First Exclusive *Endo-dig* Carbocyclization: $HfCl_4$-Catalyzed Intramolecular Allylsilylation of Alkynes

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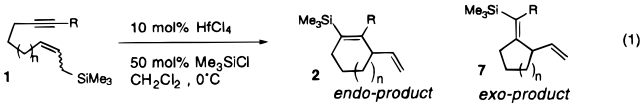
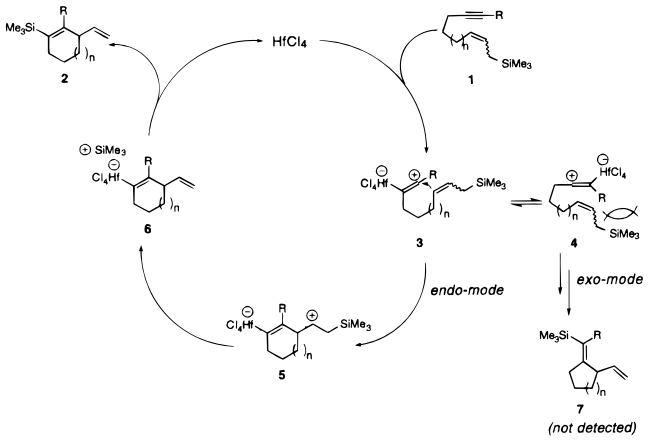
Carbocyclizations of alkenes and alkynes are extremely important and useful reactions for the synthesis of variety of a carbocyclic and heterocyclic compounds.[1] Since the early report in 1943 on the ene reaction by Alder,[2] and the first systematic studies by Lehmkuhl on metallo-ene[3] versions of this reaction, the chemistry of transition metal-catalyzed carbocyclizations became a vast field and a number of transition metal-mediated[4] and -catalyzed[5] carbocyclization methodologies were developed. Carbocyclization of alkynes is of particular interest since it allows one to obtain carbo- and heterocycles with higher degrees of unsaturation.[1,6] Apparently, the exclusive or predominant *exo*-fashion was a general regiochemical trend for the previous intramolecular carbocyclizations of alkynes.[1,7] It is clear that scope and synthetic utility of intramolecular carbocyclizations would be enhanced if methods permitting selective *endo*-cyclization could be found. As a partial solution of this problem, we wish to report $HfCl_4$-catalyzed intramolecular allylsilylation of unactivated alkynes, proceeding *exclusively in the endo-fashion* to give five-, six-, and seven-membered carbocycles **2** in moderate to high chemical yields with none of the *exo-cyclization* products **7** being produced (eq 1).



(1)

We have recently reported highly regioselective and effective Lewis acid-catalyzed intermolecular allylsilylation of unactivated alkynes.[8] Encouraged by the successful intermolecular allylsilylation of alkynes[8] and motivated by the importance of regioselective carbocyclization processes as mentioned above,[1,6,7] we attempted to apply the allylsilylation methodology to the preparation of practically important medium-sized cyclic vinylsilanes via an intramolecular mode of this reaction. Surprisingly, the initial experiments on the intramolecular allylsilylation of carbon tethered alkynyl allylsilane **1a** employing $HfCl_4$ (50 mol %) in CH_2Cl_2 (which proved to be the best catalyst system for the intermolecular allylsilylation of alkynes[8]) gave *exclusively the endo-cyclization product*—the six-membered vinylsilane **2a** in a moderate yield (35%). After considerable optimization work, it was found that even 10 mol % of $HfCl_4$ (5-fold decrease) in the combination with TMSCl (50 mol %) allowed for the preparation of **2a** in essentially better chemical yield (61%, Table 1). Accordingly, the $HfCl_4$/TMSCl catalyst system was applied for the cyclization of alkyl-, alkenyl-, and aryl-substituted carbon tethered alkynyl allylsilanes **1** (eq 1, Table 1).[9] The cyclization of alkyl-, alkenyl- and aryl-substituted alkynyl allylsilanes **1a**-**e**, bearing three methylene groups in the tether (entries 1−5), proceeded smoothly producing the six-membered carbocycles **2a**−**e** in good to nearly quantitative yields (entries 1−5). Analogously, the cyclization of **1f**−**h**, having a tether chain of four methylene groups (entries 6−8), selectively gave the seven-membered **2f**−**h** in 76, 84, and 65% isolated yields, respectively. In contrast to the above cases, the cyclization of **1i**,**j**, having a shorter carbon chain, afforded the five-membered cyclic vinylsilanes **2i**,**j** in rather low yields. Thus, the alkyl-substituted **2j** was obtained in 47% yield (entry 10), whereas **2i** was isolated in 22% only along with 20% of **1i** being recovered (entry 9). It should be pointed out that, regardless of the size of the ring obtained, the cyclization of alkyl-, alkenyl-, and aryl-substituted alkynyl allylsilanes **1a**−**j** proceeded exclusively in the *endo-fashion*, and no traces of *exo-cyclization* products **7** or any other regioisomers of **2a**−**e** were detected by ^1H NMR and capillary GC-MS analyses of crude reaction mixtures.

Scheme 1. Proposed Mechanism for the $HfCl_4$-Catalyzed *endo*-Carbocyclization of **1**



The following mechanistic rationale can explain the exclusive *endo-mode* carbocyclization of **1a**−**j** (Scheme 1). As we previously proposed for the Lewis acid-catalyzed hydro-[12] and allylstannation[13] and hydro-[14] and allylsilylation[8] of alkynes, coordination of $HfCl_4$ to the triple bond of **1** would form zwitterionic intermediate **3**.

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(4) For a review, see: (a) Oppolzer, W. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 38. See, also: (b) Courtois, G.; Masson, A.; Migniac, L. *C. R. Acad. Sci. Sér. C* **1987**, *286*, 265. (c) van der Louw, J.; Komen, C. M. D.; Knol, A.; de Kanter, F. J. J.; van der Baan, J. L.; Bickelhaupt, F.; Klumpp, G. W. *Tetrahedron Lett.* **1989**, *30*, 4453. (d) van der Louw, J.; van der Baan, J. L.; Komen, C. M. D.; Knol, A.; de Kanter, F. J. J.; Bickelhaupt, F.; Klumpp, G. W. *Tetrahedron* **1992**, *48*, 6105. (e) Oppolzer, W.; Schröder, F. *Tetrahedron Lett.* **1994**, *35*, 7939. (f) Takayama, Y.; Gao, Y.; Sato, F. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 851.

(5) See, for example: (a) Camps, F.; Coll, J.; Moretó, J. M.; Torras, J. *Tetrahedron Lett.* **1987**, *28*, 4745. (b) Oppolzer, W.; Keller, T. H.; Bedoya-Zurita, M.; Stone, C. *Tetrahedron Lett.* **1989**, *30*, 5883. (c) Oppolzer, W.; Robyr, C. *Tetrahedron* **1994**, *50*, 415. (d) See also refs 4a, e.

(6) For a review, see, for example: (a) Lautens, M.; Klute, W.; Tam, W. *Chem. Rev.* **1996**, *96*, 49. See, also: (b) Harada, T.; Otani, T.; Oku, A. *Tetrahedron Lett.* **1997**, *38*, 2855. (c) Huang, H.; Forsyth, C. J. *J. Org. Chem.* **1997**, *62*, 8595.

(7) For a review, see: Negishi, E.; Copéret, C.; Ma, S.; Liou, S.-Y., Liu, F. *Chem. Rev.* **1996**, *96*, 365.

(8) Asao, N.; Yoshikawa, E.; Yamamoto, Y. *J. Org. Chem.* **1996**, *61*, 4874. (b) Yoshikawa, E.; Gevorgyan. V.; Asao, N.; Yamamoto, Y. *J. Am. Chem. Soc.* **1997**, *119*, 6781.

(9) Other Lewis acids such as $ZrCl_4$ and $EtAlCl_2$ also catalyzed the mentioned carbocyclization, although with lower chemical yields.

(10) The preparation of **2a** is representative. A mixture of $HfCl_4$ (60 μmol, 10 mol %) and CH_2Cl_2 (1.2 mL) was stirred at room temperature for 10 min, then cooled to 0° C and followed by addition of TMSCl (300 μmol) and **1a** (600 μmol). After having been stirred for 50 min the reaction mixture was diluted with pentane (3 mL), quenched with Et_2NH (300 μL), filtered through Al_2O_3, and concentrated. The purification by column chromatography (silica gel, hexane eluent) gave 94 mg of **2a** (61%).

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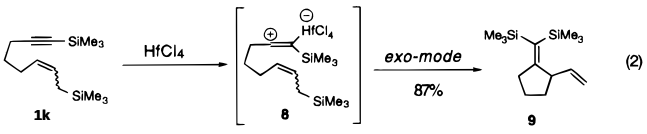
Table 1. $HfCl_4$-Catalyzed *endo*-Carbocyclization of Alkynyl-Allylsilanes **1**[10]

entry	substrate[a]	R	R^1	*n*	product	yield,[b] %
1	**1a**	Ph	H	1	**2a**	61
2	**1b**	*n*-Hex	H	1	**2b**	99
3	**1c**	*c*-hexenyl	H	1	**2c**	58
4	**1d**	*p*-tolyl	H	1	**2d**	63
5	**1e**	*n*-Hex	Me	1	**2e**	83[c]
6	**1f**	Ph	H	2	**2f**	76
7	**1g**	*n*-Hex	H	2	**2g**	84
8	**1h**	*p*-tolyl	H	2	**2h**	65
9	**1i**	Ph	H	0	**2i**	22[d]
10	**1j**	*n*-Hex	H	0	**2g**	47[e,f]

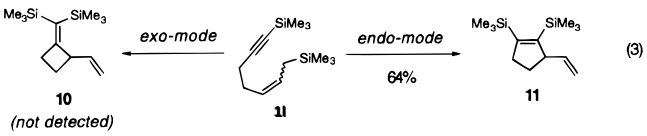
[a] A 4:1 mixture of *Z*- and *E*-isomers of **1** was used. [b] Isolated yield. [c] The *endo*-product **2e** was isolated in 83% yield along with small amount of unidentified isomeric material.[11] [d] Approximately 20% of **1i** was recovered. [e] NMR yield. [f] 30 mol % of $HfCl_4$ was used. The catalyst was added in three portions.

The carbocation of **3** would attack the double bond of internal allylsilane moiety at the γ-position affording an *endo-cyclization* product a carbenium cation **5**. The elimination of the silyl group from **5** would form ate-complex **6**, and the subsequent transmetalation of hafnium halide with silicon would produce **2** and regenerate the catalyst. Obviously, the key intermediate **3**, which is responsible for the apparent *endo-cyclization* mode, could be in the equilibrium with an isomeric **4**, which would produce an *exo-product* **7** via similar reaction pathway. The predominance of **3** over **4** could be well accounted by electronic and steric features of these vinyl cation intermediates. Indeed, in the case of the aryl- and alkenyl-substituted substrates **1a**,**c**,**d**,**f**,**h** (entries 1,3,4,6,8) the zwitterionic intermediate **3** would be favorable due to the higher stabilizing ability of the aryl and alkenyl group compared with that of the CH_2 group of the alkyl tether chain.[15] In contrast, the cation stabilizing abilities of the *n*-hexyl group and that of the alkyl tether chain in **1b**,**e**,**g** would be rather similar. Perhaps, in this case still the intermediate **3** would be more preferable over **4** due to the steric reasons; since a significant nonbonding interaction between an alkyl group and the allylsilane moiety in **4** would destabilize the intermediate **4**, and thus the formation of **7** would be unfavorable.[16]

To gain an additional support for the proposed cationic mechanism for the $HfCl_4$-catalyzed carbocyclization reaction we examined the cyclization of the trimethylsilyl-substituted substrates **1k**,**l**. Since it is well-known that the silyl group is enabled to stabilize a cation at the β-position,[17] we expected a reversal of reaction mode for these substrates, since not **3** but intermediate of type **4** or **8** would be more favorable due to the β-silicon-stabilization[17] (eq 2). Indeed, the experiment has completely satisfied the above expectations: the exclusive *exo-mode* cyclization of **1k** was observed producing five-membered **9** in 87% yield as a single product (eq 2). In contrast to **1k**, the alkynic allylsilane **1l** with shorter alkyl tether selectively underwent *endo-mode* cyclization affording **11** in 64% yield with none of the *exo*-product **10** being produced (eq 3). The force-field computations brought insight in these controversial results on cyclization modes of the silyl substituted substrates **1k** and **1l**. According to the MM3 calculations, the five-membered *endo*-product **11** is favored by 18.3 kcal/mol over the four-membered *exo*-product **10**. Accordingly, in this case not electronic but thermodynamic factors would dictate the mode of cyclization, leading to the much less strained carbocycle **11** (eq 3).



(2)



(3)

Although further investigation to settle a precise mechanism for the $HfCl_4$-catalyzed exclusive *endo-dig* carbocylization of alkynyl allylsilanes **1a**−**j**, **l** is needed, the present procedure provides a new regiospecific and synthetically useful route to medium-sized cyclic vinylsilanes.

Supporting Information Available: Spectroscopic and analytical data for compounds **1a**−**l**, **2a**−**j**, **9**, and **11** (30 pages, print/PDF). See any current masthead page for ordering information and Web access instructions.

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(11) According to GC-MS data the minor unidentified product (8%) had the same molecular weight as **2e** (278). Additionally, the low intensity multiplet was detected in the ^1H NMR spectra at 4.8 ppm. However, due to the trace amount of this product available, at this stage we are not able to assign exact structure of this isomeric compound.

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(15) For aryl-stabilyzed vinylic cations, see, for example: (a) Abram, T. S.; Watts, W. E. *J. Chem. Soc., Chem. Commun.* **1974**, 857. (b) Siehl, H.-U.; Carnahan, J. C.; Eckes, L.; Hanack, M. *Angew. Chem., Int. Ed. Engl.* **1974**, *13*, 675.

(16) As an alternative proposal, a large $HfCl_4$ group in **3** could function as a conformational bias in this acyclic system facilitating the *endo*-ring closure, whereas no such effect could be considered for **4**.

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