(CH_2), 34.3 (CH_2), 34.1 (CH_2), 33.9 (CH), 31.4 (CH_2), 27.0 (CH_2), 25.5 (CH_3), 25.4 (CH_3), 25.3 (CH_3), 21.5 (CH_2), 17.9 (CH_3), 17.8 (CH_3), 17.7 (CH_3), 17.2 (CH_3), 13.2 (CH_3), 10.8 (CH_3), 10.2 (CH_3); FABMS M^+ 787 ($C_{42}H_{68}O_{12}$ + Na); EIHRMS $M^+ - H_2O$ 746.4592 ($C_{42}H_{66}O_{11}$ ΔM -1.3 mmu); EILRMS 746, 728, 659, 582, 531, 436, 418, 385, 367, 349, 337, 301, 163, 147, 135, 121, 109.

Secoxestovanin A (2): colorless glass; ^1H NMR (see Table I); ^{13}C NMR (100 MHz, DMSO-d_6) δ 212.6 (C), 211.4 (C), 140.1 (C), 136.6 (C), 132.1 (C), 131.4 (C), 121.4 (CH), 121.4 (CH), 120.2 (CH), 117.3 (CH), 101.2 (CH), 99.1 (CH), 81.3 (CH), 76.7 (CH), 75.6 (CH), 74.3 (CH), 71.9 (CH), 70.8 (CH), 70.6 (CH), 70.0 (CH), 69.4 (CH), 68.9 (CH), 56.3 (C) 52.9 (CH), 46.8 (CH), 41.2 (CH_2), 38.4 (CH_2), 34.1 (CH_2), 31.8 (CH_2), 31.7 (CH_2), 25.9 (CH_3), 25.7 (CH_3), 25.6 (CH_3), 22.7 (CH_2), 17.8 (CH_3), 17.8 (2 × CH_3), 17.2 (CH_3), 16.4 (CH_3), 12.0 (CH_3), 10.6 (CH_3); FABMS M^+ 787 ($C_{42}H_{68}O_{12}$ + Na); EIHRMS $M^+ - H_2O$ 746.4579 ($C_{42}H_{66}O_{11}$ ΔM -2.6 mmu).

Hexaacetate 5. Xestovanin A (**1**) (20 mg) was added to acetic anhydride (1 mL) and pyridine (1 mL), and the mixture was stirred overnight at room temperature. The acetylation reagents were removed in vacuo to give a quantitative yield of the hexaacetate **5**: FTIR (film) 3384, 2965, 2936, 2876, 1752, 1710, 1440, 1371, 1244, 1224 cm^{-1}; ^1H NMR (see Table II); FABMS 1039 ($C_{54}H_{80}O_{18}$ + Na); EILRMS $M^+ - H_2O$ 998, 956, 938, 869, 503, 436, 417, 273.

Double Elimination Product 6. Xestovanin A (**1**) (40mg) was heated with stirring for 1 h at 50 °C with methanol (3 mL) and 0.05 M KOH (3 mL). The reaction mixture was cooled, diluted with 10 mL of water, neutralized with dilute HCl, and extracted with ether (3 × 25mL). The ether layers were combined, dried over sodium sulfate, and evaporated in vacuo. The resulting residue was purified by radial silica gel chromatography (3:2 hexane/ether) to give the double elimination product **6** (7 mg). **6**: FTIR (film) 3410, 2965, 2928, 2875, 1651, 1594, 1556, 1447, 1374 cm^{-1}; ^1H NMR (see Table III); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.4 (C), 142.7 (C), 139.5 (CH), 135.9 (CH), 134.7 (C), 134.0 (C), 132.7 (C), 131.0 (C), 130.9 (C), 124.4 (CH), 121.5 (CH), 120.5 (CH), 120.2 (CH), 76.8 (CH), 52.5 (C), 48.4 (CH), 36.1 (CH_2), 34.3 (CH_2), 31.3 (CH), 27.8 (CH_2), 27.0 (CH_2), 25.9 (CH_3), 25.8 (CH_3), 25.7 (CH_3), 21.6 (CH_2), 19.1 (CH_3), 18.1 (CH_3), 17.8 (CH_3), 14.0 (CH_3), 12.2 (CH_3); EIHRMS M^+ 436.3336 ($C_{30}H_{44}O_2$ ΔM -0.5 mmu).

Secoxestovanin A (**2**) (10 mg) was treated with aqueous potassium hydroxide as described above. The elimination product **6** formed from **2** in this reaction was identical by TLC and ^1H NMR comparison with that formed from xestovanin A (**1**) under the same conditions.

Identification of Fucose and Rhamnose.[13] The water soluble material from the elimination reaction of xestovanin A (**1**) described above was taken to dryness by lyophilization. Aqueous trifluoracetic acid (3 M, 10 mL) was added to the residue, and the resulting solution was heated at 90 °C for 2 h. Removal of the water and trifluoroacetic acid in vacuo gave a gum (3 mg for each reaction) that was reacted separately with (+)- and (-)-2-octanol (250 μL) and trifluroacetic acid (1 drop) at 100 °C overnight. Removal of the reagents in vacuo gave a mixture of 2-octylglycosides that were acetylated at room temperature with acetic anhydride and pyridine. Removal of the acetylation reagents under high vacuum gave a mixture of acetylated 2-octylglycosides. The mixture was dissolved in $CHCl_3$ and analyzed by capillary GC (DB-17 column; temperature program: 180°C for 2 min/increase at 5 °C per min/220 °C final temperature). The retention times and relative intensities were compared to those observed for the acetylated 2-octylglycosides of D- and L-fucose and L-rhamnose standards. The observed retention times were as follows: ((+)-2-octanol with L-fucose) 10.17, 11.00 min; ((+)-2-octanol with D-fucose) 9.91, 10.47, 10.65, 11.48 min; ((+)-2-octanol with L-rhamnose) 9.38, 9.55, 10.25 min; ((-)-2-octanol with L-rhamnose) 9.26, 10.04 min; ((+)-2-octanol with hydrolysis products) 9.36, 9.54, 9.91, 10.24, 10.47, 10.65, 11.48 min; ((-)-2-octanol with hydrolysis products) 9.26, 10.03, 10.17, 10.95.

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Supplementary Material Available: Tables II and III containing ^1H NMR data for the acetate **5** and the elimination product **6** (3 pages). Ordering information is given on any current masthead page.

Palladium-Catalyzed Selective Hydrogenolysis of Alkenyloxiranes with Formic Acid. Stereoselectivity and Synthetic Utility

Masato Oshima,[†] Hiroyuki Yamazaki,[†] Isao Shimizu,*[,†] Mohammad Nisar,[‡,1a] and Jiro Tsuji[‡,1b]

Contribution from the Department of Applied Chemistry, School of Science and Engineering, Waseda University, 3-4-1 Ookubo, Shinjuku-ku, Tokyo 169, Japan, and Department of Chemical Engineering, Faculty of Engineering, Tokyo Institute of Technology, 2-12-1 Ookayama, Meguro-ku, Tokyo 152, Japan. *Received November 22, 1988*

Abstract: Selective hydrogenolysis of alkenyloxiranes to give homoallylic alcohols was carried out using formic acid in the presence of palladium-phosphine catalyst. The selectivity of the reaction depends on a nature and an amount of phosphine ligands. The reaction proceeds stereoselectively, because the hydride derived from formic acid attacks the allyl groups intramolecularly from a palladium side of π-allylpalladium hydride intermediates. The stereoselectivity of hydride attack, which induces the ring opening of alkenyloxiranes, can be controlled by the olefin geometry of alkenyloxiranes. Thus, inversion of configuration at the oxirane carbon by the hydride attack was observed in the reaction of (*E*)-alkenyloxiranes, whereas configuration at the oxirane carbon was retained with (*Z*)-alkenyloxiranes owing to the anti-syn isomerization of the π-allylpalladium system prior to the hydride attack. On the basis of these observations, both (*S*)- and (*R*)-6,10-dimethyl-2-undecanones were synthesized with high enantiomeric purities starting from one enantiomer, (2*S*,3*S*)-6,6-(2,2-dimethylpropylenedioxy)-2,3-epoxy-2-methyl-1-heptanol.

Regio- or stereoselective epoxide-opening reaction is one of the most useful and promising synthetic methods for the preparation of optically active acyclic hydroxy compounds, because a wide variety of chiral epoxides are easily available with high enantiomeric purity by the Sharpless asymmetric epoxidation of allylic alcohols.[2,3] Although a number of ring-opening reactions of

[†] Waseda Univeristy.
[‡] Tokyo Institute of Technology.

(1) (a) Present address: Department of Chemistry, Peshawar University, Peshawar, Pakistan. (b) Present address: Department of Applied Chemistry, Okayama University of Science, Ridai-cho, Okayama 700, Japan.

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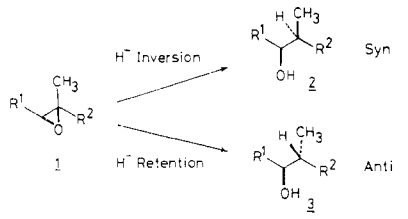
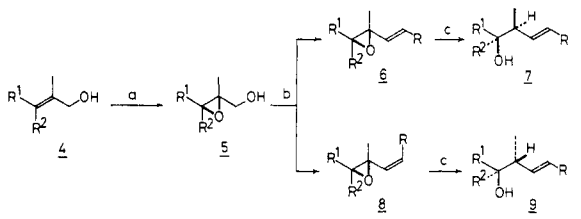
Scheme I



Scheme II[a]

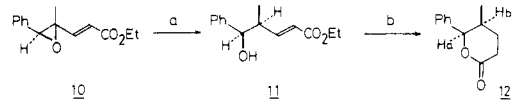


[a] Key: (a) ^{t}BuOOH, $Ti(O^iPr)_4$, (+)-DET; (b) DMSO, $(COCl)_2$, Et_3N, CH_2Cl_2; Wittig reaction; (c) $Pd_2(dba)_3CHCl_3$, n-Bu_3P, HCO_2H, Et_3N.

oxiranes with various nucleophiles have been reported,[4] reductive opening using hydride donors with high regio- and stereoselectivity is scarce.[5] Selective hydride attack on trisubstituted oxiranes such as **1** with either *inversion* or *retention* of configuration at the oxirane carbon would provide a useful synthetic method for an acyclic system **2** or **3**, which is ubiquitous in natural products (Scheme I).[6,7]

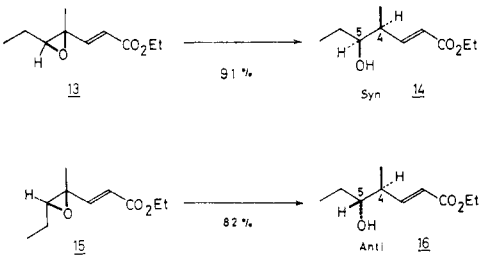
It has been reported that the ring-opening reaction of alkenyloxiranes with palladium–phosphine complexes proceeds stereoselectivity in a S_N2 manner to afford π-allylpalladium complexes, which react further with added nucleophiles to give allylic alcohols regio- and stereoselectively as 1,4-addition products.[8-10] For example, the reaction of alkenyloxiranes with active hydrogen compounds such as β-keto esters proceeds with net retention.[10a-f] On the contrary, reaction of alkenyloxiranes with organostannanes proceeds with net inversion.[10g] It is also known that allylic compounds are hydrogenolyzed via π-allylpalladium by using palladium catalyst with various reducing agents, such as formic acid,[11] $LiBHEt_3$,[12] $NaBH_4$,[13] Bu_3SnH,[14] polymethylhydrosiloxane (PMHS),[15] SmI_2,[16] alkylzinc derivatives bearing β-hydrogen,[17] NAD(P)H model,[18] and Pb cathode and Pt anode.[19] Among these reducing agents, formic acid shows wide compatibility for allylic substrates having other sensitive functional groups in the same molecules. Furthermore, the reaction of terminal allylic compounds with formic acid gives terminal olefins selectively, which is difficult with other reducing agents. We have also reported that certain alkenyloxiranes are reduced with formic acid to give homoallylic alcohols regioselectively in good yields.[20] In our recent communication the reaction of alkenyloxiranes with formic acid proceeds stereoselectively with net inversion, which appears to be useful for the construction of chiral centers bearing a methyl and a hydroxy substituent each on vicinal carbons.[21,22] In the course

Scheme III[a]

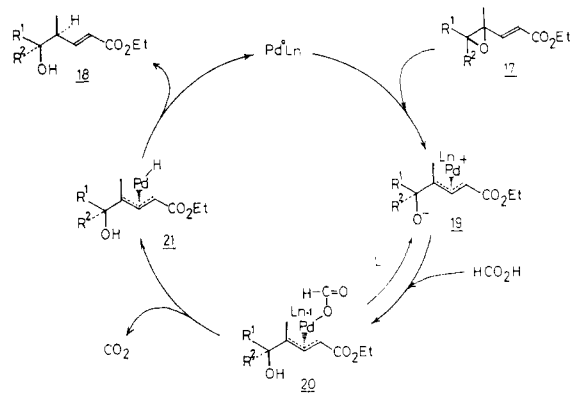


[a] Key: (a) $Pd_2(dba)_3CHCl_3$, n-Bu_3P, HCO_2H, Et_3N, dioxane, rt 97%; (b) Pd/C, H_2, AcOEt–Et_3N; NaOH, H_2O–EtOH; p-TsOH, PhH, 90%.

Scheme IV



Scheme V



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(4) For recent works, see: Behrens, C. H.; Sharpless, K. B.; Walker, F. J. *J. Org. Chem.* **1985**, *50*, 5687–5696, and reviews cited therein.

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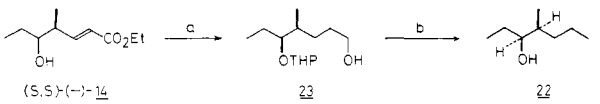
Scheme VI[a]



[a] Key: (a) DHP, *p*-TsOH; $LiAlH_4$, Et_2O 69%; (b) TsCl, $LiAlH_4$, Et_2O; 3 N HCl 31%.

of our synthetic applications, we have also found that the selectivity of the reaction is critical and strongly depends on the reaction conditions, especially on ligand effects. In this paper we report a full detail of our study on the palladium-catalyzed hydrogenolysis of alkenyloxiranes with formic acid as depicted in Scheme II. Synthetic application of this methodology to a few optically active homoallylic compounds is also presented: Both *syn*- and *anti*-2-methylhomoallylic alcohols **7** and **9** were synthesized from one enantiomeric epoxy alcohol **5** via (*E*)- or (*Z*)-alkenyloxiranes **6** and **8**, respectively.

Results and Discussion

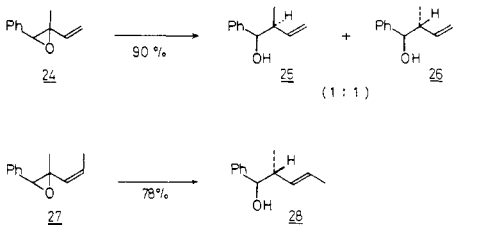
Stereoselectivity and Synthetic Utility. The alkenyloxirane **10** was prepared in three steps from (*E*)-2-methylcinnamyl alcohol by epoxidation, Swern oxidation, and Emmons–Horner reaction.[5] Reaction of **10** with formic acid using $Pd_2(dba)_3CHCl_3$ and *n*-Bu_3P (P/Pd = 0.5) as catalysts at room temperature for 1.5 h gave the homoallylic alcohol **11** in 97% yield. In order to determine the relative stereochemistry of the product **11**, **11** was hydrogenated (H_2/Pd–C), and the subsequent alkaline hydrolysis, followed by lactonization (*p*-TsOH, benzene reflux) gave the six-membered lactone **12**, whose proton H_a appeared at 5.33 ppm as a doublet having a vicinal coupling J = 3.0 Hz, the latter showing cis stereochemistry of **12**. Thus, the relative stereochemistry of **11** was determined to be syn (Scheme III).[23]

The alkenyloxiranes **13** and **15**[24] were prepared by procedures similar to those for **10**. The alkenyloxirane **13** was converted to the *syn*-homoallylic alcohol **14** in 91% yield. On the contrary, reaction of **15** (as a 5:1 mixture of **15** and **13**) gave the *anti*-homoallylic alcohol **16** (**16**:**14** = 5:1) in 82% yield. Although it is difficult to distinguish **16** from its isomer **14** by IR and ^1H NMR spectra, the stereochemistry was elucidated by comparing their ^{13}C NMR spectra with those of related systems (Scheme IV).[25]

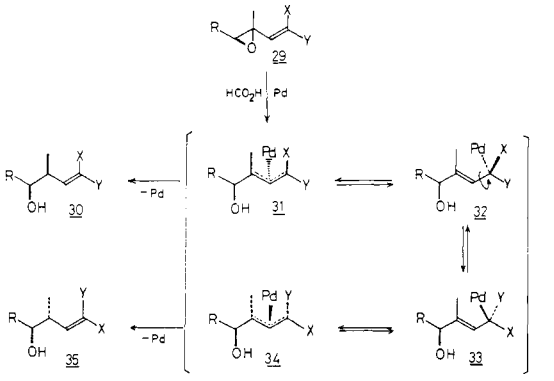
The reactions of the (*E*)-alkenoates **10**, **13**, and **15** were all stereospecific with inversion of stereochemistry, and they can be explained by Scheme V. At first, Pd(0)–phosphine complex coordinating to the olefin **17** displaces the oxide of **17** with inversion to form the π-allylpalladium alkoxide complex **19**. Then formic acid adds to the palladium complex **19** to give the π-allylpalladium formate **20**, which undergoes decarboxylation to form the π-allylpalladium hydride complex **21**.[13a] Finally, reductive elimination of palladium by internal attack of the hydride to the more substituted carbon of the π-allylpalladium **21** gives the homoallylic alcohol **18**, and the Pd(0) complex is reproduced, forming a catalytic cycle.

The present reaction is useful for the synthesis of optically active acyclic natural products and was applied to the synthesis of the optically active pheromone of the smaller European elmbark beetle, (−)-(3*S*,4*S*)-4-methyl-3-heptanol (**22**).[26] The optically active

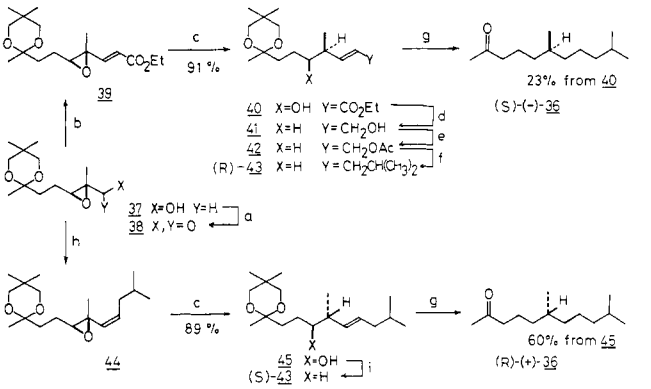
Scheme VII



Scheme VIII



Scheme IX[a]



[a] Key: (a) DMSO, $(COCl)_2$, Et_3N, CH_2Cl_2; (b) $(EtO)_2P(O)CH_2CO_2Et$, NaH, THF 65%; (c) $Pd_2(dba)_3CHCl_3$, *n*-Bu_3P, HCO_2H, Et_3N, dioxane; (d) MsCl, Et_3N; DIBAH; $LiAlH_4$; (e) Ac_2O, Py; (f) Pr^iMgBr, $CuCl_2$, LiCl; (g) Pd/C, H_2; *p*-TsOH, Me_2CO; (h) $Am^iP^+Ph_3Br^-$, *n*-BuLi 52%; (i) MsCl, Et_3N; $LiAlH_4$.

alkenyloxirane (*S*,*S*)-**13**[27] was prepared by the Sharpless oxidation of (*E*)-2-methyl-2-pentenol using (+)-diethyl tartrate, followed by Swern oxidation and subsequent Emmons–Horner reaction. Hydrogenolysis of (*S*,*S*)-**13** gave the optically active homoallylic alcohol (*S*,*S*)-**14** in 68% yield. After protecting the secondary alcohol as tetrahydropyranyl ether, both the ester and the olefin were reduced with $LiAlH_4$ in THF to give the saturated primary alcohol **23** in 69% yield. Sulfonylation of **23** with *p*-toluenesulfonyl chloride and pyridine, followed by removal of the tosylate with $LiAlH_4$ and subsequent hydrolysis, gave **22** in 31% yield from **14**

(22) Keinan reported that palladium-catalyzed reaction of allylic compounds with $NaBD_4$ or Bu_3SnH proceeds with inversion.[14] For references dealing with stereochemistry of Pd-catalyzed hydride transfer, see: (a) Greenspoon, N.; Keinan, E. *J. Org. Chem.* **1988**, *53*, 3723–3731. (b) Bäckvall, J.-E. *Acc. Chem. Res.* **1983**, *16*, 335–342.

(23) (a) By a similar procedure, the optically active (*S*,*S*)-**11** ($[\alpha]^{23}_D$ = +2.8° (*c* 2.4, $CHCl_3$)) was obtained by the reaction of (*S*,*S*)-**10** ($[\alpha]^{23}_D$ = −43.2° (*c* 3.9, $CHCl_3$)) obtained from the (2*R*,3*S*)-2,3-epoxy-2-methyl-3-phenylpropanal ($[\alpha]^{24}_D$ = +183.2° (*c* 1.7, $CHCl_3$)) [lit. $[\alpha]^{20}_D$ = +182° (*c* 2.0, $CHCl_3$)].[23b] (b) Terashima, S.; Hayashi, M.; Koga, K. *Tetrahedron Lett.* **1980**, *21*, 2733–2736.

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(27) (a) Rossiter, B. E.; Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1981**, *103*, 464–465. (b) Colvin, E. W.; Robertson, A. D.; Wakharkar, S. *J. Chem. Soc., Chem. Commun.* **1983**, 312–314 [Lit. $[\alpha]^{22}_D$ = −14.3° (*c* 1.02, $CHCl_3$)].

with 92% enantiomeric excess (Scheme VI).

As mentioned above although the palladium-catalyzed hydrogenolysis of (*E*)-alkenyloxirane proceeded with inversion of stereochemistry, hydrogenolysis of the vinyloxirane **24** gave a 1:1 mixture of the syn and anti isomers, **25** and **26**,[28] in 90% yield. Furthermore, the reaction of the (*Z*)-alkenyloxirane **27** (*Z* > 95%) gave the isomer *anti*-(*E*)-**28** as a sole product in 78% yield with higher than 95% purity. Other stereoisomers *syn*-(*Z*)-**28**, *anti*-(*Z*)-**28**, and *syn*-(*E*)-**28** were hardly detected by NMR analysis (Scheme VII).[29,30]

These results indicate that the stereoselectivity depends on the olefin geometry of alkenyloxiranes. In other words, the olefin geometry of the alkenyloxirane is important to control the stereochemistry of the hydride attack. Thus, in the reaction of (*Z*)-alkenyloxirane, the stereochemistry of asymmetric carbon is retained and the stereochemistry of olefin is isomerized simultaneously. These stereochemical results of **24** and **27** are explained by the well-known π–σ–π interconversion of π-allylpalladium intermediate (**31** → **32** → **33** → **34**) as illustrated in Scheme VIII.[31] The (*E*)-olefin **35** derived from thermodynamically stable *syn*-π-allylpalladium intermediate was obtained predominantly in this case.[32]

It is useful that both syn and anti isomers can be prepared from the same oxiranes by choosing the olefin geometry of alkenyloxiranes. Using this methodology both (*S*)-(−)- and (*R*)-(+)-dimethylundecan-2-ones **36** were synthesized from the same oxirane **37** (Scheme IX).[33] Swern oxidation of the (*S*,*S*)-epoxy alcohol **37**, followed by Emmons–Horner reaction gave the (*E*)-alkenyloxirane **39** in 65% yield. Reaction of the alkenyloxirane **39** with formic acid and Et_3N in the presence of $Pd_2(dba)_3CHCl_3$ and *n*-Bu_3P at room temperature for 1.5 h gave the homoallylic alcohol **40** in 91% yield. Methanesulfonylation of the homoallylic alcohol **40** and reduction of the ester with diisobutylaluminum hydride, followed by removal of the mesyl group with $LiAlH_4$, gave the allylic alcohol **41** in 56% yield. Acetylation of the alcohol **41** with acetic anhydride and pyridine in 89% yield, followed by coupling reaction of the acetate **42** with isopropylmagnesium bromide in presence of anhydrous cupric chloride and anhydrous lithium chloride, gave the (*R*)-olefin **43** in 42% yield. Hydrogenation of the (*R*)-olefin **43** followed by deprotection of the carbonyl group gave the (*S*)-6,10-dimethylundecan-2-one **36** in 99% yield. The rotation of (*S*)-**36** was −0.56°. The levorotation of the product indicates that asymmetric carbon has (*S*)-configuration.[34] Thus the hydride attack to the (*E*)-alkenyloxirane **39** proceeded stereospecifically with inversion.

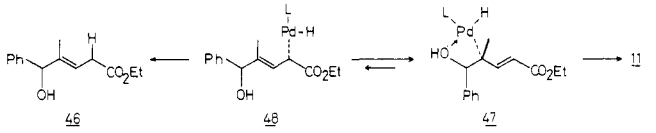
The enantiomer (*R*)-(+)-**36** was synthesized from the (*Z*)-alkenyloxirane **44**, which was prepared from the same oxirane **37** by Swern oxidation and subsequent Wittig reaction using isoamyltriphenylphosphonium iodide in 52% yield. Reaction of the (*Z*)-alkenyloxirane **44** with formic acid and Et_3N was carried out in the presence of Pd(0)–phosphine catalyst to give the homoallylic alcohol **45** as a sole product in 89% yield. Treatment of the homoallylic alcohol **45** with methanesulfonyl chloride and subsequent reduction of the mesyl group with $LiAlH_4$ gave the (*S*)-olefin **43** in 61% yield. Hydrogenation of the olefin and removal of the acetal group gave the (*R*)-6,10-dimethylundecan-2-one **36** in 99% yield. The rotation of (*R*)-**36** was +0.59°. The observed rotations of (*R*)-(+)- and (*S*)-(−)-**36** clearly support the absolute configuration of asymmetric carbons. Inversion took place by the hydride attack to (*E*)-alkenyloxirane, and retention was observed with (*Z*)-alkenyloxirane.

Table I. Reaction of **10** with HCO_2H–Et_3N Using $Pd_2(dba)_3CHCl_3$-*n*-Bu_3P[a]

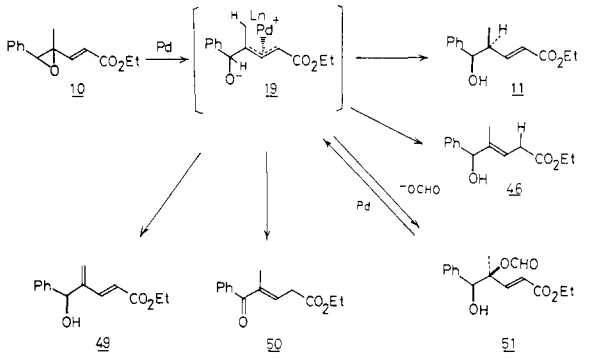
solvent	time, h	selectivity **11**:**46**	solvent	time, h	selectivity **11**:**46**
benzene	8	92:8	CH_2Cl_2	8	96:4
CH_3CN	2.5	96:4	EtOH	8	91:9
THF	5	98:2	hexane	28	92:8
DMSO	0.5	69:31	Et_2O	24	91:9
DMF	0.5	92:8	dioxane	6.5	100:0

[a] The reactions were carried out using the oxirane **10** (2 mmol), $Pd_2(dba)_3CHCl_3$ (50 μmol), *n*-Bu_3P (50 μmol), HCO_2H (10 mmol), and Et_3N (4 mmol) in solvent (10 mL). See the Experimental Section.

Scheme X



Scheme XI



Ligand and Solvent Effects. So far we have describerd that the hydrogenolysis of the alkenyloxiranes in dioxane using $^1/_2Pd_2(dba)_3CHCl_3$–*n*-Bu_3P catalyst with formic acid in dioxane proceeded regio- and stereoselectively. However, the selectivity of the reaction was influenced by the nature and the amount of ligands and solvents. The reactions of **10** carried out in various solvents are summarized in Table I. The homoallylic alcohol **11** was always obtained as a major product, accompanied by the allylic alcohol **46** as a minor product in all solvents except DMSO. This regioselectivity is explained by unsymmetrical nature of the π-allylpalladium complex.[35,36] Namely, the homoallyl alcohol **11** and its isomer **46** are considered to be formed by reductive elimination of palladium via the σ-complex **47** or **48**, respectively (Scheme X).[37] The former σ-complex **47** is considered to be much more stable than its isomer **48** by intramolecular coordination of the hydroxy group. Low regioselectivity in the reaction in DMSO is accounted for by its ability to solvate the palladium complex, which inhibits the intramolecular coordination of the hydroxy group. In addition to the selective reduction of **10** into **11** and a small amount of **46**, the reaction of the intermediate **19** would

(28) Hoffmann, R. W.; Zeiss, H.-J. *J. Org. Chem.* **1981**, *46*, 1309–1314.

(29) Authentic all four possible stereoisomers of **28** were prepared in order to determine the relative stereochemistry. NMR data for other stereoisomers are as follows. *syn*-(*E*)-**28**: ^1H NMR (90 MHz, $CDCl_3$) δ H_a 4.57 (d, J_{ab} = 5.3 Hz, 1 H), J_{cd} = 13.0 Hz; ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 132.8, 128.2, 127.9, 127.5, 126.6, 77.4 (d), 43.7 (d), 29.8 (q), 14.6 (q). *syn*-(*Z*)-**28**: ^1H NMR (90 MHz, $cDCl_3$) δ H_a 4.45 (d, J_{ab} = 7.7 Hz, 1 H), J_{cd} = 11.1 Hz; ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 132.8, 127.8, 127.6, 126.8, 126.7, 126.4, 77.2 (d), 38.8 (d), 16.4 (q), 13.0 (q). *anti*-(*Z*)-**28**: ^1H NMR (90 MHz, $CDCl_3$) δ H_a 4.27 (d, J_{ab} = 7.8 Hz, 1 H), J_{cd} = 11.1 Hz; ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 132.7, 128.1, 127.7, 127.5, 126.9, 78.6 (d), 39.9 (d), 17.1 (q), 13.3 (q).

(30) Baldwin, J. E.; Patrick, J. E. *J. Am. Chem. Soc.* **1971**, *93*, 3556–3558.

(31) Faller, J. W.; Thomsen, M. E.; Mattina, M. J. *J. Am. Chem. Soc.* **1971**, *93*, 2642–2653.

(32) Hayashi, T.; Yamamoto, A.; Hagihara, T. *J. Org. Chem.* **1986**, *51*, 723–727.

(33) $[\alpha]^{25}_D$ = +9° (*c* 2.0, EtOH): Lee, A. W. M. *J. Chem. Soc., Chem. Commun.* **1984**, 578–579.

(34) The authentic optically active (*R*)-(+)-**36** (>98% ee, $[\alpha]^{23}_D$ = −0.5°, *c* 3.2, EtOH) was prepared from optically active (*R*)-(+)-citronellol (>98% ee) by iodination and subsequent coupling with 1-lithio-2-(*tert*-butylimino)-propane, followed by hydrolysis. We thank Takasago Perfumery Co. Ltd. for a gift of optically pure (*R*)-(+)-citronellol.

(35) Keinan, E.; Roth, Z. *J. Org. Chem.* **1983**, *48*, 1769–1772.

(36) Similar contribution of hydroxy groups in the reduction of allylic substrates has been reported. Ono, N.; Hamamoto, I.; Kamimura, A.; Kaji, A. *J. Org. Chem.* **1986**, *51*, 3736–3738.

(37) Direct hydride attack from the formate complex **20** by S_Ni manner to **18** is also discussed.[13a]

Table II. Reaction of **10** with HCO_2H–Et_3N Using $Pd_2(dba)_3CHCl_3$–Phosphine or –Phosphite Catalyst in Dioxane[a]

run	phosphine or phosphite	ratio (L/Pd)	time, h	product yield,[b] % 11	46	49	50	51
1	none		48.0	58[c]	27[c]	0	0	0
2	n-Bu_3P	0.25	8.0	99	0	0	0	0
3		0.5	6.5	99	0	0	0	0
4		1.0	6.0	99	0	0	0	0
5		1.5	2.0	63	0	0	34	0
6		2.0	2.0	25	0	0	74	0
7		2.5	2.0	trace	0	0	92	0
8		4.0	1.5	trace	0	0	90	0
9	Ph_3P	0.25	7.0	99	0	0	0	trace
10		0.5	5.0	98	0	0	0	0
11		1.0	6.0	98	0	0	0	0
12		1.25	6.0	76	0	4	trace	18
13		1.5	1.5	28	0	7	11	52
14		2.0	1.0	13	0	7	16	61
15		4.0	0.5	9	0	9	14	66
16	Cy_3P	0.5	6.0	99	0	0	0	0
17		1.0	7.0	99	0	0	0	0
18		2.0	8.5	96	0	0	0	0
19		4.0	11.0	99	0	0	0	0
20	$(o\text{-tol})_3P$	2.0	19.0	97	0	0	0	0
21		4.0	19.0	99	0	0	0	0
22	dppe	0.5	4.0	99	0	0	0	0
23		1.0	5.5	98	0	0	0	0
24		1.5	5.0	86	0	0	0	0
25		2.0	22.0	78	0	0	19	0
26		2.5	50.0	70	0	5	20	0
27		4.0	120.0	47	0	23	36	0
28	$(MeO)_3P$	0.5	5.5	91	0	0	0	0
29		1.0	4.0	98	0	0	0	0
30		2.0	0.5	11	0	6	27	55
31		4.0	0.5	trace	0	4	27	68
32	$(EtO)_3P$	0.5	8.5	95	0	0	0	0
33		1.0	4.5	98	0	1	0	0
34		2.0	1.5	45	0	12	39	2
35		4.0	1.5	trace	0	10	42	47
36	$(^iPrO)_3P$	0.5	72.0	79	0	trace	0	0
37		4.0	1.5	trace	0	4	40	55
38	$(PhO)_3P$	0.5	72.0	92	0	0	0	2
39		1.0	7.0	95	0	trace	0	1
40		2.0	23.5	91	0	0	0	0
41		4.0	96.0	trace	0	0	13	4

[a] See the Experimental Section. [b] GLC analysis, unless otherwise stated. [c] Isolated yields.

involve three different courses, namely, β-elimination and isomerization to give **49** and **50**[9] and a formate attack in 1,2 manner to give **51**, respectively (Scheme XI). Actually, the composition of the reaction products from **10** was remarkably dependent on the nature of phosphine ligands and the relative ratios of the ligand to palladium (L/Pd) (Table II). As already described, the desired homoallylic alcohol **11** was obtained in an almost quantitative yield from the reaction of **10** in dioxane at room temperature with formic acid and triethylamine using 5 mol % of $^1/_2Pd_2(dba)_3CHCl_3$ and 0.5 equiv of tributylphosphine (L/Pd = 0.5) (run 3). None of the other products was detected under these conditions. As shown in Table II, satisfactory results were obtained with less than an equimolar amount of phosphine (L/Pd < 1.0) (runs 2–4). These are, indeed, the cases for any other phosphines employed, e.g., triphenylphosphine (runs 9–11). The same trend is apparent for tricyclohexylphosphine (runs 16 and 17) and even (diphenylphosphine)ethane (runs 22 and 23). Less than 1 equiv of phosphine to the palladium is essential for the selective reduction. However, the reaction of **10** without phosphine (run 1) or with a low ratio of phosphite ligands (runs 36 and 38) proceeded very slowly. In the former case, a mixture of **11** and **46** was obtained. The selectivity for **11** decreased dramatically when more than 1 equiv of tributylphosphine to the palladium was used, and isomerization of the oxirane to the enone **50** took place predominantly (runs 5–8).[9] When excess triphenylphosphine was used, the formate **51** was obtained as a major product with small amounts of the dienol **49** and the enone **50** (runs 12–15). Similarly, when other ligands, such as trimethyl phosphite (runs 28–31), triethyl phosphite (runs 32–35), triisopropyl phosphite (runs 36 and 37), and triphenyl phosphite (runs 38–41), were examined, the desired homoallylic alcohol **11** was also obtained in good yields as far as the ratio of L/Pd is smaller than 1 (runs 28–41). The use of the bidentate phosphine, dppe (runs 22–27), gave the homoallylic alcohol **11** as a major product even when more than 1 mol equiv of the ligand was used. Furthermore, when excess amounts of the bulky tricyclohexylphosphine (runs 17–19) or tri-*o*-tolylphosphine (runs 20 and 21) were used, no formation of the undesired products **49–51** was observed, but the reaction was slow. From these results, we employed tributylphosphine or triphenylphosphine as the ligand, and their amounts were kept below 1 equiv of the palladium catalyst for transformation of other alkenyloxiranes to corresponding homoallylic alcohols.

Although a precise ligand effect was unknown, the result shows that only one phosphine or phosphite coordinating to palladium is sufficient for the desired catalytic activity. The use of excess ligands favored β-elimination reaction to form the dienol **49** or the enone **50**, because excess ligands stabilize the cationic complex **19** and inhibit the formation of the formate complex **20**, which is the precursor of the hydride complex **21** (Scheme V). It is interesting to note that the formyloxy compound **51** was obtained regioselectively as a 1,2-adduct in considerable yields when more than 1 equiv of triphenylphosphine (runs 12–15) or trialkyl phosphites (runs 30, 31, 35, and 37) was used. Under these conditions nucleophilic attack of formate anion is faster than decarboxylation reaction because formation of the cationic complex **19** is favorable.[38] The formate **51** can be also converted to **11** by the reaction with formic acid using $Pd_2(dba)_3CHCl_3$–n-Bu_3P catalyst at room temperature for 24 h in 45% yield with 42% recovery of **51**. Stereoselective formation of **11** from **51** suggests the stereochemistry of the hydroxy and the formyloxy groups in **51** is syn, which is caused by external attack of formate anion to **19** and is in agreement with the well-known double-inversion stereochemistry with soft nucleophiles.[10a–f]

Conclusion

A wide variety of optically active alkenyloxiranes can be obtained with ease from the corresponding allylic alcohols, and the palladium-catalyzed hydrogenolysis of the alkenyloxiranes proceeds selectively under mild conditions. Furthermore, both syn and anti stereochemistries are accessible from the same oxirane by choosing the olefin geometry of the alkenyloxirane, and hence this method provides new entry for facile preparation of chiral acyclic compounds.

Experimental Section

General Procedures. Unless otherwise stated, experiments were carried out under argon atmosphere. Infrared spectra were obtained on a Shimadzu IR-400. ^1H NMR spectra were recorded on a Hitachi R-90H in $CDCl_3$ at 90 MHz or a Hitachi R-24 in CCl_4 at 60 MHz. ^{13}C NMR spectra were recorded on a JEOL GSX-400 in $CDCl_3$ at 100.4 MHz or a Hitachi R-90H in $CDCl_3$ at 22.5 MHz. Chemical shifts are expressed in parts per million downfield from internal tetramethylsilane. Optical rotation was taken on a Jasco DIP-4. High-resolution mass spectra were taken on a JEOL JMS-DX300. Elemental analyses were performed using a Yanaco MT-3. Ether, THF, and dioxane were distilled from benzophenone ketyl. Benzene and dichloromethane (CH_2Cl_2) were distilled on diphosphorus pentoxide. Dimethyl sulfoxide (DMSO) and triethylamine (Et_3N) were distilled on calcium hydride. Tri-*n*-butylphosphine (n-Bu_3P) was distilled in vacuo. [Tris(dibenzlideneacetone)-chloroform]dipalladium ($Pd_2(dba)_3CHCl_3$) was prepared according to the literature.[39] Thin-layer chromatography (TLC) was performed using Merck silica gel aluminum sheets (Art. 5554). Column chromatography was performed using Wakogel C-200 or Kanto silica gel 100–200 mesh.

Preparation of Ethyl (±)-(*E*)-(4*S,5*S**)-4,5-Epoxy-4-methyl-5-phenyl-2-pentenoate (10).** To a mixture of (*E*)-2-methylcinnamyl alcohol

(38) Recently, stereoselective 1,2-addition of oxygen nucleophile using carbon dioxide to alkenyloxiranes was reported by Trost. Trost, B. M.; Angle, S. R. *J. Am. Chem. Soc.* **1985**, *107*, 6123–6124. Fujinami, T.; Suzuki, T.; Kamiya, M.; Fukuzawa, S.; Sakai, S. *Chem. Lett.* **1985**, 199–200.

(39) Ukai, T.; Kawazura, H.; Ishii, Y.; Bonnet, J. J.; Ibers, J. A. *J. Organomet. Chem.* **1974**, *65*, 253–266.

(2.83 g, 19.1 mmol) and vanadium oxyacetylacetonate ($VO(acac)_2$) (0.13 g, 0.5 mmol) in dry benzene (15 mL) was added a solution of *tert*-butyl hydroperoxide (70% aqueous solution, 2.46 g, 20.0 mmol) in benzene (10 mL) over 10 min at 80 °C. The resulting mixture was stirred for 1 h. To the solution was added water (40 mL), and the organic layer was extracted with ether. The combined extracts were washed with saturated aqueous $Na_2S_2O_3$, saturated aqueous $NaHCO_3$, saturated aqueous NH_4Cl, and brine, dried over $MgSO_4$, and concentrated. The residue was chromatographed on SiO_2 using a mixture of hexane–ether (from 95:5 to 80:20) as an eluent to give (±)-(2*S**,3*S**)-2,3-epoxy-2-methyl-3-phenylpropan-1-ol (2.83 g, 90% yield): IR (neat) 3380 (s), 1450 (m), 1070 (s), 1040 (s), 850 (m), 750 (s), 700 (s) cm^{-1}; ^1H NMR (60 MHz, CCl_4) δ 7.28 (s, 5 H), 4.13 (s, 1 H), 3.69 (s, 2 H), 1.08 (s, 3 H).

To a solution of oxalyl chloride (1.58 mL, 18.1 mmol) in CH_2Cl_2 (117 mL) was added DMSO (8.3 mL, 117 mmol) in CH_2Cl_2 (8 mL) at −50 °C. To the resulting solution was added (±)-(2*S**,3*S**)-2,3-epoxy-2-methyl-3-phenylpropan-1-ol (2.54 g, 15.5 mmol) in CH_2Cl_2 (16 mL), and the mixture was stirred for 1 h. Et_3N (32.6 mL, 234 mmol) was added to the solution. The mixture was allowed to stand at room temperature with stirring for 15 min. Water was added to the solution, and the organic layer was extracted with CH_2Cl_2. The combined organic extracts were washed with saturated aqueous NH_4Cl, saturated aqueous $NaHCO_3$, and brine and dried over $MgSO_4$. The solvent was removed in vacuo, and the residue was chromatographed on SiO_2 using a mixture of hexane–ethyl acetate (from 95:5 to 80:20) as an eluent to give (±)-(2*R**,3*S**)-2,3-epoxy-2-methyl-3-phenylpropanal (1.94 g, 77% yield): IR (neat) 2980 (m), 2930 (m), 2920 (m), 1725 (s), 1445 (m), 1070 (m), 1015 (m), 890 (m), 850 (m), 740 (s), 700 (s) cm^{-1}; ^1H NMR (60 MHz, CCl_4) δ 8.92 (s, 1 H), 7.29 (s, 5 H), 4.20 (s, 1 H), 1.18 (s, 3 H).

To a suspension of sodium hydride (60 wt %, 1.12 g, 27.9 mmol) in THF (40 mL) was added triethyl phosphonoacetate (6.25 g, 27.9 mmol) over 2 min at 0 °C, and the mixture was stirred for 15 min. To the solution was added (±)-(2*R**,3*S**)-2,3-epoxy-2-methyl-3-phenylpropanal (3.47 g, 21.4 mmol), and the mixture was stirred for 30 min. Water was added to the solution, and the organic layer was extracted with ether. The combined extracts were washed with saturated aqueous NH_4Cl, saturated aqueous $NaHCO_3$, and brine. The solution was dried over $MgSO_4$, and the solvent was removed. The residue was chromatographed on SiO_2 using a mixture of hexane–ether (from 98:2 to 80:20) as an eluent to give **10** (4.53 g, 91% yield): IR (neat) 2980 (m), 1720 (s), 1650 (m), 1445 (m), 1370 (m), 1305 (s), 1270 (s), 1165 (s), 1030 (m), 980 (m), 750 (m), 705 (m) cm^{-1}; ^1H NMR (60 MHz, CCl_4) δ 7.21 (s, 5 H), 6.73 (d, J = 15.6 Hz, 1 H), 5.96 (d, J = 15.6 Hz, 1 H), 4.11 (q, J = 7.0 Hz, 2 H), 3.89 (s, 1 H), 1.30 (t, J = 7.0 Hz, 3 H), 1.22 (s, 3 H); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 165.7 (s), 148.7 (d), 134.6 (s), 128.1 (d), 127.8 (d), 126.4 (d), 121.9 (t), 65.9 (d), 61.0 (s), 60.4 (t), 14.5 (q), 14.2 (q). High-resolution mass spectrum for $C_{14}H_{16}O_3$, calcd m/z 232.1100, found m/z 232.1118.

General Procedure for the Palladium-Catalyzed Reaction of Alkenyloxiranes with Formic Acid. Ethyl (±)-(*E*)-(4*R,5*S**)-5-Hydroxy-4-methyl-5-phenyl-2-pentenoate (11).** To a mixture of $Pd_2(dba)_3CHCl_3$ (13.2 mg, 0.013 mmol) in dioxane (0.5 mL) was added n-Bu_3P (5.3 μL, 0.013 mmol). To the solution was added a solution of formic acid (98 μL, 2.55 mmol) and Et_3N (140 μL, 1.02 mmol) in dioxane (1 mL) at room temperature, and the mixture was stirred for 5 min. The alkenyloxirane **10** (119 mg, 0.51 mmol) in dioxane (1.5 mL) was added to the solution, and the mixture was stirred for 1.5 h. The solution was passed through a short SiO_2 column, and the filtrate was concentrated. The residue was chromatographed on SiO_2 using a mixture of hexane–ether (90:10) as an eluent to give **11** (116 mg, 97% yield): TLC R_f 0.49 (hexane–ethyl acetate, 2:1); IR (neat) 3430 (m), 2970 (m), 1700 (s), 1665 (m), 1270 (m), 1180 (m), 1030 (m), 980 (m), 760 (m), 700 (s), cm^{-1}; ^1H NMR (60 MHz, CCl_4) δ 7.15 (s, 5 H), 6.99 (dd, J = 7.8, 16.2 Hz, 1 H), 5.57 (d, J = 16.2 Hz, 1 H), 4.48 (d, J = 5.4 Hz, 1 H), 3.95 (q, J = 7.6 Hz, 2 H), 2.74–2.30 (m, 1 H), 1.16 (t, J = 7.6 Hz, 3 H), 0.94 (d, J = Hz, 3 H); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 166.3 (s), 150.2 (d), 142.0 (s), 128.1 (d), 127.6 (d), 126.2 (d), 121.7 (d), 76.9 (d), 60.1 (t), 43.6 (d), 14.2 (q), 13.9 (q). High-resolution mass spectrum for $C_{14}H_{18}O_3$, calcd m/z 234.1256, found m/z 234.1261.

(±)-(5*R,6*S**)-6-Phenyl-5-methyltetrahydropyran-2-one (12).** Hydrogen gas was bubbled with stirring into a mixture of **11** (1.31 g, 5.59 mmol) and palladium on charcoal (5%, 0.59 g, 0.28 mmol) in ethyl acetate (40 mL) and Et_3N (12 mL) at room temperature for 10 h. The solution was passed through Celite and concentrated to give crude ethyl (4*R**,5*S**)-5-hydroxy-4-methyl-5-phenylpentanoate (1.31 g): IR (neat) 3420 (m), 2970 (m), 1730 (s), 1450 (m), 1375 (m), 1260 (s), 1180 (s), 1030 (m), 770 (w), 710 (s) cm^{-1}; ^1H NMR (60 MHz, CCl_4) δ 7.16 (s, 5 H), 4.45 (d, J = 4.2 Hz, 1 H) 4.01 (q, J = 7.4 Hz, 2 H), 2.94 (b s, 1 H), 2.47–1.50 (m, 5 H), 1.21 (t, J = 7.4 Hz, 3 H), 1.13 (d, J = 7.2 Hz, 3 H). The ester was used in the next step without purification.

A solution containing ethyl (4*R**,5*S**)-5-hydroxy-4-methyl-5-phenylpentanoate (1.31 g) and 10% aqueous sodium hydroxide (15 mL) in ether (6 mL) was stirred for 8 h at room temperature. Dilute hydrochloric acid (2 N, 50 mL) was added to the solution, and the organic layer was extracted with CH_2Cl_2. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated to give (4*R**,5*S**)-5-hydroxy-4-methyl-5-phenylpentanoic acid (1.32 g): IR (neat) 3300 (m), 2930 (m), 1705 (s), 1480 (m), 1455 (m), 1250 (m), 685 (s) cm^{-1}; ^1H NMR (60 MHz, CCl_4) δ 7.21 (s, 5 H), 4.48 (d, J = 4.0 Hz, 1 H), 2.27 (t, J = 6.4 Hz, 2 H), 1.85–1.26 (m, 1 H), 0.80 (d, J = 6.4 Hz, 3 H). The acid was used in the next step without purification.

A solution containing crude (4*R**,5*S**)-5-hydroxy-4-methyl-5-phenylpentanoic acid (1.32 g), and a small amount of *p*-toluenesulfonic acid in benzene (30 mL) was refluxed with stirring for 2 h. Anhydrous potassium carbonate was added to the solution, and the solution was filtered. The filtrate was concentrated, and the residue was chromatographed on SiO_2 using a mixture of hexane–CH_2Cl_2–ethyl acetate (80:10:10) as an eluent to give the lactone **12**. (171 mg, 90% yield): IR (neat) 2950 (w), 1735 (s), 1455 (w), 1235 (m), 1070 (m), 705 (m) cm^{-1}; ^1H NMR (60 MHz, CCl_4) δ 7.15 (s, 5 H), 5.33 (d, J = 3.0 Hz, 1 H), 0.70 (d, J = 7.0 Hz, 3 H); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 171.0 (s), 137.8 (s), 128.1 (d), 127.5 (d), 125.5 (d), 83.4 (d), 32.0 (d), 27.0 (t), 25.7 (t), 12.7 (q). High-resolution mass spectrum for $C_{12}H_{14}O_2$, calcd m/z 190.0994, found m/z 190.1004.

Ethyl (±)-(*E*)-(4*S,5*S**)-4,5-Epoxy-4-methyl-2-heptenoate (13).** By a similar procedure to **10**, Swern oxidation of (±)-(2*S**,3*S**)-2,3-epoxy-2-methylpentan-1-ol (1.01 g) followed by Emmons–Horner reaction gave **13** (1.01 g, 63% yield): IR (neat) 2920 (m), 1700 (s), 1640 (w), 1300 (m), 1170 (m), 1030 (w), 890 (w) cm^{-1}; ^1H NMR (60 MHz, CCl_4) δ 6.71 (d, J = 15.0 Hz, 1 H), 5.95 (d, J = 15.0 Hz, 1 H), 4.20 (q, J = 7.0 Hz, 2 H), 2.77 (t, J = 6.0 Hz), 1.40 (s, 3 H), 1.52–0.98 (m, 8 H).

Ethyl (±)-(*E*)-(4*S,5*S**)-5-Hydroxy-4-methyl-2-heptenoate (14).** According to the general procedure, hydrogenolysis of **13** (368 mg) gave **14** (340 mg, in 91% yield after chromatographic purification): IR (neat) 3400 (s), 2960 (s), 1700 (s), 1640 (m), 1460 (m), 1270 (m), 1170 (m), 1030 (m), 970 (m) cm^{-1}; ^1H NMR (60 MHz, CCl_4) δ 6.96 (dd, J = 15.7 Hz, 7.7 Hz, 1 H), 5.85 (d, J = 15.7 Hz, 1 H), 4.19 (q, J = 7.0 Hz, 2 H), 3.50 (m, 1 H), 2.43 (m, 1 H), 2.12 (b s, 1 H), 1.65–1.28 (m, 2 H), 1.29 (t, J = 7.0 Hz, 3 H), 1.09 (d, J = 6.9 Hz, 3 H), 0.96 (t, J = 7.5 Hz, 3 H); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 166.6 (s), 151.4 (d), 121.1 (d), 75.7 (d), 60.2 (t), 42.4 (d), 27.4 (t), 14.2 (q), 14.1 (q), 10.3 (q).

Ethyl (±)-(*E*)-(4*R,5*S**)-4,5-Epoxy-4-methyl-2-heptenoate (15).** This compound **15** was prepared by a similar procedure to **13**. Swern oxidation of (±)-(2*S**,3*R**)-2,3-epoxy-2-methylpentan-1-ol (440 mg), followed by Emmons–Horner reaction gave **15** (390 mg, 48% yield): IR (neat) 2930 (s), 2120 (s), 1718 (s), 1450 (w), 1305 (m), 1260 (m), 1175 (s), 1030 (m), 705 (w) cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 6.76 (d, J = 15.8 Hz, 1 H), 5.88 (d, J = 15.8 Hz, 1 H), 4.18 (q, J = 7.2 Hz, 2 H), 2.83 (t, J = 6.2 Hz, 1 H), 1.44 (s, 3 H), 1.29 (t, J = 7.2 Hz, 3 H), 1.01 (t, J = 6.2 Hz, 3 H).

Ethyl (±)-(*E*)-(4*R,5*S**)-5-Hydroxy-4-methyl-2-heptenoate (16).** By the general procedure, hydrogenolysis of **15** (390 mg) gave **16** (325 mg, 82% yield): IR (neat) 3430 (m), 2960 (s), 1710 (s), 1645 (m), 1275 (s), 1180 (s), 1025 (m), 980 (m), 755 (m) cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 7.00 (dd, J = 15.8, 8.1 Hz, 1 H), 5.84 (d, J = 15.8 Hz, 1 H), 4.18 (q, J = 7.0 Hz, 2 H), 3.67 (b s, 1 H), 3.46 (dt, J = 7.5, 5.1 Hz, 1 H), 2.55–2.32 (m, 1 H), 1.28 (t, J = 7.0 Hz, 3 H), 1.10 (d, J = 6.8 Hz, 3 H), 0.96 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 166.6 (s), 150.9 (d), 121.6 (d), 76.1 (d), 60.2 (t), 42.3 (d), 27.4 (t), 15.9 (q), 14.3 (q), 10.2 (q).

(±)-(1*S,2*S**)-1,2-Epoxy-2-methyl-1-phenyl-3-butene (24).** To a suspension of methyltriphenylphosphonium bromide (1.43 g, 4.0 mmol) in THF (10 mL) was added n-butyllithium (1.60 M, 1.88 mL, 3.0 mmol) over 5 min at 0 °C. The mixture was stirred at 60 °C for 30 min. The solution was cooled to 0 °C and (±)-(2*R**,3*S**)-2,3-epoxy-2-methyl-3-phenylpropanal (322 mg, 2.0 mmol) was added to the solution. The mixture was stirred for 30 min, and the solution was filtered. Water was added to the filtrate, and the organic layer was extracted with ether. The combined extracts were washed with saturated aqueous NH_4Cl, saturated aqueous $NaHCO_3$, and brine, dried over $MgSO_4$, and concentrated in vacuo. The residue was chromatographed on SiO_2 using a mixture of hexane–ether–$CHCl_3$–Et_3N (95.9:2:2:0.1) as an eluent to give **24** (59.6 mg, 19% yield): IR (neat) 2870 (s), 1640 (m), 1495 (m), 1450 (s), 1380 (s), 1060 (m), 990 (m), 925 (s), 750 (s), 700 (s) cm^{-1}; ^1H NMR (60 MHz, CCl_4) δ 7.23 (s, 5 H), 6.04–5.04 (m, 3 H), 3.75 (s, 1 H), 1.14 (s, 3 H). High-resolution mass spectrum for $C_{11}H_{12}O$, calcd m/z 160.0888, found m/z 160.0852.

2-Methyl-1-phenyl-3-buten-1-ol (25 and 26). According to the general procedure using ammonium formate (2 equiv) instead of a mixture of formic acid and Et_3N, hydrogenolysis of **24** (1.00 g) gave the mixture

of **25** and **26**[28] (0.91 g, 82% yield, **25**:**26** = 1:1): IR (neat) 3420 (s), 2970 (s), 1625 (s), 1455 (s), 1350 (s), 1200 (m), 990 (s), 920 (s), 770 (s), 710 (s) cm^{-1}; ^1H NMR (60 MHz, CCl_4) δ 7.15 (s, 5 H), 6.04–5.42 (m, 1 H), 5.15–4.71 (m, 2 H), 4.41 (d, J = 5.6 Hz, syn, 1 H), 4.26 (d, J = 6.4 Hz, anti, 1 H), 2.72–2.10 (m, 1 H), 0.92 (d, J = 6.0 Hz, 3 H), 0.85 (d, J = 6.0 Hz, 3 H).

(±)-(*Z*)-(1*S,2*S**)-1,2-Epoxy-2-methyl-1-phenyl-3-pentene (27).** According to a similar procedure for the preparation of **24**, reaction of (±)-(2*R**,3*S**)-2,3-epoxy-2-methyl-3-phenylpropanal (337 mg) with ethyltriphenylphosphonium bromide in THF gave **27** (130 mg, 36% yield): IR (neat) 2960 (m), 1675 (s), 1440 (m), 1115 (w), 950 (w), 850 (w), 700 (s) cm^{-1}; ^1H NMR (60 MHz, CCl_4) δ 7.17 (s, 5 H), 5.72–5.16 (m, 2 H), 3.77 (s, 1 H), 1.74 (d, J = 5.6 Hz, 3 H), 1.33 (s, 3 H); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 131.2 (d), 128.7 (s), 128.0 (d), 127.4 (d), 126.3 (d), 64.7 (d), 22.1 (d), 17.3 (q), 14.3 (q). High-resolution mass spectrum for $C_{12}H_{14}O$, calcd m/z 174.1045, found m/z 174.1034.

(±)-(*E*)-(1*R,2*R**)-2-Methyl-1-phenyl-3-penten-1-ol (28).** According to the general procedure, hydrogenolysis of **27** (100 mg) gave **28**[29] (75.4 mg, 75% yield): IR (neat) 3420 (s), 2960 (s), 1450 (s), 1020 (s), 970 (s), 765 (m), 705 (s) cm^{-1}; ^1H NMR (60 MHz, CCl_4) δ 7.19 (s, 5 H), 5.57–5.06 (m, 2 H), 4.18 (d, J = 7.2 Hz, 1 H), 2.48–1.91 (m, 1 H), 1.68 (d, J = 6.0 Hz, 3 H), 0.85 (d, J = 6.0 Hz, 3 H); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 133.2 (d), 128.0 (d), 127.7 (d), 127.4 (d), 126.8 (d), 126.1 (d), 78.1 (d), 45.4 (d), 18.1 (q), 17.0 (q). High-resolution mass spectrum for $C_{12}H_{16}O$, calcd m/z 176.2002, found m/z 176.1178.

Ethyl (*E*)-(4*S*,5*S*)-4,5-Epoxy-4-methyl-2-heptenoate (13). Optically active (*E*)-(4*S*,5*S*)-**13** ($[\alpha]^{24}_D$ = +34.7°, *c* 10.5, $CHCl_3$) was prepared from (2*S*,3*S*)-2,3-epoxy-2-methylpentan-1-ol[27] (lit.[27b] $[\alpha]^{22}_D$ = −14.3°, *c* 1.02, $CHCl_3$).

Ethyl (*E*)-(4*S*,5*S*)-5-Hydroxy-4-methyl-2-heptenoate (14). According to the general procedure, hydrogenolysis of (*E*)-(4*S*,5*S*)-**13** gave (*E*)-(4*S*,5*S*)-**14**: $[\alpha]^{24}_D$ = −31.7° (*c* 9.3, $CHCl_3$).

3,5-Dinitrobenzoate of (−)-14. Anal. Calcd for $C_{17}H_{20}O_8N_2$: C, 53.68; H, 5.30; N, 7.37. Found: C, 53.65; H, 5.52; N, 7.14.

(−)-(3*S*,4*S*)-4-Methyl-3-heptanol (22) from (*E*)-(4*S*,5*S*)-14. To a solution of the homoallylic alcohol (−)-**14** (2.10 g, 11.3 mmol) and a small amount of *p*-toluenesulfonic acid in CH_2Cl_2 was added 2,3-dihydropyran (1.72 mL, 19 mmol) at 0 °C, and the mixture was stirred for 30 min. Potassium carbonate (0.2 g) was added to the solution, and the mixture was filtered. The filtrate was concentrated in vacuo to give crude tetrahydropyranyl ether, which was used in the next step without purification.

The crude tetrahydropyranyl ether in THF (5 mL) was added to a suspension of $LiAlH_4$ (0.92 g, 24 mmol) in THF (20 mL) at room temperature, and the mixture was stirred for 2 h. Water was added to the mixture, and the organic layer was extracted with ether. The combined extracts were washed with brine, and the solution was dried over $MgSO_4$. The solvent was removed, and the residual crude alcohol **23** was used in the next step without purification.

A solution of the crude alcohol **23** and *p*-toluenesulfonyl chloride (2.9 g, 15 mmol) in pyridine (8 mL) was stirred for 1 h at 0 °C. Dilute hydrochloric acid (2 N) was added, and the organic layer was extracted with ether. The combined extracts were washed with saturated aqueous NH_4Cl and brine and dried over $MgSO_4$. The solvent was removed in vacuo, and the residue was chromatographed on SiO_2 using hexane–ether (90:10) as an eluent to give the sulfonyl ester (1.79 g, 41% yield from (−)-**14**): IR (neat) 2940, 1360, 1180 cm^{-1}; ^1H NMR (60 MHz, CCl_4) δ 7.8((d, J = 8.0 Hz, 2 H), 7.35 (d, J = 8.0 Hz, 2 H), 4.65 (s, 1 H), 4.18–3.25 (m, 5 H), 2.50 (s, 3 H), 2.00–1.20 (m, 13 H), 0.95 (t, J = 6.5 Hz, 3 H).

To a suspension of $LiAlH_4$ (33.5 mg, 0.9 mmol) in THF (5 mL) was added a solution of the sulfonyl ester (1.79 g, 4.6 mmol) in THF (2 mL), and the mixture was refluxed for 10 h. Water was added to the solution, and the organic layer was extracted with ether. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The residue was dissolved in ether, and dilute hydrochloric acid (3 N) was added to the solution. The mixture was stirred for 2 h at room temperature, and the organic layer was extracted with ether. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated. The residue was chromatographed on SiO_2 using hexane–ether (90:15) as an eluent to give (−)-(3*S*,4*S*)-**22** (35.1 mg, 31% yield): $[\alpha]^{22}_D$ = −19.4° (*c* 1.2, hexane) [lit.[26a] $[\alpha]_D$ = −21.7° (hexane)]; ^1H NMR (60 MHz, CCl_4) δ 3.40 (m, 1 H), 1.70–1.20 (m, 7 H), 1.20–0.75 (m, 9 H); ^{13}C NMR δ 76.7 (d), 37.5, 35.7, 27.3, 20.5, 14.3, 13.5, 10.6.

(2*S*,3*S*)-6,6-(2,2-Dimethylpropylenedioxy)-2,3-epoxy-2-methylheptan-1-ol (37). This compound was prepared according to the literature[33] in 45% yield from 6-methyl-5-hepten-2-one: $[\alpha]^{23}_D$ = −10.6° (*c* 7.9, EtOH) [lit. $[\alpha]^{25}_D$ = +9° (*c* 2.0, EtOH)]; IR (neat) 3425 (m), 2950 (s), 1460 (m), 1370 (m), 1245 (m), 1210 (m), 1085 (s), 1035 (s), 865 (m) cm^{-1}; ^1H NMR (60 MHz, CCl_4) δ 3.51 (d, J = 10.6, 2 H), 3.40 (d, J = 10.6, 2 H), 2.91 (t, J = 4.8 Hz, 1 H), 1.33 (s, 3 H), 1.27 (s, 3 H), 1.03 (s, 3 H), 0.87 (s, 3 H).

(2*R*,3*S*)-6,6-(2,2-Dimethylpropylenedioxy)-2,3-epoxy-2-methylheptanal (38). This compound was obtained from **37** by Swern oxidation in 73% yield: $[\alpha]^{23}_D$ = +70.4° (*c* 3.7, $CHCl_3$); IR (neat) 2955 (s), 2870 (s), 1730 (s), 1460 (m), 1380 (m), 1250 (m), 1215 (m), 1100 (s), 865 (m) cm^{-1}; ^1H NMR (60 MHz, CCl_4) δ 8.68 (s, 1 H), 3.51 (d, J = 11.0 Hz, 2 H), 3.30 (d, J = 11.0 Hz, 2 H), 3.07 (t, J = 3.0 Hz, 1 H), 1.99–1.58 (m, 4 H), 1.35 (s, 3 H), 1.33 (s, 3 H), 1.05 (s, 3 H), 0.82 (s, 3 H).

Ethyl (*E*)-(4*S*,5*S*)-8,8-(2,2-Dimethylpropylenedioxy)-4,5-epoxy-4-methyl-2-nonenoate (39). This compound **39** was prepared by a similar procedure as that for **10**. Emmons–Horner reaction of the epoxyaldehyde **38** (147 mg) gave **39** (171 mg, 90% yield): $[\alpha]^{24}_D$ = +5.5° (*c* 2.4, $CHCl_3$); IR (neat) 2950 (s), 2870 (m), 1720 (s), 1655 (m), 1560 (m), 1370 (m), 1300 (s), 1260 (s), 1175 (s), 1095 (s), 980 (m), 860 (m), 760 (m) cm^{-1}; ^1H NMR (60 MHz, CCl_4) δ 6.63 (d, J = 16.0 Hz, 1 H), 5.94 (d, J = 16.0 Hz, 1 H), 4.12 (q, J = 6.8 Hz, 2 H), 3.48 (d, J = 11.0 Hz, 2 H), 3.35 (d, J = 11.0 Hz, 2 H), 2.93–2.63 (m, 1 H), 1.94–1.57 (m, 4 H), 1.41 (s, 3 H), 1.31 (s, 3 H), 1.27 (t, J = 6.8 Hz, 3 H), 1.03 (s, 3 H), 0.83 (s, 3 H); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 165.8 (s), 149.7 (d), 121.3 (d), 98.2 (s), 70.3 (t), 65.7 (d), 60.3 (t), 58.5 (s), 35.1 (t), 29.8 (s), 22.8 (q), 22.4 (q), 20.0 (q), 15.1 (q), 14.2 (q).

Ethyl (*E*)-(4*S*,5*S*)-8,8-(2,2-Dimethylpropylenedioxy)-5-hydroxy-4-methyl-2-nonenoate (40). According to the general procedure, hydrogenolysis of **39** (239 mg) gave **40** (219 mg, 91% yield): $[\alpha]^{23}_D$ = +28.3° (*c* 2.2, $CHCl_3$); IR (neat) 3430 (m), 2950 (s), 2870 (m), 1710 (s), 1645 (m), 1455 (m), 1360 (m), 1260 (s), 1175 (s), 1090 (s), 950 (m), 750 (w) cm^{-1}; ^1H NMR (60 MHz, CCl_4) δ 6.87 (dd, J = 15.6, 7.8 Hz, 1 H), 5.73 (d, J = 15.6 Hz, 1 H), 4.13 (q, J = 6.4 Hz, 2 H), 3.53 (d, J = 11.2 Hz, 2 H), 3.35 (d, J = 11.2 Hz, 2 H), 2.22–2.10 (m, 2 H), 1.31 (s, 3 H), 1.25 (t, J = 6.4 Hz, 3 H), 1.04 (s, 3 H), 0.81 (s, 3 H); ^{13}C NMR (100.4 MHz, $CDCl_3$) δ 166.6 (s), 151.2 (d), 121.3 (d), 98.8 (s), 74.6 (d), 70.3 (t), 60.1 (t), 42.8 (d), 36.3 (t), 29.8 (s), 27.9 (t), 22.9 (q), 22.3 (q), 19.1 (q), 14.3 (q), 14.2 (q).

(*S*)-(−)-6,10-Dimethylundecan-2-one (36) from 40. To a solution of **40** (1.0 g, 3.3 mmol) in CH_2Cl_2 (50 mL) was added Et_3N (0.68 mL, 4.9 mmol). The mixture was cooled to 0 °C and methanesulfonyl chloride (283 μL, 3.6 mmol) was added over 5 min. To the solution was added 10% aqueous sodium hydroxide, and the organic layer was extracted with CH_2Cl_2. The combined extracts were washed with saturated aqueous NH_4Cl, saturated aqueous $NaHCO_3$, and brine, dried over $MgSO_4$, and concentrated. The crude sulfonate (1.3 g) was used in the next step without purification.

To a solution of the crude sulfonate in ether (2 mL) was added diisobutylaluminum hydride (1 M in hexane, 6.5 mL, 6.5 mmol) at 0 °C, and the mixture was stirred for 5 min. $LiAlH_4$ was added to the solution, and the mixture was stirred for 15 h. To the solution was added dilute hydrochloric acid (1 N), and the organic layer was extracted with ether. The combined extracts were washed with saturated aqueous NH_4Cl, saturated aqueous $NaHCO_3$, and brine, dried over $MgSO_4$, and concentrated. The residue was chromatographed on SiO_2 using a mixture of hexane–ethyl acetate–CH_2Cl_2 (60:20:20) as an eluent to give the allylic alcohol **41** (475 mg, 56% yield): $[\alpha]^{25}_D$ = −7.9° (*c* 4.9, $CHCl_3$); IR (neat) 3380, 2950, 2870, 1460, 1370, 1095, 790 cm^{-1}; ^1H NMR (60 MHz, CCl_4) δ 5.64–5.34 (m, 2 H), 3.94 (d, J = 2.4 Hz, 2 H), 3.40 (d, J = 10.0 Hz, 2 H), 3.33 (d, J = 10.0 Hz, 2 H), 1.26 (s, 3 H), 0.97 (s, 3 H), 0.84 (s, 3 H).

To a solution of the allylic alcohol **41** (475 mg, 1.86 mmol) in ether (3 mL) was added pyridine (0.24 mL, 3 mmol) and acetic anhydride (0.29 mL, 3 mmol) at room temperature, and the mixture was stirred for 2 h. To the solution was added dilute hydrochloric acid (1 N), and the organic layer was extracted with ether. The combined extracts were washed with saturated aqueous NH_4Cl, saturated aqueous $NaHCO_3$, and brine, dried over $MgSO_4$, and concentrated. The residue was chromatographed on SiO_2 using a mixture of hexane–ethyl acetate (95:5) as an eluent to give the allylic acetate **42** (492 mg, 89% yield): $[\alpha]^{25}_D$ = −8.5° (*c* 4.2, EtOH); IR (neat) 2940, 2860, 1735, 1450, 1360, 1230, 1090, 1030, 970, 860 cm^{-1}; ^1H NMR (60 MHz, CCl_4) δ 5.74–5.35 (m, 2 H), 4.42 (d, J = 4.2 Hz, 2 H), 3.45 (d, J = 11.0 Hz, 2 H), 3.34 (d, J = 11.0 Hz, 2 H), 1.97 (s, 3 H), 1.26 (s, 3 H), 0.99 (s, 3 H), 0.84 (s, 3 H).

To the solution of the allylic acetate **42** (91.9 mg, 0.31 mmol) in THF (2 mL) was added a mixture of anhydrous cupric chloride (0.83 mg, 6.2 μmol) and anhydrous lithium chloride (0.52 mg, 12.4 μmol) in THF (1 mL) at −40 °C. To the solution was added isopropylmagnesium bromide (1.51 N in THF, 1.0 mL, 1.51 mmol) over 5 min, and the mixture was stirred for 30 min. Water was added to the solution, and the organic layer was extracted with ether. The combined extracts were washed with saturated aqueous NH_4Cl, saturated aqueous $NaHCO_3$, and brine, dried over $MgSO_4$, and concentrated. The residue was chromatographed on

SiO_2 using a mixture of hexane–ether (95:5) as an eluent to give the (*R*)-olefin **43** (36.8 mg, 42% yield).

Hydrogen gas was bubbled into a mixture of the (*R*)-olefin **43** (151 mg, 536 μmol) and palladium on charcoal (5%, 83.6 mg, 42 μmol) in ethanol (1 mL), and the mixture was stirred for 16 h at room temperature. The solution was passed through Celite and concentrated. The residue was dissolved in acetone (5 mL). A catalytic amount of *p*-toluenesulfonic acid was added to the solution, and the mixture was stirred for 4 h at room temperature. Potassium carbonate was added to the solution, and the mixture was filtered. The filtrate was concentrated, and the residue was chromatographed on SiO_2 using a mixture of hexane–ether (from 98:2 to 95:5) as an eluent to give (*S*)-(−)-**36** (104 mg, 99% yield): $[\alpha]^{24}_D = -0.56°$ (*c* 3.6, EtOH);[34] IR (neat) 2950, 1720, 1465, 1365, 1165, 790 cm^{-1}.

(*Z*)-(5*S*,6*S*)-2,2-(2,2-Dimethylpropylenedioxy)-5,6-epoxy-6,10-dimethyl-7-undecene (44). According to a similar procedure for the preparation of **27**, reaction of **38** with isoamyltriphenylphosphonium iodide in THF gave **44** in 52% yield from **37**: $[\alpha]^{23}_D = +26.5°$ (*c* 5.7, $CHCl_3$); IR (neat) 2960 (s), 2875 (m), 1465 (m), 1370 (m), 1250 (m), 1215 (m), 1100 (s), 865 (m), 730 (w) cm^{-1}; ^1H NMR (60 MHz, CCl_4) δ 5.76–5.13 (m, 2 H), 5.56 (d, *J* = 11.6 Hz, 2 H), 3.43 (d, *J* = 11.6 Hz, 2 H), 1.39 (s, 3 H), 1.36 (s, 3 H); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 131.0 (d), 130.7 (d), 98.3 (s), 70.3 (t), 64.2 (d), 59.1 (s), 37.4 (t), 34.9 (t), 29.8 (s), 28.5 (d), 22.9 (q), 22.8 (q), 22.4 (q), 20.2 (q), 18.2 (q).

(*E*)-(5*S*,6*R*)-2,2-(2,2-Dimethylpropylenedioxy)-5-hydroxy-6,10-dimethyl-7-undecene (45). According to the general procedure, hydrogenolysis of **44** gave **45** (89% yield): $[\alpha]^{23}_D = +6.0°$ (*c* 1.5, $CHCl_3$); IR (neat) 3430 (s), 2950 (s), 1720 (m), 1460 (s), 1370 (s), 1090 (s), 970 (m), 850 (m) cm^{-1}; ^1H NMR (60 MHz, CCl_4) δ 5.34–5.10 (m, 2 H), 3.34 (b s, 4 H), 1.24 (s, 3 H), 0.96 (s, 3 H), 0.82 (s, 3 H); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 132.9 (d), 130.7 (d), 98.9 (s), 75.1 (d), 70.2 (t), 43.3 (d), 42.0 (t), 34.6 (t), 29.8 (s), 28.4 (d), 27.9 (t), 22.8 (q), 22.5 (q), 22.3 (q), 20.2 (q), 16.9 (q).

(*R*)-(+)-6,10-Dimethylundecan-2-one (36) from 45. To a solution of **45** (290 mg, 0.97 mmol) and Et_3N (202 μL, 1.46 mmol) in CH_2Cl_2 (15 mL) was added methanesulfonyl chloride (82.5 μL, 1.1 mmol) at −20 °C over 15 min. The mixture was stirred for 30 min. The usual workup gave the crude sulfonate, which was used in the next step without purification.

To the solution of the crude sulfonate in ether (5 mL) was added $LiAlH_4$ (18.4 mg, 0.48 mmol) at room temperature over 5 min and the mixture was stirred for 16 h. Dilute hydrochloric acid (3 N) was added to the solution, and the organic layer was extracted with ether. The combined extracts were washed with saturated aqueous $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated. The residue was chromatographed on SiO_2 using a mixture of hexane–ether (95:5) as an eluent to give the (*S*)-olefin **43** (157 mg, 61% yield): $[\alpha]^{22}_D = +6.85°$ (*c* 2.6, EtOH).

Similar to (*R*)-**43**, hydrogenation of (*S*)-olefin **43** (157 mg), followed by removal of the acetal group, gave (*R*)-(+)-**36** (108 mg, 99% yield): $[\alpha]^{22}_D = +0.59°$ (*c* 3.3, EtOH); ^1H NMR (60 MHz, CCl_4) 2.41 (t, *J* = 6.4 Hz, 2 H), 2.12 (s, 3 H), 0.87 (d, *J* = 5.8 Hz, 6 H); ^{13}C NMR δ 208.4, 44.0, 39.3, 37.1, 36.6, 32.7, 29.7, 28.0, 24.8, 22.7, 22.6, 21.5, 19.6.

General Procedure for the Palladium-Catalyzed Reaction of 10 with Formic Acid Using Various Ligands and Solvents (Tables I and II). A mixture of $Pd_2(dba)_3CHCl_3$ (26 mg, 0.025 mmol) and phosphine or phosphite in solvent (5 mL) was stirred for 5 min. A solution of formic acid (0.19 mL, 5.0 mmol) and Et_3N (0.28 mL, 2.0 mmol) in solvent (2 mL) was added to the mixture, and the mixture was stirred for 5 min. The oxirane **10** (232 mg, 1.0 mmol) in solvent (3 mL) was added, and the mixture was stirred at room temperature. The reaction was monitored by TLC. After the reaction was completed, water (10 mL) was added to the solution, and the aqueous phase was extracted with ether. The organic extract was washed with saturated aqueous $NaHCO_3$, saturated aqueous NH_4Cl, and brine, dried over $MgSO_4$, and concentrated. The crude residue was analyzed by gas chromatography. The products **11**, **46**, and **49–51** were separated by column chromatography on SiO_2 using hexane–ether. Physical and analytical data of the products are as follows.

Ethyl (*E*)-5-hydroxy-4-methyl-5-phenyl-3-pentenoate (46): TLC R_f 0.42 (hexane–ethyl acetate, 2:1); IR (neat) 3420 (s), 2975 (s), 1720 (s), 1490 (m), 1445 (m), 1370 (s), 1180 (s), 1020 (s), 750 (m), 700 (s) cm^{-1}; ^1H NMR (60 MHz, CCl_4) δ 7.18 (s, 5 H), 5.71 (t, *J* = 8.0 Hz, 1 H), 5.03 (s, 1 H), 4.05 (q, *J* = 7.0 Hz, 2 H), 3.22 (s, 1 H), 3.00 (d, *J* = 8.0 Hz, 2 H), 1.42 (s, 3 H), 1.22 (t, *J* = 7.0 Hz, 3 H); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 171.9 (s), 141.9 (s), 140.6 (s), 128.1 (d), 127.2 (d), 126.2 (d), 117.8 (d), 78.6 (d), 60.6 (t), 33.3 (t), 14.2 (q), 12.3 (q). High-resolution mass spectrum for $C_{14}H_{18}O_3$, calcd *m/z* 234.1256, found *m/z* 234.1263.

Ethyl (*E*)-5-hydroxy-4-methylene-5-phenyl-2-pentenoate (49): TLC R_f 0.44 (hexane–ethyl acetate, 2:1); IR (neat) 3420 (s), 2950 (m), 1700 (s), 1620 (m), 1440 (m), 1355 (m), 1300 (s), 1260 (s), 1165 (s), 1020 (s), 970 (m), 910 (w), 855 (m), 750 (m), 690 (s) cm^{-1}; ^1H NMR (60 MHz, CCl_4) δ 7.20 (s, 5 H), 7.15 (d, *J* = 7.0 Hz, 1 H), 5.76 (d, *J* = 7.0 Hz, 1 H), 5.59 (s, 1 H), 5.50 (s, 1 H), 5.28 (s, 1 H), 3.98 (q, *J* = 8.0 Hz, 2 H), 3.46 (s, 1 H), 1.22 (t, *J* = 8.0 Hz, 3 H). High-resolution mass spectrum for $C_{14}H_{16}O_3$, calcd *m/z* 232.1100, found *m/z* 232.1066.

Ethyl (*E*)-4-methyl-5-oxo-5-phenyl-3-pentenoate (50): TLC R_f 0.58 (hexane–ethyl acetate, 2:1); IR (neat) 1750 (s), 1665 (s), 1470 (m), 1390 (m), 1290 (s), 1200 (s), 1050 (m), 730 (s) cm^{-1}; ^1H NMR (60 MHz, CCl_4) δ 7.70–7.20 (m, 5 H), 6.23 (t, *J* = 7.0 Hz, 1 H), 4.07 (q, *J* = 7.0 Hz, 2 H), 3.16 (d, *J* = 7.0 Hz, 2 H), 1.91 (s, 3 H), 1.23 (t, *J* = 7.0 Hz, 3 H); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 197.8 (s), 170.0 (s), 138.4 (s), 137.7 (s), 135.6 (d), 131.5 (d), 129.3 (d), 127.9 (d), 60.9 (t), 34.3 (t), 14.1 (q), 12.8 (q). High-resolution mass spectrum for $C_{14}H_{16}O_3$, calcd *m/z* 232.1100, found *m/z* 232.1093.

Ethyl (*E*)-4-(formyloxy)-5-hydroxy-4-methyl-5-phenyl-2-pentenoate (51): TLC R_f 0.37 (hexane–ethyl acetate, 2:1); IR (neat) 3450 (s), 2975 (m), 1710 (s), 1450 (m), 1370 (m), 1300 (s), 1160 (s), 1030 (m), 990 (m), 870 (w), 760 (w), 700 (m) cm^{-1}; ^1H NMR (60 MHz, CCl_4) δ 7.92 (s, 1 H), 7.20 (s, 5 H), 6.88 (d, *J* = 16.0 Hz, 1 H), 5.94 (d, *J* = 16.0 Hz, 1 H), 5.68 (s, 1 H), 4.18 (q, *J* = 7.0 Hz, 2 H), 3.10 (s, 1 H), 1.22 (t, *J* = 7.0 Hz, 3 H), 1.22 (s, 3 H); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 166.0 (s), 159.5 (d), 150.5 (d), 135.0 (s), 128.6 (d), 128.1 (d), 79.9 (d), 74.5 (s), 60.5 (t), 24.2 (q), 14.1 (q).

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Total Synthesis of the Highly Oxygenated Quassinoid (±)-Klaineanone

Paul A. Grieco,* Ravi P. Nargund, and David T. Parker[1]

Contribution from the Department of Chemistry, Indiana University, Bloomington, Indiana 47405. *Received January 20, 1989*

Abstract: The total synthesis of klaineanone (**1**), isolated from the seeds of *Hannoa klaineana*, is described in racemic form. The synthesis commences with the tetracyclic ketone **6**, which is transformed into tetracyclic olefinic lactone **23**, which possesses the correct configuration at C(9). Incorporation of the ring A 1β-hydroxy-2-oxo-$\Delta^{3,4}$ olefin unit into tetracyclic olefinic lactone **23**, which features a Rubottom epoxidation of silyloxy diene **35** followed by a base-catalyzed tautomerism of the resultant hydroxy ketone **36**, provides tetracyclic olefin **37**. Epoxidation of the C(11), C(12) olefin in tetracyclic compound **37** and subsequent acid-catalyzed ring opening affords *dl*-klaineanone.

The highly oxygenated carbon skeleton of quassinoids[2] coupled with their complex stereochemical arrangement of carbon atoms continues to present a formidable synthetic challenge to the organic chemist despite the advances made during the past 15 years.[3] One

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