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Intermolecular Silacarbonyl Ylide Cycloadditions: A Direct Pathway to Oxasilacyclopentenes

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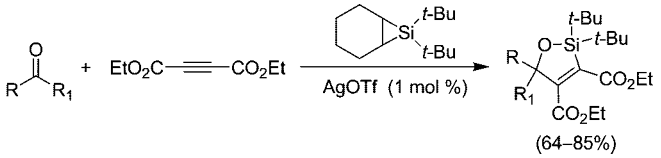
ABSTRACT

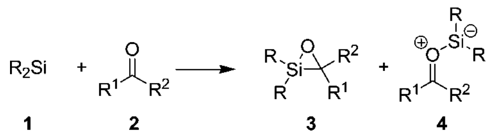


Silacarbonyl ylides, generated by metal-catalyzed silylene transfer to carbonyls, participate in formal intermolecular 1,3-dipolar cycloaddition reactions with carbonyl compounds and alkynes to form dioxasilacyclopentane acetals and oxasilacyclopentenes in an efficient, one-step process.

The reactions of silylenes with carbonyl compounds have produced a number of mechanistically and synthetically useful reactions. Silylenes (**1**) react with aldehydes and ketones (**2**) to give either oxasilacyclopropanes **3** or silacarbonyl ylides **4** (Scheme 1),[1] and these isomeric products can be interconverted.[2] The silacarbonyl ylide can be intercepted by π-bonds to form products formally arising from 1,3-dipolar cycloadditions.[3] This reaction, which creates new carbon−carbon and carbon−silicon bonds, has not been found to be preparatively useful because yields are often low, even in intramolecular examples.[1a] In addition, the generation of silylenes requires forcing conditions such as extended photolysis with excess reagents.[4]

In this paper, we report that metal-catalyzed silylene transfer to carbonyl compounds in the presence of an electron-deficient alkyne produced formal 1,3-dipolar cycloaddition products efficiently under mild conditions. The products of these reactions possess functional groups that can be functionalized with control of regioselectivity.

Scheme 1. Silylene Transfer to Carbonyl Compounds



We discovered that silylene transfer to carbonyl compounds led to three-component cyclization reactions in our attempts to form oxasilacyclopropanes. Treatment of cyclohexene silacyclopropane **6**[5] with 2 equiv of benzaldehyde (**5**) and a catalytic amount of silver triflate did not yield the expected three-membered ring. Instead, it gave the product of silylene transfer to the C−O double bond and subsequent insertion of the second equivalent of aldehyde to form dioxasilacyclopentane **7** (Scheme 2).[6] A screen of metal salts known to catalyze silylene transfer to alkenes[7] did not lead

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(1) (a) Ando, W.; Ikeno, M.; Sekiguchi, A. *J. Am. Chem. Soc.* **1978**, *100*, 3613–3615. (b) Ando, W.; Hagiwara, K.; Sekiguchi, A. *Organometallics* **1987**, *6*, 2270–2271. (c) Sakai, N.; Fukushima, I.; Minakata, S.; Ryu, I.; Komatsu, M. *Chem. Commun.* **1999**, 1857–1858.

(2) (a) Gordon, M. S.; George, C. *J. Am. Chem. Soc.* **1984**, *106*, 609–611. (b) Becerra, R.; Cannady, J. P.; Walsh, R. *J. Phys. Chem.* **1999**, *103*, 4457–4464. (c) Becerra, R.; Cannady, J. P.; Walsh, R. *Phys. Chem. Chem. Phys.* **2001**, *3*, 2343–2351.

(3) Padwa, A.; Weingarten, M. D. *Chem. Rev.* **1996**, *96*, 223–270.

(4) (a) Sakai, N.; Fukushima, T.; Okada, A.; Ohashi, S.; Minakata, S.; Komatsu, M. *J. Organomet. Chem.* **2003**, *686*, 368–372. (b) Minakata, S.; Ohashi, S.; Amano, Y.; Oderaotoshi, Y.; Komatsu, M. *Synthesis* **2007**, 2481–2484.

(5) Boudjouk, P.; Black, E.; Kumarathasan, R. *Organometallics* **1991**, *10*, 2095–2096.

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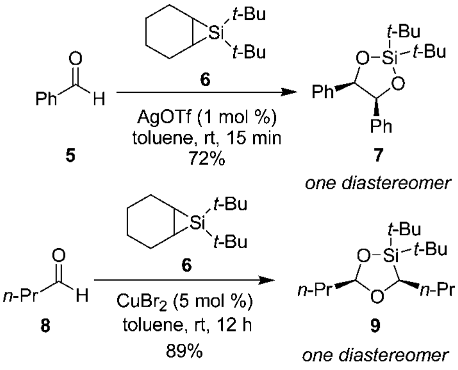
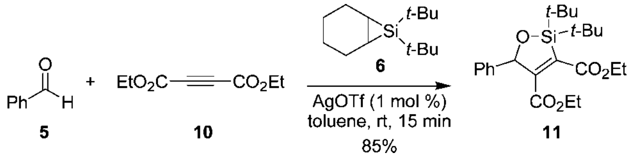
Scheme 2. Silylene Transfer to Aldehydes



to formation of oxasilacyclopropanes. When *n*-butyraldehyde (**8**) was subjected to the same catalyst screen, copper(II) bromide-catalyzed silylene transfer afforded the intermolecular 1,3-dipolar cycloaddition product, dioxasilacyclopentane acetal **9**, in 89% yield (Scheme 2). A competition experiment between aldehydes **5** and **8** yielded dioxasilacyclopentane **7** as the sole product, suggesting that the difference in regioselectivity of the corresponding products **7** and **9** is caused by a divergence in the mechanistic pathways.

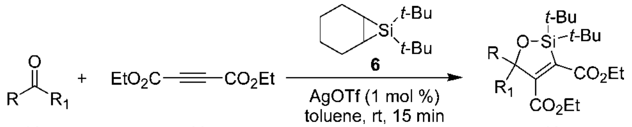
Silylene transfer to benzaldehyde in the presence of electron-deficient alkyne **10** led to a different three-component coupling reaction. When 1 equiv of alkyne **10** and 1 equiv of benzaldehyde (**5**) were treated under metal-catalyzed silylene transfer conditions, oxasilacyclopentene **11** was formed in 85% yield (Scheme 3). This reaction is complementary to our earlier synthesis of oxasilacyclopentenes.[8] That method involved a two-step process whereupon silacyclopropenes, prepared from alkynes, underwent insertion reactions with carbonyl compounds. Electron-deficient alkynes, however, did not participate in that reaction because the silylenoid intermediate is electrophilic, not nucleophilic.[9]

Scheme 3. Formation of Oxasilacyclopentene

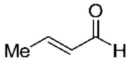
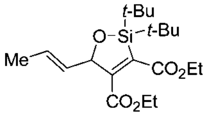
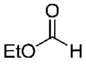
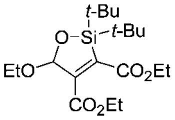
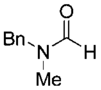
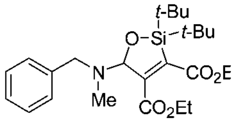
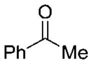
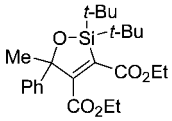
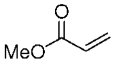
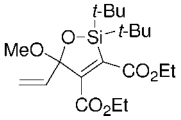


A variety of carbonyl compounds participated in the cycloaddition employing alkyne **10** as the dipolarophile (Table 1). The cycloaddition reaction tolerated α,*β*-unsaturated aldehydes and formate esters (entries 1 and 2). Formamides also reacted to form *N*,*O*-acetal oxasilacyclopentene **13c**, although the reaction was slower. Ketones underwent cyclization to form oxasilacyclopentenes containing tetrasubstituted carbon atoms (entry 4). α,*β*-Unsaturated ester **12e** reacted with alkyne **10** to form oxasilacyclopentene **13e**, although silylene transfer to the α,*β*-unsaturated ester was also observed (Scheme 4).[10] Excess ester and silacyclopropane were employed to optimize the formation of oxasilacyclopentene **13e** (entry 5).

Table 1. Silver-Catalyzed Silylcarbonyl Ylide Cycloaddition



12a-e **10** **13a-e**

entry	substrate (**12**)	product (**13**)		yield
1			**13a**	82%
2			**13b**	64%
3			**13c**	68%[a]
4			**13d**	77%[b]
5			**13e**	74%[c]

[a] At 50 °C for 12 h. [b] For 3 h. [c] 4 equiv of **6** and 4 equiv of **12e**.

The highly electron-deficient alkyne **10** was the only alkyne that participated in these reactions. Treatment of silacyclopropane **6** and carbonyl compounds with other dipolarophiles led to either silylene transfer to the alkyne to form silacyclopropenes or dimerization with the aldehyde to form dioxasilacyclopentane **7** (Scheme 5).

Control experiments indicated that the formation of the oxasilacyclopentene did not involve a silacyclopropene intermediate. When electron-deficient alkyne **10** was treated

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(6) (a) Jutzi, P.; Eikenberg, D.; Bunte, E.-A.; Möhrke, A.; Neumann, B.; Stammler, H.-G. *Organometallics* **1996**, *15*, 1930–1934. (b) Belzner, J.; Ihmels, H.; Pauletto, L.; Noltemeyer, M. *J. Org. Chem.* **1996**, *61*, 3315–3319. (c) Franz, A. K.; Woerpel, K. A. *J. Am. Chem. Soc.* **1999**, *121*, 949–957.

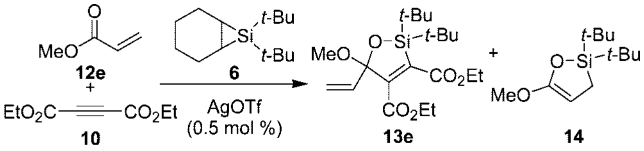
(7) Ćiraković, J.; Driver, T. G.; Woerpel, K. A. *J. Org. Chem.* **2004**, *69*, 4007–4012.

(8) (a) Seyferth, D.; Vick, S. C.; Shannon, M. L. *Organometallics* **1984**, *3*, 1897–1905. (b) Clark, T. B.; Woerpel, K. A. *J. Am. Chem. Soc.* **2004**, *126*, 9522–9523.

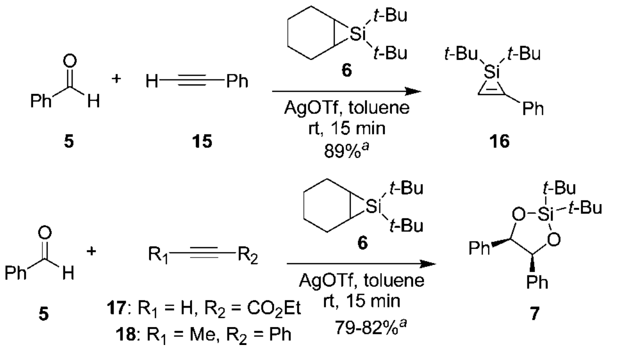
(9) Driver, T. G.; Woerpel, K. A. *J. Am. Chem. Soc.* **2004**, *126*, 9993–10002.

(10) Calad, S. A.; Woerpel, K. A. *J. Am. Chem. Soc.* **2005**, *127*, 2046–2047.

Scheme 4. Silylene Transfer to α,*β*-Unsaturated Ester



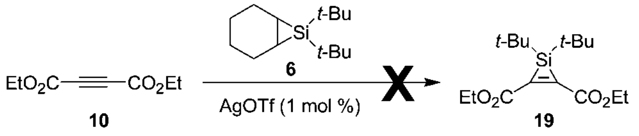
Scheme 5. Dipolarophile Screen



[a] As determined by ^{1}H NMR spectroscopic analysis of the product relative to an internal standard ($PhSiMe_3$).

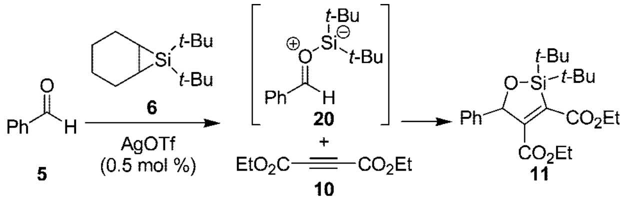
with silacyclopropane **6**, formation of silacyclopropene **19** was not detected (Scheme 6). The ^{29}Si NMR spectrum of the reaction mixture revealed two peaks at δ 18.0 and 4.8 ppm, with no peaks around δ −70 ppm, which would be expected for a silacyclopropene.[11] The silylene transfer product could not be indentified, but the chemical shifts were consistent with the presence of alkylsilanes.

Scheme 6. Silacyclopropene Control Experiment



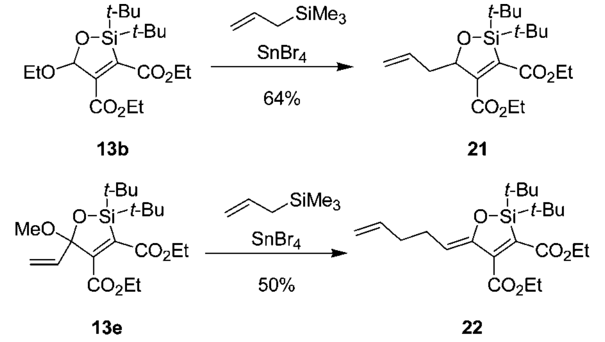
It has been previously reported that electrophilic carbenes react with aldehydes to form carbonyl ylides that then undergo 1,3-dipolar cycloadditions preferentially with electron-deficient alkynes.[12] This precedent suggests that the formation of the oxasilacyclopentenes occurs through an analogous concerted 1,3-dipolar cycloaddition pathway (Scheme 7).

Scheme 7. Proposed Cycloaddition



The oxasilacyclopentenes that possessed acetal moieties could be elaborated by nucleophilic substitution reactions. Oxasilacyclopentene **13b** was treated with allyltrimethylsilane and $SnBr_4$ to afford allylated oxasilacyclopentene **21** (Scheme 8), although the modest stabilization of the oxocarbenium ion intermediate by the electron-deficient ester required long reaction times (40 h).[13] Oxasilacyclopentene **13e** could be allylated under the same reaction conditions as **13b**, but an unanticipated product was observed. Upon Lewis acid activation to form the oxocarbenium ion, allyltrimethylsilane added to the unsubstituted terminus of the conjugated system, resulting in oxasilacyclopentene **22**.[14]

Scheme 8. Nucleophilic Substitution of Oxasilacyclopentenes



The carbonyl groups can be functionalized and appear to be sterically differentiated. Oxasilacyclopentene **11** was reduced by *i*-Bu_2AlH to form diol **23**. When oxasilacyclopentene **11** was treated with 2 equiv of methylmagnesium bromide, bicyclic α,*β*-unsaturated lactone **24** was formed (Scheme 9). Addition of 1 equiv of a Grignard reagent resulted in a 1:1 mixture of starting material and lactone **24**. These experiments reveal that the two carbonyl groups can be functionalized independently or simultaneously and suggest that the dissimilarity is due to the steric hindrance imparted by the bulky *tert*-butyl groups attached to the silicon atom.

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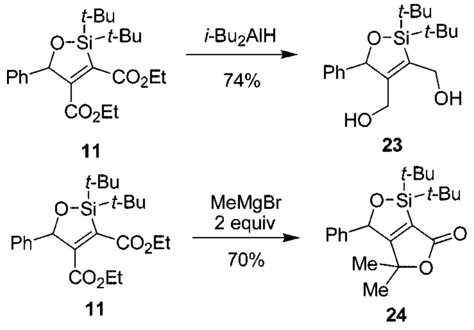
(11) Palmer, W. S.; Woerpel, K. A. *Organometallics* **1997**, *16*, 4824–4827.

(12) (a) Hodgson, D. M.; Glen, R.; Grant, G. H.; Redgrave, A. J. *J. Org. Chem.* **2003**, *68*, 581–586. (b) Russell, A. E.; Brekan, J.; Gronenberg, L.; Doyle, M. P. *J. Org. Chem.* **2004**, *69*, 5269–5274.

(13) Creary, X.; Geiger, C. C. *J. Am. Chem. Soc.* **1982**, *104*, 4151–4162.

(14) One alkene isomer was observed. We have assigned the product as the *Z*-alkene isomer because this configuration should minimize steric interactions. Spectroscopic experiments, however, showed no NOE between the vinyl hydrogen and the carboethoxy groups, so this assignment has not been established unambiguously.

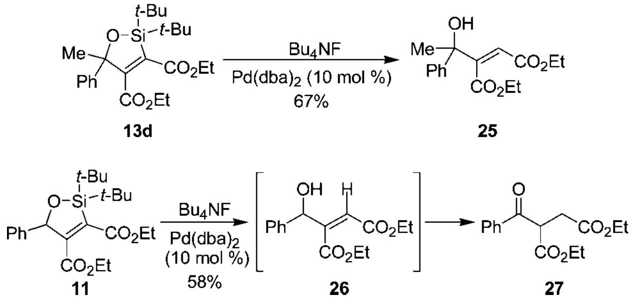
Scheme 9. Functionalization of Carbonyls



Conversion of oxasilacyclopentene **13d** to allylic alcohol **25** demonstrates the synthetic utility of the cycloaddition reaction. Initial attempts at removing the silicon atom through conventional protodesilylation methods were unsuccessful.[15] The silicon atom could be removed to form allylic alcohol **25** utilizing palladium salts and Bu_4NF as the fluoride source.[16] Oxasilacyclopentene **11** also underwent protodesilylation, but allylic alcohol **26** isomerized to provide ketone **27**.

In conclusion, silylene transfer to carbonyl compounds can be used to produce dioxasilacyclopentane acetals and oxasilacyclopentenes in a single step through formal intermolecular 1,3-dipolar cycloadditions. The oxasilacyclopentene products are useful intermediates that can be elaborated by substitution, addition, and protodesilylation reactions.

Scheme 10. Removal of Silicon



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Supporting Information Available: Experimental procedures; spectroscopic and analytical data for the products. This material is available free of charge via the Internet at http://pubs.acs.org.

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(15) Heitzman, C. L.; Lambert, W. T.; Mertz, E.; Shotwell, J. B.; Tinsley, J. M.; Va, P.; Roush, W. R. *Org. Lett.* **2005**, *7*, 2405–2408, and references therein.

(16) Copper salts have been employed in protodesilylation reactions: Trost, B. M.; Ball, Z. T.; Jöge, T. *J. Am. Chem. Soc.* **2002**, *124*, 7922–7923.