# Synthesis of 10,11-Dihydroleukotriene $B_4$ Metabolites via a Nickel-Catalyzed Coupling Reaction of *cis*-Bromides and *trans*-Alkenyl Borates

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Synthesis of 10,11-dihydro-, 10,11,14,15-tetrahydro-, and 10,11-dihydro-12-oxoleukotriene $B_4$ compounds (**2**, **4**, **5**) was accomplished stereoselectively by using the nickel-catalyzed coupling reaction illustrated in Scheme 1. The C(1)−C(7) fragments, TBS ether **10a** for **2** and **4** and ethyoxyethyl (EE) ether **10b** for **5**, were prepared in enantiomerically pure forms (>99% ee) by a modified literature procedure (ref 11a). On the other hand, boronate esters **11a** and **11b**, which correspond to the C(8)−C(20) parts of **2** and **4**, respectively, were synthesized from (*R*)-epichlorohydrin (**18**) of 99% ee. Briefly, **18** was converted into acetylenes **24** and **32** through epoxide ring-opening with $LiC{\equiv}CC_5H_{11}/BF_3{\cdot}OEt_2$ or $C_7H_{15}MgBr/CuCN$. Hydroboration of these acetylenes with (+)-$(Ipc)_2BH$ followed by reaction with MeCHO afforded the corresponding diethyl boronates, which upon ligand exchange with $Me_2C(CH_2OH)_2$ furnished boronate esters **11a** and **11b** in 75% and 77% yields, respectively. In a similar manner, racemic boronate ester *rac*-**11a**, an intermediate for synthesis of **5**, was prepared from racemic epichlorohydrin. For synthesis of **2**, borate **25** was generated from **11a** (1.5 equiv) and MeLi (1.6 equiv). Without isolation, **25** was submitted to reaction with **10a** (1 equiv) in the presence of a Ni(0) species at room temperature overnight to afford **26**, which upon treatment with TBAF furnished **2** in 64% yield from **10a**. Similarly, **11b** and **10a** furnished **4** in good yield. To synthesize **5**, *rac*-**11a** and EE ether **10b** were joined by the coupling reaction to produce **39**, which was transformed into **40** by desilylation with TBAF. After hydrolysis of **40**, oxidation with PDC followed by deprotection of the EE group furnished **5** in 36% yield from **40**. In addition, **2** was converted into amide **3** in 92% yield.

## Introduction

Recently, 10,11-dihydro derivatives of leukotriene $B_4$ ($LTB_4$) (**1**) have been isolated,[1,2] and pathway(s) leading to them and the specific enzymes involved in the route have been investigated.[3] On the basis of the biological activities,[2c,4] these metabolites are now recognized as initial products of a second metabolic pathway of **1** in addition to the $\omega$-oxidation pathway.[5] The metabolites involve 10,11-dihydro-$LTB_4$ (**2**),[2,3] 10,11-dihydro-12-*epi*-$LTB_4$ (structure not shown),[2b,c,3d] 10,11,14,15-tetrahydro-$LTB_4$ (**4**),[6] 10,11-dihydro-12-oxo-$LTB_4$ (**5**),[2a,b] etc. (Figure 1). Although these products suggest a possibility that $LTB_3$ and $LTB_5$ are metabolized similarly and **4** is formally a product from $LTB_3$, direct evidence for such a possibility has not been reported so far. From a synthetic point of view, establishment of a chemical method for synthesis of these 10,11-dihydro metabolites and those which might be produced from $LTB_3$ and $LTB_5$ would facilitate greater understanding of the pathway(s), isolation/determination of new metabolites, and examination of the biological roles at several stages.

By stimulation leukocytes produce $LTB_4$ (**1**), which, in turn, activates other leukocytes at a concentration of $10^{-9}$ M.[7] Hence, **1** is believed to be a most potent mediator of inflammation and allergic responses.[8] The activation is initiated by binding to the specific receptors, and the sequence of amino acids of the receptor has been deter-

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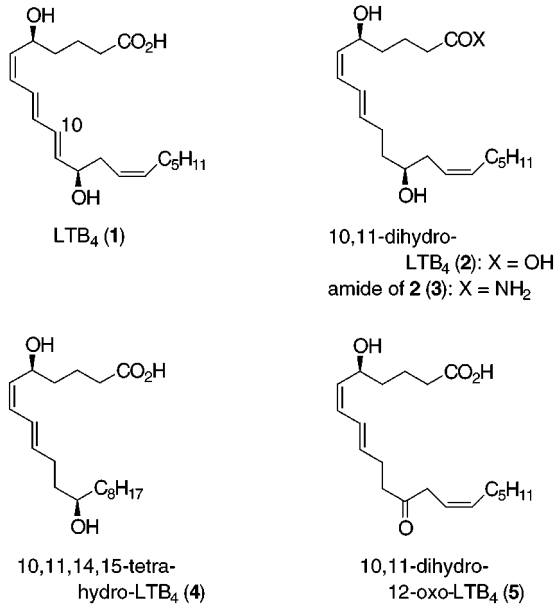



**Figure 1.** Leukotriene $B_4$ ($LTB_4$) (**1**) and dihydro-$LTB_4$ compounds **2**−**5**.

mined recently.[9] These achievements have partially been supported by supplying **1** and analogues synthesized by total synthesis,[10,11] and **1** is still required to further understand the biological action and to find a new drug against the diseases caused by leukocytes. One such investigation probably involves installation of **1** onto peptides and polymer supports. Unfortunately, the extremely unstable nature of **1** would certainly incur difficulties during the installation.[12] To this end, 10,11-dihydro-$LTB_4$ (**2**) is a good candidate for the following reasons. First, **2** still retains the biological property of **1**, though **2** is less active than **1**. Second, the chemical stability of the diene system of **2** allows use of less mild reactions which are not compatible with **1**.

Despite the importance of 10,11-dihydro metabolites as such and as a stable substitute for **1**, only two papers accomplishing synthesis of **2**, **4**, and **5** have been published so far.[13,14] The synthesis, however, suffers from low

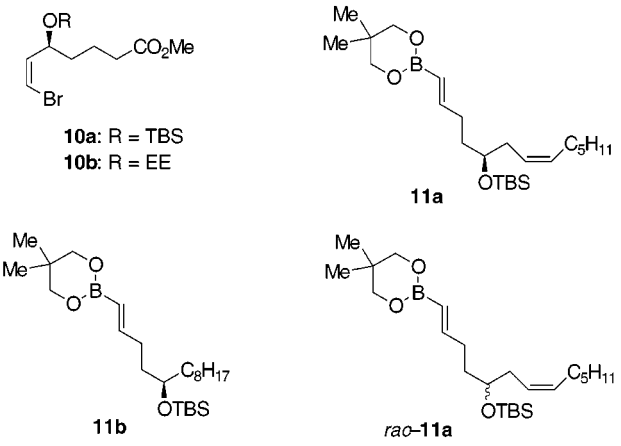
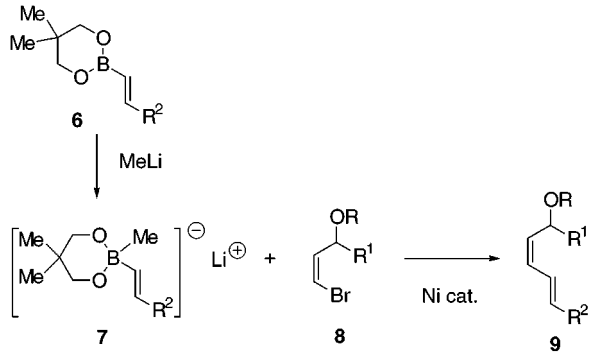



**Figure 2.** Intermediates used for synthesis of **2**−**5**: **2** and **3** from **10a** + **11a**; **4** from **10a** + **11b**; **5** from **10b** + *rac*-**11a**.

**Scheme 1**




stereoselectivity in the formation of the cis double bond at C(6) via Wittig reaction. Recently, we have developed a method for synthesis of the conjugated diene unit of type **9** as illustrated in Scheme 1.[15] Reaction of boronate esters **6** and MeLi produces lithium borates **7**, which are highly reactive species to couple with sterically hindered *cis*-bromides **8** in the presence of a nickel catalyst to afford **9** with retention of the olefin geometry. By using this reaction as a key step, synthesis of **2**, **4**, and **5** was accomplished stereoselectively, for the first time.[16] In addition, the amide of **2** (i.e., **3**) was synthesized as well. The amide might be useful as a $LTB_4$ antagonist on the analogy of $LTB_4$ amide.[17] Herein, we present details of the synthesis.

## Results and Discussion

**Synthetic Intermediates.** On the basis of the reaction summarized in Scheme 1, the following combinations of the boronate ester and the *cis*-bromide were planned for the synthesis of **2**−**5**: **10a** and **11a** for **2** and **3**; **10a** and **11b** for **4**; **10b** and *rac*-**11a** for **5** (Figure 2). Preparation of these intermediates and synthesis of **2**−**5** are described below.

**Preparation of the C(1)−C(7) Segments.** Two *cis*-bromides (**10a** and **10b**) were prepared according to the

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(12) We had the following problems in our synthesis[11a] of **1** and its analogues. (1) Treatment of an ethereal solution of **1** with diluted HCl caused decomposition within 30 min at 0 °C. (2) Gentle bubbling of nitrogen in an eluent for chromatography on silica gel was crucial to prevent isomerization to the 6*E* isomer. (3) Use of commercial $CDCl_3$ was responsible for the partial isomerization to the 6*E* isomer during a routine $^{13}C$ NMR measurement probably due to the presence of DCl. DCl-free $CDCl_3$ was prepared by passing $CDCl_3$ through a pad of $Al_2O_3$ (from Merck) before use.

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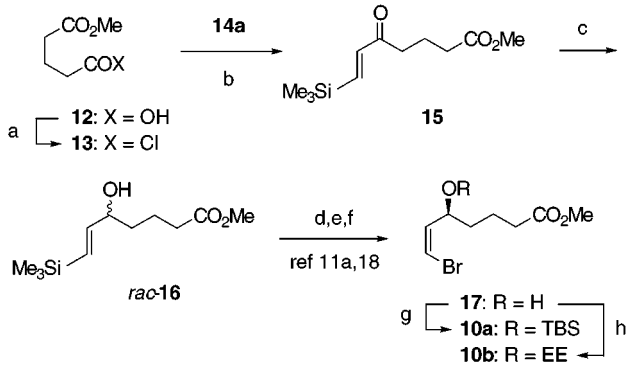
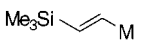
**Scheme 2**[a]




[a] Reagents and conditions: (a) $SOCl_2$, DMF (10 mol %); (b) **14a**, $PdCl_2(PPh_3)_2$ (0.4 mol %), $CHCl_3$, 77% from **12**; (c) $NaBH_4$, 81%; (d) *t*-BuOOH, $Ti(OPr)_4$, D-(−)-DIPT; (e) $Br_2$, −78 °C; (f) TBAF, −78 °C, THF; (g) TBSCl, imidazole; (h) $CH_2$=CHOEt, PPTS, $CH_2Cl_2$, 86%.

literature procedure[11a,18] with a modification as presented in Scheme 2. Originally, vinylsilane *rac*-**16** was prepared from methyl 4-formylbutanoate and aluminate **14b**, which in turn was generated from vinylstannane **14a**

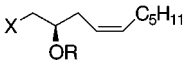



**14a**: M = $SnBu_3$
**14b**: M = $AlEt_2$

through lithiation using *n*-BuLi followed by Li/Al exchange with $Et_2AlCl$. Although the reaction proceeded efficiently, isolation of *rac*-**16** from a mixture containing a large mass of coproduced $Bu_4Sn$ by chromatography required somewhat larger volumes of silica gel and an eluent. To avoid the production of $Bu_4Sn$, the Stille reaction[19] was applied to acid chloride **13** and stannane **14a**. The reaction proceeded smoothly to furnish a mixture of ketone **15** and $Bu_3SnCl$, and the latter was simply removed by washing with aqueous NaOH, thus allowing easy purification of **15** by chromatography. Reduction of ketone **15** with $NaBH_4$ then afforded racemic alcohol *rac*-**16** in 62% overall yield from the half-acid **12**. Transformation of *rac*-**16** into *cis*-bromide **10a** exactly followed the literature procedure,[11a] which involves, as the key reaction, kinetic resolution of *rac*-**16** using the Sharpless reagent[20] to produce (*S*)-**16** (structure not shown) of >99% ee (determined by $^1H$ NMR spectroscopy of the derived MTPA ester). On the other hand, reaction of alcohol **17** with $CH_2$=CHOEt furnished **10b** in 86% yield.

**Preparation of the C(8)−C(20) Segment 11a and Synthesis of 10,11-Dihydro-LTB$_4$ (2) and Its Amide 3.** To secure a synthetic route eventually leading to **2** and **3**, a method for obtaining the key boronate ester **11a** was explored first. Among the methods so far published,[21] the protocol developed by Suzuki and Miyaura[22] was found to be suitable. Thus, hydroboration of acetylene **24** with (+)-$(Ipc)_2BH$ followed by oxidation with excess MeCHO at 40 °C and subsequent ligand exchange with the diol furnished boronate ester **11a** in 75% yield (Scheme 3).

Preparation of acetylene **24** and synthesis of 10,11-dihydro-LTB$_4$ (**2**) from boronate ester **11a** were explored by the route presented in Scheme 3. (*R*)-Epichlorohydrin (**18**) of 99% ee was transformed into alcohol **19** by the Yamaguchi method (LiC≡$CC_5H_{11}$, $BF_3$·$OEt_2$, −78 °C).[23] Since reduction of **19** in the presence of $Pd/BaSO_4$ and quinoline afforded a mixture of *cis*-olefin **27** and its trans isomer in varying ratios of >20 to 8:1, **19** was converted into TBS ether **20**. In contrast to **19**, reduction of **20** under the same conditions afforded *cis*-olefin **28** exclusively in 99% yield. Olefin **28** was treated with $Bu_4NF$ and subsequently with NaOH to furnish epoxide **21** in 95% yield. Epoxide ring-opening of **21** with allenylmagnesium bromide (**22**), prepared from propargyl bromide and Mg in the presence of $HgCl_2$,[24] afforded a mixture of alcohol **23** and bromohydrin **29**. Without separation, the

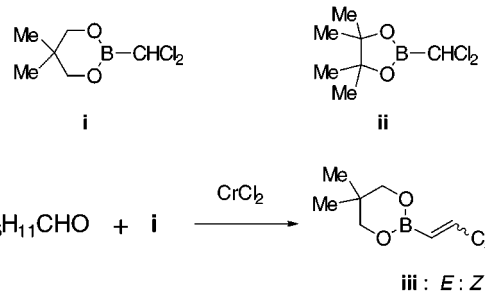



**27**: X = Cl; R = H
**28**: X = Cl; R = TBS
**29**: X = Br; R = H

mixture was treated with $K_2CO_3$ to convert **29** again to epoxide **21**, and chromatography of the resulting mixture afforded **23** and **21** in 62% and 20% yields, respectively. Silylation of **23** afforded acetylene **24** in 93% yield. Successful transformation of **24** to boronate ester **11a** is described in the above paragraph. For coupling of *cis*-bromide **10a** and boronate **11a**, lithium borate **25** and a Ni(0) species were generated by addition of MeLi (1.6 equiv) to a mixture of **11a** (1.5 equiv) and $NiCl_2(PPh_3)_2$ (10 mol %) in THF. After addition of bromide **10a** (1 equiv), the reaction was carried out at room temperature overnight to furnish diene **26** stereoselectively in 77% yield. Finally, treatment of **26** with excess $Bu_4NF$ ensued desilylation and hydrolysis to afford the target molecule **2** in 83% yield.

For conversion of acid **2** to amide **3**, **2** was esterified with $CH_2N_2$ (eq 1). The resulting methyl ester was then

(21) (a) For example, an application of the Takai reaction[21b] to boronate ester **i**[21c] produced a stereoisomeric mixture of alkene **iii**, though the original reaction using **ii** furnishes stereoselectively the corresponding trans isomer, which is, however, marginally reactive for the coupling with *cis*-bromides.[15]




**iii** : *E* : *Z* = 3 : 1

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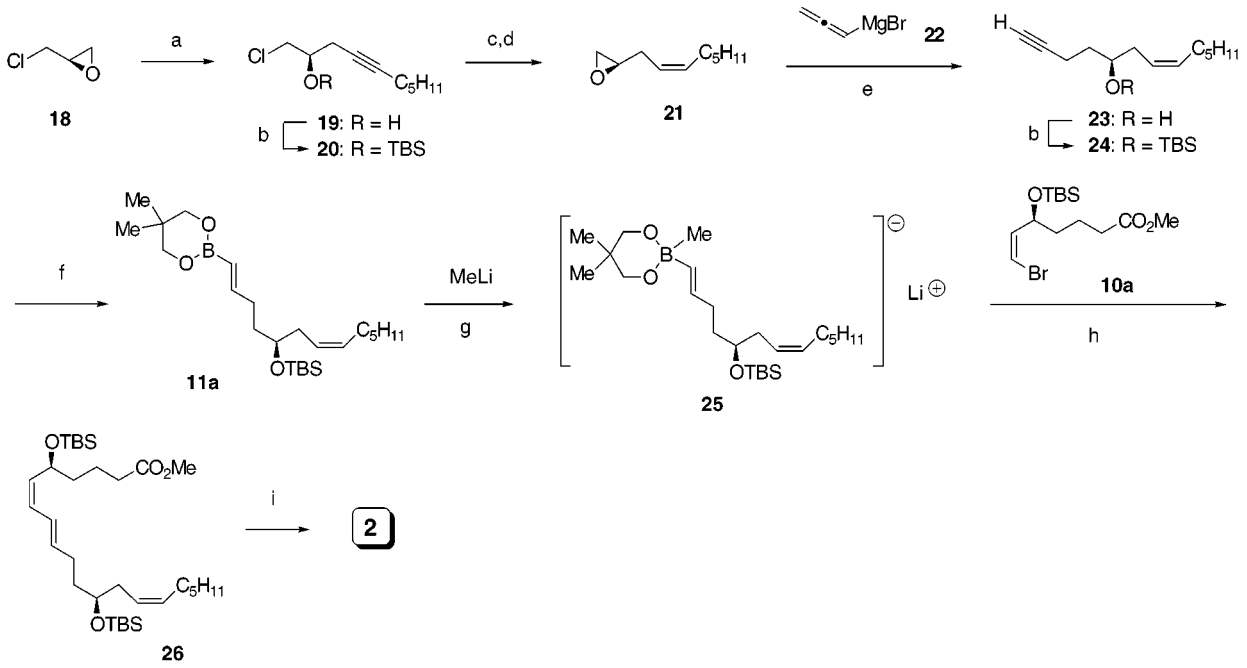
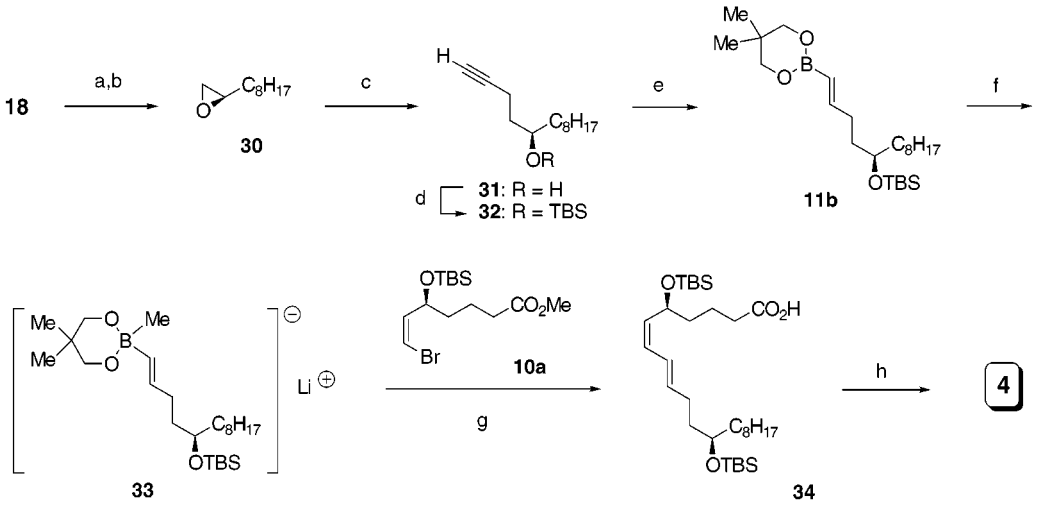
**Scheme 3**[a]




[a] Reagents and conditions: (a) LiC≡$CC_5H_{11}$, $BF_3$·$OEt_2$, 70%; (b) TBSCl, imidazole, 99% for **20**, 93% for **24**; (c) $H_2$, Pd/$BaSO_4$, quinoline, MeOH, 100%; (d) TBAF, THF then NaOH, THF, 95%; (e) **22** (1.5 equiv), $Et_2O$, −30 to 0 °C, then $K_2CO_3$, MeOH, rt, 1 h, 62%; (f) (i) (+)-$(Ipc)_2BH$ (1.2 equiv), THF, −35 to 0 °C, 2 h; (ii) MeCHO (15 equiv), 40 °C; (iii) $Me_2C(CH_2OH)_2$ (1.2 equiv), rt, 1 h, 75%; (g) **11a** (1.5 equiv), $NiCl_2(PPh_3)_2$ (10 mol %), MeLi (1.6 equiv), THF, 0 °C, 20 min; (h) **10a** (1 equiv), rt, overnight, 77% based on **10a**; (i) TBAF (10 equiv), THF, rt, overnight, 83%.

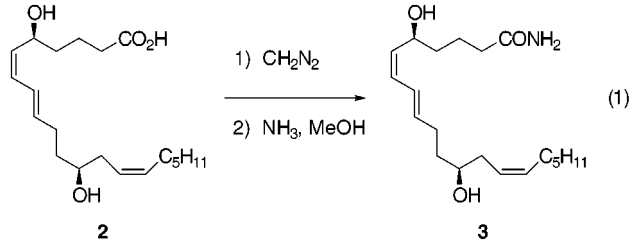
**Scheme 4**[a]




[a] Reagents and conditions: (a) $C_7H_{15}MgBr$, CuCN, THF, 100%; (b) NaOH, THF, rt, 3 h, 96%; (c) **22**, $Et_2O$, −50 to −10 °C, then $K_2CO_3$, MeOH, 57%; (d) TBSCl, imidazole, 90%; (e) (i) (+)-$(Ipc)_2BH$, THF, −35 to 0 °C, 2 h; (ii) MeCHO, 40 °C; (iii) $Me_2C(CH_2OH)_2$, rt, 1 h, 77%; (f) **11b** (1.5 equiv), $NiCl_2(PPh_3)_2$ (10 mol %), MeLi (1.6 equiv), THF, 0 °C, 20 min; (g) **10a** (1 equiv), rt, overnight, 74% based on **10a**; (h) TBAF (10 equiv), THF, 78%.

treated with $NH_3$ in MeOH for several days, furnishing amide **3** in 92% yield. During the conversion, isomerization of the cis double bond to the trans one was not observed by $^1H$ NMR spectroscopy.

**Synthesis of 10,11,14,15-Tetrahydro-LTB$_4$ (4).** To prepare the key intermediate **11b**, epoxide **18** of 99% ee was converted into another epoxide (**30**)[25] in 96% yield by copper-catalyzed epoxide ring-opening with $C_7H_{15}$-MgBr followed by reaction with NaOH (Scheme 4). Then **30** was converted into boronate ester **11b** through acetylenes **31** and **32** with yields similar to those obtained




(1)

(25) Preparation of **30** by another method: (a) Masaoka, Y.; Sakakibara, M.; Mori, K. *Agric. Biol. Chem.* **1982**, *46*, 2319−2324. (b) Sugai, T.; Mori, K. *Agric. Biol. Chem.* **1984**, *48*, 2497−2500.

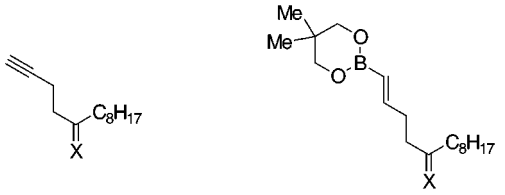
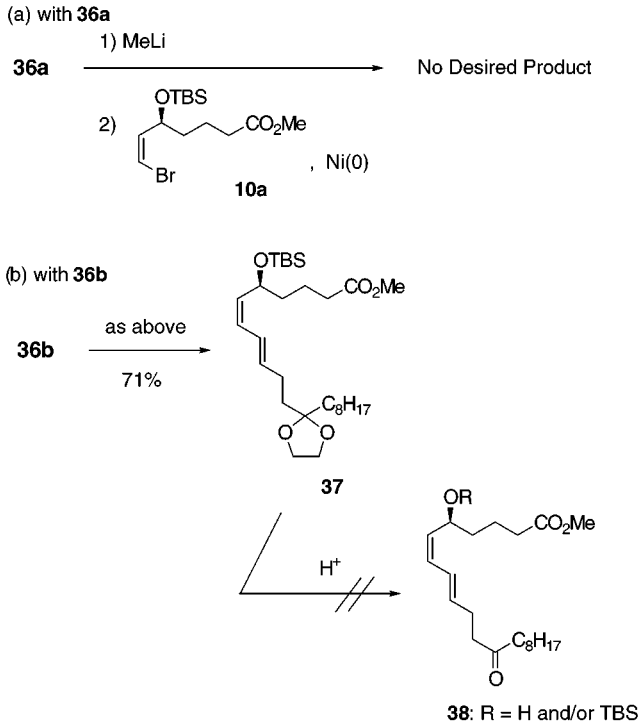



**Figure 3.** Acetylenes **35a**,**b** and boronate esters **36a**,**b** used as model compounds for synthesis of **5** (for results, see Schemes 5).

**Scheme 5. Resuts of the Model Study for Synthesis of 5**

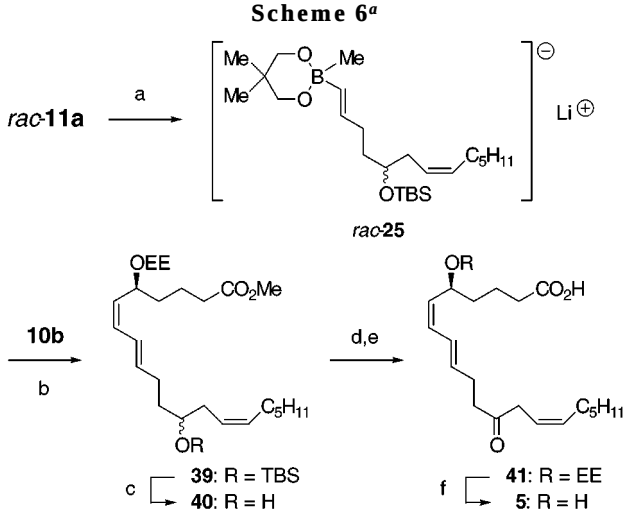



for preparation of **11a**. Coupling reaction of boronate **11b** and bromide **10a** also proceeded in a stereoselective manner to produce diene **34** in 74% yield, which upon hydrolysis afforded tetrahydro-$LTB_4$ (**4**) in 78% yield.

**Synthesis of 10,11-Dihydro-12-oxo-$LTB_4$ (5).** The coupling strategy was examined preliminarily with model boronate esters **36a** and **36b** (Figure 3). These intermediates were prepared from acetylenes **35a** and **35b** in 54% and 62% yields, respectively, by the method through hydroboration with $(Ipc)_2BH$.[22] Attempted coupling of bromide **10a** with ketone **36a** under the conditions used in Schemes 3 and 4 (MeLi, $NiCl_2(PPh_3)_2$) produced messy products (Scheme 5). On the other hand, acetal **36b** furnished the coupling product **37** in 71% yield. Unfortunately, deprotection of the ketal group in **37** under a variety of conditions resulted in recovery or decomposition of **37**.

Next, we explored another route involving oxidation of a 12-hydroxyl compound. To differentiate the two hydroxyl groups at C(5) and C(12), ethoxyethyl ether **10b** was chosen as the C(1)−C(7) part and the racemic boronate ester (*rac*-**11a**) was prepared from racemic epichlorohydrin exactly following the route summarized in Scheme 3. Treatment of *rac*-**11a** with MeLi produced

**Scheme 6**[a]




[a] Reagents and conditions: (a) *rac*-**11a** (1.5 equiv), $NiCl_2(PPh_3)_2$ (15 mol %), MeLi (1.6 equiv), THF, 0 °C, 20 min; (b) **10b** (1 equiv), rt, overnight, 48% based on **10b**; (c) TBAF (2 equiv), THF, rt, overnight, 70%; (d) 1 N NaOH, MeOH; (e) PDC (1.5 equiv), Celite, 44% from **40**; (f) PPTS, *i*-PrOH, rt, 8 h, 81%.

borate *rac*-**25**, and reaction with *cis*-bromide **10b** afforded diene **39** in 48% yield, which upon desilylation furnished alcohol **40** in 70% yield as depicted in Scheme 6. After hydrolysis, the crucial oxidation was successfully achieved with PDC, furnishing ketone **41** in 44% yield. Finally, deprotection of the EE group at C(5) completed the synthesis of 12-oxo-$LTB_4$ **5**.

## Conclusion

In summary, we have succeeded in synthesizing 10,11-dihydro-$LTB_4$ (**2**) and its amide **3** in a stereoselective fashion, for the first time. By using the present method, other dihydro-$LTB_4$ compounds (**4** and **5**) have also been synthesized stereoselectively. Since the double bond at C(14) of $LTB_4$ (**1**) is not responsible for the biological property,[17] **4** is probably more convenient as a substitute of **1** than **2** because synthesis of **4** is simpler than that of **2** due to the absence of the double bond. Furthermore, the present method is definitely applicable to stereoselective synthesis of other 10,11-dihydro-$LTB_4$ compounds. We believe that biological research of 10,11-dihydro-$LTB_4$ compounds as well as $LTB_4$ would be much accelerated with these results.

## Experimental Section

**General Methods.** Infrared (IR) spectra are reported in wavenumbers ($cm^{-1}$). Unless otherwise noted, $^1H$ NMR (300 MHz) and $^{13}C$ NMR (75 MHz) spectra were measured in $CDCl_3$ using $SiMe_4$ ($\delta$ 0 ppm) and the center line of $CDCl_3$ triplet ($\delta$ 77.1 ppm) as internal standards, respectively. The following solvents were distilled before use: THF (from Na/benzophenone), $Et_2O$ (from Na/benzophenone), and $CH_2Cl_2$ (from $CaH_2$). *N*,*N*-Dimethylformamide (DMF) was dried over $CaH_2$. Acetaldehyde (purity >99.5%) was purchased from Aldrich, and (*R*)-epichlorohydrin (**20**) (99% ee) was kindly offered by Daiso, Japan. The phosphate buffer of pH 5 was prepared by mixing $Na_2HPO_4 \cdot 12H_2O$ (7.38 g), citric acid (2.04 g), and $H_2O$ (200 mL). *trans*-1-(Trimethylsilyl)-2-(tributylstannyl)ethylene was prepared from trimethylsilylacetylene by the literature method.[26] Routinely, an organic extract was dried over $MgSO_4$ and

(26) Cunico, R. F.; Clayton, F. J. *J. Org. Chem.* **1976**, *41*, 1480−1482.

concentrated by using a rotary evaporator to leave a residual oil, which was purified by chromatography on silica gel. Some intermediates were distilled before use, and oven temperatures are given as boiling points.

**4-Methoxycarbonylbutanoic Acid (12).**[27] A solution of glutaric anhydride (6.00 g, 52.6 mmol) and NaOMe (57 mg, 1.06 mmol) in MeOH (75 mL) was stirred at room temperature overnight and most of the MeOH was removed by evaporation. A residue obtained was diluted with $H_2O$, and the resulting mixture was extracted with EtOAc twice. The combined extracts were dried and concentrated to give an oil, which was purified by chromatography to furnish **12** (7.25 g, 95%): IR (neat) 3250, 1736, 1709 $cm^{-1}$; $^1H$ NMR $\delta$ 1.86 (quintet, $J = 7$ Hz, 2 H), 2.29−2.39 (m, 4 H), 3.60 (s, 3 H), 11.62 (br s, 1 H); $^{13}C$ NMR $\delta$ 179.1, 173.6, 51.5, 32.8, 32.7, 19.6. Anal. Calcd for $C_6H_{10}O_4$: C, 49.31; H, 6.90. Found: C, 49.13; H, 6.85.

**Methyl (*E*)-5-Oxo-7-trimethylsilyl-6-heptenoate (15).** To a solution of **12** (0.96 g, 6.58 mmol) and DMF (0.05 mL, 0.65 mmol) in benzene (10 mL) was added $SOCl_2$ (0.72 mL, 9.87 mmol), and the resulting solution was heated for 2 h (bath temperature 80 °C). After the solution was cooled to room temperature, volatile materials were removed by using a vacuum pump to give crude **13**, which was used for the next reaction without further purification.

To the above acid chloride **13** dissolved in $CHCl_3$ (10 mL) were added $PdCl_2(PPh_3)_2$ (18 mg, 0.026 mmol) and **14a** (2.69 g, 6.91 mmol). The resulting solution was heated overnight (bath temperature 65 °C), cooled to room temperature, washed with 1 N NaOH, dried, and concentrated. The residue thus obtained was purified by chromatography (hexane/EtOAc) to give **15** (1.15 g, 77%): bp 125 °C (1 Torr); IR (neat) 1739, 1697, 1678, 1590 $cm^{-1}$; $^1H$ NMR $\delta$ 0.13 (s, 9 H), 1.94 (quintet, $J = 7$ Hz, 2 H), 2.37 (t, $J = 7$ Hz, 2 H), 2.67 (t, $J = 7$ Hz, 2 H), 3.67 (s, 3 H), 6.46 (d, $J = 19$ Hz, 1 H), 7.05 (d, $J = 19$ Hz, 1 H); $^{13}C$ NMR $\delta$ 199.1, 173.4, 146.4, 142.0, 51.1, 37.8, 32.6, 18.7, −2.3. Anal. Calcd for $C_{11}H_{20}O_3Si$: C, 57.85; H, 8.83. Found: C, 57.47; 9.07.

**Methyl (5*R*,6*E*)- and (5*S*,6*E*)-5-Hydroxy-7-trimethylsilyl-6-heptenoate (*rac*-16).** To an ice-cold solution of ketone **15** (701 mg, 3.07 mmol) in MeOH (10 mL) was added $NaBH_4$ (58 mg, 1.53 mmol) portionwise. The mixture was stirred at 0 °C for 30 min, and most of the MeOH was removed by using a rotary evaporator. To the residue was added brine, and the product was extracted with EtOAc repeatedly. The combined EtOAc solutions were dried and concentrated to afford an oil, which was purified by chromatography (benzene/EtOAc) to furnish *rac*-**16** (576 mg, 81%). The IR and $^{13}C$ NMR spectra of *rac*-**16** were identical with those reported previously.[18] $^1H$ NMR ($CDCl_3$) of *rac*-**16**: $\delta$ 0.07 (s, 9 H), 1.50−1.84 (m, 4 H), 2.36 (t, $J = 7$ Hz, 2 H), 2.6 (br s, 1 H), 3.67 (s, 3 H), 4.05−4.15 (m, 1 H), 5.87 (d, $J = 19$ Hz, 1 H), 6.04 (dd, $J = 19$, 5.5 Hz, 1 H).[28]

**Methyl (5*S*,6*E*)-5-[(*tert*-Butyldimethylsilyl)oxy]-7-trimethylsilyl-6-heptenoate (10a).** According to the literature procedure,[18] (*S*)-**16** of >99% ee (determined by $^1H$ NMR spectroscopy of the MTPA ester) was prepared from *rac*-**16** by the kinetic resolution using *t*-BuOOH, D-(−)-DIPT, and Ti(OPr)$_4$, and converted into TBS ether **10a** by bromination with $Br_2$ followed by reaction with TBAF and protection with TBSCl.[11a]

**Methyl (5*S*,6*Z*)-7-Bromo-5-(1-ethoxyethoxy)-6-heptenoate (10b).** A solution of **17** (1.80 g, 7.59 mmol), ethyl vinyl ether (2.18 mL, 22.8 mmol), and PPTS (190 mg, 0.76 mmol) in $CH_2Cl_2$ (10 mL) was stirred at room temperature for 2 h and poured into saturated $NaHCO_3$ with EtOAc. The layers were separated, and the aqueous layer was extracted with EtOAc. The combined extracts were dried over $NaHCO_3$ and $MgSO_4$, and concentrated to leave an oil, which was purified by chromatography (hexane/EtOAc with a few drops of $NEt_3$) to furnish **10b** (2.01 g, 86%): bp 115 °C (1 Torr); IR (neat) 3082, 1739, 1620 $cm^{-1}$; $^1H$ NMR $\delta$ 1.11 and 1.15 (2t, $J = 7$ and 7 Hz, 3 H), 1.21 and 1.25 (2d, $J = 5.5$ and 5.5 Hz, 3 H), 1.41−1.78 (m, 4 H), 2.25−2.33 (m, 2 H), 3.60 (s, 3 H), 3.29−3.66 (m, 2 H), 4.32−4.40 and 4.51−4.64 (2m, 2 H), 5.94−6.29 (m, 2 H); $^{13}C$ NMR $\delta$ 174.1, 136.8, 136.1, 109.6, 108.1, 99.7, 98.3, 73.5, 72.9, 61.7, 61.0, 51.5, 34.04, 33.94, 33.80, 33.76, 20.67, 20.49, 20.47, 20.42, 15.3, 15.1. Anal. Calcd for $C_{12}H_{21}BrO_4$: C, 46.61; H, 6.85. Found: C, 46.66; H, 6.74.

**(*R*)-1-Chloro-4-decyn-2-ol (19).** To a solution of 1-heptyne (2.83 mL, 21.6 mmol) in THF (20 mL) was added *n*-BuLi (7.0 mL, 2.31 M in hexane, 16.2 mmol) at −78 °C. After the solution was stirred for 30 min at −78 °C, $BF_3{\cdot}OEt_2$ (2.26 mL, 18.4 mmol) and, after 10 min, (*R*)-epichlorohydrin (**18**) (99% ee, 0.99 g, 10.8 mmol) were added to the solution. The resulting solution was stirred at −78 °C for 30 min and poured into a mixture of EtOAc and saturated aqueous $NH_4Cl$ with vigorous stirring. The layers were separated, and the aqueous layer was extracted with EtOAc three times. The combined organic layers were dried and concentrated to give an oil, which was subjected to chromatography (hexane:$Et_2O$ = 20:1 to 10:1) to afford **19** (1.42 g, 70%): $[\alpha]^{25}_D$ −11.0 (*c* 0.86, $CHCl_3$); bp 110 °C (1 Torr); IR (neat) 3392, 1084, 1051 $cm^{-1}$; $^1H$ NMR $\delta$ 0.89 (t, $J = 7$ Hz, 3 H), 1.20−1.40 (m, 4 H), 1.40−1.54 (m, 2 H), 2.15 (tt, $J = 7$, 2 Hz, 2 H), 2.40 (br s, 1 H), 2.46−2.54 (m, 2 H), 3.61 (dd, $J = 11$, 6 Hz, 1 H), 3.70 (dd, $J = 11$, 5 Hz, 1 H), 3.86−3.98 (m, 1 H); $^{13}C$ NMR $\delta$ 84.0, 74.4, 70.1, 48.3, 31.1, 28.5, 24.7, 22.2, 18.6, 13.9.

**(*R*)-2-[(*tert*-Butyldimethylsilyl)oxy]-1-chloro-4-decyne (20).** A solution of alcohol **19** (3.12 g, 16.5 mmol), TBSCl (3.02 g, 20.0 mmol), and imidazole (1.69 g, 24.8 mmol) in DMF (30 mL) was stirred at room temperature overnight and poured into a mixture of saturated $NaHCO_3$ and hexane. The mixture was stirred vigorously at room temperature for 1 h, the layers were separated, and the aqueous layer was extracted with hexane. The combined hexane solutions were dried and concentrated to furnish an oil, which was purified by chromatography (hexane) to afford **20** (4.95 g, 99%): IR (neat) 1255, 1113, 837, 777 $cm^{-1}$; $^1H$ NMR $\delta$ 0.10 (s, 3 H), 0.11 (s, 3 H), 0.89 (s, 12 H), 1.23−1.41 (m, 4 H), 1.41−1.54 (m, 2 H), 2.13 (tt, $J = 7$, 2 Hz, 2 H), 2.38−2.45 (m, 2 H), 3.51 (dd, $J = 11$, 6 Hz, 1 H), 3.64 (dd, $J = 11$, 5 Hz, 1 H), 3.88−3.98 (m, 1 H); $^{13}C$ NMR $\delta$ 82.4, 75.3, 71.3, 47.9, 30.6, 28.2, 25.29, 25.21, 21.8, 18.3, 17.6, 13.5, −5.2.

**(2*R*,4*Z*)-2-[(*tert*-Butyldimethylsilyl)oxy]-1-chloro-4-decene (28).** A mixture of 5% Pd/$BaSO_4$ (0.25 g) and quinoline (0.25 mL) in MeOH (60 mL) was stirred at room temperature for 30 min under argon, and argon was replaced by hydrogen. The mixture was stirred for 30 min further at room temperature, and acetylene **20** (4.95 g, 16.3 mmol) was added to it. After hydrogen uptake reached a plateau (ca. 2 h), the mixture was filtered through a pad of Celite by suction with $Et_2O$, and the filtrate was concentrated to leave an oil, which was purified by chromatography (hexane) to afford olefin **28** (4.97 g, 100%): $[\alpha]^{29}_D$ −13.6 (*c* 1.22, $CHCl_3$); IR (neat) 3008, 1103, 837, 775 $cm^{-1}$; $^1H$ NMR $\delta$ 0.08 (s, 3 H), 0.09 (s, 3 H), 0.88 (t, $J = 7$ Hz, 3 H), 0.89 (s, 9 H), 1.20−1.40 (m, 6 H), 2.03 (q, $J = 7$ Hz, 2 H), 2.29−2.37 (m, 2 H), 3.40 (dd, $J = 11$, 6 Hz, 1 H), 3.45 (dd, $J = 11$, 5 Hz, 1 H), 3.80−3.90 (m, 1 H), 5.37 (dtt, $J = 11$, 7, 1 Hz, 1 H), 5.49 (dtt, $J = 11$, 7, 1 Hz, 1 H); $^{13}C$ NMR $\delta$ 133.2, 124.2, 72.6, 48.4, 32.9, 31.6, 29.3, 27.4, 25.8, 22.6, 18.1, 14.0, −4.7.

**(2*R*,2′*Z*)-2-(2′-Octenyl)oxirane (21).** To a solution of **28** (4.97 g, 16.3 mmol) in THF (20 mL) was added TBAF (32 mL, 1.0 M in THF, 32 mmol). The resulting solution was stirred at room temperature overnight and poured into saturated $NH_4Cl$. The mixture was extracted with hexane twice. The combined extracts were rinsed with brine, dried, and concentrated to afford crude **27**, which was used for the next reaction without further purification. An analytically pure sample was obtained by chromatography (hexane/$Et_2O$): $^1H$ NMR $\delta$ 0.88 (t, $J = 7$ Hz, 1 H), 1.22−1.40 (m, 6 H), 2.03 (q, $J = 7$ Hz, 2 H), 2.23 (br d, $J = 5$ Hz, 1 H), 2.34 (t, $J = 7$ Hz, 1 H), 3.50 (dd, $J = 11$, 7 Hz, 1 H), 3.63 (dd, $J = 11$, 4 Hz, 1 H), 3.77−3.90 (m,

(27) Ohta, H.; Tetsukawa, H.; Noto, N. *J. Org. Chem.* **1982**, *47*, 2400−2404.

(28) In the original paper, the $^1H$ NMR spectrum was measured in $CCl_4$.

1 H), 5.37 (dtt, $J$ = 11, 7, 1 Hz, 1 H), 5.57 (dtt, $J$ = 11, 7, 1 Hz, 1 H); $^{13}$C NMR $\delta$ 134.3, 123.6, 71.3, 49.6, 32.2, 31.5, 29.2, 27.4, 22.5, 14.0.

To a solution of the above alcohol **27** dissolved in THF (20 mL) was added crushed NaOH (3.2 g, 80 mmol), and the mixture was stirred vigorously at room temperature for 3 h and poured into water. The product was extracted with $Et_2O$ repeatedly. The combined ethereal solutions were dried and concentrated to leave an oil, which was purified by chromatography (hexane/$Et_2O$) to afford epoxide **21** (2.38 g, 95%): bp 140 °C (12 Torr); IR (neat) 3045, 3010, 833 cm$^{-1}$; $^1$H NMR $\delta$ 0.87 (t, $J$ = 7 Hz, 3 H), 1.18−1.40 (m, 6 H), 2.02 (q, $J$ = 7 Hz, 2 H), 2.25 (dt, $J$ = 15, 7 Hz, 1 H), 2.39 (dt, $J$ = 15, 7 Hz, 1 H), 2.50 (dd, $J$ = 5, 3 Hz, 1 H) 2.73 (dd, $J$ = 5, 4 Hz, 1 H), 2.89−2.97 (m, 1 H), 5.33−5.45 (m, 1 H), 5.46−5.58 (m, 1 H); $^{13}$C NMR $\delta$ 133.4, 123.1, 51.7, 46.7, 31.4, 30.1, 29.2, 27.3, 22.5, 14.0. Anal. Calcd for $C_{10}H_{18}O$: C, 77.87; H, 11.76. Found: C, 77.50; H, 12.15.

**(5*S*,7*Z*)-7-Tridecen-1-yn-5-ol (23).** Requisite allenylmagnesium bromide **22** in $Et_2O$ (ca. 0.50 M) was prepared according to the literature procedure[24] from propargyl bromide (2.3 mL, 30 mmol), magnesium (0.80 g, 33 mmol), $HgCl_2$ (15 mg), and $Et_2O$ (13 mL), and diluted with additional $Et_2O$ (45 mL) to make a 0.5 M solution, which was used for the next reaction without titration.

To a solution of **21** (2.30 g, 14.9 mmol) in $Et_2O$ (30 mL) was added a freshly prepared solution of **22** (44.7 mL, 22.4 mmol) at −30 °C dropwise. The solution was warmed to 0 °C over 2 h and poured into saturated $NH_4Cl$. The mixture was extracted with $Et_2O$, dried, and concentrated to leave an oil, which was a mixture of **23** and **29** by $^1$H NMR spectroscopy.

To the mixture dissolved in MeOH (15 mL) was added $K_2CO_3$ (2.06 g, 14.9 mmol) portionwise. The resulting mixture was stirred at room temperature for 1 h and poured into $H_2O$. The product was extracted with $Et_2O$ several times, and the combined ethereal solutions were dried and concentrated. The residue obtained was purified by chromatography (hexane/$Et_2O$) to afford epoxide **21** (0.46 g, 20%) first and then alcohol **23** (1.80 g, 62%). Spectral data of **23**: IR (neat) 3360, 3311, 3008, 2112, 1070 cm$^{-1}$; $^1$H NMR $\delta$ 0.88 (t, $J$ = 7 Hz, 3 H), 1.20−1.45 (m, 6 H), 1.58−1.74 (m, 2 H), 1.76 (d, $J$ = 4 Hz, 1 H), 1.96 (t, $J$ = 3 Hz, 1 H), 2.04 (q, $J$ = 7 Hz, 2 H), 2.24 (t, $J$ = 7 Hz, 2 H), 2.34 (dt, $J$ = 3, 7 Hz, 2 H), 3.71−3.83 (m, 1 H), 5.39 (dtt, $J$ = 11, 7, 1 Hz, 1 H), 5.57 (dtt, $J$ = 11, 7, 1, 1 H); $^{13}$C NMR $\delta$ 134.1, 124.7, 84.3, 70.3, 68.7, 35.3, 35.1, 31.5, 29.3, 27.4, 22.5, 15.0, 14.0.

**(5*S*,7*Z*)-5-[(*tert*-Butyldimethylsilyl)oxy]-7-tridecen-1-yne (24).** A solution of **23** (1.69 g, 8.70 mmol), TBSCl (1.57 g, 10.4 mmol), and imidazole (0.89 g, 13 mmol) in DMF (10 mL) was stirred at room temperature overnight and poured into a mixture of saturated $NaHCO_3$ and hexane. After the solution was stirred vigorously at room temperature for 30 min, the layers were separated, and the aqueous layer was extracted with hexane twice. The combined hexane solutions were dried and concentrated to give an oil, which was purified by chromatography to afford **24** (2.50 g, 93%): $[\alpha]^{25}_D$ −30.4 (*c* 0.93, $CHCl_3$); bp 160 °C (1 Torr); IR (neat) 3318, 3010, 2119, 1082, 837, 775 cm$^{-1}$; $^1$H NMR $\delta$ 0.08 (s, 6 H), 0.89 (s, 12 H), 1.20−1.42 (m, 6 H), 1.54−1.75 (m, 2 H), 1.93 (t, $J$ = 3 Hz, 1 H), 2.02 (q, $J$ = 7 Hz, 2 H), 2.10−2.30 (m, 4 H), 3.75−3.85 (m, 1 H), 5.32−5.52 (m, 2 H); $^{13}$C NMR $\delta$ 132.2, 125.2, 84.7, 70.8, 68.3, 35.3, 35.2, 31.6, 29.3, 27.4, 25.9, 22.6, 18.1, 14.6, 14.0, −4.4, −4.8. Anal. Calcd for $C_{19}H_{36}OSi$: C, 73.95; H, 11.76. Found: C, 73.87; H, 11.71.

**(1′*E*,5′*S*,7′*Z*)-2-[5′-{(*tert*-Butyldimethylsilyl)oxy}-1′,7′-tridecadienyl]-5,5-dimethyl-1,3,2-dioxaborinane (11a)**. To a solution of $BH_3$·$SMe_2$ (0.96 mL, 2.0 M in THF, 1.92 mmol) was added (−)-α-pinene (0.75 mL, 4.81 mmol) at 0 °C. After the solution was stirred at 0 °C for 1 h, the white precipitate of (+)-$(Ipc)_2BH$ covered the solution. The ice−water bath was removed, and stirring was continued for 2 h further to ensure complete formation of (+)-$(Ipc)_2BH$. The mixture was cooled to −35 °C, and **24** (494 mg, 1.60 mmol) was added to the flask. The resulting mixture was gradually warmed to 0 °C over 2 h, during which time the white precipitate disappeared. Acetaldehyde (1.34 mL, 24 mmol) was added to it at 0 °C, and the resulting solution was stirred overnight at the bath temperature of 40 °C, under which the solution refluxed gently. The volatile material was removed under reduced pressure to afford the corresponding diethyl boronate, which was diluted with THF (3 mL) for the next transesterification.

To the above THF solution was added 2,2-dimethy-1,3-propanediol (200 mg, 1.92 mmol), and the resulting solution was stirred at room temperature for 1 h. Concentration and purification of the residue by chromatography (hexane/EtOAc) afforded **11a** (507 mg, 75%), which was distilled for the next reaction: $[\alpha]^{29}_D$ −10.3 (*c* 1.28, $CHCl_3$); bp 210 °C (1 Torr); IR (neat) 3006, 1639, 1089, 837, 775 cm$^{-1}$; $^1$H NMR $\delta$ 0.029 (s, 3 H), 0.033 (s, 3 H), 0.87 (s, 12 H), 0.95 (s, 6 H), 1.18−1.40 (m, 6 H), 1.45−1.60 (m, 2 H), 1.93−2.04 (m, 2 H), 2.05−2.30 (m, 4 H), 3.62 (s, 4 H), 3.66−3.71 (m, 1 H), 5.34 (d, $J$ = 18 Hz, 1 H), 5.29−5.48 (m, 2 H), 6.54 (dt, $J$ = 18, 6 Hz, 2 H). Anal. Calcd for $C_{24}H_{47}BO_3Si$: C, 68.22; H, 11.21. Found: C, 67.81; H, 11.03.

**Methyl (5*S*,6*Z*,8*E*,12*S*,14*Z*)-5,12-Bis[(*tert*-butyldimethylsilyl)oxy]-6,8,14-eicosatrienoate (26).** To an ice-cold mixture of **11a** (89 mg, 0.21 mmol), $NiCl_2(PPh_3)_2$ (10 mg, 0.015 mmol), and THF (0.3 mL) was added MeLi (0.20 mL, 1.12 M in ether, 0.22 mmol). The resulting dark red solution was stirred at 0 °C for 20 min, and bromide **10a** (>99% ee, 49 mg, 0.14 mmol) (vide supra) was added to it. Stirring was continued at room temperature overnight. A few drops of $NEt_3$, hexane, and saturated $NH_4Cl$ were added to the solution successively, and the resulting mixture was stirred for 30 min vigorously. The layers were separated, and the aqueous layer was extracted with hexane twice. The combined extracts were dried and concentrated to give an oil, which was purified by chromatography (hexane:$Et_2O$ = 50:1) to furnish **26** (63 mg, 77%): $[\alpha]^{22}_D$ +6.7 (*c* 0.60, $CHCl_3$); IR (neat) 3010, 1743, 837, 775 cm$^{-1}$; $^1$H NMR $\delta$ 0.01, 0.04, 0.049, and 0.052 (4s, 12 H), 0.87 (s, 9 H), 0.88 (t, $J$ = 7 Hz, 3 H), 0.89 (s, 9 H), 1.20−1.80 (m, 12 H), 2.01 (q, $J$ = 7 Hz, 2 H), 2.07−2.25 (m, 4 H), 2.31 (t, $J$ = 7 Hz, 2 H), 3.66 (s, 3 H), 3.62−3.74 (m, 1 H), 4.48−4.57 (m, 1 H), 5.23 (dd, $J$ = 11, 9 Hz, 1 H), 5.32−5.50 (m, 2 H), 5.68 (dt, $J$ = 15, 7 Hz, 1 H), 5.88 (t, $J$ = 11 Hz, 1 H), 6.22 (dd, $J$ = 15, 11 Hz, 1 H); $^{13}$C NMR $\delta$ 174.3, 136.5, 132.9, 132.0, 128.2, 125.6, 125.4, 71.8, 68.6, 51.5, 37.8, 36.3, 35.2, 34.0, 31.6, 29.3, 28.8, 27.4, 25.91, 25.86, 22.6, 20.9, 18.15, 18.10, 14.1, −4.27, −4.35, −4.6, −4.9. Anal. Calcd for $C_{33}H_{64}O_4Si_2$: C, 68.22; H, 11.10. Found: C, 68.16; H, 11.08.

**10,11-Dihydroleukotriene $B_4$ (2).** To a solution of **26** (100 mg, 0.172 mmol) in THF (7 mL) was added a solution of TBAF (1.72 mL, 1.0 M in THF, 1.72 mmol). After the solution was stirred at room temperature overnight, the solution was poured into a vigorously stirred mixture of $Et_2O$ and the phosphate buffer (pH 5). The layers were separated, and the aqueous layer was extracted with $Et_2O$. The combined ethereal solutions were washed with brine, dried, and concentrated. The residual oil was purified by chromatography ($Et_2O$/MeOH) to afford **2** (48 mg, 83%): IR (neat) 3383, 3016, 1714 cm$^{-1}$; $^1$H NMR $\delta$ 0.87 (t, $J$ = 7 Hz, 3 H), 1.10−1.80 (m, 12 H), 2.03 (q, $J$ = 7 Hz, 2 H), 2.12−2.29 (m, 4 H), 2.37 (t, $J$ = 7 Hz, 2 H), 3.57−3.69 (m, 1 H), 4.60 (dt, $J$ = 9, 7 Hz, 1 H), 4.66−5.20 (m, 3 H), 5.28 (dd, $J$ = 11, 9 Hz, 1 H), 5.32−5.44 (m, 1 H), 5.48−5.61 (m, 1 H), 5.72 (dt, $J$ = 15, 7 Hz, 1 H), 6.00 (t, $J$ = 11 Hz, 1 H), 6.34 (dd, $J$ = 15, 11 Hz, 1 H); $^{13}$C NMR $\delta$ 178.7, 136.6, 133.8, 131.6, 130.4, 125.8, 124.9, 70.8, 67.5, 36.4, 35.8, 35.3, 33.7, 31.5, 29.3, 29.0, 27.4, 22.5, 20.6, 14.0.

**(5*S*,6*Z*,8*E*,12*S*,14*Z*)-5,12-Dihydroxy-6,8,14-eicosatrienamide (Amide of 10,11-Dihydroleukotriene $B_4$) (3).** 10,11-Dihydroleukotriene $B_4$ (**2**) (15 mg, 0.044 mmol) was converted to methyl ester with $CH_2N_2$ in a usual manner. A solution of the methyl ester dissolved in MeOH (0.5 mL) which was saturated with $NH_3$ was placed in glass tubing. It was sealed and left at room temperature for 5 days. The volatile material was removed under reduced pressure, and the residue was purified by chromatography ($Et_2O$/MeOH) to afford amide **3** (13 mg, 92%): IR (neat) 3348, 3192, 3008, 1668, 1614 cm$^{-1}$; $^1$H NMR $\delta$ 0.87 (t, $J$ = 7 Hz, 3 H), 1.1−2.3 (m, 22 H), 3.61 (quintet, $J$ = 6 Hz, 1 H), 4.59 (q, $J$ = 7 Hz, 1 H), 5.29 (t, $J$ = 11 Hz, 1 H), 5.35−5.44 (m, 1 H), 5.50−5.62 (m, 1 H), 5.72 (dt,

$J$ = 15, 7 Hz, 1 H), 5.6−5.9 (m, 2 H), 6.00 (t, $J$ = 11 Hz, 1 H), 6.34 (dd, $J$ = 15, 11 Hz, 1 H); $^{13}$C NMR $\delta$ 175.9, 136.7, 133.7, 131.6, 130.3, 125.8, 125.1, 70.6, 67.5, 36.6, 35.9, 35.5, 35.4, 31.5, 29.3, 29.1, 27.4, 22.5, 21.2, 14.0.

**(*R*)-2-Octyloxirane (30).** To a mixture of (*R*)-epichlorohydrin (**18**) (99% ee, 3.00 mL, 38.3 mmol), CuCN (350 mg, 3.91 mmol), and THF (40 mL) was added heptylmagnesium bromide (115 mL, 0.50 M in THF, 57.5 mmol) dropwise at −78 °C. The solution was warmed to 0 °C over 2 h and poured into a mixture of saturated $NH_4Cl$ and $Et_2O$ with vigorous stirring. The layers were separated, and the aqueous layer was extracted with EtOAc. The combined extracts were dried and concentrated to furnish a residue, which was purified by chromatography (hexane/EtOAc) to afford (*R*)-1-chloro-2-decanol (7.38 g, 100%): bp 120 °C (1 Torr); IR (neat) 3379 cm$^{-1}$; $^1$H NMR $\delta$ 0.87 (t, $J$ = 7 Hz, 3 H), 1.15−1.57 (m, 14 H), 2.19 (d, $J$ = 5 Hz, 1 H), 3.47 (dd, $J$ = 11, 7 Hz, 1 H), 3.63 (dd, $J$ = 11, 3 Hz, 1 H), 3.73−3.85 (m, 1 H); $^{13}$C NMR $\delta$ 71.5, 50.6, 34.2, 31.8, 29.5, 29.4, 29.2, 25.5, 22.6, 14.1.

To a solution of the above alcohol (7.00 g, 36.3 mmol) in THF (40 mL) was added crushed NaOH (7.28 g, 182 mmol). The mixture was stirred vigorously at room temperature for 3 h and poured into water. The product was extracted with $Et_2O$ repeatedly. The combined ethereal solutions were washed with saturated $NH_4Cl$, dried, and concentrated to give an oil, which was purified by chromatography (hexane/$Et_2O$) to afford epoxide **30** (5.45 g, 96%): $[\alpha]^{27}_D$ +7.2 (*c* 0.98, $CHCl_3$); bp 90 °C (12 Torr). The $^1$H NMR spectrum of **32** thus prepared was coincident with that given in ref 29.

**(*R*)-1-Tridecyn-5-ol (31).** To a solution of **30** (3.00 g, 16.1 mmol) in THF (30 mL) was added a freshly prepared (vide supra) solution of allenylmagnesium bromide **22** (48 mL, ca. 0.50 M in $Et_2O$, 24 mmol) at −50 °C dropwise. The solution was warmed over 2 h to −10 °C and poured into a mixture of saturated $NH_4Cl$ and $Et_2O$ with vigorous stirring. The layers were separated, and the aqueous layer was extracted with EtOAc. The combined extracts were dried and concentrated to give a mixture of **31** and 1-bromo-2-decanol.

To a solution of the above mixture in MeOH (30 mL) was added $K_2CO_3$ (2.2 g, 16 mmol) portionwise. The resulting mixture was stirred at room temperature for 1 h and poured into $H_2O$. The product was extracted with EtOAc several times, and the combined organic layers were dried and concentrated. The residue was subjected to chromatography (hexane:EtOAc = 30:1 to 20:1) to afford epoxide **30** (0.41 g, 16%) and **31** (1.81 g, 57%), respectively. Spectral data of **31**: IR (neat) 3340, 3313, 2119 cm$^{-1}$; $^1$H NMR $\delta$ 0.87 (t, $J$ = 7 Hz, 3 H), 1.17−1.75 (m, 17 H), 1.96 (t, $J$ = 3 Hz, 1 H), 2.32 (ddd, $J$ = 7.4, 6.8, 2.7 Hz, 2 H), 3.67−3.80 (m, 1 H); $^{13}$C NMR $\delta$ 84.4, 70.9, 68.7, 37.4, 35.7, 31.9, 29.6, 29.5, 29.2, 25.6, 22.6, 15.0, 14.1.

**(*R*)-5-[(*tert*-Butyldimethylsilyl)oxy]-1-tridecyne (32).** According to the procedure for TBS protection of **19**, alcohol **31** (1.00 g, 5.09 mmol) was treated with TBSCl (0.92 g, 6.1 mmol), imidazole (0.52 g, 7.64 mmol), and DMF (10 mL) to afford **32** (1.43 g, 90%) after chromatography (hexane): $[\alpha]^{28}_D$ −18.4 (*c* 1.57, $CHCl_3$); bp 160 °C (1 Torr); IR (neat) 3313, 2119, 837, 775 cm$^{-1}$; $^1$H NMR $\delta$ 0.05 (s 3 H), 0.06 (s, 3 H), 0.88 (s, 12 H), 1.15−1.50 (m, 14 H), 1.54−1.72 (m, 2 H), 1.92 (t, $J$ = 3 Hz, 1 H), 2.23 (dt, $J$ = 3, 7 Hz, 2 H), 3.75 (quintet, $J$ = 6 Hz, 1 H); $^{13}$C NMR $\delta$ 84.8, 70.9, 68.2, 37.1, 35.6, 31.9, 29.8, 29.6, 29.3, 25.9, 25.1, 22.7, 18.1, 14.5, 14.1, −4.4, −4.6. Anal. Calcd for $C_{19}H_{38}OSi$: C, 73.47; H, 12.33. Found: C, 73.41; H, 12.28.

**(1′*E*,5′*R*)-2-[5′-{(*tert*-Butyldimethylsilyl)oxy}-1′-tridecenyl]-5,5-dimethyl-1,3,2-dioxaborinane (11b).** To a white suspension of (+)-$(Ipc)_2BH$ in THF, prepared according to the procedure for preparation of **11a** by using the same quantity of the reagents, was added **32** (497 mg, 1.60 mmol) at −35 °C dropwise. The resulting mixture was gradually warmed to 0 °C over 2 h, and acetaldehyde (1.34 mL, 24 mmol) was added at 0 °C. The resulting solution was stirred overnight at 40 °C (oil bath temperature; gentle reflux) and concentrated to leave the corresponding diethyl boronate, which was diluted with THF (3 mL) for the next transesterification.

2,2-Dimethyl-1,3-propanediol (200 mg, 1.92 mmol) was added to the THF solution prepared above. After 1 h at room temperature, the solution was concentrated by using a rotary evaporator to give an oily residue, which was purified by chromatography (hexane/EtOAc) to afford **11b** (523 mg, 77%), which was distilled for the next reaction: $[\alpha]^{29}_D$ +1.2 (*c*, 1.14, $CHCl_3$); bp 210 °C (1 Torr); IR (neat) 1637, 835, 773 cm$^{-1}$; $^1$H NMR $\delta$ 0.02 (s, 6 H), 0.87 (s, 12 H), 0.96 (s, 6 H), 1.16−1.46 (m, 14 H), 1.47−1.57 (m, 2 H), 2.04−2.28 (m, 2 H), 3.62 (s, 4 H), 3.59−3.69 (m, 1 H), 5.35 (dt, $J$ = 18, 1.5 Hz, 1 H), 6.55 (dt, $J$ = 18, 6 Hz, 1 H). Anal. Calcd for $C_{24}H_{49}BO_3Si$: C, 67.90; H, 11.63. Found: C, 67.75; H, 11.34.

**Methyl (5*S*,6*Z*,8*E*,12*R*)-5,12-Bis[(*tert*-butyldimethylsilyl)oxy]-6,8-eicosadienoate (34).** According to the procedure described for preparation of **26**, boronate ester **11b** (89 mg, 0.21 mmol), bromide **10a** (>99% ee, 50 mg, 0.14 mmol), $NiCl_2(PPh_3)_2$ (10 mg, 0.015 mmol), MeLi (0.20 mL, 1.12 M in $Et_2O$, 0.22 mmol), and THF (0.3 mL) furnished **34** (60 mg, 74%) after purification by chromatography (hexane/$Et_2O$): $[\alpha]^{22}_D$ +8.3 (*c* 0.40, $CHCl_3$); IR (neat) 1741, 1086, 837, 777 cm$^{-1}$; $^1$H NMR $\delta$ 0.04 (s, 12 H), 0.87 (s, 9 H), 0.88 (t, $J$ = 7 Hz, 3 H), 0.89 (s, 9 H), 1.2−1.8 (m, 20 H), 2.04−2.19 (m, 2 H), 2.31 (t, $J$ = 7 Hz, 2 H), 3.66 (s, 3 H), 3.60−3.69 (m, 1 H), 4.55 (dt, $J$ = 9, 7 Hz, 1 H), 5.23 (dd, $J$ = 11, 9 Hz, 1 H), 5.68 (dt, $J$ = 15, 7 Hz, 1 H), 5.89 (t, $J$ = 11 Hz, 1 H), 6.22 (dd, $J$ = 15, 11 Hz, 1 H); $^{13}$C NMR $\delta$ 174.3, 136.6, 132.8, 128.2, 125.3, 71.9, 68.7, 51.5, 37.8, 37.1, 36.6, 34.0, 31.9, 29.9, 29.6, 29.3, 28.6, 25.92, 25.86, 25.3, 22.7, 20.9, 18.15, 18.12, 14.1, −4.3, −4.4, −4.5, −4.9. Anal. Calcd for $C_{33}H_{66}O_4Si_2$: C, 67.98; H, 11.41. Found: C, 67.95; H, 11.44.

**10,11,14,15-Tetrahydroleukotriene B$_4$ (4).** According to the procedure for preparation of **2**, a solution of **34** (50 mg, 0.086 mmol) in THF (2 mL) was treated with TBAF (0.86 mL, 1.0 M in THF, 0.86 mmol) at room temperature overnight to afford **4** (23 mg, 78%) after chromatography ($Et_2O$/MeOH): IR (neat) 3367, 1716 cm$^{-1}$; $^1$H NMR $\delta$ 0.87 (t, $J$ = 7 Hz, 3 H), 1.1−1.8 (m, 20 H), 2.10−2.30 (m, 2 H), 2.30−2.43 (m, 2 H), 3.54−3.66 (m, 1 H), 3.80−4.70 (m, 3 H), 4.50−4.70 (m, 1 H), 5.29 (dd, $J$ = 11, 9 Hz, 1 H), 5.71 (dt, $J$ = 15, 7 Hz, 1 H), 6.00 (t, $J$ = 11 Hz, 1 H), 6.34 (dd, $J$ = 15, 11 Hz, 1 H); $^{13}$C NMR $\delta$ 178.2, 136.6, 131.6, 130.3, 125.9, 71.3, 67.5, 37.5, 36.4, 36.3, 33.6, 31.9, 29.7, 29.6, 29.3, 28.9, 25.6, 22.7, 20.6, 14.1.

**Methyl (5*S*,6*Z*,8*E*,12*S*,14*Z*)- and (5*S*,6*Z*,8*E*,12*R*,14*Z*)-12-[(*tert*-Butyldimethylsilyl)oxy]-5-(1-ethoxyethoxy)-6,8,14-eicosatrienoate (39).** According to the procedure for preparation of **26**, bromide **10b** (100 mg, 0.323 mmol), racemic boronate ester *rac*-**11a** (205 mg, 0.485 mmol), $NiCl_2(PPh_3)_2$ (30 mg, 0.046 mmol), MeLi (0.41 mL, 1.24 M in $Et_2O$, 0.51 mmol), and THF (0.6 mL) furnished **39** (83 mg, 48% based on **10b**) after chromatography (hexane:$Et_2O$ = 15:2 with a few drops of $NEt_3$): IR (neat) 1741, 835, 775 cm$^{-1}$; $^1$H NMR $\delta$ 0.047 and 0.052 (2s, 6 H), 0.88 (br s, 12 H), 1.1−1.8 (m), 1.96−2.37 (m, 8 H), 3.65 (s, 3 H), 3.33−3.73 (m, 3 H), 4.28−4.39 and 4.50−4.60 (2m, 1 H), 4.60−4.70 (m, 1 H), 5.05−5.50 (m, 3 H), 5.64−5.78 (m, 1 H), 6.02 and 6.10 (2t, $J$ = 11 Hz, 1 H), 6.18−6.38 (m, 1 H). Anal. Calcd for $C_{31}H_{58}O_5Si$: C, 69.10; H, 10.85. Found: C, 69.06; H, 10.94.

**Methyl (5*S*,6*Z*,8*E*,12*S*,14*Z*)- and (5*S*,6*Z*,8*E*,12*R*,14*Z*)-5-(1-Ethoxyethoxy)-12-hydroxy-6,8,14-eicosatrienoate (40).** A solution of **39** (150 mg, 0.278 mmol) in THF (5 mL) was treated with TBAF (0.56 mL, 1.0 M in THF, 0.56 mmol) at room temperature overnight and poured into a mixture of saturated $NH_4Cl$ and $Et_2O$ with vigorous stirring. The layers were separated, and the aqueous layer was extracted with $Et_2O$. The combined ethereal solutions were dried and concentrated to afford an oil, which was purified by chromatography (hexane:EtOAc = 5:1 to 3:1 with a few drops of $NEt_3$) to afford **40** (83 mg, 70%): IR (neat) 3462, 1741, 1095 cm$^{-1}$; $^1$H NMR $\delta$ 0.88 (t, $J$ = 7 Hz, 3 H), 1.1−1.8 (m), 1.99−2.36 (m, 8 H), 3.66 (s, 3 H), 3.33−3.70 (m, 3 H), 4.30−4.40 and 4.50−4.60 (2m, 1 H), 4.61−4.70 (m, 1 H), 5.06−5.30 (m, 1 H), 5.32−5.46 (m, 1 H), 5.50−5.64 (m, 1 H), 5.73 (dt, $J$ = 15, 7 Hz, 1 H),

(29) *The Aldrich Library of $^{13}$C and $^1$H FT NMR Spectra*, 1st ed.; Pouchert, C. J., Behnke, J., Eds.; Aldrich: Milwaukee, 1993; Vol. 1, p 365 C.

5.98−6.18 (m, 1 H), 6.24−6.44 (m, 1 H). Anal. Calcd for $C_{25}H_{44}O_5$: C, 70.72; H, 10.44. Found: C, 70.56; H, 10.46.

**(5*S*,6*Z*,8*E*,14*Z*)-5-(1-Ethoxyethoxy)-12-oxo-6,8,14-eicosatrienoic Acid (41).** A mixture of **40** (70 mg, 0.165 mmol) and 1 N NaOH (1.65 mL, 1.65 mmol) in MeOH (9 mL) was stirred at room temperature overnight, and 1 N HCl was added carefully until the solution became slightly acidic. The product was extracted with EtOAc twice. The combined extracts were dried and concentrated to give the corresponding acid, which was used for the next oxidation without further purification.

To an ice-cold solution of the acid dissolved in $CH_2Cl_2$ (1.5 mL) were added Celite (0.2 g) and PDC (93 mg, 0.25 mmol). The resulting mixture was stirred at room temperature for 4 h and filtered through a pad of Celite with $Et_2O$. The combined filtrates were concentrated, and a residual oil was purified by chromatography (hexane/$Et_2O$) to obtain **41** (30 mg, 44% from **40**): IR (neat) 3420, 1714, 1095 $cm^{-1}$; $^1H$ NMR $\delta$ 0.88 (t, $J$ = 7 Hz, 3 H), 1.1−1.8 (m), 2.01 (q, $J$ = 7 Hz, 2 H), 2.31−2.43 (m, 4 H), 2.55 (t, $J$ = 7 Hz, 2 H), 3.16 (d, $J$ = 7 Hz, 2 H), 3.32−3.72 (m, 2 H), 4.30−4.40 and 4.48−4.60 (2m, 1 H), 4.60−4.69 (m, 1 H), 5.14 and 5.28 (2t, $J$ = 11 Hz, 1 H), 5.44−5.76 (m, 3 H), 6.00 and 6.08 (2t, $J$ = 11 Hz, 1 H), 6.22−6.39 (m, 1 H).

**10,11-Dihydro-12-oxoleukotriene $B_4$ (5).** A solution of **41** (6 mg, 0.015 mmol) and PPTS (ca. 1 mg) in *i*-PrOH (0.1 mL) was stirred at room temperature for 8 h and poured into saturated $NaHCO_3$. The mixture was extracted with EtOAc twice. The combined extracts were dried and concentrated to leave an oil, which was purified by chromatography ($Et_2O$/MeOH) to furnish **5** (4 mg, 81%): $^1H$ NMR $\delta$ 0.88 (t, $J$ = 7 Hz, 3 H), 1.1−1.9 (m), 2.02 (q, $J$ = 7 Hz, 2 H), 2.34−2.42 (m, 4 H), 2.55 (t, $J$ = 7 Hz, 2 H), 3.16 (d, $J$ = 7 Hz, 2 H), 4.54−4.63 (m, 1 H), 5.31 (dd, $J$ = 11, 9 Hz, 1 H), 5.46−5.64 (m, 2 H), 5.71 (dt, $J$ = 15, 7 Hz, 1 H), 6.00 (t, $J$ = 11 Hz, 1 H), 6.34 (dd, $J$ = 15, 11 Hz, 1 H).

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**Supporting Information Available:** $^1H$ NMR spectra of compounds lacking elemental analyses. This material is available free of charge via the Internet at http://pubs.acs.org.

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