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Regioselective Rh(I)-Catalyzed Sequential Hydrosilylation toward the Assembly of Silicon-Based Peptidomimetic Analogues

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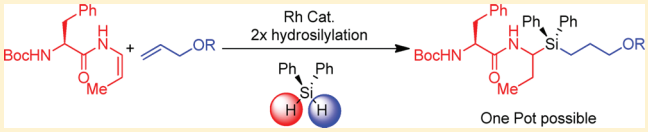
Supporting Information

ABSTRACT: A highly regioselective Rh(I)-catalyzed hydrosilylation of enamides is presented. This mild protocol allows access to a wide variety of different arylsilanes with substitution at the β-position of the enamide and functionalization on the alkyl chain tethered to the silane. This protocol is extended to include a sequential one-pot hydrosilylation. Using diphenylsilane as the appendage point, hydrosilylation of a protected allyl alcohol followed by hydrosilylation of an enamide generates a complex organosilane in one step. This highly convergent strategy to synthesize these functionalized systems now provides a way for the rapid assembly of a diverse collection of silane-based peptidomimetic analogues.



INTRODUCTION

Silicon is the second most abundant element in the earth's crust. Despite its prevalence, its utility in medicinal chemistry is still limited, possibly because of the limited number of methods for incorporating silicon into organic molecules. Nevertheless, the introduction of silicon into bioactive molecules can produce interesting biological effects, such as increased binding to the target, improved pharmacokinetic properties, as well as providing new intellectual property.[1]

One of the emerging applications for silicon is its incorporation into amino acids.[1d,2,3] Although silicon-based amino acids are not naturally occurring, introducing these building blocks into peptide chains can provide the desired modifications to the physical properties that are typically exhibited by the original peptide structure.[1b] In 1998, Sieburth and co-workers introduced the interesting concept of silicon diols representing potent inhibitors of proteases such as the ACE inhibitor **2**, which can mimic the active tetrahedral intermediate of a peptide cleavage.[1a,4,5] Silicon has most of the characteristics of the carbon element but with some slight differences. It possesses a larger radius than carbon, and hence the Si−OH bond in comparison to C−OH bond is approximately 25% longer.[1b] In contrast to carbon, silicon prefers to exist as the silanediol rather than as the silanone. Thus, replacing carbon for silicon at the peptide cleavage site becomes a viable choice.

Previously, simple silanediols were tested for bioactivity. In these cases, the silanediols showed no activity for enzyme inhibition.[1b,6] However, upon testing a silicon replica of an already known ketomethylene-based ACE inhibitor depicted as its unstable hydrate **1** (Figure 1), the silicon analogue exhibited similar inhibitory effect as the parent compound.[7] Since then, Sieburth and co-workers have reported other examples of silicon-based peptidomimetic analogues that possess a high inhibitory effect comparable to its parent carbon-based

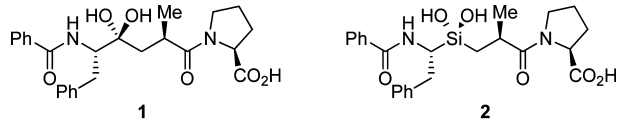


Figure 1. ACE inhibitor vs silicon-based ACE inhibitor.

inhibitor.[8] This demonstrated silicon's ability to act successfully as an active tetrahedral intermediate mimic.

Incorporating silicon into peptides whether to mimic an active tetrahedral intermediate of a protease inhibitor or to change the peptide's lipophilicity or conformation has become a growing field in drug design. As the interest into this developing area grows, the demand for a wider variety of organosilanes rises. Further exploration into alternative ways to synthesize highly functionalized organosilanes is therefore needed.

Previous Syntheses. Sieburth and co-workers reported the first synthesis incorporating silanediols into a peptide.[5] Since then, a few modications to streamline the synthesis have been reported. The modified strategy involves the formation of the first C−Si bond by deprotonation of dithiane **3** followed by attack onto Ph_2SiF_2 (Scheme 1). An organolithium reagent then attacks the silyl fluoride **4** forming the second C−Si bond.[7] After several functional group manipulations, a highly functionalized organosilane intermediate was synthesized. The silane phenyls are carried throughout the synthesis and act as masked silanediols. The silicon phenyl substituents can then be converted to the diol form by using TfOH to promote the initial C−Si bond cleavage.[5]

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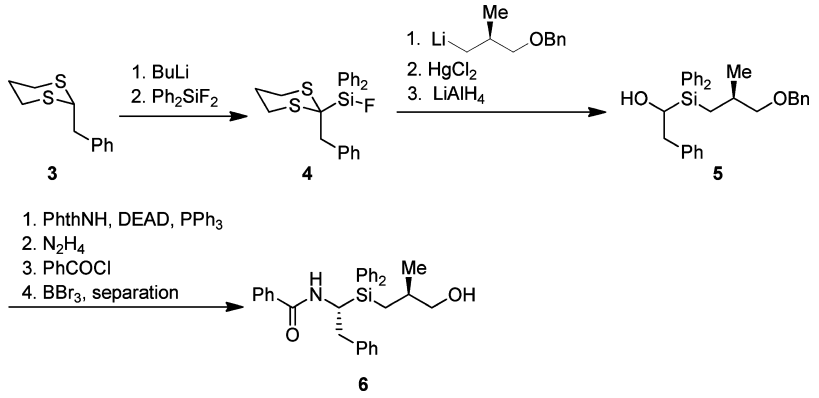
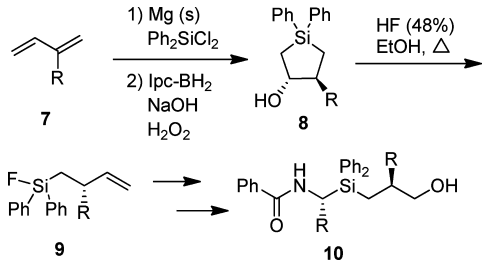
Scheme 1. Sieburth's Modified Protocol To Access ACE Inhibitor Intermediate



A more concise route was reported by the same group in 2007 (Scheme 2) involving a magnesium-mediated addition of

Scheme 2. Sieburth's Alternative Approach Using Dihydrosilole



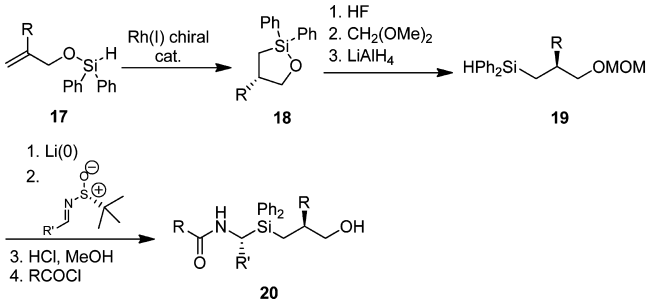
dichlorodiphenylsilane to diene **7**.[9] Hydroboration of the olefin **8** followed by ring-opening via cleavage of the Si−C bond using HF furnished an olefin tethered to a silyl fluoride as the organosilane **9**. This silyl fluoride was further manipulated in order to achieve the silanediol peptide isosteres.

Organ and Combs provided an alternative approach toward the synthesis of these isosteres by a platinum-catalyzed hydrosilylation using alkene **11** and chlorodiphenylsilane (Scheme 3).[10] The resulting chlorosilane **12** was reduced to a silyl lithium reagent, which then attacks an imine. The Scheidt group published afterward that using the Ellman auxiliary-attached imines can undergo nucleophilic attack using silyl lithium species without observing any aza-Brook rearrangement and achieving high diastereoselectivity.[11]

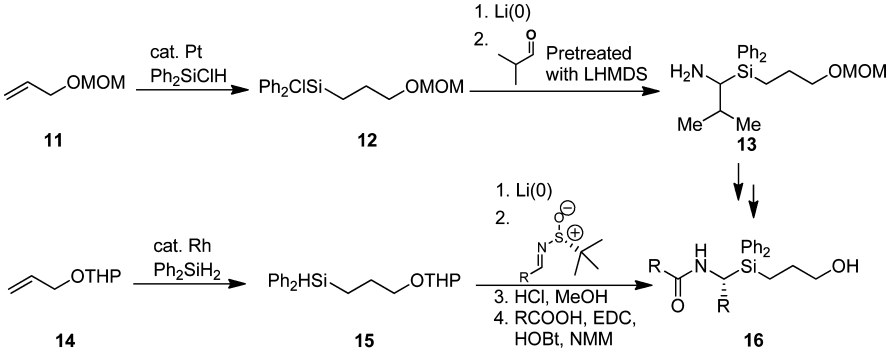
Our group presented a further exploration into synthesizing these peptidomimetics, whereby we demonstrated that the more stable diphenylsilane, Ph_2SiH_2, could be introduced in the hydrosilylation step using various olefins without any observed double hydrosilated products (Scheme 3). In order to introduce 1,1-disubstituted olefins, a radical-catalyzed strategy was employed. The silyllithium species were generated from these alkylhydridosilanes followed by attack onto a chiral sufinimine producing functionalized silanes with high diastereoselectivity.[12] The Scheidt and Skrydstrup strategies provided the compound in five steps using mild conditions starting from a protected allyl alcohol.

More recently, Sieburth and co-workers were able to extend this methodology in an elegant fashion as depicted in Scheme 4. An enantioselective intramolecular hydrosilylation was

Scheme 4. Asymmetric Intramolecular Hydrosilylation on 1,1-Disubstituted Olefins To Access Silicon-Based ACE Inhibitor



Scheme 3. Organ/Combs (Top) and Skrydstrup (Bottom) Strategy toward ACE Protease Inhibitors via Hydrosilylation/Lithiation/Nucleophilic Attack of Imine



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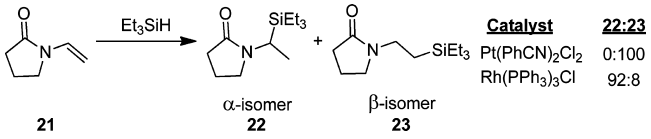
presented to allow for substitution on the olefin.[13] Using alkyldiphenylsilyl ether **17** and a chiral Rh(I) catalyst, the terminal end of the alkene underwent asymmetric hydrosilylation forming oxasilolane **18**. The oxasilolane **18** was subjected to HF to cleave the carbon−silicon bond followed by MOM protection of the generated free alcohol. The silyl lithium species was formed using Li metal and was used to attack a chiral sulfinimine to afford the desired sulfinamide product in good yields.

Although alternative strategies to achieve α-alkyl-α-aminosilane have been reported,[2a,14] the lithiation strategy to attack a chiral sulfinimine has become the common strategy employed to form C−Si bonds.[15] However, the two limitations to this Organ and Combs/Skrydstrup protocol is the generation of the silyl lithium species in order to attack the chiral sulfinimine. These conditions do not tolerate a variety of different functionalities attached on the arylsilane (furyl, thiophenyl, etc.)[16] or tethered to the terminal olefin (OBn, OAc, etc.). Also, another downside to this protocol is that the method requires the use of an auxiliary in order to induce stereochemical control in the nucleophilic attack of the imine, which will be removed subsequently. In order to access a wider variety of silyl-containing substrates in an efficient and atom-economical fashion, an asymmetric metal-catalyzed alternative would be preferred.

Hydrosilylations. The hydrosilylation of enamides provides direct access to the α-alkyl-α-aminosilanes. However, the process should optimally be high yielding, regioselective, and stereoselective. Not many reports have been published previously on the hydrosilylation of enamides. Most catalytic hydrosilylations have been reported on simple olefins with unfunctionalized hydrocarbon chains.[17] Skoda-Földes was the first to discover that hydrosilylations can occur with high regioselectivity depending on the catalyst (Scheme 5).[17j] When

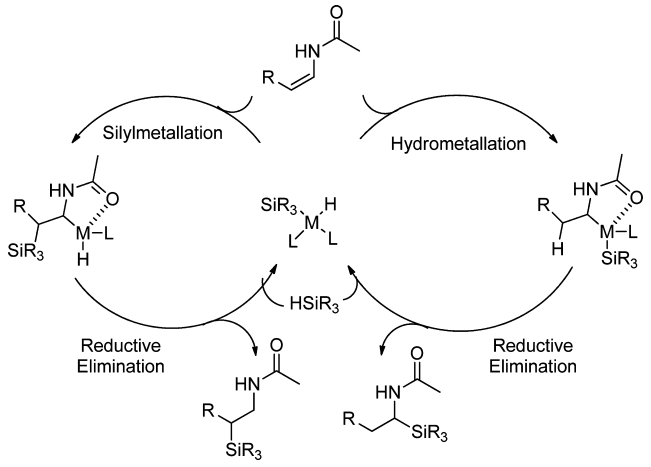
Scheme 5. Catalyst Governed Regioselectivity of Hydrosilylation



switching the catalyst from $Pt(PhCN)_2Cl_2$ to Wilkinson's catalyst in the presence of *N*-pyrrolidinone **21** and triethylsilane, the regioselectivity reverses from preferring the β-position of the enamide to the α-position.

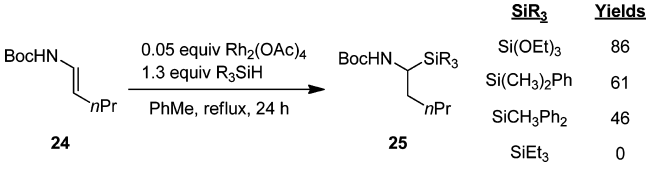
Murai and Kato, in 1998, reported a similar regioselectivity using $Rh_2(OAc)_4$ in toluene at 110 °C.[18] Different Rh catalysts were investigated including Wilkinson's catalyst. $Rh_2(OAc)_4$ proved to be the superior catalyst in the hydrosilylations giving the product in high regioselectivity for the α-position of the enamide. Murai and Kato postulated that the mechanism proceeds via a hydrometalation step with the adjoining carbonyl group directing the reaction to obtain high regioselectivity for the α-position of the enamide as depicted in Scheme 6.[18b] With the use of the Pt catalyst in the case of Skoda-Földes, the regioselectivity changes. This can be explained by a silylmetalation mechanism in which the regioselectivity is still directed by the carbonyl group (Scheme 6). However, Murai and Kato do not exclude the possibility of the Rh-catalyzed reaction occurring through a silylmetalation mechanism.[19]

Scheme 6. Proposed Catalytic Cycle of Metal-Catalyzed Enamide Hydrosilylation



In their paper, the substrate scope was moderate to high yielding but was limited to nonbulky silanes, dimethylphenylsilane, triethylsilane, and simple enamides, many lacking complexity at the β-position. Sieburth and co-workers surmised that *N*-alkenyl carbamates could also undergo hydrosilylation at the α-position with more bulky silanes (Scheme 7)[20] because

Scheme 7. Hydrosilylation of *N*-Alkenyl Carbamates



Murai and Kato demonstrated that this reaction could also proceed with *N*-alkenyl ureas.[18a] Although this strategy would have provided a more expedient and straightforward synthesis of the desired compounds, the approach was not used since then due to the low reactivity of $Rh_2(OAc)_4$ with diphenylmethylsilane and Boc-protected enamides. The low reactivity was attributed to the silane's electronic and steric effects achieving yields around 0−46% with various *N*-alkenyl carbamates. Despite the modest yields, the reaction was still regioselective as observed previously by Murai and Kato.

Metal-catalyzed hydrosilylation of enamides would provide the most direct route toward obtaining a widely diverse collection of highly functionalized organosilanes. The only deterrence from utilizing this strategy is the low yields obtained when using methyldiphenylsilane. Given new knowledge gained from similar protocols such as metal-catalyzed hydroborations[21] and hydrogenations,[22] as well as having new strategies to access a wider variety of enamides, our group surmised that hydrosilylations would be a possibility using a more reactive catalyst species. We envisioned that using one catalyst in a one pot, highly regioselective and stereoselective sequential hydrosilylation would provide the most optimal strategy toward achieving diversity in these substrates (Scheme 8). This would afford highly complex organosilanes in the most atom economical fashion. Herein, we report on our initial efforts to develop a Rh-catalyzed highly regioselective sequential hydrosilylation and its possible extension into a one-pot protocol using one catalyst. Both binuclear and mononuclear rhodium

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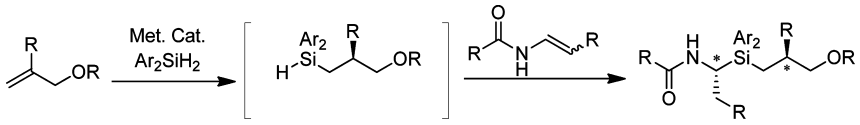
Scheme 8. Proposal for Stereoselective and Regioselective Metal-Catalyzed Sequential Hydrosilylation

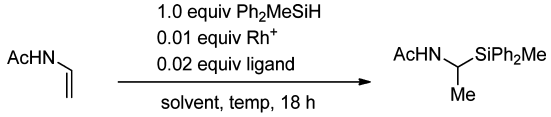


catalysts are investigated in this work. This method provides a straightforward entry to the silanediol class of peptide isosteres.

RESULTS AND DISCUSSION

Since Murai and Kato achieved good to excellent yields using *N*-vinylacetamide and methyldiphenylsilane, preliminary studies were conducted on the same enamide but using a bulkier silane, methyldiphenylsilane, as depicted in Table 1. Rhodium sources

Table 1. Optimization of Hydrosilylations Using *N*-Vinylacetamide 26 and Diphenylmethylsilane



26 **27**

entry	Rh^+ cat.	ligand	solvent	temp (^{o}C)	yield (%)
1	Rh_2OAc_4	none	DCE	65	87[a]
2	$[Rh(cod)Cl]_2$	none	DCE	65	50[a]
3	$Rh(PPh)_3Cl$	none	DCE	65	0
4	$Rh(cod)_2BF_4$	none	DCE	65	73
5	$Rh(cod)_2BF_4$	$P(OPh)_3$	DCE	65	78
6	$Rh(cod)_2BF_4$	$P(OPh)_3$	THF	65	0
7	$Rh(cod)_2BF_4$	$P(OPh)_3$	PhMe	65	0
8	$Rh(cod)_2BF_4$	$P(OPh)_3$	DCE	40	78
9	none	none	DCE	65	0
10	none	$P(OPh)_3$	DCE	65	0

[a]0.005 mol % of Rh catalyst was used.

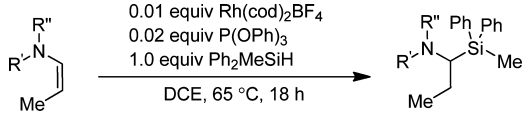
were screened as shown in entries 1−4. The dimer rhodium species, $Rh_2(OAc)_4$ (entry 1) achieved higher yield of the hydrosilylated product **27** than the $[Rh(cod)Cl]_2$. This demonstrated that the increased steric bulk of the silane from dimethylphenylsilane to diphenylmethylsilane using rhodium(II) acetate dimer did not result in significantly lower yields. However, when taking a chiral rhodium dimer species, Rh_2(*S*-DOSP)$_4$, complete conversion to the product was observed, but no enantiomeric excess was obtained.

Because there were more opportunities in developing a stereoselective reaction using a rhodium monomer catalyst, Wilkinson's catalyst and $Rh(cod)_2BF_4$ were screened. Interestingly, Wilkinson's catalyst which was originally reported by Skodes-Földes' case to give complete regioselectivity for the α-position of *N*-pyrrolidinone,[17j] achieved none of the desired product in these conditions. However, using the Rh(I) catalyst, $Rh(cod)_2BF_4$ gave the hydrosilylated product **27** in good yields (entry 4).

Addition of a phosphite ligand, $P(OPh)_3$, improved the yield giving 95% consumption of *N*-vinylacetamide **26** and a 78% isolated yield. With this rhodium complex, different solvents were screened (entries 5−7) with dichloroethane providing the highest yields. Even at lower temperatures, 40 ^{o}C, the reaction was complete in 30 min. However, it is important to note that once the enamide is substituted at the β-position, increased temperatures and reaction times are necessary.

Because of the results obtained in our initial studies, the discrepancies in yields between Murai/Kato and Sieburth and co-workers indicated that the *N*-substituent plays an important role in the hydrosilylation. Different representative *N*-substituents were therefore screened as shown in Table 2. In

Table 2. Effect of Varying *N*-Substituents



entry	enamide	monosilylated pdt	% yield
1	**28**	**32**	97
2	**29**	**33**	54
3	**30**	**34**	78
4	**31**	**35**	37

all cases, only one regioisomer was observed. *N*-Alkenylacetamide achieved 100% conversion to product and 97% isolated yield (entry 1). The carbamate provided a similar conversion; however, the yield significantly drops to 54%. Adding another *N*-substituent (entries 3 and 4) lowers the yield in comparison to the monosubstituted nitrogen counterpart (entries 1 and 2). As expected, the cyclic carbamate **31** furnished the lowest yield of the four screened. Starting material was still observed in entry 4 and proved to be inseparable from the product during flash chromatography. The marked difference in yields obtained between acetamide versus carbamate particularly in entries 3 and 4 suggests that the acetamide possesses a better donating ability to sufficiently chelate to the rhodium complex over the carbamate. This could explain the differences observed in Sieburth's results versus those of Murai and Kato.

Having optimized the necessary components for the hydrosilylation to occur in good yields, different aryl substituents on the silicon were investigated (Table 3). As indicated in a previous paper from our group, the electron-rich aromatic groups are highly desired for their ability to cleave

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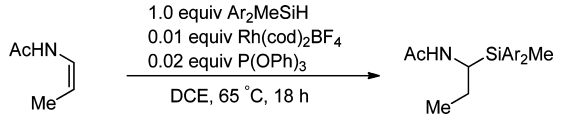
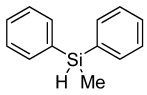
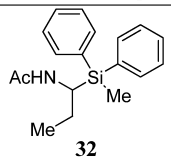
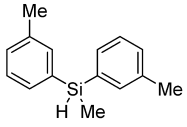
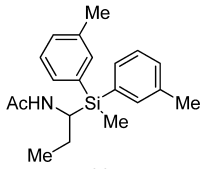
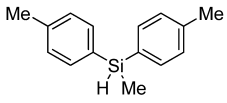
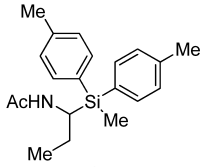
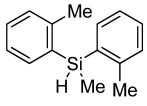
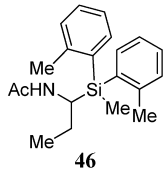
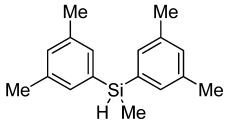
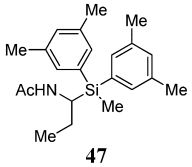
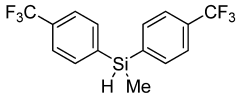
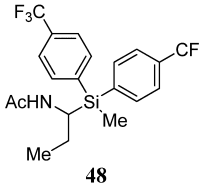
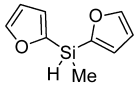
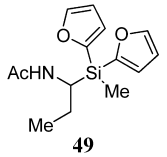
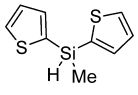
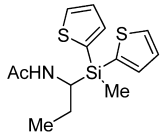
Table 3. Effect of Varying the Silane Aryl Groups on Hydrosilylation

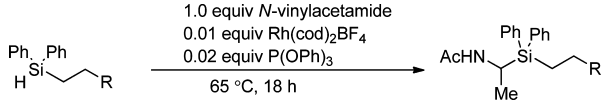


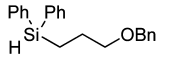
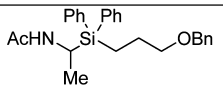
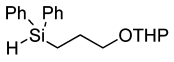
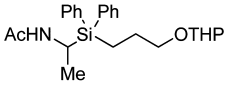
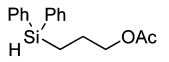
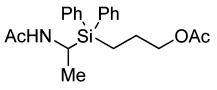
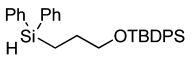
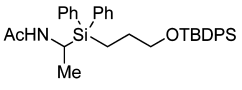
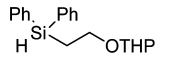
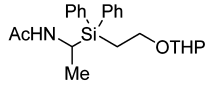
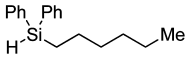
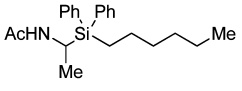
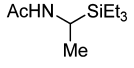
entry	aryl silane	monosilylated pdt	% yield
1	 **36**	 **32**	97
2	 **37**	 **44**	86
3	 **38**	 **45**	74
4	 **39**	 **46**	8
5	 **40**	 **47**	86
6	 **41**	 **48**	83
7	 **42**	 **49**	69
8	 **43**	 **50**	75

under milder acidic conditions to furnish the silanediol more readily.[15c] Having a methyl substituent in the meta (entry 2) or para (entry 3) positions of the aryl group gave the desired products in good yields, 86% and 74%, respectively. Carrying two methyl groups at the meta positions does not change the reactivity of the silane (entry 5). However, by placing a methyl in the ortho position of the aryl group (entry 4), the hydrosilylation is greatly impeded. Switching the methyl group with an electron-withdrawing group such as trifluoromethyl on the aryl ring (entry 6) provides comparable yields to silanes containing methyl substitution in the *m*- or *p*-position. If the aryl group is switched to furan (entry 7) or thiophene (entry 8), the reaction furnishes the desired products in 69% and 75% isolated yields, respectively. These two entries are important because lithiation of either one of these two silanes (**42** or **43**) followed by attack on a sulfinimine did not result in the formation of the desired product as seen in previous studies done in the group. However, applying this mild approach, access to these types of silanes is now possible.

Different silyl alkyl chains were also investigated (Table 4). Benzyl (entry 1) and THP (entry 2) protecting group on the 3-hydroxypropyl chain generated the hydrosilylated products in good yields. Acetyl (entry 3) and *tert*-butyldiphenylsilyl (entry 4) groups were also tolerated in the reaction. Having a hydrocarbon chain without any functionality on the silane provided the compound in good yields (entry 6). Using a

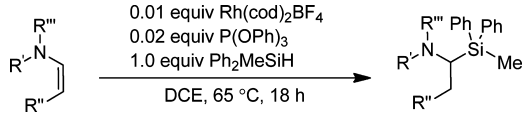
Table 4. Variation of the Functional Group on Silyl Alkyl Group

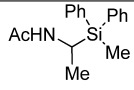
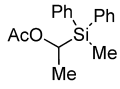
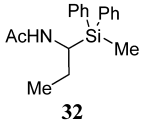
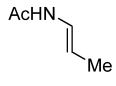
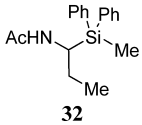
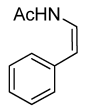
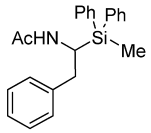
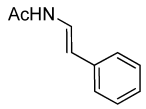
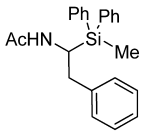
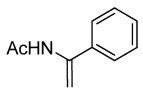
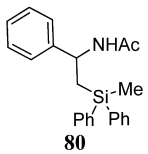
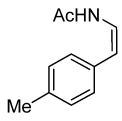
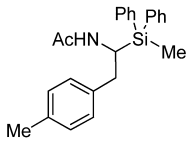
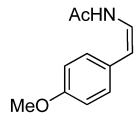
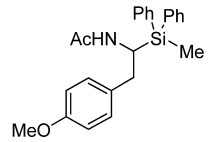
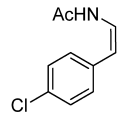
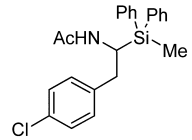
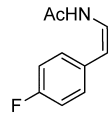
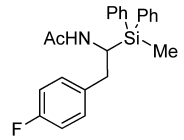
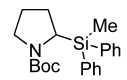
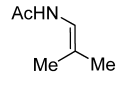
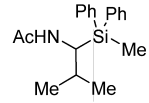
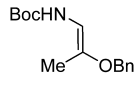
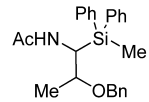
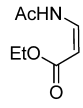
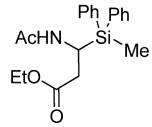


entry	silane	hydrosilylated pdt	yield
1	 **51**	 **58**	74
2	 **52**	 **59**	78
3	 **53**	 **60**	61
4	 **54**	 **61**	62
5	 **55**	 **62**	70
6	 **56**	 **63**	73
7	Et_3SiH **57**	 **64**	75

dx.doi.org/10.1021/jo300904z | *J. Org. Chem.* 2012, 77, 5894−5906

Table 5. Effect of Varying the Substituents on the Enamide Olefin



entry	enamide	silylated product	% yield
1	 **26**	 **27**	78
2	 **65**	 **78**	55
3	 **28**	 **32**	97
4	 **66**	 **32**	95
5	 **67**	 **79**	78
6	 **68**	 **79**	0
7	 **69**	 **80**	90
8	 **70**	 **81**	73
9	 **71**	 **82**	<5
10	 **72**	 **83**	64
11	 **73**	 **84**	61
12	 **74**	 **85**	58
13	 **75**	 **86**	0
14	 **76**	 **87**	0
15	 **77**	 **88**	0

typically unreactive trialkylsilane under these reaction conditions still afforded the desired product **64** (entry 7). If the alkyl chain is one carbon shorter than in entry 2, the product **62** is obtained in a 70% isolated yield (entry 5). Although it seems rather trivial to shorten the chain by one carbon, it is enough to cause problems in the lithiation of these silanes. Upon lithiation and attack on the imine, the reaction gives a mixture of undetermined compounds that are inseparable from each other. However, when the hydrosilylation strategy is used, only the desired product is observed in a 70% isolated yield.

After investigating the effect of varying the enamide's *N*-substituents and the silane's aryl and alkyl groups, variations of the substituents on the enamide were explored as depicted in Table 5. If instead of reacting methyldiphenylsilane with an enamide it is reacted with enol acetate (entry 2), the desired product is observed with complete regioselectivity for the α-position as for the enamide (entry 1). However, if a THP-protected enol is reacted with the Rh(I) catalyst and Ph_2SiH_2, complete reversal of the regioselectivity is observed providing the β-product in a 78% isolated yield (results not depicted). This gives further proof that the carbonyl adjoining the heteroatom (N or O) controls the regioselectivity. However, if the enamide is 1,1-substituted as in entry 7, sterics overrule the directing effect of the carbonyl, and the silicon ends up again at the terminal position in excellent yields.

When the β-position of the enamide is substituted with a methyl group, the *cis*- or *trans*-configuration of this particular substrate does not demonstrate a difference in isolated yield of the hydrosilylated product giving yields of 97% and 95%, respectively (entries 3 and 4). However, if the methyl

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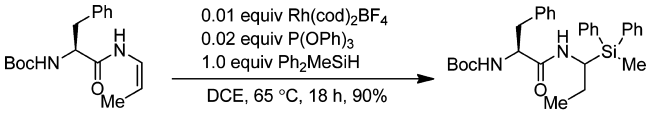
substituent is switched with an aromatic group, the configuration of the enamide becomes very important. With the *trans*-geometry, the reaction does not proceed. In order to drive the reaction forward, a *cis*-stereoisomer was tested, which resulted in complete consumption of the starting material and an isolated yield of the product of 78% was obtained.

With a methyl group in the para position, a 73% yield of **81** is achieved. However, if the aromatic group becomes more electron rich with a OMe group as in entry 9, the reaction affords only trace amounts of the desired product. These hydrosilylation conditions do tolerate aryl halides such as Cl (entry 10) and F (entry 11), providing the product in 64% and 61% yield, respectively. A cyclic enamide works as well, giving, as depicted in entry 12, silane **85** even despite the presence of a Boc-protecting group on the nitrogen. However, when the enamide double bond is trisubstituted, the reaction gave no desired product (entry 13). Having a more electron-rich trisubstituted enamide does not facilitate the reaction either (entry 14). The hydrosilylation also does not occur with esters on the β-carbon (entry 15).

Interestingly, when this methodology was applied to a highly functionalized enamide, compound **89** (Scheme 9), the hydrosilylation occurred in excellent yield providing an approximately 1:1 diastereomeric mixture of products. Epimerization of the α-center of the phenylalanine unit was also not observed.[23] This result is interesting for two reasons. First, there is no chirality transfer from the adjacent amino acid, which suggests that with a suitable asymmetric ligand control at the new stereogenic carbon center should be possible. Second, it implies that the hydrosilylation step could be performed on an intact peptide with a C-terminal enamide functionality.

Scheme 9. Hydrosilylation of a Highly Functionalized Enamide

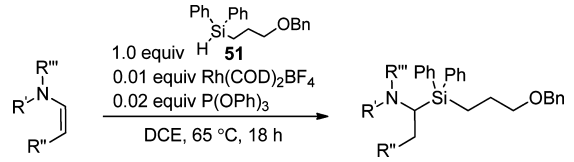


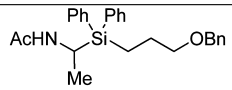
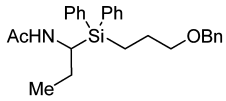
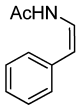
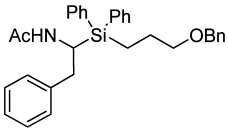
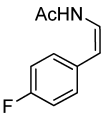
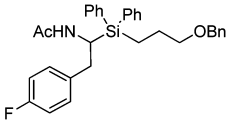
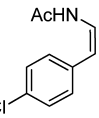
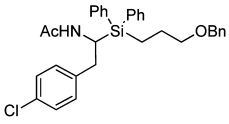
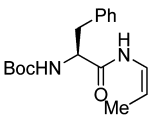
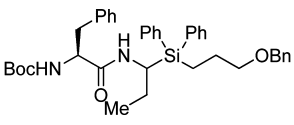
89 90

Hydrosilylation proved to be possible on a wide variety of different enamides. Taking these enamides, the hydrosilylation was further tested by using a slightly more functionalized and bulkier silane **51** (Table 6). Using $Rh(cod)_2BF_4$ and $P(OPh)_3$, *N*-vinylacetamide (entry 1) and (*Z*)-*N*-(prop-1-en-1-yl)-acetamide (entry 2) gave good yields of the hydrosilylated product. However, when the β-substituent is switched to an aromatic group, the reaction is low yielding when $Rh(COD)_2BF_4$ and triphenyl phosphite are used.

Because of its sluggish reactivity, the rhodium catalyst ends up decomposing over time. Despite catalyst decay, isomerization of the enamide configuration was not observed. $Rh_2(OAc)_4$, which has not shown quick decomposition in our studies, was used in these cases instead. The 4-fluoroaryl group reveals an improved yield using the rhodium dimer compared to the monomeric rhodium species (entry 4). However, with the phenyl group (entry 3) and the 4-chlorophenyl group (entry 5), low yields are obtained, even though in all three cases complete consumption of the starting material had occurred. The desired product and the *trans*-enamide were present in the crude mixture. This result indicates that with the bulkier silane, the reductive elimination occurs slower than the β-hydride elimination resulting in the preferred formation of the more stable *trans*-enamide. However, despite the increased sterics around the silane, functionalization of the enamide **89** does not seem to be problematic (entry 6).

Table 6. Hydrosilylation of Enamides Using Silane 51



entry	enamide	silylated pdt	% yield
1	 **26**	 **58**	74
2	 **28**	 **91**	85
3	 **67**	 **92**	38[a]
4	 **73**	 **93**	69[a]
5	 **72**	 **94**	28[a]
6	 **89**	 **95**	75

[a]0.01 equiv of $[Rh_2(OAc)_4]$ was used as catalyst for these entries.

Since the two alkyl chains on the silicon could be introduced via two Rh(I)-catalyzed hydrosilylations, exploring a sequential sequence to form two C−Si bonds in a one-pot fashion became a viable option, the results of which are depicted in Table 7. The first hydrosilylation of the allylic alcohol derivative with diphenylsilane takes place rapidly (15 min for 100% NMR conversion). If Rh_2OAc_4 is used instead, NMR conversion is 52% after 24 h for the first hydrosilylation. If the reaction time is longer than 15 min for the first step using $Rh(COD)_2BF_4$ and $P(OPh)_3$, the catalyst's reactivity decreases for the second hydrosilylation. Next, the enamide is added to the reaction mixture and heated allowing the second hydrosilylation step to proceed. The sequential hydrosilylation with vinyl acetamide proceeds in an acceptable yield for the two-step process in one pot (entry 1). Because the first step is not a quantitative reaction, the yield drops when using a one to one ratio of the protected allyl alcohol and diphenylsilane with the enamide.

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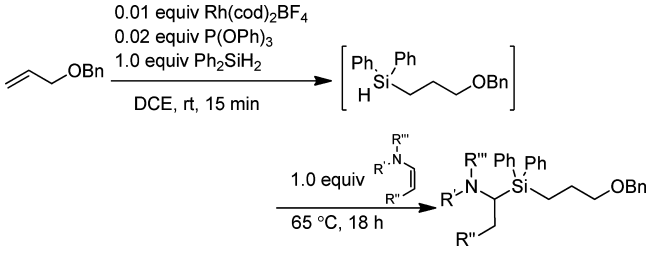
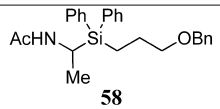
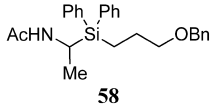
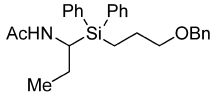
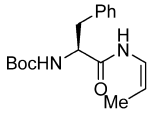
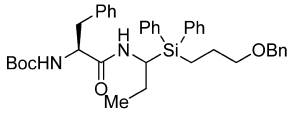
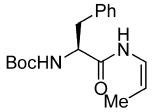
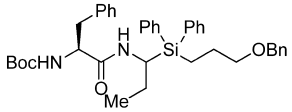
Table 7. One-Pot Sequential Hydrosilylation To Access Highly Functionalized Organosilane



entry	enamide	silylated pdt	% yield
1	 **26**	 **58**	43
2	 **26**	 **58**	64[a]
3	 **28**	 **91**	74
4	 **89**	 **95**	70
5	 **89**	 **95**	70[a]

[a]1.0 equiv of enamide, 1.2 equiv of protected allyl alcohol, and 1.2 equiv of Ph_2SiH_2 were used.

However, a higher yield of the product can be achieved if 1.2 equiv of the protected allyl alcohol and silane are used in comparison to the enamide as shown in entry 2. It should be pointed out that carrying out the sequential hydrosilylation with both the allylic alcohol derivative and enamide in the reaction flask was not fruitful, and neither was the attempt to reverse the addition of the two olefins.

The one-pot procedure for (*Z*)-*N*-(prop-1-en-1-yl)acetamide achieves good yields (entry 3). Entry 4 also demonstrates that this strategy can be applied to a highly functionalized case as well. Because not all the enamide is consumed in the reaction, the *cis* enamide is still present and is inseparable from the product using flash chromatography. However, one can resolve this issue by applying 1.2 equiv of the silane in comparison to the enamide. The desired product is achieved in good yields with the functionalities still preserved. This result is important because it demonstrates the potential of this methodology to be used as an end strategy to assemble a variety of silicon-based peptidomimetic analogues. Upon discovery of an asymmetric version of this hydrosilylation, one could dictate the stereochemical outcome of the resulting aminosilane end by the choice of ligand. Investigations on an asymmetric version of these hydrosilylations are currently undergoing.

CONCLUSIONS

In summary, a highly regioselective Rh(I)-catalyzed hydrosilylation of enamides is reported. This mild protocol is amenable to different functionalization on the silicon and the enamide. This protocol can be extended to a sequential one-pot procedure in which hydrosilylation of a protected allyl alcohol using diphenylsilane followed by hydrosilylation of the enamide occurs using the same catalyst in order to generate a complex organosilane in one step. This ability to hydrosilylate these type of highly functionalized systems without altering the chemical components of the molecule would allow for the facile assembly of a wide variety of silicon-based peptidomimetic analogues.

EXPERIMENTAL PROCEDURES

General Methods. ^{1}H NMR and ^{13}C NMR spectra were recorded at 400 and 100 MHz, and the chemical shifts are reported in ppm relative to solvent residual peak.[24] HRMS spectra were recorded on LC TOF (ES) apparatus. Flash chromatography was performed on silica gel 60 (230−400 mesh). All solvents were dried according to standard procedures.[25] Enamides (**26** **65**, **74**) and silanes (**36**, **57**) were provided by commercially available sources. Aryl vinyl bromides,[26,27] enamides,[28] diarylmethylsilanes,[15c] alkyldiphenylsilanes,[12a] and BocPheNH$_2$[29] were synthesized by known procedures. The commercial reagents were used without further purification. The reagents used in the enamide synthesis were weighed out in the argon glovebox using 8 mL vials sample vials with a Teflon-sealed screw cap.

Synthesis of Enamides 28−31, 66−77, and 89. *General Procedure A.*[28] CuI (0.05 equiv), amide/carbamate (1.2 equiv), K_2CO_3, dimethylethylenediamine (0.10 equiv), vinyl bromide, and PhMe were added to a round-bottom flask in glovebox. The reaction was placed in a preheated oil bath at 110 °C for 24 h. The reaction was cooled to room temperature and filtered through a pad of Celite using EtOAc. The reaction was purified via flash chromatography using 40−60% EtOAc/pentanes as eluent.

General Procedure B.[28,30] CuI (0.05 equiv), amide/carbamate (1.2 equiv), K_2CO_3, dimethylethylenediamine (0.10 equiv), vinyl bromide, and PhMe were added to a round-bottom flask in glovebox. The reaction was placed in a preheated oil bath at 110 °C for 24 h. The reaction was cooled to room temperature and filtered through a pad of Celite using EtOAc. The reaction was purified via flash chromatography using 40−60% EtOAc/pentanes as eluent. The *trans*-enamide was suspended in benzene and isomerized using a UV lamp at 100 W for 6−8 h. The reaction was purified via flash chromatography using 40−60% EtOAc/pentanes as eluent.

*(Z)-N-(Prop-1-en-1-yl)acetamide (**28**).* The product was obtained using general procedure A yielding **28** (1.12 g, 56%) as a colorless powder. Mp: 67−70 °C. ^{1}H NMR (400 MHz, CD_3CN): δ (ppm) 7.85 (bs, 1H), 6.59−6.62 (m, 1H), 4.66−4.74 (m, 1H), 1.94 (s, 3H), 1.61 (dd, J = 7.1, 1.8 Hz, 3H). ^{13}C NMR (100 MHz, CD_3CN): δ (ppm) 168.6, 123.1, 105.3, 23.1, 11.3 HRMS: C_5H_9NO [M + H$^+$] calcd 100.0763, found 100.0754.

*(Z)-tert-Butyl Prop-1-en-1-ylcarbamate (**29**).* The product was obtained using general procedure A yielding **29** (480 mg, 24%) as a colorless powder. Mp: 74−75 °C. ^{1}H NMR (400 MHz, CD_3CN): δ (ppm) 6.90 (bs, 1H), 6.32 (t, J = 9.2 Hz, 1H (t, J = 8.0 Hz, 2H), 4.58 (t, J = 7.0 Hz, 1H), 1.54 (dd, J = 7.0, 1.8 Hz, 3H), 1.44 (s, 9H). ^{13}C NMR (100 MHz, CD_3CN): δ (ppm) 154.0, 124.2, 103.2, 80.3, 28.5 (3C), 11.0. HRMS: $C_8H_{15}NO_2$ [M + Na$^+$] calcd 180.1001, found 180.1016.

*(Z)-1-(Prop-1-en-1-yl)pyrrolidin-2-one (**30**).*[31] The product was obtained using general procedure A yielding **30** (680 mg, 34%). The spectra are in accord with the literature.[31]

*(Z)-3-(Prop-1-en-1-yl)oxazolidin-2-one (**31**).* The product was obtained using general procedure A yielding **31** (720 mg, 36%) as a viscous oil. ^{1}H NMR (400 MHz, CD_3CN): δ (ppm) 6.15 (dq, J = 9.4, 3.4, 1.7 Hz, 1H), 4.87−4.95 (m, 1H), 4.30−4.34 (m, 2H), 3.93−3.97 (m, 2H), 1.73 (dd, J = 7.3, 1.8 Hz, 3H). ^{13}C NMR (100 MHz,

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CD_3CN): δ (ppm) 158.0, 124.9, 110.3, 63.5, 46.4, 12.2. HRMS: $C_6H_9NO_2$ [M + H^+] calcd 128.0712, found 128.0721.

*(E)-N-(Prop-1-en-1-yl)acetamide (**66**).* The product was obtained using general procedure A yielding **66** (1.10 g, 54%) as a colorless solid. Mp: 72−74 °C. ^{1}H NMR (400 MHz, CD_3CN): δ (ppm) 8.25 (bs, 1H), 6.60−6.67 (m, 1H), 5.11−5.20 (m, 1H), 1.88 (s, 3H), 1.62 (dd, *J* = 6.7, 1.7 Hz. ^{13}C NMR (100 MHz, CD_3CN): δ (ppm) 168.1, 124.6, 107.4, 22.9, 15.1. HRMS: C_5H_9NO [M + H^+] calcd 100.0763, found 100.0754.

*(Z)-N-Styrylacetamide (**67**).* The product was obtained using general procedure B yielding **67** (540 mg, 27%) as a colorless solid. Mp: 65−67 °C. ^{1}H NMR (400 MHz, CD_3CN): δ (ppm) 8.21 (bs, 1H), 7.35−7.40 (m, 4H), 7.22−7.28 (m, 1H), 6.85 (dd, *J* = 12.0, 8.0 Hz), 5.66 (d, *J* = 8.0 Hz, 1H), 1.99 (s, 3H). ^{13}C NMR (100 MHz, CD_3CN): δ (ppm) 169.3, 136.8, 129.7 (2C), 129.2 (2C), 127.6, 123.1, 110.0, 23.3. HRMS: $C_{10}H_{11}NO$ [M + Na^+] calcd 184.0738, found 184.0737.

*(E)-N-Styrylacetamide (**68**).* The product was obtained using general procedure A yielding **68** (1.10 g, 54%) as a white solid. Mp: 106−108 °C. ^{1}H NMR (400 MHz, CD_3CN): δ (ppm) 8.50 (bs, 1H), 7.46 (dd, *J* = 16.0, 12.0 Hz, 1H), 7.25−7.35 (m, 4H), 7.16 (tt, *J* = 8.0, 4.0 Hz, 1H), 6.15 (d, *J* = 16.0 Hz, 1H). ^{13}C NMR (100 MHz, CD_3CN): δ (ppm) 168.6, 137.8, 129.6 (2C), 127.2, 126.3 (2C), 124.3, 112.2, 23.1. HRMS: $C_{10}H_{11}NO$ [M + H^+] calcd 162.0920, found 162.0913.

*N-(1-Phenylvinyl)acetamide (**69**).*[32] The product was obtained using a known literature procedure. The spectra are in accord with the literature.[32]

*(Z)-N-(4-Methylstyryl)acetamide (**70**).* The product was obtained using general procedure B yielding **70** (560 mg, 28%) as an amorphous solid. ^{1}H NMR (400 MHz, CD_3CN): δ (ppm) 8.12 (bs, 1H), 7.25 (d, *J* = 8.2 Hz, 2H), 7.19 (d, *J* = 8.0 Hz, 2H), 6.80 (dd, *J* = 11.0, 9.8 Hz), 5.62 (d, *J* = 9.8 Hz, 1H), 2.33 (s, 3H), 1.99 (s, 3H). ^{13}C NMR (100 MHz, CD_3CN): δ (ppm) 169.2, 137.4, 133.9, 130.3 (2C), 129.1 (2C), 122.5, 110.0, 23.3, 21.2. HRMS: $C_{11}H_{13}NO$ [M + H^+] calcd 176.1076, found 176.1078.

*(Z)-N-(4-Methoxystyryl)acetamide (**71**).* The product was obtained using general procedure B yielding **71** (540 mg, 27%) as an amorphous solid. ^{1}H NMR (400 MHz, CD_3CN): δ (ppm) 8.09 (bs, 1H), 7.29 (d, *J* = 8.5, 2H), 6.93 (d, *J* = 6.7 Hz, 2H), 6.76 (dd, *J* = 10.9, 9.8 Hz, 1H), 5.61 (d, *J* = 9.8 Hz, 1H), 3.79 (s, 3H), 1.99 (s, 3H) . ^{13}C NMR (100 MHz, CD_3CN): δ (ppm) 169.2, 159.3, 130.5 (2C), 129.2, 121.8, 115.1 (2C), 109.9, 55.9, 23.3. HRMS: $C_{11}H_{13}NO_2$ [M + H^+] calcd 192.1025, found 192.1021.

*(Z)-N-(4-Chlorostyryl)acetamide (**72**).* The product was obtained using general procedure B yielding **72** (580 mg, 29%) as an amorphous solid. ^{1}H NMR (400 MHz, CD_3CN): δ (ppm) 8.25 (bs, 1H), 7.35 (d, *J* = 5.9, 2H), 7.31 (d, *J* = 6.6 Hz, 2H), 6.84 (dd, *J* = 10.7, 9.8 Hz, 1H), 5.67 (d, *J* = 9.8 Hz, 1H), 1.98 (s, 3H). ^{13}C NMR (100 MHz, CD_3CN): δ (ppm) 169.4, 135.6, 132.5, 130.8 (2C), 129.6 (2C), 123.7, 108.7, 23.2. HRMS: $C_{10}H_{10}ClNO$ [M + H^+] calcd 196.0530, found 196.0521.

*(Z)-N-(4-Fluorostyryl)acetamide (**73**).* The product was obtained using general procedure B yielding **73** (520 mg, 26%) as an amorphous solid. ^{1}H NMR (400 MHz, CD_3CN): δ (ppm) 8.17 (bs, 1H), 7.37 (q, *J* = 8.0, 4.0 Hz, 2H), 7.11 (t, *J* = 12.0 Hz, 2H), 6.83 (t, *J* = 10.0 Hz, 1H), 5.64 (d, *J* = 9.6 Hz, 1H), 1.98 (s, 3H). ^{13}C NMR (100 MHz, CD_3CN): δ (ppm) 169.4, 165.5 (d, *J* = 242.0), 133.2 (d, *J* = 3.3 Hz), 131.1 (d, *J* = 8.0 Hz, 2C), 123.1, 116.4 (d, *J* = 21.4 Hz, 2C), 109.0, 23.2. HRMS: $C_{10}H_{10}FNO$ [M + H^+] calcd 180.0825, found 180.0820.

*N-(2-Methylprop-1-en-1-yl)acetamide (**75**).*[33] The product was obtained using a known literature procedure. The spectra are in accord with the literature.[33]

*(E)-tert-Butyl (2-(Benzyloxy)prop-1-en-1-yl)carbamate (**76**).*[34] The product was obtained using a known literature procedure. The spectra are in accord with the literature.[34]

*(Z)-Ethyl 3-Acetamidoacrylate (**77**).*[35] The product was obtained using a known literature procedure. The spectra are in accord with the literature.[36]

*(S,Z)-tert-Butyl (1-Oxo-3-phenyl-1-(prop-1-en-1-ylamino)propan-2-yl)carbamate (**89**).* The product was obtained using general procedure A yielding **89** (480 mg, 24%) as a viscous oil. ^{1}H NMR (400 MHz, CD_3CN): δ (ppm) 8.20 (bs, 1H), 7.20−7.38 (m, 5H), 6.56−6.61 (m, 1H), 5.79 (bs, 1H), 4.78−4.85 (m, 1H), 4.45 (bs, 1H), 3.10 (dd, *J* = 12.0, 4.0 Hz, 1H), 2.89 (dd, *J* = 12.0, 8.0 Hz, 1H), 1.57 (dd, 7.2, 1.6 Hz, 3H), 1.36 (s, 9H). ^{13}C NMR (100 MHz, CD_3CN): δ (ppm) 170.6, 156.7, 138.4, 130.3 (2C), 129.3 (2C), 127.6, 122.5, 107.3, 80.2, 56.7, 38.6, 28.5 (3C), 11.4. HRMS: $C_{17}H_{24}N_2O_3$ [M + Na^+] calcd 327.1685, found 327.1684.

Synthesis of Methyldiarylsilanes 37−43. *General Procedure C.*[15c] Magnesium turnings (2.1 equiv) were suspended in THF under an atmosphere of argon. Iodine crystals were added to initiate the reaction. ArBr (2.1 equiv) was added slowly dropwise and the mixture refluxed for 3 h. In a separate flask, dichloromethylsilane (3.3 mmol, 1.0 equiv) was dissolved in THF and cooled to 0 °C under atmosphere of argon. The generated ArMgBr was added to the silane and allowed to warm to room tempertaure with stirring overnight. The reaction was diluted with Et_2O and washed with water (2×) and brine (1×). The organic layer was dried using $MgSO_4$, filtered, and concentrated in vacuo. The product was purified via flash chromatography using pentane as the eluent.

*Methyldi-m-tolylsilane (**37**).*[15c] The product was obtained using a known literature procedure. The spectra are in accord with the literature.[15c]

*Methyldi-p-tolylsilane (**38**).*[15c] The product was obtained using a known literature procedure. The spectra are in accord with the literature.[15c]

*Methyldi-o-tolylsilane (**39**).*[15c] The product was obtained using a known literature procedure. The spectra are in accord with the literature.[15c]

*Bis(3,5-dimethylphenyl)(methyl)silane (**40**).*[15c] The product was obtained using a known literature procedure. The spectra are in accord with the literature.[15c]

*Methylbis(4-(trifluoromethyl)phenyl)silane (**41**).*[36] The product was obtained using general procedure C yielding **41** (916 mg, 83%) as a viscous oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.70 (*J* = 8.3 Hz, 4H), 7.63 (d, *J* = 8.3 Hz, 4H), 5.03 (q, *J* = 7.7, 3.8 Hz), 0.71 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 139.3 (2C), 135.1 (4C), 131.9 (q, *J* = 7.5, 3.7 Hz, 4C), 124.7 (q, *J* = 64.3, 32.0 Hz, 2C), 124.1 (d, *J* = 170.0 Hz, 2C), 5.5. GCMS temp ramp: 40 °C (5 min), 40−230 °C (15 °C/min); τ = 13.2 min; GCMS *m*/*z* (rel intensity) 108 (84), 127 (64), 173 (45), 188 (28), 207 (100), 319 (84), 333 (38).

*Di(furan-2-yl)(methyl)silane (**42**).*[36] The product was obtained using general procedure C yielding **52** (182 mg, 31%) as a viscous oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.73 (d, *J* = 1.6 Hz, 2H), 6.85 (d, *J* = 3.3 Hz, 2H), 6.45 (dd, *J* = 3.3, 1.7 Hz, 2H), 4.97 (q, *J* = 7.7, 3.9 Hz, 1H), 0.65 (d, *J* = 3.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 153.3 (2C), 147.7 (2C), 122.8 (2C), 109,7 (2C), 6.4. GCMS temp ramp: 40 °C (5 min), 40−230 °C (15 °C/min); τ = 13.2 min; GCMS *m*/*z* (rel intensity) 111 (35), 126 (15), 195 (100), 210 (48).

*Methyldi(thiophene-2-yl)silane (**43**).*[36] The product was obtained using general procedure C yielding **43** (354 mg, 51%) as a viscous oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.73 (d, *J* = 4.0 Hz, 2H), 7.46−7.47 (m, 2H), 7.26−7.29 (m, 2H), 5.30−5.33 (m, 1H), 0.78−0.80 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 136.5 (2C), 133.5 (2C), 132.0 (2C), 128.4 (2C), 2.8. GCMS temp ramp: 40 °C (5 min), 40−230 °C (15 °C/min); τ = 10.1 min; GCMS *m*/*z* (rel intensity) 95 (53), 137 (89), 149 (28), 163 (68), 178 (100).

Synthesis of Alkyldiphenylsilane 51−56. *General Procedure D.*[12a] $Rh(PPh_3)_3Cl$ (0.01 equiv) was dissolved in THF in the glovebox. Alkene (1.0 equiv) was added and stirred overnight. The reaction was concentrated and purified via flash chromatography with 0−2% EtOAc/pentanes as eluent.

*(3-(Benzyloxy)propyl)diphenylsilane (**51**).*[12a] The product was obtained using a known literature procedure. The spectra are in accord with the literature.[12a]

*Diphenyl(3-((tetrahydro-2H-pyran-2-yl)oxy)propyl)silane (**52**).*[12a] The product was obtained using a known literature procedure. The spectra are in accord with the literature.[12a]

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*3-(Diphenylsilyl)propyl Acetate (**53**).* The product was obtained using general procedure D yielding **53** (427 mg, 75%) as a viscous oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.55−7.58 (m, 4H), 7.35−7.43 (m, 6H), 4.88−4.90 (m, 1H), 4.07 (t, J = 6.7 Hz, 2H), 2.04 (s, 3H), 1.75−1.82 (m, 2H), 1.15−1.20 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 171.1, 135.1 (4C), 133.8 (2C), 129.7 (2C), 128.0 (4C), 66.5, 23.7, 21.0, 8.4. HRMS: $C_{17}H_{20}O_2Si$ [M + H$^+$] calcd 285.1130, found 285.1131.

*tert-Butyl(3-(diphenylsilyl)propoxy)diphenylsilane (**54**).*[12a] The product was obtained using a known literature procedure. The spectra are in accord with the literature.[12a]

*Diphenyl(2-((tetrahydro-2H-pyran-2-yl)oxy)ethyl)silane (**55**).* The product was obtained using general procedure C yielding **55** (495 mg, 79%) as a viscous oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.57 (d, J = 7.8 Hz, 4H), 7.34−7.42, (m, 6H), 4.92 (t, J = 3.6 Hz, 1H), 4.54 (t, J = 3.8 Hz, 1H), 3.96 (q, J = 17.2, 9.3 Hz, 1H), 3.77 (t, J = 8.6 Hz, 1H), 3.56 (q, J = 18.9, 8.7 Hz, 1H), 3.40−3.44 (m, 1H), 1.47−1.77 (m, 8H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 135.1 (4C), 133.9 (2C), 129.6 (2C), 128.0 (4C), 98.4, 64.2, 62.1, 30.7, 25.4, 19.5, 14.1. HRMS: $C_{19}H_{24}O_2Si$ [M + Na$^+$] calcd 335.1444, found 335.1448.

*Hexyldiphenylsilane (**56**).*[12a] The product was obtained using a known literature procedure. The spectra are in accord with the literature.[12a]

Hydrosilylation of Enamides 27, 32−35, 44−50, 58−64, 78−88, and 90. *General Procedure E.* $Rh(cod)_2BF_4$ (0.003 mmol) and $P(OPh)_3$ (0.006 mmol) were dissolved in DCE (0.15 mL), and the mixture was stirred for 5 min. Enamide (0.30 mmol) and silane (0.30 mmol) in DCE (0.10 mL) were added in that order in the glovebox. The mixture was placed in preheated oil bath at 65 °C for 18 h. The reaction was cooled to room temperature and concentrated. The crude mixture was purified via flash chromatography using 40−60% EtOAc/pentanes as eluent.

General Procedure F. Rh_2OAc_4 (0.003 mmol) were dissolved in DCE (0.25 mL). Enamide (0.30 mmol) and silane (0.30 mmol) were added in that order in the glovebox. The mixture was placed in a preheated oil bath at 65 °C and stirred for 18 h. The reaction was cooled to room temperature and concentrated. The crude mixture was purified via flash chromatography using 40−60% EtOAc/pentanes as eluent.

*N-(1-(Methyldiphenylsilyl)ethyl)acetamide (**27**).* The product was obtained using general procedure E yielding **32** (66.0 mg, 78%) as a viscous oil. ^{1}H NMR (400 MHz, CD_3CN): δ (ppm) 7.59−7.63 (m, 4H), 7.36−7.42 (m, 6H), 6.48 (d, J = 8.8 Hz, 1H), 4.17−4.26 (m, 1H), 1.80 (s, 3H), 1.18 (d, J = 7.6 Hz, 3H), 0.68 (s, 3H). ^{13}C NMR (100 MHz, CD_3CN): δ (ppm) 169.9, 136.3, 136.2, 135.7 (2C), 135.6 (2C), 130.5, 130.4, 128.9 (2C), 128.8 (2C), 33.5, 23.1, 17.4, 6.3. HRMS: $C_{17}H_{21}NOSi$ [M + H$^+$] calcd 284.1471, found 284.1473.

*N-(1-(Methyldiphenylsilyl)propyl)acetamide (**32**).* The product was obtained using general procedure E yielding **32** (89.2 mg, 97%) as a viscous oil. ^{1}H NMR (400 MHz, CD_3CN): δ (ppm) 7.54−7.60 (m, 4H), 7.33−7.43 (m, 6H), 6.18 (d, J = 9.2 Hz, 1H), 4.03, (ddd, J = 13.6, 10.0, 3.6 Hz, 1H), 1.78 (s, 3H), 1.55−1.64 (m, 1H), 1.35−1.47 (m, 1H), 0.86 (t, J = 7.2 Hz, 3H), 0.62 (s, 3H). ^{13}C NMR (100 MHz, CD_3CN): δ (ppm) 170.3, 136.6, 136.5, 135.7 (2C), 135.6 (2C), 130.5, 130.4, 128.9 (2C), 128.8 (2C), 40.4, 25.2, 23.0, 12.5, 6.0. HRMS: $C_{18}H_{23}NOSi$ [M + H$^+$] calcd 298.1628, found 298.1625.

*tert-Butyl (1-(Methyldiphenylsilyl)propyl)carbamate (**33**).* The product was obtained using general procedure E yielding **33** (107 mg, 54%) as a viscous oil. ^{1}H NMR (400 MHz, CD_3CN): δ (ppm) 7.54−7.58 (m, 4H), 7.33−7.43 (m, 6H), 4.97 (d, 9.8 Hz, 1H), 3.64 (dt, J = 11.1, 3.6 Hz, 1H), 1.51−1.61 (m, 1H), 1.33−1.41 (m, 10H), 0.88 (t, J = 7.3 Hz, 3H), 0.61 (s, 3H). ^{13}C NMR (100 MHz, CD_3CN): δ (ppm) 157.3, 136.6, 136.5, 135.6 (4C), 130.5, 130.4, 128.9 (2C), 128.8 (2C), 78.8, 41.6, 28.6, 25.5, 12.4, 6.2. HRMS: $C_{21}H_{29}NO_2Si$ [M + Na$^+$] calcd 378.1865, found 378.1862.

*1-(1-(Methyldiphenylsilyl)propyl)pyrrolidin-2-one (**34**).* The product was obtained using general procedure E yielding **34** (75.4 mg, 78%) as a viscous oil. ^{1}H NMR (400 MHz, CD_3CN): δ (ppm) 7.53−7.62 (m, 2H), 7.33−7.40 (m, 2H), 4.10 (dd, J = 12.2, 3.7 Hz, 1H), 3.18−3.21 (m, 1H), 2.95−3.00 (m, 1H), 2.11−2.19 (m, 1H), 1.93−2.05 (m, 1H), 1.65−1.74 (m, 1H), 1.54−1.64 (m, 1H), 0.85 (t, J = 7.2, 3H), 0.66 (s, 3H). ^{13}C NMR (100 MHz, CD_3CN): δ (ppm) 175.2, 136.7, 136.3, 135.5 (2C), 135.4 (2C), 130.6, 130.5, 129.0 (2C), 128.9 (2C), 46.3, 44.1, 31.3, 21.9, 18.9, 12.8, 5.1. HRMS: $C_{20}H_{25}NOSi$ [M + H$^+$] calcd 324.1784, found 324.1782.

*3-(1-(Methyldiphenylsilyl)propyl)oxazolidin-2-one (**35**).* The product was obtained using general procedure F yielding **35** in (36.3 mg, 37%) as a viscous oil mixture with the trans enamide. ^{1}H NMR (400 MHz, CD_3CN): δ (ppm) 7.61−7.63 (m, 2H), 7.55−7.59 (m, 2H), 7.36−7.44 (m, 6H), 4.32−4.36 (m, 1H), 4.06−4.12 (m, 1H), 3.93−4.00 (m, 1H), 3.34−3.41 (m, 1H), 3.15−3.22 (m, 1H), 1.72−1.80 (m, 1H), 1.57−1.67 (m, 1H), 0.88 (t, J = 7.2 Hz, 3H), 0.69 (s, 3H). ^{13}C NMR (100 MHz, CD_3CN): δ (ppm) 159.6, 136.1, 135.9, 135.6 (2C), 135.5 (2C), 130.7 (2C), 129.1 (2C), 129.0 (2C), 62.6, 46.0, 43.7, 21.9, 12.7, 5.3. HRMS: $C_{19}H_{23}NO_2Si$ [M + Na$^+$] calcd 348.1395, found 348.1392.

*N-(1-(Methyldi-m-tolylsilyl)propyl)acetamide (**44**).* The product was obtained using general procedure E yielding **44** (84.1 mg, 86%) as a viscous oil. ^{1}H NMR (400 MHz, CD_3CN): δ (ppm) 7.33−7.41 (m, 4H), 7.19−7.28 (m, 4H), 6.18 (d, J = 9.7, 1H), 4.02 (ddd, J = 16.3, 10.1, 3.5 Hz), 2.32 (s, 3H), 2.30 (s, 3H), 1.53−1.64 (m, 1H), 1.34−1.46 (m 1H), 0.87 (t, J = 11.2 Hz, 3H), 0.60 (s, 3H). ^{13}C NMR (100 MHz, CD_3CN): δ (ppm) 170.2, 138.3, 138.1, 136.5, 136.4, 136.2 (2C), 132.7, 132.6, 131.1, 131.0, 128.8, 128.7, 40.5, 25.3, 23.0, 21.6 (2C), 12.6, 6.0. HRMS: $C_{20}H_{27}NOSi$ [M + H$^+$] calcd 326.1941, found 326.1944.

*N-(1-(Methyldi-p-tolylsilyl)propyl)acetamide (**45**).* The product was obtained using general procedure E yielding **45** (72.6 mg, 74%) as a viscous oil. ^{1}H NMR (400 MHz, CD_3CN): δ (ppm) 7.44 (dt, J = 10.1, 7.9 Hz, 4H), 7.19 (dd, J = 10.1, 7.9, 4H), 6.13 (d, J = 9.7 Hz, 1H), 3.99 (ddd, J = 14.8, 11.4, 3.5 Hz, 1H), 2.33 (s, 3H), 2.32 (s, 3H), 1.78 (s, 3H), 1.52−1.62 (m, 1H), 1.32−1.44 (m, 1H), 0.85 (t, J = 7.2 Hz, 3H), 0.57 (s, 3H). ^{13}C NMR (100 MHz, CD_3CN): δ (ppm) 170.2, 140.4, 140.3, 135.8 (2C), 135.7 (2C), 133.0, 132.9, 129.6 (2C), 129.5(2C), 40.5, 25.3, 23.0, 21.5 (2C), 12.6, 5.9. HRMS: $C_{20}H_{27}NOSi$ [M + Na$^+$] calcd 348.1760, found 348.1754.

*N-(1-(Methyldi-o-tolylsilyl)propyl)acetamide (**46**).* The product was obtained using general procedure E yielding **46** (8.0 mg, 8%) as a viscous oil. ^{1}H NMR (400 MHz, CD_3CN): δ (ppm) 7.62 (dt, J = 7.4, 1.4 Hz, 2H), 7.08−7.33 (m, 6H), 5.99 (d, J = 9.5 Hz, 1H), 4.27 (ddd, J = 13.5, 10.3, 3.2 Hz, 1H), 2.15 (s, 3H), 2.09 (s, 3H), 2.07 (s, 3H), 1.50−1.56 (m, 1H), 1.28−1.38 (m, 1H), 0.87 (t, J = 7.2 Hz, 3H), 0.65 (s, 3H). ^{13}C NMR (100 MHz, CD_3CN): δ (ppm) 170.4, 145.0, 144.8, 136.0 (2C), 135.7 (2C), 131.0, 130.9, 130.7, 130.6, 126.2, 126.0, 39.9, 30.8, 25.7, 23.2, 23.1, 12.4, 4.3. HRMS: $C_{20}H_{27}NOSi$ [M + Na$^+$] calcd 348.1759, found 348.1759.

*N-(1-(Bis(3,5-dimethylphenyl)(methyl)silyl)propyl)acetamide (**47**).* The product was obtained using general procedure E yielding **47** (91.0 mg, 86%) as a viscous oil. ^{1}H NMR (400 MHz, CD_3CN): δ (ppm) 7.15 (d, J = 11.68 Hz, 4H), 7.04 (d, J = 9.2 Hz, 2H), 6.02 (d, J = 9.8 Hz, 1H), 3.97 (ddd, J = 13.3, 10.2, 3.4, 1H), 2.28 (s, 3H), 2.26 (s, 3H), 1.78 (s, 3H), 1.52−1.58 (m, 1H), 1.32−1.40 (m, 1H), 0.85 (t, J = 7.3 Hz, 3H), 0.55 (s, 3H). ^{13}C NMR (100 MHz, CD_3CN): δ (ppm) 170.2, 138.2 (2C), 138.0 (2C), 136.5, 136.4, 133.3(4C), 132.0, 131.9, 40.5, 25.4, 23.1, 21.5 (4C), 12.6, 6.0. HRMS: $C_{22}H_{31}NOSi$ [M + Na$^+$] calcd 376.2073, found 376.2088.

*N-(1-(Methylbis(4-(trifluoromethyl)phenyl)silyl)propyl)acetamide (**48**).* The product was obtained using general procedure E yielding **47** (107.8 mg, 83%) as a viscous oil. ^{1}H NMR (400 MHz, CD_3CN): δ (ppm) 7.73−7.77 (m, 4H), 7.64−7.68 (m, 4H), 6.36 (d, J = 9.2 Hz, 1H), 3.99 (dd, J = 15.0, 9.5, 3.6 Hz, 1H), 1.76 (s, 3H), 1.53−1.61 (m, 1H), 1.41−1.50 (m, 1H), 0.87 (t, J = 7.2 Hz, 3H), 0.71 (s, 3H). ^{13}C NMR (100 MHz, CD_3CN): δ (ppm) 170.5, 141.9, 141.7, 136.4 (2C), 136.2 (2C), 131.7 (dd, J = 63.1, 7.7 Hz, 2C), 125.4 (d, J = 269.6 Hz), 125.4 (d, J = 269.4 Hz), 125.3 (q, J = 7.6, 3.8 Hz, 2C), 125.2 (q, J = 7.7, 3.9 Hz, 2C), 40.3, 25.0, 22.8, 12.5, 6.1. HRMS: $C_{20}H_{21}F_6NOSi$ [M + H$^+$] calcd 434.1376, found 434.1373.

*N-(1-(Di(furan-2-yl)(methyl)silyl)propyl)acetamide (**49**).* The product was obtained using general procedure E yielding **49** (57.1 mg, 69%) as a viscous oil. ^{1}H NMR (400 MHz, CD_3CN): δ (ppm)

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7.76 (ddd, J = 5.6, 1.6, 0.5 Hz, 2H), 6.84 (ddd, J = 11.5, 3.3, 0.5 Hz, 2H), 6.45−6.47 (m, 2H), 6.33 (d, J = 7.8 Hz, 1H), 3.69 (ddd, 13.1, 9.2, 3.9 Hz, 1H), 1.84 (s, 3H), 1.58−1.68 (m, 1H), 1.40−1.51 (m, 1H), 0.87 (t, J = 7.3 Hz, 3H), 0.55 (s, 3H). ^{13}C NMR (100 MHz, CD_3CN): δ (ppm) 170.5, 155.8, 155.7, 148.7 (2C), 123.7, 123.5, 110.8 (2C), 40.9, 24.8, 22.8, 12.3, 6.0. HRMS: $C_{14}H_{19}NO_3Si$ [M + Na^+] calcd 300.1031, found 300.1037.

*N-(1-(Methyldi(thiophene-2-yl)silyl)propyl)acetamide (**50**).* The product was obtained using general procedure E yielding **50** (69.5 mg, 75%) as a viscous oil: ^{1}H NMR (400 MHz, CD_3CN): δ (ppm) 7.75 (ddd, J = 10.5, 4.6, 3.8 Hz, 2H), 7.43 (ddd, J = 25.6, 3.4, 0.9 Hz, 2H), 7.22−7.27 (m, 2H), 6.27 (d, J = 8.6 Hz, 1H), 3.77 (ddd, J = 13.0, 9.6, 3.5 Hz, 1H), 1.84 (s, 3H), 1.61−1.71 (m, 1H), 1.39−1.51 (m, 1H), 0.88 (t, J = 7.2 Hz, 3H), 0.69 (s, 3H). ^{13}C NMR (100 MHz, CD_3CN): δ (ppm) 170.5, 137.7, 137.6, 135.2, 135.0, 133.2, 133.1, 129.4 (2C), 42.3, 25.0, 22.7, 12.5, 3.1. HRMS: $C_{14}H_{19}NOS_2Si$ [M + Na^+] calcd 332.0575, found 332.0573.

*N-(1-((3-(Benzyloxy)propyl)diphenylsilyl)ethyl)acetamide (**58**).* The product was obtained using general procedure E yielding **58** (93.0 mg, 74%) as a viscous oil. ^{1}H NMR (400 MHz, CD_3CN): δ (ppm) 7.55 (m, 4H), 7.25−7.46 (m, 11H), 6.12 (d, J = 6.9 Hz, 1H), 4.41 (s, 2H), 4.17−4.26 (m, 1H), 3.41 (t, J = 6.5 Hz, 2H), 1.76 (s, 3H), 1.55−1.63 (m, 2H), 1.17−1.21 (m, 2H), 1.13 (dd, J = 7.6 Hz, 3H). ^{13}C NMR (100 MHz, CD_3CN): δ (ppm) 169.8, 140.0, 136.4 (2C), 136.2 (2C), 134.8, 134.5, 130.6 (2C), 129.2 (2C), 128.9 (4C), 128.5 (2C), 128.3, 73.5, 73.1, 32.9, 24.8, 23.2, 17.7, 8.1. HRMS: $C_{26}H_{31}NO_2Si$ [M + H^+] calcd 418.2203, found 418.2199.

*N-(1-(Diphenyl(3-((tetrahydro-2H-pyran-2-yl)oxy)propyl)silyl)-ethyl)acetamide (**59**).* The product was obtained using general procedure E yielding **59** (96.2 mg, 78%) as a viscous oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.51−7.57 (m, 4H), 7.37−7.42 (m, 6H), 5.19 (d, J = 10.0, 1H), 4.48−4.51 (m, 1H), 4.30−4.39 (m, 1H), 3.66−3.85 (m, 1H), 3.66−3.69 (m, 1H), 3.43−3.49 (m, 1H), 3.33−3.36 (m, 1H), 1.87 (d, J = 1.6 Hz, 3H), 1.76−1.83 (m, 1H), 1.48−1.71 (8H), 1.14−1.20 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 169.3, 135.3 (4C), 132.8, 132.7, 129.8 (2C), 128.1 (4C), 98.8, 69.8, 62.4, 31.6, 30.7, 25.4, 23.6, 23.4, 19.7, 17.1, 7.5. HRMS: $C_{24}H_{33}NO_3Si$ [M + Na^+] calcd 434.2127, found 434.2122.

*3-((1-Acetamidoethyl)diphenylsilyl)propyl Acetate (**60**).* The product was obtained using general procedure E yielding **60** (67.8 mg, 61%) as a viscous oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.50−7.56 (m, 4H), 7.37−7.47 (m, 6H), 5.20 (d, J = 9.8 Hz, 1H), 4.30−4.38 (m, 1H), 3.98 (dt, J = 6.8, 1.0 Hz, 2H), 1.99 (s, 3H), 1.87 (s, 3H), 1.59−1.67 (m, 2H), 1.19 (d, J = 7.5 Hz, 3H), 1.09−1.14 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 171.0, 169.3, 135.3 (4C), 132.3, 131.9, 129.98 (2C), 128.2 (4C), 66.6, 31.5, 23.4, 22.7, 20.9, 17.1, 7.5. HRMS: $C_{21}H_{27}NO_3Si$ [M + H^+] calcd 370.1839, found 370.1838.

*N-(1-((3-((tert-Butyldiphenylsilyl)oxy)propyl)diphenylsilyl)ethyl)-acetamide (**61**).* The product was obtained using general procedure E yielding **61** (105 mg, 62%) as a viscous oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.65 (m, 4H), 7.55 (m, 4H), 7.34−7.48 (12H), 5.17 (d, J = 9.9 Hz, 1H), 4.31−4.39 (m, 1H), 3.59−3.68 (m, 2H), 1.87 (s, 3H), 1.55−1.63 (m, 2H), 1.11−1.24 (m, 5H), 1.06 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 169.4, 135.5 (4C), 135.4 (4C), 134.0 (2C), 132.9, 132.4, 129.9 (2C), 129.5 (2C), 128.2 (2C), 128.1 (2C), 127.6 (4C), 66.2, 31.7, 26.9 (3C), 26.5, 23.5, 19.2, 17.2, 7.2. HRMS: $C_{35}H_{43}NO_2Si_2$ [M + Na^+] calcd 588.2729, found 588.2720.

*N-(1-(Diphenyl(2-((tetrahydro-2H-pyran-2-yl)oxy)ethyl)silyl)-ethyl)acetamide (**62**).* The product was obtained using general procedure E yielding the viscous oil of **62** (83.7 mg, 70%) as diastereomeric mixture. Compound A: ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) inter alia, 6.50 (d, J = 9.2 Hz, 1H), 3.80−3.87 (m, 2H), 3.64−3.74 (m, 2H), 1.80 (s, 3H), 1.16 (d, J = 2.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) inter alia, 169.8, 136.2 (2C), 136.1 (2C), 135.0, 134.8, 128.9 (4C), 100.2, 64.7, 63.7, 33.0, 31.5, 26.2, 21.0, 17.5, 13.3. Compound B: ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) inter alia, 6.36 (d, J = 9.2 Hz, 1H), 3.48−3.54 (m, 2H), 3.32−3.40 (m, 2H), 1.79 (s, 3H), 1.14 (d, J = 1.9 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) inter alia, 169.8, 136.1 (4C), 134.8, 134.7, 128.9 (4C), 99.6, 64.5, 63.0, 32.8, 31.5, 26.2, 20.5, 17.4, 13.0. Since it was a mixture the last 3 carbons and 12 hydrogens were not assigned HRMS: $C_{23}H_{31}NO_3Si$ [M + H^+] calcd 398.2152, found 398.2145.

*N-(1-(Hexyldiphenylsilyl)ethyl)acetamide (**63**).* The product was obtained using general procedure F yielding **63** (77.5 mg, 73%) as a viscous oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.51−7.57 (m, 4H), 7.37−7.45 (m, 6H), 5.17 (d, J = 9.9 Hz, 1H), 4.29−4.37 (m, 1H), 1.86 (s, 3H), 1.18−1.30 (m, 11H), 1.08−1.12 (m, 2H), 0.83 (t, J = 12.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 169.3, 135.4 (2C), 135.3 (2C), 133.1, 132.6, 129.8, 129.7, 128.1 (2C), 128.0 (2C), 33.2, 31.6, 31.3, 23.5, 23.2, 22.5, 17.2, 14.0, 11.4. HRMS: $C_{22}H_{31}NOSi$ [M + Na^+] calcd 376.2072, found 376.2066.

*N-(1-(Triethylsilyl)ethyl)acetamide (**64**).* The product was obtained using general procedure F yielding **64** (45.0 mg, 75%) as a viscous oil. ^{1}H NMR (400 MHz, CD_3CN): δ (ppm) 6.07 (bs, 1H), 3.55−3.64 (m, 1H), 1.83 (s, 3H), 1.10 (d, J = 7.7 Hz, 3H), 0.96 (t, J = 8.1 Hz, 9 H), 0.59 (q, J = 8.5, 4.6 Hz, 6H). ^{13}C NMR (100 MHz, CD_3CN): δ (ppm) 169.6, 33.1, 23.2, 17.3, 7.8 (3C), 2.6 (3C). HRMS: $C_{10}H_{23}NOSi$ [M + H^+] calcd 202.1628, found 202.1624.

*1-(Methyldiphenylsilyl)ethyl Acetate (**78**).* The product was obtained using general procedure F yielding **78** (47.2 mg, 55%) as a viscous oil. ^{1}H NMR (400 MHz, CD_3CN): δ (ppm) 7.54−7.63 (m, 4H), 7.37−7.46 (m, 6H), 5.27 (q, J = 14.9, 7.5 Hz, 1H), 1.91 (s, 3H), 1.27 (d, J = 10.2 Hz, 3H), 0.62 (s, 3H). ^{13}C NMR (100 MHz, CD_3CN): δ (ppm) 171.5, 135.8 (2C), 135.7 (2C), 135.4, 135.2, 130.7 (2C), 129.0 (4C), 63.3, 21.3, 16.8, 6.5. HRMS: $C_{17}H_{20}O_2Si$ [M + Na^+] calcd 307.1131, found 307.1121.

*N-(1-(Methyldiphenylsilyl)-2-phenylethyl)acetamide (**79**).* The product was obtained using general procedure F yielding **79** (84.3 mg, 78%) as a viscous oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.60−7.66 (m, 4H), 7.36−7.48 (m, 6H), 7.09−7.27 (m, 5H), 5.20 (d, J = 9.3, 1H), 4.48 (ddd, J = 14.2, 9.8, 4.4 Hz, 1H), 3.01 (dd, J = 14.5, 4.4 Hz, 1H), 2.69 (dd, J = 14.4, 11.1 Hz, 1H), 1.74 (s, 3H), 0.61 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): 169.2, 139.3, 134.9 (2C), 134.8 (2C), 134.5, 134.3, 129.7 (2C), 128.8 (2C), 128.2 (2C), 128.1 (2C), 128.0 (2C), 126.2, 39.5, 37.3, 23.1, 5.2. δ (ppm) HRMS: $C_{23}H_{25}NOSi$ [M + H^+] calcd 360.1784, found 360.1781.

*N-(2-(Methyldiphenylsilyl)-1-phenylethyl)acetamide (**80**).* The product was obtained using general procedure F yielding **80** (96.7 mg, 90%) as a viscous oil. ^{1}H NMR (400 MHz, CD_3CN): δ (ppm) 7.54−7.57 (m, 2H), 7.47−7.50 (m, 2H), 7.31−7.41 (m, 6H), 7.18−7.27 (m, 5H), 6.75 (d, J = 8.2 Hz, 1H), 5.01−5.07 (m, 1H), 1.78 (dd, J = 14.8, 9.6 Hz, 1H), 1.64 (dd, J = 14.9, 5.9 Hz, 1H), 1.60 (s, 3H), 0.46 (s, 3H). ^{13}C NMR (100 MHz, CD_3CN): δ (ppm) 169.3, 146.7, 138.1, 137.8, 135.4 (2C), 135.2 (2C), 130.3, 130.2, 129.3 (2C), 128.9 (4C), 127.8, 127.2 (2C), 51.0, 23.6, 22.9, 4.3. HRMS: $C_{23}H_{25}NOSi$ [M + H^+] calcd 360.1784, found 360.1783.

*N-(1-(Methyldiphenylsilyl)-2-(p-tolyl)ethyl)acetamide (**81**).* The product was obtained using general procedure F yielding **81** (81.9 mg, 73%) as an amorphous solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.57−7.63 (m, 4H), 7.37−7.44 (m, 6H), 7.00−7.06 (m, 4H), 5.26 (bs, 1H), 4.43−4.50 (m, 1H), 2.98 (dd, J = 14.4, 4.3 Hz, 1H), 2.65 (dd, J = 14.4, 11.1, 1H), 2.30 (s, 3H), 1.74 (s, 3H), 0.62 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 169.2, 136.1, 135.6, 134.9 (2C), 134.8 (2C), 134.5, 134.4, 129.6 (2C), 128.9 (2C), 128.6 (2C), 128.0 (4C), 39.6, 36.9, 23.1, 21.0, 5.2. HRMS: $C_{24}H_{27}NOSi$ [M + Na^+] calcd 396.1760, found 396.1754.

*N-(2-(4-Chlorophenyl)-1-(methyldiphenylsilyl)ethyl)acetamide (**83**).* The product was obtained using general procedure F yielding **83** (75.9 mg, 64%) as an amorphous solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.55−7.61 (m, 4H), 7.37−7.47 (m, 6H), 7.17 (d, J = 8.4 Hz, 2H), 7.04 (d, J = 8.4 Hz, 2H), 5.28 (d, J = 9.8 Hz, 1H), 4.43−4.49 (m, 1H), 2.95 (dd, J = 14.5, 4.4 Hz, 1H), 2.64 (dd, J = 14.4, 11.2 Hz, 1H), 1.73 (s, 3H), 0.62 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 169.2, 137.8, 134.9 (2C), 134.7 (2C), 134.1, 133.9, 131.9, 130.1 (2C), 129.8, 129.7, 128.2 (2C), 128.1 (4C), 39.3, 36.8, 23.0, 5.4. HRMS: $C_{23}H_{24}ClNOSi$ [M + Na^+] calcd 416.1213, found 416.1217.

*N-(2-(4-Fluorophenyl)-1-(methyldiphenylsilyl)ethyl)acetamide (**84**).* The product was obtained using general procedure F yielding **84** (68.7 mg, 61%) as an amorphous solid. ^{1}H NMR (400 MHz,

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CD_3CN): δ (ppm) 7.62−7.65 (m, 2H), 7.57−7.60 (m, 2H), 7.34−7.46 (m, 6H), 7.10−7.15 (m, 2H), 6.91−6.97 (m, 2H), 6.28 (d, J = 9.8 Hz, 1H), 4.33 (ddd, J = 15.5, 10.0, 3.4 Hz, 1H), 2.84 (dd, J = 14.3, 3.4 Hz, 1H), 2.61 (dd, J = 14.2, 12.1 Hz, 1H), 1.60 (s, 3H), 0.65 (s, 3H). ^{13}C NMR (100 MHz, CD_3CN): δ (ppm) 169.7, 162.3 (d, J = 239.7 Hz), 137.4 (d, J = 3.2 Hz), 136.2, 136.1, 135.8 (2C), 135.7 (2C), 131.5 (d, J = 7.9 Hz, 2C), 130.6, 130.5, 129.0 (2C), 128.8 (2C), 115.5 (d, J = 21.1, 2C), 40.7, 36.9, 22.8, 6.0. HRMS: $C_{23}H_{24}FNOSi$ [M + H^+] calcd 378.1690, found 378.1693.

*tert-Butyl 2-(Methyldiphenylsilyl)pyrrolidine-1-carboxylate (**85**).*[15a] The product was obtained using general procedure F yielding **85** (63.8 mg, 58%) as a viscous oil.

*tert-Butyl ((2S)-1-((1-(Methyldiphenylsilyl)propyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate (**90**).* The product was obtained using general procedure F yielding **90** (136 mg, 90%) as a viscous oil. Compound A: ^1H NMR (400 MHz, CD_3CN): inter alia, δ (ppm) 6.37 (d, J = 9.9 Hz, 1H), 5.51 (d, J = 7.9 Hz, 1H), 2.98 (dd, J = 14.0, 5.4 Hz, 1H), 2.79 (dd, J = 14.1, 4.8 Hz, 1H), 0.86 (t, J = 7.2 Hz, 3H), 0.60 (s, 3H). ^{13}C NMR (100 MHz, CD_3CN): δ (ppm) inter alia, 172.4, 156.4, 57.1, 25.3, −5.7. Compound B: ^1H NMR (400 MHz, CD_3CN): δ (ppm) inter alia, 6.31 (d, J = 9.6 Hz, 1H), 5.44 (d, J = 7.4 Hz, 1H), 2.59−2.71 (m, 2H), 0.77 (t, J = 7.1 Hz, 3H), 0.61 (s, 3H), ^{13}C NMR (100 MHz, CD_3CN): δ (ppm) inter alia, 172.1, 156.2, 56.9, 25.1, −5.9. Since it contained a mixture of epimers, the last 25 carbons and 28 hydrogens were not assigned. HRMS: $C_{30}H_{38}N_2O_3Si$ [M + Na^+] calcd 525.2549, found 525.2552.

*N-(1-((3-(Benzyloxy)propyl)diphenylsilyl)propyl)acetamide (**91**).* The product was obtained using general procedure F yielding **91** (110 mg, 85%) as a viscous oil. ^1H NMR (400 MHz, CD_3CN): δ (ppm) 7.52−7.57 (m, 4H), 7.25−7.45 (m, 11H), 5.96 (d, J = 10.1 Hz, 1H), 4.41 (s, 2H), 4.08 (ddd, J = 13.4, 10.2, 3.3 Hz, 1H), 3.40 (t, J = 6.5 Hz, 2H), 1.79 (s, 3H), 1.51−1.67 (m, 3H), 1.26−1.37 (m, 1H), 1.3−1.6 (m, 2H), 0.84 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, CD_3CN): δ (ppm) 170.3, 140.1, 136.4 (2C), 136.2 (2C), 135.1, 134.8, 130.6, 130.5, 129.2 (2C), 128.9 (4C), 128.5 (2C), 128.3, 73.5, 73.0, 39.9, 25.4, 24.8, 23.0, 12.5, 8.1. HRMS: $C_{27}H_{33}NO_2Si$ [M + Na^+] calcd 454.2179, found 454.2174.

*N-(1-((3-(Benzyloxy)propyl)diphenylsilyl)-2-phenylethyl)acetamide (**92**).* The product was obtained using general procedure F yielding **92** (55.9 mg, 38%) as a viscous oil. ^1H NMR (400 MHz, CD_3CN): δ (ppm) 7.59−7.64 (m, 4H), 7.12−7.45 (m, 16H), 6.11 (d, J = 10.0 Hz, 1H), 4.39−4.45 (m, 3H), 3.41 (t, J = 6.5 Hz, 2H), 2.90 (dd, J = 14.2, 3.1 Hz, 1H), 2.52 (dd, J = 14.2, 12.4 Hz, 1H), 1.55−1.63 (m, 5H), 1.21 (t, J = 8.7 Hz, 2H). ^{13}C NMR (100 MHz, CD_3CN): δ (ppm) 169.6, 141.4, 140.1, 136.5 (2C), 136.3 (2C), 134.8, 134.4, 130.7 (2C), 129.8 (2C), 129.2 (2C), 129.0 (6C), 128.5 (2C), 128.3, 126.9, 73.5, 73.1, 40.2, 38.0, 24.8, 22.8, 8.2. HRMS: $C_{32}H_{35}NO_2Si$ [M + Na^+] calcd 516.2335, found 516.2340.

*N-(1-((3-(Benzyloxy)propyl)diphenylsilyl)-2-(4-fluorophenyl)ethyl)acetamide (**93**).* The product was obtained using general procedure F yielding **93** (106 mg, 69%) as an amorphous solid. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.54−7.58 (m, 4H), 7.37−7.43 (m, 6H), 7.23−7.29 (m, 5H), 7.03−7.09 (m, 2H), 6.86−6.90 (m, 2H), 5.21 (d, J = 10.2 Hz, 1H), 4.53−4.60 (m, 1H), 4.42 (s, 2H), 3.40 (t, J = 6.4 Hz, 2H), 2.95 (dd, J = 14.5, 4.2 Hz, 1H), 2.52 (dd, J = 14.5, 11.3 Hz, 1H), 1.71, (s, 3H), 1.59−1.66 (m, 2H), 1.15−1.19 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 169.1, 161.4 (d, J = 242.3 Hz), 138.4 (2C), 135.4 (2C), 135.2 (2C), 134.8 (d, J = 3.1 Hz), 132.8, 132.5, 130.1 (d, J = 7.8 Hz, 2C), 129.8, 128.3 (2C), 128.1 (4C), 127.6 (2C), 127.4, 114.8 (d, J = 21.0 Hz, 2C), 72.6 (2C), 38.2, 36.8, 23.6, 23.0, 7.7. HRMS: $C_{32}H_{34}FNO_2Si$ [M + H^+] calcd 512.2377, found 512.2378.

*N-(1-((3-(Benzyloxy)propyl)diphenylsilyl)-2-(4-chlorophenyl)ethyl)acetamide (**94**).* The product was obtained using general procedure F yielding **94** (44.8 mg, 28%) as a viscous oil. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.54−7.58 (4H), 7.27−7.47 (11H), 7.17 (d, J = 8.3 Hz, 2H), 7.03 (d, J = 8.3 Hz, 2H), 5.16 (d, J = 10.1 Hz, 1H), 4.55−4.61 (m, 1H), 4.43 (s, 2H), 3.40 (t, J = 6.4 Hz, 2H), 2.96 (dd, J = 14.5, 4.3 Hz, 1H), 2.53 (dd, J = 14.5, 11.3, 1H), 1.72 (s, 3H), 1.59−1.68 (m, 2H), 1.18 (t, J = 3.8 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 169.0, 138.4, 137.6, 135.4 (2C), 135.3 (2C), 132.8, 132.4, 132.0, 130.1 (2C), 129.9 (2C), 129.2 (2C), 128.3 (2C), 128.2 (2C), 128.1 (2C), 127.6 (2C), 127.5, 72.7, 72.6, 37.9, 37.0, 23.6, 23.1, 7.7. HRMS: $C_{32}H_{34}ClNO_2Si$ [M + Na^+] calcd 550.1945, found 550.1955.

*tert-Butyl ((2S)-1-((1-((3-(Benzyloxy)propyl)diphenylsilyl)propyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate (**95**).* The product was obtained using general procedure F yielding **95** (143 mg, 75%) as a viscous oil. Compound A: ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) inter alia, 5.47 (d, J = 9.9 Hz, 1H), 5.03 (bs, 1H), 0.75 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) inter alia, 170.9, 155.2, 136.8 (2C), 132.8, 132.7, 24.6, 23.5, 7.6. Compound B: ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) inter alia, 5.54 (d, J = 7.0 Hz, 1H), 4.82 (bs, 1H), 0.83 (t, J = 7.2 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) inter alia, 170.5, 154.9, 136.6 (2C), 132.5, 132.4, 24.5, 23.5, 7.4. Since it was a mixture of epimers, the last 30 carbons and 44 hydrogens were not assigned. HRMS: $C_{39}H_{48}N_2O_4Si$ [M + Na^+] calcd 659.3281, found 659.3276.

Sequential Hydrosilylation (58 and 91−95). *General Procedure G.* $Rh(cod)_2BF_4$ (0.003 mmol) and $P(OPh)_3$ (0.006 mmol) were dissolved in DCE (0.15 mL), and the mixture was stirred for 5 min. ((Allyloxy)methyl)benzene (0.30 mmol) and Ph_2SiH_2 (0.30 mmol) were added in that respective order and stirred for 15 min in the glovebox. Enamide (0.30 mmol) in DCE (0.10 mL) was added, placed in a preheated oil bath at 65 °C, and stirred for 18 h. The reaction was cooled to room temperature and concentrated. The crude mixture was purified via flash chromatography.

General Procedure H. $Rh(cod)_2BF_4$ (0.003 mmol) and $P(OPh)_3$ (0.006 mmol) were dissolved in DCE (0.15 mL), and the mixture was stirred for 5 min. ((Allyloxy)methyl)benzene (0.36 mmol) and Ph_2SiH_2 (0.36 mmol) were added in that order and the mixture stirred for 15 min in the glovebox. Enamide (0.30 mmol) in DCE (0.10 mL) was added, placed in a preheated oil bath at 65 °C, and stirred for 18 h. The reaction was cooled to room temperature and concentrated. The crude mixture was purified via flash chromatography.

*N-(1-(Diphenyl(3-((tetrahydro-2H-pyran-2-yl)oxy)propyl)silyl)ethyl)acetamide (**59**).* The product was obtained using general procedure G yielding **59** (53.0 mg, 43%). When general procedure H was used, silylated product **59** was achieved in 79.1 mg, 64% isolated yield. Characterization is reported above.

*N-(1-((3-(Benzyloxy)propyl)diphenylsilyl)propyl)acetamide (**91**).* The product was obtained using general procedure G yielding **59** (95.8 mg, 74%). Characterization is reported above.

*tert-Butyl ((2S)-1-((1-((3-(Benzyloxy)propyl)diphenylsilyl)propyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate (**95**).* The product was obtained using general procedure G yielding **94** (133.9 mg, 70%). When using general procedure H, silylated product **94** was achieved in 134.1 mg, 70% isolated yield. Characterization is reported above.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^1H and ^{13}C NMR of enamides and hydrosilylated products. This material is available free of charge via the Internet at http://pubs.acs.org.

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