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Potassium trimethylsilanolate mediated hydrolysis of nitriles to primary amides

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Abstract

Treatment of nitriles with potassium trimethylsilanolate under mild anhydrous conditions readily yields the corresponding primary amides after a simple aqueous workup. © 2000 Elsevier Science Ltd. All rights reserved.

Keywords: hydrolysis; nitriles; amides; silicon and compounds.

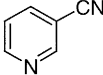
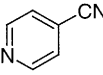
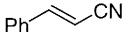
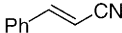


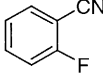
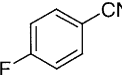
Alkali trimethylsilanolates have for some time been recognised as hydroxide anion equivalents that are conveniently soluble in organic solvents. Despite this unique property, there have been few reports of the use of these compounds since Laganis and Chenard described their role in the preparation of anhydrous carboxylate salts from the corresponding esters and acid chlorides.¹ Apart from this valuable application, trimethylsilanolates have been mainly reported as polymerisation initiators,² as a base to promote elimination of methanol from β -methoxyketones³ and in the deprotonation of propyne iminium salts,⁴ and finally as an hydroxyl synthon for fluoride S_NAr type displacements from certain activated aromatics.⁵

The reaction of benzonitriles with lithium (bis)trimethylsilylamide to form unsubstituted amidines after an aqueous workup⁶ gave rise to speculation that the oxygen analogue, lithium trimethylsilanolate, would achieve the corresponding transformation of benzonitrile to benzamide (Scheme 1). It was found that on heating lithium, sodium or potassium trimethylsilanolate with a nitrile in either THF or toluene the intermediate salt precipitates. This has two major advantages; firstly, the reaction is halted at the amide stage and secondly, as the precipitate is insoluble in most aprotic solvents any impurities can conveniently be washed away. The intermediate salt is then converted in good yield to the corresponding amide (Table 1).

In a typical procedure the trimethylsilanolate (2 mmol) was dissolved in anhydrous solvent (5 mL) with the nitrile (1 mmol). The reaction was heated to reflux until the nitrile was consumed and the solid

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Table 1
Transformation of nitriles to carboxamides by alkali metal silanolates

Entry	R	M	Solvent ^a	Time (h) ^b	Yield ^c (%)
1	PhCN	Li	THF	16	5
2	PhCN	Na	THF	16	40
3	PhCN	K	THF	16	83
4	PhCN	K	Toluene	4	82
5		K	THF	4	78
6		K	THF	4	82
7		K	THF	16	24
8		K	Toluene	2	68
9		K	THF	16	33
10		K	Toluene	2	69
11	CH ₃ (CH ₂) ₄ CN	K	THF	16	No Product formed.
12	CH ₃ (CH ₂) ₄ CN	K	Toluene	16	67
13	(CH ₃) ₃ CN	K	THF	16	7
14	(CH ₃) ₃ CN	K	Toluene	16	32
15		K	Toluene	2	80
16		K	Toluene	2	81

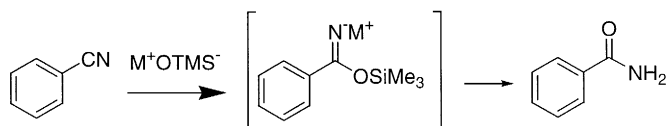
a) Reactions run in boiling solvent.

b) Reaction times of 16 hours refer to overnight runs and do not reflect the minimum time to reach completion.

c) Isolated yields of pure material >95% by HPLC/NMR. (Not optimized.)

precipitate was filtered, washed with anhydrous solvent and then poured into water and extracted into EtOAc. After drying over MgSO₄ amides were obtained in fair to good yield.

Potassium trimethylsilanolate consistently gave higher yields than either lithium or sodium trimethylsilanolate. A possible explanation for these differences may be that the intermediates are more soluble in



Scheme 1.

the case of lithium and sodium trimethylsilylanolates and that further reaction is taking place. Increasing the temperature of the reaction by replacing THF with toluene increases the rate of the reaction without compromising the yield and the higher temperature was necessary to accomplish reaction with non-activated nitriles. This reagent gives good yields with nitriles that have an acidic α -proton such as phenylacetonitrile or with substrates such as cinnamionitrile where 1,4-addition is possible. Finally, in the case of fluorobenzonitriles only hydrolysis is observed with no fluoride S_NAr displacement.

In conclusion, a convenient, mild, non-aqueous method of converting nitriles to their corresponding primary amides has been developed. Good yields combined with a simple workup procedure make it an attractive alternative to existing methods.

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