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An Oxy-Cope Approach to Hydroazulenoids. Synthetic and Mechanistic Aspects of Thermal Cyclization Reactions[1]

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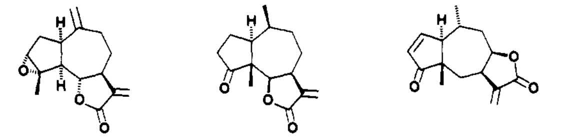
Abstract: The synthesis and thermal properties of C5-substituted oxy-Cope substrates are reported. In the *trans*-divinylcyclohexanol series, halomethyl substituents provided >80% isolated yield of the thermodynamically less stable *cis*-hydroazulenone **33** from either chloride **18** or bromide **19**. The complementary synthesis of *trans*-**35** was achieved from *cis*-divinyl-substituted bromide **25**, whereas chloride **24** underwent preferential ketonization to medium ring **38**. The energetic and stereochemical criteria of the thermoneutral oxy-Cope rearrangement–alkylation pathway were examined. Kinetic studies on the rearrangement of halides **18** and **19** established a moderately facile, highly ordered rate-determining step in which nonpolar, aprotic solvents provided the ideal reaction medium. Stereospecific labeling studies demonstrated regioselective bonding of the olefinic termini but also defined scrambling within the halomethylene carbon. Similar results were obtained under gas phase thermolysis conditions although chloride **24** was now directed to *trans*-**35**. A mechanistic interpretation of the results is presented.

The importance of cyclopentanoid natural products, interwoven with their rich diversity of molecular architecture, has continued to challenge the current level of synthetic methodologies. A prevailing trend has been to divide these systems into two main structural classes. The first group can be characterized by the presence of a tricycloundecane ring system, which is common to a growing list of natural products such as hirsutene, $\Delta^{9(12)}$-capnellene, coriolin, isocomene, pentalenene, modhephene, laurenene, and retigeranic acid.[2] The second group consists of fused-cyclopentanoid natural products. The structural characteristics of this class range from the sesquiterpene skeleton of the guaianolides and pseudoguaianolides, with their 5/7 ring system,[2-4] to the recently isolated nonisoprenoids precapnelladiene, dactylol, and poitediol, which contain a 5/8 ring system, as well as the rapidly growing list of sester- and diterpenoids of the ophiobolins, cereplastins, fusicoccin, and cycloaranosene variety, which share a 5/8/5 ring system.

Although numerous achievements in the synthesis of cyclopentanoid natural products have been reported,[2-4] most of the approaches have relied upon a stereochemical bias in the ring systems to control substitution patterns. Our strategy was to view all of these natural products as simple substituted cyclopentanoid rings; therefore, our goal was to develop new methodologies to construct five-membered rings with primary consideration given to potential mechanistic pathways that would allow a secure means of incorporating centers (and ideally relating remote centers) of stereochemistry. With these interests in mind we were intrigued by the untapped potential of sigmatropic rearrangements[5] to transfer their stereoselective generation of asymmetry into a cyclopentanoid rearrangement product.

For the initial development and subsequent application of our fundamental strategy, we envisioned a general stereocontrolled synthesis of the hydroazulenoid ring system, which constitutes the carbocyclic framework observed in the guaianolides and pseudoguaianolides (eq 1 and 2). This approach offers several ad-



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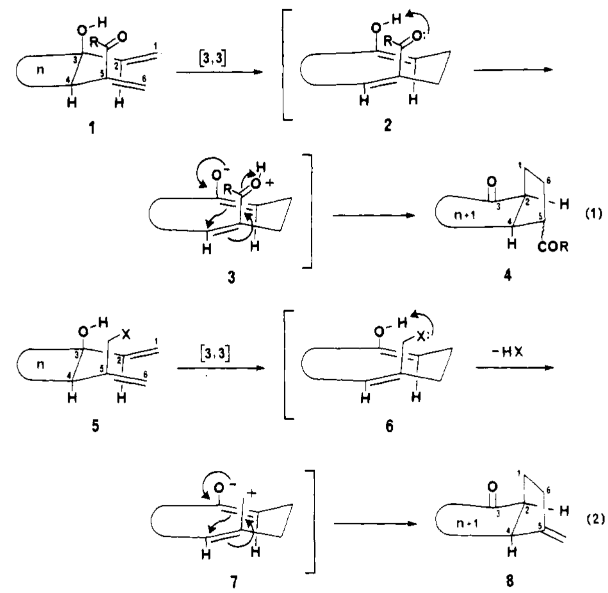
vantages over previous strategies for assembling the hydroazulene skeleton.[2,4,6] Since a successful cyclopentanoid ring closure step would also induce a one-carbon ring expansion, our pool of rearrangement precursors could be constructed from readily available six-membered ring synthons; with an important secondary benefit of having the six-membered ring as a secure template to establish stereochemistry. In addition, mild thermoneutral rearrangement conditions would provide access to the thermodynamically less stable *cis*-hydroazulenone ring system.

The Cope rearrangement and its variants are powerful reactions that transfer stereochemistry via well-defined transition states.[5] Our strategy was to incorporate latent functionality into oxy-Cope precursors which upon rearrangement would irreversibly trap the mildly nucleophilic enol (eq 1 and 2). Since an initial enolic



proton transfer step appeared to be crucial to the success of this approach, we chose to examine the effectiveness of both Michael addition (**2** → **3** → **4**)[7] and alkyl halide alkylation (**6** → **7** → **8**)

(1) For a preliminary account of part of this work, see: Sworin, M.; Lin, K.-C. *J. Org. Chem.* **1987**, *52*, 5640.

(2) For an excellent review of synthetic activity in the sesquiterpenoid area through 1980, see: Heathcock, C. H.; Graham, S. L.; Pirrung, M. C.; Plavac, F.; White, C. T. In *The Total Synthesis of Natural Products*; ApSimon, J. W., Ed.; Wiley-Interscience: New York, 1982; Vol. 5, pp 333–384, 405–423.

(3) For the distribution and biological activity of these sesquiterpenoid lactones, see: Fischer, N. H.; Olivier, E. J.; Fischer, H. D. *Fortschr. Chem. Org. Naturst.* **1979**, *38*, 47. Rodriquez, E.; Towers, G. H. N.; Mitchell, J. C. *Phytochemistry* **1976**, *15*, 1573.

(4) For recent syntheses, see: Rigby, J. H.; Senanayake, C. *J. Am. Chem. Soc.* **1987**, *109*, 3147. Schultz, A. G.; Motyka, L. A.; Plummer, M. *J. Am. Chem. Soc.* **1986**, *108*, 1056. Saha, M.; Bagby, B.; Nicholas, K. M. *Tetrahedron Lett.* **1986**, *27*, 915. Rigby, J. H.; Wilson, J. Z. *J. Am. Chem. Soc.* **1984**, *106*, 8217 and references therein.

(5) For reviews, see: Hill, R. K. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: Orlando, 1984; Vol. 3, Chapter 8. Rhoads, S. J.; Raulins, N. R. *Org. React.* **1975**, *22*, 1.

(6) Cf.: Heathcock, C. H.; DelMar, E. G.; Graham, S. L. *J. Am. Chem. Soc.* **1982**, *104*, 1907. Heathcock, C. H.; Tice, C. M.; Germroth, T. C. *J. Am. Chem. Soc.* **1982**, *104*, 6081.

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reactions to induce the intramolecular ring closure step.

When the vinyl substituents are oriented trans in oxy-Cope substrate **1** sigmatropic rearrangement through a chairlike transition state generates *trans,trans*-dienol **2**, in which H_2 and H_4 have a cis relationship. If proton transfer to the carbonyl is more facile than ketonization, then zwitterion **3** would ensue, followed by a rapid intramolecular ring closure step to provide only the cis-fused cyclopentanoid **4** (eq 1). Our hope was that this "push-pull" approach would not only enhance the Michael addition ring closure but would also ensure stereocontrol in the *cis*-divinyl-substituted series. Further activation was also envisioned via charge-accelerated catalysis[8] of the Cope sequence, which offers the secondary benefit of an enhanced ring closure step (e.g. cation transfer).

When the vinyl substituents are oriented cis, two conformers of **1** can undergo rearrangement via chairlike transition states. However, only one of the medium rings, *trans,cis*-dienol **2**, in which H_2 and H_4 have a trans relationship, has the enol and carbonyl in the proper orientation to effect an intramolecular proton transfer step (or cation exchange) and would thus provide only trans-fused cyclopentanoid **4**.

The stereochemical outcome of rearrangements in the alkylation-based series (eq 2) parallels the discussions of the Michael-type acceptors (eq 1) with some subtle differences. The overall conversion of **5** → **8** requires the irreversible loss of an HX molecule in the rearrangement-alkylation pathway.[9] If we invoke a proton transfer step, then **6** would generate zwitterion **7**; however, alternate structures that may more accurately describe the nature of **7** could also intervene.

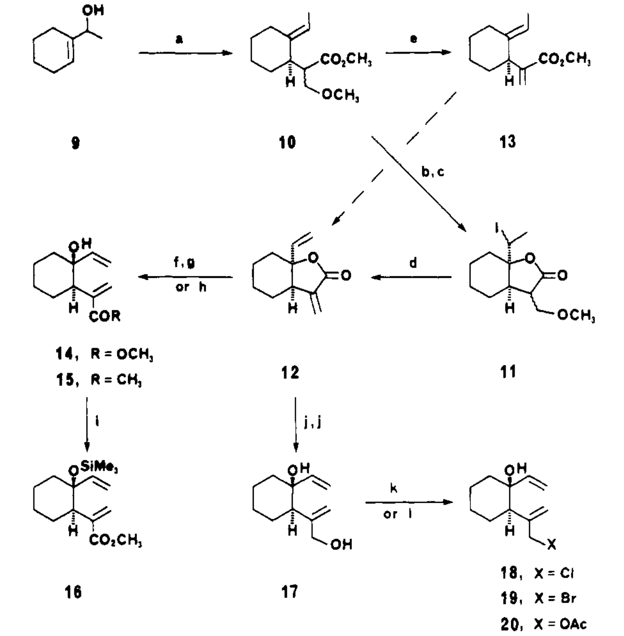
Results

Substrate Synthesis. In order to examine a variety of C5 electrophilic substituents, we required a synthesis of a highly functionalized synthon which could be converted into *trans*-divinylcyclohexanols. With this in mind, we prepared *cis*-α-methylene lactone **12** as outlined in Scheme I.

A convenient one-step assembly of the carbon framework was accomplished via the Claisen rearrangement of allylic alcohol **9**,[10] using the functionalized ortho ester described by Raucher,[11] to give masked acrylate **10** in 91% yield. The resulting strategic location of the olefinic functionality allowed the facile conversion of **10** into α-methylene lactone **12** by two related routes.[12] Saponification of ester **10**, followed by iodolactonization to **11**, and subsequent DBU-initiated elimination of both HI and MeOH provided **12** in four steps and 62% overall yield from **9**. Alternately, **10** was deprotected by *t*-BuOK-initiated elimination of MeOH to acrylate **13**, followed by a similar reaction sequence to provide **12** in five steps and 74% overall yield from **9**.

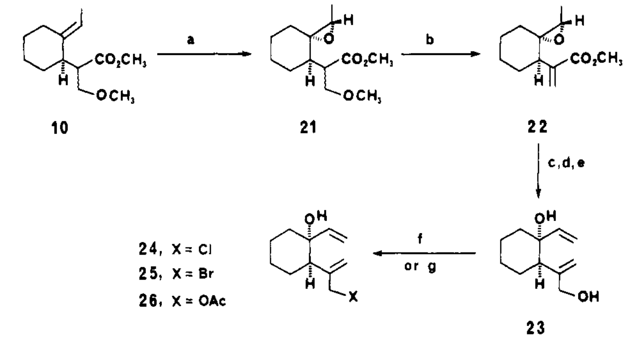
The conversion of lactone **12** into the Michael acceptors methyl ester **14** (99%) and methyl ketone **15** (96%) was accomplished by NaOH hydrolysis[13] followed by CH_2N_2 and by the addition of 1 equiv of MeLi at −78 °C, respectively (Scheme I). Ester **14** was converted to TMS ether **16** (90%) via standard silylation conditions. The alkylation-based substrates were prepared by the stepwise reduction of lactone **12** with DIBAL[14] to afford crystalline diol **17** in 89% overall yield, followed by selective exchange of the primary alcohol with Ph_3PCX_4[15] to provide chloride **18** (95%) and

Scheme I^a



^{a}Reagents: (a) $CH_3OCH_2CH_2C(OCH_3)_3$, H^+(cat.), 140 °C, 91%; (b) KOH, H_2O, CH_3OH; (c) KI_3, $NaHCO_3$, H_2O; (d) DBU, toluene, 110 °C, 69% from **10**, 83% from **13**; (e) *t*-BuOK, THF, 0 °C, 98%; (f) NaOH, H_2O; (g) CH_2N_2, Et_2O, 0 °C, 99% from **12**; (h) CH_3Li, Et_2O, THF, −78 °C, 96%; (i) TMSCl, HMDS, DMAP, pyridine, 90%; (j) DIBAL, CH_2Cl_2, hexane, −78 °C, 89% overall; (k) CCl_4 or CBr_4, PPh_3, CH_3CN, 95% for **18**, 90% for **19**; (l) Ac_2O, pyridine, 0 °C, 94%.

Scheme II^a



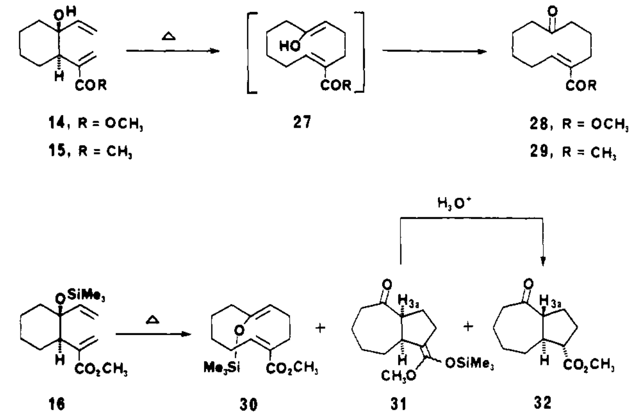
^{a}Reagents: (a) *m*-CPBA, CH_2Cl_2, $NaHCO_3$, H_2O, 0 °C, 99%; (b) *t*-BuOK, THF, −78 °C, 76%; (c) DIBAL, CH_2Cl_2, hexane, −78 °C; (d) PhSeSePh, $NaBH_4$, EtOH, 78 °C; (e) 30% H_2O_2, 0 °C → RT, 60% overall; (f) CCl_4 or CBr_4, PPh_3, CH_3CN, 90% for **24**, 80% for **25**; (g) Ac_2O, pyridine, 0 °C, 98%.

bromide **19** (90%). Diol **17** was also converted to acetate **20** (94%) with Ac_2O/pyridine (Scheme I).

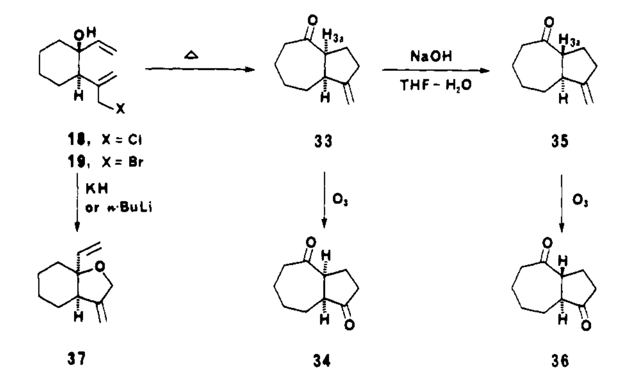
Access to the isomeric *cis*-divinyl-substituted series also employed masked acrylate **10** (Scheme II). Selective epoxidation of **10** from the equatorial face with buffered *m*-CPBA at 0 °C,[16] followed by *t*-BuOK-initiated elimination of MeOH at −78 °C,[11] provided a single epoxy ester **22** in 75% overall yield. Various attempts to convert epoxide **22** to the corresponding tertiary allylic alcohol by either deprotonation–β-elimination[17] or by benzeneselenolate opening of the epoxide[18] were unsuccessful, generally yielding complex mixtures of cyclization products via intramolecular epoxide ring opening. However, when epoxy ester **22** was first reduced with DIBAL at −78 °C[14] to the labile epoxy alcohol, followed by the dropwise addition of an ethanolic solution of this crude material into a solution of PhSeNa/EtOH at reflux[18] and

(7) Coates, R. M.; Hobbs, S. J. *J. Org. Chem.* **1984**, *49*, 140.
(8) For an excellent review through mid-1983, see: Lutz, R. P. *Chem. Rev.* **1984**, *84*, 205 and references therein.
(9) For a comprehensive discussion of alkyl halide pyrolysis reactions, see: (a) Maccoll, A. *Chem. Rev.* **1969**, *69*, 33. (b) Egger, K. W.; Cocks, A. T. In *The Chemistry of the Carbon–Halogen Bond*, Part 2; Partai, S., Ed.; Wiley: London, 1973; Chapter 10, pp 716–721, 728–739.
(10) Available on large scale from Ce(III)-catalyzed $NaBH_4$ reduction of acetylcyclohexene. Cf.: Gemal, A. L.; Luche, J.-L. *J. Am. Chem. Soc.* **1981**, *103*, 5454.
(11) Raucher, S.; Macdonald, J. E.; Lawrence, R. F. *Tetrahedron Lett.* **1980**, *21*, 4335.
(12) For a recent review on the synthesis of α-methylene lactones, see: Hoffman, H. M. R.; Rabe, J. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 94.
(13) Morton, D. R.; Thompson, J. L. *J. Org. Chem.* **1978**, *43*, 2102.
(14) Winterfeldt, E. *Synthesis* **1975**, 617. Nagaoka, H.; Kishi, Y. *Tetrahedron* **1981**, *37*, 3873.
(15) Appel, A. *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 801.
(16) Anderson, W. K.; Veysoglu, T. *J. Org. Chem.* **1973**, *38*, 2267.
(17) Thummel, R. P.; Rickborn, B. *J. Org. Chem.* **1971**, *36*, 1365.
(18) Nicolaou, K. C.; Petasis, N. A. *Selenium in Natural Products Synthesis*; CIS: Philadelphia, 1984; pp 123–127.

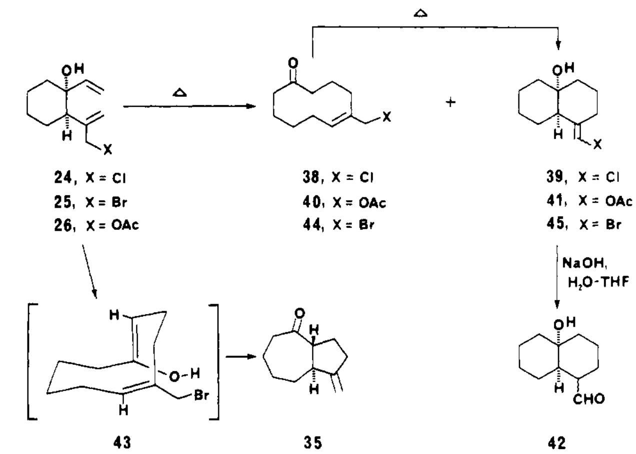
Scheme III



Scheme IV



Scheme V



subsequent in situ oxidative removal of the phenylseleno group, a 60% overall yield of crystalline diol **23** was obtained. Conversion of the *cis*-divinyl-substituted diol **23** to chloride **24** (90%), bromide **25** (80%), and acetate **26** (98%) was accomplished by identical reaction sequences as employed for *trans*-diol **17**.

Thermal Rearrangements. Our study on the feasibility of trapping an oxy-Cope intermediate commenced with methyl ester **14** and methyl ketone **15** (Scheme III). When a solution of ester **14** in dodecane was added to a preheated flask of dodecane at reflux ($T \approx 190$ °C) only the medium ring ester **28** (92%) was recovered. All attempts to employ higher reaction temperatures (up to 255 °C) to induce competitive proton transfer were unsuccessful, the sole product being ester **28** via rapid ketonization of the intermediate enol. Similar results were obtained with the methyl ketone (**15** → **29**).[7,19]

To overcome the rapid ketonization of enol **27** and to provide a protected intermediate for "proton" transfer, we investigated silyl ether **16** (Scheme III). The Cope rearrangement of **16** was extremely sluggish compared to that of the unprotected ester **14**, providing only ~10% conversion to enol ether **30** after 9 h at 190 °C versus 100% conversion after 15 min, respectively. However, when silyl ether **16** was heated at 255 °C in toluene for 22 h, all of the starting material was consumed and two major products, enol ether **30** (28%) and ketene acetal **31** (32%), were isolated after chromatographic purification.[20] Also detected in the crude reaction mixture was a minor amount of keto ester **32**, which arises from partial hydrolysis of silyl ketene acetal **31**.[20]

Although we had successfully trapped an enol ether in the Michael addition series to provide hydroazulenoid **32**, albeit in modest yields (up to ~35%), we have not pursued this approach because of more promising results in the complementary alkylation-based series.

When allylic chloride **18** was heated at 210 °C in cyclohexane for 2 h with excess propylene oxide as HCl scavenger,[21] *cis*-hydroazulenone **33** was obtained as the only product in 81% yield after chromatographic purification (Scheme IV). Propylene oxide was crucial to the stereochemical integrity of the rearrangement–alkylation sequence; amine bases were generally ineffectual,[22] the major product with Et_3N was ether **37** along with minor amounts of the isomeric *trans*-hydroazulenone **35** via in situ equilibration of the sensitive *cis*-**33**. The thermodynamic preference for the trans ring fusion was confirmed by base-catalyzed equilibration of *cis*-**33** → *trans*-**35**.[23] The stereochemistry of both hydroazulenones was unambiguously demonstrated by ozonolysis of *cis*-**33** to the known *cis*-bicyclo[5.3.0]decane-2,8-dione (**34**)[24] and of *trans*-**35** to the known *trans*-**36**[24] (Scheme IV). The isomeric composition of these hydroazulenones can be readily discerned by ^{1}H NMR spectral data. In each pair of isomers a prominent change in the chemical shift of H_{3a} was observed with the cis isomers being downfield of the trans by $\Delta\delta$ 0.30–0.36. Specifically, for *cis*-**33** H_{3a} was observed at δ 3.13 while *trans*-**35** exhibited a resonance for H_{3a} at δ 2.83. The thermal reaction of allylic bromide **19** demonstrated similar efficiency in the rearrangement–alkylation sequence providing a 75% isolated yield of *cis*-**33**.

After having accomplished one of our major goals, to efficiently prepare the thermodynamically less stable *cis*-hydroazulenone ring system from *trans*-divinyl-substituted precursors, we directed our efforts to the isomeric rearrangement series. If our original hypothesis remains valid, then *cis*-divinyl-substituted halides **24** and **25** would provide a complementary synthesis of *trans*-hydroazulenone **35**. In contrast to the earlier study, rearrangements in this series were substantially more complex (Scheme V).

When *cis*-chloride **24** was heated at 204 °C in cyclohexane for 2 h, two major products, *cis*-cyclodecenone **38** (49%) and vinyl chloride **39**, (20%) were obtained after chromatographic purification (Scheme V). A minor amount of the desired *trans*-**35** was apparent in the crude reaction mixture, but in comparison to the clean results obtained with *trans*-chloride **18**, the major pathway

(19) (a) Our results suggest that proton transfer in enol **27** to generate an allyl oxonium cation–enolate anion intermediate is unfavorable, and since the oxy-Cope rearrangement provides a quantitative enolic content, activation of the thermal Michael reaction must be largely determined by enolic acidity. (b) In a recent study Coates and Curran have eliminated the proposed Claisen rearrangement of intermediate enol ethers as the rate-determining step. Cf.: Coates, R. M.; Rogers, B. D.; Hobbs, S. J.; Peck, D. R.; Curran, D. P. *J. Am. Chem. Soc.* **1987**, *109*, 1160.

(20) On the basis of the stereochemical requirements for an intramolecular silyl migration, the ring junction stereochemistry of ketene acetal **31** has tentatively been assigned as cis. Hydrolysis of **31** provided a single ketoester **32** (81%) with the structure and relative stereochemistry assigned on the basis of its ^{1}H NMR, ^{13}C NMR, DEPT, DQCOSY, HETCOR, and IR spectral data. A trans ring junction is dictated by the upfield resonance of H_{3a} at δ 2.78; this equilibration likely occurred during the acid catalyzed hydrolysis step.

(21) Corey, E. J.; Danheiser, R. L.; Chandrasekaran, S.; Keck, G. E.; Gopalan, B.; Larsen, S. D.; Siret, P.; Gras, J.-L. *J. Am. Chem. Soc.* **1978**, *100*, 8034.

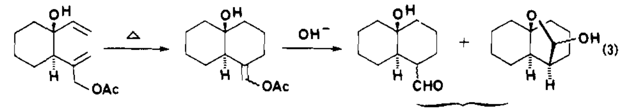
(22) Two exceptions were 2,6-di-*tert*-butylpyridine and 1,8-bis(dimethylamino)naphthalene.

(23) The observed ratio at equilibrium (mass balance >98%) was approximately 84:16 (*trans*-**35**/*cis*-**33**) via capillary GC analysis.

(24) Weller, T.; Seebach, D.; Davis, R. E.; Laird, B. B. *Helv. Chim. Acta* **1981**, *64*, 736.

now involved ketonization of the intermediate enol. The intermediacy of **38** in vinyl chloride **39** formation was clearly established by subjecting a pure sample of *cis*-cyclodecenone **38** to the rearrangement reaction conditions. This type of transannular ene closure (**38** → **39**) has previously been exploited by Wender, Williams, and others to access *trans*-decalin derivatives from photoadduct substrates.[25] To unambiguously establish the structure and relative stereochemistry of *cis*-decalin **39** beyond spectroscopic means, we examined the thermal properties of the corresponding *cis*-acetate **26** versus those of the *trans*-acetate **20**.

When *cis*-acetate **26** was heated at 204 °C in cyclohexane for 4 h, medium ring acetate **40** (30%) and vinyl acetate **41** (32%) were obtained in approximately a 1:1 ratio (Scheme V). Under identical conditions *trans*-acetate **20** provided only a single product, vinyl acetate **46**, in 96% yield (eq 3). At reaction temperatures



(3)

20 **46** **47**

as low as 166 °C no intermediates in the conversion of **20** → **46** could be detected, while the intermediacy of **40** in vinyl acetate **41** formation was established by a control reaction.

Vinyl acetates **41** and **46** exhibit similar spectroscopic properties with the most prominent difference in the chemical shift of the vinyl proton δ 6.96 (d, J = 1.9 Hz) versus δ 6.68 (s), respectively. To eliminate the possibility that we simply had isomeric olefinic acetates, each was hydrolyzed to the corresponding aldehyde. *cis*-Decalinol **42** predominantly exists in one isomeric form, while *trans*-decalinol **47** exhibits a complex mixture of aldehydes (1:7.2) and lactols (1.4:8.2) via ^{1}H NMR spectral analysis. By analogy this sequence establishes a cis ring fusion in vinyl chloride **39** and also demonstrates a highly stereospecific oxy-Cope transannular ene sequence to isomeric decalins with the overall rate of ring closure being strongly influenced by the configuration of the intermediate cyclodec-5-enones.

Although *cis*-chloride **24** proved to be ineffective at inducing ring closure, the simple substitution of *cis*-bromide **25** dramatically shifted the product distribution in this series. When bromide **25** was heated at 155 °C in benzene for 7 h, *trans*-hydroazulenone **35** and medium-ring bromide **44** were obtained in 90% yield based upon unreacted bromide **25** (14%) and in a 5:1 ratio, respectively. None of the *cis*-hydroazulenone **33** could be detected in the reaction mixture. The exclusive formation of **35** and **44** requires preferential rearrangement of bromide **25** via a single chairlike transition state to *trans,cis*-cyclodecadienol **43**, which can undergo either intramolecular ring closure or ketonization (Scheme V).

Recent work on controlling the product distribution have improved the ratio of *trans*-**35** to cyclodecenone **44** to >20:1 by the use of freshly distilled solvents along with a 3-fold increase in propylene oxide concentration.[26]

Mechanistic Overview. Because of the complexity of this bond-reorganization process, along with the contrasting behavior of the substrates to induce ring closure, we were concerned about the function of the halomethyl group and the role of subtle changes in reaction conditions on the overall mechanistic pathway. In our original working hypothesis we envisioned an initial [3,3]-sigmatropic rearrangement followed by a thermal alkylation with concurrent loss of HX. Since alternate mechanisms with similar topographical constraints are certainly possible, any mechanistic evaluation of the rearrangement pathway must delineate the involvement of the halogen in the formal loss of HX and provide information on both the electronic state and general timing of this process.[9]

(25) Wender, P. A.; Hubbs, J. C. *J. Org. Chem.* **1980**, *45*, 365. Wender, P. A.; Letendre, L. J. *J. Org. Chem.* **1980**, *45*, 367. Williams, J. R.; Callahan, J. F. *J. Org. Chem.* **1980**, *45*, 4475, 4479. Williams, J. R.; Callahan, J. F.; Lin, C. *J. Org. Chem.* **1983**, *48*, 3162. Lange, G. L.; Lee, M. *J. Org. Chem.* **1987**, *52*, 325 and references therein.

(26) Unpublished results of H. S. Ateeq. The isolated yield of *trans*-**35** under these reaction conditions was 62–68%.

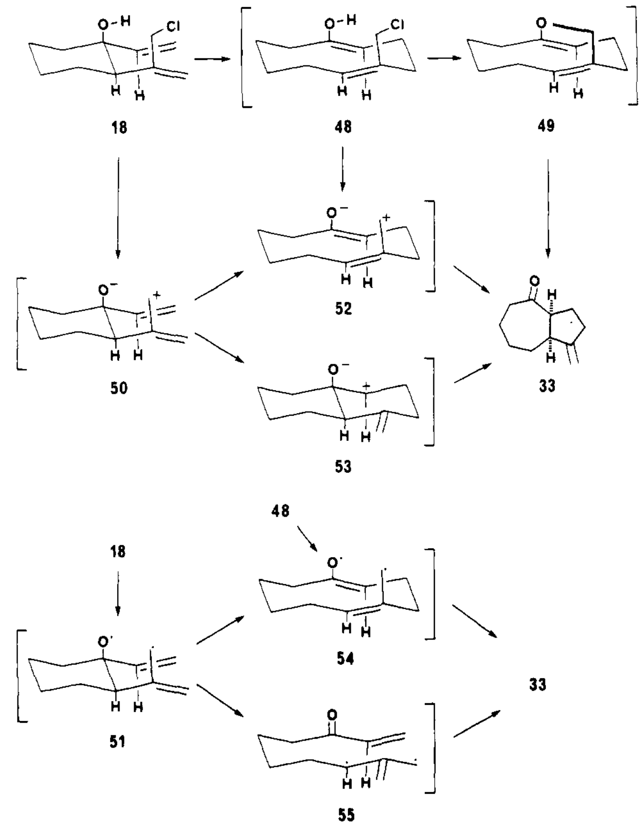


Figure 1.

Figure 1 represents a range of mechanistic possibilities for the transformation of the halomethyl substrates to hydroazulenones (the specific conversion of chloride **18** → *cis*-**33** being illustrated). In actuality these must be viewed as the mechanistic extremes since the stepwise loss of H and X along with the intervention of ion pairs or semiion pairs may be involved.[9] In what could be viewed as the ideal sigmatropic pathway, chloride **18** could undergo an oxy-Cope rearrangement to enol **48** followed by a four-centered loss of HCl to bicyclic ether **49**. A rapid Claisen rearrangement of the bridgehead diene **49** would thus provide *cis*-hydroazulenone **33** with overall retention of stereochemistry (vide infra). To invoke a Claisen rearrangement pathway does not require the intermediacy of ether **49** since loss of HCl from enol **48** could constitute a pair of isolated allyl units in which zwitterion **52** or diyl **54** could be viewed as reactive intermediates that are intercepted in the formal conversion of **49** → **33**.[27–29] If the bond-reorganization pathway involves an initial loss of HCl from chloride **18**, then either zwitterion **50** or diyl **51** could be formed. A charge-accelerated [3,3]-sigmatropic rearrangement of these "push–pull" systems[30] would provide an alternate pathway to **52** and **54**, respectively, followed by the "Claisen-like" ring closure to *cis*-hydroazulenone **33**. Zwitterion **50** could also undergo a stepwise

(27) There have been many insightful discussions on the variable nature of the transition state in [3,3]-sigmatropic rearrangements. For recent developments and leading references, see: (a) Dewar, M. J. S.; Jie, C. *J. Am. Chem. Soc.* **1987**, *109*, 5893. (b) Barluenga, J.; Aznar, F.; Liz, R.; Bayod, M. *J. Org. Chem.* **1987**, *52*, 5190. (c) Wilcox, C. S.; Babston, R. E. *J. Am. Chem. Soc.* **1986**, *108*, 6636. (d) Doering, W. von E.; Troise, C. A. *J. Am. Chem. Soc.* **1985**, *107*, 5739. (e) Gajewski, J. J.; Gilbert, K. E. *J. Org. Chem.* **1984**, *49*, 11.

(28) For a systematic study of substituent effects on the Claisen rearrangement, see: (a) Burrows, C. J.; Carpenter, B. K. *J. Am. Chem. Soc.* **1981**, *103*, 6983, 6984. (b) Cf. ref 19b.

(29) This discussion requires a less than ideal spacial orientation of the allyl groups to achieve an energy minimum on the reaction coordinate, otherwise they represent the transition state in the "concerted" rearrangement of **49** → **33**.

(30) These systems formally combine the charge-acceleration effect of a C3-alkoxide with a C5-carbocation; cf. ref 8. The additive effect of radical-stabilizing groups to accelerate Cope rearrangements has also been discussed; cf. ref 27a and 27e.

Table I. Rate Constants, Relative Rates, and Activation Parameters[a]

entry	T, °C	solvent	$10^5 k_{obs}$, s^{-1}	k_{rel}
1	188	c-C_6H_{12}	13.7 ± 0.2	(1.0)
2	188	C_6H_6	14.3 ± 0.7	~1.0
3	188	CH_2Cl_2	6.57 ± 0.20[b]	0.5
4	188	CH_3CN	*c*	*c*
5 (DBP)[d]	188	c-C_6H_{12}	9.84 ± 0.23	0.7
6 (Br)[e]	188	c-C_6H_{12}	21.6 ± 0.7	1.6
7	155.5	c-C_6H_{12}	1.79 ± 0.02	
8	166	c-C_6H_{12}	3.17 ± 0.07	
9	174.5	c-C_6H_{12}	7.05 ± 0.29	
10	202	c-C_6H_{12}	29.2 ± 1.0	

$\Delta H^{\ddagger} = 23.6 \pm 1.0$ kcal/mol
$\Delta S^{\ddagger} = -25.8 \pm 3.8$ eu
$\Delta G^{\ddagger} = 35.3 \pm 2.0$ kcal/mol

[a] Rate constants represent hydroazulenone formation, $k_{obs} = \{\ln [\mathbf{18}_0/(\mathbf{18}_0 - \mathbf{33})]\}/t$, uncertainties are standard deviations, activation parameters are reported at the mean temperature of 452 K. [b] Ether **37** was a minor product, $k_{obs} = 0.86 \times 10^{-5}$ s^{-1}. [c] Ether **37** was the major product. [d] 2,6-Di-*tert*-butylpyridine (2 equiv) was employed as HCl scavenger. [e] Rate data for bromide **19**.

cationic cyclization pathway to decalin **53** with a subsequent "pinacol-like" rearrangement yielding *cis*-**33**,[31] whereas the conversion of diyl **51** to *cis*-**33** could involve initial fragmentation of the cyclohexane ring to 1,3-diyl **55** followed by a cycloaddition reaction.[32]

In addition to the thermoneutral loss of HX, it is possible to envision several favorable stepwise processes that could catalyze the rearrangement pathway. Propylene oxide could participate as a base to induce heterolytic O–H bond cleavage in either the oxy-Cope precursors or the subsequent enols, while ionization of the C–X bond would provide a resonance-stabilized carbocation which could accelerate an electrophilic sequence.[31] Although it was possible to infer an initial oxy-Cope rearrangement from the competitive formation of cyclodecenones **38** and **44**, we examined both the energetic and stereochemical criteria of the bond-reorganization sequence to establish the ultimate role of halomethyl substituents to direct the mechanistic pathway.

Kinetic Studies. Since we could not detect any other reaction products in the conversion of *trans*-chloride **18** to *cis*-hydroazulenone **33** we investigated the rate of rearrangement of chloride **18** in various solvents, the relative rate of bromide **19** versus that of chloride **18**, and the activation parameters for **18** → **33** in cyclohexane. These results are summarized in Table I, and with the exception of entry 5 all rate constants represent pseudo-first-order kinetic data. Each experiment monitored both the disappearance of starting halide and the formation of *cis*-**33** versus the concentration of an internal standard; quantitation was achieved with relative response factors determined from a calibration curve. With the exception of entries 4 and 5, the mass balance for the conversion of **18**, **19** → **33** over several half-lives was >95%.

Protic solvents were totally detrimental to the rearrangement pathway; when anhydrous ethanol was employed as the solvent, only ether **37** was obtained. A brief evaluation of cyclohexane–ethanol solvent mixtures showed that they achieved a slower conversion of **18** → **37** but with no detectable evidence of *cis*-hydroazulenone formation. The most efficient rearrangements occurred in nonpolar, aprotic solvents (entries 1 and 2); essentially identical rates were observed in both cyclohexane and benzene for **18** → **33**. Interestingly, the use of halogenated solvents impeded this conversion; in CH_2Cl_2 (entry 3) a negative rate enhancement of 0.5-fold was observed, along with a minor, competitive pathway to ether **37**. More polar solvents[33] such as THF and CH_3CN (entry 4) strongly favored intramolecular ether formation with only a minor amount of *cis*-**33** being detected by VPC.

In view of the dramatic effect of the halogen to direct ring closure in the *cis*-divinyl-substituted precursors, the substitution of bromide **19** (entry 6) for chloride **18** provided only a modest 1.6-fold increase in the rate of *cis*-hydroazulenone **33** formation. This suggests that the primary participation and subsequent fragmentation of the C–X bond occurs after an initial rate-determining step. In an attempt to establish the reaction order, and hence the role of propylene oxide on the rearrangement pathway, several amine bases were evaluated as HCl scavengers. Unfortunately, a substantial decrease in the mass balance was observed primarily due to partial polymerization of allylic chloride **18**.[34] The only useful result was obtained with 2,6-di-*tert*-butylpyridine (entry 5), in which *cis*-**33** formation appeared to follow first-order kinetics; however, due to ~15% loss of chloride **18** over 4 h at 188 °C this observation was tentative at best and alternate experimental evidence was pursued.

Although divinylcyclohexanols have long been recognized as versatile precursors to cyclodecenones, there is surprisingly little data on the activation parameters and rate of this conversion.[35] In the original report by Marvell[35a] and a more recent reinvestigation by Kato,[35b] only general experimental conditions were given; however, Marvell has reported the rate of reaction for an oxy-Cope ene-rearrangement sequence,[35d] which upon extrapolation of our data correlates within experimental error.

The thermal rearrangement of chloride **18** → *cis*-**33** was evaluated over a ~50 °C temperature range (entries 1, 7–10) and the Eyring parameters are reported in Table I. In comparison to other Cope rearrangements[27e,36] the free energy of activation ($\Delta G^{\ddagger}$ = 35.3 kcal/mol) is within the normal range observed for a chairlike [3,3]-sigmatropic rearrangement. The modest enthalpy of activation ($\Delta H^{\ddagger}$ = 23.6 kcal/mol) for **18** → **33** suggests that some synergistic interaction of the C3 hydroxyl and C5 halomethyl substituents may exist in the transition state,[37] with this high degree of ordering being reflected by the large negative entropy term ($\Delta S^{\ddagger}$ = −25.8 eu). If these conclusions are valid, then the initial oxy-Cope rearrangement would provide an enol in which partial bonding interactions and a restricted spacial orientation would favor a rapid intramolecular loss of HCl.

From the examination of Dreiding molecular models in *trans,trans*-dienol **48** the proximity of the chloride to the enolic hydrogen after the oxy-Cope rearrangement can be estimated at 0.8 Å (with a possible approach to within 0.2 Å), well within the 1.27 Å bond length of an H–Cl molecule.[38] In the *cis*-divinyl-substituted precursors the oxy-Cope rearrangement provides a *trans,cis*-cyclodecadienol, in which the chloride–enolic hydrogen distance is lengthened to a minimum value of 1.6 Å. Substitution of bromide for chloride decreases this intraspacial separation in enol **43** to 1.2 Å, which is within the bond length of an H–Br molecule (1.41 Å).[38]

There is considerable disagreement on the interpretation of activation parameters and how they apply to a mechanistic understanding of the Cope rearrangement.[27] Gajewski favors a model based upon $\Delta G^{\ddagger}$, noting that entropy factors compensate for a decrease in the enthalpy of activation (e.g. **18** → **33**),[27e] while

(31) We have successfully developed this overall sequence as an alternate approach to cyclopentanoids via $SnCl_4$-initiated carbocation generation. See: Sworin, M.; Neumann, W. L. *J. Org. Chem.* **1988**, *53*, 4894.

(32) The chemistry of 1,3-diyls has undergone extensive development. For reviews and leading references, see: Little, R. D. *Chem. Rev.* **1986**, *86*, 875. Trost, B. M. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 1.

(33) Cf.: Swain, C. G.; Swain, M. S.; Powell, A. L.; Alunni, S. *J. Am. Chem. Soc.* **1983**, *105*, 502.

(34) This conclusion is based upon the observed loss of chloride **18** at temperatures below the experimental activation energy of **18** → **33**.

(35) (a) Marvell, E. N.; Whalley, W. *Tetrahedron Lett.* **1970**, 509. (b) Kato, T.; Kondo, H.; Nishino, M.; Tanaka, M.; Hata, G.; Miyake, A. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 2958. (c) Marvel, E. N.; Whalley, W. In *The Chemistry of the Hydroxyl Group*, Part 2; Patai, S., Ed.; Interscience: London, 1971; Chapter 13, pp 738–743. (d) Marvell, E. N.; Whalley, W. *Tetrahedron Lett.* **1969**, 1337.

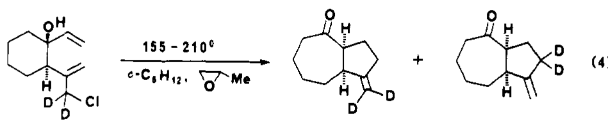
(36) Shea, K. J.; Phillips, R. B. *J. Am. Chem. Soc.* **1980**, *102*, 3156 and references therein.

(37) This hypothesis is supported by the observed facile rearrangement of methyl ester **14** ($t_{1/2}$ < 3 min), which is at least 28 times faster than that of chloride **18** ($t_{1/2}$ = 84 min) at ~190 °C, and the substantial decrease in the rate when the hydroxyl group was protected as the trimethylsilyl ether; only 10% conversion of ether **16** was detected after 9 h at 190 °C.

(38) Gordon, J.; Ford, R. A. *The Chemists Companion*; Wiley: New York, 1972; p 107. Also see p 109 for effective van der Waals radii.

Dewar has recently reported a detailed theoretical study based upon $\Delta H^{\ddagger}$ with a discussion of the biradicaloid nature of the rearrangement.[27a] Our study was limited to an investigation of the energetic criteria of a stepwise oxy-Cope rearrangement–alkylation sequence, and we have not attempted to extrapolate beyond this bond-reorganization process.

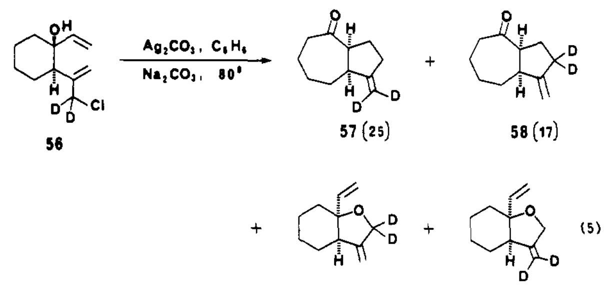
Labeling Studies. To examine the stereochemical criteria of the rearrangement pathway, chloride **56**[39] was heated in cyclohexane with excess propylene oxide as HCl scavenger at temperatures ranging from 155 to 210 °C, and the reaction stopped at 50–65% conversion; the major product (>95%) was *cis*-hydroazulenone **57**, in which the D_2 label was cleanly located on the terminal methylene carbon (eq 4). Only in reactions that



56 57(>95) 58(<5)

were conducted at significantly higher temperatures ($T \approx 255$ °C) or when crude reaction mixtures were resubmitted to the thermolysis conditions did a minor amount of **58** appear (up to 10% by ^{1}H NMR analysis).

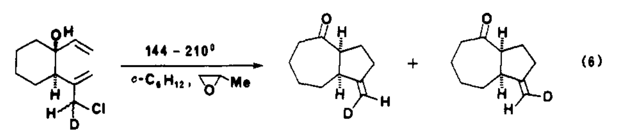
To establish the regioselectivity of a cationic pathway or more accurately the influence of carbon–halogen bond ionization versus that of the thermal oxy-Cope conditions, chloride **56** was heated at 80 °C in benzene with excess Ag_2CO_3 for 24 h (eq 5).[40]



56 57 (25) 58 (17) 59 (49) 60 (9)

Analysis of the ^{1}H NMR spectrum of the crude reaction mixture revealed four major products, ethers **59** and **60** along with *cis*-hydroazulenones **57** and **58**. Integration of the appropriate olefinic, CH_2X, and CH ring-junction resonances provided a 49:9:25:17 ratio, respectively. An indication of the conformational orientation of the diene termini in the reaction pathway can be derived from **57** + **59** versus **58** + **60**. The major conformer, in which the chloromethyl and hydroxyl groups have a cis relationship, favored "silver-assisted" ether formation[40] versus hydroazulenone synthesis by a 2:1 ratio (**59**/**57**), while the minor conformer provided a 1:2 ratio of ether **60** versus hydroazulenone **58**. These results suggest a mechanistic changeover from the thermoneutral route in which the developing cationic center induced a stepwise cationic cyclization to an intermediate decalyl cation followed by a pinacol rearrangement step.[31] The ratios of ether versus hydroazulenone thus represent the S_N2–S_N2' product spread of the allylic halide moiety.[41]

Since thermoneutral rearrangement of chloride **56** to hydroazulenone **57** clearly established the regioselective bonding of the diene termini, we hoped to demonstrate the unimolecular or bimolecular pathway of HCl expulsion[9] by an examination of the stereospecificity of chloride **61**[39] in the bond-reorganization process. If the mechanistic pathway of *pro-S* chloride **61a** involved an oxy-Cope rearrangement to the intermediate enol followed by the unimolecular loss of HCl via an intramolecular S_Ni or rapid ion pair collapse mechanism[42] to bicyclic ether **49-*d***, then the subsequent Claisen rearrangement would afford the *Z*-alkene via overall retention within the chiral carbon prior to concerted formation of hydroazulenone **62** (eq 6). By a similar analysis



61 (2.3:1) 62 (50) 63 (50)

pro-S 61a → intra

pro-R 61b → intra

pro-R chloride **61b** would only provide (*E*)-hydroazulenone **63**. It intermolecular bimolecular processes were involved, then the observed stereochemical outcome would be reversed due to neighboring-group inversion of the chloromethylene carbon, **61a** → **63** and **61b** → **62**. Finally, if bond formation does not occur between the pair of allylic units, then some degree of scrambling would be expected, determined by the lifetime of the reactive intermediate.

When chloride **61**, which was a 2.3:1 diastereomeric mixture,[39] was heated in cyclohexane with excess of propylene oxide as HCl scavenger at temperatures ranging from 144 to 210 °C, a 1:1 mixture of *cis*-hydroazulenones **62** and **63** was obtained (eq 6). Remarkably, the D_1 label was cleanly transferred to the terminal methylene carbon, but complete scrambling occurred within the deuteriated carbon. Since no premature scrambling could be detected in unconverted chloride **61**, these results suggest that the rearrangement pathway does not involve the facile formation of bicyclic ether **49** as a discrete intermediate.

FVP Rearrangements. If the observation that nonpolar, aprotic solvents were essential for a successful rearrangement pathway, and the hypothesis of the unimolecular loss of HX remained valid, then gas phase thermolysis conditions[43] should exhibit the identical stereochemical criteria that were obtained via thermoneutral solution rearrangements. Table II contains the results obtained by FVP of the allylic halide precursors. These data represent an initial evaluation of gas phase reaction conditions and are unoptimized with respect to the oven temperature and contact time.

The reactivity of *trans*-divinyl-substituted chloride **18** and deuteriated analogues **56** and **61** was examined over a 200 °C temperature range with representative data being reported in Table II (entries 1–3). At 470 °C, none of the chloride could be detected in the condensate, only hydroazulenones **33** and **35**, which were obtained in a 2:3 ratio, respectively, were detected. The sensitivity of *cis*-hydroazulenone **33** toward thermal equilibration was demonstrated by subjecting a pure sample to the thermolysis conditions

Table II. FVP Rearrangements at 0.02 mm

entry	precursor	oven T, °C	wt ratio,[a] %	NMR ratio, st mat:33:35, % st mat.	33	35
1	**18**	470	68	0	40	60
2	**61**	270		100[b]	0	0
3	**61**	370	63	~0	96[c]	4
4	**24**	400		0	14	86
5	**24**	355	69	22	7	71
6	**64**	380		15	13	72[d]
7	**25**	450	52	0	27	73
8	**33**	400	98		72	28
9	**37**	400	93	100	0	0

[a] Weight condensate/weight precursor. [b] No scrambling of the 2.3:1 diastereomeric mixture of **61** was detected. [c] A 1:1 ratio of *cis*-hydroazulenones **62** and **63** was obtained. [d] A 1:1 ratio of *trans*-hydroazulenones **65** and **66** was obtained.

(39) Available from DIBAL-D reduction of the appropriate unlabeled carbonyl precursor. For the preparation of DIBAL-D, see: Kalvin, D. M.; Woodard, R. W. *Tetrahedron* **1984**, *40*, 3387. Eisch, J. J.; Rhee, S. G. *J. Am. Chem. Soc.* **1974**, *96*, 7276.

(40) Fetizon, M.; Golfier, M.; Louis, J.-M. *Tetrahedron Lett.* **1973**, 1931.

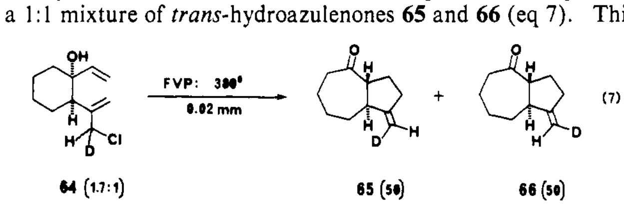
(41) DeWolfe, R. H.; Young, W. G. In *The Chemistry of Alkenes*; Patai, S., Ed.; Interscience: London, 1964; Vol. 1, Chapter 10, pp 683–706.

(42) Okamoto, K.; Yamada, H.; Nitta, I.; Shingu, H. *Bull. Chem. Soc. Jpn.* **1966**, *39*, 299. Okamoto, K.; Takeuchi, K.; Inoue, T. *J. Chem. Soc., Perkin Trans. 2* **1980**, 842 and references therein.

(43) For general reviews, see: Wiersum, U. E. *Recl. Trav. Chim. Pays-Bas* **1982**, *101*, 317, 365. For a list of practical rules, see p 322.

(entry 8). At 270 °C, only unreacted chloride was recovered, which in the case of **61** cleanly maintained the 2.3:1 diastereomeric mixture of the monodeuterio label (entry 2). When chloride **61** was subjected to FVP conditions at 370 °C, a 96:4 ratio of *cis*- to *trans*-hydroazulenones was obtained, but most important was that the D_1 label was cleanly transferred to the terminal methylene carbon with internal scrambling to provide a 1:1 mixture of *cis*-hydroazulenones **62** and **63** (entry 3). These results suggest a strong similarity in both the gas phase and solution rearrangement pathway.

Although *cis*-chloride **24** proved to be ineffective at inducing ring closure to *trans*-**35** in solution, yielding cyclodecenone **38** as the major product, this trend was completely reversed in the gas phase. FVP of *cis*-chloride **24** at 400 °C provided a 14:86 mixture of hydroazulenones **33** and **35**, respectively, with no detectable evidence of the competitive formation of medium ring **38** (entry 4). Lowering the oven temperature to 355 °C gave a 10:1 mixture of *trans*-**35** to *cis*-**33**, respectively (entry 5). When *cis*-chloride **64**, which was a 1.7:1 diastereomeric mixture,[39] was subjected to FVP conditions at 380 °C a 13:72 ratio of *cis*- to *trans*-hydroazulenones was obtained. Most significant was that *cis*-divinyl-substituted chloride **64** underwent thermal rearrangement with clean regioselective transfer of the D_1 label to the terminal methylene carbon, but internal scrambling occurred to provide a 1:1 mixture of *trans*-hydroazulenones **65** and **66** (eq 7). This



parallel gas-phase behavior between *cis*- and *trans*-divinylcyclohexanols to internally scramble the D_1 label and the known intermediacy of the enol as a precursor to *cis*-cyclodecenone **38** strongly support a mechanistic pathway that involves an initial oxy-Cope rearrangement followed by the unimolecular loss of HX along with the configurational integrity of the chloromethylene carbon prior to transannular ring closure. Finally, we also established that *cis*-ether **37** was unreactive under the reaction conditions employed in this study (entry 9).

Discussion

[3,3]-Sigmatropic rearrangements are versatile synthetic reactions that tolerate a wide range of useful functionality appended to the 1,5-diene framework. The ability of certain substituents to influence the rates of sigmatropic rearrangements has attracted considerable attention, and several theoretical models[27a,e,28a,44] have been proposed in an attempt to delineate the role of these groups on the mechanistic pathway. For the Claisen rearrangement, two systematic experimental studies have now been reported; Carpenter evaluated the cyano-substituted allyl vinyl ethers[28a] while Coates and Curran addressed the alkoxy donor groups.[19b] This latter study provides strong evidence for dipolar character in the Claisen rearrangement transition state and an incisive discussion of limitations in current theoretical models.

In the Cope rearrangement area much of the recent interest has focused on phenyl substituents,[27a,e] boatlike transition states,[27d] and the highly ionized anionic oxy-Cope rearrangement.[45-47] Although the anionic oxy-Cope process is generally presented as a concerted [3,3]-sigmatropic pathway,[45] numerous symmetry-forbidden [1,3]-migrations[46] and a fragmentation–recombination pathway could also intervene.[47] Interestingly, the thermoneutral oxy-Cope rearrangement was originally perceived by Berson to

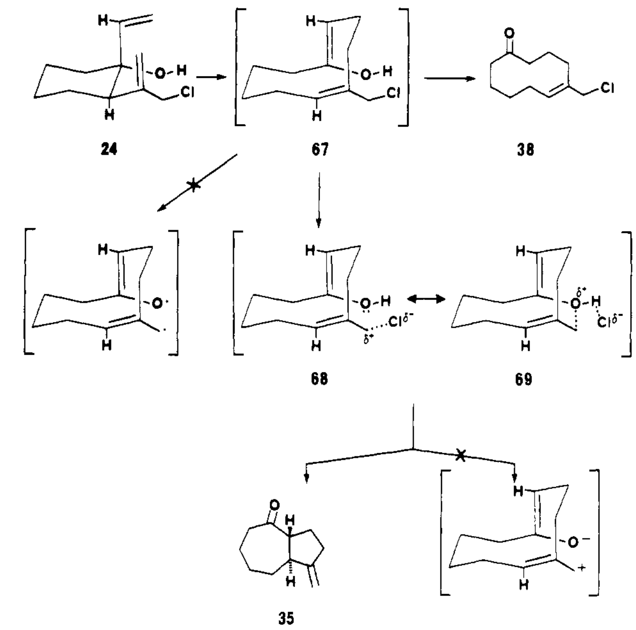


Figure 2.

proceed stepwise via diradical intermediates due to less than ideal proximity of the diene termini of the bicyclic precursors.[48] Subsequent work on substrates that could achieve better π overlap have demonstrated "concerted-like" [1,3]- and [3,3]-sigmatropic migrations,[35,49] along with carbinol bond fragmentation products.[49c,d]

Since our rearrangement precursors were designed with two potentially synergistic substituents, the uncertainty of mechanistic changeovers required a general approach to establish the role of these groups to influence the oxy-Cope rearrangement toward hydroazulenone formation. The kinetic data in Table I document a moderately facile, highly ordered rate-determining step that exhibited essentially no dependence upon the selection of bromide versus chloride. Since the labeling studies demonstrated the regioselective bonding of the olefinic termini and the *cis*-divinyl-substituted precursors yielded *cis*-cyclodecenones **38** and **44** via competitive ketonization, the best description of the rate-determining step involves an oxy-Cope rearrangement of the divinylcyclohexanols to cyclodecadienols (Figure 2, the specific conversion of chloride **24** → *trans*-**35** being illustrated). On the basis of stereospecific D_1 labeling studies, the subsequent conversion of enol **48** to *cis*-**33** (solution and gas phase) and enol **67** (gas phase) to *trans*-**35** proceeded via a unimolecular mechanistic pathway that allowed scrambling within the chloromethylene carbon.

Although the distinction between a concerted loss of HX and a two-step mechanism with the intervention of ion pairs may be subtle, in our opinion the likelihood of an ion-pair intermediate is supported by the following considerations. (1) The formation of an allyl radical pair intermediate via homolytic loss of HCl would require an activation energy in excess of the observed rate-determining step.[9,50,51] (2) Gas phase pyrolysis reactions of allylic halides exhibit heterolytic character via moderately polar transition-state complexes that disperse the formal charge and

(44) Carpenter, B. K. *Tetrahedron* **1978**, *34*, 1877.

(45) Evans, D. A.; Golob, A. M. *J. Am. Chem. Soc.* **1975**, *97*, 4765. For mechanistic studies, see: Rozeboom, M. D.; Kiplinger, J. P.; Bartmess, J. E. *J. Am. Chem. Soc.* **1984**, *106*, 1025. Evans, D. A.; Baillargeon, D. J. *Tetrahedron Lett.* **1978**, 3315, 3319.

(46) For an examination of competing 1,3 and 3,3 migrations, see: Thies, R. W.; Daruwala, K. P. *J. Org. Chem.* **1987**, *52*, 3798 and references therein.

(47) Paquette, L. A.; Pierre, F.; Cottrell, C. E. *J. Am. Chem. Soc.* **1987**, *109*, 5731.

(48) Berson, J. A.; Walsh, E. J. *J. Am. Chem. Soc.* **1968**, *90*, 4729, 4730, 4732. Berson, J. A.; Jones, M. *J. Am. Chem. Soc.* **1964**, *86*, 5017, 5019.

(49) (a) Thies, R. W.; Bolesta, R. E. *J. Org. Chem.* **1976**, *41*, 1233. (b) Thies, R. W.; Billigmeier, J. E. *J. Am. Chem. Soc.* **1974**, *96*, 200. (c) Thies, R. W.; Wills, M. T.; Chin, A. W.; Schick, L. E.; Walton, E. S. *J. Am. Chem. Soc.* **1973**, *95*, 5281. (d) Thies, R. W. *J. Am. Chem. Soc.* **1972**, *94*, 7074.

(50) In the absence of thermochemical data for 1,5-cyclodecadienes, the homolytic loss of HCl can be roughly estimated to require at least ~40 kcal/mol by the Benson group-additive method.[29,51] This barrier is similar to the 38–42 kcal/mol activation energy for the six-centered thermal elimination of HCl from allylic halides.[9]

(51) Benson, S. W. *Thermochemical Kinetics*, 2nd ed.; Wiley: New York, 1976. Benson, S. W.; Cruickshank, F. R.; Golden, D. M.; Haugen, G. R.; O'Neal, H. E.; Rodgers, A. S.; Shaw, R.; Walsh, R. *Chem. Rev.* **1969**, *69*, 279.

hence lower the activation energy.[9] (3) Theoretical studies on gas-phase substitution reactions of cationic substrates suggest a substantial ion–dipole interaction which is qualitatively related to the widely investigated gas-phase anionic process.[52] Calculations on the gas-phase anionic S_N2' substitution reaction suggest that allylic systems would exothermically add nucleophiles without activation to yield charge–dipole complexes which are minima on the energy surface.[53] (4) The product distribution from *cis*-chloride **24** strongly favored ring closure to *trans*-**35** in the gas phase, while in solution only a trace amount of **35** could be detected when cyclohexane was employed as the solvent. In the optimization of *cis*-bromide **25** → *trans*-**35** we noted that a solvent change from cyclohexane to benzene did not appreciably effect the overall rate but did significantly improve the product ratio from 40:60 to >20:1 (**35**/**44**), respectively.[26,54] Indeed, when *cis*-chloride **24** was heated at 188 °C for 4 h in benzene with propylene oxide as HCl scavenger a similar improvement in the ratio of *trans*-**35** to cyclodecenone **38** was obtained (~40:60).[26]

To summarize, the current level of experimental data support a mechanism for the thermal alkylation of enol **67** to *trans*-**35** which proceeds via the dissociation of the allylic halide to a stretched intimate ion pair **68**, which allows scrambling of the D_1 label (Figure 2). The activation energy for **67** → **68** is lowered by ion–dipole stabilization via internal participation of the enolic oxygen, which is enhanced in the gas phase,[9] and/or by electrostatic interactions with benzene in solution.[54] The resonance-stabilized, short-lived reactive intermediate **68** ↔ **69** undergoes S_N2' electrophilic capture of the nucleophilic enol with the entropy driven dissociation of HCl.

Support for the proposed mechanistic pathway can be found in Brønsted and Lewis acid catalysis reactions of Claisen rearrangements.[8] The most intensive scrutiny has been applied to the BCl_3-catalyzed aromatic Claisen rearrangement, in which a rate enhancement of $\sim 10^{10}$ was estimated.[55] Although labeling studies support a concerted pathway, the formation of cleavage products, meta and para substitution, and a substantial amount of racemization suggest a stepwise pathway. In addition, electron-withdrawing substituents on the aryl ring and α-methyl substitution in the allyl group favor fragmentation to the phenol, and BF_3 proved to be less successful than BCl_3 at catalyzing the Claisen-rearrangement pathway.[8,55] In a mechanistic sense this initial allyl phenyl ether–BCl_3 complex can be represented by protonated ether **69** in which the electrophilic boron is replaced by a proton (Figure 2).[8,55,56] Since dissociation is restricted in our tethered allylic system, a charge-accelerated rearrangement or an ion-pair capture would provide transannular ring closure to *trans*-**35**.

While the preceding points argue for ion-pair acceleration in the thermal alkylation of **67** → **35**, the incorporation of the allylic moieties within a medium ring system precludes mechanistic studies that may enhance dissociation of the ion pairs and allow capture of the free ions in addition to the examination of crossover products. Therefore, the degree of ionic separation cannot be accurately assessed but must proceed to the extent that loss of configurational integrity occurs within the chloromethylene carbon. Alternate rearrangement systems that should provide further synthesis applications and mechanistic information are currently under investigation and will be the subject of future publications.

In conclusion, the formation of carbon–carbon bonds by the alkylation of enols derived from an initial oxy-Cope rearrangement readily occurred under mild thermoneutral reaction conditions. The synthesis of *cis*- and *trans*-hydroazulenones provides a stereospecific entry to the carbocyclic framework of the guaianolides and pseudoguaianolides, whereas the mechanistic investigation presents strong evidence of ion-pair participation in the thermoneutral ring-closure step.

Experimental Section

All reactions were conducted under a positive atmosphere of dry argon. Tetrahydrofuran (THF) was distilled from potassium; diethyl ether was distilled from sodium/benzophenone ketyl; dichloromethane, hexane, cyclohexane, benzene, and toluene were distilled from calcium hydride. All other commercially available reagents were used without further purification unless otherwise noted.

Flash chromatography was performed with E. Merck silica gel 60, 230–400 mesh. Analytical thin-layer chromatography was performed on precoated glass plates (E. Merck silica gel 60 F-254, 0.25-mm layer thickness). Gas–liquid chromatography (GC) was performed on a Varian Model 3700 gas chromatograph equipped with a 15 m × 0.53 mm FSOT column packed with DB-1 1.5-μm film.

Proton nuclear magnetic resonance (^1H NMR) spectra and carbon nuclear magnetic resonance (^{13}C NMR) spectra were obtained in $CDCl_3$ solution at 300 and 75 MHz, respectively, on a Varian XL-300 FT NMR spectrometer. ^1H NMR spectra used the 7.24 ppm resonance of residual chloroform as an internal standard; ^{13}C NMR spectra used the $CDCl_3$ resonance at 77.00 ppm as an internal standard. In both ^1H NMR and ^{13}C NMR, chemical shifts are reported in δ units downfield from tetramethylsilane. ^{13}C NMR multiplicities were assigned by a DEPT pulse sequence. Multiplicities are abbreviated as follows: br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. Coupling constants (J) are reported in hertz (Hz). Infrared spectra (IR) were recorded on a Perkin-Elmer Model 783 grating spectrophotometer. High-resolution electron-impact (HREI), chemical-ionization (HRCI), and fast-atom-bombardment (HRFA) mass spectra (MS) were performed by the Midwest Center for Mass Spectroscopy, University of Nebraska. Microanalysis were performed by Galbraith Laboratories, Inc., Knoxville, TN. Melting points (mp) were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected.

Methyl 2-(2-Ethylidenecyclohexyl)-3-methoxypropanoate (10). A solution of 1-(1-hydroxyethyl)cyclohexene (12.0 g, 95 mmol),[10] trimethyl 3-methoxyorthopropanoate (78.6 g, 479 mmol),[11] and trimethylacetic acid (1.6 g total, added in 5 portions during the reaction period) was heated at ~140 °C for 24 h. After cooling, the excess ortho ester was recovered by distillation (bp 75–77 °C, 20 mm), the residue was dissolved in CH_2Cl_2 (120 mL) and hydrolyzed at room temperature for 1 h with 6 N HCl (12 mL). The aqueous portion was extracted with CH_2Cl_2 (3 × 5 mL), and the combined organic extracts were dried (Na_2SO_4) and concentrated. Purification of the residue by flash chromatography (silica gel, 50:1 hexane–ethyl acetate) followed by bulb-to-bulb distillation (bp 99–100 °C, 0.85 mm) gave 19.5 g (91%) of **10** as a colorless oil, which was a ~3.5:1 mixture of stereoisomers: ^1H NMR ($CDCl_3$, absorptions for the major isomer are listed first in each pair) δ 5.10 and 5.17 (q, J = 6.7 Hz, =CH), 3.55 and 3.66 (s, CO_2CH_3), 3.28 and 3.23 (s, OCH_3), 1.46 and 1.53 (dd, J = 6.7, 1.1 Hz, =CCH_3); ^{13}C NMR ($CDCl_3$, absorptions for the major isomer are listed first in each pair) δ 174.63 and 175.36 (s), 139.37 and 138.78 (s), 117.31 and 117.96 (d), 72.52 and 73.57 (t), 58.91 and 58.82 (q), 51.18 and 51.46 (q), 47.02 and 45.79 (d), 44.70 and 44.62 (d), 29.46 and 31.00 (t), 27.13 and 27.36 (t), 24.74 and 24.42 (t), 22.12 and 21.77 (t), 12.48 and 12.44 (q); IR (neat) 2930, 2860, 1740, 1192, 1168, 1122, 1108 cm^{-1}; MS (HREI), m/z 226.1565 (226.1569 calcd for $C_{13}H_{22}O_3$).

3aα,4,5,6,7,7a-Hexahydro-7aα-(1-iodoethyl)-3-(methoxymethyl)-benzofuran-2(3*H*)-one (11). A solution of **10** (11.3 g, 50 mmol), KOH (3.1 g, 55 mmol), MeOH (50 mL), and H_2O (25 mL) was heated at reflux for 6 h. After cooling to room temperature, the reaction mixture was adjusted to pH 6–7 by addition of 5% HCl; solid $NaHCO_3$ (2.5 g) was added, and the resulting solution was cooled to 0 °C. A solution of KI (33.2 g, 200 mmol)–I_2 (38.1 g, 150 mmol) in H_2O (50 mL) was added dropwise over ~2 h while the temperature was maintained at 0 °C. The reaction mixture was allowed to warm to room temperature and was stirred for 12 h, diluted with CH_2Cl_2 (150 mL), and quenched by the addition of saturated $Na_2S_2O_3$ (excess). The aqueous portion was extracted with CH_2Cl_2 (3 × 25 mL), and the combined organic extracts were dried (Na_2SO_4) and concentrated (light sensitive) to give 15.3 g of crude **11** as a viscous, yellow oil, which was used directly in the next experiment. Analysis of a comparable sample demonstrated a 2.5:1:0.7 (methoxy-eliminated) mixture of iodo lactones [^1H NMR ($CDCl_3$, absorptions for related resonances are listed by descending ratio) δ 6.17 (d, J = 2.5 Hz, =C*H*H), 5.52 (d, J = 2.5 Hz, =CH*H*), 4.42, 4.39, and 4.21 (q, J = 7.0 Hz, CHI), 3.28 (s, OCH_3), 1.93, 1.83, and 1.89 (d, J = 7.0 Hz, CH_3)], and separation by flash chromatography (silica gel, 40:1

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(54) For the ability of aromatic solvents to lower the energy of a polarizable transition state in the Menschutkin reaction, see: Abraham, M. H.; Grellier, P. L. *J. Chem. Soc. Perkin Trans. 2* **1976**, 1735.

(55) Borgulya, J.; Madeja, R.; Fahrni, P.; Hansen, H.-J.; Schmid, H.; Barner, R. *Helv. Chim. Acta* **1973**, *56*, 14.

(56) The rearrangement manifold for the allyl phenyl ether–BCl_3 reaction can be viewed as a divergent pathway from complex **69** to either the Claisen product **35** or the ring-cleavage product halide **67**.

(57) This resonance is ~1 ppm lower than the value given (δ 49.17) in ref 24. Since all of the remaining resonances for both isomers are essentially identical, we feel that the chemical shift should have been listed as δ 48.17.

hexane–ethyl acetate) provided the major isomer as a pale yellow oil: ^{1}H NMR ($CDCl_3$) δ 4.45 (q, *J* = 7.0 Hz, CHI), 3.61 (AB q, *J* = 9.6 Hz, Δν = 30.8 Hz, A part d, *J* = 3.3 Hz, B part d, *J* = 2.3 Hz, OCH_2), 3.32 (s, OCH_3), 2.75 (m, 2 H), 2.32 (m, 1 H), 1.96 (d, *J* = 7.0 Hz, CH_3), 1.8–1.3 (m, 7 H); ^{13}C NMR ($CDCl_3$) δ 174.92 (s), 85.17 (s), 69.66 (t), 59.05 (q), 45.18 (d), 37.79 (d), 33.11 (t), 33.02 (d), 23.26 (t), 23.25 (q), 19.64 (t), 18.04 (t); IR (neat) 2940, 2868, 1775 (br), 1154, 1120, 962 cm^{-1}.

7aα-Ethenyl-3aα,4,5,6,7,7a-hexahydro-3-methylenebenzofuran-2-(3*H*)-one (12). A solution of crude **11** (15.3 g), DBU (20 g, 131 mmol), and toluene (200 mL) was heated at reflux for 24 h, cooled to room temperature, filtered, and concentrated. After partitioning between ether (100 mL) and 5% HCl (adjust pH ~5), the aqueous layer was extracted with ether (2 × 25 mL), and the combined organic extracts were washed with 5% $NaHCO_3$ (30 mL) and brine (2 × 30 mL), dried (Na_2SO_4), and concentrated. The residue was distilled to give 6.1 g (69% from **10**) of lactone **12** as a colorless liquid: bp 101–102 °C, 0.95 mm; ^{1}H NMR ($CDCl_3$) δ 6.12 (d, *J* = 2.7 Hz, =C*H*H), 5.90 (dd, *J* = 17.3, 11.0 Hz, C*H*=CH_cH_t), 5.41 (d, *J* = 2.7 Hz, =CH*H*), 5.30 (d, *J* = 17.3 Hz, CH=CH_c*H_t*), 5.15 (d, *J* = 11.0 Hz, CH=C*H_c*H_t), 2.82 (tt, *J* = 5.5, 2.7 Hz, CH), 1.9–1.7 (m, 3 H), 1.6–1.3 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 169.78 (s), 139.51 (d), 138.48 (t), 119.55 (t), 115.15 (s), 83.69 (s), 44.26 (d), 33.91 (t), 25.47 (t), 21.16 (t), 20.35 (t); IR (neat) 3092, 3014, 2940, 2865, 1765 (br), 1669, 1644, 1255 (br), 1162, 1129, 950 (br) cm^{-1}; MS (HREI), *m/z* 178.0988 (178.0994 calcd for $C_{11}H_{14}O_2$).

1α-Ethenyl-2β-[1-(hydroxymethyl)ethenyl]cyclohexanol (17). A solution of **12** (3.60 g, 20.2 mmol) and dry hexane (250 mL)–CH_2Cl_2 (30 mL) was cooled to −78 °C, and DIBAL (41 mL, of a 1.0 M solution in hexane, 41 mmol) was added over 45 min. After an additional 45 min at −78 °C, the reaction mixture was diluted with ether (250 mL), quenched with MeOH (30 mL), followed by brine (25 mL) and $MgSO_4$ (~50 g). After warming to room temperature, the mixture was filtered and concentrated, and the residue was purified by flash chromatography (silica gel, 20:1 hexane–ethyl acetate) to give 3.45 g (95%) of a viscous oil, which was a ~2:1 mixture of hydroxy aldehyde–lactols [^{1}H NMR ($CDCl_3$) δ 9.32 (s, CHO), 5.70 (d, *J* = 5.8 Hz, CHOH) and 5.62 (d, *J* = 6.5 Hz, CHOH)].

Reduction of the aldehyde–lactols mixture (2.52 g, 14.0 mmol) using the procedure described above, followed by purification of the residue by flash chromatography (silica gel, 10:1 hexane–ethyl acetate), gave 2.40 g (94%, 89% overall) of **17** as a white solid: mp 82–83 °C; ^{1}H NMR ($CDCl_3$) δ 5.82 (dd, *J* = 17.3, 10.7 Hz, C*H*=CH_cH_t), 5.13 (dd, *J* = 17.4, 1.4 Hz, CH=H_c*H_t*), 5.02 (d, *J* = 0.9 Hz, =C*H*H), 4.95 (dd, *J* = 10.7, 1.4 Hz, CH=C*H_c*H_t), 4.85 (d, *J* = 1.9 Hz, =CH*H*), 3.96 (AB q, *J* = 12.4 Hz, Δν = 35.7 Hz, CH_2OH), 3.65 (br s, OH), 2.20 (dd, *J* = 12.7, 3.4 Hz, CH), 1.9–1.2 (m, 8 H); ^{13}C NMR ($CDCl_3$) δ 148.93 (s), 145.98 (d), 116.25 (t), 111.22 (t), 72.84 (s), 64.58 (t), 52.02 (d), 38.12 (t), 26.79 (t), 26.02 (t), 21.10 (t); IR (KBr) 3310, 3170, 3078, 3018, 2940, 2860, 1639, 1010, 1000, 994, 975, 924, 912 cm^{-1}; MS (CI), *m/z* 183 (MH^+), 166, 165, 147. Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.43; H, 9.72.

2β-[1-(Chloromethyl)ethenyl]-1α-ethenylcyclohexanol (18). To a suspension of PPh_3 (5.0 g, 19.1 mmol) in CH_3CN (2 mL)–CCl_4 (2.0 mL, 3.2 g, 20.7 mmol) at room temperature was slowly added diol **17** (2.30 g, 12.6 mmol). The reaction mixture was maintained at room temperature, stirred for 40 min, and the viscous mixture was directly transferred to a chromatography column (silica gel, 150:1 hexane–ethyl acetate then 40:1 hexane–ethyl acetate) to give 2.40 g (95%) of **18** as a colorless liquid: ^{1}H NMR ($CDCl_3$) δ 5.85 (dd, *J* = 17.2, 10.7 Hz, C*H*=CH_cH_t), 5.28 (s, =C*H*H), 5.14 (dd, *J* = 17.2, 1.2 Hz, CH=CH_c*H_t*), 5.09 (s, =CH*H*), 4.99 (dd, *J* = 10.7, 1.2 Hz, CH=C*H_c*H_t), 4.01 (AB q, *J* = 12.0 Hz, Δν = 12.4 Hz, CH_2Cl), 2.31 (dd, *J* = 12.8, 3.5 Hz, CH), 1.85–1.20 (m, 8 H); ^{13}C NMR ($CDCl_3$) δ 147.00 (s), 145.36 (d), 116.31 (t), 111.58 (t), 72.71 (s), 50.00 (t), 48.32 (d), 38.05 (t), 27.87 (t), 25.93 (t), 20.98 (t); IR (neat) 3560, 3480, 3090, 3008, 2940, 2860, 1642, 975, 922 cm^{-1}; MS (HREI), *m/z* 202.0936 (202.0938 calcd for $C_{11}H_{17}{}^{37}ClO$), 200.0966 (200.0968 calcd for $C_{11}H_{17}{}^{35}ClO$).

2β-[1-(Bromomethyl)ethenyl]-1α-ethenylcyclohexanol (19). To a suspension of PPh_3 (1.3 g, 5.0 mmol) and diol **17** (600 mg, 3.3 mmol) in CH_3CN (0.75 mL) at room temperature was slowly added CBr_4 (1.1 g, 3.3 mmol). The reaction mixture was maintained at room temperature and stirred for 20 min, and the viscous mixture was directly transferred to a chromatography column (silica gel, 150:1 hexane–ethyl acetate then 40:1 hexane–ethyl acetate) to give 730 mg (90%) of **19** as a colorless liquid: ^{1}H NMR ($CDCl_3$) δ 5.83 (dd, *J* = 17.3, 10.7 Hz, C*H*=CH_cH_t), 5.28 (s, =C*H*H), 5.12 (dd, *J* = 17.3, 1.2 Hz, CH=CH_c*H_t*), 5.06 (t, *J* = 0.8 Hz, =CH*H*), 4.97 (dd, *J* = 10.7, 1.2 Hz, CH=C*H_c*H_t), 3.91 (AB q, *J* = 10.2 Hz, Δν = 3.8 Hz, A part d, *J* = 0.9 Hz, B part d, *J* = 0.7 Hz, CH_2Br), 2.32 (dd, *J* = 12.7, 3.7 Hz, CH), 1.8–1.4 (m, 7 H), 1.3 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 147.29 (s), 145.32 (d), 117.10 (t), 111.64 (t), 72.69 (s), 48.54 (d), 39.32 (t), 37.99 (t), 28.03 (t), 25.90 (t), 20.98 (t); IR (neat) 3555, 3490, 3088, 3008, 2935, 2860, 1635, 1208, 975, 920 cm^{-1}.

2β-[1-[(Acetyloxy)methyl]ethenyl]-1α-ethenylcyclohexanol (20). A solution of **17** (182 mg, 1.0 mmol), acetic anhydride (1.02 g, 10 mmol), and pyridine (3 mL) was stirred at 0 °C for 48 h. After partitioning between ether (15 mL) and 1% HCl (20 mL) at 0 °C, the aqueous phase was extracted with ether (2 × 5 mL), and the combined organic extracts were dried (Na_2SO_4) and concentrated to give 210 mg (94%) of **20** as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 5.76 (dd, *J* = 17.3, 10.7 Hz, C*H*=CH_cH_t), 5.08 (dd, *J* = 17.3, 1.4 Hz, CH=CH_c*H_t*), 5.04 (q, *J* = 1.5 Hz, =C*H*H), 4.94 (br s, =CH*H*), 4.91 (dd, *J* = 10.7, 1.4 Hz, CH=C*H_c*H_t), 4.42 (AB q, *J* = 13.9 Hz, Δν = 19.6 Hz, A part br, B part t, *J* = 1.2 Hz, CH_2O), 2.04 (dd, *J* = 12.5, 3.3 Hz, CH), 1.99 (s, CH_3), 1.93 (s, OH), 1.85–1.30 (m, 7 H), 1.19 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 170.37 (s), 145.45 (s), 145.37 (t), 113.78 (t), 111.23 (t), 72.69 (s), 67.00 (t), 49.29 (d), 37.98 (t), 27.04 (t), 25.84 (t), 20.89 (t), 20.74 (q); IR (neat) 3510, 3090, 3010, 2940, 2860, 1740, 1645, 1240, 1045, 975, 920 cm^{-1}; MS (HREI), *m/z* 224.1419 (224.1412 calcd for $C_{13}H_{20}O_3$).

Methyl 2-[(3βS*)-2α-Methyl-1-oxaspiro[2.5]oct-4β-yl]-3-methoxypropanoate (21). A mixture of **10** (11.3 g, 50 mmol), *m*-CPBA (13 g, tech. 80%, 60 mmol), CH_2Cl_2 (250 mL), and 0.5 M $NaHCO_3$ (200 mL, 100 mmol) was stirred at 0 °C for 1 h. The organic portion was washed with 5% $Na_2S_2O_3$, 5% $NaHCO_3$, H_2O and brine, dried (Na_2SO_4), and concentrated to give 12.0 g (99%) of **21** as a colorless oil. An analytical sample was prepared by flash chromatography (silica gel, 30:1 hexane–ethyl acetate), which was a 1:1 mixture of stereoisomers: ^{1}H NMR ($CDCl_3$) δ 3.62 and 3.61, (s, CO_2CH_3), 3.45–3.35 (m, OCH_2), 3.22 (overlapping s, OCH_3), 2.95–2.80 (m, CH), 2.84 and 2.76 (q, *J* = 5.6 Hz, OCH), 1.80–1.20 (m, 9 H), 1.19 and 1.12 (d, *J* = 5.6 Hz, CH_3); ^{13}C NMR ($CDCl_3$) δ 174.31 and 173.93 (s), 72.52 and 72.44 (t), 63.03 and 62.63 (s), 59.39 and 58.99 (d), 58.88 (q), 51.55 and 51.50 (q), 46.00 and 45.16 (d), 43.00 and 42.58 (d), 27.24 and 26.36 (t), 25.40 and 25.26 (t), 23.72 and 23.67 (t), 21.14 and 21.13 (t), 13.08 and 12.94 (q); IR (neat) 2940, 2862, 1740, 1262, 1195, 1168, 1115 cm^{-1}.

Methyl 2-[(3βS*)-2α-Methyl-1-oxaspiro[2.5]oct-4β-yl]propenoate (22). To a solution of **21** (2.06 g, 8.5 mmol) in THF (35 mL) at −78 °C was added potassium *tert*-butoxide (1.15 g, 10.2 mmol, added in 3 portions during the reaction period). The reaction mixture was maintained at −78 °C for 7 h, diluted with cold brine (10 mL), and neutralized with 5% HCl, and the aqueous portion was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated. The residue was purified by flash chromatography (silica gel, 30:1 hexane–ethyl acetate) to afford 1.35 g (76%) of **22** as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 6.07 (apparent t, *J* = 0.9 Hz, =C*H*H), 5.33 (apparent t, *J* = 1.3 Hz, =CH*H*), 3.68 (s, OCH_3), 3.05 (br d, *J* = 10.4 Hz, CH), 2.70 (q, *J* = 5.6 Hz, OCH), 1.85–1.65 (m, 4 H), 1.60–1.30 (m, 4 H), 1.19 (d, *J* = 5.6 Hz, CH_3); ^{13}C NMR ($CDCl_3$) δ 168.26 (s), 141.06 (s), 123.65 (t), 64.20 (s), 53.87 (d), 51.81 (q), 43.43 (d), 30.27 (t), 29.83 (t), 25.52 (t), 25.16 (t), 13.21 (q); IR (neat) 3118, 3100, 2928, 2860, 1725, 1635, 1275, 1235, 1195, 1160 cm^{-1}; MS (HREI), parent not observed, *m/z* 195.1018 (195.1021 calcd for $C_{11}H_{15}O_3$, $M^+ - CH_3$), 178.0997 (178.0994 calcd for $C_{11}H_{14}O_2$, $M^+ - CH_3OH$).

1β-Ethenyl-2β-[1-(hydroxymethyl)ethenyl]cyclohexanol (23). By use of the procedure described for the reduction of **12**, ester **22** (5.80 g, 27.6 mmol) was converted to the very labile epoxy alcohol (4.5 g), which was used immediately in the next reaction.

To a solution of PhSeSePh (12.0 g, 38 mmol) in absolute EtOH (200 mL) at 0 °C was slowly added $NaBH_4$ (3.1 g, 82 mmol). After the yellow color had discharged, the resulting solution was heated to reflux, and a solution of the epoxy alcohol (4.5 g) in absolute EtOH (50 mL) was added via a syringe pump over 3 h. After an additional 1 h at reflux, the reaction mixture was cooled to 0 °C and excess 30% H_2O_2 (76 mL) was cautiously added from an additional funnel over 1 h. The reaction mixture was allowed to warm to room temperature, stirred for 1 h, diluted with H_2O (200 mL), and extracted with CH_2Cl_2 (3 × 250 mL). The combined organic extracts were washed with 5% $NaHCO_3$, dried (Na_2SO_4), and concentrated. Purification of the residue by flash chromatography (silica gel, 15:1 hexane–ethyl acetate) gave 3.0 g (60% overall) of **23** as a white solid: mp 71–72 °C; ^{1}H NMR ($CDCl_3$) δ 6.18 (dd, *J* = 17.3, 10.9 Hz, C*H*=CH_cH_t), 5.24 (dd, *J* = 17.3, 1.7 Hz, CH=CH_c*H_t*), 5.13 (s, =C*H*H), 5.11 (dd, *J* = 10.9, 1.7 Hz, CH=C*H_c*H_t), 4.82 (s, =CH*H*), 4.00 (AB q, *J* = 12.3 Hz, Δν = 21.0 Hz, CH_2OH), 3.70 (br s, OH), 2.24 (dd, *J* = 12.6, 3.5 Hz, CH), 1.90–1.20 (m, 8 H); ^{13}C NMR ($CDCl_3$) δ 148.80 (s), 139.18 (d), 115.06 (t), 114.08 (t), 74.35 (s), 67.69 (t), 51.89 (d), 41.07 (t), 29.46 (t), 26.15 (t), 23.57 (t); IR (KBr) 3310 (br), 3102, 3085, 3020, 2990, 2938, 2862, 1656, 1638, 1160, 1135, 1100, 1078, 1060, 995, 988, 915, 898 cm^{-1}; MS (CI), *m/z* 183 (MH^+), 166, 165, 147. Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.94; H, 10.16.

2β-[1-(Chloromethyl)ethenyl]-1β-ethenylcyclohexanol (24). By use of the procedure described for the preparation of **18**, diol **23** (800 mg, 4.39 mmol) gave 795 mg (90%) of **24** as a colorless liquid after chromatographic purification: ^{1}H NMR ($CDCl_3$) δ 6.26 (dd, J = 17.3, 10.9 Hz, $CH{=}CH_cH_t$), 5.32 (d, J = 1.0 Hz, $=CHH$), 5.27 (dd, J = 17.3, 1.6 Hz, $CH{=}CH_cH_t$), 5.16 (dd, J = 10.9, 1.6 Hz, $CH{=}CH_cH_t$), 4.96 (s, $=CHH$), 4.17 (AB q, J = 11.9 Hz, $\Delta\nu$ = 59.4 Hz, A part d, J = 1.1 Hz, B part d, J = 0.9 Hz, CH_2Cl), 2.45 (dd, J = 12.7, 3.4 Hz, CH), 1.90–1.30 (m, 8 H); ^{13}C NMR ($CDCl_3$) δ 146.13 (s), 139.23 (d), 116.91 (t), 114.09 (t), 74.87 (s), 51.49 (d), 49.75 (t), 41.57 (t), 29.16 (t), 26.08 (t), 23.57 (t); IR (neat) 3560, 3460, 3090, 3020, 2940, 2860, 1640, 1260, 1165, 993, 927, 907, 745 cm^{-1}.

2β-[1-(Bromomethyl)ethenyl]-1β-ethenylcyclohexanol (25). By use of the procedure described for the preparation of **19**, diol **23** (500 mg, 2.74 mmol) gave 535 mg (80%) of **25** as a colorless liquid after chromatographic purification: ^{1}H NMR ($CDCl_3$) δ 6.22 (dd, J = 17.3, 11.0 Hz, $CH{=}CH_cH_t$), 5.31 (s, $=CHH$), 5.23 (dd, J = 17.3, 1.6 Hz, $CH{=}CH_cH_t$), 5.13 (dd, J = 11.0, 1.6 Hz, $CH{=}CH_cH_t$), 4.92 (s, $=CHH$), 4.10 (AB q, J = 9.9 Hz, $\Delta\nu$ = 86.6 Hz, A part d, J = 0.9 Hz, B part d, J = 0.6 Hz, CH_2Br), 2.47 (dd, J = 12.5, 3.3 Hz, CH), 1.90–1.30 (m, 8 H); ^{13}C NMR ($CDCl_3$) δ 146.56 (s), 139.20 (d), 117.76 (t), 114.08 (t), 75.02 (s), 51.35 (d), 41.61 (t), 39.29 (t), 29.36 (t), 26.03 (t), 23.57 (t); IR (neat) 3460, 3090, 3020, 2940, 2860, 1635, 1210, 1160, 995, 910 cm^{-1}; MS (HREI), parent not observed, m/z 229.0414 (229.0416 calcd for $C_{11}H_{16}{}^{81}Br$, $M^+ - OH$), 165.1278 (165.1279 calcd for $C_{11}H_{17}O$, $M^+ - Br$), 164.1194 (164.1201 calcd for $C_{11}H_{16}O$, $M^+ - HBr$); MS (HRFA), m/z 227.0431 (227.0436 calcd for $C_{11}H_{16}{}^{79}Br$, $M^+ - OH$).

2β-[1-[(Acetyloxy)methyl]ethenyl]-1β-ethenylcyclohexanol (26). By use of the procedure described for the preparation of **20**, diol **23** 100 mg, 0.55 mmol) provided 120 mg (98%) of **26** as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 6.21 (dd, J = 17.2, 10.9 Hz, $CH{=}CH_cH_t$), 5.23 (dd, J = 17.2, 1.7 Hz, $CH{=}CH_cH_t$), 5.07 (dd, J = 10.9, 1.7 Hz, $CH{=}CH_cH_t$), 5.08 (q, J = 1.3 Hz, $=CHH$), 4.85 (s, $=CHH$), 4.50 (AB q, J = 13.9 Hz, $\Delta\nu$ = 27.9 Hz, A part br s, B part t, J = 1.3 Hz, CH_2OAc), 2.42 (br s, OH), 2.15 (dd, J = 12.7, 3.4 Hz, CH), 2.01 (s, CH_3), 1.80–1.20 (m, 8 H); ^{13}C NMR ($CDCl_3$) δ 170.61 (s), 144.53 (s), 139.25 (d), 113.84 (t, 2 overlapping resonances), 74.29 (s), 67.13 (t), 52.19 (d), 41.03 (t), 28.57 (t), 26.02 (t), 23.35 (t), 20.81 (q); IR (neat) 3490, 3090, 3020, 2940, 2862, 1738, 1650, 1240, 1050, 995 cm^{-1}.

2,3,3aα,5,6,7,8,8aα-Octahydro-1-methyleneazulen-4(1*H*)-one (33) from 18. A Fischer–Porter pressure bottle was charged with chloride **18** (100 mg, 0.50 mmol), propylene oxide (3 mL), and dry cyclohexane (50 mL), sealed, and carefully added to a constant-temperature refluxing-solvent bath ($T \approx 210$ °C). **Caution**: The thermolysis apparatus must be placed behind a safety shield. After 2.5 h, the pressure bottle was carefully removed, allowed to cool to room temperature, vented, and the reaction mixture was concentrated. Purification of the residue by flash chromatography (silica gel, 40:1 hexane–ethyl acetate) gave 66 mg (81%) of **33** as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 4.89 (q, J = 1.8 Hz, $=CHH$), 4.80 (q, J = 1.8 Hz, $=CHH$), 3.13 (td, J = 8.8, 7.4 Hz, H_{3a}), 2.79 (t, J = 10.3 Hz, H_{8a}), 2.6–2.2 (m, 4 H), 2.0–1.4 (m, 7 H), 1.2 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 213.50 (s), 156.34 (s), 105.88 (t), 56.45 (d), 44.40 (d), 43.24 (t), 33.70 (t), 32.40 (t), 28.70 (t), 25.50 (t), 25.02 (t); IR (neat) 3078, 2940, 2860, 1707, 1654, 1150, 884 cm^{-1}; MS (HREI), m/z 164.1196 (164.1201 calcd for $C_{11}H_{16}O$).

2,3,3aα,5,6,7,8,8aα-Octahydro-1-methyleneazulen-4(1*H*)-one (33) from 19. By use of the procedure described for the rearrangement of **18**, bromide **19** (121 mg, 0.49 mmol) was heated at 204 °C for 90 min to afford 61 mg (75%) of **33**. This material was identical in all respects with that prepared from **18**.

3aα,5,6,7,8,8aα-Hexahydroazulene-1,4(2*H*,3*H*)-dione (34).[24] A solution of *cis*-**33** (56 mg, 0.34 mmol) and MeOH (10 mL) was cooled to −78 °C, and ozone was passed through the solution until the blue color persisted. Excess ozone was removed by a steam of N_2, dimethyl sulfide (1 mL) was added, and the reaction mixture was allowed to warm to room temperature and was concentrated. The residue was partitioned between CH_2Cl_2 (15 mL) and H_2O (20 mL), the aqueous layer was extracted with CH_2Cl_2 (5 mL), and the combined organic extracts were dried (Na_2SO_4) and concentrated. Purification of the residue by flash chromatography (silica gel, 5:1 hexane–ether) gave 42 mg (74%) of **34** as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 3.36 (dt, J = 9.7, 7.7 Hz, H_{3a}), 2.6–1.7 (m, 10 H), 1.46 (m, 2 H), 1.09 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 218.74 (s), 211.61 (s), 52.60 (d), 47.98 (d),[57] 42.98 (t), 37.47 (t), 28.32 (t), 28.08 (t), 25.27 (t), 21.27 (t); IR (neat) 2940, 2860, 1740 (br), 1705 (br), 1449, 1140 cm^{-1}.

2,3,3aβ,5,6,7,8,8aα-Octahydro-1-methyleneazulen-4(1*H*)-one (35). A solution of *cis*-**33** (100 mg, 0.61 mmol), 2 M NaOH (3.3 mL), and THF (3.3 mL) was stirred at room temperature for 24 h. After partitioning between CH_2Cl_2 (40 mL) and H_2O (40 mL), the aqueous phase was extracted with CH_2Cl_2 (2 × 10 mL), and the combined organic extracts were dried (Na_2SO_4) and concentrated to give 90 mg (90%) of crude **35**. Capillary GC analysis showed an 84:16 mixture of *trans*-**35**/*cis*-**33**. An analytical sample of *trans*-**35** was obtained by chromatographic separation (silica gel, 100:1 hexane–ethyl acetate): ^{1}H NMR ($CDCl_3$) δ 4.88 (q, J = 2.4 Hz, $=CHH$), 4.77 (q, J = 2.4 Hz, $=CHH$), 2.83 (dt, J = 11.0, 6.8 Hz, H_{3a}), 2.6–1.6 (m, 11 H), 1.3 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 213.50 (s), 155.20 (s), 105.33 (t), 57.66 (d), 47.28 (d), 43.93 (t), 35.35 (t), 31.56 (t), 28.67 (t), 25.08 (t), 23.31 (t); IR (neat) 3078, 2930, 2855, 1701, 1651, 1184, 880 cm^{-1}; MS (HREI), m/z 164.1204 (164.1201 calcd for $C_{11}H_{16}O$).

3aβ,5,6,7,8,8aα-Hexahydroazulene-1,4(2*H*,3*H*)-dione (36).[24] Ozonolysis of *trans*-**35** (56 mg, 0.34 mmol) using the procedure described for the preparation of **34** and purification of the residue by flash chromatography (silica gel, 5:1 hexane–ether) followed by sublimation (oil bath 75 °C, 0.01 mm) gave 31 mg (55%) of **36** as a white solid: mp 88–89 °C (lit.[24] mp 90.5–91.5 °C); ^{1}H NMR ($CDCl_3$) δ 3.00 (distorted dt, J = 7.1, 10.2 Hz, H_{3a}), 2.64 (m, 1 H), 2.49–2.30 (m, 3 H), 2.25–1.82 (m, 6 H), 1.66 (m, 1 H), 1.28 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 217.15 (s), 211.73 (s), 54.37 (d), 51.70 (d), 43.78 (t), 36.84 (t), 30.76 (t), 28.23 (t), 23.16 (t), 21.15 (t); IR (KBr) 2980, 2940, 2870, 1735, 1695, 1171, 1147 cm^{-1}.

7aα-Ethenyl-2,3,3aα,4,5,6,7,7a-octahydro-3-methylenebenzofuran (37). A solution of **18** (103 mg, 0.51 mmol) and dry THF (5 mL) was cooled to 0 °C, and *n*-BuLi (0.43 mL, of a 1.2 M solution in hexane, 0.52 mmol) was added over ~5 min. After 3 h at 0 °C, the reaction mixture was quenched with saturated NH_4Cl and extracted with 5:1 hexane–ether (2 × 5 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated to afford 78 mg (93%) of **37** as a colorless liquid: ^{1}H NMR ($CDCl_3$) δ 5.82 (dd, J = 17.4, 10.8 Hz, $CH{=}CH_cH_t$), 5.25 (dd, J = 17.4, 1.6 Hz, $CH{=}CH_cH_t$), 5.07 (dd, J = 10.8, 1.6 Hz, $CH{=}CH_cH_t$), 4.86 (q, J = 2.0 Hz, $=CHH$), 4.82 (q, J = 2.0 Hz, $=CHH$), 4.37 (AB q, J = 13.3 Hz, $\Delta\nu$ = 17.6 Hz, A part q, J = 2.0 Hz, B part dt, J = 1.1, 2.5 Hz, CH_2O), 2.40 (t, J = 6.4 Hz, CH), 1.70–1.15 (m, 8 H); ^{13}C NMR ($CDCl_3$) δ 151.88 (s), 141.91 (d), 113.42 (t), 102.72 (t), 83.03 (s), 68.51 (t), 47.38 (d), 32.20 (t), 26.67 (t), 22.20 (t), 22.11 (t); IR (neat) 3080, 3010, 2940, 2860, 1670, 1642, 1048, 1030, 925, 882 cm^{-1}; MS (HREI), m/z 164.1194 (164.1201 calcd for $C_{11}H_{16}O$).

(*E*)-5-(Chloromethyl)-5-cyclodecen-1-one (38) and 1-(Chloromethylene)-1,2,3,4,4a,5,6,7,8,8aα-decahydro-4aα-naphthalenol (39). By use of the procedure described for the rearrangement of **18**, chloride **24** (100 mg, 0.50 mmol) was heated at 204 °C for 2 h in cyclohexane (50 mL). Purification of the residue by flash chromatography (silica gel, 50:1 hexane–ethyl acetate) afforded 49 mg (49%) of **38** as a colorless oil and 20 mg (20%) of **39** as a pale yellow oil. **38**: ^{1}H NMR ($CDCl_3$) δ 5.49 (t, J = 7.9 Hz, =CH), 3.98 (s, CH_2Cl), 2.50–1.50 (m, 14 H); ^{13}C NMR ($CDCl_3$) δ 214.37 (s), 134.62 (s), 133.46 (d), 49.48 (t), 45.60 (t), 34.68 (t), 28.19 (t), 25.50 (t), 24.01 (t), 23.34 (t), 19.20 (t); IR (neat) 2930, 2860, 1705, 1245, 1208, 974, 692 cm^{-1}. **39**: ^{1}H NMR ($CDCl_3$) δ 5.88 (d, J = 1.8 Hz, =CH), 2.71 (br d, J = 14.2 Hz, CH), 2.1–1.1 (m, 14 H); ^{13}C NMR ($CDCl_3$) δ 142.89, 111.08, 72.35, 52.52, 39.86, 31.06, 30.01, 25.68, 23.56, 23.51, 21.41; IR (neat) 3460, 2940, 2860, 1635, 1145, 960, 935, 838 cm^{-1}.

(*E*)-5-[(Acetyloxy)methyl]-5-cyclodecen-1-one (40) and 1-[(Acetyloxy)methylene]-1,2,3,4,4a,5,6,7,8,8aα-decahydro-4aα-naphthalenol (41). By use of the procedure described for the rearrangement of **18**, acetate **26** (100 mg, 0.45 mmol) was heated at 204 °C for 4 h in cyclohexane (50 mL) without propylene oxide. Purification of the residue by flash chromatography (silica gel, 15:1 hexane–ethyl acetate) afforded 30 mg (30%) of **40** and 32 mg (32%) of **41** as colorless oils. **40**: ^{1}H NMR ($CDCl_3$) δ 5.39 (t, J = 8.0 Hz, =CH), 4.47 (s, CH_2OAc), 2.50–1.50 (m, 14 H), 2.05 (s, CH_3); ^{13}C NMR ($CDCl_3$) δ 214.52 (s), 170.89 (s), 133.06 (s), 131.77 (d), 67.89 (t), 45.68 (t), 34.46 (t), 28.28 (t), 25.09 (t), 23.87 (t), 23.26 (t), 21.00 (q), 19.24 (t); IR (neat) 2940, 2860, 1740, 1705, 1235, 1025 cm^{-1}; MS (HREI), m/z 224.1407 (224.1412 calcd for $C_{13}H_{20}O_3$). **41**: ^{1}H NMR ($CDCl_3$) δ 6.96 (d, J = 1.9 Hz, =CH), 2.58 (br d, J = 13.8 Hz, CH), 2.15–1.20 (m, 14 H), 2.09 (s, CH_3); ^{13}C NMR ($CDCl_3$) δ 168.15 (s), 129.33 (d), 125.78 (s), 71.96 (s), 48.87 (d), 39.80 (t), 31.15 (t), 29.98 (t), 25.67 (t), 23.61 (t), 21.63 (t), 21.11 (t), 20.73 (q); IR (neat) 3460, 2930, 2860, 1752, 1682, 1228, 1090, 952 cm^{-1}.

1,2,3,4,4a,5,6,7,8,8aα-Decahydro-4aα-hydroxy-1-naphthalenecarboxaldehyde (42). A solution of **41** (32 mg, 0.14 mmol), 2 M NaOH (1 mL), and THF (1 mL) was stirred at room temperature for 48 h. After partitioning between ether (10 mL) and H_2O (10 mL), the aqueous phase was extracted with ether (2 × 5 mL), and the combined organic extracts were washed with 5% $NaHCO_3$ and brine, dried (Na_2SO_4), and concentrated to give 23 mg (88%) of **42** as a pale yellow oil, which was a 1:1 mixture of stereoisomers: ^{1}H NMR ($CDCl_3$) δ 9.66 (br s, CHO), 9.62 (s, CHO), 2.96 (dt, J = 12.7, 3.9 Hz, CH, 1/2 H), 2.0–1.1 (m, 15.5 H); ^{13}C NMR ($CDCl_3$) δ 205.98 and 204.51 (d), 71.38 (s), 51.05 (d), 49.25 and 43.23 (d), 42.12 (t), 30.78 (t), 25.79 (t), 24.61 (t), 23.90 (t), 20.18 (t), 19.17 (t); IR (neat) 3440, 2930, 2862, 1720 (br), 1660 (br) cm^{-1}.

2,3,3aβ,5,6,7,8,8aα-Octahydro-1-methyleneazulen-4(1*H*)-one (35) and (*E*)-5-(Bromomethyl)-5-cyclodecen-1-one (44). By use of the procedure described for the rearrangement of **18**, bromide **25** (10 mg, 0.04 mmol) was heated at 155 °C for 7 h in benzene (10 mL). Bromohydrin removal under high vacuum (<0.1 mm) afforded 7 mg, which was a mixture of **25**, **35**, and **44**. Proton integration of the olefinic resonances provided a mole ratio of 15.35:70.52:14.13, respectively. On the basis of unreacted **25** (14%), the rearrangement to **35** (75%) and **44** (15%) occurred in 90% yield and provided a 5:1 ratio (**35**/**44**).

To obtain a higher proportion of medium ring **44**, bromide **25** (122 mg, 0.50 mmol) was heated at 204 °C for 90 min in cyclohexane (50 mL). Purification of the residue by flash chromatography (silica gel, 40:1 hexane–ethyl acetate) afforded 24 mg (29%) of **35** as a colorless oil and 43 mg (35%) of **44** as a pale yellow oil. **35**: This material was identical in all respects with that prepared from **33**. **44**: ^1H NMR ($CDCl_3$) δ 5.59 (t, J = 8.0 Hz, =CH), 3.97 (s, CH_2Br), 2.50–2.20 (m, 5 H), 2.04 (m, 2 H), 1.85 (m, 4 H), 1.65 (m, 3 H); ^{13}C NMR ($CDCl_3$) δ 214.41 (s), 134.96 (s), 134.23 (d), 45.62 (t), 38.25 (t), 34.65 (t), 28.18 (t), 25.79 (t), 24.34 (t), 23.40 (t), 19.23 (t); IR (neat) 2930, 2860, 1705, 1205, 975, cm^{-1}.

1-[(Acetyloxy)methylene]-1,2,3,4,4a,5,6,7,8,8aα-decahydro-4aβ-naphthalenol (46). By use of the procedure described for the rearrangement of **26**, acetate **20** (100 mg, 0.45 mmol) afforded 96 mg (96%) of **46** as a colorless oil: ^1H NMR ($CDCl_3$) δ 6.68 (s, =CH), 2.80 (m, $H_{2\beta}$), 2.04 (s, CH_3), 1.91 (dd, J = 10.3, 4.0 Hz, H_{8a}), 1.85–1.05 (m, 13 H); ^{13}C NMR ($CDCl_3$) δ 168.05 (s), 129.02 (d), 125.97 (s), 71.31 (s), 46.94 (d), 39.53 (t), 38.48 (t), 26.47 (t), 25.68 (t), 23.08 (t), 22.05 (t), 20.96 (t), 20.55 (q); IR (neat) 3510, 3110, 2940, 2860, 1750, 1680, 1230, 1112, 1082, 952 cm^{-1}; MS (HREI), parent not observed, m/z 164.1200 (164.1201 calcd for $C_{11}H_{16}O$, $M^+ - CH_3CO_2H$); MS (HRFA), m/z 231.1568 (231.1573 calcd for $C_{13}H_{20}O_3{}^7Li$; $M^+ + {}^7Li$).

1,2,3,4,4a,5,6,7,8,8aα-Decahydro-4aβ-hydroxy-1-naphthalenecarboxaldehyde (47) and Lactols. By use of the procedure described for the hydrolysis of **41**, acetate **46** (35 mg, 0.16 mmol) afforded 26 mg (91%) of **47** as a pale yellow oil, which was a complex mixture of aldehydes (1:7.2) and lactols (1.4:8.2): ^1H NMR ($CDCl_3$, major absorptions are listed first in each pair) δ 9.52 (d, J = 3.8 Hz) and 9.85 (s, CHO), 5.31 and 5.71 (s, CHOH), 3.73 and 3.95 (s, OH); ^{13}C NMR ($CDCl_3$, major absorptions are listed first in each pair) δ 205.29 and 205.28 (d), 101.40 and 100.46 (d), 84.95 and 82.34 (s), 69.27 and 70.17 (s), 51.06 and 50.43 (d), 49.98 and 49.10 (d), 47.30 and 46.63 (d), 43.59 and 44.50 (d), (major upfield resonances only, all t) 39.90, 39.23, 39.09, 33.44, 28.53, 26.40, 26.35, 25.81, 25.76, 24.97, 21.47, 21.26, 19.84, 19.78; IR (neat) 3400, 2930, 2860, 1722, 975, 938 cm^{-1}.

Kinetic Measurements. A stock standard solution of the allylic halide (~1 mg/mL), tridecane (~0.4 mg/mL), as an internal standard, and propylene oxide (0.05 mL/mL) in dry cyclohexane or alternate solvents was prepared. An aliquot (10 mL) of the above solution was transferred to a Fischer–Porter pressure bottle (3 oz, 90 mL) under an argon atmosphere, and the sealed pressure bottle was immersed in a constant-temperature refluxing-solvent bath. The bath consisted of an insulated large-neck 2-L round-bottom flask mounted in a heating mantel and equipped with a rubber collar, reflux condenser, and thermometer. The temperature gradient and fluctuations in the working region of this bath did not vary more than ~0.5 °C. Upon removal from the temperature bath, the pressure bottle was cooled to 0 °C and opened, and the contents were transferred to a vial until analyzed by VPC. Since sampling of the reaction vessel contents could not be safely achieved, each aliquot represents a single determination, due to this limitation the calculated rate constants are probably only good to ±10%.

All VPC analyses were carried out on a Varian Model 3700 gas chromatograph equipped with a 15 m × 0.53 mm FSOT column, packed with DB-1 1.5-μm film, and a flame-ionization detector. Peak areas were determined by electronic integration, and absolute yields were determined by calibration of the allylic chloride (RRF = 0.727) and *cis*-hydroazulenone (RRF = 0.863) versus tridecane as internal standard. Rate constants and Eyring and Arrhenius parameters were determined by least-squares analysis using a RS/1 software package (Release 2 and 3), BBN Software Products Corp., running on a Micro VAX II.

Reaction of Chloride 56 with Silver(I). A mixture of chloride **56** (100 mg, 0.5 mmol), Ag_2CO_3 (700 mg, 2.5 mmol), Na_2CO_3 (400 mg, 3.8 mmol), and benzene (20 mL) was heated at reflux in a foil-wrapped flask for 24 h, cooled to room temperature, filtered, and concentrated to afford ~60 mg of a yellow oil. Analysis of the ^1H NMR spectrum indicated the absence of **56** and the presence of four major products, hydroazulenones **57** + **58** and ethers **59** + **60**. Integration of the residual proton resonances provided a mole ratio of 25:17:49:9, respectively.

FVP Rearrangements. Gas phase pyrolysis experiments were performed in a flow system. The precursor (~10 mg) in a minivial was placed in a round-bottom flask which was connected to the end of an unpacked quartz pyrolysis tube (40 cm × 12.7 mm, 55 cm overall length) mounted horizontally in a Lindberg tube furnace (30-cm reaction zone). The pyrolysis tube outlet was connected to a trap, cooled to −78 °C, which was attached to the vacuum source. The precursor was generally evaporated at ambient temperature, although for less volatile samples modest warming with a tubular oven (Kugelrohr) was employed to decrease experimental intervals. The condensate was transferred with added solvent to a vial and concentrated, and the weight ratio of volatile materials to starting precursor was determined. Analysis of the ^1H NMR spectrum and integration of the appropriate resonances provided the mole ratios reported in the text.

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Registry No. 9, 18325-75-2; **10** (isomer), 118574-50-8; **10** (isomer 2), 118574-51-9; **11**, 111615-41-9; **12**, 111615-42-0; **13**, 118495-54-8; **14**, 111615-44-2; **15**, 111615-45-3; **16**, 118495-55-9; **17**, 111615-46-4; **18**, 111615-47-5; **19**, 111615-48-6; **20**, 118495-56-0; **21** (isomer 1), 111615-58-8; **21** (isomer 2), 111765-96-9; **22**, 111615-57-7; **23**, 111634-62-9; **24**, 111615-52-2; **25**, 111615-53-3; **26**, 118495-57-1; **27** (R = OCH_3), 118495-58-2; **27** (R = CH_3), 118495-67-3; **28**, 111615-59-9; **29**, 111615-60-2; **30**, 118495-59-3; **31**, 118495-60-6; **32**, 118495-61-7; **33**, 111615-50-0; **34**, 79880-96-9; **35**, 111615-51-1; **36**, 79880-97-0; **37**, 111615-49-7; **38**, 111615-54-4; **39**, 118495-62-8; **40**, 118495-63-9; **41**, 118495-64-0; 1α-**42**, 118495-65-1; 1β-**42**, 118495-70-8; **43**, 118495-66-2; **44**, 111615-55-5; **46**, 118495-68-4; 1α-**47**, 118495-69-5; 1β-**47**, 118495-51-5; **47** (lactol 1), 118495-52-6; **47** (lactol 2), 118574-48-4; **56**, 111615-61-3; **57**, 111615-62-4; **58**, 118495-71-9; **59**, 118495-72-0; **60**, 118495-73-1; **61a**, 118574-52-0; **61b**, 118574-49-5; **62**, 118495-74-2; **63**, 118495-75-3; *pro*-(*R*)-**64**, 118495-53-7; *pro*-(*S*)-**64**, 118574-53-1; **65**, 118597-13-0; **66**, 118597-14-1; $CH_3O(CH_2)_2C(OCH_3)_3$, 77197-59-2.