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Copper-Mediated Transformation of Organosilanes to Nitriles with DMF and Ammonium Iodide

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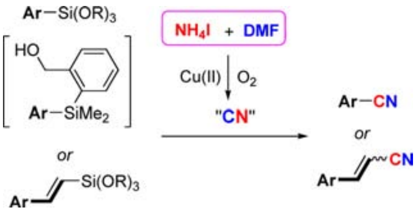
ABSTRACT



Cyanation of aryl-, diaryldimethyl-, and styrylsilanes was developed for the first time under copper-mediated oxidative conditions using ammonium iodide and DMF as the combined source of nitrogen and carbon atom of the introduced cyano unit, respectively. The reaction was observed to proceed in a two-step process: initial conversion of organosilanes to their iodo intermediates and then cyanation. This method has a broad substrate scope with high functional group tolerance.

Organo nitriles are a key building unit frequently found in numerous natural and synthetic compounds such as in dyes, herbicides, pharmaceuticals, agrochemicals, and electronic materials.[1] Moreover, the nitrile group is a versatile precursor that can readily be converted to diverse functional groups including tetrazoles, amines, amidines, amides, aldehydes and other carboxy derivatives.[2] For the preparation of nitrile compounds, conventional methods are most often used: Sandmeyer[3] and Rosenmund−von Braun procedure[4] employ stoichiometric amounts of CuCN as the cyanating reagent. On the other hand, while recent development of the transition-metal-catalyzed cyanation[5] allows using certain metal- or metalloid-bound cyanide sources such as KCN,[6] NaCN,[7] $Zn(CN)_2$,[8] or $K_4[Fe(CN)_6]$,[9]

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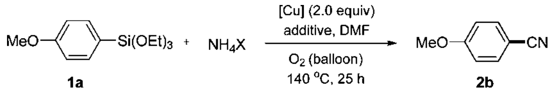
this approach also has some drawbacks. For example, the cyanation sources are usually toxic and release hazardous HCN gas, and stoichiometric amounts of metal wastes accompany the reaction. Careful control of concentration of reaction mixture is another issue to be addressed to minimize catalyst poisoning due to the in situ formation of inactive cyano transition metal complexes.[10] In response to these issues, feasibility of using nonmetallic cyanation species has been actively investigated in recent years.[11] In fact, a range of organic precursors bearing a "CN" moiety was examined; acetone cyanohydrin and its analogues,[12] alkyl nitriles,[13] malononitrile,[14] phenyl cyanates,[15] benzyl thiocyanates,[16] *N*-cyanobenzimidazole,[17] TMSCN,[18] nitromethane,[19] and *N*-cyano-*N*-phenyl-*p*-toluenesulfonamide (NCTS).[20] On the other hand, some research groups recently reported cyanation reactions employing organic precursors that do not contain the "CN" unit in their molecular skeletons.[21] Interestingly, there are two types of precursors in this approach; either using single sources or combining more than two compounds at the same time to generate the cyano unit in situ.

Recently, we reported for the first time that the cyano group could be generated in situ from the combined use of aqueous ammonia and *N*,*N*-dimethylformamide (DMF) under Cu-mediated oxidative conditions.[21a−c] Isotopic studies revealed that carbon and nitrogen atom consisting "CN" were originated from the dimethylamino moiety of DMF and ammonia, respectively. This protocol was then utilized for the cyanation of 2-phenylpyridine in the presence of a palladium cocatalyst. Subsequently, NH_4I (instead of aqueous ammonia) and DMF were combined for the cyanation of aryl boronates and electron-rich arenes[21b] and indoles[21c] under the similar conditions.

Interestingly, when ammonium iodide was used as the nitrogen source, the reaction was found to proceed in a sequential two-step process: initial iodination of substrates and then cyanation of the aryliodo intermediates with in situ generated "CN" moiety. During the course of the transformation, ammonium iodide plays a dual role as a supplier of both iodide and nitrogen atom. Jiao described an efficient Pd-catalyzed cyanation of indoles with DMF alone, but various reagents and additives were required.[21d] Cheng and co-workers reported that Pd-catalyzed cyanation of indoles[21e] and Cu-mediated cyanation of aryl halides using combined cyano sources.[21f] Bhanage et al. also revealed Pd-catalyzed cyanation of (hetero)aryl halides with formamide.[21g] Herein, we present a new advance in the cyanation of *organosilanes* under Cu-mediated oxidative conditions using NH_4I and DMF as the "CN" sources. Organosilicons have gained increasing interests in organic synthesis and materials science mainly due to their tamable reactivity, nontoxicity, high stability, and ease of preparation and handling.[22] As a result, the present result will add a promising entry into a list of synthetic utilizations of organosilanes.

Table 1. Optimization of Reaction Conditions[a]



entry	Cu species (2.0 equiv)	NH_4X	additive (2.0 equiv)	yield[b] (%)
1	$Cu(NO_3)_2\cdot 3H_2O$	aq NH_3	none	0
2	$Cu(NO_3)_2\cdot 3H_2O$	NH_4I	none	24
3	$Cu(NO_3)_2\cdot 3H_2O$	NH_4I	HOAc	40
4[c]	$Cu(NO_3)_2\cdot 3H_2O$	NH_4I	HOAc	48
5	$Cu(NO_3)_2\cdot 3H_2O$	NH_4I	CsF	60
6	$Cu(NO_3)_2\cdot 3H_2O$	NH_4I	NaF	78
7	**$Cu(NO_3)_2\cdot 3H_2O$**	**NH_4I**	**KF**	**81**
8	$Cu(NO_3)_2\cdot 3H_2O$	NH_4I	NH_4F	67
9	$Cu(CF_3COO)_2$	NH_4I	KF	74
10	CuI	NH_4I	KF	58
11	$CuBr_2$	NH_4I	KF	<5
12	$CuSO_4$	NH_4I	KF	<5
13	$Cu(OAc)_2$	NH_4I	KF	<5
14	$Cu(NO_3)_2\cdot 3H_2O$	NH_4OAc	KF	0
15	$Cu(NO_3)_2\cdot 3H_2O$	NH_4Cl	KF	0
16[d]	$Cu(NO_3)_2\cdot 3H_2O$	NH_4I	KF	52
17[e]	$Cu(NO_3)_2\cdot 3H_2O$	NH_4I	KF	73
18[f]	$Cu(NO_3)_2\cdot 3H_2O$	NH_4I	KF	66
19[g]	$Cu(NO_3)_2\cdot 3H_2O$	NH_4I	KF	71

[a] Conditions: **1a** (0.3 mmol), NH_4I (2.0 equiv), additive, and [Cu] in DMF (2.0 mL). [b] ^1H NMR yield (internal standard: 1,1,2,2-tetrachloroethane). [c] $AgBF_4$ (20 mol %) was added. [d] NH_4I and copper were used in 1.2 equiv each. [e] KF was used in 1.0 equiv. [f] Under air balloon. [g] Run at 130 °C.

We initiated our study by examining a reaction of a readily available compound (4-methoxyphenyl)triethoxysilane (**1a**)

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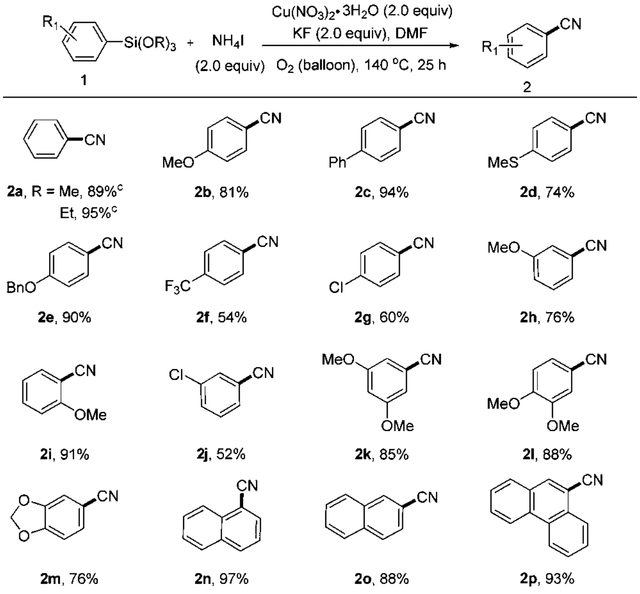
under various conditions including our previous ones (Table 1). While low conversion was observed by the action of copper species alone (entries 1−2), certain additives were found to affect the reaction efficiency. For example, the use of AcOH (2 equiv) resulted in moderate product yields (entries 3 and 4). Instead of acetic acid, which was an additive of choice in our previous procedure of the cyanation of arylboronic acids,[21b] fluoride additive turned out to be more effective. Among those species screened, KF afforded the highest product yield (entries 5−8). On the other hand, while $Cu(CF_3COO)_2$ exhibited slightly lower efficiency when compared to $Cu(NO_3)_2\cdot 3H_2O$ (entry 9), reactivity of other copper salts was lower (entries 10−13). The use of NH_4I was essential for this cyanation as demonstrated by entries 14 and 15. Upon decrease in the amount of copper species, ammonium salt, or additive, reaction efficiency was accordingly reduced (entries 16−19).

With the optimized conditions in hand, we next investigated the substrate scope of this reaction (Scheme 1). It was found that a range of functional groups (e.g., alkoxy, phenyl, methylthio, benzyloxy, trifluoromethyl, or chloro) was compatible with the employed conditions. Arylsilanes bearing substituents at the *para*-, *meta*-, and *ortho*-position were converted to the corresponding benzonitriles in good yields (**2b**, **2h**, and **2i**, respectively). The cyanation was more influenced by electronic property of substrates; electron-donating substituents induced slightly higher product yields than e-withdrawing groups. While cyanation of disubstituted arylsilanes was smooth (**2k**−**m**), fused aryl substrates also underwent the desired reaction with high efficiency (**2n**−**p**). It was interesting to observe that while trialkylarylsilanes were not reacted under the employed conditions, the alkyl moiety of working trialkoxyarylsilane substrates was more flexible leading to similar product yields (e.g., **2a**).

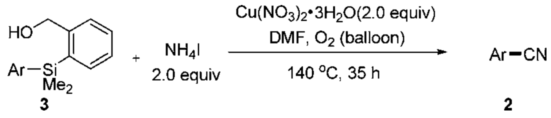
Nakao and Hiyama recently introduced a novel type of silicon cross-coupling reagent; alkenyl- and aryl[2-(hydroxymethyl)phenyl]dimethylsilanes.[23] One of the most attractive aspects of these silanes is that a fluoride activator is not required in the metal-mediated coupling reactions mainly due to an intramolecular interaction leading to a pentacoordinated silicate intermediate. We were pleased to find that conversion of aryl[2-(hydroxymethyl)phenyl]-dimethylsilanes (**3a**−**c**) was achieved indeed *in the absence of KF additive* (Table 2). Interestingly, it was observed that

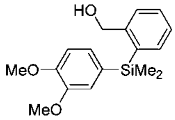
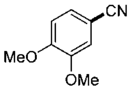
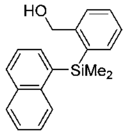
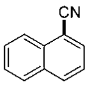
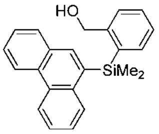
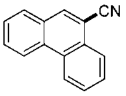
Scheme 1. Copper-Mediated Cyanatioin of Arylsilanes[a]



[a] Conditions: arylsilane (0.3 mmol), NH_4I (2.0 equiv), $Cu(NO_3)_2\cdot 3H_2O$ (2.0 equiv), KF (2.0 equiv) and DMF (2.0 mL) at 140 °C for 25 h under O_2 balloon. [b] Isolated yield. [c] KF (1.0 equiv).

Table 2. Copper-Mediated Cyanation of Hiyama Silanes[a]



entry	substrate		product[b]	
1		**3a**		**2l**, 67%
2		**3b**		**2n**, 65%
3		**3c**		**2p**, 80% (71%)[c]

[a] Conditions: arylsilane (0.3 mmol), NH_4I (2.0 equiv), $Cu(NO_3)_2\cdot 3H_2O$ (2.0 equiv) and DMF (2.0 mL) at 140 °C for 35 h under O_2 balloon. [b] Isolated yield. [c] KF(2.0 equiv) was used.

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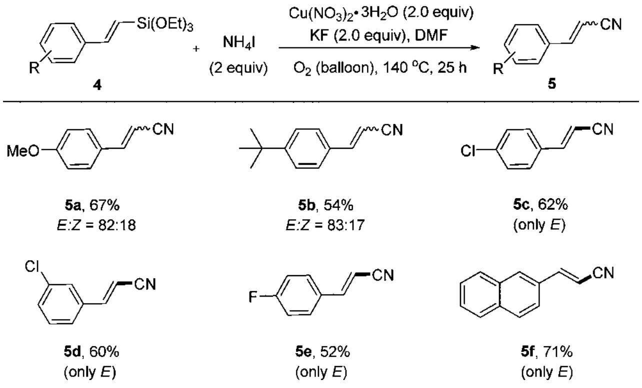
(27) When benzylamine was subjected to the current reaction conditions, benzonitrile was observed to form in high yield.

a fluoride additive slightly lowered the reaction efficiency of a phenanthrenyl derivative (**3c**). Due to the fact that vinylsilanes are readily prepared for the use of various reactions including cross-couplings,[24] we were interested in investigating their feasibility for the cyanation under our present conditions.

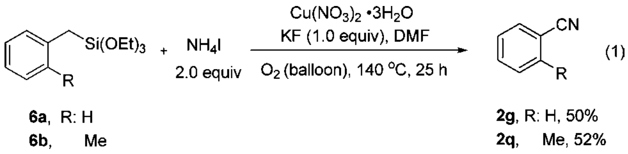
It was found that the cyanation took place smoothly giving rise to the corresponding alkenyl nitrile products (Scheme 2). Interestingly, substrates bearing electron-donating substituents at the aryl moiety underwent the cyanaton with a slight loss of stereochemistry leading to a mixture of stereoisomeric products (**5a**,**b**). In contrast, (*E*)-styrylsilanes containing e-withdrawing groups were cyanated with a complete retention of stereochemistry (**5c**−**e**). Cyanation of (*E*)-naphthalenylvinylsilane was also facile with retention (**5f**).

Scheme 2. Copper-Mediated Cyanation of Vinylsilanes[a]



[a] Conditions: styrylsilane (0.3 mmol), $Cu(NO_3)_2 \cdot 3H_2O$ (2.0 equiv), NH_4I (2.0 equiv), KF (2.0 equiv) and DMF (2.0 mL) at 140 °C for 25 h under O_2 balloon.

We next briefly examined cyanation of benzylsilane derivatives.[25] To our surprise, instead of obtaining phenylacetonitriles, benzonitriles were observed to form albeit in moderate yields (eq 1). All reagents were required for this conversion: NH_4I, copper species, KF, and O_2 in DMF. Considering a previous report by Togo and Iida that alkyl halides are oxidatively converted to nitriles with molecular iodine in aqueous ammonia,[26] this cyanation of benzylsilanes is proposed to proceed in a sequential process; initial iodination of benzylsilanes to benzyl iodides followed by formation of benzylamines which are finally oxidized to benzonitriles under the employed copper-mediated oxidative conditions.[27]



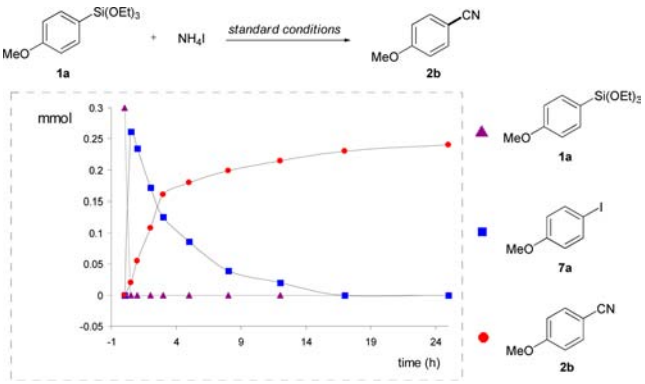
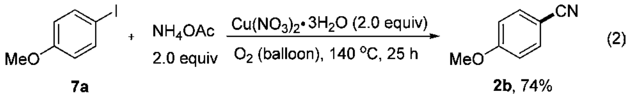


Figure 1. Reaction profile in the Cu-mediated cyanation of **1a**.

In order to gain mechanistic insight of the cyanation of arylsilanes, a reaction profile was obtained using **1a** under the standard conditions (Figure 1). Within 30 min, **1a** was converted almost quantitatively to 4-iodoanisole (**7a**), and then 4-methoxybenzonitrile (**2b**) was started to form over time with the disappearance of **7a**. In fact, when iodoarene **7a** was subject to the reaction conditions, the corresponding benzonitrile **2b** was obtained in 74% yield even in the absence of KF (eq 2), suggesting that iodoarenes are a key intermediate in the present cyanation process.



In conclusion, we have developed for the first time a copper-mediated oxidative cyanation of organosilanes using ammonium iodide and DMF as the combined source of “CN” unit. A range of substrates including aryl-, diaryldimethyl-, styryl-, and benzylsilanes were efficiently cyanated with high functional group tolerance. The reaction was proposed to proceed in two sequential steps: initial iodination and subsequent cyanation.

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Supporting Information Available. Experimental details and ^1H and ^{13}C NMR spectra of new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

The authors declare no competing financial interest.