A Short Enantiospecific Synthesis of the Ceroplastin Nucleus

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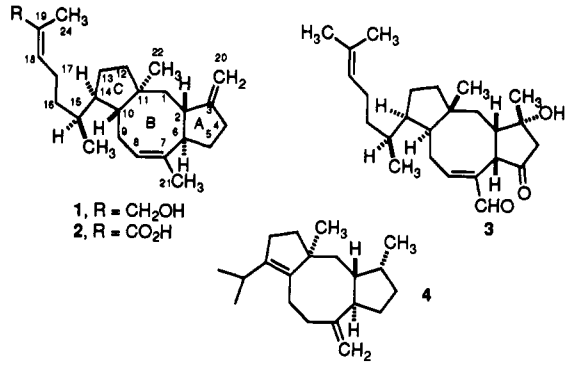
The tricyclic nucleus **9b** of ceroplastol I and ceroplasteric acid has been synthesized stereoselectively and enantiospecifically in only 10 steps from 1-cyclopentenecarboxaldehyde. Addition of (3-methyl-3-butenyl)magnesium bromide to imine **13b** and methylation with methyl iodide by Koga's procedure gave 94% of optically pure aldehyde **40** as previously described in our reiswigin A synthesis. Isomerization of the double bond of aldehyde **40** with HI afforded aldehyde **17b**. Coupling of the enolate prepared from silyl enol ether **45** with aldehyde **17b** gave a 1:1 mixture of **46a** and **46b**, which contain the complete carbon skeleton of **9b**, in only three steps. Dehydration provided enones **47a** and **47b**. Reduction of **47a** and **47b** with Li/NH_3 afforded saturated ketones **48at** and **48bt** that were reduced with $LiAlH_4$ to the saturated alcohols **49att** and **49btt**. Protection of the alcohols as the TBDMS ethers and oxidative cleavage of the dienes afforded readily separable keto aldehydes **51** and **56**. McMurry coupling of **51**, cleavage of the silyl ether, and oxidation of the alcohol with PCC completed the synthesis of **9b**.

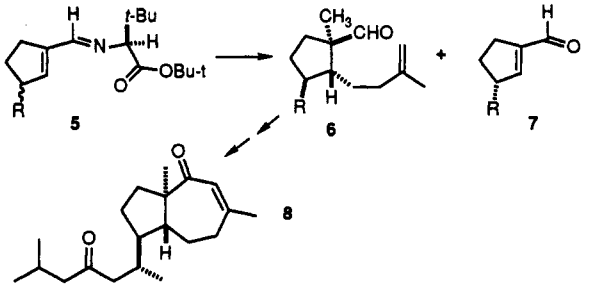
Introduction

The ceroplastins,[1] such as ceroplastol I (**1**) and ceroplasteric acid (**2**), and ophiobolins,[2] such as ophiobolin C (**3**), are sesterterpenes with a dicyclopenta[*a,d*]cyclooctene nucleus and an eight-carbon, steroid-type side chain. The fusicoccin diterpenes,[3] such as cycloaraneosene (**4**), possess the same ring system with a shorter, three-carbon side chain. The stereochemistry varies widely throughout these systems. Ceroplastins, obtained from the protective wax secreted by *Ceroplastes* scale insects, possess a trans-anti-trans ring system with the side chain at C-14 syn to the hydrogen at C-10. Ophiobolins, isolated from phytopathogenic fungi, possess a trans-syn-cis ring system with the side chain at C-14 anti to the hydrogen at C-10. The novel ring system has stimulated extensive synthetic efforts[4] that have culminated in the recent syntheses of (+)-ophiobolin C (**3**) by Kishi,[5] (±)-ceroplastol I (**1**) by Boeckman,[6] and ceroplastol II, albolic acid, cycloaraneosene (**4**), and hydroxycycloaraneosene by Kato and Takashita.[7]

We have recently reported[8] enantiospecific syntheses of



reiswigins A (**8**) and B in which the key step is the extension of Koga's procedure[9] for addition of Grignard reagents and methyl iodide to α,β-unsaturated imines of the *tert*-butyl ester of *tert*-leucine to the enantiospecific synthesis of **6**. We found that Koga's procedure can be used with aliphatic Grignard reagents and that a kinetic resolution[10] can be accomplished starting with a racemic 3-alkyl-1-cyclopentenecarboxaldehyde. Addition of (3-methyl-3-butenyl)magnesium bromide to imine **5**, prepared from the *tert*-butyl ester of (*S*)-*tert*-leucine and the racemic enal, followed by alkylation of the enamide with methyl iodide and hydrolysis affords 32% of optically pure **6** and 50% of recovered optically active **7**. Lewis acid catalyzed ene reaction of **6**, oxidation of the resulting alcohol, and conjugation of the double bond completes the synthesis of reiswigin A (**8**).



The relative and absolute stereochemistry of the three chiral centers of aldehyde **6** is identical to that at C-10, C-11, and C-14 in the C-ring of ceroplastol I (**1**) and the

(1) (a) Ríos, T.; Colunga, F. *Chem. Ind.* **1965**, 1184. (b) Iitaka, Y.; Watanabe, I.; Harrison, I. T.; Harrison, S. *J. Am. Chem. Soc.* **1968**, *90*, 1092; *Acta Crystallogr.* **1969**, *B25*, 1299. (c) Ríos, T.; Quijano, L. *Tetrahedron Lett.* **1969**, 1317. (d) Ríos, T.; Gómez, G., F. *Tetrahedron Lett.* **1969**, 2929. (e) Crews, P.; Naylor, S. G. *Prog. Chem. Org. Nat. Prod.* **1985**, *48*, 203.

(2) (a) Nozoe, S.; Morisaki, M.; Fukushima, K.; Okuda, S. *Tetrahedron Lett.* **1968**, 4457. (b) Nozoe, S.; Morisaki, M. *J. Chem. Soc., Chem. Commun.* **1969**, 1319.

(3) (a) Banerji, A.; Hunter, R.; Mellows, G.; Sim, K.; Barton, D. H. R. *J. Chem. Soc., Chem. Commun.* **1978**, 843. (b) Barrow, K. D.; Jones, R. B.; Pemberton, P. W.; Phillips, L. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1405. (c) Borschberg, H. J. Ph.D. Dissertation, Eidenössischen Technischen Hochschule, Zurich, Switzerland, 1975.

(4) (a) Das, T. K.; Dutta, P. C.; Kartha, G.; Bernassau, J. M. *J. Chem. Soc., Perkin Trans. 1* **1977**, 1287. (b) Dauben, W. G.; Hart, D. J. *J. Org. Chem.* **1977**, *42*, 922. (c) Grayson, D. H.; Wilson, J. R. H. *J. Chem. Soc., Chem. Commun.* **1984**, 1695. (d) Paquette, L. A.; Andrews, D. R.; Springer, J. P. *J. Org. Chem.* **1983**, *48*, 1148. (e) Paquette, L. A.; Colapret, J. A.; Andrews, D. R. *J. Org. Chem.* **1985**, *50*, 201. (f) Coates, R. M.; Muskopf, J. W.; Senter, P. A. *J. Org. Chem.* **1985**, *50*, 3541. (g) Mehta, G.; Krishnamurthy, N. *J. Chem. Soc., Chem. Commun.* **1986**, 1319. (h) Rigby, J. H.; Senanayake, C. *J. Org. Chem.* **1987**, *52*, 4634. (i) Rigby, J. H.; Wilson, J. A. *J. Org. Chem.* **1987**, *52*, 34. (j) Dauben, W. G.; Warshawsky, A. M. *J. Org. Chem.* **1990**, *55*, 3075.

(5) (a) Rowley, M.; Tsukamoto, M.; Kishi, Y. *J. Am. Chem. Soc.* **1989**, *111*, 2735. (b) Rowley, M.; Kishi, Y. *Tetrahedron Lett.* **1988**, *29*, 4909.

(6) Boeckman, R. K., Jr.; Arvanitis, A.; Voss, M. E. *J. Am. Chem. Soc.* **1989**, *111*, 2737.

(7) (a) Kato, N.; Nakanishi, K.; Takeshita, H. *Bull. Chem. Soc. Jpn.* **1986**, 1109. (b) Takeshita, H.; Hatsui, T.; Kato, N.; Masuda, T.; Tagoshi, H.; *Chem. Lett.* **1982**, 1153. (c) Kato, N.; Takeshita, H.; Kataoka, H.; Ohbuchi, S.; Tanaka, S. *J. Chem. Soc., Perkin Trans. 1* **1989**, 165. (d) Kato, N.; Tanaka, S.; Takeshita, H.; *Bull. Chem. Soc. Jpn.* **1988**, *61*, 3231. (e) Kato, N.; Tanaka, S.; Takeshita, H.; *Chem. Lett.* **1986**, 1989. (f) Kato, N.; Wu, X.; Tanaka, S.; Takeshita, H.; *Chem. Lett.* **1989**, 91.

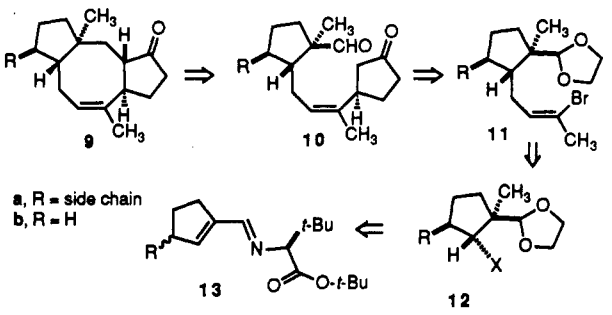
(8) Snider, B. B.; Yang, K. *Tetrahedron Lett.* **1989**, *30*, 2465; *J. Org. Chem.* **1990**, *55*, 4392.

(9) (a) Kogen, H.; Tomioka, K.; Hasimoto, S.-I.; Koga, K. *Tetrahedron* **1981**, *37*, 3951. (b) Kogen, H.; Tomioka, K.; Hashimoto, S.-I.; Koga, K. *Tetrahedron Lett.* **1980**, *21*, 4005. (c) Tomioka, K.; Koga, K. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic: New York, 1983; Vol. 2, pp 201–224. (d) Tomioka, K.; Msumi, F.; Yamashita, T.; Koga, K. *Tetrahedron* **1989**, *45*, 643.

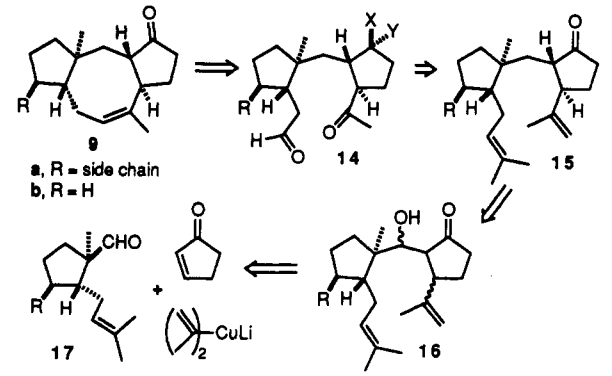
(10) For another example of a kinetic resolution using Koga's procedure, see: Paquette, L. A.; Macdonald, D.; Anderson, L. G.; Wright, J. *J. Am. Chem. Soc.* **1989**, *111*, 8037.

0022-3263/92/1957-3615$03.00/0

Scheme I



Scheme II



aldehyde provides functionality that should make it possible to close the B ring. Use of this methodology should provide a short enantiospecific entry to the ceroplastin sesterterpenes. The functionality present in ceroplastol I and the formation of a cyclopentanecarboxaldehyde in Koga's procedure suggest two approaches to close the central eight-membered ring that are shown in Schemes I and II.

Our initial plan was to close the tricyclic ring by an intramolecular aldol reaction on keto aldehyde **10a** and to reduce the conjugated double bond with lithium in ammonia. The A ring could be introduced by addition of the cuprate reagent prepared from vinyl halide **11a** to 2-cyclopentenone or optically pure 2-(arylsulfinyl)-2-cyclopentenone to give the acetal of **10a**.[11] The alkenyl bromide **11a** could be prepared from **12a**, in which X is a substituent that can be added as a Grignard reagent to imine **13a**. Model keto aldehyde **10b** was prepared efficiently and stereospecifically by this route. However, all attempts to close the eight-membered ring by an aldol condensation were unsuccessful. We therefore examined alternate procedures for closure of the central ring.

Successful closure of the eight-membered ring by formation of a bond between C-7 and C-8 has been achieved by Kishi,[5] who used an intramolecular Ni(II)/Cr(II) coupling of an iodoalkene and an aldehyde, and Dauben,[4j] who used the McMurry coupling of a keto aldehyde to close the ring and form the desired double bond directly. Ceroplastol I intermediate **9a** should be readily available by a McMurry coupling of **14a** as shown by Dauben in his model study that led to **9b**.[4j] The two carbonyl groups of **14a** can be introduced most easily by oxidative cleavage of both double bonds of diene **15a**. The required trans stereochemistry of the cyclopentanone portion of **15a** can be established by equilibration. Ketone **15a** should be readily available by dehydration and conjugate reduction of aldol adduct **16a**. Aldol adduct **16a** should be readily available in a one-pot, three-component condensation of isopropenylcuprate, cyclopentenone, and aldehyde **17a**. Since aldehyde **17a** should be readily available by Koga's procedure, this is a very short route to ceroplastol intermediate **9a**.

We chose to carry out model studies with the imine **13b**, prepared from 1-cyclopentenecarboxaldehyde and the *tert*-butyl ester of (*S*)-*tert*-leucine, to develop procedures for the elaboration of the tricyclic nucleus. Our synthesis of reiswigins A and B demonstrated that Koga's procedure can be used with side chains very similar to that required for the preparation of **1** and **2**. Therefore, we were confident that model studies that lead to **9b** could be extended to the preparation of intermediate **9a** and natural products **1** and **2**. Coates[4f] and Dauben[4j] have previously prepared enones **9b** and **60**, which will facilitate the evaluation of our model studies.

The Unsuccessful First Route

Preparation of Bromoalkene 11b. Smithers[12] and Li[13] reported that (*Z*)-alkenyl bromides can be selectively prepared by the reaction of an (α-bromoalkylidene)-phosphorane with aldehydes. We therefore turned our attention to the preparation of aldehyde **22** as a precursor of bromoalkene **11b**. Addition of allylmagnesium bromide to imine **13b** and methylation of the resulting enamide should provide an aldehyde that could be protected as the acetal and ozonylized to give **22**. However, conjugate addition of allylmagnesium bromide to imine **13b** and methylation of the resulting enamide gave 51% of tertiary amine **18a** and 40% of secondary amine **18b**, both as single diastereomers of unknown stereochemistry. Presumably, the γ-carbon of the allyl group adds to C=N rather than C=C since it can do so by a six-center transition state. Alkyl and vinyl Grignard can add to C=C by a six-center transition state but would have to add to C=N by an unfavorable four-center transition state.

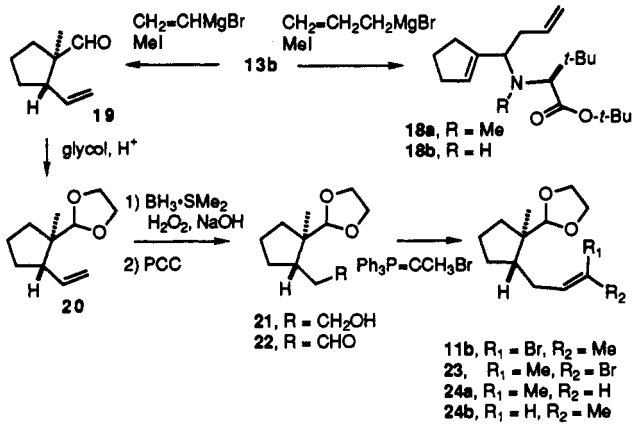
Aldehyde **19**, previously prepared by Koga,[9] was converted to the requisite aldehyde **22**. Reaction of **19** with ethylene glycol in the presence of oxalic acid and molecular sieves afforded acetal **20** in 96% yield.[14] Hydroboration[15] of acetal **20** followed by alkaline oxidation of the resulting organoborane furnished 92% of primary alcohol **21**. Oxidation with PCC gave 90% of aldehyde **22**. Reaction of ethylidenetriphenylphosphorane with 1,2-dibromotetrafluoroethane by Li's procedure[13] afforded (1-bromoethyl)triphenylphosphonium bromide that was treated with LDA and then aldehyde **22** to give 50% of an 8:1 inseparable mixture of bromoalkenes **11b** and **23** and 26% of a 4:1 *Z*-*E* mixture of **24a** and **24b**.

The stereochemistry of **11b** and **23** was assigned from analysis of the ^{1}H NMR spectral data. The vinylic proton in the (*E*)-bromoalkene **23** is deshielded by the cis vicinal bromine and resonates at lower field (δ 5.87) than the vinylic proton in the *Z* isomer **11b** (δ 5.61).[16] The vinylic methyl group in (*E*)-bromoalkene **23** is shielded by the *cis*-alkyl group and resonates upfield (δ 2.21) from the *Z* isomer **11b** (δ 2.27).[16]

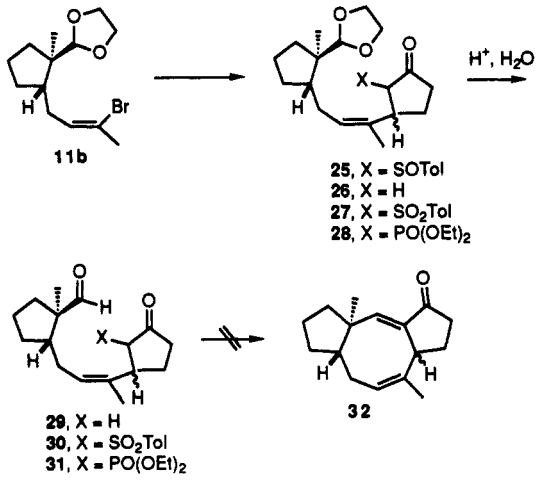
Preparation and Attempted Aldol Condensation of 29–31. With the crucial bromide **11b** in hand, we turned

(11) (a) Posner, G. H. *Acc. Chem. Res.* **1987**, *20*, 72. (b) Posner, G. H. *Chem. Scr.* **1985**, *25*, NS 157. (c) Posner, G. H. In *Asymmetric Synthesis*; Morrison, J. D.; Ed.; Academic: New York, 1983; Vol. 2, pp 225–241.

(12) Smithers, R. H. *J. Org. Chem.* **1978**, *43*, 2833.
(13) Li, X.-Y.; Hu, J.-S. *Tetrahedron Lett.* **1987**, *28*, 6317.
(14) Andersen, N. H.; Uh, H.-S. *Synth. Commun.* **1973**, *3*, 125.
(15) Lane, C. F. *J. Org. Chem.* **1974**, *39*, 1437.
(16) These data correspond closely to that reported for other 2-bromo-2-alkenes: (a) Tien, R. Y.; Abell, P. L. *J. Org. Chem.* **1970**, *35*, 956. (b) Griesbaum, K.; Seiter, W.; Schneider, H.; El Abed, M.; Rehman, Z. *Liebigs Ann. Chem.* **1979**, 1137.



our attention to methods for the introduction of the A ring. Metal–halogen exchange of bromide **11b** with *t*-BuLi and addition of MeCuCNLi gave a mixed cuprate.[17] Addition of this mixed cuprate to (*S*)-2-(tolylsulfinyl)cyclopentenone[11] in the presence of $MgCl_2$ gave the unstable sulfoxide **25**. Treatment of crude **25** with freshly prepared aluminum amalgam afforded 48% (from **11b**) of ketone **26** as single diastereomer and 47% of an 8:1 mixture of *E*–*Z* isomers **24b** and **24a**. The stereochemistry at the newly formed center of **26** was tentatively assigned as *R*, assuming that $MgCl_2$ chelates to the β-keto sulfoxide.[11] However, the important feature of this reaction is that the sulfoxide stereochemistry completely controls the stereochemistry. If the stereochemistry is *S*, the desired isomer can be easily prepared from (*R*)-2-(tolylsulfinyl)cyclopentenone.[11]



The stereochemistry of the double bond in **26** is crucial since only the *Z* isomer can undergo the desired aldol condensation. The *Z* isomer should be formed as the major product from the 8:1 mixture of **11b** and **23** since metal–halogen exchange is known to proceed with retention of stereochemistry.[17] This is confirmed by the formation of an 8:1 mixture of **24b** and **24a** by protonation of the organometallic intermediate. Finally, the stereochemical assignment is supported by the ^{13}C NMR spectral data.[18]

Since we were not sure that we had the correct stereoisomer of **26**, we prepared a mixture of both diastereomers by addition of the mixed cuprate prepared from **11b** to 2-cyclopentenone to give 61% of **26** as a 1:1 mixture of isomers. Mild acid hydrolysis of the acetal provided keto aldehydes **29** in 92% yield. Unfortunately, intramolecular aldol condensation of **29** turned out to be problematic. Treatment of **29** with 2% KOH in MeOH at reflux gave only 2% of an isolable product that might be enones **32** based on the ^1H NMR absorptions at δ 6.78 and 6.55 that are consistent with the β-H absorptions of α,β-unsaturated enones. A variety of other conditions resulted in either no reaction or the destruction of starting material.

We next attempted to construct the B ring by cyclization of sulfone **27**. Oxidation of unstable sulfoxide **25** with Oxone gave the stable sulfone **27**; hydrolysis of the acetal gave aldehyde sulfone **30** in 26% overall yield from **11b**. Treatment of aldehyde sulfone **30** with piperidine–HOAc or LDA in THF afforded only recovered starting material, while use of a 2% KOH methanol solution resulted in the decomposition of **30**.

Finally, we explored the use of an intramolecular Wittig reaction to close the B ring. Keto phosphonate **33** was prepared from cyclopentanone in 62% yield by a literature procedure.[21] Treatment of **33** with LDA followed by addition of phenylselenyl chloride gave a 91% yield of selenide **34**. Oxidation of selenide **34** with hydrogen peroxide[22] at −45 °C and then workup at rt gave a 92% yield of **35**.

Halogen–metal exchange of **11b** with *tert*-butyllithium and addition of the resulting alkenyllithium to phosphonate **35** gave a 1:1 mixture of keto acetals **28** in 20% unoptimized yield. Hydrolysis of **28** afforded 89% of keto aldehyde **31**. Unfortunately, treatment of **31** with LDA or KH at or below rt gave only recovered **31** while reaction at higher temperature resulted in the decomposition of **31**.

To determine whether the intramolecular Wittig reaction failed due to problems with the formation of the eight-membered ring or whether the keto phosphonate is inherently unreactive, we prepared phosphonate **36** by addition of isopropenyllithium to enone **35** in 84% yield. Treatment of **36** with LDA or KH followed by the addition of aldehyde **19** or nonanal did not give the desired Wittig products **37**. Treatment of the less hindered phosphonate **33** with LDA and nonanal furnished 44% of enone **38** as a 3:1 *E*/*Z* mixture.[23] These results indicate that phosphonate **36** is too hindered to undergo Wittig reactions so that it is not surprising that **31** failed to cyclize to give **32**. These results established that the aldol route to **9b** was not viable.

The Successful Second Route

Preparation of Aldehyde 17b. We therefore turned our attention to the second approach to model compound **9b** shown in Scheme II using a McMurry coupling to close the central ring as first described by Dauben. Conjugate addition of (3,3-dimethylallyl)magnesium bromide[24] to

(17) Lipshutz, B. H.; Wilhelm, R. S.; Kozlowski, J. A. *J. Org. Chem.* **1984**, *49*, 3938.

(18) The allylic methyl group of 2,3-dimethyl-1-butene resonances at δ 20.1 in the ^{13}C NMR spectrum.[19] Substitution of one of the vinylic protons with a methyl group shifts this methyl group (3-methyl) to δ 13.13 in (*E*)-3,4-dimethyl-2-pentene and to δ 17.8 in (*Z*)-3,4-dimethyl-2-pentene.[20] The allylic methyl group of 3-isopropenylcyclopentenone resonates at δ 21.0. On the basis of the above data, the calculated ^{13}C NMR chemical shift for the allylic methyl group in **26** is δ 18.7, which fits well the observed value of δ 18.8. The calculated chemical shift for the methyl group of the *E* isomer of **26** is 14.0, which is not consistent with the experimental value.

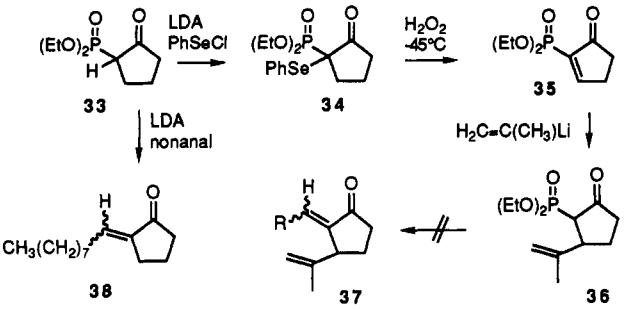
(19) *The Sadtler Standard Spectra*; Sadtler Research Laboratories Inc.; ^{13}C NMR Number 18902.

(20) De Haan, J. W.; Van de Ven, L. J. M. *Org. Magn. Reson.* **1973**, *5*, 147.

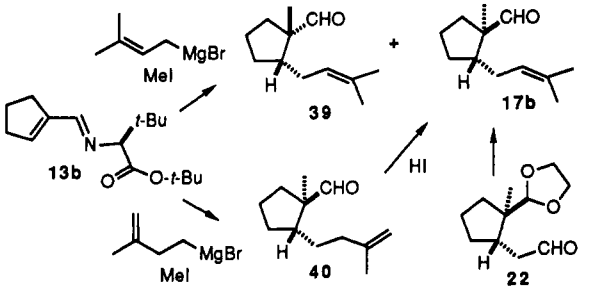
(21) Calogeropoulou, T.; Hammond, G. B.; Wiemer, D. F. *J. Org. Chem.* **1987**, *52*, 4185.

(22) Reich, H. J.; Renga, J. M.; Reich, I. L. *J. Am. Chem. Soc.* **1975**, *97*, 3434.

(23) The chemical shift of the vinylic proton in the *E* isomer (δ 6.55) and the *Z* isomer (δ 5.96) are in accord with the literature data for the *E* isomer and the other related ketones. (a) Katsin, N.; Ikan, R. *Synth. Commun.* **1977**, *7*, 185. (b) Koreeda, M.; Tanaka, Y.; Schwartz, A. *J. Org. Chem.* **1980**, *45*, 1172.



imine **13b** was examined since it provides a direct route to our initial target, aldehyde **17b**. Although allylmagnesium bromide adds to C=N, we anticipated that the two methyl groups on the double bond might prevent addition to C=N by a six-center transition state. To our delight, addition of (dimethylallyl)magnesium bromide to **13b** and methylation of the enamide at −20 °C gave 40% of a 7:1 mixture of aldehydes. However, the quaternary methyl group of the minor isomer absorbed at δ 14.0 as expected for a methyl group cis to an adjacent substituent while the methyl group of the major isomer absorbed downfield at δ 17.8. This suggests that, while conjugate addition of the Grignard reagent proceeded as desired, methylation was directed by the dimethylallyl group, rather than the chiral auxiliary, to give **39** as the major product. This assignment was confirmed by the preparation of **17b** from aldehyde **22** by reaction with isopropylidenetriphenylphosphorane and hydrolysis of the acetal in 82% yield.

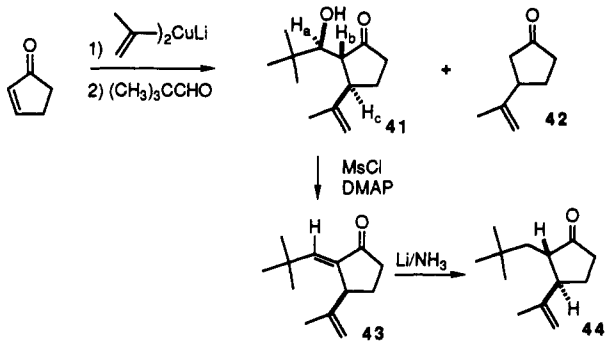


We are not sure why the stereochemistry of the methylation of the enamide precursor to **17b** and **39** is different from the other cases examined by Koga and us.[8,9] It does not appear to result from the steric bulk of the side chain, since the 3-methyl-3-butenyl side chain used in our reiswigin synthesis[8] does not prevent the chiral auxiliary from controlling the stereochemistry of methylation. Significant dimerization occurs in the formation of allylic Grignard reagents resulting in the formation of substantial amounts of 1,5-hexadienes and $MgBr_2$ in solution. It is possible that the presence of $MgBr_2$ might facilitate the isomerization of the chelated *Z* enamide that is responsible for the stereospecific methylation.[9]

Aldehyde **40**, prepared in 94% yield in a single step in our model study for reiswigin,[8] provided an alternate starting material for the preparation of **17b**. Treatment of **40** with HI/benzene[25] did not lead to clean isomerization of the alkene. Fortunately, treatment of **40** with 10 mol % of HI in CH_2Cl_2 at rt for 30 d gave the more stable aldehyde **17b** in 90% yield. Increasing the HI concentration or raising the reaction temperature accelerated the isomerization but gave **17b** in lower yield. Aldehyde **17b** is available in only two steps in 84% yield by this procedure.

(24) Barbot, F.; Miginiac, P. *Bull. Soc. Chim. Fr.* **1977**, 113.
(25) Snider, B. B.; Beal, R. B. *J. Org. Chem.* **1988**, *53*, 4508.

Preparation of the Model Ketone 44. The next three steps were explored using pivalaldehyde as a model for **17b**. Metal–halogen exchange of 2-bromopropene with *t*-BuLi afforded isopropenyllithium, which was mixed with 0.5 equiv of CuI to give lithium bis(isopropenyl)cuprate. Addition of the cuprate to cyclopentenone at −78 °C followed by trapping of the resulting enolate with pivalaldehyde at −78 °C afforded 80% of ketol **41** as a single isomer and 18% of ketone **42**. In the ^1H NMR spectrum of ketol **41**, H_b is coupled to H_c with J = 12.4 Hz, indicating that the substituents on the ring are trans, and H_a is coupled to the OH with J = 11.9 Hz. There is no coupling between H_a and H_b, suggesting that **41** exists in a locked conformation with the dihedral angle between these hydrogens close to 90°. MM2 calculations[26] verified that the most stable conformers of the *threo* isomer **41** have a dihedral angle of 96° and a predicted coupling constant of 1.2 Hz between H_a and H_b. The molecule is rigid because of the hydrogen bond between the carbonyl and hydroxyl group that is also responsible for the large H_a–OH coupling constant. The *erythro* isomer of **41** is calculated to have a coupling constant of 3.2 Hz between H_a and H_b. The formation of single stereoisomers in similar aldol reactions has been reported by Noyori[27] and Smith.[28]

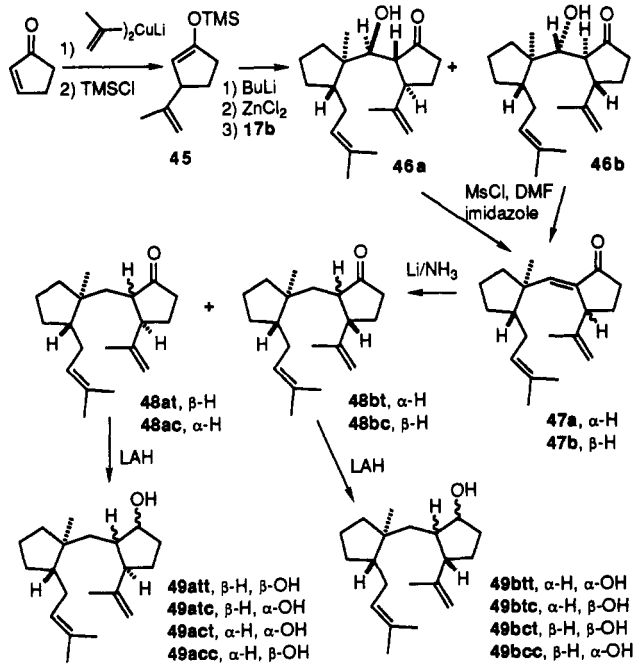


Dehydration of **41** by treatment with MsCl and DMAP in THF at reflux gave 93% of enone **43** as a single isomer. The chemical shift of the vinylic proton (δ 6.64) suggested that **43** is the *E* enone.[23] Reduction of enone **43** with lithium in ammonia provided 86% of ketone **44** as a 85:15 mixture of trans and cis isomers. The stereochemistry of **44** was determined from the ^1H NMR spectral data and the well-known[29] greater stability of trans-2,3-disubstituted cyclopentanones. The chemical shift of the allylic methine hydrogen is δ 2.99 in the cis isomer and less than δ 2.46 in the trans isomer due to the shielding by the adjacent cis alkyl group.

Three-Component Condensation To Give 46. Addition of isopropenylcuprate to cyclopentenone and trapping of the resulting enolate with aldehyde **17b** was not as straightforward, providing only 18% of a 1:1 mixture of diastereomers **46a** and **46b**. The ^1H NMR spectrum after exchange with D_2O showed two singlets at δ 3.48 and 3.40 for C*H*OH, indicating that **46a** and **46b** both have the same stereochemistry about the cyclopentanone ring as **41**. Unfortunately, the yield of ketols **46** could not be improved by using the stabilized organocopper reagent CH_2=C(Me)Cu–Bu_3P as has been reported in related examples.[27] Addition of zinc(II) chloride to the lithium enolate prior

(26) MODEL (Version 2.96) supplied by Prff. Kosta Stelious, University of Montreal, was used on a VAX 8650.
(27) Suzuki, M.; Kawagishi, T.; Yanagisawa, A.; Suzuki, T.; Okamura, N.; Noyuri, R. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 1299.
(28) Heng, K. K.; Smith, R. A. *Tetrahedron* **1979**, *35*, 425.
(29) (a) Posner, G. H.; Sterling, J. J.; Whitten, C. E.; Lentz, C. M.; Brunelle, D. J. *J. Am. Chem. Soc.* **1975**, *97*, 107. (b) Samson, M.; De Clerq, P.; Vandewalle, M. *Tetrahedron* **1975**, *31*, 1233.

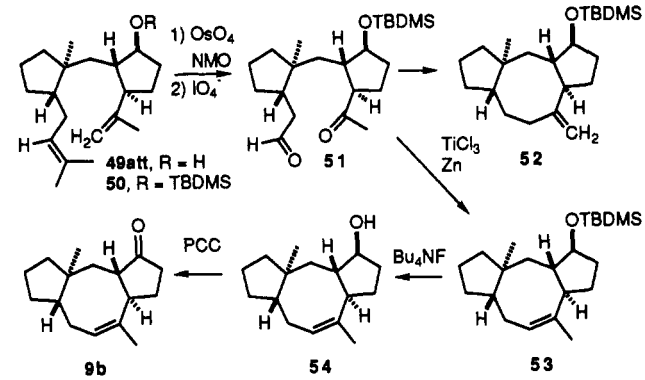
to aldehyde addition often improves the yield of the aldol products.[28,30] Unfortunately, addition of $ZnCl_2$ did not improve the yield of ketols **46**.



We therefore turned to a two-step procedure to prepare ketols **46**. Addition of isopropenylcuprate to 2-cyclopentenone and trapping of the enolate with TMSCl gave 76% of silyl enol ether **45**. Treatment of **45** with *n*-BuLi at 0 °C for 3 h and reaction of the resulting enolate with aldehyde **17b** in the presence of $ZnCl_2$ at −78 °C gave 63% of **46a** and **46b** as a 1:1 mixture. This procedure generates **46** in good yield from **17b**. A mixture of diastereomers is produced since racemic **45** is used. If **45** could be prepared in optically pure form, possibly by use of a chiral cuprate,[31] this would be a very efficient procedure for the preparation of **46a** since aldehyde **17b** is optically pure.

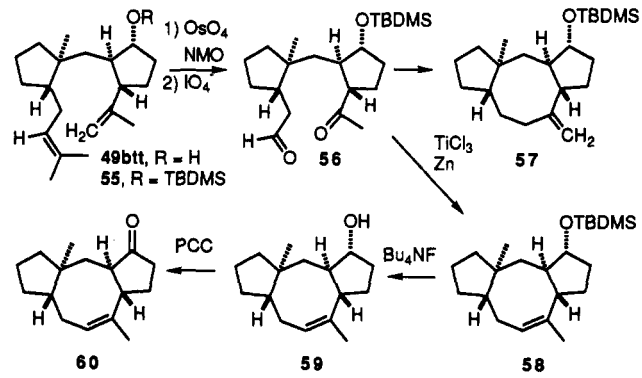
Preparation of Dienol 49. Dehydration of ketols **46** with MsCl and imidazole in DMF at reflux gave 94% of enones **47** as a 1:1 mixture of isomers. Following the same procedure used in the model study, a 1:1 mixture of enones **47** was reduced with Li/NH_3 to give 90% of an inseparable 6:1:6:1 mixture of ketones **48at**, **48ac**, **48bt**, and **48bc**, in which the thermodynamically more stable trans isomers **48at** and **48bt** predominate over cis isomers **48ac** and **48bc**. Further reduction of this mixture with $LiAlH_4$ and careful chromatography gave four fractions: 4% of **49acc**, 22% of **49bcc**, **49atc** and **49btc** as an inseparable 1:2:2 mixture, 64% of **49att** and **49btt** as a 1:1 mixture, and 5% of **49act** and **49bct** as a 1:1 mixture. The 1:1 mixture of **49att** and **49btt** was used to complete the synthesis.

Preparation of Tricyclic Ketones 9b and 60. Either ketones **48a** and **48b**, or alcohols **49att** and **49btt**, which were available in 64% yield by $LiAlH_4$ reduction of the ketones, could, in principle, be used to complete the synthesis. Attempted protection of ketone **48** as the ketal with ethylene glycol resulted in isomerization of the isopropenyl double bond into the ring. We therefore turned our attention to the longer route using alcohols **49tt**. The hydroxyl group in **49tt** was protected as the TBDMS ether since Dauben has shown that MOM ethers could not be cleaved after the McMurry cyclization without concomitant double-bond isomerization. Treatment of **49tt** with TBDMSOTf and imidazole in DMF[32] gave a 1:1 inseparable mixture of silyl ethers **50** and **55** in 97% yield. Oxidation of this mixture with OsO_4/4-methylmorpholine *N*-oxide and further oxidation of the resulting tetrols with $NaIO_4$ gave 40% of the desired keto aldehyde **51** and 42% of keto aldehyde **56**, which were easily separated by flash chromatography.



The synthesis of **9b** was completed by McMurry coupling,[33] which has been carried out by Dauben on the MOM ether corresponding to **51**.[4j] Reaction of keto aldehyde **51** with the low-valent titanium reagent prepared from $TiCl_3$–DME and zinc–copper couple afforded 31% of the desired cyclooctene **53** and 29% of the unexpected methylenecyclooctane **52**. Deprotection of the silyl ether of **53** with fluoride[32] gave the known alcohol **54** in 96% yield; oxidation of **54** with PCC afforded optically active **9b** in 78% yield, whose spectral data are identical to those of the racemic compound reported by Coates[4f] and Dauben.[4j]

Keto aldehyde **56** was converted to **60** by a similar series of reactions. McMurry coupling of **56** gave 40% of cyclooctene **58** and 29% of methylenecyclooctane **57**. Treatment of **58** with fluoride followed by oxidation of the resulting alcohol **59** furnished 76% of ketone **60**, whose spectral data are identical to those of the racemic material reported by Coates[4f] and Dauben.[4j]



It is not clear how the methylenecyclooctanes **52** and **57** are formed. The McMurry coupling is usually regiospecific and Dauben did not obtain the corresponding products in the preparation of the MOM ethers corresponding to **53** and **58**. However, Dauben did observe that the double bond migrated to give a mixture of **54**, the alcohol corresponding to methylenecyclooctane **52**, and the isomer with a tetrasubstituted double bond during acid hydrolysis of the MOM ether.[4j] It is possible that acid-catalyzed isomerization of the alkene during the McMurry coupling

(30) Johnson, C. R.; Chen, Y. F. *J. Org. Chem.* **1991**, *56*, 3344.
(31) Rossiter, B. E.; Eguchi, M.; Hernández, A. E.; Vickers, D.; Medich, J.; Marr, J.; Heinis, D. *Tetrahedron Lett.* **1991**, *32*, 3973.
(32) Corey, E. J.; Venkateswarlu, A. *J. Am. Chem. Soc.* **1972**, *94*, 6190.
(33) (a) McMurry, J. E.; Leckta, T.; Rico, J. G. *J. Org. Chem.* **1989**, *54*, 3748. (b) McMurry, J. E. *Chem. Rev.* **1989**, *89*, 1513.

converts **53** to **52**. This hypothesis is supported by MM2 calculations[26] that indicate that **52** is 2 kcal/mol more stable than **53**.

Stereochemical Assignment of Isomers of 48 and 49. Assignment of the stereochemistry of isomeric ketones **47** and **48** and the eight isomeric alcohols **49** is possible since dehydration of ketols **46** with MsCl and DMAP in THF at reflux as used in the preparation of model enone **43** gave 63% of enones **47b** and **47a** as an inseparable 2:1 mixture of isomers. Apparently one isomer of the mesylate dehydrates more readily than the other under these milder conditions. Since this 2:1 mixture of isomers can be converted to a 2:1 mixture of **60** and **9b**, whose structures are secure, we can assign the stereochemistry of the diastereomers of **47** and all later intermediates.

Li/NH_3 reduction of the 2:1 mixture of enones **47b** and **47a** gave a 12:6:2:1 mixture of ketones **48bt**, **48at**, **48bc**, and **48ac**. The spectral data of the major ketones **48bt** and **48at** can be determined from this mixture. Oxidation of alcohol **49acc**, obtained in pure form by chromatography of the mixture obtained by $LiAlH_4$ reduction of **48** as described above, with PCC gave 92% of **48ac**. Equilibration of **48ac** with NaOMe in MeOH provided an equilibrium 6:1 mixture of ketones **48at** and **48ac**. From this information the stereochemistry of all four isomers of ketones **48** can be assigned.

The stereochemistry of all eight alcohols **49** can also be established. Li/NH_3 reduction of *cis*-2,3-dialkylcyclopentanones has been shown to give mainly *trans*-1,2-*cis*-2,3-dialkylcyclopentanols, e.g. **49ct**, while reduction of *trans*-2,3-dialkylcyclopentanones has been shown to give mainly *trans*-1,2-*trans*-2,3-dialkylcyclopentanols, e.g. **49tt**.[29b] Reduction of a 2:1 mixture of enones **47b** and **47a** with Li/NH_3, protonation of the enolate with methanol, and further reduction of ketones **48** by addition of more lithium gave 30% of a 2:1 mixture of alcohols **49btt** and **49att**, 16% of a 2:1 mixture of alcohols **49bct** and **49act**, and 44% of an inseparable 6:3:4:2 mixture of ketones **48bt**, **48at**, **48bc**, and **48ac**. Protonation of the enolate gives a nonequilibrium mixture of ketones **48** richer in the cis isomers **48ac** and **48bc**. Reduction of **48c** gives **49ct** while reduction of **48t** gives **49tt**. The structures of the alcohols **49** were also partially established by interconversion with ketones **48**. For instance, oxidation of the 1:1 mixture of alcohols **49act** and **49bct**, obtained by $LiAlH_4$ reduction as described above, gave ketones **48ac** and **48bc**.

These structural assignments were confirmed by examination of the ^1H NMR spectral data. An alkyl group at C-2 shields the cis allylic C-3 methine hydrogen in 2,3-*trans*-dialkylcyclopentanols and cyclopentanones.[34] This proton resonates at δ 2.98 in cis isomers **48ac** and **48bc** and δ 2.6–2.8 in **49acc**, **49act**, **49bcc**, and **49bct**. In the corresponding trans isomers, this proton is shielded by the cis alkyl group and resonates upfield at less than δ 2.50 in **48at** and **48bt**, at less than δ 2.2 in **49att** and **49btt**, and at δ 2.39 in **49atc** and **49btc**. An alkyl group at C-2 shields the cis hydrogen at C-1 in *trans*-2-alkylcyclopentanols.[34] This hydrogen resonates at δ 4.24 and 4.29 in the *trans*-2,3-*cis*-1,2-dialkylcyclopentanols **49atc** and **49btc** and is shielded by the cis alkyl group and resonates upfield at δ 3.99 in *trans*-2,3-*trans*-1,2-dialkylcyclopentanols **49att** and **49btt**.

Conclusion. The tricyclic nucleus **9b** of ceroplastol I and ceroplasteric acid has been synthesized stereoselectively and enantiospecifically in only 10 steps from 1-cyclopentenecarboxaldehyde. Coupling of the enolate prepared from silyl enol ether **45** with aldehyde **17b** gave **46**, which contains the complete carbon skeleton of **9b**, in only three steps. Dehydration of the ketol, reduction of the α,β-unsaturated ketone to the saturated alcohol, protection of the alcohol, and oxidative cleavage of the diene afforded keto aldehydes **51** and **56**. McMurry coupling of **51**, cleavage of the silyl ether, and oxidation of the alcohol completed the synthesis of **9b**. The major stereochemical problem would be solved if we could prepare optically pure **45** by the enantioselective addition of a chiral cuprate[31] to cyclopentenone. This sequence should be readily applicable to the synthesis of ceroplastol I and ceroplasteric acid since we have developed procedures for the stereospecific introduction of the side chain in our reiswigin synthesis.

Experimental Section

General. NMR spectra were recorded at 300 MHz in $CDCl_3$. Chemical shifts are reported in δ, and coupling constants in hertz. All air-sensitive reactions were run under N_2 in flame-dried glassware with magnetic stirring. Reagents were added via oven-dried syringes through septa. Analyses were performed by Spang Microanalytical Laboratory.

Reaction of Imine 13b with Allylmagnesium Bromide. A solution of imine **13b** (63.3 mg, 0.24 mmol) in 1.0 mL of THF was cooled to −25 °C. Allylmagnesium bromide (0.95 mL, 1.0 M in ether) was added dropwise. The mixture was stirred at −25 °C for 7 h and a mixture of CH_3I (0.09 mL, 6.0 equiv), HMPA (0.3 mL, 7 equiv), and THF (0.1 mL) was added at −25 °C. The mixture was stirred at −25 °C for 0.5 h and at rt for 15 h. Citric acid (10% aqueous solution, 10 mL) was added. The solution was stirred for 1 h. The aqueous layer was extracted with ether (3 × 10 mL). The combined organic layers were washed with 10% aqueous $Na_2S_2O_3$ solution (10 mL), saturated aqueous $NaHCO_3$ solution (10 mL), and saturated aqueous NaCl solution (10 mL) and dried (Na_2SO_4). Concentration in vacuo gave 0.125 g of crude product. Flash chromatography on silica gel (25:1 hexane–EtOAc) gave 39 mg (51%) of tertiary amine **18a** followed by 29 mg (40%) of secondary amine **18b**.

18a: ^1H NMR 5.77 (dddd, 1, J = 17.2, 10.1, 6.8, 6.8), 5.56 (dt, 1, J = 1.7, 1.7), 5.05 (dddd, 1, J = 17.2, 2.1, 1.6, 1.6), 4.96 (dddd, 1, J = 10.1, 2.1, 1.1, 1.1), 3.14 (br d, 1, J = 4.7), 2.99 (s, 1), 2.40–2.60 (m, 4), 2.15–2.38 (m, 2), 2.27 (s, 3), 1.80–1.90 (m, 2), 1.48 (s, 9), 0.98 (s, 9); ^{13}C NMR 171.4 (C), 145.0 (C), 137.6 (CH), 127.5 (CH), 115.3 (CH_2), 80.4 (C), 74.2 (CH_3), 67.5 (CH), 36.1 (C) 34.2 (CH_2), 33.1 (CH_2), 33.0 (CH), 32.3 (CH_2), 28.3 (3 × CH_3), 27.1 (3 × CH_3), 23.2 (CH_2); IR 3080, 2980–2800 (2950), 1730, 1640, 1130, 990 cm^{-1}; $[\alpha]^{20}_D$ = −75.6 (c = 0.217, $CHCl_3$).

18b: ^1H NMR 5.70 (dddd, 1, J = 16.6, 9.5, 8.5, 5.9), 5.51 (dt, 1, J = 2.0, 2.0), 5.10 (dddd, 1, J = 16.6, 1.8, 1.2, 1.2), 5.06 (dddd, 1, J = 9.5, 1.8, 1.0, 1.0), 3.12 (dd, 1, J = 8.1, 6.0), 2.73 (s, 1), 2.10–2.35 (m, 6), 1.77–1.90 (m, 2), 1.68 (br s, 1), 1.47 (s, 9), 0.92 (s, 9); ^{13}C NMR 174.5 (C), 145.6 (C), 135.8 (CH), 127.4 (CH), 117.0 (CH_2), 80.4 (C), 67.9 (CH), 56.6 (CH), 39.5 (CH_2), 33.6 (C), 32.0 (CH_2), 30.1 (CH_2), 28.2 (3 × CH_3), 26.9 (3 × CH_3), 23.4 (CH_2); IR 3340, 3090, 2990–2860 (2960), 1730, 1650, 1150, 910 cm^{-1}; $[\alpha]^{20}_D$ = −47.6 (c = 0.176, $CHCl_3$).

(1*R*,2*S*)-1-Methyl-1-(1,3-dioxolan-2-yl)-2-vinylcyclopentane (20). (1*R*,2*S*)-1-Methyl-2-vinylcyclopentanecarboxaldehyde (**19**)[9] (178 mg, 1.3 mmol) was dissolved in 30 mL of acetonitrile. Oxalic acid dihydrate (0.2 g), ethylene glycol, and 4-Å molecular sieves (3.0 g) were added. The mixture was stirred at rt overnight. The mixture was filtered and 5 mL of saturated aqueous Na_2CO_3 solution was added to the filtrate. Ether (20 mL) and hexane (60 mL) were added. The solution was washed with water (3 × 25 mL) and dried (Na_2SO_4). Concentration in vacuo gave 259 mg of crude product. Flash chromatography on silica gel (40:1 hexane–EtOAc) gave 227 mg (96%) of acetal **20**: ^1H NMR 5.68 (ddd, 1, J = 17.0, 10.0, 7.5), 5.00 (ddd, 1, J = 17.0, 2.2, 1.2), 4.99 (ddd, 1, J = 10.0, 2.2, 1.1), 4.66 (s, 1), 3.80–4.00 (m, 4), 2.50 (tddd, 1, J = 8.2, 7.5, 1.2, 1.1), 1.50–2.88 (m, 5), 1.30–1.40 (m, 1), 0.87 (s, 3); ^{13}C NMR 139.7 (CH), 114.3 (CH_2), 109.4 (CH), 65.4 and 65.0 (–OCH_2CH_2O–), 48.6 (CH), 47.6 (C) 34.8 (CH_2), 30.4

(34) (a) Strickler, H.; Ohloff, G.; Kovtas, E. sz. *Helv. Chim. Acta* **1967**, *50*, 759. (b) Rei, M.-H. *J. Org. Chem.* **1978**, *43*, 2173. (c) Doerffel, V. K.; Kasper, H.; Zimmermann, G. *J. Prakt. Chem.* **1974**, *316*, 645.

(CH_2), 22.4 (CH_2) 17.4 (CH_3); IR 3080, 2960, 2870, 2740, 1640, 1095, 905 cm^{-1}; $[\alpha]^{20}_D$ = -21.7 (c = 0.377, $CHCl_3$). Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.56; H, 9.93.

(1*S*,2*R*)-2-(1,3-Dioxolan-2-yl)-2-methylcyclopentaneethanol (21). Acetal **20** (160 mg, 0.89 mmol) was dissolved in freshly distilled hexane (2.0 mL) and the solution was cooled to 0 °C. BH_3-SMe_2 (0.323 mmol, 0.323 mL, 1.0 M CH_2Cl_2) was added by syringe. The cooling bath was removed and the solution was stirred at rt overnight. Ethanol (2 mL) and NaOH (0.098 mL, 3 N aqueous solution) were added. After the solution was cooled to -5 to 0 °C, H_2O_2 (0.11 mL, 30% aqueous solution) was added. The solution was heated at reflux and then poured into 10 mL of ice water. Ether (30 mL) was added and the layers were separated. The organic layer was washed with water (2 × 5 mL) and saturated aqueous NaCl solution (5 mL) and dried (Na_2SO_4). Concentration in vacuo gave 178 mg of crude product. Flash chromatography on silica gel (2:1 hexane–EtOAc) gave 8 mg (5%) of the secondary alcohol followed by 162 mg (92%) of primary alcohol **21**: ^1H NMR 4.63 (s, 1), 3.81–4.00 (m, 4), 3.70 (ddd, 1, *J* = 10.4, 7.4, 5.5), 3.60 (ddd, 1, *J* = 10.4, 7.1, 7.1), 1.21–1.95 (m, 10), 0.87 (s, 3); ^{13}C NMR 110.1 (CH), 65.3 and 64.9 (-OCH_2CH_2O-), 62.7 (CH_2), 46.7 (C), 41.0 (CH), 36.0 (CH_2) 34.0 (CH_2), 31.7 (CH_2), 22.4 (CH_2), 16.0 (CH_3); IR 3410, 2950, 2870, 2730, 1095 cm^{-1}; $[\alpha]^{20}_D$ = -25.4 (c = 0.152, $CHCl_3$). Anal. Calcd for $C_{11}H_{20}O_3$: C, 65.97; H, 10.06. Found: C, 66.04; H, 9.94.

(1*S*,2*R*)-2-(1,3-Dioxolan-2-yl)-2-methylcyclopentaneacetaldehyde (22). Alcohol **21** (26 mg, 0.13 mmol) was dissolved in 5.0 mL of CH_2Cl_2. PCC (1.1 equiv, 31.1 mg, 0.144 mmol) was added. The solution was stirred at rt for 1 h and 20 mL of ether was added. The mixture was filtered through silica gel. Evaporation in vacuo gave 33.7 mg of crude **22**. Flash chromatography on silica gel (6:1 hexane–EtOAc) gave 25 mg (96%) of aldehyde **22**: ^1H NMR 9.74 (dd, 1, *J* = 2.2, 1.7), 4.61 (s, 1), 3.80–4.00 (m, 4), 2.80 (ddd, 1, *J* = 15.1, 2.8, 1.4), 2.15–2.35 (m, 2), 1.92–2.03 (m, 1), 1.53–1.82 (m, 3), 1.22–1.80 (m, 2), 0.86 (s, 3); ^{13}C NMR 203.1 (CHO), 110.0 (CH), 65.4 and 64.9 (-OCH_2CH_2O-), 46.5 (C), 45.9 (CH_2), 38.5 (CH), 36.0 (CH_2), 31.6 (CH_2), 22.4 (CH_2), 15.8 (CH_3); IR 2955, 2870, 2730, 1725, 1100 cm^{-1}; $[\alpha]^{20}_D$ = -3.83 (c = 0.151, $CHCl_3$). Anal. Calcd for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15. Found: C, 66.35; H, 9.36.

(1-Bromoethyl)triphenylphosphonium Bromide.[13] *n*-BuLi (2.38 mL, 2.5 M in hexane) was added dropwise to a suspension of ethyltriphenylphosphonium bromide (2.21 g, 5.95 mmol) in 70 mL of ether at -78 °C. The solution was stirred at 0 °C for 1 h and recooled to -78 °C. 1,2-Dibromotetrafluoroethane (1.43 mL, 2.0 equiv) was added dropwise. The mixture was stirred at -78 °C for 30 min and then at rt for 24 h. The mixture was filtered and the yellow solid was dried in vacuo to give 3.76 g (51%) of crude product. Recrystallization from water gave 1.36 g of the phosphonium bromide as a white solid: mp 115–117 °C; ^1H NMR (DMSO) 6.78–7.13 (m, 15), 6.14 (dq, 1, *J* = 6.8, 6.8), 0.94 (dd, 3, *J* = 17.4, 6.8); ^{13}C NMR 135.7 (d, CH, *J* = 2.9), 134.4 (d, CH, *J* = 9.9), 130.2 (d, CH, *J* = 12.6), 116.7 (d, CH, *J* = 86.6), 31.4 (d, CH_3, *J* = 51.4).

2-[(1*R*,2*S*)-2-(3-Bromo-2(*Z*)-butenyl)-1-methylcyclopentyl]-1,3-dioxolane (11b). A suspension of (1-bromoethyl)-triphenylphosphonium bromide (450 mg, 1.0 mmol) in 10 mL of THF was cooled to -78 °C. LDA (1.1 equiv, 1.1 mmol) in THF (1 mL) was added dropwise. The mixture was stirred at -78 °C for 1 h. A solution of aldehyde **22** (122 mg, 0.61 mmol) in THF (2 mL) was added. The resulting solution was stirred and was slowly warmed to -60 °C over 30 min and then to rt directly. Hexane (10 mL) was added and the mixture was filtered through silica gel. The solution was concentrated in vacuo to give 293 mg of crude **11b**. Flash chromatography on silica gel (40:1 hexane–EtOAc) gave 36 mg (26%) of a 4:1 mixture of alkenes **24a** and **24b** followed by 88 mg (51%) of an 8:1 mixture of bromoalkenes **11b** and **23**.

11b: ^1H NMR 5.61 (ddq, 1, *J* = 6.5, 6.4, 1.4), 4.65 (s, 1), 3.80–4.00 (m, 4), 2.40 (dddq, 1, *J* = 12.9, 6.7, 6.5, 1.4), 2.27 (br s, 3), 1.25–2.03 (m, 7), 0.90 (s, 3); ^{13}C NMR 129.0 (CH), 121.9 (C), 110.0 (CH), 65.4 and 65.0 (-OCH_2CH_2O-), 46.7 (C), 43.7 (CH), 35.7 (CH_2), 32.9 (CH_2), 31.3 (CH_2), 28.8 (CH_3), 22.3 (CH_2), 16.3 (CH_3); IR 2950, 2870, 1670 cm^{-1}; $[\alpha]^{20}_D$ = -12.6 (c = 0.100, $CHCl_3$).

23: ^1H NMR 5.87 (br t, 1, *J* = 6.5), 4.61 (s, 1), 2.21 (br s, 3), 0.86 (s, 3).

Preparation of a Single Diastereomer of Ketone 26. Bromides **11b** and **23** (21.8 mg, 0.075 mmol) were dissolved in 2.0 mL of dry THF at -78 °C. *t*-BuLi (103 μL, 1.6 M in pentane, 0.165 mmol) was added. The solution was stirred at -78 °C for 30 min. This solution was transferred to a solution of MeCuCNLi (0.075 mmol) in 1 mL of THF. The resulting solution was transferred to a solution of (*S*)-2-(tolylsulfinyl)-2-cyclopentenone[11c] (16.5 mg, 0.075 mmol) and $MgCl_2$ (7.9 mg, 1.1 equiv) in THF (2 mL) at -78 °C. The resulting solution was stirred at -78 °C for 30 min and warmed to 0 °C. Saturated aqueous Na_2HPO_4 solution (3 mL) was added and the solution was concentrated in vacuo at 0 °C to remove THF. The aqueous solution was extracted with ice-cold ether (3 × 5 mL). The combined ether layers were dried (Na_2SO_4). Concentration in vacuo gave 44.2 mg of crude keto sulfoxide **25** that was dissolved in 5 mL of 9:1 THF/H_2O at 0 °C and treated with freshly prepared Al–Hg (20 mg of Al treated with 2% $HgCl_2$). The resulting mixture was stirred and slowly warmed to rt. The mixture was stirred at rt overnight. The mixture was filtered through silica gel and the residue was rinsed with ether. The filtrate was concentrated in vacuo to remove THF and 3 mL of water was added. The aqueous solution was extracted with ether (2 × 15 mL). The combined ether layers were dried (Na_2SO_4) and concentrated in vacuo to give 21 mg of crude **26**. Flash chromatography on silica gel (20:1 hexane–EtOAc) gave 8 mg (47%) of an 8:1 mixture of **24b** and **24a** followed by 9 mg (48%) of a single diastereomer of acetal ketone **26**: ^1H NMR 5.28 (br dd, 1, *J* = 6.9, 6.9), 4.62 (s, 1), 3.82–4.00 (m, 4), 3.30 (dddd, 1, *J* = 11.5, 11.5, 7.3, 6.7), 1.28–2.42 (m, 15), 1.66 (br s, 3), 0.87 (s, 3); ^{13}C NMR 133.8 (C), 127.7 (CH), 110.2 (CH), 65.4 and 64.9 (-OCH_2CH_2O-), 46.6 (C), 45.4 (CH), 42.5 (CH_2), 38.8 (CH_2), 37.9 (CH), 35.9 (CH_2), 31.4 (CH_2), 28.7 (CH_2), 27.5 (CH_2), 22.2 (CH_2), 18.8 (CH_3), 16.0 (CH_3), the C=O resonates above δ 210; IR 2950, 2870, 1750, 1105 cm^{-1}; $[\alpha]^{20}_D$ = -111 (c = 0.05, $CHCl_3$). Anal. Calcd for $C_{18}H_{28}O_3$: C, 73.94; H, 9.65. Found: C, 74.00; H, 9.72.

Preparation of Both Diastereomers of Ketone 26. To a suspension of CuCN (53.7 mg, 0.6 mmol) in 3 mL of cold THF (-78 °C) was added methyllithium (0.6 mmol, 0.4 mL, 1.5 M in ether), and the temperature was raised to 0 °C until the solid was dissolved. Then the solution was recooled to -78 °C. *t*-BuLi (1.20 mmol, 0.75 mL 1.6 M in pentane) was added to a solution of racemic **11b** and **23** (173 mg, 0.60 mmol) in 5 mL of THF at -78 °C. The solution was stirred at -78 °C for 30 min and then transferred through a cannula to the MeCuCNLi solution. 2-Cyclopentenone (50 μL, 0.6 mmol) in THF (0.5 mL) was added. The solution was stirred at -78 °C for 2.5 h and a 1:1 mixture of 10% aqueous NH_4OH/saturated aqueous NH_4Cl solution (10 mL) was added. The solution was stirred at rt for 30 min. Concentration in vacuo removed the THF, and the aqueous solution was extracted with ether (3 × 15 mL). The combined ether layers were washed with saturated NaCl and dried (Na_2SO_4). Concentration in vacuo gave 230 mg of crude **26**. Flash chromatography on silica gel (20:1 hexane–EtOAc) gave 40 mg (32%) of alkene **24** followed by 107 mg (61%) of a 1:1 mixture of ketones **26**: ^1H NMR 5.28 (br dd, 1, *J* = 6.9, 6.9), 4.62 (s, 0.5 × 1), 4.61 (s, 0.5 × 1), 3.80–4.00 (m, 4), 3.25–3.38 (m, 1), 1.18–2.42 (m, 15), 1.66 (br s, 3), 0.87 (s, 3); ^{13}C NMR 133.8 and 133.7 (C), 127.7 (2 × CH), 110.20 and 110.18 (CH), 65.34, 65.39, 64.93 and 64.90 (-OCH_2CH_2O-), 46.6 and 46.5 (C), 45.4 and 45.3 (CH), 42.7 and 42.5 (CH_2), 38.8 (2 × CH_2), 37.9 (2 × CH), 35.93 and 35.88 (2 × CH_2), 31.5 and 31.4 (CH_2), 28.7 and 28.7 (CH_2), 27.5 and 27.3 (CH_2), 22.3 and 22.2 (CH_2), 18.8 (2 × CH_3), 16.03 and 15.99 (CH_3), the C=O resonates above δ 210.

Keto Aldehyde 29. The diastereomeric mixture of ketones **26** (107 mg, 0.37 mmol) was dissolved in 30 mL of acetone. Water (5 drops) and PPTs (50 mg) were added and the solution was heated at reflux overnight. Concentration in vacuo removed the acetone. Water (2 mL) was added to the residue and the aqueous solution was extracted with ether (3 × 10 mL). The combined ether layers were washed with saturated aqueous NaCl and dried (Na_2SO_4). Concentration in vacuo gave 110 mg of crude **29**. Flash chromatography on silica gel (5:1 hexane–EtOAc) gave 84 mg (92%) of **29** as 1:1 mixture of diastereomers: ^1H NMR 9.38 (s, 1), 5.15 (br dd, 1, *J* = 6.8, 6.8), 3.17–3.30 (m, 1), 1.62–2.43 (m, 13), 1.65 (br s, 3), 1.36–1.50 (m, 2), 0.99 (s, 0.5 × 3), 0.98 (s, 0.5 × 3); ^{13}C NMR 205.52 and 205.48 (CHO), 135.4 and 135.3 (C), 125.95 and 125.91 (CH), 55.8 (2 × C), 45.8 and 45.7 (CH), 42.5 and 42.3

(CH_2), 38.61 and 38.58 (CH_2), 37.79 and 37.76 (CH), 35.3 (2 × CH_2), 30.7 (2 × CH_2), 28.0 (2 × CH_2), 27.4 and 27.2 (CH_2), 22.5 (CH_2), 18.8 and 18.7 (CH_3), 14.1 (2 × CH_3), the cyclopentanone C=O absorbed above δ 210; IR 2980, 2870, 2700, 1745, 1730 cm^{-1}.

Attempted Intramolecular Aldol Condensation of Keto Aldehyde 29. Keto aldehyde **29** (45 mg, 0.18 mmol) was dissolved in 10 mL of 2% KOH solution in MeOH. The solution was heated at reflux overnight. Concentration in vacuo removed the MeOH. Water (5 mL) and ether (20 mL) were added. The aqueous layer was extracted with ether (10 mL) and the combined ether layers were dried (Na_2SO_4). Evaporation in vacuo gave 40 mg of crude product. Flash chromatography on silica gel (20:1 hexane–EtOAc) gave 1.0 mg (2.4%) of a UV-active compound that may be a 1:1 mixture of diastereomeric dienones **32**: ^1H NMR 6.78 (d, 0.5 × 1, J = 1.7), 6.65 (d, 0.5 × 1, J = 2.0), 5.44 (br dd, 0.5 × 1, J = 6.7, 6.7), 5.38 (br d, 0.5 × 1, J = 6.5), 4.51 (br d, 0.5 × 1, J = 6.5), 4.13 (br d, 0.5 × 1, J = 6.5), 0.80–2.88 (m, 13), 1.72 (br s, 0.5 × 3), 1.67 (br s, 0.5 × 3), 1.09 (s, 0.5 × 3), 0.97 (s, 0.5 × 3).

Aldehyde Sulfone 30. Bromoalkenes **11b** and **23** (41.9 mg, 0.144 mmol) in THF (1.0 mL) were cooled to −78 °C. t-BuLi (0.18 mL, 1.6 M in pentane, 0.288 mmol) was added dropwise. The solution was stirred at −78 °C for 30 min and then transferred through a cannula to a solution of MeCuCNLi (0.144 mmol) in THF (1 mL) at −78 °C (prepared as before). $MgCl_2$ (15.2 mg, 0.16 mmol) was added. (*S*)-2-(Tolylsulfinyl)-2-cyclopentenone[11c] (31.7 mg, 0.144 mol) was added. The solution was stirred at −78 °C for 2 h. A saturated aqueous NH_4Cl solution (10 mL) was added. The solution was extracted with ether (3 × 15 mL) and the combined ether layers were dried (Na_2SO_4). Concentration in vacuo at 0 °C removed the ether. The residue was redissolved in 2 mL of methanol at 0 °C. A solution of Oxone (0.25 g) in 2 mL of water was added. The milky solution was stirred at 0 °C for 3 h and extracted with CH_2Cl_2 (3 × 10 mL). The combined CH_2Cl_2 solution was dried (Na_2SO_4). Concentration in vacuo gave 71 mg of crude **27**.

Crude **27** (30 mg) was dissolved in 15 mL of acetone. PPTs (50 mg) and water (several drops) were added. The solution was heated at reflux overnight. Concentration in vacuo removed the acetone. Water (2 mL) was added and the aqueous solution was extracted with ether (3 × 5 mL). The combined ether layers were dried (Na_2SO_4) and concentrated in vacuo to give 29 mg of crude **30**. Flash chromatography on silica gel (10:1 hexane–EtOAc) gave 15 mg (61%) of aldehyde sulfone **30**: ^1H NMR 9.42 (s, 1), 7.74 (d, 2, J = 8.2), 7.36 (d, 2, J = 8.2), 5.16 (dd, 1, J = 6.2, 6.2), 3.99 (dddd, 1, J = 8.5, 8.5, 8.5, 8.5), 3.64 (d, 1, J = 8.5), 2.38–2.50 (m, 1), 2.46 (s, 3), 1.40–2.20 (m, 12), 1.60 (br s, 3), 1.03 (s, 3); ^{13}C NMR 205.9 (CHO), 169.1 (C), 145.2 (C), 133.4 (C), 129.7 (2 × CH), 129.1 (2 × CH), 127.7 (CH), 72.1 (CH), 47.0 (C), 45.6 (CH), 38.8 (CH_2), 38.6 (CH), 35.5 (CH_2), 30.8 (CH_2), 28.2 (CH_2), 24.9 (CH_2), 22.6 (CH_2), 21.7 (CH_3), 18.9 (CH_3), 14.2 (CH_3), the cyclopentanone C=O resonates above δ 210; $[\alpha]^{20}_D$ = −43.1 (c = 0.06, $CHCl_3$).

2-(Diethylphosphono)-2-(phenylselenenyl)cyclopentanone (34). n-BuLi (0.2 mL, 2.5 M in hexane, 0.5 mmol) was added to a solution of Et_2NH (0.07 mL, 0.5 mmol) in THF (3 mL) at 0 °C. The solution was stirred at 0 °C for 30 min and cooled to −78 °C. A solution of **33**[21] (0.1 g, 0.45 mmol) in THF (1 mL) was added dropwise. The resulting solution was stirred at −78 °C for 10 min and phenylselenyl chloride (96 mg, 0.5 mmol) in THF (1 mL) was added rapidly. The solution was warmed to 0 °C and acetic acid (0.05 mL, 0.83 mmol) in 5.0 mL of ether was added. Filtration of the mixture through silica gel and subsequent concentration of the filtrate in vacuo removed the solvent. The residue was redissolved in 30 mL of ether. The ether solution was washed with saturated aqueous $NaHCO_3$ (10 mL) and dried (Na_2SO_4). Concentration in vacuo gave 0.204 g of crude **34**. Flash chromatography on silica gel (4:1 EtOAc–hexane) gave 0.154 g (91%) of **34**: ^1H NMR 7.75 (dd, 2, J = 8.2, 1.3), 7.28–7.44 (m, 3), 4.10–4.35 (m, 4), 2.21–2.60 (m, 3), 1.88–2.02 (m, 3), 1.37 (td, 3, J = 7.1, 0.5), 1.30 (td, 3, J = 7.1, 0.5); ^{13}C NMR 209.2 (C=O), 138.0 (2 × CH), 129.8 (CH), 128.9 (2 × CH), 126.1 (C), 63.8 (d, CH_2, J = 7.0), 63.3 (d, CH_2, J = 7.0), 52.1 (d, C, J = 152.9), 37.5 (d, CH_2, J = 6.3), 32.5 (CH_2), 19.5 (d, CH_2, J = 10.7), 16.5 (d, CH_3, J = 5.8), 16.3 (d, CH_3, J = 5.8); IR 3030, 2990, 2900, 1735, 1580, 1480, 1240, 1040 cm^{-1}.

2-(Diethylphosphono)-2-cyclopentenone (35). A solution of 2-(diethylphosphono)-2-(phenylselenenyl)cyclopentanone (**34**) (221 mg, 0.59 mmol) in 15 mL of THF was cooled to −45 °C. Hydrogen peroxide (66.1 μL, 30% aqueous solution, 1.1 equiv) was added. The solution was stirred at −45 °C for 1.5 h. Then the solution was warmed to rt and stirred for 5 min. Concentration in vacuo removed the THF. The residue was redissolved in 30 mL of ether. The solution was washed with a saturated aqueous Na_2CO_3 (5 mL) solution and dried (Na_2SO_4). Concentration in vacuo gave 219 mg of crude **35**. Flash chromatography on silica gel (EtOAc) gave 118 mg (92%) of enone **35**: ^1H NMR 8.38 (dt, 1, J = 10.4, 2.6), 4.11–4.25 (m, 4), 2.79–2.85 (m, 2), 2.50–2.57 (m, 2), 1.35 (td, 6, J = 7.0, 0.5); ^{13}C NMR 205.0 (d, C=O, J = 12.6), 176.2 (d, CH, J = 11.3), 137.2 (d, C, J = 191.4), 62.4 (d, 2 × CH_2, J = 5.7), 35.2 (d, CH_2, J = 9.0), 28.8 (d, CH_2, J = 17.6), 16.2 (d, 2 × CH_3, J = 6.4); IR 3030, 2990, 2920, 1715, 1595, 1250, 1030 cm^{-1}; UV λ_{max} (ethanol) 224 nm (ε 367).

Acetal Ketone 28. A solution of racemic bromoalkenes **11b** and **23** (48.9 mg, 0.17 mmol) in THF (4 mL) was cooled to −78 °C. t-BuLi (2.0 equiv, 0.21 mL, 1.6 M in pentane) was added dropwise. The solution was stirred at −78 °C for 30 min. A solution of **35** (37.1 mg, 0.17 mmol) in 1 mL of THF was added. The resulting solution was stirred at −78 °C for 1 h. A saturated aqueous NH_4Cl solution (2 mL) was added. Concentration in vacuo removed the THF. The aqueous solution was extracted with ether (3 × 10 mL). The combined ether layers were dried (Na_2SO_4). Concentration in vacuo gave 108 mg of crude **28**. Flash chromatography on silica gel (2:1 hexane–EtOAc) gave 25 mg (70%) of alkene **24** followed by 14 mg (20%) of acetal ketone **28** as a 1:1 diastereomeric mixture: ^1H NMR 5.30 (dd, 0.5 × 1, J = 7.5, 7.5), 5.28 (dd, 0.5 × 1, J = 7.5, 7.5), 4.641 (s, 0.5 × 1), 4.640 (s, 0.5 × 1), 3.68–4.21 (m, 9), 2.71 (dd, 1, J = 25.9, 10.1), 2.31–2.51 (m, 2), 2.02–2.20 (m, 1), 1.43–2.00 (m, 12), 1.64 (br s, 3), 1.22–1.42 (m, 6), 0.89 (s, 0.5 × 1), 0.88 (s, 0.5 × 1); ^{13}C NMR 211.81 (d, 0.5 × C=O, J = 2.7), 211.77 (d, 0.5 × C=O, J = 3.4), 133.3 (d, 0.5 × C, J = 2.9), 133.1 (d, 0.5 × C, J = 2.5), 128.5 (0.5 × 1), 128.4 (0.5 × 1), 110.13 (0.5 × CH), 110.06 (0.5 × CH), 65.34 and 65.31 (0.5 × $-OCH_2CH_2O-$), 64.97 and 64.91 (0.5 × $-OCH_2CH_2O-$), 62.8 (d, CH_2, J = 6.2), 62.0 (d, 0.5 × CH_2, J = 6.7), 61.9 (d, 0.5 × CH_2, J = 6.8), 50.3 (d, 0.5 × CH, J = 140.3), 50.2 (d, 0.5 × CH, J = 140.1), 46.7 (0.5 × C), 46.6 (0.5 × C), 45.5 (0.5 × CH), 44.9 (0.5 × CH), 39.6 (CH), 39.3 (d, 0.5 × CH_2, J = 4.4), 39.2 (d, 0.5 × CH_2, J = 4.2), 35.84 (0.5 × CH_2), 35.77 (0.5 × CH_2), 31.6 (0.5 × CH_2), 31.4 (0.5 × CH_2), 28.84 (0.5 × CH_2), 28.78 (0.5 × CH_2), 27.0 (d, 0.5 × CH_2, J = 14.5), 26.8 (d, 0.5 × CH_2, J = 14.1), 22.31 (0.5 × CH_2), 22.26 (0.5 × CH_2), 18.9 (0.5 × CH_3), 18.8 (0.5 × CH_3), 16.5 (CH_3), 16.4 (d, 0.5 × CH_3, J = 6.3), 16.3 (d, 0.5 × CH_3, J = 6.1), 16.2 (0.5 × CH_3), 16.1 (0.5 × CH_3); IR 2980, 2870, 1700, 1625, 1250, 1040 cm^{-1}.

Keto Aldehyde 31. Acetal ketone **28** (12.2 mg, 0.0285 mmol) was dissolved in 20 mL of acetone. Water (3 drops) and TsOH (0.05 g) were added. The solution was heated at reflux for 4 h. Concentration in vacuo removed the acetone. The residue was dissolved in 25 mL of ether. The ether solution was washed with a saturated aqueous $NaHCO_3$ solution (5 mL) and dried (Na_2SO_4). Concentration in vacuo gave 13.8 mg of crude **31**. Flash chromatography on silica gel (2:1 EtOAc–hexane) gave 10 mg (89%) of keto aldehyde **31**: ^1H NMR 9.41 (br s, 1), 5.19 (dd, 0.5 × 1, J = 6.8, 6.8), 5.14 (dd, 0.5 × 1, J = 6.8, 6.8), 4.01–4.23 (m, 4), 3.60–3.80 (m, 1), 2.69 (dd, 0.5 × 1, J = 25.7, 9.7), 2.67 (dd, 0.5 × 1, J = 25.7, 9.7), 2.38–2.49 (m, 2), 1.90–2.20 (m, 5), 1.55–1.89 (m, 4), 1.62 (br s, 3), 1.22–1.54 (m, 8), 1.014 (s, 0.5 × 3), 1.005 (s, 0.5 × 3); ^{13}C NMR 210.3 (d, C=O, J = 3.5), 205.7 (CHO), 134.62 (d, 0.5 × C, J = 2.4), 134.55 (d, 0.5 × C, J = 1.4), 126.8 (CH), 62.9 (d, CH_2, J = 5.3), 62.0 (d, 0.5 × CH_2, J = 3.1), 61.9 (d, 0.5 × CH_2, J = 3.0), 55.85 (0.5 × C), 55.81 (0.5 × C), 50.2 (d, 0.5 × CH, J = 140.4), 50.1 (d, 0.5 × CH, J = 139.9), 45.7 (CH), 39.7 (0.5 × CH), 39.5 (0.5 × CH), 39.2 (d, 0.5 × CH_2, J = 4.4), 39.1 (d, 0.5 × CH_2, J = 3.2), 35.4 (0.5 × CH_2), 35.4 (0.5 × CH_2), 30.8 (CH_2), 28.14 (0.5 × CH_2), 28.12 (0.5 × CH_2), 26.8 (d, 0.5 × CH_2, J = 3.6), 26.6 (d, 0.5 × CH_2, J = 3.6), 22.6 (0.5 × CH_2), 22.5 (0.5 × CH_2), 18.6 (0.5 × CH_3), 18.5 (0.5 × CH_3), 16.5 (d, CH_3, J = 6.4), 16.3 (d, CH_3, J = 6.1), 14.2 (CH_3); IR 2960, 2870, 2975, 1750, 1725, 1625, 1240, 1040 cm^{-1}.

2-(Diethylphosphono)-3-isopropenylcyclopentanone (36). t-BuLi (0.386 mL, 1.6 M in pentane, 0.618 mmol) was added to a solution of 2-bromopropene (27.4 μL, 0.309 mmol) in THF (2 mL) at −78 °C. The solution was stirred at −78 °C for 30 min.

A solution of 2-(diethylphosphono)-2-cyclopentenone (**35**) (56.1 mg, 0.257 mmol) in THF (1 mL) was added. The resulting solution was stirred at −78 °C for 1 h and a saturated aqueous NH_4Cl solution (5 mL) and ether (5 mL) were added. The aqueous layer was extracted with ether (2 × 10 mL). The combined ether layers were washed with a saturated aqueous NaCl solution (10 mL) and dried (Na_2SO_4). Concentration in vacuo gave 71.1 mg of crude **36**. Flash chromatography on silica gel (2:1 EtOAc–hexane) gave 56.2 mg (84%) of trans ketone **36**: ^1H NMR 4.85 (dq, 1, J = 1.4, 1.4), 4.80 (br s, 1), 4.05–4.25 (m, 4), 3.28 (dddd, 1, J = 16.8, 7.3, 7.3, 7.3), 2.77 (dd, 1, J = 26.3, 7.3), 2.23–2.41 (m, 3), 1.70–1.90 (m, 1), 1.78 (br s, 3), 1.34 (td, 3, J = 7.0, 0.5), 1.31 (td, 3, J = 7.0, 0.5); ^{13}C NMR 211.5 (d, C=O, J = 4.4), 145.2 (d, C, J = 6.5), 111.3 (CH), 62.9 (d, CH_2, J = 6.6), 62.2 (d, CH_2, J = 6.7), 51.4 (d, CH, J = 133.8), 45.2 (d, CH, J = 1.7), 38.2 (d, CH_2, J = 3.2), 27.4 (d, CH_2, J = 9.4), 20.2 (CH_3), 16.34 (d, CH_3, J = 5.8), 16.25 (d, CH_3, J = 5.8); IR 3040, 2980, 2900, 1745, 1645, 1240, 1020, 885 cm^{-1}.

2-Nonylidenecyclopentanone (38). *n*-BuLi (0.15 mL, 2.5 M in hexane, 0.38 mmol) was added to a solution of Et_2NH (53.2 μL, 0.38 mmol) in THF (2 mL) at 0 °C. The solution was stirred at 0 °C for 30 min and cooled to −78 °C. A solution of **33**[21] (70.3 mg, 0.32 mmol) in THF (1 mL) was added dropwise. The resulting solution was stirred at −78 °C for 10 min and a solution of nonanal (45.5 mg, 0.32 mmol) in THF (1 mL) was added dropwise. The solution was warmed to rt and stirred for 3 h. The reaction was quenched with 5 mL of a saturated aqueous NH_4Cl solution. Concentration in vacuo removed the THF. The residue was redissolved in 30 mL of ether. The ether solution was washed with a saturated aqueous NaCl solution and dried (Na_2SO_4). Concentration in vacuo gave 121 mg of crude product. Flash chromatography on silica gel (20:1 hexane–EtOAc) gave 7 mg (10%) of (*Z*)-**38** followed by 23 mg (34%) of (*E*)-**38**.

(*Z*)-**38**: ^1H NMR 5.96 (tt, 1, J = 7.6, 2.1), 2.57–2.70 (m, 4), 2.32 (t, 2, J = 7.7), 1.88 (tt, 2, J = 7.7, 7.5), 1.15–1.50 (m, 12), 0.88 (t, 3, J = 7.0); ^{13}C NMR 141.0 (CH), 135.1 (C), 40.7 (CH_2), 31.9 (CH_2), 31.8 (CH_2), 29.4 (CH_2), 29.3 (CH_2), 29.24 (CH_2), 29.21 (CH_2), 27.8 (CH_2), 22.7 (CH_2), 20.6 (CH_2), 14.1 (CH_3), the (C=O) was not observed; IR 2920, 2850, 1720, 1640, 820 cm^{-1}.

(*E*)-**38**:[23a] ^1H NMR 6.55 (tt, 1, J = 7.5, 2.7), 2.58 (tdt, 1, J = 7.6, 2.7, 1.5), 2.33 (t, 2, J = 7.6), 2.14 (dtt, 2, J = 7.6, 7.5, 1.5), 1.93 (tt, 2, J = 7.6, 7.6), 1.18–1.50 (m, 10), 0.88 (t, 3, J = 7.0); ^{13}C NMR 207.3 (C=O), 137.1 (C), 136.4 (CH), 38.6 (CH_2), 31.8 (CH_2), 29.7 (CH_2), 29.4 (2 × CH_2), 29.23 (CH_2), 29.20 (CH_2), 26.7 (CH_2), 22.6 (CH_2), 19.8 (CH_2), 14.1 (CH_3); IR 2940, 2850, 1725, 1650, 815 cm^{-1}.

(3-Methyl-2-butenyl)magnesium Bromide.[24] 3-Methyl-2-butenyl bromide (0.5 mL) was added dropwise to Mg turnings (9.0 g, 375 mmol) in THF (25 mL). THF (120 mL) was then added, and the mixture was cooled to −15 °C. Additional 3-methyl-2-butenyl bromide (6.4 g, 43 mmol) in THF (70 mL) was added dropwise over 4 h. The mixture was stirred at 25 °C for 3 h. The solution was transferred by a cannula from the remaining Mg turnings and was concentrated to about 15 mL. The concentration was shown to be 1.04 M by addition of an aliquot to water and titration with HCl (0.1 M).

Reaction of Imine 13b with (3-Methyl-2-butenyl)magnesium Bromide. A solution of imine **13b** (379 mg, 1.43 mmol) in 5 mL of THF was cooled to −25 °C. (3-Methyl-2-butenyl)-magnesium bromide (5.5 mL, 1.04 M in THF) was added dropwise. The mixture was stirred at −25 °C for 7 h and a mixture of CH_3I (0.54 mL, 6.0 equiv), HMPA (1.4 mL, 7 equiv), and THF (1.0 mL) was added at −25 °C. The mixture was stirred at −25 °C for 0.5 h and at rt for 15 h. Citric acid (15 mL, 10%) was added. The solution was stirred at rt for 1 h. The aqueous layer was extracted with ether (3 × 20 mL). The combined organic layers were washed with a 10% aqueous $Na_2S_2O_3$ solution (15 mL), a saturated aqueous $NaHCO_3$ solution (15 mL), and a saturated aqueous NaCl solution (15 mL) and dried (Na_2SO_4). Concentration in vacuo gave 508 mg of crude product. Flash chromatography on silica gel (30:1 hexane–EtOAc) gave 101 mg (39%) of an inseparable 7:1 mixture of **39** and **17b**.

39: ^1H NMR 9.65 (s, 1), 5.07 (ddqq, 1, J = 7.1, 7.1, 1.4, 1.4), 1.24–2.26 (m, 9), 1.68 (br s, 3), 1.58 (br s, 3), 1.17 (s, 3); ^{13}C NMR 206.6 (CHO), 132.4 (C), 123.3 (CH), 55.4 (C), 52.2 (CH), 34.6 (CH_2), 32.1 (CH_2), 28.7 (CH_2), 25.7 (CH_3), 22.9 (CH_2), 21.0 (CH_3), 17.8 (CH_3); IR 2960, 2860, 2700, 1725 cm^{-1}; $[\alpha]^{20}_D$ = 40.6 (c = 0.125, $CHCl_3$). Anal. Calcd for $C_{12}H_{20}O$: C, 79.94; H, 11.18. Found: C, 79.79; H, 11.42.

(1*R*,2*S*)-1-Methyl-2-(3-methyl-2-butenyl)cyclopentanecarboxaldehyde (17b). *n*-BuLi (0.32 mL, 2.5 M in hexane, 0.80 mmol) was added to a suspension of (1-methylethyl)triphenylphosphonium bromide (0.304 g, 0.79 mmol) in 25 mL of ether at 0 °C. The solution was stirred at rt for 30 min and cooled to −78 °C. Aldehyde **22** (0.143 mg, 0.72 mmol) in 2 mL of ether was added. The mixture was stirred at rt for 10 min and filtered through silica gel. Concentration in vacuo gave 207.3 mg of the crude acetal. Flash chromatography on silica gel (50:1 hexane–EtOAc) gave 139 mg (86%) of the pure acetal.

The acetal (96.0 mg, 0.43 mmol) was dissolved in 30 mL of acetone. TsOH (0.1 g) and water (0.2 mL) were added. The solution was heated at reflux for 2 h and concentrated in vacuo to remove the acetone. The residue was redissolved in 20 mL of ether. The ether solution was washed with a saturated aqueous $NaHCO_3$ solution (2 mL) and dried (Na_2SO_4). Concentration in vacuo gave 104 mg of crude **17b**. Flash chromatography on silica gel (30:1 hexane–EtOAc) gave 74.4 mg (96%) of aldehyde **17b**: ^1H NMR 9.37 (s, 1), 5.01 (ddqq, 1, J = 7.2, 7.2, 1.5, 1.5), 1.86–2.12 (m, 5), 1.61–1.85 (m, 2), 1.65 (br s, 3), 1.58 (br s, 3), 1.33–1.47 (m, 2), 0.98 (s, 3); ^{13}C NMR 205.8 (CHO), 132.5 (C), 123.0 (CH), 55.8 (C), 46.0 (CH), 35.3 (CH_2), 30.6 (CH_2), 28.5 (CH_2), 25.7 (CH_3), 22.5 (CH_2), 17.8 (CH_3), 14.0 (CH_3); IR 2960, 2860, 2800, 1725 cm^{-1}; $[\alpha]^{20}_D$ = 21.1 (c = 0.062, $CHCl_3$). Anal. Calcd for $C_{12}H_{20}O$: C, 79.94; H, 11.18. Found: C, 80.15; H, 11.15.

Reaction of Imine 13b with (3-Methyl-3-butenyl)magnesium Bromide.[8] A solution of imine **13b** (3.94 g, 14.9 mmol) in 20 mL of THF was cooled to −20 °C. (3-Methyl-3-butenyl)-magnesium bromide (39 mL, 1.04 M in THF, 44.5 mmol) was added dropwise. The mixture was stirred at −20 °C for 15 h and a mixture of CH_3I (3.2 mL, 51.4 mmol), HMPA (20 mL), and THF (2 mL) was added at −25 °C. The mixture was stirred at −25 °C for 30 min and at rt for 15 h. Citric acid (10% aqueous solution, 120 mL) was added. The solution was stirred at rt for 2 h. The solution was extracted with ether (3 × 60 mL). The combined ether layers were washed with a 10% aqueous $Na_2S_2O_3$ solution (50 mL), a saturated aqueous $NaHCO_3$ solution (50 mL), and a saturated aqueous NaCl solution (50 mL) and dried (Na_2SO_4). Concentration in vacuo gave 3.52 g of crude **40**. Flash chromatography on silica gel (100:1 hexane–EtOAc) gave 2.53 g (94%) of (1*R*,2*S*)-1-methyl-2-(3-methyl-3-butenyl)cyclopentanecarboxaldehyde (**40**): the NMR and IR data are the same as those previously reported for the racemic material;[8] $[\alpha]^{20}_D$ = −1.04 (c = 0.23, $CHCl_3$). Anal. Calcd for $C_{12}H_{20}O$: C, 79.94; H, 11.18. Found: C, 79.99; H, 11.28.

Isomerization of 40 to 17b with 10 mol % HI in CH_2Cl_2. Aldehyde **40** (264 mg, 1.46 mmol) was dissolved in CH_2Cl_2 (30 mL). Hydroiodic acid (10% mmol, 40 mg, 47% aqueous solution) was added. The solution was stirred at rt for 30 d. The solution was washed with a saturated aqueous $NaHCO_3$ solution (5 mL) and dried (Na_2SO_4). Concentration in vacuo gave 290 mg of crude **17b**. Flash chromatography on silica gel (50:1 hexane–EtOAc) gave 240 mg (90%) of aldehyde **17b**.

2-(2,2-Dimethyl-1-hydroxylpropyl)-3-isopropenylcyclopentanone (41). *t*-BuLi (2.5 mL, 1.6 M in pentane, 4.0 mmol) was added to a solution of 2-bromopropene (0.178 mL, 2.0 mmol) in ether (25 mL) at −78 °C. The resulting solution was stirred at −78 °C for 30 min. CuI (190 mg, 1.0 mmol) was added. The mixture was warmed to rt and stirred for 3 min. The mixture turned black and was recooled to −78 °C. 2-Cyclopentenone (81.5 μL, 1.0 mmol) was added. The brown mixture was stirred at −78 °C for 2 h. Pivalaldehyde (109 μL, 1.0 mmol) was added. The mixture was stirred at −78 °C for 3 h. A saturated aqueous NH_4Cl solution (10 mL) was added and the aqueous layer was extracted with ether (2 × 10 mL). The combined ether layers were washed with a saturated aqueous NH_4Cl solution and dried (Na_2SO_4). Concentration in vacuo gave 239 mg of crude **41**. Flash chromatography on silica gel (20:1 hexane–EtOAc) gave 18 mg (15%) of ketone **42** followed by 168 mg (80%) of ketol **41**.

42: ^1H NMR 4.82 (br s, 2), 3.75 (br s, 1), 2.72–2.86 (m, 1), 2.10–2.48 (m, 4), 1.70–1.86 (m, 1), 1.80 (br s, 3); ^{13}C NMR 218.8 (C=O), 146.2 (C), 109.7 (CH_2), 43.6 (CH_2), 43.5 (CH), 38.5 (CH_2), 28.0 (CH_2), 21.0 (CH_3); IR 3040, 2970, 2890, 1750, 1645, 880 cm^{-1}.

41: ^1H NMR 4.89–4.93 (m, 2), 3.24 (d, 1, J = 11.9), 2.84 (ddd,

1, J = 12.4, 11.9, 6.1), 2.59 (d, 1, J = 11.9), 2.39 (ddd, 1, J = 18.8, 8.9, 1.8), 2.28 (br d, 1, J = 12.4), 2.21 (ddd, 1, J = 18.8, 11.4, 8.5), 2.04 (dddd, 1, J = 12.7, 8.5, 6.1, 1.8), 1.81 (dddd, 1, J = 12.7, 11.9, 11.4, 8.9), 1.72 (br s, 3), 0.91 (s, 9); ^{1}H NMR (exchange with D_2O) 3.24 (s, 1), the doublet at 2.59 disappeared; ^{13}C NMR 219.0 (C=O), 144.0 (C), 114.1 (CH_2), 78.3 (CH), 53.2 (CH), 51.0 (CH), 38.4 (CH_2), 35.5 (C), 26.3 (3 × CH_3), 25.5 (CH_2), 18.0 (CH_3); IR 3530, 3040, 2980, 2900, 1730, 1645, 890 cm^{-1}.

(*E*)-2-(2,2-Dimethylpropylidene)-3-isopropenylcyclopentanone (43). Ketol **41** (89 mg, 0.423 mmol) was dissolved in 10 mL of THF. MsCl (82 μL, 1.06 mmol) and DMAP (258 mg, 2.12 mmol) were added. The mixture was heated at reflux for 48 h and concentrated in vacuo to removed the THF. Ether (30 mL) and water (10 mL) were added. The ether solution was washed with water (10 mL) and dried (Na_2SO_4). Concentration in vacuo gave 120 mg of crude **43**. Flash chromatography on silica gel (20:1 hexane–EtOAc) gave 76 mg (93%) of enone **43**: ^{1}H NMR 6.64 (d, 1, J = 1.7), 4.82 (br s, 1), 4.60 (br s, 1), 3.76 (ddd, 1, J = 4.2, 4.2, 1.7), 2.15–2.39 (m, 2), 1.90–2.00 (m, 2), 1.85 (br s, 3), 1.11 (s, 9); ^{13}C NMR 208.6 (C=O), 147.5 (C), 147.2 (CH), 135.3 (C), 111.7 (CH_2), 45.1 (CH), 34.4 (CH_2), 34.2 (C), 29.9 (3 × CH_3), 25.0 (CH_2), 22.0 (CH_3); IR 3040, 2960, 2900, 1730, 1645, 890 cm^{-1}. Anal. Calcd for $C_{13}H_{20}O$: C, 81.20; H, 10.49. Found: C, 81.15; H, 10.56.

2-(2,2-Dimethylpropyl)-3-isopropenylcyclopentanone (44). Lithium (40 mg) was added to dry liquid NH_3 (about 25 mL). To this blue solution was added a solution of enone **43** (100 mg, 0.52 mmol) in THF (5 mL). The solution was stirred for 15 min. Ethanol (1.5 mL) was added. The solution turned white and became cloudy. After the NH_3 had evaporated, a saturated aqueous NH_4Cl solution (10 mL) was added. The aqueous layer was extracted with ether (3 × 15 mL). The combined ether layers were dried (Na_2SO_4). Concentration in vacuo gave 132 mg of crude **44**. Flash chromatography on silica gel (30:1 hexane–EtOAc) gave 86.9 mg (86%) of ketone **44** as a 85:15 mixture of trans and cis isomers: ^{1}H NMR trans isomer 4.86 (br s, 1), 4.83 (br s, 1), 2.26–2.46 (m, 3), 2.13 (ddd, 1, J = 18.6, 10.5, 8.5), 1.76–2.05 (m, 3), 1.74 (br s, 3), 1.58 (dd, 1, J = 13.9, 6.3), 1.12 (dd, 1, J = 13.9, 2.5), 0.87 (s, ×9); cis isomer 2.99 (ddd, 1, J = 7.5, 7.5, 2.7); ^{13}C NMR trans isomer 220.1 (C=O), 144.7 (C), 113.1 (CH_2), 52.6 (CH), 47.9 (CH), 41.8 (CH_2), 36.8 (CH_2), 30.5 (C), 29.7 (3 × CH_3), 25.6 (CH_2), 18.5 (CH_3); cis isomer 220.0 (C=O), 113.0 (CH_2), 50.0 (CH), 47.8 (CH), 37.5 (CH_2), 34.5 (CH_2), 29.5 (3 × CH_3), 25.0 (CH_2), 21.8 (CH_3), the two quaternary C were not observed; IR 3035, 2950, 2870, 1745, 1645 cm^{-1}.

3-Isopropenyl-1-cyclopentenyl Trimethylsilyl Ether (45). *t*-BuLi (20 mmol, 11.8 mL, 1.7 M in pentane) was added to a solution of 2-bromopropene (10 mmol, 0.89 mL) in THF (10 mL) at −78 °C. The solution was stirred at −78 °C for 30 min. CuCN (0.448 g, 5 mmol) was added. The mixture was warmed to 0 °C and stirred until the CuCN was dissolved. The solution was recooled to −78 °C and a solution of 2-cyclopentenone (0.41 mL, 5 mmol) in 2 mL of THF was added. The brown solution was stirred at −78 °C for 2 h. TMSCl (0.89 mL, 7 mmol) was added. The solution was warmed to 0 °C and stirred for 20 min. A saturated aqueous $NaHCO_3$ solution (10 mL) was added. The solution was extracted with ether (3 × 15 mL). The combined ether layers were washed with a saturated aqueous NaCl solution (15 mL) and dried (Na_2SO_4). Concentration in vacuo gave 1.51 g of crude **45**. Flash chromatography on deactivated silica gel (hexane) gave 0.75 g (76%) of silyl enol ether **45**: ^{1}H NMR 4.72 (br s, 1), 4.63 (br s, 1), 4.56 (br s, 1), 3.22–3.31 (m, 1), 2.25–2.32 (m, 1), 2.03–2.17 (m, 1), 1.69 (br s, 3), 1.53–1.65 (m, 1), 0.82–0.95 (m, 1), 0.22 (s, 9); ^{13}C NMR 155.7 (C), 150.1 (C), 108.3 (CH_2), 105.3 (CH), 49.2 (CH), 33.4 (CH_2), 27.6 (CH_2), 19.9 (CH_3), 0, (3 × CH_3); IR 3080, 2960, 2850, 1650, 1250, 920, 860, 840 cm^{-1}.

Preparation of Ketols 46. Silyl enol ether **45** (403 mg, 2.05 mmol, 1.5 equiv) was dissolved in 5 mL of dry ether. *n*-BuLi (2.05 mmol, 0.82 mL, 2.5 M in hexane) was added dropwise at 0 °C. The solution was stirred at 0 °C for 3 h. $ZnCl_2$ (2.05 mmol, 2.05 mL, 1.0 M in ether) was added. The light yellow solution was stirred at 0 °C for 5 min and recooled to −78 °C. A solution of aldehyde **17b** (288 mg, 1.41 mmol) in ether (5 mL) was added. The solution was stirred at −78 °C for 1 h and then warmed to 0 °C and stirred for 45 min. A saturated aqueous NH_4Cl solution (10 mL) was added. The aqueous layer was extracted with ether (2 × 20 mL). The combined ether layers were dried (Na_2SO_4). Concentration in vacuo gave 704 mg of crude **46**. Flash chromatography on deactivated silica gel (20:1 hexane–EtOAc) gave 81 mg (28%) of recovered **17b**, followed by 99 mg of ketone **42**, followed by 308 mg (63%) of a 1:1 mixture of ketols **46a** and **46b**: ^{1}H NMR 5.12 (br t, 0.5 × 1, J = 7.7), 5.10 (br t, 0.5 × 1, J = 7.7), 4.88–4.96 (m, 2), 3.48 (d, 0.5 × 1, J = 11.9), 3.40 (d, 0.5 × 1, J = 11.9), 2.86 (ddd, 0.5 × 1, J = 11.9, 11.9, 6.1), 2.84 (ddd, 0.5 × 1, J = 11.9, 11.9, 6.1), 2.55 (d, 0.5 × 1, OH, J = 11.9), 2.42 (d, 0.5 × 1, OH, J = 11.9), 1.18–2.39 (m, 13), 1.73 (br s, 0.5 × 3), 1.72 (br s, 0.5 × 3), 1.67 (br s, 3), 1.60 (br s, 3), 0.91 (s, 0.5 × 3), 0.75 (s, 0.5 × 3); ^{1}H NMR (exchange with D_2O) 3.48 (s, 0.5 × 1), 3.40 (s, 0.5 × 1), two doublets at 2.55 and 2.42 disappeared; ^{13}C NMR 144.2 and 144.0 (C), 131.12 and 131.09 (C), 124.6 and 124.3 (CH), 114.4 and 113.9 (CH_2), 78.8 and 74.4 (CH), 54.5 and 53.9 (CH), 51.2 and 51.0 (CH), 48.2 and 48.0 (C), 47.7 and 43.9 (CH), 38.7 and 38.5 (CH_2), 37.6 and 35.0 (CH_2), 31.4 and 30.7 (CH_2), 30.1 and 29.0 (CH_2), 25.8 (CH_3), 25.6 and 25.4 (CH_2), 21.9 and 21.8 (CH_2), 19.0 and 18.2 (CH_3), 18.0 and 17.9 (CH_3), 17.8 and 17.0 (CH_3), the (C=O) was not observed; IR 3600, 3080, 2960, 2880, 1734, 1645, 1050, 890 cm^{-1}.

Dehydration of Ketols 46a and 46b. Ketols **46a** and **46b** (116 mg, 0.381 mmol) were dissolved in 25 mL of THF. DMAP (187 mg, 1.53 mmol) and MsCl (52 μL, 0.763 mmol) were added. The mixture was heated at reflux for 4 d. The dark orange mixture was cooled to rt and concentrated in vacuo to remove the THF. Ether (30 mL) and water (10 mL) were added. The ether solution was washed with water (10 mL) and dried (Na_2SO_4). Concentration in vauco gave 175 mg of crude **47**. Flash chromatography on silica gel (100:1 hexane–EtOAc) gave 68 mg (63%) of an inseparable 2:1 mixture of **47b** and **47a**.

Ketols **46a** and **46b** (308 mg, 1.01 mmol) were dissolved in 50 mL of DMF. Imidazole (343 mg, 5.05 mmol) and MsCl (0.195 mL, 2.53 mmol) were added. The solution was heated at reflux for 2 h. The dark orange solution was cooled to rt and ether (100 mL) was added. The solution was washed with water (3 × 30 mL) and dried (Na_2SO_4). Concentration in vacuo gave 528 mg of crude **47**. Flash chromatography on silica gel (100:1 hexane–EtOAc) gave 273 mg (94%) of a 1:1 mixture of **47a** and **47b**: ^{1}H NMR **47b** 6.70 (d, 1, J = 1.6), 5.06 (br t, 1, J = 6.5), 4.81 (br s, 1), 4.53 (br s, 1), 3.73 (br s, 1), 2.12–2.48 (m, 4), 1.85 (br s, 3), 1.65 (br s, 3), 1.59 (br s, 3), 1.42–2.06 (m, 7), 1.22–1.38 (m, 2), 1.00 (s, 3); **47a** 6.74 (d, 1, J = 1.6), 5.08 (br t, 1, J = 6.5), 4.81 (br s, 1), 4.58 (br s, 1), 3.73 (br s, 1), 2.12–2.58 (m, 4), 1.85 (br s, 3), 1.67 (br s, 3), 1.59 (br s, 3), 1.42–2.06 (m, 7), 1.22–1.38 (m, 2), 0.99 (s, 3); ^{13}C NMR **47b** 208.1 (C=O), 147.5 (C), 147.4 (CH), 136.6 (C), 131.2 (C), 123.7 (CH), 111.62 (CH_2), 50.41 (CH), 47.0 (C), 45.5 (CH), 39.4 (CH_2), 34.3 (CH_2), 29.4 (CH_2), 28.8 (CH_2), 25.6 (CH_3), 25.1 (CH_2), 22.1 (CH_3), 21.66 (CH_3), 17.7 (CH_3), 16.8 (CH_3); **47a** 208.3 (C=O), 147.4 (C), 147.1 (CH), 136.7 (C), 131.4 (C), 123.7 (CH), 111.57 (CH_2), 50.4 (CH), 46.9 (C), 45.4 (CH), 39.7 (CH_2), 34.3 (CH_2), 29.4 (CH_2), 28.9 (CH_2), 25.6 (CH_3), 25.2 (CH_2), 22.0 (CH_3), 21.72 (CH_3), 18.0 (CH_3), 16.8 (CH_3); IR 3080, 2960, 2880, 1715, 1630, 875 cm^{-1}. Anal. Calcd for $C_{20}H_{30}O$: C, 83.86; H, 10.55. Found: C, 83.85; H, 10.58.

Reduction of Enones 47a and 47b. Lithium (30 mg) was added to dry ammonia (30 mL). The resulting blue solution was stirred for 5 min. To this blue solution was added a solution of a 1:1 mixture of enones **47a** and **47b** (214 mg, 0.75 mmol) in 15 mL of THF. The solution was stirred for 1 h and MeOH (10 mL) was slowly added. The reaction flask was left open to allow the ammonia to evaporate while a positive N_2 pressure was maintained. The solution was stirred at rt overnight. A saturated aqueous NH_4Cl solution (10 mL) was added. The mixture was concentrated to remove the MeOH. The aqueous solution was extracted with ether (3 × 10 mL). The combined ether layers were dried (Na_2SO_4) and concentrated in vacuo to give 272 mg of crude **48**. Flash chromatography on silica gel (100:1 hexane–EtOAc) gave 196 mg (90%) of an inseparable 6:1:6:1 mixture of ketones **48at**, **48ac**, **48bt**, and **48bc**: IR (neat) 3075, 2960, 2875, 1745, 1645, 885 cm^{-1}. Anal. Calcd for $C_{20}H_{32}O$: C, 83.27; H, 11.18. Found: C, 83.32; H, 11.23.

The data for **48bt** were determined from the mixture: ^{1}H NMR 5.11 (br t, 1, J = 6.5), 4.85 (br s, 1), 4.83 (br s, 1), 2.34–2.48 (m, 2), 1.92–2.22 (m, 4), 1.15–1.89 (m, 11), 1.75 (br s, 3), 1.67 (br s, 3), 1.60 (br s, 3), 0.69 (s, 3); ^{13}C NMR 220.1 (C=O), 144.8 (C),

130.7 (C), 124.6 (CH), 112.8 (CH_2), 52.5 (CH_2), 49.5 (2 × CH), 43.4 (C), 39.0 (CH_2), 38.9 (CH_2), 36.9 (CH_2), 30.2 (CH_2), 28.7 (CH_2), 25.8 (CH_3), 25.6 (CH_2), 21.2 (CH_3), 20.1 (CH_3), 18.7 (CH_3), 17.7 (CH_3).

Reduction of Ketones 48at, 48ac, 48bt, and 48bc with $LiAlH_4$. The mixture of ketones **48at**, **48ac**, **48bt**, and **48bc** (210 mg, 0.73 mmol) was dissolved in 10 mL of THF. $LiAlH_4$ (7.6 mg, 0.20 mmol) was added. The mixture was stirred at rt for 8 h. A saturated aqueous NH_4Cl solution (4 mL) was added slowly and the mixture was filtered through silica gel. The solution was concentrated in vacuo to remove the THF. The resulting aqueous solution was extracted with ether (2 × 10 mL). The combined ether layers were dried (Na_2SO_4). Concentration in vacuo gave 223 mg of crude **49**. Flash chromatography on silica gel (50:1 hexane–EtOAc) gave four fractions.

The first fraction contains 8 mg (4%) of **49acc**: ^1H NMR 5.12 (br s, 1, J = 7.0), 4.84 (br s, 1), 4.75 (br s, 1), 4.15–4.21 (m, 1), 2.69 (ddd, 1, J = 8.4, 8.4, 8.4), 1.92–2.11 (m, 2), 1.34–1.92 (m, 12), 1.73 (br s, 3), 1.68 (br s, 3), 1.60 (br s, 3), 1.16–1.33 (m, 2), 0.74 (s, 3); ^{13}C NMR 147.8 (C), 130.8 (C), 124.7 (CH), 112.7 (CH_2), 75.7 (CH), 49.9 (CH), 49.7 (CH), 43.9 (CH), 43.6 (C), 39.6 (CH_2), 34.8 (CH_2), 34.1 (CH_2), 30.1 (CH_2), 28.9 (CH_2), 27.5 (CH_2), 25.8 (CH_3), 22.4 (CH_3), 21.3 (CH_2), 19.6 (CH_3), 17.7 (CH_3); IR 3475, 3070, 2950, 2870, 1640, 1090, 880 cm^{-1}; $[\alpha]^{20}_D$ = –2.82 (c = 0.16, $CHCl_3$). Anal. Calcd for $C_{20}H_{34}O$: C, 82.70; H, 11.80. Found: C, 82.57; H, 11.85.

The second fraction contains 46 mg (22%) of an inseparable 1:2:2 mixture of **49bcc**, **49btc**, and **49atc**: ^1H NMR 5.05–5.13 (m, 1), 4.84 (br s, 0.2 × 1), 4.75 (br s, 0.8 × 1), 4.74 (br s, 0.8 × 1), 4.68 (br s, 0.2 × 1), 4.29 (br t, 0.4 × 1, J = 4.0), 4.24 (br t, 0.6 × 1, J = 4.0), 2.61 (dt, 0.2 × 1, J = 8.2), 2.20–2.43 (m, 0.8 × 1), 1.72 (br s), 1.68 (br s), 1.65 (br s), 1.60 (br s) (total 9 H), 1.05–2.12 (m, total 16 H), 0.82 (s, 0.4 × 3), 0.79 (s, 0.2 × 3), 0.74 (s, 0.4 × 3); IR 3080, 2960, 2870, 1645, 1100, 880 cm^{-1}. Anal. Calcd for $C_{20}H_{34}O$: C, 82.70; H, 11.80. Found: C, 82.74; H, 11.96.

The third fraction contains 135 mg (64%) of an inseparable 1:1 mixture of **49att** and **49btt**. Anal. Calcd for $C_{20}H_{34}O$: C, 82.70; H, 11.80. Found: C, 82.63; H, 11.81. The spectral data were assigned using a sample obtained by reduction of a 2:1 mixture of enones **47b** and **47a**.

The data for **49att** were determined from the mixture: ^1H NMR 5.10 (br t, 1, J = 5.7), 4.74 (br s, 2), 3.93–4.02 (m, 1), 1.98–2.12 (m, 2), 1.17–1.90 (m, 15), 1.72 (br s, 3), 1.68 (br s, 3), 1.60 (br s, 3), 0.83 (s, 3); ^{13}C NMR 146.80 (C), 130.8 (C), 124.58 (CH), 110.82 (CH_2), 80.3 (CH), 56.2 (CH), 49.6 (CH), 49.0 (CH), 45.6 (CH_2), 44.0 (CH_2), 39.0 (CH_2), 35.5 (CH_2), 29.87 (CH_2), 28.9 (CH_2), 28.7 (CH_2), 25.8 (CH_3), 21.0 (CH_2), 19.9 (CH_3), 19.3 (CH_2), 17.7 (CH_3); IR 3500, 3080, 2960, 2880, 1650, 1090, 870 cm^{-1}.

The data for **49btt** were determined from the mixture: ^1H NMR 5.10 (br t, 1, J = 5.7), 4.74 (br s, 2), 3.93–4.02 (m, 1), 1.98–2.12 (m, 2), 1.17–1.90 (m, 14), 1.72 (br s, 3), 1.68 (br s, 3), 1.60 (br s, 3), 1.10 (dd, 1, J = 14.0, 9.5), 0.76 (s, 3); ^{13}C NMR 146.76 (C), 130.8 (C), 124.64 (CH), 110.77 (CH_2), 79.7 (CH), 56.0 (CH), 50.0 (CH), 48.4 (CH), 45.3 (CH_2), 43.7 (CH_2), 39.6 (CH_2), 35.4 (CH_2), 29.93 (CH_2), 28.8 (CH_2), 28.6 (CH_2), 25.8 (CH_3), 21.3 (CH_2), 19.5 (CH_3), 19.4 (CH_2), 17.8 (CH_3).

The fourth fraction contains 11 mg (5%) of an inseparable 1:1 mixture of **49act** and **49bct**: ^1H NMR 5.09 (br t, 0.5 × 1, J = 7.8), 5.06 (br t, 0.5 × 1, J = 7.8), 4.85 (br s, 1), 4.68 (br s, 1), 4.18 (br t, 1, J = 6.5), 2.73–2.90 (m, 1), 1.20–2.12 (m, 15), 1.72 (br s, 3), 1.68 (br s, 3), 1.60 (br s, 3), 1.06 (dd, 0.5 × 1, J = 14.3, 1.9), 0.91 (dd, 0.5 × 1, J = 11, 3.4), 0.79 (s, 0.5 × 3), 0.75 (s, 0.5 × 3); ^{13}C NMR 145.7 (C), 130.3 (C), 124.5 (CH), 110.1 (0.5 × 1, CH_2), 111.0 (0.5 × 1, CH_2), 79.2 (0.5 × 1, CH), 78.5 (0.5 × 1, CH), 49.6 (0.5 × 1, CH), 49.0 (0.5 × 1, CH), 48.4 (CH), 46.8 (0.5 × 1, CH), 46.3 (0.5 × 1, CH), 43.8 (0.5 × 1, C), 43.7 (0.5 × 1, C), 39.5 (0.5 × 1, CH_2), 39.2 (0.5 × 1, CH_2), 36.3 (0.5 × 1, CH_2), 36.0 (0.5 × 1, CH_2), 32.9 (CH_2), 30.0 (0.5 × 1, CH_2), 29.8 (0.5 × 1, CH_2), 28.9 (0.5 × 1, CH_2), 28.8 (0.5 × 1, CH_2), 25.85 (0.5 × 1, CH_2), 25.81 (0.5 × 1, CH_2), 25.78 (0.5 × 1, CH_3), 25.68 (0.5 × 1, CH_3), 23.5 (0.5 × 1, CH_3), 23.3 (0.5 × 1, CH_3), 21.3 (0.5 × 1, CH_2), 21.0 (0.5 × 1, CH_2), 20.2 (0.5 × 1, CH_3), 19.7 (0.5 × 1, CH_3), 17.9 (0.5 × 1, CH_3), 17.7 (0.5 × 1, CH_3); IR 3090, 2960, 2880, 1650, 1070, 870 cm^{-1}. Anal. Calcd for $C_{20}H_{34}O$: C, 82.70; H, 11.80. Found: C, 82.79, H, 11.98.

Oxidation of Alcohol 49acc To Give Ketone 48ac. Alcohol **49acc** (6.3 mg, 0.022 mmol) was dissolved in 3 mL of CH_2Cl_2. PCC (7.1 mg, 0.033 mmol) was added. The solution was stirred for 2 h and 10 mL of ether was added. The mixture was filtered through silica gel. The filtrate was concentrated in vacuo to give 8.0 mg of crude **48ac**. Flash chromatography on silica gel (50:1 hexane–EtOAc) gave 6 mg (92%) of ketone **48ac**: ^1H NMR 5.10 (br t, 1, J = 7.2), 4.83 (br s, 1), 4.56 (br s, 1), 2.98 (ddd, 1, J = 7.4, 7.4, 3.3), 1.17–2.32 (m, 16), 1.67 (br s, 3), 1.59 (br s, 6), 0.77 (s, 3); ^{13}C NMR 220.0 (C), 144.9 (C), 130.8 (C), 124.6 (CH), 112.9 (CH_2), 50.4 (CH), 49.5 (CH), 48.1 (CH), 43.6 (C), 39.1 (CH_2), 35.2 (CH_2), 34.7 (CH_2), 30.4 (CH_2), 28.8 (CH_2), 25.8 (CH_3), 24.8 (CH_2), 22.0 (CH_3), 21.2 (CH_2), 20.2 (CH_3), 17.7 (CH_3); IR 3080, 2960, 2870, 1740, 1645, 890 cm^{-1}; $[\alpha]^{20}_D$ = –66.7 (c = 0.05, $CHCl_3$). Anal. Calcd for $C_{20}H_{32}O$: C, 83.27; H, 11.18. Found: C, 83.41; H, 11.20.

Equilibrium of Ketone 48ac with Ketone 48at. Ketone **48ac** (6 mg, 0.020 mmol) was dissolved in 3 mL of MeOH. Sodium methoxide (0.1 mL, 1 M in MeOH) was added. The solution was stirred overnight and 1 mL of a saturated aqueous NH_4Cl solution was added. Concentration in vacuo removed the MeOH. The aqueous solution was extracted with ether (3 × 5 mL). The combined ether layers were dried (Na_2SO_4) and concentrated in vacuo. Flash chromatography on silica gel (50:1 hexane–EtOAc) gave 5.6 mg (97%) of an inseparable 6:1 mixture of **48at** and **48ac**. The data for **48at** were determined from the mixture: ^1H NMR 5.08 (br t, 1, J = 6.5), 4.85 (br s, 1), 4.83 (br s, 1), 2.32–2.46 (m, 2), 1.93–2.20 (m, 4), 1.12–1.89 (m, 10), 1.74 (s, 3), 1.67 (s, 3), 1.60 9s, 3), 1.09 (dd, 1, J = 14.0, 2.6), 0.78 (s, 3); ^{13}C NMR 220.2 (C=O), 144.7 (C), 130.8 (C), 124.5 (CH), 113.2 (CH_2), 52.6 (CH), 49.8 (CH), 49.0 (CH), 43.5 (C), 39.4 (CH_2), 39.0 (CH_2), 36.7 (CH_2), 30.1 (CH_2), 28.8 (CH_2), 25.8 (CH_3), 25.5 (CH_2), 21.0 (CH_2), 20.1 (CH_3), 18.3 (CH_3), 17.8 (CH_3); IR 3080, 2970, 2880, 1745, 1645, 885 cm^{-1}.

Oxidation of Alcohols 49act and 49bct To Give Ketones 48ac and 48bc. Oxidation of the 1:1 mixture of **49act** and **49bct** as described above for **49acc** gave an inseparable 1:1 mixture of **48ac** and **48bc** in 92% yield. The data for **48bc** were determined from the mixture: ^1H NMR 5.10 (br t, 1, J = 7.2), 4.83 (br s, 1), 4.50 (br s, 1), 2.96 (ddd, 1, J = 7.4, 7.4, 3.3), 1.14–2.32 (m, 16), 1.68 (br s, 3), 1.60 (br s, 6), 0.76 (s, 3); ^{13}C NMR 220.0 (C), 144.9 (C), 130.8 (C), 124.5 (CH), 113.0 (CH_2), 50.41 (CH), 49.3 (CH), 47.7 (CH), 43.5 (C), 39.0 (CH_2), 34.7 (CH_2), 34.5 (CH_2), 30.2 (CH_2), 28.7 (CH_2), 25.8 (CH_3), 25.1 (CH_2), 21.8 (CH_3), 21.2 (CH_2), 20.2 (CH_3), 17.9 (CH_3); IR 3075, 2935, 2870, 1740, 1645, 890 cm^{-1}.

Equilibration of the 1:1 mixture of **48ac** and **48bc** with NaOMe/MeOH as described above for **48ac** gave a 6:1:6:1 mixture of **48at**, **48ac**, **48bt**, and **48bc** in 95% yield.

Protection of Alcohols 49att and 49btt as Silyl Ethers 50 and 55. A 1:1 mixture of **49att** and **49btt** was dissolved in 10 mL of DMF. TBDMSOTf (0.128 mL, 0.56 mL) and imidazole (79.1, 1.16 mmol) were added. The solution was stirred for 24 h. After 50 mL of ether was added, the solution was washed with water (3 × 10 mL) and dried (Na_2SO_4). Concentration in vacuo gave 208 mg of crude product. Flash chromatography on silica gel (hexane) gave 182 mg (97%) of an inseparable 1:1 mixture of silyl ethers **50** and **55**: IR (neat) 3080, 2960, 2860, 1645, 1095, 880 cm^{-1}. Anal. Calcd for $C_{26}H_{48}OSi$: C, 77.16; H, 11.95. Found: C, 77.26; H, 12.09.

The data for **50** were determined from the mixture: ^1H NMR 5.13 (br t, 1, J = 7.3), 4.76 (br 2, 1), 4.70 (br s, 1), 3.84 (q, 1, J = 4.0), 1.98–2.13 (m, 2), 1.75 (br s, 3), 1.70 (br s, 3), 1.65 (br s, 3), 1.10–1.88 (m, 15), 0.903 (s, 9), 0.77 (s, 3), 0.062 (s, 6); ^{13}C NMR 148.2 (C), 130.7 (C), 124.76 (CH), 110.4 (CH_2), 81.3 (CH), 55.2 (CH), 49.4 (CH), 48.7 (CH), 46.1 (CH_2), 43.9 (C), 39.1 (CH_2), 34.8 (CH_2), 32.8 (C), 29.9 (CH_2), 28.92 (CH_2), 28.7 (CH_2), 25.9 (3 × CH_3), 25.7 (CH_3), 21.2 (CH_2), 20.1 (CH_3), 19.2 (CH_3), 17.85 (CH_3), –3.9 (CH_3), –4.64 (CH_3).

The data for **55** were determined from the mixture: ^1H NMR 5.13 (br t, 1, J = 7.3), 4.76 (br s, 1), 4.70 (br s, 1), 3.90 (q, 1, J = 4.0), 1.98–2.13 (m, 2), 1.74 (br s, 3), 1.70 (br s, 3), 1.65 (br s, 3), 1.10–1.88 (m, 15), 0.898 (s, 9), 0.74 (s, 3), 0.062 (s, 6); ^{13}C NMR 148.1 (C), 130.7 (C), 124.79 (CH), 110.1 (CH_2), 80.5 (CH), 55.5 (CH), 50.2 (CH), 48.8 (CH), 46.8 (CH_2), 43.8 (C), 39.8 (CH_2), 34.9 (CH_2), 32.8 (C), 30.1 (CH_2), 28.88 (CH_2), 28.85 (CH_2), 25.9 (3 × CH_3), 25.8 (CH_3), 21.4 (CH_2), 19.7 (CH_3), 19.4 (CH_3), 17.93 (CH_3), –4.07 (CH_3), –4.56 (CH_3).

Oxidation of Unsaturated Silyl Ethers 50 and 55. A 1:1 mixture of unsaturated silyl ethers **50** and **55** (9.1 mg, 0.225 mmol) was dissolved in water (2.5 mL) and acetone (2.5 mL). OsO_4 (1%

mol, 22.9 mg, 2.5% in *t*-BuOH) and *N*-methylmorpholine *N*-oxide monohydrate (2.2 equiv, 67%) were added. The solution was stirred for 1 d. $NaHSO_3$ (0.05 g) was added and the mixture was stirred for 5 min. The mixture was filtered through the silica gel. The filtrate was concentrated in vacuo to remove the acetone. Ether (30 mL) was added and the ether layer was washed with water. Concentration in vacuo gave 138 mg of oily crude product. This crude product was redissolved in water (2.5 mL) and acetone (5 mL). $NaIO_4$ (2.2 equiv, 106 mg) was added and the mixture was stirred at rt for 3 days. Concentration in vacuo removed the acetone. Water (5 mL) and ether (15 mL) were added. The aqueous layer was extracted with ether (2 × 10 mL). The combined ether layers were dried (Na_2SO_4) and concentrated in vacuo to give 94.8 mg of crude keto aldehydes. Flash chromatography on silica gel (10:1 hexane–EtOAc) gave 34 mg (40%) of keto aldehyde **51** followed by 36 mg (42%) of keto aldehyde **56**.

51: ^{1}H NMR 9.77 (dd, 1, J = 2.8, 1.8), 3.72 (dd, 1, J = 9.2, 5.5), 2.28–2.55 (m, 4), 2.18 (s, 3), 1.21–2.10 (m, 12), 0.99 (dd, 1, J = 14.0, 6.3), 0.87 (s, 9), 0.74 (s, 3), 0.044 (s, 3), 0.037 (s, 3); ^{13}C NMR 210.0 (C=O), 202.9 (CHO), 80.8 (CH), 58.0 (CH), 45.7 (CH_2), 45.5 (CH), 45.2 (CH_2), 44.0 (C), 43.6 (CH), 38.4 (CH_2), 33.7 (CH_2), 32.2 (C), 29.6 (CH_2), 28.4 (CH_3), 26.2 (CH_2), 25.8 (3 × CH_3), 21.5 (CH_2), 19.4 (CH_3), –4.3 (CH_3), –4.7 (CH_3); IR 2960, 2860, 2720, 1730, 1715, 1110 cm^{-1}; $[\alpha]^{20}_D$ = 1.69 (c = 0.778, $CHCl_3$). Anal. Calcd for $C_{22}H_{40}O_3Si$: C, 69.42; H, 10.59. Found: C, 69.28; H, 10.43.

56: ^{1}H NMR 9.76 (dd, 1, J = 2.7, 1.8), 3.80 (dd, 1, J = 9.6, 4.8), 2.29–2.50 (m, 4), 2.18 (s, 3), 1.28–2.00 (m, 13), 0.87 (s, 9), 0.71 (s, 3), 0.044 (s, 3), 0.036 (s, 3); ^{13}C NMR 210.0 (C=O), 202.9 (CHO), 80.3 (CH), 59.0 (CH), 46.2 (CH_2), 46.2 (CH), 45.2 (CH_2), 44.1 (C), 43.6 (CH), 38.7 (CH_2), 33.7 (CH_2), 32.2 (C), 29.9 (CH_2), 28.3 (CH_3), 26.0 (CH_2), 44.1 (C), 43.6 (CH), 38.7 (CH_2), 33.7 (CH_2), 32.2 (C), 29.9 (CH_2), 28.3 (CH_3), 26.0 (CH_2), 25.8 (3 × CH_3), 21.4 (CH_2), 19.8 (CH_3), –4.3 (CH_3), –4.7 (CH_3); IR 2960, 2860, 2710, 1730, 1715, 1105 cm^{-1}; $[\alpha]^{20}_D$ = –7.0 (c = 0.102, $CHCl_3$). Anal. Calcd for $C_{22}H_{40}O_3Si$: C, 69.42; H, 10.59. Found: C, 69.55; H, 10.67.

Reductive Cyclization of Keto Aldehyde 51. In a glovebox under N_2, $TiCl_3(DME)_{1.5}$(0.233, 0.79 mmol), and zinc–copper couple (0.155 g, 2.38 mmol) were transferred to a 50-mL round-bottom flask with a condenser. The system was removed from the glovebox and DME (10 mL) was added. The mixture was heated at reflux for 10 h. To this black mixture was added a solution of keto aldehyde **51** (31.2 mg, 0.082 mmol) in 5 mL of DME over 12 h. Heating was continued for an additional 2 h. Pentane (10 mL) was added. The mixture was filtered through silica gel. The silica gel pad was washed with an additional 15 mL of pentane and the filtrate was concentrated in vacuo to 89.2 mg of crude product. Flash chromatography on silica gel (hexane) gave 8 mg (29%) of unsaturated silyl ether **52** followed by 9 mg (31%) of unsaturated silyl ether **53**.

52: ^{1}H NMR 4.85 (br s, 1), 4.78 (br s, 1), 3.64 (ddd, 1, J = 8.4, 8.4, 6.2), 2.26–2.44 (m, 2), 1.77–2.04 (m, 5), 1.13–1.75 (m, 12), 0.88 (s, 9), 0.81 (s, 3), 0.036 (s, 3), 0.032 (s, 3); ^{13}C NMR 152.2 (C), 108.7 (CH_2), 79.4 (CH), 51.4 (CH), 48.9 (CH), 42.1 (C), 41.5 (CH_2), 40.7 (CH_2), 39.9 (CH), 32.8 (CH_2), 32.3 (C), 32.1 (CH_2), 31.3 (CH_2), 31.1 (CH_2), 26.2 (CH_2), 25.9 (3 × CH_3), 19.9 (CH_2), 18.0 (CH_3), –4.2 (CH_3), –4.8 (CH_3); IR 3080, 2950, 2860, 1640, 1110, 835 cm^{-1}; $[\alpha]^{20}_D$ = 30 (c = 0.032, $CHCl_3$). Anal. Calcd for $C_{22}H_{40}OSi$: C, 75.79; H, 11.56. Found: C, 75.59; H, 10.54.

53: ^{1}H NMR 5.49 (br t, 1, J = 7.4), 4.14 (ddd, 1, J = 8.7, 8.7, 5.2), 2.88 (ddd, 1, J = 13.4, 10.8, 6.7), 1.67–2.14 (m, 6), 1.63 (br s, 3), 1.30–1.60 (m, 19), 1.23 (dd, 1, J = 15.1, 7.0), 0.96 (s, 3), 0.90 (s, 9), 0.08 (s, 3), 0.07 (s, 3); ^{13}C NMR 136.8 (C), 126.6 (CH), 77.0 (CH), 54.1 (CH), 53.0 (CH), 45.2 (C), 45.1 (CH_2), 40.8 (CH), 36.0 (CH_2), 32.9 (C), 32.1 (CH_2), 26.8 (CH_2), 26.0 (3 × CH_3), 25.1 (CH_2), 18.9 (CH_2), 18.7 (CH_3), 18.1 (CH_2), 17.4 (CH_3), –4.1 (CH_3), –4.4 (CH_3); IR 2950, 2850, 1090, 830 cm^{-1}; $[\alpha]^{20}_D$ = 48 (c = 0.040, $CHCl_3$). Anal. Calcd for $C_{22}H_{40}OSi$: C, 75.79; H, 11.56. Found: C, 75.74; H, 10.59.

Deprotection of Silyl Ether 53. Silyl ether **53** (6.8 mg, 0.02 mmol) was dissolved in 7 mL of THF. *n*-Bu_4NF (0.04 mmol, 40 μL, 1.0 M in THF) was added. The solution was stirred for 1 d and concentrated in vacuo to remove the THF. The residue was dissolved in 20 mL of ether. The solution was washed with a saturated aqueous NaCl solution (2 × 5 mL) and dried ($MgSO_4$). Concentration in vacuo gave 10 mg of crude **54**. Flash chromatography on silica gel (10:1 hexane–EtOAc) gave 4.4 mg (96%) of alcohol **54**: ^{1}H NMR 5.50 (br t, 1, J = 8.0), 4.20 (dt, 1, J = 8.8, 4.8), 2.94 (ddd, 1, J = 13.2, 11.0, 6.5), 1.24–2.13 (m, 17), 1.64 (br s, 3), 0.97 (s, 3); ^{13}C NMR 136.4 (C), 126.8 (CH), 77.0 (CH), 54.1 (CH), 53.6 (CH), 45.3 (C), 45.1 (CH_2), 41.9 (CH), 36.2 (CH_2), 32.9 (C), 32.2 (CH_2), 26.8 (CH_2), 25.6 (CH_2), 18.9 (CH_2), 18.5 (CH_3), 17.3 (CH_3); IR 3600–3100, 2960, 2870, 1070, 830 cm^{-1}; $[\alpha]^{20}_D$ = 45 (c = 0.025, $CHCl_3$). The NMR spectral data were identical to those reported by Dauben if 0.07 ppm is added to their ^{1}H NMR spectral data.[4j]

Oxidation of Alcohol 54. Alcohol **54** (4.4 mg, 0.0188 mmol) was dissolved in 2 mL of CH_2Cl_2. PCC (1.5 equiv, 6.1 mg) was added. The solution was stirred for 2 h and 5 mL of ether was added. The mixture was filtered through silica gel. Concentration of the filtrate in vacuo gave 6 mg of crude **9b**. Flash chromatography on silica gel (30:1 hexane–EtOAc) gave 3.1 mg (78%) of ketone **9b**: ^{1}H NMR 5.59 (br t, 1, J = 7.9), 3.23 (ddd, 1, J = 13.9, 12.0, 5.3), 2.43 (dd, 1, J = 18.7, 8.1), 2.33 (br d, 1, J = 14.7), 2.21 (ddd, 1, J = 18.7, 11.7, 8.7), 1.19–2.10 (m, 13), 1.68 (br s, 3), 0.72 (s, 3); ^{13}C NMR 218.19, 135.17, 126.88, 54.68, 53.76, 44.56, 44.39, 41.69, 37.55, 34.53, 32.19, 26.92, 24.38, 18.85, 18.13, 16.41; $[\alpha]^{20}_D$ = 126 (c = 0.050, $CHCl_3$). The ^{1}H and ^{13}C NMR spectral data are identical to those reported by Dauben[4j] and Coates.[4f]

Reductive cyclization of keto aldehyde 56 (33.6 mg, 0.088 mmol) as described above for **51** gave 12.3 mg (40%) of unsaturated silyl ether **58** followed by 9.0 mg (29.3%) of unsaturated silyl ether **57**.

57: ^{1}H NMR 4.83 (br s, 1), 4.73 (br s, 1), 3.58 (ddd, 1, J = 8.4, 8.4, 6.5), 2.04–2.27 (m, 2), 1.25–1.92 (m, 16), 0.97 (dd, 1, J = 13, 10.4), 0.89 (s, 9), 0.82 (s, 3), 0.043 (s, 3), 0.032 (s, 3); ^{13}C NMR 153.5 (C), 110.3 (CH_2), 79.6 (CH), 50.5 (CH), 49.1 (CH), 46.8 (CH_2), 46.6 (CH_2), 45.2 (CH), 42.6 (C), 35.6 (CH_2), 32.5 (CH_2), 32.3 (CH_2), 31.4 (CH_2), 30.9 (C), 25.9 (3 × CH_3), 21.3 (CH_2), 19.8 (CH_3), 18.1 (CH_2), –4.2 (CH_3), –4.7 (CH_3); IR 3070, 2950, 2860, 1640, 1110, 830 cm^{-1}; $[\alpha]^{20}_D$ = 4.6 (c = 0.031, $CHCl_3$). Anal. Calcd for $C_{22}H_{40}OSi$: C, 75.79; H, 11.56. Found: C, 75.56; H, 11.58.

58: ^{1}H NMR 5.19–5.27 (m, 1), 3.62 (ddd, 1, J = 4.7, 4.7, 4.7), 2.76 (ddd, 1, J = 8.2, 8.2, 8.2), 2.16–2.43 (m, 2), 1.78–1.95 (m, 4), 1.58 (br s, 3), 1.35–1.77 (m, 9), 1.10 (dd, 1, J = 12.6, 12.6), 0.88 (s, 9), 0.87 (s), 0.04 (s, 3), 0.03 (s, 3); ^{13}C NMR 136.9 (C), 123.7 (CH), 80.9 (CH), 51.9 (CH), 49.2 (CH_2), 47.1 (CH), 46.3 (CH_2), 43.6 (CH), 43.1 (C), 36.9 (CH_2), 34.7 (CH_2), 32.6 (C), 27.0 (CH_2), 25.9 (3 × CH_3), 22.4 (CH_2), 21.8 (CH_3), 20.8 (CH_3), 18.0 (CH_2), –4.49 (CH_3), –4.52 (CH_3); IR 2950, 2860, 1105, 830 cm^{-1}; $[\alpha]^{20}_D$ = –54 (c = 0.092, $CHCl_3$). Anal. Calcd for $C_{22}H_{40}OSi$: C, 75.79; H, 11.56. Found: C, 75.76; H, 10.67.

Deprotection of silyl ether 58 (9.0 mg, 0.026 mmol) as described above for **53** gave 15 mg of crude product. Flash chromatography on silica gel (10:1 hexane–EtOAc) gave 5.8 mg (95%) of alcohol **59**: ^{1}H NMR 5.20–5.28 (m, 1), 3.72 (dt, 1, J = 10.4, 5.2), 2.87 (dt, 1, J = 7.2, 7.2), 2.20–2.38 (m, 2), 1.40–1.96 (m, 12), 1.15–1.30 (m, 3), 1.70 (br s, 3), 0.89 (s, 3); ^{13}C NMR 136.2 (C), 124.2 (CH), 80.7 (CH), 52.1 (CH), 49.3 (CH_2), 46.9 (CH), 46.4 (CH_2), 43.9 (CH), 43.1 (C), 37.0 (CH_2), 34.6 (CH_2), 32.8 (C), 26.7 (CH_2), 22.6 (CH_2), 21.6 (CH_3), 21.0 (CH_3); IR 3600–3100, 2970, 2870, 1080, 800 cm^{-1}; $[\alpha]^{20}_D$ = –66.2 (c = 0.16, $CHCl_3$). Anal. Calcd for $C_{16}H_{26}O$: C, 81.99; H, 11.18. Found: C, 82.00; H, 11.22.

Oxidation of alcohol 59 (3.2 mg, 0.014 mmol) as described above for **54** followed by flash chromatography on silica gel (30:1 hexane–EtOAc) gave 2.6 mg (80%) of ketone **60**: ^{1}H NMR 5.56 (br t, 1, J = 7.1), 2.74 (dt, 1, J = 11.1, 5.5), 2.40 (dd, 1, J = 17.3, 8.0), 1.22–2.20 (m, 15), 1.73 (br s, 3), 1.14 (dd, 1, J = 14.0, 9.3), 0.84 (s, 3); ^{13}C NMR 221.04, 134.57, 126.20, 49.98, 49.93, 46.75, 44.04, 43.89, 41.96, 37.73, 34.49, 28.38, 26.34, 24.05, 21.26, 18.76; $[\alpha]^{20}_D$ = –61 (c = 0.10, $CHCl_3$). The ^{1}H and ^{13}C NMR spectral data are identical to those reported by Dauben[4j] and Coates.[4f]

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Supplementary Material Available: ^{1}H and ^{13}C NMR spectra for compounds **18a**, **18b**, **11b** and **23**, **28**, **29**, **30**, **31**, **34**, **35**, **56**, **41**, **44**, **45**, and **46** (28 pages). Ordering information is given on any current masthead page.