Supplementary Material Available: 300-MHz NMR spectra of **9**, **10**, and its endo,endo-epimer, and **14**; experimental for the X-ray structure determinations; and tables of crystal data, intensity data collection, structure refinement, final positional parameters, anisotropic thermal parameters, bond lengths, and bond angles for **8** and **10**; internal coordinates for **A–F** (Table I); and the pair of structures of Figure 5 (31 pages). Ordering information is given on any current masthead page.

Regio- and Stereoselective Oxidation of Unsaturated Bicyclo[2.2.2]octanones with Selenium Dioxide

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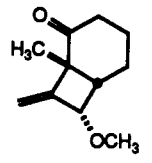
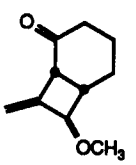
The selenium dioxide oxidation of several unsaturated bicyclo[2.2.2]octanones has been examined in connection with the projected utility of properly functionalized products in tandem oxyanionic Cope rearrangement–S_N' transformations. The oxidations studied proved to be regioselective, with attack in the olefinic sector of each molecule occurring to the exclusion of chemical reaction α to the carbonyl. Stereoselectivity was also often encountered, with steric factors appearing to contribute heavily to establishing the particular configuration of the newly introduced stereogenic center.

Earlier disclosures from this laboratory have demonstrated the feasibility of tandem anionic oxy-Cope rearrangement–S_N' allylic ether displacement as a powerful tool for multiple C–C bond construction with rapid elaboration of complex polycyclic frameworks.[1,2] The structural features essential to those alcohols that can undergo this reaction cascade can be assembled in two ways. In the first, represented by **1–3**, the alkoxy group is present in the electrophilic ketone precursor.[1] Alternatively, the ultimate leaving group can reside in the vinyl anion segment as exemplified by **4**.[2]



1



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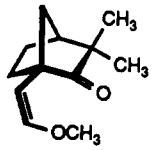

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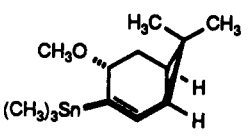

4

The serviceability of this new methodology rests to a degree upon ready access to precursor molecules of the type **1–4**. Compounds from the classes represented by **3** and **4** are readily prepared[3,4] and present no obvious availability problems. In contrast, **1** and **2** constitute small, multiply functionalized molecules of a category that has been accorded little past attention. The need for a β,γ-unsaturated ketone subunit where the double bond also forms part of an allyl ether moiety should be capable of elaboration from several diverse directions. In the case of **1** and **2**, recourse was made to the [2 + 2] photocycloaddition of methoxyallene to a 2-cyclohexenone.[5]

In the present paper, we describe a series of observations made in conjunction with an examination of the oxidation of several selected unsaturated bicyclo[2.2.2]octanones with selenium dioxide. Our goal was to gain insight into the reliability of an approach wherein an allylic oxygen was incorporated into systems in which the carbonyl group and double bond are already present. Should the regiochemistry and stereoselectivity of these oxidations proceed at acceptable levels, future implementation of this strategy would hold promise and be attractive.

Results and Discussion

As a consequence of its unique position as an oxidant, selenium dioxide has received considerable attention and several detailed reviews of its chemistry are available.[6-10] Stemming from this past work are several general reactivity patterns associated with alkene oxidation. The trends are seen to vary widely, depending on whether the olefin is cyclic or acyclic and, more critically, on the level of substitution about the double bond. Virtually without exception, the molecules studied have not also carried a ketone carbonyl, a functional group recognized in its own right to be prone to oxidation by SeO_2.

One need therefore inquire into several issues. One concern that arises immediately deals with relative reactivities at carbonyl and olefinic sites. Is there a suitably wide reactivity differential? Is allylic rearrangement a potential complication? If allylic alcohols are formed, is the oxidation regio- and/or stereoselective? Are the allylic alcohols prone to ready rearrangement and/or facile dehydration?

(1) Paquette, L. A.; Reagan, J.; Schreiber, S. L.; Teleha, C. A. *J. Am. Chem. Soc.* **1989**, *111*, 2331.
(2) (a) Paquette, L. A.; Shi, Y.-J. *J. Org. Chem.* **1989**, *54*, 5205. (b) Paquette, L. A.; Shi, Y.-J. *J. Am. Chem. Soc.*, in press.
(3) Paquette, L. A.; Teleha, C. A.; Taylor, R. T.; Maynard, G. D.; Rogers, R. D.; Gallucci, J. C.; Springer, J. P. *J. Am. Chem. Soc.* **1990**, *112*, 265.
(4) Paquette, L. A.; Ross, R. J.; Shi, Y.-J. *J. Org. Chem.* **1990**, *55*, 1589.
(5) Schreiber, S. L.; Reagan, J., unpublished observations.
(6) Campbell, T. W.; Walker, H. G.; Coppinger, G. M. *Chem. Rev.* **1952**, *50*, 279.
(7) Rabjohn, N. *Org. React.* **1949**, *5*, 331; **1976**, *24*, 261.
(8) Trachtenberg, E. N. In *Oxidation, Techniques and Applications in Organic Synthesis*; Augustine, R. L., Ed.; Marcel Dekker: New York, 1969; Chapter 3.
(9) Jerussi, A. In *Selective Organic Transformations*; Thyagarajan, B. S., Ed.; Wiley-Interscience: New York, 1970; Vol. I, p 301.
(10) Reich, H. J. In *Oxidation in Organic Chemistry*; Trahanovsky, W. S., Ed.; Academic Press: New York, 1978; Part C, Chapter 1.

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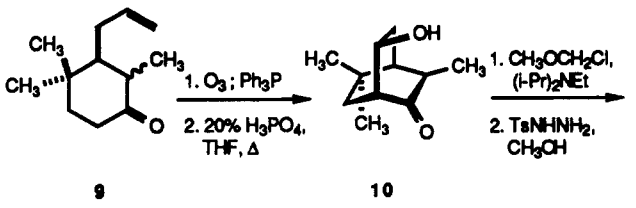
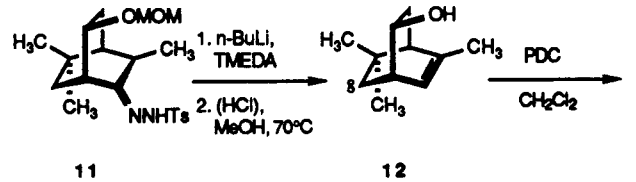
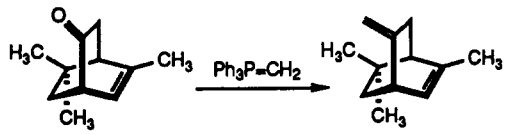
Scheme I



9 10

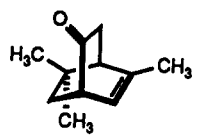


11 12

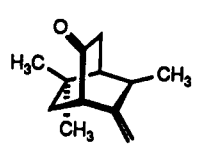


5 13

In order to probe these issues, the bicyclic enones **5**–**8** have been subjected to the action of SeO_2 in ethanol solution. While **5** and **6** are distinguished by the position of their double bond, **7** and **8** are identical in that respect, but differ in the degree to which the exocyclic π bond is substituted.



5



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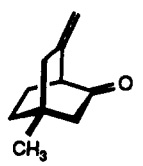
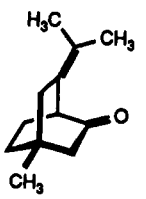


7

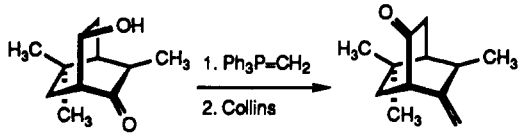


8

Of the various approaches that were considered for the synthesis of **5** and **6**, one seemed uniquely advantageous. Thus, the readily available tetrasubstituted cyclohexanone **9**[11] was ozonolyzed and subjected to intramolecular aldolization (Scheme I). Under conditions wherein catalysis was provided by 20% phosphoric acid in hot tetrahydrofuran, a 7:1 mixture of the syn and anti isomers was obtained in 84% overall yield. Two recrystallizations were adequate to provide diastereomerically pure **10**, whose stereochemistry was deduced subsequently by lanthanide-induced shifting (using $Eu(fod)_3$) on **12**. At the concentration level of 20% shift reagent, the vinyl proton experiences a downfield shift of 2.17 ppm, while the $\Delta\delta$ for exo-H-8 amounts only to 0.17 ppm. The predominant formation of **10** provides suggestive evidence that the

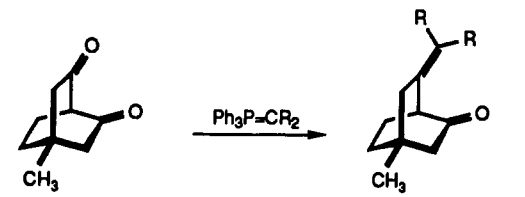
(11) Paquette, L. A.; Oplinger, J. A. *Tetrahedron* **1989**, *45*, 107.

Scheme II



10 6

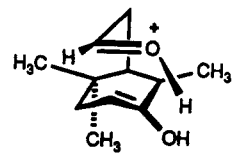
Scheme III



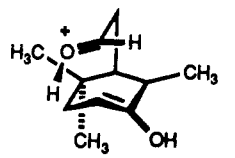
14

7, R = H
8, R = CH_3

synclinal transition state A is kinetically more favored than the antiperiplanar option B. However, the selectivity that



A



B

is observed could have a thermodynamic origin stemming from the possibility of intramolecular hydrogen bonding in the 6*S** isomer. When samples of the anti-enriched aldol mixture were resubjected to the acidic reaction conditions, little change in isomer distribution was noted. To all appearances then, **10** is formed preferentially under kinetic control.

Once the hydroxyl substituent in **10** was blocked as its MOM ether,[12] the derived tosylhydrazone **11** was subjected to the conditions of the Shapiro reaction.[13] Introduction of a double bond in this manner proceeded efficiently (73%) and without complication. Arrival at **5** was then accomplished conventionally.

For eventual comparison purposes, diene **13** was prepared by Wittig olefination of **5**.

With ample quantities of **10** in hand, a two-step protocol involving introduction of the exocyclic double bond and Collins oxidation made **6** quickly accessible (Scheme II).

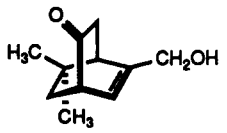
A short route to diketone **14** has previously been developed in this laboratory.[14] In the present work, the subsequent conversion to **7** was shown to be uneventful. The analogous involvement of isopropylidenetriphenylphosphorane in the Wittig condensation was similarly exploited to furnish **8** (Scheme III).

The oxidation of **5** with SeO_2 in 95% ethanol proved sluggish and required prolonged heating at the reflux temperature. After a reaction period of 48 h, 15% of unconsumed ketone could be recovered. In addition, the hydroxylated derivative **15** was isolated in 49% yield as the only identifiable product. The identification of **15** followed convincingly from its 300-MHz ^1H NMR spectrum where an allylic methyl absorption is no longer ob-

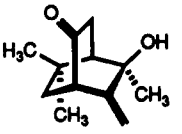
(12) Stork, G.; Takahashi, T. *J. Am. Chem. Soc.* **1977**, *99*, 1275.
(13) Shapiro, R. H. *Org. React.* **1976**, *23*, 405.
(14) (a) Poupart, M.-A.; Paquette, L. A. *Tetrahedron Lett.* **1988**, *29*, 269. (b) Poupart, M. A.; Lassalle, G.; Paquette, L. A. *Org. Synth.* **1990**, *69*, 173.

served, having been replaced by a two-proton singlet at δ 4.22 (in $CDCl_3$).

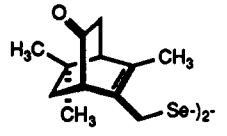
The response of **6** to the same reaction conditions was much more immediate. As a consequence of this enhanced reactivity, analysis was made of product distributions realized after reaction times of 1 and 30 h. We found following the shorter period of oxidation that three new compounds had been produced. The major constituent (56%) was identified as keto alcohol **16**. The structural elucidation of this product follows from the similarities of many of the ^1H NMR resonances to those of **6**. However, the original secondary methyl group in **6** (δ 1.10, d, J = 6.2 Hz) now appears as a singlet shifted to lower field (δ 1.67) due to the inductive influence of the geminal hydroxyl. The stereochemical assignment to **16** was also straightforward. In particular, the proximity of the hydroxyl substituent to the methylene group α to the carbonyl and especially its 1,3-diaxial relationship to the syn proton is clearly reflected in the chemical shift difference of this AB pair. While the two protons appear as a narrow multiplet centered at δ 2.30 in **6**, they are widely separated in **16** (δ 2.85 and 2.37). The hydroxyl group anisotropy clearly impacts on the syn-related methylene proton in the expected fashion.



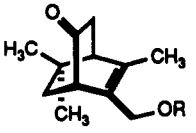
15



16



17



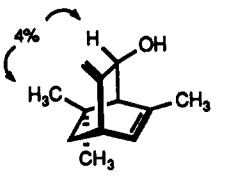
18a, R = C_2H_5
b, R=H

The second product quite unexpectedly proved to be the allylic diselenide **17** (27%). The composition of this substance was ascertained by combustion analysis and mass spectroscopy under chemical ionization conditions. The resonances of the pairs of allylic methyl (δ 1.89) and $-CH_2Se-$ groups (δ 3.87 and 3.63), with the latter assignments confirmed by C–H correlation, define the substitution pattern in that sector of the bicyclic frame where reaction has occurred.

Also obtained was a small amount of ether **18a** (3%). The more extended reaction period caused **18a** to predominate (53%). This is seemingly the result of one or more SeO_2-induced solvolytic processes involving initially formed **16** and **17**, since the related isomerized alcohol **18b** was now also present in relatively large amounts (32%).

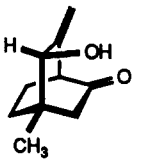
In contrast to the behavior of **5** and **6**, diene **13** was very responsive to the action of SeO_2. Simple admixing of the two reactants in 95% ethanol *at room temperature for 4 h* sufficed to consume all of the hydrocarbon. Alcohol **19** was formed predominantly (78%) in addition to several other products (14% combined yield) which were not characterized. The stereochemistry of **19** was established by an NOE experiment where double irradiation of the carbinol proton eventuates in a 4% enhancement of the signal involving the saturated methyl group. No comparable effect involving the allylic methyl group was seen.

Attention was next directed to **7**, a molecule offering the minimum level of steric congestion at its allylic and α-



19

carbonyl reaction centers. This feature was reflected in its rate of SeO_2 oxidation, the total consumption of **7** being complete within 45 min in refluxing ethanol. Two products were observed in roughy equal amounts, both resulting from allylic oxidation. The assignment of stereochemistry to keto alcohol **20** was based on NOE experiments and the appreciable chemical shift difference that materializes in the two protons of the methylene group α to the carbonyl. The syn hydroxyl configuration imparts an anisotropy effect that separates the narrow multiplet centered at δ 2.26 in **7** into a widely separated AB pair (δ 2.84 and 2.44). Diketone **21** arises as a consequence of the further oxidation of **20** under the reaction conditions.



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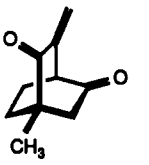
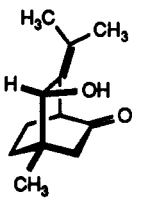
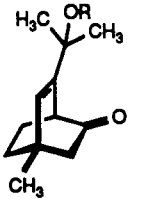


21

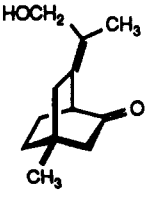


22

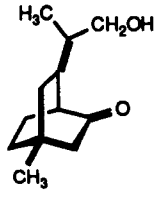


23a, R=H
b, R=CH_2CH_3

When **8** was reacted with SeO_2, a mixture of five products was obtained. These were amenable to chromatographic separation. The major component, isolated in 40% yield, was readily identified as keto alcohol **22** (δ_{AB} 2.53 and 1.94). The allylically transposed alcohol **23a** (8%) and its ethyl ether (10%), products that presumably arise from the intermediate responsible in common for the formation of **22**, were also seen. Since the final two oxidation products proved to be **24** (5%) and **25** (3%), the overwhelming preference for SeO_2 attack at the electron-rich sector was again seen.



24



25

The isolation of **15**, **16**, **20**, and **21** as major products constitutes evidence in support of the conclusion that oxidation occurred in every instance without preferential migration of the double bond. Of these examples, the production of **16** holds the most interest since the general reactivity rule ($CH_2 > CH_3 > CH$) is violated in order to

preserve the exocyclic nature of the olefinic site. The formation of **18a** arises from the capture of ethanol that is present in the reaction medium. The rigorous exclusion of water from oxidations otherwise performed in an alcohol solvent has earlier been shown to provide ethers in good yield.[7-10] The mode of formation for diselenide **17** is not known. However, selenium-containing byproducts have been isolated previously.[15,16] The co-production of **21** is believed to result from stoichiometric factors.

Oxidation about the carbonyl group in these molecules, if operative at all, is occurring at rates adequately slow that such processes do not interfere in a meaningful way. Also, while we have no reason to disagree with the mechanistic interpretation of alkene–SeO_2 oxidations that has been advanced by Sharpless and Lauer,[16] the exceptionally good stereochemical control seen here warrants proper assimilation. In the four relevant examples (**16**, **19**, **20**, and **22**), the hydroxyl is oriented toward the less sterically congested surface. We take this to be a reflection of the sensitivity of the attacking SeO_2 to prevailing steric factors rather than to some ill-defined post-equilibration scheme.[8]

In the final analysis, selenium dioxide has provided solid indication of being usefully deployable for achieving the regio- and stereoselective oxidation of unsaturated bicyclic ketones to allylic alcohols carrying carbonyl groups in close spatial proximity.

Experimental Section

Melting points are uncorrected. Infrared spectra were recorded on a Perkin-Elmer Model 1320 spectrometer. ^1H NMR spectra were recorded at 300 MHz and the ^{13}C NMR data obtained at either 75 or 20 MHz as indicated. Mass spectra were measured on a Kratos MS-30 instrument by Dick Weisenberger at The Ohio State University Chemical Instrumentation Center. Elemental analyses were performed at the Scandanavian Microanalytical Laboratory, Herlev, Denmark. All MPLC separations were conducted on Merck Lobar columns (Lichroprep Si-60) with the help of a Fluid Metering INC pump and a Waters Associates Model R403 differential refractometer detector. All reactions were performed under an inert atmosphere (nitrogen or argon) unless otherwise indicated. Solvents were reagent grade and dried prior to use.

6(*S)-Hydroxy-3(*R**),8,8-trimethylbicyclo[2.2.2]octan-2-one (10).** A cold (−78 °C), magnetically stirred solution of **9** (10.0 g, 56 mmol) in CH_2Cl_2 (150 mL) was ozonolyzed until a pale blue color developed. The reaction mixture was purged with nitrogen until colorless, whereupon a solution of triphenylphosphine in CH_2Cl_2 (166 mL of 1 M, 166 mmol) was introduced dropwise. After overnight stirring, the triphenylphosphine oxide was separated by filtration and the filtrate was concentrated. The residue was purified by chromatography on silica gel (elution with 5–20% ether in petroleum ether) to give 8.57 g (84.5%) of keto aldehyde as a coloreless oil that solidified upon storage at −10 °C: mp 112–122 °C; IR (neat, cm^{-1}) 1725, 1715; ^1H NMR (300 MHz, C_6D_6) δ 10.35 (s, 1 H), 2.16–1.92 (series of m, 5 H), 1.88–1.75 (series of m, 2 H), 1.21–1.06 (m, 3 H), 0.96–0.72 (m, 1 H), 0.69 (s, 3 H), 0.57 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 210.16, 179.72, 49.40, 46.55, 40.54, 37.95, 35.58, 33.59, 29.11, 19.26, 12.28; MS m/z (M^+) calcd 182.1307, obsd 182.1315.

A magnetically stirred solution of the keto aldehyde (2.0 g, 10.98 mmol) in 20% aqueous phosphoric acid (8 mL) and THF (8 mL) was refluxed for 10 h. After cooling, ether (20 mL) was added and the separated aqueous phase was extracted with ether (2 × 20 mL). The combined organic solutions were dried and evaporated, and the residue was recrystallized from ether–petroleum ether to give 1.67 g (84.4%) of a 7:1 diastereomeric mixture rich in **10**. A second recrystallization increased the ratio to 22:1: colorless needles; mp 92–93 °C; IR ($CHCl_3$, cm^{-1}) 3595, 3520–3300, 3059, 2963, 2940, 2876, 1715, 1505, 1422, 1315, 1110 1096, 900; ^1H NMR (300 MHz, $CDCl_3$) δ 4.24 (dt, J = 9.2, 3.7 Hz, 1 H), 2.65 (m, 1 H), 2.42 (m, 1 H), 2.32 (q, J = 3.1 Hz, 1 H), 1.84 (br s, 1 H), 1.63–1.48 (series of m, 4 H), 1.19 (d, J = 7.3 Hz, 3 H), 1.11 (s, 3 H), 1.07 (s, 3 H); ^{13}C NMR (20 MHz, $CDCl_3$) ppm 219.21, 68.88, 52.97, 45.12, 42.64, 36.14, 30.98, 30.54, 29.36, 27.94, 12.91; MS m/z (M^+) calcd 182.1307, obsd 182.1290.

Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.07; H, 9.95.

The mother liquor was evaporated and chromatographed on silica gel (elution with 40% ethyl acetate in petroleum ether) to separate residual **10** from its hydroxyl epimer: IR (neat, cm^{-1}) 3680–3060, 2968, 2950, 2865, 1712, 1449, 1388, 1367, 1292, 1124, 1083, 1060, 1040, 863; ^1H NMR (300 MHz, $CDCl_3$) δ 4.07 (m, 1 H), 2.53 (m, 1 H), 2.36 (q, J = 2.9 Hz, 1 H), 2.19 (dd, J = 9.7, 3.1 Hz, 1 H), 2.14 (dd, J = 9.7, 3.1 Hz, 1 H), 2.05 (dd, J = 14.4, 2.6 Hz, 1 H), 1.84 (dq, J = 15.1, 2.6 Hz, 1 H), 1.48 (q, J = 2.8 Hz, 1 H), 1.36 (dq, J = 13.9, 1.6 Hz, 1 H), 1.23 (s, 3 H), 1.06 (d, J = 7.3 Hz, 3 H), 1.02 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 219.01, 65.06, 53.61, 45.01, 41.56, 31.71, 31.13, 30.02, 29.60, 27.71, 14.05; MS m/z (M^+) calcd 182.1307, obsd 182.1322.

A magnetically stirred solution of pure *epi*-**10** (285 mg, 1.59 mmol) in 20% aqueous phosphoric acid (1 mL) and THF (1 mL) was refluxed for 16 h. The cooled reaction mixture was diluted with ether (5 mL), and the separated aqueous phase was extracted with ether (2 × 5 mL). The combined ethereal layers were dried and evaporated. ^1H NMR analysis of the residue indicated the **10**:epimer ratio to be 1:2.1.

Entirely comparable treatment of isomerically pure **10** delivered a mixture in which **10** still dominated (ratio 18.6:1).

6(*S)-(Methoxymethoxy)-3(*R**),8,8-trimethylbicyclo[2.2.2]octan-2-one Tosylhydrazone (11).** To a cold (0 °C), magnetically stirred solution of **10** (500 mg, 2.76 mmol) in THF (3 mL) was added diisopropylethylamine (442 mg, 3.04 mmol). After 15 min, chloromethyl methyl ether (247 mg, 3.04 mmol) in THF (3 mL) was introduced dropwise during 20 min and the reaction mixture was allowed to warm to room temperature. After 30 h, dilution with ether (20 mL) was affected, and this solution was washed with water (3 × 10 mL), dried, and evaporated. There was obtained 520 mg (83.7%) of the MOM ether as a pale yellow oil: IR (neat, cm^{-1}) 2960, 2931, 1720, 1448, 1367, 1148, 1105, 1040, 720; ^1H NMR (300 MHz, $CDCl_3$) δ 4.54 (d, J = 6.9 Hz, 1 H), 4.51 (d, J = 6.9 Hz, 1 H), 3.96 (m, 1 H), 3.25 (s, 3 H), 2.53 (m, 1 H), 2.39 (m, 1 H), 2.31 (m, 1 H), 1.60 (m, 1 H), 1.43 (dd, J = 9.8, 3.1 Hz, 2 H), 1.41 (m, 1 H), 1.09 (d, J = 7.3 Hz, 3 H), 1.04 (s, 3 H), 0.98 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 217.02, 94.67, 73.82, 73.72, 55.22, 49.44, 42.49, 36.41, 30.73, 30.47, 29.22, 26.27, 13.02; MS m/z (M^+) calcd 226.1571, obsd 226.1572.

Anal. Calcd for $C_{13}H_{22}O_2$: C, 68.99; H, 9.80. Found: C, 68.91; H, 9.80.

A solution of the above ketone (6.1 g, 27 mmol) in methanol (18 mL) was treated with tosyl hydrazide (6.02 g, 32 mmol) and stirred at room temperature for 16 h. The solvent was evaporated, and the residue was recrystallized from ether to give **11** (8.6 g, 81.6%) as a powdery, white solid: mp 116–117 °C; IR ($CHCl_3$, cm^{-1}) 2970, 2940, 2880, 1600, 1450, 1392, 1368, 1340, 1167, 1098, 1040; ^1H NMR (300 MHz, $CDCl_3$) δ 7.80 (m, 2 H), 7.26 (m, 2 H), 4.51–4.41 (m, 2 H), 3.80 (m, 1 H), 3.22 (d, J = 15.9 Hz, 3 H), 3.01–2.60 (series of m, 2 H), 2.41 (s, 3 H), 2.13 (m, 1 H), 1.38–1.15 (series of m, 5 H), 1.01–0.68 (m, 9 H); MS m/z (M^+) calcd 394.1926, obsd 394.1968.

Anal. Calcd for $C_{20}H_{30}N_2O_4S$: C, 60.89; H, 7.67. Found: C, 60.91; H, 7.79.

2,7,7-Trimethylbicyclo[2.2.2]oct-2-en-5(*S)-ol (12).** A cold (−78 °C), magnetically stirred solution of *n*-butyllithium (1.49 mL of 1.6 M in hexanes, 2.39 mmol) in dry TMEDA (3 mL) was treated dropwise with a solution of **11** (236 mg, 0.60 mmol) in TMEDA (1 mL) during 10 min. Hexane (1 mL) was introduced to facilitate stirring, which was continued for 3 h at 25 °C. The reaction mixture was quenched by the careful addition of water (5 mL) and diluted with ether (10 mL). The separated organic phase was washed with water (2 × 5 mL), dried, and evaporated. The residue was purified by silica gel chromatography (elution with 5% ethyl acetate in petroleum ether) to give 91.2 mg (72.6%) of the olefinic MOM ether: IR (neat, cm^{-1}) 2940, 2825, 1675, 1445, 1365, 1148, 1105, 1045, 922, 809, 740; ^1H NMR (300 MHz, $CDCl_3$)

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(16) Sharpless, K. B.; Lauer, R. F. *J. Am. Chem. Soc.* **1972**, *94*, 7154; **1973**, *95*, 2697; *J. Org. Chem.* **1972**, *37*, 3973.

δ 5.69 (m, 1 H), 4.63 (d, J = 6.9 Hz, 1 H), 4.59 (d, J = 6.9 Hz, 1 H), 3.84 (m, 1 H), 3.33 (s, 3 H), 2.62 (m, 1 H), 2.28 (m, 1 H), 1.85 (s, 3 H), 1.81 (m, 1 H), 1.13 (m, 2 H), 1.06–1.02 (m, 1 H), 0.97 (s, 3 H), 0.81 (s, 3 H); ^{13}C NMR (20 MHz, $CDCl_3$) ppm 144.67, 120.37, 94.66, 75.52, 54.90, 47.68, 39.56, 36.79, 32.27, 31.69, 30.92, 29.21, 21.86; MS m/z ($M^+ - C_4H_8O_2$) calcd 122.1097, obsd 122.1095.

Anal. Calcd for $C_{13}H_{22}O_2$: C, 74.24; H, 10.54. Found: C, 74.24; H, 10.56.

A solution of the above ether (17.3 mg, 0.082 mmol) and a trace of concentrated HCl in methanol (1 mL) was stirred at 70 °C for 5 h. The solvent was evaporated to give 12.8 mg (94.0%) of **12** as colorless crystals: mp 59–60 °C (from methanol–water); IR (neat, cm^{-1}) 3580–3100, 2930, 2860, 1440, 1360, 1137, 1065, 1050; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.68 (m, 1 H), 3.88 (m, 1 H), 2.53 (m, 1 H), 2.37 (m, 1 H), 1.86 (d, J = 1.6 Hz, 3 H), 1.83 (m, 1 H), 1.32 (br s, 1 H), 1.14 (m, 2 H), 0.97 (s, 3 H), 0.88 (m, 1 H), 0.82 (s, 3 H); ^{13}C NMR (20 MHz, $CDCl_3$) 145.95, 119.68, 70.02, 47.93, 39.60, 39.17, 34.34, 31.90, 30.79, 29.06, 21.84; MS m/z (M^+) calcd 166.1358, obsd 166.1358.

Anal. Calcd for $C_{11}H_{18}O$: C, 79.46; H, 10.91. Found: C, 79.46; H, 10.89.

2,7,7-Trimethylbicyclo[2.2.2]oct-2-en-5-one (5). A solution of **12** (3.41 g, 21 mmol) in dichloromethane (25 mL) was added to a rapidly stirred mixture of pyridinium dichromate (11.66 g, 31 mmol) in the same solvent (75 mL) at room temperature. After 10 h, the reaction mixture was eluted through a short pad of silica gel and concentrated. Chromatography of the residue on silica gel (elution with 5% ethyl acetate in petroleum ether) gave 2.43 g (70%) of **5** as a colorless oil: IR (neat, cm^{-1}) 2955, 2920, 2860, 1720, 1440, 1410, 1381, 1361, 1163, 1118, 1090, 1015, 810, 784, 732; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.70 (dd, J = 4.8, 2.0 Hz, 1 H), 2.89 (m, 1 H), 2.29 (m, 1 H), 2.17 (m, 1 H), 1.94 (m, 1 H), 1.87 (d, J = 1.6 Hz, 3 H), 1.55 (m, 1 H), 1.44 (m, 1 H), 1.08 (s, 3 H), 0.96 (s, 3 H); ^{13}C NMR (20 MHz, $CDCl_3$) ppm 213.15, 147.56, 118.44, 49.87, 49.43, 38.72, 36.02, 33.38, 30.99, 28.34, 21.97; MS m/z (M^+) calcd 165.1201, obsd 165.1203.

Anal. Calcd for $C_{11}H_{16}O$: C, 80.44; H, 9.82. Found: C, 80.24; H, 9.77.

6-Methylene-5(*R),8,8-trimethylbicyclo[2.2.2]octan-2-(*S**)-ol.** A cold (0 °C), magnetically stirred mixture of methyltriphenylphosphonium bromide (2.35 g, 6.59 mmol) in dry THF (20 mL) was treated with *n*-butyllithium (4.02 mL of 1.5 M in hexanes, 6.03 mmol), and the reaction mixture was warmed to 25 °C for 30 min. The temperature was again lowered to 0 °C, and a solution of **10** (500 mg, 2.74 mmol) in THF (2 mL) was introduced slowly. After 60 min at 0 °C, saturated NH_4Cl solution was added, and the product was extracted into ether and dried. Solvent evaporation followed by chromatography of the residue on silica gel (elution with 25% ether in petroleum ether) gave the unsaturated alcohol as a colorless solid: mp 54–55 °C; IR ($CHCl_3$, cm^{-1}) 3620–3490, 3068, 2964, 2929, 2865, 1641, 1448, 1399, 1386, 1367, 1276, 1243, 1192, 1169, 1125, 1084, 1040; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.89 (m, 2 H), 3.85 (m, 1 H), 2.73 (m, 1 H), 2.25 (m, 1 H), 2.13 (m, 1 H), 1.70 (br s, 1 H), 1.40 (dd, J = 7.6, 3.0 Hz, 2 H), 1.31 (m, 2 H), 1.13 (d, J = 7.0 Hz, 3 H), 1.00 (s, 3 H), 0.99 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 151.14, 109.44, 68.34, 46.93, 44.34, 39.32, 33.13, 30.87, 30.79, 29.57, 29.46, 17.93; MS m/z (M^+) calcd 180.1514, obsd 180.1543.

Anal. Calcd for $C_{12}H_{20}O$: C, 79.94; H, 11.18. Found: C, 79.71; H, 11.09.

6-Methylene-5(*R),8,8-trimethylbicyclo[2.2.2]octan-2-one (6).** To a magnetically stirred solution of dry pyridine (1.18 g, 14.9 mmol) in CH_2Cl_2 (30 mL) was added 745 mg (7.45 mmol) of chromium trioxide. The resulting mixture was stirred for 15 min prior to the addition of the above alcohol (224 mg, 1.24 mmol) dissolved in CH_2Cl_2 (1 mL). A precipitate formed immediately. After 15 min, the supernatant was decanted off and washed in turn with 1 N NaOH (2×), 1 N HCl (2×), and saturated $NaHCO_3$ solution (2×). The organic phase was dried and evaporated, and the residue was purified by chromatography (silica gel, elution with 5% ether in petroleum ether). There was isolated 239 mg (92.4%) of **6** as a colorless oil: IR (neat, cm^{-1}) 3078, 2965, 2930, 2869, 1723, 1691, 1463, 1412, 1388, 1368, 1323, 1212, 1160, 1067, 1017, 890; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.93 (d, J = 2.5 Hz, 1 H), 4.82 (d, J = 1.9 Hz, 1 H), 2.91 (m, 1 H), 2.78 (t, J = 2.9 Hz, 1 H), 2.38 (qd, J = 3.3, 2.0 Hz, 2 H), 1.61 (t, J = 2.4 Hz, 2 H), 1.50 (m, 1 H), 1.10 (d, J = 6.2 Hz, 3 H), 1.08 (s, 3 H), 0.99 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 212.98, 149.08, 110.36, 56.63, 45.82, 40.34, 35.92, 32.44, 31.77, 29.67, 29.29, 18.84; MS m/z (M^+) calcd 178.1358, obsd 178.1376.

Anal. Calcd for $C_{12}H_{18}O$: C, 80.85; H, 10.18. Found: C, 80.79; H, 10.22.

5-Methylene-2,7,7-trimethylbicyclo[2.2.2]oct-2-ene (13). The Wittig reaction was performed in the predescribed manner on **5** (240 mg, 1.46 mmol) to give **13** (192 mg, 81%) as a colorless oil: IR (neat, cm^{-1}) 3063, 3030, 2957, 2926, 2860, 1726, 1644, 1441, 1380, 1360, 1259, 1177, 1120, 1022, 915, 875, 811, 790; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.70 (d, J = 6.2 Hz, 1 H), 4.66 (m, 1 H), 4.49 (q, J = 1.9 Hz, 1 H), 2.79 (dt, J = 6.1, 3.0 Hz, 1 H), 2.47 (dd, J = 16.0, 1.6 Hz, 1 H), 1.85 (m, 2 H), 1.74 (d, J = 1.6 Hz, 3 H), 1.18 (m, 2 H), 0.96 (s, 3 H), 0.78 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 150.37, 144.16, 123.04, 103.14, 49.14, 43.27, 42.67, 33.32, 31.49, 30.59, 29.00, 21.87; MS m/z (M^+) calcd 162.1409, obsd 162.1431.

Anal. Calcd for $C_{12}H_{18}$: C, 88.82; H, 11.18. Found: C, 88.80; H, 11.22.

Selenium Dioxide Oxidation of 5. A magnetically stirred solution of **5** (348 mg, 2.12 mmol) in 95% ethanol (2 mL) was treated dropwise with a solution of selenium dioxide (250 mg, 2.26 mmol) in the same solvent (2 mL). The reaction mixture was stirred at the reflux temperature for 48 h, diluted with ether, and washed with brine. The ethereal phase was dried and concentrated to leave a residue that was purified by silica gel chromatography (elution with 5% ether in petroleum ether). There was isolated alcohol **15** (186 mg, 48.7%) and recovered starting material (52 mg, 15%).

For **15**: colorless liquid; IR ($CHCl_3$, cm^{-1}) 3603, 3560–3240, 2965, 2928, 2867, 1720, 1451, 1410, 1384, 1318, 1182, 1170, 1136, 1122, 1093, 1042, 1015, 895, 822; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.98 (dd, J = 6.3, 1.4 Hz, 1 H), 4.22 (s, 2 H), 3.01 (m, 1 H), 2.37 (dd, J = 24.6, 2.1 Hz, 1 H), 2.35 (s, 1 H), 2.04 (br s, 1 H), 1.90 (dd, J = 18.1, 2.4 Hz, 1 H), 1.62 (dd, J = 13.3, 2.2 Hz, 1 H), 1.45 (dd, J = 13.3, 3.4 Hz, 1 H), 1.11 (s, 3 H), 0.96 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 212.94, 150.64, 118.86, 64.85, 49.54, 46.97, 39.99, 36.67, 33.48, 31.37, 28.45; MS m/z (M^+) calcd 180.1150, obsd 180.1136.

Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.22; H, 8.93.

Selenium Dioxide Oxidation of 6. A. Short Reaction Time. To a magnetically stirred refluxing solution of **6** (202 mg, 1.13 mmol) in 95% ethanol (1 mL) was added dropwise a solution of SeO_2 (125 mg, 1.13 mmol) in the same solvent (1 mL). The reaction mixture was heated at reflux for 60 min, cooled, diluted with ether, and processed in the manner described above. There was obtained alcohol **16** (122 mg, 56.0%), diselenide **17** (68 mg, 26.7%), and ether **18a** (6.8 mg, 2.7%).

For **16**: colorless oil; IR ($CHCl_3$, cm^{-1}) 3600, 3555–3280, 3079, 3020, 2969, 2940, 2877, 1722, 1662, 1648, 1455, 1412, 1391, 1388, 1311, 1300, 1223, 1174, 1130, 1109, 1083, 1022, 988, 897; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.17 (s, 1 H), 4.99 (s, 1 H), 2.90 (s, 1 H), 2.85 (dd, J = 16.8, 2.8 Hz, 1 H), 2.37 (dd, J = 18.4, 3.0 Hz, 1 H), 2.03 (s, 1 H), 1.81 (t, J = 2.8 Hz, 1 H), 1.67 (s, 3 H). 1.66 (m, 2 H), 1.17 (s, 3 H), 1.05 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 213.38, 152.47, 110.44, 72.46, 55.63, 51.59, 40.44, 38.46, 32.01, 31.93, 31.14, 30.89; MS m/z (M^+) calcd 194.1307, obsd 194.1307.

Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 73.98; H, 9.39.

For **17**: yellowish oil; IR ($CHCl_3$, cm^{-1}) 2969, 2933, 2873, 1718, 1452, 1411, 1388, 1367, 1342, 1332, 1311, 1283, 1231, 1177, 1169, 1134, 1093, 1020, 994; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.87 (dd, J = 11.3, 1.9 Hz, 2 H), 3.63 (dd, J = 11.3, 4.3 Hz, 2 H), 2.93 (q, J = 2.8 Hz, 2 H), 2.33 (dd, J = 18.6, 2.4 Hz, 2 H), 2.17 (m, 2 H), 1.92 (m, 2 H), 1.89 (s, 6 H), 1.65–1.49 (m, 4 H), 1.06 (s, 6 H), 0.98 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm (212.64, 212.58), 142.66, 126.75, 54.38, (51.38, 51.32), 39.39, (36.71, 36.64), (34.26, 34.20), (31.23, 31.16), (29.67, 29.64), 28.58, 18.79; MS (EI) m/z ($M^+ - C_{12}H_{17}OSe$) calcd 257.0444, obsd 257.0489; MS (CI) m/z (M + 1) calcd 515, obsd 515.

Anal. Calcd for $C_{24}H_{34}O_2Se_2$: C, 56.25; H, 6.67. Found: C, 56.30; H, 7.03.

For **18a**: colorless oil; IR ($CHCl_3$, cm^{-1}) 2969, 2928, 2871, 1714, 1451, 1410, 1382, 1368, 1260, 1166, 1092, 1021, 894, 807, 703; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.08 (d, J = 12.0 Hz, 1 H), 3.97 (d, J = 12.0 Hz, 1 H), 3.39 (qd, J = 6.9, 2.4 Hz, 2 H), 3.06 (t, J = 2.8

Hz, 1 H), 2.35 (dd, J = 18.6, 2.3 Hz, 1 H), 2.18 (t, J = 2.7 Hz, 1 H), 1.96 (m, 1 H), 1.90 (s, 3 H), 1.62 (dd, J = 2.3, 13.2 Hz, 1 H), 1.48 (dd, J = 3.5, 13.3 Hz, 1 H), 1.17 (t, J = 6.9 Hz, 3 H), 1.10 (s, 3 H), 0.98 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 142.75, 127.51, 77.33, 67.13, 52.14, 38.91, 33.98, 31.92, 31.19, 29.35, 28.58, 22.69, 18.35, 14.10; MS m/z (M^+) calcd 222.1620, obsd 222.1616.

Anal. Calcd for $C_{14}H_{22}O_2$: C, 75.63; H, 9.97. Found: C, 75.32; H, 10.34.

B. Prolonged Heating. The oxidation of 167 mg (0.94 mmol) of **6** was carried out in the manner described above, with the exception that heating was continued for 30 h prior to workup. These conditions gave 58 mg (31.8%) of alcohol **18b**, 111 mg (53.1%) of ether **18a**, and ca. 5% of the diselenide.

For **18b**: colorless oil; IR ($CHCl_3$, cm^{-1}) 3608, 3560–3310, 2967, 2929, 2870, 1719, 1452, 1438, 1410, 1382, 1176, 1110, 1078, 995, 878; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.26 (d, J = 12.2 Hz, 1 H), 4.16 (d, J = 12.2 Hz, 1 H), 3.11 (t, J = 2.8 Hz, 1 H), 2.36 (dd, J = 18.9, 2.2 Hz, 1 H), 2.18 (t, J = 2.7 Hz, 1 H), 1.92 (m, 1 H), 1.91 (s, 3 H), 1.66 (dd, J = 13.3, 2.1 Hz, 1 H), 1.56 (br s, 1 H), 1.49 (dd, J = 13.3, 3.4 Hz, 1 H), 1.10 (s, 3 H), 0.98 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 142.26, 129.14, 77.20, 52.04, 51.11, 39.09, 36.26, 31.92, 31.13, 28.51, 22.68, 18.26; MS m/z (M^+) calcd 194.1307, obsd 194.1279.

Anal. Cacld for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 74.07; H, 9.44.

Selenium Dioxide Oxidation of 13. The standard oxidation was performed on **13** (68 mg, 0.42 mmol) at 25 °C for 4 h to give 58.4 mg (78.0%) of alcohol **19** as a colorless oil; IR (neat, cm^{-1}) 3620–3540, 1648, 1469, 1442, 1408, 1363, 1226, 1149, 1122, 1047, 1023, 884, 820; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.93 (dt, J = 6.3, 1.7 Hz, 1 H), 5.02 (t, J = 1.3 Hz, 1 H), 4.98 (s, 1 H), 4.43 (br s, 1 H), 2.92 (m, 1 H), 2.26 (br d, J = 2.2 Hz, 1 H), 1.87 (d, J = 1.7 Hz, 3 H), 1.30–1.14 (series of m, 3 H), 1.04 (s, 3 H), 0.88 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 153.89, 140.83, 123.89, 108.33, 69.48, 56.41, 41.58, 41.56, 32.65, 31.47, 28.62, 23.93; MS m/z (M^+) calcd 178.1358, obsd 178.1371.

Anal. Calcd for $C_{12}H_{18}O$: C, 80.85; H, 10.18. Found: C, 80.57; H, 10.20.

(1*S,4*R**)-4-Methyl-6-methylenebicyclo[2.2.2]octan-2-one (7).** To a magnetically stirred suspension of methyltriphenylphosphonium bromide (6.08 g, 0.018 mol) in dry THF (400 mL) was added a solution of potassium hexamethyldisilazide in toluene (32.8 mL, 0.016 mol). The yellow solution was stirred for 0.5 h at room temperature, cooled to −78 °C, and treated with a solution of **14** (2.31 g, 0.015 mol) in THF (60 mL). The temperature was allowed to rise to 25 °C during 2 h. After an additional hour of stirring, the reaction mixture was quenched with water and saturated NH_4Cl solution. The product was extracted into ether (3 × 80 mL), and the combined organic phases were washed with brine, dried, and evaporated. Flash chromatography of the residue on silica gel (elution with 5% ethyl acetate in petroleum ether) afforded 2.1 g (92%) of **7** as a colorless liquid: IR (neat, cm^{-1}) 2940, 2960, 1720, 1640, 1450, 1205, 1090, 890; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.92 (td, J = 2.4, 1.1 Hz, 1 H), 4.79 (td, J = 2.2, 1.1 Hz, 1 H), 2.88 (t, J = 2.9 Hz, 1 H), 2.32 (dddd, J = 17.0, 2.0, 2.0, 2.0 Hz, 1 H), 2.21 (dddd, J = 17.1, 2.4, 2.4, 2.4 Hz, 1 H), 2.09 (dd, J = 2.2, 1.3 Hz, 2 H), 1.89 (dt, J = 8.9, 2.9 Hz, 2 H), 1.60–1.43 (m, 2 H), 1.02 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 212.48, 143.42, 110.38, 54.17, 50.22, 41.24, 33.28, 31.85, 26.29, 24.64; MS m/z (M^+) calcd 150.1045, obsd 150.1064.

Anal. Calcd for $C_{10}H_{14}O$: C, 79.96; H, 9.39. Found: C, 79.68; H, 9.43.

(1*S,4*R**)-4-Methyl-6-isopropylidenebicyclo[2.2.2]octan-2-one (8).** To a magnetically stirred suspension of isopropyltriphenylphosphonium bromide (5.50 g, 14.2 mmol) in dry THF (300 mL) was added a solution of potassium hexamethyldisilazide (30 mL of 0.5 M in toluene, 15 mmol) under nitrogen. The resulting deep red slurry was stirred at room temperature for 3 h, cooled to −78 °C, and treated with a solution of **14** (1.98 g, 13 mmol) in dry THF (40 mL). The reaction mixture was warmed to 25 °C, refluxed for 20 h, and worked up in the predescribed manner. MPLC on silica gel afforded 1.2 g (51%) of **8** and 0.40 g (15%) of the bis(isopropylidene) derivative.

For **8**: IR ($CHCl_3$, cm^{-1}) 1710; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.21 (t, J = 2.9 Hz, 1 H), 2.16–1.95 (m, 4 H), 1.87–1.76 (m, 2 H), 1.63 (t, J = 1.9 Hz, 3 H), 1.57 (br s, 3 H), 1.44 (dd, J = 8.2, 7.8 Hz, 2 H), 1.00 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 213.17, 126.50, 125.64, 50.13, 48.25, 40.65, 33.31, 31.86, 26.74, 24.04, 20.07, 19.58.

Anal. Calcd for $C_{12}H_{18}O$: C, 80.85; H, 10.18. Found: C, 80.89; H, 10.23.

For the bis(isopropylidene) derivative: IR ($CHCl_3$, cm^{-1}) 1710, 1650, 1450, 1373; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.52 (t, J = 3.0 Hz, 1 H), 2.02 (d, J = 16.6 Hz, 2 H), 1.94 (d, J = 16.0 Hz, 2 H), 1.70 (t, J = 1.8 Hz, 6 H), 1.64–1.58 (m, 2 H), 1.56 (s, 6 H), 1.35–1.29 (m, 2 H), 0.94 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 132.96, 119.39, 41.33, 34.06, 32.84, 31.86, 28.12, 26.69, 19.67, 19.53; MS m/z (M^+) calcd 204.1888, obsd 204.1890.

Anal. Calcd for $C_{15}H_{24}$: C, 88.16; H, 11.84. Found: C, 88.17; H, 11.74.

Selenium Dioxide Oxidation of 7. A refluxing solution of **7** (1.90 g, 12.7 mmol) in 95% ethanol (15 mL) was treated portionwise with selenium dioxide (1.44 g, 1.30 mmol). After completion of the addition, the mixture was refluxed for 45 min, cooled, and filtered. After the standard isolation procedure including MPLC (silica gel, elution with petroleum ether–ether, 2:1), there was obtained 0.51 g (22%) of **20** and 0.40 g (19%) of **21**.

For **20**: IR ($CHCl_3$, cm^{-1}) 3600, 3008, 1720, 1648; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.20 (d, J = 1.6 Hz, 1 H), 5.09 (d, J = 2.0 Hz, 1 H), 3.94 (d, J = 2.0 Hz, 1 H), 2.84 (t, J = 2.9 Hz, 1 H), 2.68 (br, 1 H), 2.44 (dd, J = 2.8, 19.0 Hz, 1 H), 1.82 (d, J = 1.8, 19.0 Hz, 1 H), 1.8–1.7 (m, 2 H), 1.54–1.36 (m, 2 H), 0.98 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 212.20, 148.42, 114.04, 73.98, 53.78, 43.39, 37.37, 29.81, 23.77, 22.24; MS m/z (M^+) calcd 166.0994, obsd 166.1017.

Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.42; H, 8.51.

For **21**: oil; IR ($CHCl_3$, cm^{-1}) 1738, 1715, 1660; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.13 (s, 1 H), 5.37 (s, 1 H), 3.35 (t, J = 3 Hz, 1 H), 2.38 (s, 2 H), 2.11–1.93 (m, 2 H), 1.86–1.78 (m, 2 H), 1.14 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 207.97, 200.72, 140.21, 121.58, 54.34, 47.50, 45.52, 29.54, 23.78, 19.06; MS m/z (M^+) calcd 164.0825, obsd 164.0837.

Anal. Calcd for $C_{10}H_{12}O_2$: C, 73.15; H, 7.37. Found: C, 73.28; H, 7.17.

Selenium Dioxide Oxidation of 8. A mixture of **8** (1.00 g, 5.6 mmol) and selenium dioxide (0.62 g, 5.6 mmol) in 95% ethanol (2 mL) was refluxed for 3 h. The usual workup and chromatography furnished **22** (440 mg, 40%), **23a** (90 mg, 8%), **23b** (120 mg, 10%), **24** (50 mg, 5%), and **25** (35 mg, 3%) in addition to 100 mg of recovered starting material.

For **22**: oil; IR ($CHCl_3$, cm^{-1}) 3600, 1714, 1655; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.10 (br s, 1 H), 3.24 (dd, J = 3.5, 2.3 Hz, 1 H), 2.54 (dd, J = 19, 2.7 Hz, 1 H), 1.96 (dd, J = 19, 1.4 Hz, 1 H), 1.86 (s, 3 H), 1.83–1.67 (m, 1 H), 1.72 (s, 3 H), 1.59–1.33 (m, 4 H), 1.08 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 213.43, 133.31, 132.12, 73.59, 48.37, 43.40, 37.62, 29.17, 24.16, 22.93, 21.10, 20.14: MS m/z (M^+) calcd 194.1307, obsd 194.1331.

Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 74.19; H, 9.33.

For **23a**: oil; IR ($CHCl_3$, cm^{-1}) 3600, 3010, 1720; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.00 (d, J = 1.5 Hz, 1 H), 3.29 (dd, J = 4.4, 2.7 Hz, 1 H), 2.16 (s, 1 H), 1.96–1.87 (m, 3 H), 1.62–1.51 (m, 3 H), 1.334 (s, 3 H), 1.327 (s, 3 H), 1.27 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 213.09, 147.12, 131.18, 71.62, 49.73, 47.29, 36.96, 32.71, 28.47, 28.40, 24.34, 24.29; MS m/z (M^+) calcd 194.1307, obsd 194.1308.

Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 74.61; H, 9.31.

For **23b**: oil; IR ($CHCl_3$, cm^{-1}) 3010, 1715, 1625, 1065; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.94 (d, J = 1.5 Hz, 1 H), 3.37 (q, J = 1.5 Hz, 1 H), 3.14 (dq, J = 7.0, 2.0 Hz, 2 H), 1.95–1.81 (m, 3 H), 1.75–1.51 (m, 2 H), 1.37–1.21 (m, 4 H), 1.27 (s, 3 H), 1.26 (s, 3 H), 1.11 (t, J = 7 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 213.01, 145.07, 134.60, 75.26, 58.21, 48.83, 47.27, 37.27, 32.90, 25,77, 2494, 24.34, 23.95, 15.64; MS m/z (M^+) calcd 207.1385, obsd 207.1376.

Anal. Calcd for $C_{14}H_{22}O_2$: C, 75.63; H, 9.97. Found: C, 75.57; H, 9.91.

For **24**: oil; IR ($CHCl_3$, cm^{-1}) 3705, 1718, 1665; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.08 (d, J = 12.1 Hz, 1 H), 4.04 (d, J = 13.3 Hz, 1 H), 3.22 (t, J = 2.9 Hz, 1 H), 2.27 (d, J = 16.6 Hz, 1 H), 2.17 (d, J = 20.0 Hz, 1 H), 2.06–2.04 (m, 2 H), 1.98 (br, 1 H), 1.94–1.76

(m, 2 H), 1.72 (t, J = 2.0 Hz, 3 H), 1.47 (tm, J = 7.7 Hz, 2 H), 1.01 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 213.14, 129.79, 129.57, 62.92, 50.10, 48.47, 39.47, 33.21, 31.64, 26.57 23.80, 15.25; MS m/z (M^+) calcd 194.1307, obsd 194.1323.

Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 73.92; H, 9.35.

For **25**: oil; IR ($CHCl_3$, cm^{-1}) 3600, 1715; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.04 (s, 2 H), 3.31 (t, J = 3.0 Hz, 1 H) 2.53 (br, 1 H), 2.12-2.03 (m, 4 H), 1.88-1.75 (m, 2 H), 1.67 (dd, J = 1.5, 1.3 Hz, 3 H), 1.50-1.28 (m, 2 H), 1.02 (s, 3 H); ^{13}C NMR (75 MHz) ppm 213.36, 130.54, 130.45, 62.43, 49.95, 48.07, 40.77, 33.12, 31.69, 26.56, 24.20, 16.39; MS m/z (M^+) calcd 194.1307, obsd 194.1298.

Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 74.19; H, 9.20.

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Functionalization Reactions of a Medium-Ring Bridgehead Enone That Skirt Transannular Bond Formation

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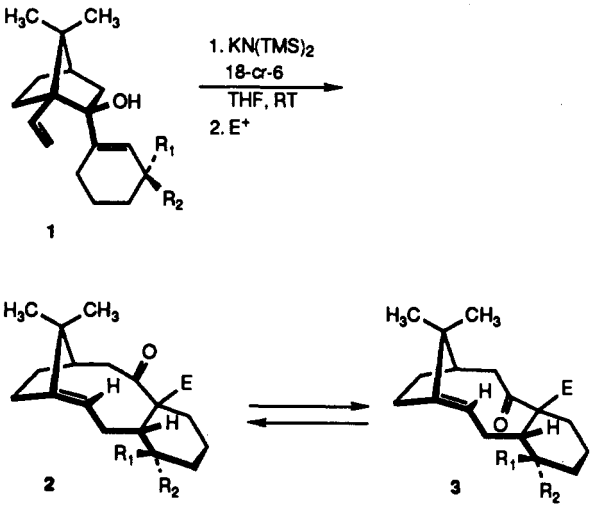
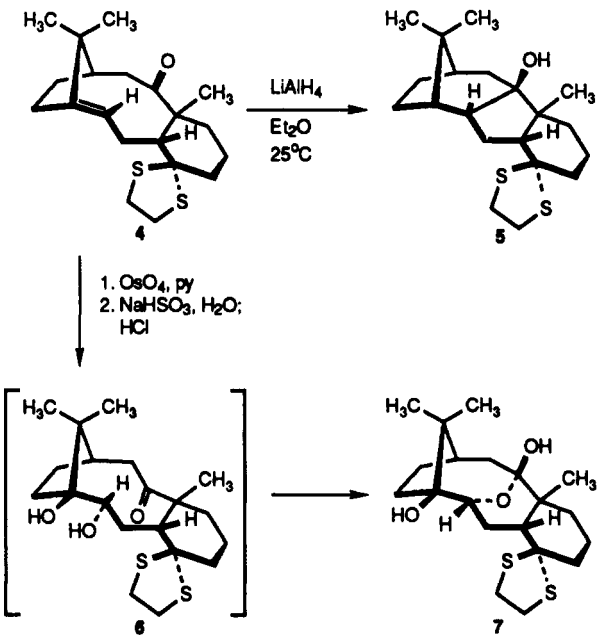
As a consequence of the close proximity of the olefinic and carbonyl centers in ketone **4**, the molecule participates readily in transannular reactions. Sequences have been developed for enhancing the level of functionality in both of these sectors within the central medium-sized ring without incurring ring closure. Osmate ester **10** is especially serviceable, permitting direct access to triol **11** and to the olefinic hydroxy acetate **17**. In a companion study, acetals **19a** and **19b** were prepared from **11** and dehydrated with the Burgess reagent. The trans cycloalkene generated in each instance was shown to possess the topography found in **21**, a conclusion that was further supported by deuterium labeling experiments. Access to this diastereomer made possible the acquisition of diacetates **23a** and **23b**, where seven of the nine carbon atoms of the central ring are stereogenic and have well-defined absolute stereochemistry.

Optically pure 1-vinyl-2-alkenyl-7,7-dimethyl-*exo*-norbornan-2-ols typified by **1** undergo anionic oxy-Cope rearrangement[1,2] with strict adherence to an endo-chair transition state to deliver *E*,syn ketones such as **2** rapidly at room temperature.[3-5] This notably efficient transformation is often atropselective and can lead to the "carbonyl up" conformer **2** or its "carbonyl down" diastereomer **3** depending upon the nature of R_1, R_2, and E.[3,4] The rate at which **2** and **3** interconvert and the magnitude and sign of K_{eq} are likewise sensitive to these substituents.[4,6]



Scheme I



The central ring in **2** and **3** is of the previously unknown[9] 5(*E*)-cyclononenone type. The minimum energy conformations of **2** and **3** (where R_1, R_2 = dithiolane and E = CH_3) have been estimated by molecular mechanics calculations (MODEL KS 2.93)[7] and are depicted in Figure 1. Despite many differing aspects of structure, both molecules

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