒド誘導体 (9) を与えた。この付加反応において、反応条件から検討すると、化合物2のジエンとしての活性はブタジエン等より数段劣ることがわかった。

Synthetic Studies Starting from β -Cyanopropionaldehyde. IX¹⁾.

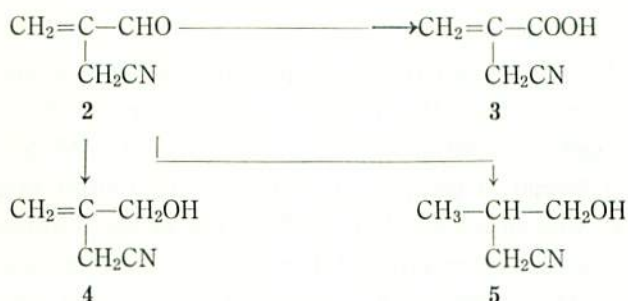
Reactions of α -Cyanomethylacrolein

As a part of synthetic studies starting from β -cyanopropionaldehyde (1), one of the authors reported that the reaction of ethyl γ -cyanopropenyl ether, which was obtained by heating the diethyl acetal of 1 with phthalic anhydride, with diethyl formal in the presence of boron trifluoride etherate as a catalyst led to α -cyanomethylacrolein (2)²⁾. This acrolein derivative was also obtained by the direct reaction of 1 with formaldehyde as in the Mannich-type reaction. The compound 2 is expected to be useful for some synthetic reactions, because it is a new vinyl compound which has an aldehyde group, a nitrile group and carbon carbon double bond conjugated with the aldehyde group. Therefore, as one of this series, studies on some basic reactions of 2 will be presented in this paper. The reaction products prepared in this investigation are all new compounds, and are hard to derive from other materials.

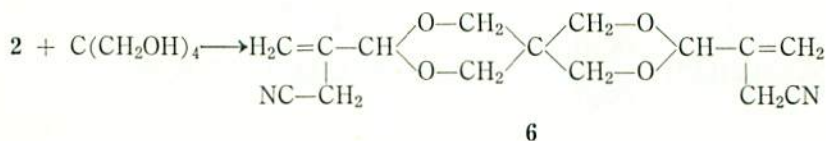


The compound 2 was readily oxidized by sodium dichromate at -5 to 0°C to α -cyanomethylacrylic acid (3), the carbon carbon double bond being preserved. This oxidation was difficult to control above 30°C , and a large amount of tarry substance was formed, because both the material and the product are likely to polymerize by heating. The selective reduction of the aldehyde group of 2 with sodium borohydride was carried out in water at room temperature, α -cyanomethylallyl alcohol (4) was obtained. The analytical values of the product were in accord with the calculated values of 4,

and the infrared spectrum showed the characteristic absorptions of hydroxyl group at 3400 cm^{-1} , of unconjugated nitrile at 2250 cm^{-1} , of the carbon carbon double bond at 1645 cm^{-1} , and no absorption in the carbonyl region at about $1750\text{--}1650\text{ cm}^{-1}$. When the reduction of **2** was carried out by the use of lithium aluminium hydride in stead of sodium borohydride in dry ether at about 35°C , both the aldehyde group and the double bond were attacked, 3-cyano-2-methyl-1-propanol (**5**) was obtained, since the carbon carbon double bond conjugated with aldehyde group.

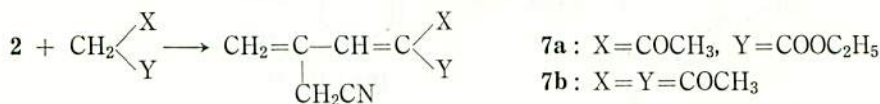


In recent years, a characteristic acetal including spirane ring has been prepared from pentaerythritol and an aldehyde³. This spiro acetal is unusually stable compound to alkali and is used for material of a binding agent. Treatment of **2** with pentaerythritol in the presence of 2% sulfuric acid at about 70°C gave 3, 9-bis-(1-cyanomethylvinyl)-2, 4, 8, 10-tetraoxaspiro-[5, 5]-undecane (**6**). Since this spiroacetal **6** has a nitrile, a carbon carbon double bond and a spirane ring, it is regarded as the organic industrial materials of wide utilities.



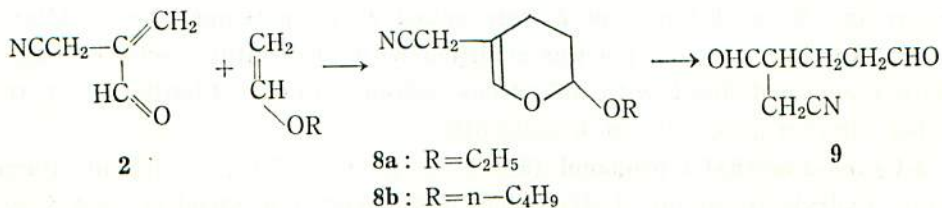
As one of this series, we have reported the reactions of β -cyanopropion-aldehyde (**1**) with several compounds having an active methylene group to prepare the new unsaturated cyanoesters⁴. This condensation was also extended to **2** in this investigation. The material **2** was readily converted into ethyl 2-cyanomethylallylideneacetate (**7a**) or 2-cyanomethylallylideneacetylacetone (**7b**) in the reaction with ethyl acetoacetate or acetylacetone, respectively. This reaction was carried out in benzene in the presence of

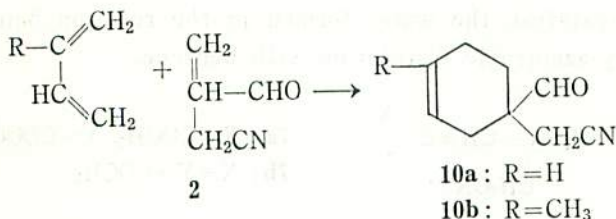
piperidine acetate as catalyst, the water formed in the reaction being removed continuously by azeotropic distillation with benzene.



One of the most useful reactions in synthetic organic chemistry is the 1,4-addition of an ethylenic compound to a conjugated diene, discovered by Diels and Alder⁵⁾, to yield a six-membered ring. The thermal dimerization of acrolein or of other conjugated carbonylic compounds involve the addition of one molecule activated at the 1, 4-positions of the conjugated system to another molecule activated at the carbon-carbon double bond. The addition has a formal similarity to the Diels-Alder reaction in that the conjugated carbonylic compounds behave both as a diene, 1, 4-addition, and as a dienophile, 1, 2-addition. As might be expected, the compound **2** can serve as a dienophile or diene analog. Therefore we examined the reactions of **2** with dienophiles, and with conjugated dienes.

The addition of **2** to ethyl vinyl ether at 190°C for 3 hr in the presence of a small amount of hydroquinone gave 2-ethoxy-5-cyanomethyl-3,4-dihydro-1,2-pyran (**8a**) in a 75% yield. Similarly, *n*-butyl vinyl ether added to **2** to give 2-*n*-butoxy-5-cyanomethyl-3,4-dihydro-1,2-pyran (**8b**). These pyran derivatives were hydrolyzed with dilute hydrochloric acid to substituted glutaraldehyde (**9**). On the other hand, the reaction of **2** with butadiene was carried out at about 100°C for 3 hr and 1-cyanomethyl-1-formyl-3-cyclohexene (**10a**) was obtained in a 76% yield. When isoprene was used as a diene component, 1-cyanomethyl-1-formyl-4-methyl-3-cyclohexene (**10b**) was obtained. On the basis of the above results, it has been concluded that C=C-C=O compounds are appreciably less reactive than C=C-C=C compounds since the former require a 90°C higher temperature for comparable yields. The reaction of **2** with styrene, cyclopentadiene or furan gave no product and the starting materials were recovered. Methacrylonitrile and acrylonitrile gave resins in the reaction of **2**, since they polymerized far more readily.





Experimental

The NMR spectra were recorded with a JNM-PMX 60 NMR spectrometer at room temperature. Carbon tetrachloride and chloroform-d were used as solvents, and tetramethylsilane was used as an internal reference. The chemical shifts were recorded in δ values, and were followed by the splitting pattern: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet.

The Mass spectra were obtained on a Hitachi RMU-7M spectrometer (ionizing potential: 70 eV; chamber temperature: 150°C). The IR spectra were measured in potassium bromide discs or liquid films using a Hitachi 285 Grating Infrared spectrometer.

The structural assignments of the reaction products were done by means of their NMR, IR and Mass spectra, and by elemental analyses.

α -Cyanomethylacrolein (2). This aldehyde was prepared as reported in the previous paper²⁾.

α -Cyanomethylacrylic Acid (3). A solution of 15 g of sodium dichromate, 20 g of concentrated sulfuric acid and 100 ml of water was added to a solution of 9.5 g (0.1 mol) of **2** and 50 ml 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 5 g of pure **3**, yield 45%. Neutralization equivalent. Found: 110. Calcd: 111.

α -Cyanomethylallyl Alcohol (4). To a solution of 1.9 g (0.05 mol) of sodium borohydride and 24 ml of water containing one drop of 10% sodium hydroxide, 9.5 g (0.1 mol) of **2** were added at room temperature. After 3 hours' stirring, the solution was acidified with 20% sulfuric acid, extracted with ether, and dried with anhydrous sodium sulfate. Distillation of the ether solution gave 6.0 g of **4**, yield 64%.

3-Cyano-2-methyl-1-propanol (5). A solution of 7.6 g of lithium aluminum hydride in 200 ml of dry ether was placed in a 500 ml of flask fitted

Table 1. Bp ($^{\circ}\text{C}/\text{mmHg}$) and IR (cm^{-1}) Data

Compd	Bp (Mp, $^{\circ}\text{C}$)	IR			
		C=N	C=O	C=C	OH or -O-
3	(79-80)	2260	1695	1640	2650
4	110-111/6	2250	-	1645	3400
5	91-94/15	2240	-	-	3350
6	(103-104)	2255	-	1645	1205 1120 1090 1030
7a	141-143/2	2260	1695 1665	1645 1610	-
7b	124-126/3	2260	1665	1640 1605	-
8a	109-110/9	2250	-	1670	1230 1145 1090 1065
8b	131-132/6	2250	-	1670	1230 1120 1065 1030
9	143-145/2	2245	1735 1725	-	-
10a	114-116/5	2245	1740	1660	-
10b	120-122/5	2245	1740	1670	-

Table 2. NMR Data

Compd	NMR (δ , ppm)						
3	11.5 (s, 1)	6.7 (d, 1)	6.4 (d, 1)	3.3 (s, 2)			
4	6.5 (d, 1)	6.2 (d, 1)	4.9 (s, 1)	3.2 (s, 2)	3.0 (s, 2)		
5	4.6 (s, 1)	2.7 (d, 2)	2.5 (d, 2)	1.4 (m, 1)	0.8 (d, 3)		
6	6.6 (d, 1)	6.3 (d, 1)	4.9 (s, 1)	3.4 (s, 4)	3.1 (s, 2)		
7a	6.9 (s, 1)	6.8 (d, 1)	6.5 (d, 1)	4.3 (q, 2)	3.1 (s, 2)	2.7 (s, 3)	1.3 (t, 3)
7b	6.9 (s, 1)	6.8 (d, 1)	6.5 (d, 1)	3.1 (s, 2)	2.9 (s, 3)	2.8 (s, 3)	
8a	6.3 (s, 1)	4.9 (t, 1)	3.6 (q, 2)	2.9 (s, 2)	1.9 (m, 4)	1.2 (t, 3)	
8b	6.3 (s, 1)	4.9 (t, 1)	3.5 (q, 2)	2.9 (s, 2)	1.9 (m, 4)	1.5 (m, 4)	0.9 (t, 3)
9	9.7 (d, 1)	9.5 (t, 1)	2.9 (m, 1)	2.8 (m, 2)	2.6 (d, 2)	2.2 (m, 2)	
10a	9.7 (s, 1)	5.8 (m, 1)	5.5 (m, 1)	3.1 (s, 2)	1.8 (m, 6)		
10b	9.7 (s, 1)	5.4 (t, 1)	3.1 (s, 2)	1.8 (m, 6)	1.3 (s, 3)		

with a stirrer, reflux condenser, dropping funnel, and calcium chloride tube. To the solution, 9.5 g (0.1 mol) of **2** was added, with stirring, at such a rate that the mixture continues to boil. While stirring was continued, water was dropped in, cautiously and with strong cooling, to decompose the excess of hydride. Then the mixture was poured into 100 ml of ice-water, treated with 10% sulfuric acid and extracted with ether. The ethereal extract was

Table 3. Analytical and Mass Spectral Data

Compd	Formula	MW	Calcd (%)			Found (%)			Mass M ⁺
			C	H	N	C	H	N	
3	C ₅ H ₅ O ₂ N	111	54.05	4.54	12.61	53.79	4.76	12.88	111
4	C ₅ H ₇ ON	97	61.84	7.27	14.42	61.45	7.53	14.66	97
5	C ₅ H ₉ ON	99	60.61	9.09	14.14	60.42	10.22	14.31	99
6	C ₁₅ H ₁₈ O ₄ N ₂	290	62.07	6.21	9.66	61.83	6.33	9.90	290
7a	C ₁₁ H ₁₃ O ₃ N	207	63.77	6.28	6.76	63.58	6.34	6.89	207
7b	C ₁₀ H ₁₁ O ₂ N	177	67.80	6.21	7.91	67.66	6.38	8.04	177
8a	C ₉ H ₁₃ O ₂ N	167	64.65	7.84	8.38	64.33	7.86	8.70	167
8b	C ₁₁ H ₁₇ O ₂ N	195	67.66	8.78	7.17	67.28	8.91	7.45	195
9	C ₇ H ₉ O ₂ N	139	60.42	6.52	10.07	59.95	6.54	10.08	139
10a	C ₉ H ₁₁ ON	149	72.48	7.38	9.40	72.20	7.50	9.67	149
10b	C ₁₀ H ₁₃ ON	163	73.62	7.98	8.59	73.46	8.11	8.73	163

dried and evaporated, and the compound **5** obtained as residue was distilled through a column. The yield was 6.9 g, 70%.

3, 9-Bis-(1-cyanomethylvinyl)-2, 4, 8, 10-tetraoxaspiro-[5, 5]-undecane (6). A mixture of 13.6 g (0.1 mol) of pentaerythritol and 50 ml of water containing 1 g of concentrated sulfuric acid was heated to about 70°C. To the solution thus obtained, 9.5 g of **2** was added over a two hour period at the same temperature. After another two hours' stirring, the reaction mixture was cooled with ice. The crude product precipitated was collected and recrystallized from ethanol to give 12 g of **6**, yield 82%.

Ethyl 2-Cyanomethylallylideneacetoacetate (7a). A mixture of 0.2 mol of ethyl acetoacetate, 0.5 g of piperidine acetate and 200 ml of benzene was gently refluxed, and 9.5 g (0.1 mol) of **2** was added slowly, the water formed in the reaction was continuously removed off by azeotropic distillation with benzene. The reaction mixture was cooled and washed with water. Distillation of the benzene solution gave 12 g of **7a**, yield 58%.

2-Cyanomethylallylideneacetylacetone (7b). Into a solution of 0.2 mol of acetylacetone, 0.5 g of piperidine acetate and 200 ml of benzene, 9.5 g (0.1 mol) of **2** was added with good agitation at room temperature. The mixture was then refluxed for two hours, the water formed being removed. Fractional distillation of this benzene solution gave 13 g of **7b**, yield 73%.

2-Ethoxy-5-cyanomethyl-3,4-dihydro-1,2-pyran (8a). A mixture of 9.5 g of **2**, 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 12.6 g of **8a**, yield 75%.

2-Butoxy-5-cyanomethyl-3, 4-dihydro-1, 2-pyran (8b). This pyran was prepared in the same manner as **8a**. From 9.5 g of **2** and 12.0 g (0.12 mol) of butyl vinyl ether, 12.3 g of **8b** was obtained, yield 63%.

α -Cyanomethylglutaraldehyde (9). A mixture of 8.4 g (0.05 mol) of **8a** and 20 g of 2% hydrochloric acid was stirred for 1 hr, during which time the temperature rose to 40° and the mixture became clear. This clear solution was then refluxed for 8 hr and cooled. The reaction mixture was neutralized with sodium bicarbonate, saturated with sodium chloride and extracted with ether. By distillation of the extract, 4.1 g of **9** was obtained, yield 59%.

Similarly, the dialdehyde **9** was obtained from **8b**, yield 48%.

1-Cyanomethyl-1-formyl-3-cyclohexene (10a). A solution of 8.1 g (0.15 mol) of butadiene in 50 ml of benzene was added to 9.5 g of **2**. The mixture was then heated in an autoclave at about 100°C for 3 hr and cooled. By distillation of this contents, 11.3 g of **10a** was obtained, yield 76%.

1-Cyanomethyl-1-formyl-4-methyl-3-cyclohexene (10b). As in the preceding experiment, 12.0 g of **10b** was obtained from 9.5 g of **2** and 10.2 g (0.15 mol) of isoprene, yield 74%.

The authors wish to thank Professor Dr. Shinichi Motoki, Science University of Tokyo, for his helpful advice and encouragement.

References

- 1) Part VIII, S. Ito, S. Satsumabayashi, T. Ohsugi and A. Fukuta, *This Bulletin*, **5**, 99 (1976).
- 2) S. Satsumabayashi and S. Motoki, *Bull. Chem. Soc. Japan*, **41**, 2538 (1968).
- 3) E. H. Pryde, R. A. Awl, H. M. Teeter and J. C. Cowan, *J. Poly. Sci.*, **59**, 1 (1962).
- 4) S. Satsumabayashi, S. Ito and S. Motoki, *This Bulletin*, **4**, 147 (1975).
- 5) O. Diels and K. Alder, *Ann. Chem.*, **460**, 111 (1928).