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Metathesis and Metallotropy: A Versatile Combination for the Synthesis of Oligoenynes

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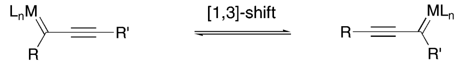
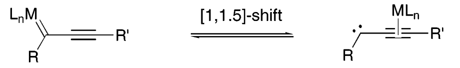
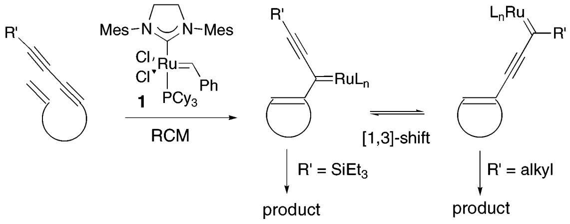
The bond reorganization processes, defined as metallotropic shift, of various alkynyl carbene complexes with Rh,[1] Mn,[2] Re,[3] Cr,[4] Mo,[4] and W[4] metals have been reported. The rearrangement involving Rh, Cr, Mo, and W is a [1,3]-shift (eq 1), while that with Mn and Re is formally defined as a [1,1.5]-shift (eq 2). However, the metallotropic shift of ruthenium alkynyl carbene complexes has not been observed until recently.[5] Because the metallotropic [1,3]-shift of a transient ruthenium carbene complex was involved in the enyne ring-closing metathesis (RCM) of diyne-containing substrates (eq 3),[6-8] we surmised that these two bond reorganization processes may share a close mechanistic relationship. Also, due to their tandem bond-forming and -breaking nature, both processes can be incorporated into a synthetic design in multiple combinations such that an efficient access to remarkably complex networks can arise. The prerequisite for this supposition is that the equilibrium composition or the reactivity of the equilibrating alkynyl ruthenium carbene species in eq 1 or 3 can be controlled to allow only one of the regioisomeric carbene complexes to react selectively. In this vein, the controlled [1,3]-shift behavior of an alkylidene derived from ruthenium complex **1**[9] depending on the substituent is highly instrumental (eq 3).[10] On the basis of this observation, we envisioned that, if properly designed, an alternating metallotropic [1,3]-shift and enyne RCM could produce a single propagating carbene species that would travel along a linear poly-1,3-diyne ($-[XCH_2CCCCCH_2]_n-$), generating an enediyne and π-conjugated oligoenynes (Scheme 1).[11] In this sequential enyne metathesis and metallotropic [1,3]-shift (M&M) event, the overall catalytic process initiated from one of the terminal alkenes would relay the metal carbene to the proximate alkyne.[12,13] Suppressed by strain from effecting a RCM reaction, the newly formed alkynyl carbene would undergo a [1,3]-shift, creating a new carbene effectively positioned for a facile metathetical closure to a five-membered ring. Herein we report one-step construction[14] of enediynes and oligoenynes enabled by the uniquely controlled repetitive metallotropic [1,3]-shift of ruthenium carbene species and its RCM.



(eq 1)



(eq 2)



(eq 3)

Scheme 1. Sequential Metathesis and Metallotropy (M&M)

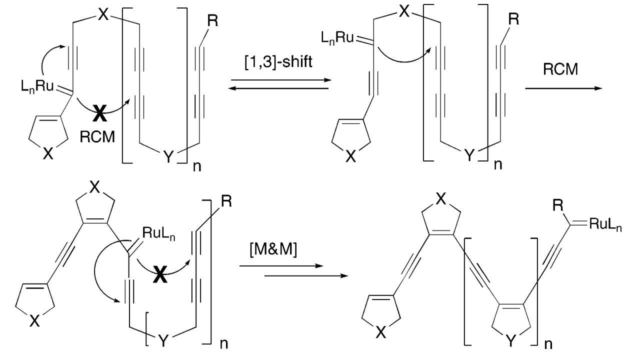
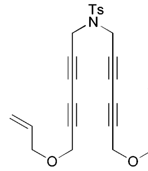
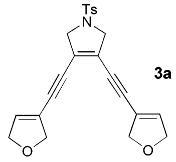
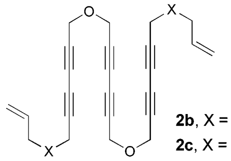
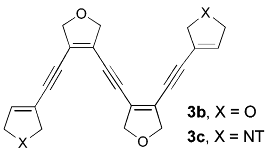
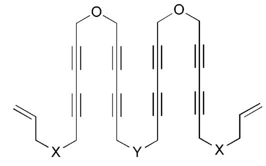
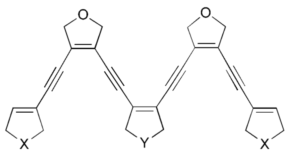
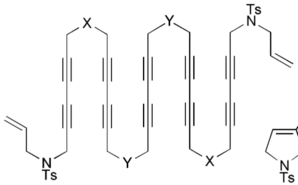
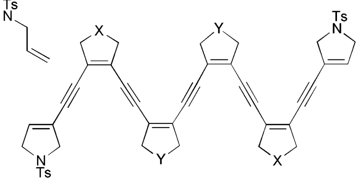


Table 1. Enyne Metathesis and Metallotropic [1,3]-Shift[a]

entry	ene-1,3-diyne	M&M product	yield (%)[b]
1	 **2a**	 **3a**	86 (67)[c]
2	 **2b**, X = O	 **3b**, X = O	63
3	**2c**, X = NTs	**3c**, X = NTs	47
4	 **2d**, X = O, Y = O	 **3d**, X = O, Y = O	51
5	**2e**, X = O, Y = NTs	**3e**, X = O, Y = NTs	45
6	 **2f**, X = O, Y = O	 **3f**, X = O, Y = O	32
7	**2g**, X = NTs, Y = O	**3g**, X = NTs, Y = O	36

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[a] With catalyst **1** (5 mol %) in CH_2Cl_2 (0.02 M) under reflux for 4−8 h. [b] Isolated yield. [c] Yield under ethylene atmosphere.

First, the planned M&M sequence was examined in a general sense with the lowest homologue **2a** (Table 1, entry 1).[15] Treatment of **2a** with **1** (5 mol %) in CH_2Cl_2 (40 °C) provided the desired product in 86% yield. The presence of ethylene during the reaction was found to be deleterious, which is contrary to the well-known beneficial ethylene effect in normal enyne metathesis.[16] It is also

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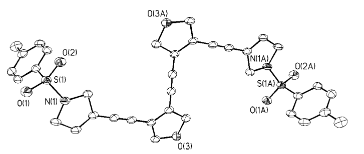
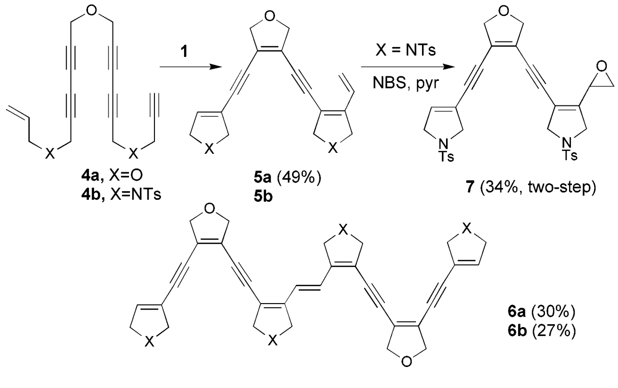


Figure 1. X-ray structure of **3c**.

Scheme 2. M&M with an Alkyne-Terminating Group



4a, X=O
4b, X=NTs

5a (49%)
5b

7 (34%, two-step)

6a (30%)
6b (27%)

surprising that the 1,3-diyne moieties in the substrate did not undergo CM with ethylene,[17] indicating that enyne RCM between the terminal alkene followed by the metallotropic [1,3]-shift and the terminating second RCM should be faster than CM of the propagating ruthenium carbene with ethylene. Next, a longer homologue with three diyne units between two terminal alkenes was tested. The all-oxygen-containing chain **2b** provided 63% yield of M&M product **3b** (entry 2), whereas the *N*-tosyl-group-bearing substrate **2c** afforded a lower yield (47%) of **3c** (entry 3). The symmetric nature of these product structures is apparent in their ^{1}H and ^{13}C NMR spectra, which was further confirmed by X-ray diffraction analysis of **3c** (Figure 1).

The effectiveness of this serial M&M sequence for the formation of oligoenynes is further demonstrated by using longer substrate homologues. Treatment of substrates **2d** and **2e** with catalyst **1** under typical RCM conditions provided *cis*-oligoenynes **3d** (X = O, Y = O) in 51% yield (entry 4) and **3e** (X = O, Y = NTs) in 45% yield (entry 5), respectively. The overall isolated yields of these longer homologue oligoenynes are marginal, and yet the theoretical yield for each bond-forming step is still higher than 90%. The longest homologues in the series, **2f** and **2g**, provided single isolated products **3f** and **3g** in 32% and 36% yield, respectively (entries 6 and 7), which remarkably involves the formation of five new triple bonds and six new double bonds in a single operation. Oligoenynes **3a**−**g** are stable even at room temperature over many weeks.[18]

An alkyne-terminating group for the metathesis can be accommodated to install a functionalizable group onto an enediyne product (Scheme 2). When **4a** was treated with **1** under ethylene,[19] RCM−[1,3]-shift−RCM reaction occurred to give **5a** (49%)[20] and its dimer **6a** (30%). Similarly, RCM of **4b** gave **5b** and **6b**. However, due to the instability of **5b**, the reaction mixture was directly treated with *N*-bromosuccinimide in pyridine, which allowed the isolation and characterization of **6b** (27%) and stable epoxide **7** (34%), respectively.

In conclusion, we have demonstrated that the combined use of enyne metathesis and metallotropic [1,3]-shift of alkynyl ruthenium carbenes is a powerful synthetic tool to construct enediynes and oligoenynes. The facile streamlining of the enyne metathesis and metallotropic [1,3]-shift of alkynyl ruthenium carbene may indicate that the electronic and geometrical constraints for both processes are similar, yet further study is necessary to provide a more accurate mechanistic picture for the latter.[21] The reaction mechanism and the utility of this bond-forming process will be further explored.

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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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(19) Although ethylene was found to be deleterious for the RCM of substrate **2a**, it was used to minimize the formation of dimeric product **6a**.
(20) Compound **5a** contains roughly 5% of styryl-group-incorporated product.
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