

Notes

[2-((Trimethylsilyl)methyl)prop-2-enyl]lithium. A Versatile Reagent for the Synthesis of 2-Substituted Propenylsilanes

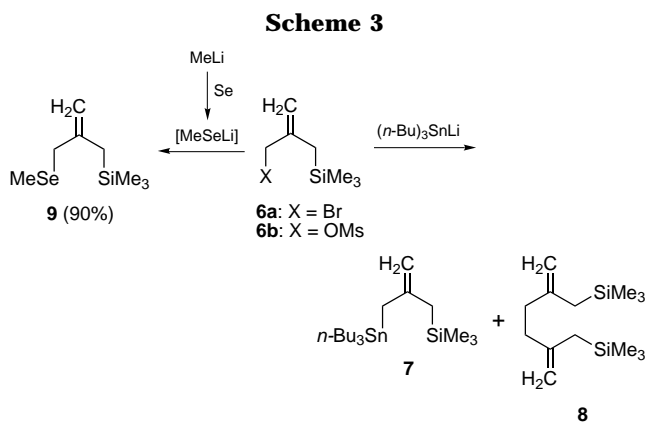
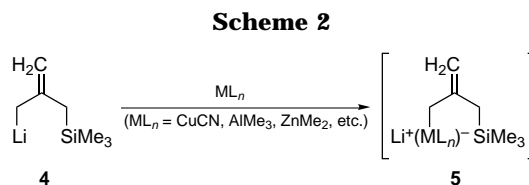
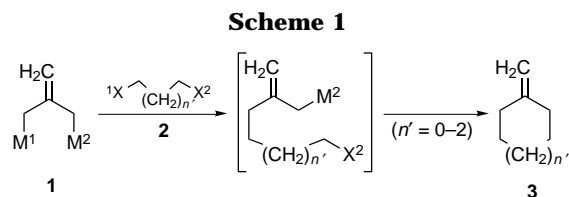
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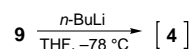
The elucidation of flexible and synthetically complementary procedures for ring formation has remained an important objective for reaction development. We have previously shown that 2-propylidene-1,3-bis(silane) moieties can serve as versatile binary nucleophiles in intramolecular cyclizations leading to isotropanes and bridged pyrrolizidines.² In principle, substitutionally differentiated 1,1-bis(metallomethyl)ethenes **1** could function as intramolecular linking agents for a wide variety of 1,*n*(*n*=2–4)-bis(electrophiles) (Scheme 1). In this Note we report the generation and synthetic utilization of [2-((trimethylsilyl)methyl)prop-2-enyl]lithium (**4**), a particularly versatile 1,3-bis(nucleophile) of the type **1**.³

Our interests in **4** were stimulated, in part, by the recognition that facile transmetalation of the highly polarized C–Li bond could give rise to a range of synthetically complementary [2-(metallomethyl)prop-2-enyl]trimethylsilanes **5** (Scheme 2). The prospect of competitive Wurtz coupling during the preparation of **4** from 1-bromo-2-((trimethylsilyl)methyl)prop-2-ene (**6a**)⁴ and Li metal prompted us to consider alternative procedures for the generation of representative allyllithiums. The reaction of allylstannanes with *n*-BuLi has been reported to give the corresponding allyllithiums in excellent yield.⁵ Unfortunately, efforts to prepare [2-(trimethylsilyl)methyl]prop-2-enyl]tri-*n*-butylstannane (**7**) via the reaction of **6a** with (*n*-Bu)₃SnLi⁶ led to the formation of substantial quantities of the coupling product **8**. In 1985, Krief reported that a rather limited series of 1-(methylseleno)prop-2-ene derivatives could be converted to the corresponding allyllithiums via *n*-BuLi-mediated Li–Se exchange.⁷

We were gratified to discover that the requisite allyl selenide **9** could be prepared in 90% distilled yield via the treatment of the readily available mesylate **6b**⁴ with CH₃SeLi (generated in situ from CH₃Li and Se) in THF at 25 °C (Scheme 3). Moreover, exposure of **9** to *n*-BuLi (THF, –78 °C, 30 min) resulted in clean Li–Se exchange to furnish **4** which could immediately be utilized in nucleophilic substitution or addition reactions. Accordingly, treatment of **4** with 1-iodododecane, representative oxiranes, ketones, or imines provided the anticipated



2-substituted allylsilanes **10–17** in excellent isolated yields (Table 1).



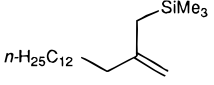

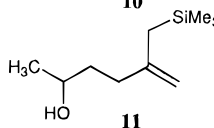

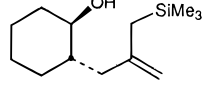
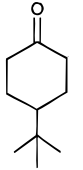
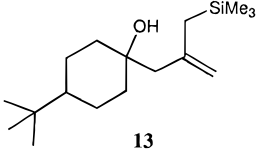
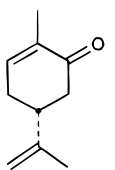
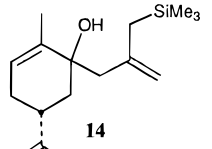
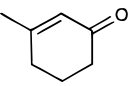
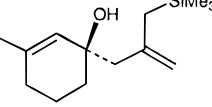
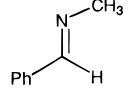
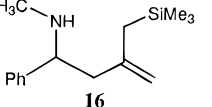
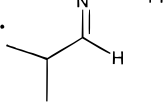
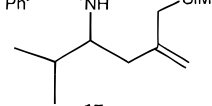
The following observations deserve comment. The reactions of **4** with simple epoxides are regio- and stereospecific (*trans*⁸), (entries b and c). Cyclic α,β -unsaturated ketones undergo exclusive 1,2-addition (entries e and f). As expected, the stereoselectivity of addition of **4** to conformationally biased cyclic ketones is only modest (entries d and e). The utilization of Cu-, Al-, and Zn-based metallate derivatives of **4** for alternative functionalization modes, as well as the subsequent use of product allylsilanes as substrates for intramolecular cycliza-

(6) Weigand, S.; Bruckner, R. *Synthesis* **1996**, 475–482.(7) Clarambeau, M.; Krief, A. *Tetrahedron. Lett.* **1984**, 25, 3629–3632.(8) The stereochemical assignment for **12** was based on the observed ¹H chemical shift of the (CH–OH) resonance in analogy with the corresponding resonance in *trans*-2-methylcyclohexanol (e.g., *trans* 2.75–3.40 ppm; *cis* 3.63–3.92 ppm); Iguchi, S.; Nakai, H.; Hayashi, M.; Yamamoto, H.; Maruoka, K. *Bull. Chem. Soc. Jpn.* **1981**, 54, 3033–3041.(9) The stereochemical assignment for alcohols **13a** and **13b** was based on the observed ¹H chemical shift of the hydroxyl (C–OH) resonance in DMSO-*d*₆ in analogy with the corresponding resonances in several 1-*R*-4-*tert*-butylcyclohexan-1-ols (e.g., R = H, Me, Et, *i*-Pr, *t*-Bu, Ph, CH₂Ph). The ¹H resonances of axial hydroxyl protons for compounds in this series were shown to possess lower chemical shift values than those of the corresponding equatorial hydroxyl protons: Meakins, G. D.; Percy, R. K.; Richards, E. E.; Young, R. N. *J. Chem. Soc. C* **1968**, 1106. For alcohols **13a_{cis}** and **13b_{trans}** the hydroxyl (C–OH) resonance was observed at (DMSO-*d*₆) δ 3.29 and 3.94 respectively.

(1) Recipient of a Japan Society for the Promotion of Science Fellowship (1997).

(2) Kercher, T.; Livinghouse, T. *J. Am. Chem. Soc.* **1996**, 118, 4200.(3) For the use of a [2-((trimethylsilyl)methyl)prop-2-enyl]indium reagent in carbonyl 1,2-addition reactions, see: Bardot, V.; Remuson, R.; Gelas-Mialhe, Y.; Gramain, J. *Synlett* **1996**, 37–38.(4) Molander, G. A.; Schubert, D. C. *Tetrahedron. Lett.* **1986**, 27, 787–790 and references therein.(5) Seyferth, D.; Weiner, M. A. *J. Org. Chem.* **1961**, 26, 4797 and references therein.

Table 1. Reaction of 4 with Representative Electrophiles

| Electrophile | Product | Yield ¹ (%) |
|--|---|------------------------|
| a. $n\text{-C}_{12}\text{H}_{25}\text{I}$ |  | 83 |
| b.  |  | 94 |
| c.  |  | 85 |
| d.  |  (<i>cis:trans</i> = 1.5:1) ² | 93 |
| e.  |  | 95 ³ |
| f.  |  | 92 |
| g.  |  | 90 |
| h.  |  | 87 |

¹All yields correspond to distilled or chromatographically purified products. ²Combined yield of purified alcohols [isolated yields: **13a**_{cis} (56%); **13b**_{trans} (37%) after chromatography].³ Combined yield of purified alcohols [isolated yields: stable diastereomer (63%); labile diastereomer (32%) after chromatography].

tion, will be discussed in future accounts from these laboratories.

Experimental Section

All reactions were performed in flame-dried glassware under an argon atmosphere. All reactions were monitored by gas chromatography (GLC) with temperature programming.

¹H NMR and ¹³C NMR spectra were recorded at 300 MHz. Coupling constants (*J*) are reported in hertz. Solvents for chromatography were reagent grade and distilled before use. Flash column chromatography was performed with silica gel 60.

Solvents used as reaction media were distilled immediately before use. Tetrahydrofuran (THF) and diethyl ether (Et₂O) were distilled from sodium-benzophenone ketyl. Solutions of *n*-butyllithium in hexanes and methylolithium in ether were titrated prior to use with 2-butanol and 2,2-bipyridine in ether at 0 °C. All starting materials were distilled or recrystallized prior to use.

Preparation of 2-((Trimethylsilyl)methyl)-2-(methylseleno)prop-1-ene (9). A 100 mL round-bottomed flask equipped

with a magnetic stirring bar and septum was flame dried under a stream of argon. Selenium powder (1.48 g, 18.8 mmol) was added, and the flask was again carefully purged with argon whereupon THF (25 mL) was added. Stirring was initiated, and the slurry was cooled to -78 °C. A solution of MeLi (14.46 mL, 18.8 mmol, 1.3 M in Et₂O) was added dropwise until the selenium had dissolved and a slight yellow color persisted. A second 100 mL flask equipped with a magnetic stirring bar and septum was purged with argon and charged with mesylate **6b**⁴ (4.17 g, 18.8 mmol) in THF (20 mL), and the solution was then cooled to -78 °C. The preformed solution of CH₃SeLi was then transferred via cannula into the flask containing the solution of **6b**. The reaction mixture was allowed to warm and stirred for 30 min at 25 °C. The solution was diluted with ether (20 mL) and poured into aqueous, saturated sodium bicarbonate (50 mL). The combined organic extracts were dried (K₂CO₃) and concentrated in vacuo. Distillation of the residue afforded allyl selenide **9** as a colorless oil [3.76 g (90%): bp 40–45 °C, 0.05 mmHg; ¹H NMR (CDCl₃) δ 4.67 (1H, app s), 4.58 (1H, app s), 3.08 (2H, s), 1.87 (3H, s), 1.66 (2H, s), 0.02 (9H, s); ¹³C NMR (CDCl₃) δ 148.5, 110.6, 33.6, 25.1, 4.5, -1.0; FTIR (neat) 2954, 2923, 2359, 1623, 1418, 1247, 858, 840 cm⁻¹; HRMS (PCI/CH₄) calcd for C₈H₁₈Si⁸⁰Se (M + H)⁺ 222.0343, found 222.0343; calcd for C₈H₁₈Si⁷⁸Se (M + H)⁺ 220.0351, found 220.0344; calcd for C₈H₁₈Si⁷⁶Se (M + H)⁺ 218.0370, found 218.0361.

General Procedure for Preparation of Allylsilanes.

Method A. 2-((Trimethylsilyl)methyl)pentadec-1-ene (10). A 10 mL flask equipped with a magnetic stirring bar and septum was purged with argon, charged with THF (1.5 mL), and cooled to -78 °C. A solution of *n*-BuLi (48 μL, 0.10 mmol, 2.11 M in hexanes) was then added via syringe, and the solution was stirred at -78 °C for 2 min. Allyl selenide **9** (22 mg, 0.10 mmol) was then added dropwise via syringe, and the solution was stirred for 30 min at -78 °C. Iodododecane (25 μL, 0.10 mmol) was then added in one portion via syringe. After being stirred for 30 min at -78 °C, the solution was allowed to warm to 25 °C. The reaction mixture was quenched by the addition of saturated, aqueous potassium bicarbonate (2.5 mL). The aqueous layer was then extracted with ether (2 × 3 mL). The combined ether extracts were washed with brine (3 mL), dried with K₂CO₃, and concentrated in vacuo. Chromatography of the residue (silica gel, 5% ether-hexane for elution) afforded allylsilane **10** as a colorless oil (26 mg, 83%). ¹H NMR (CDCl₃) δ 4.55 (1H, app s), 4.48 (1H, app s), 1.92 (2H, t, *J* = 7.2 Hz), 1.50 (2H, app s), 1.42–1.37 (2H, m), 1.24 (20H, br s), 0.86 (3H, t, *J* = 12.6) 0.01 (9H, s); ¹³C NMR (CDCl₃) δ 147.9, 107.0, 38.7, 32.3, 30.1, 29.9, 29.8, 28.3, 27.2, 23.1, 14.5, 0.9; FTIR (neat) 2956, 2924, 2853, 1466, 1377, 1248, 838 cm⁻¹; HRMS (PCI/CH₄) calcd for C₁₉H₄₀Si (M + H)⁺ 296.2899, found 296.2909.

Method B. (±)-*trans*-2-[2-((Trimethylsilyl)methyl)prop-2-enyl]cyclohexan-1-ol (12). A 10 mL flask equipped with a magnetic stirring bar and septum was purged with argon, charged with THF (2.5 mL), and cooled to -78 °C. A solution of *n*-BuLi (24 μL, 0.50 mmol, 2.11 M in hexanes) was then added via syringe, and the solution was stirred at -78 °C for 2 min. The allyl selenide **9** (111 mg, 0.50 mmol) was then added dropwise via syringe, and the solution was stirred for 30 min at -78 °C. A second 10 mL flame-dried flask equipped with a magnetic stirring bar and septum was purged with argon. Cyclohexene oxide (0.050 mL, 0.50 mmol) in THF (2.0 mL) was then added, and the solution was cooled to -78 °C. The preformed solution of **4** was then transferred via cannula into the second flask containing the cyclohexene oxide solution. The reaction mixture was quenched after being stirred for 15 min at -78 °C by the addition of a solution of Et₃N⁺H⁻O₂CCH₃ (0.8 mL, 1 M in THF). The reaction mixture was allowed to warm to 25 °C and was then diluted with ether (3 mL). The layers were separated and the aqueous layer was extracted with ether (2 mL). The combined organic solutions were washed with saturated aqueous sodium bicarbonate, dried with K₂CO₃, and concentrated in vacuo. Chromatography of the residue (silica gel, 5% Et₂O-hexanes for elution) afforded the alcohol **12** as a colorless oil (92.5 mg, 85%); ¹H NMR (C₆D₆) δ 4.83 (1H, app s), 4.74 (1H, app s), 3.09 (1H, ddd, *J* = 13.8, 9.0, 4.2 Hz), 2.69 (1H, dd, *J* = 13.8, 4.5 Hz), 1.90–1.83 (2H, m), 1.77 (1H, dd, *J* = 13.8, 9.0 Hz), 1.62 (2H, d, *J* = 3.0 Hz), 1.59–1.43 (3H, m), 1.31–1.26 (2H, m), 1.24–1.09 (2H, m), 0.87–0.75 (1H, m), 0.14 (9H, s); ¹³C NMR (C₆D₆) δ 147.5, 109.3, 75.2, 43.7, 43.0, 36.2, 31.1, 26.8, 26.1,

25.4, -1.0; FTIR (neat) 3353, 3071, 2926, 2855, 1630, 1448, 1247, 1058, 1034, 851 cm^{-1} ; HRMS (PCI/NH₃) calcd for C₁₃H₂₆OSi (M + H)⁺ 227.1831, found 227.1822. The ¹H NMR spectrum suggests that only the *trans* isomer was formed.⁹

(±)-**5-((Trimethylsilyl)methyl)hex-5-en-2-ol (11)**. Propylene oxide (7.0 μL , 0.10 mmol) was subjected to the reaction conditions described in Method A. The crude product, obtained after removal of the solvent in vacuo, was purified by flash chromatography (silica gel, 10% Et₂O–hexanes) to afford alcohol **11** as a colorless oil (17.5 mg, 94%). Spectral data were consistent with that reported in the literature.¹⁰

cis-4-(1,1-Dimethylethyl)-1-(((trimethylsilyl)methyl)prop-1-enyl)cyclohexan-1-ol (13a) and trans-4-(1,1-Dimethylethyl)-1-(((trimethylsilyl)methyl)prop-1-enyl)cyclohexan-1-ol (13b). 4-(2,2-Dimethylethyl)cyclohexan-1-one (77 mg, 0.50 mmol) was subjected to the reaction conditions described in Method A. Analysis of the product mixture by GLC showed two isomers in a ratio of 1.5:1.0. The crude product, obtained after removal of the solvent in vacuo, was purified by flash chromatography (silica gel, 2.5% Et₂O–hexanes) to provide alcohols **13a** and **13b**.⁹ **13a** as a colorless oil (79 mg, 56%): ¹H NMR (CDCl₃) δ 4.68 (1H, app s), 4.61 (1H, app s), 2.05 (2H, s), 1.67–1.65 (3H, m), 1.61 (2H, s), 1.56–1.54 (2H, m), 1.35–1.30 (5H, m), 0.84 (9H, s), 0.00 (9H, s); ¹³C NMR (CDCl₃) δ 144.8, 111.5, 70.5, 52.2, 48.4, 38.6, 32.8, 30.0, 28.0, 23.0, -1.1; FTIR (neat) 3455, 2952, 2867, 1457, 1365, 1247, 851 cm^{-1} . **13b** as a colorless oil (52 mg, 37%): ¹H NMR (CDCl₃) δ 4.72 (1H, app s, *CHH*), 4.64 (1H, app s, *CHH*), 2.17 (2H, s, *CH₂*), 2.04 (1H, s, *OH*), 1.78–1.66 (4H, m, *CH₂*), 1.64 (2H, s, *CH₂*), 1.44–1.35 (2H, m, *CH₂*), 1.12–1.04 (3H, m, *CH₂*), 0.84 (9H, s, *CH₃*), 0.01 (9H, s, *CH₃*); ¹³C NMR (CDCl₃) δ 145.0 (*C*), 112.1 (*CH₂*), 71.8 (*C*), 47.8 (*CH₂*), 44.0 (*CH*), 39.0 (*CH₂*), 32.7 (*C*), 29.6 (*CH₂*), 28.0 (*CH₃*), 25.0 (*CH₂*), -0.9 (*CH₃*); FTIR (neat) 3455, 2952, 2867, 1457, 1365, 1247, 851 cm^{-1} ; HRMS (PCI/CH₄) calcd for C₁₇H₃₄OSi (M - H)⁺ 281.2301, found 281.2292.

5-(2-Methyl-1-ethenyl)-2-methyl-1-(((2-(trimethylsilyl)methyl)prop-1-enyl)cyclohex-2-en-1-ol (14). A solution of (*R*)-(-)-carvone (63 μL , 0.40 mmol) in THF (2.0 mL) was subjected to the reaction conditions described in Method B. The product mixture contained two diastereomers in a ratio of 2.2:1.0 as determined by GLC and GCMS. The crude product, obtained after removal of the solvent in vacuo, was purified by flash chromatography (silica gel, 2.5% Et₂O–hexanes) to give two diastereomers. The major product **14** was isolated as a colorless oil (70 mg, 63%). The minor diastereomer (36 mg, 32%) proved to be very unstable and was not characterized: ¹H NMR (C₆D₆) δ 5.35 (1H, app s), 4.89 (1H, s), 4.84 (1H, s), 4.78 (1H, s), 4.76 (1H, s), 2.56 (1H, d, *J* = 13.5 Hz), 2.47–2.38 (1H, m), 2.32–2.24 (2H, m), 2.07–1.96 (3H, m), 1.88 (3H, d, *J* = 1.8 Hz), 1.72 (3H, s), 1.68 (1H, d, *J* = 13.2 Hz), 1.49 (1H, s), 1.44 (1H, app t, *J* = 12.6 Hz), 0.12 (9H, s); ¹³C NMR (C₆D₆) δ 149.2, 145.1, 139.8, 123.2, 112.2, 109.7, 74.1, 46.0, 41.0, 40.4, 31.5, 28.9, 20.7, 17.6, -1.0; FTIR (neat) 3447, 2952, 1427, 1039, 849 cm^{-1} ; HRMS (PCI/CH₄) calcd for C₁₇H₃₀OSi (M + H)⁺ 279.2144, found 279.2126.

(±)-**3-Methyl-1-[2-(((trimethylsilyl)methyl)prop-1-enyl)cyclohex-2-en-1-ol (15)**. A solution of 3-methylcyclohex-2-en-

1-one (57 μL , 0.50 mmol) in THF (2.5 mL) was subjected to the reaction conditions described in Method B. The crude product, obtained after removal of the solvent in vacuo, was purified by flash chromatography (silica gel, 10% Et₂O–hexanes) to deliver alcohol **15** as a colorless oil (110 mg, 92%): ¹H NMR (C₆D₆) δ 5.51 (1H, app s), 4.85 (2H, app s) 2.38 (1H, d, *J* = 13.2 Hz), 2.33 (1H, d, *J* = 13.2 Hz), 1.92 (1H, d, *J* = 13.2 Hz), 1.87 (1H, d, *J* = 13.2 Hz), 1.80–1.67 (5H, m), 1.60 (3H, s), 1.58–1.54 (1H, m), 1.52 (1H, app s) 0.13 (9H, s); ¹³C NMR (C₆D₆) δ 145.0, 136.3, 129.0, 111.9, 70.2, 50.9, 36.2, 30.6, 28.9, 23.9, 20.0, -1.0; FTIR (neat) 3447, 3071, 2934, 2829, 1670, 1627, 1438, 1247, 849 cm^{-1} ; HRMS (EI) calcd for C₁₄H₂₆OSi (M - H₂O)⁺ 220.1647, found 220.1641.

(±)-***N*-Methyl-4-phenyl-2-(((trimethylsilyl)methyl)but-1-enamine (16)**. A solution of *N*-benzylidene methyl amine (62 μL , 0.50 mmol) in THF (2.5 mL) was subjected to the reaction conditions described in Method B. The crude product, obtained after removal of the solvent in vacuo, was purified by flash chromatography (silica gel, 10% Et₂O–hexanes) to afford amine **16** as a colorless oil (111 mg, 90%): ¹H NMR (C₆D₆) δ 7.52 (2H, d, *J* = 7.5 Hz), 7.30 (2H, dd, *J* = 7.8, 5.1 Hz), 7.19 (1H, d, *J* = 5.1 Hz), 4.83 (1H, app s), 4.73 (1H, app s), 3.72 (1H, dd, *J* = 5.4, 3.3 Hz), 2.40–2.36 (2H, m), 2.28 (3H, s), 1.56 (2H, s), 1.39 (1H, br s), 0.07 (9H, s); ¹³C NMR (C₆D₆) δ 145.3, 128.8, 127.9, 127.7, 127.4, 110.6, 63.7, 48.9, 35.1, 26.6, -1.1; FTIR (neat) 3344, 3070, 3027, 2952, 2847, 2361, 2342, 1629, 1444, 1249, 840 cm^{-1} ; HRMS (PCI/CH₄) calcd for C₁₅H₂₅NSi (M + H)⁺ 246.1688, found 246.1674.

(±)-***N*-(Phenylmethyl)-2-(((trimethylsilyl)methyl)-4-(2-methylethyl)but-1-enamine (17)**. A solution of *N*-(2-methylpropylidene)benzilamine (81 mg, 0.50 mmol) in THF (2.5 mL) was subjected to the reaction conditions described in Method B. The crude product, obtained after removal of the solvent in vacuo, was purified by flash chromatography (silica gel, 10% Et₂O–hexanes) to furnish amine **17** as a colorless oil (125 mg, 87%): ¹H NMR (C₆D₆) δ 7.42 (2H, d, *J* = 7.5 Hz), 7.27 (2H, t, *J* = 6.9 Hz), 7.17 (1H, t, *J* = 7.2 Hz), 4.77 (1H, app s), 4.70 (1H, app s), 3.84 (1H, d, *J* = 13.2), 3.73 (1H, d, *J* = 13.2), 2.66 (1H, ddd, *J* = 17.1, 8.7, 3.9), 2.16–2.04 (2 H, m), 2.02–1.92 (1H, m), 1.55 (2H, s), 1.25 (1H, s), 1.07 (3H, d, *J* = 6.9 Hz), 0.97 (3H, d, *J* = 6.9 Hz), 0.09 (9H, s); ¹³C NMR (C₆D₆) δ 146.0, 142.1 127.2, 110.3, 60.3, 52.8, 39.7, 30.0, 26.5, 18.7, 17.8, -1.1; FTIR (neat) 3324, 3067, 3027, 2955, 1629, 1464, 1457, 1249, 843 cm^{-1} ; HRMS (PCI/CH₄) calcd for C₁₈H₃₁NSi (M + H)⁺ 290.2304, found 290.2299.

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Supporting Information Available: Spectral data for all new compounds (24 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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