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Communication

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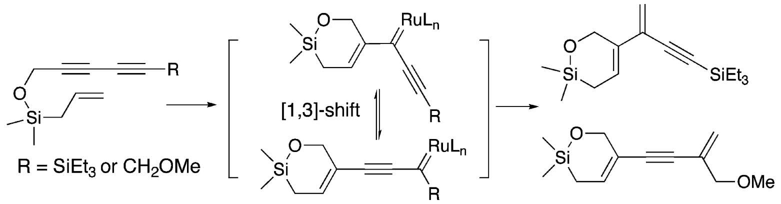

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COMMUNICATIONS

Cross and Ring-Closing Metathesis of 1,3-Diynes: Metallotropic [1,3]-Shift of Ruthenium Carbenes

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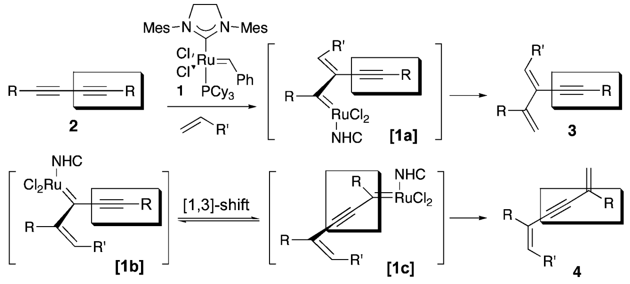
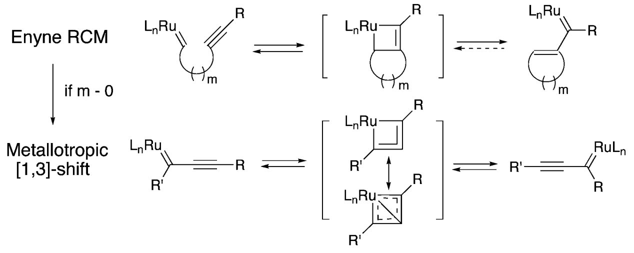
Enyne metathesisis is a powerful carbon−carbon bond-forming reaction that generates a 1,3-diene from an alkene and an alkyne.[1] In our efforts to expand the scope of the enyne ring-closing metathesis (RCM)[2] and cross metathesis (CM),[3] we became interested in 1,3-diynes as a new class of substrate. We surmised that CM of diyne **2** and alkenes catalyzed by carbene complex **1**[4] would have a certain selectivity[5] for either **3** or **4** because the formation of intermediates [**1a**] and [**1b**] would be directed by the adjacent alkyne (Scheme 1). Moreover, a metallotropic [1,3]-shift[6] might ensue in the case of [**1b**] to generate a new alkylidene [**1c**], providing 1,5-diene-3-yne **4** as a final product. The possibility of metallotropic [1,3]-shift, although not explicitly proposed, is implicated in the RCM with substrates possessing diynes reported by van Otterlo.[7] However, because neither CM nor the metallotropic [1,3]-shift involving diynes has been reported[8] the outcome of these manifolds of reaction cannot be predicted.

Scheme 1. Cross Metathesis of Diynes



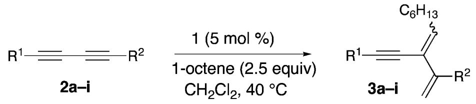
From a mechanistic standpoint,[9] we believe metallotropic [1,3]-shift and enyne RCM are in the same class of reactions. Thus, the metallotropic [1,3]-shift can be considered a special case of enyne RCM with no tether ($m = 0$) between the ene and the yne counterparts (Scheme 2). Notwithstanding the mechanistic similarity, the kinetic and thermodynamic details between the two are expected to be substantially different. For example, based on a theoretical investigation, the enyne RCM is not fully reversible yet the metallotropic [1,3]-shift is expected to be reversible.[9c,10] Herein we report the reactivity and selectivity of CM and RCM reactions of 1,3-diynes and convincing evidence for a facile metallotropic [1,3]-shift of ruthenium carbenes.

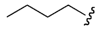
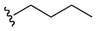
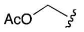
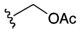
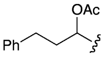
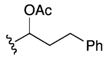
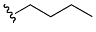
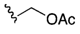
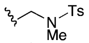
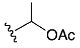
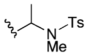
Scheme 2. Enyne RCM and Metallotropic [1,3]-Shift



The characteristic CM behavior of 1,3-diynes[11] was first examined with symmetrical and unsymmetrical diynes (Table 1). Treatment of symmetrical diynes **2a**−**d** and 1-octene (2.5 equiv)[12] with catalyst **1** (5 mol %) provided CM products **3a**−**c** (entries 1−3) as mixtures of two isomers in moderate to good yields except for diyne **2d** (entry 4). The lack of reactivity of **2d** is presumably due to the steric hindrance of the silyl groups.[13] The structure of products **3a**−**c** was established unambiguously by extensive NMR studies in combination with chemical derivatization.[14] A salient feature of this CM process is the mono-CM event at only one alkyne moiety of the diyne. The isolation of products **3a**−**c** implies that the alkyne moiety of 1,3-enynes is less reactive toward metathesis compared to that of 1,3-diynes probably due to the steric and stereoelectronic deactivation.[15] While the origin of the high *Z*/*E*-selectivity is yet to be justified, CM of substrate **2c** possessing propargylic secondary acetate provided products **3c** with excellent *Z*-selectivity (entries 3).

Table 1. CM of Symmetric and Unsymmetrical 1,3-Diynes[a]



entry	diyne **2**	R1	R2	enyne **3**	Z / E	yield (%)[b]
1	**2a**			**3a**	50:50	62
2	**2b**			**3b**	64:36	72
3	**2c**			**3c**	98:2	88
4	**2d**	Me_3Si—	—$SiMe_3$	**3d**	–	0[c]
5	**2e**	Et_3Si—		**3e**	41:59	77
6	**2f**	Et_3Si—		**3f**	69:31	91
7	**2g**	Et_3Si—		**3g**	43:57	91
8	**2h**	Et_3Si—		**3h**	98:2	76
9	**2i**	Et_3Si—		**3i**	98:2	91

[a] Diynes **2a**−**i** and 1-octene (2.5 equiv) with catalyst **1** (5 mol %) in CH_2Cl_2 (0.02 M) under reflux for 4−6 h. [b] Isolated yield. [c] Starting material was recovered.

Based on the observed CM reactivity and selectivity of symmetrical diynes **2a**−**d**, we expanded the substrate scope to unsymmetrical diynes **2e**−**i** that possess both silyl and alkyl substituents on each end of diyne. As expected, under typical CM conditions, 1,3-diynes **2e**−**i** reacted only at the alkyl substituted alkyne moiety to provide single regioisomeric CM products **3e**−**i** in high yields (entries 5−9). The substrates possessing branched and heteroatom-functionalized propargylic carbon gave excellent *Z*-selectivity (entries 8 and 9), whereas the unbranched substrates gave mixtures of *E*/*Z*-isomers (entries 5−7). The absence of the expected [1,3]-metallotropic shifted product of type **4** throughout the CM in Table 1 clearly indicates the role of an alkyne as a directing group to

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Scheme 3. Divergent RCM of Enediynes

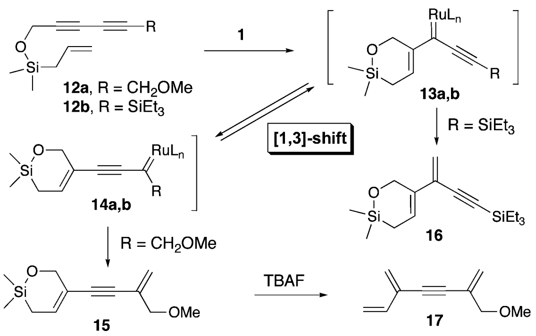
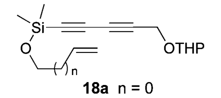
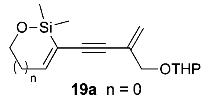
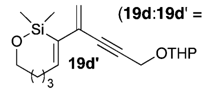
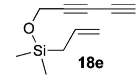
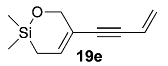
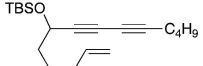
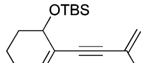
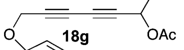
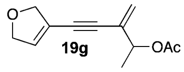
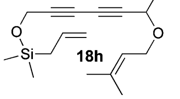
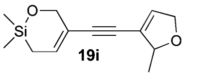


Table 2. RCM-Induced Metallotropic [1,3]-Shift[a]

entry	enediyne	CM product	yield (%)[b]
			
1	**18a** n = 0	**19a** n = 0	54
2	**18b** n = 1	**19b** n = 1	66
3	**18c** n = 2	**19c** n = 2	68
4	**18d** n = 3	**19d** n = 3	11
		(**19d**:**19d'** = 1:5)  **19d'**	55
5	 **18e**	 **19e**	69
6	 **18f**	 **19f**	96[c]
7	 **18g**	 **19g**	89[c]
8	 **18h**	 **19i**	71

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[a] With catalyst **1** (5 mol %) in CH$_2$Cl$_2$ (0.003 M) under reflux for 4−6 h. [b] NMR-based yield with internal standard (anthracene). [c] Isolated yield.

control the regioselectivity, favoring the formation of an intermediate of type [**1a**] from diynes **2a**−**i**.

We envisioned that by reversing the regioselectivity to form an intermediate of type [**1b**] via an initial RCM of 1,3-diynes, the expected [1,3]-shift might be induced. Indeed, when enediyne **12a** was treated with catalyst **1** a single product **15** was obtained in quantitative yield, the structure of which was unambiguously elucidated after its conversion to **17**,[16] while the RCM of **12b** generated **16** exclusively (Scheme 3). We believe that both **12a** and **12b** underwent initial RCM to generate intermediates **13a**,**b**, which then followed divergent reaction paths depending on the steric hindrance of substituents. Alkylidene **13a**, possessing a less hindered methoxymethylene at the terminal position of diyne, underwent [1,3]-shift to **14a**, which turned over to the observed product **15**. Another plausible scenario is based on a lower barrier of **14a** to **15** compared to that of **13a** to the corresponding final product while **13a** and **14a** are in rapid equilibrium. On the other hand, the opposite is true for **13b** because of the bulky silyl substituent at the terminal position of the alkyne, which provides **16** exclusively.

Next, we examined the generality of RCM and [1,3]-shift behavior with enediynes **18a**−**h**. Gratifyingly, the RCM reactions with these substrates provided efficient metallotropic [1,3]-shift except for one case (Table 2).[17] RCM of substrates **18a**−**c** form five- to seven-membered siloxanes accompanied by the expected [1,3]-shift to give products **19a**−**c** exclusively (entries 1−3) while that of **18d** provided eight-membered siloxane **19d** and **19d′** in a 1:5 ratio[18] (entry 4). Substrate **18e** with terminal dialkyne is a particularly good substrate for [1,3]-shift to give **9e** (entry 5). All carbon- and ether-tethered substrates **18f**,**g** yielded the corresponding 1,3-shifted product **19f**,**g** in high yield (entries 6 and 7). The efficient conversion of dienediyne **18h** to **19h** (entry 7) further supports the sequence of enyne RCM-[1,3]-shift-RCM as depicted in Scheme 3. This mechanistic hypothesis involves the formation of a 1:1 adduct between the substrate and ruthenium alkylidene followed by its metallotropic [1,3]-shift and final RCM.

In conclusion, we have demonstrated that the CM of 1,3-diynes provides excellent regioselectivity, which does not depend on the substituents on the alkynes, whereas the *E*/*Z*-selectivity showed strong dependency on the substituent. The RCM of substrates possessing a 1,3-diyne moiety undergoes smooth ring closure followed by facile metallotropic [1,3]-shift to give products that contain fully conjugated 1,5-diene-3-ynes. Further exploration of mechanistic and synthetic aspects of this bond reorganization process is in progress.

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

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