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Stereoselective Syntheses of Trisubstituted Olefins via Platinum Catalysis: α-Silylenones with Geometrical Complementarity

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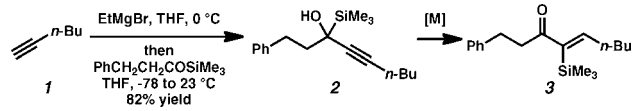
Abstract: The stereoselective syntheses of α-silylenones using catalytic $PtCl_2$ are reported. Via alkyne activation, α-hydroxypropargylsilanes are converted to (*Z*)-silylenones through a highly selective silicon migration. The complementary (*E*)-silylenones are accessed by a regioselective hydrosilylation of the ynone precursor. The synthetic utility of these compounds is demonstrated in cross-coupling reactions, highlighting the potential of these protocols for the syntheses of geometrically defined trisubstituted olefins.

The use of π-acidic metals, in particular complexes based on gold and platinum, to render an alkyne functional group electrophilic is a fundamental initiation step in a variety of chemical transformations.[1] In general, this activation step is paired with attached nucleophiles, such as alkenes, carbonyls, arenes, ethers, or strained carbocycles, to bring about isomerization-based transformations. We became curious as to whether the carbon−silicon bond, with its intrinsic electron-rich nature, could act as a nucleophile in a similar reactivity mode. Herein, we describe the realization of this hypothesis with the $PtCl_2$-catalyzed isomerization of α-hydroxypropargylsilanes to α-silylenone products (e.g., **2** → **3**, Table 1) with high levels of (*Z*)-selectivity. In addition, we illustrate the hydrosilylation of ynones, using the same $PtCl_2$ catalyst, to provide complementary geometrical selectivity. Lastly, we demonstrate the synthetic utility of these enone products, establishing a convenient method for the stereoselective synthesis of trisubstituted olefins.

In preliminary studies designed to ascertain the migratory aptitude of trialkylsilyl groups toward activated alkynes, we targeted α-hydroxypropargylsilanes such as **2** (Table 1)—it was expected that alkyne activation would initiate an interaction between the developing empty *p*-orbital and the proximal C−Si bond. These compounds are readily accessible via an alkynylide addition into an acylsilane, and a variety of α-hydroxypropargylsilanes were accessed by this protocol.[2] With substrates in hand, we began examining their reactivity in the presence of potential alkyne activators (Table 1). Although a number of these metal complexes exhibited little to no reactivity, rearrangements to enone products were observed when these silanes were treated with either gold or platinum salts. Gold species effected complete consumption of the propargylsilane (entries 6−8), but platinum-based isomerizations ultimately provided similar reactivities and higher yielding reactions (entries 9−11). Under optimized conditions (5 mol % $PtCl_2$, toluene, 80 °C), α-silylenone **3** was produced in virtually quantitative yield and with excellent stereoselectivity (ranging from 10:1 to >19:1 favoring the (*Z*)-isomer).[3]

Analogous metal-induced silyl migration has been observed previously in isolated cases. Schaumann reported examples of similar migrations using zinc chloride to provide (*E*)-silylenones; however, an acetylenic TMS group was required.[4,5] $ZnCl_2$ was ineffective in the isomerization of the compounds studied here (Table 1, entries 4, 5). One of the most pertinent comparisons is the ruthenium-catalyzed redox isomerization of propargylic alcohols to (*E*)-enones, originally reported by both Ma[6] and Trost.[7] The transformation described herein is akin to this reaction but provides additional functionality in the silicon group to allow for further manipulation.

Table 1. Reaction Optimization



entry	catalyst (5 mol %)	solvent, temp (°C)	time (h)	Conversion (%)[a]	isomer ratio (*Z*:*E*)[a]
1	$PdCl_2$	$PhCH_3$, 70	48	<5	−
2	$CpRu(CH_3CN)_3PF_6$	$PhCH_3$, 50	36	<5	−
3	$(Ph_3P)_3RuCl_2$	$PhCH_3$, 50	36	<5	−
4	$ZnCl_2$	CH_2Cl_2, 23	4	<5	−
5	$ZnCl_2$	$PhCH_3$, 50	4	<5	−
6	AuCl	$PhCH_3$, 50	5	100	1.7:1[b]
7	$AuCl_3$	$PhCH_3$, 50	5	100	1:1.7[b]
8	[Au]/[Ag][c]	$PhCH_3$, 40	1	100(76[d])	>19:1
9	$PtCl_2$	$PhCH_3$, 35	48	<5	−
10	$PtCl_2$	$PhCH_3$, 50	3.5	100	6:1
11	$PtCl_2$	$PhCH_3$, 80	1.5	100(99[d])	10:1

[a] Measured by ^1H NMR. [b] Significant quantities of protodesilylated enones were observed. [c] [Au]/[Ag]: Chloro[2-(di-*tert*-butylphosphino)-biphenyl]gold(I) (5 mol %) + $AgSbF_6$ (20 mol %). [d] Isolated yield.

With the platinum-catalyzed method fully optimized, a number of propargylsilanes were isomerized to the corresponding enones in uniformly high yields and selectivities, even with markedly low catalyst loadings (Table 2, entries 2, 4). More sterically hindered alkynes (entry 6) were isomerized cleanly, albeit with longer reaction times. Esters, carbamates, silyl ethers, acetals, and distal olefins were all tolerated in this transformation. The overall reaction times were particularly brief for substrates bearing propargylic ether substituents that were potentially capable of precoordination (entries 12, 13). This transformation likely proceeds via an initial alkyne coordination, followed by an *anti*-selective silyl migration to a vinylplatinum species (Scheme 1). Protodemetalation leads to the enone products with the observed stereochemistry.

Having selectively accessed a number of (*Z*)-silylenones via this protocol, our efforts next turned to olefin isomerization studies to

Scheme 1

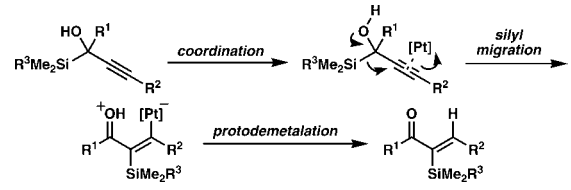


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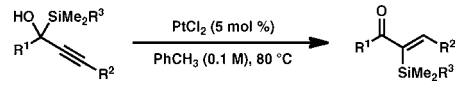
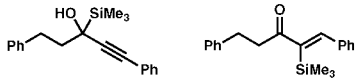
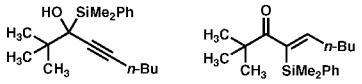
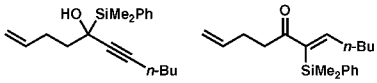
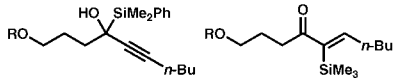
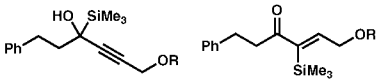
Table 2. Pt-Catalyzed Rearrangements of α-Hydroxypropargylsilanes



entry	substrate	product	time (h)	yield (%)[a]	$Z:E$[b]
1	R = CH_2CH_2Ph		1.5	99	10 : 1
2[c]	R = CH_2CH_2Ph		1.5	99	>19 : 1
3	R = *n*-Hept		1.5	98	>19 : 1
4[c]	R = *n*-Hept		1.5	99	>19 : 1
5			1.5	98	>19 : 1
6			20.5	87	>19 : 1
7			1.5	80	>19 : 1
					
8	R = TBS		1.5	93	10 : 1
9	R = Ac		1.5	93	11 : 1
10	R = CONHPh		1.5	93	>19 : 1
					
11	R = TBS		1.5	76	>19 : 1
12	R = PMB		0.2	83	>19 : 1
13[d]	R = THP		0.75	89	>19 : 1

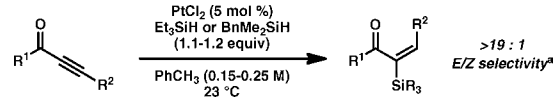
[a] Isolated yield. [b] Measured by ^{1}H NMR. [c] 1 mol % $PtCl_2$, 0.25 M in $PhCH_3$. [d] 2.5 mol % $PtCl_2$, 0.2 M in $PhCH_3$.

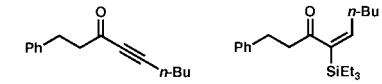
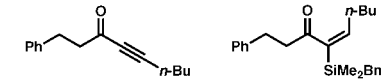
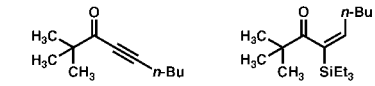
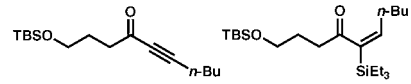
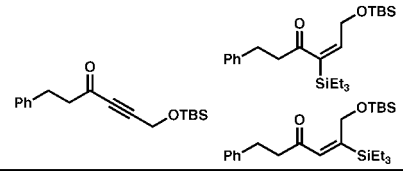
obtain the complementary (*E*)-silylenones. Attempts to achieve selectivity, however, were met with limited success under a variety of conditions.[8] Interestingly, we found that a hydrosilylation approach afforded these desired (*E*)-enone products.

Although metal-catalyzed hydrosilylation is a thoroughly studied transformation,[9] selectivities in the hydrosilylation of internal alkynes remain comparatively less explored.[10] By treatment with the same $PtCl_2$ catalyst and a silane in toluene at room temperature, a number of ynones were hydrosilylated in good yields and largely with excellent regio- and stereoselectivities (Table 3). The (*Z*)-stereoselectivity is consistent with the Chalk−Harrod mechanism frequently observed in Pt-catalyzed hydrosilylations;[11] the observed regioselectivity can be attributed to an electronic effect, wherein the metal center resides α to the carbonyl in the hydroplatinated intermediate.[12] Importantly, this transformation consistently provides the opposite geometrical isomers to those formed in the silyl migration process.[13]

With efficient protocols for accessing the above silylenone products, our efforts were then directed toward investigating the overall synthetic utility of these compounds.[14] The Hiyama coupling is an attractive method for the formation of sp^2−sp^2 carbon−carbon bonds,[15] particularly because the inherent stability of the vinylsilane nucleophiles allows them to be carried through multiple synthetic steps. In general, silanes with attached heteroatomic moieties (e.g., alkoxysilanes) are required for reactivity in these cross-couplings, but alkoxysilanes are typically more unstable than their alkylsilane counterparts. Motivated by these circumstances, there have been

Table 3. Pt-Catalyzed Hydrosilylations of Ynones



entry	substrate	product	time (h)	yield (%)[b]	α : β[a]
1			1.5	98	>19 : 1
2			1.5	99	>19 : 1
3			9	65	>19 : 1
4			2	92	>19 : 1
5			2	87[c]	2 : 1

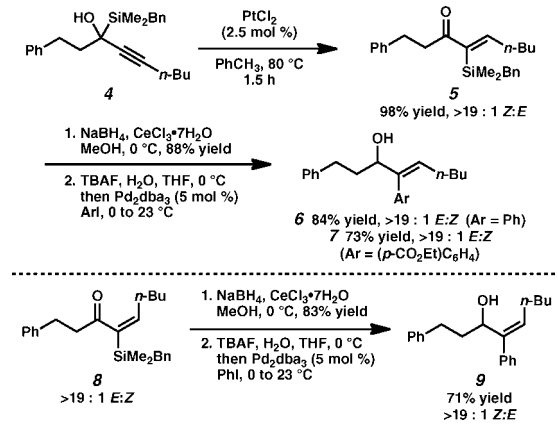
[a] Measured by ^{1}H NMR. [b] Isolated yield. [c] Isolated as a mixture of α and β isomers.

several investigations into alkylsilanes that are capable of generating a Si−X intermediate in situ.[16]

In our studies, the benzyldimethylsilyl group appeared ideal for the downstream generation of Hiyama coupling partners,[16e] its robust nature likely to be compatible with formation of the acylsilane precursor, the nucleophilic alkyne addition, and the platinum-catalyzed isomerization. Indeed, α-silylenone **5** could be formed from readily accessible alcohol **4**, with the silyl migration proceeding in excellent yield and stereoselectivity (Scheme 2). Enone **5** was reduced, and the corresponding alcohol was evaluated in representative Hiyama couplings.[17] Gratifyingly, these reactions provided the aryl alkenyl coupling products in good yield.[18] (*E*)-Silylenone **8** was also converted to the corresponding coupling product, highlighting that these two complementary platinum-catalyzed methods can be utilized in the syntheses of stereodefined trisubstituted alkenes.[19]

To summarize, we have described a platinum-catalyzed isomerization of α-hydroxypropargylsilanes. The transformation proceeds

Scheme 2



in good to excellent yield with a high degree of geometrical selectivity for a range of substrates. The substrates are readily accessible via alkyne-based nucleophilic additions into acylsilanes, this method representing a straightforward option for convergent fragment coupling. The $PtCl_2$-catalyzed hydrosilylations of the corresponding ynones, also accessible via alkyne-based nucleophilic additions, provide complementary geometry in these enone products.[20] Finally, we have demonstrated the synthetic utility of the observed silylenones, validating that the vinylsilane provides a functionality for further manipulations. The formation of geometrically pure trisubstituted olefins remains a challenge in synthetic chemistry; the methods herein provide operationally simple protocols for accessing these structural motifs. Further explorations of these unique transformations and applications will be reported in due course.

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Supporting Information Available: Experimental procedures, compound characterization data, and spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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(2) See Supporting Information for details.

(3) The isomeric ratio was higher at elevated temperatures. This observation is consistent with the initial silyl migration having a high activation energy relative to a background olefin isomerization process mediated by $PtCl_2$. Olefin isomerization occurred to some extent when the enone products were resubjected to the reaction conditions.

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(7) (a) Trost, B. M.; Livingston, R. C. *J. Am. Chem. Soc.* **1995**, *117*, 9586–9587. (b) Trost, B. M.; Livingston, R. C. *J. Am. Chem. Soc.* **2008**, *130*, 11970–11978.

(8) In general, isomerization to thermodynamic equilibrium led to an approximately 2:1 mixture of *E* and *Z* enone isomers.

(9) Hiyama, T.; Kusumoto, T. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 8, Chapter 3.12.

(10) For a recent discussion, see: Trost, B. M.; Ball, Z. T. *Synthesis* **2005**, 853–887.

(11) Chalk, A. J.; Harrod, J. F. *J. Am. Chem. Soc.* **1965**, *87*, 16–21.

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(13) Although geometrical considerations are not applicable, it should be noted that substrates based on terminal alkynes were effective in the silyl migration process but provided complex mixtures in the hydrosilylation process. See Supporting Information for details.

(14) For a review of the use of α-substituted enones in cross-coupling reactions, see: Negishi, E.-i. *J. Organomet. Chem.* **1999**, *576*, 179–194.

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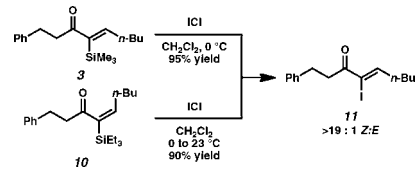
(17) The silylenone products were not effective Hiyama coupling partners, likely due to the complicating electrophilicity of the enone under the fluoride-based conditions.

(18) Water additive was crucial to the success of these transformations, most likely facilitating the formation of a disiloxane intermediate which upon fluoride activation is the active transmetallation species. For a relevant discussion, see: Denmark, S. E.; Sweis, R. F.; Wehrli, D. *J. Am. Chem. Soc.* **2004**, *126*, 4865–4875.

(19) α-Silylenones can also be converted to α-iodoenones by treatment with ICl; see: Alimardanov, A.; Negishi, E.-i. *Tetrahedron Lett.* **1999**, *40*, 3839–3842. (b) This process is generally stereoconvergent, however, as illustrated in the transformations of both **3** and **10** to **11**. In contrast, the use of Hiyama couplings enables efficient access to both isomers of the trisubstituted alkenes.



(20) For a related example of accessing alkenes with geometrical complementarity via alkyne activation processes, see: Barluenga, J.; Riesgo, L.; Vicente, R.; López, L. A.; Tomás, M. *J. Am. Chem. Soc.* **2007**, *129*, 7772–7773.

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