

Manuscript Style Guide

Synthesis of highly substituted allenylsilanes by alkylidenation of silylketenes 1

Stephen P. Marsden^{*1} and Pascal C. Ducept² 2

Address: ¹School of Chemistry, University of Leeds, Leeds LS2 9JT, United Kingdom and

²Department of Chemistry, Imperial College London, London SW7 2AY, United Kingdom

Email: Steven P. Marsden - s.p.marsden@leeds.ac.uk

* Corresponding author

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Abstract

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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.

Keywords

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allenylsilanes; rhodium(II) octanoate-mediated rearrangement; silylketenes; titanium carbenoids; ylide

3

The abstract for the manuscript should not exceed 350 words. The abstract may be a compact text or may be structured into the separate sections **Background**, the context and purpose of the study; **Results**, the main findings; **Conclusion**, brief summary and potential implications. Abbreviations should be used sparingly in the abstract. If used, then only common ones should be employed. Citations and references should not be given in abstracts.

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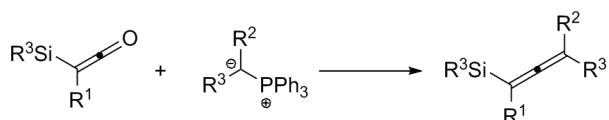
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Five keywords in alphabetical order describing the main topics of the paper should appear below the abstract for indexing purpose. They should be separated by a semicolon.

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, cyclopentenes 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).



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Figure 1: Alkylidenation approach to the synthesis of allenylsilanes.

6

The introduction section should be written from the standpoint of researchers without specialist knowledge in that area. It should clearly state the background of the research, as well as its purposes and significance, and should include a brief statement of what is being reported in the article.

7

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- Figures and schemes are consecutively numbered with Arabic numerals in the order they are first cited in the manuscript text (i.e. Figure 1, Figure 2, etc.).
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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.

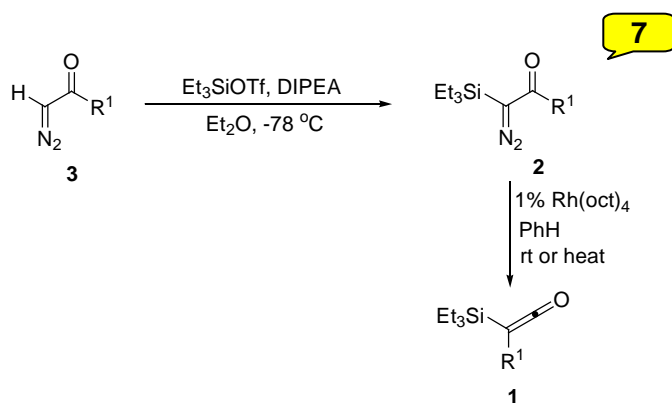
In this paper we outline the synthesis of 1,3-disubstituted and 1,3,3-trisubstituted allenylsilanes by the condensation of stabilised and semi-stabilised ylides with substituted silylketenes, and report for the first time the methylenation of silylketenes to give 1-substituted allenylsilanes using titanium-based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

8

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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.



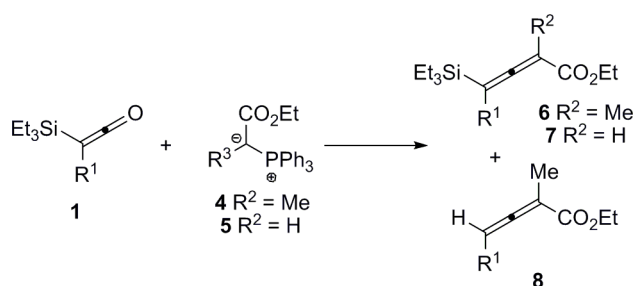
Scheme 1: Synthesis of substituted silylketenes **1**.

[...]

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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], i.e. the phosphoranes would be approaching from the same side as the R¹-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, see Supporting Information File 1 for full experimental data).



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

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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%)

^a60% of starting material recovered

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- Individual compounds must be numbered with boldface Arabic numerals in the order in which the compounds are first mentioned in the text. Boldface lower case letters may be added to distinguish compounds that differ only in the identity of substituents.
- Color and shading should not be used.

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). [...]

Supporting Information 12

Supporting information features copies of ^1H NMR spectra of silylated diazoketones **2** and silylketenes **1**, plus ^1H and ^{13}C NMR spectra of allenylsilanes **6**, **7**, and **14–19**.

Supporting Information File 1:

File Name: S1.pdf

File Format: PDF

Title: Experimental part

Supporting Information File 2:

File Name: S2.pdf

File Format: PDF

Title: NMR spectra of compounds **1,2,6** and **7**

Supporting Information File 3:

File Name: S3.pdf

File Format: PDF

Title: NMR spectra of compounds **14–19**

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Acknowledgements

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