

Rapid and efficient entry to vinyl silanes from aldehydes employing a novel metalation–Peterson sequence†

James McNulty* and Priyabrata Das

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Bis(trimethylsilyl)chloromethane undergoes a rapid and selective metalation with *s*-BuLi, yielding the nucleophilic bis(trimethylsilyl)methyl anion and providing a straightforward general entry to vinyl silanes from aromatic, aliphatic and vinyl aldehydes.

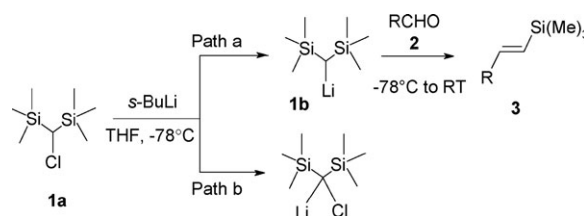
Vinyl silanes have proven to be of value in a variety of useful synthetic transformations in view of their mild reactivity, and the controlled regio- and stereoselectivity observed in their reactions.^{1,2} However, applications of vinyl silanes in total synthesis appear to be less common, possibly due to the lack of a rapid general synthetic entry to this functional group. Various methodologies are available for vinyl silane synthesis, including alkyne hydrosilylation,^{1–3} aryl/alkenyl halide–silicon exchange,⁴ as well as from carbonyl compounds.⁵ Peterson has described an interesting route using a Wittig reaction of an α -silylated ylide with an aldehyde.⁶ An obvious alternative for this purpose is [bis(trimethylsilyl)methyl]lithium (**1b**, Scheme 1), employing a Peterson reaction with a carbonyl compound to produce a vinyl silane. Unfortunately, precursor bis-silamethylenes demonstrate problematic lithium–hydrogen exchange,⁷ unless an additional stabilizing neighbouring heteroatom or electron-withdrawing group is present,^{8a} complicating this potentially valuable process.⁸ Product yields using this deprotonation–Peterson route to vinyl silanes are low to moderate (25–70%).^{5b} Given the availability of a wide range of simple aromatic and aliphatic aldehydes, we have been interested in developing a direct synthesis of vinyl silanes from aldehydes. Alternative routes to vinyl silanes from aldehydes employ reagents that are not generally available or involve several steps.⁹

Herein, we report the novel finding that commercially available†¹⁰ bis(trimethylsilyl)chloromethane (**1a**) selectively undergoes an efficient lithium–halogen exchange with *s*-BuLi, resulting in rapid generation of the desired [bis(trimethylsilyl)methyl]lithium intermediate (**1b**). The resulting bis-trimethylsilyl carbanion readily enters into Peterson olefination reactions with aldehydes, including enolizable aliphatic aldehydes, allowing a direct synthesis of vinyl silanes in high yield and with good (*E*)-stereoselectivity.

The two possible outcomes of the reaction of **1a** with an alkyl lithium reagent are outlined in Scheme 1. The reaction of **1a** with *n*-BuLi and *t*-BuLi was problematic, however we quickly determined that the desired lithium reagent **1b** was formed *via* lithium–halogen exchange upon treatment of **1a** with *s*-BuLi in THF at -78°C (Scheme 1). Steric hindrance around both the chloromethylene proton and the bulky base is the likely rationale that directs the lithium–chlorine exchange (path a) over the potential deprotonation path (path b). While both the magnesium and lithium derivatives corresponding to **1b** have been prepared through direct metalation,^{5k,5l} to the best of our knowledge, this is the first report of lithium–halogen exchange on such a bis-(trialkylsilyl)chloroalkyl group in the literature.

The synthetic utility of this novel lithium–halogen exchange as a route to vinyl silanes was investigated with a range of aromatic aldehydes, the results of which are summarized in Table 1. The isolated yields and (*E*)-stereoselectivities were invariably good in all of the cases investigated. No significant electronic effect was observed, with both electron donating and electron withdrawing derivatives (Table 1, entries 1 to 9) reacting equally well. *Ortho*-steric effects did not appear to be detrimental (Table 1, entry 4) on the part of the aldehyde.

Most interestingly, cinnamaldehyde yielded the silyldiene (Table 1, entry 3) in 81% isolated yield. The yield obtained here is considerably higher than the reported 32–37% obtained using literature methods for the preparation of intermediate **1b**.^{5b} This literature route was considered but abandoned in a previous report by Fleming *et al.* as a reliable route to silylated butadienes.^{5e} In addition, the reaction of anion **1b**, generated by lithium–proton exchange, has been reported to give only low yields of vinyl silanes upon reaction with enolizable aliphatic aldehydes (for example, 25% with 1-butanol and 45% with formaldehyde).^{5b,5e} The reaction of **1b**, generated *via* the new lithium–halogen exchange path, was therefore investigated with undecanal. This led to the formation of the corresponding vinyl silane, surprisingly isolated in 77% yield and with 4 : 1 (*E*) : (*Z*) stereoselectivity (Table 1,



Scheme 1 Halogen–lithium exchange (path a) vs. deprotonation (path b).

Department of Chemistry, McMaster University, 1280 Main Street West, Hamilton, Ontario, Canada L8S 4M1. E-mail: jmcnult@mcmaster.ca; Fax: +1 905-522-2509; Tel: +1 905-525-9140 ext. 27393

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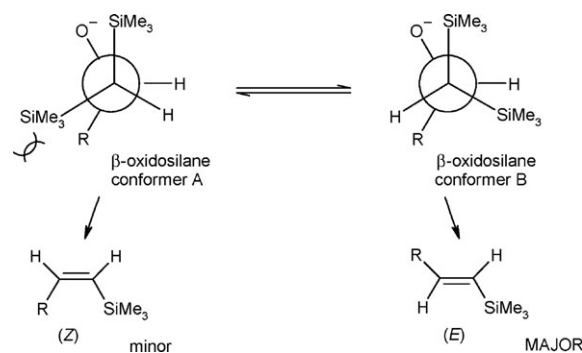
‡ This reagent is available from the Aldrich Chemical Company

Table 1 Reaction of (TMS)₂CHLi with aldehydes

Entry	2	3	(E) : (Z)	Yield (%)
1			>9 : 1	90
2			>9 : 1	95
3			>9 : 1	81
4			>9 : 1	90
5			>9 : 1	80
6			>9 : 1	85
7			>9 : 1	87
8			>9 : 1	93
9			>9 : 1	65
10			4 : 1	77

entry 10). This result proves that there is no intrinsic barrier to the use of this bis-(trimethylsilyl)-stabilized carbanion with aliphatic aldehydes (such as enolization, aldolization, *etc.*). The explanation for this unexpected higher efficiency may lie with the method of generation of **1b** via rapid lithium–chlorine exchange. In contrast, the literature protocol for the synthesis of lithium reagent **1b** involves proton–lithium exchange on the central methylene of bis(trimethylsilyl)methane using *t*-BuLi/HMPA in THF over 7.5 h.^{5b} Since it is well documented that tetraalkylsilanes are very difficult to deprotonate,⁸ the previous lengthy anion generation procedure and/or presence of unreacted *t*-BuLi may have adversely affected the yield of vinyl silanes from sensitive aldehydes.

The *trans*-olefin selectivity in the product vinyl silanes can be readily explained as follows. β -Hydroxysilanes can undergo elimination to form olefins through either a concerted *syn*-periplanar reaction pathway, typically under basic reaction conditions, or through a stepwise *anti*-periplanar pathway, typically occurring under acidic conditions.¹⁰ Conformational analysis of the present relevant β -oxidosilane intermediate is shown (conformers A and B) in Fig. 1. This intermediate possesses two diastereotopic TMS groups capable of participating in the expected *syn*-elimination. Conformer A indicates the presence of a steric non-bonding interaction that is absent in conformer B, thus favouring elimination from conformer B via an expected early transition state and leading to the (*E*)-vinyl silanes as the kinetic reaction product under these conditions.

**Fig. 1** Favoured *syn*-periplanar elimination from conformer B.

In conclusion, we have shown that bis(trimethylsilyl)chloromethane readily undergoes lithium–halogen exchange with *s*-BuLi, and that the resulting anion adds readily to aromatic, vinyl as well as enolizable aldehydes in a Peterson fashion to yield vinyl silanes in good yield and (*E*)-stereoselectivity. Further extension and application of the method is currently under investigation.

Notes and references

- I. Fleming, I. A. Barbero and D. Walter, *Chem. Rev.*, 1997, **97**, 2063.
- (a) J. Tsuji, *Palladium Reagents and Catalysts*, Wiley, Chichester, 2004, pp. 335–348; (b) T. Hiyama and E. Shirakawa, *Top. Curr. Chem.*, 2002, **219**, 61; (c) T. A. Blumenkopf and L. E. Overman, *Chem. Rev.*, 1986, **86**, 857.
- (a) A. K. Dash, J. Q. Wang and M. S. Eisan, *Organometallics*, 1999, **18**, 4724; (b) S. Bratovanov, W. Kózmínski, J. Fässler, Z. Molnar, D. Nanz and S. Bienz, *Organometallics*, 1997, **16**, 3128; (c) N. Asao, T. Sudo and Y. Yamamoto, *J. Org. Chem.*, 1996, **61**, 7654; (d) T. N. Mitchell, R. Wickenkamp, A. Amamria, R. Dicke and U. Schneider, *J. Org. Chem.*, 1987, **52**, 4868.
- (a) M. Murata, S. Watanabe and Y. Masuda, *Tetrahedron Lett.*, 1999, **40**, 9255; (b) K. Fugami, K. Oshima, K. Utimoto and H. Nozaki, *Tetrahedron Lett.*, 1986, **27**, 2161.
- (a) D. Seebach, R. Bürstinghaus, B. T. Gröbel and M. Kolb, *Justus Liebigs Ann. Chem.*, 1977, 830; (b) B. T. Gröbel and D. Seebach, *Chem. Ber.*, 1977, **110**, 852; (c) M. Isobe, M. Kitamura and T. Goto, *Tetrahedron Lett.*, 1979, 3465; (d) I. Fleming and A. Pearce, *J. Chem. Soc., Perkin Trans. 1*, 1980, 2485; (e) M. J. Carter, I. Fleming and A. Percival, *J. Chem. Soc., Perkin Trans. 1*, 1981, 2415; (f) Y. Sato and S. Takeuchi, *Synthesis*, 1983, 734; (g) D. J. Ager, *J. Org. Chem.*, 1984, **49**, 168; (h) T. Takeda, K. Ando, A. Mamada and T. Fujiwara, *Chem. Lett.*, 1985, 1149; (i) R. K. Boeckman, Jr and R. L. Chinn, *Tetrahedron Lett.*, 1985, **26**, 5005; (j) D. J. Ager and M. B. East, *J. Org. Chem.*, 1986, **51**, 3983; (k) D. R. Williams, A. I. Morales-Ramos and C. M. Williams, *Org. Lett.*, 2006, **8**, 4393; (l) L. Balazs, H. J. Breunig, I. Ghesner and E. Lork, *J. Organomet. Chem.*, 2002, **648**, 33.
- D. J. Peterson, *J. Org. Chem.*, 1968, **33**, 780.
- D. J. Peterson, *J. Organomet. Chem.*, 1967, **9**, 373.
- (a) G. A. Gornowicz and R. West, *J. Am. Chem. Soc.*, 1968, **90**, 4478; (b) M. A. Brook, *Silicon in Organic, Organometallic, and Polymer Chemistry*, John Wiley & Sons, New York, 2000; (c) E. W. Colvin, *Silicon Reagents in Organic Synthesis*, Academic Press, London, 1988; (d) W. P. Weber, *Silicon Reagents for Organic Synthesis*, Springer-Verlag, Berlin, 1983.
- (a) K. Itami, T. Nokami and J. Yoshida, *Org. Lett.*, 2000, **2**, 1299; (b) M. L. Kwan, C. W. Yeung, K. L. Breno and K. M. Doxsee, *Tetrahedron Lett.*, 2001, **42**, 1411; (c) J. M. Concellon, P. L. Bernard and E. Bardales, *Org. Lett.*, 2001, **3**, 937.
- F. P. Hudrlik, E. L. O. Agwaramgbo and M. A. Hudrlik, *J. Org. Chem.*, 1989, **54**, 5613.