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Enhanced reactivity in radical cyclizations of hydrazones using the silicon-tethered 1-bromovinyl group

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Abstract—A silicon-tethered 1-bromovinyl group was shown to function as a radical precursor for tin-mediated vinyl additions to chiral α- or β-hydroxyhydrazone. In contrast to related thiyl-mediated methods, these vinyl bromides were not limited to the 5-*exo* cyclization mode. A series of Si-tethered 5-*exo* and 6-*exo* cyclizations formed the corresponding five- and six-membered *exo*-methylene-substituted oxasilacycles. Treatment with fluoride cleaved the Si–C and Si–O bonds to afford the corresponding allylic hydrazines. Diastereoselectivities ranged from 2:1 to 25:1 (*anti*:*syn*) for the 5-*exo* cyclizations, depending on the size of the exocyclic substituent, but 6-*exo* cyclization was not diastereoselective. A variant involving Tamao oxidation of the *exo*-methylene oxasilacyclopentane intermediate afforded a methyl ketone, a net process corresponding to addition of a radical acyl anion equivalent.

1. Introduction

Radical addition to imino compounds[1] has developed into an effective strategy for synthetic access to chiral α-branched amines.[2] Diastereoselective variants of these reactions can be achieved using reliable silicon tethers,[3,4] which render the reaction intramolecular and transmit stereochemical informations from the point of attachment for heterocyclic C–C bond construction.[5] We have shown that this methodology enables stereoselective additions of functionalized carbon fragments, including hydroxymethyl,[6] vinyl,[7] and 2-(phenylthio)vinyl[8] groups, to α-hydroxyhydrazones (Fig. 1). Expanding the versatility, both in terms of the variety of radical synthons which can be introduced, and in terms of the location of the hydroxyl directing group, remains a worthwhile goal. For example, the delivery of a functionalized radical through a silicon tether attached to a β-hydroxyhydrazone (i.e., via 6-*exo* cyclization) had yet to be achieved. Although Si-tethered 6-*exo* cyclizations with carbonyl[9] and alkene[10] acceptors had been previously reported, there were also numerous examples where Si-tethers showed preference for 7-*endo* mode of ring closure.[11] Furthermore, the literature was inconsistent on whether useful stereocontrol might be available from 4-substituted 6-heptenyl systems, especially with (*E*)-configured acceptors,[12] so there was little guidance on questions of regio- and stereoselectivity in 6-*exo* cyclizations to hydrazone acceptors.

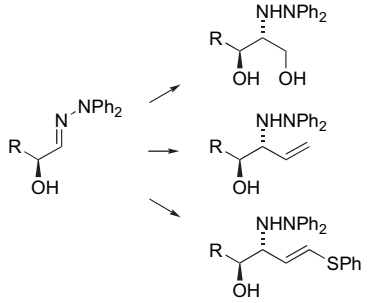

Figure 1. Addition of functionalized carbon fragments to α-hydroxyhydrazones.

By rendering radical additions intramolecular via a temporary linkage, the silicon-tether concept is ideally suited to obviate unproductive bimolecular side reactions of radicals (e.g., H-atom abstraction, dimerization, disproportionation). Of particular interest are the additions of vinyl radicals, which have never been successfully used in intermolecular additions to imino compounds.

The additions of vinyl and 2-(phenylthio)vinyl groups depicted in Figure 1 are thiyl-mediated processes. Such reactions begin with the generation of a thiyl radical from thiophenol, which then adds to a vinyl (or ethynyl) group in a reversible fashion (Scheme 1). The adduct radical can cyclize, generating an aminyl radical, which is quenched through H-atom abstraction. Treatment with fluoride removes the silicon tether for a net result of vinyl transfer from silicon to the imino carbon.

Keywords: Radical cyclization; Stereoselectivity; Silicon tether; Hydrazones.
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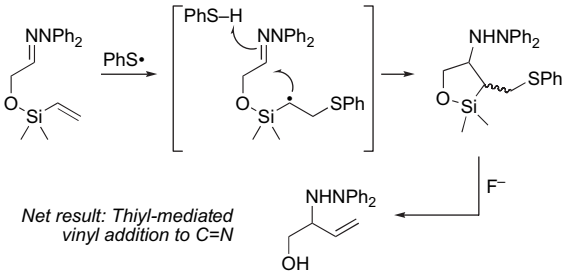


Scheme 1.

Though in our prior experience the aforementioned reversible thiyl addition method was effective in initiating 5-*exo* cyclizations to install vinyl groups, the 6-*exo* cyclization did not occur (Fig. 2).[13] We hypothesized that this failure resulted from preferred β-elimination of the thiyl radical from the slower cyclizing 7-aza-6-heptenyl system. To access relevant experimental evidence on this question, we sought to generate a similar vinyl radical, which lacked the potential for a competitive β-elimination. Here, we report studies on silicon-tethered 1-bromovinyl radical additions to imino compounds, including 5-*exo* and 6-*exo* cyclizations of oxime ethers and hydrazones.

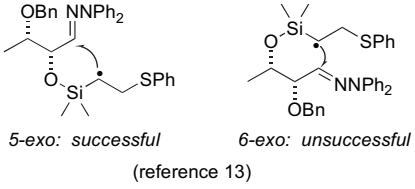


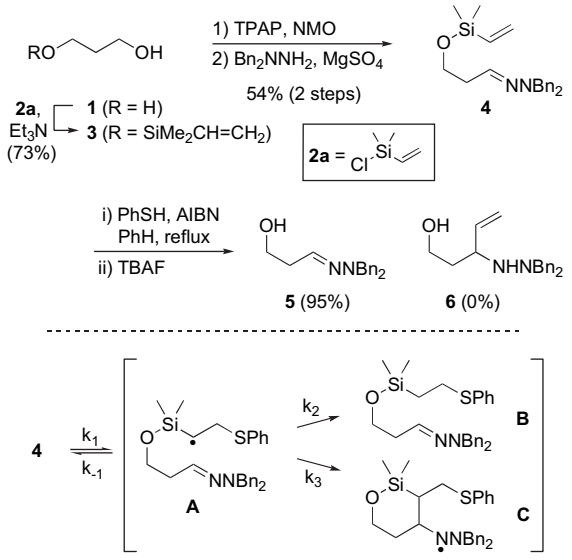
Figure 2. Prior findings on the thiyl-mediated cyclization via 5-*exo* and 6-*exo* modes.

2. Results and discussion

2.1. Thiyl-mediated 6-*exo* cyclization attempts

For a more direct test on the thiyl-mediated vinyl addition in the 6-*exo* mode, we examined 6-*exo* cyclization substrate **4**, prepared from 1,3-propanediol (**1**, Scheme 2). Monosilylation with chlorodimethylvinylsilane (**2a**) provided **3** in 73% yield; oxidation of the remaining primary alcohol of **3** and condensation with dibenzylhydrazine furnished cyclization substrate **4** in 54% yield over two steps. The compatibility of the vinylsilyl ether functionality with the oxidation and condensation steps facilitates this efficient sequence, avoiding protection and deprotection steps. Thiyl-mediated radical cyclization of **4** using the previously defined thiyl radical addition conditions[7,8] was unsuccessful, resulting only in desilylation to **5**.

A mechanistic rationale consistent with this result involves the addition of PhS• to the olefin to generate the alkyl radical **A**, a reversible process (Scheme 2). Three likely alternative reactivities of this radical include elimination of thiyl radical to regenerate **4**, hydrogen atom abstraction from the thiophenol to form the simple addition product **B**, and the desired cyclization to oxasilacycle **C**. Desilylation of **B** and/or unreacted **4** would explain the formation of hydroxyhydrazone



Scheme 2.

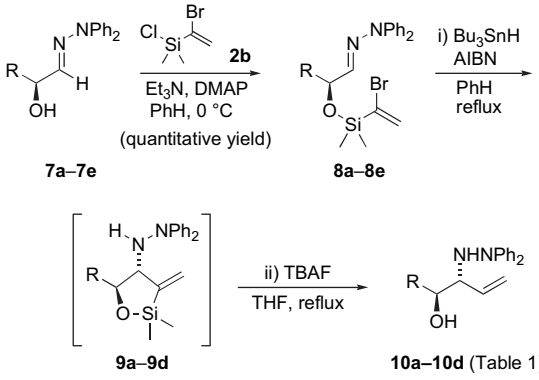
5. The rate constants k_1, k_{-1}, and k_2 are presumably independent of ring size in the cyclization (5-*exo* vs 6-*exo*). However, k_3 should depend on the ring size according to precedent: $k_{3(5\text{-}exo)}$ is known to be two orders of magnitude higher than $k_{3(6\text{-}exo)}$ for cyclization of hydrazones.[14] Most likely then, the reason for the failure of the 6-*exo* cyclizations is a relative decrease in k_3. Monitoring of the cyclization by TLC showed that **4** was consumed, excluding it as a precursor of desilylation to **5**. This strongly suggests a preferred H-atom abstraction pathway through **B**. Neither slow addition of thiophenol to decrease the rate of H-atom abstraction nor use of Lewis acids to increase the cyclization rate[15] led to the desired adduct **6**.

The results described above suggested some more aggressive modifications: first, a more rapid cyclization might avoid the premature reduction step by increasing k_3 relative to k_2. Compared to alkyl radicals, vinyl radicals are three orders of magnitude more reactive toward cyclization, having 5-*exo* cyclization rate constants in the range of 10^8 s^{-1} at 80 °C.[16] Changing radical **A** of Scheme 2 to a vinylic radical should offer an increased rate constant k_3.[17,18] Second, an irreversible generation of the vinyl radical via bromine atom abstraction by Bu_3Sn• (instead of thiyl addition to an alkyne) might facilitate cyclization by negating the competing β-elimination pathway. Tin-mediated conditions also provide for blocking the premature reduction through slow addition of the H-atom source. Based on these considerations, we identified some potential utility in bromine atom abstraction from (1-bromovinyl)silyl ethers, a process previously used by Tamao for additions to alkene acceptors.[19]

2.2. 5-*exo* Cyclizations

The use of the Si-tethered bromovinyl group with hydrazone radical acceptors was introduced with a series of positive control experiments using 5-*exo* cyclizations, enabling a direct comparison with other silicon-tethered radical precursors.[6–8] Glycolaldehyde hydrazone **7a**[7] was silylated with (1-bromovinyl)chlorodimethylsilane (**2b**) and subjected to

standard tin-mediated cyclization conditions (Scheme 3). Addition of tributyltin hydride (1.2 equiv) and AIBN (0.2 equiv) via syringe pump to refluxing solutions of the vinyl bromide **8a** in benzene led to efficient cyclization affording an intermediate which was unstable to chromatography, presumably *exo*-methylene oxasilacyclopentane **9a**. Desilylation with TBAF in refluxing THF afforded 57% of the desired vinyl adduct **10a**[7] (Table 1, entry 1). Standard chromatographic purification from tin byproducts was nontrivial, so we briefly examined alternative conditions. Related experiments (entries 2 and 3) showed that SmI_2-mediated conditions[20] in THF did not achieve cyclization, but tris(trimethylsilyl)silane could be used in place of tin although with diminished yield (24%, unoptimized). After some optimization, the removal of tin byproducts[21] was best addressed through liquid–liquid extraction; partitioning between acetonitrile and hexane left most of the tin byproducts in the hexane phase.



a: R = H, **b**: R = Me, **c**: R = ^{i}Bu, **d**: R = ^{i}Pr, **e**: R = Ph

Scheme 3.

With suitable tin-mediated conditions defined, a series of 2-hydroxyaldehyde hydrazones **7b–7e**[6,7] were subjected to silylation with **2b** to obtain radical cyclization substrates **8b–8e** (Scheme 3). As before, slow addition of Bu_3SnH and AIBN led to efficient cyclization to afford *exo*-methylene oxasilacyclopentanes **9b–9d**. Upon desilylation with fluoride (TBAF, THF), allylic hydrazines **10b–10d**[7] were obtained in moderate yields (Table 1, entries 4–6). The NMR spectra of the oxasilacyclopentane intermediates and the crude products were quite clean, indicating that the isolated yields (57–69%) were compromised by the loss of some material during removal of tin byproducts. For mandelic acid derivative **7e** (entry 7), this sequence resulted in a complex mixture, which did not contain the desired product **10e**.

Table 1. Yields and selectivities of 5-*exo* cyclization of hydrazones **8a–8d** (Scheme 3)

Entry	R	Reductant	Product, yield[a] (%)	Ratio (*anti*:*syn*)[b]
1	H	Bu_3SnH	**10a**, 57	—
2	H	$(Me_3Si)_3SiH$	**10a**, 24	—
3	H	SmI_2	**10a**, 0	—
4	Me	Bu_3SnH	**10b**, 69	66:34
5	^{i}Bu	Bu_3SnH	**10c**, 55	78:22
6	^{i}Pr	Bu_3SnH	**10d**, 59	96:4
7	Ph	Bu_3SnH	**10e**, 0	—

Conditions: 1.3 equiv reductant and 20 mol % AIBN were added via syringe pump to a solution of 0.2–0.5 mmol hydrazone in refluxing benzene (0.02 M).

[a] Isolated yield.

[b] Ratios from integration of 500 MHz ^{1}H NMR spectra prior to purification.

The stereoselectivities of these 5-*exo* cyclizations vary regularly with the size of the substituent R, consistent with previous observations.[6,7] Diastereomer ratios of **10b–10d** via vinyl radical intermediates are each lower than the corresponding cyclizations of alkyl radicals, whether generated by halogen atom abstraction[6] or thiyl addition.[7] This observation may be attributed to an earlier transition state (Fig. 3), which would presumably exhibit diminished energetic differences between chair–equatorial and the competing chair–axial and/or boat conformations.[8]

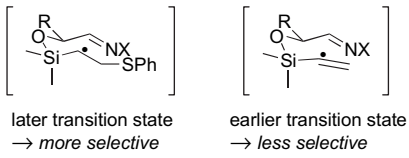
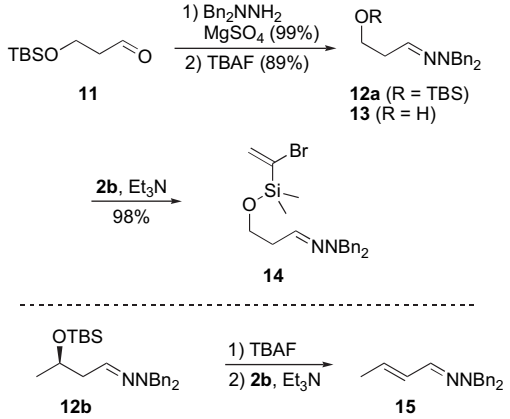


Figure 3. Transition states in alkyl versus vinyl radical cyclizations.

2.3. 6-*exo* Cyclizations

With the feasibility of the bromovinyl radical precursor established, the 6-*exo* cyclizations could next be examined. Despite the effectiveness of the 5-*exo* cyclizations, we were cognizant of the potential intrusion of competitive 1,5-hydrogen atom transfer[22] in the 6-*exo* series, and this would be a key issue to address through experiment.

The simplest cyclization substrate was prepared from 1,3-propanediol (Scheme 4). Unfortunately, the bromovinylsilyl ethers were not compatible with transformations leading to the aldehyde, so 3-(*tert*-butyldimethylsilyloxy)propanal (**11**)[23] was the starting point. Condensation with dibenzylhydrazine afforded TBS-protected hydroxyhydrazone **12a**. Desilylation to alcohol **13** and subsequent installation of the bromovinyl radical precursor in the usual way furnished cyclization substrate **14** with good overall yield.

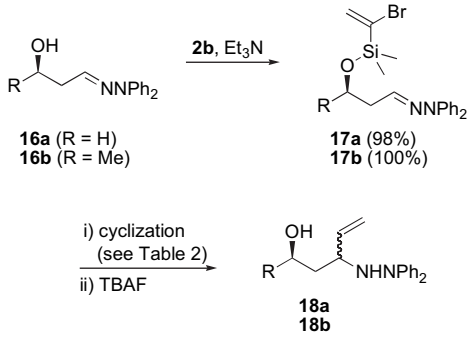


Scheme 4.

Attempts to cyclize hydrazone **14** using the tin-mediated conditions of Table 1 appeared successful in preliminary

experiments. However, the corresponding chiral substrate could not be prepared from hydrazone **12b** (Scheme 4)—elimination product **15** was observed during desilylation, and conditions to prepare the radical cyclization substrate resulted only in **15**, despite considerable experimentation. In the course of these studies, we have noted that electron-rich *N*,*N*-dibenzylhydrazones are quite prone to elimination of β-hydroxy or β-silyloxy groups. As the *N*,*N*-diphenylhydrazone analogs of these compounds proved to be more readily prepared, further studies on *N*,*N*-dibenzylhydrazones such as **14** and **12b** were not pursued.

A cyclization substrate **17a** (Scheme 5) bearing the less electron-rich diphenylhydrazone moiety was prepared in 98% yield from the previously reported alcohol **16a**.[24] Treatment of **17a** with the tributyltin hydride and AIBN resulted in cyclization, and subsequent desilylation with TBAF provided **18a** in 78% yield (Table 2, entry 1). Diphenylhydrazone **17a** was also cyclized using triethylborane as the radical initiator, but only in 40% yield (entry 2). In an attempt to simplify separation of tin byproducts, Maleczka's catalytic tin radical conditions (10 mol % Bu_3SnH, PMHS, NaOMe)[25] were also attempted leading to 39% yield (entry 3) with catalytic turnover of the tin. Unfortunately the yield could not be improved due to the incompatibility of the silyl ether with the alkoxide employed in these conditions.[26] Nevertheless, the 78% yield under more standard conditions was promising, and represents the first example of a silicon-tethered 6-*exo* radical cyclization to a C=N acceptor.



Scheme 5.

Having demonstrated the 6-*exo* cyclization, its potential for diastereoselectivity was next examined. For this purpose chiral hydroxyhydrazone **16b** (Scheme 5) was prepared in three steps from (*S*)-methyl-3-hydroxybutanoate.[24] Installation of the bromovinylsilyl ether of **17b** proceeded in quantitative yield, and cyclization and fluoride treatment then afforded **18b** in 74% yield (entry 4). Despite this quite satisfactory yield, there was no diastereoselectivity (dr 1:1), and

Table 2. Yields and selectivities of 6-*exo* cyclization of hydrazones **17a** and **17b** (Scheme 5)

Entry	R	Conditions	Product, yield[a] (%)
1	H	Bu_3SnH, AIBN	**18a**, 78
2	H	Bu_3SnH, Et_3B	**18a**, 40
3	H	10 mol Bu_3SnH, AIBN, PMHS, NaOMe	**18a**, 39
4	Me	Bu_3SnH, AIBN	**18b**, 74[b]

[a] Isolated yield.
[b] Diastereomer ratio=1:1 (^1H NMR).

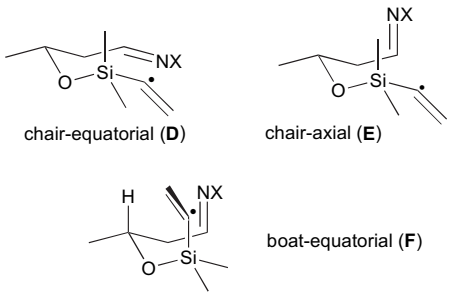


Figure 4. Plausible transition states in Si-tethered 6-*exo* vinyl radical cyclizations.

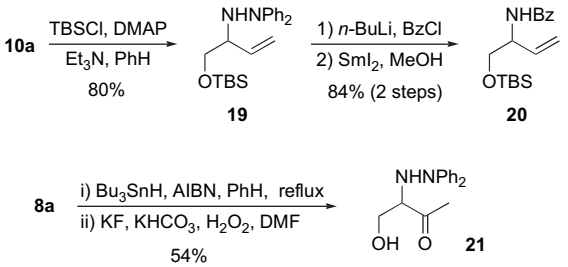
neither slow addition nor low temperature (Et_3B/O_2, −78 °C) improved upon this result.

As in the 5-*exo* cyclizations, a chair-like transition state model may be invoked, with the imino nitrogen and exocyclic alkyl substituent in pseudoequatorial positions (Fig. 4). However, in contrast to the 5-*exo* cyclizations, the pseudo-allylic strain control element is weakened as a consequence of the methylene spacer between the stereogenic center and the imino carbon, resulting in minimal differentiation of transition states **D** and **E**. Also, the usual destabilization of a boat transition state could be diminished with a vinyl radical, which bears no substituent for transannular van der Waals repulsion with the indicated hydrogen in structure **F**. As **E** and **F** converge to the same diastereomer, structure **D** would need to be considerably more stable than **E** and **F** to overcome their contributions to the product distribution. These factors may explain the apparent lack of selectivity. The larger exocyclic substituents R confer greater selectivity in the 5-*exo* cyclizations, as seen in Table 1. Unfortunately, 6-*exo* cyclization substrates bearing substituents larger than methyl could not be tested as their instability toward β-elimination in the manner described in Scheme 4 prevented any further study. This elimination presents a serious obstacle to the application of this type of method to β-hydroxyhydrazones.

2.4. Subsequent manipulations of adducts

Cleavage of the N–N bond of the adduct hydrazine **10a** was achieved by way of silyl ether **19** (Scheme 6). Thus the *N*-benzoyl derivative, prepared by lithiation of **19** and reaction with BzCl, exhibited smooth SmI_2-mediated conversion to the benzamide **20**,[27] with an 84% yield for the two-step procedure.

A noteworthy aspect of the vinyl bromide as a radical precursor is that it leads to an intermediate oxasilacycle, which can



Scheme 6.

be selectively oxidized to a ketone. After radical cyclization of glycolaldehyde-derived substrate **8a**, in the same flask, Tamao oxidation[28] (KF, $KHCO_3$, H_2O_2, DMF) of the intermediate oxasilacycle removed the silicon tether to afford the methyl ketone **21** in 54% yield for two steps (Scheme 6). This sequence expands the versatility of the vinyl addition; the net result is installation of an acetyl unit through an umpolung approach with the radical precursor serving as an acyl anion equivalent.

3. Conclusion

A new variant of silicon-tethered vinyl addition to imino compounds has been developed, as demonstrated in diastereoselective 5-*exo* radical cyclizations of hydrazones using a silicon-tethered vinyl bromide. Extension of these reactions to 6-*exo* cyclizations was achieved with yields over 70%, showing that 1,5-hydrogen atom transfer was not a serious impediment to these reactions. However, the 6-*exo* sequence proved to be limited in scope and non-selective. An useful aspect of this study is the demonstration of a rational approach for enhancing the reactivity in Si-tethered cyclizations through application of an irreversibly formed vinyl radical, needed in this case to coax along slower 6-*exo* cyclizations to imino acceptors.

4. Experimental section

4.1. Materials and methods

Reactions employed oven- or flame-dried glassware under nitrogen unless otherwise noted. THF, diethyl ether, benzene, and toluene were distilled from sodium/benzophenone ketyl under argon. CH_2Cl_2 was distilled from CaH_2 under argon or nitrogen. Alternatively, these solvents were purchased inhibitor-free and were sparged with argon and passed through columns of activated alumina prior to use (dropwise addition of blue benzophenone ketyl solution revealed the THF purified in this manner sustained the blue color more readily than the control sample purified by distillation). Nitrogen was passed successively through columns of anhydrous $CaSO_4$ and R3-11 catalyst for removal of water and oxygen, respectively. All other materials were used as received from commercial sources unless otherwise noted. Thin-layer chromatography (TLC) employed 0.25 mm glass silica gel plates with UV indicator. Flash chromatographic columns were packed with 230–400 mesh silica gel as a slurry in the initial elution solvent. Gradient flash chromatography was conducted by adsorption of product mixtures on silica gel, packing over a short pad of clean silica gel as a slurry in hexane, and eluting with a continuous gradient from hexane to the indicated solvent. Radial chromatography refers to centrifugally accelerated thin-layer chromatography performed with a Chromatotron using commercially supplied rotors. Melting points are uncorrected. Nuclear magnetic resonance (NMR) data were obtained at operating frequencies of 500 or 300 MHz for ^1H and 125 or 75 MHz for ^{13}C. Infrared spectra were recorded using a single beam FTIR spectrophotometer by standard transmission methods or by use of an attenuated total reflectance (ATR) probe. Optical rotations were determined using a digital polarimeter operating at ambient temperature. Low-resolution mass spectra were obtained using sample introduction by dip, liquid chromatography or gas chromatography. High-resolution mass spectra and combustion analyses were obtained from external commercial and institutional services.

(α-Bromovinyl)chlorodimethylsilane (**2b**) was prepared by bromination–dehydrobromination of commercially available chlorodimethylvinylsilane (**2a**) according to the literature procedure,[29] and was stored in the freezer as a solution in benzene.

4.2. Preparation and characterization data

4.2.1. 3-(Dimethyl(vinyl)silyloxy)propan-1-o1 (3). To a solution of 1,3-propanediol (**1**, 1.84 g, 24.2 mmol) and triethylamine (5.25 mL, 37.7 mmol) in THF (50 mL) was added chlorodimethylvinylsilane (**2a**, 4 mL, 29.0 mmol) and the mixture was stirred at room temperature for 90 min, diluted with ether (100 mL), and washed with 10% K_2CO_3 (aq) (2×25 mL) and brine (25 mL). The resulting organic layer was dried with $MgSO_4$, concentrated, and purified by flash chromatography (10:1 to 1:1 Hex/EtOAc) to afford **3** (3.386 g, 73%) as a yellow oil; IR (film) 3379, 2954, 1409, 1250, 1091, 1009, 960 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.19–5.75 (m, 3H), 3.79 (t, J=5.7 Hz, 2H), 3.78 (t, J=5.4 Hz, 2H), 2.38 (br s, 1H), 1.78 (quintet, J=5.7 Hz, 2H), 0.20 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.9, 133.6, 62.0 (2C), 34.2, −2.3.

4.2.2. 1,1-Dibenzyl-2-(3-(dimethyl(vinyl)silyloxy)propylidene)hydrazine (4). To a solution of **3** (1.012 g, 6.31 mmol) in CH_2Cl_2 (50 mL) was added 4 Å molecular sieves. *N*-Methylmorpholine-*N*-oxide (1.11 g, 9.47 mmol) was added and the flask was cooled in an ice/H_2O bath for 30 min. Tetrapropylammonium perruthenate (131 mg, 0.327 mmol) was added. The mixture was warmed to room temperature, stirred for 2 h, filtered through silica gel, and concentrated producing the aldehyde as a yellow oil. The aldehyde was dissolved in toluene (25 mL). Dibenzylhydrazine (1.692 g, 7.97 mmol), *p*-toluenesulfonic acid (40 mg), and sodium sulfate (150 mg) were added and the mixture was stirred for 24 h at room temperature. Concentration and flash chromatography (20:1 Hex/EtOAc) afforded **4** (1.104 g, 54%) as a colorless oil; IR (film) 3019, 2957, 1597, 1494, 1453, 1251, 1091 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.39–7.13 (m, 10H), 6.55 (t, J=5.3 Hz, 1H), 6.13–5.70 (m, 3H), 4.26 (s, 4H), 3.65 (t, J=6.7 Hz, 2H), 2.38 (td, J=6.7, 5.4 Hz, 2H), 0.12 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 138.0, 137.3, 135.0, 133.2, 128.4, 127.8, 127.0, 61.2, 58.1, 36.2, −2.2; MS (EI) *m/z* (relative intensity) 352 (M^+, 3%), 261 (40%), 237 (35%), 131 (75%), 115 (95%), 91 (100%). Anal. Calcd for $C_{21}H_{28}N_2OSi$: C, 71.54; H, 8.01; N, 7.95. Found: C, 71.70; H, 7.98; N, 7.98.

An alternative procedure: to a solution of **5** (38 mg, 0.142 mmol) in THF (2 mL) and triethylamine (0.02 mL, 0.17 mmol) were added *N*,*N*-dimethylaminopyridine (5 mg) and dimethylvinylchlorosilane (0.2 mL, 0.17 mmol), and the reaction mixture was stirred for 4 h. Concentration and flash chromatography (10:1 petroleum ether/EtOAc) afforded **4** (48 mg, 96%) as a colorless oil.

4.2.3. General procedure A: preparation of bromovinylsilyl ethers. A solution of α-hydroxyhydrazone (e.g., **7a**–**7e**) in benzene at 0 °C was treated sequentially with Et_3N (1.2 equiv), DMAP (0.1 equiv), and **2b** (1.2 equiv). Copious white precipitate formed immediately. After 10 h, the mixture was filtered through a short plug of silica gel, eluting with hexane/ethyl acetate (5:1). The filtrate was washed with brine, dried (Na_2SO_4), and concentrated. The filtration through silica gel was repeated, then concentration afforded the silyl ethers as colorless or pale yellow oils, which were not stable to prolonged storage.

4.2.3.1. Silyl ether 8a. From **7a** (633 mg, 2.8 mmol), DMAP (34 mg, 0.28 mmol), Et_3N (0.8 mL, 3.4 mmol), and **2b** (1:1 v/v solution in benzene, 1 mL, 3.4 mmol) by general procedure A was obtained **8a** (1.09 g, 100%) as a colorless oil; IR (film) 2961, 1594, 1496, 1254, 1054 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.40–7.36 (m, 4H), 7.17–7.13 (m, 2H), 7.11–7.09 (m, 4H), 6.53 (dd, apparent triplet, J=5.1 Hz, 1H), 6.35 (d, J=1.8 Hz, 1H), 6.31 (d, J=1.8 Hz, 1H), 4.40 (d, J=5.3 Hz, 2H), 0.31 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.6, 135.6, 135.2, 131.2, 129.7, 124.4, 122.4, 64.1, −2.6; MS (CI) *m/z* (relative intensity) 390 (M^+, ^{81}Br, 25%), 388 (M^+, ^{79}Br, 30%), 209 (100%), 168 (82%). Anal. Calcd for $C_{18}H_{21}N_2OSiBr$: C, 55.52; H, 5.44; N, 7.19. Found: C, 55.76; H, 5.41; N, 7.21.

4.2.3.2. Silyl ether 8b. From **7b** (136 mg, 0.57 mmol), DMAP (7 mg, 0.057 mmol), Et_3N (0.18 mL, 0.74 mmol), and **2b** (1:1 v/v solution in benzene, 0.22 mL, 0.74 mmol) by general procedure A was obtained **8b** (0.269 g, 100%) as a colorless oil; $[\alpha]_D^{20}$ −10.7 (*c* 4.46, $CHCl_3$); IR (film) 2972, 1591, 1496, 1254, 1059 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.42–7.38 (m, 4H), 7.19–7.16 (m, 2H), 7.13–7.10 (m, 4H), 6.44 (d, J=5.8 Hz, 1H), 6.36 (d, J=1.8 Hz, 1H), 6.33 (d, J=1.8 Hz, 1H), 4.65 (dddd, apparent quintet, J=6.3 Hz, 1H), 1.36 (d, J=6.4 Hz, 3H), 0.34 (s, 3H), 0.32 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.7, 140.1, 135.8, 131.0, 129.7, 124.3, 122.3, 70.2, 22.3, −2.0, −2.2; MS (LC-APCI) *m/z* (relative intensity) 405 ($[M+H]^+$, ^{81}Br, 100%), 403 ($[M+H]^+$, ^{79}Br, 90%), 223 (88%), 168 (16%). Anal. Calcd for $C_{19}H_{23}N_2OSiBr$: C, 56.57; H, 5.75; N, 6.94. Found: C, 56.80; H, 5.68; N, 6.93.

4.2.3.3. Silyl ether 8c. From **7c** (155 mg, 0.55 mmol), DMAP (7 mg, 0.057 mmol), Et_3N (0.17 mL, 0.71 mmol), and **2b** (1:1 v/v solution in benzene, 0.22 mL, 0.74 mmol) by general procedure A was obtained **8c** (0.312 g, 100%) as a colorless oil; $[\alpha]_D^{20}$ +4.1 (*c* 3.7, $CHCl_3$); IR (film) 2956, 1589, 1494, 1248, 1052 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.41–7.37 (m, 4H), 7.18–7.14 (m, 2H), 7.11–7.09 (m, 4H), 6.36–6.30 (m, 3H), 4.54 (ddd, J=7.7, 6.4, 6.4 Hz, 1H), 1.76–1.67 (m, 1H), 1.56 (ddd, J=13.9, 7.8, 6.6 Hz, 1H), 1.39 (ddd, J=13.6, 7.4, 6.6 Hz, 1H), 0.95 (d, J=6.7 Hz, 3H), 0.93 (d, J=6.7 Hz, 3H), 0.32 (s, 3H), 0.31 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.7, 139.7, 135.8, 131.0, 129.7, 124.3, 122.3, 72.6, 45.2, 24.2, 23.0, 22.5, −1.9, −2.1; MS (LC-APCI) *m/z* (relative intensity) 447 ($[M+H]^+$, ^{81}Br, 4%), 445 ($[M+H]^+$, ^{79}Br, 6%), 265 (100%), 168 (66%). Anal. Calcd for $C_{22}H_{29}N_2OSiBr$: C, 59.32; H, 6.56; N, 6.29. Found: C, 59.23; H, 6.56; N, 6.21.

4.2.3.4. Silyl ether 8d. From **7d** (116 mg, 0.43 mmol), DMAP (6 mg, 0.043 mmol), Et_3N (0.14 mL, 0.56 mmol), and **2b** (1:1 v/v solution in benzene, 0.18 mL, 0.56 mmol) by general procedure A was obtained **8d** (0.233 g, 100%) as a colorless oil; $[\alpha]_D^{21}$ +37.1 (*c* 1.85, $CHCl_3$); IR (film) 2959, 1592, 1496, 1253, 1046 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.41–7.37 (m, 4H), 7.17–7.14 (m, 2H), 7.11–7.08 (m, 4H), 6.36 (d, J=7.0 Hz, 1H), 6.33 (d, J=1.8 Hz, 1H), 6.30 (d, J=1.9 Hz, 1H), 4.14 (dd, apparent triplet, J=6.9 Hz, 1H), 1.82–1.75 (m, 1H), 0.94 (d, J=6.7 Hz, 3H), 0.84 (d, J=6.8 Hz, 3H), 0.31 (s, 3H), 0.30 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.8, 139.2, 135.8, 130.9, 129.7, 124.2, 122.4, 79.1, 33.7, 18.3, −1.9, −2.1; MS (LC-APCI) *m/z* (relative intensity) 433 ($[M+H]^+$, ^{81}Br, 10%), 431 ($[M+H]^+$, ^{79}Br, 16%), 251 (100%), 168 (5%). Anal. Calcd for $C_{21}H_{27}N_2OSiBr$: C, 58.46; H, 6.31; N, 6.49. Found: C, 58.50; H, 6.33; N, 6.48.

4.2.4. General procedure B: radical addition and desilylation. A solution of the (α-bromovinyl)silyl ether (**8a**–**8d**) in benzene (ca. 0.02 M) was deoxygenated (nitrogen was bubbled through the solution via a syringe needle for 20 min) and heated to reflux. A solution of AIBN (0.2 equiv) and Bu_3SnH (1.3 equiv) in benzene (ca. 10% of the total reaction volume) was added through a syringe pump over 10 h, and reflux was continued for another 10 h. If necessary, additional portions of AIBN (0.2 equiv) were added until the reaction was complete, as judged by TLC. A solution of TBAF (1 M in THF, 6 equiv) was added and reflux was continued for another 3 h. The reaction mixture was passed through a short plug of silica gel, eluting with EtOAc. After concentration and analysis of diastereomer ratio by ^1H NMR (integration of alkene peaks), the crude product was partitioned between CH_3CN and hexane to remove most of the tin components with the hexane fraction. Flash chromatography afforded **10a**–**10d**, with yields shown in Table 1. These known compounds were identified by comparison with characterization data previously reported.[7b]

4.2.4.1. *N*-(Diphenylamino)vinylglycinol (10a). From **8a** (0.551 mmol) and Bu_3SnH (0.19 mL) by general procedure B was obtained **10a** (80.3 mg, 57%).

4.2.4.2. (2*S*,3*R*)-3-(*N*,*N*-Diphenylhydrazino)-4-penten-2-ol (10b). From **8b** (0.285 mmol) and Bu_3SnH (0.12 mL) by general procedure B was obtained **10b** (53 mg, 69%, *anti*/*syn*=66:34).

4.2.4.3. (3*R*,4*S*)-3-(*N*,*N*-Diphenylhydrazino)-6-methyl-1-hepten-4-ol (10c). From **8c** (0.236 mmol) and Bu_3SnH (0.086 mL) by general procedure B was obtained **10c** (40.1 mg, 55%, *anti*/*syn*=78:22).

4.2.4.4. (3*S*,4*R*)-4-(*N*,*N*-Diphenylhydrazino)-2-methyl-5-hexen-3-ol (10d). From **8d** (0.267 mmol) and Bu_3SnH (0.10 mL) by general procedure B was obtained **10d** (46.6 mg, 59%, *anti*/*syn*=96:4).

4.2.5. 1,1-Dibenzyl-2-(3-(*tert*-butyldimethylsilyloxy)propylidene)hydrazine (12a). To a solution of aldehyde **11**[23] (1.521 g, 8.07 mmol) in toluene (16 mL) were added *N*,*N*-dibenzylhydrazine (1.78 g, 8.07 mmol) and magnesium sulfate (200 mg), and the mixture was stirred at room

temperature for 16 h. Concentration and flash chromatography (7:1 to 3:1 Hex/EtOAc) afforded **12a** (1.941 g, 85%) as a colorless oil; IR (film) 2927, 2855, 1603, 1494, 1453, 1253, 1097, 940 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.45–7.12 (m, 10H), 6.65 (t, J=5.4 Hz, 1H), 4.34 (s, 4H), 3.75 (t, J=6.5 Hz, 2H), 2.45 (q, J=6.5 Hz, 2H), 0.92 (s, 9H), 0.06 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 138.0, 135.4, 128.3, 127.7, 126.9, 61.6, 58.2, 36.4, 25.9, 18.2, −5.4; MS (EI) m/z (relative intensity) 382 (M^+, 7%), 325 (66%), 237 (36%), 233 (40%), 131 (70%), 91 (100%). Anal. Calcd for $C_{23}H_{34}N_2OSi$: C, 72.20; H, 8.96; N, 7.32. Found: C, 72.42; H, 9.03; N, 7.34.

4.2.6. 3-(2,2-Dibenzylhydrazono)propan-1-ol (13). To a solution of hydrazone **12a** (313 mg, 0.818 mmol) in THF (10 mL) was added tetrabutylammonium fluoride (1 M solution in THF, 0.90 mL, 0.90 mmol) and the mixture was stirred at room temperature for 1 h. Concentration and flash chromatography (5:1 to 1:1 Hex/EtOAc) afforded **13** (195 mg, 89%) as a yellow oil; IR (film) 3371 (br), 2921, 1597, 1491, 1450, 1070 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.40–7.18 (m, 10H), 6.66 (t, J=3.90 Hz, 1H), 4.29 (s, 4H), 3.78 (t, J=5.4 Hz, 2H), 3.00 (s, 1H), 2.34 (td, J=5.4, 4.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 137.7, 136.1, 128.5, 127.8, 127.1, 60.4, 58.4, 34.5; MS (EI) m/z (relative intensity) 268 (M^+, 30%), 210 (30%), 177 (10%), 159 (35%), 131 (45%), 92 (80%), 91 (100%), 65 (40%). Anal. Calcd for $C_{17}H_{20}N_2O$: C, 76.09; H, 7.51; N, 10.44. Found: C, 76.41; H, 7.39; N, 10.11.

4.2.7. 1,1-Dibenzyl-2-(3-((1-bromovinyl)dimethylsilyloxy)propylidene)hydrazine (14). To a solution of hydroxyhydrazine **13** (406 mg, 1.51 mmol) in THF (15 mL) at 0 °C were added triethylamine (0.30 mL, 2.0 mmol) and DMAP (20 mg, 0.151 mmol) followed by addition of (1-bromovinyl)chlorodimethylsilane (**2b**, 7.0 M in benzene, 0.40 mL, 2.8 mmol). The reaction mixture was stirred for 4 h, concentrated, diluted with EtOAc, and extracted with brine. The organic phase was dried and filtered through a plug of silica gel affording **14** (640 mg, 98%) as a colorless oil; IR (film) 2958, 2917, 1589, 1491, 1454, 1254, 1090, 833, 796, 731, 698 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ ppm 8.02–7.75 (m, 10H), 7.19 (t, J=5.3 Hz, 1H), 6.92 (ABq, J=1.8 Hz, $\Delta\nu$= 18.4 Hz, 2H), 4.91 (s, 4H), 4.37 (t, J=6.6 Hz, 2H), 3.06 (dt, J=11.94, 6.6 Hz, 1H), 0.87 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 138.0, 135.4, 134.5, 130.9, 128.4, 127.8, 127.0, 61.8, 58.1, 36.0, −2.9; MS (EI) m/z (relative intensity) 432 (M^+, ^{81}Br, 8%), 430 (M^+, ^{79}Br, 8%), 237 (24%), 139 (46%), 131 (86%), 91 (100%). Anal. Calcd for $C_{21}H_{27}BrN_2OSi$: C, 58.46; H, 6.31; N, 6.49. Found: C, 58.56; H, 6.50; N, 6.24.

4.2.8. (*S*)-1,1-Dibenzyl-2-(3-(*tert*-butyldimethylsilyloxy)-butylidene) hydrazine (12b). To a solution of methyl (*S*)-3-(*tert*-butyldimethylsilyloxy)butanoate[30] (1.707 g, 7.34 mmol) in hexane (8.8 mL) was added diisobutylaluminum hydride (1 M in hexane, 8.8 mL, 8.8 mmol) over 30 min at –78 °C. After 1 h, the reaction was quenched with saturated aqueous Na/K tartrate solution (35 mL), then diluted with diethyl ether (25 mL) and CH_2Cl_2 (25 mL), and stirred vigorously for 30 min. The organic phase was separated and the aqueous phase was washed with diethyl ether (3×25 mL). The combined organic layers were dried and concentrated. The crude aldehyde was dissolved in toluene (20 mL) and dibenzylhydrazine (2.50 g, 10.9 mmol) was added. After 16 h at room temperature, concentration and flash chromatography (10:1 to 1:1 Hex/EtOAc) afforded **12b** (2.93 g, 100%) as a colorless oil; $[\alpha]_D^{24}$ −6.94 (*c* 0.605, $CHCl_3$); IR (film) 2927, 2897, 2852, 1605, 1255 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.45–7.04 (m, 10H), 6.59 (dd, J=5.65, 5.65 Hz, 1H), 4.29 (unresolved ABq, 4H), 3.90 (apparent sextet, J=6.0 Hz, 1H), 2.36–2.26 (m, 2H), 1.06 (d, J=6.1 Hz, 3H), 0.84 (s, 9H), 0.01 (s, 3H), −0.03 (s, 3H); MS (EI) m/z (relative intensity) 397 ([M+H]$^+$, 100%), 301 (13%), 265 (12%). Anal. Calcd for $C_{24}H_{36}N_2OSi$: C, 72.67; H, 9.15; N, 7.06; Si, 7.08. Found: C, 72.89; H, 9.18; N, 7.13.

4.2.9. 2-(3-((1-Bromovinyl)dimethylsilyloxy)propylidene)-1,1-diphenylhydrazine (17a). To a solution of hydroxyhydrazine **16a**[24] (474 mg, 2.09 mmol) in benzene (21 mL) at 0 °C were added triethylamine (0.38 mL, 2.7 mmol) and *N*,*N*-dimethylaminopyridine (26 mg, 0.21 mmol) followed by the addition of **2b** (7.0 M in benzene, 0.40 mL, 2.7 mmol). The reaction mixture was stirred for 4 h, concentrated, diluted with EtOAc, and washed with brine. The organic phase was dried and filtered through a plug of silica gel affording **17a** (794 mg, 98%) as a colorless oil; IR (film) 3064, 2960, 2591, 2494, 1300, 1254, 1090 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.47–7.38 (m, 4H), 7.21–7.08 (m, 6H), 6.60 (t, J=5.2 Hz, 1H), 6.35 (ABq, J=1.8 Hz, $\Delta\nu$=16.5 Hz, 2H), 3.90 (t, J=6.7 Hz, 2H), 2.61 (td, J=6.7, 5.3 Hz, 2H), 0.32 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.2, 136.4, 135.3, 131.0, 130.0, 124.0, 122.3, 61.5, 35.8, −2.9; MS (EI) m/z (relative intensity) 404 (M^+, ^{81}Br, 20%), 402 (M^+, ^{79}Br, 20%), 195 (25%), 169 (35%), 168 (100%), 167 (68%). Anal. Calcd for $C_{19}H_{23}BrN_2OSi$: C, 56.57; H, 5.75; Br, 19.81; N, 6.94. Found: C, 56.84; H, 5.84; Br, 19.54; N, 7.04.

4.2.10. 3-(2,2-Diphenylhydrazinyl)pent-4-en-1-ol (18a). A solution of hydrazone **17a** (165 mg, 0.41 mmol) in benzene (20 mL) was deoxygenated (nitrogen was bubbled through the solution via a syringe needle for 20 min). To this was added a solution of AIBN (33 mg, 0.20 mmol) and tributyltin hydride (0.16 mL, 0.57 mmol) in benzene (1.6 mL). The solution was heated at reflux for 16 h. A solution of TBAF (1 M in THF, 0.9 mL, 0.90 mmol) was added and reflux was continued for 4 h. Filtration through silica gel, concentration, and flash chromatography (5:1 to 1:2 petroleum ether/EtOAc) afforded **18a** (86 mg, 78%) as a colorless oil; IR (film) 3362 (br), 3060, 2917, 2852, 1588, 1491, 1270 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.30–7.26 (m, 4H), 7.15–7.13 (m, 4H), 7.01–6.98 (m, 2H), 6.92 (m, 1H), 5.86 (ddd, J=17.0, 10.4, 8.2 Hz, 1H), 5.15–5.10 (m, 2H), 3.78 (ddd, J=11.7, 5.9, 5.9 Hz, 1H), 3.66 (ddd, J=11.0, 7.4, 5.4 Hz, 1H), 3.62–3.58 (m, 1H), 1.90 (dddd, J=18.1, 7.3, 5.4, 5.4 Hz, 1H), 1.79 (ddd, J=12.4, 6.9, 6.6, 5.9 Hz, 1H), 1.27 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.9, 138.9, 129.1, 122.3, 120.5, 117.6, 60.4, 59.4, 35.8; MS (CI) m/z (relative intensity) 269 ([M+H]$^+$, 10%), 184 (40%), 168 (100%). Anal. Calcd for $C_{17}H_{20}N_2O$: C, 76.09; H, 7.51; N, 10.44. Found: C, 75.99; H, 7.53; N, 10.25.

Alternative procedure, catalytic Bu_3SnH: to a solution of hydrazone **17a** (86 mg, 0.21 mmol) in benzene (2 mL) were

added AIBN (3 mg, 0.02 mmol), tributyltin hydride (5.8 μL, 0.02 mmol), PMHS (45 μL), and sodium methoxide (42 mg, 0.75 mmol). The mixture was heated at reflux for 16 h, concentrated, diluted with diethyl ether (10 mL), and washed with saturated aqueous NH_4Cl (7 mL), water (5 mL), and brine (5 mL). The organic phase was concentrated and the residue was treated with TBAF (1 M in THF, 0.5 mL, 0.5 mmol) at room temperature for 6 days. The reaction mixture was filtered through silica gel, concentrated, and purified by flash chromatography (5:1 to 1:2 petroleum ether/EtOAc) to afford **18a** (22 mg, 39%) as a colorless oil.

Alternative procedure, Et_3B/O_2 initiation: to a solution of hydrazone **17a** (75 mg, 0.19 mmol) in deoxygenated dichloromethane (11 mL) were added triethylborane (1 M in hexane, 0.5 mL, 0.5 mmol) and tributyltin hydride (70 μL, 0.27 mmol) at −78 °C. The mixture was allowed to warm to room temperature over 40 h, and oxygen was introduced by diffusion through a balloon.[31] The mixture was concentrated, dissolved in EtOAc (4 mL), and treated with TBAF (1 M in THF, 0.7 mL, 0.7 mmol) at room temperature for 12 h. The reaction mixture was filtered through Celite, concentrated, and purified by flash chromatography (5:1 to 1:2 petroleum ether/EtOAc) to afford **18a** (40 mg, 40%) as a colorless oil.

4.2.11. (*S*)-2-(3-((1-Bromovinyl)dimethylsilyloxy)butylidene)-1,1-diphenylhydrazine (17b). To a solution of hydroxyhydrazone **16b**[24] (217 mg, 0.85 mmol) and imidazole (174 mg, 2.56 mmol) in THF (8 mL) was added (1-bromovinyl)chlorodimethylsilane (7.0 M in benzene, 0.4 mL, 2.72 mmol). The mixture was stirred at room temperature for 15 min. The solution was filtered through silica gel and concentrated. Flash chromatography (10:1 petroleum ether/EtOAc) afforded **17b** (362 mg, 100%) as a colorless oil; $[\alpha]_D^{21}$ −1.0 (*c* 4.1, $CHCl_3$); IR (film) 3060, 2968, 1596, 1493, 1377, 1300, 1254, 1211, 1089 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.39–7.34 (m, 4H), 7.15–7.07 (m, 6H), 6.55 (dd, J=5.6, 5.6 Hz, 1H), 6.27 (ABq, J=1.7 Hz, $\Delta\nu$=11.0, 2H), 4.18–3.97 (apparent sextet, J=6.2 Hz, 1H), 2.54–2.39 (m, 2H), 1.21 (d, J=6.1 Hz, 3H), 0.23 (s, 3H), 0.22 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.1, 136.9, 135.8, 130.9, 129.7, 123.9, 122.4, 68.59, 42.4, 23.7, −2.1, −2.2; MS (EI) *m*/*z* (relative intensity) 418 (M^+, ^{81}Br, 14%), 416 (M^+, ^{79}Br, 16%), 209 (46%), 167 (100%), 139 (52%), 77 (16%). Anal. Calcd for $C_{20}H_{25}BrN_2OSi$: C, 57.55; H, 6.04; N, 6.71. Found: C, 57.74; H, 6.18; N, 6.70.

4.2.12. (2*S*,4*S*)- and (2*S*,4*R*)-4-(2,2-diphenylhydrazinyl)-hex-5-en-2-ol (18b). By the procedure described above for **18a**, cyclization and desilylation of **17b** (0.20 mmol) afforded **18b** (42 mg, 74%) as a 1:1 mixture of diastereomers separable by careful radial chromatography. Diastereomer i: colorless oil; IR (film, $CDCl_3$) 3375 (br), 3060, 2958, 2848, 1588, 1493, 1270, 1123, 923 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.31–7.25 (m, 4H), 7.17–7.13 (m, 4H), 7.01–6.95 (m, 2H), 5.86–5.74 (m, 1H), 5.15–5.06 (m, 2H), 4.44 (s, 1H), 3.94–3.84 (m, 1H), 3.61 (ddd, J=7.8, 6.4, 6.4 Hz, 1H), 1.74 (ddd, J=14.3, 9.7, 6.0 Hz, 1H), 1.63–1.55 (m, 1H), 1.59 (br s, 1H), 1.19 (d, J=6.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.9, 139.6, 129.1, 122.1, 120.4, 117.5, 77.3, 59.7, 42.3, 24.7; MS (EI) *m*/*z* (relative intensity) 282 (M^+, 100%), 168 (35%). Diastereomer ii: colorless oil; IR (film) 3358 (br), 2921, 1588, 1491, 1115 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.32–7.26 (m, 4H), 7.12–7.10 (m, 4H), 7.03–6.99 (m, 2H), 5.95 (ddd, J=17.1, 10.4, 8.3 Hz, 1H), 5.16 (d, J=10.3 Hz, 1H), 5.13 (d, J=17.4 Hz, 1H), 4.27–4.11 (br s, 1H), 4.07–4.00 (m, 1H), 3.67–3.59 (m, 1H), 2.79 (s, 1H), 1.76–1.66 (m, 2H), 1.12 (d, J=6.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.7, 138.7, 129.2, 122.5, 120.5, 117.9, 65.4, 59.2, 42.1, 23.4; MS (EI) *m*/*z* (relative intensity) 282 (M^+, 100%), 168 (42%).

4.2.13. Silyl ether 19. From **10a** (47 mg, 0.19 mmol), DMAP (ca. 2 mg), Et_3N (0.07 mL, 0.28 mmol), and TBSCl (43 mg, 0.28 mmol) in benzene (3 mL, 0.06 M) by general procedure A was obtained **19** (54.3 mg, 80%) as a colorless oil; IR (film) 2928, 1589, 1497, 1258, 1088 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.29–7.25 (m, 4H), 7.20–7.18 (m, 4H), 7.00–6.96 (m, 2H), 5.75 (ddd, J=17.4, 10.1, 7.2 Hz, 1H), 5.14 (dd, J=17.4, 1.5 Hz, 1H), 5.12 (dd, J=10.4, 1.4 Hz, 1H), 4.71 (s, 1H), 3.65–3.60 (m, 3H), 0.91 (s, 9H), 0.07 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.8, 136.6, 128.9, 121.9, 120.3, 118.5, 64.7, 62.2, 25.8, 18.2, −5.5; MS (CI) *m*/*z* (relative intensity) 369 ([M+H]$^+$, 80%), 281 (60%), 200 (50%). Anal. Calcd for $C_{22}H_{32}N_2OSi$: C, 71.69; H, 8.75; N, 7.60. Found: C, 71.88; H, 8.60; N, 7.64.

4.2.14. Benzamide 20 (N–N bond cleavage). To a solution of hydrazine **19** (52.5 mg, 0.143 mmol) in THF (3 mL) at −78 °C was added *n*-BuLi (2.5 M in hexane, 0.15 mL, 0.36 mmol). After 1 h, benzoyl chloride (0.06 mL, 0.5 mmol) was added, and the mixture was allowed to warm to ambient temperature. After 10 h, the reaction mixture was diluted with Et_2O, washed with saturated aqueous $NaHCO_3$, concentrated, and purified by column chromatography to afford the benzamide derivative, which was used immediately. The benzamide was dissolved in anhydrous MeOH (0.2 mL) and SmI_2 (ca. 0.2 M in THF) was added until a blue color was maintained (3 mL, ca. 0.6 mmol). After 30 min, concentration and column chromatography gave the pure amide **20** (35 mg, 85%) as a pale yellow oil; IR (film) 3309, 1637, 1539, 1256, 1113 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.80–7.77 (m, 2H), 7.52–7.48 (m, 1H), 7.45–7.42 (m, 2H), 6.56 (d, J=7.1 Hz, 1H), 5.93 (ddd, J=17.1, 10.5, 5.6 Hz, 1H), 5.28 (dd, J=17.2, 1.2 Hz, 1H), 5.20 (dd, J=10.5, 1.2 Hz, 1H), 4.74–4.70 (m, 1H), 3.82 (dd, J=10.0, 4.2 Hz, 1H), 3.78 (dd, J=10.0, 3.5 Hz, 1H), 0.91 (s, 9H), 0.07 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.6, 136.0, 134.7, 131.4, 128.6, 126.8, 116.2, 65.0, 53.0, 25.8, 18.2, −5.4; MS (CI) *m*/*z* (relative intensity) 306 ([M+H]$^+$, 100%), 248 (15%).

4.2.15. Methyl ketone 21 (Tamao oxidation). A solution of **8a** (299 mg, 0.68 mmol) in benzene (34 mL, 0.02 M) was deoxygenated (nitrogen was bubbled through the solution via a syringe needle for 20 min) and heated to reflux. A solution of AIBN (22 mg, 0.14 mmol) and Bu_3SnH (0.24 mL, 0.81 mmol) in benzene (4 mL) was added via syringe pump over 4 h, and reflux was continued for another 10 h. The mixture was concentrated and partitioned between CH_3CN (30 mL) and hexane (5×25 mL) to remove most of the tin components with the hexane fraction. Hexane fractions 3–5 were extracted with CH_3CN (2×25 mL) and these were washed again with hexane (2×25 mL). Concentration of the combined CH_3CN fractions afforded the oxasilacycle

9a (0.152 g). To a solution of **9a** in DMF (10 mL) were added KF (0.15 g, 2.7 mmol), $KHCO_3$ (0.17 g, 1.7 mmol), and H_2O_2 (50% aqueous solution, 0.23 mL, 2.7 mmol). After 3 h, the reaction mixture was diluted with EtOAc (80 mL), washed with brine (3×20 mL), and dried over Na_2SO_4. Concentration and flash chromatography afforded ketone **21** (98.2 mg, 0.36 mmol, 54%) as a colorless oil; IR (film) 3431, 1710, 1588, 1493 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.31–7.27 (m, 4H), 7.11–7.05 (m, 4H), 7.04–7.02 (m, 2H), 5.04 (s, 1H), 4.03–3.96 (m, 2H), 3.71 (dd, apparent triplet, J=3.3 Hz, 1H), 2.28 (dd, J=9.2, 3.2 Hz, 1H), 2.24 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.9, 147.8, 129.3, 123.0, 120.5, 68.5, 61.2, 27.2; MS (LC-APCI) *m/z* (relative intensity) 271 ($[M+H]^+$, 60%), 239 (44%), 168 (100%). Anal. Calcd for $C_{16}H_{18}N_2O_2$: C, 71.09; H, 6.71; N, 10.36. Found: C, 71.08; H, 6.67; N, 10.27.

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