Suitability of the Claisen Ring Expansion Protocol for Crenulide Diterpene Construction

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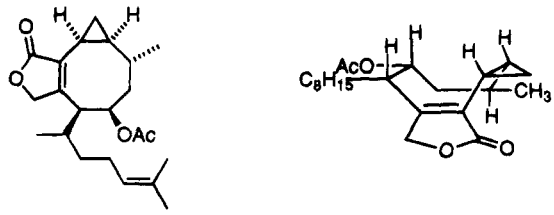
An enantiospecific synthesis of optically pure **2**, a molecule possessing the ring system characteristic of the crenulide diterpenes, is reported. The nine-step sequence began with the previously described *R* lactone **6**. The early bond-forming reactions include an aldol condensation with crotonaldehyde and intramolecular selenonium ion-promoted cyclization with participation by the neighboring hydroxyl group. Selenoxide elimination made possible the acquisition of allyl vinyl ether **4**. Thermal activation of the latter in hot mesitylene proceeded via a Claisen ring expansion pathway to give **36a**. This key intermediate was then ketalized, subjected to Simmons–Smith cyclopropanation, and carried through a selenoxide elimination step to arrive ultimately at **2**. Selected transformations of the medium-ring bicyclic lactones are described, accompanied by X-ray crystallographic studies to substantiate the stereochemical assignments advanced throughout the investigation.

Among the seaweeds that survive in the most competitive of tropical and subtropical habitats, the small brown Phaeophyta of the family Dictyotaceae are the most conspicuous.[2] The ability of these algae to coexist in such environments has been attributed to their production of toxic secondary metabolites, the most prevalent of which appears to be acetoxycrenulide (**1**).[3-5] This diterpenoid possesses a bicyclo[6.1.0]nonane framework never encountered before in nature. Its unusual structural features also include an α,β-unsaturated lactone functionality, a side chain formally derived from 2-methyl-2-heptene,[6] and six stereogenic centers. The polycyclic skeleton is rigid, with the eight-membered ring locked into a tub conformation having the cyclopropane unit and all three additional ring substituents projected equatorially.



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Acetoxycrenulide constitutes an attractive synthetic target for a number of reasons.[7] A potentially concise retrosynthetic analysis for construction of its tricyclic nucleus is shown in Scheme 1. Disconnection of the three-membered ring from **2** in tandem with reductive saturation (trans) of the conjugated double bond leads to **3**. Recognition of the possibility that **3** is interconnected with **4** via [3,3] sigmatropy considerably simplifies the synthetic problem at hand. Rupture of various bonds in **4** allows for retrosynthetic conversion back to **6**. Since optically pure **6** has previously been described, the promise of an enantiospecific pathway emerged and merited investigation.

Thus, our focus in this report is to examine the feasibility of producing **4** and to test its suitability for entering into Claisen ring expansion.[8,9] We also detail the level and direction of stereocontrol that operates during thermal activation of an epimer of **4**. Made clear by the present investigation are the several advantages associated with this important new methodology for medium-ring construction.[10]

Results and Discussion

As specified above, lactone **6**[11] was to be utilized as our starting material. Its preparation from L-glutamic acid (**7**)[12] via (*R*)-(−)-γ-[(trityloxy)methyl]-γ-butyrolactone[13] proceeded uneventfully according to literature precedent with but two exceptions. In our hands, the diazotization

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(6) Optically pure C6-functionalized 2-methyl-2-heptenes are available: Liang, S.; Paquette, L. A. *Tetrahedron Asymmetry* **1990**, *1*, 445.

(7) (a) Paquette, L. A.; Wang, T.-Z.; Pinard, E. *J. Am. Chem. Soc.* **1995**, *117*, 1455. (b) Preliminary report: Paquette, L. A.; Ezquerra, J.; He, W. *Tetrahedron Lett.* **1990**, *31*, 6505.

(8) (a) Demole, E.; Enggist, P.; Borer, M. C. *Helv. Chim. Acta* **1971**, *54*, 1845. (b) Petrzilka, M. *Helv. Chim. Acta* **1978**, *61*, 2286, 3075. (c) Pitteloud, R.; Petrzilka, M. *Helv. Chim. Acta* **1979**, *62*, 1319.

(9) (a) Kinney, W. A.; Coghlan, M. J.; Paquette, L. A. *J. Am. Chem. Soc.* **1984**, *106*, 6868, **1985**, *107*, 7352. (b) Kang, H.-J.; Paquette, L. A. *J. Am. Chem. Soc.* **1990**, *112*, 3252. (c) Paquette, L. A.; Kang, H.-J. *J. Am. Chem. Soc.* **1991**, *113*, 2610. (d) Paquette, L. A.; Sweeney, T. J. *J. Org. Chem.* **1990**, *55*, 1703; *Tetrahedron* **1990**, *46*, 4487. Paquette, L. A.; Friedrich, D.; Rogers, R. D. *J. Org. Chem.* **1991**, *56*, 3841.

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(11) (a) Takano, S.; Yonaga, M.; Morimoto, M.; Ogasawara, K. *J. Chem. Soc. Perkin Trans. 1* **1985**, 305. (b) Takano, S.; Tamura, N.; Ogasawara, K. *J. Chem. Soc. Chem. Commun.* **1981**, 1155.

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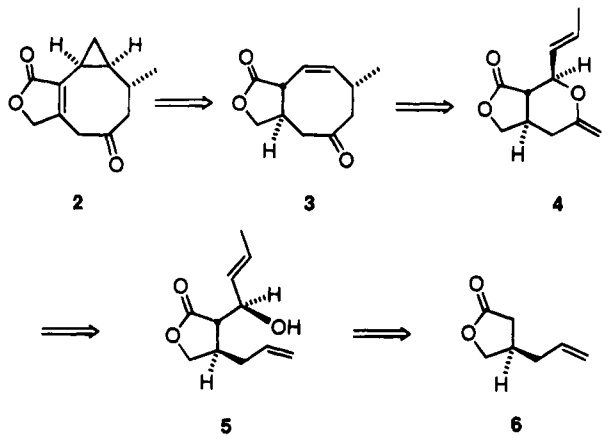
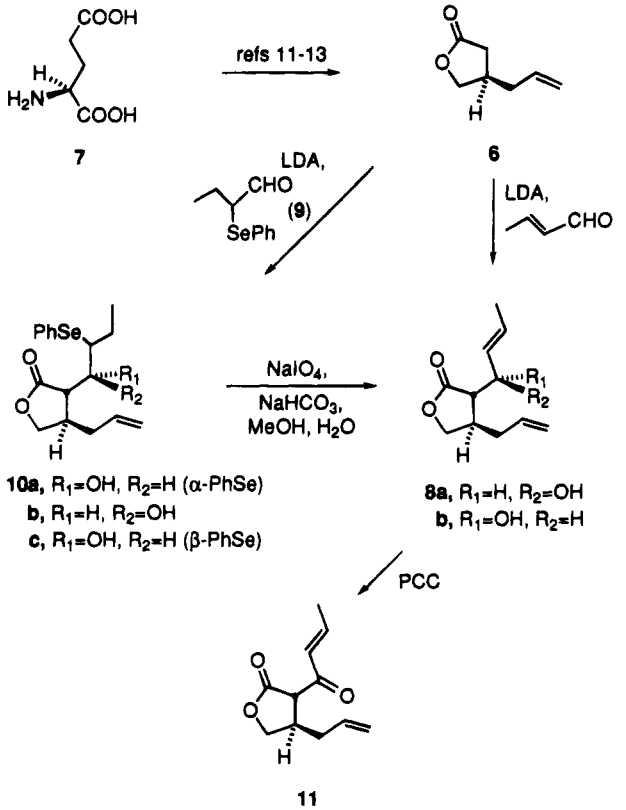
Scheme 1



Scheme 2



of **7** to give (*S*)-(+)-γ-(ethoxycarbonyl)-γ-butyrolactone was reproducibly accomplished in 30–37% yield rather than at the 76% level quoted by Yamada and coworkers.[12] Also, the optical rotation of **6**, at $[\alpha]^{20}_{D}$ +20.8°, exceeded the previously reported value by approximately 6°.[11]

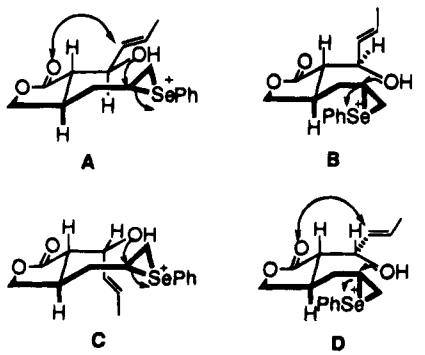
The synthesis began as outlined in Scheme 2. Conversion of **6** to its lithium enolate and treatment with crotonaldehyde at −78 °C gave the aldols **8a** and **8b** in a 1:1 ratio and 91% yield. These diastereomers, which lent themselves to ready chromatographic separation, were shown to be epimeric by independent oxidation to **11**. Their individual configurational assignments rest on X-ray crystallographic studies of compounds derived from them as described below.

The trans exclusivety of the aldol reaction is fully maintained during comparable condensation of **6** with α-(phenylseleno)butyraldehyde (**9**). This reagent had previously been prepared by Baudat and Petrzilka in a four-step sequence from *n*-butyraldehyde.[14] For our purposes, it proved more expedient to expose the aldehyde to phenylselenenyl chloride in ethyl acetate solution at room temperature (34%).[15] The chiral center in **9** opens up the possibility for producing four stereoisomeric aldols. Careful high pressure chromatography resulted in the isolation of pure **10a–c** in yields of 30, 23, and 8%, respectively. While the configurations of the hydroxyl-bearing centers in **10** were established by conversion to either **8a** or **8b** via selenoxide elimination, no attempt was made to unravel the stereochemistry of the selenium-substituted carbons.

These observations indicated the direct route via crotonaldehyde to be superior to that involving **9**. Furthermore, since **8a** is the aldol ultimately required for arrival at **2**, the conversion of **8b** to **11** allows in principle for the recycling of this diastereomer as required for large-scale preparations.

To continue the sequence, an efficient method was needed to promote cyclization of the hydroxyl function onto the allylic double bond in that regiochemical sense that would culminate in formation of a tetrahydropyran ring. Further, the potential for introducing the exocyclic vinyl ether double bond without risk of internal migration[9] was mandatory. These requirements were best met by making recourse to *N*-(phenylseleno)phthalimide[16] in dichloromethane solution at room temperature. Formation of the transient phenylselenonium ion with this reagent lent itself well to neighboring group participation because of the weakly nucleophilic character of the phthalimide counterion. This was not the case with phenylselenenyl chloride, where simple 1,2-addition to the double bond *without ring closure* was kinetically preferred.[17]

Scheme 3 illustrates that **8a** responds exclusively via the 6-endo-trig option to give both possible diastereomers **12** and **13** in equal proportions and 67% combined yield. Epimer **8b**, in contrast, cyclizes at both π-bond termini to generate **14** (55%) and **15** (17%), both as single isomers. The erosion of diastereoselectivity observed in the Scheme 3 case of **8a** can be attributed to the rather severe nonbonded steric compression involving the carbonyl oxygen and *E*-propenyl side chain in **A**. As a consequence, the boatlike alternative **B** finds it possible



to compete effectively, producing an equal amount of **13**. When the stereochemistry at the hydroxyl-substituted

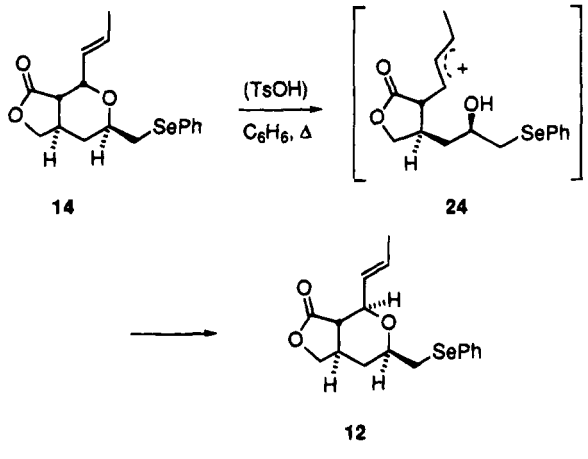
(14) Baudat, R.; Petrzilka, M. *Helv. Chim. Acta* **1979**, *62*, 1406.
(15) Sharpless, K. B.; Lauer, R. F.; Teranishi, A. Y. *J. Am. Chem. Soc.* **1973**, *75*, 6137.
(16) (a) Nicolaou, K. C.; Claremon, D. A.; Barnette, W. E.; Seitz, S. P. *J. Am. Chem. Soc.* **1979**, *101*, 3704. (b) Grieco, P. A.; Jaw, J. Y.; Claremon, D. A.; Nicolaou, K. C. *J. Org. Chem.* **1981**, *46*, 1215.
(17) Ezquerra, J. Unpublished results.

center is reversed as in **8b**, then strain relief and the advantages of a chair topography are both met in **C**. Option **D** is doubly disadvantaged and no evidence was found for isomerization via this arrangement. The stereochemical assignments made to **14** and **15** follow from these mechanistic considerations.

The nonutility of **14** and **15** for gaining access to keto lactone **35a** prompted the exploration of an alternative means for skirting the production of these unwanted intermediates. Following the discovery that **6** reacts efficiently with N-PSP in a $H_2O-CH_2Cl_2$ solvent system to give **19** and **20** (89%), these intermediates were separated and individually subjected to aldol condensation with crotonaldehyde (Scheme 4).

Although each substrate afforded two dihydroxy lactones [**21a,b** (91%) and **22a,b** (70%), respectively], their chromatographic separation was not necessary since each pair converged to a single pyran, *viz.* **13** or **12**, when heated with a catalytic quantity of *p*-toluenesulfonic acid in benzene. The stereoselectivity of these cyclizations implicates kinetically controlled ionization of the allylic hydroxyl with formation of the cations **23** and **24**. The second hydroxyl, functioning as a neighboring group, captures the cation exclusively via the six-centered transition state that eventuates in equatorial orientation of the propenyl substituent. With the limited evidence available, it is not possible to rule out the operation of a more elaborate mechanistic scheme wherein **23** and **24** lose a proton to generate conjugated diastereomeric diene lactone systems that undergo ring closure by an acid-catalyzed Michael reaction.

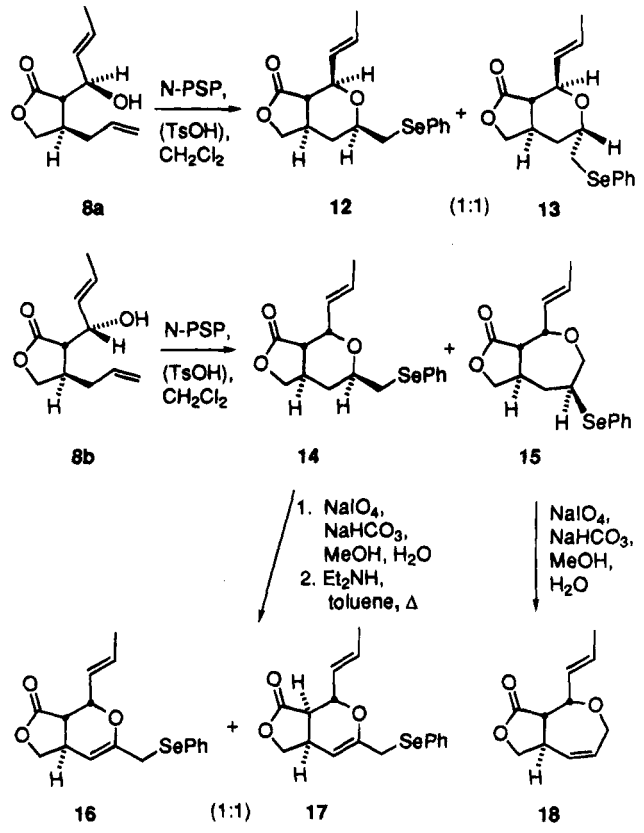
These findings prompted a return to **14**, which when subjected to the identical acid-catalyzed conditions, was completely isomerized to **12** (92% isolated) within 2 h.



This smooth conversion opened a much more direct and expeditious pathway to **35a** (see below).

The finding that **C** is capable of seven-membered ring closure to give **15** is nonetheless noteworthy. Oxidation of **15** with sodium periodate and sodium bicarbonate gave the tetrahydroxepin **18** (56%) after a short reaction time at room temperature. The strong bias for regioselective formation of the allyl ether follows from the usual inductive considerations. In contrast, the structural features of **12**–**14** are such that selenoxide elimination can only proceed by abstraction of a hydrogen atom that is geminal to oxygen. Consequently, **25** and its diastereomers are unusually stable compounds that require forcing conditions for conversion to the respective vinyl ethers. In the event, heating **25** in toluene containing

Scheme 3



diethylamine resulted in conversion to a 1:1 mixture of **16** and **17** (48%). Evidently, the PhSeOH produced simultaneously with **26** under these conditions serves as a source of $PhSe^+$ (Scheme 5). The high reactivity of the exocyclic double bond in **26** is conducive to the ready formation of **27**, subsequent opening of which is likely facilitated by the base. Diethylamine is presumably also responsible for the α epimerization.

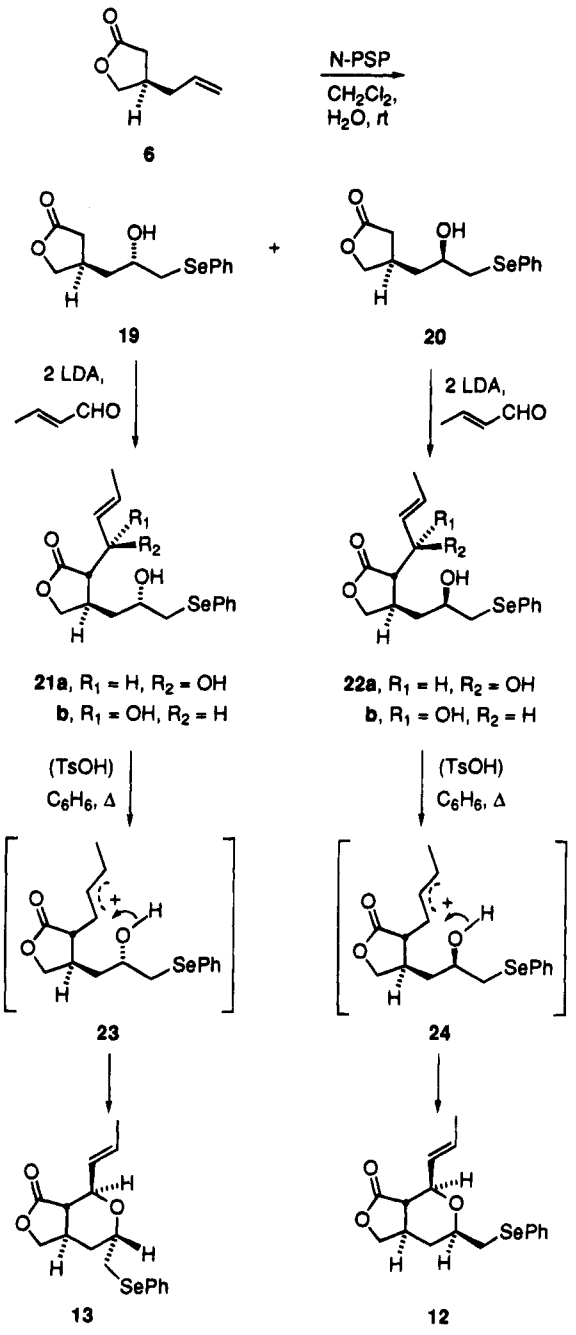
When recourse was made instead to triethylamine, the product mixture consisted of more closely balanced amounts of **16** (21%) and **28** (37%). While this base curtails selenonium ion formation to an appreciable degree, internalization of the exocyclic double bond is not impeded.

We reasoned that the temperature provided by hot toluene was insufficient to provide for an adequately fast rate of Claisen rearrangement. Indeed, performing the elimination in a sealed tube at 175–180 °C resulted instead in the formation of **29** (49%). Still further modification of the conditions was required to curtail migration of the β,γ-double bond into conjugation. Movement in this direction was realized when **25** was heated with diethylamine in mesitylene in open vessels to furnish a 1:1 mixture of **29** and **30** (48%, Scheme 6). At this point, sufficient synthetic promise had been demonstrated to prompt advance in the correct configurational series.

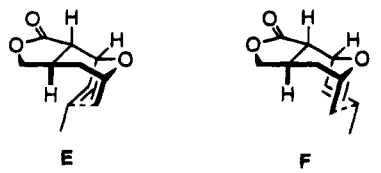
The stereochemical assignments given to **29** and **30** follow from two fundamental considerations. The first is the normal kinetic bias of the Claisen rearrangement to proceed via a chair transition state.[18] Additionally, the Claisen ring expansion is most often *Z*-selective,[9] since this reaction channel generates the new endocyclic

(18) Ziegler, F. E. *Chem. Rev.* **1988**, *88*, 1423 and references cited therein.

Scheme 4



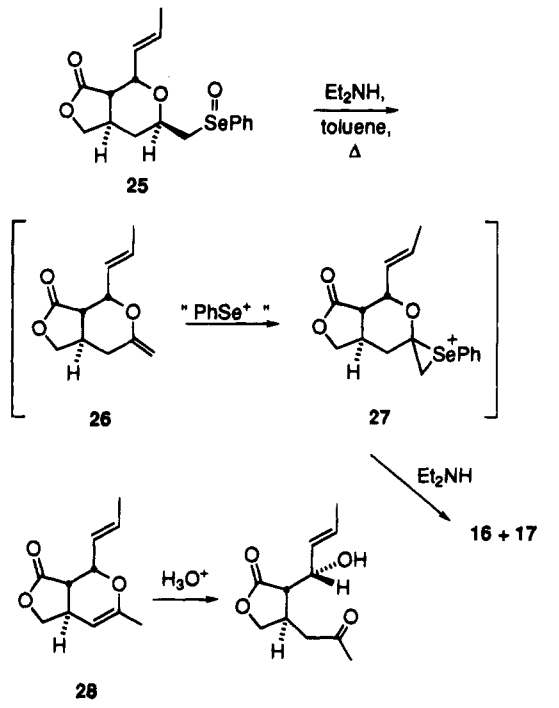
double bond in its less strained geometry. When these criteria are applied to **26**, the transition state depicted by **E** is deduced to be substantially favored over **F**. Adoption of the chairlike topography also guarantees β orientation of the secondary methyl group.



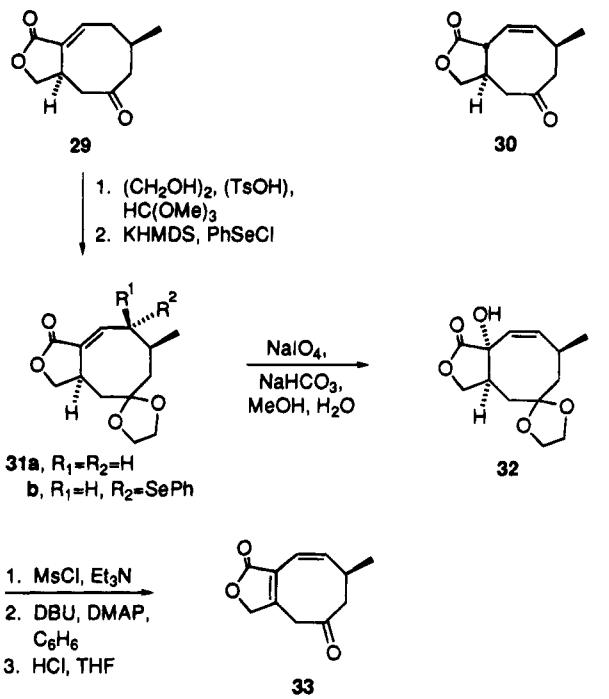
E F

With **29** in hand, it was possible to examine a modest amount of functional group manipulation. Once ketalization had been effected, **31a** was deprotonated and exposed to phenylselenenyl chloride. This reaction probed the relative reactivity of the nucleophilic sites along the extended enolate backbone. Derivative **31b** was formed

Scheme 5



Scheme 6

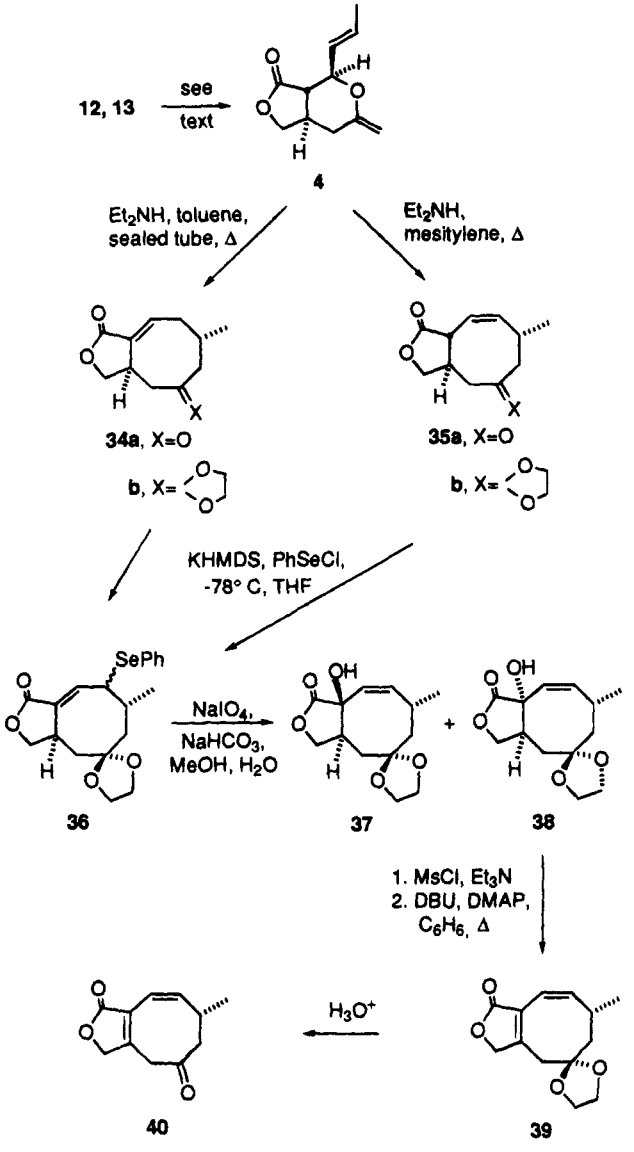


exclusively (72% isolated). Its subsequent oxidation resulted in the expected[19] [2,3] sigmatropic shift to deliver, after hydrolysis, the α-carbinol stereoselectively. Conversion of **32** to its mesylate made possible E_2 elimination to give keto lactone **33** (42%).

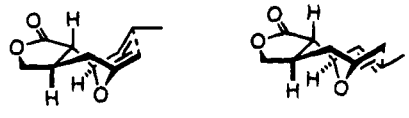
With this reactivity profile established, we turned our attention to appropriate chemical modification of **12** and **13**. Their separation was not necessary because elimination from the corresponding selenoxides leads uniquely to vinyl ether **4** (see Scheme 7). Entry of **4** into the Claisen rearrangement should be accompanied by a

(19) Reich, H. J. In *Organoselenium Chemistry*; Liotta, D., Ed.; John Wiley and Sons, Inc.: New York, 1987; Chapter 8.

Scheme 7



preference for utilization of transition state **G** relative to **H**. Indeed, this chairlike arrangement is singularly



G **H**

adopted during the thermal activation process. Moreover, the control that can be exercised over the location of the double bond in the ring-expanded product is impressive. Thus, the use of diethylamine and toluene in a sealed tube at 175–180 °C led straightforwardly to **34a** (49%). On the other hand, recourse to diethylamine in refluxing mesitylene resulted in clean conversion to **35a** (50% isolated). The lesser effective concentration of amine base residing in solution at these temperatures when an open vessel is utilized may be responsible for this dichotomy. The high crystallinity of **34a** warranted that its structure be established beyond doubt by X-ray crystallography. As shown in Figure 1, the mechanistic assumptions made earlier were fully corroborated in this manner.

The enolate derived by deprotonation of either **34b** or **35b** also experiences selenenylation at the γ position.

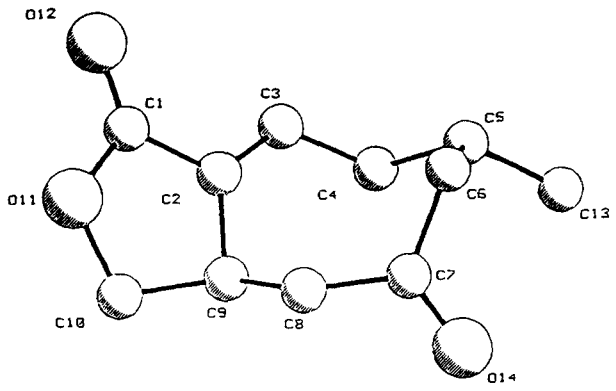


Figure 1. A computer-generated drawing of **34a** derived from the X-ray coordinates with hydrogens omitted for clarity (courtesy of J. P. Springer).

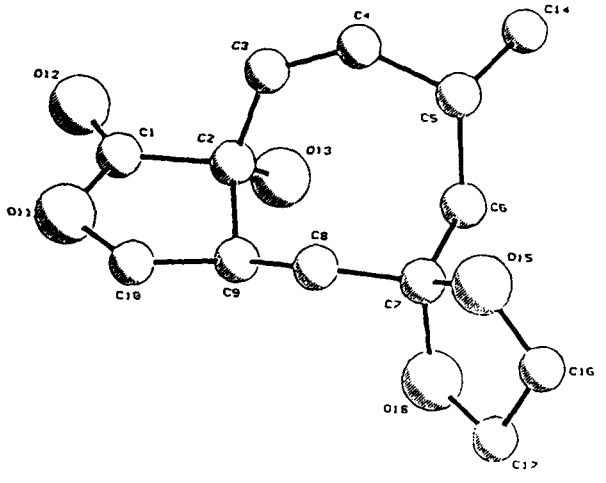


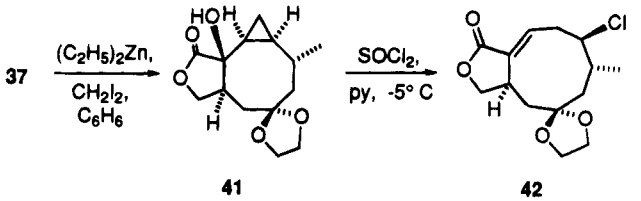
Figure 2. A computer-generated drawing of **38** derived from the X-ray coordinates with hydrogens omitted for clarity (courtesy of J. P. Springer).

However, the α orientation of the adjacent methyl group discourages cleanly stereoselective α attack that is seen to operate in **31a**. Approximately 33% of the β selenide is formed. Intermediates **36** were converted directly into **37** and **38** (64% combined). These isomers were separated and distinguished by X-ray crystallographic analysis of the major constituent **38** (Figure 2). Sequential dehydration and deketalization of **38** gave **40**. Since this product was clearly antipodal to **33**, this sequence confirmed the stereochemical assignments advanced in Scheme 6.

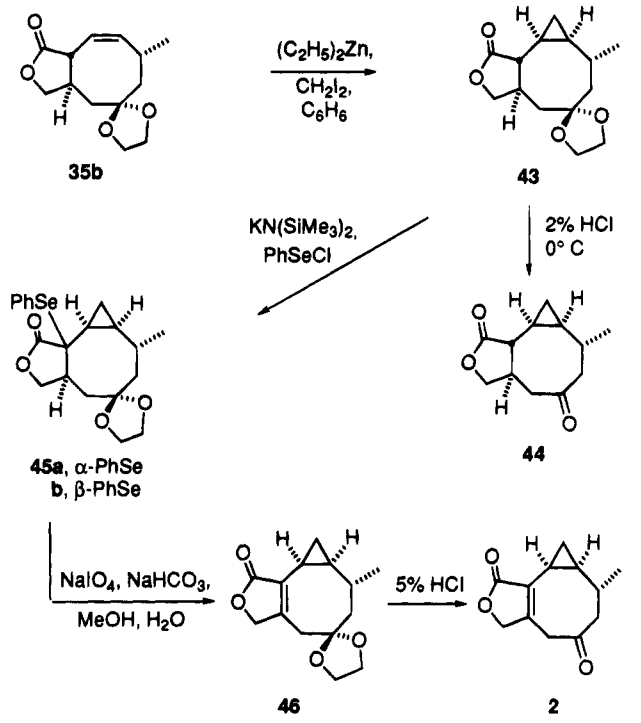
Fusion of the cyclopropane ring onto the bicyclic lactone framework was next undertaken. Use can be made of the hydroxyl-directing capability[20] present in **37** to gain access to **41** (73%, Scheme 8). However, the appreciable sensitivity of the cyclopropylcarbinyl alcohol subunit in **41** to ionic ring opening as exemplified by the conversion to **42** (67%) caused this approach to be abandoned. Therefore, **35b** was subjected to Simmons–Smith cyclopropanation according to the protocol developed by Sawada and Inoue.[21] Reaction occurred smoothly to give a single stereoisomer, assumed to be **43** (83%) in line with

(20) (a) Simmons, H. E.; Cairns, T. L.; Vladuchick, S. A.; Hoiness, C. M. *Org. React. (N.Y.)* **1973**, *20*, 1. (b) Winstein, S.; Sonnenberg, J.; de Vries, L. *J. Am. Chem. Soc.* **1959**, *81*, 6523. (c) Winstein, S.; Sonnenberg, J. *J. Am. Chem. Soc.* **1961**, *83*, 3235. (d) Kawabata, N.; Nakagawa, T.; Nakao, T.; Yamashita, S. *J. Org. Chem.* **1977**, *42*, 3031.

Scheme 8

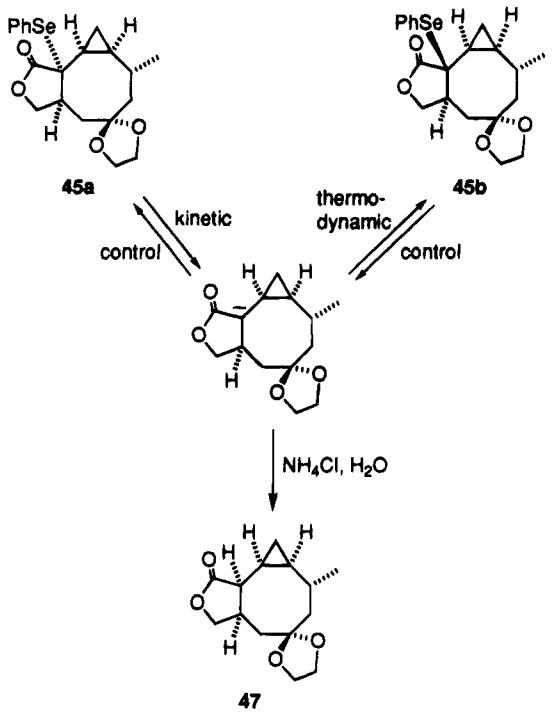


Scheme 9



introduction of the three-membered ring from the less sterically congested π surface (Scheme 9). The chemical shifts of the methyl doublet in **41** (δ 1.00) and **43** (δ 1.05) are nearly identical as expected on this basis. The extreme lability of **43** to acidic conditions is notable. For example, ketal hydrolysis is complete within a few minutes in cold 2% HCl solution.

With all of the carbon atoms necessary for the northern sector properly set, the time had arrived to remove the original centers of stereoinduction and introduce the intraring double bond. To this end, the enolate of **43** was allowed to react with phenylselenenyl chloride in the presence of HMPA to provide mixtures of the cis and trans isomers **45a** and **45b**. The product ratio and extent of reaction are highly dependent on the conditions employed. The pertinent features of the process are as follows: (a) if the concentration of reactants fell below 0.4 mmol/3 mL, product formation was not observed; (b) the presence of HMPA was crucial to success; (c) normal or inverse addition of KHMDS had no impact on the efficiency with which **45** was produced; (d) the ratio of THF to DME affected the distribution of **45a** to **45b** (further study is warranted); (e) quenching with methanol at −78 °C gave essentially quantitative yields; and (f) reaction temperature and time were important variables. Stirring at 78 °C for 1 h led ultimately to the



isolation of **45a** and **45b** in a 2.3:1 ratio (61%). Longer reaction times led to an increase in the proportion of **45b** (to as high as 1:2.5). If the reaction mixture was allowed to warm to 0 °C before being returned to −78 °C for quenching, **45b** became heavily dominant. We interpret these observations to be indicative of the existence of the following equilibrium. Short reaction times and low temperatures favor **45a**, the obvious product of kinetic control. As the duration of reaction is prolonged and/or temperatures are increased, the level of **45b** is enhanced because it is thermodynamically favored. The existence of this equilibrium allows for the channeling of unwanted **45b** back to **45a**. Also, quenching of the intermediate enolate ion afforded the previously unknown cis-fused lactone **47**.

Oxidative elimination within **45a** produced **46** quantitatively. This ketal was considerably less prone to deketalization than **43**. A reaction time of 48 h was necessary to complete the conversion to **2** in 5% HCl. Thus, the presence of the added double bond has striking kinetic consequences.

Significantly for our purposes, the hydrolysis to give **2** proceeded efficiently without any evidence of double bond migration. An X-ray crystallographic analysis of **2** was completed not only to demonstrate beyond doubt that the tricyclic nucleus had been properly assembled, but to gain additional stereochemical insight. As seen in Figure 3, neither of the potentially enolizable allylic α-carbonyl protons is properly stereoaligned for abstraction by a base. Molecular models implicate a quite rigid conformation for **2** and suggest that the solution structure may be as geometrically constrained as that in the solid state. This working assumption has received substantitation by virtue of our inability to realize any fruitful level of enolization. The C_8 side chain required for arriving at **1** needs therefore to be present from the outset.[10]

Conclusion

A fully functionalized tricyclic system (**2**) corresponding to the ring framework of crenulide diterpenes has been

(21) Sawada, S.; Inoue, Y. *Bull. Chem. Soc. Jpn.* **1969**, *42*, 2669. See also Furukawa, J.; Kawabata, N.; Nishimura, J. *Tetrahedron* **1968**, *24*, 53 and Denmark, S.; Edwards, J. P. *J. Org. Chem.* **1991**, *56*, 6974.

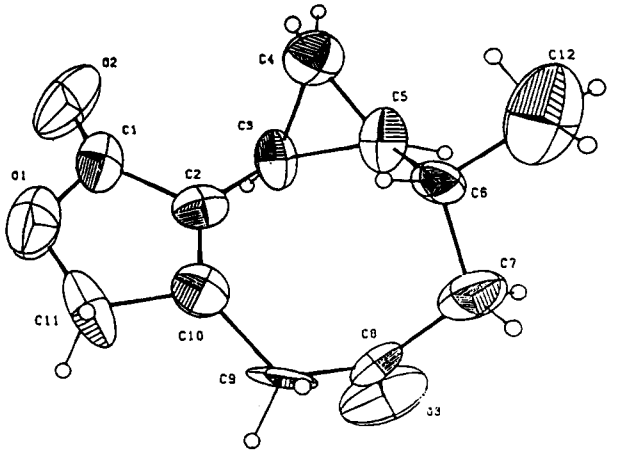


Figure 3. Computer-generated perspective drawing of **2** as determined by X-ray analysis (courtesy of R. D. Rogers).

synthesized in optically active form from L-glutamic acid. The described construction, which makes extensive use of organoselenium chemistry, features a stereocontrolled Claisen ring expansion. The overall scheme represents another demonstration of the power of this [3,3] sigmatropic process for the stereochemically reliable construction of relatively complex 4-cyclooctenones and has set the stage for an eventual total synthesis of (+)-acetoxycrenulide.[7a]

Experimental Section

Melting points are uncorrected. Infrared spectra were recorded on a Perkin-Elmer Model 1320 spectrometer. ^{1}H NMR spectra were recorded at 300 MHz and the ^{13}C NMR data obtained at 75, 62.5, and 20 MHz. Mass spectra were measured on a Kratos MS-30 instrument by Mr. Dick Weisenberger at The Ohio State University Chemical Instrumentation Center. Elemental analyses were performed at the Scandinavian 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.

Direct Condensation of 6 with Crotonaldehyde. To a solution of diisopropylamine (21.6 mL, 0.154 mmol) in dry THF (180 mL) was added dropwise *n*-butyllithium in hexane (82.8 mL of 1.6 M, 0.132 mol) at −78 °C. This solution was stirred for 30 min before **6** (15.12 g, 0.120 mol) dissolved in dry THF (60 mL) was introduced dropwise. After completion of the addition, the mixture was stirred at −78 °C for 1 h and treated with crotonaldehyde (8.82 g, 0.126 mol) in one portion. Stirring was maintained at −78 °C for 2 h, at which time saturated NH_4Cl solution was added. The aqueous solution was extracted with ether (3 × 300 mL) and the combined organic phases were washed with brine (100 mL), dried, and concentrated. The light yellow residue was subjected to preparative HPLC (Waters Prep 500) on silica gel with 16% ethyl acetate in petroleum ether as eluant. There was obtained 9.06 g (39%) of **8a** and 13.24 g of a mixture of **8a** and **8b** (total yield of 91%).

For **8a**: colorless oil; IR (neat, cm^{-1}) 3455, 2920, 1750, 1440, 1380, 1150; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.76 (dq, J = 15.4, 6.5 Hz, 1 H), 5.62 (m, 1 H), 5.44 (ddd, J = 15.4, 6.4, 1.5 Hz, 1 H), 5.07 (d, J = 1.5 Hz, 1 H), 5.02 (d, J = 3.0 Hz, 1 H), 4.50 (br s, 1 H), 4.33 (t, J = 8.5 Hz, 1 H), 3.86 (dd, J = 8.9, 6.7 Hz, 1 H), 2.95 (br s, 1 H), 2.59 (dq, J = 15.2, 7.2 Hz, 1 H), 2.41 (dd, J = 7.3, 3.4 Hz, 1 H), 2.27 (m, 1 H), 2.15 (m, 1 H), 1.68 (d, J = 6.5 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 178.36, 134.06, 130.10, 128.31, 117.76, 71.86, 70.93, 50.78, 37.31, 34.85, 17.47; MS m/z ($M^+ - H_2O$) calcd 179.1072, obsd 179.1068; $[\alpha]^{20}_D$ +64.6° (c 1.75, $CHCl_3$). Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.32; H, 8.21. Found: C, 67.27; H, 8.25.

Condensation of 6 with α-(Phenylseleno)butyraldehyde. To a solution of diisopropylamine (3.34 mL, 23.9 mmol) in dry THF (30 mL) was added *n*-butyllithium in hexane (14.9 mL of 1.6 M, 23.9 mmol) at −78 °C with stirring. After 10 min, **6** (3.01 g, 23.8 mmol) in THF (30 mL) was introduced over a period of 1 h. Stirring was continued for an additional 2 h at −78 °C before **9** (5.46 g, 24.1 mmol) was added during 5 min. After 3 h at −78 °C, the reaction mixture was treated with saturated Na_2SO_4 solution, the organic phase was separated, and the aqueous layer was extracted with benzene. The combined organic layers were washed with brine, dried, and evaporated. The residual yellow oil was purified by HPLC on silica gel (elution with 25% ethyl acetate in petroleum ether) to give (in order of elution) 647 mg (8%) of **10c**, 1.96 g (23%) of **10b**, and 2.55 g (30%) of **10a**.

For **10a**: colorless crystals, mp 69−71 °C; IR ($CHCl_3$, cm^{-1}) 3450, 1750, 1575, 1475, 1435, 1380, 1145, 1022; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.49−7.45 (m, 2 H), 7.21−7.16 (m, 3 H), 5.67−5.61 (m, 1 H), 5.09−5.01 (m, 2 H), 4.37 (t, J = 7.8 Hz, 1 H), 3.83 (t, J = 8.9 Hz, 1 H), 3.65 (td, J = 12.2, 3.1 Hz, 1 H), 3.14 (dd, J = 9.8, 2.8 Hz, 1 H), 2.66−2.60 (m, 1 H), 2.38 (m, 1 H), 2.24 (m, 1 H), 2.17 (m, 1 H), 1.96−1.88 (m, 1 H), 1.65−1.57 (m, 1 H), 1.14 (t, J = 7.3 Hz, 3 H), 0.88 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 177.19, 134.30, 133.79, 129.17, 129.00, 127.64, 118.22, 73.24, 71.30, 51.29, 48.25, 38.57, 36.00, 23.90, 11.96; MS m/z (M^+) calcd 354.0734, obsd 354.0736; $[\alpha]^{20}_D$ +6.7° (c 0.45, $CHCl_3$). Anal. Calcd for $C_{17}H_{22}O_3Se$: C, 57.79; H, 6.27. Found: C, 57.64; H, 6.42.

For **10b**: faint yellow oil; IR ($CHCl_3$, cm^{-1}) 3450, 1755, 1580, 1480, 1440, 1382, 1022; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48−7.44 (m, 2 H), 7.22−7.16 (m, 3 H), 5.69−5.55 (m, 1 H), 5.02 (s, 1 H), 4.98 (d, J = 5.2 Hz, 1 H), 4.25 (t, J = 8.3 Hz, 1 H), 3.99 (t, J = 6.0 Hz, 1 H), 3.85 (dd, J = 8.9, 6.0 Hz, 1 H), 3.35 (m, 1 H), 2.88 (t, J = 5.8 Hz, 1 H), 2.69−2.58 (m, 1 H), 2.46−2.32 (m, 1 H), 2.31−2.24 (m, 1 H), 2.08−1.94 (m, 1 H), 1.93−1.67 (m, 1 H), 1.55−1.47 (m, 1 H), 1.09 (t, J = 7.3 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 178.26, 135.00, 134.74, 134.34, 129.22, 127.91, 117.82, 72.99, 71.67, 52.17, 48.62, 37.69, 36.05, 22.75, 12.42; MS m/z (M^+) calcd 354.0733, obsd 354.0724; $[\alpha]^{20}_D$ +59° (c 1.0, $CHCl_3$).

For **10c**: yellowish oil; IR (neat, cm^{-1}) 3490, 2960, 1760, 1485, 1380, 1020; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.57−7.49 (m, 2 H), 7.32−7.23 (m, 3 H), 5.74−5.60 (m, 1 H), 5.08 (s, 1 H), 5.03 (d, J = 5.4 Hz, 1 H), 4.46 (dd, J = 8.8, 7.4 Hz, 1 H), 3.92 (dd, J = 8.8, 5.7 Hz, 1 H), 3.68 (ddd, J = 8.1, 3.1, 1.8 Hz, 1 H), 3.59 (dd, J = 16.8, 4.2 Hz, 1 H), 3.58 (br s, 1 H), 2.66−2.58 (m, 2 H), 2.30−2.14 (m, 2 H), 1.97−1.83 (m, 1 H), 1.63−1.51 (m, 1 H), 1.13 (t, J = 7.2 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 177.02, 134.69, 133.96, 129.08, 127.77, 127.40, 118.02, 72.74, 71.71, 54.81, 46.93, 38.47, 37.32, 24.99, 12.42; MS m/z (M^+) calcd 354.0733, obsd 354.0764; $[\alpha]^{20}_D$ +46.3° (c 0.95, $CHCl_3$).

Oxidative Elimination of the Diastereomers of 10. A. Seleno Alcohol 10a. To a well stirred solution of **10a** (2.43 g, 6.87 mmol) in methanol (176 mL) and water (29 mL) was added solid sodium bicarbonate (635 mg, 7.56 mmol) and sodium metaperiodate (2.21 g, 10.3 mmol). A thick white precipitate formed rapidly. After 1 h, the reaction mixture was poured into water (100 mL) and extracted with dichloromethane (3 × 100 mL). The organic layer was washed with brine, dried, and evaporated. The residue was purified by MPLC on silica gel (elution with 30% ethyl acetate in petroleum ether) to give 599 mg (44%) of **8b** as a pale yellow oil: IR (neat, cm^{-1}) 3460, 2920, 1760, 1445, 1385, 1175, 1020; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.73 (dq, J = 15.5, 6.7 Hz, 1 H), 5.64 (m, 1 H), 5.53 (ddm, J = 15.5, 7.7 Hz, 1 H), 5.06 (d, J = 1.2 Hz, 1 H), 5.01 (dd, J = 6.6, 1.4 Hz, 1 H), 4.31 (dd, J = 9.1, 7.7 Hz, 1 H), 4.22 (m, 1 H), 3.83 (dd, J = 9.1, 7.7 Hz, 1 H), 3.10 (br s, 1 H), 2.44−2.36 (m, 2 H), 2.34 (dd, J = 8.5, 6.6 Hz, 1 H), 2.09 (m, 1 H), 1.68 (dd, J = 6.4, 1.4 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 178.20, 133.90, 130.06, 129.80, 118.01, 73.03, 71.51, 50.09, 37.25, 36.89, 17.60; MS m/z (M^+ − OH) calcd 179.1072, obsd 179.1092; $[\alpha]^{20}_D$ +60.9° (c 2.2, $CHCl_3$). Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.32; H, 8.21. Found: C, 67.40; H, 8.35.

B. Seleno Alcohol 10b. Application of the above procedure to **10b** (4.08 g, 11.5 mmol) in methanol (296 mL) and water (48 mL) with $NaHCO_3$ (1.06 g) and $NaIO_4$ (3.20 g) gave after MPLC (silica gel, elution with 30% ethyl acetate in petroleum ether) 1.25 g (55%) of **8a**, identical in all respects to the alcohol described earlier.

C. Seleno Alcohol 10c. Treatment of **10c** (929 mg, 2.62 mmol) in methanol (66 mL) and water (11 mL) with $NaHCO_3$ (242 mg) and $NaIO_4$ (841 mg) afforded following chromatography 198 mg (39%) of **8b**.

(3*S*,4*R*)-4-Allyl-3-[(*E*)-crotonyl]dihydro-2(3*H*)-furanone (11). To a solution of **8b** (1.48 g, 7.55 mmol) in dichloromethane (20 mL) was added pyridinium chlorochromate (3.0 g, 13.4 mmol) and sodium acetate (250 mg, 3.0 mmol). The black suspension was stirred at room temperature for 1 h, diluted with water (20 mL), and extracted with ether (3 × 20 mL). The combined organic layers were washed with brine (20 mL), dried, and evaporated. The dark residue was purified by chromatography on silica gel (elution with 30% ethyl acetate in petroleum ether) to give 1.14 g (78%) of **11** as a colorless oil consisting of a 4.1:1 keto–enol mixture: IR (neat, cm^{-1}) 2980, 2920, 1770, 1690, 1660, 1630, 1440, 1380, 1230, 1160, 1020; ^1H NMR (300 MHz, $CDCl_3$) (keto tautomer) δ 7.02 (dq, J = 6.9, 15.6 Hz, 1 H), 6.37 (dq, J = 1.6, 15.6 Hz, 1 H), 5.67 (m, 1 H), 5.10 (m, 1 H), 5.05 (m, 1 H), 4.43 (dd, J = 7.5, 9.0 Hz, 1 H), 3.98 (dd, J = 8.0, 9.0 Hz, 1 H), 3.58 (d, J = 6.4 Hz, 1 H), 3.12 (m, 1 H), 2.21 (m, 2 H), 1.94 (dd, J = 1.6, 6.9 Hz, 3 H); ^{13}C NMR (62.5 MHz, $CDCl_3$) (keto tautomer) ppm 191.21, 172.56, 146.64, 133.85, 130.08, 118.32, 71.77, 55.85, 37.04, 36.62, 18.52; MS m/z (M^+) calcd 194.0943, obsd 194.0936; $[\alpha]^{20}_D$ +88.1° (c 0.78, $CHCl_3$). Anal. Calcd for $C_{11}H_{14}O_3$: C, 68.02; H, 7.27. Found: C, 67.61; H, 7.30.

(3a*S*,4*R*,6*R*,7a*R*)-Hexahydro-6-[(phenylselenyl)methyl]-4-[(*E*)-propenyl]-3*H*-furo[3,4-*c*]pyran-3-one (12) and Its Epimer 13. To a solution of **8a** (127 mg, 0.648 mmol) in dichloromethane (12 mL) were added *N*-(phenylseleno)phthalimide (254 mg, 0.841 mmol) and *p*-toluenesulfonic acid (12 mg, 0.06 mmol). The mixture was stirred under nitrogen at room temperature for 1 h, filtered to remove the precipitated phthalimide, and concentrated. The residue was subjected to MPLC (silica gel, elution with 30% ethyl acetate in petroleum ether) to give 152 mg (67%) of a 1:1 mixture of **12** and **13**: IR (neat, cm^{-1}) 2920, 1770, 1470, 1430, 1360, 1160, 990; ^1H NMR (300 MHz, $CDCl_3$) δ 7.47–7.40 (m, 2 H), 7.19–7.16 (m, 3 H), 5.82–5.53 (m, 2 H), 4.32–4.29 (m, 1 H), 4.26–4.23 (m, 1 H), 3.90–3.85 (m, 0.5 H), 3.80–3.70 (m, 1 H), 3.56–3.48 (m, 0.5 H), 3.20–2.89 (m, 2 H), 2.34–1.85 (m, 3 H), 1.66 (d, J = 7.3 Hz, 3 H), 1.39–1.15 (m, 1 H); MS m/z (M^+) calcd 352.0577, obsd 352.0577.

(3a*S*,4*S*,6*R*,7a*R*)-Hexahydro-6-[(phenylselenyl)methyl]-4-[(*E*)-propenyl]-3*H*-furo[3,4-*c*]pyran-3-one (14) and (3a*S*,4*S*,7*S*,8a*R*)-Hexahydro-7-(phenylselenenyl)-4-[(*E*)-propenyl]-1*H*,3*H*-furo[3,4-*c*]oxepin-3-one (15). A solution of **8b** (653 mg, 3.33 mmol) in dichloromethane (75 mL) was treated in analogous fashion with *N*-(phenylseleno)phthalimide (1.31 g, 4.33 mmol) and *p*-TsOH (63 mg, 0.33 mmol). MPLC purification gave 200 mg (17%) of **15** followed by 660 mg (56%) of **14**.

For **14**: colorless crystals, mp 65–68 °C (from ethyl acetate/petroleum ether); IR ($CHCl_3$, cm^{-1}) 1760, 1370, 1305, 1050, 995, 715; ^1H NMR (300 MHz, $CDCl_3$) δ 7.46–7.41 (m, 2 H), 7.23–7.18 (m, 3 H), 5.81 (dqd, J = 15.6, 6.5, 1.7 Hz, 1 H), 5.39 (ddq, J = 15.7, 4.8, 1.7 Hz, 1 H), 4.81 (br s, 1 H), 4.35 (dd, J = 8.4, 6.1 Hz, 1 H), 3.82–3.74 (m, 2 H), 3.05 (dd, J = 6.4, 12.4 Hz, 1 H), 2.92 (dd, J = 5.9, 12.3 Hz, 1 H), 2.50–2.39 (m, 2 H), 2.02 (dm, J = 12.2 Hz, 1 H), 1.64 (dt, J = 6.6, 1.5 Hz, 3 H), 1.36–1.24 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 173.58, 132.54, 131.34, 129.09, 127.00, 124.08, 123.56, 72.44, 71.58, 68.76, 46.78, 36.01, 34.91, 32.80, 18.05; MS m/z (M^+) calcd 352.0577, obsd 352.0567.

For **15**: colorless oil; IR (neat, cm^{-1}) 2910, 1760, 1470, 1160, 1050, 1015, 740; ^1H NMR (300 MHz, $CDCl_3$) δ 7.61–7.50 (m, 2 H), 7.33–7.22 (m, 3 H), 5.87 (dqd, J = 15.3, 7.8, 1.2 Hz, 1 H), 5.43 (ddq, J = 15.2, 6.4, 1.6 Hz, 1 H), 4.61 (t, J = 6.9 Hz, 1 H), 4.40 (t, J = 8.7 Hz, 1 H), 4.04 (ddd, J = 13.1, 3.3, 1.7 Hz, 1 H), 3.71 (dd, J = 9.0, 10.2 Hz, 1 H), 3.61 (dd, J = 13.0, 11.2 Hz, 1 H), 3.37–3.25 (m, 1 H), 3.01 (dd, J = 11.4, 7.5 Hz, 1 H), 2.82 (dddd, J = 20.9, 19.7, 8.3, 2.7 Hz, 1 H), 2.38 (dm, J = 13.2 Hz, 1 H), 1.68 (ddd, J = 6.6, 1.6, 0.8 Hz, 3 H), 1.44–1.26 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 175.26, 135.03, 131.01, 129.25, 128.17, 127.46, 126.22, 74.96, 70.66, 70.33, 49.44, 41.96, 37.92, 36.36, 17.91; MS m/z (M^+) calcd 352.0577, obsd 352.0589.

(3a*S*,4*S*,7a*R*)-1,3a,4,7a-Tetrahydro-6-[(phenylselenyl)-methyl]-4-[(*E*)-propenyl]-3*H*-furo[3,4-*c*]pyran-3-one (16) and Its Epimer 17. To a solution of **14** (43 mg, 0.121 mmol) in methanol (3.1 mL) and water (0.5 mL) were added solid $NaHCO_3$ (11.2 mg, 0.134 mmol) and $NaIO_4$ (33 mg, 0.158 mmol). The mixture was stirred at room temperature for 1 h, poured into water (15 mL), and extracted with dichloromethane (3 × 20 mL). The combined organic phases were washed with brine, dried, and evaporated to dryness at room temperature. The resulting selenoxide was dissolved in toluene (2 mL) containing diethylamine (0.37 μL, 0.364 mmol) and heated at reflux for 18 h. The solvent was removed in vacuo and the residue was purified by MPLC on silica gel (elution with 30% ethyl acetate in petroleum ether) to give 10 mg (24%) of **16** followed by 10 mg (24%) of **17**.

For **16**: colorless liquid; IR (neat, cm^{-1}) 2920, 1775, 1640, 1480, 1440, 1330, 1190, 1070; ^1H NMR (300 MHz, $CDCl_3$) δ 7.55–7.50 (m, 2 H), 7.29–7.23 (m, 3 H), 5.87 (dqd, J = 15.4, 6.6, 1.7 Hz, 1 H), 5.42 (dmd, J = 15.4, 1.7 Hz, 1 H), 5.13 (ddd, J = 1.5, 4.5, 4.6 Hz, 1 H), 4.62 (d, J = 1.4 Hz, 1 H), 4.37 (dd, J = 6.7, 7.9 Hz, 1 H), 3.73 (dd, J = 8.0, 11.3 Hz, 1 H), 3.45 (s, 2 H), 2.97–2.86 (m, 1 H), 2.54 (dd, J = 4.5, 14.0 Hz, 1 H), 1.72 (dt, J = 6.6, 1.5 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 172.29, 152.01, 134.13, 130.03, 129.80, 128.93, 127.58, 125.09, 95.07, 73.81, 70.86, 60.36, 32.44, 30.23, 17.81; MS m/z (M^+) calcd 350.0428, obsd 350.0399.

For **17**: colorless liquid; IR (neat, cm^{-1}) 2910, 1770, 1660, 1475, 1440, 1170, 1000; ^1H NMR (300 MHz, $CDCl_3$) δ 7.53–7.50 (m, 2 H), 7.27–7.23 (m, 3 H), 5.85 (dqd, J = 15.4, 6.6, 1.2 Hz, 1 H), 5.57 (ddd, J = 15.4, 6.6, 1.6 Hz, 1 H), 4.75 (dd, J = 5.1, 5.5 Hz, 1 H), 4.43 (d, J = 3.1 Hz, 1 H), 4.30 (dd, J = 6.2, 8.8 Hz, 1 H), 3.82 (dd, J = 3.3, 8.8 Hz, 1 H), 3.39 (s, 2 H), 3.02–2.98 (m, 1 H), 2.68 (dd, J = 4.2, 7.8 Hz, 1 H), 1.74 (dt, J = 6.1, 1.2 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 175.23, 152.20, 134.30, 129.88, 129.74, 128.87, 127.50, 127.24, 97.08, 72.37, 72.27, 42.68, 30.84, 30.56, 17.79; MS m/z (M^+) calcd 350.0428, obsd 350.0429.

(3a*S*,4*S*,8a*R*)-3a,4,6,8a-Tetrahydro-4-[(*E*)-propenyl]-1*H*,3*H*-furo[3,4-*c*]oxepin-3-one (18). Oxidation of **15** (117 mg, 0.331 mmol) in methanol (8.4 mL) and water (1.5 mL) with $NaHCO_3$ (30.5 mg, 0.364 mmol) and $NaIO_4$ (91 mg, 0.430 mmol) at room temperature for 1 h gave after the usual workup and MPLC purification (silica gel, elution with 30% ethyl acetate in petroleum ether) 36.2 mg (56%) of **18** as a pale yellow oil: IR (neat, cm^{-1}) 2890, 1775, 1450, 1380, 1300, 1190, 1110, 1020; ^1H NMR (300 MHz, $CDCl_3$) δ 5.97 (dqd, J = 15.3, 6.6, 1.2 Hz, 1 H), 5.76 (ddd, J = 10.5, 5.1, 2.5 Hz, 1 H), 5.60 (dm, J = 10.5 Hz, 1 H), 5.54 (ddq, J = 15.4, 5.9, 1.6 Hz, 1 H), 4.65 (dd, J = 6.9, 6.2 Hz, 1 H), 4.51 (t, J = 8.5 Hz, 1 H), 4.38 (ddt, J = 17.2, 5.2, 0.6 Hz, 1 H), 4.25 (dddd, J = 17.3, 4.0, 1.9, 1.9 Hz, 1 H), 3.81 (dd, J = 8.5, 11.3 Hz, 1 H), 3.56–3.50 (m, 1 H), 3.23 (dd, J = 7.2, 12.2 Hz, 1 H), 1.73 (dt, J = 6.6, 1.2 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 174.71, 131.99, 130.61, 127.70, 125.73, 75.46, 70.07, 66.06, 49.61, 36.83, 17.94; MS m/z (M^+) calcd 194.0942, obsd 194.0946. Anal. Calcd for $C_{11}H_{14}O_3$: C, 68.02; H, 7.65. Found: C, 67.87; H, 7.32.

Phenylselenenylation of 6. A mixture of **6** (126 mg, 1.00 mmol), N-PSP (393 mg, 1.30 mmol), catalytic amount of $TsOH{\cdot}H_2O$, water (1 mL), and dichloromethane (4 mL) was vigorously stirred at room temperature overnight. Following the predescribed workup, there was isolated 266 mg (89%) of a 1:1 mixture of **19** and **20**. Their separation was achieved by MPLC on silica gel (elution with ether).

For **19**: IR (neat, cm^{-1}) 3420, 1760; ^1H NMR (300 MHz, $CDCl_3$) δ 7.50 (m, 2 H), 7.27 (m, 3 H), 4.45 (dd, J = 9.2, 7.5 Hz, 1 H), 3.95 (dd, J = 9.2, 7.9 Hz, 1 H), 3.65 (m, 1 H), 3.06 (dd, J = 12.8, 4.0 Hz, 1 H), 2.85 (dd, J = 12.8, 8.3 Hz, 1 H), 2.72 (dd, J = 16.0, 7.6 Hz, 1 H), 2.58 (dd, J = 17.2, 8.3 Hz, 1 H), 2.15 (dd, J = 17.2, 9.0 Hz, 1 H), 1.69 (dd, J = 7.2, 3.1 Hz,

1 H), 1.63 (dd, J = 9.4, 6.8 Hz, 1 H), 1.25 (br s, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) ppm 176.98, 133.13, 129.29, 128.86, 127.58, 73.85, 68.59, 39.34, 37.08, 34.39, 33.70; MS m/z (M^+) calcd 300.0264, obsd 300.0275; $[\alpha]^{20}_D$ +27.2° (c 1.3, $CHCl_3$).

For **20**: IR (neat, cm^{-1}) 3430, 1760; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52 (m, 2 H), 7.28 (m, 3 H), 4.39 (dd, J = 9.0, 7.3 Hz, 1 H), 3.89 (dd, J = 9.0, 7.3 Hz, 1 H), 3.66 (hept, J = 4.0 Hz, 1 H), 3.08 (dd, J = 12.8, 3.9 Hz, 1 H), 2.85 (dd, J = 12.8, 8.6 Hz, 1 H), 2.74 (dd, J = 15.0, 7.3 Hz, 1 H), 2.64 (dd, J = 17.0, 8.3 Hz, 1 H), 2.23 (dd, J = 17.1, 8.3 Hz, 1 H), 1.67 (m, 2 H), 1.26 (br s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 171.06, 133.31, 129.38, 129.07, 127.72, 72.92, 68.05, 39.20, 37.15, 34.98, 33.12; MS m/z (M^+) calcd 300.264 , obsd 300.0281; $[\alpha]^{20}_D$ +23.7° (c 1.3, $CHCl_3$).

(3*S*,4*R*)-Dihydro-3-[(1*R*,2*E*)- and (3*S*,4*R*)-Dihydro-3-[(1*S*,2*E*)-1-hydroxy-2-butenyl]-4-[(2*R*)-2-hydroxy-3-(phenylseleno)propanyl]-2(3*H*)-furanone (22a and 22b). To diisopropylamine (0.297 mL, 2.12 mmol) in 5 mL of dry tetrahydrofuran was added dropwise 1.4 M n-butyllithium in hexane (1.3 mL, 1.77 mmol) at −20 °C. After 15 min, the solution was cooled to −78 °C and a solution of **20** (240 mg, 0.803 mmol) in 3 mL of dry tetrahydrofuran was added dropwise. An additional 7 mL of dry tetrahydrofuran was introduced dropwise at −78 °C to dissolve the precipitated solid, and the white, milky suspension was stirred at −78 °C for 2 h. Neat crotonaldehyde (149 μL, 1.80 mmol) was introduced via syringe, and the mixture was stirred at −78 °C for an additional 1 h. After being quenched with saturated NH_4Cl solution at −78 °C, the mixture was diluted with ether (200 mL), washed with brine (50 mL), and dried. The residue after concentration was subjected to MPLC on silica gel (ether as eluent) to give 99 mg (33%) of **22a** and 108 mg (37%) of **22b** as colorless liquids. The overall yield was 70%.

For **22a**: IR (neat, cm^{-1}) 3430 (br), 1750; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50 (m, 2 H), 7.27 (m, 3 H), 5.78 (m, 1 H), 5.50 (m, 1 H), 4.48 (m, 1 H), 4.42 (dd, J = 8.4, 8.8 Hz, 1 H), 3.86 (dd, J = 8.8, 8.1 Hz, 1 H), 3.64 (m, 1 H), 3.02 (dd, J = 12.7, 4.3 Hz, 1 H), 2.88 (dd, J = 12.7, 8.3 Hz, 1 H), 2.83−2.52 (series of m, 1 H), 2.49 (dd, J = 8.8, 3.7 Hz, 1 H), 1.79 (m, 1 H), 1.70 (dd, J = 5.1, 0.8 Hz, 3 H), 1.70−1.53 (series of m, 3 H); ^{13}C NMR (62.5 MHz, $CDCl_3$) ppm 178.08, 133.28, 129.90, 129.35, 129.12, 128.61, 127.69, 72.32, 71.13, 67.67, 51.13, 39.40, 36.93, 33.26, 17.67; MS m/z (M^+) calcd 370.0683 obsd 370.0689; $[\alpha]^{20}_D$ +12.1° (c 0.61, $CHCl_3$).

For **22b:** IR (neat, cm^{-1}) 3400 (br), 1750; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52 (m, 2 H), 7.28 (m, 3 H), 5.79 (m, 1 H), 5.54 (m, 1 H), 4.42 (dd, J = 9.0, 8.3 Hz, 2 H), 3.86 (t, J = 8.7 Hz 1 H), 3.67 (m, 1 H), 3.05 (dd, J = 12.8, 4.1 Hz, 1 H), 2.87 (dd, J = 12.8, 8.4 Hz, 1 H), 2.83−2.60 (series of m, 1 H), 2.50 (dd, J = 9.1, 6.0 Hz, 1 H), 1.87 (m, 1 H), 1.72 (dd, J = 6.5, 1.4 Hz, 3 H), 1.70−1.54 (series of m, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 177.79, 133.19, 133.11, 129.82, 129.56, 129.24, 127.56, 72.67, 72.09, 67.88, 50.66, 39.32, 36.84, 34.50, 17.57; MS m/z (M^+) calcd 370.0683, obsd 370.0668; $[\alpha]^{20}_D$ +3.1° (c 0.49, $CHCl_3$).

(3*S*,4*R*)-Dihydro-3-[(1*R*,2*E*)- and (3*S*,4*R*)-Dihydro-3-[(1*S*,2*E*)-1-hydroxy-2-butenyl]-4-[(2*S*)-2-hydroxy-3-(phenylseleno)propanyl]-2(3*H*)-furanone (21a and 21b). The condensation of **19** (235 mg, 0.786 mmol) with crotonaldehyde was carried out in the same manner as described above. Inseparable diastereoisomers **21a** and **21b** (222 mg, 77%) and starting material (37 mg, 16%) were isolated by MPLC on silica gel (ether as eluent). The overall yield was 91% based on recovered starting material. The pale yellow oil exhibited the following: IR (neat, cm^{-1}) 3400 (br), 1750; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51 (m, 2 H), 7.28 (m, 3 H), 5.77 (m, 1 H), 5.52 (m, 1 H), 4.48 (m, 1.5 H), 4.32 (m, 0.5 H), 3.92 (m, 1 H), 3.66 (m, 1 H), 3.07 (m, 1 H), 2.85 (m, 1 H), 2.69−2.52 (series of m, 2 H), 2.45 (m, 1 H), 1.88 (m, 1 H), 1.69 (dm, J = 6.3 Hz, 3 H), 1.70 (s, 1 H), 1.59 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 178.09, 177.74, 133.21 (2C), 129.92, 129.81, 129.67, 129.34(2C), 129.00, 127.64, 127.58, 73.14, 72.95, 72.63, 71.06, 68.77, 68.74, 51.11, 50.55, 39.85, 39.67, 37.16, 36.89, 35.75, 34.70, 17.63 (2C); MS m/z (M^+) calcd 370.0683, obsd 370.0679.

Dehydration−Cyclization of 21a/21b. The diastereomeric diols **21a** and **21b** (30 mg, 0.0810 mmol) were dissolved in 25 mL of dry benzene and treated with 1 mg of $TsOH·H_2O$. The solution was refluxed for 3 h and cooled to room temperature. After dilution with ether (50 mL), the mixture was washed with saturated $NaHCO_3$ solution and dried. The residue after concentration was subjected to MPLC on silica gel (50% ether/petroleum ether as eluent) to give 24 mg (84%) of pure **13**: IR (neat, cm^{-1}) 1770; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52 (m, 2 H), 7.25 (m, 3 H), 5.87 (dqd, J = 15.4, 6.5, 1.1 Hz, 1 H), 5.64 (ddq, J = 15.4, 5.7, 1.5 Hz, 1 H), 4.34 (dd, J = 8.4, 6.5 Hz, 1 H), 4.20 (m, 2 H), 3.82 (dd, J = 10.9, 8.4 Hz, 1 H), 3.24 (dd, J = 12.4, 6.5 Hz, 1 H), 3.05 (dd, J =12.4, 8.5 Hz, 1 H), 2.40 (m, 1 H), 2.11 (ddd, J = 13.0, 4.2, 2.4 Hz, 1 H), 2.00 (dd, J = 13.8, 9.9 Hz, 1 H), 1.75 (dd, J = 6.5, 1.1 Hz, 3 H), 1.70 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 173.44, 133.11, 129.50, 129.23, 129.12, 127.81, 127.37, 71.47, 71.40, 71.34, 47.16, 36.24, 30.37, 29.63, 17.88; MS m/z (M^+) calcd 352.0577, obsd 352.0574; $[\alpha]^{20}_D$ +39.8° (c 0.60, $CHCl_3$).

Dehydration−Cyclization of 22a and 22b. Comparable treatment of **22a** (23 mg, 0.0623 mmol) but with a reduction in reflux time to 2 h gave 18 mg (82%) of **12**. Diastereomer **22b** (29.9 mg, 0.0180 mol) gave 25 mg (88%) of **12** after 1 h of heating: IR (neat, cm^{-1}) 1770; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52 (m, 2 H), 7.27 (m, 3 H), 5.87 (dqd, J = 15.5, 6.5, 0.7 Hz, 1 H), 5.74 (ddq, J = 15.5, 5.3, 1.2 Hz, 1 H), 4.39 (dd, J = 8.4, 6.5 Hz, 1 H), 3.97 (dd, J = 9.4, 5.4 Hz, 1 H), 3.87 (dd, J = 11.0, 8.5 Hz, 1 H), 3.62 (m, 1 H), 3.22 (dd, J = 12.5, 5.6 Hz, 1 H), 3.01 (dd, J = 12.5, 6.8 Hz, 1 H), 2.34 (m, 1 H), 2.16 (ddd, J = 12.4, 3.2, 2.5 Hz, 1 H), 1.98 (dd, J = 13.6, 9.5 Hz, 1 H), 1.76 (d, J = 6.2 Hz, 3 H), 1.36 (q, J = 12.1 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 173.10, 132.61, 130.17, 129.19, 129.11, 127.35, 127.05, 76.94, 76.27, 70.92, 47.77, 41.80, 33.69, 32.50, 17.90; MS m/z (M^+) calcd 352.0577, obsd 352.0572; $[\alpha]^{20}_D$ +18.8° (c 0.60, $CHCl_3$).

Isomerization of 14. Lactone **12** (235 mg, 92%) was isolated when **14** (255 mg, 0.691 mmol) was refluxed in benzene (40 mL) in the presence of a catalytic amount of $TsOH·H_2O$ for 2 h.

(3a*S*,4*S*,7a*R*)-1,3a,4,7a-Tetrahydro-6-methyl-4-[(*E*)-propenyl]-3*H*-furo[3,4-*c*]pyran-3-one (28). To a solution of **14** (60 mg, 0.169 mmol) in methanol (4.3 mL) and water (0.7 mL) were added solid $NaHCO_3$ (15.6 mg, 0.186 mmol) and $NaIO_4$ (47 mg, 0.22 mmol). After 1 h, the usual workup gave the selenoxide that was directly dissolved in toluene (2 mL) containing triethylamine and refluxed under nitrogen for 18 h. The solvent was removed in vacuo, and the residue was subjected to MPLC on silica gel (elution with 30% ethyl acetate in petroleum ether) to give 7 mg (21%) of **16** followed by 12.2 mg (37%) of **28**: colorless oil; IR (neat, cm^{-1}) 2920, 1775, 1655, 1385, 1330, 1205, 1100; ^{1}H NMR (300 MHz $CDCl_3$) δ 5.74 (dqd, J = 15.3, 6.5, 1.5 Hz, 1 H), 5.45 (dmd, J = 15.3, 1.6 Hz, 1 H), 5.08 (ddd, J = 3.9, 3.8, 1.6 Hz, 1 H), 4.62 (s, 1 H), 4.44 (dd, J = 6.7, 7.9 Hz, 1 H), 3.87 (dd, J = 8.0, 11.2 Hz, 1 H), 2.96−2.93 (m, 1 H), 2.68 (dd, J = 5.6, 14.0 Hz, 1 H), 1.80 (dd, J = 2.1, 0.8 Hz, 3 H), 1.73 (dt, J = 6.5, 1.5 Hz, 3 H); MS m/z (M^+) calcd 194.0942, obsd 194.0935.

Acid-Catalyzed Hydrolysis of 28. A solution of **28** in $CDCl_3$ was allowed to stand open to the atmosphere. Quantitative conversion to the ring-opened hydroxy ketone occurred after several hours: IR (neat, cm^{-1}) 3450, 2905, 1755, 1700, 1375, 1260, 1020, 970; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.82 (dq, J = 15.3, 6.5 Hz, 1 H), 5.55 (ddd, J = 15.3, 7.5, 1.5 Hz, 1 H), 4.62 (dd, J = 8.6, 8.9 Hz, 1 H), 4.39 (dd, J = 6.8, 7.0 Hz, 1 H), 3.79 (dd, J = 8.0, 9.3 Hz, 1 H), 3.10 (br s, 1 H), 2.95 (dd, J = 4.5, 8.1 Hz, 1 H), 2.83 (m, 1 H), 2.56 (dd, J = 8.9, 18.1 Hz, 1 H), 2.44 (dd, J = 6.3, 8.8 Hz, 1 H), 2.16 (d, J = 2.0 Hz, 3 H), 1.73 (dd, J = 6.5, 1.5 Hz, 3 H); MS m/z (M^+ − OH) calcd 195.1021, obsd 195.1007.

(3a*S*,7*R*)-3a,6,7,8-Tetrahydro-7-methylcycloocta[*c*]furan-1,5(3*H*,4*H*)-dione (29). A 23 mg (0.065 mmol) sample of **14** was dissolved in methanol (1.7 mL) and water (0.3 mL) and oxidized with $NaIO_4$ (18 mg, 0.084 mmol) in the presence of $NaHCO_3$ (5.9 mg, 0.071 mmol). The resulting selenoxide was taken up into toluene (1 mL) containing diethylamine (30 mL, 0.290 mmol) and heated in a sealed Pyrex tube at 175−180 °C for 24 h. Direct MPLC purification (silica gel, elution with 30% ethyl acetate in petroleum ether) afforded 6.2 mg

(49%) of **29** as colorless needles: mp 90–92 °C; IR (KBr, cm^{-1}) 2960, 2920, 1755, 1705, 1250, 1200, 1110, 1040; ^1H NMR (300 MHz, $CDCl_3$) δ 7.04 (td, J = 8.2, 2.0 Hz, 1 H), 4.47 (dd, J = 7.7, 9.4 Hz, 1 H), 4.06 (dd, J = 9.4, 1.8 Hz, 1 H), 3.22 (m, 1 H), 2.78 (dd, J = 10.5, 13.1 Hz, 1 H), 2.58 (dd, J = 10.5, 4.2 Hz, 1 H), 2.38–2.03 (series of m, 5 H), 1.05 (d, J = 5.2 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 209.92, 169.66, 138.34, 131.44, 71.04, 52.43, 47.40, 34.21, 33.98, 28.34, 20.56; MS m/z (M^+) calcd 194.0942, obsd 194.0954; $[\alpha]^{20}_D$ −61.5° (c 1.35, $CHCl_3$). Anal. Calcd for $C_{11}H_{14}O_3$: C, 68.02; H, 7.65. Found: C, 68.26; H, 7.42.

(3a*R*,7*S*,9a*R*)-3a,6,7,9a-Tetrahydro-7-methylcycloocta[*c*]furan-1,5(3*H*,4*H*)-dione (30). A 1.00 g (2.82 mmol) sample of **14** was transformed into **25** in the predescribed manner and the crude selenoxide so formed was dissolved in mesitylene (80 mL) containing dimethylamine (1.2 mL). This solution was refluxed under nitrogen for 2 h, cooled, and filtered through silica gel. Following the removal of mesitylene (elution with petroleum ether), the ketones were flushed out with ether. The ethereal eluate was concentrated to give a dark oil that was subjected to MPLC (silica gel, elution with 30% ethyl acetate in petroleum ether) to give 265 mg (48%) of a 1:1 mixture of **29** and **30**.

For **30**: ^1H NMR (300 MHz, $CDCl_3$) the characteristic methyl signal of this diastereomer appears at δ 1.15 (d, J = 6.0 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 208.75, 177.01, 141.07, 120.91, 71.34, 53.97, 42.25, 40.71, 37.43, 30.26, 22.09.

(3a*R*,7*R*)-3a,6,7,8-Tetrahydro-7-methylspiro[cycloocta[*c*]furan-5(3*H*),2′-[1,3]dioxolan]-1(4*H*)-one (31a). A solution of **29** (46 mg, 0.237 mmol) in dichloromethane (1.5 mL) was treated with ethylene glycol (0.33 mL), trimethyl orthoformate (0.125 mL), and *p*-toluenesulfonic acid (4.5 mg) and stirred under a nitrogen atmosphere for 16 h. The reaction mixture was poured into water (10 mL) and extracted with dichloromethane (3 × 30 mL). The combined organic layers were washed with brine, dried, and evaporated. MPLC purification of the residue (silica gel, elution with 30% ethyl acetate in petroleum ether) gave 54.8 mg (98%) of **31a** as a colorless oil: IR (neat, cm^{-1}) 2960, 1705, 1675, 1200, 1140, 1100, 1040; ^1H NMR (300 MHz, $CDCl_3$) δ 6.95 (td, J = 7.7, 2.1 Hz, 1 H), 4.41 (dd, J = 8.9, 7.8 Hz, 1 H), 4.00–3.89 (series of m, 4 H), 3.94 (dd, J = 3.8, 8.9 Hz, 1 H), 3.34 (dd, J = 7.8, 15.7 Hz, 1 H), 2.67 (m, 1 H), 2.26–2.14 (m, 2 H), 1.91 (d, J = 10.0 Hz, 1 H), 1.90 (d, J = 6.0 Hz, 1 H), 1.76 (dd, J = 4.2, 14.8 Hz, 1 H), 1.59 (dd, J = 10.1, 14.8 Hz, 1 H), 0.95 (d, J = 6.7 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 170.58, 138.90, 131.66, 109.16, 72.26, 65.26, 63.63, 46.42, 43.77, 35.20, 33.28, 27.93, 22.25; MS m/z (M^+) calcd 238.1204, obsd 238.1203.

(3a*R*,7*S*,8*R*)-3a,6,7,8-Tetrahydro-7-methyl-8-(phenylselenyl)spiro[cycloocta[*c*]furan-5(3*H*),2′-[1,3]dioxolan]-1(4*H*)-one (31b). A magnetically stirred solution of **31a** (36 mg, 0.151 mmol) in anhydrous tetrahydrofuran (1.4 mL) was cooled to −78 °C and treated dropwise with potassium hexamethyldisilazide (0.45 mL of 0.5 M in toluene, 0.227 mmol). After 1 h, a solution of phenylselenenyl chloride (43 mg, 0.227 mmol) in THF (0.72 mL) was added at once and allowed to react for 1 h. The reaction mixture was quenched with saturated NH_4Cl solution (5 mL) and extracted with dichloromethane (3 × 30 mL). The combined organic phases were washed with brine, dried, and evaporated. MPLC of the residue on silica gel (elution with 30% ethyl acetate in petroleum ether) gave 43 mg (72%) of **31b** as a yellow oil: IR (neat, cm^{-1}) 2980, 1750, 1650, 1480, 1440, 1250, 1200, 1120, 1040; ^1H NMR (300 MHz, $CDCl_3$) δ 7.52 (m, 2 H), 7.32 (m, 3 H), 6.97 (dd, J = 1.4, 6.6 Hz, 1 H), 3.98–3.82 (m, 4 H), 3.62 (d, J = 5.9 Hz, 1 H), 3.61 (d, J = 2.8 Hz, 1 H), 3.46 (dd, J = 6.7, 12.4 Hz, 1 H), 2.29 (m, 1 H), 2.17 (m, 1 H), 1.81 (dd, J = 4.5, 14.8 Hz, 1 H), 1.75 (d, J = 13.5 Hz, 1 H), 1.66 (dm, J = 14.8 Hz, 1 H), 1.51 (d, J = 13.8, Hz, 1 H), 1.41 (d, J = 6.7 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 171.66, 138.65, 138.38, 129.21, 128.90, 127.42, 125.87, 108.90, 73.06, 64.91, 64.32, 52.87, 44.89, 42.96, 32.69, 29.05, 24.99; MS m/z (M^+ − SePh) calcd 237.1125, obsd 237.1159.

(3a*S*,7*S*,9a*S*)-3a,6,7,9a-Tetrahyro-9a-hydroxy-7-methylspiro[cycloocta[*c*]furan-5(3*H*),2′-[1,3]dioxolan]-1(4*H*)-one (32). To a solution of **31b** (43 mg, 0.109 mmol) in methanol (2.8 mL) and water (0.4 mL) were added solid $NaHCO_3$ (10 mg, 0.120 mmol) and $NaIO_4$ (30 mg, 0.142 mmol), and the mixture was stirred at room temperature for 1 h before being poured into water (10 mL). The product was extracted into dichloromethane (3 × 10 mL), and the combined organic layers were washed with brine, dried, and evaporated. The residue was subjected to MPLC (silica gel, elution with 30% ethyl acetate in petroleum ether) to give 24 mg (86%) of **32** as a colorless oil: IR (neat, cm^{-1}) 3400, 2960, 1765, 1200, 1150, 1090; ^1H NMR (300 MHz, $CDCl_3$) δ 5.83 (dd, J = 7.9, 11.4 Hz, 1 H), 5.55 (dd, J = 1.4, 11.4 Hz, 1 H), 4.43 (dd, J = 7.8, 8.9 Hz, 1 H), 3.90–3.88 (m, 4 H), 3.70 (t, J = 8.6 Hz, 1 H), 3.26 (br s, 1 H), 3.24–3.14 (m, 1 H), 3.08 (dm, J = 2.9 Hz, 1 H), 1.97 (dd, J = 10.8, 14.5 Hz, 1 H), 1.88 (dt, J = 14.1, 1.6 Hz, 1 H), 1.73 (ddd, J = 1.3, 3.0, 14.5 Hz, 1 H), 1.62 (dd, J = 11.1, 14.1 Hz, 1 H), 1.06 (d, J = 6.9 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 178.23, 145.56, 123.13, 109.68, 76.20, 71.12, 64.88, 64.10, 45.47, 43.28, 38.26, 27.46, 22.53; MS m/z (M^+) calcd 254.1155, obsd 254.1172.

(7*S*)-6,7-Dihydro-7-methylcycloocta[*c*]furan-1,5(3*H*,4*H*)-dione (33). A cold (0 °C), magnetically stirred solution of **32** (39 mg, 0.154 mmol) in dichloromethane (6.5 mL) was blanketed with nitrogen and treated sequentially with triethylamine (48 μL, 0.351 mmol) and then methanesulfonyl chloride (14 μL, 0.184 mmol). The reaction mixture was stirred at 0 °C for 30 min, diluted with dichloromethane (30 mL), and washed with 10% HCl (10 mL) and saturated $NaHCO_3$ solutions. The dried organic phase was evaporated, and the mesylate was taken up in benzene (8 mL), treated with DBU (73 μL, 0.461 mmol) and DMAP (18 mg, 0.154 mmol), and refluxed under nitrogen for 20 h. The cooled solution was washed with 10% HCl (10 mL), saturated $NaHCO_3$ solution (10 mL), and brine (10 mL) before being dried and concentrated. The resulting oil was dissolved in THF (8 mL), treated with concentrated HCl (1 drop), stirred at room temperature for 24 h, poured into saturated $NaHCO_3$ solution (10 mL), and extracted with dichloromethane (3 × 10 mL). The combined extracts were dried, evaporated, and subjected to MPLC purification (silica gel, elution with 50% ethyl acetate in petroleum ether). There was obtained 12.5 mg (42%) of **33** as a faint yellow oil: IR (neat, cm^{-1}) 2960, 1750, 1715, 1455, 1040, 1000; ^{13}C NMR (300 MHz, $CDCl_3$) δ 6.03 (d, J = 11.3 Hz, 1 H), 5.76 (dd, J = 8.0, 11.2 Hz, 1 H), 4.82 (d, J = 17.2 Hz, 1 H), 4.64 (d, J = 17.2 Hz, 1 H), 3.82 (d, J = 16.4 Hz, 1 H), 3.15 (d, J = 16.3 Hz, 1 H), 3.18–3.09 (m, 1 H), 2.82 (dd, J = 3.6, 13.5 Hz, 1 H), 2.49 (t, J = 13.0 Hz, 1 H), 1.20 (d, J = 6.6 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 203.22, 172.68, 154.34, 141.40, 124.58, 117.90, 72.33, 54.54, 42.19, 31.02, 20.91; MS m/z (M^+) calcd 192.0786, obsd 192.0797; $[\alpha]^{20}_D$ −140° (c 1.1, $CHCl_3$).

(3a*R*,7*S*)-3a,6,7,8-Tetrahydro-7-methylcycloocta[*c*]furan-1,5(3*H*,4*H*)-dione (34a). The selenoxide obtained from oxidation of 70 mg (0.198 mmol) of the **12/13** mixture in the predescribed manner was dissolved in toluene (5.5 mL) containing diethylamine (81 μL, 0.791 mmol) and placed in a sealed Pyrex tube. Following heating of the tube at 175–180 °C for 24 h, the cooled dark reaction mixture was concentrated and subjected to MPLC purification (silica gel, elution with 30% ethyl acetate in petroleum ether) to give 18.7 mg (49%) of **34a** as white needles: mp 83–84 °C; IR (neat, cm^{-1}) 2960, 2930, 1755, 1705, 1460, 1225, 1175, 1040; ^1H NMR (300 MHz, $CDCl_3$) δ 7.01 (td, J = 9.5, 1.9 Hz, 1 H), 4.43 (dd, J = 7.2, 9.3 Hz, 1 H), 4.06 (dd, J = 1.7, 9.5 Hz, 1 H), 3.36 (dd, J = 8.5, 16.2 Hz, 1 H), 2.66 (dd, J = 9.0 Hz, 2 H), 2.63 (dd, J = 5.0, 12.5 Hz, 1 H), 2.43 (m, 1 H), 2.23 (dd, J = 4.2, 12.3 Hz, 1 H), 2.04–1.82 (m, 1 H), 1.90 (dd, J = 9.6, 11.7 Hz, 1 H), 1.19 (d, J = 6.3 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 209.22, 169.73, 139.74, 131.03, 70.76, 52.14, 46.45, 36.19, 33.81, 28.21, 21.49; MS m/z (M^+) calcd 194.0942, obsd 194.0932; $[\alpha]^{20}_D$ −10° (c 1.2, $CHCl_3$).

X-ray Crystal Structure Analysis of 34a. Suitable crystals of **34a** for X-ray diffraction studies formed with space group symmetry of $P4_32_12$ and cell constants of a = 7.318(1) Å and c = 36.744(4) Å for Z = 8 and a calculated density of 1.276 g/cm^3. Of the 889 reflections measured with an automatic four circle diffractometer equipped with Cu radiation, 689 were observed ($I > 3\sigma I$). The structure was solved with a

direct methods approach and difference Fourier analysis and refined using full-matrix least-squares techniques.[22] Hydrogens were assigned isotropic temperature factors corresponding to their attached atoms. The function $\sum w(|F_o| - |F_c|)^2$ with $w = 1/(\sigma F_o)^2$ was minimized to give an unweighted residual of 0.048. No abnormally short intermolecular contacts were noted. Tables VI–VIII containing the final fractional coordinates, temperature parameters, bond distances, and bond angles are available from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK. Figure 2 is a computer generated perspective drawing of **34a** from the final X-ray coordinates showing the correct absolute stereochemistry.

(3a*R*,7*S*)-3a,6,7,8-Tetrahydro-7-methylspiro[cycloocta-[*c*]furan-5(3*H*),2′-[1,3]dioxolan]-1(4*H*)-one (34b). A solution of **34a** (41 mg, 0.211 mmol) in dichloromethane (3 mL) was treated with ethylene glycol (0.25 mL), trimethyl orthoformate (0.13 mL), and *p*-toluenesulfonic acid (4 mg) and stirred under nitrogen for 16 h. The reaction mixture was poured into water (10 mL) and extracted with dichloromethane (3 × 30 mL). The usual workup followed by MPLC on silica gel (elution with 30% ethyl acetate in petroleum ether) furnished 49.2 mg (98%) of **34b** as a faintly yellowish oil: IR (neat, cm^{-1}) 2950, 1755, 1675, 1190, 1135, 1100, 1040; ^1H NMR (300 MHz, $CDCl_3$) δ 6.94 (td, J = 7.9, 2.2 Hz, 1 H), 4.41 (t, J = 8.4 Hz, 1 H), 3.97–3.85 (m, 5 H), 3.26 (m, 1 H), 2.37 (d, J = 8.1 Hz, 1 H), 2.35 (dd, J = 4.4, 9.4 Hz, 1 H), 2.04–1.84 (series of m, 4 H), 1.69 (dd, J = 4.3, 14.9 Hz, 1 H), 1.11 (d, J = 6.8 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 171.05, 139.69, 130.99, 110.66, 71.21, 64.76, 63.86, 43.82, 41.90, 35.29, 34.48, 28.87, 23.00; MS m/z (M^+) calcd 238.1204, obsd 238.1227.

(3a*R*,7*R*,9a*R*)-3a,6,7,9a-Tetrahydro-7-methylcycloocta-[*c*]furan-1,5(3*H*,4*H*)-dione (35a). The selenoxide resulting from oxidation of the **12/13** mixture (905 mg, 2.56 mmol) in the predescribed manner was dissolved in mesitylene (70 mL, dried over P_2O_5), treated with diethylamine (1.05 mL, 10.22 mmol), and stirred at the reflux temperature under nitrogen for 1 h. The cooled reaction mixture was passed through a column of silica gel (3 cm × 30 cm) and washed with petroleum ether until mesitylene was no longer eluted. Subsequent washing with ethyl acetate (500 mL) and concentration of the eluate to dryness left a dark oil that was purified by MPLC on silica gel (elution with 30% ethyl acetate in petroleum ether). There was isolated 247 mg (50%) of **35a**, an analytical sample of which was obtained by preparative GC (5% SE-30, 150 °C): colorless oil; IR (neat, cm^{-1}) 2970, 1770, 1705, 1385, 1350, 1160, 1015; ^1H NMR (300 MHz, $CDCl_3$) δ 5.71 (dd, J = 6.5, 10.5 Hz, 1 H), 5.62 (m, 1 H), 4.39 (t, J = 7.5 Hz, 1 H), 3.85 (dd, J = 8.9, 11.1 Hz, 1 H), 3.35 (dd, J = 6.3, 12.7 Hz, 1 H), 3.21–3.06 (m, 1 H), 2.87 (t, J = 11.5 Hz, 1 H), 2.76 (dd, J = 4.5, 14.0 Hz, 1 H), 2.39–2.29 (m, 3 H), 1.15 (d, J = 6.4 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 207.83, 176.27, 139.92, 123.92, 70.45, 56.07, 45.32, 41.94, 41.14, 29.31, 20.65; MS m/z (M^+) calcd 194.0942, obsd 194.0922; $[\alpha]^{20}_D$ +7.1° (c 0.85, $CHCl_3$). Anal. Calcd for $C_{11}H_{14}O_3$: C, 68.02; H, 7.65. Found: C, 68.26; H, 7.41.

When **8a** (2.35 g, 12.0 mmol) was exposed to *N*-(phenylseleno)phthalimide (4.00 g, 13.2 mmol) and the resulting **12/13** mixture was directly oxidized and heated in mesitylene without isolation of the intermediates, **35a** was isolated in 66% overall yield (1.53 g).

(3a*R*,7*R*,9a*R*)-3a,6,7,9a-Tetrahydro-7-methylspiro[cycloocta[*c*]furan-5(3*H*),2′-[1,3]dioxolan]-1(4*H*)-one (35b). A 247 mg (1.27 mmol) sample of **35a** was ketalized as described above to give 292 mg (96%) of **35b** as a colorless crystalline solid: mp 71–73 °C; IR (KBr, cm^{-1}) 2970, 1770, 1360, 1170, 1070, 975, 955; ^1H NMR (300 MHz, $CDCl_3$) δ 5.75 (dd, J = 6.2, 10.2 Hz, 1 H), 5.68 (m, 1 H), 4.29 (t, J = 8.0 Hz, 1 H), 3.90 (m, 4 H), 3.79 (dd, J = 8.4, 11.4 Hz, 1 H), 3.27 (dd, J = 6.1, 12.7 Hz, 1 H), 2.72–2.49 (m, 2 H), 2.06 (m, 1 H), 2.01 (m, 1 H), 1.82 (dd, J = 2.0, 11.9 Hz, 1 H), 1.73 (d, J = 14.2 Hz, 1 H), 1.04 (d, J = 6.5 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 177.80, 139.80, 123.30, 109.24, 70.72, 64.95, 63.02, 49.72, 45.50, 39.63, 38.40, 29.18, 21.65; MS m/z (M^+) calcd 238.1204, obsd 238.1227; $[\alpha]^{20}_D$ −22.1° (c 0.95, $CHCl_3$). Anal. Calcd for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61. Found: C, 65.54; H, 7.59.

Selenenylation–Oxidation of 35b. To a solution of **35b** (99 mg, 0.416 mmol) in cold (−78 °C), anhydrous tetrahydrofuran (4 mL) was added potassium hexamethyldisilazide (1.24 mL of 0.5 M in toluene, 0.620 mmol). After 1 h, phenylselenenyl chloride (119 mg, 0.624 mmol) in THF (1 mL), was added in one portion. Following the predescribed workup and MPLC on silica gel (elution with 30% ethyl acetate in petroleum ether), **36** was obtained as a mixture of diastereomers (140 mg, 86%), that was directly oxidized with $NaIO_4$ (99 mg, 0.463 mmol) in the presence of $NaHCO_3$ (32.9 mg, 0.392 mmol) in methanol (9.1 mL) and water (1.5 mL). MPLC purification (silica gel, elution with 30% ethyl acetate in petroleum ether) afforded 18 mg (20%) of **37** followed by 40 mg (44%) of **38**.

For **37**: colorless crystals, mp 109–111 °C; IR (KBr, cm^{-1}) 3400, 2960, 1770, 1360, 1215, 1090; ^1H NMR (300 MHz, $CDCl_3$) δ 5.93 (dd, J = 0.7, 11.0 Hz, 1 H), 5.79 (dd, J = 8.7, 11.0 Hz, 1 H), 4.21 (t, J = 7.6 Hz, 1 H), 4.02 (m, 1 H), 3.95–3.78 (m, 4 H), 3.40–3.35 (m, 1 H), 2.72–2.62 (m, 2 H), 2.38 (br s, 1 H), 1.94 (dd, J = 4.0, 14.7 Hz, 1 H), 1.77 (dd, J = 10.7, 14.7 Hz, 1 H), 1.52–1.42 (m, 1 H), 1.03 (d, J = 6.7 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 177.24, 145.06, 126.12, 110.41, 73.05, 70.16, 64.77, 63.41, 49.41, 42.21, 30.93, 26.73, 22.10; MS m/z (M^+) calcd 254.1154, obsd 254.1190; $[\alpha]^{20}_D$ −30° (c 1.3, $CHCl_3$).

For **38**: colorless crystals, mp 137–140 °C; IR ($CHCl_3$, cm^{-1}) 3450, 1780, 1205, 1145, 1080, 1035, 955; ^1H NMR (300 MHz, $CDCl_3$) δ 6.04 (dd, J = 4.5, 12.6 Hz, 1 H), 5.39 (dd, J = 2.0, 12.5 Hz, 1 H), 4.36 (t, J = 8.8 Hz, 1 H), 4.12–3.85 (m, 4 H), 3.54 (dd, J = 9.1, 10.9 Hz, 1 H), 3.19 (br s, 1 H), 3.09 (dd, J = 12.1, 14.8 Hz, 1 H), 2.98–2.86 (m, 1 H), 2.51–2.43 (m, 1 H), 1.94 (dd, J = 12.0, 14.1 Hz, 1 H), 1.57 (t, J = 14.2 Hz, 2 H), 1.08 (d, J = 7.2 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 180.56, 147.02, 121.00, 110.47, 75.22, 69.47, 64.64, 64.42, 42.72, 39.61, 36.08, 32.64, 22.82; MS m/z (M^+) calcd 254.1154, obsd 254.1111; $[\alpha]^{20}_D$ +34.8° (c 1.35, $CHCl_3$).

X-Ray Crystal Structure Analysis of 38. Suitable crystals of **38** for X-ray diffraction studies formed with space group symmetry of $P2_12_12_1$ and cell constants of a = 8.676(2) Å, b = 9.362(1) Å, and c = 15.454(2) Å for Z = 4 and a calculated density of 1.345 g/cm^3. Of the 1006 reflections measured with an automatic four circle diffractometer equipped with Cu radiation, 952 were observed ($I > 3\sigma I$). The structure was solved with a direct methods approach and difference Fourier analysis and refined using full-matrix least-squares techniques.[22] Hydrogens were assigned isotropic temperature factors corresponding to their attached atoms. The function $\sum w(|F_o| - |F_c|)^2$ was minimized to give an unweighted residual of 0.043. No abnormally short intermolecular contacts were noted. Tables IX–XI containing the final fractional coordinates, temperature parameters, bond distances, and bond angles are available from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK. Figure 3 is a computer generated perspective drawing of **38** from the final X-ray coordinates.

(7*R*)-6,7-Dihydro-7-methylspiro[cycloocta[*c*]furan-5(3*H*),2′-[1,3]dioxolan]-1(4*H*)-one (39). To an ice-cold, magnetically stirred solution of **38** (17 mg, 0.067 mmol) in dichloromethane (3.5 mL) containing triethylamine (22.4 μL, 0.172 mmol) and blanketed with nitrogen was added methanesulfonyl chloride (6.5 μL, 0.084 mmol). After 1.5 h of stirring at 0 °C, the reaction mixture was placed in a refrigerator at −5 °C for 12 h, poured into 10% HCl, and extracted with dichloromethane (3 × 10 mL). The combined organic layers were washed with saturated $NaHCO_3$ and brine solutions, dried, and evaporated. The residue was taken up in benzene (5 mL), treated with DBU (41.9 μL, 0.28 mmol) and DMAP (8.5 mg, 0.070 mmol), and heated at reflux under nitrogen for 24 h. The reaction mixture was cooled to room temperature and worked up in the usual manner. MPLC purification (silica gel, elution with 30% ethyl acetate in petroleum ether) afforded **39** (6.5 mg, 41%) as a colorless oil: IR (neat, cm^{-1}) 2960, 2930, 1750, 1660, 1440, 1330, 1050, 740;

(22) The following library of crystallographic programs was used: SHELXS-86, Sheldrick, G. M., University of Gottingen, Gottingen, West Germany (1986); SDP Plus V1.1, Ikaya, Y.; Frenz, B. A., B. A. Frenz and Associates, College Station, Texas (1984).

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.99 (dd, J = 1.8, 11.8 Hz, 1 H), 5.77 (dd, J = 4.9, 11.8 Hz, 1 H), 4.77 (s, 2 H), 4.04–3.88 (m, 4 H), 2.88 (d, J = 13.2 Hz, 1 H), 2.54 (d, J = 13.2 Hz, 1 H), 2.58–2.52 (m, 1 H), 1.93 (dd, J = 10.9, 14.5 Hz, 1 H), 1.51 (d, J = 14.4 Hz, 1 H), 1.11 (d, J = 7.1 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 173.21, 157.42, 142.93, 126.76, 116.12, 108.62, 72.80, 64.80 (2C), 41.20, 36.44, 30.96, 24.48; MS m/z (M^+) calcd 236.1048, obsd 236.1033.

(7*R*)-6,7-Dihydro-7-methylcycloocta[*c*]furan-1,5(3*H*,4*H*)-dione (40). A solution of **40** (6.5 mg, 0.028 mmol) in tetrahydrofuran (3 mL) was treated with concentrated HCl (2 drops), stirred at room temperature for 16 h, poured into water (10 mL), and extracted with dichloromethane (3 × 10 mL). The combined organic layers were washed with saturated $NaHCO_3$ and brine solutions, dried, and evaporated. the residue was purified by MPLC on silica gel (elution with 50% ethyl acetate in petroleum ether) to give 3 mg (56%) of **40** and 3 mg of unreacted **39**.

For **40**: colorless oil; IR (neat, cm^{-1}) 2930, 1750, 1715, 1455, 1040, 1000; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.03 (d, J = 11.2 Hz, 1 H), 5.77 (dd, J = 8.2, 11.2 Hz, 1 H), 4.82 (d, J = 17.5 Hz, 1 H), 4.64 (d, J = 17.5 Hz, 1 H), 3.82 (d, J = 16.5 Hz, 1 H), 3.15 (d, J = 16.3 Hz, 1 H), 3.18–3.09 (m, 1 H), 2.82 (dd, J = 3.8, 13.3 Hz, 1 H), 2.49 (t, J = 13.0 Hz, 1 H), 1.20 (d, J = 6.6 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 203.25, 172.70, 154.36, 141.40, 124.56, 117.89, 72.35, 54.56, 42.19, 31.01, 20.91; MS m/z (M^+) calcd 192.0786, obsd 192.0794; $[\alpha]^{20}_D$ +121° (c 0.85, $CHCl_3$).

(3a*S*,7*R*,7a*S*,8a*S*,8b*S*)-Octahydro-8b-hydroxy-7-methylspiro[1*H*-cyclopropa[3,4]cycloocta[1,2-*c*]furan-5(3*H*),2′-[1,3]dioxolan]-1-one (41). A solution of **37** (22 mg, 0.087 mmol) in benzene (4 mL) was treated with diethylzinc (0.15 mL of 1.1 M in toluene, 0.165 mmol). Diiodomethane (55 μL, 0.683 mmol) was introduced dropwise during 1 min, and the mixture was stirred under nitrogen for 20 min, poured into 10% HCl (10 mL), and extracted with dichloromethane (3 × 10 mL). The combined organic layers were washed with saturated $NaHCO_3$ and brine solutions, dried, and evaporated. The residue was subjected to MPLC (silica gel, elution with 30% ethyl acetate in petroleum ether), affording 17 mg (73%) of **41** as white needles: mp 138–140 °C; IR ($CHCl_3$, cm^{-1}) 3420, 2970, 1765, 1225, 1090, 1070, 1015; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.23 (t, J = 7.8 Hz, 1 H), 4.03–3.88 (m, 4 H), 3.82 (m, 1 H), 2.88 (dddd, J = 1.7, 7.6, 7.8, 11.2 Hz, 1 H), 2.20 (dd, J = 11.2, 14.7 Hz, 1 H), 2.13 (br s, 1 H), 1.87 (dd, J = 4.3, 15.3 Hz, 1 H), 1.61 (dd, J = 12.3, 15.3 Hz, 1 H), 1.44 (dd, J = 1.0, 14.3 Hz, 1 H), 1.26 (m, 1 H), 1.04–0.97 (m, 1 H), 1.0 (d, J = 6.4 Hz, 3 H), 0.88 (d, J = 3.6, 8.7 Hz, 1 H), 0.74 (m, 1 H), 0.32 (dd, J = 5.6, 11.0 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 177.80, 110.41, 73.33, 70.20, 64.83, 63.12, 47.15, 42.78, 30.78, 28.13, 22.79, 21.02, 20.63, 5.92; MS m/z (M^+) calcd 268.1310, obsd 268.1318; $[\alpha]^{20}_D$ −58° (c 0.50, $CHCl_3$).

(3a*R*,7*R*,8*S*)-8-Chloro-3a,4,6,7,8,9-hexahydro-7-methylspiro[1*H*-cyclonona[*c*]furan-5(3*H*),2′-[1,3]dioxolan]-1-one (42). Alcohol **41** (14 mg, 0.052 mmol) was dissolved in dry pyridine (0.2 mL), cooled to 0 °C, treated with thionyl chloride (0.2 mL), and stored at −5 °C for 2 days. The reaction mixture was poured into ice–water and extracted with dichloromethane (3 × 10 mL). The combined extracts were washed with brine, dried, and evaporated. The residue was purified by chromatography on silica gel (elution with 30% ethyl acetate in petroleum ether) to furnish 10 mg (67%) of **42** as a faint yellow oil: IR (neat, cm^{-1}) 2930, 1750, 1675, 1455, 1270, 1195, 1095, 1035; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.86 (dd, J = 2.1, 8.7 Hz, 1 H), 4.77–4.70 (m, 1 H), 4.45 (dd, J = 7.5, 9.1 Hz, 1 H), 4.03–3.72 (m, 6 H), 3.35–3.27 (m, 1 H), 2.16–1.50 (series of m, 4 H), 1.31 (d, J = 7.1 Hz, 3 H), 1.25–0.82 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 169.65, 140.62, 129.51, 109.88, 71.69, 65.35, 63.69, 61.99, 45.91, 42.44, 37.27, 33.84, 29.68, 18.94; MS m/z (M^+ − Cl) calcd 251.1283, obsd 251.1286.

(3a*R*,7*R*,7a*S*,8a*S*,8b*R*)-Octahydro-7-methylspiro[1*H*-cyclopropa[3,4]cycloocta[1,2-*c*]furan-5(3*H*),2′-[1,3]dioxolan]-1-one (43). A solution of **35b** (103 mg, 0.433 mmol) in benzene (19 mL) was treated in turn with diethylzinc (0.47 mL of 1.1 M in toluene, 0.517 mmol) and diiodomethane (995 mg, 3.72 mmol). After being stirred at room temperature for 20 min, the reaction mixture was poured into saturated NH_4Cl solution and extracted with dichloromethane (3 × 30 mL). The combined organic layers were washed with brine, dried, and evaporated. MPLC of the residue on silica gel (elution with 30% ethyl acetate in petroleum ether) afforded 90 mg (83%) of **43** as colorless needles: mp 104–105 °C (from ethyl acetate in petroleum ether); IR ($CHCl_3$, cm^{-1}) 2960, 1765, 1360, 1085, 1075, 1025; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.27 (dd, J = 7.7, 8.3 Hz, 1 H), 3.96 (m, 3 H), 3.80 (m, 1 H), 3.66 (dd, J = 8.5, 11.6 Hz, 1 H), 2.76 (m, 1 H), 1.88 (dd, J = 4.4, 14.5 Hz, 1 H), 1.89–1.70 (m, 2 H), 1.77 (d, J = 11.0 Hz, 1 H), 1.63 (dd, J = 11.7, 14.5 Hz, 1 H), 1.31–1.13 (m, 1 H), 1.05 (d, J = 6.4 Hz, 3 H), 0.99–0.91 (m, 2 H), 0.69 (m, 1 H), 0.12 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 178.73, 110.02, 70.32, 65.11, 63.07, 48.43, 47.50, 39.66, 38.77, 30.58, 22.23, 20.25, 16.34, 10.82; MS m/z (M^+) calcd 252.1361, obsd 252.1365; $[\alpha]^{20}_D$ −50.5° (c 0.39, $CHCl_3$). Anal. Calcd for $C_{14}H_{20}O_4$: C, 66.64; H, 7.98. Found: C, 66.47; H, 8.10.

(3a*R*,7*R*,7a*S*,8a*S*,8b*R*)-Octahydro-7-methyl-1*H*-cyclopropa[3,4]cycloocta[1,2-*c*]furan-1,5(3*H*)-dione (44). To a solution of **43** (10 mg, 0.040 mmol) in tetrahydrofuran (4 mL) was added two drops of concentrated HCl, and the solution was stirred at room temperature for 10 min, poured into saturated $NaHCO_3$ solution, and extracted with dichloromethane (3 × 10 mL). The combined extracts were washed with brine, dried, and concentrated. The residue was purified by silica gel chromatography (elution with 30% ethyl acetate in petroleum ether) to give 7.5 mg (91%) of **44** as a colorless oil: IR ($CHCl_3$, cm^{-1}) 2960, 2930, 2860, 1780, 1705, 1380, 1350, 1150; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.39 (dd, J = 7.4, 8.7 Hz, 1 H), 3.73 (dd, J = 8.7, 10.9 Hz, 1 H), 2.72 (dd, J = 4.5, 13.2 Hz, 1 H), 2.57 (t, J = 11.3 Hz, 1 H), 2.34 (dd, J = 2.5, 11.1 Hz, 1 H), 2.27 (d, J = 12.8 Hz, 1 H), 1.90 (dd, J = 10.9, 12.1 Hz, 1 H), 1.74 (m, 1 H), 1.16 (d, J = 6.6 Hz, 3 H), 1.06 (td, J = 8.4, 5.5 Hz, 1 H), 0.87 (m, 2 H), 0.66 (tt, J = 2.4, 8.4 Hz, 1 H), 0.28 (dd, J = 5.4, 11.0 Hz, 1 H); ^{13}C NMR (20 MHz, $CDCl_3$) ppm 210.28, 176.47, 68.85, 53.35, 46.77, 42.78, 40.41, 29.42, 20.40, 19.95, 14.83, 9.65; MS m/z (M^+) calcd 208.1099, obsd 208.1131.

Phenylselenenylation of 43. Lactone **43** (101 mg, 0.40 mmol) in dry DME (1.5 mL) was added dropwise via cannula to a cold (−78 °C) solution of potassium hexamethyldisilazide in toluene (1.0 mL of 0.5 M, 0.50 mmol) during 10 min. The reaction mixture was stirred for 45 min prior to the introduction of a solution of phenylselenenyl chloride (95.7 mg, 0.50 mmol) in 0.5 mL of dry 1,2-dimethoxyethane containing 100 mg of HMPA all at once. The decolorized solution was stirred at −78 °C for 1 h, quenched with methanol at that temperature, and extracted with dichloromethane (3 × 70 mL). The combined organic layers were washed with brine (20 mL), dried, and evaporated. The residue was subjected to MPLC (silica gel, elution with 50% ether in petroleum ether) to give 70 mg (43%) of **45a** and 30 mg (18%) of **45b**, together with 30 mg of recovered **43**. The overall yield was quantitative based on recovered starting material.

For **45a**: colorless crystals, mp 116–120 °C; IR ($CHCl_3$, cm^{-1}) 2960, 1440, 1205, 1105, 1005, 750; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.71 (m, 2 H), 7.36–7.27 (m, 3 H), 4.45 (dd, J = 7.3, 8.8 Hz, 1 H), 4.33 (d, J = 8.8 Hz, 1 H), 3.93 (m, 2 H), 3.82 (m, 2 H), 2.79 (td, J = 6.4, 3.5 Hz, 1 H), 2.44 (dd, J = 3.5, 15.3 Hz, 1 H), 1.93 (ddd, J = 1.1, 6.4, 15.3 Hz, 1 H), 1.64 (d, J = 13.8 Hz, 1 H), 1.52–1.40 (m, 2 H), 1.30 (dd, J = 6.2, 13.0 Hz, 1 H), 1.19 (dd, J = 6.2, 11.3 Hz, 1 H), 0.89 (d, J = 6.6 Hz, 3 H), 0.57 (tt, J = 2.1, 8.7 Hz, 1 H), 0.37 (td, J = 5.0, 9.0 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 175.26, 138.42, 129.78, 128.65, 127.02, 110.37, 68.38, 65.16, 63.44, 51.35, 47.94, 45.51, 40.22, 27.62, 25.89, 23.11, 22.86, 6.03; MS m/z (M^+) calcd 408.0840, obsd 408.0827; $[\alpha]^{20}_D$ +88° (c 0.34, $CHCl_3$).

For **45b**: colorless oil; IR ($CHCl_3$, cm^{-1}) 2960, 1765, 1440, 1185, 1085, 1070, 1025; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64 (m, 2 H), 7.40–7.25 (m, 3 H), 4.08 (t, J = 8.0 Hz, 1 H), 4.00–3.78 (series of m, 5 H), 3.03 (m, 1 H), 2.32 (dd, J = 10.0, 15.1 Hz, 1 H), 1.89 (dd, J = 3.1, 12.8 Hz, 1 H), 1.82 (m, 1 H), 1.75 (dd, J = 3.2, 12.7 Hz, 1 H), 1.54 (d, J = 15.1 Hz, 1 H), 1.31–1.16 (series of m, 1 H), 1.11 (d, J = 6.1 Hz, 3 H), 1.09–0.98 (m, 1 H), 0.93 (dd, J = 5.8, 11.3 Hz, 1 H), 0.81 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 175.81, 137.40, 129.63, 129.13, 126.43,

110.53, 69.74, 64.80, 63.41, 60.47, 46.70, 45.32, 34.75, 29.49, 23.18, 22.84, 12.27; MS m/z (M^+ − SePh) calcd 251.1283, obsd 251.1256; $[\alpha]^{20}_D$ −4.8° (*c* 1.56, $CHCl_3$).

Deselenenylation of 45b. To a cold (−78 °C), magnetically stirred solution of **45b** (34.0 mg, 0.083 mmol) in dry THF (4 mL) was added dropwise a solution of potassium hexamethyldisilazide in toluene (0.30 mL of 0.5 M, 0.150 mmol). The light yellow solution was stirred at −78 °C for 2 h before being quenched with saturated NH_4Cl solution at this temperature. The product was extracted into ether (3 × 25 mL) and the combined organic phases were dried, evaporated, and subjected to MPLC purification (silica gel, elution with 70% ether in petroleum ether) to give 16.0 mg (76%) of **47** as a colorless oil: IR (neat, cm^{-1}) 2960, 2920, 1765, 1365, 1145, 1100, 995, 950; ^1H NMR (300 MHz, $CDCl_3$) δ 4.43 (dd, *J* = 7.4, 6.9 Hz, 1 H), 4.06 (dd, *J* = 8.5, 1.4 Hz, 1 H), 3.87−3.70 (m, 4 H), 2.56 (tdd, *J* = 7.2, 3.9, 1.4 Hz, 1 H), 2.19 (dd, *J* = 15.4, 4.0 Hz, 1 H), 1.87 (ddd, *J* = 15.4, 7.4, 1.1 Hz, 1 H), 1.58 (ddd, *J* = 14.0, 2.3, 1.0 Hz, 1 H), 1.52−1.46 (m, 2 H), 1.15 (m, 2 H), 0.91 (d, *J* = 6.6 Hz, 3 H), 0.79−0.60 (series of m, 2 H), 0.53 (td, *J* = 3.8, 4.4 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 176.53, 110.20, 70.03, 64.82, 63.76, 47.84, 44.69, 38.89, 28.24, 23.73, 23.27, 21.65, 3.97; MS m/z (M^+) calcd 252.1361, obsd 252.1370; $[\alpha]^{20}_D$ +32.0° (*c* 0.50, $CHCl_3$).

(7*R*,7a*S*,8a*S*)-4,6,7,7a,8,8a-Hexahydro-7-methylspiro-[1*H*-cyclopropa[3,4]cycloocta[1,2-c]furan-5(3*H*),2′-[1,3]dioxolan]-1-one (46). A solution of **45a** (70.0 mg, 0.172 mmol) in methanol (4 mL) and water (0.1 mL) was treated with $NaIO_4$ (110 mg, 0.516 mmol) and $NaHCO_3$ (43 mg, 0.516 mmol) and stirred vigorously at room temperature for 3 h. The usual workup and MPLC purification gave 43.0 mg (100%) of **46** as colorless crystals: mp 115−117 °C; IR ($CHCl_3$, cm^{-1}) 2960, 2925, 1750, 1670, 1120, 1065, 1025; ^1H NMR (300 MHz, $CDCl_3$) δ 4.69 (ddd, *J* = 0.6, 2.5, 7.0 Hz, 1 H), 4.50 (dd, *J* = 3.1, 17 Hz, 1 H), 4.01−3.83 (series of m, 4 H), 3.09 (d, *J* = 14.7 Hz, 1 H), 2.40 (d, *J* = 14.7 Hz, 1 H), 1.92 (dd, *J* = 5.2, 8.9 Hz, 1 H), 1.74 (d, *J* = 14.5 Hz, 1 H), 1.49−1.42 (m, 1 H), 1.04−0.81 (series of m, 3 H), 1.00 (s, 3 H), 0.17 (dd, *J* = 5.0, 10.8 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 174.76, 159.06, 127.11, 109.21, 72.43, 64.60, 64.43, 48.55, 37.13, 31.06, 24.69, 23.07, 10.53, 9.19; MS m/z (M^+) calcd 250.1205, obsd 250.1202; $[\alpha]^{20}_D$ +105.7° (*c* 0.35, $CHCl_3$). Anal. Calcd for $C_{14}H_{18}O_4$: C, 67.18; H, 7.25. Found: C, 66.86; H, 7.44.

(7*R*,7a*S*,8a*S*)-4,6,7,7a,8,8a-Hexahydro-7-methyl-1*H*-cyclopropa[3,4]cycloocta[1,2-c]furan-1,5(3*H*)-dione (2). Ketal **46** (43.0 mg, 0.172 mmol) was dissolved in tetrahydrofuran (80 mL) containing 6 mL of 5% HCl and stirred at room temperature for 48 h. Following dilution with more THF (100 mL), the reaction mixture was washed with saturated $NaHCO_3$ (20 mL) and NaCl solutions (20 mL) prior to drying and solvent evaporation. The residue was subjected to MPLC on silica gel (ether elution) to return 2.0 mg (5%) of unreacted **46** and give 32.0 mg (90%) of **2** as a crystalline solid: mp 111−112 °C; IR ($CHCl_3$, cm^{-1}) 2960, 1750, 1710, 1675, 1400, 1350, 1120, 1035; ^1H NMR (300 MHz, $CDCl_3$) δ 4.61 (m, 2 H), 3.47 (d, *J* = 6.1 Hz, 1 H), 3.18 (d, *J* = 6.1 Hz, 1 H), 2.78 (dd, *J* = 3.9, 12.8 Hz, 1 H), 2.43 (dd, *J* = 12.8, 12.8 Hz, 1 H), 1.51−1.41 (m, 1 H), 1.17 (d, *J* = 6.7 Hz, 3 H), 1.25−1.19 (m, 1 H), 1.05−0.85 (m, 2 H), 0.22 (dd, *J* = 5.8, 11.0 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 206.33, 174.01, 153.87, 126.32, 71.44, 54.48, 41.61, 32.85, 24.00, 21.12, 11.32, 11.00; MS m/z (M^+) calcd 206.0943, obsd 206.0955. Anal. Calcd for $C_{12}H_{14}O_3$: C, 69.89; H, 6.84. Found: C, 69.66; H, 7.07.

X-ray Crystallographic Analysis of 2. A transparent single crystal of **2** was mounted on a pin and transferred to the goniometer. The space group was determined to be either the centric $P2_1/n$ or acentric $P2_1$ from the systematic absences. Statistical tests indicated that the space group was acentric and the subsequent solution and successful refinement of the structure was carried out in the acentric space group $P2_1$. Least-squares refinement with isotropic thermal parameters led to R = 0.110. The geometrically constrained hydrogen atoms were placed in calculated positions 0.95 Å from the bonded carbon atom and allowed to ride on that atom with B fixed at 5.5 Å^2. The methyl hydrogen atoms were included as a rigid group with rotational freedom at the bonded carbon atom (C−H = 0.95 Å, B = 5.5 Å^2). Refinement of nonhydrogen atoms with anisotropic temperature factors led to the final values of R = 0.053 and R_w = 0.061. The data collection parameters and the final values of the positional parameters can be obtained from the Cambridge Crystallographic Data Centre.

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Supplementary Material Available: 300-MHz ^1H NMR and 75-MHz ^{13}C NMR spectra of those compounds lacking combustion data (53 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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