Highly Stereocontrolled Total Synthesis of Leukotriene B_4, 20-Hydroxyleukotriene B_4, Leukotriene B_3, and Their Analogues

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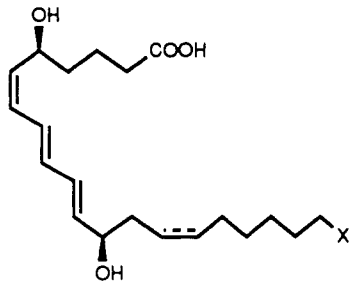
A highly stereocontrolled and practical new method for synthesis of LTB_4 (1), 20-OH-LTB_4 (2), and LTB_3 (3) has been developed, which uses the palladium-catalyzed coupling reaction of the vinylborane **5**, derived from the C(1)–C(9) fragment **4**, with the corresponding C(10)–C(20) fragments **6a–c**. The acetylene **4** was synthesized by palladium–copper-catalyzed coupling reaction of (trimethylsilyl)acetylene with the bromide **12**, which was prepared from γ-(trimethylsilyl)allylic alcohol (*S*)-**10** by bromination followed by debromosilylation. The alcohol (*S*)-**10** was obtained by the kinetic resolution of the racemate *dl*-**10** using the Sharpless reagent. The vinyl iodides **6a** and **6b** were prepared from racemic γ-(trimethylsilyl)allylic alcohols *dl*-**17** and *dl*-**28**, respectively, by the Sharpless kinetic resolution followed by the reactions taking advantage of the reactivity of vinylsilane moiety, while the segment **6c** was prepared by the Sharpless kinetic resolution of racemic γ-iodoallylic alcohol *dl*-**34** followed by protection. By using this method, precursors of the radiolabeled LTB_4 and 20-OH-LTB_4, i.e., 14,15-didehydro-LTB_4 (**40**) and 14,15-didehydro-20-OH-LTB_4 (**41**), respectively, were also synthesized. Similarly the novel structural analogues of LTB **42–44** were prepared.

In the past several years, the leukotriene cascade has attracted much interest in the scientific community because of the biologically important nature of these molecules.[1] Among the rest, leukotriene B_4 (LTB_4, 1), biosynthesized from arachidonic acid via the 5-lipoxygenase pathway, has been shown to be one of the most potent inducers of chemotaxis, chemokinesis, aggregation, and degranulation of leukocytes.[2] LTB_4 is rapidly oxidized



LTB_4 (**1**): X = H, $\Delta^{14,15}$
20-OH-LTB_4 (**2**): X = OH, $\Delta^{14,15}$
LTB_3 (**3**): X = H, 14,15-dihydro

in vivo by hydroxylation at C-20 to provide 20-hydroxyleukotriene B_4 (20-OH-LTB_4, **2**).[3] 5,8,11-Eicosatrienoic acid is also metabolized in vivo into LTB_3 (**3**) via the 5-lipoxygenase pathway and has been reported to possess similar biological activities to LTB_4.[4] Since these LTBs **1–3** are available in minute quantity from biological sources, their chemical synthesis has attracted much interest in recent years for further evaluation of their biological properties, and several total syntheses have been reported.[5-7] Despite their elegance, however, these syntheses have certain drawbacks such as lengthy reaction sequences, low selectivity, and/or low overall yield. Herein we report a short and completely stereocontrolled approach to the synthesis of LTB_4, 20-OH-LTB_4, and LTB_3.[8] By using this approach, we also synthesized 14,15-didehydro-LTB_4, 14,15-didehydro-20-OH-LTB_4, and some novel structural analogues of LTB.

Our synthesis of LTBs **1–3** is summarized in Scheme I. The characteristic feature of our synthesis is the stereospecific construction of the 6-cis,8-trans,10-trans conjugated triene unit of LTBs **1–3** from the acetylene **4** and the corresponding trans vinyl iodides **6a–c** according to the procedure developed by Suzuki and his co-workers.[9] The highly enantioselective and practical preparation of the chiral fragments **4** and **6a–c** using the kinetic resolution of γ-heteroatom-substituted allylic alcohols by the Sharpless asymmetric epoxidation is another characteristic feature.[10,11]

The enantiomerically pure compound **4** was synthesized as outlined in Scheme II. Addition reaction of **8**[12] with **9** (M = $AlEt_2$)[13] afforded racemic allylic alcohol *dl*-**10** in

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(8) For a preliminary communication, see: Kobayashi, Y.; Shimazaki, T.; Sato, F. *Tetrahedron Lett.* **1987**, *28*, 5849.

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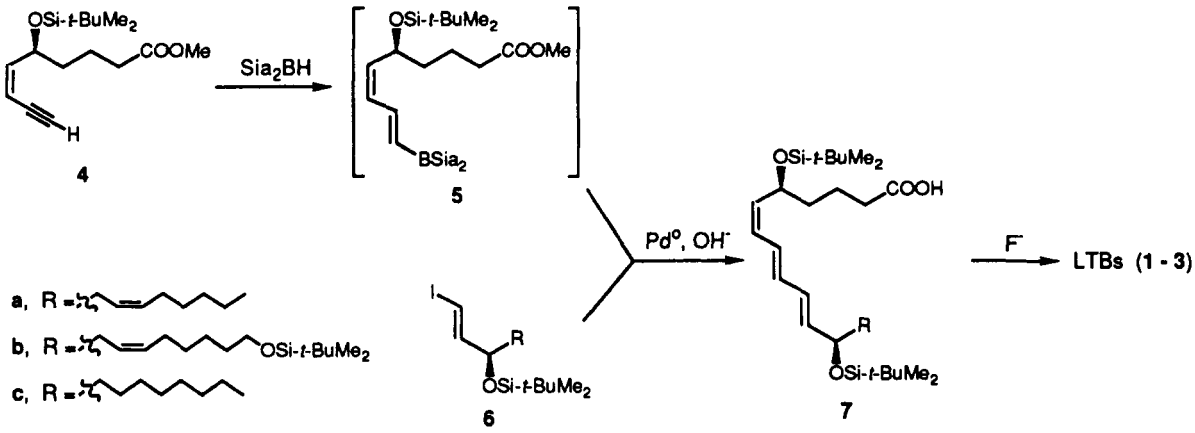
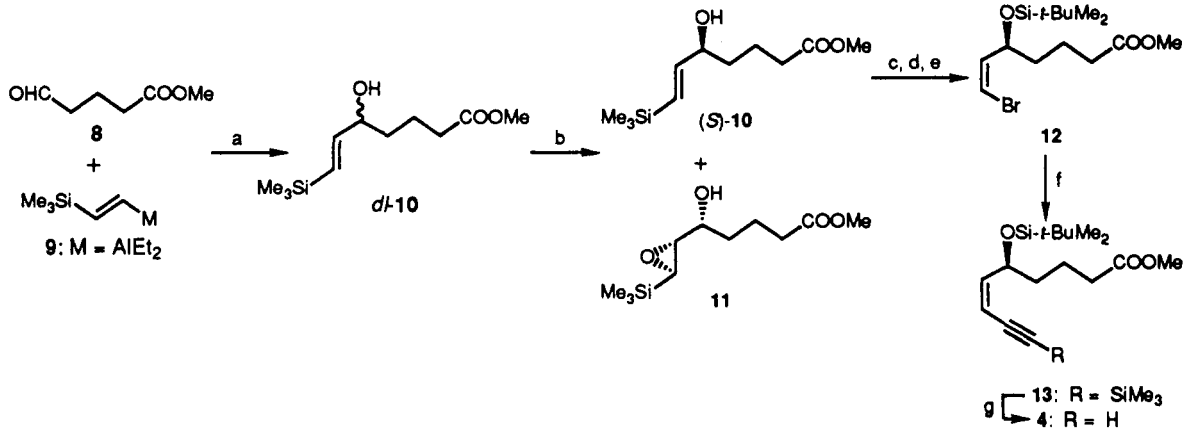
Scheme I



Scheme II[a]



[a] (a) THF, −78 °C to room temperature, then cat. NaOMe, MeOH; (b) Ti(O-*i*-Pr)$_4$ (1.0 equiv), D-(−)-DIPT (1.2 equiv), *t*-BuOOH (1.5 equiv), −21 °C, 21 h; (c) Br_2, CH_2Cl_2, −70 °C; (d) *n*-Bu_4NF, THF, −70 °C; (e) *t*-$BuMe_2SiCl$, imidazole, DMF; (f) $Me_3SiC{\equiv}CH$ (2.0 equiv), *n*-$PrNH_2$ (3.0 equiv), $Pd(PPh_3)_4$ (0.03 equiv), CuI (0.07 equiv), PhH; (g) KCN (7.0 equiv), $AgNO_3$ (4.0 equiv), THF–EtOH–H_2O (1:1:1).

65% yield, which was subjected to the kinetic resolution using the Sharpless reagent (*t*-BuOOH, Ti(O-*i*-Pr)$_4$, and D-(−)-DIPT) to provide the alcohol (*S*)-**10** (>99% ee) and the epoxy alcohol **11** (>99% ee) in 43% and 45% yields, respectively.[10] The alcohol (*S*)-**10** thus prepared was transformed into cis bromide **12** stereospecifically in 74% overall yield by the three-step reactions of bromination, debromosilylation with *n*-Bu_4NF, and protection with *t*-$BuMe_2SiCl$.[14] The coupling reaction of **12** with (trimethylsilyl)acetylene using $Pd(PPh_3)_4$ and CuI as catalysts in benzene–*n*-$PrNH_2$ at room temperature afforded **13** quantitatively.[15,16] Selective desilylation of **13** with KCN and $AgNO_3$[16] at 0 °C produced the key fragment **4** in 95% yield. The compound **4** thus prepared was homogeneous by ^1H and ^{13}C NMR spectroscopy and the enantiomeric excess of **4** was confirmed to be >99% by ^1H NMR spectroscopy of the corresponding MTPA ester.[17]

Synthesis of the iodide **6a**, the requisite fragment for synthesis of LTB_4 (**1**), is summarized in Scheme III. The hydromagnesiation reaction[18] of acetylene **14**, prepared quantitatively by reaction of bromoacetaldehyde diethyl acetal with the lithium anion of 1-heptyne, using *i*-BuMgBr and a catalytic amount of Cp_2TiCl_2 afforded stereospecifically cis olefin **15** in 81% yield. Noteworthy here is the fact that semi-hydrogenation of **14** using Pd on $BaSO_4$ poisoned with quinoline resulted in the contamination of ca. 5% of the trans isomer. Hydrolysis of **15** with aqueous oxalic acid afforded **16**,[19] which was in turn reacted with the anion **9** (M = Li) to give racemic allylic alcohol *dl*-**17** in 75% yield. Kinetic resolution of *dl*-**17** using *t*-BuOOH, Ti(O-*i*-Pr)$_4$, and L-(+)-DIPT afforded (*R*)-**17** (>99% ee) and **18** (>99% ee) in 44% and 43% yields, respectively.[10] Regioselective epoxidation of (*R*)-**17** using *t*-BuOOH, Ti(O-*i*-Pr)$_4$, and D-(−)-DIPT and subsequent protection with *t*-$BuMe_2SiCl$ afforded **19** in 86% yield.[20] Reaction of the epoxide **19** with *n*-Bu_3SnLi in THF at 0 °C resulted in regiospecific ring opening and in situ Peterson olefination reaction to furnish **20**, which upon treatment with I_2 afforded the key intermediate **6a** in 90% yield from **19**. The enantiomeric excess of **6a** thus prepared was confirmed to be >99% by ^1H NMR spectroscopy of the corresponding MTPA ester.[17] The epoxide **18** was also converted into **6a** in high overall yield. Thus, the Mitsunobu inversion[21] of **18** followed by hydrolysis and

(13) Aluminum anion **9** (M = $AlEt_2$) gave a better yield of *dl*-**10** than lithium anion **9** (M = Li).

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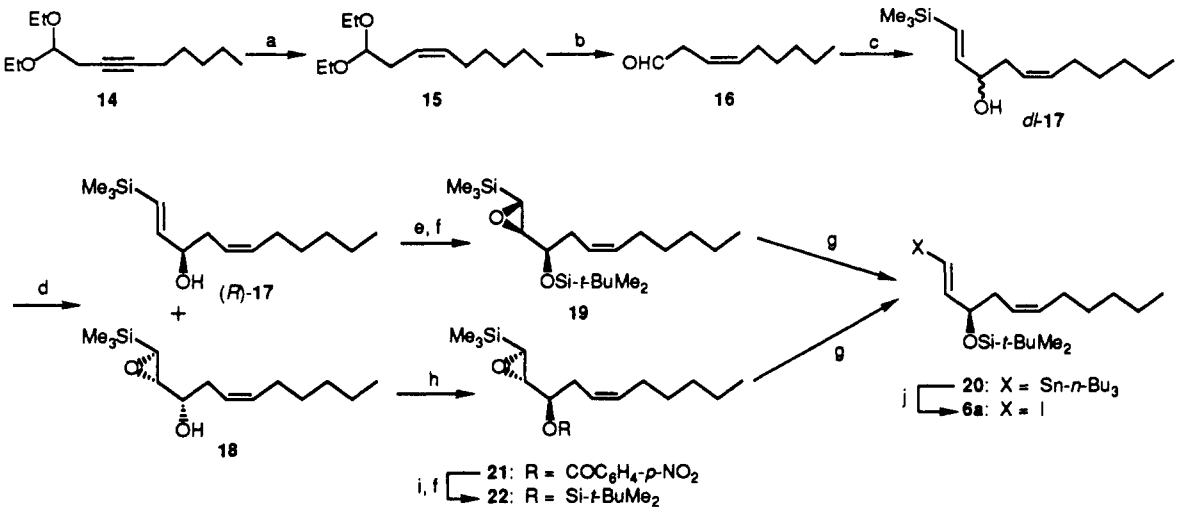
(20) Epoxidation of (*R*)-**17** by using *t*-BuOOH/VO(acac)$_2$ or *t*-BuOOH/Ti(O-*i*-Pr)$_4$ afforded the diepoxide in addition to the desired monoepoxide.

Scheme III[a]



[a] (a) *i*-BuMgBr, cat. Cp_2TiCl_2, Et_2O, 26 to 28 °C; (b) $(COOH)_2$, acetone–H_2O (4:1), 60 °C, 2 h; (c) **9** (M = Li), THF, 178 to 0 °C; (d) Ti(O-*i*-Pr)$_4$ (1.0 equiv), L-(+)-DIPT (1.2 equiv), *t*-BuOOH (1.5 equiv), −21 °C, 3.5 h; (e) Ti(O-*i*-Pr)$_4$ (0.3 equiv), D-(−)-DIPT (0.37 equiv), *t*-BuOOH (2 equiv), 4A molecular sieves, −21 °C, 4 h; (f) *t*-BuMe$_2$SiCl, imidazole, DMF; (g) LDA (1.4 equiv), *n*-Bu_3SnH (1.05 equiv), THF, 0 °C, 3 h; (h) Ph_3P (1.5 equiv), (=NCOOEt)$_2$ (1.6 equiv), *p*-$NO_2C_6H_4COOH$ (1.4 equiv), 0 °C, 1 h; (i) 2 N NaOH, THF–MeOH (1:1), 0 °C, 1 h; (j) I_2 (1.05 equiv), Et_2O, 0 °C, 0.5 h.

protection afforded **22** in 88% yield. Reaction of **22** with *n*-Bu_3SnLi followed by iodination with I_2 yielded **6a** (>99% ee) in 96% yield.

Preparation of **6b**, the intermediate for synthesis of 20-OH-LTB_4 (**2**), is shown in Scheme IV. Reaction of the aldehyde **23**[22] with propargyl bromide in the presence of Zn dust (1.2 equiv) and $TiCl_4$ (0.005 equiv) in THF at 0 °C afforded the acetylene **24**, the hydroxyl group of which was protected with ethyl vinyl ether to afford **25** quantitatively. Alkylation of **25** with $I(CH_2)_5OEE$ (EE, α-ethoxyethyl) furnished **26** in 80% yield. Cis reduction of **26** via hydroboration with Sia_2BH followed by deprotection with 3 N HCl afforded a 71% yield of **27**, which upon selective protection with *t*-$BuMe_2SiCl$ gave racemic alcohol *dl*-**28** in 88% yield. The Sharpless kinetic resolution of *dl*-**28** with *t*-BuOOH, Ti(O-*i*-Pr)$_4$, and D-(−)-DIPT produced (*S*)-**28** (>99% ee) in 43% yield and **29** (>99% ee) in 42% yield. Both products were converted into the iodide **6b** in 72% and 93% overall yields, respectively, by the same sequence of the reactions described for the preparation of **6a**.

The fragment **6c** (>99% ee), corresponding to C(10)–C(20) portion of LTB_3 (**3**), was synthesized quantitatively by protection of (*R*)-**34**, which was prepared in 44% (88% of theory) yield by the Sharpless kinetic resolution of racemic 1-iodo-1(*E*)-undecen-3-ol (*dl*-**34**),[11] obtained from nonanoyl chloride (**33**) by the literature procedure (Scheme V).[23]

With the segments **4** and **6a–c** in hand, we carried out the coupling reaction[9] (Scheme I). Thus, **4** was reacted with Sia_2BH (1.5 equiv) in THF at 0 °C for 1 h. To this solution were added aqueous 2 N LiOH (7 equiv), **6a** (1.4 equiv), and Pd(PPh$_3$)$_4$ (0.05 equiv) successively. The resulting mixture was stirred at 40 °C for 18 h under argon to afford the coupling product **7a** in 68–76% yield after chromatography on silica gel. The compound **7a** thus obtained was found to be homogeneous by ^1H and ^{13}C NMR spectroscopy and also by TLC. Finally, deprotection of **7a** with excess *n*-Bu_4NF in THF under argon followed by chromatography on silica gel provided a 79–85% yield

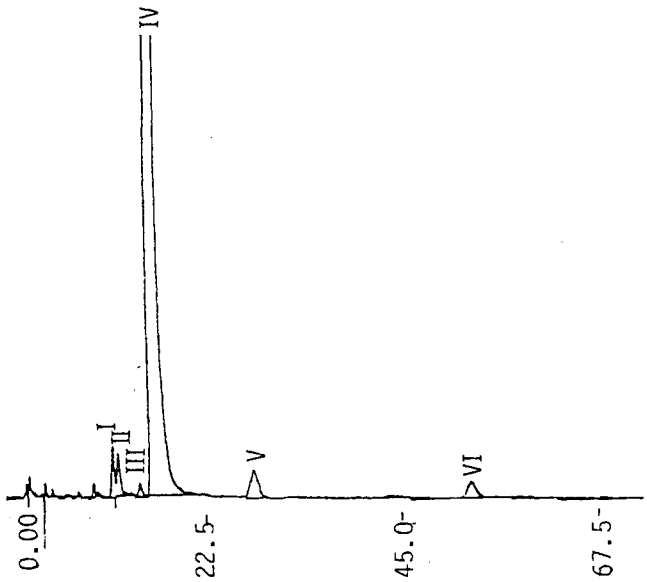


Figure 1. RP-HPLC analysis of synthetic LTB_4: column, Beckman Ultrasphere ODS, 5-μm, 250 × 4.6 mm; mobile phase, MeOH–H_2O–NH_4OH–AcOH (66:33:0.08:0.08); flow rate, 0.8 mL/min.

Table I. RP-HPLC Data of Synthetic LTB_4

peak	t_R	rel ratio (%)	compd
I	12.2	0.4	**36**
II	12.9	0.5	**37** and/or **38**
III	15.3	0.1	**35**
IV	16.8	97.7	**1**
V	28.4	0.6	nd[a]
VI	53.4	0.5	**39**

[a] Not determined.

of LTB_4 (**1**, mp 25–28 °C (recrystallized from hexane–Et_2O), $[\alpha]^{25}_D$ +13.1° (*c* 0.26, $CDCl_3$); lit.[5g] $[\alpha]^{25}_D$ +12.6° (*c* 0.46, $CDCl_3$)). Spectroscopic data (IR and ^1H NMR) of **1** thus synthesized were in good agreement with those reported[5f,g] and the ^{13}C NMR spectrum of **1** supported the structure. The chemical purity of **1** (even before recrystallization) was found to be >95% by RP-HPLC analysis (Figure 1) and the retention time of **1** was identical with

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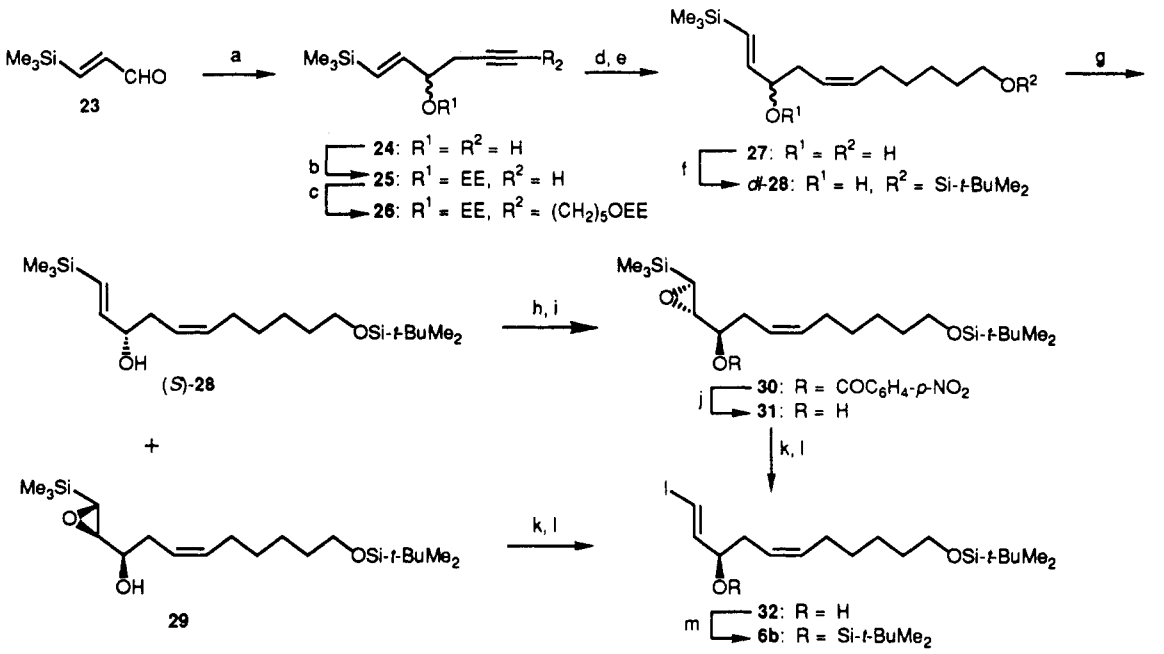
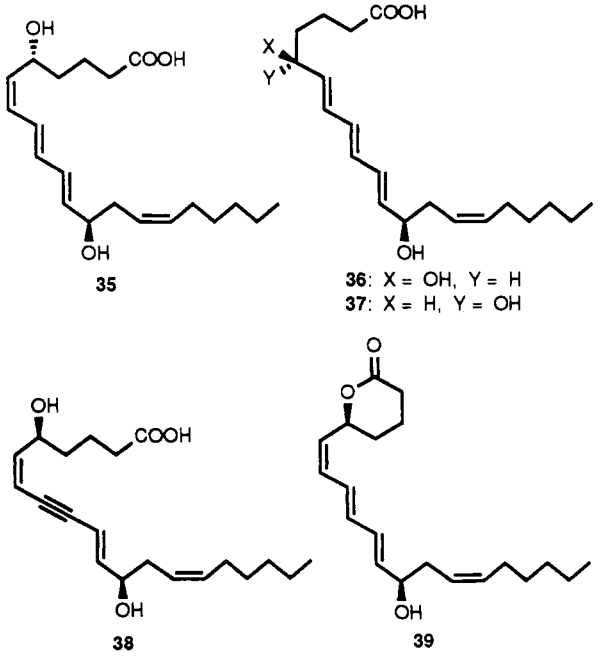
(22) Jung, M. E.; Gaede, B. *Tetrahedron* **1979**, *35*, 621.
(23) Luo, F.-T.; Negishi, E. *J. Org. Chem.* **1985**, *50*, 4762.

Scheme IV[a]



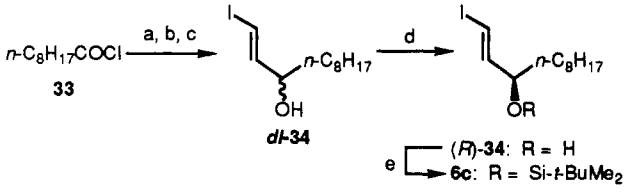
[a] (a) Propargyl bromide (1.5 equiv), Zn (1.5 equiv), cat. $TiCl_4$, 0 °C to room temperature; (b) ethyl vinyl ether, PPTS; (c) *n*-BuLi (1.05 equiv), $I(CH_2)_5OEE$ (1.3 equiv), HMPA (2.0 equiv), THF, −78 °C to room temperature; (d) Sia_2BH, 0 °C, 1 h, then AcOH, 25 °C, 4 h; (e) 3 N HCl, MeOH; (f) *t*-$BuMe_2SiCl$ (1.2 equiv), pyridine (1.5 equiv), CH_3CN, 0 °C; (g) $Ti(O\text{-}i\text{-}Pr)_4$ (1.0 equiv), D-(−)-DIPT (1.2 equiv), *t*-BuOOH (1.5 equiv), CH_2Cl_2, −21 °C, 16 h; (h) $Ti(O\text{-}i\text{-}Pr)_4$ (1.0 equiv), L-(+)-DIPT (1.2 equiv), *t*-BuOOH (1.5 equiv), −21 °C; (i) *p*-NOC_6H_4COOH (2.0 equiv), $(=NCOOEt)_2$ (1.7 equiv), PPh_3 (1.9 equiv), THF, 0 °C, 1 h; (j) 1 N NaOH, MeOH, 0 °C, 1 h; (k) LDA (4.0 equiv), *n*-BuSnH (1.6 equiv), THF, 0 °C, 3 h; (l) I_2 (1.2 equiv), Et_2O, 0 °C; (m) *t*-$BuMe_2SiCl$, imidazole, DMF.

that of authentic LTB_4. The compounds corresponding to the minor peaks (I–III, VI) of Figure 1 were assigned as summarized in Table I by comparison of the retention times with those of the authentic compounds **35–39**, which were prepared unambiguously as described below. Compound **35**, 5*R* epimer of **1**, was prepared as a 1:1 mixture with **1** from racemic acetylene *dl*-**4** and the iodide **6a** (>99% ee) by the procedure shown in Scheme I. Isomerization of a mixture of **1** and **35** in the presence of a catalytic amount of I_2 afforded a mixture of **36** and **37** (isomerization of pure **1** with I_2 gave **36**). 8,9-Di-



dehydro-LTB_4 **38** was prepared by the coupling reaction[15] of **4** with **6a** in the presence of $Pd(PPh_3)_4$ (0.1 equiv) and

Scheme V[a]



[a] (a) HC≡CH, $AlCl_3$ (1.4 equiv), 0 °C; (b) NaI (1.6 equiv), cat. $AlCl_3$, acetone, reflux; (c) $NaBH_4$, EtOH, 0 °C; (d) $Ti(O\text{-}i\text{-}Pr)_4$ (0.3 equiv), L-(+)-DIPT (0.37 equiv), *t*-BuOOH (1.5 equiv), −21 °C, 40 h; (e) *t*-$BuMe_2SiCl$, imidazole, DMF.

CuI (0.2 equiv) in benzene–*n*-Pr_2NH followed by deprotection with *n*-Bu_4NF. δ-Lactone **39**[24] was prepared by dehydration of **1** at 50 °C under vacuum (0.1 mmHg).

Similarly, hydroboration of **4** followed by the coupling reaction with the iodides **6b** and **6c** furnished after desilylation a 67% yield of 20-OH-LTB_4 (**2**) ($[\alpha]^{20}_D$ +9.4° (*c* 0.50, MeOH)) and a 74% yield of LTB_3 (**3**) ($[\alpha]^{21}_D$ +7.8° (*c* 0.23, $CDCl_3$)) (Scheme I), respectively. Chemical purities of **2** and **3** thus prepared were found to be 96% and 97%, respectively, (RP-HPLC analysis) and spectral data support their structures. Although syntheses of **2**[6] and **3**[7] have been published previously, their spectral and physical properties were not reported presumably due to the difficulty in obtaining a sufficient quantity of them. With **2** and **3** in hand, we could record for the first time their $[\alpha]_D$, molar absorption coefficient (ϵ) of λ_{max}, and ^1H NMR, ^{13}C NMR, and IR data (see Experimental Section).

As described above the present method for synthesis of LTBs **1–3** provides a general and practical entry into structurally related compounds. Thus, we were interested in synthesizing the LTB analogues **40–44** for of the fol-

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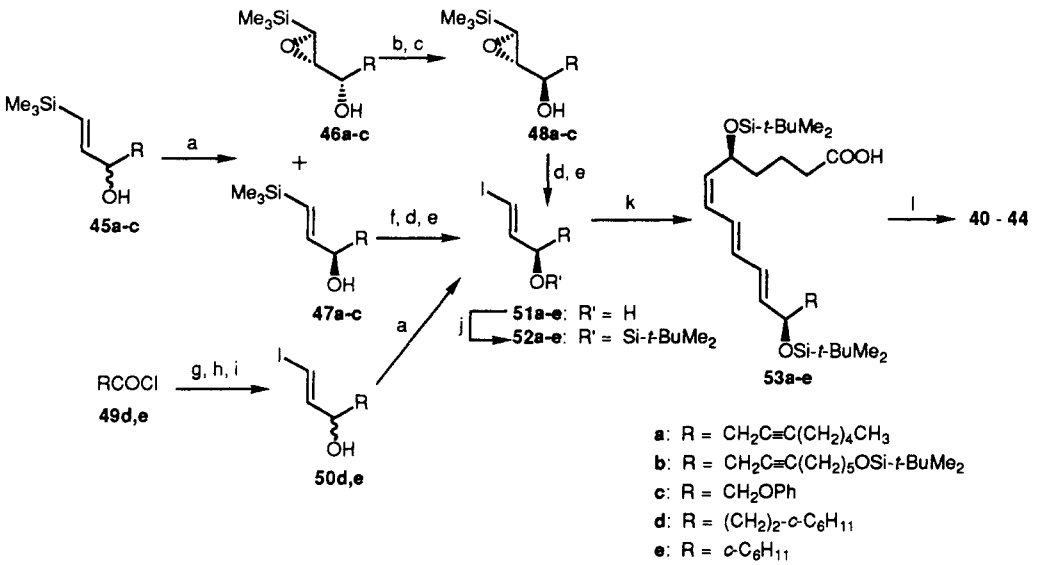
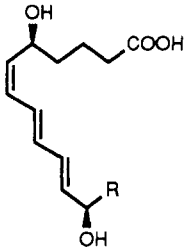
Scheme VI[a]



a: R = $CH_2C{\equiv}C(CH_2)_4CH_3$
b: R = $CH_2C{\equiv}C(CH_2)_5OSi$-*t*-$BuMe_2$
c: R = CH_2OPh
d: R = $(CH_2)_2$-*c*-C_6H_{11}
e: R = *c*-C_6H_{11}

[a] (a) Ti(O-*i*-Pr)$_4$, L-(+)-DIPT, *t*-BuOOH, CH_2Cl_2); (b) (=NCOOEt)$_2$, *p*-$NO_2C_6H_4COOH$, PPh_3, THF; (c) 1 N NaOH, MeOH; (d) LDA, *n*-Bu_3SnH, THF; (e) I_2, Et_2O; (f) *t*-BuOOH, VO(acac)$_2$ or Ti(O-*i*-Pr)$_4$; (g) HC≡CH, $AlCl_3$, CCl_4; (h) NaI, cat. $AlCl_3$ acetone; (i) $NaBH_4$, EtOH; (j) *t*-$BuMe_2SiCl$, imidazole, DMF; (k) **5**, $Pd(PPh_3)_4$, LiOH, THF–H_2O; (l) *n*-Bu_4NF, THF.

lowing reasons. 14,15-Didehydro-LTB$_4$ (**40**) and 14,15-didehydro-20-OH-LTB$_4$ (**41**) are precursors of 14,15-



40: R = $CH_2C{\equiv}C(CH_2)_4CH_3$
41: R = $CH_2C{\equiv}C(CH_2)_5OH$
42: R = CH_2OPh
43: R = $(CH_2)_2$-*c*-C_6H_{11}
44: R = *c*-C_6H_{11}

[^{3}H]LTB$_4$ and 14,15-[^{3}H]-20-OH-LTB$_4$, respectively, both of which are important radiolabeled materials for biological studies.[25] The analogues **42**–**44** lack a methyl group at C-20, which is susceptible to ω-oxidation in vivo,[3] thus they are expected to act as stable agonists of LTB$_4$. The synthetic route to **40**–**44**, which was found to proceed successfully, is summarized in Scheme VI. The iodides **52a**–**c**, requisite intermediates for synthesis of **40**–**42**, were prepared by using the Sharpless kinetic resolution of racemic γ-(trimethylsilyl)allylic alcohols **45a**–**c** as the key step, while the iodides **52d,e**, intermediates for synthesis of **43** and **44**, were prepared by the Sharpless kinetic resolution of racemic γ-iodoallylic alcohols **50d,e**. The coupling reaction of the iodides **52a**–**e** with the C(1)–C(9) fragment **4** provided **40**–**44** after desilylation in good yields.

In conclusion, we have succeeded in developing an efficient and stereoselective new method for the synthesis of LTB$_4$ (**1**), 20-OH-LTB$_4$ (**2**), and LTB$_3$ (**3**). We have also shown that this method can be applicable to the synthesis of a wide variety of structural analogues, which is demonstrated by the synthesis of **40**–**44**. With a sufficient amount of LTBs (**1**, **2**, and **3**), we could measure for the first time $[\alpha]_D$ values and spectral (λ_{max} (ϵ), ^{1}H NMR, and ^{13}C NMR) data of 20-OH-LTB$_4$ (**2**) and LTB$_3$ (**3**) as well as ^{13}C NMR data of LTB$_4$ (**1**). The biological evaluation of new LTB analogues **42**–**44** will be reported in due course.[26]

Experimental Section

General. ^{1}H NMR spectra were recorded on a Hitachi R-40 (90 MHz), a JEOL FX-90Q (90 MHz), a Varian NMRG-200 (200 MHz), or a Varian VXR-500S (500 MHz) instrument. Chemical shifts are reported in ppm (δ) downfield from Me_4Si (δ = 0 ppm) or residual $CHCl_3$ (δ = 7.26 ppm) as an internal standard unless otherwise noted. Signal patterns are indicated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br s, broad singlet. Coupling constants (*J*) are given in hertz. ^{13}C NMR spectra were obtained on a JEOL FX-90Q (22.5 MHz) or a Varian NMRG-200 (50 MHz) instrument. IR spectra were recorded on a JASCO A-100 spectrophotometer. Optical rotations were measured on a YANAKO OR-50 polarimeter. RP-HPLC analyses were carried out on a NSP-800-9DX (Nihon Seimitsu Kagaku Co., Ltd.) instrument with a Beckman Ultrasphere ODS (4.6 × 250 mm, 5 μm) and a Soma UV-VIS/S-7302 detector at 280 nm. Elemental analyses were performed at the Research Laboratory of Resources Ultilization, Tokyo Institute of Technology, and high-resolution mass spectra (HRMS) were obtained at Nissan Chemical Industries, Ltd.

All reactions sensitive to oxygen or moisture were carried out under an argon atmosphere. Column chromatography was conducted by using Wakogel C-200 or C-300 (silica gel, Wako Pure Chemical Industries Ltd.).

Materials. Diethyl ether and tetrahydrofuran (THF) were freshly distilled from sodium benzophenone ketyl. Dichloromethane was freshly distilled from calcium hydride. Hexamethylphosphoric triamide (HMPA) was distilled from calcium hydride and stored over calcium hydride. *N*,*N*-Dimethylformamide (DMF) and diisopropylamine were dried over calcium hydride. A stock solution of *t*-BuOOH in CH_2Cl_2 was prepared and stored as described by Sharpless.[27] Disiamylborane (Sia_2BH) was freshly prepared before use according to the procedure of Brown.[28] (Trimethylsilyl)acetylene and *trans*-1-(trimethylsilyl)-2-(tri-*n*-butylstannyl)ethylene were prepared by the literature procedures,[29,30] respectively.

Methyl 5(*S*)-Hydroxy-7-(trimethylsilyl)-6(*E*)-heptenoate ((*S*)-10). Racemic alcohol *dl*-**10** was prepared by a previously described procedure[10a] with modification. To a solution of

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trans-1-(trimethylsilyl)-2-(tri-*n*-butylstannyl)ethylene (74 g, 0.19 mol) in THF (300 mL) at −78 °C was added *n*-BuLi dropwise (100 mL, 1.83 M in hexane, 0.183 mol). After the solution had been stirred for 2 h at −60 °C, Et_2AlCl (180 mL, 1.0 M in hexane, 0.18 mol) was added at −78 °C, and the solution was stirred for a further 30 min to generate **9** (M = $AlEt_2$). To this solution was added **8**[12] (20.0 g, 0.154 mol) dropwise at −78 °C. Stirring was continued for 2 h at room temperature, and H_2O (10 mL), NaF (38 g), and Celite (30 g) were successively added at 0 °C. The resulting white mixture was vigorously stirred at room temperature for 1 h and filtered through a pad of Celite. The filtrate was concentrated in vacuo and the residue was passed through a short silica gel column to separate off the nonpolar compounds. The above semipurified product and NaOMe (5.0 g, 93 mmol) in MeOH (200 mL) were stirred for 15 h at room temperature, and most of the MeOH was removed in vacuo to leave an oil, which was diluted with Et_2O (300 mL). This ethereal solution was washed with saturated aqueous NH_4Cl (100 mL), and the aqueous layer was extracted with Et_2O (200 mL). The combined extracts were dried ($MgSO_4$) and concentrated in vacuo to give the residue, which was purified by chromatography on silica gel to provide *dl*-**10** (23 g, 65%).

The kinetic resolution of *dl*-**10** using *t*-BuOOH (1.5 equiv), $Ti(O\text{-}i\text{-}Pr)_4$ (1 equiv), and D-(−)-DIPT (1.2 equiv) was carried out as described previously[10a] to give (*S*)-**10** (>99% ee) and **11** (>99% ee).

Methyl 7-Bromo-5(*S*)-[(*tert*-butyldimethylsilyl)oxy]-6-(*Z*)-heptenoate (12). To a solution of (*S*)-**10** (1.71 g, 7.43 mmol) in CH_2Cl_2 (30 mL) at −70 °C was added bromine (0.39 mL, 7.6 mmol) dropwise. After 10 min, excess bromine was quenched with aqueous $Na_2S_2O_3$. The mixture was extracted with hexane twice. The combined organic layers were dried ($MgSO_4$) and concentrated in vacuo to give the bromine adduct. To a solution of this product in THF (5 mL) at −70 °C was slowly added *n*-Bu_4NF (14 mL, 0.63 M in THF, 8.8 mmol). The solution was stirred for 15 min at −70 °C and poured into brine. The product was extracted with Et_2O three times. The combined organic layers were dried ($MgSO_4$) and concentrated in vacuo to afford the cis bromide, which was used for the next reaction without further purification. Analytically pure cis bromide was obtained by chromatography on silica gel: ^1H NMR (90 MHz, CCl_4, C_6H_6) δ 1.23–1.88 (m, 5 H), 2.17–2.38 (m, 2 H), 3.56 (s, 3 H), 4.37–4.61 (m, 1 H), 5.82–6.38 (m, 2 H); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 173.5, 137.4, 107.4, 69.0, 51.0, 35.1, 33.4, 20.2.

A solution of the above product, *tert*-butyldimethylsilyl chloride (1.68 g, 11.1 mmol), and imidazole (1.52 g, 22.3 mmol) in DMF (20 mL) was stirred for 5 h at room temperature and poured into a mixture of hexane and saturated aqueous $NaHCO_3$. The organic layer was separated and the aqueous layer was extracted with hexane twice. The combined organic layers were dried ($MgSO_4$) and concentrated in vacuo to give the residue, which was purified by chromatography on silica gel to afford **12** (1.92 g, 74% from (*S*)-**10**): $[\alpha]^{25}_D$ +15.2° (*c* 1.01, $CHCl_3$); ^1H NMR (90 MHz, CCl_4, C_6H_6) δ 0.02 and 0.07 (2s, 6 H), 0.88 (s, 9 H), 1.18–1.84 (m, 4 H), 2.11–2.38 (m, 2 H), 3.58 (s, 3 H), 4.36–4.69 (m, 1 H), 5.93–6.18 (m, 2 H); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 173.4, 138.5, 106.1, 70.6, 51.1, 36.4, 33.9, 25.8, 20.5, 18.0, −4.5, −4.9; IR (neat) 1737, 1249, 1088, 836, 779 cm^{-1}.

Methyl 5(*S*)-[(*tert*-Butyldimethylsilyl)oxy]-6(*Z*)-nonen-8-ynoate (4). To a solution of **12** (1.54 g, 4.39 mmol), (trimethylsilyl)acetylene (1.24 mL, 8.77 mmol), and *n*-propylamine (1.08 mL, 13.1 mmol) in benzene (20 mL) were added $Pd(PPh_3)_4$ (150 mg, 0.13 mmol) and CuI (59 mg, 0.31 mmol). The solution was stirred for 20 h at room temperature and poured into saturated aqueous NH_4Cl. The mixture was extracted with hexane three times. The combined organic layers were dried ($MgSO_4$) and concentrated in vacuo to give **13**, which was used for the next reaction without further purification. Analytically pure **13** was obtained by chromatography on silica gel: ^1H NMR (90 MHz, CCl_4, C_6H_6) δ 0.01 and 0.06 (2s, 6 H), 0.18 (s, 9 H), 0.88 (s, 9 H), 1.30–1.82 (m, 4 H), 2.11–2.38 (m, 2 H), 3.58 (s, 3 H), 4.48–4.76 (m, 1 H), 5.39 (d, *J* = 11 Hz, 1 H), 5.80 (dd, *J* = 8.4, 11 Hz, 1 H).

To a solution of the above acetylene **13** dissolved in THF (15 mL), EtOH (15 mL), and H_2O (15 mL) at 0 °C was added $AgNO_3$ (2.98 g, 17.5 mmol) in one portion. After 30 min at 0 °C, KCN (2.0 g, 31 mmol) was added portionwise. The resulting mixture was vigorously stirred for 3 h at 0 °C, poured into brine, and extracted with Et_2O twice. The combined organic layers were dried ($MgSO_4$) and concentrated in vacuo. The residue was purified by chromatography on silica gel to provide **4** (1.24 g, 95% from **12**). The enantiomeric excess of **4** thus prepared was reconfirmed to be >99% by ^1H NMR spectroscopy of the derived MTPA ester. **4**: $[\alpha]^{25}_D$ +49.6° (*c* 1.15, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$) δ 0.03 and 0.07 (2s, 6 H), 0.87 (s, 9 H), 1.41–1.79 (m, 4 H), 2.33 (t, *J* = 7.2 Hz, 2 H), 3.11 (dd, *J* = 0.9, 2.4 Hz, 1 H), 3.66 (s, 3 H), 4.65 (dt, *J* = 8.6, 5.7 Hz, 1 H), 5.44 (ddd, *J* = 0.9, 2.4, 11 Hz, 1 H), 5.92 (ddd, *J* = 0.9, 8.6, 11 Hz, 1 H); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 173.0, 148.0, 107.4, 82.5, 79.5, 70.2, 50.8, 36.8, 33.6, 25.7, 20.4, 12.9, −4.6, −5.1; IR (neat) 3290, 1737, 1249, 1083, 838, 774 cm^{-1}; HRMS calcd for $C_{12}H_{19}O_3Si$ ($M^+ - C_4H_9$) 239.1103, found 239.1073.

1,1-Diethoxy-3(*Z*)-nonene (15). To a solution of 1-heptyne (105 mL, 0.80 mol) in THF (800 mL) at 0 °C was slowly added *n*-BuLi (400 mL, 173 M in hexane, 0.692 mol). After 15 min at 0 °C, bromoacetaldehyde diethyl acetal (70 mL, 0.40 mol) and HMPA (280 mL, 1.6 mol) were added. The reaction was continued for 24 h at room temperature and quenched with saturated aqueous NH_4Cl. The mixture was extracted with hexane. The extract was washed with H_2O twice, dried ($MgSO_4$), and concentrated in vacuo. Distillation of the residue gave **14** (86.7 g, 100%): bp 82–83 °C (0.8 mmHg); ^1H NMR (90 MHz, CCl_4) δ 0.89 (t, *J* = 6 Hz, 3 H), 1.0–1.7 (m, 12 H), 1.95–2.23 (m, 2 H), 2.27 (dt, *J* = 5, 2 Hz, 2 H), 3.23–3.76 (m, 4 H), 4.37 (t, *J* = 6 Hz, 1 H); IR (neat) 1118, 1060 cm^{-1}.

To an ice-cooled solution of *i*-BuMgBr (250 mL, 1.85 M in Et_2O, 0.46 mol) was added Cp_2TiCl_2 (1.5 g, 6.0 mmol). The solution was stirred for 30 min at 0 °C, and **14** (80.0 g, 0.376 mol) was added. Stirring was continued for 12 h at 26–28 °C, and the solution was slowly poured into a mixture of ice (200 g) and saturated aqueous NH_4Cl (200 mL) with vigorous stirring. The organic layer was separated, dried ($MgSO_4$), and concentrated in vacuo to afford the residue, which was passed through a short silica gel column (hexane–Et_2O). The filtrate was concentrated in vacuo to leave an oil, which was distilled to give **15** (65.1 g, 81%): bp 114–117 °C (12 mmHg); ^1H NMR (90 MHz, CCl_4) δ 0.87 (t, *J* = 6 Hz, 3 H), 1.05–1.65 (m, 12 H), 1.85–2.10 (m, 2 H), 2.23 (t, *J* = 6 Hz, 2 H), 3.10–3.76 (m, 4 H), 4.30 (t, *J* = 6 Hz, 1 H), 5.07–5.52 (m, 2 H); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 132.1, 123.8, 102.7, 61.1, 32.1, 31.5, 29.2, 27.4, 22.5, 15.2, 13.9; IR (neat) 1448, 1383, 1346, 1120, 1060 cm^{-1}. Anal. Calcd for $C_{13}H_{26}O_2$: C, 72.84; H, 12.23. Found: C, 71.96; H, 12.39.

1-(Trimethylsilyl)-1(*E*),5(*Z*)-undecadien-3(*R*)-ol ((*R*)-17) and 2(*S*)-[1′(*S*)-Hydroxy-3′(*Z*)-nonenyl]-3(*S*)-(trimethylsilyl)oxirane (18). The aldehyde **16** was prepared by the procedure of Winter[19] with modification. A solution of **15** (2.0 g, 9.33 mmol and 2,5-di-*tert*-butylhydroquinone (ca. 30 mg) in acetone–H_2O (4:1, 50 mL) was heated to 60 °C, and oxalic acid (170 mg, 1.9 mmol) was added. The mixture was gently refluxed for 2 h, cooled to 0 °C, and extracted with hexane–Et_2O (1:1, 100 mL). The extract was washed successively with saturated aqueous $NaHCO_3$ (20 mL) and brine (20 mL) and dried ($MgSO_4$). Evaporation of the solvent afforded the crude aldehyde **16** (1.22 g), which was used for the next reaction without further purification.

To a solution of *trans*-1-(trimethylsilyl)-2-(tri-*n*-butylstannyl)ethylene (6.2 g, 16 mmol) in THF (25 mL) at −78 °C was slowly added *n*-BuLi (10 mL, 1.53 M in hexane, 15.3 mmol). After stirring for 1 h at −60 °C, the above aldehyde **16** (1.22 g) was added. The solution was stirred for 1 h at 0 °C, and saturated aqueous NH_4Cl (10 mL) was added. The mixture was extracted with hexane twice. The combined extracts were dried ($MgSO_4$) and concentrated in vacuo. The residue was purified by chromatography on silica gel to give *dl*-**17** (1.69 g, 75% from **15**). The spectral data (^1H NMR, ^{13}C NMR, IR) were identical with those reported before.[10a]

The kinetic resolution of *dl*-**17** using *t*-BuOOH (1.5 equiv), $Ti(O\text{-}i\text{-}Pr)_4$ (1 equiv), and L-(+)-DIPT (1.2 equiv) was carried out as described before to provide (*R*)-**17** (>99% ee) and **18** (>99% ee).[10a]

2(*R*)-[1′(*R*)-[(*tert*-Butyldimethylsilyl)oxy]-3′(*Z*)-nonenyl]-3(*R*)-(trimethylsilyl)oxirane (19). To a mixture of D-(−)-DIPT (1.2 mL, 5.65 mmol), $Ti(O\text{-}i\text{-}Pr)_4$ (1.4 mL, 4.7 mmol),

and 4A molecular sieves (1 g) in CH_2Cl_2 (15 mL) at −21 °C was added (*R*)-**17** (3.65 g, 15.2 mmol) dissolved in CH_2Cl_2 (8 mL). After 10 min, *t*-BuOOH (7.5 mL, 4.09 M in CH_2Cl_2, 30.7 mmol) was added dropwise at −40 °C. The mixture was stirred for 4 h at −21 °C and then dimethyl sulfide (4 mL, 54 mmol) was added to destroy excess *t*-BuOOH. After 30 min at −21 °C, aqueous 10% tartaric acid (4 mL), Et_2O (50 mL), NaF (1.2 g), and Celite (1 g) were added to the solution. The resulting white mixture was vigorously stirred for 1 h at room temperature and filtered through a pad of Celite with Et_2O. Evaporation of the filtrate and chromatography on silica gel (hexane–Et_2O containing 0.5% of NEt_3) afforded the enantiomer of **18** (3.35 g, 86%): $[\alpha]^{25}_D$ +4.25° (*c* 1.15, $CHCl_3$).

The above alcohol (2.78 g, 10.8 mmol) was converted into the silyl ether **19** (4.04 g, 100%) with *tert*-butyldimethylsilyl chloride (2.5 g, 16.6 mmol), imidazole (1.5 g, 22 mmol), and DMF (20 mL) by the procedure for the preparation of **12**. **19**: $[\alpha]^{25}_D$ −0.18° (*c* 1.11, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$) δ 0.02, 0.04, and 0.05 (3s, 15 H), 0.80–0.95 (m, 12 H), 1.18–1.42 (m, 6 H), 1.97–2.10 (m, 2 H), 2.18 (d, *J* = 3.5 Hz, 1 H), 2.31–2.39 (m, 2 H), 2.75 (dd, *J* = 3.5, 5.4 Hz, 1 H), 3.49 (q, *J* = 5.6 Hz, 1 H), 5.33–5.57 (m, 2 H); ^{13}C NMR (50 MHz, $CDCl_3$) 132.4, 124.9, 73.4, 58.5, 49.8, 33.8, 31.5, 29.3, 27.3, 25.7, 22.5, 18.0, 14.0, −3.8, −4.6, −4.9; IR (neat) 1250, 1090, 840 cm^{-1}; HRMS calcd for $C_{16}H_{33}O_2Si_2$ ($M^+ - C_4H_9$) 313.2019, found 313.1937.

1-Iodo-3(*R*)-[(*tert*-butyldimethylsilyl)oxy]-1(*E*),5(*Z*)-undecadiene (6a). To a solution of *i*-Pr_2NH (4.5 mL, 32 mmol) in THF (30 mL) at 0 °C was added *n*-BuLi (15.0 mL, 1.53 M in hexane, 23 mmol). After 30 min at 0 °C, *n*-Bu_3SnH (4.55 g, 16.9 mmol) was added. The solution was stirred for additional 30 min at 0 °C, and then **19** (5.97 g, 16.1 mmol) was added. After 3 h at 0 °C, the reaction was quenched with saturated NH_4Cl and the mixture was extracted with hexane repeatedly. The combined organic layers were dried ($MgSO_4$) and concentrated in vacuo to afford **20** (9.9 g), which was used for the next reaction without further purification. The following spectroscopic data of **20** were recorded after purification by chromatography on silica gel: ^1H NMR (90 MHz, CCl_4, C_6H_6) δ 0.07 (s, 6 H), 0.7–2.3 (m), 3.89–4.13 (m, 1 H), 5.27–5.47 (m, 2 H), 5.95 (m, 2 H); IR (neat) 1605, 1070, 840 cm^{-1}.

To a solution of above **20** (9.9 g) in Et_2O (50 mL) at 0 °C was added I_2 (4.31 g, 16.9 mmol) portionwise. The resulting dark solution was stirred for 30 min, and excess I_2 was quenched with aqueous $Na_2S_2O_3$. The mixture was extracted with hexane twice. The combined organic phases were washed with aqueous 3 N NaOH, dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by chromatography on silica gel to provide **6a** (5.20 g, 90% based on **19**). The enantiomeric excess of **6a** thus obtained was reconfirmed to be >99% by ^1H NMR spectroscopy of the derived MTPA ester. **6a**: $[\alpha]^{25}_D$ +7.4° (*c* 1.24, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$) δ 0.03 and 0.05 (2s, 6 H), 0.84–0.93 (m, 12 H), 1.17–1.42 (m, 6 H), 1.93–2.07 (m, 2 H), 2.23 (t, *J* = 6.6 Hz, 2 H), 4.07 (dq, *J* = 1.2, 6.6 Hz, 1 H), 5.25–5.56 (m, 2 H), 6.21 (dd, *J* = 1.2, 14 Hz, 1 H), 6.53 (dd, *J* = 5.6, 14 Hz, 1 H); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 148.8, 132.6, 124.2, 75.6, 75.1, 35.8, 31.6, 29.3, 27.5, 25.8, 22.6, 18.2, 14.0, −4.6, −4.8; IR (neat) 1605, 1250, 1085, 940, 835, 776 cm^{-1}. Anal. Calcd for $C_{17}H_{33}OISi$: C, 44.99, H, 8.14; I, 31.07. Found: C, 50.23; H, 8.19; I, 31.88.

The title compound **6a** was also prepared from **22** (see below for the preparation of **22**) by the same procedure described above in 96% yield. The enantiomeric excess of **6a** thus obtained was found to be >99% by ^1H NMR spectroscopy of the derived MTPA ester.

2(*S*)-[1′(*R*)-[(*p*-Nitrobenzoyl)oxy]-3′(*Z*)-nonenyl]-3(*S*)-(trimethylsilyl)oxirane (21). To a solution of diethyl azodicarboxylate (0.22 g, 1.4 mmol) and *p*-nitrobenzoic acid (0.22 g, 1.3 mmol) in THF (3 mL) at 0 °C was added a solution of **18** (230 mg, 0.898 mmol) and PPh_3 (350 mg, 1.33 mmol) dissolved in THF (3 mL). The resulting solution was stirred for 30 min at 0 °C and concentrated in vacuo. The residue was dissolved in Et_2O and filtered through a pad of Celite with Et_2O. The filtrate was washed with saturated aqueous $NaHCO_3$, and the aqueous layer was extracted with Et_2O twice. The combined ethereal solutions were dried ($MgSO_4$) and concentrated in vacuo. The residue was purified by chromatography on silica gel to give **21** (340 mg, 93%): $[\alpha]^{25}_D$ −17.8° (*c* 1.13, $CHCl_3$); ^1H NMR (90 MHz, CCl_4, C_6H_6) δ 0.06 (s, 9 H), 0.86 (t, *J* = 5 Hz, 3 H), 1.1–1.7 (m, 6 H), 1.89–2.22 (m, 3 H), 2.35–2.67 (m, 2 H), 2.97 (dd, *J* = 3, 7 Hz, 1 H), 4.78 (q, *J* = 7 Hz, 1 H), 5.16–5.66 (m, 2 H), 8.17 (s, 4 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 164.1, 150.7, 135.7, 134.1, 131.0, 123.5, 122.5, 77.7, 56.3, 49.5, 31.3, 29.6, 29.0, 27.2, 22.3, 13.8, −4.0; IR (neat) 1725, 1610, 1530, 1270, 1105, 840, 720 cm^{-1}; HRMS calcd for $C_{13}H_{16}NO_5Si$ ($M^+ - C_8H_{15}$) 294.0797, found 294.0805.

2(*S*)-[1′(*R*)-[(*tert*-Butyldimethylsilyl)oxy]-3′(*Z*)-nonenyl]-3(*S*)-(trimethylsilyl)oxirane (22). A mixture of **21** (340 mg, 0.835 mmol), THF (2 mL), MeOH (2 mL), and aqueous 2 N NaOH (2 mL) was vigorously stirred for 1 h at 0 °C and poured into saturated aqueous NH_4Cl. The mixture was extracted with hexane repeatedly. The combined extracts were dried ($MgSO_4$) and concentrated in vacuo. The residue was purified by chromatography on silica gel to provide the corresponding alcohol (214 mg, 100%): $[\alpha]^{25}_D$ −7.40° (*c* 1.27, $CHCl_3$); ^1H NMR (90 MHz, CCl_4, C_6H_6) δ 0.05 (s, 9 H), 0.88 (t, *J* = 6 Hz, 3 H), 1.1–1.6 (m, 6 H), 1.90–2.19 (m, 2 H), 2.09 (d, *J* = 4 Hz, 1 H), 2.18–2.42 (m, 2 H), 2.75 (t, *J* = 5 Hz, 1 H), 3.10–3.45 (m, 2 H), 5.18–5.62 (m, 2 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 133.2, 124.1, 73.0, 58.9, 49.4, 32.3, 31.3, 29.1, 27.2, 22.4, 13.8, −4.0; IR (neat) 3410, 1250, 865, 840 cm^{-1}.

The above alcohol (2.97 g, 11.6 mmol) was transformed into **22** (4.08 g, 95%) with *tert*-butyldimethylsilyl chloride (2.2 g, 14.6 mmol), imidazole (1.58 g, 23.2 mmol), and DMF (30 mL) by the procedure described for the preparation of **12**. **22**: $[\alpha]^{25}_D$ −9.7° (*c* 1.05, $CHCl_3$); ^1H NMR (90 MHz, $CDCl_3$) δ 0.06 (s, 9 H), 0.07 and 0.11 (2s, 6 H), 0.91 (br s, 12 H), 1.10–1.42 (m, 6 H), 1.95–2.12 (m, 3 H), 2.28 (t, *J* = 7 Hz, 2 H), 2.78 (dd, *J* = 3.6, 7.2 Hz, 1 H), 3.25 (q, *J* = 7 Hz, 1 H), 5.18–5.61 (m, 2 H); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 132.0, 124.9, 76.3, 59.5, 48.9, 33.4, 31.6, 29.4, 27.5, 26.0, 22.6, 18.2, 14.1, −3.6, −4.3, −4.9; IR (neat) 1245, 1090, 835, 770 cm^{-1}; HRMS calcd for $C_{16}H_{33}O_2Si_2$ ($M^+ - C_4H_9$) 313.2019, found 313.2130.

1-(Trimethylsilyl)-1(*E*)-hexen-5-yn-3-ol (24). To an ice-cooled mixture of the aldehyde **23**[22] (20 g, 156 mmol) and Zn dust (15.3 g, 234 mmol) in THF (200 mL) was added $TiCl_4$ (0.1 mL), and the mixture was stirred for 5 min. Propargyl bromide (21 mL, 236 mmol) dissolved in THF (20 mL) was dropwise added over 20 min at 0 °C. After the addition, the mixture was stirred for 30 min at room temperature, and H_2O (8.4 mL, 468 mmol) and hexane (200 mL) were added successively. The resulting mixture was vigorously stirred for 1 h and then filtered through a pad of silica gel with Et_2O. The filtrate was concentrated in vacuo to leave an oil, which was semipurified by being passed through a short silica gel column using a mixture of hexane and Et_2O (5:1) as eluent to afford **24** (29 g, 100%): ^1H NMR (90 MHz, CCl_4, CH_2Cl_2) δ 0.10 (s, 9 H), 1.91 (t, *J* = 3 Hz, 1 H), 2.31 (dd, *J* = 3, 6 Hz, 1 H), 2.90 (br s, 1 H), 4.11 (dt, *J* = 3.3, 6 Hz, 1 H), 5.80 (d, *J* = 18 Hz, 1 H), 6.10 (dd, *J* = 3.3, 18 Hz, 1 H); IR (neat) 3370, 3290, 1620, 1245, 872, 840 cm^{-1}.

4-(1′-Ethoxyethoxy)-6-(trimethylsilyl)-5(*E*)-hexen-1-yne (25). To an ice-cooled solution of **24** (16.2 g, 96.4 mmol) and PPTS (0.80 g, 3.2 mmol) in CH_2Cl_2 (200 mL) was dropwise added ethyl vinyl ether (18 mL, 190 mmol). The solution was stirred for 1 h at room temperature and poured into a mixture of hexane and saturated aqueous $NaHCO_3$. The organic layer was separated and the aqueous layer was extracted with hexane twice. The combined extracts were dried ($MgSO_4$) and concentrated in vacuo to leave an oil, which was purified by chromatography on silica gel to afford **25** (21.9 g, 95%): ^1H NMR (90 MHz, CCl_4, CH_2Cl_2) δ 0.10 (s, 9 H), 0.99–1.32 (m, 6 H), 1.77–1.88 (m, 1 H), 2.19–2.40 (m, 2 H), 3.10–3.62 (m, 2 H), 3.88–4.16 (m, 1 H), 4.44–4.79 (m, 1 H), 5.59–6.12 (m, 2 H); IR (neat) 3280, 1618, 1129, 1085, 865, 840 cm^{-1}.

1-(1′-Ethoxyethoxy)-5-iodopentane. A solution of 1,5-pentanediol (25 g, 240 mmol), TsCl (20.6 g, 108 mmol), and pyridine (19 mL, 235 mmol) in CH_2Cl_2 (400 mL) was stirred overnight at room temperature and poured into brine. The mixture was extracted with ether twice. The combined extracts were washed with aqueous 3 N HCl, dried ($MgSO_4$), and concentrated in vacuo to afford 1,5-pentanediol monotosylate. A mixture of this tosylate and NaI (25 g, 167 mmol) in acetone (500 mL) was refluxed for 2 h and filtered through a pad of Celite. The filtrate was concentrated in vacuo to afford the residue, which was diluted with Et_2O. This ethereal solution was washed with aqueous $Na_2S_2O_3$, dried ($MgSO_4$), and evaporated to afford 5-iodo-1-pentanol: ^1H

NMR (90 MHz, CCl_4) δ 1.2–2.0 (m, 6 H), 3.12 (t, J = 6.5 Hz, 2 H), 3.49 (t, J = 6 Hz, 2 H), 3.78 (s, 1 H).

The above iodide was protected with ethyl vinyl ether (15.5 mL, 162 mmol) and PPTS (1.5 g, 5.97 mmol) in CH_2Cl_2 (150 mL) by the procedure described for the preparation of **25** to provide the title compound (16.39 g, 53%): ^1H NMR (90 MHz, CCl_4) δ 0.9–2.0 (m, 12 H), 2.98–3.67 (m, 6 H), 4.50 (q, J = 5.2 Hz, 1 H); IR (neat) 1135, 1088, 1061 cm^{-1}.

3,11-Bis(1′-ethoxyethoxy)-1-(trimethylsilyl)-1(*E*)-undecen-5-yne (26). To a solution of **25** (8.30 g, 34.6 mmol) and bipyridyl (ca. 5 mg) in THF (42 mL) at −78 °C was dropwise added *n*-BuLi (17.3 mL, 2.1 M in hexane, 36.3 mmol). After the solution had been stirred for 1 h at −78 °C, HMPA (12.8 mL, 73.6 mmol) and 1-(1′-ethoxyethoxy)-5-iodopentane (13.0 g, 45.5 mmol) were added successively. The reaction was continued for 24 h at room temperature and quenched with saturated aqueous NH_4Cl. The mixture was extracted with hexane repeatedly. The combined extracts were dried ($MgSO_4$) and evaporated to leave the residue, which was purified by chromatography on silica gel to afford **26** (10.6 g, 80%): ^1H NMR (90 MHz, CCl_4, C_6H_6) δ 0.17 (s, 9 H), 1.0–1.7 (m), 1.89–2.28 (m, 4 H), 3.04–3.76 (m, 6 H), 3.87–4.13 (m, 1 H), 4.46–4.82 (m, 2 H), 5.66–6.17 (m, 2 H); IR (neat) 1618, 1123, 1092, 839 cm^{-1}.

11-(Trimethylsilyl)-6(*Z*),10(*E*)-undecadiene-1,9-diol (27). To a solution of **26** (4.2 g, 11 mmol) in THF (30 mL) at 0 °C was added freshly prepared Sia_2BH (50 mL, 0.5 M in THF, 25 mmol). Stirring was continued for 1 h at 0 °C and then AcOH (3 mL, 52 mmol) was added. The solution was stirred for a further 4 h at room temperature and cooled to 0 °C. To this were added an aqueous 3 N NaOH solution (20 mL) and 35% H_2O_2 (11 mL) successively. After 30 min, the mixture was poured into brine and extracted with hexane twice. The combined extracts were dried ($MgSO_4$) and concentrated in vacuo to give the ethoxyethyl ether of **27**. A solution of the above product and aqueous 3 N HCl (1.5 mL) in MeOH (30 mL) was stirred for 1.5 h at room temperature and poured into brine. The mixture was extracted with Et_2O three times. The combined extracts were dried ($MgSO_4$) and concentrated in vacuo. Chromatography of the residue on silica gel afforded **27** (2.01 g, 71%): ^1H NMR (200 MHz, $CDCl_3$) δ 0.03 (s, 9 H), 1.24–1.58 (m, 6 H), 1.93–2.09 (m, 2 H), 2.26 (t, J = 7 Hz, 2 H), 2.58 (br s, 2 H), 3.53 (t, J = 6.5 Hz, 2 H), 4.07 (q, J = 5.6 Hz, 1 H), 5.27–5.58 (m, 2 H), 5.82 (dd, J = 1.1, 18 Hz, 1 H), 6.01 (dd, J = 4.8, 18 Hz, 1 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 148.0, 133.1, 129.4, 124.9, 73.8, 62.6, 34.8, 32.4, 29.2, 27.2, 25.2, −1.5; IR (neat) 3330, 1621, 1250, 1054, 867, 840 cm^{-1}.

11-[(*tert*-Butyldimethylsilyl)oxy]-1-(trimethylsilyl)-1(*E*),5(*Z*)-undecadien-3-ol (*dl*-28). A solution of **27** (1.86 g, 7.26 mmol), *tert*-butyldimethylsilyl chloride (1.35 g, 8.96 mmol), and pyridine (0.87 mL, 11 mmol) in acetonitrile (24 mL) was stirred for 1 h at 0 °C and poured into a mixture of hexane and saturated aqueous $NaHCO_3$. The organic layer was separated and the aqueous layer was extracted with hexane twice. The combined extracts were dried ($MgSO_4$) and concentrated in vacuo to afford the residue, which was purified by chromatography on silica gel to afford *dl*-**28** (2.36 g, 88%): ^1H NMR (200 MHz, $CDCl_3$) δ 0.03 and 0.06 (2s, 15 H), 0.88 (s, 9 H), 1.23–1.59 (m, 6 H), 1.72 (br s, 1 H), 1.96–2.11 (m, 2 H), 2.29 (t, J = 6 Hz, 2 H), 3.58 (t, J = 6.5 Hz, 2 H), 4.12 (q, J = 6 Hz, 1 H), 5.38 (dt, J = 5, 6 Hz, 1 H), 5.55 (dt, J = 5, 6 Hz, 1 H), 5.88 (d, J = 18 Hz, 1 H), 6.06 (dd, J = 5, 18 Hz, 1 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 148.2, 133.3, 129.3, 124.8, 73.8, 63.1, 34.9, 32.6, 29.3, 27.3, 25.8, 25.4, 18.2, −1.5, −5.5; IR (neat) 3340, 1620, 1247, 1099, 835 cm^{-1}; HRMS calcd for $C_{16}H_{31}OSi_2$ (M^+ − (C_4H_9 and H_2O)) 295.1913, found 295.1891.

11-[(*tert*-Butyldimethylsilyl)oxy]-1-(trimethylsilyl)-1(*E*),5(*Z*)-undecadien-3(*S*)-ol ((*S*)-28) and 2(*R*)-[9′-[(*tert*-Butyldimethylsilyl)oxy]-1′(*R*)-hydroxy-3′(*Z*)-nonenyl]-3(*R*)-(trimethylsilyl)oxirane (29). To a solution of *dl*-**28** (775 mg, 2.09 mmol), D-(−)-DIPT (0.53 mL, 2.5 mmol), and $Ti(O\text{-}i\text{-}Pr)_4$ (0.62 mL, 2.1 mmol) in CH_2Cl_2 (14 mL) at −40 °C was slowly added *t*-BuOOH (1.02 mL, 3.07 M in CH_2Cl_2, 3.13 mmol). The reaction was continued for 16 h at −21 °C and quenched with dimethyl sulfide (2 mL). To this were added aqueous 10% tartaric acid (2 mL), NaF (0.9 g), and Et_2O (10 mL). The resulting mixture was stirred vigorously for 3 h at room temperature and filtered through a pad of Celite with Et_2O. The filtrate was concentrated in vacuo to afford the residue, which was diluted with Et_2O (20 mL). This solution was treated with aqueous 1 N NaOH (10 mL, 10 mmol) for 30 min at 0 °C with vigorous stirring. The products were extracted with Et_2O three times. The combined extracts were dried ($MgSO_4$) and concentrated in vacuo. The crude products were purified by chromatography on silica gel to give (*S*)-**28** (336 mg, 43%) and **29** (341 mg, 42%). The enantiomeric excesses of (*S*)-**28** and **29** were confirmed to be both >99% by ^1H NMR spectroscopy of the derived MTPA esters. (*S*)-**28**: TLC, R_f 0.38 (hexane/Et_2O = 3:1); $[\alpha]^{20}_D$ −4.7° (*c* 2.01, $CHCl_3$). **29**: TLC, R_f 0.27 (hexane/Et_2O = 3:1); $[\alpha]^{20}_D$ +6.2° (*c* 1.51, acetone); ^1H NMR (90 MHz, $CDCl_3$) δ 0.04 and 0.08 (2s, 15 H), 0.89 (s, 9 H), 1.1–2.5 (m, 6 H), 2.91 (t, J = 3.8 Hz, 1 H), 3.60 (t, J = 6.1 Hz, 2 H), 3.71–3.98 (m, 1 H), 5.28–5.78 (m, 2 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 133.1, 124.2, 69.4, 63.1, 58.0, 47.6, 32.6, 31.7, 29.3, 27.3, 25.8, 25.4, 18.2, −3.9, −5.5; IR (neat) 3420, 1248, 1098, 836 cm^{-1}; HRMS calcd for $C_{16}H_{33}O_3Si_2$ (M^+ − C_4H_9) 329.1968, found 329.1813.

2(*S*)-[9′-[(*tert*-Butyldimethylsilyl)oxy]-1′(*R*)-hydroxy-3′(*Z*)-nonenyl]-3(*S*)-(trimethylsilyl)oxirane (31). The alcohol (*S*)-**28** (1.30 g, 3.51 mmol) was converted into the enantiomer of **29** (1.21 g, 89%, $[\alpha]^{25}_D$ −6.5° (*c* 1.30, acetone)) with *t*-BuOOH (1.2 mL, 4.33 M in CH_2Cl_2, 5.2 mmol), $Ti(O\text{-}i\text{-}Pr)_4$ (1.04 mL, 3.49 mmol), L-(+)-DIPT (0.88 mL, 4.14 mmol), and CH_2Cl_2 (10 mL) in the same way as (*R*)-**17**.

The above alcohol (540 mg, 1.46 mmol) was treated with PPh_3 (730 mg, 2.78 mmol), *p*-nitrobenzoic acid (500 mg, 3.0 mmol), and diethyl azodicarboxylate (0.4 mL, 2.5 mmol) in THF (5 mL) in the same way as **18** to provide **30** (866 mg). Analytically pure *p*-nitrobenzoate **30** was obtained by chromatography on silica gel: $[\alpha]^{25}_D$ −12.9° (*c* 1.38, $CHCl_3$); ^1H NMR (90 MHz, CCl_4, C_6H_6) δ 0.17 (s, 15 H), 0.92 (s, 9 H), 1.2–2.2 (m, 9 H), 2.44–2.68 (m, 2 H), 2.97 (dd, J = 3.6, 6.5 Hz, 1 H), 3.52 (t, J = 5.7 Hz, 1 H), 4.78 (q, J = 6.5 Hz, 1 H), 5.17–5.67 (m, 2 H), 8.16 (s, 4 H); IR (neat) 1722, 1262, 1251, 1099, 838 cm^{-1}.

The above ester **30** was hydrolyzed with aqueous 1 N NaOH (2.5 mL, 2.5 mmol) and MeOH (5 mL) in the same way as **21** to afford **31** (490 mg, 87% from the enantiomer of **29**): $[\alpha]^{25}_D$ −3.9° (*c* 1.25, $CHCl_3$); ^1H NMR (90 MHz, CCl_4, C_6H_6) δ 0.16 and 0.19 (2s, 15 H), 0.96 (s, 9 H), 1.2–1.7 (m, 6 H), 1.94–2.44 (m, 5 H), 2.60 (d, J = 5.4 Hz, 1 H), 2.72 (dd, J = 3.3, 5.4 Hz, 1 H), 3.14–3.47 (m, 1 H), 3.55 (t, J = 6 Hz, 2 H), 5.17–5.59 (m, 2 H); IR (neat) 3400, 1253, 1100, 837 cm^{-1}.

11-[(*tert*-Butyldimethylsilyl)oxy]-1-iodo-1(*E*),5(*Z*)-undecadien-3(*R*)-ol (32). According to the procedure described for **6a**, the reaction involving **31** (490 mg, 1.27 mmol), $i\text{-}Pr_2NH$ (0.89 mL, 6.35 mmol), *n*-BuLi (2.4 mL, 2.1 M in hexane, 5.04 mmol), $n\text{-}Bu_3SnH$ (0.53 mL, 1.97 mmol), bipyridyl (ca. 5 mg), and THF (6 mL) and the next reaction with I_2 (390 mg, 1.54 mmol) and Et_2O (10 mL) gave **32** (520 mg, 97%): $[\alpha]^{25}_D$ +14.8° (*c* 1.77, $CHCl_3$); ^1H NMR (90 MHz, CCl_4, C_6H_6) δ 0.13 (s, 6 H), 0.96 (s, 9 H), 1.3–1.7 (m, 6 H), 1.90–2.12 (m, 2 H), 2.27 (t, J = 6.5 Hz, 2 H), 3.57 (t, J = 5.7 Hz, 2 H), 3.90–4.18 (m, 1 H), 5.12–5.68 (m, 2 H), 6.28 (d, J = 14.4 Hz, 1 H), 6.47 (dd, J = 5.1, 14.4 Hz, 1 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 148.1, 134.4, 123.7, 77.3, 73.9, 63.2, 34.6, 32.6, 29.3, 27.3, 25.9, 25.4, 18.2, −5.4; IR (neat) 3340, 1606, 1251, 1196, 832, 775 cm^{-1}; HRMS calcd for $C_{13}H_{24}IO_2Si$ (M^+ − C_4H_9) 367.0592, found 367.0693.

The title compound **32** was also prepared from the epoxide **29** in 97% yield in the same way as **6a**.

3(*R*),11-Bis[(*tert*-butyldimethylsilyl)oxy]-1-iodo-1(*E*),5(*Z*)-undecadiene (6b). The alcohol **32** (116 mg, 0.274 mmol) was silylated to **6b** (141 mg, 96%) with *tert*-butyldimethylsilyl chloride (54 mg, 0.36 mmol), imidazole (37 mg, 0.54 mmol), and DMF (3 mL) by the procedure described for the preparation of **12**. **6b**: ^1H NMR (90 MHz, CCl_4, C_6H_6) δ 0.11 (s, 12 H), 0.93 (s, 18 H), 1.15–1.76 (m, 6 H), 1.92–2.12 (m, 2 H), 2.21 (t, J = 6 Hz, 2 H), 3.55 (t, J = 5.4 Hz, 2 H), 4.03 (q, J = 6 Hz, 1 H), 5.09–5.66 (m, 2 H), 6.17 (d, J = 15 Hz, 1 H), 6.44 (dd, J = 6, 15 Hz, 1 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 149.0, 132.7, 124.5, 75.8, 75.1, 63.2, 35.6, 32.7, 29.4, 27.4, 25.9, 25.8, 25.5, 18.3, 18.1, −4.8, −5.0, −5.4; IR (neat) 1608, 1248, 1092, 827, 770 cm^{-1}; HRMS calcd for $C_{19}H_{38}IO_2Si_2$ (M^+ − C_4H_9) 481.1456, found 481.1275.

1-Iodo-1(*E*)-undecen-3-ol (*dl*-34). The title compound *dl*-**34** was prepared from nonanoyl chloride (**33**) by the procedure descriabed by Negishi et al.[23] An ice-cooled suspension of $AlCl_3$ (26 g, 0.195 mol) in CCl_4 was flushed with acetylene. To this was

added nonanoyl chloride (**33**, 25 g, 0.141 mol) over 15 min. After the addition the mixture was stirred for 4 h at 0 °C under a slow stream of acetylene and poured into a mixture of ice (200 g) and brine (100 mL) with vigorous stirring. The product was extracted with $CHCl_3$ twice. The combined organic layers were washed with aqueous Na_2CO_3, dried ($MgSO_4$), and concentrated in vacuo. The residue was distilled to give 1-chloro-1(*E*)-undecen-3-one (25.6 g, 90%, bp 94–96 °C (0.6 mmHg)). A mixture of this chloride (25.6 g, 0.126 mol), NaI (37.5 g, 0.25 mol), and $AlCl_3$ (0.85 g, 6.4 mmol) in acetone (200 mL) was refluxed for 2 h and filtered through a pad of Celite. The filtrate was diluted with hexane and H_2O. The organic layer was separated and the aqueous layer was extracted with hexane. The combined extracts were dried ($MgSO_4$) and concentrated in vacuo to give crude 1-iodo-1(*E*)-undecen-3-one. A solution of this iodide dissolved in EtOH (50 mL) was added to an ice-cooled solution of $NaBH_4$ (3.4 g, 90 mmol) in EtOH (150 mL) over 30 min. After 2 h at 0 °C, the solution was concentrated in vacuo to afford the residue, which was diluted with hexane and water. The organic layer was separated and the aqueous layer was extracted with hexane. The combined extracts were dried ($MgSO_4$) and concentrated in vacuo. Distillation of the residue gave *dl*-**34** (32.4 g, 87% from 1-chloro-1(*E*)-undecen-3-one): ^1H NMR (90 MHz, CCl_4) δ 0.86 (t, J = 6 Hz, 3 H), 1.1–1.6 (m, 14 H), 2.85–3.00 (br s, 1 H), 3.90 (q, J = 6 Hz, 1 H), 6.12 (d, J = 16 Hz, 1 H), 6.38 (dd, J = 6, 16 Hz, 1 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 148.9, 77.1, 74.6, 36.4, 31.7, 29.3, 29.1, 25.0, 22.5, 13.9; IR (neat) 3350, 1605, 942 cm^{-1}; HRMS calcd for C_4H_7IO ($M^+ - C_7H_{15}$) 197.9543, found 197.9521.

1-Iodo-1(*E*)-undecen-3(*R*)-ol ((*R*)-34). To a mixture of $Ti(O\text{-}i\text{-}Pr)_4$ (1.70 mL, 5.71 mmol), L-(+)-DIPT (1.45 mL, 6.83 mmol), and 4A molecular sieves (3 g) in CH_2Cl_2 (20 mL) at −15 °C was added racemic alcohol *dl*-**34** (5.4 g, 18.2 mmol) dissolved in CH_2Cl_2 (15 mL). After 10 min at −15 °C, *t*-BuOOH (6.32 mL, 4.32 M in CH_2Cl_2, 27.3 mmol) was added dropwise at −30 °C. The reaction mixture was stirred for 40 h at −21 °C and dimethyl sulfide (2 mL, 27 mmol) was added. After 1 h at −21 °C, aqueous 10% tartaric acid (4 mL), Et_2O (50 mL), NaF (1.4 g), and Celite (1 g) were successively added. The mixture was vigorously stirred for 1 h at room temperature and filtered through a pad of Celite. The filtrate was concentrated to give the residue, which was diluted with Et_2O (50 mL). To this was added aqueous 1 N NaOH (25 mL), and the resulting mixture was stirred for 2 h at room temperature. The organic layer was separated, dried ($MgSO_4$), and concentrated in vacuo. The residue was chromatographed on silica gel to afford (*R*)-**34** (2.39 g, 44%). The enantiomeric excess of (*R*)-**34** was confirmed to be >99% by ^1H NMR spectroscopy of the derived MTPA ester. (*R*)-**34**: $[\alpha]^{25}_D$ −7.8° (*c* 1.23, $CHCl_3$).

1-Iodo-3(*R*)-[(*tert*-butyldimethylsilyl)oxy]-1(*E*)-undecene (6c). The alcohol (*R*)-**34** (2.39 g, 8.07 mmol) was converted into **6c** (3.15 g, 95%) with *tert*-butyldimethylsilyl chloride (1.64 g, 10.9 mmol) and imidazole (1.1 g, 16.2 mmol) in DMF (15 mL) by the procedure described for the preparation of **12**. **6c**: $[\alpha]^{25}_D$ +25.8° (*c* 1.12, $CHCl_3$); ^1H NMR (90 MHz, CCl_4, C_6H_6) δ 0.02 (s, 6 H), 0.88 (br s, 12 H), 1.1–1.6 (m, 14 H), 3.92 (q, J = 6 Hz, 1 H), 6.03 (d, J = 16 Hz, 1 H), 6.29 (dd, J = 6, 16 Hz, 1 H); IR (neat) 1610, 1460, 1245, 1080, 940, 830, 770 cm^{-1}.

5(*S*),12(*R*)-Bis[(*tert*-butyldimethylsilyl)oxy]-6(*Z*),8(*E*),10(*E*),14(*Z*)-eicosatetraenoic Acid (7a). To a solution of **4** (46 mg, 0.155 mmol) in THF (3 mL) at 0 °C was dropwise added freshly prepared Sia_2BH (0.46 mL, 0.5 M in THF, 0.23 mmol). The solution was stirred for 1 h at 0 °C, and aqueous 2 N LiOH (0.54 mL, 10.8 mmol) and **6a** (89 mg, 0.218 mmol) were added. Argon was bubbled into the reaction mixture for 15 min and then $Pd(PPh_3)_4$ (18 mg, 0.016 mmol) was added. The mixture was vigorously stirred at 40 °C for 18 h under argon atmosphere and then slowly poured into a vigorously stirred and ice-cooled mixture of saturated aqueous NH_4Cl (20 mL) and Et_2O (30 mL). The organic layer was separated, washed with brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by chromatography on silica gel using a deoxygenated mixture of hexane and Et_2O as an eluent to give **7a** (67 mg, 76%): $[\alpha]^{25}_D$ +4.3° (*c*, 0.60, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 0.02 (s, 3 H), 0.05 (s, 6 H), 0.07 (s, 3 H), 0.88 (s, 12 H), 0.91 (s, 9 H), 1.23–1.78 (m, 10 H), 2.01 (q, J = 7 Hz, 2 H), 2.22–2.38 (m, 4 H), 4.18 (q, J = 7 Hz, 1 H), 4.57 (q, J = 7 Hz, 1 H), 5.32–5.41 (m, 2 H), 5.44 (dt, J = 12, 7 Hz, 1 H), 5.72 (dd, J = 7, 14 Hz, 1 H), 5.96 (t, J = 12 Hz, 1 H), 6.13–6.25 (m, 2 H), 6.36 (dd, J = 12, 14 Hz, 1 H); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 179.8, 137.8, 134.9, 133.8, 132.0, 129.3, 128.1, 127.1, 125.2, 73.3, 68.8, 37.8, 36.5, 34.1, 31.6, 29.4, 27.5, 26.0, 22.6, 20.7, 18.3, 18.2, 14.1, −4.1, −4.3, −4.7; IR (neat) 3000, 1706, 1252, 1080, 836, 774 cm^{-1}.

Leukotriene B_4 (1). To a solution of **7a** (61 mg, 0.11 mmol) in THF (3 mL) at 0 °C was added *n*-Bu_4NF (1.6 mL, 0.67 M in THF, 1.1 mmol). The solution was stirred for 17 h at room temperature and poured into a vigorously stirred and ice-cooled mixture of Et_2O (30 mL) and McIlvaine's phosphate buffer solution (pH 5, 15 mL), prepared from $Na_2HPO_4 \cdot 12H_2O$ (7.38 g), citric acid (2.04 g), and H_2O (200 mL). The organic phase was separated, washed with brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by chromatography on silica gel using a deoxygenated mixture of Et_2O and MeOH as an eluent to give **1** (31 mg, 85% yield). RP-HPLC analysis (see Figure 1 and Table I) showed 98% purity for **1**. The spectroscopic data (^1H NMR (500 MHz), IR) were identical with those reported before.[5f,g] Other data of **1**: UV (MeOH) λ_{max} 260, 269, 281 nm (ϵ 39 000, 53 000, 43 000) (lit.[5g] λ_{max} 260, 270.5, 281 nm (ϵ 43 000, 52 000, 42 000)); $[\alpha]^{25}_D$ +13.1° (*c* 0.26, $CDCl_3$) (lit.[5g] $[\alpha]^{25}_D$ +12.6° (*c* 0.46, $CDCl_3$)); ^{13}C NMR (50 MHz, $CDCl_3$) δ 178.7, 136.9, 134.3, 134.1, 133.7, 130.4, 127.7, 124.2, 72.0, 67.6, 36.4, 35.2, 33.6, 31.4, 29.2, 27.3, 22.5, 20.4, 14.0; mp 25–28 °C (recrystallized from hexane-Et_2O).

Large-Scale Preparation of LTB_4 (1). According to the procedure described above, **4** (1.12 g, 3.78 mmol) in THF (30 mL) was treated with Sia_2BH (11 mL, 0.5 M in THF, 5.5 mmol) and then reacted with **6a** (2.01 g, 4.92 mmol), $Pd(PPh_3)_4$ (220 mg, 0.19 mmol), and aqueous 2 N LiOH (13.2 mL, 26.4 mmol) for 18 h at 40 °C to afford after chromatography **7a** (1.46 g, 69%).

The above silyl ether **7a** (1.46 g, 2.59 mmol) was treated with *n*-Bu_4NF (26 mL, 1.0 M in THF, 26 mmol) in THF (40 mL) for 14 h at room temperature to provide **1** (0.69 g, 80% yield, 97% purity by RP-HPLC analysis) after chromatography.

5(*S*),12(*R*)-Dihydroxy-6(*Z*),10(*E*),14(*Z*)-eicosatrien-8-ynoic Acid (8,9-Didehydro-LTB_4, 38). To a solution of the acetylene **4** (77 mg, 0.26 mmol), the iodide **6a** (138 mg, 0.338 mmol), and *n*-$PrNH_2$ (0.21 mL, 2.6 mmol) in benzene (4 mL) were added $Pd(PPh_3)_4$ (30 mg, 0.026 mmol) and CuI (5 mg, 0.026 mmol). The resulting solution was stirred for 12 h at room temperature and poured into a mixture of Et_2O and saturated aqueous NH_4Cl. The ethereal solution was separated, washed with brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by chromatography on silica gel to afford methyl ester of the corresponding silyl ether of **38** (142 mg, 97%): ^1H NMR (90 MHz, CCl_4, C_6H_6) δ 0.12 and 0.16 (2s, 12 H), 0.92 and 0.95 (2s), 1.2–1.9 (m, 10 H), 1.89–2.10 (m, 2 H), 2.14–2.37 (m, 4 H), 3.58 (s, 3 H), 4.16 (q, J = 5.7 Hz, 1 H), 4.47–4.78 (m, 1 H), 5.15–5.90 (m, 5 H), 6.05 (dd, J = 5.7, 16 Hz, 1 H); IR (neat) 1741, 1095 cm^{-1}.

To a solution of the above silyl ether (34 mg, 0.060 mmol) in THF (3 mL) was added *n*-Bu_4NF (1.1 mL, 0.67 M in THF, 0.74 mmol). The solution was stirred for 6 day at room temperature and poured into an ice-cooled mixture of Et_2O and the phosphate buffer solution (pH 5) with vigorous stirring. The organic layer was washed with brine, dried ($MgSO_4$), and concentrated in vacuo. Chromatography of the residue on silica gel gave **38** (13 mg, 65%): ^1H NMR (200 MHz, $CDCl_3$) δ 0.88 (t, J = 6 Hz, 3 H), 1.18–1.87 (m, 10 H), 1.96–2.13 (m, 3 H), 2.26–2.49 (m, 4 H), 1.9–2.9 (br peak, 3 H), 4.22 (q, J = 5.5 Hz, 1 H), 4.67 (q, J = 6.7 Hz, 1 H), 5.27–5.44 (m, 1 H), 5.53–5.63 (m, 1 H), 5.66 (d, J = 10.7 Hz, 1 H), 5.88 (d, J = 15.8 Hz, 1 H), 5.91 (dd, J = 6.7, 10.7 Hz, 1 H), 6.18 (dd, J = 5.5, 16.0 Hz, 1 H); IR (neat) 3360, 1711, 1250, 1042, 958 cm^{-1}.

LTB_4 δ-Lactone (39). LTB_4 (1, 6 mg, 0.018 mmol) was heated at 50 °C for 14 h under reduced pressure (0.1 mmHg), and the product was purified by chromatography on silica gel to afford the lactone **39**[24] (3 mg, 53%); ^1H NMR (200 MHz, $CDCl_3$) δ 0.88 (t, J = 6 Hz, 3 H), 1.16–2.12 (m), 2.25–2.73 (m, 6 H), 4.14–4.31 (m, 1 H), 5.18–5.68 (m, 4 H), 5.82 (dd, J = 6.3, 14 Hz, 1 H), 6.17 (t, J = 10.5 Hz, 1 H), 6.23–6.51 (m, 3 H); IR (neat) 3380, 1720, 1238, 1034 cm^{-1}.

5(*S*),12(*R*),20-Tris[(*tert*-butyldimethylsilyl)oxy]-6(*Z*),8(*E*),10(*E*),14(*Z*)-eicosatetraenoic Acid (7b). According to the procedure described for the preparation of **7a**, the acetylene **4** (72 mg, 0.24 mmol) in THF (4 mL) was treated with a solution

of Sia_2BH (1.3 mL, 0.36 M in THF, 0.47 mmol) at 0 °C for 1 h and then coupled with the iodide **6b** (178 mg, 0.330 mmol) in the presence of $Pd(PPh_3)_4$ (30 mg, 0.026 mmol) and aqueous 2 N LiOH (0.9 mL, 1.8 mmol) for 12 h at 40 °C to provide **7b** (141 mg, 85%): $[\alpha]^{23}_D$ +4.9° (*c* 1.5, $CDCl_3$); ^1H NMR (200 MHz, $CDCl_3$) δ 0.01, 0.04, and 0.05 (3s, 18 H), 0.87, 0.886, and 0.895 (3s, 27 H), 1.2–1.9 (m, 10 H), 1.94–2.07 (m, 2 H), 2.21–2.42 (m, 4 H), 3.59 (t, *J* = 6.5 Hz, 2 H), 4.17 (q, *J* = 6.2 Hz, 1 H), 4.47–4.62 (m, 1 H), 5.28–5.56 (m, 3 H), 5.71 (dd, *J* = 6.7, 14.0 Hz, 1 H), 5.96 (t, *J* = 11.1 Hz, 1 H), 6.08–6.27 (m, 2 H), 6.37 (dd, *J* = 11.8, 13.7 Hz, 1 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 179.4, 138.0, 135.1, 134.0, 132.1, 129.4, 128.2, 127.2, 125.4, 73.2, 68.8, 63.3, 37.7, 36.3, 33.8, 32.7, 29.4, 27.4, 25.9, 25.8, 25.5, 20.5, 18.3, 18.2, 18.1, -4.4, -4.5, -4.9, -5.0, -5.4; IR (neat) 3000, 1708, 1250, 1075, 834, 773 cm^{-1}.

20-Hydroxyleukotriene B_4 (2). The silyl ether **7b** (45 mg, 0.065 mmol) was treated with *n*-Bu_4NF (1 mL, 0.67 M in THF, 0.67 mmol) in THF (2 mL) for 18 h at room temperature. The solution was cooled to 0 °C and poured into an ice-cooled and vigorously stirred mixture of AcOEt (20 mL) and McIlvaine's phosphate buffer (pH 4, 15 mL) to afford 20-OH-LTB_4 (**2**) (18 mg, 79%). RP-HPLC analysis (t_R 27.4 min, MeOH/H_2O/AcOH/NH_4OH = 50:50:0.08:0.08, flow rate = 0.8 mL/min) showed 96% purity for **2**: $[\alpha]^{20}_D$ +9.4° (*c* 0.50, MeOH); UV (MeOH) λ_{max} 259, 269, 281 nm (ε 42 000, 56 000, 44 000) (lit.[3] λ_{max} 260, 270, 281 nm); ^1H NMR (500 MHz, $CDCl_3$ and acetone-d_6 (4:1)) δ 1.08–1.17 (m, 4 H), 1.23–1.34 (m, 3 H), 1.38–1.53 (m, 3 H), 1.77–1.83 (m, 2 H), 2.01–2.13 (m, 4 H), 3.34 (t, *J* = 6.6 Hz, 2 H), 2.3–3.6 (br peak, 4 H), 3.94 (q, *J* = 6.4 Hz, 1 H), 4.34 (dt, *J* = 10, 6 Hz, 1 H), 5.13–5.20 (m, 2 H), 5.21–5.28 (m, 1 H), 5.52 (dd, *J* = 6.4, 14.9 Hz, 1 H), 5.79 (t, *J* = 11.4 Hz, 1 H), 5.95 (dd, *J* = 10.7, 14.9 Hz, 1 H), 6.03 (dd, *J* = 10.7, 14.4 Hz, 1 H), 6.24 (dd, *J* = 11.4, 14.4 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$ and acetone-d_6 (4:1)) δ 174.9, 136.9, 134.2, 133.4, 132.2, 129.6, 129.0, 127.3, 124.7, 71.3, 66.7, 61.9, 36.4, 34.9, 33.1, 32.1, 28.8, 26.8, 24.9, 20.2; IR (neat) 3340, 1705, 1037, 994 cm^{-1}.

5(*S*),12(*R*)-Bis[(*tert*-butyldimethylsilyl)oxy]-6(*Z*),8-(*E*),10(*E*)-eicosatrienoic Acid (7c). According to the procedure described for the preparation of **7a**, the acetylene **4** (72 mg, 0.24 mmol) in THF (2.5 mL) was treated with Sia_2BH (1.0 mL, 0.5 M in THF, 0.5 mmol) and then reacted with **6c** (140 mg, 0.34 mmol) in the presence of $Pd(PPh_3)_4$ (50 mg, 0.043 mmol) and aqueous 2 N LiOH (1.0 mL, 2.0 mmol) with vigorous stirring for 18 h at 40 °C to provide **7c** (123 mg, 90%): $[\alpha]^{20}_D$ +8.4° (*c* 1.04, $CDCl_3$); ^1H NMR (200 MHz, $CDCl_3$) δ 0.01, 0.03, 0.04, and 0.06 (4s, 12 H), 0.87 and 0.89 (2s, 21 H), 1.16–1.79 (m), 2.36 (t, *J* = 6.2 Hz, 2 H), 4.14 (q, *J* = 6.0 Hz, 1 H), 4.54 (q, *J* = 6.7 Hz, 1 H), 5.36 (t, *J* = 9.7 Hz, 1 H), 5.56–5.79 (m, 1 H), 5.96 (t, *J* = 11.0 Hz, 1 H), 6.08–6.26 (m, 2 H), 6.34 (dq, *J* = 3.2, 10.8 Hz, 1 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 178.8, 138.7, 135.0, 134.1, 129.2, 128.2, 127.0, 73.3, 68.8, 38.3, 37.7, 33.7, 31.8, 29.6, 29.5, 29.2, 25.9, 25.8, 25.2, 22.6, 20.5, 18.2, 18.1, 14.0, -4.37, -4.43, -4.9, -5.0; IR (neat) 3100, 3030, 1710, 1630, 1462, 1250, 1080, 1000, 835 cm^{-1}.

Leukotriene B_3 (3). According to the procedure described for **1**, LTB_3 (**3**) (60 mg, 82%) was prepared from **7c** (123 mg, 0.22 mmol), *n*-Bu_4NF (3.5 mL, 0.67 M in THF, 2.3 mmol), and THF (2 mL) with stirring for 20 h at room temperature. RP-HPLC analysis (t_R 41.7 min, MeOH/H_2O/AcOH/NH_4OH = 66:33:0.08:0.08, flow rate = 0.8 mL/min) showed 97% purity for **3**: $[\alpha]^{21}_D$ +7.8° (*c* 0.23, $CDCl_3$); UV (MeOH) λ_{max} 261, 270, 281 nm (ε 38 000, 52 000, 41 000); ^1H NMR (200 MHz, $CDCl_3$) δ 0.86 (t, *J* = 6.3 Hz, 3 H), 1.1–1.8 (m), 2.35 (t, *J* = 6.6 Hz, 2 H), 4.14 (q, *J* = 6.2 Hz, 1 H), 4.50–4.66 (m, 1 H), 4.6–5.0 (br signal, 3 H), 5.40 (t, *J* = 9.7 Hz, 1 H), 5.73 (dd, *J* = 6.6, 14 Hz, 1 H), 6.06 (t, *J* = 11 Hz, 1 H), 6.14–6.54 (m, 3 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 178.5, 137.7, 134.3, 133.7, 130.4, 130.3, 127.6, 72.6, 67.5, 37.1, 36.4, 33.7, 31.8, 29.5, 29.2, 25.3, 22.6, 20.5, 14.0; IR (neat) 3380, 3020, 1705, 1215, 995, 750 cm^{-1}.

1-(Trimethylsilyl)-1(*E*)-undecen-5-yn-3-ol (45a). To a well-stirred solution of **25** (2.4 g, 10 mmol) and bipyridyl (ca. 5 mg) in THF (50 mL) at -60 °C was added *n*-BuLi (6.7 mL, 1.56 M in hexane, 10.5 mmol) dropwise. After stirring for 1 h at -60 °C, HMPA (5.2 mL, 30 mmol) and pentyl bromide (1.86 mL, 15 mmol) were successively added. The reaction was continued for 36 h at room temperature and quenched with H_2O. The product was extracted with hexane repeatedly. The combined extracts were dried ($MgSO_4$) and concentrated in vacuo to afford the ethoxyethyl ether of **45a**. A solution of this compound in MeOH (70 mL) and aqueous 3 N HCl (10 mL) was stirred at room temperature for 20 min and poured into brine. The product was extracted with hexane three times. The combined extracts were dried ($MgSO_4$) and concentrated in vacuo. The residue was purified by chromatography on silica gel to provide **45a** (1.84 g, 77%): ^1H NMR (90 MHz, CCl_4, CH_2Cl_2) δ 0.12 (s, 9 H), 0.94 (t, *J* = 6 Hz, 3 H), 1.1–1.7 (m, 6 H), 1.99–2.45 (m, 4 H), 2.4–2.8 (br peak, 1 H), 3.94–4.22 (m, 1 H), 5.87 (d, *J* = 18 Hz, 1 H), 6.03 (dd, *J* = 3, 18 Hz, 1 H); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 146.4, 130.2, 83.2, 75.6, 75.5, 72.4, 31.0, 28.6, 27.6, 22.1, 18.6, 13.8, -1.5; IR (neat) 3370, 1621, 1245, 865, 837 cm^{-1}; HRMS calcd for $C_{14}H_{25}Si$ (M^+ - OH) 221.1725, found 221.1721.

2(*S*)-[1′(*S*)-Hydroxy-3′-nonynyl]-3(*S*)-(trimethylsilyl)-oxirane (46a) and 1-(Trimethylsilyl)-1(*E*)-undecen-5-yn-3-(*R*)-ol (47a). According to the procedure for the kinetic resolution of *dl*-**28**, racemic alcohol **45a** (6.61 g, 27.8 mmol) was reacted with *t*-BuOOH (9.6 mL, 2.9 M in CH_2Cl_2, 27.8 mmol), L-(+)-DIPT (5.84 mL, 27.5 mmol), and $Ti(O\text{-}i\text{-}Pr)_4$ (8.27 mL, 27.8 mmol) in CH_2Cl_2 (160 mL) at -21 °C for 4 h, and the crude products were purified by chromatography on silica gel to give **46a** (3.32 g, 47%) and **47a** (2.72 g, 41%). The enantiomeric excesses of **46a** and **47a** were both >99% by ^1H NMR spectroscopy of the derived MTPA esters. **46a**: $[\alpha]^{25}_D$ +16.1° (*c* 1.65, $CHCl_3$); ^1H NMR (90 MHz, CCl_4, C_6H_6) δ 0.07 (s, 9 H), 0.88 (t, *J* = 6 Hz, 3 H), 1.1–1.7 (m, 6 H), 1.90–2.15 (m, 2 H), 2.18–2.46 (m, 3 H), 2.62 (br s, 1 H), 2.84 (t, *J* = 4 Hz, 1 H), 3.70 (dt, *J* = 4, 6 Hz, 1 H); IR (neat) 3440, 1250, 835 cm^{-1}. **47a**: $[\alpha]^{25}_D$ -55.3° (*c* 1.25, acetone).

2(*S*)-[1′(*R*)-Hydroxy-3′-nonynyl]-3(*S*)-(trimethylsilyl)-oxirane (48a). According to the procedure for **18**, **46a** (3.10 g, 12.2 mmol) was treated with *p*-nitrobenzoic acid (4.35 g, 26.0 mmol), PPh_3 (6.82 g, 26.0 mmol), and diethyl azodicarboxylate (3.76 mL, 23.9 mmol) in THF (40 mL) to afford the corresponding ester (3.66 g, 74%), which was hydrolyzed with aqueous 1 N NaOH (20 mL) and MeOH (30 mL) at 0 °C for 1 h to provide **48a** (1.90 g, 61%): $[\alpha]^{25}_D$ -29.8° (*c* 1.28, $CHCl_3$); ^1H NMR (90 MHz, CCl_4, CH_2Cl_2) δ 0.09 (s, 9 H), 0.90 (t, *J* = 6 Hz, 3 H), 1.1–1.7 (m, 6 H), 1.94–2.48 (m, 5 H), 2.78 (dd, *J* = 3.6, 4.8 Hz, 1 H), 2.95–3.47 (m, 2 H); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 82.7, 75.2, 71.8, 58.4, 49.3, 31.0, 28.6, 24.8, 22.1, 18.7, 13.8, -3.8; IR (neat) 3390, 1250, 842 cm^{-1}.

1-Iodo-1(*E*)-undecen-5-yn-3(*R*)-ol (51a). According to the procedure described for **6a**, the reaction involving **48a** (1.90 g, 7.48 mmol), *i*-Pr_2NH (4.21 mL, 30.0 mmol), *n*-BuLi (13.4 mL, 1.68 M in hexane, 22.5 mmol), *n*-Bu_3SnH (2.82 mL, 10.5 mmol), bipyridyl (ca. 5 mg), and THF (45 mL) and the subsequent reaction with I_2 (2.3 g, 9.1 mmol) in Et_2O (50 mL) gave **51a** (1.26 g, 58%): $[\alpha]^{25}_D$ +5.7° (*c* 1.20, $CHCl_3$); ^1H NMR (90 MHz, CCl_4) δ 0.89 (t, *J* = 6 Hz, 3 H), 1.1–1.7 (m, 6 H), 1.90–2.45 (m, 4 H), 3.10 (br s, 1 H), 4.05 (dt, *J* = 5, 6 Hz, 1 H), 6.39 (d, *J* = 15 Hz, 1 H), 6.55 (dd, *J* = 5, 15 Hz, 1 H); IR (neat) 3340, 1605, 1250, 1035, 945, 843 cm^{-1}.

The title compound **51a** was also prepared in the same way as above in 77% yield from the diastereomeric mixture of the epoxide, which was prepared from **47a** with *t*-BuOOH (1.6 equiv), and $Ti(O\text{-}i\text{-}Pr)_4$ (1.3 equiv) in CH_2Cl_2 in 92% yield.

3(*R*)-[(*tert*-Butyldimethylsilyl)oxy]-1-iodo-1(*E*)-undecen-5-yne (52a). The alcohol **51a** (355 mg, 1.21 mmol) was silylated with *tert*-butyldimethylsilyl chloride (260 mg, 1.72 mmol), imidazole (160 mg, 2.35 mmol), and DMF (2 mL) to provide **52a** (478 mg, 97%) by the procedure described for the preparation of **12**. **52a**: $[\alpha]^{25}_D$ -33.5° (*c* 1.07, $CHCl_3$); ^1H NMR (90 MHz, CCl_4, C_6H_6) δ 0.05 (s, 6 H), 0.7–1.0 (m, 12 H), 1.10–1.65 (m, 6 H), 1.97–2.36 (m, 4 H), 4.06 (q, *J* = 6 Hz, 1 H), 6.16 (d, *J* = 15 Hz, 1 H), 6.53 (dd, *J* = 5, 15 Hz, 1 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 147.9, 82.9, 76.6, 75.8, 74.3, 31.0, 28.5, 28.1, 25.6, 22.1, 18.6, 18.1, 13.9, -4.9, -5.1; IR (neat) 1670, 1610, 1465, 1250, 1095, 940, 835, 770 cm^{-1}; HRMS calcd for $C_{13}H_{22}IOSi$ ($M^+ - C_4H_9$) 349.0486, found 349.0510.

5(*S*),12(*R*)-Dihydroxy-6(*Z*),8(*E*),10(*E*)-eicosatrien-14-ynoic Acid (14,15-Didehydroleukotriene B_4, 40). According to the procedure described for the preparation of **7a**, the acetylene **4** (82 mg, 0.28 mmol) in THF (4 mL) was treated with Sia_2BH (0.83 mL, 0.5 M in THF, 0.42 mmol) and then reacted with the iodide **52a** (157 mg, 0.39 mmol), $Pd(PPh_3)_4$ (32 mg, 0.028 mmol), and aqueous 2 N LiOH (1.4 mL, 2.8 mmol) to afford crude **53a**,

which was used for the next reaction without further purification. An analytically pure sample was obtained by chromatography on silica gel: ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.04, 0.06, 0.07, and 0.08 (4s, 12 H), 0.87 (s, 12 H), 0.90 (s, 9 H), 1.20–1.85 (m, 10 H), 2.06–2.19 (m, 2 H), 2.23–2.48 (m, 4 H), 4.28 (q, J = 6.3 Hz, 1 H), 4.49–4.62 (m, 1 H), 5.37 (dd, J = 8.8, 10 Hz, 1 H), 5.81 (ddd, J = 3.0, 6.5, 14 Hz, 1 H), 5.97 (t, J = 11 Hz, 1 H), 6.12–6.48 (m, 3 H).

The above silyl ether **53a** was treated with n-Bu_4NF (4.2 mL, 0.67 M in THF, 2.8 mmol) in THF (2 mL) for 12 h at room temperature, and the product was purified in the same way as **1** to provide **40** (51 mg, 55%): 96% purity by RP-HPLC analysis (t_R 11.0 min, MeOH/H_2O/AcOH/NH_4OH = 66:33:0.08:0.08, flow rate = 0.8 mL/min); ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.89 (t, J = 6 Hz, 3 H), 1.2–1.8 (m, 10 H), 2.09–2.22 (m, 2 H), 2.28–2.49 (m, 4 H), 2.9–4.1 (br peak, 3 H), 4.29 (q, J = 5.9 Hz, 1 H), 4.54–4.67 (m, 1 H), 5.42 (t, J = 9.7 Hz, 1 H), 5.81 (dd, J = 5.9, 14.3 Hz, 1 H), 6.08 (t, J = 11.0 Hz, 1 H), 6.16–6.42 (m, 2 H), 6.49 (dd, J = 11.9, 13.2 Hz, 1 H); IR (neat) 3380, 1712, 1385 cm^{-1}.

11-[(*tert*-Butyldimethylsilyl)oxy]-1-(trimethylsilyl)-1-(*E*)-undecen-5-yn-3-ol (45b). Acetylene **25** (6.22 g, 25.9 mmol) was converted into crude **26** with 1-(1′-ethoxyethoxy)-5-iodopentane (11.1 g, 38.8 mmol), n-BuLi (17.8 mL, 1.53 M in hexane, 27.2 mmol), HMPA (9.75 mL, 56.0 mmol), and THF (30 mL) as described earlier. The crude product **26** was treated with aqueous 1 N HCl (7 mL) in MeOH (30 mL) for 2 h at room temperature to give 3,11-dihydroxy-1-(trimethylsilyl)-1(*E*)-undecen-5-yne (3.90 g, 59% from **25**): ^{1}H NMR (90 MHz, CCl_4, C_6H_6) δ 0.11 (s, 9 H), 1.1–1.7 (m, 6 H), 1.92–2.34 (m, 4 H), 3.47 (t, J = 6 Hz, 2 H), 3.78 (br s, 2 H), 3.90–4.17 (m, 1 H), 5.80 (d, J = 18 Hz, 1 H), 6.04 (dd, J = 3.6, 18 Hz, 1 H); IR (neat) 3330, 1247, 1038, 861, 838 cm^{-1}.

According to the procedure described for the preparation of *dl*-**28**, the above diol (3.90 g, 15.3 mmol) was selectively silylated with *tert*-butyldimethylsilyl chloride (4.87 g, 32.3 mmol), pyridine (3 mL, 37 mmol), and acetonitrile (86 mL) to provide racemic **45b** (4.67 g, 83%): ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.03 and 0.06 (2s, 15 H), 0.88 (s, 9 H), 1.32–1.61 (m, 6 H), 2.09–2.23 (m, 3 H), 2.36–2.46 (m, 2 H), 3.59 (t, J = 6.2 Hz, 2 H), 4.18 (m, 1 H), 5.96 (d, J = 19 Hz, 1 H), 6.16 (dd, J = 4.4, 19 Hz, 1 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 146.7, 130.4, 83.2, 75.8, 72.4, 63.1, 32.2, 28.7, 27.6, 25.9, 25.0, 18.6, 18.2, −1.5, −5.5; IR (neat) 3350, 1249, 1098, 833 cm^{-1}.

2(*S*)-[9′-[(*tert*-Butyldimethylsilyl)oxy]-1′(*S*)-hydroxy-3-nonynyl]-3(*S*)-(trimethylsilyl)oxirane (46b) and 11-[(*tert*-Butyldimethylsilyl)oxy]-1-(trimethylsilyl)-1(*E*)-undecen-5-yn-3(*R*)-ol (47b). According to the procedure for the kinetic resolution of *dl*-**28**, racemic alcohol **45b** (2.09 g, 5.67 mmol) was treated with *t*-BuOOH (2.0 mL, 4.32 M in CH_2Cl_2, 8.64 mmol), L-(+)-DIPT (1.44 g, 6.80 mmol), and Ti(O-*i*-Pr)$_4$ (1.62 g, 5.44 mmol) in CH_2Cl_2 (30 mL) at −21 °C for 12 h to give **46b** (1.02 g, 47%) and **47b** (0.90 g, 43%). Enantiomeric excesses of **46b** and **47b** were 98% and >99%, respectively, by ^{1}H NMR spectroscopy of the derived MTPA esters. **46b**: $[\alpha]^{25}_D$ +11.2° (*c* 1.02, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.03 and 0.07 (2s, 15 H), 0.87 (s, 9 H), 1.33–1.60 (m, 6 H), 2.11–2.22 (m, 3 H), 2.37 (d, J = 3.7 Hz, 1 H), 2.42–2.51 (m, 2 H), 3.00 (t, J = 3.7 Hz, 1 H), 3.59 (t, J = 6.3 Hz, 1 H), 3.79–3.90 (m, 1 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 82.9, 75.0, 68.3, 62.9, 57.5, 47.8, 32.2, 28.6, 25.8, 24.9, 24.1, 18.6, 18.1, −4.0, −5.6; IR (neat) 3430, 1249, 1101, 835, 772 cm^{-1}; HRMS calcd for $C_{16}H_{31}O_3Si_2$ ($M^+ - C_4H_9$) 327.1811, found 327.1795. **47b**: $[\alpha]^{25}_D$ −40.8° (*c* 1.10, acetone).

1-[(*tert*-Butyldimethylsilyl)oxy]-1-iodo-1(*E*)-undecen-5-yn-3(*R*)-ol (51b). According to the procedure described for **6a**, **51b** was prepared from **47b** in 76% overall yield. **51b**: $[\alpha]^{25}_D$ +6.3° (*c*, 1.11, $CHCl_3$); ^{1}H NMR (90 MHz, CCl_4, CH_2Cl_2) δ 0.06 (s, 6 H), 0.88 (s, 9 H), 1.2–1.7 (m, 6 H), 1.98–2.38 (m, 4 H), 2.4–2.8 (m, 1 H), 3.53 (t, J = 5.4 Hz, 2 H), 3.90–4.21 (m, 1 H), 6.30 (d, J = 15 Hz, 1 H), 6.51 (dd, J = 4.5, 15 Hz, 1 H); IR (neat) 3370, 1249, 1099, 835, 770 cm^{-1}.

3(*R*),11-Bis[(*tert*-butyldimethylsilyl)oxy]-1-iodo-1(*E*)-undecen-5-yne (52b). The alcohol **51b** was silylated to **52b** in 85% yield by the same procedure as described for the preparation of **12**. **52b**: $[\alpha]^{25}_D$ −24.8° (*c* 1.18, $CHCl_3$); ^{1}H NMR (90 MHz, CCl_4, CH_2Cl_2) δ 0.02 and 0.07 (2s, 12 H), 0.89 (s, 18 H), 1.2–1.7 (m, 6 H), 1.94–2.32 (m, 4 H), 3.52 (t, J = 6 Hz, 2 H), 4.08 (q, J = 5.5 Hz, 1 H), 6.19 (d, J = 14 Hz, 1 H), 6.52 (dd, J = 5.4, 14 Hz, 1 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 148.0, 82.8, 76.5, 76.0, 74.3, 63.1, 32.3, 28.7, 28.1, 25.9, 25.7, 25.0, 18.7, 18.2, 18.1, −4.9, −5.0, −5.4; IR (neat) 1249, 1100, 835, 774 cm^{-1}; HRMS calcd for $C_{19}H_{37}O_2ISi_2$ ($M^+ - C_4H_9$) 480.1378, found 480.1307.

5(*S*),12(*R*),20-Tris[(*tert*-butyldimethylsilyl)oxy]-6(*Z*),8-(*E*),10(*E*)-eicosatrien-14-ynoic Acid (53b). According to the procedure described for the preparation of **7a**, the acetylene **4** (49 mg, 0.165 mmol) in THF (4 mL) was treated with Sia_2BH (0.66 mL, 0.5 M in THF, 0.33 mmol) and then reacted with **52b** (120 mg, 0.224 mmol) in the presence of $Pd(PPh_3)_4$ (20 mg, 0.017 mmol) and aqueous 2 N LiOH (1.0 mL, 2.0 mmol) with vigorous stirring for 14 h at 40 °C to provide **53b** (61 mg, 53%): ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.01, 0.05, 0.06, and 0.08 (4s, 18 H), 0.87, 0.89, and 0.90 (3s, 27 H), 1.1–1.9 (m, 10 H), 2.07–2.18 (m, 2 H), 2.28–2.41 (m, 4 H), 3.62 (t, J = 6.5 Hz, 2 H), 4.27 (q, J = 6 Hz, 1 H), 4.50–4.62 (m, 1 H), 5.37 (dd, J = 9, 11 Hz, 1 H), 5.79 (dd, J = 6, 15 Hz, 1 H), 5.96 (t, J = 11 Hz, 1 H), 6.11–6.28 (m, 2 H), 6.36 (dd, J = 11, 14 Hz, 1 H); IR (neat) 3050, 1713, 1256, 1090, 848, 778 cm^{-1}.

5(*S*),12(*R*),20-Trihydroxy-6(*Z*),8(*E*),10(*E*)-eicosatrien-14-ynoic Acid (14,15-Didehydro-20-OH-LTB$_4$, 41). According to the procedure described for **7b**, the silyl ether **53b** (57 mg, 0.082 mmol) was treated with n-Bu_4NF (0.82 mL, 1 M in THF, 0.82 mmol) for 13 h at room temperature to afford **41** (19 mg, 66%): 95% purity by RP-HPLC analysis (t_R 10.9 min, MeOH/H_2O/AcOH/NH_4OH = 50:50:0.08:0.08, flow rate = 0.7 mL/min); ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.2–1.8 (m, 10 H), 2.0–2.6 (m, 10 H), 3.62 (t, J = 5.9 Hz, 2 H), 4.31 (q, J = 6.0 Hz, 1 H), 4.53–4.67 (m, 1 H), 5.44 (dd, J = 9.2, 10.7 Hz, 1 H), 5.77 (dd, J = 6.0, 14.5 Hz, 1 H), 6.06 (t, J = 11.4 Hz, 1 H), 6.26 (dd, J = 10.5, 14.5 Hz, 1 H), 6.33 (dd, J = 10.5, 14.5 Hz, 1 H), 6.53 (dd, J = 11.4, 14.5 Hz, 1 H).

1-Phenoxy-4-(trimethylsilyl)-3(*E*)-buten-2-ol (45c). To a solution of allyl phenyl ether (24 g, 180 mmol) in MeOH (150 mL) at −78 °C was passed ozone at a rate of gentle bubbling. After all of the ether had disappeared, argon was bubbled at −78 °C for 15 min and then dimethyl sulfide (20 mL) was added. The resulting solution was warmed up to room temperature gradually over 1.5 h and concentrated in vacuo. Distillation of the residue gave a 4:1 mixture of phenoxyacetaldehyde and dimethyl sulfoxide (19.3 g), which was used for the next reaction without further separation: ^{1}H NMR (90 MHz, CCl_4) δ 4.38 (s, 2 H), 6.65–7.35 (m, 5 H), 9.70 (s, 1 H).

To an ice-cooled solution of MeLi (84 mL, 1.48 M in Et_2O, 124 mmol) was added slowly (trimethylsilyl)acetylene (19.1 mL, 135 mmol). After 30 min at 0 °C, the above aldehyde (19.3 g) was added at 0 °C. The solution was stirred for 30 min at 0 °C and poured into a mixture of aqueous 1 N HCl and ice with vigorous stirring. The mixture was extracted with hexane three times. The combined organic layers were dried ($MgSO_4$) and concentrated in vacuo to give 1-phenoxy-4-(trimethylsilyl)-3-butyn-2-ol (26.9 g, 64% from allyl phenyl ether): ^{1}H NMR (90 MHz, CCl_4, C_6H_6) δ 0.17 (s, 9 H), 3.46 (br s, 1 H), 3.99 (d, J = 6 Hz, 2 H), 4.63 (t, J = 6 Hz, 1 H), 6.67–7.22 (m, 5 H).

To an ice-cooled solution of $[(CH_3O(CH_2)_2O)_2AlH_2]Na$ (40 mL, 3.56 M in toluene, 142 mmol) in Et_2O (200 mL) was added dropwise the above acetylene (17.8 g, 76.1 mmol). The resulting solution was refluxed overnight and cooled to 0 °C, and then H_2O (10 mL), NaF (15 g), and Celite (15 g) were slowly added at 0 °C. The mixture was stirred for 2 h and filtered through a pad of Celite with Et_2O (50 mL). Concentration of the filtrate gave an oil, which was distilled to afford **45c** (17.1 g, 95%): bp 150–160 °C (0.15 mmHg); ^{1}H NMR (90 MHz, CCl_4, CH_2Cl_2) δ 0.15 (s, 9 H), 2.83 (br s, 1 H), 3.93 (dd, J = 7.8, 10.2 Hz, 1 H), 4.04 (dd, J = 4.0, 10.2 Hz, 1 H), 4.36–4.55 (m, 1 H), 6.21 (s, 2 H), 6.85–7.50 (m, 5 H); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 158.5, 143.4, 131.9, 129.3, 121.0, 114.6, 72.3, 71.7, −1.4; IR (neat) 3350, 3080, 1590, 1235, 1174, 1080, 1045, 945, 750, 685 cm^{-1}. Anal. Calcd for $C_{13}H_{20}O_2Si$: C, 66.05; H, 8.53. Found; C, 66.04; H, 8.50.

2(*S*)-(1′(*S*)-Hydroxy-2′-phenoxy)-3(*S*)-(trimethylsilyl)-oxirane (46c) and 1-Phenoxy-4-(trimethylsilyl)-3(*E*)-buten-2(S)-ol (47c). According to the procedure for the kinetic resolution of *dl*-**28**, **45c** provided **46c** (46%) and **47c** (47%) as white solids, enantiomeric excesses of which were found to be both >99% by ^{1}H NMR spectroscopy of the derived MTPA esters. **46c**: $[\alpha]^{25}_D$ −17.0° (*c* 0.978, $CHCl_3$); ^{1}H NMR (90 MHz, CCl_4, CH_2Cl_2) δ 0.19 (s, 9 H), 2.36 (d, J = 3.7 Hz, 1 H), 2.80 (br s, 1 H), 2.95–3.12

(m, 1 H), 3.73–4.37 (m, 3 H), 6.74–7.45 (m, 5 H); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 158.6, 129.5, 121.3, 114.7, 69.8, 69.5, 55.7, 48.8, -3.7; IR (Nujol) 3400, 1598, 1585 cm^{-1}; mp 61.5–62.5 °C (recrystallized from pentane–Et_2O). **47c**: mp 49–50 °C (recrystallized from pentane–Et_2O).

3(*S*)-[(*tert*-Butyldimethylsilyl)oxy]-1-iodo-4-phenoxy-1(*E*)-butene (52c). According to the procedure described for the preparation of **6a**, **52c** was prepared in 83% yield: $[\alpha]^{25}_D$ +8.2° (*c* 0.93, $CHCl_3$); ^{1}H NMR (90 MHz, CCl_4, CH_2Cl_2) δ 0.14 (s, 6 H), 0.93 (s, 9 H), 3.83 (d, *J* = 8.8 Hz, 2 H), 4.35–4.60 (m, 1 H), 6.52 (d, *J* = 15.6 Hz, 1 H), 6.64 (dd, *J* = 4.6, 15.6 Hz, 1 H), 6.72–7.32 (m, 5 H); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 158.5, 145.4, 129.4, 121.0, 114.6, 78.0, 73.7, 71.4, 25.8, 18.3, -4.7; IR (neat) 1605, 1248, 830 cm^{-1}; HRMS calcd for $C_{12}H_{17}IO_2Si$ ($M^+ - C_4H_8$) 348.0044, found 348.0014.

5(*S*),12(*S*)-Dihydroxy-13-phenoxy-6(*Z*),8(*E*),10(*E*)-tridecatrienoic Acid (42). Acetylene **4** (49 mg, 0.165 mmol) was treated with Sia_2BH (0.5 mL, 0.5 M in THF, 0.25 mmol) and then coupled with **52c** (90 mg, 0.22 mmol) in the presence of $Pd(PPh_3)_4$ (17 mg, 0.015 mmol) and aqueous 2 N LiOH (1.0 mL, 2.0 mmol) to afford **53c** (85 gm, 91%): ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.01, 0.04, 0.06, and 0.09 (4s, 12 H), 0.84 (s, 9 H), 0.88 (s, 9 H), 1.10–1.80 (m, 4 H), 2.23–2.40 (m, 2 H), 3.86 (d, *J* = 6.0 Hz, 2 H), 4.48–4.65 (m, 2 H), 5.39 (t, *J* = 9.6 Hz, 1 H), 5.80 (dd, *J* = 5.6, 15.1 Hz, 1 H), 5.96 (t, *J* = 11.1 Hz, 1 H), 6.21 (dd, *J* = 11.1, 14.6 Hz, 1 H), 6.28–6.50 (m, 2 H), 6.82–7.35 (m, 5 H).

The above silyl ether **53c** (85 mg, 0.15 mmol) was treated with *n*-Bu_4NF (1.5 mL, 1.0 M in THF, 1.5 mmol) in THF (2 mL) to furnish **42** (42 mg, 84%): 96% purity by RP-HPLC analysis (t_R 7.6 min, MeOH/H_2O/AcOH/NH_4OH = 66:33:0.08:0.08, flow rate = 0.8 mL/min; ^{1}H NMR (200 MHz, acetone-d_6) δ 1.50–1.80 (m, 4 H), 2.33 (t, *J* = 7.2 Hz, 2 H), 3.87–4.04 (m, 2 H), 4.50–4.68 (m, 2 H), 5.44 (t, *J* = 9.9 Hz, 1 H), 5.90 (dd, *J* = 5.7, 15.2 Hz, 1 H), 6.05 (t, *J* = 11.1 Hz, 1 H), 6.29 (dd, *J* = 10.6 Hz, 14.5 Hz, 1 H), 6.52 (ddd, *J* = 1.2, 10.6, 15.2 Hz, 1 H), 6.65 (dd, *J* = 11.2, 14.6 Hz, 1 H), 6.88–7.32 (m, 5 H); IR (neat) 3400, 1705, 1245, 1115, 750 cm^{-1}.

5-Cyclohexyl-1-iodo-1(*E*)-penten-3-ol (50d). To a solution of 3-cyclohexylpropionic acid (50 g, 0.32 mol) in benzene (100 mL) was slowly added oxalyl chloride (56 mL, 0.64 mol). After the addition, the solution was stirred overnight at room temperature and then most of the volatile materials were removed by evaporation to leave an oil, which was distilled to afford 3-cyclohexylpropionyl chloride (**49d**, 55.3 g, 99%; bp 75–76 °C (1 mmHg)).

The above acid chloride (**49d**) was converted into **50d** in 81% yield by the procedure described for the preparation of *dl*-**34**. **50d**: ^{1}H NMR (90 MHz, CCl_4) δ 0.65–1.80 (m, 15 H), 2.55–3.15 (br peak, 1 H), 3.84 (q, *J* = 6 Hz, 1 H), 6.14 (d, *J* = 15 Hz, 1 H), 6.40 (dd, *J* = 6, 15 Hz, 1 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 148.9, 77.2, 74.9, 37.4, 33.8, 33.2, 32.6, 26.5, 26.2; IR (neat) 3260, 1610, 1250, 945 cm^{-1}. Anal. Calcd for $C_{11}H_{19}IO$: C, 44.91; H, 6.51; I, 43.14. Found: C, 45.24; H, 6.62; I, 42.89.

3(*R*)-[(*tert*-Butyldimethylsilyl)oxy]-5-cyclohexyl-1-iodo-1(*E*)-pentene (52d). According to the procedure described for *dl*-**34**, racemic alcohol **50d** (10 g, 34 mmol) was treated with *t*-BuOOH (12 ml, 4.33 M in CH_2Cl_2, 52 mmol), L-(+)-DIPT (2.4 g, 11 mmol), Ti(O-*i*-Pr)$_4$ (2.4 g, 8.06 mmol), 4A molecular sieves (3 g), and CH_2Cl_2 (80 mL) for 40 h at -21 °C to give **51d** (4.1 g, 41%), the enantiomeric excess of which was analyzed to be >99% by ^{1}H NMR spectroscopy of the derived MTPA ester: $[\alpha]^{25}_D$ -6.1° (*c* 2.0, $CHCl_3$).

The alcohol **51d** (4.05 g, 13.8 mmol) was converted into **52d** (4.99 g, 89%) with *tert*-butyldimethylsilyl chloride (2.7 g, 18 mmol) and imidazole (1.7 g, 25 mmol) in DMF (30 mL) by the procedure described for the preparation of **12**. **52d**: $[\alpha]^{25}_D$ +23.9° (*c* 1.33, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.02 and 0.04 (2s, 6 H), 0.88 (s), 0.78–1.75 (m), 4.04 (dq, *J* = 1.2, 6.0 Hz, 1 H), 6.18 (dd, *J* = 1.2, 14.3 Hz, 1 H), 6.51 (dd, *J* = 6.0, 14.4 Hz, 1 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 149.6, 75.5, 37.6, 34.8, 33.3, 32.4, 26.6, 26.3, 25.8, 18.1, -4.7, -5.0; IR (neat) 1610, 1450, 1250, 1080, 830, 770 cm^{-1}.

14-Cyclohexyl-5(*S*),12(*R*)-dihydroxy-6(*Z*),8(*E*),10(*E*)-tetradecatrienoic Acid (43). Acetylene **4** (110 mg, 0.37 mmol) was treated with Sia_2BH (1.2 mL, 0.5 M in THF, 0.6 mmol) and then coupled with **52d** (210 mg, 0.51 mmol) in the presence of $Pd(PPh_3)_4$ (30 mg, 0.026 mmol) and aqueous 2 N LiOH (1.3 mL, 2.6 mmol) to afford **53d** (188 mg, 88%): ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.01, 0.03, and 0.04 (3s, 12 H), 0.80–1.78 (m), 2.36 (t, *J* = 7.2 Hz, 2 H), 4.11 (q, *J* = 6.1 Hz, 1 H), 4.49–4.61 (m, 1 H), 5.36 (dd, *J* = 8.7, 10.5 Hz, 1 H), 5.60–5.78 (m, 1 H), 5.96 (t, *J* = 11.0 Hz, 1 H), 6.09–6.44 (m, 3 H); IR (neat) 3100, 1705, 1248, 1080, 905, 835, 720 cm^{-1}.

The above silyl ether **53d** (188 mg, 0.32 mmol) was treated with *n*-Bu_4NF (5 mL, 1 M in THF, 5 mmol) in THF (5 mL) to furnish **43** (74 mg, 69%): 96% purity by RP-HPLC analysis (t_R 22.7 min, MeOH/H_2O/AcOH/NH_4OH = 66:33:0.08:0.08, flow rate = 0.8 mL/min); ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.73–1.78 (m, 19 H), 2.39 (t, *J* = 6.8 Hz, 2 H), 2.9–3.9 (br peak, 3 H), 4.73 (q, *J* = 6.4 Hz, 1 H), 4.53–4.66 (m, 1 H), 5.42 (t, *J* = 9.9 Hz, 1 H), 5.75 (dd, *J* = 6.7, 14.3 Hz, 1 H), 6.08 (t, *J* = 11.0 Hz, 1 H), 6.16–6.34 (m, 2 H), 6.49 (dd, *J* = 11.0, 13.5 Hz, 1 H); IR (neat) 3360, 1705, 1215, 993, 748 cm^{-1}.

1-Cyclohexyl-3-iodo-2(*E*)-propen-1-ol (50e). Cyclohexanecarbonyl chloride (**49e**) was converted into **50e** in 53% yield (three steps) by the procedure described for the preparation of *dl*-**34**. **50e**: bp 129 °C (1 mmHg); ^{1}H NMR (90 MHz, CCl_4) δ 0.7–2.1 (m, 11 H), 2.86 (br s, 1 H), 3.72 (t, *J* = 6.4 Hz, 1 H), 6.10 (d, *J* = 15.6 Hz, 1 H), 6.46 (dd, *J* = 6.4, 15.6 Hz, 1 H); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 147.6, 79.0, 77.0, 43.6, 28.8, 28.3, 26.5, 26.1; IR (neat) 3320, 1605, 1010, 948 cm^{-1}. Anal. Calcd for $C_9H_{15}IO$: C, 40.62; H, 5.68; I, 47.69. Found: C, 40.37; H, 5.59; I, 47.22.

1(*R*)-[(*tert*-Butyldimethylsilyl)oxy]-1-cyclohexyl-3-iodo-2(*E*)-propene (52e). According to the procedure described for *dl*-**34**, racemic alcohol **50e** (5.33 g, 20.0 mmol) was treated with *t*-BuOOH (10.4 mL, 2.9 M in CH_2Cl_2, 30 mmol), L-(+)-DIPT (1.69 g, 7.96 mmol), Ti(O-*i*-Pr)$_4$ (1.72 g, 5.78 mmol), 4A molecular sieves (2.0 g), and CH_2Cl_2 (30 mL) for 53 h at -21 °C to give **51e** (2.24 g, 42%), the enantiomeric excess of which was analyzed to be >99% by ^{1}H NMR spectroscopy of the derived MTPA ester: $[\alpha]^{25}_D$ -11.4° (*c* 1.40, $CHCl_3$).

The above alcohol **51e** (4.05 g, 15.2 mmol) was converted into **52e** (4.99 g, 86%) with *tert*-butyldimethylsilyl chloride (2.7 g, 18 mmol) and imidazole (1.7 g, 25 mmol) in DMF (30 mL) by the procedure described for the preparation of **12**. **52e**: $[\alpha]^{25}_D$ +31.6° (*c* 1.54, $CHCl_3$); ^{1}H NMR (90 MHz, CCl_4, C_6H_6) δ 0.09 (s, 6 H), 0.95 (s), 0.7–1.9 (m), 3.73 (t, *J* = 6 Hz, 1 H), 6.06 (d, *J* = 14 Hz, 1 H), 6.41 (dd, *J* = 6, 14 Hz, 1 H); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 148.3, 79.7, 75.8, 44.2, 28.8, 28.4, 26.6, 26.3, 25.9, 18.3, -4.3, -4.8; IR (neat) 1608, 1455, 1255, 1105, 838, 775 cm^{-1}; HRMS calcd for $C_{11}H_{20}IOSi$ ($M^+ - C_4H_9$) 323.0330, found 323.0316.

12-Cyclohexyl-5(*S*),12(*R*)-dodecatrienoic Acid (44). Acetylene **4** (45 mg, 0.15 mmol) was treated with Sia_2BH (0.61 mL, 0.5 M in THF, 0.31 mmol) and then coupled with **52e** (75 mg, 0.20 mmol) in the presence of $Pd(PPh_3)_4$ (18 mg, 0.016 mmol) and aqueous 2 N LiOH (0.53 mL, 1.1 mmol) to afford **53e** (70 mg, 86%): ^{1}H NMR (200 MHz, $CDCl_3$) δ -0.01, 0.01, 0.03, and 0.04 (4s, 12 H), 0.87 (s, 9 H), 0.89 (s, 9 H), 0.90–1.90 (m, 15 H), 2.35 (t, *J* = 6.6 Hz, 2 H), 3.84 (t, *J* = 6.6 Hz, 1 H), 4.47–4.62 (m, 1 H), 5.36 (dd, *J* = 7.6, 10.9 Hz, 1 H), 5.67 (q, *J* = 7.1 Hz, 1 H), 5.95 (t, *J* = 11.0 Hz, 1 H), 6.06–6.44 (m, 3 H); IR (neat) 3100, 1710, 1250, 1088, 835, 775 cm^{-1}.

The above silyl ether **53e** (29 mg, 0.054 mmol) was treated with *n*-Bu_4NF (0.81 mL, 0.67 M in THF, 0.54 mmol) in THF (2 mL) to furnish **44** (12 mg, 72%) as a white solid: 96% purity by RP-HPLC analysis (t_R 16.2 min, MeOH/H_2O/AcOH/NH_4OH = 60:40:0.08:0.08, flow rate = 0.54 mL/min); ^{1}H NMR (200 MHz, acetone-d_6) δ 0.85–1.90 (m, 15 H), 2.30 (t, *J* = 7.2 Hz, 2 H), 2.75–3.00 (br peak, 1 H), 3.6–3.9 (br peak, 2 H), 3.83 (t, *J* = 6.3 Hz, 1 H), 4.54–4.59 (m, 1 H), 5.40 (dd, *J* = 8.8, 10.7 Hz, 1 H), 5.78 (dd, *J* = 6.6, 14.2 Hz, 1 H), 6.04 (dt, *J* = 1.0, 11.1 Hz, 1 H), 6.18–6.66 (m, 3 H); IR (Et_2O) 3410, 1695, 1245, 1000 cm^{-1}; mp 95–98 °C (recrystallized from hexane–Et_2O).

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Supplementary Material Available: ^{1}H NMR and ^{13}C NMR spectra of the compounds described in this paper (89 pages). Ordering information is given on any current masthead page.