Tandem Cope–Cope Rearrangements

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Abstract: The first examples of tandem Cope–Cope rearrangements have been identified. When (1*R**,4*S**,6*R**)-1,6-divinylbicyclo[2.2.2]oct-2-ene (**6**) was rearranged thermally, smooth conversion to (1*R**,8a*S**)-1,2,3,5,6,8a-hexahydro-1-vinylnaphthalene (**8**) occurred. The mechanistic course of this isomerization was established by deuterium substitution as in **6**-d_1 and by placement of a methoxyl group as in **14**. The specific positioning of these labels in the corresponding products following upon thermal activation constitutes an especially stringent test of the operation of two [3,3] sigmatropic shifts in tandem. Since the intermediate in these reactions was not spectroscopically visible, the Cope-2 stage must be accelerated relative to the more energy-demanding Cope-1 lead-in step. This ordering is attributed to the kinetic benefits of strain release that materialize during passage to the final product. The discovery was also made that by positioning of an electron-rich aromatic ring at the distal carbon of the C(1) vinyl group, additional intramolecular acid-promoted cyclization can operate. The specific example is defined by the formation of **33**. Finally, the consequences of anionic acceleration on the interruption of the tandem sigmatropic events were determined. The conversion of both **39** and **40** to their alkoxides did induce rearrangement at room temperature. The greater the concentration of negative charge on oxygen, the greater the kinetic acceleration and the greater the extent to which alternative pathways operate competitively.

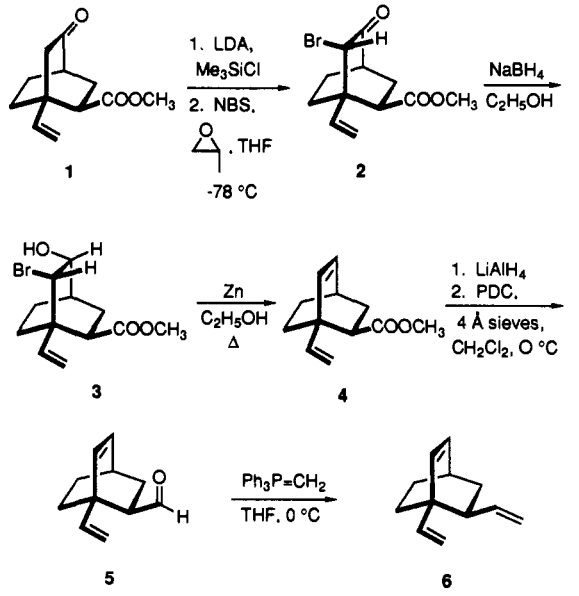
Increasing attention is being paid to tandem organic reactions[2] as a means of enhancing structural complexity rapidly and efficiently. Frequently, high stereocontrol is achieved because the second stage occurs intramolecularly. Although sigmatropic transformations are known to be easily assimilated into reaction cascades having these features,[2] we are unaware of any reported examples of sequential Cope–Cope rearrangements.[3] Herein we probe the feasibility of this reaction principle and illustrate its synthetic potential.

Our first step in this direction was intentionally limited to starting materials offering the possibility for regioselective competition between two [3,3] sigmatropic reaction channels. Prior to our earlier work in this field,[4] intramolecularly competitive Cope rearrangements were unknown. The extent to which kinetic differentiation along these lines becomes understood can be expected to impact directly on the range and power of the methodology.

Results and Discussion

The 1,6-Divinylbicylo[2.2.2]oct-2-ene Example. Structurally, triene **6** represents the simplest of the bicyclic starting materials suited to our purposes. The known keto ester **1**[5] was envisioned to be a possible precursor to **6**. Although reduction of **1** with $NaBH_4$[6] proceeded regioselectively to provide a 9:1 mixture of stereoisomeric hydroxy esters, their mesylate derivatives could not be made to undergo successful E_2 elimination[7] to provide diene ester **4**. Nor was the enol phosphate[8] of **1** useful in this regard. The successful pathway began by bromination of the silyl enol ether with *N*-bromosuccinimide in the presence of propylene oxide,[9] a process that led exclusively to the *anti*-bromo ketone **2** (Scheme 1). This highly crystalline intermediate was smoothly transformed into bromohydrin **3** as a prelude to reductive elimination with zinc in ethanol.[10] Arrival at **6** was accomplished via a straightforward sequence in which **4** was converted seriatim into the alcohol, aldehyde, and the corresponding chain-extended olefin.

Scheme 1



* Abstract published in *Advance ACS Abstracts*, February 15, 1994.

(1) (a) Bourse Lavoisier recipient and Elf-Aquitaine grantee (1988–1989). (b) Lubrizol Fellow, 1992.

(2) (a) Ho, T. L. *Tandem Organic Reactions*; John Wiley and Sons, Inc.: New York, 1992. (b) Ziegler, F. E. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Ed.; Pergamon Press: Oxford, 1991; Vol. 5, Chapter 7.3.

(3) (a) The possibility that such a rearrangement may be operating to a minor extent in the reactions of 5-alkoxy-1,3,7,9-tetraenes has been considered (the primary pathway seems to be a [5,5] sigmatropic rearrangement) but not unequivocally established: Wender, P. A.; Ternansky, R. J.; Sieburth, S. M. *Tetrahedron Lett.* **1985**, *26*, 4319. (b) An example of a Claisen–Cope–Cope sequence has been reported: Cookson, R. C.; Rogers, N. R. *J. Chem. Soc., Perkin Trans. 1* **1973**, 2741.

(4) Paquette, L. A.; Guevel, R.; Sauer, D. R. *Tetrahedron Lett.* **1992**, *33*, 923.

(5) Schinzer, D.; Kalesse, M. *Synlett* **1989**, 34.

(6) Brown, H. C.; Muzzio, J. *J. Am. Chem. Soc.* **1966**, *88*, 2811.

(7) Compare: Williams, R. M.; Maruyama, L. K. *J. Org. Chem.* **1987**, *52*, 4044.

(8) Ireland, R. E.; Muchmore, D. C.; Hengartner, U. *J. Am. Chem. Soc.* **1972**, *94*, 5098.

(9) (a) Roberts, R. M.; Schlessinger, R. H. *J. Am. Chem. Soc.* **1981**, *103*, 724. (b) Reuss, R. H.; Hassner, A. *J. Org. Chem.* **1974**, *39*, 1785.

(10) James, D. R.; Rees, R. W.; Shoppee, C. W. *J. Chem. Soc.* **1955**, 1370.

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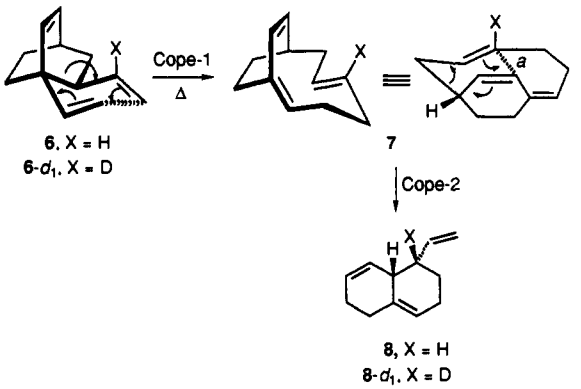
Scheme 2

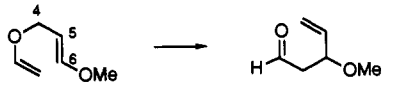


The thermal rearrangement of **6** was effected in chlorobenzene-d_5 solution at 220 °C for 20 h in a sealed tube. Direct spectroscopic analysis of the reaction mixture indicated that a single isomeric product had been generated. This substance was shown to be the hexahydronaphthalene **8** on the strength of ^{1}H decoupling, 2D-COSY, C/H correlation, and semiselective DEPT-45 experiments (see supplementary material).

A hypothetical pathway from **6** to **8**, illustrated in Scheme 2, incorporates the fundamental feature of a first-stage Cope rearrangement (Cope-1) that leads to the intermediate triene **7**. By making and breaking bonds in this manner, one generates a belted structural isomer that experiences substantial steric compression. In particular, an olefinic carbon in the six-membered ring is forcibly compressed against a carbon atom from the trans double bond across the gap labeled as *a* in **7**. The intrinsic property of **7** and the structurally enforced chairlike geometry of this particular 1,5-diene subunit are expectedly conducive to a second Cope rearrangement. In fact, the Cope-2 step should be kinetically more accelerated than the first in light of the strain release accompanying the conversion to **8**. In agreement with this prediction, no buildup of **7** was noted during the thermal conversion of **6** to **8**.

Greater assurance that the pathway advanced in Scheme 2 corresponded to reality was derived from an analogous experiment performed on **6**-d_1. Introduction of a deuterium atom at this specific site was achieved by reduction of **4** with $LiAlD_4$, followed by PDC oxidation and Wittig olefination as before. The intervention of **7** would require that the isotopic label be attached directly to the trans olefinic carbon that is a seat of reaction at the Cope-2 stage. As a consequence, the deuterium would ultimately arise as the substituent geminal to the exo vinyl group in **8**-d_1. Since this proton is clearly evident as a doublet of doublets of doublets at δ 2.58 in **8** and is absent in the high-field ^{1}H NMR spectrum of **8**-d_1 (with attendant consequences), full consistency with the proposed mechanism is seen.

Consequences of 3-Methoxy Substitution. Exclusive adherence by **6** to that Cope rearrangement option involving its exocyclic double bonds provides no direct information concerning the extent to which the alternative [3,3] sigmatropic option is kinetically disadvantaged. In their exhaustive study of the classical Claisen rearrangement,[11] Coates and Curran found that introduction of alkoxy groups at C(4) or C(6) results in 9.5–159-fold acceleration of the [3,3] sigmatropic shift (see **9**). Substitution at C(4) had

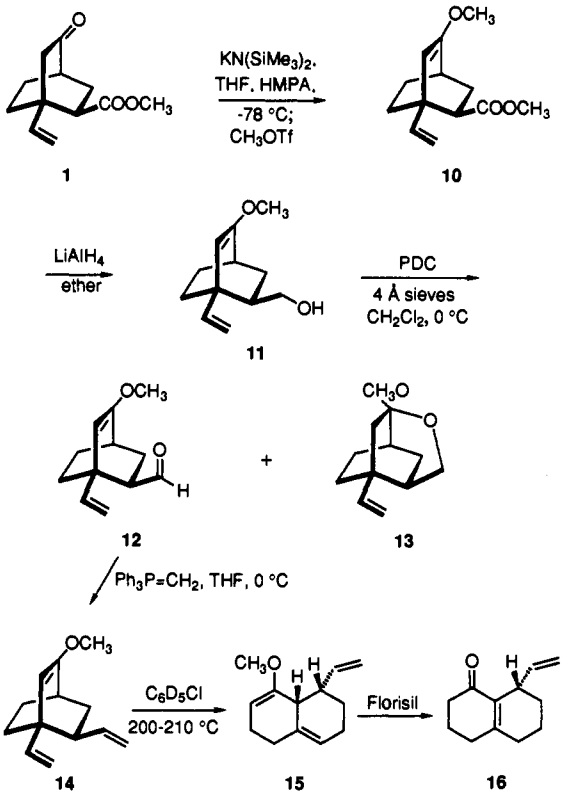


9

generally greater impact than that at C(6). Positioning of a methoxyl group at C(3) as in **14** might bring matters into closer balance if a reasonable correspondence in rates existed. Relevantly, however, the Claisen and Cope rearrangements feature quite different transition states, with the former involving a buildup of charge and the latter exhibiting neutral characteristics. On this basis, no electronic advantage should be expected from the methoxyl group, although synthetic utility would be heightened.

(11) Coates, R. M.; Rogers, B. D.; Hobbs, S. J.; Peck, D. R.; Curran, D. P. *J. Am. Chem. Soc.* **1987**, *109*, 1160.

Scheme 3



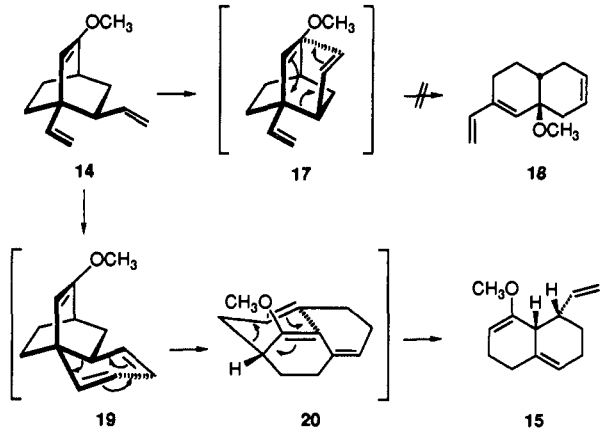
The route employed for the preparation of **14** was again dependent on the availability of **1**.[5] Its deprotonation and subsequent exposure to methyl triflate[12] furnished **10** (Scheme 3). Introduction of the requisite vinyl group to give **14** was carried out in the predescribed manner. The PDC oxidation had necessarily to be perfomed with greater care than usual because of competing cyclization to the ketal **13** even when pyridine was present in the reaction mixture. Furthermore, aldehyde **12** was a particularly sensitive compound, requiring that it be subjected to Wittig olefination without delay.

The thermal rearrangement of **14**, conducted in C_6D_5Cl solution at 200–210 °C as in the earlier example, could be conveniently monitored by ^{1}H NMR. Particularly helpful in this regard was the disappearance of the methoxyl singlet of **14** at δ 3.24 and its replacement by the equivalent absorption for **15** at δ 3.31. This change correlated well with alterations in several other regions of the spectrum. After 20 h, the data indicated that a single isomer had been produced. Its structural features were determined to be those described by **15**, in keeping with the results of a battery of advanced NMR experiments (see supplementary material). Furthermore, in our attempts to purify **15** by chromatography on Florisil, a modest amount of hydrolysis occurred to give dienone **16**.

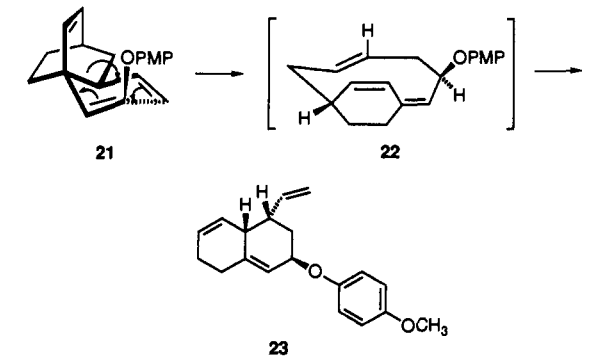
Thus, the behavior of **14** is in keeping with that of **6**. The adoption of a boat [3,3] mutant at the Cope-1 stage, viz. **17**, in order to involve the methoxyl group directly and give **18** does not operate (Scheme 4). Evidently, this alternative is of sufficiently high energy so as to have no opportunity to compete with the exocyclic chair alternative **19**. The complete specificity is noteworthy and signals that systems of types **8** and **15** can be readily accessed in this manner.

(12) Paquette, L. A.; Oplinger, J. A. *Tetrahedron* **1989**, *45*, 107.

Scheme 4



Scheme 5

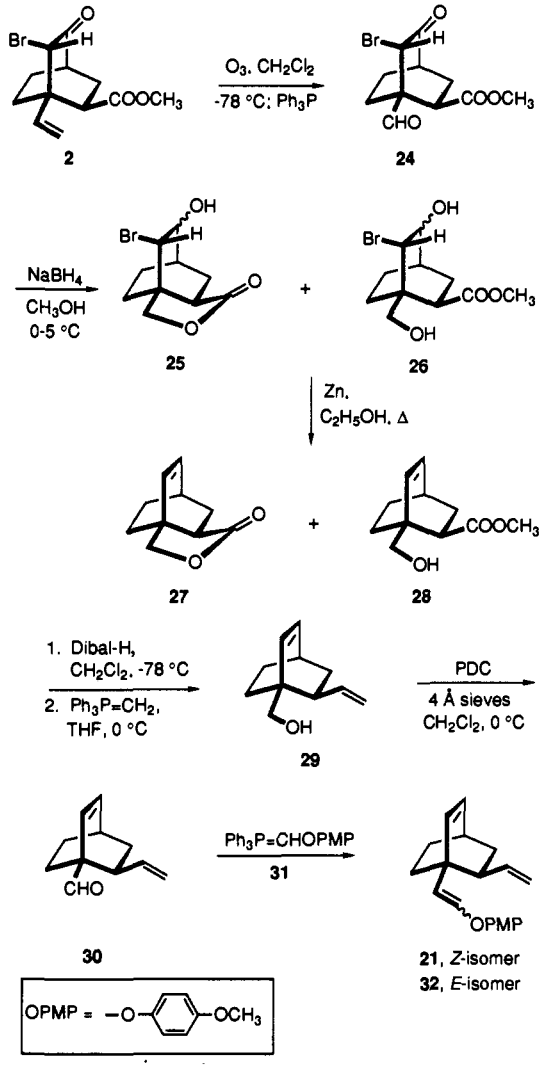


Acid-Catalyzed Cyclization of an Aryl-Substituted Hexahydronaphthalene. The ease of generating hexahydronaphthalenes by tandem Cope–Cope rearrangement and the well-defined relationship of positional substitution in the 1,6-divinylbicyclo-[2.2.2]oct-2-ene precursor and end product prompted us to consider yet another utilitarian role for the process. More specifically, it was of interest to take advantage of the well-recognized capability of electron-rich aromatic rings to engage in intramolecular electrophilic substitution.[13] An important consequence of topologically controlled sigmatropic transfers is predictable chirality transfer. Accordingly, the connectivities present in **21** should without any suppositions be expected to translate stereospecifically into **23** if the suprafaciality defined in **22** is indeed the kinetically favorable pathway (Scheme 5). As will be seen, **23** is particularly susceptible to acid-catalyzed ring closure.

To arrive at **21**, the bromo keto ester **2** was first ozonolyzed. When this olefinic bond cleavage was performed in methanol at −78 °C with dimethyl sulfide as the eventual reducing agent, a quantitative yield of **24** was realized on occasion. In light of the irreproducibility of this process, however, recourse was made instead to the use of triphenylphosphine,[15] which consistently furnished the aldehyde in 88% yield (Scheme 6). Exposure of **24** to sodium borohydride in methanol[16] at 0–5 °C afforded the needed lactone **25** and its hydroxy ester progenitor **26** in a ratio of approximately 8:1.

This mixture was heated in ethanol containing powdered zinc in order to introduce the intracyclic double bond. At this point, it proved convenient to separate **27** from **28**, although it was not necessary that this be done. Their conversion to the isomerically pure diene alcohol **29** was achieved by low-temperature reduction

Scheme 6



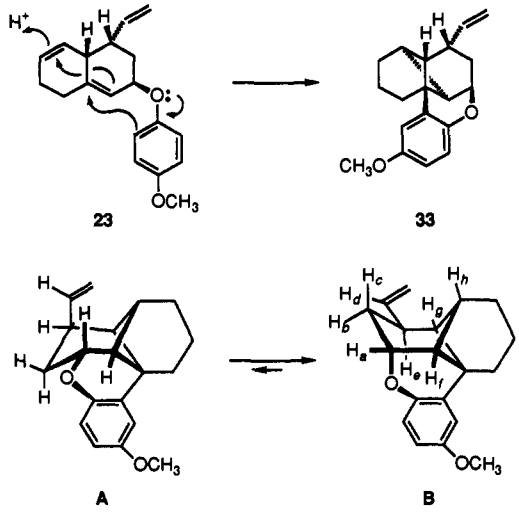
with Dibal-H[17] and direct olefination with methylenetriphenylphosphorane.[18] Finally, PDC oxidation made available the aldehyde **30**, condensation of which with the ylide **31**[19] provided a *ca.* 1:1 mixture of **21** and **32**. The *Z*-isomer **21** was the less polar vinyl ether and could therefore be obtained more readily in pure condition.

The thermal isomerization of **21** was performed in standard fashion (C_6H_5Cl, 200–210 °C, 16 h). Direct chromatography of the reaction mixture on Florisil in order to remove the reaction solvent did not afford **23**. Rather, the isolated material was seen by ^1H NMR to have lost its two core olefinic centers. Protonation of the less sterically congested double bond evidently engages the second π system in transannular bonding, perhaps in a concerted setting (Scheme 7). The outcome of this electron flow is to position positive charge preferentially at the tertiary carbon atom for the usual inductive reasons. The adventitiously positioned *p*-methoxyphenoxy substituent ultimately becomes bonded to this site from its more sterically available β surface to deliver **33**.

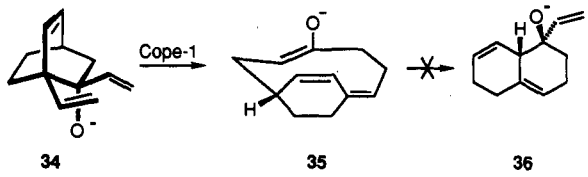
As before, the carbon–carbon connectivities in **33** were established by semiselective DEPT-45 studies as described in the supplementary material. MM2 calculations performed on this structure (MODEL version KS 2.99)[20] indicated conformer **B** to

(13) A classical example can be found in an early synthesis of *dl*-lycopodine: Stork, G.; Kretchmer, R. A.; Schlessinger, R. H. *J. Am. Chem. Soc.* **1968**, *90*, 1647.
(14) Pappas, J. J.; Keaveney, W. P.; Gancher, E.; Berger, M. *Tetrahedron Lett.* **1966**, 4273.
(15) Lorenz, O.; Park, C. R. *J. Org. Chem.* **1965**, *30*, 1976.
(16) Chairkin, S. W.; Brown, W. G. *J. Am. Chem. Soc.* **1949**, *71*, 122.
(17) Grieco, P. A. *J. Org. Chem.* **1972**, *37*, 2363.
(18) (a) Enholm, E. J.; Trivellas, A. *J. Am. Chem. Soc.* **1989**, *111*, 6463. (b) Little, R. D.; Muller, G. W. *J. Am. Chem. Soc.* **1981**, *103*, 2744.
(19) Paquette, L. A.; Huber, S. K.; Thompson, R. C. *J. Org. Chem.* **1993**, *58*, 6874–6882.
(20) (a) Allinger, N. L. *J. Am. Chem. Soc.* **1977**, *99*, 8127. (b) Burkett, U.; Allinger, N. L. *Molecular Mechanics*; ACS Monograph 177; American Chemical Society: Washington, DC, 1982. The 2.99 version of this software package was provided to us by Professor Kosta Steliou.

Scheme 7



Scheme 8



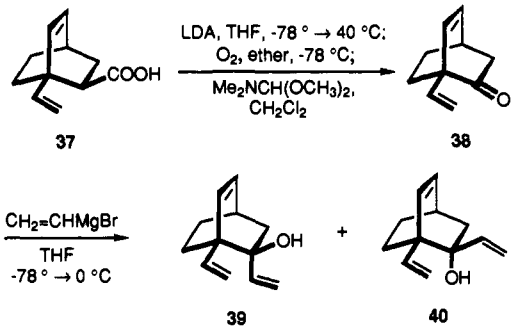
be more stable than **A** to an extent greater than 5 kcal/mol. Support for this conclusion was gained from NOE measurements, which indicated *inter alia* the following integral enhancements to be operative: H_a/H_c = 6.6%, H_a/H_f = 7%, H_c/H_d = 0.9%, and $H_d/H_e + H_h$ = 3.8%. Significantly, no H_a/H_d interaction was seen.

A particularly noteworthy observation is that the *E*-isomer **32** does not respond in a comparable manner. As a consequence of the high stereochemical control operative in the preliminary tandem Cope–Cope rearrangement, the *p*-methoxyphenoxy substituent in the resultant hexahydronaphthalene must necessarily be projected to the α surface. Cyclization by intramolecular electrophilic aromatic substitution is now rendered kinetically prohibitive because structural constraints dictate that the new bond to the aromatic ring continue to be β-directed. An inside–outside bridge would necessarily result. This unlikely event is not observed, uncharacterizable polymeric products resulting instead.

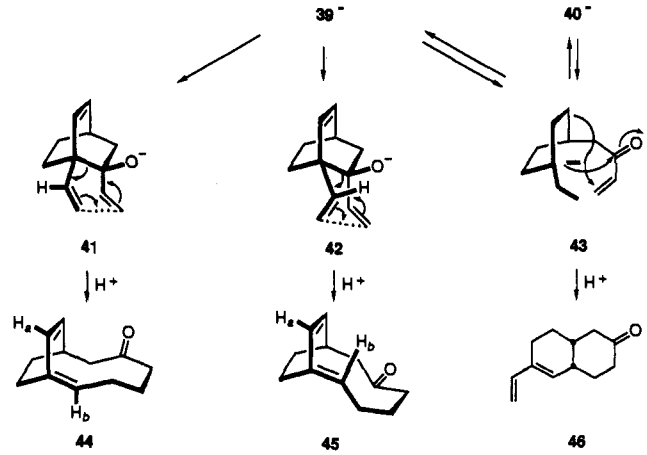
An Anionic Oxy-Cope Variant. The mechanistic model advanced above adumbrates the likelihood that a charge-accelerated variant might well be interrupted after the Cope-1 stage. The basis for this conclusion is depicted in Scheme 8. Once alkoxide **34** is generated, the usual driving force[21] for kinetically enhanced [3,3] sigmatropy[22] should become available to generate **35**. A major underlying driving force to the facile operation of this rearrangement is the significantly enhanced thermodynamic stability of a resonance-stabilized enolate anion, viz. **35**, relative to a harder alkoxide, e.g., **34**. Conventional isomerization of **35** to **36** cannot be considered probable since the accrued stabilization would necessarily be sacrificed. Stated differently, the independent generation of **36** would be expected to eventuate in rapid conversion to **35** via a Cope transition state!

While this conclusion was perceived as valid, we were aware of the possibility that recourse to charge acceleration might make available alternative reaction pathways not encountered during processes driven solely by thermal activation.[23] The possible operation of other competing transformations further stimulated our interest in this line of mechanistic inquiry.

Scheme 9



Scheme 10



For this purpose, it was necessary to obtain ketone **38**. This intermediate was prepared by saponification of **4** and oxygenative degradation of the derived carboxylate dianion (Scheme 9).[24] Addition of vinylmagnesium bromide[25] to **38** afforded **39** (46%) and **40** (43%) as chromatographically separable colorless oils. These stereoisomers were readily distinguished on the basis of NOE measurements.

The endo orientation of the vinyl substituent in **39** was expected to provide a forum for operation of the chairlike transition state **42** and ultimate delivery of ketone **45** following protonation (Scheme 10). Beyond that, passage through the boatlike conformation **41** was presupposed to be energetically accessible as well. Should this pathway be utilized, its involvement would be recognized by formation of the *Z*-dienone **44**. As a third option, complete bond heterolysis[23] within **39**⁻ could deliver the pentadienyl anion **43**, thereby setting the stage for the possible formation of ketone **46** in addition to possible isomerization to **40**⁻.

When **39** was treated with excess ethylmagnesium bromide in THF at room temperature for 4 days, ketone **45** was produced as the exclusive rearrangement product (expt 1, Table 1). Mechanistic cogency requires that this impressive selectivity be reflective of a strong kinetic bias on the part of **39**⁻ for adoption of transition state **42**, at least when significant ion pairing operates. As the "nakedness" of the alkoxide ion is progressively heightened through utilization of sodium hydride and then potassium hydride as base (expts 2 and 3), increasing amounts of **46** begin to make their appearance. Maximum charge buildup on alkoxide oxygen

(21) (a) Evans, D. A.; Baillargeon, D. J. *Tetrahedron Lett.* **1978**, 3315; 3319. (b) Steigerwald, M. L.; Goddard, W. A., III; Evans, D. A. *J. Am. Chem. Soc.* **1979**, *101*, 1994. (c) Carpenter, B. K. *Tetrahedron* **1978**, *34*, 1877. (d) Ahlgren, G. *Tetrahedron Lett.* **1979**, 915. (e) Rozeboom, M. D.; Kiplinger, J. P.; Bartmess, J. E. *J. Am. Chem. Soc.* **1984**, *106*, 1025. (f) Dewar, M. J. S.; Xie, C. *J. Am. Chem. Soc.* **1987**, *109*, 5893.

(22) Evans, D. A.; Golob, A. M. *J. Am. Chem. Soc.* **1975**, *97*, 4765.

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

(24) (a) Wasserman, H. H.; Lipshutz, B. H. *Tetrahedron Lett.* **1975**, 4611. (b) Adam, W.; Cueto, O.; Ehrig, V. *J. Org. Chem.* **1976**, *41*, 370. (c) Konen, D. A.; Silbert, L. S.; Pfeffer, P. E. *J. Org. Chem.* **1975**, *40*, 3253.

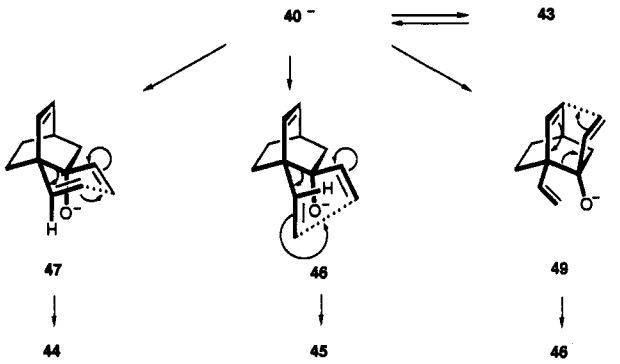
(25) Fieser, L. F.; Fieser, M. *Reagents for Organic Synthesis*; John Wiley and Sons, Inc.: New York, 1967; Vol. I, p 584.

Table 1. Anionic Rearrangements of 39 and 40[a]

expt	substrate	base	reaction time	product distribution 44	45	46
1	39	excess C_2H_5MgBr, THF	4 days	0	100	0
2	39	excess NaH, THF	3 h	0	30	1
3	39	excess KH, THF	40 min	0	2.5	1
4	39	excess KH, 18-cr-6	2 min	1	2.2	3.5
5	40	excess C_2H_5MgBr, THF	4 days	16.5	0	1
6	40	excess NaH, THF	2.5 h	1.4	1	2.6
7	40	excess KH, THF	15 min	1	1.5	7.7
8	40	excess KH, 18-cr-6	2 min	2.5	1	6.4

[a] All reactions performed at room temperature with yields ranging from 68 to 93%.

Scheme 11



is achieved when 18-crown-6 is added to sequester the potassium counterion. Under these circumstances (expt 4), 39⁻ is transformed into a 1:2.2:3.5 mixture of 44, 45, and 46. Quite obviously, the extent of intramolecular competition increases in proportion to the degree to which negative charge is concentrated on the oxygen atom.

The configurational relationships present in 40⁻ potentially allow for the operation of transition states 47–49 in addition to bond fragmentation that would give rise to 43 (Scheme 11). Similar probe experiments performed on this epimer (Table 1) showed first that the bromomagnesium salt in this instance isomerized predominantly, although not exclusively, to 44 (expt 5). A modest amount of 46 was detected as well (ratio 16.5:1). Under conditions where sodium hydride served as the base (expt 6), ketone 45 also surfaced. The product compositions observed in the presence of potassium hydride, with and without added 18-crown-6 (expts 7 and 8), were dominated by elevated proportions of 46. Consequently, as the oxido ion in 39⁻ and 40⁻ is made increasingly independent of the cation, the predilection for ring cleavage to generate 43 increases, as seen earlier in structurally related anions.[23] The source of 46 from the direction of 40⁻ could also reside in the boat-like transition state 49, although this is considered less likely. In this connection, 39-MgBr is seen *not* to fragment to 43 during 4 days at room temperature. Although it is likely that 40⁻ is equally recalcitrant to such C–C bond heterolysis, this conclusion has not been substantiated. Indeed, if this were not the case, then the 16.5:1 product ratio observed in expt 5 should be regarded as the lower limit of partitioning between the reaction channels mediated by 47 and 49.

The structural assignments to ketones 44 and 45 conform to the NOE effects, or lack thereof, exhibited by their olefinic protons. The differing interrelationships of H_a to H_b are particularly diagnostic. In 45, the spatial proximity of these hydrogen atoms gives rise to a 1.6% integral enhancement. Their distal arrangement in 44 is sufficient to reveal no interaction at all.

We conclude on the basis of our analysis of the reaction profiles of 6, 14, and 21 that a strong kinetic preference exists for initial [3,3] sigmatropic rearrangement (the Cope-1 phase) via a chairlike arrangement involving exclusively the pair of vinyl groups external to the bicyclic framework. For the future, guidance is now available on the predictability of related intramolecularly competitive thermal processes. Once intermediates such as 7, 20, and 22 are accessed, a second [3,3] sigmatropic event (the Cope-2 phase) operates more rapidly than the first, thereby precluding the buildup of a detectable concentration of this triene in the reaction mixture. The kinetic acceleration is attributed to the release of strain energy. In a system such as 23, which was designed to undergo electrophilically-induced ring closure beyond the tandem Cope–Cope stage, smooth conversion to 33 was indeed observed. When charge acceleration is incorporated into these systems as it is, for example, in 40⁻, the neighboring C(1)–C(2) bond can become sufficiently weakened to allow other processes to compete effectively. The specific operational mode(s) that is (are) followed is (are) directly linked to the extent of anionic charge that is initially localized on the alkoxide oxygen.

Experimental Section

General Considerations. Melting points were uncorrected. The column chromatographic separations were performed with Woelm silica gel (230–400 mesh). Solvents were reagent grade and in most cases dried prior to use. The purity of all compounds was shown to be >95% by TLC and high-field ^1H NMR (300 MHz) and ^{13}C NMR (75 MHz). The high-resolution, chemical ionization, and fast-atom-bombardment mass spectra were obtained at The Ohio State University Campus Chemical Instrumentation Center. Elemental analyses were performed at the Scandinavian Microanalytical Laboratory, Herlev, Denmark.

Methyl (1*R,2*R**,4*R**,6*S**)-6-Bromo-5-oxo-1-vinylbicyclo[2.2.2]octane-2-carboxylate (2).** To an LDA solution prepared at 0 °C from diisopropylamine (9 mL, 64.3 mmol) and 1.6 M *n*-butyllithium in hexanes (34.3 mL, 54.8 mmol) in dry THF (200 mL) was slowly added at −78 °C a solution of 1[5] (10.3 g, 49.5 mmol) in dry THF (80 mL) over a 1-h period. At the end of the addition, the yellow reaction mixture was stirred for an additional 15 min, and TMSCl (8.8 mL, 69.3 mmol, freshly distilled from $N(n\text{-}Bu)_3$) was added to the vigorously stirred mixture at −78 °C. After 1 h of being stirred at −78 °C, the reaction mixture was allowed to warm to 0 °C and transferred via cannula into a dry 1-L flask, concentrated in vacuo, taken up in pentane, filtered, and concentrated in vacuo. The last three operations were repeated until all of the amine hydrochloride had been removed. The resulting crude silyl enol ether was taken up in dry THF (150 mL) along with propylene oxide (5 mL, 74.2 mmol) and cooled to −78 °C under N_2. Freshly recrystallized *N*-bromosuccinimide (9.7 g, 54.5 mmol) was added to this vigorously stirred solution. The reaction mixture was stirred for 35 min at 0 °C and quenched by inverse addition to a saturated $NaHCO_3$ solution (200 mL). The aqueous layer was extracted several times with ether. The combined organic extracts were washed with brine (200 mL), dried, and concentrated in vacuo. The crude product was crystallized from a 9:1 mixture of petroleum ether and ether to give 11.4 g (80%) of 2 as colorless crystals: mp 71–73 °C; IR ($CHCl_3$, cm^{-1}) 1745, 1640, 1480, 1450, 1440, 1360, 1210, 1170, 1060, 930; ^1H NMR (300 MHz, $CDCl_3$) δ 5.72 (dd, *J* = 17.5, 11 Hz, 1 H), 5.17 (d, *J* = 11 Hz, 1 H), 5.07 (d, *J* = 17.5 Hz, 1 H), 4.96 (d, *J* = 2 Hz, 1 H), 3.62 (s, 3 H), 2.93 (dd, *J* = 11, 6 Hz, 1 H), 2.50 (quint, *J* = 3 Hz, 1 H), 2.18–1.79 (series of m, 5 H), 1.65 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.5, 174.2, 139.0, 115.9, 52.6, 51.8, 46.2, 45.2, 41.4, 27.4, 25.2, 22.1; MS *m/z* (M^+) calcd 286.0204, obsd 286.0206.

Anal. Calcd for $C_{12}H_{15}O_3Br$: C, 50.19; H, 5.27. Found: C, 50.26; H, 5.28.

Methyl (1*R,2*R**,4*R**,5*R**,6*S**)-6-Bromo-5-hydroxy-1-vinylbicyclo-[2.2.2]octane-2-carboxylate (3).** To a cold (5 °C), magnetically stirred solution of 2 (15 g, 52.4 mmol) in absolute ethanol (400 mL) was added sodium borohydride (2.2 g, 57.7 mmol) in six small portions. After 3 h, the reaction mixture was carefully quenched by slow addition of saturated NH_4Cl solution and extracted with several portions of ether. The combined organic phases were washed with brine (200 mL), dried, and concentrated in vacuo to give 14 g (93%) of the desired bromohydrin as a white solid, mp 49–50 °C. This material was used in subsequent reactions without further purification. An analytically pure sample was obtained by MPLC on silica gel (elution with 9% dichloromethane and 22% ethyl acetate in petroleum ether): IR ($CHCl_3$, cm^{-1}) 3550, 1730, 1640, 1440, 1375, 1200, 1180, 1080, 930; ^1H NMR (300 MHz, $CDCl_3$) δ 5.69 (dd, *J* = 17, 10 Hz, 1 H), 5.15 (dd, *J* = 8, 2 Hz, 1 H), 5.09 (dd, *J* = 10, 0.7 Hz, 1 H), 5.00 (dd, *J* = 17, 0.7 Hz, 1 H), 4.01 (ddd, *J* = 8, 3, 1 Hz, 1 H), 3.64 (s, 3 H), 2.70 (dd, *J* = 10, 7 Hz, 1 H), 2.34 (br s, 1 H), 2.08–1.85 (series of m, 4 H), 1.73 (m, 1 H), 1.38 (m, 2 H); ^{13}C NMR (75 MHz,

$CDCl_3$) δ 175.2, 141.3, 114.7, 67.2, 63.3, 51.6, 47.2, 41.7, 31.6, 27.9, 24.7, 18.1; CI MS *m/z* ($M^+ + 1$) calcd 289.05, obsd 289.08.

Anal. Calcd for $C_{12}H_{17}O_3Br$: C, 49.84; H, 5.93. Found: C, 49.94; H, 5.96.

Methyl (1*R,2*S**,4*S**)-1-Vinylbicyclo[2.2.2]oct-5-ene-2-carboxylate (4).** A vigorously stirred mixture of **3** (7.5 g, 26 mmol) and powdered zinc (7 g) in absolute ethanol (150 mL) was refluxed for 20 h under N_2, cooled to room temperature, diluted with ether (200 mL), and filtered through a pad of Celite, which was subsequently washed thoroughly with ether. The filtrate was carefully concentrated in vacuo and chromatographed over 60 g of silica gel (elution with 10% ether in petroleum ether) to give 4.7 g (94%) of **4** as an odoriferous, volatile, colorless oil: IR (neat, cm^{-1}) 1745, 1635, 1430,1350, 1250, 1150, 1000, 900; ^1H NMR (300 MHz, $CDCl_3$) δ 6.36 (dd, *J* = 8, 6.6 Hz, 1 H), 6.21 (d, *J* = 8 Hz, 1 H), 5.99 (dd, *J* = 17.6, 10.8 Hz, 1 H), 5.12 (dd, *J* = 17.6, 1 Hz, 1 H), 5.07 (dd, *J* = 10.8, 1 Hz, 1 H), 3.54 (s, 3 H), 2.62 (m, 2 H), 1.89 (ddd, *J* = 13, 9.7, 2.7 Hz, 1 H), 1.60–1.44 (series of m, 3 H), 1.30 (m, 1 H), 1.17 (dd, *J* = 12, 7.3 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.4, 142.4, 133.6, 132.7, 113.1, 51.1, 48.2, 41.6, 33.1, 32.9, 30.1, 25.1; MS *m/z* (M^+) calcd 192.1150, obsd 192.1150.

Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 74.82; H, 8.47.

(1*R,2*S**,4*S**)-1-Vinylbicyclo[2.2.2]oct-5-ene-2-carboxaldehyde (5).** To a magnetically stirred suspension of lithium aluminum hydride (680 mg, 17.9 mmol) in dry ether (50 mL) at 0 °C was added a solution of **4** (3.37 g, 17.5 mmol) in dry ether (20 mL). The reaction mixture was stirred for 4 h at 0 °C and subsequently quenched at 0 °C according to the Fieser and Fieser procedure.[25] The resulting white solids were filtered, and the filtrate was concentrated in vacuo to afford 2.67 g (93%) of the alcohol as a colorless oil: IR (neat, cm^{-1}) 3400, 1635, 1605, 1460, 1440, 1410, 1375, 1105, 1065, 1035, 995, 905, 725, 690; ^1H NMR (300 MHz, $CDCl_3$) δ 6.34 (dd, *J* = 8.3, 6.5 Hz, 1 H), 6.20 (d, *J* = 8.4 Hz, 1 H), 6.00 (dd, *J* = 17.7, 10.8 Hz, 1 H), 5.20 (dd, *J* = 17.7, 1.1 Hz, 1 H), 5.13 (dd, *J* = 10.8, 1.1 Hz, 1 H), 3.45 (dd, *J* = 10.9, 5.8 Hz, 1 H), 3.11 (dd, *J* = 10.9, 6 Hz, 1 H), 2.56 (m, 1 H), 1.79 (series of m, 2 H), 1.55 (series of m, 3 H), 1.31 (m, 1 H), 1.10 (series of m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.8, 135.0, 131.5, 112.6, 66.9, 45.5, 41.8, 33.9, 31.7, 30.6, 26.1; MS *m/z* (M^+) calcd 164.1201, obsd 164.1177.

Anal. Calcd for $C_{11}H_{16}O$: C, 80.44; H, 9.82. Found: C, 80.13; H, 9.82.

To a suspension of pyridinium dichromate (1.38 g, 3.66 mmol) and 3-Å molecular sieves (1.5 g) in CH_2Cl_2 (60 mL) at 0 °C was added a solution of the above alcohol (300 mg, 1.83 mmol) in CH_2Cl_2 (25 mL). The reaction mixture was stirred at 0 °C for 3 h and at room temperature for 10 h, concentrated in vacuo, taken up in a 10% ether in petroleum ether solution, poured onto a Florisil column, and chromatographed (elution with 10% ether in petroleum ether) to give 250 mg (84%) of **5** as a colorless liquid, which should be stored as a benzene solution to preclude decomposition: IR ($CHCl_3$, cm^{-1}) 1725, 1640, 1450, 1420, 1380, 1000, 920, 700; ^1H NMR (300 MHz, C_6D_6) δ 9.26 (d, *J* = 3 Hz, 1 H), 6.12 (dd, *J* = 8.3, 8 Hz, 1 H), 6.01 (d, *J* = 8.3 Hz, 1 H), 5.81 (dd, *J* = 17.7, 10.8 Hz, 1 H), 5.03 (m, 2 H), 2.26 (m, 1 H), 2.17 (m, 1 H), 1.52 (m, 1 H), 1.30 (m, 3 H), 1.04 (m, 2 H); ^{13}C NMR (75 MHz, C_6D_6) δ 202.2, 142.2, 135.9, 132.1, 114.1, 55.3, 41.4, 33.1, 30.5, 28.2, 26.3; MS *m/z* (M^+) calcd 162.1045, obsd 162.1035.

(1*R,4*S**,6*R**)-1,6-Divinylbicyclo[2.2.2]oct-2-ene (6).** To a suspension of methyltriphenylphosphonium bromide (1.98 g, 5.55 mmol) in dry THF (40 mL) was added a solution of *n*-butyllithium (2.9 mL of a 1.6 M solution in hexanes) at 0 °C under N_2. The resulting yellow slurry was stirred for 1 h at 0 °C and for 1 h at room temperature prior to being treated with a solution of **5** (250 mg, 1.54 mmol) in dry THF (10 mL). After 2 h of being stirred at 0 °C, the reaction mixture was quenched with water (20 mL), and the aqueous phase was extracted with ether (5 × 50 mL). The combined organic layers were dried and concentrated carefully in vacuo to leave a residue which was purified by twofold chromatography on Florisil (elution with petroleum ether). There was obtained 151 mg (61%) of **6** as a volatile, colorless oil: IR (neat, cm^{-1}) 1637, 1610, 1464, 1450, 1418, 994, 908, 697; ^1H NMR (300 MHz, C_6D_6) δ 6.22 (dd, *J* = 8.4, 6.6 Hz, 1 H), 6.12 (br d, *J* = 8.4 Hz, 1 H), 5.94 (dd, *J* = 17.7, 10.3 Hz, 1 H), 5.45 (ddd, *J* = 17, 13, 9 Hz, 1 H), 5.07 (m, 2 H), 4.84 (m, 2 H), 2.32 (m, 1 H), 2.10 (ddd, *J* = 9.5, 9.5, 4.5 Hz, 1 H), 1.73 (ddd, *J* = 12, 11.2, 2.5 Hz, 1 H), 1.50–1.05 (series of m, 5 H); ^{13}C NMR (75 MHz, C_6D_6) δ 144.4, 143.7, 134.6, 133.5, 113.4, 112.5, 48.8, 42.8, 35.2, 32.9, 30.9, 26.3; MS *m/z* (M^+) calcd 160.1252, obsd 160.1250.

Anal. Calcd for $C_{12}H_{16}$: C, 89.94; H, 10.06. Found: C, 89.95; H, 10.45.

(1*R,8a*S**)-1,2,3,5,6,8a-Hexahydro-1-vinylnaphthalene (8).** A solution of **6** (15 mg, 0.093 mmol) in chlorobenzene-d_5 (1.5 mL) was heated in a sealed tube to 220 °C for 20 h. ^1H NMR analysis showed formation of only **8**: ^1H NMR (300 MHz, C_6D_5Cl) δ 5.96 (ddd, *J* = 17, 10, 9 Hz, 1 H), 5.81 (m, 1 H), 5.53 (br d, 1 H), 5.49 (m, 1 H), 5.20 (ddd, *J* = 17, 2, 1 Hz, 1 H), 5.12 (ddd, *J* = 10, 2, 0.7 Hz, 1 H), 3.04 (m, 1 H), 2.58 (ddd, *J* = 9, 4, 3 Hz, 1 H), 2.36–2.27 (m, 2 H), 2.26–2.10 (series of m, 3 H), 2.07–1.95 (br d, *J* = 17 Hz, 1 H), 1.84 (m, 2 H); ^{13}C NMR (75 MHz, C_6D_5Cl) δ 139.1, 136.0, 130.2, 126.5, 120.0, 114.7, 41.5, 39.5, 31.9, 28.7, 27.1, 21.7; MS *m/z* (M^+) calcd 160.1252, obsd 160.1251.

(1*R,2*S**,4*S**)-1-Vinylbicyclo[2.2.2]oct-5-ene-2-carboxaldehyde-*formyl-d* (5-d_1).** To a cold (0 °C), magnetically stirred suspension of lithium aluminum deuteride (0.81g, 19.3 mmol) in dry ether (50 mL) was slowly added a solution of **4** (0.7 g, 3.64 mmol) in ether (20 mL). After 1 h at 0 °C, the reaction mixture was quenched according to the Fieser and Fieser procedure.[25] The resulting solids were filtered and rinsed thoroughly with ether. The filtrate was concentrated in vacuo to afford 550 mg (91%) of the dideuterated alcohol as a colorless oil: IR (neat, cm^{-1}) 3500, 1640, 1450, 1420, 1380, 1190, 1130, 1110, 970, 700; ^2H NMR (46 MHz, C_6D_6) δ 3.42, 2.98; ^1H NMR (300 MHz, C_6D_6) δ 6.17 (dd, *J* = 8.3, 6.5 Hz, 1 H), 6.09 (d, *J* = 8.3 Hz, 1 H), 5.86 (dd, *J* = 17.7, 10.8 Hz, 1 H), 5.05 (dd, *J* = 17.7, 1.1 Hz, 1 H), 4.99 (dd, *J* = 10.8, 1.1 Hz, 1 H), 2.32 (m, 1 H), 1.70–1.56 (m, 2 H), 1.49 (br s, 1 H), 1.44–1.29 (m, 2 H), 1.28–0.99 (m, 3 H); ^{13}C NMR (75 MHz, C_6D_6) δ 144.1, 134.8, 132.1, 112.4, 66.02 (quint, $^1J_{C,D}$ = 20 Hz), 45.8, 42.0, 34.2, 31.7, 31.0, 26.5; MS *m/z* (M^+) calcd 166.1327, obsd 166.1330.

To a suspension of pyridinium dichromate (458 mg, 1.22 mmol) and 4-Å molecular sieves (500 mg) in CH_2Cl_2 (30 mL) at 0 °C was added a solution of the above alcohol (100 mg, 0.61 mmol) in CH_2Cl_2 (5 mL). The reaction mixture was stirred at 0 °C for 6 h and at room temperature for 10 h prior to concentration in vacuo. The residue was taken up in 10% ether in petroleum ether, poured on a Florisil column, and chromatographed (elution with 10% ether in petroleum ether) to give 77 mg (78%) of **5**-d_1: IR (neat, cm^{-1}) 1710, 1640, 1452, 1420, 1379, 1180, 1121, 1076, 1027, 998, 964, 913, 696, 671; ^2H NMR (46 MHz, C_6D_6) δ 9.26; ^1H NMR (300 MHz, C_6D_6) δ 6.12 (dd, *J* = 8.3, 6.7 Hz, 1 H), 6.01 (d, *J* = 8.3 Hz, 1 H), 5.81 (dd, *J* = 17.7, 10.8 Hz, 1 H), 5.03 (m, 2 H), 2.24 (m, 1 H), 2.15 (dd, *J* = 9.7, 4.5 Hz, 1 H), 1.54 (dm, *J* = 13 Hz, 1 H), 1.28 (m, 3 H), 1.00 (m, 2 H); ^{13}C NMR (75 MHz, C_6D_6) δ 201.9 (t, $^1J_{C,D}$ = 27 Hz), 142.2, 135.9, 132.1, 114.1, 55.1 (t, $^2J_{C,D}$ = 3 Hz), 41.3, 33.1, 30.5, 28.1, 26.2; MS *m/z* (M^+) calcd 163.1107, obsd 163.1111.

(1*R,4*S**,6*R**)-1-Vinyl-6-(vinyl-*1-d*)bicyclo[2.2.2]oct-2-ene (6-d_1).** To a suspension of methyltriphenylphosphonium bromide (420 mg, 1.18 mmol) in dry THF (20 mL) was added a solution of *n*-butyllithium (0.39 mL of a 2.5 M solution in hexanes) at 0 °C under N_2. The resulting yellow slurry was stirred for 3 h at 0 °C. To this mixture was added a solution of **5**-d_1 (77 mg, 0.47 mmol) in dry THF (3 mL). After 2 h of being stirred at 0 °C, the resulting reaction mixture was quenched with water (5 mL), the aqueous layer was extracted with ether (3 × 50 mL), and the combined organic layers were dried and concentrated carefully in vacuo. The resulting liquid was purified by twofold chromatography on Florisil (elution with petroleum ether) to afford 35 mg (46%) of **6**-d_1: IR (neat, cm^{-1}) 1630, 910, 697; ^2H NMR (46 MHz, C_6D_6) δ 5.82; ^1H NMR (300 MHz, C_6D_6) δ 6.22 (dd, *J* = 8.3, 6.6 Hz, 1 H), 6.12 (br d, *J* = 8.3 Hz, 1 H), 5.94 (dd, *J* = 17.7, 10.5 Hz, 1 H), 5.07 (m, 2 H), 4.85 (m, 2 H), 2.30 (m, 1 H), 2.10 (dd, *J* = 9.3, 4.3 Hz, 1 H), 1.72 (ddd, *J* = 12.6, 9.6, 2.5 Hz, 1 H), 1.46–1.05 (series of m, 5 H); ^{13}C NMR (75 MHz, C_6D_6) δ 144.5, 143.4 (t, $^1J_{C,D}$ = 20 Hz), 134.6, 133.4, 113.2, 112.5, 48.7, 42.8, 35.1, 32.9, 30.9, 26.3; MS *m/z* (M^+) calcd 161.1315, obsd 161.1315.

(1*R,8a*S**)-1,2,3,5,6,8a-Hexahydro-1-vinylnaphthalene-*1-d* (8-d_1).** A solution of **6**-d_1 (25 mg, 0.093 mmol) in chlorobenzene-d_5 (1.5 mL) was heated in a sealed tube to 200 °C for 20 h. ^1H NMR analysis of the solution showed formation of only **8**-d_1; ^1H NMR (300 MHz, C_6D_5Cl) δ 5.96 (dd, *J* = 17, 10 Hz, 1 H), 5.82 (m, 1 H), 5.53 (br d, *J* = 8 Hz, 1 H), 5.50 (m, 1 H), 5.21 (dd, *J* = 17, 2.2 Hz, 1 H), 5.13 (dd, *J* = 10, 2.2 Hz, 1 H), 3.04 (m, 1 H), 2.36–2.28 (m, 2 H), 2.28–2.10 (series of m, 3 H), 2.04–1.97 (br d, *J* = 17 Hz, 1 H), 1.83 (dd, *J* = 9, 4.1 Hz, 2 H); ^{13}C NMR (75 MHz, C_6D_5Cl) δ 139.1, 136.0, 130.2, 126.5, 120.0, 114.7, 41.0 (t, $^1J_{C,D}$ = 20 Hz), 39.4, 31.9, 28.6, 27.1, 21.7; MS *m/z* (M^+) calcd 161.1315, obsd 161.1310.

Methyl (1*R,2*S**,4*S**)-5-methoxy-1-vinylbicyclo[2.2.2]oct-5-ene-2-carboxylate (10).** To a solution of **1** (4.45 g, 21.4 mmol) and dry HMPA (7.45 mL, 43 mmol) in THF (200 mL) was slowly added at −78 °C a solution of potassium hexamethyldisilazide (55 mL of a 0.47 M solution in toluene). After 30 min of being stirred at −78 °C, the reaction mixture

was treated with methyl triflate (6 mL, 53 mmol), stirred for an additional 30 min, allowed to warm to room temperature, and concentrated in vacuo. The residue was taken up in 10% ether in petroleum ether (50 mL), poured onto a Florisil column, and chromatographed directly (elution with 10% ether and 2% triethylamine in petroleum ether) to give 3.1 g (65%) of **10** as a colorless oil: IR (neat, cm^{-1}) 1745, 1650, 1640, 1470, 1455, 1440, 1385, 1360, 1325, 1265, 1230, 1205, 1170, 1095, 1065, 1035, 1000, 920; ^1H NMR (300 MHz, C_6D_6) δ 6.20 (dd, J = 17.6, 11 Hz, 1 H), 5.20 (dd, J = 17.6, 1 Hz, 1 H), 5.14 (dd, J = 11, 1 Hz, 1 H), 4.91 (d, J = 2 Hz, 1 H), 3.37 (s, 3 H), 3.35 (s, 3 H), 2.57 (m, 1 H), 2.54 (dd, J = 10, 5.6 Hz, 1 H), 1.92 (m, 1 H), 1.88 (m, 1 H), 1.62 (ddd, J = 12, 10, 2.7 Hz, 1 H), 1.49–1.21 (series of m, 3 H); ^{13}C NMR (75 MHz, C_6D_6) δ 174.5, 161.9, 143.7, 112.5, 94.6, 54.2, 50.6, 49.3, 43.6, 35.1, 34.8, 32.7, 25.5; MS m/z (M^+) calcd 222.1256, obsd 222.1261.

Anal. Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16. Found: C, 70.29; H, 8.10.

(1*R,2*R**,4*R**)-5-Methoxy-1-vinylbicyclo[2.2.2]oct-5-ene-2-methanol (11).** To a suspension of lithium aluminum hydride (380 mg, 10 mmol) in dry ether (40 mL) was added at 0 °C a solution of **10** (1 g, 4.5 mmol) in dry ether (20 mL). After 2 h at 0 °C, the reaction mixture was carefully quenched by the addition of water (0.4 mL) followed by 2 N NaOH solution (0.4 mL) and distilled water (1.2 mL). The resulting solids were filtered and the organic layer was concentrated in vacuo to afford 0.81 g (92%) of **11** as a colorless oil which was used without further purification. An analytical sample was prepared by chromatography on Florisil: IR (neat, cm^{-1}) 3500, 1650, 1535, 1460, 1380, 1260, 1225, 1140, 1035, 910, 860, 775; ^1H NMR (300 MHz, C_6D_6) δ 5.93 (dd, J = 17.6, 11 Hz, 1 H), 5.08 (dd, J = 17.6, 1.5 Hz, 1 H), 5.03 (dd, J = 11, 1.5 Hz, 1 H), 4.68 (d, J = 2 Hz, 1 H), 3.54 (dd, J = 10.6, 5.5 Hz, 1 H), 3.21 (s, 3 H), 3.14 (dd, J = 10.6, 6.7 Hz, 1 H), 2.47 (m, 1 H), 1.67 (m, 1 H), 1.57 (ddd, J = 12, 10, 2.5 Hz, 1 H), 1.46–1.14 (series of m, 6 H); ^{13}C NMR (75 MHz, C_6D_6) δ 163.0, 144.7, 112.0, 93.1, 66.8, 54.0, 46.6, 42.9, 35.9, 35.3, 32.0, 26.5; MS m/z (M^+) calcd 194.1307, obsd 194.1301.

Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 74.25; H, 9.34.

(1*R,2*S**,4*S**)-5-Methoxy-1-vinylbicyclo[2.2.2]oct-5-ene-2-carboxaldehyde (12) and (1*R**,3*R**,6*R**,8*R**)-3-Methoxy-1-vinyl-4-oxatricyclo-[4.4.0.0^{3,8}]decane (13).** To a suspension of pyridinium dichromate (776 mg, 2.06 mmol) and 4-Å molecular sieves (1 g) in CH_2Cl_2 (30 mL) was slowly added a solution of **11** (200 mg, 1.03 mmol) in CH_2Cl_2 (10 mL) at 0 °C. The resulting brown reaction mixture was stirred for 5 h at 0 °C, subsequently diluted with a mixture of 10% ether and 2% triethylamine in petroleum ether, and filtered over a small pad of Celite. The filtrate was carefully concentrated in vacuo. Chromatography of the residue on Florisil (elution with 10% ether in petroleum ether) afforded 123 mg (62%) of **12** as a colorless oil, which decomposes readily if not stored as a benzene solution, and 62 mg (31%) of **13**.

For **12**: IR (neat, cm^{-1}) 1725, 1635, 1625, 1460, 1380, 1340, 1220, 1110, 1005, 905; ^1H NMR (300 MHz, C_6D_6) δ 9.45 (d, J = 2.7 Hz, 1 H), 5.95 (dd, J = 17.7, 10 Hz, 1 H), 5.11 (m, 2 H), 4.67 (d, J = 2 Hz, 1 H), 3.20 (s, 3 H), 2.49 (m, 1 H), 2.19 (m, 1 H), 1.89 (m, 1 H), 1.44–1.10 (series of m, 5 H); ^{13}C NMR (75 MHz, C_6D_6) δ 202.7, 163.8, 142.9, 113.8, 93.5, 55.9, 54.2, 42.7, 35.0, 34.8, 28.0, 26.5; MS m/z (M^+) calcd 192.1150, obsd 192.1151.

For **13**: IR (neat, cm^{-1}) 1640, 1460, 1340, 1160, 1110, 1010, 905; ^1H NMR (300 MHz, C_6D_6) δ 5.64 (dd, J = 17.4, 10.7 Hz, 1 H), 4.88 (dd, J = 10.7, 1 Hz, 1 H), 4.82 (dd, J = 17.4, 1 Hz, 1 H), 3.87 (dd, J = 9, 1.6 Hz, 1 H), 3.57 (dd, J = 9, 2.9 Hz, 1 H), 3.26 (s, 3 H), 2.09 (m, 1 H), 2.00 (dm, J = 12 Hz, 1 H), 1.60 (m, 2 H), 1.51 (m, 1 H), 1.25 (m, 5 H); ^{13}C NMR (75 MHz, C_6D_6) δ 143.8, 110.9, 102.4, 67.5, 48.6, 37.9, 37.9, 37.2, 35.7, 29.3, 28.3, 23.0; MS m/z (M^+) calcd 194.1307, obsd 194.1311.

Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 74.22; H, 9.46.

(1*R,4*R**,6*S**)-3-Methoxy-1,6-divinylbicyclo[2.2.2]oct-2-ene (14).** To a suspension of methyltriphenylphosphonium bromide (1.67 g, 4.69 mmol) in dry THF (40 mL) was added a solution of 1.6 M n-butyllithium in hexanes (2.5 mL, 3.9 mmol) at 0 °C. The resulting yellow slurry was stirred at 0 °C for 1 h and at room temperature for 1 h, returned to 0 °C, and treated with a solution of **12** (250 mg, 1.3 mmol) in dry THF (10 mL). The reaction mixture was stirred for 2.5 h at 0 °C, diluted with petroleum ether, filtered over a pad of basic Al_2O_3 (Type I), washed thoroughly with dry pentane, and carefully concentrated in vacuo. The product was chromatographed (Florisil, elution with 1% triethylamine in petroleum ether) to give 181 mg (73%) of **14** as a colorless oil: IR (neat, cm^{-1}) 1631, 1450, 1417, 1376, 1259, 1220, 1153, 1080, 995, 907, 866, 774; ^1H NMR (300 MHz, C_6D_6) δ 6.01 (dd, J = 17.8, 10.5 Hz, 1 H), 5.58 (ddd, J = 17, 10.2, 9.2 Hz, 1 H), 5.10 (m, 2 H), 4.87 (m, 2 H), 4.70 (d, J = 1 Hz, 1 H), 3.24 (s, 3 H), 2.48 (m, 1 H), 2.09 (ddd, J = 10, 9.5, 4.6 Hz, 1 H), 1.70 (ddd, J = 12, 11, 2.6 Hz, 1 H), 1.50–1.26 (series of m, 5 H); ^{13}C NMR (75 MHz, C_6D_6) δ 162.6, 145.1, 143.8, 113.3, 112.0, 94.5, 54.1, 49.6, 43.7, 35.3, 35.1, 34.6, 26.3; MS m/z (M^+) calcd 190.1358, obsd 190.1360.

(1*R,8a*S**)-1,2,3,5,6,8a-Hexahydro-8-methoxy-1-vinylnaphthalene (15).** A solution of **14** (25 mg, 0.131 mmol) in chlorobenzene-d_5 (1.5 mL) was heated in a sealed tube to 210 °C for 20 h. ^1H NMR analysis of the reaction mixture showed formation of **15**. The crude mixture was purified by flash chromatography on Florisil (elution with petroleum ether) to give 15 mg (60%) of **15** as a colorless oil along with 6 mg (24%) of ketone **16**.

For **15**: IR (neat, cm^{-1}) 1677, 1658, 1436, 1359, 1225, 1203, 1166, 1152, 1033, 910; ^1H NMR (300 MHz, C_6D_6) δ 5.95 (ddd, J = 17.5, 10, 8 Hz, 1 H), 5.38 (m, 1 H), 5.19 (ddd, J = 17.5, 2, 1 Hz, 1 H), 5.06 (ddd, J = 10, 2, 1 Hz, 1 H), 4.62 (ddd, J = 5, 5, 1 Hz, 1 H), 3.22 (s, 3 H), 3.11 (m, 1 H), 3.08 (m, 1 H), 2.14 (m, 2 H), 2.09 (m, 2 H), 2.10–1.75 (m, 2 H), 1.75–1.61 (m, 2 H); ^{13}C NMR (75 MHz, C_6D_6) δ 156.0, 138.5, 135.7, 121.0, 115.0, 94.8, 53.8, 42.8, 38.6, 32.9, 28.4, 24.6, 21.7; MS m/z (M^+) calcd 190.1358, obsd 190.1370.

Anal. Calcd for $C_{13}H_{18}O$: C, 82.06; H, 9.53. Found: C, 81.47; H, 9.69.

For **3,4,5,6,7,8-hexahydro-8-vinyl-1(2*H*)-naphthalenone (16)**: IR ($CHCl_3$, cm^{-1}) 1680, 1640, 1420, 1380, 1330, 1260, 1190, 910; ^1H NMR (300 MHz, C_6D_6) δ 5.90 (ddd, J = 17, 11, 6 Hz, 1 H), 5.07 (ddd, J = 10, 2, 1 Hz, 1 H), 4.98 (ddd, J = 17, 2, 1 Hz, 1 H), 3.67 (m, 1 H), 2.17 (m, 2 H), 1.70–1.40 (series of m, 7 H), 1.38–1.20 (m, 3 H); ^{13}C NMR (75 MHz, C_6D_6) δ 195.8, 155.6, 141.3, 133.8, 114.2, 38.4, 34.4, 31.5, 31.4, 27.3, 22.6, 17.7; MS m/z (M^+) calcd 176.1201, obsd 176.1206.

Methyl (1*R,2*S**,4*S**,6*R**)-6-Bromo-1-formyl-5-oxobicyclo[2.2.2]-octane-2-carboxylate (24).** A solution of **2** (3.16 g, 11 mmol) in dry CH_2Cl_2 (60 mL) was treated with ozone (about 0.8 mL/min) at –78 °C until a blue color persisted. The excess ozone was removed by a flow of dry N_2. The reaction mixture was then treated with triphenylphosphine (7 g), allowed to warm slowly to room temperature over 5 h, stirred for 16 h at this temperature, and concentrated in vacuo. The residue was chromatographed on Florisil (elution with petroleum ether followed by 20% ethyl acetate in petroleum ether) to afford 2.85 g (89%) of **24**: IR ($CHCl_3$, cm^{-1}) 1745, 1730, 1455, 1445, 1360, 1340, 1285, 1220, 1185, 1080, 1060, 920; ^1H NMR (300 MHz, C_6D_6) δ 9.62 (s, 1 H), 5.01 (d, J = 2.1 Hz, 1 H), 3.11 (s, 3 H), 2.73 (dd, J = 11.8, 5.8 Hz, 1 H), 2.04 (m, 1 H), 1.83 (ddd, J = 11.2, 4.9, 4.4 Hz, 1 H), 1.62 (m, 1 H), 1.30 (m, 2 H), 1.25 (m, 1 H), 0.99 (m, 1 H); ^{13}C NMR (75 MHz, C_6D_6) δ 204.6, 200.5, 172.8, 52.1, 51.9, 48.4, 43.7, 42.0, 26.0, 22.5, 21.5; MS m/z (M^+) calcd 287.9996, obsd 287.9992.

Anal. Calcd for $C_{11}H_{13}O_4Br$: C, 45.70; H, 4.53. Found: C, 45.68; H, 4.57.

(3a*R,4*R**,6*S**,7a*S**)-4-Bromotetrahydro-5-hydroxy-3*H*-3a,6-ethanoisobenzofuran-1(4*H*)-one (25) and Methyl (1*R**,2*S**,4*S**,6*R**)-6-Bromo-5-hydroxy-1-(hydroxymethyl)bicyclo[2.2.2]octane-2-carboxylate (26).** To a solution of **24** (0.87 g, 3 mmol) in distilled methanol (30 mL) cooled to 0–5 °C was added sodium borohydride (0.22 g, 5.82 mmol) portionwise to guard against overreduction. After 20 min, the reaction mixture was carefully treated with saturated NH_4Cl solution (5 mL) and extracted several times with ether. The combined organic layers were dried and concentrated in vacuo to leave 920 mg of a white waxy solid consisting of an 8:1 mixture of **25** and **26**, which was carried onto the next step without further purification.

For **25**: IR ($CHCl_3$, cm^{-1}) 3400, 1760, 1120, 1000; ^1H NMR (300 MHz, $CDCl_3$) δ 4.43 (br s, 1 H), 4.13 (d, J = 10 Hz, 1 H), 3.98 (d, J = 10 Hz, 1 H), 2.54 (br s, 1 H), 2.17 (m, 2 H), 2.02 (br s, 1 H), 1.96–1.74 (series of m, 5 H), 1.35 (m, 1 H); ^{13}C NMR (62 MHz, $CDCl_3$) δ 176.2, 73.0, 71.7, 34.7, 34.2 (2 C), 29.6 (2 C), 18.6, 18.5; MS m/z (M^+) calcd 260.0048, obsd 260.0019.

(3a*R,6*S**,7a*S**)-7,7a-Dihydro-3*H*-3a,6-ethanoisobenzofuran-1(6*H*)-one (27).** A solution of the **25/26** mixture (2.2 g, 8.5 mmol) and powdered Zn (0.8 g, 12 mmol) in absolute ethanol (90 mL) was refluxed for 22 h and subsequently cooled to room temperature and concentrated in vacuo. The residue was diluted with 20% ethyl acetate in petroleum ether, poured onto a pad of Celite, and washed thoroughly with ether. After concentration of the filtrate, the residual oil was purified by MPLC (elution with 10% ethyl acetate in petroleum ether) to give 877 mg (63%) of **27** as a colorless oil that slowly crystallized and 19 mg (9%) of **28** as a colorless oil.

For **27**: colorless crystals, mp 53–56 °C after sublimation at 70 °C and 1 Torr; IR ($CHCl_3$, cm^{-1}) 1785, 1380, 1360, 1150, 1130, 1080, 1050,

1030, 1000; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.41 (dd, J = 8, 7 Hz, 1 H), 5.96 (d, J = 8 Hz, 1 H), 4.35 (d, J = 8.6 Hz, 1 H), 4.08 (d, J = 8.6 Hz, 1 H), 2.64 (m, 1 H), 2.40 (dd, J = 10.1, 6.4 Hz, 1 H), 1.85 (ddd, J = 13, 11, 3.4 Hz, 1 H), 1.68–1.36 (m, 3 H), 1.35–1.21 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.6, 138.2, 132.3, 75.4, 43.5, 42.7, 29.9, 28.8, 28.6, 22.7; MS m/z (M^+) calcd 164.0837, obsd 164.0814.

Anal. Calcd for $C_{10}H_{12}O_2$: C, 73.15; H, 7.37. Found: C, 73.15, H, 7.34.

For **28**: IR ($CHCl_3$, cm^{-1}) 3400, 1725, 1630, 1465, 1445, 1375, 1350, 1320, 1270, 1170, 1100, 1050, 970, 860, 700; ^{1}H NMR (300 MHz, C_6D_6) δ 6.24 (dd, J = 8.3, 6.7 Hz, 1 H), 5.95 (d, J = 8.3 Hz, 1 H), 3.86 (q, J = 7.1 Hz, 2 H), 3.75 (d, J = 11.3 Hz, 1 H), 3.62 (d, J = 11.1 Hz, 1 H), 2.57 (dd, J = 9.5, 6.0 Hz, 1 H), 2.30 (m, 1 H), 2.15 (m, 1 H), 1.57 (m, 3 H), 1.22 (m, 2 H), 1.04 (m, 1 H), 0.90 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) δ 174.9, 134.5, 132.0, 67.3, 60.2, 44.4, 42.3, 32.3, 30.5, 30.0, 25.4, 14.2; MS m/z (M^+) calcd 210.1556, obsd 210.1252.

(1*R,4*S**,6*R**)-6-Vinylbicyclo[2.2.2]oct-2-ene-1-methanol (29).** To a solution of **27** (46 mg, 0.28 mmol) in CH_2Cl_2 (8 mL) at −78 °C was added a 1.0 M solution of Dibal-H in hexanes (0.3 mL). The resulting cloudy reaction mixture was stirred for 10–15 min at −78 °C, quenched with 10% sodium potassium tartrate solution (10 mL), allowed to warm to room temperature, and stirred until both layers were clear (2–3 h). The aqueous phase was extracted with CH_2Cl_2 (2 × 50 mL), and the combined organic layers were dried and concentrated in vacuo to afford 45 mg (96%) of a colorless oil consisting of a mixture of epimeric lactols (I and II) and the hydroxyaldehyde (III) (ratio of 32.7:21.7:7.4) as an inseparable mixture: IR (neat, cm^{-1}) 3400, 1720, 1190, 1130, 1100, 1070, 1010, 990, 900; ^{1}H NMR (300 MHz, C_6D_6) δ 9.3 (d, J = 4.5 Hz, 1 H (III)), 6.16–5.95 (series of m, 2 H (I, II, III)), 5.19 (dd, J = 8, 5 Hz, 1 H (II)), 4.93 (d, J = 6.8 Hz, 1 H (I)), 4.72 (br s, 1 H (I)), 3.96 (d, J = 8 Hz, 1 H (II)), 3.82 (d, J = 7.8 Hz, 1 H (I)), 3.78 (d, J = 7.8 Hz, 1 H (I)), 3.60 (d, J = 10.7 Hz, 1 H (III)), 3.50 (d, J = 10.7 Hz, 1 H (III)), 3.50 (d, J = 10.7 Hz, 1 H (III)), 3.36 (d, J = 8 Hz, 1 H (II)), 3.00 (d, J = 9 Hz, 1 H (II)), 2.79 (br s, 1 H (III)), 2.39–2.22 (series of m, 1 H (I, II, III)), 1.96 (m, 1 H (I, II)), 1.73 (ddd, J = 12, 11, 3.4 Hz, 1 H (I)), 1.59 (m, 1 H (II, III)), 1.51–0.87 (series of m, 5 H (I, III) + 6 H (II)); ^{13}C NMR (75 MHz, C_6D_6) δ 203.8, 135.9, 135.8, 135.7, 135.6, 135.4, 132.5, 105.1, 97.9, 75.0, 74.6, 66.7, 53.2, 50.0, 46.9, 45.9, 43.6, 42.3, 31.5, 31.1, 30.8, 30.2, 30.1, 29.2, 28.7, 28.6, 27.9, 25.6, 23.9, 23.7; MS m/z (M^+) calcd 166.0994, obsd 166.0994.

To a suspension of predried methyltriphenylphosphonium bromide (1.46 g, 4.1 mmol) in dry THF (45 mL) was added n-butyllithium (2.5 mL of 1.4 M solution in hexanes) at 0 °C. The resulting deep yellow suspension was stirred for 1 h at 0 °C and for 30 min at room temperature. A solution of the above mixture (189 mg, 1.14 mmol) in dry THF (15 mL) was introduced at 0 °C, and stirring was maintained for 1 h at 0 °C and for 1 h at room temperature before quenching with distilled water (20 mL). The aqueous layer was extracted several times with ether. The combined organic phases were dried and concentrated in vacuo. Chromatography of the residue on silica gel (elution with 10% ether in petroleum ether) afforded 146 mg (78%) of **29** as a colorless liquid: IR (neat, cm^{-1}) 3400, 1640, 1460, 1420, 1380, 1035, 1000, 915, 740, 700; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.36 (dd, J = 7.5, 7.4 Hz, 1 H), 5.99 (d, J = 8.3 Hz, 1 H), 5.46 (ddd, J = 17, 9.9, 9.1 Hz, 1 H), 4.96 (dd, J = 17, 1.4 Hz, 1 H), 4.85 (dd, J = 10.0, 1.7 Hz, 1 H), 3.65 (d, J = 11.2 Hz, 1 H), 3.64 (d, J = 11.2 Hz, 1 H), 2.52 (m, 1 H), 2.30 (ddd, J = 10.8, 9.6, 4.6 Hz, 1 H), 1.88 (ddd, J = 13.2, 12, 2.3 Hz, 1 H), 1.63–0.80 (series of m, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.8, 135.3, 131.9, 113.4, 67.9, 45.7, 42.0, 35.0, 30.4, 29.0, 25.7; MS m/z (M^+) calcd 164.1201, obsd 164.1189.

Anal. Calcd for $C_{11}H_{16}O$: C, 80.44; H, 9.82. Found: C, 80.43; H, 9.91.

(1*R,4*S**,6*R**)-6-Vinylbicyclo[2.2.2]oct-2-ene-1-carboxaldehyde (30).** To a suspension of pyridinium dichromate (275 mg, 0.73 mmol) and 4-Å molecular sieves (350 mg) in CH_2Cl_2 (10 mL) was added a solution of **29** (60 mg, 0.367 mmol) in CH_2Cl_2 (4 mL) at 0 °C. The resulting brown reaction mixture was stirred for 5 h at 0 °C and carefully concentrated in vacuo, taken up in 10% ether solution in petroleum ether, and chromatographed on Florisil (elution with the same solvent mixture) to afford 39 mg (66%) of **30** as a colorless oil, which decomposes readily to a white polymer if not stored as a benzene solution and used as rapidly as possible; IR (neat, cm^{-1}) 1725, 1685, 1637, 1450, 1159, 996, 916, 717, 692, 634; ^{1}H NMR (300 MHz, C_6D_6) δ 9.42 (d, J = 0.6 Hz, I H), 6.54 (d, J = 8.3 Hz, 1 H), 6.14 (dd, J = 6.9, 6.8 Hz, 1 H), 5.25 (ddd, J = 17, 10, 9 Hz, 1 H), 4.77 (dd, J = 17, 1.5 Hz, 1 H), 4.72 (dd, J = 10, 1.5 Hz, 1 H), 2.31 (ddd, J = 10.5, 10, 4.5 Hz, 1 H), 2.20 (m, 1 H), 1.56 (ddd, J = 12, 9, 2.2 Hz, 1 H), 1.38 (m, 1 H), 1.17 (m, 1 H), 1.00 (m, 1 H), 0.90 (m, 2 H); ^{13}C NMR (75 MHz, C_6D_6) δ 202.3, 141.9, 135.2, 128.4, 114.5, 51.6, 44.4, 34.5, 31.0, 27.6, 24.8; MS m/z (M^+) calcd 162.1045, obsd 162.1045.

(1*R,4*S**,6*R**)-1-[(*Z*)-2-(*p*-Methoxyphenoxy)vinyl]-6-vinylbicyclo-[2.2.2]oct-2-ene (21) and (1*R**,4*S**,6*R**)-1-[(*E*)-2-(*p*-Methoxyphenoxy)-vinyl]-6-vinylbicyclo[2.2.2]oct-2-ene (32).** To a slurry of ((*p*-methoxyphenoxy)methyl)triphenylphosphonium chloride (240 mg, 0.866 mmol) in dry THF (20 mL) was added n-butyllithium (0.45 mL of 1.6 M solution in hexanes) at 0 °C. The resulting deep red solution was stirred at 0 °C for 1.5 h, allowed to warm to room temperature for 15 min, returned to 0 °C, and treated with a solution of **30** (39 mg, 0.241 mmol) in THF (2 mL). After 2 h, the reaction mixture was diluted with water (10 mL) and extracted with ether. The combined organic layers were dried, filtered, and concentrated in vacuo. Purification of the residue by MPLC (elution with 2.5% ether and 1% triethylamine in petroleum ether) gave 19 mg (28%) of the less polar Z-isomer **21** as a colorless oil, 30 mg (44%) of a mixture of the E- and Z-isomers, and 11 mg (16%) of the more polar E-isomer **32** as a colorless oil.

For **21**: IR (neat, cm^{-1}) 1667, 1636, 1611, 1591, 1505, 1464, 1441, 1418, 1390, 1295, 1227, 1180, 1110, 1039, 998, 953, 908, 826, 736, 699, 644; ^{1}H NMR (300 MHz, C_6D_6) δ 6.84 (dm, J = 9 Hz, 2 H), 6.63 (dm, J = 9 Hz, 2 H), 6.51 (d, J = 8 Hz, 1 H), 6.25 (dd, J = 8, 7 Hz, 1 H), 6.18 (d, J = 9 Hz, 1 H), 5.64 (ddd, J = 17, 9.8, 9.7 Hz, 1 H), 4.96 (ddd, J = 17, 1.2, 1 Hz, 1 H), 4.94 (ddd, J = 9.8, 1.2, 1 Hz, 1 H), 4.74 (d, J = 7 Hz, 1 H), 3.26 (s, 3 H), 2.50 (ddd, J = 9.4, 9.2, 4.6 Hz, 1 H), 2.33 (m, 1 H), 1.79 (m, 3 H), 1.46 (m, 1 H), 1.32 (m, 1 H), 1.17 (m, 1 H); ^{13}C NMR (75 MHz, C_6D_6) δ 155.8, 152.0, 144.3, 141.8, 136.7, 133.6, 117.9 (2 C), 117.0, 115.0 (2 C), 113.3, 55.1, 48.5, 41.1, 34.8, 32.6, 30.4, 26.4; MS m/z (M^+) calcd 282.1620, obsd 282.1602.

Anal. Calcd for $C_{19}H_{22}O_2$: C, 80.82; H, 7.85. Found: C, 81.23; H, 7.91.

For **32**: ^{1}H NMR (300 MHz, C_6D_6) δ 6.94 (dm, J = 9 Hz, 2 H), 6.70 (dm, J = 9 Hz, 2 H), 6.42 (d, J = 12.5 Hz, 1 H), 6.20 (dd, J = 8.5, 6.7 Hz, 1 H), 5.99 (d, J = 8.3 Hz, 1 H), 5.60 (d, J = 12.5 Hz, 1 H), 5.48 (ddd, J = 17, 10, 9.5 Hz, 1 H), 4.90 (ddd, J = 10, 2 , 1 Hz, 1 H), 4.85 (ddd, J = 17, 2, 1 Hz, 1 H), 3.29 (s, 3 H), 2.30 (m, 1 H), 2.09 (ddd, J = 9.4, 9.3, 4.5 Hz, 1 H), 1.71 (ddd, J = 11, 9.6, 2.5 Hz, 1 H), 1.39 (m, 2 H), 1.29 (m, 2 H), 1.10 (m, 1 H); ^{13}C NMR (75 MHz, C_6D_6) δ 155.8, 152.1, 143.9, 143.3, 134.6, 134.4, 118.6, 118.2 (2 C), 115.0 (2 C), 113.8, 55.1, 49.3, 39.9, 35.1, 33.6, 30.6, 26.4.

(6*R,6a*R**,7*S**,10a*S**,11*S**,12*S**)-6,6a,7,8,9,10-Hexahydro-2-methoxy-12-vinyl-6,7,10α-[1]propanyl[3]ylidene-10a*H*-dibenzo[*b*,*d*]pyran (33).** A solution of **21** (15 mg, 0.053 mmol) in chlorobenzene (1.5 mL) was heated in a sealed tube at 200–210 °C for 16 h. The cooled reaction mixture was chromatographed on Florisil (elution with petroleum ether followed by 5% ether in petroleum ether) to give 10 mg (66%) of **33**; IR (neat, cm^{-1}) 1630, 1600, 1485, 1270, 1250, 1200, 1100, 1030, 1000, 900, 795; ^{1}H NMR (300 MHz, C_6D_6) δ 6.73 (d, J = 9 Hz, 1 H), 6.71 (d, J = 3 Hz, 1 H), 6.58 (dd, J = 9, 3 Hz, 1 H), 5.62 (ddd, J = 17, 11, 7 Hz, 1 H), 4.89 (br d, J = 5 Hz, 1 H), 4.78 (ddd, J = 11, 2, 1 Hz, 1 H), 4.73 (ddd, J = 17, 2, 1 Hz, 1 H), 3.36 (s, 3 H), 2.38 (dd, J = 13, 9 Hz, 1 H), 2.32 (br dd, J = 6.5, 5 Hz, 1 H), 2.06 (ddd, J = 8.5, 7, 6 Hz, 1 H), 2.02 (m, 1 H), 1.71 (ddd, J = 13, 11, 6 Hz, 1 H), 1.60 (br s, 1 H), 1.56 (ddd, J = 13, 6.5, 3 Hz, 1 H), 1.50–1.30 (m, 2 H), 1.40–1.20 (m, 2 H), 1.16 (m, 1 H); ^{13}C NMR (75 MHz, C_6D_6) δ 156.6, 154.9, 143.5, 132.5, 113.3, 112.3, 110.7, 109.4, 89.8, 56.2, 55.4, 54.9, 47.9, 47.2, 39.9, 34.1, 30.2, 24.7, 19.9; MS m/z (M^+) calcd 282.1620, obsd 282.1619.

Anal. Calcd for $C_{19}H_{22}O_2$: C, 80.82; H, 7.85. Found: C, 81.28; H, 8.09.

(1*R,2*S**,4*S**)-1-Vinylbicyclo[2.2.2]oct-5-ene-2-carboxylic acid (37).** To a solution of **4** (4.73 g, 24.6 mmol) in methanol (150 mL) was added 2 M lithium hydroxide solution. The reaction mixture was stirred at 40–45 °C for 36 h, acidified to pH ≈ 3–4, extracted with ether (6 × 100 mL), dried, and concentrated in vacuo to give 4.27 g (96%) of **37** as a very viscous oil which slowly crystallized as a white solid: mp 46–48 °C (from pentane at −78 °C); IR ($CHCl_3$, cm^{-1}) 3580–3050, 2860, 1725, 1660, 1440, 1340, 1230, 1150, 1150, 1020, 980; ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.0 (br s, 1 H), 6.37 (dd, J = 8.3, 6.7 Hz, 1 H), 6.21 (d, J = 8.3 Hz, 1 H), 6.05 (dd, J = 17.6, 10.9 Hz, 1 H), 5.17 (dd, J = 17.6, 1 Hz, 1 H), 5.12 (dd, J = 11.5, 1 Hz, 1 H), 2.63 (m, 2 H), 1.94 (ddd, J = 12.5, 10, 2.7 Hz, 1 H), 1.62–1.48 (series of m, 3 H), 1.36 (m, 1 H), 1.17 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 181.1, 142.1, 133.7, 132.9, 113.6, 48.2, 41.2, 33.0, 32.9, 30.0, 25.0; MS m/z (M^+) calcd 178.0994, obsd 178.1007.

Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 74.09; H, 8.00.

1-Vinylbicyclo[2.2.2]oct-5-en-2-one (38). To an LDA solution prepared at 0 °C from diisopropylamine (3.3 mL, 23.2 mmol) and 1.6 M

n-butyllithium in hexanes (13.5 mL, 22.3 mmol) in dry THF (35 mL) was slowly added at −20 °C a solution of **37** (1.59 g, 8.9 mmol) in dry THF (15 mL) over a 40-min period. The reaction mixture was allowed to warm to room temperature for 1 h and heated to 45 °C for 2 h in order to ensure dianion formation. The yellow dianion solution was cooled to −78 °C and added over 2-h period via cannula to a reaction flask containing diethyl ether (140 mL) at −78 °C, into which dry oxygen was continuously being introduced below the surface. The reaction mixture was acidified at −78 °C with 5% HCl. In the cold, the water layer was separated and extracted with ether (4 × 150 mL) and CH_2Cl_2 (100 mL). The combined organic layers were dried and concentrated in vacuo to *ca.* 10 mL. As the remaining ether was removed in vacuo, CH_2Cl_2 was added to maintain a volume of *ca.* 10 mL. The slightly yellow solution of α-hydroperoxy acid was diluted with CH_2Cl_2 (100 mL) at −78 °C under N_2, and dimethylformamide dimethyl acetal (4.75 mL, 35.7 mmol) was slowly introduced. This mixture was stirred for 2 h at −78 °C and at room temperature for 30 h, concentrated to *ca.* 10 mL, and directly chromatographed on silica gel (elution with 10% ether in petroleum ether) to give a colorless liquid which was subjected to MPLC (silica gel, elution with 4% ether in petroleum ether). There was isolated 672 mg (51%) of **35** as a colorless, volatile liquid that crystallizes at −30 °C: IR (neat, cm^{-1}) 1720, 1645, 1250, 1090, 1000, 920, 710; ^1H NMR (300 MHz, $CDCl_3$) δ 6.52 (dd, *J* = 8.1, 6.6 Hz, 1 H), 6.30 (dd, *J* = 17.7, 11 Hz, 1 H), 6.09 (d, *J* = 8.2 Hz, 1 H), 5.32 (dd, *J* = 11, 1 Hz, 1 H), 5.19 (dd, *J* = 17.7, 1 Hz, 1 H), 2.97 (br s, 1 H), 2.09 (m, 2 H), 1.81 (m, 2 H), 1.59 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 211.0, 136.9, 136.7, 131.0, 115.3, 54.5, 40.4, 32.1, 28.6, 25.4; MS *m/z* (M^+) calcd 148.0888, obsd 148.0864.

Anal. Calcd for $C_{10}H_{12}O$: C, 81.04; H, 8.16. Found: C, 81.04; H, 8.16.

(1*R,2*R**,4*S**)-1,2-Divinylbicyclo[2.2.2]oct-5-en-2-ol (39) and (1*R**,2*S*,4*S**)-1,2-Divinylbicyclo[2.2.2]oct-5-en-2-ol (40).** To a stirred solution of **38** (0.490 g, 3.31 mmol) in THF (50 mL) at −78 °C was added under N_2 a 1 M solution of vinylmagnesium bromide in THF (19 mL, 19.0 mmol). The reaction mixture was slowly warmed to 0 °C during 30 min, at which point it was quenched carefully with saturated NH_4Cl solution (50 mL), diluted with ether (200 mL), washed with brine (100 mL), dried, and concentrated. The alcohol isomers were separated by MPLC on silica gel (elution with 20% ether in petroleum ether) to give 251 mg (43%) of the less polar **40** and 272 mg (46%) of **39** as colorless oils.

For **39**: IR (neat, cm^{-1}) 3500, 1645, 1610, 1465, 1450, 1415, 1370, 1350, 1320, 1090, 1130, 1000, 920, 700; ^1H NMR (300 MHz, $CDCl_3$) δ 6.46 (dd, *J* = 8.2, 6.6 Hz, 1 H), 6.19 (br d, *J* = 8.3 Hz, 1 H), 6.04 (dd, *J* = 17.5, 11 Hz, 1 H), 5.97 (dd, *J* = 17.1, 10.8 Hz, 1 H), 5.23 (dd, *J* = 17.2, 1.5 Hz, 1 H), 5.22 (dd, *J* = 10.9, 1.5 Hz, 1 H), 5.20 (dd, *J* = 17.6, 1.3 Hz, 1 H), 5.12 (dd, *J* = 10.8, 1.5 Hz, 1 H), 2.65 (br s, 1 H), 1.86 (dd, *J* = 17.3, 2.3 Hz, 1 H), 1.73 (br s, 1 H), 1.70 (ddd, *J* = 12, 9, 3.5 Hz, 1 H), 1.51 (m, 2 H), 1.38 (m, 1 H), 1.20 (ddd, *J* = 13, 12, 4.5 Hz, 1 H); ^{13}C NMR (62 MHz, $CDCl_3$) δ 141.6, 140.2, 135.1, 133.8, 115.2, 113.2, 77.2, 48.1, 44.5, 31.1, 27.2, 25.5; MS *m/z* (M^+) calcd 176.1201, obsd 176.1226.

Anal. Calcd for $C_{12}H_{16}O$: C, 81.77; H, 9.15. Found: C, 82.01; H, 9.36.

For **40**: IR (neat, cm^{-1}) 3500, 1640, 1615, 1470, 1450, 1420, 1380, 1310, 1010, 925, 710; ^1H NMR (300 MHz, $CDCl_3$) δ 6.32 (dd, *J* = 8.2, 6.5 Hz, 1 H), 6.06 (br d, *J* = 8.1 Hz, 1 H), 6.02 (dd, *J* = 17.6, 11 Hz, 1 H), 5.85 (dd, *J* = 17.3, 10.7 Hz, 1 H), 5.20 (dd, *J* = 10.9, 1.5 Hz, 1 H), 5.14 (dd, *J* = 17.6, 1.5 Hz, 1 H), 5.04 (dd, *J* = 17.3, 1.5 Hz, 1 H), 4.92 (dd, *J* = 10.7, 1.5 Hz, 1 H), 2.61 (br s, 1 H), 2.25 (ddd, *J* = 12.3, 9.5, 3.9 Hz, 1 H), 1.75 (ddd, *J* = 12, 4.5, 2.5 Hz, 1 H), 1.65 (br s, 1 H), 1.64 (m, 1 H), 1.61 (m, 1 H), 1.38 (m, 1 H), 1.02 (ddd, *J* = 12, 12, 4.5 Hz, 1 H); ^{13}C NMR (62 MHz, $CDCl_3$) δ 146.0, 141.0, 134.9, 134.4, 115.6, 110.2, 77.9, 48.1, 42.0, 31.1, 25.6, 23.8; MS *m/z* (M^+) calcd 176.1201, obsd 176.1204.

Anal. Calcd for $C_{12}H_{16}O$: C, 81.77; H, 9.15. Found: C, 81.84; H, 9.23.

Representative Anionic Oxy-Cope Rearrangements. (7*E*)-Bicyclo[6.2.2]dodeca-7,9-dien-3-one (44), (7*Z*)-Bicyclo[6.2.2]dodeca-7,9-dien-3-one (45), and *cis*-3,4,4a,7,8,8a-Hexahydro-6-vinyl-2(1*H*)-naphthalenone (46). (A) Action of Sodium Hydride in THF on 40. To a suspension of 97% sodium hydride (100 mg, 4.16 mmol) in dry THF (10 mL) under argon was added a solution of **40** (60 mg, 0.34 mmol) in THF (5 mL). The reaction mixture was stirred for 2.5 h, carefully quenched with saturated NH_4Cl solution, and extracted with ether (3 × 80 mL). The combined organic layers were washed with brine (80 mL), dried, and concentrated in vacuo to give 1.4:1:2.6 mixture of 44, 45, and 46 as determined by analytical HPLC. The three isomers were separated by MPLC on silica gel (elution with 5% ether in petroleum ether) to give 21 mg (35%) of 44, 25 mg (41%) of 46, and 11 mg (18%) of 45, all as a colorless oils.

For **44**: IR (neat, cm^{-1}) 1695, 1440, 1410, 1360, 1120; ^1H NMR (300 MHz, $CDCl_3$) δ 6.67 (br d, *J* = 9.5 Hz, 1 H), 5.97 (br dd, *J* = 9.5, 6.7 Hz, 1 H), 4.97 (br t, *J* = 7.9 Hz, 1 H), 2.76 (br dd, *J* = 17, 11.5 Hz, 1 H), 2.70 (m, 1 H), 2.51 (dd, *J* = 10.1, 3.5 Hz, 1 H), 2.31–2.09 (series of m, 5 H), 2.08–1.85 (series of m, 4 H), 1.76 (m, 1 H); ^{13}C NMR (62 MHz, $CDCl_3$) δ 213.0, 135.4, 133.9, 132.0, 128.9, 49.2, 43.6, 32.3, 32.2, 30.1, 27.3, 23.8; MS *m/z* (M^+) calcd 176.1201, obsd 176.1202.

For **45**: IR (neat, cm^{-1}) 1685, 1455, 1430, 1410, 1350, 1210, 1115; ^1H NMR (300 MHz, $CDCl_3$) δ 6.52 (br d, *J* = 9.5 Hz, 1 H), 5.88 (br dd, *J* = 9.5, 6.3 Hz, 1 H), 4.93 (br t, *J* = 6.5 Hz, 1 H), 2.70 (m, 2 H), 2.53 (m, 1 H), 2.52 (dd, *J* = 11, 4 Hz, 1 H), 2.31 (dd, *J* = 11, 5.5 Hz, 1 H), 2.25–1.92 (series of m, 7 H), 1.82 (m, 1 H); ^{13}C NMR (62 MHz, $CDCl_3$) δ 209.2, 134.9, 134.7, 128.6, 127.9, 51.8, 41.3, 33.1, 28.1, 26.7, 26.6, 23.0; MS *m/z* (M^+) calcd 176.1201, obsd 176.1196.

For **46**: IR (neat, cm^{-1}) 1715, 1640, 1605, 1450, 1355, 1340, 1310, 1285, 1275, 1190, 1170, 1000, 900; ^1H NMR (300 MHz, $CDCl_3$) δ 6.35 (dd, *J* = 17.5, 10.7 Hz, 1 H), 5.65 (br s, 1 H), 5.10 (d, *J* = 17.5 Hz, 1 H), 4.96 (d, *J* = 10.7 Hz, 1 H), 2.61 (br s, 1 H), 2.30 (m, 5 H), 2.21–2.06 (series of m, 2 H), 2.03–1.57 (series of m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 212.1, 139.3, 136.3, 131.5, 111.2, 43.8, 38.6, 36.0, 34.9, 30.3, 25.5, 21.3; MS *m/z* (M^+) calcd 176.1201, obsd 176.1201.

(B) Action of Potassium Hydride/18-Crown-6 on 39. To a suspension of 121 mg (3.01 mmol) of potassium hydride, obtained after pentane washing (3 × 15 mL) of a 24% suspension in oil, in dry THF (10 mL) under argon was added a solution of **39** (80 mg, 0.45 mmol) in THF (5 mL). After 2 min, reaction was judged complete (TLC analysis), and the reaction mixture was quenched by careful addition of saturated NH_4Cl solution, extracted with ether (3 × 80 mL), washed with brine, dried, and concentrated in vacuo to give 72 mg of an oil consisting of a 1:2.2:3.5 mixture of **44**, **45**, and **46** (HPLC analysis).

(C) Action of Ethylmagnesium Bromide on 39. To a solution of freshly prepared ethylmagnesium bromide in THF (10 mL of 1.6 M solution, 16 mmol) under argon was added a solution of **39** (80 mg, 0.45 mmol) in THF (4 mL). After 4 days of being stirred at room temperature, the reaction mixture was carefully quenched by inverse addition to saturated NH_4Cl solution, extracted with ether, washed with brine, dried, and concentrated in vacuo to give 74 mg (93%) of **45** admixed with *ca.* 5% of unreacted **39**.

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Supplementary Material Available: Details of the semiselective DEPT-45 experiments performed on **8**, **15**, and **33**, as well as the final atomic coordinates for the global minimum-energy conformation of **33** (5 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.