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Silylene Transfer to Carbonyl Compounds and Subsequent Ireland−Claisen Rearrangements to Control Formation of Quaternary Carbon Stereocenters

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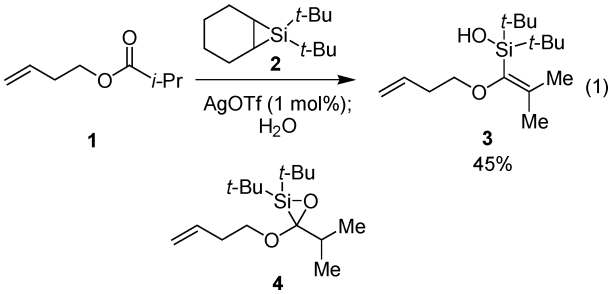
Silylenes (R_2Si) react with the carbon−oxygen double bond of carbonyl compounds to afford a variety of products. For example, silylene transfer to aldehydes and ketones produce cyclic siloxanes[1−7] and silyl enol ethers[8−10] via oxasilacyclopropane[11] or silacarbonyl ylide[12] intermediates. Reactions of silylenes with α,β-unsaturated ketones provide oxasilacyclopentenes containing a cyclic silyl enol ether functionality.[5,13,14] Although the reactions of silylenes with carbonyl compounds were first reported nearly 30 years ago, these reactions have not been applied to organic synthesis. In this communication, we demonstrate that silylene transfer to α,β-unsaturated carbonyl compounds provides a stereoselective method for the synthesis of compounds possessing quaternary carbon stereocenters.[15,16]

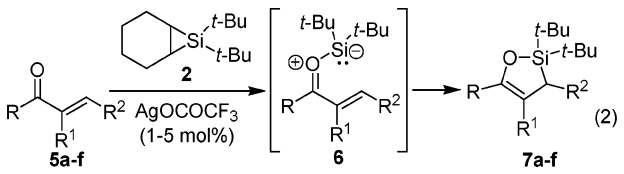
We became interested in silylene transfer to carbonyl compounds during our studies on the metal-catalyzed silacyclopropanation of alkenes.[17,18] While alkenes substituted with a hindered pivaloate ester underwent silylene transfer to the alkene, those bearing an enolizable ester reacted preferentially at the carbonyl group. When isobutyrate **1** was treated with cyclohexene silacyclopropane **2** and a catalytic amount of AgOTf, silylene transfer to the carbonyl group was observed, providing silanol **3** as the major product (eq 1).[19] Oxasilacyclopropane **4** likely formed as an intermediate in the reaction,[20] and rearrangement of this intermediate led to formation of the product. The enhanced reactivity of the carbonyl group over the alkene is consistent with the electrophilic nature of the metal silylenoid intermediate that is transferred.[21,22]



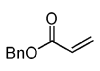
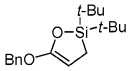
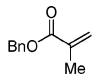
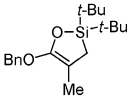
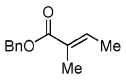
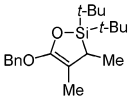
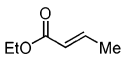
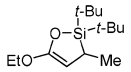
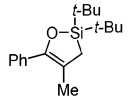
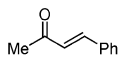
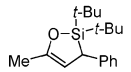
(1)

Silver-catalyzed silylene transfer to a range of α,β-unsaturated carbonyl compounds demonstrated that both carbonyl and alkene functional groups reacted to afford oxasilacyclopentene products (eq 2, Table 1). These reactions likely occurred through nucleophilic attack of the carbonyl group onto an electrophilic silver silylenoid intermediate[21] to form a silacarbonyl ylide **6** followed by an electrocyclic ring closure (eq 2).[9,23,24] With enoates **5a**−**d**, highly reactive oxasilacyclopentenes were obtained and characterized by NMR spectroscopy because isolation of these silyl ketene acetals proved difficult.[25,26] Oxasilacyclopentenes **7e**−**f** derived from ketones **5e**−**f** were found to be more stable than those derived from esters,[25] and these compounds were isolated by column chromatography. Entry 6 is noteworthy, because silylene transfer to the α,β-unsaturated ketone results in the synthetic equivalent of regioselective enolization.[27]

Table 1. Silylene Transfer to α,β-Unsaturated Esters

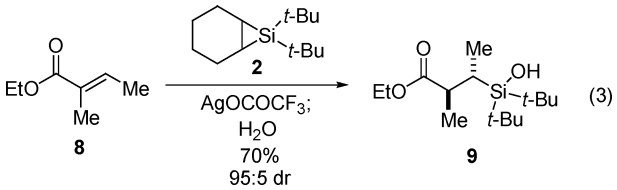


(2)

Entry	Substrate (**5**)	Product (**7**)		Yield (%)
1			**7a**	98[a,b]
2			**7b**	93[a]
3			**7c**	99[a]
4			**7d**	98[a]
5			**7e**	71[c]
6			**7f**	58[c]

[a] As determined by ^{1}H NMR spectroscopic analysis of the product relative to an internal standard ($PhSiMe_3$). [b] Oxasilacyclopentene **7a** was isolated in a drybox and obtained by recrystallization in 76% yield. [c] Isolated yields.

When the α,β-unsaturated ester ethyl tiglate (**8**) was exposed to silylene transfer conditions followed by treatment with water, β-silyl ester **9** was obtained with high diastereoselectivity (eq 3). Observation of the reaction mixture by NMR spectroscopy revealed the presence of an oxasilacyclopentene in 92% yield, which hydrolyzed to form ester **9**.[9] The high diastereoselectivity obtained in this hydrolysis suggested that oxasilacyclopentenes might serve as useful intermediates for stereoselective synthetic transformations.



(3)

Since oxasilacyclopentenes obtained from α,β-unsaturated esters contain the silyl enol ether functionality embedded within the ring, we considered silylene transfer as a method for the stereoselective

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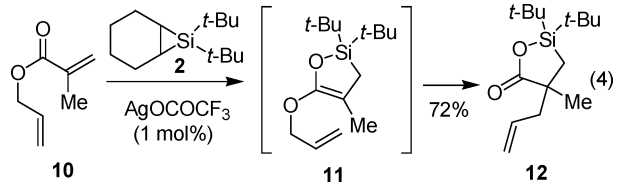
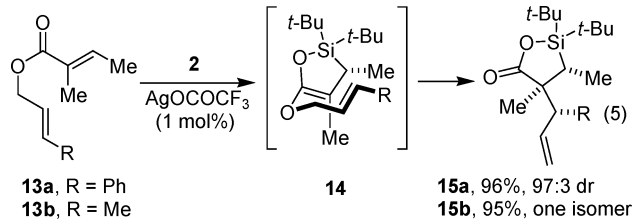
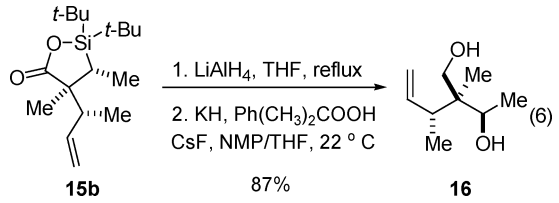
formation of tetrasubstituted silyl ketene acetals.[28] Silylene transfer to the α,β-unsaturated ester moiety of allyl methacrylate (**10**) occurred instead of transfer to the terminal alkene (eq 4). Intermediate oxasilacylopentene **11** underwent an Ireland−Claisen rearrangement[29,30] to provide silalactone **12** with the formation of an all-carbon quaternary center.[31] Adding substitution to the β-position of the unsaturated ester afforded products **15a**−**b** with high diastereoselectivities and three contiguous stereocenters (eq 5).[32] This stereochemistry may arise through a chairlike transition structure (**14**) in which the allyl fragment approaches the face opposite to the β-methyl group.

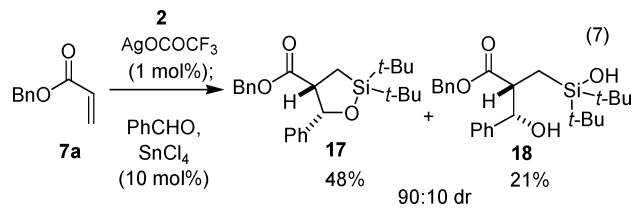




Conversion of silalactone **15b** to a functionalized diol demonstrates the synthetic utility of this silylene transfer/Ireland−Claisen reaction (eq 6). Reduction of silalactone **15b** followed by oxidation of the carbon−silicon bond[33,34] afforded 1,3-diol **16** in 83% yield over three steps starting from crotyl tiglate **13b**.



In addition to Ireland−Claisen rearrangements, preliminary studies show that these silyl ketene acetal intermediates also participate in aldol addition reactions.[35,36] Treatment of benzyl acrylate under silylene transfer conditions followed by benzaldehyde in the presence of a Lewis acid formed Mukaiyama aldol products **17** and **18** with 90:10 overall diastereoselectivity (eq 7).



Silylene transfer to α,β-unsaturated esters produces oxasilacyclopentenes and provides a new effective method for regio- and stereoselective enolate formation. These oxasilacyclopentenes are useful synthetic intermediates that can undergo facile and selective Ireland−Claisen rearrangements and aldol addition reactions to provide products with multiple contiguous stereocenters and quaternary carbon centers.

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Supporting Information Available: Experimental procedures; spectroscopic, analytical, and X-ray data for the products (PDF, CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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