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Silylene-Mediated Polarity Reversal of Dienoates: Additions of Dienoates to Aldehydes at the *δ*-Position To Form *trans*-Dioxasilacyclononenes

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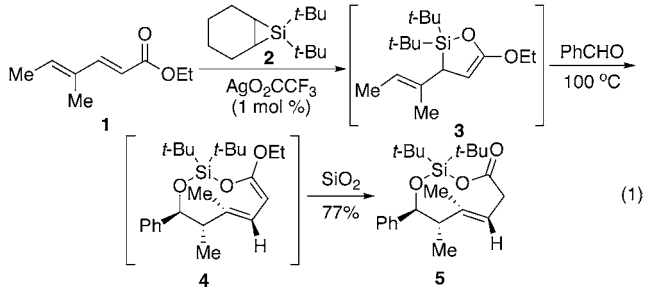
Abstract: Silylene transfer to α,*β*,*γ*,*δ*-unsaturated carbonyl compounds produced oxasilacyclopentenes that underwent thermal additions to aldehydes to produce *trans*-dioxasilacyclononenes as single stereoisomers. This reaction, which converts the *δ*-position of the unsaturated carbonyl compound into a nucleophilic center, represents an inversion of polarity from the normal pattern of reactivity. The stereospecificity of the reaction suggests that the addition to aldehydes occurred through a closed, chairlike six-membered transition state. This reaction can be used to prepare enantiomerically pure materials by the use of chiral auxiliaries to control the formation of the oxasilacyclopentenes. Functionalization of the resulting *trans*-cycloalkene occurred with complete stereoselectively.

The different positions of unsaturated carbonyl compounds exhibit predictable patterns of reactivity. While the α- and *γ*-positions are donor sites, the *β*- and *δ*-positions are acceptors.[1] For example, the aldol reaction, in which the α-position is nucleophilic, is a common transformation,[2] and the vinylogous aldol reaction uses the *γ*-position as a nucleophile.[3] Conjugate addition reactions capitalize on the electrophilicity of the *β*- and *δ*-positions.[4] The polarity of these positions can be reversed in some cases. For example, formal homoaldol reactions employ the *β*-position as a nucleophilic site.[5] Umpolung reactivity where the *δ*-position is nucleophilic, on the other hand, is uncommon.[6]

In this communication, we present a method for addition of aldehydes to dienoates at the *δ*-carbon. Silylene transfer to a dienoate forms a vinyl oxasilacyclopentene in which the *δ*-carbon becomes the nucleophilic site. These intermediates undergo nucleophilic additions to aldehydes, forming *trans*-dioxasilacyclononenes stereoselectively and stereospecifically.

The one-flask conversion of dienoate **1** and benzaldehyde to the protected adduct **5** illustrates this transformation. Silver-catalyzed silylene transfer[7] to dienoate **1** afforded vinyl oxasilacyclopentene **3** cleanly. Heating strained[8] vinyl oxasilacyclopentene **3** with benzaldehyde produced the dienol ether **4** as a single diastereomer. Filtration through silica gel hydrolyzed the silyl ketene acetal to provide the corresponding *trans*-dioxasilacyclononene **5** as one diastereomer.[9]



(1)

The anti configuration of the addition product **4** is likely established through a Zimmerman−Traxler-like[10] transition state in which the aldehyde is activated by coordination to the silicon center (**A**, Figure 1). Although *E*-allylic silanes typically react with

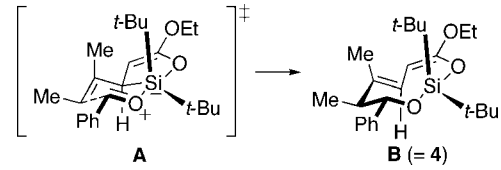
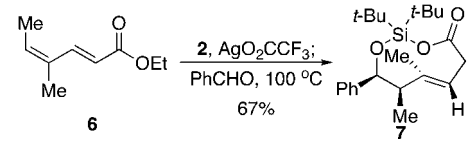


Figure 1

aldehydes in the presence of Lewis acids through open transition states to give syn products,[11,12] allylic silanes can react through closed transition states if the silicon atom is particularly Lewis acidic.[8,13] Three facts support the closed transition state for the formation of adduct **4**: (1) an external Lewis acid was not required to activate the addition of silane **3** to an aldehyde; (2) the *E*-allylic silane gave the anti product, not the syn product; and (3) no Mukaiyama[14] α-aldol products were formed by reaction of the more nucleophilic silyl ketene acetal moiety.[15]

The stereospecificity of the addition reaction also indicates that it proceeds through a closed transition state.[16] The product obtained from the *Z*-dienoate **6** was the syn isomer of the *trans*-dioxasilacyclononene (**7**, eq 2).[9] The relative configuration of *trans*-dioxasilacyclononene **7** is also consistent with its formation through a closed, chairlike transition state.[11,12]



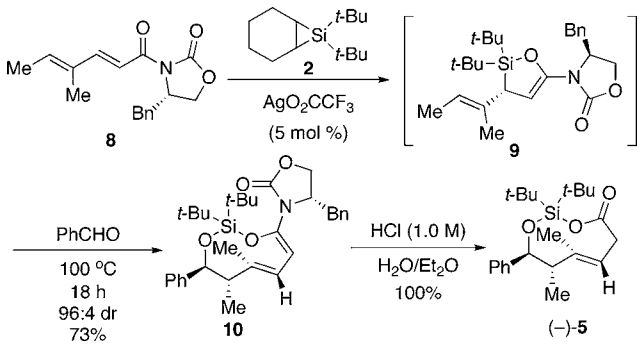
(2)

The *trans*-cyclononene products can be formed with control of absolute stereochemistry. The chiral auxiliary of dienimide **8** controlled the silylene transfer reaction, resulting in stereoselective formation of intermediate **9** (Scheme 1). Heating this silane with benzaldehyde promoted the diastereoselective formation of *trans*-dioxasilacyclononadiene **10**.[17] Treatment of diene **10** with acid under biphasic conditions removed the chiral auxiliary, providing enantioenriched *trans*-dioxasilacyclononene (−)-**5**.

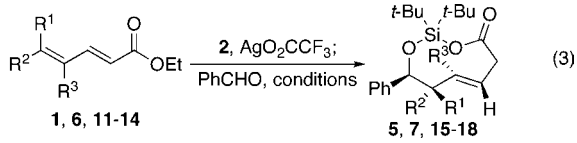
The addition of aldehydes at the *δ*-position of dienoates is general for a number of unsaturated esters (eq 3). Reaction times, however, depend upon the nucleophilicity of the allylic silane formed after silylene transfer. Substrates that possessed a methyl substituent at the *γ*-position (Table 1, entries 1, 2, and 4) produced methallyl silanes that underwent faster addition relative to substrates that only had a hydrogen atom at that position.[15]

10.1021/ja109631z

Scheme 1. Asymmetric Formation of *trans*-Dioxasilacyclononene



The longer reaction times of the substrates that only had a hydrogen atom at the γ-position led to more decomposition products and lower yields.



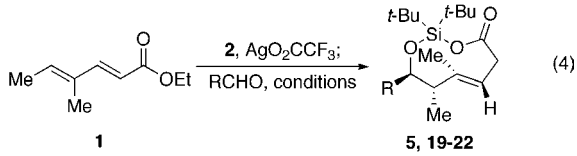
(3)

Table 1. Dienoate Scope in Formation of *trans*-Dioxasilacyclononenes (eq 3)[a]

entry	Dienoate	R^1	R^2	R^3	Conditions	Product	Yield
1	**1**	H	Me	Me	100 °C, 18 h	**5**	77%
2	**6**	Me	H	Me	100 °C, 18 h	**7**	67%
3	**11**	H	Me	H	100 °C, 5 d	**15**	59%
4	**12**	H	H	Me	100 °C, 2 d	**16**	53%
5	**13**	Me	Me	H	100 °C, 10 d	**17**	38%
6	**14**	H	H	H	100 °C, 5 d	**18**	37%

[a] Products were formed as one isomer as determined by ^{1}H NMR spectroscopy and GCMS. Yields reported are isolated yields.

A number of aldehydes participated in the addition reaction (eq 4). Reactions of sterically hindered aldehydes required longer reaction times (Table 2, entries 3 and 4). A Lewis acid catalyzed the allylation, leading to faster reactions, even at room temperature (entry 4). The relative stereochemistry of the products



(4)

Table 2. Aldehyde Scope (eq 4)[a]

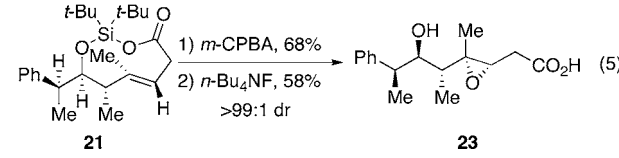
entry	RCHO	Conditions, yield		Product
		Thermal	$SnBr_4$ (10 mol %), rt	
1	PhCHO	100 °C, 18 h, 77%	3 h, 37%	**5**
2	*n*-BuCHO	100 °C, 18 h, 72%	3 h, 37%	**19**
3	*i*-PrCHO	130 °C, 3 d, 73%	18 h, 40%	**20**
4	Ph, Me, CHO	130 °C, 5 d, 72%	18 h, 94%	**21**
5	Me, CHO	100 °C, 18 h, 80%	decomposition	**22**

[a] Products were formed as one isomer as determined by ^{1}H NMR spectroscopy and GCMS. Yields reported are isolated yields.

formed by the Lewis acid catalyzed process was again consistent with a closed, chairlike transition state. The Lewis acid likely coordinated to the oxygen atom of the O−Si bond of the vinyl oxasilacyclopentene **3**, increasing the electrophilicity of the silicon center.[18]

Stereochemically homogeneous products can be made by kinetic resolution. Addition to a chiral aldehyde (Table 2, entry 4) produced the adduct as a single diastereomer.[17] The relative stereochemistry of *trans*-dioxasilacyclononene **21** is consistent with a closed, chairlike transition state where the vinyl oxasilacyclopentene approached the chiral aldehyde on a Felkin trajectory.[19] This result suggests that the use of chiral, nonracemic aldehydes would give enantioenriched products.

Because substituted *trans*-cyclononenes adopt specific conformations and are slow to isomerize,[20] functionalization of the carbon−carbon double bond only occurred on the outside face. Treatment of *trans*-dioxasilacyclononene **21** with *m*-CPBA followed by deprotection afforded epoxide **23** as a single diastereomer. This selectivity is noteworthy because epoxidations of acyclic alkenes with *m*-CPBA in which the faces of the alkene are only differentiated by $A_{1,2}$ strain are generally not diastereoselective.[21] In addition, hydroxyl-directed epoxidation of free alcohols with structures analogous to cyclononene **21** would give epoxides with the opposite relative configuration compared to epoxide **23**.[21]



(5)

In summary, silylene transfer to dienoates afforded intermediates that function as δ-enolate equivalents that react with aldehydes to form addition products stereoselectively and stereospecifically. Enantiopure products can be synthesized by employing a chiral auxiliary to control silylene transfer. Further functionalization of the *trans*-cycloalkene occurred diastereoselectively. This methodology has potential application for the synthesis of polypropionate natural products and related structures.[22]

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

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