Stereoselective Construction of the Dicyclopenta[*a,d*]cyclooctene Core of the Ceroplastin Sesterterpenes by Way of the Anionic Oxy-Cope Rearrangement

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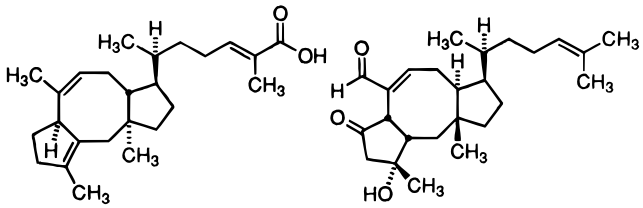
Bicyclo[3.2.1]octanediones such as **9**, which are readily available by double carbonylation of (1,3-cyclohexadiene)iron tricarbonyl complexes according to Eilbracht, are amenable to regiospecific methylenation under Wittig conditions. Reduction of **10** with copper hydride leads to **11**, which can be resolved by application of Johnson's sulfoximine technology and oxidized to give the enantiopure antipodes of **10**. Variously substituted cyclopentenyl anions undergo 1,2-addition to **10**, providing carbinols which are capable of anionic oxy-Cope rearrangement via chair transition states. These structural reorganizations are fully stereocontrolled and lead directly to functionalized dicyclopenta[*a,d*]cyclooctenes. When **11** is treated analogously, only [1,3] sigmatropy is observed and inversion of stereochemistry at the migrating carbon prevails. Both processes exhibit impressive scaffolding powers and are characterized by brevity.

The carbocyclic ring system shared by the ceroplastin sesterterpenes and the fusicoccin diterpenes is the relatively uncommon dicyclopenta[*a,d*]cyclooctene substructure. The pharmacological effects attributed to this class of natural products are as diverse as their level of unsaturation, extent of oxygenation, and ring juncture stereochemistry. Widespread interest in these substances has led to the successful total synthesis of albolic acid (**1**),[3] ophiobolin C (**2**),[4] ceroplastol I (**3**),[4,5] and cotylenol (**4**).[7] Our goal for the present research program was to develop an enantioselective route to **1** that would prove more expedient and generally applicable than that originally devised by this group.[6]



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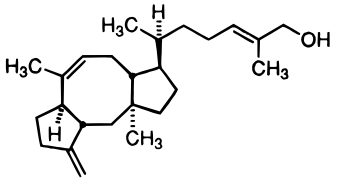

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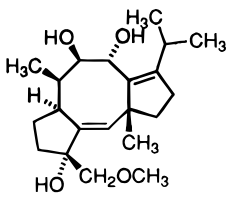

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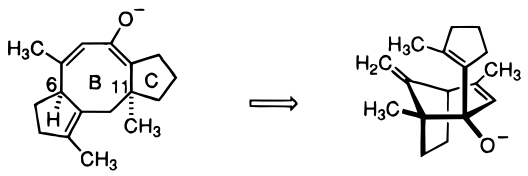
The challenge of elaborating the central eight-membered ring has previously been addressed by appropriate medium-ring cyclization reactions,[3,4,7] fragmentation of a suitably functionalized bicyclo[3.3.1]nonanone,[5] and adaptation of a Tebbe olefination/Claisen ring expansion sequence.[6] The present report details an alternative approach for gaining rapid access to the entire dicyclopenta[*a,d*]cyclooctene core. The strategy takes advantage of the charge-accelerated oxy-Cope rearrangement[8,9] for molecular construction, with full control over the relevant stereochemical features. More specifically, the [3,3] sigmatropic interrelationship of enolate anion **5** with alkoxide **6** was recognized to represent a direct means for establishing the requisite carbocyclic framework.[10] Several additional advantages were also apparent. Thus, the structurally enforced geometry in effect during the rearrangement was guaranteed to resolve the stereochemical issue of fixing the distal H-6 and C-11 methyl substituent in a cis relationship. Furthermore, two of the three unsaturated centers in **5** would be set in locales identical to those present in the target. The third π-bond forms part of a reactive enolate system, whose destiny it was ultimately to allow for side chain attachment to ring C.



5 **6**

Results and Discussion

Preparation and Resolution of Ketone 10. The plan contemplated for arrival at intermediates such as **6** was exo 1,2-addition of a cyclopentenyl anion to bicyclic unsaturated ketone **10**. The methodology developed by Eilbracht for smoothly effecting the 2-fold carbonylation

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(3) Kato, N.; Takeshita, H.; Kataoka, H.; Ohbuchi, S.; Tanaka, S. *J. Chem. Soc., Perkin Trans. 1* **1989**, 165.

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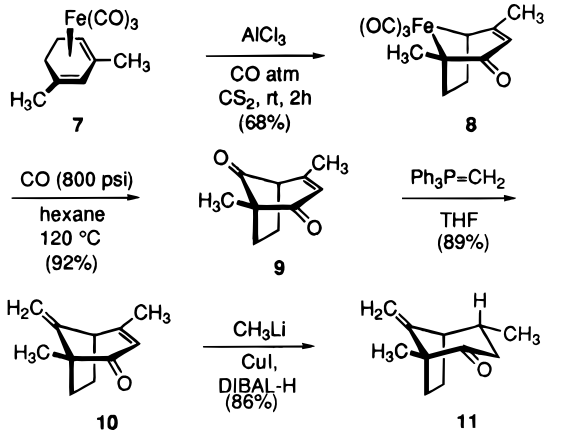
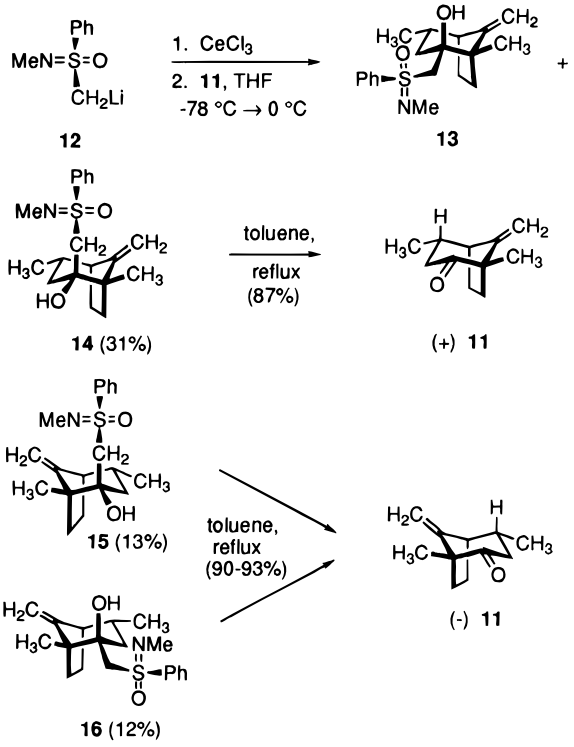
Scheme 1



Scheme 2



of 1,3-cyclohexadienes[11] was expected to play an especially useful role. At the experimental level, the iron tricarbonyl complex **7** was found to be conveniently transformed via **8** to **9** in the previously detailed manner (Scheme 1). The two carbonyl groups in **9** exhibit widely divergent reactivity, such that conventional Wittig olefination can be utilized to produce **10** efficiently (89%). In order to evaluate the difference in steric screening surrounding the two faces of the enone chromophore in **10**, its reduction with copper hydride was performed under the Saegusa conditions.[12] Only **11** resulted (86% isolated), indicating exo approach to be strongly favored kinetically. The stereochemistry of **11** was defined on the basis of convincing NOE experiments (see Experimental Section).

At this juncture, it was considered advisable to investigate means for the resolution of **10**, and the sulfoximine method pioneered by Johnson[13] was selected for this

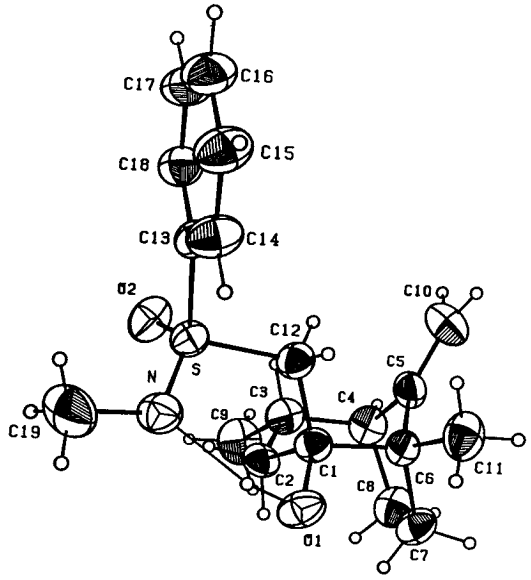
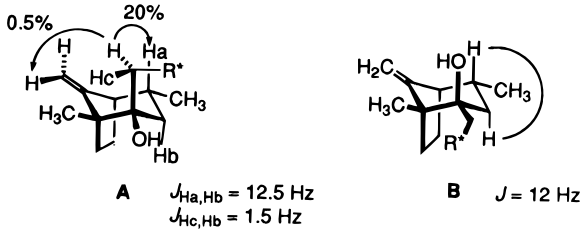


Figure 1. Computer-generated perspective drawing of **14** as determined by X-ray crystallography.

purpose. When attempts were first undertaken to add the α-lithio derivative **12** to **10**, no reaction was observed. Enolization at the γ-position of the enone was considered to be responsible for this observation. Alternative coupling of **12** to **11** initially gave low conversion to adducts, with starting materials again being recovered. However, exposure of **12** to anhydrous cerium trichloride[14] prior to the introduction of **11** led to satisfactory conversion (Scheme 2). The three major adducts **14** (31%), **15** (13%), and **16** (12%) were obtained pure by chromatography on silica gel with increasing solvent polarity. A trace amount of the endo adduct **13** was also present, but was not fully characterized. The unreacted **11** recovered from this process proved to be enriched in the levorotatory enantiomer to the extent of 25% ee.

The separation of **14** from the other diastereomers could be easily accomplished by direct crystallization of the adduct mixture from ethyl acetate−petroleum ether. The absolute configuration of **14** was convincingly established by X-ray crystallographic analysis (Figure 1).[38] The structural assignments to **15** and **16** rest upon appropriate analysis of coupling constants and NOE measurements as summarized in **A** and **B**. Thermolysis of individual samples of **14**−**16** in refluxing toluene occurred smoothly to deliver enantiopure samples of (+)-**11** and (−)-**11**.



Deprotonation of either antipode with potassium hexamethyldisilazide (KHMDS) in THF at −78 °C followed

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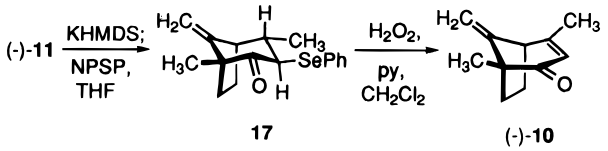
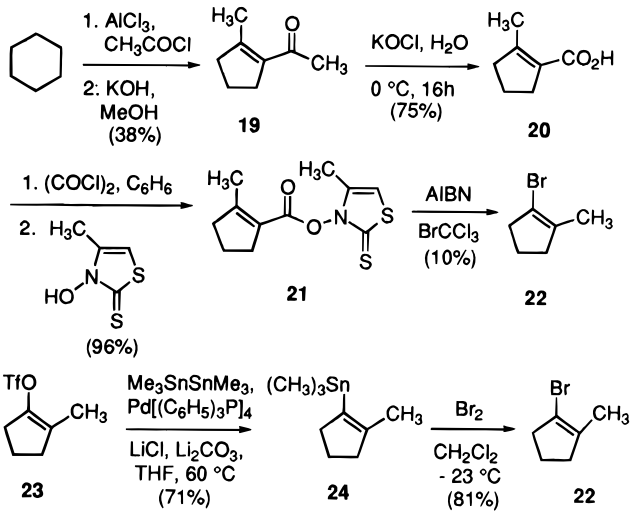
(13) (a) Johnson, C. R.; Zeller, J. R. *J. Am. Chem. Soc.* **1982**, *104*, 4021. (b) Johnson, C. R.; Schroeck, C. W.; Shanklin, J. R. *J. Am. Chem. Soc.* **1973**, *95*, 7424.
(14) Imamoto, T.; Takiyama, N.; Nakamura, K.; Hatajima, T.; Kamiya, Y. *J. Am. Chem. Soc.* **1989**, *111*, 4392.

Scheme 3



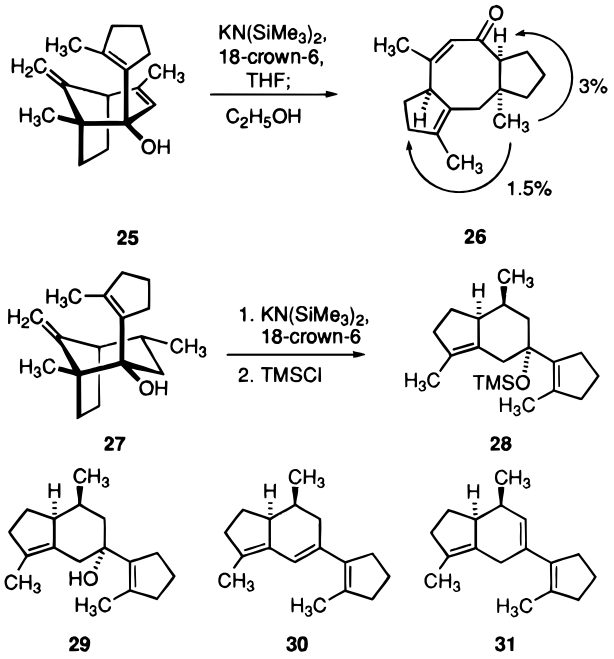
Scheme 4



by the addition of solid *N*-(phenylseleno)phthalimide (NPSP)[15] gave the exo α-phenylseleno ketones **17** and **18** (Scheme 3). Less than 5% of the endo isomers were apparent by ^{1}H NMR analysis at 300 MHz. Treatment of these intermediates with hydrogen peroxide in the presence of pyridine[16] furnished (−)-**10** and (+)-**10**, respectively, in 65−75% overall yield.

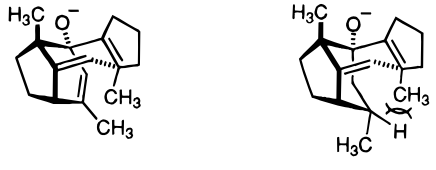
Pilot Studies Involving 1-Bromo-2-methylcyclopentene. In order to establish the feasibility of projected oxy-Cope rearrangements of the **6** → **5** type, attention was turned to bromide **22** as the first nucleophilic reaction partner. Two routes for its preparation were examined (Scheme 4). In the first, the unsaturated carboxylic acid **20** was readily arrived at by adopting Harding's method.[17] Thus, cyclohexane was treated with acetyl chloride and aluminum chloride in chloroform and the crude product was exposed to potassium hydroxide in methanol to provide ketone **19**. Subsequent haloform oxidation of **19** afforded **20** in 75% yield. The acid chloride derived from **20** was reacted with 3-hydroxy-4-methylthiazole-2(3*H*)-thione[18] to give **21**, an ester which proved easy to purify and was entirely stable at rt. Slow addition of **21** to a refluxing solution of AIBN in bromotrichloromethane[18,19] produced **22**. The low yield of isolated **22** (10%) stems from the close similarities of its boiling point to that of $BrCCl_3$ which was present in excess.

Scheme 5



These complications led us to pursue a more rapid and efficient route to **22**. Thermodynamic deprotonation of 2-methylcyclopentanone with LDA followed by exposure to *N*-phenyltriflimide gave rise to **23**. Adaptation of Wulff's palladium-catalyzed stannylation conditions[20] to **23** gave **24**, bromination of which at −23 °C afforded **22** in 81% yield.

Once halogen−metal exchange involving **22** had been effected with *sec*-butyllithium in THF, racemic **10** was introduced at −20 °C. As expected, exo attack prevailed, and alcohol **25** was obtained in 57% yield; starting enone was also recovered (12%) (Scheme 5). An alternative approach involving *tert*-butyllithium in ether as solvent resulted in the formation of a 6.9:1 ratio of **25** and its endo counterpart (50% combined), alongside 36% of unreacted enone. The relative stereochemistry depicted for **25** follows from the remarkable rapidity (less than 30 min at 20 °C) with which this alcohol underwent oxy-Cope rearrangement once it was converted to its potassium salt. Quenching of the enolate with ethanol resulted in the installation of a cis B/C ring junction in **26** as determined by NOE methods. This stereochemical outcome is as expected if **25**$^-$ adopts the energetically favorable chairlike transition state **C** in the course of its unidirectional pathway to product.



C **D**

When the analogous process was applied to **27**, which was obtained in a parallel manner from **11**, no [3,3] sigmatropic rearrangement materialized. Instead, a base-promoted [1,3] shift occurred,[9,21] and the resultant potassium alkoxide was silylated to afford **28**. Direct

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characterization of alcohol **29** was thwarted because of its exceptional sensitivity to dehyration during purification to give triene **30** along with a trace amount of isomer **31**. The inability of **27** to enter into oxy-Cope rearrangement is believed to stem from the serious nonbonded steric compression that necessarily must arise between the cyclopentenyl methyl group and the cyclohexyl methine carbon as depicted in **D**. When compared to **C**, it can be seen that the added double bond so alters the conformation of the six-membered ring that heightened proximity considerations no longer apply.

Consideration of Direct Introduction of the Side Chain. If a suitably functionalized cyclopentenyl halide was added to **10** and the alcohol so formed subjected to [3,3] sigmatropic rearrangement, an unrivaled opportunity could exist to arrive most expediently at targets such as **1**. As a result, the pursuit of **44**, **45**, and allied compounds proved unresistable. The requirement that two adjacent stereogenic centers in **44/45** be properly established was met, as shown in Scheme 6. In light of existing precedent,[22] it was anticipated that Cu(I)-promoted conjugate addition of Grignard reagent **32**[23] to 4-methylcyclopentenone (**33**)[24] would result in formation of the trans product **34**. Indeed, with chlorotrimethylsilane present,[25] **34** was formed in highly stereoselective fashion (14:1, capillary GC analysis). Subsequent acidic hydrolysis furnished diketone **35** in 86% overall yield.

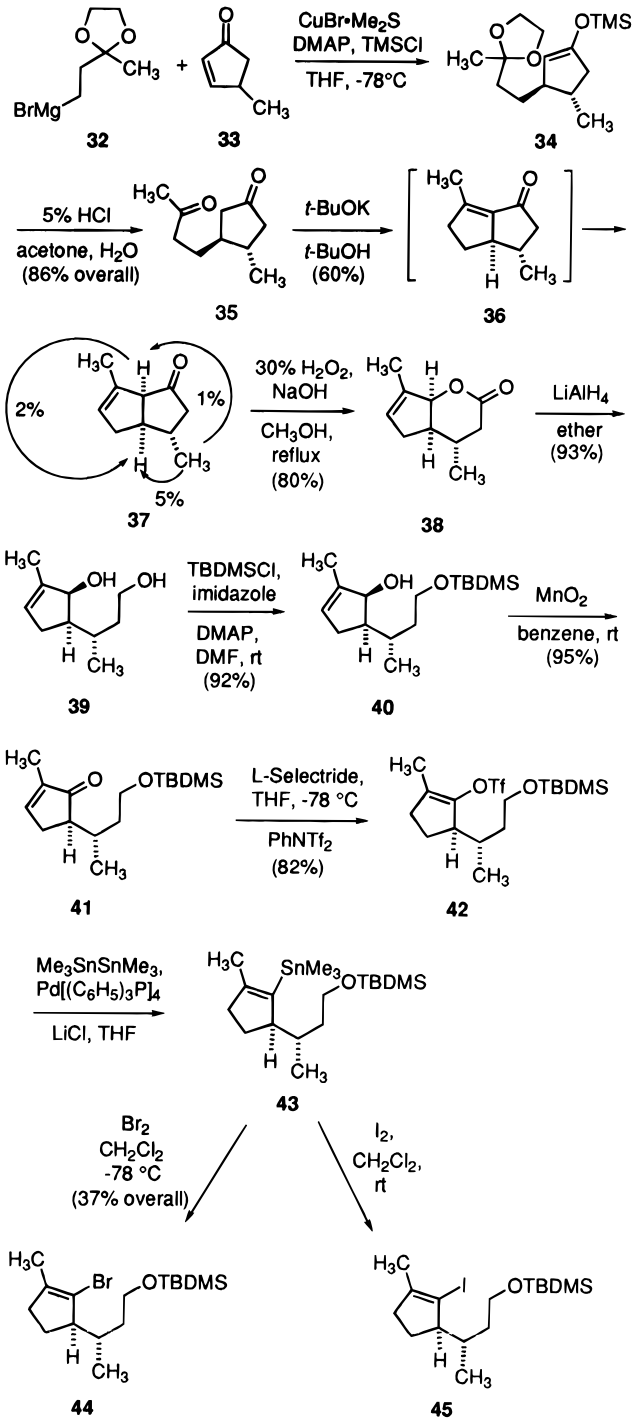
Intramolecular aldol condensation within **35**, achieved by heating with potassium *tert*-butoxide in *tert*-butyl alcohol at 50 °C, resulted initially in the formation of **36**, which underwent double-bond migration to arrive at β,γ-unsaturated ketone **37** in 60% yield. The conjugated isomer can be isolated if shorter reaction times are employed. The formation of **37**, which is well precedented,[26] is thermodynamically controlled and results because disconnection of the two π-systems generates a more stable compound. A driving force of ca. 2.4 kcal/mol has been estimated for related *cis*-bicyclo[3.3.0]octan-2-ones.[26] NOE studies performed on **37** confirmed that the cuprate had indeed been guided to the π-face of **33** opposite to that occupied by the methyl group.

Baeyer−Villiger oxidation[27] of **37** was smoothly accomplished by heating with 30% hydrogen peroxide in alkaline methanol. Recourse to 3 equiv each of H_2O_2 and NaOH provided the highest yield (80%) of **38** at short reaction times. When *m*-chloroperbenzoic acid was used in the presence of $NaHCO_3$,[28] no **38** was formed and only epoxides resulted.

Hydride reduction of **38** gave rise to diol **39** (93%), which was regioselectively silylated so as to lead to **40** (92%). Manganese dioxide oxidation[29,30] of **40** proceeded smoothly at rt without any evidence of epimerization to make enone **41** available (95%). In contrast, Swern oxidation proved inefficient in this instance, and the use of PCC resulted in erosion of stereochemical integrity,[31] particularly with prolongation of the reaction time.

Reduction of **41** with L-Selectride[32] resulted in 1,4-addition to the enone and regiospecific formation of the enolate, which was trapped in turn as the triflate (82% of **42**). A key requirement for the success of this reaction was that **41** be added to a slight excess (1.2 equiv) of the hydride reagent in THF at −78 °C. The reverse order of

Scheme 6



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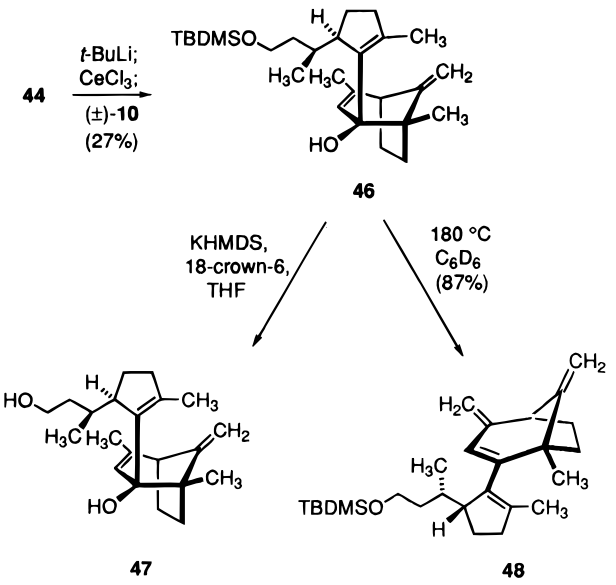
Scheme 7



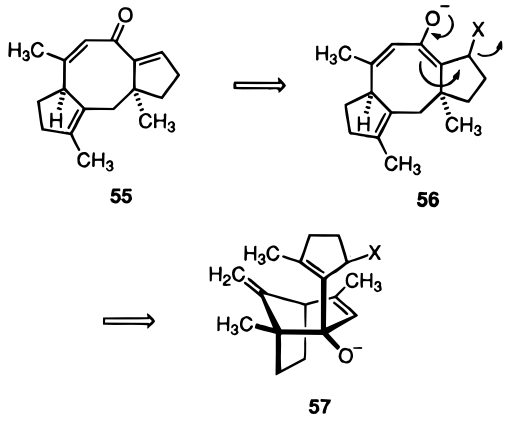
addition is particularly conducive to epimerization. With arrival at vinyl stannane **43** as before,[20,33] direct treatment with either elemental bromine or iodine resulted in conversion to **44** and **45**, respectively. These cycloalkenyl halides were easily purified by means of chromatography on silica gel which had been pretreated with 20% triethylamine in petroleum ether. Elution with a solvent system consisting of 1% triethylamine in petroleum ether was particularly advantageous.

While metal−halogen exchange of bromide **44** with *n*- or *sec*-butyllithium at −10 °C could not be driven to completion even after 24 h, the conversion of either **43** or **45** into the cyclopentenyllithium was accomplished at −78 °C in less than 20 min by treatment with 2.2 equiv of *tert*-butyllithium. Attempts to couple this intermediate with (±)-**10** were again thwarted by competing enolization. This problem was overcome by prior conversion to the cerate. In this way, alcohol **46** was obtained as the only detectable diastereomer in 27% yield (Scheme 7). The relative stereochemistry of this adduct has not been unequivocally determined.

Quite unexpectedly, attempted base-promoted rearrangement of **46** resulted principally in recovery of unreacted carbinol alongside a small amount of desilylated **47**. This diol was identical to that obtained by treatment of **46** with tetra-*n*-butylammonium fluoride. Prolongation of the reaction time or modest increases in reaction temperature simply generated increased proportions of **47**. Attempted thermal rearrangement of **46** in benzene at 180 °C in a sealed NMR tube uniquely gave the tetraene **48** (87%), the obvious product of dehydration.

The cerate-mediated coupling of **44** to (+)-**11** occurred in a highly diastereoselective manner to afford **49** and **50** in a 10:1 ratio (Scheme 8). Base-promoted rearrangement of these adducts occurred readily in the presence of potassium hexamethyldisilazide and 18-crown-6 in THF at 0 °C, being complete in less than 30 min. Spectral analysis of the products immediately revealed that [1,3] sigmatropy had prevailed. The isomerization of less polar adduct **49** gave rise to a mixture of **51a**, **51b**, and **52**, which was directly transformed into pure diol **52** by exposure to fluoride ion. The more polar **50** behaved analogously. In light of our ability to establish the stereochemistry of **53b** by a detailed analysis of COSY and NOE data,[33] the structural assignments to **51**−**54** were thereby confirmed. The finding that the [1,3] shifts proceed suprafacially with inversion of configuration at the migrating carbon (that bearing the alkoxide group) is consistent with operation of a concerted unimolecular rearrangement.[9,21,34]

Preincorporation of a Leaving Group in the Nucleophilic Component. The results just detailed indicate that the size of the side chain in **44** and **45** is too cumbersome to allow operation of the necessary [3,3] sigmatropic shift. In an unrelated study, we have demonstrated that proper positioning of a leaving group β to an incipient enolate anion results in kinetically controlled elimination and regiocontrolled formation of an α,β-unsaturated ketone.[35] The relevance of this innovation in the present context is reflected in the structural ensemble **55**−**57**. Past experience has shown



that recourse to a methoxy substituent for X allows not only for ready formation of the alkenyl anion but for ultimate ejection once the enolate anion has been formed as in **56**.[35,36] Consequently, the functionalized cyclopentenyl bromide **59b** was prepared, subjected to lithium−halogen exchange with *sec*-butyllithium, and coupled to (±)-**10** at −10 °C (Scheme 9). All four possible diastereomers (**60**−**63**) resulted in a combined yield of 85%. The 2.1:1.0:1.3:1.8 ratio of these carbinols proved to be virtually unchanged by solvent modification (ether vs THF) or base (*sec*- vs *tert*-butyllithium). A sensitivity to reaction temperature was noted. For example, at −78 °C, the product ratio (1.0:1.5:0.8:3.3) reflected an increased preference for endo attack. Direct crystallization of the crude product allowed for the isolation of pure **63**. Flash chromatography of the mother liquor afforded clean **60** and a mixture of **61** and **62**. The last two isomers were more difficult to separate.

Not unexpectedly, the exo alcohols **61** and **63** proved unreactive to base-promoted isomerization. Endo alcohol **62** was equally unreactive toward potassium hydride or potassium hexamethyldisilazide and 18-crown-6 in THF at 0 °C. This inability on the part of **62** to engage in [3,3] sigmatropy can be traced to severe nonbonded interaction

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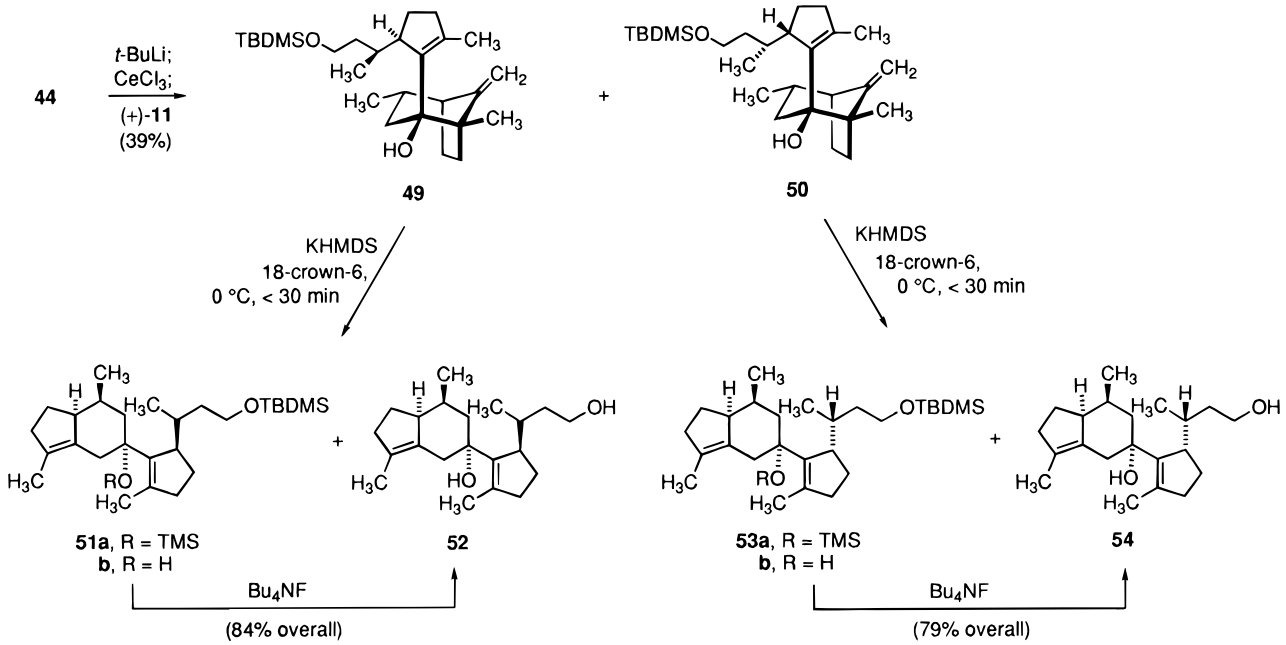
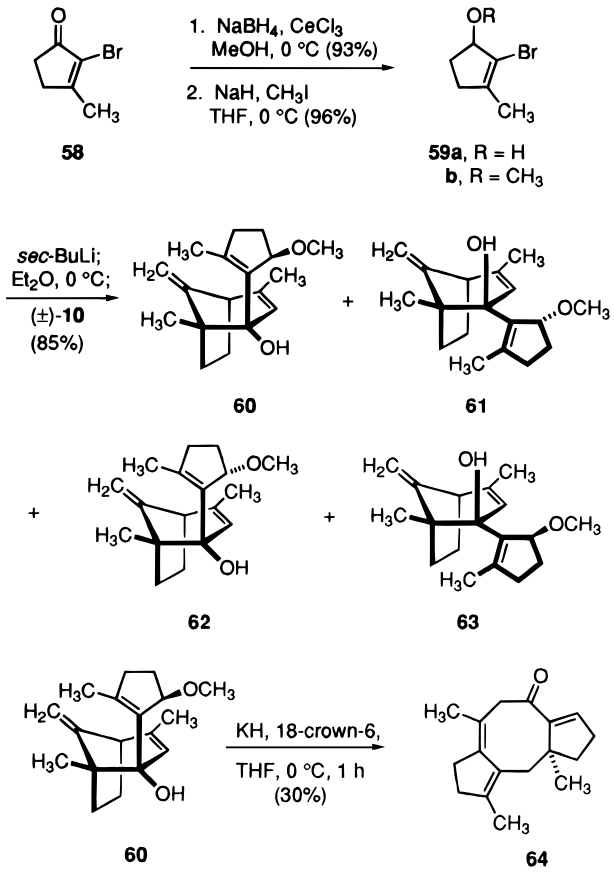
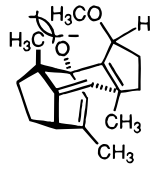
Scheme 8



Scheme 9



between the methoxy and tertiary methyl substituents as the chair alignment depicted in **E** develops. In **60**, the configuration of the methoxy carbon is now matched, such that progress is realized along this reaction channel. In this instance, however, **64** is isolated in only 30% yield along with two unidentified products. While it is necessary that trienone **55** be formed first, no conditions were found to retard deconjugation of the double bond internal to the medium-sized ring, a process which operates very readily. Thus, although the methoxy group is expelled under mild conditions in the projected manner, introduction of a double bond in the C-ring in this manner is accompanied by strain which is alleviated under the present circumstances by π-bond shifting to give **64**. Although the translocation associated with the unbridled postisomerization of **55** to **64** might be subsequently rectified, the inefficiency of the **10** → **60** → **64** sequence was not considered to be either useful or promising.



E

Conclusion

The synthetic effort described above illustrates several possibilities for realizing direct enantioselective construction of the dicyclopenta[*a*,*d*]cyclooctene core of the ceroplastin sesterterpenes and fusicoccin diterpenes. At the most basic level, full stereocontrolled assembly of the novel carbocyclic framework can be accomplished in only five steps from 2-methylcyclopentanone or six steps from 1,3-dimethyl-1,3-cyclohexadiene. The ease with which bicyclic ketones such as **10** and **11** can be resolved is detailed herein. However, it should be recognized that dieneiron tricarbonyl complexes such as **7** are equally amenable to separation into their enantiomers.[37]

While certain of the coupling reactions reported here are highly diastereoselective, others are not. These significant variations are considered to be dependent on the characteristics of the organolithium nucleophile. For example, the lithium derivative produced from the methoxy-substituted cyclopentenyl bromide **59b** is undoubt-

(37) Eilbracht, P.; Hittinger, C.; Kufferath, K.; Schmitz, A.; Gilsing, H.-D. *Chem. Ber.* **1990**, *123*, 1089.

(38) 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.

edly internally chelated, whereas that derived from **22** does not have this option. If the logical assumption is made that internally chelated lithium anions are less aggregated and significantly smaller than normal tetrameric species, their smaller size could facilitate a more closely balanced partitioning of exo and endo attack.

Finally, a new base-promoted [1,3] sigmatropic rearrangement has been discovered. The scaffolding potential of this process in total synthesis remains to be tested.

Experimental Section

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

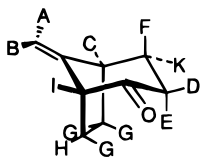
1,4-Dimethyl-8-methylenebicyclo[3.2.1]oct-3-en-2-one (10). A suspension of methyltriphenylphosphonium bromide (2.6 g, 7.3 mmol) in THF (40 mL) was treated with *n*-butyllithium (4.2 mL of 1.6 M in hexane, 6.7 mmol). After 15 min, the reaction mixture was cooled to −78 °C and a solution of **9**[11] (1.0 g, 6.7 mmol) in THF (14 mL) was introduced via cannula. The mixture was allowed to warm slowly to rt and after a total of 3 h was poured into saturated $NaHCO_3$ solution. The aqueous phase was extracted with CH_2Cl_2 (4×), and the combined organic phases were dried and evaporated. Chromatography of the residue on silica gel (elution with 10% ethyl acetate in petroleum ether) afforded 0.88 g (89%) of **10** as a colorless liquid: IR (neat, cm^{-1}) 1680, 1660, 1630, 1440, 1340, 1180, 1100, 900; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.68 (br s, 1 H), 4.71 (s, 1 H), 4.59 (s, 1 H), 3.09 (d, J = 6.2 Hz, 1 H), 2.20−1.95 (m, 1 H), 2.04 (d, J = 1.4 Hz, 3 H), 1.85−1.70 (m, 2 H), 1.70−1.55 (m, 1 H), 1.31 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 202.7, 167.7, 157.8, 123.3, 100.1, 55.8, 51.2, 33.6, 28.4, 22.4, 15.2; MS *m/z* (M^+) calcd 162.1045, obsd 162.1006.

Anal. Calcd for $C_{11}H_{14}O$: C, 81.44; H, 8.70. Found: C, 81.33; H, 8.76.

1,4-Dimethyl-8-methylenebicyclo[3.2.1]octan-2-one (11). To a suspension of copper(I) iodide (0.36 g, 1.85 mmol) in THF at 0 °C was added methyllithium (1.3 mL of 1.4 M in ether, 1.85 mmol). The reaction mixture was cooled to −50 °C prior to the addition of HMPA (10 mL) and diisobutylaluminum hydride (24.7 mL of 1.0 M in toluene, 24.7 mmol). After 30 min of stirring, a solution of **10** (1.0 g, 6.17 mmol) in THF (7 mL) was introduced via cannula. The mixture was stirred for 1.5 h and poured into a 10% hydrochloric acid solution, the aqueous phase was extracted with ether (4×), and the combined organic extracts were washed with 10% hydrochloric acid prior to drying. After removal of solvent, chromatography of the residue on silica gel (elution with 10% ethyl acetate in petroleum ether) gave 0.87 g (86%) of **11** as a colorless oil: IR (neat, cm^{-1}) 1710, 1660, 1470, 1450, 1420, 1380, 1350, 1330, 1165, 1150, 1120, 1070, 1030, 900; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.90 (s, 1 H), 4.66 (s, 1 H), 2.59 (br s, 1 H), 2.35−2.20 (m, 1 H), 2.20−2.06 (m, 1 H), 2.05−1.90 (m, 1 H), 1.88−1.75 (m, 3 H), 1.72−1.60 (m, 1 H), 1.17 (s, 3 H), 1.00 (d, J = 6.5 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 210.1, 157.2, 103.0, 56.4, 48.8, 42.9, 37.2, 35.7, 20.9, 18.7, 15.2; MS *m/z* (M^+) calcd 164.1201, obsd 164.1191.

Anal. Calcd for $C_{11}H_{16}O$: C, 80.44; H, 9.82. Found: C, 80.55; H, 9.93.

Resolution of Ketone 11. Anhydrous cerium trichloride (1.85 g, 7.5 mmol) was further dried at 140 °C under high vacuum for 16 h and then cooled under argon. To this was added THF (25 mL), and the suspension was stirred for 2 h before being cooled to −78 °C and treated with several drops of *sec*-butyllithium until a pale yellow color persisted. A solution of enantiopure sulfoximine (846 mg, 5 mmol)[13] in THF (15 mL) was treated with *sec*-butyllithium (4.6 mL of 1.3 M solution in cyclohexane, 6 mmol) at −78 °C under argon. After 30 min of stirring, the solution containing **12** was transferred to the cerium chloride suspension via cannula at −78 °C. The resulting mixture was stirred for 3 h at this temperature before introduction of a solution of ketone **11** (821.2 mg, 5 mmol) in THF (15 mL) via cannula. After 16 h of stirring at −78 °C, the mixture was slowly warmed to rt and then quenched with brine at 0 °C. The aqueous phase was extracted with ether, and the combined organic phases were dried and evaporated. Treatment with 10% ethyl acetate in petroleum ether afforded 380 mg of **14**. The mother liquor was subjected to MPLC (silica gel, elution with 10% ethyl acetate in petroleum ether) to give an additional 140 mg of **14** (total 520 mg, 31%), 215 mg (13%) of **15**, and 198 mg (12%) of **16**, along with 300 mg (37%) of recovered **11** which was 25% enriched in the levorotatory enantiomer.



resonance	δ [ppm]	multiplicity
A	4.90	s
B	4.66	s
C	2.59	br s
D	2.28	dd
E	2.11	dd
F	1.98	ddd
G(3H)	1.82	m
H	1.66	m
I (3H)	1.17	s
K(3H)	1.00	d

Couplings (Hz): $J_{C,F}$ = 3 (e,a); $J_{E,F}$ = 12 (a,a); $J_{D,E}$ = 15 (gem); $J_{D,F}$ = 6 (e,a); $J_{F,K}$ = 6; $J_{C,D}$ = 1 (w); $J_{C,H}$ < 1 (w); $J_{E,H}$ < 1 (w)

NOE's: I → B (5%), I → H (2.5%), G → C (5%), G → E (5%)

(+)-(*S*)-*S*-[[(1*S*,2*R*,4*S*,5*S*)-2-Hydroxy-1,4-dimethyl-8-methylenebicyclo[3.2.1]oct-2-yl]methyl]-*N*-methyl-*S*-phenylsulfoximine (14): white crystals, mp 164−165 °C (from ethyl acetate); IR (KBr, cm^{-1}) 3270, 1470, 1450, 1410, 1400, 1390, 1365, 1355, 1295, 1265, 1250, 1230, 1215, 1155, 1110, 1085, 1075, 1035, 995, 945, 900, 855; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88−7.83 (m, 2 H), 7.66−7.54 (m, 3 H), 6.65 (br s, 1 H), 4.78 (d, J = 0.8 Hz, 1 H), 4.43 (d, J = 0.8 Hz, 1 H), 3.33 (d, J = 14.1 Hz, 1 H), 3.20 (dd, J = 14.1, 2.0 Hz, 1 H), 2.72 (dd, J = 14.2, 4.4 Hz, 1 H), 2.60 (s, 3 H), 2.29−2.19 (m, 2 H), 1.85−1.67 (m, 1 H), 1.62−1.41 (m, 3 H), 1.26−1.15 (m, 1 H), 1.00 (s, 3 H), 0.88 (d, J = 6.6 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 159.5, 139.3, 133.0, 129.6 (2 C), 129.0 (2 C), 102.1, 77.2, 58.5, 50.7, 49.4, 39.4, 35.0, 32.4, 28.8, 21.9, 18.8, 16.1; MS *m/z* (M^+) calcd 333.1763, obsd 333.1766; $[\alpha]^{23}_D$ +7.4 (*c* 0.01, $CHCl_3$).

Anal. Calcd for $C_{19}H_{27}NO_2S$: C, 68.43; H, 8.16. Found: C, 68.35; H, 8.16.

(+)-(*S*)-*S*-[[(1*R*,2*S*,4*R*,5*R*)-2-Hydroxy-1,4-dimethyl-8-methylenebicyclo[3.2.1]oct-2-yl]methyl]-*N*-methyl-*S*-phenylsulfoximine (15): colorless oil; IR (neat, cm^{-1}) 3490, 1660, 1650, 1475, 1440, 1420, 1390, 1370, 1295, 1270, 1240, 1195, 1150, 1110, 1085, 1045, 1000, 975, 950, 890, 840, 780, 740, 690; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.85−7.82 (m, 2 H), 7.62−7.51 (m, 3 H), 5.97 (br s, 1 H), 4.76 (s, 1 H), 4.54 (s, 1 H), 3.48 (d, J = 4.9 Hz, 1 H), 3.29 (dd, J = 4.9, 1.5 Hz, 1 H), 2.75 (s, 3 H), 2.18−2.08 (m, 2 H), 1.90 (dd, J = 12.5, 3.7 Hz, 1 H), 1.48−1.40 (m, 2 H), 1.27−1.07 (m, 3 H), 1.05 (s, 3 H), 0.58 (d, J = 6.4 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 159.0, 140.3, 132.9, 129.4 (2 C), 128.9 (2 C), 102.3, 74.9, 59.9, 50.5, 49.1, 39.6, 34.7, 32.5, 29.2, 21.6, 18.4, 16.12; MS *m/z* (M^+) calcd 333.1763, obsd 333.1750; $[\alpha]^{23}_D$ +35.3 (*c* 0.01, $CHCl_3$).

Anal. Calcd for $C_{19}H_{27}NO_2S$: C, 68.43; H, 8.16. Found: C, 68.28; H, 8.17.

(+)-(*S*)-*S*-[[(1*R*,2*R*,4*R*,5*R*)-2-Hydroxy-1,4-dimethyl-8-methylenebicyclo[3.2.1]oct-2-yl]methyl]-*N*-methyl-*S*-phenylsulfoximine (16): white crystals, mp 131−131.5 °C (from petroleum ether at −20 °C); IR (film, cm^{-1}) 3260, 1660, 1440, 1375, 1340, 1230, 1170, 1150, 1110, 1080, 1055, 1025, 1000, 980, 950, 875, 860; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89−7.80 (m, 2 H), 7.66−7.25 (m, 3 H), 6.39 (br s, 1 H), 4.89 (s, 1 H), 4.61 (s, 1 H), 3.30 (d, J = 13.5 Hz, 1 H), 3.10 (d, J = 13.5

Hz, 1 H), 2.58 (s, 3 H), 2.42 (dd, J = 14.3, 4.6 Hz, 1 H), 2.35 (br d, J = 4.6 Hz, 1 H), 2.25−2.11 (m, 1 H), 1.59−1.39 (m, 4 H), 1.32−1.19 (m, 1 H), 0.98 (s, 3 H), 0.92 (d, J = 6.8 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 159.2, 139.2, 133.1, 129.6 (2 C), 129.0 (2 C), 101.8, 78.1, 61.6, 49.6, 49.2, 38.8, 35.0, 32.9, 28.8, 20.8, 18.9, 16.8; MS m/z (M^+ + H) calcd 334.1841, obsd 334.1859; $[\alpha]^{23}_D$ +54.8 (c 0.004, $CHCl_3$).

Anal. Calcd for $C_{19}H_{27}NO_2S$: C, 68.43; H, 8.16. Found: C, 68.66; H, 8.17.

(+)-(1*S*,4*S*,5*S*)-1,4-Dimethyl-8-methylenebicyclo[3.2.1]-octan-2-one ((+)-11). A solution of **14** (293 mg, 0.879 mmol) in toluene (50 mL) was deoxygenated for 30 min with argon and heated to reflux. After 12 h, the cooled solution was placed on silica gel and eluted with petroleum ether to remove toluene followed by 5% ethyl acetate in petroleum ether to give 125 mg (87%) of (+)-**11**, $[\alpha]^{23}_D$ +38.4 (c 0.01, $CHCl_3$).

(−)-(1*R*,4*R*,5*R*)-1,4-Dimethyl-8-methylenebicyclo[3.2.1]-octan-2-one ((−)-11). A. By Cleavage of 16. A solution of **16** (19 mg, 0.057 mmol) in toluene (3 mL) was heated as described above to give 8.7 mg (93%) of (−)-**11**, $[\alpha]^{23}_D$ −37.9 (c 0.01, $CHCl_3$).

B. By Cleavage of 15. Heating **15** as above gave the same levorotatory ketone as did **16** in 90% yield.

(−)-(1*R*,5*R*)-1,4-Dimethyl-8-methylenebicyclo[3.2.1]oct-3-en-2-one ((−)-10). A solution of (−)-**11** (32.8 mg, 0.2 mmol) in THF (4 mL) was treated with KHMDS (0.6 mL, 0.5 M in toluene, 0.3 mmol) at −78 °C under argon. After 30 min, solid *N*-(phenylseleno)phthalimide (60.4 mg, 0.2 mmol) was added. The resulting mixture was stirred at this temperature for 2 h before being allowed to warm slowly to rt and quenched with brine. The aqueous phase was extracted with ether, and the combined organic phases were washed with brine and dried. After solvent removal, the residue was purified by chromatography on silica gel (elution with 2.5% ethyl acetate in petroleum ether) to give 52 mg (81%) of selenide **17** as a yellow oil: IR (neat, cm^{-1}) 1710, 1660, 1575, 1475, 1445, 1435, 1370, 1325, 1300, 1290, 1270, 1250, 1160, 1110, 1070, 1050, 1025, 1000, 900; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48−7.44 (m, 2 H), 7.19−7.15 (m, 3 H), 4.81 (s, 1 H), 4.62 (s, 1 H), 3.48 (d, J = 11.3 Hz, 1 H), 2.61 (br s, 1 H), 1.95−1.55 (series of m, 5 H), 1.20 (s, 3 H), 1.18 (d, J = 6.6 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 205.7, 155.5, 134.7 (2 C), 129.4, 128.9 (2 C), 127.5, 104.0, 56.9, 56.8, 49.5, 43.9, 35.7, 21.2, 18.9, 16.5; MS m/z (M^+) calcd for 320.0679, obsd 320.0646.

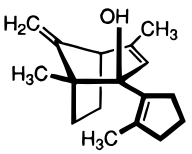
To a mixture of **17** (32 mg, 0.1 mmol) and pyridine (8.1 μL) in CH_2Cl_2 (1 mL) was added 34 mL of 30% H_2O_2 at 0 °C. This mixture was warmed to rt, stirred for 30 min, and poured into saturated $NaHCO_3$ solution. The aqueous phase was extracted with ether, and the combined organic phases were washed with brine, dried, and evaporated. Purification of the residue by chromatography on silica gel (elution with 5% ethyl acetate in petroleum ether) gave 13 mg (80%) of (−)-**10**, $[\alpha]^{23}_D$ −52.7 (c 0.01, $CHCl_3$).

(+)-(1*S*,5*S*)-1,4-Dimethyl-8-methylenebicyclo[3.2.1]oct-3-en-2-one ((+)-11). A solution of (+)-**11** (32.8 mg, 0.2 mmol) in THF (4 mL) was treated with KHMDS (0.6 mL, 0.5 M in toluene, 0.3 mmol) at −78 °C under argon. After 30 min, solid *N*-(phenylseleno)phthalimide (60.4 mg, 0.2 mmol) was added. The resulting mixture was stirred at this temperature for 2 h before being allowed to warm slowly to rt and quenched with brine. The aqueous phase was extracted with ether, and the combined organic phases were washed with brine and dried. After solvent removal, selenide **18** was dissolved in CH_2Cl_2 (2 mL), treated with pyridine (18 μL), and cooled to 0 °C prior to treatment with 70 μL of 30% H_2O_2. The reaction mixture was warmed to rt, stirred for 30 min, and poured into saturated $NaHCO_3$ solution. The aqueous phase was extracted with ether, and the combined organic phases were washed with brine prior to drying and solvent evaporation. Purification of the residue by chromatography on silica gel (elution with 5% ethyl acetate in petroleum ether) gave 24 mg (74% overall) of (+)-**11**, $[\alpha]^{23}_D$ +53.0 (c 0.01, $CHCl_3$).

(1*R*,2*R*,5*R*)-1,4-Dimethyl-2-(2-methyl-1-cyclopenten-1-yl)-8-methylenebicyclo[3.2.1]oct-3-en-2-ol (25). A. Use of *sec*-Butyllithium in THF. A solution of **22** (120.8 mg, 0.75 mmol) in THF (3 mL) was treated with *sec*-butyllithium (538.5 μL of 1.3 M in cyclohexane, 0.70 mmol) at −20 °C under argon. The reaction mixture was stirred for 40 min before **10** (81.1 mg, 0.5 mmol) dissolved in THF (1 mL) was introduced. The mixture was stirred for 1 h at −20 °C and for 1 h at rt, cooled to −20 °C, and quenched with brine. The aqueous phase was extracted with ether, and the combined organic phases were washed with saturated $NaHCO_3$ solution and brine and then dried and evaporated. Chromatography of the residue on silica gel (elution with 0.5% ethyl acetate in petroleum ether) gave 70 mg (57%) of **25**. Starting enone **10** (26 mg, 12%) was recovered by increasing the eluant polarity (5% ethyl acetate in petroleum ether). The yield of alcohol **25** based on recovery of starting enone was 65%: IR (neat, cm^{-1}) 3490, 1680, 1440, 1375, 1150, 1030, 990, 885; ^{1}H NMR (300 MHz, C_6D_6) δ 4.84 (d, J = 1.1 Hz, 1 H), 4.69 (d, J = 1.0 Hz, 1 H), 4.56 (d, J = 1.0 Hz, 1 H), 2.65−2.35 (m, 4 H), 2.35−2.20 (m, 2 H), 1.97−1.82 (m, 3 H), 1.76−1.20 (series of m, 6 H), 1.54 (d, J = 1.5 Hz, 3 H), 1.25 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 158.6, 139.3, 138.1, 134.8, 127.2, 100.6, 82.9, 50.7, 49.6, 41.5, 38.8, 32.1, 29.8, 22.6, 21.3, 18.5, 16.9; MS m/z (M^+) calcd 244.1827, obsd 244.1860.

Anal. Calcd for $C_{17}H_{24}O$: C, 83.54; H, 9.91. Found: C, 83.35; H, 9.87.

B. Use of *tert*-Butyllithium in Ether. A solution of **22** (76 mg, 0.46 mmol) in anhydrous ether (1.5 mL) was treated with *tert*-butyllithium (0.9 mL of 1.7 M in pentane, 1.53 mmol) at −78 °C and stirred for 1 h. The reaction mixture was allowed to warm to 0 °C for 15 min, at which time a solution of **10** (72 mg, 0.45 mmol) in ether (4.1 mL) was introduced. The resulting mixture was stirred at 0 °C for 2 h and warmed to rt for 2 h before being quenched with brine (2 mL). Workup in the predescribed manner gave 54 mg (50%) of a 6.9:1 mixture of **25** and **i**, together with 26 mg (36%) of recovered **10**.



i

For **i**: colorless oil; IR (neat, cm^{-1}) 3472, 1666, 1625, 1455, 1377, 1347, 1173, 1070, 894, 694; ^{1}H NMR (300 MHz, C_6D_6) δ 5.19 (d, J = 1.7 Hz, 1 H), 4.68 (s, 1 H), 4.62 (s, 1 H), 2.56 (d, J = 7.7 Hz, 1 H), 2.47−2.30 (m, 1 H), 2.28 (m, 1 H), 2.17 (t, J = 7.2 Hz, 1 H), 1.79−1.66 (m, 4 H), 1.56 (s, 3 H), 1.64−1.40 (m, 2 H), 1.35 (s, 3 H), 1.37−1.22 (m, 2 H), 1.05 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 160.0, 146.2, 136.2, 134.9, 130.5, 100.3, 74.9, 54.7, 46.0, 38.7, 38.1, 38.0, 24.4, 23.8, 22.7, 18.0, 14.9; MS m/z (M^+) calcd 244.1827, obsd 244.1843.

Anal. Calcd for $C_{17}H_{24}O$: C, 83.54; H, 9.91. Found: C, 83.55; H, 9.95.

(3a*S*,6a*S*,10a*S*)-1,3,3a,6a,7,8,10,10a-Octahydro-6,9,10a-trimethyldicyclopenta[*a*,*d*]cycloocten-4(2*H*)-one (26). A mixture of 18-crown-6 (21.7 mg, 0.082 mmol), alcohol **25** (16.7 mg, 0.0683 mmol), and dry THF (2 mL) was treated with potassium hexamethyldisilazide (0.18 mL of 0.5 M solution in toluene, 0.26 mmol) at 0 °C under argon. The reaction mixture was allowed to warm to rt and stirred for 30 min before being cooled to 0 °C and quenched with absolute ethanol (0.5 mL). The mixture was filtered through neutral alumina (the filter cake was washed with ether), the solvent was removed, and the residue was purified chromatographically on silica gel (elution with 2.5% ethyl acetate in petroleum ether) to give 10 mg (61%) of **26** as a colorless oil: ^{1}H NMR (300 MHz, C_6D_6) δ 6.23 (s, 1 H), 3.97 (br s, 1 H), 2.87 (m, 1 H), 2.65−2.40 (m, 1 H), 2.30−1.80 (m, 3 H), 1.80−1.55 (m, 3 H), 1.53 (s, 3 H), 1.45 (s, 3 H), 1.40−1.00 (m, 2 H), 0.98−0.78 (m, 3 H), 0.74 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 201.5, 152.0, 134.3, 132.6, 132.5, 58.7, 54.9, 50.7, 39.4, 37.5, 34.7, 26.0, 25.8, 25.2, 24.0, 21.6, 14.5; MS m/z (M − CH_3)$^+$ calcd 229.1592, obsd 229.1644.

(1*R*,2*R*,4*R*,5*R*)-1,4-Dimethyl-2-(2-methyl-1-cyclopenten-1-yl)-8-methylenebicyclo[3.2.1]octan-2-ol (27). A solution

of **22** (121 mg, 0.75 mmol) in THF (3 mL) was treated with *tert*-butyllithium (0.97 mL of 1.7 M in pentane, 1.65 mmol) at −78 °C under argon. After 40 min of stirring, a solution of **11** (82 mg, 0.5 mmol) in THF (1 mL) was introduced via syringe. The reaction mixture was stirred for 30 min at −78 °C before being warmed to rt. After an additional hour of stirring, the reaction mixture was quenched with brine, the aqueous phase was extracted with ether, and the combined organic phases were washed with brine, dried, and evaporated. After solvent removal, chromatography of the residue on silica gel (elution with 3% ethyl acetate in petroleum ether) gave 69 mg (56%) of **27** as a colorless oil and 32 mg (39%) of recovered **11**.

For **27**: IR (neat, cm^{-1}) 3540, 1650, 1470, 1450, 1370, 1330, 1320, 1280, 1040, 1000, 890, 690; ^1H NMR (300 MHz, $CDCl_3$) δ 4.97 (d, J = 0.9 Hz, 1 H), 4.70 (d, J = 0.9 Hz, 1 H), 2.60−2.40 (m, 2 H), 2.36−2.25 (m, 3 H), 2.19 (s, 1 H), 2.05−1.94 (m, 2 H), 1.93 (dd, J = 0.9, 0.8 Hz, 3 H), 1.75−1.27 (series of m, 7 H), 1.04 (s, 3 H), 0.88 (d, J = 6.66 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 161.6, 136.4, 134.7, 102.7, 79.8, 52.2, 49.3, 40.9, 40.3, 38.3, 35.2, 33.4, 22.4, 20.6, 18.9, 17.7, 17.2; MS m/z (M^+) calcd 246.1983, obsd 246.2001.

Anal. Calcd for $C_{17}H_{26}O$: C, 82.87; H, 10.64. Found: C, 82.64; H, 10.72.

[[(5*S*,7*S*,7a*S*)-2,4,5,6,7,7a-Hexahydro-3,7-dimethyl-5-(2-methyl-1-cyclopenten-1-yl)inden-5-yl]oxy]trimethylsilane (28). A solution of 18-crown-6 (63.4 mg, 0.24 mmol) and **27** (49.3 mg, 0.2 mmol) in THF (3 mL) was treated with potassium hexamethyldisilazide (0.25 mL of 0.5 M in toluene, 0.26 mmol) via syringe at 0 °C under argon. The reaction mixture was allowed to warm to rt, stirred for 30 min, and cooled to −78 °C prior to being quenched with freshly distilled chlorotrimethylsilane (76.2 mL, 0.6 mmol). After 30 min of stirring, the mixture was warmed to rt and poured into a stirred mixture of ether and saturated $NaHCO_3$ solution. The aqueous phase was extracted with ether, and the combined organic phases were washed with saturated $NaHCO_3$ solution and brine, dried, and evaporated. The crude product was filtered through Florisil (elution with 0.5% ether in petroleum ether) to give 51 mg (81%) of silyl ether **28** as a colorless oil: IR (neat, cm^{-1}) 1440, 1250, 1075, 1050, 1035, 840, 755; ^1H NMR (300 MHz, C_6D_6) δ 3.01 (dd, J = 13.4, 1.9 Hz, 1 H), 2.77 (br s, 1 H), 2.65−1.92 (series of m, 10 H), 1.91 (dd, J = 1.0, 0.9 Hz, 3 H), 1.85−1.45 (series of m, 4 H), 1.57 (br s, 3 H), 0.75 (d, J = 7.4 Hz, 3 H), 0.18 (s, 9 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 140.6, 136.0, 133.9, 130.5, 76.0, 50.4, 47.0, 40.7, 40.2, 38.4, 35.1, 31.8, 24.1, 22.5, 16.8, 14.7, 14.0, 2.4 (3 C); MS m/z (M^+) calcd 318.2379, obsd 318.2435.

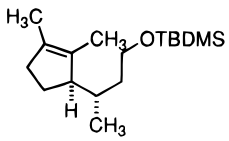
Anal. Calcd for $C_{20}H_{34}OSi$: C, 75.40; H, 10.76. Found: C, 75.42; H, 10.80.

(7*S*,7a*S*)-2,6,7,7a-Tetrahydro-3,7-dimethyl-5-(2-methyl-1-cyclopenten-1-yl)indene (30). When silyl ether **28** was treated with silica gel, triene **30** was obtained as a colorless oil contaminated with a trace of isomer **31**. For the major triene **30**: ^1H NMR (300 MHz, C_6D_6) δ 6.43 (br s, 1 H), 3.05−2.80 (m, 1 H), 2.70−2.50 (m, 3 H), 2.50−2.00 (series of m, 6 H), 1.88−1.50 (series of m, 4 H), 1.86 (s, 3 H), 1.78 (br s, 3 H), 0.94 (d, J = 6.9 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 137.6, 134.1, 133.9, 133.3, 132.8, 119.3, 48.6, 40.7, 38.3, 38.1, 36.5, 29.6, 26.0, 22.2, 16.2, 13.7, 13.3; MS m/z (M^+) calcd 228.1878, obsd 228.1843.

(5*R*)-5-[(1*S*)-3-(*tert*-Butyldimethylsiloxy)-1-methylpropyl]-1-hydroxy-2-methylcyclopentenyl Trifluoromethanesulfonate (42). To a solution of L-Selectride (4.25 mL of 1 M solution, 4.25 mmol) in THF (50 mL) was added a solution of **41** (1.00 g, 3.54 mmol) in THF (5 mL) via cannula at −78 °C under argon. After 30 min, solid *N*-phenyltriflimide (1.52 g, 4.25 mmol) was added and the mixture was allowed to warm to rt. After 16 h, the mixture was poured into cold saturated $NaHCO_3$ solution, the aqueous phase was extracted with petroleum ether, and the combined organic phases were washed with saturated $NaHCO_3$ solution and brine prior to drying and solvent removal. Chromatography of the residue on silica gel (elution with 1.25% ethyl acetate in petroleum ether) gave 1.21 g (82%) of **42** as a colorless oil: IR (neat, cm^{-1}) 1460, 1420, 1380, 1250, 1210, 1145, 1105, 1055, 1000, 940, 900, 850, 780; ^1H NMR (300 MHz, $CDCl_3$) δ 3.63 (m, 2 H), 3.01 (br s, 1 H), 2.35−2.17 (m, 2 H), 2.03−1.88 (m, 2 H), 1.73 (s, 3 H), 1.72−1.63 (m, 1 H), 1.56−1.32 (m, 2 H), 0.89 (s, 9 H), 0.78 (d, J = 6.9 Hz, 3 H), 0.04 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 144.5, 129.5, 118.5 (q, J = 319.9 Hz, CF_3), 61.2, 47.6, 37.7, 32.2, 29.8, 25.9 (3 C), 20.5, 18.3, 13.7, 12.3, −5.4, −5.5; MS m/z ($M^+ - C_4H_9$) calcd 359.0961, obsd 359.0973.

Anal. Calcd for $C_{17}H_{31}F_3O_4SSi$: C, 49.02; H, 7.50. Found: C, 48.67; H, 7.38.

Sequential Palladium-Catalyzed Stannylation and Halogenation of Vinyl Triflate 42. A mixture of **42** (1.50 g, 3.6 mmol), lithium chloride (916 mg, 21.6 mmol), hexamethylditin (1.31 g, 4.0 mmol), and $Pd(Ph_3P)_4$ (416 mg, 0.36 mmol) in THF (60 mL) was deoxygenated for 30 min with argon and heated gently at reflux for 16 h under argon. After cooling, petroleum ether was added, followed by saturated $NaHCO_3$ solution. The aqueous layer was extracted with petroleum ether, and the combined organic phases were washed with saturated $NaHCO_3$ solution and brine prior to drying and solvent removal. The product was taken up in petroleum ether and filtered through silica gel (pretreated with 20% triethylamine in petroleum ether; elution with 1% triethylamine in petroleum ether) to give crude vinyltin **43** (1.56 g, which contained a trace amount of methylated compound **ii** and a small amount of hexamethylditin) as a colorless oil. This material was dissolved in CH_2Cl_2 (50 mL) and treated with bromine (1 M solution in dichloromethane) at −78 °C until the reaction mixture turned slightly yellow. After 5 min, pentane (30 mL) was added, and the mixture was poured into saturated Na_2SO_3 solution. The aqueous phase was extracted with petroleum ether, and the combined organic phases were washed with 1.5% aqueous NH_4OH solution prior to drying and solvent evaporation. The crude product was purified by column chromatography on silica gel (elution with petroleum ether) to give 456 mg (37% overall) of vinyl bromide **44** as a colorless oil; 180 mg (12%) of triflate **42** was recovered. The overall yield of **44** based on the recovered starting material was 43%.



ii

***tert*-Butyldimethyl[(3*S*)-3-[(1*R*)-3-methyl-2-(trimethylstannyl)-2-cyclopenten-1-yl]butoxy]silane (43):** IR (neat, cm^{-1}) 1615, 1470, 1460, 1440, 1385, 1370, 1360, 1190, 1110, 1005, 980, 900, 835, 810, 775; ^1H NMR (300 MHz, C_6D_6) δ 3.68−3.62 (m, 2 H), 2.99 (br s, 1 H), 2.28−2.22 (m, 2 H), 2.10−1.90 (m, 1 H), 1.80−1.30 (series of m, 4 H), 1.74 (dd, J = 0.8, 0.9 Hz, 3 H), 1.00 (s, 9 H), 0.74 (d, J = 6.9 Hz, 3 H), 0.26 (s, 9 H), 0.09 (s, 6 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 149.5, 140.2, 61.6, 57.1, 39.8, 39.7, 33.0, 26.2 (3 C), 24.1, 18.5, 18.4, 13.5, −5.1, −5.2, −8.8 (3 C); MS m/z (M^+) calcd for $C_{19}H_{40}OSi^{120}Sn$ 432.1870, obsd 432.1634.

***tert*-Butyl[(3*S*)-3-[(1*R*)-2,3-dimethyl-2-cyclopenten-1-yl]butoxy]dimethylsilane (ii):** ^1H NMR (300 MHz, $CDCl_3$) δ 3.70−3.60 (m, 2 H), 2.59 (br s, 1 H), 2.18 (m, 2 H), 2.00−1.85 (m, 1 H), 1.80−1.64 (m, 1 H), 1.61 (br s, 3 H), 1.52 (br s, 3 H), 1.60−1.40 (m, 3 H), 0.90 (s, 9 H), 0.63 (d, J = 6.8 Hz, 3 H), 0.60 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 132.4, 131.7, 61.6, 53.6, 38.6, 37.3, 29.8, 25.8 (3 C), 21.6, 18.2, 13.7, 13.2, 11.8, −5.4 (2 C); MS m/z ($M^+ - C_4H_9$) calcd 225.1674, obsd 225.1653.

***tert*-Butyldimethyl[(3*S*)-3-[(1*R*)-2-bromo-3-methyl-2-cyclopenten-1-yl]butoxy]silane (44):** IR (neat, cm^{-1}) 1655, 1465, 1460, 1435, 1375, 1355, 1250, 1100, 1000, 985, 935, 900, 835, 810, 775; ^1H NMR (300 MHz, C_6D_6) δ 3.71−3.57 (m, 2 H), 2.90 (br s, 1 H), 2.41−2.31 (m, 1 H), 2.04−1.84 (m, 2 H), 1.65 (dd, J = 0.9, 1.0 Hz, 3 H), 1.61−1.40 (m, 4 H), 1.06 (s, 9 H), 0.80 (d, J = 6.9 Hz, 3 H), 0.14 (s, 6 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 137.3, 121.3, 61.5, 54.2, 38.3, 35.7, 30.7, 26.2 (3 C), 21.7, 18.5, 15.7, 13.3, −5.2, −5.2; MS m/z ($M^+ - CH_3$) calcd 331.1093, obsd 331.1093, ($M^+ - C_4H_9$) calcd 289.0623, obsd 289.0619.

***tert*-Butyldimethyl[(3*S*)-3-[(1*R*)-2-iodo-3-methyl-2-cyclopenten-1-yl]butoxy]silane (45).** To a solution of **43** (1 equiv) in CH_2Cl_2 (50 mL/g vinyltin) was added iodine crystals (1.1 equiv) at rt. After 15 min, the mixture was diluted with pentane and poured into saturated $NaHSO_3$ solution. The organic phase was washed with 1.5% aqueous NH_4OH solution, dried, and freed of solvent. The crude product was purified by column chromatography on silica gel (elution with 1% triethylamine in petroleum ether) to give vinyl iodide **45** as a colorless oil: IR (neat, cm^{-1}) 1640, 1470, 1460, 1430, 1375, 1250, 1100, 1005, 985, 940, 900, 835, 810, 775; ^1H NMR (300 MHz, C_6D_6) δ 3.65 (m, 2 H), 2.87 (br s, 1 H), 2.36 (m, 1 H), 2.01 (m, 2 H), 1.68 (t, J = 0.8 Hz, 3 H), 1.66−1.41 (m, 4 H), 1.08 (s, 9 H), 0.75 (d, J = 6.8 Hz, 3 H), 0.15 (s, 6 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 144.1, 100.1, 61.5, 56.8, 38.4, 36.4, 31.7, 29.2 (3 C), 22.3, 19.1, 18.5, 13.0, −5.1, −5.2; MS *m*/*z* ($M^+ - CH_3$) calcd 379.0913, obsd 379.0962.

(1*S*,2*R*,5*S*)-2-[(5*R*)-5-[(1*S*)-3-(*tert*-Butyldimethylsiloxy)-1-methylpropyl]-2-methyl-1-cyclopenten-1-yl]-1,4-dimethyl-8-methylenebicyclo[3.2.1]oct-3-en-2-ol (46). Anhydrous cerium trichloride (160 mg, 0.648 mmol) was further dried at 140 °C under high vacuum for 16 h and then cooled under argon. To this solid was added anhydrous THF (2 mL), and the suspension was stirred for 3 h before being cooled to −78 °C and treated with several drops of *tert*-butyllithium until a slightly yellow color persisted. A solution of **44** (75 mg, 0.216 mmol) in THF (2 mL) was treated with *tert*-butyllithium (0.28 mL of 1.7 M solution in pentane, 0.475 mmol) at −78 °C under argon. After 2 h of stirring, this solution was transferred to the cerium chloride suspension via cannula at −78 °C. The resulting mixture was stirred for 1 h at this temperature before a solution of (±)-**10** (70 mg, 0.216 mmol) in THF (2 mL) was introduced via cannula. After being stirred for 8 h at −78 °C and 4 h at −20 °C, the mixture was slowly warmed to rt and quenched with brine at 0 °C. The aqueous phase was extracted with ether, and the combined organic phases were dried and evaporated. Purification of the residue by chromatography on silica gel (elution with 2.5% ethyl acetate in petroleum ether) gave 25 mg (27%) of **46** as a colorless oil and 40 mg of recovered starting enone **10**.

For **46**: IR (neat, cm^{-1}) 3490, 1660, 1460, 1440, 1375, 1260, 1095, 1020, 880, 840, 780; ^1H NMR (300 MHz, $CDCl_3$) δ 5.04 (d, J = 1.2 Hz, 1 H), 4.68 (d, J = 0.8 Hz, 1 H), 4.54 (d, J = 0.8 Hz, 1 H), 3.50 (dd, J = 7.6, 7.7 Hz, 2 H), 2.70 (br d, J = 8.5 Hz, 1 H), 2.59 (br d, J = 5.1 Hz, 1 H), 2.43−2.27 (m, 2 H), 2.08−1.98 (m, 1 H), 1.96 (s, 3 H), 1.93−1.80 (m, 1 H), 1.71 (d, J = 1.4 Hz, 3 H), 1.69−1.50 (m, 4 H), 1.62 (s, 1 H), 1.42−1.30 (m, 3 H), 1.14 (s, 3 H), 0.90 (s, 9 H), 0.68 (d, J = 7.0 Hz, 3 H), 0.04 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 158.3, 138.7, 138.2, 137.7, 126.6, 100.1, 83.6, 62.7, 54.3, 50.9, 49.3, 41.0, 39.7, 33.3, 32.1, 29.7, 26.1 (3 C), 23.5, 21.3, 18.4, 18.2, 17.4, 13.7, −5.2 (2 C); MS *m*/*z* (M^+) calcd 430.3267, obsd 430.3255.

Attempted Base-Promoted Rearrangement of 46. A solution of **46** (11 mg, 0.0255 mmol) and 18-crown-6 (13.5 mg, 0.051 mmol) in THF (3 mL) was treated with KHMDS (0.102 mL, 0.5 M in toluene). After 2 h of stirring at rt, the mixture was quenched with brine and the aqueous phase was extracted with ether. The combined organic phases were dried, solvent was removed, and the residue was subjected to chromatography on silica gel (elution first with 2.5% ethyl acetate in petroleum ether followed by 20% ethyl acetate in petroleum ether) to give 6 mg of recovered **46** and 2 mg of **47**, spectroscopically identical to the product obtained from fluoride-induced desilylation (see below).

(1*S*,2*R*,5*S*)-2-[(5*R*)-5-[(1*S*)-3-Hydroxy-1-methylpropyl]-2-methyl-1-cyclopenten-1-yl]-1,4-dimethyl-8-methylenebicyclo[3.2.1]oct-3-en-2-ol (47). A solution of **46** (2 mg, 0.0046 mmol) in THF (1 mL) was treated with tetrabutylammonium fluoride (0.014 mL, 1 M solution in THF, 0.014 mmol). After 16 h of stirring at rt, the mixture was diluted with ether and poured into ice water, the aqueous phase was extracted with ether, and the combined organic phases were washed with brine prior to drying. After solvent removal, the residue was purified by chromatography on silica gel (elution with 30% ethyl acetate in petroleum ether) to give 1.2 mg (82%) of **47**: ^1H NMR (300 MHz, $CDCl_3$) δ 5.06 (br s, 1 H), 4.71 (s, 1 H), 3.54 (ddd, J = 7.0, 2.0, 2.0 Hz, 2 H), 2.62 (br d, J = 5.3 Hz, 1 H), 2.77 (br d, J = 8.7 Hz, 1 H), 2.45−2.25 (m, 3 H), 2.10−1.90 (m, 2 H), 1.97 (s, 3 H),1.73 (d, J = 1.4 Hz, 3 H), 1.72−1.25 (m, 9 H), 1.15 (s, 3 H), 0.72 (d, J = 7.0 Hz, 3 H); MS *m*/*z* (M^+) calcd 316.2402, obsd 316.2415.

***tert*-Butyldimethyl[(3*S*)-3-[(1*R*)-3-methyl-2-[(1*S*,5*S*)-1-methyl-4,8-dimethylenebicyclo[3.2.1]oct-2-en-2-yl]-2-cyclopenten-1-yl]butoxy]silane (48).** A solution of **46** (6 mg, 0.014 mmol) in C_6D_6 was sealed in an NMR tube (nonbase washed) and heated at 180 °C for 20 h. The NMR spectrum indicated that clean dehydration had occurred. Purification was achieved by filtration through silica gel (elution with 2% ethyl acetate in petroleum ether) to give 5 mg (87%) of pure **48**: IR (neat, cm^{-1}) 1620, 1465, 1460, 1435, 1400, 1375, 1365, 1255, 1100, 1005, 985, 890, 860, 840, 775, 735; ^1H NMR (300 MHz, $CDCl_3$) δ 5.57 (s, 1 H), 4.68 (s, 1 H), 4.63 (d, J = 1.5 Hz, 1 H), 4.53 (s, 1 H), 4.48 (d, J = 1.5 Hz, 1 H), 3.62 (m, 2 H), 3.22 (d, J = 7.0 Hz, 1 H), 2.93 (br s, 1 H), 2.26 (m, 2 H), 2.15−1.98 (m, 2 H), 1.85−1.30 (series of m, 7 H), 1.67 (br s, 3 H), 1.20 (s, 3 H), 0.88 (s, 9 H), 0.56 (d, J = 6.7 Hz, 3 H), 0.03 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 159.7, 153.6, 139.1, 137.1, 127.5, 100.6, 104.4, 97.5, 62.0, 51.3, 45.5, 41.5, 39.2, 37.5, 31.1, 30.5, 26.0 (3 C), 22.5, 19.1, 18.3, 15.4, 13.8, 5.2, −5.3 (2 C); MS *m*/*z* (M^+) calcd 412.3161, obsd 412.3158.

Coupling of (+)-Ketone 44 to (+)-10. Cerium chloride heptahydrate (537 mg, 1.44 mmol) was dried at 140 °C under high vacuum for 16 h and then cooled under argon. To this solid was added THF (5 mL), and the suspension was stirred for 3 h before being cooled to −78 °C and treated with several drops of *tert*-butyllithium until a pale yellow color persisted. A solution of **44** (250 mg, 0.72 mmol) in THF (3 mL) was treated with *tert*-butyllithium (0.932 mL of 1.7 M solution in pentane, 1.58 mmol) at −78 °C under argon. After 2 h, the solution was transferred to the cerium chloride suspension via cannula at −78 °C. The resulting mixture was stirred for 1 h at this temperature before introduction of a solution of (+)-**10** (118 mg, 0.72 mmol) in THF (2 mL) via cannula. After 3 h at −78 °C, the mixture was slowly warmed to rt and then quenched with brine at 0 °C. The aqueous phase was extracted with ether, and the combined organic phases were dried and evaporated. Purification of the residue by chromatography on silica gel (elution with 1% ethyl acetate in petroleum ether) gave 75 mg (17%) of **49** as a colorless oil followed by 8 mg (2%) of the more polar **50** and 60 mg (51%) of **10**. The combined yield of adducts was 39%, based on the recovered enone.

(1*S*,2*R*,4*S*,5*S*)-2-[(5*R*)-5-[(1*S*)-3-(*tert*-Butyldimethylsiloxy)-1-methylpropyl]-2-methyl-1-cyclopenten-1-yl]-1,4-dimethyl-8-methylenebicyclo[3.2.1]octan-2-ol (49): IR (neat, cm^{-1}) 3540, 1650, 1465, 1460, 1405, 1370, 1355, 1340, 1310, 1275, 1250, 1220, 1090, 1000, 990, 890, 830, 810, 775, 660; ^1H NMR (300 MHz, $CDCl_3$) δ 4.96 (s, 1 H), 4.68 (s, 1 H), 3.64 (dd, J = 7.5, 7.1 Hz, 2 H), 2.82 (m, 1 H), 2.46−2.37 (m, 2 H), 2.26 (m, 1 H), 2.16−1.78 (series of m, 4 H), 1.97 (s, 3 H), 1.68−1.41 (series of m, 7 H), 1.30−1.18 (m, 2 H), 1.02 (s, 3 H), 0.89 (s, 9 H), 0.88 (d, J = 6.7 Hz, 3 H), 0.71 (d, J = 7.1 Hz, 3 H), 0.05 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 162.0, 139.9, 133.5, 102.8, 79.6, 62.6, 54.7, 54.4, 49.1, 42.6, 40.1, 40.0, 35.7, 33.7, 32.3, 26.0 (3 C), 22.7, 20.3, 18.9, 18.7, 18.4, 17.5, 14.2, −5.2 (2 C); MS *m*/*z* (M^+) calcd 432.3424, obsd 432.3407; $[\alpha]^{23}_D$ +9.0 (*c* 0.007, $CHCl_3$).

(1*S*,2*R*,4*S*,5*S*)-2-[(5*S*)-5-[(1*R*)-3-(*tert*-Butyldimethylsiloxy)-1-methylpropyl]-2-methyl-1-cyclopenten-1-yl]-1,4-dimethyl-8-methylenebicyclo[3.2.1]octan-2-ol (50): IR (neat, cm^{-1}) 3540, 1650, 1470, 1460, 1385, 1375, 1360, 1320, 1255, 1100, 1035, 1000, 980, 890, 830, 810, 780; ^1H NMR (300 MHz, $CDCl_3$) δ 4.97 (s, 1 H), 4.02 (s, 1 H), 3.68 (m, 2 H), 2.79 (br d, J = 6.4 Hz, 1 H), 2.36−2.23 (m, 2 H), 2.19−1.86 (series of m, 4 H), 1.97 (s, 3 H), 1.79−1.66 (m, 2 H), 1.64−1.44 (m, 6 H), 1.45−1.11 (m, 2 H), 1.04 (s, 3 H), 0.91 (s, 9 H), 0.88 (d, J = 6.7 Hz, 3 H), 0.76 (d, J = 6.9 Hz, 3 H), 0.06 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 162.0, 139.6, 136.4, 102.7, 80.4, 61.6, 54.0, 52.9, 49.3, 41.5, 40.6, 39.9, 35.6, 33.4, 33.2, 26.1 (3C), 24.3, 20.7, 19.0, 18.4, 18.0, 17.8, 13.4, −5.3 (2 C); MS *m*/*z* (M^+) calcd 432.3424, obsd 432.3425; $[\alpha]^{23}_D$ −73.8 (*c* 0.002, $CHCl_3$).

(5*S*,7*S*,7a*S*)-2,4,5,6,7,7a-Hexahydro-5-[(5*R*)-5-[(1*S*)-3-hydroxy-1-methylpropyl]-2-methyl-1-cyclopenten-1-yl]-3,7-dimethylinden-5-ol (52). A solution of alcohol **49** (29 mg, 0.067 mmol) and 18-crown-6 (53 mg, 0.201 mmol) in THF (5 mL) was treated with KHMDS (0.402 mL, 0.5 M in toluene, 0.201 mmol) at 0 °C. After 30 min, the mixture was quenched with brine, the aqueous phase was extracted with ether, and the combined organic phases were dried and evaporated. The residue was filtered through silica gel (elution with 30% ethyl acetate in petroleum ether) to give a mixture of **51a**, **51b**, and **52**, which was not separated but dissolved directly in THF (10 mL) and treated with tetrabutylammonium fluoride (0.70 mL, 1 M in THF, 0.7 mmol). After being stirring for 2 h at rt, the mixture was diluted with ether and poured in ice water, the aqueous phase was extracted with ether, and the combined organic phases were washed with brine and dried. After solvent removal, purification of the residue by chromatography on silica gel (elution with 25% ethyl acetate in petroleum ether) gave 18 mg (84% overall) of **52** as white crystals, mp 80−81 °C (from ether−petroleum ether): IR (CCl_4, cm^{-1}) 3620, 3400, 1455, 1440, 1380, 1090, 1065, 1040; ^1H NMR (300 MHz, C_6D_6) δ 3.50 (m, 2 H), 2.94 (br s, 1 H), 2.90 (br s, 1 H), 2.87 (br s, 1 H), 2.45−2.05 (series of m, 8 H), 1.92−1.45 (series of m, 9 H), 1.82 (br s, 3 H), 1.64 (br s, 3 H), 0.92 (d, J = 7.2 Hz, 3 H), 0.82 (d, J = 6.9 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 145.4, 134.9, 133.5, 131.5, 74.4, 60.7, 50.9, 47.9, 44.2, 40.7, 39.5, 39.3, 37.6, 32.3, 27.9, 26.1, 23.1, 17.1, 16.1, 14.3, 14.0; MS m/z ($M^+ - H_2O$) calcd 300.2453, obsd 300.2448; $[\alpha]^{23}_D$ +26.1 (c 0.01, CCl_4).

[[(5*S*,7*S*,7a*S*)-5-[(5*R*)-5-[(1*S*)-3-(*tert*-Butyldimethylsiloxy)-1-methylpropyl]-2-methyl-1-cyclopenten-1-yl]-2,4,5,6,7,7a-hexahydro-3,7-dimethylinden-5-yl]oxy]trimethylsilane (51a): IR (neat, cm^{-1}) 1460, 1375, 1360, 1250, 1090, 1040, 1020, 980, 940, 900, 840, 775, 750; ^1H NMR (300 MHz, C_6D_6) δ 3.69 (m, 2 H), 3.06 (d, J = 15.0 Hz, 1 H), 2.90 (m, 1 H), 2.81 (br d, J = 8.0 Hz, 1 H), 2.60 (br d, J = 15.0 Hz, 1 H), 2.40−1.93 (series of m, 6 H), 1.91 (br s, 3 H), 1.89−1.40 (series of m, 8 H), 1.60 (br s, 3 H), 1.00 (s, 9 H), 0.91 (d, J = 7.0 Hz, 3 H), 0.80 (d, J = 7.0 Hz, 3 H), 0.20 (s, 9 H), 0.10 (s, 6 H); MS m/z ($M^+ - HOSiC_3H_9$) calcd 414.3318, obsd 414.3316.

(5*S*,7*S*,7a*S*)-2,4,5,6,7,7a-Hexahydro-5-[(5*R*)-5-[(1*S*)-3-(*tert*-butyl-dimethylsiloxy)-1-methylpropyl]-2-methyl-1-cyclopenten-1-yl]-3,7-dimethylinden-5-ol (51b): IR (neat, cm^{-1}) 3620, 3450, 1650, 1440, 1375, 1360, 1255, 1100, 1010, 840, 775; ^1H NMR (300 MHz, C_6D_6) δ 3.67 (m, 2 H), 2.99 (br d, J = 15.5 Hz, 1 H), 2.92 (br d, J = 8.0 Hz, 2 H), 2.40−2.01 (series of m, 6 H), 1.98−1.85 (m, 1 H), 1.82 (br s, 3 H), 1.81−1.40 (series of m, 9 H), 1.61 (br s, 3 H), 1.00 (s, 9 H), 0.87 (d, J = 6.9 Hz, 3 H), 0.79 (d, J = 6.9 Hz, 3 H), 0.10 (s, 6 H); MS m/z ($M^+ - H_2O$) calcd 414.3318, obsd 414.3312.

(5*S*,7*S*,7a*S*)-2,4,5,6,7,7a-Hexahydro-5-[(5*S*)-5-[(1*R*)-3-hydroxy-1-methylpropyl]-2-methyl-1-cyclopenten-1-yl]-3,7-dimethylinden-5-ol (54). Adaptation of the predescribed procedure to the rearrangement of **50** gave a mixture of **53**, **53b**, and **54**, which was directly subjected to desilylation conditions. Diol **54** was obtained in 79% overall yield.

For **54**: white crystals, mp 110−111 °C (petroleum ether at −20 °C); IR (CCl_4, cm^{-1}) 3620, 3400, 1460, 1435, 1375, 1090, 1060, 1015, 960; ^1H NMR (300 MHz, C_6D_6) δ 3.71−3.51 (m, 2 H), 3.09 (br d, J = 9.0 Hz, 1 H), 2.98 (m, 1H), 2.86 (br d, J = 15.3 Hz, 1 H), 2.40−2.05 (series of m, 8 H), 1.90−1.25 (series of m, 9 H), 1.68 (br s, 3 H), 1.56 (br s, 3 H), 0.89 (d, J = 7.1 Hz, 3 H), 0.82 (d, J = 7.0 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 145.4, 135.4, 131.6, 131.4, 75.1, 60.6, 50.6, 47.1, 43.8, 41.2, 39.3, 38.9, 37.4, 32.1, 27.5, 26.4, 22.6, 17.7, 15.8, 14.2, 14.0; MS m/z ($M^+ - H_2O$) calcd 300.2453, obsd 300.2447; $[\alpha]^{23}_D$ +7.0 (c 0.003, CCl_4).

[[(5*S*,7*S*,7a*S*)-5-[(5*S*)-5-[(1*R*)-3-(*tert*-Butyldimethylsiloxy)-1-methylpropyl]-2-methyl-1-cyclopenten-1-yl]-2,4,5,6,7,7a-hexahydro-3,7-dimethylinden-5-yl]oxy]trimethylsilane (53a): IR (neat, cm^{-1}) 1650, 1465, 1440, 1380, 1360, 1250, 1100, 1040, 970, 890, 840, 780, 760; ^1H NMR (300 MHz, C_6D_6) δ 3.65 (m, 2 H), 3.34 (br s, 1 H), 2.90 (br d, J = 9.5 Hz, 1 H), 2.80 (br d, J = 17.5 Hz, 1 H), 2.62 (br d, J = 17.5 Hz, 1 H), 2.40−2.00 (series of m, 7 H), 1.95 (br s, 3 H), 1.90−1.30 (series of m, 7 H), 1.60 (br s, 3 H), 0.97 (s, 9 H), 0.90 (d, J = 7.0 Hz, 3 H), 0.79 (d, J = 6.9 Hz, 3 H), 0.17 (s, 9 H), 0.07 (s, 6 H); MS m/z (M^+) calcd 504.3819, obsd 504.3812.

(5*S*,7*S*,7a*S*)-2,4,5,6,7,7a-Hexahydro-5-[(5*S*)-5-[(1*R*)-3-(*tert*-butyldimethylsiloxy)-1-methylpropyl]-2-methyl-1-cyclopenten-1-yl]-3,7-dimethylinden-5-ol (53b): IR (neat, cm^{-1}) 3600, 3480, 1470, 1460, 1435, 1380, 1360, 1255, 1100, 1010, 980, 900, 840, 810, 780; ^1H NMR (500 MHz, C_6D_6) δ 3.70 (m, 2 H), 3.11 (br s, 1 H), 3.01 (br d, J = 9.4 Hz, 1 H), 2.89 (d, J = 15.6 Hz, 1 H), 2.50−2.20 (series of m, 5 H), 2.18−2.10 (m, 2 H), 1.83−1.50 (series of m, 9 H), 1.76 (br s, 3 H), 1.60 (br s, 3 H), 1.00 (s, 9 H), 0.90 (d, J = 7.1 Hz, 3 H), 0.84 (d, J = 6.9 Hz, 3 H), 0.10 (s, 6 H); ^{13}C NMR (125 MHz, C_6D_6) ppm 145.1, 135.4, 132.8, 131.2, 74.7, 61.9, 52.3, 47.1, 43.9, 41.0, 39.9, 38.9, 37.5, 32.8, 27.8, 26.4, 26.2 (3 C), 23.1, 18.5, 17.8, 16.0, 14.0, 13.8, −5.1 (2 C); MS m/z ($M^+ - H_2O$) calcd 414.3318, obsd 414.3305; $[\alpha]^{23}_D$ +11.5 (c 0.002, $CHCl_3$).

Coupling of 59b to (±)-10. To solution of **58** (4.43 g, 25.3 mmol) in dry methanol (70 mL) was added cerium trichloride heptahydrate (10.38 g, 27.8 mmol), and the mixture was cooled to 0 °C while sodium borohydride (1.05 g, 27.8 mmol) was introduced in portions. Stirring was maintained for 30 min prior to quenching with water (50 mL) and extraction with ethyl acetate. The combined organic phases were washed with brine, dried, and concentrated to leave a residue, purification of which by chromatography on silica gel (elution with 2:1 hexanes/ethyl acetate) afforded **59a** as a colorless oil (4.15 g, 93%): ^1H NMR (300 MHz, C_6D_6) δ 4.40 (m, 1 H), 2.01−1.82 (m, 3 H), 1.71−1.52 (m, 2 H), 1.47 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 140.5, 121.4, 79.8, 34.1, 31.5, 15.8; MS m/z (M^+) calcd 175.9817, obsd 175.9827.

A solution of **59a** (3.58 g, 20.2 mmol) and iodomethane (2.52 mL, 40.4 mmol) in THF (40 mL) was cooled to 0 °C and treated with sodium hydride (730 mg, 30.3 mmol). The reaction mixture was allowed to warm to rt, stirred for 3 h, quenched with water (20 mL), and extracted with ether. The combined organic phases were washed with brine, dried, and concentrated. Chromatography of the residue on silica gel (elution with 50:1 hexanes/ethyl acetate) furnished **59b** as a colorless oil (3.72 g, 96%): ^1H NMR (300 MHz, $CDCl_3$) δ 4.36 (m, 1 H), 3.35 (s, 3 H), 2.48−2.37 (m, 1 H), 2.25−2.12 (m, 2 H), 1.98−1.83 (m, 1 H), 1.78 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 142.8, 117.4, 88.1, 55.6, 34.5, 27.9, 15.9; MS m/z (M^+) calcd 174.9797, obsd 174.9778.

A solution of **59b** (700 mg, 3.66 mmol) in anhydrous ether (18.3 mL) was cooled to −10 °C under N_2, treated with *sec*-butyllithium (2.81 mL of 1.3 M in cyclohexane, 3.65 mmol), and stirred for 40 min prior to the addition of (±)-**10** (296 mg, 1.83 mmol). After an additional hour of stirring, the reaction mixture was quenched with brine (100 mL) and the aqueous phase was extracted with ether. The combined organic layers were washed with brine, dried, and concentrated. The crude product was taken up in benzene (0.5 mL) and stored overnight at rt. The deposited colorless crystals were filtered and dried to give 123 mg (25%) of **63**. The mother liquor was chromatographed on silica gel (elution with 20:1 hexanes/ethyl acetate) to give pure **60** (146 mg, 29%) and a mixture of **61** and **62** (156 mg, 31%) in a 1.5:2.0 ratio. Rechromatography was necessary to achieve separation of the latter two carbinols.

For **60**: colorless oil; IR (neat, cm^{-1}) 3471, 1668, 1446, 1375, 1076, 1018, 1005, 994, 880; ^1H NMR (300 MHz, C_6D_6) δ 5.12 (s, 1 H), 4.66 (d, J = 8.2 Hz, 2 H), 4.50 (s, 1 H), 4.48 (br s, 1 H), 3.19−3.11 (m, 1 H), 2.93 (s, 3 H), 2.49 (d, J = 4.0 Hz, 1 H), 2.46−2.36 (m, 1 H), 1.98 (dd, J = 16.4, 8.0 Hz, 1 H), 1.73 (s, 3 H), 1.68−1.37 (m, 8 H), 1.28 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 158.7, 142.7, 137.8, 136.4, 129.0, 100.6, 91.2, 81.0, 54.8, 51.0, 49.8, 39.0, 31.7, 29.8, 25.4, 21.3, 18.7, 16.9; MS m/z (M^+) calcd 274.1933, obsd 274.1947.

Anal. Calcd for $C_{18}H_{26}O_2$: C, 78.78; H, 9.56. Found: C, 78.82; H, 9.56.

For **61**: colorless oil; IR (neat, cm^{-1}) 3473, 1669, 1446, 1376, 1352, 1078, 993, 880; ^1H NMR (300 MHz, C_6D_6) δ 5.68 (d, J = 1.3 Hz, 1 H), 4.75 (d, J = 0.6 Hz, 1 H), 4.63 (d, J = 1.0 Hz, 1 H), 4.16 (d, J = 5.2 Hz, 1 H), 3.10 (s, 3 H), 3.10−2.56 (m, 1 H), 2.46 (d, J = 5.9 Hz, 1 H), 1.97 (s, 3 H), 1.98−1.88 (m, 3 H), 1.76−1.60 (m, 3 H), 1.58 (d, J = 1.5 Hz, 3 H), 1.46−1.38 (m, 2 H), 1.36 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 159.8, 143.6,

141.8, 136.9, 128.6, 100.5, 90.3, 80.9, 55.6, 52.4, 49.6, 38.3, 32.3, 29.5, 28.5, 21.6, 18.7, 17.7; MS *m*/*z* (M^+) calcd 274.1933, obsd 274.1929.

For **62**: colorless oil; IR (neat, cm^{-1}) 3459, 1666, 1446, 1375, 1352, 1080, 993, 885; ^1H NMR (300 MHz, C_6D_6) δ 5.24 (d, J = 0.7 Hz, 1 H), 4.91 (d, J = 16.1 Hz, 2 H), 4.45 (d, J = 5.8 Hz, 1 H), 4.22 (s, 1 H), 2.97 (s, 3 H), 2.55 (d, J = 5.9 Hz, 1 H), 2.45−2.38 (m, 1 H), 1.97−1.85 (m, 2 H), 1.78−1.33 (series of m, 5 H), 1.69 (s, 3 H), 1.57 (d, J = 1.5 Hz, 3 H), 1.40 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 158.1, 141.8, 139.7, 137.5, 128.6, 100.5, 90.7, 79.7, 55.0, 51.1, 49.2, 37.9, 31.8, 28.9, 26.5, 21.3, 18.9, 16.5; MS *m*/*z* (M^+) calcd 274.1933, obsd 274.1934.

For **63**: colorless crystals, mp 155−156 °C; IR (film, cm^{-1}) 3429, 1666, 1462, 1377, 1346, 1072, 893; ^1H NMR (300 MHz, C_6D_6) δ 5.35 (d, J = 0.9 Hz, 1 H), 4.67 (d, J = 1.1 Hz, 1 H), 4.51 (s, 1 H), 4.09 (br s, 1 H), 3.00 (s, 3 H), 2.85−2.75 (m, 1 H), 2.50 (d, J = 5.0 Hz, 1 H), 2.49−2.42 (m, 1 H), 2.00−1.91 (m, 1 H), 1.90 (s, 3 H), 1.75−1.52 (m, 5 H), 1.64 (d, J = 1.4 Hz, 3 H), 1.41 (ddd, J = 13.5, 10.7, 2.8 Hz, 1 H), 1.26 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 158.8, 141.6, 139.0, 128.8, 128.0, 99.7, 91.3, 82.5, 55.6, 50.8, 49.5, 37.9, 31.8, 29.9, 27.5, 21.2, 18.8, 17.5; MS *m*/*z* (M^+) calcd 274.1933, obsd 274.1938.

Anal. Calcd for $C_{18}H_{26}O_2$: C, 78.78; H, 9.56. Found: C, 78.76; H, 9.52.

Rearrangement−Elimination of 60. A slurry of potassium hydride (158 mg, 1.34 mmol) in dry THF (4 mL) cooled to 0 °C was treated with a solution of **60** (123 mg, 0.44 mmol) and 18-crown-6 (135 mg, 0.51 mmol) in dry THF (6 mL), stirred for 1 h, and quenched with brine. The separated aqueous phase was extracted with ether, and the combined organic layers were dried and concentrated to leave a yellow oil, which was purified by chromatography on silica gel (elution with 20:1:0.1 hexanes/ethyl acetate/triethylamine). There were isolated 33 mg (30%) of **64** and two unidentified oils (32%).

For **64**: colorless solid, mp 127−128 °C; IR (film, cm^{-1}) 1667, 1651, 1600, 1434, 1257; ^1H NMR (300 MHz, $CDCl_3$) δ 6.65 (t, J = 2.6 Hz, 1 H), 4.20 (d, J = 12.0 Hz, 1 H), 2.75 (d, J = 15.1 Hz, 1 H), 2.60 (d, J = 12.0 Hz, 1 H), 2.54 (d, J = 15.1 Hz, 1 H), 2.50−2.13 (m, 6 H), 1.95−1.84 (m, 1 H), 1.79 (s, 3 H), 1.72 (s, 3 H), 1.69−1.20 (m, 1 H), 1.14 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 195.3, 149.3, 146.0, 145.4, 142.2, 134.3, 113.4, 49.1, 47.7, 38.4, 37.0, 35.2, 29.1, 28.7, 27.7, 22.7, 15.6; MS *m*/*z* (M^+) calcd 242.1671, obsd 242.1678.

Anal. Calcd for $C_{17}H_{22}O$: C, 84.24; H, 9.16. Found: C, 84.18; H, 9.02.

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Supporting Information Available: Experimental procedures for the preparation of **21**−**24** and **35**−**41** as well as ^1H and/or ^{13}C NMR spectra of those compounds lacking combustion data (32 pages). This material is contained in libraries, 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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