Highly diastereoselective titanium(II)-mediated cyclizations of 1,7-(silyloxy)enynes

Nicole M. Barbour and Andrew J. Phillips*

Department of Chemistry and Biochemistry, University of Colorado, Boulder, CO 80309-0215, USA
E-mail: andrew.phillips@colorado.edu

Dedicated to Professor Johann Mulzer on the occasion of his 65th birthday

Abstract
Cyclization of 1,7-(silyloxy)enynes with Ti(*i*-PrO)$_4$ and *n*-BuLi yields 6-membered cyclic siloxanes in moderate to good yields. The reaction is highly diastereoselective (typical d.r.'s >15:1).

Keywords: Enyne, cyclization, silicon-tethered reactions, low-valent titanium, cyclic siloxanes

Introduction

We recently described the highly diastereoselective cyclization of 1,6-(silyloxy)enynes with ClTi(*i*-PrO)$_3$ and Grignard reagents to give 5-membered cyclic siloxanes (Figure 1).[1] Excision of the silicon gives rise to homoallylic alcohols, and these building blocks were used as part of the syntheses of dictyostatin[2] and 7-demethylpericidin A$_1$.[3] In conjunction with our interest in exploring the utility of these types of cyclization, we have examined the cyclization of 1,7-(silyloxy)enynes (see also Figure 1), and in this paper we report our preliminary studies.

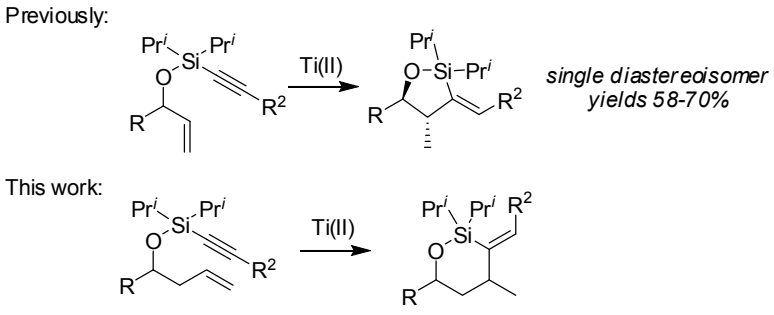
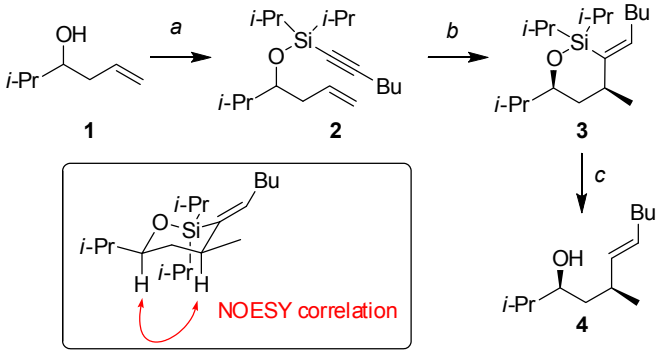


Figure 1. Cyclizations of 1,6- and 1,7-(silyloxy)enynes.

Results and Discussion

Our initial studies focused on readily accessible 1,7-(silyloxy)enyne **2**, which was prepared by silylation of alcohol **1**[4] with bromodiisopropylhexynylsilane (Scheme 1).[5] In our earlier work on the cyclization of 1,6-(silyloxy)enynes the combination of $ClTi(OPr^i)_3$ as the titanium source with *i*-PrMgCl (two equivalents with respect to the Ti) at -40 ºC had proven optimal. Although these conditions resulted in cyclization of **2**, there was a significant amount of unreacted starting material, and the isolated yields of **3** were never greater than ~35%. Although more starting material could be consumed by the addition of further equivalents of $ClTi(OPr^i)_3$ and the Grignard reagent after 3 hours, we viewed this approach as cumbersome and sub-optimal. Variation of temperature and solvents also failed to appreciably effect the levels of conversion and the combination of $Ti(OPr^i)_4$/*i*-PrMgCl was also fruitless.

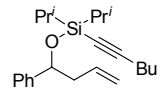
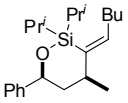
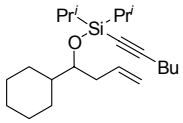
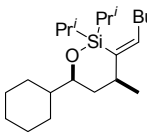
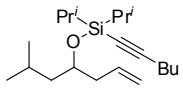
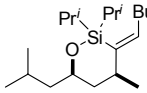
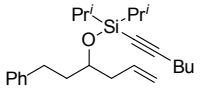
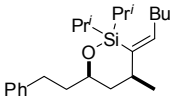
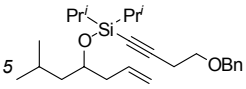
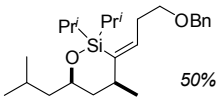
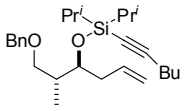
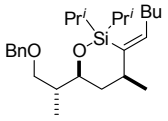
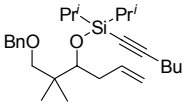
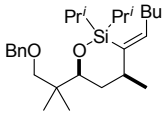
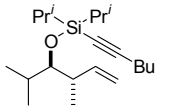
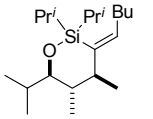
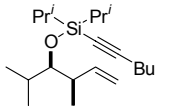
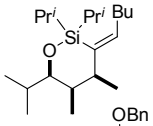
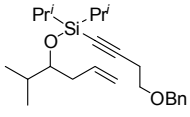
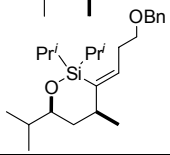
Gratifyingly, turning to *n*-BuLi as the reductant provided increased reactivity and in the case of **2**, cyclization provided the desired cyclic siloxane **3** in 70% yield as essentially a single diastereoisomer (d.r. >15:1). NOESY NMR experiments showed a strong correlation between the hydrogen adjacent the alcohol and the hydrogen adjacent to the methyl group, which strongly suggested that the reaction occurs with 1,3-*syn* stereoinduction. Desilylation using TBAF provided the alcohol **4** in quantitative yield.[6]



Scheme 1. *Reagents and conditions*: (a) bromodiisopropylhexynylsilane, DMAP, DMF, quantitative; (b) Ti(*i*-PrO)$_4$, *n*-BuLi, THF, -40 ºC → rt, 70%, *d.r.* >15:1; (c) TBAF, DMF, 60 ºC quant.

A variety of substrates that were cyclized and that provide some measure of the broad utility of the reaction are shown in Table 1. The reaction is highly diastereoselective with typical diastereoisomer ratios being >15:1 as determined by ^{1}H NMR analysis of the crude reaction mixtures.[7] Of particular note are substrates cyclized in entries 8 and 9, which produce stereochemical arrays that are difficult to access by alternative methods. In these cases the combination of *anti*- or *syn*- crotylation of an aldehyde, followed by (silyloxy)enyne cyclization provides a concise route to systems bearing adjacent methyl-group stereocenters.

Table 1. *Reagents and conditions*: Ti(*i*-PrO)$_4$, *n*-BuLi, THF, -40 ºC → rt

Entry	Substrate	Product	Yield (d.r.)
1			62% (>15:1)
2			67% (>15:1)
3			52% (>15:1)
4			49% (>15:1)
5			50% (>15:1)
6			64% (>15:1)
7			52% (>15:1)
8			65% (>15:1)
9			56% (>15:1)
10			83% (>15:1)

Although we have not performed extensive mechanistic studies, a simple mnemonic for the observed 1,3-*syn* stereoinduction can be proposed by employing a six membered chair-like transition state (Figure 2). In this model, the alkene orients itself to avoid a pseudo-1,3-diaxial interaction with an isopropyl group on silicon and cyclization occurs from conformer A.

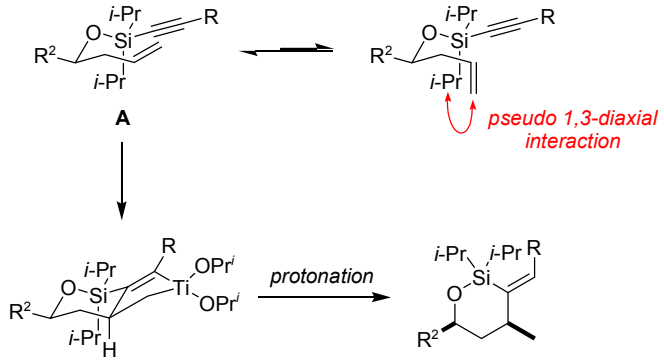


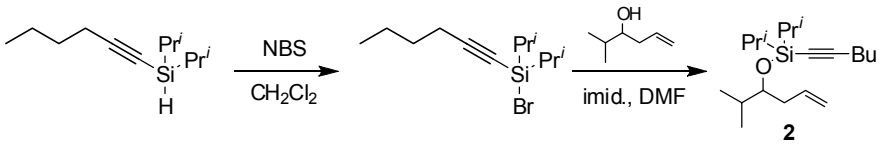
Figure 2. A simple model for the observed stereochemistry

In conclusion, we have described the cyclization of 1,7-(silyloxy)enynes to produce cyclic siloxanes. The reaction employs readily accessible reagents and provides high levels of 1,3-*syn* stereoinduction. Applications of this chemistry in the context of complex molecule synthesis are ongoing and will be reported in due course.

Experimental Section

General Procedures. ^{1}H and ^{13}C spectra were recorded at 25 ºC on a Varian Inova spectrometer operating at 500 and 100 MHz, respectively, using $CDCl_3$ as the solvent and internal reference. Coupling constants are reported in Hertz, Hz. All non-aqueous reactions were run in flame-dried glassware under a dry N_2 atmosphere. Toluene, THF, CH_2Cl_2, and Et_2O were obtained from Aldrich (Pure-Pac) and further dried by passage through activated alumina. All flash chromatography was performed with normal phase silica gel (Silicycle, 35-75 μm particle size, 60 Å pore size).

Representative procedure for the synthesis of a bromoalkynyl(diisopropyl)silane and silylation of an alcohol. Hex-1-ynyl-diisopropyl-(1-isopropyl-but-3-enyloxy)-silane, 2



Hexynyl(diisopropyl)silane (250 mg, 1.27 mmol) in dichloromethane (5 mL) was cooled to 0 ºC, then *N*-bromosuccinimide (277 mg, 1.57 mmol) was added in a portionwise fashion. The cold bath was removed and the reaction was stirred for 90 min at room temperature. The solvent was removed on a rotary evaporator and the residue was diluted with pentane and filtered. The filtrate was evaporated and diluted with *dry* DMF (2 mL) and was then added to a separate flask containing the alcohol (97 mg, 0.85 mmol) and imidazole (145 mg, 2.13 mmol) in DMF (2.25 mL). The reaction was stirred for 10 h at room temperature and was then diluted with ethyl acetate, washed with saturated aqueous NH_4Cl solution and brine (4x), dried with $MgSO_4$, filtered, and concentrated in vacuo. The residue was then purified by flash chromatography on silica gel eluting with 10% CH_2Cl_2/90% hexanes to yield the **2** (246 mg, 94 %).

Hex-1-ynyl-diisopropyl-(1-isopropyl-but-3-enyloxy)-silane(2).IR: 3074, 2911, 2169, 1642, 1460 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.80 (m, 1H), 5.00 (m, 2H), 3.70 (m, 1H), 2.24-2.32 (m, 4H), 1.79-1.83 (m, 1H), 1.43-1.56 (m, 5H), 1.06-0.87 (m, 22H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.2, 116.3, 109.4, 80.2, 77.8, 38.4, 32.5, 30.9, 22.0, 19.6, 18.7, 17.7, 17.6, 17.5, 17.4, 17.3, 14.1, 13.8, 13.7; HRMS: calculated for $C_{19}H_{36}OSiNa^+$ ($M+Na^+$) 331.2427, found 331.2424.

Hex-1-ynyl-diisopropyl-(1-phenyl-but-3-enyloxy)-silane, 4: IR: 2952, 2173, 1639, 1468 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.34-7.23 (m, 5H), 5.82-5.74 (m, 1H), 5.03-4.96 (m, 3H), 2.60-2.49 (m, 2H), 2.28-2.26 (m, 2H), 1.58-1.43 (m, 5H), 1.11-0.80 (m, 16H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.7, 135.2, 128.1, 127.1, 126.4, 117, 110.0, 79.4, 75.8, 45.2, 30.9, 22.1, 19.6, 17.6, 17.5, 17.3, 17.2, 13.8, 13.6, 13.3; HRMS: calculated for $C_{22}H_{34}OSiNa^+$ ($M+Na^+$) 365.2271, found 365.2273.

(1-Cyclohexyl-but-3-enyloxy)-hex-1-ynyl-diisopropyl-silane, 6: IR: 3070, 2919, 2846, 2169, 1729 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 5.90-5.83 (m, 1H), 5.06-5.01 (m, 2H), 3.73-3.69 (m, 1H), 2.34-2.25 (m, 4H), 1.65-1.72(m, 3H), 1.67-1.65 (m, 2H), 1.56-1.43 (m, 5H), 1.22-0.92 (m, 22H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.2, 116.2, 109.4, 80.3, 42.7, 38.5, 30.9, 29.2, 28.1, 27.0, 26.7, 22.0, 19.7, 17.7, 17.6, 13.8, 13.7; HRMS: calculated for $C_{22}H_{40}OSiNa^+$ ($M+Na^+$) 371.2741, found 371.2748.

Hex-1-ynyl-(1-isobutyl-but-3-enyloxy)-diisopropyl-silane, 8: IR: 2956, 2866, 2173 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.29-7.18 (m, 5H), 5.91-5.84 (m, 1H), 5.11-5.06 (m, 2H), 4.04-4.02 (m, 1H), 2.80-2.75 (m, 1H), 2.67-2.64 (m, 1H), 2.42-2.37 (m, 2H), 2.31-2.27 (m, 2H), 1.90-1.80 (m, 2H), 1.58-1.44 (m, 6H), 1.10-0.93 (m, 15H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 135.6, 116.8, 109.6, 79.9, 71.4, 46.0, 42.1, 30.9, 24.5, 23.4, 23.0, 22.1, 19.6, 17.6, 17.6, 13.8, 13.6; HRMS: calculated for $C_{20}H_{38}OSiNa^+$ ($M+Na^+$) 345.2584, found 345.2584.

Hex-1-ynyl-diisopropyl-(1-phenethyl-but-3-enyloxy)-silane, 10: IR: 3058, 3021, 2935, 2866, 2169, 1639, 1602, 1464 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.27-7.16 (m, 5H), 5.89-5.84 (m, 1H), 5.09-5.04 (m, 2H), 4.02-4.00 (m, 1H), 2.75-2.73 (m, 1H), 2.65-2.62 (m, 1H), 2.40-2.35 (m, 2H), 2.29-2.25 (m, 2H), 1.88-1.78 (m, 2H), 1.56-1.42 (m, 6H), 1.08-0.91 (m, 15H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.1, 135.3, 128.6, 128.5, 125.8, 117.0, 109.7, 79.8, 72.9, 41.7, 38.4, 31.9, 30.9, 22.1, 19.7, 17.6, 17.5, 17.3, 13.8, 13.8, 13.7, 13.6; HRMS: calculated for $C_{24}H_{38}OSiNa^+$ ($M-Na^+$) 393.2584, found 393.2580.

(4-Benzyloxy-but-1-ynyl)-(1-isobutyl-but-3-enyloxy)-diisopropyl-silane, 12: IR: 3062, 3025, 2952, 2858, 2177, 1631, 1360, 1093 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.38-7.29 (m, 5H), 5.90-5.84 (m, 1H), 5.08-5.04 (m, 2H), 4.58 (s, 2H), 4.02-4.00 (m, 2H), 3.67-3.64 (m, 2H), 2.63-2.60 (t, 2H), 2.34-2.32 (m, 2H), 1.78-1.75 (m, 1H), 1.59-1.39 (m, 1H), 1.33-1.28 (m, 1H), 1.11-1.05 (m, 15H), 0.99-0.90 (m, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.3, 135.5, 128.6, 127.9, 127.9, 116.8, 105.6, 81.5, 73.3, 71.5, 68.8, 68.2, 46.0, 42.1, 24.5, 23.5, 23.0, 21.5, 17.6, 13.7, 13.6; HRMS: calculated for $C_{25}H_{40}O_2SiNa^+$ ($M+Na^+$) 423.2690, found 423.2687.

(±)-[1-(2-Benzyloxy-1-methyl-ethyl)-but-3-enyloxy]-hex-1-ynyl-diisopropyl-silane, 14: IR: 3066, 3029, 2895, 2165, 1636, 1464, 1354, 1243, 1080, 877, 685 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.41-7.33 (m, 5H), 6.00-5.96 (m, 1H), 5.12-4.61 (m, 2H), 4.59-4.06 (m, 2H), 4.05-3.67 (m, 1H), 3.42-2.45 (m, 1H), 2.44-2.37 (m, 2H), 2.32-2.30 (m, 2H), 1.59-1.49 (m, 4H), 1.18-0.99 (m, 25H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.2, 135.7, 128.5, 127.7, 127.6, 116.8, 109.6, 80.1, 74.9, 73.1, 72.8, 38.4, 30.9, 22.1, 19.7, 17.7, 13.8; HRMS: calculated for $C_{26}H_{42}O_2SiNa^+$ ($M+Na^+$) 437.2846, found 437.2849.

[1-(2-Benzyloxy-1,1-dimethyl-ethyl)-but-3-enyloxy]-hex-1-ynyl-diisopropyl-silane, 16: IR: 3070, 3021, 2944, 2866, 2169, 1460, 1370, 1084, 877, 734, 591 cm^{-1};^1H NMR (500 MHz, $CDCl_3$): δ 7.36-7.23 (m, 5H), 6.05-6.00 (m, 1H), 5.05-4.97 (m, 2H), 4.50 (q, 2H), 3.94-3.92 (q, 1H), 3.30 (q, 2H), 2.49-2.45 (m, 1H), 2.33-2.30 (m, 1H), 2.27-2.24 (t, 2H), 1.54-1.43 (m, 5H), 1.21-0.91 (m, 30H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.4, 137.9, 128.4, 127.6, 127.5, 115.6, 109.4, 80.8, 73.3, 40.8, 38.2, 30.9, 22.1, 21.9, 21.4, 19.7, 18.0, 17.9, 17.7, 17.5, 17.4, 14.1, 14.0, 13.9, 13.8; HRMS: calculated for $C_{27}H_{44}O_2SiNa^+$ ($M-Na^+$) 451.3002, found 451.2487.

(*3R*,4*S*)-Hex-1-ynyl-diisopropyl-(1-isopropyl-2-methyl-but-3-enyloxy)-silane, 18: IR: 3078, 2964, 2862, 2165, 1645, 1635, 1464, 1382, 1243 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 6.01-5.94 (m, 1H), 5.03-4.97 (m, 2H), 3.60-3.58 (m, 1H), 2.51-2.49 (m, 1H), 2.30-2.25 (m, 2H), 1.87-1.81 (m, 1H), 1.56-1.46 (m, 5H), 1.11-0.88 (m, 25H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.2, 113.6, 109.3, 77.2, 76.9, 42.3, 32.3, 30.9, 22.0, 20.1, 19.6, 19.0, 17.9, 17.8, 17.7, 17.6, 17.3, 14.1, 14.0, 13.9, 13.7; HRMS: calculated for $C_{20}H_{38}OSiNa^+$ ($M+Na^+$) 345.2584, found 345.2576.

(*3R*,4*R*)-Hex-1-ynyl-diisopropyl-(1-isopropyl-2-methyl-but-3-enyloxy)-silane, 20: IR: 3074, 2895, 2711, 2356, 2328, 2165, 1639, 1460, 1378, 1064, 872, 677 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 5.92-5.87 (m, 1H), 5.02-4.94 (m, 2H), 3.58-3.56 (m, 1H), 2.42 (q, 1H), 2.28-2.24 (m, 3H), 1.84-1.83 (m, 1H), 1.54-1.43 (m, 6H), 1.09-0.86 (m, 23 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.9, 113.2, 109.3, 81.9, 80.3, 42.4, 32.0, 30.9, 22.0, 20.4, 19.6, 17.9, 17.8, 17.7, 17.6, 17.4, 17.3, 16.5, 14.1, 14.0, 13.8, 13.7; HRMS: calculated for $C_{20}H_{38}OSiNa^+$ ($M+Na^+$) 345.2584, found 345.2584.

4-Benzyloxy-but-1-ynyl)-diisopropyl-(1-isopropyl-but-3-enyloxy)-silane, 22: IR: 3433, 3066, 3021, 2866, 2169, 1704, 1468, 1362, 1093 cm^{-1}; **^1H NMR** (500 MHz, $CDCl_3$): δ 7.41-7.29 (m, 5H), 5.93-5.87 (m, 1H), 5.10-5.03 (m, 1H), 4.61-4.58 (m, 2H), 3.66 (q, 2H), 2.61 (q, 2H), 2.35-2.31 (m, 2H), 1.86-1.83 (m, 1H), 1.13-0.91 (m, 26H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 138.3, 138.3, 136.1, 128.7, 128.6, 127.9, 116.4, 105.5, 81.2, 77.8, 73.3, 73.2, 68.9, 68.6, 38.5, 32.5, 21.5, 21.4, 19.0, 18.7, 17.8, 17.7, 17.6, 17.5, 17.3, 17.3, 17.1, 13.8, 13.7, 13.3; **HRMS:** calculated for $C_{24}H_{38}O_2SiNa^+$ ($M+Na^+$) 409.2533, found 409.2531.

Representative procedure for the enyne cyclization. 2,2,6-Triisopropyl-4-methyl-3-pentylidene-[1,2]oxasilinane, 3

A solution of $Ti(OPr^i)_4$ (0.364 mL, 1.21 mmol) in THF (2.2 mL) was cooled to -78 ºC, then *n*-BuLi (1.60 mL, 1.6 M, 2.56 mmol) was added. This solution was stirred 15 min, then warmed to 0 ºC and the dark red colored solution was stirred for 20 min. The reaction was then cooled to -40 ºC and the substrate alcohol **2** was added to the reaction as a solution in THF. This was warmed to room temperature over 10h. This was quenched with NH_4Cl, diluted with ethyl acetate, washed with brine, dried with $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by flash chromatography on silica gel eluting with 10 % CH_2Cl_2/90 % hexanes to yield the siloxane (90.2 mg, 62 %).

2,2,6-Triisopropyl-4-methyl-3-pentylidene-[1,2]oxasilinane, 2: IR: 2829, 2169, 1610 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 5.99-5.96 (m, 1H), 3.65 (m, 1H), 2.33-2.29 (m, 1H), 2.06-1.98 (m, 2H), 1.60-1.54 (m, 2H), 1.38-1.31 (m, 5H), 1.26-0.86 (m, 22H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.8, 138.1, 79.9, 41.4, 38.3, 35.4, 33.2, 32.6, 22.9, 20.6, 19.0, 18.2, 18.1, 18.0, 17.5, 15.3, 14.3, 14.3; HRMS: calculated for $C_{19}H_{38}OSiNa^+$ ($M+Na^+$) 333.2583, found 333.2587.

2,2-Diisopropyl-4-methyl-3-pentylidene-6-phenyl-[1,2]oxasilinane, 5 (Table 1, Entry 1): IR: 2956, 2854, 1464 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.40-7.22 (m, 5H), 6.07-6.04 (m, 1H), 5.08-5.06 (m, 1H), 2.58-2.55 (m, 1H), 2.12-2.04 (m, 2H), 1.85-1.82 (m, 1H), 1.43-1.34 (m, 5H),

1.26-0.91 (m, 20H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.3, 139.1, 137.5, 128.3, 136.9, 125.4, 47.9, 39.8, 38.8, 33.3, 32.6, 22.9, 20.4, 18.2, 18.0, 17.6, 15.4, 14.3; HRMS: calculated for $C_{22}H_{36}OSiNa^+$ ($M+Na^+$) 367.2428, found 367.2431.

6-Cyclohexyl-2,2-diisopropyl-4-methyl-3-pentylidene-[1,2]oxasilinane, 7 (Table 1, Entry 2): IR: 2948, 2854 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.99-5.97 (m, 1H), 3.67-3.64 (m, 1H), 2.32-2.29 (m, 1H), 2.07-2.00 (m, 2H), 1.89-1.86 (m, 1H), 1.75-1.74 (m, 2H), 1.67-1.65 (m, 2H), 1.58-1.55 (m, 1H), 1.39-0.92 (m, 27H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.9, 138.1, 79.4, 45.5, 41.4, 38.3, 33.3, 32.6, 29.3, 28.5, 27.0, 26.7, 26.6, 22.9, 20.6, 18.2, 18.1, 17.5, 15.3, 14.3; HRMS: calculated for $C_{22}H_{42}OSiNa^+$ ($M+Na^+$) 373.2897, found 373.2903.

6-Isobutyl-2,2-diisopropyl-4-methyl-3-pentylidene-[1,2]oxasilinane, 9 (Table 1, Entry 3): IR: 2952, 2862, 1733, 1615 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.98-5.95 (m, 1H), 3.99-3.96 (m, 1H), 2.34-2.32 (m, 1H), 2.05-1.98 (m, 2H), 1.88-1.82 (m, 1H), 1.56-1.53 (m, 1H), 1.40-1.31 (m, 7H), 1.15-0.88 (m, 26H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.9, 138.0, 73.0, 48.5, 45.1, 38.0, 33.2, 32.6, 24.6, 23.7, 22.9, 22.5, 20.4, 18.2, 18.1, 18.0, 17.5, 15.2, 14.3, 14.1; HRMS: calculated for $C_{20}H_{40}OSiNa^+$ ($M+Na^+$) 347.2741, found 347.2746.

2,2-Diisopropyl-4-methyl-3-pentylidene-6-phenethyl-[1,2]oxasilinane, 11 (Table 1, Entry 4): IR: 2931, 2862, 2165, 1606, 1456 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.33-7.20 (m, 5H), 6.01-6.00 (m, 1H), 3.96-3.91 (m, 1H), 2.86-2.83 (m, 1H), 2.77-2.71 (m, 1H), 2.37-2.33 (m, 1H), 2.11-2.02 (m, 2H), 1.77-1.71 (m, 2H), 1.61-1.59 (m, 1H), 1.43-1.35 (m, 5H), 1.13-0.94 (m, 20H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.1, 138.7, 138.1, 128.9, 128.5, 126.8, 73.8, 44.6, 41.2, 37.9, 33.3, 32.6, 32.0, 22.9, 20.4, 18.2, 18.1, 17.5, 15.3, 14.4, 14.1; HRMS: calculated for $C_{24}H_{40}OSiNa^+$ ($M+Na^+$) 395.2741, found 395.2755.

3-(3-Benzyloxy-propylidene)-6-isobutyl-2,2-diisopropyl-4-methyl-[1,2]oxasilinane, 13 (Table 1, Entry 5): IR: 2952.2, 2858, 1464, 1358, 1101, 1064, 987 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.39-7.29 (m, 5H), 6.02-6.0 (m, 1H), 4.56-4.55 (s, 2H), 4.02-0.01 (m, 1H), 3.54-3.51 (t, 2H), 2.45-2.37 (m, 3H), 1.90-1.87 (m, 1H), 1.59-1.56 (m, 1H), 1.47-1.39 (m, 2H), 1.18-0.90 (m, 28H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.9, 138.7, 133.1, 128.6, 127.8, 127.8, 73.1, 73.0, 70.3, 48.5, 45.0, 38.2, 33.9, 23.6, 23.7, 22.5, 20.3, 18.1, 18.0, 17.8, 17.6, 17.5, 15.2, 14.0; HRMS: calculated for $C_{25}H_{42}O_2SiNa^+$ ($M+Na^+$) 425.2846, found 425.2848.

6-(2-Benzyloxy-1-methyl-ethyl)-2,2-diisopropyl-4-methyl-3-pentylidene-[1,2]oxasilinane, 15 (Table 1, Entry 6): IR: 3062, 3029, 2948, 1941, 1859, 1802, 1602, 1455, 1370, 1101, 877, 779, 709 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.41-7.29 (m, 5H), 6.06-6.03 (m, 1H), 4.57 (s, 2H), 3.92-3.89 (m, 1H), 3.71-3.69 (m, 1H), 3.50-3.47 (m, 1H), 2.37 (m, 1H), 2.10-2.05 (m, 2H), 1.88-1.85 (m, 1H), 1.69-1.67 (d, 1H), 1.43-0.97 (m, 28H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.3, 138.7, 138.3, 128.5, 127.8, 127.6, 73.3, 72.8, 41.5, 41.4, 38.2, 33.3, 32.6, 22.9, 20.6, 18.2, 18.1, 17.6, 15.3, 14.4, 14.2; HRMS: calculated for $C_{26}H_{44}O_2SiNa^+$ ($M+Na^+$) 439.3003, found 439.3004.

6-(2-Benzyloxy-1,1-dimethyl-ethyl)-2,2-diisopropyl-4-methyl-3-pentylidene-[1,2]oxasilinane, 17 (Table 1, Entry 7): IR: 3066, 3029, 2952, 2923, 2858, 2169, 1455, 1374, 1097, 1019 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.37-7.29 (m, 5H), 6.02-6.00 (m, 1H), 4.53 (q,

2H), 3.90 (d, 1H), 3.45 (d, 1H), 3.20 (d, 1H), 2.34-2.25 (m, 2H), 2.07-2.01 (m, 2H), 1.56 (d, 2H), 1.41-0.78 (m, 29H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.3, 138.5, 138.4, 128.4, 127.6, 127.5, 127.4, 78.7, 73.5, 60.5, 39.9, 38.7, 38.2, 33.2, 32.6, 30.5, 30.0, 22.9, 21.9, 21.2, 20.8, 20.1, 18.2, 18.1, 17.7, 17.6, 17.5, 17.4, 17.3, 15.4, 14.4, 14.3; HRMS: calculated for $C_{27}H_{46}O_2SiNa^+$ ($M+Na^+$) 453.3159, found 453.3175.

(4*S*,5*S*,6*R*)-2,2,6-Triisopropyl-4,5-dimethyl-3-pentylidene-[1,2]oxasilinane, 19 (Table 1, Entry 8): IR: 2952, 2862, 1741, 1606, 1460, 1378, 1243, 1048, 901 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.06-6.03 (m, 1H), 3.32 (m, 1H), 2.09-2.03 (m, 4H), 1.82-1.79 (m, 1H), 1.37-1.27 (m, 14H), 1.12-0.91 (m, 19H); ^{13}C NMR (100 MHz, $CDCl_3$); δ 142.1, 138.4, 82.6, 46.2, 41.7, 33.5, 32.5, 31.4, 30.0, 22.9, 21.6, 20.8, 18.6, 18.4, 18.3, 18.2, 18.1, 17.8, 17.6, 17.2, 15.3, 14.5, 14.3; HRMS: calculated for $C_{20}H_{40}OSiNa^+$ ($M+Na^+$) 347.2741, found 347.2747.

(4*S*,5*R*,6*R*)-2,2,6-Triisopropyl-4,5-dimethyl-3-pentylidene-[1,2]oxasilinane, 21 (Table 1, Entry 9): IR: 2960, 2915, 2858, 1460, 1382, 1117, 991 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$): δ 5.89-5.87 (m, 1H), 3.44-3.42 (m, 1H), 2.51-2.50 (m, 1H), 2.19-2.01 (m, 2H), 1.72-1.60 (m, 2H), 1.40-1.27 (m, 7H), 1.12-0.64 (m, 26 H); **^{13}C NMR** (100 MHz, $CDCl_3$); δ 139.1, 136.2, 84.6, 43.9, 39.8, 33.3, 32.8, 32.3, 22.9, 20.4, 18.8, 18.4, 18.3, 18.2, 17.6, 14.9, 14.5, 14.3, 5.8; **HRMS:** calculated for $C_{20}H_{40}OSiNa^+$ ($M+Na^+$) 347.2742, found 347.2770.

3-(3-Benzyloxy-propylidene)-2,2,6-triisopropyl-4-methyl-[1,2]oxasilinane, 23 (Table 1, Entry 10): IR: 2964, 2862, 1468, 1101, 1052 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.39-7.29 (m, 5H), 6.04-6.02 (m, 1H), 4.56 (s, 2H), 3.70-3.67 (m, 1H), 3.55-3.52 (m, 2H), 2.45-2.32 (m, 4H), 1.64-1.58 (m, 2H), 1.48 (s, 1H), 1.31 (s, 1H), 1.16-0.89 (m, 38H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.9, 138.8, 133.2, 128.6, 127.8, 127.8, 79.9, 73.2, 70.3, 41.3, 38.5, 35.4, 33.9, 20.6, 19.0. 18.2, 18.1, 18.0, 17.4, 15.4, 14.2; HRMS: calculated for $C_{24}H_{40}NaO_2SiNa^+$ ($M+Na^+$) 411.2690, found 411.2699.

Acknowledgements

This research was supported by the National Science Foundation CAREER Program (Award # 0645787).

References

1. O'Neil, G. W.; Phillips, A. J. *Tetrahedron Lett.* **2004***, 45*, 4253
2. O'Neil, G. W.; Phillips, A. J. *J. Am. Chem. Soc.* **2006**, *128*, 5340.
3. Keaton, K. A.; Phillips, A. J. *J. Am. Chem. Soc.* **2006**, *128*, 408.
4. Readily prepared by Barbier-type allylation using allyl bromide and zinc. See Hoffman, R.; Brueckner, R.; *Chem. Ber.* **1992,** *125*, 2731.

5. A variety of functionalized bromodiisopropylalkynylsilanes are readily accessible by alkylation of lithioacetylides with chlorodiisopropylsilane. Subsequent bromination and reaction with an alcohol provides the (silyloxy)enyne. See the experimental section for a representative procedure.
6. Ozonolysis of this alkene and reduction of the aldehyde provided a diol for which data could be compared to the known 2,4-*anti*-2,5-dimethylhexane-1,4-diol. See: Still, W. C.; Darst, K. P. *J. Am. Chem. Soc.* **1980,** *102,* 7385.
7. The stereochemistry of the examples in Table 1 was assigned by analogy to that for **3**.