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Enantioselective total syntheses of kudtriol, 5-*epi*-kudtriol and their C-11 epimers

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Abstract

Two approaches for the enantioselective syntheses of naturally occurring kudtriol **2a** and 5-*epi*-kudtriol **3a** as well as their C-11 epimers are presented, both using the Sharpless asymmetric dihydroxylation as the key reaction. Through comparison of the spectral data of natural triols and synthetic samples, we could confirm the absolute configuration of the natural triols.

1. Introduction

Sesquiterpenic compounds of the eudesmane family have attracted considerable attention due to their intriguing biological properties,[1,2] particularly significant being anti-feedant activity, cell growth inhibitory and plant growth regulating activities. *Jasonia glutinosa* (in Spanish) is well known as traditional medicine, which is named 'mountain tea' or 'rock tea'. From the aerial parts of *J. glutinosa*, Kudtdiol **1**, a representative member of this class of natural products, was first isolated by Teresa and co-workers in 1978.[3] The stereochemistry of **1** was firmly determined based on spectroscopic analysis and chemical correlation. Reinvestigation on the chemical constituents of *J. glutinosa* by Teresa et al. in 1980 resulted in the isolation of kudtriol **2a** and 5-*epi*-kudtriol **3a**, two epimeric eudesmane derivatives, and structural characterization by spectroscopic methods and chemical correlations, as (+)-(11*R*)-eudesm-4(14)-en-5α,11,12-triol and (–)-(11*R*)-eudesm-4(14)-en-5β,11,12-triol, respectively.[4] The stereochemistry at C-11 was deduced from chemical correlation with Kudtdiol **1** and the stereochemistry at C-5 was assigned spectroscopically based on the relative deshielding effect of 5-hydroxy group. The proposed structure of kudtriol **2a** was further unequivocally determined[5] by means of synthesis starting from 1-α-santonin **4** through an eleven-step process.

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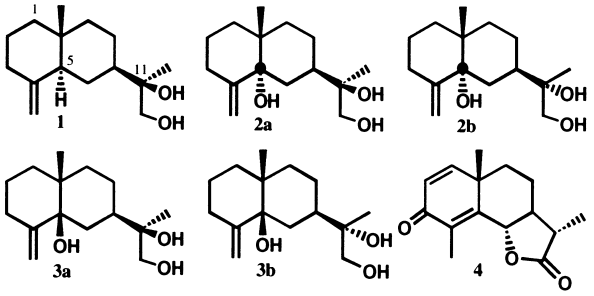
In connection with our interest in confirming the absolute configurations of natural products and our ongoing project on the asymmetric synthesis of bioactive sesquiterpenoids, we are stimulated to develop a facile approach for the total synthesis of this kind of sesquiterpenoids. Reported herein are two efficient approaches for the total synthesis of **2a**, **3a** and their C-11 epimeric isomers **2b** and **3b**, respectively. As a part of our work, natural products **15** and **16** have also been obtained as intermediates.

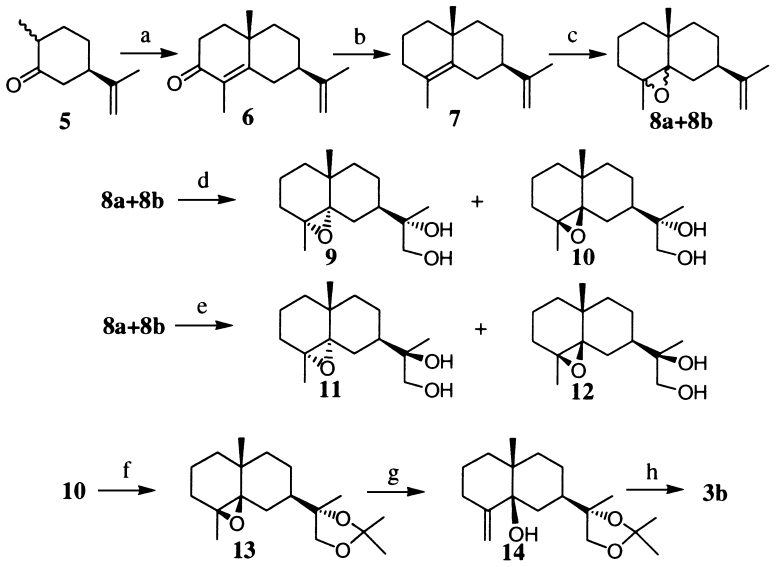


2. Results and discussion

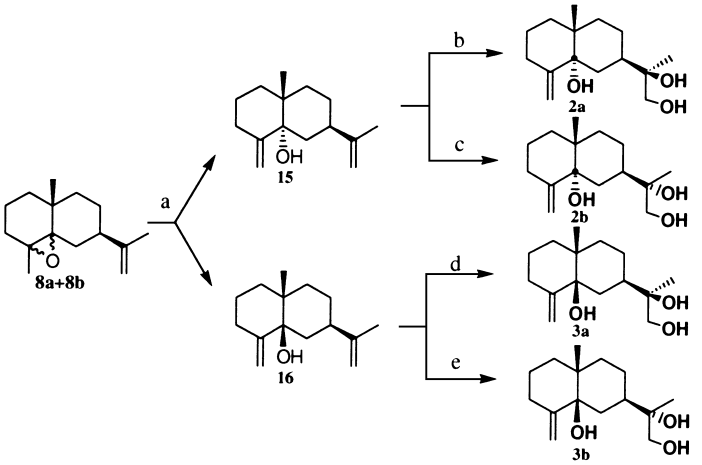
Our synthesis began with (+)-dihydrocarvone[6] (Scheme 1). By the published method,[7] (+)-α-cyperone **6** was easily prepared from (+)-dihydrocarvone **5** in 50% yield. Reductive deoxygenation[8] of **6** was effected with $AlCl_2H$ in ether to give diene **7** in 85% yield (purity > 95%, determined by GC), which was epoxidized[9] regioselectively with *m*CPBA at 0°C to afford an inseparable epimeric epoxide mixture **8a+8b** in a ratio of ca. 2:1 as determined by the ^1H NMR (400 MHz) spectral analysis. Diastereomeric 4,5-epoxides **9**, **10**, **11** and **12** were prepared readily from epoxide mixture **8a+8b** by Sharpless dihydroxylation[10] with AD-mix-α or AD-mix-β and chromatographic separation on silica gel, respectively, in good yield. Their absolute configurations were assigned according to the face-selection rule of the Sharpless AD process.[10,11] After all attempts were made unsuccessfully to obtain directly allylic alcohols **2** and **3** by epoxide rearrangement (LDA, $Al(OPr^i)_3$, $Ti(OPr^i)_4$[12]) of the above four compounds severally, we turned our attention to protection of the glycol. Ketalization[13] of the resulting dihydroxy epoxide **10** with acetone catalyzed by *p*-TsOH according to Ikekawa's procedure afforded pure corresponding acetonide **13**, which was subjected to the LDA mediated rearrangement to produce the corresponding title compound **3b** smoothly after deacetonization.

An alternative synthetic approach for the syntheses of the title compounds was investigated due to the inconvenience of the former approach (Scheme 2). Treatment of epoxides **8a+8b** with lithium diisopropylamine in THF at 0–23°C for 24 h gave the corresponding allylic alcohols **15** [60% yield; $[\alpha]_D^8$ +125.9 (*c* 0.72, $CHCl_3$)] and **16** [32% yield; $[\alpha]_D^8$ –95.2 (*c* 0.32, $CHCl_3$)] respectively, after chromatographic purification of the crude product on silica gel, which showed identical spectral data with those of natural products[14] isolated from the aerial parts of an Australian *Cassinia subtrapic*, respectively. Therefore, epoxides **8a** and **8b** should correspond to the configurations 4α,5α and 4β,5β, respectively.

Standard dihydroxylation[10] of **15** with commercially available AD-mix-α or AD-mix-β in *t*-BuOH:H_2O (v/v 1:1) provided a mixture of triols **2b** (29% de) and **2a** (25% de), respectively[15] in good combined yield (85–90%), which are chromatographically inseparable on silica gel. Analytically pure triols **2a** and **2b** were obtained by fractional recrystallization from petroleum ether–ether.



Scheme 1. *Reagents and conditions*: (a) Ref. 7, 50%; (b) $AlCl_2H$, ether, rt, 3 h, 85%; (c) *m*CPBA (0.9 equiv.), CH_2Cl_2, 0°C, 2 h, 84%; (d) AD-mix-α, *t*-BuOH–H_2O, 0°C, 24 h, 98% for **9** and **10** combined; (e) AD-mix-β, *t*-BuOH–H_2O, 0°C, 24 h, 95% for **11** and **12** combined; (f) *p*-TsOH, acetone, rt, 10 min, 58%; (g) LDA, diethyl ether, rt, 24 h, 84%; (h) 1N HCl, THF, reflux, 3 h, 90%



Scheme 2. *Reagents and conditions*: (a) LDA, diethyl ether, rt, 24 h, 60% for **15**, 32% for **16**; (b) AD-mix-β, *t*-BuOH–H_2O, 0°C, 24 h, 90% altogether; (c) AD-mix-α, *t*-BuOH–H_2O, 0°C, 24 h, 85% altogether; (d) AD-mix-β, *t*-BuOH–H_2O, 0°C, 24 h, 92% altogether; (e) AD-mix-α, *t*-BuOH–H_2O, 0°C, 24 h, 95% altogether

Accordingly, dihydroxylation of **16** with AD-mix-α or AD-mix-β furnished epimeric isomers **3b** and **3a** in ratios of 8:5 and 3:5, respectively,[15] in excellent combined yield (92–95%). The diastereoselectivity of dihydroxylation of **16** could be calculated directly after chromatographic purification on silica gel.[16]

As listed in Table 1, the ^1H NMR spectral data of the title compounds synthesized were compared with those of natural products reported in the literature. It is obvious that the synthetic triols **2a** and **3a** were identical with natural products, respectively, although the instrument used

for synthetic samples was operated at higher resolution.[17] The absolute stereochemistry of naturally occurring kudtriol and 5-*epi*-kudtriol was established unambiguously.

Table 1
^{1}H NMR spectral data (δ_H) of natural triols (60 MHz) and synthetic triols (400 MHz)[a]

H	Kudtriol	Synthetic **2a**	Synthetic **2b**	5-*Epi*-kudtriol	Synthetic **3a**	Synthetic **3b**
15	0.83 s	0.85 s	0.85 s	0.99 s	1.02 s	1.02 s
13	1.16 s	1.13 s	1.12s	1.13 s	1.17 s	1.15 s
12	3.40 d, 3.56 d (J = 12Hz)	3.45 d, 3.59 d (J = 11.2 Hz)	3.42 d, 3.64 d (J = 11.2 Hz)	3.35 d, 3.55 d (J = 11 Hz)	3.43 d, 3.59 d (J = 10.8Hz)	3.45 d, 3.65 d (J = 10.8Hz)
14	4.65 s	4.71 s	4.64 s	4.90 brs	4.94 s	4.95 s
14	4.76 s	4.82 s	4.80 s	(2H)	4.97 s	5.06 s

[a] Due to different instrument resolving power and conditions, there are some chemical-shift difference for the synthetic form and the natural form.

In summary, the enantioselective synthesis of eudesmane natural sesquiterpenoids **2a** and **3a** as well as their C-11 epimers **2b** and **3b** has been accomplished starting from dihydrocarvone via two synthetic approaches. The synthesis disclosed herein features the efficient regioselective Sharpless dihydroxylation and an LDA-induced stereospecific rearrangement of 4,5-epoxide derivatives of eudesmane, which would be useful and applicable for the synthesis of another member of eudesmane sesquiterpenes. The application of the present methodology to the synthesis of more complex, biologically active sesquiterpenoids will be investigated in due course.

3. Experimental

Melting points were determined on a Kolfer apparatus and are uncorrected. IR spectra were recorded on an FT-170SX(film) spectrometer. ^{1}H NMR spectra were measured on a Bruker AC-80 or AM-400 spectrometer using $CDCl_3$ as a solvent and TMS as an internal standard. Mass spectra were measured on a VG ZAB-HS spectrometer by direct inlet at 70 eV, and signals given in m/z with relative intensity (%) in brackets. Elemental analyses were determined on a Vario EL instrument. Optical rotation measurements were carried out on a Perkin–Elmer 141 polarimeter. All solvents were distilled prior to use. All anhydrous solvents were prepared by standard methods. All reactions were conducted under an argon atmosphere unless otherwise noted, and monitored by TLC. All products prepared were purified by flash column chromatography on silica gel (200–300 mesh) purchased from Qingdao Marine Chemical Company.

3.1. 7β,10β-Selina-4,11-diene 7

To a solution of $AlCl_2H$ (1 M in ether, 100 mL) was added a solution of (+)-α-cyperone **6** (1.03 g) in dry ether (20 mL) under argon in an ice–salt bath. After stirring at room temperature for 6 h, the reaction mixture was poured into crushed ice. The organic layer was separated and the aqueous layer was extracted with ether (3×30 mL). The combined organic fractions were washed with water (2×10 mL), satd aq. $NaHCO_3$ (2×10 mL), brine (2×10 mL), and dried ($MgSO_4$). After removal of the solvents, the oily residue was chromatographed on silica gel using petroleum ether

(30–60°C) as eluent to afford diene **7** (810 mg, 85%) as a colorless oil. IR: 3078, 1642, 1451, 1373, 882 cm^{-1}; ^1H NMR (80 MHz, $CDCl_3$): δ (ppm) 1.06 (s, 3H, 10-Me), 1.62 (s, 3H, 4-Me), 1.77 (s, 3H, 11-Me), 2.56 (br d, $J=11.8$ Hz, 1H), 4.72 (br t, $J=1.0$ Hz, 1H, 12-H), 4.74 (br s, 1H, 12-H); EIMS m/z (%): 204 (M^+, 46), 189 (100), 161 (20), 147 (31), 133 (74), 119 (24), 105 (52), 91 (60); EIMS HR: calcd for $C_{15}H_{24}$ (M^+): 204.18748. Found: 204.18725.

3.2. 4,5-Oxidoselina-11-ene *8a* and *8b*

A mixture of diene **7** (500 mg), $NaHCO_3$ (500 mg) and *m*CPBA (70%, 600 mg) in CH_2Cl_2 (20 mL) was stirred at 0°C for 2 h. The reaction mixture was then diluted with ether (60 mL), washed successively with 10% aq. Na_2SO_3 (2×10 mL), 5% aq. NaOH (2×10 mL), water (2×10 mL), brine (2×10 mL), and dried ($MgSO_4$). After removal of the solvents, the oily residue was chromatographed on silica gel eluting with petroleum ether:ether (15:1) to give a mixture of epoxides **8a** and **8b** as colorless oils (450 mg, 84%). The spectral data of mixtures **8a** and **8b**: IR: 3078, 1644, 1456, 1376, 887 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.06 (s, 1H, 10-Me for **8b**), 1.07 (s, 2H, 10-Me for **8a**), 1.25 (s, 2H, 4-Me for **8a**), 1.33 (s, 1H, 4-Me for **8b**), 1.74 (s, 3H, 11-Me for **8a** and **8b**), 4.71 (br s, 2H, 12-H for **8a** and **8b**); EIMS m/z (%): 220 (M^+, 7), 205 (5), 202 (9), 187 (6), 177 (6), 162 (19), 147 (12), 135 (27), 119 (33), 107 (74), 91 (35), 79 (54), 5 (48), 43 (100).

3.3. (+)-4α,5α-Oxidoeudesm-11S,12-diol *9* and (−)-4β,5β-oxidoeudesm-11S,12-diol *10*

A mixture of AD-mix-α (1.4 g) in *tert*-butyl alcohol (5 mL) and water (5 mL) was stirred at room temperature until both phases were clear, and then cooled to 0°C. Epoxide mixture **8a** and **8b** (220 mg, 1 mmol) in 50% aq. *t*-BuOH (2 mL) was added dropwise. The resulting mixture was stirred at 0°C for 24 h before it was quenched by addition of Na_2SO_3 (1.5 g) at 0°C. After stirring for a further 1 h, the reaction mixture was extracted several times with ethyl acetate. The combined organic fractions were washed with 5% KOH (2×10 mL), water (2×10 mL), brine (2×10 mL), and dried ($MgSO_4$). After removal of the solvents, the oily residue was chromatographed on silica gel to afford **9** (163 mg, 64%) and **10** (86 mg, 34%), both as colorless oils.

Compound **9** (39% de): $[\alpha]_D^9$ +31.9 (*c* 2.82, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.03 (s, 3H, 10-Me), 1.07 (s, 3H, 11-Me), 1.35 (s, 3H, 4-Me), 3.43 and 3.55 (dd, 2H, AB, $J=11.22$ Hz, 12-H); EIMS m/z (%): 254 (M^+, 1), 239 (3), 236 (2), 223 (21), 205 (50), 178 (71), 161 (60), 147 (21), 43 (100); IR: 3410, 2890, 1457, 1365, 1131, 1049 cm^{-1}. Anal. calcd for $C_{15}H_{26}O_3$: C, 70.87; H, 10.24. Found: C, 70.50; H, 10.39.

Compound **10** (42% de): $[\alpha]_D^9$ −5.3 (*c* 1.90, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.02 (s, 3H, 10-Me), 1.10 (s, 3H, 11-Me), 1.31 (s, 3H, 4-Me), 3.42 and 3.52 (dd, 2H, $J=10.8$ Hz, 12-H); EIMS m/z (%): 254 (M^+, 1), 239 (3), 236 (2), 223 (21), 205 (25), 178 (31), 161 (58), 147 (42), 121 (85), 43 (100); IR: 3346, 2936, 1458, 1377, 1131, 1096 cm^{-1}. Anal. calcd for $C_{15}H_{26}O_3$: C, 70.87; H, 10.24. Found: C, 71.04; H, 10.01.

3.4. (+)-4α,5α-Oxidoeudesm-11R,12-diol *11* and (+)-4β,5β-oxidoeudesm-11R,12-diol *12*

A procedure similar to the above gave **11** in 63% yield and **12** in 32% yield.

Compound **11** (33% de): $[\alpha]_D^{16}$ +53.0 (*c* 0.95, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.05 (s, 3H, 10-Me), 1.13 (s, 3H, 11-Me), 1.33 (s, 3H, 4-Me), 3.44 and 3.55 (dd, 2H, $J=10.83$ Hz, 12-H); EIMS m/z (%): 254 (M^+, 1), 239 (4), 223 (16), 205 (39), 187 (35), 178 (47), 161 (67), 147

(72), 121 (69), 107 (50), 95 (24), 43(100); IR: 3410, 2940, 1595, 1458, 1375, 1105, 1046 cm^{-1}. Anal. calcd for $C_{15}H_{26}O_3$: C, 70.87; H, 10.24. Found: C, 70.40; H, 10.50.

Compound **12** (30% de): $[\alpha]_D^{16}$ +4.2 (*c* 2.4, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.02 (s, 3H, 10-Me), 1.09 (s, 3H, 11-Me), 1.28 (s, 3H, 4-Me), 3.43 and 3.53 (dd, 2H, $J=11.06$ Hz, 12-H); EIMS m/z (%): 254 (M^+, 1), 239 (2), 223 (10), 205 (29), 187 (35), 178 (17), 161 (67), 147 (42), 121 (29), 43 (100); IR: 3385, 2934, 1594, 1460, 1377, 1107, 1030 cm^{-1}. Anal. calcd for $C_{15}H_{26}O_3$: C, 70.87; H, 10.24. Found: C, 70.39; H, 10.34.

3.5. (–)-[11S]-4β,5β-Epoxyeudesm-11S,12-isopropylidene ketal **13**

The diol **10** (80 mg) in acetone (3 mL) was treated with *p*-toluenesulfonic acid (cat.) for 10 min at room temperature. The reaction mixture was diluted with ethyl acetate (20 mL), and the organic layer was washed successively with aq. Na_2CO_3 (2×10 mL), water (2×10 mL), brine (2×10 mL), and dried over $MgSO_4$. Evaporation of the solvent and separation on silica gel gave the acetonide **13** of **10** as colorless oil (54 mg, 58%) and acetonide of **12** (20 mg, 21%). Compound **13**: ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.05 (s, 3H, 10-Me), 1.25 (s, 3H, 11-Me), 1.34 (s, 3H, 4-Me), 1.38 (s, 3H, acetonide), 1.42 (s, 3H, acetonide), 3.67 and 3.82 (dd, 2H, $J=8.5$ Hz, 12-H); EIMS m/z (%): 294 (M^+, 2), 279 (10), 261 (3), 236 (45), 219 (13), 201 (54), 187 (6), 115 (100), 95 (10), 55 (48), 43 (25); IR: 2990, 2929, 2880, 1467, 1376, 887 cm^{-1}.

3.6. (–)-[11S]-5β-Hydroxyeudesm-4(14)-en-11S,12-isopropylidene ketal **14**

To a freshly prepared solution of LDA (0.17 M in THF, 5 mL) was added a solution of **13** (50 mg) in dry THF (4 mL) under argon. The reaction mixture was stirred at room temperature for 24 h. Then some water was added to the reaction mixture at 0°C, and stirring was continued for additional 10 min. The organic layer was separated and aqueous layer was extracted with ether (2×20 mL). The combined organic fractions were washed with H_2O (2×10 mL), brine (2×10 mL), and dried ($MgSO_4$). After removal of the solvents, the crude products were chromatographed on silica gel eluting with petroleum ether:ether (6:1) to yield **14** (42 mg, 84%) as colorless oil. Compound **14**: $[\alpha]_D^{20}$ –27.3 (*c* 0.55, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.06 (s, 3H, 10-Me), 1.30 (s, 3H, 11-Me), 1.40 (s, 3H, acetonide), 1.44 (s, 3H, acetonide), 3.70 and 3.95 (dd, 2H, $J=8.3$ Hz, 12-H), 4.96 (br s, 2H, 14-H); EIMS m/z (%): 294 (M^+, 7), 279 (23), 276 (14), 236 (20), 201 (55), 187 (60), 137 (20), 115 (100), 43 (35); IR: 3485, 3085, 2982, 2928, 2871, 1637, 1377, 1209, 1067, 1039, 895 cm^{-1}. Anal. calcd for $C_{18}H_{30}O_3$: C, 73.47; H, 10.20. Found: C, 73.22; H, 10.79.

3.7. (–)-[11S]-Eudesm-4(14)-en-5β,11S,12-triol **3b**

Some drops of aqueous HCl (1N, 0.5 mL) were added dropwise to a solution of **14** (20 mg) in THF (5 mL), and the mixture was refluxed for 3 h. After cooling, the reaction mixture was diluted with ethyl acetate (20 mL). The organic layer was washed with 10% aq. Na_2CO_3 (2×10 mL), H_2O (2×10 mL), brine (2×10 mL), and dried over $MgSO_4$. Evaporation of the solvents afforded the crude products which were chromatographed on silica gel to yield **3b** (15 mg, 90%) as colorless oil: $[\alpha]_D^{11}$ –42.3 (*c* 0.36, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.02 (s, 3H, 10-Me), 1.13 (s, 3H, 11-Me), 3.44 and 3.63 (dd, 2H, AB, $J=10.8$ Hz, 12-H), 4.94 (brs, 1H, 14-H), 5.07 (brs, 1H, 14-H); EIMS m/z (%): 254 (M^+, 3), 239 (3), 236 (5), 222 (2), 205 (15), 187 (12), 161 (56), 147 (27), 43 (100); IR: 3400, 2932, 2869, 1641, 1449, 1378, 1281, 1028 cm^{-1}.

3.8. (+)-5α-Hydroxy-β-selinene **15** and (−)-5β-hydroxy-β-selinene **16**

To a freshly prepared solution of LDA (1 M in ether, 12 mL) was added a solution of epoxides **8a** and **8b** (160 mg) in dry ether (10 mL) under argon. The reaction mixture was stirred at room temperature for 24 h, then some water was added to the reaction mixture at 0°C, and stirring was continued for additional 10 min. The organic layer was separated and aqueous layer was extracted with ether (3×30 mL). The combined organic fractions were washed with 5% aq. HCl (2×10 mL), aq. $NaHCO_3$ (2×10 mL), brine (2×10 mL), and dried ($MgSO_4$). After removal of the solvents, the crude products were chromatographed on silica gel eluting with petroleum ether:ether (8:1) to yield **15** (96 mg, 60%) and **16** (52 mg, 32%), both as colorless oils.

Compound **15**: $[\alpha]_D^8$ +125.9 (*c* 0.72, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 0.88 (s, 3H, 10-Me), 1.76 (s, 3H, 11-Me), 2.52 (m, 1H), 2.58 (dt, J = 13.2, 6.4 Hz, 1H), 4.69 (br s, 1H), 4.73 (br s, 1H), 4.75 (br s, 1H), 4.82 (br s, 1H); EIMS m/z (%): 220 (M^+, 7), 205 (23), 202 (29), 187 (67), 137 (20), 109 (31), 107 (30), 95 (57), 43 (100); IR: 3446, 3081, 1644, 1446, 1376, 894 cm^{-1}. Anal. calcd for $C_{15}H_{24}O$: C, 81.76; H, 10.98. Found: C, 81.50; H, 10.79.

Compound **16**: $[\alpha]_D^8$ –95.2 (*c* 0.32, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.05 (s, 3H, 10-Me), 1.76 (s, 3H, 11-Me), 4.73 (br s, 1H), 4.75 (br s, 1H), 4.95 (br s, 2H); EIMS m/z (%): 220 (M^+, 13), 205 (19), 202 (14), 187 (28), 169 (44), 162 (22), 135 (36), 125 (43), 109 (42), 95 (61), 81 (48), 67 (54), 55 (61), 41 (100); IR: 3438, 3084, 2930, 1447, 887 cm^{-1}. Anal. calcd for $C_{15}H_{24}O$: C, 81.76; H, 10.98. Found: C, 81.63; H, 11.14.

3.9. Typical experimental procedure for dihydroxylation of **15** and **16**

A mixture of AD-mix (1.4 g/1 mmol of substrate) in *tert*-butyl alcohol (4 mL) and water (4 mL) was stirred at room temperature until both phases were clear, and then cooled to 0°C. Substrate (1 mmol) in 2 mL of 50% aq. *t*-BuOH was added dropwise. The resulting mixture was stirred vigorously at 0°C for 24 h before it was quenched by the addition of Na_2SO_3 (1.5 g) at 0°C. After stirring for an additional 1 h, the reaction mixture was extracted three times with ethyl acetate. The combined organic fractions were washed with water (3×5 mL), brine (3×5 mL) and dried. After evaporation of the solvents, the oily residue was chromatographed on silica gel to afford target triol.

3.10. (+)-(11S)-Eudesm-4(14)-en-5α,11S,12-triol **2b**

Colorless oil: 85% yield; 29% de; $[\alpha]_D^{20}$ +126.5 (*c* 2.5, $CHCl_3$); after recrystallization $[\alpha]_D^{11}$ +137 (*c* 0.36, $CHCl_3$); mp 157°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 0.85 (s, 3H, 10-Me), 1.12 (s, 3H, 11-Me), 3.42 and 3.64 (dd, 2H, J = 11.2 Hz, 12-H), 4.64 (s, 1H, 14-H), 4.80 (s, 1H, 14-H); EIMS m/z (%): 254 (M^+, 3), 239 (3), 236 (5), 205 (13), 161 (66), 95 (43), 43 (100); IR (film): 3463, 2980, 1646 cm^{-1}; EIMS HR: calcd for $C_{15}H_{26}O_3$ (M^+): 254.18865. Found: 254.18764.

3.11. (+)-(11R)-Eudesm-4(14)-en-5α,11R,12-triol **2a**

Colorless oil: 90% yield; 25% de; $[\alpha]_D^{11}$ +134.3 (*c* 0.95, $CHCl_3$); after recrystallization $[\alpha]_D^{11}$ +77.6 (*c* 0.13, $CHCl_3$), lit.[4] $[\alpha]_D$ +76.5 (*c* 1.03, $CHCl_3$); mp 177°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 0.85 (s, 3H, 10-Me), 1.13 (s, 3H, 11-Me), 3.45 and 3.59 (dd, 2H, J = 11.2 Hz, 12-H), 4.71 (s, 1H, 14-H), 4.82 (s, 1H, 14-H); EIMS m/z (%): 254 (M^+, 3), 239 (5), 236 (5), 205 (17), 95 (37), 43 (100);

IR (film): 3351, 3325, 2932 cm^{-1}; EIMS HR: calcd for $C_{15}H_{26}O_3$ (M^+): 254.18865. Found: 254.18760.

3.12. (–)-(11S)-Eudesm-4(14)-en-5β,11S,12-triol **3b**

Colorless oil: $[\alpha]_D^{11}$ –40.5 (*c* 0.79, $CHCl_3$). Anal. calcd for $C_{15}H_{26}O_3$: C, 70.87; H, 10.24. Found: C, 70.56; H, 10.49.

3.13. (–)-(11R)-Eudesm-4(14)-en-5β,11R,12-triol **3a**

Colorless oil: $[\alpha]_D^{11}$ –9.2 (*c* 1.67, $CHCl_3$), lit.[4] $[\alpha]_D$ –10.4 (*c* 0.79, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.02 (s, 3H, 10-Me), 1.17 (s, 3H, 11-Me), 3.43 and 3.59 (dd, 2H, $J = 10.8$ Hz, 12-H), 4.94 (s, 1H, 14-H), 4.97 (s, 1H, 14-H); EIMS m/z (%): 254 (M^+, 4), 239 (4), 236 (5), 205 (13), 162 (25), 147 (37), 95 (24), 84 (50), 43 (100); IR (film): 3413, 2926, 2856 cm^{-1}. Anal. calcd for $C_{15}H_{26}O_3$: C, 70.87; H, 10.24. Found: C, 70.75; H, 10.30.

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15. The low diastereoselectivity in dihydroxylation of this kind of compound with AD-mix might result from the rigid and big deca-hydronaphthalene substitute in the substrate. For the chiral olefins **15** and **16**, it is obvious that the $(DHQD)_2PHAL$ and $(DHQ)_2PHAL$ are mismatching ligands in this AD reaction. See also: Chen, Y. G.; Xiong, Z. M.; Gang, Z.; Liu, L.; Li, Y. L. *Tetrahedron: Asymmetry* **1998**, *9*, 1923.
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17. Authentic samples of natural kudtriol and 5-*epi*-kudtriol are not available for direct comparison.