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ADDITION REACTIONS OF α-DIMETHYLAMINONITRILES WITH ACRYLONITRILE: A SIMPLE SYNTHESIS OF γ-KETONITRILES

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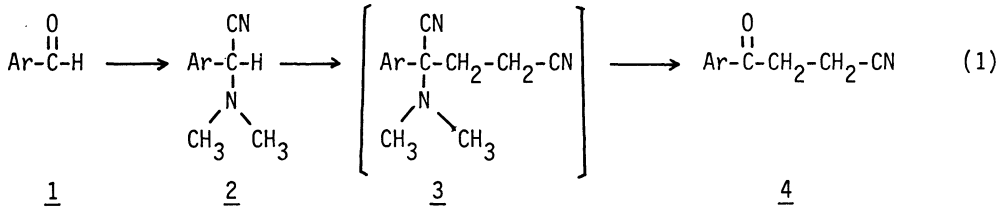
The reaction of the anion derived from α-dialkylaminonitriles with acrylonitrile, followed by hydrolysis with aqueous acids or cupric sulfate in 95% ethanol gave γ-ketonitriles in good yields. This procedure is highly convenient for the synthesis of various γ-ketonitriles.

A recent report by Büchi et.al.[1] on the chemistry of α-dialkylaminonitriles prompts us to communicate our findings. Our results represent a simple and convenient synthesis of γ-ketonitriles[2] from the corresponding aldehydes as shown in equation (1). The sequence of reactions, starting from α-dimethylaminonitriles 2 to give the γ-ketonitriles 4, can be effected in one-pot (in the case of acid hydrolysis).

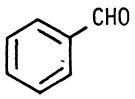
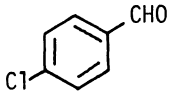
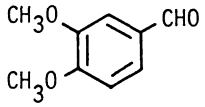
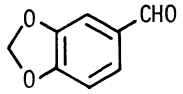
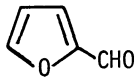


(1)

The following procedure is representative: 2-(p-chlorophenyl)-2-dimethylaminoacetonitrile[3] (0.025 mol) was added, under nitrogen, to a suspension of sodium methoxide (0.025 mol) in dry 1,2-dimethoxyethane (DME, 75 ml). The solution was then stirred at room temperature (RT) for 15 min. A solution of acrylonitrile (3 ml) in DME (10 ml) was slowly added and the whole mixture was stirred for additional 2 hr. The reaction mixture was hydrolyzed with hydrochloric acid (75 ml, 2N) for 2 hr at RT. The product was isolated with chloroform and further purified by recrystallization from 1:1 benzene-hexane to give 4-(p-chlorophenyl)-4-oxobutyronitrile in 75% yield. The results are summarized in Table 1.

An alternative hydrolytic procedure for the adduct 3 was also investigated. Preliminary experiments[4] employing α-dimethylaminonitriles 2 and cupric sulfate, cupric acetate, or ferrous sulfate in 95% ethanol indicated that the cupric sulfate gave the best yields of the corresponding aldehydes. For this reason, cupric sulfate was used in the subsequent hydrolysis of 3. It was found that a cleaner product 4 could be obtained if the crude 3 was isolated prior to the hydrolysis.

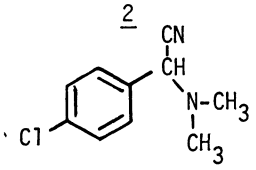
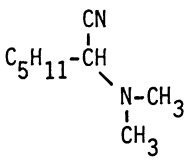
Table 1

1	4, Yields %[a] (Mp.°C)[b](Method)[c]
	71 (71-72) (1) 78 (71-72) (2)
	75 (72-73) (1) 74 (72-73) (2)
	70 (112-113) (1) 70 (112-113) (2)
	71 (92-93) (1) 70 (92-93) (2)
	72 (77-78) (3) 70 (77-78) (2)

[a]Yields refer to overall yields from 2. [b]Products were purified on recrystallization from 1:1 benzene-hexane. [c]Method of hydrolysis 1, 2N HCl/2hr/RT; 2, $CuSO_4.5\ H_2O$/95% CH_3CH_2OH/reflux, 15 min; 3, 50% CH_3CO_2H/24 hr/RT.

REFERENCES AND NOTES

1. G. Büchi, P.H. Liang, and H. Wüest, Tetrahedron Lett., 2763 (1978) and references therein.
2. M. Bogavac, H. Lapin, V. Arsenijervic, and A. Horeau, Bull.Soc.Chim.Fr., 4437 (1969); H.C. Ho, T.L. Ho, and C.M. Wong, Can.J.Chem., 50, 2718 (1972); W. Steglich and P. Gruber, Angew.Chem.Int.Ed., 10, 655 (1971); H. Stetter, Angew.Chem.Int.Ed., 15, 639 (1976); H. Stetter and H. Kuhlmann, Tetrahedron, 33, 353 (1977).
3. All α-dimethylaminonitriles were prepared from the corresponding aldehydes according to S.F. Dyke, E.P. Tiley, A.W.C. White, and D.P. Gale, Tetrahedron, 31, 1219 (1975).
4. Hydrolysis of parent α-dimethylaminonitriles in 95% ethanol to the corresponding aldehydes investigated were:

2	Reagents	1,Yields %
	$CuSO_4.5\ H_2O$	75
	$Cu(OAc)_2.H_2O$	53
	$FeSO_4.7\ H_2O$	56
	$CuSO_4.5\ H_2O$	76
	$Cu(OAc)_2.H_2O$	52
	$FeSO_4.5\ H_2O$	66

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