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2-ALKOXY AND 2,2-DIALKOXY NITRILES FROM ACETALS AND ORTHOESTERS —— EXCHANGE OF ALKOXY INTO CYANO GROUP BY MEANS OF CYANOTRIMETHYLSILANE

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Summary: Title transformation is accomplished by the catalytic action of $SnCl_2$ or $BF_3 \cdot OEt_2$. Lithio derivative of 2,2-dimethoxyacetonitrile is used as synthetic equivalent of methyl lithioformate.

Organosilicon compounds have found important roles in organic synthesis.[1,2] In this context cyanotrimethylsilane has been used as a versatile cyanation agent.[3,4] This paper describes a novel synthetic utility of Me_3SiCN, whose reaction with acetals and orthoesters under the catalytic action of $SnCl_2$ or $BF_3 \cdot OEt_2$ gives 2-alkoxy or 2,2-dialkoxyalkanenitriles, respectively, in excellent yield.[5]

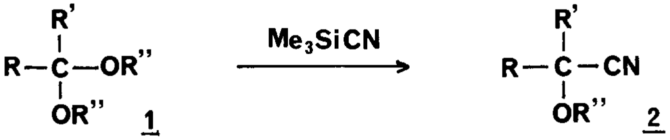


Table 1. 2-Alkoxy and 2,2-Dialkoxy Nitriles 2

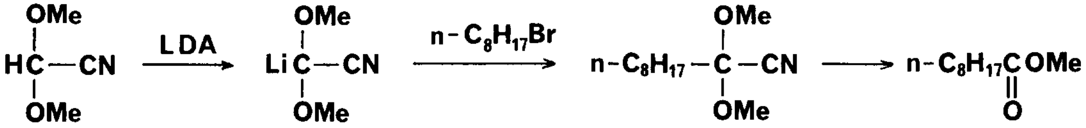
Entry	R	R'	R"	Catalyst	Yield (%)[a]
1	H	H	Me	$SnCl_2$	64
2	Me	H	Me	$BF_3 \cdot OEt_2$	73
3	Me	H	Et	$BF_3 \cdot OEt_2$	97
4	$n\text{-}C_6H_{13}$	H	Me	$SnCl_2$	83
5	$PhCH_2$	H	Me	$BF_3 \cdot OEt_2$	88
6	Ph	H	Me	$SnCl_2$	94
7	$ClCH_2$	H	Me	$SnCl_2$	80[b]
8	$H_2C{=}CH$	H	Me	$SnCl_2$	72
9	$n\text{-}C_6H_{13}C{\equiv}C$	H	Me	$BF_3 \cdot OEt_2$	94
10	H	OMe	Me	$BF_3 \cdot OEt_2$	80
11	H	OEt	Et	$BF_3 \cdot OEt_2$	84
12	Me	OMe	Me	$BF_3 \cdot OEt_2$	70
13	OMe	OMe	Me	$SnCl_2$	83[b]

a) Isolated yields are shown. Glc yields are quantitative. b) Reaction catalyzed by $BF_3 \cdot OEt_2$ gives unsatisfactory result.

Preparation of dimethoxyacetonitrile from trimethyl orthoformate is illustrative (entry 10, Table 1). A mixture of trimethyl orthoformate (3.3 ml, 30 mmol) and cyanotrimethylsilane (3.8 ml, 30 mmol) was added with 0.3 ml (2 mmol) of $BF_3{\cdot}OEt_2$ at room temperature. After stirring for 3 h, the completion of the reaction was observed by nmr and glc. The reaction mixture was worked up with $NaHCO_3$ aq. solution and extracted with ether. Drying (Na_2SO_4) and distillation gave dimethoxyacetonitrile (2.4 g, 24 mmol, 80% yield). In place of $BF_3{\cdot}OEt_2$, $SnCl_2$ could be used as catalyst affording similar results with exception of entries 7 and 13 in Table 1 where $BF_3{\cdot}OEt_2$ gave unsatisfactory results.

The known synthetic utility of 2-alkoxyalkanenitrile[9] can be extended to 2,2-dimethoxyacetonitrile which serves as a "methyl lithioformate" equivalent.

A THF solution of LDA was prepared from diisopropylamine (597 mg, 5.9 mmol), n-BuLi (5.9 mmol, 4.1 ml of 1.44 M hexane solution) and 20 ml of THF. A solution of dimethoxyacetonitrile (546 mg, 5.4 mmol) in THF-HMPT (4:1, 5 ml) was added to LDA solution maintained at -78°C. The whole was stirred for 90 min at -78°C, then 1-bromooctane (1.1 ml, 6.0 mmol) was added at the same temperature. After stirring for 90 min at -78°C then 30 min at room temperature, the reaction mixture was added with ether and worked up with ice-water. Organic layer was dried (Na_2SO_4) and concentrated. Chromatography (silica gel, hexane-benzene) gave 2,2-dimethoxydecanenitrile (630 mg, 3.0 mmol, 55% yield). A solution of the product (180 mg, 0.85 mmol) and p-toluenesulphonic acid (10 mg) in acetone-water (5:1, 12 ml) was heated at reflux for 3 h. Usual workup afforded methyl nonanate (140 mg, 0.81 mmol, 96% yield).



$$\mathrm{H\underset{OMe}{\overset{OMe}{C}}{-}CN} \xrightarrow{\mathrm{LDA}} \mathrm{Li\underset{OMe}{\overset{OMe}{C}}{-}CN} \xrightarrow{n\text{-}C_8H_{17}Br} n\text{-}\mathrm{C_8H_{17}{-}\underset{OMe}{\overset{OMe}{C}}{-}CN} \longrightarrow n\text{-}\mathrm{C_8H_{17}\underset{\overset{\|}{O}}{C}OMe}$$

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