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Alkyne Metathesis: Catalysts and Synthetic Applications

Wei Zhang[a] and Jeffrey S. Moore[b,*]

[a] Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139, USA
[b] Roger Adams Laboratory, Department of Chemistry and Materials Science & Engineering, University of Illinois at Urbana-Champaign, Urbana, Illinois 61801, USA
Fax: (+1)-217-244-8024; e-mail: jsmoore@uiuc.edu

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Dedicated to the inspiring and pioneering work of Bob Grubbs and Dick Schrock in the field of carbon-carbon multibond metathesis.

Abstract: There has been rapid progress and growing interest in alkyne metathesis within the past decade. The availability of highly active catalysts as well as their applications in both organic synthesis and polymer chemistry has served to motivate the advancement of this field. In this article, the development of several different metathesis catalysts, including two heterogeneous ones, are reviewed with an emphasis on comparing strengths and weaknesses. In Section 4, the applications of alkyne metathesis to synthesis of natural products, conjugated polymers as well as shape-persistent macrocycles are discussed. In the last section, a comparison of alkyne metathesis to the well established alkene metathesis is given. Developing an alkyne metathesis catalyst with both high reactivity and robustness to air and moisture remains an unsolved problem of this important and useful reaction.

Keywords: acyclic diyne synthesis; cyclooligomerization; metathesis; poly(arylene-ethynylene)s; ring-closing alkyne metathesis; shape-persistent macrocycles

1 Introduction

The past decade has witnessed the tremendous impact of alkene metathesis on organic synthesis and polymer chemistry.[1] The extraordinary generality and chemoselectivity of this synthetic method as well as the ready availability of the catalysts have greatly facilitated the wide application of alkene metathesis in a variety of research areas. However, despite the great success of alkene metathesis, the analogous alkyne metathesis reaction is a less developed synthetic method. Its application is impeded by the availability and performance of the alkyne metathesis catalysts, especially with regard to convenience of catalyst synthesis, substrate compatibility, and temperature required for catalytic activity. As catalysts improve, alkyne metathesis has started to gain attention as a powerful tool holding great synthetic promise.[2–4] The catalysts that have been most widely used in organic synthesis and preparation of arylene-ethynylene polymers are based on molybdenum or tungsten complexes, in which alkoxide or phenoxide ligands are most common. Both homogeneous and heterogeneous catalysts have been successfully developed. In this review, the historical mechanistic understanding on alkyne metathesis will be discussed first. Comparison of various homogeneous catalyst systems and theoretical investigation of alkyne metathesis catalyzed by tungsten or molybdenum alkylidyne complexes will be covered in Section 3.1. Two newly developed heterogeneous catalytic systems will be discussed in Section 3.2, and the recent applications of alkyne meta-

Jeffrey Moore was born near Joliet, IL in 1962. He received his BS in chemistry (1984) from the University of Illinois, and his PhD in Materials Science and Engineering with Samuel Stupp (1989). After am NSF position at Caltech with Robert Grubbs and research at the University of Michigan in Ann Arbor, he returned in 1993 to the University of Illinois, where he is currently the William H. and Janet G. Lycan Professor of Chemistry and Materials Science and Engineering. His research focuses on molecular self-assembly, structure-controlled macromolecules and foldamers, stimuli-responsive materials, and self-healing polymers.

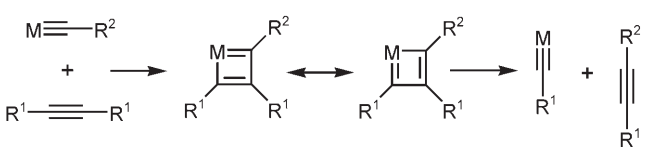
Wei Zhang was born in China in 1977. After completing his BS in chemistry in 2000 at Peking University and one year graduate study in University of Utah, he transferred to the University of Illinois at Urbana-Champaign in 2001, where he completed his PhD in chemistry with Prof. Jeffrey Moore, working on the development of a molybdenum-based alkyne metathesis catalyst and its application in the synthesis of shape-persistent macrocycles and conjugated polymers (2005). In March 2006 he assumed a postdoctoral position at MIT with Prof. Timothy M. Swager.

thesis in organic synthesis and polymer chemistry will be covered in Section 4. Finally, a comparison of alkyne metathesis to alkene metathesis is made in Section 5. Although there have been several previous articles reviewing related topics,[1b,h,3,5] here we emphasize the most recently developed catalyst systems and their high efficiency in addressing synthetic challenges in the field of organic and polymer chemistry.

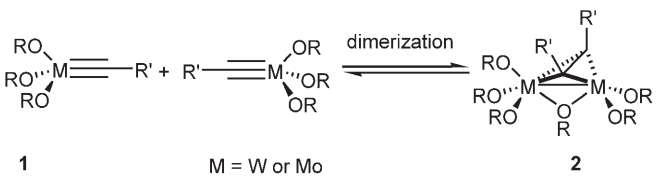
2 Mechanistic Overview

Analogous to alkene metathesis, in which the alkylidene units between two olefin compounds are mutually exchanged, alkyne metathesis refers to the exchange of alkylidyne units between a pair of acetylenes. Catalytic alkyne metathesis has been known for over three decades. In the late 1960s, a heterogeneous mixture of tungsten trioxide and silica was found to be able to catalyze alkyne metathesis at a very high temperature (200–450 °C).[6] A few years later, Mortreux reported the first homogeneous catalyst system generated from $Mo(CO)_6$ and resorcinol, which can catalyze the metathesis of *p*-tolylphenylacetylene at 160 °C.[7] However, the mechanism of this transformation was not well understood until 1975 when Katz first proposed the concept of an alkylidyne complex metathesizing acetylenes (Scheme 1).[8] In the proposed alkylidyne mechanism, metallacyclobutadienes are initially formed from acetylenes and alkylidyne complexes, analogous to metallacyclobutanes that are formed in alkene metathesis from olefins and metal alkylidene complexes.[9] The metathesis product is obtained following cycloreversion along the alternative metallocycle bonds. This mechanism was later experimentally established by Schrock using well-defined tungsten(VI) neopentylidyne complexes.[10] The isolated metallacyclobutadiene intermediates, which were generated from a formal [2+2] cycloaddition of alkylidynes and alkynes, were proven to be catalytically active toward metathesis.[11] This represents the first rational design of well-defined homogeneous catalyst for alkyne metathesis.

Both tungsten- and molybdenum-based alkylidyne species $(RO)_3M{\equiv}CR'$ (M = W or Mo) (**1**) are commonly in equilibrium with alkyne adducts of formula $M_2(OR)_6(\mu\text{-}C_2R'_2)$ (**2**) (Scheme 2), and the position of equilibrium is dependent on the nature of R and R′.[12,13] Bulky R and R′ combinations favor the alkylidyne species and the position of equilibrium is more



Scheme 1. Alkylidyne mechanism of alkyne metathesis.



Scheme 2. Dimerization pathway leading to catalyst deactivation.

sensitive to R rather than R′ group. If the formation of alkyne adduct **2** is strongly favored, the catalyst will essentially lose its activity, which is also known as the dimerization pathway leading to catalyst deactivation.[13] To avoid such problem, approaches manipulating the steric bulkiness and electronic properties of the ligands have been utilized, which will be discussed in the following section.

Another commonly encountered side reaction in alkyne metathesis is polymerization of small alkyne by-products, such as 2-butyne (Scheme 3). The polymerization is proposed to go through "ring expansion" mechanism, in which the small alkynes are repeatedly inserted into the metal-carbon bond.[10,14] In this scenario, the metathesis catalysts are transformed into vinyl alkylidyne species **3**, which would be unavailable for alkyne metathesis. This undesirable pathway could be prevented if the alkyne by-product is either more sterically bulky or insoluble in the reaction media, which will be discussed in Section 3.

In addition to the above-mentioned side reactions leading to catalyst deactivation, the efficiency of the metathesis reaction is also largely dependent on the competition between the productive and non-productive manifold ("pseudopoisoning" effect of the by-product on the metathesis catalyst), especially in the metathesis of alkyl aryl disubstituted substrates (e.g., butynyl-substituted aromatic substrate **4** in Scheme 4).[15] In alkyne metathesis, alkyl-substituted alkynes are more reactive than arylalkynes, and electron-deficient arylalkynes react slower than electron-rich arylalkynes.[14,16] Hence, the reaction of the catalyst with small alkyne by-product (e.g., 3-hexyne) is presumably favored over its reaction with starting aryl-substituted monomers or intermediate arylene-ethynylene oligomers. The catalyst is thus kinetically occupied with by-product rather than the desired elongation and/or cyclization; the non-productive route can dominate the catalytic activity. In such cases the dialkyl-substituted alkyne by-products should be avoided (or efficiently removed) if the metathesis of electron-deficient aryl substrates is to proceed with high conversion. Utilizing a benzoylbiphenyl-based endgroup in metathesis leading to the formation of an insoluble by-product represents a novel strategy[17] to overcome this "pseudopoisoning" problem, which will be discussed in Section 4.

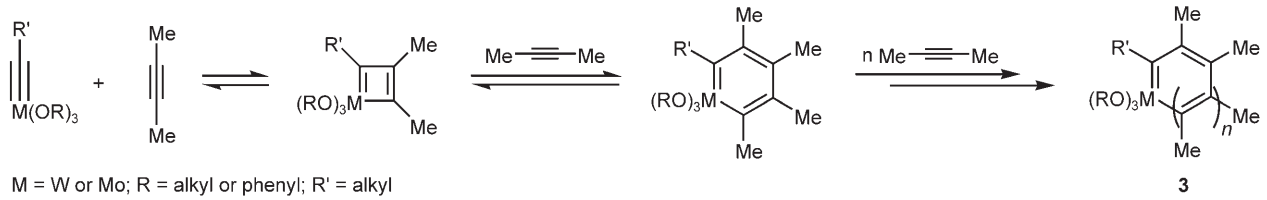
3 Catalyst Synthesis

Alkyne metathesis catalysts, either homogeneous or heterogeneous, are mainly tungsten or molybdenum-based with alkoxides or phenoxides as the ligand. The summary below is divided into homogeneous and heterogeneous systems and further subdivided by metal center.

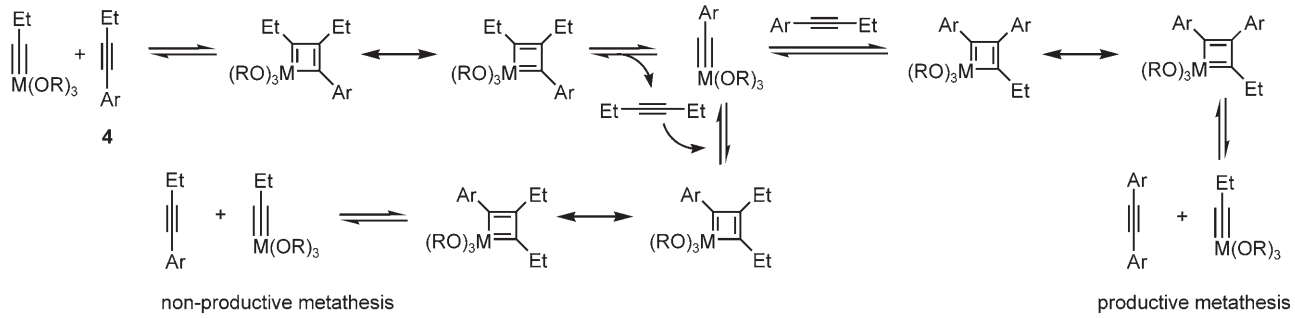
3.1 Homogeneous Systems

3.1.1 Tungsten-Based

In the early 1980s, Schrock and co-workers prepared several tungsten(VI) oxoalkylidene complexes (alkylidene ligand counted as a dianion), which catalyzed olefin metathesis at 25 °C.[18] They reasoned that if an alkylidyne complex was to catalyze the metathesis of



Scheme 3. Postulated ring expansion mechanism of polymerization of 2-butyne by-product.



Scheme 4. Productive metathesis *vs.* non-productive metathesis. Propylidyne catalyst and butynyl substituted aromatic substrate were used for illustration.

acetylenes, it probably should also contain tungsten(VI) (alkylidyne ligand counted as a trianion). The discovery of neopentylidyne complexes W(C-*t*-Bu)(CH_2-*t*-Bu)$_3$ (**5**),[19] which was the only tungsten(VI) alkylidyne species known at that time, created the possibility of preparing active alkyne metathesis catalysts.

Reaction between WCl_6 and neopentyllithium generates alkylidyne **5**, which is not a good candidate for metathesis catalyst due to the reactivity of those alkyl ligands. Further treatment of complex **5** with HCl and 1,2-dimethoxyethane (DME) provides another alkylidyne species, tungsten(VI) trichloride **6**. Although a stable tungstacyclobutadiene complex forms readily upon addition of one equivalent of an internal alkyne to complex **6**, the metallacyclic species **7**, instead of going through desired cycloreversion, reacts further with alkyne to yield reduced tungsten side products **8** that contain a peralkylated cyclopentadienyl ring. In contrast, the trialkoxytungsten(VI) alkylidyne complex **9**, prepared *via* replacing chloride in **6** with *tert*-butoxy group using lithium *tert*-butoxide, is highly active for the metathesis of ordinary internal alkynes (Scheme 5a).[20] The bulky alkoxide ligands are utilized to prevent or significantly slow down the dimerization pathway (Scheme 2). Complexes containing other common bulky ligands (e.g. alkyls, thiolates, amides) were also tested and showed little activity, presumably owing to the fact that the element bound to the metal (i.e., C, N, S) is not as electronegative as oxygen.[21] Chloride ligands are sufficiently electronegative, but they also readily bridge between metals and promote rapid disproportionation or other decomposition reactions. Thus, bulky alkoxides represent the best ligand for alkyne metathesis activity. More recently, it was reported that compound **9** can also be prepared from metathesis between $(Me_3CO)_3W{\equiv}W(OCMe_3)_3$ (**10**)[22] and neoheptyne **11** (Scheme 5b), which is a more convenient synthetic approach.[5]

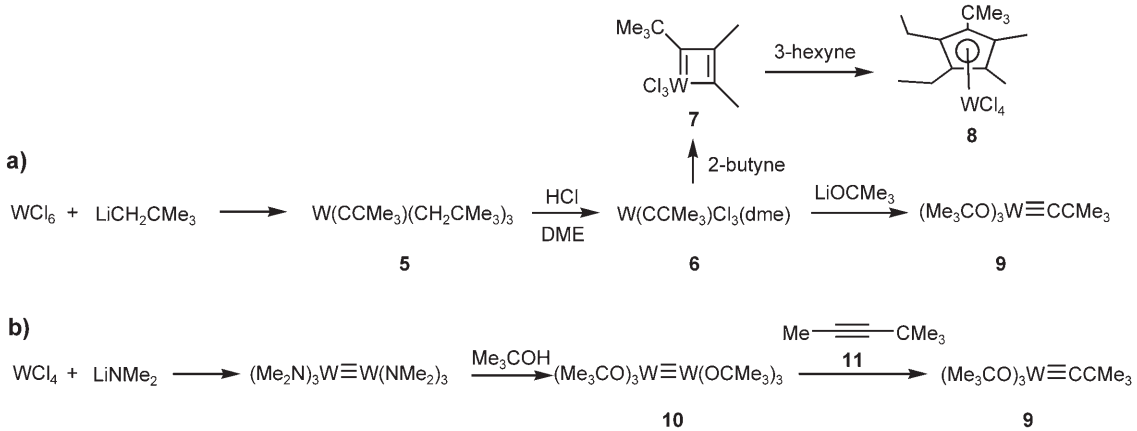
Schrock's neopentylidyne catalyst **9** represents the only catalytically active, well-defined tungsten-based species among all the alkyne metathesis catalysts that have been utilized. Complex **9** is metathesis active under fairly mild conditions (room temperature to 90 °C) and its behavior is well understood at the molecular level.[21] The utility of this complex is evident from its role in performing the first ring-closing alkyne metathesis (RCAM) reactions,[23] and since then has been successfully employed in natural product syntheses.[24–27] Although this catalyst tolerates many functional groups, the metathesis becomes problematic when the substrates used contain thio ethers, amines or crown either segments.[24] It is suggested that these donor sites might deactivate catalyst **9** by coordination to its high-valent tungsten center.[28]

3.1.2 Molybdenum-Based

3.1.2.1 Trialkoxymolybdenum(VI) Alkylidynes Prepared from Mo(C-*t*-Bu)(CH_2-*t*-Bu)$_3$

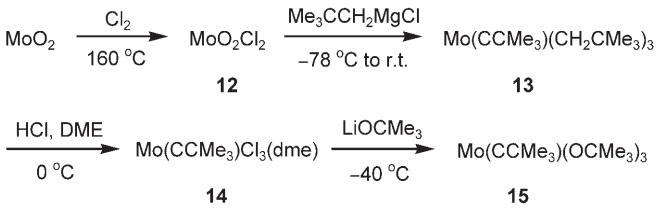
Given the successful development of tungsten-based metathesis catalyst, investigation of the feasibility of using d^0 molybdenum alkylidyne complexes to catalyze alkyne metathesis attracted attention, since the known classical homogeneous catalysts contained molybdenum metal centers, not tungsten.[7] It was deemed possible to enhance and control the activity of these ill-defined molybdenum-based catalysts through ligand variation, as has been achieved in the tungsten system. The idea of a well-defined molybdenum catalyst was thus very appealing.

Initial studies on molybdenum-based catalysts were impeded by the problematic synthesis of molybdenum(VI) propylidyne **15**, which only gave low and irreproducible yields.[19] In the middle 1980s, Schrock and co-workers made progress in optimizing the synthesis, which produced Mo(C-*t*-Bu)(CH_2-*t*-Bu)$_3$ in 35 % yield on a moderate scale (6–7 g).[16] The synthesis starts from reaction of MoO_2 with chlorine gas, providing MoO_2Cl_2 (**12**). Treatment of **12** with the



Scheme 5. Synthetic routes to trialkoxytungsten(VI) alkylidyne **9**.

Grignard reagent *t*-BuCH$_2$MgCl followed by hydrochloric acid, afforded molybdenum alkylidyne **14**, which upon alcoholysis furnished trialkoxymolybdenum(VI) complex **15** (Scheme 6). Although internal alkynes did not react with **15**, replacing the *tert*-butoxide with fluoroalkoxide ligands generated active species, which could react smoothly with internal alkynes.



Scheme 6. Synthetic route for trialkoxymolybdenum(VI) alkylidyne **15**.

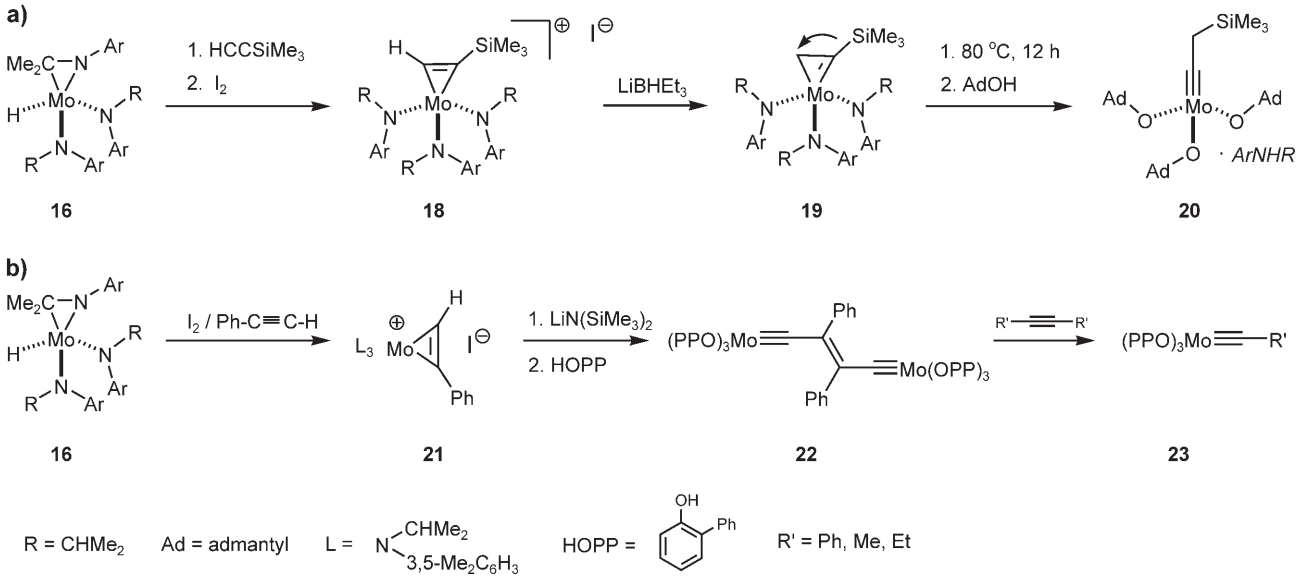
3.1.2.2 Trialkoxymolybdenum(VI) Alkylidynes Prepared from Metallaaziridine-Hydride

Over one decade later, Cummins reported an improved synthetic route to molybdenum-based alkylidyne catalysts.[29] The synthesis starts with a metallaaziridine-hydride complex **16**, which is known[30] to serve as a source of the three-coordinate molybdenum(III) complex Mo[N(*i*-Pr)Ar]$_3$ **17** (Scheme 7a). Treatment of **16** with excess trimethylsilylacetylene followed by iodine oxidation produced the yellow salt **18**. Further reaction of **18** with [Li][BHEt$_3$] provided the η^2-vinyl derivative **19**, which rearranges to the alkylidyne complex *via* a 1,2-migration of the trimethylsilyl group.[31] Upon addition of 3 equivs. of 1-adamantyl alcohol, the trialkoxymolybdenum(VI) alkylidyne complex **20** could be isolated as a crystalline solid that retained 1 equiv. of ArNHR. So far only adamantoxymolybdenum derivatives have been insoluble enough to isolable in pure form.[5] In this case, the bulky alkoxide ligand was again used to prevent catalyst deactivation through a dimerization pathway. More recently, Cummins also reported a new synthetic route utilizing the reductive coupling of molybdenum(IV) acetylides toward the construction of trialkoxy alkylidynes **23** (Scheme 7b).[32] It turned out that the enedialkylidyne **22** itself can also serve as an efficient metathesis precatalyst.

All the molybdenum catalysts with either adamantoxy or phenoxy ligand have shown metathesis activity at ambient temperature. The above synthetic routes to trialkoxymolybdenum(VI) alkylidynes represent a significant improvement compared to the original route to trialkoxyalkylidyne complexes,[16,33] which was more time-consuming and not amenable to large-scale production. However, the scope of these catalysts is yet to be fully studied, leaving questions about the strength and limitations of these catalytic species.

3.1.2.3 Molybdenum-Based Catalyst generated from Mo(III) Triamide and CH_2Cl_2

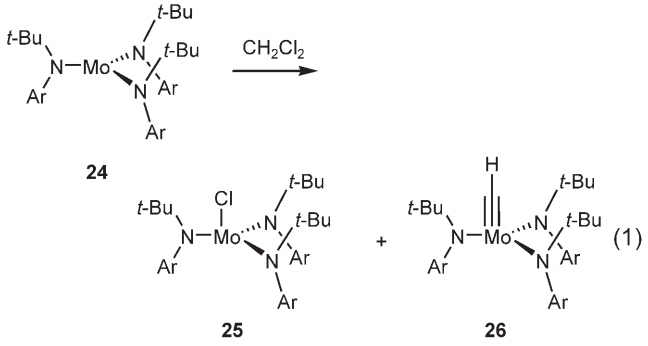
Following on the pioneering work of Cummins' on the molybdenum species of the general type Mo[N(*t*-Bu)Ar]$_3$ **24** (the analogue of compound **17**),[34–37] which activate the triple bond of dinitrogen in a stoichiometric fashion, Fürstner and co-workers investigated the reactivity of this type of compounds for alkyne metathesis. Although compound **24** (Ar = 3,5-dimethylbenzene) was not metathesis active on its



Scheme 7. Synthetic route to trialkoxymolybdenum(VI) alkylidyne **20** and **23**.

own, treatment of **24** in toluene with >2 equivs. of CH_2Cl_2 at 80 °C produced a mixture capable of efficiently catalyzing the metathesis of acetylenes bearing various aliphatic or aromatic substituents.[38] Using CH_2Cl_2 as the solvent turned out to be equally effective as using toluene as solvent with CH_2Cl_2 addition. Activation of **24** with other geminal dihalides (e.g., CH_2Br_2, $PhCHCl_2$, etc) also generated catalytically active species for alkyne metathesis.

Analysis of the products derived from the reaction of molybdenum triamide **24** with CH_2Cl_2 indicated the presence of several molybdenum species by NMR and MS. The major components of this mixture with a ratio of about 1:2 were the molybdenum monochloride species **25** and molybdenum methylidyne complex **26**[39] [Eq. (1)].[28] The reactivities of these two species



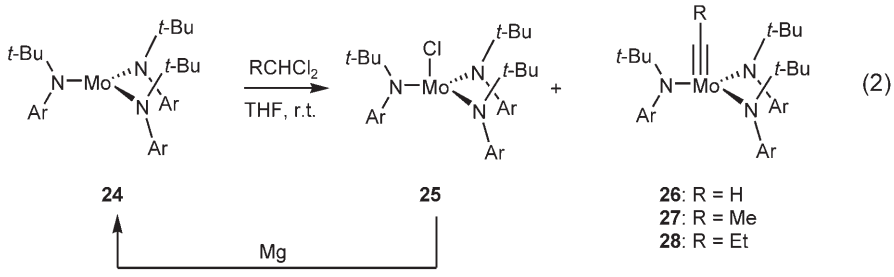
were studied in a model reaction, which showed that the monochloride compound **25** is the catalytically active species, while the terminal alkylidyne **26** was only poorly effective, which may be explained by the known propensity of terminal alkylidynes to suffer ligand loss, forming "deprotio metallacyclobutadiene" complexes along the reaction pathway.[5,21,40] The catalytic activity of the terminal alkylidyne was also studied by subjecting 2-butynylbenzene to metathesis conditions catalyzed by pure **26**, which was obtained *via* reductive recycle strategy (see below).[41] The observed low conversion (11%) of starting acetylene further demonstrated that **26** is catalytically inactive.

Although only monochloride **25** is metathesis active, the generated mixture in Eq. (1) can serve as the catalyst, making this "*in situ*" approach very convenient. This catalytic system is fully operative at 80 °C, compatible with a variety of functional groups, including thio ethers, crown ether segments, or amines which completely inactivate the tungsten alkylidyne catalyst **9**.[38] Such favorable reactivity is rationalized by the crowded coordination sphere around the molybdenum center of the precatalyst which could attenuate its effective Lewis acidity and prevents coordination of potential donor sites to the central metal leading to catalyst deactivation.[28] However, limits were encountered with substrates containing the thiophene moiety or the protons of a secondary amide.[38] Also, detailed understanding of the catalytically active species and the pathway from **25** is highly desirable, potentially benefiting the future design of more active catalysts.

3.1.2.4 Molybdenum-Based Catalysts Prepared *via* Reductive Recycle Strategy

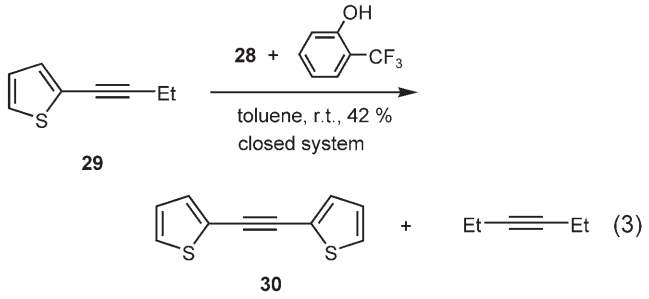
Although trialkoxymolybdenum(VI) alkylidynes (i.e., complex **20**) can be conveniently obtained from alcoholysis of the metathesis inactive triamide, the starting complex (i.e., complex **26**) requires a time-consuming, multistep synthetic procedure and presents a practical limitation.[29,42] Therefore, development of an alternative strategy for the preparation of trisamidomolybdenum(VI) alkylidynes was pursued.

Taking advantage of the reaction discovered by Fürstner, which generated an inseparable mixture of molybdenum(IV) monochloride **25** and molybdenum(VI) methylidyne **26** [Eq. (1)], we developed a strategy for selective formation of alkylidyne complexes.[14,41] Our original thinking was that if molybdenum triamide **24** reacted with a *gem*-dihalide such as 1,1-dichloropropane to produce propylidyne **28** and monochloride **25**, it should be possible to find conditions that selectively reduced **25** in the presence of **28** returning this undesired product to the parent trisamido compound **24**. Indeed in the presence of magnesium and excess 1,1-dichloropropane, an 89% yield of **28** was obtained. We called this procedure the reductive recycle approach, although to date we have not investigated the mechanism to confirm that this is indeed the actual pathway. Other mechanisms could be conceived. The strategy is generally useful for preparing various molybdenum alkylidynes **26**–**28**. By



using the reductive recycle strategy, molybdenum(VI) propylidyne **28** was successfully prepared on the multi-gram scale [Eq. (2)].[43]

Alcoholysis of **28** with 3 equivs. of phenol or alcohol generated a catalytically active species, which was directly applied to metathesis studies. The catalyst is metathesis active in a variety of solvents, even in acetonitrile and THF which are usually considered coordinating solvents. However, because alkoxide ligands are displaced by water or methanol, protic solvents and adventitious water should be avoided, which represents a general drawback for most of the alkyne metathesis catalysts currently utilized. The catalyst is also compatible with a broad range of functional groups, even protons of a secondary amide, which is problematic to the catalyst generated from molybdenum(IV) monochloride **25**.[38] Moreover, for the first time the catalyst enabled the metathesis of thiophene-containing substrate **29** [Eq. (3)], which had not previ-

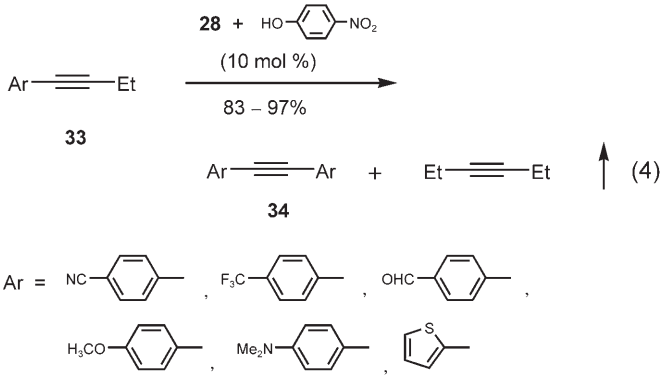


ously been achieved by any other homogeneous alkyne metathesis catalyst.[4,28] Realizing the full substrate scope greatly benefited from investigations of the alkynyl substituent effect on metathesis reaction, from which we found that in the metathesis of small molecules, the butynyl substituent is superior to the propynyl group due to the inertness of hexyne by-product (*vs.* butyne by-product generated from propynyl substrates) toward catalyst-initiated polymerization side reaction (Scheme 3).[44]

Owing to the importance of electronic effects of the ligands on metathesis activity, further optimization on the catalyst efficiency was accomplished by a ligand survey, in which a variety of phenols and alcohols were tested as ligands.[14] Reactivity studies showed that the catalytic activity of molybdenum complexes was improved upon increasing the electron-withdrawing character of the ligands, and the catalyst from *p*-nitrophenol **31** or 2,3,5,6-tetrafluoro-4-trifluoromethylphenol **32** displayed the highest activity. In addition to the fast reaction rates, the low cost of *p*-nitrophenol prompted us to select this ligand for further studies.

It was surprising to see the high activity of the catalyst generated from *p*-nitrophenol, which is just a simple phenol, not bulky at all. Usually bulky alkoxides are used as catalyst ligands to prevent catalyst deactivation *via* the dimerization pathway (Scheme 2).[21] However, the success of the *p*-nitrophenol catalyst seems to indicate that the bulkiness of the ligand is not a prerequisite for high catalyst activity. Presumably, bulky ligands not only prevent catalyst dimerization, but also slow down the desired metathesis reaction, making the catalyst less reactive. On the other hand, small ligands (e.g., *p*-nitrophenol) greatly facilitate the desired metathesis. In these cases the metathesis equilibrium reaches completion before catalyst dimerization significantly occurs.

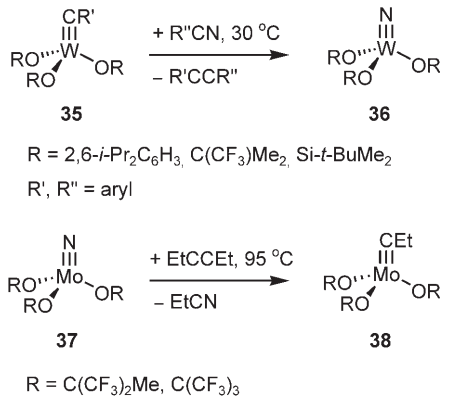
By using the catalyst generated from molybdenum triamide **28** and *p*-nitrophenol, under dynamic vacuum conditions, the metathesis of butynyl-substituted substrates **33** with various functional groups provided alkyne dimer products **34** in 83–97% isolated yield [Eq. (4)], which represents a synthetic ap-



proach to acetylene derivatives. Such highly active catalysts also enabled the preparation of defect-free arylene-ethynylene conjugated polymers[45] as well as provided a highly efficient, one-step synthesis of shape-persistent macrocycles,[15,17,46] which will be discussed in detail in Section 4. High sensitivity of this catalyst to air and moisture represents a limitation and identifies a grand challenge for future catalyst development.

3.1.2.5 Molybdenum-Based Catalyst Prepared from Nitrides by Metathesis with Alkynes

Recently Johnson reported another synthetic route to trialkoxymolybdenum(VI) alkylidyne complexes *via* metathesis of molybdenum nitride with alkynes.[47] Complex **38** was first prepared two decades ago by Schrock, who demonstrated its activity in alkyne metathesis reactions.[16] Johnson found that although in the case of trialkoxytungsten(VI) complex **35**, the formation of nitride **36** from alkylidyne **35** and nitrile is favored,[48–50] the molybdenum(VI) analogue showed thermodynamic preference for the formation of alkylidyne complex from nitride species and alkynes (Scheme 8). Although no terminal nitrido com-



Scheme 8. Conversion of tungsten alkylidyne to nitride complex *vs.* conversion of molybdenum nitride to alkylidyne species.

plexes were formed in the reaction between propylidyne complex **38** and nitriles, heating nitride **37**[51] with 3-hexyne and 1 equiv. of DME at 95 °C for several days generated compound **38**. This indicated that the alkylidyne complexes are formed irreversibly from the nitride complexes, but with a large activation barrier. Higher reaction rate was achieved in the absence of DME and conversion to the propylidyne **38** is quantitative after 14.5 h at 95 °C. The generated catalyst **38** with highly fluorinated alkoxide ligands showed metathesis activity in the homodimerization of propynylbenzene at room temperature. However, the scope of this catalyst has not been reported.

3.1.2.6 Molybdenum-Based Catalyst Generated *in situ* from $Mo(CO)_6$ and Phenol

Another type of homogeneous catalyst is based on $Mo(CO)_6$ and phenol additives, which was briefly mentioned in Section 2. A catalytically active species is generated *in situ* from $Mo(CO)_6$ or related molybdenum sources and phenols at elevated temperatures. Such a catalyst system was initially discovered by Mortreux,[7,52] and later improved and widely used by Bunz,[4,53,54] Mori,[55] Fürstner[3] and more recently Grela.[56,57] This "instant" method is attractive because all the ingredients are inexpensive, commercially available and stable "off the shelf" reagents can be used directly without the rigorous purifications and an inert atmosphere.[58] However, this catalytic system shows poor compatibility with some heteroatom functional groups, such as esters, aldehydes, pyridines etc.[53] Moreover, this system requires high temperatures ($\geq$ 130 °C) to be catalytically active, restricting its application to only robust substrates.

To improve this catalyst system, a variety of approaches were examined, including purging the reaction mixture with nitrogen to facilitate by-product removal,[53,59] temperature adjustment and the utilization of chelating 1,2-diphenyloxyethane additive,[60] which improved the reaction yields and reaction rates to some extent. Further extension of the scope and the use of lower temperature was achieved by a pre-activation approach, in which $Mo(CO)_6$ and phenols were heated either with[54] or without[60] 3-hexyne prior to substrate addition. More recently, Grela and co-workers surveyed a variety of phenols as catalyst additives and identified 2-fluorophenol and 2-fluoro-5-methylphenol as optimal.[57]

Despite considerable optimization on this catalyst system, its relatively harsh operative conditions as well as the low activity towards highly functionalized substrates present limitations in its wide application in organic synthesis and polymer chemistry. Moreover, the exact nature of the catalytically active species is still not clear. Better mechanistic understanding on this system would help further improving its catalytic activity.[61]

3.1.3 Comparison of Available Catalysts

There is, as of yet, no ideal catalyst system for alkyne metathesis. Each catalyst has its own advantages and drawbacks. An attempt to compare the known catalysts is made in Table 1, regarding the convenience of catalyst preparation, functional group incompatibility, operative temperature, commercial availability, sensitivity to air/moisture, and realized synthetic applications.

3.1.4 Theoretical Investigation of Alkyne Metathesis Catalyzed by W/Mo Alkylidynes

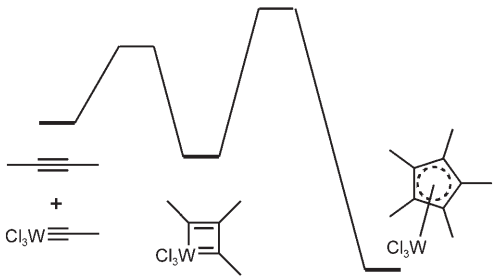
Given that many theoretical studies previously conducted on olefin metathesis have improved the understanding of the reaction mechanism and enabled the development of new catalysts,[62] detailed theoretical studies on alkyne metathesis are expected to be of great help in gaining deeper insight into the current catalyst systems.[63]

Recently, Jia and Lin performed theoretical calculations based on the B3LYP density functional theory to examine structural and energetic aspects related to the possible reaction pathways of alkyne metathesis.[64] Their calculations showed that the alkyne binding capability of the metal alkylidyne species correlates to the stability of the transition states in the initial metallacyclobutadiene formation step and the following cycloreversion step. Compared with tungsten alkylidyne compounds bearing alkoxide ligands, those analogues with amide ligands have poorer alkyne binding ability due to the stronger W(VI)-NR_2 π-bonding interaction, consistent with known catalytic

Table 1. Comparison of alkyne metathesis catalysts.

Catalyst	$(t\text{-BuO})_3W{\equiv}CC(Me)_3$	$(AdO)_3Mo{\equiv}CCH_2SiMe_3$	$Mo[NAr(t\text{-}Bu)]_3+CH_2Cl_2$	$EtCMo[NAr(t\text{-}Bu)]_3$ + *p*-nitrophenol	$EtCMo[OC(CF_3)_2Me]_3$	$Mo(CO)_6$ + phenol
Steps from commercial sources	4	8	4	5	4	0
Functional group incompatibility	amines, thioethers, polyether, thiophene	unknown	thiophene, secondary amide	acidic hydrogen	unknown	Lewis basic heteroatom functional groups
Operative temperature	r.t. to 90 °C	r.t.	80 °C	r.t.	r.t.	130 to 160 °C
Commercial availability	yes	no	no	no	no	yes
Sensitivity to air/H_2O	high	high	high	high	high	low[58]
Demonstrated synthetic applications	cross-metathesis, RCAM, polymer synthesis	cross-metathesis	cross-metathesis, RCAM	cross-metathesis, polymer synthesis, cyclooligomeri- zation	cross-metathesis	cross-metathesis, polymer synthesis, cyclooligomerization

performance. For trialkoxymolybdenum(VI) alkylidyne species with electron-rich ligands, the transition state structure leading to the metallacyclobutadiene is strongly disfavored. The difficulties stem from the significant deformation of the complex and the alkyne substrate due to the less diffuse *d* orbitals at the Mo center compared to W. However, introduction of electron-withdrawing groups to the alkoxide ligands significantly increases the alkyne binding capability of Mo(VI) alkylidyne species, lowering the barrier to the metallacyclic intermediate. Calculations also revealed that the poor metathesis activity of alkylidyne complexes containing chloride ligands (**6**) is due to a high energy barrier for the cycloreversion step and a relatively low barrier for the formation of cyclopentadienyl (Cp) side products (**8**) through a second alkyne insertion into the metallacyclobutadiene intermediate (Scheme 9).[65] While the calculation results are consistent with experimental findings, they reinforce the importance of the electronic effects of ligands on catalyst activity.



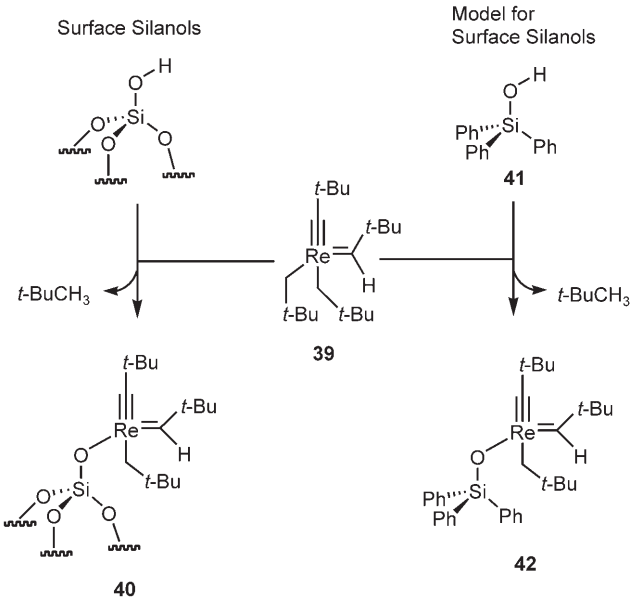
Scheme 9. Schematic representation of the energy profile for cycloreversion *vs.* cyclopentadiene formation from tungsten trichloride-based metallacyclobutadiene intermediate.

3.2 Heterogeneous Systems

Much effort has been devoted to development of "well-defined" heterogeneous catalysts. The advantages of heterogeneous catalysis include avoiding catalyst deactivation through a bimolecular dimerization pathway,[13,21] easy separation of products from metals and catalyst recycling. Although the first heterogeneous catalyst for alkyne metathesis, which consists of a mixture of tungsten trioxide and silica, was discovered over three decades ago, its extremely harsh operative conditions (200–450 °C) has greatly impeded practical use.[6] In contrast to the many homogeneous catalyst systems reported so far, heterogeneous catalysis for alkyne metathesis is less developed. Within the past a few years, two different silica-supported transition metal catalysts were reported.[66,67]

3.2.1 Silica-Supported Rhenium Catalyst

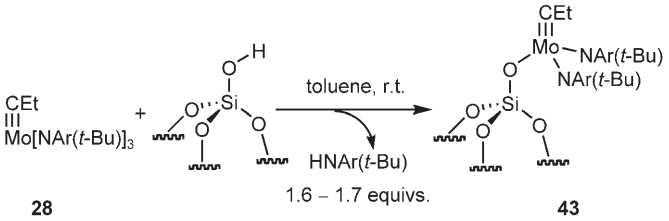
In 2001 Basset and co-workers reported a silica-supported rhenium catalyst, which represents the first example of a heterogeneous catalyst for alkyne metathesis.[66] Catalyst **40** was generated from mixing a d^0-Re(VII) complex **39** with SiO_2 in pentane at 20 °C (Scheme 10). The product was characterized by ^1H and ^{13}C NMR. Microanalysis results indicated the grafting of one Re per silanol. Additional evidence for **40** was gained from model compound **42** with a triphenylsiloxy substituent in place of a siloxy group of the silica surface. The obtained rhenium species can catalyze the metathesis of 2-pentyne at room temperature with equilibrium reached being in 20 min. However, further work on this catalyst toward alkyne metathesis has yet to be reported. Further studies exploring the substrate scope of this system is desired.



Scheme 10. Preparation of Re(VII)-based heterogeneous catalyst **40** and its model species **42**.

3.2.2 Silica-Supported Molybdenum Catalyst

Very recently we described the molybdenum-based heterogeneous catalyst **43**, which was prepared simply by mixing triamide **28** with a suspension of silica in toluene at room temperature (Scheme 11).[67] Elemental analysis of the impregnated silica indicated an average Mo/aniline ratio of 1:1.35 on the surface. Further evidence for the formation of **43** was obtained from IR, X-ray photoelectron spectroscopy (XPS) and ^{13}C-MAS NMR. The scope of the metathesis activity of **43** was probed with acetylene substrates with



Scheme 11. Preparation of Mo(VI)-based heterogeneous catalyst **43**.

alkyl, thienyl, benzoate and anisole substituents. Half-lives at room temperature of less than 1 h were generally observed, even with as little as 0.8 mol % catalyst loading. The fact that catalyst **43** was able to metathesize propynyl derivatives, including the well known problematic thiophene-containing substrate,[4,14] without the undesirable interference of polymerization, demonstrates the practical success of the heterogeneous approach in controlling the coordination sphere around the molybdenum center. The recyclability of catalyst **43** was tested on propynyl thiophene with an initial 4.0 mol % catalyst loading. Three cycles produced conversions in the range of 32–52 %, respectively. The three-phase test demonstrated that the metal center does not dissociate from the silica support. The applicability of this system for preparative synthesis was demonstrated by the gram-scale metathesis of 1-phenyl-1-propyne at room temperature under vacuum conditions, providing the homodimer in 88 % isolated yield. Such a readily accessible heterogeneous catalyst system, with high catalytic activity and good stability, represents another useful synthetic tool in the field of alkyne metathesis.

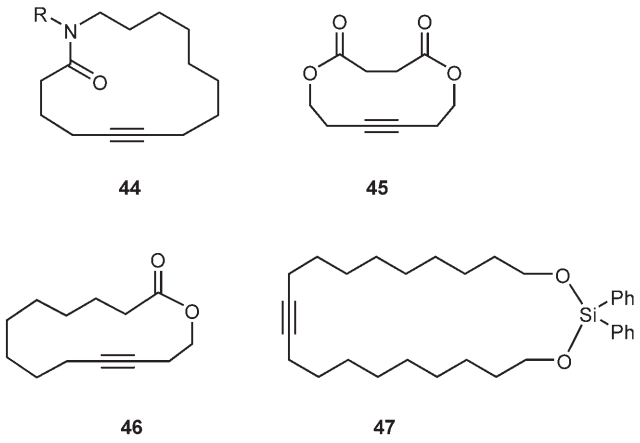
4 Synthetic Applications of Alkyne Metathesis

4.1 Ring-Closing Alkyne Metathesis (RCAM)

Given the successful application of ring-closing metathesis (RCM) in macrocycle formation,[1,68,69] Fürstner and co-workers investigated the possibility of closing acyclic diynes to generate large cyclics by using alkyne metathesis.[3] In their early studies, they found that efficient preparations of functionalized macrocycles were achieved by RCAM, catalyzed by tungsten alkylidyne **9** at 80 °C under high dilution in either trichlorobenzene, chlorobenzene or toluene. In some cases higher conversions were obtained with removal of butyne or hexyne by-product under vacuum. More importantly, they showed that cyclic products with ring size 12 or greater can be obtained in good to excellent yields,[23] demonstrating the general usefulness of RCAM in synthesizing large cyclic alkynes

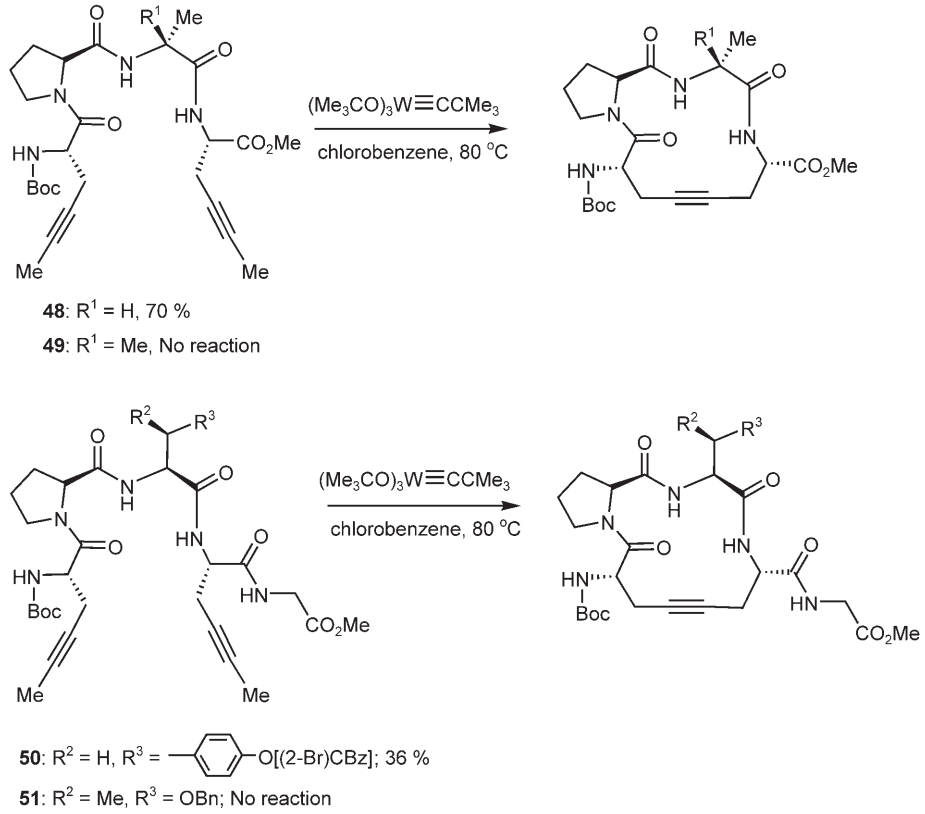
(Scheme 12). They also tested the "instant approach", generating catalytic species *in situ* from $Mo(CO)_6$ and phenol additives, in RCAM reactions and showed that this system is also applicable to macrocycle synthesis at 135 °C but displays a narrower substrate scope due to its poor functional group compatibility.[24]

Recently Overhand and co-workers reported the synthesis of conformationally restricted peptidic β-turn mimics.[70] A range of oligopeptides **48**–**51** containing two acetylenic amino acids were prepared and subjected to metathesis cyclization conditions in the presence of tungsten catalyst **9** (Scheme 13). In contrast to the productive cyclization of **48** (70% yield) and **50** (36% yield), cyclization of **49** and **51** proved to be unsuccessful. The results indicate that the nature of the dipeptide (mimic) linking the two acetylenic amino acid moieties plays a key role for a productive RCAM event. 2D NMR analysis of the cyclic products indicates that replacement of a disulfide bridge with an acetylene moiety makes the cyclic peptides more rigid, thus favoring additional interstrand proton-proton interactions.

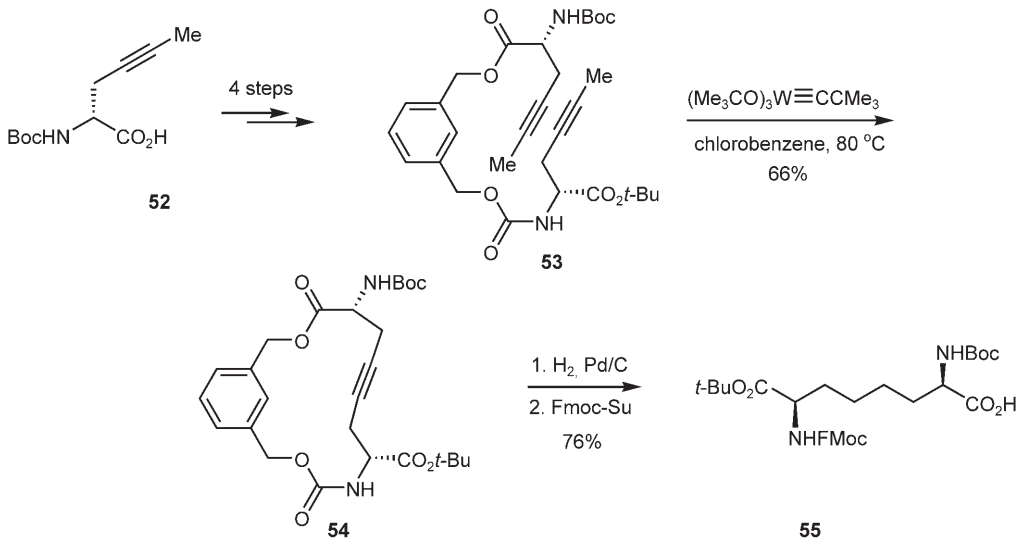


Scheme 12. Representative examples of large cyclic alkynes prepared *via* RCAM.

van Boom et al. reported the synthesis of diaminosuberic acid (DAS) derivatives *via* RCAM.[71] As shown in Scheme 14, the orthogonally protected adduct **53** was prepared from **52** in four steps. Tungsten alkylidyne **9** mediated cyclization of **53** provided cyclic alkyne **54** in 66% yield. Catalytic hydrogenation of **54** followed by protection of the resulting amine with an Fmoc group gave the orthogonally protected diaminosuberic acid product **55** in 76% yield. Alternatively, the *Z*-alkene derivative can also be obtained from **54** by Lindlar reduction. Such a synthetic approach allows the preparation of stereochemically pure saturated and unsaturated cysteine isosters as the free diaminodicarboxylic acids or in orthogonally protected form. With both enantiomers of the starting amino acids available, thus ensuring access to all possible diastereomers, selective reduction of the triple



Scheme 13. Synthesis of conformationally restricted peptidic β-turn mimics *via* RCAM.



Scheme 14. Synthesis of diaminosuberic acid derivative **55** *via* RCAM.

bond allows the synthesis of geometrically pure and conformationally restricted DAS derivatives.

Recently Gladysz and co-workers reported the synthesis of metallamacrocycles catalyzed by either tungsten alkylidyne **9** or molybdenum catalyst of "instant approach".[72,73] As shown in Scheme 15a–c, reaction of complex **56–58** with phosphine ligand **59** gave the linear precursor **60–62** in 30–54% isolated yield. In the presence of tungsten complex **9**, metathesis of **60–62** went smoothly, even in the case of complex **62**, which involves antiperiplanar- or *trans*-directed groups making cyclization intrinsically more difficult. Metallamacrocycles **63–65** were obtained in 47–59% isolated yield. Further hydrogenation of **65** in the presence of Pd/C catalyst provided **66** with a saturated carbon bridge between the phosphorus atoms in 87% yield. Interestingly, in the presence of molybdenum catalyst, metathesis of **60** provided *trans*-chelate product **67** instead of the isomeric *cis*-chelate product **63** as obtained from the tungsten-catalyzed reaction. Surprisingly, the nature of the catalyst could affect the metallamacrocycle product. All these macrocycles exhibit good thermal stabilities and showed no tendency to cyclooligomerize. This synthetic approach provides a valuable complement to earlier developed alkene metathesis and improves the applicability of metal-catalyzed metathesis reactions to the preparation of architecturally unusual inorganic and organometallic complexes.[74]

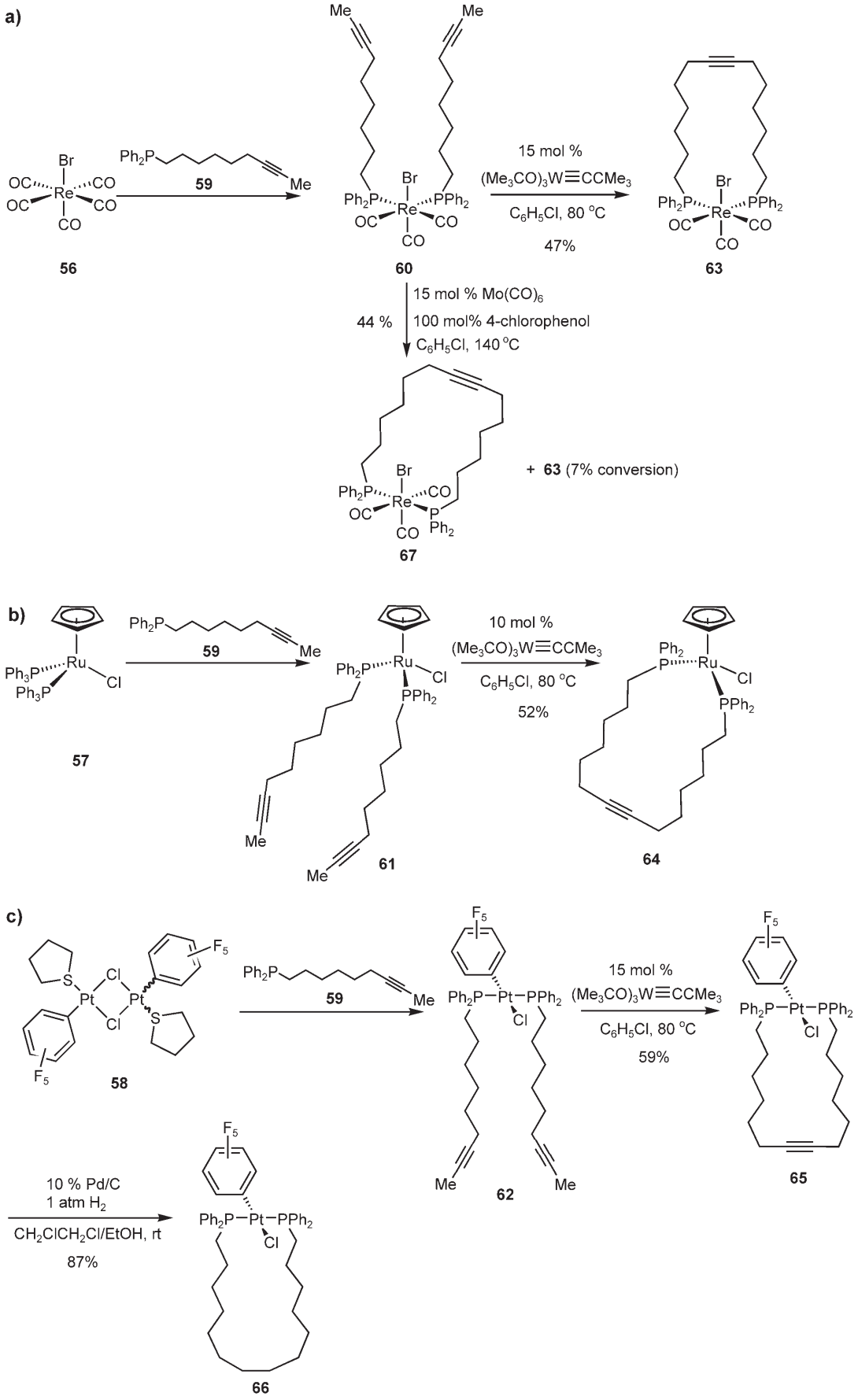
4.2 Natural Product Synthesis

4.2.1 Macrocyclic (*Z*)-Alkenes

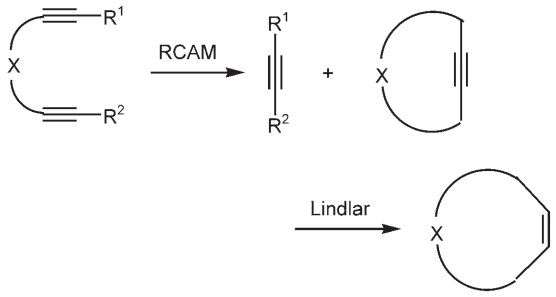
RCM of acyclic dienes has been widely applied to the synthesis of carbo- and heterocycles of almost any size including medium and macrocyclic products.[1,68] However, a significant drawback remains with these cyclization reactions: while RCM generally enables formation of large rings in good to excellent yields, the stereochemistry of the newly formed double bond can hardly be predicted and in many cases is difficult to control. Often mixtures of both geometrical isomers are obtained, and the separation of these is usually difficult. This problem strongly affected the key cyclization step in the synthesis of epothilone A, in which the 16-membered ring was formed *via* RCM.[75] To address this deficiency of RCM, Fürstner envisioned RCAM/semireduction as a viable solution.[28] The combination of RCAM and Lindlar reduction of the resulting cycloalkynes constitutes a stereoselective route to (*Z*)-alkenes, which are often the less favorable product of RCM (Scheme 16). This two-step process applies similar retrosynthetic logic as RCM while having the advantage of better control on double bond stereochemistry.

Fürstner pioneered the synthesis of natural products *via* the RCAM approach.[3] They first utilized the RCAM/semireduction method to synthesize naturally occurring musks containing (*Z*)-configured alkenes.[24] As shown in Scheme 17, RCAM of diyne **68** proceeded smoothly in the presence of either a catalytic amount of tungsten alkylidyne (71% isolated yield of **69**) or by means of the "instant approach" using $Mo(CO)_6$ and *p*-chlorophenol (67% isolated yield of **69**). Lindlar reduction of the resulting cycloalkyne **69** followed by deprotection of the N-Fmoc group with TBAF gave epilachnene **70** in good overall yield. Its higher homologue homoepilachnene **71** was also obtained by following a similar synthetic route.

The catalyst system of Mo(III) triamide **24** and CH_2Cl_2 was also applied to the synthesis of cyclic natural products.[76,77] As shown in Scheme 18, esterifica-



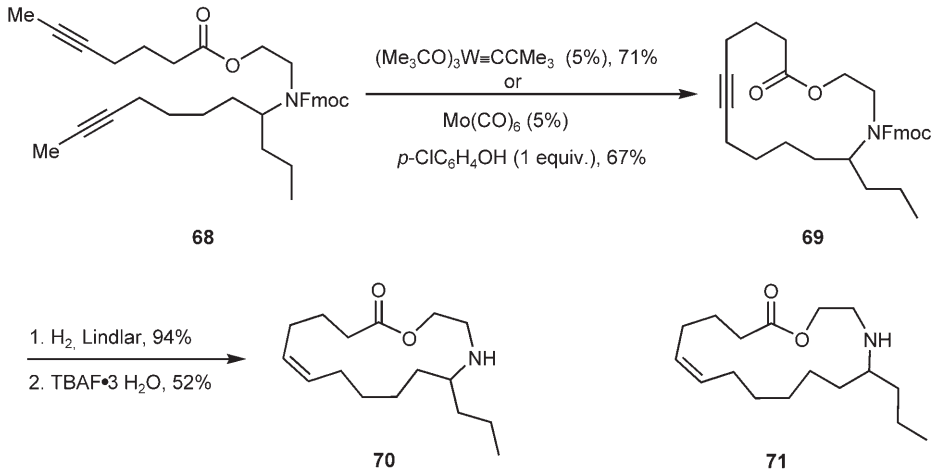
Scheme 15. Synthesis of metallamacrocycles **63**–**67** *via* RCAM.



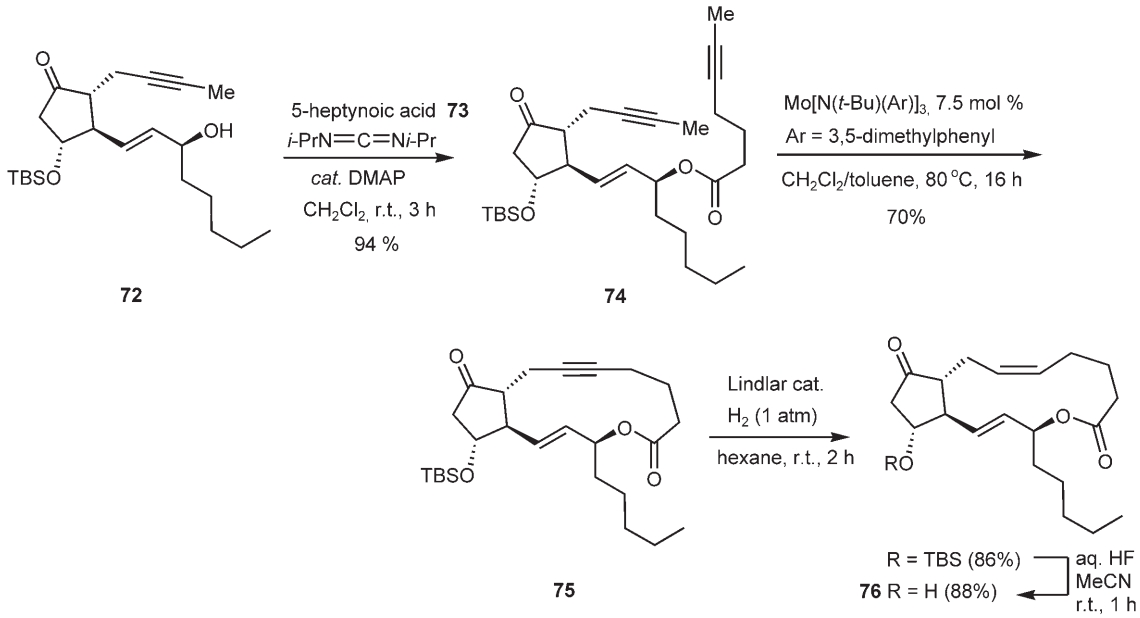
Scheme 16. RCAM/semireduction approach toward stereoselective synthesis of macrocyclic (*Z*)-alkenes.

tion of secondary alcohol **72** with 5-heptynoic acid **73** provided diyne **74**, the precursor for RCAM. The key macrocyclization step proceeded very well in the presence of the metathesis catalyst (**24**/CH_2Cl_2), affording the desired cycloalkyne **75** in 70% yield. Standard Lindlar hydrogenation of **75** followed by deprotection of the residual TBS ether completes the total synthesis of the marine natural product prostaglandin E2-1,15-lactone **76**. It should be noted that this RCAM approach into the prostaglandin series is inherently flexible. Esterification of **72** with alkynoic acids other than **73** followed by RCAM opens a rather general way for the assembly of prostaglandin libraries.

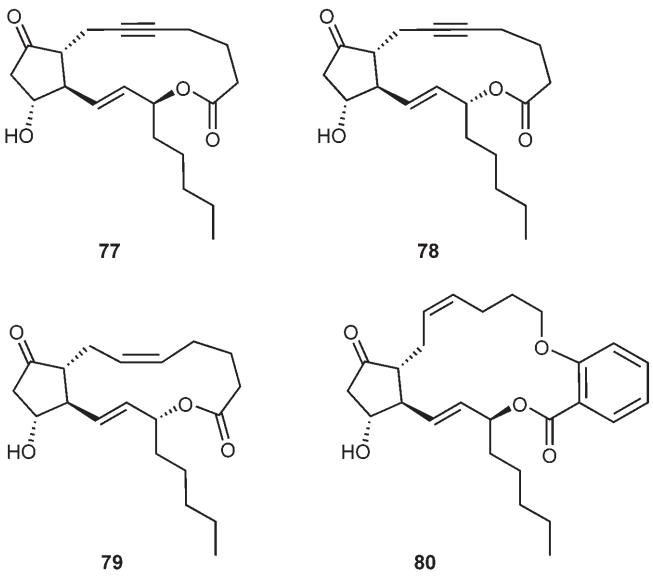
This approach does not require installation of modified α-chains and has been successfully applied to the synthesis of several analogues of **76** (**77**–**80**) (Scheme 19), further demonstrating its strategic advantages over more conventional approaches. The



Scheme 17. Synthesis of epilachnene **70** by using RCAM/semireduction approach.



Scheme 18. Synthesis of prostaglandin E2-1,15-lactone **76**.



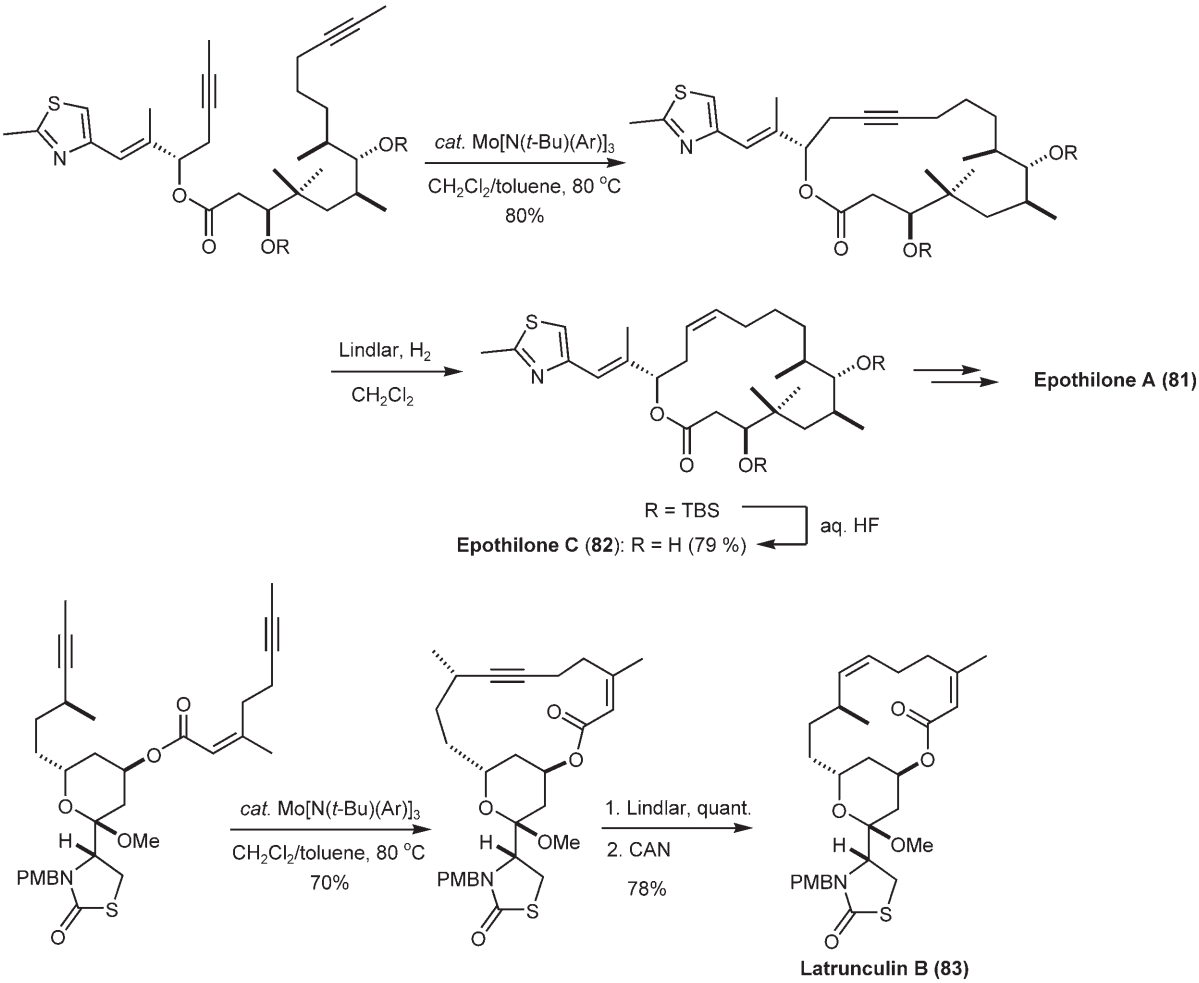
Scheme 19. Analogues of prostaglandin E2-1,15-lactone **76**.

route also demonstrates the ability to conduct alkyne metathesis in the presence of alkenes. In contrast, alkene metathesis in the presence of alkynes is more problematic.[1]

Recently, application of this RCAM/semireduction method to more challenging synthetic targets was reported.[78] Epothilones A (**81**) and C (**82**) as well as lactrunculins (**83**) were successfully prepared in good yield (Scheme 20). In all cases, the pre-existing alkene moieties were unaffected, demonstrating the high chemoselectivity of the alkyne metathesis catalyst.

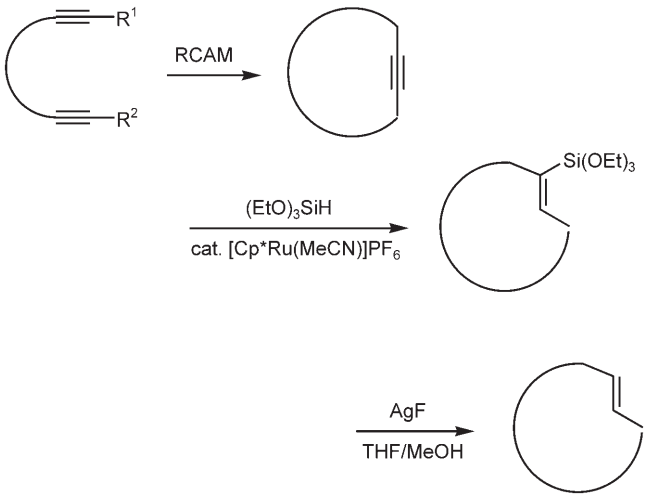
4.2.2 Macrocyclic (*E*)-Alkenes

Although the synthesis of macrocyclic (*Z*)-alkenes *via* RCAM/semireduction is well established, the complementary stereoselective synthesis of (*E*)-alkenes *via* semi-reduction has been less thoroughly developed. Many of the known methods for transforming acetylenes to (*E*)-alkenes either have poor selectivity or are incompatible with functional groups.[79] Recently,



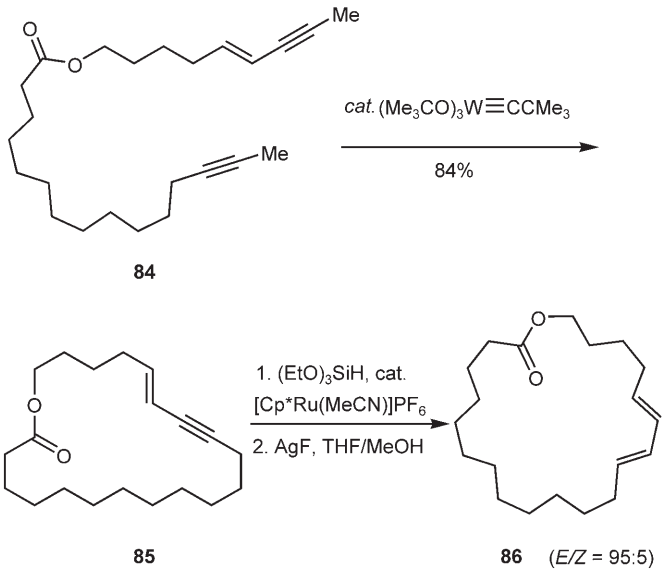
Scheme 20. Synthesis of epothilones A and C and lactrunculins *via* RCAM/semireduction approach.

Trost[80] and Fürstner[81] independently developed a general and mild procedure based on a hydrosilylation/protodesilylation strategy. The use of ruthenium complex $[Cp^*Ru(MeCN)_3]PF_6$ and $(EtO)_3SiH$ for hydrosilylation of the alkynes enabled a highly chemo- and stereoselective *trans* addition[82] in good yields and also showed good compatibility with a variety of functional groups. In the desilylation step, AgF was used as a mild fluoride source, which led to rapid, quantitative and selective desilylation under mild conditions (Scheme 21). The overall set of conditions holds promise for the application of this three-step procedure (RCAM/hydrosilylation/protodesilylation) to synthesis of natural products containing (*E*)-cycloalkene skeletons.



Scheme 21. RCAM/hydrosilylation/protodesilylation approach for synthesis of (*E*)-cycloalkenes.

The feasibility of this three-step method was demonstrated in the synthesis of (*E,E*)-cycloalkadienes **86** (Scheme 22).[81] RCAM of enyne-yne substrate **84** catalyzed by tungsten alkylidyne **9** provided lactone **85** in good yield. Subsequent chemoselective *trans*-hydrosilylation at the alkyne site, followed by protodesilylation with AgF afforded 1,3-diene product **86**. This work also represents the first step of applying the RCAM approach towards the total synthesis of natural products containing macrocyclic diene structures.



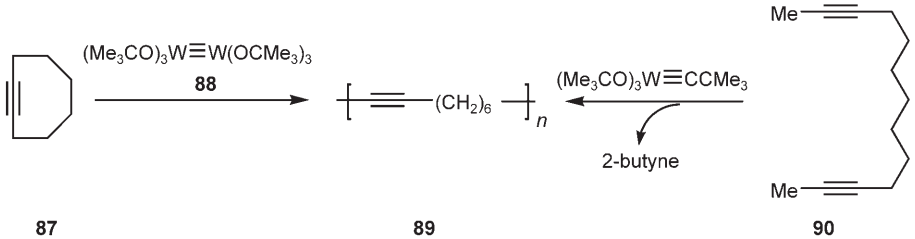
Scheme 22. Synthesis of cycloalkadiene **86** *via* RCAM/hydrosilylation/protodesilylation approach.

4.3 Polymer Synthesis

4.3.1 Ring-Opening Alkyne Metathesis Polymerization

In contrast to the wide application of RCAM in organic synthesis, ring-opening alkyne metathesis has not been intensively investigated. Probably the main reason for this is the lack of suitable substrates. Two examples are briefly discussed below.

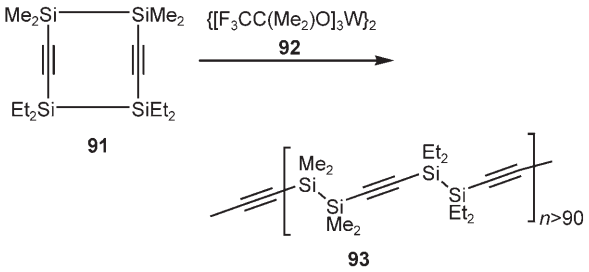
In the late of 1980s, Schrock reported the polymerization of the strained cyclic monomer **87** by ring-opening metathesis, in which tungsten dimer complex **88** was utilized as catalyst precursor (Scheme 23).[83] The insoluble elastomer **89** was obtained as polymeric product with a wide molecular weight distribution, $M_w/M_n > 4$. This result indicates either the initiation step occurs sluggishly or the polymer already formed is partially degraded (back-biting) to cyclooligomers, which suggests this polymerization cannot be regarded as "living". The corresponding polymer **89** can also be obtained by the step growth process known as acyclic diyne metathesis (ADIMET) (see Section 4.3.2).



Scheme 23. Ring-opening metathesis polymerization of monomer **87**.

Removal of 2-butyne from 2,10-dodecadiyne **90** gives **89** in good yield.

Bazan and co-workers later reported a further application of ring opening alkyne metathesis in the polymerization of cyclodiyne **91** (Scheme 24).[84] By using catalyst precursor **92**, monomer **91** was regiospecifically polymerized to the head-to-tail product **93**, which was rationalized by the steric effect of alkyl substituents. The disilane polymer **93** became conducting upon treatment with SbF_5, and also showed attractive optical properties.



Scheme 24. Ring-opening metathesis polymerization of monomer **91**.

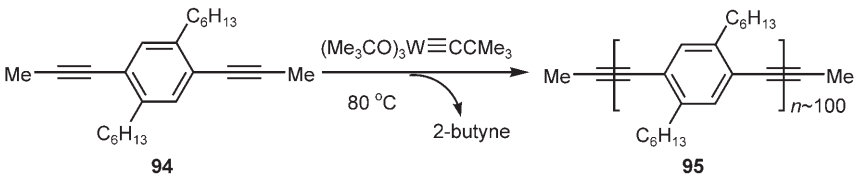
4.3.2 Acyclic Diyne Metathesis Polymerization

Poly(*p*-phenylene-ethynylene)s (PPEs)[4,85] or poly(arylene-ethynylene)s[86] (PAEs) are the dehydrogenated analogues of the PPVs,[87] and they have been intensively studied due to their desirable electronic and optical properties.[4,85,86,88] The conventional synthesis of PAEs is mainly restricted to Pd/Cu-catalyzed coupling reactions, which is often limited in its ability to achieve high molecular weight and well-defined endgroups without the presence of diyne defects in the polymer backbone.[89] The drawbacks of Pd-catalyzed coupling reactions make it desirable to develop a complementary synthetic route to PAEs, and alkyne metathesis was envisioned as an attractive alternative.[4]

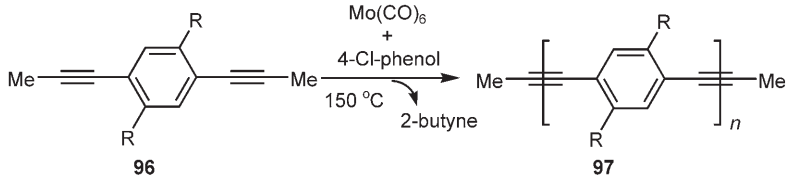
Weiss and co-workers first reported the synthesis of PPEs by alkyne metathesis (Scheme 25).[90] Catalyzed by tungsten alkylidyne **9** at 80 °C, ADIMET of 2,5-dihexyl-1,4-dipropynylbenzene monomer **94** provided PPE **95** in good yield, and the degree of polymerization (P_n) reached almost 100 repeating units. The NMR and mass spectra of **95** confirmed the presence of propynyl endgroups. The optical and spectroscopic properties of **95** are identical with those of the polymer synthesized by cross-coupling methods, thus indicating the ADIMET route to PPE is competitive with the more common Pd-catalyzed synthetic scheme.

The catalyst system $Mo(CO)_6$/phenol has been extensively applied to PPE synthesis due to its convenient generation. A series of dipropynylated benzenes **96** was prepared and subjected to ADIMET, providing PPEs **97** in quantitative yields and high purity (Scheme 26).[91,92] It was found that the degree of polymerization (P_n) is strongly dependent on the side-chains. Although PPE **97** with hexyl side-chains never exceed a P_n of 100, due to insufficient solubility of the polymer in the reaction medium, PPEs with up to 1200 repeating units were reported when long side-chains were employed as solubilizing groups.[92]

Given the success in synthesizing PPEs **97**, metathesis of other propynylated aromatic monomers was also tested. Metathesis copolymerization of monomer **98** and **96b** afforded a series of random copolymers



Scheme 25. Synthesis of PPEs **95** *via* acyclic diyne metathesis polymerization of monomer **94**.



a R = C_6H_{13}
b R = $C_{12}H_{25}$
c R = 2-ethylhexyl
d R = 3,7-dimethyloctyl
e 1:1 copolymer from **a** and **b**

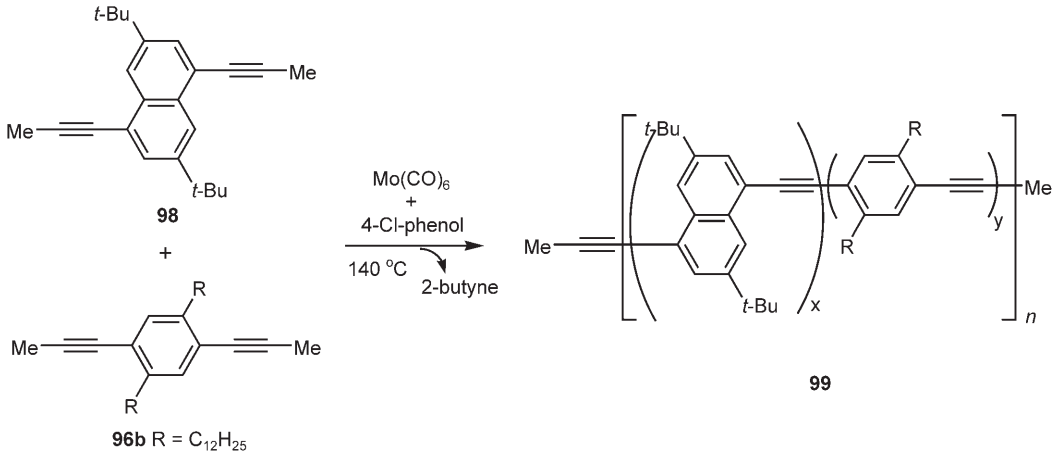
Scheme 26. Synthesis of PPEs **97** *via* acyclic diyne metathesis polymerization of monomers **96**.

99, in which naphthyl and phenylene units are separated by an alkynyl group (Scheme 27).[93] These copolymers were obtained in high yield, with moderate to high degrees of polymerization ($30 < P_n < 100$). With a high solid-state photoluminescent quantum yield of blue light emission, PPE **99** is an attractive candidate for OLED applications.

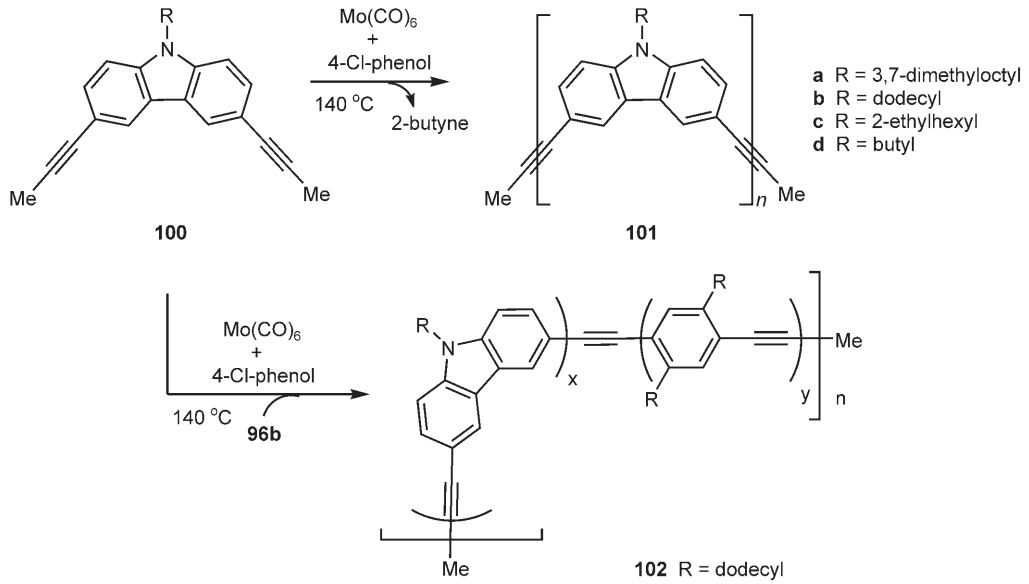
More recently, Bunz and co-workers also reported the metathesis of carbazole-based monomers **100**, which gave polymers **101** in good yields (Scheme 28).[94] These polymers show a blue shift in their fluorescence upon addition of a poor solvent. Copolymerization of monomer **100b** and **96b** was also conducted and the degree of polymerization increased with decreasing carbazole content, possibly because heteroatom-containing monomers react relatively sluggishly in ADIMET as compared with pure hydrocarbon monomers when the Mortreux catalytic system is utilized.[53] The fluorescence of emissive polymer **102** can be reversibly quenched by the addition or removal of TFA.

Although the Mortreux catalytic system has been intensively applied to polymer synthesis *via* ADIMET, its limited functional group tolerance and requirement of high temperatures restrict its use mainly to hydrocarbon PPE synthesis. At temperatures above 150 °C, the polymer products contain defect structures which limit extended conjugation.[92] Moreover, small-scale polymerizations are reported to give material of lower P_n, making this approach not generally useful for the laboratory synthesis of PPEs.[92]

Recently we applied the molybdenum-based catalyst from **28** and *p*-nitrophenol[14,41] to poly(thieny-

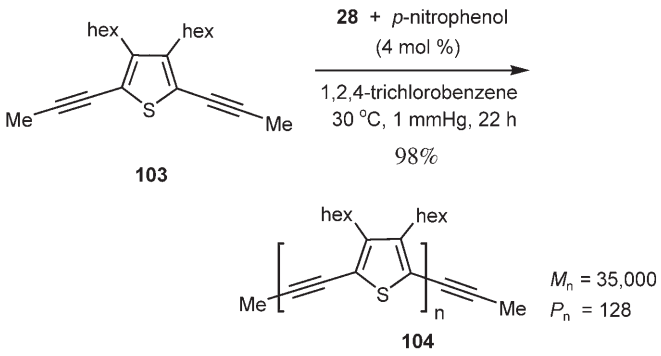


Scheme 27. Synthesis of copolymer **99** *via* acyclic diyne metathesis of monomers **98** and **96b**.



Scheme 28. Synthesis of carbazole-based polymer **101** and copolymer **102** *via* acyclic diyne metathesis polymerization.

lene-ethynylene) (PTE) synthesis, which represents much milder conditions for PAE preparation *via* ADIMET.[45] Polymerization of thiophene monomer **103** was conducted in 1,2,4-tricholobenzene at room temperature under open driven conditions,[95] providing defect-free, high molecular weight PTEs with P_n = 128 (Scheme 29). Polymer **104** showed similar absorption and emission features to the previously reported PPEs.[96] The well known incompatibility issue of the thiophene functional group in alkyne metathesis[4,28] prevented other catalytic systems from accomplishing this transformation.



Scheme 29. Synthesis of PTEs **104** *via* acyclic diyne metathesis polymerization of monomer **103**.

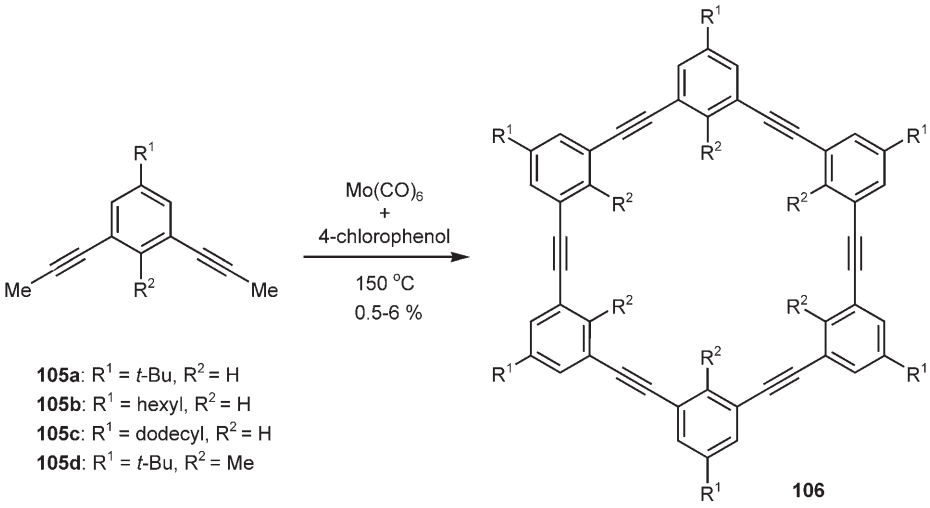
4.4 Cyclooligomerization

Shape-persistent arylene-ethynylene macrocycles have attracted great attention in supramolecular chemistry and materials science due to their unique structures and novel properties.[2,97] Conventional macrocycle synthesis mainly relies on cross-coupling approaches.[98] The primary disadvantage of the coupling methods is the kinetically determined product distribution, in which a significant portion of oligomers grow beyond the length of the cyclic targets ("overshooting").[2] Such problems can be resolved by using a dynamic covalent approach involving reversible alkyne metathesis reactions that afford macrocycles in one step starting from simple monomers.

Bunz and co-workers first reported the synthesis of hexakis(phenylene-ethynylene) macrocycles *via* alkyne metathesis utilizing the Mortreux catalytic system.[99] Metathesis of dipropynylated monomer **105** in 1,2-dichlorobenzene at 150 °C provided macrocycles **106** in 0.5–6 % yield (Scheme 30). An X-ray crystal structure analysis revealed that hydrocarbon macrocycle **106a** arranges into stacked tubular structures with internal channels, even without the help of hydrogen bonding or long alkyl chains. van der Waals interactions alone are suggested to be sufficient to line up these rings into tubular forms.

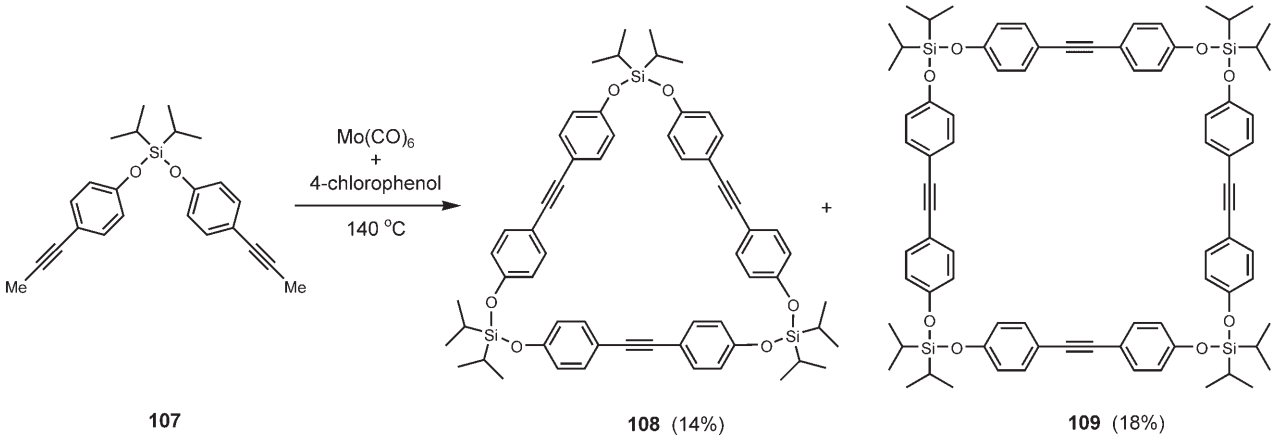
Similarly, silicon-containing phenylene-ethynylene cyclic trimer **108** and tetramer **109** were prepared from metathesis of corresponding dipropynylated monomer **107** with isolated yields of 14 % and 18 %, respectively (Scheme 31).[100] Crystalline **109** exhibits a rhomboidal structure that contains a large interior cavity occupied by two molecules of hexane, indicating the potential applications of these box-shaped molecules in host-guest chemistry.

Schrock's tungsten catalyst was also utilized in macrocycle synthesis as reported by Vollhardt and coworkers.[101] Metathesis of diyne monomer **110** at 80 °C in toluene provided trimeric macrocycles **111** in yields of 12–54 % (Scheme 32). However, the doubly *ortho*-substituted precursors **110e–f** did not undergo cyclization, presumably due to the steric hindrance caused by the substituents beside the alkyne groups, impeding the metathesis reactions.



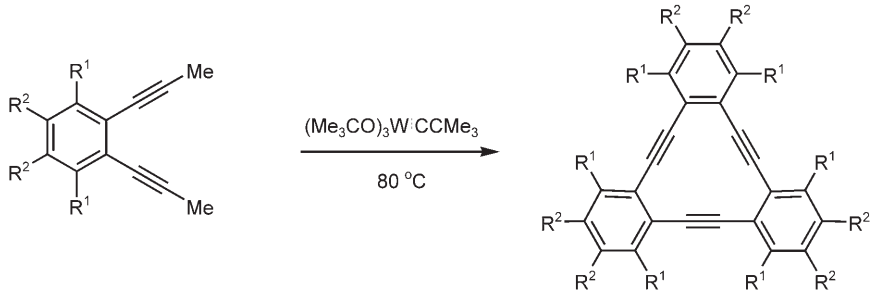
105a: R^1 = *t*-Bu, R^2 = H
105b: R^1 = hexyl, R^2 = H
105c: R^1 = dodecyl, R^2 = H
105d: R^1 = *t*-Bu, R^2 = Me

Scheme 30. Synthesis of hexameric phenylene-ethynylene macrocycles **106** *via* alkyne metathesis.



107 **108** (14%) **109** (18%)

Scheme 31. Synthesis of macrocycle **108** and **109** *via* alkyne metathesis of monomer **107**.



110a: $R^1 = R^2 = H$
110b: $R^1 = H$, $R^2 = Me$
110c: $R^1 = H$ $R^2 = OMe$
110d: $R^1 = H$, $R^2 = Br$
110e: $R^1 = R^2 = Me$
110f: $R^1 = Br$, $R^2 = H$

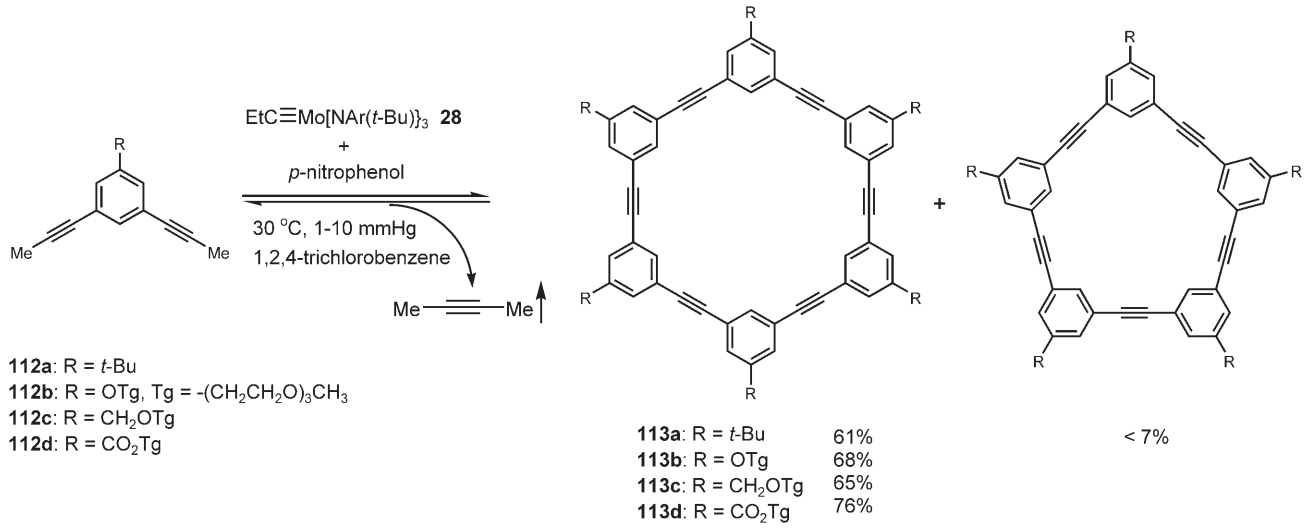
111a: $R^1 = R^2 = H$ (54%)
111b: $R^1 = H$, $R^2 = Me$ (27%)
111c: $R^1 = H$ $R^2 = OMe$ (28%)
111d: $R^1 = H$, $R^2 = Br$ (12%)
111e: $R^1 = R^2 = Me$ (0%)
111f: $R^1 = Br$, $R^2 = H$ (0%)

Scheme 32. Synthesis of trimeric macrocycles **111** *via* alkyne metathesis.

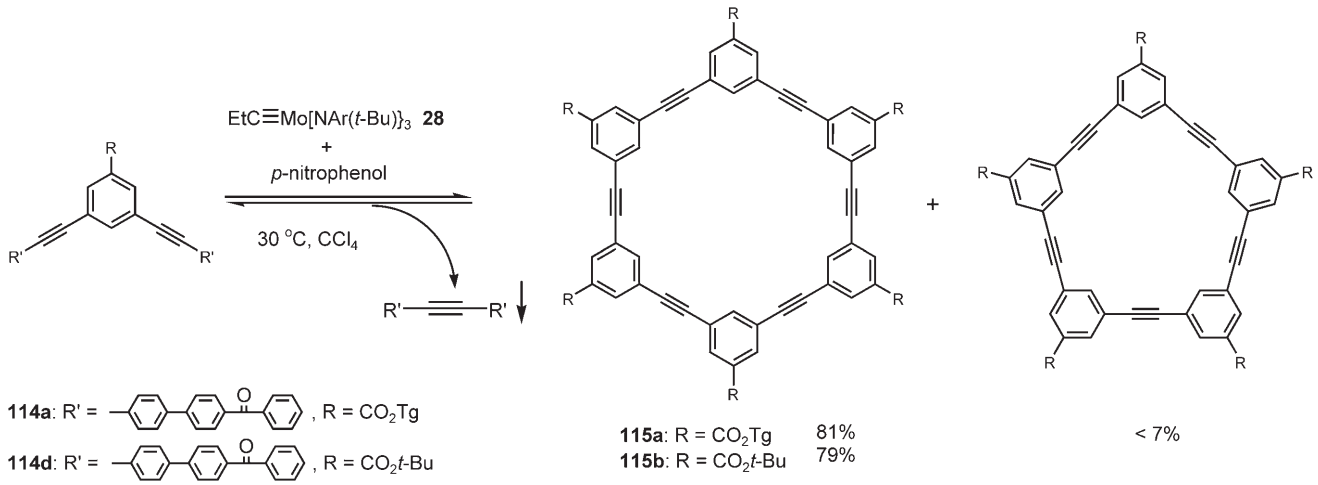
To further improve the efficiency (higher product yield, less catalyst loading) of macrocycle synthesis and more importantly to enable low-temperature dynamic covalent approaches, we investigated the macrocycle synthesis *via* alkyne metathesis utilizing the room temperature molybdenum catalyst derived from **28** and *p*-nitrophenol.[17]

Although the metathesis of dipropynylated monomers **112** under conventional vacuum-driven conditions afforded hexameric macrocycyles **113** in good yields on a small scale (15–33 mg) (Scheme 33), further increasing the scale of the vacuum-driven strategy turned out to be problematic and macrocycles were obtained in poor yields and with considerable amounts of unreacted starting monomers and oligomeric products. Failure to scale the reaction was thought to be due to the "pseudopoisoning" effect of the by-product on the metathesis catalyst (Scheme 4);[15] the catalyst is occupied in the non-productive metathesis with 2-butyne (3-hexyne) and not available to perform the desired cyclooligomerization. The accumulated 2-butyne by-product may also deactivate the catalyst *via* polymerization through ring-expansion mechanism (Scheme 3).

To overcome this pseudopoisoning effect and improve the efficiency of alkyne metathesis for macrocycle preparation, we developed a precipitation-driven alkyne metathesis approach, in which a poorly soluble, less-reactive diarylacetylene by-product enables the efficient removal of the by-product from the reaction mixture, thus allowing the desired metathesis reaction to be performed in a closed system.[17] Precipitation rather than evaporation serves as the driving force to shift the metathesis equilibrium. This approach has the additional advantage that all substrates react at comparable rates and none of the by-products are prone to polymerize. The high efficiency of this novel approach was demonstrated by successful metathesis of diynes **114** at 30 °C, providing macrocycles **115** in high yields (Scheme 34). Moreover, the multigram synthesis of **115a** was accomplished in one step by using this precipitation-driven method (5.68 g,



Scheme 33. Synthesis of hexameric macrocycles **113** under vacuum-driven conditions.

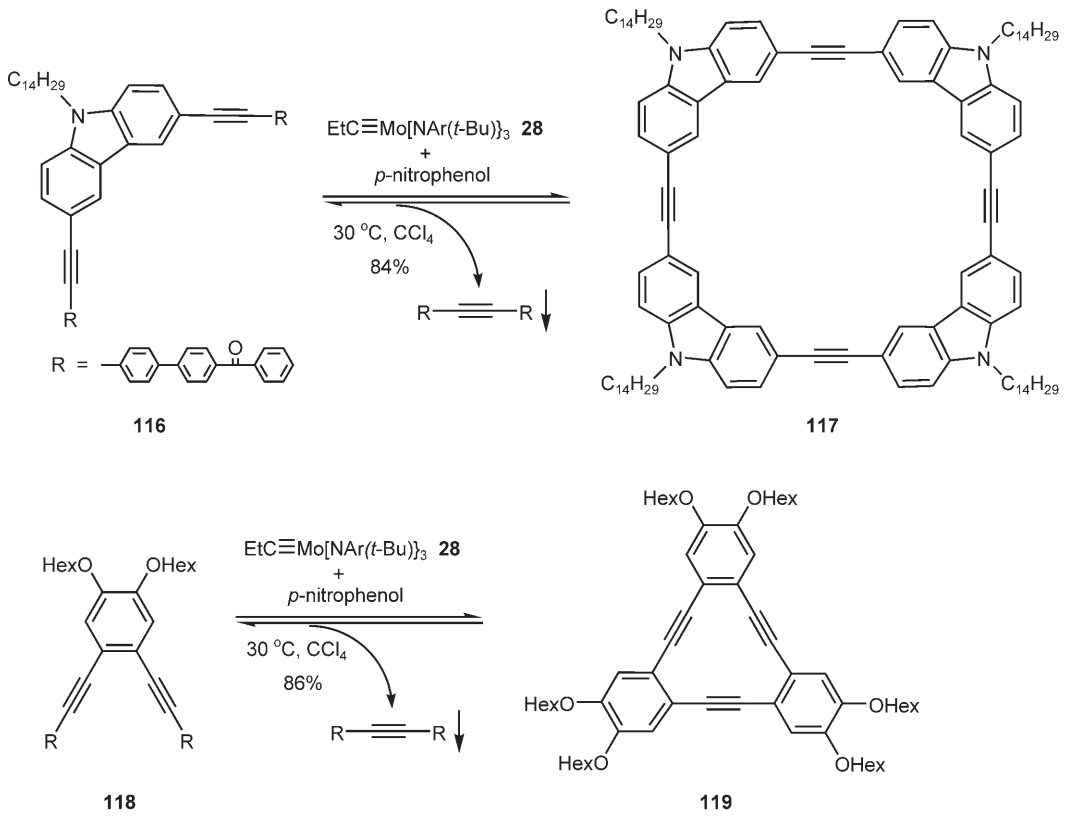


Scheme 34. Synthesis of hexameric macrocycles **115** under precipitation-driven conditions.

77%), which represents the first successful large-scale preparation of hexakis(phenylene-ethynylene) macrocycles.[17] These results highlight the significant advantages of precipitation-driven alkyne metathesis over the traditional vacuum-driven approach. Moreover, the product is isolated simply by filtration followed by concentration of the solution.

The generality of this precipitation-driven strategy was further demonstrated by the high-yielding syntheses of tetrameric carbazole-based macrocycle **117** (84%)[17,102] and trimeric macrocycle **119** (86%)[46] from their corresponding diyne monomers **116** and **118** (Scheme 35). In both cases, the target macrocycles are the only products observed in the reaction mixtures. It is interesting to note that the low temperature route using catalyst form **28** in Scheme 35 generates macrocycles while the high temperature route using *in situ* catalyst from $Mo(CO)_6$ in Scheme 28 gives polymeric products. Very recently, nanofibril structures were prepared from macrocycle **117** through a gelating process.[103] The favorable 1D molecular assembly is proposed to result from the decreased mobility of molecules during the gelation, which minimizes the steric hindrance of side-chains. In addition to the large cavity size (9.5 Å), macrocycle **117** has a highly rigid, π-conjugated backbone in a totally planar conformation, which holds great promise for its 1D self-assemblies to produce a new type of nanomaterials with well-fined, non-collapsible internal channels, that have interesting potential applications in nanoscale optoelectronic devices.

We further conducted a series of experiments toward mechanistic understanding on the reaction pathway of marocycle formation, which successfully



Scheme 35. Synthesis of carbazole-based tetrameric macrocycle **117** and catechol-based trimeric macrocycle **119** *via* precipitation-driven alkyne metathesis.

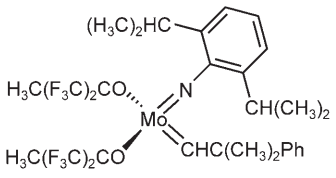
revealed the underlying "energy gap" principle for the selective generation of certain arylene-ethynylene macrocycles *via* alkyne metathesis.[2,15] We also demonstrated that the reaction is a truly thermodynamically controlled, reversible process.[15] Both enthalpy and entropy factors should be taken into consideration for rational design of building blocks for constructing macrocycles. The highly efficient one-step preparation of macrocycles using precipitation-driven alkyne metathesis may open the way to other two-dimensional or three-dimensional arylene-ethynylene structures as well as alkyne-bridged oligomers and polymers.

5 Alkyne Metathesis *vs.* Alkene Metathesis

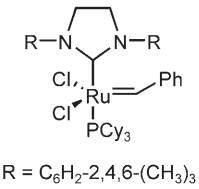
Although alkyne metathesis and alkene metathesis are closely related and share analogous mechanistic pathways, there also exists a great difference between these two types of transformation. A comparison of these two processes can help to highlight the unique advantages of both and point to deficiencies that represent challenges for further development.

5.1 Catalysts

From Schrock's molybdenum alkylidene catalyst **120**[104] to Grubbs' second generation of ruthenium carbene catalyst **121**,[105] the past three decades have witnessed the successful development of a series of



120



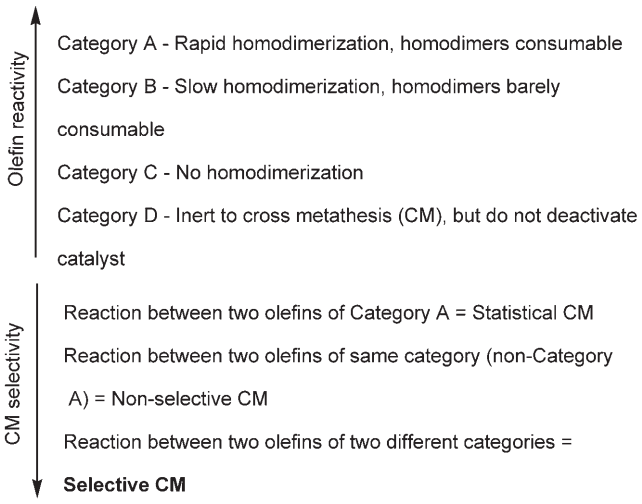
R = C_6H_2-2,4,6-$(CH_3)_3$

121

alkene metathesis catalysts, which have shown enormous applications in both organic synthesis and polymer chemistry. Both commercially available catalysts **120** and **121** are well defined, operative at ambient temperatures and show a good compatibility with a variety of functional groups. Although complex **121** is generally considered as less reactive than **120**, its broader substrate scope and robustness to air and moisture greatly facilitate its wide applications. In

both cases, strong ligand effects play important roles in catalyst optimization,[106,107] indicating the importance of electronic effect of the ligand to catalyst activity.

For alkyne metathesis, although there have been several types of catalysts developed so far, except the tungsten alkylidyne **9** and the Mortreux catalytic system, all other catalysts are not commercially available, which partially impedes their applications. Moreover, most of the catalysts are highly sensitive to air/moisture and require Schlenk or glove-box technique. Only the Mortreux system is robust enough to air/moisture,[58] but it exhibits low reactivity and poor functional group tolerance. Obviously, the development of alkyne metathesis catalyst has lagged behind alkene metathesis. Analogous to alkene metathesis catalysts, the ligand electronics and sterics are also critical to alkyne metathesis catalyst activity. Usually more electron-withdrawing ligands lead to more reactive catalysts.[14,21]

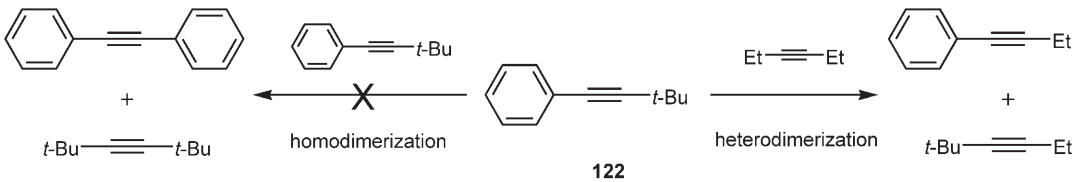


Scheme 36. Olefin categorization and rules for alkene cross-metathesis selectivity.[108]

5.2 Cross-Metathesis

In recent years, alkene cross-metathesis has emerged as a powerful and convenient synthetic technique in organic synthesis.[1i] However, the lack of predictability in olefin geometry and stereoselectivity can limit its practical use. To overcome this problem, Grubbs and co-workers investigated the alkene cross-metathesis with several classes of olefins, including substituted and functionalized styrenes, secondary allylic alcohols, tertiary allylic alcohols, and olefins with α-quaternary centers, and they found a general empirical model useful for the prediction of cross-metathesis selectivity, in terms of product selectivity, regioselectivity and chemoselectivity (Scheme 36).[108] The reactivity of olefins in cross-metathesis is ranked by their relative ability to undergo homodimerization and the susceptibility of their homodimers toward secondary metathesis reactions. Product selectivity can be achieved by suppressing the tendency of homodimerization of one component and manipulating the rate of secondary metathesis of the desired cross-product. These rates can be controlled by utilizing olefins with significantly different activities, which can be modified by altering their steric and electronic properties through substituents, functionalities, or protecting groups. Moreover, an appropriate choice of olefin metathesis catalyst is suggested to be another critical factor for achieving high product selectivity.[108] This empirical approach toward understanding cross-metathesis selectivity by categorizing the substrate reactivity opens a new possibility for predicting and designing new, selective cross-metathesis reactions, including multicomponent processes.

For alkyne metathesis, there are only a few reports of synthetically useful cross-metathesis reactions[55,109] and there has been no useful model, which can predict the product selectivity. During the investigation of our molybdenum-based catalyst, we found that the *tert*-butyl-substituted alkyne **122** cannot homodimerize; instead, cross-metathesis between **122** and 3-hexyne was observed (Scheme 37).[14] Presumably, due to the steric bulkiness of the *tert*-butyl group, formation of the productive metallacyclobutadiene intermediate is strongly disfavored, thus blocking the homodimerization pathway. This represents an interesting example of using substrate steric effects to achieve selective heterodimer formation. Better understanding of the selectivity issue in alkyne cross-metathesis will definitely further broaden the application scope of alkyne metathesis. Therefore, the development of a predictive model for alkyne cross-metathesis is highly desired and could be facilitated by using the knowledge gained from studies of alkene cross-metathesis.



Scheme 37. Homodimerization of *tert*-butyl substituted acetylene **122** *vs.* heterodimerization of **122** with 3-hexyne.

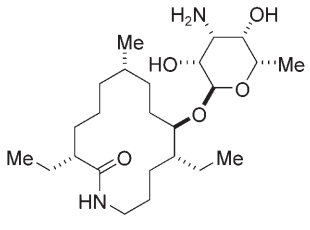
5.3 Ring-Opening Metathesis

Ring-opening alkene metathesis polymerization of cyclic olefins had been studied many years before well-defined catalysts were developed.[110] By utilizing molybdenum alkylidene and ruthenium carbene catalysts, Schrock and Grubbs demonstrated that in the right circumstances, these well-defined catalysts could catalyze olefin polymerization in a "living" fashion; that is, intermediate alkylidenes that contain the growing polymer chain would not decompose, nor undergo back-biting or chain transfer reactions.[111] It was also found that the polymerization process could be controlled through minute, but critical changes in the catalyst structure to yield polymers with highly regular repeating units.[112] In great contrast, ring-opening alkyne metathesis polymerization has been rarely applied in polymer chemistry, presumably due to the lack of readily available monomers.

5.4 Ring-Closing Metathesis

Ruthenium-catalyzed ring-closing alkene metathesis has become a standard transformation in organic synthesis, especially in the late stage of a total synthesis owing to the chemoselectivity exhibited by the catalyst and the mild reaction conditions required.[1k] On the other hand, molybdenum species **120** was also applied to natural product synthesis (fluvirucin-B1 **123**),[113] in spite of its sensitivity to air, moisture and some functionalities. In addition to total synthesis, given the useful feature of the reaction's reversibility, ring-closing alkene metathesis has proven to be advantageous for producing interlocked, "magic" ring systems in high yield.[114] While this approach generally allows formation of large rings in good to excellent yields, the stereochemistry (*E/Z*) of the newly formed double bond can hardly be predicted or controlled, which represents a limitation in the current field of ring-closing alkene metathesis.

The use of alkyne metathesis catalysts in the synthesis of cyclic compounds was also realized in the 1990s, pioneered by Fürstner and co-workers, who showed that large rings could be prepared through ring-closing alkyne metathesis (see Section 4.2).[23] A cyclic alkyne then could be hydrogenated selectively (Lindlar reduction) to yield a *cis* olefin (Scheme 16). This alternative to alkene metathesis circumvented the aforementioned unsolved selectivity problem, presenting a practically useful synthetic approach toward (*Z*)-cycloalkene compounds.

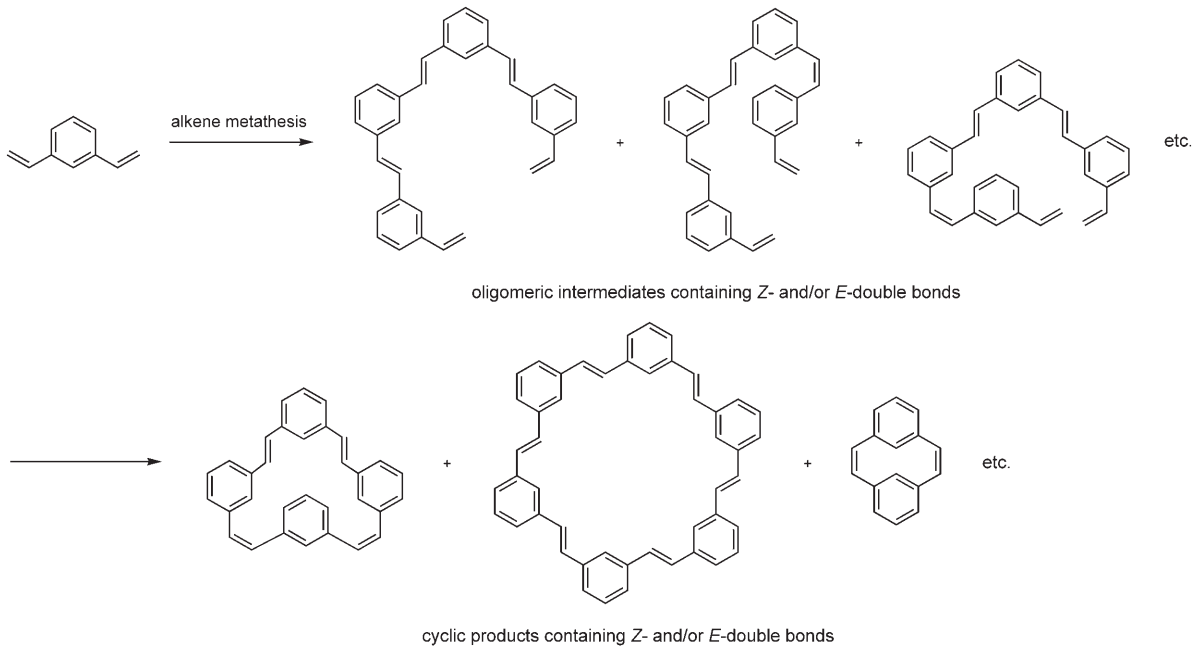


Fluvirucin B_1 (**123**)

5.5 Cyclooligomerization

Although ring-closing alkene metathesis has been intensively used in synthesis of flexible large cyclic compounds, there has been no report on its application in shape-persistent macrocycle synthesis by cyclooligomerization. In contrast to conformationally flexible cycles, shape-persistent macrocycles generally have a regular repeating unit with few degrees of conformational freedom. Macrocyclic strain and entropy considerations determine the preferred ring size, with macrocycles having the smallest number of monomer units being entropically favored. The bond angles and conformational rigidity of the monomer determine if a particular macrocycle is strained or strain-free. The energy gap between the most stable product and the second most stable product determines whether a unique product will be formed under reversible condtions.[2] The uncontrolled double bond configuration (*E/Z*) in alkene metathesis represents a potential problem in the high-yielding synthesis of shape-persistent macrocycles. The presence of both *E*- and *Z*-double bonds will lead to a variety of macrocyclic products with different angles and geometry. The lack of a strong thermodynamic preference of this system might impede the generation of a unique product (Scheme 38). Moreover, the significantly higher reactivity of the alkene metathesis catalyst on endgroups than on internal double bonds may also hamper selective generation of a complex, thermodynamically most stable structure: formation of some intermediate compounds may not be truly reversible due to the relative inertness of the internal double bonds. Nonetheless, it would be of interest to experimentally test the feasibility of utilizing alkene metathesis to synthesize shape-persistent macrocycles.

In great contrast to the few applications of alkene metathesis in this area, alkyne metathesis has been successfully applied to synthesis of a variety of shape-persistent macrocycles. The linear geometry of ethynylene group avoids the potential stereochemistry issue as in alkene metathesis. Therefore, a unique, thermodynamically favored, macrocyclic product can often be obtained based on rational design. Both trimeric,[46] tetrameric and hexameric macrocycles[17,102] have been prepared in one step starting from monomers *via* alkyne metathesis. The newly developed precipitation-driven approach[17] represents a general and highly efficient synthetic method towards shape-persistent macrocycle synthesis.



Scheme 38. Possible oligomeric intermediates and cyclic products formed during cyclooligomerization *via* alkene metathesis (simple *m*-divinylbenzene monomer is used for illustration). Due to the presence of both *Z*- and *E*-double bonds in the cyclic products, no significant thermodynamic driving force may exist for selective generation of a single product.

5.6 Acyclic Diene/Diyne Metathesis

Acyclic diene metathesis (ADMET) polymerization[115] is mainly used for synthesizing polymers with flexible backbones. High molecular weight polymers are usually obtained by removing the ethene by-product under refluxing conditions. However, there has been no report on its application toward conjugated polymer synthesis, which, if realized, would serve as an alternative synthetic route toward poly(phenylenevinylene) (PPV)[87] materials.

Acyclic diyne metathesis (ADIMET) polymerization has also been widely used in polymer chemistry. Polymers with both flexible and rigid backbones have been prepared by this method. In particular, a variety of poly(phenylene-ethynylene)s (PPEs) or poly(arylene-ethynylene)s (PAEs) conjugated polymers have been successfully synthesized and studied, showing interesting electronic and optical properties.[4,45] Compared to the conventional cross-coupling approach to PAEs, the ADIMET polymerization is superior with respect to purity, yield and molecular weight of the product.

6 Conclusion and Outlook

After three decades of development, alkyne metathesis now represents a widely applicable synthetic approach in both organic and polymer chemistry. From the early development of Mortreux's *in situ* catalytic system, which requires high temperature and is only applicable to hydrocarbon species, catalysts are now available that allow metathesis of highly functionalized substrates under mild conditions. However, the current catalysts still have their own disadvantages, such as inconvenient preparation, high sensitivity to air/moisture, or poor functional group tolerance etc. Therefore, development of a "dream" catalyst that functions at or below ambient temperature and overcomes the above-mentioned drawbacks, especially with robustness to air and moisture, represents a challenging task in this field. Commercialization of well-defined, molybdenum-based catalysts would also greatly facilitate the application of this approach.

Alkyne metathesis, combined with subsequent Lindlar reduction is now emerging as an indirect but stereoselective tool in the synthesis of (*Z*)-cycloalkenes under mild conditions. Such a strategy by-passes the requirement for isomer separation and allows modular synthesis to be incorporated. The utility of this approach has been demonstrated in various flexible syntheses of natural products. Transformation of (cyclo)-alkynes to (*E*)-alkene products still needs further investigation, and will provide a complementary approach to RCM.

ADIMET has greatly improved the current synthesis of PAEs and shape-persistent macrocycles. In the presence of highly active catalysts, metathesis of rigid, angular, aromatic diyne monomers is under thermodynamic control, leading the reaction toward the formation of the thermodynamically most stable cyclics.

It should also be noted that the concept of the energy gap principle illustrated for macrocyclization *via* alkyne metathesis also applies broadly to other dynamic covalent methods, as long as the reaction is a fully reversible process.

Finally, given the history of alkene metathesis development, it is reasonable to say that as catalysts becoming better understood, more readily accessible and more user-friendly, alkyne metathesis will likely become a widely-utilized, powerful approach in synthesis.

Acknowledgements

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References

[1] For reviews see: a) Y. Chauvin, *Angew. Chem. Int. Ed.* **2006**, *45*, 3741; b) R. R. Schrock, *Angew. Chem. Int. Ed.* **2006**, *45*, 3748; c) R. H. Grubbs, *Angew. Chem. Int. Ed.* **2006**, *45*, 3760; d) D. Astruc, *New. J. Chem.* **2005**, *29*, 42; e) R. H. Grubbs, *Tetrahedron* **2004**, *60*, 7117; f) A. Deiters, S. F. Martin, *Chem. Rev.* **2004**, *104*, 2199; g) S. T. Diver, A. J. Giessert, *Chem. Rev.* **2004**, *104*, 1317; h) R. R. Schrock, A. H. Hoveyda, *Angew. Chem. Int. Ed.* **2003**, *42*, 4592; i) S. J. Connon, S. Blechert, *Angew. Chem. Int. Ed.* **2003**, *42*, 1900; j) T. M. Trnka, R. H. Grubbs, *Acc. Chem. Res.* **2001**, *34*, 18; k) A. Fürstner, *Angew. Chem. Int. Ed.* **2000**, *39*, 3012; l) *Handbook of Metathesis*, (Ed.: R. H. Grubbs), vols. 1–3, Wiley-VCH, Weinheim, **2003**; m) *Alkene Metathesis in Organic Synthesis*, (Ed.: A. Fürstner), Springer, Berlin, **1998**.

[2] W. Zhang, J. S. Moore, *Angew. Chem. Int. Ed.* **2006**, *45*, 4416.

[3] A. Fürstner, P. W. Davies, *Chem. Commun.* **2005**, 2307.

[4] U. H. F. Bunz, *Acc. Chem. Res.* **2001**, *34*, 998.

[5] a) A. Mortreux, O. Coutelier, *J. Mol. Catal. A: Chem.* **2006**, *254*, 96; b) R. R. Schrock, in: *Handbook of Metathesis*, (Ed.: R. H. Grubbs), Wiley-VCH, Weinheim, **2003**, vol. 1, pp 173; c) R. R. Schrock, *Chem. Rev.* **2002**, *102*, 145.

[6] F. Pennellar, R. L. Banks, G. C. Bailey, *J. Chem. Soc., Chem. Commun.* **1968**, 1548.

[7] a) A. Mortreux, M. Blanchard, *J. Chem. Soc., Chem. Commun.* **1974**, 786; b) A. Mortreux, J. C. Delgrange, M. Blanchard, B. Lubochinsky, *J. Mol. Catal.* **1977**, *2*. 73; c) A. Mortreux, F. Petit, M. Blanchard, *J. Mol. Catal.* **1980**, *8*, 97; d) A. Bencheick, M. Petit, A. Mortreux, F. Petit, *J. Mol. Catal.* **1982**, *15*, 93.

[8] T. J. Katz, J. McGinnis, *J. Am. Chem. Soc.* **1975**, *97*, 1592.

[9] J.-L. Hérisson, Y. Chauvin, *Makromol. Chem.* **1971**, *141*, 161.

[10] J. H. Wengrovius, J. Sancho, R. R. Schrock, *J. Am. Chem. Soc.* **1981**, *103*, 3932.

[11] S. F. Pedersen, R. R. Schrock, M. R. Churchill, H. J. Wasserman, *J. Am. Chem. Soc.* **1982**, *104*, 6808.

[12] M. H. Chisholm, K. Folting, D. M. Hoffman, J. C. Huffman, *J. Am. Chem. Soc.* **1984**, *106*, 6794.

[13] M. H. Chisholm, B. K. Conroy, B. W. Eichhorn, K. Folting, D. M. Hoffman, J. C. Huffman, N. S. Marchant, *Polyhedron* **1987**, *6*, 783.

[14] W. Zhang, S. Kraft, J. S. Moore, *J. Am. Chem. Soc.* **2004**, *126*, 329.

[15] W. Zhang, J. S. Moore, *J. Am. Chem. Soc.* **2005**, *127*,11863.

[16] L. G. McCullough, R. R. Schrock, J. C. Dewan, J. C. Murdzek, *J. Am. Chem. Soc.* **1985**, *107*, 5987.

[17] W. Zhang, J. S. Moore, *J. Am. Chem. Soc.* **2004**, *126*, 12796.

[18] a) R. R. Schrock, S. M. Rocklage, J. H. Wengrovius, G. Rupprecht, J. Fellmann, *J. Mol. Catal.* **1980**, *8*, 73; b) J. H. Wengrovius, R. R. Schrock, M. R. Churchill, J. R. Missert, W. J. Youngs, *J. Am. Chem. Soc.* **1980**, *102*, 4515.

[19] D. N. Clark, R. R. Schrock, *J. Am. Chem. Soc.* **1978**, *100*, 6774.

[20] a) R. R. Schrock, D. N. Clark, J. Sancho, J. H. Wengrovius, S. M. Rocklage, S. F. Pedersen, *Organometallics* **1982**, *1*, 1645; b) J. H. Freudenberger, R. R. Schrock, M. R. Churchill, A. L. Rheingold, J. W. Ziller, *Organometallics* **1984**, *3*, 1563; c) M. L. Listemann, R. R. Schrock, *Organometallics* **1985**, *4*, 74.

[21] R. R. Schrock, *Polyhedron* **1995**, *14*, 3177.

[22] The cleavage reaction was first reported by Schrock, see: a) R. R. Schrock, M. L. Listemann, L. G. Sturgeoff, *J. Am. Chem. Soc.* **1982**, *104*, 4291 and ref.[20c]; compound **10** was first reported by Chisholm, see: b) M. Akiyama, M. H. Chisholm, F. A. Cotton, M. W. Extine, D. A. Haitko, D. Little, P. E. Fanwick, *Inorg. Chem.* **1979**, *18*, 2266.

[23] A. Fürstner, G. Seidel, *Angew. Chem. Int. Ed.* **1998**, *37*, 1734.

[24] A. Fürstner, O. Guth, A. Rumbo, G. Seidel, *J. Am. Chem. Soc.* **1999**, *121*, 11108.

[25] A. Fürstner, A. Rumbo, *J. Org. Chem.* **2000**, *65*, 2608.

[26] A. Fürstner, T. Dierkes, *Org. Lett.* **2000**, *2*, 2463.

[27] A. Fürtstner, G. Seidel, *J. Organomet. Chem.* **2000**, *606*, 75.

[28] A. Fürstner, C. Mathes, C. W. Lehmann, *Chem. Eur. J.* **2001**, *7*, 5299.

[29] Y.-C. Tsai, P. L. Diaconescu, C. C. Cummins, *Organometallics* **2000**, *19*, 5260.

[30] Y.-C. Tsai, M. J. A. Johnson, D. J. Mindiola, C. C. Cummins, W. T. Klooster, T. F. Koetzle, *J. Am. Chem. Soc.* **1999**, *121*, 10426.

[31] S. R. Allen, R. G. Beevor, M. Green, A. G. Orpen, K. E. Paddick, I. D. Williams, *J. Chem. Soc., Dalton Trans.* **1987**, 591.

[32] J. M. Blackwell, J. S. Figueroa, F. H. Stephens, C. C. Cummins, *Organometallics* **2003**, *22*, 3351.

[33] J. S. Murdzek, R. R. Schrock, *Organometallics* **1987**, *6*, 1373.

[34] C. E. Laplaza, A. L. Odom, W. M. Davis, C. C. Cummins, J. D. Protasiewicz, *J. Am. Chem. Soc.* **1995**, *117*, 4999.

[35] C. E. Laplaza, C. C. Cummins, *Science* **1995**, *268*, 861.

[36] C. C. Cummins, *Chem. Commun.* **1998**, 1777.

[37] Molybdenum triamide **24** is readily available on gram quantities starting from $MoCl_3(thf)_3$, which is prepared from $MoCl_5$ *via* Poli's procedure, see: F. Stoffelbach, D. Saurenz, R. Poli, *Eur. J. Inorg. Chem.* **2001**, *10*, 2699.

[38] A. Fürstner, C. Mathes, C. W. Lehmann, *J. Am. Chem. Soc.* **1999**, *121*, 9453.

[39] J. C. Peters, A. L. Odom, C. C. Cummins, *Chem. Commun.* **1997**, 1995.

[40] a) L. G. McCullough, M. L. Listemann, R. R. Schrock, M. R. Churchill, J. W. Ziller, *J. Am. Chem. Soc.* **1983**, *105*, 6729; b) J. H. Freudenberger, R. R. Schrock, *Organometallics* **1986**, *5*, 1411; c) A. Bray, A. Mortreux, F. Petit, M. Petit, T. Szymanska-Buzar, *J. Chem. Soc., Chem. Commun.* **1993**, 197.

[41] W. Zhang, S. Kraft, J. S. Moore, *Chem. Commun.* **2003**, 832.

[42] The most recent synthesis of trisamidomolybdenum(VI) methylidyne complex **26** reported by Cummins involved using 7-chloronorbornadiene as a methane source in conjunction with chlorine atom abstraction and benzene elimination, see T. Agapie, P. L. Diaconescu, C. C. Cummins, *J. Am. Chem. Soc.* **2002**, *124*, 2412.

[43] W. Zhang, Y. Lu, J. S. Moore, *Org. Synth.* in press.

[44] Polymerization of alkynes by a tungsten alkylidyne catalyst was reported before, see: a) K. Weiss, R. Goller, G. Lössel, *J. Mol. Catal.* **1988**, *46*, 267; b) S. A. Krouse, R. R. Schrock, *Macromolecules* **1989**, *22*, 2569; c) T. J. Katz, T. H. Ho, N. Y. Shih, Y. C. Ying, V. I. W. Stuart, *J. Am. Chem. Soc.* **1984**, *106*, 2659.

[45] W. Zhang, J. S. Moore, *Macromolecules* **2004**, *37*, 3973.

[46] W. Zhang, S. M. Brombosz, J. L. Mendoza, J. S. Moore, *J. Org. Chem.* **2005**, *70*, 10198.

[47] R. L. Gdula, M. J. A. Johnson, *J. Am. Chem. Soc.* **2006**, *128*, 9614.

[48] J. H. Freudenberger, R. R. Schrock, *Organometallics* **1986**, *5*, 398.

[49] M. H. Chisholm, K. Folting-Streib, D. B. Tiedtke, F. Lemoigno, O. Eisenstein, *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 110.

[50] M. H. Chisholm, K. Folting-Streib, M. L. Lynn, D. B. Tiedtke, F. Lemoigno, O. Eisenstein, *Chem. Eur. J.* **1999**, *5*, 2318.

[51] R. L. Gdula, M. J. A. Johnson, N. W. Ockwig, *Inorg. Chem.* **2005**, *44*, 9140.

[52] A. Mortreux, N. Dy, M. Blanchard, *J. Mol. Catal.* **1975/76**, *1*, 101.

[53] N. G. Pschirer, U. H. F. Bunz, *Tetrahedron Lett.* **1999**, *40*, 2481.

[54] G. Brizius, U. H. F. Bunz, *Org. Lett.* **2002**, *4*, 2829.

[55] a) N. Kaneta, T. Hirai, M. Mori, *Chem. Lett.* **1995**, 627; b) N. Kaneta, K. Hikichi, S. Asaka, M. Uemura, M. Mori, *Chem. Lett.* **1995**, 1055.

[56] K. Grela, J. Ignatowska, *Org. Lett.* **2002**, *4*, 3747.

[57] V. Sashuk, J. Ignatowska, K. Grela, *J. Org. Chem.* **2004**, *69*, 7748.

[58] The catalytic active species of this system are probably trisphenoxides in a low concentration. Under the reaction condition employed for the metathesis (130–150 °C), the apparent higher stability of this system to air could be (partially)due to the slow reaction between trisphenoxides and oxygen/moisture, which are all present in a small amount.

[59] L. Kloppenburg, D. Song, U. H. F. Bunz, *J. Am. Chem. Soc.* **1998**, *120*, 7973.

[60] V. Huc, R. Weihofen, I. Martin-Jimenez, P. Oulié, C. Lepetit, G. lavigne, R. Chauvin, *New. J. Chem.* **2003**, *27*, 1412.

[61] U. H. F. Bunz, *Science* **2005**, *308*, 216.

[62] a) B. F. Straub, *Angew. Chem. Int. Ed.* **2005**, *44*, 5974; b) C. Adlhart, P. Chen, *J. Am. Chem. Soc.* **2004**, *126*, 3496; c) L. Cavallo, *J. Am. Chem. Soc.* **2002**, *124*, 8965; d) S. E. Vyboishchikov, M. Buhl, W. Thiel, *Chem. Eur. J.* **2002**, *8*, 3692; e) Y. D. Wu, Z. H. Peng, *J. Am. Chem. Soc.* **1997**, *119*, 8043.

[63] For pioneer work, see a) T. Woo, E. Folga, T. Ziegler, *Organometallics* **1993**, *12*, 1289; b) S. Fantacci, N. Re, M. Rosi, A. Sgamellotti, M. F. Guest, P. Sherwood, C. Floriani, *J. Chem. Soc., Dalton Trans.* **1997**, 3845.

[64] J. Zhu, G. Jia, Z. Lin, *Organometallics* **2006**, *25*, 1812.

[65] R. R. Schrock, S. F. Pedersen, M. R. Churchill, J. W. Ziller, *Organometallics* **1984**, *3*, 1574.

[66] M. Chabanas, A. Baudouin, C. Copéret, J.-M. Basset, *J. Am. Chem. Soc.* **2001**, *123*, 2062.

[67] H. Weissman, K. N. Plunkett, J. S. Moore, *Angew. Chem. Int. Ed.* **2006**, *45*, 585.

[68] K. C. Nicolaou, P. G. Bulger, D. Sarlah, *Angew. Chem. Int. Ed.* **2005**, *44*, 4490.

[69] C. Pariya, K. N. Jayaprakash, A. Sarkar, *Coord. Chem. Rev.* **1998**, *168*, 1.

[70] M. IJsselstijn, B. Aguilera, G. A. van der Marel, J. H. van Boom, F. L. van Delft, H. E. Schoemaker, H. S. Overkleeft, F. P. J. T. Rutjes, M. Overhand, *Tetrahedron Lett.* **2004**, *45*, 4379.

[71] B. Aguilera, L. B. Wolf, P. Nieczypor, F. P. J. T. Rutjes, H. S. Overkleeft, J. C. M. van Hest, H. E. Schoemaker, B. Wang, J. C. Mol, A. Fürstner, M. Overhand, G. A. van der Marel, J. H. van Boom, *J. Org. Chem.* **2001**, *66*, 3584.

[72] E. B. Bauer, F. Hampel, J. A. Gladysz, *Adv. Synth. Catal.* **2004**, *346*, 812.

[73] E. B. Bauer, S. Szafert, F. Hampel, J. A. Gladysz, *Organometallics* **2003**, *22*, 2184.

[74] For synthesis of metallamacrocycles *via* alkene metathesis, see a) E. B. Bauer, J. A. Gladysz, in: *Handbook of Metathesis*, (Ed.: R. H. Grubbs), Wiley-VCH, Weinheim, **2003**, Vol. 2, pp. 403; b) M. Weck, B. Mohr, J.-P. Sauvage, R. H. Grubbs, *J. Org. Chem.* **1999**, *64*, 5463; c) T. Shima, F. Hampel, J. A. Gladysz, *Angew. Chem. Int. Ed.* **2004**, *43*, 5537; d) J. Stahl, J. C. Bohling, E. B Bauer, T. B. Peters, W. Mohr, J. M. Martín-Alvarez, F. Hampel, J. A. Gladysz, *Angew. Chem. Int. Ed.* **2002**, *41*, 1871; e) V. Martinez, J.-C. Blais, D. Astruc, *Angew. Chem. Int. Ed.* **2003**, *42*, 4366.

[75] a) P. Bertinato, E. J. Sorensen, D. Meng, S. Danishefsky, *J. Org. Chem.* **1996**, *61*, 8000; b) K. C. Nicolaou,

Y. He, D. Vourloumis, H. Vallberg, F. Roschangar, F. Sarabia, S. Ninkovic, Z. Yang, J. I. Trujillo, *J. Am. Chem. Soc.* **1997**, *119*, 7960; c) D. Schinzer, A. Limberg, A. Bauer, O. M. Böhm, M. Cordes, *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 523.
[76] A. Fürstner, K. Grela, *Angew. Chem. Int. Ed.* **2000**, *39*, 1234.
[77] A. Fürstner, K. Grela, C. Mathes, C. W. Lehmann, *J. Am. Chem. Soc.* **2000**, *122*, 11799.
[78] A. Fürstner, C. Mathes, K. Grela, *Chem. Commun.* **2001**, 1057.
[79] a) T. K. Jones, S. E. Denmark, *Org. Synth.* **1986**, *64*, 182; b) L. Brandsma, W. F. Nieuwenhuizen, J. W. Zwikker, U. Mäeorg, *Eur. J. Org. Chem.* **1999**, 775; c) C. E. Castro, R. D. Stephens, *J. Am. Chem. Soc.* **1964**, *86*, 4358; d) A. B. Smith, P. A. Levenberg, J. Z. Suits, *Synthesis* **1986**, 184.
[80] B. M. Trost, Z. T. Ball, T. Jöge, *J. Am. Chem. Soc.* **2002**, *124*, 7922.
[81] a) A. Fürstner, K. Radkowski, *Chem. Commun.* **2002**, 2182; b) F. Lacombe, K. Radkowski, G. Seidel, A. Fürstner, *Tetrahedron* **2004**, *60*, 7315.
[82] B. M. Trost, Z. T. Ball, *J. Am. Chem. Soc.* **2001**, *123*, 12726.
[83] a) S. A. Krouse, R. R. Schrock, *Macromolecules* **1989**, *22*, 2569; b) S. A. Krouse, R. R. Schrock, *Macromolecules* **1987**, *20*, 903.
[84] X.-P. Zhang, G. C. Bazan, *Macromolecules* **1994**, *27*, 4627.
[85] D. T. McQuade, A. E. Pullen, T. M. Swager, *Chem. Rev.* **2000**, *100*, 2537.
[86] U. H. F. Bunz, *Chem. Rev.* **2000**, *100*, 1605.
[87] J. H. Burroughes, D. D. C. Bradley, A. R. Brown, R. N. Marks, K. Mackey, R. H. Friend, P. L. Burns, A. B. Holmes, *Nature* **1990**, *347*, 539.
[88] J. M. Tour, *Chem. Rev.* **1996**, *96*, 537.
[89] F. E. Goodson, T. I. Wallow, B. M. Novak, *J. Am. Chem. Soc.* **1997**, *119*, 12441.
[90] K. Weiss, A. Michel, E. M. Auth, U. H. F. Bunz, T. Mangel, K. Müllen, *Angew. Chem. Int. Ed.* **1997**, *36*, 506.
[91] L. Kloppenburg, D. Song, U. H. F. Bunz, *J. Am. Chem. Soc.* **1998**, *120*, 7973.
[92] L. Kloppenburg, D. Jones, U. H. F. Bunz, *Macromolecules* **1999**, *32*, 4194.
[93] N. G. Pschirer, M. W. Vaughn, Y. B. Dong, H.-C. zur Loye, U. H. F. Bunz, *Chem. Commun.* **2000**, 85.
[94] G. Brizius, S. Kroth, U. H. F. Bunz, *Macromolecules* **2002**, *35*, 5317.
[95] K. B. Wagener, J. M. Bonella, J. G. Nell, R. P. Duttweiler, M. A. Hillmyer, *Makromol. Chem.* **1990**, *191*, 365.
[96] M. I. Sluch, A. Godt, U. H. F. Bunz, M. A. Berg, *J. Am. Chem. Soc.* **2001**, *123*, 6447.
[97] a) S. Höger, *Angew. Chem. Int. Ed.* **2005**, *44*, 3806; b) D. Zhao, J. S. Moore, *Chem. Commun.* **2003**, 807; c) C. Grave, A. D. Schlüter, *Eur. J. Org. Chem.* **2002**, 3075; d) U. H. F. Bunz, Y. Rubin, Y. Tobe, *Chem. Soc. Rev.* **1999**, *28*, 107; e) S. Höger, *J. Polym. Sci. Part A* **1999**, *37*, 2685; f) J. S. Moore, *Acc. Chem. Res.* **1997**, *30*, 402.
[98] E. Negishi, L. Anastasia, *Chem. Rev.* **2003**, *103*, 1979.
[99] P.-H. Ge, W. Fu, W. A. Herrmann, E. Herdtweck, C. Campana, R. D. Adams, U. H. F. Bunz, *Angew. Chem. Int. Ed.* **2000**, *39*, 3607.
[100] N. G. Pschirer, W. Fu, R. D. Adams, U. H. F. Bunz, *Chem. Commun.* **2000**, 87.
[101] O. Š. Miljanić, K. P. C. Vollhardt, G. D. Whitener, *Synlett* **2003**, 29.
[102] The gram-scale synthesis of tetrameric macrocycle **117** was also accomplished in one step starting from diyne monomers: W. Zhang, H. M. Cho, J. S. Moore, *Org. Synth.* in press.
[103] K. Balakrishnan, A. Datar, W. Zhang, X. Yang, T. Naddo, J. Huang, J. Zuo, M. Yen, J. S. Moore, L. Zang, *J. Am. Chem. Soc.* **2006**, *128*, 6576.
[104] a) R. R. Schrock, J. S. Murdzek, G. C. Bazan, J. Robbins, M. DiMare, M. O'Regan, *J. Am. Chem. Soc.* **1990**, *112*, 3875; b) G. C. Bazan, J. H. Oskam, H.-N. Cho, L. Y. Park, R. R. Schrock, *J. Am. Chem. Soc.* **1991**, *113*, 6899.
[105] a) M. Scholl, S. Ding, C. W. Lee, R. H. Grubbs, *Org. Lett.* **1999**, *1*, 953; b) C. W. Bielawski, R. H. Grubbs, *Angew. Chem. Int. Ed.* **2000**, *39*, 2903.
[106] a) J. H. Oskam, R. R. Schrock, *J. Am. Chem. Soc.* **1992**, *114*, 7588; b) J. H. Oskam, R. R. Schrock, *J. Am. Chem. Soc.* **1993**, *115*, 11831.
[107] a) E. L. Dias, S. T. Nguyen, R. H. Grubbs, *J. Am. Chem. Soc.* **1997**, *119*, 3887; b) M. S. Sanford, M. Ulman, R. H. Grubbs, *J. Am. Chem. Soc.* **2001**, *123*, 749; c) J. A. Love, M. S. Sanford, M. W. Day, R. H. Grubbs, *J. Am. Chem. Soc.* **2003**, *125*, 10103.
[108] A. K. Chatterjee, T.-L. Choi, D. P. Sanders, R. H. Grubbs, *J. Am. Chem. Soc.* **2003**, *125*, 11360.
[109] A. Fürstner, C. Mathes, *Org. Lett.* **2001**, *3*, 221.
[110] a) K. J. Ivin, *Olefin Metathesis*, Academic Press, New York, **1983**; b) K. J. Ivin, J. C. Mol, *Olefin Metathesis and Metathesis Polymerization*, Academic Press, San Diego, **1997**.
[111] R. R. Schrock, J. Feldman, L. Cannizzo, R. H. Grubbs, *Macromolecules* **1987**, *20*, 1169.
[112] a) K. M. Totland, T. J. Boyd, G. G. Lavoie, W. M. Davis, R. R. Schrock, *Macromolecules* **1996**, *29*, 6114; b) D. H. McConville, J. R. Wolf, R. R. Schrock, *J. Am. Chem. Soc.* **1993**, *115*, 4413.
[113] A. F. Houri, Z. M. Xu, D. A. Cogan, A. H. Hoveyda, *J. Am. Chem. Soc.* **1995**, *117*, 2943.
[114] a) J.-P. Sauvage, B. Mohr, R. H. Grubbs, M. Weck, *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 1308; b) A. F. M. Kilbinger, S. J. Cantrill, A. W. Waltman, M. W. Day, R. H. Grubbs, *Angew. Chem. Int. Ed.* **2003**, *42*, 3281.
[115] K. B. Wagener, J. M. Bonella, J. G. Nell, R. P. Duttweiler, M. A. Hillmeier, *Makromol. Chem.* **1990**, *191*, 365.

