

## Reaction of Silyldihalomethyllithiums with Nitriles: Formation of $\alpha$ -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.<sup>1</sup> We have also disclosed a domino reaction of silyldibromomethyllithium **1a** with aldehydes and electrophiles (Scheme 1).<sup>2</sup> 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  $\beta$ -oxidosilanes **2**. This concept has been recently expanded to multicomponent linchpin coupling reactions with silylated 1,3-dithianes.<sup>3</sup>

In contrast, there have been few reports on rearrangement from C to N (aza-Brook rearrangement).<sup>4</sup> 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 sp<sup>2</sup>-nitrogen. In addition, a synthesis of  $\alpha$ -keto acylsilanes, where 2-bromo-2*H*-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  $\alpha$ -keto acylsilanes. Although functionalized acylsilanes have been extensively explored in organic synthesis,<sup>5</sup> only two reports of  $\alpha$ -keto acylsilane preparation have appeared in the literature, both of which entail a multistep operation.<sup>6</sup> 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,  $\alpha$ -keto acylsilane **8a** was obtained in 74% yield. The reaction proceeded with aromatic nitriles bearing an electrondonating or -withdrawing group, giving 8b or 8c in 76 or 54% vield respectively (Table 1). Unfortunately, alkyl nitriles provided none of the desired products.  $\alpha$ -Keto acylsilane 8a was also obtained in 47% yield from silvldiiodomethyllithium 1b. The lower yield was ascribed to the instability of 1b. Interestingly, the use of silvldichloromethyllithium 1c furnished  $\alpha,\alpha$ -dichloro-4-methoxyacetophenone (7b), which can be regarded as the rearrangement product of the silvl group (vide infra). The triisopropylsilvl analogue 1d afforded the corresponding  $\alpha$ -keto acylsilane 8g in 63% yield (entry 9), whereas dimethylphenylsilyl and trimethylsilyl did not furnish the corresponding  $\alpha$ -keto acylsilanes.

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

## Scheme 1



Scheme 2



Table 1

	SiXLi X X 1	1) [[ Y 2) 1N	(2.4 equiv)		Si 8
Entry	$R_3$ Si	Х	Y	Product	Yield (%)
1	t-BuMe <sub>2</sub> Si	Br 1a	Н	<b>8</b> a	74
2			4-MeO	<b>8</b> b	76
3			4-Br	8c	54
4			2-Me	8d	40
5			4-i-Pr <sub>3</sub> SiO	8e	63
6			Ph-==-	8f	45
7		I 1b	4-MeO	<b>8</b> b	47
8		Cl 1c	4-MeO	<b>8</b> b	4 <sup>a</sup>
9	<i>i</i> -Pr <sub>3</sub> Si	Br 1d	4-MeO	8g	63

<sup>*a*</sup>  $\alpha, \alpha$ -Dichloro ketone **7b** was obtained in 77% yield.

by the action of LiAlH<sub>4</sub> or allylmagnesium chloride giving the corresponding aziridine **10**. Furthermore, 2*H*-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).<sup>8</sup> 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  $\alpha$ , $\alpha$ -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

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Figure 1. ORTEP drawing of azirine 11a.

Scheme 3



## Scheme 4



<sup>a</sup> After acidic hydrolysis of imines to ketones.

iodomethane provided *C*-methylated product **13a**, along with *N*-methyl imine **12a** (Scheme 4).<sup>9</sup> 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  $\alpha$ -keto acylsilanes in a one-pot operation (Scheme 5). To a mixture of dibromomethane



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  $\alpha$ -keto acylsilane **8b** in 55% overall yield.

In conclusion, we have achieved a novel route to  $\alpha$ -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.

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**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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