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Diastereoselective Synthesis of Seven-Membered-Ring *trans*-Alkenes from Dienes and Aldehydes by Silylene Transfer

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Supporting Information

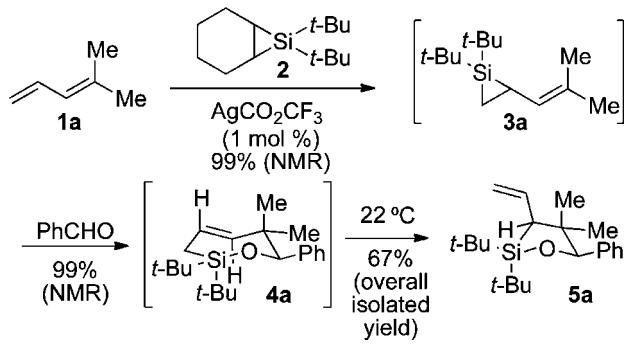
ABSTRACT: Silver-catalyzed silylene transfer to alkenes forms vinylsilacyclopropanes regioselectively. These allylic silanes undergo additions to aldehydes to form seven-membered-ring *trans*-alkenes with high diastereoselectivity. The high reactivity of the *trans*-alkenes is evidenced by their formal [1,3]-sigmatropic rearrangement reactions and the rapid additions of oxygen−hydrogen bonds across the carbon−carbon double bonds.

Investigations of the chemistry of seven-membered-ring *trans*-alkenes have been limited by the difficulty of making such highly strained alkenes.[1] The development of methods for the synthesis of seven-membered cyclic *trans*-alkenes should lead to useful applications of these strained compounds, considering that advances in the preparation of the larger eight- and nine-membered-ring *trans*-alkenes have enabled these highly reactive compounds to be used in synthesis[2−5] and bioconjugation.[6] In contrast to the larger cyclic *trans*-alkenes, however, no methods have been developed for the synthesis of functionalized seven-membered-ring cyclic *trans*-alkenes. Photoisomerization of *cis*-cycloheptene provided minute quantities of the trans isomer, which was unstable at −30 °C.[7] Trapping of transient *trans*-cycloheptenes has not proven to be synthetically useful,[8,9] and syntheses of seven-membered-ring *trans*-alkenes containing heteroatoms in the ring are lengthy and not general.[10,11]

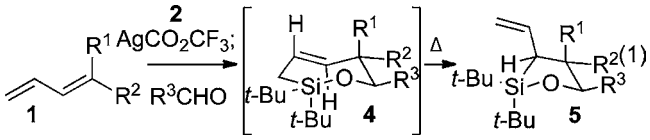
In this communication, we report a one-flask synthesis of seven-membered-ring *trans*-alkenes by regioselective, catalytic silylene transfer to a diene followed by a rapid diastereoselective addition of an aldehyde. Initial studies indicate that these strained alkenes are highly reactive.

Our diastereoselective synthesis of seven-membered-ring *trans*-alkenes was predicated on the high reactivity of strained allylic silanes with aldehydes.[12−15] The preparation of the requisite allylic silane (e.g., **3a** in Scheme 1) could be challenging because it would require a formal [2 + 1] cycloaddition of a silylene with a diene instead of the formal [4 + 2] cycloaddition that is typically observed.[16−19] The silver-catalyzed silylene transfer reaction to diene **1a**, however, gave vinyl silacyclopropane **3a** regioselectively (Scheme 1).[20] After the silylene transfer reaction was complete (less than 10 min), 1 equiv of benzaldehyde was added, and within 10 min, the allylic silane underwent quantitative insertion of the aldehyde to afford the cyclic *trans*-alkene **4a** as a single diastereomer (as determined by ^{1}H NMR spectroscopy).[21] This seven-membered-ring *trans*-alkene was highly reactive: attempts to isolate alkene **4a** led to addition reactions (see below). Even in the absence of additional reagents, *trans*-cycloalkene **4a** underwent formal [1,3]-sigmatropic rearrangement over several hours to form oxasilacyclopentane **5a**, which could be isolated and purified.

Scheme 1. One-Flask Synthesis of Seven-Membered-Ring *trans*-Alkenes



A number of seven-membered-ring *trans*-alkenes were synthesized using different substituted dienes and aldehydes (eq 1 and Table 1). In all cases, the silylene transfer reaction



was regioselective and complete in less than 10 min, and the addition to the aldehyde was diastereoselective and rapid (less

Table 1. Formation and Rearrangement of *trans*-Oxasilacycloheptenes

entry	R^1	R^2	R^3	4	%	5	%
1	Me	Me	Ph	**a**	99	**a**	67[a]
2	H	Me	Ph	**b**	99	**b**	51[a]
3	H	OTIPS	Ph	**c**	99	**c**	99[b]
4	H	OTIPS	*i*-Pr	**d**	75	**d**	80[b]
5	H	OTIPS	(*E*)-CHCHCH$_3$	**e**	84	**e**	86[b]
6	H	OTIPS	CHCH$_3$Ph	**f**	75	**f**	71[b]

[a]Reaction run at room temperature, isolated yield. [b]Reaction run at 60 °C, ^{1}H NMR yield based on comparison to mesitylene as an internal standard.

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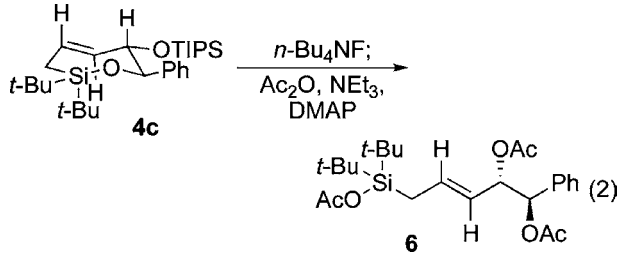
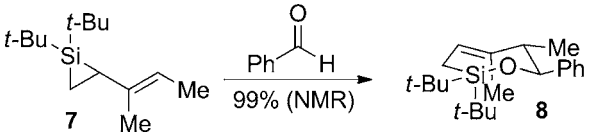
than 10 min, except for branched alkyl aldehydes, which required 3 h). Silylene transfer to (*E*)-1-(triisopropylsiloxy)-1,3-butadiene (diene **1c**) occurred at the less electron-rich double bond, even though silylene transfer generally occurs at the more electron-rich alkene.[22] The resulting vinylsilacyclopropane, however, reacted not as the enol ether but as the allylic silane.[15,23]

The stereochemical configuration of the seven-membered-ring *trans*-alkene was determined by ^{1}H NMR spectroscopy and is consistent with the high reactivity of these compounds (see below). The vinyl protons of the unstable seven-membered-ring *trans*-alkenes couple with coupling constants (*J*) ranging from 17.2 to 17.6 Hz. These values are consistent with the reported coupling constants of *trans*-cycloheptene measured by low-temperature NMR spectroscopy (J = 18 Hz).[7] In contrast, the vinyl protons of a stable *cis*-oxasilacycloheptene exhibit a much smaller coupling constant (J = 10.9 Hz).[16] The results of nuclear Overhauser effect (NOE) experiments are consistent with the assignment of the alkene geometry and the overall conformational preference depicted for compounds **4**: irradiation of each vinyl proton led to enhancements of NOEs to substituents on opposite faces of the ring. Further evidence for the stereochemical assignment was obtained from cleavage of the silicon−oxygen bond in **4c** and isolation of the stable allylic silane **6** (eq 2), which exhibited coupling between the vinylic protons (J = 15.2 Hz) consistent with that in other (*E*)-allylic silanes.[24,25]



(2)

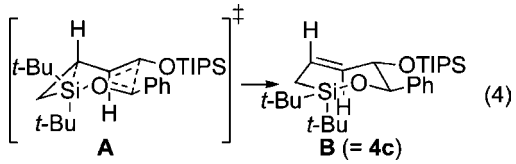
Although the seven-membered-ring *trans*-alkene products hydrolyzed readily upon handling, they isomerized slowly to products that could be isolated and purified (alkenes **5**; eq 1). This [1,3]-silyl rearrangement to give stable oxasilacyclopentanes, which would be expected to require high temperatures (500 °C),[26] occurred readily at room temperature in most cases. In the case of the *trans*-alkene derived from 3-methylpentadiene, isomerization did not occur, likely because the product would be sterically congested (eq 3). The half-lives



(3)

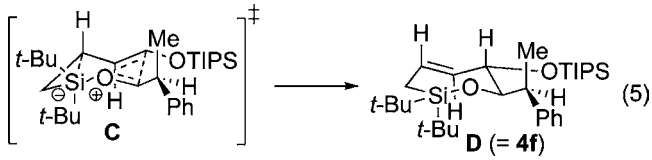
for the formal [1,3]-sigmatropic rearrangements at room temperature averaged 10 to 12 h. The rearrangement from the seven-membered-ring *trans*-alkenes to the oxasilacyclopentanes is likely a thermal process, because irradiation under a UV lamp (254 nm) did not accelerate the rearrangement. On the other hand, heating the *trans*-alkenes at 60 °C reduced the half-life to 30 min and improved the yield (Table 1). The ease of this transformation in comparison with known 1,3-silyl rearrangements[26] provides additional confirmation that the cyclic *trans*-alkene is highly strained.

The formation of the trans double bond in the seven-membered ring can be explained by considering the mechanism of insertion of the aldehyde. The Lewis acidic silicon atom[12,13,27,28] of the vinylsilacyclopropane intermediate enables complexation of the aldehyde. Cyclization through the closed, chairlike transition state[14,15,29] **A** would form the observed trans double bond in the product (eq 4).



(4)

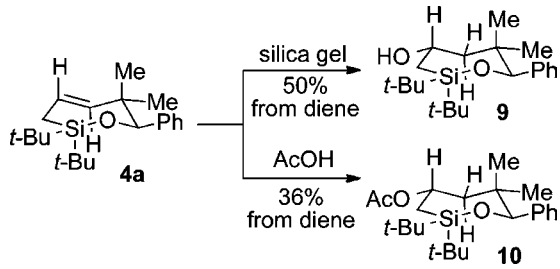
The highly organized transition state for the insertion also enables the mutual kinetic resolution[30] of a vinylsilacyclopropane and a chiral aldehyde. Insertion of racemic 2-phenylpropanal into the silacyclopropane derived from silyloxydiene **1c** provided *trans*-oxasilacycloheptene **4f** as a single diastereomer (Table 1, entry 6). The X-ray crystal structure obtained after rearrangement to the oxasilacyclopentane revealed that the mutual kinetic resolution matched (*S*)-2-phenylpropanal with (*S*)-vinylsilacyclopropane **3c** (and the *R* isomers with each other). Formation of this diastereomer is consistent with Felkin−Anh addition to the aldehyde, which minimizes *syn*-pentane interactions[31] (as shown for the *S*,*S* pair in eq 5).



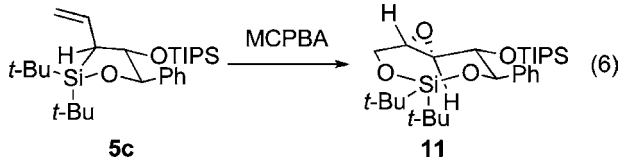
(5)

Preliminary studies revealed the high reactivity of the alkenes formed by these new reactions. Attempts to purify *trans*-alkene **4a** by silica gel chromatography resulted in the regioselective and stereoselective hydration of the double bond (Scheme 2).

Scheme 2. Reactivity of Seven-Membered-Ring *trans*-Alkene 4a



Acetic acid also added selectively across *trans*-cycloheptene **4a** (Scheme 2).[32] The double bond of oxasilacyclopentane **5c** also underwent a highly stereoselective reaction: when it was treated with *m*-chloroperoxybenzoic acid (MCPBA), a single diastereomer of the trans-fused epoxide **11** was formed (eq 6). The



(6)

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oxasilacyclopentane likely underwent epoxidation followed by acid-catalyzed rearrangement to the eight-membered-ring *trans*-alkene[33] and then rapid epoxidation of this strained carbon–carbon double bond.

In conclusion, we have developed a rapid synthesis of seven-membered-ring *trans*-alkenes by a single-flask reaction. This process involves silylene transfer to a diene followed by diastereoselective insertion of an aldehyde into the resultant allylic silane. The highly ordered transition state of this reaction enables a chiral aldehyde to discriminate between the enantiomers of the vinylsilacyclopropane.

■ ASSOCIATED CONTENT

Supporting Information

Experimental procedures and characterization data, including X-ray crystallographic data (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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(21) A control experiment suggested that silver trifluoroacetate plays no role in the reaction with the aldehyde. Addition of tetramethylethylenediamine, which should complex silver (see: Comuzzi, C.; Novelli, R.; Portanova, R.; Tolazzi, M. *Supramol. Chem.* **2001**, *13*, 455), before addition of the aldehyde had no impact on the insertion reaction.

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(23) This methodology can be employed on a preparative scale: *trans*-oxasilacycloheptene **4c** was prepared on a 1 mmol scale during the preparation of allylic silane **6**. Details are provided in the Supporting Information.

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