Efficient Synthesis of Aroyl Cyanides and Hetero Analogs from Aroyl Chlorides and Potassium Cyanide

Masato TANAKA*, Masayuki KOYANAGI

National Chemical Laboratory for Industry, Yatabe, Tsukuba, Ibaraki 305, Japan

According to a recent report[1], cyanohydrin esters may be obtained in high yield by treatment of carboxylic anhydrides with sodium cyanide/sodium borohydride in aqueous dioxan. The reaction is assumed to proceed via the *in situ* formation and reduction of acyl cyanides. It was stated that the carboxylic anhydrides cannot be replaced by the acid chlorides because in the latter case the reaction does not proceed without considerable hydrolysis taking place. Prompted by the report of Ref.[1], we publish here our results obtained in the synthesis of aroyl cyanides.

In a previous paper[2], one of us reported that acyl cyanides may be conveniently prepared by reaction of acyl chlorides with tributyltin cyanide. In continuation of our investigations on this subject we tried to catalyze the reaction of acyl chlorides with potassium cyanide by tributyltin cyanide but we found that the desired conversion proceeds quite fast even in the absence of the phase-transfer catalyst tributyltin cyanide when acetonitrile is used as solvent.

1 2

In particular, the reactions of 2-methylbenzoyl, furan-2-carbonyl, and thiophene-2-carbonyl chloride proceeded cleanly to give the corresponding acyl cyanides **(2)** in high yields. The use of propanenitrile, benzonitrile, benzene, dimethylformamide, or sulfolane as solvent did not improve the results to an appreciable extent. We further tried to promote the reaction by 18-crown-6 and/or tributyltin chloride; however, the use of these additives was found to be favorable only in few cases. It occurred to us that the addition of a small amount of water to the reaction mixture might attack the crystal lattice of the solid potassium cyanide in the mixture and thus promote the reaction. This is indeed the case; in the presence of a small amount of water, the reaction proceeds much faster. If only a limited amount of water is used hydrolysis of the starting acyl chloride **(1)** and of the product aroyl cyanide **(2)** is not a serious problem. Figure 1 shows that the time/conversion curve of the reaction of benzoyl chloride is a function of the amount of water used and that too long reaction times lead to a decrease in yield due to hydrolysis of the product. On the other hand, the effect of water on the reaction largely depends on the structure of the starting acyl chlorides (Figure 2).

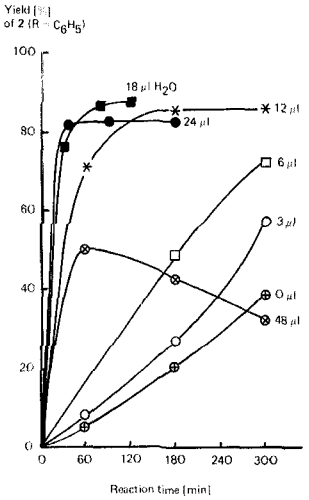


Figure 1.

The effect of added water on the reaction of benzoyl chloride with potassium cyanide in acetonitrile (3 ml) at 80 °C.

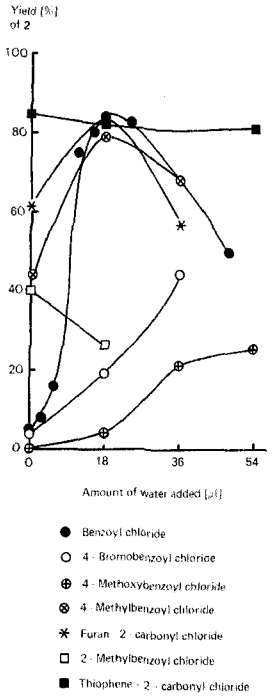


Figure 2.

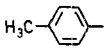
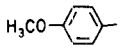
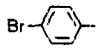
The effect of added water on the reaction of acid chlorides with potassium cyanide in acetonitrile (3 ml) at 80 °C *(60 min)*.

In summary, the conversion of aroyl chlorides **(1)** into aroyl cyanides **(2)** using potassium cyanide is strongly promoted in acetonitrile, or, depending on the structure of acid halides, in aqueous acetonitrile. The conventional synthesis of acyl cyanides usually involves the use of heavy metal cyanides such as copper and silver cyanides[3]. With regard to availability and cost of the cyanogen source, hydrogen cyanide, sodium cyanide, and potassium cyanide should be preferable. However, the conversion of acyl chlorides into acyl cyanides using these reagents is known either to fail at all or to afford acyl cyanide dimers [R—CO—O—C(CN)$_2$—R][3]. It has been reported that the use of phase-transfer catalysts in the liquid-liquid two-phase reaction of acyl chlorides with potassium cyanide allows the synthesis under ambient conditions, but this method also causes considerable dimer formation[4]. Recent patents claim the use of heavy metal compounds as catalysts[5,6,7]. The present procedure compares favorably with these methods since our reaction proceeds under mild conditions without any catalysts and dimer formation is negligible unless too much water is added.

Aroyl Cyanides and Hetero Analogs (2); Analytical Procedure:
Dry potassium cyanide powder (426 mg, 6.5 mmol), the acid chloride **1** (6.0 mmol), and acetonitrile (3 ml) are placed in a 10 ml Schlenk tube. Additives are added if necessary. The mixture is vigorously stirred at 80 °C for the period given in the Table. The resultant mixture is analyzed by G. L. C. for acyl cyanide using biphenyl as internal standard (column: diethylene glycol succinate polyester on Neopak AS, 2 m × 3 mm). Analysis for acyl cyanide dimers is performed on a column

0039-7881/81/1232-0973 $ 03.00

Table. Aroyl Cyanides (**2**, Arylglyoxylonitriles) and Hetero Analogs

R	Additive (for 6 mmol of **1**)	Reaction time[a] [min]	Yield of **2**		m.p. [°C] or b.p. [°C]/torr	
			by G.L.C. Analysis	Isolated Product	found	reported
	–	300	38			
	H_2O (18 µl)	90	85	68	33–34°	32–33°[9]
	H_2O (18 µl)	180	77[b]			
	18-crown-6 (5%)	300	45			
	18-crown-6 (5%) + $(n\text{-}C_4H_9)_3SnCl$ (5%)	300	59			
	–	300	86			
	H_2O (9 µl)	60	76	71	27–28°	30°[10]
	H_2O (18 µl)	60	79			
	H_2O (36 µl)	300	19			
	18-crown-6 (5%)	300	81			
	H_2O (36 µl)	60	46			
	–	90	81			
	H_2O (18 µl)	90	94	78	140°/23	84–85°/11[11]
	–	60	85	67	54–55°	52°[8]

[a] Reaction conditions: aroyl chloride (6 mmol) + potassium cyanide (426 mg) in acetonitrile (3 ml), 80°C.
[b] Propanenitrile was used as solvent in place of acetonitrile.

packed with SE 30 on Chromsorb W (40 cm × 3 mm) using *o*-terphenyl as internal standard. Identity of the products is confirmed by comparison of G.L.C. retention times with those of authentic samples prepared by different routes.

Benzoyl Cyanide; Typical Preparative-Scale Procedure:
Benzoyl chloride (6.92 ml, 60 mmol) and water (180 µl, 10 mmol) are added to a stirred suspension of powdered potassium cyanide (4.25 g, 65 mmol) in dry acetonitrile (30 ml). The mixture is vigorously stirred at 80°C for 1.5 h, then diluted with ether (30 ml), dried with magnesium sulfate, and filtered. The volatile materials are removed in vacuo and the residue is distilled in vacuo; yield: 5.32 g (68%); b.p. 82.5–86.5°C/12 torr. An analytical sample is obtained by recrystallization from hexane; m.p. 33–34°C.

Received: March 20, 1981
(Revised form: June 9, 1981)

* Address for correspondence.

[1] J. M. Photis, *J. Org. Chem.* **46**, 182 (1981).
[2] M. Tanaka, *Tetrahedron Lett.* **21**, 2959 (1980).
[3] J. Thesing, D. Witzel, A. Brehm, *Angew. Chem.* **68**, 425 (1956). O. Bayer, in: Houben-Weyl, *Methoden der Organischen Chemie*, 4th Edn., E. Müller, Ed., Vol. 7/2C, Georg Thieme Verlag, Stuttgart, 1977, p. 2487.
[4] K. E. Koenig, W. P. Weber, *Tetrahedron Lett.* **1974**, 2275.
[5] K. Findeisen, *German Patent (DOS)* 2614242 (1978), Bayer AG; *C. A.* **88**, 22421 (1978).
[6] *Belgian Patent* 855255 (1978), DEGUSSA; *C. A.* **88**, 190425 (1978).
[7] H. Klenk et al., *German Patents (DOS)* 2753656, 2753657 (1979), DEGUSSA; *C. A.* **91**, 74363, 74362 (1979).
[8] P. Cagniant, P. Cagniant, *C. R. Acad. Sci.* **229**, 1150 (1949).
[9] *Handbook of Chemistry and Physics*, 55th Ed., CRC Press, Cleveland, 1974.
[10] D. Demozay, R. Caffiero, D. Phillon, *German Patents (DOS)* 1813184 (1969), Pechiney. Progil; *C. A.* **72**, 100331 (1970).
[11] G. N. Sausen, V. A. Engelhardt, W. J. Middleton, *J. Am. Chem Soc.* **80**, 2815 (1958).

0039-7881/81/1232-0974 $ 03.00