Preparation of Two Diastereoisomeric Decalin Synthons and (−)-Ambrox

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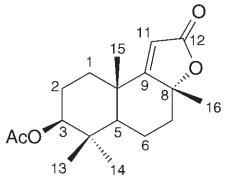
Two diastereoisomeric decalins, (2*S*,4a*S*,5*S*,6*R*)- and (2*S*,4a*S*,5*R*,6*R*)-5-(2-hydroxyethyl)-1,1,4a,6-tetramethyldecalin-2,6-diol (**5** and **6**) were prepared from the degradation products of oleanolic acid. Starting from **6**, (−)-ambrox (**4**) was synthesized.

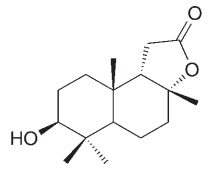
Introduction. – *trans*-4,4,8,10-Tetramethyldecalin is a common structural unit in natural products, especially in the large family of terpenoids. The dominating construction methods of decalins are *Diels–Alder* reactions, *Robinson* annulation, and cation- or radical-induced polyene cyclization [1]. However, in the synthesis of the corresponding natural products, these methods are often limited with respect to suitable starting substrates, selectivity control, and product resolution. Asymmetric syntheses of natural products containing the 4,4,8,10-tetramethyldecalin unit are commonly based on chiral synthons from natural terpenes (*e.g.*, sclareol, manool, abietic acid, communic acid, larixol, carvone, or thujone), as well as from well-established synthetic chiral materials such as the *Wieland–Miescher* ketone.

We have obtained the intermediates **1** (seven steps, 42% total yield) and **2** from oleanolic acid [2]. Natural products possessing a decalin skeleton with a 9β-side chain are more prevalent, but those with a 9α-side chain play also a very important role. Polygodial with a 9β-side chain, for example, is an active antifeedant, but polygodial with a 9α-side chain is inactive [3]. However, (−)-9-*epi*-ambrox (**3**) has a lower threshold concentration than (−)-ambrox (**4**) [4]. Thus, the preparation of intermediates such as **5** and **6** from the same starting material by only adjusting some procedures is fascinating, since they could be adapted conveniently for the synthesis of related natural products and their 9-epimers.

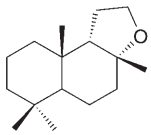
(−)-Ambrox is a very important and a rather expensive ambergris odorant. Therefore, many natural materials have been utilized for its preparation, but the commercial synthesis of (−)-ambrox uses exclusively sclareol [5]. Sclareol is obtained predominantly from the plant *Salvia sclarea*; the available amount and the price can fluctuate enormously depending on the harvest of *Salvia sclarea*. Oleanolic acid is distributed throughout the plant kingdom, and also commercially available for approximately a third of the price of that of sclareol. Therefore, it is of interest to use oleanolic acid in natural product synthesis and transformation.



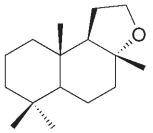
1



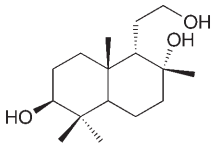
2



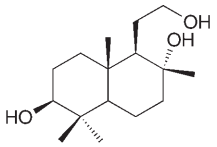
(–)-9-*epi*-Ambrox (**3**)



(–)-Ambrox (**4**)



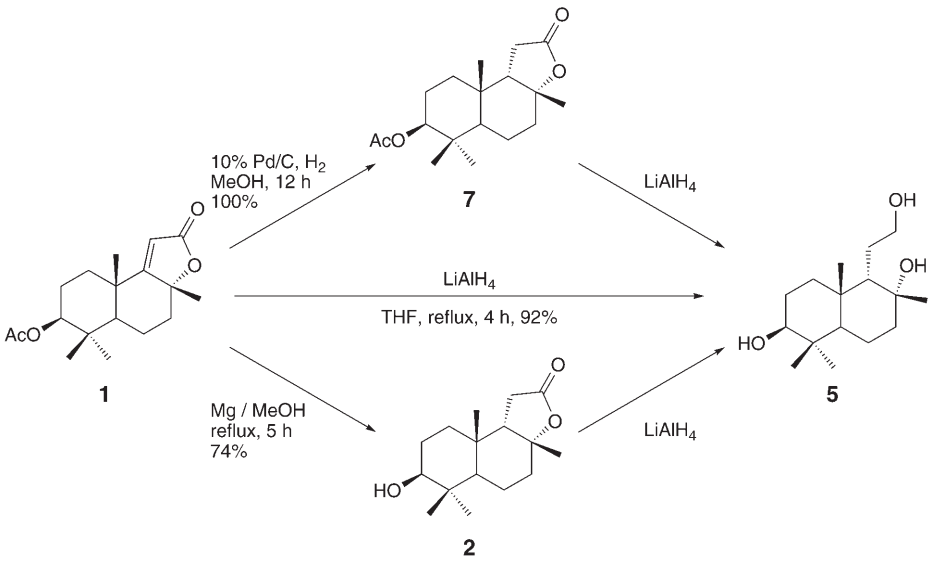
5



6

Results and Discussion. – For the catalytic hydrogenation of **1**, the product with a 9β-side chain was expected, considering the conformation observed in the single-crystal X-ray structure of **1** [2]. But to our surprise, only product **7** with a 9α-side chain was obtained in the presence of H_2 and 10% Pd/C (*Scheme 1*). The reduction of compound **1** by Mg/MeOH afforded compound **2** with the same configuration as observed for **7**. Thus, the conformational stability of the five-membered lactone may determine the stereocontrol.

Scheme 1

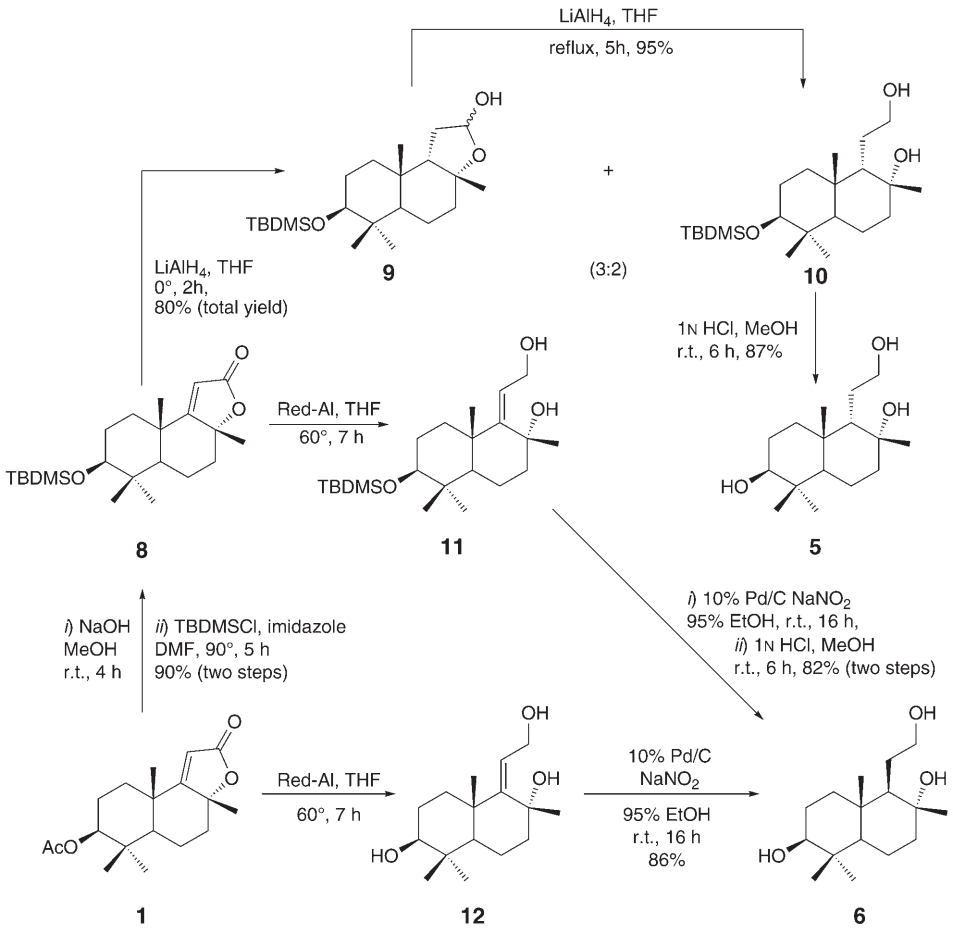


We assumed that the lactone-ring-opened product may be suitable as a starting material to obtain the 9-epimer **6** instead of **5**. The stereochemical course of the

hydrogenation may be influenced by a neighboring heteroatom [6][7]. In compound **1**, there is a potential α-OH group adjacent to the C=C bond. Its affinity to the Pd/C catalyst surface may result in the addition of H_2 *syn* to the α-OH group [7].

At first, as starting material, the 3-OH *tert*-butyl(dimethyl)silyl (TBDMS)-protected compound **8** was used. The lactone ring could not be opened by base hydrolysis or ester exchange. Referring to the reductive lactone ring opening by $LiAlH_4$ [8][9], even at low temperature (0°), the double bond was reduced as well; acetal **9** and compound **10** with a saturated 9α-side chain were isolated (*Scheme 2*). The reduction of the unsaturated lactone with $LiAlH_4$ is a 1,4-reduction process [10]. When DIBAL-H is used [11][12], and followed by reduction with $LiAlH_4$ or $NaBH_4$, most starting material **8** was recovered at low temperature (−70 to 0°.) At elevated temperature (40–60°), the reduction of **8** led to a complex product mixture. Using $NaBH_4$ and with LiCl as additive in 1,2-dimethoxyethane, the desired product **11** containing a C=C

Scheme 2



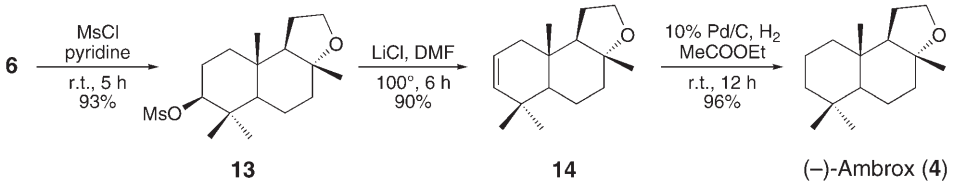
bond was obtained, but the yield was low (40%). After examining various reduction reagents, it was found that the reduction of **8** and **1**, respectively, by Red-Al (sodium bis(2-methoxyethoxy)aluminumhydride) gave triols **11** and **12** in 70 and 75% yield, respectively (*Scheme 2*).

With compound **12** in hand, we tested and verified our speculation by catalytic hydrogenation. Hydrogenation of **12** with 10% Pd/C in 95% EtOH in the presence of $NaNO_2$ [13][14] gave the saturated triol **6** with a 9β-side chain in 86% yield. Without $NaNO_2$, a considerable amount of by-products, resulting from hydrogenolysis and isomerization of the allylic alcohol, were formed.

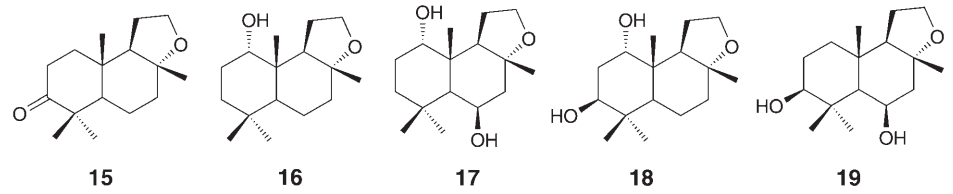
Based on the results obtained from the reduction of compound **8**, the unsaturated lactone **1** was reduced directly to the saturated triol **5** with 9α-side chain with $LiAlH_4$ under reflux in THF (*Scheme 1*).

(−)-Ambrox (**4**) was synthesized following the procedure for (−)-9-*epi*-ambrox (**3**) [2] (*Scheme 3*) with modifications. Intermediate **13** was prepared directly by mesylation of triol **6** with methanesulfonyl chloride. The primary OH group at C(12) was probably first mesylated, followed by intramolecular nucleophilic attack by the 8-OH group to complete the cyclization, and then mesylation of the OH group at C(3) gave compound **13**.

Scheme 3



Ring-*A*-substituted derivatives of (−)-ambrox, such as **15**–**19** are usually obtained by the biotransformation of (−)-ambrox [15]. The yields for these derivatives of (−)-ambrox are usually very low, and the fermentation time is long. The inhibitory activity of these compounds against thymidine phosphorylase *in vitro* has been evaluated [15d], but none of them has exhibited substantial potency.



Conclusions. – In summary, (2*S*,4a*S*,5*S*,6*R*)- and (2*S*,4a*S*,5*R*,6*R*)-5-(2-hydroxyethyl)-1,1,4a,6-tetramethyldecalin-2,6-diol (**5** and **6**, resp.) were prepared from the same starting material **1** by using different reduction sequences of the C=C bond and the lactone ring. (−)-Ambrox (**4**) was synthesized from **6**. These intermediates could be used for the synthesis of compounds with a 4,4,8,10-tetramethyldecalin skeleton possessing 9α- or 9β-side chains.

The authors are grateful to the *National Natural Science Foundation of China* (Grant 20572107) and *Chengdu Municipal Bureau of Science & Technology* for financial support.

Experimental Part

General. All solvents including petroleum ether (PE; 60–90°) were distilled prior to use. Anh. THF was distilled from Na and benzophenone. Commercial reagents were used without purification. M.p.: *X-6* melting point apparatus; uncorrected. Optical rotations: *Perkin-Elmer 341* automatic polarimeter. IR Spectra: *Perkin-Elmer* FT-IR spectrophotometer. NMR Spectra: *Bruker Avance-600* spectrometer with TMS as internal standard. Electrospray ionization mass spectra (ESI-MS) on a *Finnigan LCQ^{DECA}* mass spectrometer, and electron ionization mass spectra (EI-MS) on a *VG Micromass VG7070E* mass spectrometer.

*(2*S*,4a*S*,5*S*,6*R*)-5-(2-Hydroxyethyl)-1,1,4a,6-tetramethyldecahydronaphthalene-2,6-diol* (**5**). $LiAlH_4$ (49 mg, 1.3 mmol) was added to a soln. of compound **1** (100 mg, 0.32 mmol) in 5 ml THF at r.t. under Ar. The mixture was refluxed for 4 h, allowed to cool to r.t. The reaction was quenched with H_2O (50 µl), 15% NaOH (50 µl), and additional H_2O (150 µl). The resulting suspension was filtered and washed with THF. The combined filtrate was concentrated under reduced pressure and purified by silica gel (SiO_2) chromatography (PE/acetone 2:1) to afford **5** (79 mg, 92%). Colorless crystals (MeOH). M.p. 164–165°. $[\alpha]_D^{20} = -2.9$ ($c = 1.0$, MeOH). IR (KBr): 3406, 3370, 2961, 2913, 2857, 1343, 1114, 1033, 932. ^{1}H-NMR (600 MHz, CD_3OD): 3.46 (*t*, *J* = 7.6, 2 H); 3.15 (*dd*, *J* = 11.4, 4.2, 1 H); 2.03–1.99 (*m*, 1 H); 1.82–1.70 (*m*, 2 H); 1.62–1.48 (*m*, 4 H); 1.44 (*s*, 3 H); 1.41–1.36 (*m*, 1 H); 1.15–1.12 (*m*, 1 H); 1.12 (*s*, 3 H); 1.06 (*dd*, *J* = 12.09, 2.49, 1 H); 0.97 (*s*, 3 H); 0.75 (*s*, 3 H). ^{13}C-NMR (150 MHz, CD_3OD): 78.2; 72.1; 63.7; 56.7; 45.7; 38.2; 37.9; 36.5; 34.4; 30.5; 29.5; 27.0; 26.5; 23.9; 19.9; 14.1. HR-ESI-MS (pos.): 293.2082 ($[M + Na]^+$, $C_{16}H_{30}NaO_3^+$; calc. 293.2087).

*$\Delta^{9(11)}$-3β-[(*tert*-Butyl)dimethylsilyloxy]sclareolide* (*=(3a*R*,7*S*,9a*S*)-7-({[(*tert*-Butyl)dimethylsilyl]-oxy}methyl)-3a,6,6,9a-tetramethyl-4,5,5a,6,7,8,9,9a-octahydronaphtho[2,1-*b*]furan-2(3a*H*)-one*; **8**). To a soln. of **1** (100 mg, 0.33 mmol) in 10 ml MeOH was added NaOH (40 mg, 1 mmol). The mixture was stirred at r.t. for 4 h. Most of the solvent was removed under reduced pressure, and 30 ml AcOEt was added. The resulting mixture was washed with H_2O and brine, and dried (Na_2SO_4). After concentration under reduced pressure, the crude product was obtained and used directly without purification. DMF (5 ml) was added to the above product and then *tert*-butyl(chloro)dimethylsilane (TBDMSCl) (230 mg) and imidazole (113 mg). This mixture was stirred at 90° for 5 h and then cooled to r.t., diluted with 30 ml AcOEt, washed with brine, and dried (Na_2SO_4). Concentration of the filtrate under reduced pressure followed by chromatography (SiO_2; PE/AcOEt 10:1) afforded **8** (110 mg, 90%). Off-white solid. IR (KBr): 2949, 2934, 2860, 1747, 1625, 1463, 1253, 1218, 1191, 1115, 1094, 1076, 955, 881, 837, 775. ^{1}H-NMR (600 MHz, $CDCl_3$): 5.51 (*s*, 1 H); 3.21 (*dd*, *J* = 11.0, 4.7, 1 H); 2.30–2.28 (*m*, 1 H); 1.85–1.82 (*m*, 1 H); 1.78–1.71 (*m*, 2 H); 1.70–1.66 (*m*, 1 H); 1.64–1.62 (*m*, 1 H); 1.55 (*s*, 3 H); 1.20 (*s*, 3 H); 0.93 (*s*, 3 H); 0.90 (br., 9 H); 0.85 (*s*, 3 H); 0.06 (*s*, 3 H); 0.04 (*s*, 3 H). ^{13}C-NMR (150 MHz, $CDCl_3$): 184.2; 172.2; 109.6; 87.1; 78.6; 54.7; 40.6; 40.3; 39.4; 35.2; 28.6; 27.3; 25.8 (3 C); 25.3; 19.5; 18.2; 18.1; 15.9; −3.8; −5.0. HR-ESI-MS (pos.): 401.2487 ($[M + Na]^+$, $C_{22}H_{38}NaO_3Si^+$; calc. 401.2482).

*(3a*R*,7*S*,9a*S*,9b*S*)-7-({[(*tert*-Butyl)dimethylsilyl]oxy}methyl)-3a,6,6,9a-tetramethyldodecahydro-naphtho[2,1-*b*]furan-2-ol* (**9**). To a soln. of **8** (100 mg, 0.26 mmol) in anh. THF (10 ml) was added 20 mg (0.53 mmol) of $LiAlH_4$ at 0° under Ar atmosphere. The soln. was stirred at 0° for 2 h, followed by addition of H_2O (0.1 ml), 15% NaOH (0.1 ml), and additional H_2O (0.3 ml). The suspension was filtered, and the precipitate was washed with THF. The filtrate was combined and concentrated under reduced pressure. Purification of the residue by chromatography (SiO_2; PE/AcOEt 4:1) afforded compound **9** (49 mg, 48%) as an off-white solid. IR (KBr): 3434, 2951, 2858, 1651, 1465, 1389, 1361, 1253, 1095, 1073, 880, 836, 774. ^{1}H-NMR (600 MHz, $CDCl_3$): 5.48–5.45, 5.34–5.33 (2*m*, 1 H); 3.17 (*dd*, *J* = 7.0, 4.4, 1 H); 1.97–1.94, 1.90–1.87 (2*m*, 2 H); 1.46, 1.45 (2*s*, 3 H); 1.11, 1.09 (2*s*, 3 H); 0.94, 0.93 (2*s*, 3 H); 0.89 (br., 9 H); 0.75, 0.74 (2*s*, 3 H); 0.05, 0.04, 0.03, 0.02 (4*s*, 6 H). ^{13}C-NMR (150 MHz, $CDCl_3$): 97.2; 95.9; 83.3; 82.4; 79.6; 59.4; 55.2; 46.2; 45.5; 39.1; 38.2; 37.7; 37.6; 36.6; 36.5; 36.3; 35.8; 35.3; 29.3; 28.9; 28.8; 27.8; 27.6; 27.6; 25.9; 22.9; 22.9; 20.5; 20.1; 18.1; 16.2; 16.0; −3.8; −4.9. HR-ESI-MS (pos.): 405.2791 ($[M + Na]^+$, $C_{22}H_{42}NaO_3Si^+$; calc. 405.2795).

*(1Z,2*R*,6*S*,8a*S*)-6-({[(*tert*-Butyl)dimethylsilyl]oxy}methyl)-1-(2-hydroxyethylidene)-2,5,5,8a-tetramethyldecahydronaphthalen-2-ol* (**11**). To a stirred soln. of **8** (40 mg, 0.11 mmol) in anh. THF (10 ml) was syringed 90 µl of Red-Al (70 wt.-% in toluene, 0.32 mmol) at r.t. under Ar. The mixture was stirred at 60° for 7 h, followed by quenching the reaction with 2 ml of 23% aq. potassium sodium tartrate (*Rochelle* salt), and the mixture was stirred vigorously until the soln. turned clear. AcOEt (10 ml) was added to the mixture, the org. layer was separated, and the aq. layer was extracted with AcOEt. The combined org. layers were washed with brine, dried (Na_2SO_4), filtered, and concentrated under reduce pressure. The residue was purified by chromatography (SiO_2; PE/AcOEt 2:1) to afford **11** (28 mg, 70%) as off-white solid. IR (KBr): 3411, 2930, 2857, 1473, 1463, 1386, 1368, 1251, 1110, 1074, 1008, 943, 886, 837, 771. ^{1}H-NMR (600 MHz, $CDCl_3$): 5.52 (*t*, *J* = 6.3, 1 H); 4.44 (*dd*, *J* = 13.2, 6.5, 1 H); 4.30 (*dd*, *J* = 13.2, 6.1, 1 H); 3.17 (*dd*, *J* = 11.2, 4.9, 1 H); 1.98 (*dt*, *J* = 12.4, 3.3, 1 H); 1.81 (*dt*, *J* = 13.0, 3.4, 1 H); 1.72–1.66 (*m*, 2 H); 1.65–1.61 (*m*, 2 H); 1.57–1.52 (*m*, 3 H); 1.41–1.37 (*m*, 1 H); 1.26 (*s*, 3 H); 1.09 (*s*, 3 H); 1.01 (*dd*, *J* = 11.7, 2.5, 1 H); 0.92 (*s*, 3 H); 0.89 (br., 9 H); 0.77 (*s*, 3 H); 0.05 (*s*, 3 H); 0.03 (*s*, 3 H). ^{13}C-NMR (150 MHz, $CDCl_3$): 157.7; 122.0; 78.8; 74.4; 60.2; 52.0; 45.4; 40.4; 39.8; 37.3; 30.6; 28.6; 28.2; 25.9 (3 C); 23.7; 19.8; 18.1; 15.9; −3.8; −5.0. HR-ESI-MS (pos.): 405.2805 ($[M+Na]^+$, $C_{22}H_{42}NaO_3Si^+$; calc. 405.2795).

*(2*S*,4a*S*,5*Z*,6*R*)-5-(2-Hydroxyethylidene)-1,1,4a,6-tetramethyldecahydronaphthalene-2,6-diol* (**12**). The process was similar to the preparation of **11**. Yield: 75%. Colorless crystal (MeOH). M.p. 201–202.5°. $[\alpha]_D^{20} = +5.3$ (*c* = 1.0, MeOH). IR (KBr): 3351, 2971, 2933, 2861, 1622, 1471, 1073, 1043, 975, 930. ^{1}H-NMR (600 MHz, CD_3OD): 5.37 (*dd*, *J* = 5.9, 4.1, 1 H); 4.49 (*dd*, *J* = 14.8, 6.1, 1 H); 4.40 (*dd*, *J* = 14.8, 3.8, 1 H); 3.14 (*dd*, *J* = 9.4, 7.0, 1 H); 1.93–1.90 (*m*, 2 H); 1.73–1.68 (*m*, 3 H); 1.61–1.57 (*m*, 1 H); 1.55–1.50 (*m*, 1 H); 1.48–1.43 (*m*, 1 H); 1.41 (*s*, 3 H); 1.12 (*s*, 3 H); 1.03 (*dd*, *J* = 11.4, 2.2, 1 H); 0.99 (*s*, 3 H); 0.80 (*s*, 3 H). ^{13}C-NMR (150 MHz, CD_3OD): 154.7; 124.0; 77.8; 73.0; 60.1; 52.1; 44.4; 40.0; 38.9; 37.4; 28.4; 27.4; 27.1; 23.1; 19.3; 14.7. HR-ESI-MS (pos.): 291.1926 ($[M+Na]^+$, $C_{16}H_{28}NaO_3^+$; calc. 291.1931).

*(2*S*,4a*S*,5*R*,6*R*)-5-(2-Hydroxyethyl)-1,1,4a,6-tetramethyldecahydronaphthalene-2,6-diol* (**6**). *a*) *Starting from* **12**. To a soln. of **12** (80 mg, 0.3 mmol) in 95% EtOH (10 ml) was added 10% Pd/C (10 mg) and $NaNO_2$ (1 mg). After stirring for 30 min, the mixture was hydrogenated for 16 h at r.t. Pd/C was removed by filtration, and the filtrate was concentrated. The residue was purified by chromatography (SiO_2; PE/acetone 2:1) to give **6** (69 mg, 86%) as an off-white solid.

b) *Starting from* **11**. Substrate **11** (50 mg, 0.13 mmol) was used. The hydrogenation procedure was analogous to the hydrogenation of **12**. After removal of Pd/C and the solvent, a residue was obtained, to which MeOH (5 ml) and 1N HCl (0.5 ml) were added. The mixture was stirred at r.t. for 6 h. AcOEt (30 ml) was added, and the resulting soln. was washed with sat. aq. $NaHCO_3$, brine, and dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The residue was purified by chromatography (SiO_2; PE/acetone 2:1) to give **6** (29 mg, 82% two steps). Colorless crystal (MeOH). M.p. 207–208°. $[\alpha]_D^{20} = -8.4$ (*c* = 1.0, MeOH). IR (KBr): 3406, 3352, 2958, 2931, 2874, 2855, 1629, 1130, 1043, 905. ^{1}H-NMR (600 MHz, CD_3OD): 3.60–3.51 (*m*, 2 H); 3.15 (*dd*, *J* = 11.4, 4.9, 1 H); 1.87–1.84 (*m*, 1 H); 1.74–1.71 (*m*, 1 H); 1.70–1.66 (*m*, 2 H); 1.64–1.54 (*m*, 3 H); 1.16 (*s*, 3 H); 1.09–1.04 (*m*, 2 H); 0.97 (*s*, 3 H); 0.92–0.90 (*m*, 1 H); 0.84 (*s*, 3 H); 0.76 (*s*, 3 H). ^{13}C-NMR (150 MHz, CD_3OD): 78.1; 72.4; 63.6; 58.1; 55.1; 43.5; 38.5; 38.3; 37.8; 27.9; 27.3; 26.4; 22.7; 19.8; 14.6 (2 C). HR-ESI-MS: 293.2082 ($[M+Na]^+$, $C_{16}H_{30}NaO_3^+$; calc. 293.2087).

Compound **6** has also been obtained from the biotransformation of (−)-ambrox (**4**) [15c][16].

3β-(Mesyloxy)-9-ambrox (=*[(3a*R*,7*S*,9a*S*,9b*R*)-3a,6,6,9a-Tetramethyldodecahydronaphtho[2,1-b]furan-7-yl]methyl Methanesulfonate*; **13**). MsCl (0.05 ml) was added to a mixture of **6** (50 mg, 0.20 mmol), pyridine (0.2 ml), and CH_2Cl_2 (3 ml), the mixture was stirred at r.t. for 5 h, and then AcOEt (15 ml) was added. The resulting soln. was washed with 5% HCl (aq.), sat. aq. $NaHCO_3$, and brine, and dried (Na_2SO_4). The filtrate was concentrated under reduced pressure, and the residue was purified by chromatography (SiO_2; PE/AcOEt 4:1) to give **13** (57 mg, 93%). Colorless crystals (AcOEt). M.p. 150–151.5°. $[\alpha]_D^{20} = -15.6$ (*c* = 1.0, $CHCl_3$). IR (KBr): 2971, 2951, 2927, 2878, 1350, 1332, 1170, 1004, 923, 906. ^{1}H-NMR (600 MHz, $CDCl_3$): 4.36 (*dd*, *J* = 11.1, 5.8, 1 H); 3.90–3.94 (*m*, 1 H); 3.84 (*q*, *J* = 8.0, 1 H); 3.02 (*s*, 3 H); 2.03–1.95 (*m*, 3 H); 1.80–1.71 (*m*, 3 H); 1.59–1.57 (*m*, 1 H); 1.44–1.33 (*m*, 3 H); 1.26–1.21 (*m*, 1 H); 1.09 (*s*, 3 H); 1.05 (*s*, 3 H); 1.02–0.99 (*m*, 1 H); 0.89 (*s*, 3 H); 0.88 (*s*, 3 H). ^{13}C-NMR (150 MHz,

$CDCl_3$): 90.0; 79.6; 64.9; 59.8; 56.1; 39.4; 38.8; 38.6; 37.8; 35.7; 28.4; 25.1; 22.6; 21.0; 20.4; 16.0; 15.1. HR-ESI-MS (pos.): 683.3624 ($[2\,M+Na]^+$, $C_{34}H_{60}NaO_8S_2^+$; calc. 683.3622).

The procedures for the syntesis of $\Delta^{2(3)}$-ambrox (**14**) from 3β-(mesyloxy)-9-ambrox (**13**), and (−)-ambrox (**4**) are similar to those in [2] (*Scheme 3*).

$\Delta^{2(3)}$-Ambrox (=*(3a*R,*9a*S,*9b*R*)-3a,6,6,9a-Tetramethyl-1,2,3a,4,5,5a,6,9,9a,9b-decahydronaphtho[2,1-*b*]furan*; **14**). Colorless crystals (AcOEt). M.p. 88–89°. $[\alpha]_D^{20} = +12.2$ ($c = 1.0$, $CHCl_3$). IR (KBr): 2925, 2866, 1632, 1380, 1132, 1115, 1093, 1055, 1039, 723. ^{1}H-NMR (600 MHz, $CDCl_3$): 5.45 (*ddd*, *J* = 10.0, 5.3, 2.4, 1 H); 5.40 (*dd*, *J* = 10.1, 2.4, 1 H); 3.93 (*dt*, *J* = 9.0, 3.0, 1 H); 3.84 (*q*, *J* = 8.3, 1 H); 1.99–1.97 (*m*, 1 H); 1.83–1.73 (*m*, 5 H); 1.47–1.37 (*m*, 3 H); 1.30–1.26 (*m*, 1 H); 1.11 (*s*, 3 H); 0.99 (*s*, 3 H); 0.91 (*s*, 3 H); 0.88 (*s*, 3 H). ^{13}C-NMR (150 MHz, $CDCl_3$): 138.6; 121.2; 79.8; 64.9; 58.9; 52.9; 40.5; 39.1; 35.2; 34.5; 31.9; 22.7; 22.2; 21.5; 20.5; 15.2. ESI-MS: 257.1 ($[M+Na]^+$).

(−)-Ambrox (=*(3a*R,*9a*S,*9b*R*)-3a,6,6,9a-Tetramethyldodecahydronaphtho[2,1-*b*]furan*; **4**). Colorless crystals (AcOEt). M.p. 73–75° ([17a]: 74–76°, [17b]: 77–77.5°). $[\alpha]_D^{20} = -25.0$ ($c = 1.0$, $CHCl_3$) ([17a]: $[\alpha]_D^{20} = -24.7$, $c = 1.0$, $CHCl_3$; [17b]: $[\alpha]_D^{25} = -25.1$, $c = 1.0$, $CHCl_3$). IR (KBr): 2924, 2854, 1463, 1260, 1098, 1060, 1048, 1025, 802. The ^{1}H- and ^{13}C-NMR, and MS data were identical with those in [17][18].

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