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Intramolecular nucleophilic attack at silicon in *o*-silylbenzyl alcohols. Generation of allyl and benzyl anion equivalents

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ABSTRACT

Substituted silyl ethers of *o*-bromobenzyl alcohols and the derived *o*-silylbenzyl alcohols were used to transfer allyl and benzyl groups from silicon to the electrophiles benzaldehyde and benzophenone in excellent yields. γ-Oxidosilane intermediates (and possibly hypercoordinated silicon intermediates) are postulated.

1. Introduction

1.1. Silicon beyond trimethylsilyl

Organosilicon compounds are now widely used in organic synthesis. Gilbert Stork's early work in organosilicon chemistry[1–3] starting in 1968 was a major factor in stimulating interest in this area to the organic synthesis community.[4] Some of Stork's important early contributions are the facile preparation of silyl enol ethers and their conversion to lithium enolates,[1] conversion of epoxysilanes to carbonyl compounds,[2] and development of annulation methods using epoxysilanes[2b] and α-silylated vinyl ketones.[3]

Much of the early work with organosilicon compounds used trimethylsilyl groups. Stork was one of the first synthetic chemists to make use of the other bonds to silicon. In 1968, he introduced the *tert*-butyldimethylsilyl (TBDMS) group, the first (and probably the mostly widely used) hindered trialkylsilyl protecting group.[1] Subsequently many other hindered silyl groups have been introduced.[5,6] To quote a widely used book on protecting groups,[6] 'Silyl groups have found broad appeal as protective groups because their reactivity and stability can be tailored by varying the nature of the substituents on the silicon'.

Stork also recognized that a silicon atom could be used as a link to connect two reaction partners, and wrote a series of papers[7–9] on the 'temporary silicon connection'. He used this concept for radical reactions[7] and cycloadditions,[8] and demonstrated how it could be used in the synthesis of sugars.[7e,9] This concept was quickly accepted and has been widely applied.[10]

1.2. Summary of prior work

Many important reactions of organosilicon compounds involve nucleophilic attack at the silicon (e.g., generation of reactive anionic intermediates, removal of silyl protecting groups, elimination reactions, rearrangements, etc.). For some time we have been investigating the possibility of using intramolecular nucleophiles for such reactions.[11–15] We anticipated that an intramolecular nucleophile would have a number of advantages: (a) Control of regiochemistry and stereochemistry. (b) Control of stoichiometry. With an intermolecular nucleophile, excess reagent (nucleophile) may be harmful. (c) Control of reagent purity. For example, fluoride is often used for nucleophilic reactions of silicon compounds, but it is not easily obtained or kept in anhydrous form. (d) Reaction rate. An intramolecular reaction is often much faster than an intermolecular one. In addition, we wanted a system in which the nucleophile could be in a relatively unreactive (protected) form, which could be activated when needed.

We began by investigating the use of the γ-oxidopropyl group. We found that acyclic substrates having a γ-hydroxypropyl group ($Si-(CH_2)_3OH$) undergo base-induced cleavage of allyl and benzyl groups attached to silicon.[12] (Rearrangement reactions were also demonstrated.[11]) With lithium as the counter ion, and in the presence of HMPA, capture of these groups by some carbonyl compounds was demonstrated.[12]

Then we found that more rigid substrates having a γ-hydroxypropyl group incorporated in an *ortho*-substituted aromatic ring

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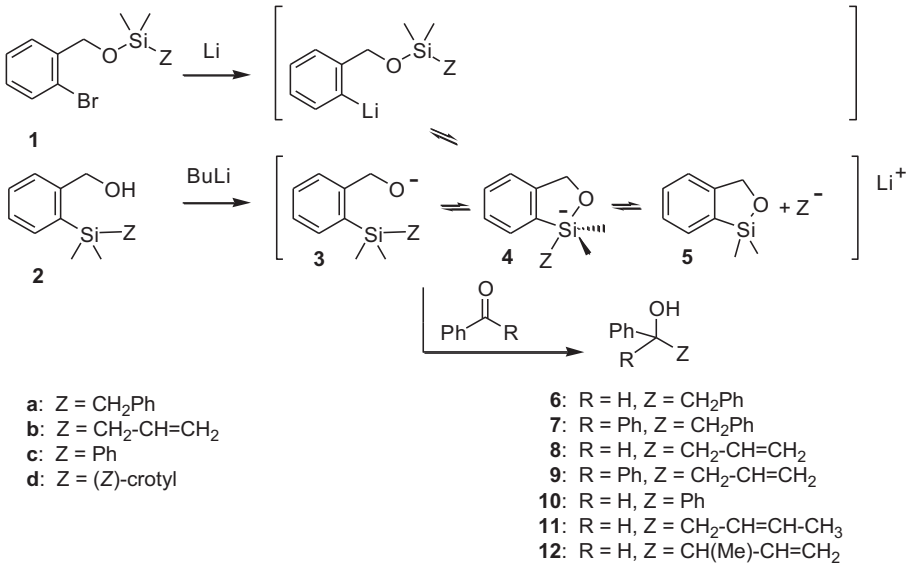
(the *ortho*-silylbenzyl alcohol system) underwent cleavage reactions much more readily than the acyclic compounds (presumably via a γ-oxidopropyl intermediate **3** (see Scheme 1)). We reported a convenient synthesis of this sytem,[13] used it to study the stereochemistry of the rearrangement of α-halosilanes,[14] and began to study the generation of anionic (benzyl and silyl) intermediates.[15] We also found that the silyl ether **1a** could undergo a rearrangement reaction, acting as a precursor to an intermediate, such as **3**. Treatment of **1a** with lithium in ether followed by benzophenone in THF resulted in cleavage of the benzyl group with capture by benzophenone in moderate yield. No HMPA was necessary. [Cleavage and capture of a Me_3Si group was also demonstrated using both a silyl ether (**1**) and silyl alcohol (**2**) (Z=$SiMe_3$) as precursors to intermediates **3**–**5** (Scheme 1). Oxasilacyclopentane **5** was trapped with MeLi to give the silyl alcohol **2** (Z=Me), illustrating the possibility of reusing **5**.[15]]



Scheme 1.

Subsequently Nakao and Hiyama[16,17] and others[18] have used the *o*-silylbenzyl alcohol system for the generation of intermediates for various reactions, including transition metal-catalyzed cross-coupling reactions[16,18b] and various rhodium-catalyzed addition reactions.[17,18a] Other oxasilacyclopentanes,[19,20] and other heterocyclic five-membered ring systems[21] (cf. structure **4** below) have also been used for the transfer of nucleophilic organic groups from silicon.

We report here the optimization and extensions of some of our reactions, transferring benzyl and allyl groups to benzaldehyde and benzophenone. The preparation of benzyl- and allyllithium compounds from the corresponding halides and lithium metal is frequently complicated by Wurtz coupling.[22,23] Benzyllithium compounds have not been used a great deal in organic synthesis, partly because of difficulties in their preparation.[24] Allylation reactions are very important in synthesis, and a large number of methods for allylation of carbonyl compounds have been reported.[25]

2. Results and discussion

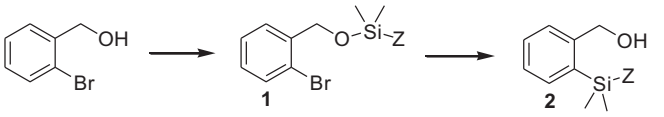
In our previous work, we found that treatment of benzylsilyl ether **1a** with lithium in ether followed by 1.1 equiv of benzophenone in THF resulted in 1,1,2-triphenylethanol (**7**) in 57% yield.[15] The mechanistic rationale (Scheme 1) involves halogen–metal exchange followed by rearrangement to alkoxide **3a** (Z=CH_2Ph). Intermediate **3a** appeared to be stable in ether, but in the presence of THF, a cleavage reaction occurred to give oxasilacyclopentane **5**, possibly via pentacoordinate intermediate **4a**. The group cleaved (Z=CH_2Ph) was trapped with benzophenone to give **7**.

To extend and optimize this idea, we initially prepared as substrates, silyl ethers **1a**–**c** and silyl alcohols **2a**–**c** (Table 1) using our previously developed procedures.[13] The silyl ethers were prepared from *o*-bromobenzyl alcohol and the corresponding chlorosilanes with Et_3N in ether (rt, 2–3 h). The silyl alcohols were prepared by treatment of the silyl ethers with lithium in ether (rt, 2 h) followed by aqueous workup. The conversion **1**→**2** presumably involves a rearrangement reaction to give lithium alkoxide **3**[13,15] (see Scheme 1).

2.1. Reactions of *o*-bromobenzylsilyl ethers 1a and 1b

We first treated silyl ethers **1a** and **1b** with lithium in ether followed by benzaldehyde and benzophenone in THF to give alcohols **6**–**9** (together with oxasilacyclopentane **5**). We found (by GC analysis of aliquots) that the conversion to lithium alkoxide **3** was complete within 2 h at rt. We obtained the most reproducible results when we cannulated the ether solution away from excess lithium before adding the carbonyl compound in THF.

Table 1
Preparation of *o*-bromobenzylsilyl ethers and *o*-silylbenzyl alcohols



Z	Product	Yield (%)	Product	Yield (%)
CH_2Ph	**1a**	91–98	**2a**	91–98
CH_2–CH=CH_2	**1b**	97	**2b**	85–90
Ph	**1c**	91	**2c**	90–98
(*Z*)-Crotyl	**1d**	94	**2d**	58 (not optimized)

Benzyl transfer using benzylsilyl ether **1a** was never very efficient. Preliminary experiments using GC yields (with a hydrocarbon standard) gave 37–43% yield of **6** from benzaldehyde and 63–64% yield of **7** from benzophenone using this procedure. Isolated yields of pure products (by chromatography) were determined to be 26% for **6** and 49% for **7**.

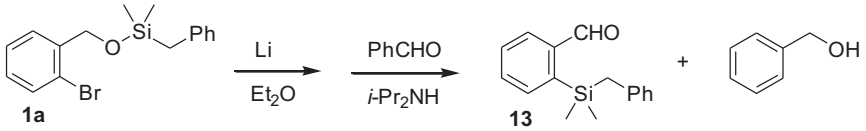
GC analyses of the crude products indicated the presence of several impurities. We were concerned that reactive anions were being destroyed by reaction with THF. We tried a few experiments using tetrahydropyran as solvent instead of THF. The GC yields were lower (14–16% of **6**, and 39% of **7**).

In some of the reactions of **1a** (and **2a**) with benzophenone, some benzhydrol was observed in the crude products. And in many of the reactions of **1a** with benzaldehyde, we observed a byproduct, which was eventually identified as *o*-(benzyldimethylsilyl)benzaldehyde (**13**). These products appear to result from hydride transfer, analogous to Cannizzaro reactions and Oppenauer oxidations.[26]

Compound **13** was isolated from a reaction using diisopropylamine. In some of the reactions of the benzyl alcohol substrate **2a** (below), we tried using amine additives to reduce byproducts. We additionally found some amines could be used in place of THF in some cleavage reactions, and briefly looked at the use of amines with silyl ether **1a** as well as with **2a**. In a reaction in which diisopropylamine was used as a solvent (**1a**, Li in ether, rt, 2 h, followed by benzaldehyde in diisopropylamine) both aldehyde **13** (30% yield) and benzyl alcohol (44% yield) were isolated.

ether followed by benzaldehyde or benzophenone in THF led to alcohols **6** or **7**, respectively. GC analyses of the crude products indicated fewer impurities from the benzyl alcohol substrate **2a** than from the silyl ether substrate **1a**. From the reactions using benzophenone, GC and GC/MS analyses suggested the presence of 1,1-diphenylpentan-1-ol (**14**), presumably formed by addition of excess *n*-BuLi to benzophenone. We therefore tried adding diisopropylamine to react with excess BuLi. This resulted in a crude product without **14**, which was easier to purify, and **7** was obtained in 74–76% yields. We had initially used a small excess of the carbonyl compounds. The best results were obtained without the amine, and using the carbonyl compounds as the limiting reagents, with an excess of benzyl alcohol substrate **2a** and an equivalent amount of *n*-BuLi. Thus, treatment of 1.5 equiv of **2a** with 1.5 equiv of *n*-BuLi in ether (0.5 h, 0 °C) followed by 1.0 equiv of benzophenone in THF (3 h, rt) led to alcohol **7** in 92% yield. And similar treatment of **2a** with *n*-BuLi in ether followed by benzaldehyde in THF led to alcohol **6** in 94% yield.

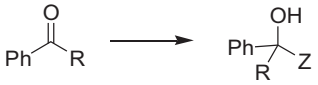
In earlier experiments, we briefly looked into the possibility of benzyl transfer to the enolizable ketone, cyclohexanone, from the



In contrast to the benzyl transfer from the silyl ether, allyl transfer was very efficient (using silyl ether **1b** with lithium in ether followed by benzaldehyde or benzophenone in THF to give **8** or **9**, respectively). The GC and GC/MS of the crude products showed mainly the desired trapping products (**8** or **9**) together with some unreacted benzaldehyde or benzophenone (as well as oxasilacyclopentane **5**).

Up to this point the silyl ether substrates were used as the limiting reagents. But if the reactions are to be useful in synthesis, the carbonyl compounds should be the limiting reagents. Using these conditions, the carbonyl compounds were not observed in the crude products, and the product alcohols were easy to purify, and were obtained in high yields. Treatment of allylsilyl ether **1b** with Li/Et_2O followed by benzaldehyde in THF led to homoallyl alcohol **8** in 97% yield. And treatment of **1b** with Li/Et_2O followed by benzophenone in THF led to homoallyl alcohol **9** in 91% yield. Table 2 summarizes the results using the best conditions.

Table 2
Trapping with carbonyl compounds



R	Z	Substrate	Product	Yield (%)
H	CH_2Ph	**2a**	**6**	94
Ph	CH_2Ph	**2a**	**7**	92
H	$CH_2–CH=CH_2$	**1b**	**8**	97
Ph	$CH_2–CH=CH_2$	**1b**	**9**	91
H	$CH_2–CH=CH_2$	**2b**	**8**	97
H	Ph	**2c**	**10**	28[a]
H	$CH_2–CH=CH_2$	**15**	**8**	83
H	$CH_2–CH=CH–CH_3$	**1d**	**11**, **12**	88

[a] HMPA added to the reaction mixture.

2.2. Reactions of *o*-silylbenzyl alcohols 2a and 2b

Benzyl transfer could be accomplished efficiently using benzylsilyl alcohol **2a** as a substrate. Treatment of **2a** with *n*-BuLi in silyl ether substrate **1a** and from the benzyl alcohol substrate **2a**. The yields were lower, and this was not pursued. For example, using benzyl alcohol substrate **2a** (1.0 equiv) and 1.4 equiv of *n*-BuLi in ether (0.5 h, 0 °C), followed by cyclohexanone (1.6 equiv) in THF (warm to rt, 15 h) gave 1-benzylcyclohexanol in 28% yield by GC. Under analogous conditions, benzophenone (1.4 equiv) gave alcohol **7** in GC yields of 90–98%.

The use of sodium hydride as a base in place of *n*-BuLi was also briefly investigated. As mentioned earlier, intermediate **3a** as the lithium salt appeared to be stable in ether, but underwent cleavage when THF was added. In contrast, intermediate **3a** as the sodium salt undergoes cleavage in ether. For example, treatment of benzyl alcohol substrate **2a** (with a hydrocarbon standard) with NaH in ether, taking aliquots with aqueous workup, resulted in 62% of **2a** remaining at 1 h, 2% at 3 h, and none at 4 h (with oxasilacyclopentane **5** as the other observed product).[27] The reaction was repeated, except that benzophenone (1.4 equiv) was added after 20 min at rt, and the reaction was followed by aliquots. After 4 h, 66% GC yield of alcohol **7** was obtained. Since the GC yield for trapping benzyl from **2a** with benzophenone to give **7** was 90–98% using the BuLi procedure (above), the NaH procedure was not investigated further.

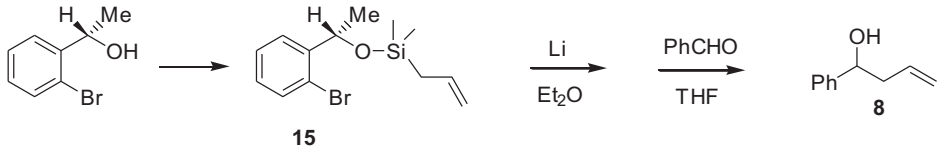
Allylsilyl alcohol **2b** also appeared to be an efficient substrate for allyl transfer. For example, treatment of 1.5 equiv of **2b** with 1.5 equiv of *n*-BuLi in ether (0.5 h, 0 °C) followed by 1.0 equiv of benzaldehyde in THF (6 h, rt) led to homoallylic alcohol **8** in 97% yield. This route was not pursued since it involves an extra step, and the route from allylsilyl ether **1b** worked well.

2.3. Reaction of (phenylsilyl)benzyl alcohol 2c

We next attempted phenyl transfer using phenylsilyl alcohol substrate **2c**. Treatment of **2c** with *n*-BuLi in ether followed by benzaldehyde in THF gave starting materials. (An analogous reaction of a mixture of **2a** and **2c** in the presence of a hydrocarbon standard led to alcohol **6**, but no benzhydrol (**10**).) However, when the reaction was run in the presence of 6.4 equiv of HMPA, a 28% yield of benzhydrol (**10**) was isolated.

2.4. Chiral substrate

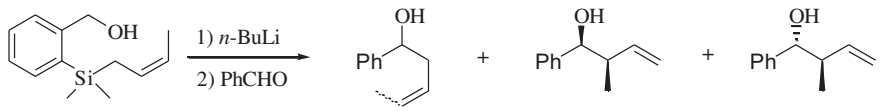
The allyl and benzyl transfer reactions were quite efficient, and an interesting question is what is the nature of the transition state, and could these reactions be used in asymmetric synthesis. We therefore prepared the chiral allylsilyl ether **15** from commercially available (*S*)-(−)-2-bromo-α-methylbenzyl alcohol and allyldimethylchlorosilane (76% yield). Treatment of **15** with lithium in ether followed by benzaldehyde in THF gave homoallyl alcohol **8** in 83% yield. Using GC analysis on a chiral column, alcohol **8** was found to be racemic. This could have resulted from diastereomeric transition states having similar energies, or more likely, from a reaction mechanism in which the allyl group is dissociated from the silyl substrate.



15 **8**

2.5. Crotyl substrates 1d and 2d

To shed more light onto these questions, the crotyl substrates **1d** and **2d** were prepared (Table 1). Treatment of **2d** with *n*-BuLi in ether followed by benzaldehyde in THF gave an 88% yield of a mixture of homoallyl alcohols **11** and **12** in a GC ratio of 1:1.3 to 1.6. Samples of **11** (14% yield) and **12** (28% yield) were obtained by column chromatography. Compound **11** was predominantly the *Z* isomer. Compound **12** was found to be a mixture of *syn* (**12s**) and *anti* (**12a**) isomers. By NMR integration, the *syn*/*anti* ratio was estimated to be about 1.6:1.



2d **11** **12s** **12a**

2.6. Mechanism

The fact that the reaction of the chiral silyl ether **15** gives racemic alcohol **8**, together with the observation that the reaction of the crotylsilyl alcohol **2d** gives a mixture of isomers (**11** and **12** (*syn* and *anti*)), suggest that these reactions take place by a transition state, which is not 'tight' but rather more 'open'.

Allylsilanes are of considerable importance in synthesis, and numerous methods for allylation of carbonyl compounds have been developed.[28] A number of types of allylation reactions have been developed, which are believed to take place by a closed, cyclic transition structure. These reactions are believed to involve penta- or hexacoordinate silicon anions, and generally take place in a stereospecific manner, with *E*- and *Z*- crotylsilanes giving predominantly *anti* and *syn* products, respectively. Examples include reactions of allyltrifluorosilanes with fluoride ion (or other bases),[29] and reactions of allyltrichlorosilanes with (a) catechol (or other diols),[30] (b) DMF or other amides,[31] (c) HMPA or other phosphoramides,[31d,32] and (d) various amine oxides.[33]

Earlier allylations by allylsilanes used acidic or electrophilic conditions (showing γ-regioselectivity, but little or no stereoselectivity),[30m,34] or fluoride ion (giving mixtures of regio- and stereoisomers).[35] These reactions (both acid and fluoride-induced reactions) have been described as taking place through an open transition structure. Our allylation reactions appear to proceed via an open transition structure, and most resemble the fluoride-induced reactions. Our observations are consistent with the mechanistic rationale shown in Scheme 1. They do not tell us the extent to which a pentacoordinate silicon intermediate (**4**) may be involved.[36]

3. Conclusion

This work demonstrates that *o*-bromobenzylsilyl ethers (**1**) and *o*-silylbenzyl alcohols (**2**) can be used to generate allyl and benzyl anion equivalents, which can be trapped with non-enolizable carbonyl compounds in high yield.

4. Experimental

4.1. General

All reactions were carried out under argon or nitrogen in oven dried glassware; liquids were transferred with argon or nitrogen-flushed syringes. Column chromatography was carried out as flash chromatography using 200–425 or 170–400 mesh silica gel. The verb 'concentrated' refers to removal of solvent on a rotary evaporator. When reactions were followed by aliquots, a 0.2–0.4 mL aliquot of the reaction mixture was added to 3 mL of saturated $NaHCO_3$ and 1 mL of ether, and the ether layer was dried (Na_2SO_4) and analyzed by GC.

Nuclear magnetic resonance (NMR) spectra were obtained in $CDCl_3$ (^1H NMR at 300 MHz and ^{13}C NMR at 75 MHz or ^1H NMR at 400 MHz and ^{13}C NMR at 100 MHz). Chemical shifts are reported in δ relative to CH_2Cl_2 at δ 5.32 for ^1H NMR unless otherwise specified and to $CDCl_3$ (δ 77.0) for ^{13}C NMR. Assignments in ^{13}C NMR were made using DEPT. Gas chromatography/mass spectrometry analyses (GC/MS) were obtained in the EI mode. The high resolution mass spectrum (HRMS) was determined by the Midwest Center for Mass Spectrometry, University of Nebraska. Gas chromatography (GC) analyses were carried out with a flame ionization detector and using helium as the carrier gas.[37]

Anhydrous ether and THF were distilled from sodium and benzophenone under nitrogen. Triethylamine and diisopropylamine were distilled from CaH_2. The lithium wire (containing 1% sodium) was cut, gouged with a spatula, and quickly blotted with a paper towel before adding to the reaction flask.

The benzyldimethylsilyl ether (**1a**)[13] and the allyldimethylsilyl ether (**1b**)[13] of *o*-bromobenzyl alcohol were prepared from the corresponding chlorosilanes ($PhCH_2Me_2SiCl$ and $allylMe_2SiCl$) and triethylamine in ether (2 h, rt).[13] *o*-(Benzyldimethylsilyl)benzyl alcohol (**2a**) and *o*-(allyldimethylsilyl)benzyl alcohol (**2b**) and were prepared from **1a** and **1b**, respectively, by treatment with lithium in ether.[13] Comparison samples of alcohols **6**, **7**, and **8** were prepared

as follows: 1,2-diphenylethanol (**6**)[23] by $NaBH_4$ reduction of deoxybenzoin; 1,1,2-triphenylethanol (**7**)[23] by reaction of benzylmagnesium chloride with benzophenone; 1-phenyl-3-buten-1-ol (**8**)[23] by reaction of allylmagnesium bromide with benzaldehyde. (*Z*)-Crotyldimethylchlorosilane was prepared by $Ni(acac)_2$-catalyzed hydrosilylation of butadiene with dimethylchlorosilane according to the method of Fürstner and Voigtlander.[38]

4.2. Phenyldimethylsilyl ether (1c) of *o*-bromobenzyl alcohol

To a solution of 4.0 g (21.4 mmol) of *o*-bromobenzyl alcohol in 75 mL of anhydrous ether was added 4.0 mL (28.7 mmol) of triethylamine followed by 3.6 mL (21.4 mmol) of phenyldimethylchlorosilane (dropwise). The reaction mixture was stirred at rt for 3 h and then added to 100 mL of saturated $NaHCO_3$. The aqueous layer was extracted with ether (2×40 mL). The combined organic layers were dried (Na_2SO_4), concentrated, chromatographed (silica gel, 25×2.5 cm, petroleum ether/ether 9:1), and placed under oil pump vacuum (0.07 mm, 2.75 h) to give 6.19 g (91% yield) of phenylsilyl ether **1c** as clear and colorless oil: IR (film): 3069, 2959, 1591, 1570, 1443, 1428, 1254, 1119, 1094, 1026, 831, 786, 747, 700 cm^{-1}; ^1H NMR (300 MHz): δ 0.50 (s, 6H), 4.79 (s, 2H), 7.15–7.68 (m, 9H); ^{13}C NMR (75 MHz): δ −1.7 (CH_3), 64.6 (CH_2), 121.4 (C) 127.3 (CH), 127.9 (CH), 128.1 (CH), 128.3 (CH), 129.7 (CH), 132.1 (CH), 133.4 (CH), 137.5 (C), 139.8 (C). GC analysis[37a] showed major peaks at 16.2 min (92.0%, **1c**), 17.5 min (2.8%), and 20.8 min (1.6%).

4.3. *o*-(Phenyldimethylsilyl)benzyl alcohol (2c)

To a solution of 2.87 g (8.94 mmol) of phenylsilyl ether **1c** in 50 mL of anhydrous ether was added 1.00 g (143 mmol) of lithium wire. The reaction mixture was stirred at rt for 2 h and then decanted from the excess lithium into 150 mL of saturated $NaHCO_3$. The aqueous layer was extracted with ether (2×20 mL). The combined organic layers were dried ($MgSO_4$), concentrated, chromatographed on silica gel (petroleum ether/ether 9:1; then 1:1), and placed under oil pump vacuum (2 h, 0.1 mm) to give 2.13 g (98% yield) of phenylsilyl alcohol **2c**[16a] as a clear and colorless oil. GC analysis[37a] showed the major peak at 14.9 min (97%); $C_{18}H_{38}$ at 14.2 min; GC/MS *m*/*z* (relative intensity, tentative assignment): 242 (not visible, M^+), 227 (50, M^+-CH_3), 209 (100), 181 (10), 165 (67, $M^+-C_6H_5$), 149 (40), 147 (30), 105 (28, $C_6H_5Si^+$), 91 (34, $C_7H_7^+$), 77 (72, $C_6H_5^+$). The IR, ^1H NMR, and ^{13}C NMR spectra correspond to those reported.[16a]

4.4. Reaction of the benzyldimethylsilyl ether (1a) of *o*-bromobenzyl alcohol with diisopropylamine and benzaldehyde: isolation of *o*-(benzyldimethylsilyl)benzaldehyde (13) and benzyl alcohol

To a solution of 0.214 g (0.639 mmol) of benzylsilyl ether **1a** in 10 mL of anhydrous ether was added 0.10 g (14.3 mmol) of lithium wire. The resulting mixture was stirred at rt for 2 h. The liquid mixture (cloudy light violet) was transferred via cannula into a new reaction flask. Benzaldehyde (0.09 mL, 0.89 mmol) was added via syringe followed by 0.5 mL (3.6 mmol) of diisopropylamine. The reaction mixture was allowed to stir at rt, and was followed by GC analysis of aliquots. After 1.5 h, GC analysis[37a] showed major peaks at 2.9 min (41%, PhCHO), 3.4 min (8%, $PhCH_2OH$), 15.4 min (22%, aldehyde (**13**)), and 16.2 min (27%, benzylsilyl alcohol **2a**). After 24 h, the remaining reaction mixture was added to 50 mL of saturated $NaHCO_3$. The aqueous layer was extracted with ether (2×10 mL), and the combined organic layers were washed with water (2×20 mL), brine (20 mL), and then dried ($MgSO_4$). GC analysis[37a] showed major peaks at 3.0 min (19%, PhCHO), 3.4 min (14%, $PhCH_2OH$), 15.5 min (45%, **13**), and 16.3 min (6%, **2a**). The crude product was chromatographed (30 g of silica gel, 19.4×2.4 cm, hexanes followed by hexanes/ethyl acetate 7:3) to give 0.022 g (13% yield) of *o*-(benzyldimethylsilyl)benzaldehyde (**13**) as a clear colorless oil having 100% GC purity[37a] (15.5 min; $C_{22}H_{46}$ at 18.5 min). A second fraction was further purified by bulb-to-bulb distillation (100 °C, 0.15–0.2 mm) to give 0.028 g (17.3% yield) of **13** as a clear colorless oil having 96% GC purity (total yield 30%). Compound **13** had the following spectra: IR (film): 3024, 2955, 2733, 1707, 1599, 1561, 1492, 1294, 1246, 1203, 827, 798, 755, 700 cm^{-1}; ^{13}C NMR (75 MHz): δ −1.8, 25.8, 124.1, 128.1, 128.4, 129.5, 132.9, 133.0, 136.1, 139.9, 140.8, 141.3, 193.4; GC/MS *m*/*z* (relative intensity, tentative assignment): 254 (not visible, M^+), 239 (5, M^+-CH_3), 163 (100, M^+-benzyl), 91 (20, $C_7H_7^+$). The ^1H NMR spectrum was in complete agreement with that reported for compound **13**.[39]

Further fractions were combined to give 0.031 g (44% yield) of benzyl alcohol as a clear and colorless oil, having 99% GC purity, and identified by IR, ^1H NMR, and ^{13}C NMR comparison with a commercial sample.

4.5. Reaction of the allyldimethylsilyl ether (1b) of *o*-bromobenzyl alcohol with benzaldehyde: 1-phenyl-3-buten-1-ol (8)

To a solution of 0.257 g (0.902 mmol) of the allylsilyl ether **1b** in 5 mL of anhydrous ether was added 0.10 g (14.3 mmol) of lithium wire. The resulting mixture was stirred at rt for 2 h. The liquid mixture was transferred via cannula into a new reaction flask. Benzaldehyde (0.06 mL, 0.59 mmol) was added followed by 5 mL of THF. After 3 h at rt, GC analysis[37a] of an aliquot showed major peaks at 5.3 min (51%, oxasilacyclopentane **5**) and 6.2 min (40%, **8**). After 3.5 h, the reaction mixture was added to 40 mL of saturated $NaHCO_3$. The aqueous layer extracted with ether (2×10 mL), and the combined organic layers were dried ($MgSO_4$) and concentrated, and chromatographed twice (6 g of silica gel, 18.4×1 cm, petroleum ether/ether 18:1). The product was placed under oil pump vacuum (2 h, 0.03–0.05 mm) to give 0.085 g (97% yield) of homoallyl alcohol **8** as a clear and colorless oil. GC analysis showed a GC purity of 98%. The IR, ^1H NMR and ^{13}C NMR spectra, and GC retention time were equivalent to those of the comparison sample of **8**.

4.6. Reaction of the allyldimethylsilyl ether (1b) of *o*-bromobenzyl alcohol with benzophenone: 1,1-diphenyl-3-buten-1-ol (9)

In a procedure similar to that for the conversion of **1b** to **8** (0.240 g (0.842 mmol) of allylsilyl ether **1b**, 5 mL of anhydrous ether, 0.10 g (14.3 mmol) of lithium, 2 h, rt; then liquid cannulated into 0.1135 g (0.6236 mmol) of benzophenone, 5 mL of THF, 8 h, rt), 0.127 g (91% yield) of homoallyl alcohol **9** was obtained as a clear and colorless oil having IR, ^1H NMR, ^{13}C NMR, and mass spectra equivalent to those reported.[23] GC analysis[37a] showed one major peak at 13.8 min (96%); $C_{22}H_{46}$ at 18.5 min.

4.7. Reaction of *o*-(benzyldimethylsilyl)benzyl alcohol (2a) with benzaldehyde: 1,2-diphenylethanol (6)

To an ice-cooled solution of 0.232 g (0.905 mmol) of *o*-benzylsilyl alcohol **2a** in 9 mL of anhydrous ether was added 0.36 mL (0.9 mmol) of *n*-butyllithium (2.5 *M* in hexanes) dropwise. The resulting mixture was stirred for 0.5 h at 0 °C. Benzaldehyde (0.06 mL, 0.59 mmol) was added followed by 9 mL of THF. The ice bath was removed and the reaction mixture was stirred at rt.

After 3 h, GC analysis[37b] of an aliquot showed major peaks at 5.6 min (56%, oxasilacyclopentane **5**) and 12.7 min (39%, **6**). After 3.5 h, the reaction mixture was added to 40 mL of saturated

$NaHCO_3$. The aqueous layer extracted with ether (2×10 mL), and the combined organic layers were dried ($MgSO_4$), concentrated, and chromatographed twice (15 g of silica gel, 7.5×2.5 cm, hexanes/ethyl acetate 9:1). The product was placed under oil pump vacuum (1.5 h, 0.03 mm) to give 0.110 g (94% yield) of alcohol **6** as a white solid, mp 62.4–63.1 °C (lit.[40] mp 64–65.5 °C). GC analysis[37b] showed one major peak at 12.2 min (99%); $C_{22}H_{46}$ at 17.9 min. The IR, ^{1}H NMR and ^{13}C NMR spectra were equivalent to those of the comparison sample of **6**.

4.8. Reaction of *o*-(benzyldimethylsilyl)benzyl alcohol (2a) with benzophenone: 1,1,2-triphenylethanol (7)

To an ice-cooled solution of 0.233 g (0.907 mmol) of benzylsilyl alcohol **2a** in 9 mL of anhydrous ether was added 0.36 mL (0.9 mmol) of *n*-butyllithium (2.5 *M* in hexanes) dropwise. The resulting mixture was stirred for 0.5 h at 0 °C. Benzophenone (0.111 g, 0.606 mmol) was added followed by 9 mL of THF. The ice bath was removed and the reaction mixture was stirred at rt.

After 3 h, GC analysis[37b] of an aliquot showed major peaks at 5.1 min (48%, oxasilacyclopentane **5**) and 18.6 min (49%, **7**). After 3.5 h, the reaction mixture was added to 40 mL of saturated $NaHCO_3$. The aqueous layer extracted with ether (2×10 mL), and the combined organic layers were dried ($MgSO_4$), concentrated, and chromatographed twice (15 g of silica gel, 7.4×2.5 cm, petroleum ether/ether 15:1). The product was placed under oil pump vacuum (2 h, 0.025 mm) to give 0.153 g (92% yield) of alcohol **7** as a white solid: mp 85.6–86.4 °C (lit.[41] mp 87–89 °C). GC analysis[37b] showed one major peak at 18.7 min (92%); $C_{24}H_{50}$ at 20.3 min. The IR, ^{1}H NMR, and ^{13}C NMR spectra were equivalent to those of the comparison sample of **7**.

[In a preliminary experiment, the peak at 5.1 min in the GC was assigned as oxasilacyclopentane **5** from the mass spectrum: *m*/*z* 164 (33), 149 (100), 105 (10), 89 (6), which is equivalent to that reported[15] (and the peak at 18.6 min in the GC had the mass spectrum of **7**)].

In an early experiment in which benzylsilyl alcohol **2a** was used as the limiting reagent, GC/MS of the crude product showed major peaks in the GC at 5.2 min (oxasilacyclopentane **5**), 9.2 min (benzophenone), 10.6 min, and 12.4 min (1,1,2-triphenylethanol (**7**)). The peak at 10.6 min was tentatively assigned as 1,1-diphenylpentan-1-ol (**14**) and had the following mass spectrum: *m*/*z* 240 (0.1, M^+), 222 (28, M^+-H_2O), 193 (40, M^+-H_2O-Et), 183 (100, M^+-Bu), 105 (37).

4.9. Reaction of *o*-(phenyldimethylsilyl)benzyl alcohol (2c) with benzaldehyde: benzhydrol (10)

To an ice-cooled solution of 0.364 g (1.503 mmol) of phenylsilyl alcohol **2c** in 9 mL of anhydrous ether was added 0.6 mL (1.5 mmol) of *n*-butyllithium (2.5 M in cyclohexane) dropwise. The resulting mixture was stirred for 0.5 h at 0 °C. Benzaldehyde (0.10 mL, 0.984 mmol) was added followed by 9 mL of THF and 1.1 mL (6.32 mmol) of HMPA. The ice bath was removed and the reaction mixture was stirred at rt. After 3 h, GC analysis[37a] of an aliquot showed major peaks at 2.9 min (11%, PhCHO), 4.9 min (16%, oxasilacyclopentane **5**), 11.9 min (11%, benzhydrol (**10**)), and 14.9 min (43%, **2c**). After 8 h, GC analysis[37a] of an aliquot showed major peaks at 3.0 min (2.6%, PhCHO), 5.0 min (16%, **5**), 12.1 min (19%, **10**), and 15.0 min (23%, **2c**). Under the same conditions a commercial sample of benzhydrol (**10**) had a retention time of 12.1 min.

After 10 h, the reaction mixture was added to 40 mL of saturated $NaHCO_3$. The aqueous layer extracted with ether (2×10 mL), and the combined organic layers were washed with water (2×40 mL), brine (40 mL), dried ($MgSO_4$), and concentrated. The crude product was chromatographed (20 g of silica gel, 13×2.4 cm, hexanes followed by hexanes/ethyl acetate 8:2) to give a solid product, which was recrystallized from hexanes and placed under oil pump vacuum (2 h, 0.2–0.6 mm) to give 0.051 g (28% yield) of benzhydrol (**10**) as a white solid, mp 63.0–64.6 °C (lit.[42] mp 65.5–66 °C). The IR, ^{1}H NMR, ^{13}C NMR, and mass spectrum, and GC retention time were equivalent to those of a commercial sample of **10**.

4.10. Allyldimethylsilyl ether (15) of (*S*)-(−)-2-bromo-α-methylbenzyl alcohol

In a procedure analogous to that for the preparation of phenylsilyl ether **1c**, allylsilyl ether **15** was prepared from 1.011 g (5.026 mmol) of (*S*)-(−)-2-bromo-α-methylbenzyl alcohol (25 mL of anhydrous ether, 1.0 mL (7.2 mmol) of triethylamine, 1.0 mL (5.2 mmol) of allyldimethylchlorosilane, 19 h, rt). Chromatography (25 g of silica gel, 16×2.4 cm, petroleum ether/ether 9:1) gave 1.019 g (68% yield) of **15** as a clear and colorless oil: IR (film): 3076, 2974, 2926, 1631, 1469, 1255, 1131, 1097, 1023, 957, 843, 754 cm^{-1}; ^{1}H NMR (400 MHz, acetone as standard at δ 2.09): δ 0.00 (s) and 0.02 (s) (total 6H), 1.32 (d, *J*=6.2 Hz, 3H), 1.51 (appears as d, *J*=7.9 Hz, 2H), 4.82–4.72 (m, 2H), 5.16–5.08 (m, 1H), 5.72–5.59 (m, 1H), 7.01 (t, *J*=7.55 Hz, 1H), 7.23 (t, *J*=7.4 Hz, 1H), 7.39 (d, *J*=7.7 Hz, 1H), 7.51 (d, *J*=7.7 Hz, 1H); ^{13}C NMR (100 MHz): δ −2.1 (CH_3), 24.7 (CH_2), 25.4 (CH_3), 69.8 (CH), 113.7 (CH_2), 120.8 (C), 127.4 (CH), 127.6 (CH), 128.3 (CH), 132.2 (CH), 133.8 (CH), 145.4 (C). GC analysis[37a] showed a major peak at 12.9 min (99%); $C_{24}H_{50}$ at 23.5 min. A second chromatography fraction (0.114 g, 8% yield) had a GC purity of 97%. The combined yield was 76%.

4.11. Reaction of the allyldimethylsilyl ether (15) of (*S*)-(−)-2-bromo-α-methylbenzyl alcohol with benzaldehyde: 1-phenyl-3-buten-1-ol (8)

In a procedure similar to that for the conversion of **1b** to **8**, 0.280 g (0.936 mmol) of **15** in 5 mL of anhydrous ether was treated with 0.10 g (14.3 mmol) of lithium wire (1.5 h, rt); then 0.07 mL (0.69 mmol) of benzaldehyde in 5 mL of THF, (8 h, rt). The crude product was chromatographed (6 g of silica gel, 18.6×0.9 cm, hexanes/ethyl acetate 18:1) to give homoallyl alcohol **8** as a slightly yellow oil. GC analysis using a chiral column[37c] showed major peaks at 12.4 min (40%) and 13.0 min (40%). (The comparison sample of **8** (racemic) showed 12.5 min (52%) and 13.1 min (48%).) The product was rechromatographed (15 g of silica gel, 9.5×2.4 cm, hexanes/ethyl acetate 18:1), and the product placed under oil pump vacuum (2 h, 0.05 mm) to give 0.085 g (83% yield) of 1-phenyl-3-buten-1-ol (**8**) as a clear and colorless oil. GC analysis[37a] showed a major peak at 6.5 min (97%). The mass spectrum was equivalent to that of the comparison sample of **8**.

4.12. (*Z*)-Crotyldimethylsilyl ether (1d) of *o*-bromobenzyl alcohol

In a procedure analogous to that for the preparation of silyl ether **1c**, crotylsilyl ether **1d** was prepared from 4.003 g (21.40 mmol) of *o*-bromobenzyl alcohol (75 mL of anhydrous ether, 4.0 mL (28.7 mmol) of triethylamine, 3.45 g (23.2 mmol) of (*Z*)-crotyldimethylchlorosilane, 2 h, rt) giving 6.026 g (94% yield) of **1d** as a clear and colorless oil: IR (film) 3069, 3016, 2958, 2918, 2883, 1649, 1570, 1467, 1442, 1376, 1252, 1120, 1097, 1026, 859, 840, 748 cm^{-1}; ^{1}H NMR (400 MHz, $CHCl_3$ as standard at δ 7.24): δ 0.18 (s, 6H), 1.55–1.60 (crude d, $J\approx6$ Hz, 3H), 1.62–1.68 (crude d, $J\approx8$ Hz, 2H), 4.73 (s, 2H), 5.35–5.50 (m, 2H), 7.10 (t, *J*=7.6 Hz, 1H), 7.31 (t, *J*=7.6 Hz, 1H), 7.55–7.45 (m, 2H); ^{13}C NMR (100 MHz): δ −2.2 (CH_3), 12.7 (CH_3), 17.8 (CH_2), 64.4 (CH_2), 121.2 (C), 122.5 (CH), 124.8 (CH), 127.3 (CH), 127.8 (CH), 128.3 (CH), 132.1 (CH),

139.9 (C). GC analysis[37b] showed a major peak at 12.7 min (96%); $C_{24}H_{50}$ at 21.3 min.

4.13. *o*-((*Z*)-Crotyldimethylsilyl)benzyl alcohol (2d)

To a solution of 3.000 g (10.025 mmol) of crotylsilyl ether **1d** in 50 mL of anhydrous ether was added 0.70 g (101 mmol) of lithium wire. The reaction mixture was stirred at rt for 2 h, and then added to 100 mL of saturated $NaHCO_3$. The aqueous layer was extracted with ether (2×20 mL), and the combined organic layers were dried ($MgSO_4$), concentrated, and chromatographed (40 g of silica gel, 19.0×2.5 cm, petroleum ether/ether 9:1) giving 1.274 g (58% yield) of crotylsilyl alcohol **2d** as a clear and colorless oil: IR (film): 3318 (br), 3057, 3014, 2957, 1650, 1436, 1397, 1250, 1150, 1079, 837, 750 cm^{-1}; ^1H NMR (400 MHz, 1,4-dioxane as standard at δ 3.71): δ 0.40 (s, 6H), 1.58 (d, J=5.1 Hz, 3H), 1.84 (d, J=7.4 Hz, 2H), 2.01 (s, 1H), 4.80 (s, 2H), 5.51–5.39 (m, 2H), 7.33 (td, J=7.4, 1.0 Hz, 1H) 7.44 (td, J=7.5, 1.2 Hz, 1H), 7.51 (d, J=7.6 Hz, 1H), 7.58 (dd, J=7.2, 0.7 Hz, 1H); ^{13}C NMR (100 MHz): δ −1.6 (CH_3), 12.6 (CH_3), 17.7 (CH_2), 65.4 (CH_2), 122.3 (CH), 125.9 (CH), 127.0 (CH), 127.9 (CH), 129.6 (CH), 135.0 (CH), 136.8 (C), 146.2 (C); GC/MS *m*/*z* (relative intensity, tentative assignment): 220 (not visible, M^+), 165 (63, M−crotyl), 147 (100), 145 (58). HRMS (ESI) calcd for $C_{13}H_{20}OSiNa$ (M+Na), 243.1181. Found, 243.1183. (For examples of mass spectra of similar compounds, see Ref. [13].) GC analysis[37a] showed a major peak at 12.1 min (98%); $C_{24}H_{50}$ at 21.7 min. From earlier chromatography fractions was obtained an additional 0.604 g (27% yield) of **2d** as a clear and colorless oil, which was 85% pure by GC.

4.14. Reaction of *o*-((*Z*)-crotyldimethylsilyl)benzyl alcohol (2d) with benzaldehyde: 1-phenyl-3-penten-1-ol (11) and 2-methyl-1-phenyl-3-buten-1-ol (12s and 12a)

To an ice-cooled solution of 0.317 g (1.437 mmol) of the crotylsilyl alcohol **2d** in 9 mL of anhydrous ether was added 0.60 mL (1.5 mmol) of *n*-butyllithium (2.5 *M* in hexanes) dropwise. The resulting mixture was stirred for 0.5 h at 0 °C. Benzaldehyde (0.12 mL, 1.18 mmol) was added followed by 9 mL of THF. The ice bath was removed and the reaction mixture was stirred at rt for 18.5 h, then added to 40 mL of saturated $NaHCO_3$. The aqueous layer was extracted with ether (2×10 mL), and the combined organic layers were dried ($MgSO_4$). GC analysis[37b] showed major peaks at 5.5 min (50%, oxasilacyclopentane **5**), 7.3 min (25%, *syn* and *anti* isomers of **12**: **12s**, **12a**), and 8.05, 8.14 min (4%, 15%, not well resolved, **11** (*E* and *Z*)). The product was quickly chromatographed on silica gel to remove oxasilacyclopentane **5**, and then purified by bulb-to-bulb distillation (90 °C, 0.25 mm) to give 0.169 g (88% yield) of a clear and colorless oil as a mixture of **11** (*E* and *Z*) and **12** (*syn* and *anti*). GC analysis[37b] showed major peaks at 7.1 min (55%, **12s**, **12a**) and 7.8, 7.9 min (7%, 28%, not well resolved, **11** (*E* and *Z*)). The proton NMR spectrum of the oil showed peaks that are consistent with the purified isomers of **11** and **12** (below). The oil was chromatographed (8 g of silica gel, petroleum ether/ether 9:1) to give (a) 0.053 g (28% yield) of **12**, (b) 0.060 g of a mixture of **11** and **12**, and (c) 0.026 g (14% yield) of **11**, all as clear and colorless oils.

The first portion (a) had IR, ^1H NMR, and ^{13}C NMR spectra consistent with a mixture of **12s** and **12a**. In particular, the peaks in the ^1H NMR were those of the reported[43] spectra of the *syn* and *anti* isomers of **12**; the integration (especially the peaks at δ 0.87, 1.01, 4.35, 4.61) indicated a *syn*/*anti* ratio of 1.5–1.7/1. GC analysis[37b] gave major peaks at 7.3 min (96%, **12s**, **12a**) and 8.1 min (2%).

The second portion (b) in the GC analysis[37b] showed major peaks at 7.4 min (60%, **12**) and 8.1, 8.2 min (14%, 25%, not well resolved, **11** (*E* and *Z*)).

The third portion (c) had ^1H NMR, and ^{13}C NMR spectra containing all of the peaks reported for (*Z*)-1-phenyl-3-penten-1-ol (**11**),[44] with a few additional smaller peaks in the NMR spectra. The IR spectrum had only a very small shoulder at 963 cm^{-1} (possibly *E* isomer) suggesting the major isomer was *Z*. (For the IR spectra of the *E* and *Z* isomers of **11**, see ref 45.) GC analysis[37b] gave major peaks at 8.1, 8.2 min (14%, 81%, not well resolved, **11** (*E* and *Z*)).

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