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[(*E*)-γ-(Dimethylphenylsilyl)allyl]diisopinocampheylborane: a highly enantioselective reagent for the synthesis of *anti*-β-hydroxyallylsilanes†

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Abstract

anti-β-Hydroxyallylsilanes are prepared with 88–95% e.e. via the asymmetric allylboration reactions of aldehydes and [(*E*)-γ-(dimethylphenylsilyl)allyl]diisopinocampheylborane (**7**). © 2000 Published by Elsevier Science Ltd.

In 1990 we introduced diisopropyl 2-[(*E*)-γ-(dimethylphenylsilyl)]allyl-1,3,2-dioxaborolane-4,5-dicarboxylate (**1**) as a reagent for the formal γ-hydroxyallylation of aldehydes.[1,2] This process involved allylboration of aldehydes using **1** to give the *anti*-β-hydroxyallylsilanes **3** which were epoxidized with dimethyldioxirane. Subsequent treatment of the intermediate epoxysilane with acetic acid effected Peterson elimination, thereby providing the targeted diols **4** in excellent yield. Other γ-silylallylboronate reagents—with different substituents on silicon—were developed in our laboratory to permit Fleming–Tamao oxidation to be performed at the stage of **3**, thereby facilitating the synthesis of *anti*-3,4-but-1-enediols.[2–4] Of greater significance is the realization that this allylboration sequence constitutes an exceptionally simple route to chiral, non-racemic allylsilanes which are of interest as reagents for subsequent C–C bond forming events.[5,6] For example, we recently demonstrated that the *anti*-β-hydroxyallylsilanes, after conversion to a silyl ether (e.g. **5**), undergo highly diastereoselective Lewis acid promoted [3+2]-additions to aldehydes.[7] A representative example is the chelate controlled addition of **5** to benzyloxyacetaldehyde, which provides tetrahydrofuran **6** with >20:1 diastereoselectivity. Additional applications of *anti*-β-hydroxyallylsilanes as nucleophilic chiral allylmetal reagents are under investigation in our laboratory.[8]

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† This paper is dedicated to Professor Harry H. Wasserman on the occasion of his 80th birthday.

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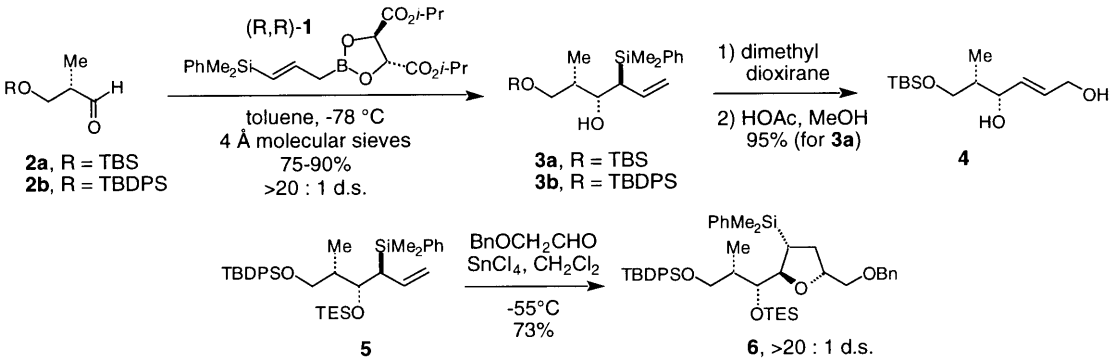
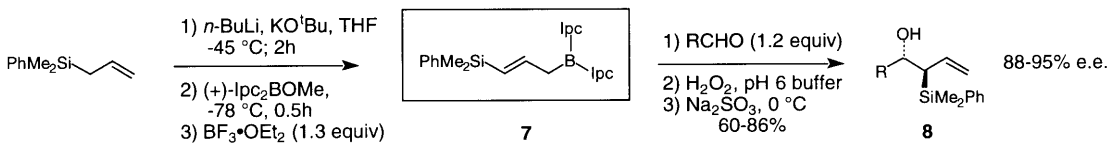


This exceptionally simple synthesis of chiral allylsilanes, illustrated by the conversion of **2** to **3**, is a potentially important addition to the allylsilane literature since highly diastereo- and enantioselective syntheses of chiral allylsilanes are not generally available, especially for the parent allylsilanes lacking substituents on the vinyl group.[5,9,10] However, while the reactions of **1** with chiral aldehydes proceed with excellent diastereoselectivity,[2] especially when performed in the stereochemically matched manifold,[11] this reagent has proven to be only moderately enantioselective in reactions with achiral aldehydes (75–87% e.e. with the most favorable classes of substrates).[7,12] Therefore, we elected to develop a new reagent, [(*E*)-γ-(dimethylphenylsilyl)allyl]diisopinocampheylborane (**7**), which incorporates the diisopinocampheylboranyl chiral auxiliary developed by H. C. Brown and coworkers.[13] Allylboranes incorporating this group have consistently proven to be more enantioselective than those based on the tartrate ester auxiliary in **1**.[14,15] Accordingly, we expected that the new reagent **7** would provide access to the targeted *anti*-β-hydroxyallylsilanes from achiral aldehydes with excellent enantioselectivity.[4,16]

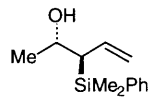
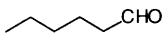
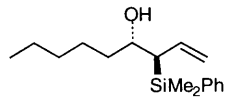
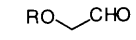
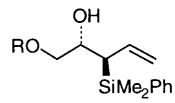
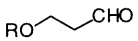
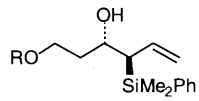
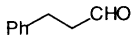
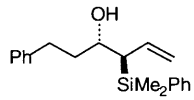
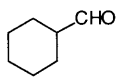
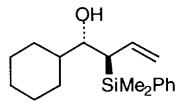
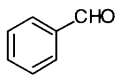
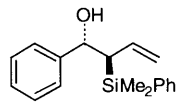
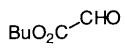
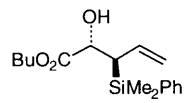
Reagent **7** was synthesized by metallation of allyldimethylphenylsilane[17] with *n*-BuLi and KO*t*Bu (1 equiv. each) in THF at –45°C,[2] followed by addition of *B*-methoxydiisopinocampheylborane (Ipc_2BOMe).[18] The mixture was stirred at –78°C for 30 min, then $BF_3{\cdot}OEt_2$ (1.3 equiv.) was added to sequester MeOLi/MeOK and generate a –78°C solution of reagent **7** to which was added a slight excess of aldehyde (typically 1.2 equiv.). The reaction mixture was stirred at –78°C for 4 h, then was worked up oxidatively to give the product β-hydroxyallylsilanes **8** in 60–86% yields following purification by silica gel chromatography. In no cases did we observe any of the diastereomeric *syn*-β-hydroxyallylsilanes. As shown in Table 1,[19] each of the *anti*-β-hydroxy allylsilanes was obtained with an enantiomeric purity of 88–95% e.e., as determined by Mosher ester analysis[20] or ^1H NMR chiral shift studies. In one case (reaction with hydrocinnamaldehyde), the product % e.e. was confirmed by chiral HPLC analysis.[8] Stereochemical assignments for allylsilanes **8a**, **8b**, **8e** and **8f** were made by comparison with spectroscopic data for samples previously generated in our laboratory.[2,7] Absolute stereochemical assignments for **8e** and **8h** were made by using the Mosher method,[21] thereby confirming that the sense of asymmetric induction of the Ipc auxiliary is the same in reagent **7** as for other allylboranes containing this directing group.[13] All other stereochemical assignments were made by analogy to the cases outlined here.



The results summarized in Table 1 clearly indicate that reagent **7** is substantially more enantioselective than **1** (comparative enantioselectivity data for reactions performed with the tartrate ester modified γ-silylallylboronate **1** are included in Table 1).[2,7] In principle, even higher levels of enantiomeric purity should be achievable by using the carene-derived auxiliaries developed by Brown,[22] if the enantioselectivity obtained using **7** is insufficient for a specific synthetic problem. It should also be possible to incorporate other substituents at silicon,[2–4] in order to fine tune the reactivity of the allylsilane reagent for subsequent C–C or C–X bond forming events.

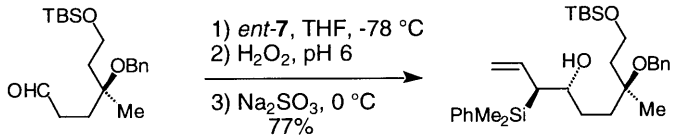
Although we have concentrated here on the synthesis of β-hydroxyallylsilanes **8** from achiral aldehydes, it is expected that reagent **7** will also be useful in reactions with chiral aldehydes. One such example is summarized below, in which aldehyde **9** with a remote chiral quaternary center

Table 1
Enantioselective reactions of achiral aldehydes with **7**

Entry	Aldehyde	Yield	Product	Enantioselectivity
a	Me—CHO	80%		93% e.e. (84% e.e.)[a]
b		86%		95% e.e. (81% e.e.)[a]
c		85% 70%		88% e.e.[b] (R = Bn) 90% e.e. (R = TBDPS)
d		72% 74%		95% e.e. (R = PMB) 90% e.e.[b] (R = Bn)
e		76%		95% e.e. (75% e.e.)[a]
f		85%		91% e.e. (87% e.e.)[a]
g		81%		93% e.e.
h		60%		95% e.e

(a) Enantioselectivity obtained using the tartrate ester modified γ-silylallylboronate, **1**.
(b) % E.e. determined via ^{1}H NMR chiral shift analysis using Eu(hfc)$_3$.

was used as the substrate. This reaction, using *ent*-**7** prepared from (–)-Ipc_2BOMe, provided the β-hydroxyallylsilane **10** with 90:10 diastereoselectivity. The seemingly low selectivity of this reaction is a direct consequence of the fact that the enantiomeric purity of **9** was only 92% e.e. The observed diastereoselectivity is consistent with reagent *ent*-**7** functioning at a ≥90% e.e. level in this reaction, with the minor enantiomer of **9** being funneled selectively into the minor product diastereomer, and with the enantiomeric purity of the major product (**10**) being correspondingly enhanced.[23]



9 (92% e.e.) **10** (90 : 10 d.r.)

A representative experimental procedure follows. Potassium *t*-butoxide (177 mg, 1.58 mmol, 1 equiv.) was dissolved in dry THF (3 mL) and cooled to −78°C. Phenyldimethylallylsilane (0.35 mL, 1.74 mmol, 1.1 equiv.) was added via syringe in one portion followed by dropwise addition of *n*-BuLi (0.73 mL of 2.16 M solution in hexanes, 1.58 mmol, 1 equiv.) over 5 min. The mixture was stirred at −78°C for 10 min, then the flask was transferred into a −45°C bath (dry ice–acetonitrile) and stirred for 2 h. The flask was returned to the −78°C bath and freshly prepared[18] (+)-Ipc_2BOMe (500 mg, 1.58 mmol, 1 equiv.; generated from recrystallized Ipc_2BH) in THF (2 mL) was added slowly via cannula. The mixture was stirred at −78°C for 30 min, then $BF_3{\cdot}OEt_2$ (0.26 mL, 2.06 mmol, 1.33 equiv.) was added dropwise followed immediately by slow addition of neat hexanal (0.23 mL, 1.9 mmol, 1.2 equiv.). After being stirred at −78°C for 4 h, the reaction mixture was diluted with 1 M KH_2PO_4–KOH buffer (3 mL; pH 6) and 30% H_2O_2 (1 mL). The cooling bath was removed and the reaction mixture was stirred at ambient temperature for 1 h, then cooled to 0°C and aqueous 1 M Na_2SO_3 solution (7 mL) was added portionwise to destroy excess H_2O_2 (exothermic!). The resulting mixture was stirred for 15 min at 0°C, then was extracted with ethyl acetate and washed with $NaHCO_3$ solution, dried over Na_2SO_4 and concentrated in vacuum. The residue was purified by chromatography over silica gel using hexane–ether (95:5 to 90:10) mixtures as eluant to afford the product **8b** as a colorless oil, 377 mg (86% yield, based on Ipc_2BOMe), $[\alpha]_D = +2°$ (*c* 2.4, $CHCl_3$), with an enantiomeric purity of 95% e.e. based on Mosher ester analysis. In cases where separation of the allylation product from residual aldehyde is difficult (as in the reaction using benzaldehyde as substrate), the excess aldehyde was removed by treatment of the crude material with $NaBH_4$ in THF–MeOH at 0°C prior to chromatographic purification.

In summary, we have demonstrated that the chiral γ-silylallylborane **7** undergoes highly enantioselective reactions with a range of achiral aldehydes, thereby providing general access to enantiomerically enriched β-hydroxyallylsilanes which are of interest for a range of C–C bond forming processes. Additional studies using these compounds as reagents for organic synthesis will be reported in due course.

Acknowledgements

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