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Synthesis of α,β-Unsaturated Acylsilanes via Perrhenate-Catalyzed Meyer−Schuster Rearrangement of 1-Silylalkyn-3-ols

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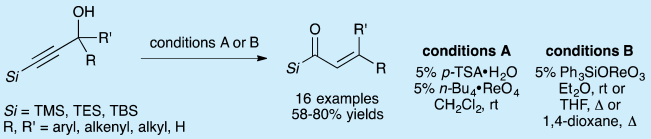
Supporting Information

ABSTRACT: We report the synthesis of α,β-unsaturated acylsilanes via the perrhenate-catalyzed Meyer−Schuster rearrangement of 1-silylalkyn-3-ols. Propargylic alcohols derived from TES-acetylene and substituted benzaldehydes can be converted to acylsilanes using a combination of *p*-TSA·H_2O and *n*-Bu_4N·ReO_4, or $Ph_3SiOReO_3$ in good yields. Some propargylic alcohols derived from ketones, as well as aliphatic and unsaturated aldehydes, can also be converted to acylsilanes; however, they were often prone to side reactions.



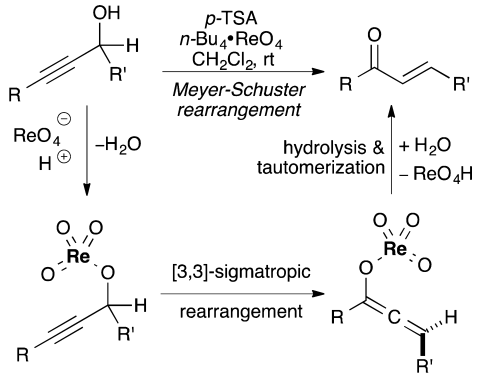
Acylsilanes display unique, nonintuitive reactivity patterns, making them valuable *umpolung* synthons in retrosynthetic planning. The Brook rearrangement[1] enables the use of acylsilanes in cascade processes, generating multiple bonds in a single reaction and dramatically increasing molecular complexity in the products.[2] Many methods for the preparation of acylsilanes have been developed; however, none are general.[3]

We required a practical route to α,β-unsaturated acylsilanes to advance ongoing research in our laboratory and envisioned that the Meyer−Schuster rearrangement[4] of easily prepared 1-silylalkyn-3-ols would provide expedient access to these compounds.[5] Although there are a number of ways to promote this rearrangement, many involve elevated temperatures and require expensive catalysts or anhydrous conditions. In 1991, Hayashi showed that the combination of tetra-*n*-butylammonium perrhenate and toluenesulfonic acid in wet dichloromethane promotes the Meyer−Schuster rearrangement at ambient temperature.[6] In analogy with other oxometal-catalyzed rearrangements, this reaction is thought to occur through formation of a propargyl perrhenate ester, [1,3]-transposition[7] of the oxygen through a [3,3]-sigmatropic rearrangement leading to the allenoate ester, hydrolysis, and tautomerization to the α,β-unsaturated ketone (Scheme 1).

Mechanistic and substrate scope studies[8] of the related [1,3]-transposition of allylic alcohols with similar high oxidation rhenium catalysts[9] have shown that the course of the reaction is sensitive to substrate structure. Highly stereoselective allylic alcohol transposition reactions support a mechanism involving [3,3]-sigmatropic rearrangement of perrhenate ester intermediates via a highly organized chairlike transition state as a key step. Allylic alcohols that are prone to ionization (i.e., those bearing cation stabilizing groups) undergo transposition with decreased stereoselectivity, implicating an ionic mechanism.

Hayashi's report contained the first and, to our knowledge, only example of the synthesis of acylsilanes via the Meyer−Schuster rearrangement.[6] Since it is clear that perrhenate-catalyzed 1,3-transpositions are substrate sensitive, and because this reaction represents a practical route to acylsilanes, we have explored their synthesis using a broad range of substrates, revealing interesting reactivity trends. In addition, we have also found that Osborn's reagent ($Ph_3SiOReO_3$) is capable of generating acylsilanes from substrates that are too reactive under standard conditions.

Scheme 1. Meyer−Schuster Rearrangement of Propargylic Alcohols via [3,3]-Sigmatropic Rearrangement of Perrhenate Esters



Propargylic alcohols were prepared by deprotonation of the commercially available silyl acetylenes with *n*-butyllithium and addition of the resulting anion to a series of aldehydes and ketones (eq 1).

We began by exploring the effect of the silyl group on the rearrangement. Scheme 2 shows that substrates **1a−c** bearing TMS, TES, and TBS groups at the terminal alkyne position are readily transformed to the corresponding acyl silanes **2a−c** in good yields. Control experiments with substrate **1b** confirmed that both acid and ammonium perrhenate are necessary for this rearrangement. Substrate **1d** bearing a TIPS group did not yield the desired acylsilane under standard conditions but rather gave

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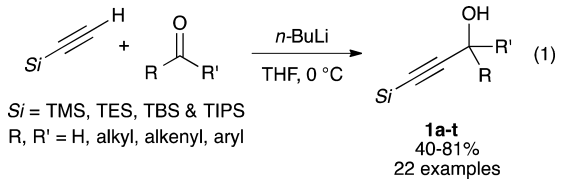
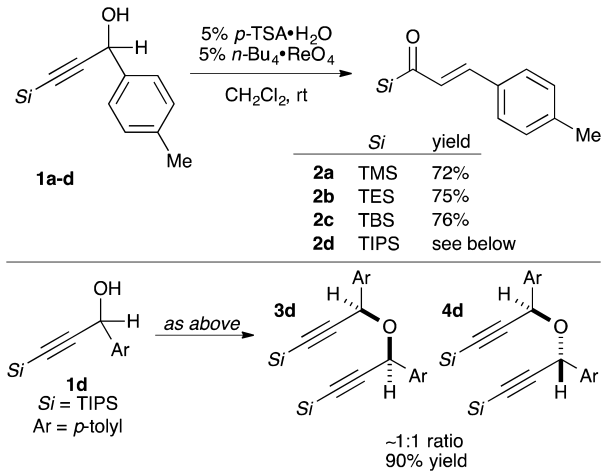


Scheme 2. Effect of the Silyl Group on the Synthesis of α,β-Unsaturated Acylsilanes via Meyer−Schuster Rearrangement

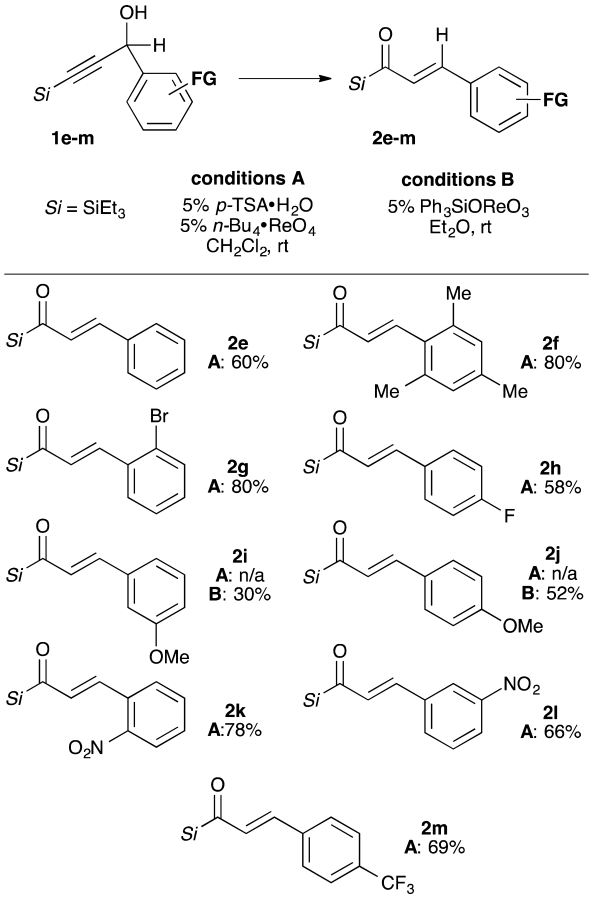


a mixture of diastereomeric ethers **3d** and **4d**. These products likely arise through acid-catalyzed ionization of the propargylic alcohol to the corresponding cation, which is then intercepted by another equivalent of alcohol. This result reflects the increased steric demand of the TIPS vs TBS groups, which likely precludes the 3,3-sigmatropic rearrangement. Changing the reaction temperature, the solvent, or the catalyst did not generate the desired product.

A series of propargylic alcohols prepared from substituted benzaldehydes and TES-acetylene were explored next (Scheme 3). In general, substrates with electron-poor or electron-neutral aryls provided the expected acylsilane under standard conditions (**2e−h,k−m**). The steric demands of the aryl group do not appear to affect the reaction (**2f**). Similarly, the position of the electron-withdrawing groups on the aryl ring had little effect on the yield of acylsilane (**2k** vs **2l**). In contrast, substrates bearing an electron-donating methoxy group on the aryl ring (**2i** and **2j**) underwent decomposition under standard conditions, irrespective of the position of the substituent. This result is consistent with observations in the related 1,3-transposition of allylic alcohols and suggests that formation of a benzylic carbocation may interfere with the reaction. Since it is likely that ionization of the propargylic alcohol is catalyzed by Brönsted acid, we decided to use Osborn's reagent, which presumably would avoid generation of strong acid in the medium. Under these conditions, the expected acylsilanes were formed, albeit in lower yields than all the other analogues explored.

Next, we explored a range of tertiary propargylic alcohols prepared from TES-acetylene and the corresponding ketones (Scheme 4). Alcohol **1n**, derived from benzophenone, unexpectedly gave β-silyl-1-indanone **3n** as the main product under standard conditions, with no evidence of acylsilane **2n**. The same result was observed when Osborn's reagent was used. The mechanism for this transformation is unclear. A similar result was observed by Maraval and co-workers in their

Scheme 3. Synthesis of α,β-Unsaturated Acylsilanes from Aryl-Substituted Secondary Propargylic Alcohols



investigation of Brönsted acid catalyzed rearrangements of diphenylpropargylic alcohols.[8] They proposed the formation of an acylsilane, followed by electrophilic aromatic substitution and consecutive 1,2-shifts of the silyl group. In contrast, alcohol **1o**, bearing two *p*-chlorophenyl substituents, provided the expected β,β-diaryl-unsaturated acylsilane **2o** with no evidence of the corresponding indanone product **3o**. Taken together, these results are consistent with an electrophilic aromatic substitution step in the formation of indanones, since the *p*-chloro substituent deactivates the aromatic ring. Alcohol **1p**, derived from acetophenone, gave the conjugated enyne **3p** when treated under conditions A, presumably due to acid-catalyzed dehydration. The desired unsaturated acylsilane **2p** could be obtained in good yield when treated with Osborn's catalyst. Finally, substrate **1q** underwent Rupe rearrangement (i.e., dehydration of the tertiary propargylic alcohol followed by hydration of the alkyne) to α-silyl ketone **3q** irrespective of the conditions used.

Curiously, secondary propargylic alcohols derived from aliphatic aldehydes (**1r−t**, Scheme 5) did not undergo the Meyer−Schuster rearrangement at room temperature, nor did they decompose via dehydration pathways. Furthermore, only alcohol **1t**, bearing a quaternary center adjacent to the carbinol carbon, was converted to the corresponding acylsilane **2t** when the reaction was conducted at elevated temperature. The reasons behind this unexpected reactivity trend are unclear; however, we note that all staggered conformations of substrate **1t** present an alkyl group antiperiplanar to the departing oxygen

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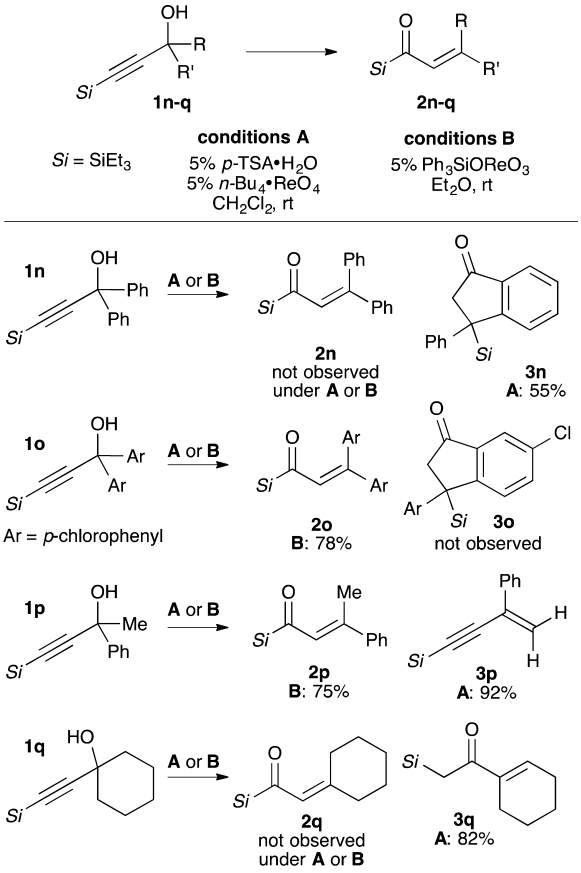
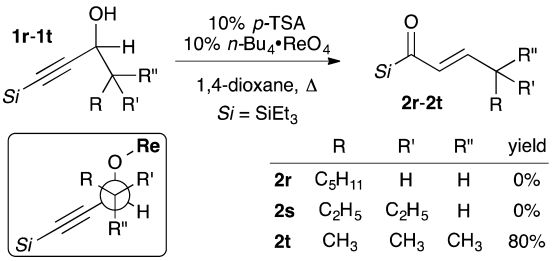
Scheme 4. Synthesis of α,β-Unsaturated Acylsilanes from Tertiary Propargylic Alcohols



Scheme 5. Attempted Meyer–Schuster Rearrangement of Propargylic Alcohols Derived from Aliphatic Aldehydes

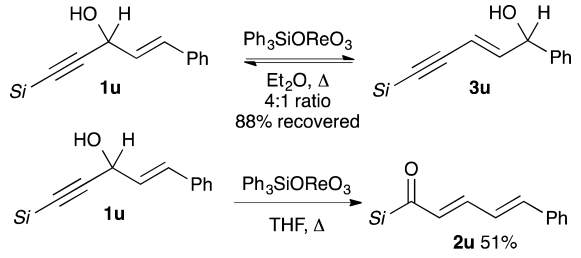


	R	R'	R"	yield
2r	C_5H_{11}	H	H	0%
2s	C_2H_5	C_2H_5	H	0%
2t	CH_3	CH_3	CH_3	80%

(inset), which may help stabilize the transition state for the [3,3]-sigmatropic rearrangement.

The Meyer–Schuster rearrangement of propargylic alcohols derived from α,β-unsaturated aldehydes would give rise to α,β,γ,δ-unsaturated acylsilanes. We expected, however, that these substrates would be very prone to ionization under acidic conditions, and it was unclear if the desired products could be prepared. Subjecting the allylic and propargylic alcohol **1u** derived by addition of TES-acetylene to cinnamaldehyde to standard conditions (conditions A in Scheme 4) provided a mixture of compounds consisting largely of ethers, which probably arise through self-condensation reactions (not shown). When the same substrate was treated with Osborn's catalyst in refluxing Et_2O only a mixture of alcohols arising from reversible 1,3 allylic transposition of the substrate was observed (Scheme 6). Conjugation is often used as a thermodynamic driving force in perrhenate-catalyzed allylic

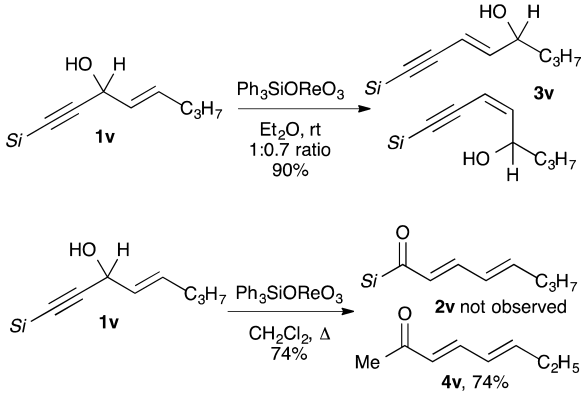
Scheme 6. Attempted Meyer–Schuster Rearrangement of a Propargylic Alcohol Derived from Cinnamaldehyde



transpositions. In the present example, the mixture of products observed likely reflects the small energy difference between substrate **1u** and the transposed alcohol **3u**, both of which have a conjugated double bond. On geometric grounds, we reasoned that the activation energy for the required [3,3]-sigmatropic rearrangement between the perrhenate ester and the alkyne function should be higher than that of the [3,3]-sigmatropic rearrangement between the perrhenate ester and the alkene function, which proceeds through a chairlike transition state. We therefore conducted the reaction at higher temperatures and were pleased to find that in refluxing THF substrate **1u** was converted to α,β,γ,δ-unsaturated acylsilane **2u**, albeit in modest yield.

Not surprisingly, alcohol **1v**, derived from *trans*-2-hexenal, underwent allylic transposition to a mixture of conjugated alcohols **3v** when treated with Osborn's reagent in Et_2O at ambient temperature (Scheme 7). In contrast to alcohol **1u**,

Scheme 7. Attempted Meyer–Schuster Rearrangement of a Propargylic Alcohols Derived from *trans*-2-Hexenal



conducting the reaction with **1v** at elevated temperatures did not yield the desired acylsilane but rather led to the known α,β,γ,δ-unsaturated ketone **4v**. This product is likely the result of a Rupe rearrangement (dehydration, followed by hydration of the alkyne) and desilylation.

We have studied the synthesis of acylsilanes via the perrhenate-catalyzed Meyer–Schuster rearrangement using a broad range of substrates. Propargylic alcohols derived from benzaldehydes are readily converted to the desired acylsilanes using a combination of *p*-TSA·H_2O and *n*-Bu_4N·ReO_4 unless the aryl ring is electron rich. With these substrates, the use of Osborn's catalyst ($Ph_3SiOReO_3$) gave the desired products, presumably by avoiding Bronsted acid catalyzed ionization of the alcohols. Most tertiary propargylic alcohols could also be transformed to the corresponding acylsilanes but were prone to side reactions. In contrast, secondary propargylic alcohols

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derived from aliphatic aldehydes proved generally unreactive. Finally, propargylic alcohols derived from unsaturated aldehydes underwent 1,3-allylic transposition reactions as expected, and in one instance, the α,β,γ,δ-unsaturated acylsilane could be obtained.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.5b02909.

General experimental procedures and characterization data, including ^{1}H, ^{13}C, ^{29}Si, and ^{19}F NMR, IR, and HRMS (PDF)

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Notes

The authors declare no competing financial interest.

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