# Vinylcyclobutanols: A Composite Functional Group?

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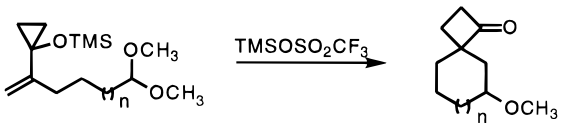
**Abstract:** The effect of small strained rings on chemical reactivity was probed by the examination of the behavior of vinylcyclobutanols as terminators in cyclization reactions. The substrates were readily available by the addition of vinyllithium reagents bearing acetals as cyclization initiators to cyclobutanone. Bronsted and Lewis acids both promoted cyclization in contrast to vinylcyclopropanol terminators for which Bronsted acids failed. The products are spirocycles consisting of a cyclopentanone derived from ring expansion of the cyclobutanol and the second ring derived by attack of the terminator on the initiator. Spirocyclization to [4.5] and [4.6] systems proceeded smoothly, whereas spirocyclization to a [4.7] system failed. Attaching the cyclization termini to a preexisting ring system (whereby tricycles consisting of a fused bicycle and a spirocycle are formed) expands the scope of the cyclization to include the [4.7] ring system even at 0.01 M, a rather high concentration for such an unfavorable ring system. The diastereoselectivity generally placed the initiator substituent and the carbon−carbonyl bond of the cyclopentanone ring *trans* on the newly formed ring. Cyclic acetals and the free aldehyde also served as initiators. The mechanistic implications of these observations are discussed.

## Introduction

The chemistry of strained rings represents a continuing field of endeavor— fascinating from both theoretical-physical[1] and synthetic[2] points of view. While much effort has focused on the cyclopropyl unit as the most strained member, the cyclobutyl moiety offers nearly the same strain energy,[3] although the bonding characteristics of the C−C bonds appear to be quite different. In considering the effects of small rings on chemical transformations, ground state effects do not necessarily reveal what may be important in the transition state. We have undertaken studies of the development of potentially useful synthetic reactions based upon the chemistry of small rings.

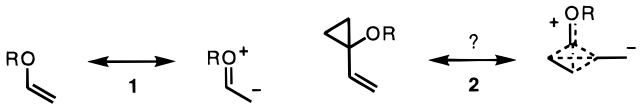
The effectiveness of cyclization reactions depends on both the initiator and the terminator.[4] In a study wherein vinylcyclopropanols were employed as terminators, as depicted in eq 1, a number of observations suggested that these terminators behaved differently from standard ones.[5] While five-membered




(1)

rings could not be formed, eight-membered rings were formed with remarkable ease and with good diastereoselectivities without resorting to high dilution. Even a 13-membered ring formed in acceptable yields under such conditions.

This remarkable behavior led us to consider whether the vinylcyclopropanol had some special bonding characteristics that affected transition state energies. One way to consider this question is to compare it to an enol **1** (R = H), which is a composite of an alcohol and a double bond. The conjugation




of the two groups permits electron delocalization from oxygen to carbon that facilitates attack of electrophiles at the carbon $\beta$ to the oxygen substituent—a structural feature that forms the heart of a vast domain of synthetic chemistry. By interposing a cyclopropane ring between the oxygen and the double bond as in **2**, does the cyclopropane still transmit electronic information as depicted by the potential resonance structure? While such interactions will likely be minimally important in the ground state, their importance should increase significantly in the transition state for electrophilic addition. The $\pi$ like character of cyclopropyl bonds[6] and the importance of delocalization contributing to the stability of the cyclopropylcarbinyl cations[7] support this interpretation. Thus, this composite functional group juxtaposes an oxygen, a cyclopropyl ring, and a double bond in such a way that they act in concert when challenged by an electrophile. A second structural issue deals with release of ring strain in the transition state that accompanies the ring enlargement. In the case of a cyclopropyl to cyclobutyl ring adjustment, this effect is minimal since the difference in ring strain is only on the order of 1−2 kcal/mol.[3]

The vinylcyclobutanol system is of particular interest because the cyclobutane ring also possesses the capability of interacting with an adjacent alkenyl group or $sp^2$-hybridized center, albeit less effectively than the cyclopropane ring. The direct conjugation of the Walsh orbitals in a cyclobutane ring with the $\pi$-orbitals of adjacent double bonds has been investigated by semiempirical[9,10] and *ab initio*[11] calculations and photoelectron spectroscopy.[12,13] These studies suggest a resonance integral $\beta$ value for a vinylcyclobutane similar to that of a

⊗ Abstract published in *Advance ACS Abstracts,* November 15, 1996.

(1) Wiberg, K. B. *Acc. Chem. Res.* **1996**, *29*, 229. Also see: Karasakov, P. B.; Gerratt, J.; Cooper, D. L.; Raimondi, M. *J. Am. Chem. Soc.* **1994**, *116*, 7714.

(2) Small Ring Compounds in Organic Synthesis, Parts I, II, III; de Meijere, A., Ed.; Springer Verlag: Berlin, 1988. The Chemistry of the Cyclopropyl Group, Rappoport, Z., ed.; Wiley: Chichester, 1995.

(3) Pell, A. S.; Pilcher, G. *Trans. Faraday Soc.* **1965**, *61*, 71.

(4) Cf. Johnson, W. S.; Telfer, S. J. *J. Am. Chem. Soc.* **1987**, *109*, 2517. For reviews, see: Johnson, W. S. *Angew. Chem., Int. Ed. Engl.* **1976**, *15*, 9; *Biorg. Chem.* **1976**, *5*, 51.

(5) Trost, B. M.; Lee, D. C. *J. Am. Chem. Soc.* **1988**, *110*, 6556.

(6) Walsh, A. D. *Trans. Faraday Soc.* **1949**, *45*, 179.

(7) For a review, see: Wiberg, K. B.; Hess, B. A., Jr.; Ashe, A. J., III In Carbonium Ions, Olah, G. A., Schleyer, P. v. R., Eds.; Wiley: New York, 1972; Vol. 3.

(8) Gleiter, R. *Top. Curr. Chem.* **1979**, *86*, 197.

(9) Hoffmann, R.; Davidson, R. B. *J. Am. Chem. Soc.* **1971**, *93*, 5699.

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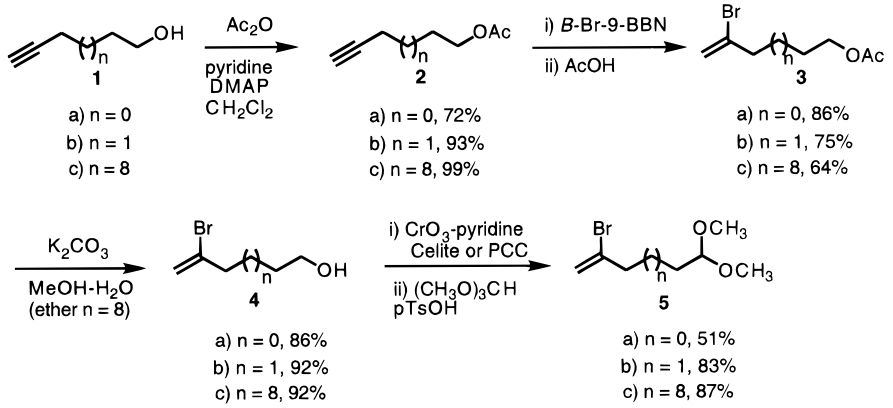
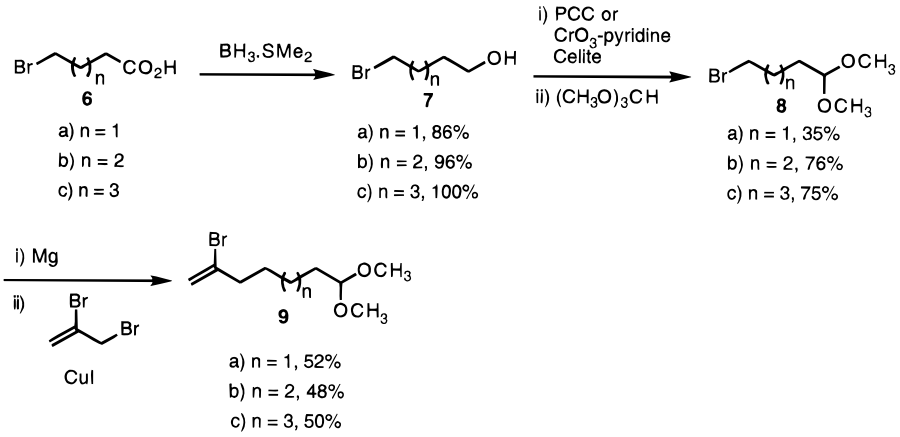
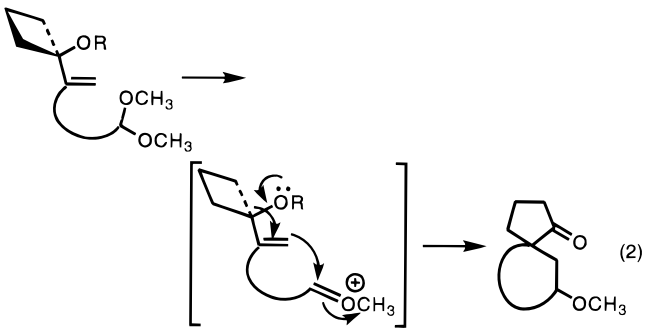
**Scheme 1.** Preparation of Vinyl Bromides via Bromoboronation




**Scheme 2.** Preparation of Vinyl Bromides via 2,3-Dibromopropene

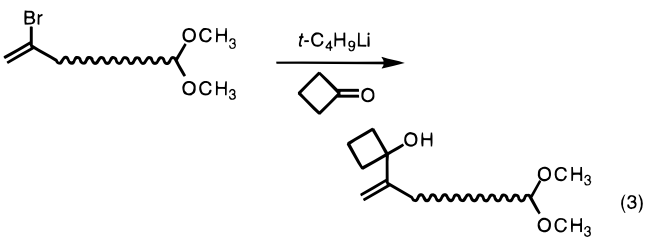



vinylcyclopropane although the interaction integral is diminished. While the bonding of the cyclobutane attenuates its ability to delocalize charge, the approximately 20 kcal/mol of strain energy released by expansion of the four- to a five-membered ring may compensate for the electronic deficits. We undertook a study of vinylcyclobutanol terminators in cyclizations according to eq 2 to evaluate these issues.




(2)

**Preparation of Substrates.** Equation 3 outlines the general strategy for the synthesis of the vinylcyclobutanols which reduces the problem to a facile synthesis of the vinyl bromide. Two routes were employed. The first route relied upon the




(3)

bromoboronation of alkynes as outlined in Scheme 1. The ready availability of terminal alkynols either commercially or via addition of terminal alkynes to carbonyl groups or epoxides followed by base promoted migration of the triple bond to a terminal position (the so called zip reaction)[14] makes such compounds attractive starting materials. Following the method of Suzuki et al.,[15] 9-BBN-Br (9-borabicyclo[3.3.1]nonyl-9-bromide) adds chemoselectively in Markovnikov-like fashion to alkynes at 0 °C. Addition of acetic acid at 0 °C effects deboronation to produce the internal vinyl bromide in good yields.

A second strategy employed copper catalyzed cross-coupling of Grignard reagents with 2,3-dibromopropene as outlined in Scheme 2. This strategy takes advantage of the availability of

(10) (a) Gleiter, R.; Kobayashi, T. *Helv. Chim. Acta* **1971**, *54*, 1081. (b) Jorgensen, W. L. *J. Am. Chem. Soc.* **1975**, *97*, 3082. (c) Jorgensen, W. L.; Borden, W. T. *J. Am. Chem. Soc.* **1973**, *95*, 6649. (d) Gleiter, R.; Bischof, P.; Volz, W. E.; Paquette, L. A. *J. Am. Chem. Soc.* **1977**, *99*, 8. (e) Bischof, P.; Gleiter, R.; Haider, R. *J. Am. Chem. Soc.* **1978**, *100*, 1036. (f) Borden, W. T.; Gold, A.; Jorgensen, W. L. *J. Org. Chem.* **1978**, *43*, 491.

(11) Hehre, W. J. *J. Am. Chem. Soc.* **1972**, *94*, 6592.

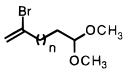
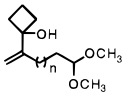
(12) (a) Bischof, P.; Gleiter, R.; de Meijere, A.; Meyer, L. U. *Helv. Chim. Acta* **1974**, *57*, 1519. (b) Bischof, P.; Gleiter, R.; Kukla, M. K.; Paquette, L. A. *J. Electron Spectrosc. Relat. Phenom.* **1974**, *4*, 177. (c) Bischof, P.; Gleiter, R.; Gubernator, K.; Haider, R.; Musso, H.; Schwarz, W.; Trautmann, W.; Hopf, H. *Chem. Ber.* **1981**, *114*, 994. (d) Gleiter, R.; Haider, R.; Spanget-Larsen, J.; Bischof, P. *Tetrahedron Lett.* **1983**, 1149. (e) Gleiter, R.; Haider, R.; Gubernator, K.; Bischof, P.;*Chem. Ber.* **1983**, *116*, 2983. (f) Gleiter, R.; Haider, R.; Bischof, P.; Lindner, H.-*J. Chem. Ber.* **1983**, *116*, 3736. (g) Borden, W. T.; Young, S. D.; Frost, D. C.; Westwood, N. P. C.; Jorgensen, W. L. *J. Org. Chem.* **1979**, *44*, 737.

(13) Bruckmann, P.; Klessinger, M. *Chem. Ber.* **1978**, *111*, 944.

(14) Brown, C. A.; Yamashita, A. *J. Am. Chem. Soc.* **1975**, *97*, 891. Abrams, S. R. *Can. J. Chem.* **1984**, *62*, 1333.

(15) Hara, S.; Dojo, H.; Takinami, S.; Suzuki, A. *Tetrahedron Lett.* **1983**, *24*, 731.

**Table 1.** Preparation of Vinylcyclobutanols from Vinyl Bromides[a]

| Starting material | Product | Yield |
|---|---|---|
|  |  | |
| **5a**, n = 1 | **10a**, n = 1 | 70% |
| **5b**, n = 2 | **10b**, n = 2 | 100% |
| **9a**, n = 3 | **10c**, n = 3 | 90% |
| **9b**, n = 4 | **10d**, n = 4 | 82% |
| **9c**, n = 5 | **10e**, n = 5 | 79% |
| **5c**, n = 9 | **10f**, n = 9 | 81% |

[a] *t*-$C_4H_9Li$, cyclobutanone, THF, −78 °C.

**Table 2.** Cyclization of 6,6-Dimethoxy-2-(1′-hydroxycyclobutyl)-1-hexene 10b

| entry | catalyst | temp (°C) | concn (M) | yield (%) | **33a:33b** |
|---|---|---|---|---|---|
| 1 | 1 equiv of $TMSOSO_2CF_3$[a] | 0 | 0.01 | 80 | 9:1 |
| 2 | 1.5 equiv of $TMSOSO_2CF_3$[b] | 0 | 0.05 | 81 | 3.8:1 |
| 3 | 0.1 equiv of $TMSOSO_2CF_3$ | 0 | 0.1 | N.D. | 8.7:1 |
| 4 | 10% $CF_3SO_3H$ | 0 | 0.01 | N.D. | 9.0:1 |
| 5 | 2 equiv of $SnCl_4$ | −20 | 0.01 | 100 | 4.3:1 |
| 6 | 10% $Ph_3CSbCl_6$ | −78 | 0.01 | 62[c] | ONLY *trans* |

[a] 0.7 equiv of 2,6-di-*tert*-butylpyridine added. [b] 1.0 equiv of pyridine added. [c] The product consisted of a 17% yield of **33a** and a 45% yield of the corresponding alcohol (loss of methyl group).

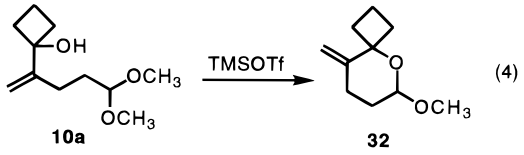
bromoacetals as precursors. As summarized in Table 1, formation of the vinylcyclobutanols occurs smoothly according to eq 3.

Effects of conformational constraints were also explored in terms of formation of fused bicycles. The conformational rigidity of the six-membered ring led us to prepare substrates that would cyclize to both *trans*- and *cis*-decalins. The 2,3-dibromopropene strategy proves effective as outlined in Scheme 3. Initially, **12** was isolated with the intention to equilibrate the two isomers to the thermodynamically more stable *trans* series. Its instability, however, thwarted such plans. As a result, the aldehyde **12** is directly acetalized to the dimethyl acetal **13**. MPLC (medium pressure liquid chromatography) achieves a partial separation from which the pure *trans* acetal can be isolated. Hydrolysis to the *trans*-aldehyde **12** ($H_2SO_4$, $H_2O$, THF, 25 °C, 87%), allows establishment of the stereochemistry by the proton coupling constants. This pure *trans*-acetal is converted to the *trans* substrate **14** in 75% yield. Alternatively, a separable 2:1 mixture of **14** and **15** forms in 53% yield from the mixture of *trans* and *cis* acetals **13**. A small byproduct in this reaction is the internal mixed acetal **16**. In this way, pure *trans* (**14**) and *cis* (**15**) substrates are available.

A cyclopentyl template represents a conformationally more flexible system. In building a substrate directed at the perhydroazulene skeleton, the alkyne strategy was adopted. As shown in Scheme 4, the aldehyde obtained upon hydrolysis of the enol ether **19**, which is initially a 7.8:1 mixture of *trans* and *cis* isomers, equilibrates to a 23:1 mixture upon treatment with magnesium methoxide. Flash chromatography following acetalization removes the minor *cis* isomer to give pure *trans* **21**. The efficiency of this sequence is readily apparent from the isolation of the terminal alkyne **22** in 72% overall yield from **18**. The dimethyl acetal proves incompatible with the bromoboronation protocol. On the other hand, stannylcupration proves effective to give the vinylstannane **23**.[16] Since the lithium−tin exchange proved more troublesome than the bromide−lithium exchange, the vinyl stannane **23** is converted to the vinyl bromide **24** which participates uneventfully in the reaction with cyclobutanone to give substrate **25**.

A homolog of 2,3-dibromopropene sets the route for the synthesis of a substrate that potentially will cyclize to a [5.8.5] ring system as outlined in Scheme 5. The homologation of the alkylated ketone **26** via the enol ether **27** gives aldehyde **28** initially as a 12:1 mixture of *trans* ($\delta$ 9.68) and *cis* ($\delta$ 9.53) isomers which equilibrates to the more stable *trans* isomer when exposed to methanolic magnesium methoxide. The acetal **29** is isolated in 69% overall yield from the cyclopentanone **26**.

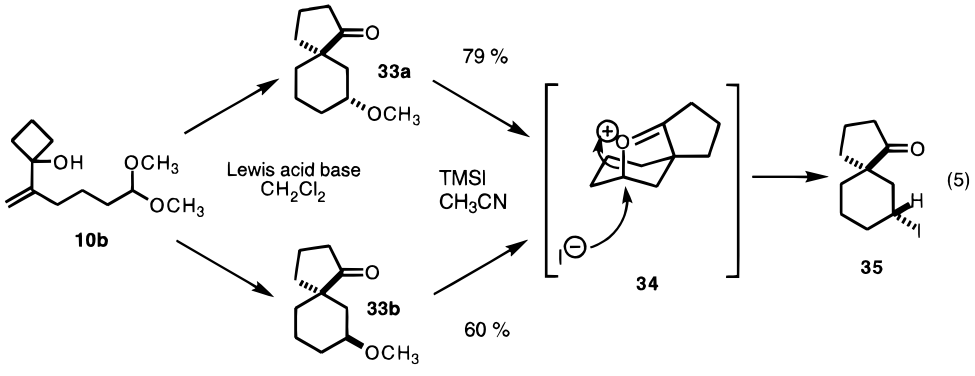
**Cyclizations.** Treatment of vinylcyclobutanol **10a** with trimethylsilyl trifluoromethanesulfonate (TMSOTf) at subambient to ambient temperature yielded mainly cyclic acetal **32** formed by transacetalization (eq 4). Attempts to form the five-membered carbocycle by raising the temperature to 50 °C gave a complicated mixture of intractable products.



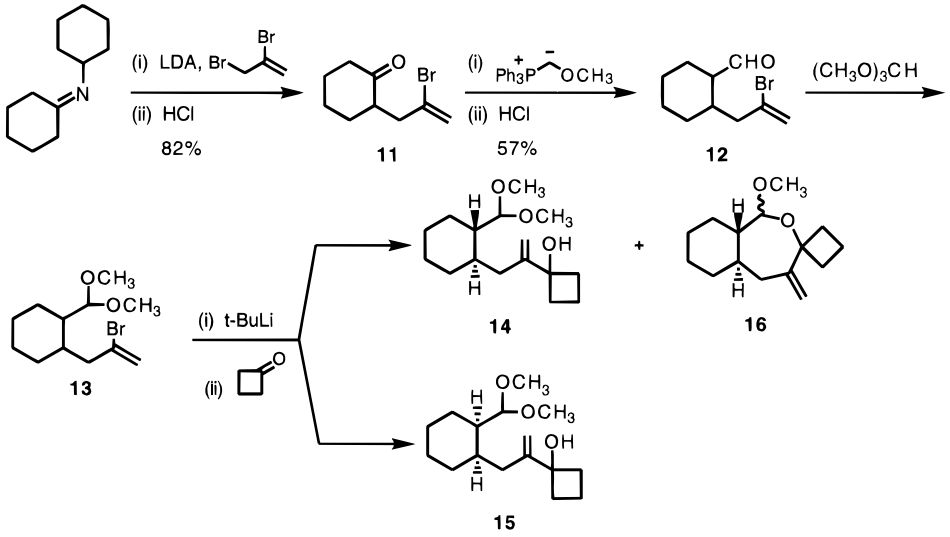
**10a** **32** (4)

On the other hand, cyclization proceeded smoothly with vinylcyclobutanol **10b** to give the [4.5]spiro compound **33** with high diastereoselectivities (eq 5). As shown in Table 2, a good diastereoselectivity of 9:1 can be observed under "standard" vinylcyclopropanol cyclization conditions of 1.0 equiv of TMSOTf and 0.7 equivs of 2,6-di-*tert*-butylpyridine in methylene chloride which became the standard conditions here too. It is curious to note that switching to pyridine affects the diastereoselectivity of the cyclization (Table 2, entry 1 vs 2).

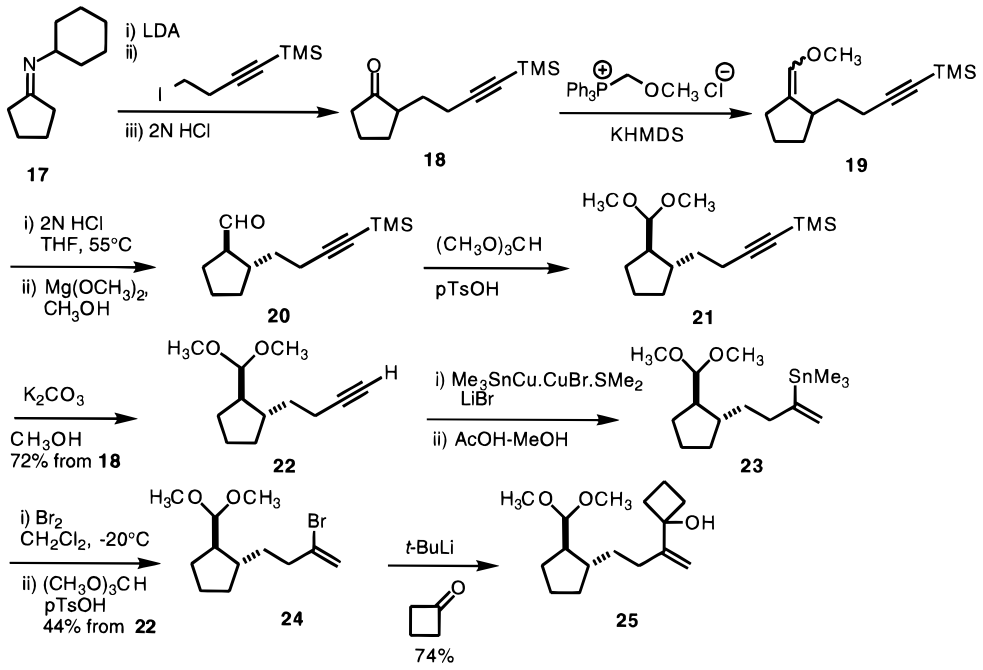
The analogous cyclization carried out with a vinylcyclopropanol terminator gave only a 2:1 diastereoselectivity.[17] $^1H$ NMR shift studies establish the major isomer to have the methoxy and carbonyl groups *trans* to each other and the minor isomer, *cis*. Using Resolve -Al[Eu(thd)$_3$, tris (2,2,6,6-tetramethyl-3,5-heptanedionato)europium)], the methine proton adjacent to the methoxy group shifts from $\delta$ 3.64 to $\delta$ 3.79 upon adding 0.2 equiv of the shift reagent in the major isomer, but is virtually



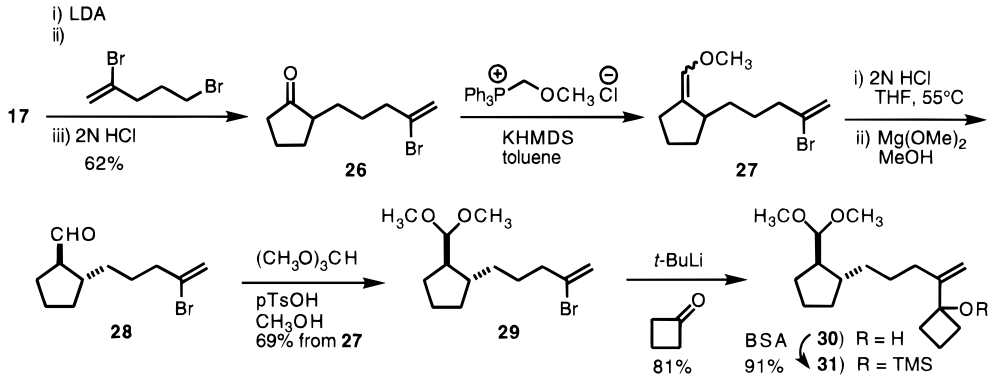
**Scheme 3.** Preparation of Decalin Cyclization Substrates




**Scheme 4.** A Synthesis of Precursor of [5.7.5]Tricycle

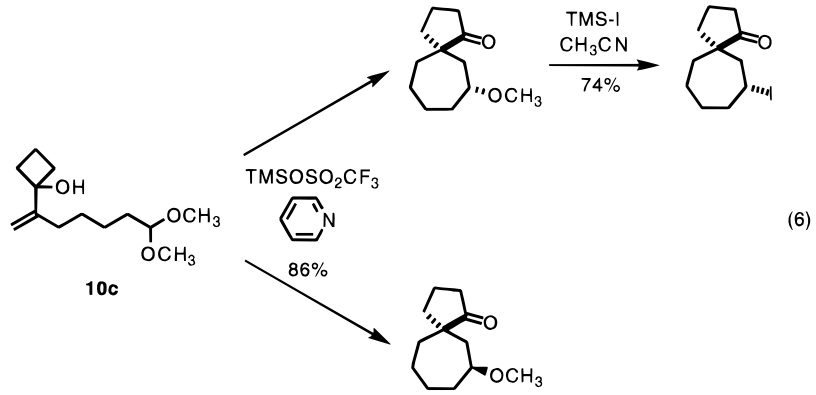



**Scheme 5.** A Synthesis of Precursor of [5.8.5]Tricycle.




unchanged ($\delta$ 3.18 to $\delta$ 3.19) in the minor isomer. A catalytic amount of the silyl triflate suffices (entry 3) and the reaction can be performed at higher concentrations. Interestingly, the reaction is also catalyzed by triflic acid (entry 4), which is in sharp contrast to the case of the vinylcyclopropanols where extraneous protons had to be rigorously excluded from the reaction mixture. The cyclization was also found to be compatible with Lewis acids such as tin(IV) chloride (entry 5) and trityl hexachloroantimonate (entry 6). The dependence of the diastereoselectivity on the catalyst is quite interesting.

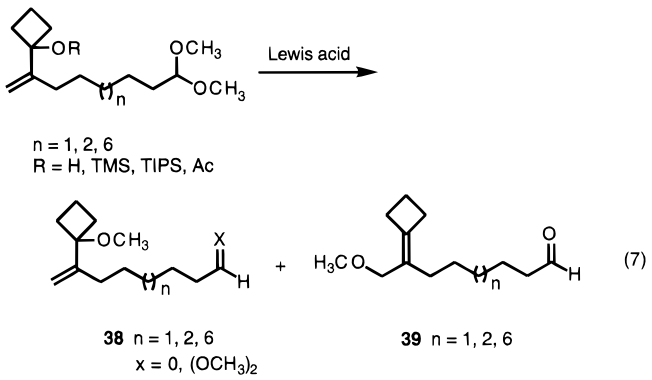
(16) Piers, E.; Chong, J. M. *Can. J. Chem.* **1988**, *66*, 1425.
(17) Trost, B. M.; Brandi, A. *J. Am. Chem. Soc.* **1984**, *106*, 5041.




In an attempt to achieve further characterization as the alcohol, the *trans* (**33a**) and *cis* (**33b**) isomers were independently exposed to trimethylsilyl iodide.[18] Instead of effecting demethylation, the methoxy group was substituted to give a single iodide **35** regardless of the stereochemistry of the starting material (eq 5). This result suggests the participation of the carbonyl oxygen as in **34** and therefore assignment of **35** as the stereochemistry of the product. The somewhat smoother conversion of the major diastereomer **33a** to iodide **35** supports its stereochemical assignment wherein formation of **34** is facilitated by direct participation of the carbonyl oxygen during the ionization step. The methine hydrogen adjacent to iodine exhibits coupling constants of 11.5 and 4.1 Hz ($\delta$ 4.79) indicative of this hydrogen being axial. A shift study using 2 mol% Eu $(fod)_3$ shifted the methine proton on the carbon bearing iodide from $\delta$ 4.78 to $\delta$ 5.12, a magnitude of shift consistent with the assigned stereochemistry.

Diastereoselective formation of a seven-membered ring occurred equally well (eq 6). The standard cyclization conditions produces an 86% yield of a 4.6:1 ratio of **36a** and **36b**. With dioxane or hexane instead of methylene chloride as solvent, the dr dropped to 1-2:1. The stereochemistry is assigned based upon analogy to the previous example and NMR shift studies with $Eu(fod)_3$. Addition of 3 mol% of the reagent effects a shift of the methine proton in the major isomer from $\delta$ 3.49 to $\delta$ 3.72 but almost no shift in the minor one ($\delta$ 3.21 to $\delta$ 3.24) in accord with predictions based upon the assigned structures. The major diastereomer reacts readily with trimethylsilyl iodide to give the iodide **37** with no trace of the methyl cleavage product (eq 6).

Extension of this cyclization to formation of 8-, 9-, or 13-membered rings using substrates **10d**, **e**, or **f** failed. As shown in eq 7, the standard conditions produce mostly a mixture of

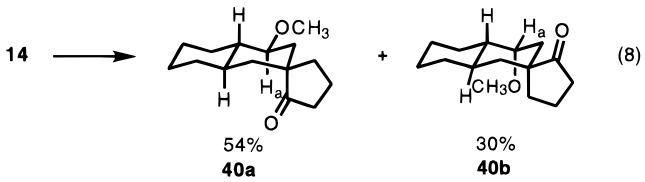



methyl ethers **38** and **39**. To address the question of the role that the free hydroxyl group plays, the trimethyl and triisopropylsilyl ethers as well as the acetate were also subjected to the standard conditions with no cyclization products being obtained.

(18) Schmidt, A. H. *Aldrich. Acta* **1981**, *14*, 31. Jung, M. E.; Lyster, M. A. *J. Org. Chem.* **1977**, *42*, 3761.

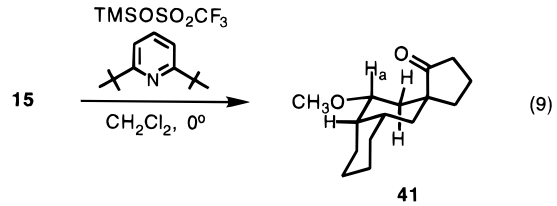
The failure to obtain eight-membered rings stood in contrast to the use of vinylcyclopropanols as terminators where such a ring size does form. Constraining the degrees of freedom may influence the cyclization. As a result, initial studies explored the effect of employing a cyclic substrate to form six- and seven-membered rings.

Subjecting the *trans* isomer **14** to the standard conditions at 0 °C gives an approximately 2:1 separable mixture of two cyclized isomers **40a** and **40b** (eq 8). The axial nature of the

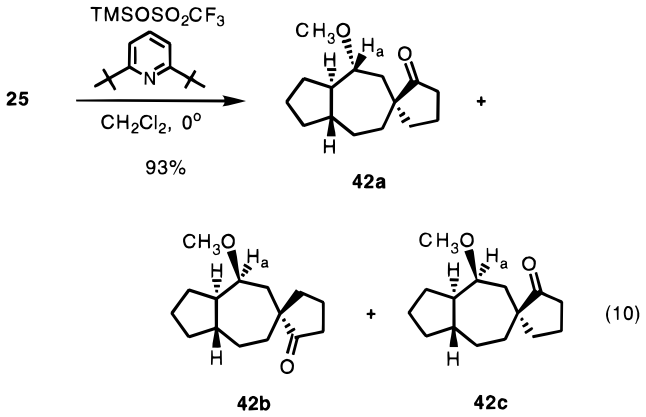



methine proton in **40a** ($\delta$ 3.65) is clearly indicated by its coupling constants (ddd, $J$ = 10.9, 9.8, 4.5 Hz) which reveal two axial−axial and one axial−equatorial couplings. The shift study with $Eu(fod)_3$, wherein the methine proton $H_a$ moves from $\delta$ 3.39 to $\delta$ 4.42, supports the assignment of the carbonyl group being in close proximity to this proton as in **40a**. Complete assignments of the $^{13}C$ and $^{1}H$ NMR spectra are possible by a combination of HETCOR, DEPT, and COSY experiments in benzene-$d_6$. The minor product **40b** has its methine proton $H_a$ ($\delta$ 3.16) as a quartet, $J$ = 2.7 Hz, which indicates it must be equatorial. The stereochemistry of the spiro center is suggested by the shift study with $Eu(fod)_3$ wherein the methoxy protons show a relatively small shift ($\delta$ 3.22 to $\delta$ 3.43). This shift is comparable to that of the methine proton $H_a$ ($\delta$ 3.16 to 3.38)—a proton that cannot come into close proximity with the spiro center in either isomer. These observed shifts likely derive solely from complexation of the europium with the ether oxygen. Thus, the carbonyl group appears distal both to the methine proton and the methoxy group as depicted in **40b**. The cyclic ether **16** also participates in the process in chloroform to give a 33% yield of **40a** and a 15% yield of **40b**.

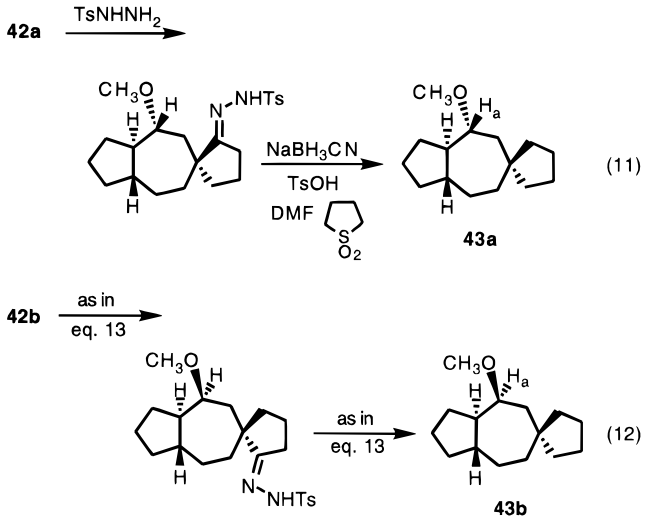
Interestingly, the *cis* isomer **15** produces a single tricycle **41** (eq 9). The $^{1}H$ NMR coupling constants indicate a fairly rigid ring system. The appearance of $H_a$ ($\delta$ 3.82) as a dt ($J$ = 12.0, 4.8 Hz) indicates this proton is axial with only one axial−axial coupling constant. The large shift of this proton to $\delta$ 4.30 upon addition of only 3 mol% of $Eu(fod)_3$ supports the assigned stereochemistry.



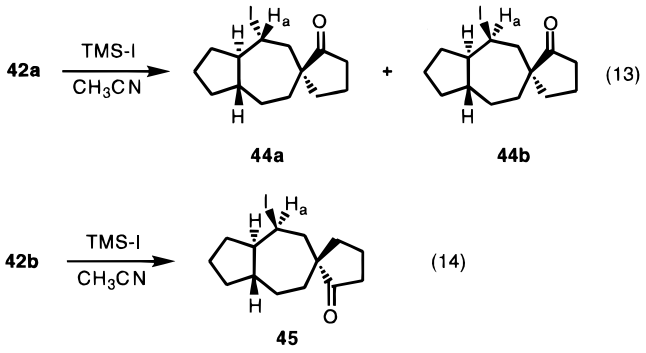
Cyclization of cyclopentyl substrate **25** proceeds well to the perhydroazulene system in 93% yield (eq 10) as a 3.9:3.4:1 separable mixture. Reductions of the tosylhydrazones derived from the two major diastereomers **42a** and **42b** (eqs 11 and 12)




give non-identical spirocyclopentanes **43a** and **43b**. Thus, these two isomers clearly differ at the carbon bearing the




methoxy group. Reaction of **42a** with trimethylsilyl iodide gives two iodides **44a** and **44b** (eq 13) neither of which corresponds to the single isomer **45** obtained from **42b** (eq 14). Thus,




thesemajor isomers also differ in the stereochemistry of the spiro center as well. The diastereochemical assignments for the major isomers must be as depicted in **42a** and **42b** although which is which cannot be unambiguously assigned.

The methine proton $H_a$ shows a distinct pattern throughout these series. In **42a**, it appears as a dt, $J = 9.3$ and 3.9 Hz ($\delta$ 3.25), in **44a** as a dt, $J = 10.7$ and 5.4 Hz ($\delta$ 4.24), and in **44b**

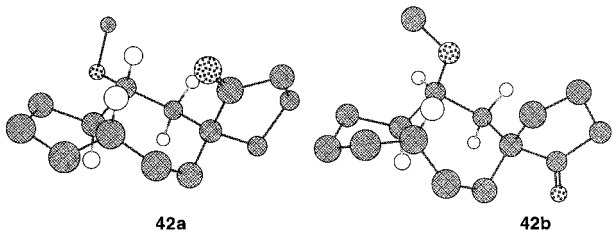
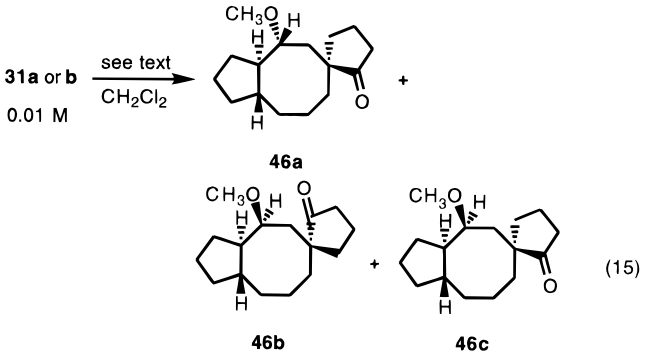



**Figure 1.** Molecular mechanics calculated conformations of **42a** and **42b**. Nonessential hydrogens omitted for clarity.

as a ddd, $J = 10.1$, 7.4, and 5.2 Hz ($\delta$ 4.75). In **42b** and **45**, it appears as a multiplet ($\delta$ 3.54 and 4.82 respectively). Thus, the stereochemistry of the spiro fused center is clearly visible in the multiplicity of the methine proton $H_a$. The minor product, **42c**, exhibits a ddd, $J = 9.6$, 7.8, and 5.8 ($\delta$ 2.94) for this proton thereby suggesting it has the same stereochemistry at the spiro center as **42a**. It is therefore assigned as epimeric at the methoxy carbon as depicted. In support of this suggestion, the coupling pattern is the same as that observed for iodide **44b** which suggests the two have the same stereochemistry at this center.

Molecular mechanics calculations indicate that **42a** and **42b** have as their low energy conformations those depicted in Figure 1. The presence of an axial−axial like coupling between the bridgehead hydrogen and the methoxy methine hydrogen ($H_a$) in **42a** and the absence of any such large coupling constants for this hydrogen ($w_{1/2} = 8.8$ Hz) in **42b** lead us to make the assignments as depicted.

Having established the viability of forming polycycles, we turned to the issue of eight-membered ring construction. Gratifyingly, using our standard conditions at 0 °C, cyclization does occur at 0.01 M concentration to form a 4.4:1.9:1 ratio of diastereomers, albeit only in 32% yield (eq 15). Using 10% triflic acid at 0 °C in the absence of any base increases both the yield to 55% and the diastereoselectivity to 6.4:2.2:1. Trityl




hexachloroantimonate (10%) maintains good diastereoselectivity (5.4:2.4:1) but proceeds in diminished yield (34%). The best yield, 70%, is obtained with 2 equiv of titanium tetrachloride at −78 °C to room temperature in the presence of 1 equiv of 2,6-di-*tert*-butylpyridine which produces a 2.1:1.6:1 mixture of diastereomers.

A series of transformations involving the two newly created stereogenic centers were performed to help establish the stereochemical relationships. Removal of the methoxy group takes advantage of the replacement of the methoxy substituent by iodide that we observe upon treating all of these spiroketones with trimethylsilyl iodide followed by radical deiodination[19] as in eqs 16 and 17. Both **46a** and **46c** produce the identical

(19) Kuivila, H. G.; Menapace, L. W. *J. Org. Chem.* **1963**, *28*, 2165.

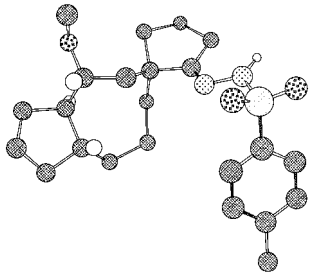
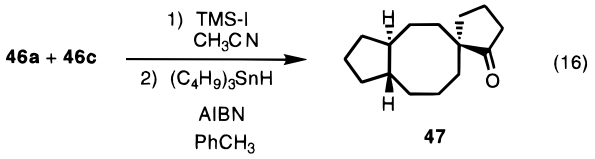
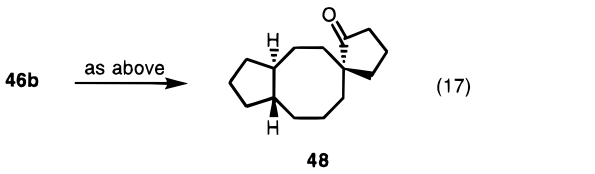


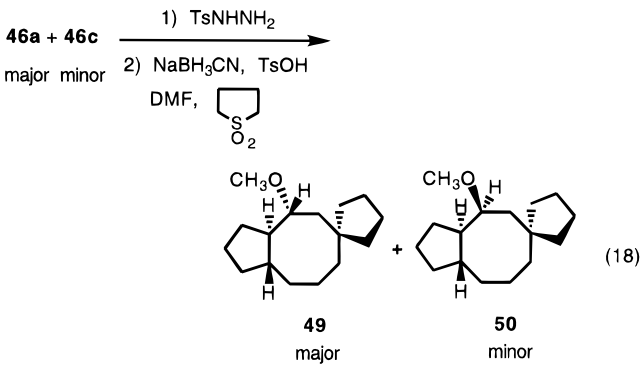
**Figure 2.** X-ray structure of **46a**. Nonessential hydrogens omitted for clarity.

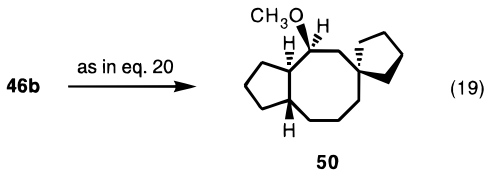
product **47**, whereas the spiroketone **48** from **46b** is different.




Thus, **46a** and **46c** differ only in the stereochemistry of the methoxy group, but **46b** differs at the spiro center. Reduction of the carbonyl group to a methylene unit[20] as in eqs 18 and 19




probes the stereochemical relationships with respect to the latter. A mixture of **46a** (major) and **46c** (minor) is converted to a mixture of a major (**49**) and a minor (**50**) deoxygenated product. It is assumed that the major starting material produces the major product and the minor starting material the minor product. The deoxygenated product from **46b** corresponds to the minor deoxygenated product in the first case. It is reasonable to conclude that the spiropentane **49** obtained from **46a** is different than the one obtained from both **46b** and **46c**, i.e., **50**. Thus, **46a** and **46c** share the same stereochemistry with respect to the spiro center and **46b** and **46c** share the same stereochemistry with respect to the carbon bearing the methoxy group. In this way, the three diastereomers are those depicted in **46a**, **46b**, and **46c** but the assignment of the exact stereochemistry to the specific compound is not possible with this data. Fortunately, the tosylhydrazone of the major diastereomeric ketone **46a** crystallizes satisfactorily to give X-ray quality crystals. Figure 2 depicts the X-ray structure[21] which establishes the stereochemistry of **46a** unambiguously and by extension that of **46b** and **46c**.

## Discussion

Vinylcyclobutanols appear to be somewhat less effective than vinylcyclopropanols as cyclization terminators as illustrated by the difference in ease of formation of eight-membered rings. Nevertheless, in some respects they give superior results. For example, the diastereoselectivity of cyclization of **10b** and **10c** of 9:1 and 4.6:1, respectively, is higher than that observed for the corresponding substrates bearing a vinylcyclopropanol terminator (~2:1). This selectivity also relates to the choice of acid with the bulky trityl hexachloroantimonate giving only a single diastereomer.

The reaction is consistent with ring expansion proceeding in concert with the cyclization. Consider the cyclization of **10b**. If six-membered ring formation preceded ring expansion, the carbocation **51** would presumably be the preferred intermediate over **52**. Little, if any, diastereoselectivity might have been expected for bond migration. Indeed, the steric interactions developing between the carbonyl group and the six-membered ring leading to **33a** should disfavor this isomer. Earlier results involving an analogous cyclopropyl-carbinyl cation support this interpretation.[22] The observed good selectivity favoring **33a** is inconsistent with these arguments.

On the other hand, a ring expansion concurrent with cyclization involving a *trans* addition across the double bond as depicted in **53** and **54** nicely accommodates the observations. Clearly, the unfavorable interactions in **54** disfavor that transition state relative to **53** and account for diastereomer **33a** being strongly preferred. The greater conformational flexibility of a seven-membered ring compared to a six-membered ring accounts for its selectivity being somewhat diminished but still in the same direction.

The fused-spirocyclization of eqs 10 and 11 are also rationalized by this mechanism as illustrated in Figures 3 and 4. For the cyclization of **14**, both chair and boat-type transition states must be considered to explain the observed products. The unfavorable eclipsing interactions between the cyclobutyl portion and the methoxycarbonium ion disfavor the "chair-2" and "boat-2" transition states and rationalize the absence of the corresponding products. The axial−like orientation of the cyclobutyl unit in the "chair-1" transition state may explain the ability of the "boat-1" transition state to compete.

In the case of **15** only the two chair transition states need to be considered. The 1,3-diaxial-like interaction between the cyclopentanone ring and the methoxy group in the chair-2 transition state disfavors this pathway. The chair-1 transition state is virtually devoid of any such unfavorable interactions.

The efficiency of the cyclization with the cyclobutyl terminator can be improved by conformational constraints. The failure of the formation of an eight-membered ring in the acyclic system and its success by simply attaching the chains to a ring system highlight this fact. It is particularly noteworthy that the eight-membered ring formed in good yield even at 0.01 M concentration. Thus, the vinylcylobutanol terminator does appear to enhance the ease of cyclization compared to many other nucleophiles wherein cyclization to eight-membered rings require much higher dilutions.

(20) Hutchins, R. O.; Milewski, C. A.; Maryanoff, B. E. *J. Am. Chem. Soc.* **1973**, *96*, 3662.

(21) The X-ray analysis was performed by Athar Masood of Stanford University.

(22) Trost, B. M.; Scudder, P. H. *J. Am. Chem. Soc.* **1977**, *99*, 7601.

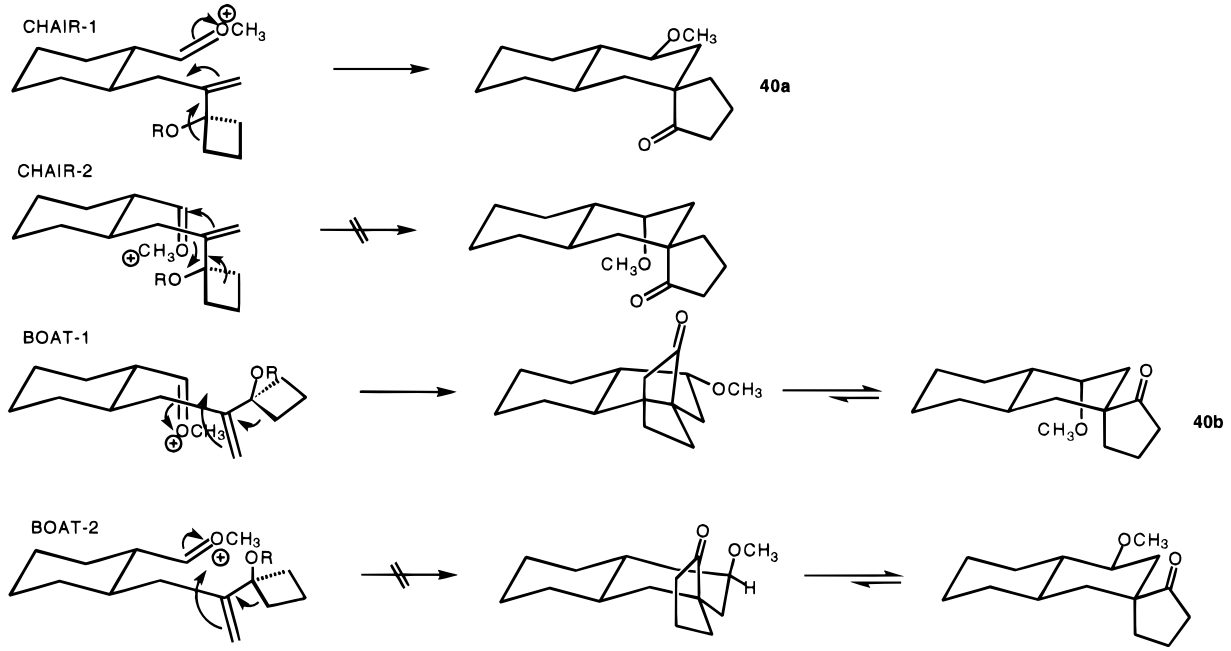



**Figure 3.** Possible transition states for cyclization of **14**.

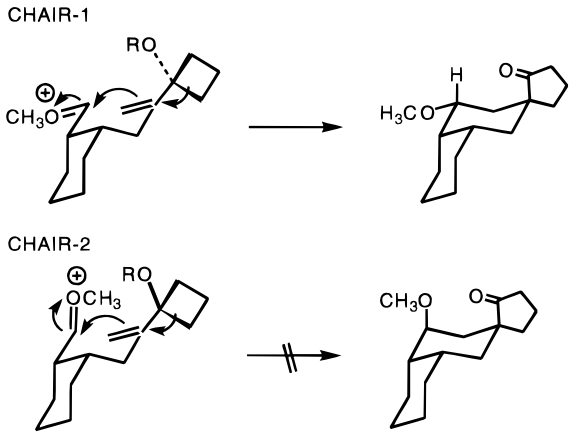
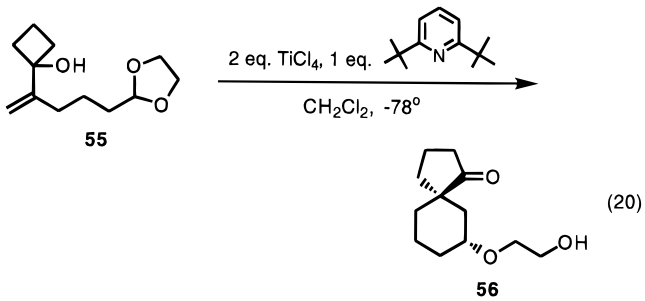



**Figure 4.** Possible Transition states for cyclization of **15**.

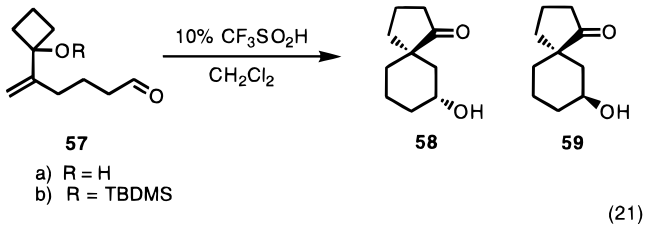
In no case is cyclization not accompanied by ring expansion. Furthermore, in those cases where cyclizations fail, ring expansion also does not occur. For example, as shown in eq 9, the vinylcyclobutanol simply reacts as an allyl alcohol. Thus, the two events appear intimately tied.

The effect of initiator was briefly examined. The cyclic acetal **55** does not cyclize well upon exposure to trimethylsilyl triflate. On the other hand, the conditions that proved most successful for formation of the eight-membered ring **46a**−**c** also proved successful here. A single diastereomeric product **56** is obtained in 56% yield (eq 20). Performing this reaction under standard




(20)

conditions gives **56** in a reduced yield of 36% along with the alcohol **58** in 16% yield. The stereochemistry of **58** is established by its quantitative methylation ($CH_3I$, $Ag_2O$) to give a methyl ether **33a** that is identical to that obtained in the

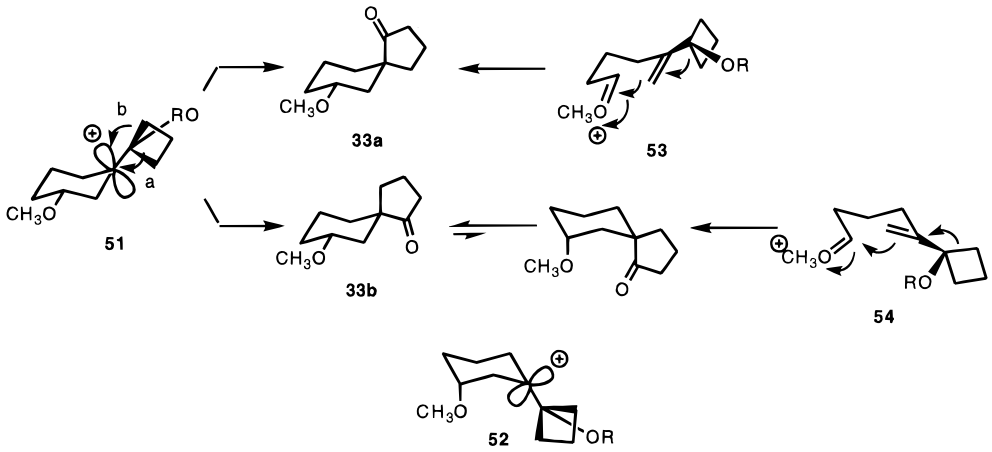



(21)

cyclization of the acetal **10b**. The formation of the free alcohol from **55** suggests that hydrolysis and cyclization of the resultant aldehyde **57a** competes with direct cyclization. To examine this issue, the TBDMS ether of **10b** is carefully hydrolyzed (HOAc, $H_2O$, THF) to aldehyde **57b** and the latter subjected to 10% triflic acid. A 90% yield of a 1:1.3 ratio of **58** and **59** is obtained. Thus, a protonated carbonyl group is adequate as an initiator. Consistent with the lower steric demands of such an initiator, a lower diastereoselectivity in the cyclization is observed.

What do we mean when we refer to a vinylcyclobutanol as a composite functional group? We do not propose that this effect is a ground state phenomenon. The evidence for a ground state interaction between a cyclobutane and a double bond is debatable.[1,9−13] For the case of a vinylcyclobutanol, compelling evidence for such ground state interactions is lacking. For example, the difference in $^{13}C$ shifts for the double bond for vinylcyclobutanol ($\Delta\delta = 3.6$) falls between vinylcyclopropanol ($\Delta\delta = 4.0$) and vinylcyclopentanol or vinylcyclohexanol ($\Delta\delta$ 3.3−3.4). While the larger difference may be associated with increased polarization of the double bond, the closeness of the numbers makes any such interpretation highly tenuous. The lack of reactivity of cyclobutane toward electrophiles compared to cyclopropane also suggests that the $\sigma$ bonding electrons of cyclobutane are not easily accessible. However, this may be a kinetic issue. In the case of vinylcyclobutanol, the $\pi$-system of the double bond overcomes the kinetic barrier for interaction with an electrophile. Once that interaction commences, then much is to be gained by delocalizing the developing positive charge throughout the cyclobutane framework and onto oxygen as depicted in eq 2 in terms of stabilization by delocalization

**Scheme 6**




and strain relief. The expanded scope of the cyclization with a vinylcyclopropanol terminator compared to the vinylcyclobutanol terminator may derive from the much higher $\pi$ character of the cyclopropyl bonds compared to those of a cyclobutane which is only partially compensated for by the much larger strain release in the transition state in the cyclobutyl case. To the extent that the $\pi$ bond, the strained ring bonds, and the oxygen are behaving in concert to lower transition state energies for the attack of an electrophile, the concept of considering vinylcyclobutanols as composite functional groups has validity.

## Experimental Section

**General Methods.** Solvents were generally freshly distilled before use: acetonitrile, benzene, dichloromethane, diisopropylamine, dimethylformamide, hexane, pyridine, and triethylamine from calcium hydride; diethyl ether, dimethoxyethane, dioxane, tetrahydrofuran, and toluene from sodium benzophenone ketyl; methanol and ethanol from magnesium methoxide and magnesium ethoxide, respectively. Trimethylsilyl trifluoromethanesulfonate was distilled over calcium hydride.

Flash chromatography was carried out by the method of Still[25] employing E. Merck silica gel (Kieselgel 60, 200−400 mesh), and analytical thin layer chromatography (TLC) was performed on 0.2 mm precoated commercial silica gel plates (E. Merck, DC-Platten Kieselgel 60 $F_{254}$). Solvents for chromatography are listed as volume/volume ratios. Analytical gas chromatography (GC) was performed on a Varian Model 3700 gas chromatograph or a Hewlett Packard 5890 Series II gas chromatograph using an Alltech 25m × 25m ID bonded FSOT polymethylsiloxane (SE-30, OV-1) column with flame ionization detector. The following settings were used: initial temperature: 50 °C, initial time: 4 min, final temperature: 250 °C, rate: 20 °C/min.

Proton ($^1$H) nuclear magnetic resonance spectra were recorded using a Varian XL-400 (400 MHz) or Varian Gemini 200 (200 MHz) or 300 (300 MHz). Carbon-13 ($^{13}$C) nuclear magnetic resonance spectra were recorded using a Varian XL-400 (100 MHz) or Varian Gemini 200 (50 MHz) or 300 (75 MHz). Infrared spectra were recorded on a Nicolet 205 FT-IR spectrometer. Solution spectra were recorded in 0.1 mm path length sodium chloride cells. Melting points were determined using a Thomas-Hoover oil bath apparatus and were not corrected. Combustion analyses were performed by M-H-W Laboratories, Phoenix, AZ.

**12-Bromo-12-tridecen-1-yl acetate (3c).** To a solution of *B*-Br-9-BBN (1.0 M in dichloromethane, 49 mL, 49 mmol) in 100 mL of dichloromethane at 0 °C was added a solution of 12-tridecyn-1-yl acetate[26] (5.32 g, 22.3 mmol) in 10 mL of dichloromethane. The reaction was stirred at 0 °C for 3 h, and glacial acetic acid (16.7 mL) was added. After an additional hour at 0 °C, 3 M aqueous sodium acetate solution (200 mL) was added followed by 30% aqueous hydrogen peroxide (33 mL). This was stirred at room temperature for 45 min. The layers were separated, and the aqueous layer was extracted with hexane (3 × 100 mL). The combined organic layers were washed with water (2 × 100 mL), saturated sodium bicarbonate solution (2 × 100 mL), and water (2 × 100 mL) and dried over magnesium sulfate. Removal of solvents *in vacuo* yielded a cloudy liquid. Flash column chromatorgraphy (10:1 hexane/ether) yielded the titled compound as a colorless liquid (4.54 g, 64%). IR ($CDCl_3$): 1728, 1253 cm$^{-1}$. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 5.53 (d, $J$ = 1.3 Hz, 1H), 5.35 (d, $J$ = 1.4 Hz, 1H), 4.03 (t, $J$ = 6.8 Hz, 2H), 2.39 (t, $J$ = 7.1 Hz, 2H), 2.03 (s, 3H), 1.56 (m, 4H), 1.26 (br s, 14H). $^{13}$C NMR (75.5 MHz, $CDCl_3$) $\delta$ 171.1, 134.8, 116.1, 64.5, 41.3, 29.4 (2), 29.2 (2), 28.5, 28.3, 27.8, 25.8, 20.9. $^1$H NMR (300 MHz, $C_6D_6$): $\delta$ 6.27 (d, $J$ = 1.4 Hz, 1H), 5.25 (d, $J$ = 1.3 Hz, 1H), 3.98 (t, $J$ = 6.7 Hz, 2H), 2.20 (t, $J$ = 7.4 Hz, 2H), 1.70 (s, 3H), 1.43 (m, 4H), 1.17 (br s, 14H). $^{13}$C NMR (75.5 MHz, $C_6D_6$): $\delta$ 170.1, 135.2, 116.4, 64.4, 41.6, 29.9 (2), 29.6, 29.0, 28.7, 28.2, 26.3, 20.6. HRMS: Calcd for $C_{13}H_{23}Br$ ($M - CH_3CO_2H$)$^+$: 260.0962. Found: 260.0950.

**12-Bromo-12-tridecen-1-ol (4c).** 12-Bromo-12-tridecen-1-yl acetate (**4c**) (2.0 g, 6.26 mmol) was taken up in 5.4 mL of methanol, 3.6 mL of water, and 2.0 mL of ether and treated with 0.95 g (6.89 mmol) of potassium carbonate at room temperature. The reaction was stirred overnight, and an additional 0.95 g (6.89 mmol) of potassium carbonate and 2 mL of ether were added. After another 24 h, another 0.45 g (3.26 mmol) of potassium carbonate was added. After stirring overnight, the reaction was added to dichloromethane (10 mL) and water (10 mL). The aqueous layer was extracted with dichloromethane (1 × 10 mL). The combined organic layers were washed with brine (3 × 15 mL) and dried ($MgSO_4$). After evaporation of the solvent, purification by silica gel chromatography (3:1 pentane/ether) gave 1.52 g (92%) of **4c**. IR ($CDCl_3$): 3623, 1631, 1466 cm$^{-1}$. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 5.54 (s, 1H), 5.37 (s, 1H), 3.63 (t, $J$ = 6.6 Hz, 2H), 2.40 (t, $J$ = 7.3 Hz, 2H), 1.55 (m, 4H), 1.27 (br s, 14H). $^{13}$C NMR ($CDCl_3$, 75.5 MHz): $\delta$ 134.9, 116.2, 63.0, 41.4, 32.7, 29.5 (2), 29.4 (2), 29.2, 28.3, 27.8, 25.7. HRMS: Calcd for $C_{13}H_{25}O$ ($M - Br$)$^+$: 197.1905. Found: 197.1896.

**2-Bromo-13,13-dimethoxy-1-tridecene (5c).** A solution of 12-bromo-12-tridecen-1-ol (**4c**) (1.41 g, 5.09 mmol) in 2.5 mL of dichloromethane was added dropwise to a suspension of pyridinium chlorochromate (1.64 g, 7.63 mmol) in 10 mL of dichloromethane at 0 °C. The resulting black suspension was stirred at room temperature for 3 h. Pentane (20 mL) was added, and the mixture was filtered through Celite, rinsing the residue with additional pentane (2 × 10 mL). Removal of solvents yielded 1.22 g (87%) of the corresponding aldehyde as a greenish-brown liquid. This was taken up in 10 mL of

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(24) Bartlett, P. A.; Johnson, W. S.; Elliott, J. D. *J. Am. Chem. Soc.* **1983**, *105*, 2088; Johnson, W. S.; Elliot, J. D.; Hanson, G. J. *J. Am. Chem. Soc.* **1984**, *106*, 1138.

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(26) Trost, B. M.; Matsubara, S.; Caringi, J. *J. Am. Chem. Soc.* **1989**, *111*, 8745.

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**Table 3.** Experimental Details for Preparation of Vinylcyclobutanols from Vinyl Bromides

| Entry | Vinyl Bromide (mg, mmol) | *t*-$C_{4H9Li\ (1.7\ M)}$[a] mL, mmol | Cyclobutanone $\mu$L, mmol | THF mL | Product mg, % yield |
|---|---|---|---|---|---|
| 1 | **5a** (137, 0.655) | 0.72, 1.2 | 33, 0.442 | 1.4 | **10a** 61, 70 |
| 1 | **5b** (1900, 8.50) | 10.5, 17.9 | 510, 6.80 | 14 | **10b** 1500, 100 |
| 3 | **9a** (1070, 4.51) | 5.0, 8.5 | 263, 3.52 | 16.8 | **10c** 720, 90 |
| 4 | **9b** (793, 3.16) | 3.7, 6.3 | 208, 2.79 | 13.4 | **10d** 550, 82 |
| 5 | **9c** (1200, 4.52) | 5.2, 8.8 | 280, 3.75 | 30.4 | **10e** 760, 79 |
| 6 | **5c** (750, 2.33) | 2.75, 4.7 | 166, 2.22 | 4.6 | **10f** 563, 81 |
| 7 | *trans* **13** (70, 0.25) | 0.30, 0.5 | 19, 0.25 | 1.4 | **14** 51, 75[b] |
| 8 | *cis*+*trans* **13** (200, 0.72) | 0.85, 1.5 | 54, 0.72 | 2.8 | **14** 72, 37; **15** 30, 16[b] |
| 9 | **24** (169, 0.61) | 0.76, 1.3 | 68, 0.92 | 2.4 | **25** 121, 74[c] |
| 10 | **30** (1350, 4.64) | 5.5, 9.3 | 390, 5.22 | 18.6 | **31a** 1060, 81[b] |

[a] In pentane. [b] Eluted with 10:1 followed by 2:1 pentane/ether. [c] Eluted with 10:1 followed by 5:2 pentane ether.

methanol and treated with 970 $\mu$L (8.86 mmol) of trimethyl orthoformate and *p*-toluenesulfonic acid (42 mg, 0.222 mmol) at room temperature. After 2.5 h, the reaction was diluted with dichloromethane (10 mL) and washed with 1% aqueous sodium carbonate solution (1 × 20 mL). The aqueous layer was extracted with dichloromethane (3 × 10 mL), and the combined organic layers were dried ($MgSO_4$). After evaporation of the solvents *in vacuo*, silica gel chromatography (10:1 pentane/ether) afforded 1.23 g (87%) of **5c**. IR ($CDCl_3$): 2992, 1631, 1465, 1446, $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 5.55 (dd, $J$ = 1.4, 1.3 Hz, 1H), 5.38 (d, $J$ = 1.5 Hz, 1H), 4.36 (t, $J$ = 5.7 Hz, 1H), 3.32 (s, 6H), 2.41 (td, $J$ = 7.4, 1.2 Hz, 2H), 1.56 (m, 4H), 1.28 (br s, 14H). $^{13}C$ NMR (75.5 MHz, $CDCl_3$): $\delta$ 134.9, 116.2, 104.5, 52.6, 41.4, 32.5, 29.5, 29.4, 29.3, 29.2, 29.1 (2), 28.4, 27.9, 24.6. HRMS: Calcd for $C_{14}H_{26}O^{81}Br$ $(M - OCH_3)^+$: 291.1146. Found: 291.1140. Anal. Calcd for $C_{15}H_{29}BrO_2$: C, 56.07; H, 9.10. Found: C, 56.24; H, 8.95.

**2-Bromo-7,7-dimethoxy-1-heptene[27] (9a).** Crushed magnesium turnings (1.55 g, 63.6 mmol) were placed in a flask, and 1-bromo-4,4-dimethoxybutane (2.50 g, 12.7 mmol) in 13 mL of THF was added. The reaction was heated to reflux for 1 h after addition of the bromoacetal was complete. The reaction mixture was then cannulated into a suspension of 2,3-dibromopropene (2.11 g, 10.6 mmol) and copper(I) iodide (101 mg, 0.5 mmol) in 8 mL of THF at 0 °C. The reaction mixture was then stirred for 2 h and was quenched by adding to 30 mL of saturated ammonium chloride solution. Extraction with ether (1 × 30 mL, 2 × 20 mL) was followed by washing the ether extracts with brine (2 × 50 mL) and drying over anhydrous sodium sulfate. Removal of solvents *in vacuo* yielded a residue which was purified by silica gel chromatography (4:1 pentane/ether) to afford 1.30 g (52%) of pure 2-bromo-7,7-dimethoxy-1-heptene as a yellow liquid. IR ($CDCl_3$): 1650, 1602 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 5.57 (d, $J$ = 1.3 Hz, 1H), 5.40 (d, $J$ = 1.4 Hz, 1H), 4.37 (t, $J$ = 5.7 Hz, 1H), 3.32 (s, 6H), 2.43 (t, $J$ = 7.3 Hz, 2H), 1.59 (m, 4H), 1.37 (m, 2H). $^{13}C$ NMR (75.5 MHz, $CDCl_3$): $\delta$ 134.4, 116.3, 104.0, 52.1, 40.8, 31.7, 27.2, 22.9. HRMS: Calcd for $C_9H_{16}O_2{}^{81}Br$ $(M - H)^+$: 237.0313. Found: 237.0309.

**2-Bromo-8,8-dimethoxy-1-octene (9b).** Following the above protocol, 1-bromo-5,5-dimethoxypentane (2.3 g, 10.9 mmol), magnesium turnings (1.3 g, 54.5 mmol), copper(I) iodide (86 mg, 0.45 mmol), and 2,3-dibromopropene (1.8 g, 9.0 mmol) in 20 mL of THF gave 1.1 g (48%) of **9b**. IR ($CDCl_3$): 1631 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 5.53 (d, $J$ = 1.4 Hz, 1H), 5.36 (s, 1H), 4.34 (t, $J$ = 5.7 Hz, 1H), 3.29 (s, 6H), 2.39 (t, $J$ = 7.3 Hz, 2H), 1.55 (m, 4H), 1.31 (m, 4H). $^{13}C$ NMR (75.5 MHz, $CDCl_3$): $\delta$ 134.8, 116.4, 104.4, 52.4, 41.0, 32.1, 27.9, 27.5, 24.0. HRMS: Calcd for $C_{10}H_{19}{}^{81}BrO_2$ $(M^+)$: 252.0547. Found: 252.0521.

**2-Bromo-8,8-dimethoxy-1-octene (9c).** Following the above protocol, 1-bromo-6,6-dimethoxypentane (2.4 g, 10.7 mmol), magnesium turnings (1.6 g, 64.0 mmol), copper(I) iodide (85 mg, and 2,3-dibromopropene (1.8 g, 8.9 mmol) in 20 mL of THF gave 1.2 g (50%) of **9c**. IR ($CDCl_3$): 1630, 1602 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 5.53 (d, $J$ = 1.3 Hz, 1H), 5.36 (d, $J$ = 1.4 Hz, 1H), 4.34 (t, $J$ = 5.7 Hz, 1H), 3.30 (s, 6H), 2.39 (t, $J$ = 7.3 Hz, 2H), 1.56 (m, 4H), 1.31 (m, 6H). $^{13}C$ NMR (75.5 MHz, $CDCl_3$): $\delta$ 134.9, 116.3, 104.5, 52.4, 41.1, 32.2, 28.9, 28.0, 27.5, 24.2. HRMS: Calcd for $C_{11}H_{20}{}^{81}BrO_2$ $(M - H)^+$: 265.0626. Found: 265.0626.

**Preparation of Vinylcyclobutanols from Vinyl Bromides. Typical Procedure of 6,6-Dimethoxy-2-(1′-hydroxy)cyclobutyl-1-hexene (10b).** A solution of 2-bromo-6,6-dimethoxy-1-hexene (**5b**)[28] (1.9 g, 8.5 mmol) in 7 mL of THF was added to a solution of *tert*-butyllithium (1.7 M in pentane, 10.5 mL, 17.9 mmol) in 7 mL of THF at −78 °C. After 20 min, cyclobutanone (0.51 mL, 6.8 mmol) was added. The reaction was stirred for 1.5 h and was then added to a mixture of 1 M aqueous sodium hydrogen phosphate (30 mL) and ether (30 mL). The organic layer was dried ($Na_2CO_3$), and solvents were removed in vacuo to yield a colorless liquid. Purification by silica gel chromatography (1:1 pentane/ether) yielded 1.5 g (100%) of **10b**. IR ($CDCl_3$): 3593 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 5.07 (s, 1H), 4.88 (d, $J$ = 1.0 Hz, 1H), 4.38 (t, $J$ = 5.5 Hz, 1H), 3.30 (s, 6H), 2.29 (m, 2H), 2.11 (t, $J$ = 8.0 Hz, 2H), 2.02 (m, 2H), 1.90 (m, 1H), 1.68−1.50 (m, 6H). $^{13}C$ NMR (75.5 MHz, $CDCl_3$): $\delta$ 152.0, 108.0, 104.4, 78.0, 52.3, 34.3, 31.9, 29.5, 22.9, 12.7. HRMS: Calcd for $C_{11}H_{22}O$ $(M - CH_5O_2)^+$: 165.1279. Found: 165.1281. Anal. Calcd for $C_{12}H_{22}O_3$: C, 67.26; H, 10.35. Found: C, 67.10; H, 10.15.

Experimental details for the remaining examples are summarized in Table 3.

**Characterizing Data. 10a**: IR ($CDCl_3$): 3592, 3436, 1650, 1600 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 5.06 (s, 1H), 4.86 (d, $J$ = 0.9 Hz, 1H), 4.38 (t, $J$ = 5.7 Hz, 1H), 3.28 (s, 6H), 2.27 (m, 2H), 2.14 (t, $J$ = 7.9 Hz, 2H), 2.02 (m, 2H), 1.80 (m, 4H), 1.17 (m, 1H). $^{13}C$ NMR (75.5 MHz, $CDCl_3$): $\delta$ 151.6, 108.7, 104.3, 78.3, 52.5, 34.6, 31.1, 25.1, 12.8. HRMS: Calcd for $C_{11}H_{19}O_3$ $(M - H)^+$: 199.1334. Found: 199.1344. Anal. Calcd for $C_{11}H_{20}O_3$: C, 65.97; H, 10.07. Found: C, 66.15; H, 9.96.

**10c**: IR ($CDCl_3$): 3600, 3450, 1650, 1610 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 5.07 (s, 1H), 4.88 (s, 1H), 4.38 (t, $J$ = 5.8 Hz, 1H), 3.32 (s, 6H), 2.32 (m, 2H), 2.12 (t, $J$ = 7.2 Hz, 2H), 2.03 (m, 2H), 1.91 (m, 2H), 1.75 (br s, 1H), 1.67−1.37 (m, 7H). $^{13}C$ NMR (75.5 MHz, $CDCl_3$): $\delta$ 152.4, 108.2, 104.5, 78.4, 52.5, 34.5, 32.2, 30.0, 28.0, 24.4, 12.9. HRMS: Calcd for $C_{13}H_{23}O_3$ $(M - H)^+$: 227.1647. Found: 227.1658. Anal. Calcd for $C_{13}H_{24}O_3$: C, 68.38; H, 10.59. Found: C, 68.49; H, 10.44.

**10d**: IR ($CDCl_3$): 3592, 3450, 1650, 1610, 1464, 1445 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 5.07 (s, 1H), 4.87 (d, $J$ = 1.2 Hz, 1H), 4.37 (t, $J$ = 5.7 Hz, 1H), 3.32 (s, 6H), 2.32 (m, 2H), 2.11 (t, $J$ = 7.6 Hz, 2H), 2.10−1.85 (m, 2H), 1.68−1.35 (m, 11H). $^{13}C$ NMR (75.5 MHz, $CDCl_3$): $\delta$ 152.5, 108.1, 104.6, 78.5, 52.5, 34.5, 32.3, 29.9, 29.3, 28.1, 24.3, 12.9. HRMS: Calcd for $C_{14}H_{25}O_3$ $(M - H)^+$: 241.1804. Found: 241.1817. Anal. Calcd for $C_{14}H_{26}O_3$: C, 69.38; H, 10.81. Found: C, 69.20; H, 10.84.

**10e**: IR ($CDCl_3$): 3693, 3593, 1650, 1610 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 5.04 (s, 1H), 4.85 (s, 1H), 4.34 (t, $J$ = 5.6 Hz, 1H), 3.30 (s, 6H), 2.30 (m, 2H), 2.06 (dd, $J$ = 15.6, 7.0 Hz, 2H), 2.02−1.98 (m, 2H), 1.58−1.32 (m, 12H). $^{13}C$ NMR (75.5 MHz, $CDCl_3$): $\delta$ 152.6, 107.9, 104.5, 78.4, 52.4, 34.4, 32.2, 29.9, 29.3, 29.2, 28.1, 24.3, 12.8. HRMS: Calcd for $C_{15}H_{27}O_3$ $(M - H)^+$: 255.1960. Found: 255.1940.

**10f**: IR ($CDCl_3$): 3594, 1602, 1465, 1446 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 5.07 (s, 1H), 4.88 (d, $J$ = 1.1 Hz, 1H), 4.37 (t, $J$ = 5.7 Hz, 1H), 3.32 (s, 6H), 2.33 (m, 2H), 2.12−1.89 (m, 4H), 1.64−1.44 (m, 7H), 1.28 (m, 14H). $^{13}C$ NMR (75.5 MHz, $CDCl_3$): $\delta$ 152.4, 107.6, 104.3, 78.2, 52.3, 34.5, 32.3, 30.1, 29.6, 29.5 (2), 29.4 (2), 29.3, 28.3, 24.5, 13.0. HRMS: Calcd for $C_{18}H_{32}O_2$ $(M - CH_3OH)^+$: 280.2402. Found: 280.2402. Anal. Calcd for $C_{19}H_{36}O_3$: C, 73.03; H, 11.61. Found: C, 73.05; H, 11.42.

**14**: IR ($CDCl_3$): 3633, 3450, 1650, 1600 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 5.09 (s, 1H), 4.86 (s, 1H), 4.36 (d, $J$ = 3.8 Hz, 1H), 3.41

(s, 3H), 3.38 (s, 3H), 2.64 (dd, $J$ = 14.2, 2.9 Hz, 1H), 2.28 (m, 2H), 2.07 (m, 2H), 1.90 (m, 2H), 1.78−1.51 (m, 6H), 1.42 (m, 1H), 1.21 (m, 4H), 0.91 (m, 1H). $^{13}$C NMR (75.5 MHz, $CDCl_3$): $\delta$ 150.4, 109.8, 107.8, 78.3, 56.1, 55.3, 44.6, 35.7, 35.3, 34.7, 31.2, 25.4, 25.0, 13.2. HRMS: Calcd for $C_{14}H_{20}O$ ($M - C_2H_8O_2$)$^+$: 204.1514. Found: 204.1518.

**15**: IR ($CDCl_3$): 3600, 3451, 1650, 1600 cm$^{-1}$. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 5.10 (d, $J$ = 1.2 Hz, 1H), 4.86 (d, $J$ = 1.0 Hz, 1H), 4.32 (d, $J$ = 8.8 Hz, 1H), 3.32 (s, 3H), 3.30 (s, 3H), 2.29 (m, 2H), 2.17−1.53 (m, 11H), 1.43 (m, 2H), 1.25 (m, 4H). $^{13}$C NMR (75.5 MHz, $CDCl_3$): $\delta$ 151.0, 110.0, 105.4, 78.2, 53.5, 51.3, 41.9, 35.9, 34.9, 31.7, 28.6, 28.0, 25.8, 23.2, 20.4, 13.3. HRMS: Calcd for $C_{15}H_{24}O_2$ ($M - CH_3OH$)$^+$: 236.1776. Found: 236.1780.

**25:** IR ($CDCl_3$): 3592, 3466, 1639, 1450, 1364 cm$^{-1}$. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 5.06 (s, 1H), 4.89 (d, $J$ = 1.0 Hz, 1H), 4.13 (d, $J$ = 7.3 Hz, 1H), 3.34 (s, 3H), 3.31 (s, 3H), 2.32 (m, 2H), 2.16 (m, 1H), 2.05 (m, 4H), 1.80 (m, 7H), 1.52 (m, 4H), 1.35 (m, 1H). $^{13}$C NMR (75.5 MHz, $CDCl_3$): $\delta$ 152.2, 108.3, 108.1, 78.4, 54.3, 52.7, 47.3, 41.2, 34.6, 34.4, 32.6, 28.8, 27.8, 24.7, 13.1. HRMS: Calcd for $C_{15}H_{23}O$ ($M - CH_3O - H_2O$)$^+$: 219.1748. Found: 219.1766.

**31a**: IR ($CDCl_3$): 3592, 3460, 1717, 1642, 1450, 1361, 1319 cm$^{-1}$. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 5.07 (s, 1H), 4.89 (d, $J$ = 1.3 Hz, 1H), 4.14 (d, $J$ = 7.0 Hz, 1H), 3.35 (s, 3H), 3.33 (s, 3H), 2.33 (m, 2H), 2.10 (m, 2H), 2.02 (m, 2H), 1.96−1.46 (m, 13H), 1.22 (m, 2H). $^{13}$C NMR (75.5 MHz, $CDCl_3$): $\delta$ 152.3, 108.3, 108.0, 78.4, 54.1, 53.0, 47.3, 41.4, 35.7, 34.6, 32.5, 30.2, 27.7, 27.0, 24.6, 13.1. Anal. Calcd for $C_{17}H_{30}O_3$: C, 72.30; H, 10.71. Found: C, 72.11; H, 10.50.

**2-(2-Bromo-2-propen-1-yl)cyclohexanone (11).** A solution of LDA, prepared from diisopropylamine (8.60 mL, 61.3 mmol) and *n*-butyllithium (1.40 M in hexane, 440 mL, 61.3 mmol) in 60 mL of THF, was cooled to −78 °C, and the *N*-cyclohexylimine of cyclohexanone (9.62 g, 53.7 mmol) was added. The resulting yellow solution was allowed to warm to −50 °C over 2 h and then to 0 °C for 1 h. It was recooled to −30 °C, and 2,3-dibromopropene (5.80 mL, 56.1 mmol) was added dropwise. The solution became colorless, and it was warmed to room temperature slowly. After 2 h at room temperature, solvents were removed to give a yellow liquid. This was taken up in ether (60 mL) and 2 M aqueous hydrochloric acid solution (90 mL), and the mixture was heated at reflux for 2 h. The reaction was cooled and ether (60 mL) was added. The aqueous layer was extracted with ether (2 × 40 mL). The combined organic layers were washed with brine (3 × 50 mL) and dried ($MgSO_4$). Removal of solvents followed by silica gel chromatography (9:1 pentane/ether) of the residue yielded 2-(2-bromo-2-propen-1-yl)cyclohexanone as a yellow liquid (9.48 g, 82%). IR ($CDCl_3$): 1708, 1631, 1449, 1428 cm$^{-1}$. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 5.61 (d, $J$ = 0.8 Hz, 1H), 5.45 (d, $J$ = 0.8 Hz, 1H), 3.00 (dd, $J$ = 14.8, 4.6 Hz, 1H), 2.69 (m, 1H), 2.40 (m, 2H), 2.27 (dd, $J$ = 14.8, 9.0 Hz, 1H), 2.22−2.08 (m, 2H), 1.90 (m, 1H), 1.69 (m, 2H), 1.23 (m, 1H). $^{13}$C NMR (75.5 MHz, $CDCl_3$): $\delta$ 210.5, 132.0, 118.2, 47.9, 41.7, 40.7, 32.5, 27.5, 24.7. HRMS: Calcd for $C_9H_{13}O$ ($M - Br$)$^+$: 137.0966. Found: 137.0969.

**2-(2-Bromo-2-propen-1-yl)-1-(dimethoxymethyl)cyclohexane (13).** To a suspension of (methoxymethyl)triphenylphosphonium chloride (5.21 g, 15.2 mmol) in 15 mL of THF at 0 °C was added phenyllithium (1.8 M in 7:3 cyclohexane/ether, 7.7 mL, 14 mmol). The resulting red suspension was stirred at 0 °C for 30 min and then cooled to −70 °C. A solution of 2-(2-bromo-2-propen-1-yl)cyclohexanone (**11**) (1.50 g, 6.91 mmol) was then added dropwise. The suspension was stirred at −70 °C for 1 h and then at room temperature for 2 h. The mixture was then added to saturated aqueous ammonium chloride solution (30 mL) and ether (20 mL). The aqueous layer was extracted with ether (3 × 15 mL), and the combined organic layers were washed with brine (2 × 60 mL) and dried ($MgSO_4$). Removal of solvents in vacuo yielded a brown residue which was passed through a short column of silica gel, eluting with 7:1 pentane/ether, to give the crude methyl enol ether as a yellow liquid.

The methyl enol ether was taken up in 9 mL of THF and 6 mL of 2 M aqueous hydrochloric acid and heated at 55 °C for 3 h. Ether (6 mL) was added, and the layers were separated. The aqueous layer was extracted with ether (3 × 5 mL), and the organic layers were washed with brine (3 × 15 mL) and dried ($Na_2SO_4$). Removal of solvents in vacuo gave a mixture of *cis*- and *trans*-aldehyde **12** (915 mg, 57% over two steps) which decomposes upon standing at room temperature.

A portion of the above mixture was taken up in 5 mL of methanol and treated with trimethyl orthoformate (600 $\mu$L, 5.48 mmol) containing a catalytic amount of concentrated sulfuric acid at room temperature. The reaction was stirred at room temperature for 1 h, and solvents were removed in vacuo to yield a yellow residue which was filtered through silica gel (5:1 pentane/ether). Further purification by MPLC (25:1 hexane/ether) yielded 88 mg of pure *trans*-**13** and two fractions of a mixture of *cis*- and *trans*-isomers (109 mg, 211 mg). *trans* **13**: IR ($CDCl_3$): 1721, 1629, 1449 cm$^{-1}$. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 5.56 (s, 1H), 4.43 (d, $J$ = 1.4 Hz, 1H), 4.35 (d, $J$ = 4.6 Hz, 1H), 3.43 (s, 3H), 3.39 (s, 3H), 2.81 (dd, $J$ = 14.2, 4.1 Hz, 1H), 2.18 (dd, $J$ = 14.3, 9.3 Hz, 1H), 1.88−1.19 (m, 9H), 0.91 (m, 1H). $^{13}$C NMR (75.5 MHz, $CDCl_3$): $\delta$ 133.8, 117.7, 106.9, 55.6, 55.1, 45.6, 43.9, 35.1, 30.1, 25.0, 24.8, 24.6. HRMS: Calcd for $C_{11}H_{18}OBr$ ($M - OCH_3$)$^+$: 245.0541. Found: 245.0532.

**2-(1-Trimethylsilyl-1-butyn-4-yl)cyclopentanone (18).** A solution of LDA prepared from 6.0 mL of diisopropylamine (42.8 mmol) and 32.0 mL of *n*-butyllithium (1.40 M in hexane, 44.8 mmol) in 43.0 mL of THF was cooled to −78 °C. The cyclohexylimine of cyclopentanone (6.50 g, 39.3 mmol) was added dropwise. The reaction was allowed to warm to 0 °C slowly. It was then recooled to −78 °C, and 4-iodo-1-trimethylsilylbut-1-yne (10.4 g, 41.5 mmol) was added. The reaction was allowed to warm to room temperature slowly and stirred overnight. The solvents were partially removed, and the residue was taken up in 40 mL of ether and 60 mL of 2 M aqueous hydrochloric acid and heated to reflux. After 8 h, the layers were separated and the aqueous layer was extracted with ether (3 × 50 mL). The combined organic layers were extracted with saturated, aqueous sodium bicarbonate solution solution (2 × 60 mL) and brine (2 × 60 mL) and dried ($Na_2SO_4$). Removal of solvents in vacuo yielded a brown liquid. Flash column chromatography (10:1 pentane/ether) gave the titled compound as a yellow liquid (5.88 g, 72%). IR ($CDCl_3$): 2172, 1733, 1454, 1431, 1406, 1354 cm$^{-1}$. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 2.41−1.96 (m, 8H), 1.79 (m, 1H), 1.48 (m, 2H), 0.14 (s, 9H). $^{13}$C NMR (75.5 MHz, $CDCl_3$): $\delta$ 220.6, 106.3, 85.0, 48.1, 37.9, 29.3, 28.5, 20.6, 18.0, −0.03. HRMS: Calcd for $C_{12}H_{20}OSi$ ($M^+$): 208.1283. Found: 208.1281.

***trans*-1-Dimethoxymethyl-2-(1-butyn-4-yl)cyclopentane (22).** A solution of potassium hexamethyldisilazide in toluene was prepared from 1.69 g (42.1 mmol) of potassium hydride and 1,1,1,3,3,3-hexamethyldisilazane (8.9 mL, 42.2 mmol) in 42 mL of toluene. To a suspension of (methoxymethyl)triphenylphosphonium chloride (7.54 g, 22.0 mmol) in 22.0 mL of toluene at 0 °C was added 25.5 mL of the potassium hexamethyldisilazide solution. The suspension was then stirred for 30 min at 0 °C. To the resulting red suspension was added cyclopentanone **18** (2.08 g, 10.0 mmol) dropwise, and the reaction was stirred at 0 °C for 30 min and then at room temperature for 4 h. The suspension was added to saturated aqueous ammonium chloride solution (1 × 75 mL) and ether (25 mL). The aqueous layer was extracted with ether (3 × 50 mL). The combined organic layers were washed with brine (2 × 75 mL) and dried ($Na_2SO_4$). Removal of solvents in vacuo yielded a yellow liquid. Partial purification by silica gel chromatography (10:1 hexane/ether) yielded crude **19**.

Enol ether **19** was taken up in 9 mL of THF and 6 mL of 2 M aqueous hydrochloric acid at room temperature. The mixture was then heated at 55 °C for 5 h. The layers were separated and the aqueous layer was extracted with ether (2 × 10 mL). The combined organic layers, were washed with saturated aqueous sodium bicarbonate solution (1 × 15 mL) and brine (3 × 15 mL) and dried ($Na_2SO_4$). Removal of solvents in vacuo yielded a yellow liquid which was taken up in 8 mL of methanol and treated with magnesium methoxide. The suspension was stirred at room temperature for 36 h. It was then taken up in brine (10 mL) and ether/hexane (10 mL). The aqueous layer was extracted with ether/hexane (2 × 10 mL). The organic layers were washed with brine (3 × 15 mL) and dried ($Na_2SO_4$). Removal of solvents in vacuo yielded the aldehyde **20**.

Aldehyde **20** was taken up in 10 mL of methanol and treated with 4 mL of trimethyl orthoformate and 50 mg of *p*-toluenesulfonic acid at room temperature. The reaction was stirred for 3 h. It was then taken up in ether (30 mL) and saturated aqueous sodium bicarbonate solution (30 mL). The aqueous layer was extracted with ether (2 x 30

mL). The combined organic layers were washed with brine (3 × 40 mL) and dried ($Na_2SO_4$). Removal of solvents in vacuo yielded **21**. IR ($CDCl_3$): 2956, 1452, 1382, 1253 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 4.11 (d, $J$ = 6.7 Hz, 1H), 3.35 (s, 3H), 3.31 (s, 3H), 2.21 (m, 2H), 1.85−1.63 (m, 4H), 1.56−1.37 (m, 4H), 1.19 (m, 2H), 0.13 (s, 9H). $^{13}C$ NMR (75.5 MHz, $CDCl_3$): $\delta$ 108.2, 107.9, 83.9, 54.7, 52.9, 47.4, 41.0, 34.9, 32.3, 27.7, 24.7, 18.9, 0.1. HRMS: Calcd for $C_{15}H_{27}O_2Si$ $(M - H)^+$: 267.1780. Found: 267.1770.

Acetal **21** was taken up in 50.0 mL of methanol and potassium carbonate (6.91 g, 50.0 mmol) was added at room temperature. After 2.5 h, the reaction mixture was filtered, rinsing the residue with ether. The solvents were removed in vacuo to yield a yellow liquid. Flash column chromatography using 25:1 hexane/ether as eluent afforded 1.40 g of the titled compound (72% over 5 steps). IR ($CDCl_3$): 3308, 1452, 1365 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 4.14 (d, $J$ = 6.6 Hz, 1H), 3.38 (s, 3H), 3.34 (s, 3H), 2.21 (m, 2H), 1.94 (t, $J$ = 2.7 Hz, 1H), 1.91−1.19 (m, 10H). Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.30; H, 10.15.

***trans*-1-(Dimethoxymethyl)-2-(3-bromo-3-buten-1-yl)cyclopentane (24).** Methyllithium (1.4 M in ether, 2.0 mL, 2.8 mmol) was added to a solution of hexamethylditin (917 mg, 2.80 mmol) in 2.8 mL of ether at room temperature.[24] After 30 min, the reaction was cooled to −45 °C, and copper(I) bromide−dimethyl sulfide complex (576 mg, 2.80 mmol) was added in one portion.[25] The resulting dark suspension was kept at −45 °C for 30 min and then further cooled to −78 °C. It was then cannulated into a solution of **22** (275 mg, 1.40 mmol) in 2.80 mL of THF and methanol (3.40 mL) at −78 °C. After 30 min, the reaction was stirred at −63 °C. After stirring overnight, glacial acetic acid (3 mL) and methanol (3 mL) were added as a mixture via syringe. The reaction was stirred for 1 h. The reaction was then diluted with ether (80 mL), and saturated aqueous ammonium chloride solution (pH = 8) (20 mL) was added. The mixture was stirred at room temperature until the organic layer became clear. The aqueous layer was then extracted with ether (2 × 20 mL). The combined organic layers were washed with saturated aqueous ammonium chloride solution (pH = 8) (2 × 20 mL) and dried ($MgSO_4$). Following evaporation in vacuo, purification by silica gel chromatography (pentane then 10:1 pentane/ether) yielded **23**. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 5.66 (m, 1H), 5.13 (m, 1H), 4.14 (d, $J$ = 7.0 Hz, 1H), 3.35 (s, 3H), 3.33 (s, 3H), 2.28 (m, 2H), 1.87−1.63 (m, 6H), 1.53 (m, 2H), 1.23 (m, 2H), 0.15 (s, 9H).

Vinylstannane **23** was dissolved in 20 mL of dichloromethane and cooled to −20 °C. Bromine was then added dropwise until a faint yellow color persisted. The reaction was diluted with ether (20 mL), washed with saturated aqueous sodium thiosulfate solution (1 × 20 mL) and brine (1 × 20 mL), and dried ($Na_2SO_4$). Removal of solvents in vacuo yielded a yellow liquid. The yellow liquid was taken up in methanol and treated with trimethyl orthoformate and a catalytic amount of *p*-toluenesulfonic acid at room temperature. Solvents were removed in vacuo, and the residue was loaded directly onto a silica gel column and eluted with 10:1 pentane/ether to afford the titled compound (169 mg, 44% from **22**). IR ($CDCl_3$): 2954, 2873, 2834, 1630, 1602, 1452 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 5.55 (d, $J$ = 1.3 Hz, 1H), 5.35 (d, $J$ = 1.4 Hz, 1H), 4.11 (d, $J$ = 7.0 Hz, 1H), 3.34 (s, 3H), 3.30 (s, 3H), 2.42 (m, 2H), 1.91−1.62 (m, 5H), 1.58−1.15 (m, 5H). $^{13}C$ NMR (75.5 MHz, $CDCl_3$): $\delta$ 134.9, 116.0, 108.2, 54.5, 52.8, 47.4, 40.5, 40.2, 34.1, 32.4, 27.7, 24.6. HRMS: Calcd for $C_{11}H_{18}O^{81}Br$ $(M - OCH_3)^+$: 247.0520. Found: 247.0530.

**2-(4-Bromo-4-penten-1-yl)cyclopentanone (26).** A solution of LDA prepared from diisopropylamine (4.70 mL, 33.5 mmol) and *n*-butyllithium (1.40 M in hexane, 24.0 mL, 33.6 mmol) in 33 mL of THF was cooled to −78 °C. The cyclohexylimine of cyclopentanone (5.00 g, 30.3 mmol) was then added dropwise. The reaction was allowed to warm to 0 °C slowly and then stirred at that temperature for 30 min. The solution was then recooled to −70 °C, and 2,5-dibromo-1-pentene[29] (10.4 g, 45.5 mmol) was added dropwise. The reaction was allowed to warm to room temperature overnight. After 16 h, solvents were evaporated in vacuo, and the light yellow residue was taken up in ether (30 mL) and 2 M aqueous hydrochloric acid (42 mL). The mixture was heated to reflux for 20 h. Ether (30 mL) was added, and the layers were separated. The aqueous layer was extracted with ether (3 × 30 mL), and the combined organic layers were washed with saturated aqueous sodium bicarbonate solution solution (1 × 100 mL) and brine (3 × 75 mL) and dried ($Na_2SO_4$). Removal of solvents in vacuo followed by flash column chromatography (10:1 pentane/ether) afforded 4.37 g (62%) of **26**. IR ($CDCl_3$): 2966, 2944, 2879, 2866, 1732, 1631, 1455, 1405 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 5.56 (d, $J$ = 1.4 Hz, 1H), 5.39 (d, $J$ = 1.6 Hz, 1H), 2.43 (t, $J$ = 7.2 Hz, 2H), 2.38−1.97 (m, 5H), 1.78 (m, 2H), 1.59 (m, 3H), 1.26 (m, 1H). $^{13}C$ NMR (75.5 MHz, $CDCl_3$): $\delta$ 221.1, 134.1, 116.8, 48.9, 41.3, 38.1, 29.5, 28.3, 25.8, 20.7. HRMS: Calcd for $C_{10}H_{15}{}^{81}BrO$ $(M^+)$: 232.0285. Found: 232.0309.

***trans*-2-(4-Bromo-4-penten-1-yl)-1-(dimethoxymethyl)cyclopentane (29).** Following the protocol for the preparation of **19**, (methoxymethyl)triphenylphosphonium chloride (7.54 g, 22.0 mmol), **27** (2.17 g, 10.0 mmol), and 25.5 mL (1.00 M, 25.5 mmol) of a toluene solution of potassium hexamethyldisilamide gave crude methyl enol ether **27**.

Following the protocol for the preparation of **18**, methyl enol ether **27** was hydrolyzed in 9 mL of THF and 6 mL of 2 M aqueous hydrochloric acid to give aldehyde **28** (*trans*:*cis* = 16:1 by GC). As for the preparation of **21**, aldehyde **28** in 10 mL of methanol and 4.0 mL of trimethyl orthoformate gave, after overnight reaction and flash column chromatography (pentane then 20:1 pentane/ether followed by 10:1 pentane/ether), 2.02 g (69% over 4 steps) of **29**. IR ($CDCl_3$): 1630, 1452 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 5.57 (d, $J$ = 1.3 Hz, 1H), 5.39 (d, $J$ = 1.4 Hz, 1H), 4.13 (d, $J$ = 7.1 Hz, 1H), 3.36 (s, 3H), 3.33 (s, 3H), 2.42 (m, 2H), 1.86−1.44 (m, 10H), 1.22 (m, 2H). $^{13}C$ NMR (75.5 MHz, $CDCl_3$): $\delta$ 134.9, 116.3, 108.3, 54.4, 53.0, 47.4, 41.5, 41.3, 34.6, 32.6, 27.7, 26.6, 24.7. HRMS: Calcd for $C_{12}H_{22}O_2$-Br $(M - CH)^+$: 277.0803. Found: 277.0795.

**Standard Cyclizations of Vinylcyclobutanol Acetals. 7-Methoxyspiro[4.5]decan-1-one (33).** To a solution of **10b** (198 mg, 0.924 mmol) in 18.4 mL of methylene chloride cooled to 0 °C was added 2,6-di-*tert*-butylpyridine (124 mg, 0.627 mmol) followed by trimethylsilyl triflate (205 mg, 0.924 mmol) dropwise. After 15 min, aqueous sodium bicarbonate was added. The organic layer was dried ($MgSO_4$) and evaporated *in vacuo*, and the resulting oil purified by flash chromatography (4:1 pentane−ether) to give 121 mg (72%) of **33a** and 14 mg (8%) of **33b**.

**33a**: IR ($CDCl_3$): 1727 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 3.63 (tt, $J$ = 7.7, 3.9 Hz, 1H), 3.30 (s, 3H), 3.24 (m, 2H), 1.89−1.79 (m, 6H), 1.62−1.50 (m, 2H), 1.40−1.23 (m, 4H). $^{13}C$ NMR (75.5 MHz, $CDCl_3$): $\delta$ 223.5, 75.1, 55.8, 53.3, 48.7, 37.7, 37.5, 36.3, 31.8, 30.3, 18.6, 18.4. HRMS: Calcd for $C_{11}H_{18}O_2$ $(M^+)$: 182.1306. Found: 182.1302.

**33b**: IR ($CDCl_3$): 2937, 2863, 1728, 1454, 1166, 1118, 1094 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 3.30 (s, 3H), 3.15 (tt, $J$ = 11.3, 4.1 Hz, 1H), 2.24 (dt, $J$ = 6.5, 2.3 Hz, 2H), 2.04 (dt, $J$ = 11.2, 3.3 Hz, 1H), 1.90−1.61 (m, 5H), 1.40−1.11 (m, 6H). $^{13}C$ NMR (75.5 MHz, $CDCl_3$): $\delta$ 222.5, 55.4, 50.2, 37.2, 37.1, 33.5, 31.4, 30.9, 29.5, 20.9, 18.9. HRMS: Calcd for $C_{11}H_{18}O_2$ $(M^+)$: 182.1306. Found: 182.1309.

**7-Iodospiro[4.5]decan-1-one (35).** From **33a**: To a solution of **33a** (100 mg, 0.549 mmol) in 1.1 mL of acetonitrile in a flask protected from light was added trimethylsilyl iodide (101 $\mu$L, 0.713 mmol). After 4 h, another 101 $\mu$L (0.713 mmol) of trimethylsilyl iodide was added. The reaction was stirred overnight and was then diluted with ether (3 mL). The organic layer was washed with saturated sodium thiosulfate solution (2 × 2 mL) and brine (1 × 2 mL) and dried ($MgSO_4$). Removal of solvents followed by silica gel chromatography using 8:1 pentane/ether as eluent yielded **35** (120 mg, 79%).

From **33b**: Following the above procedure, methyl ether **33b** (14 mg, 0.0768 mmol) reacted with trimethylsilyl iodide (2 × 14.2 $\mu$L, 0.200 mmol total) in 0.5 mL of acetonitrile gave 12.9 mg (60%) of **35**. IR ($CDCl_3$): 1728, 1448, 1406, 1326 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 4.79 (tt, $J$ = 11.5, 4.1 Hz, 1H), 2.40 (m, 2H), 2.27 (m, 2H), 1.87 (m, 8H), 1.46 (m, 1H), 1.30 (m, 1H). $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 221.6, 50.8, 45.9, 39.5, 39.3, 38.0, 31.5, 26.7, 23.4, 18.6. HRMS: Calcd for $C_{10}H_{15}IO$: C, 43.18; H, 5.44. Found: C, 43.11; H, 5.33.

**7-Methoxyspiro[4.6]undecan-1-one (36).** A solution of 7,7-dimethoxy-2-(1′-hydroxycyclobutyl)-1-heptene **10c** (200 mg, 0.876 mmol) in 88 mL of dichloromethane was cooled to 0 °C, and pyridine (50 $\mu$L, 0.618 mmol) was added. After 15 min, trimethylsilyl triflate (170 $\mu$L, 0.880 mmol) was added dropwise. The colorless solution turned light orange immediately. After 15 min, the reaction was

quenched by addition to saturated aqueous sodium bicarbonate solution (80 mL) and ether (25 mL). The organic layers were dried ($MgSO_4$) and evaporated *in vacuo*. Purification of the yellow residue by silica gel chromatography (4:1 pentane/ether) gave **36** (148 mg, 86%) as a 4.6:1 diastereomeric mixture by GC.

**36a**: IR ($CDCl_3$): 1729, 1459 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 3.52 (tt, $J$ = 8.6, 2.1 Hz, 1H), 3.27 (s, 3H), 2.26 (m, 2H), 2.03 (m, 1H), 1.96−1.25 (m, 13H). $^{13}C$ NMR (75.5 MHz, $CDCl_3$): $\delta$ 223.8, 78.0, 56.0, 49.1, 40.6, 38.4, 36.7, 35.6, 34.5, 25.8, 23.4, 18.3. HRMS: Calcd for $C_{12}H_{20}O_2$ ($M^+$): 196.1463. Found: 196.1474. Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.19; H, 10.13.

**36b**: IR ($CDCl_3$): 1729, 1463, 1455 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 3.23 (s, 3H), 3.14 (tt, $J$ = 9.6, 2.9 Hz, 1H), 2.20 (m, 2H), 2.00−1.12 (m, 14H).

**7-Iodospiro[4.6]undecan-1-one (37).** Following the procedure for formation of **35**, **36a** (18 mg, 0.09 mmol) and trimethylsilyl iodide (2 × 17.0 $\mu$L, 0.24 mmol total) in 0.5 mL of acetonitrile gave **37** (20 mg, 74%) after flash chromatography (8:1 pentane/ether). IR ($CDCl_3$): 1730, 1457, 1406 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 4.69 (tt, $J$ = 10.5, 2.5 Hz, 1H), 2.56 (m, 2H), 2.27 (m, 2H), 2.09 (m, 2H), 1.94−1.35 (m, 10H). $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 222.5, 49.0, 44.8, 38.4, 36.8, 34.2, 30.9, 28.9, 23.2, 18.6. HRMS: Calcd for $C_{11}H_{17}O$ ($M - I$)$^+$: 165.1279. Found: 165.1278.

**Cyclization of *trans*-2-(2-(1′-Hydroxycyclobutyl)-2-propen-1-yl)-1-(dimethoxymethyl)cyclohexane (14).** Following the standard protocol, **14** (67 mg, 0.25 mmol), 2,6-di-*tert*-butylpyridine (39.3 $\mu$L, 0.175 mmol), and trimethylsilyl triflate (48.2 $\mu$L, 0.250 mmol) in 7.5 mL of methylene chloride gave 32 mg (54%) of **40a** and 18 mg (30%) of **40b** after flash chromatography (10:1 pentane/ether).

**40a**: IR ($CDCl_3$): 1728, 1602, 1450 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 3.39 (ddd, $J$ = 11.0, 9.8, 4.6 Hz, 1H), 3.34 (s, 3H), 2.30 (m, 2H), 2.13 (m, 1H), 2.07 (ddd, $J$ = 13.0, 4.5, 2.1 Hz, 1H), 1.93 (m, 2H), 1.80−1.43 (m, 6H), 1.33−1.10 (m, 2H), 1.11 (dd, $J$ = 12.9, 11.0 Hz, 1H), 1.06−0.82 (m, 5H). $^1H$ NMR (300 MHz, $C_6D_6$): $\delta$ 3.65 (ddd, $J$ = 10.8, 9.8, 4.4 Hz, 1H), 3.24 (s, 3H), 2.43 (m, 1H), 1.99 (ddd, $J$ = 12.8, 4.5, 2.0 Hz, 1H), 1.89 (m, 2H), 1.75 (m, 1H), 1.62 (m, 2H), 1.48−1.28 (m, 7H), 1.21 (m, 2H), 1.04 (dd, $J$ = 12.9, 11.0 Hz, 1H), 0.96 (m, 1H), 0.79 (m, 1H), 0.65 (dd, $J$ = 13.2, 12.6 Hz, 1H). $^{13}C$ NMR (75.5 MHz, $CDCl_3$): $\delta$ 222.4, 79.8, 57.1, 48.7, 48.5, 40.2, 39.9, 38.0, 37.4, 35.6, 33.7, 28.7, 26.1, 26.06, 18.6. HRMS: Calcd for $C_{15}H_{24}O_2$ ($M^+$): 236.1776. Found: 236.1804.

**40b**: IR ($CDCl_3$): 1732, 1602, 1462, 1450, 1378 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 3.22 (s, 3H), 3.16 (ddd, $J$ = 2.7, 2.7, 2.7 Hz, 1H), 2.49 (m, 2H), 2.21−1.14 (m, 15H), 1.02−0.75 (m, 3H). $^1H$ NMR (300 MHz, $C_6D_6$): $\delta$ 3.00 (s, 3H), 2.86 (ddd, 2.7, 2.7, 2.7 Hz, 1H), 2.57 (tdt, $J$ = 23.3, 11.7, 3.6 Hz, 1H), 2.18 (m, 2H), 1.93−1.01 (m, 14H), 0.97−0.63 (m, 3H). $^{13}C$ NMR (75.5 MHz, $CDCl_3$): $\delta$ 219.8, 79.7, 77.2, 57.2, 46.8, 46.6, 39.8, 35.7, 34.6, 31.5, 29.7, 28.8, 26.7, 26.0, 16.7. HRMS: Calcd for $C_{15}H_{24}O_2$ ($M^+$): 236.1776. Found: 236.1784.

**Cyclization of *cis*-2-(2-(1′-hydroxycyclobutyl)-2-propen-1-yl)-1-(dimethoxymethyl)cyclohexane (15).** Following the standard protocol, **15** (25 mg, 0.093 mmol), 2,6-di-*tert*-butylpyridine (14.6 $\mu$L, 0.065 mmol) and trimethylsilyl triflate (18.0 $\mu$L, 0.093 mmol) in 9.3 mL of methylene chloride gave 18 mg (82%) of **41** after flash chromatography (10:1 pentane/ether). IR ($CDCl_3$): 1726, 1467, 1450, 1407, 1374 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 3.82 (dt, $J$ = 12.0, 4.8 Hz, 1H), 3.32 (s, 3H), 2.29 (td, $J$ = 7.6, 2.7 Hz, 2H), 2.09 (m, 2H), 1.91 (dt, $J$ = 14.8, 7.0 Hz, 2H), 1.80 (d, $J$ = 6.5 Hz, 1H), 1.77 (m, 2H), 1.68 (ddd, $J$ = 13.2, 4.7, 1.4 Hz, 1H), 1.59−1.16 (m, 10H). $^1H$ NMR (300 MHz, $C_6D_6$): $\delta$ 4.08 (dt, $J$ = 12.0, 4.9 Hz, 1H), 3.17 (s, 3H), 2.32 (m, 1H), 2.04 (m, 1H), 1.87 (m, 2H), 1.71 (ddd, $J$ = 13.3, 4.6, 1.6 Hz, 2H), 1.65 (m, 1H), 1.50−1.11 (m, 12H), 1.06 (ddd, $J$ = 13.8, 4.1, 1.7 Hz, 1H). $^{13}C$ NMR (75.5 MHz, $CDCl_3$): $\delta$ 222.2, 77.2, 55.6, 48.4, 40.4, 38.0, 37.9, 32.5, 31.5, 31.1, 29.6, 26.1, 20.9, 18.6, 17.8. HRMS: Calcd for $C_{15}H_{24}O_2$ ($M^+$): 236.1776. Found: 236.1782.

**Cyclization of *trans*-1-(dimethoxymethyl)-2-(1′-hydroxymethyl)-2-((1′-hydroxycyclobutyl)-3-buten-1-yl) cyclopentane (25).** Following the standard procedure, **25** (121 mg, 0.451 mmol), 2,6-di-*tert*-butylpyridine (71 $\mu$L, 0.32 mmol), and trimethylsilyl triflate (87 $\mu$L, 0.45 mmol) in 45 mL of methylene chloride gave 100 mg (93%) of **42** after flash chromatography (10:1 then 6:1 pentane/ether) as a 3.9:3.4:1 ratio of diastereomers.

**42a**: IR ($CDCl_3$): 1727, 1450 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 3.29 (s, 3H), 3.25 (dt, $J$ = 9.3, 3.9 Hz, 1H), 2.26 (m, 2H), 2.11 (m, 2H), 1.87 (m, 4H), 1.75 (d, $J$ = 4.1 Hz, 2H), 1.70−1.16 (m, 10H). $^{13}C$ NMR (75.5 MHz, $CDCl_3$): $\delta$ 223.6, 85.7, 56.9, 52.7, 50.7, 43.1, 36.6, 36.1, 34.9, 34.7, 33.7, 33.5, 31.7, 24.0, 18.8. HRMS: Calcd for $C_{15}H_{24}O_2$ ($M^+$): 236.1776. Found: 236.1787. Anal. Calcd for $C_{15}H_{24}O_2$: C, 76.23; H, 10.24. Found: C, 76.46; H, 10.09.

**42b**: IR ($CDCl_3$): 1726, 1452 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 3.54 (m, 1H), 3.34 (s, 3H), 2.32 (m, 1H), 2.19−1.53 (m, 16H), 1.46 (dt, $J$ = 14.8, 5.0 Hz, 1H), 1.32 (m, 1H), 1.16 (m, 1H). $^{13}C$ NMR (75.5 MHz, $CDCl_3$): $\delta$ 222.9, 81.0, 57.5, 51.1, 49.0, 38.1, 36.6, 36.1, 36.0, 35.4, 31.6, 30.2, 28.1, 24.2, 18.9. HRMS: Calcd for $C_{15}H_{24}O_2$ ($M^+$): 236.1776. Found: 236.1787. Anal. Calcd for $C_{15}H_{24}O_2$: C, 76.23; H, 10.24. Found: C, 76.47; H, 9.99.

**42c**: IR ($CDCl_3$): 1728, 1455 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 3.30 (s, 3H), 2.94 (ddd, $J$ = 9.6, 7.8, 5.8 Hz, 1H), 2.28 (m, 2H), 2.00 (m, 2H), 1.92−1.71 (m, 8H), 1.67−1.26 (m, 9H). $^{13}C$ NMR (75.5 MHz, $CDCl_3$): $\delta$ 222.5, 83.9, 56.2, 52.5, 43.5, 38.7, 36.3, 36.1, 34.6, 32.8, 31.0, 29.7, 28.4, 22.8, 18.7. HRMS: Calcd for $C_{15}H_{24}O_2$ ($M^+$): 236.1776. Found: 236.1770.

**Deoxygenation of Cyclopentanones 42.** Of **42a**. A solution of 4**2a** (10 mg, 0.04 mmol) and *p*-toluenesulfonylhydrazine (9.8 mg, 0.05 mmol) in 100 $\mu$L of absolute ethanol was heated to reflux. Solvents were removed in vacuo after 24 h. The residue was then taken up in 1:1 DMF-sulfolane (200 $\mu$L), and sodium cyanoborohydride (10.6 mg, 0.168 mmol) and *p*-toluenesulfonic acid (2.1 mg, 0.01 mmol) were added. The reaction was then heated to 110 °C. After 2 h, the reaction was cooled, taken up in water (2 mL), and extracted with hexane (2 × 2 mL), and the latter was dried ($MgSO_4$). Following evaporation, the residue was chromatographed with 10:1 pentane/ether to yield **43a** (6.2 mg, 66%). IR ($CDCl_3$): 1712, 1602, 1452 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 3.32 (s, 3H), 3.01 (ddd, $J$ = 9.6, 6.0, 4.5 Hz, 1H), 2.04 (m, 1H), 1.85−1.16 (m, 21H). $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 86.0, 56.5, 52.4, 44.2, 43.7, 43.4, 41.1, 40.2, 38.9, 34.9, 32.5, 31.3, 24.2, 24.0, 23.5.

**Of 42b**. Following the above protocol, **42b** (10 mg, 0.04 mmol) gave 6.4 mg (68%) of **43b** after flash chromatography. IR ($CDCl_3$): 1602, 1450 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 3.41 (td, $J$ = 6.0, 3.3 Hz, 1H), 3.34 (s, 3H), 1.90−1.11 (m, 22H). $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 80.2, 57.6, 49.9, 44.8, 44.0, 41.9, 39.9, 39.0, 37.8, 35.3, 32.2, 29.5, 24.7, 24.3, 24.2.

**2-Methoxybicyclo[6.3.0]undecane-4-spiro-1′-cyclopentan-2′-one (46).** To a solution of **31** (280 mg, 0.991 mmol) and 2,6-di-*tert*-butylpyridine (222.6 $\mu$L, 0.991 mmol) in 99 mL of dichloromethane at −78 °C was added titanium(IV) chloride (1.00 M in dichloromethane, 1.98 mL, 1.98 mmol) dropwise. The reaction was then allowed to warm to room temperature slowly. After 6 h, methanol (1 mL) was added. After another 30 min, the reaction was diluted with hexane (50 mL) and washed with 1 M aqueous hydrochloric acid solution (1 × 100 mL), saturated aqueous sodium bicarbonate solution (1 × 100 mL), and brine (1 × 100 mL) and dried ($Na_2SO_4$). Following solvent removal in vacuo, the residue was chromatographed (10:1 pentane/ether then 1.5 ether/pentane) to yield 47.3 mg (19%) of a white crystalline solid as a single diastereomer, **46b** (minor), and 125.7 mg (51%) of a mixture of two diastereomers, **46a** (major) and **46c** (trace), for a total yield of 70%.

**46a**: IR ($CDCl_3$): 1725, 1604, 1458 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 3.31 (s, 3H), 3.07 (ddd, $J$ = 10.5, 4.7, 2.0 Hz, 1H), 2.39−0.86 (m, 22H). $^{13}C$ NMR (75.5 MHz, $CDCl_3$): $\delta$ 222.6, 77.2, 56.9, 49.6, 49.3, 41.9, 37.9, 36.8, 36.6, 35.7, 33.0, 31.5, 29.7, 23.9, 21.9, 18.5. HRMS: Calcd for $C_{16}H_{26}O_2$ ($M^+$): 250.1932. Found: 250.1934. Anal. Calcd for $C_{16}H_{26}O_2$: C, 76.75; H, 10.47. Found: C, 77.00; H, 10.54.

**46b**: mp 71−72 °C (recrystallized from hexane). IR ($CDCl_3$): 1727, 1602, 1465, 1452 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 3.37 (dt, $J$ = 10.2, 4.3 Hz, 1H), 3.31 (s, 3H), 2.4 −2.18 (m, 4H), 2.01−1.08 (m, 18H). $^{13}C$ NMR (75.5 MHz, $CDCl_3$): $\delta$ 222.9, 80.2, 58.2, 50.3, 46.0, 40.2, 38.8, 38.0, 37.4, 36.9, 34.2, 33.1, 31.0, 25.8, 22.6, 18.6. Anal. Calcd for $C_{16}H_{26}O_2$: C, 76.75; H, 10.47. Found: C, 76.87; H, 10.25.

**Deoxygenation of Cyclopentanones (46a−c). Of 46a + c**: A mixture of **46a** and **46c** (20 mg, 0.08 mmol) was deoxygenated as before using *p*-toluenesulfonylhydrazine (17.9 mg, 0.096 mmol) in 200 $\mu$L of ethanol followed by sodium cyanoborohydride (20 mg, 0.32 mmol)

and *p*-toluenesulfonic acid (3.8 mg, 0.02 mmol) in 250 $\mu$L of DMF and 250 $\mu$L of sulfolane to give, after purification by silica gel chromatography (10:1 pentane/ether), a diastereomeric mixture of **49** (major) and **50** (minor) (by GC) (3.1 mg, 16%). IR ($CDCl_3$): 1711, 1602, 1452, 1364 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 3.34 (s) and 3.33 (s) (total 3H), 3.30 (m) and 2.91 (ddd, $J$ = 10.5, 4.8, 2.5 Hz) (total 1H), 2.07 (m, 1H), 1.98−1.02 (m, 47H). $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 86.2, 81.5, 57.6, 56.3, 51.6, 46.2, 45.3, 42.3, 41.7, 41.3, 40.9, 38.9, 38.8, 38.5, 37.9, 37.5, 37.3, 36.6, 35.7, 34.2, 32.9, 30.3, 29.7, 25.4, 24.7, 24.6, 23.8, 23.7, 23.4, 23.2, 23.1, 22.4.

**Of 46b**: Cyclopentanone **46b** (10 mg, 0.04 mmol) and *p*-toluenesulfonylhydrazine (8.9 mg, 0.05 mmol) in 100 $\mu$L of ethanol was heated at reflux for 24 h, and solvents were removed *in vacuo*. The residue was then taken up in 1:1 DMF−sulfolane (200 $\mu$L), and sodium cyanoborohyride (10 mg, 0.16 mmol) and *p*-toluenesulfonic acid (1.9 mg, 0.01 mmol) were added. The reaction was heated to 110 °C for 2 h. Another 10 mg (0.16 mmol) of sodium cyanoborohydride and 1.9 mg (0.01 mmol) of *p*-toluenesulfonic acid were then added. After 5.5 h, the reaction was cooled, taken up in water (1 × 2 mL), and extracted with hexane (2 × 2 mL), and the latter was dried ($MgSO_4$). Removal of solvents yielded a residue which was purified by silica gel chromatography (10:1 pentane/ether) to afford the titled compound (6.1 mg, 64%) as a single diastereomer (by GC) which corresponds to the minor isomer in the above mixture by both NMR and GC. IR ($CDCl_3$): 1602, 1465, 1451 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 3.34 (s, 3H), 3.30 (dt, $J$ = 10.4, 4.1 Hz, 1H), 2.07 (m, 1H), 1.92−1.02 (m, 23H). $^{13}C$ NMR (75.5 MHz, $CDCl_3$): $\delta$ 81.5, 57.6, 46.2, 43.7, 42.3, 38.9, 38.8, 37.9(2), 37.3, 36.6, 30.3, 25.4, 24.7, 23.4, 23.2. Anal. Calcd for $C_{16}H_{28}O$: C, 81.29; H, 11.94. Found: C, 81.06; H, 12.13.

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**Supporting Information Available:** 2D NMR studies of **40a**, X-ray data for **46a**, and cyclizations of **55** and **57** (22 pages). See any current masthead page for ordering and Internet access instructions.

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