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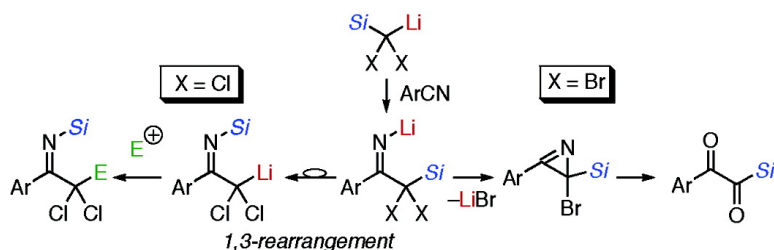
Reaction of Silyldihalomethyllithiums with Nitriles: Formation of -Keto Acylsilanes via Azirines and 1,3-Rearrangement of Silyl Group from C to N

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Reaction of Silyldihalomethyllithiums with Nitriles: Formation of α-Keto Acylsilanes via Azirines and 1,3-Rearrangement of Silyl Group from C to N

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Rearrangement of a silyl group from C to O has been successfully applied to sequential carbon–carbon bond formation.[1] We have also disclosed a domino reaction of silyldibromomethyllithium **1a** with aldehydes and electrophiles (Scheme 1).[2] The key of this process is solvent-controlled 1,3-Brook rearrangement of silicon from carbon to oxygen (**2** to **3**) prior to Peterson elimination of β-oxidosilanes **2**. This concept has been recently expanded to multicomponent linchpin coupling reactions with silylated 1,3-dithianes.[3]

In contrast, there have been few reports on rearrangement from C to N (aza-Brook rearrangement).[4] With the hope to find the aza-Brook rearrangement, we investigated the reaction of **1a** with nitriles. Here we present 1,3-rearrangement of a silyl group from carbon to negatively charged sp²-nitrogen. In addition, a synthesis of α-keto acylsilanes, where 2-bromo-2H-azirine participates as a key intermediate, is reported.

tert-Butyldimethylsilyldibromomethyllithium (**1a**) was easily prepared by deprotonation of dibromomethylsilane with lithium diisopropylamide (LDA) in THF at −78 °C. An addition of benzonitrile and subsequent acidic workup did not furnish the expected rearrangement product **7a** but yielded deep crimson 1-silyl-2-phenylethanedione **8a** as a stable compound (Scheme 2). The result was intriguing enough to lead us to develop a new synthetic route of α-keto acylsilanes. Although functionalized acylsilanes have been extensively explored in organic synthesis,[5] only two reports of α-keto acylsilane preparation have appeared in the literature, both of which entail a multistep operation.[6] It then proved to be necessary to employ 1.5 equiv of LDA and stir more than 5 min after quenching with 1 M HCl to improve the yield. After optimization, α-keto acylsilane **8a** was obtained in 74% yield. The reaction proceeded with aromatic nitriles bearing an electron-donating or -withdrawing group, giving **8b** or **8c** in 76 or 54% yield respectively (Table 1). Unfortunately, alkyl nitriles provided none of the desired products. α-Keto acylsilane **8a** was also obtained in 47% yield from silyldiiodomethyllithium **1b**. The lower yield was ascribed to the instability of **1b**. Interestingly, the use of silyldichloromethyllithium **1c** furnished α,α-dichloro-4-methoxy-acetophenone (**7b**), which can be regarded as the rearrangement product of the silyl group (vide infra). The triisopropylsilyl analogue **1d** afforded the corresponding α-keto acylsilane **8g** in 63% yield (entry 9), whereas dimethylphenylsilyl and trimethylsilyl did not furnish the corresponding α-keto acylsilanes.

We presumed the reaction mechanism involved an intermediacy of 2-bromo-2H-azirine for the unexpected formation of α-keto acylsilane (Scheme 3).[7] Nucleophilic attack of **1a** to nitrile produces an initial adduct **5**, which intramolecularly cyclizes to 2-bromo-2H-azirine **9**. Hydrolysis of **9** furnishes α-keto acylsilanes **8**. Chemical evidence for the presence of 2H-azirine was provided
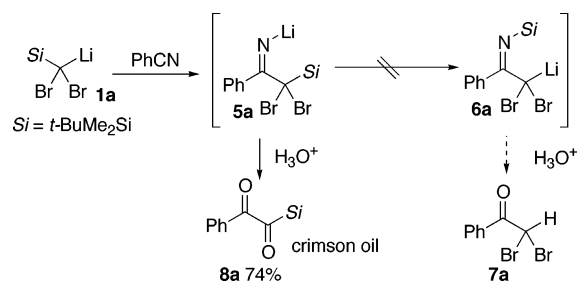

Scheme 1
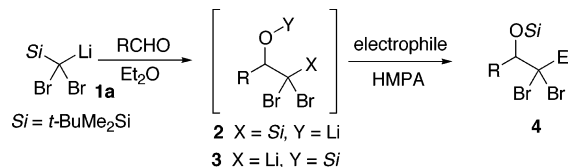
Scheme 2

Table 1

Entry	R₃Si	X	Y	Product	Yield (%)
1	*t*-BuMe₂Si	Br **1a**	H	**8a**	74
2			4-MeO	**8b**	76
3			4-Br	**8c**	54
4			2-Me	**8d**	40
5			4-*i*-Pr₃SiO	**8e**	63
6			Ph—≡—	**8f**	45
7		I **1b**	4-MeO	**8b**	47
8		Cl **1c**	4-MeO	**8b**	4 [a]
9	*i*-Pr₃Si	Br **1d**	4-MeO	**8g**	63

[a] α,α-Dichloro ketone **7b** was obtained in 77% yield.

by the action of LiAlH₄ or allylmagnesium chloride giving the corresponding aziridine **10**. Furthermore, 2H-azirine **11** was obtained as a major product in the reaction with phenyl- or butylmagnesium bromide. An X-ray diffraction unambiguously elucidated that direct halide displacement and not nucleophlic addition to the C–N double bond provides **11a** (Figure 1).[8] Azirine **11** still has a reactive imine bond, and sequential additions of butyl and allyl Grignard reagents to **9** provided **10c**.

As briefly mentioned above, aza-1,3-Brook rearrangement can explain the formation of α,α-dichloro ketone **7b** from **1c**. If this is the case, an addition of electrophiles to the reaction mixture would capture the resulting carbanionic species **6**. In fact, treatment with
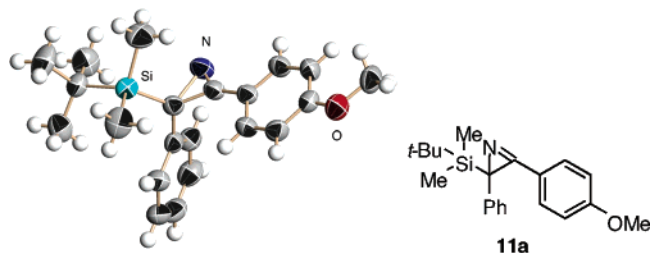
Figure 1. ORTEP drawing of azirine **11a**.

Scheme 3

Entry	Nucleophiles	Nu¹	Nu²	10 (isomeric ratio)	11
				Yield (%)	
1	AllylMgCl	allyl	allyl	**10a** 95 (82/18)	–
2	LiAlH₄	H	H	**10b** 66 (>99/1)	–
3	PhMgBr	Ph	–	–	**11a** 43
4	*n*-BuMgBr	*n*-Bu	–	–	**11b** 40
5	*n*-BuMgBr/AllylMgCl	*n*-Bu	allyl	**10c** 34 (>99/1)	–

Scheme 4

| Entry	Electrophile	E	12	13
			Yield (%)	
1	MeI	Me	**12a** 37 [a]	**13a** 42 [a]
2	PhCHO/Me₃SiCl	PhCH(OSiMe₃)	–	**13b** 88
3	PhCOCl/cat. DMAP	PhCO	–	**13c** 67 [a]
4	CH₂=CHCH₂Br	CH₂=CHCH₂	**12d** 19	**13d** 74 [a]
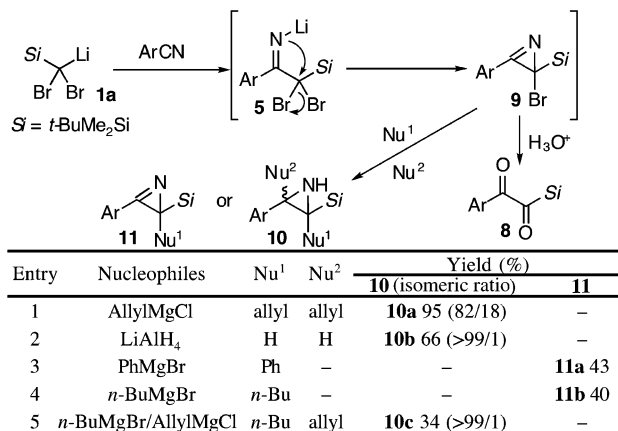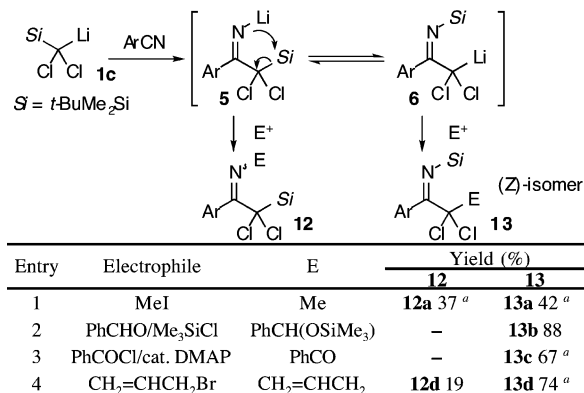
[a] After acidic hydrolysis of imines to ketones.

iodomethane provided *C*-methylated product **13a**, along with *N*-methyl imine **12a** (Scheme 4).[9] Benzaldehyde, which is reactive with **6** but not with **5**, afforded **13b** in excellent yield. Importantly, a single isomer of *N*-silyl imine **13** was exclusively obtained in each case. The stereochemistry of the C–N double bond was assigned as *Z*-configuration on the basis of NOE experiments.

Finally, we conducted this novel preparation of α-keto acylsilanes in a one-pot operation (Scheme 5). To a mixture of dibromomethane

Scheme 5
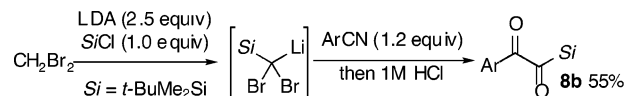
and *tert*-butyldimethylsilyl chloride in THF was added LDA at −78 °C. To the resulting mixture was added 4-methoxybenzonitrile. Quenching with 1 M HCl afforded α-keto acylsilane **8b** in 55% overall yield.

In conclusion, we have achieved a novel route to α-keto acylsilanes from aryl nitriles with silyldi*bromo*methyllithium. This reaction involves 2-bromo-2*H*-azirine as a key intermediate, allowing the synthesis of aziridines or azirines with nucleophiles. Furthermore, we have observed novel silyl 1,3-rearrangement from carbon to negatively charged nitrogen in the reaction with silyldi-*chloro*methyllithium, which enables sequential carbon−carbon bond formation.

Supporting Information Available: General procedures and spectral data for compounds X-ray crystallographic file in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

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(9) The addition of HMPA did not improve the yield of **13a**.

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