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Enantioselective Syntheses and Configuration Assignments of γ-Chiral Butenolides from *Plagiomnium undulatum*: Butenolide Synthesis from Tetronic Acids

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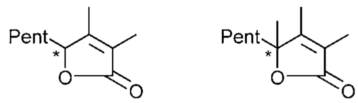
Abstract: Both enantiomers of the γ-chiral α,β-dimethylated butyrolactones *nat*-**1** and *nat*-**2** from the moss *Plagiomnium undulatum* were synthesized stereoselectively through butenolides and tetronic acids, respectively. The configuration of the natural products was determined by GLC comparisons with mono(3-*O*-acetyl-6-*O*-*tert*-butyldimethylsilyl-2-*O*-methyl)hexakis(6-*O*-*tert*-butyldimethylsilyl-2,3-di-*O*-methyl)-β-cyclodextrin as a stationary phase.

Keywords: Arndt-Eistert homologation · asymmetric synthesis · butyrolactones · configuration determination · dihydroxylation · tetronic acids

Introduction

Bryophytes (mosses) are known to generate a great variety of secondary metabolites. However, this property mainly applies to liverworts (Hepaticae), whereas common mosses (Musci) are considered to be poor in their production of volatile constituents. A recent investigation of the hydrodistillation products of a selection of mosses revealed that many of them also produce complex mixtures of volatiles, although in much smaller amounts (approximately 10%) than liverworts. From the genus *Plagiomnium undulatum*, in addition to (+)-dauca-8,11-diene (a new sesquiterpene hydrocarbon), two Δ^2-butenolides,[1] *nat*-**1** and *nat*-**2** (Scheme 1), with the latter exhibiting a very intense, pleasant, floral fragrance, were isolated and their structures were derived by NMR spectroscopy and mass spectrometry analysis.[2] However, the absolute configuration at their stereocenters remained unknown.

In order to establish the latter, we compared extracts from *Plagiomnium undulatum*, which contained both *nat*-**1** and *nat*-**2** (plus other compounds), with synthetic specimens of (*S*)-**1**, (*R*)-**1**, (*S*)-**2**, and (*R*)-**2** by enantioselective gas chromatography with appropriately modified cyclodextrins.[3] This was the only way of determining the absolute configuration of compound *nat*-**1** because it had been inaccessible in pure form from the natural source. In contrast, GLC comparisons between *nat*-**2** (which had been isolated in pure form) and stereochemically unambiguously assigned reference compounds (*S*)-**2** and (*R*)-**2** were an obvious means of absolute configuration assignment, since "easier" methods like CD spectroscopy[4] or ^{1}H NMR spectroscopy analysis in the presence of an enantiopure lanthanide shift reagent[5] were not readily applicable.



Scheme 1. Butenolides from *Plagiomnium undulatum*.[2]

Reference compounds (*S*)-**1**, (*R*)-**1**, (*S*)-**2**, and (*R*)-**2** qualified, in principle, for being accessible by the asymmetric dihydroxylation[6] (AD) of sterically homogeneous β,γ-unsaturated carboxylic esters, since this reaction provides β-hydroxy-γ-butyrolactones in a single step and in essentially enantiopure form.[7] Having accessed a variety of saturated[8] and unsaturated butyrolactones[9] in this manner,[7,10] we found the latter did not include trisubstituted (for example, **1**) or tetrasubstituted (for example, **2**) Δ^2-butenolides. This gap is closed by the present study. Concomitantly, we disclose the first examples each of a novel access to optically active tetronic acids (**11**→**10**→**18**; **5**→**4**→**21**) and of a novel preparation of β-substituted butenolides (**18**→**19**→**2**).

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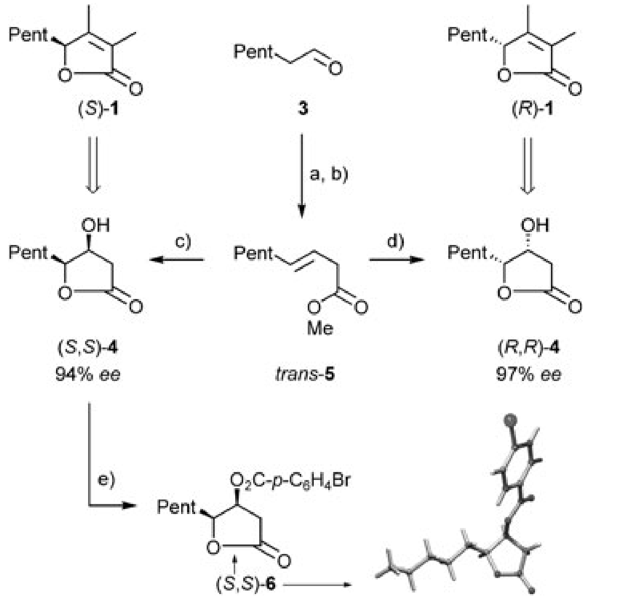
Results and Discussion

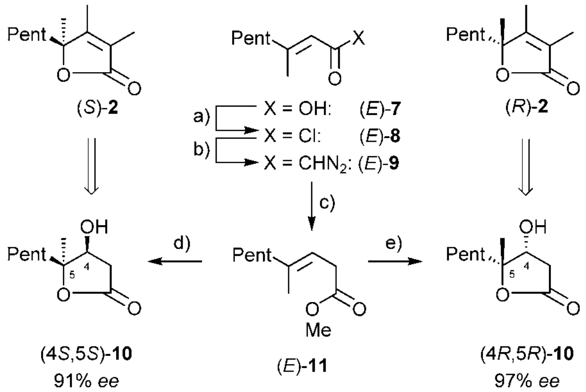
Following the β,γ-unsaturated ester→β-hydroxy-γ-lactone strategy, the two enantiomers of trisubstituted butenolides (*S*)- and (*R*)-**1** were traced back to ester *trans*-**5**[11] (Scheme 2). This originated from the deconjugative Knoeve-



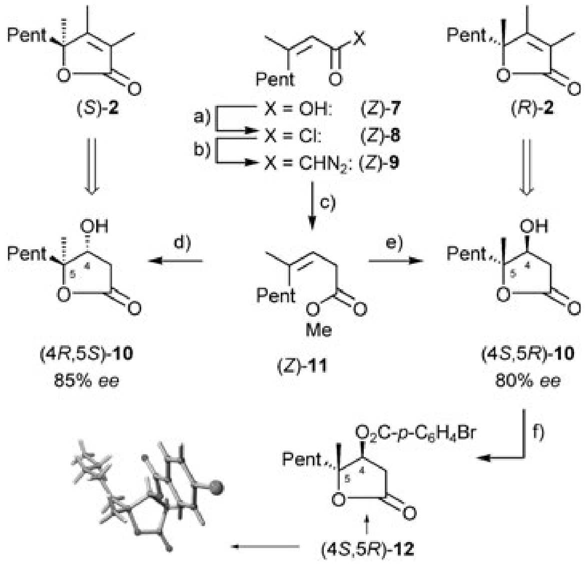
Scheme 2. Approaching butenolides (*S*)- and (*R*)-**1**. a) Malonic acid (1.1 equiv), NEt_3 (3.0 equiv), 90 °C, 18 h; b) H_2SO_4 (cat.), MeOH, Δ, 2 h; 82 %; c) $K_2OsO_2(OH)_4$ (0.8 mol %), $(DHQ)_2PHAL$ (0.01 equiv), $K_3Fe(CN)_6$ (3.0 equiv), K_2CO_3 (3.0 equiv), $MeSO_2NH_2$ (1.0 equiv), *t*BuOH/H_2O (1:1), 0 °C, 12 h; 91 %; d) $K_2OsO_2(OH)_4$ (0.8 mol %), $(DHQD)_2PHAL$ (0.01 equiv), $K_3Fe(CN)_6$ (3.0 equiv), K_2CO_3 (3.0 equiv), $MeSO_2NH_2$ (1.0 equiv), *t*BuOH/H_2O (1:1), 0 °C, 12 h; 90 %; e) *p*Br$C_6H_4CO_2H$ (1.1 equiv), DCC (1.1 equiv), DMAP (cat.), CH_2Cl_2, RT, 4 h, Δ, 1 h; 81 %. A Pluton/Povray plot[15] of the solid-state structure of (*S,S*)-**6** is also depicted. Pent = pentyl, $(DHQ)_2PHAL$ = 1,4-bis(dihydroquininyl)phthalazine, $(DHQD)_2PHAL$ = 1,4-bis(dihydroquinidinyl)-phthalazine, DCC = *N,N'*-dicyclohexylcarbodiimide, DMAP = 4-dimethyl-aminopyridine.

nagel condensation[12] of aldehyde **3** with malonic acid followed by methyl esterification. Oxidation of ester *trans*-**5** with AD mixes α and β (containing $(DHQ)_2PHAL$ and $(DHQD)_2PHAL$, respectively, as the chiral auxiliary) provided hydroxylactones (*S,S*)-**4** (94 % *ee*;[13] absolute configuration ascertained by X-ray crystal structure analysis[14] of a crystal of the *para*-bromobenzoate (*S,S*)-**6**) and (*R,R*)-**4** (97 % *ee*[13]), respectively.

Application of our unsaturated ester→β-hydroxy-γ-lactone strategy to obtain the optically active tetrasubstituted butenolides (*S*)- and (*R*)-**2** allowed us to start both from ester (*E*)-**11**[16] (Scheme 3) or from its isomer (*Z*)-**11** (Scheme 4). AD mix α converted the former into a hydroxylactone, (4*S*,5*S*)-**10,** with 91 % *ee*,[13] and the latter into the hydroxylactone (4*S*,5*R*)-**10** with 80 % *ee*.[13] Likewise, dihydroxylation of esters (*E*)- and (*Z*)-**11** with AD mix β occurred with 97 % *ee*[13] (→(4*R*,5*R*)-**10**) and 85 % *ee*[13] (→



Scheme 3. Approaching butenolides (*S*)- and (*R*)-**2**, variant 1. a) $SOCl_2$ (1.0 equiv), DMF (cat.), CH_2Cl_2, 0 °C→RT, 3 h; b) CH_2N_2 (2.0 equiv), Hünig's base (1.0 equiv), Et_2O, 0 °C→RT, 1 h; 55 % over 2 steps; c) AgOBz (0.3 equiv), NEt_3 (4.7 equiv), MeOH, RT, 5 h; 88 %; d) $K_2OsO_2(OH)_4$ (0.8 mol %), $(DHQ)_2PHAL$ (0.016 equiv), $K_3Fe(CN)_6$ (3.0 equiv), K_2CO_3 (3.0 equiv), $MeSO_2NH_2$ (1.0 equiv), *t*BuOH/H_2O (1:1), 0 °C, 1 d; 83 %; e) $K_2OsO_2(OH)_4$ (0.8 mol %), $(DHQD)_2PHAL$ (0.016 equiv), $K_3Fe(CN)_6$ (3.0 equiv), K_2CO_3 (3.0 equiv), $MeSO_2NH_2$ (1.0 equiv), *t*BuOH/H_2O (1:1), 0 °C, 1 d; 82 %. DMF = *N,N*-dimethylformamide.

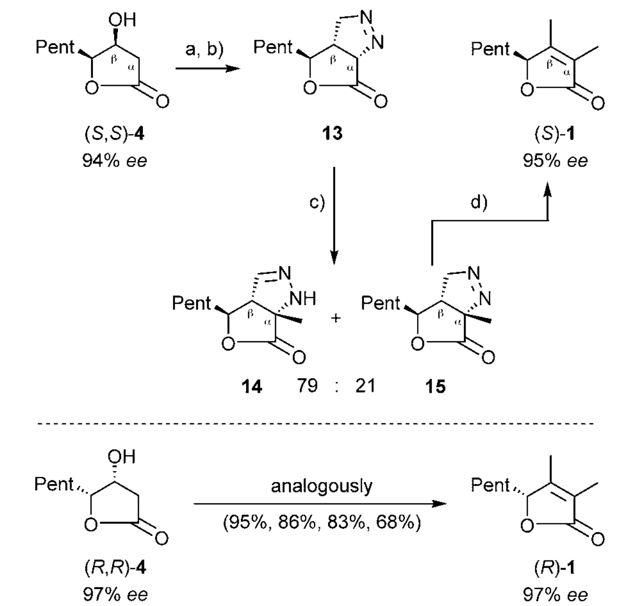


Scheme 4. Approaching butenolides (*S*)- and (*R*)-**2**, variant 2. a) $SOCl_2$ (1.1 equiv), DMF (cat.), CH_2Cl_2, 0 °C→RT, 2.5 h; b) CH_2N_2 (3.0 equiv), Hünig's base (1.0 equiv), Et_2O, 0 °C→RT; 57 % over 2 steps; c) AgOBz (0.3 equiv), NEt_3 (4.7 equiv), MeOH, RT, 4 h; 95 %; d) $K_2OsO_2(OH)_4$ (0.8 mol %), $(DHQD)_2PHAL$ (0.016 equiv), $K_3Fe(CN)_6$ (3.0 equiv), K_2CO_3 (3.0 equiv), $MeSO_2NH_2$ (1.0 equiv), *t*BuOH/H_2O (1:1), 0 °C, 1 d; 85 %; e) $K_2OsO_2(OH)_4$ (0.8 mol %), $(DHQ)_2PHAL$ (0.016 equiv), $K_3Fe(CN)_6$ (3.0 equiv), K_2CO_3 (3.0 equiv), $MeSO_2NH_2$ (1.0 equiv), *t*BuOH/H_2O (1:1), 0 °C, 1 d; 92 %; f) *p*BrC_6H_4COCl (1.2 equiv), NEt_3 (1.3 equiv), DMAP (cat.), CH_2Cl_2, RT, 6 h, Δ, 2 h; 56 %. A Pluton/Povray plot[15] of the solid-state structure of (4*S*,5*R*)-**12** is also depicted.

(4*R*,5*S*)-**10**), respectively. The β,γ-unsaturated C_{10} esters (*E*)- and (*Z*)-**11** had been obtained stereospecifically from the α,β-unsaturated C_9 acids (*E*)-**7**[17] and (*Z*)-**7**,[18] respectively by Arndt–Eistert homologations[19] proceeding through the corresponding acid chlorides (*E*)- and (*Z*)-**8** and the derived diazoketones (*E*)- and (*Z*)-**9**.[20]

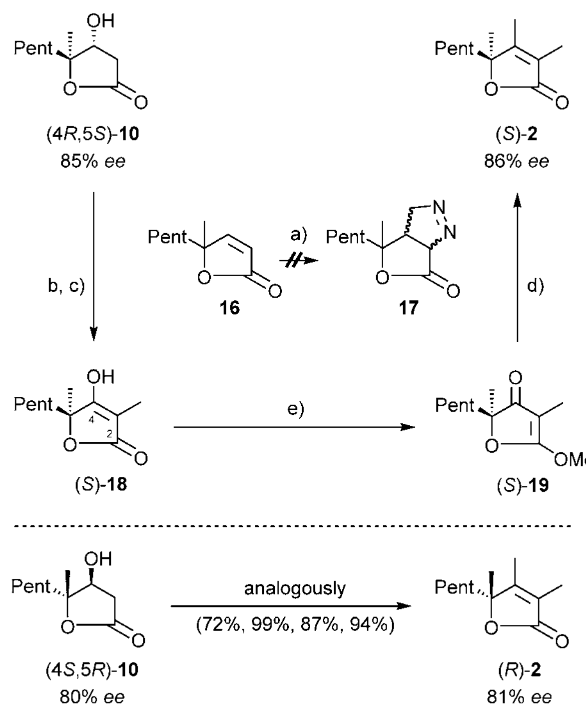
The anomalous X-ray diffraction[14] of the *para*-bromobenzoate first obtained from these lactones as nice crystals revealed its stereostructure to be that depicted for (4*S*,5*R*)-**12**; this proves that the configuration of the underlying hydroxylactone, namely the α-osmylation product of ester (*Z*)-**11**, is (4*S*,5*R*)-**10** (Scheme 4). The configurations of the hydroxylactone isomers obtained according to Scheme 3 emerged from correlations with those shown in Scheme 4. According to chiral GLC,[13] α-methylation/oxidation of the α-osmylation product (4*S*,5*S*)-**10** of ester (*E*)-**11** (Scheme 3) provided the *same* tetronic acid enantiomer ((*S*)-**18**, Scheme 6) as α-methylation/oxidation of compound (4*R*,5*S*)-**10** from Scheme 4. Similarly, α-methylation/oxidation of the β-osmylation product of ester (*E*)-**11** (Scheme 3)—which was hence designated (4*R*,5*R*)-**10**—gave the identical tetronic acid enantiomer (not depicted) to that obtained by α-methylation/oxidation of hydroxylactone (4*S*,5*R*)-**10** (Scheme 4).

Hydroxylactones (*S*,*S*)-**4** and (*R*,*R*)-**4** were transformed into the trisubstituted butenolides (*S*)-**1** and (*R*)-**1**, respectively, as detailed in Scheme 5 for the former compound. Dehydration with mesyl chloride/triethylamine produced the expected Δ^1-butenolide in 94% *ee* (92% yield). Its $C^{\beta}H{=}C^{\alpha}H$ moiety was elaborated into the desired $C^{\beta}Me{=}C^{\alpha}Me$ moiety by Hanessian and Murray's β-methylation/α-alkylation protocol for butenolides.[21] Cycloaddition of diazomethane gave the Δ^1-pyrazoline **13** with the C^{β}–Me "bond-to-be" (96% yield). Enolate formation with LDA and treatment with methyl iodide afforded a Δ^2:Δ^1 mixture of pyrazolines **14** and **15**, thereby establishing the C^{α}–Me bond (80% yield). Pyrolysis in refluxing dioxane provided the desired butenolide (*S*)-**1** in 75% yield with an undiminished *ee* value (95%). A specimen of (*R*)-**1** (97% *ee*) was similarly obtained.



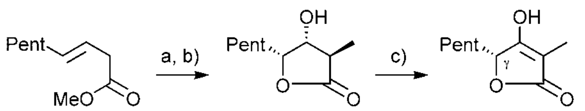
Scheme 5. Completing the synthesis of butenolides (*S*)- and (*R*)-**1**. a) MsCl (1.5 equiv), NEt_3 (2.8 equiv), CH_2Cl_2, 0°C, 30 min; 92%, 94% *ee*; b) CH_2N_2 (5.0 equiv), Et_2O, 0°C→RT, 15 h; 96%; c) LDA (1.7 equiv), THF, −78°C, 30 min; MeI (1.8 equiv), −78°C, 18 h; 80%; d) 1,4-dioxane, 110°C, 5 d; 75%. Ms = mesyl = methanesulfonyl, LDA = lithium diisopropylamide, THF = tetrahydrofuran.

The methodology of Hanessian and Murray[21] was unsuitable for converting hydroxylactones (4*R*,5*S*)-**10** and (4*S*,5*R*)-**10** into the tetrasubstituted butenolides (*S*)-**2** and (*R*)-**2**, respectively, since butenolide **16**—obtained by dehydrating an isomeric mixture of hydroxylactones **10**—did not react with diazomethane (Scheme 6). We circumvented this inertia by adding tetronic acids to the product palette of AD reactions of β,γ-unsaturated esters and by establishing a novel way for converting the C^{β}–OH motif of tetronic acids into the C^{β}–hydrocarbon subunit of Δ^2-butenolides.



Scheme 6. Completing the synthesis of butenolides (*S*)- and (*R*)-**2**. a) CH_2N_2 (5.0 equiv), Et_2O, RT, 5 d; b) LDA (2.8 equiv), THF, −78°C, 30 min; MeI (1.8 equiv), THF/DMPU, −78°C→−40°C, 14 h; 74%; c) DMSO (3.5 equiv), $(F_3CCO)_2O$ (2.0 equiv), CH_2Cl_2, −78°C, 2 h; NEt_3 (4.0 equiv), −78°C, 14 h; 99%; d) MeLi (2.0 equiv), THF, −50°C→0°C, 2 h; HCl, 30 min, RT; 87%, 86% *ee*; e) $Me_3O^+ \cdot BF_4^-$ (3.0 equiv), CH_2Cl_2, RT, 28 h; 85%. DMPU = 1,3-dimethyltetrahydro-2-(1*H*)-pyrimidinone.

The *S* enantiomer of butenolide **2** was targeted from hydroxylactone (4*R*,5*S*)-**10** by lithioalkoxide/enolate formation followed by methylation[22] (Scheme 6). A single diastereomer of the expected α-methyl-β-hydroxylactone was isolated. Working in THF/DMPU, the α-methyl and β-hydroxy groups were probably oriented *trans*.[10a,22] Swern oxidation[23] including enol formation yielded tetronic acid (*S*)-**18** almost quantitatively. There appears to be little precedence[24] for such an approach to these compounds.[25] The method could be extended to tetronic acid **21** which, unlike (*S*)-**18**, might—but did not—racemize due to the possibility of C^{γ},H acidity (Scheme 7).



trans-**5** **20** (97% *ee*) **21** (96% *ee*)

Scheme 7. Synthesis of an optically active tetronic acid, **21**, from a β,γ-unsaturated ester. a) Same as step d of Scheme 2; b) LDA (5.0 equiv), THF, −78 °C, 1 h; MeI (10 equiv), THF, −78 °C, 2 h; 83 %; c) DMSO (3.5 equiv), $(F_3CCO)_2O$ (2.0 equiv), CH_2Cl_2, −78 °C, 1 h; NEt_3 (4.0 equiv), −78 °C, 45 min; 92 %.

Tetronic acid (*S*)-**18** was methylated by Meerwein's salt regioselectively at C^2=*O*, rather than at C^4–*O*H, thereby yielding methoxyfuranone (*S*)-**19** (Scheme 6).[26] Addition of MeLi followed by acid hydrolysis provided target structure (*S*)-**2** in 87 % yield. This reaction, to the best of our knowledge, represents the first example of the overall transformation O=C–C=C(OR^1)$_2$ + R^{2}M → R^2–C=C–C(=O)(OR^1) in heterocycle synthesis. It consists of the sequential transformations 1) HO–C=CH–C(=O)OR^1 + R^{1}X → O=C–C=C(OR^1)$_2$ and 2) O=C–C=C(OR^1)$_2$ + R^{2}M → R^2–C=C–C(=O)(OR^1). The same sequence of steps might be applicable to the conversion of *other* β-ketolactones into *other* α,β-unsaturated lactones containing a β-substituent; conceivably, this could entail the two-step conversion of tetrahydropyran-2,4-diones into 4-substituted 5,6-dihydro-(2*H*)-2-pyranones or the two-step conversion of benzo-3,4-dihydro-(2*H*)-2,4-pyrandiones into 4-substituted cumarins. It should be noted that the *related* transformation O=C–C=C–OR^1 + R^{2}M → R^2–C=C–C=O, which proceeds at a lower oxidation state than (*S*)-**19**→(*S*)-**2**, has been amply used for the preparation of 3-substituted 2-cycloalken-1-ones.[27]

Having made enantiomer (*R*)-**2** available by the same sequence of steps (Scheme 6, bottom), we were in possession of all the materials needed for the GLC analysis of compounds *nat*-**1** and *nat*-**2**. As demonstrated by enantioselective GLC (Figure 1), the predominant *nat*-**2** is the enantiopure *S* enantiomer, while the minor component *nat*-**1** is a mixture of enantiomers with a small excess of the *R* enantiomer (9 % *ee*).

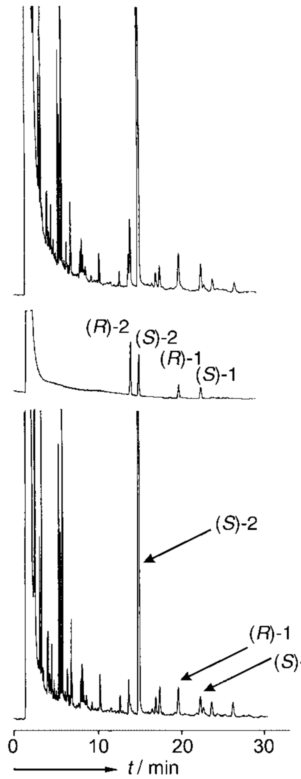


Figure 1. GLC analyses of natural plant extract and synthetic reference compounds by using a 25 m fused-silica capillary column with monokis(3-*O*-acetyl-6-*O*-*tert*-butyldimethylsilyl-2-*O*-methyl)hexakis(6-*O*-*tert*-butyldimethylsilyl-2,3-di-*O*-methyl)-β-cyclodextrin[3a] at 150 °C (isothermal). H_2 at an inlet pressure of 0.5 bar was used as the carrier gas with split injection (ratio 1:30). Bottom: natural plant extract; center: synthetic reference compounds; top: coinjection of natural plant extract and synthetic reference compounds.

Experimental Section

General: All reactions were performed in oven-dried (110 °C) glassware under N_2. THF was freshly distilled from K, CH_2Cl_2 was distilled from CaH_2. Diazomethane was prepared as an ethanol-free diethyl ether solution according to the literature[28] by using the ALDRICH Diazald kit; the diazomethane concentrations were determined prior to use.[28] Products were purified by flash chromatography[29] on Merck silica gel 60. Yields refer to analytically pure samples. ^{1}H NMR ($CHCl_3$ (δ = 7.26 ppm) as the internal standard in $CDCl_3$; C_6HD_5 (δ = 7.15 ppm) as the internal standard in C_6D_6) and ^{13}C NMR ($CDCl_3$ (center peak of the triplet δ = 77.0 ppm) as the internal standard in $CDCl_3$; C_6D_6 (center peak of the triplet δ = 128.0 ppm) as the internal standard in C_6D_6) spectroscopy was performed on Varian Mercury VX 300 and Bruker DRX 500 spectrometers. Integrals are in accordance with the assignments; coupling constants are given in Hz. The assignments of ^{1}H and ^{13}C NMR signals refer to the IUPAC nomenclature except within substituents where primed numbers are used. Combustion analyses were performed by E. Hickl, Institut für Organische Chemie und Biochemie, Universität Freiburg. MS analyses were obtained by Dr. J. Wörth and C. Warth, Institut für Organische Chemie und Biochemie, Universität Freiburg. IR spectra were obtained on a Perkin–Elmer Paragon 1000 apparatus. Optical rotations measured with a Perkin–Elmer polarimeter 341 at 589 nm and 20 °C and were calculated according to the Drude equation ($[\alpha]_D = (\alpha_{exp} \times 100)/(c \times d)$); rotational values are the average of five measurements of α_{exp} in a given solution of the respective sample. Melting points were measured on a Dr. Tottoli apparatus (Büchi) and are uncorrected. The *ee* values were determined by chiral GC, by using a Carlo Erba Instruments HRC 5160 Mega series apparatus with a Varian CP7502 (β-cyclodextrin/dimethylpolysiloxane) column.

(*S*)-3,4-Dimethyl-5-pentyl-2-(5*H*)-furanone ((*S*)-1): A solution of **15** (70 mg, 0.33 mmol) in 1,4-dioxane (3 mL) was heated at 110 °C for 5 d. The solvent was evaporated in vacuo. Subsequent purification by flash chromatography (cyclohexane/EtOAc 10:1) afforded the title compound (45 mg, 75 %): $[\alpha]_D$ = −6.5 (c = 0.6 in $CHCl_3$); IR (film): $\tilde{\nu}$ = 2955, 2930, 2860, 1755, 1685, 1465, 1460, 1440, 1385, 1330, 1130, 1115, 1095, 1060, 1010, 965, 925, 765, 745, 730, 660, 610, 575, 550 cm^{-1}; $t_r(S)$ = 18.25 min, $t_r(R)$ = 17.27 min (120 °C, 100 kPa); 95 % *ee*.

(*R*)-3,4-Dimethyl-5-pentyl-2-(5*H*)-furanone ((*R*)-1): The neat enantiomer of **15** ("*ent*-**15**"; 99 mg, 0.47 mmol) was heated for 4 h at 150 °C. Purification by flash chromatography (cyclohexane/EtOAc 9:1) afforded the title compound (58 mg, 68 %): $[\alpha]_D$ = +7.1 (c = 0.6 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.89 (m$_c$, 5'-CH_3), 1.25–1.48 (m, 1'-H^1, 2'-H_2, 3'-H_2, 4'-H_2), 1.81 (m$_c$, 3-CH_3), 1.84–1.91 (m, 1'-H^2), 1.94 (m$_c$, 4-CH_3), 4.71–4.73 (m, 5-H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$; *,** = distinguishable by a C,H correlation spectrum): δ = 8.39 (3-CH_3)*, 11.93 (4-CH_3)*, 13.92 (C-5'), 22.41, 24.10, and 31.49 (C-2', C-3', C-4'), 32.08 (C-1')**, 83.21 (C-5), 123.38 (C-3), 159.17 (C-4), 174.67 (C-2) ppm; $t_r(S)$ = 15.81 min, $t_r(R)$ = 17.07 min (120 °C, 100 kPa); 97 % *ee*; HRMS: m/z calcd for $C_{11}H_{18}O_2$: 182.130694; found 182.130680; elemental analysis calcd (%) for $C_{11}H_{18}O_2$ (182.3): C 72.50, H 9.96; found: C 72.47, H 10.07.

(*R*)-3,4,5-Trimethyl-5-pentyl-2-(5*H*)-furanone ((*R*)-2): Methyllithium (1.08 M in diethyl ether, 1.48 mL, 1.60 mmol, 2.0 equiv) was added at −50 °C to a solution of (*R*)-**19** (170 mg, 0.802 mmol) and stirred for 15 min. The solution was allowed to warm to 0 °C and stirred for 2 h. After addition of aq. HCl (0.5 M, 10 mL) the mixture was stirred for 30 min at room temperature. The solution was extracted with EtOAc (5 × 15 mL) and the combined organic extracts were dried over $MgSO_4$. After evaporation in vacuo, the residue was purified by flash chromatography (cyclohexane/EtOAc 10:1) to afford the title compound (148 mg, 94 %): $[\alpha]_D$ = −7.8 (c = 0.4 in $CHCl_3$); ^{1}H NMR (500 MHz, C_6D_6; * = distinguishable by a C,H correlation spectrum): δ = 0.80 (t, $J_{5',4'}$ = 7.23 Hz, 5'-CH_3), 0.98 (s, 5-CH_3), 0.84–0.94 and 1.00–1.20 (2m, 1- and 6-H, 1'-H^1, 2'-H_2, 3'-H_2, 4'-H_2), superimposed with 1.19 (s, 4-CH_3)*, 1.44–1.49 (m, 1'-H^2), 1.58 (s, 3-CH_3)* ppm; ^{13}C NMR (125 MHz, C_6D_6; * = distinguished by comparison with the corresponding signals of a $CDCl_3$ solution of (*R*)-**2** (δ = 8.58 (3-CH_3), 11.23 (4-CH_3) ppm); **,*** = distinguishable by a C,H correlation spectrum): δ = 8.51 (3-CH_3)*, 10.35 (4-CH_3)*, 14.13 (C-5')**, 22.69, 22.93, and 31.98 (C-2', C-3', C-4'), 23.63 (5-CH_3)**, 37.07 (C-1')***, 86.75 (C-5), 123.34 (C-3), 161.03 (C-4), 172.71 (C-2) ppm; $t_r(R)$ = 12.07 min, $t_r(S)$ = 12.57 min (120 °C, 100 kPa); 81 % *ee*; HRMS: m/z calcd for $C_{12}H_{20}O_2$: 196.146330; found 196.145939; elemental analysis calcd (%) for $C_{12}H_{20}O_2$ (196.2): C 73.43, H 10.27; found: C 73.32, H 10.41.

(*S*)-3,4,5-Trimethyl-5-pentyl-2-(5*H*)-furanone ((*S*)-2): The title compound (125 mg, 87 %) was prepared from (*S*)-**19** (159 mg, 0.736 mmol) by an analogous procedure to that described for (*R*)-**2**: $[\alpha]_D$ = +10.3 (c = 0.9 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$; * = distinguishable by the NOE observed at 4-CH_3 (δ = 1.88 ppm) while irradiating 5-CH_3 (δ = 1.38 ppm)): δ = 0.86 (t, $J_{5',4'}$ = 7.0 Hz, 5'-H_3), 0.95–1.07 and 1.18–1.31 (2m, 1- and 5-H, 2'-H_2, 3'-H_2, 4'-H_2), 1.38 (s, 5-CH_3), 1.52–1.60 and 1.77–1.83 (2m, 1-H, 1'-H_2), superimposed by 1.80 (q, $^5J_{3\text{-Me},4\text{-Me}}$ = 1.0 Hz, 3-CH_3)*, 1.88 (q, $^5J_{4\text{-Me},3\text{-Me}}$ = 1.1 Hz, 4-CH_3)* ppm; ^{13}C NMR (125 MHz, $CDCl_3$; *,**,*** = distinguishable by a C,H correlation spectrum;): δ = 8.58 (3-CH_3)*, 11.23 (4-CH_3)*, 14.02 (C-5')**, 22.50, 22.72 and 31.77 (C-2', C-3', C-4'), 23.76 (5-CH_3)**, 37.01 (C-1')***, 88.00 (C-5), 122.96 (C-3), 162.69 (C-4), 173.99 (C-2) ppm; $t_r(S)$ = 12.24 min, $t_r(R)$ = 11.95 min (120 °C, 100 kPa); 86 % *ee*.

(4*S*,5*S*)-4,5-Dihydro-4-hydroxy-2-(3*H*)-furanone ((*S*,*S*)-4): $(DHQ)_2$PHAL (63 mg, 0.081 mmol, 1 mol %), $K_3Fe(CN)_6$ (8.00 g, 24.3 mmol, 3.0 equiv), K_2CO_3 (3.36 g, 24.3 mmol, 3.0 equiv), $MeSO_2NH_2$ (771 mg, 8.11 mmol, 1.0 equiv), and $K_2OsO_2(OH)_4$ (24 mg, 0.065 mmol, 0.8 mol %) were dissolved in *t*BuOH (50 mL) and H_2O (50 mL). After cooling to 0 °C *trans*-**5** (1.38 g, 8.11 mmol) was added. After 12 h at 0 °C, aq. Na_2SO_3 (34 mL) was added and the mixture was stirred for 1 h at room temperature. The solution was extracted with EtOAc (3 × 50 mL) and the combined organic extracts were dried over $MgSO_4$. After evaporation in vacuo the residue was purified by flash chromatography (cyclohexane/EtOAc 2:1) to afford the title compound (1.27 g, 91 %): $[\alpha]_D$ = −60.7 (c = 1.1 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$; * = interchangeable, ** = distinguishable by a C,H correlation spectrum): δ = 0.89–0.93 (m, 5'-H_3), 1.30–1.56 (m, 2'-H_2, 3'-H_2, 4'-H_2), AB signal (δ_A = 1.72, δ_B = 1.87, J_{AB} = 13.8 Hz, A part in addition split by $J_{A,2'\text{-H(1)}}$ = 10.2, $J_{A,5}$ = $J_{A,2'\text{-H(2)}}$ = 5.7 Hz, B part in addition split by $J_{B,2'\text{-H(2)}}$ = 9.9*, $J_{B,5}$ = 8.3, $J_{B,2'\text{-H(1)}}$ = 5.4* Hz, 1'-H_2), 2.22 (br d, $J_{4\text{-OH},4}$ = 4.8 Hz, 4-OH), AB signal (δ_A = 2.55, δ_B = 2.79, J_{AB} = 17.7 Hz, A part in addition split by $J_{A,4}$ = 0.9 Hz, B part in addition split by $J_{B,4}$ = 5.5 Hz, 3-H_2), 4.37 (ddd, $J_{5,1'\text{-H(B)}}$ = 8.5, $J_{5,1'\text{-H(A)}}$ = 5.7, $J_{5,4}$ = 3.6 Hz, 5-H)**, 4.48 (br ddd, $J_{4,5} \approx J_{4,4\text{-OH}} \approx J_{4,3\text{-H(B)}} \approx$ 4.4 Hz, $J_{4,3\text{-H(A)}}$ not resolved, 4-H)** ppm; ^{13}C NMR (125 MHz, $CDCl_3$; * = distinguishable by a C,H correlation spectrum, ** = assignment is based on increment calculation[30] which predicts δ = 30.5 ppm (C-3'), *** = distinction is based on increment calculation[30] which predicts δ = 65.0 ppm (C-4) and δ = 77.9 ppm (C-5)): δ = 13.92 (C-5'), 22.44 and 25.20 (C-2', C-4'), 28.20 (C-1')*, 31.59 (C-3')**, 39.47 (C-3), 69.01 (C-4)***, 84.95 (C-5)***, 175.84 (C-2) ppm; elemental analysis calcd (%) for $C_9H_{16}O_3$ (172.2): C 62.77, H 9.36; found: C 62.60, H 9.27.

(4*R*,5*R*)-4,5-Dihydro-4-hydroxy-2-(3*H*)-furanone ((*R*,*R*)-4): The title compound (1.13 g, 90 %) was prepared from *trans*-**5** (1.24 g, 7.30 mmol) by an analogous procedure to that described for (*S*,*S*)-**4** but with $(DHQD)_2$PHAL as a ligand: $[\alpha]_D$ = +62.9 (c = 1.1 in $CHCl_3$).

Methyl (*trans*-3-nonenoate) (*trans*-5): A mixture of triethylamine (8.8 mL, 6.4 g, 63 mmol, 3.0 equiv), heptanal (2.40 g, 21.0 mmol), and malonic acid (2.40 g, 23.1 mmol, 1.1 equiv) was heated at 90 °C for 18 h. After the mixture had been cooled to room temperature, the solution was poured into precooled (0 °C) aq. H_2SO_4 (20 %, 12.5 mL). The solution was extracted with CH_2Cl_2 (3 × 15 mL) and evaporated in vacuo. The residue was dissolved in methanol (12.5 mL). After addition of conc. H_2SO_4 (0.60 mL, 0.11 g, 1.1 mmol, 0.05 equiv), the mixture was heated for 2 h under reflux and then cooled to 0 °C. Aq. $NaHCO_3$ (9.5 mL) was added. After extraction with CH_2Cl_2 (3 × 10 mL) the combined organic extracts were washed with aq. NaCl (3 × 10 mL) and dried over $MgSO_4$. The solvent was evaporated in vacuo and the residue was purified by distillation (110–112 °C, 30 mbar) to afford the title compound (2.95 g, 82 %): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.88 (t, $J_{9,8}$ = 6.8 Hz, 9-H_3), 1.20–1.42 (m, 6-H_2, 7-H_2, 8-H_2), 1.98–2.07 (m, 5-H_2), 3.03 (m$_c$, presumably interpretable as br d, $J_{2,3}$ = 5.4 Hz, 2-H_2), 3.68 (s, $COOCH_3$), 5.46–5.62 (m, 3-H, 4-H) ppm.

(4*S*,5*S*)-4-(4-Bromobenzoyloxy)-4,5-dihydro-5-pentyl-2-(3*H*)-furanone ((*S*,*S*)-6): DCC (0.12 g, 0.57 mmol, 1.1 equiv), *p*-bromobenzoic acid (0.11 g, 0.57 mmol, 1.1 equiv), and DMAP (cat.) were added to a solution of (4*S*,5*S*)-**4**. After heating for 1 h under reflux, the mixture was cooled to room temperature and stirred for 4 h. After addition of aq. NH_4Cl (15 mL) and extraction with CH_2Cl_2 (4 × 20 mL), the combined organic extracts were dried over $MgSO_4$. Purification by flash chromatography (cyclohexane/EtOAc 10:1) afforded the title compound (149 mg, 81 %) as a white solid: m.p. 81 °C; ^{1}H NMR (500 MHz, $CDCl_3$; * = interchangeable): δ = 0.84–0.89 (m, 5'-H_3), 1.25–1.34 (m, 3'-H_2, 4'-H_2), 1.35–1.44 (m, 2'-H^1), 1.49–1.60 (m, 2'-H^2), 1.68–1.75 (m, 1'-H^1), 1.84–1.91 (m, 1'-H^2), AB signal (δ_A = 2.72, δ_B = 3.00, J_{AB} = 18.3 Hz, A part in addition split by $J_{A,4} \approx$ 0.5 Hz, B part in addition split by $J_{B,4}$ = 5.9 Hz, 3-H_2), 4.62 (ddd, $J_{5,1'\text{-H(1)}}$ = 8.8*, $J_{5,1'\text{-H(2)}}$ = 4.9*, $J_{5,4}$ = 4.1 Hz, 5-H), 5.71 (ddd, $J_{4,3\text{-H(B)}}$ = 5.4, $J_{4,5}$ = 4.1, $J_{4,3\text{-H(A)}} \approx$ 1.1 Hz, 4-H), AA'BB' signal with signal centers at 7.62 and 7.88 (2 × 2 ArH) ppm; IR (film): $\tilde{\nu}$ = 3035, 3025, 3015, 3010, 2960, 2935, 2875, 2860, 1925, 1785, 1725, 1590, 1485, 1400, 1355, 1270, 1235, 1195, 1175, 1165, 1145, 1115, 1100, 1070, 1050, 1015, 920, 850, 800 cm^{-1}; proof of the absolute configuration was obtained by X-ray crystal structure analysis.[14]

(*E*)-3-Methyl-2-octenoic acid ((*E*)-7): At −78 °C, *t*BuLi (1.7 M in pentane, 14.3 mL, 24.3 mmol, 9.7 equiv) was added to a solution of pentyl iodide (1.50 mL, 2.28 g, 11.5 mmol, 4.6 equiv) in pentane (45 mL) and diethyl ether (30 mL). After being stirred for 5 min, the solution was allowed to reach room temperature then it was stirred for 1.5 h. The mixture was cooled to 0 °C and added to a cooled (−5 °C) suspension of CuI (1.10 g, 5.75 mmol, 2.3 equiv) in THF (5 mL). After 10 min, the solution was cooled to −78 °C and a solution of 2-butynoic acid (210 mg, 2.50 mmol) in THF (5 mL) was added. The mixture was stirred for 10 min at −78 °C and was then allowed to reach −15 °C. After 30 min, the mixture was poured into cold (0 °C) aq. HCl (1 M, 40 mL) and the solution was warmed to room temperature. After extraction with EtOAc (4 × 50 mL), the combined organic extracts were dried over $MgSO_4$ and evaporated in vacuo. The residue was purified by flash chromatography (cyclohexane/EtOAc 10:1) to afford the title compound (336 mg, 86 %): ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.90 (t, $J_{8,7}$ = 7.2 Hz, 8-H_3), 1.24–1.36 (m, 6-H_2, 7-H_2), 1.46–1.52 (m, 5-H_2), 2.14–2.18 (m, 4-H_2), superimposed by 2.16 (m$_c$, presumably interpretable as d, ${}^4J_{allyl}=1.2$ Hz, 3-CH_3), 5.69 (incomplete resolved qd, ${}^4J_{2,3\text{-Me}}={}^4J_{2,4}=1.2$ Hz, 2-H), 11.89 (brs, COO*H*) ppm; elemental analysis calcd (%) for $C_9H_{16}O_2$ (156.21): C 69.20, H 10.32; found: C 69.32, H 10.16.

(*Z*)-3-Methyl-2-octenoic acid ((*Z*)-7): At −5°C MeLi (1.6 M in diethyl ether, 57.5 mL, 92.0 mmol, 4.6 equiv) was added to a suspension of CuI (8.76 g, 46.0 mmol, 2.3 equiv) in THF (200 mL). The solution was stirred for 20 min at this temperature and then cooled to −78°C. A solution of 2-octynoic acid (2.80 g, 20.0 mmol) in THF (9 mL) was added. After stirring for 1.5 h at this temperature, the mixture was warmed to −15°C and stirred for another 5 h. The mixture was poured into cold (0°C) aq. HCl (1 M, 400 mL). After extraction with EtOAc (4×100 mL), the combined organic extracts were dried over $MgSO_4$ and evaporated in vacuo. The residue was purified by flash chromatography (cyclohexane/EtOAc 10:1) to afford the title compound (3.04 g, 97%): ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=0.89$ (m_c, 8-H_3), 1.28–1.37 (m, 6-H_2, 7-H_2), 1.47 (m_c, 5-H_2), 1.92 (d, ${}^4J_{3\text{-Me},2}=1.4$ Hz, 3-CH_3), 2.63 (m_c, 4-H_2), 5.67 (m_c, 2-H), 11.89 (brs, COO*H*) ppm.

(*E*)-3-Methyl-2-octenoyl chloride ((*E*)-8): At 0°C, $SOCl_2$ (0.33 mL, 0.53 g, 4.5 mmol, 1.0 equiv) and DMF (1 drop) were added to a solution of (*E*)-3-methyl-2-octenoic acid (701 mg, 4.49 mmol) in CH_2Cl_2 (19 mL). The solution was stirred for 3 h at room temperature. After evaporation in vacuo, the crude residue was used for the preparation of (*E*)-**9** without further purification.

(*Z*)-3-Methyl-2-octenoyl chloride ((*Z*)-8): At 0°C, $SOCl_2$ (0.051 mL, 83 mg, 0.70 mmol, 1.1 equiv) and DMF (1 drop) were added to a solution of (*Z*)-3-methyl-2-octenoic acid (0.10 g, 0.64 mmol) in CH_2Cl_2 (4 mL). The solution was stirred for 2.5 h at room temperature. After evaporation in vacuo, the crude residue was used for the preparation of (*Z*)-**9** without further purification.

(*E*)-1-Diazo-4-methyl-3-nonen-2-one ((*E*)-9): At 0°C, the crude acid chloride (*E*)-**8** was added to a solution of CH_2N_2 (0.42 M in diethyl ether, 21.4 mL, 8.98 mmol, 2.0 equiv) and Hünig's base (0.78 mL, 0.58 g, 4.5 mmol, 1.0 equiv). After the mixture had been stirred for 1 h at room temperature, the solvent was evaporated in vacuo. The residue was purified by flash chromatography (cyclohexane/EtOAc 30:1) to afford the diazoketone (*E*)-**9** (447 mg, 55% over 2 steps) as a yellow oil: ^{1}H NMR (500 MHz, $CDCl_3$; *=distinguishable by a C,H correlation spectrum): $\delta=0.89$ (t, $J_{9,8}=7.2$ Hz, 9-H_3), 1.23–1.36 (m, 7-H_2, 8-H_2), 1.43–1.50 (m, 6-H_2), 2.10 (m_c, 5-H_2), 2.19 (d, ${}^4J_{4\text{-Me},3}=0.8$ Hz, 4-CH_3), 5.18 (brs, 1-H)*, 5.74 (brs, 3-H)* ppm; IR (film): $\tilde{\nu}=2960$, 2930, 2870, 2860, 2095, 1690, 1645, 1615, 1445, 1385, 1335, 1145, 1115, 1085, 785 cm^{-1}; HRMS: *m*/*z* calcd for $C_{10}H_{16}N_2O$: 180.126211; found 180.126263.

(*Z*)-1-Diazo-4-methyl-3-nonen-2-one ((*Z*)-9): At 0°C, a solution of the crude acid chloride (*Z*)-**8** in Et_2O (3 mL) was added to a solution of CH_2N_2 (0.43 M in diethyl ether, 4.5 mL, 1.92 mmol, 3.0 equiv) and Hünig's base (0.11 mL, 84 mg, 0.65 mmol, 1.0 equiv). After the mixture had been stirred for 15 min at 0°C and for 1 h at room temperature, the solvent was evaporated in vacuo. The residue was purified by flash chromatography (petroleum ether/diethyl ether 10:1) to afford the diazoketone (*Z*)-**9** (66 mg, 57% over 2 steps) as a yellow oil: ^{1}H NMR (500 MHz, $CDCl_3$; *=distinguishable by a C,H correlation spectrum): $\delta=0.89$ (m_c, 9-H_3), 1.29–1.37 (m, 7-H_2, 8-H_2), 1.43–1.51 (m, 6-H_2), 1.87 (d, ${}^4J_{4\text{-Me},3}=1.4$ Hz, 4-CH_3), 2.65 (brt, $J_{5,6}=7.9$ Hz, 5-H_2), 5.16 (brs, 1-H)*, 5.73 (brs, 3-H)* ppm; IR (film): $\tilde{\nu}=3080$, 2960, 2930, 2870, 2860, 2095, 1645, 1615, 1445, 1385, 1335, 1145, 1115, 1085, 1005, 960, 845, 785, 725 cm^{-1}; elemental analysis calcd (%) for $C_{10}H_{16}N_2O$ (180.1): C 66.69, H 8.88, N 15.55; found: C 66.57, H 8.97, N 15.62.

(4*R*,5*R*)-4,5-Dihydro-4-hydroxy-5-methyl-5-pentyl-2-(3*H*)-furanone ((4*R*,5*R*)-10): $(DHQD)_2$PHAL (6 mg, 0.008 mmol, 1.6 mol%), $K_3Fe(CN)_6$ (494 mg, 1.50 mmol, 3.0 equiv), K_2CO_3 (207 mg, 1.50 mmol, 3.0 equiv), $MeSO_2NH_2$ (48 mg, 0.50 mmol, 1.0 equiv), and $K_2OsO_2(OH)_4$ (1.5 mg, 0.004 mmol, 0.8 mol%) were dissolved in *t*BuOH (2.5 mL) and H_2O (2.5 mL). After the solution had been cooled to 0°C, (*E*)-**11** (92 mg, 0.50 mmol) was added. After 24 h at 0°C, aq. Na_2SO_3 (2.5 mL) was added and the mixture was stirred for 30 min at room temperature. The solution was extracted with EtOAc (3×40 mL). The combined organic extracts were dried over $MgSO_4$. After evaporation in vacuo, the residue was purified by flash chromatography (cyclohexane/EtOAc 2:1) to afford the title compound (76 mg, 82%): $[\alpha]_D=+15.7$ ($c=1.2$ in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$; *=interchangeable): $\delta=0.90$ (m_c, 5′-H_3), 1.29–1.47 (m, 2′-H_2, 3′-H_2, 4′-H_2), superimposed with 1.33 (s, 5-CH_3), AB signal ($\delta_A=1.73$, $\delta_B=1.81$, $J_{AB}=13.8$ Hz, A part in addition split by $J_{A,2'\text{-H(1)}}=10.1$, $J_{A,2'\text{-H(2)}}=6.1$ Hz, B part in addition split by $J_{B,2'\text{-H(1)}}=10.5$*, $J_{B,2'\text{-H(2)}}=5.8$* Hz, 1′-H_2), 2.46 (brs, 4-OH), 2.52 (dd, $J_{gem}=18.0$, $J_{3\text{-H(1)},4}=2.5$ Hz, 3-H^1), 2.95 (dd, $J_{gem}=18.0$, $J_{3\text{-H(2)},4}=6.2$ Hz, 3-H^2), 4.21 (m_c, 4-H) ppm; IR (film): $\tilde{\nu}=3445$, 2955, 2935, 2870, 1755, 1460, 1385, 1320, 1295, 1265, 1235, 1200, 1170, 1135, 1120, 1100, 1075, 955, 930 cm^{-1}; $t_r(4R,5R)=39.82$ min, $t_r(4S,5S)=45.61$ min (140°C, 100 kPa); 97% *ee*; elemental analysis calcd (%) for $C_{10}H_{18}O_3$ (186.2): C 64.50, H 9.74; found: C 64.46, H 9.72.

(4*S*,5*S*)-4,5-Dihydro-4-hydroxy-5-methyl-5-pentyl-2-(3*H*)-furanone ((4*S*,5*S*)-10): The title compound (167 mg, 83%) was prepared from (*E*)-**11** (200 mg, 1.09 mmol) by an analogous procedure to that described for (4*R*,5*R*)-**10** but with $(DHQ)_2$PHAL as the ligand: $[\alpha]_D=-16.1$ ($c=1.1$ in $CHCl_3$); $t_r(4S,5S)=42.19$ min, $t_r(4R,5R)=37.79$ min (140°C, 100 kPa); 91% *ee*.

(4*R*,5*S*)-4,5-Dihydro-4-hydroxy-5-methyl-5-pentyl-2-(3*H*)-furanone ((4*R*,5*S*)-10): The title compound (909 mg, 85%) was prepared from (*Z*)-**11** (1.06 g, 5.75 mmol) by an analogous procedure to that described for (4*R*,5*R*)-**10** but with $(DHQD)_2$PHAL as the ligand: $[\alpha]_D=-4.0$ ($c=1.2$ in $CHCl_3$); $t_r(4R,5S)=39.50$ min, $t_r(4S,5R)=37.33$ min (140°C, 100 kPa); 85% *ee*.

(4*S*,5*R*)-4,5-Dihydro-4-hydroxy-5-methyl-5-pentyl-2-(3*H*)-furanone ((4*S*,5*R*)-10): The title compound (618 mg, 92%) was prepared from (*Z*)-**11** (665 mg, 3.61 mmol) by an analogous procedure to that described for (4*R*,5*R*)-**10**: $[\alpha]_D=+3.8$ ($c=1.1$ in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=0.89$ (t, $J_{5',4'}=7.0$ Hz, 5′-H_3), 1.25–1.45 (m, 2′-H_2, 3′-H_2, 4′-H_2), superimposed with 1.40 (s, 5-CH_3), 1.59 (m_c, 1′-H_2), 2.55 (dd, $J_{gem}=18.1$, $J_{3\text{-H(1)},4}=4.1$ Hz, 3-H^1; superimposes, in line with the integral, on the brs of 4-OH), 2.91 (dd, $J_{gem}=18.1$, $J_{3\text{-H(2)},4}=6.8$ Hz, 3-H_2), 4.26 (m_c, 4-H) ppm; IR (film): $\tilde{\nu}=3445$, 2955, 2935, 2870, 1755, 1385, 1320, 1295, 1265, 1195, 1175, 1135, 1120, 1105, 1065, 1040, 950 cm^{-1}; $t_r(4S,5R)=36.79$ min, $t_r(4S,5R)=40.54$ min (140°C, 100 kPa); 80% *ee*; elemental analysis calcd (%) for $C_{10}H_{18}O_3$ (186.2): C 64.49, H 9.74; found: C 64.27, H 9.87.

Methyl (*E*)-4-methyl-3-nonenoate ((*E*)-11): Under exclusion of light, a solution of silver benzoate (130 mg, 0.568 mmol, 0.29 equiv) in triethylamine (1.28 mL, 929 mg, 9.18 mmol, 4.70 equiv) was added dropwise to a solution of (*E*)-**9** (352 mg, 1.95 mmol) in methanol (8 mL). After the mixture had been stirred for 5 h at room temperature, the solvent was evaporated in vacuo and the residue was purified by flash chromatography (petroleum ether/diethyl ether 50:1) to afford the title compound (318 mg, 88%) as a colorless liquid: ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=0.88$ (t, $J_{9,8}=7.2$ Hz, 9-H_3), 1.21–1.34 (m, 7-H_2, 8-H_2), 1.37–1.43 (m, 6-H_2), 1.62 (brs, 4-CH_3), 2.01 (brt, $J_{5,6}=7.6$ Hz, 5-H_2), 3.05 (brd, $J_{2,3}=7.1$ Hz, 2-H_2), 3.68 (s, $COOCH_3$), 5.31 (tm_c, $J_{3,2}=6.7$ Hz, 3-H) ppm; proof of the *E* configuration was obtained from the NOE observed at 3-H ($\delta=5.31$ ppm) while irradiating 5-H_2 ($\delta=2.01$ ppm).

Methyl (*Z*)-4-methyl-3-nonenoate ((*Z*)-11): The title compound (799 mg, 95%) was prepared from (*Z*)-**9** (824 mg, 4.58 mmol) by an analogous procedure to that described for (*E*)-**11**: ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=0.89$ (t, $J_{9,8}=7.2$ Hz, 9-H_3), 1.19–1.41 (m, 6-H_2, 7-H_2, 8-H_2), 1.73 (dt, ${}^4J_{4\text{-Me},3}={}^5J_{4\text{-Me},2}=1.3$ Hz, 4-CH_3), 2.01 (brt, $J_{5,6}=7.7$ Hz, 5-H_2), 3.04 (m_c, presumably interpretable as a incomplete resolved dq, $J_{2,3}=7.2$, ${}^5J_{2,4\text{-Me}}=1.2$ Hz, 2-H_2), 3.68 (s, $COOCH_3$), 5.31 (tm_c, $J_{3,2}=7.2$ Hz, 3-H) ppm.

(4*S*,5*R*)-4-(4-Bromobenzoyloxy)-4,5-dihydro-5-methyl-5-pentyl-2-(3*H*)-furanone ((4*S*,5*R*)-12): Triethylamine (0.08 mL, 0.05 g, 0.5 mmol, 1.3 equiv), *p*-bromobenzoyl chloride (0.11 g, 0.49 mmol, 1.2 equiv), and DMAP (cat.) were added to a solution of (4*S*,5*R*)-**10** (70 mg, 0.41 mmol) in CH_2Cl_2 (1 mL). After the mixture had been stirred for 6 h at room temperature, the solution was heated under reflux for 2 h. It was then allowed to cool to room temperature, diluted with H_2O (15 mL), and extracted with CH_2Cl_2 (4×15 mL). The combined organic extracts were dried over $MgSO_4$ and evaporated in vacuo. The residue was purified by flash chromatography (cyclohexane/EtOAc 8:1) to afford the title compound (85 mg, 56 %): ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=0.91$ (m_c, 5′-H_3), 1.22–1.55 (m, 2′-H_2, 3′-H_2, 4′-H_2), superimposed with 1.44 (s, 5-CH_3), 1.63–1.79 (m, 1′-H_2), AB signal ($\delta_A=2.69$, $\delta_B=3.15$, $J_{AB}=18.6$ Hz, A part in addition split by $J_{A,4}=2.6$ Hz, B part in addition split by $J_{B,4}=7.0$ Hz, 3-H_2), 5.48 (dd, $J_{4,3\text{-H(B)}}=7.0$, $J_{4,3\text{-H(A)}}=2.6$ Hz, 4-H), AA′BB′ signal with signal centers at 7.62 and 7.89 (2×2 ArH) ppm; proof of the absolute configuration was obtained by X-ray crystal structure analysis.[14]

(3a*R*,4*S*,6a*S*)-3,3a,4,6a-Tetrahydro-4-pentylfuro[3,4c]pyrazol-6-one (13): a) At 0 °C, triethylamine (2.70 mL, 1.97 g, 19.5 mmol, 2.8 equiv) and $MeSO_2Cl$ (0.81 mL, 1.2 g, 11 mmol, 1.5 equiv) were added to a solution of (*S*,*S*)-**4** (1.20 g, 6.97 mmol) in CH_2Cl_2 (20 mL). After the mixture had been stirred for 30 min, aq. NH_4Cl (15 mL) was added. The mixture was extracted with CH_2Cl_2 (4×40 mL), dried over $MgSO_4$ and evaporated in vacuo. The residue was purified by flash chromatography (cyclohexane/EtOAc 6:1) to afford (*S*)-5-pentyl-2-(5*H*)-furanone (992 mg, 92 %): $[\alpha]_D=+91.0$ ($c=1.2$ in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$; * = interchangeable): $\delta=0.88$–0.92 (m, 5′-H_3), 1.29–1.35 (m, 3′-H_2, 4′-H_2), 1.38–1.52 (m, 2′-H_2), 1.63–1.70 (m, 1′-H^1), 1.73–1.80 (m, 1′-H^2), 5.04 (dddd, $J_{5,1'\text{-H(1)}}=7.3$*, $J_{5,1'\text{-H(2)}}=5.4$*, $J_{5,4}\approx{}^4J_{5,3}\approx1.7$ Hz, 5-H), 6.10 (dd, $J_{3,4}=5.7$, $^4J_{3,5}=2.0$ Hz, 3-H), 7.45 (dd, $J_{4,3}=5.8$, $J_{4,5}=1.5$ Hz, 4-H) ppm; $t_r(S)=34.50$ min, $t_r(R)=33.18$ min (100 °C, 100 kPa); 94 % *ee*; elemental analysis calcd (%) for $C_9H_{14}O_2$ (154.2): C 70.01, H 9.15; found: C 70.01, H 9.18.

b) At 0 °C, diazomethane (0.45 M in diethyl ether, 43 mL, 19.5 mmol, 5.0 equiv) was added to a solution of (*S*)-5-pentyl-2-(5*H*)-furanone (600 mg, 3.89 mmol, 94 % *ee*) in diethyl ether (6 mL). The solution was allowed to reach room temperature and was stirred for 15 h. After evaporation in vacuo, the residue was purified by flash chromatography (cyclohexane/EtOAc 5:1) to afford the title compound (730 mg, 96 %): IR (film): $\tilde{\nu}=2960$, 2935, 2865, 1770, 1355, 1225, 1205, 1185, 1025, 1000, 945, 905, 765, 755, 730, 720, 695, 655 cm^{-1}; elemental analysis calcd (%) for $C_{10}H_{16}N_2O_2$ (196.3): C 61.20, H 8.23, N 14.27; found: C 61.27, H 8.08 N 14.09.

(3a*S*,4*R*,6a*R*)-3,3a,4,6a-Tetrahydro-4-pentylfuro[3,*R*4c]pyrazol-6-one (*ent*-13): a) (*R*)-5-Pentyl-2-(5*H*)-furanone (852 mg, 95 %) was prepared from (*R*,*R*)-**4** (1.00 g, 5.80 mmol) by an analogous procedure to that described for **13** (part a): $[\alpha]_D=-94.8$ ($c=0.9$ in $CHCl_3$); IR (film): $\tilde{\nu}=3090$, 2955, 2930, 2860, 1750, 1600, 1465, 1330, 1165, 1115, 1100, 1030, 1000, 960, 920, 900, 815 cm^{-1}; $t_r(R)=29.75$ min, $t_r(S)=33.80$ min (140 °C, 100 kPa); 97 % *ee*.

b) The title compound (219 mg, 86 %) was prepared from (*R*)-5-pentyl-2-(5*H*)-furanone (200 mg, 1.30 mmol, 97 % *ee*) by an analogous procedure to that described for **13** (part b): ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=0.90$ (m_c, 5′-H_3), 1.27–1.49 (m, 2′-H_2, 3′-H_2, 4′-H_2), 1.63–1.78 (m, 1′-H_2), 2.67 (dddd, $J_{3a,6a}=9.0$, $J_{3a,3\text{-H(A)}}=7.9$, $J_{3a,4}=5.2$, $J_{3a,3\text{-H(B)}}=2.8$ Hz, 3a-H), 3.92 (dt, $J_{4,1'\text{-H(1)}}=7.5$, $J_{4,3a}=J_{4,1'\text{-H(2)}}=5.3$ Hz, 4-H), AB signal ($\delta_A=4.75$, $\delta_B=4.83$, $J_{AB}=18.5$ Hz, A part in addition split by $J_{A,3a}=8.2$, $^5J_{A,6a}=2.0$ Hz, B part in addition split by $J_{B,3a}={}^5J_{B,6a}=2.6$ Hz, 3-H_2), 5.52 (dt, $J_{6a,3a}=9.1$, $^5J_{6a,3\text{-H(A)}}={}^5J_{6a,3\text{-H(B)}}=2.2$ Hz, 6a-H) ppm.

(3a*S*,4*S*,6a*S*)-1,3a,4,6a-Tetrahydro-6a-methyl-4-pentylfuro[3,4c]pyrazol-6-one (14) and (3a*R*,4*S*,6a*S*)-3,3a,4,6a-tetrahydro-6a-methyl-4-pentylfuro[3,4c]pyrazol-6-one (15): At −78 °C, *n*BuLi (2.05 M in hexane, 0.84 mL, 1.73 mmol, 1.7 equiv) was added to a solution of diisopropylamine (0.242 mL, 175 mg, 1.73 mmol, 1.7 equiv) in THF (1.7 mL). After the mixture had been stirred for 30 min, a solution of **13** (200 mg, 1.02 mmol) in THF (1.5 mL) was added and the mixture was stirred for 30 min at −78 °C. Methyl iodide (0.13 mL, 0.29 g, 2.0 mmol, 2.0 equiv) was added. The solution was allowed to warm to −40 °C and stirred for 18 h. After addition of H_2O the mixture was allowed to reach room temperature, extracted with EtOAc (4×20 mL), and dried over $MgSO_4$. Evaporation in vacuo followed by flash chromatography (cyclohexane/EtOAc 6:1) afforded the separated title compounds in a 79:21 ratio (**14**: 138 mg, 65 %; **15**: 33 mg, 15 %).

14: IR (film): $\tilde{\nu}=3030$, 2960, 2935, 2860, 1770, 1380, 1235, 1230, 1215, 1210, 1200, 1190, 1145, 1115, 1100, 800 cm^{-1}; HRMS: *m*/*z* calcd for $C_{11}H_{18}N_2O_2$: 210.137130; found 210.136828; elemental analysis calcd (%) for $C_{11}H_{18}N_2O_2$ (210.3): C 62.84, H 8.63, N 13.32; found: C 62.78, H 8.82, N 13.19.

15: IR (film): $\tilde{\nu}=2955$, 2935, 2860, 1770, 1550, 1455, 1435, 1375, 1355, 1290, 1255, 1240, 1175, 1110, 1015, 995, 945, 935, 905 cm^{-1}; elemental analysis calcd (%) for $C_{11}H_{18}N_2O_2$ (210.3): C 62.84, H 8.63, N 13.32; found: C 62.94, H 8.75, N 13.05.

(3a*R*,4*R*,6a*R*)-1,3a,4,6a-Tetrahydro-6a-methyl-4-pentylfuro[3,4c]pyrazol-6-one (*ent*-14) and (3a*S*,4*R*,6a*R*)-3,3a,4,6a-tetrahydro-6a-methyl-4-pentylfuro[3,4c]pyrazol-6-one (*ent*-15): The title compounds (*ent*-**14**: 62 mg, 32 %; *ent*-**15**: 98 mg, 51 %) were prepared in a 42:58 ratio from *ent*-**13** (180 mg, 0.917 mmol) by an analogous procedure to that described for **14** and **15**.

ent-**14**: ^{1}H NMR (500 MHz, $CDCl_3$; * = interchangeable): $\delta=0.90$–0.93 (m, 5″-H_3), 1.30–1.56 (m, 2″-H_2, 3″-H_2, 4″-H_2), superimposed by 1.54 (s, 1′-H_3), 1.63–1.70 (m, 1″-H^1), 1.76–1.84 (m, 1″-H^2), 3.24 (m, 3a-H), 4.38 (ddd, $J_{4,1''\text{-H(1)}}=8.6$*, $J_{4,1''\text{-H(2)}}=5.9$*, $J_{4,3a}=3.1$ Hz, 4-H), 6.03 (brs, NH), 6.70 (d, $J_{3,3a}=1.1$ Hz, 3-H) ppm.

ent-**15**: ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=0.90$ (m_c, 5″-H_3), 1.27–1.50 (m, 2″-H_2, 3″-H_2, 4″-H_2), 1.58–1.76 (m, 1′-H_2), superimposed with 1.59 (s, 1′-H_3), 2.29 (ddd, $J_{3a,3\text{-H(A)}}=7.5$, $J_{3a,4}=5.5$, $J_{3a,3\text{-H(B)}}=2.0$ Hz, 3a-H), 3.78 (ddd, $J_{4,1''\text{-H(1)}}=7.5$, $J_{4,1''\text{-H(2)}}=J_{4,3a}=5.5$ Hz, 4-H), AB signal ($\delta_A=4.71$, $\delta_B=4.82$, $J_{AB}=18.5$ Hz, A part in addition split by $J_{A,3a}=7.5$ Hz, B part in addition split by $J_{B,3a}=2.0$ Hz, 3-H_2) ppm.

(5*S*)-4-Hydroxy-3,5-dimethyl-5-pentyl-2-(3*H*)-furanone ((*S*)-18): a) At −78 °C, *n*-BuLi (2.27 M in THF, 2.47 mL, 5.60 mmol, 2.8 equiv) was added to a solution of diisopropylamine (0.79 mL, 0.57 g, 5.6 mmol, 2.8 equiv) in THF (8 mL). After the mixture had been stirred for 30 min, a solution of (4*R*,5*S*)-**10** (370 mg, 2.00 mmol, 84 % *ee*) in THF (3 mL) was added and the mixture was stirred for 1 h. A solution of methyl iodide (0.22 mL, 0.51 g, 3.6 mmol, 1.8 equiv) in DMPU (5.4 mL) and THF (7.1 mL) was added to this mixture during 90 min. It was then warmed to −40 °C and stirred overnight at this temperature. Aqueous HCl (2 %, 30 mL) was added and the mixture was allowed to reach room temperature. After extraction with EtOAc (3×30 mL), the combined organic extracts were washed with aq. NaCl (2×30 mL) and dried over $MgSO_4$. Evaporation in vacuo followed by flash chromatography (cyclohexane/EtOAc 3:1) afforded (3*R*,4*R*,5*S*)-4,5-dihydro-4-hydroxy-3,5-dimethyl-5-pentyl-2-(3*H*)-furanone (295 mg, 74 %): $[\alpha]_D=-5.0$ ($c=0.3$ in $CHCl_3$); $t_r(3R,4R,5S)=30.70$ min, $t_r(3S,4S,5R)=28.51$ min (140 °C, 100 kPa); 86 % *ee*; elemental analysis calcd (%) for $C_{11}H_{20}O_3$ (200.3): C 65.97, H 10.07; found: C 65.85, H 9.87.

b) At −78 °C, trifluoroacetic anhydride (0.33 mL, 0.49 g, 2.3 mmol, 2.0 equiv) was added to a solution of DMSO (0.29 mL, 0.32 g, 4.1 mmol, 3.5 equiv) in CH_2Cl_2 (6 mL). The resulting mixture was stirred for 30 min. After addition of a solution of (3*R*,4*R*,5*S*)-4,5-dihydro-4-hydroxy-3,5-dimethyl-5-pentyl-2-(3*H*)-furanone (232 mg, 1.16 mmol, 86 % *ee*) in CH_2Cl_2 (6 mL), the mixture was stirred for 2 h at −78 °C. Triethylamine (0.65 mL, 0.47 g, 4.6 mmol, 4.0 equiv) was then added and the mixture was stirred for 14 h. After addition of H_2O (15 mL) the solution was allowed to reach room temperature and was extracted with CH_2Cl_2 (5×20 mL). Drying over $MgSO_4$ and evaporation in vacuo followed by flash chromatography (cyclohexane/EtOAc 3:1) afforded the title compound (229 mg, 99 %): $[\alpha]_D=+0.6$ ($c=1.1$ in $CHCl_3$); IR (film): $\tilde{\nu}=2955$, 2930, 2870, 2865, 1720, 1650, 1460, 1405, 1370, 1335, 1310, 1265, 1170, 1105, 1050 cm^{-1}; $t_r(S)=15.58$ min, $t_r(R)=12.69$ min (140 °C, 100 kPa); 85 % *ee*; elemental analysis calcd (%) for $C_{11}H_{18}O_3$ (198.2): C 66.64, H 9.15; found: C 66.42, H 9.34.

(5*R*)-4-Hydroxy-3,5-dimethyl-5-pentyl-2-(3*H*)-furanone ((*R*)-18): a) (3*S*,4*S*,5*R*)-4,5-Dihydro-4-hydroxy-3,5-dimethyl-5-pentyl-2-(3*H*)-furanone (471 mg, 72 %) was prepared from (4*S*,5*R*)-**10** (611 mg, 3.28 mmol, 80 % *ee*) by an analogous procedure to that described for (*S*)-**18** (part a): $[\alpha]_D=+4.3$ ($c=0.6$ in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=0.90$ (t, $J_{5',4'}=7.0$ Hz, 5′-H), 1.25–1.46 (m, 2′-H_2, 3′-H_2, 4′-H_2), superimposed with 1.30 (d, $J_{3\text{-Me},3}=7.1$ Hz, 3-CH_3) and 1.33 (s, 5-CH_3), 1.63–1.75 (m, 1′-H_2), 2.44 (brd, $J_{4\text{-OH},4}=5.2$ Hz, 4-OH), 2.66 (dq, $J_{3,4}=9.8$, $J_{3,3\text{-Me}}=7.1$ Hz, 3-H), 3.86 (dd, $J_{4,3}=9.9$, $J_{4,4\text{-OH}}=5.2$ Hz, 4-H) ppm; IR (film): $\tilde{\nu}=3445$, 2955, 2935, 2875, 1755, 1750, 1460, 1385, 1350, 1310, 1255, 1245, 1200, 1125, 1110, 1075, 1040, 945, 620 cm^{-1}; $t_r(3S,4S,5R)=27.13$ min, $t_r(3R,4R,5S)=30.08$ min (140 °C, 100 kPa); 78 % *ee*.

b) The title compound (278 mg, 99 %) was prepared from (3*S*,4*S*,5*R*)-4,5-dihydro-4-hydroxy-3,5-dimethyl-5-pentyl-2-(3*H*)-furanone (248 mg, 1.42 mmol, 80 % *ee*) by an analogous procedure to that described for (*S*)-**18** (part b): $[\alpha]_D = -1.0$ ($c = 1.0$ in $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): $\delta = 0.86$ (m_c, 5′-H_3), 1.13–1.35 (m, 2′-H_2, 3′-H_2, 4′-H_2), 1.47 (s, 5-CH_3), 1.71–1.86 (m, 1′-H_2), superimposed with 1.73 (s, 3-CH_3), 10.07 (br s, 4-OH) ppm; $t_r(R) = 13.88$ min, $t_r(S) = 16.81$ min (140 °C, 100 kPa); 82 % *ee*.

(5*S*)-2-Methoxy-3,5-dimethyl-5-pentyl-4-(5*H*)-furanone ((*S*)-19): At room temperature, $Me_3O^+ \cdot BF_4^-$ (199 mg, 1.35 mmol, 3.0 equiv) was added to a solution of (*S*)-**18** (89 mg, 0.45 mmol) in CH_2Cl_2 (7 mL). After the mixture had been stirred for 28 h, aq. $NaHCO_3$ (9 mL) was added. The solution was extracted with CH_2Cl_2 (5 × 10 mL) and dried over $MgSO_4$. After evaporation in vacuo the residue was purified by flash chromatography (cyclohexane/EtOAc 3:1) to afford the title compound (81 mg, 85 %): $[\alpha]_D = -54.5$ ($c = 0.5$ in $CHCl_3$); $t_r(S) = 11.14$ min, $t_r(R) = 11.68$ min (120 °C, 100 kPa), 87 % *ee*; IR (film): $\tilde{\nu} = 3000$, 2960, 2930, 2875, 2865, 1595, 1480, 1455, 1400, 1375, 1195, 1125, 980, 800, 785, 765, 760, 750, 745, 730, 725, 715, 710, 675, 665 cm^{-1}; elemental analysis calcd (%) for $C_{12}H_{20}O_3$ (212.3): C 67.95, H 9.43; found: C 68.04, H 9.73.

(5*R*)-2-Methoxy-3,5-dimethyl-5-pentyl-4-(5*H*)-furanone ((*R*)-19): The title compound (173 mg, 87 %) was prepared from (*R*)-**18** (185 mg, 0.933 mmol) by an analogous procedure to that described for (*S*)-**19**: $[\alpha]_D = +50.6$ ($c = 0.7$ in $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): $\delta = 0.86$ (m_c, 5′-H_3), 1.17–1.34 (m, 2′-H_2, 3′-H_2, 4′-H_2), 1.39 (s, 5-CH_3), 1.59 (s, 3-CH_3), 1.69–1.80 (m, 1′-H_2), 4.01 (s, 2-OCH_3); $t_r(R) = 11.58$ min, $t_r(S) = 11.17$ min (120 °C, 100 kPa); 81 % *ee*.

(3*R*,4*R*,5*R*)-4,5-Dihydro-4-hydroxy-3-methyl-5-pentyl-2-(3*H*)-furanone (20): At −78 °C, *n*-BuLi was added to a solution of diisopropylamine (1.41 mL, 1.02 g, 10.1 mmol, 5.0 equiv) in THF (7 mL). After the mixture had been stirred for 30 min, a solution of (*R*,*R*)-**4** (347 mg, 2.02 mmol, 97 % *ee*) in THF (2 mL) was added. The solution was stirred for 1 h at −78 °C, then a solution of methyl iodide (1.25 mL, 2.86 g, 20.2 mmol, 10.0 equiv) in THF (7 mL) was added. After the mixture had been stirred for 2 h, a solution of glacial acetic acid (1.7 mL) in THF (7 mL) was added and the mixture was allowed to reach room temperature. Aqueous $NaHCO_3$ (35 mL) was added and the aqueous phase was extracted with EtOAc (4 × 30 mL). The combined organic extracts were dried over $MgSO_4$ and evaporated in vacuo. The residue was purified by flash chromatography (cyclohexane/EtOAc 4:1) to afford the title compound (311 mg, 83 %): $[\alpha]_D = +78.3$ ($c = 1.2$ in $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): $\delta = 0.90$ (m_c, 5′-H_3), 1.26–1.46 (m, 2′-H^1, 3′-H_2, 4′-H_2), superimposed with 1.30 (d, $J_{3\text{-Me},3} = 7.7$ Hz, 3-CH_3), 1.48–1.58 (m, 2′-H^2), 1.69–1.80 (m, 1′-H_2), 2.42 (d, $J_{4\text{-OH},4} = 4.9$ Hz, 4-OH), 2.61 (qd, $J_{3,3\text{-Me}} = 7.6$, $J_{3,4} = 3.8$ Hz, 3-H), 4.14 (ddd, $J_{4,4\text{-OH}} = J_{4,5} = 4.9$, $J_{4,3} = 3.9$ Hz, 4-H), 4.46 (m_c, 5-H) ppm; IR (film): $\tilde{\nu} = 3450$, 2955, 2930, 2875, 2860, 1760, 1460, 1380, 1355, 1330, 1235, 1205, 1130, 1085, 1045, 1025, 1000, 955 cm^{-1}.

(3*S*,4*S*,5*S*)-4,5-Dihydro-4-hydroxy-3-methyl-5-pentyl-2-(3*H*)-furanone (*ent*-20): The title compound (945 mg, 87 %) was prepared from (*S*,*S*)-**4** (1.0 g, 5.8 mmol, 94 % *ee*) by an analogous procedure to that described for **20**: $[\alpha]_D = -74.6$ ($c = 1.5$ in $CHCl_3$); elemental analysis calcd (%) for $C_{10}H_{18}O_3$ (186.3): C 64.50, H 9.74; found: C 64.23, H 9.94.

(5*R*)-4-Hydroxy-3-methyl-5-pentyl-2-(3*H*)-furanone (21): At −78 °C, trifluoroacetic anhydride (0.47 mL, 0.70 g, 3.3 mmol, 2.0 equiv) was added to a solution of DMSO (0.41 mL, 0.45 g, 5.8 mmol, 3.5 equiv) in CH_2Cl_2 (9 mL). After the mixture had been stirred for 30 min, a solution of **20** (309 mg, 1.66 mmol) in CH_2Cl_2 (9 mL) was added and the mixture was stirred for 1 h at −78 °C. After addition of triethylamine (0.93 mL, 0.67 mg, 6.6 mmol, 4.0 equiv) and stirring for 45 min, H_2O (20 mL) was added and the solution was allowed to reach room temperature. After the mixture had been stirred for 30 min, the aqueous phase was extracted with CH_2Cl_2 (4 × 30 mL) and the combined organic extracts were dried over $MgSO_4$. Evaporation in vacuo followed by flash chromatography (cyclohexane/EtOAc 2:1) afforded the title compound (281 mg, 92 %): $[\alpha]_D = +15.6$ ($c = 1.0$ in $CHCl_3$).

(5*S*)-4-Hydroxy-3-methyl-5-pentyl-2-(3*H*)-furanone (*ent*-21): The title compound (776 mg, 94 %) was prepared from *ent*-**20** (831 mg, 4.46 mmol) by an analogous procedure to that described for **20**: $[\alpha]_D = -14.5$ ($c = 1.0$ in $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$; *,** = interchangeable): $\delta = 0.87$ (m_c, 5′-H_3), 1.23–1.46 (m, 2′-H_2, 3′-H_2, 4′-H_2), 1.61 (dddd, $J_{gem} = 14.5$, $J_{1'\text{-H(1)},2'\text{-H(1)}} = 9.8$, $J_{1'\text{-H(1)},5} = 7.8$, $J_{1'\text{-H(1)},2'\text{-H(2)}} = 5.2$ Hz, 1′-H^1), 1.73 (d, $^5J_{3\text{-Me},5} = 1.2$ Hz, 3-CH_3), 1.98 (dddd, $J_{gem} = 14.1$, $J_{1'\text{-H(2)},2'\text{-H(1)}} = 9.6$*, $J_{1'\text{-H(2)},2'\text{-H(2)}} = 6.1$*, $J_{1'\text{-H(2)},5} = 3.6$ Hz, 1′-H^2), 4.76 (incompletely resolved ddq, $J_{5,1'\text{-H(1)}} = 7.7$**, $J_{5,1'\text{-H(2)}} = 3.4$**, $^5J_{5,3\text{-Me}} = 1.2$ Hz, 5-H), 10.71 (br s, 4-OH) ppm; IR (KBr): $\tilde{\nu} = 2970$, 2955, 2925, 2875, 2855, 1710, 1645, 1270, 1230, 1220, 1100, 1080 cm^{-1}; elemental analysis calcd (%) for $C_{10}H_{16}O_3$ (184.2): C 65.20, H 8.76; found: C 65.20, H 8.90.

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