Enhanced Channeling of the Squarate Cascade through the Dianionic Oxy-Cope Option. Oxy Substitution Markedly Augments Syn Delivery of the Second Alkenyllithium

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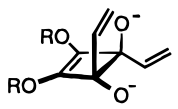
Abstract: A general means for enhancing the extent to which squarate esters enter into cascade processes involving a dianionic oxy-Cope rearrangement as the key step is presented. Adoption of this sigmatropic process requires that the two alkenyllithium reagents being introduced add cis to each other, a kinetic bias which can be realized simply by the proper incorporation of ethereal oxygen substituents in the first organometallic reagent. Structural reorganization occurs via boat-like transition states such that stereoinduction manifests itself with high fidelity.

About five years ago, we initiated an investigation into the consequences of adding a pair of alkenyl anions to squarate esters in anticipation of realizing a direct, single-operation pathway to polycyclic end-products.[1] As this study broadened in scope,[2] it became clearly apparent that trans addition of the two nucleophiles to generate dialkoxides such as **1** was heavily preferred and often exclusive. As concerns **1**, conrotatory 4π



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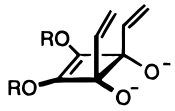

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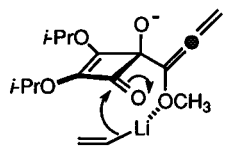
electrocyclic ring opening occurs under control of the oxido anions to generate a *cis,cis*-1,3,5,7-octatetraene capable in turn of a second conrotatory (now 8π) event, culminating ultimately in the formation of multicyclic ring systems housing several stereogenic centers. The stereochemical outcome of this mechanistic tandem is not governed by the diastereoselection associated with the initial addition step because of helical equilibration at the tetraene stage.[2g,h] The scenario is rather different when cis addition operates since concerted dianionic oxy-Cope rearrangement ensues and transmission of stereochemical information occurs with high fidelity via a boat-like intermediate.[3]

Several examples have come to light recently where cis addition was found to be competitive with the production of **1** (see **3**−**5**).[4,5] Without exception, an ethereal oxygen atom was attached to a carbon atom situated proximate to the four-membered ring. This phenomenon was attributed to coordination of the methoxy oxygen to the lithium atom of the second-stage nucleophile, thereby facilitating its syn delivery.



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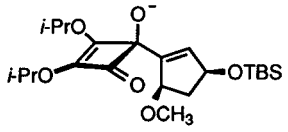

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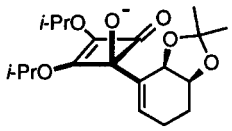

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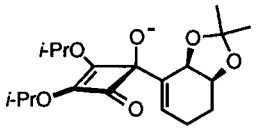

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Nonetheless, critical examination of the diastereomeric monoadducts **5** and **6** suggested that the working hypothesis advanced above may be too simplistic. While **5** responded to cyclopentenyllithium by generating a 3.5:1 mixture of Cope and electrocyclic products, analogous treatment of **6** proceeded only along the latter trajectory.[5] The dearth of examples of this type of behavior has prompted an investigation having as its explicit goal the purposeful incorporation of structural modifications designed to scrutinize this matter explicitly.

Results and Discussion

Chiral Acetals as Directing Groups. The use of β-eliminatable groups has proven to be highly utilitarian, bringing complete regiocontrol to the final transannular aldolization, thereby limiting the number of products formed and improving yields.[2c,g,h,4] For these reasons, recourse was made to this feature throughout the present investigation. In accord with this plan, the lithiated acetals **8** and **17** were first prepared by reaction of 2-bromo-2-cyclopenten-1-one[6] and the corresponding enan-

[⊗] Abstract published in *Advance ACS Abstracts,* March 15, 1997.

(1) Negri, J. T.; Morwick, T.; Doyon, J.; Wilson, P. D.; Hickey, E. R.; Paquette, L. A. *J. Am. Chem. Soc.* **1993**, *115*, 12189.

(2) (a) Morwick, T.; Doyon, J.; Paquette, L. A. *Tetrahedron Lett.* **1995**, *36*, 2369. (b) Paquette, L. A.; Morwick, T. *J. Am. Chem. Soc.* **1995**, *117*, 1451. (c) Paquette, L. A.; Doyon, J. *J. Am. Chem. Soc.* **1995**, *117*, 6799. (d) Wilson, P. D.; Friedrich, D.; Paquette, L. A. *J. Chem. Soc., Chem. Commun.* **1995**, 1351. (e) Paquette, L. A.; Morwick, T. M.; Negri, J. T.; Rogers, R. D. *Tetrahedron* **1996**, *52*, 3075. (f) Paquette, L. A.; Morwick, T. M. Submitted for publication. (g) Paquette, L. A.; Doyon, J.; Kuo, L. H.; *Tetrahedron Lett.* **1996**, *37*, 3299. (h) Paquette, L. A.; Hamme, A. T., II; Kuo, L. H.; Doyon, J.; Kreuzholz, R. *J. Am. Chem. Soc.* **1997**, *119*, 1242.

(3) Brands, M.; Wey, H. G.; Bruckmann, J.; Krüger, C.; Butenschön, H. *Chem. Eur. J.* **1996**, *2*, 182 and references cited therein.

(4) (a) Morwick, T. M.; Paquette, L. A. *J. Am. Chem. Soc.* **1997**, *119*, 1230. (b) Paquette, L. A.; Kuo, L. H.; Hamme, A. T., II; Kreuzholz, R.; Doyon, J. *J. Org. Chem.* **1997**, *62*, in press.

(5) Paquette, L. A.; Kuo, L. H.; Doyon, J. *Tetrahedron* **1996**, *52*, 11625.

(6) (a) Johnson, C. R.; Sakaguchi, H. *Synlett* **1992**, 813. (b) Johnson, C. R.; Adams, J. P.; Braun, M. P.; Senanayake, C. B. W.; Wovkulich, P. M.; Uskokovic, M. R. *Tetrahedron Lett.* **1992**, *33*, 917.

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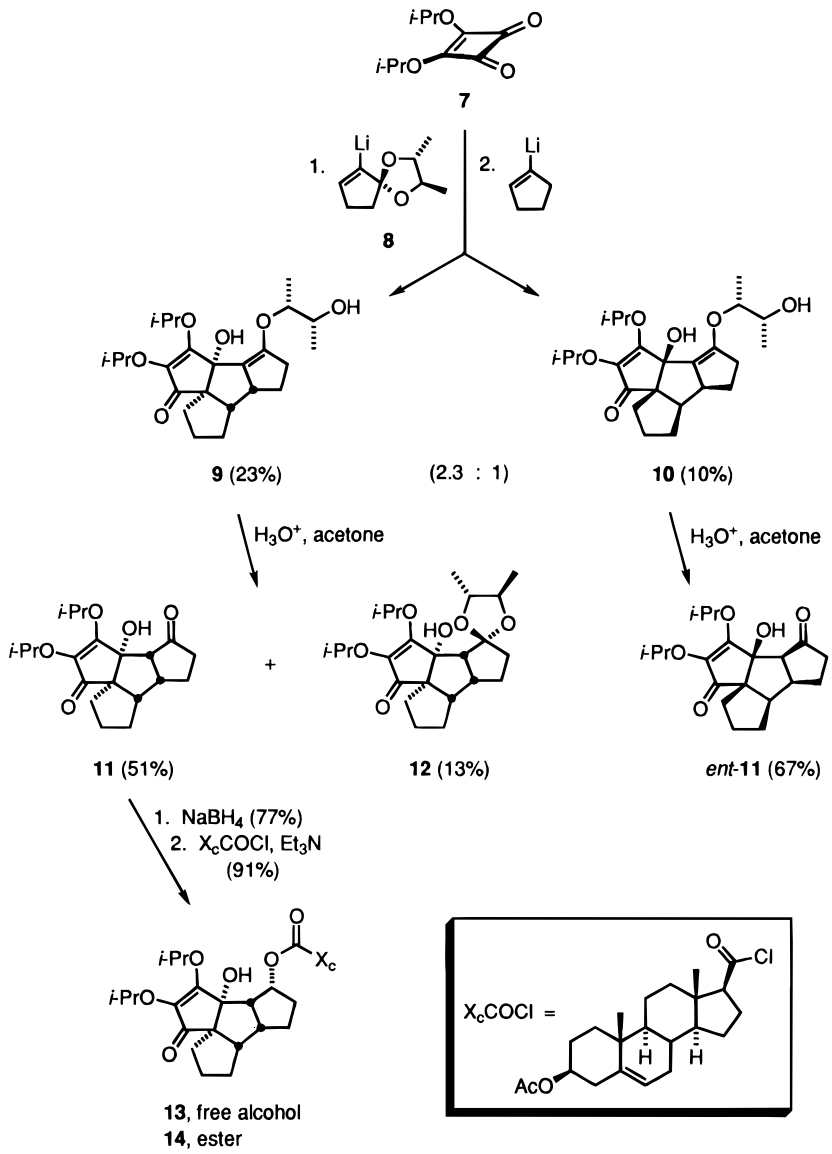
Scheme 1



tiopure diols,[7,8] followed by halogen−metal exchange with *tert*-butyllithium.[9] The addition of 1 equiv of **8** to diisopropyl squarate (**7**) followed by cyclopentenyllithium gave the two diasteromeric enol ethers **9** and **10** as a 2.3:1 mixture, readily separated by flash chromatography on silica gel (Scheme 1).

The absolute stereochemical assignments to these tetraquinanes were convincingly established on the following grounds. Acidic hydrolysis of major product **9** in aqueous acetone provided the dextrorotary ketone **11** along with its acetal **12** in good yield. Sodium borohydride reduction of **11** in methanol at 0 °C proceeded chemo- and regioselectively to furnish carbinol **13**, which was esterified with 3β-acetoxyetienoyl chloride[10] to implement conversion to the highly crystalline ester **14**. X-ray crystallographic analysis of **14** (Figure 1) not only defined unambiguously the six nonsteroidal stereogenic centers but also demonstrated beyond doubt that **9** had evolved from an anionic oxy-Cope sequence. Since the hydrolysis of **10** gave rise to a tetracyclic ketone antipodal to **11**, this product had also to materialize by [3,3] sigmatropic rearrangement of a diastereomeric cis adduct to **7**.

In the spirit of our operating paradigm, **8** and **17** were added to **7** as lead-in reagents, to be followed by 2-propenyllithium (Scheme 2). The objective was to sharpen our insight regarding the possible impact of the dioxolane substituents on stereocontrol. Perhaps not surprisingly in light of the distance involved between the methyl or cyclohexyl groups and the carbonyl site in the monoadducts, the two reaction systems gave closely

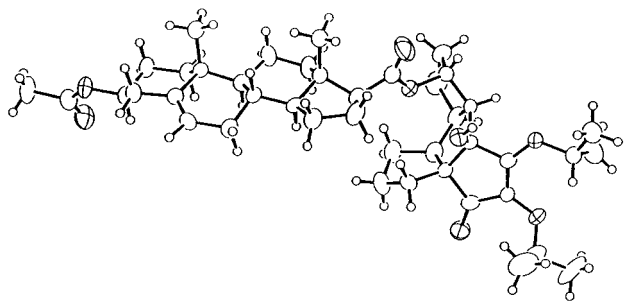


Figure 1. Computer-generated X-ray drawing of the final X-ray model of **14**.

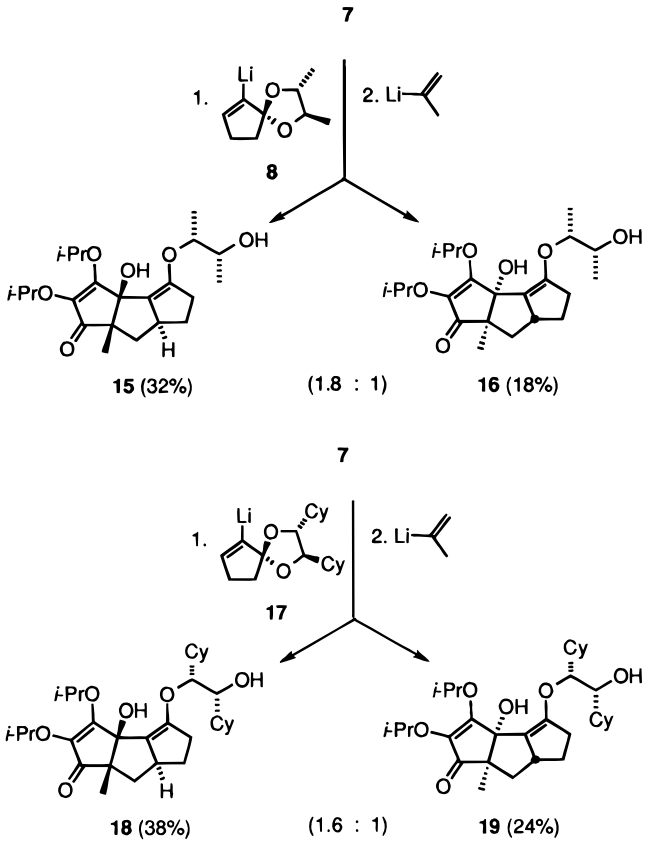
(7) (2*R*,3*R*)-(−)-Butane-2,3-diol was purchased from the Aldrich Chemical Company.

(8) The dicyclohexyl-substituted diol was generously provided by Prof. Reinhard Hoffmann, University of Marburg.

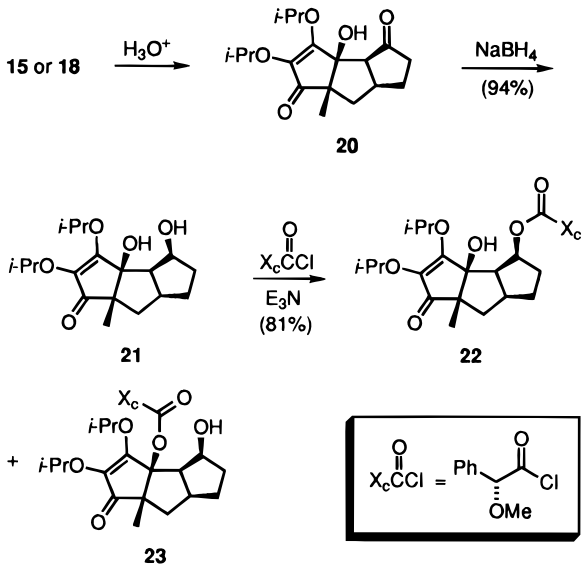
(9) (a) Shih, C.; Fritzen, E. L.; Swenton, J. S. *J. Org. Chem.* **1980**, *45*, 4462. (b) Smith, A. B., III; Branca, S. J.; Pilla, N. N.; Guaciaro, M. A. *J. Org. Chem.* **1982**, *47*, 1855. (c) Smith, A. B., III; Branca, S. J.; Guaciaro, M. A.; Wovkulich, P. M.; Korn, A. *Organic Syntheses*; Wiley: New York, 1990; Collect. Vol. VII, p 271.

(10) Djerassi, C.; Staunton, J. *J. Am. Chem. Soc.* **1961**, *83*, 736.

Scheme 2



Scheme 3



comparable product distributions (1.6−1.8:1). To confirm that identical stereoinduction had materialized in the two major products **15** and **18**, these enol ethers were separately hydrolyzed as before. The identical levorotatory triquinane ketone **20** was produced in these experiments, although conversion was much faster for **15** (12 h) than for **18** (48 h) (Scheme 3).

For the purpose of comparing the sense of stereochemical induction in **20** relative to **11**, the tricyclic ketone was reduced to **21** and subsequently treated with (*R*)-*O*-methylmandelic acid chloride.[11] Monoesters **22** and **23** were isolated in 86% yield. The formation of **23** occurs by intramolecular acyl transfer as

(11) Prepared from commercially available (*R*)-*O*-methylmandelic acid by treatment with oxalyl chloride in CH_2Cl_2 at 0 °C.

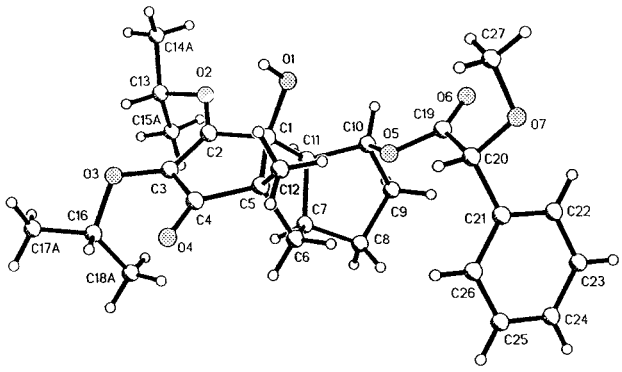
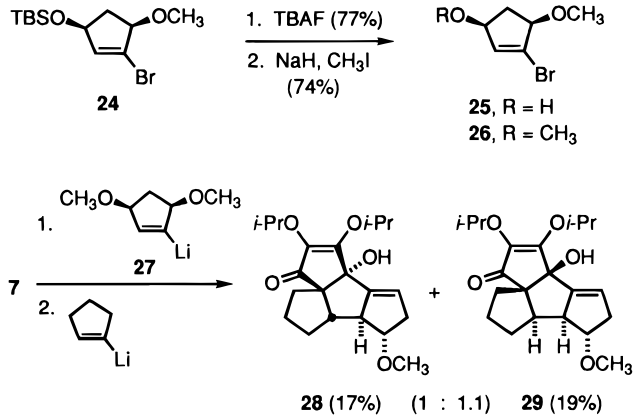


Figure 2. Computer-generated X-ray drawing of the final X-ray model of **22**.

Scheme 4



evidenced by independent TLC monitoring of the fate of **22** under the reaction conditions. With time, **23** was observed to form at the expense of **22**. Single crystal X-ray analysis of **22** (Figure 2) revealed the stereogenic centers in the triquinane moiety to be enantiotopic to those in **11**. Consequently, the major monoadduct diastereomer, experimentally determined to be in excess by a factor of only 1.16:1, must be transformed more efficiently into product in one instance than in the other. Revealed thereby is the fact that the distribution of final products need not be related directly to the selectivities of the first addition. As a consequence of the several diastereomerically related steps that must be traversed, their individual efficiencies need not be identical and very likely are not.

The *cis*-3,5-Dimethoxycyclopentene Substitution Plan. Mindful of the diagnostic role capable of being played by chiral, nonracemic *cis*-3,5-disubstituted cyclopentenyllithium reagents,[4] we selectively deprotected the known levorotatory bromide **24** with tetra-*n*-butylammonium fluoride. Subsequent O-methylation provided the dimethoxy bromide **26** of 85% ee (Scheme 4). Addition of the derived lithium reagent **27** to **7** in advance of cyclopentenyllithium-generated tetraquinanes **28** and **29** in approximately equal amounts (ratio 1:1.1). These products hold the advantage of retaining one of the two stereogenic centers resident in the lead-in nucleophile. Notwithstanding the fact that the C-5 methoxyl in **27** suffers β-elimination in order to control the direction of transannular aldolization, the C-3 methoxyl is not configurationally perturbed and can therefore be utilized in assignment of absolute stereochemistry at the four newly introduced stereogenic sites. This protocol was implemented with **29** whose highly crystalline nature permitted elucidation of its three-dimensional structural features by means of X-ray crystallography (Figure 3). Comparative analysis of the NMR spectral data for **29** and **28** formed the basis of the structural assignment to the latter product (see Experimental

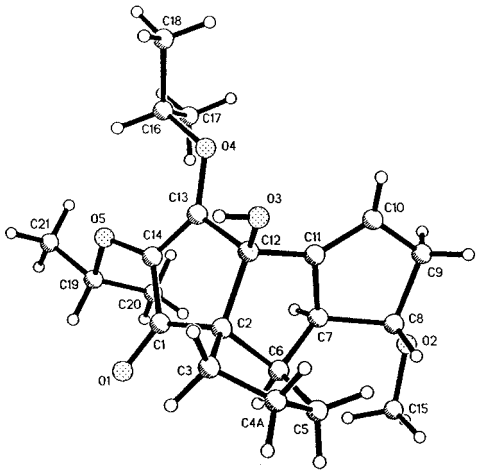
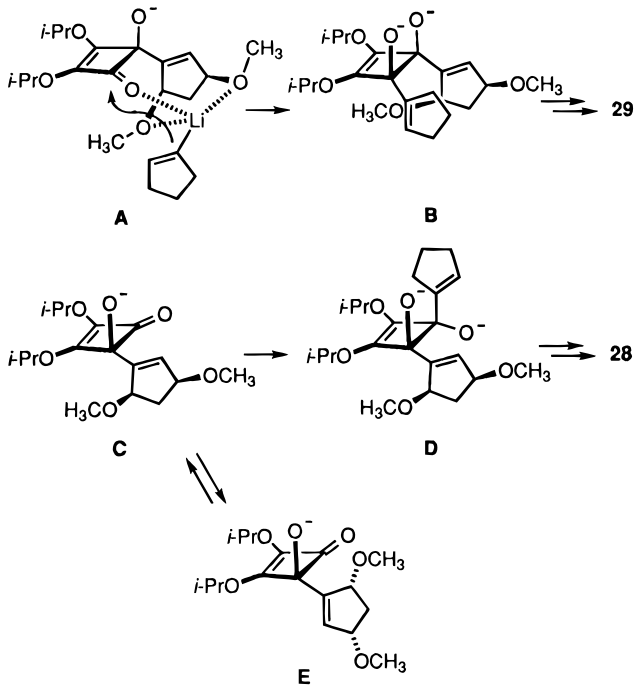


Figure 3. Computer-generated X-ray drawing of the final X-ray model of **29**.

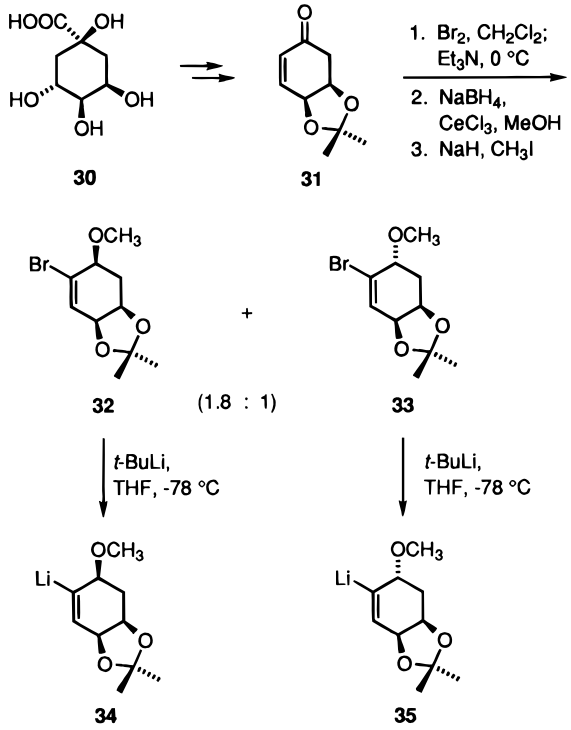
Section). Particularly significant is the finding that the methoxy substituents in monoadduct diastereomer **A** have found it possible to accomplish "oxy-Cope engineering" by coaxing the cyclopentenyllithium to form only the syn diadduct **B**. This is



not the case for **C**, which serves as the major and perhaps exclusive percursor to **D**. These findings alert us to the possibility that the reactive conformations of the monoadducts may be those with an exo-oriented double bond as depicted in **A** and **C**. Under these circumstances, **A** features two methoxyl oxygens amenable to coordination to the incoming alkenyllithium reagent and **C** does not. We recognize that the latter diastereomer could engage in syn delivery if its endo-oriented rotamer **E** were populated. However, this is evidently not a kinetically relevant geometry. Finally, when **B** is generated, the pair of cyclopentenyl double bonds must now become endo oriented in order to allow for development of the boat-like topography demanded for conversion to **29**.

Cyclohexenyl Anions Based on (−)-Quinic Acid. The point of departure for the preparation of cyclohexenyl bromides featuring an oxygenated substituent closer to the bond-forming site than the methoxyl leaving group was (−)-quinic acid (**30**).

Scheme 5



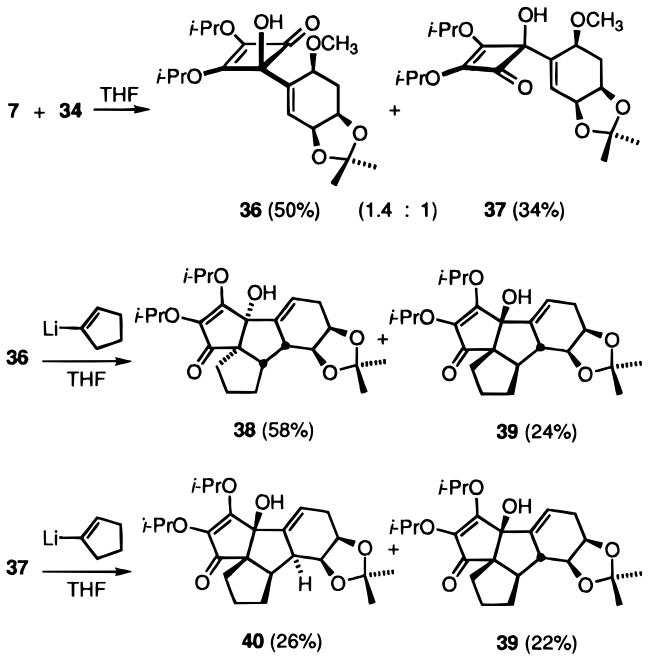
Following its conversion to **31** by literature methods,[12] the same bromination−reduction−alkylation sequence as employed in earlier examples was applied (Scheme 5). At the reduction stage, both alcohol stereoisomers were formed, with the cis isomer predominating (1.8:1), as determined by NOESY techniques. Chromatographic separation was undertaken prior to the O-methylation step, and the independent conversion of **32** and **33** to **34** and **35**, respectively, was accomplished in the predescribed manner.

These optically pure organolithium reagents were independently added to diisopropyl squarate (**7**). In the first case, the resultant pair of diastereomeric monoadducts[3] **36** and **37** proved conveniently separable by chromatography. Subsequently, both alcohols entered smoothly into reaction with excess cyclopentenyllithium (Scheme 6). Each of these experiments gave rise to two products, with that arising from cis addition and ensuing dianionic oxy-Cope rearrangement predominating. Since such sigmatropic rearrangements transfer chirality efficiently, **38** and **40** would need to be diastereomerically related, and this indeed was found to be the case. The less-predominant trans-fused polycyclic acetonide **39** arises from trans addition and rearrangement along the electrocyclic cascade. In light of the nature of this process and the very specific location of the acetonide unit in the octatetraene intermediate, full control of product stereochemistry can be achieved by ring closure from the less sterically congested helix. Only one mode of 8π conrotatory ring closure appears to be operative since only **39** was isolated from both experiments and no evidence was found for formation of a second trans-fused diastereomer.

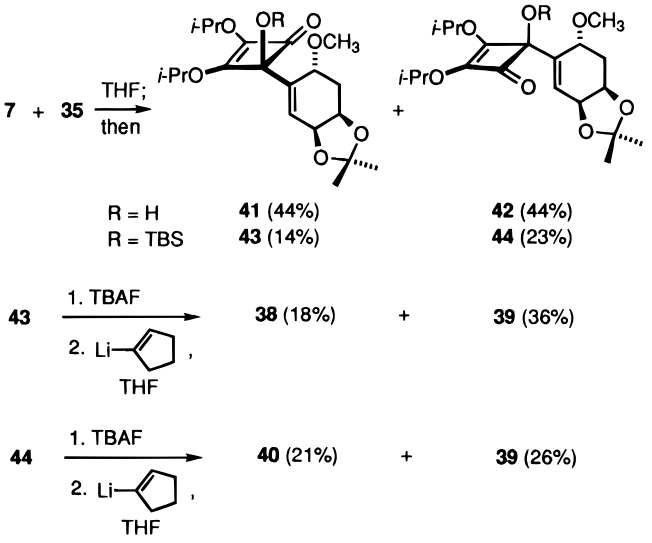
The relative configuration of the triad of tertiary protons in the southeastern sector of **38**−**40** was made unambiguously apparent on the basis of NOE experiments (see Experimental Section). Since the configuration of the oxygenated center derives from quinic acid, the absolute stereochemistry of these products was established simultaneously.

(12) (a) Audia, J. E.; Boisvert, L.; Patten, A. D.; Villalobos, A.; Danishefsky, S. J. *J. Org. Chem.* **1989**, *54*, 3738. (b) Trost, B. M.; Romero, A. G. *J. Org. Chem.* **1986**, *51*, 2332.

Scheme 6



Scheme 7



When **35** was added to **7**, carbinols **41** and **42** were found to co-elute (as is often observed). In this instance, however, the *tert*-butyldimethylsilyl derivatives **43** and **44** proved amenable to chromatographic separation (Scheme 7). Once accomplished, deprotection was effected with fluoride ion to return isomerically pure samples of the individual alcohols. These intermediates were subjected in turn to the action of cyclopentenyllithium as before. Careful spectroscopic analysis and chromatography of the product mixtures revealed that **39** was the more dominant ketone in both of these examples. These results demonstrate that the stereogenicity of the methoxyl-substituted carbon plays no controlling role in the electrocyclic cascade, which is totally regulated by the acetonide unit. On the other hand, since **41** is the precursor of **38**, and **42** leads uniquely to **40**, the oxy-Cope pathway proceeds with telltale residual evidence of the specific monoadduct stereoisomer from which the sigmatropic rearrangement is initiated.

Conclusions

In light of the predescribed results, we now can interpret more sharply the options available to squarate esters during their treatment with a pair of alkenyllithiums. Properly positioned basic oxygen substituents resident in the initially formed monoadduct do indeed have the capability of overriding the customary sterically-driven kinetic tendency for trans entry of the second alkenyl anion. This can be explained by complexation of the lithium atom from this reagent to the pendant oxygen atom in the monoadduct such that intramolecular cis delivery can become kinetically competitive. It is important to note that the acetal groups in **8** and **17** give evidence of directing exclusive syn attack in the diastereomeric pairs of monoadducts derived from them. Despite the higher level of oxidation resident in **34** and **35**, this particular substitution pattern is not superior to the others. This is not a simple case of matched and mismatched arrangements since neither diastereomer exerts exceptional control. More subtle effects of a type previously discussed[5] may be operative here.

Our investigation into the control of facial selectivity of 2-fold nucleophilic addition to squarate esters makes evident a range of other options associated with the rapid synthetic elaboration of extensively functionalized polycyclic compounds. In this context, it is of utmost importance to keep in mind that stereoinductive transmission operates superbly well in the oxy-Cope rearrangement channel. However, when the electrocyclic cascade is followed, a chaperone substituent must reside in sufficient proximity to one of the termini of the octatetraene helix to guide the directionality of its conrotatory closure and achieve equally high levels of chirality transfer.

Experimental Section

The general experimental protocols followed in this study parallel those described earlier in refs 2f,g.

(2*R*,3*R*)-6-Bromo-2,3-dimethyl-1,4-dioxaspiro[4.4]non-6-ene. 2-Bromocyclopenten-1-one (3.0 g, 18.6 mmol), (2*R*,4*R*)-2,4-butanediol (1.68 g, 18.6 mmol), and a crystal of *p*-toluenesulfonic acid were dissolved in 30 mL of benzene and placed in a 50 mL flask equipped with a Dean−Stark trap. The reaction mixture was refluxed for 2 d, cooled, and treated with solid K_2CO_3 (300 mg). Evaporation of the solvent and chromatography of the residue on silica gel (elution with 30% ethyl acetate in hexanes) gave 3.0 g (69%) of the ketal and 0.70 g (23%) of recovered starting ketone. For the ketal: IR (neat, cm^{-1}) 1621, 1377, 1314, 1158; ^1H NMR (300 MHz, C_6D_6) δ 5.77 (t, J = 2.4 Hz, 1 H), 3.98−3.88 (m, 1 H), 3.40 (m, 1 H), 2.09−2.01 (m, 2 H), 1.99−1.87 (m, 2 H), 1.10 (d, J = 6.0 Hz, 3 H), 0.99 (d, J = 6.0 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 135.8, 125.9, 117.1, 79.8, 79.1, 35.9, 28.8, 16.8, 16.3; MS *m/z* (M^+) calcd 232.0099, obsd 232.0104; $[\alpha]^{21}_D$ +10.1° (*c* 1.10, $CHCl_3$).

(2*R*,3*R*)-6-Bromo-2,3-dicyclohexyl-1,4-dioxaspiro[4.4]non-6-ene. The title compound was prepared in the predescribed manner (7-d reflux) in 88% yield; IR (neat, cm^{-1}) 1622, 1450, 1317, 1214, 1170; ^1H NMR (300 MHz, $CDCl_3$) δ 6.17 (t, J = 2.7 Hz, 1 H), 3.83 (t, J = 6.5 Hz, 1 H), 3.63 (t, J = 6.5 Hz, 1 H), 2.38−2.32 (m, 2 H), 2.13 (m, 2 H), 2.00−1.50 (series of m, 10 H), 1.40−1.43 (m, 1 H), 1.40−1.00 (series of m, 10 H), 0.95−0.80 (t, J = 3.5 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 136.6, 125.1, 117.1, 84.3, 83.2, 40.8 (2 C), 35.6, 30.3, 30.2, 28.8, 28.0, 26.4 (2 C), 26.3 (2 C), 26.0 (2 C); MS *m/z* (M^+) calcd 368.1349, obsd 368.1350; $[\alpha]^{21}_D$ +28° (*c* 0.80, $CHCl_3$).

(3a*R*,6a*S*,6b*R*,9b*R*)-4,5,6,6a,6b,7,7,9b-Octahydro-9b-hydroxy-9-[(1*R*,2*R*)-2-hydroxy-1-methylpropoxy]-1,2-diisoproxy-3*H*-dicyclopenta-[*a*,*b*]pentalen-3-one (9) and (3a*S*,6a*R*,6b*S*,9b*S*)-4,5,6,6a,6b,7,7,9b-Octahydro9b-hydroxy-9-[(1*R*,2*R*)-2-hydroxy-1-methylpropoxy]-1,2-diisoproxy-3*H*-dicyclopenta[*a*,*b*]pentalen-3-one (10). The lithium reagent **8** was prepared by treating a solution of the bromo acetal (0.42 g, 1.80 mmol) in dry THF (9 mL) with *tert*-butyllithium (2.3 mL of 1.7 M in pentane, 3.91 mmol) dropwise at −78 °C. The mixture was stirred at this temperature for 1 h before **7** (0.36 g, 1.81 mmol) dissolved in THF (9 mL) was introduced. After an additional 2.5 h of stirring at −78 °C, a solution of cyclopentenyllithium [from 0.70 g (3.60 mmol) of the iodide in THF (18 mL) and *tert*-butyllithium (4.7 mL of 1.7 M in pentane, 7.99 mmol)] was transferred in via cannula. Afer the

mixture had stirred at 22 °C for 20 h, the reaction mixture was quenched with deoxygenated, saturated NH_4Cl solution (10 mL) and extracted with ether (2 × 20 mL). The combined organic layers were washed with water (20 mL) and brine (20 mL), dried, and concentrated. Flash chromatography of the residue on silica gel (elution with 3:1 hexanes/ethyl acetate) gave 76 mg (10%) of **10** and 170 mg (23%) of **9**.

For **9**: yellowish oil; IR (neat, cm^{-1}) 3400, 1691, 1613, 1379, 1101; ^1H NMR (300 MHz, C_6D_6) δ 5.55 (heptet, J = 6.0 Hz, 1 H), 5.24 (heptet, J = 6.0 Hz, 1 H), 4.92−4.88 (br, 1 H), 4.67−4.42 (br, 1 H), 3.69 (quint, J = 6.3 Hz, 1 H), 3.56 (quint, J = 6.3 Hz, 1 H), 2.98−2.91 (m, 1 H), 2.57−2.49 (m, 1 H), 2.43−2.37 (m, 1 H), 2.34−2.27 (m, 1 H), 2.20−2.11 (m, 1 H), 1.92−1.74 (m, 2 H), 1.71−1.59 (m, 2 H), 1.57−1.49 (m, 1 H), 1.47−1.32 (m, 1 H), 1.28 (d, J = 6.0 Hz, 3 H), 1.26 (d, J = 6.0 Hz, 3 H), 1.23 (d, J = 6.0 Hz, 3 H), 1.21 (d, J = 6.0 Hz, 3 H), 1.08 (d, J = 6.3 Hz, 3 H), 1.00 (d, J = 6.3 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 202.4, 166.3, 151.6, 133.3, 120.4, 80.4, 78.1, 73.2, 71.4, 71.3, 70.6, 51.4, 44.6, 33.8, 30.3, 28.0, 27.3, 22.7, 22.6, 22.5, 22.4, 22.3, 18.6, 17.2; MS *m/z* (M^+) calcd 420.2518, obsd 420.2515; $[\alpha]^{22}_D$ −200° (*c* 0.32, C_6H_6).

For **10**: yellowish oil; IR (neat, cm^{-1}) 3407, 1692, 1614, 1379, 1103; ^1H NMR (300 MHz, C_6D_6) δ 5.43 (heptet, J = 6.5 Hz, 1 H), 5.40 (heptet, J = 6.5 Hz, 1 H), 4.49−4.37 (br, 1H), 3.84 (quint, J = 6.3 Hz, 1 H), 3.63 (quint, J = 6.3 Hz, 1 H), 3.38−3.16 (br, 1 H), 3.04−2.96 (m, 1 H), 2.64−2.52 (m, 2 H), 2.49−2.42 (m, 1 H), 2.39−2.29 (m, 1 H), 2.24−2.05 (m, 1 H), 1.91−1.81 (m, 2 H), 1.70−1.64 (m, 2 H), 1.62−1.45 (m, 1 H), 1.42−1.30 (m, 1 H), 1.29 (d, J = 6.5 Hz, 3 H), 1.27 (d, J = 6.5 Hz, 3 H), 1.20 (d, J = 6.5 Hz, 3 H), 1.18 (d, J = 6.5 Hz, 3 H), 1.12 (d, J = 6.3 Hz, 3 H), 0.99 (d, J = 6.3 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 202.7, 165.3, 152.3, 132.8, 118.1, 80.7, 77.5, 73.6, 71.8, 71.2, 71.0, 51.2, 45.9, 35.9, 30.3, 28.0, 27.1, 23.1, 22.7, 22.6, 22.5, 22.3, 18.5, 17.3; MS *m/z* (M^+) calcd 420.2518, obsd 420.2524; $[\alpha]^{22}_D$ +213° (*c* 0.46, C_6H_6).

(3a*R*,6a*S*,6b*R*,9a*R*,9b*R*)-5,6,6b,7,8,9a,9b-Octahydro-9b-hydroxy-1,2-diisopropoxy-3*H*-dicyclopenta[*a,b*]pentalene-3,9(4*H*)-dione (11) and (3a*R*,4′*R*,5′*R*,6a*R*,6b*R*,9a*R*,9b*S*)-2,3,6a,6b,8,9,9a,9b-Octahydro-6a-hydroxy-5,6-diisopropoxy-4′,5′-dimethylspiro(7*H*-dicyclopenta-[*a,b*]-pentalene-7,2′-[1,3]dioxolan)-4(1*H*)-one (12). A solution of **9** (0.10 g, 0.23 mmol) in acetone (8 mL) and water (4 mL) was treated with concentrated HCl (4 drops) and stirred at 22 °C for 24 h. The mixture was extracted with ether (2 × 15 mL), and the combined organic layers were washed with water (15 mL) and brine (15 mL) prior to drying and evaporation. The residue was subjected to flash chromatography on silica gel (elution with 6:1 hexanes/ethyl acetate) and afforded 13 mg (13%) of **12** and 42 mg (51%) of **11**.

For **11**: pale yellowish oil; IR (neat, cm^{-1}) 3441, 1698, 1625, 1102; ^1H NMR (300 MHz, $CDCl_3$) δ 5.34 (heptet, J = 6.1 Hz, 1 H), 5.12 (s, 1 H), 4.94 (heptet, J = 6.1 Hz, 1 H), 2.84 (d, J = 9.2 Hz, 1 H), 2.72 (dd, J = 15.8, 8.5 Hz, 1 H), 2.61 (dd, J = 17.1, 8.5 Hz, 1 H), 2.46−2.42 (m, 1 H), 2.41 (d, J = 9.2 Hz, 1 H), 2.38−2.06 (m, 1 H), 2.03−1.89 (m, 2 H), 1.84−1.78 (m, 2 H), 1.76−1.62 (m, 2 H), 1.34 (d, J = 6.1 Hz, 3 H), 1.30 (d, J = 6.1 Hz, 3 H), 1.21 (d, J = 6.1 Hz, 3 H), 1.11 (d, J = 6.1 Hz, 3 H), 1.16−1.10 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 223.3, 203.0, 166.0, 131.9, 83.4, 73.9, 72.0, 66.8, 55.2, 52.8, 39.9, 39.0, 31.0, 29.5, 28.0, 22.8, 22.7, 22.6, 22.5, 21.8; MS *m/z* (M^+) calcd 348.1940, obsd 348.1938; $[\alpha]^{22}_D$ +13.9° (*c* 0.55, $CHCl_3$).

Anal. Calcd. for $C_{20}H_{28}O_5$: C, 68.93; H, 8.10. Found: C, 69.03; H, 8.12.

For **12**: pale yellowish oil; IR (neat, cm^{-1}) 3485, 1698, 1625, 1102; ^1H NMR (300 MHz, $CDCl_3$) δ 5.32 (heptet, J = 6.2 Hz, 1 H), 4.92 (s, 1 H), 4.88 (heptet, J = 6.2 Hz, 1 H), 3.83−3.74 (m, 1 H), 3.59−3.50 (m, 1 H), 2.77−2.66 (m, 2 H), 2.50 (d, J = 6.0 Hz, 1 H), 2.17−2.06 (m, 2 H), 2.03−1.86 (m, 1 H), 1.84−1.71 (m, 4 H), 1.69−1.61 (m, 2 H), 1.59−1.48 (m, 1 H), 1.33 (d, J = 6 Hz, 3 H), 1.32 (d, J = 6.2 Hz, 3 H), 1.26 (d, J = 6.2 Hz, 3 H), 1.23 (d, J = 6.2 Hz, 3 H), 1.22 (d, J = 6.2 Hz, 3 H), 1.17 (d, J = 6.2 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 204.3, 169.0 128.6, 118.2, 82.4, 79.2, 77.3, 73.4, 71.8, 70.4, 62.2, 48.5, 47.0, 39.6, 32.3, 29.2, 29.1, 24.8, 23.0, 22.9, 22.7, 22.4, 16.6, 16.4; MS *m/z* (M^+) calcd 420.2517, obsd 420.2514; $[\alpha]^{22}_D$ −48.7° (*c* 0.16, $CHCl_3$).

Anal. Calcd. for $C_{24}H_{36}O_6$: C, 68.53; H, 8.63. Found: C, 68.62; H, 8.62.

(3a*R*,6a*S*,6b*R*,9*R*,9a*S*,9b*R*)-4,5,6,6a,6b,7,8,9,9a,9b-Decahydro-9,-9b-dihydroxy-1,2-diisopropoxy-3*H*-dicyclopenta[*a,b*]pentalen-3-one (13). A cold (0 °C), magnetically stirred solution of **11** (66 mg, 0.18 mmol) in methanol (3 mL) was treated with sodium borohydride (7.0 mg, 0.18 mmol), stirred at 22 °C for 2 h, and quenched with water (3 mL). The mixture was extracted with ether (2 × 10 mL), and the combined organic layers were washed with water (10 mL) and brine (10 mL), dried, and concentrated. Purification of the residue by flash chromatography on silica gel (elution with 6:1 hexanes/ethyl acetate) gave **13** (51 mg, 77%) as a white solid: mp 134−136 °C; IR (neat, cm^{-1}) 3550, 1691, 1612, 1306, 1101; ^1H NMR (300 MHz, $CDCl_3$) δ 5.36 (heptet, J = 6.1 Hz, 1 H), 4.93 (heptet, J = 6.1 Hz, 1 H), 4.45−4.43 (m, 1 H), 4.32−4.07 (br, 1 H), 3.05−2.71 (br, 1 H), 2.69−2.66 (m, 1 H), 2.64−2.53 (m, 2 H), 1.98−1.70 (m, 7 H), 1.68−1.54 (m, 3 H), 1.34 (d, J = 6.1 Hz, 1 H), 1.32 (d, J = 6.1 Hz, 3 H), 1.20 (d, J = 6.1 Hz, 3 H), 1.18 (d, J = 6.1 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 205.0, 167.2, 130.5, 83.2, 75.1, 73.9, 71.9, 69.7, 57.8, 51.1, 43.3, 36.6, 31.2, 29.1, 28.8, 25.8, 22.8 (2 C), 22.7, 22.5; MS *m/z* (M^+) calcd 350.2097, obsd 350.2095; $[\alpha]^{22}_D$ −9.5° (*c* 0.37, $CHCl_3$).

Anal. Calcd. for $C_{20}H_{30}O_5$: C, 68.53; H, 8.63. Found: C, 68.44; H, 8.63.

3*β*-Acetoxyandrost-5-ene-17*β*-carboxylic Acid, 9-Ester with (3a*R*,-6a*S*,6b*R*,9*R*,9a*S*,9b*R*)-4,5,6,6a,6b,7,8,9,9a,9b-decahydro-9,9b-dihydroxy-1,2-diisopropoxy-3*H*-dicyclopenta[*a,b*]pentalen-3-one (14). A solution of **13** (82 mg, 0.23 mmol) in CH_2Cl_2 (5 mL) cooled to 0 °C was treated with 3*β*-acetoxyetienoyl chloride (0.13 g, 0.34 mmol) and triethylamine (0.10 mL, 0.71 mmol), and the mixture was stirred at room temperature for 5 h. Water (5 mL) was added, and the product was extracted into CH_2Cl_2 (2 × 10 mL). The combined organic layers were washed with water (10 mL) and brine (10 mL), dried, and concentrated. Purification of the product by flash chromatography on silica gel (elution with 8:1 hexanes/ethyl acetate) gave **14** (0.15 g, 91%) as a white solid: mp 139−141 °C; IR (neat, cm^{-1}) 3561, 1731, 1697, 1622, 1247; ^1H NMR (300 MHz, $CDCl_3$) δ 5.51−5.44 (m, 1 H), 5.36−5.26 (m, 2 H), 4.84 (heptet, J = 6.1 Hz, 2 H), 4.57−4.52 (m, 1 H), 3.45 (br, 1 H), 2.66−2.53 (m, 3 H), 2.38−1.99 (m, 6 H), 1.98 (s, 3 H), 1.95−1.62 (m, 10 H), 1.61−1.40 (m, 8 H), 1.35−1.03 (series of m, 18 H), 0.97 (s, 3 H), 0.65 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 204.2, 172.7, 170.4, 168.3, 139.6, 128.8, 122.2, 82.1, 75.6, 73.7, 73.6, 71.8, 70.4, 57.1, 56.5, 55.4, 49.8, 48.6, 46.7, 44.2, 38.6, 38.0, 36.9, 36.5, 33.3, 32.0, 31.9, 31.7, 29.2 (2 C), 27.7, 24.9, 24.5, 23.6, 22.8 (3 C), 22.3, 21.4, 21.0, 19.3, 13.5; MS *m/z* (M^+) calcd 692.4242, obsd 692.4265; $[\alpha]^{22}_D$ −54.2° (*c* 0.8, $CHCl_3$).

Anal. Calcd. for $C_{42}H_{60}O_8$: C, 72.79; H, 8.73. Found: C, 72.69; H, 8.70.

(3a*S*,6a*R*,6b*S*,9b*S*)-5,6,6a,6b,7,8,9a,9b-Octahydro-9b-hydroxy-1,2-diisopropoxy-3*H*-dicyclopent[*a,b*]pentalene-3,9(4*H*)-dione (*ent*-11). A solution of **10** (39 mg, 0.09 mmol) in aceteone (4 mL) and water (2 mL) was treated with concentrated HCl (2 drops), and the mixture was stirred at 22 °C for 21 h prior to extraction with ether (2 × 20 mL). The combined organic layers were washed with water (10 mL) and brine (10 mL), dried, and concentrated. The residue was subjected to flash chromatography on silica gel (elution with 6:1 hexanes/ethyl acetate) and gave 22 mg (67%) of *ent*-**11**, $[\alpha]^{22}_D$ −13.0° (*c* 0.28, $CHCl_3$).

(3a*S*,6a*S*,7a*S*)-3a,5,6,6a,7,7a-Hexahydro-3a-hydroxy-4-[(1*R*,2*R*)-2-hydroxy-1-methylpropoxy]-2,3-diisopropoxy-7a-methyl-1*H*-cyclopenta[*a*]pentalen-1-one (15) and (3a*R*,6a*R*,7a*R*)-3a,5,6,6a,7,7a-Hexahydro-3a-hydroxy-4-[(1*R*,2*R*)-2-hydroxy-1-methylpropoxy]-2,3-diisopropoxy-7a-methyl-1*H*-cyclopenta[*a*]pentalen-1-one (16). Reaction of **8** [from 932 mg (4.0 mmol) of bromo acetal] with **7** (400 mg, 2.0 mmol) and 2-lithiopropene [from 484 mg (4.0 mmol) of 2-bromopropene] in the predescribed manner was followed by overnight stirring at room temperature, an aqueous NH_4Cl quench, and the usual workup. The thick oil so obtained was subjected to flash chromatography on silica gel (elution with 1:1 hexanes/ethyl acetate) to give 254 mg (32%) of **15** and 143 mg (18%) of **16**.

For **15**: thick colorless oil; IR (neat, cm^{-1}) 3412, 1692, 1614, 1452, 1380, 1330; ^1H NMR (300 MHz, C_6D_6) δ 5.41 (heptet, J = 6.1 Hz, 1 H), 5.32 (heptet, J = 6.1 Hz, 1 H), 3.90 (br s, 1 H), 3.57−3.46 (m, 2 H), 3.10 (br s, 1 H), 2.66−2.56 (m, 1 H), 2.51 (m, 1 H), 2.41−2.20 (m, 2 H), 1.72 (m, 1 H), 1.41 (s, 3 H), 1.40−1.20 (m, 1 H), 1.22 (d, J

= 6.1 Hz, 3 H), 1.20 (d, *J* = 6.1 Hz, 3 H), 1.17 (d, *J* = 6.1 Hz, 3 H), 1.13 (d, *J* = 6.1 Hz, 3 H), 1.09 (m, 1 H), 0.97 (d, *J* = 5.9 Hz, 3 H), 0.93 (d, *J* = 5.8 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 202.3, 165.7, 151.4, 132.4, 124.0, 80.5, 78.6, 73.7, 71.7, 71.5, 61.2, 43.34, 43.28, 34.4, 28.4, 22.9, 22.83, 22.78, 22.6, 20.0, 18.8, 17.4; MS *m/z* (M^+) calcd 394.2380, obsd 394.2368; $[\alpha]^{22}_D$ −296° (*c* 0.86, $CHCl_3$).

For **16**: pale yellow oil; IR (neat, cm^{-1}) 3400, 1695, 1653, 1453, 1380, 1320; ^{1}H NMR (300 MHz, C_6D_6) *δ* 5.38 (heptet, *J* = 6.1 Hz, 1 H), 5.33 (heptet, *J* = 6.1 Hz, 1 H), 4.07 (quint, *J* = 6.2 Hz, 1 H), 3.55 (quint, *J* = 6.2 Hz, 1 H), 3.05 (br s, 1 H), 2.70−2.60 (m, 1 H), 2.55−2.40 (m, 2 H), 2.30−2.20 (m, 1 H), 1.80−1.60 (m, 2 H), 1.42 (s, 3 H), 1.40−1.00 (series of m, 2 H), 1.23 (d, *J* = 6.1 Hz, 3 H), 1.22 (d, *J* = 6.1 Hz, 3 H), 1.16 (d, *J* = 6.1 Hz, 3 H), 1.10 (d, *J* = 6.1 Hz, 3 H), 1.06 (d, *J* = 6.2 Hz, 3 H), 0.93 (d, *J* = 6.2 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 202.6, 165.1, 152.2, 132.3, 120.4, 81.0, 78.3, 74.0, 72.2, 71.6, 61.4, 44.6, 43.4, 36.3, 28.7, 22.9, 22.8, 22.6, 22.5, 20.2, 18.8, 17.7; MS *m/z* (M^+) calcd 394.2355, obsd 394.2355; $[\alpha]^{22}_D$ +211° (*c* 0.63, $CHCl_3$).

(3a*S*,6a*S*,7a*S*)-4-[(1*R*,2*R*)-1,2-Dicyclohexyl-2-hydroxyethoxo]-3a,5,6,6a,7,7a-hexahydro-3a-hydroxy-2,3-diisopropoxy-7a-methyl-1*H*-cyclopenta[*a*]pentalen-1-one (18) and (3a*R*,6a*R*,7a*R*)-1,2-Dicyclohexyl-2-hydroxyethoxo]-3a,5,6,6a,7,7a-hexahydro-3a-hydroxy-2,3-diisopropoxy-7a-methyl-1*H*-cyclopenta[*a*]pentalen-1-one (19). Reaction of **17** [from 738 mg (2.0 mmol) of the bromo acetal] with **7** (200 mg, 1.0 mmol) (reaction time of 1 h) and then 2-lithiopropene [from 242 mg (2.0 mmol) of 2-bromopropene] for 14 h at room temperature followed by the usual workup provided a residual gum that was subjected to chromatography on silica gel (elution with 15% ethyl acetate in hexanes containing 1% triethylamine). There was isolated 205 mg (38%) of **18** and 125 mg (24%) of **19**.

For **18**: pale yellowish oil; IR (neat, cm^{-1}) 3348, 1684, 1608, 1380, 1332, 1263; ^{1}H NMR (300 MHz, C_6D_6) *δ* 5.53 (heptet, *J* = 6.1 Hz, 1 H), 5.19 (heptet, *J* = 6.1 Hz, 1 H), 4.40 (br s, 1 H), 3.75 (br s, 1 H), 3.69 (t, *J* = 4.7 Hz, 1 H), 3.47 (t, *J* = 4.7 Hz, 1 H), 2.70−2.40 (m, 3 H), 2.20−2.35 (m, 1 H), 1.80−1.40 (series of m, 12 H), 1.36 (s, 3 H), 1.29 (d, *J* = 6.1 Hz, 3 H), 1.26 (d, *J* = 6.1 Hz, 3 H), 1.18 (d, *J* = 6.1 Hz, 3 H), 1.16 (d, *J* = 6.1 Hz, 3 H), 1.40−1.00 (series of m, 12 H), 0.90−0.80 (m, 1 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 202.2, 166.3, 152.7, 132.9, 120.7, 82.4, 78.8, 76.0, 73.6, 71.7, 65.9, 61.1, 43.7, 43.3, 40.4, 39.8, 33.5, 30.9, 30.6, 28.2, 27.6, 27.4, 26.95, 26.90, 26.8, 26.7, 23.1, 22.9, 22.88, 22.6, 20.1, 15.5; MS *m/z* (M^+) calcd 530.3636, obsd 530.3612; $[\alpha]^{22}_D$ −259° (*c* 0.72, $CHCl_3$).

For **19**: thick colorless oil; IR (neat, cm^{-1}) 3560, 3345, 1695, 1614, 1380, 1321, 1259; ^{1}H NMR (300 MHz, C_6D_6) *δ* 5.38 (heptet, *J* = 6.1 Hz, 1 H), 5.34 (heptet, *J* = 6.1 Hz, 1 H), 4.20 (br s, 1 H), 3.96 (dd, *J* = 7.1, 3.0 Hz, 1 H), 3.61 (dd, *J* = 7.1, 3.0 Hz, 1 H), 2.80−2.60 (series of m, 2 H), 1.46 (s, 3 H), 1.33 (d, *J* = 6.0 Hz, 3 H), 1.26 (d, *J* = 6.0 Hz, 3 H), 1.14 (d, *J* = 6.0 Hz, 3 H), 1.09 (d, *J* = 6.0 Hz, 3 H), 1.40−0.90 (series of m, 20 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 202.6, 165.2, 153.6, 132.2, 119.6, 84.5, 78.2, 76.3, 74.4, 71.6, 61.4, 44.1, 43.6, 40.1, 39.7, 35.9, 30.9, 30.6, 29.2, 26.9, 26.85, 26.76, 26.71, 26.6, 26.51, 26.46, 23.1, 22.9, 22.8, 22.52, 22.49, 20.1; MS *m/z* (M^+) calcd 530.3616, obsd 530.3612; $[\alpha]^{22}_D$ +100° (*c* 0.55, $CHCl_3$).

(3a*S*,3b*S*,6a*S*,7a*S*)-3b,4,6,6a,7,7a-Hexahydro-3a-hydroxy-2,3-diisopropoxy-7a-methyl-1*H*-cyclopenta[*a*]pentalene-1,4-(3a*H*)-dione (20). A solution of **15** (40 mg, 0.10 mmol) in 5 mL of wet acetone was treated with 1 drop of 10% HCl, stirred overnight at room temperature, and quenched with 1 mL of saturated $NaHCO_3$ solution. The acetone was evaporated, and the resulting aqueous solution was extracted with ether. The combined organic extracts were dried and concentrated. Following a short flash chromatography (silica gel, elution with 20% ethyl acetate in hexanes) and solvent removal, 32 mg (100% of **20** was obtained as a colorless oil.

The hydrolysis of **18** was slower, and it was necessary to heat the reaction mixture at reflux for 2 d to obtain the identical ketone.

For **20**: IR (film, cm^{-1}) 3450, 1723, 1698, 1621, 1381, 1300; ^{1}H NMR (300 MHz, C_6D_6) *δ* 5.33 (heptet, *J* = 6.1 Hz, 1 H), 5.27 (heptet, *J* = 6.1 Hz, 1 H), 5.12 (s, 1 H), 2.44 (d, *J* = 7.5 Hz, 1 H), 2.16 (m, 1 H), 2.03 (m, 1 H), 1.85 (dq, *J* = 8.5, 3.6 Hz, 1 H), 1.72 (br dd, *J* = 8.5, 3.6 Hz, 1 H), 1.26 (s, 2 H), 1.17 (d, *J* = 6.1 Hz, 3 H), 1.16 (d, *J* = 6.1 Hz, 3 H), 1.15 (d, *J* = 6.1 Hz, 3 H), 1.06 (d, *J* = 6.1 Hz, 3 H), 1.20−1.05 (m, 2 H), 0.90 (m, 1 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 221.8, 201.5, 165.7, 132.4, 84.4, 73.7, 71.7, 56.8, 56.6, 39.9, 38.2, 35.7, 22.9, 22.7, 22.6, 22.55, 22.4, 19.8; MS *m/z* (M^+) calcd 322.1780, obsd 322.1773; $[\alpha]^{22}_D$ −16° (*c* 1.0, $CHCl_3$).

(3a*S*,3b*R*,4*S*,6a*S*,7a*S*)-3a,3b,4,6,6a,7,7a-Octahydro-3a,4-dihydroxy-2,3-diisopropoxy-7a-methyl-1*H*-cyclopenta[*a*]pentalen-1-one (21). Sodium borohydride (5.0 mg, 0.132 mmol) was added in one portion to a solution of **20** (20 mg, 0.62 mmol) in methanol (0.5 mL). The reaction mixture was left to stir overnight, concentrated, diluted with saturated NH_4Cl solution, and extracted with ether. Drying of the organic extracts and concentration gave an oil which was purified by flash chromatography (silica gel, elution with 50% ethyl acetate in hexanes) to obtain 10 mg (94%) of **21** as a colorless solid: mp 117−119 °C (from ethyl acetate/hexanes); IR (film, cm^{-1}) 3373, 1693, 1614, 1454, 1381, 1310; ^{1}H NMR (300 MHz, C_6D_6) *δ* 5.38 (heptet, *J* = 6.1 Hz, 1 H), 5.33 (heptet, *J* = 6.1 Hz, 1 H), 4.21 (t, *J* = 3.8 Hz, 1 H), 3.75 (s, 1 H), 2.58−2.45 (m, 3 H), 2.15−1.95 (m, 1 H), 1.80−1.35 (series of m, 5 H), 1.31 (s, 3 H), 1.18 (d, *J* = 6.1 Hz, 3 H), 1.17 (d, *J* = 6.1 Hz, 3 H), 1.15 (d, *J* = 6.1 Hz, 3 H), 1.11 (d, *J* = 6.1 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 203.0, 166.5, 132.0, 84.4, 75.5, 73.5, 71.5, 58.4, 57.3, 44.7, 40.0, 36.7, 29.4, 22.83, 22.78, 22.73, 22.5, 19.1; MS *m/z* (M^+) calcd 324.1935, obsd 324.1936; $[\alpha]^{22}_D$ −263° (*c* 0.45, $CHCl_3$).

Anal. Calcd. for $C_{18}H_{28}O_5$: C, 66.64; H, 8.70. Found: C, 66.64; H, 8.69.

(3a*S*,3b*R*,3b*S*,6a*S*,7a*S*)-2,3,3a,3b,6,6a,7,7a-Octahydro-3b-hydroxy-4,5-diisopropoxy-6a-methyl-6-oxo-1*H*-cyclopenta[*a*]pentalen-3-yl (*R*)-methoxyphenylacetate (22) and (3a*S*,3b*R*,4*S*,6a*S*,7a*S*)-1,3b,4,5,6,-6a,7,7a-Octahydro-4-hydroxy-2,3-diisopropoxy-7a-methyl-1-oxo-3a*H*-cyclopenta[*a*]pentalen-3a-yl (*R*)-methoxyphenylacetate (23). (*R*)-*O*-Methylmandelic acid (50 mg, 0.3 mmol) was dissolved in 2 mL of CH_2Cl_2, and the solution was cooled to 0 °C in advance of the addition of 0.6 mmol of oxalyl chloride. After overnight stirring at room temperature, the solvent was evaporated under vacuum and 40 mg (0.12 mmol) of **21** in 2 mL of CH_2Cl_2 was added, followed by 75 mg of triethylamine and a crystal of 4-(dimethylamino)pyridine. After 2 h, the alcohol could no longer be detected by TLC. The volatile organics were removed under vacuum, and the resulting mixture was applied directly to a column of silica gel (elution with 20% ethyl acetate in hexanes). Esters **23** and **22** were isolated (total 47 mg, 81%) in order of elution.

For **22**: 28 mg (48%); colorless solid, mp 69−71 °C (from ethyl acetate); IR (film, cm^{-1}) 3464, 1743, 1698, 1621; ^{1}H NMR (300 MHz, $CDCl_3$) *δ* 7.44−7.32 (m, 5 H), 5.40 (heptet, *J* = 6.1 Hz, 1 H), 5.30−5.27 (m, 1 H), 4.95 (heptet, *J* = 6.1 Hz, 1 H), 4.75 (s, 1 H), 3.35 (s, 3 H), 3.19 (s, 1 H), 2.71 (m, 1 H), 2.30−2.10 (m, 2 H), 2.05−1.83 (m, 2 H), 1.82−1.70 (m, 1 H), 1.50−1.15 (m, 2 H), 1.36 (d, *J* = 6.1 Hz, 3 H), 1.31 (d, *J* = 6.1 Hz, 3 H), 1.21 (d, *J* = 6.1 Hz, 3 H), 1.20 (d, *J* = 6.1 Hz, 3 H), 1.09 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 202.3, 169.6, 162.2, 135.3, 131.5, 129.1, 128.9, 128.9, 127.0, 127.0, 82.6, 83.4, 80.0, 73.9, 71.9, 57.6, 56.9, 55.0, 43.0, 39.8, 34.4, 28.2, 22.7, 22.7, 22.65, 22.4, 17.9; MS *m/z* (M^+) calcd 472.2461, obsd 472.2437.

For **23**: 19 mg (33%); colorless oil; IR (neat, cm^{-1}) 3422, 1748, 1700, 1622; ^{1}H NMR (300 MHz, $CDCl_3$) *δ* 7.45−7.25 (m, 5 H), 5.45−5.35 (m, 1 H), 5.38 (heptet, *J* = 6.1 Hz, 1 H), 4.97 (heptet, *J* = 6.1 Hz, 1 H), 4.75 (s, 1 H), 3.41 (s, 3 H), 2.66 (t, *J* = 7.3 Hz, 1 H), 2.58 (s, 1 H), 2.16 (q, *J* = 6.8 Hz, 2 H), 1.93−1.70 (series of m, 3 H), 1.40 (m, 1 H), 1.35 (d, *J* = 6.1 Hz, 3 H), 1.30 (d, *J* = 6.1 Hz, 3 H), 1.30−1.00 (m, 1 H), 1.20 (d, *J* = 6.1 Hz, 3 H), 1.19 (d, *J* = 6.1 Hz, 3 H), 1.15 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 203.5, 170.1, 166.9, 136.0, 131.3, 128.8, 128.7, 128.7, 127.2, 127.2, 82.9, 82.8, 78.5, 74.0, 71.8, 57.5, 57.2, 55.4, 43.6, 39.5, 34.4, 28.4, 22.7, 22.7, 22.7, 22.4, 18.4; MS *m/z* (M^+) calcd 472.2461, obsd 472.2432.

(1*S*,4*R*)-3-Bromo-4-methoxy-2-cyclopentenol (25). A solution of **24** (1.10 g, 3.58 mmol) in THF (24 mL) was cooled to 0 °C and treated dropwise with tetra-*n*-butylammonium fluoride (7.2 mL of 1 M in THF, 7.2 mmol), and the mixture was stirred at room temperature for 30 min before the addition of water (10 mL) and extraction with ether (2 × 20 mL). The combined organic phases were washed with water (20 mL) and brine (20 mL), dried, and concentrated. The residue was purified by flash chromatography (silica gel, elution with 3:1 hexanes/

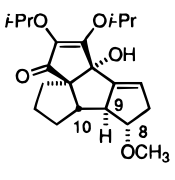
ethyl acetate) to give **25** as a yellowish liquid (0.53 g, 77%): IR (neat, cm^{-1}) 3384, 1689, 1356, 1077; ^1H NMR (300 MHz, $CDCl_3$) δ 6.07 (br, 1 H), 4.45−4.41 (m, 1 H), 4.11−3.96 (m, 1 H), 3.78 (br, 1 H), 3.31 (s, 3 H), 2.62 (dt, J = 14.0, 7.4 Hz, 1 H), 1.60 (dt, J = 14.0, 4.0 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 137.3, 126.8, 84.6, 72.5, 56.1, 39.3; MS *m/z* (M^+) calcd 191.9728, obsd 191.9757; $[\alpha]^{22}_D$ −36.9° (*c* 0.74, $CHCl_3$).

(3*S*,5*R*)-1-Bromo-3,5-dimethoxycyclopentene (26). Alcohol **25** (0.51 g, 2.64 mmol) in THF (10 mL) was added dropwise at 0 °C to a magnetically stirred suspension of sodium hydride (0.17 g of 60% dispersion in mineral oil, 4.25 mmol) in the same solvent (10 mL). After 1 h at room temperature, methyl iodide (0.90 mL, 14.5 mmol) was introduced at 0 °C and stirring was maintained at 22 °C for 2 h. Water (5 mL) was added, the mixture was extracted with ether (2 x 10 mL), and the combined organic solutions were washed with water (10 mL) and brine (10 mL), dried, and concentrated. The residue was subjected to flash chromatography (silica gel, elution with 20:1 hexanes/ethyl acetate) to provide **26** as a pale yellowish liquid (0.40 g, 74%): IR (neat, cm^{-1}) 1620, 1455, 1358, 1097; ^1H NMR (300 MHz, $CDCl_3$) δ 6.17 (br, 1 H), 4.43−4.16 (m, 1 H), 4.14−4.09 (m, 1 H), 3.31 (s, 3 H), 3.25 (s, 3 H), 2.56 (dt, J = 13.9, 7.4 Hz, 1 H), 1.72 (dt, J = 13.9, 4.0 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 134.4, 128.3, 84.1, 80.9, 55.8, 55.4, 35.6; MS *m/z* (M^+) calcd 205.9918, obsd 205.9930; $[\alpha]^{22}_D$ −56.7° (*c* 0.56, $CHCl_3$).

(3a*R*,6a*S*,6b*R*,7*S*,9b*R*)-4,5,6,6a,6b,7,8,9b-Octahydro-9b-hydroxy-1,2-diisopropoxy-7-methoxy-3*H*-dicyclopenta[*a,b*]pentalen-3-one (28) and (3a*S*,6a*R*,6b*S*,7*S*,9b*S*)-4,5,6,6a,6b,7,8,9b-Octahydro-9b-hydroxy-1,2-diisopropoxy-7-methoxy-3*H*-dicyclopenta[*a,b*]pentalen-3-one (29). Reaction of **27** [from 0.39 g (1.88 mmol) of **26**] in THF (10 mL) with **7** (0.37 g, 1.88 mmol) (reaction time of 1 h) and then cyclopentenyllithium [from 0.74 g (3.81 mmol) of the iodide] for 18 h at 22 °C followed by the usual workup procedure provided a brown liquid that was purified by flash chromatography on silica gel (elution with 6:1 hexanes/ethyl acetate). There were isolated 0.12 g (17%) of **28** and 0.13 g (19%) of **29**.

For **28**: pale yellowish oil; IR (neat, cm^{-1}) 3398, 1691, 1613, 1306, 1108; ^1H NMR (300 MHz, $CDCl_3$) δ 5.56 (br, 1 H), 5.34 (heptet, J = 6.1Hz, 1 H), 4.85 (heptet, J = 6.1 Hz, 1 H), 3.77 (q, J = 6.3 Hz, 1 H), 3.28 (s, 3 H), 2.95−2.90 (m, 1 H), 2.68−2.63 (m, 2 H), 2.50−2.41 (m, 1 H), 2.20−2.10 (m, 2 H), 1.84−1.78 (m, 2 H), 1.75−1.67 (m, 2 H), 1.52−1.45 (m, 1 H), 1.32 (d, J = 6.1 Hz, 3 H), 1.18 (d, J = 6.1 Hz, 3 H), 1.14 (d, J = 6.1 Hz, 3 H), 1.14 (d, J = 6.1 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 203.5, 165.6, 150.8, 129.0, 119.6, 90.6, 75.7, 74.1, 71.9, 71.3, 62.2, 57.6, 51.8, 42.1, 33.6, 32.1, 27.5, 23.0, 22.8, 22.7, 22.2; MS *m/z* (M^+) calcd 362.2099, obsd 362.2096; $[\alpha]^{22}_D$ −74.2° (*c* 0.38, $CHCl_3$).

Anal. Calcd. for $C_{21}H_{30}O_5$: C, 69.57; H, 8.35. Found: C, 69.48; H, 8.38.



Irradiate	Observe	%n.O.e.
H-8 (δ 3.77)	H-9	2.1
	H-10	9.1
H-9 (δ 2.93)	H-8	1.7
	H-10	2.0

For **29**: white solid, mp 108−110 °C; IR (neat, cm^{-1}) 3410, 1693, 1614, 1308, 1104; ^1H NMR (300 MHz, $CDCl_3$) δ 5.61 (br, 1 H), 5.28 (heptet, J = 6.1 Hz, 1 H), 4.90 (heptet, J = 6.1 Hz, 1 H), 3.97 (q, J = 6.3 Hz, 1 H), 3.22 (s, 3 H), 2.87−2.76 (m, 2 H), 2.60−2.54 (m, 1 H), 2.52−2.40 (m, 1 H), 1.93−1.80 (m, 1 H), 1.78−1.60 (m, 6 H), 1.26 (d, J = 6.1 Hz, 3 H), 1.21 (d, J = 6.1 Hz, 3H), 1.17 (d, J = 6.1 Hz, 3 H), 1.15 (d, J = 6.1 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 203.2, 165.1, 148.8, 132.8, 121.1, 84.7, 77.0, 73.9, 71.9, 69.7, 57.2, 52.7, 69.7, 57.2, 52.7, 49.8, 42.5, 29.3, 29.0, 27.1, 22.6, 22.5 (2 C), 22.4; MS *m/z* (M^+) calcd 362.2099, obsd 362.2094; $[\alpha]^{22}_D$ +20.6° (*c* 0.49, $CHCl_3$).

Anal. Calcd. for $C_{21}H_{30}O_5$: C, 69.57; H, 8.35. Found: C, 69.64; H, 8.33

(3a*R*,5*S*,7a*S*)-6-Bromo-3a,4,5,7a-tetrahydro-5-methoxy-2,2-dimethyl-1,3-benzodioxole (32). A cold (0 °C) solution of **31** (500 mg, 3.0 mmol) in CH_2Cl_2 (10 mL) was treated dropwise during 5 min with a CH_2Cl_2 solution (5 mL) of bromine (0.17 mL, 3.29 mmol), followed by triethylamine (0.95 mL, 6.82 mmol). After an additional 5 min at 0 °C, the reaction mixture was warmed to room temperature, filtered through a short pad of silica gel, and freed of solvent. The residue was chromatographed on silica gel (elution with 20% ethyl acetate in hexanes containing 0.1% triethylamine) to give 636 mg (87%) of the bromo enone as a white crystalline solid: mp 108−110 °C; IR (neat, cm^{-1}) 1703, 1613, 1383, 1371, 1226; ^1H NMR (300 MHz, $CDCl_3$) δ 7.08 (dd, J = 3.0, 1.8 Hz, 1 H), 4.75 (dd, J = 4.8, 3.0 Hz, 1 H), 4.67 (m, 1 H), 3.16 (dd, J = 17.4, 2.6 Hz, 1 H), 2.79 (dd, J = 17.4, 3.6 Hz, 1 H), 1.38 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 187.3, 146.1, 124.2, 110.4, 73.3, 72.9, 38.6, 27.7, 26.5; MS *m/z* ($M^+ - CH_3$) calcd 230.9656, obsd 230.9660; $[\alpha]^{22}_D$ −20.8° (*c* 1.09, $CHCl_3$).

The bromo enone (76 mg, 0.31 mmol) was dissolved in dry methanol (1.5 mL) containing cerium trichloride heptahydrate (126 mg, 0.34 mmol) at 0 °C and treated with sodium borohydride (58 mg, 1.5 mmol) in two portions. After 15 min, saturated NH_4Cl solution was introduced and the products were extracted into CH_2Cl_2, dried, and concentrated. The 1.8:1 cis/trans mixture of alcohols (^1H NMR analysis) was separated into its components by chromatography on silica gel (elution with 20% ethyl acetate in hexanes). There was isolated 48 mg (62%) of the cis isomer and 27 mg (35%) of the trans isomer, both as white crystalline solids.

For the cis alcohol: colorless crystals, mp 69−70 °C; IR (neat, cm^{-1}) 3512, 1645, 1292, 1227, 1154; ^1H NMR (300 MHz, $CDCl_3$) δ 6.07 (dd, J = 3.1, 1.1 Hz, 1 H), 4.51 (m, 2 H), 4.14 (s, 1 H), 3.31 (d, J = 9.6 Hz, 1 H), 2.56 (ddd, J = 15.4, 3.5, 2.4 Hz, 1 H), 2.22 (ddd, J = 15.4, 4.6, 2.1 Hz, 1 H), 1.46 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 128.7, 128.1, 110.2, 74.0, 71.9, 69.4, 32.4, 28.1, 26.5; MS *m/z* ($M^+ - CH_3$) 232.9813, obsd 232.9813; $[\alpha]^{22}_D$ −141° (*c* 1.03, $CHCl_3$).

For the trans alcohol: colorless crystals, mp 125−126 °C; IR (neat, cm^{-1}) 3589, 1643, 1299, 1212, 1154; ^1H NMR (300 MHz, $CDCl_3$) δ 6.09 (m, 1 H), 4.48 (m, 1 H), 4.38 (m, 1 H), 2.61 (ddd, J = 14.3, 5.6, 4.3 Hz, 1 H), 2.04 (s, 1 H), 1.87 (ddd, J = 14.3, 8.9, 2.5 Hz, 1 H), 1.38 (s, 3 H), 1.36 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 130.6, 129.2, 109.3, 73.3, 72.3, 66.2, 33.7, 27.8, 26.4; MS *m/z* ($M^+ - CH_3$) calcd 232.9813, obsd 232.9807; $[\alpha]^{22}_D$ −67.4° (*c* 1.08, $CHCl_3$).

To a THF (10 mL) suspension of sodium hydride (290 mg, 12.0 mmol) at 0 °C under N_2 was added over 1 h a THF solution (5 mL) of the cis alcohol (1.5 g, 6.0 mmol) and methyl iodide (2.23 g, 15 mmol). The reaction was stirred at 22 °C for 12 h, quenched with saturated NH_4Cl solution, and extracted with ether. The usual workup was followed by chromatography on silica gel (elution with 40% ethyl acetate in hexanes) to give 1.5 g (95%) of **32** as a colorless solid: mp 64−65 °C; ^1H NMR (300 MHz, C_6D_6) δ 6.08 (br s, 1 H), 3.96−3.93 (m, 1 H), 3.82−3.77 (m, 1 H), 3.42 (m, 1 H), 3.14 (s, 3 H), 1.96 (m, 1 H), 1.62−1.58 (m, 1 H), 1.40 (s, 3 H), 1.22 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 129.5, 129.2, 110.1, 76.0, 73.3, 71.0, 56.8, 31.1, 28.3, 26.5; $[\alpha]^{22}_D$ −50.5° (*c* 1.03, $CHCl_3$).

Anal. Calcd. for $C_{10}H_{15}BrO_3$: C, 45.65; H, 5.75. Found: C, 45.77; H, 5.80.

(3a*R*,5*R*,7a*S*)-6-Bromo-3a,4,5,7a-tetrahydro-5-methoxy-2,2-dimethyl-1,3-benzodioxole (33). Analogous O-methylation of the trans alcohol from above (2.55 g, 10.28 mmol) provided **33** (2.31 g, 86%) as a faintly yellowish oil: IR (neat, cm^{-1}) 1642, 1379, 1236, 1060; ^1H NMR (300 MHz, $CDCl_3$) δ 6.08 (br, 1 H), 4.42−4.35 (m, 2 H), 3.90−3.85 (m, 1 H), 3.39 (s, 3 H), 2.31 (dt, J = 13.9, 5.3 Hz, 1 H), 1.96−1.84 (m, 1 H), 1.32 (s, 3 H), 1.28 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 129.7, 127.7, 109.1, 75.7, 72.9, 71.4, 57.5, 31.5, 27.7, 26.1; MS *m/z* (M^+) calcd 262.0148, obsd 262.0176; $[\alpha]^{22}_D$ −35.2° (*c* 0.72, $CHCl_3$).

(*S*)-4-Hydroxy-2,3-diisopropoxy-4-[(3*S*,4*R*,6*S*)-3,4-(isopropylidenedioxy)-6-methoxy-1-cyclohexen-1-yl]-2-cyclobuten-1-one (36) and (*R*)-4-Hydroxy-2,3-diisopropoxy-4-[(3*S*,4*R*,6*S*)-3,4-(isopropylidenedioxy)-6-methoxy-1-cyclohexen-1-yl]-2-cyclobuten-1-one (37). *tert*-Butyllithium (3.0 mL of 1.7 M in pentane, 5.10 mmol) was added dropwise at −78 °C to a solution of **32** (0.60 g, 2.29 mmol) in dry THF (12 mL), and the mixture was stirred at this temperature for 1 h

prior to the introduction of **7** (0.23 g, 1.16 mmol) as a solution in THF (6 mL). One hour later, water (10 mL) was carefully added, and the products were extracted into ether (2 × 20 mL), washed with water (20 mL) and brine (20 mL), dried, and concentrated. Chromatography of the residue on silica gel (elution with 4:1 hexanes/ethyl acetate) gave **36** (0.22 g, 50%), followed by **37** (0.15 g, 34%).

For **36**: faint yellowish oil; IR (neat, cm^{-1}) 3386, 1769, 1384, 1101; ^1H NMR (300 MHz, C_6D_6) δ 6.47 (d, $J = 3.4$ Hz, 1 H), 4.94 (br, 1 H), 4.86 (heptet, $J = 6.0$ Hz, 1 H), 4.81 (heptet, $J = 6.0$ Hz, 1 H), 4.38−4.32 (m, 1 H), 4.02−3.97 (m, 1 H), 3.65−3.62 (m, 1 H), 3.06 (s, 3 H), 2.06 (dt, $J = 14.4$, 4.9 Hz, 1 H), 1.56 (dt, $J = 14.5$, 4.2 Hz, 1 H), 1.41 (s, 3 H), 1.28 (s, 3 H), 1.25−1.14 (m, 12 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 183.8, 168.2, 138.0, 132.8, 126.1, 109.4, 88.0, 77.2, 73.2, 72.9, 72.0, 71.3, 56.2, 28.4, 28.3, 26.5, 22.8, 22.7, 22.6, 22.2; MS *m/z* (M^+) calcd 382.1961, obsd 381.1976; $[\alpha]^{22}_D$ +63.6° (*c* 0.55, C_6H_6).

Anal. Calcd. for $C_{20}H_{30}O_7$: C, 62.79; H, 7.91. Found: C, 62.89; H, 7.94.

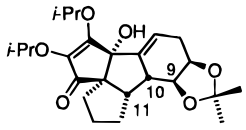
For **37**: faint yellowish oil; IR (neat, cm^{-1}) 3417, 1769, 1614, 1372, 1098; ^1H NMR (30 MHz, C_6D_6) δ 6.12 (d, $J = 2.4$ Hz, 1 H), 5.35 (br, 1 H), 4.89 (heptet, $J = 6.1$ Hz, 1 H), 4.76 (heptet, $J = 6.1$ Hz, 1 H), 4.12−4.09 (m, 2 H), 3.87−3.83 (m, 1 H), 3.12 (s, 3 H), 1.92−1.83 (m, 1 H), 1.69 (dt, $J = 14.9$, 4.5 Hz, 1 H), 1.41 (s, 3 H), 1.23 (s, 3 H), 1.12−1.06 (m, 12 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 185.3, 164.4, 139.5, 132.6, 124.1, 109.6, 89.1, 76.7, 75.4, 73.4, 71.4, 71.3, 56.4, 29.4, 28.4, 26.4, 22.7, 22.6, 22.4, 22.2; MS *m/z* (M^+) calcd 382.1961, obds 382.2005; $[\alpha]^{22}_D$ +62.2° (*c* 0.59, C_6H_6).

Anal. Calcd. for $C_{20}H_{30}O_7$: C, 62.79; H, 7.91. Found: C, 62.71; H, 7.94.

(3a*R*,6a*S*,6b*R*,7*S*,8*R*,10b*R*)-5,6,6a,6b,7,8,9,10b-Octahydro-10b-hydroxy-1,2-diisopropoxy-7,8-(isopropylidenedioxy)dicyclopent[*a,b*]-inden-3(4*H*)-one (38) and (3a*S*,6a*R*,6b*R*,7*S*,8*R*,10b*S*)-5,6,6a,6b,7,8,9,-10b-Octahydro-10b-hydroxy-1,2-diisopropoxy-7,8-(isopropylidenedioxy)dicyclopent[*a,b*]inden-3(4*H*)-one (39). *tert*-Butyllithium (6.5 mL of 1.7 M in pentane, 11.05 mmol) was added dropwise at −78 °C to cyclopentenyl iodide (0.96 g, 4.94 mmol) dissolved in dry THF (25 mL). After 1 h at this temperature, a solution of **36** (0.47 g, 1.23 mmol) in dry THF (13 mL) was introduced, and the reaction was allowed to proceed at room temperature for 13 h prior to implementation of the usual workup. Flash chromatography on silica gel (elution with 5:1 hexanes/ethyl acetate) gave 0.12 g (24%) of **39** and 0.29 g (58%) of **38**.

For **38**: faint yellowish oil; IR (neat, cm^{-1}) 3437, 1692, 1613, 1380, 1054; ^1H NMR (300 MHz, $CDCl_3$) δ 5.91−5.86 (m, 1 H), 5.29 (heptet, $J = 6.1$ Hz, 1 H), 4.97 (heptet, $J = 6.1$ Hz, 1 H), 4.11 (q, $J = 5.1$ Hz, 1 H), 4.05 (t, $J = 4.7$ Hz, 1 H), 2.70 (dt, $J = 10.8$, 7.3 Hz, 1 H), 2.57 (dt, $J = 17.4$, 6.0 Hz, 1 H), 2.52−2.41 (m, 1 H), 2.34−2.24 (m, 2 H), 2.01−1.80 (m, 3 H), 1.76−1.66 (m, 2 H), 1.41 (s, 3 H), 1.34 (s, 3 H), 1.32 (d, $J = 6.1$ Hz, 3 H), 1.22 (d, $J = 6.1$ Hz, 3 H), 1.20 (d, $J = 6.1$ Hz, 3 H), 1.18 (d, $J = 6.1$ Hz, 3 H), 1.07−0.99 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 202.7, 165.8, 141.3, 132.3, 119.5, 107.4, 80.0, 75.3, 73.8, 71.7, 71.4, 64.9, 53.3, 49.9, 29.5, 29.4, 28.4, 28.3, 26.4, 25.9, 22.6, 22.5 (2 C), 22.3; MS *m/z* (M^+) calcd 418.2378, obsd 418.2356; $[\alpha]^{22}_D$ −200° (*c* 0.42, $CHCl_3$).

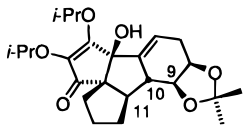
Anal. Calcd. for $C_{24}H_{34}O_6$: C, 68.86; H, 8.19. Found: C, 68.79; H, 8.26.



Irradiate	Observe	%n.O.e.
H-10 (δ 2.45)	H-9	1.9
	H-11	6.3

For **39**: faint yellowish oil; IR (neat, cm^{-1}) 3443, 1694, 1614, 1380, 1053; ^1H NMR (300 MHz, $CDCl_3$) δ 6.07−6.03 (m, 1 H), 4.90 (heptet, $J = 6.1$ Hz, 1 H), 4.10 (q, $J = 6.2$ Hz, 1 H), 3.79 (t, $J = 6.1$ Hz, 1 H), 2.61 (dt, $J = 16.9$, 7.1 Hz, 1 H), 2.48−2.17 (m, 3 H), 2.16−2.03 (m, 2 H), 1.99−1.55 (m, 4 H), 1.44 (s, 3 H), 1.40−1.28 (m, 9 H), 1.23−1.04 (m, 7 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 203.0, 165.7, 146.0, 129.3, 119.4, 108.0, 80.8 (2 C), 73.9, 72.6, 71.8, 66.8, 53.9, 50.2, 33.9, 30.8, 27.9, 26.9, 25.4, 25.2, 22.7 (3 C), 22.3; MS *m/z* (M^+) calcd 418.2378, obsd 418.2366; $[\alpha]^{22}_D$ +27.0° (*c* 0.57, $CHCl_3$).

Anal. Calcd. for $C_{24}H_{34}O_6$: C, 68.86; H, 8.19. Found: C, 69.01; H, 8.23.

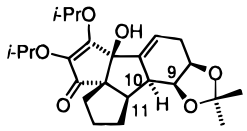


Irradiate	Observe	%n.O.e.
H-10 (δ 2.39)	H-9	1.8
	H-11	1.0

(3a*S*,6a*R*,6b*S*,7*S*,8*R*,10b*S*)-5,6,6a,6b,7,8,9,10b-Octahydro-10b-hydroxy-1,2-diisopropoxy-7,8-(isopropylidenedioxy)dicyclopent[*a,b*]-inden-3(4*H*)-one (40). *tert*-Butyllithium (1.4 mL of 1.7 M in pentane, 2.4 mmol) was added dropwise at −78 °C to cyclopentenyl iodide (0.20 g, 1.03 mmol) dissolved in dry THF (5 mL). After 1 h at this temperature, a solution of **37** (95 mg, 0.24 mmol) in THF (3 mL) was introduced, allowed to react for 17 h at room temperature, and processed as described above to give 27 mg (26%) of **40** and 23 mg (22%) of **39**.

For **40**: faint yellowish oil; IR (neat, cm^{-1}) 3426, 1691, 1613, 1380, 1052; ^1H NMR (300 MHz, $CDCl_3$) δ 6.06−6.04 (m, 1 H), 5.31 (heptet, $J = 6.0$ Hz, 1 H), 4.47−4.44 (m, 1 H), 4.39−4.31 (m, 1 H), 2.80−2.73 (m, 1 H), 2.48−2.40 (m, 1 H), 2.34−2.24 (m, 1 H), 2.14−1.97 (m, 2 H), 1.96−1.63 (m, 5 H), 1.60−0.90 (m, 19 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 203.4, 166.1, 144.5, 131.2, 120.9, 108.0, 79.8, 75.0, 73.9, 73.5, 72.0, 68.0, 48.5, 41.2, 30.8, 30.6, 30.4, 27.8, 27.0, 25.2, 22.7 (2 C), 22.4, 22.3; MS *m/z* (M^+) calcd 418.2378, obsd 418.2363; $[\alpha]^{22}_D$ +139° (*c* 0.50, $CHCl_3$).

Anal. Calcd. for $C_{24}H_{34}O_6$: C, 68.86; H, 8.19. Found: C, 68.59; H, 8.25.



Irradiate	Observe	%n.O.e.
H-10 (δ 2.48)	H-9	9.6
	H-11	12.0

(*S*)-4-(*tert*-Butyldimethylsiloxy)-2,3-diisopropoxy-4-[(3*S*,4*R*,6*R*)-3,4-(isopropylidenedioxy)-6-methoxy-1-cyclohexen-1-yl]-2-cyclobuten-1-one (43) and (*R*)-4-(*tert*-Butyldimethylsiloxy)-2,3-diisopropoxy-4-[(3*S*,4*R*,6*R*)-3,4-(isopropylidenedioxy)-6-methoxy-1-cyclohexen-1-yl]-2-cyclobuten-1-one (44). *tert*-Butyllithium (4.6 mL of 1.7 M in pentane, 7.8 mmol) was added dropwise at −78 °C to a solution of **33** (0.93 g, 3.5 mmol) in dry THF (18 mL), and the mixture was stirred at this temperature for 1 h prior to the introduction of **7** (0.35 g, 1.76 mmol) as a solution in THF (9 mL). One hour later, the usual workup was applied and an inseparable 1:1 mixture (^1H NMR analysis) of **41** and **42** was obtained in 88% yield.

A 0.94 g (2.46 mmol) sample of this mixture was dissolved in DMF (8 mL), treated with *tert*-butyldimethylsilyl chloride (0.74 g, 4.91 mmol) and imidazole (0.50 g, 7.4 mmol), and heated at 70 °C for 14 h. Water (10 mL) was added and the resulting mixture was extracted with ether (2 × 20 mL). The combined organic layers were washed with water (20 mL) and brine (20 mL), dried, and concentrated. Chromatography of the residue on silica gel (elution with 6:1 hexanes/ethyl acetate gave 0.17 g (14%) of **43** and 0.28 g (23%) of **44**, both as yellow liquids.

For **43**: IR (film, cm^{-1}) 1770, 1622, 1384, 1099; ^1H NMR (300 MHz, C_6D_6) δ 6.53 (d, $J = 3.2$ Hz, 1H), 4.94 (heptet, $J = 6.1$ Hz, 1 H), 4.74 (heptet, $J = 6.1$ Hz, 1 H), 4.43−4.38 (m, 2 H), 3.85 (t, $J = 3.6$ Hz, 1 H), 3.01 (s, 3 H), 2.15−2.06 (m, 1 H), 1.72−1.65 (m, 1 H), 1.45 (s, 3 H), 1.25 (s, 3 H), 1.17 (d, $J = 6.1$ Hz, 3 H), 1.15−1.09 (m, 9 H), 1.00 (s, 9 H), 0.35 (s, 3 H), 0.28 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 182.9, 166.2, 139.7, 132.9, 125.9, 108.7, 89.5, 76.3, 73.3, 73.1, 71.4, 70.9, 56.1, 30.0, 28.0, 25.8 (3 C), 25.6, 22.6 (2 C), 22.3, 22.0, 18.3, −3.4, −3.5; MS *m/z* (M^+) calcd 496.2828, obsd 496.2842; $[\alpha]^{22}_D$ +74.9° (*c* 0.62, $CHCl_3$).

For **44**: IR (film, cm^{-1}) 1777, 1633, 1383, 1098; ^1H NMR (300 MHz, C_6D_6) δ 6.50 (d, $J = 3.1$ Hz, 1 H), 4.95 (heptet, $J = 6.1$ Hz, 1 H), 4.69 (heptet, $J = 6.1$ Hz, 1 H), 4.40−4.34 (m, 2 H), 3.91 (t, $J = 3.8$ Hz, 1 H), 3.06 (s, 3 H), 2.19−2.12 (m, 1 H), 1.76−1.65 (m, 1 H), 1.41 (s, 3 H), 1.24 (s, 3 H), 1.17 (d, $J = 6.1$ H, 3 H), 1.14−1.01 (m, 9 H), 0.98 (s, 9 H), 0.33 (s, 3 H), 0.25 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 182.6, 163.8, 139.3, 133.3, 125.8, 108.5, 88.9, 76.0, 73.2, 72.9, 71.4, 71.0, 55.8, 30.0, 27.9, 25.7 (3 C), 25.6, 22.7, 22.5, 22.2,

22.0, 18.3, −3.4, −3.5; MZ *m/z* (M^+) calcd 496.2828, obsd 496.2862; $[\alpha]^{22}_D$ +30.0° (*c* 0.96, $CHCl_3$).

(*S*)-4-Hydroxy-2,3-diisopropoxy-4-[(3*S*,4*R*,6*R*)-3,4-(isopropylidenedioxy)-6-methoxy-1-cyclohexen-1-yl]-2-cyclobuten-1-one (41). Tetra-*n*-butylammonium fluoride (0.65 mL of 1 M in THF, 0.65 mL) was added to a solution of **43** (0.16 g, 0.32 mmol) in THF (3 mL), and the reaction mixture was stirred at room temperature for 30 min. Water (5 mL) was added, and the mixture was extracted with ether (2 × 10 mL). The combined organic layers were washed with water (10 mL) and brine (10 mL), dried, and concentrated. Chromatography of the residue on silica gel (elution with 4:1 hexanes/ethyl acetate) gave **41** as a yellow liquid (81 mg, 66%); IR (film, cm^{-1}) 3402, 1769, 1621, 1384, 1099; ^{1}H NMR (300 MHz, C_6D_6) δ 6.45 (d, J = 3.1 Hz, 1 H), 4.95 (heptet, J = 6.1 Hz, 1 H), 4.72 (heptet, J = 6.1 Hz, 1 H), 4.33−4.30 (m, 1 H), 4.27−4.21 (m, 1 H), 4.05 (t, J = 5.0 Hz, 1 H), 3.02 (s, 3 H), 1.98−1.90 (m, 1 H), 1.86−1.78 (m, 1 H), 1.41 (s, 3 H), 1.26 (s, 3 H), 1.21−1.07 (m, 13 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 183.3, 166.2, 138.7, 132.6, 125.4, 108.6, 87.9, 76.5, 73.8, 73.1, 71.4, 71.3, 55.8, 29.8, 27.9, 25.9, 22.5, 22.4, 21.9; MS *m/z* (M^+) calcd 382.1961, obsd 382.1962; $[\alpha]^{22}_D$ −71.9° (*c* 0.93, C_6H_6).

Anal. Calcd. for $C_{20}H_{30}O_7$: C, 62.79; H, 7.91. Found: C, 62.86; H, 7.98.

(*R*)-4-Hydroxy-2,3-diisopropoxy-4-[(3*S*,4*R*,6*R*)-3,4-(isopropylidenedioxy)-6-methoxy-1-cyclohexen-1-yl]-2-cyclobuten-1-one (42). Comparable treatment of **44** (0.28 g, 0.56 mmol) provided 0.16 g (76%) of **42** as a yellow liquid; IR (film, cm^{-1}) 3405, 1769, 1633, 1384, 1098; ^{1}H NMR (300 MHz, C_6D_6) δ 6.20 (d, J = 2.6 Hz, 1 H), 5.37−5.03 (br, 1 H), 4.91 (heptet, J = 6.1 Hz, 1 H), 4.73 (heptet, J = 6.1 Hz, 1 H), 4.45−4.41 (m, 1 H), 4.31−4.29 (m, 1 H), 4.18−4.13 (m, 1 H), 3.10 (s, 3 H), 2.09−2.01 (m, 1 H), 1.71−1.63 (m, 1 H), 1.33 (s, 3 H), 1.24 (s, 3 H), 1.18−1.06 (m, 12 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 184.8, 164.1, 138.5, 132.3, 124.8, 108.5, 88.7, 76.3, 74.8, 73.1, 71.5, 71.4, 56.1, 29.8, 27.9, 26.1, 22.4 (2 C), 22.1, 21.8; MS *m/z* (M^+) calcd 382.1961, obsd 382.2021; $[\alpha]^{22}_D$ −47.5° (*c* 0.52, C_6H_6).

Anal. Calcd. for $C_{20}H_{30}O_7$: C, 62.79; H, 7.91. Found: C, 62.76; H, 7.97.

Formation of 38 and 39 from 41. A cold (−78 °C), magnetically stirred solution of cyclopentenyl iodide (0.16 g, 0.82 mmol) in dry THF (4 mL) was treated dropwise with *tert*-butyllithium (1.1 mL of 1.7 M in pentane, 1.87 mmol). After 1 h at this temperature, a solution of **41** (77 mg, 0.20 mmol) of dry THF (2 mL) was introduced. The resulting solution was then stirred at room temperature for 16 h and diluted with deoxygenated saturated NH_4Cl solution (5 mL) at 0 °C and, 10 min later, with water (5 mL) and ether (20 mL). The organic phase was washed with water (10 mL) and brine (10 mL), dried, and concentrated. Submission of the residue to flash chromatography (silica gel, elution with 4:1 hexanes/ethyl acetate) gave 30 mg (36%) of **39** and 15 mg (18%) of **38**.

Formation of 39 and 40 from 42. When **42** was processed in the predescribed manner, flash chromatography (silica gel, elution with 5:1 hexanes/ethyl acetate) furnished 34 mg (21%) of **40** and 43 mg (26%) of **39**.

Acknowledgment. This contribution is dedicated with admiration to Prof. Fabian Gerson, a longtime friend and collaborator, on the occasion of his retirement from the University of Basel. The authors thank the National Science Foundation for generous financial support and Dr. Kurt Loening for nomenclature expertise..

Supporting Information Available: Crystallographic experimental sections and tables of X-ray crystal data, bond lengths and angles, final fractional coordinates, and thermal parameters for **14**, **22**, and **29** (36 pages). See any current masthead page for ordering and Internet access instructions. The authors have deposited the atomic coordinates for the X-ray structures with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, U.K.

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