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[Bis(2-pyridyldimethylsilyl)methyl]lithium. New Reagent for the Stereoselective Synthesis of Vinylsilanes

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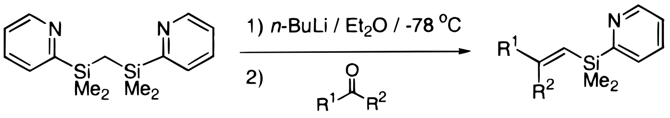
ABSTRACT

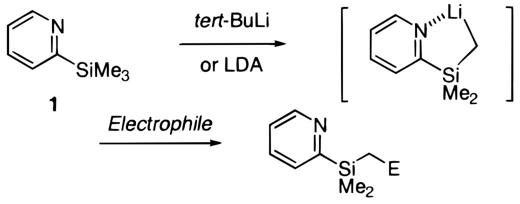


>99% Stereoselectivity

The generation of (2-PyMe$_2$Si)$_2$CHLi was easily accomplished by the deprotonation of (2-PyMe$_2$Si)$_2$CH$_2$ using *n*-BuLi in Et$_2$O. Thus generated (2-PyMe$_2$Si)$_2$CHLi was found to react with a variety of aldehydes and ketones to give the corresponding vinylsilanes in extremely high yields with complete stereoselectivities.

The generation and reactions of α-silyl carbanions are subjects of great interest in organic synthesis.[1] Despite many useful reactions such as the Peterson olefination,[2] nucleophilic hydroxymethylation,[3] and their variants, α-silyl carbanion chemistry still suffers from its substrate dependence. In most cases, the deprotonation methodology is only feasible when the additional stabilizing effects by neighboring heteroatom or electron-withdrawing groups can be expected.[1] Recently, we have embarked on a program directed toward the development of removable intramolecular ligands (directing groups), which control the metal-mediated and -catalyzed processes by a complex induced proximity effect (CIPE).[4] For example, the facile deprotonation of the otherwise difficult trimethylsilyl group[5] was achieved by utilizing a 2-pyridyldimethylsilyl (2-PyMe$_2$Si) group as the intramolecular ligand (Scheme 1).[6] We envisioned that appending multiple 2-PyMe$_2$Si groups should lead to interesting reactivity. Herein, we report on our investigations of α-silyl carbanion chemistry using (2-PyMe$_2$Si)$_2$CH$_2$ (**2**).

Scheme 1



The starting material **2** can be easily prepared in 63% yield by the reaction of 2-PyMe$_2$SiCH$_2$Li, generated from **1**, and

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[1] (a) Brook, M. A. *Silicon in Organic, Organometallic, and Polymer Chemistry*; John Wiley & Sons: New York, 2000. (b) Colvin, E. W. *Silicon Reagents in Organic Synthesis*; Academic Press: London, 1988. (c) Weber, W. P. *Silicon Reagents for Organic Synthesis*; Springer-Verlag: Berlin, 1983. (d) Magnus, P. *Aldrichimica Acta* **1980**, *13*, 238.

[2] Peterson, D. J. *J. Org. Chem.* **1968**, *33*, 780. For an excellent review, see: Ager, D. J. *Org. React.* **1990**, *38*, 1.

[3] Tamao, K.; Ishida, N.; Ito, Y.; Kumada, M. *Org. Synth.* **1990**, *69*, 96.

[4] For a review on CIPE, see: Beak, P.; Meyers, A. I. *Acc. Chem. Res.* **1986**, *19*, 356. See also: Hoveyda, A. H.; Evans, D. A.; Fu, G. C. *Chem. Rev.* **1993**, *93*, 1307.

[5] (a) Peterson, D. J. *J. Organomet. Chem.* **1967**, *9*, 373. (b) Gornowicz, G. A.; West, R. *J. Am. Chem. Soc.* **1968**, *90*, 4478. (c) Frye, C. L.; Salinger, R. M.; Fearon, F. W. G.; Klosowski, J. M.; DeYoung, T. *J. Org. Chem.* **1970**, *35*, 1308. (d) Pinkerton, F. H.; Thames, S. F. *J. Organomet. Chem.* **1971**, *29*, C4. (e) Hosomi, A.; Kohra, S.; Tominaga, Y.; Shoji, M.; Sakurai, H. *Chem. Pharm. Bull.* **1987**, *35*, 1663. (f) Friesen, R. W.; Sturino, C. F.; Daljeet, A. K.; Kolaczewska, A. *J. Org. Chem.* **1991**, *56*, 1944. (g) Imanieh, H.; Quayle, P.; Voaden, M.; Conway, J.; Street, S. D. A. *Tetrahedron Lett.* **1992**, *33*, 543. (h) Luitjes, H.; de Kanter, F. J. J.; Schakel, M.; Schmitz, R. F.; Klumpp, G. W. *J. Am. Chem. Soc.* **1995**, *117*, 4179. (i) Brough, P. A.; Fisher, S.; Zhao, B.; Thomas, R. C.; Snieckus, V. *Tetrahedron Lett.* **1996**, *37*, 2915. (j) Abele, B. C.; Strohmann, C. In *Organosilicon Chemistry III*; Auner, N., Weis, J., Eds.; Wiley-VCH: Weinheim, 1998; p 206.

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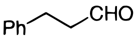
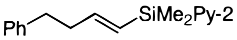
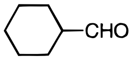
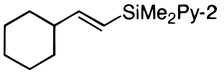
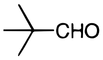
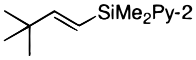
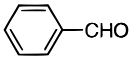
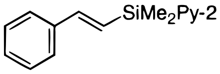
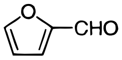
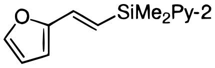
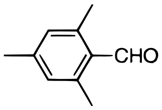
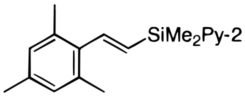
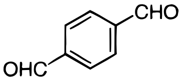
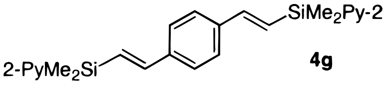
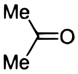
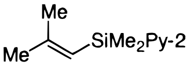
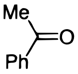
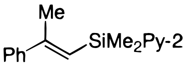
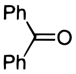
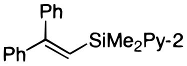
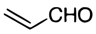
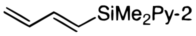
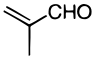
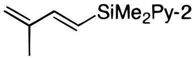
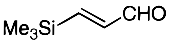
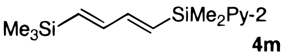
Table 1. Reactions of $(2\text{-PyMe}_2\text{Si})_2\text{CHLi}$ with Carbonyl Compounds[a]

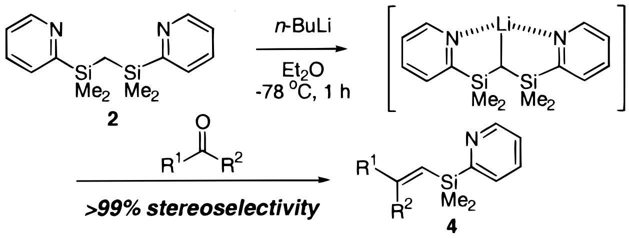
entry	carbonyl compound	product	yield[b]	selectivity[c]
1		 **4a**	quant	>99% *E*
2		 **4b**	quant	>99% *E*
3		 **4c**	quant	>99% *E*
4		 **4d**	90%	>99% *E*
5		 **4e**	quant	>99% *E*
6		 **4f**	94%	>99% *E*
7[d]		 **4g**	98%	>99% *E*
8		 **4h**	73%	-
9		 **4i**	56%	>99% *E*
10		 **4j**	84%	-
11		 **4k**	53%	>99% *E*
12		 **4l**	quant	>99% *E*
13		 **4m**	51%	>99% *E*

[a] Unless otherwise noted, the reactions were performed in dry Et_2O using $(2\text{-PyMe}_2\text{Si})_2\text{CHLi}$ and carbonyl compounds (1.5 equiv) at −78 °C for 30 min and then at room temperature for 1 h under argon. [b] Isolated yields. [c] Determined by ^1H and ^{13}C NMR analysis and NOE experiments. [d] The reaction was performed using $(2\text{-PyMe}_2\text{Si})_2\text{CHLi}$ (2.5 equiv).

$2\text{-PyMe}_2\text{SiH}$, as reported previously.[6c] At the outset, we examined the deprotonation of **2** to generate $(2\text{-PyMe}_2\text{Si})_2\text{CHLi}$. It has been reported that the deprotonation of **1** is highly dependent on the lithiating agent employed: *t*-BuLi leads to quantitative deprotonation, whereas *n*-BuLi leads to a complex mixture.[6b] As in the case for **1**, the deprotonation of **2** was successfully accomplished by 1.1 equiv of *t*-BuLi in Et_2O at −78 °C, and subsequent reaction with allyl bromide gave the corresponding adduct $(2\text{-PyMe}_2\text{Si})_2\text{CHCH}_2\text{CH=CH}_2$ (**3**) in 82% yield. Anticipating the increased reactivity of **2**, we next employed *n*-BuLi under otherwise identical conditions, and **3** was isolated in 92% yield. Simple alkyl bromides were not applicable in this reaction because of their lower reactivities toward nucleophiles.

Having established the facile deprotonation of **2**, we further investigated the reactions of $(2\text{-PyMe}_2\text{Si})_2\text{CHLi}$ with various carbonyl compounds. It has been reported[6c] that the reactions of 2-$PyMe_2SiCH_2Li$ with aldehydes and ketones gave the β-hydroxysilanes without any formation of alkenes by a Peterson-type elimination.[2] However, in the case of **2**, Peterson-type olefination was found to take place, after or concurrently with the addition, to give the corresponding vinylsilanes stereoselectively (Scheme 2). The results are depicted in Table 1.

Scheme 2



The reactions with primary, secondary, and tertiary aliphatic and aromatic aldehydes gave the corresponding vinylsilanes in quantitative yields (entries 1−7). Noteworthy is that the reaction is also applicable to the sterically hindered aldehydes (entries 3 and 6) and bisaldehyde (entry 7). Ketones gave the disubstituted vinylsilanes with somewhat lower yields (entries 8−10). Presumably, proton transfer competed with addition for enolizable ketones such as acetophenone (entry 9), where $(2\text{-}PyMe_2Si)_2CHLi$ serves as the base. The reaction can be applied to the stereoselective synthesis of dienylsilanes as well (entries 11−13).

The extremely high stereoselectivities (>99% *E*) are worth mentioning. It has been well documented that acid- or base-catalyzed elimination from isolated β-hydroxysilanes is highly stereoselective.[7] However, this is not the case for the direct addition/elimination sequences.[7,8] For example, the condensation of $(Me_3Si)_2CHLi$ with benzaldehyde gave a mixture of stereoisomers ($E/Z = 1.4/1$).[8b] If the selectivities are governed by the well-accepted *syn*-elimination[2,7] from the β-silyl alkoxide (**A** or **B**), the selectivity differences between $(2\text{-}PyMe_2Si)_2CHLi$ and $(Me_3Si)_2CHLi$ should not be as dramatic as it is (Figure 1). Moreover, the use of the more sterically demanding $t\text{-}BuMe_2Si$ group instead of a Me_3Si group only led to a slight increase in the *E* selectivity, indicating that the steric factor is not a sole decisive factor for the high selectivity.[7] There must be some contribution from the pyridyl group in the observed high stereoselectivity. We surmise that, before the elimination of the siloxy group, the chairlike conformer (**C** or **D**) might be involved as a stereodetermining intermediate where the intramolecular coordination of the pyridyl group locks the conformation.[8o] Of the two, **D** should be preferred over **C**, since both silyl and R_L groups can occupy the equatorial positions. Thus preferred **D** may lead to the observed *E*-isomer. However, we must stress that these discussions are purely speculative with no experimental evidence.

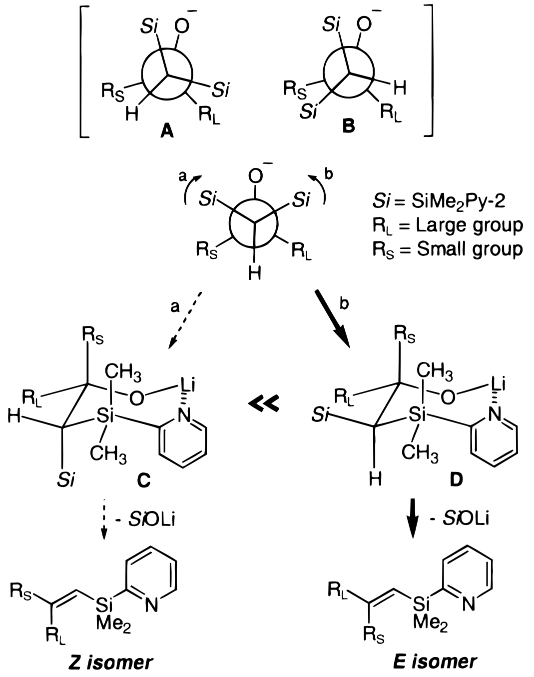


Figure 1. The origin of stereoselectivity.

To assess the elimination aptitude of the 2-$PyMe_2Si$ group in the Peterson-type elimination, we next conducted a control experiment using 2-$PyMe_2SiCH_2SiMe_2Ph$ (**5**). As reported previously, **5** can be prepared in 99% yield by the reaction of 2-$PyMe_2SiCH_2Li$ and $PhMe_2SiCl$.[6c] The generation of 2-$PyMe_2SiCH(Li)SiMe_2Ph$ was successfully accomplished by the reaction of **5** with *t*-BuLi in Et_2O. The carbanion thus generated was subsequently allowed to react with benzaldehyde to give the $PhMe_2Si$-substituted styrene **6** in 95% yield (Scheme 3). The formation of a 1:1 mixture of two

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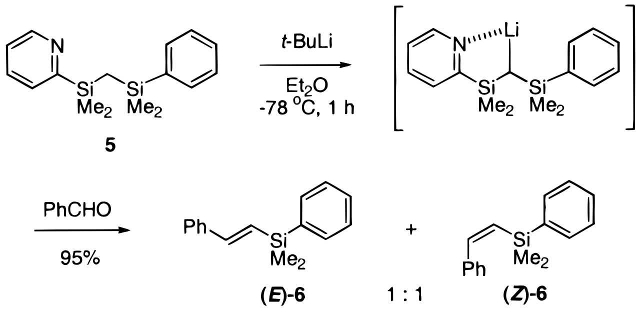
(6) (a) Yoshida, J.; Itami, K.; Mitsudo, K.; Suga, S. *Tetrahedron Lett.* **1999**, *40*, 3403. (b) Itami, K.; Mitsudo, K.; Yoshida, J. *Tetrahedron Lett.* **1999**, *40*, 5533. (c) Itami, K.; Mitsudo, K.; Yoshida, J. *Tetrahedron Lett.* **1999**, *40*, 5537.

(7) Hudrlik, P. K.; Agwaramgbo, E. L. O.; Hudrlik, A. M. *J. Org. Chem.* **1989**, *54*, 5613.

(8) Although similar *E* selectivities for [bis(silyl)methyl]lithium were previously reported, they are not as high as ours or not sited in the literature; see: (a) Sakurai, H.; Nishiwaki, K.; Kira, M. *Tetrahedron Lett.* **1973**, 4193. (b) Gröbel, B.-T.; Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1974**, *13*, 83. (c) Hartzell, S. L.; Rathke, M. W. *Tetrahedron Lett.* **1976**, 2737. (d) Sachdev, K. *Tetrahedron Lett.* **1976**, 4041. (e) Carter, M. J.; Fleming, I. *J. Chem. Soc., Chem. Commun.* **1976**, 679. (f) Seyferth, D.; Lefferts, J. L.; Lambert, R. L., Jr. *J. Organomet. Chem.* **1977**, *142*, 39. (g) Seebach, D.; Bürstinghaus, R.; Gröbel, B.-T.; Kolb, M. *Liebigs Ann. Chem.* **1977**, 830. (h) Gröbel, B.-T.; Seebach, D. *Chem. Ber.* **1977**, *110*, 852. (i) Isobe, M.; Kitamura, M.; Goto, T. *Tetrahedron Lett.* **1979**, 3465. (j) Fleming, I.; Pearce, A. *J. Chem. Soc., Perkin Trans. 1* **1980**, 2485. (k) Carter, M. J.; Fleming, I.; Percival, A. *J. Chem. Soc., Perkin Trans. 1* **1981**, 2415. (l) Sato, Y.; Takeuchi, S. *Synthesis* **1983**, 734. (m) Ager, D. J. *J. Org. Chem.* **1984**, *49*, 168. (n) Takeda, T.; Ando, K.; Mamada, A.; Fujiwara, T. *Chem. Lett.* **1985**, 1149. (o) Boeckman, R. K., Jr.; Chinn, R. L. *Tetrahedron Lett.* **1985**, *26*, 5005. (p) Ager, D. J.; East, M. B. *J. Org. Chem.* **1986**, *51*, 3983. (q) Inoue, S.; Sato, Y. *Organometallics* **1986**, *5*, 1197. (r) Terao, Y.; Aono, M.; Takahashi, I.; Achiwa, K. *Chem. Lett.* **1986**, 2089. (s) Marchand, A. P.; Huang, C.; Kaya, R.; Baker, A. D.; Jemmis, E. D.; Dixon, D. A. *J. Am. Chem. Soc.* **1987**, *109*, 7095. (t) Kira, M.; Hino, T.; Kubota, Y.; Matsuyama, N.; Sakurai, H. *Tetrahedron Lett.* **1988**, *29*, 6939. (u) Bates, T. F.; Thomas, R. D. *J. Org. Chem.* **1989**, *54*, 1784.

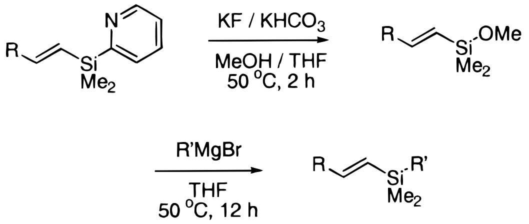
Scheme 3



stereoisomers (*E* and *Z*) strongly denotes that the addition process is nonselective, giving the two diastereomeric intermediates. Moreover, it should be noted that the 2-PyMe$_2$Si-substitued styrene was not observed at all in this reaction. This observation underscores the greater elimination aptitude of the 2-PyMe$_2$Si group, and we assume the following as plausible explanations: (i) the coordination of the pyridyl group may force the conformation as in **C** or **D** (Figure 1), thereby making the 2-PyMe$_2$Si group eliminate and (ii) the greater electrophilicity of the 2-PyMe$_2$Si group facilitates the alkoxide attack more readily.[8u]

Although the 2-pyridyl-substituted vinylsilane itself can be expected to exert interesting reactivity, its conversion to other vinylsilanes is also viable (Scheme 4). By using a recently developed protocol, the 2-Py−Si bond can be cleaved in a KF/MeOH system to afford methoxy(vinyl)silane.[9] The resultant methoxysilane can be further allowed to react with a Grignard reagent such as PhMgBr to give the corresponding vinylsilane.[10]

Scheme 4



In conclusion, we have developed the facile generation and reactions of $(2\text{-PyMe}_2\text{Si})_2\text{CHLi}$ with a variety of aldehydes and ketones, affording the corresponding vinylsilanes and dienylsilanes in extremely high yields with complete stereoselectivities. This expeditious and versatile protocol will find use in many organic reactions using vinylsilanes and dienylsilanes.[11]

Acknowledgment. This research was supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science, Sports and Culture, Japan, and in part by the Mitsubishi Foundation.

Supporting Information Available: Experimental procedures and characterization data for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

OL005735N

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(9) Itami, K.; Mitsudo, K.; Yoshida, J. *J. Org. Chem.* **1999**, *64*, 8709.

(10) For example, aryl(vinyl)silane (R = 2,4,6-$\text{Me}_3\text{C}_6\text{H}_2$, R′ = Ph) can be prepared in 57% overall yield.

(11) (a) Fleming, I.; Dunoguès, J.; Smither, R. *Org. React.* **1989**, *37*, 57. (b) Larson, G. L. *J. Organomet. Chem.* **1992**, *422*, 1. (c) Fleming, I.; Barbero, A.; Walter, D. *Chem. Rev.* **1997**, *97*, 2063.