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First enantioselective total synthesis of glutinone and its C(7) and C(11) epimers

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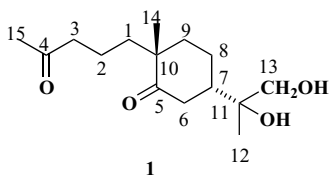
Abstract—A facile and efficient asymmetric synthesis of glutinone **1** and its C(7) and C(11) epimers **1b–d** is presented, using the Sharpless asymmetric dihydroxylation reaction as the key step. By comparing the spectral data of the natural product with that of the synthetic samples, we could confirm the absolute configuration of glutinone **1**. © 2001 Published by Elsevier Science Ltd.

1. Introduction

Sesquiterpenoids exist widely in higher plants as important chemical constituents and constitute a large family of natural products.[1,2] *Jasonia glutinosus* is an annual medicinal plant occurring in the Mediterranean littoral area of the Iberian Peninsula,[3] the South of France and Malta.[4] It is used in traditional medicine as an antispasmodic drug.[3] Two new sesquiterpenoids, glutinone **1** and lucinone **2**, were isolated by Castillo et al. from the aerial parts of this plant in 1995.[5] Their structures were characterized by spectroscopic methods as 4,5-dioxo-4,5-*seco*-eudesman-11,13-diol **1** and 5β,11,12-trihydroxyiphionan-4-one **2**, respectively. However, the stereochemistry at C(7) and C(11) of glutinone **1** is still unknown. Our interest in confirming the absolute configurations of natural products and our ongoing project on the asymmetric synthesis of bio-active sesquiterpenoids,[6,7] stimulated us to develop an enantioselective approach for the total synthesis of this class of sesquiterpenoids. Reported herein is the first asymmetric synthesis of **1a** and its three C(7) and C(11) epimers **1b–d**.



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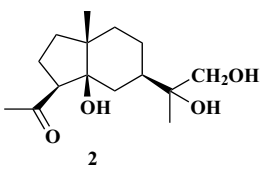

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2. Results and discussion

Our synthesis began with (+)-dihydrocarvone **3a** (Scheme 1). (+)-α-Cyperone **4a** was prepared from (+)-dihydrocarvone **3a** in 50% yield using the published method.[8] Reductive deoxygenation[9] of **4a** was effected with $AlCl_2H$ in ether to give diene **5a** in 90% yield (purity >95%, determined by GC). Diastereoisomers **6a** and **6b** were prepared readily from **5a** by Sharpless dihydroxylation[10] with commercially available AD-mix-β or AD-mix-α, respectively, in good yield. Their absolute configurations were assigned according to the face-selection rule of the Sharpless AD process. Ketalization[11] of the resulting diols with acetone catalyzed by *p*-TsOH according to Ikekawa's procedure afforded the corresponding **7a** and **7b**, which were oxidized using O_3 to give **8a** and **8b**, respectively. After deacetonization, two epimers **1a** and **1b** were produced.

Starting from (−)-dihydrocarvone **3b**, the same reactions were repeated, allowing the other epimers, **1c** and **1d**, to be obtained.

Standard dihydroxylation of **5a** and **5b** with commercially available AD-mix-β or AD-mix-α provided a mixture of **6a** (45% d.e.), **6b** (52% d.e.), **6c** (85% d.e.) and **6d** (85% d.e.), respectively, in good yield,[12] which are chromatographically inseparable on silica gel. However, the mixture was used in the next reactions and analytically pure compounds **1a** (75% d.e.), **1b** (80% d.e.), **1c** (90% d.e.), and **1d** (90% d.e.) could be obtained by very careful chromatographic separation on silica gel after the final hydrolysis step.

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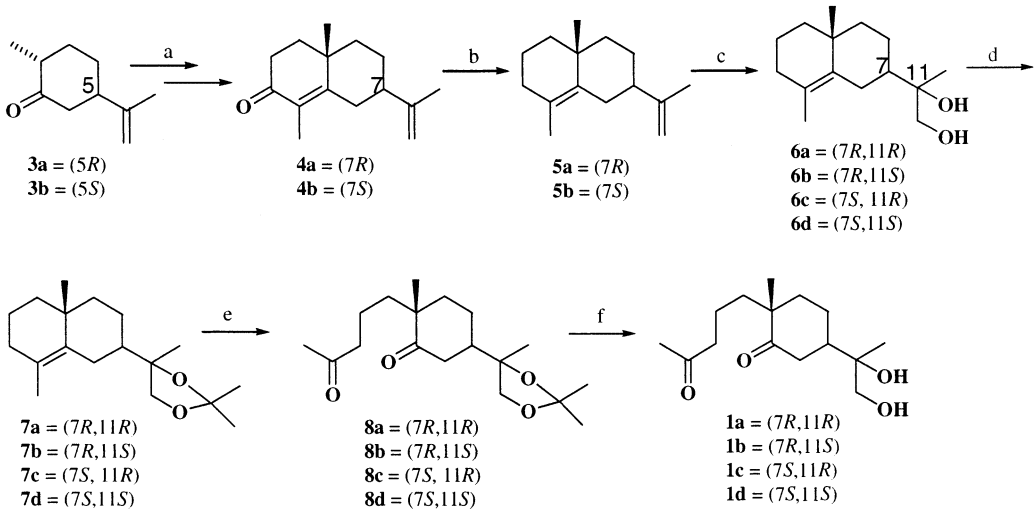

Scheme 1. *Reagents and conditions*: (a) Ref. 4, 70%; (b) $AlCl_2H$, ether, 92%; (c) AD-mix-β and AD-mix-α, *tert*-BuOH–H_2O, 0°C, over 85%; (d) cat. TsOH, acetone, over 88%; (e) O_3, Py, CH_2Cl_2, 56–65%; (f) 60% HAc, 40°C, 71–90%.

As listed in Tables 1 and 2, the ^1H and ^{13}C NMR spectral data of the four compounds synthesized were compared with those of the natural product reported in the literature. It is obvious that the synthetic compound **1a** was identical with the natural product.[13] Thus, the absolute stereochemistry of naturally occurring glutinone was established unambiguously as (7*R*,11*R*).

3. Conclusion

In conclusion, the enantioselective synthesis of glutinone **1** and its C(7) and C(11) epimers has been accomplished starting from (+)-dihydrocarvone **3a** and (−)-dihydrocarvone **3b**. The absolute configuration of naturally occurring glutinone **1** was confirmed at the same time. The application of the present

Table 1. ^1H NMR spectral data (δ_H) of natural glutinone **1** and synthetic products **1a–d**

H	Glutinone **1**	Synthetic **1a**	Synthetic **1b**	Synthetic **1c**	Synthetic **1d**
12	1.12	1.09	1.16	1.17	1.17
13	3.41d and 3.56d (J=10.8 Hz)	3.37d and 3.52d (J=10.5 Hz)	3.43d and 3.48d (J=10.8 Hz)	3.43d and 3.59d (J=10.8 Hz)	3.43d and 3.59d (J=10.8 Hz)
14	**1.11**	**1.07**	**1.14**	**1.02**	**1.02**
15	2.11	2.07	2.15	2.13	2.12

Table 2. ^{13}C NMR spectral data (δ_H) of natural glutinone **1** and synthetic products **1a–d**

C	Glutinone **1**	Synthetic **1a**	Synthetic **1b**	Synthetic **1c**	Synthetic **1d**
1	**37.35**	**37.29**	**37.27**	**39.95**	**39.94**
2	18.30	18.23	18.19	17.94	17.96
3	**44.37**	**44.28**	**44.28**	**43.42**	**43.43**
4	**209.27**	**209.12**	**209.13**	**208.44**	**208.35**
5	215.79	215.75	215.33	215.38	215.24
6	**38.91**	**38.84**	**39.88**	**38.41**	**38.40**
7	**45.25**	**45.18**	**45.33**	**45.92**	**45.92**
8	**22.35**	**22.26**	**21.18**	**20.95**	**20.97**
9	36.42	36.35	36.19	36.32	36.33
10	**47.39**	**47.32**	**47.35**	**48.05**	**48.04**
11	73.90	73.81	73.78	73.64	73.63
12	20.50	20.45	20.43	20.58	20.63
13	68.26	68.18	68.05	68.09	68.12
14	23.23	23.13	23.19	21.73	21.74
15	29.99	29.88	29.92	29.93	29.92

methodology to the synthesis of more complex biologically active sesquiterpenoids will be investigated in due course.

4. Experimental

For column chromatography, silica gel (200–300 mesh) and light petroleum ether (PE, bp 60–90°C) were used. IR spectra were recorded on a Nicolet FT-170SX spectrometer as liquid films. ^1H and ^{13}C NMR spectra were obtained on a Bruker AM-400 spectrometer with TMS as an internal standard and $CDCl_3$ as solvent. Mass spectra were determined on a VG ZAB-HS spectrometer (EI, 70 eV). Elemental analysis was performed on an Italian 1106 analyzer. Optical rotation measurements were carried out on a Perkin–Elmer 141 polarimeter.

4.1. General experimental procedure for reductive deoxygenation of 4a and 4b

To a solution of $AlCl_2H$ (1 M in dry ether, 40 mL) was added a solution of substrate (2 mmol) in dry ether (5 mL) under argon in an ice bath. After stirring at rt for 6 h, the reaction mixture was poured into crushed ice. The organic layer was separated and the aqueous layer was extracted with ether (3×20 mL). The combined organic extracts were washed with water (2×15 mL), satd aq. $NaHCO_3$ (15 mL×2), brine (2×15 mL), and dried ($MgSO_4$). After evaporation of the solvents under reduced pressure, the oily residue was chromatographed on silica gel eluting with petroleum ether to give the target diene as a colorless oil.

4.2. (7*R*,10*R*)-Selina-4,11-diene 5a

Colorless oil; yield 85%; $[\alpha]_D^{16}$ +45.2 (*c* 1.25, $CHCl_3$); IR: 3078, 1642, 1451, 1373, 882 cm^{-1}; EIMS *m*/*z* (%) 204 (M^+, 46), 189 (100), 161 (20), 147 (31), 133 (74), 119 (24), 105 (52), 91 (60); ^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). Anal. calcd for $C_{15}H_{24}$: C, 88.16; H, 11.84. Found: C, 88.04; H, 11.96%.

4.3. (7*S*,10*R*)-Selina-4,11-diene 5b

Colorless oil; yield 88%; $[\alpha]_D^{16}$ +46.5 (*c* 0.85, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$): δ (ppm) 1.08 (s, 3H, 10-Me), 1.62 (s, 3H, 4-Me), 1.71 (s, 3H, 11-Me), 2.72 (dt, J=14.6 Hz, 2.0 Hz, 1H), 4.78 (br s, 2H, 12-H). Anal. calcd for $C_{15}H_{24}$: C, 88.16; H, 11.84. Found: C, 88.11; H, 11.88%.

4.4. General experimental procedure for dihydroxylation of 5a and 5b

A mixture of AD-mix (1.4 g) in 50% aq. *tert*-BuOH (8 mL) was stirred at rt until both phases were clear, and then cooled to 0°C. Substrate (1 mmol) in 50% aq. *tert*-BuOH (2 mL) 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 a further 0.5 h at rt, the reaction mixture was extracted with EtOAc (3×50 mL). The combined organic fractions were washed with brine (2×15 mL) and dried ($MgSO_4$). After evaporation of the solvents under reduced pressure, the oily residue was chromatographed on silica gel to afford the target diol.

4.5. (7*R*,10*R*,11*R*)-Eudesm-4-en-11,12-diol 6a

(Substrate: **5a**; reagent: AD-mix-β) Colorless oil; yield 92% (45% d.e.); $[\alpha]_D^{16}$ +79.4 (*c* 1.22, $CHCl_3$); IR: 3389, 2927, 1457, 1373, 1044 cm^{-1}; EIMS *m*/*z* (%) 238 (M^+, 8), 220 (18), 189 (100), 147 (30), 133 (14), 119 (16), 105 (25), 91 (42); ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.02 (s, 3H, 10-Me), 1.16 (s, 3H, 11-Me), 1.61 (s, 3H, 4-Me), 2.68 (br d, J=13.6 Hz, 1H), 3.47 (d, J=11.1 Hz, 1H, 12-H), 3.61 (d, J=11.1 Hz, 1H, 12-H). Anal. calcd for $C_{15}H_{26}O_2$: C, 75.58; H, 10.99. Found: C, 75.50; H, 11.09%

4.6. (7*R*,10*R*,11*S*)-Eudesm-4-en-11,12-diol 6b

(Substrate: **5a**; reagent: AD-mix-α) Colorless oil; yield 90% (52% d.e.); $[\alpha]_D^{16}$ +76.1 (*c* 0.92, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.02 (s, 3H, 10-Me), 1.15 (s, 3H, 11-Me), 1.59 (s, 3H, 4-Me), 2.49 (br d, J=13.1 Hz, 1H), 3.48 (d, J=11.5 Hz, 1H, 12-H), 3.62 (d, J=11.5 Hz, 1H, 12-H). Anal. calcd for $C_{15}H_{26}O_2$: C, 75.58; H, 10.99. Found: C, 75.33; H, 11.24%.

4.7. (7*S*,10*R*,11*R*)-Eudesm-4-en-11,12-diol 6c

(Substrate: **5b**; reagent: AD-mix-β) Colorless oil; yield 92% (85% d.e.); $[\alpha]_D^{26}$ +14.2 (*c* 0.45, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$): δ (ppm) 1.09 (s, 3H, 10-Me), 1.21 (s, 3H, 11-Me), 1.63 (s, 3H, 4-Me), 2.64 (br d, J=15.0 Hz, 1H), 3.44 (d, J=10.6 Hz, 1H, 12-H), 3.62 (d, J=10.6 Hz, 1H, 12-H). Anal. calcd for $C_{15}H_{26}O_2$: C, 75.58; H, 10.99. Found: C, 75.48; H, 11.11%.

4.8. (7*S*,10*R*,11*S*)-Eudesm-4-en-11,12-diol 6d

(Substrate: **5b**; reagent: AD-mix-α) Colorless oil; yield 89% (85% d.e.); $[\alpha]_D^{26}$ +25.0 (*c* 1.70, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$): δ (ppm) 1.09 (s, 3H, 10-Me), 1.20 (s, 3H, 11-Me), 1.66 (s, 3H, 4-Me), 2.63 (br d, J=15.2 Hz, 1H), 3.40 (d, J=11.0 Hz, 1H, 12-H), 3.61 (d, J=11.0 Hz, 1H, 12-H). Anal. calcd for $C_{15}H_{26}O_2$: C, 75.58; H, 10.99. Found: C, 75.32; H, 11.20%.

4.9. General experimental procedure for ketalization of 6a–d

The diol (1 mmol) in acetone (2 mL) was treated with *p*-toluenesulfonic acid (cat. amount) for 15 min at rt. The solvent was removed under reduced pressure and the resulting oily residue was chromatographed on silica gel to afford the target ketal.

4.10. (7*R*,10*R*,11*R*)-Eudesm-4-en-11,12-isopropylidene ketal 7a

Colorless oil; yield 90%; $[\alpha]_D^{16}$ +44.5 (*c* 1.15, $CHCl_3$); IR: 2979, 2926, 2858, 1457, 1372, 1058 cm^{-1}; EIMS *m*/*z* (%) 278 (M^+, 15), 220 (8), 205 (28), 189 (13), 162 (26), 147 (31), 115 (100), 105 (16), 91 (26); ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.02 (s, 3H, 10-Me), 1.25 (s, 3H, 11-Me), 1.38 (s, 3H, acetonide), 1.42 (s, 3H, acetonide), 1.61 (s, 3H, 4-Me), 3.66 (d, $J=8.3$ Hz, 1H, 12-H), 3.88 (d, $J=8.3$ Hz, 1H, 12-H). Anal. calcd for $C_{18}H_{30}O_2$: C, 77.65; H, 10.86. Found: C, 77.51; H, 10.93%.

4.11. (7*R*,10*R*,11*S*)-Eudesm-4-en-11,12-isopropylidene ketal 7b

Colorless oil; yield 88%; $[\alpha]_D^{16}$ +51.2 (*c* 0.84, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.01 (s, 3H, 10-Me), 1.25 (s, 3H, 11-Me), 1.38 (s, 3H, acetonide), 1.41 (s, 3H, acetonide), 1.62 (s, 3H, 4-Me), 3.67 (d, $J=9.0$ Hz, 1H, 12-H), 3.88 (d, $J=9.0$ Hz, 1H, 12-H). Anal. calcd for $C_{18}H_{30}O_2$: C, 77.65; H, 10.86. Found: C, 77.48; H, 10.88%.

4.12. (7*S*,10*R*,11*R*)-Eudesm-4-en-11,12-isopropylidene ketal 7c

Colorless oil; yield 90%; $[\alpha]_D^{26}$ +3.6 (*c* 0.91, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.06 (s, 3H, 10-Me), 1.24 (s, 3H, 11-Me), 1.39 (s, 3H, acetonide), 1.42 (s, 3H, acetonide), 1.62 (s, 3H, 4-Me), 3.67 (d, $J=8.2$ Hz, 1H, 12-H), 3.88 (d, $J=8.2$ Hz, 1H, 12-H). Anal. calcd for $C_{18}H_{30}O_2$: C, 77.65; H, 10.86. Found: C, 77.65; H, 10.87%.

4.13. (7*S*,10*R*,11*S*)-Eudesm-4-en-11,12-isopropylidene ketal 7d

Colorless oil; yield 91%; $[\alpha]_D^{26}$ +8.5 (*c* 0.45, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.07 (s, 3H, 10-Me), 1.24 (s, 3H, 11-Me), 1.38 (s, 3H, acetonide), 1.42 (s, 3H, acetonide), 1.59 (s, 3H, 4-Me), 3.66 (d, $J=8.2$ Hz, 1H, 12-H), 3.89 (d, $J=8.2$ Hz, 1H, 12-H). Anal. calcd for $C_{18}H_{30}O_2$: C, 77.65; H, 10.86. Found: C, 77.48; H, 10.93%.

4.14. General experimental procedure for O_3 oxidation of 7a–d

A solution of ketal (0.5 mmol) in CH_2Cl_2 (10 mL) was treated at −78°C with a stream of ozone until TLC analysis revealed all of the ketal substrate was consumed. The solution was purged with argon for 10 min and the mixture was stirred at rt overnight. The solvent was removed under reduced pressure and the resulting oily residue was chromatographed on silica gel to afford the target dione.

4.15. (7*R*,10*R*,11*R*)-4,5-Dioxo-4,5-*seco*-eudesman-11,13-isopropylidene ketal 8a

Colorless oil; yield 65% (75% d.e.); $[\alpha]_D^{16}$ +36.5 (*c* 0.98, $CHCl_3$); IR: 2981, 2936, 2870, 1706, 1375, 1057 cm^{-1}; EIMS *m*/*z* (%) 310 (M^+, 7), 295 (10), 217 (11), 196 (66), 115 (100), 97 (8), 57 (15), 43 (58); ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.14 (s, 3H, 10-Me), 1.27 (s, 3H, 11-Me), 1.39 (s, 3H, acetonide), 1.42 (s, 3H, acetonide), 2.14 (s, 3H, 4-Me), 3.69 (d, $J=8.6$ Hz, 1H, 12-H), 3.88 (d, $J=8.6$ Hz, 1H, 12-H). Anal. calcd for $C_{18}H_{30}O_4$: C, 69.64; H, 9.74. Found: C, 69.52; H, 9.80%.

4.16. (7*R*,10*R*,11*S*)-4,5-Dioxo-4,5-*seco*-eudesman-11,13-isopropylidene ketal 8b

Colorless oil; yield 59% (80% d.e.); $[\alpha]_D^{16}$ +38.5 (*c* 0.85, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.14 (s, 3H, 10-Me), 1.26 (s, 3H, 11-Me), 1.37 (s, 3H, acetonide), 1.41 (s, 3H, acetonide), 2.14 (s, 3H, 4-Me), 3.68 (d, $J=8.4$ Hz, 1H, 12-H), 3.85 (d, $J=8.4$ Hz, 1H, 12-H). Anal. calcd for $C_{18}H_{30}O_4$: C, 69.64; H, 9.74. Found: C, 69.49; H, 9.87%.

4.17. (7*S*,10*R*,11*R*)-4,5-Dioxo-4,5-*seco*-eudesman-11,13-isopropylidene ketal 8c

Colorless oil; yield 56% (90% d.e.); $[\alpha]_D^{26}$ −62.9 (*c* 0.46, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.02 (s, 3H, 10-Me), 1.27 (s, 3H, 11-Me), 1.38 (s, 3H, acetonide), 1.41 (s, 3H, acetonide), 2.13 (s, 3H, 4-Me), 3.69 (d, $J=8.4$ Hz, 1H, 12-H), 3.87 (d, $J=8.4$ Hz, 1H, 12-H). Anal. calcd for $C_{18}H_{30}O_4$: C, 69.64; H, 9.74. Found: C, 69.46; H, 9.86%.

4.18. (7*S*,10*R*,11*S*)-4,5-Dioxo-4,5-*seco*-eudesman-11,13-isopropylidene ketal 8d

Colorless oil; yield 60% (90% d.e.); $[\alpha]_D^{26}$ −67.6 (*c* 1.27, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$): δ (ppm) 1.02 (s, 3H, 10-Me), 1.27 (s, 3H, 11-Me), 1.37 (s, 3H, acetonide), 1.41 (s, 3H, acetonide), 2.12 (s, 3H, 4-Me), 3.68 (d, $J=8.6$ Hz, 1H, 12-H), 3.86 (d, $J=8.6$ Hz, 1H, 12-H). Anal. calcd for $C_{18}H_{30}O_4$: C, 69.64; H, 9.74. Found: C, 69.58; H, 9.77%.

4.19. General experimental procedure for deacetonization of 8a–d

A solution of substrate (0.2 mmol) in aq. HOAc (60%, 2 mL) was stirred at 40°C for 4 h. After cooling, the reaction mixture was poured into water (8 mL). The aqueous layer was extracted with EtOAc (3×15 mL). The combined organic fractions were washed with satd aq. $NaHCO_3$ (3×10 mL), brine (2×10 mL) and dried ($MgSO_4$). Evaporation of the solvents under reduced pressure, afforded an oily residue, which was chromatographed on silica gel to afford the target diol.

4.20. (7*R*,10*R*,11*R*)-4,5-Dioxo-4,5-*seco*-eudesman-11,13-diol 1a

Colorless oil; yield 71% (75% d.e.); $[\alpha]_D^{16}$ +64.3 (*c* 0.70, $CHCl_3$);IR: 3420, 2985, 1702, 1370, 1044 cm^{-1}; EIMS *m*/*z* (%) 252 (M^+-H_2O, 30), 239 (12), 221 (25), 186 (100), 161 (31), 149 (18), 111 (34), 75 (20); ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.07 (s, 3H, 10-Me), 1.09 (s, 3H, 11-Me), 2.07 (s, 3H, 4-Me), 3.37 (d, $J=10.5$ Hz,

1H, 12-H), 3.52 (d, $J=10.5$ Hz, 1H, 12-H); ^{13}C NMR (400 MHz, $CDCl_3$): δ (ppm) 215.75, 209.12, 73.81, 68.18, 47.32, 45.18, 44.28, 38.84, 37.29, 36.35, 29.88, 23.13, 22.26, 20.45, 18.23. Anal. calcd for $C_{15}H_{26}O_4$: C, 66.64; H, 9.69. Found: C, 66.38; H, 9.82%.

4.21. (7*R*,10*R*,11*S*)-4,5-Dioxo-4,5-*seco*-eudesman-11,13-diol 1b

Colorless oil; yield 82% (80% d.e.); $[\alpha]_D^{16}$ +22.1 (*c* 0.58, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.14 (s, 3H, 10-Me), 1.16 (s, 3H, 11-Me), 2.15 (s, 3H, 4-Me), 3.43 (d, $J=10.8$ Hz, 1H, 12-H), 3.58 (d, $J=10.8$ Hz, 1H, 12-H); ^{13}C NMR (400 MHz, $CDCl_3$): δ (ppm) 215.33, 209.13, 73.78, 68.05, 47.35, 45.33, 44.28, 39.88, 37.27, 36.19, 29.92, 23.19, 21.18, 20.43, 18.19. Anal. calcd for $C_{15}H_{26}O_4$: C, 66.64; H, 9.69. Found: C, 66.45; H, 9.72%.

4.22. (7*S*,10*R*,11*R*)-4,5-Dioxo-4,5-*seco*-eudesman-11,13-diol 1c

Colorless oil; yield 90% (90% d.e.); $[\alpha]_D^{26}$ −49.1 (*c* 0.88, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.02 (s, 3H, 10-Me), 1.17 (s, 3H, 11-Me), 2.13 (s, 3H, 4-Me), 3.43 (d, $J=10.8$ Hz, 1H, 12-H), 3.59 (d, $J=10.8$ Hz, 1H, 12-H); ^{13}C NMR (400 MHz, $CDCl_3$): δ (ppm) 215.38, 208.44, 73.64, 68.09, 48.05, 45.92, 43.42, 39.95, 38.41, 36.32, 29.93, 21.73, 20.95, 20.58, 17.94. Anal. calcd for $C_{15}H_{26}O_4$: C, 66.64; H, 9.69. Found: C, 66.53; H, 9.77%.

4.23. (7*S*,10*R*,11*S*)-4,5-Dioxo-4,5-*seco*-eudesman-11,13-diol 1b

Colorless oil; yield 84% (90% d.e.); $[\alpha]_D^{26}$ −53.7 (*c* 0.85, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.02 (s, 3H, 10-Me), 1.17 (s, 3H, 11-Me), 2.12 (s, 3H, 4-Me), 3.43 (d, $J=10.8$ Hz, 1H, 12-H), 3.59 (d, $J=10.8$ Hz, 1H, 12-H); ^{13}C NMR (400 MHz, $CDCl_3$): δ (ppm) 215.24, 208.35, 73.63, 68.12, 48.04, 45.92, 43.43, 39.94, 38.40, 36.33, 29.92, 21.74, 20.97, 20.63, 17.96. Anal. calcd for $C_{15}H_{26}O_4$: C, 66.64; H, 9.69. Found: C, 66.59; H, 9.74%.

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12. For the chiral olefin **5a**, it is obvious that the $(DHQD)_2PHAL$ and $(DHQ)_2PHAL$ are mismatching ligands in this AD reaction.
13. The slight difference of the ^{1}H and ^{13}C NMR data between **1** and **1a** is due to the different instruments used.