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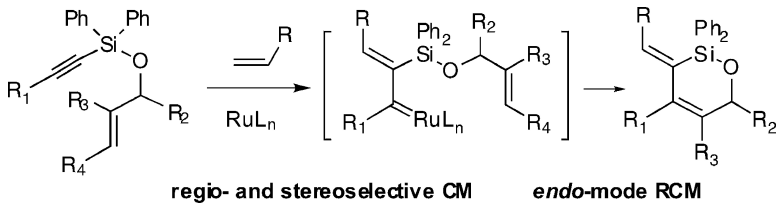

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Tandem Sequence of Cross Metathesis−Ring-Closing Metathesis Reaction of Alkynyl Silyloxy-Tethered Enynes

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Abstract: A tandem cross metathesis (CM)−ring-closing metathesis (RCM) sequence to form cyclic siloxanes is reported. This new enyne metathesis platform expands the scope and utility of the regio- and stereoselective cross metathesis reaction between silylated alkynes and terminal alkenes. The initial cross metathesis was directed to occur on the alkyne by employing sterically hindered mono-, di-, and trisubstituted alkenes tethered to the alkyne via silyl ether. The regio- and stereoselectivity feature of the initial CM step in this tandem CM−RCM process is identical to that of the CM reactions of silylated alkynes and alkenes. This tandem sequence provides both synthetically useful silylated 1,3-diene building blocks and insights into the reaction mechanism of the enyne metathesis reaction.

Introduction

Enyne metathesis,[1] a subclass of olefin metathesis,[2,3] is a powerful carbon−carbon bond-forming process to generate 1,3-dienes from the reaction of alkenes and alkynes. Despite the versatility of this reaction, the ring-closing metathesis (RCM) of enynes has been limited to form small-sized rings while most cross metathesis (CM)[4] reactions of enynes have been performed with terminal alkynes and alkenes to generate 1,3-disubstituted 1,3-dienes. One of the major encumbrances of the enyne CM with internal alkynes and alkenes has been the lack of control in regioselectivity and stereoselectivity. For reactions of terminal alkynes, the regiochemistry can be controlled, but the stereoselectivity problem has yet to be addressed to avoid the formation of an inseparable mixture of *E*/*Z* isomers (eq 1). To address these selectivity problems associated with enyne CM, we developed a silyloxy temporary tether-based RCM approach (eq 2).[5] The basis for the choice of silyloxy tether[6−8] is not only its easy formation and removal but also its well-known steric and stereoelectronic biasing effect in a variety of synthetic transformations.[9]

We recently reported the tartrate-based enyne RCM[10] reaction catalyzed by ruthenium complex **1**,[11] which showed a characteristic transition from exo-mode to endo-mode ring closure going from the formation of small-membered rings to that of larger rings. In sharp contrast, the CM of enyne **2** possessing a silyloxy tether provided exclusively the exo-mode ring-closure product **3** possessing *Z*-stereochemistry of the endocyclic double

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(6) For reviews of silicon tethers, see: (a) Bols, M.; Skrydstrup, T. *Chem. Rev.* **1995**, *95*, 1253−1277. (b) Fensterbank, L.; Malacria, M.; Sieburth, S. McN. *Synthesis* **1997**, 813−854. (c) Gauthier, D. R., Jr.; Zandi, K. S.; Shea, K. J. *Tetrahedron* **1998**, *54*, 2289−2338.

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(9) (a) Antras, F.; Ahmar, M.; Cazes, B. *Tetrahedron Lett.* **2001**, *42*, 8157−8160. (b) Trost, B. M.; Machacek, M.; Schnaderbeck, M. J. *Org. Lett.* **2000**, *2*, 1761−1764. (c) Wender, P. A.; Deschamps, N. M.; Williams, T. J. *Angew. Chem., Int. Ed.* **2004**, *43*, 3076−3079.

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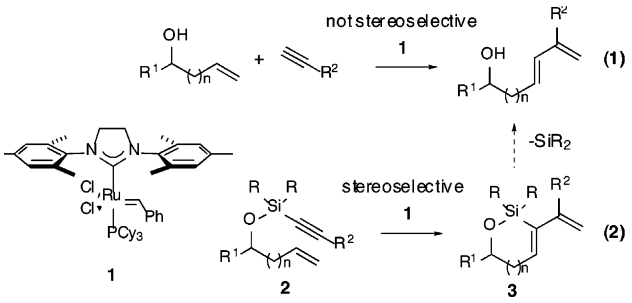
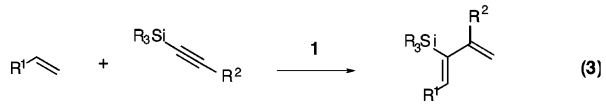
(11) Scholl, M.; Ding, S.; Lee, C. W.; Grubbs, R. H. *Org. Lett.* **1999**, *1*, 953−956.

10.1021/ja0520159 CCC: $30.25



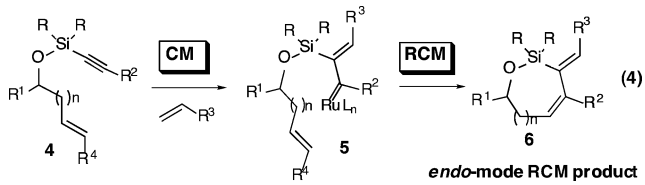
bond[5] regardless of the tether size ($n = 0-8$). We believed that the observed exo-mode selectivity (regioselectivity in CM reaction) is the consequence of the sterically hindered nature of the silyl group attached to the alkyne,[12] which plays a dominant role in directing the formation of the metathesis intermediate.[5] In terms of stereoselectivity, the exclusive *Z*-stereochemistry differs from that of the macrocyclic enyne RCM reactions with the tartrate tether, which normally generates mixtures of *E*- and *Z*-stereoisomers.

We surmised that the observed exo-mode selectivity in the RCM reaction depicted in eq 2 could be extrapolated to the CM reaction between silylated alkynes and alkenes (eq 3).[13] If the bulky silyl substituent has a profound directing effect in the regio- and stereoselectivity-determining steps for both the RCM and CM reactions, an identical regio- and stereochemical outcome would be obtained in both processes.



Notwithstanding the resolution of the regioselectivity and stereoselectivity problems in enyne metathesis by employing silylated alkynes, another outstanding issue to be addressed is the initiation of the process. Depending on whether the metathesis starts from an alkene (*alkene initiation*) or an alkyne (*alkyne initiation*), different propagating species would carry the catalytic cycle.[14] This, in turn, would be contingent upon the relative reactivity of alkene and alkyne substrates. To expand the scope of the enyne metathesis reaction as a general synthetic tool as well as to obtain further insight into the reaction mechanism, the initiation event should be clearly understood.

At this juncture, we envisioned that the combination of the reactivity and selectivity features of CM in eq 1 and the RCM in eq 2 could be juxtaposed in a CM–RCM sequence[15] to establish a new tandem metathesis process (eq 4). Assuming that the reactivity of the double bond of enyne **4** is lower than that of the triple bond due to the presence of the R group, the initial CM reaction between a propagating species derived from the external alkene and the triple bond would generate a new alkylidene **5**. If the rate of ring closure of **5** is faster than that of intermolecular methylene transfer, cyclic siloxane **6** would be formed, which is a formal endo-mode RCM product, the connectivity of which is unachievable via direct RCM reaction of **4**.[16]



Herein we report a regio- and stereoselective tandem CM–RCM reaction of silyloxy-tethered enyne **4** with both terminal and internal alkene counterparts to achieve a new connectivity pattern of siloxane-based 1,3-dienes **6**. This tandem process not only expands the scope of silicon-tethered enyne metathesis reactions but also provides a clear mechanistic picture and a measure of the relative reactivity of variously substituted alkenes and silylated alkynes.

Results and Discussions

Substrate Scope and Substituent Effect: The reactivity of silylated internal alkynes is generally much lower than that of regular internal alkynes due to the sterically hindered nature of the silyl group. However, it was observed that the reactivity of silylated internal alkynes can be reconstituted by introducing an oxygen substituent at the propargylic position.[17] More importantly, introducing additional oxygen substituents at the silicon further increases the reactivity of the alkyne toward the CM reaction without perturbation of the regioselectivity in the product. Therefore, the metathesis reaction of enynes **2a**–**c**[13,18] possessing a tethered trisubstituted cyclic alkene provided CM products **7a**–**f**, and a minor amount of **8a**–**f** (Table 1). The trisubstituted cyclic alkenes were found to be inert under the reaction conditions, which did not allow ring opening by intermediate **5**.

The involvement of intermediate **5** in the reaction can be deduced unambiguously on the basis of the connectivity of CM products **7a**–**f**, albeit the minor products indicate the existence of a different intermediate derived from the methylidene propagating species.[13,19] Due to the low reactivity of the trisubstituted cyclic olefin, differently substituted acyclic olefins were introduced into the enyne substrate **9a**–**f**. When these enynes were reacted under the same reaction conditions in the presence of a variety of terminal alkenes, the expected CM–RCM products **10a**–**f** were isolated in moderate to good yields (Table 2). The styryl moiety-containing enyne **9a** reacted with 5-hexenyl-1-acetate to generate the CM–RCM product **10a** in 52% yield and CM-only product **11** in 15% yield (entry 1). The connectivity of **10a** and **11** clearly indicates that the CM reaction occurs between the alkyne moiety and the 5-hexenyl-1-acetate-

(12) For the inhibition of RCM by a silyl substituent at the terminal position of alkynes, see: (a) Kim, S.-H.; Zeurcher, W. J.; Bowden, N. B.; Grubbs, R. H. *J. Org. Chem.* **1996**, *61*, 1073–1081. (b) Clark, S. J.; Elustondo, F.; Trevitt, G. P.; Boyall, D.; Robertson, J.; Blake, A. J.; Wilson, C.; Stammen, B. *Tetrahedron* **2002**, *58*, 1973–1982.

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(14) For a discussion of preferred alkene initiation, see: Hansen, E. C.; Lee, D. *J. Am. Chem. Soc.* **2004**, *126*, 15074–15080.

(15) For related CM–RCM sequences with an alkene and a diyne, see: Stragies, R.; Schuster, M.; Blechert, S. *Chem. Commun.* **1999**, 237–239.

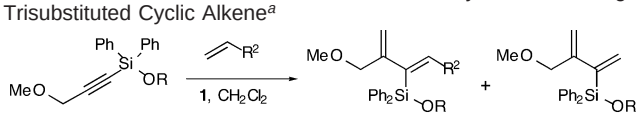
(16) An endo-mode ring closure to form a six-membered ring has been observed with substrates that have 1,1-disubstituted alkene moieties: (a) Kitamura, T.; Sato, Y.; Mori, M. *Chem. Commun.* **2001**, 1258–1259. (b) Kitamura, T.; Sato, Y.; Mori, M. *Adv. Synth. Catal.* **2002**, *344*, 678–693. (c) Dolhem, F.; Lievre, C.; Demailly, G. *Eur. J. Org. Chem.* **2003**, 2336–2342.

(17) Tonogaki, K.; Mori, M. *Tetrahedron Lett.* **2002**, *43*, 2235–2238.

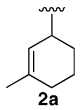
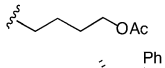
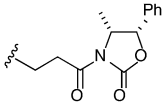
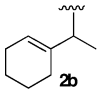
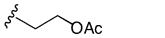
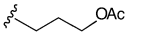
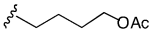
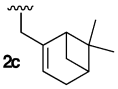
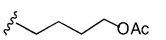
(18) For methods for the formation of alkynylsilyl ethers, see: (a) Stork, G.; Keitz, P. F. *Tetrahedron Lett.* **1989**, *30*, 6981–6984. (b) Grimm, J. B.; Lee, D. *J. Org. Chem.* **2004**, *69*, 8967–8970.

(19) For an early mechanistic proposal relying on methylidene as a propagating species, see: Stragies, R.; Schuster, M.; Blechert, S. *Angew. Chem., Int. Ed.* **1997**, *36*, 2518–2520.

Table 1. CM between Terminal Alkenes and Enynes Possessing Trisubstituted Cyclic Alkene[a]



2 7 8

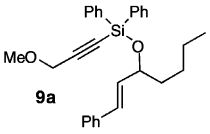
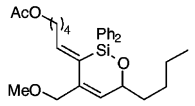
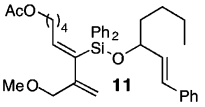
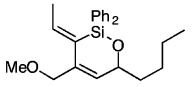
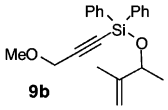
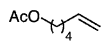
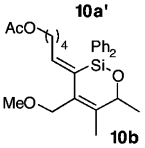
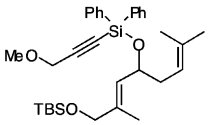
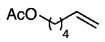
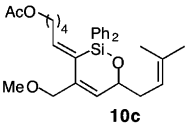
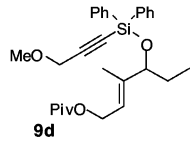
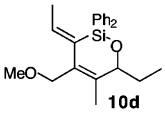
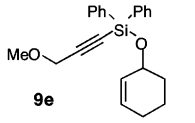
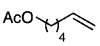
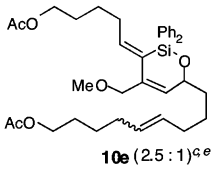
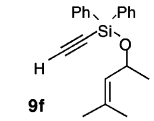
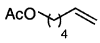
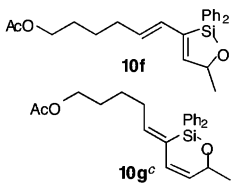
Entry	R	R_2	yield of **7** (%)(*Z*/*E*)[b,c]		**8**
1	 **2a**	 OAc	**7a**	83 (97:3)	12
2		 Ph N O O	**7b**	44 (100:0)	n.d.[d]
3	 **2b**	 OAc	**7c**	64 (93:7)	n.d.
4		 OAc	**7d**	65 (96:4)	n.d.
5		 OAc	**7e**	60 (96:4)	20
6	 **2c**	 OAc	**7f**	84 (95:5)	13

[a] Catalyst **1** (7−15 mol %) and 1-alkene (4 equiv) in CH_2Cl_2 (0.03 M) at 40 °C for 3−4 h. [b] Ratio was determined by ^{1}H NMR. [c] The trisubstituted double bond on the cyclohexene moiety remained intact. [d] Not detected.

derived alkylidene to generate an intermediate of type **5**, which cyclizes onto the styryl group or reacts with 5-hexenyl-1-acetate to afford **10a** and **11**, respectively. It was assumed that, if an internal alkene is employed, the ring-closure efficiency should be improved because of the slower rate of alkenyl group transfer compared to that of the methylene transfer.[20] Indeed, when **9a** was reacted with *cis*-2-butene, CM−RCM product **10a′** was obtained in 84% yield without formation of the prematurely terminated CM-only product. Enyne **9b** possessing a 1,1-disubstituted alkene also underwent tandem CM−RCM reaction with 5-hexenyl-1-acetate to yield siloxane **10b** in moderate yield (46%) (entry 3). Enynes **9c** and **9d** tethered with different trisubstituted alkene moieties provided CM−RCM products **10c** and **10d** in 51 and 91% yields from the reactions with 5-hexenyl-1-acetate and *cis*-2-butene, respectively. Enyne **9e**, which possesses a disubstituted cyclohexenyl moiety, reacted with 5-hexenyl-1-acetate to undergo CM followed by a ring-opening metathesis sequence to deliver a 1:2 adduct **10e** in 67% yield (entry 6). The reaction of enyne **9f** possessing a terminal alkyne with 5-hexenyl-1-acetate generated a 1.3:1 mixture of five- and six-membered ring CM−RCM products **10f** and **10g** (entry 7). This is a very unexpected result because the silylated terminal alkyne invariably undergoes enyne metathesis with the regioselectivity that leads to **10f** only.[21] The origin of this perturbed regioselectivity leading to **10g** is not fully understood. However, we strongly suspect that the oxygen substituent on the silicon tether plays an important role as a chelating group.

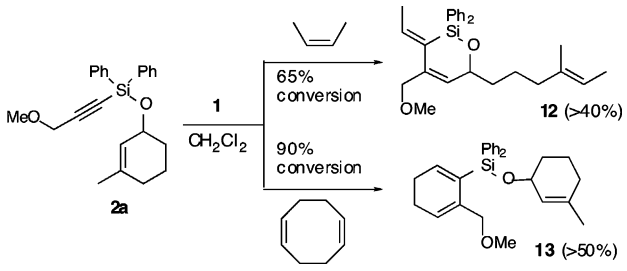
The methylene-free condition[20] is instrumental for the CM−RCM reactions of enynes carrying sterically hindered unreactive alkenes (Scheme 1). Enyne **2a**, which provides only the CM product in the reaction with 5-hexenyl-1-acetate (entry 1 in Table 1), reacted with *cis*-2-butene to deliver the CM−RCM product

Table 2. Tandem CM−RCM Reaction of Silyloxy-Tethered Enynes and Terminal Alkenes[a]

Entry	enyne **9**	alkene	product	yield (%)[b]
1	 **9a**		 **10a**[c]	52
			 **11**	15
2	**9a**		 **10a'**	84[d]
3	 **9b**		 **10b**	46
4	 **9c**		 **10c**	51
5	 **9d**		 **10d**	91[d]
6	 **9e**		 **10e** (2.5 : 1)[e]	67
7	 **9f**		 **10f** **10g**[c]	53 (1.3:1)

[a] Catalyst **1** (7−15 mol %) and 1-alkene (4 equiv) in CH_2Cl_2 (0.03 M) at 40 °C. [b] Isolated yields. [c] Full characterization was done after the conversion of siloxanes to **10a″**, **10e′**, and **10g′** via the removal of the silyl moiety; see Supporting Information. [d] *cis*-2-Butene was directly bubbled into the reaction. [e] *E*/*Z*-isomers only at the acyclic disubstituted double bond.

Scheme 1

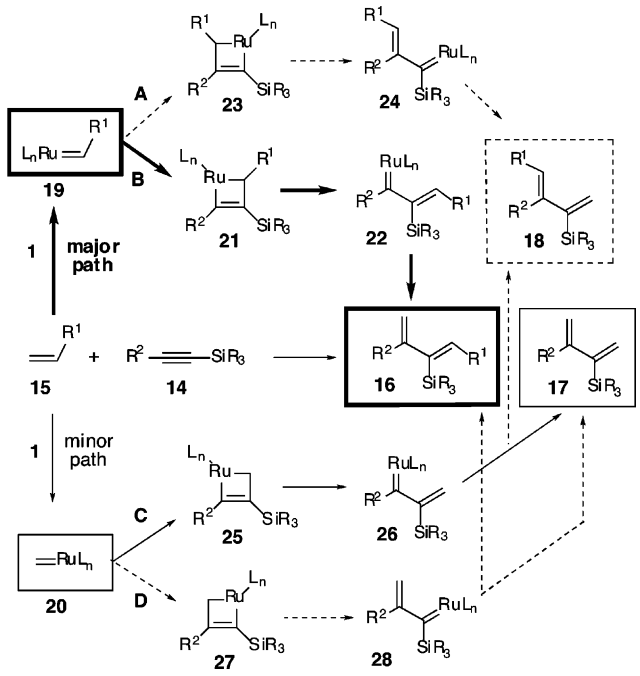


12, albeit in moderate yield (40% yield at 65% conversion).[22] This difference is probably the consequence of the faster

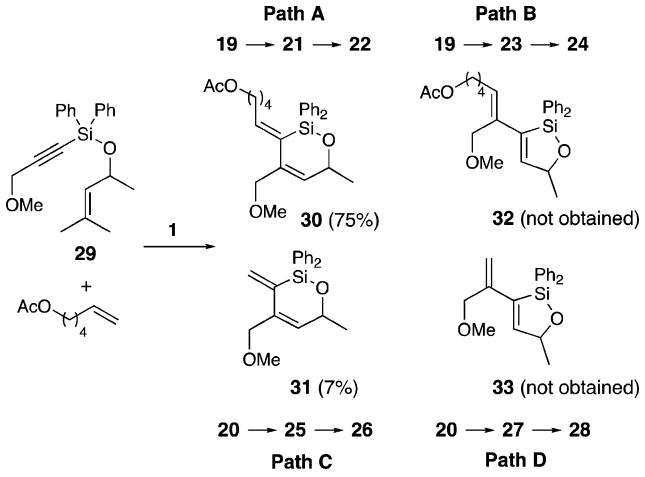
(20) Kulkarni, A. A.; Diver, S. T. *J. Am. Chem. Soc.* **2004**, *126*, 8110−8111.
(21) For examples of terminal silylated alkyne metathesis, see. (a) Tonogaki, K.; Mori, M. *Tetrahedron Lett.* **2002**, *43*, 2235−2238. (b) Stragies, R.; Voigtmann, U.; Blechert, S. *Tetrahedron Lett.* **2000**, *41*, 5465−5468. (c) Lee, H.-Y.; Kim, B. G.; Snapper, M. L. *Org. Lett.* **2003**, *5*, 1855−1858. (d) Clark, J. S.; Trevitt, G. P.; Boyall, D.; Stammen, B. *Chem. Commun.* **1998**, 2629−2630.

(22) Full characterization of the CM product was achieved after the conversion of **12** to **12′** via the removal of the silyl moiety; see Supporting Information.

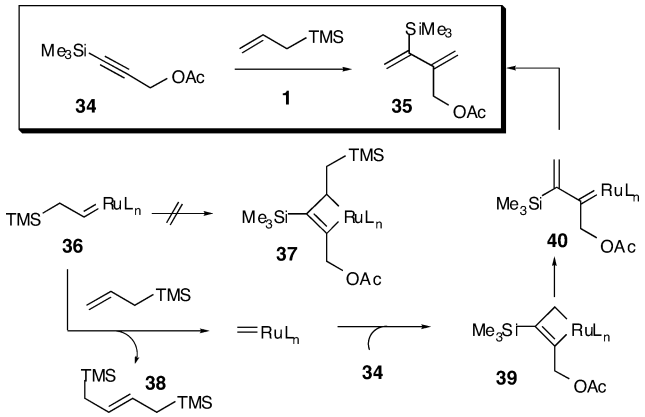
Scheme 2



Scheme 3



Scheme 4



methylene transfer from the terminal alkene compared to that of alkenyl transfer, thereby allowing the intermediate alkylidene to undergo cyclization in the latter case.

Furthermore, the reaction of **2a** with 1,5-cyclooctadiene generated 1,3-cyclohexadiene derivative **13** in >50% yield, while the use of 1,5-hexadiene[23] provided much lower yield of **13** (Scheme 1). The moderate yield even at 90% consumption of **2a** is due to the formation of co-oligomerized material with 1,5-cyclooctadiene.

Mechanism: As shown in Tables 1 and 2, the enyne cross metathesis between alkene **15** and silylated alkyne **14** consistently yielded **16** as a predominant product and **17** as a minor; however, **18** was not detected (Scheme 2). In terms of mechanistic details, one of the most undefined aspects of the enyne metathesis is the nature of the propagating species, which is intimately related to the initiation event.[12a,19,24] Fortunately, in the current enyne metathesis between silylated alkynes (**14**) and terminal alkenes (**15**), we can exclude the possibility of the initiation of the metathesis on the alkyne due to the sterically hindered nature of the silylated alkyne **14**.[14,25] Deconvolution of the initiation event in the metathesis process involving silylated alkynes greatly simplifies the mechanistic interpretation, thus giving a much clearer picture of the overall reaction mechanism compared to that with terminal alkynes. Deduced from the product distribution in combination with the known preference for the formation of alkylidene **19** over methylidene **20**,[26] four possible reaction pathways (**A**−**D**) are depicted in Scheme 2. In the proposed mechanism, alkylidene **19** will react with internal alkyne **14** ($R^2 \neq H$) to generate a metallacyclobutene intermediate **21** favorably (path **B**). The preferred formation of **21** is assumed to be the consequence of positioning the bulky silyl group away from the sterically hindered NHC ligand-bearing ruthenium metal center. The electrocyclic ring opening of **21** to **22** followed by methylene transfer would deliver the predominantly observed product **16**. Although it is not unreasonable to assume that **16** can be derived from path **D** via intermediates **27** and **28**, the contribution from this path should be minimal. The absence of product **18** indicates that the reaction path going through **23** to **24** (path **A**) is not operating in the current metathesis reaction. As an exception, however, the CM of terminal silylated alkynes (**14** with $R^2 = H$) prefers to follow path **A** to give exclusively **18**.[1a] The formation of varying amounts of **17** can be rationalized based on the involvement of methylidene intermediate **20**. Although **20** generally forms slowly at lower concentration compared to that of **19**, it can play an important role if **19** cannot participate in the next step (see Scheme 4). To avoid the unfavorable interaction between the bulky silyl group and the sterically hindered NHC ligand on the ruthenium metal center, methylidene **20** will favorably form metallacyclobutene **25** over **27**.

(23) Smulik, J. A.; Diver, S. T. *Tetrahedron Lett.* **2001**, *42*, 171−174.
(24) For the mechanistic view in preference of an alkyne initiation−methylidene propagation, see: (a) Katz, T. J.; Sivavec, T. M. *J. Am. Chem. Soc.* **1985**, *107*, 737−738. (b) Kinoshita, A.; Mori, M. *Synlett* **1994**, 1020−1022. (c) Stragies, R.; Schuster, M.; Blechert, S. *Chem. Commun.* **1999**, 237−238. For an alkene initiation−alkylidene propagation, see: (d) Kim, S.-H.; Bowden, N.; Grubbs, R. H. *J. Am. Chem. Soc.* **1994**, *116*, 10801−10802.
(25) For other evidence of an alkene initiation, see: (a) Hoye, T. R.; Donaldson, S. M.; Vos, T. *Org. Lett.* **1999**, *1*, 277−280. (b) Schramm, M. P.; Reddy, D. S.; Kozmin, S. A. *Angew. Chem., Int. Ed.* **2001**, *40*, 4274−4277. (c) Giessert, A. J.; Diver, S. T. *Org. Lett.* **2005**, *7*, 351−354. For theoretical support for alkene initiation, see: (d) Straub, B. F.; Lippstreu, J. J. *J. Am. Chem. Soc.* **2005**, *127*, 7444−7457.
(26) (a) Randall, M. L.; Tallarico, J. A.; Snapper, M. L. *J. Am. Chem. Soc.* **1995**, *117*, 9610−9611. (b) Tallarico, J. A.; Bonitatebus, P. J., Jr.; Snapper, M. L. *J. Am. Chem. Soc.* **1997**, *119*, 7157−7158. (c) Ulman, M.; Grubbs, R. H. *Organometallics* **1998**, *17*, 2484−2489.

The electrocyclic ring opening of **25** to **26** (path **C**) followed by methylene transfer will provide the minor product **17**, which requires a net dimerization of alkene **15** to supply additional methylene. Indeed, it was found that there is a strong correlation between the formation of **17** and alkene dimerization. Although theoretically it is possible that alkylidene **26** can provide **18**, the absence of **18** is strong evidence that alkylidene **26** has very low tendency to react with terminal alkene **15** to generate a propagating methylidene **20**, which is consistent with the predominant initial partitioning of **15** toward **19** over **20**. Another possible reaction path for the formation of **17** is the route involving **27** and **28** (path **D**). However, the contribution of this path should be negligible due to the disfavored formation of **27** compared to **25**.

The mechanistic picture depicted in Scheme 2 is further supported by the product distribution from the CM−RCM sequence of reaction between **29** and 5-hexenyl-1-acetate, which provides information regarding the history of each step (Scheme 3). From this reaction, only two products, **30** and **31**, were isolated in 75 and 7% yields, respectively. On the basis of the identity of **30** and **31**, we can infer that the major compound **30** was generated via the path **A** (**19**−**21**−**22**), while the minor product **31** was generated via the path **C** (**20**−**25**−**26**). The absence of two additional possible compounds, **32** and **33**, indicates that the reactions via the path **B** (**19**−**21**−**22**) and path **D** (**20**−**25**−**26**) were not or only minimally involved in this reaction.

The enyne metathesis of silylated alkyne **34** and allyl trimethylsilane yielded only the unexpected ethylene crossed product **35** in low yield, which affords further insight into the mechanistic picture (Scheme 4). The formation of **35** can be readily explained on the basis of the lack of reactivity of alkylidene **36** toward **34** to form metallacyclobutene intermediate **37**, probably due to the severe steric interaction caused by two silyl groups. Thus, **36** reacted with allyl trimethylsilane to generate dimer **38** and sterically less encumbered methylidene, which readily forms **39** by reaction with **34**. Subsequent electrocyclic ring opening of **39** to **40** followed by methylene transfer from allyl trimethylsilane would provide **35**.[27] The low yield is due to the slow step involving the formation of methylidene[26] and the dimer **38**.

Reactivity and *E*/*Z* Selectivity in the CM of Silylated Alkynes: The increased reactivity caused by the oxygen substituent on the silicon seems to be much greater than that of the propargylic position. This oxygen substituent effect can be clearly seen by comparing the reaction time required for the metathesis reaction of **2a**−**c** and **41a**,**b** (Scheme 5). The reactions of **2a**−**c** that possess an oxygen substituent on the silicon took about 4 h for near complete conversion (Table 1), while **41a**,**b** that have no oxygen substituent took 40 h for a similar level of conversion (Table 3).[13] We speculated that this difference is not emulated from simple steric or inductive effects of the oxygen, instead, it is related to some type of complexation of the ruthenium metal to the oxygen. The difference between **2a**−**c** and **41a**,**b** is not only the reactivity but also the stereoselectivity. While the CM of **2a**−**c** typically generates mixtures of *Z*/*E*-isomers in the range of 93:7 to 98:2, that of **41a**,**b** generates only *Z*-isomer. The increased reactivity in

Scheme 5

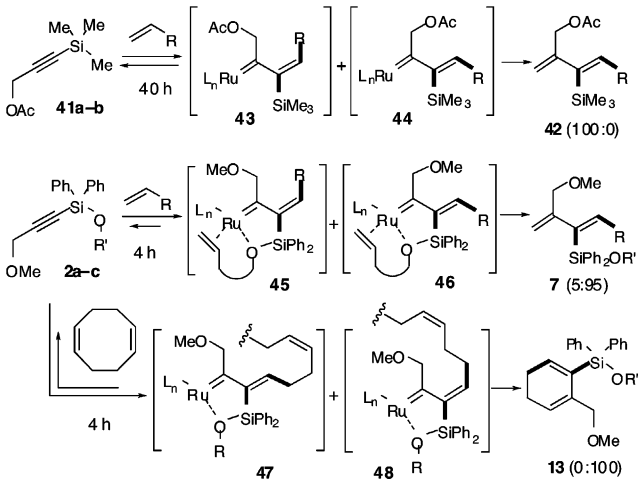
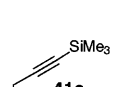
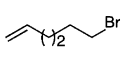
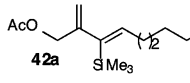
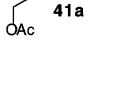
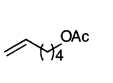
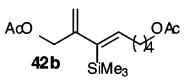
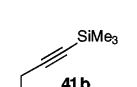
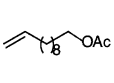
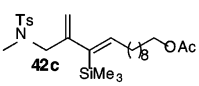
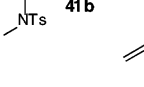
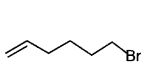
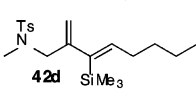


Table 3. CM between Terminal Alkenes and Internal Alkynes Possessing Trimethylsilyl Substituent[a]

Entry	alkyne	alkene	1,3-diene[b]	yield (%)[c]
1				79
2				80
3				65
4				79

[a] Catalyst **1** (7−15 mol %) and 1-alkene (4−8 equiv) in CH_2Cl_2 (0.03 M) at 40 °C for 40 h. [b] Only a single isomer of product was observed within the ^{1}H NMR detection limit. [c] Isolated yields.

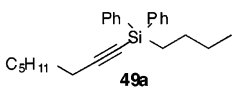
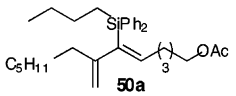
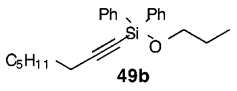
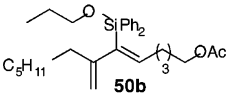
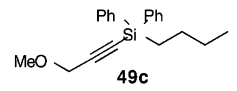
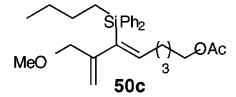
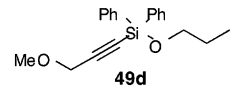
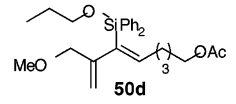
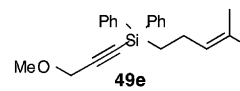
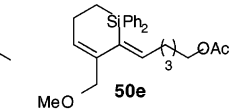
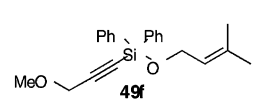
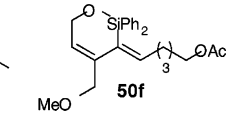
concert with the decreased *Z*/*E* selectivity in the CM reaction of **2a**−**c** and the complete reversal of *Z*/*E* selectivity for the formation of **13** indicates that the early metathesis steps to form intermediates (e.g., **19**−**21**−**22** in Scheme 2) are reversible, and thus are not the stereochemistry-determining steps. Therefore, the rate for the formation of **43** and **44** from **41a**,**b** and their reversion rates are comparable, while only **44** slowly turns over to the major compound **42**. On the other hand, once the intermediates **45** and **46** are formed from **2a**−**c**, their reversion rates are slower compared to those of **43** and **44** due to the presumed chelation of the oxygen[28] and possibly tethered alkene[29] that stabilize these intermediates. The slower reversion rate maintains the higher concentration of these reactive intermediates **45** and **46**, which is the source of the reduced reaction time. The reduced reversion rate of **45** will allow some fraction of this intermediate to turn over to the minor product **7**. In the metathesis reaction of **2a**−**c** with 1,5-cyclooctadiene, the intermediate **47** has proper cis-geometry of the double bond

(27) The metathesis of **34** with ethylene produced **35** in quantitative yield within an hour.

(28) For the related ethereal oxygen chelate formation, see: (a) Garber, S. B.; Kingsbury, J. S.; Gray, B. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2000**, *122*, 8168−8179. (b) Kingsbury, J. S.; Harrity, J. P. A.; Bonitatebus, P. J.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1999**, *121*, 791−799. (c) Harrity, J. P. A.; Visser, M. S.; Gleason, J. D.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1997**, *119*, 1488−1489. (d) Harrity, J. P. A.; La, D. S.; Cefalo, D. R.; Visser, M. S.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1998**, *120*, 2343−2351. (e) Engelhardt, F. C.; Schmitt, M. J.; Taylor, R. E. *Org. Lett.* **2001**, *3*, 2209−2212.

(29) For the formation of a stable alkene chelate, see ref 26b.

Table 4. CM of Silylated Alkynes Possessing Different Substituent at the Propargylic Carbon and Silicon Center[a]

entry	alkyne	1,3-diene	conversion (%)[b]
1	 **49a**	 **50a**	0
2	 **49b**	 **50b**	<5
3	 **49c**	 **50c**	<20
4	 **49d**	 **50d**	100
5	 **49e**	 **50e**	<20
6	 **49f**	 **50f**	100

[a] Catalyst **1** (7−15 mol %) and 1-alkene (4 equiv) in CH_2Cl_2 (0.03 M) at 40 °C. [b] Conversion was determined by ^1H NMR after 4 h.

to undergo facile cyclization, thereby providing 1,3-cyclohexadiene products, whereas the other intermediate **48** possessing trans-geometry of the double bond can only react intermolecularly to generate oligomers.

Propargylic Heteroatom Effect: In the enyne CM−RCM sequence of reactions with enynes, with alkynyl silyloxy tethers, the oxygen heteroatom substituents at the propargylic site seem to play a significant role in increasing the CM reactivity of silylated alkynes.[30] The heteroatom substituent effect caused by each oxygen, one at the propargylic carbon and one at the silicon center, was further examined separately by comparing the conversion of each starting material **49a**−**f** in the CM reaction to the product at a given time frame (Table 4). When straight alkyl group-containing silylated alkynes **49a** and **49b** were treated with 5-hexenyl-1-acetate, virtually no conversion was observed (entries 1 and 2), whereas the corresponding alkynes **49c** and **49d** possessing methoxy substituents gave much higher conversion (entries 3 and 4). This result clearly indicates that the oxygen substituent at the propargylic carbon center is necessary to maintain a certain level of reactivity of the silylated alkynes. Specifically, silylated alkynes **49d** and **49f**, which carry an additional oxygen substituent at the propargylic silicon center in addition to the one at the propargylic carbon, gave complete conversion within the same length of reaction time (entries 4 and 6). The higher reactivity of **49c**,**d** compared to that of **49a**,**b** and additional comparison between **49c** and **49d** clearly indicates that the oxygen substituent at both carbon and siliconpropargylic centers increases the metathesis reactivity of these silylated alkynes. The effect of the double bond on enyne substrates was examined by comparing the relative CM reactivity of **49c** with **49e** (entries 3 and 5) and that of **49d** with **49f**, respectively (entries 4 and 6). Overall, the rate of conversion for both substrates **49c** and **49e** is identical, as is that of **49d** and **49f**. This outcome implicates that the activating role of double bond functionality for the metathesis is minimal at best.

The heteroatom substituent effect observed in Tables 1−3 was further confirmed by the systematic variation of the substituents at the propargylic center (Table 4). Although the exact activating mechanism and the role of the propargylic heteroatoms should wait further study, one plausible justification is the stabilization of the ruthenium alkylidene intermediates formed during the reaction via the formation of chelate, as suggested in Scheme 5.

Conclusion

The scope and utility of the regio- and stereoselective cross metathesis reaction between silylated alkynes and terminal alkenes were expanded by employing a tandem cross metathesis (CM)−ring-closing metathesis (RCM) sequence. This selective tandem metathesis process not only allowed the formation of novel cyclic siloxanes but also provided insight into the reaction mechanism of the enyne metathesis reaction. Furthermore, the systematic variation of the substituent on the silicon center clearly identified the activating role of the heteroatom at the propargylic sites.

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Supporting Information Available: General experimental procedures, characterization data of compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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(30) For early observations of the activating effect of oxygen and nitrogen substituent in enyne metathesis, see: (a) Mori, M.; Tonogaki, K.; Nishiguchi, N. *J. Org. Chem.* **2002**, *67*, 224−226. (b) Tonogaki, K.; Mori, M. *Tetrahedron Lett.* **2002**, *43*, 2235−2238. (c) Randl, S.; Lucas, N.; Connon, S. J.; Blechert, S. *Adv. Synth. Catal.* **2002**, *344*, 631−633.