Studies Directed to the Synthesis of the Antifungal Antibiotic Aleurodiscal. Enantioselective Construction of an Advanced β-D-Xyloside Congener

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Abstract: The first synthesis of a highly functionalized congener of aleurodiscal is reported. An enantiocontrolled route to tricyclic ketone **8** was first developed by taking advantage of regiodirected tandem methylation and vinylation of a phenylsulfanyl precursor, as **23** → **24** → **8**. These experiments formed the basis for the coupling of **8** to **30**, in turn prepared from (4*S*)-(-)-*tert*-butyldimethylsiloxycyclopentenone, prior to oxy-anionic Cope rearrangement. Phenylselenenylation of the enolate ion generated in this manner ultimately led to a pair of dienone isomers, whose distinctively different chemistries were made apparent at several levels. Notable features of the overall approach include the introduction of stereogenic centers positioned remotely from each other across a medium-sized ring and stereoselective bond construction via a boatlike transition state following efficient conjoining of the two key segments.

Key words: anionic sigmatropy, oxy-Cope reaction, chiral sulfoximine, cyclobutanones

In 1989, a team of researchers from three West German universities reported on the isolation and characterization of aleurodiscal (**1**), an antifungal antibiotic produced by mycelial cultures of *Aleurodiscus mirabilis* collected from the bark of *Cinnamonum camphora* endemic to Japan.[1] Structure elucidation, accomplished by combined application of spectroscopic and X-ray crystallographic methods, revealed the substance to constitute a fundamentally new type of sesterterpenoid. Hydrolysis of **1** in methanolic hydrochloric acid released D-(+)-xylose, thereby making possible the assignment of absolute configuration as shown. Aleurodiscal, believed to be biogenetically related to retigeranic acid (**2**),[2,3] has structural components similar to those found in precapnelladiene (**3**),[4,5] albolic acid (**4**) and related ophiobolins,[6,7] as well as variecolin (**5**).[8]

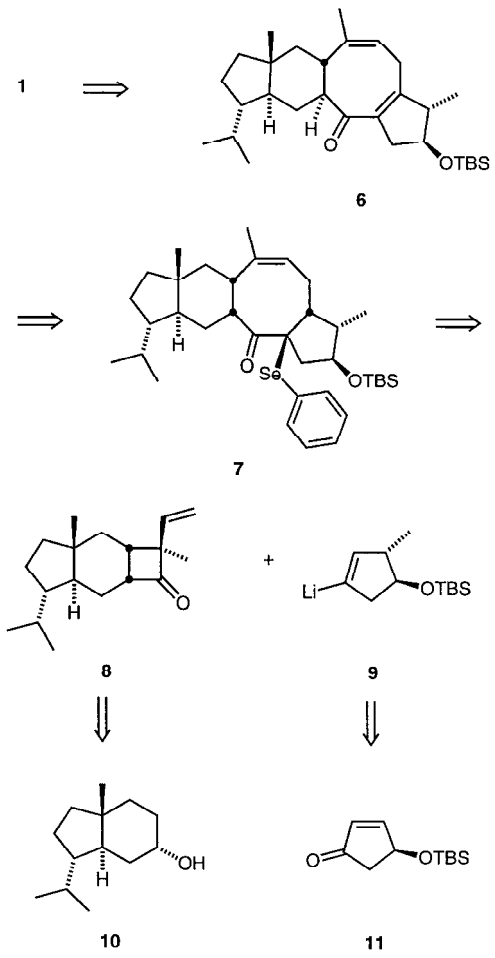
The novel structural framework and therapeutic potential of **1** were among the considerations that prompted the design of a strategy for its *de novo* construction. In particular, the intention was to extend our earlier work involving the synthesis of structurally complex targets by proper deployment of oxy-anionic sigmatropy.[9] Therefore, the theme that will be developed in the present context is the convergent coupling of optically pure cyclobutanone **8** with cyclopentenyllithium **9** of >98% ee as a means of establishing the central eight-membered ring (Scheme 1). The primary initial concerns necessarily become those associated with the crafting of **8** and **9** from precursors such as **10** and **11**, respectively. Subsequently, consideration will be given to the chemistry of **7** and related advanced intermediates including, but not restricted to, dienones such as **6**.

Discussion of Results

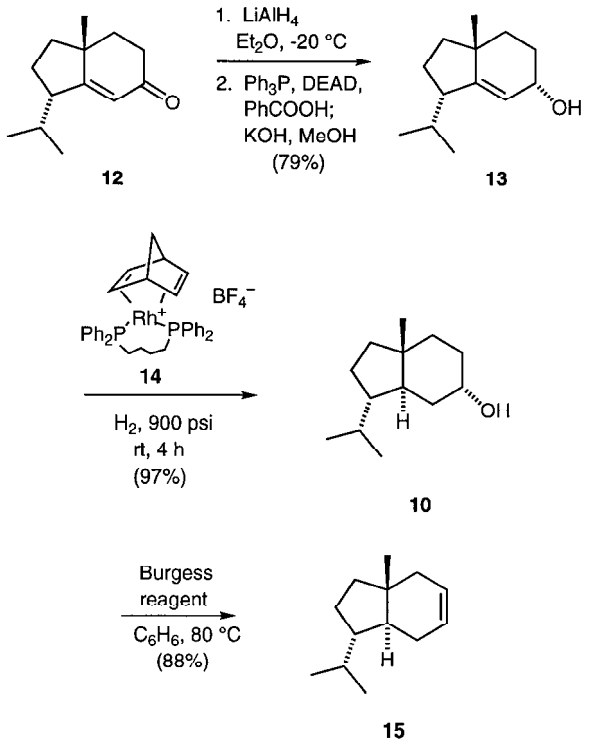
Enantiocontrolled Route to the Left Half. The starting point for accessing **8** was the hydrindenone **12**, which was conveniently obtained from commercially available (±)-2,6-dimethylhept-5-enal (melonal) according to the protocols developed by Snider[10] and by Corey.[3a,11] In order to set the rather elusive *trans* intra-ring stereochemistry, **12** was subjected sequentially to stereoselective hydride reduction from the α-face, Mitsunobu inversion to generate the α-allylic alcohol **13**, and facially controlled hydrogenation of **13** in the presence of norbornadienerhodium(I) diphosphine complex **14**.[12] This route, originally devised by Engler,[11,13] delivered **10** efficiently without evidence of contamination from the more thermodynamically stable *cis* isomer (Scheme 2).

In preparation for annulation of the cyclobutanone ring, attention was given to the regiodirected dehydration of **10**. The most effective of the reagents examined proved to be (methoxycarbonylsulfamoyl)triethylammonium hydroxide inner salt.[14] The elimination of **10**, realized in hot benzene solution, led uniquely to **15** as confirmed spectroscopically, in a reproducible 88% yield.

Advantage was taken of the face selectivity with which **12** is attacked by nucleophiles for resolution purposes. To this end, this ketone was transformed by reaction with the lithium salt of Johnson's (+)-(*S*)-sulfoximine[15] into the chromatographically separable 1,2-adducts **16** and **17**

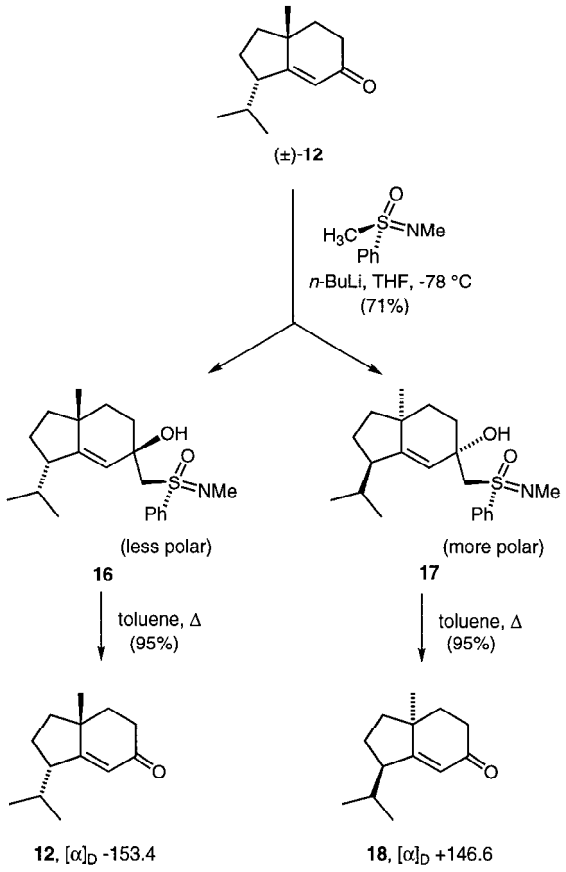


Scheme 1



Scheme 2

(Scheme 3). The absolute stereochemistry of **16** was defined by X-ray crystallographic analysis (Figure 1). Release of the optical antipodes of **12** was readily accomplished by heating **16** and **17** separately in toluene. Since the less polar diastereomer **16** was more easily purified, the desired levorotatory enantiomer of **12** was routinely accessed in optically pure form, i.e., ≥99% ee.



Scheme 3

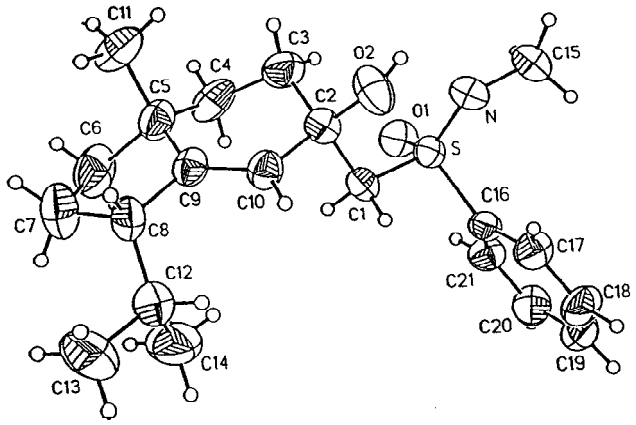
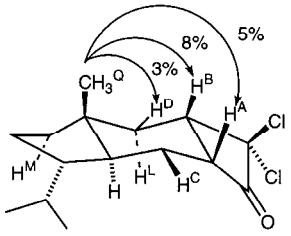


Figure 1

After considerable experimentation, the [2+2] cycloaddition of dichloroketene to **15** was successfully implemented by the slow addition of trichloroacetyl chloride to a suspension of zinc–copper couple and the alkene in diethyl ether at room temperature.[16] These conditions gave rise

to **19** (74%) with the proper regio- and stereochemistry as deduced by NOE experiments (Figure 2) and X-ray crystallography (Figure 3). High-field ^{1}H NMR analysis revealed the existence of W couplings between H^Q and both H^L and H^M. The vicinal coupling between H^A and H^C is characteristic of a 90° dihedral angle relationship (J < 1 Hz). The relative positioning of the carbonyl in this adduct follows from the chemical shifts of H^A (α to carbonyl) and H^B (α to CCl_2). The most diagnostic NOE effect is the 8% enhancement of the H^B signal that arises from irradiation of H^Q.



19

H^Q

with	% NOE
H^A	3
H^B	8
H^D	0.5

Figure 2

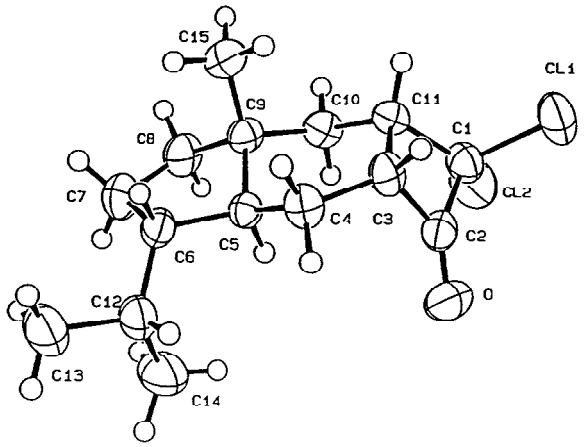
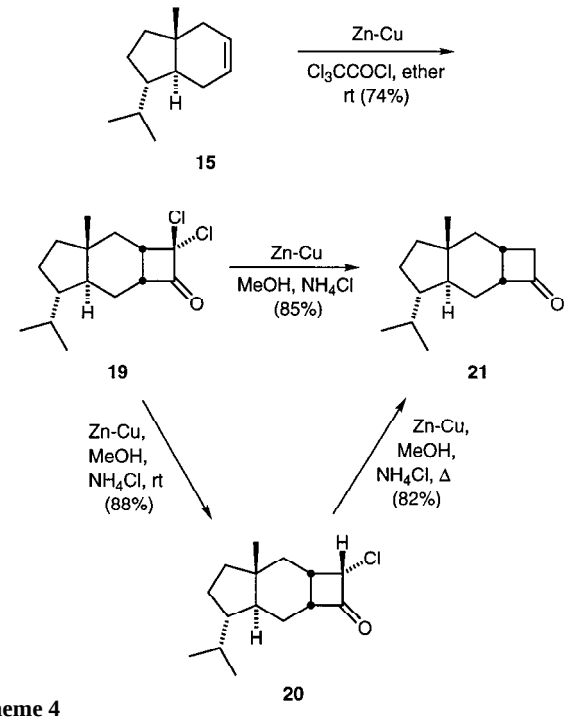


Figure 3

Initial attempts to accomplish the reductive removal of the chlorine atoms in **19** proved unsatisfactory (Scheme 4). Powdered zinc in acetic acid gave the monochloro ketone **20** readily, but the prolonged heating (110°C, 2 h) required to bring about the second dechlorination caused substantial decomposition and led to a poor yield of **21**. Neither were chromium(II) chloride in aqueous acetone,[17] tributyltin hydride and AIBN in hexanes, or other prescribed methods[18] useful. In contrast, a mixture of zinc–copper couple and ammonium chloride in hot methanol[19] resulted in clean, complete reduction to **21** (85%). Nonetheless, the optimum protocol for this conversion was to effect initial monoreduction to **20** during 5 min at room temperature, since **20** proved much easier to purify than **21**. The final step was subsequently performed for 1–2 h at the reflux temperature.

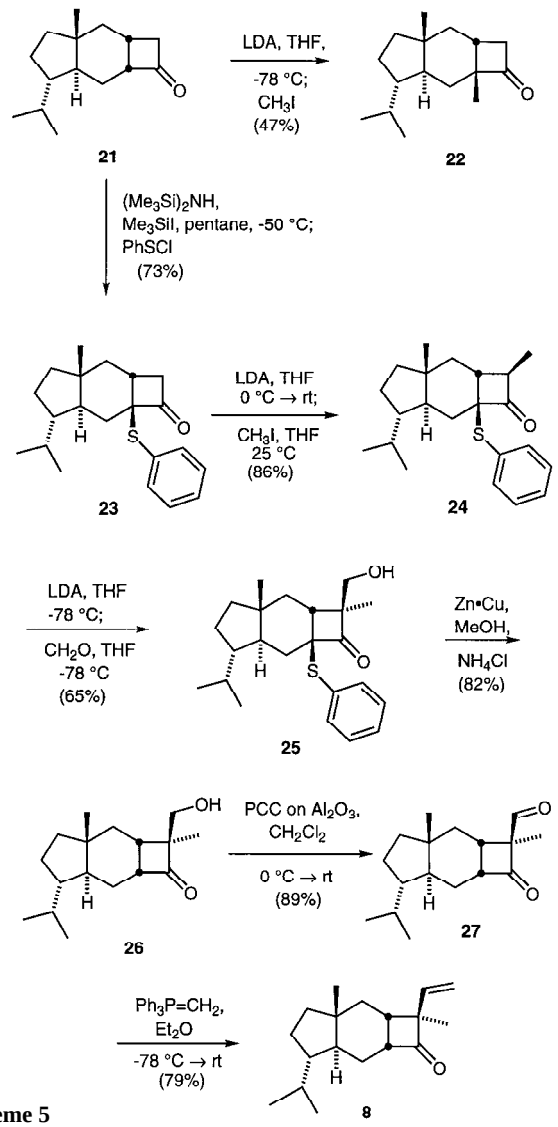


Scheme 4

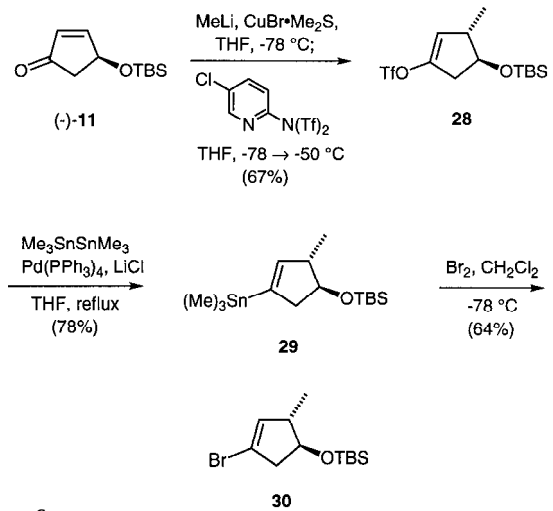
Although the [2+2] cycloaddition of vinyl ketenes to alkenes has been extensively exploited in synthesis,[20] the use of such reagents in the present context followed by *C*-methylation would culminate in formation of the incorrect stereoisomer of **8**. These considerations demanded, therefore, that **20** or **21** serve as the appropriate precursor. As our point of departure, **21** was subjected to kinetic deprotonation with LDA and the resulting enolate anion was trapped with methyl iodide. However, these and related conditions led to **22** (47%) alongside unreacted cyclobutanone (Scheme 5). When **20** was found to respond to methylation with the identical regiochemistry,[21] recourse was made instead to treatment of the kinetically (and thermodynamically) favored silyl enol ether of **21** with phenylsulfenyl chloride.[22] The phenylsulfanyl ketone **23** so obtained responded well to directed methylation, with **24** arising in 86% isolated yield following swamping with methyl iodide at 25°C.[23] Since **23** had given no evidence of *S*-methylation after 5 h at room temperature in the presence of a vast excess of CH_3I, the obviously slow bimolecular rate eased concern about possible competing side reactions during the conversion to **24**. The methylation of **23** occurred exclusively from the β-face as confirmed by NOE measurements.

Of the several methods probed for the vinylation of **24**, that involving initial base-promoted condensation with monomeric formaldehyde[24] proved to be highly successful. Removal of the phenylsulfanyl blocking group in **25** was again accomplished with zinc–copper couple. Oxidation of **26** to oxo aldehyde **27** with pyridinium chlorochromate on alumina[25] set the stage for arrival at **8** via chemoselective Wittig alkenation.

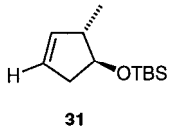
Assembly of the Right Hand Segment. With subtarget **8** in hand, attention was directed to generation of enantiopure nucleophile **9**. Our approach exploited the ready avail-



Scheme 5



Scheme 6

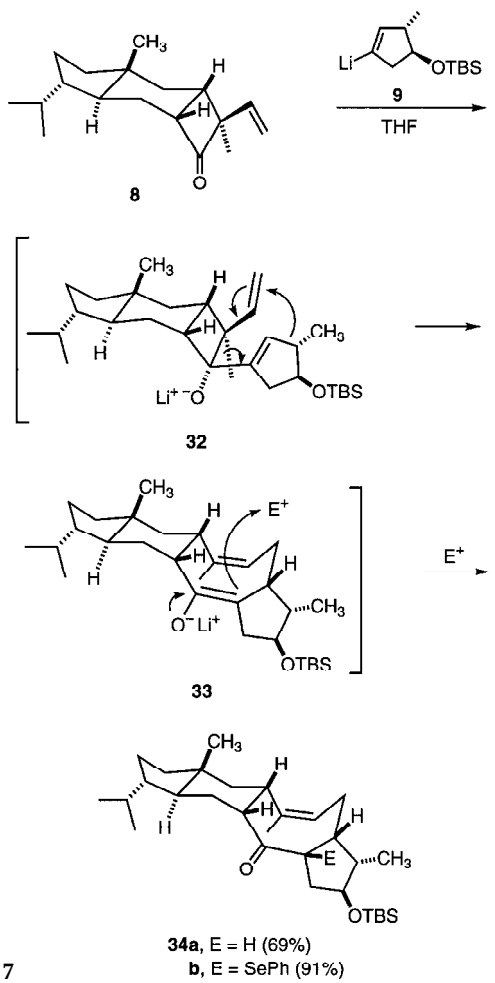


ability of (–)-**11**[26] and the excellent stereoselectivity with which lithium dimethylcuprate undergoes conjugate addition to its enone chromophore (Scheme 6). Trapping of the resulting enolate with *N*-(5-chloro-2-pyridyl)-triflimide[27] afforded **28**, from which the vinylstannane **29** was secured by reaction with hexamethylditin in the presence of tetrakis(triphenylphosphine)palladium(0) and lithium chloride.[28] Bromide **30** was subsequently obtained by titration of **29** with bromine in dichloromethane at –78 °C.[29] NOE studies of **28–30** confirmed the *trans* arrangement of the substituents.

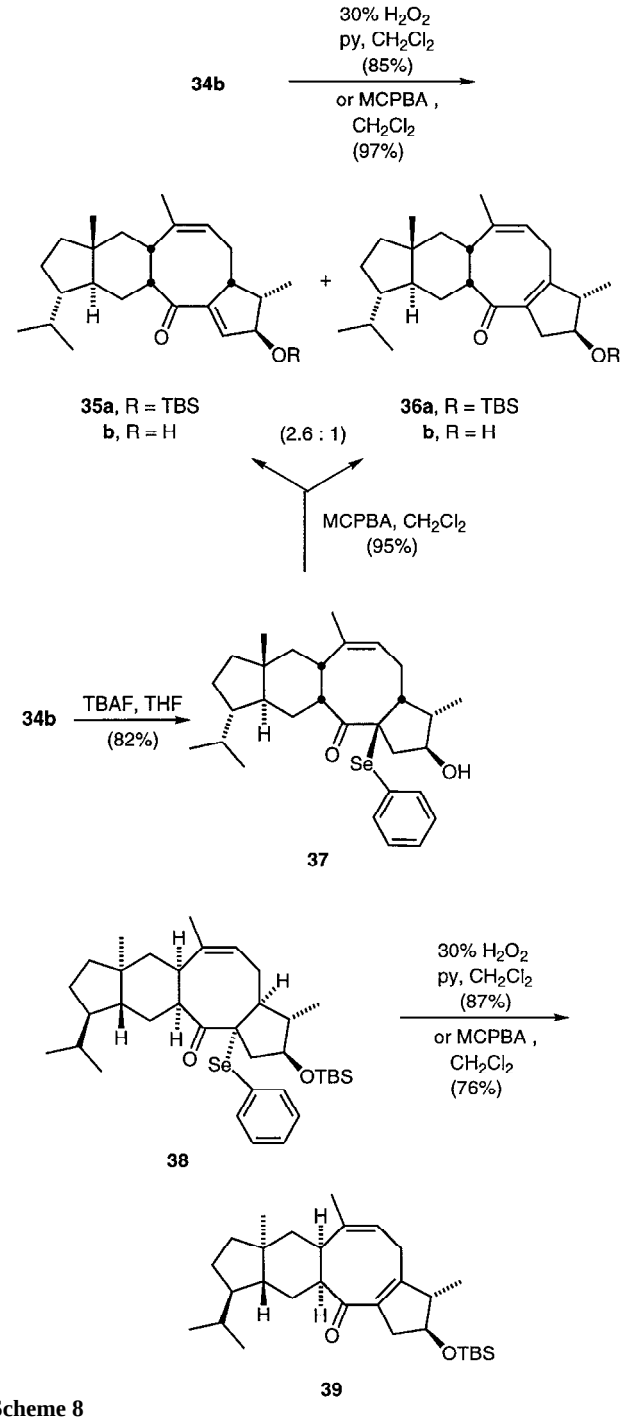
The possibility of transmetalating **29** was skirted because of the inherent difficulties of removing the tin byproducts of this process. In contrast, the halogen–metal exchange involving **30** and *tert*-butyllithium proceeded very efficiently. When solutions of **9** generated in this manner were quenched with methanol, **31** was isolated in 86% yield.

Coupling of the Sectors. Arrival at the Aleurodiscal Core. The anionic oxy-Cope reaction, with its ability to deliver high levels of chirality transfer and regiocontrol under mild conditions, is a powerful variant of the [3,3] sigmatropic rearrangement. When this transformation is accompanied by significant strain release, the process is irreversible. In light of the ground state conformation adopted by **8** (Scheme 7), the approach of cycloalkenyllithium **9** to its carbonyl group is relegated exclusively to β-face attack. With arrival at divinylcyclobutanoxide **32**, spontaneous rearrangement via a boat-like transition state to deliver **33** was anticipated. As discussed elsewhere,[30] this transition state geometry is adopted to skirt the introduction of a pair of *trans* double bonds in the emerging eight-membered ring. Electrophilic capture by **33** proceeds from the molecular exterior to set the final substituent *syn* to the three pre-existing tertiary hydrogens. The tetracyclic ketones **34a** and **34b**, obtained following the addition of water and phenylselenenyl chloride, respectively, to **33**, were securely identified on the basis of NOE data (see Experimental Section). The remarkable efficiency (91%) of the one-pot, four-step process (including the lithiation of **30**) leading to **34b** is noteworthy.

With generous amounts of **34b** now available, oxidative elimination of the phenylseleno substituent was next pursued. When exposed to 30% hydrogen peroxide in dichloromethane containing pyridine, conversion to a 2.6:1 mixture of **35a** and **36a** was realized (Scheme 8). These dienones, easily distinguished by ^{1}H NMR spectroscopy, are considered to be the end result of sterically controlled intramolecular proton abstraction within the two selenoxide diastereomers. In order to test this operating assumption, efforts were made to redirect the regioselectivity of the process. Recourse to sodium periodate in methanol–tetrahydrofuran–water (5:1:l) gave rise to solubility problems as evidenced by the need for long reaction times and the extensive recovery of **34b**. Alternative use of 3-chloroperbenzoic acid at –78 °C and at –10 °C surprisingly had no effect on the originally observed distribution of **35a** and **36a**. In order to evaluate the role of the TBS group on the regioselectivity of the elimination, the free



Scheme 7



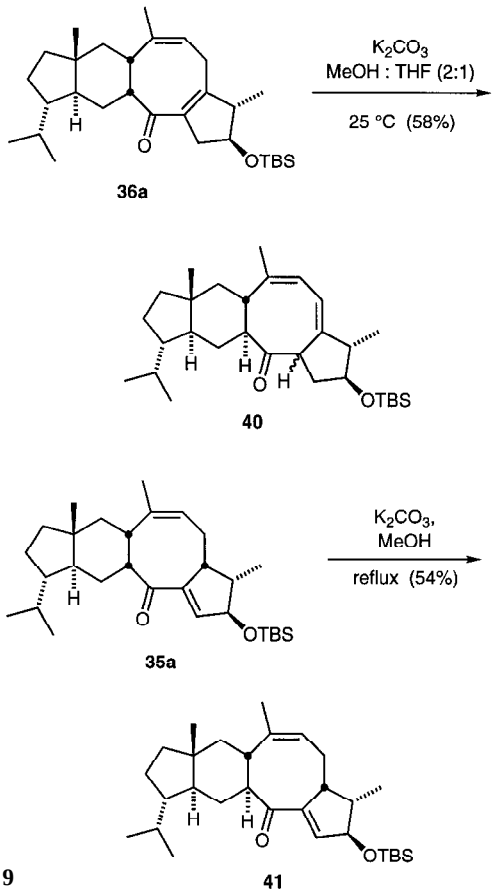
Scheme 8

hydroxy selenide **37** was generated and subjected to peracid oxidation. Under these circumstances, **35b** and **36b** were generated in a parallel 2.6:1 ratio. In contrast, the oxidation of diastereomer **38**, prepared independently, gave **39** very predominantly.

Evaluation of End Game Tactics. The predominant formation of **35a** and **35b** prompted initial investigation of their isomerization to **36a** and **36b**. Iodine in benzene solution had no effect on either intermediate at room temperature; heating to reflux induced decomposition. However, the desired transformations were accomplished instead with rhodium trichloride trihydrate in hot ethanol,[31] but only modest yields (32–35%) were realized in these conversions. Since chromatographic separation of the isomers was straightforward, this pathway was routinely used to obtain quantities of **36a**.

Arrival at aleurodiscal (**1**) requires that several of its unique structural features be addressed. The necessary chemical transformations include epimerization at C-12, oxidation of the allylic methyl group at position 25, installation of a methyl group (C-23) in the lower portion of the eight-membered ring, and coupling to the xylose moiety. Each of these changes has been accorded preliminary attention.

One's ability to accomplish epimerization α to the carbonyl group rests on the relative positioning of the two double bonds.[32] Thus, stirring **36a** with potassium carbonate in a 2:1 mixture of methanol and tetrahydrofuran at room temperature for 2 days resulted in conversion to the conjugated dienone **40** (Scheme 9). This isomerization can be attributed to the substantial acidity of the doubly allylic protons in **36a**, a situation that does not exist in **35a**. The latter dienone is indeed amenable to conversion to its more stable diastereomer **41**, although refluxing conditions were necessary to bring the configurational inversion about in a reasonable timeframe (12 h).

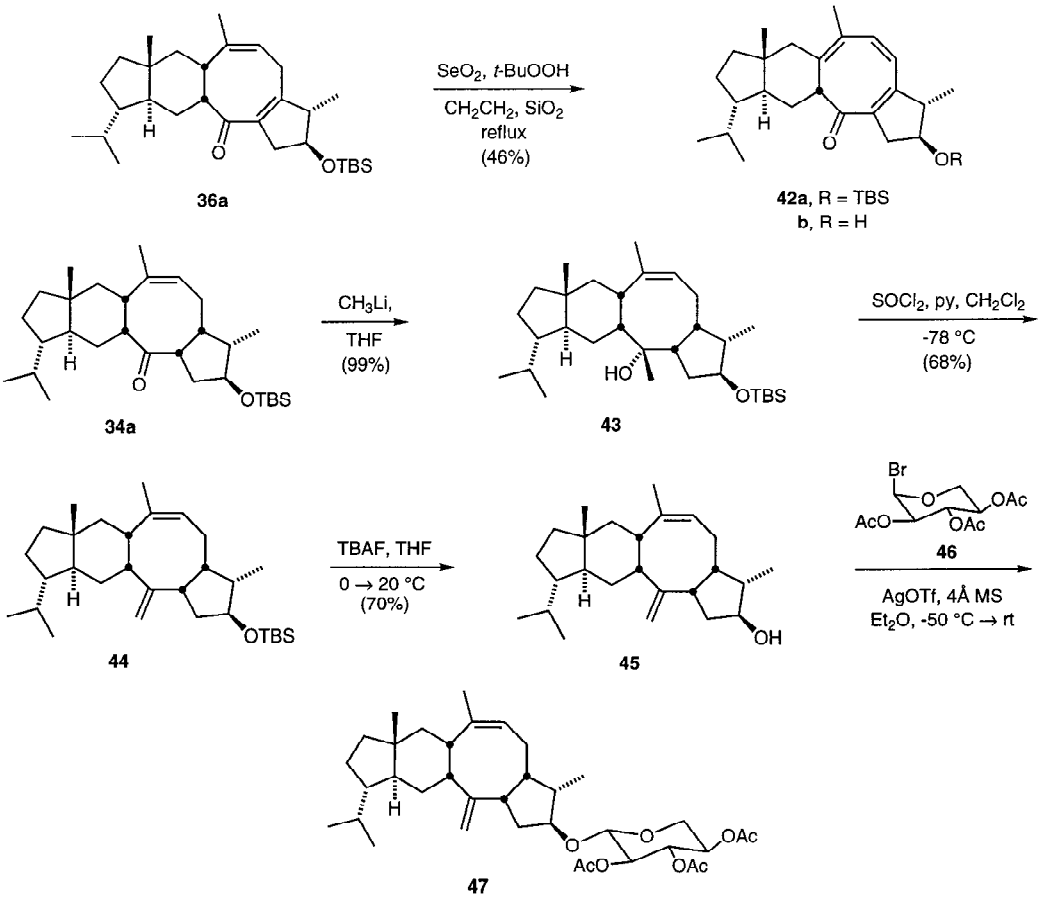


Scheme 9

The intra-ring activation available to **36a** manifested itself again during attempts to oxidize C-25 to the aldehyde level. For example, heating **36a** with selenium dioxide, *tert*-butyl hydroperoxide, and silica gel in dichloromethane[33] for a few hours led to the isolation of **42a** and **42b** (Scheme 10). Alternative radical-based methods involving *N*-bromosuccinimide or the chromium trioxide/3,5-dimethylpyrazole reagent failed to give recognizable products.

The final methyl group in aleurodiscal was installed by reaction of **34a** with methyllithium in tetrahydrofuran at 0 °C. Strict attention must be paid to acid-free conditions during workup in order to avoid cyclization with formation of a bridged ether.[21] Exposure of **43** to thionyl chloride and pyridine led exclusively to the exocyclic double bond isomer **44**. Since **44** was not smoothly isomerized to the desired internal diene following heating with rhodium trichloride, the introduction of C-23 must be accomplished by an alternative route.

At this point, it was considered timely to investigate the coupling of an activated xylose derivative with a representative aglycone. To this end, **44** was desilylated and the alcohol **45** so formed was brought into reaction with bromo triacetate **46**[34] under catalysis by silver triflate[35] in diethyl ether at –50 °C, with subsequent warming to room temperature. Although this single experiment returned a large amount (69%) of the acetate of **45**, sufficient **47** (24%) was obtained to permit full characterization. The ready acetyl transfer operative under these conditions points up



Scheme 10

the likelihood that a different protecting group may ultimately be preferred.

Summary

Recourse to a 1,2-addition/anionic oxy-Cope reaction sequence provides a very concise route to the aleurodiscal framework. The protocol allows for the direct introduction of six of the eight stereogenic centers resident in **1**. Proper absolute configuration is set at all of these sites. In addition, several advanced intermediates are adequately functionalized to permit arrival at **1** in principle. While this has not yet been achieved, some useful and important insight has been gained that should allow future implementation of a proper end game. Some of the key lessons learned include (i) an appreciable kinetic bias exists for selenoxide elimination to occur exocyclic to the cyclooctenyl core; (ii) epimerization at C-12 is thermodynamically favored under the proper conditions; (iii) the central eight-membered ring is prone to transannular effects and is amenable to setting resident double bonds in conjugation; (iv) the sensitivity of this medium-sized ring is such that oxidation of C-25 to the aldehyde level will need to be accomplished indirectly; and (v) introduction of the allylic methyl group at C-23 and its associated double bond must be approached in a manner that skirts the dehydration of a tertiary alcohol since the latter tactic is clearly conducive to elimination in the exocyclic direction.

Finally, arrival at (–)-**34b** was accomplished from (–)-**8** in 12 steps and 6.8% overall yield. It is hoped that the lessons learned in this series of experiments can be applied to the acquisition of aleurodiscal and bioactive analogs thereof.

Most reactions were carried out under N_2. Solvents were reagent grade, and in most cases dried before use. Benzene, Et_2O, THF, toluene, and dioxane were distilled from Na/benzophenone ketyl. CH_2Cl_2, diisopropylamine, DMSO, DMF, Et_3N, Hunig's base, and most other reaction solvents were distilled from CaH_2. MeOH was distilled from the magnesium salt. Flash chromatography was performed on silica gel (230–400 mesh, 60 Å) or Fluka silica gel H with the indicated solvents. Mps were determined in open capillaries and are uncorrected. HRMS (Kratos MS-30 or VG-70-2505) were recorded at The Ohio State University Chemical Instrumentation Center. Elemental analyses were performed at the Scandinavian Microanalytical Laboratory, Herlev, Denmark or at Atlantic Microlab, Inc., Norcross, Georgia, USA.

(–)-(3*S*,7a*R*)-7,7a-Dihydro-3-isopropyl-7a-methylindan-5(6*H*)-one (12):

Melonal (80% tech. grade, 100 g, 0.57 mol) was heated to reflux under N_2 with pyrrolidine (127 mL, 1.52 mol) in benzene (3 L) for 40 h using a Dean–Stark trap to separate the water (about 14 mL). The excess pyrrolidine and benzene were removed by simple distillation. After cooling, anhyd benzene (2 L) was added to the solution followed by methyl vinyl ketone (115 mL of 95% freshly distilled, 1.42 mol) in a solution of anhyd benzene (200 mL) over 2 h. The mixture was heated for an additional 15 h and cooled. Glacial HOAc (75 mL) and NaOAc (100 mL of 4.3 M) were introduced and heating at reflux was resumed for 3 h. The mixture was diluted with Et_2O (750 mL), washed with 10% HCl (2 × 200 mL) and sat. $NaHCO_3$ (3 × 200 mL), dried, filtered, and evaporated. Purification was accomplished by distillation, bp 120°C at 0.5 mm Hg, to furnish 77.6 g (71%) of (±)-4-methyl-4-(4-methylpent-3-enyl)cyclohex-2-en-1-one as a clear yellow oil.
IR (neat, cm^{-1}): ν = 1680, 1610, 1450, 1375.
^1H NMR (300 MHz, $CDCl_3$): δ = 6.66 (d, J = 10.2 Hz, 1 H), 5.84 (d, J = 10.2 Hz, 1 H), 5.06 (t, J = 1.3 Hz, 1 H), 2.44–2.40 (m, 2 H), 2.00–1.92 (m, 3 H), 1.81–1.70 (m, 1 H), 1.65 (s, 3 H), 1.57 (s, 3 H), 1.48–1.41 (m, 2 H), 1.12 (s, 3 H).
^{13}C NMR (75 MHz, $CDCl_3$): δ = 199.5, 159.1, 131.9, 127.3, 123.9, 40.9, 35.6, 34.1, 33.4, 25.6, 24.8, 22.8, 17.6.

(+)-2,6-Dimethyl-2-(3-oxobutyl)hept-5-enal could be isolated in yields up to 10% as a side product.

A single-necked flask was fitted with an addition funnel and charged with the above ketone (80.0 g, 0.42 mol) and anhyd CH_2Cl_2 (2 L) at 10°C under N_2. Ethylaluminum dichloride (660 mL of 1 M in hexanes, 0.66 mol) was transferred via cannula to the addition funnel and added dropwise over 1.5 h. The clear yellow-orange solution was allowed to react over 4 h at r.t., quenched with aq NH_4Cl (200 mL), diluted with Et_2O (500 mL), and washed with H_2O (300 mL) and sat. $NaHCO_3$ (2 × 200 mL). The aluminum salts were rinsed with Et_2O. The combined organic solutions were dried and concentrated, and the residue was chromatographed on silica gel (elution with 10–15% EtOAc in hexanes) to give racemic **12** as a colorless oil (60 g, 73%).
IR (neat, cm^{-1}): ν = 1665, 1460, 1205.
^1H NMR (300 MHz, $CDCl_3$): δ = 5.74 (s, 1 H), 2.82 (m, 1 H), 2.55 (m, 1 H), 2.35 (m, 1 H), 2.06–1.60 (m, 6 H), 1.46–1.30 (m, 1 H), 1.18 (s, 3 H), 0.98 (d, J = 6.8 Hz, 3 H), 0.72 (d, J = 6.8 Hz, 3 H).
^{13}C NMR (75 MHz, $CDCl_3$): δ = 199.6, 180.8, 120.4, 47.3, 43.3, 39.9, 35.9, 33.8, 29.4, 23.5, 22.6, 21.8, 16.4.
MS m/z (M^+) calcd 192.1514, obsd 192.1505.

Pyrolysis of **16** as described below for the diastereomer gave (–)-**12** exhibiting $[\alpha]_D^{20}$ –153.4 (c = 0.78, $CHCl_3$).
Anal. Calcd for $C_{13}H_{20}O$: C, 81.20; H, 10.48. Found: C, 81.21; H, 10.51.

(–)-(3*R*,5*S*,7a*R*)-5,6,7,7a-Tetrahydro-3-isopropyl-7a-methylindan-5-ol (13):

Hydrindenone **12** (6.0 g, 36 mmol) was diluted with anhyd Et_2O (40 mL) and added dropwise over 40 min to a solution of $LiAlH_4$ (1.5 g, 39 mmol) in Et_2O (50 mL) at –25°C. After 1.5 h of stirring, sat. NH_4Cl and Et_2O were introduced and the aluminum salts were filtered and rinsed (3 × 50 mL) with Et_2O. The filtrate was dried and concentrated, and the residue was purified on silica gel by elution with 15% EtOAc in hexanes to give 5.7 g (95%) of the β-alcohol as a waxy, white solid, mp 46–48°C.

IR (neat, cm^{-1}): ν = 3340, 1560.
^1H NMR (300 MHz, $CDCl_3$): δ = 5.21 (br s, 1 H), 4.33–4.07 (m, 1 H), 2.57–2.45 (m, 1 H), 2.02–1.14 (m, 10 H), 1.04 (s, 3 H), 0.92 (d, J = 6.8 Hz, 3 H), 0.68 (d, J = 6.8 Hz, 3 H).
^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.9, 119.1, 68.8, 45.1, 41.9, 40.1, 36.1, 29.9, 28.6, 25.1, 22.2, 22.1, 15.9.
MS m/z (M^+) calcd 194.1671, obsd 194.1670.
$[\alpha]_D^{20}$ –89.0 (c = 2.61, $CHCl_3$)
Anal. Calcd for $C_{13}H_{22}O$: C, 80.36; H, 11.41. Found: C, 80.11; H, 11.37.
The above alcohol (40 g, 21 mmol) was dissolved in anhyd Et_2O (2 L) along with Ph_3P (55 g, 21 mmol) and benzoic acid (26.3 g, 22 mmol). Diethyl azodicarboxylate (DEAD) (33 mL, 21 mmol) was added dropwise via syringe and the yellow solution was stirred for 10 min before a white precipitate developed. After another 20 min, the mixture was concentrated, placed atop a column of silica gel, and filtered through with 15% EtOAc in hexanes. The ester was concentrated and hydrolyzed with 5% KOH in MeOH (900 mL) during 12 h at r.t. $NaHCO_3$ (40 g) was added, the solution was evaporated, and the concentrate was dissolved in Et_2O and washed with H_2O prior to drying and solvent removal. Purification on silica gel by elution with 10% EtOAc in hexanes furnished 33 g (83%) of (–)-**13** as a waxy solid.
IR (neat, cm^{-1}): ν = 3350, 1010.
^1H NMR (300 MHz, $CDCl_3$): δ = 5.40 (br s, 1 H), 4.20–4.15 (m, 1 H), 2.60–2.50 (m, 1 H), 2.08–1.15 (m, 10 H), 0.95 (d, J = 6.7 Hz, 3 H), 0.95 (s, 3 H), 0.70 (d, J = 6.7 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ =155.0, 117.5, 64.0, 45.1, 41.8, 40.0, 31.0, 28.4, 28.1, 23.6, 22.2, 22.0, 15.9.
$[\alpha]_D^{20}$ –176.6 (c = 1.30, $CHCl_3$).

(–)-(3*S*,5a*S*,5*S*,7a*R*)-Hexahydro-3-isopropyl-7a-methylindan-5-ol (10):
Norbornadiene (1,4-bisdiphenylphosphinobutane)rhodium(I) tetrafluoroborate (**14**, 500 mg) and allylic alcohol (–)-**13** (4.83 g, 25.2 mmol) were dissolved in THF (60 mL) and placed under H_2 atmosphere of 900 psi in a bomb. The resulting suspension was filtered through silica gel and purified on silica gel by elution with 20% EtOAc in hexanes to give 4.73 g (97%) of (–)-**10** as a white solid, mp 44–46 °C.
IR (neat, cm^{-1}): ν = 3430, 1210, 740.
^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.08 (m, 1 H), 1.75–1.25 (m, 14 H), 0.89 (d, J = 6.7 Hz, 3 H), 0.80 (d, J = 6.7 Hz, 3 H), 0.74 (s, 3 H).
^{13}C NMR (75 MHz, $CDCl_3$): δ = 66.9, 45.9, 42.8, 41.5, 39.2, 34.1, 32.8, 29.1, 29.0, 22.9, 22.1, 17.8, 16.7.
MS m/z (M^+) calcd 196.1827, obsd 196.1828.
$[\alpha]_D^{20}$ –61 (c = 1.01, $CHCl_3$).
Anal. Calcd for $C_{13}H_{24}O$: C, 79.35; H, 12.32. Found: C, 79.59; H, 12.37.

(–)-(1*S*,3a*R*,7a*S*)-3a,4,7,7a-Tetrahydro-1-isopropyl-3a-methylindan (15):
Alcohol (–)-**10** (9.0 g, 46 mmol) was diluted with benzene (250 mL) and added to a solution of Burgess reagent (12.6 g, 53.0 mmol) in benzene (50 mL). This solution was stirred for 3 h, heated to reflux overnight, cooled, and diluted with Et_2O (100 mL). The organic solution was washed with brine (2 × 100 mL), and the aqueous solution was extracted with Et_2O (1 × 50 mL). The organic layer was dried, the solvent was removed, and the residue was chromatographed on silica gel with hexane elution to give 7.2 g (88%) of (–)-**15** as a colorless oil.
IR (neat, cm^{-1}): ν = 1460, 1375.
^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.64–5.60 (m, 2 H), 2.20–2.10 (m, 1 H), 1.97 (br s, 2 H), 1.77–1.48 (m, 5 H), 1.37–1.17 (m, 3 H), 0.91 (d, J = 6.7 Hz, 3 H), 0.84 (d, J = 6.7 Hz, 3 H), 0.76 (s, 3 H).
^{13}C NMR (75 MHz, $CDCl_3$): δ = 126.7, 126.6, 47.5, 46.3, 41.0, 40.3, 39.2, 30.4, 28.4, 24.3, 21.8, 18.8, 18.1.
MS m/z (M^+) calcd 178.1721, obsd 178.1708.
$[\alpha]_D^{20}$ –116 (c = 4.74, $CHCl_3$).
Anal. Calcd for $C_{13}H_{22}$: C, 87.56; H, 12.44. Found: C, 87.75; H, 12.47.

(*S*)-*N*-Methyl-*S*-phenyl-*S*-{[(3*S*,5*R*,7a*R*)-5,6,7,7a-tetrahydro-5-hydroxy-3-isopropyl-7a-methyl-5-indanyl]methyl}sulfoximine (16) and Diastereomer 17:
A solution of Johnson's (+)-(*S*)-sulfoximine (9.0 g, 53 mmol) in THF (150 mL) was cooled to –5 °C and treated with BuLi (34 mL, 1.58 M in hexanes, 53 mmol). The anion solution, which formed over 25 min, was cooled to –78 °C before racemic **12** (10 g , 53 mmol) was added slowly via cannula. After 20 min, the mixture was quenched with sat. NH_4Cl (50 mL). Hexanes (100 mL) were added and the separated organic phase was dried and evaporated. Chromatographic separation on silica gel with 20% EtOAc in hexanes gave 6.4 g (34%) of **16** and 7.0 g (37%) of **17**. Compound **16** was a white solid, mp 105–106 °C.
IR (neat, cm^{-1}): ν = 3310, 1450, 1370, 1225, 1150, 1110, 1005.
^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.89–7.86 (m, 2 H); 7.65–7.54 (m, 3 H), 5.00 (s, 1 H), 3.28 (dd, J = 1.4, 2.5 Hz, 1 H), 3.11 (d, J = 14 Hz, 1 H), 2.84 (m, 1 H), 2.61 (s, 3 H), 2.58–2.51 (m, 1 H), 2.11–2.00 (m, 1 H), 1.87–1.70 (m, 3 H), 1.60–1.53 (m, 1 H), 1.46–1.39 (m, 2 H), 1.38–1.10 (m, 1 H), 1.06 (s, 3 H), 1.03–0.93 (m, 1 H), 0.88 (d, J = 6.7 Hz, 3 H), 0.54 (d, J = 6.7 Hz, 3 H).
^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.7, 139.1 (2 C), 133.1, 129.6, 129.0 (2 C), 120.9, 72.7, 62.0, 44.7, 42.3, 40.0, 35.5, 31.9, 28.8, 28.5, 24.9, 22.0, 21.9, 15.8.
MS m/z (M^+) calcd 361.2075, obsd 361.2059.
Anal. Calcd for $C_{21}H_{31}O_2SN$: C, 69.77; H, 8.64. Found: C, 69.27; H, 8.71.

For the X-ray crystallographic analysis, see Figure 1.

For **17**: colorless crystals, mp 110–111 °C.
IR (neat, cm^{-1}): ν = 3240, 2160, 1670, 1460, 1250.
^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.87–7.84 (m, 2 H), 7.62–7.55 (m, 3 H), 5.78 (s, 1 H), 3.27 (m, 2 H), 2.62 (s, 3 H), 2.60–2.56 (m, 1 H), 2.10–1.96 (m, 2 H), 1.85–1.45 (m, 6 H), 1.29–1.16 (m, 1 H), 1.04 (s, 3 H), 1.12–0.98 (m, 1 H), 0.94 (d, J = 6.7 Hz, 3 H), 0.74 (d, J = 6.7 Hz, 3 H).
^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.0, 139.0 (2 C), 133.0, 129.5, 129.0 (2 C), 119.6, 72.1, 65.8, 44.9, 42.1, 40.1, 34.8, 34.5, 28.9, 28.5, 24.4, 22.1 (2 C), 15.7.
MS m/z (M^+) calcd 361.2075, obsd 361.2037.
Anal. Calcd for $C_{21}H_{31}O_2SN$: C, 69.77; H, 8.64. Found: C, 69.55; H, 8.72.

(+)-(3*R*,7a*S*)-7,7a-Dihydro-3-isopropyl-7a-methylindan-5(6*H*)-one (18):
Sulfoximine **17** (20.15 g, 56.5 mmol) was dissolved in toluene (200 mL) and heated to reflux. Progress of the reaction was followed by TLC every 15 min. After 45 min, the mixture was cooled and the toluene was removed on a rotary evaporator. The residue was chromatographed on silica gel, elution with 20% EtOAc in hexanes providing 10.3 g (95%) of ketone **18**.
$[\alpha]_D^{20}$ +146.6 (c = 0.73, $CHCl_3$).

(–)-(2a*S*,3a*R*,6*S*,6a*S*,7a*R*)-2,2-Dichlorodecahydro-6-isopropyl-3a-methyl-1*H*-cyclobut[*f*]inden-1-one (19):
Hydrindene **15** (10.8 g, 56.0 mmol) and zinc–copper couple (9.5 g, 146 mmol) were suspended in Et_2O (200 mL). A solution of trichloroacetyl chloride (7.5 mL, 67 mmol) in Et_2O (90 mL) was added over 2 h and the suspension was stirred for an additional 2 h, filtered through Celite with Et_2O, concentrated to one-quarter volume, and diluted with pentane to the original volume. The viscous aqueous layer was removed and extracted with Et_2O (3 × 20 mL). The combined organic phases were washed with brine, sat. $NaHCO_3$, and brine (25 mL each), dried, filtered, and evaporated. Chromatography on silica gel with 4% EtOAc in hexanes yielded **19** (13.0 g, 74%).
IR (neat, cm^{-1}): ν = 1800, 1500, 1380, 1265.
^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.08 (t, J = 9.2 Hz, 1 H), 3.13–3.03 (m, 1 H), 2.26–2.12 (m, 2 H), 1.75–0.92 (m, 9 H), 0.89 (d, J = 6.7 Hz, 3 H), 0.80 (d, J = 6.7 Hz, 3 H), 0.75 (s, 3 H).
^{13}C NMR (75 MHz, $CDCl_3$): δ = 195.7, 87.9, 53.9, 47.3, 46.4, 43.3, 40.9, 39.7, 38.5, 29.8, 23.7, 23.0, 21.7, 18.3, 17.1.
MS m/z (M^+) calcd 288.1048, obsd 288.1056.
$[\alpha]_D^{20}$ –110 (c = 0.9, $CHCl_3$).
Anal. Calcd for $C_{15}H_{22}OCl_2$: C, 62.29; H, 7.66. Found: C, 62.19; H, 7.66.

For the X-ray crystallographic analysis, see Figure 3.

(–)-(2*S*,2a*S*,3a*R*,6*S*,6a*S*,7a*R*)-2-Chlorodecahydro-6-isopropyl-3a-methyl-1*H*-cyclobut[*f*]inden-1-one (20):
Dichlorocyclobutanone **19** (200 mg, 0.69 mmol) was dissolved in a 3% solution of NH_4Cl in MeOH (20 mL) and mixed with a suspension of zinc–copper couple (300 mg). The reduction proceeded to completeness nearly instantaneously at r.t. Et_2O was added and the suspension was filtered through Celite. Monochloro ketone **20** (195 mg, 88%) was recovered as a fine white crystalline compound following chromatography on silica gel with elution by 5% EtOAc in hexanes; mp 108–110 °C.
IR (neat, cm^{-1}): ν = 1795, 1450.
^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.98 (dd, J = 9.0, 2.3 Hz, 1 H), 3.37 (t, J = 8.7 Hz, 1 H), 2.96 (m, J = 9.4 Hz, 1 H), 2.17 (dd, J = 14.4, 4.5 Hz, 1 H), 1.94 (dd, J = 8.2, 14.5 Hz, 1 H), 1.76–1.51 (m, 2 H), 1.01–0.93 (m, 7 H), 0.89 (d, J = 6.7 Hz, 3 H), 0.80 (d, J = 6.7 Hz, 3 H), 0.77 (s, 3 H).
^{13}C NMR (75 MHz, $CDCl_3$): δ = 200.9, 63.4, 53.0, 47.1, 46.0, 40.7, 38.5, 37.3, 29.7, 28.7, 23.7, 22.9, 21.8, 18.2, 17.1.
MS m/z (M^+) calcd 254.1437, obsd 254.1438.

(–)-(2a*R*,3a*R*,6*S*,6a*S*,7a*R*)-Decahydro-6-isopropyl-3a-methyl-1*H*-cyclobut[*f*]inden-1-one (21):
Dichlorocyclobutanone **19** (16 g, 55.4 mmol), zinc–copper couple (10 g, 166 mmol), and solid NH_4Cl (15 g) were suspended in MeOH

(400 mL) and stirred for 1 h at r.t., and at reflux for 1 h. The mixture was cooled, diluted with Et_2O (300 mL), filtered through Celite, and evaporated to dryness. Chromatography of the residue on silica gel with 3% EtOAc in hexanes gave 10.3 g (85%) of **21** as a colorless to slightly yellow oil.
IR (neat, cm^{-1}): ν = 1780, 1460, 1380, 1230, 1050.
^1H NMR (300 MHz, $CDCl_3$): δ = 3.40 (t, *J* = 8.8 Hz, 1 H), 3.25–3.16 (m, 1 H), 2.67–2.54 (m, 1 H), 2.41–2.35 (m, 1 H), 2.21 (dd, *J* = 8.1, 5.2 Hz, 1 H), 2.10 (dd, *J* = 4.4, 9.4 Hz, 1 H), 1.74–1.50 (m, 3 H), 1.50–1.24 (m, 3 H), 1.22–0.92 (m, 3 H), 0.88 (d, *J* = 6.8 Hz, 3 H), 0.79 (d, *J* = 6.8 Hz, 3 H), 0.76 (s, 3 H).
^{13}C NMR (75 MHz, $CDCl_3$): δ = 210.0, 58.0, 52.4, 47.4, 46.8, 44.2, 41.7, 38.7, 29.7, 23.8, 23.3, 22.1, 21.8, 18.2, 17.1.
MS *m/z* (M^+) calcd 220.1827, obsd 220.1827.
$[\alpha]_D^{20}$ –57.7 (*c* = 4.00, $CHCl_3$).
Anal. Calcd for $C_{15}H_{24}O$: C, 81.76; H, 10.98. Found: C, 81.53; H, 11.05.

(±)-(2a*R,3a*R**,6*S**,6a*S**,7a*R**)-Decahydro-6-isopropyl-3a,7a-dimethyl-1*H*-cyclobut[*f*]inden-1-one (22):**
Cyclobutanone **21** (0.050 g, 0.23 mmol) was dissolved in THF (4 mL) at –78 °C, and potassium hexamethyldisilazide (1.13 mL of 0.4 M in toluene, 0.45 mmol) was added dropwise. The solution was stirred for 90 min before MeI (15 mL, 0.28 mmol) was slowly introduced. After 2 h at –78 °C and overnight at r.t., H_2O (3 mL) was added and the products were extracted into Et_2O. The organic layers were dried and the residue was chromatographed on silica gel with 5% EtOAc in hexanes to give 25 mg (47%) of **22** as a colorless oil.
^1H NMR (300 MHz, $CDCl_3$): δ = 3.50–3.41 (m, 1 H), 2.35 (dd, *J* = 2.4, 14.2 Hz, 1 H), 2.28–2.18 (m, 3 H), 1.76–1.56 (m, 3 H), 1.46–1.32 (m, 3 H), 1.31 (s, 3 H), 1.26–0.90 (m, 3 H), 0.88 (d, *J* = 6.7 Hz, 3 H), 0.79 (d, *J* = 6.7 Hz, 3 H), 0.72 (s, 3 H).
^{13}C NMR (75 MHz, $CDCl_3$): δ = 213.9, 62.7, 51.7, 47.7, 47.6, 45.0, 42.1, 38.7, 31.2, 30.4, 29.9, 25.9, 24.2, 21.8, 18.4, 17.6.

(+)-(2a*R*,3a*R*,6*S*,6a*S*,7a*S*)-Decahydro-6-isopropyl-3a-methyl-7a-(phenylsulfanyl)-1*H*-cyclobut[*f*]inden-1-one (23):
A solution of cyclobutanone **21** (3.25 g, 14.7 mmol) and hexamethyldisilazane (3.50 mL, 19.7 mmol) in pentane (325 mL) was cooled to -50 °C before iodotrimethylsilane (2.40 mL, 16.9 mmol) was added. The mixture was stirred at r.t. overnight, cooled to –50 °C, treated with phenylsulfanyl chloride (3.1 mL), and warmed to r.t. with stirring for 30 min. After dilution with CH_2Cl_2, the mixture was washed with sat. $Na_2S_2O_3$, dried, and concentrated. Chromatography of the residue was performed on silica gel with elution by 3% Et_2O in hexanes to furnish 3.40 g (70%, or 90% based on recovered starting material) of **23** as a white solid, mp 50–51 °C.
IR (neat, cm^{-1}) ν = 1770, 1450, 1380, 1060.
^1H NMR (300 MHz, $CDCl_3$): δ = 7.53–7.48 (m, 2H), 7.38–7.28 (m, 3H), 3.79 (dd, *J* = 16.3, 7.5 Hz, 1H), 2.50–2.28 (m, 3H), 2.13 (dd, *J* = 13.9, 4.5 Hz, 1H), 1.77–1.54 (m, 1H), 1.53–1.31 (m, 5H), 1.14–0.86 (m, 3H), 0.80 (d, *J* = 6.5 Hz, 3 H), 0.79 (s, 3 H), 0.71 (d, *J* = 6.5 Hz, 3 H).
^{13}C NMR (75 MHz, $CDCl_3$): δ = 204.7, 135.2 (2 C), 131.2, 129.0, 128.7 (2 C), 69.4, 53.1, 47.7, 47.5, 45.0, 41.7, 38.4, 31.7, 30.5, 29.3, 23.8, 21.8, 17.8, 17.5.
MS *m/z* (M^+) calcd 328.1861, obsd 328.1867.
$[\alpha]_D^{20}$ +118 (*c* = 1.66, $CHCl_3$).
Anal. Calcd for $C_{21}H_{28}OS$: C, 76.79; H, 8.60. Found: C, 76.42; H, 8.59.

(2*R*,2a*R*,3a*R*,6*S*,6a*S*,7a*S*)-Decahydro-6-isopropyl-2,3a-dimethyl-7a-(phenylsulfanyl)-1*H*-cyclobut[*f*]inden-1-one (24):
A stock solution of LDA (15.0 ml of 0.5 M in THF, 7.50 mmol) was added rapidly to a solution of **23** (1.52 g, 4.63 mmol) in THF (200 mL) at 0 °C and stirred for 1 h at r.t. MeI (10 ml, 160 mmol) was added rapidly and the mixture was stirred for 30 min at r.t. before being washed with H_2O (20 mL). The aqueous layer was extracted with Et_2O (2 × 20 mL) and the combined organic phases were dried and evaporated. Chromatography of the residue was performed with 3% Et_2O in hexane to give **24** (1.36 g, 86%) as a colorless oil.
IR (neat, cm^{-1}): ν = 1770, 1580, 1450, 1385, 1085.
^1H NMR (300 MHz, $CDCl_3$): δ = 7.54–7.50 (m, 2 H), 7.49–7.28 (m, 3 H), 2.81–2.72 (m, 1 H), 2.40 (dd, *J* = 9.7, 3.4 Hz, 1 H), 2.23–2.04 (m, 2 H), 1.78–1.57 (m, 1 H), 1.57–1.26 (m, 5 H), 1.50 (d, *J* = 7.6 Hz, 3 H), 1.26–0.88 (m, 3 H), 0.83 (s, 3 H), 0.78 (d, *J* = 6.7 Hz, 3 H), 0.72 (d, *J* = 6.7 Hz, 3 H).
^{13}C NMR (75 MHz, $CDCl_3$): δ = 210.3, 135.4 (2 C), 131.4, 128.9, 128.7 (2 C), 66.2, 63.4, 47.8, 47.6, 45.6, 42.1, 39.0, 32.6, 29.4, 24.0, 21.8, 18.6, 17.9.
MS *m/z* (M^+) calcd 342.2017, obsd 342.2018.

(2*S*,2a*R*,3a*R*,6*S*,6a*S*,7a*S*)-Decahydro-2-(hydroxymethyl)-6-isopropyl-2,3a-dimethyl-7a-(phenylsulfanyl)-1*H*-cyclobut[*f*]inden-1-one (25):
Methylcyclobutanone **24** (2.0 g, 5.8 mmol) in THF (100 mL) was deprotonated with LDA (11.7 mL of 0.5 M solution in THF) over 45 min at –78 °C. Excess monomeric formaldehyde (15 mL of formaldehyde solution in THF) was added quickly and the mixture was stirred for 20 min at –78 °C, quenched with H_2O (30 mL) at –78 °C, and diluted with Et_2O (20 mL) after warming to 20 °C. The aqueous layer was extracted with Et_2O (3 × 15 mL) and the extracts were dried and evaporated. Chromatography of the residue was performed on silica gel using 20% EtOAc in hexanes to give **25** (1.41g, 65%) as a white solid.
IR (neat, cm^{-1}): ν = 3600–3100, 1770, 1440, 1390, 1030.
^1H NMR (300 MHz, $CDCl_3$): δ = 7.55–7.50 (m, 2 H), 7.37–7.26 (m, 3 H), 4.03 (dd, *J* = 9.9, 8.5 Hz, 2 H), 2.50 (dd, *J* = 8.9, 2.8 Hz, 1 H), 2.15 (dd, *J* = 4.9, 9.2 Hz, 1 H), 1.96 (dd, *J* = 10.8, 2.7 Hz, 1 H), 1.76–1.66 (m, 1 H), 1.57–1.32 (m, 8 H), 1.17 (s, 3 H), 1.11–0.93 (m, 1 H), 0.88 (s, 3 H), 0.78 (d, *J* = 6.7 Hz, 3 H), 0.71 (d, *J* = 6.7 Hz, 3 H).
^{13}C NMR (75 MHz, $CDCl_3$): δ = 211.1, 135.0 (2 C), 131.2, 128.9, 128.7 (2 C), 70.3, 66.6, 64.5, 47.9, 47.7, 41.7, 39.3, 38.4, 37.1, 33.1, 29.6, 24.2, 21.8, 19.3, 18.0, 15.1.

(–)-(2*S*,2a*S*,3a*R*,6*S*,6a*S*,7a*R*)-Decahydro-2-(hydroxymethyl)-6-isopropyl-2,3a-dimethyl-1*H*-cyclobut[*f*]inden-1-one (26):
Ketone **25** (1.15 g, 3.09 mmol) in MeOH (100 mL) with NH_4Cl (1.25 g, 23.3 mmol) and zinc–copper couple (4 g, 62 mmol) was stirred overnight at r.t. To this was added Et_2O (80 mL) and the suspension was filtered through Celite. Solvent was evaporated and the residue was chromatographed on silica gel with 25% EtOAc in hexanes to give **26** (0.670 g, 82%) as a white solid, mp 73–74 °C.
IR (neat, cm^{-1}): ν = 3470, 1740, 1470, 1380, 1040.
^1H NMR (300 MHz, $CDCl_3$): δ = 3.75 (br s, 2 H), 3.62 (dd, *J* = 9.9, 1.9 Hz, 1 H), 2.51–2.42 (m, 1 H), 2.13 (dd, *J* = 4.9, 9.1 Hz, 1 H), 1.87 (dd, *J* = 8.4, 4.8 Hz, 1 H), 1.76–1.56 (m, 3 H), 1.52–1.30 (m, 3 H), 1.27–1.12 (m, 3 H), 1.09 (s, 3 H), 1.05–0.92 (m, 1 H), 0.88 (d, *J* = 6.6 Hz, 3 H), 0.80 (d, *J* = 6.6 Hz, 3 H), 0.76 (s, 3 H).
^{13}C NMR (75 MHz, $CDCl_3$): δ = 213.0, 69.1, 67.1, 54.8, 47.8, 47.1, 41.3, 38.9, 37.9, 29.8, 29.6, 23.9, 23.1, 21.8, 18.4, 17.2, 12.6.
MS *m/z* (M^+) calcd 264.2089, obsd 264.2082.
$[\alpha]_D^{20}$ –63 (*c* = 2.02, $CHCl_3$).
Anal. Calcd for $C_{17}H_{28}O_2$: C, 77.23; H, 10.67. Found: C, 77.02; H, 10.68.

(1*S*,2a*R*,3a*S*,4*S*,6a*R*,7a*S*)-Decahydro-4-isopropyl-1,6a-dimethyl-2-oxo-1*H*-cyclobut[*f*]indene-1-carboxaldehyde (27):
Cyclobutanone **26** (420 mg, 1.52 mmol) was dissolved in CH_2Cl_2 (30 mL) and cooled to 0 °C. Pyridinium chlorochromate on alumina (1.6 g, 1.6 mmol) was added in one portion and the mixture was stirred for 10 h at r.t. The suspension was filtered through silica gel and eluted with 25% EtOAc in hexanes. Clear white crystals of **27** formed on standing: 357 mg (89%); mp 65–67 °C.
IR (neat, cm^{-1}): ν = 1785, 1720, 1470.
^1H NMR (300 MHz, $CDCl_3$): δ = 9.55 (s, 1 H), 3.69 (dd, *J* = 8.0, 3.1 Hz, 1 H), 3.03–2.93 (m, 1 H), 2.13 (dd, *J* = 4.8, 9.4 Hz, 1 H), 1.89 (dd, *J* = 8.2, 5.0 Hz, 1 H), 1.74–1.37 (m, 5 H), 1.36 (s, 3 H), 1.34–0.94 (m, 4 H), 0.89 (d, *J* = 6.8 Hz, 3 H), 0.81 (d, *J* = 6.8 Hz, 3 H), 0.80 (s, 3 H).
^{13}C NMR (75 MHz, $CDCl_3$): δ = 201.3, 197.1, 79.9, 57.5, 47.5, 46.8, 41.2, 38.9, 37.3, 29.8, 28.5, 23.8, 22.8, 21.8, 18.3, 17.0, 10.9.

MS *m/z* (M^+) calcd 262.1933, obsd 262.1943.
Anal. Calcd for $C_{17}H_{26}O_2$: C, 77.80; H, 9.99. Found: C, 78.18; H, 9.74.

(–)-(2*R*,2a*S*,3a*R*,6*S*,6a*R*,7a*R*)-Decahydro-6-isopropyl-2,3a-dimethyl-2-vinyl-1*H*-cyclobut[*f*]inden-1-one (8):
To a solution of methyltriphenylphosphonium bromide (366 mg, 1.02 mmol) in anhyd Et_2O (45 mL) at –70 °C was added potassium hexamethyldisilazide (2.05 mL, 1.5 M solution in toluene, 1.02 mmol) and the mixture was stirred for 40 min. Oxo aldehyde **27** (257 mg, 0.98 mmol) dissolved in Et_2O (10 mL) was added dropwise at –78 °C. After 45 min at r.t., the yellow mixture turned white and was quenched with sat. $NaHCO_3$ (15 mL). The separated organic phase was dried and concentrated. Chromatography of the residue on silica gel with 5% EtOAc in hexanes gave **8** (200 mg, 79%) as a colorless oil.
IR (neat, cm^{-1}): ν = 1760, 1630, 1460, 1390.
^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.98 (dd, *J* = 10.4, 6.9 Hz, 1 H), 5.08 (d, *J* = 17.5 Hz, 1 H), 5.05 (d, *J* = 10.5 Hz, 1 H), 3.66 (dd, *J* = 8.1, 2.5 Hz, 1 H), 2.58–2.48 (m, 1 H), 2.12 (dd, *J* = 4.8, 9.1 Hz, 2 H), 1.88 (dd, *J* = 8.1, 5.2 Hz, 2 H), 1.73–1.53 (m, 3 H), 1.49–1.15 (m, 4 H), 1.13 (s, 3 H), 0.89 (d, *J* = 6.7 Hz, 3 H), 0.80 (d, *J* = 6.7 Hz, 3 H), 0.76 (s, 3 H).
^{13}C NMR (75 MHz, $CDCl_3$): δ = 210.9, 142.1, 113.1, 67.8, 54.3, 47.6, 46.9, 41.3, 38.9, 38.0, 32.2, 29.8, 23.9, 22.8, 21.8, 18.4, 17.1, 15.2.
MS *m/z* (M^+) calcd 260.2140, obsd 260.2147.
$[\alpha]_D^{20}$ –92 (*c* = 0.715, $CHCl_3$).
Anal. Calcd for $C_{18}H_{28}O$: C, 83.02; H, 10.84. Found: C, 82.77; H, 10.93.

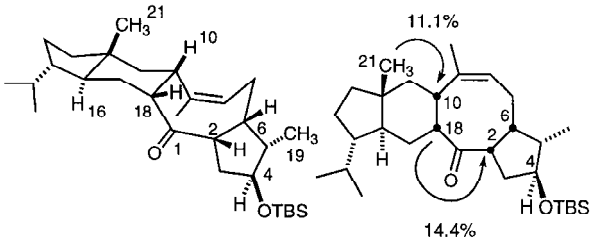
(3*S*,4*S*)-4-(*tert*-Butyldimethylsiloxy)-3-methylcyclopent-1-en-1-yl Trifluoromethanesulfonate (28):
Copper(I) bromide–dimethyl sulfide complex (1.87 g, 9.1 mmol) was dried under vacuum, suspended in THF (120 mL), cooled to –78 °C and treated with MeLi (12 mL, 18 mmol). The slightly yellow solution was stirred for 1 h before (–)-**11** (1.75 g, 8.24 mmol) in cold (–78 °C) THF (40 mL) was added dropwise via cannula. After 15 min, *N*-(5-chloro-2-pyridyl)triflimide (6.00 g, 15.2 mmol) dissolved in THF (40 mL) was added via cannula at –50 °C, and the mixture was stirred at –50 °C for 45 min and poured into 15% ammonium hydroxide (100 mL). Hexanes (100 mL) were added followed by extraction of the aqueous layer with Et_2O (3 × 25 mL). The combined organic layers were dried and evaporated, and the residue was chromatographed on silica gel with 3% Et_2O in hexanes to give **28** (1.99 g, 67%) as a clear light oil.
IR (neat, cm^{-1}): ν = 1665, 1435, 1260, 1220, 1150.
^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.47 (br s, 1 H), 4.01 (m, 1 H), 2.87–2.78 (m, 1 H), 2.71–2.61 (m, 1 H), 2.56–2.48 (m, 1 H), 1.50 (d, *J* = 6.1 Hz, 3 H), 0.89 (s, 9 H), 0.71 (s, 3 H), 0.63 (s, 3 H).
^{13}C NMR (75 MHz, $CDCl_3$): δ = 145.5, 120.7, 45.9, 40.7, 25.7 (3 C), 18.0, –4.7, –4.8 (CF_3 not detected).
MS *m/z* (M^+) calcd 360.1038, obsd 360.1038.
$[\alpha]_D^{20}$ –27.6 (*c* = 2.42, $CHCl_3$).

(–)-[(3*S*,4*S*)-4-(*tert*-Butyldimethylsiloxy)-3-methylcyclopent-1-en-1-yl]trimethylstannane (29):
Vinyl triflate **28** (312 mg, 0.87 mmol) was dissolved in THF (30 mL) and treated in order with hexamethylditin (312 mg, 0.95 mmol), LiCl (280 mg, 6.6 mmol; dried under vacuum and heated prior to addition), and tetrakis(triphenylphosphine)palladium(0) (115 mg, 0.1 mmol). The mixture was stirred at 20 °C for 1 h and heated for 45 min at 65 °C. The product was isolated by adding hexanes (15 mL) and washing with H_2O (2 x 15 mL). The aqueous layer was extracted with hexanes (2 × 5 mL) and the combined organic solutions were dried, filtered and concentrated. Chromatography of the residue on silica gel with 2% Et_2O in hexanes containing 1% Et_3N gave **29** (260 mg, 78%) as a colorless oil.
IR (neat, cm^{-1}): ν = 1465, 1365, 1255, 1110.
^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.76–5.62 (m, 1 H), 4.00–3.94 (m, 1 H), 2.71–2.58 (m, 2 H), 2.34–2.26 (m, 1 H), 1.01 (d, *J* = 7.2 Hz, 3 H), 0.90 (s, 9 H), 0.11 (s, 6 H), 0.10–0.06 (m, 9 H).
^{13}C NMR (75 MHz, $CDCl_3$): δ = 145.1, 140.5, 81.6, 50.3, 47.5, 25.9 (3 C), 18.2, 18.1, –4.5, –4.6, –10.2.
MS *m/z* (M^+) calcd 376.1244, obsd 376.1245.
$[\alpha]_D^{20}$ –34.8 (*c* = 1.73, $CHCl_3$).

(+)-{[(1*S*,2*S*)-4-Bromo-2-methylcyclopent-3-en-1-yl]oxy}-*tert*-butyldimethylsilane (30):
Lithium chloride (192 mg, 4.55 mmol) was placed in a 50-mL round-bottomed flask and dried under vacuum with a flame. $Pd(PPh_3)_4$ (90 mg, 0.078 mmol) was added and dissolved in THF (15 mL). Hexamethylditin (210 mg, 0.64 mmol) was introduced followed by **28** (235 mg, 0.65 mmol) in THF (5 mL) . The mixture was stirred at 20 °C for 30 min and heated to 75 °C for 3 h. The stirring bar was removed and the THF was evaporated to 1/3 volume. The remainder was poured into hexanes (50 mL), filtered through a pad of Celite with 1% triethylamine in hexanes, washed with $NaHCO_3$ (15 mL) and dried. The solvent was removed and the crude tin compound (204 mg) was redissolved in CH_2Cl_2 (10 mL). Br_2 (96 mg, 0.60 mmol) was added as a 0.1 M solution in CH_2Cl_2 (6 mL) at –78 °C. After 5 min, the mixture was washed with 5 mL each of NH_4OH, H_2O, and brine, then dried and concentrated. Chromatography of the residue on silica gel (elution with 2% Et_2O in hexanes) furnished **30** as a colorless oil (122 mg, 64%).
IR (neat, cm^{-1}): ν = 1475, 1370, 1260, 1120.
^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.71 (t, *J* = 1.9 Hz, 1 H), 4.03–3.97 (m, 1 H), 2.87–2.78 (m, 1 H), 2.62–2.50 (m, 2 H), 1.05 (d, *J* = 7.1 Hz, 3 H), 0.89 (s, 9 H), 0.065 (s, 3 H), 0.06 (s, 3 H).
^{13}C NMR (75 MHz, $CDCl_3$): δ = 134.7, 117.3, 79.7, 49.6, 48.8, 25.8 (3 C), 18.1, 17.9, –4.7, –4.8.
MS *m/z* (M^+) calcd 290.0701, obsd 290.0710.
$[\alpha]_D^{20}$ +50.3 (*c* = 6.2, $CHCl_3$).

(2*S*,3*S*,3a*R*,6a*S*,7a*R*,10*S*,10a*S*,11a*R*,12a*S*)-2-(*tert*-Butyldimethylsiloxy)-2,3,3a,4,6a,7,7a,8,9,10,10a,11,11a,12a-tetradecahydro-10-isopropyl-3,6,7a-trimethylcyclopenta[4,5]cyclooct[1,2-*f*]inden-12(1*H*)-one (34a):
Vinyl bromide **30** (173 mg, 0.60 mmol) was placed in a flame-dried flask with a stirring bar and anhyd THF (15 mL) at –78 °C, and *t*-BuLi (0.70 mL, 1.19 mmol) was added via syringe. After 45 min, a solution of **8** (140 mg, 0.54 mmol) in THF (5 mL) was added via cannula at –78 °C. The mixture was stirred for 20 min, H_2O (5 mL) was added, and the solution was warmed to 20 °C. Hexane (5 mL) was added, the organic layer was separated, and the aqueous phase was extracted with Et_2O (2 × 10 mL), and dried. The residue was chromatographed on TLC grade silica gel (elution with hexane to 2% Et_2O in hexanes) to give **34a** (175 mg, 69%) as a colorless oil.
IR (neat, cm^{-1}): ν = 1695, 1460, 1375, 1255, 1080.
^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.46 (m, 1 H), 4.13 (m, 1 H), 3.34 (m, 1 H), 3.03 (m, 1 H), 2.51–2.28 (m, 2 H), 2.22–2.05 (m, 2 H), 1.90–1.84 (m, 5 H), 1.80 (s, 3 H), 1.78–1.23 (m, 8 H), 1.20–0.98 (m, 4 H), 0.91 (d, *J* = 7.2 Hz, 6 H), 0.89 (s, 6 H), 0.87 (s, 3 H), 0.78 (s, 3 H), 0.03 (s, 6 H).

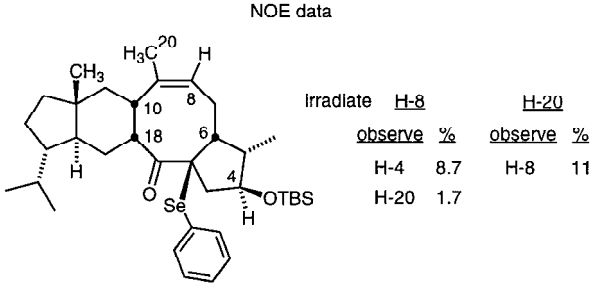
NOE data



irradiate	H-4		H-2		H-18		H-21	
	observe	%	observe	%	observe	%	observe	%
	H-3	4.9	H-18	11.5	H-2	14.4	H-10	11.1
	H-5	3.1	H-6	9.5	H-10	6.6	H-11'	3.4
	H-19	3.6	H-3	5.2	H-17	2.1	H-15'	7.9
					H-17'	4.4	H-17'	3.0

^{13}C NMR (75 MHz, $CDCl_3$): δ = 219.4, 138.1, 126.0, 81.5, 52.9, 52.1, 46.2, 46.1, 44.4, 42.4, 41.9, 41.7, 41.3, 38.9, 38.2, 28.9, 28.2, 28.1, 27.1, 25.9 (3 C), 22.8, 22.1, 18.1, 17.6, 17.3, 13.4, –4.7 (2 C).
MS *m/z* (M^+) calcd 472.3737, obsd 472.3728.
Anal. Calcd for $C_{30}H_{52}O_2Si$: C, 76.21; H, 11.08. Found: C, 76.26; H, 11.12.

(–)-(2*S*,3*S*,3a*R*,6a*S*,7a*R*,10*S*,10a*S*,11a*R*,12a*R*)-2-(*tert*-Butyldimethylsiloxy)-2,3,3a,4,6a,7,7a,8,9,10,10a,11,11a,12a-tetradecahydro-10-isopropyl-3,6,7a-trimethyl-12a-(phenylseleno)cyclopenta-[4,5]cyclooct[1,2-*f*]inden-12(1*H*)-one (34b):
Vinyl bromide **30** (175 mg, 0.60 mmol) in THF (20 mL) was cooled to –78 °C and reacted with *tert*-butyllithium (860 μL, 1.20 mmol) for 15 min. A solution of **8** (135 mg, 0.52 mmol) in THF (5 mL) was cooled to –78 °C and added dropwise via cannula. After the mixture had been stirred for 40 min, a solution of phenylselenyl chloride (33 mg, 0.173 mmol) in THF (3 mL) cooled to –78 °C was added dropwise via cannula. The mixture was stirred for 20 min, warmed to –50 °C, and quenched with H_2O (5 mL). The aqueous portion was extracted with Et_2O (2 × 10 mL) and the organic solution was dried and concentrated. Chromatography of the residue on silica gel with 2% Et_2O in hexanes gave 297 mg (91%) of **34b** as a white solid, mp 123–125 °C.
IR (neat, cm^{-1}): ν = 1680, 1420, 1120.
^{1}H NMR (300 MHz, C_6D_6): δ = 7.62–7.59 (m, 2 H), 7.12–7.02 (m, 3 H), 5.18 (t, *J* = 7.8 Hz, 1 H), 3.85–3.73 (m, 2 H), 2.98–2.94 (m, 1 H), 2.81–2.73 (m, 2 H), 2.50 (dd, *J* = 3.7, 13.9 Hz, 2 H), 2.32–2.23 (m, 1 H), 2.22–2.16 (m, 2 H), 2.01–1.66 (m, 6 H), 1.62 (s, 3 H), 1.59–1.22 (m, 4 H), 1.06–0.86 (m, 18 H), 0.76 (s, 3 H), 0.02 (s, 3 H), –0.05 (s, 3 H).
^{13}C NMR (75 MHz, C_6D_6): δ = 208.0, 143.5, 136.8, 129.9, 129.1, 129.0, 128.2, 128.1, 127.9, 123.9, 78.6, 64.2, 49.6, 47.3, 45.6, 44.5, 44.4, 42.2, 41.6, 41.5, 40.0, 36.9, 31.3, 29.2, 26.1, 25.8 (3 C), 24.2, 22.7, 22.5, 18.3, 17.5, 17.2, 13.7, –4.4, –4.8.
MS *m/z* (M^+) calcd 628.3215, obsd 628.3218.
$[\alpha]_D^{20}$ –8.3 (*c* = 0.42, $CHCl_3$).
Anal. Calcd for $C_{36}H_{56}O_2SeSi$: C, 68.87; H, 8.99. Found: C, 68.93; H, 9.01.



(+)-(2*R*,3*S*,3a*R*,6a*S*,7a*R*,10*S*,10a*S*,11a*R*)-2-(*tert*-Butyldimethylsiloxy)-3,3a,4,6a,7,7a,8,9,10,10a,11,11a-dodecahydro-10-isopropyl-3,6,7a-trimethylcyclopenta[4,5]cyclooct[1,2-*f*]inden-12(2*H*)-one (35a) and (2*S*,3*S*,6a*S*,7a*R*,10*S*,10a*S*,11a*R*)-2-(*tert*-Butyldimethylsiloxy)-2,3,4,6a,7,7a,8,9,10,10a,11,11a-dodecahydro-10-isopropyl-3,6,7a-trimethylcyclopenta[4,5]cyclooct[1,2-*f*]inden-12(1*H*)-one (36a):
Method A. Oxidation with Hydrogen Peroxide:
Oxo selenide **34b** (40 mg, 0.064 mmol) was dissolved in CH_2Cl_2 (10 mL) and pyridine (0.4 mL). H_2O_2 (0.5 mL, 30% solution) was added at 0 °C and the mixture was allowed to warm to r.t. during 2 h. H_2O (5 mL) was added and the organic phase was washed with H_2O (2 × 5 mL). The organic layer was dried, freed of solvent, and chromatographed on silica gel with 2% Et_2O in hexanes to furnish **35a** (19 mg, 62%) and **36a** (7 mg, 23%).

For **35a**:
IR (neat, cm^{-1}): ν = 2960, 1675, 1610, 1460, 1370, 1250, 1040, 835.
^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.38 (t, *J* = 2.2 Hz, 1 H), 5.35 (t, *J* = 8.6 Hz, 1 H), 4.29 (br s, 1 H), 3.69 (t, *J* = 7.5 Hz, 1 H), 3.47 (t, *J* = 7.2 Hz, 1 H), 3.01–2.92 (m, 1 H), 2.80–2.69 (m, 1 H), 2.28–2.13 (m, 1 H), 1.89–1.54 (m, 3 H), 1.63 (s, 3 H), 1.45–1.03 (m, 9 H), 0.97 (d, *J* = 7.4 Hz, 3 H), 0.95–0.79 (m, 15 H), 0.77 (s, 3 H), 0.07 (s, 3 H), 0.06 (s, 3 H).
^{13}C NMR (75 MHz, $CDCl_3$): δ = 205.7, 149.0, 139.6, 137.7, 125.2, 99.6, 82.8, 77.2, 46.9, 46.0, 45.8, 45.1, 44.5, 41.4, 40.8, 39.5, 36.2, 29.6, 26.9, 26.3, 25.9 (3 C), 25.8, 24.4, 23.3, 21.9, 18.3, 17.0, 14.9, –4.6, –4.7.
MS *m/z* (M^+) calcd 470.3580, obsd 470.3592.
$[\alpha]_D^{20}$ +34 (*c* = 0.31, $CHCl_3$).
Anal. Calcd for $C_{30}H_{50}O_2Si$: C, 76.53; H, 10.70. Found: C, 76.40; H, 10.72.

For **36a**:
IR (neat, cm^{-1}): ν = 1650, 1450, 1360, 1240, 1100.
^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.47 (t, *J* = 8.5 Hz, 1 H), 3.90–3.86 (m, 1 H), 3.63 (t, *J* = 6.5 Hz, 1 H), 3.15 (dd, *J* = 7.1, 6.8 Hz, 1 H), 2.79–2.50 (m, 5 H), 1.83–1.11 (m, 11 H), 1.69 (s, 3 H), 1.07 (d, *J* = 7.2 Hz, 3 H), 0.88 (s, 9 H), 0.87 (d, *J* = 6.8 Hz, 3 H), 0.84 (d, *J* = 6.8 Hz, 3 H), 0.80 (s, 3 H), 0.05 (s, 3 H), 0.04 (s, 3 H).
^{13}C NMR (75 MHz, $CDCl_3$): δ = 207.7, 153.6, 140.5, 136.9, 127.7, 123.2, 77.9, 54.5, 49.0, 46.5, 44.5, 42.6, 41.8, 39.6, 39.3, 37.9, 29.4, 28.8, 28.5, 25.9 (3 C), 23.0, 22.1, 18.2, 18.1, 17.3, 15.9, –4.6, –4.8.
MS *m/z* (M^+) calcd 470.3580, obsd 470.3579.

Method B. Peracid Oxidation.
A solution of **34b** (297 mg, 0.47 mmol) in CH_2Cl_2 (100 mL) cooled to –5 °C was treated with MCPBA (81 mg, 172 mmol) in one portion. The mixture turned yellow and then almost clear before more peracid was added at 45 minute intervals. The solution was washed with sat. $NaHCO_3$ (2 × 10 mL) and the organic phase was dried and concentrated. Chromatography as before furnished both **35a** (154 mg, 70%) and **36a** (59 mg, 27%).

(2*S*,3*S*,3a*R*,6a*S*,7a*R*,10*S*,10a*S*,11a*R*,12a*R*)-2,3,3a,4,6a,7,7a,8,9,10,10a,11,11a,12a-Tetradecahydro-2-hydroxy-10-isopropyl-3,6,7a-trimethyl-12a-(phenylseleno)cyclopenta[4,5]cyclooct[1,2-*f*]-inden-12(1*H*)-one (37):
A solution of **34b** (30 mg, 0.048 mmol) in THF (10 mL) at –5 °C was reacted with tetrabutylammonium fluoride (60 µL, 0.06 mmol) in THF over 10 min at r.t. Product **37** (20 mg, 82%) was isolated as a white solid, mp 160 °C, after chromatography on silica gel with 35% EtOAc in hexanes.
IR (neat, cm^{-1}): ν = 3440, 1630, 1420.
^{1}H NMR (300 MHz, C_6D_6): δ = 7.57–7.53 (m, 2 H), 7.10–7.02 (m, 3 H), 5.10 (t, *J* = 8.1 Hz, 1 H), 3.85 (t, *J* = 7.3 Hz, 1 H), 3.56–3.48 (m, 1 H), 2.77–2.68 (m, 3 H), 2.44 (dd, *J* = 10.2, 3.6 Hz, 1 H), 2.33–2.13 (m, 3 H), 1.93–1.85 (m, 3 H), 1.82–1.74 (m, 1 H), 1.72–1.62 (m, 3 H), 1.63 (s, 3 H), 1.57–1.42 (m, 3 H) 1.40–1.18 (m, 2 H), 1.04–0.97 (m, 6 H), 0.93 (d, *J* = 6.9 Hz, 3 H), 0.75 (s, 3 H).
^{13}C NMR (75 MHz, C_6D_6): δ = 208.5, 143.2, 136.2 (2 C), 130.2, 128.9, 128.6, 127.9, 123.9, 78.1, 64.4, 50.1, 47.3, 45.6, 44.5, 44.4, 42.3, 41.6, 41.5, 39.9, 37.1, 31.2, 29.1, 25.9, 24.4, 22.8, 22.5, 17.5, 17.2, 13.6.
MS *m/z* (M^+) calcd 514.2350, obsd 514.2348.
Anal. Calcd for $C_{30}H_{42}O_2Se$: C, 70.15; H, 8.24. Found: C, 69.86; H, 8.22.

(2*R*,3*S*,3a*R*,6a*S*,7a*R*,10*S*, 10a*S*,11a*R*)-3, 3a,4,6a,7,7a,8,9,10,10a, 11,11a-Dodecahydro-2-hydroxy-10-isopropyl-3,6,7a-trimethylcyclopenta[4,5]cyclooct[1,2-*f*]inden-12(2*H*)-one (35b) and (2*S*,3*S*,6a*S*,7a*R*, 10*S*,10a*S*,11a*R*)-2,3,4,6a,7,7a,8,9,10,10a,11,11a-Dodecahydro-2-hydroxy-10-isopropyl-3,6,7a-trimethylcyclopenta[4,5]cyclooct[1,2-*f*]inden-12(1*H*)-one (36b):
Compound **37** (12 mg, 0.024 mmol) was dissolved in CH_2Cl_2 (10 mL) and cooled to –10 °C. MCPBA (4.8 mg, 0.028 mmol) was added in one portion and allowed to react for 1 h while being allowed to warm to r.t. The mixture was washed with sat. $NaHCO_3$ (2 × 5 mL), dried, filtered, and evaporated. Purification of the residue on silica gel with elution by 40% EtOAc in hexanes furnished **35b** (8.0 mg) and **36b** (3.1 mg) (96% combined).

For **35b:** white solid, mp 148–151 °C.
IR (neat, cm^{-1}): ν = 3240, 1720, 1600, 1460, 1375.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.46 (t, *J* = 2.4 Hz, 1 H), 5.33 (t, *J* = 7.8 Hz, 1 H), 4.32 (m, 1 H), 3.70 (t, *J* = 7.4 Hz, 1 H), 3.50 (m, 1 H), 2.97 (m, 1 H), 2.85–2.70 (m, 1 H), 2.32–2.27 (m, 1 H), 2.24–2.16 (m, 1 H), 1.90–1.77 (m, 3 H), 1.71–1.65 (m, 2 H), 1.64 (s, 3 H), 1.62–1.53 (m, 2 H), 1.46–1.32 (m, 4 H), 1.26–1.20 (m, 1 H), 1.01 (d, *J* = 7.4 Hz, 3 H), 0.91 (d, *J* = 6.8 Hz, 3 H), 0.87 (d, *J* = 6.8 Hz, 3 H), 0.77 (s, 3 H).
^{13}C NMR (75 MHz, $CDCl_3$): δ = 205.6, 150.2, 139.9, 136.8, 124.9, 82.4, 46.9, 46.3, 46.0, 45.2, 44.6, 41.5, 40.8, 39.5, 36.3, 29.7, 27.0, 26.3, 24.5, 23.5, 21.9, 18.4, 17.0, 14.8.
MS *m/z* (M^+) calcd 356.2715, obsd 356.2714.
Anal. Calcd for $C_{24}H_{36}O_2$: C, 80.85; H, 10.18. Found: C, 81.22; H, 9.98.

For **36b**: heavy, colorless oil.
IR (neat, cm^{-1}): ν = 3420, 2930, 2780, 1640, 1440, 1370.
^{1}H NMR (300 MHz, C_6D_6): δ = 5.38 (t, *J* = 7.7 Hz, 1 H), 3.88–3.85 (m, 1 H), 3.61 (t, *J* = 6.0 Hz, 1 H), 3.13 (dd, *J* = 8.4, 8.6 Hz, 1 H), 2.85 (dd, *J* = 5.9, 10.7 Hz, 1 H), 2.66–2.48 (m, 3 H), 2.36 (d, *J* = 6.6 Hz, 1 H), 1.79–1.57 (m, 2 H), 1.58 (s, 3 H), 1.56–1.03 (m, 9 H), 0.98 (d, *J* = 7.3 Hz, 3 H), 0.93–0.82 (m, 1 H), 0.78 (d, *J* = 6.8 Hz, 3 H), 0.73 (d, *J* = 6.8 Hz, 3 H), 0.70 (s, 3 H).

Rhodium Trichloride-Promoted Isomerizations.
Method A: To a solution of **35a** (91 mg, 0.19 mmol) in EtOH (30 mL) was added $RhCl_3 \cdot 3H_2O$ (14 mg, 0.054 mmol) and the orange mixture was heated to reflux for 20 h. The residue was purified by chromatography on silica gel with 30% EtOAc in hexanes to give 24 mg (35%) of **36a**.

Method B: A solution of **35b** (7.7 mg, 0.022 mmol) in EtOH (10 mL) was treated with rhodium trichloride (4.6 mg, 0.022 mmol) and the solution was heated to reflux for 17 h. The EtOH was removed and the residue was placed atop a column of silica gel and eluted with 20–25% EtOAc in hexanes to deliver 3 mg (35%) of **36b**.

(2*S*,3*S*,6a*S*,7a*R*,10*S*,10a*S*)-2-(*tert*-Butyldimethylsiloxy)-2,3,6a,7,7a,8,9,10,10a,11,11a,12a-dodecahydro-10-isopropyl-3,6,7a-trimethylcyclopenta[4,5]cyclooct[1,2-*f*]inden-12(1*H*)-one (40):
Ketone **36a** (4.3 mg, 9.1 mmol) was dissolved in a solution of K_2CO_3 (3 mg) in MeOH (3 mL) and THF (0.5 mL) and stirred for 48 h. The mixture was concentrated, CH_2Cl_2 (10 mL) was added, and the organic solution was dried, filtered, and evaporated. The residue was purified on silica gel with elution by 1.5% Et_2O in hexanes to furnish **40** (2.5 mg, 58%) as a white solid, mp 110–127 °C.
^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.06 (t, *J* = 10.6 Hz, 1 H), 5.85 (m, 1 H), 3.91–3.88 (m, 1 H), 3.28 (dd, *J* = 0.5, 4.9 Hz, 1 H), 3.02 (dd, *J* = 6.2, 8.0 Hz, 1 H), 2.77 (m, 1 H), 2.45 (dd, *J* = 9.0, 1.4 Hz, 1 H), 2.25–2.15 (m, 1 H), 2.12–2.05 (m, 1 H), 1.96–1.90 (m, 1 H), 1.80–1.10 (m, 10 H), 1.01 (d, *J* = 7.3 Hz, 3 H), 0.99–0.80 (m, 18 H), 0.75 (s, 3 H), 0.07 (s, 6 H).
^{13}C NMR (75 MHz, $CDCl_3$): δ = 205.1, 149.7, 145.8, 137.2, 124.7, 53.9, 50.1, 46.2, 45.5, 45.0, 41.6, 41.4, 40.3, 39.0, 36.8, 29.0, 27.0, 25.9 (3 C), 23.1, 22.0, 18.6, 18.2, 17.8, 17.7, 16.8, –4.5, –4.8.
MS *m/z* (M^+) calcd 470.3580, obsd 470.3590.

(+)-(2*R*,3*S*,3a*R*,6a*S*,7a*R*,10*S*,10a*S*,11a*S*)-2-(*tert*-Butyldimethylsiloxy)-3,3a,4,6a,7,7a,8,9,10,10a,11,11a-dodecahydro-10-isopropyl-3,6,7a-trimethylcyclopenta[4,5]cyclooct[1,2-*f*]inden-12(2*H*)-one (41):
Ketone **35a** (28 mg, 59 mmol) was dissolved in MeOH (10 mL), K_2CO_3 (5 mg) was added, and the suspension was stirred for 12 h at r.t. After an additional 12 h at 60 °C, the MeOH was removed and CH_2Cl_2 (3 mL) was added. The mixture was dried and concentrated, and the residue was purified by chromatography on silica gel with 1.5% Et_2O in hexanes to furnish **41** (15 mg, 53%) as a white solid, mp 95–110 °C.
^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.58 (s, 1 H), 5.16 (br d, *J* = 7.2 Hz, 1 H), 4.46 (d, *J* = 8.2 Hz, 1 H), 3.75–3.67 (m, 1 H), 3.45 (t, *J* = 3.3 Hz, 1 H), 2.48–2.25 (m, 3 H), 2.00–1.85 (m, 1 H), 1.80–1.60 (m, 4 H), 1.56 (s, 4 H), 1.52–1.30 (m, 4 H), 1.30–1.13 (m, 5 H), 1.10 (d, *J* = 7.0 Hz, 3 H), 0.95–0.82 (m, 12 H), 0.79 (d, *J* = 6.8 Hz, 3 H), 0.08 (s, 6 H).
^{13}C NMR (75 MHz, $CDCl_3$): δ = 203.3, 146.9, 145.0, 139.7, 122.7, 81.1, 58.5, 50.4, 47.5, 45.8, 45.1, 42.9, 41.9, 38.9, 36.6, 29.1, 28.8, 28.4, 25.8 (3 C), 23.0, 21.9, 19.1, 18.9, 18.1, 17.6, 12.2, –4.5, –4.8.
MS *m/z* (M^+) calcd 470.3580, obsd 470.3581.
$[\alpha]_D^{20}$ +167 (*c* = 1.11, $CHCl_3$).

(2*S*,3*S*,7a*S*,10*S*,10a*S*)-2-(*tert*-Butyldimethylsiloxy)-2,3,7,7a,8,9,10,10a,11,11a-decahydro-10-isopropyl-3,6,7a-trimethylcyclopenta[4,5]cyclooct[1,2-*f*]inden-12(1*H*)-one (42a) and (2*S*,3*S*,7a*S*,10*S*,10a*S*)-2,3,7,7a,8,9,10,10a,11,11a-Decahydro-2-hydroxy-10-isopropyl-3,6,7a-trimethylcyclopenta[4,5]cyclooct[1,2-*f*]inden-12(1*H*)-one (42b):
SeO_2 on silica gel (260 mg, 0.11 mmol) was suspended in CH_2Cl_2 (5 mL) and *tert*-butyl hydroperoxide (20 mg, 0.22 mmol) was added. After 10 min, **36a** (35 mg, 0.074 mmol) in CH_2Cl_2 (5 mL) was introduced at r.t. and stirred for 72 h. The mixture was heated to reflux and more SeO_2 on silica gel was added. Products **42a** (9.6 mg, 27%) and **42b** (6.6 mg, 19%) were collected following chromatography on silica gel with elution by 2% Et_2O in hexanes.

For **42a**: white solid, mp 160 °C (dec).
IR (neat, cm^{-1}): ν = 1680, 1510, 1410, 1300, 1150.
^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.35 (d, *J* = 12.3 Hz, 1 H), 6.05 (d, *J* = 12.3 Hz, 1 H), 3.85 (m, 1 H), 3.37 (dd, *J* = 6.2, 17.1 Hz, 1 H), 3.10 (d, *J* = 5.8 Hz, 1 H), 2.89 (dd, *J* = 4.1, 17.1 Hz, 1 H), 2.79 (m, 1 H), 2.62 (d, *J* = 14 Hz, 1 H), 2.51 (td, *J* = 4.2, 12.4 Hz, 1 H), 2.36 (dd, *J* = 12.9, 4.0 Hz, 1 H), 1.92 (m, 1 H), 1.75 (br d, *J* = 12.7 Hz, 2 H), 1.62 (s, 3 H), 1.57–1.22 (m, 4 H), 1.39 (s, 1 H), 1.19 (d, *J* = 6.7 Hz, 3 H), 1.19 (s, 1 H), 1.14 (d, *J* = 6.8 Hz, 3 H), 1.06 (d, *J* =7.2 Hz, 3 H), 0.92 (s, 9 H), 0.78 (s, 3 H), 0.04 (s, 3 H), 0.02 (s, 3 H).
^{13}C NMR (75 MHz, $CDCl_3$): δ = 192.4, 148.6, 143.6, 138.4, 137.3, 131.1, 123.1, 77.4, 55.9, 49.1, 47.2, 46.1, 43.0, 42.1, 42.0, 38.6, 30.2, 26.1, 26.0 (3 C), 24.3, 22.0, 18.5, 18.2, 18.0, 17.9, 16.3, –4.4, –4.6.
MS *m/z* (M^+) calcd 468.3424, obsd 468.3420.

For **42b**: white solid, mp 158–159 °C.
IR (neat, cm^{-1}): ν = 3390, 2950, 1640, 1440, 1370, 1200.
^{1}H NMR (300 MHz, C_6D_6): δ = 6.29 (d, *J* = 12.4 Hz, 1 H), 5.94 (d, *J* = 12.4 Hz, 1 H), 3.54 (m, 1 H), 3.18 (dd, *J* = 5.7, 17.8 Hz, 1 H), 3.00 (d, *J* = 5.9 Hz, 1 H), 2.74 (d, *J* = 17.9 Hz, 1 H), 2.58 (m, 2 H), 2.50–2.40 (m, 1 H), 2.28 (m, 1 H), 1.87 (m, 1 H), 1.75–1.64 (m, 3 H), 1.58 (s, 3 H), 1.56–1.14 (m, 4 H), 1.12 (d, *J* = 6.8 Hz, 3 H), 1.13 (s, 1 H), 1.08 (d, *J* = 6.8 Hz, 3 H), 0.87 (d, *J* = 7.3 Hz, 3 H), 0.72 (s, 3 H).
^{13}C NMR (75 MHz, C_6D_6): δ = 192.5, 149.4, 143.2, 138.3, 137.3, 131.0, 123.5, 75.3, 56.2, 49.2, 46.2, 43.0, 42.5, 42.1, 38.6, 30.2, 26.1, 24.3, 22.0, 18.6, 18.0, 17.9, 16.6.
MS *m/z* (M^+) calcd 354.2559, obsd 354.2577.

(2*S*,3*S*,3a*R*,6a*S*,7a*R*,10*S*,10a*S*,11a*R*,12*S*,12a*S*)-2-(*tert*-Butyldimethylsiloxy)-1,2,3,3a,4,6a,7,7a,8,9,10,10a,11,11a,12,12a-hexadecahydro-10-isopropyl-3,6,7a,12-tetramethylcyclopenta[4,5]-cyclooct-[1,2-*f*]inden-12-ol (43):
Ketone **34a** (20 mg, 0.042 mmol) was dissolved in THF (5 mL) at 0 °C before MeLi (36.4 µL, 0.051 mmol) was added via syringe. The mixture was stirred at 20 °C for 30 min and quenched with brine (3 mL). The separated organic phase was dried and concentrated. The crude material was purified by chromatography on silica gel with 5% EtOAc in hexanes to give **43** (21 mg, 99%) as a colorless oil.
IR (neat, cm^{-1}): ν = 3320, 1470, 1370, 1260, 1090.
^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.06 (br s, 1 H), 5.41 (br s, 1 H), 4.18–4.13 (m, 1 H), 3.84–3.73 (m, 1 H), 3.22 (br s, 1 H), 2.97–2.91 (m, 1 H), 2.56–2.04 (m, 4 H), 2.00–1.87 (m, 2 H), 1.83 (s, 3 H), 1.75–1.25 (m, 14 H), 1.05 (s, 3 H), 0.95 (d, *J* = 6.8 Hz, 3 H), 0.91 (s, 3 H), 0.89 (s, 9 H), 0.81 (d, *J* = 6.8 Hz, 3 H), 0.04 (s, 6 H).
^{13}C NMR (75 MHz, $CDCl_3$): δ = 141.4, 127.0, 85.2, 78.5, 76.8, 76.4, 52.5, 48.9, 48.4, 44.1, 41.7, 39.6, 39.1, 35.8, 31.6, 29.4, 28.1, 25.9 (3 C), 25.3, 24.5, 24.4, 23.9, 21.9, 18.2, 18.1, 13.4, –4.4, –4.7.
MS *m/z* (M^+) calcd 488.4050, obsd 488.4047.

(–)-*tert*-Butyl{[(2*S*,3*S*,3a*S*,6a*S*,7a*R*,10*S*,10a*S*,11a*R*,12a*R*)-1,2,3,3a,4,6a,7,7a,8,9,10,10a,11,11a,12,12a-hexadecahydro-10-isopropyl-3,6,7a-trimethyl-12-methylenecyclopenta[4,5]cyclooct[1,2-*f*]inden-2-yl]oxy}dimethylsilane (44):

Alcohol **43** (50 mg, 0.103 mmol) was dissolved in CH_2Cl_2 (3 mL) and pyridine (2 mL) and cooled to –78 °C. $SOCl_2$ (50 µL, 0.68 mmol) was added via syringe and reaction was complete within 5 min. Ice (10 g) was added followed by EtOAc (10 mL), and the mixture was allowed to warm to r.t. The aqueous layer was extracted with EtOAc (3 × 5 mL) and the combined organic phases were dried and concentrated. The residue was purified by chromatography on silica gel with 1.5 to 2% Et_2O in hexanes to deliver **44** (34 mg, 68%) as a heavy, colorless oil.

^{1}H NMR (300 MHz,C_6D_6): δ = 5.48 (s, 1 H), 5.42 (dt, *J* = 3.1, 1.5 Hz, 1 H), 5.11 (s, 1 H), 4.30–4.28 (m, 1 H), 2.86 (td, *J* = 3.1, 1.5 Hz, 1 H), 2.56–2.49 (m, 2 H), 2.49–2.37 (m, 1 H), 2.20–2.16 (m, 1 H), 2.15–1.77 (m, 3 H), 1.76 (s, 3 H), 1.74–1.05 (m, 8 H), 1.03 (d, *J* = 7.8 Hz, 3 H), 1.01 (s, 9 H), 0.95 (d, *J* = 6.8 Hz, 3 H), 0.90 (d, *J* = 6.7 Hz, 3 H), 0.88–0.80 (m, 3 H), 0.79 (s, 3 H), 0.12 (s, 3 H), 0.11 (s, 3 H).

^{13}C NMR (75 MHz, C_6D_6): δ = 157.9, 138.9, 126.2, 112.2, 83.6, 50.0, 46.8, 46.7, 45.8 (2 C), 44.8, 43.5, 42.8, 42.6, 42.5, 39.6, 31.2, 28.9, 27.8, 27.5, 26.2 (3 C), 22.8, 22.7, 18.3, 17.8, 17.7, 16.3, –4.2, –4.6.

MS *m/z* (M^+) calcd 470.3944, obsd 470.3953.

$[\alpha]_D^{24}$ –15.0 (*c* = 2.34, $CHCl_3$).

(2*S*,3*S*,3a*S*,6a*S*,7a*R*,10*S*,10a*S*,11a*R*,12a*R*)-1,2,3,3a,4,6a,7,7a,8,9,10,10a,11,11a,12,12a-Hexadecahydro-10-isopropyl-3,6,7a-trimethyl-12-methylenecyclopenta[4,5]cyclooct[1,2-*f*]inden-2-ol (45):

A solution of **44** (20 mg, 0.042 mmol) in THF (10 mL) was cooled to 0 °C. TBAF (300 µL of a 1 M soln in THF) was added via syringe and the solution was allowed to warm to 20 °C and stirred for 8 h. The mixture was quenched with sat. $NaHCO_3$ (5 mL), and the organic layer was dried and evaporated. Chromatography of the residue on silica gel with 15% to 30% EtOAc in hexanes afforded **45** (11 mg, 70%) and recovered **44** (11%).

For **45**: white solid, mp 105–107 °C.

^{1}H NMR (300 MHz, C_6D_6): δ = 5.46 (s, 1 H), 5.41 (t, *J* = 7.8 Hz, 1 H), 5.02 (s, 1 H), 4.08–4.02 (m, 1 H), 2.79 (dt, *J* = 3.1, 3.0 Hz, 1 H), 2.54–2.43 (m, 2 H), 2.36–2.26 (m, 1 H), 2.17–2.02 (m, 1 H), 2.00–1.77 (m, 3 H), 1.76 (s, 3 H), 1.69–1.54 (m, 3 H), 1.50–1.27 (m, 4 H), 1.10 (t, *J* = 10.1 Hz, 1 H), 1.04–0.92 (m, 3 H), 0.96 (s, 3 H), 0.95 (d, *J* = 6.7 Hz, 3 H), 0.89 (d, *J* = 6.8 Hz, 3 H), 0.91–0.81 (m, 2 H), 0.78 (s, 3 H).

^{13}C NMR (75 MHz, C_6D_6): δ = 157.6, 138.8, 126.2, 112.4, 82.5, 50.0, 46.8, 46.6, 45.9, 45.8, 45.0, 43.1, 42.7, 42.6, 42.5, 39.6, 31.3, 28.9, 27.8, 27.4, 22.8, 22.6, 17.8, 17.7, 16.3.

(–)-(2*S*,3*S*,3a*S*,6a*S*,7a*R*,10*S*,10a*S*,11a*R*,12a*S*)-1,2,3,3a,4,6a,7,7a,8,9,10,10a,11,11a,12,12a-Hexadecahydro-10-isopropyl-3,6,7a-trimethyl-12-methylenecyclopenta[4,5]cyclooct[1,2-*f*]inden-2-yl β-D-Xylopyranoside Triacetate (47):

Molecular sieves (4 Å, 100 mg, dried under vacuum), alcohol **45** (10 mg, 0.028 mmol), and **46** (14 mg, 0.042 mmol) were suspended in Et_2O (10 mL) for 10 min before being cooled to –50 °C. Silver triflate (10 mg, 0.039 mmol) was added in one portion and the suspension was stirred for 1 h. The mixture was filtered and washed with $NaHCO_3$. The separated organic phase was dried, refiltered and evaporated. The residue was purified by chromatography on silica gel (elution with 5–15% EtOAc in hexanes) to furnish 7.5 mg (69%) of the acetate of **45** as a colorless oil.

^{1}H NMR (300 MHz, C_6D_6): δ = 5.43 (s, 1 H), 5.40–5.36 (m, 2 H), 5.06 (s, 1 H), 2.76 (t, *J* = 7.1 Hz, 1 H), 2.45–2.32 (m, 3 H), 2.28–1.78 (m, 5 H), 1.81–1.68 (m, 3 H), 1.75 (s, 3 H), 1.66–1.49 (m, 3 H), 1.48–1.23 (m, 5 H), 1.10 (d, *J* = 7.6 Hz, 3 H), 0.96 (d, *J* = 6.8 Hz, 3 H), 0.89 (d, *J* = 6.8 Hz, 3 H), 0.78 (s, 3 H).

^{13}C NMR (75 MHz, C_6D_6): δ = 170.1, 156.7, 139.1, 126.0, 113.5, 85.2, 50.0, 46.8, 46.1, 45.9, 45.4, 43.7, 42.9, 42.7, 42.5, 40.2, 39.6, 31.2, 28.8, 28.0, 27.3, 22.8, 22.7, 20.9, 17.8, 17.7, 16.0.

MS *m/z* (M^+) calcd 398.3185, obsd 398.3188.

$[\alpha]_D^{20}$–38.1 (*c* = 0.75, $CHCl_3$).

Also isolated was 4 mg (24%) of **47** as a thick, colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.37–5.35 (t, *J* = 2.9 Hz, 1 H), 5.30 (s, 1 H), 5.20 (t, *J* = 9.6 Hz, 1 H), 4.95–4.87 (m, 2 H), 4.89 (s, 1 H), 4.26–4.20 (m, 1 H), 4.13–4.09 (m, 1 H), 3.78 (dd, *J* = 5.8, 5.0 Hz, 1 H), 3.61–3.55 (m, 1 H), 3.60 (t, *J* = 10.6 Hz, 1 H), 2.77–2.74 (m, 1 H), 2.56–2.51 (m, 1 H), 2.40–2.45 (m, 1 H), 2.31–2.26 (m, 1 H), 2.11 (s, 3H), 2.10 (s, 3 H), 2.03 (s, 3 H), 2.05–1.81 (m, 2 H), 1.80–1.59 (m, 3 H), 1.74 (s, 3 H), 1.52–1.23 (m, 8 H), 1.02 (d, *J* = 7.5 Hz, 3 H), 0.91 (d, *J* = 6.8 Hz, 3 H), 0.89–0.80 (m, 2 H), 0.84 (d, *J* = 6.8 Hz, 3 H), 0.82 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 183.1, 181.6, 177.0, 156.7, 144.1, 140.7, 140.5, 125.3, 124.2, 101.1, 97.0, 88.5, 73.1, 70.8, 69.0, 57.8, 46.3, 45.5, 45.4, 44.9, 42.9, 42.4, 39.3, 31.6, 30.8, 28.4, 22.7(3 C), 22.3, 21.0, 20.8, 17.6, 17.5, 16.4, 14.1.

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