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Lipase-mediated kinetic resolution of tricyclic acyloins, *endo*-3-hydroxytricyclo[4.2.1.$0^{2,5}$]non-7-en-4-one and *endo*-3-hydroxytricyclo[4.2.2.$0^{2,5}$]dec-7-en-4-one

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Abstract: Kinetic resolution of tricyclic acyloins, *endo*-3-hydroxytricyclo[4.2.1.$0^{2,5}$]non-7-en-4-one and *endo*-3-hydroxytricyclo[4.2.2.$0^{2,5}$]dec-7-en-4-one, and their acetates has been examined using a lipase. It has been found that a facile and stereoselective kinetic resolution occurs both in organic solvent and an aqueous solution in enantiocomplementary ways to afford both enantiomers of the acyloins and their acetates in enantiomerically pure forms. Enantiomerization of (+)-acyloins leading to (−)-acyloin acetates has also been achieved by the same lipase in an organic solvent by addition of a catalytic amount of triethylamine. © 1997 Elsevier Science Ltd

Quite recently, we found that the racemic tricyclic acyloin *endo*-3-hydroxytricyclo[4.2.1.$0^{2,5}$]non-7-en-4-one (±)-**1a** is transformed into one particular enantiomeric acetate (−)-**3a** in a satisfactory yield with an excellent enantiomeric excess of 97% ee on stirring with vinyl acetate in tetrahydrofuran containing a catalytic amount of triethylamine in the presence of lipase PS (*Pseudomonas* sp., Amano).[1] The reaction was reasoned to involve a dynamic interconversion[2] between the enantiomers (+)-**1a** and (−)-**1a**, *via* the *meso* ene-1,2-diol **2a**, in which the former enantiomer is selectively acetylated under these enzyme-mediated transesterification conditions to give rise to the single acetate (−)-**3a**. The acetate (−)-**3a** served as a good starting material for the construction of a versatile chiral building block ketodicyclopentadiene[3,4] (−)-**4** whose formation also determined the absolute configuration of the starting acetate (−)-**3a** (Scheme 1). Since this dynamic transesterification procedure provides only one particular enantiomeric product, we further examined the lipase-mediated kinetic resolution using the same racemic acyloin (±)-**1a** and its one carbon homologue racemic *endo*-3-hydroxytricyclo[4.2.2.$0^{2,5}$]dec-7-en-4-one (±)-**1b** in order to obtain both enantiomeric products as well as to extend applicability of the enzymatic reaction.[5] This paper describes an efficient procedure for an enantiocomplementary preparation of pairs of both enantiomeric acyloins **1a,b** and their acetates **3a,b** by employing the lipase-mediated kinetic resolution[6] carried out in both organic and aqueous media.

The racemic substrates **1a,b** and **3a,b** were prepared according to the established procedure[7] from the bicyclic *endo* diesters **5a,b** *via* the tricyclic *endo* ene-1,2-diol bis-silyl ethers **6a,b** without difficulty. Thus, the acyloin condensation of the diesters **5a,b** in the presence of trimethylsilyl chloride (TMS-Cl) gave the *meso* bis-silyl ethers **6a,b** which on hydrolysis with 5% hydrochloric acid gave stereoselectively the corresponding acyloins (±)-**1a,b** having *endo* hydroxy group in good overall yields. Acetylation of (±)-**1a,b** with acetic anhydride in pyridine afforded stereoselectively the *endo*-acetates (±)-**3a,b** each as a sole product, respectively. In these conversions it was noted that only the single diastereomers (±)-**1a,b** having an *endo*-hydroxy group and (±)-**3a,b** having an *endo*-acetoxy group were generated by stereoselective protonation from the convex face of the molecules. The *exo*-hydroxy and the *exo*-acetoxy products were not generated even under more forcing conditions. The *meso* ene-1,2-diol bis-acetate substrates **7a,b** were also prepared in moderate yields

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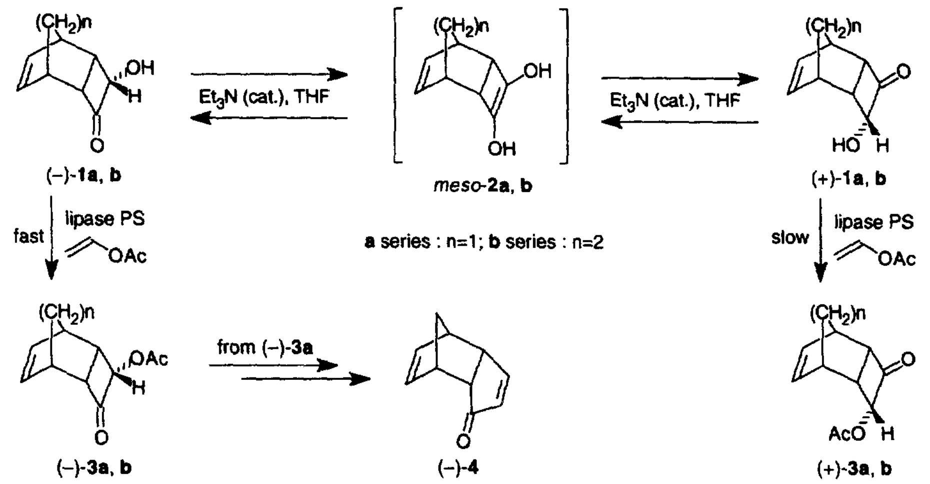
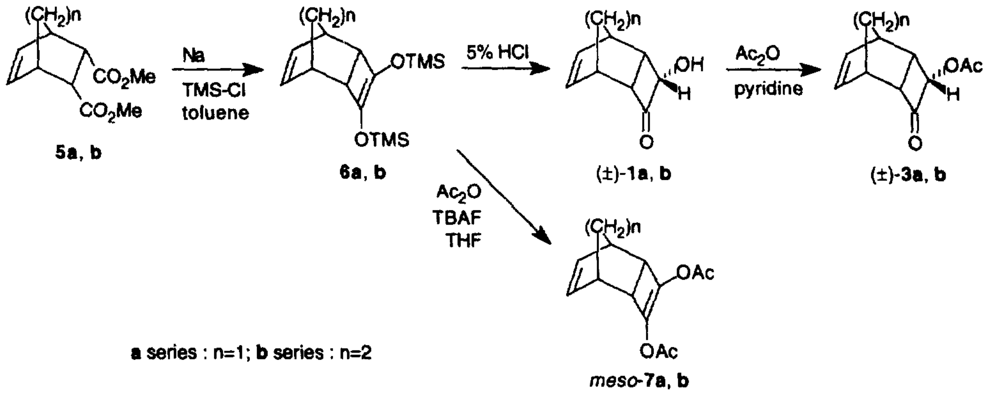


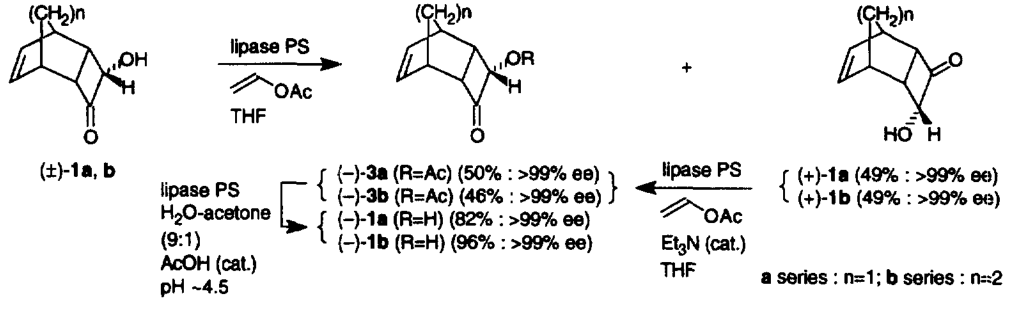
Scheme 1.

(≈50%) accompanied by the racemic acetates (±)-**3a**,**b** (≈50%) when the bis-silyl ethers **6a**,**b** were directly treated with acetic anhydride in THF in the presence of tetrabutylammonium fluoride (TBAF) (Scheme 2).



Scheme 2.

We first examined the kinetic resolution of the racemic acyloins (±)-**1a**,**b** under neutral conditions in organic solvent. Thus, on stirring with lipase PS in THF containing vinyl acetate (1.2 equiv.) at room temperature, (±)-**1a** furnished the optically active acetate (−)-**3a** in 50% yield accompanied by the unreacted acyloin (+)-**1** in 49% recovery. Similarly, the homologue acyloin (±)-**1b** furnished the homologue acetate (−)-**3b** and the unreacted homologue acyloin (+)-**1b** in yields of 46 and 49%. Enantiomeric excesses of the products were determined by HPLC using a chiral column which revealed all of the products to be enantiomerically pure (>99% ee). As the matter of course, the enantiomerically pure (+)-acyloins (+)-**1a**,**b** were inert under the same neutral resolution conditions, but they were readily transformed into the acetate (−)-**1a**,**b**, respectively, in yields of 63 and 71% both with >98% ee (by HPLC) with inversion of configuration when a catalytic amount of triethylamine was added to the each reaction mixture.[1] The single enantiomeric acetates (−)-**3a** and (−)-**3b** were also obtained in yields of 75 and 67% with 97 and 99% ee, respectively, when the racemic acyloins (±)-**1a**,**b** were treated as above in THF containing a catalytic amount of triethylamine. These indicated that the added amine induced the dynamic interconversion between the enantiomers of the acyloins **1a,b** intervening the *meso* ene-1,2-diol intermediates **2a,b** to afford the single enantiomeric acetates (−)-**3a,b** by lipase-mediated enantioselective transesterification of the (−)-acyloins **1a,b** under these equilibrium conditions,[1] respectively (Schemes 1 and 3).

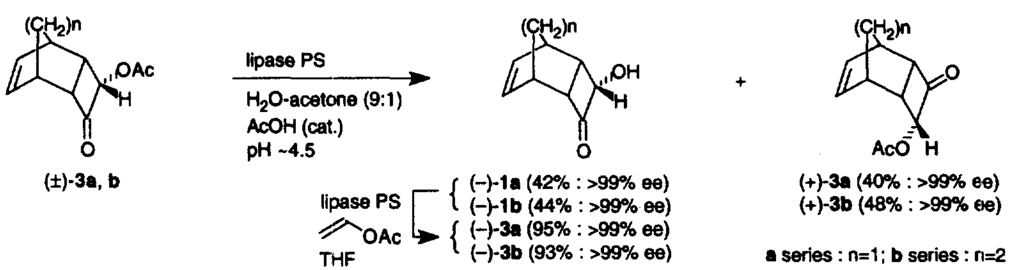


Scheme 3.

Chemical conversion of the enantiomerically pure acetates (−)-**3a,b** into the corresponding (−)-acyloins **1a,b** under alkaline conditions was found to be difficult to carry out without some racemization. However, when the enantiomerically pure acetates (−)-**3a,b** were stirred with lipase PS in a mixture of aqueous and acetone (9:1) containing a catalytic amount of acetic acid (pH≈4.5), the enantiomerically pure acyloins (−)-**1a,b** were obtained in excellent yields without losing their original enantiomeric excesses[8] (Scheme 3).

Employing the same procedure, we next examined the enzymatic hydrolysis of the racemic acetates (±)-**3a,b** in a weak acidic aqueous solution. Thus, the racemates **3a,b**, on stirring with lipase PS in a mixture of aqueous acetone (9:1) containing a catalytic amount of acetic acid (pH≈4.5) at room temperature, afforded the optically active acyloins (−)-**1a** and (−)-**1b** in yields of 42 and 44% with the unreacted optically active acetates, (+)-**3a** and (+)-**3b**, in recoveries of 40 and 48%, respectively. Enantiomeric excesses of all products were determined to be >99% by HPLC using a chiral column. The recovered enantiomerically pure acetates (+)-**3a,b** were stable under the same lipase-mediated aqueous conditions even after a prolonged stirring.

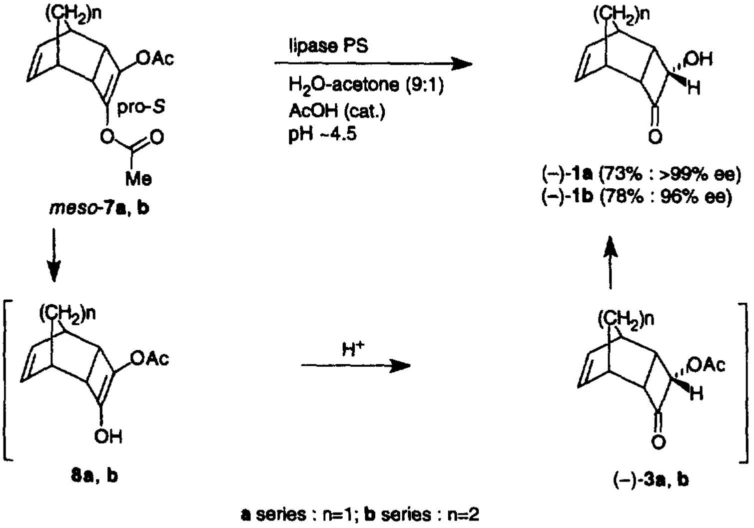
Acetylation of the optically active acyloins (−)-**1a,b** was also found to be difficult to carry out as basic conditions necessarily required for acylation induced partial racemization. This was again overcome by use of the lipase. Thus, the enantiomerically pure (−)-**1a,b** were stirred with vinyl acetate (1.2 equiv.) in THF in the presence of lipase PS[8] to furnish the acetates **3a** in 95% with >99% ee (by HPLC) and **3b** in 93% yield with 99% ee (by HPLC), respectively (Scheme 4).



Scheme 4.

On the other hand, the *meso* ene-1,2-diol bis-acetates **7a,b** exhibited an interesting stereochemical behavior under the lipase-mediated hydrolysis conditions. Thus, when **7a** was stirred with lipase PS in an aqueous acetone (9:1) containing a catalytic amount of acetic acid (pH≈4.5), asymmetric hydrolysis occurred to give the optically active acyloin (−)-**1a** in 73% yield with >99% ee. Similarly,

7b gave (−)-**1b** in 78% yield with 96% ee. The formation of the acyloins (−)-**1a,b** must involve the chemoselective reaction at the functionality that located on the opposite carbogenic center to the above *endo*-monoacetate substrates **3a,b**. Namely, in the bis-acetates **7a,b**, the first enzymatic hydrolysis occurred at the acetoxy functionality on the pro-*S* center selectively to give the acetoxy-enols **8a,b** which sequentially collapsed to the acyloins (−)-**1a,b** by stereoselective protonation followed by the second enzymatic hydrolysis of the resulting acetates (−)-**3a,b** otherwise the single acyloins (−)-**1a,b** could not be generated (Scheme 5).



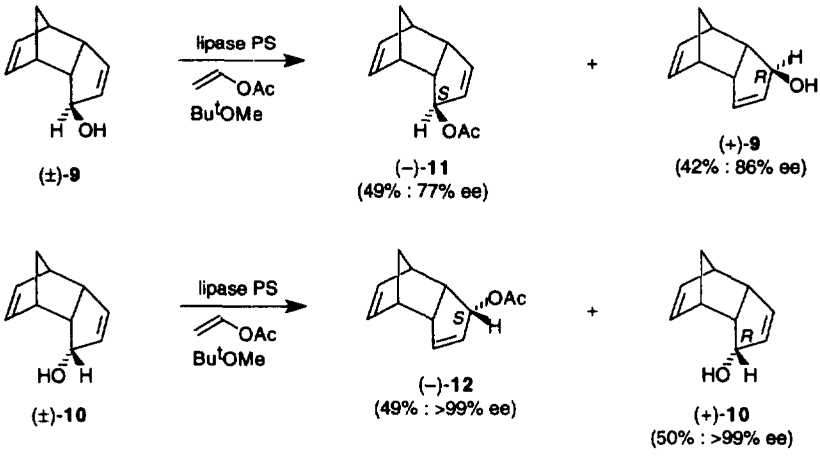
Scheme 5.

The observed outcome may be due to the steric interference existing in the tricyclic ene-1,2-diol bis-acetates **7a,b** which forces the acetoxy groups to extrude to the convex face. Of these acetoxy groups, the one that is located on the pro-*S* center could have a similar stereochemical situation to that of the *endo*-acetates (−)-**3a,b** to undergo stereoselective enzymatic reaction to give the transient enols **8a,b** leading to the acyloins (−)-**1a,b**. A similar stereochemical relationship in an enzymatic reaction has been observed in the kinetic transesterification of two diastereomeric racemic tricyclic alcohols, having the same stereochemical background, (±)-**9** and (±)-**10**, in which the selective reaction occurred at the opposite carbogenic centers, but at the same stereogenic *S* centers[9,10] (Scheme 6).

In summary, we have described an efficient kinetic resolution of two tricyclic acyloins, *endo*-3-hydroxytricyclo[4.2.1.$0^{2,5}$]non-7-en-4-one and *endo*-3-hydroxytricyclo[4.2.2.$0^{2,5}$]dec-7-en-4-one, and their acetates by employing lipase-mediated transesterification in an organic solvent for the former pair and lipase-mediated hydrolysis in aqueous solution for the latter pair. The transesterification reaction has also been shown to transform dynamically the optically active and the racemic acyloins into the one particular enantiomeric acyloin acetates with excellent enantiomeric excesses by addition of a catalytic amount of triethylamine to the reaction medium.

Experimental

Melting points were determined on a Yanagimoto hotstage instrument and are uncorrected. IR spectra were recorded on a JASCO-IR 700 spectrometer. ^{1}H NMR spectra were recorded on a Varian Gemini-2000 (300 MHz) spectrometer. Optical rotations were measured with a JASCO-DIP-370 digital polarimeter. Optical purities were determined on a Gilson Model-307 instrument equipped with a chiral column.



Scheme 6.

endo-*3,4-Bis-acetoxytricyclo[4.2.1.0^{2,5}]nona-3,7-diene 7a*

To a stirred solution of the bis-silyl ether[7] **6a** (3.0 g, 10 mmol) in THF (50 ml) was added successively acetic anhydride (2.4 ml, 25 mmol) and tetrabutylammonium fluoride (TABF) (1.0 M in THF, 25 ml, 25 mmol) at 0°C and the mixture was stirred at the same temperature for 1 h and at room temperature for 1 h. The mixture, after dilution with ether, was washed with brine, dried over $MgSO_4$, evaporated under reduced pressure, and chromatographed (SiO_2, 90 g, elution with Et_2O–hexane, 1:3) to give the bis-acetate **7a** (600 mg, 25%) as colorless crystals and the racemic acetate (±)-**3a** (1.4 g, 70%) as colorless crystals.

The bis-acetate **7a**: mp 33–35°C (Et_2O–hexane). IR (Nujol): ν=1761 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ=5.95 (2H, t, *J*=6.0 Hz), 3.20 (2H, d, *J*=7.4 Hz), 2.72 (2H, br s), 2.02 (6H, s), 1.94 (1H, d, *J*=8.2 Hz), 1.53 (1H, d, *J*=8.2 Hz). HRMS: Calcd for $C_{13}H_{14}O_4$: 234.0891 (M$^+$). Found: 234.0871.

endo-*3,4-Bis-acetoxytricyclo[4.2.2.0^{2,5}]deca-3,7-diene 7b*

To a stirred solution of the bis-silyl ether[7] **6b** (700 mg, 2.3 mmol) in THF (20 ml) was added successively acetic anhydride (540 µl, 5.7 mmol) TBAF (1.0 M in THF, 5.7 ml, 5.7 mmol) at 0°C and the mixture was stirred at the same temperature for 1 h and at room temperature for 1 h. The mixture, after dilution with ether, was washed with brine, dried over $MgSO_4$, evaporated under reduced pressure, and chromatographed (SiO_2, 30 g, elution with Et_2O–hexane, 1:3) to give the bis-acetate **7b** (282 mg, 50%) as colorless crystals and the racemic acetate (±)-**3b** (187 mg, 50%) as colorless crystals.

The bis-acetate **7b**: mp 56–57°C (Et_2O–hexane). IR (Nujol): ν=1755 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ=6.01 (2H, dd, *J*=4.7, 3.2 Hz), 2.83–2.79 (2H, m), 2.71–2.63 (2H, m), 2.10 (6H, s), 1.46–1.30 (4H, m). HRMS: Calcd for $C_{14}H_{16}O_4$: 248.1048 (M$^+$). Found: 248.1055.

(−)-(1R,2S,3S,5R,6S)-3-Acetoxytricyclo[4.2.1.0^{2,5}]non-7-en-4-one 3a via *dynamic conditions*

A suspension of the racemic acyloin[7] (±)-**1a** (4.5 g, 30 mmol) and lipase PS-on-Celite (4.5 g) in THF (80 ml) containing vinyl acetate (3.3 ml, 36 mmol) and triethylamine (0.4 ml, 3 mmol) was stirred at room temperature for 48 h. After filtration of the mixture through a Celite pad, the filtrate was evaporated under reduced pressure. The residue dissolved in ether was washed with brine, dried over $MgSO_4$, evaporated under reduced pressure, and chromatographed (SiO_2, 150 g, elution with Et_2O–hexane, 1:3) to give the acetate (−)-**3a** (4.3 g, 75%): mp 56–58°C (Et_2O–hexane), $[\alpha]_D^{24}$ −120.7 (*c* 2.0, $CHCl_3$), 97% ee (CHIRALCEL OD, 5% Pr^{i}OH–hexane).

IR (Nujol): ν=1786, 1743 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ=6.14 (1H, dd, *J*=5.5, 3.0 Hz), 6.01 (1H, dd, *J*=5.5, 3.0 Hz), 5.35 (1H, dd, *J*=8.8, 3.3 Hz), 3.63 (1H, ddd, *J*=7.4, 5.5, 3.3 Hz), 3.39 (1H, ddd,

J=8.8, 5.5, 4.7 Hz), 3.23–3.17 (1H, m), 3.15–3.09 (1H, m), 2.08 (3H, s), 1.77 (1H, br d, J=8.5 Hz), 1.53 (1H, br d, J=8.5 Hz). HRMS: Calcd for $C_{11}H_{12}O_3$: 192.0786 (M^+). Found: 192.0828.

*(−)-(1R,2S,3S,5R,6S)-3-Acetoxytricyclo[4.2.2.0^{2,5}]dec-7-en-4-one **3b*** via *dynamic conditions*

A suspension of the racemic acyloin[7] (±)-**1b** (2.0 g, 12.2 mmol) and lipase PS-on-Celite (2 g) in THF (40 ml) containing vinyl acetate (1.3 ml, 14.6 mmol) and triethylamine (0.2 ml, 1.2 mmol) was stirred at room temperature for 48 h. The reaction mixture was treated as above to give the acetate (−)-**3b** (1.7 g, 67%) and the unreacted acyloin **1b** (320 mg, 16%) after chromatographic separation (SiO_2, 60 g, elution with Et_2O–hexane, 1:3). (−)-**3b**: mp 63–65°C (Et_2O–hexane), $[\alpha]_D^{27}$ −127.5 (*c* 1.0, $CHCl_3$), 99% ee (CHIRALCEL OD, 5% Pr^iOH–hexane).

IR (Nujol): ν=1785, 1745 cm^{-1}. ^1H NMR ($CDCl_3$): δ=6.21 (1H, ddd, J=7.3, 6.3, 1.4 Hz), 6.13 (1H, td, J=7.3, 1.1 Hz), 5.50 (1H, dd, J=9.3, 3.3 Hz), 3.29 (1H, ddd, J=8.2, 4.9, 3.6 Hz), 2.90–2.97 (2H, m), 2.74–2.78 (2H, m), 2.09 (3H, s), 1.23–1.65 (4H, m). HRMS: Calcd for $C_{12}H_{14}O_3$: 206.0942 (M^+). Found: 206.0949.

*Kinetic transesterification of the racemic acyloin (±)-**1a**, a formation of (−)-(1R,2S,3S,5R,6S)-3-acetoxytricyclo[4.2.1.0^{2,5}]non-7-en-4-one **3a** and (+)-(1S,2R,3R,5S,6R)-3-hydroxytricyclo-[4.2.1.0^{2,5}]non-7-en-4-one **1a***

A suspension of the racemic acyloin[7] (±)-**1a** (100 mg, 0.67 mmol) and lipase PS-on-Celite (100 mg) in THF (3 ml) containing vinyl acetate (74 µl, 0.8 mmol) was stirred at room temperature for 33 h. After filtration of the mixture through a Celite pad, the filtrate was evaporated under reduced pressure. The residue dissolved in ether was washed with brine, dried over $MgSO_4$, evaporated under reduced pressure, and chromatographed (SiO_2, 3 g, elution with Et_2O–hexane, 1:2) to give the (−)-acetate (−)-**3a** (64 mg, 50%) as colorless crystals and the (+)-acyloin (+)-**1a** (49 mg, 49%) as colorless crystals.

*(−)-Acetate (−)-**3a***

Mp 56–58°C (Et_2O–hexane), $[\alpha]_D^{29}$ −123.9 (*c* 1.0, $CHCl_3$), >99% ee (CHIRALCEL OD, 5% Pr^iOH–hexane). Spectral data (IR and ^1H NMR) and tlc were identical with those of (−)-**3a** obtained by the dynamic conditions above.

*(+)-Acyloin (+)-**1a***

Mp 104–106°C (Et_2O–hexane), $[\alpha]_D^{29}$ +216.9 (*c* 0.4, $CHCl_3$), >99% ee (CHIRALCEL OD, 5% Pr^iOH–hexane). IR (Nujol): ν=3376, 1761 cm^{-1}. ^1H NMR ($CDCl_3$): δ=6.19 (1H, dd, J=5.8, 3.0 Hz), 6.13 (1H, dd, J=5.8, 2.5 Hz), 4.43 (1H, m), 3.57 (1H, m), 3.09 (1H, m), 2.07 (1H, d, J=8.0 Hz), 1.77 (1H, d, J=8.2 Hz), 1.54 (1H, d, J=8.2 Hz). HRMS: Calcd for $C_9H_{10}O_2$: 150.0680 (M^+). Found: 150.0676.

*Kinetic transesterification of the racemic acyloin (±)-**1b**, a formation of (−)-(1R,2S,3S,5R,6S)-3-acetoxytricyclo[4.2.2.0^{2,5}]dec-7-en-4-one **3b** and (+)-(1S,2R,3R,5S,6R)-3-hydroxytricyclo-[4.2.2.0^{2,5}]dec-7-en-4-one **1b***

A suspension of the racemic acyloin[7] (±)-**1b** (200 mg, 1.2 mmol) and lipase PS-on-Celite (200 mg) in THF (8 ml) containing vinyl acetate (130 µl, 1.4 mmol) was stirred at room temperature for 20 h. After filtration of the mixture through a Celite pad, the filtrate was evaporated under reduced pressure. The residue dissolved in ether was washed with brine, dried over $MgSO_4$, evaporated under reduced pressure, and chromatographed (SiO_2, 6 g, elution with AcOEt–hexane, 1:9) to give the (−)-acetate (−)-**3b** (15 mg, 46%) as colorless crystals and the (+)-acyloin (+)-**1b** (97 mg, 49%) as colorless crystals.

(−)-Acetate (−)-3b

Mp 63–65°C (Et_2O–hexane), >99% ee (CHIRALCEL OD, 5% Pr^iOH–hexane). Spectral data (IR and ^1H NMR) and tlc were identical with those of (−)-**3a** obtained by the dynamic conditions above.

(+)-Acyloin (+)-1b

Mp 113–115°C (AcOEt–hexane), $[\alpha]_D^{30}$ +254.8 (*c* 1.0, $CHCl_3$), >99% ee (CHIRALCEL OD, 10% Pr^iOH–hexane). IR (Nujol): ν=3367, 1765 cm^{-1}. ^1H NMR ($CDCl_3$): δ=6.29 (1H, ddd, *J*=8.2, 6.3, 1.4 Hz), 6.20 (1H, dd, *J*=7.3, 6.3 Hz), 4.65 (1H, m), 3.21 (1H, td, *J*=8.2, 4.2 Hz), 2.96–2.80 (2H, m), 2.43 (1H, d, *J*=9.1 Hz), 1.67–1.22 (4H, m). HRMS: Calcd for $C_{10}H_{12}O_2$: 164.0837 (M^+). Found: 164.0836.

Kinetic hydrolysis of the racemic acetate (±)-3a, a formation of (−)-(1R,2S,3S,5R,6S)-3-hydroxytricyclo[4.2.1.0^{2,5}]non-7-en-4-one 1a and (+)-(1S,2S,3S,5S,6R)-3-acetoxytricyclo[4.2.1.0^{2,5}]non- 7-en-4-one 3a

To a stirred solution of the racemic acetate[7] (±)-**3a** (100 mg, 0.52 mmol) in a mixture of H_2O and acetone (9:1, 3 ml) adjusted at pH 4.5 by addition of acetic acid was suspended with lipase PS-on-Celite (100 mg) at room temperature and the mixture was stirred at the same temperature for 20 h. After filtration of the mixture through a Celite pad, the filtrate was evaporated under reduced pressure. The residue dissolved in ether was washed with brine, dried over $MgSO_4$, evaporated under reduced pressure, and chromatographed (SiO_2, 3 g, elution with Et_2O–hexane, 1:2) to give the (+)-acetate (+)-**3a** (40 mg, 40%) as colorless crystals and the (−)-acyloin (−)-**1a** (33 mg, 42%) as colorless crystals.

(+)-Acetate (+)-3a

Mp 56–58°C (Et_2O–hexane), $[\alpha]_D^{29}$ +123.0 (*c* 0.5, $CHCl_3$), >99% ee (CHIRALCEL OD, 5% Pr^iOH–hexane). Spectral data (IR and ^1H NMR) and tlc were identical with those of an authentic material.

(−)-Acyloin (−)-1a

Mp 104–106°C (AcOEt–hexane), $[\alpha]_D^{27}$ −217.3 (*c* 0.7, $CHCl_3$), >99% ee (CHIRALCEL OD, 5% Pr^iOH–hexane). Spectral data (IR and ^1H NMR) and tlc were identical with those of an authentic material.

Kinetic hydrolysis of the racemic acetate (±)-3b, a formation of (−)-(1R,2S,3S,5R,6S)-3-hydroxytricyclo[4.2.2.0^{2,5}]dec-7-en-4-one 1b and (+)-(1S,2R,3R,5S,6R)-3-acetoxytricyclo[4.2.2.0^{2,5}]dec- 7-en-4-one 3b

To a stirred solution of the racemic acetate[7] (±)-**3b** (100 mg, 0.5 mmol) in a mixture of H_2O and acetone (9:1, 3 ml) adjusted at pH 4.5 by addition of acetic acid was suspended with lipase PS-on-Celite (100 mg) at room temperature and the mixture was stirred at the same temperature for 24 h. After filtration of the mixture through a Celite pad, the filtrate was evaporated under reduced pressure. The residue dissolved in ether was washed with brine, dried over $MgSO_4$, evaporated under reduced pressure, and chromatographed (SiO_2, 3 g, elution with AcOEt–hexane, 1:9) to give the (+)-acetate (+)-**3b** (48 mg, 48%) as colorless crystals and the (−)-acyloin (−)-**1b** (35 mg, 44%) as colorless crystals.

(+)-Acetate (+)-3b

Mp 56–58°C (Et_2O–hexane), $[\alpha]_D^{30}$ +127.6 (*c* 0.3, $CHCl_3$), >99% ee (CHIRALCEL OD, 5% Pr^iOH–hexane). Spectral data (IR and ^1H NMR) and tlc were identical with those of an authentic material.

*(−)-Acyloin (−)-**1b***

Mp 113–115°C (AcOEt–hexane), $[\alpha]_D^{27}$ −255.1 (*c* 0.4, $CHCl_3$), >99% ee (CHIRALCEL OD, 10% Pr^iOH–hexane). Spectral data (IR and ^1H NMR) and tlc were identical with those of an authentic material.

Kinetic hydrolysis of the meso *bis-acetate **7a***

To a stirred solution of the bis-acetate **7a** (100 mg, 0.43 mmol) in a mixture of H_2O and acetone (9:1, 3 ml) adjusted at pH 4.5 by addition of acetic acid was suspended with lipase PS-on-Celite (100 mg) at room temperature and the mixture was stirred at the same temperature for 15 h. After filtration of the mixture through a Celite pad, the filtrate was evaporated under reduced pressure. The residue dissolved in AcOEt was washed with brine, dried over $MgSO_4$, evaporated under reduced pressure, and chromatographed (SiO_2, 5 g, elution with AcOEt–hexane, 1:1) to give the acyloin (−)-**1a** (60 mg, 73%) as colorless crystals: mp 104–106°C (AcOEt–hexane), >99% ee (CHIRALCEL OD, 5% Pr^iOH–hexane). Spectral data (IR and ^1H NMR) and tlc were identical with those of an authentic material.

Kinetic hydrolysis of the meso *bis-acetate **7b***

To a stirred solution of the bis-acetate **7b** (100 mg, 0.4 mmol) in H_2O and acetone (9:1, 3 ml) adjusted at pH 4.5 by addition of acetic acid was suspended with lipase PS-on-Celite (100 mg) at room temperature and the mixture was stirred at the same temperature for 17 h. After filtration of the mixture through a Celite pad, the filtrate was evaporated under reduced pressure. The residue dissolved in AcOEt was washed with brine, dried over $MgSO_4$, evaporated under reduced pressure, and chromatographed (SiO_2, 3 g, elution with AcOEt–hexane, 1:4) to give the acyloin (−)-**1b** (65 mg, 78%) as colorless crystals: mp 113–115°C (AcOEt–hexane), >96% ee (CHIRALCEL OD, 10% Pr^iOH–hexane). Spectral data (IR and ^1H NMR) and tlc were identical with those of an authentic material.

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