Enzymatic Kinetic Resolution of 5-Hydroxy-4-oxa-*endo*-tricyclo[5.2.1.$0^{2,6}$]dec-8-en-3-ones: A Useful Approach to D-Ring Synthons for Strigol Analogues with Remarkable Stereoselectivity

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Received May 31, 1996[⊗]

Racemic 5-hydroxy-4-oxa-*endo*-tricyclo[5.2.1.$0^{2,6}$]dec-8-en-3-one and its 2-methyl analogue were resolved employing a lipase-catalyzed acetylation reaction. The latter compound thus gave access to a homochiral D-ring synthon for strigolactones. The enzymatic acetylation reaction occurred with a remarkable inversion of configuration at C-5, through which it is possible to achieve a highly efficient asymmetric synthesis of 5-acetoxy-2(5*H*)-furanone.

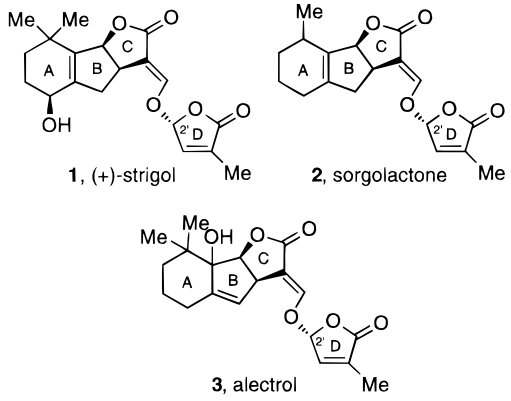
(+)-Strigol (**1**) and some structurally related sesquiterpene lactones sorgolactone (**2**) and alectrol (**3**) are members of the "strigolactone" family,[1] which induce germination of seeds of the parasitic weeds *Striga* and *Orobanche*.[2−4]

These weeds cause severe damage to graminaceous and leguminous crops in tropical and semitropical areas in the eastern hemisphere.[5−7] As part of our interest in the (asymmetric) synthesis of the strigolactones and their synthetic analogues[8−12] we recently devised an asymmetric synthesis of the tricyclic *exo*-chloro lactone **4a** (Scheme 1),[13] which can be regarded as a homochiral D-ring synthon. This D-ring is a common structural feature of the strigolactones and is of prime importance for full biological activity. Even the absolute stereochemistry at C-2′ is essential for optimal stimulation of germination.[12,14,15]

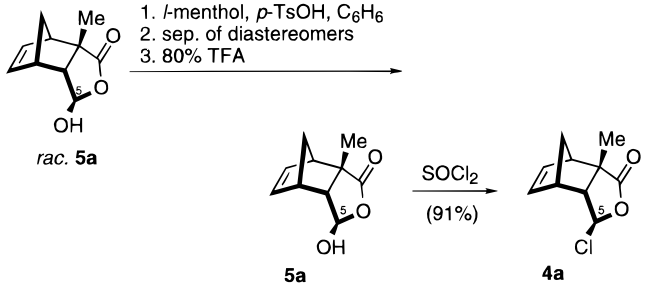
The key step in the synthesis of **4a** involves menthylation with *l*-menthol to give a 1:1 mixture of diastereomeric menthyl ethers, separation of the diastereomers, followed by acidic hydrolysis to give the enantiopure hydroxy lactone **5a**. This method provides access to both enantiomers of **5a** by choosing the appropiate enantiomer of menthol. However, the resolution is quite laborious since it requires two steps and a careful selective recrystallization. Moreover, 1 equiv of the chiral auxiliary is required. In order to circumvent these problems, a study was undertaken to improve the resolution, using an enzymatic approach.

Enzymes currently find widespread use in synthetic organic chemistry.[16a−d] A prominent example of an enzymatic asymmetric transformation is the kinetic resolution of a racemic alcohol R*OH in the presence of

Chart 1



Scheme 1



[⊗] Abstract published in *Advance ACS Abstracts,* September 15, 1996.

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S0022-3263(96)01022-5 CCC: $12.00

Scheme 2

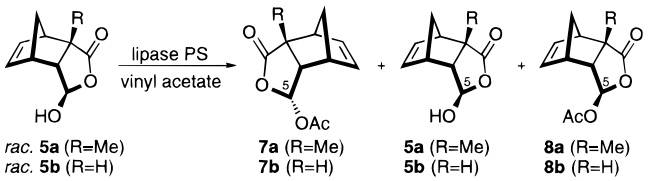


Table 1. Lipase PS-Catalyzed Transesterification of *endo*-Tricyclic Hydroxy Lactone *rac*-5a

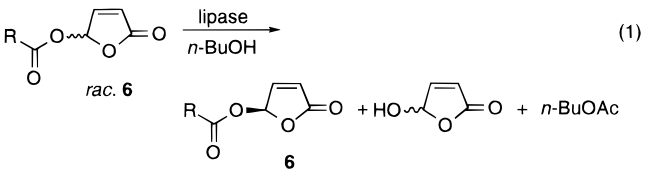
			product distribution (%)		
entry	time, h	conversion (%)	**7a** (% ee)	**5a** (% ee)	**8a**
1	22	30.8	30.2 (>90)	69.2 (41)	0.6
2	46	48.0	45.7 (87)	52.0 (79)	2.3
3	70	56.2	51.6 (87)	43.8 (85)	4.6

an acyl donor $R^2C(O)OR^3$, catalyzed by a lipase. The charm of this methodology lies in the facts that organic solvents can be used, workup is extremely simple, and a large variety of substrates is tolerated in this transformation. The application of enol esters as irreversible acyl donors[16b] makes this type of resolution even more attractive. In the present paper we describe the kinetic resolution of racemic *endo*-tricyclic hydroxy lactones **5** employing vinyl acetate as irreversible acyl donor, catalyzed by lipase PS.

Results and Discussion

Starting *endo*-tricyclic *exo*-hydroxy lactones **5** were obtained by standard literature procedures. Hydroxy lactone **5a** was prepared by a Diels−Alder reaction of citraconic anhydride and cyclopentadiene, followed by partial reduction according to the procedure of Canonne.[17] Hydroxy lactone **5b** was obtained by photooxidation of furfural[18] and subsequent Diels−Alder reaction with cyclopentadiene.

Kinetic Resolution. In a recent paper Kellogg *et al.* described the lipase-mediated transesterification of 5-acyloxy-2(5*H*)-furanones *rac*-**6** with 1-butanol resulting in ee's ranging from 68−98% (eq 1) with hitherto unknown stereochemistry.[19]



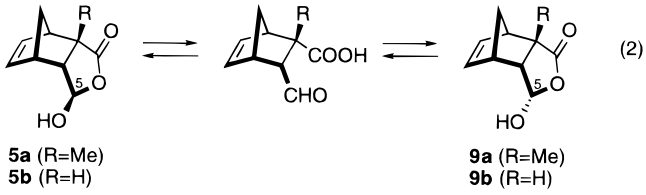
(1)

We have studied the irreversible acetylation of *endo*-tricyclic *exo*-hydroxy lactones **5** in the presence of vinyl acetate in dichloromethane catalyzed by lipase PS (Scheme 2). The results are collected in Tables 1 and 2.

As can be deduced from the data shown in Tables 1 and 2, the lipase PS-mediated acetylation of hydroxy lactones **5** is accomplished in good to excellent ee's. It should be emphasized that this conversion does not take place when other lipases were employed (lipase A, lipase R). Along with the *endo*-acetates **7a** and **7b**, *exo*-acetates **8a** and **8b** were formed in minor amounts (Tables 1 and 2). A striking observation is the fact that this reaction takes place with epimerization at C-5. The formation of the *endo*-acetates **7a** and **7b** could readily be deduced from ^{1}H-NMR analysis. The acetal proton H_5 of the *endo*-isomers **7a** and **7b** exhibited a doublet (^3J = 7 Hz for **7a** and 6 Hz for **7b**) at ca. 0.6 ppm lower field as compared to the corresponding *exo*-isomers (^3J = 1 Hz), which is in agreement with previous observations.[13] These results suggest that the reaction takes place via the thermodynamically unfavorable *endo*-hydroxy epimers **9**, which can be formed from the corresponding *exo*-isomers by *mutarotation* (eq 2). During NMR experiments in $CDCl_3$, we never observed the presence of the *endo*-epimers in the solution.

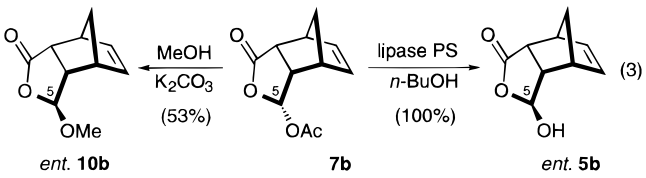
Table 2. Lipase PS-Catalyzed Transesterification of *endo*-Tricyclic Hydroxy Lactone *rac*-5b

			product distribution (%)		
entry	time, h	conversion (%)	**7b** (% ee)	**5b** (% ee)	**8b**
1	17	39.0	39.0 (>90)	61.0 (56)	0
2	47	53.5	50.0 (>90)	46.5 (>90)	3.5
3	17 days	60.8	45.2 (>90)	39.2 (>90)	15.6



(2)

It should be noted that it is not possible to obtain the *endo*-acetates by any other means. Acetylation reactions under conventional conditions, such as Ac_2O/pyridine or Ac_2O/*p*-TsOH, gave exclusively the *exo*-acetates **8**. In order to gain information about the existence of the *exo*/*endo* equilibrium (eq 2), we subjected the *endo*-acetate **7b** to a transesterification reaction. However, employing MeOH as a solvent in the presence of K_2CO_3 the expected *exo*-hydroxy lactone *ent*-**5b** was not obtained, but *exo*-methoxy lactone *ent*-**10b** was isolated as the main product (eq 3). Therefore, we switched to the enzymatic approach. Lipase PS-catalyzed transesterification in the presence of 10 equiv of *n*-BuOH in CH_2Cl_2 led to the exclusive formation of *exo*-hydroxy lactone *ent*-**5b** (eq 3). Again, no trace of *endo*-hydroxy lactone could be detected.



(3)

The results obtained with lipase PS-catalyzed acetylation of racemic hydroxy lactones **5** (Scheme 2) fit into a model in which only one enantiomer of the thermodynamically unfavorable *endo*-hydroxy lactones **9** is withdrawn from the *exo*/*endo* equilibrium (eq 2) to undergo a relatively fast enzymatic acetylation reaction. This sequence is an example of the *Curtin−Hammett* principle.[20] This remarkably large kinetic difference between

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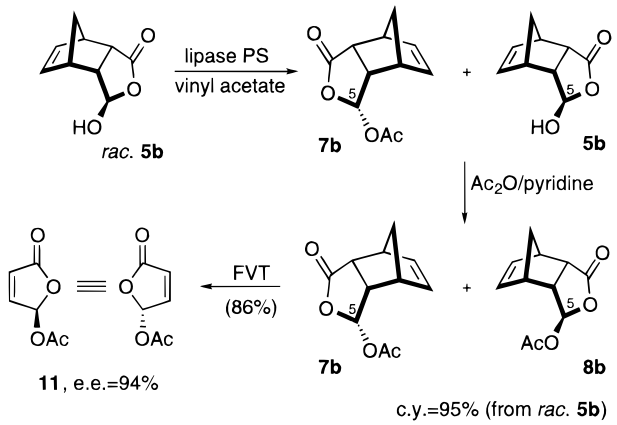
Scheme 3



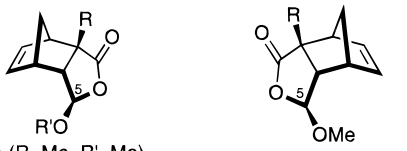
the *endo*- and *exo*-hydroxy lactones results in an excellent selectivity of product formation. It should be noted that in the absence of the lipase no conversion into **7a,b** or **8a,b** was observed even after 17 days. This implies that the formation of *exo*-acetates **8a,b** (*e.g.* Table 2, entry 3) is also catalyzed by the lipase, albeit in a much lower rate. The formation of the *exo*-acetates **8a** and **8b**, which are diastereomeric to the initially formed products **7a,b**, takes place via the *exo*-epimers **5a** and **5b**, respectively. This formation of diastereomers **7** and **8**, which is the ultimate result of the *exo*/*endo* equilibrium as depicted in eq 2, is quite unusual in kinetic resolutions.

The interesting finding shown in Scheme 2 can be advantageously utilized to achieve a sequence with full *chiral economy* (Scheme 3) in the following manner.

The crude mixture of **7b** and **5b**, obtained by kinetic resolution of *rac*-**5b** is acetylated under standard conditions to give the diastereomeric products **7b** and **8b**. Without further purification this mixture was subjected to a cycloreversion reaction, employing the technique of flash vacuum pyrolysis (FVT). This reaction led to the formation of one single isomer of 5-acetoxy-2(5*H*)-furanone **11**. This remarkable result can be rationalized by taking into account that a double stereodifferentiation has taken place. These results demonstrate the successful application of an enzymatic kinetic resolution of a racemic mixture, providing one single enantiomer without purification of any intermediate.

Determination of Enantiomeric Excess and Absolute Configuration. The ee's of the tricyclic hydroxy lactones **5a** and **5b** were established after menthylation with *l*-menthol to give the corresponding *l*-menthyloxy lactones **12a** and **12b** as a mixture of diastereomers with known absolute stereochemistry.[13,21] The de's could thus be determined by comparison of the relative intensities of the acetal H_5 proton signals in the ^{1}H-NMR spectrum. As there is no stereochemical preference in the menthylation reaction,[13] this derivatization allows the determination of the ee's of the hydroxy lactones **5**. Moreover, this derivatization to menthyl acetals **12** with known stereochemistry enables the unambigious assignment of the absolute stereochemistry as is shown (Scheme 2). Although effective, a more convenient procedure to determine the respective ee's involves the conversion of hydroxy lactones **5** and *endo*-acetoxy lactones **7** into the corresponding methyl acetals **10a,b** and *ent*-**10a,b**. These methylations occurred with complete *exo* selectivity in almost quantitative yields.

Chart 2



The ee's then were determined employing 400 MHz ^{1}H-NMR analysis in the presence of the chiral shift reagent Eu(hfc)$_3$ (1.5 equiv). In the case of methoxy lactones **10a** and *ent*-**10a** a difference of 0.03 ppm was observed for the α-methyl protons. On the other hand, the ee of methoxy lactone **10b**[22] was calculated on the basis of a 0.03 ppm difference of chemical shift of the acetal proton H_5 as compared to its enantiomer *ent*-**10b**. The determination of ee of acetoxy-2(5*H*)-furanone **11** was accomplished by comparison of the relative intensities of the CH_3 signals in the ^{1}H-NMR spectrum using 0.4 equiv of Eu(hfc)$_3$, which resulted in a downfield shift of approximately 0.8 ppm and a difference of 0.16 ppm for both enantiomers. On the basis of the above assignment of the absolute stereochemistry the levorotatory 5-acetoxy-2(5*H*)-furanone **11**, obtained by Kellogg *et al.* according to eq 1,[19] can be assigned as 5(*R*).

Conclusion

Lipase PS-mediated acetylation proved to be a simple, highly efficient method for the kinetic resolution of racemic tricyclic hydroxy lactones **5**. Employing this methodology it is possible to synthesize both enantiomers of *exo*-chloro lactones **4a**. These optically active latent butenolides are useful synthons for the preparation of homochiral strigolactones.[13] The kinetic resolution was accompanied with a remarkable epimerization, which could be used to demonstrate the synthesis of enantiopure 5-acetoxy-2(5*H*)-furanone **11** with optimal "chiral economy".

Experimental Section

General. For general methods and instrumentation, see ref 13. GC-MS spectra were run on a Varian Saturn 2 GC-MS ion-trap system. Separation was carried out on a fused-silica capillary column (DB-5, 30 m × 0.25 mm). Helium was used as carrier gas, and electron impact (EI) was used as ionization mode. Lipase PS was obtained from Amano as a gift.

General Procedure for the Enzymatic Kinetic Resolution of the Tricyclic Hydroxy Lactones *rac*-5a and *rac*-5b. To a solution containing *exo*-hydroxy tricyclic lactone *rac*-**5a**[17] (500 mg, 2.79 mmol) and vinyl acetate (2.57 mL, 27.9 mmol) in CH_2Cl_2 (25 mL) were added lipase PS (1.0 g) and powdered 4A molecular sieves (0.5 g). The suspension was stirred vigorously at room temperature. At given intervals (Tables 1 and 2) samples were taken (3 mL) and filtered over hyflo. The hyflo was washed with CH_2Cl_2, and the crude mixture was analyzed by 100 MHz ^{1}H-NMR ($CDCl_3$) for conversion. Purification by chromatography (SiO_2, hexane/ethyl acetate 3:1) afforded *endo*-acetate **7a** as a white solid and *exo*-alcohol **5a** as a white solid, which were analyzed for ee (*vide infra*).

Enantiomeric Excess Determination. The hydroxy lactones **5a** and **5b** were transformed into the corresponding

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l-menthyl ethers **12**.[13,21] Alternatively, **5a** and **5b** were converted into the corresponding *exo*-methoxy lactones **10a**, **10b** and subsequently analyzed by 400 MHz ^{1}H-NMR ($CDCl_3$) in the presence of ca. 1.5 equiv of Eu(hfc)$_3$ (*vide infra*). Similarly, *endo*-acetates **7a** and **7b** were methylated to give *ent*-**10a** and *ent*-**10b**, respectively (*vide infra*), which were analyzed for ee in the same manner.

5(*R*)-Acetoxy-2(*R*)-methyl-4-oxa-*endo*-tricyclo[5.2.1.0^{2,6}]-dec-8-en-3-one (7a) and 5(*R*)-hydroxy-2(*S*)-methyl-4-oxa-*endo*-tricyclo[5.2.1.0^{2,6}]dec-8-en-3-one (5a). These compounds were synthesized according to the general procedure starting from *rac*-**5a**[17] (3.00 g, 16.7 mmol). The reaction was stopped after 73 h. Purification by chromatography (SiO_2, hexane/ethyl acetate 3:1) gave **7a** (1.28 g, 34%) as a white solid and **5a** (1.18 g, 39%) as a white solid. Analytical samples of **5a** and **7a** were obtained by recrystallization from hexane/ethyl acetate.

7a: mp 98.5−101.5 °C; $[\alpha]_D$ −88.4° (*c* 0.4, CH_2Cl_2); ^{1}H-NMR ($CDCl_3$, 100 MHz): δ 1.54 (s, 3H), 1.69 (m, 2H), 2.15 (s, 3H), 2.85 (m, 1H), 2.87 (dd, J = 3.9, 7.0 Hz, 1H), 3.04 (m, 1H), 6.26 (m, 2H), 6.50 (d, J = 7.0 Hz, 1H); GC-MS (EI, *m*/*z*, rel int (%)): 163 (M^+ − OAc, 90.4), 157 (1.7), 152 (23.4), 97 (13.6), 91 (16.9), 66 (100). Anal. Calcd for $C_{12}H_{14}O_4$: C, 64.85; H, 6.35. Found: C, 65.28; H, 6.31.

5a: All analytical data (Mp, $[\alpha]_D$, ^{1}H-NMR, and mass data) were in complete agreement with those reported previously.[13]

5(*R*)-Acetoxy-4-oxa-*endo*-tricyclo[5.2.1.0^{2,6}]dec-8-en-3-one (7b) and 5(*R*)-Hydroxy-4-oxa-*endo*-tricyclo[5.2.1.0^{2,6}]-dec-8-en-3-one (5b). These compounds were synthesized according to the general procedure starting from *rac*-**5b**[17] (3.00 g, 18.1 mmol). The reaction was stopped after 46 h. Purification by chromatography (SiO_2, hexane/ethyl acetate 3:1) gave **7b** (1.65 g, 44%) as a white solid and **5b** (1.41 g, 47%) as a white solid. Analytical samples of **5b** and **7b** were obtained by recrystallization from hexane/ethyl acetate.

7b: mp 116.5−118 °C; $[\alpha]_D$ −126.0° (*c* 1.0, CH_2Cl_2); ^{1}H-NMR ($CDCl_3$, 100 MHz): δ 1.47 (dt, J = 1.0 Hz, 9.0 Hz, 1H), 1.65 (dt, J = 1.0 Hz, 9.0 Hz, 1H), 2.15 (s, 3H), 3.11 (m, 1H), 3.36 (m, 3H), 6.25 (m, 2H), 6.48 (d, J = 6.0 Hz, 1H); GC-MS (EI, *m*/*z*, rel int (%)): 166 (M^+ + 1 − Ac, 12.2), 149 (M^+ − OAc, 49.2), 137 (12.2), 91 (42.3), 83 (9.1), 66 (100). Anal. Calcd for $C_{11}H_{12}O_4$: C, 63.45; H, 5.81. Found: C, 63.55; H, 5.79.

5b: mp 134−136.5 °C; $[\alpha]_D$ +53.2° (*c* 0.2, CH_2Cl_2); ^{1}H-NMR ($CDCl_3$, 100 MHz): δ 1.37 (dt, J = 1.0 Hz, 8.5 Hz, 1H), 1.56 (dt, J = 1.0 Hz, 8.5 Hz, 1H), 2.86 (m, 1H), 3.33 (m, 3H), 4.83 (br s, 1H), 5.16 (br s, 1H), 6.14 (m, 2H); GC-MS (EI, *m*/*z*, rel int (%)): 167 (M^+ + 1, 1.9), 149 (2.0), 91 (29.3), 83 (3.1), 66 (100). Anal. Calcd for $C_9H_{10}O_3$: C, 65.05; H, 6.07. Found: C, 64.97; H, 6.00.

5(*S*)-Hydroxy-4-oxa-*endo*-tricyclo[5.2.1.0^{2,6}]dec-8-en-3-one (*ent*-5b). A solution containing **7b** (50 mg, 0.24 mmol) and *n*-BuOH (0.22 mL, 24 mmol) in CH_2Cl_2 (3 mL) were treated with lipase PS (100 mg) and powdered 4A molecular sieves (50 mg). The suspension was stirred vigorously at room temperature. After 24 h the suspension was filtered over hyflo and washed with CH_2Cl_2, and the filtrate was concentrated *in vacuo*. Yield 39.0 mg, 98% of pure *ent*-**5b** as a white solid. An analytical sample was obtained by recrystallization from hexane/ethyl acetate. Mp 130.5−131.5 °C; $[\alpha]_D$ −48.6° (*c* 0.2, CH_2Cl_2); ^{1}H-NMR and mass data were the same as for compound **5b**.

Racemic *exo*-5-Methoxy-2-methyl-4-oxa-*endo*-tricyclo-[5.2.1.0^{2,6}]dec-8-en-3-one (*rac*-10a). For determination of ee of 5(*R*)-hydroxy lactone **5a**. *rac*-**5a** (50 mg, 0.28 mmol) was treated with methanol (2 mL) and 1 drop of thionyl chloride. The solution was stirred for 30 min and concentrated *in vacuo* to give pure *rac*-**10a** (53.4 mg, 96%) as a white solid: mp 86.5−89.5 °C; ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 1.45 (s, 3H), 1.59 (m, 2H), 2.40 (dd, J = 1.0, 4.2 Hz, 1H), 2.75 (m, 1H), 3.05 (m, 1H), 3.36 (s, 3H), 4.66 (d, J = 1.0 Hz, 1H), 6.10 (m, 1H), 6.19 (m, 1H). Addition of 1.5 equiv of the chiral shift reagent Eu(hfc)$_3$ gave a splitting of the α-methyl signal of 0.03 ppm (1.07 ppm downfield shift). GC-MS (EI, *m*/*z*, rel int (%)): 195 (M^+ + 1, 59.0), 163 (10.4), 135 (15.2), 129 (39.4), 97 (20.1), 91 (26.9), 66 (100). Anal. Calcd for $C_{11}H_{14}O_3$: C, 68.02; H, 7.26. Found: C, 67.80; H, 7.19.

5(*S*)-Methoxy-2(*R*)-methyl-4-oxa-*endo*-tricyclo[5.2.1.0^{2,6}]-dec-8-en-3-one (*ent*-10a). For determination of ee of *endo*-5(*R*)-acetoxy lactone **7a.** A solution of **7a** (25 mg, 0.11 mmol) in methanol (2 mL) was treated with 1 drop of thionyl chloride. The solution was stirred for 30 min and concentrated *in vacuo* to give pure *ent*-**10a** (21.1 mg, 97%), which was analyzed for ee as described for *rac*-**10a**.

Racemic *exo*-5-Methoxy-4-oxa-*endo*-tricyclo[5.2.1.0^{2,6}]-dec-8-en-3-one (*rac*-10b).[22] For determination of ee of 5(*R*)-hydroxy lactone **5b**. A solution of *rac*-**5b** (50 mg, 0.31 mmol) in methanol (2 mL) was treated with 1 drop of thionyl chloride. The solution was stirred for 30 min and concentrated *in vacuo* to give crude *rac*-**10b**, which was not sufficiently pure for ee determination. Purification by chromatography (SiO_2, hexane/ethyl acetate 9:1) gave pure *rac*-**10b** (47.2 mg, 84%) as a white solid: mp 54.5−55.5 °C; ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 1.44 (dt, J = 1.0 Hz, 8.6 Hz, 1H), 1.62 (dt, J = 1.0 Hz, 8.6 Hz, 1H), 2.91 (m, 1H), 3.19 (m, 1H), 3.31 (m, 2H), 3.43 (s, 3H), 4.79 (d, J = 1.1 Hz, 1H), 6.20 (m, 1H), 6.25 (m, 1H). Addition of 1.5 equiv of the chiral shift reagent Eu(hfc)$_3$ gave a splitting of the signal of the acetal proton H_5 of 0.03 ppm (1.37 ppm downfield shift). GC-MS (EI, *m*/*z*, rel int (%)): 181 (M^+ + 1, 10.7), 149 (12.6), 121 (14.4), 115 (9.4), 91 (54.6), 83 (15.3), 66 (100). Anal. Calcd for $C_{10}H_{12}O_3$: C, 66.65; H, 6.71. Found: C, 66.12; H, 6.62.

5(*S*)-Methoxy-4-oxa-*endo*-tricyclo[5.2.1.0^{2,6}]dec-8-en-3-one (*ent*-10b). For determination of ee of *endo*-5(*R*)-acetoxy lactone **7b.** This compound was prepared from **7b** (40 mg, 0.19 mmol) in the same way as described for the synthesis of *ent*-**10a**. Yield after chromatography (SiO_2, hexane/ethyl acetate 9:1) 28.2 mg, 83%. The ee was determined according to the procedure as described for *rac*-**10b**.

Racemic *exo*-5-Acetoxy-2-methyl-4-oxa-*endo*-tricyclo-[5.2.1.0^{2,6}]dec-8-en-3-one (*rac*-8a). *rac*-**5a** (100 mg, 0.56 mmol) was dissolved in pyridine/acetic anhydride 2:1 v/v (1 mL) and stirred for 17 h at room temperature. The solvents were removed *in vacuo*, and the residue was coevaporated with toluene. Yield 121.8 mg, 98% of pure *rac*-**8a** as a colorless oil: ^{1}H-NMR ($CDCl_3$, 100 MHz): δ 1.50 (s, 3H), 1.62 (m, 2H), 2.04 (s, 3H), 2.50 (dd, J = 0.9, 4.2 Hz, 1H), 2.80 (m, 1H), 3.12 (m, 1H), 5.87 (d, J = 0.9 Hz, 1H), 6.19 (m, 2H), GC-MS (EI, *m*/*z*, rel int (%)): 163 (M^+ − OAc, 36.3), 157 (3.0), 97 (18.2), 91 (11.5), 66 (100); HRMS/EI: *m*/*z* calcd for $C_{12}H_{14}O_4$: 222.0892. Found 222.08931 ± 0.00088.

Racemic *exo*-5-Acetoxy-4-oxa-*endo*-tricyclo[5.2.1.0^{2,6}]-dec-8-en-3-one (*rac*-8b). This compound was prepared from *rac*-**5b** (100 mg, 0.60 mmol) in the same way as described for the synthesis of *rac*-**8a**. Purification by chromatography (SiO_2, hexane/ethyl acetate 3:1) afforded *rac*-**8b** (119.8 mg, 87%) as a white solid. An analytically pure sample was obtained by recrystallization from hexane/ethyl acetate: mp 82.5−84 °C; ^{1}H-NMR ($CDCl_3$, 100 MHz): δ 1.39 (dt, J = 1.0 Hz, 8.7 Hz, 1H), 1.60 (dt, J = 1.0 Hz, 8.7 Hz, 1H), 2.03 (s, 3H), 2.96 (m, 1H), 3.25 (m, 3H), 5.86 (d, J = 1.2 Hz, 1H), 6.19 (m, 2H); GC-MS (EI, *m*/*z*, rel int (%)): 149 (M^+ − OAc, 10.2), 143 (1.6), 91 (23.6), 83 (11.6), 66 (100). Anal. Calcd for $C_{11}H_{12}O_4$: C, 63.45; H, 5.81. Found: C, 63.50; H, 5.79.

5(*R*)-Acetoxy-2(*S*)-methyl-4-oxa-*endo*-tricyclo[5.2.1.0^{2,6}]-dec-8-en-3-one (8a). This compound was prepared from **5a** (100 mg, 0.56 mmol) in the same way as described for the synthesis of *rac*-**8a**. Yield 123.1 mg, 99% of **8a** as a colorless oil: $[\alpha]_D$ −79.3° (*c* 0.4, CH_2Cl_2). ^{1}H-NMR and mass data were the same as for compound *rac*-**8a**.

5(*R*)-Acetoxy-4-oxa-*endo*-tricyclo[5.2.1.0^{2,6}]dec-8-en-3-one (8b). This compound was prepared from **5b** (100 mg, 0.60 mmol) in the same way as described for the synthesis of *rac*-**8b**. Yield 119.8 mg, 87% of **8b** as a white solid. An analytically pure sample was obtained by recrystallization from hexane/ethyl acetate: mp 84−86.5 °C; $[\alpha]_D$ −27.2° (*c* 0.4, CH_2Cl_2). ^{1}H-NMR and mass data were the same as for compound *rac*-**8b**.

5(*R*)-Acetoxy-2(5*H*)-furanone (11). Flash vacuum thermolysis of **7b** (52.4 mg, 0.25 mmol) [sample temp: 80 °C; oven temp: 500 °C; cold trap temp: −78 °C; pressure: 5×10^{-2} mbar] provided pure **11** (32.7 mg, 92%) as a colorless oil: $[\alpha]_D$ −30.9° (*c* 0.7, CH_2Cl_2); ^{1}H-NMR data were the same as reported

for *rac*-**11**.[23] Addition of $Eu(hfc)_3$ (0.4 equiv) gave a separation of CH_3 signals amounting 0.16 ppm for the corresponding enantiomers (0.8 ppm downfield shift), ee 94%.

The same compound **11** was obtained by FVT [sample temp: 120 °C; oven temp: 500 °C; cold trap temp: −78 °C; pressure: 5×10^{-2} mbar] starting from a 1:1 mixture of diastereomeric acetates **7b** and **8b** (110 mg, 0.53 mmol). Yield 64.9 mg, 86% as a colorless oil. $[\alpha]_D$ −34.2° (*c* 0.5, CH_2Cl_2), ee 94%.

Acknowledgment. We thank Amano Enzyme Europe Ltd. for a generous gift of lipase PS and several other lipases. We thank H. Amatdjais, P. v Galen, and A. Swolfs for conducting elemental analysis, mass, and 400 MHz ^{1}H-NMR measurements, respectively. These investigations were supported by the Netherlands Foundation of Chemical Research (SON) with financial aid from the Netherlands Organization for the Advancement of Research (NWO).

(23) Nagao, Y.; Dai, W.; Ochiai, M.; Shiro, M. *J. Org. Chem.* **1989**, *54*, 5211−5217.

Supporting Information Available: Copies of ^{1}H NMR spectra of *rac*-**8a**, *rac*-**8b**, **7a**, **7b** (4 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO9610220