Pergamon

Tetrahedron: *Asymmetry* 12 (2001) 1779–1784

TETRAHEDRON: *ASYMMETRY*

Enantioselective syntheses of isoprostane and iridoid lactones intermediates by enzymatic transesterification

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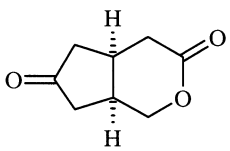
Received 12 June 2001; accepted 5 July 2001

Abstract—Crude *Pseudomonas cepacia* lipase (Amano PS-30) is a suitable biocatalyst for the kinetic resolution of the 1,2-*cis*-disubstituted cyclopentanoid building block (3a*R**,4*R**,6a*S**)-(±)-4-hydroxymethyl-3,3a,4,6a-tetrahydrocyclopenta[*b*]furan-2-one through enantioselective transesterification. Enantiomerically enriched acetic acid (3a*S*,4*S*,6a*R*)-(+)-2-oxo-3,3a,4,6a-tetrahydro-2*H*-cyclopenta[*b*]furan-4-yl methyl ester was utilized in a formal synthesis of the iridoids (+)-isoiridomyrmecin and (−)-teucrium-lactone.

1. Introduction

Recently, we have described the facile and efficient conversion of bicyclic lactone (±)-**1** into 4-epimeric Corey-like lactone (±)-**2a**.[1] Compound **1** is readily prepared on multigram scale by a regiocontrolled Baeyer–Villiger oxidation of the Weiss diketone *cis*-bicyclo[3.3.0]-octane-3,7-dione **3**.[2]



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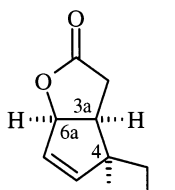
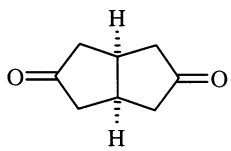


2a R = H
2b R = Bn
2c R = Ac



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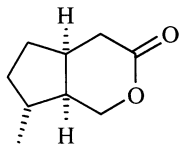

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Both compounds **1** and **2a** are attractive building blocks for the synthesis of 1,2-*cis*-dialkyl substituted cyclopentanoids. In fact, lactone **1** contains two *cis* fused rings of different size, each functionalized in a different manner, thus allowing for chemo-, regio-, and stereoselective reactions. Indeed, we exploited these interesting features of (±)-**1** in a formal synthesis of (±)-loganin.[2] The isomeric lactone (±)-**2a** was utilized as the starting material in a straightforward synthesis of compounds of the 12-oxophytodienoic cascade.[1] In addition, the *O*-benzyl ether **2b**[3–5] was employed in the total synthesis of iridoids.[3,4] We anticipate that **2a** will serve also as a key intermediate in the syntheses of isoprostane-like cyclopentanoids such as preclavulone A[6] and 12-*epi*-PGA and 11-deoxy-12-*epi*-PG isoprostaglandins.[7]

Given the ready access to lactones **1** and **2a**, their synthetic importance and usefulness would be greatly enhanced by a procedure leading to them in an enantiomerically pure form. Herein, we report the results of our efforts in this field using biocatalytic methods, the assignment of absolute configurations to (+)-**2a** and (+)-**2c**, and the conversion of (+)-**2c** into (−)-7-*epi*-boschnialactone **4**. In the accompanying paper[8] we describe a complementary approach to enantiomerically enriched **1** and **2a** through asymmetric synthesis.†

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† A recent paper describes the synthesis of (+)-**2b** by an application of lithium amide-induced asymmetric rearrangements of 4-substituted cyclopentene oxides to cyclopentenols (Ref. 4).

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PII: S0957-4166(01)00311-1

2. Results and discussion

The lipase-catalyzed transesterification of alcohols[9,10] seemed the simplest biocatalytic approach to the synthesis of enantiomerically pure compounds **1** and **2a**, and since **1** is a precursor of **2a**,[1] initially we decided to investigate the resolution of the former lactone through the enzymatic acylation of the corresponding secondary alcohol.

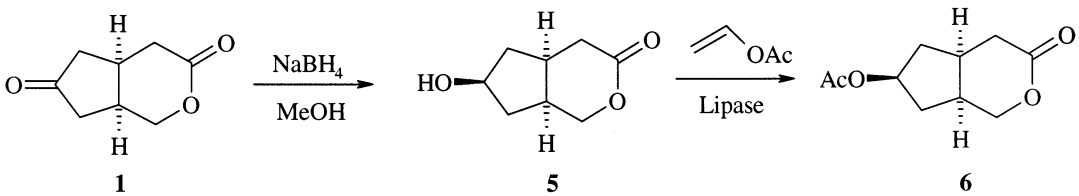
2.1. Enzymatic resolution of alcohol (±)-5

Chemoselective reduction of (±)-**1** with $NaBH_4$ in MeOH at −30°C readily afforded the *endo* alcohol (±)-**5**, with d.e. of 90%, in 95% chemical yield.[1] To find a suitable enzyme for the kinetic resolution, compound **5** was then exposed to various lipases of different origin using vinyl acetate as solvent and acyl donor (Scheme 1). The reactions were performed at 22°C using 1.0 mmol of substrate (±)-**5** and 25 mg of each enzyme, and they were stopped when high resolution gas chromatographic analysis indicated about 50% conversion of the starting material. Neither the enantiomers **5** nor enantiomers **6** could be separated on HRGC or HPLC chiral columns available to us; *E* values[11] were therefore estimated by measuring the e.e. of the enantiomerically enriched acetate **6** by ^1H NMR in the presence of (+)-Eu(hfc)$_3$. All NMR experiments were performed by comparing the results for racemic products, obtained by reaction of alcohol (±)-**5** with acetic anhydride and pyridine, and the enantiomerically enriched acetate **6**. The absolute configuration of the latter was not established. The following lipases were tested: Amano PS (PSL, from *Pseudomonas cepacia*), Amano AK (PFL, from *Pseudomonas fluorescens*), Amano AYS (CRL, from *Candida rugosa*), *Candida antartica* lipase (CAL), *Candida cylindracea* lipase (CCL), *Candida lipolytica* lipase, Porcine pancreatic lipase, Amano A (from *Aspergillus niger*), Amano M (from *Mucor javanicus*), *Penicillium roqueforti* lipase, hog liver esterase, *Rhizopus arrhizus* lipase.

Notably, all of the 12 enzymes examined showed the same enantiomer preference, though enantiodifferentiation was rather modest. Amano PS proved to be the best lipase with an *E* of 4.9 (Table 1, entry 1). Lowering the temperature of the PSL-catalyzed transesterification had a small beneficial effect on the enantioselectivity which increased to $E = 6.1$ at 0°C and to 7.2 at −20°C. No significant improvements were also observed when the kinetic resolutions were performed in organic solvents at 22°C (Table 1, entries 2–6), showing an *E* value slightly higher in $CHCl_3$ (entry 6) than in ethers or toluene. To our surprise, no acylation of alcohol **5** occurred in the presence of either trifluoroethyl pivalate, trifluoroethyl butyrate or *N*-tosyl-L-proline trifluoroethyl ester as acyl donors.

We realized that the difficulties encountered in the resolution of (±)-**5** might be ascribed to the local pseudo C_S symmetry of the cyclopentanol moiety in compound **5** which was not substantially altered by the *cis*-fused lactone ring. In order to enhance the chemical and steric differences between the 1,2-*cis*-substituents, lactone (±)-**1** was converted into the monocyclic ester **7** which was then exposed to vinyl acetate in the presence of PSL (Scheme 2) under a number of reaction conditions (Table 1, entries 7–9).

The e.e.s of the enantiomerically enriched acetate **8** were estimated by integration of the CO_2Me doubled singlets in the ^1H NMR spectrum in the presence of



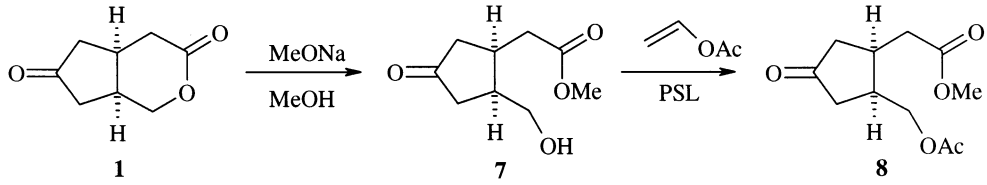
1 **5** **6**

Scheme 1.

Table 1. PSL-catalyzed transesterifications of alcohols (±)-**5** and (±)-**7**

Entry	Substrate	Solvent system	Reaction time (h)	Substrate conversion (%)	E.e. of product[a] (%)	*E*
1	**5**	Vinyl acetate	2	56	47	4.9
2	**5**	MeO*t*Bu[b]	2	54	45	4.3
3	**5**	THF[b]	2	49	33	2.6
4	**5**	1,4-Dioxane[b]	2.5	66	42	5.7
5	**5**	Toluene[b]	1.5	47	52	4.9
6	**5**	$CHCl_3$[b]	18	65	44	6.0
7	**7**	Vinyl acetate	3	34	66	6.8
8	**7**	THF–Et_3N[b,c]	4.5	47	61	7.0
9	**7**	1,4-Dioxane[b]	4.5	55	60	8.5

[a] Acetate **6** or **8** where appropriate.
[b] Vinyl acetate (10 equiv.) as acyl donor.
[c] 2 equiv. of NEt_3.



Scheme 2.

(+)-Eu(hfc)$_3$. The *E* values of these enzymatic resolutions were, as expected, generally higher than those observed for alcohol (±)-**5**, but still unsatisfactory to our purposes. The absolute configuration of the predominant enantiomer **8** was not established; however, chemical conversion to alcohol **5** (i. ester and acetate hydrolysis with NaOH; ii. *p*-TsOH-promoted relactonization; iii. ketone reduction[1] with $NaBH_4$) proved that the stereochemistry corresponded to the faster acylated enantiomer (+)-**5** (Scheme 1 and Table 1, entry 1). It was therefore worthy to explore a double asymmetric resolution[12] of lactone (±)-**1**, coupling the PSL-mediated acylation of hydroxyester (±)-**7** with that of **5**. In the event, enzymatic resolution of (±)-**7** in 1,4-dioxane yielded acetate **8** with 62% e.e. at a conversion of 53%, while the following PSL-catalyzed acylation of enantiomerically enriched alcohol (+)-**5** in 1,4-dioxane afforded, at a conversion of about 70%, lactone (−)-**6**, $[\alpha]_D^{20}$ −16.7 (*c* 1.1, CH_2Cl_2), 87% e.e., in 20% isolated overall yield from the racemic starting material.

2.2. Enzymatic resolution of alcohol (±)-2a

In principle, enantiomerically enriched **2a** could be obtained from (−)-**6** by simple chemical reactions;[1] however, the direct enzymatic resolution of (±)-**2a** appeared more suitable to preparative purposes. In fact, we expected that, thanks to the substitution pattern of the cyclopentene ring, the local symmetry about the hydroxyl group of **2a** was reduced with respect to carbinol **5**, thus facilitating the biocatalytic enantiomer recognition. In addition, we were encouraged by a few successful enzymatic resolutions of bicyclic alcohols similar to **2a** already existing in the literature.[13,14] After having tested the entire stock of our lipases (see above) we discovered that Amano PS was the lipase of choice. Table 2 reports the results of resolutions performed in different solvents at 22°C in the presence of PSL and with vinyl acetate as acyl donor; lipase from *P. cepacia*, immobilized in Sol-Gel-AK, and lipase Amano AK are also included for comparison (entry 4 and 5, respectively). The highest *E* value was observed when the PSL-mediated irreversible acetylation of (±)-**2a** was carried out in vinyl acetate/triethylamine as solvent (entry 3). Under this biocatalytic condition, the sluggish reacting enantiomer (+)-**2a**, $[\alpha]_D^{20}$ +4.5 (*c* 0.5, CH_2Cl_2), could be obtained with an e.e.of $\geq$97% when acetylation of (±)-**2a** was brought to about 60%. On a preparative scale, however, an earlier termination of the reaction was required in order to have acceptable chemical yields. Thus, at 55% conversion of (±)-**2a**, unreacted alcohol (+)-**2a** was obtained with an e.e. of 91% and in 40% isolated yield from the racemic material. On the other hand, given the *E* value, an iterative resolution[12] of **2a** was mandatory in order to upgrade the enantiomeric purity of the product (+)-**2c**. In the first experiment, the reaction was terminated at about 52% of the complete acylation of (±)-**2a**, affording acetate (+)-**2c** with an e.e. of 78%. After cleavage (K_2CO_3 in MeOH) of the acetate group, enzymatic acetylation of the enantiomerically enriched alcohol (−)-**2a** was terminated at a conversion of 90%, yielding (+)-**2c**, $[\alpha]_D^{20}$ +33.7 (*c* 0.5, CH_2Cl_2), with an e.e. of 95%. Enantiomerically enriched lactones (+)-**2c** and (+)-**2a** gave (−)-**2a**, e.e. 95%, and (−)-**2c**, e.e. 97%, respectively, under standard condition.

2.3. Absolute configurations of (+)-2a and (+)-2c, and synthesis of (−)-7-*epi*-boschnialactone 4

To demonstrate the synthetic potential and to establish the absolute configuration, lactone (+)-**2c** was con-

Table 2. Lipase-catalyzed transesterifications of alcohols (±)-**2a**

Entry	Solvent system	Substrate conversion (%)	E.e. of substrate (+)-**2a** (%)	E.e. of product (+)-**2c** (%)	*E*
1[a]	Vinyl acetate	58	96	68	20
2[a,b]	Vinyl acetate	53	77	68	12
3[a]	Vinyl acetate/NEt_3 (5:1)	55	91	74	21
4[c]	Vinyl acetate	39	52	81	16
5[d]	Vinyl acetate/NEt_3 (5:1)	52	83	77	19
6[a]	THF[e]	53	77	68	12
7[a]	1,4-Dioxane[e]	50	75	75	15
8[a]	1,2-Dimethoxyethane[e]	43	59	78	15
9[a]	Toluene[e]	63	44	40	4.5

[a] Lipase Amano PS.
[b] Reaction performed at 50°C.
[c] Lipase from *P. cepacia*, immobilized in Sol-Gel-AK.
[d] Lipase Amano AK.
[e] Vinyl acetate (10 equiv.) as acyl donor.

verted to the known (−)-7-*epi*-boschnialactone **4**[15–17] under conditions shown in Scheme 3. S_N2' ring opening of (+)-**2c** according to Curran's methodology[18] led to a mixture of *exo*- and *endo*-methyl derivatives **9**, showing a diastereomeric ratio higher than 49:1 when the reaction was performed at −45°C. Acid **9** was then converted into lactone (−)-**4** using standard reactions.

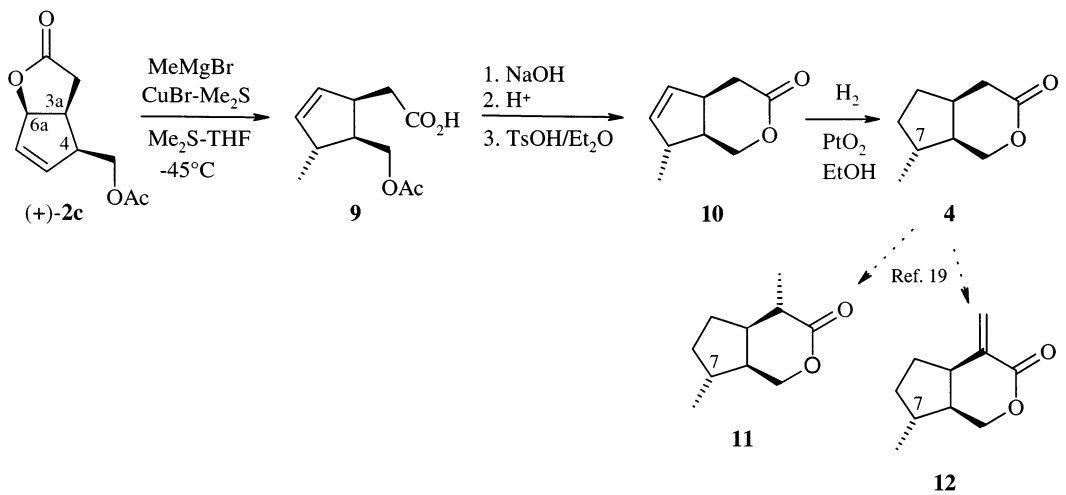
The present enantioselective synthesis of (−)-7-*epi*-boschnialactone compares with previous asymmetric syntheses[15–17] using substrates from the 'chiral pool' and constitutes a formal synthesis of the iridoids (+)-isoiridomyrmecin **11** and (−)-teucriumlactone **12**.[19] Moreover, it demonstrates the (3a*S*,4*S*,6a*R*) configuration of the acetate (+)-**2c** and hence the (3a*R*,4*R*,6a*S*) configuration of the slow reacting enantiomer (+)-**2a** in the PSL-catalyzed resolution of (±)-**2a**.

3. Conclusion

In this study we have shown that lipase Amano PS-catalyzed kinetic resolutions could provide three synthetically useful building block lactones (−)-**6**, (+)-**2a**, and (+)-**2c** in good e.e. Lactone (+)-**2c** was converted into (−)-7-*epi*-boschnialactone **4** in high yield, thus accomplishing a formal synthesis of the iridoids (+)-isoiridomyrmecin **11** and (−)-teucriumlactone **12**. Our results on the exploitation of (+)-**2a**, (+)-**2c**, and the corresponding enantiomers in enantioselective syntheses of isoprostanes will be reported in incoming papers.

4. Experimental

Melting points were determined on a Fisher–Johns hot plate and are uncorrected. IR spectra were recorded as thin films on a Perkin–Elmer FT-IR Paragon 100 PC spectrometer ^{1}H NMR (300 MHz) and ^{13}C NMR (75.47 MHz) spectra were recorded in $CDCl_3$ solution unless indicated otherwise with a Bruker CXP 300 spectrometer. Chemical shifts are reported in δ units relative to $CHCl_3$ [δ_H 7.26, δ_C (central line of t) 77.0]; the abbreviations s = singlet, d = doublet, t = triplet, q = quartet, qu = quintuplet, m = multiplet, and br = broad are used throughout. Coupling constants (J) are given in Hz. The multiplicity (in parentheses) of each carbon atom was determined by DEPT experiments. Mass spectra (direct inlet system) were recorded at 70 eV (0.5 mA) with a Finnigan MAT 8222 instrument. All experiments were completed in flame-dried glassware under an atmosphere of argon. Syringes and needles for the transfer of reagents were dried at 140°C and allowed to cool in a desiccator over P_2O_5 before use. Analytical TLC was carried out on glass-backed plates, pre-coated with a 0.25 mm layer of silica gel, and visualization was effected with short-wavelength UV light (254 nm) or with 0.5% vanillin solution in H_2SO_4–EtOH (4:1) followed by heating. Flash column chromatography was accomplished with Kieselgel 60 (40–63 μm). E.e. values were determined by HRGC using a Hewlett–Packard model 5890II instrument, equipped with an EASY-SEP capillary column purchased from Analytical Technology (25 m×0.32 mm id and 0.25 μm film thickness); injector (split spitless, split ratio 1:36) temperature 250°C, detector (FID) temperature 280°C, carrier gas He, 1.27 mL min^{-1}. Retention times (t_R) are given in min. Optical activity was measured with a Perkin–Elmer 241 polarimeter. $[\alpha]_D$ values are given in 10^{-1} deg cm^2 g^{-1}. All commercial reagent grade solvents were dried and degassed by standard techniques just before use. Yields are reported for chromatographically and spectroscopically pure isolated compounds. *P. cepacia* lipase (PSL, Amano PS), *P. fluorescens* lipase (PFL, Amano AK), *C. rugosa* lipase (CRL, Amano AYS), *A. niger* lipase (Amano A), *M. javanicus* lipase (Amano M) were a generous gift of Amano Pharmaceutical Co. Ltd. *C. antartica* lipase (CAL), *C. cylindracea* lipase (CCL), *C. lipolytica* lipase, Porcine pancreatic lipase (PPL, type II), *P. roqueforti* lipase, hog liver esterase, *R. arrhizus* lipase, and *P. cepacia* lipase, immobilized in SOL-Gel-AK, were purchased from Fluka.



Scheme 3.

4.1. Enzymatic acylations of alcohols (±)-5, (±)-7, and (±)-2a

Alcohols (±)-**5** and (±)-**2a** were obtained as reported in the literature.[1] A solution of MeONa in MeOH (0.35 M, 1 mL) was added to a solution of lactone (±)-**1**[2] (500 mg, 3.25 mmol) in anhydrous MeOH (25 mL). The mixture was stirred at 21°C for 12 h, then it was treated with saturated NH_4Cl (300 μL) and evaporated to dryness under reduced pressure. The residue was dissolved in MeOH and EtOAc (50 mL), and the suspension was filtered on a plug of Celite. Evaporation of the solution under reduced pressure gave hydroxyester (±)-**7** (556 mg, 92%) as an oil (IR 3320, 1740 cm^{-1}) which was immediately submitted to the enzymatic reaction.

In a round-bottomed flask were placed the alcohol (1.0 mmol), a solution of vinyl acetate (10 mmol) in the indicated solvent (5 mL) and the indicated lipase (25 mg) (see Tables 1 and 2). Alternatively, to a solution of the alcohol (1.0 mmol) in vinyl acetate (10 mL) was added the indicated lipase (25 mg). The mixture was vigorously stirred at the desired temperature and monitored by HRGC on a HP-5 (cross-linked 5% PhMe silicone) capillary column (25 m, 0.25 mm id and 0.33 μm film thickness). The reaction was stopped by filtration of the enzyme on a plug of Celite. Volatiles were evaporated under reduced pressure and the residue was separated by flash chromatography on silica gel (eluent: EtOAc–hexane gradient) to afford, in order of elution, the desired monoacetate and unreacted starting alcohol. The e.e. values of enantiomerically enriched (−)-**6** and **8** were estimated by integration of the –OCO*Me* and COO*Me* doubled singlets, respectively, in the ^1H NMR spectra in the presence of (+)-Eu(hfc)$_3$. E.e. of enantiomerically enriched **2a** and **2c** were determined by HRGC on the capillary column indicated above; programmed temperature of the column: 1 min at 180°C, then increased from 180°C to 220°C with a gradient of 2°C min^{-1}, followed by 10 min at 220°C. The elution order was found to be (3a*S*,4*S*,6a*R*)-(+)-**2c** (t_R = 12.5 min), (3a*R*,4*R*,6a*S*)-(−)-**2c** (t_R = 13.8 min), (3a*S*,4*S*,6a*R*)-(−)-**2a** (t_R = 15.9 min), and (3a*R*,4*R*,6a*S*)-(+)-**2a** (t_R = 17.5 min). For comparison, monoacetates (±)-**6**, (±)-**8**, and (±)-**2c** were prepared from the corresponding racemic alcohol under standard conditions.

(±)-**6**. Colorless oil. IR: 2934, 1733, 1430, 1376, 1246, 1165, 1118, 1085, 1046, 905, 815 cm^{-1}; ^1H NMR: δ 1.5–1.8 (2H, m), 2.03 (s, 3H), 2.12–2.3 (2H, m), 2.48 (1H, dd, J = 17 and 9.5), 2.55–2.75 (m, 3H), 4.15 (1H, dd, J = 11.5 and 7.0), 4.30 (1H, dd, J = 11.5 and 5.0), 5.12 (1H, qu, J = 5.5); ^{13}C NMR: δ 21.2 (3), 32.5 (1), 34.5 (2), 34.7 (2), 34.8 (1), 38.8 (2), 69.6 (2), 75.2 (1), 170.5 (0), 173.1 (0).

(±)-**8**. Colorless oil. ^1H NMR: δ 2.05 (3H, s), 2.12 (1H, dd, J = 19.5 and 8.5), 2.20 (1H, dd, J = 19.5 and 4.5), 2.40–2.52 (3H, m), 2.58 (1H, dd, J = 15.3 and 7.0), 2.75 (1H, m), 2.95 (1H, m), 3.70 (3H, s), 4.10 (1H, dd, J = 12.5 and 7.0), 4.20 (1H, dd, J = 12.5 and 7.0).

(±)-**2c**. Colorless oil. IR: 2923, 1772, 1736, 1422, 1366, 1241, 1116, 1033 cm^{-1}; ^1H NMR: δ 2.05 (3H, s), 2.52 (1H, dd, J = 18.3 and 5.5), 2.65 (1H, J = 18.3 and 10.0), 3.10–3.30 (2H, m), 4.10 (1H, dd, J = 11.8 and 4.6), 4.26 (1H, J = 11.8 and 6.0), 5.45 (1H, brd, J = 7.2), 6.0 (2H, m); ^{13}C NMR: δ 20.6 (3), 29.9 (2), 37.8 (1), 46.2 (1), 62.6 (2), 88.2 (1), 130.1 (1), 137.4 (1), 170.7 (0), 176.5 (0); EIMS m/z (rel. int.) 196 [M^+] (8), 166 (7), 148 (10), 136 (38), 124 (63), 108 (27), 92 (23), 91 (27), 43 (100). Anal. calcd for $C_{10}H_{12}O_4$: C, 61.22; H, 6.16. Found: C, 61.35; H, 6.31%.

4.2. (4a*R*,7*R*,7a*S*)-(−)-7-Methyl-4,4a,7,7a-tetrahydro-1*H*-cyclopenta[*c*]pyran-3-one (−)-10

A solution of MeMgBr (3 M in Et_2O; 430 μL, 1.29 mmol) was added dropwise to a stirred solution of CuBr·Me_2S (273 mg, 1.33 mmol) in THF (2.6 mL) and Me_2S (1.3 mL) at −20°C (cryostat). After stirring the mixture for 1 h, the temperature of the mixture was lowered to −40°C and lactone (+)-**2c** (126 mg, 0.64 mmol) in THF (1.5 mL) was slowly added by syringe. After 5 h the reaction was warmed to rt, poured onto aqueous NaOH (1 M, 5 mL) and the mixture stirred for an additional 2 h. Aqueous HCl (1 M, ca. 5 mL) was added and the aqueous layer extracted with Et_2O (3×15 mL). The combined organic layers were washed with H_2O (5 mL), brine (5 mL), and concentrated under reduced pressure to a volume of ca. 15 mL. The resultant solution was treated with *p*-TsOH (3 mg) and stirred for 8 h at rt until TLC indicated complete lactonization to compound **10**. The reaction was washed with 5% aqueous $NaHCO_3$, followed by brine, dried ($MgSO_4$) under reduced pressure. Purification of the residue by column chromatography (hexane–EtOAc, 4:1) gave a white solid of lactone **10** (83 mg, 85%); mp 77–78°C; $[\alpha]_D^{20}$ −164 (*c* 0.5, CH_2Cl_2); IR: 2925, 1728, 1461, 1380, 1238, 1150, 1070, 978, 770 cm^{-1}; ^1H NMR: δ 1.11 (3H, d, J = 7.0), 2.20–2.28 (1H, m), 2.34 (1H, dd, J = 15.0 and 6.0), 2.68 (1H, dd, J = 15.0 and 7.0), 3.33–3.42 (1H, m), 4.08 (1H, dd, J = 11.5 and 6.5), 4.32 (1H, dd, J = 11.5 and 4.5), 5.52 (1H, dt, J = 5.5 and 2.0), 5.70 (1H, dt, J = 5.5 and 2.0); ^{13}C NMR: δ 173.4 (0), 137.2 (1), 130.8 (1), 69.7 (2), 43.9 (1), 42.9 (1), 41.7 (1), 33.8 (2), 21.3 (3). Anal. calcd for $C_9H_{12}O_2$: C, 71.03; H, 7.95. Found: C, 71.22; H, 7.83%.

4.3. (4a*S*,7*R*,7a*S*)-(−)-7-Methylhexahydrocyclopenta[*c*]-pyran-3-one (−)-4

H_2 was added to a previously evacuated and vigorously stirred suspension of PtO_2 (ca. 15 mg) and lactone (−)-**10** (70 mg, 0.46 mmol) in EtOH (5 mL) at rt. The mixture was stirred for 45 h, the catalyst was removed by filtration and the filtrate was evaporated under reduced pressure. Purification of the residue by column chromatography (hexane–EtOAc, 7:3) gave a white solid of (−)-7-*epi*-boschnialactone **4** (63 mg, 89%); mp 55–56°C (hexane); [lit.[20] (enantiomer) 55–56°C]; $[\alpha]_D^{20}$ −82.5 (*c* 0.4, $CHCl_3$); [lit.[17] $[\alpha]_D^{25}$ −92 (*c* 1.0, $CHCl_3$); ^1H NMR: δ 1.06 (3H, d, J = 6.0), 1.12–1.31 (2H, m), 1.77–1.93 (3H, m), 1.97–2.07 (1H, m), 2.30–2.40 (1H,

m), 2.55–2.65 (2H, m), 4.10 (1H, dd, $J=11.5$ and 4.5), 4.27 (1H, dd, $J=11.5$ and 4.5); ^{13}C NMR: δ 173.6 (0), 68.9 (2), 44.5 (1), 37.4 (1), 34.7 (2), 34.6 (1). 34.5 (2), 33.3 (2), 18.6 (3). Anal. calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 70.25; H, 9.33%.

Acknowledgements

We are indebted to Amano Pharmaceutical Co. Ltd for the kind supply of lipases Amano AK, Amano PS, Amano A, Amano M, and Amano AYS. We thank the Italian CNR and MURST (funds COFIN 1999), and the University of Pavia (funds FAR) for financial support, and Prof. Mariella Mella and Professor Giorgio Mellerio for NMR and MS spectra, respectively.

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