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Synthesis of Diverse Allylsilanes Employing Brønsted Acid Catalyzed Reductive Functionalization

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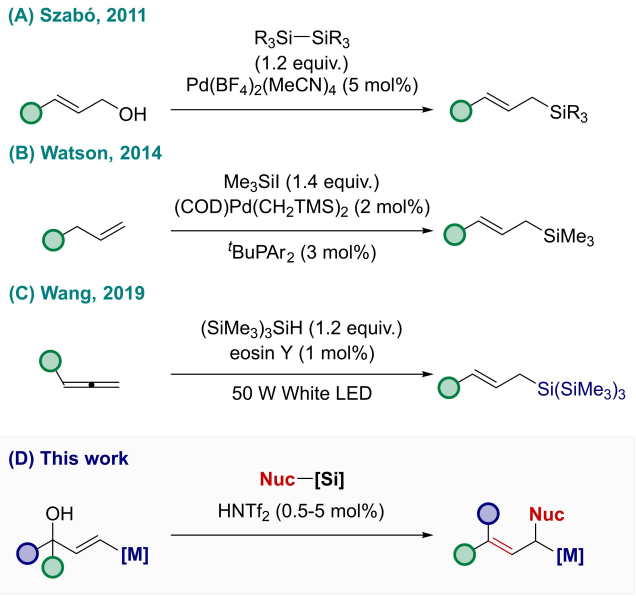
Abstract: We present a rapid (0.25–1 h), method to produce functionalised allylsilanes from readily available vinylsilanes. Employing a Brønsted acid catalysed dehydration as the key step, allylsilanes are produced in good yields (22–98%) and, in most cases, as a single geometric isomer. Furthermore, a possible allylation-Cope pathway was discovered for certain substrates and attempts to optimise this are described.

Keywords: Brønsted Acid; Allylsilane; Dehydration;; Allylation; Cope rearrangement

Allylsilanes are important building blocks within organic synthesis due to their varied reactivity, stability, and low toxicity.[1] Of note is their use as a carbon nucleophile in a range of important reactions including Hosomi-Sakurai allylations,[2] and Hiyama cross-couplings.[3] Furthermore, their use in desilylative transformations,[4] as well as successful use in ring-forming reactions cements their place in the synthetic chemist's toolbox.[5]

As a result of their wide-ranging use, novel methodologies have been developed to access them (Scheme 1). These include more traditional approaches employing allylic organometallics[6] and Wittig chemistry[7] to more modern methods applying metal-catalysed silylation of allyl electrophiles with a range of silylation reagents (Scheme 1A).[8] Further methodologies such as silyl-Heck cross couplings



Scheme 1. Selected examples.

(Scheme 1B),[9] metal-catalysed hydrosilylation of dienes[10]/allenes[11]) and propargyl displacement have all been described.[12] Finally, recent reports suggest that visible light driven radical processes can also access these valuable building blocks (Scheme 1C).[13]

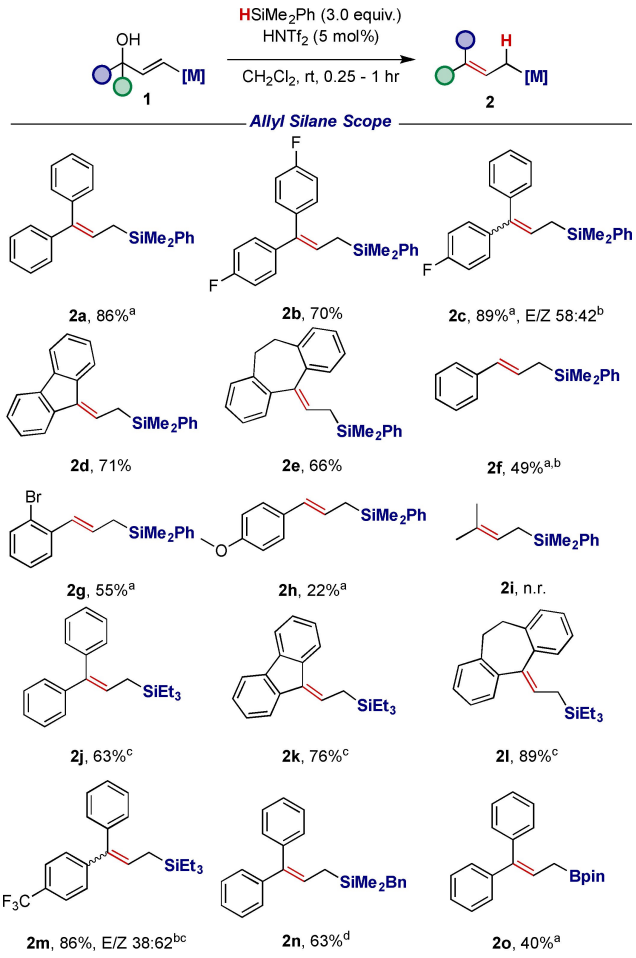
Although these methodologies present an elegant approach to allylsilanes, they are not without issue. In many cases both regioisomers are formed in the reaction mixture, or ligand divergence is noted. Furthermore, reagents are often difficult to access,

with catalyst systems consisting of non-commercial ligands and metal salts. Finally, many of the methodologies required anhydrous and air-free conditions, or specialist laboratory setups, which limits their usefulness. With these in mind, we reasoned that we could employ our lab's experience in both Lewis[14] and Brønsted[15] acid catalysed dehydration reactions to furnish highly substituted allylsilanes from readily available starting materials (Scheme 1D).[16]

We began our study focussing on the dehydration of **1a**, and employing hydridic nucleophiles (Table 1). We chose to initially focus on this area as there is clear literature precedent for the synthesis of these allylsilanes,[17] and therefore their usefulness is in no doubt. Based on our previously published work employing triflimide as a highly active super Brønsted acid,[15] we were confident that this catalyst would perform well in this reaction. This assumption turned out to be entirely justified, with complete consumption of starting material in all cases. As such, initial work concentrated on the nature of the hydride source, with silanes being the only promising lead. Further optimisation resulted in the discovery of the need for matched silanes, with transsilylation occurring when different silanes were used. Additional experimentation furnished optimised conditions, affording the allyl silane in low to excellent yields under mild conditions. It should be noted here that no attempts were made to ensure the system was air or moisture free and, in most cases, the corresponding allyl silane could be purified by filtration through silica.

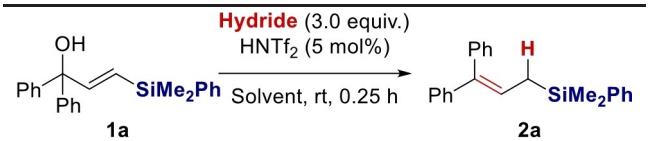
With conditions now optimised, we subjected a range of vinylsilanes to our reductive dehydration (Scheme 2). Pleasingly the reaction tolerated a range of functional groups, affording the allylsilanes in generally good yields. As shown (Scheme 2) varying the electronics and sterics of the reaction proved amenable, providing the allyl silane in moderate to excellent yields. Changing the silane to triethylsilane (TES) or dimethylbenzyl was also well tolerated. In addition, the vinyl pinacol boronate ester derivative **1o**, gave allylborane **2o** in synthetically useful yields. Where the parent vinyl silane was unsymmetrical ($R^1 \neq R^2$), the reaction was unselective relative to double bond geometry. Attempts to rectify this, including reducing the temperature of the reaction and slow addition of both catalyst and hydride source, proved fruitless.

We then turned our attention to other nucleophiles, and given our experience in this area, we decided to employ allylsilane itself (Scheme 3). This was borne out of the fact that the Brønsted acid used would, currently, not tolerate basic nucleophiles. To this end, we subjected **1a** to our previously optimised conditions, replacing the silanes for allyltrimethylsilane, and found that the reaction proceeded smoothly providing **3a** in excellent yield. We found that we could reduce the catalyst loading to 0.5 mol% without any decrease in efficiency.

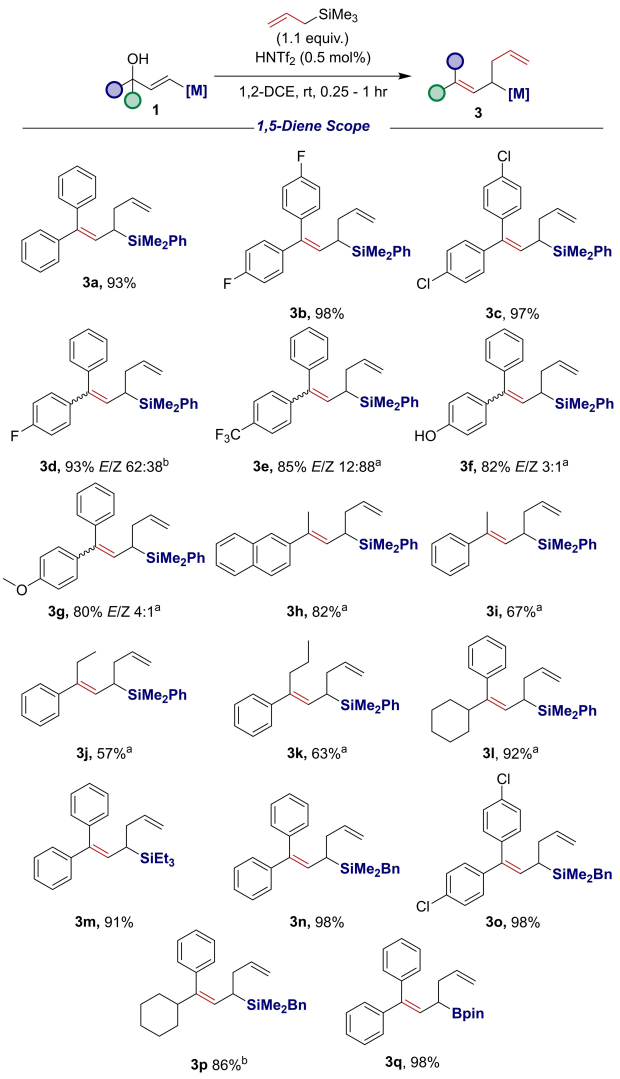


Scheme 2. Allyl silane substrate scope. [a] NMR yield calculated based on crude reaction mixtures; [b] *E*/*Z* assignments determined using 1D selective NOESY and 2D selHSQMBC experiments (see SI for more detail). [c] $HSiEt_3$ used. [d] $SiMe_2Bn$ was used.

Table 1. Optimisation study for the synthesis of allylic silane.



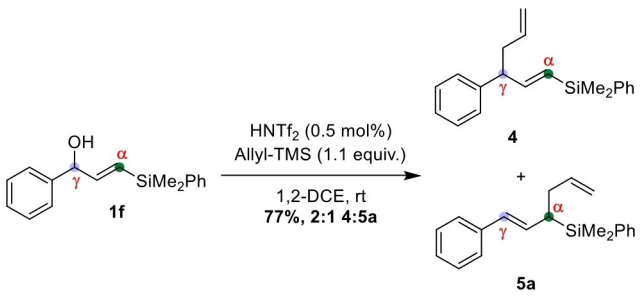
Entry	Solvent	Hydride source	Yield 2a (%)
1	CH_2Cl_2	$HSiEt_3$	20
2	PhMe	$HSiMe_2Ph$	43
3	CH_2Cl_2	$HSiMe_2Ph$	86
4	CH_2Cl_2	$NaBH_4$	complex
5	CH_2Cl_2	HBPin	n.r
6	CH_2Cl_2	Hanztsch Ester	n.r
7	CH_2Cl_2	None	complex



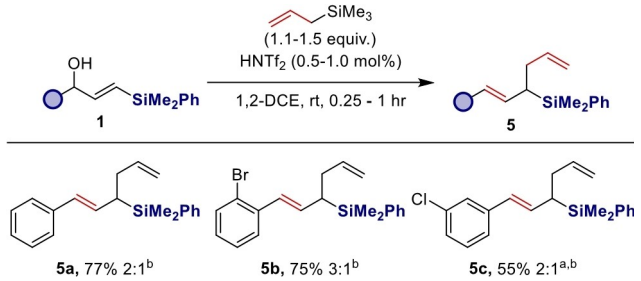
Scheme 3. Dehydrative allylations to form 1,5-dienes. [a] *E*/*Z* ratio determined by NMR analysis; [b] 1 mol% $HNTf_2$, 1.5 equiv. allyl-TMS.

As such, we proceeded to explore the utility of this reaction, starting our study with tertiary motifs. Once again, the reaction was tolerant to a range of functional groups, allowing for the access to allyl, homoallylsilanes in good to excellent yields throughout. When unsymmetrical scaffolds bearing two aryl groups were used, we obtained mixtures of regioisomers, however switching from diaryl to aryl, alkyl resulted in complete control of regiochemistry. Interestingly, the electronics of the system appears to have a pronounced effect on the outcome of the reaction, with strongly electron-withdrawing groups providing the *Z*-isomer as the major product whilst electron donating groups provide the *E*-isomer predominantly. The nature of this electronic dependence is currently under investigation, and we will report our findings in due course. We also explored the use of other silanes, and again all were well tolerated. The boron derivative also performed excellently, however given the difficulty in accessing the vinyl borane starting materials, we were limited to this single example. We finished our investigation looking at monosubstituted substrates, which we assumed would simply provide a mixture of regioisomers. With this in mind, we reacted **1f** under the previously described conditions, and obtained, as expected two products (Scheme 4). However, upon close inspection of the ^{1}H-NMR obtained from the mixture, we realised that we did not have E/Z isomers, but a mixture of allyl and vinyl silane.

Clearly these products are the result of direct allylation at either the α or γ positions relative to silicon, with the allylation at γ occurring with double bond transposition. In saying that, **4** could be transformed into **5a** through a Cope rearrangement, and we wondered if this could therefore be achieved. After extensive experimentation focussing on trying to mediate a thermal Cope rearrangement, we concluded that the energy barrier was too high, even after prolonged (168 h) heating at temperatures in excess of 200 °C. As such, we wanted to ascertain if ring functionalization played a role in both the allylation and potential subsequent Cope (Scheme 5). Ortho- and meta-substituted system were synthesized and subjected to our allylation conditions. As shown, this had little effect on the ratio of the product obtained, and the Cope rearrangement did not progress with either scaffold.



Scheme 4. Allylation of Mono-Substituted VinylsSilane.



Scheme 5. Representative Dehydrative-Allylations. [a] 1 mol% $HNTf_2$, 1.5 equiv. allyl-TMS; [b] Vinyl:allyl ratio determined by NMR analysis.

Given our failure to realise a Cope rearrangement with secondary substrates, we wanted to explore if a more constrained motif would be more amenable. To this end we synthesised **6** and reacted it under our allylation conditions (Scheme 6). After complete consumption of the starting material, ^{1}H-NMR analysis of the crude mixture indicated an vinyl:allyl ratio of 1:2 in 63% yield. Once again, experimentation concentrating on realising a thermal Cope rearrangement was attempted, this time with marked success. Heating the mixture obtained at a relatively mild 85 °C for 12 hours in a pressure vial resulted in complete conversion to the allylsilane without any noticeable reduction in yield. Although we were not able to reproduce the Cope rearrangement in other systems, we are confident that it can be realised, and work is currently underway to achieve this.

In conclusion, we have developed a facile dehydrative functionalisation approach to allylsilanes. The work shows that with low loadings of catalyst, and under mild conditions, a range of allylsilanes can be produced. We have also described preliminary work focussed on an allylation-Cope strategy to more complex allylsilanes.

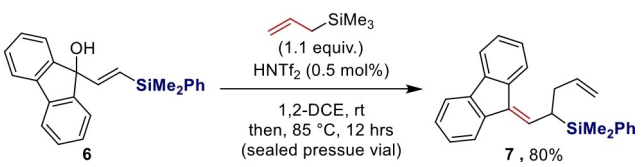
Experimental Section

Synthesis of Allylsilanes/Borane (2)

To a solution of vinyl silane/borane in DCM (0.5 M) was added $HSiR_3$ (3.0 equiv.) and triflimide (5.0 mol%, 0.05 M solution in DCM). This solution was stirred at room temperature for 15 minutes. After this time, the reaction was quenched with K_2CO_3 (1 equiv.) and reduced under vacuum. The residue was then purified via column chromatography to afford the corresponding (E)-allyl silane/borane.

Synthesis of Allylsilanes/Boranes (3)

To a solution of vinyl silane/borane in DCE (0.5 M) was added trimethylallylsilane (1.1–1.5 equiv.) and $HNTf_2$ (0.5–1.0 mol%, 0.01 M solution in DCM). This solution was stirred at room temperature for 15 minutes. After this time, the reaction was quenched with K_2CO_3 (1 equiv.) and reduced under vacuum. The residue was then purified via column chromatography to afford the corresponding (E)-allyl silane/borane.



Scheme 6. Optimized Allylation-Cope.

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