APPLICATION AND GENERATION OF SILACYCLOPROPANES

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INTRODUCTION

Silacyclopropanes (siliranes) are three-membered, silicon heterocycles with exceptional properties and synthetic potential. The 3p bonding orbitals on silicon effect extensive structural deformation of the three-membered ring. In particular, the bond lengths and internal bond angles are considerably different from those of the analogous cyclopropane.[1] Quantum mechanical calculations as well as spectroscopic data show the carbon silicon bond in siliranes to be on average 0.3 Å longer than the corresponding carbon-carbon bonds in cyclopropanes. Additionally, the endocyclic C-Si-C bond angles deviate 5 to 10 degrees (average of 54 degrees) off from the ideal 60 degrees in a three-membered ring.[1]

This structural deformation manifests itself chemically, as both an increase in difficulty of preparation and handling as well as an increase in reactivity. The extreme reactivity of this class of compounds has hindered the development of siliranes as practical synthetic tools. This report outlines the successful generation of the silacyclopropanes as well the development of unique reactions that are characteristic of this class of compounds.

METHODS OF SILIRANE FORMATION

Reduction of 1,3-Dihalides

Wurtz-type reductive coupling of 1,3-dihalides with divalent metals is an effective way to construct cyclopropanes.[2] Seyferth and coworkers have successfully applied this strategy for the construction of silacyclopropanes.[3] Using magnesium turnings as the reducing agent, highly substituted siliranes **1** can be synthesized in low to moderate yields (Scheme 1). Unfortunately, the substrate scope using this method of silirane formation is not as broad as it is for cyclopropane construction.[4]

Scheme 1. Hexamethylsilirane Formation

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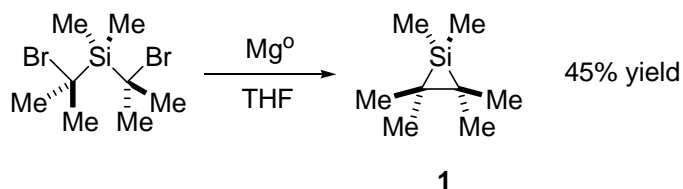
Photochemical Generation and Trapping of Silylenes

A conceptually distinct approach to constructing siliranes is the direct addition of a silylene to an alkene. Silylenes are dicoordinate silicon analogs of carbenes and can be produced in a variety of ways. The earliest reported method involves photochemical extrusion of dimethylsilylene **3** from dodecamethylcyclohexasilane **2**.[5a] Other ways of generating diorganosilylenes photochemically involve irradiation of linear and cyclic trisilanes.[5b]

Silyenes exist in a singlet ground state and react in many of the same ways as singlet carbenes. Ando and coworkers have shown that direct reaction of dimesitylsilylene with alkenes produces siliranes in good yield.[6] The addition of silylenes to geometrically defined alkenes produces siliranes in a stereospecific fashion (Scheme 2).[6]

**Scheme 2. Photochemically Induced Silylene Trapping**
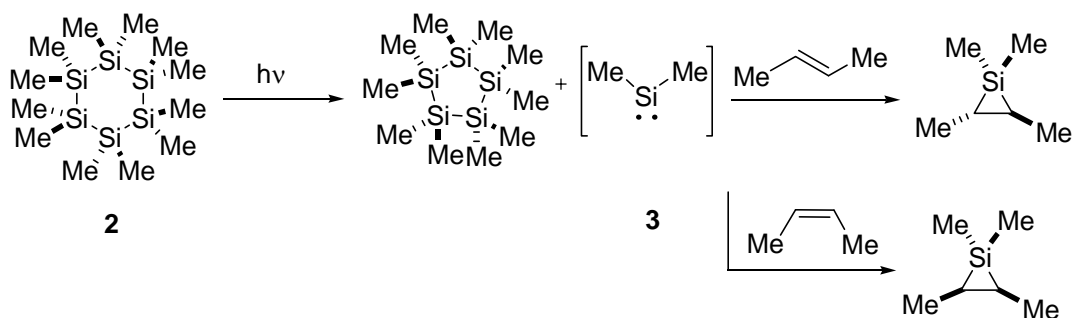
Siliranes from Silylenoids

The photochemical generation of silylenes is not practical for the synthesis of siliranes in quantity. The preparative scale synthesis of siliranes is accomplished through the use of metal-mediated silylene transfer.[7] Upon treatment of dichloro-dialkylsilanes with reducing metals, a metal-silylene complex can be generated, that adds to alkenes stereospecifically and in good yields.[7]

If the alkene bears a proximal stereogenic center, silylene-metal complexes produce siliranes with high diastereoselectivity.[8] Steric interactions, not coordination, account for the high level of stereocontrol in metal-silylene based silacyclopropanations (Scheme 3).

Scheme 3. Stereospecific Silylenoid Transfer
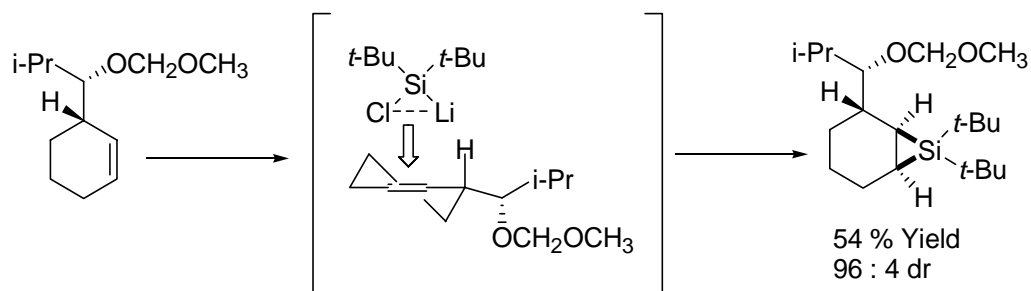
Silylene Transfer Reactions

The most widely employed method for the selective formation of siliranes utilizes the thermal transfer of a silylene unit from one silirane to create another. Seyferth and coworkers serendipitously discovered that upon heating, siliranes cheletropically extrude dialkylsilylene, which can then re-insert into a second available alkene (Scheme 4).[9] Mechanistic investigations have shown that silylene extrusion is a reversible process, and that the product distribution is governed by the thermodynamic stabilities of the siliranes.

Scheme 4. Thermally Induced Silylene Transfer
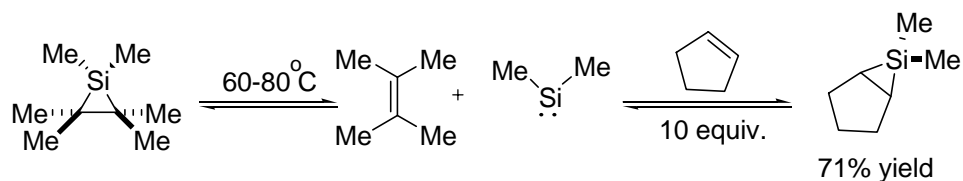
Woerpel and coworkers expanded the synthetic practicality of this silylene transfer reaction by developing a protocol that uses catalytic quantities of silver triflate.[10] This modification allows for the silylene transfer reaction to proceed at lower temperatures in good yield. Furthermore, the catalyzed silylene transfer is compatible with a larger substrate scope.

REACTIONS OF SILIRANES: INSERTION

Thermally-Based Insertions into Siliranes

When siliranes are heated in the presence of styrene derivatives, a two-atom insertion reaction occurs with the double bond to give a silacyclopentane instead of the expected silirane product. This type of ring expansion has also been observed with carbonyl functionalities, specifically aromatic and

α,β-unsaturated aldehydes which yield 1-sila-2-oxycyclopentanes **4** in moderate yield. Aliphatic aldehydes are unreactive in the presence of siliranes even at elevated temperature; however, under photochemical UV-irradiation, aliphatic aldehydes will insert into siliranes (Scheme 5).[11]

Scheme 5. Thermal Two-Atom Insertion Reactions
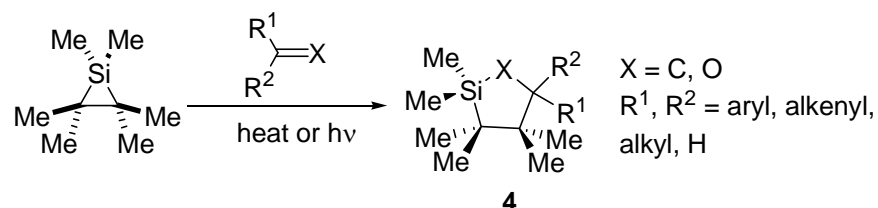
Alkoxide Catalyzed Aldehyde Insertions into Siliranes

Woerpel and coworkers have found that the stereo- and regiochemical outcome of aldehyde insertions into either *cis* or *trans* dimethyl-di-tert-butylsilirane **5** is highly dependent on the reaction conditions and the presence of additives (Table 1).[12] Thermally promoted additions of benzaldehyde to *cis*- or *trans*-**5** produces the thermodynamically most favorable trans-trans oxysilacyclopentane diastereomer as the major product. However, in the presence of a catalytic amount of potassium *tert*-butoxide, the insertion of benzaldehyde into *cis*-**5** produces the trans-trans and trans-cis diastereomers, whereas the insertion into *trans*-**5** produces the cis-cis and cis-trans diastereomers. The product distribution for the *tert*-butoxide-catalyzed insertion reveals that the reaction occurs with near complete inversion of configuration at the silirane-carbon that reacts with the aldehyde.[12]

**Table 1. Diastereomeric Distribution of Benzaldehyde Insertions**
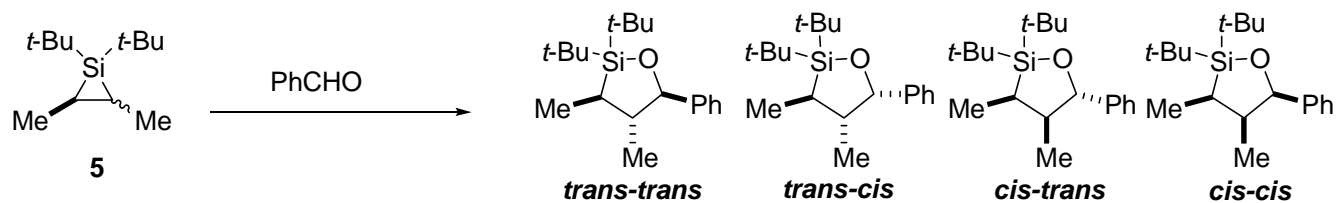
silirane	conditions	trans-trans	trans-cis	cis-trans	cis-cis
		product composition, %			
trans	100 °C	**75**	7	8	10
cis	100 °C	**48**	6	32	14
trans	25% KO*t*-Bu/18-crown-6, RT	3	1	13	**83**
cis	10% KO*t*-Bu/18-crown-6, RT	**69**	30	<1	<1

4

Unsymmetrically substituted siliranes show a regiochemical preference to undergo insertion of benzaldehyde into the more substituted carbon in both thermal and *tert*-butoxide catalyzed reactions.[12] The catalyzed reaction is much higher yielding in comparison to the thermally promoted reaction.

Formamide Insertions into Siliranes

In addition to aldehydes, formamides also will insert into siliranes. At elevated temperatures (120 °C), 1-formylpyrrolidine reacts with *trans*-**5**, to give the oxysilacyclopentane aminal **6** in high yield and as a single stereoisomer (Scheme 6). In contrast, the *cis* silirane decomposes under the same reaction conditions.

Scheme 6. Formation of *trans*-Oxysilacyclopentane Acetates

trans-**5**　　　　　　　　　　**6**　　　　　　　　**7**

86% yield
from silirane
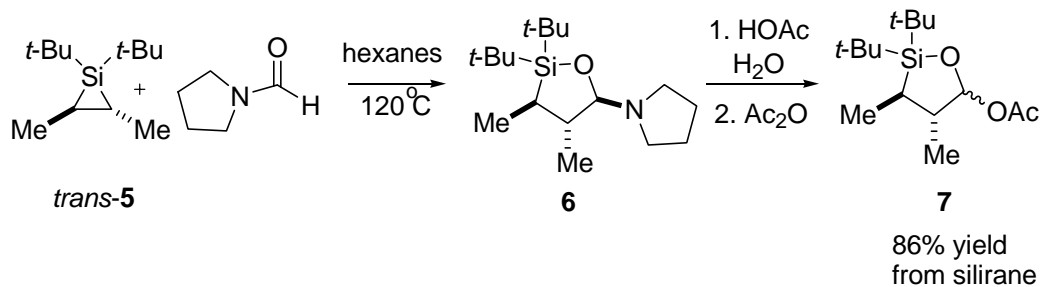
The formamide insertion, unlike benzaldehyde insertion, occurs with retention of configuration at the substituted carbon; therefore the only product formed is the trans-trans diastereomer **6**.[13] The regioselectivity of insertion into mono-substituted siliranes favors the more substituted carbon atom much like the 1,2-substitution pattern in benzaldehyde insertion.

The aminal product of the formamide insertion is particularly acid labile. Hydrolysis of the product with acetic acid affords a mixture of hemiacetal anomers. After acylation, the more stable oxasilacyclopentane acetate **7** can be isolated in high yield.[13]

Insertion of Isocyanides into Siliranes

Treatment of cis and trans siliranes with isocyanides at elevated temperatures produces iminosilacyclobutanes **8** stereospecifically in high yield.[14] The regioselectivity of the insertion process occurs primarily at the more substituted carbon atom, though, as the size of the substituent on the silirane increases the regioselectivity erodes considerably. Iminosilacyclobutanes are hydrolyzed with

aqueous copper sulfate to oxasilacyclopentane hemiacetals (as a mixture of anomers) which can be acylated in high yield (Scheme 7).[15]

Scheme 7. Isocyanide Insertion followed by Hydrolysis
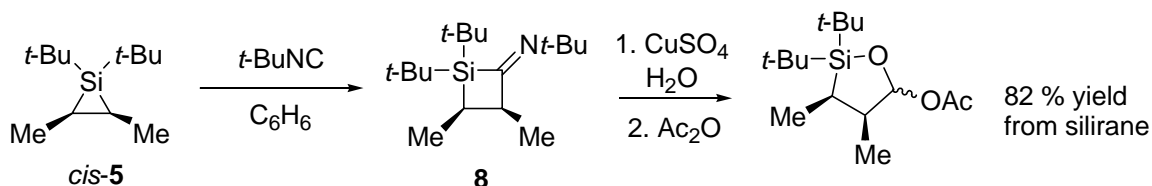

Metal Catalyzed Insertions into Siliranes

Copper halides catalyze the insertion of the carbonyl group of aromatic, α,β-unsaturated aldehydes, formamides, formate esters and α,β-unsaturated ketones into siliranes with good yields and excellent diastereoselectivities.[16] In all cases, the product retains the stereochemical configurations at the silirane carbon centers. With mono-substituted siliranes, insertion occurs exclusively at the more substituted carbon atom to afford the 1,2-disubstituted oxysilacyclopentanes.

Zinc halides also catalyze the insertion of a variety of carbonyl compounds into siliranes. Interestingly, zinc and copper exhibit complementary regioselectivities for the insertion process (Scheme 8). In all examples, insertion occurs at the less substituted carbon atom to afford the 1,3-disubstituted oxysilacyclopentane. The substrate scope for this reaction includes formate esters, aromatic, α,β-unsaturated, and aliphatic aldehydes. In most cases the insertion proceeds in high yield, albeit with low diastereoselectivity.[17]

Scheme 8. Regioselectivities of Copper and Zinc Catalyzed Insertions


6
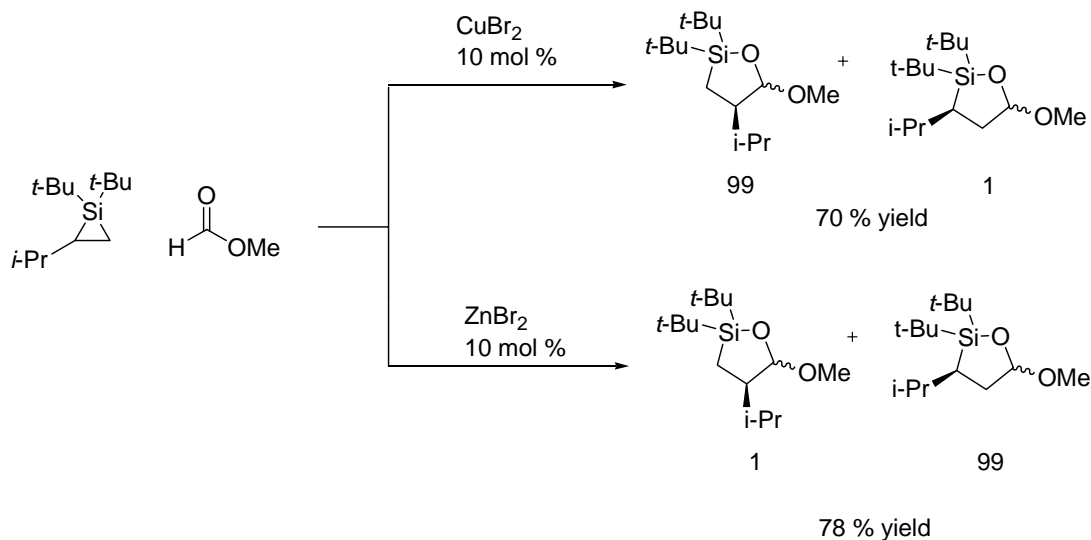
ADDITIONS TO OXASILACYCLOPENTANE RINGS

The products of carbonyl insertion reactions, oxasilacyclopentane acetates, are in themselves synthetically useful. In the presence of a Lewis acid (e.g. tin tetrabromide), oxasilacyclopentane acetates **7** generate putative oxocarbenium ions **9** that can be trapped with nucleophiles. The substituted oxasilacyclopentanes can then be further transformed by Tamao oxidation to the corresponding 1,3-diol **10** bearing three contiguous stereocenters (Scheme 9).[18]

Scheme 9. Oxasilacyclopentane Acetate Transformations
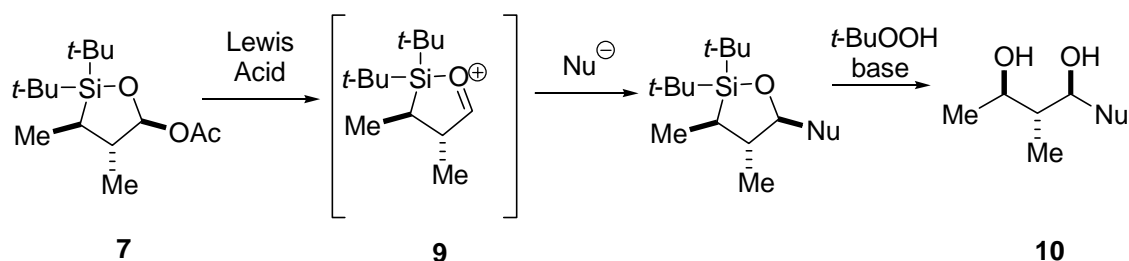
Silyl enol ethers and allylic trimethylsilanes can serve as carbon nucleophiles for the addition to oxocarbenium ions.[19] The stereochemical outcome of the addition of several silyl enol ethers to both trans and cis oxasilacyclopentane acetates proceeds with high 3,4-trans diastereoselectivity (Scheme 10).[19] The addition of α-substituted enolates is a stereoconvergent process and is independent of the geometry of the enol silane. Syn diastereoselectivity between the α-carbon stereocenter and the newly formed stereocenter from the oxocarbenium ion is observed in all cases.[20]

Scheme 10. Aldol Addition to Oxocarbenium Ion
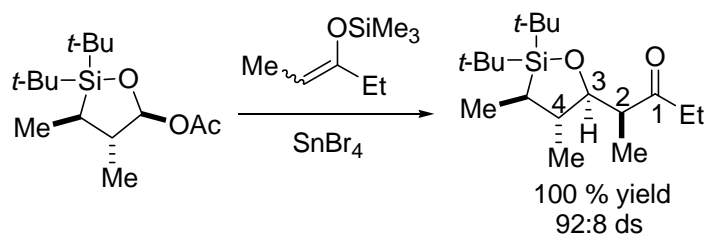
CONCLUSIONS

Silacyclopropanes undergo a variety of unique transformations that are absent in the chemistry of other three-membered ring systems. Stereo- and regioselective insertions into silacyclopropanes followed by further manipulation provide poly-oxygenated molecules bearing several stereogenic

centers. Unfortunately the number of preparatively useful silirane transformations is limited because of the high of reactivity of the ring system. Also, high stereoselectivity can only be achieved with sterically unencumbered, symmetrical siliranes. For this chemistry to be truly synthetically practical, considerable expansion of the substrate scope of silirane formation is needed, as is the development of an asymmetric variant of the silacyclopropanation reaction.

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