Heteroatomic Effects on the Acid-Catalyzed Rearrangements of Dispiro[4.0.4.4]tetradeca-11,13-dienes

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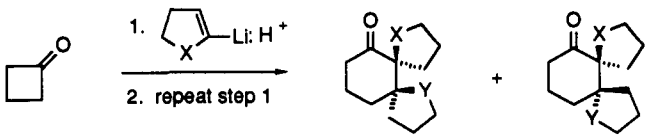
Abstract: The synthesis of dispiro[4.0.4.4]tetradeca-11,13-dienes containing one or two heteroatoms (O,S) is described. In all cases, a suitably functionalized cyclohexanone served as the precursor. Bromination–dehydrobromination delivered the cyclohexenone, which was subjected to 1,2-reduction and elimination by reaction with 2,4-dinitrobenzenesulfenyl chloride and thermal activation. The pathways by which the 1,3-cyclohexadienes undergo acid-catalyzed isomerization have been identified. The choice between aromatization and conversion to a [4.4.4]propelladiene gives evidence for being dependent on an interplay between steric and electronic factors. The generation of a transient oxonium ion causes both pathways to operate at approximately equivalent levels. When a thermodynamically less favorable thionium ion intermediate is involved, selectivity increases to the point where only aromatization occurs in the presence of *p*-toluenesulfonic acid. A neighboring sulfhydryl group is shown to be capable of intercepting the spirocyclic carbocationic intermediate. The regiochemistry of the epoxidation of **30** and the stereoselectivity of Diels–Alder cycloaddition of the [4.4.4]propelladienes to *N*-methyltriazolinedione are also detailed.

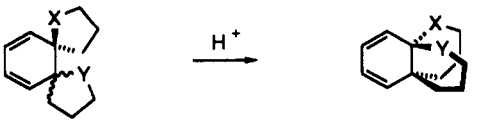
Oxonium ion-activated pinacol rearrangements[2] have established themselves as synthetically useful reactions,[3] particularly when utilized in a reiterative mode.[4] We have reported, inter alia, that twofold addition of 5-lithio-2,3-dihydrofuran and -thiophene[5] to cyclobutanone constitutes a highly efficient synthetic entry to *cis*- (**1**) and *trans*-hetero-2,3-dispirocyclohexanones (**2**). Heterocyclic compounds of this general type have



1 **2**

been scrutinized to determine their preferred conformation.[4d] Once resolved, these ketones undergo acid-catalyzed epimerization and racemization, thereby establishing their ease of fragmentation to tethered onium ion–enol pairs and the ready recombination of these achiral intermediates.[4d]

As part of a program designed to develop our base of knowledge surrounding polyspirocyclic heteroatomic systems, the cyclohexadienes corresponding to **1** and **2** have now been prepared. First to be surveyed was the response of cyclic conjugated olefins of type **3** to acid-catalyzed rearrangement.[6] In the course of this study, the discovery has been made that conversion to a previously unknown type of [4.4.4]propelladiene, *viz.*, **4**, can be achieved from either isomer of **3**. An aromatization pathway also operates,



3 **4**

and this paper details the mechanistic basis of these carbocationic processes as well as the role played by oxygen and sulfur atoms in channeling the possible competitive reaction alternatives.

Results

Preparation of the Spirocyclic Dienes. Although the major focus of this study was a detailed examination of the manner in which dihetero-substituted systems respond to acid-catalyzed rearrangement, an important reference point involved the presence of a lone oxygen atom in the spirocyclic network. Ketone **5**, previously described by Krieger et al.,[7] has provided the means for the direct acquisition of **11** starting from cyclopentanone (Scheme 1). Condensation of **5** with the cerate derived from 5-lithio-2,3-dihydrofuran[4d] was necessary in order to curtail in a significant way the tendency of this ketone to undergo enolization.[8] The resulting carbinol proved quite amenable to ring expansion simply upon being stirred with Dowex-50 ion-exchange resin in CH_2Cl_2 at room temperature. This process led to the isolation of **6** in 91% yield.

When the monobromination of **6** with pyridinium hydrotribromide in THF at 0 °C was found to give a 4.75:1 distribution of α-bromo stereoisomers, curiosity as to the preferred direction of electrophilic capture prompted the chromatographic separation of **7** from **8** and submission of the minor diastereomer to X-ray crystallographic analysis. Two important issues emerge from the ORTEP diagram of **8** depicted in Figure 1. The more obvious is the cis relative stereochemistry of the bromine and oxygen substituents. This observed product distribution reveals that the more reactive enol conformation of **6** must be **A**, with axial attack

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(1) Procter and Gamble Graduate Fellow, 1993.

(2) Paquette, L. A.; Lawhorn, D. E.; Teleha, C. A. *Heterocycles* **1990**, *30*, 765.

(3) (a) Paquette, L. A.; Lord, M. D.; Negri, J. T. *Tetrahedron Lett.* **1993**, *34*, 5693. (b) Paquette, L. A.; Dullweber, U.; Cowgill, L. D. *Tetrahedron Lett.* **1993**, *34*, 8019.

(4) (a) Negri, J. T.; Rogers, R. D.; Paquette, L. A. *J. Am. Chem. Soc.* **1991**, *113*, 5073. (b) Paquette, L. A.; Negri, J. T.; Rogers, R. D. *J. Org. Chem.* **1992**, *57*, 3947. (c) Paquette, L. A.; Andrews, J. F. P.; Vanucci, C.; Lawhorn, D. E.; Negri, J. T.; Rogers, R. D. *J. Org. Chem.* **1992**, *57*, 3956. (d) Paquette, L. A.; Branan, B. M.; Friedrich, D.; Edmondson, S. D.; Rogers, R. D. *J. Am. Chem. Soc.* **1994**, *116*, 506.

(5) Paquette, L. A.; Dullweber, U.; Branan, B. M. *Heterocycles* **1994**, *37*, 187.

(6) The subject dienes are also prone to isomerization in the presence of TCNE: Paquette, L. A.; Branan, B. M. *Heterocycles*, in press.

(7) Krieger, H.; Routsalainen, H.; Montin, J. *Chem. Ber.* **1966**, *99*, 3715.

(8) (a) Imamoto, T.; Takiyama, N.; Nakamura, K.; Hatajima, T.; Kamiya, Y. *J. Am. Chem. Soc.* **1989**, *111*, 4392. (b) Paquette, L. A.; He, W.; Rogers, R. D. *J. Org. Chem.* **1989**, *54*, 2291 and relevant references cited therein.

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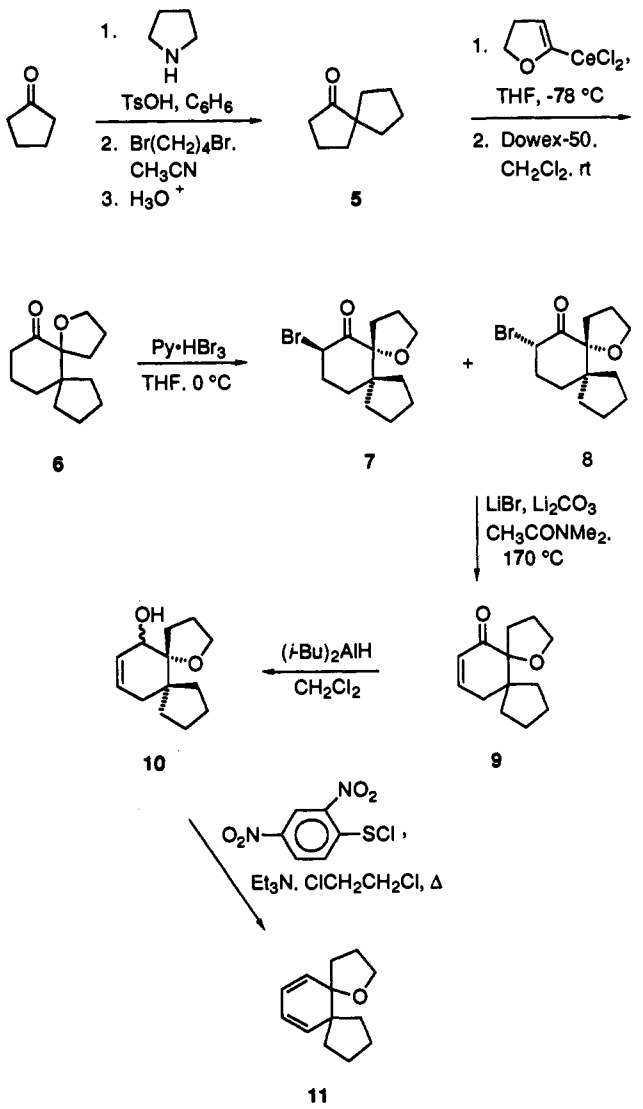
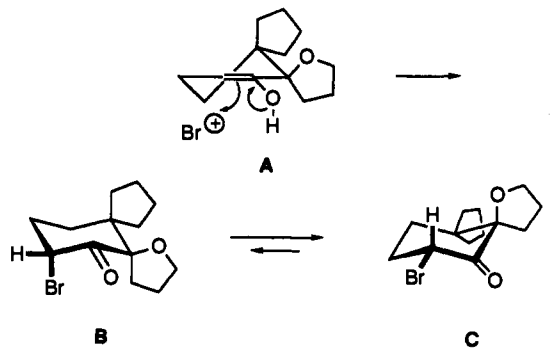
Scheme 1



by the positive bromine source occurring on the face of the six-membered ring opposite that occupied by the equatorially disposed ether oxygen. Once **B** is produced, conformational chair-to-chair interconversion can occur to deliver **C**. Since 2-bromo- and



2-methoxycyclohexanones prefer to exist as the axial conformers and to appreciable levels (85%[9] and 63%,[10] respectively), conformation **B** may well be favored for the trans isomer except for the 1,3-diaxial Br/CH_2 interaction present therein. A referee has, in fact, indicated to us that MMX shows **C** to be more stable

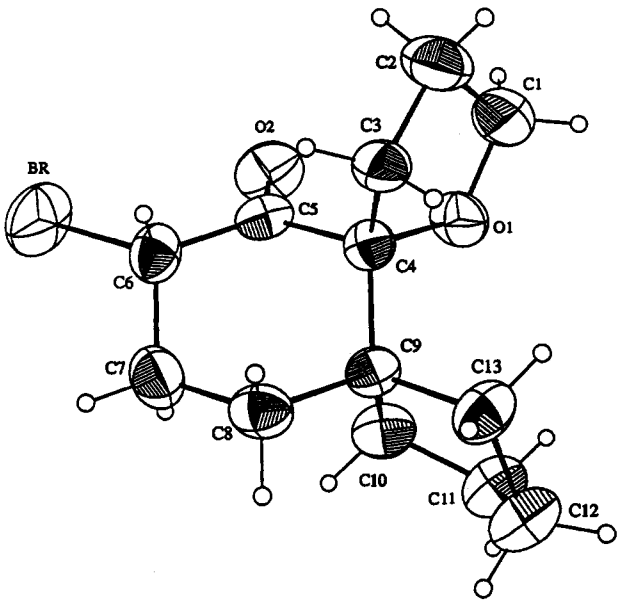


Figure 1. Computer-generated perspective drawing of **8** as determined by X-ray crystallography.

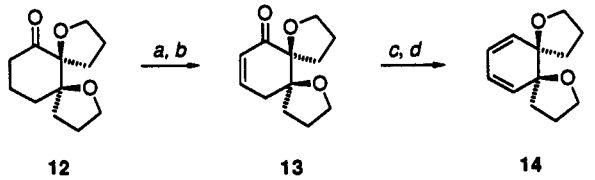
than **B** by 3.4 kcal/mol. The geometry adopted by *cis*-**8** in the crystalline state projects both the bromine and oxygen atoms equatorially (see Figure 1). This particular bias would appear to be sterically driven.[4b]

In the ensuing dehydrobrominations, both stereoisomers gave evidence of reacting equally well. These substrates delivered **9** in good yield upon being heated with lithium bromide and lithium carbonate in dimethylacetamide (DMA) at 170 °C for the purpose of introducing the conjugated double bond. Reduction of **9** with diisobutylaluminum hydride in CH_2Cl_2 proceeded to give an inseparable 2.3:1 mixture of allylic alcohols **10**. Subsequent treatment of this mixture with 2,4-dinitrobenzenesulfenyl chloride and triethylamine in refluxing 1,2-dichloroethane[11] provided **11** in 57% yield. In view of the established sensitivity of this sigmatropic rearrangement–elimination sequence to steric effects,[12] it is highly probable that **11** is produced with rather different efficiencies from its two stereoisomeric precursors. The structural assignment to **11** rests securely on its 300-MHz ^1H NMR spectrum which consists, inter alia, of two vinyl proton multiplets each of area 2 at δ 5.80–5.72 and 5.70–5.61, a pair of protons α to the ether oxygen which are well separated (δ 3.77–3.70 and 3.67–3.60) as a consequence of their appreciable chemical nonequivalence, and two protons from the adjoining cyclopentane ring (δ 2.47–2.37 and 2.03–1.92) which are strongly differentiated by virtue of their divergent spatial relationships relative to the magnetic anisotropies generated by the oxygen center and diene π network.

A comparable sequence has proven effective in gaining access to the dioxa dienes **14** and **17** (Scheme 2). The only significant change was recourse to the Luche procedure[13] for effecting the 1,2-reduction of **13** and **16**. This process does not bring the diastereofacial aspects of allylic alcohol production under control but greatly facilitates workup. Notably, **13** and **16** respond quite differently toward the $NaBH_4$–$CeCl_3$ complex. In the syn dioxa example, the two carbinols are produced in a 6.8:1 ratio. When the oxygen atoms are disposed trans, a closer correspondence is seen between the two isomers (1.4:1). No effort was expended to ascertain the relative stereochemistry either of these alcohols or of their α-bromo ketone precursors.

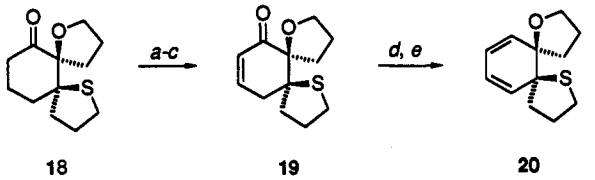
(9) Bingham, R. C. *J. Am. Chem. Soc.* **1976**, *98*, 535.
(10) Lambert, J. B. In *The Conformational Analysis of Cyclohexenes, Cyclohexadienes, and Related Hydroaromatic Compounds*; Rabideau, P., Ed.; VCH: Weinheim, Germany, 1989; Chapter 2.
(11) (a) Reich, H. J.; Wollowitz, S. *J. Am. Chem. Soc.* **1982**, *104*, 7051. (b) Wang, T.-Z.; Paquette, L. A. *J. Org. Chem.* **1986**, *51*, 5232.
(12) (a) Wang, T.-Z.; Paquette, L. A. *Tetrahedron Lett.* **1988**, *29*, 41. (b) Paquette, L. A.; Wang, T.-Z.; Luo, J.; Cottrell, C. E.; Clough, A. E.; Anderson, L. B. *J. Am. Chem. Soc.* **1990**, *112*, 239.
(13) Gemal, A. L.; Luche, J.-L. *J. Am. Chem. Soc.* **1981**, *103*, 5454.

Scheme 2



[a] Py·HBr$_3$, THF. [b] LiBr, Li_2CO_3, DMA, reflux. [c] $NaBH_4$, $CeCl_3 \cdot 7H_2O$. [d] 2,4-$(NO_2)_2C_6H_3SCl$, Et_3N, $ClCH_2CH_2Cl$, reflux.

Scheme 3



[a] LDA, THF; Me_3SiCl, Et_3N. [b] NBS, propylene oxide, THF. [c] LiBr, Li_2CO_3, DMA, reflux. [d] $NaBH_4$, $CeCl_3 \cdot 7H_2O$, CH_3OH. [e] 2,4-$(NO_2)_2$-C_6H_3SCl, Et_3N, $ClCH_2CH_2Cl$, reflux.

The route followed in Schemes 1 and 2 is not viable for the production of sulfide congeners of **14** and **17** because of the reactivity of divalent sulfur toward electrophilic brominating agents such as Py·HBr$_3$. For this reason, arrival at the oxathia dienes **20** and **23** required that ketones **18** and **21** be converted into enones **19** and **22** by the initial action of *N*-bromosuccinimide on the respective trimethylsilyl enol ethers[14] under conditions where propylene oxide served as a buffer. These conditions gave the α-bromo derivatives of **18** and **21** in 94% and 99% yield, respectively (Scheme 3).

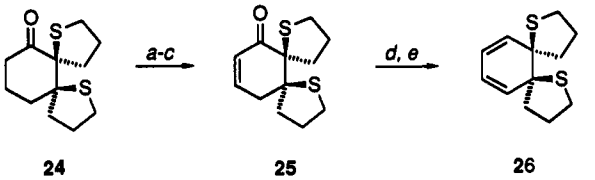
In keeping with this successful series of reactions, the syn and anti dithia ketones **24** and **27** were satisfactorily transfomed into dienes **26** and **29** by comparable means (Scheme 4). These products proved to be crystalline solids with good shelf stability. In fact, none of the dienes exhibited sensitivity to oxidation or some alternative destructive process when stored under standard laboratory conditions for prolonged periods of time.

Acid-Catalyzed Rearrangements. A systematic investigation of the fate of the structurally and stereochemically varied cyclohexadienes described above under acidic conditions was next undertaken. After preliminary experiments demonstrated that certain rearrangement products did not stain well on thin-layer chromatography, the decision was made to follow the progress of these reactions directly in the probe of an NMR spectrometer. Although a variety of options can be envisioned for the selection of a catalyst, recourse was made throughout to the use of *p*-toluenesulfonic acid in $CDCl_3$ solution.

Following exposure of **11** to approximately 8 mol % of *p*-TsOH at 25 °C, no remaining diene could be detected by ^{1}H NMR after

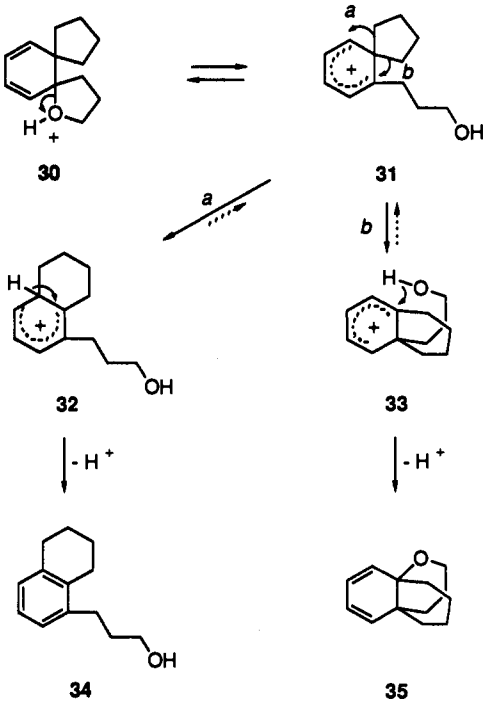
(14) Reuss, R. H.; Hassner, A. *J. Org. Chem.* **1974**, *39*, 1785.

Scheme 4



[a] LDA, THF; Me_3SiCl, Et_3N. [b] NBS, propylene oxide, THF. [c] LiBr, Li_2CO_3, DMA, reflux. [d] $NaBH_4$, $CeCl_3 \cdot 7H_2O$, CH_3OH. [e] 2,4-$(NO_2)_2$-C_6H_3SCl, Et_3N, $ClCH_2CH_2Cl$, reflux.

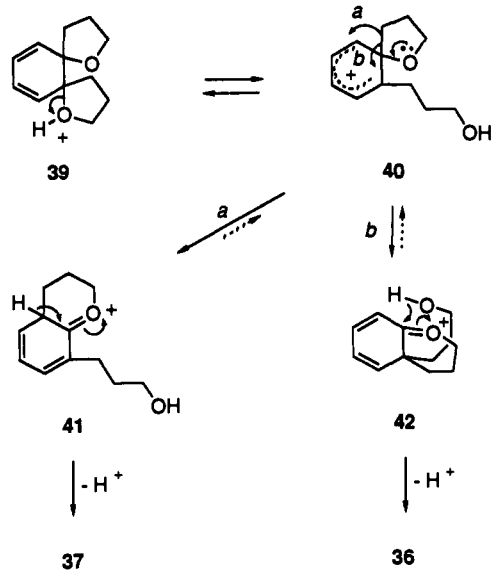
Scheme 5



5 min. Chromatography of the sample on silica gel led to the isolation of propelladiene **35** and alcohol **34** in a 2:1 ratio. Ether **35** proved stable to chromatography on silica gel (a characteristic of all the propellanes described here) and to further rearrangement when exposed to camphorsulfonic acid in benzene. In a formal sense, these isomerizations are consistent with initial bond heterolysis within the protonated dispiro ether **30** to generate pentadienyl cation **31** (Scheme 5). Arrival at this intermediate sets the stage for two possible 1,2-Wagner–Meerwein shifts labeled as *a* and *b*, both of which lead to dismantling of the second spirocyclic center. Adherence to path *a* gives rise to **32**, irreversible proton loss from which results in the establishment of benzenoid aromaticity. Pathway *b* defines an alkyl migration that eventuates in the generation of a new quaternary carbon center as in **33**. Intramolecular nucleophilic attack by the hydroxyl oxygen completes the conversion to **35**.

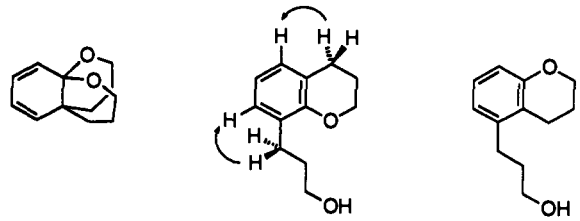
The reproducibility with which **11** experiences such rearrangement has made it abundantly clear that the *b* process is kinetically favored. Although inspection of molecular models of **31** has not provided us with a convincing rationale for this contrasteric migratory preference, it was considered important

Scheme 6



to ascertain how a second heteroatom might impact on the course of events.

Comparable treatment of **14** furnished a 1.1:1 mixture of **36** and **37** in good yield. The trans dioxa diene **17** responded in an

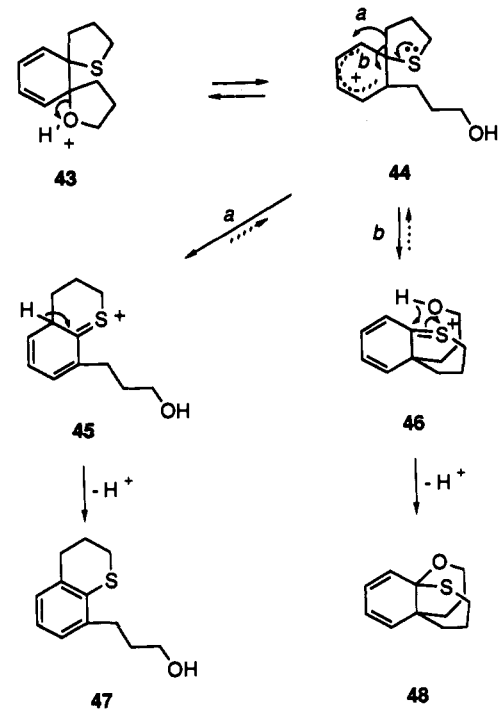


identical manner, both systems requiring approximately 2 h to be completely consumed. The C_s symmetry of **36** was apparent from its nine-line ^{13}C NMR spectrum and the appearance of four distinctive olefinic proton signals at 300 MHz. The structural features assigned to **37** were confirmed on the basis of NOE experiments in which the two pairs of benzylic protons were separately irradiated. In both experiments, an integral enhancement was observed for the signal arising from the neighboring aromatic proton. On this basis, the isomer **38** can be dismissed from further explicit consideration.

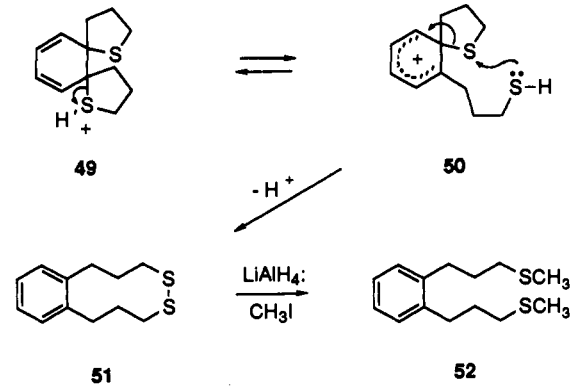
The mechanistic profile likely followed by the dioxa isomers is diagrammed in Scheme 6. In these examples, we have obtained no evidence indicating that the ether oxygen atom in **40** enters into 1,2-migration. Furthermore, the near-identical amounts of **36** and **37** suggest that the need to involve oxonium ions **41** and **42** brings the mechanistic options *a* and *b* closer into balance.

The oxathia dienes **20** and **23** offer attractive chemical elements designed to probe still more deeply into these mechanistic issues. The presence of both an oxygen and a sulfur atom provides the opportunity to determine which C–X bond heterolysis will initiate the reaction cascade. Beyond that, the intervention of less electronically favorable[5] thionium ions should offer further indication as to whether the competitive *a*/*b* migratory profile can experience increased selectivity. Isomerization of **20** or **23** under the influence of *p*-TsOH in $CDCl_3$ solution ultimately gave rise to a lone isomeric product identified as **47**. These strikingly chemospecific conversions imply that the C–S bond is less prone to cleavage than its C–O counterpart and that cation **44** is first generated (Scheme 7). Impressively, intemediate **44** advances to product uniquely by pathway *a*, at least under conditions where a sulfonic acid catalyst is involved.

Scheme 7



Scheme 8



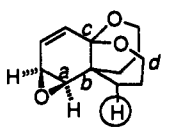
In a serendipitous experiment performed almost simultaneously, a $CDCl_3$ solution of **23** was allowed to evaporate slowly over the course of 2 weeks at room temperature. Redissolution of the sample and a second recording of the NMR spectrum revealed that isomerization to a mixture of **47** and **48** (ratio 4:1) had occurred during this period. The catalyst was presumably the Brønsted acid slowly liberated upon degradation of the isotopically labeled solvent. Tetracyanoethylene (TCNE) likewise promotes (in a shorter time frame) the conversion of **23** predominantly to **48**, although a different mechanism is likely operative under these circumstances.[6] It must be emphasized that one cannot be fully committed to the **44** → **46** → **48** pathway outlined in Scheme 7. The reverse timing of the C–X bond ruptures could be operative and not be recognized. However, some might want to invoke Occam's razor in order to simplify matters in favor of **44**.

The syn dithia analog **26** was transformed uniquely during 48 h into disulfide **51** following addition of 10 mol % *p*-toluenesulfonic acid to $CDCl_3$ solutions. Anti isomer **29** likewise gave **51** exclusively when kept in $CDCl_3$ at room temperature in an NMR tube for several days. The formation of this end product correlates well with initial ionization to pentadienyl cation **50** followed by intramolecular nucleophilic attack by mercapto sulfur at the sulfide center with direct aromatization of the benzene ring (Scheme 8). Thus, we see for the first time that the spirocyclic cations invoked as the initially formed intermediates can indeed be intercepted prior to Wagner–Meerwein shift when the

heteroatom residing at the terminus of the propyl chain is made sufficiently nucleophilic.

The structural constitution of **51**, deduced initially on the basis of its simplified ^1H and ^{13}C (six-line) NMR spectra, was confirmed by chemical conversion to **52** via lithium aluminum hydride reduction and direct S-methylation. The bisthioether exhibits the same symmetry characteristics as **51**, thereby requiring that the disulfide linkage present in **51** reside in the mirror plane responsible for the meso nature of these compounds.

Selected Reactions of the [4.4.4]Propelladienes. With several heteroatomic propelladienes of type **4** in hand, some attention was accorded to the regio- and stereochemical aspects of epoxidation and cycloaddition reactions. Thus, treatment of **36** with buffered *m*-chloroperbenzoic acid was found to proceed slowly at room temperature with the formation of **53**. There is,

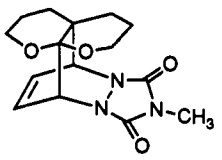


a, 61.7 ppm
b, 33.9 ppm
c, 96.1 ppm
d, 61.9 ppm

53

of course, no issue of facial selectivity in this instance. However, the fact that the double bond most distal from the oxygen atoms was the seat of reaction was determined by a 5-Hz tuned semiselective INEPT experiment capable of detecting ^3J and ^4J interactions. Saturation of the γ-pyranyl proton that appears at δ 1.62 (dddd, J = 13, 3.5, 3.5, 2 Hz) produced enhancements at the four carbons labeled *a*–*d*. Since one of these four carbon centers belongs to the epoxide subunit, the proximal relationship shown is required. The observed regioselectivity is attributed to inductive effects.

Although **36** was unreactive toward *N*-phenylmaleimide even under forcing conditions (175 000 psi, CH_2Cl_2), cycloaddition occurred slowly in the presence of *N*-methyltriazolinedione (MTAD) at room temperature (CH_2Cl_2 solution). After 5 days, the extent of conversion to **54** was 73%. The processing of **35** under analogous conditions was accompanied by the interesting observation that dienophile capture occurs only from that direction syn to the cyclohexane ring. The identity of **55** was established



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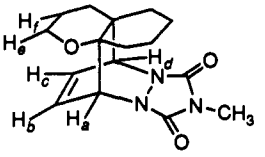

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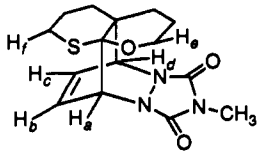

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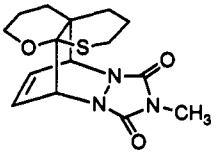

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by ^1H–^1H COSY, ^1H–^{13}C COSY, and INEPT experiments which permitted all relevant protons and carbons to be identified. Once accomplished, NOE data such as those indicated below confirmed the relative spatial proximity of the tetrahydropyranyl ring to the unsaturated bridge.

The condensation of **48** with MTAD afforded two adducts, **56** and **57**, in 86% yield and a ratio of 20:1. As before, the proximity of the sulfur-containing six-membered ring to the ethylene π-bond was corroborated by NOE results.

It is noteworthy that MTAD adds anti to oxygen when the monooxapropelladiene **35** is involved but preferentially syn to oxygen in the oxathia example. Competition experiments, undertaken to gauge the relative reactivity of the three dienes toward MTAD, revealed **48** to be most reactive and **36** the least. The experimentally derived ratios for **48**:**35**:**36** were 2.1:1.4:1. The higher reactivity of **48** suggests that inductive effects do not alone contribute to the ability of these dienes to engage in (4 + 2) cycloaddition.

NOE's for **55**:

H_b (δ 6.49-6.45)
→ H_a : 4.5%
→ H_e : 1.1%
H_c (δ 6.45-6.38)
→ H_d : 4.5%
→ H_f : 1.8%

NOE's for **56**:

H_b (δ 6.56-6.51)
→ H_f (δ 2.57) : 1.4%
H_c (δ 6.37-6.32)
→ H_f (δ 2.57) : 0.2%
H_e (δ 3.88-3.81)
no effect on H_b or H_c

Discussion

The present survey of the acid-catalyzed isomerization of dispiro[4.0.4.4]tetradeca11,13-dienes containing one or two heteroatoms has provided insight into those control elements that dictate regioselectivity. If **11** is viewed as a suitable point of reference, we see that this system is inherently capable of producing only the cyclohexadienyl carbocation **31**. Once generated, this intermediate partitions itself along two Wagner–Meerwein reaction channels, with that involving the greater buildup of steric congestion being favored by a factor of 2.

Subsequent to the mechanistically related conversions of **14** and **17** to **40**, the pair of 1,2-shift options now operate with essentially equal efficiency. In this specific example, migration of the methylene group may perhaps be facilitated because of the involvement of nonbonded electron pairs from the tetrahydrofuranyl oxygen atom. One might inquire whether the evolution of oxonium ions **41** and **42** so levels the energetics of the competing Wagner–Meerwein steps that they are no longer kinetically imbalanced.

This working assumption is lent credence by the regioselectivity exhibited by **44**. Formed by heterolytic scission of the C–O bond in the oxathia dispiro diene, **44** is expected to be less favorably inclined than either **31** or **40** to advance to thionium ion(s) **45** and/or **46** because of their lower stability and higher reactivity.[5,15] This diminution in driving force is anticipated to result in a substantive enhancement in the selectivity of the ensuing Wagner–Meerwein shift. Indeed, the resident sulfur atom in **44** causes the pathway leading to the sterically less crowded intermediate **45** to operate as the exclusive exit step. Our ability to isolate **48** under different reaction conditions suggests that the partitioning between **45** and **46** may be subject to modulation.

In support of the preceding mechanistic detail, it is noted that **50** is sufficiently reluctant to enter into the Wagner–Meerwein manifold (with requisite development of thionium ion character) and that it is entirely prone to intramolecular nucleophilic attack at sulfur by the pendant sulfhydryl group.

Thus, we have shown that heteratomic effects manifest themselves in clear-cut fashion during acid-catalyzed rearrangement of the title dienes. A new class of [4.4.4]propelladienes can be accessed in this manner. Rationalization of the stereoselectivity with which these propelladienes enter into Diels–Alder reaction with *N*-methyltriazolinedione is deferred to a future paper which will also detail the cycloaddition stereochemistry exhibited by **11**, **14**, **17**, **20**, **23**, and **26**.

Experimental Section

Melting points are uncorrected. ^1H and ^{13}C NMR spectra were recorded at the indicated field strengths. High resolution mass spectra were recorded at The Ohio State University Chemical Instrumentation

(15) (a) Trost, B. M.; Mikhail, G. K. *J. Am. Chem. Soc.* **1987**, *109*, 4124. (b) Trost, M. B.; Sato, T. *J. Am. Chem. Soc.* **1985**, *107*, 719. (c) Trost, B. M.; Murayama, E. *Tetrahedron Lett.* **1982**, *23*, 1047.

Center. Elemental analyses were performed at the Scandinavian Microanalytical Laboratory, Herlev, Denmark. All reactions were carried out under a nitrogen atmosphere, and the ensuing separations were effected under flash chromatography conditions on Merck silica gel HG_{254}. The organic extracts were dried over anhydrous magnesium sulfate. Solvents were reagent grade and in many cases dried before use.

1-Oxadispiro[4.0.4.4]tetradecan-14-one (6). Cerium trichloride heptahydrate (11.64 g, 31.2 mmol) was heated at 140 °C and 1 Torr overnight. After the solid had cooled, anhydrous THF (90 mL) was introduced, and the slurry was stirred at room temperature for 3 h, cooled to −78 °C, and treated dropwise with *tert*-butyllithium until a pink color persisted. A solution of 5-lithio-2,3-dihydrofuran in dry THF (25 mL) [prepared from 2.190 g (31.2 mmol) of 2,3-dihydrofuran[16] and 20.22 mL of 1.7 M *tert*-butyllithium] was next introduced, and the reaction mixture was stirred at −78 °C for 3 h before the introduction via cannula of **5**[7] (3.598 g, 26.0 mmol) dissolved in dry THF (2 mL). After an additional 4 h in the cold, the mixture was allowed to warm to room temperature, poured into saturated $NaHCO_3$ solution, and extracted into ether (2×) and CH_2Cl_2 (2×). The combined extracts were washed with brine and dried prior to solvent evaporation. The unpurified carbinol was stirred with Dowex-50X resin (2.0 g) in CH_2Cl_2 (200 mL) for 20 h, filtered, and concentrated. Chromatography of the oil on silica gel (elution with 15% ethyl acetate in hexanes) furnished 4.913 g (90.6%) of **6**: IR (neat, cm^{-1}) 2960, 2880, 1715, 1445, 1300, 1090, 1050; ^1H NMR (300 MHz, $CDCl_3$) δ 3.92–3.85 (m, 1 H), 3.77–3.69 (m, 1 H), 2.72–2.63 (m, 1 H), 2.38–2.20 (m, 2 H), 1.89–1.69 (m, 7 H), 1.68–1.23 (m, 8 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 212.4, 93.6, 68.5, 53.5, 37.8, 35.4, 33.9, 33.3, 28.2, 26.2, 25.9, 25.7, 22.7; MS *m/z* (M^+) calcd 208.1463, obsd 208.1469.

Anal. Calcd for $C_{13}H_{20}O_2$: C, 74.96; H, 9.68. Found: C, 75.06; H, 9.73.

(5*R,13*R**)-13-Bromo-1-oxadispiro[4.0.4.4]tetradecan-14-one and (5*R**,13*S**)-13-Bromo-1-oxadispiro[4.0.4.4]tetradecan-14-one (7 and 8).** A solution of **6** (500 mg, 2.40 mmol) in THF (5 mL) was transferred by cannula to a stirred mixture of pyridinium hydrobromide perbromide (806 mg, 2.52 mmol) in THF (5 mL) at 0 °C. Additional brominating agent (100 mg) was added after 30 min and again after 1 h. After an additional 2 h of being stirred, the reaction mixture was diluted with ether, washed with 10% $Na_2S_2O_3$ solution and brine, and then dried. Evaporation of the solvent and chromatography of the residue on silica gel (elution with 20% ethyl acetate in hexanes) gave first the anti isomer **7** (524 mg, 76%) and subsequently the syn isomer **8** (111 mg, 16%).

For **7**: IR (neat, cm^{-1}) 2955, 2875, 1735, 1450, 1290, 1050; ^1H NMR (300 MHz, $CDCl_3$) δ 5.36 (dd, J = 12.5 Hz, 6.5 Hz, 1 H), 3.89–3.81 (m, 1 H), 3.68–3.60 (m, 1 H), 2.70–2.61 (m, 1 H), 2.51–2.43 (m, 1 H), 2.22–1.96 (m, 2 H), 1.88–1.74 (m, 3 H), 1.67–1.41 (m, 6 H), 1.40–1.29 (m, 2 H), 1.26–1.18 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.0, 94.8, 68.9, 54.3, 53.6, 36.0, 35.5, 32.1, 26.2, 26.1, 25.9, 25.8; MS *m/z* (M^+) calcd 286.0569, obsd 286.0568.

For **8**: mp 85–86 °C (from hexanes); IR (CH_2Cl_2, cm^{-1}) 2960, 2880, 1740, 1450, 1260, 1200, 1115, 1095, 1055, 990, 910; ^1H NMR (300 MHz, $CDCl_3$) δ 4.82 (dd, J = 12.8 Hz, 6.8 Hz, 1 H), 3.99–3.84 (m, 2 H), 2.49–2.40 (m, 1 H), 2.21–2.00 (m, 2 H), 1.97–1.78 (m, 3 H), 1.77–1.55 (m, 7 H), 1.49–1.33 (m, 2 H), 1.24–1.14 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 202.1, 93.7, 68.6, 53.5, 53.4, 36.1, 34.6, 34.2, 32.2, 32.1, 26.4, 25.7, 25.1; MS *m/z* (M^+) calcd 286.0569, obsd 286.0580.

Anal. Calcd for $C_{13}H_{19}BrO_2$: C, 54.37; H, 6.67. Found: C, 54.47; H, 6.71.

1-Oxadispiro[4.0.4.4]tetradec-12-en-14-one (9). Lithium bromide (5.643 g, 65.0 mmol) was heated to 140 °C and 1 Torr for 3 h. After the solid had cooled, *N*,*N*-dimethylacetamide (200 mL) was introduced followed by Li_2CO_3 (4.072 g, 55.1 mmol). The mixture was heated to 100 °C, a solution of **7** and **8** (4.78 g, 16.6 mmol) in *N*,*N*-dimethylacetamide (10 mL) was added, and the temperature was raised to 170 °C. After 75 min at this temperature, none of the starting material remained. The cooled mixture was diluted with ether and filtered through a pad of Celite. Concentration of the filtrate followed by Kugelrohr distillation of the acetamide left a dark residue which was triturated with ether. Filtration and evaporation of the solvent followed by chromatography of the oil on silica gel (elution with 10% ether in hexanes) afforded 2.85 g (83%) of **9**: IR (neat, cm^{-1}) 3035, 2955, 2875, 1680, 1450, 1425, 1380, 1090, 795; ^1H NMR (300 MHz, $CDCl_3$) δ 6.68 (dt, J = 10.0 Hz, 4.0 Hz, 1 H), 5.86 (dt, J = 10 Hz, 1.7 Hz, 1 H), 4.00–3.85 (br m, 1 H), 3.85–3.78 (m, 1 H), 2.40–2.21 (m, 2 H), 2.04–1.58 (m, 5 H), 1.52 (br d, J = 7.4 Hz, 5 H), 1.32–1.25 (m, 2 H); ^{13}C NMR (62.5 MHz, 330 K, $CDCl_3$) δ 200.0, 147.4, 127.9, 90.3, 69.4, 51.2, 39.6, 33.8, 33.7, 29.2, 25.7, 25.4, 25.2; MS *m/z* (M^+) calcd 206.1307, obsd 206.1304.

Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.79. Found: C, 75.98; H, 8.82.

1-Oxadispiro[4.0.4.4]tetradec-12-en-14-ol (10). A stirred mixture of **9** (2.85 g, 13.8 mmol) and cerium trichloride heptahydrate (5.66 g, 15.2 mmol) in methanol (50 mL) was treated with sodium borohydride (575 mg, 15.2 mmol). When TLC analysis indicated that starting material remained after 10 min, small additional quantities of hydride reagent were added until UV-active compounds were no longer detected. The reaction mixture was poured into 5% HCl and extracted with ether. The organic phases were dried and evaporated, and the residual oil was chromatographed on silica gel (elution with 40% ethyl acetate in hexanes) to afford 2.631 g (91%) of a 2.3:1 mixture of allylic alcohols **10**: IR (neat, cm^{-1}) 3635–3095, 3030, 2955, 2875, 1655, 1450, 1425, 1300, 1230, 1100, 1050, 975, 910, 825, 740; ^1H NMR (300 MHz, C_6D_6) δ 5.79 (dq, J = 10.0 Hz, 4.4 Hz, 2.4 Hz, 1 H), 5.69 (dm, J = 10 Hz, 0.43 H), 5.62–5.55 (m, 1 H), 5.45–5.38 (m, 0.43 H), 4.34 (br s, 0.43 H), 3.95–3.88 (m, 0.43 H), 3.83 (br d, J = 8.4 Hz, 1 H), 3.73–3.60 (m, 2.62 H), 2.29 (d, J = 8.4 Hz, 1 H), 2.19–2.05 (m, 2 H), 2.02–1.85 (m, 1.2 H), 1.82–1.65 (m, 6 H), 1.63–1.32 (m, 11 H), 1.28–1.23 (m, 2.4 H), 1.09–1.01 (m, 0.6 H); ^{13}C NMR (75 MHz, C_6D_6) δ 131.3, 129.8, 128.4, 127.1, 89.1, 87.9, 73.8, 72.6, 70.4, 70.1, 51.1, 49.9, 38.5, 36.9, 34.6, 34.4, 34.1, 32.5, 30.8, 28.4, 28.1, 27.3, 25.5, 24.7, 24.4 (one signal not resolved); MS *m/z* ($M^+ - H_2O$) calcd 190.1358, obsd 190.1383.

Anal. Calcd for $C_{13}H_{20}O_2$: C, 74.96; H, 9.68. Found: C, 74.58; H, 9.72.

1-Oxadispiro[4.0.4.4]tetradeca-11,13-diene (11). To a stirred solution of allylic alcohols **10** (363 mg, 1.74 mmol) and triethylamine (1.0 mL, 7.0 mmol) in 1,2-dichloroethane (15 mL) was added 2,4-dinitrobenzenesulfenyl chloride (1.23 g, 5.23 mmol). The mixture was stirred at reflux for 8 h, cooled, poured into ether, and filtered through Celite. Evaporation of the solvent afforded a dark oil that was chromatographed on silica gel (elution with 5% ethyl acetate and 1% triethylamine in hexanes) to afford 187 mg (57%) of **11** as a colorless oil: IR (neat, cm^{-1}) 3040, 2960, 2880, 1725, 1450, 1070, 735; ^1H NMR (300 MHz, C_6D_6) δ 5.80–5.72 (m, 2 H), 5.70–5.61 (m, 2 H), 3.77–3.70 (m, 1 H), 3.67–3.60 (m, 1 H), 2.47–2.37 (m, 1 H), 2.03–1.92 (m, 1 H), 1.78–1.44 (m, 10 H); ^{13}C NMR (75 MHz, C_6D_6) δ 140.3, 136.6, 122.5, 121.0, 86.2, 67.9, 51.3, 34.3, 33.5, 33.2, 26.3, 25.21, 25.1; MS *m/z* (M^+) calcd 190.1358, obsd 190.1359.

Anal. Calcd for $C_{13}H_{18}O$: C, 82.06; H, 9.53. Found: C, 81.76; H, 9.62.

(5*R,6*R**)-1,7-Dioxadispiro[4.0.4.4]tetradec-12-en-11-one (13) (Procedure A).** To a stirred solution of pyridinium hydrobromide perbromide (3.838 g, 12.00 mmol) in THF (35 mL) at 0 °C was added via cannula a solution of **12** (2.41 g, 11.5 mmol) in THF (10 mL). After being stirred for 30 min, the reaction mixture was diluted with ether and washed consecutively with 10% $Na_2S_2O_3$ solution, water, and brine. The organic layer was dried and evaporated, and the residue was chromatographed on silica gel (elution with 30% ethyl acetate in hexanes) to furnish 2.19 g (66%) of the major diastereomer followed by 0.59 g (17.8%) of the minor diastereomer.

For the major diastereomer: mp 63–64 °C; IR ($CDCl_3$, cm^{-1}) 2980, 1730, 1440, 1075; ^1H NMR (300 MHz, $CDCl_3$) δ 5.21 (dd, J = 11.3 Hz, 6.7 Hz, 1 H), 3.93–3.85 (m, 3 H), 3.81–3.75 (m, 1 H), 2.61–2.44 (m, 2 H), 2.34–2.24 (m, 1 H), 1.98–1.85 (m, 3 H), 1.83–1.63 (m, 4 H), 1.61–1.57 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 201.3, 94.5, 87.6, 69.4, 69.0, 52.7, 33.1, 32.2, 31.2, 26.2, 26.1, 25.9; MS *m/z* (M^+) calcd 288.0362, obsd 288.0347.

A solution of the above bromo ketones (2.758 g, 9.537 mmol) in *N*,*N*-dimethylacetamide (10 mL) was added to a mixture of lithium bromide (2.930 g, 23.84 mmol) [heated overnight at 140 °C and 1 Torr before use] and lithium carbonate (2.114 g, 28.61 mmol) in the same solvent (40 mL). The mixture was heated to 170 °C for 3 h, cooled, poured into ether, and filtered through Celite. Rotary evaporation of the ether and Kugelrohr distillation of the acetamide left a solid that was triturated with ether. Filtration of the extracts and evaporation afforded an oil that was chromatographed on silica gel (elution with 1:1 ethyl acetate–hexanes) to furnish 1.331 g (67%) of **13** as a colorless oil: IR (neat, cm^{-1}) 2990, 1690, 1450, 1380, 1200, 1100, 1050; ^1H NMR (300 MHz, 373 K, toluene-d_8) δ 6.26 (dt, J = 10.1 Hz, 4.3 Hz, 1 H), 5.85 (dt, J = 10.1 Hz, 2.1 Hz, 1 H), 3.84–3.71 (m, 2 H), 3.69–3.65 (m, 2 H), 2.63 (br d, J = 7.9 Hz, 1 H), 2.16–2.09 (br m, 1 H), 2.05–1.44 (m, 7 H), 1.33–1.22 (m, 1 H); ^{13}C NMR (75 MHz, 373 K, toluene-d_8) δ 145.2, 128.5, 91.1, 87.4, 69.5,

(16) Boeckman, R. K., Jr.; Bruza, K. J. *Tetrahedron Lett.* **1977**, 4187.

68.8, 38.2, 33.1, 26.4, 26.1 (two signals not observed); MS *m/z* (M^+) calcd 208.1099, obsd 208.1101.

Anal. Calcd for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74. Found: C, 69.24; H, 7.89.

(5*R,6*S**)-1,7-Dioxadispiro[4.0.4.4]tetradeca-11,13-diene (14). Use of Dibal-H (Procedure B).** A solution of **13** (2.140g, 10.27 mmol) in CH_2Cl_2 (100 mL) was cooled to 0 °C and treated with a solution of diisobutylaluminum hydride in hexanes (11.3 mL, 11.3 mmol). The reaction mixture was stirred for 1 h, methanol (3 mL) was added, and stirring was maintained for 8 h. The mixture was poured into 50 mL each of 10% HCl and brine and extracted with ether. The combined organic phases were dried and evaporated, and the residual oil was chromatographed on silica gel (elution with 1:1 ethyl acetate–hexanes) to afford a quantitative yield of one allylic alcohol: IR (neat, cm^{-1}) 3700–3120, 3040, 2990, 2880, 1465, 1430, 1070, 930, 840, 740, 710; ^1H NMR (250 MHz, 350 K, C_6D_6) δ 5.72–5.65 (m, 1 H), 5.52–5.44 (m, 1 H), 3.98–3.79 (m, 3 H), 3.70–3.56 (m, 2 H), 2.65 (br s, 1 H), 2.47 (dd, J = 17.3 Hz, 2.2 Hz, 1 H), 1.81–1.68 (m, 5 H), 1.61–1.43 (m, 3 H), 1.40–1.29 (m, 1 H); ^{13}C NMR (62.5 MHz, 350 K, C_6D_6) δ 130.7, 127.0, 87.9, 87.5, 72.6, 70.1, 68.3, 36.2, 33.0, 29.6, 27.0, 25.5; MS *m/z* (M^+) calcd 210.1256, obsd 210.1228.

Anal. Calcd for $C_{12}H_{18}O_3$: C, 68.55; H, 8.63. Found: C, 68.22; H, 8.72.

Use of $NaBH_4$–$CeCl_3$ (Procedure C). To a mixture of **13** (500 mg, 2.4 mmol) and $CeCl_3 \cdot 7H_2O$ (895 mg, 2.4 mmol) in methanol (6 mL) was added sodium borohydride (91 mg, 2.4 mmol). Two additional amounts of $NaBH_4$ (*ca.* 20 mg each) were added until none of the enone could be detected by TLC analysis. The reaction mixture was poured into 5% HCl and extracted with ether. The organic phases were dried and evaporated, and the residual oil was chromatographed on silica gel (elution with 60% ethyl acetate in hexanes) to afford 307 mg (61%) of the alcohol described above, followed by 45 mg (9%) of its epimer: IR (neat, cm^{-1}) 3700–3120, 3040, 2995, 2985, 1465, 1430, 1070, 930, 840, 735, 710; ^1H NMR (300 MHz, $CDCl_3$) δ 5.67–5.54 (m, 2 H), 4.56 (br s, 1 H), 4.10–4.01 (m, 1 H), 3.98–3.91 (m, 1 H), 3.86–3.75 (m, 2 H), 2.21–1.74 (m, 9 H), 1.59–1.48 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 130.1, 126.1, 89.3, 87.2, 72.8, 70.3, 68.3, 38.1, 32.1, 29.0, 27.2, 25.9; MS *m/z* (M^+) calcd 210.1256, obsd 210.1251.

To a stirred solution of the above alcohol (1.279 g, 6.08 mmol) and triethylamine (2.5 mL, 18 mmol) in 1,2-dichloroethane (30 mL) was added 2,4-dinitrobenzenesulfenyl chloride (2.854 g, 12.2 mmol). The mixture was stirred and heated to reflux for 12 h then poured into saturated $NaHCO_3$ solution and extracted with CH_2Cl_2. The combined organic phases were dried and evaporated. Chromatography of the residual brown oil on silica gel (elution with 1:1 ethyl acetate–hexanes) followed by rechromatography of the diene-containing fractions on neutral alumina (elution with 10% ethyl acetate in hexanes) afforded 663 mg (57%) of **14** as a colorless solid: mp 52–54 °C (sublimation); IR (KBr, cm^{-1}) 3050, 2950, 2870, 1450, 1405, 1310, 1200, 1100, 1075, 1050, 935, 865, 725, 660; ^1H NMR (300 MHz, $CDCl_3$) δ 5.92–5.83 (m, 4 H), 4.00–3.94 (m, 2 H), 3.90–3.82 (m, 2 H), 2.16–2.06 (m, 2 H), 1.98–1.89 (m, 4 H), 1.83–1.76 (quint, J = 5.6 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.6, 123.1, 85.3, 68.7, 33.5, 26.2; MS *m/z* (M^+) calcd 192.1150, obsd 192.1147.

Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 74.88; H, 8.54.

(5*R,6*S**)-1,7-Dioxadispiro[4.0.4.4]tetradec-12-en-11-one (16).** To a solution of pyridinium hydrobromide perbromide (2.71 g, 8.85 mmol) in THF (35 mL) at 0 °C was added dropwise a solution of **15** (1.77 g, 8.36 mmol) in THF (10 mL). The reaction mixture was allowed to warm to room temperature for 15 min. Workup according to procedure A and purification by MPLC (silica gel, elution with 10% ether in petroleum ether) afforded 1.84 g (76%) of the major diastereomer, accompanied by 0.60 g (24%) of the minor diastereomer.

For the major diastereomer: IR (neat, cm^{-1}) 2980, 1740, 1450, 1290, 1060, 920; ^1H NMR (300 MHz, $CDCl_3$) δ 5.14 (dd, J = 11.6 Hz, 6.7 Hz, 1 H), 3.87–3.79 (m, 2 H), 3.74–3.42 (m, 2 H), 2.65 (quintet, J = 6.6 Hz, 1 H), 2.35–2.21 (m, 2 H), 2.19–2.05 (m, 1 H), 1.99–1.58 (m, 8 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.5, 92.2, 88.7, 69.1, 68.2, 53.5, 34.1, 33.4, 32.8, 26.2, 25.9, 25.9; MS *m/z* (M^+) calcd 288.0361, obsd 288.0354.

For the minor diastereomer: IR ($CHCl_3$, cm^{-1}) 2960, 2885, 1735, 1055; ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.4, 94.5, 87.8, 69.0, 69.0, 52.5, 35.8, 32.0, 31.6, 31.3, 26.5, 26.0; MS *m/z* (M^+) calcd 288.0361, obsd 288.0322.

The above α-bromo ketones (1.74 g, 6.02 mmol) when dehydrobrominated according to procedure A gave 1.09 g (87%) of **16** as a colorless oil: IR (neat, cm^{-1}) 2990, 1690, 1380, 1220, 1090, 1060; ^1H NMR (300 MHz, $CDCl_3$) δ 6.82 (ddd, J = 10.1 Hz, 5.7 Hz, 2.5 Hz, 1 H), 5.99 (ddd, J = 10.1 Hz, 3.0 Hz, 0.7 Hz, 1 H), 4.15–4.09 (m, 1 H), 3.96–3.77 (m, 3 H), 2.65 (dt, J = 18.9 Hz, 2.7 Hz, 1 H), 2.50–2.35 (m, 2 H), 2.23–2.12 (m, 1 H), 2.12–1.75 (m, 5 H), 1.65–1.57 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.8, 146.7, 128.1, 91.8, 86.1, 69.9, 69.2, 39.7, 32.3, 29.4, 26.3, 25.6; MS *m/z* (M^+) calcd 208.1099, obsd 208.1105.

Anal. Calcd for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74. Found: C, 68.97; H, 7.88.

(5*R,6*R**)-1,7-Dioxadispiro[4.0.4.4]tetradeca-11,13-diene (17).** To a mixture of **16** (3.24 g, 15.6 mmol) and $CeCl_3 \cdot 7H_2O$ (5.79 g, 15.6 mmol) in methanol (50 mL) was added sodium borohydride (617 mg, 16.3 mmol). The mixture was stirred for 10 min and worked up according to procedure C to afford 2.33 g (71.4%) of a 1.4:1 mixture of alcohols: IR (neat, cm^{-1}) 3675–3095, 3035, 2965, 2875, 2685, 1740, 1720, 1435, 1240, 1055; ^1H NMR (300 MHz, $CDCl_3$) δ 5.70–5.69 (m, 0.62 H), 5.60–5.55 (m, 0.88 H), 4.11–4.09 (m, 0.41 H), 3.97–3.62 (m, 4.16 H), 2.66 (d, J = 4.2 Hz, 0.32 H), 2.55 (d, J = 4.5 Hz, 0.46 H), 2.28–2.11 (m, 3.0 H), 2.10–1.77 (m, 6.3 H), 1.65–1.49 (m, 1.42 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 129.5, 128.5, 127.7, 126.4, 88.6, 86.6, 86.2, 84.6, 73.2, 73.1, 69.7, 69.3, 68.1, 67.7, 38.5, 37.8, 32.3, 31.9, 30.4, 27.9, 26.8, 26.6, 26.5, 26.2; MS *m/z* (M^+) calcd 210.1256, obsd 210.1253.

Anal. Calcd for $C_{12}H_{18}O_3$: C, 68.55; H, 8.63. Found: C, 68.38; H, 8.74.

Dehydration of the above alcohols (2.118 g, 10.1 mmol) as described earlier yielded 1.34 g (69%) of **17**: IR (neat, cm^{-1}) 3039, 2974, 2866, 1400, 1075, 1031, 993, 945, 707; ^1H NMR (300 MHz, $CDCl_3$) δ 5.79–5.74 (m, 2 H), 5.69–5.65 (m, 2 H), 3.91–3.77 (m, 4 H), 2.79–2.70 (m, 2 H), 2.01–1.76 (m, 4 H), 1.65–1.56 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.8, 121.7, 88.4, 68.7, 31.7, 26.4; MS *m/z* (M^+) calcd 192.1150, obsd 192.1189.

Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 74.98; H, 8.40.

(5*R,6*S**)-1-Oxa-7-thiadispiro[4.0.4.4]tetradec-12-en-14-one (19) (Procedure D).** A solution of *n*-butyllithium in hexanes (8.27 mL, 13.2 mmol) was added via syringe to a solution of dry diisopropylamine (1.94 mL, 13.9 mmol) in anhydrous THF (40 mL) at –78 °C. This solution was stirred for 15 min before being treated with a solution of **18** (2.852 g, 12.6 mmol) in dry THF (10 mL). The reaction mixture was quenched after 30 min by the addition of premixed trimethylsilyl chloride (1.78 mL, 14.0 mmol) and triethylamine (0.49 mL, 3.5 mmol). After being allowed to warm to room temperature during 1 h, the mixture was poured into saturated $NaHCO_3$ solution and extracted with ether. The extracts were dried and evaporated, and the residual oil was dissolved immediately in THF (40 mL) containing propylene oxide (0.98 mL, 14.0 mmol) at 0 °C. *N*-Bromosuccinimide (2.492 g, 14.0 mmol) was added, and stirring was maintained for 1 h. Solvent evaporation followed by chromatography of the residue on silica gel (elution with 20% ethyl acetate in hexanes) afforded 3.611 g (94%) of a mixture of epimeric α-bromo ketones.

These bromo ketones (3.611 g, 11.8 mmol) were dehydrobrominated according to procedure A to afford 2.10 g (79%) of **19**: IR (neat, cm^{-1}) 3040, 2960, 2880, 1680, 1440, 1380, 1045; ^1H NMR (300 MHz, C_6D_6) δ 6.19–6.13 (m, 1 H), 5.95 (dd, J = 10.0 Hz, 2.1 Hz, 1 H), 3.84–3.73 (br m, 1 H), 3.64–3.46 (br m, 1 H), 3.03–2.91 (br m, 1 H), 2.62–2.56 (br m, 1 H), 2.55–2.39 (br m, 1 H), 2.34–2.22 (br m, 1 H), 2.11 (dd, J = 19.0 Hz, 5.3 Hz, 1 H), 2.03–1.66 (br m, 2 H), 1.65–1.26 (br m, 4 H), 1.24–0.84 (br m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.2, 148.5, 127.3, 90.4, 68.9, 65.4, 40.4, 37.0, 33.2, 30.4, 27.0, 26.0; MS *m/z* (M^+) calcd 224.0871, obsd 224.0872.

Anal. Calcd for $C_{12}H_{16}O_2S$: C, 64.25; H, 7.19. Found: C, 64.10; H, 7.25.

(5*R,6*S**)-1-Oxa-7-thiadispiro[4.0.4.4]tetradeca-11,13-diene (20).** A stirred mixture of **19** (1.127 g, 5.02 mmol) and cerium trichloride heptahydrate (2.059 g, 5.53 mmol) in methanol (20 mL) was treated with sodium borohydride (212 mg, 5.60 mmol) according to procedure C to furnish 1.077 g (95%) of a 7.6:1 mixture of epimeric allylic alcohols with R_f = 0.4 and 0.25, respectively.

For the major epimer: IR (KBr, cm^{-1}) 3680–3095, 3035, 2945, 2865, 1655, 1445, 1055; ^1H NMR (300 MHz, $CDCl_3$) δ 5.66–5.57 (m, 1 H), 5.56–5.53 (br d, J = 10.2 Hz, 1 H), 4.05–3.90 (m, 3 H), 2.89–2.83 (m, 1 H), 2.75–2.65 (m, 1 H), 2.56 (br d, J = 18.1 Hz, 1 H), 2.28–1.79 (m, 9 H), 1.42–1.32 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 129.6, 128.2, 88.5, 73.0, 70.6, 65.4, 39.5, 37.2, 33.0, 31.6, 29.6, 27.5; MS *m/z* (M^+) calcd 226.1028, obsd 226.1027.

The above allylic alcohols (239 mg, 1.05 mmol) were dehydrated according to procedure C to give 110 mg (50%) of **20** as a white solid:

mp 61–63 °C (sublimation); IR (neat, cm^{-1}) 3040, 2960, 2870, 1440, 1340, 1050, 865, 730, 680; ^1H NMR (300 MHz, C_6D_6) δ 6.10 (br d, J = 9.3 Hz, 1 H), 5.77–5.67 (m, 2 H), 5.62–5.57 (ddd, J = 9.3 Hz, 4.8 Hz, 1.4 Hz, 1 H), 3.76–3.70 (m, 2 H), 2.68–2.58 (m, 2 H), 2.19–2.06 (m, 1 H), 1.80–1.51 (m, 7 H); ^{13}C NMR (75 MHz, C_6D_6) δ 140.0, 135.7, 123.2, 120.3, 85.3, 68.2, 66.1, 38.8, 34.1, 32.6, 31.2, 26.4; MS m/z (M^+) calcd 208.0922, obsd 208.0923.

Anal. Calcd for $C_{12}H_{16}OS$: C, 69.19; H, 7.74. Found: C, 69.15; H, 7.75.

(5*R,6*R**)-1-Oxa-7-thiadispiro[4.0.4.4]tetradec-12-en-14-one (22).** A 2.426 g (10.72 mmol) sample of **21** was brominated according to procedure D to give 3.232 (99%) of the α-bromo ketones as a mixture of epimers. These bromo ketones (3.232 g, 10.6 mmol), when subjected to procedure A, afforded 1.687 g (71%) of **22** as a white crystalline solid, mp 58–59 °C (from hexanes): IR ($CDCl_3$, cm^{-1}) 3040, 2960, 2880, 2245, 1685, 1625, 1440, 1420, 1380, 1265, 1180, 1090, 1050, 990; ^1H NMR (300 MHz, $CDCl_3$) δ 6.74 (dt, J = 10.1 Hz, 4.0 Hz, 1 H), 5.92 (dt, J = 10.1 Hz, 1.9 Hz, 1 H), 4.03 (br s, 1 H), 3.95 (dd, J = 14.2 Hz, 7.7 Hz, 1 H), 2.79 (dd, J = 7.6 Hz, 4.8 Hz, 2 H), 2.68 (br d, J = 1.9 Hz, 2 H), 2.21–2.13 (m, 1 H), 2.03–1.81 (m, 6 H), 1.74–1.67 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 199.2, 147.6, 127.7, 91.0, 70.4, 65.8, 42.2, 36.8, 33.3, 31.0, 25.3; MS m/z (M^+) calcd 224.0871, obsd 224.0875.

Anal. Calcd for $C_{12}H_{16}O_2S$: C, 64.25; H, 7.19. Found: C, 64.75; H, 7.20.

(5*R,6*R**)-1-Oxa-7-thiadispiro[4.0.4.4]tetradeca-11,13-diene (23).** A 1.034 g (4.61 mmol) sample of **22** was reduced according to procedure C to afford 1.000 g (96%) of allylic alcohols, a portion of which (248 mg, 1.10 mmol) was dehydrated as previously described to give 146 mg (64%) of **23** as a colorless oil: IR (neat, cm^{-1}) 3045, 2960, 2870, 1440, 1080, 1045, 805; ^1H NMR (300 MHz, C_6D_6) δ 5.96 (br d, J = 9.3 Hz, 1 H), 5.71–5.70 (m, 2 H), 5.58 (ddd, J = 9.4 Hz, 3.7 Hz, 2.6 Hz, 1 H), 3.78–3.65 (m, 2 H), 2.71–2.54 (m, 2 H), 2.27–2.11 (m, 2 H), 1.94–1.86 (m, 3 H), 1.84–1.58 (m, 3 H); ^{13}C NMR (75 MHz, C_6D_6) δ 139.3, 135.5, 123.3, 119.6, 85.8, 69.0, 64.7, 36.7, 36.2, 33.5, 30.8, 26.3; MS m/z (M^+) calcd 208.0922, obsd 208.0919.

Anal. Calcd for $C_{12}H_{16}OS$: C, 69.19; H, 7.74. Found: C, 68.78; H, 7.81.

(5*R,6*S**)-1,7-Dithiadispiro[4.0.4.4]tetradec-12-en-11-one (25).** A 874 mg (3.61 mmol) sample of **24** was brominated according to procedure D to give first 873 mg (75%) of one bromo ketone, followed subsequently by 212 mg (18%) of its epimer. The above bromo ketones (1.085 g, 3.38 mmol) were dehydrobrominated according to procedure A to give first unreacted α-bromo ketone (261 mg, 24%) followed closely by **25** (552 mg, 68%): mp 86–87 °C (from hexanes); IR (KBr, cm^{-1}) 2935, 2860, 1660 (s), 1435, 1415, 1380, 1305, 1250, 1220, 975, 815, 680; ^1H NMR (300 MHz, $CDCl_3$) δ 6.69–6.63 (m, 1 H), 5.96 (dd, J = 10.2 Hz, 2.8 Hz, 1 H), 3.00–2.69 (m, 5 H), 2.61 (dd, J = 19.6 Hz, 5.5 Hz, 1 H), 2.57–2.38 (br m, 1 H), 2.30–2.10 (m, 4 H), 2.06–1.90 (m, 1 H), 1.87–1.80 (m, 1 H), 1.68–1.43 (br m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.1, 146.3, 127.8, 71.3, 67.8, 43.1, 37.4, 33.9, 33.0, 32.6, 32.2, 31.7; MS m/z (M^+) calcd 240.0643, obsd 240.0645.

Anal. Calcd for $C_{12}H_{16}OS_2$: C, 59.96; H, 6.71. Found: C, 59.81; H, 6.82.

(5*R,6*S**)-1,7-Dithiadispiro[4.0.4.4]tetradeca-11,13-diene (26).** A 679 mg (2.82 mmol) sample of **25** was reduced according to procedure C to furnish 665 mg (97%) of separately eluting alcohols (15:1, respectively).

For the major epimer: colorless crystals, mp 79.5–81.5 °C (from ether); ^1H NMR (300 MHz, $CDCl_3$) δ 5.65–5.49 (m, 2 H), 4.09–4.04 (m, 1 H), 3.00–2.89 (m, 1 H), 2.88–2.66 (m, 5 H), 2.46–1.88 (m, 8 H), 1.63–1.51 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 131.7, 127.7, 73.3, 72.6, 65.7, 42.1, 37.5, 36.8, 34.2, 33.2, 32.8, 31.0.

The above allylic alcohols (190 mg, 0.783 mmol) were dehydrated as detailed above to afford 103 mg (58%) of **26** as colorless crystals: mp 69.5–71.5 °C (from hexanes); IR (KBr, cm^{-1}) 3040, 2940, 2860, 1435, 1260, 1000, 740; ^1H NMR (300 MHz, $CDCl_3$) δ 6.11 (dd, J = 7.6 Hz, 2.9 Hz, 2 H), 5.76 (dd, J = 7.6 Hz, 3.0 Hz, 2 H), 2.94–2.82 (m, 4 H), 2.27–2.20 (m, 2 H), 2.19–1.93 (m, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.1, 120.8, 66.3, 38.1, 32.8, 31.2; MS m/z (M^+) calcd 224.0693, obsd 224.0690.

Anal. Calcd for $C_{12}H_{16}S_2$: C, 64.24; H, 7.19. Found: C, 64.32; H, 7.21.

(5*R,6*R**)-1,7-Dithiadispiro[4.0.4.4]tetradec-12-en-11-one (28).** A 570 mg (2.35 mmol) sample of **27** was brominated according to procedure D to give 690 mg (91%) of a closely eluting mixture of α-bromo ketones. These bromo ketones (3.660 g, 11.40 mmol) were dehydrobrominated according to procedure A to give 2.628 g (96%) of the **28** as colorless crystals: mp 60–63 °C (from ether); IR (KBr, cm^{-1}) 2970, 2940, 2870, 1720, 1675, 1435, 1415, 1380, 1265, 1235, 1130, 1000, 840, 775, 685; ^1H NMR (300 MHz, C_6D_6) δ 6.23 (ddd, J = 10.1 Hz, 5.7 Hz, 2.2 Hz, 1 H), 6.06 (dd, J = 10.2 Hz, 2.8 Hz, 1 H), 2.94–2.87 (m, 1 H), 2.76–2.65 (m, 1 H), 2.60–2.44 (m, 4 H), 2.29 (dd, J = 18.9 Hz, 5.7 Hz, 1 H), 2.24–2.15 (m, 1 H), 1.89–1.54 (m, 6 H); ^{13}C NMR (75 MHz, C_6D_6) δ 194.1, 145.6, 128.7, 71.9, 66.1, 43.6, 39.0, 34.7, 34.2, 33.4, 32.9, 30.6; MS m/z (M^+) calcd 240.0643, obsd 240.0642.

Anal. Calcd for $C_{12}H_{16}OS_2$: C, 59.96; H, 6.71. Found: C, 59.62; H, 6.68.

(5*R,6*R**)-1,7-Dithiadispiro[4.0.4.4]tetradeca-11,13-diene (29).** A 2.628 g (10.9 mmol) sample of **28** was reduced according to procedure A to furnish 2.595 g (98%) of coeluting epimeric alcohols: IR (neat, cm^{-1}) 3600–3100, 3030, 2930, 2860, 1435, 1265, 1225, 1065; ^1H NMR (300 MHz, $CDCl_3$) δ 5.80–5.52 (m, 2 H), 4.19–4.11 (m, 1 H), 3.04–2.81 (m, 4 H), 2.76 (br d, J = 10.2 Hz, 1 H), 2.71–2.52 (m, 1 H), 2.50–2.39 (m, 1 H), 2.37–1.76 (m, 8 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 128.9, 127.9, 127.8, 127.3, 73.9, 73.2, 72.9, 66.0, 41.5, 40.8, 40.2, 40.0, 36.4, 35.1, 34.9, 34.1, 33.7, 33.3, 32.5, 31.1 (remaining absorptions not observed); MS m/z (M^+) calcd 242.0799, obsd 242.0803.

These allylic alcohols (142 mg, 0.587 mmol) were dehydrated in the predescribed manner to furnish 49 mg (37%) of **29** as colorless crystals: mp 96.5–97.5 °C (from hexanes); IR (KBr, cm^{-1}) 3030, 2950, 2925, 2850, 1435, 1255, 1150, 750; ^1H NMR (300 MHz, $CDCl_3$) δ 6.01 (dd, J = 7.4 Hz, 3.0 Hz, 2 H), 5.84 (dd, J = 7.4 Hz, 3.0 Hz, 2 H), 3.02–2.95 (m, 2 H), 2.87 (dd, J = 15.9 Hz, 5.2 Hz, 1 H), 2.86 (dd, J = 15.9 Hz, 5.4 Hz, 1 H), 2.42–2.35 (m, 2 H), 2.32–2.20 (m, 2 H), 2.18–2.04 (m, 2 H), 2.00–1.90 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.5, 120.2, 64.6, 37.9, 33.5, 30.1; MS m/z (M^+) calcd 224.0693, obsd 224.0689.

Anal. Calcd for $C_{12}H_{16}S_2$: C, 64.24; H, 7.19. Found: C, 64.35; H, 7.30.

Acid-Catalyzed Rearrangement of 11. To an NMR tube was added a mixture of **11** (52 mg, 0.27 mmol) and *p*-toluenesulfonic acid (3.9 mg, 2.1×10^{-5} mol) in $CDCl_3$ (1 mL). After 5 min, none of the starting material was detected by NMR analysis. The solvent was evaporated, and the residue was chromatographed on silica gel (elution with 10% ethyl acetate and 1% triethylamine in hexanes). The first compound to elute was **35** (21 mg, 40%): IR (neat, cm^{-1}) 3035, 2940, 2865, 1445, 1165, 1140, 1120, 1080, 1010, 690; ^1H NMR (300 MHz, $CDCl_3$) δ 5.92 (ddd, J = 9.7 Hz, 5.0 Hz, 1.1 Hz, 1 H), 5.81 (dd, J = 9.6 Hz, 5.0 Hz, 1 H), 5.62 (dd, J = 9.7 Hz, 3.0 Hz, 2 H), 3.85–3.66 (m, 2 H), 2.02–1.93 (m, 1 H), 1.81–1.61 (m, 3 H), 1.60–1.19 (m, 7 H), 1.14–1.08 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.0, 135.2, 123.8, 121.8, 78.1, 63.7, 38.0, 33.6, 31.4, 31.1, 22.8, 20.7, 19.7; MS m/z (M^+) calcd 190.1358, obsd 190.1355.

Anal. Calcd for $C_{13}H_{18}O$: C, 82.06; H, 9.53. Found: C, 81.95; H, 9.61.

The second compound to elute was **34** (13 mg, 20%): IR (neat, cm^{-1}) 3670–3090, 3010, 2930, 2860, 1580, 1450, 1050; ^1H NMR (300 MHz, $CDCl_3$) δ 7.38–6.95 (m, 3 H), 3.73 (t, J = 6.4 Hz, 2 H), 2.81 (t, J = 6.0 Hz, 2 H), 2.74 (t, J = 6.2 Hz, 2 H), 2.68 (t, J = 7.8 Hz, 2 H), 1.91–1.75 (m, 6 H), 1.60 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.9, 137.4, 135.0, 127.2, 12616, 125.2, 62.7, 32.9, 30.1, 28.9, 26.1, 23.4, 22.8; MS m/z (M^+) calcd 190.1358, obsd 190.1365.

Anal. Calcd for $C_{13}H_{18}O$: C, 82.06; H, 9.53. Found: C, 81.95; H, 9.48.

Acid-Catalyzed Rearrangement of 14. Into an NMR tube was placed **14** (77 mg, 0.40 mmol) and *p*-toluenesulfonic acid (4.8 mg, 2.6×10^{-5} mol) in $CDCl_3$ (1 mL). After 2 h, NMR analysis showed none of the starting material to remain. The solvent was evaporated, and the residue was chromatographed on silica gel (elution with 20% ethyl acetate in hexanes). The first compound to elute was **36**, a colorless solid: mp 68–70 °C (25 mg, 33%); IR ($CDCl_3$, cm^{-1}) 3035, 2960, 2870, 2250, 1435, 1210, 1085, 1070, 1030, 905, 720; ^1H NMR (300 MHz, $CDCl_3$) δ 6.72 (ddd, J = 9.6 Hz, 5.2 Hz, 1.4 Hz, 1 H), 5.97 (dd, J = 9.5 Hz, 5.2 Hz, 1 H), 5.76 (br d, J = 9.5 Hz, 1 H), 5.63 (br d, J = 9.6 Hz, 1 H), 3.95–3.87 (m, 2 H), 3.65–3.58 (m, 2 H), 1.88–1.80 (m, 2 H), 1.70–1.45 (m, 4 H), 1.43–1.34 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.4, 128.9, 127.9, 121.9, 98.4, 62.2, 38.0, 30.9, 21.1; MS m/z (M^+) calcd 192.1150, obsd 192.1152.

Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.38. Found: C, 74.54; H, 8.50.

The second compound to elute was **37** (22 mg, 29%): IR (neat, cm^{-1}) 3690–3100, 3020, 2950, 2870, 1590, 1470, 1455, 1215, 1190, 1050, 765, 740; ^1H NMR (300 MHz, $CDCl_3$) δ 6.95 (d, J = 7.3 Hz, 1 H), 6.91 (d, J = 7.5 Hz, 1 H), 6.78 (t, J = 7.4 Hz, 1 H), 4.21 (t, J = 5.2 Hz, 2 H),

3.60 (t, J = 6.2 Hz, 2 H), 2.80 (t, J = 6.5 Hz, 2 H), 2.68 (t, J = 7.2 Hz, 2 H), 2.04–1.95 (m, 3 H), 1.89–1.80 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.8, 129.3, 127.9, 127.8, 121.9, 119.9, 66.6, 61.9, 33.0, 25.6, 25.1, 22.5; MS m/z (M^+) calcd 192.1150, obsd 192.1150.

Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 75.02; H, 8.48.

Comparable treatment of a 1:1 mixture of **14** and **17** (316 mg, 1.64 mmol) with *p*-toluenesufonic acid (30 mg, 0.16 mmol) in dry CH_2Cl_2 (5 mL) for 24 h afforded 52 mg (17%) of **36** and 133 mg (42%) of **37**.

Acid-Catalyzed Rearrangement of 23. To an NMR tube was added a mixture of **23** (48 mg, 0.23 mmol) and *p*-toluenesulfonic acid (2.7 mg, 1.4×10^{-5} mol) in $CDCl_3$ (1 mL). After several hours, the solvent was evaporated, and the residue was chromatographed on silica gel (elution with 40% ethyl acetate and 1% triethylamine in hexanes) to give 25 mg (53%) of **47** as a colorless solid: mp 64–65 °C (from 10% ethyl acetate in hexanes); IR (neat, cm^{-1}) 3700–3120, 2950, 2880, 1455, 1060; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.00–6.97 (m, 2 H), 6.91–6.86 (m, 1 H), 3.70 (t, J = 6.3 Hz, 2 H), 2.99 (t, J = 6.0 Hz, 2 H), 2.80–2.76 (m, 2 H), 2.70–2.64 (m, 2 H), 2.18–2.10 (m, 2 H), 1.87–1.77 (m, 2 H), 1.38 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.5, 133.2, 132.2, 125.9, 125.3, 125.0, 62.5, 33.1, 29.3, 27.2, 25.1, 23.5; MS m/z (M^+) calcd 208.0922, obsd 208.0928.

Anal. Calcd for $C_{12}H_{16}OS$: C, 69.19; H, 7.74. Found: C, 68.95; H, 7.76.

Comparable treatment of **20** (34 mg) with *p*-toluenesulfonic acid (1.7 mg) in $CDCl_3$ (1 mL) for 2.5 days and silica gel chromatography furnished 14 mg (40%) of **47**.

(4a*R,8a*S**)-3,4,6,7-Tetrahydro-4a,8a-[1,3]butadieno-2*H*,5*H*-thiopyrano[2,3-*b*]pyran (48).** A solution of **23** (96 mg, 0.46 mmol) in $CDCl_3$ (5 mL) was kept at room temperature for 2 weeks on the benchtop. Periodic TLC analysis revealed the original disappearance of **23** and appearance of **47** and **48**. The solvent was evaporated, and the residue was chromatographed on silica gel (gradient elution with 20% ethyl acetate in hexanes and then 1:1 ethyl acetate–hexanes). The first compound to elute was **48** (11 mg, 11%), followed by the aromatic alcohol **47** (41 mg, 42%).

For **48**: colorless oil; IR (neat, cm^{-1}) 3040, 2960, 2860, 1720, 1685, 1460, 1445, 1290, 1250, 1210, 1150, 1080, 850, 725, 685; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.04–5.92 (m, 3 H), 5.75–5.72 (m, 1 H), 3.88–3.81 (m, 1 H), 3.75–3.67 (m, 1 H), 2.77–2.61 (m, 1 H), 2.55–2.47 (m, 1 H), 2.03–1.84 (m, 3 H), 1.79–1.65 (m, 3 H), 1.63–1.55 (m, 1 H), 1.53–1.42 (m, 1 H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 138.8, 134.9, 124.3, 123.8, 75.1, 62.6, 47.2, 32.0, 31.1, 25.7, 23.0, 21.7; MS m/z (M^+) calcd 208.0922, obsd 208.0924.

Anal. Calcd for $C_{12}H_{16}OS$: C, 69.19; H, 7.74. Found: C, 69.07; H, 7.80.

Acid-Catalyzed Rearrangement of 26. Into an NMR tube was added a mixture of **26** (54 mg, 0.24 mmol) and *p*-toluenesulfonic acid (4.6 mg, 2.5×10^{-5} mol) in $CDCl_3$ (1 mL). After 48 h, no remaining **26** was evident by NMR analysis, nor was the formation of any byproduct in evidence. The reaction mixture was flash chromatographed on neutral alumina (dichloromethane elution). Evaporation left **51** as a colorless oil: IR (neat, cm^{-1}) 3020, 2940, 2870, 1490, 1450, 1290, 1250, 750; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.19–7.11 (m, 4 H), 2.85–2.60 (m, 8 H), 2.05–1.89 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.2, 129.3, 126.2, 38.4, 31.2, 30.3; MS m/z (M^+) calcd 224.0693, 224.0700.

***o*-Bis[3-(methylthio)propyl]benzene (52).** A solution of **51** (49 mg, 0.22 mmol) in dry THF (5 mL) at 0 °C was treated with lithium aluminum hydride (14 mg, 0.37 mmol). After 10 min, methyl iodide (0.20 mL, 0.67 mmol) was introduced via syringe, and stirring was maintained for 30 min. The solvent was evaporated, and the residue was chromatographed on silica gel (elution with 5% ethyl acetate in hexanes) to furnish 32 mg (57%) of **52** as a colorless oil: IR (neat, cm^{-1}) 2914, 2851, 1487, 1436, 1287, 1256, 749; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.19–7.12 (m, 4 H), 2.80–2.71 (m, 4 H), 2.59–2.53 (m, 4 H), 2.12 (s, 6 H), 1.94–1.84 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.4, 129.3, 126.1, 34.0, 31.5, 30.4, 15.5; MS m/z (M^+) calcd 254.1163, obsd 254.1160.

Anal. Calcd for $C_{14}H_{22}S_2$: C, 66.09; H, 8.71. Found: C, 66.23; H, 8.78.

11,12-Epoxy-3,4,6,7-tetrahydro-8a,4a-[1]buteno-2*H*,5*H*-pyrano[2,3-*b*]-pyran (53). A solution of **36** (35 mg, 0.18 mmol) in CH_2Cl_2 (2 mL) was stirred vigorously with an aqueous solution of $NaHCO_3$ (46 mg, 0.55 mmol) in water (2 mL). This two-phase mixture was treated over 5 min with MCPBA (32 mg, 0.18 mmol) in approximately 10 mg lots. Additional MCPBA was added (50 mg, in 10 mg lots every 12 h) when TLC analysis revealed that starting material remained. Stirring was maintained for 4 days, after which time the organic phase was separated, and the aqueous phase was extracted with CH_2Cl_2. The combined organic layers were washed successively with 10% NaOH solution and water, dried, and evaporated. The residual oil was chromatographed on silica gel (elution with 30% ethyl acetate in hexanes) to afford 20 mg (53%) of **53** as a colorless solid: mp 96–104 °C; IR ($CDCl_3$, cm^{-1}) 2975, 2955, 2880, 1450, 1225, 1175, 1080, 1035, 975, 840; ^{1}H NMR (300 MHz, acetone-d_6) δ 6.19 (dd, J = 10.0 Hz, 3.9 Hz, 1 H), 5.62 (dd, J = 1.6 Hz, 10.0 Hz, 1 H), 3.86–3.73 (m, 2 H), 3.50–3.41 (m, 2 H), 3.14 (dt, J = 3.9 Hz, 1.6 Hz, 1 H), 3.01 (d, J = 4.0 Hz, 1 H), 2.26 (dt, J = 13.3 Hz, 4.2 Hz, 1 H), 2.02–1.92 (m, 1 H), 1.86–1.70 (m, 1 H), 1.62 (dddd, J = 13 Hz, 3.5 Hz, 3.5 Hz, 2 Hz, 1 H), 1.48–1.27 (m, 4 H); ^{13}C NMR (75 MHz, acetone-d_6) δ 136.9, 129.6, 96.1, 64.8, 61.9, 61.7, 45.2, 33.9, 32.1, 28.2, 23.2, 21.0; MS m/z (M^+) calcd 208.1099, obsd 208.1104.

Anal. Calcd for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74. Found: C, 68.76; H, 7.69.

Diels–Alder Addition of *N*-Methyltriazolinedione to the [4.4.4]Propelladienes. (A) 3,4-Dihydro-*N*-methyl-8a,4a-(epoxypropano)-5,8-etheno-2*H*-pyrano[2,3-*d*]pyridazine-6,7(5*H*,8*H*)-dicarboximide (54). A solution of freshly sublimed *N*-methyltriazolinedione (12 mg, 0.11 mmol) in CH_2Cl_2 (2 mL) at –78 °C was added via cannula to a solution of **36** (20 mg, 0.10 mmol) in CH_2Cl_2 (3 mL) at the same temperature. The red solution was warmed to room temperature, where stirring was maintained for 5 days. Chromatography on silica gel (elution with 1:1 ethyl acetate in hexanes) yielded unreacted **36** (3 mg, 15%), followed by **54** (23 mg, 73%) as a colorless solid: mp 202–203 °C (from 30% ethyl acetate in hexanes); IR (KBr, cm^{-1}) 3080, 2970, 2900, 1780, 1720, 1455, 1395, 1275, 1210, 1090, 1065, 785; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.44–6.35 (m, 2 H), 4.54 (dd, J = 5.3 Hz, 2.0 Hz, 1 H), 4.29 (dd, J = 5.2 Hz, 2.0 Hz, 1 H), 4.05–3.84 (m, 3 H), 3.76–3.67 (m, 1 H), 2.99 (s, 3 H), 2.20–2.10 (m, 1 H), 1.92–1.62 (m, 5 H), 1.59–1.51 (m, 1 H), 1.47–1.37 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.9, 157.5, 129.5, 129.3, 96.4, 63.6, 61.5, 60.1, 60.0, 37.5, 31.7, 30.1, 25.4, 21.1, 19.1; MS m/z (M^+) calcd 305.1376, obsd 305.1362.

Anal. Calcd for $C_{15}H_{19}N_3O_4$: C, 59.01; H, 6.27. Found: C, 59.03; H, 6.59.

(B) (4a*R,5*S**,8*R**,8a*R**)-3,4-Dihydro-*N*-methyl-4a,8a-butano-5,8-etheno-2*H*-pyrano[2,3-*d*]pyridazine-6,7(5*H*,8*H*)-dicarboximide (55).** A solution of freshly sublimed *N*-methyltriazolinedione (46 mg, 0.40 mmol) in CH_2Cl_2 (2 mL) at –78 °C was added via cannula to a solution of **35** (70 mg, 0.37 mmol) in CH_2Cl_2 (3 mL) at the same temperature. The red solution was warmed to room temperature, where stirring was maintained for 5 days. The solvent was evaporated, and the residue was chromatographed on silica gel (elution with 30% ethyl acetate in hexanes) to furnish 14 mg (21%) of recovered **35**, followed by 78 mg (70%) of **55**, a colorless solid: mp 131–133 °C (from 20% ethyl acetate in hexanes); IR (KBr, cm^{-1}) 2975, 2935, 2885, 1770, 1750, 1455, 1390, 1195, 785; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.49–6.38 (m, 2 H), 4.39 (dd, J = 5.4 Hz, 1.7 Hz, 1 H), 4.23 (dd, J = 5.5 Hz, 1.6 Hz, 1 H), 3.77–3.69 (m, 1 H), 3.65–3.57 (m, 1 H), 2.98 (s, 3 H), 2.18–2.01 (m, 2 H), 1.68–1.56 (m, 8 H), 1.49–1.33 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.9, 157.8, 129.9, 129.7, 75.1, 61.8, 61.2, 60.4, 38.3, 32.6, 32.1, 30.8, 25.4, 20.8, 18.3, 17.0; MS m/z (M^+) calcd 303.1583, obsd 303.1578.

Anal. Calcd for $C_{16}H_{21}N_3O_3$: C, 63.35; H, 6.98. Found: C, 63.26; H, 7.07.

(C) (4a*R,5*S**,8*R**,8a*R**)-3,4-Dihydro-*N*-methyl-8a,4a-(epithiopropano)-5,8-etheno-2*H*-pyrano[2,3-*d*]pyridazine-6,7(5*H*,8*H*)-dicarboximide (56).** A solution of freshly sublimed *N*-methyltriazolinedione (33 mg, 0.29 mmol) in CH_2Cl_2 (3 mL) at –78 °C was added via cannula to a solution of **48** (55 mg, 0.27 mmol) in CH_2Cl_2 (3 mL) at the same temperature. The red solution was warmed to room temperature, where stirring was maintained for 5 days. The solvent was evaporated, and the residue was chromatographed on silica gel (elution with 1:1 ethyl acetate–hexanes) to give 3.5 mg (4%) of **57**, followed by 70 mg (82%) of **56** as a colorless solid: mp 196–197 °C (from 75% ethyl acetate in hexanes); IR (KBr, cm^{-1}) 2950, 2890, 1775, 1460, 1395, 1195; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.56–6.51 (m, 1 H), 6.37–6.32 (m, 1 H), 4.54–4.50 (m, 2 H), 3.88–3.81 (m, 2 H), 2.94 (s, 3 H), 2.57 (t, J = 7.0 Hz, 2 H), 2.37 (td, J =13.5 Hz, 3.9 Hz, 1 H), 2.21–1.98 (m, 2 H), 1.96–1.86 (m, 1 H), 1.78–1.62 (m, 2 H), 1.46–1.37 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.1, 157.0, 130.9, 127.2, 73.2, 61.1, 59.8, 59.6, 47.3, 31.2, 28.8, 25.3, 24.8, 20.1, 17.5; MS m/z (M^+) calcd 321.1147, obsd 321.1142.

Anal. Calcd for $C_{15}H_{19}N_3O_3S$: C, 56.06; H, 5.96. Found: C, 56.00; H, 5.92.

The minor adduct **57** exhibited the following characteristic signals: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.48–6.43 (m, 1 H), 6.43–6.4 (m, 1 H), 4.60–4.54 (m, 2 H), 3.73–3.61 (m, 2 H), 3.02 (s, 3 H), 2.70–2.60 (m, 2 H).

Competition Experiments. (A) **Between 35 and 36.** A solution of freshly sublimed *N*-methyltriazolinedione (22 mg, 0.19 mmol) in CH_2Cl_2 (5 mL) at −78 °C was added via cannula to a solution containing **35** (41 mg, 0.21 mmol) and **36** (41 mg, 0.21 mmol) in CH_2Cl_2 (5 mL) at the same temperature. The red solution was warmed to room temperature, where stirring was maintained for 4 days. The solvent was evaporated, and the residue was chromatographed on silica gel (gradient elution with 30–40% ethyl acetate in hexanes) to give 20 mg (49%) of **35**, 25 mg (61%) of **36**, 13 mg (22%) of **55**, and 9 mg (16%) of **54**.

(B) **Between 36 and 48.** A solution of freshly sublimed *N*-methyltriazolinedione (10 mg, 9.1×10^{-5} mol) in CH_2Cl_2 (2 mL) at −78 °C was added via cannula to a solution containing **48** (23 mg, 0.11 mmol) and **36** (21 mg, 0.11 mmol) in CH_2Cl_2 (3 mL) at the same temperature. The red solution was warmed to room temperature and stirred for 4 days. ^{1}H NMR analysis revealed a 2.15:1 ratio of **56** to **54** to have been produced.

(C) **Between 35 and 48.** A solution of freshly sublimed *N*-methyltriazolinedione (14 mg, 0.12 mmol) in CH_2Cl_2 (2 mL) at −78 °C was added via cannula to a solution containing **48** (30 mg, 0.14 mmol) and **35** (27 mg, 0.14 mmol) in CH_2Cl_2 (3 mL) at the same temperature. The red solution was warmed to room temperature and stirred for 4 days. The solvent was evaporated, and the residue was chromatographed on silica gel (gradient elution with 10–70% ethyl acetate and 1% triethylamine in hexanes) to provide (in order) **35** (18 mg, 66%), **48** (13 mg, 42%), **55** (7 mg, 20%), and **56** (15 mg, 39%).

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Supplementary Material Available: Crystallographic experimental procedures and tables of X-ray crystal data, bond lengths and angles, final fractional coordinates, and thermal parameters for **8** (6 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.