Lipase-Mediated Synthesis of Both Enantiomers of Levoglucosenone from Acrolein Dimer

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Received April 20, 2001; Accepted June 22, 2001

Abstract: A synthesis of both enantiomers of levoglucosenone from acrolein dimer has been developed by employing lipase-mediated kinetic hydrolysis. Thus, acrolein dimer is transformed into racemic dihydrolevoglucosenone by sequential hydride reduction, oxidative acetalization, and Swern oxidation. Employing Saegusa-Larock conditions, dihydrolevoglucosenone is transformed into racemic levoglucosenone. The lipase-mediated resolution was best carried out under hydrolysis conditions with the *endo*-acetate generated from racemic levoglucosenone to give rise to highly enantioenriched (+)-alcohol and enantiopure (–)-acetate serving as the precursors of enantiopure levoglucosenone having the corresponding chirality.

Keywords: chiral pool; chiral resolution; dehydrogenation; enzymatic resolution; heterocycles

Introduction

(–)-Levoglucosenone [1,6-anhydro-3,4-dideoxy-β-D-glycerohex-3-enopyranos-2-ulose); (–)-**1**] is a pyrolysis product of cellulose[1] (Figure 1). Owing to the high chemical potential exhibited by an enone functionality and masked formyl and 1,2-glycol functionalities and the inherent stereochemical potential exhibited by the biased framework, this molecule has received considerable attention as a versatile chiral building block and actually is being utilized for enantio- and diastereoselective construction of a variety of optically active compounds.[2,3] However, its utilization is still limited as its preparation from cellulose affords only the (–)-enantiomer in very low yield (<10%). Therefore, the development of an efficient synthesis of levoglucosenone **1** in both enantiomeric forms is essential for its more versatile utilization. Three methods which are capable of producing enantiomeric (+)-levoglucosenone [(+)-**1**] have been reported: two utilizing natural sugar precursors with a multi-step sequence[4,5] and one employing the Sharpless asymmetric dihyroxylation[6] or lipase-mediated resolution[7] with a circuitous sequence via isolevoglucosenone. We report here a fourth method which involves an efficient synthesis of racemic levoglucosenone [(±)-**1**] and its lipase-mediated resolution[7] through the allyl acetate intermediate (±)-**9**.

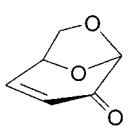

Figure 1. (–)-Levoglucosenone [(–)-**1**].

Results and Discussion

Commercially available acrolein dimer [2*H*-3,4-dihydropyran-2-carbaldehyde; (±)-**2**] was reduced with sodium borohydride to give the primary alcohol[8] (±)-**3**. Internal acetal formation of (±)-**3** under oxidative conditions proceeded in a one-pot, two-step sequence involving oxidative treatment in methanol and intramolecular acetalization to give **5** having a dioxabicyclo[3.2.1]octane framework as a mixture of epimers, presumably via the methyl acetal **4**. When the oxidation was carried out without using methanol, a complex mixture of products was generated. Thus, (±)-**3** was first stirred with *m*-chloroperbenzoic acid (*m*-CPBA) in methanol at 0 °C to give a mixture of oxidation products which, after evaporation of the solvent, was refluxed with a catalytic amount of *p*-toluenesulfonic acid in benzene to afford the bicyclic acetal **5** in acceptable overall yield. We first examined the direct conversion of **5** into racemic levoglucosenone [(±)-**1**] using *o*-iodoxybenzoic acid (IBX) which was recently employed by Nicolaou[9] to convert a cyclic alcohol into the corresponding enone in one step. Indeed, the desired reaction did occur to give a mixture containing levoglucosenone [(±)-**1**] as a ma-

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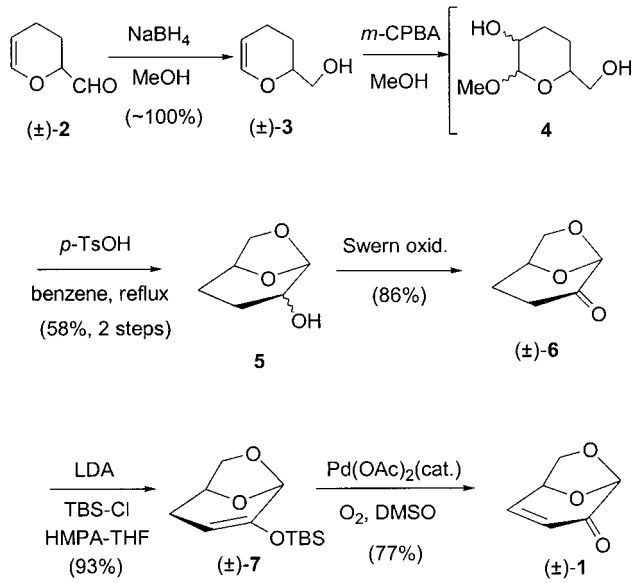
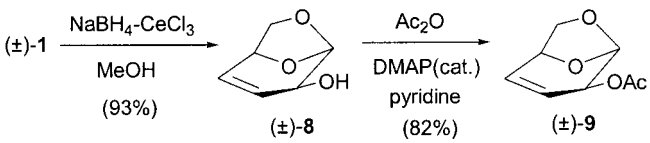


Scheme 1. Synthesis of racemic levoglucosenone [(±)-**1**].

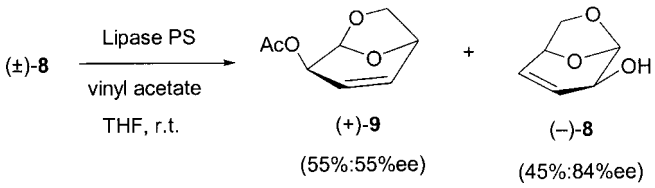
jor component, but the by-products could not be removed in a practical manner. Swern oxidation[10] of **5** was thus carried out to give racemic dihydrolevoglucosenone [(±)-**6**] whose ^{1}H NMR spectral data were identical with those reported for optically active (–)-**6** from a natural origin.[11] IBX oxidation of (±)-**6** again generated the same inseparable mixture together with levoglucosenone [(±)-**1**].

In order to carry out the requisite dehydrogenation under more familiar conditions,[12] ketone (±)-**6** was transformed into the *tert*-butyldimethylsilyl (TBS) enol ether (±)-**7** under standard conditions. Employing the Larock modification[13] of the Saegusa reaction,[12] (±)-**7** was exposed to oxygen in DMSO in the presence of a catalytic amount of palladium(II) acetate. The reaction proceeded in the desired way to give rise to racemic levoglucosenone [(±)-**1**] in satisfactory yield. The overall yield of racemic levoglucosenone [(±)-**1**] from acrolein dimer (±)-**2** was 36% in six steps (Scheme 1).

Having established a new synthesis of racemic levoglucosenone [(±)-**1**], we next examined its resolution by employing lipase-mediated conditions. To carry out the resolution under transesterification or ester hydrolysis conditions, (±)-**1** was transformed diastereoselectively into the *endo*-alcohol (±)-**8** and the *endo*-acetate (±)-**9** by sequential 1,2-reduction[14] and acetylation (Scheme 2).



Scheme 2. Preparation of resolution substrates.



Scheme 3. Lipase-mediated transesterification.

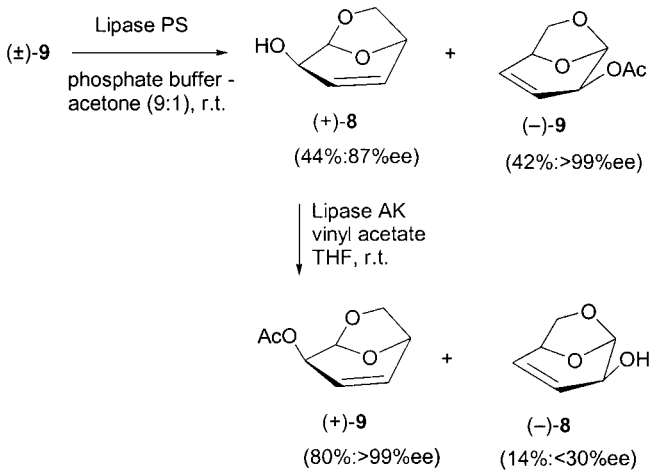
Resolution of the alcohol (±)-**8** under transesterification conditions[7] was first examined using four immobilized lipases in THF containing an excess amount of vinyl acetate (10 equiv.) at room temperature. Among the lipases examined, three catalyzed the transesterification to give enantioenriched acetate (+)-**9** and enantioenriched alcohol (–)-**8** in good yields. Fortunately, since both products were prepared in enantiomerically pure forms from natural carbohydrate precursors,[1c,15,16,17] their absolute configurations were assigned as shown (Scheme 3). However, the optical purity of both products was found to be less than satisfactory for practical use in every case (Table 1).

On the other hand, resolution of acetate (±)-**9** under hydrolysis conditions in a mixture of a phosphate buffer and acetone using the same four immobilized lipases proceeded in an enantiocomplementary way to the transesterification reaction above to give the enantiomeric alcohol (+)-**8** and the enantiomeric acetate (–)-**9**, respectively; this way was much superior to the transesterification. In particular, lipase PS brought about excellent resolution giving rise to highly enantioenriched alcohol[1c,15,16,17] (+)-**8** (87% ee) and enantiopure acetate[15,17] (–)-**9** in good yields (Scheme 4 and Table 2). The enantioenriched alcohol (+)-**8** obtained could be optically purified using lipase AK which exhibited the best result among the lipases examined (Table 1, entry 4). Thus, (+)-**8** (87% ee), on stirring with a limited amount of vinyl acetate (1 equiv.) at room temperature, furnished the enantiopure (+)-acetate (+)-**9** in 80% yield with some re-

Table 1. Kinetic transesterification of allyl alcohol (±)-**8**.[a]

Entry	Lipase[b]	Time (h)	(–)-**8** (%:% ee)[c]	(+)-**9** (%:% ee)[c]
1	Novozyme	12	-:-[d]	-:-[d]
2	Lipase LIP	12	53:38	42:61
3	Lipase AK	12	60:70	45:84
4	Lipase PS	12	46:70	44:70

[a] Reaction was carried out in THF at room temperature with ten equivalents of vinyl acetate.
[b] Novozyme (*Candida antarctica*, Roche); Lipase LIP (*Pseudomonas* sp., Toyobo); Lipase PS (*Pseudomonas cepacia*, Amano); Lipase AK (*Pseudomonas* sp., Amano).
[c] Enantiomeric excess was determined by HPLC equipped with a chiral column (CHIRALCEL OJ) after conversion into the benzoate.
[d] Reaction did not proceed.



Scheme 4. Lipase-mediated resolution and optical purification.

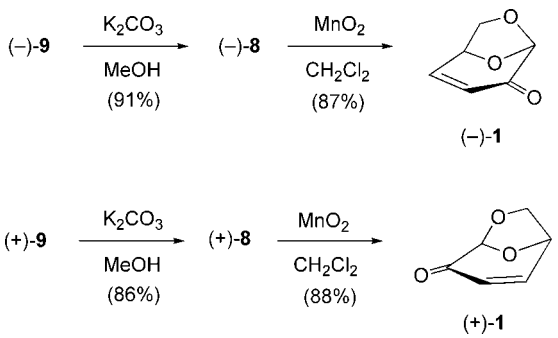
Table 2. Kinetic hydrolysis of allyl acetate (±)-**9**.[a]

Entry	Lipase[b]	Time (h)	(+)-**8** (%:% ee)[c]	(–)-**9** (%:% ee)[c]
1	Novozyme	216	30:76	53:26
2	Lipase LIP	16	40:48	43:26
3	Lipase AK	288	60:70	34:90
4	Lipase PS	27	44:87	42:>99

[a] Reaction was carried out in phosphate buffer-acetone mixture (9:1 v/v) at room temperature.
[b] Novozyme (*Candida antarctica*, Roche); Lipase LIP (*Pseudomonas* sp., Toyobo); Lipase PS (*Pseudomonas cepacia*, Amano); Lipase AK (*Pseudomonas* sp., Amano).
[c] Enantiomeric excess was determined by HPLC equipped with a chiral column (CHIRALCEL OJ) after conversion into the benzoate.

covery of the (–)-alcohol (–)-**8** (14% with <30% ee). The configuration and structure of the products were deduced unambiguously by comparison of the spectroscopic data with those reported[1c,15,16,17] (Scheme 4).

Conversion of the enantiopure products into enantiopure levoglucosenone (**1**) having the corresponding chirality could be carried out satisfactorily under standard conditions. Thus, both enantiomers of acetate **9** were first transformed into alcohol **8**, under



Scheme 5. Synthesis of enantiopure levoglucosenone.

methanolysis conditions in the presence of potassium carbonate, which furnished the corresponding levoglucosenone (**1**) on oxidation with manganese(IV) oxide[6] (Scheme 5).

Conclusion

We have developed a new route to racemic levoglucosenone. Employing a lipase-mediated kinetic hydrolysis reaction, the racemic acetate generated from racemic levoglucosenone was resolved and reconverted into both enantiomers of enantiopure levoglucosenone. The present synthesis involving an efficient acquisition of racemic levoglucosenone and its resolution is highly promising for the stereocontrolled construction of a variety of both natural and unnatural optically active compounds.

Experimental Section

General Remarks

The solvents used were distilled prior to use. IR spectra were recorded on a JASCO-IR-700 spectrometer. ^{1}H NMR and ^{13}C NMR were obtained in $CDCl_3$ using a Varian Gemini (300 and 75 MHz). Optical rotations were measured using a JASCO DIP-370 digital polarimeter. Optical purity was determined on a Gilson Model-307 instrument equipped with a chiral column. Mass spectra were obtained using a JMS-AX-500 and a JMX-MX-303 instrument.

7,8-Dioxabicyclo[3.2.1]octan-2-ol (5)

To a stirred solution of alcohol (±)-**3** (100 mg, 0.88 mmol) in MeOH (2 mL) was added *m*-CPBA (259 mg, 1.05 mmol) at 0 °C and the stirring was continued for 30 min at the same temperature. The solvent was evaporated under reduced pressure to give a residue containing **4**. This was dissolved in benzene (10 mL) containing *p*-TsOH (8.3 mg, 0.04 mmol) and the mixture heated at reflux for 5 h. The solvent was evaporated under reduced pressure and the residue chromatographed (SiO_2 7 g, elution with Et_2O-hexane, 20:1 v/v) to give **5** as a colorless oil; yield: 67 mg (58%); IR (film): ν = 3450, 2950, 1095, 1014, 884 cm^{-1}; ^{1}H NMR: δ = 5.32 (br. s, 1H, H-1), 4.50 (m, 1H, H-5), 3.93 (d, $J_{6,5}$ = 7 Hz, 0.5H, H-6), 3.87 – 3.79 (m, 1.5H, H-6), 3.63 – 3.58 (m, 1H, H-2), 2.10 – 1.90 (m, 2H,), 1.67 – 1.40 (m, 2H); HRMS: calcd. for $C_6H_{10}O_3$: 130.0629; found: *m/z* = 130.0595; anal. calcd. for $C_6H_{10}O_3$: C 55.35, H 7.74; found: C 55.06, H 7.56.

(±)-7,8-Dioxabicyclo[3.2.1]octan-2-one [(±)-6]

To a stirred solution of oxalyl chloride (4 mL, 46 mmol) in CH_2Cl_2 (40 mL) was added DMSO (6.5 mL, 92 mmol) at –70 °C and, after 30 min, **5** (2.0 g, 15.4 mmol) in CH_2Cl_2 (10 mL) was added at the same temperature. After stirring for 1 h at the same temperature, Et_3N (19 mL, 138 mmol) was added and the mixture was gradually warmed to room temperature. The

reaction was quenched by addition of saturated aqueous NH_4Cl and extracted with CH_2Cl_2. The extract was washed with brine, dried ($MgSO_4$), evaporated under reduced pressure, and the residue chromatographed (SiO_2 150 g, elution with Et_2O-hexane, 3:1 v/v) to give (±)-**6** as a pale yellow oil; yield: 1.70 g (86%); IR (film): ν = 2966, 2898, 1716, 1105, 971, 890, 831 cm^{-1}; ^1H NMR: δ = 5.11 (s, 1H, H-1), 4.72–4.70 (m, 1H, H-5), 4.05 (dd, $J_{6,6'}$ = 7.4 and $J_{6,5}$ = 0.8 Hz, 1H, H-6), 3.99 – 3.94 (m, 1H, H-6'), 2.72 – 2.52 (m, 1H, H-3), 2.43 – 2.25 (m, 2H, H-3' and H-4'), 2.05 – 1.98 (m, 1H, H-4'); HRMS: calcd. for $C_6H_8O_3$: 128.0473; found: *m/z* = 128.0483. ^1H NMR data were identical with those reported.[11]

(±)-2-(*tert*-Butyldimethylsiloxy)-7,8-dioxabicyclo[3.2.1]oct-2-ene [(±)-7]

To a stirred solution of LDA [prepared *in situ* by treating *i*-Pr_2NH (77 μL, 0.6 mmol) in THF (2 mL) at –78 °C with BuLi (1.56 M in hexane, 0.3 mL, 0.47 mmol) in the same flask] was added (±)-**6** (50 mg, 0.39 mmol) in THF (1 mL) at 0 °C. After 20 min at the same temperature, the mixture was cooled to –78 °C and to this mixture was added TBS-Cl (90 mg, 0.6 mmol) and HMPA (0.08 mL, 0.47 mmol) in THF (1 mL) and the mixture was warmed gradually to 0 °C. The reaction was quenched by addition of 5% aqueous $NaHCO_3$ and extracted with a mixture of Et_2O-AcOEt (6:1, v/v). The extract was dried ($MgSO_4$), evaporated under reduced pressure, and the residue chromatographed (SiO_2 5 g, elution with AcOEt-hexane, 1:20 v/v) to give (±)-**7** as a pale yellow oil; yield: 88 mg (93%); IR (film): ν = 2957, 2894, 2859, 1664, 1220, 1101, 868, 841 cm^{-1}; ^1H NMR: δ = 5.17 (d, $J_{3,4}$ = 1.4 Hz, 1H, H-3), 4.65 – 4.62 (m, 2H, H-1 and H-5), 3.95 – 3.90 (m, 1H, H-6'), 3.64 (dd, $J_{6,6'}$ = 6.9 and $J_{6,5}$ = 1.6 Hz, 1H, H-6), 2.76–2.69 (m, 1H, H-4), 1.83 (dd, $J_{4',4}$ = 17.0 and $J_{4',3}$ = 5.8 Hz, 1H), 0.925 (s, 9H), 0.164 (s, 3H), 0.158 (s, 3H); HRMS: calcd. for $C_{12}H_{22}O_3Si$: 242.1337; found: *m/z* = 242.1313.

(±)-Levoglucosenone [(±)-1]

A solution of (±)-**7** (118 mg, 0.49 mmol) and $Pd(OAc)_2$ (10 mg, 0.05 mmol) in DMSO (2 mL) was stirred under an oxygen atmosphere at 80 °C for 48 h. The mixture was diluted with CH_2Cl_2 and water and the organic layer was separated. The organic layer was washed, dried ($MgSO_4$), evaporated under reduced pressure, and the residue chromatographed (SiO_2 10 g elution with Et_2O-hexane, 4:1 v/v) to give (±)-**1** as a colorless oil; yield: 47 mg (77%); IR (film): ν = 2976, 2899, 1699, 1107, 972, 892, 832 cm^{-1}; ^1H NMR: δ = 7.29 (dd, $J_{4,3}$ = 9.9 and $J_{4,5}$ = 4.7 Hz, 1H, H-4), 6.14 (dd, $J_{3,4}$ = 9.9 and $J_{3,1}$ = 1.6 Hz, 1H, H-3), 5.38 (d, $J_{1,3}$ = 1.6 Hz, 1H, H-1), 5.02 (t, $J_{5,4}$ = 4.7 and $J_{5,6'}$ = 4.7 Hz, 1H, H-5), 3.91(dd, $J_{6',6}$ = 6.9 and $J_{6',5}$ = 4.7 Hz, 1H, H-6'), 3.78 (d, $J_{6,6'}$ = 6.9 Hz, 1H, H-6); HRMS: calcd. for $C_6H_6O_3$: 126.0313; found: *m/z* = 126.0280. Spectra and TLC were identical with those of an authentic sample.[6]

(±)-7,8-Dioxabicyclo[3.2.1]oct-3-en-2-ol [(±)-8]

To a stirred solution of (±)-**1** (1.53 g, 12.1 mmol) in MeOH (20 mL) was added $CeCl_3 \cdot 7\,H_2O$ (4.51 g, 12.1 mmol) followed by $NaBH_4$ (229 mg, 6.1 mmol) at –50 °C and the stirring was continued for 20 min at the same temperature. The reaction was quenched by addition of acetone and the mixture was evaporated under reduced pressure. The residue was diluted with water and extracted with Et_2O. The extract was washed with brine, dried ($MgSO_4$), evaporated under reduced pressure, and the residue chromatographed (SiO_2 60 g, elution with Et_2O-hexane, 5:1 v/v) to give (±)-**8** as a colorless oil; yield: 1.39 g (89%); IR (film): ν = 3457, 3017, 2960, 2894, 1123, 1046, 983, 885, 820 cm^{-1}; ^1H NMR: δ = 6.12 (dd, $J_{4,5}$ = 9.9 and $J_{4,3}$ = 4.4 Hz, 1H, H-4), 5.72 (dt, $J_{3,4}$ = 9.9, $J_{3,2}$ = 2.5, and $J_{3,1}$ = 2.5 Hz 1H, H-3), 5.52 (dd, $J_{1,2}$ = 2.5 and $J_{1,3}$ = 2.5 Hz, 1H, H-1), 4.66 (dd, $J_{5,4}$ = 4.4 and $J_{5,6}$ = 4.4 Hz, 1H, H-5), 4.34(d, $J_{2,OH}$ = 11.8 Hz, 1H, H-2), 3.84 (d, $J_{6,6'}$ = 6.6 Hz, 1H, H-6), 3.78–3.74 (m, 1H, H-6'), 2.08 (d, $J_{OH,2}$ = 12.1 Hz, 1H, OH); ^{13}C NMR: δ = 130.8, 129.2, 101.3, 71.1, 70.6, 68.7. HRMS: calcd. for $C_6H_8O_3$: 128.0473; found: *m/z* = 128.0459; anal. calcd. for $C_6H_8O_3$: C 56.50, H 6.29; found: C 56.50, H 6.41. The ^1H NMR spectra were identical with those reported,[1c,16] but not identical with those of the epimeric alcohol.[6]

(±)-2-Acetoxy-7,8-dioxabicyclo[3.2.1]oct-3-ene [(±)-9]

To a stirred solution of (±)-**8** (1.30 g, 10.2 mmol) in CH_2Cl_2 (30 mL) were added pyridine (1.64 mL, 20 mmol), 4-*N*,*N*-dimethylaminopyridine (DMAP; 12 mg, 0.1 mmol), and acetic anhydride (1.43 mL, 15 mmol) at room temperature and the stirring was continued for 5 h at the same temperature. The mixture was diluted with Et_2O and washed successively with 10% HCl and brine, dried ($MgSO_4$), evaporated under reduced pressure, and the residue chromatographed (SiO_2 70 g, elution with AcOEt-hexane, 1:20 v/v) to give (±)-**9** as a colorless oil; yield: 1.42 g (82%); IR (film): ν = 2968, 2892, 1730, 1372, 1237, 1125, 1041, 984, 901, 885, 803 cm^{-1}; ^1H NMR: δ = 6.20 (ddd, $J_{4,3}$ = 10.4, $J_{4,5}$ = 4.1 and $J_{4,2}$ = 1.4 Hz, 1H, H-4), 5.66–5.62 (m, 2H, H-2 and H-3), 5.53 (s, 1H, H-1), 4.70 (t, $J_{5,4}$ = 4.1, $J_{5,6'}$ = 4.1 Hz, 1H, H-5), 3.99 (d, $J_{6,6'}$ = 6.9 Hz, 1H, H-6), 3.81 (m, 1H, H-6'), 2.15 (s, 3H, OAc); HRMS: calcd. for $C_8H_{10}O_4$: 170.0578; found: *m/z* = 170.0576; anal. calcd. for $C_8H_{10}O_4$: C 56.47, H 5.92; found: C 56.57, H 5.92. The ^1H NMR spectra were identical with those reported for the optically active product.[15,17]

Kinetic Transesterification of Racemic Alcohol (±)-8: Typical Example

A suspension of (±)-**8** (30 mg, 0.23 mmol), vinyl acetate (215 μL, 2.3 mmol), and immobilized lipase (Lipase AK; 39 mg) in THF (1 mL) was stirred at room temperature for 12 h. The mixture was filtered through a Celite pad and the filtrate was evaporated under reduced pressure and the residue chromatographed (SiO_2 2 g, elution with Et_2O-hexane, 1:4 v/v) to give the (+)-acetate (+)-**9** (yield: 18 mg, 46%) and the (–)-alcohol (–)-**8** (yield: 13 mg, 44%), each as a colorless oil. The enantiomeric excess of the products was determined by HPLC equipped with a chiral column (CHIRALCEL OJ, elution with *i*-PrOH-hexane, 1:9 v/v) after transformation of each product into the benzoate: (+)-**9** (70% ee) and (–)-**8** (70% ee).

Kinetic Hydrolysis of Racemic Acetate (±)-9: Typical Example

A suspension of (±)-**9** (1.0 g, 6.0 mmol) and immobilized lipase (Lipase PS 680 mg) in 0.1 M phosphate buffer (pH 7.6; 16 mL) and acetone (1.7 mL) was stirred at room temperature for 27 h. The mixture was diluted with Et_2O and filtered through a Celite pad, and the organic layer was separated. The organic layer was washed with brine, dried ($MgSO_4$), evaporated under reduced pressure, and the residue chromatographed (SiO_2 70 g, elution with Et_2O-hexane, 1:4 v/v) to give (–)-**9** (yield: 425 mg, 42%), $[\alpha]_D^{26}$: –34.5 (*c* 1.1, $CHCl_3$) {lit.: $[\alpha]_D^{26}$: –26 (*c* 1.2, $CHCl_3$)[15]; $[\alpha]_D^{27}$: –40.7 (*c* 1.3, $CHCl_3$)[17]}, and (+)-**8** (yield: 340 mg, 44%), $[\alpha]_D^{26}$: +22.1 (*c* 1.0, $CHCl_3$), each as a colorless oil. The enantiomeric excess of the products was determined as above by HPLC equipped with a chiral column which revealed (–)-**9** as >99% ee and (+)-**8** as 87% ee. The spectroscopic data (^{1}H NMR and MS) and TLC of the products were identical with those of (±)-**8** and (±)-**9**.

Optical Purification of Enantioenriched (+)-Alcohol (+)-8

A suspension of (+)-**8** (87% ee: 290 mg, 2.27 mmol), vinyl acetate (251 μL, 2.27 mmol), and Lipase AK (290 mg) in THF (5 mL) was stirred at room temperature for 7 h. The mixture was filtered through a Celite pad, the filtrate was evaporated under reduced pressure, and the residue chromatographed (SiO_2 15 g, elution with Et_2O-hexane, 1:4 v/v) to give enantiopure (+)-acetate (+)-**9** (yield: 310 mg, 80%), $[\alpha]_D^{29}$: +35.7 (*c* 0.8, $CHCl_3$), and poorly enantioenriched (–)-alcohol (–)-**8** (yield: 41 mg, 14%), $[\alpha]_D^{29}$: –9.2 (*c* 0.8, $CHCl_3$). The optical purity of (+)-**9** was determined as >99% ee by HPLC equipped with a chiral column (CHIRALCEL OJ, elution with *i*-PrOH-hexane, 1:9 v/v) after transformation into the benzoate by sequential alkaline methanolysis and benzoylation. The spectroscopic data (^{1}H NMR and MS) and TLC of the products were identical with those of (±)-**8** and (±)-**9**.

(–)-(1*R*,2*S*,5*S*)-7,8-Dioxabicyclo[3.2.1]oct-3-en-2-ol [(–)-8] from Enantiopure (–)-Acetate (–)-9

To a stirred solution of K_2CO_3 (276 mg, 2 mmol) in MeOH (5 mL) was added (–)-**9** (334 mg, 1.96 mmol) at room temperature and the stirring was continued for 30 min at the same temperature. The mixture was evaporated under reduced pressure, the residue was diluted with water and extracted with Et_2O. The extract was washed with brine, dried ($MgSO_4$), evaporated under reduced pressure, and the residue chromatographed (SiO_2 10 g, elution with Et_2O-hexane 3:1, v/v) to give (–)-**8** as colorless needles; yield: 229 mg (91%); mp 66–68 °C, $[\alpha]_D^{20}$: –28.8 (*c* 1.0, $CHCl_3$){lit.: mp 65–66.5 °C, $[\alpha]_D^{20}$: –35.3 (*c* 1.0, $CHCl_3$)[1c]; mp 70 °C, $[\alpha]_D^{20}$: –6.5 (*c* 1.7, $CHCl_3$)[15]; mp 67–69 °C, $[\alpha]_D$: –34 (*c* 1, $CHCl_3$)[16]}. The spectroscopic data (^{1}H NMR and MS) and TLC were identical with those of (±)-**8**.

(+)-(1*R*,2*S*,5*S*)-7,8-Dioxabicyclo[3.2.1]oct-3-en-2-ol [(+)-8] from Enantiopure (+)-Acetate +-(9)

To a stirred solution of K_2CO_3 (187 mg, 1.35 mmol) in MeOH (3 mL) was added (+)-acetate (+)-**9** (230 mg, 1.35 mmol) at room temperature and the stirring was continued for 30 min at the same temperature. The mixture was evaporated under reduced pressure, the residue was diluted with water and extracted with Et_2O. The extract was washed with brine, dried ($MgSO_4$), evaporated under reduced pressure, and the residue chromatographed (SiO_2 6 g, elution with Et_2O-hexane, 3:1 v/v) to give the (+)-alcohol (+)-**8**; yield: 149 mg (86%); mp 67–68 °C, $[\alpha]_D^{20}$: +28.1 (*c* 1.0, $CHCl_3$). The spectroscopic data (^{1}H NMR and MS) were identical with those of (±)-**8**.

(–)-Levoglucosenone [(–)-1]

To a stirred solution of (–)-**8** (34 mg, 0.27 mmol) in CH_2Cl_2 (2 mL) was added MnO_2 (342 mg, 3.94 mmol) at room temperature and the stirring was continued for 5 h at the same temperature. After filtration through a Celite pad, the filtrate was evaporated under reduced pressure and the residue chromatographed (SiO_2 1.5 g, elution with Et_2O-hexane, 5:1 v/v) to give (–)-**1** as a pale yellow oil; yield: 29 mg (87%); $[\alpha]_D^{28}$: –525 (*c* 1.2, $CHCl_3$) {lit.: $[\alpha]_D$: –460 (*c* 1.0, $CHCl_3$)[1a]; $[\alpha]_D^{27}$: –518 (*c* 1, $CHCl_3$)[1c]; $[\alpha]_D$: –458 (*c* 3.97, $CHCl_3$)[1d]}. The spectroscopic data and TLC were identical with those of an authentic material.[6]

(+)-Levoglucosenone [(+)-1]

Alcohol (+)-**8** (20 mg, 0.16 mmol) was oxidized with MnO_2 (203 mg, 2.3 mmol) as above to give (+)-**1** as a pale yellow oil; yield: 18 mg (88%); $[\alpha]_D^{28}$: +533 (*c* 1.5, $CHCl_3$) {lit.[4]: $[\alpha]_D$: +518 (*c* 1.2, $CHCl_3$)}. The spectroscopic data and TLC were identical with those of an authentic material.[6]

Acknowledgements

This research was supported by the Ministry of Science, Culture, and Sports, Japan.

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