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Chiral Decalins: Preparation from Oleanolic Acid and Application in the Synthesis of (−)-9-*epi*-Ambrox

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A novel and versatile process was developed to prepare the *trans*-decalins $\Delta^{9(11)}$-3β-acetoxysclareolide (**2**) and $\Delta^{9(11)}$-3β-acetoxy-8-*epi*-sclareolide (**3**), respectively, with 4a-methoxycarbonyl-2,7,7-trimethyl-1-oxo-*cis*-decalin-2-ene (**4**) and its C-3 hydroxyl derivative **5** from oleanolic acid (3β-hydroxyolean-12-en-28-oic acid, **1**). Three key steps were (a) introduction of the AcO-12 group and the C-9,C-11 double bond at ring C of methyl 3β-acetoxyolean-12-en-28-oate (**8**) to afford the diene, methyl 3,12-diacetoxyolean-9(11),12-dien-28-oate (**11**); (b) photolytic cleavage of the C-8,C-14 bond in the diene to give an acetoxy-substituted triene **14**; and (c) oxidative cleavage of the triene or its hydrolyzed α,β-unsaturated ketone product with m-CPBA/TsOH to give the *cis*- and *trans*-decalins **2**−**5**. $\Delta^{9(11)}$-3β-Acetoxysclareolide (**2**) was stereospecifically reduced to give 3β-acetoxy-9-*epi*-sclareolide (**23**), from which (−)-9-*epi*-ambrox (**7**) was synthesized.

Decalin is one of the most prevalent structural units present in natural products possessing diverse and significant biological activities[1] and olfactory and fixative properties.[2] To date, numerous syntheses of these kinds of compounds have been accomplished.[1,3] Most of the syntheses are based on transformation of terpenes such as sclareolide,[4] abietic acid,[5] labdanolic acid,[6] sclareol,[7] manool,[8] larixol,[9] and communic acid[10] or well-established synthetic chiral materials such as Wieland−Miescher ketone.[11] Nevertheless, almost all these semisynthetic materials are comparatively rare and expensive, bear no functional groups on ring A (C-1 to C-4), possess a Me-8β functionality, and may not be employed to synthesize compounds with functional groups on ring A or those with a Me-8α group. Thus, it would be highly advantageous to obtain chiral decalins suitable for the versatile syntheses of these compounds with or without functional groups on ring A and those with either Me-8α or -8β substituents.

Oleanolic acid (3β-hydroxyolean-12-en-28-oic acid, **1**), a pentacyclic triterpene, is abundant as a natural resource.[12] Both the A/B and D/E rings of **1** constitute decalin ring systems. The framework of the A/B rings, a 3β-hydroxy-4,4,8,10-tetramethyl-*trans*-decalin, could be used as a versatile precursor for a large number of natural products.[1] In addition, the *cis*-decalin fragment of the D/E rings could also be transformed into triterpenoids, such as achilleol B[13] and camelliols A and B.[14] Thus, it would be of importance to generate simultaneously *cis*- and *trans*-decalins derived from the A/B and D/E fragments of **1** by cleavage of ring C in a facile manner.

Ring C of **1** was converted into the triene **G1**, which could not be directly cleaved with different oxidants. Indirectly, the C-11,C-12 double bond in **G2** was cleaved with $RuCl_3/NaIO_4$ to give **G3** and **G4** in a total yield of 30% from **G1** (Scheme 1a).[15] Compounds **G3** and **G4** are unstable, and **G3** possesses no chiral centers at C-8 and C-9. The yield for the cleavage of the C-9,C-11 bond is even poorer with low selectivity.[15] To date, there have been no examples reported concerning the cleavage of the C-12,C-13 bond.

Enol acetates can be transformed into ketols or α-acetoxy ketones via enol acetate epoxide[16] or hydrolyzed to ketones and then they might undergo a Baeyer−Villiger reaction with peracids. It was presumed that AcO-11 or AcO-12 trienes could thus be easily cleaved and the cleavage of the C-9,C-11, C-11,C-12, or C-12,C-13 bonds could probably be selectively realized. In this study, we have explored a route to cleave ring C of **1**, which involves

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Scheme 1. Key Steps of Ring C Cleavage of Oleanolic Acid

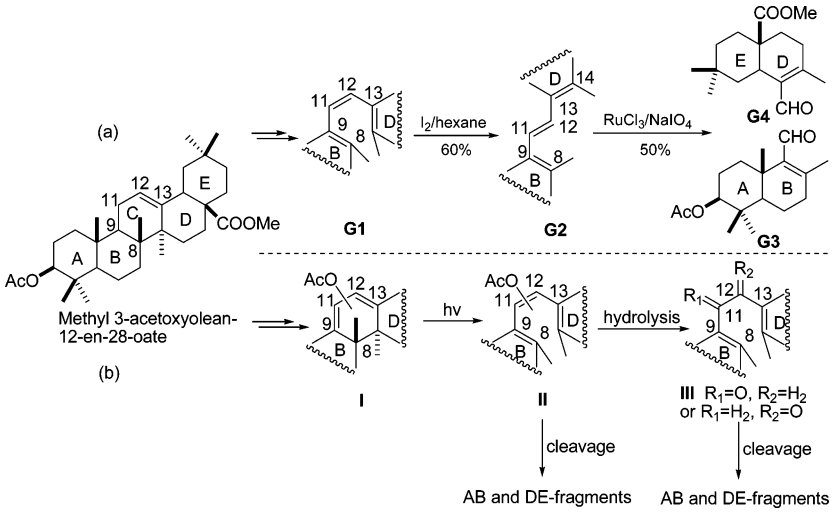
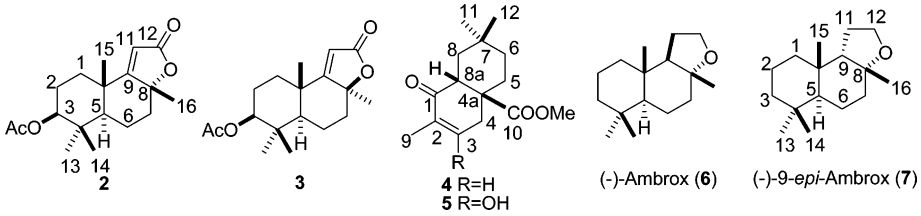
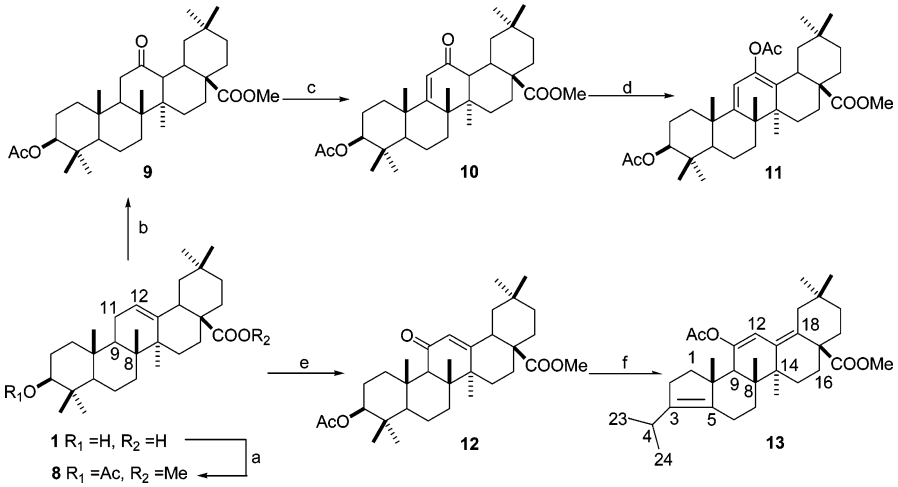


Chart 1. Ring C Cleaved Products **2**−**5** of Oleanolic Acid, (−)-Ambrox (**6**), and (−)-9-*epi*-Ambrox (**7**)



Scheme 2. Synthesis of Acetoxy-Substituted Dienes[a]



[a] Reagents and conditions: (a) (i) Ac_2O, pyridine, $CHCl_3$, reflux; (ii) CH_2N_2, THF, 0→5 °C, 81%; (b) O_3, $CHCl_3$, then $BF_3{\cdot}Et_2O$, −5→0 °C, 85% or H_2O_2/HCOOH, $CHCl_3$, rt, 82%; (c) Br_2, HBr in CH_3COOH (33%) (cat.), CH_3COOH, rt, 92%; (d) Ac_2O, H_2SO_4/TsOH (cat.), rt, 87%; (e) $CrO_3{\cdot}2$pyridine, CH_2Cl_2, 65%; (f) Ac_2O, H_2SO_4/TsOH (cat.), 80 °C, 46%.

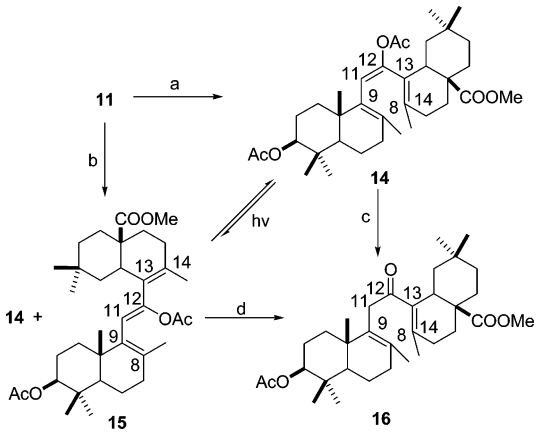
oxidative cleavage of the acetoxy-substituted trienes **II** or their hydrolyzed dienone products **III** (Scheme 1b). Cleavage of the AcO-12 triene or its hydrolyzed product was carried out, and selective access was realized to the *trans*-decalin $\Delta^{9(11)}$-3β-acetoxysclareolide (**2**) or its 8-epimer, $\Delta^{9(11)}$-3β-acetoxy-8-*epi*-sclareolide (**3**), respectively, with *cis*-decalins **4** and **5** (Chart 1).

As one of the most valuable animal perfumes, ambergris possesses unique olfactive and fixative properties,[2b] which is related principally to the presence of (−)-ambrox (**6**) (Chart 1). To date, several syntheses of **6** have been reported.[17] Studies on the configuration−odor relationship revealed that (−)-9-*epi*-ambrox (**7**)[2a,b,18] possesses the strongest scent and lowest threshold concentration (0.15 ppb) among all stereoisomers of (−)-ambrox (**6**). However synthetic methods of compound **7** are few and need to be improved in view of long reaction routes, low yields, or rigorous conditions.[2a,19] In this study, (−)-9-*epi*-ambrox (**7**) was synthesized starting from $\Delta^{9(11)}$-3β-acetoxysclareolide (**2**).

Results and Discussion

Cleavage of Ring C of Oleanolic Acid (1). The α,β-unsaturated ketone **10** was prepared via oxidation of **8**[20] with H_2O_2/HCOOH or O_3[21] and then dehydrogenation with Br_2/HBr[22] in acetic acid. In the enol acetylation of **10** with Ac_2O, different catalysts such as H_2SO_4/TsOH,[23] PPA, CF_3COOH, pyridine,[24] and CH_3COONa[24b,25] were tested. It was found that H_2SO_4/TsOH was effective, and the enol acetate **11** was obtained in 87% yield (Scheme 2), whereas long reaction times were needed and low conversion rates were obtained when pyridine or CH_3COONa was used. When synthesizing the enol acetate of the Δ^{12}-11-oxo compound **12**,[26] no reaction occurred when pyridine and CH_3COONa were used and a very low

Scheme 3. Photochemical Ring Opening of Acetoxy-Substituted Diene **11**[a]



[a] Reagents and conditions: (a) *hν* (high-pressure mercury lamp), Pyrex, CH_3COOEt, rt, 94%; (b) *hν* (high-pressure mercury lamp), quartz, CH_3COOEt, rt, 49% (**14**) and 35% (**15**); (c) (i) KOH, CH_3OH, H_2O, rt, (ii) Ac_2O, pyridine, 91%; (d) (i) KOH, CH_3OH, H_2O, rt, (ii) Ac_2O, pyridine, 87%.

conversion rate was observed when H_2SO_4/TsOH was employed at room temperature. Using H_2SO_4/TsOH as catalyst at 80 °C, ring A was transformed into a five-membered ring and the double bond was rearranged to give **13** (Scheme 2). A similar example using PCl_5 has also been documented.[27]

In ring C of **11**, the conjugated double bonds and *trans*-disposition between Me-8β and Me-14α allowed a six-electron-system antarafacial reaction,[28] which led to the cleavage of the bond between C-8 and C-14 (Scheme 3). Irradiation of **11** in CH_3COOEt in a Pyrex flask under argon using a 500 W high-pressure Hg lamp gave the (8*Z*,11*E*,13*E*)-triene **14** in 94% yield. The ring C opening took place by a conrotatory photochemical electrocyclic reaction similar to that evident in the transformation of ergosterol to previtamin D.[29] This process could be accomplished in different solvents such as CH_2Cl_2, $CHCl_3$, and EtOH. Interestingly, when **11** was irradiated in a quartz flask, **14** and its isomer (8*Z*,11*Z*,-13*E*)-triene **15** were obtained in 49% and 35% yields, respectively. The two isomers could interconvert when irradiated in a quartz flask, indicating that compound **15** is a further photochemical product of **14**. The different results in Pyrex and quartz flasks are probably due to the light of different wavelengths allowed to penetrate. In fact, both compounds are unstable when irradiated in a quartz flask, and thus long reaction times should be avoided to prevent further reactions.

The spectroscopic data of **14** and **15** did not provide conclusive evidence for their configurations. X-ray crystallographic analysis of **14** confirmed the configuration of **14** as a (8*Z*,11*E*,13*E*)-triene (Figure 1).[30] Acetylation of the hydrolyzed products of **14** or **15** with Ac_2O gave the same product, **16** (Scheme 3), and thus, the structure of compound **15** was indirectly established as a (8*Z*,11*Z*,-13*E*)-triene.

A [1,7]H sigmatropic shift in the transformation of provitamin D_2 to vitamin D_2[29] and a [1,5]H sigmatropic migration of a triterpenoid *cis*-triene[15] have been reported. However, no H sigmatropic shift reactions occurred when compound **14** or **15** was irradiated with ultraviolet light. It is probably because the serious distortion of these molecules as shown from the crystal structure of **14** (Figure 1) destroys the conjugations of the trienes and prevents the molecules from any antarafacial or suprafacial [1,7]H or [1,5]H sigmatropic migration. The unconjugated triene is also revealed by the fact that **14** possesses no ultraviolet absorption in the region of a normal conjugated triene.

The oxidation of compound **14** with $KMnO_4$, $KMnO_4$/$NaIO_4$, or O_3 gave complex mixtures. Enol acetates can be transformed into ketols or α-acetoxy ketones via enol acetate epoxides[16] or hydrolyzed to ketones, and then they might undergo a Baeyer−

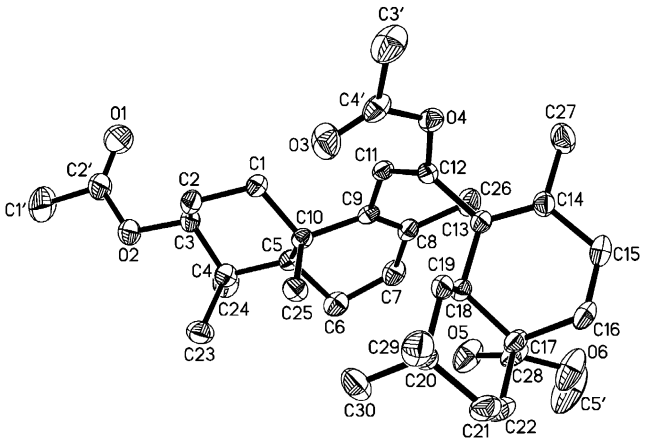


Figure 1. ORTEP diagram of triene **14**.

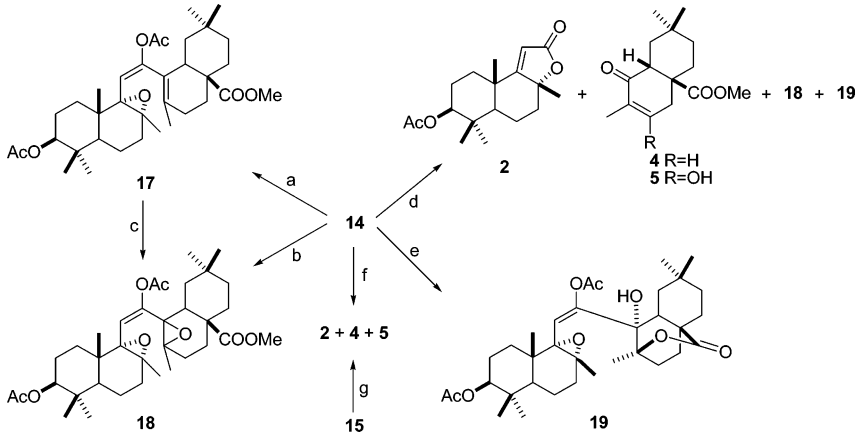
Villiger reaction with peracids; thus, m-CPBA was chosen for the cleavage of compound **14** (Scheme 4). Oxidation of **14** with m-CPBA in the presence of $NaHCO_3$ or phosphate buffer (pH 7.5) gave epoxide **17** or **18** as the major product without triene cleavage. Direct oxidation of **14** with m-CPBA gave compounds **2**, **4**, **5**, and diepoxide **18**, as well as lactone **19**. Compound **19** was the major product when **14** was oxidized with H_2O_2/HCOOH at 50 °C. The configurations of **2**, **17**, and **19** were confirmed by X-ray crystallographic analysis.[30] The triene cleaved products **2**, **4**, and **5** were detected even if **14** was oxidized directly with less than 1 molar equiv of m-CPBA. On the basis of products from oxidation of **14** with m-CPBA or m-CPBA and $NaHCO_3$, the triene cleavage is presumed to be an acid-catalyzed process. Different acids including TsOH, H_2SO_4, and CF_3COOH were tested. It was found that a catalytic amount of TsOH could largely inhibit the production of diepoxide **18** and lactone **19** and obviously improve the reaction. Other oxidants such as H_2O_2/CH_3COOH and *t*-BuOOH gave no satisfactory results. Here, the introduction of an acetoxy group at C-12 and application of m-CPBA/TsOH made cleavage of the C-12,C-13 bond of the triene facile and selective. At the same time, oxidation of (8*Z*,11*Z*,13*E*)-triene **15** with m-CPBA/TsOH rendered the same products **2**, **4**, and **5** (Scheme 4).

Significantly, oxidation of **16** with m-CPBA/TsOH gave **3**, an 8-epimer of **2**, and **2**, **4**, and **5** (Scheme 5). The ratio of **3**/**2** was 5:1, as determined from the ^1H NMR spectrum. Slow recrystallization of the mixture of **3** and **2** from *n*-hexane/acetone (8:1) gave crystals with two different shapes, which could be manually separated to give pure **3** and **2**. Similar to **14**, compound **16** was oxidized with m-CPBA in the presence of $NaHCO_3$ to give epoxide **20** or **21**. The configurations of **3** and **21** were determined by X-ray crystallographic analysis.[30]

Compounds **2** and **3** possess a 3β-acetoxy-4,4,8,10-tetramethyl-*trans*-decalin system and consequently are versatile synthons for the syntheses of natural products with Me-8α or -8β groups and with or without functional groups on ring A. Compounds **4** and **5**, with a *cis*-decalin framework, are also important intermediates for the syntheses of tricyclic triterpenoids, such as achilleol B[13] and camelliols A and B.[14]

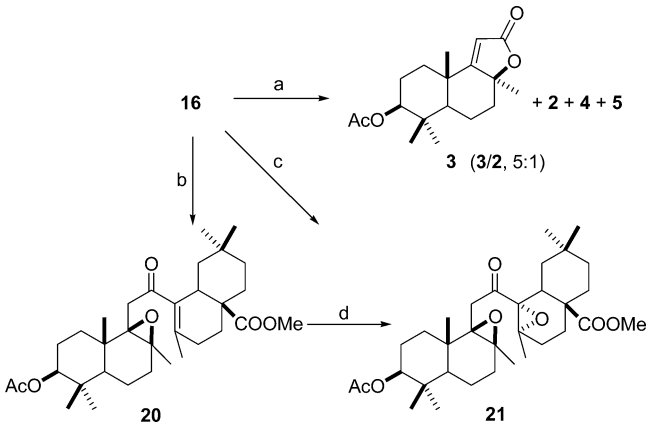
Synthesis of (−)-9-*epi*-Ambrox (7) from 2. Compound **2** possesses substitution patterns and configurations similar to those of (−)-9-*epi*-ambrox (**7**) and could be used as a starting material for the synthesis of **7** (Scheme 6). The key step for the synthesis of **7** from **2** was to reduce the C-9,C-11 double bond stereospecifically. Unsaturated lactone **2** was reduced with Mg in CH_3OH to give **22**. The ^1H NMR and ^{13}C NMR data of **22** were quite different from those of 3β-hydroxysclareolide.[31] Acetylation of **22** with Ac_2O gave the product **23**, which could also be obtained directly from **2** in high yields by reduction with $NaBH_4$/$NiCl_2 \cdot 6H_2O$[32] or by hydrogenation with H_2 in the presence of 10% Pd/C.

Scheme 4. Oxidation of Trienes **14** and **15**[a]



[a] Reagents and conditions: (a) m-CPBA (1 equiv), $NaHCO_3$, CH_2Cl_2, rt, 74%; (b) m-CPBA (2 equiv), $NaHCO_3$, CH_2Cl_2, rt, 56%; (c) m-CPBA (1 equiv), $NaHCO_3$, CH_2Cl_2, rt, 71%; (d) m-CPBA(3 equiv), CH_2Cl_2, rt, 51% (**2**), 23% (**4**), 22% (**5**), 8% (**18**), and 16% (**19**); (e) H_2O_2/HCOOH, $CHCl_3$, 50 °C, 60%; (f) m-CPBA(3 equiv), TsOH (cat.), CH_2Cl_2, rt, 82% (**2**), 57% (**4**), and 8% (**5**); (g) m-CPBA(3 equiv), TsOH (cat.), CH_2Cl_2, rt, 76% (**2**), 52% (**4**), and 10% (**5**).

Scheme 5. Oxidation of Dienone **16**[a]



[a] Reagents and conditions: (a) m-CPBA (3 equiv), TsOH (cat.), CH_2Cl_2, rt, 69% (**3** + **2**, **3**/**2** = 5:1), 49% (**4**) and 7% (**5**); (b) m-CPBA (1 equiv), $NaHCO_3$, CH_2Cl_2, rt, 84%; (c) m-CPBA (2 equiv), $NaHCO_3$, CH_2Cl_2, rt, 45%; (d) m-CPBA (1 equiv), $NaHCO_3$, CH_2Cl_2, rt, 57%.

The X-ray crystallographic analysis of **23** suggested that **22** is 3β-hydroxy-9-*epi*-sclareolide.[30]

Reductive removal of a sulfonate group with LAH can transform sulfonate to the corresponding hydrocarbon.[33] However, reduction of sulfonate **24** or **25** with LAH in THF and then cyclization with $TsOH{\cdot}H_2O$[34] in CH_3NO_2 did not afford the target compound **7** but its 3β-hydroxylated derivative, 3β-hydroxy-9-*epi*-ambrox (**26**). Cleavage of the S−O bond occurred probably because the C−O bond of the sulfonate was sterically hindered.[35] At the same time, compound **26** was also obtained via reduction of **23** with LAH in THF and then cyclization with $TsOH{\cdot}H_2O$ in CH_3NO_2. The configuration of **26** was confirmed by X-ray crystallographic analysis.[30]

Compound **26** was mesylated with methanesulfonyl chloride to give the mesylate **27** in 93% yield (Scheme 6). Then, Zn/NaI[35] was used to reductively remove the mesyloxy group in dimethoxyethane (DME) under reflux, but a mixture of (−)-9-*epi*-ambrox (**7**), **28**, and **29** was obtained. However, removal of the mesyloxy group in **27** with LiCl in DMF at 100 °C rendered the alkene **28** in 80% yield. Hydrogenation of **28** gave the target compound **7** quantitatively.

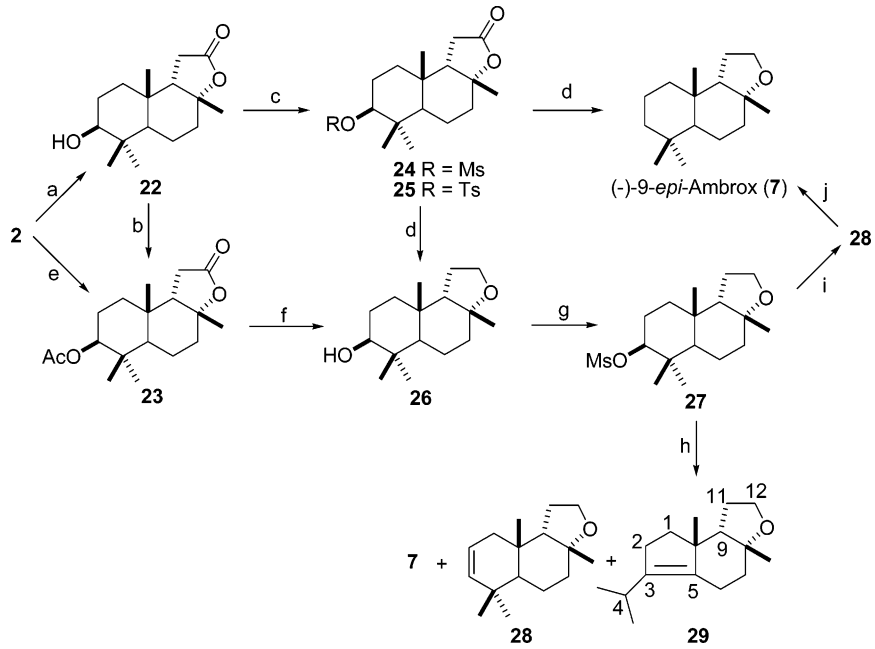
An efficient and convenient process was developed to prepare the *trans*-decalin $\Delta^{9(11)}$-3β-acetoxysclareolide (**2**) or its 8-epimer, $\Delta^{9(11)}$-3β-acetoxy-8-*epi*-sclareolide (**3**), respectively, with 4a-methoxycarbonyl-2,7,7-trimethyl-1-oxo-*cis*-decalin-2-ene (**4**) and its C-3 hydroxyl derivative **5** from oleanolic acid (**1**). This process relies on the introduction of an AcO-12 group and a C-9,C-11 double bond at ring C of methyl 3-acetoxyolean-12-en-28-oate (**8**), photolytic cleavage of the C-8,C-14 bond in the resulting diene, methyl 3,12-diacetoxyolean-9(11),12-dien-28-oate (**11**), and oxidative cleavage of the resulting acetoxy-substituted triene **14** or its hydrolyzed product **16**, with a novel method using m-CPBA/TsOH. All of the decalins, especially the *trans* ones, are useful and versatile precursors for the syntheses of important natural products possessing a decalin framework, with Me-8α or Me-8β groups and with or without functional groups on ring A. The stereospecific reduction of $\Delta^{9(11)}$-3β-acetoxysclareolide (**2**) gave 3β-acetoxy-9-*epi*-sclareolide (**23**). Compound **23**, an important synthon with 9*S* configuration, is difficult to prepare from other natural compounds. From **23**, (−)-9-*epi*-ambrox (**7**) was synthesized.

Experimental Section

General Experimental Procedures. Melting points were determined with an X-6 melting point apparatus and are uncorrected. Optical rotations were measured on a Perkin-Elmer 341 automatic polarimeter. UV and IR spectra were obtained on a Lambda 35 spectrometer and a Perkin-Elmer FT-IR spectrometer, respectively. NMR spectra were recorded on a Bruker Advance 600 spectrometer with TMS as internal standard. Electrospray ionization mass spectra (ESIMS) were acquired on a Finnigan LCQ^{DECA} mass spectrometer, and electron ionization mass spectra (EIMS) were recorded on a VG7070E mass spectrometer. HRESIMS were carried out on a BioTOF-Q mass spectrometer. Silica gel (200−300 mesh) was used for column chromatography. Precoated plates (silica gel GF254, 0−40 μm) activated at 110 °C for 2 h were used for TLC detected with an UV lamp, I_2, and an 8% ethanol solution of phosphomolybolic acid or a 5% ethanol solution of H_2SO_4. Commercial reagents were used without purification. All solvents including petroleum ether (60−90 °C) were distilled prior to use. Anhydrous THF was distilled from Na and benzophenone.

Methyl 3,12-Diacetoxyolean-9(11),12-dien-28-oate (11). To a solution of compound **10** (1 g, 1.9 mmol) in acetic anhydride (10 mL) were added a drop of concentrated H_2SO_4 and a catalytic amount of TsOH (20 mg). The reddish reaction mixture was stirred at room temperature for 5 h and then poured into a mixture of ice/water. The solid precipitate was filtered, washed with saturated aqueous $NaHCO_3$ and water, dried, and purified over a silica gel column (eluted by petroleum ether/AcOEt, 20:1) to render **11** (0.939 g, 87%). Compound **11** (colorless cubic crystals): mp 165.8−167.9 °C; $[\alpha]^{20}_D$ +194.4 (*c* 0.29, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 278 (3.96) nm; IR (KBr) ν_{max} 2946, 2867, 1729, 1656, 1240 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz) δ 5.40 (1H, s, H-11), 4.51 (1H, dd, J = 11.6, 4.7 Hz, H-3), 3.63 (3H, s, $-COOCH_3$), 3.22 (1H, dd, J = 13.3, 3.8 Hz, H-18), 2.16 (3H, s, CH_3COO-12), 2.06 (3H, s, CH_3COO-3), 1.22, 1.07, 1.06, 0.95, 0.92, 0.90, 0.87 (each 3H, s, Me); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 177.9, 171.0, 169.2, 156.5, 140.8, 129.0, 114.9, 80.4, 51.7, 51.0, 45.3, 43.0,

Scheme 6. Synthesis of (−)-9-*epi*-Ambrox (**7**)[a]



[a] Reagents and conditions: (a) Mg, CH_3OH, reflux, 74%; (b) Ac_2O, pyridine, CH_2Cl_2, rt, 95%; (c) MsCl or TsCl, pyridine, 0 °C, 96% (**24**) and 78% (**25**); (d) (i) LAH, THF, N_2, reflux, (ii) TsOH·H_2O, CH_3NO_2, 73% from **24**; (e) $NaBH_4$, $NiCl_2$·$6H_2O$, MeOH, 0 °C to rt, 97%; (f) (i) LAH, LiCl, THF, N_2, reflux, (ii) TsOH·H_2O, CH_3NO_2, 77%; (g) MsCl, pyridine, 0 °C, 93%; (h) Zn, NaI, DME, reflux, 42% (**28**), 14% (**29**), and 28% (**7**); (i) LiCl, DMF, 100 °C, 80%; (j) 10% Pd/C, H_2 (4 MPa), 100%.

41.4, 40.4, 38.8, 37.9, 36.7, 33.8, 32.8, 32.7, 32.1, 32.0, 30.5, 28.1, 27.0, 25.0, 24.1, 23.4, 23.3, 21.3, 20.7, 20.2, 20.0, 18.0, 16.7; ESIMS *m*/*z* 1158.9 $[2M + Na]^+$ (64), 591.3 $[M + Na]^+$ (100); HRESIMS *m*/*z* $[M + Na]^+$ 591.3665 (calcd for $C_{35}H_{52}NaO_6$, 591.3656).

Methyl 3,12-Diacetoxy-8,14-*seco*-olean-8*Z*,11*E*,13*E*-trien-28-oate (14). A solution of compound **11** (100 mg) in ethyl acetate (20 mL) in a Pyrex flask under argon was irradiated using a 500 W high-pressure Hg lamp at room temperature until compound **11** disappeared (monitored by TLC). Then, the solvent was evaporated under reduced pressure to give a syrup, which was purified over a silica gel column (petroleum ether/AcOEt, 25:1) to afford **14** (94 mg, 94%) as a colorless oil. An oily solution of **14** in a small amount of petroleum ether/AcOEt (25:1) stood for several days, and colorless cubic crystals were obtained. Compound **14** (colorless cubic crystals): mp 128.5−129.7 °C; $[\alpha]^{20}_D$ +170.6 (*c* 0.14, $CHCl_3$); IR (KBr) ν_{max} 2946, 2863, 1732, 1455, 1366, 1247, 1207, 1027 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz) δ 5.78 (1H, s, H-11), 4.54 (1H, dd, J = 11.2, 3.7 Hz, H-3), 3.65 (3H, s, $-COOCH_3$), 2.86 (1H, br s), 2.10 and 2.07 (each 3H, s, CH_3COO-3 and CH_3COO-12), 1.62 and 1.60 (each 3H, s, H-26 and H-27), 0.91 (6H, s, Me), 0.90 (3H, s, Me), 0.88 (6H, s, Me); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 178.0, 171.0, 169.0, 147.1, 134.2, 133.3, 132.6, 132.0, 119.0, 80.8, 51.7, 51.2, 44.9, 41.9, 38.8, 37.8, 36.6, 35.4, 34.9, 33.9, 33.0, 30.6, 29.9, 28.2, 24.6, 24.3, 22.3, 22.1, 21.9, 21.6, 21.4, 18.6, 16.7; ESIMS *m*/*z* 607.4 $[M + K]^+$ (5), 591.3 $[M + Na]^+$ (100), 568.5 $[M + H]^+$ (3), 509.2 $[M + H - CH_3COOH]^+$ (17), 449.3 (26); HRESIMS *m*/*z* $[M + Na]^+$ 591.3642 (calcd for $C_{35}H_{52}NaO_6$, 591.3656).

Methyl 3β-Acetoxy-12-oxo-8,14-*seco*-olean-8*Z*,13*E*-dien-28-oate (16). (1) Starting from **14**: To a solution of compound **14** (100 mg, 0.18 mmol) in methanol (5 mL) were added KOH (15 mg, 0.27 mmol) and water (0.2 mL). The reaction mixture was stirred at room temperature for 12 h. Then, water (20 mL) was added and the mixture was extracted with CH_2Cl_2 three times. The combined organic layer was washed with water and brine and dried over $MgSO_4$. After removal of the $MgSO_4$ via filtration, pyridine (0.5 mL) and acetic anhydride (0.2 mL) were added directly. The resulting solution was stirred at room temperature for 5 h and then washed with water, 5% HCl(aq), saturated aqueous $NaHCO_3$, and brine, dried over $MgSO_4$, and filtered. Then, the solvent was evaporated under reduced pressure to give a residue, which was purified over a silica gel column (petroleum ether/AcOEt, 25:1) to afford compound **16** (84 mg, 91%).

(2) Starting from **15** with the same procedure as (1), yield: 87%.

Compound 16: colorless cubic crystals; mp 145.6−146.7 °C; $[\alpha]^{20}_D$ +159.2 (*c* 0.25, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 244 (3.74) nm; IR (KBr) ν_{max} 2956, 1736, 1719, 1685, 1628, 1243 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz) δ 4.53 (1H, dd, J = 11.7, 4.6 Hz, H-3), 3.71 (3H, s, $-COOCH_3$), 3.47 and 3.19 (each 1H, d, J = 19.0 Hz, H-11), 3.08 (1H, dd, J = 12.9, 3.2 Hz, H-18), 2.05 (3H, s, CH_3COO-), 1.62 (3H, s, H-27), 1.44 (3H, s, H-26), 0.96 (3H, s, Me), 0.92 (3H, s, Me), 0.90 (6H, s, Me), 0.88 (3H, s, Me); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 204.9, 177.8, 170.8, 139.0, 133.0, 132.9, 129.8, 80.6, 51.8, 50.3, 44.9, 42.2, 39.9, 37.9, 37.7, 34.2, 34.1, 33.7, 33.4, 32.5, 31.8, 30.6, 29.9, 28.0, 23.9, 23.8, 22.6, 21.3, 20.4, 20.0, 19.9, 18.6, 16.6; ESIMS *m*/*z* 565.3 $[M + K]^+$ (2), 549.4 $[M + Na]^+$ (100), 489.3 (26); HRESIMS *m*/*z* $[M + Na]^+$ 549.3527 (calcd for $C_{33}H_{50}NaO_5$, 549.3550).

$\Delta^{9(11)}$-3β-Acetoxysclareolide (2), *cis*-Decalin 4, and *cis*-Decalin 5. (1) Starting from **14**: To a solution of **14** (100 mg, 0.18 mmol) in CH_2Cl_2 (10 mL) were added a catalytic amount of TsOH and then m-CPBA (75%) (120 mg, 0.52 mmol). The reaction mixture was stirred for 12 h at room temperature. The resulting solution was washed with saturated aqueous $NaHSO_3$, saturated aqueous $NaHCO_3$, and brine, dried over $MgSO_4$, filtered, and evaporated to dryness. The residue was separated over a silica gel column (petroleum ether/AcOEt, 25:1, and then petroleum ether/AcOEt, 4:1) to afford compounds **2** (44 mg, 82%), **4** (25 mg, 57%), and **5** (4 mg, 8%).

(2) Starting from **15** with the same procedure as (1): **2** (75%), **4** (52%), and **5** (10%).

Compound 2: colorless cubic crystals; mp 171.1−171.9 °C; $[\alpha]^{20}_D$ −118.8 (*c* 0.14, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 215 (4.12) nm; IR (KBr) ν_{max} 3006, 2982, 2955, 2932, 2864, 1757, 1731, 1628, 1374, 1254, 1027, 955 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz) δ 5.56 (1H, s, H-11), 4.50 (1H, dd, J = 10.9, 4.5 Hz, H-3), 2.33 (1H, dt, J = 12.1, 2.8 Hz, H-7), 2.09 (3H, s, CH_3COO-), 1.84−1.91 (3H, m, H-1, H-2 and H-6), 1.76−1.82 (2H, m, H-1 and H-2), 1.59 (1H, m, H-6), 1.58 (3H, s, H-16), 1.52 (1H, dt, J = 12.8, 3.7 Hz, H-7), 1.24 (3H, s, H-15), 1.04 (1H, dd, J = 12.1, 2.3 Hz, H-5), 0.98 (3H, s, H-14), 0.92 (3H, s, H-13); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 183.3 (C-9), 172.0 (C-12), 170.7 (CH_3COO-), 109.9 (C-11), 86.9 (C-8), 79.5 (C-3), 54.7 (C-5), 40.4 (C-7), 39.3 (C-10), 38.5 (C-4), 34.9 (C-1), 28.1 (C-13), 25.3 (C-16), 23.2 (C-2), 21.1 (CH_3COO-), 19.2 (C-6), 18.2 (C-15), 16.6 (C-14); ESIMS *m*/*z* 329.2 $[M + Na]^+$ (63), 307.2 $[M + H]^+$ (100); HRESIMS *m*/*z* $[M + Na]^+$ 329.1726 (calcd for $C_{18}H_{26}NaO_4$, 329.1723).

Compound 4: white amorphous powder; $[\alpha]^{20}_D$ +8.3 (*c* 0.05, AcOEt), $[\alpha]^{20}_{578}$ +10.4 (*c* 0.05, AcOEt), $[\alpha]^{20}_{546}$ +8.3 (*c* 0.05, AcOEt), $[\alpha]^{20}_{436}$ −50.0 (*c* 0.05, AcOEt), $[\alpha]^{20}_{365}$ −547.9 (*c* 0.05, AcOEt); UV (MeOH) λ_{max} (log ϵ) 236 (3.84) nm; IR (KBr) ν_{max} 2951, 2864, 1731, 1673, 1453, 1255, 1200, 1169 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz) δ

6.60 (1H, d, J = 5.5 Hz, H-3), 3.65 (3H, s, $-COOCH_3$), 3.02 (1H, dd, J = 13.6, 4.2 Hz, H-8a), 2.69 (1H, dt, J = 18.7, 2.1 Hz, H-4), 2.56 (1H, dd, J = 18.7, 5.9 Hz, H-4), 1.74 (3H, s, H-9), 1.70 (1H, dd, J = 13.7, 4.6 Hz, H-5), 1.63 (1H, dt, J = 13.7, 3.5 Hz, H-5), 1.46 (1H, dd, J = 13.8, 4.4 Hz, H-6), 1.42 (1H, m, H-8), 1.36 (1H, m, H-6), 1.26 (1H, t, J = 13.5 Hz, H-8), 0.99, 0.96 (each 3H, s, H-11 and H-12); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 201.1 (C-1), 177.2 (C-10), 141.8 (C-3), 134.4 (C-2), 52.4 ($-COOCH_3$), 47.9 (C-4a), 46.1 (C-8a), 38.3 (C-8), 34.4 (C-6), 32.5 (C-11 or 12), 29.7 (C-5), 29.6 (C-7), 27.8 (C-4), 24.2 (C-11 or 12), 16.0 (C-9); ESIMS m/z 289 $[M + K]^+$ (2), 251 $[M + H]^+$ (100), 191.1 $[M + H - HCOOCH_3]^+$ (94); HRESIMS m/z $[M + Na]^+$ 273.1457 (calcd for $C_{15}H_{22}NaO_3$, 273.1461).

Compound 5: white amorphous powder; $[\alpha]^{20}_D$ −43.7 (c 0.05, AcOEt), $[\alpha]^{20}_{578}$ −45.8 (c 0.05, AcOEt), $[\alpha]^{20}_{546}$ −56.3 (c 0.05, AcOEt), $[\alpha]^{20}_{436}$ −160.4 (c 0.05, AcOEt), $[\alpha]^{20}_{365}$ −718.7 (c 0.05, AcOEt); UV (MeOH) λ_{max} (log ϵ) 244 (4.03) nm; IR (KBr) ν_{max} 3438, 2953, 2920, 1728, 1668, 1628, 1291, 1203 cm^{-1}; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 3.68 (3H, s, $-COOCH_3$), 3.10 (1H, br d, J = 18.5 Hz, H-4), 3.06 (1H, dd, J = 13.7, 4.4 Hz, H-8a), 2.93 (1H, d, J = 18.5 Hz, H-4), 1.87 (3H, s, H-9), 1.76 (1H, dt, J = 13.7, 4.8 Hz, H-5), 1.64 (1H, dt, J = 14.3, 3.4 Hz, H-5), 1.46 (1H, m, H-8), 1.42 (1H, dd, J = 13.3, 4.2 Hz, H-6), 1.38 (1H, m, H-6), 1.25 (1H, t, J = 13.5 Hz, H-8), 0.99, 0.97 (each 3H, s, H-11 and H-12); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 198.0 (C-1), 176.2 (C-10), 150.0 (C-3), 132.0 (C-2), 52.6 ($-COOCH_3$), 46.9 (C-4a), 45.4 (C-8a), 38.3 (C-8), 36.3 (C-4), 34.2 (C-6), 32.4 (C-11 or 12), 29.7 (C-7), 29.3 (C-5), 24.1 (C-11 or 12), 12.4 (C-9); ESIMS m/z 265.6 $[M - H]^-$ (100); HRESIMS m/z $[M - H]^-$ 265.1450 (calcd for $C_{15}H_{21}O_4$, 265.1434).

$\Delta^{9(11)}$-3β-Acetoxy-8-*epi*-sclareolide (3). To a solution of **16** (82 mg, 0.16 mmol) in CH_2Cl_2 (5 mL) were added a catalytic amount of TsOH and then m-CPBA(75%) (110 mg, 0.48 mmol). The reaction mixture was stirred for 12 h at room temperature. The resulting solution was washed with saturated aqueous $NaHSO_3$, saturated aqueous $NaHCO_3$, and brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was separated over a silica gel column (petroleum ether/AcOEt, 25:1, and then petroleum ether/AcOEt, 4:1) to afford a mixture of compounds **3** and **2** (ratio of **3**/**2** = 5:1) (33 mg, 69%), **4** (19 mg, 49%), and **5** (3 mg, 7%). Slow recrystallization of the mixture of **3** and **2** from *n*-hexane/acetone (8:1) gave different crystal shapes, which could be manually separated to give pure **3** as colorless needle crystals and **2** as colorless cubic crystals. Compound **3** (colorless needle crystals): mp 65.5−66.8 °C; $[\alpha]^{25}_D$ +211.8 (c 0.09, $CHCl_3$); UV ($CHCl_3$) λ_{max} (log ϵ) 240 (3.12) nm; IR (KBr) ν_{max} 2924, 1755, 1714, 1624, 1259, 1025 cm^{-1}; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 5.71 (1H, s, H-11), 4.56 (1H, dd, J = 11.5, 4.5 Hz, H-3), 2.24 (1H, dt, J = 11.4, 3.2 Hz), 2.08 (3H, s, CH_3COO-), 1.89 (1H, dt, J = 13.1, 3.3 Hz), 1.80−1.86 (3H, m), 1.71−1.79 (2H, m), 1.64−1.69(2H, m), 1.63, 1.26, 0.96, and 0.92 (each 3H, s, Me); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 186.6, 172.4, 170.8, 113.4, 86.7, 79.8, 44.3, 39.2, 37.8, 36.2, 30.3, 28.4, 27.3, 25.3, 24.1, 21.2, 16.6, 16.2; ESIMS m/z 345.1 $[M + K]^+$ (10), 329.2 $[M + Na]^+$ (100), 307.2 $[M + H]^+$ (20); HRESIMS m/z $[M + Na]^+$ 329.1716 (calcd for $C_{18}H_{26}NaO_4$, 329.1723).

3β-Hydroxy-9-*epi*-sclareolide (22). To a stirred solution of compound **2** (100 mg, 0.33 mmol) in methanol (5 mL) was added magnesium turnings (16 mg, 0.67 mmol). The reaction mixture was heated and kept refluxing slowly. When Mg was consumed, a second portion of Mg (16 mg) was added; then the addition was repeated until the reaction was complete (monitored by TLC). The mixture was cooled to room temperature, and 5% HCl(aq) was added. The resulting mixture was extracted with ethyl acetate, and the combined organic layer was washed with saturated aqueous $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated in vacuo. Separation of the residue via silica gel chromatography (petroleum ether/AcOEt, 4:1) yielded **22** (64 mg, 74%) as crystals. Compound **22**: mp 151.9−154.9 °C; $[\alpha]^{20}_D$ −64.3 (c 0.12, CH_3OH), $[\alpha]^{20}_{578}$ −66.1 (c 0.12, CH_3OH), $[\alpha]^{20}_{546}$ −76.5 (c 0.12, CH_3OH), $[\alpha]^{20}_{436}$ −130.4 (c 0.12, CH_3OH), $[\alpha]^{20}_{365}$ −212.2 (c 0.12, CH_3OH); IR (KBr) ν_{max} 3462, 2928, 1758, 1739, 1388, 1062, 946 cm^{-1}; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 3.24 (1H, dd, J = 10.6, 5.6 Hz, H-3), 2.58 (1H, dd, J = 17.2, 13.6 Hz, H-11), 2.42 (1H, dd, J = 17.2, 8.3 Hz, H-11), 2.06 (1H, dd, J = 13.6, 8.3 Hz, H-9), 2.03 (1H, m, H-7), 1.62−1.68 (3H, m, 1H-6 and 2H-2), 1.57 (3H, s, H-16), 1.55 (1H, m, H-7), 1.32−1.39 (2H, m, H-1 and H-6), 1.26 (1H, m, H-1), 1.12 (3H, s, H-15), 1.11 (1H, m, H-5),1.05 (3H, s, H-13), 0.81 (3H, s, H-14); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 175.3 (C-12), 85.8 (C-8), 78.6 (C-3), 56.5 (C-9), 45.6 (C-5), 38.5 (C-4), 36.8 (C-7), 36.1 (C-1), 35.8 (C-10), 32.6 (C-11), 28.3 (C-13), 27.3 (C-16), 26.8 (C-2), 22.9 (C-15), 19.0 (C-6), 15.7 (C-14); ESIMS m/z 305.4 $[M + K]^+$ (30), 289.4 $[M + Na]^+$ (100); HRESIMS m/z $[M + Na]^+$ 289.1778 (calcd for $C_{16}H_{26}NaO_3$, 289.1774).

3β-Acetoxy-9-*epi*-sclareolide (23). (1) Starting from **2**: $NaBH_4$ (32 mg, 0.8 mmol) at 0 °C was added under stirring to a solution of **2** (55 mg, 0.18 mmol) and $NiCl_2 \cdot 6H_2O$ (10 mg, 0.05 mmol) in MeOH (20 mL). The mixture was stirred for 1 h at 0 °C and then 2 h at room temperature, quenched with saturated aqueous NH_4Cl, and extracted with AcOEt. The combined organic layer was washed with brine, dried over $MgSO_4$, and filtered. Concentration of the filtrate in vacuo followed by flash chromatography (petroleum ether/AcOEt 4:1) afforded **23** (54 mg, 97%).

(2) Starting from **2**: To a stainless steel autoclave of 20 mL were added a solution of compound **2** (50 mg) in ethyl acetate (5 mL) and 10% Pd/C (10 mg). The autoclave was evacuated and purged with hydrogen three times, and then the pressure of hydrogen was kept at 4 MPa. The reaction mixture was stirred at room temperature for 24 h. Then, stirring was stopped and the autoclave was vented slowly. Removal of the Pd/C by filtration and concentration in vacuo gave **23** quantitatively.

(3) Starting from **22**: To a solution of **22** (20 mg, 0.08 mmol) in pyridine (2 mL) was added acetic anhydride (0.2 mL). The reaction mixture was stirred at room temperature for 5 h, poured into water, and extracted with ethyl acetate. The combined extracts were washed with 5% HCl(aq), water, saturated aqueous $NaHCO_3$, and brine, dried over $MgSO_4$, and filtered. Concentration of the filtrate in vacuo followed by flash chromatography (petroleum ether/AcOEt 4:1) afforded **23** (22 mg, 95%).

Compound 23: colorless cubic crystals; mp 189.2−189.8 °C; $[\alpha]^{20}_D$ −35.9 (c 0.20, CH_3OH), $[\alpha]^{20}_{578}$ −33.8 (c 0.20, CH_3OH), $[\alpha]^{20}_{546}$ −39.5 (c 0.20, CH_3OH), $[\alpha]^{20}_{436}$ −71.3 (c 0.20, CH_3OH), $[\alpha]^{20}_{365}$ −116.4 (c 0.20, CH_3OH); IR (KBr) ν_{max} 2982, 2951, 1769, 1756, 1726, 1627, 1267, 1245, 1025, 942 cm^{-1}; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 4.47 (1H, dd, J = 11.5, 5.1 Hz, H-3), 2.58 (1H, dd, J = 17.2, 13.6 Hz, H-11), 2.43 (1H, dd, J = 17.2, 8.2 Hz, H-11), 2.07 (3H, s, CH_3COO-), 2.02−2.08 (2H, m), 1.65−1.72 (3H, m), 1.59 (1H, m, H-7), 1.57 (3H, s, H-16), 1.30−1.39 (3H, m), 1.21 (1H, dd, J = 12.2, 1.8 Hz), 1.15, 0.93 and 0.88 (each 3H, s, Me); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 175.1, 170.8, 85.6, 80.1, 56.5, 45.8, 37.3, 3.67, 35.7, 35.6, 32.5, 28.3, 27.3, 23.2, 22.9, 21.2, 18.9, 16.8; ESIMS m/z 655.3 $[2M + K]^+$ (5), 639.5 $[2M + Na]^+$ (60), 347.2 $[M + K]^+$ (33), 331.3 $[M + Na]^+$ (100); HRESIMS m/z $[M + Na]^+$ 331.1878 (calcd for $C_{18}H_{28}NaO_4$, 331.1880).

3β-Mesyloxy-9-*epi*-sclareolide (24). A solution of **22** (50 mg, 0.19 mmol) in pyridine (2 mL) was cooled to −5→0 °C in an ice/NaCl bath, and then methanesulfonyl chloride (0.05 mL) was added. The reaction mixture was stirred at the same temperature for 2 h, and ethyl acetate was added. The mixture was washed with 5% HCl(aq), water, saturated aqueous $NaHCO_3$, and brine, dried ($MgSO_4$), filtered, and concentrated in vacuo. The yellow residue was separated over a silica gel column (petroleum ether/AcOEt, 4:1) to give compound **24** (62 mg, 96%) as crystals. Compound **24**: mp 164.9−165.8 °C; $[\alpha]^{20}_D$ −35.1 (c 0.21, AcOEt), $[\alpha]^{20}_{578}$ −38.9 (c 0.21, AcOEt), $[\alpha]^{20}_{546}$ −44.3 (c 0.21, AcOEt), $[\alpha]^{20}_{436}$ −78.2 (c 0.21, AcOEt), $[\alpha]^{20}_{365}$ −127.5 (c 0.21, AcOEt); IR (KBr) ν_{max} 2935, 1759, 1631, 1349, 1172, 941, 914 cm^{-1}; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 4.33 (1H, dd, J = 11.3, 5.2 Hz, H-3), 3.04 (3H, s, CH_3SO_3-), 2.56 (1H, dd, J = 17.1, 13.7 Hz, H-11), 2.43 (1H, dd, J = 17.1, 8.4 Hz, H-11), 1.57 (3H, s, H-16), 1.16, 1.09, and 0.89 (each 3H, s, Me); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 174.8, 88.9, 85.4, 56.3, 46.0, 38.9, 38.2, 36.6, 35.7, 35.5, 32.4, 28.4, 24.8, 22.9, 22.8, 19.1, 16.5; ESIMS m/z 383.1 $[M + K]^+$ (40), 367.2 $[M + Na]^+$ (100); HRESIMS m/z $[M + Na]^+$ 367.1536 (calcd for $C_{17}H_{28}NaO_5S$, 367.1550).

3β-Hydroxy-9-*epi*-ambrox (26). (1) Starting from **24**: $LiAlH_4$ (33 mg, 0.88 mmol) was added to a stirred solution of compound **24** (77 mg, 0.22 mmol) in THF (5 mL) under argon. The mixture was refluxed slowly for 2 h and then cooled to room temperature. Then, 5% HCl(aq) was added, and the mixture was extracted with Et_2O three times. The combined Et_2O layer was washed with saturated aqueous $NaHCO_3$ and saturated aqueous Na_2SO_4, dried over Na_2SO_4, filtered, and concentrated in vacuo. Nitromethane (10 mL) and then $TsOH \cdot H_2O$ (19 mg, 0.10 mmol) were directly added to the residue. This mixture was stirred at room temperature for 6 h, diluted with Et_2O, washed with saturated aqueous $NaHCO_3$ and brine, dried over $MgSO_4$, and filtered.

The filtrate was concentrated in vacuo and purified over a silica gel column (petroleum ether/AcOEt, 4:1) to afford compound **26** (41 mg, 73%).

(2) Starting from **23** with the same procedure as (1), yield: 77%.

Compound 26: colorless needle crystals; mp 132.5−134.6 °C; $[\alpha]^{25}_{D}$ −8.0 (*c* 0.97, $CHCl_3$); $[\alpha]^{25}_{578}$ −8.1 (*c* 0.97, $CHCl_3$); $[\alpha]^{25}_{546}$ −9.0 (*c* 0.97, $CHCl_3$); $[\alpha]^{25}_{436}$ −14.6 (*c* 0.97, $CHCl_3$); $[\alpha]^{25}_{365}$ −21.1 (*c* 0.97, $CHCl_3$); IR (KBr) ν_{max} 3451, 2965, 2929, 1462, 1384, 1123, 1063, 1037 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz) δ 3.85 (1H, dt, J = 9.1, 2.9 Hz), 3.77 (1H, q, J = 8.5 Hz), 3.22 (1H, dd, J = 9.0, 7.3 Hz), 1.96−2.05 (1H, m), 1.88−1.94 (1H, m), 1.64−1.68 (3H, m), 1.56−1.62 (3H, m), 1.52 (1H, dt, J = 13.2, 4.2 Hz), 1.38 (3H, s, Me), 1.17 (1H, dd, J = 12.1, 2.0 Hz), 1.10, 1.02, and 0.79 (each 3H, s, Me); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 80.6, 79.1, 64.0, 58.7, 45.8, 38.6, 36.5, 35.8, 35.4, 28.8, 28.4, 27.6, 27.2, 22.9, 20.1, 15.6; EIMS *m*/*z* 252 $[M]^+$ (3), 237 $[M - Me]^+$ (45), 219 $[M - Me - H_2O]^+$ (19), 152 (29), 135 (80), 97 (42), 84 (35), 55 (42), 43 (100).

3β-Mesyloxy-9-*epi*-ambrox (27). A mixture of **26** (50 mg, 0.20 mmol), pyridine (0.2 mL), and CH_2Cl_2 (3 mL) was cooled to −5 → 0 °C in an ice/NaCl bath, and then methanesulfonyl chloride (0.05 mL) was added. The mixture was kept at −5→0 °C for 2 h, and additional CH_2Cl_2 was added. The mixture was washed with 5% HCl(aq), water, saturated aqueous $NaHCO_3$, and brine, dried ($MgSO_4$), filtered, and concentrated in vacuo. The yellow residue was separated over a silica gel column to give **27** (61 mg, 93%). Compound **27** (pale yellow cubic crystals): mp 114.8−116.6 °C; $[\alpha]^{25}_{D}$ −4.8 (*c* 0.08, $CHCl_3$); IR (KBr) ν_{max} 2925, 2858, 1465, 1354, 1334, 1174, 939, 912, 873 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz) δ 4.34 (1H, dd, J = 9.2, 8.0 Hz, H-3), 3.86 (1H, dt, J = 8.4, 3.2 Hz, H-12), 3.78 (1H, q, J = 8.4 Hz, H-12), 3.03 (3H, s, CH_3SO_3−), 1.89−2.01 (4H, m), 1.38, 1.14, 1.06 and 0.87 (each 3H, s, Me); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 90.0, 80.4, 64.0, 58.5, 46.1, 38.9, 38.3, 36.1, 35.5, 35.2, 28.7, 28.5, 27.6, 25.2, 22.7, 20.2, 16.4; EIMS *m*/*z* 330 $[M]^+$ (1), 315 $[M - Me]^+$ (58), 234 $[M - CH_3SO_3H]^+$ (15), 219 (43), 201 (5), 191 (16), 175 (10), 135 (100).

$\Delta^{2(3)}$-9-*epi*-Ambrox (28). To a solution of compound **27** (30 mg, 0.09 mmol) in DMF (5 mL) was added anhydrous LiCl (20 mg, 0.47 mmol). The mixture was stirred at 100 °C for 4 h and then cooled to room temperature. Ethyl acetate was added, and the resulting solution was washed with water three times and brine, dried over $MgSO_4$, and filtered. Evaporation in vacuo and purification over a silica gel column (*n*-hexane/AcOEt, 50:1) gave **28** (17 mg, 80%) as a colorless oil. Compound **28**: $[\alpha]^{20}_{D}$ −4.3 (*c* 0.24, $CHCl_3$), $[\alpha]^{20}_{578}$ −5.1 (*c* 0.24, $CHCl_3$), $[\alpha]^{20}_{546}$ −6.4 (*c* 0.24, $CHCl_3$), $[\alpha]^{20}_{436}$ −10.2 (*c* 0.24, $CHCl_3$), $[\alpha]^{20}_{365}$ −13.6 (*c* 0.24, $CHCl_3$); IR (KBr) ν_{max} 2928, 2866, 1630, 1380, 1132, 1115, 1093, 1055, 1039, 723 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz) δ 5.46 (1H, ddd, J = 9.9, 6.0, 1.6 Hz, H-2), 5.35 (1H, dd, J = 9.9, 2.7 Hz, H-3), 3.86 (1H, dt, J = 8.4, 2.7 Hz, H-12), 3.78 (1H, q, J = 8.4 Hz, H-12), 2.00−2.07 (2H, m, H-1 and H-11), 1.93 (1H, m, H-11), 1.69 (1H, dd, J = 12.2, 8.2 Hz, H-9), 1.63 (1H, dd, J = 16.4, 6.0 Hz, H-1), 1.54−1.60 (3H, m, 1H-6 and 2H-7), 1.50 (1H, dd, J = 12.5, 2.6 Hz, H-5), 1.39 (3H, s, H-16), 1.35 (1H, m, H-6), 1.11 (3H, s, H-15), 0.98 and 0.88 (each 3H, s, H-13 and H-14); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 137.8 (C-3), 121.6 (C-2), 80.6 (C-8), 63.9 (C-12), 56.9 (C-9), 43.7 (C-5), 38.2 (C-1), 35.1 (C-10), 34.6 (C-7), 34.5 (C-4), 31.7 (C-13 or 14), 29.4 (C-11), 26.9 (C-16), 23.1 (C-15), 22.9 (C-13 or 14), 21.3 (C-6); ESIMS *m*/*z* 257.1 $[M + Na]^+$ (90), 235.2 $[M + H]^+$ (100); HRESIMS *m*/*z* $[M + H]^+$ 235.2059 (calcd for $C_{16}H_{27}O$, 235.2056).

(-)-9-*epi*-Ambrox (7). To a stainless steel autoclave of 20 mL with a magnetic stirrer were added a solution of **28** (50 mg) in ethyl acetate (5 mL) and 10% Pd/C (10 mg). The autoclave was evacuated and purged with hydrogen three times, and then the pressure of hydrogen was kept at 4 MPa during the entire reaction process. After 12 h, the stirring was stopped and the autoclave was vented slowly. Removal of the Pd/C by filtration and concentration in vacuo gave **7** quantitatively as a colorless oil. The spectroscopic data were the same as those published.[2a,36] Compound **7**: $[\alpha]^{25}_{D}$ −6.2 (*c* 1.0, $CHCl_3$) (lit.[19a] $[\alpha]^{25}_{D}$ −6.0, *c* 1.0, $CHCl_3$); IR (KBr) ν_{max} 2924, 2854, 1463, 1260, 1098, 1060, 1048, 1025, 802 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz) δ 3.85 (1H, dt, J = 8.5, 3.0 Hz, H-12), 3.77 (1H, q, J = 8.5 Hz, H-12), 2.04 (1H, m, H-11), 1.91 (1H, m, H-11), 1.64 (1H, m, H-2), 1.51−1.59 (4H, m, H-6, 2H-7, and H-9), 1.39−1.42 (2H, m, H-2 and H-3), 1.37 (3H, s, H-16), 1.21−1.28 (3H, m, 2H-1 and H-6), 1.19 (1H, dd, J = 12.4, 1.4 Hz, H-5), 1.15 (1H, ddd, J = 12.8, 12.8, 4.3 Hz, H-3), 1.10 (3H, s, H-15), 0.89 and 0.82 (each 3H, s, H-13 and H-14); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 80.8 (C-8), 64.1 (C-12), 59.0 (C-9), 46.7 (C-5), 42.3 (C-3), 38.7 (C-1), 36.0 (C-10), 35.8 (C-7), 33.6 (C-13 or C-14), 32.9 (C-4), 28.8 (C-11), 27.7 (C-16), 22.8 (C-15), 21.8 (C-13 or C-14), 20.4 (C-6), 18.5 (C-2); EIMS *m*/*z* 236 $[M]^+$ (13), 221 $[M - Me]^+$ (100), 206 (19), 151 (6),137 (72), 121 (15), 109 (24), 97 (31), 81 (28), 67 (30), 55 (59), 41 (69).

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Supporting Information Available: Experimental data of compounds **13**, **15**, **17**−**21**, **25**, and **29**, NMR and selected HRMS spectra of compounds **2**−**5**, **7**, **11**, and **13**−**29**, and ORTEP diagrams of **2**, **3**, **14**, **17**, **19**, **21**, **23**, and **26**. This material is available free of charge via the Internet at http://pubs.acs.org.

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