Chiral Preparation of C_2-Symmetric 4-Cyclopentene-1,3-diol

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Abstract: Optically pure C_2-symmetric 4-cyclopentene-1,3-diol has been prepared in both enantiomeric forms from racemic (3a*S**,4*R**,7*S**,7a*S**)-3a,4,7,7a-tetrahydro-4,7-methano-1*H*-inden-1-one by employing lipase-mediated kinetic resolution as the key step. As a result, the known (3a*S**,4*R**,7*S**,7a*S**)-3a,4,7,7a-tetrahydro-4,7-methano-1*H*-inden-1-one is transformed into (1′*S**,3′*S**,3′a*R**,4′*S**,7′*R**,7′a*S**)- 2′,3′,3′a,4′,7′,7′a-hexahydro-3′-hydroxy-4′,7′-methano-1′*H*-inden-1′-yl benzoate, via stereo- and regioselective hydride reduction of epoxy ketone and sequential benzoylation, which is resolved under transesterification conditions in the presence of lipase. The hydride reduction of benzoate and acetate gives the corresponding chiral diols, which are further transformed into both enantiomers of C_2-symmetric 4-cyclopentene-1,3-diol via a retro-Diels–Alder reaction.

Key words: enzymes, stereoselective synthesis, Diels–Alder reactions, diols, epoxides

4-Cyclopentene-1,3-diol[1] serves as an important precursor for enantiocontrolled syntheses of a variety of biologically active natural and synthetic compounds, especially prostanoids[2] and carbocyclic nucleosides.[3] In connection with cyclopentanoid synthesis, much effort has been made to develop efficient preparations and practical uses of *meso*-4-cyclopentene-1,3-diol (**1**) (Figure 1). Many asymmetric procedures have been developed on the basis of the desymmetrization of **1**.[4]

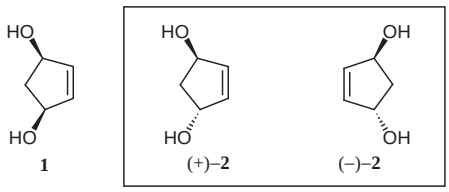
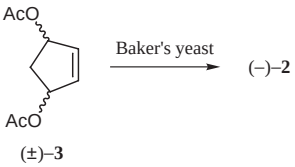


Figure 1

But, because of the difficulty of stereoselectively constructing *trans*-diol functionalities on a cyclopentene ring, no efficient chiral preparation of C_2-symmetric 4-cyclopentene-1,3-diol (**2**) has been reported, except for a report by Kurozumi[5] and one by Fuchs.[6] Kurozumi et al. reported that asymmetric hydrolysis of a stereoisomeric mixture of diacetate **3** using baker's yeast furnished (–)-**2** in 7–17% yield with 10–32% optical purity (Scheme 1). On the other hand, Fuchs et al. obtained (+)–**2** from chiral sulfide alcohol **4** with 90% ee, via [2,3]-sigmatropic rearrangement of sulfoxide **5** as the key step. In that communication, (+)–**2** was immediately trapped with diphenyl disulfide to convert it into a chiral epoxide synthon **6** for the synthesis of prostaglandin E2 intermediate (Scheme 2).[7] Thus, (+)- and (–)-**2** have never been isolated in optically pure forms. Because of the symmetrical form of C_2 and allylic *trans*-diol functionalities in **2**, high potentiality would be expected in the chiral synthesis of cyclopentanoids. So, an efficient chiral preparation of **2** in both enantiomeric forms would be required. We report herein an efficient chiral preparation of both enantiomers of **2** starting from the known racemic (3a*S**,4*R**,7*S**,7a*S**)-3a,4,7,7a-tetrahydro-4,7-methano-1*H*-inden-1-one **7**[8,9] by employing a lipase-mediated kinetic transesterification[10] as the key step.[11]



Scheme 1

Dienone (±)-**7** was first transformed into racemic epoxy ketone **8** by the established method, which was reported by Chapman.[12] Treatment of **8** with LAH in refluxing THF gave *trans*–diol **9** as a single isomer in high yield via stereoselective 1,2-reduction of ketone and regioselective epoxide ring-opening.[13] Zwanenburg reported that this reduction at a lower temperature yielded the corresponding epoxy alcohol with a trace amount of diol **9**.[14] To distinguish between the two alcohol functionalities in the molecule, diol **9** was exposed to NBS to block the *endo*-oriented alcohol regioselectively by generating the single bromo ether **10**, whose remaining alcohol was protected with a benzoyl group to furnish benzoate **11**, in 54% yield from **8**. Treatment of **11** with zinc in the presence of HOAc in EtOH regenerated olefin and alcohol functionality to furnish *endo*-alcohol (±)-**12** (Scheme 3).

Treatment of the racemic alcohol (±)-**12** with vinyl acetate in organic solvent in the presence of lipase[15] at 37 °C yielded the acetate (+)-**13** and unreacted starting alcohol (+)-**12**, which were readily separated by silica gel column chromatography (Scheme 4, Table). Alcohol (+)-**12** was converted to the corresponding acetate (–)-**13** to determine its optical purity. Both the ee of (+)- and of (–)-**13** were determined by HPLC analysis using a chiral column

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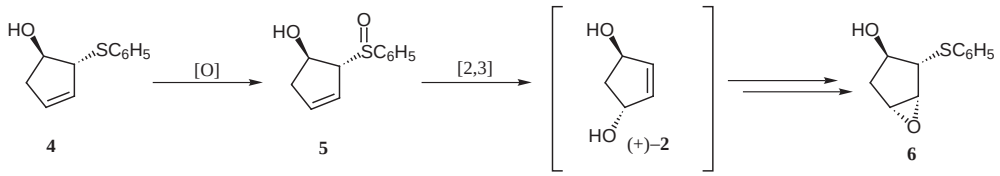
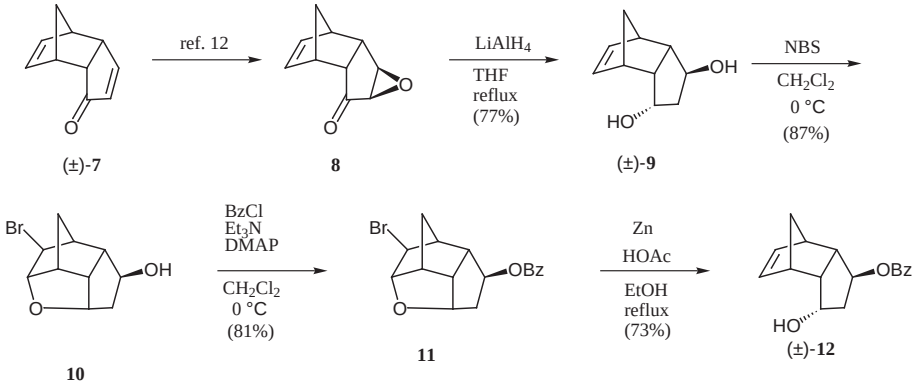


Scheme 2



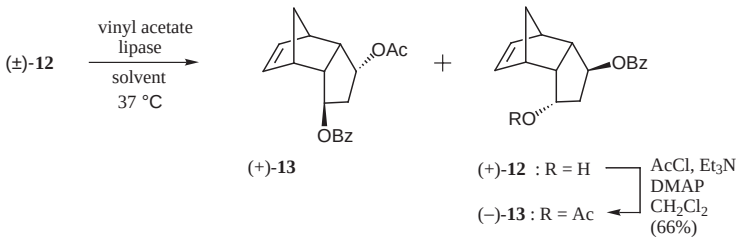
Scheme 3

(Chiralcel OD). As shown in the Table, when a catalytic amount of lipase PS-D or lipase AK-20 was used with vinyl acetate in *t*-BuOMe, acetate (+)-**13** and alcohol (+)-**12** were obtained in good recovery with moderate ee (entries 1, 2 and 7). THF and diisopropyl ether (IPE) were not good solvents for this reaction, because the reaction in either case proceeded very slowly and gave the acetate (+)-**13** in lower yield (entries 3 and 4). When some other lipases were used, such as lipase AS and lipase AYS, no reaction occurred (entries 5 and 6). Next, we demonstrated the

Table Lipase-Mediated Asymmetric Esterification of (±)-**12**

Entry	Scale (g)	Lipase (weight%)		Vinyl Acetate (mol equiv)	Solvent	Time (h)	Yield[a] (%) (ee)[b] (+)-**12**	(+)-**13**
1	0.5	PS-D[c]	(10)	1.5	*t*-BuOMe	82	48 (82)	48 (90)
2	0.5	PS-D	(10)	1.0	*t*-BuOMe	57	51 (82)	45 (97)
3	0.5	PS-D	(10)	1.0	IPE	57	76 (21)	18 (89)
4	0.5	PS-D	(10)	1.0	THF	57	82 (1)	1 (99)
5	0.5	AS[d]	(10)	1.0	*t*-BuOMe	57	no reaction	
6	0.5	AYS[e]	(10)	1.0	*t*-BuOMe	57	no reaction	
7	0.5	AK-20[f]	(10)	1.0	*t*-BuOMe	57	54 (32)	45 (23)
8	0.5	PS-D	(100)	1.0	*t*-BuOMe	48	45 (93)	54 (92)
9	0.5	PS-D	(100)	0.8	*t*-BuOMe	24	48 (92)	46 (96)
10	25.0	PS-D	(100)	0.8	*t*-BuOMe	24	40 (95)	52 (95)

[a] Isolated yield.
[b] HPLC analysis of acetate (+)- and (–)-**13**.
[c] *Pseudomonas cepasia*, immobilized on diatomaceous earth (AMANO).
[d] *Aspergillus niger* (AMANO).
[e] *Candida rugosa* (AMANO).
[f] *Pseudomonas fluorescens* (AMANO).

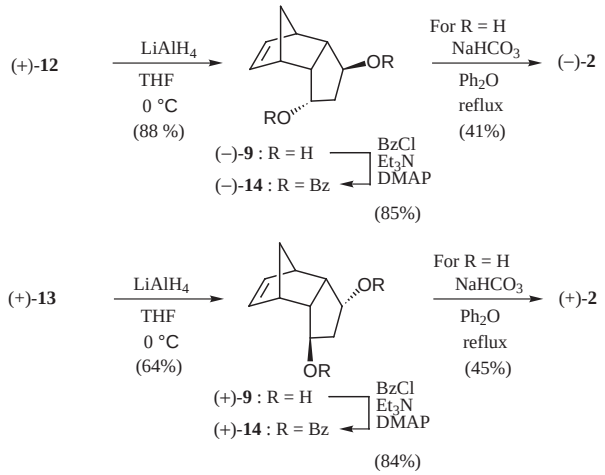


Scheme 4

amounts of lipase and vinyl acetate in the reaction. As entry 8 shows, when 100 weight% of lipase PS-D with 1.0 mol equiv of vinyl acetate was used, both (+)-**12** and (+)-**13** were obtained in good yield with high ee. The most efficient reaction condition, using lipase PS-D with 0.8 mol equiv of vinyl acetate in *t*-BuOMe, yielded (+)-**13** and (+)-**12** in 46% yield with 96% ee and 48% yield with 92% ee, respectively (entry 9). Under this reaction condition, the same result was obtained when 25 g of (±)-**12** was used as a starting material (entry 10).

Acetate (+)-**13** and alcohol (+)-**12** were easily converted to (+)- and (–)-diol **9** by LAH reduction, respectively. Fortunately, chiral diol **9** was readily recrystallized from *i*-PrOH and hexane to give enantiopure materials. Thus, the enantiopure diol **9** was obtained in both enantiomeric forms. The optical purity of (+)- and (–)-**9** was determined by HPLC using a chiral column (Chiralcel OD), after the conversion to corresponding dibenzoate **14**. Next, (+)- and (–)-diol **9** were heated in refluxing diphenyl ether[16] in the presence of sodium hydrogen carbonate[17] to give (+)- and (–)-diol **2**, respectively, via retro-Diels–Alder reactions (Scheme 5).

In conclusion, we have established an efficient chiral preparation of **2** in both enantiomeric forms by employing lipase-mediated kinetic transesterification as the key step. On the basis of the C_2 symmetry and allylic *trans*–diol functionalities in **2**, this study may have established the enantiocontrolled syntheses of natural and unnatural products involving prostanoids and aminopentitols. We have just begun to investigate the practical uses of the prepared enantiopure **2** as a chiral building block.



Scheme 5

Melting points are uncorrected. IR spectra were recorded on a JASCO-FT-IR-5000 spectrometer. ^{1}H NMR spectra were recorded on a JEOL-EX-270 (270 MHz) spectrometer and on a JEOL-GSX-400 (400 MHz) spectrometer. Mass spectra were recorded on a JEOL-DX-303 spectrometer. Enantiomeric excess was determined using a Waters-HPLC 600 instrument equipped with a chiral column. Optical rotations were measured with a JASCO-DIP-370 digital polarimeter.

(±)-(1*S,3*S**,3a*R**,4*S**,7*R**,7a*S**) -2,3,3a,4,7,7a-Hexahydro-4,7-methano-1*H*-indene-1,3-diol [(±)-9]**

To a stirred suspension of $LiAlH_4$ (10.34 g, 0.27 mol) in THF (300 mL) was added keto epoxide **8** (36.8 g, 0.23 mol) in THF (400 mL) over 25 min at 0 °C. After further stirring at 80 °C for 6 h, the reaction was quenched by adding 28% aq ammonia and Celite at 0 °C. After further stirring for 2 h at r.t., the mixture was filtered through a Celite pad, and the filtrate was extracted with THF (5 × 300 mL). The extract was washed with brine (100 mL), dried ($MgSO_4$), and evaporated under reduced pressure. The residue was recrystallized from MeOH to give the diol **9**.

Yield: 29 g, 77%; colorless crystals; mp 134–136 °C.

IR (film): 3182 cm^{-1}.

^{1}H NMR (270 MHz, $CDCl_3$–CD_3OD): δ = 1.32–1.36 (1 H, m), 1.43–1.47 (1 H, m), 1.69–1.88 (2 H, m), 2.18–2.33 (2 H, br s), 2.64 (1 H, dd, *J* = 8.6, 4.5 Hz), 2.94–3.02 (3 H, m), 3.79 (1 H, d, *J* = 5.3 Hz), 4.56 (1 H, td, *J* = 17.2, 8.3 Hz), 6.00 (1 H, dd, *J* = 5.6, 3.1 Hz), 6.28 (1 H, dd, *J* = 5.6, 2.8 Hz).

^{13}C NMR (270 MHz, $CDCl_3$–CD_3OD): δ = 45.08, 45.16, 45.31, 51.23, 52.38, 55.80, 72.66, 73.09, 133.68, 137.63.

MS: *m*/*z* = 166 (M^+), 66 (100%).

HRMS: *m*/*z* Calcd for $C_{10}H_{12}O_2$: 166.0994. Found: 166.0976.

Anal. Calcd for $C_{10}H_{12}O_2$: C, 72.26; H, 8.49. Found: C, 72.11; H, 8.78.

(±)-(1*S,3*S**,3a*S**,4*R**,5*S**,6*S**,7*S**,7a*R**)-6-Bromo-3,5-epoxy-2,3,3a,4,5,6,7,7a-octahydro-4,7-methano-1*H*-inden-1-ol (10)**

To a stirred solution of (±)-**9** (42.2 g, 0.25 mol) in CH_2Cl_2 (250 mL) was added NBS (56.0 g, 0.31 mol) portionwise over 10 min at 0 °C. After stirring at the same temperature for 30 min, the reaction mixture was diluted with CH_2Cl_2 (100 mL), washed with sat. aq $NaHCO_3$ (100 mL), aq $Na_2S_2O_3$ (10%, 100 mL) and brine (100 mL), dried ($MgSO_4$), and evaporated under reduced pressure. The residue was recrystallized from hexane–Et_2O to give the bromo ether **10**.

Yield: 54.0 g (87%); colorless crystals; mp 74–75 °C.

IR (film): 3210 cm^{-1}.

^{1}H NMR (270 MHz, $CDCl_3$): δ = 1.59 (1 H, br s), 1.77–1.81 (1 H, m), 1.90 (1 H, td, *J* = 15.3, 5.4 Hz), 2.30 (1 H, d, *J* = 11.2 Hz), 2.55–

2.63 (3 H, m), 2.77–2.83 (1 H, m), 2.97–3.04 (1 H, m), 3.81 (1 H, d, *J* = 2.3 Hz), 4.36–4.46 (1 H, m), 4.47–4.51 (2 H, m).

^{13}C NMR (270 MHz, $CDCl_3$): δ = 38.78, 45.55, 48.06, 48.39, 49.54, 56.17, 56.71, 72.67, 84.52, 89.03.

MS: *m*/*z* = 246 (M^+ + 2), 244 (M^+), 165, 99 (100%).

HRMS: *m*/*z* Calcd for $C_{10}H_{13}{}^{79}BrO_2$: 244.0099 (M^+). Found: 244.0113; calcd for $C_{10}H_{13}{}^{81}BrO_2$: 246.0079 (M^+ + 2). Found: 246.0086.

Anal. Calcd for $C_{10}H_{13}BrO_2$: C, 49.00; H, 5.35. Found: C, 48.86; H, 5.23.

(±)-(1′*S,3′*S**,3′a*R**,4′*R**,5′*S**,6′*S**,7′*S**,7′a*R**)-6′-Bromo-3′,5′-epoxy-2′,3′,3′a,4′,5′,6′,7′,7′a-octahydro-4′,7′-methano-1′*H*-inden-1′-yl Benzoate (11)**

A solution of bromo ether **10** (59.6 g, 0.24 mol) in CH_2Cl_2 (600 mL) was stirred with Et_3N (37.1 mL, 0.27 mol), DMAP (34.0 g, 0.27 mol) and benzoyl chloride (BzCl, 30.9 mL, 0.27 mol) at 0 °C for 3 h. The reaction mixture was washed with aq. HCl (10%, 300 mL), sat. aq $NaHCO_3$ (300 mL) and brine (300 mL), dried ($MgSO_4$) and evaporated under reduced pressure. The residue was recrystallized from hexane–EtOAc to give benzoate **11**.

Yield: 68.0 g (81%); colorless crystals; mp 90–91 °C.

IR (film): 1714 cm^{-1}.

^{1}H NMR (270 MHz, $CDCl_3$): δ = 1.81 (1 H, dd, *J* = 11.1, 0.8 Hz), 2.16 (1 H, td, *J* = 15.7, 5.8 Hz), 2.34 (1 H, d, *J* = 10.9 Hz), 2.68–2.80 (3 H, m), 2.81–2.88 (1 H, m), 2.99–3.06 (1 H, m), 3.95 (1 H, d, *J* = 2.3 Hz), 4.53–4.57 (2 H, m), 5.30–5.36 (1 H, m), 7.41–7.47 (2 H, m), 7.53–7.64 (1 H, m), 7.99–8.03 (2 H, m).

^{13}C NMR (270 MHz, $CDCl_3$): δ = 38.77, 44.47, 45.52, 48,43, 49.70, 54.09, 55.97, 75.96, 83.86, 89.07, 128.40, 129.53, 130.13, 133.07, 166.37.

MS: *m*/*z* = 350 (M^+ + 2), 348 (M^+), 228, 269, 105 (100%).

HRMS: *m*/*z* Calcd for $C_{17}H_{17}{}^{79}BrO_3$: 348.0361 (M^+). Found: 348.0323; calcd for $C_{17}H_{17}{}^{81}BrO_3$: 350.0341 (M^+ + 2). Found: 350.0440.

Anal. Calcd for $C_{17}H_{17}BrO_3$: C, 58.47; H, 4.91. Found C, 58.16; H, 4.55.

(±)-(1′*S,3′*S**,3′a*R**,4′*S**,7′*R**,7′a*S**)-2′,3′,3′a,4′,7′,7′a-Hexahydro-3′-hydroxy-4′,7′-methano-1′*H*-inden-1′-yl Benzoate [(±)-12]**

A solution of benzoate **11** (75.0 g, 0.21 mol) in HOAc (61.4 mL) and EtOH (1000 mL) was stirred at 90 °C with zinc dust (140.0 g, 0.21 mol) for 4 h. After cooling, the mixture was filtered through a Celite pad and the filtrate was evaporated under reduced pressure. The residue was diluted with EtOAc (500 mL), washed with sat. aq $NaHCO_3$ (300 mL) and brine (300 mL), dried ($MgSO_4$) and evaporated under reduced pressure. The residue was recrystallized from hexane–EtOAc to give alcohol (±)-**12**.

Yield: 42.3 g (73%); colorless crystals; mp 98 °C.

IR (film): 3240 cm^{-1}.

^{1}H NMR (270 MHz, $CDCl_3$): δ = 1.35–1.42 (2 H, m), 1.48–1.52 (1 H, m), 1.86–1.97 (1 H, m), 2.05–2.17 (1 H, m), 2.81–2.86 (1 H, m), 3.00–3.07 (2 H, m), 3.12–3.15 (1 H, m), 4.58–4.70 (1 H, m), 4.92 (1 H, d, *J* = 6.1 Hz), 6.17 (1 H, dd, *J* = 5.5, 3.1 Hz), 6.34 (1 H, dd, *J* = 5.5, 2.5 Hz), 7.40–7.47 (2 H, m), 7.52–7.59 (1 H, m), 7.99–8.03 (2 H, m).

^{13}C NMR (400 MHz, $CDCl_3$): δ = 42.98, 45.33, 45.55, 51.44, 52.48, 53.52, 73.13, 77.23, 128.32, 129.51, 130.64, 132.86, 134.26, 137.73, 166.10.

MS: *m*/*z* = 270 (M^+), 148, 66 (100%).

HRMS: *m*/*z* Calcd for $C_{17}H_{18}O_3$: 270.1256. Found: 270.1226.

Anal. Calcd for $C_{17}H_{18}O_3$: C, 75.53; H, 6.71. Found: C, 75.52; H, 6.53.

Asymmetric Transesterification of (±)-12; Typical Procedure

A solution of alcohol (±)-**12** (25.0 g, 92.6 mmol) and vinyl acetate (6.8 mL, 74.1 mmol) in *t*-BuOMe (500 mL) was suspended with lipase PS-D (*Pseudomonas* sp. AMANO, 25.0 g) and the suspension was stirred at 37 °C for 24 h. After filtration through a Celite pad, the filtrate was evaporated under reduced pressure. The residue was chromatographed (silica gel 400 g; hexane–EtOAc, 8:1 v/v) to give the acetate (+)-**13** (15.1 g, 52%) as a colorless oil and alcohol (+)-**12** (10.0 g, 40%) as colorless crystals.

(+)-(1′*R*,3′*R*,3′a*S*,4′*R*,7′*S*,7′a*R*)-3′-Acetoxy-2′,3′,3′a,4′,7′,7′a-hexahydro-4′,7′-methano-1′*H*-inden-1′-yl Benzoate [(+)-13]

$[\alpha]_D{}^{21}$+49.5 (*c* 1.00, $CHCl_3$).

IR (film):1717, 1735 cm^{-1}.

^{1}H NMR (270 MHz, $CDCl_3$): δ = 1.44–1.45 (1 H, m), 1.47–1,48 (1 H, m), 1.93–2.08 (1 H, m), 2.09 (3 H, s), 2.10–2.21 (1 H, m), 2.83–2.88 (2 H, m), 3.13–3.15 (1 H, m), 3.23 (1 H, dt, *J* = 8.2, 4.0 Hz), 4.97 (1 H, d, *J* = 6.1 Hz), 5.34 (1 H, td, *J* = 10.1, 8.6 Hz), 6.15 (1 H, dd, *J* = 5.5, 3.0 Hz), 6.22 (1H, dd, *J* = 5.5, 3.0 Hz), 7.40–7.46 (2 H, m), 7.52–7.58 (1 H, m), 7.99–8.03 (2 H, m).

^{13}C NMR (400 MHz, $CDCl_3$): δ = 21.05, 39.65, 45.59, 45.74, 49.00, 52.02, 53.14, 75.45, 76.27, 128.34, 129.53, 130.47, 132.93, 133.90, 137.63, 166.01, 170.89.

MS: *m*/*z* = 312 (M^+), 187, 66 (100%).

HRMS: *m*/*z* Calcd for $C_{19}H_{20}O_4$: 312.1362. Found: 312.1357.

Anal. Calcd for $C_{19}H_{20}O_4$: C, 73.06; H, 6.45. Found: C, 72.10; H, 6.51.

Optical purity was determined to be 95% ee by HPLC using a chiral column with chiral stationary phase (Chiralcel OD; hexane–*i*-PrOH, 25:1 v/v).

(+)-(1′*S*,3′*S*,3′a*R*,4′*S*,7′*R*,7′a*S*)-2′,3′,3′a,4′,7′,7′a-Hexahydro-3′-hydroxy-4′,7′-methano-1′*H*-inden-1′-yl Benzoate [(+)-12]

Mp 88 °C; $[\alpha]_D{}^{22}$+13.8 (*c* 1.00, $CHCl_3$).

The spectroscopic data were identical to those of (±)-**12**. Optical purity was determined to be 95% ee by HPLC using a chiral column with chiral stationary phase (Chiralcel OD; hexane–*i*-PrOH, 25:1 v/v) after the following conversion into acetate (–)-**13**.

(–)-(1′*S*,3′*S*,3′a*R*,4′*S*,7′*R*,7′a*S*)-3′-Acetoxy-2′,3′,3′a,4′,7′,7′a-hexahydro-4′,7′-methano-1′*H*-inden-1′-yl Benzoate [(–)-13]

A solution of alcohol (+)-**12** (0.10 g, 0.37 mmol) in CH_2Cl_2 (5 mL) was stirred at 0 °C with Et_3N (57 μL, 0.41 mmol), DMAP (52 mg, 0.43 mmol) and AcCl (29 μL, 0.41 mmol) for 2 h. The reaction mixture was diluted with CH_2Cl_2 (15 mL), washed with aq HCl (10%,10 mL), sat. aq $NaHCO_3$ (10 mL) and brine (10 mL), dried ($MgSO_4$) and evaporated under reduced pressure. The residue was chromatographed (silica gel 20 g; hexane–EtOAc, 10:1 v/v) to give acetate (–)-**13**.

Yield: 76 mg (66%); colorless oil; $[\alpha]_D{}^{22}$ –49.5 (*c* 1.00, $CHCl_3$).

The spectroscopic data were identical to those of (+)-**13**.

(–)-(1*S*,3*S*,3a*R*,4*S*,7*R*,7a*S*)-2,3,3a,4,7,7a-Hexahydro-4,7-methano-1*H*-indene-1,3-diol [(–)-9]

To a stirred suspension of $LiAlH_4$ (1.01g, 26.7 mmol) in THF (100 mL) was added alcohol (+)-**12** (6.0 g, 22.2 mmol) in THF (50 mL) at 0 °C over 30 min, and the mixture was stirred for 1.5 h. The reaction was quenched by adding of 28% aq ammonia and Celite. After further stirring for 12 h at r.t., the mixture was filtered through a Celite pad, and the filtrate was extracted with THF (5 × 100 mL).

The extract was dried ($MgSO_4$) and evaporated under reduced pressure. The residue was chromatographed (silica gel 200 g; hexane–EtOAc, 1:1 v/v) to give diol (–)-**9** (3.23 g, 88%) as colorless crystals. Diol (–)-**9** (3.2 g, 95% ee) was recrystallized from hexane–*i*-PrOH to give optically pure diol (–)-**9** (1.2 g), whose optical purity was determined to be >99% ee by HPLC using a chiral column with chiral stationary phase (Chiralcel OD; hexane–*i*-PrOH, 99:1 v/v) after the following conversion into dibenzoate (–)-**14**.

Mp 123–126 °C; $[\alpha]_D^{24}$ – 29.3 (*c* 1.00, MeOH).

The spectroscopic data were identical to those of (±)-**9**.

(+)-(1*R*,3*R*,3a*S*,4*R*,7*S*,7a*R*)-2,3,3a,4,7,7a-Hexahydro-4,7-methano-1*H*-indene-1,3-diol [(+)-9]

To a stirred suspension of $LiAlH_4$ (2.27 g, 60.0 mmol) in THF (200 mL) was added the acetate (+)-**13** (15.6 g, 50.0 mmol) in THF (100 mL) at 0 °C over 30 min. The mixture was stirred at that temperature for 3 h. The reaction was quenched by adding 28% aq ammonia and Celite. After further stirring for 12 h at r.t., the mixture was filtered through a Celite pad, and the filtrate was extracted with THF (5 × 100 mL). The extract was dried ($MgSO_4$) and evaporated under reduced pressure. The residue was chromatographed (silica gel 200 g; hexane–EtOAc, 1:1 v/v) to give diol (+)-**9** (5.32 g, 64%) as colorless crystals. The diol (+)-**9** (0.72 g, 95% ee) was recrystallized from hexane–*i*-PrOH to give optically pure diol (+)-**9** (0.40 g), whose optical purity was determined to be >99% ee by HPLC using a chiral column with chiral stationary phase (Chiralcel OD; hexane–*i*-PrOH, 99:1 v/v) after the following conversion into dibenzoate (+)-**14**.

Mp 123–126 °C;$[\alpha]_D^{26}$ + 30.3 (*c* 1.00, MeOH).

The spectroscopic data were identical to those of (±)-**9**.

(–)-(1′*S*,3′*S*,3′a*R*,4′*S*,7′*R*,7′a*S*)–3′-Benzoyloxy-2′,3′,3′a,4′,7′,7′a-hexahydro-4′,7′-methano-1′*H*-inden-1′-yl Benzoate [(–)-14]

To a stirred solution of diol (–)-**9** (100 mg, 0.60 mmol) with Et_3N (0.19 mL, 1.33 mmol) and DMAP (169 mg, 1.39 mmol) in CH_2Cl_2 was added BzCl (0.15 mL, 1.33 mmol) at 0 °C. After stirring at r.t. for 1 h, the reaction mixture was diluted with CH_2Cl_2 (15 mL), washed with aq HCl (10%, 15 mL), sat. aq $NaHCO_3$ (15 mL) and brine (15 mL), dried ($MgSO_4$) and evaporated under reduced pressure. The residue was chromatographed (silica gel 15 g; hexane–EtOAc, 20:1 v/v) to give dibenzoate (–)-**14**.

Yield: 191 mg (85%); colorless oil; $[\alpha]_D^{22}$ –81.3 (*c* 1.00, $CHCl_3$).

IR (film): 1707 cm^{-1}.

^1H NMR (270 MHz, $CDCl_3$): δ = 1.39 (1 H, d, *J* = 8.2 Hz), 1.48 (1 H, td, *J* = 10.2, 1.7 Hz), 2.09–2.19 (1 H, m), 2.32 (1 H, dd, *J* = 14.7, 8.4 Hz), 2.90–2.95 (2 H, m), 3.17–3.20 (1 H, m), 3.36 (1 H, dt, *J* = 8.7, 4.0 Hz), 5.04 (1 H, d, *J* = 6.3 Hz), 5.61 (1 H, td, *J* = 10.1, 8.4 Hz), 6.20 (1 H, dd, *J* = 5.6, 3.0 Hz), 6.32 (1 H, dd, *J* = 5.6, 3.0 Hz), 7.42–7.51 (4 H, m), 7.54–7.65 (2 H, m), 8.01–8.10 (4 H, m).

^{13}C NMR (270 MHz, $CDCl_3$): δ = 39.85, 45.67, 45.83, 49.25, 52.09, 53.24, 76.02, 76.39, 128.36, 128.49, 129.56, 129.59, 130.30, 130.47, 132.96, 133.02, 134.13, 137.73, 166.07, 166.32.

MS: *m*/*z* = 374 (M^+), 130, 105 (100%).

HRMS: *m*/*z* Calcd for $C_{24}H_{22}O_4$: 374.1518. Found: 374.1526.

Anal. Calcd for $C_{24}H_{22}O_4$: C, 76.99; H, 5.92. Found: C, 76.87; H, 5.90.

(+)-(1′*R*,3′*R*,3′a*S*,4′*R*,7′*S*,7′a*R*)-3′-Benzoyloxy-2′,3′,3′a,4′,7′,7′a-hexahydro-4′,7′-methano-1′*H*-inden-1′-yl Benzoate [(+)-14]

In the same manner as described for (–)-**14**, (+)-**9** gave (+)-**14**.

Yield: 189 mg (84%); colorless oil; $[\alpha]_D^{24}$ +79.3 (*c* 1.00, $CHCl_3$).

The spectroscopic data were identical to those of (–)-**14**.

(1*R*,3*R*)-4-Cyclopentene-1,3-diol [(+)-2]

A suspension of (+)-**9** (500 mg, 3.01 mmol) and $NaHCO_3$ (1.91 g, 22.6 mmol) in Ph_2O (5 mL) was sonicated under bubbling argon gas for 20 min. The suspension was stirred at 280 °C for 3 h. After cooling, the mixture was directly chromatographed (silica gel 30 g; hexane–EtOAc, 10:1 v/v) to give diol (+)-**2**.

Yield: 141 mg (47%); colorless crystals; mp 67–69 °C; $[\alpha]_D^{27}$+228.1 (*c* 1.04, MeOH), {lit.[5] (antipode): $[\alpha]_D$ –237 (MeOH)}.

IR (film): 3250 cm^{-1}.

^1H NMR (270 MHz, $CDCl_3$–CD_3OD): δ = 2.04 (2 H, t, *J* = 5.1 Hz), 4.99 (2 H, t, *J* = 5.1, 1.0 Hz), 5.99 (2 H, d, *J* = 1.0 Hz).

^{13}C NMR (270 MHz, $CDCl_3$–CD_3OD): δ = 43.60, 75.73, 136.90.

MS: *m*/*z* = 100 (M^+), 99 (M^+ – 1), 43 (100%).

HRMS: *m*/*z* Calcd for $C_5H_8O_2$: 100.0524. Found: 100.0524.

Anal. Calcd for $C_5H_8O_2$: C, 59.98; H, 8.05. Found: C, 60.18; H, 8.34.

(1*S*,3*S*)-4-Cyclopentene-1,3-diol [(–)-2]

In the same manner as described for (+)-**2**, (–)-**9** gave (–)-**2**.

Yield: 123 mg (41%); colorless crystals; mp 68–69 °C; $[\alpha]_D^{23}$ – 233.8 (*c* 0.95, MeOH), {lit.[5] $[\alpha]_D$ –237 (MeOH)}.[5]

The spectroscopic data were identical to those of (+)-**2**.

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