vinylallenone 61 as a colorless liquid (229.4 mg, 62%).

(1(1′)*Z*,2*Z*)-3-*tert*-Butyl-1-(6′,6′-dimethyl-2′-methylenecyclohexylidene)pent-2-en-4-one (62) and Its 1(1′)*Z*,2*E* Isomer 63. A solution of vinylallenone **61** (210 mg, 0.806 mmol) in benzene (1.5 mL) was added to an ampoule under a nitrogen atmosphere. The solution was cooled to dry ice temperature and evacuated, and then the ampoule was sealed. The ampoule containing the vinylallenone was heated in an oil bath at 68.5 °C for 17.5 h. The ampoule was cooled and then opened. Three drops of the solution was transferred to C_6D_6 in an NMR tube in order to determine the (1(1′)*Z*,2*Z*)-**62**/(1(1′)*Z*,2*E*)-**63** ratio (62:38 ratio by ^{1}H NMR). Finally, HPLC purification (Partisil, 2% EtOAc/hexanes) gave the trienones in the following order of elution: (1(1′)*Z*,2*Z*)-**62** (111.4 mg, 53%, major isomer A, less polar) and (1(1′)*Z*,2*E*)-**63** (77.2 mg, 37%, minor isomer B, more polar) as colorless liquids. The ratio of geometric isomers was 61/39: 62/38 (^{1}H NMR); 61/39 (HPLC); 59/41 (yield). In separate control experiments, the two geometric isomers were stable to the thermal conditions described above.

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Supplementary Material Available: Spectral data for all new compounds and general experimental details (80 pages). Ordering information is given on any current masthead page.

Stereo- and Enantiospecific Syntheses of (−)-Reiswigins A and B. Assignment of Absolute and Relative Configuration

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The first synthesis of reiswigin A (**20**) was accomplished in only eight steps providing optically pure material in 7% overall yield with control of the relative and absolute stereochemistry at carbons 1, 7, and 8. The synthesis was designed to provide a mixture of isomers at carbon 13 since the stereochemistry at this center was not assigned in the structure determination. Sakurai reaction of allylic silane **12** with enone **13** affords ketone **5** as a mixture of diastereomers. Protection of the ketone, cleavage of the double bond, and intramolecular aldol reaction gives cyclopentenecarboxaldehyde **4**. Addition of 3-methyl-3-butenylmagnesium bromide to imine **17** by Koga's procedure followed by alkylation of the enamide with methyl iodide gives **3**. This crucial step not only controls the relative stereochemistry at carbons 1, 7, and 8 but also effects a kinetic resolution, permitting assignment of absolute stereochemistry to reiswigin A as shown in **20**. Me_2AlCl-catalyzed ene reaction of **3** gives alcohol **19**. Oxidation of the alcohol and acid-catalyzed conjugation of the double bond and hydrolysis of the ketal gives a mixture of reiswigin A (**20**) and **21**. The stereochemistry at carbon 13 is assigned based on NMR shifts. Addition of cyclohexenylpotassium to crotonaldehyde gives dienol **26b**. Anionic oxy-Cope rearrangement gives aldehyde **28**, which was used for stereo- and enantiospecific syntheses of both reiswigins A (**20**) (11 steps, 12%) and B (**36**) (11 steps, 6%).

Diterpenes reiswigins A (**1**) and B (**2**) were recently isolated by Koehn and co-workers from a deepwater marine organism *Epipolasis reiswigi* collected by submersible at 330 m.[1] These compounds show potent in vitro activity against Herpes simplex type I virus and murine A59 hepatitis virus. The structure and relative stereochemistry at three of the four chiral centers (carbons 1, 7, and 8) were determined by a combination of one- and two- dimensional NMR spectroscopy and mass spectroscopy. The relative configuration at carbon 13 and the absolute stereochemistry could not be assigned from the available data. The structural novelty and potentially useful biological activity of these unusual hydroazulenoid diterpenes encouraged us to develop a practical synthesis of these compounds which would permit complete structure assignment and allow the preparation of analogues for biological testing.

Initially, we chose to develop a synthesis of **1** which would control the relative and absolute stereochemistry at carbons 1, 7, and 8 but would lead to a mixture of isomers at carbon 13 so that we would be assured of producing both reiswigin A and its epimer at carbon 13.[2] It was our expectation that, with both isomers in hand, we would be able to assign the stereochemistry of reiswigin A. It was therefore important that the synthesis be designed to permit modification of the stereochemistry at carbon 13 once we had assigned it.

Retrosynthetic analysis suggested that the cycloheptenone moiety of **1** could be most easily made by a type II intramolecular ene reaction of unsaturated aldehyde **3** as developed by Marshall and Andersen,[3] followed by oxidation of the alcohol and conjugation of the double bond. An intramolecular aldol condensation was a less attractive method for ring closure since two regioisomeric enones could be formed. Aldehyde **3** could be prepared by conjugate addition to enal **4** followed by methylation of the enolate. Conjugate addition to **4** should occur selectively from the β-face. Methylation of the enolate, however, would be expected to occur predominantly from the less hindered undesired α-face rather than the desired β-face. Enal **4** should be readily available by oxidative cleavage of cyclohexene **5** followed by intramolecular aldol

(1) Kashman, Y.; Hirsch, S.; Koehn, F.; Cross, S. *Tetrahedron Lett.* **1987**, *28*, 5461.

(2) For a preliminary report see: Snider, B. B.; Yang, K. *Tetrahedron Lett.* **1989**, *30*, 2465.

(3) Oppolzer, W.; Snieckus, V. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 476.

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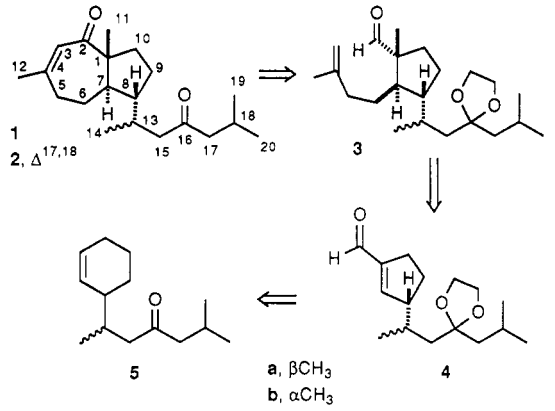
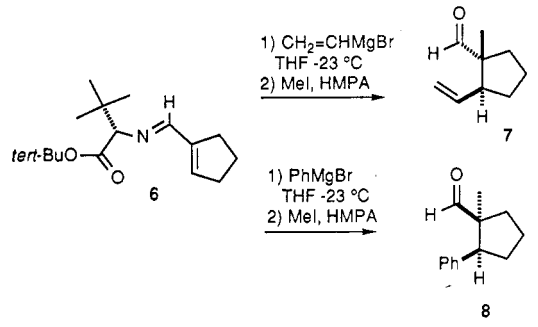
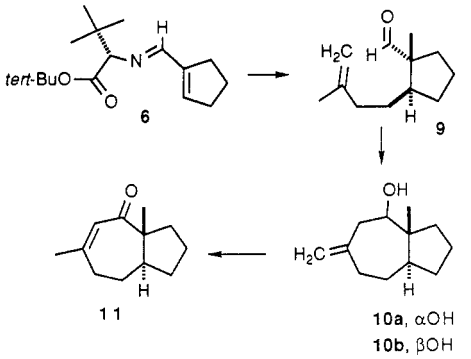
condensation of the resulting dial.



The elegant studies of Koga and co-workers provide an efficient solution to this problem.[4] They found that addition of vinylmagnesium bromide to the *tert*-leucine *tert*-butyl ester imine of 1-cyclopentenecarboxaldehyde (**6**) followed by alkylation of the resulting enamide with methyl iodide and hydrolysis of the imine gives **7** in 62% yield and 92% enantiomeric excess. The chiral auxiliary directs both the addition of the Grignard reagent from the β-face and the addition of the methyl group from the "more hindered" β-face. This result suggested that the conversion of **4** to **3** proposed above could be accomplished. However, addition of phenylmagnesium bromide and methyl iodide to **6** affords the other diastereomer **8**, and the addition of aliphatic Grignard reagents have not been reported.



We carried out model studies with racemic **6**, prepared from 1-cyclopentenecarboxaldehyde[5] and racemic *tert*-leucine *tert*-butyl ester.[6] Addition of 4 equiv of 3-methyl-3-butenylmagnesium bromide to **6** in THF at −25 °C, followed by addition of 6 equiv of methyl iodide and 7 equiv of HMPA, and hydrolysis provides **9** in 66% yield. The stereochemistry of **9** was assigned based on its ^{13}C NMR spectrum in which the ring methyl group absorbed at δ 13.9 as expected for a methyl group cis to an adjacent substituent.[4] The intramolecular ene reaction can be easily accomplished by treatment of **9** with 1.1 equiv of Me_2AlCl[7,8] in CH_2Cl_2 at 0 °C for 30 min to give 91% of **10** as predominantly a single diastereomer. Oxidation of **10** with PCC in CH_2Cl_2 followed by conjugation of the double bond with toluenesulfonic acid in benzene at reflux gives 82% of the desired enone **11**. The ^1H and ^{13}C NMR, IR, and UV spectra of **11** are similar to those of reiswigin A.



The intramolecular ene reaction of **9** gives **10** as predominantly a single diastereomer. The proton on the hydroxyl-bearing carbon of the major isomer is coupled to the adjacent methylene group with coupling constants of 4.8 and 2.4 Hz, suggesting that the proton is pseudoequatorial and the hydroxyl group is pseudoaxial. Since the cycloheptane ring is conformationally mobile the stereochemistry cannot be assigned unambiguously from this data. Calculations of the energy of conformers using MODEL[9] suggest that **10a**, but not **10b**, should exist predominantly in conformations with a pseudoaxial hydroxyl group and pseudoequatorial proton. The major isomer is tentatively assigned structure **10a**.

Synthesis of Reiswigin A. Having established that Koga's procedure could be used to convert **4** to **3**, we developed an efficient route to enal **4**. Sakurai reaction[10] of 2-cyclohexenyltrimethylsilane (**12**)[11] with 6-methyl-*trans*-2-hepten-4-one (**13**)[12] with $TiCl_4$ at −40 °C gives 88% of **5** as a mixture of diastereomers. Protection of the ketone as the ketal with ethylene glycol and toluenesulfonic acid in benzene at reflux gives 90% of **14**. Hydroxylation with 1 mol % of osmium tetroxide and *N*-methylmorpholine *N*-oxide[13] in aqueous acetone affords 88% of diol **15**. Oxidative cleavage of the diol with sodium periodate in aqueous acetone gives **16**, which undergoes an aldol condensation[14] catalyzed by piperidine and acetic acid in toluene at 0 °C to give 69% of **4** from **15** as a racemic mixture of diastereomers.

Reaction of L-*tert*-leucine *tert*-butyl ester[15] and racemic **4** in hexane for 12 h at 25 °C in the presence of 4A molecular sieves[4] gives 94% of a 1:1 mixture of diastereomeric imines **17** and **18**. Reaction of this mixture with (3-methyl-3-butenyl)magnesium bromide in THF at −25 °C followed by alkylation of the enamide with methyl iodide and hydrolysis as described above gives 32% of **3**, minor amounts of other diastereomers, and 50% of recovered optically active **4**. This crucial step in the synthesis not only controls the relative stereochemistry at carbons 1, 7, and 8 but also effects a kinetic resolution, converting **17**

(4) Kogen, H.; Tomioka, K.; Hashimoto, S.-I.; Koga, K. *Tetrahedron* **1981**, *37*, 3951; *Tetrahedron Lett.* **1980**, *21*, 4005. Tomioka, K.; Koga, K. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1983; Vol. 2, Chapter 7. Tomioka, K.; Masumi, F.; Yamashita, T.; Koga, K. *Tetrahedron* **1989**, *45*, 643.

(5) Brown, J. B.; Henbest, H. B.; Jones, E. R. H. *J. Chem. Soc.* **1950**, 3634.

(6) Izumiya, N.; Fu, S.-C. J.; Birnbaum, S. M.; Greenstein, J. P. *J. Biol. Chem.* **1953**, *205*, 221. Jaeger, D. A.; Broadhurst, M. D.; Cram, D. J. *J. Am. Chem. Soc.* **1979**, *101*, 717.

(7) Snider, B. B.; Rodini, D. J.; Karras, M.; Kirk, T. C.; Deutsch, E. A.; Cordova, R.; Price, R. T. *Tetrahedron* **1981**, *37*, 3927.

(8) Quinkert, G.; Schmalz, H.-G.; Walzer, E.; Gross, S.; Kowalczyk-Przewloka, T.; Schierloh, C.; Dürner, G.; Bats, J. W.; Kessler, H. *Justus Leibigs Ann. Chem.* **1988**, 283.

(9) MODEL (Version 2.94) supplied by Prof. Kosta Steliou, University of Montreal, was used on a VAX 8650.

(10) Sakurai, H.; Hosomi, A.; Hayashi, J. *Org. Synth.* **1984**, *62*, 86.

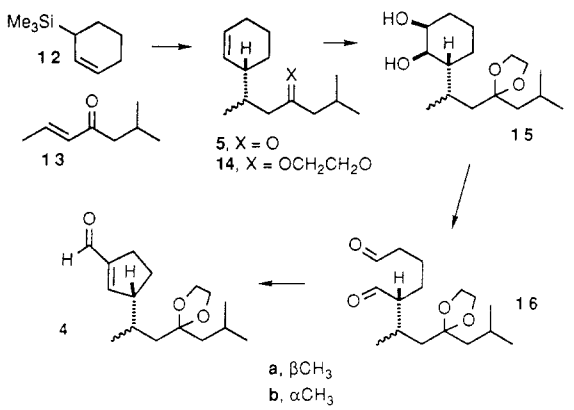
(11) Eaborn, C.; Jackson, R. A.; Pearce, R. *J. Chem. Soc., Perkin Trans. 1* **1974**, 2055.

(12) Birch, A. J.; Macdonald, P. L.; Powell, V. H. *J. Chem. Soc. C* **1970**, 1469.

(13) VanRheenen, V.; Cha, D. Y.; Hartley, W. M. *Org. Synth.* **1978**, *58*, 43.

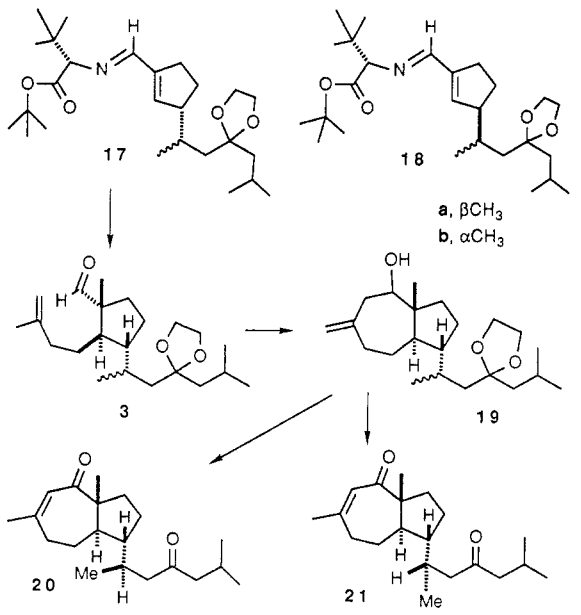
(14) Barrière, J.-C.; Cléophax, J.; Géro, S. D.; Vuilhorgne, M. *Helv. Chim. Acta* **1983**, *66*, 296.

(15) We thank Dr. Karl Heinz Drauz of Degussa AG for a generous gift of L-*tert*-leucine.



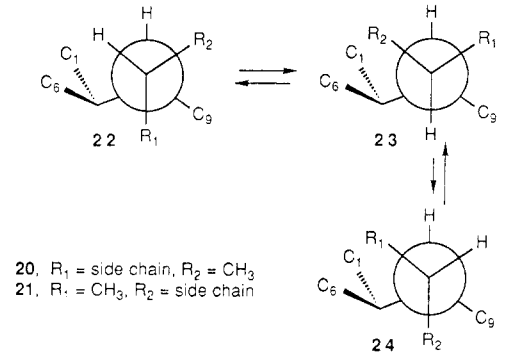
selectively to reiswigin precursor **3**, leaving the diastereomer **18** largely unreacted. The *tert*-butyl group of the imine and the side chain on the cyclopentane in **17** both direct the delivery of the 3-methyl-3-butenyl and methyl groups from the less hindered β-face. In **18**, the *tert*-butyl group of the imine directs delivery from the β-face while the side chain directs delivery from the α-face. Imine **18** therefore reacts much more slowly than **17** and gives rise largely to recovered **4** and small amounts of diastereomers, rather than enantiomers, of **3**.

The synthesis is completed by treatment of **3** with Me_2AlCl in CH_2Cl_2 at 0 °C for 30 min to give a mixture of **19** and the corresponding keto alcohol resulting from hydrolysis of the ketal. Oxidation of the alcohol to the ketone with PCC in CH_2Cl_2, followed by treatment with toluenesulfonic acid in wet benzene at reflux for 12 h to complete hydrolysis of the ketal and bring the double bond into conjugation, gives an HPLC separable 3:2 mixture of reiswigin A (**20**) and **21**, the epimer at carbon 13, in 84% yield from **3**. The ^1H and ^{13}C NMR and IR spectral data and the HPLC retention time of synthetic reiswigin A are identical with those of the natural product.[16]



The availability of both **20** and **21** permits the assignment of structure **20** to natural reiswigin A. The ^1H and ^{13}C NMR spectra of **20** and **21** are quite similar except for the chemical shift of the 14-methyl group, which absorbs at δ 0.90 in the proton NMR and δ 20.1 in the carbon NMR in reiswigin A (**20**) and δ 0.80 and 13.6 in **21**, and the chemical shift of carbon 15, which occurs at δ 45.4 in **20** and δ 49.9 in **21**. Although the use of chemical shift data to assign configuration to conformationally mobile molecules is dangerous, the differences in this case, coupled with molecular mechanics calculations of the energies of the conformers about the 8–13 bond, are sufficient to permit tentative assignment as shown.

The origins of these shift differences can be seen in the Newman projections **22**–**24** of the three conformers of **20** and **21**. Molecular mechanics calculations[9] suggest that conformations **22** and **23** are similar in energy while conformation **24** is much higher in energy. Using $R_1 = R_2 = CH_3$ as a model to minimize conformational flexibility of the side chain, **22** is calculated to be the most stable conformer with a dihedral angle between the hydrogens of 61°. Conformation **23** with a dihedral angle of −170° is less stable by 0.25 kcal/mol. Conformation **24** with a dihedral angle of −66° is less stable by 0.92 kcal/mol. Conformation **23** has only two gauche butane interactions but has a high energy syn-axial interaction between R_2 and carbon 6. Conformation **22** has three gauche butane interactions but no high energy interactions with carbon 6. The least stable conformation **24** has three gauche butane interactions and a high energy syn-axial interaction between R_2 and carbon 6.



The 14-methyl group of **21** (R_1) in conformation **22** is in a gauche relationship with carbons 7 and 9 and should be shifted upfield from the 14 methyl group of **20** (R_2) in conformation **22**, which is in a gauche relationship only with carbon 9. The methyl groups of both **20** and **21** are in a gauche relationship with one carbon in conformation **23**. However, the 14-methyl group of **20** (R_2) is in a deshielding syn-axial relationship with carbon 6.[17] Therefore, in each conformation the 14-methyl group of **20** should absorb downfield from the 14-methyl group of **21**, permitting a tentative structural assignment to be made. Similar analysis predicts that the 15-methylene group of **20** should absorb upfield from the 15-methylene group of **21** as is observed. Support for this assignment can be found in the limited spectral data available for related sesqui- and diterpenes. The methyl group in the stereoisomer corresponding to **20** absorbs downfield by 0.1–0.2 ppm in the ^1H NMR spectrum and downfield by 4–7 ppm in the ^{13}C NMR spectrum.[18]

(16) We thank Dr. Frank Koehn for spectral data and a sample of natural reiswigin A. The ^1H NMR data reported for **1** in ref 1 are not referenced correctly; 0.08 ppm should be subtracted from the reported δ values.

(17) Stothers, J. B.; Tan, C. T.; Teo, K. C. *J. Magn. Reson.* **1975**, *20*, 570. Batchelor, J. G. *Ibid.* **1975**, *18*, 212.

(18) (a) Look, S.; Fenical, W. *Tetrahedron* **1987**, *43*, 3363. (b) Forster, P. G.; Ghisalberti, E. L.; Jefferies, P. R.; Poletti, V. M.; Whiteside, N. J. *Phytochemistry* **1986**, *25*, 1377. (c) Mori, K.; Waku, M. *Tetrahedron* **1984**, *40*, 305. (d) Narwid, T. A.; Cooney, K. E.; Uskokovic, M. R. *Helv. Chim. Acta* **1974**, *57*, 771. (e) Trachtenberg, E. N.; Byon, C.; Gut, M. *J. Am. Chem. Soc.* **1977**, *99*, 6145. (f) Crews, P.; Naylor, S. *Prog. Chem. Org. Nat. Prod.* **1985**, *48*, 204. (g) Köster, F.-H.; Wolf, H.; Kluge, H. *Justus Leibigs Ann. Chem.* **1986**, 78.

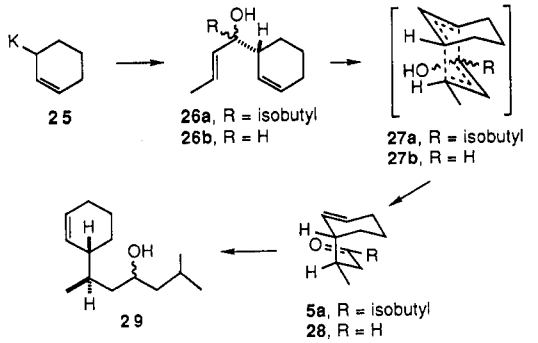
The absolute configuration of reiswigin A (1) can be assigned as shown in **20** by comparison of the CD spectrum and optical rotation with that of the synthetic material. Both natural and synthetic reiswigin A have a CD maximum of $[\theta] = -4400°$ at 300 nm and $[\alpha]^{25}_D = -10°$. The absolute stereochemistry of synthetic **20** and **21** is known since Koga determined that Grignard reagents add to L-*tert*-leucine *tert*-butyl ester imines of cyclopentenecarboxaldehydes as shown in the conversion of **17** to **3**. Natural (−)-reiswigin A therefore has the absolute configuration shown in **20**. Furthermore, kinetic resolution[19] in the Grignard addition to **17** and **18** must be very efficient since $[\theta]$ and $[\alpha]^{25}_D$ for synthetic **20** is comparable to that of the natural product.

Stereospecific Synthesis of Reiswigin A. The first synthesis of reiswigin A was accomplished in only eight steps, providing optically pure material in 7% overall yield with control of the relative and absolute stereochemistry at carbons 1, 7, and 8. The synthesis was designed to provide a mixture of isomers at carbon 13 since the stereochemistry at this center was not assigned in the structure determination. Once the stereochemistry was assigned this mixture of isomers is less than ideal since the separation of **20** and **21** can only be accomplished with difficulty on a small scale by HPLC. We chose to modify the synthesis to permit control of the stereochemistry of the side chain methyl group in order to produce **20** stereospecifically. This will permit the preparation of adequate quantities of material for in vivo testing of the antiviral activity and confirm the stereochemistry at carbon 13 tentatively assigned above based on NMR chemcial shift data.

The desired enone **5a** should be available stereospecifically by an oxy-Cope rearrangement of dienol **26a**, which should be readily available by addition of the 2-cyclohexenyl anion to enone **13**. We expected that both diastereomers of **26a** would give the desired diastereomer **5a** selectively since the oxy-Cope rearrangement should proceed through chair transition state **27a** with the stereochemistry of **5a** controlled by the stereochemistry of the double bonds.

2-Cyclohexenylpotassium (**25**), prepared by deprotonation of cyclohexene by Schlosser's procedure,[20] was added to enone **13** at 0 °C to give 18% of **5** as a mixture of diastereomers and 33% of **26a** as a mixture of diastereomers. An anionic oxy-Cope rearrangement[21] was effected by heating **26a** with potassium hydride and 18-crown-6 in DME at reflux to give 83% of a 3:1 mixture of **5a** and **5b**. This approach to **5a** is clearly not acceptable. The oxy-Cope rearrangement is not as selective as we anticipated, and the addition of **25** to **13** gives a mixture of 1,4-addition product **5** in addition to the desired 1,2-addition product **26a**. 1,4-Addition could not be prevented by reaction at −78 °C or by reaction in the presence of $CeCl_3$.

Addition of **25** to crotonaldehyde was explored since 1,4-addition should be less of a problem with an aldehyde. Addition of **25** to crotonaldehyde at 0 °C gives 81% of **26b** as a 1:1 mixture of diastereomers and a trace of 1,4-addition product. Anionic oxy-Cope rearrangement of **26b** with potassium hydride and 18-crown-6 in DME at reflux proceeds stereospecifically through transition state **27b** to give 77% of the desired enal **28** containing less than 5% of the undesired diastereomer. This approach has several advantages over addition to the enone: reaction of **25** with



crotonaldehyde gives only the desired 1,2-addition product, the oxy-Cope reaction is stereospecific, and **28** should be useful as an intermediate for the syntheses of both reiswigins A and B. Addition of isobutylmagnesium bromide to crude **28** produces alcohol **29** in 71% yield from **26b**. Oxidation with PCC gives 95% of **5a**.

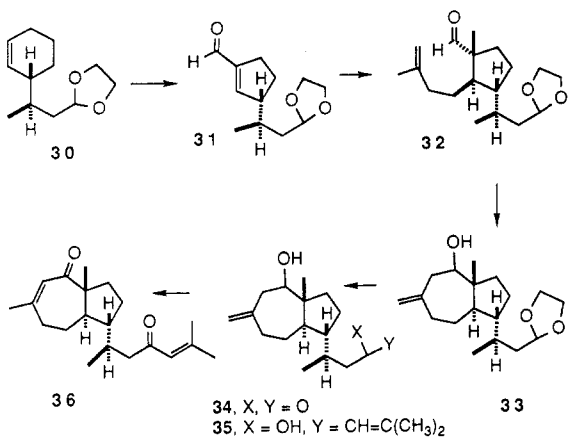
Use of a single diastereomer **5a** poses a major problem that was not encountered with the mixture of diastereomers **5a** and **5b**. The dial **16a**, and, to a lesser extent, the enal **4a** are susceptible to epimerization. This cannot be detected if a mixture of diastereomers is used. If **5a** is used, epimerization will regenerate a mixture of diastereomers. We expected that the desired transformations could be carried out without epimerization since the aldol reaction is carried out with piperidine and acetic acid in toluene at 0 °C, conditions which have been reported to convert dials to cyclopentenecarboxaldehydes without epimerization in related systems.[14]

The conversion of racemic **5a** to (−)-reiswigin A (**20**), contaminated with less than 5% of the desired isomer **21**, was carried out as described for the racemic mixture in 20% yield for the seven-step sequence. Very little epimerization occurs in the conversion of **5a** to **4a**. This stereospecific synthesis provides **20** stereo- and enantiospecifically in 12% overall yield from cyclohexene in 11 steps and confirms the stereochemistry previously assigned at carbon 13 in reiswigin A.

Synthesis of Reiswigin B (36). We chose to add the unsaturated side chain of reiswigin B late in the synthesis since it was anticipated that the double bond would interfere with oxidative cleavage of the cyclohexene. Reaction of **28** with ethylene glycol and toluenesulfonic acid in benzene at reflux gives 72% of acetal **30**. Hydroxylation, cleavage with periodate, and aldol condensation produces enal **31** in 67% yield. Reaction of the L-*tert*-leucine *tert*-butyl ester imine of **31** with (3-methyl-3-butenyl)-magnesium bromide and methyl iodide gives 35% of **32** and 50% of recovered optically active **31**. Ene reaction with Me_2AlCl at 0 °C affords 83% of **33**. Concomitant partial hydrolysis of the acetal does not occur since it is more stable than the ketal of **19**. Hydrolysis of the acetal with pyridinium tosylate in aqueous acetone at reflux provides 95% of hydroxyaldehyde **34**. Addition of **34** to 3 equiv of (2-methyl-1-propenyl)lithium (prepared by transmetallation of the bromide with 2 equiv of *tert*-butyllithium at −78 °C) in THF at −78 °C affords 55% (65% based on recovered **34**) of a mixture of diols **35**. Oxidation with PCC in CH_2Cl_2 to give the dione followed by heating at reflux in benzene containing toluenesulfonic acid to bring the exomethylene double bond into conjugation affords 92% of reiswigin B (**36**) with ^1H and ^{13}C NMR and IR spectral and optical rotation data identical with those described.[1] This route provides reiswigin B stereo- and enantiospecifically from cyclohexene and crotonaldehyde in 6% overall yield in 11 steps.

The relative and absolute stereochemistry of reiswigins

(19) For another example of a kinetic resolution using Koga's procedure, see: Paquette, L. A.; Macdonald, D.; Anderson, L. G.; Wright, J. *J. Am. Chem. Soc.* **1989**, *111*, 8037.
(20) Hartmann, J.; Schlosser, M. *Helv. Chim. Acta* **1976**, *59*, 453.
(21) Evans, D. A.; Nelson, J. V. *J. Am. Chem. Soc.* **1980**, *102*, 774.



A and B have been determined. Short, practical, stereo- and enantiospecific syntheses have been developed. We have shown that alkyl Grignard reagents can be used in Koga's procedure for the enantiospecific synthesis of 1,2-dialkylcycloalkanecarboxaldehydes and that kinetic resolution occurs in the addition to racemic 3-alkyl-1-cyclopentenecarboxaldehydes.

Experimental Section

(3-Methyl-3-butenyl)magnesium Bromide. 4-Bromo-2-methyl-1-butene (12.4 g, 0.083 mol) in THF (20 mL) was added dropwise to magnesium (4.35 g) in THF (40 mL) over 1.5 h. The solution was stirred at 25 °C for 1 h to give a 0.9 M solution of the Grignard reagent as determined by addition of an aliquot to water and titration of the resulting solution with HCl (0.1 M) to a phenolphthalein end point.

(1*R,2*S**)-1-Methyl-2-(3-methyl-3-butenyl)cyclopentanecarboxaldehyde (9).** A solution of imine **6**[4] (0.178 g, 0.67 mmol) in 1.2 mL of THF was cooled to −25 °C. (3-Methyl-3-butenyl)magnesium bromide (3.0 mL, 0.9 M in THF, 2.7 mmol) was added dropwise by syringe. The solution was stirred at −25 °C for 8 h. A mixture of CH_3I (0.25 mL, 4 mmol, 6 equiv), HMPA (0.80 mL, 7 equiv), and THF (0.3 mL) was added dropwise. The solution was stirred at −25 °C for 30 min and then at 25 °C for 15 h. Citric acid (6 mL, 10% aqueous) was added. The mixture was stirred at room temperature for 1 h and was extracted with ether (2 × 20 mL). The ethereal extracts were combined, washed with 10% aqueous $Na_2S_2O_3$ solution, saturated aqueous $NaHCO_3$ solution, and saturated aqueous NaCl solution, dried (Na_2SO_4), and concentrated in vacuo to give 100 mg of crude product. Flash chromatography on silica gel (8:1 hexane–EtOAc) gave 80.2 mg (66%) of aldehyde **9**: ^1H NMR δ 9.39 (s, 1), 4.68 (br s, 1), 4.64 (br s, 1), 1.71–2.10 (m, 6), 1.70 (s, 3), 1.25–1.48 (m, 5), 0.98 (s, 3); ^{13}C NMR δ 206.0, 145.5, 110.0, 56.0, 44.4, 36.7, 35.5, 30.5, 28.0, 22.6, 22.3, 13.9; IR (neat) 3079, 2970–2930, 2870, 2690, 1728, 1651 cm^{-1}. Anal. Calcd for $C_{12}H_{20}O$: C, 79.94; H, 11.18. Found: C, 79.79; H, 11.23.

(3a*R,4*S**,8a*S**)-Decahydro-3a-methyl-6-methylene-4-azulenol (10a).** A solution of aldehyde **8** (30.7 mg, 0.17 mmol) in CH_2Cl_2 (13 mL) was treated with Me_2AlCl (0.10 mL, 1.93 M in hexane) at 0 °C for 30 min. The solution was then stirred with HCl (0.5 mL, 1 N) and water (2 mL) at 25 °C for 5 min. The aqueous layer was extracted with CH_2Cl_2 (2 × 5 mL), and the combined organic layers were washed with 1 N HCl (2 × 5 mL), saturated aqueous $NaHCO_3$ solution, saturated aqueous NaCl solution and dried (Na_2SO_4). The solution was concentrated in vacuo to give 60 mg of crude product. Flash chromatography on silica gel (6:1 hexane–EtOAc) gave 28 mg (91%) of alcohol **10** as predominantly a single diastereomer, **10a**: ^1H NMR δ 4.93 (br s, 1), 4.82 (br s, 1), 3.53 (br s, 1), 2.56 (dd, 1, *J* = 13.4, 2.2 Hz), 2.42 (dd, 1, *J* = 13.4, 4.8 Hz), 2.34 (t, 2, *J* = 7.7 Hz), 1.95–2.15 (m, 2), 1.20–1.80 (m, 7), 0.85 (s, 3); ^{13}C NMR δ 145.0, 115.8, 71.3, 48.4, 39.9, 39.1, 36.5, 34.7, 32.0, 25.0, 21.0, 19.1; IR (neat) 3461, 3048, 2930, 2865, 1633 cm^{-1}. Anal. Calcd for $C_{12}H_{20}O$: C, 79.94; H, 11.18. Found: C, 79.86; H, 11.33.

(3a*R,8a*S**)-2,3,3a,7,8,8a-Hexahydro-3a,6-dimethyl-4(1*H*)-azulenone (11).** Alcohol **10** (32 mg, 0.18 mmol) was dissolved in dry CH_2Cl_2 (5 mL), and 44 mg (0.20 mmol, 1.1 equiv) of PCC was added. The mixture was stirred for 2 h and filtered through a fritted funnel packed with silica gel. The solvent was evaporated under reduced pressure, and the residue was dissolved in 25 mL of benzene to which *p*-toluenesulfonic acid (2.0 mg) and a few drops of water were added. The mixture was heated at reflux overnight. The solution was cooled to room temperature, and saturated aqueous $NaHCO_3$ solution (10 mL) was added. The aqueous layer was extracted with ether (3 × 15 mL). The combined organic layers were washed with saturated aqueous NaCl solution and dried (Na_2SO_4). The solution was concentrated in vacuo to give 33 mg of crude product. Flash chromatography on silica gel (8:1 hexane–EtOAc) gave 26.1 mg (83%) of enone **11**: ^1H NMR δ 5.82 (br s, 1), 2.25–2.42 (m, 3), 1.90 (s, 3), 1.4–2.1 (m, 10), 1.11 (s, 3); ^{13}C NMR δ 207.5, 152.2, 127.4, 55.6, 43.1, 36.3, 34.9, 30.9, 28.6, 25.7, 19.4, 19.0; IR (neat) 2880, 1660 cm^{-1}; UV λ_{max} (ethanol) 239 nm (ε 1.0 × 10^4). Anal. Calcd for $C_{12}H_{18}O$; C, 80.85; H, 10.18. Found: C, 80.73; H, 10.21.

2-(2-Cyclohexenyl)-6-methyl-4-heptanone (5). A solution of $TiCl_4$ in CH_2Cl_2 (17.2 mL, 1 M) was added through a syringe to a solution of **13**[12] (2.17 g, 17.2 mmol) in 9 mL of CH_2Cl_2 at −40 °C. The solution was stirred for 5 min, and **12**[11] (3.45 g, 22.4 mmol) in 26 mL of CH_2Cl_2 was added dropwise over 40 min. The mixture was stirred at −40 °C for 30 min. Water (34 mL) and ether (43 mL) were added, and the solution was warmed to 25 °C. The organic and aqueous layers were separated. The aqueous layer was extracted with ether (3 × 40 mL). The combined organic layers were washed with 40 mL of saturated aqueous $NaHCO_3$ solution and 40 mL of saturated aqueous NaCl solution and dried (Na_2SO_4). The solution was concentrated in vacuo to give 3.44 g of crude product. Flash chromatography on silica gel (15:1 hexane–EtOAc) of 0.59 g of the crude product gave 0.53 g (86%) of a ≈3:2 mixture of ketones **5a** and **5b**. The data for **5a** are identical with those described below. The data for **5b** were determined from the mixture: ^{13}C NMR δ 210.7 (C=O), 130.2 (CH), 128.2 (CH), 52.3 (CH_2), 47.6 (CH_2), 40.1 (CH), 32.9 (CH), 25.3 (CH_2), 25.26 (CH_2), 24.9, (CH), 22.6 (CH_3), 22.5, (CH_3), 22.1 (CH_2), 16.4 (CH_3).

α-((*E*)-1-Propenyl)-2-cyclohexene-1-methanol (26b). To a suspension of potassium *tert*-butoxide (0.34 g, 3.0 mmol) in 3 mL of dry cyclohexene was added *sec*-butyllithium (2.3 mL, 3.0 mmol, 1.3 M in cyclohexane) at 0 °C. The solution was stirred at 0 °C for 24 h, and a solution of crotonaldehyde (0.21 g, 3.0 mmol) in 2 mL of hexane was then added dropwise. The mixture was stirred at 0 °C for 1 h, and the reaction mixture was worked up by adding hydrochloric acid (3 mL, 1.0 M) and H_2O (3 mL). The aqueous layer was extracted with ether (3 × 15 mL). The combined organic layers were washed with saturated $NaHCO_3$ solution (10 mL) and saturated NaCl solution (10 mL) and dried (Na_2SO_4). Concentration in vacuo gave 0.56 g of crude product. Flash chromatography on silica gel (10:1 hexane–EtOAc) gave 0.37 g (81%) of alcohol **26b** as a 1:1 mixture of diastereomers: ^1H NMR δ 5.45–5.88 (m, 4), 3.92 (dd, 0.5 × 1, *J* = 6.8, 6.8 Hz), 3.89 (dd, 0.5 × 1, *J* = 6.8, 6.8 Hz), 2.22 (m, 1), 1.98 (m, 2), 1.72 (dd, 0.5 × 3, *J* = 6.3, 1.3 Hz), 1.71 (dd, 0.5 × 3, *J* = 6.3, 1.3 Hz), 1.63–1.82 (m, 1), 1.30–1.60 (m, 3); ^{13}C NMR δ (132.8, 132.1) (CH), (129.67, 129.70) (CH), (128.0, 128.2) (CH), (127.0, 127.2) (CH), (76.4, 76.3) (CH), (41.6, 41.4) (CH), (25.7, 24.3) (CH_2), 25.3 (both isomers, CH_2), (21.3, 21.5) (CH_2), (17.8, 17.7) (CH_3); IR (neat) 3370, 3020, 2925, 2860, 1675, 1650, 964 cm^{-1}. Anal. Calcd for $C_{10}H_{16}O$: C, 78.90; H, 10.61. Found: C, 78.72; H, 10.61.

(1*R,β*R**)-β-Methyl-2-cyclohexene-1-propanal (28).** Alcohol **26b** (0.13 g, 0.85 mmol) was dissolved in 40 mL of dry DME under N_2. Potassium hydride (0.069 g, 1.72 mmol) and 18-crown-6 (0.211 g, 0.80 mmol) were added. The mixture was heated at reflux for 15 h. The solution was cooled to room temperature, and 20 mL of saturated aqueous NH_4Cl solution and 50 mL of pentane were added. The aqueous layer was extracted with 20 mL of pentane. The combined organic layers were washed with water (3 × 20 mL), dried (Na_2SO_4), and concentrated in vacuo to give 0.125 g of crude product. Flash chromatography on silica gel (15:1 pentane–ether) gave 0.10 g (77%) of aldehyde **28**: ^1H NMR δ 9.76 (dd, 1, *J* = 2.8, 1.6 Hz), 5.75 (m, 1), 5.50 (ddt, 1, *J* = 10.1, 3.2, 2.0 Hz), 2.49 (ddd, 1, *J* = 15.0, 2.3, 1.6 Hz), 2.22 (ddd, 1, *J* = 15.0, 9.0, 2.8 Hz), 2.13 (m, 1), 1.95 (m, 2), 1.68–1.83 (m, 2), 1.43–1.59 (m, 1), 1.15–1.33 (m, 2), 0.96 (d, 3, *J* = 6.4 Hz); ^{13}C NMR δ 203.1

(CHO), 129.6 (CH), 129.0 (CH), 47.7 (CH_2), 40.4 (CH), 32.1 (CH), 25.30 (CH_2), 25.27 (CH_2), 22.1 (CH_2), 17.3 (CH_3); IR 3200, 2960–2830, 2710, 1725, 1650, 720 cm^{-1}. Anal. Calcd for $C_{10}H_{16}O$: C, 78.90; H, 10.59. Found: C, 79.01; H, 10.67.

(1*R,3*R**)-γ-Methyl-α-(2-methylpropyl)-2-cyclohexene-1-propanol (29).** A solution of crude aldehyde **28** (0.11 g), obtained from 0.10 g (0.60 mmol) of alcohol **26b**, in 5 mL of dry ether was added to isobutylmagnesium chloride (0.5 mL, 2 M in ether) at 0 °C. The solution was stirred at 0 °C for 1 h, and hydrochloric acid (2 mL, 1.0 M) and water (10 mL) were added. The aqueous layer was extracted with ether (2 × 20 mL). The combined organic phase was washed with saturated aqueous $NaHCO_3$ solution and saturated aqueous NaCl solution and dried (Na_2SO_4). The solution was concentrated in vacuo to give 0.123 g of crude **29**. Flash chromatography on silica gel (8:1 hexane–EtOAc) gave 99.2 mg (71% from **26b**) of alcohol **29** as a mixture of diastereomers: ^1H NMR δ 5.73 (m, 1), 5.33 (br d, 1 *J* = 10.5 Hz), 3.74 (m, 1), 2.02–2.20 (m, 1), 1.92–2.10 (m, 1), 1.18–1.84 (m, 12), 0.85–0.95 (m, 9); ^{13}C NMR δ (130.6, 129.9) (CH), (128.1, 128.2) (CH), (67.8, 68.6) (CH), (47.9, 46.9) (CH_2), (41.8, 42.3) (CH_2), (41.3, 40.1) (CH), (33.3, 33.9) (CH), 26.02 (both isomers CH_2), (25.50, 25.46) (CH_2), (24.7, 24.6) (CH), (23.3, 23.6) (CH_2), (25.5, 22.4) (CH_3), (22.2, 21.9) (CH_3), (16.4, 17.2) (CH_3); IR 3360, 3020, 2960–2840, 1650, 735, 720 cm^{-1}. Anal. Calcd for $C_{14}H_{28}O$: C, 79.94; H, 12.46. Found: C, 80.03; H, 12.52.

(2*R)-2-((1*R**)-2-Cyclohexenyl)-6-methyl-4-heptanone (5a).** A solution of alcohol **29** (27.7 mg, 0.132 mmol) and PCC (31.5 mg, 0.146 mmol) in 20 mL of dry CH_2Cl_2 was stirred at room temperature for 3.5 h. The solution was filtered through silica gel and concentrated in vacuo to give 31.6 mg of crude **5a**. Flash chromatography on silica gel (20:1 hexane–EtOAc) yielded 26.1 mg (95%) of ketone **5a**: ^1H NMR δ 5.70–5.80 (m, 1), 5.49 (br d, 1, *J* = 10.0 Hz), 2.41 (dd, 1, *J* = 15.4, 3.2 Hz), 2.27 (d, 2, *J* = 6.8 Hz), 2.02–2.24 (m, 4), 1.92–2.00 (m, 2), 1.63–1.82 (m, 2), 1.40–1.55 (m, 1), 1.17–1.28 (m, 1), 0.91 (d, 3, *J* = 6.5 Hz), 0.90 (d, 3, *J* = 6.5 Hz), 0.88 (d, 3, *J* = 6.2 Hz); ^{13}C NMR δ 211.0 (C=O), 130.0 (CH), 128.6 (CH), 52.4 (CH_2), 47.0 (CH_2), 40.4 (CH), 33.0 (CH), 25.40 (CH_2), 25.35 (CH_2), 24.5 (CH), 22.6 (CH_3), 22.5 (CH_3), 22.2 (CH_2), 17.0 (CH_3); IR (neat) 3020, 2955, 2930, 2870, 2815, 1712, 1650 cm^{-1}. Anal. Calcd for $C_{14}H_{24}O$: C, 80.71, H, 11.61. Found: C, 80.78, H, 11.70.

3-(3-(Ethylenedioxy)-1,5-dimethylhexyl)cyclohexene (14). A solution of 0.353 g (1.69 mmol) of ketone **5**, 1.5 mL of ethylene glycol, and 0.02 g of *p*-toluenesulfonic acid in 125 mL of benzene was heated at reflux for 12 h with azeotropic removal of water. The solution was cooled to room temperature, and 10 mL of 10% aqueous NaOH solution was added. The aqueous layer was extracted with ether (2 × 15 mL). The combined organic solution was washed with saturated aqueous NaCl solution and dried (Na_2SO_4). The solution was concentrated in vacuo to give 0.40 g of crude product. Flash chromatography on silica gel (10:1 hexane–EtOAc) yielded 0.37 g (87%) of a ≈3:2 mixture of **14a** and **14b**. The data for **14a** are identical with those described below. The data for **14b** were determined from the mixture: ^{13}C NMR δ 131.3 (CH), 128.7 (CH), 112.5 (C), 64.41 and 64.27 (OCH_2CH_2O), 45.51 (CH_2), 41.4 (CH_2), 40.8 (CH), 32.7 (CH), 25.46 (CH_2), 25.38 (CH_2), 24.5 (CH_3), 23.95 (CH_3), 24.00 (CH), 22.4 (CH_2), 17.3 (CH_3).

(3*R)-3-((1*R**)-3-(Ethylenedioxy)-1,5-dimethylhexyl)-cyclohexene (14a)** was obtained in 85% yield from **5a** by the procedure used for the mixture of diastereomers: ^1H NMR δ 5.69–5.79 (m, 1), 5.51 (br d, 1, *J* = 10.0 Hz), 3.94 (br s, 4), 2.08–2.18 (m, 2), 1.90–2.00 (m, 2), 1.61–1.82 (m, 5), 1.52 (d, 2, *J* = 6.2 Hz), 1.38–1.45 (m, 1), 1.15–1.30 (m, 1), 0.951 (d, 3, *J* = 6.6 Hz), 0.942 (d, 3, *J* = 6.6 Hz), 0.938 (d, 3, *J* = 6.2 Hz); ^{13}C NMR δ 130.7 (CH), 128.2 (CH), 112.6 (C), 64.4 and 64.2 (OCH_2CH_2O), 45.5 (CH_2), 41.7 CH), 40.3 (CH_2), 32.6 (CH), 25.54 (CH_2), 25.46 (CH_2), 24.2 (CH_3), 24.01 (CH_3), 24.00 (CH), 22.4 (CH_2), 18.1 (CH_3); IR (neat) 3015, 2950, 2925, 2870, 1650, 1080 cm^{-1}. Anal. Calcd for $C_{16}H_{28}O_2$: C, 76.14; H, 11.18. Found: C, 76.19; H, 11.25.

(1*S,2*R**,3*R**)-3-(3-(Ethylenedioxy)-1,5-dimethylhexyl)-cyclohexane-1,2-diol (15).** Ketal **14** (0.175 g, 0.69 mmol) was dissolved in 7 mL of 50% aqueous acetone. *N*-Methylmorpholine *N*-oxide monohydrate (0.99 g, 0.73 mmol) and a solution of 2.5 wt % osmium tetroxide in *tert*-butanol (75 mg) were added. The solution was stirred at room temperature for 16 h. Sodium hydrosulfite (0.07 g), Florisil (0.8 g), and water (6 mL) were added. The mixture was stirred for 5 min and filtered through a short column packed with silica gel. The filtrate was concentrated in vacuo to remove acetone. The aqueous solution was acidified to pH 2 with 10% sulfuric acid. Sodium chloride was added to saturate the solution, and the solution was then extracted with ether (3 × 15 mL). The combined organic layers were dried (Na_2SO_4). The solution was concentrated in vacuo to give 0.20 g of crude product. Flash chromatography on silica gel (7:5 hexane–EtOAc) gave 0.186 g (94%) of a ≈3:2 mixture of **15a** and **15b**. The data for **15a** are given below. The data for **15b** were determined from the mixture: ^1H NMR δ 0.94 (d, 3, *J* = 6.6 Hz), 0.92 (d, 3, *J* = 6.6 Hz), 0.88 (d, 0.5 × 3, *J* = 6.9 Hz).

(1*S,2*R**,3*R**)-3-((1*R**)-3-(Ethylenedioxy)-1,5-dimethylhexyl)cyclohexane-1,2-diol (15a)** was obtained in 95% yield from **14a** by the procedure used for the mixture of diastereomers: ^1H NMR δ 4.08 (ddd, 1, *J* = 2.8, 2.8, 2.8 Hz), 3.97 (br s, 4), 3.72 (d, 1, *J* = 4.2 Hz, OH), 3.34 (ddd, 1, *J* = 10.6, 4.28 2.8 Hz), 2.44 (br s, 1, OH), 1.31–2.01 (m, 13), 1.03 (d, 3, *J* = 6.9 Hz), 0.94 (d, 3, *J* = 6.8 Hz), 0.92 (d, 3, *J* = 6.8 Hz); ^{13}C NMR δ 113.1 (C), 72.9 (CH), 70.1 (CH), 64.5 and 64.4 (OCH_2CH_2O), 45.0 (CH_2), 42.8 (CH), 37.5 (CH_2), 31.1 (CH_2), 26.3 (CH), 24.2 (CH_3), 24.1 (CH_3), 24.0 (CH_2), 23.8 (CH), 20.3 (CH_3), 19.6 (CH_2); IR (neat) 3420, 2960–2870, 1072 cm^{-1}.

2-(1,5-Dimethyl-3-(ethylenedioxy)hexyl)hexanedial (16). Diol **15** (91.8 mg, 0.32 mmol) in water (1 mL) and acetone (2 mL) was stirred with $NaIO_4$ (75.4 mg, 0.35 mmol) at 25 °C for 3 h. The solution was concentrated in vacuo to remove acetone. The resulting aqueous solution was extracted with EtOAc (3 × 15 mL). The combined organic layers were washed with saturated aqueous NaCl solution and dried (Na_2SO_4). The solution was concentrated in vacuo to give 88.2 mg of a crude mixture of dials **16a** and **16b**. The data for **16a** are given below. The data for **16b** were determined from the mixture: ^1H NMR δ 9.77 (t, 1, *J* = 1.7 Hz), 9.66 (d, 1, *J* = 1.7 Hz), 0.96 (d, 6, *J* = 6.6 Hz), 0.90 (d, 3, *J* = 7.2 Hz).

(2*R)-2-((1*R**)-1,5-Dimethyl-3-(ethylenedioxy)hexyl)-hexanedial (16a)** was prepared in 107% crude yield from **15a** by the procedure used for the mixture of diastereomers: ^1H NMR δ 9.77 (t, 1, *J* = 1.7 Hz), 9.69 (d, 1, *J* = 2.3 Hz), 3.91 (br s, 4), 2.47 (td, 2, *J* = 7.0, 1.7 Hz), 2.30–2.40 (m, 1), 2.05–2.14 (m, 1), 1.20–1.80 (m, 9), 1.03 (d, 3, *J* = 7.2 Hz), 0.94 (d, 6, *J* = 6.6 Hz); ^{13}C NMR δ 205.3 (CHO), 202.1 (CHO), 111.8 (C), 64.28 and 64.26 (OCH_2CH_2O), 56.6 (CH), 45.3 (CH_2), 43.7 (CH_2), 40.5 (CH_2), 29.3 (CH), 25.4 (CH_2), 24.1 (CH), 24.0 (CH_3), 23.9 (CH_3), 20.4 (CH_2), 18.5 (CH_3); IR (neat) 2955, 2930, 2870, 2710, 1725, 1078 cm^{-1}.

3-(1,5-Dimethyl-3-(ethylenedioxy)hexyl)-1-cyclopentene-carboxaldehyde (4). Crude dial **16** was dissolved in 15 mL of anhydrous toluene. A solution of pyrrolidine acetate (1 N in dry benzene) (0.1 mL) was added. The solution was stirred at 0 °C for 14 h. A 10% aqueous solution of citric acid (5 mL) was added. The organic and aqueous layers were separated. The aqueous layer was extracted with ether (2 × 10 mL). The combined organic layers were washed with saturated aqueous NaCl solution, and dried (Na_2SO_4). The solution was concentrated in vacuo to give 65 mg of crude product. Flash chromatography on silica gel (6:1 hexane–EtOAc) gave 59.0 mg (69% from diol **14**) of a ≈3:2 mixture of enals **4a** and **4b**. The data for **4a** are given below. The data for **4b** were determined from the mixture: ^{13}C NMR δ 190.0 (CHO), 155.9 (CH), 147.8 (C), 112.0 (C), 64.40 and 64.35 (OCH_2CH_2O), 52.8 (CH), 45.5 (CH_2), 41.6 (CH_2), 32.5 (CH), 28.1 (CH_2), 26.7 (CH_2), 24.5 (two CH_3), 24.0 (CH), 18.2 (CH_3).

(3*R)-3-((1*R**)-1,5-Dimethyl-3-(ethylenedioxy)hexyl)-1-cyclopentenecarboxaldehyde (4a)** was prepared from **16a** in 79.8% yield (from diol **15a**) by the procedure used for the mixture of diastereomers: ^1H NMR δ 9.89 (s, 1), 6.81 (ddd, 1, *J* = 2.2, 1.9, 1.9 Hz), 3.93 (br s, 4), 2.90–3.00 (m, 1), 2.39–2.62 (m, 2), 2.05–2.18 (m, 1), 1.45–1.89 (m, 7), 1.00 (d, 3, *J* = 6.5 Hz), 0.946 (d, 3, *J* = 6.6 Hz), 0.942 (d, 3, *J* = 6.6 Hz); ^{13}C NMR δ 190.1 (CHO), 155.2 (CH), 147.9 (C), 112.2 (C), 64.5 and 64.3 (OCH_2CH_2O), 53.1 (CH), 45.5 (CH_2), 41.5 (CH_2), 32.4 (CH), 28.0 (CH_2), 27.0 (CH_2), 24.12 (CH_3), 24.09 (CH_3), 23.94 (CH), 18.8 (CH_3); IR (neat) 2955, 2925, 2870, 2710, 1683, 1620, 1075 cm^{-1}; UV λ_{max} (ethanol) 237 nm (ε 1.57 × 10^4). Anal. Calcd for $C_{16}H_{26}O_3$: C, 72.14; H, 9.84. Found: C, 72.03; H, 9.78.

Imines 17 and 18. Aldehyde **4** (47.3 mg, 0.178 mmol) and L-*tert*-leucine *tert*-butyl ester (33.2 mg, 0.178 mmol) in hexane

(2 mL) were stirred with 4A molecular sieves (0.1 g) at 25 °C overnight. The solution was filtered through a fritted funnel packed with silica gel. The filtrate was concentrated in vacuo to give 72.5 mg (94%) of imines **17** and **18**: ^{1}H NMR δ 8.00 (br s, 1), 6.11 (br s, 1), 3.90 (br s, 4), 3.37 (br s, 1), 2.48–2.90 (m, 2), 1.95–2.10 (m, 2), 1.50–1.80 (m, 7), 1.482 (s, 0.25 × 9), 1.476 (s, 0.25 × 9), 1.470 (s, 0.25 × 9), 1.460 (s, 0.25 × 9), 0.80–1.02 (m, 9), 0.98 (s, 0.5 × 9), 0.97 (s, 0.5 × 9).

Imines 17a and 18a were prepared in 93% yield from **4a** by the procedure used for the mixture of diastereomers: ^{1}H NMR δ 8.00 (br s, 1), 6.11 (br s, 1), 3.90 (br s, 4), 3.37 (br s, 1), 2.50–2.85 (m, 2), 2.00–2.09 (m, 2), 1.05–1.80 (m, 7), 1.47 (s, 0.5 × 9), 1.46 (s, 0.5 × 9), 1.20–1.27 (m, 1), 0.98 (s, 0.5 × 9), 0.97 (s, 0.5 × 9), 0.80–1.02 (m, 9); ^{13}C NMR δ 170.9 (C), 159.7 (CH), 145.0 (CH), (142.92, 142.89) (CH), (111.30, 111.28) (C), (83.08, 83.06) (CH), (80.7) (C), (64.5, 64.4 and 64.25, 64.23) (OCH_2CH_2O), (52.9, 52.8) (CH), (45.54, 45.51) (CH_2), (41.4, 41.3) (CH_2), (32.9, 32.8) (CH), (30.41, 30.38) (CH_2), (28.22, 28.18) (3 × CH_3), (26.93, 26.90) (CH_2), 26.8 (3 × CH_3), 24.1 (CH_3), 24.0 (CH_3), 23.9 (CH), (19.94, 18.92) (CH_3), one carbon not observed; IR (neat) 2980–2930, 2875, 1740, 1720, 1640, 1610, 1140 1078 cm^{-1}.

(1*R*,2*R*,3*R*)-3-(1,5-Dimethyl-3-(ethylenedioxy)hexyl)-1-methyl-2-(3-methyl-3-butenyl)cyclopentanecarboxaldehyde (3). A solution of imines **17** and **18** (239 mg, 0.517 mmol) in THF (1.0 mL) was cooled to −25 °C. (3-Methyl-3-butenyl)magnesium bromide (2.3 mL, 0.9 M in THF) was added dropwise. The solution was stirred at −25 °C for 7.5 h. A mixture of methyl iodide (0.20 mL, 3.1 mmol), HMPA (0.63 mL, 3.6 mmol), and THF (0.2 mL) was added. The mixture was stirred at −25 °C for 30 min and then at 25 °C for 15 h. Workup as described above for the preparation of **9** gave 150 mg of crude product. Flash chromatography on silica gel (8:1 hexane–EtOAc) gave 58 mg (32%) of a ≈3:2 mixture of aldehydes **3a** and **3b** and 69 mg (50%) of recovered unsaturated aldehyde **4** which showed a (+) CD spectrum.

The data for **3b** were determined from the mixture: ^{13}C NMR δ 206.0, 145.4, 112.3, 110.1, 64.33, 64.30, 56.36, 49.02, 46.18, 45.52, 43.5, 36.3, 31.6, 28.9, 27.5, 24.20, 24.03, 24.06, 23.4, 22.64, 14.6, 14.1.

(1*R*,2*R*,3*R*)-3-((1*R*)-1,5-Dimethyl-3-(ethylenedioxy)hexyl)-1-methyl-2-(3-methyl-3-butenyl)cyclopentanecarboxaldehyde (3a) was synthesized from **4a** in 36.6% yield by the procedure used for the mixture of diastereomers: ^{1}H NMR δ 9.41 (s, 1), 4.67 (br s, 1), 4.63 (br s, 1), 3.93 (br s, 4), 1.25–1.95 (m, 16), 1.68 (s, 3), 1.04 (d, 3, *J* = 6.7 Hz), 1.02 (s, 3), 0.952 (d, 3, *J* = 6.6 Hz, 0.948 (d, 3, *J* = 6.6 Hz); ^{13}C NMR δ 206.2 (CHO), 145.7 (C), 112.4 (C), 110.0 (CH_2), 64.5 and 64.4 (OCH_2CH_2O), 56.3 (C), 51.0 (CH), 47.0 (CH), 45.6 (CH_2), 38.6 (CH_2), 36.5 (CH_2), 34.9 (CH_2), 29.4 (CH), 28.1 (CH_2), 24.8 (CH_2), 24.2 (CH_3), 24.1 (CH_3), 24.0 (CH), 22.4 (CH_3), 22.0 (CH_3), 14.2 (CH_3); IR (neat) 3070, 2940, 2920, 2860, 2680, 1725, 1650, 1072 cm^{-1}. Anal. Calcd for $C_{22}H_{38}O_3$: C, 75.38; H, 10.92. Found: C, 75.43; H, 10.92.

(1*R*,3a*R*,4*S*,8a*R*)-Decahydro-1-(1,5-dimethyl-3-(ethylenedioxy)hexyl)-3a-methyl-6-methylene-4-azulenol (19). A solution of aldehyde **3** (17.0 mg, 0.049 mmol) in CH_2Cl_2 (10 mL) was cooled to 0 °C. Me_2AlCl (0.03 mL, 1.93 M in hexane) was added dropwise. The solution was stirred at 0 °C for 30 min, and HCl (0.3 mL, 1 N aqueous solution) and water (3 mL) were added. The aqueous layer was extracted with CH_2Cl_2 (2 × 6 mL). The combined organic layers were washed with saturated aqueous $NaHCO_3$ solution and saturated aqueous NaCl solution and dried (Na_2SO_4). The solution was concentrated in vacuo to give 14.1 mg of a mixture of alcohol **19** and the corresponding keto alcohol resulting from hydrolysis of the ketal.

(1*R*,3a*R*,4*S*,8a*R*)-Decahydro-1-((1*R*)-1,5-dimethyl-3-(ethylenedioxy)hexyl)-3-methyl-6-methylene-4-azulenol (19a). A 3:1 mixture (15.8 mg) of desired diastereomer of **19a** and the corresponding keto alcohol resulting from hydrolysis of the ketal was obtained from aldehyde **3a** (17.7 mg) by the procedure used for the mixture of diastereomers. The data for **19a** were determined from the mixture: ^{1}H NMR δ 4.93 (br s, 1), 4.82 (br s, 1), 3.92 (br s, 4), 3.45–3.53 (m, 1), 2.57 (dd, 1, *J* = 13.3, 2.2 Hz), 2.25–2.41 (m, 4), 1.90–2.05 (m, 2), 1.48–1.60 (m, 7), 1.12–1.40 (m, 5), 1.05 (s, 3), 0.80–1.02 (m, 9); IR (neat) 3525, 3060, 2945, 2865, 1632, 1073 cm^{-1}.

Reiswigin A (20). The mixture of ketal alcohol **19** and the corresponding keto alcohol from the above reaction (10.1 mg) in CH_2Cl_2 (5 mL) was stirred with PCC (10 mg, 0.046 mmol) in CH_2Cl_2 (10 mL) at 25 °C for 5 h. The mixture was filtered through a fritted funnel packed with silica gel. The solvent was evaporated in vacuo. The residue was dissolved in benzene (20 mL), and *p*-toluenesulfonic acid (2 mg) and 5 drops of water were added. The solution was heated at reflux overnight. The solution was cooled to room temperature, and saturated aqueous Na_2CO_3 solution (3 mL) was added. The inorganic layer was extracted with ether (2 × 10 mL). The combined organic layers were washed with saturated aqueous NaCl solution and dried (Na_2SO_4). The solution was concentrated in vacuo to give 11.3 mg of crude product. Flash chromatography on silica gel (8:1 hexane–EtOAc) gave 8.9 mg (83% from aldehyde **3**) of reiswigin A (**20**) and its epimer **21**. HPLC analysis showed that the product consisted of a 3:2 mixture of reiswigin A (**20**) and its epimer **21**. HPLC separation was accomplished on a 10 mm × 25 cm ODS column with 70:30 methanol–water as eluent at a flow rate of 2 mL/min. The retention times are 128 min (**20**) and 137 min (**21**).

Reiswigin A (**20**) was also prepared from the mixture of ketal alcohol **19a** and keto alcohol by the procedure used for preparing the mixture of **20** and **21**. Flash chromatography gave **20** contaminated with <5% of **21** in 85.8% yield from **3a**.

The ^{1}H and ^{13}C NMR and IR data of synthetic reiswigin A (**20**) are identical with those of an authentic sample.[1,16] The ^{1}H NMR data reported for reiswigin A (**20**) are not referenced correctly;[16] 0.08 ppm should be subtracted from the reported δ values. Both the UV and CD spectra of synthetic **20** are identical with those of a natural sample provided by Dr. Koehn. Synthetic **20**: UV λ_{max} (ethanol) 239 nm (ε 1.1 × 10^4); $[\alpha]^{25}_D$ −11.5° (*c* = 0.075, $CDCl_3$); CD λ_{max} (ethanol) 300 nm ($[\theta]_{25}$ −5.0 × 10^3). Natural **20**: UV λ_{max} (ethanol) 239 nm (ε 1.1 × 10^4); $[\alpha]^{25}_D$ −10° (*c* = 0.1, $CDCl_3$); CD λ_{max} (ethanol) 300nm ($[\theta]_{25}$ −4.4 × 10^3).

The data for **21**: ^{1}H NMR δ 5.80 (br s, 1), 1.90 (br s, 3), 1.10 (s, 3), 0.93 (d, 6, *J* = 6.6 Hz), 0.80 (d, 3, *J* = 6.5 Hz); ^{13}C NMR 210.3 (C_2), 152.5 (C_4), 127.4 (C_3), 56.4 (C_1), 52.6 (C_{17}), 49.9 (C_{15}), 46.4 and 44.8 (C_7 and C_8), 35.2 and 34.9 (C_5 and C_{10}), 28.6 (C_{12}), 28.6 (C_{13}), 24.5 (C_{18}), 24.2 (C_6), 22.6 and 22.6 (C_{19} and C_{20}), 20.5 (C_9), 19.8 (C_{11}), 13.6 (C_{14}); carbon 16 was not observed; UV λ_{max} (ethanol) 239 nm (ε 1.0 × 10^4); CD λ_{max} (ethanol) 300 nm ($[\theta]_{25}$ −5.9 × 10^3).

(3*R)-3-((1*R**)-3-(Ethylenedioxy)-1-methylpropyl)cyclohexene (30).** Aldehyde **28** (98.7 mg, 0.648 mmol) in 50 mL of benzene was treated with 0.1 g of toluene sulfonic acid and 0.3 mL of ethylene glycol. The solution was heated at reflux with azeotropic removal of water for 12 h. The solution was cooled to room temperature, washed with 3 mL of saturated aqueous $NaHCO_3$ solution and 20 mL of H_2O, dried (Na_2SO_4), and concentrated in vacuo to give 99.2 mg of crude acetal. Flash column chromatography on silica gel (20:1 hexane–EtOAc) gave 91.0 mg (72%) of acetal **30**: ^{1}H NMR δ 5.74 (m, 1), 5.52 (br d, 1, *J* = 10.5 Hz), 4.90 (dd, 1, *J* = 5.8, 4.0 Hz), 3.80–4.00 (m, 4), 2.10–2.20 (m, 1), 1.91–2.00 (m, 2), 1.63–1.82 (m, 4), 1.42–1.60 (m, 2), 1.18–1.33 (m, 1), 0.97 (d, 3, *J* = 7.1 Hz); ^{13}C NMR δ 130.1 (CH), 128.3 (CH), 104.2 (CH), 64.8 and 64.6 (OCH_2CH_2O), 40.9 (CH), 37.5 (CH_2), 33.4 (CH), 25.5 (CH_2), 24.2 (CH_2), 22.3 (CH_2), 16.9 (CH_3); IR (neat) 3020, 2960–2840, 1650, 1130, 1040, 720 cm^{-1}. Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.56; H, 10.12.

(3*R)-3-((1*R**)-1-Methyl-3-(ethylenedioxy)propyl)-1-cyclopentenecarboxaldehyde (31).** (1*S**,2*R**,3*R**)-3-((1*R**)-3-(Ethylenedioxy)-1-methylpropyl)-3-cyclohexane-1,2-diol was prepared in 96% yield by the procedure used for the preparation of **15**: ^{1}H NMR δ 4.91 (dd, 1, *J* = 6.6, 6.3 Hz), 3.81–4.10 (m, 5), 3.44 (dd, 1, *J* = 10.6, 2.8 Hz), 1.30–2.15 (m, 11), 1.02 (d, 3, *J* = 7.0 Hz), 0.78–0.95 (m, 1); ^{13}C NMR δ 104.3 (CH), 72.7 (CH), 70.3 (CH), 64.9 and 64.8 (OCH_2CH_2O), 42.6 (CH), 35.3 (CH_2), 31.2 (CH_2), 27.4 (CH), 24.4 (CH_2), 19.5 (CH_2), 18.9 (CH_3); IR (neat) 3430, 2960–2875, 1135, 1115, 1040 cm^{-1}.

(2*R**)-2-((1*R**)-1-Methyl-3-(ethylenedioxy)propyl)hexanedial was prepared in 96.1% crude yield by the procedure used for the preparation of **16**: ^{1}H NMR δ 9.76 (t, 1, *J* = 1.5 Hz), 9.70 (d, 1, *J* = 2.5 Hz), 4.91 (dd, 1, *J* = 5.7, 5.7 Hz), 3.80–4.00 (m, 4), 2.46 (td, 2, *J* = 7.0, 1.5 Hz), 2.25–2.33 (m, 1), 2.11–2.21 (m, 1), 1.52–1.80 (m, 5), 1.39–1.49 (m, 1), 1.04 (d, 3, *J* = 7.1 Hz); ^{13}C NMR δ 204.9 (CHO), 201.9 (CHO), 103.2 (CH), 64.8 and 64.7 (OCH_2CH_2O), 56.5

(CH), 43.8 (CH_2), 37.9 (CH_2), 29.8 (CH), 25.4 (CH_2), 20.3 (CH_2), 17.5 (CH_3); IR 2960, 2890, 2730, 1725, 1145, 1120, 1035 cm^{-1}.

Enal **31** was prepared in 69% overall yield from cyclohexene **30** by the procedure used for the preparation of **4**: ^1H NMR δ 9.79 (s, 1), 6.81 (ddd, 1, J = 2.1, 1.8, 1.8 Hz), 4.92 (dd, 1, J = 8.3, 6.0 Hz), 3.80–4.00 (m, 4), 2.90–3.00 (m, 1), 2.39–2.62 (m, 2), 2.13 (dddd, 1, J = 13.0, 9.0, 9.0, 4.5 Hz), 1.82–1.92 (m, 1), 1.51–1.74 (m, 3), 1.00 (d, 3, J = 6.7 Hz); ^{13}C NMR δ 190.0 (CHO), 154.5 (CH), 147.9 (C), 103.5 (CH), 64.8 and 64.7 (OCH_2CH_2O), 52.7 (CH), 38.6 (CH_2), 33.2 (CH), 28.1 (CH_2), 26.9 (CH_2), 17.6 (CH_3); IR (neat) 2960, 2880, 2710, 1680, 1620, 1145, 1035, 710 cm^{-1}; UV λ_{max} (ethanol) 240 nm (ϵ 1.64 × 10^4). Anal. Calcd for $C_{12}H_{18}O_3$: C, 68.54; H, 8.63. Found: C, 68.19; H, 8.42.

(1*R*,2*R*,3*R*)-3-((1*R*)-1-Methyl-3-(ethylenedioxy)propyl)-1-methyl-2-(3-methyl-3-butenyl)cyclopentanecarboxaldehyde (32). Aldehyde **31** (56 mg, 0.27 mmol) was converted to a mixture of imines in 95% yield by the procedure used for the preparation of **17** and **18**: ^1H NMR δ 7.99 (s, 0.5 × 1), 7.98 (s, 0.5 × 1), 6.13 (dt, 1, J = 1.9, 1.9 Hz), 4.92 (dd, 0.5 × 1, J = 8.4, 5.9 Hz), 4.91 (dd, 0.5 × 1, J = 8.4, 5.9 Hz), 3.80–4.00 (m, 4), 3.38 (s, 1), 2.45–2.85 (m, 4), 1.99–2.12 (m, 1), 1.50–1.83 (m, 3), 1.47 (s, 0.5 × 9), 1.46 (s, 0.5 × 9), 1.00 (d, 3, J = 6.5 Hz), 0.97 (s, 0.5 × 9), 0.96 (s, 0.5 × 9); ^{13}C NMR δ 170.9 (C), (159.57, 159.55) (CH), (145.24, 145.22) (C), (142.12, 142.07) (CH), 103.8 (CH), (83.1, 83.0) (CH), 80.7 (C), 64.8, 64.6) (OCH_2CH_2O), (52.21, 52.18) (CH), (38.56, 38.49) (CH_2), (35.01, 35.01) (CH_2), (33.5, 33.6) (CH), 30.3 (CH_2), 28.16 (3 CH_3), 26.8 (3 CH_3), (17.57, 17.61) (CH_3), one carbon not observed; IR (neat) 3050 2985–2880, 1745, 1645, 1615, 1145, 1040, 735 cm^{-1}.

The mixture of imines was treated as described above for the preparation of **3** to give 28.0 mg (51%) of recovered aldehyde **31** and 26.8 mg (35%) of aldehyde **32**: ^1H NMR δ 9.39 (s, 1), 4.92 (dd, 1, J = 6.2, 6.2 Hz), 4.68 (br s, 1), 4.63 (br s, 1), 3.80–4.00 (m, 4), 1.95–1.22 (m, 13), 1.68 (s, 3), 1.03 (d, 3, J = 7.3 Hz), 1.02 (s, 3); ^{13}C NMR δ 206.0 (CHO), 145.4 (C), 110.1 (CH_2), 104.1 (CH), 64.9 and 64.6 (OCH_2CH_2O), 56.4 (C), 50.3 (CH), 46.3 (CH), 36.2 (CH_2), 35.5 (CH_2), 34.7 (CH_2), 30.4 (CH), 27.8 (CH_2), 24.7 (CH_2), 22.3 (CH_3), 20.2 (CH_3), 14.2 (CH_3); IR (neat) 3070, 2950, 2880, 2690, 1725, 1650, 1135, 1040, 890 cm^{-1}. Anal. Calcd for $C_{18}H_{30}O_3$: C, 73.43; H, 10.27. Found, C, 73.30; H, 10.19.

(1*R*,3a*R*,4*S*,8a*R*)-Decahydro-1-((1*R*)-1-methyl-3-(ethylenedioxy)propyl)-3a-methyl-6-methylene-4-azulenol (33). A solution of aldehyde **32** (22.8 mg, 0.077 mmol) in CH_2Cl_2 (20 mL) was treated with Me_2AlCl (0.045 mL, 1.93 M in hexane, 1.1 equiv) and worked up as described above to give 29.3 mg of crude product. Flash chromatography on silica gel (10:1 hexane–EtOAc) gave 18.8 mg (83%) of alcohol **33**: ^1H NMR δ 4.93 (br s, 1), 4.89 (dd, 1, J = 6.2, 4.1 Hz), 4.82 (br s, 1), 3.80–4.00 (m, 4), 3.47–3.52 (m, 1), 2.56 (dd, 1, J = 13.4, 2.3 Hz), 2.28–2.42 (m, 3), 1.92–2.02 (m, 2), 1.52–1.80 (m, 6), 1.12–1.48 (m, 4), 0.92 (d, 3, J = 6.8 Hz), 0.88 (s, 3); ^{13}C NMR δ 145.0 (C), 115.9 (CH_2), 104.4 (CH), 71.6 (CH), 64.8 and 64.5 (OCH_2CH_2O), 49.5 (C), 49.3 (CH), 40.8 (CH), 39.8 (CH_2), 35.9 (CH_2), 35.0 (CH_2), 34.7 (CH_2), 30.7 (CH), 24.2 (CH_2), 23.6 (CH_2), 19.9 (CH_3), 19.8 (CH_3); IR (neat) 3500, 3070, 2960–2870, 1690, 1140, 1040, 890, 880 cm^{-1}. Anal. Calcd for $C_{18}H_{30}O_3$: C, 73.43; H, 10.27. Found: C, 73.24; H, 10.12.

(1*R*,3a*R*,4*S*,8a*R*)-Decahydro-1-((1*R*)-1-methyl-3-oxopropyl)-3a-methyl-6-methylene-4-azulenol (34). Acetal **33** (12.0 mg, 0.041 mmol) was dissolved in 30 mL of acetone. Water (3 drops) and pyridinium tosylate (10 mg) were added. The solution was heated at reflux for 12 h. The solution was cooled to room temperature and concentrated in vacuo. The residue was redissolved in 20 mL of ether and 5 mL of water. The aqueous layer was extracted with ether (2 × 5 mL). The combined organic layers were washed with saturated aqueous NaCl solution and dried (Na_2SO_4). The solution was concentrated in vacuo to give 19.3 mg of crude aldehyde. Flash chromatography on silica gel (8:1 hexane–EtOAc) gave 9.8 mg (95%) of aldehyde **34**: ^1H NMR δ 9.78 (dd, 1, J = 2.5, 1.7 Hz), 4.95 (br s, 1), 4.83 (br s, 1), 3.48–3.52 (m, 1), 2.57 (dd, 1, J = 13.5, 2.4 Hz), 2.31–2.50 (m, 3), 2.13–2.25 (m, 2), 1.93–2.02 (m, 2), 1.60–1.80 (m, 3), 1.13–1.48 (m, 5), 0.96 (d, 3, J = 6.4 Hz), 0.90 (s, 3); ^{13}C NMR δ 203.2 (CHO), 144.7 (C), 116.2 (CH_2), 71.3 (CH), 49.6 (C), 48.6 (CH), 46.5 (CH_2), 41.3 (CH), 39.8 (CH_2), 35.0 (CH_2), 34.5 (CH_2), 29.4 (CH), 24.2 (CH_2), 23.7 (CH_2), 20.0 (CH_3), 19.8 (CH_3); IR (neat) 3530, 3080, 2960–2890, 1735, 1640, 1060, 900, 880 cm^{-1}. Anal. Calcd for $C_{16}H_{26}O_2$: C, 76.75; H, 10.47. Found: C, 76.75; H, 10.32.

(1*R*,3a*R*,4*S*,8a*R*)-Decahydro-1-((1*R*)-1,5-dimethyl-3-hydroxyhex-4-enyl)-3a-methyl-6-methylene-4-azulenol (35a and 35b). 1-Bromo-2-methylpropene (0.019 mL, 0.206 mmol) in 1 mL of THF was cooled to −78 °C. *tert*-Butyllithium (0.240 mL, 0.412 mmol, 1.7 M in hexane) was added dropwise. The solution was stirred at −78 °C for 30 min, and aldehyde **34** (17.0 mg, 0.068 mmol) in 0.5 mL of THF was added. The solution was stirred at −78 °C for 30 min, and the reaction was quenched with 2.5 mL of hydrochloric acid (0.1 M) and 2.5 mL of H_2O. The solution was warmed to room temperature, and 5 mL of ether was added. The aqueous layer was extracted with ether (2 × 10 mL). The combined organic layers were washed with saturated aqueous $NaHCO_3$ solution (5 mL) and saturated aqueous NaCl solution (5 mL) and dried (Na_2SO_4). The solution was concentrated in vacuo to give 30.8 mg of crude diol. Flash chromatography on silica gel (4:1 hexane–EtOAc) gave 2.8 mg (16%) of recovered **34**, followed by 4.7 mg (27% based on recovered **34**) of one epimer **35a**, followed by 6.6 mg (38.0% based on recovered **34**) of the other epimer **35b**.

The data for **35a**: mp 86.0–87.0 °C; ^1H NMR δ 5.17 (dqq, 1, J = 9.0, 1.3, 1.3 Hz), 4.94 (br s, 1), 4.83 (br s, 1), 4.40 (ddd, 1, J = 9.0, 9.0, 3.7 Hz), 3.48–3.52 (m, 1), 2.57 (dd, 1, J = 13.4, 2.2 Hz), 2.28–2.41 (m, 3), 1.90–2.30 (m, 2), 1.72 (d, 3, J = 1.3 Hz), 1.69 (d, 3, J = 1.3 Hz), 1.05–1.68 (m, 9), 0.94 (d, 3, J = 6.8 Hz), 0.89 (d, 3, J = 0.6 Hz); ^{13}C NMR δ 145.0 (C), 134.2 (C), 128.9 (CH), 115.9 (CH_2), 71.6 (CH), 66.9 (CH), 49.5 (C), 49.2 (CH), 40.7 (CH), 39.8 (CH_2), 39.6 (CH_2), 35.1 (CH_2), 34.7 (CH_2), 30.4 (CH), 25.7 (CH_2), 24.3 (CH_3), 23.7 (CH_2), 19.9 (CH_3), 19.2 (CH_3), 18.1 (CH_3); IR ($CHCl_3$) 3615, 3540, 3080, 2960–2880, 1670, 1635, 1050 cm^{-1}. Anal. Calcd for $C_{20}H_{34}O_2$: C, 78.38; H, 11.18. Found: C, 78.21; H, 11.47.

The data for **35b**: mp 97.5–99.0 °C; ^1H NMR δ 5.07 (dqq, 1, J = 8.9, 1.3, 1.3 Hz), 4.93 (br s, 1), 4.83 (br s, 1), 4.39 (ddd, 1, J = 8.9, 8.9, 3.0 Hz), 3.48–3.52 (m, 1), 2.57 (dd, 1, J = 13.6, 2.2 Hz), 2.30–2.41 (m, 3), 1.92–2.05 (m, 2), 1.75 (d, 3, J = 1.3 Hz), 1.70 (d, 3, J = 1.3 Hz), 1.13–1.68 (m, 9), 0.91 (d, 3, J = 6.4 Hz), 0.87 (d, 3, J = 0.7 Hz); ^{13}C NMR δ 145.1 (C), 135.8 (C), 128.3 (CH), 115.8 (CH_2), 71.5 (CH), 67.8 (CH), 49.4 (C), 49.2 (CH), 40.9 (CH), 39.8 (CH_2), 39.6 (CH_2), 34.9 (CH_2), 34.8 (CH_2), 30.9 (CH), 25.9 (CH_2), 24.0 (CH_3), 23.5 (CH_2), 20.1 (CH_3), 20.0 (CH_3), 18.3 (CH_3); IR ($CHCl_3$) 3610, 3530, 3070, 2960–2850, 1680, 1635, 1050 cm^{-1}. Anal. Calcd for $C_{20}H_{34}O_2$: C, 78.38; H, 11.18. Found: C, 78.02; H, 11.50.

Reiswigin B (36). A mixture of diols **35a** (1.9 mg, 0.0062 mmol) and **33b** (2.5 mg, 0.0082 mmol) was dissolved in 5 mL of dry CH_2Cl_2 under N_2. PCC (4.0 mg, 0.018 mmol) was added. The solution was stirred at room temperature for 1.5 h and then filtered through silica gel. The solution was concentrated in vacuo to remove CH_2Cl_2. The residue was redissolved in 15 mL of benzene. Water (5 drops) and toluenesulfonic acid (6.1 mg, 0.032 mmol) were added. The solution was heated at reflux for 12 h. The solution was cooled to room temperature, and saturated aqueous $NaHCO_3$ solution was added. The aqueous layer was extracted with ether (10 mL). The combined organic layers were washed with saturated aqueous NaCl solution and dried (Na_2SO_4). The solution was concentrated in vacuo to give 7.0 mg of crude product. Flash chromatography on silica gel (5:1 hexane–EtOAc) gave 4.0 mg (92%) of reiswigin B (**36**). The ^1H and ^{13}C NMR data of synthetic reiswigin B (**36**) are identical with those reported: UV λ_{max} (ethanol) 239 nm (ϵ 1.8 × 10^4); $[\alpha]^{25}_D$ −23° (c = 0.052, $CDCl_3$).

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Supplementary Material Available: ^1H and/or ^{13}C NMR spectra for compounds without combustion analyses and other key intermediates (18 pages). Ordering information is given on any current masthead page.