[7] The reaction of **7** with $AuCl_3$ as catalyst afforded exclusively phenol **8** (69%).[3] In the platinum(II)-catalyzed reaction, traces (ca. 1%) of a phenol tentatively assigned as 1,3-dihydro-6-methyl-5-isobenzofuranol were also obtained.

[8] a) The calculations were performed with Gaussian 98.[8b] The geometries of all complexes were optimized at the DFT level of theory with the generalized gradient approximation and the B3LYP hybrid functional.[8c, d] The standard 6-31G(d) basis set was used for C, H, O and Cl, and the default LANL2DZ pseudorelativistic potential and basis set were used for Pt. Harmonic frequencies were calculated at B3LYP level to characterize the stationary points and to determine the zero-point energies (ZPE). The starting approximate geometry for the transition states (TS) were located graphically; b) Gaussian 98 (Revision A.7), M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, V. G. Zakrzewski, J. A. Montgomery, R. E. Stratmann, J. C. Burant, S. Dapprich, J. M. Millam, A. D. Daniels, K. N. Kudin, M. C. Strain, O. Farkas, J. Tomasi, V. Barone, M. Cossi, R. Cammi, B. Mennucci, C. Pomelli, C. Adamo, S. Clifford, J. Ochterski, G. A. Petersson, P. Y. Ayala, Q. Cui, K. Morokuma, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. Cioslowski, J. V. Ortiz, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. Gomperts, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, C. Gonzalez, M. Challacombe, P. M. W. Gill, B. G. Johnson, W. Chen, M. W. Wong, J. L. Andres, M. Head-Gordon, E. S. Replogle, J. A. Pople, Gaussian, Inc., Pittsburgh, PA, **1998**.; c) P. J. Stephens, F. J. Devlin, C. F. Chabalowski, M. J. Frisch, *J. Phys. Chem.* **1994**, *98*, 11623–11627; d) W. Kohn, A. D. Becke, R. G. Parr, *J. Phys. Chem.* **1996**, *1000*, 12974–12980.

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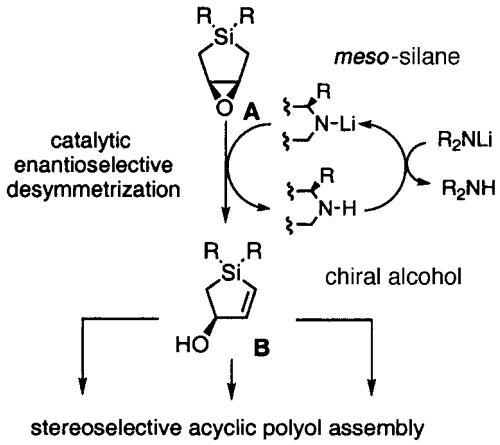
Catalytic Enantioselective Isomerization of Silacyclopentene Oxides: New Strategy for Stereocontrolled Assembly of Acyclic Polyols**

Dong Liu and Sergey A. Kozmin*

Creation of molecular chirality by desymmetrization of readily available prochiral precursors is a powerful synthetic strategy.[1] This approach is particularly attractive when a substoichiometric amount of chiral catalyst is utilized to mediate such transformations with high efficiency and enantioselectivity.[2] We have been engaged in the development of new catalytic desymmetrization approaches based on the use of cyclic silicon-containing templates. Herein, we disclose a highly enantioselective base-promoted rearrangement of silacyclopentene oxide, which resulted in the development of a novel strategy for the preparation of acyclic polyol-containing motifs. To our knowledge, enantioselective desymmetrization of cyclic silanes has not been documented prior to this work.[3, 4]

Pioneered by Whitesell and Felman,[5] base-mediated epoxide isomerization utilizing chiral lithium amides has become a valuable method for the preparation of allylic alcohols.[6] With this as a precedent, we devised a strategy for desymmetrization of *meso*-silane **A** (Scheme 1). Enantioselective deprotonation, followed by β-elimination would result in the formation of enantiomerically enriched allylic alcohol **B**. Importantly, the use of a catalytic amount of chiral base in combination with an appropriate agent capable of regenerat-



Scheme 1. General strategy for the desymmetrization of *meso*-silane **A** to give enatiomerically enriched allylic alcohol **B**.

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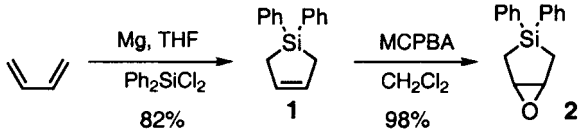
[**] Initial funding of this work was provided by the University of Chicago. We are grateful to the donors of the Petroleum Research Fund for further financial support.

Supporting information for this article is available on the WWW under http://www.angewandte.com or from the author.

ing the active catalyst would result in the development of a catalytic enantioselective process.[7] Silane **B**, which incorporates structural features of both the vinyl silane and allylic alcohol, was envisioned to serve as a versatile precursor for the assembly of a wide range of synthetically valuable acyclic polyol fragments.

Silacyclopentene oxides can be readily assembled on a preparative scale according to the general sequence illustrated in Scheme 2. In the case of the diphenyl-substituted derivative, silylation of magnesium–butadiene,[8] followed by oxidation of the resulting silacyclopentene **1** with 3-chloroperoxybenzoic acid (MCPBA) furnished epoxide **2** in an overall yield of 80% for the two steps.[9]



Scheme 2. Preparation of diphenylsilacyclopentene oxide (**2**).

We anticipated that the presence of the silicon atom would have two beneficial effects on the epoxide rearrangement: 1) α-Si-carbanion stabilization favoring initial deprotonation; and 2) the ability to maximize the level of asymmetric induction by adjusting the exocyclic silicon substituents positioned in the direct proximity to the deprotonation site. Systematic cross-examination of three silacyclopentene oxides and four chiral amide bases (Figure 1) revealed that the

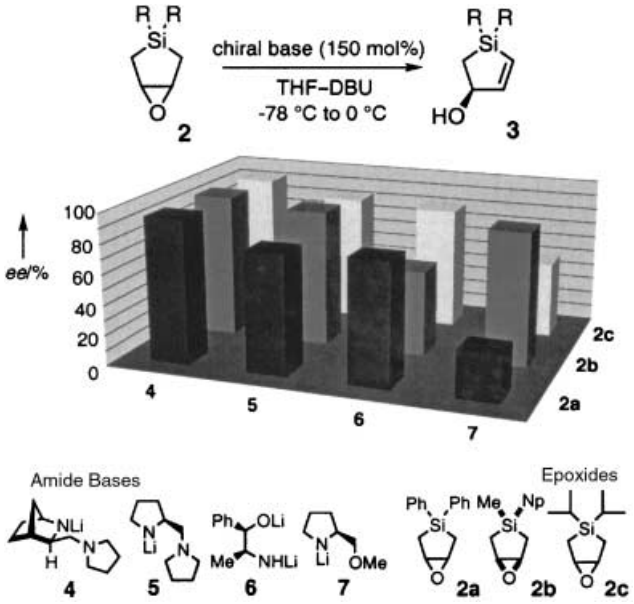
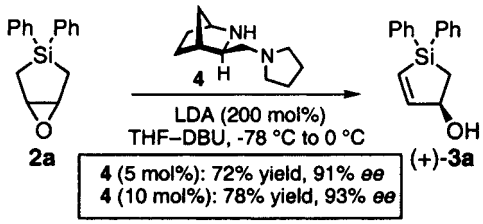


Figure 1. Base-mediated rearrangement of silacyclopentene oxides **2** to give allylic alcohols **3**.

use of diphenylsilacyclopentene oxide **2a** in combination with bicyclic amide **4**[10] resulted in the highest level of enantioselectivity (95% *ee*). Furthermore, we found that the rearrangement can be performed efficiently using a catalytic amount of **4** and two equivalents of lithium disopropylamide (LDA), in agreement with results obtained by Andersson and co-workers for the rearrangement of carbocyclic epoxides.[10] While 91% *ee* was obtained with a 5 mol% loading, the use of 10 mol% of amide **4** resulted in 93% *ee* and 78% yield (Scheme 3).[11, 12]

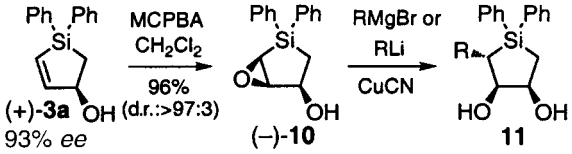


Scheme 3. Catalytic enantioselective isomerization of **2** to give (+)-**3a**.

Having secured an efficient access to alcohol (+)-**3a** in high enantiomeric purity, our subsequent efforts focused on the stereoselective construction of tetraol fragment **12** (see Table 2). The approach commenced with a diastereoselective hydroxy-directed epoxidation of (+)-**3a** to give (−)-**10** (d.r.: >97:3),[9] followed by Si-guided cuprate addition to afford silacyclic diol **11** (Table 1).[13] The latter transformation was found to be highly regioselective and general for incorporating a variety of alkyl, aryl, and alkenyl fragments. Importantly, potential products resulting from either the Peterson elimination or fragmentation were not observed under these highly nucleophilic conditions.

Our studies on the oxidative cleavage of silacyclic diols **11** began with the examination of the Tamao[14] and the Fleming[15] protocols, which generally resulted in incomplete reactions and isolation of multiple products. We soon uncovered that the oxidative cleavage of the silacyclopentane

Table 1. Epoxidation/cuprate addition sequence.[a]



Entry	R	**11**	Yield [%][b]	d.r.
1		(−)-**11a**	91[c]	>97:3
2		(−)-**11a**	72[d]	>97:3
3		(−)-**11b**	78[c]	>97:3
4		(−)-**11c**	92[c]	>97:3
5		(−)-**11d**	87[c]	>97:3
6		(−)-**11e**	92[c]	>97:3
7		(−)-**11f**	86[c]	>97:3
8		(−)-**11g**	91[d]	>97:3
9	 ($LiAlH_4$)	(−)-**11f**	64[e]	>97:3

[a] For detailed experimental procedures and compound characterization, see Supporting Information. [b] Refers to the yield of spectroscopically pure product isolated after silica gel chromatography. [c] Organocuprate was generated from the corresponding Grignard reagent. [d] Organocuprate was generated from the corresponding organolithium reagent. [e] Reduction was carried out on the methoxymethyl(MOM)-protected alcohol (−)-**10** to prevent formation of the *meso* product.

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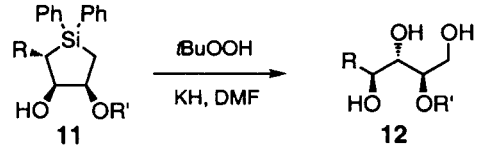
Table 2. Oxidative cleavage of cyclic silanes.[a]



Entry	Silane	R	R′	**12**	Yield [%][b]
1	(−)-**11a**		H	(−)-**12a**	78
2	(+)-**11b**		H	(−)-**12b**	76
3	(+)-**11c**		H	(−)-**12c**	79
4	(−)-**11f**		H	(−)-**12d**	70
5	(−)-**11h**		MOM	(−)-**12e**	74

[a] For detailed experimental procedures and compound characterization, see Supporting Information. [b] Refers to the yield of spectroscopically pure product isolated after silica gel chromatography.

scaffold can be efficiently accomplished according to the Woerpel procedure employing the use of basic *t*BuOOH in DMF.[16] Several representative tetraols **12** were prepared in good yields *with complete overall diastereoselectivity* illustrating the generality of this strategy (Table 2). The occurrence of a polyol motif **12** in a number of bioactive natural products is noteworthy. Representative examples include the side chain portion of bacteriohopanoid.[17a] and the central macrolide segment of herbarumin I, a highly potent phytotoxic agent.[17b]

In summary, we have demonstrated a highly enantioselective catalytic isomerization of silacyclopentene oxide, a pivotal point in our strategy for the stereoselective assembly of acyclic polyols. Development of an arsenal of new asymmetric processes utilizing cyclic silanes is currently in progress.

Received: September 6, 2001 [Z17864]

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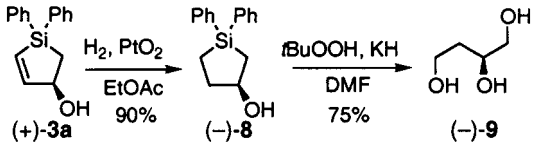
[11] Determination of the enantiomeric excess was carried out by the Mosher ester ^{1}H NMR analysis; see Supporting Information for details. The attempts to resolve alcohol **3a** using six different chiral HPLC stationary phases proved unsuccessful.

[12] The absolute configuration of silane (*R*)-**3a** was later confirmed by its conversion to the known (*S*)-triol **9**, as illustrated below.



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The First Catalytic, Diastereoselective, and Enantioselective Crossed-Aldol Reactions of Aldehydes**

Scott E. Denmark* and Sunil K. Ghosh

The apotheosis of the aldol addition reaction is one of the most well-documented chapters of modern organic synthesis; the generality, versatility, and selectivity associated with this process have been the subject of countless reviews and authoritative summaries. Stimulated by the challenge posed by nature, a generation of synthetic organic chemists has constructed an impressive edifice of knowledge which constitutes insightful, elegant, and practical solutions to the structural and stereochemical problems presented by polypropionate-derived natural products. Yet, at this advanced vantage, it is remarkable that the most basic of aldol

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[**] We are grateful to the National Science Foundation for generous financial support (NSF CHE 9803124).

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