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Facile generation of α-silyl carbanion of trimethylsilyl group assisted by intramolecular pyridyl group coordination

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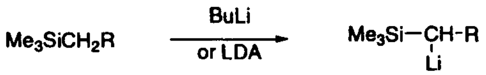
Abstract

Novel methodology for the generation of α-silyl carbanion by the deprotonation of trimethylsilyl group with *tert*-butyllithium or LDA has been developed. This newly developed α-lithiation protocol is based on the intramolecular pyridyl group coordination to stabilize the α-silyl carbanion, together with the inherent silicon α effect. The importance of the use of the 2-pyridyl group in 'pyridyl'- and 'silyl'-directed α-lithiation has been confirmed by the control experiments utilizing phenyltrimethylsilane and (3-pyridyl)trimethylsilane. © 1999 Elsevier Science Ltd. All rights reserved.

Since their introduction to organic synthesis by Peterson in 1968,[1] α-silyl carbanions[2] have been extensively studied and have emerged as extremely important synthons in organic synthesis.[3] They have been widely used in Peterson olefination,[1] nucleophilic hydroxymethylation,[4] and their variants. Representatively, α-silyl carbanions are generated in three different ways: (1) Grignard reagent formation from the corresponding α-halosilane; (2) deprotonation by lithiating reagent such as butyllithium; and (3) addition of alkyllithium to vinylsilane. Among these α-silyl carbanion generating methods, deprotonation by butyllithium is by far the most convenient way, since α-halosilanes and vinylsilanes are not always readily available. In most cases, together with the stabilization of the carbanion by the α-silyl group, stabilization effects by neighboring hetero atoms or electron-withdrawing groups have been exploited for their generation (Eq. 1).[5]



$$\mathrm{Me_3SiCH_2R} \xrightarrow[\text{or LDA}]{\text{BuLi}} \mathrm{Me_3Si{-}}\underset{\mathrm{Li}}{\mathrm{CH}}\mathrm{{-}R} \qquad (1)$$

R = $SiMe_3$, OMe, SMe, SPh, SOPh, SePh, PPh_2, $P(O)(OEt)_2$, $P(S)Ph_2$, N_2, Cl, Ph, CO_2-*t*-Bu, CN, vinyl etc.

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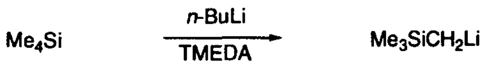
However, without such additional effects, the generation of α-silyl carbanion is known as a formidable task by means of hydrogen–metal exchange, and to our knowledge, there are only a few reports on trimethylsilyl group deprotonation.[6] For example, in the case of Me_4Si, the deprotonation is extremely slow and inefficient giving the corresponding α-silyl carbanion in 36% yield after 4 days (Eq. 2).[6a] Presumably, this sluggish deprotonation stems from the lack of additional stabilization effects.



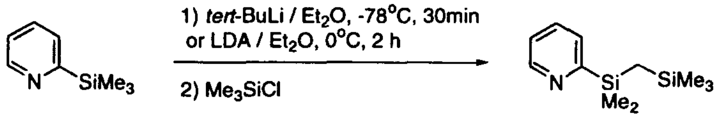
$$Me_4Si \xrightarrow[\text{TMEDA}]{n\text{-BuLi}} Me_3SiCH_2Li \qquad (2)$$

36% after 4 days

Herein, we report on a novel methodology for the efficient deprotonation of the trimethylsilyl group based on the intramolecular pyridyl group coordination to stabilize thus generated α-silyl carbanion (Eq. 3).

(3)

The reaction is simple to perform. To a solution of (2-pyridyl)trimethylsilane[7] (**1**) in dry Et_2O was added dropwise a solution of *tert*-butyllithium (1.1 equiv.) at −78°C. Instantaneously, the color of the solution changed to orange which indicated a generation of α-silyl carbanion of trimethylsilyl group as shown in Eq. 3. The generation of α-silyl carbanion was unambiguously confirmed by the treatment with chlorotrimethylsilane (1.2 equiv.) to give its adduct **2** in 93% yield (Eq. 4).[8] Surprisingly, lithium diisopropylamide (LDA) was also found to be effective and gave **2** in 69% yield (92% purity) when the deprotonation was conducted at 0°C for 2 h (Eq. 4). It is interesting to note that the purification of **2** was found to be very easy without any chromatographic isolation technique. By virtue of the possession of the pyridyl group, **2** has been isolated only by simple acid–base extraction with >95% purity as judged by ^1H NMR and capillary GC analysis.



(4)

1 **2**

93% yield (>95% purity) from *tert*-BuLi
69% yield (92% purity) from LDA

Other lithiating reagents were also examined. The lithiation of **1** with *n*-butyllithium at −78°C did not occur at all. Raising the temperature to 0°C seemed to generate some anionic species but gave a complex mixture of unidentified products after the treatment with chlorotrimethylsilane. On the other hand, the lithiation proceeded with *sec*-butyllithium at −78°C. However, **2** was isolated in much lower yield (~60%) together with some unidentified products. It seems that nucleophilicities as well as basicities of the bases employed are very important for the successful deprotonation of **1**. After all, *tert*-butyllithium and LDA were found to be the lithiating reagents of choice for **1**. Especially, the successful deprotonation by LDA is of great importance, since most of the functional groups are known to tolerate LDA.

Next, we examined the structure of (2-pyridyldimethylsilyl)methyl lithium in solution using ^1H NMR spectroscopy in $Et_2O\text{-}d_{10}$ at −78°C (Fig. 1). When compared to **1**, noticeable changes in the pyridine ring chemical shift were observed for (2-pyridyldimethylsilyl)methyl lithium. Downfield shifts in the

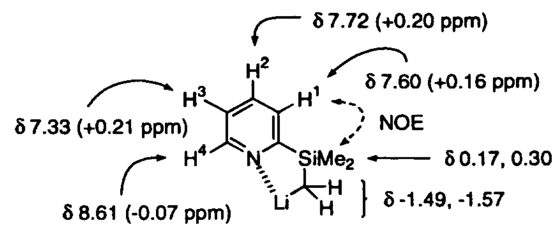
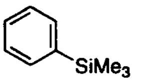


Figure 1. ^{1}H NMR of (2-pyridyldimethylsilyl)methyl lithium in Et_2O-d_{10} at −78°C

chemical shift were observed for H^1, H^2, and H^3 which clearly indicate the intramolecular pyridyl group coordination to the metal. Moreover, a positive nuclear Overhauser effect was observed between the methyl groups on the silicon and H^1, which is also in line with aforementioned discussions.

In order to substantiate that this facile generation of α-silyl carbanion is attributed to the intramolecular pyridyl group coordination together with the inherent silicon α effect, we next examined the α-lithiation of phenyltrimethylsilane (**3**) and (3-pyridyl)trimethylsilane (**4**) with *tert*-butyllithium. Upon treatment with *tert*-butyllithium, neither **3** nor **4** generated the desired α-silyl carbanion. This pronounced difference between **1** and **3** or **4** supports our hypothesis that the 2-pyridyl group is required for the generation and stabilization of α-silyl carbanion of the trimethylsilyl group.



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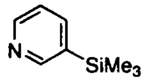

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In conclusion, we have developed a novel methodology for the generation of α-silyl carbanion by virtue of the intramolecular assistance of the 2-pyridyl group. This appears to be the first bona fide case of the efficient and practical deprotonation of trimethylsilyl group. This newly developed α-lithiation protocol would expand the scope and limitation of the chemistry of α-silyl carbanion. Moreover, easy purification (simple acid–base extraction), without any chromatographic isolation technique, will fulfil today's economically and environmentally conscious climate. Clearly, we are now in a position to use the resulting (2-pyridyldimethyl)methyl lithium reagent in organic synthesis, as reported in the following paper.[9]

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8. To a solution of **1** (151 mg, 1.0 mmol) in dry Et_2O (2 mL) was added dropwise a solution of *tert*-butyllithium (1.1 mmol, 1.64 M solution in pentane) at −78°C. After stirring for an additional 30 min, chlorotrimethylsilane (130 mg, 1.2 mmol) was added and stirred overnight. 1N aq. HCl (5 mL) was added and stirred for 15 min, and then separated. The organic phase was additionally extracted with 1N aq. HCl (4×5 mL). The aqueous phase was neutralized by adding NaOH pellet and was extracted with Et_2O (3×10 mL). Drying over $MgSO_4$ and removal of solvent under reduced pressure afforded **2** (208 mg, 93%, >95% pure as judged by ^1H NMR and capillary GC) as a colorless oil: ^1H NMR (300 MHz, $CDCl_3$): δ −0.05 (s, 9H), 0.07 (s, 2H), 0.33 (s, 6H), 7.14 (ddd, J=7.5, 5.1, 1.5 Hz, 1H), 7.48 (ddd, J=7.5, 1.5, 1.2 Hz, 1H), 7.54 (td, J=7.5, 1.8 Hz, 1H), 8.75 (ddd, J=5.1, 1.8, 1.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ −1.0, 1.0, 2.1, 122.5, 128.6, 133.9, 150.1, 169.2.
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