A Practical Method for Using Alkoxide-Accelerated Vinylcyclobutane Ring Expansions in the Synthesis of Six-Membered Rings. Unexpected Orbital Symmetry Allowed and Forbidden 1,3-Sigmatropic Rearrangements

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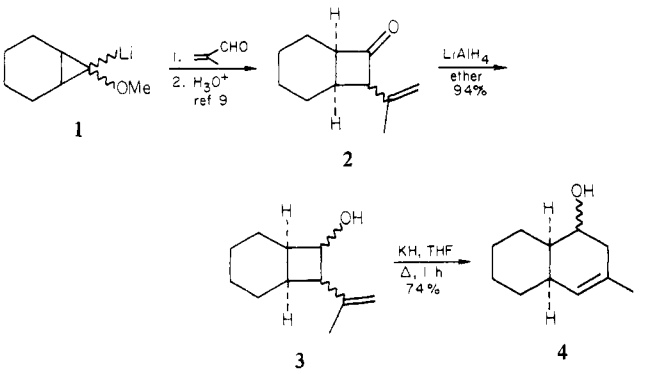
Abstract: A practical method for utilizing the ring expansion of 2-vinylcyclobutanols to cyclohex-3-en-1-ols, even in cases in which very acid-sensitive groups are present, consists of the addition of 1-lithio-1-methoxycyclopropanes to conjugated enals, brief treatment in the cold of the resulting alcohols with dilute acid, conversion of the resulting 2-vinylcyclobutanones to the corresponding alcohols, and treatment of the latter with potassium hydride in tetrahydrofuran. The utility of this method has been demonstrated by a synthesis of (−)-β-selinene starting from (−)-perillaldehyde and by the stereoselective preparation of an unsaturated decalol, which is a model for a key intermediate in the synthesis of compactin. In the latter study, it has been ascertained that a 2-dienylcyclobutanol in which the groups are arranged in a trans manner rearranges to the axial decalol diene in an apparent suprafacial retention mode whereas the cis epimer yields mainly the same alcohol by a suprafacial inversion pathway; the steric courses of both reactions are contrary to expectations based on the literature.

In this paper, we propose a practical method for utilizing the alkoxide-accelerated vinylcyclobutane rearrangement for the synthesis of six-membered rings, we demonstrate the method by a simple synthesis of (−)-β-selinene and a highly stereoselective and efficient preparation of a decalol diene bearing much of the functionality present in an important intermediate[2] in the synthesis of compactin, the inhibitor of a key step in cholesterol biosynthesis,[3] and we reveal two highly unusual steric courses of this type of 1,3-sigmatropic rearrangement that are essentially the opposite of those recently reported in a closely related system.[4] The papers by Danheiser[4] and Carpenter[5] reference most of the pertinent literature. It is sufficient here to mention that the landmark finding by Evans and Golob[6] that a properly placed alkoxide anion substituent could greatly accelerate a 3,3-sigmatropic rearrangement has stimulated a number of uses of this principle to accelerate 1,3-sigmatropic rearrangements; the first example of its use in a vinylcyclobutane rearrangement is due to Wilson and Mao,[7] and a more extensive study by Danheiser[4] recently appeared at a time when much of the work that we here report was complete.

The 2-vinylcyclobutanol substrates were prepared from the corresponding 2-vinylcyclobutanones, our synthesis of which involves the addition of conjugated enals to 1-lithio-1-methoxycyclopropanes[8] and acid-catalyzed rearrangement of the resulting allylic alcohols.[9] This procedure, one example of which is illustrated in Scheme I, involves such mild conditions that particularly acid-sensitive functionality is preserved (see below).

Our earlier work[10] had shown that 2-vinylcyclobutanones such as **2** undergo a rearrangement to conjugated cyclohexenones when exposed to strong acid. Since cyclohexenols such as **4** can be oxidized to such cyclohexenones (see below), the rearrangement shown in Scheme I constitutes a method of performing the ring expansion to a cyclohexenone under basic conditions.

Scheme I



The utility of the base-induced rearrangement in a case in which the acid-catalyzed version would be expected to destroy a group within the molecule has been demonstrated in the preparation of the eudesmane sesquiterpene (−)-β-selinene (**14**)[11] starting from the commercially available (−)-perillaldehyde (**6**)[12] (Scheme II). Addition of the latter to 1-lithio-1-methoxycyclopropane (**5**)[8] followed by exposure of the crude product **7** to 5% HBF_4 in THF (10-fold dilution of 48% aqueous HBF_4 with THF) for 10 min yields the vinylcyclobutanone **8**; it is noteworthy that this type of rearrangement[9] can be conducted under conditions that do not affect the sensitive isopropenyl group. Not unexpectedly, strong enough acid treatment of **8** to effect 1,3-acyl rearrangement[10] causes migration of the isopropenyl double bond into the ring and

(1) Andrew Mellon Predoctoral Fellow.
(2) Wang, N.-Y.; Hsu, C.-T.; Sih, C. J. *J. Am. Chem. Soc.* **1981**, *103*, 6538. Funk, R. L.; Zeller, W. E. *J. Org. Chem.* **1982**, *47*, 180. Heathcock, C. H.; Taschner, M. J.; Thomas, J. A. "Abstract of Papers", 183rd National Meeting of the American Chemical Society, Las Vegas, NV, March 1982; American Chemical Society: Washington, D.C., 1982; ORGN 12.
(3) Brown, A. G.; Smale, T. C.; King, T. J.; Hasenkamp, R.; Thompson, R. H. *J. Chem. Soc., Perkin Trans. 1* **1976**, 1165. Brown, M. S.; Faust, J. R.; Goldstein, J. L.; Kaneko, I.; Endo, A. *J. Biol. Chem.* **1978**, *253*, 1121 and citations therein.
(4) Danheiser, R. L.; Martinez-Davila, C.; Sard, H. *Tetrahedron* **1981**, *37*, 3943.
(5) Zoeckler, M. T.; Carpenter, B. K. *J. Am. Chem. Soc.* **1981**, *103*, 7661.
(6) Evans, D. A.; Golob, A. M. *J. Am. Chem. Soc.* **1975**, *97*, 4765.
(7) Wilson, S. R.; Mao, D. T. *J. Chem. Soc., Chem. Commun.* **1978**, 479.
(8) Cohen, T.; Matz, J. R. *J. Am. Chem. Soc.* **1980**, *102*, 6900.
(9) Cohen, T.; Matz, J. R. *Tetrahedron Lett.* **1981**, *22*, 2455.
(10) Matz, J. R.; Cohen, T. *Tetrahedron Lett.* **1981**, *22*, 2459.
(11) (a) Gopichand, Y.; Pednekar, P. R.; Chakravarti, K. K. *Ind. J. Chem., Sect. B* **1978**, *16B*, 148. (b) Naya, T.; Miyamoto, F.; Takemoto, T. *Experientia* **1978**, *34*, 984.
(12) (a) Aldrich Chemical Co. Our sample showed $[\alpha]_D$ −123.4° (*c* 9.23, $CHCl_3$); literature values are −106° (for a sample prepared from β-pinene)[12b] and −146° (for the natural product).[12c] (b) Buchi, G.; Hofheinz, W.; Paukstelis, J. V. *J. Am. Chem. Soc.* **1969**, *91*, 6573. (c) Semmler, F. W.; Zaar, B. *Chem. Ber.* **1911**, *44*, 52. The (+) and (−) aldehydes are both obtainable from natural sources so that it is also possible by this scheme to synthesize (+)-β-selinene, which is likewise a natural product.[13]
(13) (a) Cocker, W.; McMurry, T. B. H. *Tetrahedron* **1960**, *8*, 181. (b) Trivedi, B.; Motl, O.; Herout, V.; Sorm, F. *Collect. Czech. Chem. Commun.* **1964**, *29*, 1675. (c) Ganter, C.; Keller-Wojtkiewicz, B. *Helv. Chim. Acta* **1971**, *54*, 183.

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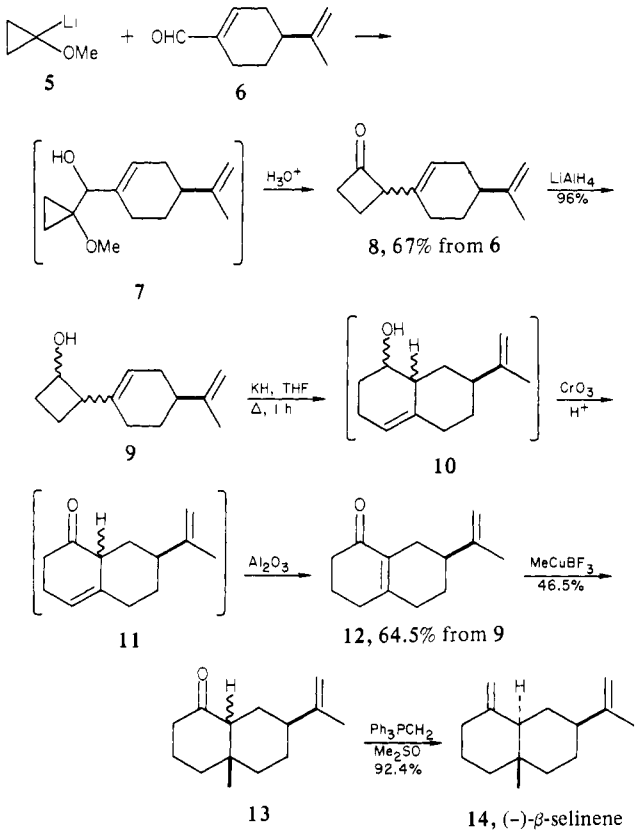
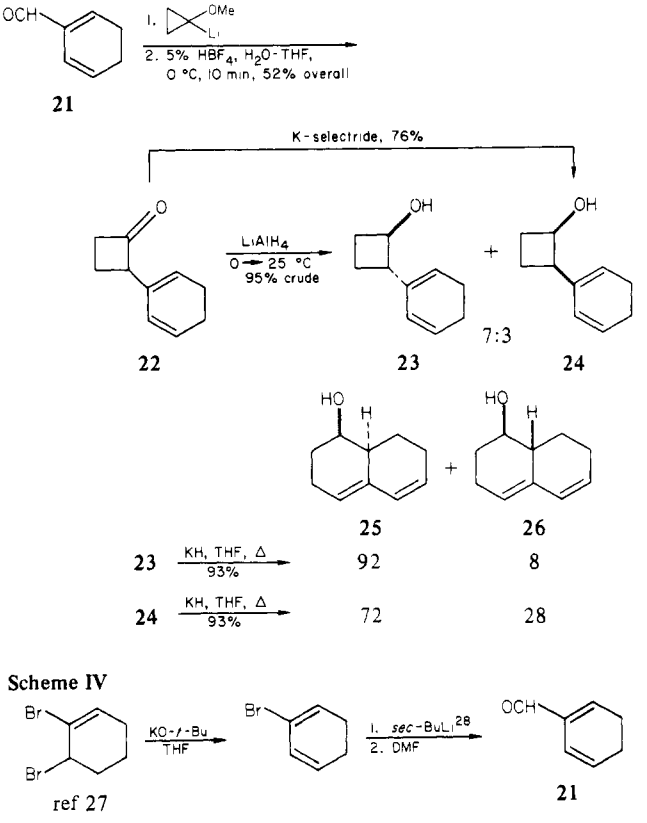
Scheme II



Scheme III

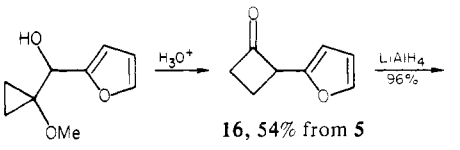


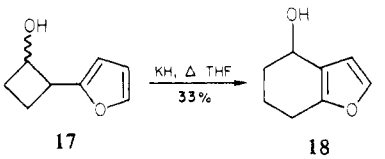
Scheme IV

disproportionation of the resulting dihydrobenzene. Reduction of **8** with $LiAlH_4$ yields the 2-vinylcyclobutanols **9**,[14] which upon treatment with KH in refluxing THF for 1 h produce the cyclohexenols **10**. Oxidation of unpurified **10** with Jones reagent yields the nonconjugated enone **11**, which is converted to the conjugated enone **12** ($[\alpha]^{25}_D$ −187.9°, CCl_4) by rapid passage through a short column of basic, activity 3 EM alumina 90 (3% ethyl acetate in hexanes). Conjugate addition of a methyl group is accomplished by the use of CH_3CuBF_3,[15] which gives ketone **13** (a mixture of two stereoisomers with one very predominant) in 46.5% yield and 33% of a diene presumably arising from 1,2-addition followed by dehydration.[15,16] In the enantiomeric series, a mixture analogous to **13** (but partially racemic and exhibiting the same spectroscopic properties) has previously been converted to (+)-β-selinene (as well as to another eudesmane, neointermedeol).[17] In our hands, a Wittig reaction in Me_2SO converted **13** in 92.4% yield (based on the 34% of recovered **13**) to (−)-β-selinene,[18] contaminated (capillary GLC) with about 5% of an isomer.[19] The product exhibits $[\alpha]^{25}_D$ −49.5° (*c* 6.55, hexanes).[20] The only other synthesis of optically active β-selinene yielded partially racemic material $[\alpha]^{25}_D$ +21.5° (*c* 6.62, hexane).[17]

A stereochemical study revealed that the alcohol **9**, produced by $LiAlH_4$ reduction, is 82% trans and 18% cis (about the cyclobutane ring); when K-Selectride is used to reduce ketone **8**, the pure cis cyclobutanol is obtained.[21,23] *cis*-**9** isomerizes almost quantitatively to *trans*-**9** when exposed to KH in THF for 30 min at 25 °C. *trans*-**9** yields a mixture of alcohols (**10**) in 87% yield when heated at reflux with KH for 1 h.

This type of rearrangement is even capable of violating the aromaticity of a furan ring. The product (**15**) of reaction of **5**





with furfural rearranges in acid without much destruction of the sensitive furan ring. When the resulting 2-(2-furyl)cyclobutanone (**16**) is reduced to the alcohol **17** and the latter is treated with KH, the furanocyclohexenol **18** is produced, albeit in a less than satisfactory yield.[25,26]

(14) The characterization of the alcohol mixture used in the synthetic study is given below.

(15) Yamamoto, Y.; Yamamoto, S.; Yatagai, H.; Ishihara, Y.; Maruyama, K. *J. Org. Chem.* **1982**, *47*, 119.

(16) Lithium dimethylcuprate gave only a trace of conjugate addition product; most of the product apparently resulted from 1,2 addition.

(17) MacKenzie, B. D.; Angelo, M. M.; Wolinsky, J. *J. Org. Chem.* **1979**, *44*, 4042.

(18) The NMR and IR spectra compared favorably with those reported for the (+) enantiomer.[17]

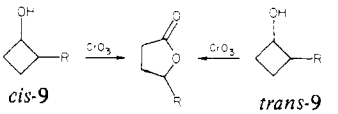
(19) This Wittig procedure is known to convert a cis–trans mixture of such decalones to the trans epimer.[17]

(20) Literature values reported for the natural (−) isomer are −35° [11a] and −85° [11b] and for the (+) isomer, +60°,[11b] +38°,[13a] +40.7°,[13b] and +43° [13c]

(21) The chromatographic and NMR ($CDCl_3$) characteristics of these epimeric 2-vinylcyclobutanols are completely in accord with those found by Trost for analogous vinylcyclobutanols.[22]

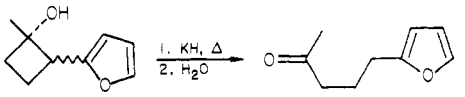
(22) Trost, B. M.; Jungheim, L. N. *J. Am. Chem. Soc.* **1980**, *102*, 7910.

(23) Upon oxidation with Jones reagent, both epimeric alcohols produce the same γ-lactone in nearly quantitative yield.[24]



(24) Jeanne-Carlier, R.; Bourelle-Wargnier, F. *Tetrahedron Lett.* **1975**, 1841.

The tertiary alcohol **19**, when heated with KH in THF, produces the ketone **20** in 83% yield and no detectable ring-expansion product. This result is consistent with Danheiser's finding[4] that



19 20

2-vinyl-1-alkylcyclobutanols give significantly poorer yields of ring-expansion product than do the secondary alcohols; a 1,5 proton or hydrogen atom transfer must occur either in the alkoxide during a concerted ring opening or in a fragmentation product such as a ketone–anion or an anion–diradical. Presumably the same type of intermediate is responsible for the isomerization of the cis to the trans cyclobutanols.

The generation of cyclohex-3-en-1-ols by such rearrangements could be of use in natural product synthesis as illustrated in Scheme III. Aldehyde **21** (Scheme IV) reacts with **5** to yield, after rearrangement with dilute acid, the acid-sensitive cyclobutanone **22**. The major product of reduction of **22** with $LiAlH_4$, the trans alcohol **23**,[21] rearranges in the presence of KH in refluxing THF to give the axial and equatorial cyclohexenols **25** and **26** in a ratio of 92:8. The cis cyclobutanol **24**, formed uncontaminated with the trans isomer (**23**) by reduction with K-Selectride, reacts with KH under similar conditions to give the same cyclohexenols in a ratio of 72:28. At −23 °C in the presence of KH, the cis cyclobutanol **24** is completely converted to a mixture of the trans cyclobutanol **23** (25%), the axial cyclohexenol **25** (57%), and the equatorial cyclohexenol **26** (18%); the trans cyclobutanol **23** is unchanged under the same conditions while the axial cyclohexenol **25** is stable even in refluxing THF.

Thus, the potassium salt of the *trans*-2-vinylcyclobutanol (**23**) rearranges by an apparent suprafacial *retention* (sr) mechanism, whereas the cis isomer (**24**) undergoes both isomerization to the trans epimer and ring expansion by a predominantly suprafacial *inversion* (si) mechanism. These ring-expansion results are very nearly the opposite of those of Danheiser[4] in a system lacking the conjugating double bond;[29] his results are consistent with his previous findings with regard to alkoxide-accelerated vinylcyclopropane rearrangements[30] as well as Berson's results in the rearrangements of vinylcyclobutanes possessing cis and trans substituents at the 2-position of the cyclobutane ring.[31] These previous results[30,31] have been rationalized on the basis that the *trans*-2-substituted-vinylcyclobutanes undergo the orbital symmetry allowed processes while the epimeric substrates undergo the "forbidden" processes because the transition states of the allowed transformations are destabilized by severe steric compression due to the cis substituent being thrust into the allylic system; the transition state for the forbidden process is considered to have certain electronic stabilizing features.[31,32]

A possible explanation of our results involves a fragmentation to an anion diradical or an anion aldehyde [as appears to occur in the cis–trans isomerisms of the 2-vinylcyclobutanols and possibly in the 1,5-hydrogen transfer (**19** → **20**)] followed by ring closure to the six-membered rings; however, it is not at all clear why the (apparently) less stable cyclohexenol is the major product in both cases and why Danheiser[4] observed the opposite behavior. Another, and a particularly interesting, rationalization of the sr mechanism observed for **23** is based on Carpenter's predictions[32] that both the alkoxide substituent and the double bond which is conjugated with that involved in the rearrangement favor the "forbidden" far more than the allowed process. Carpenter[5] has recently reported an example of an alkoxide-accelerated 1,3-sigmatropic rearrangement in which the ratio of sr to si is at least 2:1; however, the high ratio that we have observed in the case of **23** is apparently unprecedented. It is even more difficult to rationalize the allowed si path observed for the rearrangement of the cis alcohol **24**; if this transformation is concerted, and this is not at all certain, there must be a previously unobserved attraction between the alkoxide functionality and the conjugated allylic system. Further work designed to throw light on this unprecedented stereochemical result is planned.

In any event, it is clear that the 2-(1,3-cyclohexadien-2-yl)-cyclobutanone (**22**), which is now readily available, can be converted rather stereoselectively and efficiently to the alcohol **25**. This augues well for the possibility of using this methodology to synthesize compactin.[3] A class of key intermediates[2] in compactin synthesis differs from **25** only in possessing at the 7- and 8-positions cis substituents that are also cis to the bridgehead hydrogen atom. Such a pair of cis substituents should have a strong tendency during the ring expansion to arrange themselves cis to the bridgehead hydrogen atom since in the other possible configuration the substituent at the 8-position would very seriously crowd the alkoxide group at the 1-position.

Experimental Section

All reactions involving anions were carried out under an atmosphere of prepurified argon. Solvents were dried by using standard procedures and distilled immediately before use. In experiments involving the cyclohexadiene system, the organic solvents and aqueous solutions were deaerated with argon prior to use; purification of these compounds by distillation and flash chromatography was performed in the presence of the radical inhibitor 3-*tert*-butyl-4-hydroxy-5-methylphenyl sulfide. A dry ice/2-propanol slush bath was used to obtain a temperature of −78 °C and dry ice/1-hexanol for −45 °C. The temperatures recorded during the Kugelrohr distillations refer to the temperatures of the oven and are thus not true boiling points. The reported boiling points are uncorrected. Infrared spectra were recorded using a Perkin-Elmer Model 247 grating infrared spectrophotometer calibrated with a polystyrene film and recorded in units of cm^{-1}. ^1H NMR spectra were recorded on either a Varian T-60 or a Bruker WH-300 spectrometer. Chemical shift data are reported in units of δ relative to tetramethylsilane used as an internal standard. Carbon tetrachloride deuterated chloroform was used as the solvent. Low-resolution mass spectra were recorded on an LKB-9000 combined gas chromatograph–mass spectrometer, and high-resolution mass spectra were recorded on a CH-5 double focusing Varian Mat mass spectrometer. Optical rotations were obtained as solutions in a 1-dm cell in a Perkin-Elmer 241 polarimeter. The R_f values reported are from thin layer chromatograms run on glass-supported 250-μm silica gel GF plates (Analtech). Flash chromatography was performed with 40–63-μm silica gel 60 (E. Merck No. 9385).

7-Methoxy-7-(phenylthio)bicyclo[4.1.0]heptane.[33] To a Fischer–Porter tube were added 3.78 g (12.1 mmol) of 7,7-bis(phenylthio)bicyclo[4.1.0]heptane,[34] 3.44 g (12.6 mmol) of $HgCl_2$, 2.58 g (12.2 mmol) of HgO, a stirring bar, and 60 mL of methanol. The reaction mixture was heated with stirring for 24 h at 100 °C. After cooling, the methanol solution was filtered and the solvent removed in vacuo. The reaction mixture was taken up in pentane and washed twice with H_2O to remove mercuric salts. The organic phase was dried ($MgSO_4$), and the solvent was removed under reduced pressure to give a yellow oil. Kugelrohr distillation, 110 °C (0.2 mmHg), gave 2.45 g (87%) of the product as a pale yellow oil: ^1H NMR (CCl_4) δ 7.0–7.5 (m, 5 H, phenyl), 3.27 (s, 3 H, OCH_3), 1.2–1.8 (m, 10 H, cyclohexyl); IR (neat) 2925, 1595, 1480, 1438, 1102, 735, 687 cm^{-1}; exact mass calcd for $C_{14}H_{18}OS$: 234.1078; found: 234.1063.

1-Methoxy-1-(phenylthio)cyclopropane. To a solution of cyclopropyl phenyl sulfide[35] (5.53 g, 36.9 mmol) in 125 mL of THF at 0 °C was

(25) Jung had previously shown that an alkoxide-assisted 3,3-rearrangement could lead to dearomatization of a furan ring, but in that case the furan ring was not reestablished. The present case appears to be the first example of annulation onto a furan ring using a sigmatropic rearrangement. Jung, M. E.; Hudspeth, J. P. *J. Am. Chem. Soc.* **1978**, *100*, 4309. See also: Jung, M. E.; Hudspeth, J. P. *Ibid.* **1980**, *102*, 2463.

(26) For an example of a 3,3-sigmatropic rearrangement (nonannulative) into a furan ring in which the latter was reestablished, see: Raucher, S.; Lui, A. S. T.; Macdonald, J. E. *J. Org. Chem.* **1979**, *44*, 1885.

(27) Stevens, C. L.; Valicenti, J. A. *J. Am. Chem. Soc.* **1965**, *87*, 838.

(28) Miller, R. B.; McGarvey, G. *J. Org. Chem.* **1979**, *44*, 4623.

(29) Cis → trans isomerization in the cyclobutanols was not ruled out in this case, but even if it does occur the results are very different from our own.

(30) Danheiser, R. L.; Martinez-Davila, C.; Auchus, R. J.; Kadonaga, J. T. *J. Am. Chem. Soc.* **1981**, *103*, 2443.

(31) Berson, J. A. *Acc. Chem. Res.* **1972**, *5*, 406.

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

(33) Shöllkopf, U.; Ruban, E.; Tonne, P.; Riedel, K. *Tetrahedron Lett.* **1970**, 5077.

(34) Braun, M.; Seebach, D. *Chem. Ber.* **1976**, *109*, 669. We have found that the yield is improved when methyllithium is substituted for butyllithium in the ring closure step, since butyllithium causes significant sulfur–lithium exchange in the product.

added 30 mL (42 mmol) of 1.4 M BuLi in hexane. The reaction mixture was stirred for 3 h at 0 °C before the mixture was cooled to −78 °C. I_2 (11.2 g, 44.1 mmol) was added to the mixture, which was then stirred for an additional 0.5 h. The reaction mixture acquired the brown color of I_2 and became quite viscous due to the precipitation of LiI. A 10% $Na_2S_2O_3$ solution was added to destroy excess I_2, and the mixture was warmed to room temperature. The yellow reaction mixture was taken up in ether, the organic phase was washed twice with H_2O and dried ($MgSO_4$), and the solvent was removed in vacuo. The reddish oil was taken up in methanol (100 mL) containing Na_2CO_3 (10 g, 0.10 mol), and the mixture was heated at reflux for 3 h. The mixture was filtered, and the solvent was removed in vacuo. The resulting oil was taken up in ether, and the ethereal solution was washed twice with H_2O. The organic phase was dried over $MgSO_4$, and the solvent was removed under reduced pressure. Kugelrohr distillation, 70–75 °C (0.2 mmHg), gave 5.5 g (83%) of the mixed ketal as a yellow oil: ^1H NMR (CCl_4) δ 7.0–7.4 (m, 5 H, phenyl), 3.37 (s, 3 H, OCH_3), 1.2–1.9 (m, 4 H, cyclopropyl); IR (neat) 1587, 1482, 1440, 1258, 1205, 1167, 1060, 810, 738, 690 cm^{-1}; exact mass calcd for $C_{10}H_{12}OS$: 180.0609; found: 180.0608.

1-Lithio-1-methoxycyclopropane (5). To a three-necked, round-bottom flask equipped with a glass stirring bar under argon were added 10 mL of THF and lithium foil (~40 mg, ~5.8 mmol) cut into 5–10-mg pieces. The reaction mixture was cooled to −45 °C before 1-(dimethylamino)naphthalene (DMAN) (0.84 mL, 5.2 mmol) was added, and stirring was continued for 3.5 h. It is essential to maintain the temperature below −45 °C during the preparation of LDMAN, otherwise the latter decomposes to 1-lithionaphthalene. The dark green reaction mixture was cooled to −78 °C and 1-methoxy-1-(phenylthio)cyclopropane (450 mg, 2.5 mmol) in 4 mL of THF was added. The reaction mixture was stirred for 0.75 h before use.

8-(2-Propenyl)bicyclo[4.2.0]octan-7-one (2). To 30 mL of a solution of LDMAN (0.5 M, 15 mmol), prepared as above, was added a solution of 1.32 g (5.64 mmol) of 7-methoxy-7-(phenylthio)bicyclo[4.1.0]heptane in 10 mL of THF at −78 °C. After the mixture had been stirred for 45 min, methacrolein (0.75 mL, 9.1 mmol) was added. The dark color of the reaction mixture disappeared within 10 s. After 10 min, water was added and the reaction mixture was partitioned between water and ether. The organic phase was washed twice with water to remove lithium thiophenoxide and twice with 5% HCl to remove DMAN. The solvent was removed from the dried ($MgSO_4$) organic phase to give the crude alcohol as a yellow oil. The latter was taken up in 10 mL of THF, and HBF_4 (3 mL of a 48% aqueous solution) was added. An exothermic reaction ensued with the mixture taking on a golden yellow color. The reaction mixture was stirred for 5 min and then partitioned between ether and water. The ether phase was washed with 5% $NaHCO_3$ and dried ($MgSO_4$), and the solvent was removed in vacuo. Chromatography on silica gel (5% ethyl acetate in hexanes) gave the product as a yellow liquid. Kugelrohr distillation, 75–80 °C (0.35 mmHg), provided 806 mg (87%) of **2** as a colorless oil: ^1H NMR (CCl_4) δ 5.8 (m, 2 H, vinyl), 2.9–3.6 (m, 2 H, C*H*COC*H*), 1.2–2.7 (m, 9 H, cyclohexyl), 1.77 (br s, 3 H, CH_3); IR (neat) 1770 cm^{-1}; exact mass calcd for $C_{13}H_{18}O$: 164.1201; found: 164.1198.

8-(2-Propenyl)bicyclo[4.2.0]octan-7-ol (3). To a solution of 770 mg (4.70 mmol) of **2** in 20 mL of anhydrous ether was added $LiAlH_4$ (0.52 g, 13.7 mmol). The mixture was stirred for 0.5 h and quenched as follows: water (0.8 mL) was added dropwise with stirring (care is required since H_2 is evolved), 15% aqueous sodium hydroxide (1.6 mL) was added, and finally 2.4 mL of water was added; this procedure[36] afforded a granular precipitate of aluminum salts that could be easily removed by filtration. The filtrate was washed with water and dried ($MgSO_4$), and the solvent was removed in vacuo to give a yellow oil. Kugelrohr distillation, 75–80 °C (0.3 mmHg), gave 730 mg (94%) of **3** as a colorless oil: ^1H NMR (CCl_4) 4.7 (m, 2 H, vinyl), 3.85 (t, J = 5 Hz, 1 H, C*H*OH), 3.0 (br s, 1 H, OH), 2.63 (t, J = 6 Hz, 1 H, allylic, cyclobutane), 2.30 (br t, J = 5 Hz, 1 H), 1.0–1.9 (m, 9 H, cyclohexyl), 1.77 (s, 3 H, CH_3); IR (neat) 3350, 2940, 2860, 1645, 1450, 1143, 1077, 1048, 885 cm^{-1}; exact mass calcd for $C_{11}H_{18}O$: 166.1358; found: 166.1358.

Rearrangement of 3. To a solution of 402 mg (2.42 mmol) of **3** in 13 mL of anhydrous THF was added excess KH (the pentane washed solid was added until evolution of H_2 ceased). The reaction mixture was heated at reflux for 1 h and was quenched by the slow addition of H_2O. The reaction mixture was taken up in ether, and the solution was washed twice with water. The ether was dried ($MgSO_4$) and the solvent was removed in vacuo. Column chromatography on silica gel (10% EtOAc in hexanes) gave the alcohol **4** as a solid. Kugelrohr distillation, 100–105 °C (0.35 mmHg), gave 298 mg (74%) of **4** as an oily white solid: ^1H NMR (CCl_4) 5.0–5.3 (m, 1 H, vinyl), 3.7–4.1 (m, 1 H, C*H*OH) 2.58 (s, 1 H, alicyclic), 1.0–2.5 (m, 12 H, alicyclic + OH), 1.65 (br s, 3 H, CH_3); exact mass calcd for $C_{11}H_{18}O$: 166.1358; found: 166.1358.

2-(4-(2-Propenyl)cyclohexen-1-yl)cyclobutanone (8). To a preformed solution of 40 mmol of **5** in 200 mL of THF at −78 °C was added (−)-Perillaldehyde **6** (5.7 mL, 37 mmol), and the mixture was stirred for 0.5 h. The reaction mixture was quenched with water and partitioned between ether and water. The organic layer was washed twice with water to remove lithium thiophenoxide and twice with 5% HCl to remove the DMAN. Evaporation of the dried ($MgSO_4$) organic layer afforded the crude alcohol **7** as a yellow oil.

The latter was taken up in 60 mL of THF, and 6 mL of HBF_4 (48% aqueous solution) was added slowly at 25 °C. The reaction mixture was stirred for 15 min and then poured into ether. The organic layer was washed twice with 5% $NaHCO_3$ and once with water. Evaporation of the dried ($MgSO_4$) organic layer gave a deep yellow oil, from which 4.7 g (67%) of **8** was isolated as a colorless liquid by fractional distillation: bp 105–108 °C (0.5 mmHg); ^1H NMR ($CDCl_3$) δ 5.58 (br s, 1 H, C=CH), 4.72 (m, 2 H, C=CH_2), 3.88 (t, J = 7.6 Hz, 1 H, COCH), 3.05 (m, 2 H, $COCH_2$), 1.77–2.25 (m, 8 H, alicyclic), 1.73 (s, 3 H, CH_3), 1.45 (m, 1 H, alicyclic); IR (neat) 2975, 2925, 2840, 1785, 1640, 1450, 1430, 1070, 885 cm^{-1}; exact mass calcd for $C_{13}H_{18}O$: 190.1358; found: 190.1364.

Reduction of 8 with Lithium Aluminum Hydride. To a stirred solution of 3.46 g (18.2 mmol) of **8** in 75 mL of anhydrous ether at 0 °C was added $LiAlH_4$ (1.58 g, 41.5 mmol). After 30 min, water (1.6 mL), 15% NaOH (1.6 mL), and then water (4.8 mL) were carefully added. The white granular precipitate was removed by filtration, and the filtrate was washed with water. The organic phase was dried ($MgSO_4$) and the solvent removed by evaporation. The yellow oil thus obtained gave a colorless oil on Kugelrohr disstillation, 90 °C (1 mmHg). The product (**9**) was found to be a mixture of 18% (*Z*)-2-(4-(2-propenyl)cyclohexen-1-yl)cyclobutanol (*Z*-**9**) (R_f 0.38, 20% ethyl acetate in hexanes) and 82% of *E*-**9** (R_f 0.25, 20% ethyl acetate in hexanes). These were separated by flash chromatography (22% ethyl acetate in hexanes).

***Z* isomer of 9**: ^1H NMR ($CDCl_3$) δ 5.64 (br s, 1 H, C=CH), 4.69 (br s, 2 H, C=CH_2), 4.31 (m, 1 H, C*H*OH), 3.00 (m, 1 H, allylic, cyclobutane), 1.80–2.35 (m, 11 H, alicyclic and OH), 1.76 (s, 3 H, CH_3), 1.55 (m, 1 H, alicyclic); IR (neat) 3400, 2950, 2925, 2850, 2825, 1640, 1450, 1435, 1100, 885 cm^{-1}; exact mass calcd for $C_{13}H_{20}O$: 192.1514; found: 192.1514.

***E* isomer of 9**: ^1H NMR ($CDCl_3$) δ 5.46 (br s, 1 H, C=CH), 4.71 (br s, 2 H, C=CH_2), 3.97 (m, 1 H, C*H*OH), 2.60 (m, 1 H, allylic, cyclobutane), 1.30–2.18 (m, 12 H, alicyclic and OH), 1.73 (s, 3 H, CH_3); IR (neat) 3325, 2975, 2940, 2910, 2880, 2825, 1640, 1450, 1440, 1100, 885 cm^{-1}; exact mass calcd for $C_{13}H_{20}O$: 192.1514; found: 192.1514. The stereochemical assignments are based on (1) the preparation of the *Z* isomer exclusively by the sterically hindered reducing agent K-Selectride (see below) and (2) the chromatographic and NMR characteristics that are completely in accord with those found by Trost for analogous 2-vinylcyclobutanols.[22]

(*Z*)-2-(4-(2-Propenyl)cyclohexen-1-yl)cyclobutanol (9). To a solution of 210 mg (1.09 mmol) of **8** in 1 mL of THF at 0 °C was added 2.5 mL (1.25 mmol) of a 0.50 M THF solution of K-Selectride (Aldrich). After 30 min, 1 mL of 20% aqueous sodium hydroxide and 1 mL of 30% aqueous hydrogen peroxide solutions were carefully added. After 30 min more, the mixture was poured into ether and washed with 5% aqueous sodium thiosulfate solution and with brine. The organic phase was dried ($MgSO_4$) and the solvent removed by evaporation. Flash chromatography (13% ethyl acetate in hexanes) gave 198 mg (94%) of the title compound as a colorless oil. The spectral characteristics were identical with those of the *Z* isomer prepared by reduction using lithium aluminum hydride.

Oxidation of (*Z*)- and (*E*)-2-(4-(2-Propenyl)cyclohexen-1-yl)cyclobutanol (9).[23] To a solution of 70 mg (0.35 mmol) of the *Z* or *E* alcohol in acetone was added Jones reagent in drops at 25 °C, until the reaction mixture attained a permanent yellowish tinge. The reaction mixture, which contained a green precipitate, was poured into ether, and the organic layer was washed twice with 5% $NaHCO_3$ and once with water. The dried ($MgSO_4$) organic layer gave, after evaporation, a colorless oil in 98% yield from the *Z* alcohol and in 96% yield from the *E* alcohol. The product was found to be the same γ-lactone, 4,5-dihydro-5-(4-(2-propenyl)cyclohexen-1-yl)-2(3*H*)-furanone, from either the *Z* or *E* isomer. The compound gave a single spot on analytical TLC (R_f 0.16, 20% ethyl acetate in hexanes): ^1H NMR ($CDCl_3$) δ 5.81 (br s, 1 H, C=CH), 4.87 (t, J = 7.5 Hz, 1 H, COOCH), 4.73 (m, 2 H, C=CH_2), 2.55 (m, 2 H, $COCH_2$), 1.46–2.36 (m, 9 H, alicyclic), 1.74 (s, 3 H, CH_3); IR (neat) 2900, 1770, 1640, 1450, 1430, 1180, 1170, 1140, 920, 890 cm^{-1}; exact mass calcd for $C_{13}H_{18}O_2$: 206.1307; found: 206.1307.

(35) Tanaka, K.; Uneme, H.; Matsui, S.; Tanikaga, R.; Kaji, A. *Chem. Lett.* **1980**, 287.

(36) Fieser, L. F.; Fieser, M. "Reagents for Organic Synthesis"; Wiley: New York, 1967; Vol. I, p 584.

Rearrangement of *Z* Alcohol 9 to *E* Alcohol 9. To a solution of 88 mg (0.46 mmol) of the *Z* alcohol **9** in 5 mL of THF at 0 °C was added excess potassium hydride, and the reaction was followed by TLC. Even after 30 min, there was no observable change. Hence, the reaction mixture was warmed to 25 °C. Over a 30-min period, the starting material (R_f 0.38, 20% ethyl acetate in hexanes) completely disappeared and a new spot (R_f 0.25, 20% ethyl acetate in hexanes), due to the *E* alcohol **9**, appeared. The reaction mixture was quenched with water and poured into ether. The organic layer was washed with water and dried ($MgSO_4$). Rotary evaporation of the solvent gave 87 mg (99%) of a colorless oil, which was found to have identical spectral characteristics with those of the *E* alcohol **9**.

Rearrangement of the Mixture of Cyclobutanols 9 to the Cyclohexenols 10. To a solution of 4.24 g (22.1 mmol) of **9** in 50 mL of THF was added excess potassium hydride, and the mixture was heated at reflux for 1 h. The reaction mixture was cooled to 25 °C, quenched with water, and poured into ether. The organic layer was washed with water and dried ($MgSO_4$). Removal of the solvent gave **10** as a yellow oil. The crude compound gave a single spot on analytical TLC, but its NMR spectrum showed that it consisted of at least two stereoisomers: ^{1}H NMR ($CDCl_3$) δ 5.39 (m, 1 H, C=CH), 4.94 (m, 1 H, C=CH_2), 4.68 (d, 1 H, C=CH_2), 3.45–3.97 (m, 1 H, C*H*OH), 1.21–2.47 (m, 13 H, alicyclic and OH), 1.76 and 1.73 (s, 3 H, CH_3); IR (neat) 3350, 2900, 2850, 1640, 1440, 1430, 1050, 880 cm^{-1}.

3,4,5,6,7,8-Hexahydro-7-(2-propenyl)-1(2*H*)-naphthalenone (12). To a solution of the crude alcohol **10** in 80 mL of acetone was added Jones reagent in drops. A green precipitate formed. The addition was continued until the reaction mixture attained a permanent yellow tinge. The reaction mixture was partitioned between ether and water, and the organic layer was washed twice with 10% $NaHCO_3$ and once with water. The dried ($MgSO_4$) organic layer, upon evaporation, gave crude **11** as a red oil: IR (neat) 2960, 2925, 2850, 1710, 1640, 1440, 1200, 885 cm^{-1}. The unconjungated ketone **11** was passed through a column of basic, activity 3 EM alumina 90 (3% ethyl acetate in hexanes) to obtain the conjugated ketone **12**. Kugelrohr distillation, 105 °C (0.5 mmHg), of the product gave 2.71 g (64.5% from **9**) of **12** as a pale yellow oil: $[\alpha]^{25}_D$ − 187.9° (*c* 12.8, CCl_4); ^{1}H NMR (CCl_4) δ 4.7 (br s, 2 H, C=CH_2), 1.1–2.7 (m, 13 H, alicyclic), 1.75 (s, 3 H, CH_3); IR (neat) 2950, 2875, 1665, 1640, 1455, 1430, 1390, 1260, 1200, 890, 870 cm^{-1}; exact mass calcd for $C_{13}H_{18}O$: 190.1358; found: 190.1358.

7-(2-Propenyl)-4a-methyl-3,4,4a,5,6,7,8,8a-octahydro-1(2*H*)-naphthalenone (13). A suspension of 4.48 g (23.5 mmol) of purified (Soxhlet extraction with THF overnight) cuprous iodide in 30 mL of anhydrous ether was cooled to −40 °C (dry ice/ethylene dichloride), and 15.7 mL (23.5 mmol) of methyllithium (Alfa, 1.5 M in ether) was added in drops. After 5 min, the reaction mixture was cooled to −70 °C and BF_3·Et_2O (2.9 mL, 24 mmol) was slowly added. After 2 min, a solution of 1.49 g (7.84 mmol) of the enone **12** in 10 mL of ether was added at −70 °C. The mixture was allowed to warm slowly to room temperature, and the reaction mixture was quenched with water, stirred in ammonium chloride solution, and filtered through a sintered-glass filter. The filtrate was partitioned between ether and water. The dried ($MgSO_4$) organic layer, upon evaporation, gave a yellow oil. Silica gel chromatography (5% ethyl acetate in hexanes) gave 0.75 g (46%) of the title compound as the second fraction. This fraction gave two spots (R_f 0.31 and 0.37 in 5% EtOAc) on analytical TLC: ^{1}H NMR (CCl_4) δ 4.7 (br s, 2 H, C=CH_2), 0.9–2.4 (m, 14 H, alicyclic), 1.75 (s, 3 H, C=CCH_3), 0.8 (s, 3 H, CCH_3); IR (neat) 2950, 1715, 1640, 1450, 1390, 895 cm^{-1}; exact mass calcd for $C_{14}H_{22}O$: 206.1671; found: 206.1669. The first fraction (0.53 g, 33%) obtained in the chromatographic separation was a hydrocarbon (R_f 0.8 in 5% EtOAc), probably formed by 1,2 addition followed by dehydration.

(−)-β-Selinene (14). Sodium hydride (Ventron Corp, 50% in oil, 92 mg, 1.92 mmol) was washed with pentane in the reaction flask under argon. Freshly distilled (over CaH_2) dimethyl sulfoxide (4 mL) was injected into the system, and the mixture was stirred at 80 °C until hydrogen evolution ceased (30 min). The flask was then cooled to 0 °C, a solution of 0.93 mg (2.6 mmol) of methyltriphenylphosphonium bromide in 4 mL of Me_2SO was added, and the mixture was warmed to 25 °C. After 10 min, a solution of 0.38 g (1.8 mmol) of **13** in 3 mL of Me_2SO was added. The mixture was stirred at 80 °C for 70 h, cooled, and poured into an equal amount of water. The mixture was extracted with four 10-mL portions of pentane. The combined pentane extract was washed twice with 1:1 Me_2SO/H_2O and finally with water. The dried ($MgSO_4$) organic layer upon evaporation gave a yellow oil, which was adsorbed on a short silica gel column and eluted with pentane to give 0.23 g (61%) of the title compound. Then the column was eluted with 5% ethyl acetate in hexanes to recover 0.13 g (34%) of unreacted **13**. Capillary GLC (pentaphenyl ether column) of the product showed that 95.5% of the product was the title compound and the remainder was a single isomer: $[\alpha]^{25}_D$ −49.5° (*c* 6.55, hexanes); ^{1}H NMR (CCl_4) δ 4.7 (s, 3 H, vinyl), 4.4 (s, 1 H, vinyl), 0.9–2.15 (m, 14 H, alicyclic), 1.7 (s, 3 H, C=CCH_3), 0.75 (s, 3 H, CCH_3); IR (neat) 3080, 2925, 2840, 1640, 1440, 1380, 890 cm^{-1}; exact mass calcd for $C_{15}H_{24}$: 204.1878; found: 204.1876.

2-(2-Furyl)cyclobutanone (16). To a solution of 31 mmol of 1-lithio-1-methoxycyclopropane in 55 mL of THF at −78 °C was added freshly distilled furfural (2.50 mL, 30.2 mmol). After 10 min, the product was worked up in the same manner as **2**. Considerable heat was evolved during the extraction with 5% HCl, but TLC indicated that very little rearrangement to **16** had occurred. The crude alcohol was taken up in 18 mL of THF, and 2 mL of concentrated HBF_4 was added; the reaction was mildly exothermic. After the reaction mixture had been stirred for 10 min, it was partitioned between ether and water. The organic phase was washed with 5% $NaHCO_3$, dried ($MgSO_4$), and evaporated to give a reddish oil. Silica gel chromatography (5% ethyl acetate in hexanes) gave the crude product as a yellow oil. Kugelrohr distillation, 60–65 °C (0.35 mmHg), provided 2.21 g (54%) of the ketone as very pale yellow oil; ^{1}H NMR (CCl_4) δ 7.31 (m, 1 H, 5-furyl H), 6.28 (m, 1 H, 3- or 4-furyl H), 6.10 (m, 1 H, 3- or 4-furyl H), 4.43 (m, 1 H, CH_2CHCO), 2.92–3.12 (m, 2 H, CH_2CO), 1.98–2.60 (m, 2 H, CH_2CH_2CO); IR (neat) 2950, 1790, 1595, 1500, 1145, 1075, 1004, 726 cm^{-1}; exact mass calcd for $C_8H_8O_2$: 136.0524; found: 136.0524.

2-(2-Furyl)cyclobutanol (17). The procedure was the same as that used to prepare **3**. From 708 mg (5.21 mmol) of 2-(2-furyl)cyclobutanone was obtained, after Kugelrohr distillation, 65–70 °C (0.3 mmHg), 689 mg (96%) of the mixture of cyclobutanols **17** as a colorless oil; ^{1}H NMR (CCl_4) δ 7.37 (d, J = 1 Hz) and 7.28 (d, J = 1 Hz, 1 H, aryl), 6.3–6.5 (m, 1 H, aryl), 6.13 (d, J = 3 Hz) and 5.97 (d, J = 3 Hz, 1 H, aryl), 4.0–4.6 (m, 1 H, C*H*OH), 3.6–3.8 and 3.0–3.4 (m, 1 H, ArC*H*), 1.5–2.4 (m, 5 H, alicyclic + OH); IR (neat) 3350, 2980, 2950, 1592, 1305, 1230, 1145, 1105, 1008, 980, 790, 730 cm^{-1}; exact mass calcd for $C_8H_{10}O_2$: 138.0681; found: 138.0683.

Rearrangement of 17. The procedure was the same as that for the rearrangement of **3** except that it was performed at 25 °C for 16 h; from 288 mg (7.09 mmol) of **17** in 10 mL of THF was isolated, after column chromatography on silica gel (10% ethyl acetate in hexanes) and Kugelrohr distillation, 65–70 °C (0.3 mmHg), 95 mg (33%) of **18** as a colorless oil; ^{1}H NMR (CCl_4) δ 7.21 (d, J = 1 Hz, H_5 of furan), 6.32 (d, J = 1 Hz, H_4 of furan), 4.54 (m, 1 H, HOC*H*Ar), 3.02 (br s, 1 H, OH), 3.4–3.6 (m, 2 H, CH_2Ar), 1.5–2.1 (m, 4 H, alicyclic); IR (neat) 3350, 2940, 2850, 1625, 1505, 1438, 1420, 1222, 1127, 1058, 1030, 980, 950, 935, 885, 720 cm^{-1}; exact mass calcd for $C_8H_{10}O_2$: 138.0681; found: 138.0678.

2-(2-Furyl)-1-methylcyclobutanol (19). To a solution of 645 mg (4.74 mmol) of 2-(2-furyl)cyclobutanone in 7.5 mL of pentane at 0 °C was added 2.5 mL of MeMgBr in ether (3.0 M, 7.5 mmol). Upon addition of the Grignard reagent, a solid formed immediately, thus making stirring of the solution impossible. After addition was complete, the reaction mixture was allowed to stand for 10 min before it was poured into ice. This solution was extracted with ether, and the organic phase was dried ($MgSO_4$). TLC indicated the presence of unreacted starting material with the mixture of cyclobutanols. The solvent was removed under reduced pressure to give a yellow oil. This oil was taken up in anhydrous ether (8 mL), and the Grignard reagent was again added (2.5 mL, 7.5 mmol). The reaction mixture was worked up as described above. Again TLC showed some starting cyclobutanone. The alcohols were purified by chromatography on silica gel by using 5% EtOAc in hexanes (completely separated the cis–trans alcohols). The alcohols were combined to give 342 mg (48%) of the cyclobutanols as a colorless oil (an accident caused some loss of product, so this represents a minimum yield): ^{1}H NMR (CCl_4) δ 7.37 (d, J = 1 Hz) and 7.30 (d, J = 1 Hz) (combined peak = 1 H, H_5 of furan), 6.3–6.5 (m, 1 H, H_3 or H_4 of furan), 6.13 (d, J = 3 Hz) and 5.99 (d, J = 3 Hz) (combined peaks = 1 H, H_3 or H_4 of furan), 3.3–3.5 (m, 1 H, cyclobutane carbinyl H), 1.7–2.3 (m, 5 H, alicyclic + OH), 1.33 and 1.07 (s, 3 H, CH_3); IR (neat) 3400, 2960, 1595, 1505, 1255, 1145, 1010, 985, 948, 800, 730 cm^{-1}; exact mass calcd for $C_9H_{12}O_2$: 152.0837; found: 152.0839.

Rearrangement of 19. The procedure was the same as for the rearrangement of **3** except that it was complete after 1 h at 25 °C; from 222 mg (1.46 mmol) of **19** in 8 mL of THF was isolated, after Kugelrohr distillation, 65–70 °C (0.3 mmHg), 184 mg (83%) of the ketone **20** as a pale yellow oil: ^{1}H NMR (CCl_4) δ 7.20 (d, J = 1 Hz, 1 H, H_5 of furan), 6.2–6.3 (m, 1 H, H_4 of furan), 5.90 (d, J = 4 Hz, 1 H, H_3 of furan), 2.60 (t, J = 7 Hz, 2 H, CH_2COCH_3), 2.34 (t, J = 7 Hz, 2 H, ArCH_2), 2.02 (s, 3 H, CH_3), 1.84 (m, $CH_2CH_2CH_2CO$); IR (neat) 2950, 1718, 1600, 1510, 1370, 1150, 1010, 730 cm^{-1}; exact mass calcd for $C_9H_{12}O_2$: 152.0837; found: 152.0837.

2-Bromo-1,3-cyclohexadiene. To a clear, stirred solution of 0.436 g (3.89 mmol) of potassium *tert*-butoxide in 25 mL of THF at 0 °C was

added slowly a solution of 0.765 g (3.2 mmol) of 2,3-dibrmocyclohexene[27] in 5 mL of THF. The reaction mixture turned pale brown and then a white precipitate appeared. When TLC showed the absence of starting material, the reaction mixture was quenched with ammonium chloride solution and poured into ether. The organic layer was washed with ammonium chloride solution and water. The dried ($MgSO_4$) organic layer gave a yellow oil on evaporation of the solvent. This oil, upon fractional distillation in the presence of the radical inhibitor 3-*tert*-butyl-4-hydroxy-5-methylphenyl sulfide, gave 246 mg (39.7%) of the title compound as a pale yellow liquid: bp 48 °C (18 mmHg); ^1H NMR ($CDCl_3$) δ 6.04 (m, 1 H, vinyl), 5.92 (m, 1 H, vinyl), 5.83 (m, 1 H, vinyl), 2.20 (m, 4 H, allylic); IR (neat) 3050, 2940, 2870, 2810, 1620, 1420, 1390, 1340, 1320, 1280, 1165, 1000, 940, 800, 710 cm^{-1}; exact mass calcd for C_6H_7Br: 159.9711; found: 159.9711.

1,3-Cyclohexadiene-2-carboxaldehyde (21). To a solution of 606 mg (3.8 mmol) of 2-bromo-1,3-cyclohexadiene in 8 mL of THF at −78 °C was added slowly 4.2 mL (4.2 mmol) of *sec*-butyllithium (Aldrich, 1.01 M in cyclohexane). The reaction mixture turned canary yellow. After 40 min, freshly distilled DMF was added at −78 °C; the reaction mixture turned clear. It was warmed to 0 °C, and after 1 h it was quenched with 5% acetic acid and poured into ether. The organic layer was washed with water and dried ($MgSO_4$). Evaporation of the solvent gave a yellow oil, which on Kugelrohr distillation, 65 °C (16 mmHg), gave 296 mg (72.1%) of the title compound as a pale yellow oil; ^1H NMR ($CDCl_3$) δ 9.38 (s, 1 H, CHO), 6.76 (m, 1 H, vinyl), 6.40 (m, 1 H, vinyl), 6.02 (m, 1 H, vinyl), 2.50 (m, 2 H, allylic), 2.28 (m, 2 H, allylic); IR (neat) 3050, 2950, 2825, 2730, 1690, 1640, 1600, 1440, 1420, 1360, 1310, 1250, 1190, 950, 835, 810, 750, 710 cm^{-1}; exact mass calcd for C_7H_8O: 108.0575; found: 108.0576.

2-(1,3-Cyclohexadien-2-yl)cyclobutanone (22). To a solution of 2.5 mmol of 1-lithio-1-methoxycyclopropane (**5**) in 14 mL of THF at −78 °C was added a solution of 250 mg (2.31 mmol) of **21** in 3 mL of THF. The dark green color of the reaction mixture disappeared almost immediately. After 15 min, the reaction mixture was quenched with water and poured into ether. The organic layer was washed twice with water to remove lithium thiophenoxide and twice with 5% HCl to remove DMAN. Evaporation of the dried ($MgSO_4$) organic layer afforded crude 1-(1,3-cyclohexadien-2-yl)-1-methoxy-1-cyclopropylmethanol as a yellow oil.

To a solution of the crude alcohol in 10 mL of THF at 0 °C was added HBF_4 (1 mL of 48% aqueous solution); an endothermic reaction ensued. When the rearrangement was monitored by TLC, it appeared that the product slowly decomposed during its formation. The reaction was terminated after 20 min; at this time some starting material was still present, but substantial decomposition of product had not occurred. The recovered starting material was sometimes recycled. The reaction mixture was poured into ether, and the mixture was washed twice with 10% $NaHCO_3$ and once with water. The dried ($MgSO_4$) organic layer gave a yellow oil upon evaporation of the solvent. The title compound was isolated as a colorless oil (178 mg, 52%) by flash chromatography (10% ethyl acetate in hexanes): ^1H NMR ($CDCl_3$) δ 5.87 (m, 2 H, vinyl), 5.63 (m, 1 H, vinyl), 3.95 (t, J = 7.9 Hz, 1 H, COCH), 3.01 (m, 2 H, $COCH_2$), 1.93–2.31 (m, 6 H, alicyclic); IR (neat) 3050, 2940, 2875, 2825, 1780, 1650, 1420, 1395, 1350, 1240, 1200, 1070, 820, 730 cm^{-1}; exact mass calcd for $C_{10}H_{12}O$: 148.0888; found: 148.0888.

Reduction of Cyclobutanone 22 with Lithium Aluminum Hydride. To a solution of 363 mg (2.45 mmol) of **22** in 40 mL of ether at 0 °C was carefully added lithium aluminum hydride (280 mg, 7.4 mmol). After 15 min, the reaction mixture was warmed to 25 °C. After 20 min, 1.3 mL of water, 1.3 mL of 15% NaOH, and 4.0 mL of water were carefully added successively. The white granular precipitate was removed by filtration, and the filtrate was washed with water. The organic phase was dried ($MgSO_4$) and the solvent removed by evaporation. TLC of the product showed two spots; the faster moving component (R_f 0.34, 20% ethyl acetate in hexanes) was identified as (*Z*)-2-(1,3-cyclohexadien-2-yl)cyclobutanol (**24**) and the slower moving component (R_f 0.27, 20% ethyl acetate in hexanes) as the E isomer **23**. Flash chromatography (22% ethyl acetate in hexanes) of the mixture gave 105 mg (28.5%) of **24** and 237 mg (64.5%) of **23**.

24: ^1H NMR ($CDCl_3$) δ 5.87 (m, 2 H, vinyl), 5.72 (br s, 1 H, vinyl), 4.36 (br s, 1 H, C*H*OH), 3.15 (m, 1 H, allylic, cyclobutane), 1.67–2.34 (m, 9 H, alicyclic and OH); IR (neat) 3410, 3050, 2940, 2860, 2830, 1640, 1420, 1385, 1340, 1210, 1090, 830, 720 cm^{-1}; exact mass calcd for $C_{10}H_{14}O$: 150.1045; found: 150.1044.

23: ^1H NMR ($CDCl_3$) δ 5.91 (m, 2 H, vinyl), 5.62 (m, 1 H, vinyl), 4.00 (m, 1 H, C*H*OH), 2.65 (m, 2 H, allylic), 1.33–2.26 (m, 8 H, alicyclic and OH); IR (neat) 3380, 3050, 2965, 2870, 2825, 1640, 1420, 1380, 1350, 1200, 1090, 830, 730 cm^{-1}; exact mass calcd for $C_{10}H_{14}O$: 150.1045; found: 150.1042.

(*Z*)-2-(1,3-Cyclohexadien-2-yl)cyclobutanol (24). To a solution of 163 mg (1.09 mmol) of **22** in 1 mL of THF was added K-Selectride (2.5 mL, 1.25 mmol, Aldrich, 0.5 M in THF). After 30 min, solutions of 20% aqueous sodium hydroxide (1 mL) and 30% aqueous hydrogen peroxide (1 mL) were slowly added. After 30 min, the mixture was poured into ether and washed with 5% aqueous sodium thiosulfate solution and brine. The organic phase was dried ($MgSO_4$) and the solvent removed by evaporation. Flash chromatography (30% ethyl acetate in hexanes) of the product gave 125 mg (76%) of the title compound, the spectral characteristics of which were identical with that of **24** isolated from the reduction with $LiAlH_4$.

Rearrangement of (*Z*)-2-(1,3-Cyclohexadien-2-yl)cyclobutanol (24) with KH at −23 °C. To a solution of 16 mg (0.11 mmol) of **24** in 2 mL of THF at −23 °C was added excess KH, and the reaction was followed by TLC. After 3 h, the starting material had disappeared and the reaction mixture was quenched with water and poured into ether. The organic layer was washed with water and dried ($MgSO_4$). The solvent was removed by evaporation to provide 15.8 mg (98.7%) of the product. A 300-MHz NMR spectrum of the product mixture showed the presence of **23**, **25**, and **26** in the ratio of 25:57:18.

In Refluxing THF. To a solution of 30 mg (0.20 mmol) of **24** in 3 mL of THF was added excess KH, and the reaction mixture was heated at reflux for 1 h, cooled to 25 °C, and quenched with water. The mixture was poured into ether, and the organic layer was washed with water. Evaporation of the dried ($MgSO_4$) organic layer gave 27.8 mg (92.6%) of the product. Flash chromaotgraphy (25% ethyl acetate in hexanes) gave **25** as a white solid and **26** as a colorless liquid in the ratio 72:28.

Axial Alcohol 25: ^1H NMR ($CDCl_3$) δ 6.04 (d, J = 9.7 Hz, 1 H, vinyl), 5.73 (m, 1 H, vinyl), 5.69 (br s, 1 H, vinyl), 4.01 (s, half-width 15.0 Hz, 1 H, C*H*OH), 1.40–2.39 (m, 10 H, alicyclic and OH) [The peak at δ 4.01 narrowed to a multiplet with half-width 8.8 Hz after removing the coupling with the OH proton by addition of diisopropyl amine. The three remaining coupling constants are approximately 2.6, 2.6, and 3.6 Hz.]; exact mass calcd for $C_{10}H_{14}O$: 150.1045; found: 150.1044. The equatorial alcohol **26**, as isolated from the rearrangement of **24**, was contaminated with its epimer **25**.

26: ^1H NMR ($CDCl_3$) δ 6.04 (d, J = 9.5 Hz, 1 H, vinyl), 5.72 (m, 1 H, vinyl), 5.43 (br s, 1 H, vinyl), 3.51 (m, 1 H, C*H*OH), 1.2–2.4 (m, 10 H, alicyclic and OH) [When the peak at δ 3.51 was decoupled from the OH hydrogen by the addition of diisopropyl amine, it narrowed by 4.66 Hz, and the remaining coupling constants were revealed to be 11.12, 8.08 and 3.64 Hz.]; exact mass calcd for $C_{10}H_{14}O$: 150.1045; found: 150.1044.

Rearrangement of (*E*)-2-(1,3-Cyclohexadien-2-yl)cyclobutanol (23). To a solution of 114 mg (0.76 mmol) of **23** in 8 mL of THF was added excess potassium hydride. After the mixture had been heated at reflux for 1 h, it was cooled to 25 °C and quenched with water. The reaction mixture was poured into ether, and the organic layer was washed with water. Rotary evaporation of the dried ($MgSO_4$) organic layer gave 106 mg (93%) of a white solid; 300-MHz NMR showed the product to be a mixture of **25** and **26** in the ratio 92:8.

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