

Full Research Paper

Synthesis of highly substituted allenylsilanes by alkylidenation of silylketenes

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Abstract

Background: Allenylsilanes are useful intermediates in organic synthesis. An attractive, convergent but little used approach for their synthesis is the alkylidenation of stable silylketenes. Reactions thus far have been limited to the use of unsubstituted silylketenes (or equivalents) with stabilised or semi-stabilised ylides only. The current study explores the reactions of substituted ketenes prepared through rhodium(II)-mediated rearrangement of silylated diazoketones.

Results: A range of novel 1,3-disubstituted and 1,3,3-trisubstituted allenylsilanes were prepared using stabilised and semi-stabilised ylides. Alkylidenation with non-stabilised phosphorus ylides was not viable, but the use of titanium-based methylenating reagents was successful, allowing access to 1-substituted allenylsilanes.

Conclusion: Many novel allenylsilanes may be accessed by alkylidenation of substituted silylketenes. Importantly, for the first time, simple methylenation of silylketenes has been achieved using titanium carbenoid-based reagents.

Introduction

Allenylsilanes are versatile intermediates for organic synthesis.[1,2] They have two main modes of reactivity: firstly, as propargyl anion equivalents in thermal [3,4] or Lewis acid-mediated [5,6] addition to carbonyls, acetals and imines, and secondly as three-carbon partners in [3+2] annulation reactions. Thus, reaction with aldehydes,[7] imines/iminiums,[7,8] enones [9-11] and nitrosyl cations [12] leads to dihydrofurans, dihydropyrroles, cyclopentenones and isoxazoles respectively.[13] In most cases the silicon is retained in the final product and can be used as a handle for further synthetic elaboration.

Amongst the myriad methods to prepare allenylsilanes,[1,14] an attractive disconnection is to consider a Wittig-type alkylidenation of a silylketene, Figure 1.

This convergent approach potentially allows for tremendous variation in substitution pattern at both termini of the allenylsilane, yet has been little exploited thus far. Ruden first demonstrated that the stabilised phosphorane carbethoxymethylenetriphenylphosphorane underwent Wittig condensation with trimethylsilylketene at sub-ambient temperature in high yield, but found that non-stabilised phosphoranes led to complex mixtures of products.[15] Other workers later extended this chemistry to include a wider range of stabilised phosphoranes, but attempts to promote the reaction with semi-stabilised ylides such as benzylidenetriphenylphosphorane were unsuccessful unless bis(trialkylsilyl)ketenes were used as substrates.[16,17] Thus, only 3-substituted and 3,3-disubstituted allenylsilanes have thus far been accessed by alkylidenation of silylketenes, whilst no reports of the

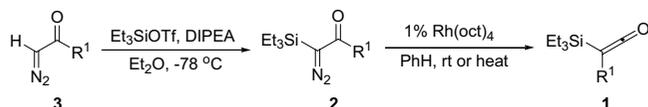
successful introduction of non-stabilised ylide equivalents have been forthcoming.

A second impediment to the generalisation of the approach has been the paucity of methods for preparing substituted silylketenes. [18,19] Methods based upon the thermolysis of siloxyalkynes [20] and dehydrohalogenation of substituted α -silyl acid halides [21,22] have not found general application. We recently reported a mild and functional group tolerant approach to substituted silylketenes based upon a rhodium-mediated formal Wolff rearrangement of silylated diazoketones. [23] Related photolytic approaches also hold some promise. [24-27] These methods allow access for the first time to a wide range of substituted silylketenes which will allow the chemistry of these fascinating persistent ketenes [18] to be better delineated.

In this paper we outline the synthesis of 1,3-disubstituted and 1,3,3-trisubstituted allenylsilanes by the condensation of stabilised and semi-stabilised ylides with substituted silylketenes, and report for the first time the methylenation of silylketenes to give 1-substituted allenylsilanes using titanium-based methodology.

Results and Discussion

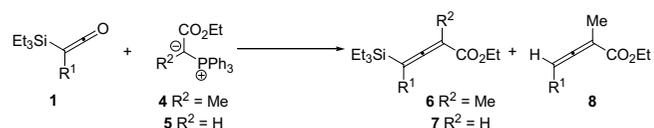
Our investigations began with the preparation of substituted silylketenes **1** as substrates for the alkylidenation chemistry. This was carried out under our previously reported conditions for rhodium(II) octanoate-mediated rearrangement of silyl diazoketones **2**, [23] which in turn were prepared by *C*-silylation of the parent diazoketones **3** with triethylsilyl triflate, [28] Scheme 1, Table 1. It should be noted that while the alkyl-substituted silylketenes are relatively stable and show little decomposition at room temperature over several days, the (hetero)aromatic-substituted silylketenes are much less robust and should be used quickly or stored in a freezer.



Scheme 1: Synthesis of substituted silylketenes 1

With the requisite silylketenes in hand, attention turned to their reaction with the carboethoxy-stabilised phosphoranes **4** and **5**. At the outset, it was by no means certain that these would react efficiently with substituted silylketenes **1** since it is well documented that nucleophiles attack silylketenes *anti* to the silicon, [29] *ie* the phosphoranes would be approaching from the same side as the R^1 -substituent. Since in all previous examples this substituent has been a hydrogen atom, the extension to bulkier substituents could not be taken for granted. In the event, however, we were pleased to find that in nearly all

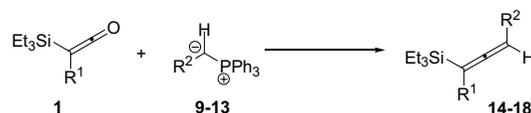
cases the desired allenylsilanes were formed in moderate to excellent yield, Scheme 2, Table 2.



Scheme 2: Reaction of substituted silylketenes with ester-stabilised phosphoranes

As expected, reactions with the more substituted ylide **4** were significantly slower than those with the parent ylide **5** (compare reaction temperatures and times, entries 1, 3 and 5 versus entries 2, 4 and 6). Increasing the steric bulk of the ketene substituent also slows the reaction, in line with our expectations, exemplified by the reactions of cyclohexyl-substituted ketene **1d** (entries 7 and 8, compared with entries 16). In almost all cases, if reactions were left for extended periods beyond consumption of starting material, small quantities of desilylated allenes were observed. With alkyl-substituted ketenes this could be avoided by careful reaction monitoring, but was unavoidable in the (somewhat sluggish) reaction of ylide **4** with aromatic substituted ketenes **1e/f**, while in the case of furyl and thiophenyl-substituted ketenes **1h** and **1i**, these were the sole or predominant products of reaction. It appears that the presence of the (hetero)aryl group labilises the silicon to cleavage under the reaction conditions, likely reflecting the silyl group acting as an electrofuge with the (hetero)aryl substituent stabilising incipient anionic character at the adjacent carbon.

We next investigated the reaction of silylketenes **1** with other ylides (Scheme 3). Pleasingly, ylides stabilised by alternative electron-withdrawing groups such as cyano (**9**), acetyl (**10**) and benzoyl (**11**) were also successfully employed in allenylsilane formation. Likewise, the semi-stabilised aromatic-substituted ylides **12** and **13** also gave good yields of the allenylsilanes. The incorporation of the 4-bromophenyl group from **13** is particularly interesting since the bromide provides a handle for further functionalisation either of the allenylsilane or of the products of its subsequent reaction.

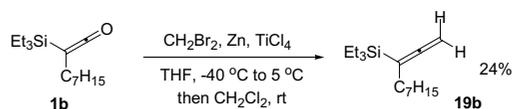


Scheme 3: Reaction of silylketenes with various ylides

Finally, the reactions of the non-stabilised ylides $Ph_3P=CHSPh$, $Ph_3P=CHOMe$ and $Ph_3P=CH_2$ were examined. In all cases, rapid decomposition of the silylketenes to complex mixtures of unidentified products was observed, even at sub-ambient temperatures. One possible mechanism proposed for the decomposition of

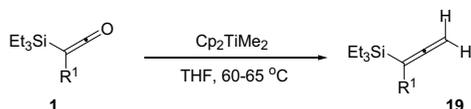
unsubstituted silylketenes with reactive ylides involves deprotonation by the basic reagent to generate ynoate anions. Clearly, since such a pathway cannot operate with the substituted ketenes used here other mechanisms are at play, which may include nucleophilic desilylation or ketene oligomerisation initiated by nucleophilic addition to the ketene carbonyl group. If the former pathway were occurring, then increasing the size of the silyl substituent ought to retard this pathway, but reaction of the *tert*-butyldimethylsilyl analogue of **1b** with $\text{Ph}_3\text{P}=\text{CH}_2$ also gave no observable allenylsilane product. The lack of identifiable products from these reactions precludes further speculation on the mechanism of decomposition at this stage.

The confirmation that non-stabilised ylides such as methylenetriphenylphosphorane were unsuitable reaction partners for condensation with even substituted silylketenes was disappointing, since the 1-substituted allenylsilanes **19** that would be thus formed are useful synthetic intermediates. Our attention therefore turned to the application of milder (and specifically less basic/nucleophilic) methylenating reagents. We first investigated the Lombardo reagent, [30] and were pleased to find that a modest yield of allenylsilane **19b** was obtained from this reaction (Scheme 4).



Scheme 4: Methylenation of silylketene **1b with the Lombardo reagent**

Although the Lombardo reaction had several disadvantages (including the lengthy preparation of the reagent and the heterogeneous nature of the reaction medium) which led us to discount it as a long term solution to the problem, it gave us the encouragement to screen other titanium carbenoid-based methylenating reagents. The Petasis reagent (dimethyltitanocene) [31,32] was our next choice, and we were pleased to find that it afforded modest to excellent yields of the allenylsilanes in reaction with most of the ketene substrates examined (Scheme 5, Table 4).



Scheme 5: Methylenation of silylketenes with the Petasis reagent

The low yield with phenyl-substituted ketene **1e** is likely attributable to the instability of the ketene at the elevated temperatures for the Petasis reaction. Consistent with this, attempted reaction of the heteroaryl-substituted ketenes **1h/j** failed to return any allenylsilane product. We have not as yet examined the use of the more reactive Tebbe

reagent which may function effectively at lower temperatures and hence offer a solution to this current limitation. Additionally, it will be of future interest to investigate the chromium-based Takai procedures for olefination with higher alkylidene reagents, [33] since this has the potential to deliver alkyl-substituted allenylsilanes.

In summary, we have further developed the reaction of stabilised and semi-stabilised ylides with silylketenes to include, for the first time, carbon-substituted silylketenes leading to a range of novel 1,3-disubstituted and 1,3,3-trisubstituted allenylsilanes. Additionally, we have demonstrated for the first time that titanium carbenoids can be used to methylenate silylketenes, providing the first access to 1-substituted allenylsilanes from these substrates. Given the broad range of useful chemistry undertaken by allenylsilanes, we expect that these new highly functionalised members of the class will find broad synthetic utility. Our own studies on their application in heterocyclic synthesis will be disclosed in due course.

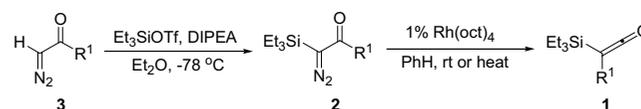


Figure 1
Alkylidene approach to the synthesis of allenylsilanes.

Table 1: Synthesis of substituted silylketenes I

Entry	R ¹	Yield (2)	Yield (1)
a	CH ₃	82%	50%
b	C ₇ H ₁₅	95%	65%
c	PhCH ₂	90%	72%
d	cC ₆ H ₁₁	94%	77%
e	Ph	80%	43%
f	4-MeOPh	35%	24%
g	4-BrPh	90%	40%
h	2-furyl	74%	40%
i	2-thienyl	72%	27%
j	3-(<i>N</i> -Boc-indolyl)	46%	51%

Description of Additional Material

Additional material features copies of ¹H nmr spectra of silylated diazoketones **2** and silylketenes **1**, plus ¹H and ¹³C nmr spectra of allenylsilanes **6**, **7**, and **1419**.

Table 2: Reaction of substituted silylketenes with ester-stabilised phosphoranes

Entry	Ketene	Ylide	Temp (°C)	t (h)	Solvent	Yield 6/7 (8)
1	1a	4	80	24	PhH	54%
2	1a	5	rt	3	CH ₂ Cl ₂	60%
3	1b	4	110	24	toluene	45%
4	1b	5	reflux	24	CH ₂ Cl ₂	77%
5	1c	4	80	24	PhH	60%
6	1c	5	rt	6	CH ₂ Cl ₂	81%
7	1d	4	110	48	toluene	22% ^a
8	1d	5	80	48	toluene	78%
9	1e	4	80	24	PhH	55% (7%)
10	1f	4	60	5	CH ₂ Cl ₂	44% (3%)
11	1h	4	rt	6	CH ₂ Cl ₂	0% (57%)
12	1h	4	50	1	CH ₂ Cl ₂	7% (23%)
13	1i	4	rt	10	CH ₂ Cl ₂	0% (67%)
14	1i	5	rt	2	CH ₂ Cl ₂	98%
15	1j	4	80	12	PhH	74% (19%)

^a 60% of starting material recovered

Table 3: Reaction of silylketenes with various ylides

Entry	Ketene	Ylide	R ²	Temp (°C)	t (h)	Solvent	Allene	Yield
1	1a	9	CN	rt	1	CH ₂ Cl ₂	14a	53%
2	1b	9	CN	rt	16	CH ₂ Cl ₂	14b	94%
3	1a	10	COMe	rt	8	CH ₂ Cl ₂	15a	52%
4	1a	11	COPh	50	5	CH ₂ Cl ₂	16a	62%
5	1b	11	COPh	60	24	CH ₂ Cl ₂	16b	62%
6	1a	12	Ph	rt	0.5	THF	17a	65%
7	1b	12	Ph	rt	0.5	THF	17b	68%
8	1g	12	Ph	rt	0.5	THF	17g	58%
9	1b	13	4-BrPh	rt	0.5	THF	18b	53%

^a the TBDMS ketene was employed in place of the TES ketene

Table 4: Methylenation of silylketenes with the Petasis reagent

Entry	Ketene	Time (h)	Yield
1	1b	6	78%
2	1b*	2	79%
3	1c	5	74%
4	1d	26	82%
5	1e	5	38%

^a the TBDMS ketene was employed in place of the TES ketene

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