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Benzhydryldimethylsilyl Allylic Silanes: Syntheses and Applications to [3 + 2] Annulation Reactions

Zhi-Hui Peng and K. A. Woerpel*

Department of Chemistry, University of California, Irvine, California 92697-2025

kwoerpel@uci.edu

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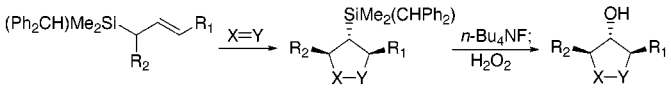
ABSTRACT



A new silyl group, the benzhydryldimethylsilyl group, has been developed that is easily synthesized and that undergoes facile oxidation. The [3 + 2] annulation reactions of allylic silanes with this silyl group provide a variety of highly substituted five-membered carbocycles and heterocycles with high stereoselectivities. The silyl groups of these cyclic compounds have been oxidized to hydroxyl groups to demonstrate the general synthetic utility of the method.

The [3 + 2] annulation reactions of allylic silanes[1] have received much attention because they provide highly stereoselective methods for the synthesis of functionalized five-membered-ring carbocycles and heterocycles.[2−8] Sterically demanding silyl groups have been previously employed to retard elimination processes[9] and thus to favor the silyl migration leading to the [3 + 2] annulation products. The use of these hindered silanes has created other difficulties, such as attenuated reactivity of the allylic silane and difficult removal of the silyl moiety from the annulation product.[10] Meyers et al. have introduced the trityldimethylsilyl moiety as a solution to these problems, because the allylic silane bearing this group is highly reactive, and the trityl unit may be removed as trityl anion by fluoride ion, making this silane readily oxidizable.[5b,c]

Although we had hoped to make use of the trityldimethylsilyl group in our own investigations of allylic silane annulation chemistry,[7a] this moiety was not ideal for the applications we envisioned. We required a short synthesis of the silyl group, preferably as the silyl halide, but the synthesis of trityldimethylsilyl bromide required three steps.[11] In addition, the exceedingly large silyl moiety was anticipated to be incompatible with our method for making highly substituted allylic silanes by allylic substitution reactions.[12] In this Letter, we describe the annulation reactions of allylic silanes bearing the benzhydryldimethylsilyl group for the synthesis of cyclopentanes,[2,5] tetrahydrofurans,[4,6] and pyr-

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(8) Other annulation pathways are also possible. For [2 + 2] annulations, see: (a) Akiyama, T.; Kirino, M. *Chem. Lett.* **1995**, 723−724. (b) Knölker, H.-J.; Baum, G.; Graf, R. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1612−1615. For a formal [4 + 2] annulation, see: Angle, S. R.; El-Said, N. A. *J. Am. Chem. Soc.* **1999**, *121*, 10211−10212.
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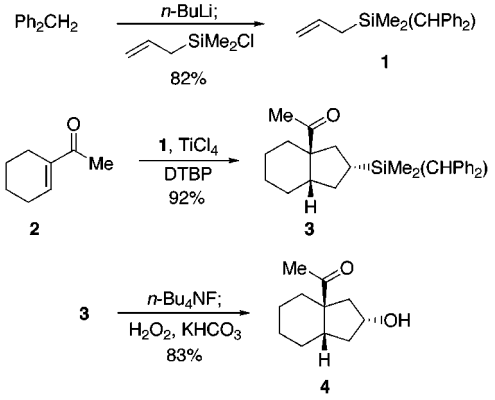
rolidinones.[7] This silyl group has several attributes that render it well suited for annulation processes: (1) it can be easily introduced to allylic silanes, including highly substituted allylic silanes; (2) it is bulky enough to suppress Sakurai-type products[9] and to obtain [3 + 2] annulation products with a variety of electrophiles; (3) it is tolerant to a variety of synthetic procedures; and (4) it can be easily oxidized to a hydroxyl group under mild conditions.

The utility of the benzhydryldimethylsilyl moiety was demonstrated by the reactions of the simplest allylic derivative allylbenzhydryldimethylsilane **1** with α,β-unsaturated ketones. Allylbenzhydryldimethylsilane **1** could be prepared by deprotonation of diphenylmethane followed by quenching with commercially available allyldimethylchlorosilane (82% yield, Scheme 1). The $TiCl_4$-promoted [3 + 2] annulation

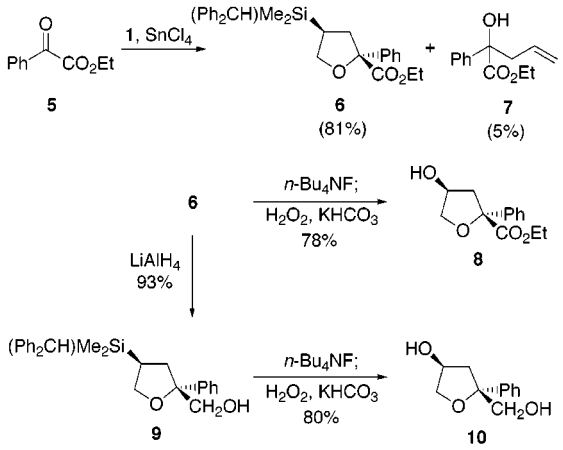
Scheme 1



of allylic silane **1** with enone **2** in the presence of 2,6-di-*tert*-butylpyridine (DTBP) provided entirely the annulation product **3** in 92% yield (Scheme 1).[2,5b,c,13] Meyers' procedure for the oxidation of the trityldimethylsilyl group[5b,c] oxidized the corresponding benzhydryldimethylsilyl group smoothly.[14] Treatment of silane **3** with *n*-Bu_4NF displaced the benzhydryl group,[15] and the resulting reaction mixture was exposed to the Tamao conditions to yield alcohol **4** in high yield.

Allylbenzhydryldimethylsilane **1** can be used for the synthesis of five-membered heterocycles as well as carbocycles. The [3 + 2] annulation of **1** and α-keto ester **5**[4a] gave tetrahydrofuran **6** in 81% yield (Scheme 2).[13] Only 5% of the Sakurai product **7** was obtained, again indicating that

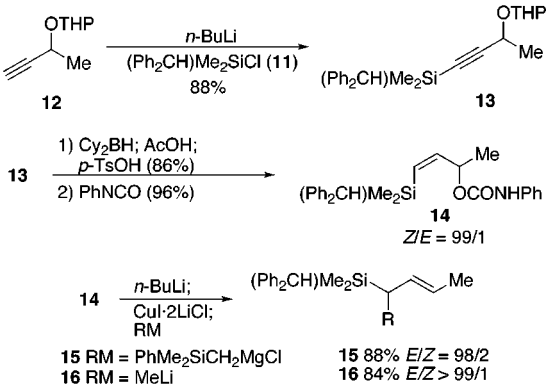
Scheme 2



the benzhydryldimethylsilyl group was sufficiently bulky to undergo the 1,2-silyl migration over nucleophilic attack. The benzhydryldimethylsilyl group of tetrahydrofuran **6** was oxidized to afford alcohol **8** in good yield (Scheme 2). To demonstrate that the benzhydryldimethylsilyl group could withstand strongly reducing conditions, the ester moiety of **6** was reduced to provide alcohol **9** in high yield. Oxidation of **9** provided diol **10** cleanly.

Having demonstrated the utility of the simple benzhydryldimethylsilyl allylic silane in the [3 + 2] annulations, we were interested in the use of substituted allylic silanes to prepare more functionalized annulation products. The α-substituted (*E*)-benzhydryldimethylcrotylsilanes were prepared using the procedure developed in our laboratory (Scheme 3).[12] The requisite chlorosilane **11** was prepared directly from

Scheme 3



diphenylmethane and dichlorodimethylsilane in 70% yield. Silylation of the THP ether of 3-butyn-2-ol (**12**) with chlorosilane **11**, followed by hydroboration and protonolysis of the alkyne and removal of the THP group, afforded the allylic alcohol with high (*Z*)-selectivity. This alcohol was then treated with phenyl isocyanate to afford carbamate **14**. The copper-mediated S_N2' reactions of **14** provided (*E*)-crotylsilanes **15** and **16** with high selectivities.[12]

(12) (a) Smitrovich, J. H.; Woerpel, K. A. *J. Am. Chem. Soc.* **1998**, *120*, 12998−12999. (b) Smitrovich, J. H.; Woerpel, K. A. *J. Org. Chem.* **2000**, *65*, 1601−1614.

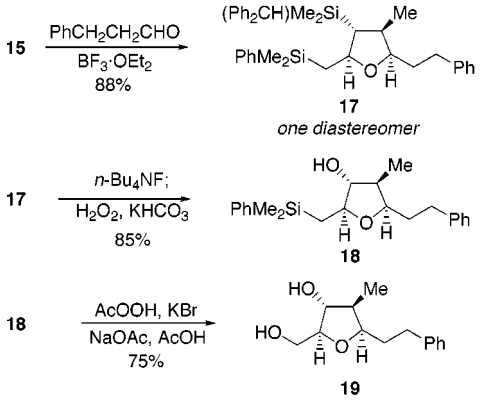
(13) For the annulation products **3**, **6**, and **20**, only one diastereomer was detected by ^1H NMR spectroscopy, and the stereochemistry was assigned by comparison to the analogous reported compounds (see refs 2, 4, 5, and 7). Furthermore, spectral data (^1H and ^{13}C NMR) obtained for **4** were identical to those reported by Knölker and Meyers (refs 2c and 5c).

(14) The benzhydryl group was expected to be as good a leaving group as the trityl group because they have comparable basicities: Bordwell, F. G. *Acc. Chem. Res.* **1988**, *21*, 456−463.

(15) A recent work has shown that the benzylsilyl group can also be oxidized to a hydroxy group with the same procedure: Miura, K.; Hondo, T.; Nakagawa, T.; Takahashi, T.; Hosomi, A. *Org. Lett.* **2000**, *2*, 385−388.

Highly substituted benzhydryldimethylsilyl allylic silanes **15** and **16** undergo annulation reactions with high efficiency. In the presence of $BF_3{\cdot}OEt_2$, allylic silane **15** reacted with hydrocinnamaldehyde to give tetrahydrofuran **17** in high yield as a single diastereomer by ^1H NMR spectroscopic analysis (Scheme 4). The two silyl groups of **17** could then

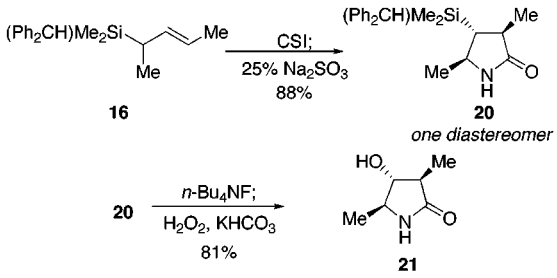
Scheme 4



be oxidized sequentially (Scheme 4). The benzhydryldimethylsilyl was first oxidized using the two-step, one-pot procedure (n-Bu_4NF/H_2O_2) to afford alcohol **18**. Oxidation of the terminal dimethylphenylsilyl group under acidic conditions[10] was not attempted because of concern about β-elimination.[16] Oxidation under basic conditions (t-BuOK/DMSO)[17] yielded none of the desired diol **19**.[18] Successful oxidation was achieved by one-pot bromodesilylation/oxidation (AcOOH/KBr),[19] affording **19** in 75% yield. The stereochemistry of diol **19** was proven by X-ray diffraction analysis of its bis(3,5-dinitrobenzoate) derivative.[20]

Benzhydryldimethylsilyl allylic silanes can also be utilized for the preparation of nitrogen-containing heterocycles. Previous work from our laboratory has shown that the [3 + 2] annulation of *N*-chlorosulfonyl isocyanate (CSI) with allylic silanes provides a stereoselective synthesis of trisubstituted 2-pyrrolidinones.[7a] Benzhydrylsilane **16** underwent annulation with CSI to furnish lactam **20** in 88% yield as a single stereoisomer after in situ reduction with 25% Na_2SO_3 (Scheme 5).[13] Oxidation of the benzhydryldimethylsilyl

Scheme 5



group of **20** provided 4-hydroxy-2-pyrrolidinone **21** in 81% yield without epimerization.

In conclusion, the benzhydryldimethylsilyl group has been developed as a useful new silyl moiety for [3 + 2] annulation reactions of allylic silanes. We have utilized this group to prepare a variety of oxygenated five-membered ring systems in high yields and with high stereoselectivities. The utility of benzhydryldimethyl allylic silanes in annulation processes has been demonstrated by our recent formal synthesis of (±)-peduncularine with a [3 + 2] annulation as a key step.[21]

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Supporting Information Available: Full experimental and analytical data for all new compounds; X-ray data for a derivative of **19**; ^1H NMR spectra of **3**, **6**, **15**, **16**, **17**, and **20**; and GC traces of **15** and **16**. This material is available free of charge via the Internet at http://pubs.acs.org.

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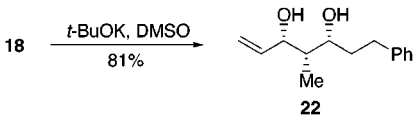
(16) For example, see: Boons, G. J. P. H.; van der Marel, G. A.; van Boom, J. H. *Tetrahedron Lett.* **1989**, *30*, 229−232.

(17) Murakami, M.; Suginome, M.; Fujimoto, K.; Nakamura, H.; Anderson, P. G.; Ito, Y. *J. Am. Chem. Soc.* **1993**, *115*, 6487−6498.

(18) The β-elimination product **22** was obtained in 81% yield.



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(20) The stereochemistry is consistent with the anti-S_E' pathway through an antiperiplanar transition state. See refs 1 and 6a,b.

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