

New metallation and synthetic applications of isonitriles

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Abstract – Insertions of isonitriles into silicon–tin linkage of organo-silylstannanes and silicon–silicon linkage of polysilanes are catalyzed by palladium complexes. [(N-2,6-xylylimino)trialkylsilylmethyl]stannanes thus prepared undergo transmetalation with n-butyllithium to generate in situ [(N-2,6-xylylimino)trialkylsilylmethyl]lithiums, which may serve as acyl anion equivalent in organic synthesis. Organozincs undergo the insertion reaction with aryl isocyanides to generate the corresponding α -(N-aryl-imino)alkylzincs, which may be synthetically used. Successive insertions of 1,2-diisocyanoarenes into Grignard reagent result in the formation of quinoxaline oligomers up to hexamer.

INTRODUCTION

Acylmetals are often involved as important intermediates in transition-metal-catalyzed reaction with carbon monoxide. Synthetic utilities of some acylmetal compounds such, as acylferrate anions and related organometallic compounds have been demonstrated. However, acylmetals, which are readily available and widely utilizable as synthetic reagents for nucleophilic introduction of acyl group have been so far limited. On the other hand, isonitriles, which are of isoelectronic structure with carbon monoxide, react similarly with organometallic compounds to give the corresponding α -(N-substituted imino)alkylmetal compounds. As reported by Walbosky, α -(N-tert-alkylimino)alkyllithiums and magnesiums were generated in situ and utilized synthetically as acyl anion equivalent. However, extensive studies on metallation at the isocyano carbon of isonitrile have not been so far done. This paper describes new metallation reactions of isonitrile, which give structurally interesting organometallic compounds and are synthetically useful.

INSERTION OF ISONITRILES INTO SILICON–TIN LINKAGE OF SILYLSTANNANES – PREPARATIONS AND REACTIONS OF [(N-SUBSTITUTED IMINO)SILYLMETHYL]STANNANES

Organosilylstannanes react with isonitriles in the presence of tetrakis(triphenylphosphine)-palladium or palladium acetate catalyst to afford [(N-substituted imino)organosilylmethyl]-stannanes (**1**) in moderate yields (Table 1) (ref. 1).

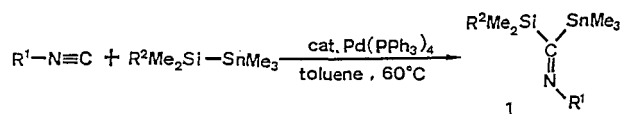


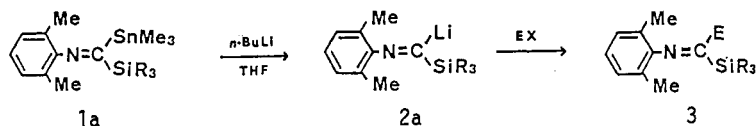
Table 1.

R ¹	R ²	Yield (%)
<i>n</i> -C ₆ H ₁₃ -	Me	59
<i>i</i> -Pr-	Me	71 ^a
<i>c</i> -C ₆ H ₁₁ -	Me	58
<i>t</i> -Bu-	Me	No Reaction ^b
EtOOCCH(CH ₃)-	Me	85
<i>o</i> -Tolyl-	Me	69
2,6-Xylyl-	Me	87
	<i>t</i> -Bu	78 ^c

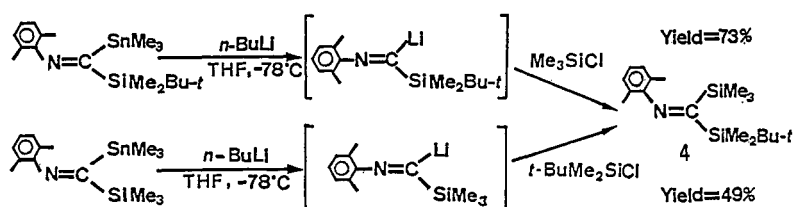
a: Neat . b: Me₃SiSiMe₃+Me₃SnSnMe₃
 c: Reflux

The palladium mediated insertion of isonitrile into the Si-Sn bond of organosilylstannanes may be reasonably explained by a mechanism involving the following catalytic cycle (i) oxidative addition of the organosilylstannane on Pd(0) catalyst, (ii) insertion of isonitrile into the resultant Pd-Sn or Pd-Si bond, (iii) reductive elimination leading to 1 with regeneration of the Pd(0) catalyst.

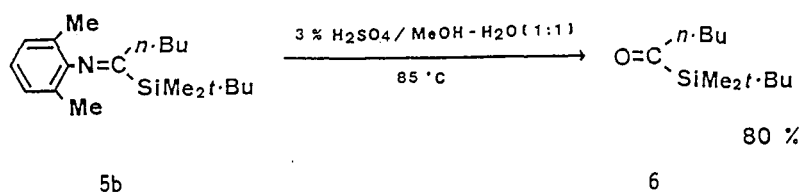
Stable [(N-2,6-xylylimino)trialkylsilylmethyl]stannane (1a) thus prepared is selectively transmetalated at -78°C with *n*-butyllithium to generate in situ [(N-2,6-xylylimino)-trialkylsilylmethyl]lithium (2a), which serves as a versatile acylmetal equivalent reacting with various electrophiles (ref. 2).



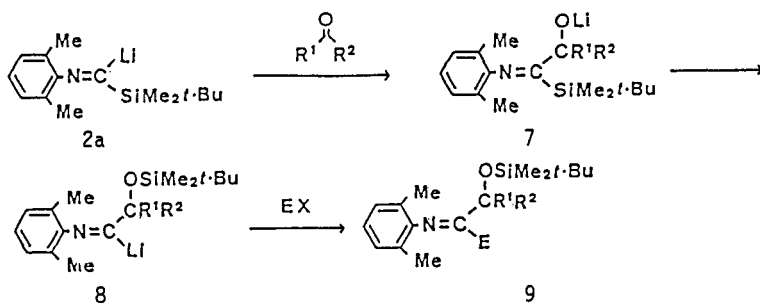
The reaction of 2a with trialkylchlorosilanes provides symmetrical and unsymmetrical bis (organosilyl)imines (4).



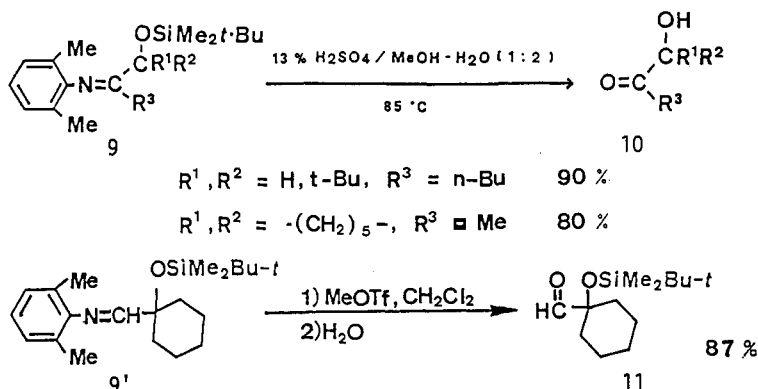
Alkylations of 2a with alkyl halides give the corresponding [α -(N-2,6-xylylimino)alkyl]-silanes (5) in moderate yields, e.g., 5a (R=Et) 75%; 5b (R = *n*-Bu) 76%. The alkylated product was successfully hydrolyzed to afford the corresponding acylsilane in good yield. For instance, 5b was treated with 3% solution of H₂SO₄ in MeOH-H₂O (1:1) at 85°C for 12 h to give the acylsilane 6 in 80% yield. The present reaction provides a general and facile method for preparation of a variety of acylsilanes.



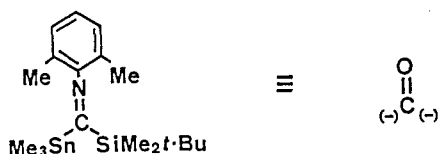
Of interest is the reaction of 2a with carbonyl compounds, in which the expected adduct (7) is readily converted to [α -(N-2,6-xylylimino)alkyl]lithium (8) by the Brook-type migration of trialkylsilyl group from the imino carbon to the alkoxy oxygen. The resultant organolithium intermediates (8) are subsequently treated with electrophiles to give 9.



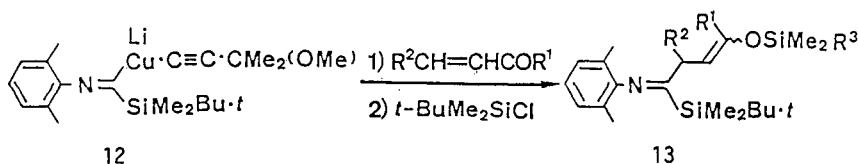
The imines (9) produced are hydrolyzed by the treatment with dilute H₂SO₄ to give the corresponding α -hydroxy ketones (10) in good yields. The imines (9') are also converted to α -silyloxy carbonyl compounds (11) by the reaction with methyl triflate at room temperature followed by quenching with water.



In the present reactions, [(N-2,6-xylylimino)trialkylsilylmethyl]stannanes (1a) functions as a synthetic equivalent to a carbonyl dianion which can introduce two different electrophiles on the carbonyl carbon atom. Noteworthy is that two carbon-carbon bond formations on carbonyl carbon can be achieved in one pot with 1a by use of 1 equiv of n-butyllithium.



Furthermore, the mixed cuprates (12) generated by treatment of [(N-2,6-xylylimino)trialkylsilylmethyl]lithium (2a) with cuprous acetylide react with α,β -unsaturated ketones or aldehydes in the presence of trialkylchlorosilane to afford the conjugate adducts (13) in moderate yields (ref. 3).



$\text{R}^2\text{CH}=\text{CHCOR}^1$	Yield (%)
	68
	74
	70
	70

INSERTION OF ISONITRILES INTO SILICON-SILICON LINKAGE OF POLYSILANES

Bis(silyl)ketones have been intrigued in view of their reactions and spectroscopic properties. However, only a few bis(silyl)ketones (15) such as bis(triphenylsilyl)ketone have been isolable and characterized, because of the instability. We found that N-substituted bis(silyl)imines (14), nitrogen analogue of bis(silyl)ketones, are readily prepared by palladium catalyzed reaction of isonitriles with disilanes (Table 2). In general, N-substituted bis(silyl)imines thus prepared are yellow liquid and thermally stable, but decomposed gradually under air, turning to dark-brown. The synthesis of bis(silyl)imines may be mechanistically closely related with the Pd(0)-mediated insertion of isonitrile into silicon-tin bond of organosilylstannane, as mentioned above (ref. 4).

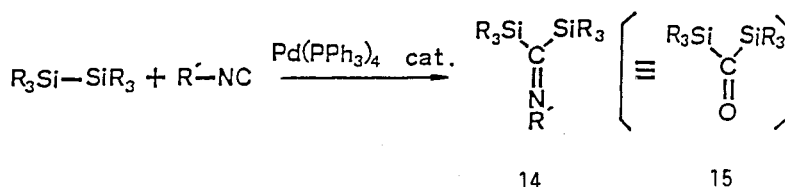

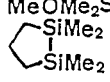


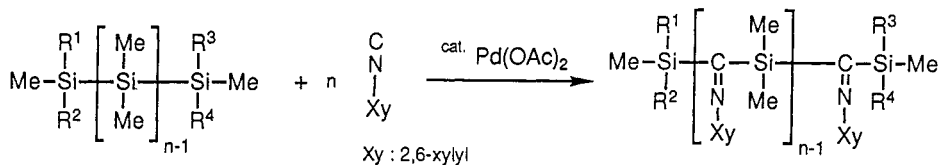


Table 2.

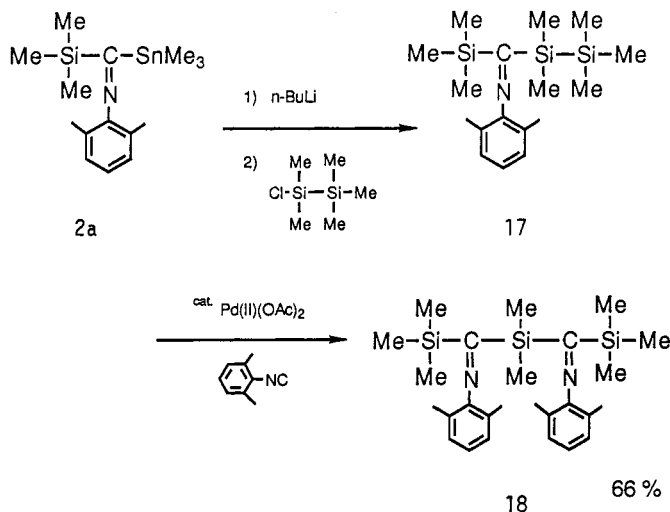
Disilane	Isonitrile	Yield(%)
Me ₃ SiSiMe ₃		25
PhMe ₂ SiSiMe ₂ Ph		88
FMe ₂ SiSiMe ₂ F		59
F ₂ MeSiSiMe ₃		57
MeOMe ₂ SiSiMe ₂ OMe		47
		38
PhC≡CMe ₂ SiSiMe ₃		77
FMe ₂ SiSiMe ₂ F		71
PhMe ₂ SiSiMe ₂ Ph		63

Poly-insertion of isocyanides into polysilanes is also catalyzed by palladium acetate to give poly[sila(N-substituted)imines] (**16**). Noteworthy is that an isocyanide molecule is regularly inserted into each silicon-silicon linkage of polysilanes when an excess of isocyanide is reacted with polysilanes (ref. 5).



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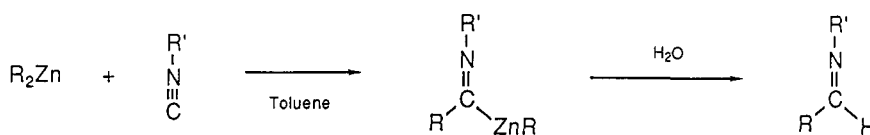
2,4-Bis(N-2,6-xylylimino)-1,3,5-trisilapentane (**18**) is also obtained by a palladium-catalyzed reaction of 2,6-xylyl isocyanide with 1-[(N-2,6-xylylimino)trimethylsilylmethyl]-1,1,2,2,2-pentamethyldisilane (**17**), which is prepared from [(N-2,6-xylylimino)trimethylsilylmethyl]-lithium (**2a**) and chloropentamethyldisilane.



The palladium-catalyzed poly-insertion of isonitriles into polysilane is successfully applied to tetrasilane and hexasilane; e.g., the reaction of decamethyltetrasilane with 2,6-xylyl isocyanide produces the expected 1,1,1,3,3,5,5,7,7,7-decamethyl-2,4,6-tris-(N-2,6-xylylimino)-1,3,5,7-tetrasilane in 34% isolated yield as a yellow crystalline solid [UV(cyclohexane solution) max 407 nm (ϵ 540)].

INSERTION OF ISONITRILES INTO ZINC-CARBON LINKAGE OF ORGANOZINC COMPOUNDS

Dialkylzinc and diarylzinc are reluctant to react with aryl isocyanides in toluene at room temperature. On heating, however, insertion of 2,6-xylyl isocyanide and 2,6-bis-(trifluoromethyl)phenyl isocyanide into organozinc takes place cleanly and smoothly to give in situ α -(N-arylimino)alkylzinc compounds (**19**) in moderate yields (Table 3). It is to be noted that not only dialkylzinc and diarylzinc, but also divinylzinc affords the corresponding α -(N-2,6-xylylimino)alkylzinc (**19**). However, use of *o*-tolyl isocyanide results in the concomitant formation of by-products having much higher boiling point. Alkyl isocyanides do not give the expected insertion products (ref. 6).

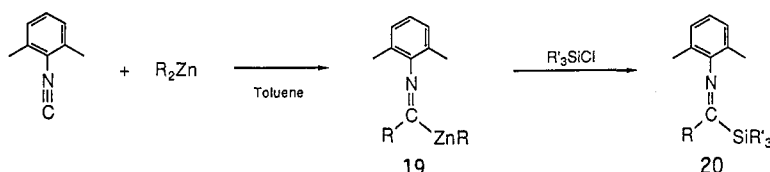


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Table 3.

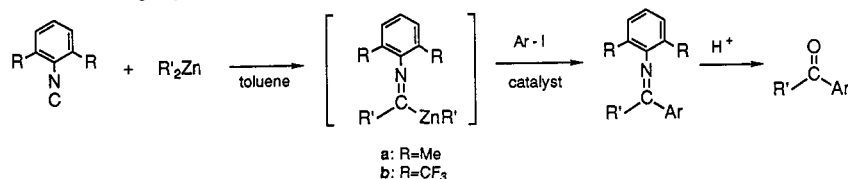
R	R'	reaction conditions	yield, %
Et	2,6-xylyl	90 °C, 6 h	63
<i>i</i> -Pr	2,6-xylyl	95 °C, 2 h	73
CH ₂ =CH	2,6-xylyl	40 °C, 40 h	11
CH ₃ CH=CH	2,6-xylyl	40 °C, 12 h	71
Ph	2,6-xylyl	90 °C, 3 h	74
<i>i</i> -Pr	<i>o</i> -tolyl	60 °C, 2.5 h	33

$[\alpha$ -(N-arylimino)alkyl]zincs (**19**) thus generated are trapped with trialkylchlorosilane. When trialkylchlorosilane is added at room temperature to a toluene solution of **19** containing DMF, HMPA and DMAP as additives, $[\alpha$ -(N-arylimino)alkyl]silanes (**20**) are obtained in moderate yields and are hydrolyzed to the corresponding acylsilanes, as mentioned above.



Coupling reactions of $[\alpha$ -(N-arylimino)alkyl]zincs (**19**) with aromatic iodides are catalyzed by transition metal complexes. The coupling of $[\alpha$ -(arylimino)alkyl]zinc (**19**), prepared from 2,6-xylyl isocyanide, is efficiently catalyzed by palladium catalyst to give the corresponding N-aryl aryimine derivatives (**21**). On the other hand, NiCl₂(dppp) [dppp: 1,3-bis(diphenylphosphino)propane] is a catalyst of choice for the coupling reaction of $[\alpha$ -(arylimino)alkyl]zinc (**19**) prepared from 2,6-bis(trifluoromethyl)phenyl isocyanide. Use of other catalysts, including PdCl₂(PPh₃)₂, PdCl₂(dppf), Pd(PPh₃)₄, Pd(PEt₃)₄ and NiCl₂(PPh₃)₂ requires a longer reaction time and gives **21** in lower yields. Attempts of the coupling of **19** with alkenyl iodides have so far failed (ref. 7).

N-Aryl aromatic imines (**21**) thus prepared are readily hydrolyzed to the corresponding aromatic ketones in high yields.

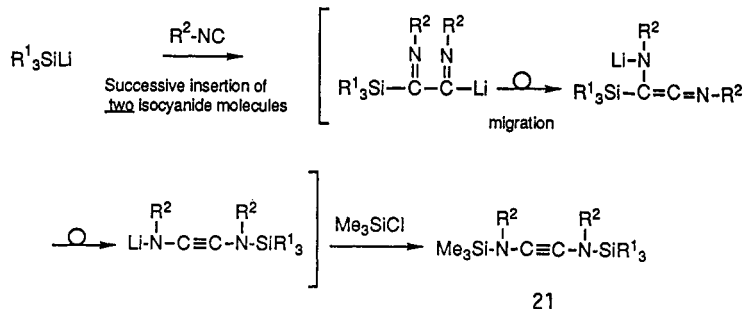


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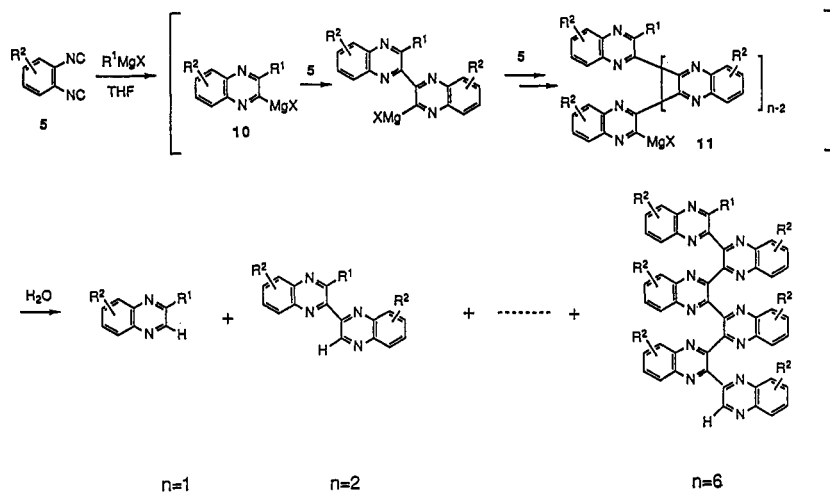
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SUCCESSIVE INSERTIONS OF ISONITRILES INTO LITHIUM-SILICON LINKAGE AND MAGNESIUM-CARBON LINKAGE

Alkyl isocyanides are readily dimerized by organosilyllithium to produce di-[N-(organosilyl)-N-alkylamino]acetylenes (21) in moderate yields, after quenching with trialkylchlorosilanes. The dimerizations of isocyanides, which present a novel double insertion of isocyanides into organolithium, may be explained by a reaction scheme involving a successive insertion of two isocyanides into the lithium-silicon bond of organosilyllithium, followed by anionic 1,2-migration of silyl group (ref. 8).



Oligomerization of isocyanide by successive insertion of isocyanides into organometallic compound has been found in the reaction of 1,2-diisocyanoarene with Grignard reagent. The reaction of 1,2-diisocyano-3,4,5,6-tetramethylbenzene with Grignard reagent gives a mixture of quinoxaline oligomers up to hexamer. The quinoxaline oligomers produced are separated and isolated by HPLC. Of noteworthy is the formation of the quinoxaline hexamer, which arises from twelve successive insertion of the isocyno group of 1,2-diisocyanoarene into carbon-magnesium linkage (ref. 9).



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