Systematic Analysis of the Intramolecular Competition Associated with the Ring Closing Metathesis of Ene-Diene Systems of Differing Chain Length with a Pair of Ruthenium Catalysts

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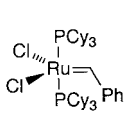
Dedicated to Professor *Dieter Seebach* on the occasion of his 65th birthday

The (alkylidene) ruthenium complexes **1** and **2b** were examined as catalysts for the ring-closing metathesis of the homologous series of ene-dienes **16** to ascertain the extent to which a divergence in product distribution would be observed. In each case, the levels of cyclic alkene and conjugated diene were determined (see *Table 1*). Double bond geometric assignments were made on the basis of vinyl proton ^{1}H-NMR chemical shifts and coupling constants. MM3 Calculations were undertaken to gauge the levels of steric strain in end products of varying ring size. The global ensemble of facts, including key control experiments, demonstrate the striking differences between **1** and **2b**. Finally, the steric energies are seen not to correlate with the product distributions, most probably due to the distinctive reactivity patterns of the metathesis reagents.

1. Introduction. – Intramolecular cyclization reactions have played a pivotal role in our appreciation of those factors that gain importance in the assembly of medium to large rings [1]. The breadth of reaction types has been subjected to impressive variation, ranging from C–C bond-formation (*e.g.*, the generation of carbocyclic malonates [2]) to the formation of C–O (*e.g.*, the elaboration of cyclic ethers [3] and lactones [1][4]) and C–N bonds (*e.g.*, closure to produce *N*-tosylated amines [5]). On the strength of the seminal investigations performed by *Ziegler* and co-workers [6] and by *Stoll* and co-workers [7] among others, it was soon recognized that the probability for chain ends to meet in a bifunctional linear precursor decreases as the chain is made increasingly longer. In 1935, *Ruzicka* advanced the hypothesis that this probability factor contributes independently of ring-strain effects to the global disincentive toward cyclization [8]. The ensuing experimental determination of activation parameters for a number of cases suggested that simple relationships between $\Delta H^{\neq}$ and the strain energy likely do not exist for this generic class of reactions [9].

During the past two decades, the advent of effective new methods with which to accomplish intramolecular macrocyclization has stimulated interest at many levels [10]. The current perception is that one or another of these protocols should enable the synthetic chemist to arrive at the targeted goal. This is particularly true when the step involved is metal-mediated [11]. Among these applications, the area of ring-closing diene metathesis (RCM) involving air-stable ruthenium catalysts has experienced tremendous growth and commanded a major share of the attention [12]. There remains little awareness today that, in the 1998 *Armstrong* review of this field [13], examples of 8-membered- to 21-membered ring closures were indeed quite uncommon. Success or failure was attributed more to the substrate conformation than to the properties of the

catalyst. However, the advent of new, more reactive catalysts [14] has shown that this viewpoint is no longer tenable. While **1** has become recognized to offer good functional group tolerance and reliable performance levels with many substrates, **2a** and **2b** exhibit higher reactivity, increased efficiency, and improved sensitivity toward functional groups as a direct result of their more favorable steric and electronic properties.



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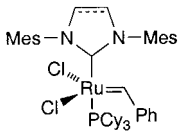


2a unsaturated
b saturated

Notwithstanding the apparent broad scope of RCM reactions promoted by **1** and **2**, little effort has yet been expended on the elucidation of possible *divergences* in their chemical reactivity. One possible direction is to take advantage of the capacity of competing *intramolecular* cyclization options to reveal the adoption of different reaction pathways. In the first of the examples of which we are aware, *Wagner* and co-workers examined the conversion of **3** and **4** into macrolides under catalysis by two of the above ruthenium catalysts [15] (*Scheme 1*). Quite unexpectedly for them, distinctively different pathways were followed. With catalyst **1**, the (*E,E*)-dienes **5** and **6** were formed with remarkably good efficiency (57–62%). Less than 5% of the (*E,Z*)-isomer was found, and no other end products were detected. In contrast, the heterocyclic carbene complex **2a** showed the opposite selectivity and gave rise chiefly to the (*E*)-cycloalkenes **7** and **8** (40–45%). Therefore, while **1** reacts regioselectively with the less sterically hindered terminal C=C bond, **2a** opts instead to engage the more substituted, electron-rich internal C=C bond in metathesis. The consequences are quite dramatic. Although solvent, temperature, and concentration effects were examined by these authors, no control experiments were reported.

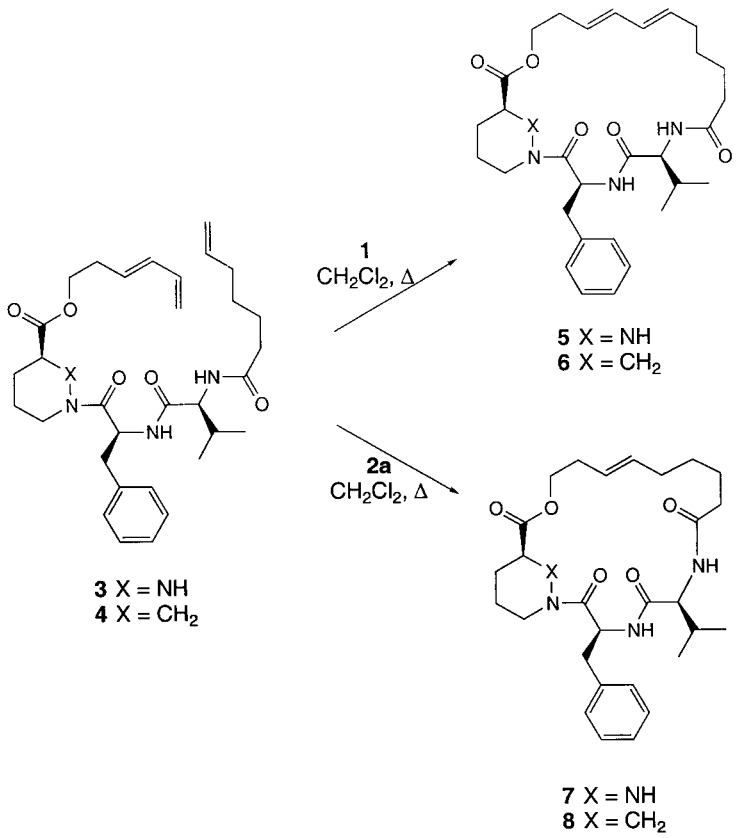
In a recent study targeting the asymmetric synthesis of radicol and monocillin I, the *Danishefsky* group examined the RCM of dithianes **9** and **11** (*Scheme 2*) [16]. Whereas the use of commercial **1** resulted in essentially no reaction of **9**, application of **2b** gave diene **10** (55% yield) as the only monomeric product. This scenario was repeated with **11**, which cyclized to the 14-membered **12** (60%) notwithstanding the presence of dithiane and epoxide functionality. This common convergence to the larger-ring dienes was left unexplained.

In a third report, *Mioskowski* and co-workers demonstrated that when C- *vs.* O-membered-ring cyclizations are both possible, formation of the heterocycle is favored [17]. The example given in *Scheme 3* is illustrative.

To explore possible trends in regioselectivity as a function of ring size, we carried out a systematic analysis of RCM behavior in the compound series defined by **16** (see below, *Scheme 4*)[1]). Throughout this study, the conjugated-dienyl unit bonded to the N-atom was retained while the ω-alkenyl chain linked to the O-atom was progressively lengthened. To achieve a semblance of electronic equivalence, the degree of alkyl

[1]) For a preliminary report covering a portion of this investigation, see [18].

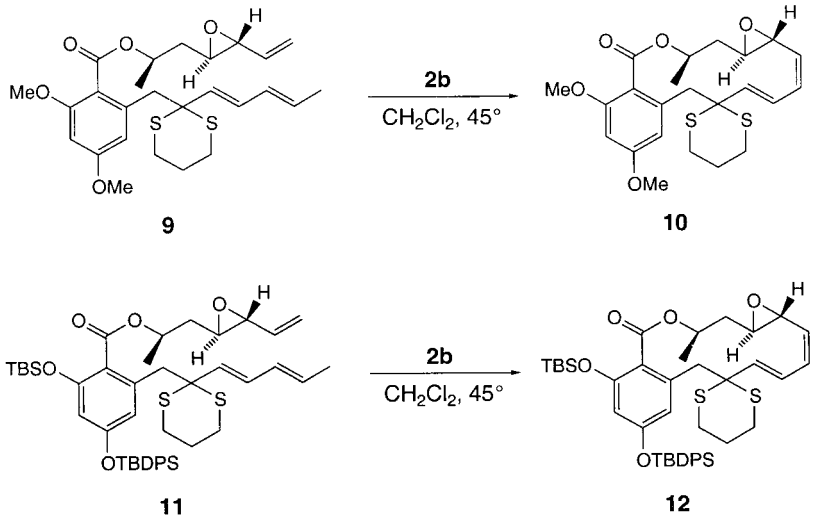
Scheme 1



substitution about both double bonds in the conjugated-diene segment was equalized. The commercially available catalysts **1** and **2b** were independently evaluated. Since significant differences in ring size are involved in each instance, we also performed a series of *Monte-Carlo* conformational searches [19] using the MM3 force field [20] to provide insight into the differing steric energies involved. To take advantage of improved parametrization, these calculations involved the *N*-methyl derivatives of **16**. The elimination of the sulfonamide side chain was not expected to impact meaningfully on the prevailing steric considerations. By this means, steric-energy data would be made available over a wide range of ring sizes. This limitation has hampered past investigations of intramolecular cyclization processes [21–24].

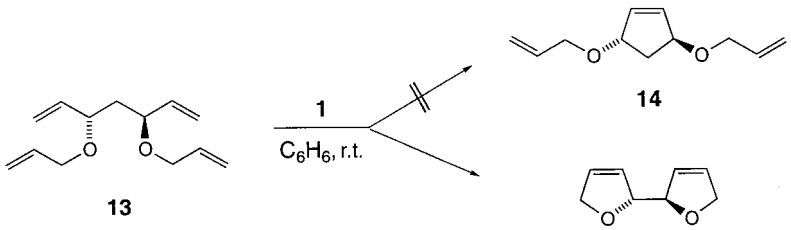
2. Synthetic Considerations. – The point of departure for access to **16** was the azidocyclohexanol **17**, readily available from reaction of sodium azide with cyclohexene oxide in refluxing aqueous ethanol [25] (*Scheme 4*). *O*-Pivaloylation, chemoselective reduction over 10% Pd/C, and *N*-tosylation [26] subsequently provided the generic

Scheme 2



9 **10** **11** **12**

Scheme 3



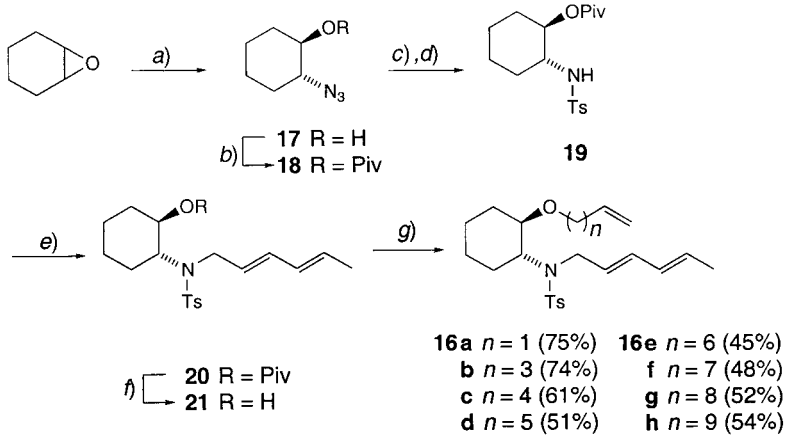
13 **14** **15** (90%)

intermediate **19**. Addition of (2*E*,4*E*)-1-bromo-hexa-2,4-diene[2]) [27] to the sodium salt of **19** in DMF solution [28] led to the desired **20**, reduction of which with Dibal-H [29] made available the functionalized cyclohexanol **21**. The construction of **16a**–**h** was concluded by bringing the sodium salt of **21** into contact with the appropriate ω-alkenyl bromide *via* a protocol previously defined by others [30]. A progressive dropoff in coupling efficiency from 75 to 50% was noted as n was increased from 1 to 5. Greater extension of the methylene chain beyond this level was not accompanied by a further erosion in reaction efficiency. The example involving $n = 2$ was met with wholesale E_2 elimination, thus causing us to dispense with further consideration of this substrate.

3. Intramolecular Competition Studies. – The results obtained with **16a** (*Entries 1* and *2*) and **16b** (*Entries 3* and *4*) provide important calibration points for the smaller-sized rings (*Table 1*). In the first instance, the (*Z*)-monoene **22** was formed efficiently

[2]) Prepared from commercially available (2*E*,4*E*)-hexa-2,4-dien-1-ol by the method described in [27].

Scheme 4



a) NaN_3, NH_4Cl, EtOH/H_2O 5:1, reflux (88%). *b*) PivCl, Et_3N, CH_2Cl_2 (96%). *c*) H_2, 10% Pd/C, MeOH. *d*) TsCl, Et_3N, CH_2Cl_2 (65% over two steps). *e*) NaH, (*E,E*)-MeCH=CHCH=CHCH$_2$Br, DMF (70%). *f*) (i-Bu)$_2$AlH, CH_2Cl_2, $-78° \rightarrow$ r.t. (80%). *g*) NaH, CH_2=CH(CH$_2$)$_n$Br, DMF.

(71–75% yield) in the presence of either metathesis catalyst (*Scheme 5*). None of the starting ene-diene was recovered after a standardized reaction time of 24 h. The insertion of two additional methylene groups (**16b**) effectively retards the ability of this system to cyclize (15–20% recovery of starting material). Also, neither the (*E*)- nor the (*Z*)-monoene corresponding to **22** was observed. In contrast, the (*E,Z*)-diene **23** was formed uniquely (exclusive of oligomers) in isolated yields ranging from 27–33%.

The (*Z*)-geometry of **22** was readily ascertained on the basis of its two widely spaced *m* positioned upfield and downfield of 5.5 ppm. The (*E*)-counterpart is characterized by a narrow *m* of area 2 in this region [31][32]. The olefinic-proton absorptions displayed by **23** consist of three *m*. The two located at δ 7.12–6.98 and 6.24–6.17, each of area 1, are attributable to the central olefinic protons of the conjugated diene. The third, positioned at δ 5.51–5.36, is twice as intense and originates from the remaining vinylic H-atoms. Since irradiation at δ 6.24 causes the downfield signal to collapse to a *d* (J = 15.5 Hz) and the reciprocal experiment at δ 7.11 leaves a *d* (J = 9.9 Hz) at δ 6.24, the (*E,Z*)-geometric arrangement as in **23** is unequivocally defined [33].

The identical processing of **16c** resulted in notably inefficient ring closure with either catalyst (67–70% oligomerization, *Entries 5* and *6*). Although a choice between the formation of an 11- or 13-membered ring exists in this instance, only an inseparable *ca.* 1:1 mixture (^{13}C-NMR analysis) of the (*E*)-isomer **24** and the (*Z*)-isomer **27** materialized. In the ^{1}H-NMR spectrum of these combined isomers, the vinylic proton signals consist of two br. *m* (δ 5.70–5.61 and δ 5.44–5.39). There is a strong likelihood that the inner regions of these absorptions arise from the (*E*)-olefin. The two monomeric cyclization products derived from **16d** (*Entries 7* and *8*) proved to be conveniently amenable to chromatographic separation. The less-polar substance was determined to be the (*E*)-monoene **28** based on the strength of its overlapping olefinic absorptions at δ *ca.* 5.4. The ^{1}H-NMR spectrum of the second product was nearly

Scheme 5

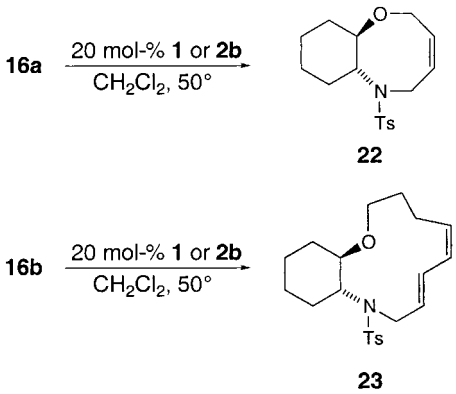


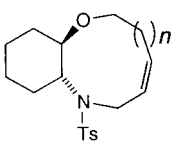
Table 1. *Results of Intramolecularly Competitive Ring-Closing Metathesis*[a])

Entry	Ene-diene reactant	Catalyst	Product composition [%][b])					
			Recovered starting material	(*Z*)-Monoene	(*E*)-Monoene	(*E*,*Z*)-1,3-Diene	(*E*,*E*)-1,3-Diene	Oligomers[c])
1	**16a**	**1**		71				29
2	**16a**	**2b**		75				25
3	**16b**	**1**	20			33		37
4	**16b**	**2b**	15			27		58
5	**16c**	**1**	17	8	8			67
6	**16c**	**2b**	13	9	8			70
7	**16d**	**1**	18		22	25		35
8	**16d**	**2b**	12		43	10		35
9	**16e**	**1**	29		31			40
10	**16e**	**2b**	19		49			32
11	**16f**	**1**	15		35			50
12	**16f**	**2b**	18		39			43
13	**16g**	**1**	60	9			17	14
14	**16g**	**2b**	13	40			16	31
15	**16h**	**1**	21	8			33	38
16	**16h**	**2b**	10	30			23	37

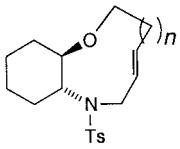
[a]) All reactions were carried out in CH_2Cl_2 solution at a catalyst concentration of 0.003M according to the general procedure. [b]) All values, except those given for the oligomers, represent actual isolated yields with an accuracy level of ±3%. [c]) These values represent the balance of material not otherwise accounted for.

identical to that exhibited by **23**. Also consistent with its formulation as the (*E*,*Z*)-diene **31** were a number of selective decoupling experiments. Furthermore, the strikingly different spectral appearance of the downfield portion of the ^{1}H-NMR spectra subsequently recorded for **32** and **33** proved reinforcing.

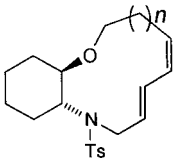
The incremental intercalation of yet more methylene groups as in **16e** and **16f** was met with the exclusive generation of the (*E*)-monoenes **29** and **30**, respectively



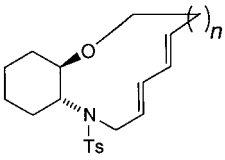
24 $n = 3$
25 $n = 7$
26 $n = 8$



27 $n = 3$
28 $n = 4$
29 $n = 5$
30 $n = 6$



31 $n = 4$



32 $n = 7$
33 $n = 8$

(*Entries 9–12*). In these homologues, the already modest chemical-shift differences of the olefinic protons so evident in **28** (δ 5.48–5.30) are mirrored closely in **30** (δ 5.56–5.45) but less so in **29** (δ 5.61–5.52; δ 5.48–5.39), probably as the result of ring-size effects.

The introduction of eight- and nine-membered methylene chains as in **16g** and **16h** was equally revealing (*Entries 13–16*). These ene-dienes gave rise to the (*Z*)-monoenes defined by **25** and **26**, respectively, and to the (*E*,*E*)-dienes characterized as **32** and **33**. *The divergence in product distribution exhibited by catalysts* **1** *and* **2b** *was greatest for these most structurally extended substrates.* The pattern of olefinic signals displayed by **25** and **26** is strikingly comparable to that exhibited by the lower homologue **24**. Clearly apparent in the 300- and 500-MHz spectra of **32** and **33** are four distinctively separated *m*.

In the specific case of **33**, irradiation of the δ 6.06 *m* causes simplification of the δ 5.91 signal to a *d* with $J =$ 15.0 Hz. Additionally, irradiation at δ 5.91 leaves a *d* ($J = 14.2$ Hz) at δ 6.06. Therefore, both of its constituent C=C bonds are necessarily (*E*)-configured. The spectrum of **32** is almost superimposable upon that of **33**.

4. The Consequences of Chain Length. – As each compound of type **16** engages in ring-closing metathesis, two distinctive modes of cyclization are set in competition, each with a different ring-size outcome. Noteworthily, in the case of **16a**, both ruthenium catalysts are notably effective in generating the 8-membered ring monoene **22** to the exclusion of any geometric isomer of the conjugated cyclodecadiene. The higher homolog **16b** is, in principle, amenable to formation of a 10-membered cycloalkene or a 12-membered cyclic diene such as **23**. Once again, the pathway leading to an unsaturated cyclodecane derivative is not followed, leading one to conclude that a kinetic deterrent is likely associated with this ring size.

Since **16c** cyclizes only in the direction of the 11-membered cycles **24** and **27**, the corollary would mean that the transition states associated with possible generation of a

13-membered diene are too energetic to be easily reached. Furthermore, as noted earlier, the pathway found to be operational here is seen to be marginally competitive with oligomerization. In contrast, the circumstances surrounding **16d**, *i.e.*, competition between 12- and 14-membered-ring formation, do not serve as a deterrent to either pathway. While catalyst **2b** exhibits a greater preference for generation of the smaller monoene **28** than does **1**, the product distributions conform well to the notion that near-isoenergetic transition states are involved.

Neither **16e** nor **16f** give evidence of proceeding to generate the larger-ring diene products (now 15- and 16-membered) (*Entries 9–12*). Instead, reaction proceeds with formation of the (*E*)-monoenes **29** and **30** where the ring sizes are constituted of 13 and 14 atoms, respectively. By the time that **16g** and **16h** are arrived at, little discrimination between the two pathways manifests itself (*Entries 13–16*). With either catalyst, the production of (*E,E*)-dienes **32** and **33** is heightened. This may be a reflection of recognition within the associated transition states of the stabilizing effects of more extended conjugation and/or the energetic advantage of minimizing nonbonded transannular interactions by increasing the number of double bonds within the loop. Alternatively, the rigid group effect of the 1,3-diene in the backbone could be responsible [34], but we consider this to be unlikely.

5. Results of Molecular-Mechanics Calculations. – In an effort to obtain comparative information within six series of unsaturated heterocyclic systems, we have made recourse to molecular-mechanics calculations based on the MM3 force field [20]. Utilization of the stochastic method of optimizing the molecular geometries [35] of **34**–**39** provided the steric energies compiled in *Tables 2* and *3*. The structures corresponding to the low-energy minima are depicted in *Fig. 1* from the perspective above the equatorial plane in each case. Clearly revealed by plots of steric energy *vs.* ring size is the rather monotonous relationship between these parameters, except for the smaller values of *n*. Thus, the gap between the (*Z*)-isomer **34** and (*E*)-isomer **35** at the level of the 8-membered ring is expectedly biased more favorably toward the less strained (*Z*)-isomer (*Fig. 2*). We find this divergence to be even greater when (*E,E*)-isomer **39** is involved (*Fig. 3*). The energetic costs of maintaining the two (*E*)-configured C=C bonds in **39** relative to the (*Z,Z*)-diene option **36** reaches a value of *ca.* 20 kcal/mol at the level of the 8-membered ring. The steric phenomenon begins to manifest itself at the 11-membered-ring level. When 16-membered rings are involved, the (*Z,Z*)-diene isomer **36** is modestly more strained than the other three geometric forms.

Given the assumption that MM3 has generated fairly good estimates of these structures and their energies, the deviations are seen to be quite small, except at the lower end of the medium-ring range. While direct comparison of monoenes **34** and **35** with dienes **36**–**39** is not warranted, a parallelism is apparent within these separate groups of compounds. When diverse intricacies are at play as the value of *n* increases in these systems, appropriate conformational adjustments materialize such that a more or less global normalization operates. We have no reason to be skeptical about the correctness of the calculated values. The internal consistency of the steric strain energies is not easily correlated with the product distributions experimentally determined for the ring-closing metatheses (shown below).

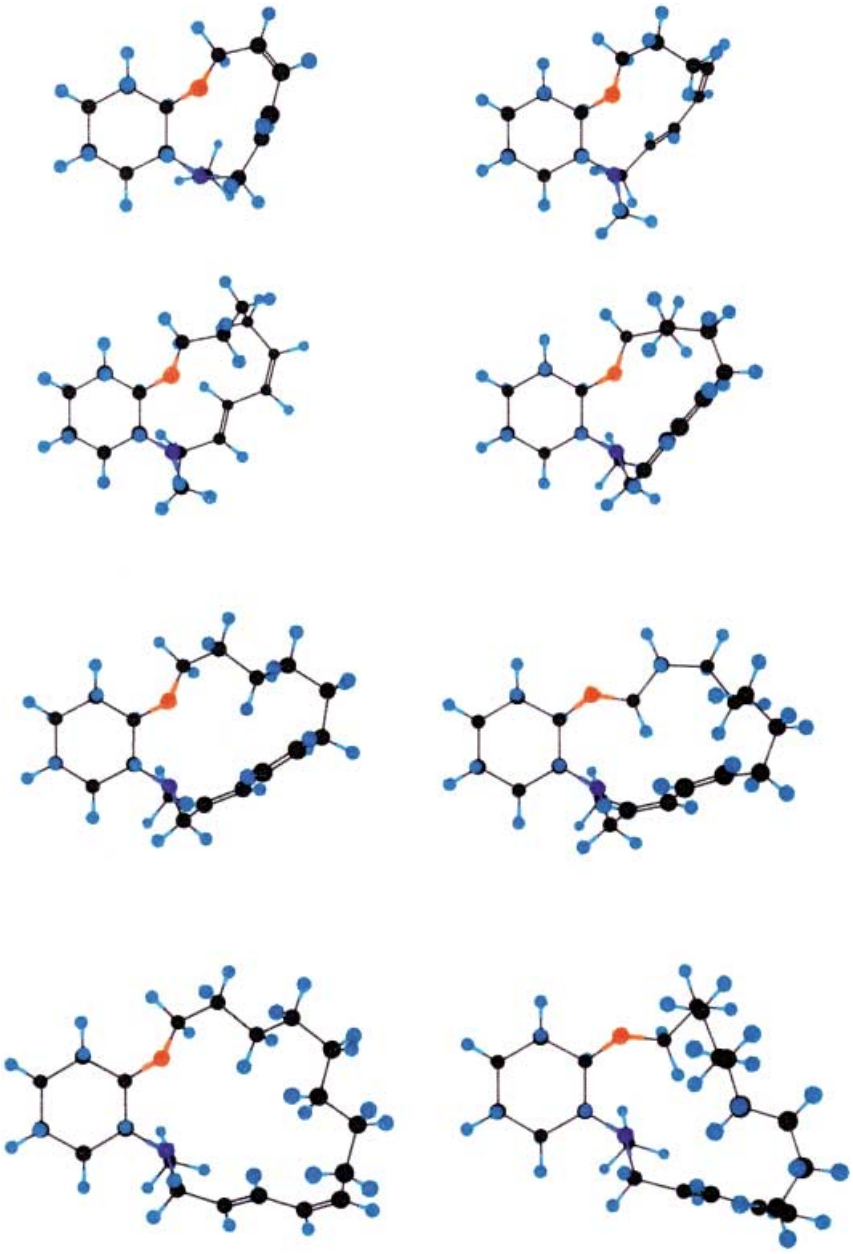


Fig. 1. *Top views of the minimum-energy conformers of eight homologous* (E,Z)*-1,3-dienes as calculated* via *MM3*

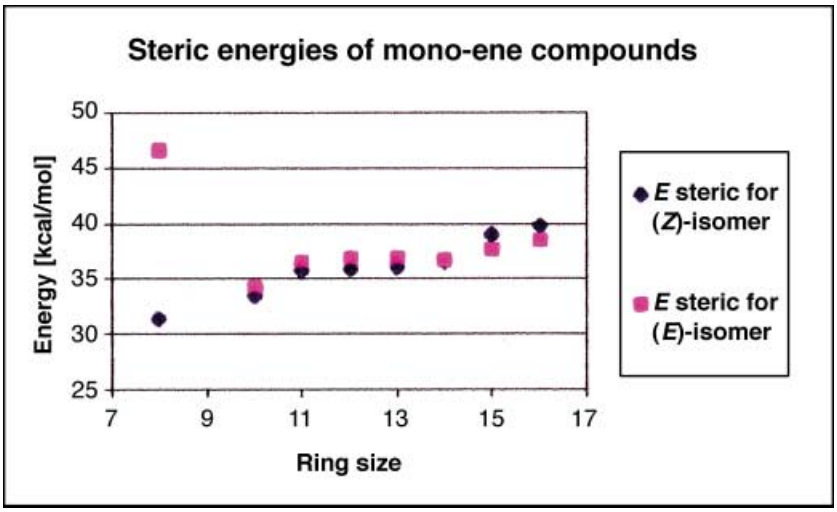


Fig. 2. *Steric energies of the* (E)*- and* (Z)*-monoenes as a function of ring size* (MM3 calculations)

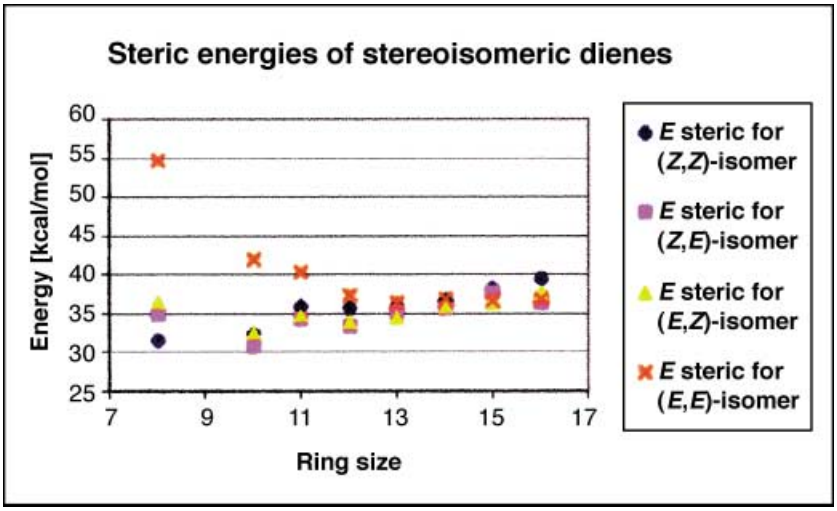


Fig. 3. *Steric energies of the four stereoisomeric series of 1,3-dienes as a function of ring size* (MM3 calculations)

6. Mechanistic Analysis. – In light of the presence of three olefinic moieties in **16**, initial reaction with the ruthenium catalysts **1** and **2b** can operate at three different sites. On the basis of results described earlier and those recorded for **40**, which is transformed into **41** (96%) without evidence for the generation of **42** [36] (*Scheme 6*), we believe that the pathway involving preferential attack at the lesser-substituted isolated C=C bond in **16** is likely to be operative as well. Once the ruthenium carbenoid **43** is generated, intramolecular cyclization can, in principle, result in capture of the more proximal (as in **44** or **45**) or the more distal conjugated C=C bond (see **46** and **47**,

Table 2. *Steric Energies of the (*Z*)- and (*E*)-Monoenes*[a])

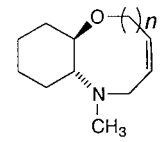
Ring size	(*Z*)-Series	(*E*)-Series
8	31.4	46.6
10	33.5	34.3
11	35.7	36.6
12	35.8	36.9
13	36.1	36.9
14	36.5	36.7
15	38.9	37.6
16	39.7	38.5

[a]) All values are in kcal/mol.

Table 3. *Steric Energies of the Stereoisomeric 1,3-Dienes*[a])

Ring size	(*Z*,*Z*)-Isomer	(*Z*,*E*)-Isomer	(*E*,*Z*)-Isomer	(*E*,*E*)-Isomer
8	31.5	35.0	36.4	54.7
10	32.4	30.9	32.4	41.9
11	35.8	34.2	34.7	40.3
12	35.7	33.4	33.8	37.2
13	36.0	35.1	34.6	36.3
14	36.7	35.7	35.9	36.8
15	38.1	37.7	36.4	36.7
16	39.4	36.3	37.5	36.9

[a]) All values in kcal/mol.



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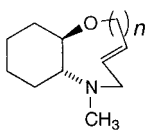

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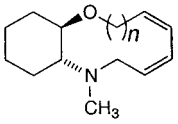

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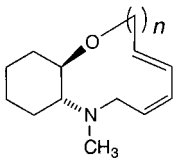

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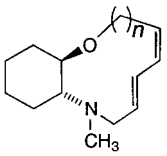
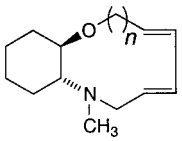
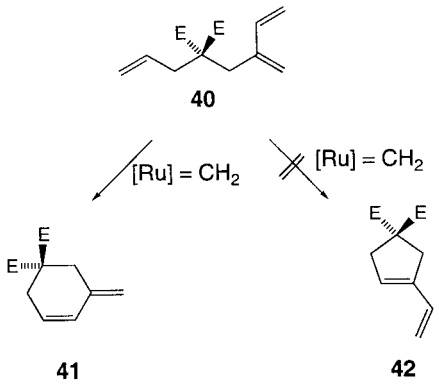


38



39

Scheme 6



Scheme 7). Subsequent [2 + 2] retrograde fragmentation within the first two metallocyclobutanes affords the (*Z*)- or (*E*)-monoene product, respectively. As is illustrated, the analogous chemical transformation within **46** and **47** provides for the formation of the (*E*,*Z*)- and (*E*,*E*)-dienes.

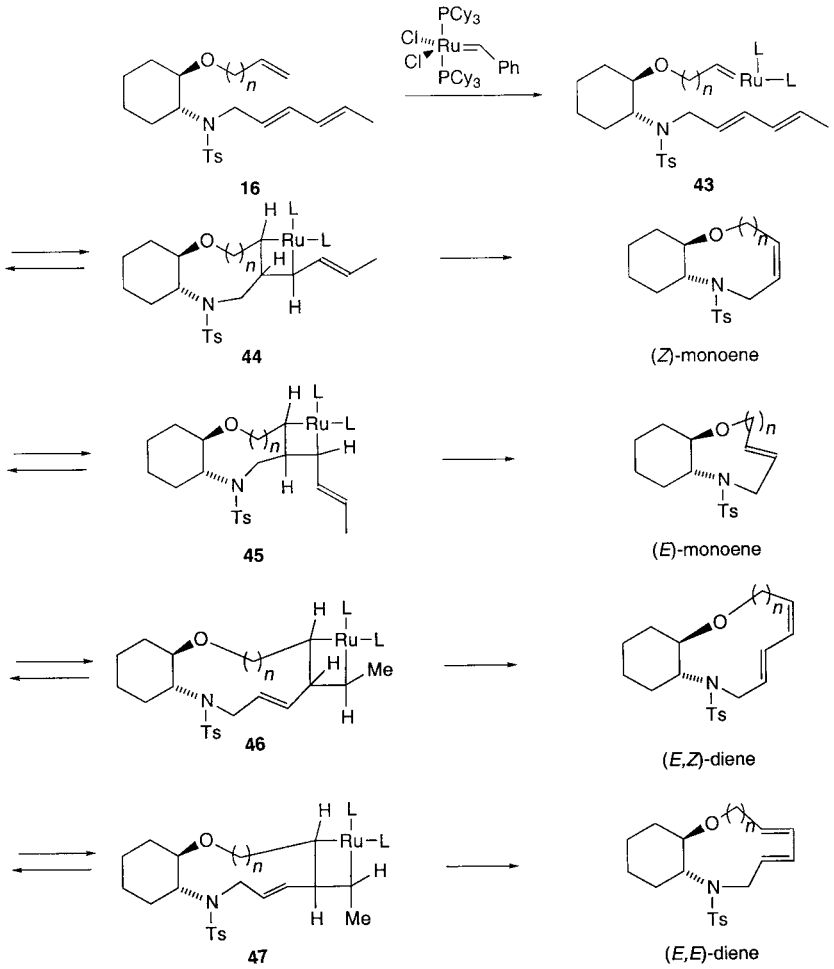
The (*E*/*Z*)-selectivity ratios generated during RCM are customarily difficult to predict or control, and the present study is no exception. The changes in selectivity as a function of ring size [37], the position of the C=C bond, and the remoteness of heteroatom functionality from the metathesis-reaction site [38] have been examined in other contexts. With very few exceptions, the product distributions do not vary as significantly as they do with **3** and **4**. Thus, the observations made by *Wagner* [15] and by *Danishefsky* [16] do not appear to carry over to **16a**–**h**.

When large, strainless rings are being formed, the transition states are widely recognized to be independent of strain-energy consequences [9b]. As the medium-ring region is approached, steric and strain effects increasingly begin to surface, and the resulting unfavorable enthalpic contributions must be added to the entropy loss arising from ring closure. These effects are considered to play a role in the preferred ring-closure modes uncovered in the present study. A comparable conclusion regarding product double-bond stereochemistry is not warranted because significant secondary metathesis isomerization is known to operate during RCM [14c].

7. Control Experiments. – Our analysis of the products formed in the RCM of **16a**–**h** is based on the expectation that kinetic control is operative under these conditions. If reversibility is inherent to these processes, more so for the more reactive catalyst **2b** than **1**, the door is open for possible ring contraction of the dienes to monoenes under the proper conditions. The ensuing data provide compelling evidence that these mechanistically relevant transformations are possible. This scenario sheds considerable light on the dichotomy of the product distributions.

Selected as the test case was **16d** in light of its unique capability to produce both types of cyclization products. Its behavior is such that exposure to catalyst **1** affords approximately equal amounts of (*E*)-monoene **28** and the (*E*,*Z*)-diene **31** (*Table 1*). With **2b** as the promoter, it is immediately clear that **28** is significantly more

Scheme 7

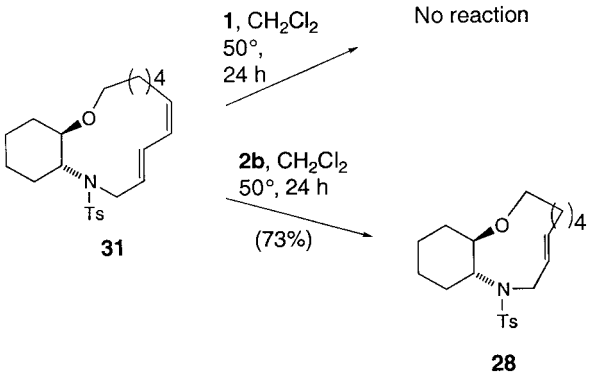


predominant (ratio 4 : 1). At issue is the question of whether **31** is being converted into **28** under either set of conditions, most particularly when the more reactive catalyst is utilized. To probe this issue, **31** was resubjected to the original RCM conditions (*Scheme 8*). In the presence of **1**, no reaction was observed, and the diene was recovered quantitatively. By way of contrast, the use of **2b** resulted in the complete disappearance of **31** and isolation of **28** in 73% yield.

These findings suggest that the conversion of **3** and **4** to **7** and **8** by **2b** may proceed *via* the intermediacy of **5** and **6**, respectively. Why ring contraction is not observed with dienes **10** and **12** remains in need of clarification; it may be either of kinetic or thermodynamic origin.

Taken together, the scenario that has developed to this point shows the product distributions not to necessarily parallel the calculated steric strain energies for **34**–**39**. Additional probes of such RCM reactions are clearly warranted.

Scheme 8



8. Conclusion. – Ene-dienes **16** are shown to be useful probes for the study of the effect of chain length on the mode of ring-closing metathesis. The regio- and stereoselectivities vary widely, and all four possible mechanistic pathways are represented. Thus, **16a** furnishes the (*Z*)-monoene **22** in good yield without any evidence for formation of a 10-membered ring diene. For **16b**, the preferred process lies very much in favor of generating the (*E*,*Z*)-diene **23**. Systematic chain extension to the level of **16e** is met with a return to preferred cycloalkene production, but now (*E*)-configured as in **29**. As concerns **16h**, the longest chain homolog examined, ring-size effects are less distinctive, and both monoene **26** and diene **33** are formed, the latter being favored by as much as 4:1. Although these processes lead to rather diverse structural motifs, strong evidence is provided that the diene product **31** is convertible to the monoene **28** under RCM conditions, provided that the more reactive **2b** serves as the catalyst. The ability to trigger these events reveal the complexity associated with the implementation of such ring closures. Reversible ruthenacyclobutane formation always remains a distinct mechanistic possibility. The further chemical evolution of these intermediates is dependent on prevailing kinetic and thermodynamic factors.

The financial support of *the National Science Foundation* is greatly appreciated. We thank Dr. *Claudio Sturino* (*Merck Frosst*, Montreal) for a generous gift of the ruthenium catalysts. *J. E. H.* was a trainee in the NIH Chemistry/Biology Interface Program and *J. C. E* was an undergraduate research participant.

Experimental Part

General. Solvents were reagent grade and in most cases dried prior to use. Column chromatography (CC): *Woelm* silica gel (230–400 mesh). The purity of all compounds was shown to be $>95\%$ by TLC and high-field ^{1}H-and ^{13}C-NMR spectroscopy. IR: in cm^{-1}. The high-resolution mass spectra (in *m*/*z*) were recorded in the Department of Chemistry at The Ohio State University. Elemental analyses were performed at *Atlantic Microlab, Inc.*, Norcross, GA.

Compound **18**. Alcohol **17** (44.4 g, 314.9 mmol) was dissolved in dry CH_2Cl_2 (400 ml), cooled to 0°, and treated with Et_3N (63.7 g, 629.7 mmol) and pivaloyl chloride (57.0 g, 472.4 mmol). The resulting mixture was stirred at r.t. for 36 h and quenched with 1N HCl (200 ml) followed by H_2O (500 ml). The aq. layer was extracted with CH_2Cl_2, the combined org. phase dried and evaporated, and the residue purified by CC (SiO_2; petroleum ether/Et_2O 40:1): 68.1 g (96%) of **18**. Colorless liquid. IR (neat): 1728, 1170. ^{1}H-NMR (300 MHz, $CDCl_3$): 4.69–4.61 (*m*, 1 H); 3.46–3.36 (*m*, 1 H); 2.09–2.01 (*m*, 2 H); 1.78–1.68 (*m*, 2 H); 1.45–1.15 (*m*, 13 H).

^{13}C-NMR (75 MHz, $CDCl_3$): 178.1; 75.0; 63.5; 38.8; 30.4; 30.3; 27.1 (2 C); 23.8; 23.3. HR-ES-MS: 248.1381 ($[M+Na]^+$; calc. 248.1369).

Compound **19**. An 80.7 g (358 mmol) sample of **18** dissolved in MeOH (300 mg) was admixed with 10% Pd/C (1.5 g), saturated with H_2, and stirred under H_2 overnight. The mixture was filtered through *Celite*, rinsed with Et_2O (200 ml), and evaporated to leave the amine as a colorless oil that was used directly.

To a soln. of the above oil in anh. CH_2Cl_2 (500 ml) were added dry Et_3N (46.5 g, 71.6 mmol) and tosyl chloride (88.7 g, 465 mmol) at r.t. under N_2. The resulting soln. was stirred overnight at r.t. and quenched with 1N HCl (100 ml) and H_2O (300 ml). The aq. layer was extracted with CH_2Cl_2, the combined org. phase dried and evaporated, and the residue was purified by CC (SiO_2; petroleum ether/Et_2O 2:1): 82.7 g (65%) of **19**. White solid. M.p. 93–95°. IR (neat): 3402, 3278, 1728, 1651. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.72 (*d*, *J* = 8.3, 2 H); 7.25 (*d*, *J* = 8.3, 2 H); 5.96–5.89 (*m*, 1 H); 4.75–4.61 (*m*, 1 H); 3.88–3.75 (*m*, 1 H); 3.38–3.20 (*m*, 1 H); 2.39 (*s*, 3 H); 2.17–2.08 (*m*, 1 H); 1.97–1.15 (*m*, 15 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 177.9; 142.9; 138.9; 129.5 (2 C); 126.7 (2 C); 73.9; 56.5; 38.7; 32.1; 30.6; 27.1 (3 C); 24.1; 23.4; 21.4. HR-ES-MS: 376.1547 ($[M+Na]^+$; calc. 376.1553).

Compound **20**. A soln. of **19** (24.4 g, 69.2 mmol) in anh. DMF (100 ml) was treated portionwise with NaH (3.32 g of a 60% mixture in oil, 83.1 mmol) at 0° and stirred at 0° for 30 min prior to the addition of (*E*,*E*)–MeCH=CHCH=$CHCH_2$Br (13.2 g, 83.1 mmol). The resulting mixture was stirred at 0° for 1 h and at r.t. overnight, carefully quenched with H_2O (200 ml), and diluted with Et_2O (300 ml). The aq. layer was extracted with Et_2O, the combined org. layer washed with H_2O, dried, and evaporated. The residue was purified by CC (SiO_2; petroleum ether/Et_2O 5:1): 25.4 g (70%) of pure **20**. White solid. M.p. 122–124°. IR (neat): 1728. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.75–7.68 (*m*, 2 H); 7.35–7.20 (*m*, 2 H); 6.10–6.01 (*m*, 1 H); 5.95–05.86 (*m*, 1 H); 5.72–5.61 (*m*, 1 H); 5.37–5.27 (*m*, 1 H); 4.79–4.72 (*m*, 1 H); 3.97–3.88 (*m*, 1 H); 3.82–3.67 (*m*, 2 H); 2.41 (s, 3 H); 2.12–2.08 (*m*, 1 H); 1.76–1.58 (*m*, 8 H); 1.33–1.07 (*m*, 11 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 177.9; 142.7; 139.1; 133.1; 130.5; 130.0; 129.5 (2 C); 127.1; 126.9 (2 C); 71.2; 60.4; 46.1; 38.7; 31.8; 30.7; 27.0 (3 C); 25.2; 23.9; 21.4; 18.0. HR-ES-MS: 456.2165 ($[M+Na]^+$; calc. 456.2179). Anal. calc. for $C_{24}H_{35}NO_4S$: C 66.48, H 8.14; found: C 66.58, H 8.25.

Compound **21**. To a soln. of **20** (25.4 g, 58.7 mmol) in anh. CH_2Cl_2 (200 ml) was slowly added 1M Dibal-H in hexane (146.8 ml, 146.8 mmol) at −78°. The resulting mixture was stirred at −78° for 2 h, warmed to r.t., carefully quenched with sat. sodium potassium tartrate soln. (150 ml), and stirred overnight. The aq. layer was extracted with CH_2Cl_2, the combined org. phase dried and evaporated, and the residue purified by CC (SiO_2; petroleum ether/Et_2O 2:1): 16.4 g (80%) of **21**. Yellow oil. IR (neat): 3520, 1598, 1334. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.74–7.69 (*m*, 2 H); 7.29–7.27 (*m*, 2 H); 6.18–6.09 (*m*, 1 H); 6.03–5.93 (*m*, 1 H); 5.73–5.63 (*m*, 1 H); 5.56–5.47 (*m*, 1 H); 4.06–3.95 (*m*, 1 H); 3.79–3.67 (*m*, 1 H); 3.51–3.44 (*m*, 2 H); 2.41 (*s*, 3 H); 2.12–2.07 (*m*, 1 H); 1.80–1.63 (*m*, 5 H); 1.43–1.12 (*m*, 6 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 143.0; 137.8; 133.2; 130.2; 130.07; 130.04; 129.4 (2 C); 126.9 (2 C); 69.7, 63.8; 45.6; 34.2; 28.9; 25.2; 23.8; 21.2; 17.8. HR-ES-MS: 372.1595. ($[M+Na]^+$; calc. 372.1604). Anal. calc. for $C_{19}H_{27}NO_3S$: C 65.30, H 7.79; found: C 65.40, H 7.94.

Compound **16a**. A soln. of **21** (0.50 g, 1.3 mmol) in anh. DMF (10 ml) was treated portionwise with NaH (0.1 g of 60% mixture in oil, 2.6 mmol) at 0°, and stirred at 0° prior to the addition of allyl bromide (0.24 g, 2.0 mmol) along with a catalytic amount of Bu_4NI. The resulting mixture was stirred at 0° for 1 h and at r.t. overnight, carefully quenched with H_2O (30 ml), and diluted with Et_2O (30 ml). The aq. layer was extracted with Et_2O, the combined org. layer was washed with H_2O, dried, and evaporated. The residue was purified by CC (SiO_2; petroleum ether/Et_2O 5:1): 0.38 g (75%) of **16a**. Yellowish oil. IR (neat): 1450, 1334, 1152. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.75 (*d*, *J* = 8.3, 2 H); 7.25 (*d*, *J* = 8.3, 2 H); 6.09–5.91 (*m*, 2 H); 5.68–5.57 (*m*, 2 H); 5.53–5.45 (*m*, 1 H); 5.13–5.02 (*m*, 2 H); 4.02–3.96 (*m*, 1 H); 3.95–3.66 (*m*, 4 H); 3.33–3.29 (*m*, 1 H); 2.39 (*s*, 3 H); 2.19–2.15 (*m*, 1 H); 1.86–1.56 (*m*, 7 H); 1.29–1.12 (*m*, 3 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 142.2; 138.8; 135.1; 132.1; 130.5; 129.5; 128.9 (2 C); 128.1; 127.5 (2 C); 115.9; 77.4; 68.9; 62.2; 46.5; 31.9; 31.3; 25.4; 23.9; 21.3; 17.9; HR-ES-MS: 412.1895 ($[M+Na]^+$; calc. 412.1917).

Compound **16b**. Yellowish oil; 74% yield. IR (neat): 1334, 1153. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.75 (*d*, *J* = 8.3, 2 H); 7.27–7.20 (*m*, 2 H); 6.09–5.92 (*m*, 2 H); 5.79–5.62 (*m*, 2 H); 5.54–5.44 (*m*, 1 H); 4.99–4.94 (*m*, 2 H); 3.94–3.62 (*m*, 3 H); 3.52–3.45 (*m*, 1 H); 3.23–3.16 (*m*, 1 H); 3.11–3.04 (*m*, 1 H); 2.39 (*s*, 3 H); 2.19–2.17 (*m*, 1 H); 1.95–1.85 (*m*, 3 H); 1.76–1.55 (*m*, 6 H); 1.41–1.07 (*m*, 5 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 142.2; 138.8; 138.2; 132.1; 130.5; 129.4; 128.9 (2 C); 128.2; 127.4 (2 C); 114.3; 77.3; 67.0; 62.3; 46.2; 32.4; 31.2; 30.1; 28.9; 25.4; 23.9; 21.4; 17.9. HR-ES-MS: 440.2205 ($[M+Na]^+$; calc. 440.2229). Anal. calc. for $C_{24}H_{35}NO_3S$: C 69.03, H 8.45; found: C 68.79, H 8.55.

Compound **16c**. Yellowish oil; 61% yield. IR (neat): 1450, 1335, 1153. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.76–7.72 (*m*, 2 H); 7.27–7.19 (*m*, 2 H); 6.09–5.91 (*m*, 2 H); 5.82–5.71 (*m*, 1 H); 5.68–5.61 (*m*, 1 H); 5.53–5.46 (*m*, 1 H); 5.03–4.93 (*m*, 2 H); 3.92–3.63 (*m*, 3 H); 3.49–3.44 (*m*, 1 H); 3.23–3.19 (*m*, 1 H); 3.08–3.03 (*m*, 1 H);

2.39 (*s*, 3 H); 2.19–2.18 (*m*, 1 H); 2.17–1.95 (*m*, 2 H); 1.89–1.84 (*m*, 1 H); 1.75–1.55 (*m*, 7 H); 1.33–1.07 (*m*, 6 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 142.2; 138.9; 138.7; 132.1; 130.6; 129.5; 128.9 (2 C); 128.3; 127.5 (2 C); 114.4; 77.4; 67.7; 62.4; 46.4; 33.5; 32.4; 31.3; 29.4; 25.43; 25.40; 24.1; 21.4; 18.0. HR-ES-MS: 454.2418 ($[M+Na]^+$; calc. 454.2386). Anal. calc. for $C_{25}H_{37}NO_3S$: C 69.57, H 8.64; found: C 69.51, H 8.68.

Compound **16d**. Yellowish oil; 51% yield. IR (neat): 1451, 1334. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.75 (*d*, J = 8.3, 2 H); 7.22 (*d*, J = 8.3 Hz, 2 H); 6.09–5.91 (*m*, 2 H); 5.85–5.74 (*m*, 1 H); 5.68–5.61 (*m*, 1 H); 5.54–5.46 (*m*, 1 H); 5.03–4.93 (*m*, 2 H); 3.90–3.64 (*m*, 3 H); 3.49–3.44 (*m*, 1 H); 3.21–3.19 (*m*, 1 H); 3.09–3.01 (*m*, 1 H); 2.39 (*s*, 3 H); 2.19–2.17 (*m*, 1 H); 2.05–1.98 (*m*, 2 H); 1.89–1.85 (*m*, 1 H); 1.76–1.55 (*m*, 7 H); 1.35–1.07 (*m*, 8 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 142.1; 138.9; 138.8; 132.1; 130.6; 129.4; 128.9 (2 C); 128.3; 127.5 (2 C); 114.2; 77.4; 67.8; 62.3; 46.3; 33.6; 32.4; 31.2; 29.8; 28.7; 25.6; 25.4; 24.0; 21.4; 18.0. HR-ES-MS: 468.2549 ($[M+Na]^+$; calc. 468.2543). Anal. calc. for $C_{26}H_{39}NO_3S$: C 70.07, H 8.82; found: C 70.25, H 8.89.

Compound **16e**. Yellowish oil; 45% yield. IR (neat): 1450, 1335. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.75–7.72 (*m*, 2 H); 7.27–7.18 (*m*, 2 H); 6.08–5.90 (*m*, 2 H); 5.89–5.74 (*m*, 1 H); 5.67–5.59 (*m*, 1 H); 5.52–5.45 (*m*, 1 H); 5.03–4.91 (*m*, 2 H); 3.91–3.63 (*m*, 3 H); 3.47–3.42 (*m*, 1 H); 3.21–3.18 (*m*, 1 H); 3.05–2.99 (*m*, 1 H); 2.38 (*s*, 3 H); 2.18–2.16 (*m*, 1 H); 2.07–1.99 (*m*, 2 H); 1.87–1.83 (*m*, 1 H); 1.78–1.54 (*m*, 7 H); 1.37–1.06 (*m*, 10 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 142.1; 138.92; 138.90; 132.1; 130.6; 129.4; 128.9 (2 C); 128.3; 127.5 (2 C); 114.2; 77.4; 67.8; 62.3; 46.3; 33.7; 32.4; 31.2; 29.9; 28.9; 28.8; 25.9; 25.4; 24.0; 21.3; 18.0. HR-ES-MS: 482.2680 ($[M+Na]^+$; calc. 482.2699). Anal. calc. for $C_{27}H_{41}NO_3S$: C 70.55, H 8.99; found: C 70.41, H 9.01.

Compound **16f**. Yellowish oil: 48% yield. IR (neat): 1463, 1336. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.76–7.73 (*m*, 2 H); 7.27–7.20 (*m*, 2 H); 6.09–5.91 (*m*, 2 H); 5.86–5.75 (*m*, 1 H); 5.68–5.61 (*m*, 1 H); 5.53–5.46 (*m*, 1 H); 5.04–4.92 (*m*, 2 H); 3.92–3.63 (*m*, 3 H); 3.49–3.43 (*m*, 1 H); 3.20–3.19 (*m*, 1 H); 3.06–3.01 (*m*, 1 H); 2.39 (*s*, 3 H); 2.19–2.18 (*m*, 1 H); 2.09–2.01 (*m*, 2 H); 1.89–1.85 (*m*, 1 H); 1.75–1.55 (*m*, 7 H); 1.45–1.07 (*m*, 12 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 142.2; 139.0; 138.9; 132.1; 130.6; 129.5; 129.0 (2 C); 128.4; 127.6 (2 C); 114.2; 77.4; 67.9; 62.4; 46.4; 33.7; 32.5; 31.3; 30.0; 29.4; 29.1; 28.9; 26.1; 25.5; 24.1; 21.4; 18.0. HR-ES-MS: 496.2848 ($[M+Na]^+$; calc. 496.2856). Anal. calc. for $C_{28}H_{43}NO_3S$: C 70.99, H 9.15; found: C 71.00, H 9.26.

Compound **16g**. Yellowish oil; 52% yield. IR (neat): 1460, 1336. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.76–7.73 (*m*, 2 H); 7.27–7.19 (*m*, 2 H); 6.09–5.91 (*m*, 2 H); 5.89–5.75 (*m*, 1 H); 5.68–5.61 (*m*, 1 H); 5.54–5.47 (*m*, 1 H); 5.04–4.92 (*m*, 2 H); 3.91–3.67 (*m*, 3 H); 3.48–3.43 (*m*, 1 H); 3.21–3.19 (*m*, 1 H); 3.06–3.01 (*m*, 1 H); 2.39 (*s*, 3 H); 2.18–2.17 (*m*, 1 H); 2.09–2.02 (*m*, 2 H); 1.95–1.80 (*m*, 1 H); 1.74–1.56 (*m*, 7 H); 1.44–1.07 (*m*, 14 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 142.2; 139.1; 139.0; 132.1; 130.6; 129.5; 129.0 (2 C); 128.4; 127.6 (2 C); 114.1; 77.5; 67.9; 62.4; 46.4; 33.8; 32.5; 31.3; 30.0; 29.48; 29.45; 29.1; 28.9; 26.2; 25.5; 24.1; 21.4; 18.0; HR-ES-MS: 510.2999 ($[M+Na]^+$; calc. 510.3012). Anal. calc. for $C_{29}H_{45}NO_3S$: C 71.41, H 9.30; found: C 71.85, H 9.50.

Compound **16h**. Yellowish oil; 54% yield. IR (neat): 1463, 1335. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.78–7.73 (*m*, 2 H); 7.27–7.20 (*m*, 2 H); 6.09–5.91 (*m*, 2 H); 5.87–5.76 (*m*, 1 H); 5.68–5.61 (*m*, 1 H); 5.54–5.47 (*m*, 1 H); 5.04–4.92 (*m*, 2 H); 3.91–3.64 (*m*, 3 H); 3.48–3.43 (*m*, 1 H); 3.21–3.19 (*m*, 1 H); 3.06–3.01 (*m*, 1 H); 2.39 (*s*, 3 H); 2.19–2.17 (*m*, 1 H); 2.08–2.01 (*m*, 2 H); 1.89–1.85 (*m*, 1 H); 1.76–1.55 (*m*, 7 H); 1.42–1.07 (*m*, 16 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 142.1; 139.0; 138.9; 132.1; 130.6; 129.4; 128.9 (2 C); 128.4; 127.5 (2 C); 114.1; 77.6; 67.9; 62.4; 46.5; 33.8; 32.5; 31.3; 30.0; 29.53; 29.51; 29.50; 29.1; 28.9; 26.1; 25.5; 24.1; 21.4; 18.0. HR-ES-MS: 524.3123 ($[M+Na]^+$; calc. 524.3169).

General Ring-Closing-Metathesis Procedure. All reactions were performed at a substrate concentration of 0.003M. The ruthenium catalyst (20 mol-%) was carefully weighed in a dry box and placed in a flame-dried flask inside the dry box. A 0.03M stock soln. of **16** in CH_2Cl_2 was prepared earlier. The remainder of the required solvent volume was added to the catalyst, and the proper volume of the substrate soln. was introduced by syringe pump over 12 h while stirring was maintained at 50°. The mixture was agitated at 50° for an additional 12 h, cooled to r.t., quenched with lead tetraacetate (10 mg, 0.022 mmol), and stirred overnight under N_2. The products were purified by CC. The results are compiled in *Table 1*. The spectroscopic characterizations follow.

Cyclization of **16a**: *Formation of* **22**. White solid. M.p. 91–93°. IR (neat): 1600. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.70 (*d*, J = 8.3, 2 H); 7.23 (*d*, J = 8.1, 2 H); 5.59–5.53 (*m*, 1 H); 5.44–5.35 (*m*, 1 H); 4.41–4.33 (*m*, 2 H); 4.03–3.96 (*m*, 1 H), 3.81–3.65 (*m*, 2 H); 3.41–3.32 (*m*, 1 H); 2.38 (*s*, 3 H); 1.97–1.91 (*m*, 1 H); 1.71–1.56 (*m*, 3 H); 1.42–1.11 (*m*, 4 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 142.5; 138.9; 129.1 (2 C); 128.5; 127.2 (2 C); 126.2; 74.7, 64.7; 62.3; 42.8; 32.7; 28.8; 24.6; 24.3; 21.4. HR-ES-MS: 344.1308 ($[M+Na]^+$; calc. 344.1291).

Cyclization of **16b**: *Formation of* **23**. Colorless gum. IR (neat): 1600. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.76 (*d*, J = 8.3, 2 H); 7.26 (*d*, J = 8.6, 2 H); 7.12–6.98 (*m*, 1 H); 6.24–6.17 (*m*, 1 H); 5.51–5.36 (*m*, 2 H); 4.46–4.39 (*m*, 1 H); 3.92–3.83 (*m*, 1 H); 3.61–3.56 (*m*, 2 H); 2.79–2.66 (*m*, 2 H); 2.40–2.28 (*m*, 5 H); 1.81–0.86 (*m*, 10 H).

^{13}C-NMR (75 MHz, $CDCl_3$): 142.6; 139.1; 129.74; 129.71; 129.3 (2 C); 128.3; 127.2; 123.5; 77.5; 63.6; 61.3; 44.1; 30.5; 29.3; 28.2; 25.1; 24.0; 22.4; 21.4. HR-ES-MS: 398.1766 ($[M+Na]^+$; calc. 398.1759).

Cyclization of **16c**: *Formation of* **24/27**. Colorless gum. IR (neat): 1600. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.82–7.77 (*m*, 2 H); 7.26–7.20 (*m*, 2 H); 5.69–5.62 (*m*, 1 H); 5.44–5.39 (*m*, 1 H); 3.95–3.55 (*m*, 2 H); 3.44–3.39 (*m*, 1 H); 2.40 (*s*, 3 H); 2.19–2.17 (*m*, 1 H); 1.98–1.96 (*m*, 1 H); 1.70–1.09 (*m*, 15 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 142.4; 136.2; 129.2 (2 C); 128.8; 127.3 (2 C); 124.1; 78.3; 68.6; 62.1; 39.7; 31.2; 31.1; 30.8; 27.9; 26.1; 25.1; 24.0; 21.5. HR-ES-MS:186.1758 ($[M+Na]^+$; calc. 386.1760).

Cyclization of **16d**: *Formation of* **28** *and* **31**. Data of **28**: Colorless gum. IR (neat): 1600. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.82–7.78 (*m*, 2 H); 7.29–7.18 (*m*, 2 H); 5.48–5.30 (*m*, 2 H); 4.21–4.15 (*m*, 1 H); 3.75–3.73 (*m*, 1 H); 3.65–3.59 (*m*, 1 H); 3.45–3.38 (*m*, 1 H); 3.10–3.08 (*m*, 1 H); 2.98–2.92 (*m*, 1 H); 2.39 (*s*, 3 H); 2.28–2.26 (*m*, 1 H); 2.09–2.07 (*m*, 1 H); 1.77–1.05 (*m*, 14 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 142.3; 139.5; 131.7; 128.9 (2 C); 128.5; 127.5 (2 C); 78.2; 63.9; 61.9; 44.3; 31.1; 30.9; 30.4; 28.2; 25.1; 24.0; 23.2; 21.4; 19.6. HR-ES-MS: 400.1923 ($[M+Na]^+$; calc. 400.1917).

Data of **31**: Colorless gum. IR (neat): 1600. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.83–7.78 (*m*, 2 H); 7.33–7.21 (*m*, 2 H); 6.65–6.56 (*m*, 1 H); 6.00–5.92 (*m*, 1 H); 5.44–5.33 (*m*, 2 H); 4.09–4.02 (*m*, 1 H); 3.81–3.74 (*m*, 1 H); 3.62–3.55 (*m*, 1 H); 3.20–3.18 (*m*, 1 H); 2.40 (*s*, 3 H); 2.28–2.02 (*m*, 1 H); 1.88–1.17 (*m*, 17 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 142.7; 139.2; 131.2; 129.2; 129.1 (2 C); 128.5; 127.5 (2 C); 125.8; 77.4; 67.2; 62.1; 46.8; 31.4; 29.5; 27.3; 25.8; 24.7; 24.0; 23.7; 23.6; 21.4. HR-ES-MS: 426.2079 ($[M+Na]^+$; calc. 426.2073).

Cyclization of **16e**: *Formation of* **29**. Colorless gum. IR (neat): 1600. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.80–7.75 (*m*, 2 H); 7.27–7.19 (*m*, 2 H); 5.61–5.52 (*m*, 1 H); 5.48–5.39 (*m*, 1 H); 3.85–3.54 (*m*, 3 H); 3.46–3.37 (*m*, 2 H); 2.39 (*s*, 3 H); 2.27–2.19 (*m*, 1 H); 2.03–1.99 (*m*, 2 H); 1.69–1.06 (*m*, 16 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 142.3; 139.5; 132.2; 128.9 (2 C); 127.4; 77.8; 65.8; 58.3; 46.9; 31.7; 30.4; 30.2; 29.8; 28.4; 25.5; 25.0; 24.0; 22.9; 21.4. HR-ES-MS: 414.2070 ($[M+Na]^+$; calc. 414.2073).

Cyclization of **16f**: *Formation of* **30**. Colorless gum. IR (neat): 1600. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.83–7.77 (*m*, 2 H); 7.28–7.21 (*m*, 2 H); 5.54–5.44 (*m*, 2 H); 3.91–3.86 (*m*, 1 H); 3.64–3.55 (*m*, 3 H); 3.28–3.18 (*m*, 2 H); 2.40 (*s*, 3 H); 2.24–2.22 (*m*, 1 H); 2.04–2.02 (*m*, 2 H); 1.71–1.08 (*m*, 17 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 142.3; 139.3; 133.3; 129.1 (2 C); 127.7 (2 C); 127.5; 77.7; 66.6; 62.8; 45.9; 31.8; 30.3; 29.8; 29.6; 28.3; 25.5; 25.4; 25.2; 24.8; 24.1; 21.4. HR-ES-MS: 428.2228 ($[M+Na]^+$; calc. 428.2229).

Cyclization of **16g**: *Formation of* **25** *and* **32**. Data of **25**: Colorless gum. IR (neat): 1600. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.78 (*d*, $J=8.3$, 2 H); 7.21 (*d*, $J=8.1$, 2 H); 5.53–5.46 (*m*, 1 H); 5.34–5.30 (*m*, 1 H); 3.78–3.73 (*m*, 2 H); 3.60–3.45 (*m*, 3 H); 3.23–3.18 (*m*, 1 H); 2.39 (*s*, 3 H); 2.29–2.26 (*m*, 1 H); 2.03–1.84 (*m*, 3 H); 1.73–1.62 (*m*, 3 H); 1.46–1.06 (*m*, 15 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 142.2; 139.7; 132.7; 129.0 (2 C); 127.6 (2 C); 126.0; 77.4; 66.3; 63.8; 47.5; 31.3; 30.2; 29.7; 29.6; 28.3; 26.2; 26.1; 25.5; 25.4; 25.0; 24.4; 24.0; 21.4. HR-ES-MS: 442.2372 ($[M+Na]^+$; calc. 442.2386).

Data of **32**: Colorless gum. IR (neat): 1600. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.82–7.77 (*m*, 2 H); 7.29–7.21 (*m*, 2 H); 5.98–5.86 (*m*, 2 H); 5.56–5.45 (*m*, 2 H); 4.15–4.05 (*m*, 1 H); 3.67–3.57 (*m*, 1 H); 3.51–3.44 (*m*, 1 H); 3.28–3.23 (*m*, 1 H); 3.01–2.98 (*m*, 1 H); 2.41 (*s*, 3 H); 2.38–2.09 (*m*, 3 H); 1.75–1.09 (*m*, 20 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 142.3; 139.5; 132.8; 131.1; 131.0; 129.1 (2 C); 127.7 (2 C); 127.6; 77.6; 68.4; 62.5; 47.4; 31.9; 30.6; 30.2; 29.6; 27.7; 27.4; 26.3; 25.7; 25.5; 24.6; 24.0; 21.5. HR-ES-MS: 468.2549 ($[M+Na]^+$; calc. 468.2543).

Cyclization of **16h**: *Formation of* **26** *and* **33**. Data of **26**: Colorless gum. IR (neat): 1600. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.79–7.74 (*m*, 2 H); 7.24–7.19 (*m*, 2 H); 5.61–5.52 (*m*, 1 H); 5.25–5.16 (*m*, 1 H); 3.99–3.73 (*m*, 1 H); 3.73–3.56 (*m*, 2 H); 3.30–3.29 (*m*, 1 H); 3.08–3.02 (*m*, 1 H); 2.38 (*s*, 3 H); 2.27–2.21 (*m*, 1 H); 1.92–1.81 (*m*, 2 H); 1.73–1.55 (*m*, 3 H); 1.44–1.15 (*m*, 19 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 142.1; 139.8; 133.1; 128.9 (2 C); 127.8; 126.2 (2 C); 77.9; 67.2; 62.5; 45.9; 31.2; 30.2; 30.0; 28.4; 26.3; 26.1; 26.0; 25.3; 25.0; 24.8; 24.1; 23.3; 21.4. HR-ES-MS: 456.2547 ($[M+Na]^+$; calc. 456.2543).

Data of **33**: Colorless gum. IR (neat): 1600. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.79–7.75 (*m*, 2 H); 7.27–7.19 (*m*, 2 H); 6.06–5.98 (*m*, 1 H); 5.88–5.83 (*m*, 1 H); 5.57–5.47 (*m*, 1 H); 5.46–5.29 (*m*, 1 H); 4.26–4.18 (*m*, 1 H); 3.81–3.72 (*m*, 1 H); 3.61–3.46 (*m*, 2 H); 3.11–3.03 (*m*, 1 H); 2.99–2.92 (*m*, 1 H); 2.38 (*s*, 3 H); 2.21–2.09 (*m*, 3 H); 1.75–1.68 (*m*, 4 H); 1.59–1.08 (*m*, 17 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 142.2; 139.3; 133.6; 131.9; 130.6; 128.9 (2 C); 128.3; 127.7 (2 C); 77.9; 68.5; 61.8; 44.4; 31.3; 30.1; 29.9; 29.1; 27.2; 26.9; 26.3; 25.2; 25.1; 25.09; 24.0; 23.9; 21.4. HR-ES-MS: 482.2706 ($[M+Na]^+$; calc. 482.2699).

Control Experiments. Catalyst **2b** (12.65 mg, 0.015 mmol) was weighed in a dry box, placed in a flame-dried flask, and diluted with CH_2Cl_2 (22.2 ml). A soln. of **31** (30 mg, 0.074 mmol) in CH_2Cl_2 (2.47 ml to give a 0.03M soln.) was introduced to the catalyst soln. *via* a syringe pump over 3 h with stirring and heating of the mixture to 50°. After an additional 21 h under these conditions, the contents were cooled to r.t., quenched with lead

tetraacetate (10 mg, 0.022 mmol), and stirred overnight under N_2. Purification of the residue by CC (SiO_2) gave **28** (20.4 mg, 73%) with no evidence of residual **31**.

Submission of **31** to the action of **1** under identical conditions led to the complete recovery of starting material.

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