Catalytic Ring-Closing Metathesis of Doubly Armed, Bridged Bicyclic Sulfones. Evaluation of Chain Length and Possible Intramolecular SO_2 Group Ligation to the Ruthenium Carbenoid

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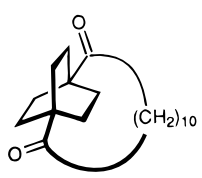
Abstract: Disubstituted bicyclic sulfones **3a**−**3d**, which were prepared by the 2-fold alkylation of 1,6-dilithio-9-thiabicyclo[4.2.1]nonane dioxide, undergo ring-closing metathesis to give a select few of the possible dimers and trimers. Only in the case of **3d** were monomeric end products formed. The pronounced diastereoselectivities observed, particularly with the two lowest homologues, are suggested to be kinetically favored because of the operation of internal ruthenium/sulfonyl oxygen coordination during generation of the first intermolecular double bond. This ligation appears to be an important component of the overall reaction in that it serves to maximize unfavorable nonbonded steric interactions when the sulfone bridges adopt a syn relationship. MM3 calculations indicate the anti sulfone dimers also to be thermodynamically favored when $n = 3$. The preference for the anti sulfone arrangement appears to erode with an increase in the length of the tethers. Not unexpectedly, a ring size dependency is likely at play. The development of a ring-closing metathesis strategy for the incorporation of sulfone groups into stereochemically defined polybicyclic molecules has been realized.

The utilitarian potential of diene ring-closing metathesis (RCM), most particularly for macrocycle synthesis, has attracted the attention of numerous research groups.[1,2] Interest in this catalytic organometallic route to cyclic olefins derives from three features of the methodology: (1) the availability of efficient molybdenum[3] and ruthenium[4] precatalysts having sufficiently well-balanced electronic and coordinative unsaturation to allow convenient use and high-turnover performance; (2) the exceptional tolerance of these initiators to diverse functional groups, including the capacity of the Lewis-acidic metal carbene centers to engage in intramolecular coordination to polar substituents in order to maximize proper orientation of the reacting centers;[5] and (3) one's ability to profit from the gain in entropy that drives the macrocyclization by ensuring that ethylene is the volatile byproduct.

As extensive as studies of the RCM process have been, no attention appears to have been paid to its possible utilization for the construction of unsaturated paddlanes. This class of molecules, originally described by Ginsburg,[6] encompasses a fascinating group of tricyclic compounds in which all four constituent bridges are conjoined to a pair of bridgehead carbon atoms. The paddlanedione **1**[7] and doubly bridged sulfide **2**[8] are



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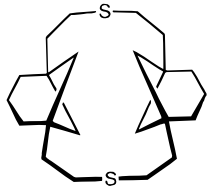

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representative examples.[9] Theoretical contributions by Wiberg[10] and by Schleyer[11] have focused on the fact that reduction in the bridge lengths to extreme limits as in [2.2.2.2]paddlane should induce considerable distortion of the bridgehead carbons toward square-planar geometry. A summary of the experimental

(1) Recent reviews: (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) Fürstner, A. *Top. Catal.* **1997**, *4*, 285. (d) Schuster, M.; Blechert, S. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2037. (e) Armstrong, S. K. *J. Chem. Soc., Perkin Trans. 1* **1998**, 371. (f) Pariya, C.; Jayaprakash, K. N.; Sarkar, A. *Coord. Chem. Rev.* **1998**, *168*, 1. (g) Randall, M. L.; Snapper, M. L. *J. Mol. Catal. A: Chem.* **1998**, *133*, 29. (h) Grubbs, R. H.; Chang, S. *Tetrahedron* **1998**, *54*, 4413. (i) Ivin, K. J. *J. Mol. Catal. A: Chem* **1998**, *133*, 1. (j) Wright, D. L. *Curr. Org. Chem.* **1999**, *3*, 211.

(2) *Alkene Metathesis in Organic Synthesis*; Fürstner, A., Ed.; Springer: Berlin, 1998.

(3) Schrock, R. R.; Murdzek, J. S.; Bazan, G. C.; Robbins, J.; DiMare, M.; O'Regan, M. *J. Am. Chem. Soc.* **1990**, *112*, 3875.

(4) (a) Nguyen, S. T.; Johnson, L. K.; Grubbs, R. H. *J. Am. Chem. Soc.* **1992**, *114*, 3974. (b) Schwab, P.; France, M. B.; Ziller, J. W.; Grubbs, R. H. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2039.

(5) (a) Fürstner, A.; Langemann, K. *J. Org. Chem.* **1996**, *61*, 3942. (b) Fürstner, A.; Langemann, K. *Synthesis* **1997**, 792. (c) Fürstner, A.; Müller, T. *Synlett* **1997**, 1010. (d) Fürstner, A.; Langemann, K. *J. Am. Chem. Soc.* **1997**, *119*, 9130. (e) Fürstner, A.; Müller, T. *J. Org. Chem.* **1998**, *63*, 424. (f) Fürstner, A.; Seidel, G.; Kindler, N. *Tetrahedron* **1999**, *55*, 8215. (g) Hoye, T. R.; Zhao, H. *Org. Lett.* **1999**, *1*, 1123.

(6) Hahn, E. H.; Bohm, H.; Ginsburg, D. *Tetrahedron Lett.* **1973**, 507.

(7) Eaton, P. E.; Leipzig, B. D. *J. Am. Chem. Soc.* **1983**, *105*, 1656.

(8) Warner, P.; Chen, B.-L.; Bronski, C. A.; Karcher, B. A.; Jacobson, R. A. *Tetrahedron Lett.* **1981**, *22*, 375.

(9) Additional selected examples: (a) Allen C. F. H.; Van Allan, J. A. *J. Org. Chem.* **1953**, *18*, 882. (b) Mori, T.; Kimoto, K.; Kawanisi, M.; Nozaki, H. *Tetrahedron Lett.* **1969**, 3653. (c) Thornber, C. W. *Chem. Commun.* **1973**, 238. (d) Helder, R.; Wynberg, H. *Tetrahedron Lett.* **1973**, 4321. (e) Vögtle, F.; Koo Tze Mew, P. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 60. (f) Wiberg, K. B.; O'Donnell, M. J. *J. Am. Chem. Soc.* **1979**, *101*, 6660. (g) Tobe, Y.; Fujita, H.; Wakaki, I.; Terashima, K.; Kobiro, K.; Kakiuchi, K.; Odaira, Y. *J. Chem. Soc., Perkin Trans. 1* **1984**, 2681. (h) Li, Y. Q.; Thiemann, T.; Mimura, K.; Sawada, T.; Mataka, S.; Tashiro, M. *Eur. J. Org. Chem.* **1998**, *1841*, 1.

(10) (a) Wiberg, K. B.; Hiatt, J. E.; Burgmaier, G. *Tetrahedron Lett.* **1968**, 5855. (b) Wiberg, K. B. *Tetrahedron Lett.* **1985**, *26*, 5967.

(11) Würthwein, E.-U.; Chandrasekhar, J.; Jemmis, E. D.; Schleyer, P. v. R. *Tetrahedron Lett.* **1981**, *22*, 843.

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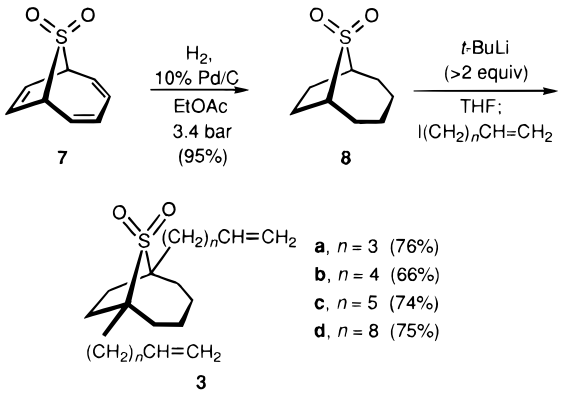
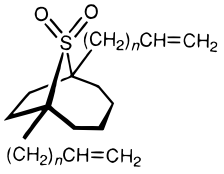
Scheme 1



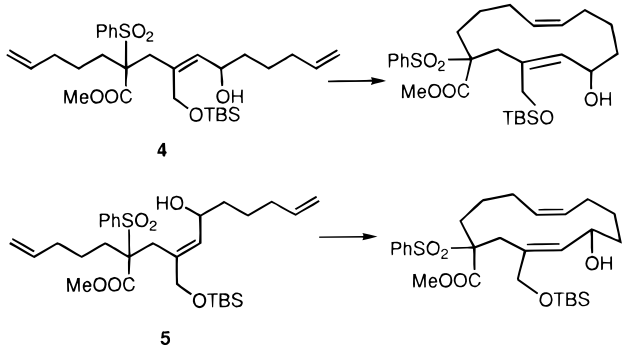
efforts directed toward the possible realization of these angle deformations is available.[12]

The present effort seeks as one of several goals an experimental resolution to the questions of whether the carbons contained in the terminal double bonds of **3** can be brought into effective contact and, if so, the value of *n* at which this can be done. Experimental fact has shown that neither the conformational predisposition of sites of unsaturation in properly designed substrates nor the ring size being generated is of major importance.[5] Seemingly more decisive are the presence of polar "relay" substituents suitably positioned relative to the sites of reaction and minimal steric hindrance close to the double bonds. However, **3** represents an extreme situation where the pair of

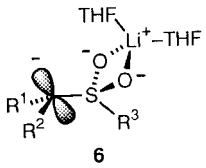


side chains are prominently projected approximately 180° away from each other. Consequently, dienes of type **3** must necessarily be regarded as minimally predisposed toward cyclization.

To render matters workable, it appeared necessary that the sulfone group in **3** exert a key influence as a properly situated center for intramolecular coordination to the ruthenium carbenoid. The cyclization behavior of sulfones **4** and **5** has been



previously described,[13] and unsaturated sulfonamides are well-known to experience RCM with reasonable efficiency.[14] In all of these cases, the sulfone group is not called upon to drive the reaction forward in the manner being considered for **3**. Nevertheless, the ability of sulfones to ligate metal ions in other contexts is well appreciated. For example, the characteristic structural feature of lithiated α-sulfonyl carbanions is the staggered conformation where the lone pair orbital on carbon is gauche to the two oxygens that are engaged in contact ion pairing to the metal ion as in **6**.[15,16] Thus, while there exists the



likelihood that the sulfone functionality in **3** might well be capable of serving as a relay complexing site for ruthenium during metathesis,[17] it is equally unlikely that this coordination would be so stable as to sequester the metal and curtail ring closure. These factors were considered to bode well for ultimate success.

Finally, as will be demonstrated below, this investigation brings to the fore a number of intriguing stereochemical questions that may not be initially apparent because of the meso nature of **3**.

Results

9-Thiabicyclo[4.2.1]nona-2,4,7-triene 9,9-dioxide (**7**) is readily available from the reaction of cyclooctatetraene with SbF_5 in liquid sulfur dioxide below −30 °C.[18,19] Catalytic hydrogenation of **7** over 10% palladium on carbon provided **8**,[20] the bisdeprotonation of which has previously been studied[21] (Scheme 1). Rather unexpectedly, the alkylation of **8** with several ω-alkenyl iodides[22] proved to be highly sensitive to the base employed. The use of *n*-butyllithium invariably led to the generation of unknown contaminants[23] that proved inseparable from **3**. Lithium hexamethyldisilazide gave rise predominantly to the

(12) Agosta, W. C. In *Chemistry of Alkanes and Cycloalkanes*; Patai, S., Rappoport, Z., Eds.: Wiley, Chichester, U.K., 1992; pp 927−962.

(13) Fürstner, A.; Gastner, T.; Weintritt, H. *J. Org. Chem.* **1999**, *64*, 2361.

(14) For example: (a) Paquette, L. A.; Leit, S. M. *J. Am. Chem. Soc.* **1999**, *121*, 8126. (b) Hanson, P. R.; Probst, D. A.; Robinson, R. E.; Yau, M. *Tetrahedron Lett.* **1999**, *40*, 4761. (c) Cerezo, S.; Cortés, J.; Moreno-Mañas, M.; Pleixats, R.; Roglans, A. *Tetrahedron* **1998**, *54*, 14869. (d) Fürstner, A.; Picquet, M.; Bruneau, C.; Dixneuf, P. H. *Chem. Commun.* **1998**, 1315. (e) Visser, M. S.; Heron, N. M.; Didiuk, M. T.; Sagal, J. F.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1996**, *118*, 4291.

(15) (a) Boche, G. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 277 and relevant references therein. (b) Raabe, G.; Gais, H.-J.; Fleischhauer, J. *J. Am. Chem. Soc.* **1996**, *118*, 4622 and earlier reports by the Gais group.

(16) Terrier, F.; Kizilian, E.; Goumont, R.; Faucher, N.; Wakselman, C. *J. Am. Chem. Soc.* **1998**, *120*, 9496.

(17) Examples of complexation to other metal ions: (a) Oppolzer, W.; Mills, R. J.; Pachinger, W.; Stevenson, T. *Helv. Chim. Acta* **1986**, *69*, 1542. (b) Oppolzer, W.; Schneider, P. *Helv. Chim. Acta* **1986**, *69*, 1817. (c) Oppolzer, W. *Pure Appl. Chem.* **1988**, *60*, 39. (d) Oppolzer, W.; Kingma, A. J.; Poli, G. *Tetrahedron* **1989**, *45*, 479. (e) Oppolzer, W.; Tamura, O.; Deerberg, J. *Helv. Chim. Acta* **1992**, *75*, 1965. (f) Wu, M.-J.; Wu, C.-C.; Tseng, T.-C. *J. Org. Chem.* **1994**, *59*, 7188.

(18) Gasteiger, J.; Huisgen, R. *J. Am. Chem. Soc.* **1972**, *94*, 6541.

(19) Paquette, L. A.; Jacobsson, U.; Ley, S. V. *J. Am. Chem. Soc.* **1976**, *98*, 152.

(20) (a) Mock, W. L.; McCausland, J. H. *J. Org. Chem.* **1976**, *41*, 242. (b) Jones, D. N.; Hill, D. R.; Lewton, D. A.; Sheppard, C. *J. Chem. Soc., Perkin Trans. 1* **1977**, 1574.

(21) Paquette, L. A.; Meisinger, R. H.; Gleiter, R. *J. Am. Chem. Soc.* **1973**, *95*, 5414.

(22) Alternative recent applications of these iodides: (a) Bailey, W. F.; Nurumi, T. T.; Patricia, J. J.; Wang, W. *J. Am. Chem. Soc.* **1987**, *109*, 2442. (b) Baldwin, J. E.; Bischoff, L.; Claridge, T. D. W.; Heupel, F. A.; Spring, D. R.; Whitehead, R. C. *Tetrahedron* **1997**, *53*, 2271. (c) Kita, Y.; Sano, A.; Yamaguchi, T.; Oka, M.; Gotanda, K.; Matsuzi, M. *Tetrahedron Lett.* **1997**, *38*, 3549.

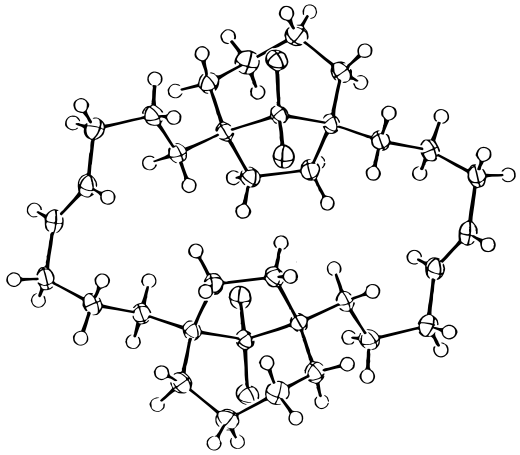
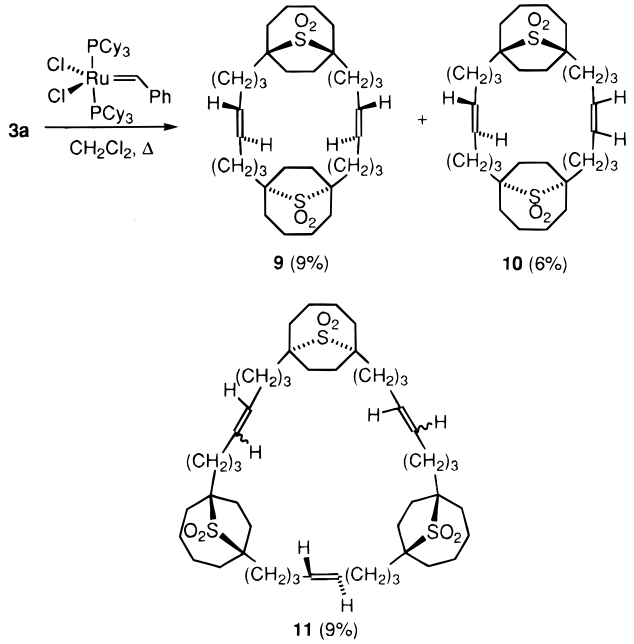


Figure 1. Computer-generated perspective drawing of the final X-ray model of **9**.

Scheme 2



monoalkylation product in low yield. The best conditions uncovered involved the use of more than 2 equiv of *tert*-butyllithium in THF at low temperatures. Under these conditions, the unoptimized yields of **3a**−**3d** ranged from 66 to 76%.

The RCM experiments were initially conducted on **3a**, the smallest member of the homologous series. Under high dilution conditions in the presence of $[RuCl_2(=CHPh)(PCy_3)_2]$, this substrate was transformed at the reflux temperature of CH_2Cl_2 into two dimeric compounds and a trimer in addition to oligomers (Scheme 2). The first of the bis(sulfones) exhibited only eight ^{13}C NMR signals. This inherent symmetry can be accommodated by several structural options. For this reason, recourse was made to X-ray crystallographic analysis, which clearly showed **9** to possess an anti arrangement of its sulfone bridges and trans geometry at the pair of parallel olefinic sites (Figure 1). Definition of the unsymmetrical structural features of **10** was arrived at in a comparable fashion (Figure 2). Although this molecule exhibited some disorder in the crystal, it was possible to corroborate that the alignment of the sulfones is again anti. The possible underlying reasons for the absence

(23) These contaminants exhibited a signal for a teminal CH_3 group in the ^1H NMR spectrum.

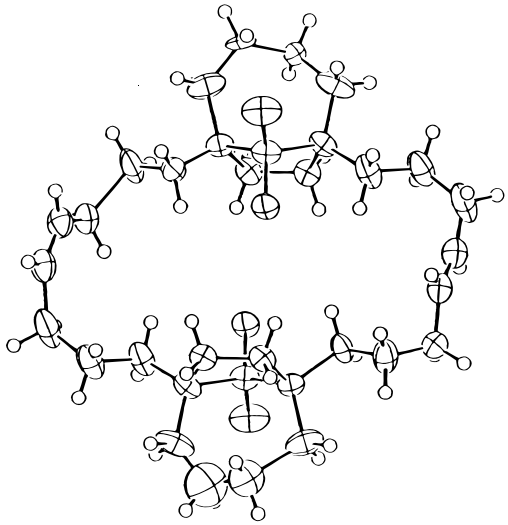
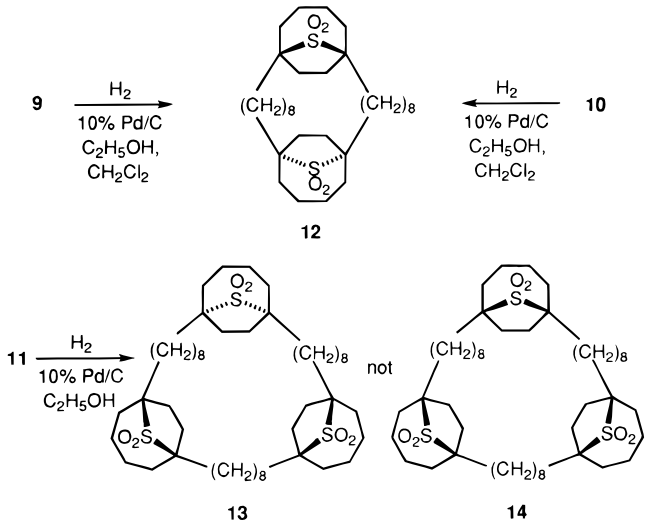


Figure 2. Computer-generated perspective drawing of the final X-ray model of **10**.

Scheme 3

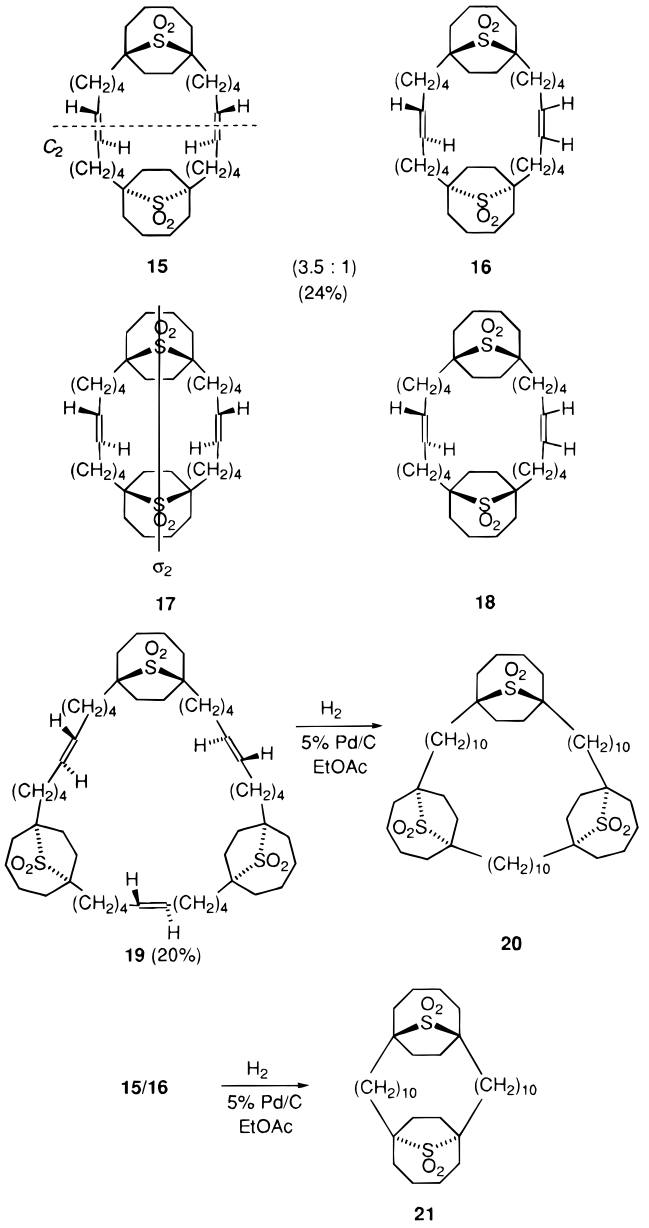


of any detectable syn product will be presented in the sequel. As expected, the catalytic hydrogenation of **9** and **10** led exclusively to the formation of the same saturated dimer **12** (Scheme 3).

Proper determination of the structure of trimeric compound **11** proved difficult at the alkene stage. This complication was shown to be attributable uniquely to double-bond geometry as a result of an exhaustive hydrogenation experiment. At this stage, FAB MS data defined the molecular weight and ^{13}C NMR spectroscopy indicated the saturated trisulfone *not* to be the C_{3v}-symmetric (only eight signals expected) isomer **14**. The end product was therefore **13**, a conformationally flexible, amorphous solid.

When very similar conditions were applied to homologue **3b**, we observed comparable conversion to a pair of dimers (24%) and a trimer (20%) (Scheme 4). The major dimer proved to be symmetrical, a feature compatible with either **15** or **17**. Comparison of the ^{13}C NMR spectrum of this dimer with that of **10** showed them to be essentially superimposable. Although the extent to which the spectrum of **17** might differ from that observed is not known, it would be rather surprising if **3b** differed significantly from **3a** in its reactivity pattern. Consequently, we favor the assignment **15** at the present time. The same arguments prompt us to believe the unsymmetrical dimer

Scheme 4

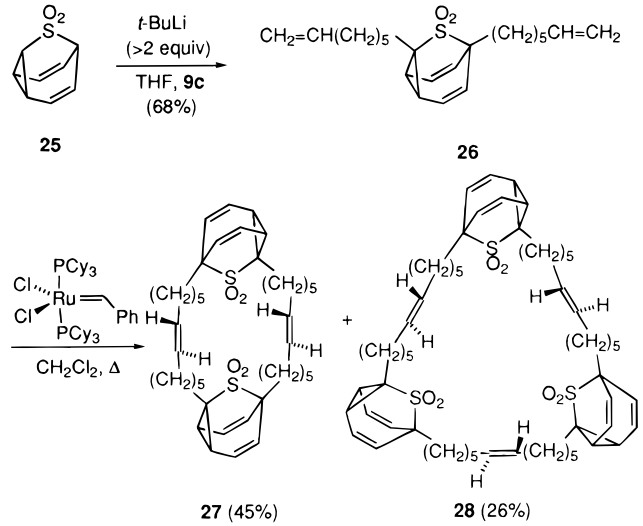


to be **16** and not **18**. A check that catalytic hydrogenation of **15** and **16** led only to **21** was also carried out.

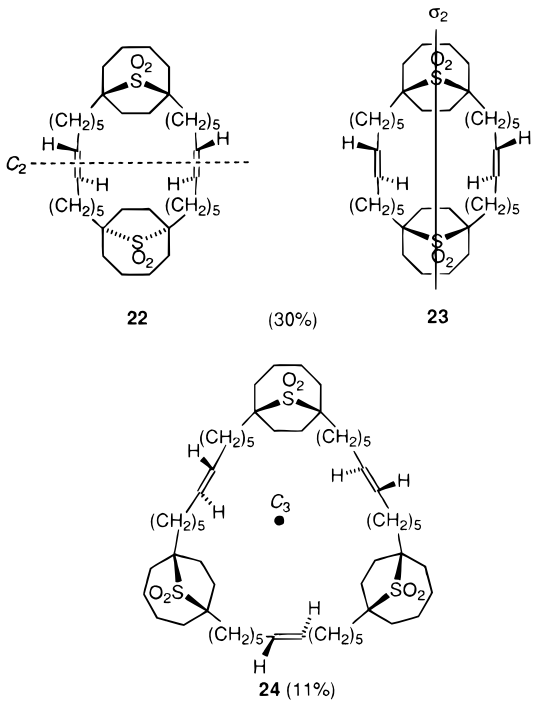
In this instance, the trimer was formed in 20% yield. Its formulation as **19** derives from its nine-line ^{13}C NMR spectrum, which requires that all three double bonds have the same geometry. For the usual steric reasons, the all-cis olefin arrangement can be precluded. The fact that the majority of the carbon signals appear as clusters of multiplets rules out an all-syn orientation for the three sulfone bridges. This important spectral feature is equally apparent once the double bonds are saturated as in **20**.

The harbinger of a possible change in metathesis behavior arose from the self-coupling reaction of **3c** in the presence of the Grubbs catalyst. This experiment resulted in the formation of a lone dimer (30%) and trimer (11%). The high crystallinity of both solids, neither of which could be isolated in a form suited to X-ray structural analysis, made possible their ready purification. The ^{13}C NMR spectrum of each the two products features 10 lines in accord with either the C_2 axially symmetric **22** or C_s planar symmetric depiction **23** of the dimer. The data

Scheme 5



for **24** reflect its C_3 symmetry. To all appearances, the possible *Z* diastereomers of **22**−**24** were not end products of the metathesis process.

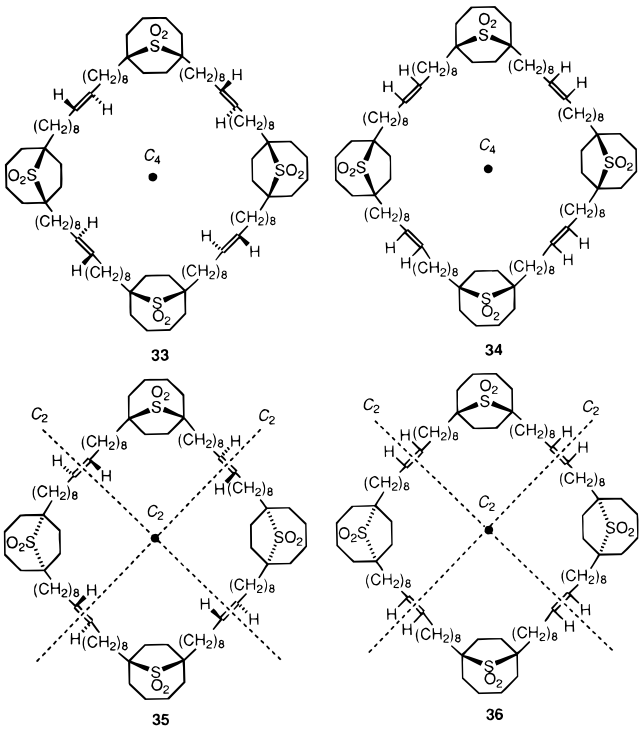


To facilitate rationalization of these findings in terms of a reasonable transition state model, comparison was made directly with sulfone **26** where the distance between the olefinic termini had been meaningfully altered. Rapid Cope rearrangement within the thiabarbaralane substructure provided a means for the rapid symmetrization of the two chains. Like that of **3c**, the formation of any cyclic polyolefin must "encapsulate" space-demanding sulfone groups (Scheme 5). Sulfone **25**, likewise available from the cyclooctatetraene−SO_2 reaction that provides **7**,[18,19] was smoothly dialkylated to give **26**. The parallelism between **26** and **3c** under RCM conditions was as straightforward as originally anticipated. In this instance, dimer **27** and trimer **28** were formed more efficiently in a combined yield exceeding 70%, a likely consequence of the considerably smaller angle between the reacting terminal vinyl groups. No evidence was found for monomer formation via an intramo-

lecular pathway. Particularly noteworthy is the fact that no ROMP/RCM product involving the divinylcyclopropane was isolated; this exclusion can be rationalized by the untoward geometrical features of the hypothetical ruthenium carbenoid−sulfone complexes.

To minimize structural constraints and achieve geometry optimization, the final experiments were conducted in **3d** (Scheme 6). Significantly, the lengths of the pendant chains were now such as to favor the formation of the monomeric paddlanes **29** and **30** to the extent of 25%. The *E*:*Z* ratio was determined to be 6.5:3.5 by ^{13}C NMR analysis.

This ring closure was not so favored as to preclude concomitant transformation into dimer **31** (29%) and trimer **32** (17%). On this occasion, it was not possible to distinguish between the C_s- or C_2-symmetric forms of **31**. A tetramer (8%) was also separated from the mixture during the chromatographic purification process. No attempt was made to distinguish which of the four suitably symmetric candidates from the group **33**−**36** represents the correct structural assignment.

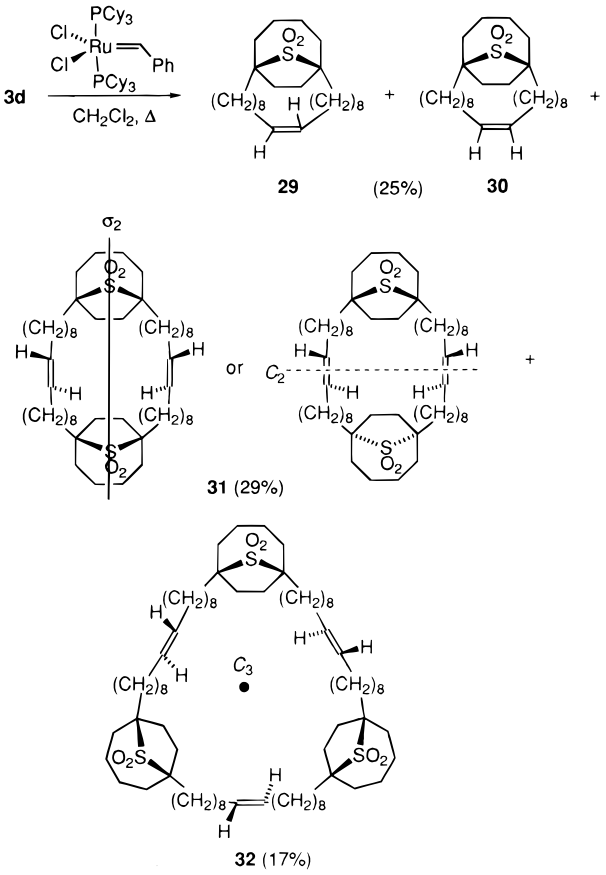


Discussion

The use of bicyclic sulfone **8** as a template offers several avenues for expanding our view of certain features of the ring-closing metathesis process. The readiness with which its dianion can be prepared provides direct entry into the doubly alkylated RCM substrates **3a**−**d**. Since the two chains in **3** have been restricted to being identical in this study, the C_s symmetry of **8** is preserved in all four reactants. In this regard, it matters not which olefin terminus is first transformed into a ruthenium carbenoid. Importantly, diastereomeric discrimination must enter into consideration as reaction proceeds from this point.

A possible working model that accounts for the conversion of **3a** into **9** and **10** is outlined in Scheme 7. Following the formation of **37** with loss of ethylene, two choices are open for coupling to a second molecule of dienyl sulfone reactant. Should the ruthenium atom coordinate in an anti arrangement as defined by **38**, the prevailing steric congestion on the front surface as well as rear side of the complex is minimized. In contrast, the

Scheme 6

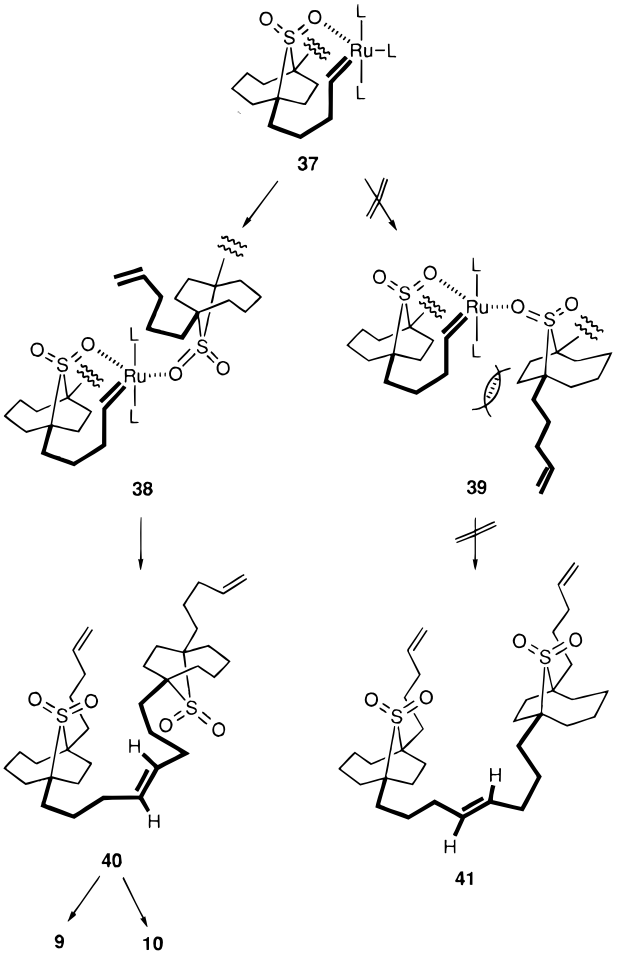


syn sulfone alternative **39** experiences serious nonbonded pairwise compression of all four alkenyl chains. One need recognize that the even more massive tris(cyclohexyl)phosphine ligands, which are reduced to "L" in these illustrations to simplify visualization, further complicate the distinction between **38** and **39**. The likely lowest energy structure is therefore **38**, which leads via **40** to **9** and presumably also **10**. The possibility that a minor amount of the cis isomer of **40** is generated at this stage of the RCM process cannot be ruled out. The *assumed* ligating interactions between sulfonyl oxygens and the ruthenium center serve to confer structural rigidity on the intermediates in question, with further enhancement of product-determining steric discrimination.

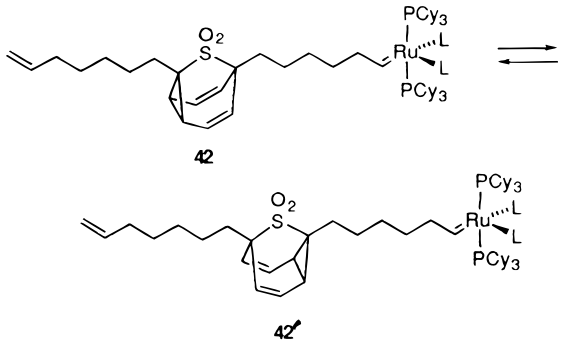
In an attempt to secure spectral evidence for ruthenium−sulfonyl oxygen coordination, the monoalkylated analogue of **3c** was admixed with 1 equiv of the Grubbs catalyst in CD_2Cl_2 and the progress of reaction was monitored by ^{1}H and ^{13}C NMR. Concentrations much higher than those normally utilized were obviously necessary. Although the progressive buildup of styrene was easily recognized, minimal concomitant change in the chemical shifts of the bridgehead proton and bridgehead carbon atoms was seen. Nor were signals attributable to the uncoordinated ruthenium carbenoid visible. Such intermediates appear to be too short-lived under these conditions for direct observation.

As in the preceding examples, there is no unequivocal experimental evidence that **3c** engages in metathesis via a mechanistic pathway that is kinetically controlled in a comparable fashion. However, Fürstner has demonstrated that increased distances between ester linkages and terminal alkene groups result in significantly improved yields.[5b] The implication is that large-ring chelation of ruthenium by the carbonyl oxygen might likewise be accommodated by longer chain lengths. The

Scheme 7



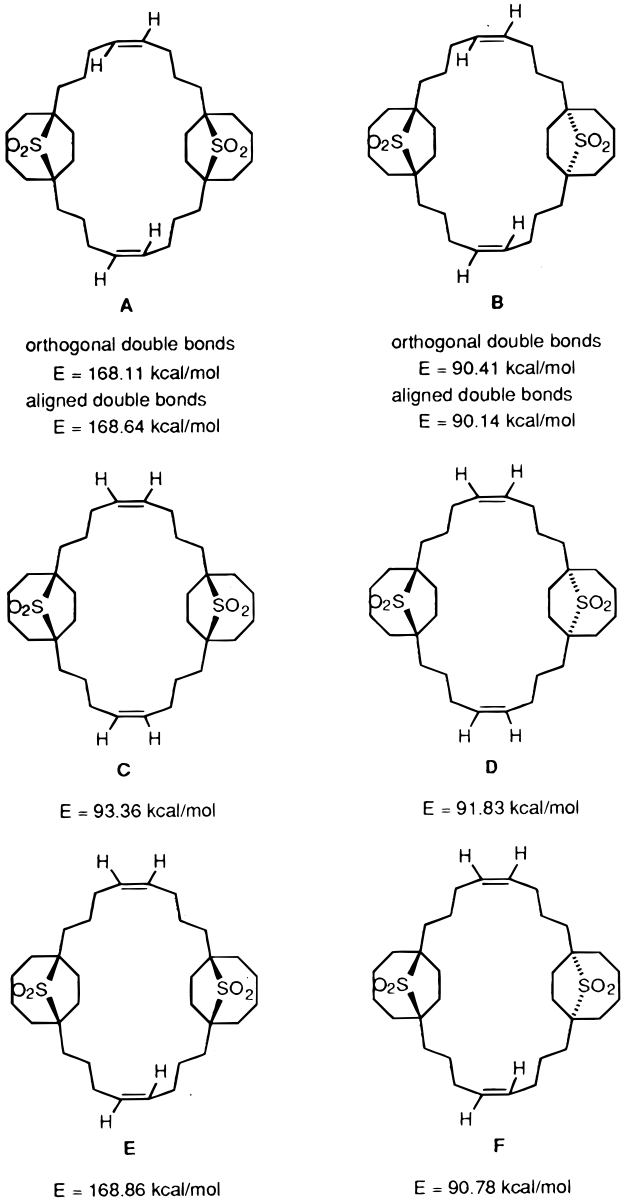
Scheme 8



similarity with which **3c** and **26** are transformed into a single dimer and but one trimer holds interest. It will be recognized that the initially formed ruthenium carbenoid **42** is not capable of generating diastereomerically distinguishable coupling products because of the rapidity of the Cope rearrangement, which results in unbridled interconversion with **42′** (Scheme 8). When these conditions are operative, product formation could result possibly from internal ligation to sulfonyl oxygen in combination with more subtle effects that dictate the partitioning among dimer, tetramer, and (in the case of **3d**) tetramer production. Perhaps relevant to this mechanistic assumption is the absence of products derived from insertion into the divinylcyclopropane substructure, a process that is not geometrically feasible should internal chelation to the sulfone operate.

To the best of our knowledge, the results described herein represent the first examples of the use of RCM methodology for preparing paddlanes. While **28** and **29** constitute the only two monosulfonyl paddlanes obtained by way of this protocol, the structurally unusual dimeric and trimeric sulfones represent macromolecular species worthy of further investigation.

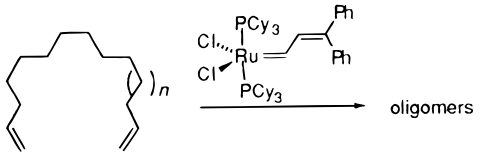
Table 1. Global Minimum Energies of the Six Possible Diastereomers Derivable from the Dimerization Metathesis of **3a** as Determined by MM3 Calculations



While the rationalization presented here has a certain heuristic value for qualitative prediction of the predominant stereoisomers produced upon RCM of the lower analogues **3a** and **3b**, the thermodynamic aspects of the process are not addressed by the model. In particular, it is not clear, a priori, whether certain dimers are intrinsically of lower energy than their isomeric counterparts. Also unclear is the degree to which this might be true. In an effort to probe these relevant issues, we carried out a series of Monte Carlo conformational energy searches with the MM3 force field. The results are summarized in Table 1. The conformers of interest were selected by scanning the local minima and reminimizing those of interest according to the full-matrix Newton−Raphson method in order to ensure that accurate relative energies were found. The lowest energy structure **B** thus obtained was found to correspond to **9**. Only a

fraction of 1 kcal less stable than **B** is **F**, the cis,trans,anti isomer previously characterized as **10**. Since **D** placed in third position, it is clear that the three possible anti-bridged disulfones enjoy a stabilization not resident in the syn diastereomers, with the possible exception of **C**. The very high energy levels displayed by **A** and **E** were not entirely expected and are not completely understood. The relative alignment of the double bonds in **A** and **B** has little impact on the overall energetics.

These computational studies reveal that the kinetically favored dimers produced by **3a** are also the most thermodynamically favored. Does this finding rule out the mechanistic role earlier advanced for internally ligated complexes such as **37**−**39**? Not necessarily so. Were the sulfonyl groups not serving as relays to help assemble the reaction sites, oligomerization would likely materialize. A noteworthy comparison can be made with 1,13-tetradecadiene (**43**) and 1,15-hexadecadiene (**44**), neither of



43, $n = 1$
44, $n = 2$

which gives rise to cyclic monomers to any measurable extent under RCM conditions.[5b] In contrast, the notion that the proper locus of a ligating group is critical for smooth macrocyclization has been demonstrated repeatedly by others. Its effectiveness is due to the consequent lowering of the enthalpic barrier during ring formation. The comparison with **43** and **44** suggests that coordination to the sulfonyl group may actually be pivotal for productive RCM.

Experimental Section

General Procedure for the Dialkylation of 8. A. A cold (−78 °C) solution of **8** (500 mg, 2.97 mmol) was treated with *tert*-butyllithium (5.57 mL of 1.6 N, 8.91 mmol), and the mixture was stirred at this temperature for 40 min. 1-Iodo-4-pentene (1.58 g, 8.06 mmol) in dry THF (5 mL) was introduced, and the reaction mixture was stirred for an additional 1 h at −78 °C and warmed to room temperature for 3 h prior to quenching with saturated NH_4Cl solution (5 mL). The mixture was then diluted with water (50 mL) and extracted with ether (3 × 50 mL). After the combined organic phases had been dried and concentrated, the residue was chromatographed on silica gel (elution with 5% ethyl acetate in hexanes) to give **3a** (594 mg, 59%) as a colorless oil: IR (neat, cm^{-1}) 1643, 1462, 1285, 1123; ^1H NMR (300 MHz, $CDCl_3$) δ 5.85−5.70 (m, 2 H), 5.07−4.90 (m, 4 H), 2.15−1.30 (series of m, 24 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.2, 115.2, 63.9, 36.2, 34.5, 34.2, 31.3, 24.1, 23.4; HRMS (EI) *m*/*z* (M^+) calcd for $C_{18}H_{30}O_2S$ 310.1966, obsd 310.1966.

General Procedure for Ring-Closing Metathesis. To an N_2-blanketed refluxing CH_2Cl_2 solution (500 mL) of the Grubbs catalyst (233 mg, 0.264 mmol, 15 mol %) was added **3a** (546 mg, 1.76 mmol) dissolved in dry CH_2Cl_2 (200 mL) under high-dilution conditions. An additional 15 mol % of the ruthenium complex was added after 10 h. Complete addition of the diene sulfone required 20 h. The reaction mixture was refluxed a further 4 h, concentrated, and chromatographed on silica gel (elution with 20% ethyl acetate in hexanes) to give 45 mg (9%) of **9**, 37 mg (6%) of **10**, and 45 mg (9%) of **11**.

For **9**: colorless crystals, mp 289−291 °C (from CH_2Cl_2−hexanes); IR (neat, cm^{-1}) 1430, 1260, 1100; ^1H NMR (300 MHz, $CDCl_3$) δ 5.42−5.34 (m, 4 H), 2.20−1.35 (series of m, 48 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 130.6, 63.5, 34.9, 34.6, 32.1, 31.2, 24.2, 23.0; HRMS (EI) *m*/*z* (M^+) calcd 564.3307, obsd 564.3298. Anal. Calcd for $C_{32}H_{52}O_4S_2$: C, 68.04; H, 9.28. Found: C, 67.98; H, 9.25.

For **10**: colorless crystals, mp 245−247 °C (from CH_2Cl_2−hexanes); IR (neat, cm^{-1}) 1435, 1260, 1110; ^1H NMR (300 MHz, $CDCl_3$) δ 5.50−5.35 (m, 4 H), 2.30−1.25 (series of m, 48 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 131.0, 130.2, 64.1 (2 C), 36.0, 34.8, 34.3 (2 C), 32.4, 31.3, 31.0, 27.8, 24.9, 24.3, 24.1, 23.9; HRMS (EI) *m*/*z* (M^+) calcd 564.3307, obsd 564.3321. Anal. Calcd for $C_{32}H_{52}O_4S_2$: C, 68.04; H, 9.28. Found: C, 67.63; H, 9.19.

For **11**: colorless oil; IR (neat, cm^{-1}) 1445, 1280, 1105; ^1H NMR (300 MHz, $CDCl_3$) δ 5.45−5.35 (br s, 4 H), 2.15−1.30 (series of m, 72 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 130.7 (m), 63.9 (m), 35.8 (m), 34.4 (m), 32.7 (m), 31.4 (m), 24.2 (m), 23.6 (m); HRMS (EI) *m*/*z* (M^+) molecular ion too fleeting for accurate mass measurement.

Hydrogenation of 9. A solution of **9** (15 mg, 0.027 mmol) in 10:1 ethanol−dichloromethane (2.2 mL) containing 10% palladium on charcoal (20 mg) was placed under an atmosphere of hydrogen (balloon) and stirred at 20 °C for 2 h, followed by filtration and concentration. Chromatography of the residue on silica gel (elution with 20% ethyl acetate in hexanes) gave **12** in quantitative yield (15 mg) as a white solid: mp 243−245 °C; IR (neat, cm^{-1}) 1425, 1250, 1085; ^1H NMR (300 MHz, $CDCl_3$) δ 2.15−1.25 (series of m, 56 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 64.0, 35.0, 34.5, 30.9, 28.1, 26.0, 24.2, 22.2; HRMS (EI) *m*/*z* (M^+SO_2) calcd 504.4001, obsd 504.4020. Anal. Calcd for $C_{32}H_{56}O_4S_2$: C, 67.56; H, 9.92. Found: C, 67.29; H, 10.04.

Hydrogenation of 10. Catalytic reduction of **10** (15 mg) in the predescribed manner afforded 15 mg (100%) of **12**, identical in all respects to the above sample.

Hydrogenation of 11. Catalytic reduction of **11** (40 mg, 0.047 mmol) gave **13** (40 mg, 100%) as a colorless crystalline solid: mp 256−258 °C; IR (neat, cm^{-1}) 1435, 1265, 1105; ^1H NMR (300 MHz, $CDCl_3$) δ 2.10−1.20 (series of m, 84 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 63.8 (s), 36.1 (m), 34.2 (m), 30.9 (m), 29.4 (m), 28.3 (m), 23.9 (m), 23.4(m); FAB MS *m*/*z* ($M^+ + H$) calcd 853.55, obsd 853.57. Anal. Calcd for $C_{48}H_{84}O_6S_3$: C, 67.56; H, 9.92. Found: C, 67.62; H, 10.89.

1,5-Di-6-heptenyl-9-thiatricyclo[3.3.1.0^{2,8}]nona-3,6-diene 9,9-Dioxide (26). To a solution of **25** (275 mg, 1.63 mmol) in dry THF (12 mL) cooled to −78 °C under N_2 was added a solution of *tert*-butyllithium in pentane (2.1 mL of 1.7 M, 3.59 mmol). After 1 h of stirring, 7-iodo-1-heptene (400 mg, 1.78 mmol) was introdued via syringe and the reaction mixture was stirred at −78 °C for 6 h prior to quenching with saturated NH_4Cl solution and extraction with ether. The combined organic phases were dried and concentrated, and the residue was purified by flash chromatography on silica gel (elution with 30% ether in hexanes) to afford **26** (200 mg, 68%) as colorless platelets: mp 63−64 °C; IR (neat, cm^{-1}) 1285; ^1H NMR (300 MHz, $CDCl_3$) δ 5.94−5.71 (m, 4 H), 5.06−4.90 (m, 4 H), 4.27−4.06 (m, 4 H), 2.15−1.84 (m, 8 H), 1.67−1.53 (m, 4 H), 1.49−1.29 (m, 8 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.8, 122.7, 114.4, 79.8, 47.2, 33.5, 29.3, 28.7, 28.5, 24.2; HRMS (EI) *m*/*z* ($M^+ - SO_2$) calcd 296.2504, obsd 296.2483. Anal. Calcd for $C_{22}H_{32}O_2S$: C, 73.29; H, 8.95. Found: C, 73.41; H, 8.83.

Ring-Closing Metathesis of 26. Reaction of **26** (500 mg, 1.38 mmol) with 100 mg (0.11 mmol) of Grubbs catalyst in the predescribed manner afforded 205 mg (45%) of **27** and 140 mg (26%) of **28**.

For **27**: colorless crystals; mp 207−210 °C; IR (neat, cm^{-1}) 1280, 1120; ^1H NMR (300 MHz, $CDCl_3$) δ 5.93−5.83 (m, 4 H), 5.42−5.34 (m, 4 H), 4.27−4.06 (m, 8 H), 2.09−1.88 (series of m, 16 H), 1.68−1.54 (m, 8 H), 1.46−1.30 (series of m, 16 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 130.5, 122.8, 80.0, 47.1, 32.1, 29.2, 29.1, 29.0, 28.8, 28.5, 28.2, 26.6, 24.2, 24.0, 23.8; FAB MS *m*/*z* ($M^+ + H$) calcd 664.36, obsd 664.31. Anal. Calcd for $C_{40}H_{56}O_4S_2$: C, 72.25; H, 8.48. Found: C, 72.39; H, 8.51.

For **28**: colorless crystals; mp 185−187 °C; IR (neat, cm^{-1}) 1285, 1260; ^1H NMR (300 MHz, $CDCl_3$) δ 5.92−5.83 (m, 4 H), 5.39−5.33 (m, 4 H), 4.22−4.13 (m, 8 H), 2.04−1.88 (series of m, 16 H), 1.66−1.54 (m, 8 H), 1.43−1.30 (series of m, 16 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 130.3, 122.7, 79.8, 47.3, 32.1, 29.4, 29.3, 29.1, 29.0, 28.8, 24.2, 24.1; FAB MS *m*/*z* ($M^+ + H$) calcd 966.54, obsd 966.49. Anal. Calcd for $C_{60}H_{84}O_6S_3$: C, 72.25; H, 8.48. Found: C, 72.35; H, 8.48.

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Supporting Information Available: Text presenting experimental details and full spectral data for all new compounds not given in the Experimental Section, the computed lowest energy conformations for **A**−**F**, and tables giving the crystal data and structure refinement information, bond lengths and angles, atomic and hydrogen coordinates, and isotropic and anisotropic displacement coordinates for **9** and **10** (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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