Ruthenium-Catalyzed Polycyclization Reactions

Thesis by
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Dedicated to my Mother, Father, and Brother

To Richard and Gene

And to the memory of Bruce Hansen

Acknowledgments

It has been a great privilege to study chemistry under the direction of Professor Robert Grubbs these past four and a half years. Bob has been a superlative advisor in the laboratory. Despite granting his students a significant degree of autonomy in their research and maintaining a "hands off" approach, he was always available to help out no matter how busy he was. These past years with the Tall Guy has also been a lot of fun, especially the summer camping trips (may the Old Smuggler tradition continue!) and the occasional day of rock climbing.

The members of my committee, Professors Andy Myers, Bill Goddard, and Erick Carreira, are thanked for their assistance and input. Dennis Dougherty has generously agreed to become a part of the team on rather short notice.

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Caltech has been wonderful, and I am grateful to several professors from Grinnell College for encouraging me to go west. My first taste of organic chemistry came from Jim Swartz every Tuesday and Thursday morning at 8:30. In spite of the early hour, he piqued my interest in the topic. Lee Sharpe was a terrific advisor, and Leslie Lyons, Martin Minelli, Luther Erickson, Gene Wubbels, and Tony Watson all taught me a great deal of chemistry and made my undergraduate experience very rewarding. Outside the chemistry department, my thanks go to Professors Henry Walker, Dennis Perri, and Margarita Pillado-Miller.

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ponderables that the universe has presented humankind (Is Mr. Brown controlled by remote? What does the walking man do?). Toby, Shirley, Ramsey, Patrick, and Bill took me in during two Thanksgivings and provided well-needed respite, great turkey dinners, and the opportunity to sleep in a snow cave (gotta watch out for that post-nasal drip, though); I am grateful for their Northwest hospitality. Many a Car Appreciation Day was spent in the role of Grease Monkey Understudy with Lou "Only about a million times" "Eighteen years I'm in the business" "My eyes is goin' crazy!" Madsen. Others who deserve thanks include Chris Kankel, Erik Severin, Dinorah Alan, Paul Ellingstad, Bruce Shapiro, Neal "You gotta light 'em up!" Hines, Seth Miller, Ken Brameld, and of course, the members of the nefarious North Shore Nine.

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And finally, a word to referee fk, who has examined more than one paper from the Grubbs group: er, you see, I think you're missing something!

And now that we have returned to the desultory life of the plains, let us endeavor to impart a little of the mountain grandeur into it. We will remember within what walls we lie, and understand that this life too has its summit, and why from the mountain top deepest valleys have the tinge of blue; that there is elevation every hour, as no part of the earth is so low that the heavens may not be seen and we have only to stand on the summit of our hour to command an uninterrupted horizon.

-Henry David Thoreau

Abstract

Ruthenium carbene $Cl_2(PCy_3)_2Ru{=}CHCH{=}CPh_2$ mediates the efficient and selective conversion of acyclic dienynes to fused bicyclic [*n.m.*0] dienes containing five-, six- and seven-membered rings. Studies with various X-substituted acetylenes (X = H, alkyl, Ph, CO_2Me, $SnBu_3$, $SiMe_3$, halogen) suggest that the dienyne metathesis is not only sensitive to these substituents but also to the catalysts employed. Among the various metal alkylidenes examined, only the ruthenium catalyst **1** exhibited metathesis activity for a range of substrates. In no case, however, were acetylenes with heteroatomic substituents metathesized; these substrates either underwent simple diene RCM or failed to react with the catalyst in a productive fashion. These observations further expand the scope of catalytic RCM for the construction of complex organic compounds.

Ruthenium alkylidene $Cl_2(PCy_3)_2Ru{=}CHPh$ has been utilized in the tandem ring-opening/ring-closing metathesis of cycloolefins. This reaction produces a bicyclic molecules conatining nonconjugated dienes. Reactivity of the precursors is dependent upon strain, and thus ring size, of the cycloolefins. Competing oligomerization is observed in substrates having low ring strain; this process is inhibited by increasing dilution of the reaction or by adding alkyl substitution to the acyclic olefins.

The application of ruthenium alkylidene $Cl_2(PCy_3)_2Ru{=}CHPh$ to the catalysis of polycyclization reactions is detailed. Several acyclic precursors have been synthesized and reacted with the ruthenium alkylidene. These precursors vary in topology and contain either acetylenic or cyclic olefin metathesis relays or both. The cyclization reactions proceed in moderate to good yield to produce polycyclic polyenes when the precursors are subjected to catalytic amounts of the ruthenium complex. Precursors bearing *n* relay units generate polycycles containing (*n* + 1) rings.

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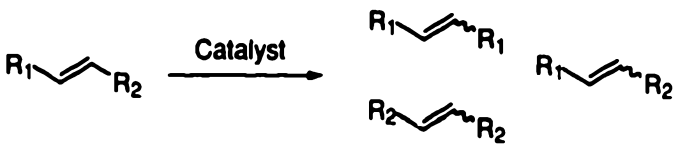
Introduction

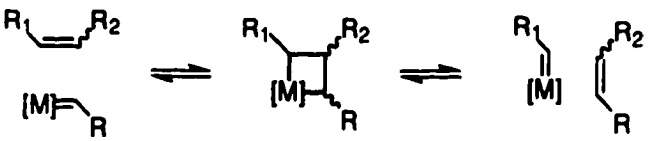
The olefin metathesis reaction (Scheme 1) involves the exchange of alkylidene fragments of two olefins; in the example shown, the *trans*-disubstituted starting material is converted into a statistical mixture of olefins.[1] In 1971 Chauvin and coworkers proposed what is now the commonly accepted mechanism of olefin metathesis.[2] The fundamental components of this mechanism are illustrated in the scheme: the initial step involves formation of a metallacyclobutane, formally a [2 + 2] cycloaddition between an olefin and a metallaolefin. Productive cleavage of this intermediate generates a new olefin and new metallaolefin. The steps of this mechanism are generally reversible, and the reaction is typically under thermodynamic control.

Scheme 1

Olefin Metathesis:



Chauvin Mechanism:



Olefin metathesis is catalyzed by transition metal carbenes. Classically, catalyst systems were ill-defined, multiple component mixtures. More recently, well-defined, single component systems have been developed (Figure 1). Most of these catalysts are early transition metal alkylidenes or metallacyclobutanes which cleave to generate alkylidenes. Many of these systems exhibit high metathesis activity, but consequently, suffer from instability and low functional group tolerance; the rigorous exclusion of oxygen

and water is requisite for the use of these catalysts. The difficulty of synthesis has been an additional obstacle to their widespread use, a problem which has been alleviated by the commercial availability of the tungsten and molybdenum catalysts of Schrock and coworkers.

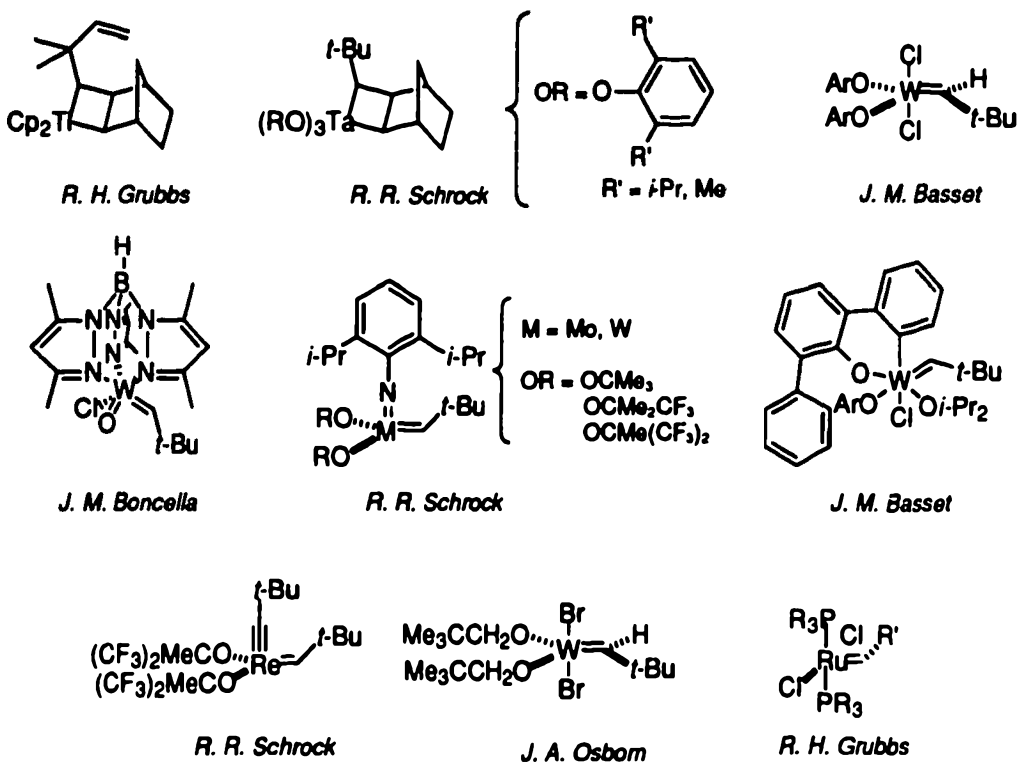


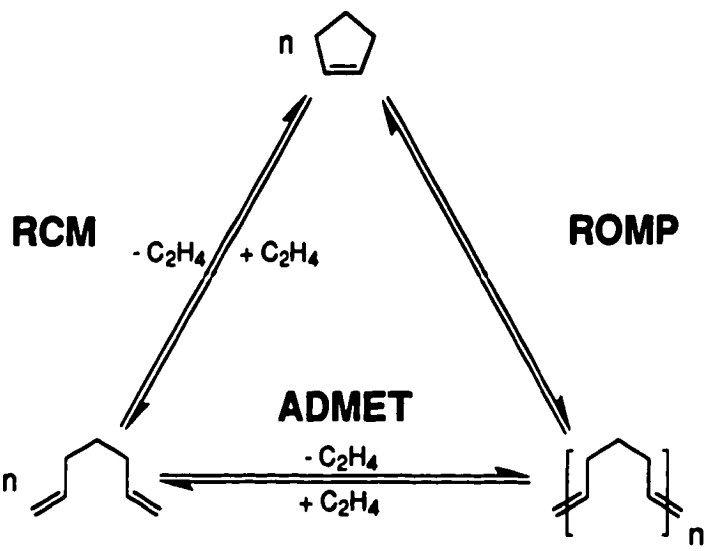
Figure 1. Well-defined olefin metathesis catalysts.[3]

Although it typically exhibits lower metathesis activity than the early transition metal systems, the ruthenium alkylidene system (R = CHPh, $CH{=}CPh_2$, H, alkyl, CO_2R) developed by Grubbs and coworkers offers several advantages.[4] It has shown remarkable functional group tolerance and a correspondingly high stability. For example, the ruthenium alkylidene exhbits metathesis activity in the presence of air, water, and strong

acids. Additionally, the catalyst is readily available through several inexpensive and straightforward preparations which have recently been developed, including reaction of the appropriate ruthenium precursor with cyclopropenes, diazo compounds, *gem*-dihalo compounds, and propargyl and vinyl chlorides.[5]

As new olefin metathesis catalysts have evolved, so have applications of the reaction. The reaction depicted in Scheme 1, acyclic cross metathesis, is one of the simpler metathesis processes, and its utility is greatly enhanced when proper selectivity (*e.g.*, product, *cis*/*trans*) can be achieved. In the reaction of α,ω-dienes, several additional metathesis pathways are possible (Scheme 2).[6] The competition among these three processes, ROMP (ring-opening metathesis polymerization), ADMET (acyclic diene metathesis)[7] polymerization, and RCM (ring-closing metathesis), is affected by such factors as ring strain, olefin concentration, ethylene pressure, and temperature. Although ROMP and ADMET are extremely useful in the synthesis of functionalized macromolecules,[8] the present work focuses on RCM to produce small, cyclic molecules.

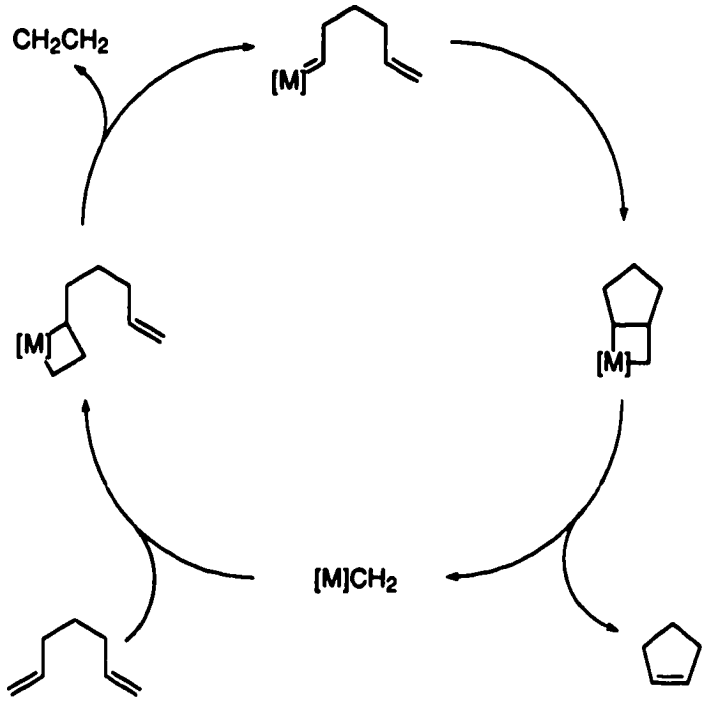
Scheme 2



Diene RCM (Scheme 3), although a relatively new application of olefin metathesis catalysts, has been employed with increasing frequency in the synthesis of cyclic olefins.[9] Thermodynamic considerations include the creation of ring strain and the formation of two molecules from one, and the mechanism for the process involves an intramolecular olefin metathesis as the key step.

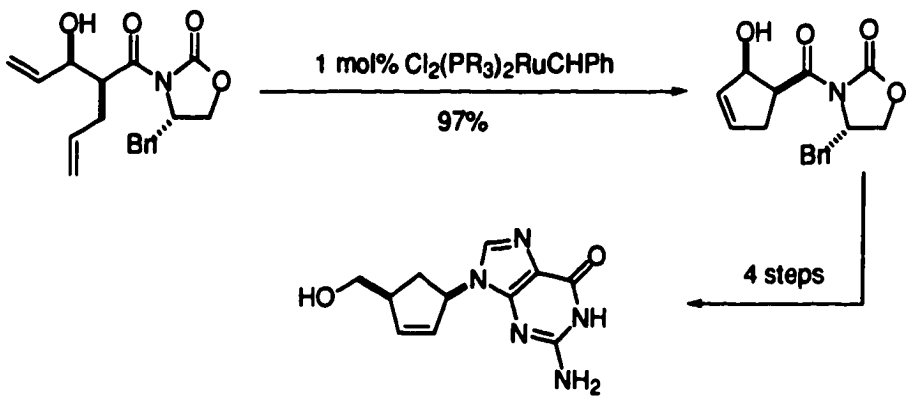
Scheme 3

Mechanism of Diene RCM:



The application of diene RCM in the formation of five- to eight-membered rings as well as macrocycles has recently found its place as an established technique in the armamentarium of synthetic organic chemistry. Because of its ability to form carbon-carbon double bonds and because these bonds provide the possibility of further functionalization, RCM has recently been utilized in the synthesis of compounds with biological activity.[10] For example, Crimmins and King recently reported the synthesis of HIV reverse transcriptase inhibitor 1592U89 (Scheme 4); key steps include RCM to form the cycloolefin and palladium-catalyzed allylic amination to attach the purine moeity.[11]

Scheme 4



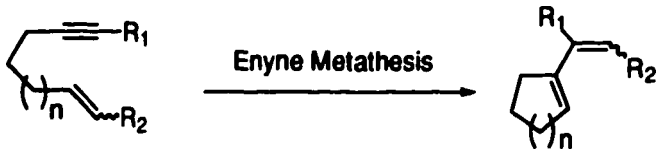
1592U89

A related reaction involving cyclization of enynes (Scheme 4) has been reported. Enyne metathesis begins in a manner analogous to diene RCM, but the cyclization step is an intramolecular acetylene metathesis which forms the ring and a vinylcarbene. This latter species reacts with the olefin of another enyne molecule to start the catalytic cycle once again. Unlike diene RCM, enyne metathesis is not entropically driven by the production of two molecules from one. Rather the reaction proceeds by the stabilization of the product diene over the enyne starting material; in the process, a π-bond is converted to a σ-bond

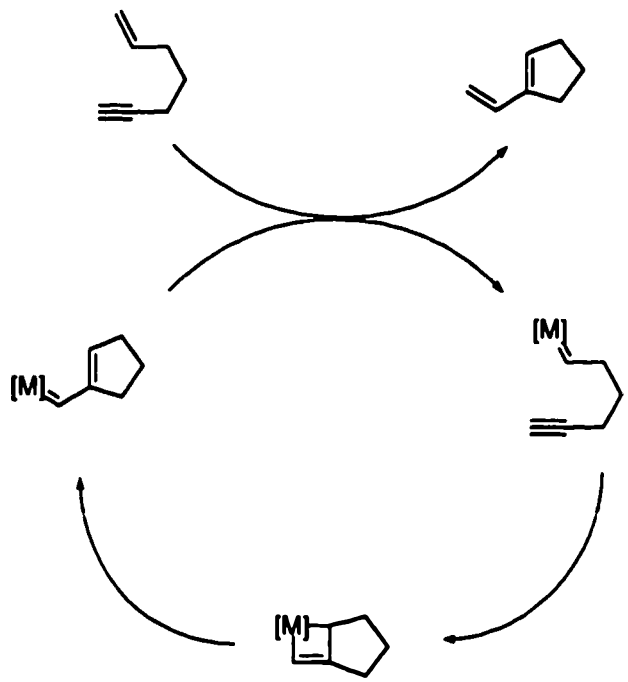
($\Delta H \approx -20$ kcal mol^{-1}). Reports of enyne RCM mediated by tungsten and ruthenium alkylidenes has been reported,[12] and the process shows some potential for applications in synthetic chemistry.[13]

The extension of RCM to the formation of systems containing more than one ring is an attractive goal in terms of greater synthetic efficiency. One strategy for such a polycyclization reaction involves the intermediate vinylcarbene of enyne metathesis. If an

Scheme 5



Mechanism of Enyne Metathesis



additional olefinic tether were present in this species, a second ring-closure would occur and the overall result would be formation of a bicyclic. In this manner, we envisioned the

acetylene acting as an olefin metathesis relay. A cycloolefin instead of an acetylene should also function in this manner as a relay, albeit with different thermodynamic parameters.

Thesis Research

The first chapter of this thesis describes the utility of acetylenes as relay units in RCM. The synthesis of variety of dienyne precursors and their reaction with well-defined metathesis catalysts are detailed. Specifically, the nature of the acetylene substituent is examined in the context of dienyne RCM. Alkyl groups smaller than *t*-butyl are productively cyclized, but in no cases do precursors bearing heteroatomic acetylenic substituents undergo dienyne RCM. A competing diene RCM is observed to varying extents, depending on the transition metal alkylidene catalyst employed.

Extending the concept of an olefin metathesis relay from acetylenes to cycloolefins, so-called tandem ring-opening/ring-closing metathesis, is detailed in Chapter 2. When cycloolefins bearing two olefinic tethers are exposed to metal alkylidenes, the formation of bicyclics is observed. Yield, reaction rate, and the presence of competing intermolecular metathesis are dependent upon ring size of the cycloolefin precursor and the presence of alkyl substitution on the acyclic olefins.

The final chapter extends the application of acetylene and cycloolefin relays to the synthesis of polycyclic molecules. The synthesis and cyclization reactions of precursors bearing more than one relay unit are described. A wide variety of topologies are present in the polycyclic products; fused and nonfused polycyclic systems containing either conjugated or nonconjugated polyenes are formed. In general, a precursor with n relay units will form a product bearing $n + 1$ rings.

The application of this research to the synthesis of natural and unnatural products appears promising. These catalytic reactions proceed under mild conditions in the presence

of a diversity of functional groups. It is hoped that the findings reported in this thesis will contribute both to the continued development of metathesis-based reactions.

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[3]Adapted from Nguyen, S.T. Ph.D. Thesis, California Institute of Technology, 1995.

[4]Nguyen, S.T.; Johnson, L.K.; Grubbs, R.H. *J. Am. Chem. Soc.* **1992**, *114*, 3974.

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[6]Adapted from Dias, E.L. Ph.D. Thesis, California Institute of Technology, 1998.

[7]ADMET is also referred to as DOMP (Diolefin Metathesis Polymerization).

[8]For general references on ROMP, see: (a) Ivin, K. J. *Olefin Metathesis*; Academic Press: London, 1983. (b) Grubbs, R. H.; Tumas, W. *Science* **1989**, *243*, 907-915. (c) Schrock, R. R. *Acc. Chem. Res.* **1990**, *23*, 158-165. (d) Breslow, D. S. *Prog. Polym. Sci.* **1991**, *18*, 1141-1195. For leading references on ADMET, see (e) Wagener, K.B.; Nel, J.G.; Duttweiler, R.P.; Hillmyer, M. A.; Boncella, J.M.; Konzelman, J.; Smith, D.W., Puts, R.; Willoughby, L. *Rubber Chem. & Tech.* **1991**, *64*, 83. (f) Wolfe, P.S.; Gomez, F.J.; Wagener, K.B. *Macromolecules* **1997**, *30*, 714. (g) Chauvin, Y.; Saussine, L. *Macromolecules* **1997**, *29*, 1163.

[9](a) Grubbs, R.H.; Miller, S.J.; Fu, G.C. *Acc. Chem. Res.* **1995**, *28*, 446. (b) Schmalz, H.-G. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1833. (c) Hashimi, A.S.K. *J. Prakt. Chem.* **1997**, *339*, 195.

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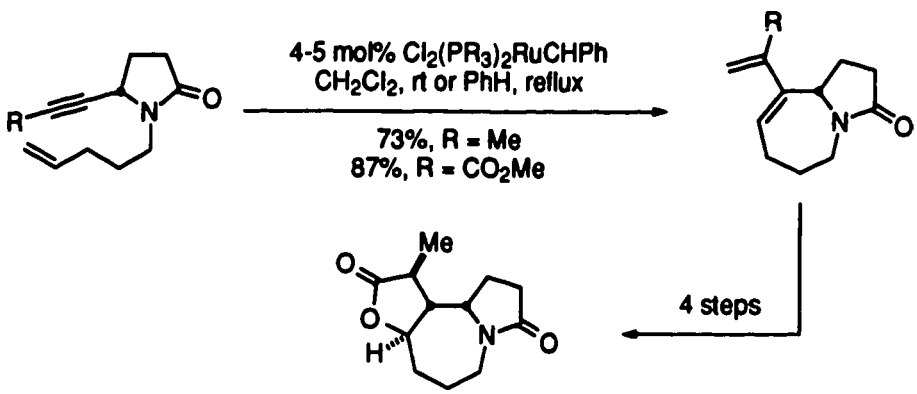
[13]For example, enyne RCM was recently utilized as a key step in the total synthesis of (-)-stemoamide. Kinoshita, A.; Mori, M. *J. Org. Chem.* **1996**, *61*, 8356.



(-)-Stemoamide

Chapter 1:

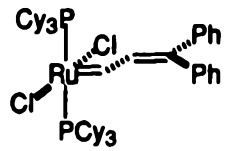
Catalytic Ring-Closing Metathesis (RCM) of Dienynes: Construction of Fused Bicyclic [*n.m*.0] Systems and Effects of Acetylene Substitution[†]

Abstract

Ruthenium carbene **1** ($Cl_2(PCy_3)_2Ru=CHCH=CPh_2$) mediates the efficient and selective conversion of acyclic dienynes to fused bicyclic [*n.m.*0] dienes containing five-, six- and seven-membered rings. Studies with various X-substituted acetylenes (X = H, alkyl, Ph, CO_2Me, $SnBu_3$, $SiMe_3$, halogen) suggest that the dienyne metathesis is not only sensitive to these substituents but also to the catalysts employed. Among the various metal alkylidenes examined, only the ruthenium catalyst **1** exhibited metathesis activity for a range of substrates. In no case, however, were acetylenes with heteroatomic substituents metathesized; these substrates either underwent simple diene RCM or failed to react with the catalyst in a productive fashion. These observations further expand the scope of catalytic RCM for the construction of complex organic compounds.

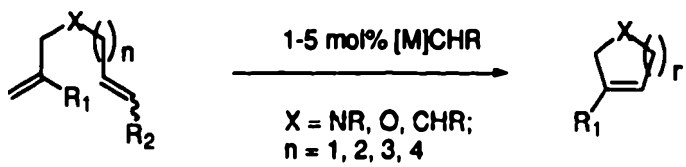
Introduction

Fused bicyclic [*n.m*.0] structural frameworks represent an important substructure in many natural products, and the efficient synthesis of functionalized fused bicyclic rings remains an important goal.[1] Strategies and methods that accomplish the rapid construction of functionalized fused bicyclic rings from simple precursors are therefore desired. We recently reported a short and highly convergent metathesis-based strategy for the construction of functionalized fused bicyclic rings.[2] The key step of this approach involves the ruthenium carbene **1** catalyzed ring-closing metathesis (RCM) of dienynes.[3]



1

Previous reports have established transition metal alkylidene-mediated catalytic RCM of dienes as a general approach to the construction of carbocycles and heterocyles (Eq. 1).[4] To expand the scope of this reaction, a metathesis-based strategy for double ring (or multiple) cyclization of a single substrate to construct a fused bicyclic [*n.m*.0] ring system was explored.

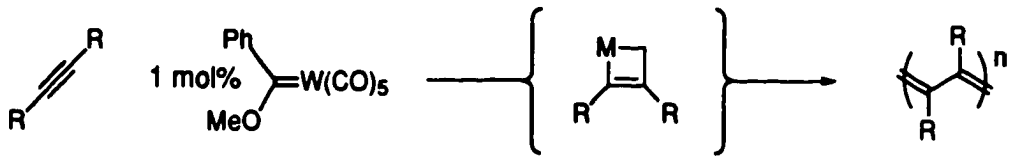


(1)

A starting point for the development of this new strategy was to be found in the reaction of metal carbene species with triple bonds, a process which has been documented in the metathesis polymerization of acetylenes (Scheme 1). For example, exposure of

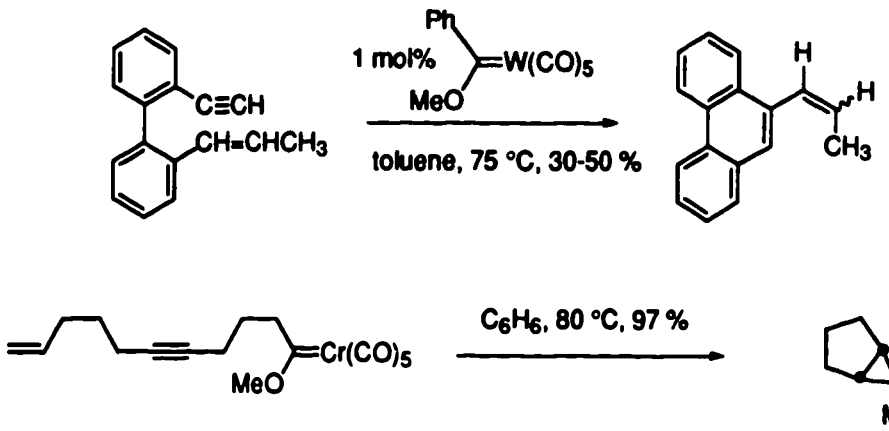
mono- or disubstituted acetylenes to a pentacarbonyltungsten carbene produces the conjugated poly(acetylene) (Scheme 2).[5] The polymerization proceeds despite the inherently unfavorable entropy change, because during the course of every acetylene metathesis, a π bond is converted into a σ bond, a stabilization of approximately 20 kcal mol^{-1}. In the context of bicyclic ring systems, we envisioned the acetylene acting as a metathesis relay: intramolecular reaction with the acetylene would form the first ring and a vinyl carbene species which could react further to produce the second.

Scheme 1



The utilization of acetylenes as relays was based on precedent: several researchers have reported that intramolecular enyne metathesis can be used to construct ring structures. Katz and Sivavec utilized pentacarbonyltungsten carbene in the catalytic intramolecular enyne metathesis (single ring closure) to generate substituted 1-vinylcycloolefins (Scheme 2).[6] Subsequently, other researchers have studied the ene-yne-ene transformation (bis-ring annulation) with electrophilic (Fischer) carbenes and rhodium-catalyzed decomposition of α-diazo ketones to generate compounds containing two rings linked with a single bond. With the Fischer carbenes, pre-formed carbenes were required in stoichiometric quantities, and the second ring closure was followed by reductive elimination of the intermediate metallacyclobutane to form the cyclopropane.[7] With the rhodium-catalyzed decomposition of α-diazo ketones, a complex product distribution arising from several competing processes was observed.[8]

Scheme 2



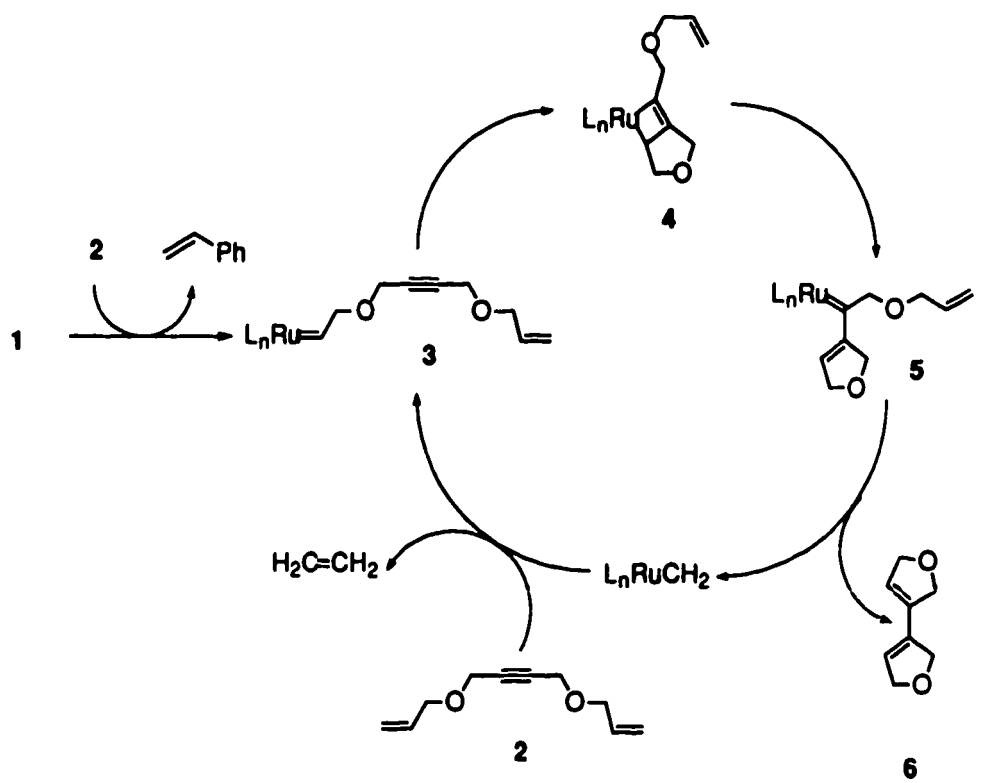
These studies demonstrated that the course of enyne metathesis is dependent on the metal complex employed. Furthermore, these synthetic methods are somewhat limited due to their limited substrate flexibility,[9] several unpredictable competing pathways,[10] modest yields, and stoichiometry of reaction.[11] Nevertheless, an important principle was demonstrated: the acetylene acts as an olefin metathesis relay. In the process, the enyne metathesis generates the first ring in addition to the regenerated carbene which undergoes *diene RCM* to generate a second ring. This property of dienyne cyclization was utilized for a new metathesis-based strategy for the construction of fused bicyclic [*n.m.*0] rings (*vide infra*).

Results and Discussion

Initial Model Studies. Earlier studies from our group and others have established that the ruthenium carbene **1** is a efficient catalyst for diene RCM.[4d,f] Our first objective was to determine the reactivity of ruthenium carbene **1** (and other RCM catalysts) toward the dienyne metathesis.

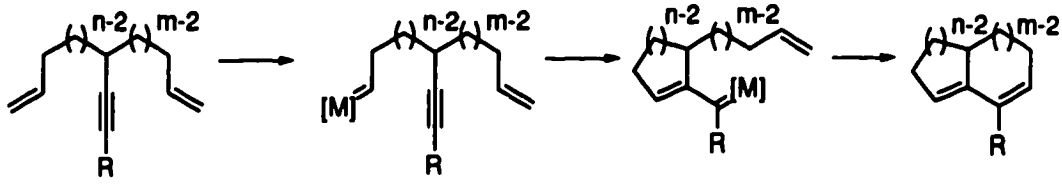
From the readily prepared compound **2**[12] under standard diene RCM conditions (3 mol % **1**, 0.04 M in C_6H_6, rt, 4 h), product **6** is obtained in 90% yield. The reaction proceeds cleanly; no side products or intermediates are observable by ^1H NMR. The proposed mechanism of conversion of dienyne **2** to product **6** is shown in Scheme 3. The first step involves intermolecular acyclic metathesis to generate intermediate **3**, which undergoes intramolecular acetylene metathesis to form **5**, which contains the first ring of **6** and a reactive vinylcarbene. A second intramolecular olefin metathesis produces the second ring and the propagating ruthenium methylidene species **7**. During this process, two rings are generated, and the resulting bicyclics contain olefins that may be further functionalized.

Scheme 3



*Construction of Fused [*n.m.*0] Rings.* The strategy to generate fused bicyclic [*n.m*.0] frameworks (the smallest unit of fused polycyclic structure) is shown in Scheme 4. The key feature is the location of the acetylene group in a *branched* position between the two olefins. An intramolecular acetylene metathesis forms the first ring and a vinylcarbene species which undergoes an intramolecular olefin metathesis to produce the fused bicyclic [*n.m*.0] ring system. The studies contained herein suggest that the strategy is general and allows for the efficient and rapid construction of a variety of fused bicyclic rings. Futhermore, they suggest that the rurthenium carbene **1** is the catalyst of choice. Among the metal alkylidenes examined, only the ruthenium complex catalyzed dienyne cyclization for a range of substrates.

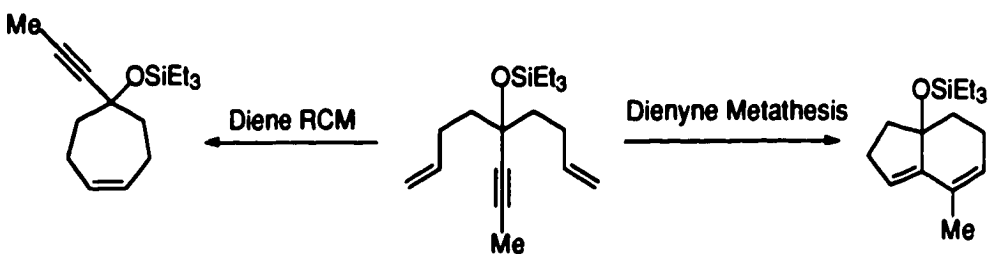
Scheme 4



Branched dienynes **9-16** were synthesized via Grignard addition to the appropriate acetylenic acid derivative and protected as the triethylsilyl ethers.[13] These dienynes were reacted with **1**, and all reactions were initially monitored by ^{1}H NMR spectroscopy.[14] Both the starting vinylcarbene and propagating methylidene α proton resonances are observed downfield in the range 19-20 ppm. As dienyne metathesis proceeds, the vinylcarbene doublet disappears as the methylidene singlet emerges. Each catalytic cycle produces one molecule of ethylene which appears as a sharp singlet at 5.35 ppm. Additionally, the characteristic signal pattern for a terminal olefin disappears as the reaction progresses. Product formation is also observable by thin layer chromatography; the product dienes absorb in the UV region while the dienyne precursors do not.

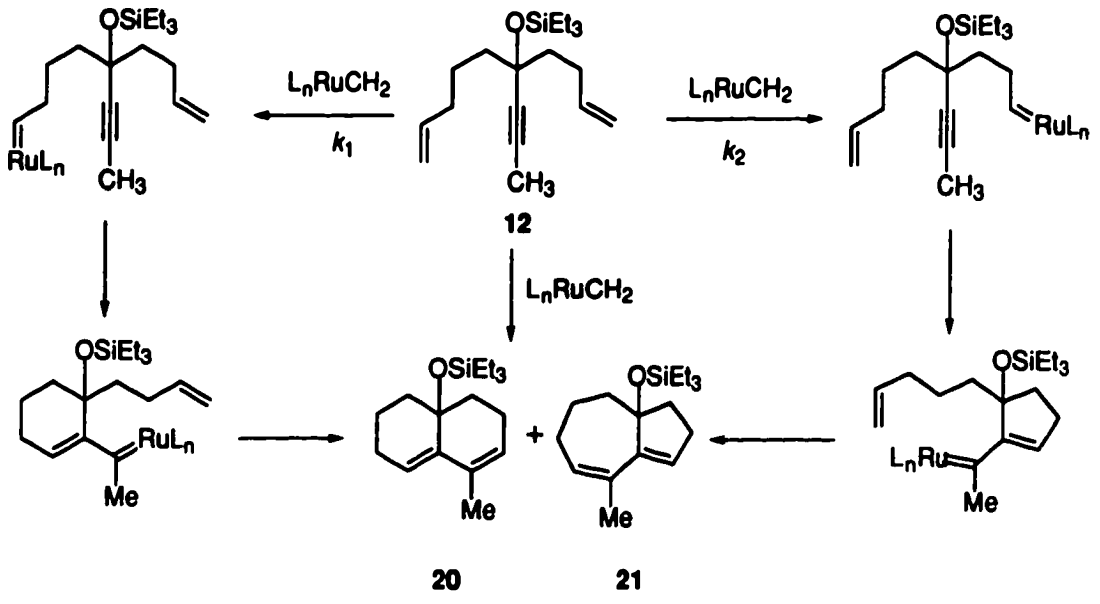
The first substrate to be examined was dienyne **9**, which shares several structural similarities with dienyne **2**. The acetylenes are disubstituted and the length of the diene tether is the same. One important difference was the possibility of a competing diene RCM to give cycloheptene (Scheme 5).[15] This possible side reaction is absent in the linear dienyne **2** since diene RCM would involve the unfavorable formation of a ten-membered cycloalkyne. When dienyne **9** was treated with 3 mol % ruthenium carbene **1** in CH_2Cl_2, the fused bicyclo[4.3.0] ring **18** was isolated in 95% yield along with trace amount (<3%) of cycloheptene **17** arising from competing RCM of dienes. Thus, the dienyne metathesis is largely favored over competing diene RCM. The reaction can be carried out in variety of solvents and temperatures (Table 1). For instance, the same substrate cyclized (quantitative conversion) in two hours in benzene at 65°C with only 1 mol % catalyst. As shown in entry 3, increasing each olefinic tether by one methylene unit leads to the bicyclo[5.4.0] ring **19** in 88% yield. As expected, no product arising from competing diene RCM is detected.

Scheme 5



When the unsymmetrical dienyne **12** was treated with the ruthenium catalyst (entry 3, Table I), two bicyclic compounds possessing [4.4.0] and [5.3.0] ring systems were isolated in equal amounts. The steps leading to these products differ only in the site of initial metathesis (Scheme 6). Presumably, the 1:1 product ratio arises from the nonselective initial step ($k_1 \approx k_2$).

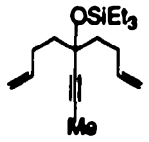
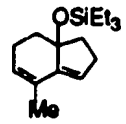
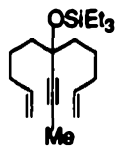
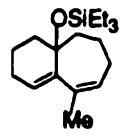
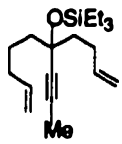
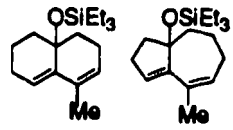
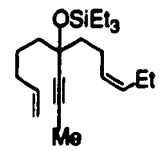
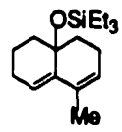
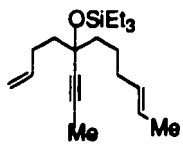
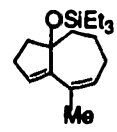
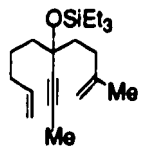
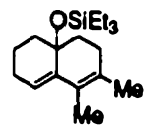
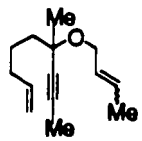
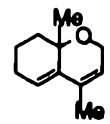
Scheme 6



Earlier work from these laboratories on diene RCM have shown that monosubstituted olefins undergo intermolecular acyclic metathesis faster than disubstituted olefins.[4b] These studies suggested a straightforward solution for the control of product distribution: the site of initial acyclic metathesis, and thus regiochemical control of the cyclized products, could be realized through differentiation of the olefins by alkyl substitution. Accordingly, the precursors **13** and **14** were synthesized.

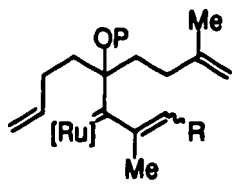
The sterically biased dienyne **13** leads to the bicyclic [4.4.0] diene **20** in 83% yield (entry 4, Table 1). Furthermore, the corresponding bicyclic[5.3.0] ring **21** is isolated as the sole product when the substitution of the olefin is reversed (entry 5, Table 1). Not only do these observations greatly expand the scope of this methodology, they also provide further evidence for the proposed mechanism. The dienyne **15** with an internally substituted olefin also displays high regioselectivity, leading to the formation of the tetrasubstituted bicyclic [4.4.0] compound **22** (entry 6, Table 1). It also represents the first

Table 1. Catalytic RCM of Dienynes

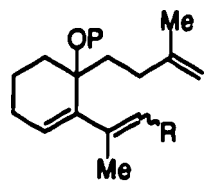
Entry	Substrate	Product	Conditions (Yield)
1			3 mol % **1**, 8 h, 25 °C, 95%, CH_2Cl_2 (0.06 M)
	9	**18**	
2			6 mol % **1**, 8 h, 65 °C, 88%, C_6H_6 (0.06 M)
	10	**19**	
3			3 mol % **1**, 15 h, 65 °C, 86%, C_6H_6 (0.02 M), 1:1 of [4.4.0] and [3.5.0]
	12	**20** **21**	
4			3 mol % **1**, 6 h, 65 °C, 83%, C_6H_6 (0.03 M)
	13	**20**	
5			15 mol % **1**, 1.5 h, 100 °C, 78%, toluene (0.01 M)
	14	**21**	
6			15 mo l% **1**, 12 h, 65 °C, 89%, C_6H_6 (0.05 M)
	15	**22**	
7			3 mul % **1**, 6 h, 65 °C, 88%, C_6H_6 (0.05 M)
	16	**23**	

example in which a sterically congested tetrasubstituted olefin has been constructed using the ruthenium catalyst.[16] Finally, the presence of a heteroatom within the diene tether does not alter the expected outcome (entry 7, Table 1); a single bicyclic product **23** is obtained. No complications arise from possible chelation involving the ether moeity.

Although the formation of the products in Table 1 is consistent with the mechanism described in Scheme 3, an alternative mechanism for dienyne RCM involving initial metathesis at the acetylene has been discussed.[17] Several observations serve to invalidate this "acetylene first" mechanism. During the course of the dienyne cyclization of **15**, for example, the acetylene would react with catalyst **1** to produce the vinylcarbene species **49**. In order to account for the observed product formation, it would be necessary for this intermediate to be formed *with complete regioselectively*; there is no clear reason why this should be true. Additionally, an intramolecular metathesis of the vinylcarbene would produce cyclic triene **50**, an intermediate which should increase to some steady state concentration during the course of the reaction; however, no intermediates of any type are observed in the dienyne RCM reactions.[18] Despite the indirect nature of these arguments against the alternative mechanism, we believe that the initial metathesis occurs at the olefinic tethers.



49

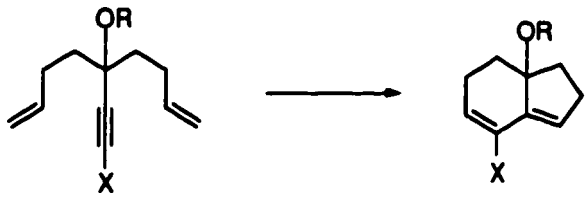


50

Effect of Acetylene Substituent. During the course of dienyne RCM, the acetylenic substituent is transformed into a vinylic substituent (Scheme 7). If suitably substituted precursors were capable of undergoing dienyne RCM, the vinylic substituents of the

product might then be further functionalized by any of a number of available techniques. In order to survey the reactivity of substituted dienynes, several different substrates with varying acetylenic substituents X were synthesized and subjected to ruthenium-catlyzed dienyne metathesis. Concurrently, the reactivity of these dienynes with well-defined tungsten[19] and molybdenum[20] alkylidenes was examined.

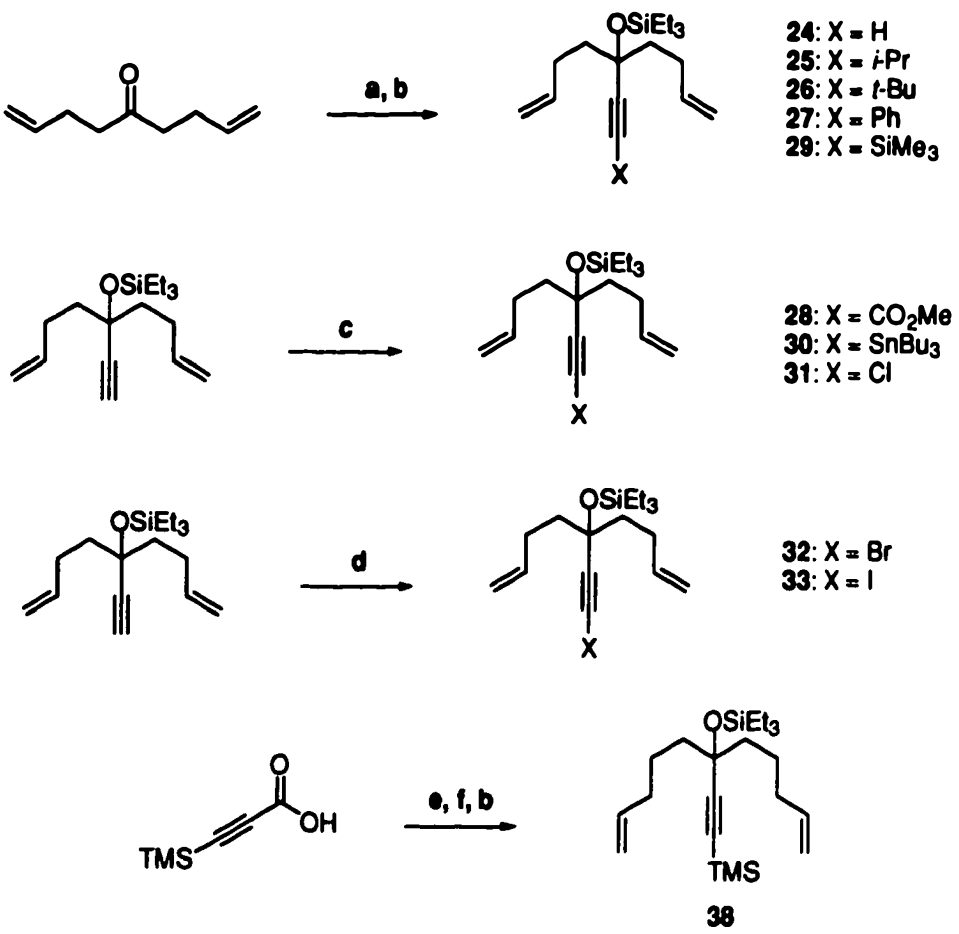
Scheme 7



X = SiR_3, SnR_3, Br, CO_2R, etc.

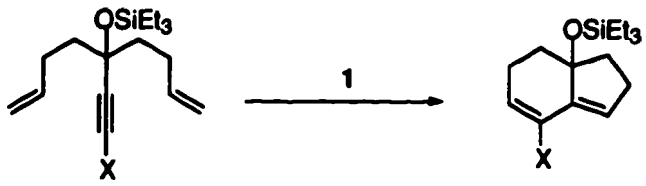
The substituted dienynes **24-33** were readily prepared from 1,8-nonadien-5-one (Scheme 8).[21] The appropriate acetylide anions were added to the ketone, and the resultant alcohols were protected as the triethylsilyl ethers. For those substrates not accessible by acetylide addition, **28-31**, the terminal acetylene dienyne **24** was deprotonated with *n*-BuLi and quenched with the appropriate electrophile. The iodo- and bromoalkyne substrates **32** and **33** were synthesized by reaction of **24** with *N*-halosuccinimide and a catalytic amount of $AgNO_3$.[22] Compounds **24-33** were isolated as clear, colorless oils, and all were stable at ambient temperature.

Scheme 8



Synthesis of Substituted Acetylenes: (a) XCCH, BuLi, THF; (b) Et_3SiOTf, NEt_3, CH_2Cl_2; BuLi, [$ClCO_2Me$, $ClSnBu_3$, NCS], THF; (d) [NBS, NIS], $AgNO_3$ (cat.), acetone; (e) DBU, BnBr, MeCN; (f) $MgBrCH_2CH_2CH_2CH{=}CH_2$, THF.

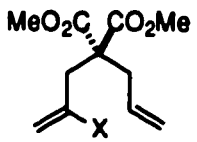
Table 2. Metathesis of Substituted Dienynes using Ruthenium Catalyst **1**



Entry	Acetylene substituent X		Yield, conditions
1	H	**24**	**39**, >98%, 15 min, RT
2	Me	**9**	**18**, 95%, 8 h, RT
3	*i*-Pr	**25**	**40**, 78%, 4 h, 60 °C
4	*t*-Bu	**26**	NR
5	Ph	**27**	**41**, 96%, 3 h, 60 °C
6	CO_2Me	**28**	**42**, 82%, 4h, 60 °C
7	TMS	**29**	NR
8	$SnBu_3$	**30**	NR
9	Cl	**31**	NR
10	Br	**32**	NR
11	I	**33**	NR

Results of the RCM reactions of ruthenium alkylidene **1** with compounds **24-33** are summarized in Table 2.[23] The ruthenium catalyst **1** shows activity with various carbon-based substituents and without exception, it favors dienyne metathesis over the competing diene RCM. With alkyl substitution, steric effects are important and reaction rates follow the expected trend (X = H > Me > *i*-Pr ≈ Ph). With the bulky *t*-butyl substituent, the dienyne cyclization is not observed. The ester-substituted dienyne **28** cyclizes cleanly and with rates similar to the isopropyl-substituted substrate **25** (entry 6, Table 2).

Electronic effects in the reaction of **24-28** with **1** are negligible. Conjugation of an aromatic or an ester with the acetylene has little effect on the rate or the overall yield of bicyclic product. In contrast, diene RCM is much more sensitive to these electronic effects: olefinic substitution of an ester or a phenyl group has an extremely detrimental effect on the outcome of diene RCM. For example, ring closure of **47** and **48** proceeds to 25% and 5% conversion over a period of days, respectively, while the RCM of the parent dimethyl diallylmalonate **46** in which X = H is quantitative on a much shorter timescale.[24]

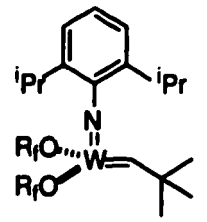


46: X = H
47: X = Ph
48: X = CO_2Me

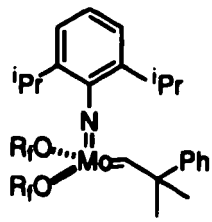
Substrates containing heteroatoms directly attached to the acetylene (**29-33**) are not cyclized by **1**. Because no diene RCM to form the cycloheptene is observed in these reactions, it was thought that the acetylenic substituents were involved in the decomposition of **1**. However, control experiments were conducted with **29-33** which suggested that this was not the case. Exposure of **29-33** to **1** in the presence of the terminal acetylene dienyne **24** or dimethyl diallylmalonate **46** led to cyclization of **24** or **46** while **29-33** remained unreacted even as a ruthenium alkylidene species was observed in the reaction mixture.[25] At higher catalyst loadings, cycloheptene formation is observed (*e.g.*, dienyne **29** in which X = $SiMe_3$ proceeds to >90% conversion of cycloheptene with 10 mol % **1** after 24 h at rt).[26]

The reactions of tungsten catalyst **34** and molybdenum catalyst **35** are summarized in Table 3.[27] Molybdenum alkylidene **35** is the least productive catalyst; it produced a bicyclic product only with the unsubstituted acetylene (X = H, compound **24**, entry 1,

Table 3). With the other substrates (entries 2-11), only the unreacted starting material was recovered in reaction with **35**.

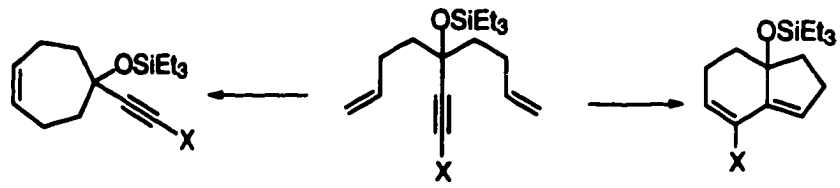


34 (R_f = $CMe(CF_3)_2$)



35 (R_f = $CMe(CF_3)_2$)

Table 3. Metathesis of Substituted Dienynes using Tungsten Catalyst **34** and Molybdenum Catalyst **35**.

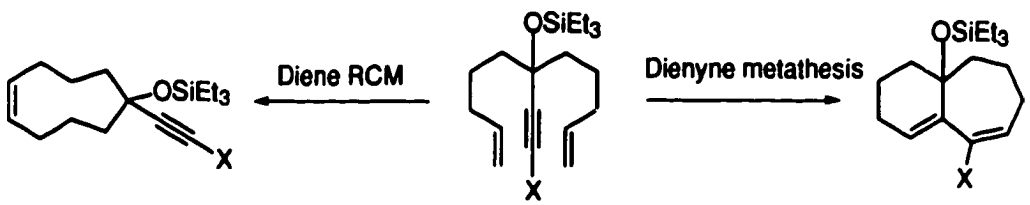


Entry	Acetylene substituent X		Catalyst **34**	Catalyst **35**
1	H	**24**	**39**, >98%, 20 min, RT	**39**, 97%, 20 min, RT
2	Me	**9**	cycloheptene and [4.3.0] (1:4)	NR
3	*i*-Pr	**25**	cycloheptene	NR
4	*t*-Bu	**26**	**43**, cycloheptene	NR
5	Ph	**27**	cycloheptene	NR
6	CO_2Me	**28**	NR	NR
7	TMS	**29**	**44**, cycloheptene	NR
8	$SnBu_3$	**30**	cycloheptene	NR
9	Cl	**31**	NR	NR
10	Br	**32**	NR	NR
11	I	**33**	NR	NR

The tungsten catalyst **34** cleanly converted the unsubstituted acetylene (X=H, entry 1, Table 2) to the bicyclic product. However, with several substrates containing a variety of acetylenic substitution (*i*-Pr, *t*-Bu, phenyl, $SiMe_3$, $SnBu_3$), diene RCM is favored over dienyne metathesis, yielding the cycloheptene instead of the bicyclic compound. The methyl-substituted dienyne **9** yields a mixture (95 : 3) of the cycloheptene and the bicyclic product. A homologous methyl-substituted dienyne substrate **10** is cyclized to the bicyclic [5.4.0] ring **19** (Scheme 9), and no cyclononene product is observed. The homologous

$SiMe_3$ substituted dienyne **38** gave no observable product, and only the unreacted starting dienyne was recovered. The reactions of **10** and **38**, in which diene RCM was expected to be highly unfavorable since it would involve the formation of a nine-membered ring, supported the former explanation: the $SiMe_3$ group effectively shuts down olefin-acetylene metathesis, leaving diene RCM as the only available pathway. However, the RCM reaction of substrate **9** reflects competitive rates of the two processes. In any case, it is evident that the product distribution is critically dependent on the steric bulk of the acetylenic substituents when using tungsten catalyst **34**.

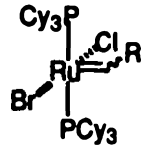
Scheme 9



38: X = TMS
10: X = Me

The bromo- and iodoalkyne dienyne substrates **32** and **33** did not cyclize under standard catalytic RCM conditions with any of the catalysts listed.[28] However, reaction with a *stoichiometric* amount of ruthenium carbene **1** resulted in a halide exchange reaction. After 2 hours at 60 °C, a new vinyl carbene species is observed in the ^1H NMR spectrum of the reaction mixture. The α proton resonance of the new carbene species is upfield and the β proton is downfield compared to the starting carbene. These two signals coincide with the resonances of an intermediate observed in the reaction of **1** with 20 equivalents of LiBr in benzene to produce the dibromo analogue of **1** and are consistent with a mixed halide vinyl carbene species such as **45**.[29] Additionally, the presence of 1,1-

diphenylbutadiene in the reaction mixture indicates at least some degree of metathesis with the olefinic tethers of **32** and **33**.



45

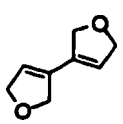
Conclusions

We have presented metathesis-based methodology for the construction of fused bicyclic [*n.m.*0] rings, an important structural framework in a variety of natural products. The ruthenium carbene **1** catalyzes the conversion of acyclic dienynes to fused bicyclic rings containing five, six and seven membered rings. The key step in the strategy involves the metal alkylidene catalyzed dienyne metathesis. During this process, two rings are formed in a single catalytic step. The acetylene plays a critical strategic role by relaying one RCM to another. Studies with different substituents on the acetylene and other well-defined alkylidenes have revealed important reactivity patterns. Product distribution is largely catalyst dependent. Among the well-defined catalysts examined, only the ruthenuim alkylidene **1** exhibited dienyne metathesis for a variety of substituents in good yields. These properties of the catalyst and the dienyne reaction significantly expand the scope of catalytic RCM for the construction of complex organic compounds.

Experimental Section

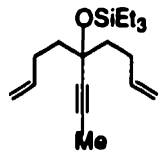
High resolution mass spectra were obtained from the Southern California Mass Spectrometry Facility (University of California, Riverside). Analytical thin-layer chromatography (tlc) was performed using Silica Gel 60 F254 precoated plates (0.25 mm thickness) with a fluorescent indicator. Flash column chromatography was performed using Silica Gel 60 (230-400 mesh) from EM Science.[30] Catalysts **1**, **34**, and **35** were prepared according to published procedures.[3,15] All reactions were carried out under an argon atmosphere with dry, degassed solvents under anhydrous conditions.

2-Butyne-1,4-diol bis(allyl) ether (2): NaH (92 mg, 3.9 mmol) was added to a solution of 2-butyne-1,4-diol (200 mg, 1.75 mmol) in 50 ml of DMF at room temperature. Allyl iodide (650 mg, 3.9 mmol) was added, and the resulting suspension was stirred for 2 hours. The reaction was quenched with water (50 ml), extracted with hexanes (3 × 50 ml), dried over $MgSO_4$, concentrated and purified by flash chromatography to give 250 mg (74%) of **2** as colorless oil. ^{1}H NMR (C_6D_6, 300 MHz) δ 5.21 (dq, J = 17.1, 1.8 Hz, 1H), 4.99 (dq, J = 10.5, 1.5 Hz, 1H), 5.73 (m, 1H), 3.87 (dt, J = 5.4, 1.5 Hz, 2H), 3.94 (s, 2H); ^{13}C NMR (C_6D_6, 75 MHz) δ 117.9, 133.9, 82.3, 70.6, 57.4; IR (neat, cm^{-1}) 3081, 2924, 2854, 1250; HRMS calcd for $C_{10}H_{14}O_2$ (M^+) 166.0994, found 166.0989.



1-(4-Oxa-1-cyclopentenyl)-4-oxacyclopentene (6): Ruthenium catalyst **1** (30 mg, 0.032 mmol) was added to a solution of dienyne **2** (190 mg, 1.14 mmol) in 35 ml

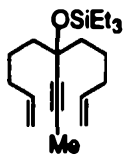
of C_6H_6. The resulting light brown solution was maintained at room temperature for 4 hours. The solution was quenched by opening to air, concentrated under reduced pressure and purified by flash chromatography to produce **6**, which was isolated as a colorless oil (140 mg, 90% yield). ^{1}H NMR (C_6D_6, 300 MHz) δ 4.92 (br s, 1H), 4.61 (m, 2H), 4.47 (m, 2H); ^{13}C NMR (C_6D_6, 75 MHz) δ 132.0, 123.2, 76.2, 75.0; IR (neat, cm^{-1}) 2922, 2867, 1743, 1459; HRMS calcd for $C_8H_{10}O_2$ (M^+) 138.0681, found 138.0680.



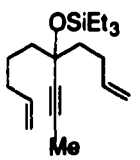
A representative procedure for the synthesis of symmetrical dienynes: 5-(1-Propynyl)-5-triethylsilyloxy-1,8-nonadiene (9): Allyl bromide (5.8 g, 43 mmol) in 10 ml of THF was added dropwise over a period of 20 minutes to a suspension of Mg (1.4 g, 57.4 mmol) in 100 ml of THF at room temperature. The suspension was then stirred at room temperature for an additional 40 minutes. The reaction mixture was then transferred via cannula to $MeCCCO_2Bn$ **8** (2.5 g, 14.3 mmol) in 50 ml of THF at 0 °C. After 15 minutes, saturated NH_4Cl was added (200 ml) and the aqueous layer was extracted with Et_2O (2 × 100 ml). The combined organic layers were washed with saturated NaCl (2 × 100 ml), dried over Na_2SO_4, and concentrated under reduced pressure. The crude reaction mixture was dried with benzene azeotrope (2 × 5 ml) and taken to the next step without further purification.

$Et_3SiOSO_2CF_3$ (3.25 ml, 14.3 mmol) was added to crude alcohol and NEt_3 (4.0 ml, 28.7 mmol) in 50 ml of CH_2Cl_2 at 0 °C. After 30 minutes, the reaction was quenched over saturated $NaHCO_3$ (100 ml) and extracted with CH_2Cl_2 (2 × 50 ml), dried over Na_2SO_4, concentrated and purified by flash chromatography (pet. ether) to give 1.9 g (45%, two steps) of **9** as colorless oil. ^{1}H NMR (C_6D_6, 300 MHz) δ 5.89-5.76 (m, 2H), 5.10-4.94 (m, 4H), 2.35-2.30 (m, 4H), 1.83-1.77 (m, 4H), 1.43 (s, 3H), 1.07 (t, J = 7.5

Hz, 9H), 0.78 (q, J = 7.8 Hz, 6H); ^{13}C NMR (C_6D_6, 75 MHz) δ 138.9, 114.5, 83.1, 81.1, 72.1, 42.5, 29.4, 7.5, 6.7, 3.1; IR (neat, cm^{-1}) 2952, 2918, 2876, 2247, 1426, 1239; HRMS calcd for $C_{18}H_{33}OSi$ (MH^+) 293.2302, found 293.2301.



6-(1-Propynyl)-6-triethylsilyloxy-1,10-undecadiene (10): Isolated 62% (two steps) of **10** as colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.89-5.75 (m, 2H), 4.99-4.92 (m, 4H), 2.09-2.01 (m, 4H), 1.82 (s, 3H), 1.55 (m, 8H), 0.96 (t, J = 7.6 Hz, 9H), 0.66 (q, J = 7.7 Hz, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 138.9, 114.3, 83.2, 80.2, 71.9, 42.3, 33.9, 23.6, 7.1, 6.2, 3.5; IR (neat, cm^{-1}) 3077, 2950, 2918, 2876, 2244, 1415, 1238; HRMS calcd for $C_{20}H_{37}OSi$ (MH^+) 321.2615, found 321.2614.

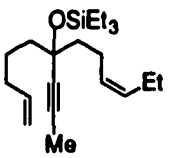


A representative procedure for the synthesis of unsymmetrical dienynes: 5-(1-Propynyl)-5-triethylsilyloxy-1,9-decadiene (12): Allyl bromide (1.6 ml, 15.7 mmol) in 5 ml of THF was added dropwise over a period of 30 minutes to a suspension of Mg (575 mg, 23.6 mmol) in 10 ml of THF at room temperature. The suspension was then stirred at room temperature for an additional 30 minutes. The reaction mixture was then transferred via cannula to MeCCCON(OMe)Me **11** (1.0 g, 7.9 mmol) in 10 ml of THF at -78 °C. After 60 minutes, saturated NH_4Cl was added (100 ml) and the aqueous layer was extracted with Et_2O (2 × 50 ml). The combined organic layers were washed with saturated NaCl (2 × 100 ml), dried over Na_2SO_4, and

concentrated under reduced pressure. The crude ketone was taken to the next step without further purification.

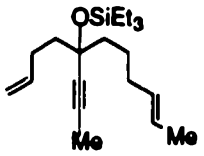
$BrCH_2CH_2CH_2CH=CH_2$ (1.9 ml, 15.7 mmol) in 5 ml of THF was added dropwise over a period of 30 minutes to a suspension of Mg (575 mg, 23.6 mmol) in 10 ml of THF at room temperature. The suspension was then stirred at room temperature for an additional 30 minutes. The reaction mixture was then transferred via cannula to the crude ketone in 10 ml of THF at -78 °C. After 60 minutes, saturated NH_4Cl was added (100 ml) and the aqueous layer was extracted with Et_2O (2 × 50 ml). The combined organic layers were washed with saturated NaCl (2 × 100 ml), dried over Na_2SO_4, and concentrated under reduced pressure. The crude alcohol was dried with benzene azeotrope (2 X 5 ml) and taken to the next step without further purification.

$Et_3SiOSO_2CF_3$ (1.75 ml, 7.86 mmol) was added to the crude alcohol and NEt_2 (2.2 ml, 15.7 mmol) in 10 ml of CH_2Cl_2 at 0 °C. After 30 minutes, the reaction was quenched over saturated $NaHCO_3$ (50 ml) and extracted with CH_2Cl_2 (2 × 50 ml), dried over Na_2SO_4, concentrated, and purified by flash chromatography (petroleum ether) to give 900 mg (38%, three steps) of **12** as colorless oil. ^1H NMR ($CDCl_3$, 300 MHz) δ 5.89-5.78 (m, 2H), 5.06-4.91 (m, 4H), 2.23-2.13 (m, 2H), 2.09-2.02 (m, 2H), 1.82 (s, 3H), 1.69-1.47 (m, 6H), 0.97 (t, J = 7.8 Hz, 9H), 0.66 (q, J = 7.8 Hz, 6H); ^{13}C NMR (C_6D_6, 75 MHz) δ 138.89, 138.94, 114.4, 113.5, 82.9, 80.4, 71.8, 42.3, 41.8, 33.9, 28.8, 23.6, 7.1, 6.2, 3.5; IR (neat, cm^{-1}) 3078, 2952, 2918, 2876, 2244, 1416, 1238; HRMS calcd for $C_{19}H_{35}OSi$ (MH^+) 307.2458, found 307.2457.

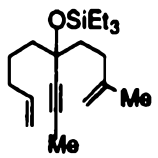


***Z*-5-(1-Propynyl)-5-triethylsilyloxy-1,9-undecadiene (13):** Isolated 31% (three steps) of **13** as colorless, clear oil. ^1H NMR (C_6D_6, 300 MHz) δ 5.93-5.80 (m,

1H), 5.50-5.36 (m, 2H), 5.13-4.96 (m. 2H), 2.45-2.35 (m, 2H), 2.06-1.98 (m, 2H), 1.88-1.82 (m, 2H), 1.80-1.62 (m, 4H), 1.58 (d, J = 4.7 Hz, 3H), 1.44 (s, 3H), 1.11 (q, J = 7.5 Hz, 6H), 0.82 (t, J = 7.5 Hz, 9H); ^{13}C NMR (C_6D_6, 75 MHz) δ 139.0, 131.6, 125.2, 114.4, 83.5, 80.9, 72.4, 42.9, 42.5, 33.2, 29.4, 24.8, 18.1, 7.5, 6.7, 3.1; IR (neat, cm^{-1}) 2951, 2876, 2244, 1415, 1238; HRMS calcd for $C_{21}H_{37}OSi$ (MH^+) 321.2615, found 321.2614.

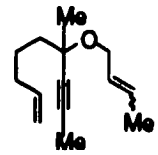


***E*-6-(1-Propynyl)-6-triethylsilyloxy-1,9-dodecadiene (14):** Isolated 15% (three steps) of **14** as colorless, clear oil. ^{1}H NMR (C_6D_6, 300 MHz) δ 5.86-5.72 (m, 1H), 5.53-5.40 (m, 2H), 5.07-4.94 (m, 2H), 2.45-2.35 (m, 2H), 2.17-2.06 (m, 2H), 2.04-1.97 (m, 2H), 1.85-1.60 (m, 6H), 1.45 (s, 3H), 1.11 (t, J = 7.8 Hz, 9H), 0.94 (t, J = 7.5 Hz, 6H); ^{13}C NMR (C_6D_6, 75 MHz) δ 138.9, 131.9, 129.2, 114.8, 83.5, 80.9, 72.5, 43.4, 42.8, 34.3, 24.2, 22.9, 20.9, 14.5, 7.5, 6.7, 3.2; IR (neat, cm^{-1}) 3006, 2953, 2876, 2243, 1415, 1238; HRMS calcd for $C_{21}H_{39}OSi$ (MH^+) 335.2772, found 335.2770.

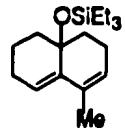


2-Methyl-5-(1-propynyl)-5-triethylsiloxy-1,9-decadiene (15): Isolated 21% (three steps) of **15** as colorless, clear oil. ^{1}H NMR (C_6D_6, 300 MHz) δ 5.86-5.73 (m, 1H), 5.10-4.95 (m, 2H), 4.88 (m, 1H), 4.81 (m, 1H), 2.42-2.34 (m, 2H), 2.07-1.92 (m, 4H), 1.80-1.62 (m, 7H), 1.44 (s, 3H), 1.12 (t, J = 7.5 Hz, 9H), 0.83 (q, J = 7.5 Hz, 6H); ^{13}C NMR (C_6D_6, 75 MHz) δ 146.0, 138.9, 114.8, 110.0, 83.5, 80.9, 72.4, 42.8,

41.6, 34.3, 33.1, 24.2, 22.9, 7.5, 6.7, 3.1; IR (neat, cm^{-1}) 3076, 2952, 2876, 2917, 2242, 1415, 1238; HRMS calcd for $C_{20}H_{37}OSi$ (MH^+) 321.2615, found 321.2614.

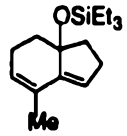


6-Methyl-6-(1-propynyl)-7-oxa-1,9-undecadiene (16): Two sequential Grignard reactions ($BrMgCH_2CH_2CH_2CH{=}CH_2$ and MeMgBr): 60% yield (two steps) of crude alcohol. Alkylation of crude tertiary alcohol: NaH (95%, 130 mg, 5.3 mmol) was added to the crude tertiary alcohol (540 mg, 3.5 mmol) in 5 ml of DMF. After 15 minutes, excess crotyl chloride (3.4 ml, 35 mmol) was added and the resulting mixture was heated to 80 °C for 6 hours. The reaction was quenched with saturated NH_4Cl (50 ml), extracted with hexanes, dried over Na_2SO_4, concentrated and purified by flash chromatography (5% diethyl ether/pet. ether) to give 340 mg (47%) of **16** as colorless oil. ^1H NMR (C_6D_6, 300 MHz, *ca.* 4:1 mixture of *Z:E* isomers) δ 5.85-5.60 and 5.55-5.42 (m, 3H), 5.05-4.92 (m, 2H), 4.40-4.08 (m, 2H), 2.05-1.95 (m, 2H), 1.86-1.60 (m, 4H), 1.55-1.53 (m, 3H), 1.49 (s, 3H), 1.42 (d, J = 2.4 Hz, 3H); ^{13}C NMR (C_6D_6, 75 MHz) δ 139.0, 129.5, 129.0, 127.0, 125.9, 114.7, 81.5, 80.9, 80.8, 73.4, 73.3, 64.9, 60.0, 42.1, 42.0, 34.3, 26.9, 24.1, 17.8, 13.3, 3.2; IR (neat, cm^{-1}) 2978, 2944, 2929, 2858, 2242, 1441, 1248; HRMS calcd for $C_{11}H_{17}O$ (MH^+) 207.1750, found 207.1749.

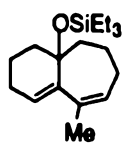


A representative procedure for catalytic dienyne metathesis: 2-Methyl-6-triethylsilyloxybicyclo[4.4.0]deca-2,10-diene (20): Ruthenium catalyst **1** (F.W. 925.1, 0.03 eq, 5.6 mg) in C_6H_6 (1.0 ml) was added through a cannula to

a solution of dienyne **13** (F.W. 334.6, 1.0 eq, 0.2 mmol, 67 mg, entry 4) in C_6H_6 (5.7 ml, 0.03 M). The resulting light brown solution was placed in a 65 °C oil bath. After 6.5 hours, the starting material was completely converted to a compound with $R_f = 0.4$ (pet. ether) on tlc. The solution was concentrated under reduced pressure and purified by flash chromatography. The fused bicyclo[4.4.0] ring **20** was isolated as a colorless, volatile oil (46 mg, 83% yield). ^{1}H NMR (C_6D_6, 300 MHz) δ 5.54-5.47 (br m, 2H), 2.55-2.40 (br m, 1H), 2.12-2.02 (br m, 1H), 1.97-1.77 (m, 4H), 1.76-1.72 (br m, 3H), 1.75-1.3 (m, 4H), 1.03 (t, J = 7.8 Hz, 9H), 0.65 (q, J = 7.8 Hz, 6H); ^{13}C NMR (C_6D_6, 75 MHz) δ 138.7, 131.0, 125.5, 123.1, 70.0, 38.9, 38.2, 26.5, 22.8, 20.2, 18.2, 7.7, 7.0; IR (neat, cm^{-1}) 2937, 2875, 1440, 1237; HRMS calcd for $C_{17}H_{30}OSi$ (M^+) 278.2067, found 278.2066.

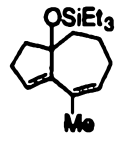


2-Methyl-6-triethylsilyloxybicyclo[4.3.0]nona-2,9-diene (18): ^{1}H NMR (C_6D_6, 300 MHz) δ 5.47 (d, J = 3.9 Hz, 1H), 5.42 (br s, 1H), 2.65-2.47 (br m, 2H), 2.18-1.87 (m, 4H), 1.78 (q, J = 1.1 Hz), 1.71 (ddt, J = 8.6, 8.6, 13.6 Hz, 1H), 1.47-1.35 (m, 1H), 1.01 (t, J = 8.1 Hz, 9H), 0.59 (q, J = 8.1 Hz, 6H); ^{13}C NMR (C_6D_6, 75 MHz) δ 145.6, 128.7, 126.7, 124.3, 83.3, 39.6, 37.5, 30.1, 24.2, 19.3, 7.5, 6.5; IR (neat, cm^{-1}) 2935, 2876, 1455, 1237; HRMS calcd for $C_{16}H_{28}OSi$ (M^+) 264.1910, found 264.1909.

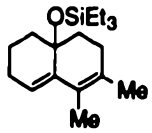


2-Methyl-7-triethylsilyloxybicyclo[5.4.0]undeca-2,11-diene (19): ^{1}H NMR (C_6D_6, 300 MHz) δ 5.59 (dt, J = 5.4, 1.3 Hz, 1H), 5.48 (t, J = 3.8 Hz, 1H), 2.3-

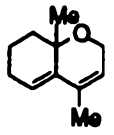
2.17 (br m, 1H), 2.13-1.96 (br m, 1H), 1.94 (q, J = 1.5 Hz, 3H), 1.92-1.68 (m, 6H), 1.65-1.45 (m, 4H), 1.06 (t, J = 7.8 Hz, 9H), 0.64 (q, J = 7.8 Hz); ^{13}C NMR (C_6D_6, 75 MHz) δ 145.1, 135.1, 125.9, 124.3, 76.3, 43.7, 40.4, 29.2, 26.3, 25.7, 23.6, 20.7, 7.6, 7.4; IR (neat, cm^{-1}) 2937, 2834, 1456, 1238; HRMS calcd for $C_{18}H_{32}OSi$ (M^+) 292.2224, found 292.2222.



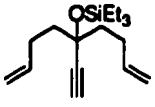
2-Methyl-7-triethylsilyloxybicyclo[5.3.0]deca-2,11-diene (21): ^{1}H NMR (C_6D_6, 300 MHz) δ 5.58 (t, J = 5 Hz, 1H), 5.5 (t, J = 2.5 Hz, 1H), 2.47-2.26 (m, 2H), 2.17-1.92 (m, 4H), 1.9 (d, J = 1.2 Hz, 3H), 1.87-1.8 (m, 2H), 1.66-1.45 (m, 4H), 1.04 (t, J = 8 Hz, 9H), 0.64 (q, J = 8 Hz, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 150.0, 130.3, 128.2, 127.9, 87.2, 42.4, 41.9, 29.3, 29.2, 24.8, 22.5, 7.2, 6.3; IR (neat, cm^{-1}) 2951, 2875, 1455, 1237: HRMS calcd for $C_{17}H_{31}OSi$ (MH^+) 279.2145, found 279.2144. Somewhat unstable compound when concentrated; sample contains a small amount (<3%) of unidentified decomposition substance.



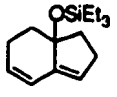
2,3-Dimethyl-6-triethylsilyloxybicyclo[4.4.0]deca-2,10-diene (22): ^{1}H NMR (C_6D_6, 300 MHz, sample contains a small amount (<3%) of unknown decomposition product) δ 5.54-5.51 (br m, 1H), 2.56-2.4 (br m, 1H), 2.2-1.95 (br m, 1H), 1.94-1.76 (m, 4H), 1.68 (br s, 3H), 1.72 (br s, 3H), 1.55-1.32 (m, 4H), 1.03 (t, J = 7.9 Hz, 9H), 0.63 (q, J = 7.7 Hz, 6H); ^{13}C NMR (C_6D_6, 75 MHz) δ 139.4, 130.2, 124.6, 121.3, 69.9, 39.4, 38.2, 29.5, 26.7, 20.5, 18.1, 14.6, 7.7, 6.9; IR (neat, cm^{-1}) 2936, 2829, 1455, 1237; HRMS calcd for $C_{18}H_{33}OSi$ (MH^+) 293.2302, found 293.2301.



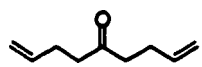
2,6-Dimethyl-5-oxabicyclo[4.4.0]deca-2,10-diene (23): ^{1}H NMR (C_6D_6, 300 MHz, somewhat unstable compound when concentrated) δ 5.39 (m, 1H), 5.21 (br s, 1H), 5.37 (br d, J = 17 Hz, 1H), 4.04 (br d, J = 17 Hz, 1H), 1.97-1.89 (m, 2H), 1.87-1.76 (m, 1H), 1.69 (br s, 3H), 1.58-1.47 (m, 2H), 1.27 (d, J = 0.5 Hz, 3H); ^{13}C NMR (C_6D_6, 75 MHz) δ 138.3, 129.0, 122.4, 120.0, 71.1, 60.8, 36.9, 25.8, 21.9, 20.2, 18.9; IR (neat, cm^{-1}) 2971, 2938, 2830, 1452, 1391, 1366; HRMS calcd for $C_{11}H_{16}O$ (M^+) 164.1202, found 164.1201.



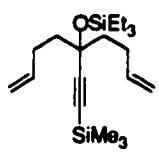
5-Ethynyl-5-triethylsilyloxy-1,8-nonadiene (24): To a stirred solution of the dienyne alcohol (0.95 g, 5.8 mmol) and anhydrous NEt_3 (1.9 ml, 13 mmol) in CH_2Cl_2 (60 ml) at 0°C was added Et_3SiOTf (1.1 ml, 5.8 mmol). The addition was followed by tlc. When finished by tlc, the reaction mixture was quenched with 60 ml sat. aq. $NaHCO_3$, dried over Na_2SO_4, and extracted with CH_2Cl_2 (3 × 50 ml). Purification by chromatography (petroleum ether elution) yielded the product as a clear, colorless oil: 1.25 g, 78%. ^{1}H NMR (C_6D_6, 300 MHz) δ 5.84-5.74 (m, 2H), 5.09-4.94 (m, 4H), 2.34-2.27 (m, 4H), 1.97 (s, 1H), 1.82-1.76 (m, 4H), 1.05 (t, J = 7.8 Hz, 9H), 0.78 (q, J = 7.6 Hz, 6H); ^{13}C NMR (C_6D_6, 75 MHz) δ 138.5, 114.6, 87.2, 73.7, 71.9, 42.1, 29.1, 7.4, 6.6; IR (neat, cm^{-1}) 3307, 3079, 2953, 2914, 2109; HRMS calcd for $C_{17}H_{31}OSi$ (MH^+) 279.2136, found 279.2144.



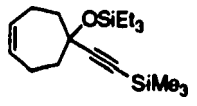
6-Triethylsilyloxybicyclo[4.3.0]nona-2,9-diene (39): ^{1}H NMR (C_6D_6, 300 MHz) δ 6.20 (dd, *J* = 9.9, 2.4 Hz, 1 H), 5.73-5.68 (m, 1H), 5.35 (d, *J* = 0.9 Hz, 1H), 2.59-2.47 (m, 2H), 2.12-1.86 (m, 4H), 1.70-1.35 (m, 2H), 1.02 (t, *J* = 7.9 Hz, 9H), 0.62 (q, *J* = 7.8 Hz, 6H); ^{13}C NMR (C_6D_6, 75 MHz) δ 143.2, 129.8, 125.6, 122.7, 82.5, 38.9, 36.9, 29.9, 23.7, 7.2, 6.2; IR (neat, cm^{-1}) 3030, 2953, 2875; HRMS calcd for $C_{15}H_{26}OSi$ (M^+) 250.1746, found 250.1743.



1,8-Nonadien-5-one. In a dry 500 ml round bottomed flask was placed Mg (40-80 mesh powder, 3.6 g, 147 mmol), I_2 (10 mg), and THF (200 ml). To this mixture 4-bromo-1-butene (15 ml, 147 mmol) in anhydrous THF (50 ml) was added dropwise over 15 min and stirred for an additional 30 min. The Grignard reagent was transferred to an addition funnel connected to a 1000 ml round-bottom flask containing *N*-methoxy-*N*-methyl-4-pentenamide[31] (12.7 g, 89 mmol) in THF (500 ml) at -10 °C. The Grignard reagent was added dropwise to a solution of the Weinreb amide in THF over 20 min. After addition was complete, the reaction was stirred until complete by tlc (ca. 45 min). The reaction was quenched with NH_4Cl (sat. aq., 200 ml) and extracted with Et_2O (3 × 200 ml). The organics were combined, dried over Na_2SO_4, and concentrated under vacuum to yield a yellow oil. This oil was purified by flash chromatography (10% EtOAc in petroleum ether elution) to yield the desired product: 9.4 g, 76%. ^{1}H NMR (C_6D_6, 300 MHz) δ 5.74-5.61 (m, 2H), 4.97-4.88 (m, 4H), 2.22-2.15 (m, 4H), 1.98-1.94 (m, 4H); ^{13}C NMR (C_6D_6, 75 MHz) δ 206.8, 137.7, 115.0, 41.7, 28.0; IR (neat, cm^{-1}) 3080, 2979, 1715.

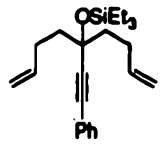


A representative procedure for the synthesis of dienynes via acetylide addition to ketone: 5-Trimethylsilylethynyl-5-triethylsilyloxy-1,8-nonadiene (29): To a solution of trimethylsilylacetylene (0.25 ml, 1.8 mmol) in THF (10 ml) at -78 °C was added BuLi (1.1 ml, 1.6 M in hexanes, 1.8 mmol) and stirred for 10 min. The deprotonated acetylene was then added via canula to a stirring solution of 1,8-nonadien-5-one (202 mg, 1.46 mmol) in THF (10 ml) over 3 min. The reaction was stirred at -78 °C until complete by tlc (about 30 min). The reaction was quenched with NH_4Cl (sat. aq., 20 ml) and extracted with EtOAc (3 × 10 ml). The organic fractions were combined, dried over Na_2SO_4, and concentrated under vacuum to yield a brown oil. The oil was dissolved in 10 ml CH_2Cl_2 and NEt_3 (1.0 ml, 3.0 mmol) was added to the solution. The solution was cooled to 0 °C and Et_3SiOTf (0.55 ml) was added until the reaction was complete by tlc (petroleum ether elution). The reaction mixture was quenched with $NaHCO_3$ (aq., 20 ml) and extracted with Et_2O (3×10 ml). The organics were combined, dried over Na_2SO_4, and concentrated under vacuum to yield a yellow oil. This oil was purified by silica gel chromatography (10% EtOAc in petroleum ether elution) to yield the product as a clear, colorless oil: 330 mg, 96%. ^1H NMR (C_6D_6, 300 MHz) δ 5.87-5.78 (m, 2H), 5.10-4.94 (m, 4H), 2.39-2.33 (m, 4H), 1.87-1.81 (m, 4H), 1.09 (t, J = 7.8 Hz, 9H), 0.84 (q, J = 7.8 Hz, 6H), 0.15 (s, 9H); ^{13}C NMR (C_6D_6, 75 MHz) δ 138.7, 114.6, 110.0, 89.7, 72.4, 42.2, 29.3, 7.4, 6.7, -0.2; IR (neat, cm^{-1}) 3079, 2954, 2914, 2164; HRMS calcd for $C_{20}H_{39}OSi_2$ (MH^+) 351.2529, found 351.2539.

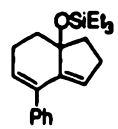


5-Triethylsilyloxy-5-trimethylsilylethynylcycloheptene (44): ^1H NMR (C_6D_6, 300 MHz) δ 5.76-5.73 (m, 2H), 2.22-1.84 (m, 8H), 1.12 (t, J = 7.8 Hz, 9H), 0.84 (q, J = 7.8 Hz, 6H), 0.16 (s, 9H); ^{13}C NMR (C_6D_6, 75 MHz) δ 132.2, 111.0, 89.5,

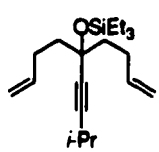
73.8, 42.3, 23.3, 7.5, 7.4, -0.2; IR (neat, cm^{-1}) 3022, 2954, 2162; HRMS calcd for $C_{18}H_{34}OSi_2$ (M^+) 322.2139, found 322.2148.



5-Phenylethynyl-5-triethylsilyloxy-1,8-nonadiene (27): ^1H NMR (C_6D_6, 300 MHz) δ 7.41-7.38 (m, 2H), 6.97-6.95 (m, 3H), 5.88-5.82 (m, 2H), 5.13-4.98 (m, 4H), 2.45-2.41 (m, 4H0, 1.97-1.91 (m, 4H), 1.08 (t, *J* = 7.8 Hz, 9H), 0.85 (q, *J* = 7.8 Hz, 6H); ^{13}C NMR (C_6D_6, 75 MHz) δ 138.7, 131.7, 128.6, 128.4, 123.4, 114.7, 93.2, 85.8, 72.5, 42.2, 29.4, 7.4, 6.7; IR (neat, cm^{-1}) 3079, 3034, 2952, 2913, 2226; HRMS calcd for $C_{23}H_{34}OSi$ (M^+) 354.2370, found 354.2359.

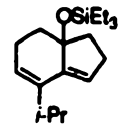


2-Phenyl-6-triethylsilyloxybicyclo[4.3.0]nona-1,9-diene (41): ^1H NMR (C_6D_6, 300 MHz) δ 7.47-7.12 (m, 5H), 5.81-5.79 (m, 1H), 5.63 (s, 1H), 2.16-2.00(m, 4H), 1.80-1.69 (m, 2H), 1.52-1.44 (m, 2H), 1.04 (t, *J* = 7.9 Hz, 9H), 0.66 (q, *J* = 7.7 Hz, 6H); ^{13}C NMR (C_6D_6, 75 MHz) δ 143.6, 141.7, 135.7, 128.8, 128.5, 128.4, 127.3, 127.2, 85.6, 39.3, 37.4, 30.1, 24.7, 7.6, 6.6; IR (neat, cm^{-1}) 3078, 3055, 3022, 2952; HRMS calcd for $C_{21}H_{31}OSi$ (MH^+) 327.2137, found 327.2153.

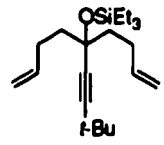


5-(3-Methyl-1-butynyl)-5-triethylsilyloxynona-1,8-diene (25): ^1H NMR (C_6D_6, 300 MHz) δ 5.92-5.78 (m, 2H), 5.12-4.95 (m, 4H), 2.39-2.32 (m, 5H), 1.86-1.80 (m, 4H), 1.09 (t, *J* = 7.9 Hz, 9H), 1.01 (d, J = 6.8 Hz, 6H), 0.82 (q, *J* = 7.7

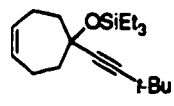
Hz, 6H); ^{13}C NMR (C_6D_6, 75 MHz) δ 138.8, 114.5, 90.9, 83.3, 72.1, 42.6, 29.4, 23.0, 20.7, 7.6, 6.6; IR (neat, cm^{-1}) 3078, 2952, 2235: HRMS calcd for $C_{20}H_{37}OSi$ (MH^+) 321.2605, found 321.2622.



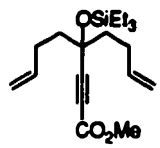
2-(2-Propyl)-6-triethylsilyloxybicyclo[4.3.0]nona-1,9-diene (40): ^1H NMR (C_6D_6, 300 MHz) δ 5.56 (d, *J* = 5.1 Hz, 1H), 5.49 (s, 1H), 2.60-2.49 (m, 2H), 2.18-1.96 (m, 3H), 1.75-1.65 (m, 2H), 1.46-1.36 (m, 2H), 1.13 (d, *J* = 3.0 Hz, 3H), 1.11 (d, *J* = 2.7 Hz, 3H), 1.02 (t, *J* = 8.0 Hz, 9H), 0.61 (q, J = 8.0 Hz, 6H); ^{13}C NMR (C_6D_6, 75 MHZ) δ 144.5, 139.3, 123.4, 122.5, 83.9, 39.4, 37.4, 30.4, 30.2, 24.2, 23.0, 22.1, 7.4, 6.7; IR (neat, cm^{-1}) 3044, 2957, 2929; HRMS calcd for $C_{18}H_{34}OSi$ (MH^+) 293.2293, found 293.2300.



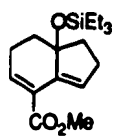
5-(*tert*-Butylethynyl)-5-triethylsilyloxynona-1,8-diene (26): ^1H NMR (C_6D_6, 300 MHz) δ 5.91-5.82 (m, 2H), 5.14-4.96 (m, 4H), 2.41-2.33 (m, 4H), 1.87-1.81 (m, 4H), 1.13 (s, 9H), 1.10 (t, *J* = 7.8 Hz, 9H), 0.83 (q, *J* = 7.8 Hz, 6H); ^{13}C NMR (C_6D_6, 75 MHz) δ 139.0, 114.5, 93.6, 82.6, 72.0, 42.7, 30.9, 29.5, 27.5, 7.5, 6.7; IR (neat, cm^{-1}) 3078, 2951, 2239; HRMS calcd for $C_{21}H_{39}OSi$ (MH^+) 335.2760, found 335.2770.



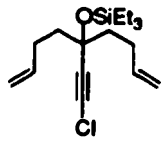
5-*tert*-Butylethynyl-5-triethylsilyloxycycloheptene (43): ^{1}H NMR (C_6D_6, 300 MHz) δ 5.81-5.78 (m, 2H), 2.22-2.00 (m, 4H), 1.90-1.82 (m, 4H), 1.13 (t, *J* = 7.8 Hz, 9H), 1.15 (s, 9H), 0.84 (q, *J* = 7.8 Hz, 6H); ^{13}C NMR (C_6D_6, 75 MHz) δ 132.3, 94.2, 83.4, 73.7, 42.8, 31.0, 27.5, 23.5, 7.5, 6.8; IR (neat, cm^{-1}) 3021, 2951, 2237; HRMS calcd for $C_{19}H_{34}OSi$ (M^+) 306.2370, found 306.2379.



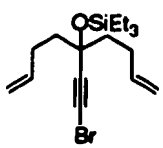
A representative procedure for synthesis of substituted acetylenes via deprotonation of substrate 24: 5-(Carbomethoxyethynyl)-5-triethylsilyloxynona-1,8-diene (28): To a stirring solution of **24** (316 mg, 1.13 mmol) in 8 ml THF at -78 °C was added BuLi (2.5 M in hexanes, 0.50 ml, 1.2 mmol, 1.1 eq) and allowed to stir for 3 min. The acetylide was transferred via canula to a stirring solution of $ClCO_2Me$ (119mg, 1.26 mmol, 1.1 eq) in 12 ml THF. The reaction was slowly warmed to ambient temperature. When tlc showed complete conversion, the reaction was quenched by addition of 25 ml sat. aq. NH_4Cl. The aqueous solution was extracted with EtOAc (3 × 25 ml), dried over Na_2SO_4, and purified by silica gel chromatography (10% Et_2O in petroleum ether elution) to yield the product as a clear, colorless oil: 351 mg, 92 %. ^{1}H NMR (C_6D_6, 300 MHz) δ 5.72-5.67 (m, 2H, 5.03-4.92 (m, 4H), 3.21 (s, 3H), 2.26-2.20 (m, 4H), 1.03 (t, *J* = 7.8 Hz, 9H), 0.77 (q, *J* = 7.8 Hz, 6H); ^{13}C NMR (C_6D_6, 75 MHz) δ 153.6, 138.0, 115.0, 90.3, 77.8, 72.0, 52.1, 41.5, 28.8, 7.3, 6.5; IR (neat, cm^{-1}) 3079, 2954, 2914, 2232, 1827, 1721; HRMS calcd for $C_{19}H_{33}O3Si$ (MH^+) 337.2190, found 337.2199.



2-(Carbomethoxy)-6-triethylsilyloxybicyclo[4.3.0]nona-1,9-diene (42): Isolated as an orange oil which was somewhat unstable at ambient temperature. ^{1}H NMR (C_6D_6, 300 MHz) δ 6.96 (m, 1H), 6.66 (m, 1H), 3.41 (s, 3H), 2.61-2.46 (m, 2H), 2.19-2.10 (m, 1H), 2.02-1.87 (m, 3H), 1.80-1.58 (m, 1H), 1.39-1.09 (m, 1H), 0.97 (t, *J* = 7.9 Hz, 9H), 0.58 (q, *J* = 7.8 Hz, 6H); ^{13}C NMR (C_6D_6, 75 MHZ) δ 166.3, 140.6, 138.7, 131.8, 130.1, 83.9, 51.0, 38.4, 36.6, 30.7, 24.8, 7.4, 6.5; IR (neat, cm^{-1}) 3044, 2951, 2934, 1721, 1255; HRMS calcd for $C_{17}H_{29}O3Si$ (MH^+) 309.1886, found 309.1895.

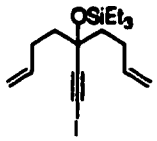


5-Chloroethynyl-5-triethylsilyloxynona-1,8-diene (31): ^{1}H NMR (C_6D_6, 300 MHz) δ 5.82-5.70 (m, 2H), 5.05-4.93 (m, 4H), 2.27-2.18 (m, 4H), 1.76-1.70 (m, 4H), 1.03 (t, *J* = 8.0 Hz, 9H), 0.73 (q, *J* = 7.8 Hz, 6H); ^{13}C NMR (C_6D_6, 75 MHz) δ 138.3, 114.7, 73.2, 72.5, 63.8, 42.0, 29.0, 7.3, 6.5; IR (neat, cm^{-1}) 3080, 2954, 2914, 2223; HRMS calcd for $C_{17}H_{30}ClOSi$ (MH^+) 313.1754, found 313.1762.

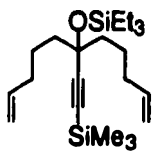


A representative procedure for the synthesis of bromo- or iodoacetylenic dienynes: 5-Bromoethynyl-5-triethylsilyloxynona-1,8-diene (32): The terminal acetylene substrate **24** (306 mg, 1.10 mmol) was dissolved in acetone (8 ml). To this solution was added NBS (231 mg, 1.30 mmol) followed by $AgNO_3$ (42 mg, 0.25 mmol). After stirring for 25 minutes the reaction was complete as judged by tlc and was quenched by pouring into 10 ml ice water. The aqueous solution was extracted with EtOAc (5 × 15 ml), dried over Na_2SO_4, and purified by silica gel chromatography to

yield the product as a clear oil: 383 mg, 97 %. ^{1}H NMR (C_6D_6, 300 MHz) δ 5.79-5.70 (m, 2H), 5.04-4.92 (m, 4H), 2.27-2.21 (m, 4H), 1.77-1.71 (m, 4H), 1.03 (t, *J* = 7.8 Hz, 9H), 0.74 (q, *J* = 7.8 Hz, 6H); ^{13}C NMR (C_6D_6, 75 MHz) δ 138.4, 114.7, 83.9, 73.1, 45.7, 42.0, 29.0, 7.4, 6.5; IR (neat, cm^{-1}) 3078, 2955, 2931, 2140; HRMS calcd for $C_{17}H_{30}BrOSi$ (MH^+) 357.1235, found 357.1249.



5-Iodoethynyl-5-triethylsilyloxynona-1,8-diene (33): ^{1}H NMR (C_6D_6, 300 MHz) δ 5.81-5.68 (m, 2H), 5.05-4.92 (m, 4H), 2.30-2.21 (m, 4H), 1.78-1.72 (m, 4H), 1.04 (t, *J* = 8.0 Hz, 9H), 0.75 (t, *J* = 7.6 Hz, 6H); ^{13}C NMR (C_6D_6, 75 MHz) δ 138.4, 114.7, 102.9, 98.2, 73.7, 42.2, 29.1, 7.4, 6.5; IR (neat, cm^{-1}) 3078, 2952, 2913, 2176; HRMS calcd for $C_{17}H_{30}IOSi$ (MH^+) 405.1111, found 405.1127.



6-Triethylsilyloxy-6-trimethylsilylethynyl-1,10-undecadiene (38): ^{1}H NMR (C_6D_6, 300 MHz) δ 5.86-5.72 (m, 2H), 5.08-4.95 (m, 4H), 2.04-1.98 (m, 4H), 1.80-1.68 (m, 8H), 1.13 (t, *J* = 7.8 Hz, 9H), 0.87 (q, *J* = 7.9 Hz, 6H), 0.16 (s, 9H); ^{13}C NMR (C_6D_6, 75 MHz) δ 138.8, 114.8, 110.7, 89.2, 72.7, 42.1, 34.1, 23.8, 7.4, 6.6, -0.5; IR (neat, cm^{-1}) 3075, 2953, 2924, 2280, 2163; HRMS calcd for $C_{22}H_{43}OSi$ (MH^+) 379.2852, found 379.2830.

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References and Notes

† Parts of this chapter have been published as Kim, S.H.; Zuercher, W.J.; Bowden, N.B. Grubbs, R.H. *J. Org. Chem.* **1996**, *61*, 1073-1081. It is necessary to acknowledge the contributions of Ned Bowden (synthesis of compounds **2** and **6**) and Andres Kim (synthesis of compounds **9**, **10**, **12-16**, **18-23**).

[1]See for instance, *Natural Products Chemistry*, Nakanishi, K., Ed.; Academic Press: New York, 1974; Volumes 1-3.

[2]Preliminary work was reported in a communication. Kim, S.H.; Bowden, N.; Grubbs, R.H. *J. Am. Chem. Soc.* **1994**, *116*, 10801.

[3]For the preparation and characterization of catalyst **1**: (a) Nguyen, S.T.; Johnson, L.K.; Grubbs, R.H.; Ziller, J.W. *J. Am. Chem. Soc.* **1992**, *114*, 3974. (b) Nguyen, S.T.; Grubbs, R.H.; Ziller, J.W. *J. Am. Chem. Soc.* **1993**, *115*, 9858.

[4]Previous reports on RCM from this laboratory: (a) Fu, G.C.; Grubbs, R.H. *J. Am. Chem. Soc.* **1992**, *114*, 5426. (b) Fu, G.C.; Grubbs, R. H. *J. Am. Chem. Soc.* **1992**, *114*, 7324. (c) Fu, G.C.; Grubbs, R.H. *J. Am. Chem. Soc.* **1993**, *115*, 3800. (d) Fu, G C.; Nguyen, S.T.; Grubbs, R. H. *J. Am. Chem. Soc.* **1993**, *115*, 9856. (e) Fujimura, O.; Fu, G.C.; Grubbs, R.H. *J. Org. Chem.* **1994**, *59*, 4029. (f) Miller, S.J.; Kim, S.H.; Chen, Z.; Grubbs, R.H. *J. Am. Chem. Soc.* **1995**, 117, 2108. (g) Miller, S.J.; Grubbs, R.H. *J. Am. Chem. Soc.* **1995**, *117*, 5855-5856. (h) Grubbs, R.H.; Miller, S.J.; Fu, G C. *Acc. Chem. Res.* in press. For recent applications of RCM to natural product synthesis: (i) Martin, S.F.; Liao, Y.; Rein, T. *Tetrahedron Lett.* **1994**, *35*, 691. (j) Borer, B.C.; Deerenberg, S.; Bieraugel, H.; Pandit, U.K. *Tetrahedron Lett.* **1994**, *35*, 3191. (k) Wagman, A.S.; Martin, S.F. *Tetrahedron Lett.* **1995**, *36*, 1169. (l) Houri, A.F.; Xu, Z.; Logan, D.A.; Hoveyda, A.H. *J. Am. Chem. Soc.* **1995**, *117*, 2943. For a review on applications of olefin metathesis in organic synthesis: Grubbs, R.H.; Pine, S.H. In *Comprehensive Organic Synthesis*; Trost, B.M., Ed.; Pergamon: New York, 1991; Vol.

5, Chapter 9.3.

[5]Katz, T.J.; Lee, S.J. *J. Am. Chem. Soc.* **1980**, *102*, 424.

[6]Katz, T.J.; Sivavec, T.M. *J. Am. Chem. Soc.* **1985**, *107*, 737.

[7](a) Korkowski, P.F.; Hoye, T.R.; Rydberg, D.B. *J. Am. Chem. Soc.* **1988**, *110*, 2676. (b) Harvey, D.F.; Brown, M.F. *J. Org. Chem.* **1992**, *57*, 5559. For a review on the chemistry of Fischer carbenes with enyne substrates see: Wulff, W.D. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon: New York, 1991; Vol. 5, Chapter 9.2.

[8]Hoye, T.R.; Dinsmore, C.J. *J. Am. Chem. Soc.* **1991**, *113*, 4343.

[9]Some substrates possess specific structural requirements such as pre-formed carbenes and specific α-diazocarbonyl compounds.

[10]For instance, the rhodium-catalyzed reaction showed a complex product distribution arising from several competing processes (reference 8).

[11]The dienyne cyclization shown in Scheme 2 required a stoichiometric amount of pre-formed Fischer carbene (reference 7a).

[12]Dienyne **2** was synthesized from 2-butyne-1,4-diol: NaH, CH_2=$CHCH_2Br$, DMF.

[13]The dienyne precursors have been protected as trialkylsilyl ethers. Cyclization proceeds without this protection, but the reaction rate is slowed dramatically, possibly due to intramolecular chelation.

[14]NMR reactions were conducted in 0.2-0.3 mmol scale at 0.01-0.07M substrate concentration.

[15]Another noteworthy difference is that the olefinic tethers of the branched precursors **9** and **10** are enantiotopic (*i.e.*, they are related by a plane of symmetry) while the tethers of **2** are homotopic. The site of initial metathesis of the branched precursors thus determines the absolute configuration of the product.

[16]Additionally, the formation of **22** directly contradicts this "acetylene first" mechanism (*vide supra*): in no case has the formation of a tetrasubstituted olefin from an α,ω-diene been possible using ruthenium catalysts such as **1**.

[17]Ivin, K.J.; Mol, J.C. *Olefin Metathesis and Metathesis Polymerization*; 2nd. Ed.; Academic: San Diego, 1997.

[18]Furthermore, in order for this alternative "acetylene first" mechanism to be operant, it must be true that metathesis of the acetylene is faster than metathesis of the olefin ($k_{acetylene} > k_{olefin}$). In solution, reaction of **1** with 2-butene occurs on the order of minutes at room temperature while the reaction with 2-butyne proceeds over hours at higher temperatures.

[19]**34**: (a) Schrock, R.R.; DePue, R.T.; Feldman, J.; Schaverien, C.J.; Dewan, J.C.; Liu, A.H. *J. Am. Chem. Soc.* **1988**, *110,* 1423. (b) Schrock, R.R.; DePue, R.T.; Feldman, J.; Yap, K.B.; Yang, D.C.; Davis, W.M.; Park, L.; DiMare, M.; Schofield, M.; Anhaus, J.; Walborsky, E.; Evitt, E.; Kruger, C.; Betz, P. *Organometallics* **1990**, *9*, 2262.

[20]**35**: (a) Schrock, R.R.; Murdzek, J.S.; Bazan, G.C.; Robbins, J.; DiMare, M.; O'Regan, M. *J. Am. Chem. Soc.* **1990**, *112*, 3875. (b) Bazan, G.C.; Oskam, J.H.; Cho, H.-N.; Park, L.Y.; Schrock, R.R. *J. Am. Chem. Soc.* **1991**, *113*, 6899. Both the tungsten **34** and molybdenum **35** alkylidenes have been employed in diene RCM.

[21]Notably absent from the list of acetylenic substituents are X = OR, NRR', and SR. The acetylenic substituent X is transformed to an α-carbon substituent in the intermediate vinylcarbene in the mechanism of dienyne RCM, and ruthenium alkylidenes containing these groups as α-carbon substituents have been prepared and are not active in olefin metathesis. Wu, Z.; Nguyen, S.T.; Grubbs, R.H.; Ziller, J.W. *J. Am. Chem. Soc.* **1995**, *117*, 5503.

[22]Hofmeister, H.; Annen, K.; Laurent, H.; Wiechert, R. *Angew. Chem. Int. Ed. Engl.*

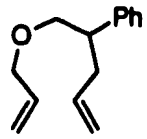
1984, *23*, 727-729.

[23]Reactions were conducted at 0.05-0.1 M concentration in C_6D_6 with 3-5 mol % catalyst. "NR" signifies no productive dienyne RCM. In some cases, diene RCM is observed (see text).

[24]Additionally, when X = methyl, the reaction produces the substituted cyclopentene derivative in greater than 95% yield. Kirkland, T.A.; Grubbs, R.H. *J. Org. Chem.* **1997**, *62*, 7310.

[25]This type of process, in which seemingly reactive partners fail to undergo any observable reaction, has been dubbed the "high school dance reaction" by a former member of the Grubbs group. Fujimura, O. Personal Communication.

[26]To compare, ruthenium alkylidene **1** catalyzes the cycloheptene formation of **49** in 72% yield (8h, rt, 4 mol % **1**) as reported in Reference 4d.



49

[27]The dienyne **9** was treated with other metal alkylidenes. With Basset's tungsten catalyst,[a] the reaction failed to go to completion and only 30% of the bicyclo[4.3.0] compound **18** was observed. Only unreacted starting material was recovered upon treatment of 18 with Tebbe reagent.[b] (a) Couturier, J.-M.; Pailet, C.; Leconte, M.; Basset, J.-M.; Weiss, K. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 628. (b) Tebbe, F.N.; Parshall, G.W.; Overall, D.W. *J. Am. Chem. Soc.* **1979**, *101*, 5074.

[28]Catalyst **1** fails to metathesize vinyl halide species as well. Reference 23 and Kim, S-H.; Grubbs, R. H. Unpublished results.

[29]Dias, E.L.; Grubbs, R.H. Unpublished results. For more information on the synthesis and reactivity of derivatives of **1** bearing differing halides and phosphines as well as a

detailed description of the mechanism of **1**, see Dias, E.L.; Nguyen, S.T.; Grubbs, R.H. *J. Am. Chem. Soc.* **1997**, *119*, 3887.

[30]Still, W.C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

[31]Nahm, S.; Weinreb, S.M. *Tet. Lett.* **1981**, *22*, 3815-3818.

Chapter 2:
Tandem Ring-Opening/Ring-Closing Metathesis of Cyclic Olefins†

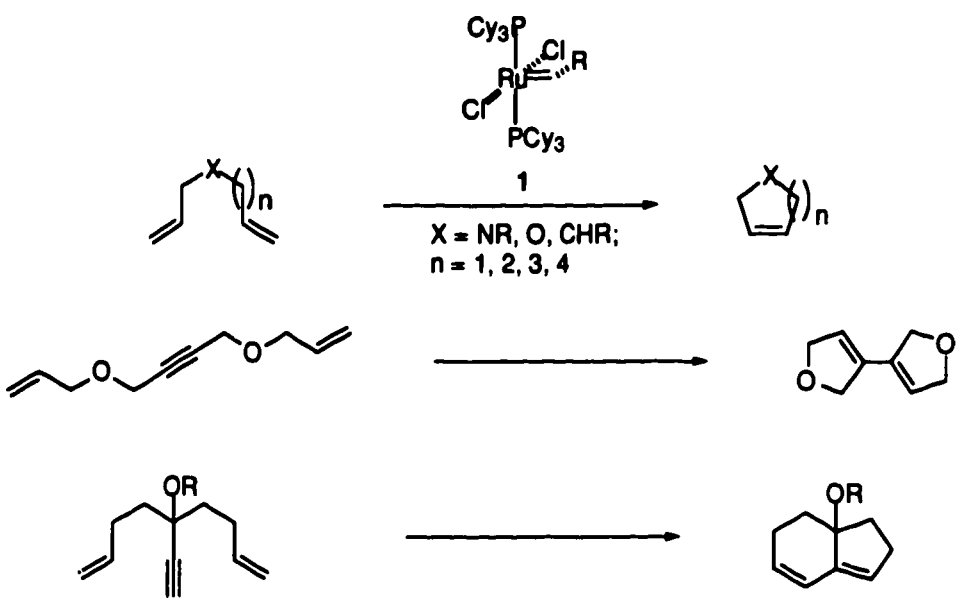
Abstract

Ruthenium alkylidene **1** has been utilized in the tandem ring-opening/ring-closing metathesis of cycloolefins. This reaction produces bicyclic molecules conatining nonconjugated dienes. Reactivity of the precursors is dependent upon ring strain, and thus ring size, of the cycloolefins. Competing oligomerization is observed in substrates having low ring strain; this process is inhibited by increasing dilution of the reaction or through alkyl substitution of an acyclic olefins.

Introduction

As new catalysts have been developed which are more tolerant of functionality and commercially available, the olefin metathesis reaction has played an increasingly significant role in organic synthesis. Many of the applications to date have been ring-closing metathesis (RCM) of dienes. Ruthenium carbene complexes such as **1** (R = Ph, $CH{=}CPh_2$) effectively catalyze the ring-closing metathesis of dienes to yield unsaturated carbocycles and heterocycles (Scheme 1).[1] In order to obtain more complex ring systems, it was demonstrated that an acetylene between the two olefins of the diene acts as a relay, allowing the metathesis catalyst to proceed from one ring to the next to produce a bicyclic product.[2] In this manner, both fused and nonfused bicycles containing conjugated dienes are accessible.

Scheme 1



In addition to the utility of RCM in the synthesis of cyclic molecules, these same metathesis catalysts also promote the ring-opening metathesis polymerization (ROMP) of

cyclic olefins.[3,4] In ROMP, ring strain (Table 1) is a requisite driving force because the reaction is entropically disfavored; those monomers possessing higher ring strains are generally more active in ROMP. Monomers such as norbornene and cyclobutene are readily polymerized with a range of catalysts; more active catalysts will promote the ROMP of cyclopentene and cyclooctene.[4] Additionally, there are a limited number of cases of cycloheptene ROMP.[5]

Table 1. Ring strain values for common cycloolefins[6]

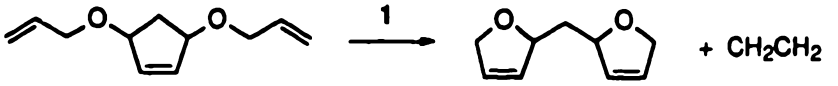
Cycloolefin	Ring Strain / kcal mol^{-1}
Cyclopropene	54-56
Cyclobutene	31-34
Cyclopentene	6.8-6.9
Cyclohexene	2.5-2.6
Cycloheptene	6.7-7.2
Cyclooctene	7.4-8.8
Norbornene	24-27

In contrast to the other ring systems, cyclohexenes exhibit extremely low activity in this regard.[7] This failure to polymerize is largely due to the low ring strain of cyclohexene; the enthalpic component of the polymerization is not sufficiently negative to offset unfavorable entropy change. The entropic component, which is temperature dependent, may be attenuated by conducting the reaction at lower temperature, an approach which has shown limited success in cyclohexene ROMP: using a heterogeneous tungsten catalyst system, a 50% by volume solution of cyclohexene in toluene proceeds to a mixture of oligomers ($N < 20$) to a 12% conversion at -77 °C but quickly reverts to pure cyclohexene

as the temperature is increased.[8] Even under a pressure of 10^4 psig of ethylene, cyclohexene ring-opening metathesis proceeds to only 6.8% conversion of 1,7-octadiene.[9]

The combination of enthalpically driven ring-opening from ROMP and the entropically driven dienyne RCM constitutes a new strategy for the synthesis of organic ring systems. Rather than using an acetylene to relay the metathesis catalyst, this method utilizes the unsaturation of a cycloolefin. A typical substrate molecule (Eq. 1) has a strained cycloolefin located between olefinic side chains. The products of this reaction are bicyclics with nonconjugated dienes.

The thermodynamics of the proposed ring-opening/ring-closing metathesis reaction may be viewed as a combination of RCM and ROMP. To a first approximation, the enthalpic contribution will be determined by the balance of ring strain in the starting material and product, and those cyclics which may be successfully polymerized through ROMP (or those cyclics successfully produced by RCM) represent a starting point for our investigations. Unlike ROMP, the reaction is entropically driven by the production of ethylene, similar to diene or dienyne RCM, and may proceed if enthalpically neutral or even slightly disfavored.



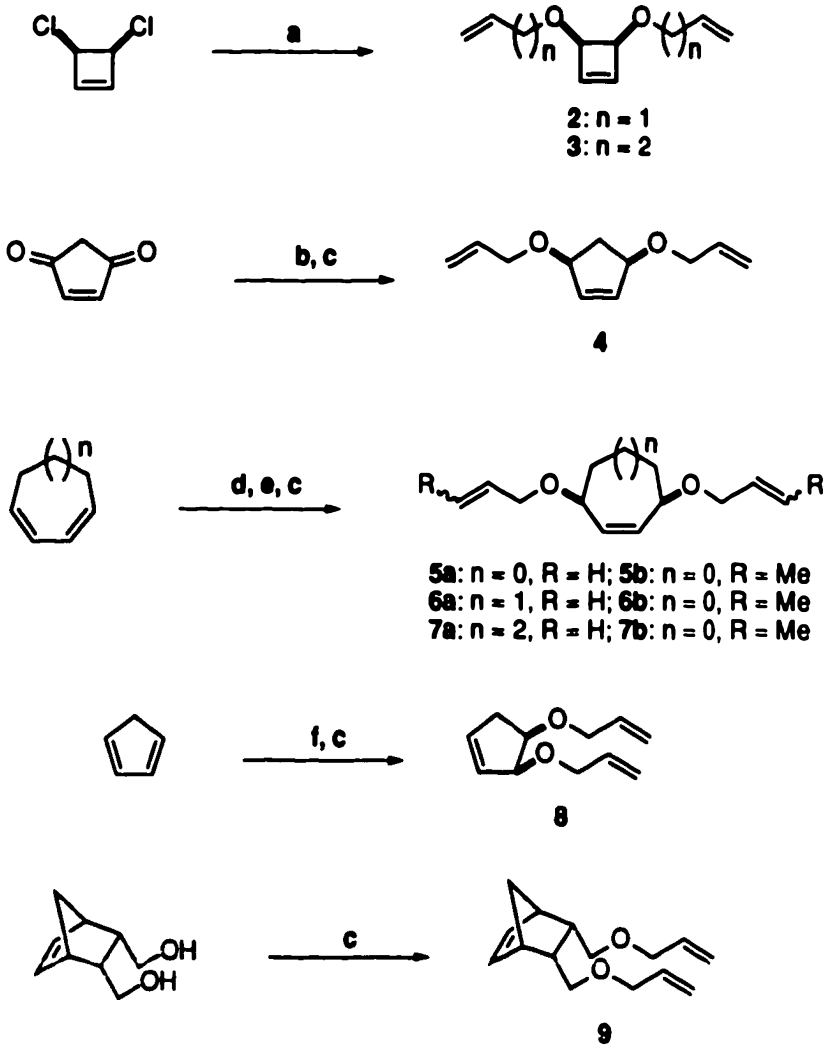
4 **10** (1)

For our initial studies concerning the ring-opening/ring-closing metathesis of cycloolefins, we have focused on the synthesis of polycyclic ethers. In addition to the straightforward synthesis of the precursors, the product polycyclic ethers are structural motifs common to many natural and synthetic ionophores, and the development of new methods for their synthesis remains an important goal.[10]

Results and Discussion

Substrate Synthesis. The bis(allyl) ethers of several cycloolefin diols were prepared for the study (Scheme 2). These substrates contain four- to eight-membered rings

Scheme 2



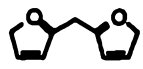
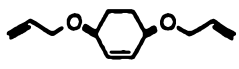
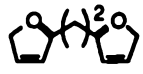
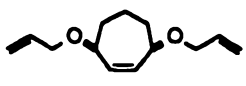
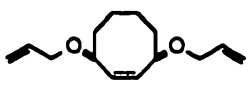
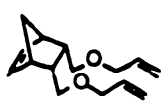
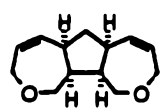
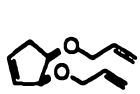
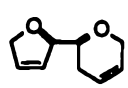
Synthesis of ring opening-ring closing metathesis cyclic ether substrates: (a) NaH, CH_2=$CH(CH_2)_nOH$, 75 °C, 40-66%; (b) $NaBH_4$, $CeCl_3$, MeOH, 58%; (c) NaH, CH_2=$CHCH_2Br$ or CH_3CH=$CHCH_2Br$, DMF, 50-80%; (d) $Pd(OAc)_2$ (cat), LiOAc, HOAc/pentane, 40-75%; (e) $LiAlH_4$, THF, 75-86%; (f) OsO_4 (cat), $tBuOH/H_2O$, 89%

as well as a norbornene ring system. The cyclobutenes **2** and **3** were obtained by heating a solution of commercially available *cis*-3,4-dichlorocyclobutene and sodium allyl or homoallyl alkoxide in the parent alcohol.[11] Luche reduction[12] of 3,5-cyclopentenedione followed by standard *O*-allylation conditions produced the cyclopentene substrate **4**. Three steps were required to produce **5-7** from the cyclic 1,3-dienes: palladium-catalyzed *cis*-1,4-diacetoxylation,[13] reduction of the acetate to produce the diol, and *O*-alkylation with either allyl or (*E/Z*)-crotyl bromide. Osmylation of cyclopentadiene[14] followed by *O*-allylation produced the substrate **8**. The *endo, endo*-norbornenediol bis(allyl) ether **9** is made in two steps by reduction of the commercially available anhydride followed by *O*-allylation.

Ring-Opening/Ring-Closing Metathesis. Treatment of substrates **2-9** with 3-6 mol % **1** at slightly elevated temperature affords the expected bicyclic products in good to excellent yields (Table 2) depending on ring size and reaction concentration. The catalyst efficiently produces dihydrofuran and dihydropyran systems as well as the tricyclic compound **16** which incorporates two oxacycloheptene substructures. Reaction times parallel ring strain energies for the homologous series of cycloolefin starting compounds (entries 1-5):[6] cyclobutene **2** is opened fastest, followed by the five- and eight-membered rings of **4** and **7**. Cycloheptene **6** and cyclohexene **5** appear to be the slowest rings to open.

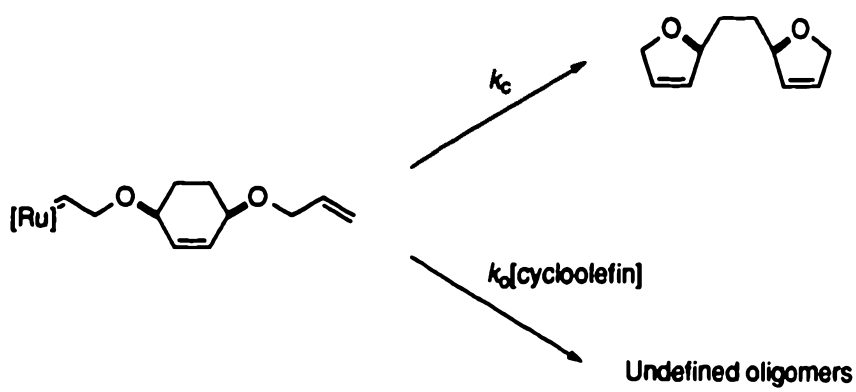
Because of their low strain energy, cyclohexenes were expected to be poor relay rings in ring-opening/ring-closing reactions. These factors, in addition to potential conformational constraints on the intermediate metallacycle, made it questionable at the outset whether the ring would open at all, much less at a synthetically useful rate. However, it was noted that conversion of a six-membered ring to two five-membered rings with concomitant production of ethylene should be thermodynamically favorable due to the entropy change. Accordingly, cyclohexene ring-opening/ring-closing metathesis was attempted.[15]

Table 2. Results of ring opening-ring closing metathesis reactions

Entry	Substrate	Product	Yield and Conditions
1	 **2**	 **10**	82%, 3 mol % **1**, 0.1 M (C_6H_6), 45 °C, 1.5h
2	 **4**	 **11**	90%, 5 mol % **1**, 0.1 M (C_6H_6), 60 °C, 2h
3	 **5a**	 **12**	73%, 0.008 M (C_6H_6), 45 °C, 6h
4	 **6a**	 **13**	57%, 0.02 M (C_6H_6), 45 °C, 6h
5	 **7a**	 **14**	85%, 0.01 M (C_6H_6), 45 °C, 6h
6	 **3**	 **15**	70 %, 3 mol % **1**, 0.07 M (C_6H_6), 45 °C, 6h
7	 **9**	 **16**	68 %, 6 mol % **1**, 0.04 M (C_6H_6), 45 °C, 2h
8	 **8**	 **17**	92 %, 5 mol % **1**, 0.04 M (C_6H_6), 60 °C, 3h

Initial experiments with the six-membered ring relay system suggested that our ring opening-ring closing strategy would be limited to the more strained ring systems. The reactions of **5a**, **6a**, and **7a** yielded multiple products when the reactions were conducted at concentrations near those used for the other substrates. The failure to produce the expected bicyclics was attributed to a competing intermolecular metathesis, which was not observed in systems having high ring strain (cyclobutene or norbornene). It appeared that the acyclic olefins were reacting via acyclic diene metathesis (ADMET)[16] to produce dimers or other oligomeric species (Scheme 3). Competing intermolecular metathesis has been observed previously for systems in which the rate of cyclization is slower than oligomerization.[17]

Scheme 3



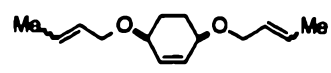
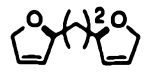
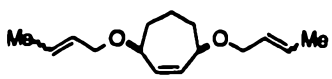
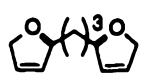
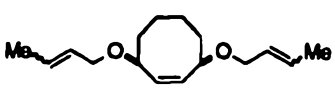
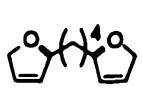
If this scheme for the competing process is indeed correct, there are two terms which contribute to the rate of oligomerization: concentration and k_o, the oligomerization rate constant. Decreasing either of these terms should steer the reaction to the desired bicyclic product. When conducted at higher dilution, the rates of intermolecular metathesis were effectively decreased relative to the intramolecular reaction. For example, the conversion of **5a** to **12** proceeds cleanly and efficiently at 0.008 M in 73% yield (compared

to 16% at 0.12 M). A similar dependence of reaction yield on concentration is observed for **6a** and **7a**.

We envisioned the oligomers being formed by intermolecular metathesis through the acyclic olefins, and in order to decrease k_O, the bis(crotyl) cycloolefin diol ethers were prepared in order to make the acyclic olefins less active for metathesis relative to the cyclic olefin.[18] There is ample precedent that increasing substitution on an olefin decreases the rate of olefin metathesis.[2] Alkyl substitution should slow the undesired process and allow the metathesis catalyst to react via ring-opening.

Indeed, when the crotyl ethers **5b-7b** are reacted with catalyst **1**, the reactions proceed in moderate yield at concentrations similar to those used for the other substrates (Table 3). These yields are among the lowest for all of the substrates included in this

Table 3. Results of ring opening-ring closing metathesis reactions of crotyl-substituted ethers

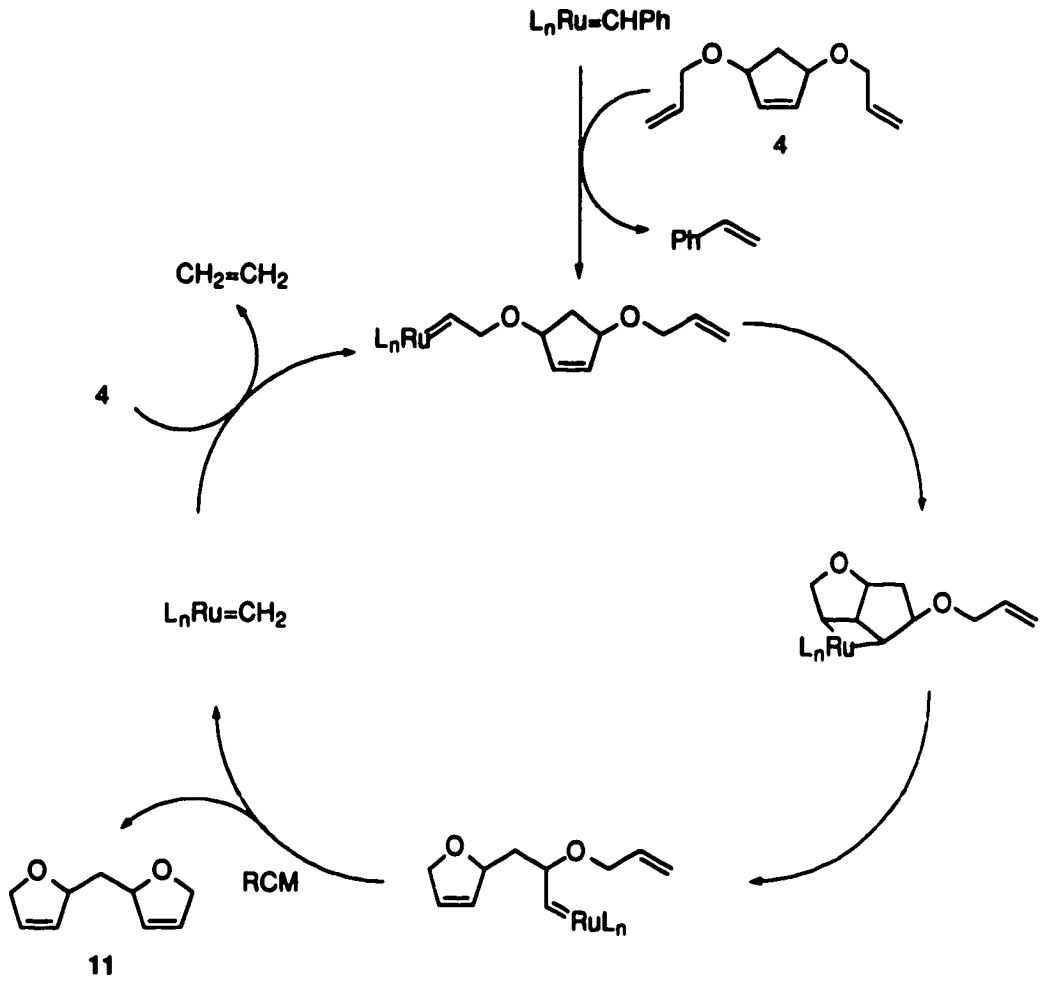
Entry	Substrate	Product	Yield and Conditions
3b	 **5b**	 **12**	42%, 6 mol % 1, 0.2 M (C_6H_6), 45 °C, 6h
4b	 **6b**	 **13**	56%, 4 mol % 1, 0.2 M (C_6H_6), 45 °C, 6h
5b	 **7b**	 **14**	71 %, 6 mol % 1, 0.1 M (C_6H_6), 45 °C, 4h

study, and the mass balance is presumably to be found in a small amount of oligomeric byproducts. The reaction times are somewhat longer than for the other substrates in the

homologous series. This observation is consistent with the substitution decreasing the rate of metathesis at the acyclic olefin. Olefin substitution appears to slow the intramolecular (desired) process to a lesser extent, and the relative rate of cyclization is effectively increased to allow for product formation.

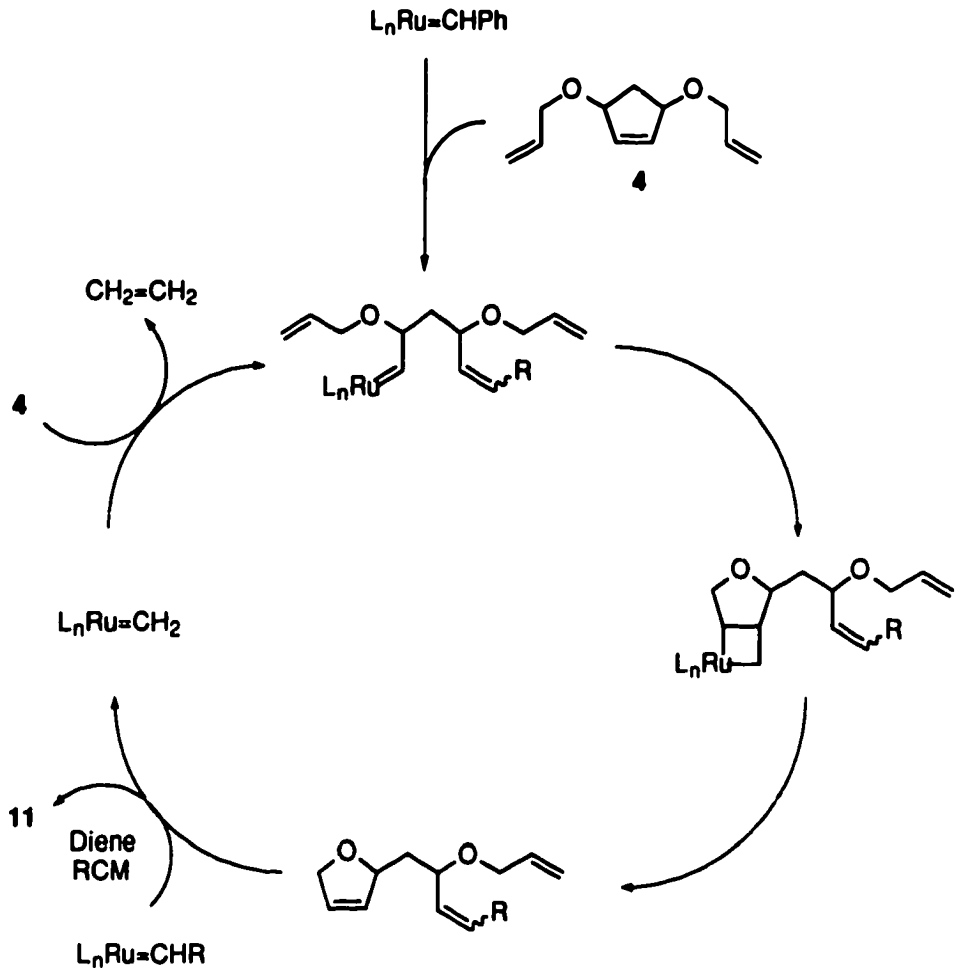
The formation of the observed products is consistent with two mechanisms. Mechanism 1 (Scheme 4) involves initial metathesis at the terminal olefin of the allyl group.

Scheme 4



Productive cleavage of the subsequently formed metallacyclobutane produces the first ring and metal alkylidene. The final step is closure of the ring through intramolecular olefin metathesis. Mechanism 1 is analogous to the quantitative ring closing metathesis of 1,2-poly(butadiene).[19] In mechanism 2 (Scheme 5) the initial metathesis occurs at the disubstituted cyclic olefin and is followed by two diene ring closing steps.

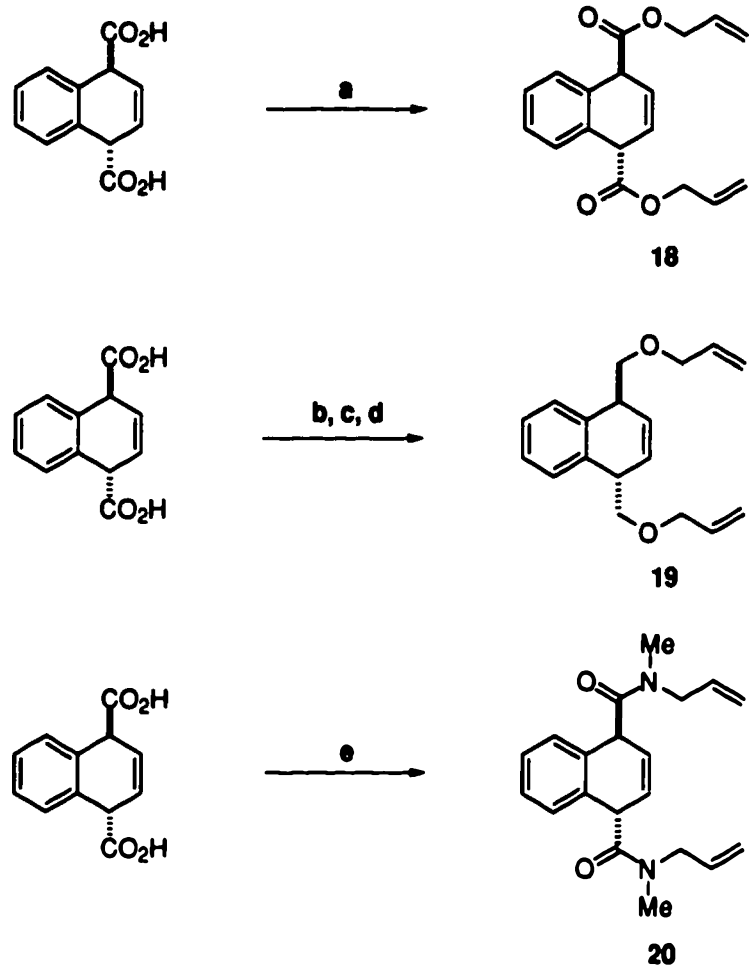
Scheme 5



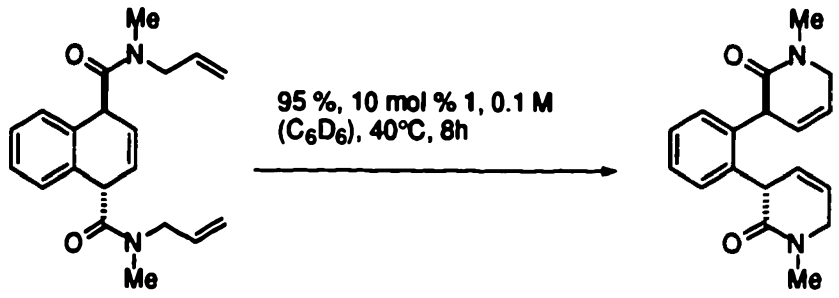
Because increasing olefinic substitution decreases the rate of olefin metathesis, mechanism 1 is expected to predominate over mechanism 2. That no intermediates are observed in the ring-opening/ring-closing reactions is consistent with the former mechanism. Additionally, the results of dilution and of tether substitution support mechanism 1 (*vide supra*). However, mechanism 2 has not been excluded; ring strain may activate the cyclic olefin and favor this mechanism in some cases. The conformational constraints imposed on the metallacyclobutane intermediate of the first intramolecular metathesis in mechanism 1 are additional consideration.[20]

To increase the complexity of the system and to further test the utility of cyclohexene systems, a series of compounds based on 1,4-dihydronapthalene (Scheme 6) were synthesized using standard methods from *trans*-1,4-dihydronapthalene dicarboxylic acid. Using **1** as catalyst, ester and ether derivatives **18** and **19** fail to ring open, but the *N*-allyl-*N*-methyl amide **20** efficiently produced the tricyclic species **21** (Eq. 2). A contrast in reactivity of this type between amide and ester was observed previously in the formation of eight-membered rings.[1b] Presumably, **20** is able to undergo ring-opening/ring-closing metathesis because the favorable conformations of the amide are more energetically accessible than those of the related ether and ester.

Scheme 6



Synthesis of *trans*-1,4-dihydronapthalene-based ring opening-ring closing metathesis substrates: (a) CH_2=$CHCH_2OH$, DCC, CH_2Cl_2, 8%; (b) MeOH, H_2SO_4 (cat), 75%; (c) $LiAlH_4$, Et_2O, 68%; (d) NaH, CH_2=$CHCH_2Br$, DMF, 23%; (e) PCl_5, PhH then $MeNH(CH_2CH{=}CH_2)$, NEt_3, CH_2Cl_2, 19%.



20 **21** (2)

Conclusions

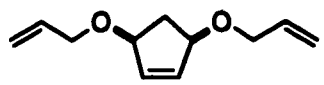
We have demonstrated that cyclic unsaturation, similar to acteylenic unsaturation, is an effective relay for olefin metathesis. This approach has been utilized in the tandem ring-opening/ring-closing metathesis of four- to eight-membered cycloolefins, as well as norbornenes, to produce polycyclic ethers. The reactivity as a function of ring size parallels strain energies. Competing intermolecular reactions were observed for six-, seven-, and eight-membered rings. The relative rates of these intermolecular reactions may be lowered by conducting the reaction at high dilution or by increasing the substitution of the acyclic olefins involved. Although ring-opening reactions involving six-membered rings are not well known, systems have been presented in which a cyclohexene ring is utilized for a metathesis relay.

Experimental Section

High resolution mass spectra were obtained from the Southern California Mass Spectrometry Facility (University of California, Riverside). Analytical thin-layer chromatography (tlc) was performed using Silica Gel 60 F254 precoated plates (0.25 mm thickness) with a fluorescent indicator. Flash column chromatography was performed using Silica Gel 60 (230-400 mesh) from EM Science.[21] Catalyst **1** was prepared according to published procedures.[3b] *trans*-1,4-Dihydronapthalene dicarboxylic acid was prepared according to the procedure of Lyssy.[22] The metathesis reactions were carried out under an argon atmosphere with dry, degassed solvents under anhydrous conditions.

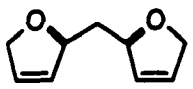
3

***cis*-3,4-Cyclobutenediol bis(3-butenyl) ether (3).** To a stirring solution of 3-buten-1-ol (10 ml, 120 mmol) at 0 °C was slowly added NaH (1.3 g, 56 mmol). After allowing the solution to stir for 5 min, *cis*-3,4-dichlorocyclobutene (1.3 g, 10 mmol) was added. The mixture was heated to 75 °C and stirred for 18 h. The reaction was quenched by addition to NH_4Cl (sat aq., 25 ml) and extracted with Et_2O (4 × 25 ml). After concentrating to a dark orange oil, the product was purified on silica gel (10% Et_2O in petroleum ether) to yield **3** (1.25 g, 66%) as a clear, colorless oil. ^1H NMR (C_6D_6, 300 MHz) δ 6.08 (d, J = 1.4 Hz, 2H), 5.95-5.81 (m, 2H), 5.11-4.99 (m, 4H), 4.36 (d, J = 1.4 Hz, 2H), 3.58-3.42 (m, 4H), 2.37-2.30 (m, 4H); ^{13}C NMR (C_6D_6, 75 MHz) δ 141.8, 136.0, 116.1, 82.4, 68.2, 35.1; IR (neat, cm^{-1}) 3073, 2953, 2916, 2873, 1111; HRMS calcd for $C_{12}H_{19}O_2$ (MH^+) 195.1385, found 195.1388.



4

***cis*-3,5-Cyclopentenediol bis(allyl) ether (4).** To a stirring solution of *cis*-3,5-cyclopentenediol (600 mg, 6.0 mmol) in DMF (50 ml) at 0 °C was slowly added NaH (420 mg, 18 mmol). After stirring for 1h, allyl bromide (5.0 ml, 30 mmol) was added and the reaction mixture was allowed to warm up to room temperature. After 14 h the reaction was partitioned between Et_2O and water (150 ml each) and extracted with Et_2O (4 × 100 ml). After concentrating to a yellow oil, the product was purified on silica gel (10% EtOAc in petroleum ether) to yield **3** (640 mg, 60%) as a clear, colorless oil. ^1H NMR (C_6D_6, 300 MHz) δ 5.92-5.77 (m, 4H), 5.00-5.29 (m, 2H), 4.19-4.14 (m, 2H), 3.78-3.87 (m, 4H), 2.40-2.32 (m, 1H), 1.83-1.74 (m, 1H); ^{13}C NMR (C_6D_6, 75 MHz) δ 135.9, 134.6, 115.7, 81.6, 69.4, 38.2; IR (neat, cm^{-1}) 3078, 3014, 2979, 2934, 2855, 1082; HRMS calcd for $C_{11}H_{17}O_2$ (MH^+) 181.1228, found 181.1226.



11

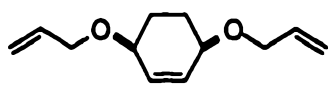
***meso*-Bis(5-oxa-2-cyclopentenyl)methane (11).** To a vial containing ruthenium catalyst **1** (10 mg, 12 μmol, 3 mol %) in benzene (2 ml) was added ether **4** (65 mg, 360 μmol). The vial was capped and placed in a 45 °C oil bath and stirred 5 h. The reaction mixture was concentrated and purified on silica gel (10% Et_2O in petroleum ether) to yield the product **11** (47 mg, 85%) as a clear, colorless oil. ^1H NMR (C_6D_6, 300 MHz) δ 5.64-5.59 (m, 2H), 5.46-5.41 (m, 2H), 5.08-4.96 (m, 2H), 4.52-4.38 (m, 4H), 2.03-1.94 (m, 1H), 1.87-178 (m, 1H); ^{13}C NMR (C_6D_6, 75 MHz) δ 130.3, 126.5, 83.4, 74.9, 42.5; IR (neat, cm^{-1}) 3078, 3014, 2978, 2931, 2854, 1081; HRMS calcd for $C_9H_{13}O_2$ (MH^+) 153.0916, found 153.0915.

2

***cis*-3,4-Cyclobutenediol bis(allyl) ether (2).** Substrate **2** was prepared in a fashion analogous to cylobutene **3**. **2** was isolated as a clear oil (40%). ^{1}H NMR (C_6D_6, 300 MHz) δ 6.08 (d, J = 0.9 Hz, 2H), 5.95-5.84 (m, 2H), 5.33-5.26 (m, 2H), 5.06-5.00 (m, 2H), 4.42 (d, J = 0.9 Hz, 2H), 4.11-3.94 (m, 4H); ^{13}C NMR (C_6D_6, 75 MHz) δ 141.9, 136.0, 115.6, 81.9, 69.4; IR (neat, cm^{-1}) 3125, 3078, 3051, 3015, 2983, 2861, 1122; HRMS calcd for $C_{10}H_{15}O_2$ (MH^+) 167.1072, found 167.1068.

10

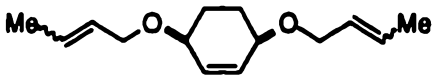
***meso*-1,1'-Bi(5-oxa-2-cyclopentene) (10).** Bicyclic ether **10** was obtained as a clear, colorless oil (82%) under conditions analogous to the reaction producing **11**. ^{1}H NMR (C_6D_6, 300 MHz) δ 5.81-5.77 (m, 2H), 5.49-5.45 (m, 2H), 4.80-4.76 (m, 2H), 4.52-4.40 (m, 4H); ^{13}C NMR (C_6D_6, 75 MHz) δ 128.2, 127.7, 89.3, 75.8; IR (neat, cm^{-1}) 3079, 2852, 1082; HRMS calcd for $C_8H_{11}O_2$ (MH^+) 139.0759, found 139.0754.



5a

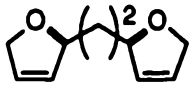
***cis*-3,6-Cyclohexenediol bis(allyl) ether (5a).** The ether **5a** was prepared in a manner similar to **4** using allyl bromide and *cis*-3,6-cyclohexenediol prepared by the method of Bäckvall. **5a** was isolated as a clear, colorless oil (78%). ^{1}H NMR C_6D_6, 300 MHz) δ 5.91-5.78 (m, 4H), 5.28-5.20 (m, 2H), 5.05-5.00 (m, 2H), 3.88-3.75 (m, 4H), 3.63-3.59 (m, 2H), 1.91-11.82 (m, 2H), 1.51-1.42 (m, 2H); ^{13}C NMR (C_6D_6, 75 MHz) δ

136.1, 131.0, 115.6, 72.3, 69.2, 25.3; IR (neat, cm^{-1}) 3079, 3031, 2946, 2854, 1086; HRMS calcd for $C_{12}H_{19}O_2$ (MH^+) 195.1385, found 195.1391.



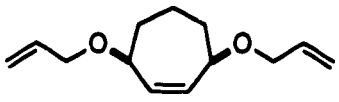
5b

***cis*-3,6-Cyclohexenediol bis((*E*/*Z*)-2-butenyl) ether (5b).** The ether **5b** was prepared in a manner similar to **4** using crotyl bromide and *cis*-3,6-cyclohexenediol prepared by the method of Bäckvall. **5b** was isolated as a clear, colorless oil (87%). ^1H NMR (C_6D_6, 300 MHz) δ 5.93-5.90 (m, 2H), 5.70-5.45 (m, 4H), 3.99-3.79 (m, 4H), 3.69-3.67 (m, 2H), 1.97-1.88 (m, 2H), 1.57-1.44 (m, 8H); ^{13}C NMR (C_6D_6, 75 MHz) δ 131.1, 131.0, 129.1, 128.6, 126.4, 72.2, 71.9, 69.0, 64.0, 25.4, 17.8, 13.2; IR (neat, cm^{-1}) 3027, 2939, 2854, 1092.



12

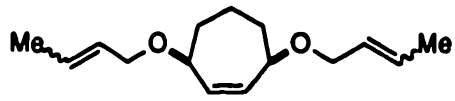
***meso*-1,2-Bis(5-oxa-2-cyclopentenyl)ethane (12).** Bicyclic ether **12** was obtained as a clear, colorless oil (73%) under conditions analogous to the reaction producing **10**. ^1H NMR (C_6D_6, 300 MHz) δ 5.45-5.40 (m, 4H), 4.84-4.81 (m, 2H), 4.47-4.45 (m, 4H), 1.78-1.56 (m, 4H); ^{13}C NMR (C_6D_6, 75 MHz) δ 130.0, 126.8, 86.2, 75.1, 32.1; IR (neat, cm^{-1}) 3076, 3025, 2930, 1086.



6a

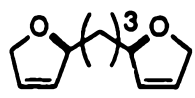
***cis*-3,7-Cycloheptenediol bis(allyl) ether (6a).** The ether **6a** was prepared in a manner similar to **4** using allyl bromide and *cis*-3,7-cycloheptenediol

prepared by the method of Bäckvall. **6a** was isolated as a clear, colorless oil (52%). ^{1}H NMR (C_6D_6, 300 MHz) δ 5.90-5.78 (m, 4H), 5.26 (dd, *J* = 17.2, 1.7 Hz, 2H), 5.04 (dd, *J* = 10.4, 1.3 Hz, 2H), 3.88-3.73 (m, 6H), 1.82-1.66 (m, 3H), 1.50-1.29 (m, 3H); ^{13}C NMR (C_6D_6, 75 MHz) δ 135.8, 135.2, 115.6, 79.0, 69.3, 32.9, 25.1; IR (neat, cm^{-1}) 3079, 3015, 2982, 2932, 2856, 1082; HRMS calcd for $C_{13}H_{21}O_2$ (MH^+) 209.1542, found 209.1538.



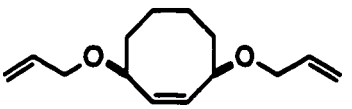
6b

***cis*-3,7-Cycloheptenediol bis((*E*/*Z*)-2-butenyl) ether (6b).** The ether **6b** was prepared in a manner similar to **4** using crotyl bromide and *cis*-3,7-cycloheptenediol prepared by the method of Bäckvall. **6b** was isolated as a clear, colorless oil (73%). ^{1}H NMR (C_6D_6, 300 MHz) δ 5.94-5.90 (m, 2H), 5.72-5.45 (m, 4H), 3.98-3.78 (m, 6H), 1.88-1.34 (m, 12H); ^{13}C NMR (C_6D_6, 75 MHz) δ135.5, 135.4, 128.8, 126.6, 78.9, 78.7, 69.2, 64.2, 33.0, 25.3, 17.8, 13.2; IR (neat, cm^{-1}) 3023, 2933, 2856, 1093.



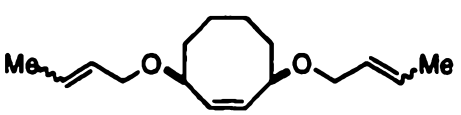
13

***meso*-1,3-Bis(5-oxa-2-cyclopentenyl)propane (13).** Bicyclic ether **13** was obtained as a clear, colorless oil (57%) under conditions analogous to the reaction producing **10**. ^{1}H NMR (C_6D_6, 300 MHz) δ 5.47-5.42 (m, 4H), 4.82-4.76 (m, 2H), 4.54-4.42 (m, 4H), 1.65-1.43 (m, 6H); ^{13}C NMR (C_6D_6, 75 MHz) δ 130.2, 126.7, 86.1, 75.0, 36.5, 21.6; IR (neat, cm^{-1}) 3076, 3025, 2930, 1086.



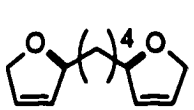
7a

***cis*-3,8-Cyclooctenediol bis(allyl) ether (7a).** The ether **7a** was prepared in a manner similar to **4** using allyl bromide and *cis*-3,8-cyclooctenediol prepared by the method of Bäckvall. **7a** was isolated as a clear, colorless oil (62%). ^{1}H NMR (C_6D_6, 300 MHz) δ 5.95-5.82 (m, 2H), 5.57-5.54 (m, 2H), 5.27 (dd, *J* = 17.2, 1.9 Hz, 2H), 5.05 (dd, *J* = 10.4, 2.0 Hz, 2H), 4.10-3.96 (m, 4H), 3.82-3.74 (m, 2H), 1.94-1.86 (m, 2H), 1.54-1.20 (m, 6H); ^{13}C NMR (C_6D_6, 75 MHz) δ 135.9, 134.3, 115.9, 76.0, 69.6, 36.4, 24.0; IR (neat, cm^{-1}) 3078, 3016, 2982, 29313, 2858, 1082; HRMS calcd for $C_{14}H_{23}O_2$ (MH^+) 223.1698, found 223.1704.

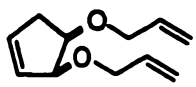


7b

***cis*-3,8-Cyclooctenediol bis((*E*/*Z*)-2-butenyl) ether (7b).** The ether **7b** was prepared in a manner similar to **4** using crotyl bromide and*cis*-3,8-cyclooctenediol prepared by the method of Bäckvall. **7b** was isolated as a clear, colorless oil (74%). ^{1}H NMR (C_6D_6, 300 MHz) δ 5.74-5.47 (m, 6H), 4.17-3.96 (m, 4H), 3.84-3.91 (m, 2H), 1.99-1.89 (m, 2H), 1.56-1.18 (m, 18H); ^{13}C NMR (C_6D_6, 75 MHz) δ 134.3, 134.2, 134.1, 128.6, 128.1, 127.6, 126.4, 75.6, 75.3, 69.1, 36.3, 36.2, 23.8, 17.5; IR (neat, cm^{-1}) 3018, 2932, 2857, 1095; HRMS calcd for $C_{16}H_{27}O_2$ (MH^+) 251.2011, found 251.2013.

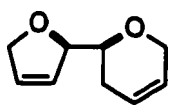


***meso*-1,4-Bis(5-oxa-2-cyclopentenyl)butane (14).** Bicyclic ether **14** was obtained as a clear, colorless oil (71%) under conditions analogous to the reaction producing **10**. ^{1}H NMR (C_6D_6, 300 MHz) δ 5.48-5.43 (m, 4H), 4.80-4.77 (m, 2H), 4.52-4.44 (m, 2H), 1.54-1.32 (m, 8H); ^{13}C NMR (C_6D_6, 75 MHz) δ 130.2, 126.7, 86.1, 75.0, 36.5, 25.8; IR (neat, cm^{-1}) 3077, 2932, 2853, 1078; HRMS calcd for $C_{12}H_{19}O_2$ (MH^+) 195.1385, found 195.1383.



8

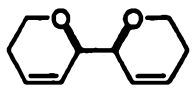
***cis*-3,4-Cyclopentenediol bis(allyl) ether (8).** The ether **8** was prepared in a manner similar to **4** using allyl bromide and *cis*-3,4-cyclopentenediol prepared by the method of Sharpless from cyclopentadiene. **8** was isolated as a clear, colorless oil (52%). ^{1}H NMR (C_6D_6, 300 MHz) δ 5.99-5.83 (m, 2H), 5.74-5.70 (m, 1H), 5.5.66-5.63 (m, 1H), 5.35-5.25 (m, 2H), 5.06-5.01 (m, 2H), 4.20-3.77 (m, 6H), 2.46-2.38 (m, 1H), 2.23-2.15 (m, 1H); ^{13}C NMR (C_6D_6, 75 MHz) δ 136.4, 135.9, 133.5, 130.2, 115.6, 115.4, 80.4, 79.0, 70.8, 69.7, 37.0; IR (neat, cm^{-1}) 3077, 3014, 2982, 2917, 2855, 1124; HRMS calcd for $C_{11}H_{17}O_2$ (MH^+) 181.1228, found 181.1238.



17

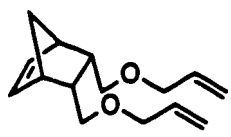
4-(5-Oxa-2-cyclopentenyl)-5-oxacyclohexene (17). Bicyclic ether **15** was obtained as a clear, colorless oil (92%) under conditions analogous to the reaction producing **10**. ^{1}H NMR (C_6D_6, 300 MHz) δ 5.88-5.84 (m, 1H), 5.66-5.60 (m, 1H), 5.51-5.48 (m, 1H), 5.41-5.36 (m, 1H), 4.84-4.81 (m, 1H), 4.48-4.43 (m, 2H), 4.03-3.96 (m, 2H), 3.47-3.40 (m, 1H), 2.18-2.00 (m, 2H); ^{13}C NMR (C_6D_6, 75 MHz) δ

127.8, 127.7, 126.6, 124.1, 88.8, 76.6, 75.7, 65.8, 27.7; IR (neat, cm^{-1}) 3035, 2919, 2848, 1090; HRMS calcd for $C_9H_{13}O_2$ (MH^+) 153.0916, found 153.0916.



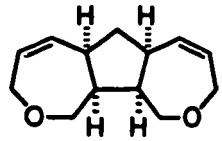
15

***meso*-1,1'-Bi(6-oxa-2-cyclohexene) (15).** Bicyclic ether **15** was obtained as a clear, colorless oil (70%) under conditions analogous to the reaction producing **10**. ^1H NMR (C_6D_6, 300 MHz) δ 5.76-5.69 (m, 2H), 4.13 (s, 2H), 3.85-3.78 (m, 2H), 3.47-3.38 (m, 2H), 2.07-1.98 (m, 2H), 1.56-1.47 (m, 2H); ^{13}C NMR (C_6D_6, 75 MHz) δ 128.4, 125.5, 76.4, 63.5, 25.6; IR (neat, cm^{-1}) 3040, 2960, 2918, 2852, 1091; HRMS calcd for $C_{10}H_{15}O_2$ (MH^+) 167.1080, found 167.1072.



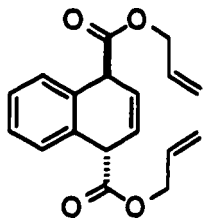
9

***endo, endo*-5,6-Bis(2-oxa-4-pentenyl)bicyclo[2.2.1]hept-2-ene (9).** The ether **9** was prepared in a manner similar to **4** using allyl bromide and *endo,endo*-5-norbornene-2,3-dimethanol. **9** was isolated as a clear, colorless oil (55%). ^1H NMR (C_6D_6, 300 MHz) δ 6.09-6.08 (m, 2H), 5.91-5.78 (m, 2H), 5.28-5.20 (m, 2H), 5.06-5.01 (m, 2H), 3.78-3.73 (m, 4H), 3.27-3.22 (m, 2H), 3.02-2.93 (m, 4H),2.52-2.46 (m, 2H), 1.50-1.46 (m, 1H), 1.18-1.14 (m, 1H); ^{13}C NMR (C_6D_6, 75 MHz) δ 135.9, 135.5, 115.8, 71.9, 70.7, 49.3, 46.1, 42.0; IR (neat, cm^{-1}) 3059, 2961, 2919, 2864, 1092; HRMS calcd for $C_{15}H_{23}O_2$ (MH^+) 235.1698, found 235.1698.

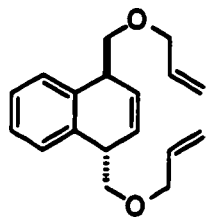


16

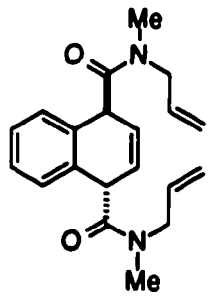
***cis, cis*-5,10-Dioxatricyclo[8.5.0.0^{8,14}]pentadeca-2,12-diene (16).** Tricyclic ether **14** was obtained as a clear, colorless oil (68%) under conditions analogous to the reaction producing **10**. ^{1}H NMR (C_6D_6, 300 MHz) δ 5.46-5.39 (m, 2H), 5.17-5.11 (m, 2H), 4.16-4.08 (m, 2H), 3.95-3.74 (m, 2H), 3.46- 3.39 (m, 2H), 2.53-2.36 (m, 4H), 1.92-1.84 (m, 1H), 1.37-1.26 (m, 2H); ^{13}C NMR (C_6D_6, 75 MHz) δ 130.8, 127.1, 71.2, 69.6, 47.5, 42.1, 41.9; IR (neat, cm^{-1}) 3003, 2928, 2873, 2817, 1124; HRMS calcd for $C_{13}H_{19}O_2$ (MH^+) 207.1385, found 207.1375.



Diallyl *trans*-1,4-dihydronapthalene 1,4-dicarboxylate (18). To a stirring solution of *trans*-1,4-dihydronapthalene 1,4-dicarboxylic acid (655 mg, 3 mmol) and allyl alcohol (0.48 ml, 7 mmol) in CH_2Cl_2 (15ml) at ambient temperature was added DCC (1.4 g, 7 mmol). The reaction mixture was allowed to stir 12h. After purification on silica gel (CH_2Cl_2 elution) the product **18** (70 mg, 8%) was isolated as a white crystalline solid. ^{1}H NMR (C_6D_6, 300 MHz) δ 7.25-7.22 (m, 2H), 7.05-7.02(m, 2H), 6.01-5.99 (m, 2H), 5.67-5.54 (m, 2H), 5.02-4.86 (m, 4H), 4.35-4.32 (m, 4H), 4.22-4.21 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 135.8, 134.8, 127.7, 126.3, 123.5, 116.7, 75.4, 72.0, 39.3; IR (neat, cm^{-1}) 3082, 3027, 2983, 2936, 2886, 2864, 1732, 1119; HRMS calcd for $C_{18}H_{22}NO_4$ (MNH_4^+) 316.1549, found 316.1563.



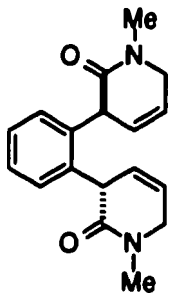
***trans*-1,4-Bis(2-oxa-4-pentenyl)-1,4-dihydronapthalene (19).** To a stirring solution of *trans*-1,4-dihydronapthalene-1,4-dimethanol in DME was added NaH. After 30 min, allyl bromide was added and stirring was continued for 2h. The reaction was quenched with 1.0 N HCl (20 ml) and extracted with CH_2Cl_2 (3× 30 ml). The extracts were combined, concentrated *in vacuo*, and purified on silica gel to yield **19** (320 mg, 23%) as a clear, colorless oil. ^1H NMR ($CDCl_3$, 300 MHz) δ 7.38-7.34 (m, 2H), 7.25-7.20 (m, 2H), 6.10 (s, 2H), 5.96-5.85 (m, 2H), 5.32-5.16 (m, 4H), 4.03-3.98 (m, 4H), 3.74-3.50 (m, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 135.8, 134.8, 127.7, 126.3, 123.5, 75.4, 72.0, 39.3; IR (neat, cm^{-1}); HRMS calcd for $C_{18}H_{26}NO_2$ (MNH_4^+) 288.1963, found 288.1972.



20

***N, N'*-Diallyl-*N, N'*-dimethyl-*trans*-1,4-dihydronapthalene 1,4-dicarboxamide (20).** A solution containing *trans*-1,4-dihydronapthalene dicarboxylic acid (500 mg, 2.3 mmol) and PCl_5 (1.0 g, 4.8 mmol) in benzene (50 ml) was heated to reflux for 2 h. The reaction mixture was then cooled and the benzene was removed *in vacuo*. The residue was dissolved in a minimum amount of CH_2Cl_2 and passed through a plug of silica gel. The solution was again concentrated and the residue was dissolved in

CH_2Cl_2 along with *N*-methylallylamine (0.64 ml, 4.6 mmol) and NEt_3 (0.44 ml, 3.1 mmol). The reaction mixture was stirred 12 h and then quenched with 1.0 N HCl and extracted with Et_2O (3×30 ml). The diamide **20** (140 mg, 19%) was isolated as a white crystalline solid after recrystallization from Et_2O/petroleum ether. ^1H NMR ($CDCl_3$, 300 MHz) δ 7.26-7.12 (m, 4H), 6.13-6.08 (m, 2H), 5.78-5.64 (m, 2H), 5.23-5.12 (m, 4H), 4.88-4.78 (m, 2H), 4.02-4.01 (m, 4H), 2.95 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.2, 172.6, 132.7, 127.4, 127.2, 126.0, 125.8, 125.7, 117.4, 117.2, 52.4, 50.7, 45.8, 45.6, 45.2, 45.0, 34.9, 34.0; IR (neat, cm^{-1}) 3078, 2981, 2930, 1636; HRMS calcd for $C_{20}H_{25}N_2O_2$ (MH^+) 325.1916, found 325.1904.



21

1,2- Bis(*N*-methyl-2-cyclohexamid-3-enyl)benzene (21). Tricyclic amide **21** was obtained from **20** as a clear oil (95%) under conditions analogous to the reaction producing **10**. ^1H NMR ($CDCl_3$, 300 MHz) δ 7.16-7.14 (m, 4H), 6.08-6.02 (m, 2H), 5.96-5.90 (m, 2H), 5.15-5.11 (m, 2H), 4.17-3.96 (m, 4H), 2.99 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 169.0, 139.8, 128.2, 127.9, 127.1, 120.2, 51.2, 43.0, 34.3; IR (neat, cm^{-1}) 3048, 2920, 1639; HRMS calcd for $C_{18}H_{21}N_2O_2$ (MH^+) 297.1603, found 297.1605.

Acknowledgement. This work was supported by the NSF, NIH, and Nippon Zeon.

References and Notes

[†] Parts of this chapter have been published in Zuercher, W.J.; Hashimoto, M.; Grubbs, R.H. *J. Am. Chem. Soc.* **1996**, *118*, 6634-6640. The laboratory work of Masakazu Hashimoto (synthesis of compounds **18-21**) is acknowledged.

[1](a) Fu, G. C.; Nguyen, S. T.; Grubbs, R. H. *J. Am. Chem. Soc.* **1993**, *115*, 9856-9857. (b) Miller, S. J.; Kim, S-H.; Chen, Z-R.; Grubbs, R. H. *J. Am. Chem. Soc.* **1995**, *117*, 2108-2109. (c) Grubbs, R. H.; Miller, S. J.; Fu, G. C. *Acc. Chem. Res.* **1995**, *28*, 446-452 and references cited therein.

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[4]For general references on ROMP, see: (a) Ivin, K. J. *Olefin Metathesis*; Academic Press: London, 1983. (b) Grubbs, R. H.; Tumas, W. *Science* **1989**, *243*, 907-915. (c) Schrock, R. R. *Acc. Chem. Res.* **1990**, *23*, 158-165. (d) Breslow, D. S. *Prog. Polym. Sci.* **1991**, *18*, 1141-1195.

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[6] Greenberg, A.; Liebmann, J. F. *Strained Organic Molecules*, Academic Press: New York, 1978 and references cited therein. A range of strain values are shown, including theoretical and experimental determinations.

[7]Although cyclohexene ROMP has been dubbed "the impossible reaction," cyclohexene has been found to polymerize under nonequilibrium conditions (*vide infra*). Patton, P. A.; Lillya, C. P.; McCarthy, T. J. *Macromol.* **1986**, *19*, 1266-1268.

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[9]D.L. Crain and A. Reusser, ACDS meeting 1972 (New York), Symposium on Advances in Petrochemical Technology.

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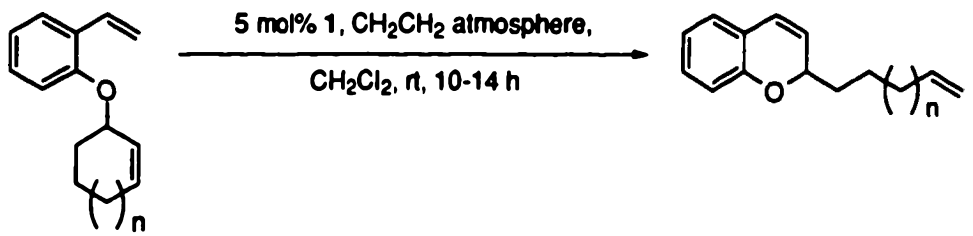
[18]Presumably, this is the case because oligomerization is only observed with low strain cycloolefins.

[19]Coates, G. W.; Grubbs, R. H. *J. Am. Chem. Soc.* **1996**, *118*, 230-231.

[20]Hoveyda and coworkers have reported a ruthenium-catalyzed rearrangement of styrenyl ethers to produce substituted chromenes as shown. In this process, yields are high (>90%) when $n = 2$ or 3 and low (35%) when $n = 1$. There is no such rearrangement in the case of $n = 0$. Rather than ring strain, it appears that conformational issues, particularly those of the intermediate metallacyclobutanes, are the critical factor in this reaction. Harrity, J.P.A.; Visser, M.S.; Gleason, J.D.; Hoveyda, A.H. *J. Am. Chem. Soc.* **1997**, *119*, 1488.



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Chapter 3

Ruthenium-Catalyzed Polycyclization Reactions[†]

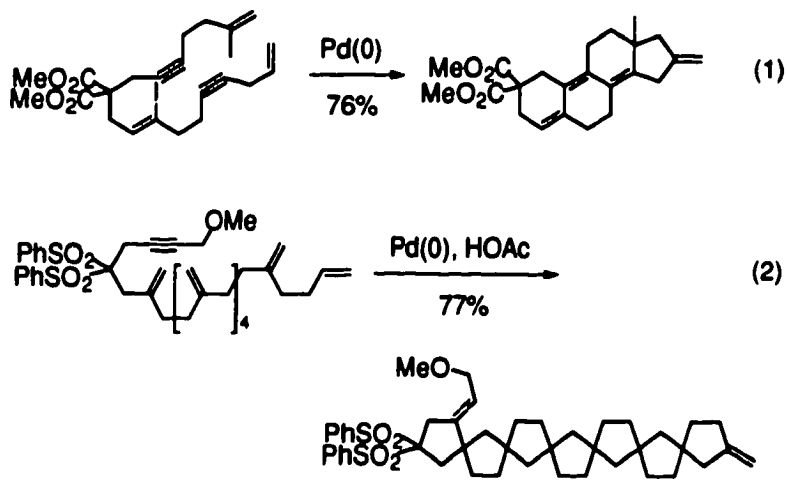
Abstract

The application of ruthenium alkylidene **1** to the catalysis of polycyclization reactions is detailed. Several acyclic precursors have been synthesized and reacted with **1**. These precursors vary in topology and contain both acetylenic and cycloolefin metathesis relays. The cyclization reactions proceed in moderate to good yield to produce polycyclic polyenes when the precursors are subjected to catalytic amounts of **1**. In general, precursors bearing *n* relay units generate polycycles containing (*n* + 1) rings.

Introduction

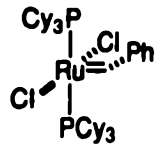
Cascade reactions have proven effective in the assembly of complex polycyclic systems from simple acyclic precursors.[1] These cascade cyclizations are characterized by the formation of a reactive intermediate which undergoes a series ring-forming steps before termination, and examples have been reported for cationic,[2] anionic,[3] radical,[4] and transition-metal mediated cascade processes. The application of homogeneous transition metal catalysts to cascade cyclizations of polyenes and polyynes appears very promising. For example, the groups of Negishi (Eq. 1)[5] and Trost (Eq. 2)[6] have utilized cyclic carbopalladation cascades in the one-step, catalytic assembly of systems containing up to seven rings (Scheme 1). Despite tremendous progress in this area, the development of efficient methods for the construction of polycyclic systems remains an important goal of synthetic chemistry.

Scheme 1

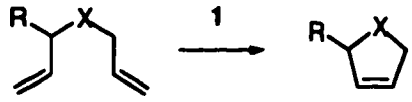


Previous reports from this laboratory[7] demonstrate the possibility of extending catalytic diene ring-closing metathesis[8] (RCM, Eq. 3) to the formation of polycyclic structures by a cascade of ring-opening olefin metathesis or carbene-alkyne metathesis

reactions.[9] When a precursor diene containing an acetylene or a cyclic olefin is exposed to ruthenium alkylidene **1**,[10] bicyclics are produced (Eqs. 4-5). Extending this reaction to analogous precursors bearing two or more of these olefin metathesis relays should lead to the production of polycyclic molecules. Herein we report the synthesis of such precursors and their cascade cyclization reactions catalyzed by ruthenium alkylidene **1**.



1



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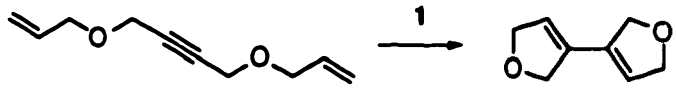

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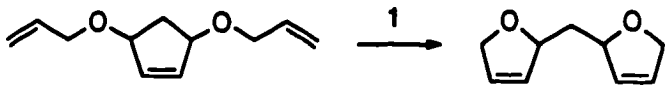


(5)

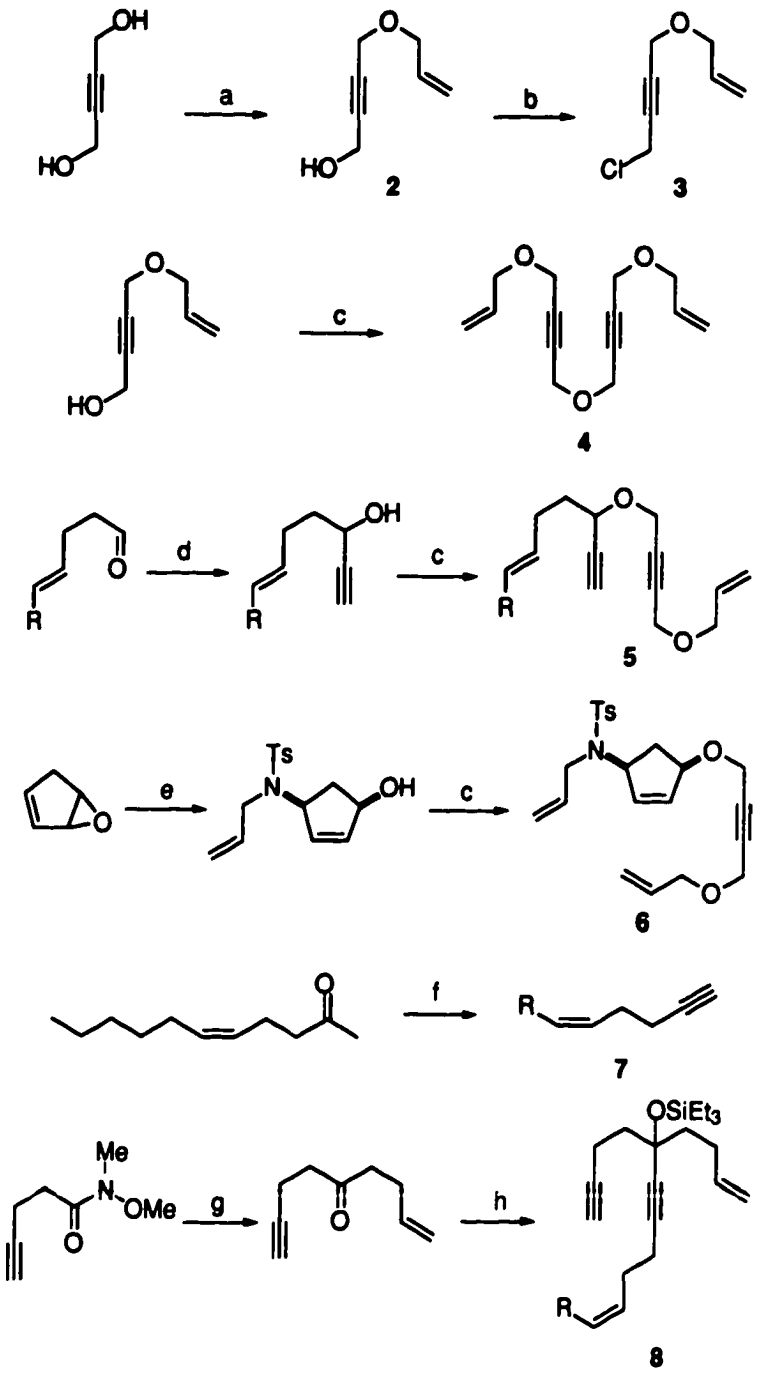
Results and Discussion

Precursor Synthesis. Several dienes containing two or more olefin metathesis relay units were prepared in order to study the possibility of ruthenium-catalyzed polycyclization (Scheme 2). The linear precursor **4** was prepared by alkylation of the anion of 2-butyne-1,4-diol monoallyl ether **2** with propargyl chloride **3**.[11] Lithium

trimethylsilylacetylide was added to *trans*-4-decenal; after desilylation, *O*-alkylation with **3** produced **5**. Palladium-catalyzed ring opening of cyclopentadiene monoepoxide with *N*-allyl-*p*-toluenesulfonamide and *O*-alkylation of the resulting amino alcohol with propargyl chloride **3** produced **6**. The branched precursor **8** was formed via sequential addition of 3-butenylmagnesium bromide and the lithium anion of **7** to the Weinreb amide[12] of 4-pentynoic acid[13] followed by silylation with triethylsilyl triflate. Enyne **7** was prepared from *cis*-4-decenal, (bromomethyl)triphenylphosphonium bromide, and KO(*t*-Bu).[14]

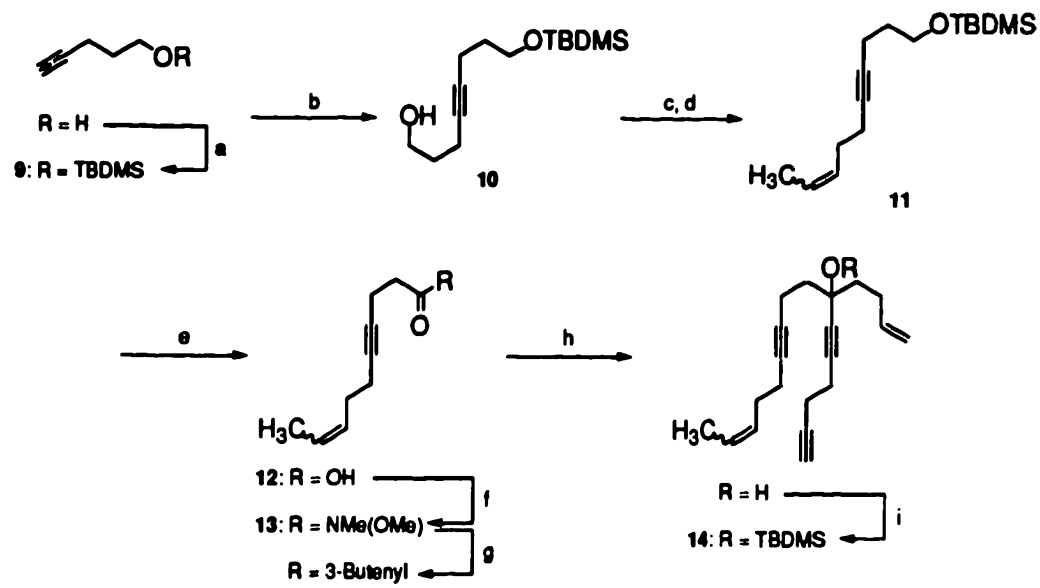
The synthesis of dientriyne **14** (Scheme 3) began with silylation of 4-pentyn-1-ol with TBSCl. Deprotonation of **9** and ring opening of oxetane promoted by $BF_3 \cdot OEt_3$ afforded the monoprotected acetylenic diol **10**. Oxidation and olefination of the resultant aldehyde produced **11**. Desilylation and oxidation with Jones reagent produced the carboxylic acid **12**. The conversion of **12** to the Weinreb amide **13** was accomplished via the acid chloride. Sequential addition of 3-butenylmagnesium bromide and the lithium monoanion of 1,5-hexadiyne produced the tertiary alcohol which was protected with TBSOTf to afford dientriyne **14**.

Scheme 2



(a) NaH, AllBr, DMF, 70%; (b) TsCl, NEt_3, DMAP, CH_2Cl_2; (c) NaH, DMF, **13**, 60-82%; (d) i. TMSCCH, BuLi, THF, ii. K_2CO_3, MeOH, 86%; (e) Allyl-NHTs, Pd_2dba_3•$CHCl_3$, dppe, BSA, THF, %; (f) 3-ButenylMgBr, THF, 89%; (g) Ph_3PCH_2Br, *t*-BuOK, THF, 70%; (h) i. BuLi, THF then **14**, ii. Et_3SiOTf, NEt_3, CH_2Cl_2, two steps 60%.

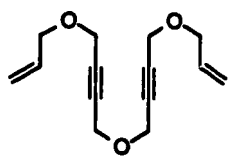
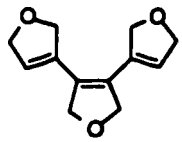
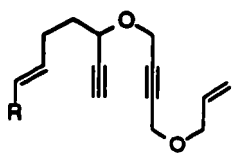
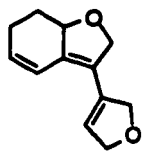
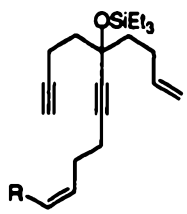
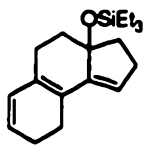
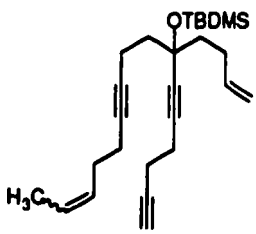
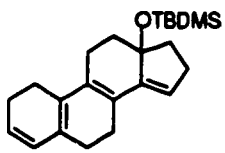
Scheme 3



(a) TBDMSCl, NEt_3, CH_2Cl_2, 98%; (b) BuLi, THF then oxetane, $BF_3{\cdot}OEt_2$, 84%; (c) PDC, CH_2 (d) BuLi, Ph_3PEtBr, THF, 64% from **10**; (e) CrO_3, H_2SO_4, *i*-PrOH, 83%; (f)$(COCl)_2$, CH_2Cl_2 the $H_2NMe(OMe)Cl$, NEt_3, 72%; (g) 3-ButenylMgBr, THF, 86%; (h) 1,5-Hexadiyne, 1.0 equiv. BuL THF, 48%; (i) TBDMSOTf, NEt_3, CH_2Cl_2, 96%.

Polycyclization reactions. Treatment of the acyclic precursors containing acetylenic relay units with a catalytic amount of **1** at ambient or slightly elevated temperature results in the formation of fused and nonfused carbo- and heterocyclic products in moderate to good yields (Table 1).[15] Both fused and nonfused systems containing conjugated polyenes may be obtained.

Table 1. Results of ruthenium-catalyzed polycyclizations

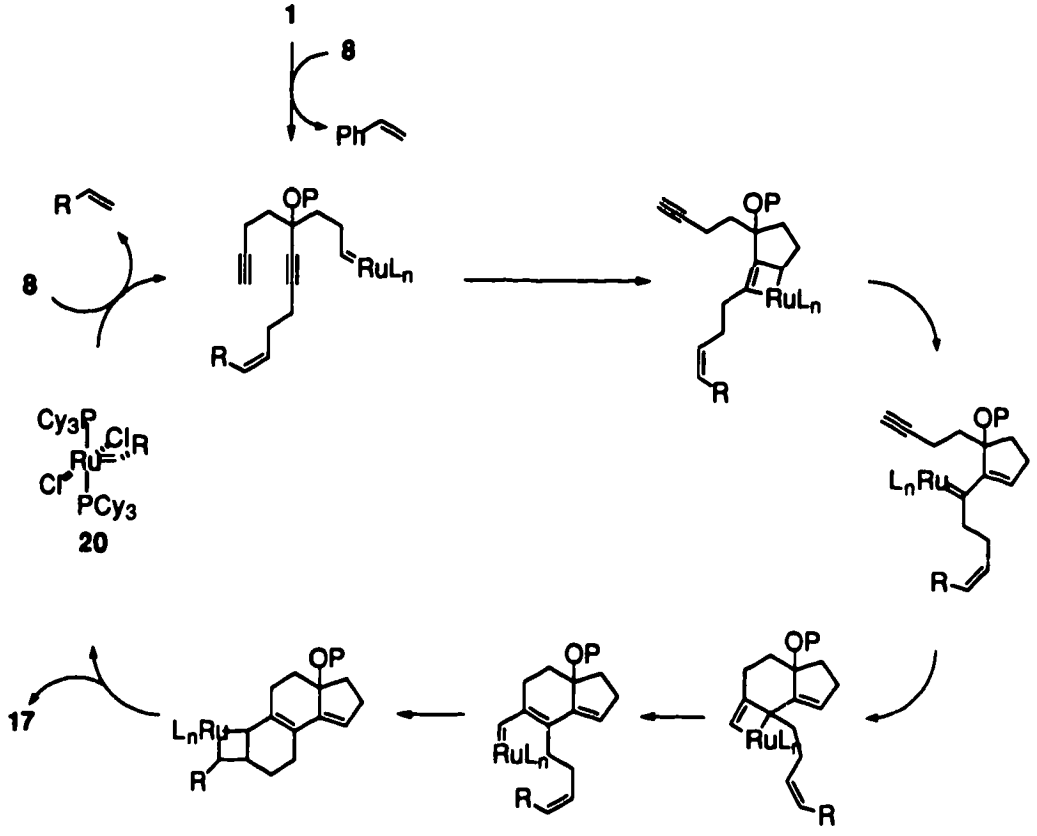
Precursor	Product	Yield and Conditions
 **4**	 **15**	8 mol% **1**, 0.1 M (C_6H_6), 45°C, 4h, 60%
 **5** (R = pentyl)	 **16**	5 mol% **1**, 0.05 M (C_6H_6), 40°C, 5h, 79%
 **8** (R = pentyl)	 **17**	4 mol% **1**, 0.05 M (C_6H_6), 45°C, 4h, 84%
 **14**	 **18**	4 mol% **1**, 0.05 M (C_6H_6), rt, 4h, 70%

In general, fused polycyclics are formed in higher yield than nonfused ring systems (i.e., **17** and **18** vs. **15**). In the intermediate case where the product contains both types of ring linkages, **16**, yields are also high. However, it is not known whether this originates

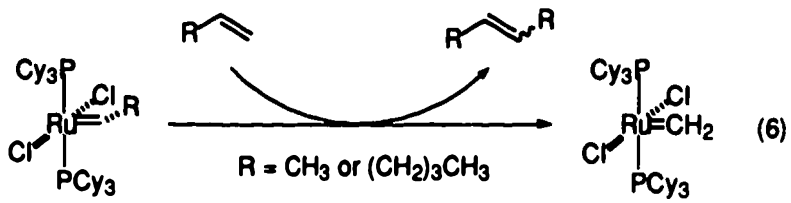
from the thermodynamic stability of product due to increased conjugation, a kinetic factor of conformational origin, or some other effect.

The mechanism of the polycyclizations involves initial formation of a ruthenium alkylidene which undergoes a series of intramolecular metatheses with the relay units prior to termination by a final ring closure. For example, the conversion of **8** to **17** (Scheme 4) presumably begins with metathesis of **1** with the monosubstituted olefin of **8**.[16] The newly-formed carbene subsequently undergoes two intramolecular carbene-alkyne metatheses[17] involving the respective metallacyclobutene intermediates. The cyclization is completed by metathesis of the vinylcarbene with the disubstituted olefin to yield product **17** and propagating alkylidene **20**.

Scheme 4

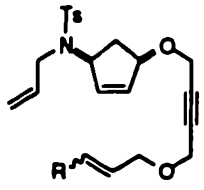


The initiation and subsequent reactions of **1** are followed by observing the ^{1}H NMR signal of the α-proton of the ruthenium alkylidene. As the benzylidene (singlet 20.02 ppm in CD_2Cl_2) is consumed, a signal for the propagating alkylidene **12** appears. In the reactions of **5**, **8**, and **14**, this species is expected to be ethylidene or *n*-pentylidene and is observed initially as a multiplet (ethylidene: quartet at 19.26 ppm in CD_2Cl_2; *n*-pentylidene: triplet at 19.24 ppm). However, as the reaction progresses, a singlet corresponding to the ruthenium methylidene **21** (18.94 ppm in CD_2Cl_2) grows as the alkylidene signal decays. Additionally, the formation of ethylene (singlet, 5.35 ppm in CD_2Cl_2) and either 2-butene or 5-decene is observed in the reaction mixture. These observations indicate a secondary metathesis with the α-olefin byproduct of the cyclization reaction (Eq. 6) and are consistent with the reported reactivity of **1** with α-olefins.[9a]

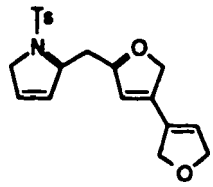


12 **21** (6)

Cycloolefins as well as acetylenes are effective relays in these polycyclization reactions. Initially, the presence of a cyclopentene as a relay was observed to have a detrimental effect the cyclization reaction. When precursor **6a** is exposed to 4 mol % **1**, tricycle **19** is recovered in only 40% yield, and the mass balance is found in an uncharacterized side product which appears to be oligomerized starting material. This type



6a: R = H
6b: R = Me



19

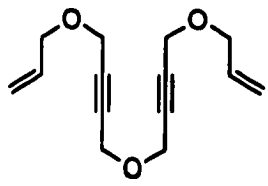
of side reaction has been observed previously in the application of cycloolefins as metathesis relay units, and the problem was ameliorated through alkyl substitution of one of the acyclic olefins of **6a**, thereby slowing the relative rate of the competing side reaction.[5c] This strategy works in the present study as well: when **6b** is exposed to 4 mol % **1**, cyclization proceeds cleanly to a single product, and **19** is isolated in 70% yield.

Conclusions

We have presented an efficient, catalytic method for the production of polycyclic molecules from acyclic precursors. The reaction proceeds through a cascade of metathesis steps with either acetylenic or cycloalkenyl relay units. A variety of structural types are accessible depending on the topology of the precursor and relay unit employed. The use of more and varied metathesis relays as well as the further functionalization of the resulting cyclic olefin systems are currently under investigation.

Experimental Section

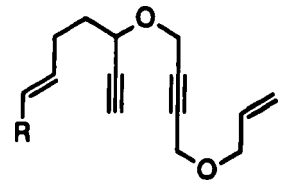
General. NMR spectra were recorded on either a General Electric QE-300 spectrometer at ambient temperature. Chemical shifts are reported in parts per million (ppm) downfield from tetramethylsilane (TMS) with reference to internal solvent. Infrared spectra were recorded on a Perkin-Elmer 1600 Series FT-IR. High-resolution mass spectra were provided by the Southern California Mass Spectrometry Facility (University of California at Riverside). Analytical thin-layer chromatography (tlc) was performed using silica gel 60 F254 precoated plates (0.25 mm thickness) with a fluorescent indicator. Visualization was accomplished with one or more of the following: UV light, $KMnO_4$, phosphomolybdic acid (PMA), cerric ammonium nitrate (CAN), or *p*-anisaldehyde solution followed by heating. Flash chromatography was performed using silica gel 60 (230-400 mesh) from EM Science.[18] All reactions were carried out under an inert atmosphere in oven-dried glassware unless otherwise specified. Catalyst **1** was prepared according to published procedure.[9a] Solvents were purified by passage through a column containing A-5 alumina (all solvents) followed by a column containing Q-5 reactant (non-ethereal solvents). Cyclopentadiene monoepoxide was prepared following published procedure.[19]



4

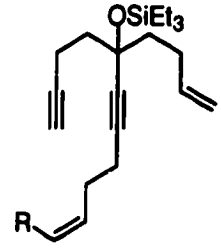
4,9,16-Trioxa-1,16-heptadecadien-6,11-diyne (4). ^{1}H NMR (C_6D_6, 300 MHz) δ 5.74-5.63 (m, 1H), 5.18-5.10 (m, 1H), 4.96-4.91 (m, 1H), 4.04 (t, *J* = 1.8 Hz, 2H), 3.86 (t, J = 1.8 Hz, 2H), 3.81-3.78 (m, 2H); ^{13}C NMR (C_6D_6, 100 MHz) δ 134.7,

116.8, 83.1, 81.6, 70.0, 56.8, 56.1; IR (neat, cm^{-1}) 3080, 3015, 2982, 2943, 2854, 1074; HRMS calcd for $C_{14}H_{18}O_3$ (MNH_4^+) 252.1600, found 252.1599.



5 (R = pentyl)

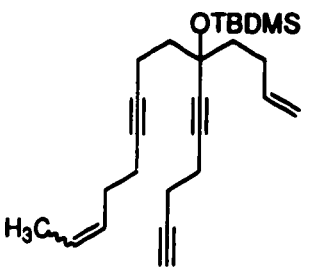
(*E*)-10-Ethynyl-4,9-Dioxa-1,13-nonadecadien-6-yne (5). ^1H NMR (C_6D_6, 300 MHz) δ 5.96-5.83 (m, 1H), 5.48-5.19 (m, 4H), 4.31 (m, 3H), 4.19 (t, *J* = 1.2 Hz, 2H), 4.05 (dt, J = 5.8, 1.3 Hz, 2H) 2.45 (d, *J* = 2.1 Hz, 1H), 2.15 (q, *J* = 7.2 Hz, 2H), 1.96 (q, *J* = 6.6 Hz, 2H), 1.84 (m, 2H), 1.35-1.23 (m, 6H), 0.87 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 133.9, 131.6, 128.5, 117.9, 82.3, 82.0, 81.9, 74.4, 70.6, 67.4, 57.4, 56.0, 35.2, 32.5, 31.3, 29.2, 28.1, 22.5, 14.1: IR (neat, cm^{-1}) 3304, 3080, 3017, 2954, 2925, 2854, 2112, 1071; HRMS calcd for $C_{19}H_{27}O_2$ ($[M-H]^+$) 287.2011, found 287.1999.



8 (R = pentyl)

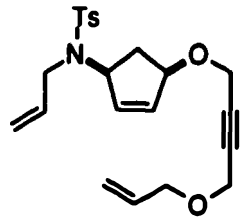
(*Z*)-5-(3-Butynyl)-5-triethylsilyloxy-1,10-hexadecadien-6-yne (8). ^1H NMR (C_6D_6, 300 MHz) δ 5.85-5.72 (m, 1H), 5.06 (dd, *J* = 17.1, 1.6 Hz, 1H), 4.96 (dd, *J* = 10.0, 0.7 Hz, 1H), 5.08-4.94 (m, 2H), 2.54-2.47 (m, 2H), 2.30-2.23 (m, 2H), 2.15-

1.93 (m, 8H), 1.79-1.72 (m, 3H), 1.29-1.23 (m, 6H), 1.04 (t, J = 7.9 Hz, 9H), 0.89 (t, J = 6.9, 3H), 0.76 (q, J = 7.9 Hz, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 138.56, 131.43, 127.65, 114.27, 85.50, 84.85, 82.67, 71.15, 67.79, 42.01, 41.56, 31.50, 29.31, 28.80, 27.28, 26.40, 22.56, 19.14, 14.08, 13.90, 7.09, 6.11; IR (neat, cm^{-1}) 3313, 3078, 3007, 2956, 2875, 2236, 2121, 1642, 1090; HRMS calcd for $C_{26}H_{45}OSi$ (MH^+) 401.3240, found 401.3247.



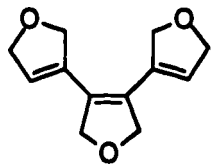
14

Compound (14). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.89-5.76 (m, 1H), 5.55-5.40 (m, 2H), 5.01 (dd, J = 17.2, 1.8 Hz, 1H), 4.93 (dd, J = 10.0, 1.8 Hz, 1H), 2.45-2.14 (m, 12H), 2.01 (t, J = 2.4 Hz, 1H), 1.84-1.77 (m, 3H), 1.69-1.61 (m, 4H), 0.85 (s, 9H), 0.14 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 138.7, 129.8, 129.0, 125.9, 125.0, 114.2, 83.9, 83.8, 82.6, 80.3, 79.5, 71.4, 69.4, 42.4, 42.2, 32.3, 28.8, 26.7, 25.8, 19.0, 18.8, 18.6, 18.2, 14.2, 12.8, -2.9; IR (neat, cm^{-1}) 3311, 3078, 3015, 2928, 2856, 2236, 2122, 1641, 1254, 1090; HRMS calcd for $C_{26}H_{40}OSi$ (MH^+) 397.2927, found 397.2912.



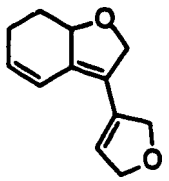
6

Compound (6). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.70 (d, *J* = 8.4 Hz, 2H), 7.28 (d, *J* = 8.4 Hz, 2H), 5.99-5.76 (m, 3H), 5.62-5.59 (m, 1H), 5.32-5.07 (m, 4H), 4.97-4.93 (m, 1H), 4.46-4.42 (m, 1H), 4.15-4.12 (m, 4H), 4.03-4.00 (m, 2H), 3.72-3.54 (m, 2H), 2.43 (dt, *J* = 14.7, 8.0 Hz, 1H), 2.41 (s, 3H), 1.38 (dt, *J* = 14.4, 4.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 143.2, 137.3, 135.9, 134.3, 134.2, 133.8, 129.6, 127.2, 117, 9, 116.9, 82.2, 80.9, 70.6, 61.7, 57.3, 56.6, 45.6, 34.9, 21.5; IR (neat, cm^{-1}) 3078, 3020, 2980, 2922, 2854, 1645, 1088; HRMS calcd for $C_{22}H_{31}N_2O_4S$ (MNH_4^+) 419.2004, found 419.2004.



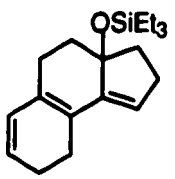
15

3,4-Bis(2,5-dihydrofuran-3-yl)-2,5-dihydrofuran (15). ^{1}H NMR (CD_2Cl_2, 300 MHz) δ 5.78 (s, 2H), 4.74 (s, 4H), 4.65 (s, 8H); ^{13}C NMR (CD_2Cl_2, 100 MHz) δ 132.2 (s), 128.1 (s), 125.9 (d, *J* = 179 Hz), 78.2 (t, *J* = 147 Hz), 75.6 (t, *J* = 147 Hz), 75.5 (t, *J* = 147 Hz); IR (neat, cm^{-1}) 3076, 2846, 1078, 1064; HRMS calcd for $C_{12}H_{14}O_3$ (M^+) 206.0943, found 206.0937.



16

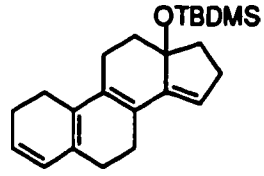
3-(2,5-Dihydrofuran-3-yl)-1,6,7,8-tetrahydrobenzofuran (16). To a stirring solution of **5** (305 mg, 1.1 mmol) in benzene (20 ml, 0.05 M) is added **1** (36 mg, 44 μmol, 0.04 equiv). The reaction is stirred at 45 °C until complete consumption of starting material is observed by tlc (product R_f = 0.2; 10% EtOAc in hexanes), about 4 h. The solvent is removed under reduced pressure, and the remaining colored oil is purified by flash chromatography (10% EtOAc in hexanes) to yield the product **17** as a clear, light yellow oil (158 mg, 79%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.18 (dt, J = 9.9, 2.0 Hz, 1H), 5.90 (m, 1H), 5.64 (t, J = 2.0 Hz), 4.28-4.87 (m, 2H), 4.78-4.67 (m, 5H), 2.32-2.18 (m, 3H), 1.70-1.59 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 134.2, 133.6, 132.5, 123.0, 121.0, 120.2, 84.3, 75.3, 75.2, 75.1, 29.9, 25.1; IR (neat, cm^{-1}) 3033, 2942, 2840, 1099, 1086; HRMS calcd for $C_{12}H_{14}O_2$ (M^+) 190.0994, found 190.0985.



17

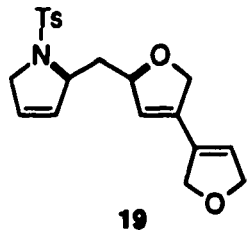
10-Triethylsilyloxytricyclo[8.3.0.0^{1,10}]trideca-1(13),2(7),5-triene (17). To a stirring solution of **1** (9.9 mg, 12 μmol, 0.04 equiv) in benzene (10 ml, 0.05 M) is added **8** (199 mg, 0.50 mmol). The reaction is stirred at 45 °C until complete consumption of starting material is observed by tlc (product R_f = 0.3; 2% Et_2O in

hexanes), about 4 h. The solvent is removed under reduced pressure, and the remaining dark oil is purified by flash chromatography (2% Et_2O in hexanes) to yield the product **17** as a clear, light yellow oil (126 mg, 84%). ^1H NMR ($CDCl_3$, 300 MHz) δ 5.84-5.82 (m, 2H), 5.60 (s, 1H), 2.68-2.51 (m, 4H), 2.39-1.78 (m, 6H), 1.57-1.45 (m, 2H), 0.88 (t, *J* = 7.9 Hz, 9H), 0.49 (q, *J* = 7.9, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 145.10, 130.32, 128.54, 126.45, 123.58, 123.48, 82.94, 39.44, 37.05, 30.33, 27.03, 23.10, 22.99, 7.18, 6.06; IR (neat, cm^{-1}) 3028, 2953, 2875, 1622, 1080; HRMS calcd for $C_{19}H_{30}OSi$ (M^+) 302.2066, found 302.2051.



18

Compound (18). To a stirring solution of **14** (42 mg, 0.1 mmol) in C_6H_6 (2 ml, 0.05 M) was added **1** (3.5 mg, 4 μmol, 0.04 equiv). After stirring for 4h at rt, **14** was not detectable by tlc (product R_f = 0.5; 1% NEt_3 in hexanes), and the reaction mixture was purified by flash chromatography (1% NEt_3 in hexanes elution). The product **18** was isolated as a viscous, light yellow oil: 26 mg, 70%. ^1H NMR ($CDCl_3$, 300 MHz) δ 5.95-5.91 (m, 1H), 5.75-5.69 (m, 1H), 5.46 (s, 1H), 2.64-2.53 (m, 2H), 2.40-2.34 (m, 2H), 2.21-2.02 (m, 4H), 1.82-1.71 (m, 1H), 1.52-1.42 (m, 1H), 0.99 (s, 9H), 0.09 (s, 3H), 0.00 (s, 3H); ^{13}C NMR (C_6D_6, 100 MHz) δ 145.0, 132.6, 128.5, 125.3, 124.3, 124.0, 82.9, 46.8, 39.7, 37.1, 30.6, 27.7, 26.2, 25.9, 24.1, 23.8, 18.7, 14.2, 12.5, -2.7, -3.1; IR (neat, cm^{-1}) 3037, 2954, 2929, 2855, 1634, 1472, 1252, 1076.



19

Compound (19). ^{1}H NMR (CD_2Cl_2, 300 MHz) δ 7.66 (d, *J* = 8.4 Hz, 2H), 7.32 (d, *J* = 8.4 Hz, 2H), 5.73-5.57 (m, 4H), 5.03-4.93 (m, 1H), 4.82-4.67 (m, 6H), 4.52-4.46 (m, 1H), 4.16-4.01 (m, 2H), 2.41 (s, 3H), 2.21-2.13 (m, 1H), 2.00-1.90 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 143.7, 132.2, 132.0, 130.1, 129.8, 127.4, 126.4, 124.2, 123.4, 84.0, 76.2, 75.0, 74.5, 64.7, 55.5, 42.3, 21.2; IR (neat, cm^{-1}) 2847, 1597, 1470, 1162, 1088; HRMS calcd for $C_{20}H_{24}NO_4S$ (MH^+) 374.1426, found 374.1423.

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References and Notes

[†] The laboratory work described in this chapter was done with Matthias Scholl who synthesized compounds **4** and **15** and helped in the synthesis of **5**, **6**, and **19**.

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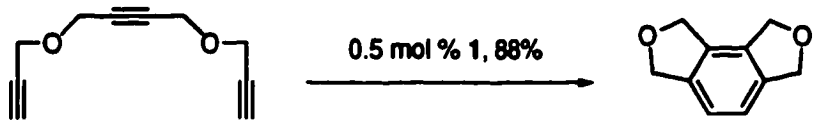
[15]Compounds **4** and **5** have been protected as trialkylsilyl ethers. Cyclization proceeds without this protection, but the reaction rate is slowed dramatically, possibly due to intramolecular chelation.

[16]The extra substituent on the disubstituted olefin is employed to increase the relative rate of metathesis at the monosubstituted "productive" olefin. When the reaction is conducted with an acyclic precursor containing two monosubstituted olefins, product formation is observed at a slower rate and to a lesser extent.

[17]A related process involving carbene-acetylene metathesis, enyne metathesis ring-closure, has been reported utilizing tungsten and ruthenium carbene complexes. (a) Katz, T. J.; Sivavec, T. M. *J. Am. Chem. Soc.* **1985**, *107*, 737. (b) Kinoshita, A.; Mori, M. *Synlett* **1994**, 1020. (c) Kinoshita, A.; Mori, M. *J. Org. Chem.* **1996**, *61*, 8356. Similarly, carbene-acetylene metathesis allows for the recently reported rearrangement-cyclization of triynes to produce aromatics, an example of which is shown. (d) Peters, J.U.; Blechert, S. *Chem. Commun.* **1997**, 1983.



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