BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN VOL. 43 963—965 (1970)

Reaction of Acetonitrile with Carboxylic Esters

Akira UCHIDA, Akio DOYAMA and Sumio MATSUDA

Faculty of Engineering, Osaka University, Yamadakami, Suita

(Received June 21, 1969)

Acetonitrile is metalated by means of alkali amide,[1,2] sodium,[2] alkyllithium,[3] lithium diethylamide[4] or sodium with naphthalene,[5] using ether, petroleum ether, benzene or ethylene glycol dimethyl ether as the solvent.

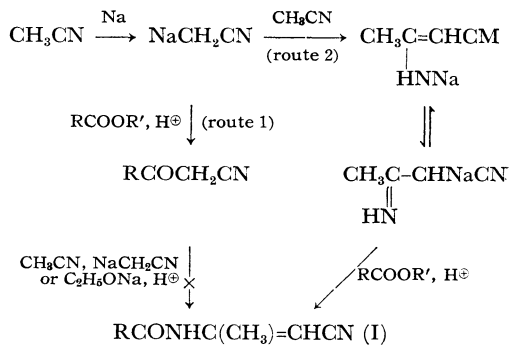
In a previous paper, a large excess of acetonitrile was treated with sodium, and then the reaction of the resultant cyanomethylsodium with aromatic carbonyl compounds was attempted.[7]

It is well known that cyanomethyl carbanion

1) H. Lettré, G. Meiners and H. Wickmann, *Naturwissenschaften*, **33**, 158 (1946).
2) R. Holtzwart, *J. Prakt. Chem.* [2], **39**, 230 (1885).
3) E. M. Kaiser, *J. Org. Chem.*, **33**, 3402 (1968).
4) K. Ziegler and H. Ohlinger, *Ann.*, **495**, 84 (1932).
5) Du Pont de Memours & Co., U. S. 2307643 (1940).
6) E. Mohr, *J. Prakt. Chem.* [2], **56**, 125 (1897).
7) A. Uchida, S. Saito and S. Matsuda, This Bulletin, **42**, 2989 (1969).

adds to acetonitrile to form diacetonitrile (β-aminocrotononitrile or β-iminobutyronitrile),[2,4,5] and that diacetonitrile condenses with carbonyl compounds.[6] However, when the reaction of cyanomethylsodium with aromatic carbonyl compounds was attempted in acetonitrile, the derivatives of hydroxypropionitrile or the derivatives of cinnamonitrile were obtained.[7] These results suggest that the cyanomethyl carbanion in acetonitrile did not add to the solvent molecule, but instead reacted predominantly with aromatic carbonyl compounds.

The present study will deal with the reaction of cyanomethyl carbanion (or cyanomethylsodium) with carboxylic esters in acetonitrile.



Results and Discussion

Lettré *et al.* attempted the condensation reaction of acetonitrile with various esters using sodium amide in ether and obtained the derivatives of acylacetonitrile.[1] According to the results described in a previous paper,[7] the formation of acylacetonitrile can be expected in the reaction of cyanomethylsodium with esters in acetonitrile.

When a solution of ethyl acetate and cyanomethylsodium in acetonitrile was heated under reflux for an hour, a crystalline solid was formed in a fairly good yield. This solid was identified as β-acetamidocrotononitrile from the spectroscopic data and from the results of elementary analysis, although the mp was not identical with that reported in the literature.[8] Similarly, β-benzamidocrotononitrile was obtained by the reaction of methyl benzoate.

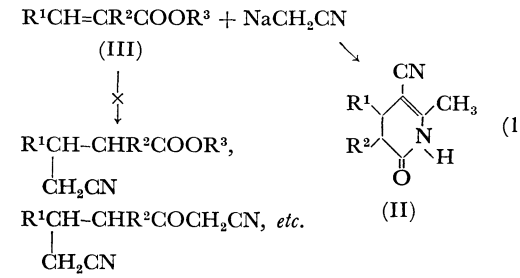
The reaction of diethyl carbonate with acetonitrile in ether or alcohol, using sodium amide[9,10] or sodium ethoxide[11] as the catalysts, has been reported to give ethyl cyanoacetate. The reaction of diethyl carbonate with cyanomethylsodium in acetonitrile, however, resulted in the production of β-ethoxycarbonylaminocrotononitrile. These results are completely different from those to be expected on the basis of the previous paper.[7]

There might be at least two possible routes for the formation of β-acylaminocrotononitrile (I) by the reaction of an ester with cyanomethylsodium in acetonitrile.

If acylacetonitrile is formed by the reaction of cyanomethylsodium with esters, and if the resultant acylacetonitrile is added to a solvent molecule, any rearrangement will give I (route 1). On the other hand, if the reactivities of esters towards cyanomethylsodium are less than that of acetonitrile, cyanomethylsodium will add to acetonitrile preferentially to form diacetonitrile and the reaction of diacetonitrile with the esters will give I (route 2).

When a mixture of acetonitrile, acylacetonitrile (α-cyanoacetophenone or ethyl cyanoacetate,) and sodium ethoxide or cyanomethylsodium was heated under reflux for an hour, almost all of the acylacetonitrile was recovered. This means that the most plausible process is not the route 1 but the route 2. The discrepancies which exist between the aromatic carbonyl compounds and the esters may be supposed to be due to the differences in the reactivities of these two kinds of reactants towards cyanomethyl carbanion.

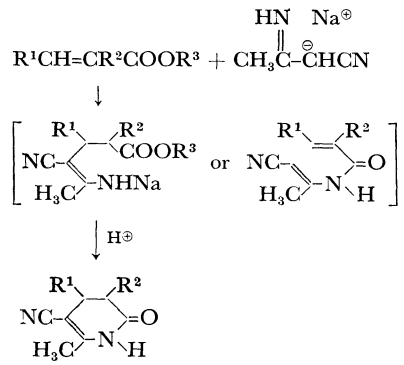
In the case of the reaction of the α,β-unsaturated ester with cyanomethylsodium in acetonitrile, the Michael-type addition was expected to occur. However, no Michael-type addition product was obtained; only the derivative of dihydropyridone (II) was obtained.



		R^1	R^2	R^3
II, III	a	H	H	CH_3
	b	H	CH_3	C_2H_5
	c	C_6H_5	H	CH_3
	d	CH_3	H	C_2H_5
	e	CH_3	$COOC_2H_5$	C_2H_5

Although the mechanism of the reaction (1) is not clearly known, the following process seems plausible.

8) Du Pont de Memours & Co., U. S. 2333493 (1941).
9) R. Levine and C. R. Hauser, *J. Amer. Chem. Soc.*, **68**, 761 (1946).
10) Mallinchrodt Chem. Works, U.S. 2342385 (1941).
11) V. H. Wallingford, D. M. Jones and A. H. Homeyer, *J. Amer. Chem. Soc.*, **64**, 577 (1942).



Experimental

The same instruments as those described in the previous paper[7] were used for the spectroscopic measurements.

The esters (unless otherwise noted, 0.5 mol per 1.0-g atom of sodium) was added to a solution which had previously been prepared by the dissolution of sodium in acetonitrile (375 *ml* per 1.0-g atom of sodium)and was cooled in an ice-water bath. Then the mixture was heated under reflux for an hour and neutralized with dilute sulfuric acid. The organic phase was separated and dried over anhydrous magnesium sulfate, and the solvent was removed by distillation. From the residues, the following products were isolated.

β-Acetamidocrotononitrile, from ethyl acetate, in a 64% yield; mp 107—110°C (ethanol-water) (lit,[8] mp 53°C); IR (KBr Disk) 2220 cm^{-1} (CN), 1720 cm^{-1} (CO), 1640 cm^{-1} (C=C); NMR ($CDCl_3$) τ 7.89, 7.85 (3H×2, s, C$\underline{H}_3$), 3.60 (1H, s, C=C$\underline{H}$), 1.79 (1H, broad, CON$\underline{H}$).

Found: C, 57.82; H, 6.75; N, 22.72%; M^+, 124. Calcd for C_6H_8ON: C, 58.05; H, 6.50; N, 22.75%; mol wt, 124.14.

β-Benzamidocrotononitrile, from 0.46 mol of methyl benzoate per 1.0-g atom of sodium, in an 88% yield; mp 81—83°C (benzene); IR (KBr Disk) 2220 cm^{-1} (CN), 1685 cm^{-1} (C=C); NMR ($CDCl_3$) τ 7.75 (3H, s, C$\underline{H}_3$), 3.47 (1H, s, C=C$\underline{H}$CN), 2.5 (6H, m, aryl $\underline{H}$+N$\underline{H}$).

Found: C, 70.67; H, 5.46; N, 15.09%; M^+, 186. Calcd for $C_{11}H_{10}ON_2$: C, 70.95; H, 5.41; N, 15.05%; mol wt, 186.21.

β-Ethoxycarbonylaminocrotononitrile, from diethyl carbonate, in a 69% yield; mp 87—90°C(acetone); IR (KBr Disk) 2200 cm^{-1} (CN), 1750 cm^{-1} (CO), 1640 cm^{-1} (C=C); NMR ($CDCl_3$) τ 8.71 (3H, t, J=7 Hz, C$\underline{H}_3$CH$_2$), 7.82 (3H, s, C$\underline{H}_3$), 5.81 (2H, q, J=7 Hz, CH$_3$C$\underline{H}_2$), 4.04 (1H, s, C$\underline{H}$CN), 2.65 (1H, broad, CON$\underline{H}$).

Found: C, 54.67; H, 6.86; N, 18.17%; M^+, 154. Calcd for $C_7H_{10}O_2N_2$: C, 54.53; H, 6.54; N, 18.17%; mol wt, 154.17.

3,4-Dihydro-5-cyano-6-methyl-2-pyridone (IIa), from methyl acrylate, in a 69% yield; mp 213—214°C (THF); IR (KBr Disk) 3200, 3150 cm^{-1} (NH), 2200 cm^{-1} (CN), 1690 cm^{-1} (CO), 1650 cm^{-1} (C=C); NMR ($CDCl_3$) τ 7.88 (3H, s, C$\underline{H}_3$), 7.57 (4H, s, C$\underline{H}_2$C$\underline{H}_2$), 1.50 (1H, broad, CON$\underline{H}$).

Found: C, 61.58; H, 6.05; N, 20.43%; M^+, 136. Calcd for $C_7H_8ON_2$: C, 61.75; H, 5.92; N, 20.85%; mol wt, 136.15.

3,4-Dihydro-3,6-dimethyl-5-cyano-2-pyridone (IIb), from ethyl methacrylate, in a 75% yield; mp 148—150°C (ethanol); IR (KBr Disk) 3200, 3100 cm^{-1} (NH), 2200 cm^{-1} (CN), 1690 cm^{-1} (CO), 1650 cm^{-1} (C=C); NMR ($CDCl_3$) τ 8.77 (3H, d, J=6.0 Hz, C$\underline{H}_3$-CH), 7.86 (3H, s, C$\underline{H}_3$), 7.1—7.7 (3H, m, C$\underline{H}_2$C$\underline{H}$), 1.10 (1H, broad, CON$\underline{H}$).

Found: C, 64.00; H, 7.02; N, 18.77%; M^+, 150. Calcd for $C_8H_{10}ON_2$: C, 63.98; H, 6.71; N, 18.65%; mol wt, 150.18.

3,4-Dihydro-4-phenyl-5-cyano-6-methyl-2-pyridone (IIc), from 0.4 mole of methyl cinnamate per 1.0-g atom of sodium, in a 72% yield; mp 188—190°C (methanol); IR (KBr Disk) 3200, 3100 cm^{-1} (NH), 2200 cm^{-1} (CN), 1685 cm^{-1} (CO), 1634 cm^{-1} (C=C); NMR ($CDCl_3$) τ 7.86 (3H, s, C$\underline{H}_3$), 7.16 (2H, m, C$\underline{H}_2$), 6.12 (1H, m, C_6H_5C$\underline{H}$), 2.73 (5H, m, aryl $\underline{H}$), 1.12 (1H, broad, CON$\underline{H}$).

Found: C, 73.65; H, 5.45; N, 13.23%; M^+, 212. Calcd for $C_{13}H_{12}ON_2$: C, 73.56; H, 5.70; N, 13.20%; mol wt, 212.24.

3,4-Dihydro-4,6-dimethyl-5-cyano-2-pyridone (IId), from ethyl crotonate, in a 57% yield; mp 130—132°C (acetonitrile); IR (KBr Disk) 3200, 3100 cm^{-1} (NH), 2200 cm^{-1} (CN), 1670 cm^{-1} (CO), 1620 cm^{-1} (C=C); NMR ($CDCl_3$) τ 8.78 (3H, d, J=6.3 Hz, C$\underline{H}_3$-CH), 7.87 (3H, s, C$\underline{H}_3$C=C), 7.85—7.04 (3H, m, C$\underline{H}$-C$\underline{H}_2$), 1.02 (1H, broad, CON$\underline{H}$).

Found: C, 64.04; H, 7.08; N, 19.07%; M^+, 150. Calcd for $C_8H_{10}ON_2$: C, 63.98; H, 6.71; N, 18.69%; mol wt, 150.18.

3,4-Dihydro-3-ethoxycarbonyl-4,6-dimethyl-5-cyano-2-pyridone (IIe), from 0.4 mole of diethyl ethylidenemalonate per 1.0-g atom of sodium, in 60% yield; mp 91—93°C (ethanol-water); IR (neat) 3250 cm^{-1} (NH), 2200 cm^{-1} (CN), 1700 cm^{-1} (CO), 1640 cm^{-1} (C=C); NMR ($CDCl_3$) τ 8.73 (3H, d, J=7.0 Hz, C$\underline{H}_3$CH), 8.70 (3H, t, J=7.0 Hz, C$\underline{H}_3$CH$_2$), 7.83 (3H, s, C$\underline{H}_3$ C=C), 6.6—7.2 (2H, m, CH$_3$C$\underline{H}$C$\underline{H}$COOC$_2$H$_5$), 5.73 (2H, q, J=7.0 Hz, CH$_3$C$\underline{H}_2$), 1.20 (1H, broad, CON$\underline{H}$).

Found: C, 59.17; H, 6.40; N, 12.60%; M^+, 222. Cacld for $C_{11}H_{14}O_3N_2$: C, 59.45; H, 6.35; N, 12.60%; mol wt, 222.24.