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Ethylene Transposition: Ruthenium Hydride Catalyzed Intramolecular *trans*-Silylvinylation of Internal Alkynes

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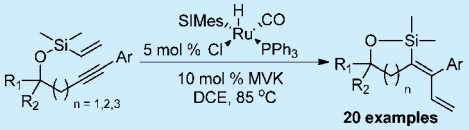
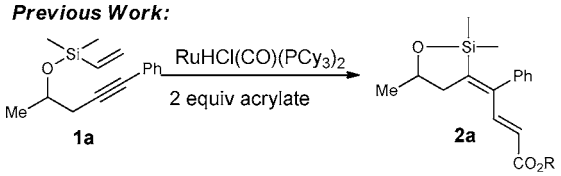
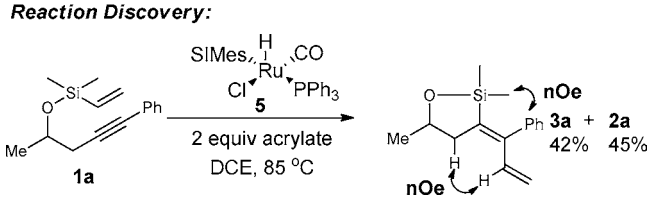
Supporting Information

ABSTRACT: A highly selective intramolecular *trans*-silylvinylation of internal alkynes catalyzed by RuHCl(CO)(SIMes)(PPh_3) has been accomplished. The use of methyl vinyl ketone as an additive increased the efficiency of this transformation. This process was used to successfully form five-, six-, and seven-membered oxasilacycles by a formal anti-exo-dig cyclization.



Silicon tethers are widely applicable in organic synthesis, having found uses in a variety of reactions including metathesis, cross-coupling, carbocyclization, and hydro- and carbosilylation. Their use to create highly functionalized systems in a regio- and stereodefined manner has spurred renewed interest of late.[1] In addition to being highly selective, these reactions create complex silanes which offer a versatile functional handle for further manipulation.[2] The majority of work in this area has focused on hydrosilylation chemistry.[3−7] Recently, a number of ruthenium catalyzed protocols have emerged for the synthesis of trisubstituted olefins using an intramolecular hydrosilylation of alkynes.[8−15] These complementary routes to trisubstituted vinylsilanes are inherently limited due to the mandatory inclusion of a hydrogen atom into the product alkene. Subsequent studies on silylcarbonylation and silylcyanation[16] of alkynes have been described to circumvent this limitation.[17−20] Specifically, Ojima and Denmark have studied the silylformylation of alkynes and found that five- and six-membered rings could be formed readily in this reaction.[21−25] Silylformylation and silylcyanation reactions afford the *syn*-alkene isomers selectively. Intermolecular versions of silylcarbocyclization reactions also afford the *syn*-isomers.[26−28] We have recently reported that vinyl-silicon tethers can be used to control both the regio- and stereochemistry in the silylvinylation of pendent alkynes with acrylates.[29] The subsequent vinyl ruthenium species intercept





acrylates to give highly substituted dienes. Unlike the aforementioned reactions, this process affords the *trans*-isomer selectively, a rare example of an intramolecular *trans*-substitution across an alkyne.[15,30,31]

While examining catalysts for this transformation, we discovered that ruthenium hydride complex **5** gave a nearly 1:1 mixture of acrylate product **2a** and vinylation product **3a**. A careful examination of the product indicated, as previously observed with the acrylate products, that the *anti*-5-exo-dig isomer was obtained. Given the novelty of this transformation, we set out to find an optimized protocol for the synthesis of vinylated product **3a**. Simply adding alkyne **1a** in DCE and hydride **5** to a sealed tube and heating to 85 °C overnight gave a 70% conversion of the starting material. Under these conditions, we observed a mixture of the expected vinylated product **3a** and diene **4a** (Table 1). Cycloisomerization of substituted enyne compounds with ruthenium hydrides has been reported previously.[32] These compounds were separated by column chromatography, and NOE experiments confirmed the assigned stereochemistry shown.[33]

Specifically, irradiation of the internal vinyl proton (at C2) displayed an enhancement of both diastereotopic allylic protons (at C5) in the oxasilylcyclopentane ring. Also, NOESY data displayed cross-peaks for the silylmethyl groups and protons on the aromatic ring.

Our previous results indicated full consumption of **1a** in only 9 h; thus, we theorized that the acrylate may play a beneficial role in the reaction.[29] Therefore, we screened electron-deficient olefins as additives in this reaction. As shown in Table 1, methyl methacrylate and acrylonitrile were beneficial to the reaction affording 50% and 55% conversion of the starting material, respectively (entries 2−3). No reaction was observed with phenylvinylsulfone as an additive (entry 4). Pleasingly, vinylphosphonates and acrylamides afforded a good conversion and high yield by ^{1}H NMR (entries 5−7). Moreover, acyclic vinylketones afforded a full conversion and high yield of the product with an excellent ratio of **3A** to **4A** (entry 8). The use

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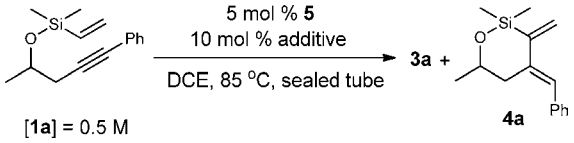
Table 1. Screen of Additives



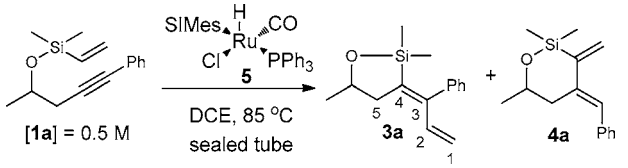
entry	additive	crude yield[a] (%)	ratio[b] (3a:4a)
1	-	70	53:17
2	CO_2Me, Me	50	30:16
3	CN	55	45:10
4	SO_2Ph	trace	-
5	$PO(OEt)_2$	77	53:14
6	$CONMe_2$	76	52:14
7	CONH*t*-Bu	100	81:14
8	COMe	***100***	***85:15***
9	O	80	60:20
10[c]	$C_2H_{4(g)}$ 1 atm	100	85:5

[a]Yield based on remaining **1a** by ^{1}H NMR versus mesitylene internal standard. [b]Ratio of **3a** and **4a** was determined by ^{1}H NMR versus mesitylene internal standard. [c]**3a** was obtained as a mixture of isomers (10:1, *Z*/*E*) as observed by ^{1}H NMR.

of cyclohexanone as an additive suggests that η-4-coordination of the additive may not be a requirement (entry 9). We also examined using ethylene (entry 10); however, a mixture of inseparable stereoisomers of **3a** were obtained. Methyl vinyl ketone (MVK) was chosen as our additive, as it provided the highest ratio of **3a** to **4a**, and its volatility facilitated removal of the additive from the reaction mixture.

Examination of other ruthenium hydride complexes revealed that complex **5** was particularly well suited for this reaction.[34] Attempts to generate complex 5 *in situ* from commercially available $RuHCl(CO)(PPh_3)_3$ and SIMes·HCl completely failed. No conversion of **1a** was observed after 24 h indicating that **5** may not have formed under the reaction conditions. To further optimize this reaction, the catalyst loading was scrutinized; in particular, the amount of **5** in relation to MVK was analyzed (Table 2). As previously mentioned, exclusion of MVK from the reaction gave only a 70% conversion after 24 h.

Table 2. Optimization for Silylvinylation Product 3a



entry	hydride **5** (mol %)	MVK (mol %)	time (h)	conversion (%)	ratio (3a:4a)
1	5	none	24	70	53:17
2	5	5	5	83	55:09
3	5	10	5	100	85:15
4	5	20	5	98	68:11
5	2.5	5	24	46	22:10
6	2.5	25	24	100	88:12
7	1	2	48	27	6:13
8	1	25	48	91	76:8

In a 1:1 ratio of MVK to catalyst **5**, an 83% conversion was attained in only 5 h. Addition of 10 mol % MVK provided the best results for both the yield and ratio of **3a:4a**. Additional MVK showed no further beneficial effect at a 5 mol % loading of complex **5**. Interestingly, it was found that the loading of complex **5** could be lowered provided the concentration of MVK was kept high. This of course came at the expense of the reaction time. Our current hypothesis is that the MVK protects the ruthenium catalyst from decomposition.[32,35]

Next, we examined the substrate scope of this reaction (Figure 1). Use of 5 mol % catalyst **5** and 10 mol % MVK was implemented in an attempt to keep the reaction time less than 24 h. Alkynes bearing a phenyl group at the terminus were examined first. Dienes **3a**−**3f** were produced from the corresponding phenyl alkynes. These substrates performed admirably, providing reaction products in good yields with **3** to **4** ratios consistently between 5:1 and 10:1 for compounds **3a**−**3f** (ratios in parentheses). Both electron-rich functionality as in the case of the anisole substituted diene **3g** and electron-withdrawing acetyl and nitro groups on the aryl ring were well tolerated. Crystallization of compound **3j** allowed for unambiguous verification of its structure through X-ray diffraction. As anticipated from NOESY experiments, the structure of **3j** is as depicted in Figure 1. All other structures have been determined through NOESY experiments or by analogy. Compound **3h** which bears a fluorine moiety was prepared in 71% yield. Methyl groups were also tolerated at the 3 and 5 positions and provided diene **3k** in 73% yield. Bulky groups at the ortho position such as chlorine were well tolerated and afforded **3l** in 73% yield while the 1-naphthyl analogue **3m** was provided in 63% yield. These structures (**3l** and **3m**) appear as mixtures of atropisomers by proton NMR. Substrates **1p** and **1q** which possess both propargylic and homopropargylic functionality provided >15:1 ratios favoring products **3p** and **3q** in 64% and 65% yield, respectively. Six-membered silylcycles could also be formed efficiently regardless of Thorpe−Ingold factors.[36] Compounds **3r** and **3s** were obtained in 59% and 74% yields, respectively. Of note, seven-membered ring product **3t** was formed in 53% yield using this methodology. Ojima et al. have noted the formation of seven-membered rings using rhodium catalyzed silylformylation provides a mixture of products with only trace amounts of the desired product observable by ^{1}H NMR and GC-MS.[37,38] In this case, the corresponding eight-membered ring was not observed in the ^{1}H NMR of the crude reaction mixture.

In our previous investigations alkyl groups at the alkyne terminus provided *trans*-silylvinylated products.[29] Evaluation of alkyl bearing alkyne substrates in the ethylene transposition reaction was also undertaken. Alkyne **1u** was subjected to conditions previously utilized for ethylene transposition; to our surprise, this led to the formation of **4u** as the sole product in 82% yield (Table 3). Alkyne **1v**, which also possesses a *tert*-butyl substituent, afforded **4v** in 66% isolated yield. Concerned that this switch in reactivity was due to sterics arising from the bulky *tert*-butyl group, we investigated methyl substituted alkynes. Under analogous conditions we again observed only cycloisomerization product **4w** in 72% yield by ^{1}H NMR (66% isolated yield) and **4x** in 59% isolated yield. Given the similar steric impediment of the alkyne methyl versus the propargylic methylene in **1w** and **1x** we surmise that this change in reactivity cannot be caused solely by steric congestion. Cycloisomerization products from tethered enynes have been reported by Mori in the presence of ruthenium hydrides.[32,39]

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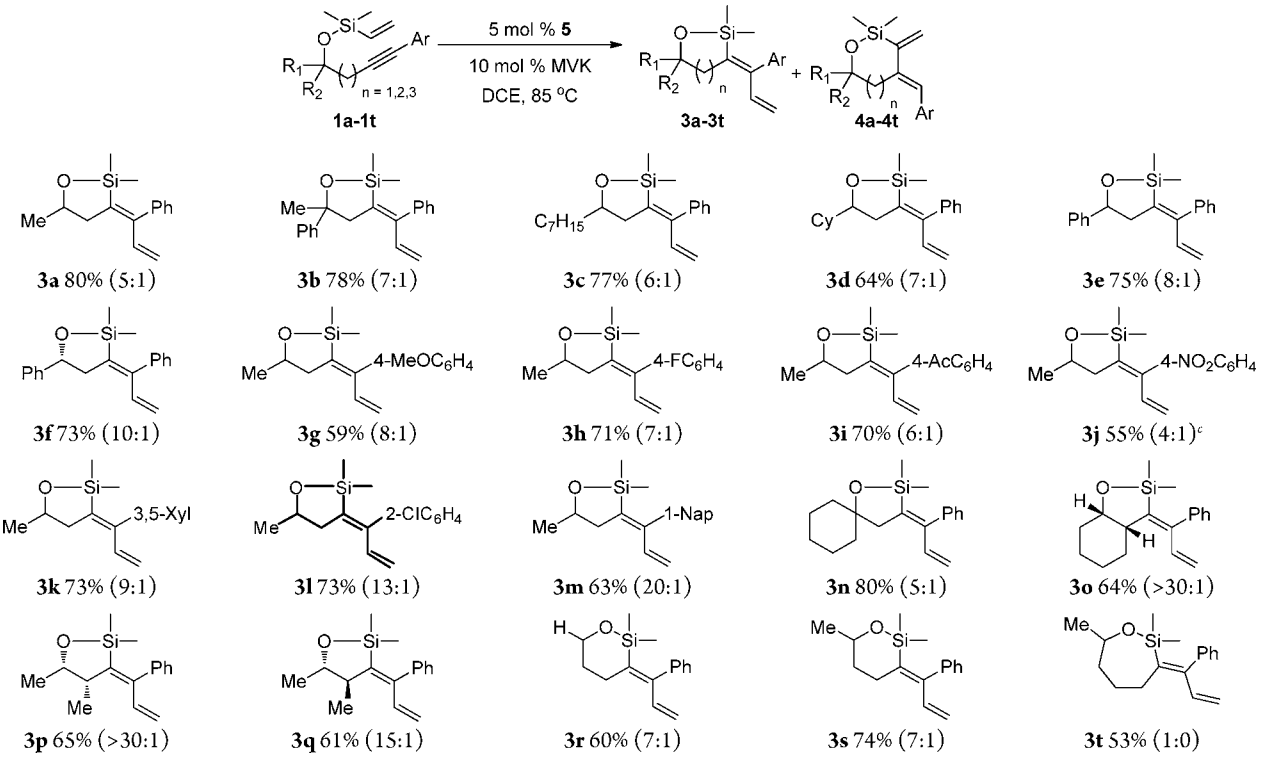
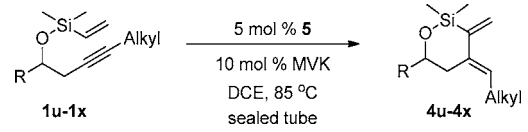
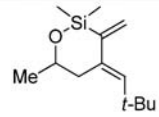
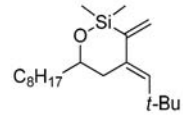
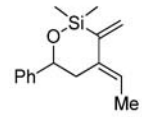
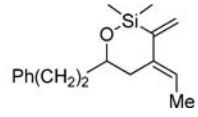


Figure 1. Scope of silylvinylation with aryl-substituted alkynes.[a,b] [a] Yields represent only isolated vinylation products **3**. [b] Ratios in parentheses represent the ratio of vinylation product **3** to cycloisomerization product **4** as determined by ^{1}H NMR of the crude reaction mixture. [c] Structure verified by X-ray crystallography.

Table 3. Diene Formation with Alkyl-Substituted Alkynes

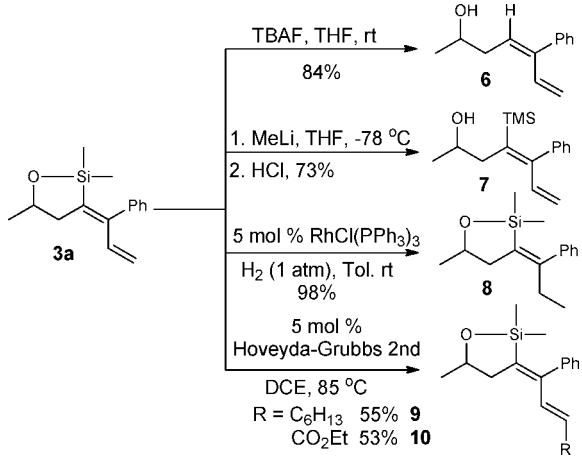


entry	product	compound	yield (%)
1		4u	82
2		4v	66
3		4w	66
4		4x	59

We are currently investigating the factors determining this switch in product formation, as well as related methods for the synthesis of dienes such as **3u−x** and **4a−t** using ruthenium catalysis.

Synthetic utility of the silylvinylation products was demonstrated using representative example **3a** (Scheme 1). Fluoride mediated removal of silicon afforded hydrovinylation product **6** in 84% yield. Addition of methyl lithium to **3a** provided alcohol **7** in 73% yield. Selective hydrogenation of the terminal olefin in diene **3a** provided tetrasubstituted olefin **8** in near quantitative yield. Finally, olefin metathesis of **3a** provided diene **9** in 55% yield using 1-octene, and diene **10** in 53% yield using ethyl acrylate as a cross partner. Both diene moieties were isolated as a single isomer by ^{1}H NMR. The silylvinylation and metathesis reaction can also be performed in tandem to afford similar overall yields.

Scheme 1. Derivatization of Diene 3a



In summary, we have demonstrated an effective protocol for a formal *anti*-exo-dig silylvinylation of internal alkynes. The reaction was amenable to various aryl alkynes and the diene products were further functionalized to afford tetra substituted olefins. Alkyl substituted alkynes afforded 1,3-dienes possibly through cycloisomerization. Further studies on mechanism,

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selective formation of product **3** with alkyl and product **4** with aryl substituted alkynes are ongoing.

■ ASSOCIATED CONTENT

Supporting Information

Experimental procedures and spectral data. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

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Author Contributions

‡S.L. and J.Z. contributed equally.

Notes

The authors declare no competing financial interest.
§Please send correspondence regarding X-ray crystal structure data to Dr. Nadia Marino (nmarino@syr.edu).

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