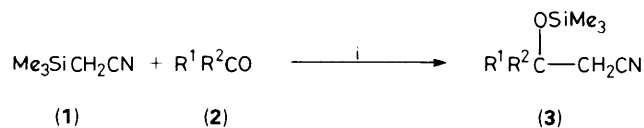


Fluoride-ion Mediated Reaction Between Trimethylsilylacetonitrile and Carbonyl Compounds. A New Synthesis of β -Trimethylsilyloxy Nitriles

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A new way of cyanomethylating carbonyl compounds under nucleophilic catalysis is described.

In recent years organosilicon chemistry has become important in the development of new methodologies in organic synthesis.¹ As an example of this, the Peterson reaction between metallated α -silyl carbanions and carbonyl compounds has found widespread utility in carbonyl olefination.^{1,2} Following this methodology various groups³ have reported the preparation of alkene-2-nitriles from the reaction between trimethylsilylacetonitrile (TMSAN) (1) and carbonyl compounds. Recently there has been increased interest in the use of fluoride ion as a promoter of carbon nucleophiles from organosilicon compounds in the formation of carbon-carbon bonds.⁴ We report here that commercially available TMSAN (1) under nucleophilic catalysis provides a new way of cyanomethylating carbonyl compounds to give β -trimethylsilyloxy nitriles (3).⁵



Scheme 1. Reagents and conditions: i, TASF or NaOMe, CH₂Cl₂ or THF, -15 °C, 1–2 h

We found that TMSAN (1.3 equiv.) reacted with carbonyl compounds (1 equiv.), in either methylene dichloride or tetrahydrofuran (THF) as solvents, in the presence of a catalytic amount of tris(dimethylamino)sulphonium difluorotrimethylsiliconate (TASF),⁶ to afford the expected β -trimethylsilyloxy nitrile (3) in excellent yields. Various carbonyl compounds have been used in this reaction and the results, summarized in the Table, illustrate the efficiency, the applicability, and the scope of the method. As shown in the Table, the reaction works especially well with non-enolizable carbonyl compounds to give β -trimethylsilyloxy nitriles in excellent yields. With enolizable ketones the corresponding silyloxy nitrile was obtained in lower yield, together with the corresponding trimethylsilyl enol ether.⁷ The use of higher reaction temperatures, or a change of solvent (*i.e.* MeCN or HMPA) failed to modify the reaction course and the corresponding trimethylsilyl enol ethers were the chief products. When the reaction was tested for cyclic ketones no silyl enol ethers were formed, but spontaneous elimination took place giving the alkenenitrile in high yield. With α,β -unsaturated aldehydes only 1,2-addition occurred to give the expected siloxy nitrile in good yield. Particularly noteworthy is that the reaction proceeds under mild, almost neutral, conditions *via* metal-free

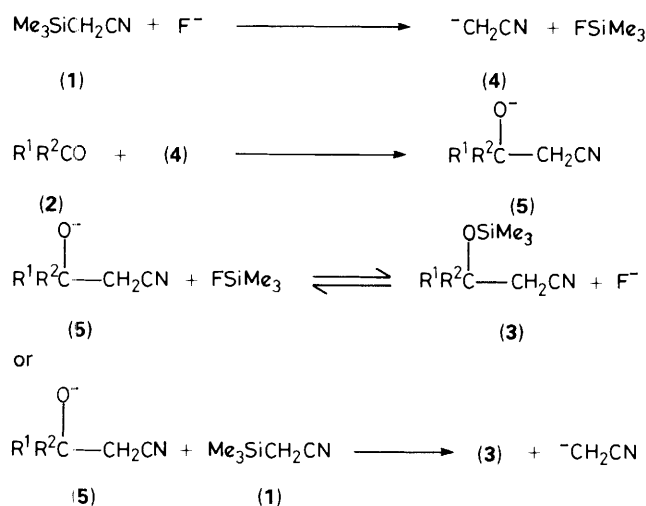
Table. Preparation of trimethylsilyloxynitriles (3) from TMSAN (1) and carbonyl compounds (2)^a

Carbonyl compound	Product (3) ^{b,c} % yield	B.p. (°C)/mmHg ^d	N.m.r. (δ)	
			CH ₂ CN	CHOSiMe ₃
Benzaldehyde	93	105/0.02	2.63	4.96
4-Methoxybenzaldehyde	80, 77 ^e	120/0.01—0.02	2.60	4.87
4-Chlorobenzaldehyde	63	140/0.01	2.58	4.80
4-Cyanobenzaldehyde	56	150/0.01—0.02	2.65	5.03
4-Methoxycarbonylbenzaldehyde	73 ^e	140/0.4	2.73	5.10 ^f
Isobutyraldehyde	65	160/760	2.33	—
Pivalaldehyde	50 ^e	100/12	2.40	3.56
α-Methylcinnamaldehyde	94	140/0.02	2.62	4.50
Cinnamaldehyde	45	125/0.2—0.3	2.56	4.60
Crotonaldehyde	(45)	90/12	—	—
Benzophenone	(95)	130/0.01	—	—
Acetophenone	20 (60)	—	—	—
	35 ^e	90/0.08	2.63	—
Cyclohexanone	20 (80)	120/20	2.45	—

^a All reactions were conducted on a 3 mmol scale using TASF as catalyst unless otherwise stated. ^b Yields refer to isolated materials which gave satisfactory microanalytical data (C, H, and N ± 0.30). ^c The number in parentheses indicates the proportion of alkene-2-nitrile produced during distillation. ^d Observed during distillation with Kugelröhr apparatus and are uncorrected. ^e NaOMe as catalyst. ^f Isolated as β-hydroxy nitriles.

carbanionic species.* Consequently the reaction could be applied to compounds possessing base or acid sensitive functionalities.

Although the reaction mechanism is not clear, it can be assumed (Scheme 2) that the reaction is initiated by fluoride

**Scheme 2.**

ion to generate the cyanomethyl carbanion (4), which then reacts with the carbonyl compound (2) to give the corresponding β-cyanomethyl alkoxide (5). The alkoxide (5) could be further silylated to (3) with regeneration of the catalyst or react with (1) to generate (3) and the cyanomethyl carbanion (4). In fact, we found that TMSAN (1) upon treatment with various aldehydes and sodium methoxide or potassium t-butoxide as catalyst in THF as solvent afforded the corresponding β-trimethylsilyloxy nitrile (3) in excellent yield, clearly supporting the proposed mechanism.

In conclusion we have developed a versatile procedure for cyanomethylation of carbonyl compounds under mild condi-

tions. Further studies are in progress in our laboratory to exploit the scope of this method.

Experimental

Aldehydes or ketones (3 mmol) and TMSAN (0.4 g, 3.5 mmol) were mixed at -15 °C in anhydrous methylene dichloride or THF (5 ml), containing molecular sieves (4 Å) and a catalytic amount of TASF (10% equiv.) was added. Instantaneously, a dark colour developed (the reaction was also slightly exothermic), and the reaction mixture was allowed to stand at room temperature. After being stirred at the same temperature for 1–2 h, the reaction mixture was poured into the water (3 ml) and the organic layer separated and dried. Evaporation of the solvent under reduced pressure gave the corresponding β-trimethylsilyloxy nitrile, which was purified by Kugelröhr distillation. Unless otherwise stated, results in the Table were obtained by similar reaction and work-up conditions.

Acknowledgements

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