Total Synthesis of 1233A

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The total synthesis of the HMG-CoA synthase inhibitor 1233A (1), starting from either (*R*)-pulegone (6) or diketo ester 12, is described. The key transformations included the diastereoselective [2,3] rearrangements of allylic ethers 9 and 19 to alcohols 10 and 11b, respectively, and the diastereoselective hydroboration of 11b to form 19. A Pd-mediated coupling of iodo olefin 31a with *tert*-butyl crotonate under newly devised conditions provides an efficient preparation of the diene portion of 1233A.

The natural product 1233A (1), a member of a small but growing group of naturally occurring β-lactones, is a novel antibiotic first isolated over two decades ago by Turner.[1,2] Renewed interest in 1 has been aroused by the observation of its interference with the cholesterol biosynthetic pathway. This biological activity is due to a specific inhibition of HMG-CoA synthase, which, remarkably, occurs without the inhibition of acetoacetyl thiolase or HMG-CoA reductase, enzymes utilized in steps just preceding and following the action of HMG-CoA synthase.[3] Only recently have the relative and absolute configurations of 1233A been established.[4] Two previous syntheses,[5] which appeared since the initiation of this work, utilized convergent strategies wherein chiral units were prepared by separate means and subsequently joined. Striving to develop tactics which refrained from the repeated use of resolutions or chiral auxilliaries or reagents, we pursued a philosophically different approach, one which would utilize an initial stereogenic center to guide the formation of the remaining ones.[6] Inherent in such a plan would be a solution to the problem posed by the 1,6 relationship of the remote stereogenic centers. We now describe, herein, a new synthesis of 1233A (1) which addresses the remote diastereoselection issue and provides an improved method for the preparation of the diene portion of the molecule.

As outlined in Scheme I, generation of the stereogenic centers would be attended to in the early part of the synthesis, with the lone methyl-bearing methine carbon serving as the key stereodirecting center. One tactic to amplify the asymmetric influence of that center would be to incorporate it into a ring such as in 3 and rely on a chirality transfer operation (i.e. 5 → 4) to provide a new stereogenic center on the acyclic portion of the substrate. From there, well-established methods for 1,2-asymmetric induction could be employed for the creation of the third center. The possibility for such a transformation emerged during the course of a pravastatin synthesis where an allylic ether related to 5 (i.e. *ent*-5, with R = H) was found to undergo a [2,3] rearrangement with high diastereoselectivity.[7] In this instance a suitable latent CH_2OH group for R in 5 would be required.

An abundant supply of allylic alcohol 7 was available from (*R*)-pulegone (6) via the same three-step protocol outlined for the enantiomeric series (Scheme II).[8] O-Alkylation of 7 with the previously unknown allylic halide 8 (readily produced from the reaction of methallyl dichloride and *tert*-butyldimethylsilanol anion[9]) generated ether 9 in 71% yield. On treatment with *n*-butyllithium,

(1) Aldridge, D. C.; Giles, D.; Turner, W. B. *J. Chem. Soc. D* **1970**, 639. Aldridge, D. C.; Giles, D.; Turner, W. B. *J. Chem. Soc. C* **1971**, 3888.

(2) The other β-lactone containing natural products include the following. Lipstatin: Weibel, E. K.; Hadvary, P.; Hochuli, E.; Kupfer, E.; Lengsfeld, H. *J. Antibiot.* **1987**, *40*, 1081. Hochuli, E.; Kupfer, E.; Maurer, R.; Meister, W.; Mercadal, Y.; Schmidt, K. *J. Antibiot.* **1987**, *40*, 1086. Barbier, P.; Schneider, F. *Helv. Chim. Acta* **1987**, *70*, 196. Valilactone: Kitahara, M.; Asano, M.; Naganawa, H.; Maeda, K.; Hamada, M.; Aoyagi, T.; Umezawa, H.; Iitaka, Y.; Nakamura, H. *J. Antibiot.* **1987**, *40*, 1647. Esterastin: Umezawa, H.; Aoyagi, T.; Hazato, T.; Uotani, K.; Kojima, F.; Hamada, M.; Takeuchi, T. *J. Antibiot.* **1978**, *31*, 639. Kondo, S.; Uotani, K.; Miyamoto, M.; Hazato, T.; Naganawa, H.; Aoyagi, T.; Umezawa, H. *J. Antibiot.* **1978**, *31*, 797. Ebelactones A and B: Umezawa, H.; Aoyagi, T.; Uotani, K.; Hamada, M.; Takeuchi, T.; Takahashi, S. *J. Antibiot.* **1980**, *33*, 1594. Uotani, K.; Naganawa, H.; Kondo, S.; Aoyagi, T.; Umezawa, H. *J. Antibiot.* **1982**, *35*, 1495. Oxazolomycin and curromycins A and B: Mori, T.; Takahashi, K.; Kashiwabara, M.; Uemura, D.; Katayama, C.; Iwadare, S.; Shizuri, Y.; Mitomo, R.; Nakano, F.; Matsuzaki, A. *Tetrahedron Lett.* **1985**, *26*, 1073. Ogura, M.; Nakayama, H.; Furihata, K.; Shimazu, A.; Seto, H.; Otake, N. *J. Antibiot.* **1985**, *38*, 669. Ogura, M.; Nakayama, H.; Furihata, K.; Shimazu, A.; Seto, H.; Otake, N. *Agric. Biol. Chem.* **1985**, *49*, 1909. Ikeda, Y.; Kondo, S.; Naganawa, H.; Hattori, S.; Hamada, M.; Takeuchi, T. *J. Antibiot.* **1991**, *44*, 453. And the only β-lactones isolated from plant sources, anisatin and neoanisatin: Yamada, K.; Takada, S.; Nakamura, S.; Hirata, Y. *Tetrahedron* **1968**, *24*, 199. Takada, S.; Nakamura, S.; Yamada, K.; Hirata, Y. *Tetrahedron Lett.* **1966**, 4739. Niwa, H.; Nisiwaki, M.; Tsukada, I.; Ishigaki, T.; Ito, S.; Wakamatsu, K.; Mori, T.; Ikagawa, M.; Yamada, K. *J. Am. Chem. Soc.* **1990**, *112*, 9001.

(3) Omura, S.; Tomoda, H.; Kumagai, H.; Greenspan, M. D.; Yodkovitz, J. B.; Chen, J. S.; Alberts, A. W.; Martin, I.; Mochales, S.; Monaghan, R. L.; Chabala, J. C.; Schwartz, R. E.; Patchett, A. A. *J. Antibiot.* **1987**, *40*, 1356. Tomoda, H.; Kumagai, H.; Tanaka, H.; Omura, S. *Biochim. Biophys. Acta* **1987**, *922*, 351. Greenspan, M. D.; Yudkovitz, J. B.; Lo, C. L.; Chen, J. S.; Alberts, A. W.; Hunt, V. M.; Chang, M. N.; Yang, S. S.; Thompson, K. L.; Chiang, Y. P.; Chabala, J. C.; Monaghan, R. L.; Schwartz, R. L. *Proc. Natl. Acad. Sci. U.S.A.* **1987**, *84*, 7488. Tomoda, H.; Kumagai, H.; Takahashi, Y.; Tanaka, Y.; Iwai, Y.; Omura, S. *J. Antibiot.* **1988**, *41*, 247. Mayer, R. J.; Louis-Flamberg, P.; Elliot, J. D.; Fisher, M.; Leber, J. *Biochem. Biophys. Res. Commun.* **1990**, *169*, 610.

(4) Chiang, Y. P.; Chang, M. N.; Yang, S. S.; Chabala, J. C.; Heck, J. V. *J. Org. Chem.* **1988**, *53*, 4599.

(5) Chiang, Y. P.; Yang, S. S.; Heck, J. V.; Chabala, J. C.; Chang, M. N. *J. Org. Chem.* **1989**, *54*, 5708. Mori, K.; Takahashi, Y. *Liebigs Ann. Chem.* **1991**, 1057.

(6) We have successfully applied such a strategy to the synthesis of other natural products. See, for example: Wovkulich, P. M.; Baggiolini, E. G.; Hennessy, B. M.; Uskoković, M. R.; Mayer, E.; Norman, A. W. *J. Org. Chem.* **1983**, *48*, 4433 (calcitriol lactone). Wovkulich, P. M.; Barcelos, F.; Batcho, A. D.; Sereno, J. F.; Baggiolini, E. G.; Hennessy, B. M.; Uskoković, M. R. *Tetrahedron* **1984**, *40*, 2283 (1α,25*S*,25-trihydroxycholecalciferol). Wovkulich, P. M.; Tang, P. C.; Chadha, N. K.; Batcho, A. D.; Barrish, J. C.; Uskoković, M. R. *J. Am. Chem. Soc.* **1989**, *111*, 2596 (mevinolin). Chadha, N. K.; Batcho, A. D.; Tang, P. C.; Courtney, L. F.; Cook, C. M.; Wovkulich, P. M.; Uskoković, M. R. *J. Org. Chem.* **1991**, *56*, 4714 (tetrahydrolipstatin). Daniewski, A. R.; Wovkulich, P. M., Uskoković, M. R. *J. Org. Chem.* **1992**, *57*, 7133.

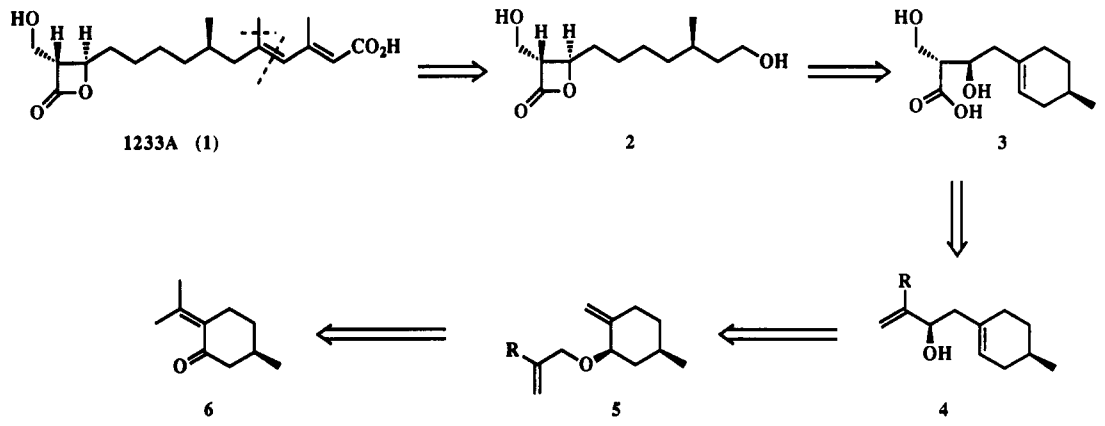
(7) Barrish, J. C.; Wovkulich, P. M.; Tang, P. C.; Batcho, A. D.; Uskoković, M. R. *Tetrahedron Lett.* **1990**, *31*, 2235.

(8) Wovkulich, P. M.; Tang, P. C.; Chadha, N. K.; Batcho, A. D.; Barrish, J. C.; Uskoković, M. R. *J. Am. Chem. Soc.* **1989**, *111*, 2596.

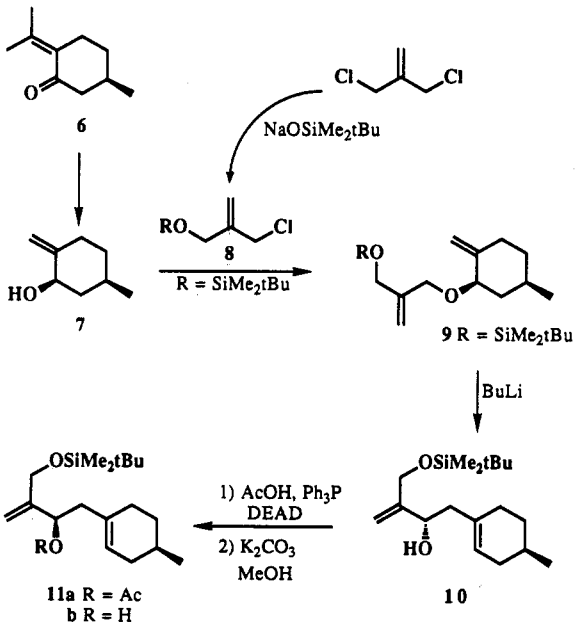
(9) Other bifunctional isobutylene derivatives have been described which could conceivably be used to produce 8: for example ($AcOCH_2C(CH_2Br)=CH_2$) Magnusson, G.; Lindqvist, F. *J. Chem. Soc., Chem. Commun.* **1990**, 1080. ($HOCH_2C(CH_2Br)=CH_2$) Nishizawa, M.; Adachi, K.; Hayashi, Y. *J. Chem. Soc., Chem. Commun.* **1984**, 1637. ($AcOCH_2C(CH_2Cl)=CH_2$ and $HOCH_2C(CH_2Cl)=CH_2$) Chalova, O. B.; Chistoedova, G. P.; Kiladze, T. K.; Germash, E. V.; Kantor, E. A.; Rakhmankulov, D. L. *Zh. Prikl. Khim. (Leningrad)* **1988**, *61*, 934; Chem. Abstr. **1988**, *110* (5), 38603b.

0022-3263/93/1958-0832$04.00/0

Scheme I



Scheme II



bis-allylic ether **9** underwent a smooth [2,3] rearrangement to form **10** as a single diastereomer in 68% yield.[10] This was a most gratifying result, not only for the high diastereoselection, but also for the apparent regioselectivity of the deprotonation preceding the rearrangement (i.e. CH_2OCH vs CH_2OSi). Inversion of the allylic alcohol to the required diastereomer **11b** was accomplished by a two-step Mitsunobu process (68%).[11]

From consideration of steric interactions in the transition state for the [2,3] rearrangement, it was anticipated that the desired diastereomer **11b** could be produced directly if one were to start with the epimer of allylic ether **9**,[12] thereby eliminating the need for an inversion step. An alternate synthesis of the required (*trans*-1*S*,3*R*)-3-methyl-6-methylene-1-cyclohexanol was therefore undertaken. Asymmetric hydrogenation of diketo ester **12**[13] in the presence of a catalytic amount of the {RuCl(C_6H_6)-[(S)BiNAP]}$^+Cl^-$ complex[14] produced ketol ester **13** in 81% yield (97% ee crude, 99% ee after crystallization, Scheme III). Silylation of alcohol **13**, Wittig methylenation to **14b**, and ester reduction with DiBAL gave alcohol **15** in 73% overall yield. Hydrogenation of **15** in the presence of Rh($Ph_3P)_3Cl$ produced an 80:20 mixture of saturated alcohols **16** and **17**, respectively. Aryl selenide mediated elimination[15] of the primary alcohol group in **16** followed by acidic desilylation produced the (*trans*-1*S*,3*R*)-3-methyl-6-methylene-1-cyclohexanol (**18b**), which was identical by NMR and rotation to material obtained by Mitsunobu inversion of alcohol **7**. When viewed in terms of the number of steps taken from a catalytic asymmetric reaction to produce the initial stereogenic center, this seven-step procedure compares favorably with the (*R*)-pulegone → **7** → **18b** route, since (*R*)-pulegone may be obtained from *N*,*N*-diethylgeranylamine via a four-step process which begins with the catalytic isomerization to (*R*)-*N*,*N*-diethylcitronellalenamine.[16] Such considerations are particularly relevant for planning future ventures such as labeling studies and synthesis of the enantiomeric series.

O-Alkylation of **18b** with allylic chloride **8**, using the same conditions as described for the epimeric series, gave ether **19** in 60% yield (Scheme IV). Unlike the clean rearrangement observed for **9**, the [2,3] rearrangement of **19** to form **11b** was accompanied by the formation of a number of unidentified byproducts. Although the yield of **11b** is presently only in the 40% range, it is formed as a single diastereomer.[17] Initial observations suggest that the difference in reactivity between **9** and **19** may reside in a lower regioselectivity at the deprotonation step with

(10) The other diastereomer, **11b**, which is inseparable from **10** under the purification conditions used, was not observed by ^{13}C NMR at a S/N = 50:1.

(11) Mitsunobu, O. *Synthesis* **1981**, 1. Under the typical inversion conditions, dehydration to the corresponding triene was a significant side reaction. This could be suppressed by conducting the reaction in the presence of pyridine.

(12) The stereochemical outcome of the reaction **9** → **10** may be rationalized in terms of steric effects and is similar to the result for *ent*-**5** (R = H). See, for example: Barrish, J. C.; Wovkulich, P. M.; Tang, P. C.; Batcho, A. D.; Uskoković, M. R. *Tetrahedron Lett.* **1990**, *31*, 2235. For theoretical calculations of [2,3] rearrangements, see: Houk, K. N.; Marshall, J. A. *J. Org. Chem.* **1990**, *55*, 1421 and references therein.

(13) Yates, P.; Bichan, D. J. *Can. J. Chem.* **1975**, *53*, 2045.

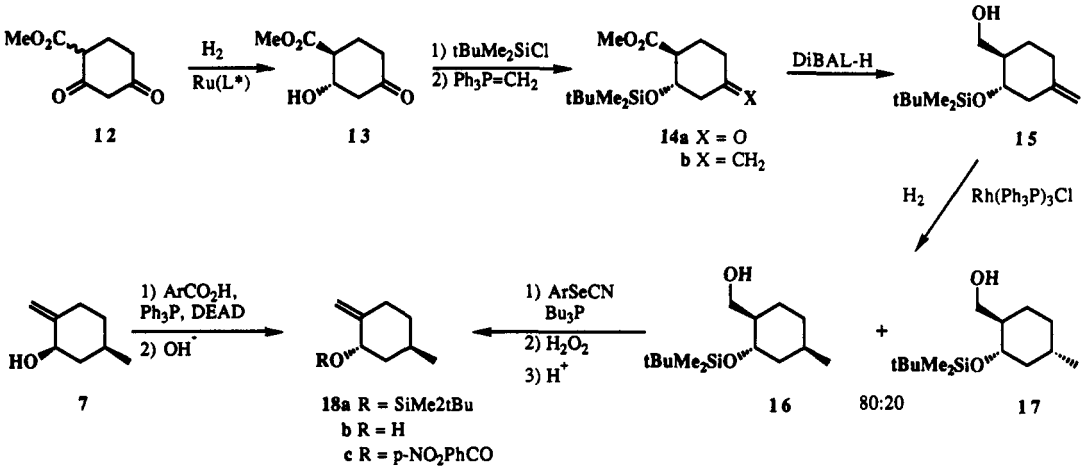
(14) Noyori, R.; Ikeda, T.; Ohkuma, T.; Widhalm, M.; Kitamura, M.; Takaya, H.; Akutagawa, S.; Sayo, N.; Saito, T.; Taketomi, T.; Kumobayashi, H. *J. Am. Chem. Soc.* **1989**, *111*, 9134. Ohta, T.; Takaya, H.; Noyori, R. *J. Org. Chem.* **1988**, *27*, 566. Mashima, K.; Kusano, K.; Ohta, T.; Noyori, R.; Takaya, H. *J. Chem. Soc. Chem. Commun.* **1989**, 1208. Kitamura, M.; Ohkuma, T.; Tokunaga, M.; Noyori, R. *Tetrahedron Asymmetry* **1990**, *1*, 1.

(15) Grieco, P. A.; Gilman, S.; Nishizawa, M. *J. Org. Chem.* **1976**, *41*, 1485.

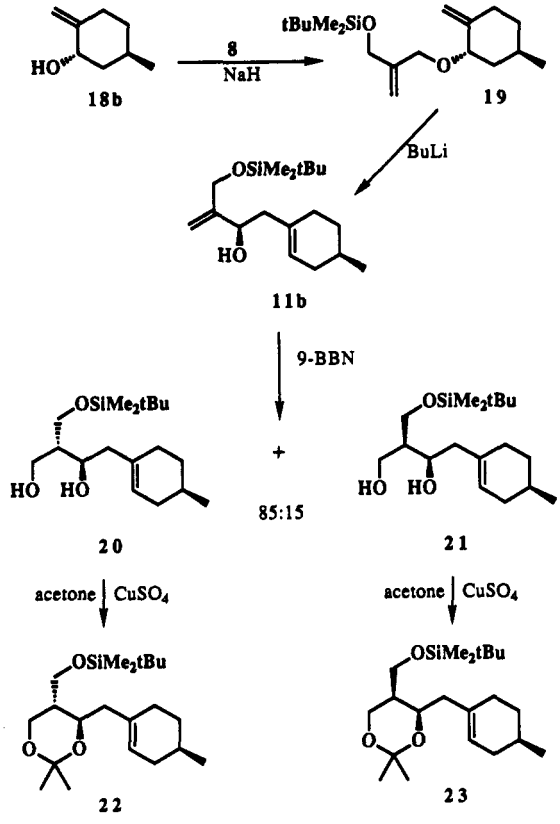
(16) Tani, K.; Yamagata, T.; Akutagawa, S.; Kumobayashi, H.; Taketomi, T.; Takaya, H.; Miyashita, A.; Noyori, R.; Otsuka, S. *J. Am. Chem. Soc.* **1984**, *106*, 5208 and references therein. Corey, E. J.; Ensley, H. E.; Suggs, J. W. *J. Org. Chem.* **1976**, *41*, 380.

(17) None of the diastereomer was observed by ^{13}C NMR at a S/N = 50:1.

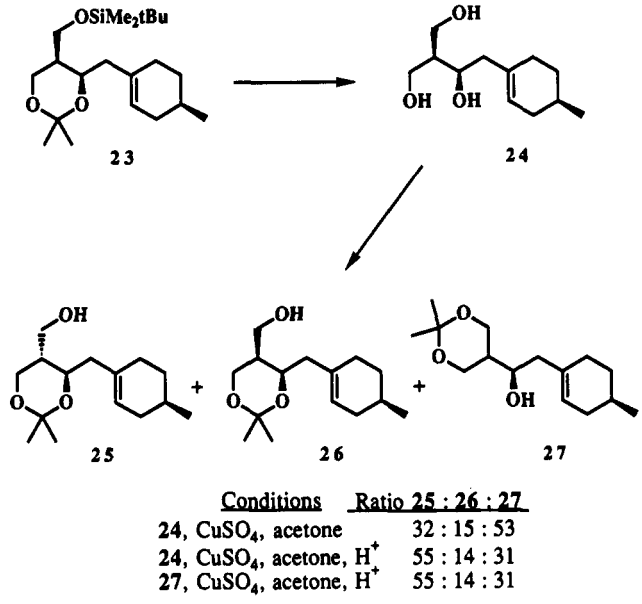
Scheme III



Scheme IV



Scheme V



Conditions	Ratio 25 : 26 : 27
24, $CuSO_4$, acetone	32 : 15 : 53
24, $CuSO_4$, acetone, H^+	55 : 14 : 31
27, $CuSO_4$, acetone, H^+	55 : 14 : 31

19, although further investigation is underway to establish this effect.[18]

Having addressed the formation of the 1,6-disposed stereogenic centers, attention was directed next to the third stereogenic center. Hydroboration of **11b** with 9-BBN produced diols **20** and **21** as an 85:15 mixture, respectively, which were converted directly to their respective acetonides **22** and **23** on treatment with acetone and anhydrous $CuSO_4$. Before continuing with the synthesis, however, it was of interest to explore the interrelationships of **20** and **21**.

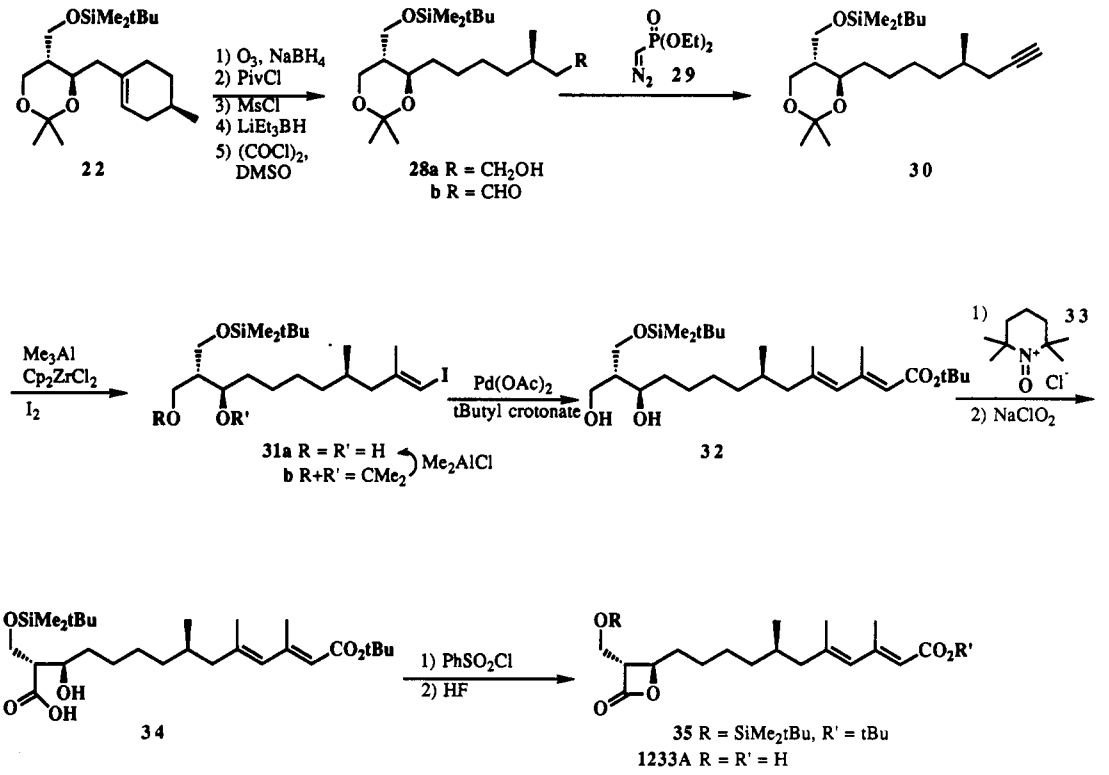
Since the CH_2O moieties of diol **21** (or **20**) are diastereotopically related, any operation which shifts the position of the *tert*-butyldimethylsilyl group from one CH_2O group to another will accomplish an interconversion between **20** and **21**. It seemed likely that the ability of acetonides to isomerize under mild conditions might provide the means for such a transformation. To examine this possibility, acetonide **23** was first deprotected under acidic conditions (Dowex 50X8, MeOH) to form triol **24** (Scheme V). Under nonequilibrating conditions (acetone, $CuSO_4$), diol **24** formed acetonides **25**, **26**, and **27** as a 32:15:53 mixture.[19] Under thermodynamic conditions (TsOH, acetone, $CuSO_4$) however, the desired acetonide **25** was the predominant isomer (**25**/**26**/**27** = 55:14:31, starting from either triol **24** or acetonide **27**). In this manner acetonide **25** was conveniently isolated from the mixture and converted to **22** by silylation, while **26** and **27** were reisomerized to the equilibrium mixture and reprocessed further. The production of acetonide **27** also provided the opportunity to confirm the assignment of the absolute configuration at the secondary alcohol position in **11b** by inspection of the NMR data for the (*R*)- and (*S*)-MTPA esters of **27**.[20]

Having served its purpose for the introduction of the new stereogenic centers, the cyclohexene ring could now

(18) Under some conditions, byproducts, which appear to be enol ethers derived from **11b** are observed. However, it has not yet been rigorously established whether their formation is due a deprotonation preceding or following the [2,3] rearrangement.

(19) The order of elution on a 4.6- × 250-mm μPorasil column (hexane/EtOAc, 4:1) is **27**, **25**, **26**. $CDCl_3$ used for NMR was passed through basic alumina prior to use to remove traces of acid.

Scheme VI



be severed. A four-step procedure, consisting of ozonolysis with reductive workup, monopivalylation of the primary alcohol, mesylation of the secondary alcohols, and reduction with lithium triethylborohydride, allowed the conversion of **22** to alcohol **28a** in 71% overall yield (Scheme VI). At this point, the stereospecific formation of the diene section of 1233A had to be addressed. Unlike the ubiquitous trisubstituted olefin pattern found in retinoids, the *tetra*substituted diene portion of 1233A represents a surprisingly uncommon substitution pattern. Unfortunately the presence of that additional substituent thwarted the usual strategies employed for the introduction of a diene (i.e. using derivatives of $XCH_2C(CH_3)=CHCO_2R$) giving low yields and/or serious olefin mixtures. Model studies suggested that the most promising approach would entail a Negishi type carboalumination[21] followed by a Heck type palladium-mediated coupling reaction.[22] For this approach, alcohol **28a** was oxidized to aldehyde **28b** under Swern conditions and transformed to the homologated acetylene **30** with diethyl (diazomethyl)phosphonate (**29**) using Gilbert's conditions,[23] in 70% overall yield. On exposure to trimethylaluminum and zirconocene dichloride followed by treatment with iodine, acetonide–acetylene **30** formed *diol* iodide **31a** stereospecifically in 63% yield and was accompanied by **31b** (23%), the product bearing an intact acetonide group. Selective ketal cleavage in the presence of the *tert*-butyldimethylsilyl group was realized by the use of Me_2AlCl, which gave **31a** in 86% yield from **31b**. These conditions for ketal cleavage, which are not unlike the reaction conditions above, succeeded where literature methods failed, a likely consequence of the proximity of the hydroxyl groups.[24,25] Application of the original Heck conditions (**31a**, *tert*-butyl crotonate, organic base, Pd catalyst, with or without phosphine ligands, ca. 100 °C) produced the desired *E,E* olefin **31** along with a substantial amount of α,β double bond isomerization to the *Z,E* olefin. This problem was alleviated significantly through the use of the phase-transfer conditions developed by Jeffery[26] (Aliquat 336, K_2CO_3, DMF, $Pd(OAc)_2$, *tert*-butyl crotonate, rt, 8–12 days) but was not eliminated. In other Pd-catalyzed reactions, the presence of silver salts has been reported to enhance reaction rates and reduce bond isomerizations.[27] When such conditions were applied to the present problem, the degree of bond isomerization was reduced to less than a few percent, but the reaction was still very slow at room temperature. Subsequent investigation, however, uncovered a remarkable solvent effect. Whereas under the typical conditions with silver carbonate using DMF or THF as solvent, the reaction required 5–8 days, the same reaction run in methylene chloride took place in about 1 h at room temperature

(20) The (*R*)- and (*S*)-methoxy(trifluoromethyl)phenylacetic acid esters were prepared under standard conditions. Dale, J. A.; Mosher, H. S. *J. Am. Chem. Soc.* **1973**, *95*, 512.

(21) Negishi, E.; Van Horn, D. E.; King, A. O.; Okukado, N. *Synthesis* **1979**, 501. Rand, C. L.; Van Horn, D. E.; Moore, M. W.; Negishi, E. *J. Org. Chem.* **1981**, *46*, 4096. Negishi, E.; Van Horn, D. E.; Toshida, T. *J. Am. Chem. Soc.* **1985**, *107*, 6639. Negishi, E. *Pure Appl. Chem.* **1981**, *53*, 2333.

(22) Kim, J. I.; Patel, B. A.; Heck, R. F. *J. Org. Chem.* **1981**, *46*, 1067. Heck, R. F. *Pure Appl. Chem.* **1981**, *53*, 2323.

(23) Gilbert, J. C.; Weerasooriya, U. *J. Org. Chem.* **1979**, *44*, 4997. Colvin, E. W.; Hamill, B. J. *J. Chem. Soc., Perkin Trans. 1* **1977**, 869.

(24) See, for example: Otera, J.; Nozaki, H. *Tetrahedron Lett.* **1986**, *27*, 5743. Me_2AlCl has been used previously for the cleavage of THP ethers, although MEM and MOM ethers produced ethyl ethers. Ogawa, Y.; Shibasaki, M. *Tetrahedron Lett.* **1984**, *25*, 663. See also: Takano, S.; Ohkawa, T.; Ogasawara, K. *Tetrahedron Lett.* **1988**, *29*, 1823.

(25) The ketal equilibration process (i.e. **24** → **25**, Scheme V) in conjunction with this selective acetonide cleavage process provides an opportunity for alternate synthetic approaches. The corresponding triol, generated from **31b** during the study of procedures to selectively remove the acetonide group, was converted to **31a** by application of the ketal equilibration process described above (acetone, $CuSO_4$, TsOH, similar ketal ratio as observed for **24**), silylation, and acetonide cleavage.

(26) Jeffery, T. *J. Chem. Soc., Chem. Commun.* **1984**, 1287. Jeffery, T. *Tetrahedron Lett.* **1985**, *26*, 2667.

(27) Karabelas, K.; Westerlund, C.; Hallberg, A. *J. Org. Chem.* **1985**, *50*, 3896. Abelman, M. M.; Oh, T.; Overman, L. E. *J. Org. Chem.* **1987**, *52*, 4133.

forming diene **32** in 65% yield from **31a**, accompanied by only a few percent of the *ZE* isomer. It is anticipated that this solvent effect should find general application in the Heck type coupling for hindered systems, especially where recourse to organo-tin reagents had previously been made in order to achieve reasonable reaction rates. Oxidation of diol **32** with the *N*-oxammonium chloride **33**[28] gave an unstable hydroxyaldehyde which was oxidized directly with sodium chlorite to the corresponding hydroxy acid **34** in 79% yield. Closure of the hydroxy acid to the β-lactone **35** ($PhSO_2Cl$, pyridine, 70%) followed by cleavage of both the silyl ether and *tert*-butyl ester under carefully controlled conditions (aqueous HF, THF, 78%)[29] gave 1233A (**1**), the spectral properties of which were in accord with the natural material.

Experimental Section

General Procedure. Unless otherwise noted all reactions were run under an argon atmosphere. THF was distilled from sodium benzophenone; CH_2Cl_2 was stored over 4-Å molecular sieves. Chromatography was performed on 230–400-mesh silica gel 60. When noted, chromatography conducted on reverse-phase silica gel was done with Partisil 40, ODS-3. Extracted reaction mixtures were dried over anhydrous Na_2SO_4 and filtered, and solvent was removed under reduced pressure. Rotations were carried out at 25 °C. NMR spectra were obtained in $CDCl_3$ at 200 or 400 MHz for ^1H and 50 MHz for ^{13}C, significant chemical shifts are reported in ppm (δ units) downfield from TMS, and *J* values are given in hertz.

***cis*-(1*R*,3*R*)-3-Methyl-6-methylenecyclohexanol (7).** Prepared from the commercially abundant (*R*)-pulegone (**6**) following the same procedure outlined in our previous work using the enantiomeric series for the synthesis of mevinolin[30] (i.e. (1) $NaBH_4$, $CeCl_3$; (2) O_3 then Me_2S; (3) $Ph_3P{=}CH_2$ from $Ph_3P^+CH_3Br^-$, KOtBu, THF): $[\alpha]^{25}_D = +19.5°$ (*c* = 0.946, $CHCl_3$); ^1H NMR δ 0.91 (d, *J* = 6.3 Hz, 3 H), 2.34 (ddd, *J* = 2.1, 3.6, 13.6 Hz, 1 H), 4.01 (dm, *J* = 11.5 Hz, 1 H), 4.73 (bd, *J* = 1.8 Hz, 1 H), 4.89 (bd, *J* = 1.4 Hz, 1 H); ^{13}C NMR (C) 151.6; (CH) 72.0, 31.8; (CH_2) 103.7, 45.7, 36.1, 33.9; (CH_3) 21.8. Anal. Calcd for $C_8H_{14}O$: C, 76.14; H, 11.18. Found: C, 75.75; H, 11.29.

(1,1-Dimethylethyl)dimethyl[[2-(chloromethyl)-2-propenyl]oxy]silane (8). To an ice-cooled mixture of NaH (18.00 g (0.45 mol) of a 60% oil dispersion, prewashed under argon with pentane) and 300 mL of THF was added 66.400 g (0.50 mol) of *tert*-butyldimethylsilanol in 200 mL of THF (15 min).[31] The mixture was stirred at room temperature for 30 min, and then 125.00 g (1.00 mol) of freshly distilled 3-chloro-2-(chloromethyl)-1-propene was added in one portion followed by 9.2345 g (0.025 mol) of tetrabutylammonium iodide. The mixture was heated at 55–60 °C for 23 h, cooled, taken up in 1.5 L of hexane, washed successively with water, aqueous $NaHSO_3/Na_2SO_3$, and brine, and dried over anhydrous Na_2SO_4. Distillation at 20 mmHg through a Vigreux column over a range of 98–105 °C gave 77.89 g (53%) of the product **8**, which contained ca. 25% (by weight) of 1,3-bis(1,1-dimethylethyl)-1,1,3,3-tetramethyldisiloxane [i.e. $(tBuMe_2Si)_2O$]. Although the $(tBuMe_2Si)_2O$ could be removed by careful fractionation, its presence in the next step was not detrimental and consequently the material was used as such: ^1H NMR δ 0.08 (s, 6 H), 0.91 (s, 9 H), 4.09 (s, 2 H), 4.23 (s, 2 H), 5.21 (m, 2 H); ^{13}C NMR (C) 144.5, 18.3; (CH_2) 114.3, 63.3, 44.9; (CH_3) 25.8 (3), −5.5 (2).

***cis*-(2*R*,4*R*)-2-[[2-[[[(1,1-Dimethylethyl)dimethylsilyl]oxy]methyl]-1-prop-2-enyl]oxy]-4-methyl-1-methylenecyclohexane (9).** To a mixture of 110 mL of THF and NaH (6.00 g (0.150 mol) of a 60% oil dispersion prewashed with pentane) was added 15.120 g (0.120 mol) of **7** in 10 mL of THF (10 min). The mixture was heated at 62 °C for 1.5 h and cooled, and then 44.100 g (0.150 mol) of the chloro olefin (**8**) above (containing ca. 25% of $(tBuMe_2Si)_2O$) was added, followed by a 5-mL THF rinse and 3.6938 g (0.01 mol) of tetrabutylammonium iodide. The mixture was heated at 62 °C for 20 h, quenched by the addition of water, taken up in ether, and washed successively with water and brine. The concentrated product was filtered through silica gel, eluting with hexane/EtOAc (95:5), and distilled (0.15 mmHg, 120–126 °C) to give 26.2471 g (71%) of **9**: $[\alpha]^{25}_D = +20.8$ (*c* = 1.004, $CHCl_3$); ^1H NMR δ 0.06 (s, 6 H), 0.90 (s, 9 H), 0.93 (d, *J* = 6.6 Hz, 3 H), 2.33 (ddd, *J* = 2.3, 3.6, 13.4 Hz, 1 H), 3.67 (dd, *J* = 4.8, 11.8 Hz, 1 H), 4.02 (d, *J* = 12.8 Hz, 1 H), 4.11 (d, *J* = 12.8 Hz, 1 H), 4.18 (bs, 2 H), 4.73 (nm, 1 H), 4.92 (bs, 1 H), 5.10 (bs, 1 H), 5.16 (bs, 1 H); ^{13}C NMR (C) 148.7, 145.9, 18.3; (CH) 78.7, 31.7; (CH_2) 111.0, 104.5, 69.7, 63.9, 42.8, 36.3, 33.9; (CH_3) 25.9 (3), 21.8, −5.5 (2). Anal. Calcd for $C_{18}H_{34}O_2Si$: C, 69.62; H, 11.04. Found: C, 69.93; H, 11.18.

[*S*-(*R)]-4-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-1-(4-methylcyclohexen-1-yl)-3-methylene-2-butanol (10).** To a solution of 1.3576 g (4.38 mmol) of ether **9** in 33 mL of THF at −78 °C was added 3.8 mL of 2.3 M butyllithium in hexane solution. After 30 min the mixture was set in a bath at −20 °C and stirred for 45 min. The reaction was quenched by the addition of brine and extracted with Et_2O. The crude product was chromatographed, eluting with hexane/EtOAc (94:6), to give 0.9176 g (68%) of alcohol **10**: $[\alpha]^{25}_D = +28.5°$ (*c* = 0.994, $CHCl_3$); ^1H NMR δ 0.08 (s, 6 H), 0.91 (s, 9 H), 0.93 (d, *J* = 6.2 Hz, 3 H), 4.18 (d, *J* = 13.5 Hz, 1 H), 4.30 (d, *J* = 13.5 Hz, 1 H), 5.09 (s, 2 H), 5.48 (bs, 1 H); ^{13}C NMR (C) 149.6, 134.2, 18.3; (CH) 124.4, 70.9, 28.2; (CH_2) 110.4, 64.1, 44.8, 33.8, 31.1, 28.1; (CH_3) 25.8 (3), 21.6, −5.5 (2). Anal. Calcd for $C_{18}H_{34}O_2Si$: C, 69.62; H, 11.04. Found: C, 69.80; H, 11.17.

[*R*-(*R)]-1-[2-(Acetyloxy)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3-methylene-1-butyl]-4-methylcyclohexene (11a).** To a mixture of 0.9166 g (2.957 mmol) of alcohol **10**, 18 mL of THF, 1.5493 g (5.91 mmol) Ph_3P, 0.239 mL (2.957 mmol) of pyridine and 0.847 mL (14.78 mmol) of acetic acid at −45 °C was added 1.0299 g (5.913 mmol) of diethyl azodicarboxylate in 1 mL of THF. The mixture was stirred for 5 h during which time the bath was allowed to warm to 0 °C. The mixture was taken up in hexane/EtOAc (1:1) and washed successively with water, saturated $NaHCO_3$, and brine. The crude product was chromatographed, eluting with hexane/EtOAc (98:2), to give 0.7995 g (77%) of **11a**: $[\alpha]^{25}_D = +72.0°$ (*c* = 0.972, $CHCl_3$); ^1H NMR δ 0.06 (s, 6 H), 0.90 (s, 9 H), 0.90 (d, *J* = 5.5 Hz, 3 H), 2.01 (s, 3 H), 4.11 (d, *J* = 15.1 Hz, 1 H), 4.20 (d, *J* = 15.1 Hz, 1 H), 5.09 (s, 1 H), 5.18 (d, *J* = 1.4 Hz, 1 H), 5.39 (t, *J* = 6.6 Hz, 1 H); ^{13}C NMR (C) 170.0, 147.2, 133.1, 18.3; (CH) 124.1, 72.5, 28.0; (CH_2) 110.8, 63.2, 42.4, 33.9, 31.0, 28.3; (CH_3) 25.8 (3), 21.6, 21.0, −5.5 (2). Anal. Calcd for $C_{20}H_{36}O_3Si$: C, 68.13; H, 10.29. Found: C, 67.98; H, 10.38. The triene elimination product [(*R*)-4-methyl-1-(3-methylene-1-buteneyl)cyclohexene] was also isolated: yield, 0.1017 g (12%); ^1H NMR δ 0.08 (s, 6 H), 0.91 (s, 9 H), 0.96 (d, *J* = 6.6 Hz, 3 H), 4.32 (s, 2 H), 5.05 (bs, 1 H), 5.22 (bs, 1 H), 5.73 (nm, 1 H), 6.12 (d, *J* = 16.0 Hz, 1 H), 6.24 (d, *J* = 16.0 Hz, 1 H)].

[*R*-(*R)]-4-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-1-(4-methylcyclohexen-1-yl)-3-methylene-2-butanol (11b).** Treatment of **11a** (4.758 g) with MeOH (160 mL)/K_2CO_3 (18.6 g) gave (2.5 h) the alcohol **11b** (3.848 g, 91%). The analytical sample was distilled bulb to bulb (oven = 70 °C, 0.07 mmHg): $[\alpha]^{25}_D = +70.9°$ (*c* = 0.454, $CHCl_3$); ^1H NMR δ 0.07 (s, 6 H), 0.90 (s, 9 H), 0.93 (d, *J* = 5.5 Hz, 3 H), 4.19 (d, *J* = 13.6 Hz, 1 H), 4.29 (d, *J* = 13.6 Hz, 1 H), 5.09 (s, 2 H), 5.49 (bs, 1 H); ^{13}C NMR (C) 149.7, 134.0, 18.3; (CH) 124.5, 70.7, 28.2; (CH_2) 110.3, 64.1, 45.3, 33.9, 31.0, 28.2; (CH_3) 25.8 (3), 21.6, −5.5 (2). Anal. Calcd for $C_{18}H_{34}O_2Si$: C, 69.62; H, 11.04. Found: C, 69.95; H, 11.14.

[1*S*,2*S*]-2-Hydroxy-4-oxocyclohexanecarboxylic Acid Methyl Ester (13). A solution of 7.08 g (0.0416 mol) of **12**,[13] 0.200

(28) The use of stoichiometric **33** gave better results, in general, than catalytic use of TEMPO. See: Siedlecka, R.; Skarzewski, J.; Mlochowski, J. *Tetrahedron Lett.* **1990**, *31*, 2177. Inokuchi, T.; Matsumoto, S.; Nishiyama, T.; Torii, T. *J. Org. Chem.* **1990**, *55*, 462.

(29) The desilylation is very rapid under these conditions, followed by a much slower cleavage of the *tert*-butyl ester. Although reaction times could be made shorter with more concentrated HF solutions, the formation of a byproduct generated from an apparent hydration of the diene resulted in decreased yields of the final product.

(30) Routinely carried out on 0.49-mol scale, cf. ref 8.

(31) Formation of the disiloxane $(tBuMe_2Si)_2O$ predominates when NaH is used in excess, relative to *tert*-butyldimethylsilanol.

g (0.229 mmol) of the {RuCl(C_6H_6)[(*S*)-BiNAP]}$^+Cl^-$ complex,[32] and 100 mL of CH_2Cl_2 (passed through basic alumina) was stirred mechanically at 55 °C under 1500 psi of H_2 for 22 h. Volatiles were removed under reduced pressure and the residue chromatographed, eluting with hexane/ethyl acetate/(EtOAc) (1:1) to give 5.805 g (81%) of **13**. The product was 97% ee by ^1H NMR in the presence of Eu(hfc)$_3$. An analytical sample was crystallized from diethyl ether to give **13** as colorless crystals (99% ee by NMR): mp 37.0–38.0 °C; $[\alpha]^{25}_D$ = +41.5° (*c* = 1.11, EtOH); ^1H NMR δ 1.69–1.80 (m, 1 H), 2.28–2.47 (m, 4 H), 2.72 (ddd, *J* = 3.9, 9.2, 13.2 Hz, 1 H), 2.81 (ddd, *J* = 2.0, 5.0, 14.5 Hz, 1 H), 3.78 (s, 3 H), 4.16–4.23 (m, 1 H); IR ($CHCl_3$) 1722 cm^{-1}. Anal. Calcd for $C_8H_{12}O_4$: C, 55.81; H, 7.03. Found: C, 55.68; H, 7.25.

***trans*-(1*S*)-2-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-4-oxocyclohexanecarboxylic Acid Methyl Ester (14a).** To a stirred solution of 5.20 g (0.0302 mol) of **13** in 25 mL of DMF at room temperature was added 3.29 g (0.0483 mol) of imidazole and 6.83 g (0.0453 mol) of *tert*-butyldimethylchlorosilane. After the mixture was stirred for 3 h, H_2O was added, and the mixture was extracted with Et_2O (2 × 30 mL). Chromatography of the crude product, eluting with hexane/EtOAc (6:1), gave 8.30 g (96%) of **14a** as a colorless oil: $[\alpha]^{25}_D$ = +52.9° (*c* = 0.92, EtOH); ^1H NMR δ 0.04 (s, 3 H), 0.06 (s, 3 H), 0.85 (s, 9 H), 1.87–1.98 (m, 1 H), 2.13–2.47 (m, 4 H), 2.67 (ddd, *J* = 1.5, 4.3, 14.4 Hz, 1 H), 2.71–2.77 (m, 1 H), 3.73 (s, 3 H), 4.31 (dt, *J* = 4.3, 7.8 Hz, 1 H); IR ($CHCl_3$) 1730, 1722 cm^{-1}. Anal. Calcd for $C_{14}H_{26}O_4Si$: C, 58.70; H, 9.15. Found: C, 58.47; H, 9.44.

***trans*-(1*S*)-2-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-4-methylenecyclohexanecarboxylic Acid Methyl Ester (14b).** A solution of 8.22 g (0.0287 mol) of **14a** in 20 mL of THF was added dropwise (5 min) to methylene triphenylphosphorane (prepared from 20.505 g (0.0574 mol) of methyltriphenylphosphonium bromide, 5.797 g (0.05166 mol) of potassium *tert*-butoxide, and 150 mL of THF). After the mixture was stirred for 20 min at room temperature, 200 mL of H_2O was added and the mixture was extracted with Et_2O. Chromatography of the crude product, eluting with hexane/EtOAc (15:1), gave 7.18 g (88%) of **14b**: $[\alpha]^{25}_D$ = +36.9° (*c* = 1.21, EtOH); ^1H NMR δ 0.02 (s, 3 H), 0.07 (s, 3 H), 0.85 (s, 9 H), 1.45–1.56 (m, 1 H), 1.89–2.53 (m, 6 H), 3.67 (s, 3 H), 3.82 (dt, *J* = 3.9, 10.1 Hz, 1 H), 4.70 (s, 1 H), 4.72 (s, 1 H); IR ($CHCl_3$) 1731 cm^{-1}. Anal. Calcd for $C_{15}H_{28}O_3Si$: C, 63.33; H, 9.92. Found: C, 63.05; H, 9.92.

***trans*-(1*R*)-2-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-4-methylenecyclohexanemethanol (15).** To a stirred solution of 7.05 g (0.0248 mol) of **14b** in 200 mL of dry CH_2Cl_2 at −50 °C was added 99 mL of a 1.0 M CH_2Cl_2 solution of diisobutylaluminum hydride (DIBAL-H) over 10 min. After addition, the mixture was allowed to reach 0 °C (15 min) and 20 mL of H_2O was added cautiously with vigorous stirring. After 10 min the mixture was transferred to a separatory funnel, 200 mL of H_2O added, and the mixture extracted with Et_2O. Chromatography of the crude product, eluting with hexane/EtOAc (10:1), afforded 5.46 g (86%) of **15**: $[\alpha]^{25}_D$ = +38.5° (*c* = 0.86, EtOH); ^1H NMR δ 0.12 (s, 6 H), 0.91 (s, 9 H), 1.03 (dq, *J* = 4.2, 12.8 Hz, 1 H), 1.67 (m, 1 H), 1.76 (m, 1 H), 2.00 (dt, *J* = 3.6, 12.8 Hz, 1 H), 2.10 (t, *J* = 12.8 Hz, 1 H), 2.26 (dm, *J* = 12.8 Hz, 1 H), 2.50 (m, 2 H), 3.48 (dt, *J* = 4.6, 10.7 Hz, 1 H), 3.55 (m, 1 H), 3.69 (dd, *J* = 6.8, 10.7 Hz, 1 H), 4.66 (d, *J* = 1.8 Hz, 1 H), 4.70 (d, *J* = 1.8 Hz, 1 H). Anal. Calcd for $C_{14}H_{28}O_2Si$: C, 65.57; H, 11.01. Found: C, 65.46; H, 11.19.

(1*R*-(1α,2β,4α))- and (1*R*-(1α,2β,4β))-2-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-4-methylcyclohexanemethanols (16 and 17). A solution of 5.36 g (0.0209 mol) of **15**, 0.967 g (0.001 045 mol) of tris(triphenylphosphine)rhodium chloride, and CH_2Cl_2 was placed in a Paar hydrogenation apparatus. After shaking for 16 h at room temperature under 70 psi of H_2, the mixture was concentrated under reduced pressure and chromatographed, eluting with hexane/EtOAc (10:1) to give 4.22 g (78%) of **16** (colorless oil) [$[\alpha]^{25}_D$ = +26.8° (*c* = 0.99, EtOH); ^1H NMR δ 0.08 (s, 3 H), 0.10 (s, 3 H), 0.90 (s, 9 H), 0.94 (d, *J* = 7.2 Hz, 3 H), 1.22–1.35 (m, 2 H), 1.45–1.63 (m, 5 H), 2.04 (m, 1 H), 3.53 (dd, *J* = 4.3, 10.7 Hz, 1 H), 3.65 (dd, *J* = 7.3, 10.7 Hz, 1 H), 3.79 (dt, *J* = 4.3, 8.6 Hz, 1 H); ^{13}C NMR (C) 18.0; (CH) 71.6, 46.8, 27.7; (CH_2) 66.6, 40.8, 30.4, 22.6; (CH_3) 25.8 (3), 19.5, −4.0, −4.8. Anal. Calcd for $C_{14}H_{30}O_2Si$: C, 65.06; H, 11.70. Found: C, 65.17; H, 11.64] and 1.08 g (20%) of **17** (colorless oil): $[\alpha]^{25}_D$ = +72.5° (*c* = 0.99, EtOH); ^1H NMR δ 0.10 (s, 3 H), 0.11 (s, 3 H), 0.90 (s, 9 H), 0.92 (d, *J* = 6.6 Hz, 3 H), 1.35–1.54 (m, 2 H), 1.60–1.69 (m, 2 H), 1.74 (dm, *J* = 11.6 Hz, 1 H), 3.49 (dd, *J* = 4.1, 10.7 Hz, 1 H), 3.52 (dd, *J* = 4.1, 10.5 Hz, 1 H), 3.67 (dd, *J* = 7.0, 10.7 Hz, 1 H); ^{13}C NMR: (C) 17.9; (CH) 76.5, 46.9, 31.4; (CH_2) 67.4, 44.7, 34.0, 27.4; (CH_3) 25.8 (3), 22.2, −3.7, −4.7. Anal. Calcd for $C_{14}H_{30}O_2Si$: C, 65.06; H, 11.70. Found: C, 65.23; H, 11.96.

[1*S*-*trans*]-(1,1-Dimethylethyl)dimethyl[(5-methyl-2-methylenecyclohexyl)oxy]silane (18a). Tributylphosphine (7.203 mL, 0.0289 mol) was added dropwise over 10 min to a stirred solution of 4.15 g (0.01606 mol) of **16**, 5.470 g (0.0241 mol) of *o*-nitrophenyl selenocyanate, and 80 mL of THF at 0 °C. After the mixture was stirred at room temperature for 1 h, 36.4 mL (0.36 mol) of 30% aqueous H_2O_2 was added. The mixture was stirred at room temperature for 1 h and then at 55 °C for 1 h. The cooled mixture was diluted with 100 mL of H_2O and extracted with hexane. Chromatography of the crude material, eluting with hexane/EtOAc (40:1), gave 3.40 g of an oil, which on bulb-to-bulb distillation (oven temperature = 100 °C, 2 mmHg) gave 3.05 g (79%) of **18a** as a colorless oil: $[\alpha]^{25}_D$ = +65.1° (*c* = 1.21, EtOH); ^1H NMR δ 0.01 (s, 3 H), 0.05 (s, 3 H), 0.88 (s, 9 H), 0.88 (d, *J* = 6.7 Hz, 3 H), 1.01 (dq, *J* = 4.1, 10.9 Hz, 1 H), 1.19 (ddd, *J* = 2.9, 11.0, 13.3 Hz, 1 H), 1.68–1.80 (m, 2 H), 1.97–2.11 (m, 2 H), 2.40 (dt, *J* = 4.7, 13.5 Hz, 1 H), 4.21 (nm, 1 H), 4.65 (t, *J* = 1.9 Hz, 1 H), 4.71 (s, 1 H). Anal. Calcd for $C_{14}H_{28}OSi$: C, 69.93; H, 11.74. Found: C, 69.80; H, 11.95.

***trans*-(1*S*)-5-Methyl-2-methylenecyclohexanol (18b). A. By Deprotection of 18a.** A solution of 3.00 g (0.01248 mol) of **18a** and 0.475 g (0.00249 mol) of *p*-toluenesulfonic acid monohydrate in 25 mL of MeOH was stirred at room temperature for 6 h. A 25-mL portion of saturated aqueous $NaHCO_3$ was added, and the mixture was extracted with Et_2O (2 × 20 mL). The residue was fractionally distilled (10-cm Vigreux column) to give 1.15 g (73%) of **18b**. An analytical sample was distilled bulb-to-bulb (oven = 45–50 °C, 25 mmHg): $[\alpha]^{25}_D$ = +89.3° (*c* = 1.02, $CHCl_3$); ^1H NMR δ 0.88 (d, *J* = 6.7 Hz, 3 H), 1.05 (m, 1 H), 1.25 (ddd, *J* = 3.5, 11.2, 13.9 Hz, 1 H), 2.11 (ddd, *J* = 4.3, 13.2, 13.2 Hz, 1 H), 2.40 (dddd, *J* = 1.5, 4.3, 13.2, 13.2 Hz, 1 H), 4.26 (t, *J* = 3.5 Hz, 1 H), 4.72 (t, *J* = 1.5 Hz, 1 H), 4.80 (bs, 1 H); ^{13}C NMR (C) 150.4; (CH) 72.2, 26.1; (CH_2) 109.0, 42.5, 35.7, 29.8; (CH_3) 21.5. Anal. Calcd for $C_8H_{14}O$: C, 76.14; H, 11.18. Found: C, 76.16; H, 11.29.

B. By Mitsunobu Inversion of 7. Mitsunobu inversion of (1*R*,3*R*)-3-methyl-6-methylene-1-cyclohexanol (12.619 g of **7**, 250 mL of THF, 39.3 g of Ph_3P, 26.12 g of diethyl azodicarboxylate, 25.07 g of *p*-nitrobenzoic acid, −15 °C, 2 h) gave a ca. 70:30 mixture of desired inversion product **18c** and the S_N2' product (i.e. the primary *p*-nitrobenzoate). Basic hydrolysis (30 mL of THF, 108 mL of MeOH, 3.24 mL of H_2O, 5.18 g NaOH, room temperature, 30 min) of the mixture gave, after chromatography and distillation, 3.466 g (29%, the yield was not optimized) of the alcohol **18b**: bp 89–91 °C at 38 mmHg; $[\alpha]^{25}_D$ = +88.9° (*c* = 0.85, $CHCl_3$).

***trans*-(2*S*,4*R*)-2-[[2-[[[(1,1-Dimethylethyl)dimethylsilyl]oxy]methyl]-1-prop-2-enyl]oxy]-4-methyl-1-methylenecyclohexane (19).** **19** was prepared by the same procedure used with the epimeric series (60% yield). Distilled bulb-to-bulb (oven temperature = 85 °C, 0.2 mmHg). **19**: $[\alpha]^{25}_D$ = +27.9° (*c* = 0.977, $CHCl_3$); ^1H NMR δ 0.06 (s, 6 H), 0.86 (d, *J* = 6.5 Hz, 3 H), 0.89 (s, 9 H), 1.03 (m, 1 H), 1.75 (m, 1 H), 1.95 (dm, *J* = 11.1 Hz, 1 H), 2.08 (dt, *J* = 13.1, 3.6 Hz, 1 H), 2.59 (tm, *J* = 12.7 Hz, 1 H), 3.75 (d, *J* = 12.8 Hz, 1 H), 3.80 (nm, 1 H), 3.91 (d, *J* = 12.8 Hz, 1 H), 4.11 (d, *J* = 15.0 Hz, 1 H), 4.18 (d, *J* = 15.0 Hz, 1 H), 4.76 (t, *J* = 1.5 Hz, 1 H), 4.85 (t, *J* = 2.0 Hz, 1 H), 5.06 (nm, 1 H), 5.16 (bs, 1 H); ^{13}C NMR (C) 147.5, 145.8, 18.3; (CH) 78.4, 26.5; (CH_2) 111.0, 110.9, 67.7, 63.9, 41.7, 36.1, 30.3; (CH_3) 25.9 (3), 21.9, −5.4 (2). Anal. Calcd for $C_{18}H_{34}O_2Si$: C, 69.62; H, 11.04. Found: C, 69.82; H, 11.28.

[2*S*,3*R*,(4*R)]-2-[[[(1,1-Dimethylethyl)dimethylsilyl]oxy]methyl]-4-(4-methyl-1-cyclohexen-1-yl)-1,3-butanediol (20) and [4*R*(4α,4(*R**),5β)]-5-[[[(1,1-Dimethylethyl)dimethylsilyl]oxy]methyl]-2,2-dimethyl-4-[(4-methyl-1-cyclohexen-1-yl)methyl]-1,3-dioxane (22).** To 2.680 g (8.629 mmol) of olefin **11b** in 25 mL of THF at 0 °C was added 77.7 mL of 0.5 M

(32) Mashima, K. K.; Ohta, T.; Noyori, R.; Takaya, H. *J. Chem. Soc., Chem. Commun.* **1989**, 1208.

9-borabicyclononane in THF solution. The mixture was stirred for 5 h during which time the temperature was allowed to rise to room temperature. The mixture was quenched by the addition of 16 mL of water followed by addition of 33 g of $NaHCO_3$ and 39 mL of 30% H_2O_2. After 45 min the mixture was taken up in EtOAc and washed successively with saturated $NaHCO_3$ and brine. In a separate experiment the major diol (**20**) was purified by chromatography: $[\alpha]^{25}_D = +45.3°$ ($c = 0.177$, $CHCl_3$); ^1H NMR δ 0.08 (s, 6 H), 0.90 (s, 9 H), 0.95 (d, $J = 6.3$ Hz, 3 H), 3.77–3.98 (m, 5 H), 5.52 (bs, 1 H); ^{13}C NMR (C) 134.0, 18.2; (CH) 125.0, 69.3, 46.9, 28.4; (CH_2) 63.6, 62.5, 44.2, 33.9, 31.0, 28.4; (CH_3) 25.8 (3), 21.7, –5.5 (2). Anal. Calcd for $C_{18}H_{36}O_3Si$: C, 65.80; H, 11.04. Found: C, 65.94; H, 11.05.

The crude diol mixture from above was stirred with 65 mL of acetone and 20.657 g of anhydrous $CuSO_4$ powder overnight, filtered, and concentrated under reduced pressure. Chromatography (hexane/EtOAc, 97:3) gave 1.892 g (60%) of the more polar acetonide **22** [$[\alpha]^{25}_D = +59.0°$ ($c = 0.256$, $CHCl_3$); ^1H NMR δ 0.01 (s, 6 H), 0.87 (s, 9 H), 0.91 (d, $J = 5.7$ Hz, 3 H), 1.34 (s, 3 H), 1.39 (s, 3 H), 2.24 (bd, $J = 15.4$ Hz, 1 H), 3.51 (d, $J = 5.2$ Hz, 2 H), 3.79 (d, $J = 7.8$ Hz, 2 H), 3.88 (ddd, $J = 3.2, 7.2, 10.3$ Hz, 1 H), 5.40 (bs, 1 H); ^{13}C NMR (C) 134.5, 98.0, 18.1; (CH) 122.5, 68.8, 41.4, 28.3; (CH_2) 61.9, 61.3, 41.9, 34.0, 31.3, 29.1; (CH_3) 29.1, 25.7 (3), 21.8, 19.6, –5.6 (2). Anal. Calcd for $C_{21}H_{40}O_3Si$: C, 68.42; H, 10.94. Found: C, 68.52; H, 11.03] and 0.335 g (11%) of the less polar acetonide **23**: ^1H NMR δ 0.047 (s, 3 H), 0.05 (s, 3 H), 0.88 (s, 9 H), 0.91 (d, $J = 6.3$ Hz, 3 H), 1.35 (s, 3 H), 1.43 (s, 3 H), 3.72–4.07 (m, 4 H), 4.16 (ddd, $J = 2.9, 6.9, 6.9$ Hz, 1 H), 5.42 (bs, 1 H); ^{13}C NMR (C) 133.7, 98.6, 18.3; (CH) 122.8, 69.4, 39.3, 28.2; (CH_2) 61.2, 58.0, 40.4, 33.8, 31.1, 28.5; (CH_3) 29.7, 25.9 (3), 21.6, 18.9, –5.4 (2).

[4*R*-(4α,4(*R),5β)]-5-(Hydroxymethyl)-2,2-dimethyl-4-[(4-methyl-1-cyclohexen-1-yl)methyl]-1,3-dioxane (25).** The major acetonide **22** was desilylated (99%) using 1.5 equiv of Bu_4NF in THF (45 min at room temperature): ^1H NMR δ 0.91 (d, $J =$ 5.6 Hz, 3 H), 1.35 (s, 3 H), 1.40 (s, 3 H), 2.25 (bd, $J = 15$ Hz, 1 H), 3.56 (m, 2 H), 3.84 (m, 3 H), 5.43 (bs, 1 H).

[4*R*-(4α,4(*R),5α)]-5-(Hydroxymethyl)-2,2-dimethyl-4-[(4-methyl-1-cyclohexen-1-yl)methyl]-1,3-dioxane (26).** The minor acetonide **23** was desilylated (95%) using 1.5 equiv of Bu_4NF in THF (4 h at room temperature): ^1H NMR δ 0.92 (d, $J = 5.8$ Hz, 3 H), 1.37 (s, 3 H), 1.46 (s, 3 H), 3.84 (dd, $J = 4.4, 10.4$ Hz, 1 H), 4.03 (m, 4 H), 4.20 (dt, $J = 2.6, 7.0$ Hz, 1 H), 5.43 (bs, 1 H).

[3*R*-(4*R)]-2-(Hydroxymethyl)-4-(4-methylcyclohexenyl)-butane-1,3-diol (24).** Removal of the protecting groups of **23** to generate **24** (66%, plus monosilylated material) was carried out using acidic ion-exchange resin Dowex 50X8 in methanol at room temperature (4.5 h): ^1H NMR δ 0.91 (d, $J = 6.1$ Hz, 3 H), 3.68–4.03 (m, 5 H), 5.49 (bs, 1 H); ^{13}C NMR (C) 133.7; (CH) 125.0, 69.6, 46.0, 28.2; (CH_2) 63.2, 61.4, 43.9, 33.9, 30.9, 28.2; (CH_3) 21.6.

Kinetic Acetonide Formation from Triol 24. Triol **24** (0.0317 g, 0.148 mmol) was stirred with 0.1182 g (0.741 mmol) of anhydrous $CuSO_4$ and 0.8 mL of acetone for 1 h and then analyzed by HPLC [hexane/EtOAc (4:1)]. The mixture of **25**:**26**:**27** was 32.5:14.7:52.8.

Thermodynamic Acetonide Formation from Triol 24. Triol **24** (0.0303 g, 0.142 mmol), 0.1129 g (0.708 mmol) of anhydrous $CuSO_4$, 0.8 mL of acetone, and 0.0027 g (0.014 mmol) toluenesulfonic acid monohydrate were stirred at room temperature for 17 h. The mixture was taken up in EtOAc and washed successively with water, saturated $NaHCO_3$, and brine. Analysis by HPLC [hexane/EtOAc (4:1)] showed a 55:14.1:30.9 mixture of **25**:**26**:**27**.

Equilibration of **27** under the same conditions as the thermodynamic acetonide formation above produced essentially the same **25**:**26**:**27** ratio. **27**: ^1H NMR δ 0.92 (d, $J = 5.9$ Hz, 3 H), 1.39 (s, 3 H), 1.40 (s, 3 H), 3.65 (m, 1 H), 3.78 (m, 2 H), 3.96 (m, 2 H), 5.49 (bs, 1 H); ^{13}C NMR (C) 133.5, 97.8; (CH) 125.5, 67.1, 39.5, 28.3; (CH_2) 61.7, 61.0; 43.8, 33.9, 30.9, 28.3; (CH_3) 25.9, 21.9, 21.6.

(*R*)-MTPA ester of 27: ^1H NMR δ 0.91 (d, $J = 6.3$ Hz, 3 H), 1.34 (s, 3 H), 1.38 (s, 3 H), 2.21 (dd, $J = 5.1, 14.2$ Hz, 1 H), 2.31 (dd, $J = 8.3, 14.2$ Hz, 1 H), 3.47 (d, $J = 0.8$ Hz, 3 H), 3.70 (dd, $J = 9.2, 11.8$ Hz, 1 H), 3.78 (dd, $J = 8.9, 11.8$ Hz, 1 H), 3.82 (ddd, $J = 1.1, 5.0, 11.8$ Hz, 1 H), 3.88 (ddd, $J = 1.1, 4.9, 11.8$ Hz, 1 H), 5.22 (dt, $J = 8.3, 5.1$ Hz, 1 H), 5.36 (bs, 1 H).

(*S*)-MTPA ester of 27: ^1H NMR δ 0.93 (d, $J = 6.3$ Hz, 3 H), 1.26 (s, 3 H), 1.35 (s, 3 H), 2.26 (dd, $J = 5.3, 14.5$ Hz, 1 H), 2.36 (dd, $J = 8.8, 14.5$ Hz, 1 H), 3.55 (d, $J = 1.1$ Hz, 3 H), 3.60 (dd, $J = 9.0, 11.7$ Hz, 1 H), 3.71 (dd, $J = 9.0, 11.7$ Hz, 1 H), 3.74 (ddd, $J = 1.3, 4.7, 11.7$ Hz, 1 H), 3.82 (ddd, $J = 1.3, 4.9, 11.7$ Hz, 1 H), 5.26 (dt, $J = 8.8, 5.3$ Hz, 1 H), 5.45 (bs, 1 H).

Cyclohexene Ring Cleavage Sequence: [4*R*-(4α,4(*R),5β)]-5-[[[(1,1-Dimethylethyl)dimethylsilyl]oxy]methyl]-β-methyl-2,2-dimethyl-1,3-dioxane-4-heptanol (28a).** Ozone was passed through a solution of 3.48 g (9.2 mmol) of the acetonide **22** in 100 mL of CH_2Cl_2/MeOH (1:1) at –78 °C until a blue color persisted. The mixture was flushed with argon to remove excess ozone, 2.0 g (52.9 mmol) of $NaBH_4$ was added, and the mixture was stirred overnight, during which time the temperature was allowed to warm to room temperature. After aqueous workup the crude material was filtered through silica gel, eluting with hexane/EtOAc (40:60), to give 3.48 g (93%) of diols as a 1:1 mixture. The mixture of diols was stirred at 0 °C with 8 mL of pyridine, 0.105 g (0.86 mmol) of 4-(*N*,*N*-dimethylamino)pyridine, and 1.1 mL (9.0 mmol) of pivaloyl chloride. After 2 h, the mixture was taken up in Et_2O and washed successively with water, saturated $CuSO_4$, and brine. Chromatography of the crude monopivaloyl ester, eluting with hexane/EtOAc (3:1), gave 3.80 g (91%) of the product. To 4.0260 g (8.238 mmol) of the monopivaloyl ester, 3.23 mL (18.54 mmol) of diisopropylethylamine, and 22 mL of CH_2Cl_2 at 0 °C was added 0.80 mL (10.33 mmol) of methanesulfonyl chloride. After 30 min water was added, and the mixture was taken up in EtOAc and washed with brine. The crude product was filtered through silica gel, eluting with hexane/EtOAc (2:1). The mesylate in 5 mL of THF was added to 49.4 mL of 1.0 M $LiEt_3BH$ in THF solution. The mixture was refluxed for 70 min, cooled, and quenched by the addition of water. After aqueous workup, chromatography of the crude material, eluting with hexane/EtOAc (2:1), gave 3.167 g of product which contained ca. 10% of an olefin mixture resulting from mesylate elimination. While it was possible to remove this byproduct chromatographically, on a large scale it was more convenient to simply hydrogenate the double bond without separation. Stirring an EtOAc solution of the reaction mixture under an atmosphere of hydrogen in the presence of 10% Pd on carbon and solid $NaHCO_3$ saturated the byproduct double bond to give 2.673 g (84%) of the product **28a**: $[\alpha]^{25}_D = +32.3°$ ($c =$ 0.177, $CHCl_3$); ^1H NMR δ 0.01 (s, 6 H), 0.86 (d, $J = 5.7$ Hz, 3 H), 0.86 (s, 9 H), 1.35 (s, 3 H), 1.39 (s, 3 H), 3.49–3.79 (m, 7 H); ^{13}C NMR (C) 98.0, 18.1; (CH) 70.1, 41.6, 29.4; (CH_2) 62.0, 61.3, 61.1, 40.0, 37.0, 33.4, 26.2, 25.2; (CH_3) 29.1, 25.7 (3), 19.6, 19.5, –5.6, –5.7. Anal. Calcd for $C_{21}H_{44}O_4Si$: C, 64.90; H, 11.41. Found: C, 64.76; H, 11.44.

[4*R*-(4α,4(*R),5β)]-5-[[[(1,1-Dimethylethyl)dimethylsilyl]oxy]methyl]-2,2-dimethyl-4-(5-methyl-7-octynyl)-1,3-dioxane (30).** Swern oxidation[33] of 2.673 g (6.889 mmol) of the alcohol **28a** gave, after filtration through silica gel eluting with hexane/EtOAc (1:1), the corresponding aldehyde **28b**, which was used directly in the next step [^1H NMR δ 0.03 (s, 6 H), 0.85 (s, 9 H), 0.92 (d, $J = 6.0$ Hz, 3 H), 1.37 (s, 3 H), 1.41 (s, 3 H), 3.45–3.85 (m, 5 H), 9.74 (t, $J = 2.5$ Hz, 1 H)]. To a mixture of 1.119 g (9.99 mmol) of potassium *tert*-butoxide and 30 mL of THF at –78 °C, was added 1.837 g (10.320 mmol) of (diazomethyl)phosphonic acid, diethyl ester (**29**) in 15 mL of THF. After 10 min the aldehyde in 10 mL of THF was added, and the mixture was stirred overnight, during which time the bath was allowed to warm to room temperature. After aqueous workup, chromatography of the crude material, eluting with hexane/EtOAc (70:30), gave 1.836 (70% for the two steps) of acetylene **30**: ^1H NMR δ 0.01 (s, 6 H), 0.87 (s, 9 H), 0.95 (d, $J = 6.1$ Hz, 3 H), 1.37 (s, 3 H), 1.39 (s, 3 H), 1.93 (t, $J = 2.7$ Hz, 1 H), 3.45–3.85 (m, 5 H); ^{13}C NMR (C) 98.0, 83.3, 18.1; (CH) 70.1, 68.9, 41.6, 32.2; (CH_2) 62.0, 61.3, 35.9, 33.4, 26.9, 25.7, 25.1; (CH_3) 29.1, 25.7 (3), 19.6, 19.2, –5.6, –5.7. Anal. Calcd for $C_{22}H_{42}O_3Si$: C, 69.05; H, 11.06. Found: C, 68.98; H, 10.95.

[1*E*,4*R*,9*R*,10*R*]-10-[[[(1,1-Dimethylethyl)dimethylsilyl]oxy]methyl]-2,4-dimethyl-1-iodoundec-1-ene-9,11-diol (31a). To 0.5816 g (1.989 mmol) of zirconocene dichloride was added

(33) Mancuso, A. J.; Swern, D. *Synthesis* **1981**, 165.

3.96 mL of 2.51 M trimethylaluminum in dichloroethane. After 15 min 0.7601 g (1.989 mmol) of acetylene **30** in 1 mL of dichloroethane was added. The mixture was stirred for 23.5 h and then cooled to −25 °C, and 2.2724 g (8.954 mmol) of iodine in 2 mL of THF was added. The mixture was stirred for 140 min, during which time the bath was allowed to warm to −10 °C. The mixture was cooled to −20 °C and quenched by the addition of 3 mL of THF/H_2O (1:1). After aqueous workup and chromatography [hexane/EtOAc (60:40)], 0.6390 g (66%) of **31a** was obtained [^{1}H NMR δ 0.08 (s, 6 H), 0.81 (d, J = 7.6 Hz, 3 H), 0.90 (s, 9 H), 1.80 (s, 3 H), 1.99 (dd, J = 7.7, 13.8 Hz, 1 H), 2.18 (dd, J = 6.9, 13.8 Hz, 1 H), 3.8–3.95 (m, 5 H), 5.82 (s, 1 H); ^{13}C NMR (C) 147.2, 18.1; (CH) 75.2, 72.8, 46.6, 30.9; (CH_2) 64.2, 61.8, 47.6, 36.6, 35.1, 27.0, 26.2; (CH_3) 25.9 (3), 23.8, 19.3, −5.5 (2)] along with 0.2403 g (23%) of acetonide **31b**: ^{1}H NMR δ 0.02 (s, 6 H), 0.79 (d, J = 6.6 Hz, 3 H), 0.88 (s, 9 H), 1.36 (s, 3 H), 1.40 (s, 3 H), 1.78 (s, 3 H), 1.98 (dd, J = 8.5, 13.0 Hz, 1 H), 2.19 (dd, J = 6.0, 13.0 Hz, 1 H), 3.45–3.85 (m, 5 H), 5.80 (s, 1 H); ^{13}C NMR (C) 147.3, 98.2, 18.2; (CH) 75.2, 70.2, 41.7, 30.9; (CH_2) 62.2, 61.4, 47.7, 36.7, 33.5, 27.0, 25.2; (CH_3) 29.2, 25.9 (3), 23.8, 19.7, 19.3, −5.5 (2).

Selective Removal of Acetonide in the Presence of the *tert*-Butyldimethylsilyl Ether (31b → 31a). To 0.2378 g (0.4539 mmol) of acetonide **31b** and 5 mL of CH_2Cl_2 at −20 °C was added 1.82 mL of 1.0 M dimethylaluminum chloride in hexane solution. After 2 h (−20 to −15 °C) the mixture was quenched by the addition of THF/H_2O (1:1). After aqueous workup and chromatography (hexane/EtOAc, 70:30), 0.1884 g (86%) of diol **31a** was isolated.

[2*E*,4*E*,7*R*,12*R*,13*R*]-13-[[[(1,1-Dimethylethyl)dimethylsilyl]oxy]methyl]-12,14-dihydroxy-3,5,7-trimethyltetradeca-2,4-dienoic Acid 1,1-Dimethylethyl Ester (32). To a vigorously stirred mixture of 2.9934 g (6.186 mmol) of iodide **31a**, 35 mL of *tert*-butyl crotonate, 1.8763 g (6.804 mmol) of Ag_2CO_3, 1.89 mL (13.61 mmol) of triethylamine, 7.26 mL (0.124 mol) of ethanol,[34] and 25 mL of CH_2Cl_2 was added 0.1388 g (0.619 mmol) of $Pd(OAc)_2$ dissolved in 23 mL of CH_2Cl_2. After being stirred in the dark for 75 min, the mixture was diluted with hexane and filtered through a pad of silica gel, eluting with hexane/EtOAc (70:30). Volatiles were removed under reduced pressure, and the residue was chromatographed [hexane/EtOAc (65:35)] to give 2.5777 g (84%)[35] of **32**: $[\alpha]^{25}_D$ = +0.88° (c = 1.023, $CHCl_3$). ^{1}H NMR δ 0.07 (s, 6 H), 0.81 (d, J = 6.2 Hz, 3 H), 0.89 (s, 9 H), 1.47 (s, 9 H), 1.77 (s, 3 H), 2.06 (dd, J = 6.0, 13.2 Hz, 1 H), 2.18 (bs, 3 H), 2.43 (bs, OH), 2.74 (bs, OH), 3.87 (m, 5 H), 5.56 (bs, 1 H), 5.65 (s, 1 H); ^{13}C NMR (C) 166.7, 152.7, 140.5, 79.5, 18.1; (CH) 129.5, 119.3, 72.7, 46.5, 30.9; (CH_2) 64.1, 61.7, 48.9, 36.7, 35.1, 27.0, 26.1; (CH_3) 28.3 (3), 25.8 (3), 19.4, 19.3, 18.3, −5.6 (2); IR ($CHCl_3$) 1698 cm^{-1}. Anal. Calcd for $C_{28}H_{54}O_5Si$: C, 67.42; H, 10.91. Found: C, 67.29; H, 10.77.

[2*E*,4*E*,7*R*,12*R*,13*S*]-13-[[[(1,1-Dimethylethyl)dimethylsilyl]oxy]methyl]-12-hydroxy-3,5,7-trimethyltetradeca-2,4-dienedioic Acid 1,1-Dimethylethyl Ester (34). To 0.4227 g (0.848 mmol) of diol **31** in 28.5 mL of CH_2Cl_2 at −20 °C was added 0.2278 g (1.188 mmol) of 2,2,6,6-tetramethyl-1-oxopiperidinium chloride over 10 s. The mixture was stirred in the dark for 10 min and then for 2 h at −15 °C. A 1.15-mL (10.18-mmol) portion of 2-methylbutene was added, followed by the addition (20 s) of a freshly prepared solution of 0.7676 g (6.789 mmol) of 80% $NaClO_2$, 0.7846 g (5.68 mmol) of NaH_2PO_4·H_2O, and 25.4 mL of H_2O. The cooling bath was removed, and the mixture was taken up in EtOAc and washed successively with 0.05 M HCl and brine. The crude product was chromatographed on reverse-phase silica gel, eluting with CH_3CN/H_2O (83:17) to give 0.3427 g (79%) of hydroxy acid **34**: ^{1}H NMR δ 0.06 (s, 6 H), 0.80 (d, J = 6.4 Hz, 3 H), 0.87 (s, 9 H), 1.47 (s, 9 H), 1.76 (s, 3 H), 2.03 (m, 1 H), 2.16 (s, 3 H), 2.67 (bs, 1 H), 3.96 (m, 3 H), 5.55 (s, 1 H), 5.64 (s, 1 H); ^{13}C NMR (C) 176.8, 167.0, 152.7, 140.5, 79.8, 18.1; (CH) 129.5, 119.2, 70.4, 52.4, 30.7; (CH_2) 62.6, 49.0, 36.4, 35.0, 26.7, 25.8; (CH_3) 28.3 (3), 25.7 (3), 19.5, 19.4, 18.3, −5.7 (2); IR ($CHCl_3$) 1745, 1699 cm^{-1}. Anal. Calcd for $C_{28}H_{52}O_6Si$: C, 65.58; H, 10.22. Found: C, 65.44; H, 10.28.

[2*R*-[2α,(2*E*,4*E*,7*R),3β]]-11-[3-[[[(1,1-Dimethylethyl)dimethylsilyl]oxy]methyl]-4-oxo-2-oxetanyl]-3,5,7-trimethyl-2,4-undecadienoic Acid 1,1-Dimethylethyl Ester (35).** To 0.1290 g (0.252 mmol) of hydroxy acid **34** in 3 mL of pyridine at ca. 0 °C was added 0.1335 g (0.756 mmol) of benzenesulfonyl chloride in 0.25 mL of pyridine. The mixture was stirred for 18.5 h, during which time the bath temperature was allowed to rise to 10 °C. The reaction was quenched by the addition of brine. After aqueous workup and chromatography [hexane/EtOAc (95:5)] 0.0875 g (70%) of the product **35** was obtained: $[\alpha]^{25}_D$ = +11.6° (c = 0.56, $CHCl_3$); ^{1}H NMR δ 0.06 (s, 6 H), 0.81 (d, J = 6.5 Hz, 1 H), 0.88 (s, 9 H), 1.47 (s, 9 H), 1.77 (s, 3 H), 2.18 (s, 3 H), 3.32 (ddd, J = 3.3, 3.8, 4.9 Hz, 1 H), 3.81 (dd, J = 3.3, 11.1 Hz, 1 H), 3.96 (dd, J = 4.9, 11.1 Hz, 1 H), 4.52 (dt, J = 3.8, 6.6 Hz, 1 H), 5.56 (bs, 1 H), 5.65 (bs, 1 H); ^{13}C NMR (C) 169.5, 166.7, 152.6, 140.3, 79.5, 18.1; (CH) 129.6, 119.3, 74.8, 58.8, 30.9; (CH_2) 58.2, 48.9, 36.6, 33.9, 26.7, 25.2; (CH_3) 28.3 (3), 25.7 (3), 19.4, 19.3, 18.3, −5.6 (2); IR ($CHCl_3$) 1819, 1698 cm^{-1}. Anal. Calcd for $C_{28}H_{50}O_5Si$: C, 67.97; H, 10.19. Found: C, 67.59; H, 9.88.

1233A (1). A mixture of 0.3370 g (0.658 mmol) of silyl β-lactone **35**, 2.5 mL of 49% aqueous HF, and 4.0 mL of THF was stirred in a polyethylene vessel for 8.5 h. The mixture was taken up in CH_2Cl_2 and washed with brine. The product was chromatographed on reverse-phase silica gel eluting with CH_3CN/H_2O (1:1) to give 0.1655 g (78%) of 1233A (**1**) along with 0.0424 g (17%) of the *tert*-butyl ester of 1233A (i.e. **35**, R = H, R′ = *tert*-butyl). 1233A: $[\alpha]^{25}_D$ = +27.5° (c = 1.08, $CHCl_3$) [lit.[4] $[\alpha]^{25}_D$ = +28.6° (c = 0.62, $CHCl_3$)]; ^{1}H NMR δ 0.83 (d, J = 6.4 Hz, 3 H), 1.80 (s, 3 H), 2.08 (dd, J = 6.3, 12.8 Hz, 1 H), 2.23 (s, 3 H), 3.39 (q, J = 4.2 Hz, 1 H), 3.87 (dd, J = 4.0, 11.6 Hz, 1 H), 4.04 (dd, J = 5.0, 11.6 Hz, 1 H), 4.57 (ddd, J = 4.5, 6.2, 7.0 Hz, 1 H), 5.67 (s, 1 H), 5.71 (s, 1 H); ^{13}C NMR (C) 171.7, 169.8, 157.0, 142.1; (CH) 129.5, 116.6, 74.9, 58.6, 30.9; (CH_2) 58.0, 48.9, 36.5, 33.9, 26.6, 25.1; (CH_3) 19.9, 19.4, 18.5. The ^{1}H and ^{13}C NMR spectra are in accord with authentic material. Anal. Calcd for $C_{18}H_{28}O_5$: C, 66.64; H, 8.70. Found: C, 66.31; H, 8.72.

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(34) The presence of ethanol helped to suppress oxidation of the secondary alcohol to the corresponding hydroxy ketone.

(35) The NMR spectra for the olefins is quite distinct: the desired *E,E* isomer shows broad singlets (one proton each) at δ 5.56 and 5.66, while the *Z,E* olefin has the corresponding peaks at 5.56 and 6.34 ppm.