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Acyl Polysilanes: New Acyl Anion Equivalents for Additions to Electron-Deficient Alkenes

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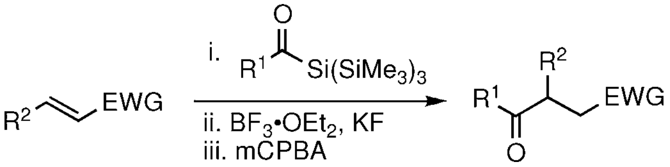
ABSTRACT



Silenes, generated through thermolysis of acylpolysilanes, add to α,β-unsaturated esters to form cyclobutanes and silylsubstituted cyclopropanes in moderate yields. Upon Si−C bond oxidation the cyclopropanes are converted directly to 1,4-dicarbonyl compounds, thus demonstrating the formal acyl anion chemistry of acyl polysilanes.

The addition of an acyl anion to an α,β-unsaturated carbonyl compound is a classical and valuable method to generate synthetically useful 1,4-dicarbonyl compounds.[1] Its simplest form, the Stetter reaction, involves cyanide or thiazolium salt promoted addition of an aldehyde to the acceptor enone.[2] However, the high reactivity of the aldehyde under these conditions can result in problems owing to self-condensation, and consequently, many alternative acyl anion equivalents have been described. One such class of acyl anion equivalents are the acyl silanes, which have found widespread application in synthesis.[3] While these have proven to be effective for Stetter-type reactions,[4] in many cases their application requires the use of basic or toxic promoters such as cyanide or fluoride. In this Letter we describe the application of acyl polysilanes as a neutral, thermally activated acyl anion equivalent for the addition to α,β-unsaturated carbonyl compounds.

As part of a general program exploring the use of silenes, compounds containing a C=Si bond, in synthesis,[5−8] we had previously explored the thermal [4 + 2] cycloaddition of Brook-type silenes [$R(R'_3SiO)C{=}Si(SiR'_3)_2$] with various alkyl-substituted dienes. These proceeded as predicted to afford the corresponding silacyclohexene in good yields and moderate diastereoselectivity (Scheme 1).[7]

Although initial experiments had suggested that electron-deficient dienes behaved similarly, a more detailed analysis

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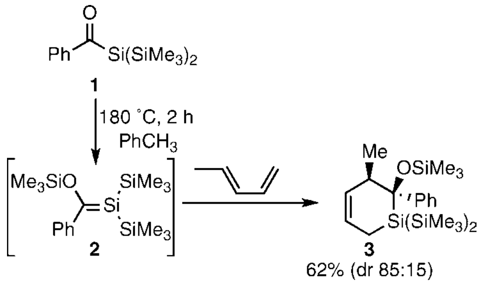
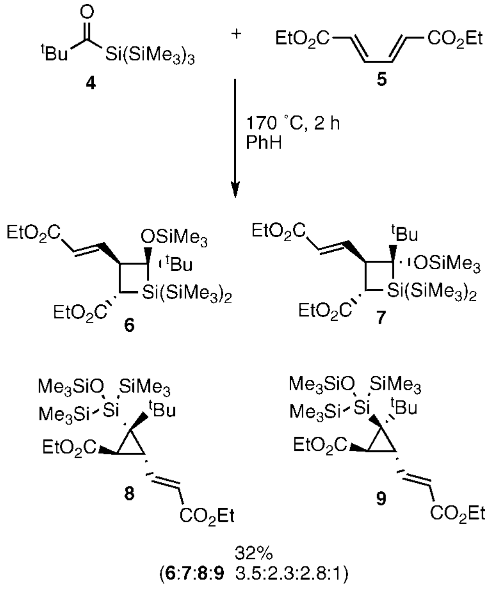
Scheme 1. Reaction of Siloxysilenes with Alkyl-Substituted Dienes



of the reaction mixture suggested that the process was more complex, involving the formation of isomeric silacyclobutanes through a [2 + 2] cycloaddition pathway. Consequently we re-examined this process heating pivaloyl polysilane **4** with (*E*,*E*)-diethylhexa-2,4-dienoate **5** in benzene in a sealed tube at 170 °C for 2 h (Scheme 2). Following flash chromatography, two discrete fractions could be obtained, each containing a mixture of two diastereoisomers in an overall 32% yield. The structures of these compounds were determined by 2D NMR spectroscopy and, ultimately, by single crystal X-ray diffraction of compound **8** (Figure 1a). The configuration of the silacyclobutanes **6** and **7** could be deduced from 2D NMR correlation experiments (Figure 1b). The regiochemistry of the "cycloaddition" was confirmed by HMBC experiments that, for both isomers, showed a 3-bond correlation from proton 1′-H to ring carbon C-2, and stereochemistry was elucidated through ^{1}H NOESY experiments.

Scheme 2. Initial Thermal Reaction of Pivaloylpolysilane **4** with Diethyl Hexadienedioate **5**



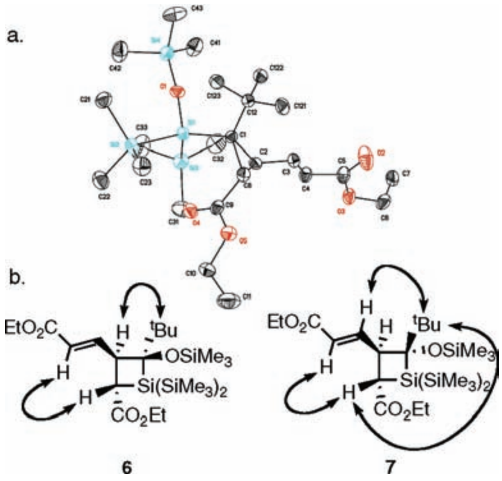


Figure 1. (a) X-ray structure for **8**. (b) Selected NOESY correlations for **6** and **7**.

Attempts to enhance the reaction by varying the reaction temperature, time, and ratio of the reagents produced variable results. Ultimately, the optimum reaction conditions involved heating the polysilane **4** with a 4-fold excess of the diene at 200 °C for 3 h, which afforded a 1.9:0:2.7:1 mixture of isomers in 69% yield, (Table 1 entry 2). The minor silacyclobutane isomer was only observed at lower temperatures, while prolonged heating resulted in diminished yields probably due to product decomposition. This suggested that silacyclobutanes are potential intermediates on the reaction pathway. In support of this, heating a solution of silacyclobutane **6** in benzene at 200 °C for 1.5 h afforded the cyclopropane **8** in 25% yield along with 46% unchanged silacyclobutane **6** (Scheme 3). Intrigued by this unusual cyclopropanation we then examined other electron-deficient silenophiles (Table 1 entries 1−10). With the exception of phenyl vinyl sulfone (entry 9), which afforded only cyclobutanes, and chalcone **11** (entry 10), all of these substrates led to the preferential if not exclusive formation of the cyclopropane. The reaction with chalcone **11** produced the [4 + 2] adduct **12** in which the α,β-unsaturated enone had behaved as the 4π component (Scheme 4). While this latter outcome is consistent with the earlier reports by Brook describing the reaction of photochemically generated siloxysilenes with enals and enones, the formation of cyclopropanes contrasts with similar studies examining reactions with cinnamate esters.[9] The reasons for this difference in reaction outcome between these two approaches to silene generation are not obvious and remain a subject of ongoing investigation.[10] In order to avoid the need for sealed tube apparatus, we then explored the potential to undertake the same conversion in a microwave vessel. Whereas for the reaction of pivaloyl polysilane and diethyl hexadienoate, it was initially found that by running the reaction at higher temperature (220 °C)

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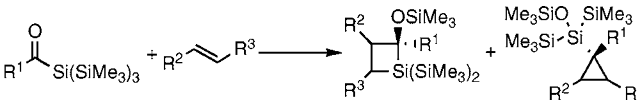
[9] Brook, A. G.; Hu, S. S.; Chatterton, W. J.; Lough, A. J. *Organometallics* **1991**, *10*, 2752–2757. Brook, A. G.; Hu, S. S.; Saxena, A. K.; Lough, A. J. *Organometallics* **1991**, *10*, 2758–2767.

[10] A model study in which a mixture of acylpolysilane **10**, ethyl cinnamate and 1,3-pentadiene were heated in benzene produced a mixture of cyclopropane **13d** and the expected adduct arising from [4 + 2] cycloaddition of a siloxysilene with pentadiene.

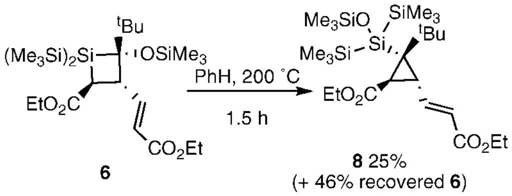
Table 1. Thermal Reactions of Acyl Polysilanes with Electron-Deficient Alkenes



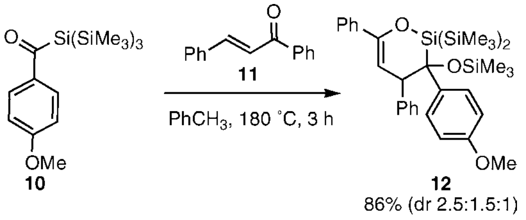
entry	R^1	R^2	R^3	method[a]	yield (%)[b] cyclobutanes	yield (%)[b] cyclopropanes
1	^{t}Bu	CO_2Me	CO_2Me	A		33 (1:0)
2	^{t}Bu	CH=CH CO_2Et	CO_2Me	A	23 (1.9:0)	46 (2.7:1)
3	^{t}Bu	CH=CHMe	CO_2Et	A		7 (1:0)
4	^{t}Bu	Ph	CO_2Me	A		49 (1:0)
5	^{t}Bu	Ph	NO_2	A	nr	
6	^{t}Bu	Ph	CN	A	11 (7.2:2:1)	32 (2.4:2.4:1:1)
7	Ph	Ph	$CONH_2$	B (90 min)	nr	
8	4-MeOC_6H_4	Ph	$CONEt_2$	B (5 min)		77[c] (2.9:1)
9	4-MeOC_6H_4	Ph	SO_2Ph	B (5 min)	40 (1:1)	
10	4-MeOC_6H_4	Ph	COPh	B (5 min)	*d*	
11	Ph	Ph	CO_2Me	B (90 min)		49 (2.7:1)
12	^{t}Bu	Ph	CO_2Me	B (240 min)		42 (1:0)
13	$4\text{-CF}_3C_6H_4$	Ph	CO_2Me	B (60 min)		56 (4.9:1)
14	4-MeOC_6H_4	Ph	CO_2Me	B (5 min)		67 (2:1)
15	2-furyl	Ph	CO_2Me	B (50 min)		40 (1:0)
16	Me	Ph	CO_2Me	B (180 min)		50 (2.3:1)
17	Me	Ph	CO_2Me	A		24 (1:0)

[a] Method used. A = sealed tube, PhH, 200 °C, 3 h; B = microwave reactor, $PhCH_3$, 180 °C, time in parentheses required to achieve complete conversion of acyl polysilane. [b] Figures in parentheses refer to diastereoselectivity as determined by ^1H NMR or GC−MS analysis of crude reaction mixture. [c] Product unstable. [d] [4 + 2] cycloaddition product **12** isolated in 86% ds (2.5:1.5:1); see Scheme 4.

Scheme 3. Thermal Rearrangement of Silacyclobutane **6**



Scheme 4. Reaction of Acylpolysilane **10** with Chalcone



and short times (30 min) good yields could be obtained using only 1 equiv of the silenophile, the high pressures generated in the tube made it practically difficult to translate this observation to other substrates. However, the use of microwave heating at slightly lower temperatures addressed this issue, and using this somewhat operationally simpler protocol, we then explored a selection of different polysilanes using methyl cinnamate as a model silenophile, (Table 1 entries 7−16). In all, cases the cyclopropane was the only isolable product, with no evidence for silacyclobutane being detected in the crude reaction mixture. At this stage, we had developed a simple, neutral synthesis of silylated cyclopropanes from cinnamate esters and various related analogues, and it was of interest to explore how these could be elaborated in a synthetically useful manner. We anticipated that Fleming−Tamao oxidation of the silyl group would provide 2-hydroxycyclopropane carboxylates that resemble the donor−acceptor cyclopropanes elegantly exploited by Reissig and others.[11] Despite the presence of the siloxy group, initial attempts to directly oxidize the C−Si bond using the classic Tamao conditions (H_2O_2, KF, $KHCO_3$) failed.[12] In such situations it can be beneficial to convert the silane precursors to the analogous fluorosilane. Following the precedents from our earlier studies,[8] siloxysilylcyclopropane **13a** was treated with $BF_3{\cdot}2AcOH$ to afford, after 30 min at room temperature, the fluorosilane **14a** (Scheme 5). Surprisingly, this too was resistant to oxidation with hydrogen peroxide. However, enhancing the reactivity of the silicon center by conversion to the difluorosilane **15** through prolonged treatment with $BF_3{\cdot}2AcOH$ overcame this problem. The subsequent Tamao oxidation now proceeded smoothly to afford a mixture of ketoester **17a** and associated acid, presumably arising from opening of the intermediate

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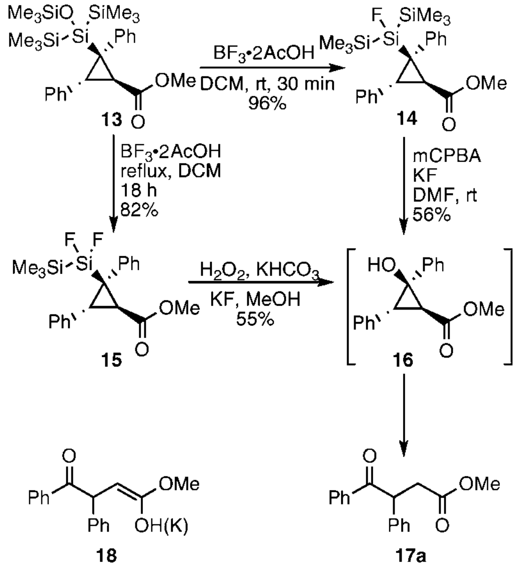
[11] Jones, G. R.; Landais, Y. *Tetrahedron* **1996**, *52*, 7599–7662. Yu, M.; Pagenkopf, B. L. *Tetrahedron* **2005**, *61*, 321–347. Reissig, H. U.; Zimmer, R. *Chem. Rev.* **2003**, *103*, 1151–1196.

[12] Tamao, K.; Ishida, N.; Tanaka, T.; Kumada, M. *Organometallics* **1983**, *2*, 1694–1696.

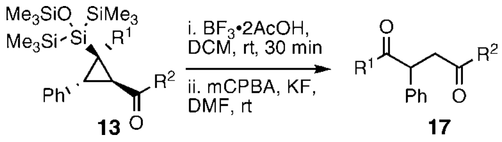
Scheme 5. Oxidative Elaboration of Silylcyclopropanes



hydroxycyclopropane under the reaction conditions and concomitant ester hydrolysis. Disappointingly, attempts to extend this protocol to other silyl cyclopropanes resulted in only low yields of the intermediate difluorosilane accompanied by extensive decomposition. Consequently we explored different methods for the oxidation and ultimately found that, following the precedent established by Tamao,[13] the monofluorosilane could be oxidized, albeit slowly, using mCPBA in DMF. Following further optimization, it was found that the addition of KF to this oxidation provided both enhanced yields and shorter reaction times. Pleasingly, this two-step procedure proved to be applicable to all of the other silylcyclopropanes to provide the corresponding 1,4- dicarbonyl compounds in reasonable yields (Table 2).

Presumably the ring opening of the cyclopropane proceeds via the intermediate enolate anion **18**, but to date, all attempts to trap this with a variety of electrophiles have proven unsuccessful. Practically, the process can be simplified into a one-pot conversion with the intermediate fluorosilyl cyclopropane being used directly in the subsequent oxidation.

Table 2. Oxidation of Silylcyclopropanes **13**



entry	13	R^1	R^2	yield **14** (%)	yield **17**(%)
1	**a**	Ph	OMe	96	56
2	**b**	Me	OMe	94	50
3	**c**	^{t}Bu	OMe	97	61
4	**d**	4-MeOC$_6$H$_4$	OMe	98	51
5	**e**	4-CF$_3$C$_6$H$_4$	OMe	98	45
6	**f**	2-furyl	OMe	61	78
7	**g**	4-MeOC$_6$H$_4$	NEt$_2$	[a]	22

[a] Fluorosilane **14g** was not stable to silica gel and was used directly in the oxidation without purification.

Overall, this two-step sequence, involving silene generation and “cycloaddition”, followed by oxidative cleavage of the cyclopropyl ring, represents the product of the formal addition of an acyl anion to the cinnamate group. In conclusion, acyl polysilanes represent a new acyl anion equivalent and in particular one that reacts under nonbasic conditions. These results continue to demonstrate that the unusual chemistry exhibited by silenes offers new prospects for synthetic methodology. Further explorations of their chemistry, together with mechanistic studies to underpin these observations, are in progress and will be reported in due course.

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Supporting Information Available: Experimental procedures and NMR spectra for all new products. This information is available free of charge via the Internet at http://pubs.acs.org.

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[13] Tamao, K.; Kakui, T.; Akita, M.; Iwahara, T.; Kanatani, R.; Yoshida, J.; Kumada, M. *Tetrahedron* **1983**, *39*, 983–990.