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CARBONYL COMPOUNDS FROM α-DIALKYLAMINONITRILES BY HYDROLYSIS IN THE PRESENCE OF CUPRIC SULFATE

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The pioneering work of Hauser[1] on the deprotonation and alkylation of α-dialkylaminonitriles provided the stimulus to explore this class of compounds as carbonyl anion equivalents.[2-5] The utility of these intermediates was extended further when ylides derived from allylic N-cyanomethyl pyrrolidinium salts were found to rearrange to γ,δ-unsaturated α-pyrolidinonitriles.[6-9] Traditionally α-aminonitriles are hydrolyzed to the corresponding carbonyl compounds with either acids or strong bases, but both methods have their limitations. Aminonitrile 8[8] did not give aldehyde 16 on hydrolysis with aqueous oxalic acid[7] but diols derived from the aldehyde by acid induced cyclization. Similarly, citronellal (14) is known to cyclize to isopulegol in the acidic medium necessary for its generation from nitrile 6. Hydrolysis of nitrile 6 with 1N ethanolic sodium hydroxide also failed to produce 14 and this general instability of aldehydes to strong alkali led us to search for a superior method. We found cupric sulfate in aqueous methanol to greatly accelerate the hydrolysis of aminonitriles by removing cyanide from the aminonitrile-imminium cyanide equilibrium according to equation $4\ CN^- + 2\ CuSO_4 \rightarrow 2\ CuCN$[10] $+ (CN)_2$[11] $+ 2\ SO_4^=$. Procedure a is recommended for volatile substances. The reaction mixtures in both procedures a and b become acidic (pH 3.5 - 4.0) and for highly sensitive aldehydes procedure c should be utilized in which a pH of 5.0 - 5.5 is maintained by addition of K_2HPO_4. Hydrolyses *do* require copper sulfate and reaction rates are low at neutrality even in its presence.

Procedures a and b: A stirred suspension of the amino nitrile (30 mmol) and $CuSO_4 \cdot 5H_2O$ (30 mmol) in 35 ml of aqueous methanol[13] was heated at reflux for 1.5 h. a: Volatile products were separated from inorganic salts by distillation at 20 mm into a cooled receiver. The distillate was then fractionated. b: Addition of pentane to the reaction mixture was followed by filtration, drying and evaporation of the solvents under reduced pressure.

Procedure c: A suspension of dibasic potassium phosphate (1.5 mmol) and $CuSO_4 \cdot 5\ H_2O$ (7.5 mmol) in 70 ml of methanol-water (3:1) was stirred for 10 minutes at 20°. The amino nitrile (5.0 mmol) was added, and stirring was continued for 6 h at 20°. After 2 h an additional 1.0 mmol of K_2HPO_4 was added. The reaction mixture was diluted with pentane, filtered and the insoluble material was washed with pentane. The filtrate was dried and after the solvents were evaporated the residue was purified by distillation.

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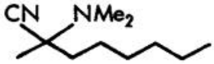
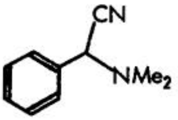
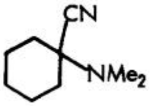
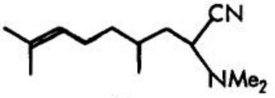
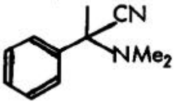
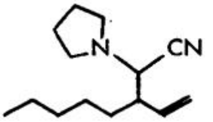
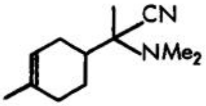
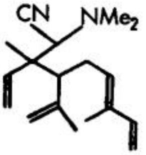
Table. Cupric Sulfate Assisted Hydrolysis of α-Dialkylaminonitriles

	Aminonitrile[12]	Ketone (procedure, yield %)		Aminonitrile[12]	Aldehyde (procedure yield %)
1		9 (a, 83)	5		13 (b, 85)
2		10 (a, 78)	6		14 (c, 94)
3		11 (b, 80)	7		15[14] (c, 65)
4		12 (b, 90)	8[8]		16[8] (b, 82)

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10. Identified by its ir spectrum "The Sadtler Standard Spectra Inorganics", vol. I No Y213K.
11. Cyanogen was not detectable in the reaction mixtures and was hydrolyzed to oxamide identified by ir and t.l.c. comparison with authentic material.
12. Aminonitriles 1 - 6 were prepared according to D. B. Luten, Jr., J. Org. Chem., 3, 588 (1939). Compound 7 was prepared by [2,3] sigmatropic rearrangement of the ammonium ylide.[7]
13. Use of absolute methanol leads to acetals and ketals.
14. A mixture of α,β- and β,γ-unsaturated aldehydes was obtained.