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Synthesis of (+)-Ginnol, a Type R_{long}–CH(OH)–R'_{long} Alcohol, by an Asymmetric β,γ-Unsaturated Ester → γ-Butyrolactone Conversion

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Abstract

An enantioselective synthesis of (+)-ginnol (**17**) illustrates how Sharpless' asymmetric dihydroxylation may be used for the asymmetric synthesis of monoalcohols. The dihydroxylation was perfomed with AD mix α and the unsaturated ester *trans*-**9**. The resulting lactone *cis*-**13** was dehydrated giving butenolide **13** (96.2% *ee*) from where we proceeded to the title compound **17** in three steps. Butenolide **13** showed 88-94%*ee* when ester *trans*-**9** contained *cis*-isomer due to too forcing reaction condition on the way to the precursor acids *trans*- and *cis*-**7**.

Keywords: Alcohols; Asymmetric Synthesis; Lactones; Osmylation

Recently, we have developed a straightforward asymmetric synthesis of γ-lactones [1] from β,γ-unsaturated carboxylic esters **1** (Scheme 1) [2-5]. With Sharpless' AD mix α or AD mix β [6] these esters gave glycols of the expected [7] absolute configurations which lactonized spontaneously giving the hydroxylactones **2** and *ent*-**2**, respectively. The *ee*-values of the lactones varied with the substituent R from 78% (R = Me) to 97% (R = Oct). They remained unaffected upon dehydration to the corresponding Δ^2-butenolides **3** and *ent*-**3**, respectively. From the hydroxylactones **2** (*ent*-**2**) or the butenolides **3** (*ent*-**3**) possibilities for synthesizing optically active γ-lactones **4** (*ent*-**4**) have been investigated and continue to be scrutinized. The present study is based upon a *different* application of a type-**3** butenolide: The latter was transformed into an enantiopure secondary alcohol **6**, namely into (+)-ginnol (**17**; Scheme 3) [8]. (+)-Ginnol is a constituent of the lipid tubes in the cuticula of many plants [9].

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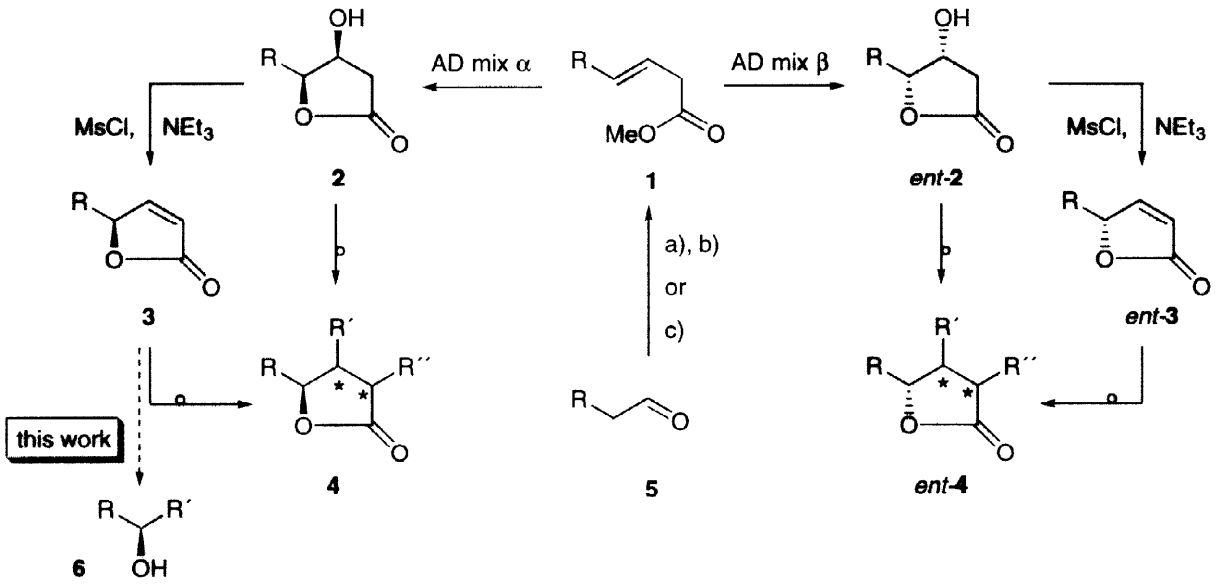
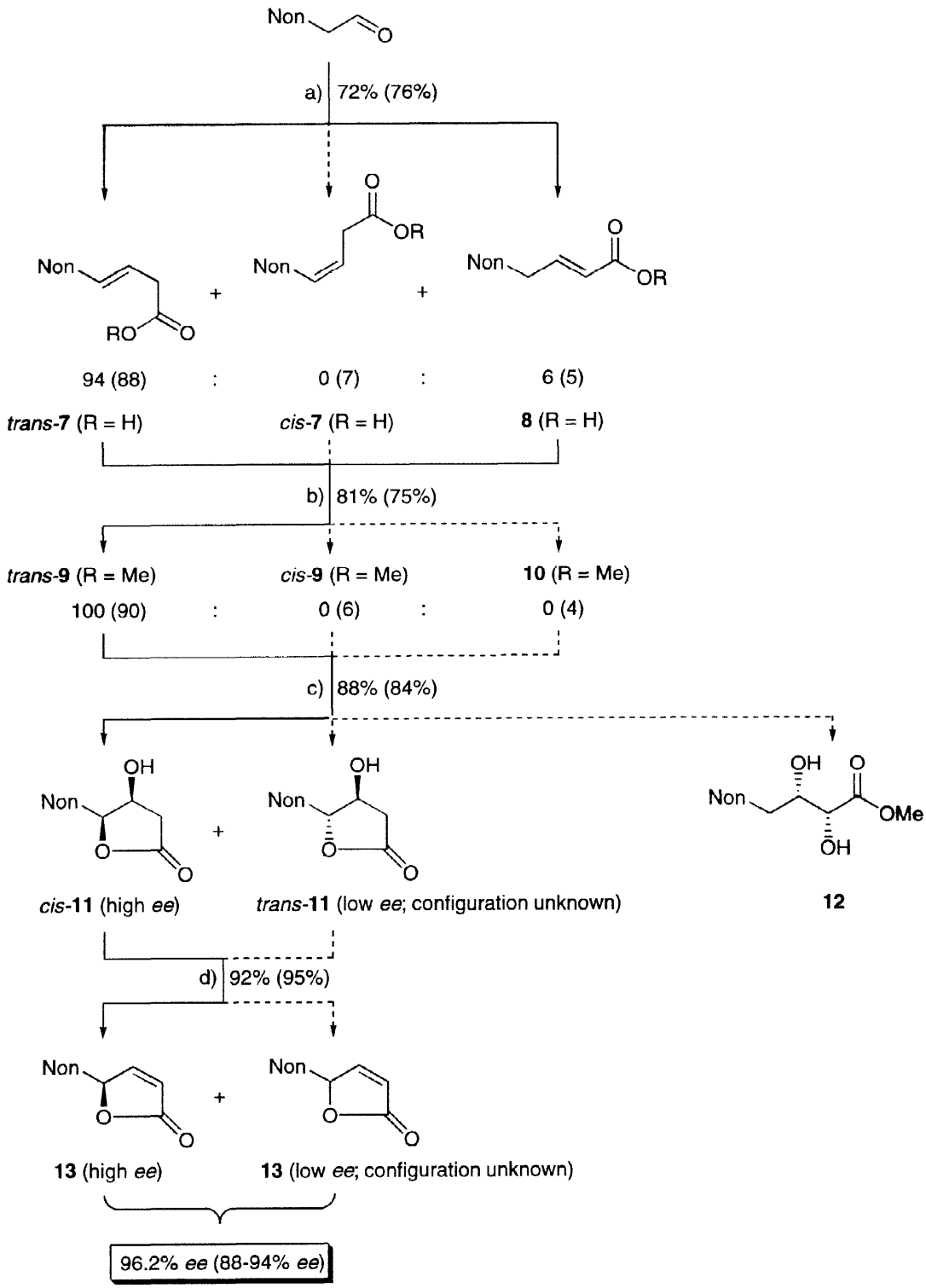


Scheme 1.

Our synthesis began with the preparation of butenolide **13** (Scheme 2). Undecanal and malonic acid were subjected to a decarboxylative deconjugating Knoevenagel condensation. First, we followed a protocol of Ragoussis [10] heating the components in the presence of 0.5 mol-% of piperidine in xylene solution at reflux temperature. We obtained a 88:7:5 mixture of the desired deconjugated carboxylic acid *trans*-**7**, its stereoisomer *cis*-**7**, and its conjugated isomer **8**. These species were unseparable by flash chromatography on silica gel [11]. Esterification with methanol provided a similarly composed 90:6:4 mixture of the corresponding esters *trans*-**9**, *cis*-**9**, and **10**. They, too, were chromatographically unseparable. Accordingly, we performed the subsequent asymmetric dihydoxylation ("AD") *with this mixture* and AD mix α [6]. We obtained the β-hydroxy-γ-nonyl-γ-lactone *cis*-**11**. It furnished butenolide **13** upon dehydration with mesyl chloride and triethylamine.

Surprisingly, the optical purity of **13** varied between 88% and 94% *ee* from one preparation to the next. We had the impression that low yields of the AD step correlated with high *ee* values and *vice versa*. We concluded that the presence of 6% ester *cis*-**9** in our dihydroxylation substrate *trans*-**9** caused the scattering and lower than possible [2,5] *ee* values of butenolide **13**. This was due to the combination of three effects: (1) A kinetic resolution arises in the AD step. Ester *trans*-**9** being a *trans*-olefin is dihydroxylated faster and with higher enantioselectivity than ester *cis*-**9** being a *cis*-olefin. This is commonly found in ADs [7]. Since the dihydroxylation products of *trans*-**9** and *cis*-**9** lactonize under the AD conditions, lactone *cis*-**11** forms rapidly and lactone *trans*-**11** slowly. The 90:6 *trans*-**9**:*cis*-**9** mixture will therefore give a 90:6 *cis*-**11**:*trans*-**11** mixture at complete conversion and pure *cis*-**11** at low conversion. (2) We had apparently been unable to separate the desired actone *cis*-**11** from *trans*-**11** chro-

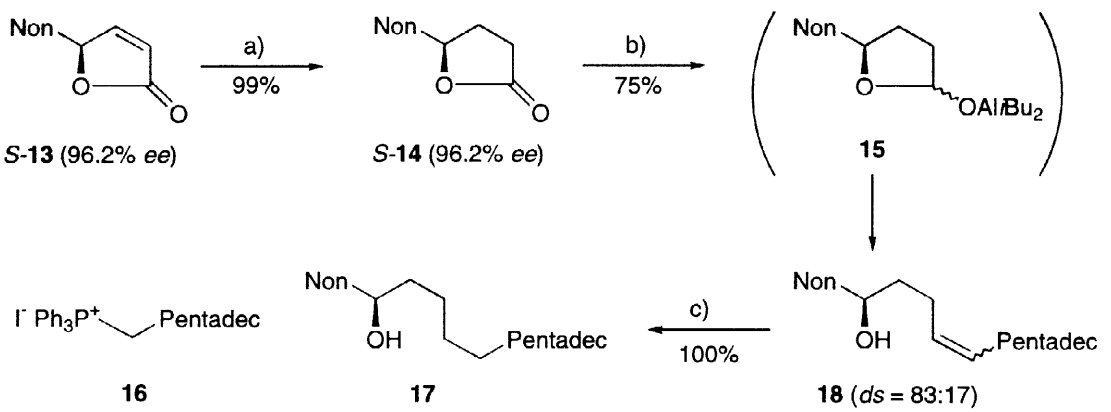


Scheme 2. a) Malonic acid (1.0 equiv.), NEt_3 (1.0 equiv.), reflux, 10.5 h; [alternative: addition of undecanal to refluxing solution of malonic acid (3.1 equiv.) and piperidine (0.5 mol-%) in xylene, azeotropic removal of H_2O, 5 h].– b) MeOH (3.7 equiv.), camphorsulfonic acid (1.5 mol-%), $CHCl_3$, reflux, azeotropic removal of H_2O, 10 h.– c) AD mix a (1.40 g per mmol trans-**9**), methanesulfonamide (1.0 equiv.), $tBuOH/H_2O$ (1:1), 0°C, 39 h.– d) NEt_3 (2.9 equiv.), MsCl (1.6 equiv.), CH_2Cl_2, room temp., 1.5 h.

atographically. We were even unaware of its presence because an abundance of only ≤6% in the product mixture would have left it undetected by ^1H NMR spectroscopy. (3) Both lactone diastereomers were dehydrated to butenolide **13**, *cis*-**11** giving *S*-**13** with high *ee* and *trans*-**11**

giving **13** with unknown configuration and low *ee*. Consequently, the obtained sample of *S*-**13** would reveal a sub-optimum *ee* value as soon as some contaminating lactone *trans*-**11** had formed following some dihydroxylation of the contaminating ester *cis*-**9**.

Avoiding such a *ee*-decreasing dihydroxylation of ester *cis*-**9** completely was tantamount to dihydroxylating *pure trans*-**9** rather than the so far used 90:6 *trans*-**9**:*cis*-**9** mixture. To this end, we replaced Ragoussis' protocol [10] by a procedure from Yamanaka *et al.* [12], i. e. heated undecanal, malonic acid, and 1.0 equiv. of triethylamine without solvent at ca. 90°C (Scheme 3). A 94:6 mixture of the deconjugated carboxylic acid *trans*-**7** and its conjugated isomer **8** resulted but no stereoisomer *cis*-**7**. This mixture could be esterified with methanol such that the more stable acid **8** remained unchanged and the *pure* ester *trans*-**9** formed in 81% yield. AD with AD mix α [6] provided lactone *cis*-**11** (88% yield). Its *ee* value was measured after dehydration with mesyl chloride / triethylamine (→ butenolide *S*-**13**) reproducibly as 96%. Clearly, any β,γ-unsaturated ester to be converted by our AD strategy with optimum enantiomeric purity into the corresponding β-hydroxy-γ-lactone or Δ^2-butenolide should be 100% free from its *cis*-isomer.



Scheme 3. a) H_2 (4 bar), Pd/C (5 mol-%), AcOEt, 2½ d.– b) DIBAL (1.0 equiv.), toluene, -78°C, 2¼ h; transferred to solution [from **24** (3.7 equiv.), nBuLi (3.4 equiv.), THF, room temp., 30 min] at room temp., 1½ d.– c)H_2 (4 bar), Pd/C (7 mol-%), AcOEt, 2½ d.

Scheme 3 shows the terminating steps of our ginnol synthesis. Butenolide *S*-**13** (96.2% *ee*) was hydrogenated over Pd/C rendering the saturated lactone *S*-**14** of identical optical purity. Reduction with a stoichometric amount of DIBAL in toluene afforded the aluminum lactolate **15**. It was transferred without work-up [13] into a THF solution of an excess of the phosphorus ylid obtained from phosphonium iodide **16** and nBuLi. The Wittig olefination product **18** resulted in 75% yield as a 83:17 mixture of unassigned stereoisomers. Catalytic hydrogenation delivered (+)-ginnol (**17**) quantitatively. It was identical with the natural product according to its 300 MHz ^{1}H NMR spectrum ($CDCl_3$) and the specific rotation $[\alpha]_D$ 0.5 (*c* = 0.91, $CHCl_3$) [14].

Previous syntheses of ginnol furnished material of slightly (92% *ee* [15]) or considerably (76% *ee* [9b]) lower optical purity. Accordingly, the 96.2% *ee* achieved here represent some progress. In fact our study indicates that – if enantiopurity is a concern – it can be advantageous to synthesize chiral secondary alcohols from hydroxylactones obtained by the asymmetric dihydroxylation of β,γ-unsaturated esters.

EXPERIMENTAL

General methods. All reactions were performed in oven-dried (80°C) glassware under N_2. THF was freshly distilled from K, CH_2Cl_2 from CaH_2. Products were purified by flash chromatography on Merck silica gel 60 (eluents given in brackets). Yields refer to analytically pure samples.– ^{1}H NMR [300 MHz; $CHCl_3$ (7.26 ppm) as internal standard in $CDCl_3$] and ^{13}C NMR [$CDCl_3$ (77.00 ppm) as internal standard in $CDCl_3$; APT ^{13}C-NMR: assignments in accordance with signal phases]: Varian VXR 200 and Bruker AMX 300; integrals in accordance with assignments; coupling constants in Hz. The assignments of ^{1}H- and ^{13}C-NMR resonances refer to the IUPAC nomenclature; primed numbers belong to side-chain. Combustion analyses: F. Hambloch, Institute of Organic Chemistry, University of Göttingen. MS: G. Remberg, Institute of Organic Chemistry, University of Göttingen. IR spectra: Perkin-Elmer 1600 Series FTIR; film or KBr. Optical rotations: Perkin-Elmer polarimeter 241 at 589 nm; rotational values are the average of 5 measurements of α in a given solution of the respective sample. Chiral capillary gas chromatography: 20% heptakis-(2,6-di-*O*-methyl-3-*O*-pentyl-ß-cyclodextrin in 80% OV1701, 25 m, 70 kPa H_2, isothermal. Melting points (uncorrected): Dr. Tottoli apparatus (Fa. Büchi).

***trans*-3-Tridecenoic acid** (*trans*-**7**). A mixture of undecanal (25.0 ml, 20.7 g, 122 mmol), NEt_3 (16.9 ml, 12.3 g, 122 mmol, 1.0 equiv.), and malonic acid (12.7 g, 122 mmol, 1.0 equiv.) was refluxed for 10.5 h. After cooling to room temp. sulfuric acid (20%, 70 ml) was added and the aqueous layer extracted with petroleum ether / *tert*-butylmethyl ether (2:1, 4 × 60 ml). Drying of the combined organic extracts with $MgSO_4$, evaporation of the solvent, and distillation at 137-139°C / 0.3 torr yielded the title compound (18.6 g, 72%); ^{1}H NMR [contained 6 mol-% of isomer **8** as evidenced through δ = 5.81 (dt, J_{trans} = 15.4, J_{allyl} = 1.5, 2-H) and 7.08 (dt, J_{trans} = 15.4, $J_{3,4}$ = 7.2, 3-H)]: δ = 0.88 (t, $J_{13,12}$ = 6.8, 13-H_3), 1.26-1.40 (m, 6-H_2, 7-H_2, 8-H_2, 9-H_2, 10-H_2, 11-H_2, 12-H_2), 2.03 (dt, $J_{5,4}$ = $J_{5,6}$ = 6.7, 5-H_2), 3.06 (d, $J_{2,3}$ = 6.1, 2-H_2), extreme AB signal (δ_A = 5.51, δ_B = 5.58, J_{AB} = 15.8, in addition split by $J_{A,5}$ = 6.4, $J_{B,2}$ = 6.2, A: 4-H, B: 3-H),

12.00 (br. s, CO_2H); APT ^{13}C-NMR (50 MHz): δ = 14.11 (C-13), 22.69, 29.11, 29.15, 29.33, 29.49, 29.57, 31.91, and 32.48 (C-5, C-6, C-7, C-8, C-9, C-10, C-11, C-12), 37.85 (C-2), 120.58 and 135.56 (C-3, C-4), 178.80 (C-1); IR (film): 2925, 2855, 2675, 1710, 1650, 1465, 1420, 1285, 1220, 970, 940 cm^{-1}; Anal calcd. for $C_{13}H_{24}O_2$ (212.3), C 73.54, H 11.39; found 73.38, H 11.59.

Methyl *trans*-3-tridecenoate (*trans*-**9**). A mixture of acid *trans*-**7** (16.9 g, 77.7 mmol), MeOH (12 ml, 9.5 g, 0.30 mol, 3.7 equiv.), and camphorsulfonic acid (270 mg, 1.16 mmol, 1.5 mol-%) in $CHCl_3$ (130 ml) was refluxed under azeotropic removal of H_2O for 10 h. After cooling to room temp. the mixture was washed with satd. aqueous solutions of $NaHCO_3$ (2 × 40 ml) and NaCl (60 ml). Drying of the organic layer with $MgSO_4$, evaporation of the solvent, and distillation at 90-92°C / 0.2 Torr afforded the title compound (14.5 g, 81%); ^{1}H NMR: δ = 0.88 (t, $J_{13,12}$ = 6.6, 13-H_3), 1.24-1.41 (m, 6-H_2, 7-H_2, 8-H_2, 9-H_2, 10-H_2, 11-H_2, 12-H_2), 2.02 (td, $J_{5,6}$ = $J_{5,4}$ = 6.4, 5-H_2), 3.03 (d, $J_{5,6}$ = 5.2, 3-H_2), 3.68 (s, CO_2Me), 5.45-5.62 (m, 3-H, 4-H); ^{13}C NMR (50 MHz): δ = 14.00 (C-13), 22.60, 29.08 (rel. intensity = 2), 29.26, 29.42, 29.51, 31.83, and 32.40 (C-5, C-6, C-7, C-8, C-9, C-10, C-11, C-12), 37.82 (C-2), 51.56 (OMe), 121.29 and 134.84 (C-3, C-4), 172.47 (C-1); IR (film): 2955, 2925, 2855, 1745, 1465, 1435, 1250, 1165, 970 cm^{-1}; Ana calcd. for $C_{14}H_{26}O_2$ (226.4), C 74.29, H 11.58; found C 74.00, H 11.80.

(4*S*,5*S*)-4,5-Dihydro-4-hydroxy-5-nonyl-2(3*H*)-furanone (*cis*-**11**). At 0°C ester *trans*-**9** (2.53 g, 11.2 mmol) and methanesulfonamide (1.08 g, 11.3 mmol, 1.0 equiv.) were added to a stirred suspension of AD mix α (15.5 g) in *t*BuOH / H_2O (1:1, 110 ml). After 39 h the reaction was quenched by adding Na_2SO_3 (16.5 g). After extraction with *tert*-butylmethyl ether (5 × 100 ml) the combined organic extracts were washed with KOH (1 M, 2 × 50 ml) and a satd. aqueous solution of NaCl (60 ml). Drying with $MgSO_4$, evaporation of the solvent, and flash chromatography on silica gel (eluent: petroleum ether / *tert*-butylmethyl ether 1:2 → 1:3) yielded the title compound (2.24 g, 88%) as white crystals; mp 71°C; $[\alpha]_D^{25}$ = -50.6 (*c* = 2.74 in $CHCl_3$); ^{1}H NMR: δ = 0.88 (t, $J_{9',8'}$ = 6.6, 9′-H_3), 1.22-1.58 (m, 2′-H_2, 3′-H_2, 4′-H_2, 5′-H_2, 6′-H_2, 7′-H_2, 8′-H_2), 1.65-1.78 (m, 1′-H^1), 1.81-1.94 (m, 1′-H^2), 2.02 (d, $J_{OH,4}$ = 4.5, OH), AB signal (δ_A = 2.56, δ_B = 2.80, J_{AB} = 17.8, in addition split by $J_{A,4}$ = 1.1, $J_{B,4}$ = 5.2, 3-H_2), 4.37 (ddd, $J_{4,5}$ = 8.2*, $J_{4,3\text{-H(B)}}$ = 5.7*, $J_{4,OH}$ = 3.7, 4-H), 4.48 (dddm$_c$, $J_{5,1'\text{-H(1)}} \approx J_{5,1'\text{-H(2)}} \approx J_{5,4} \approx$ 4.6, 5-H), *assignments interchangeable; APT ^{13}C-NMR (50 MHz): δ = 14.07 (C-9′), 22.62, 25.53, 28.22, 29.26, 29.45 (rel. intensity = 3), and 31.83 (C-1′, C-2′, C-3′, C-4′, C-5′, C-6′, C-7′, C-8′), 39.50 (C-3), 68.81 (C-4), 85.36 (C-5), 176.51 (C-2); IR (KBr): 3415, 3135, 2955, 2925, 2850, 1740, 1615,

1465, 1400, 1315, 1240, 1185, 1100, 1060, 1045, 1015, 970, 880, 810, 780, 725, 690 cm^{-1}; Anal calcd. for $C_{13}H_{24}O_3$ (228.3), C 68.38, H 10.59; found C 68.65, H 10.89.

(5*S*)-5-Nonyl-2(5*H*)-furanone (*S*-**13**). At 0°C NEt_3 (5.10 ml, 3.70 g, 36.6 mmol, 2.9 equiv.) and methanesulfonyl chloride (1.60 ml, 2.35 g, 20.5 mmol, 1.6 equiv.) were added dropwise to a solution of hydroxylactone *cis*-**11** (2.86 g, 12.5 mmol) in CH_2Cl_2 (80 ml). After stirring for 1.5 h the reaction was quenched by adding a satd. aqueous solution of NH_4Cl (65 ml). Extraction with *tert*-butylmethyl ether (3 × 50 ml), drying of the combined organic extracts with $MgSO_4$, evaporation of the solvent, and flash chromatography on silica gel (eluent: petroleum ether / *tert*-butylmethyl ether 2:3 → 1:1) yielded the title compound (2.49 g, 95%) as a colorless liquid; chiral gas chromatography (125°C, R_T = 109.1 min for *S*-**13** and R_T = 107.6 min for *R*-**13**) revealed *ee* = 96.2%; $[\alpha]_D^{25}$ = +74.0 (*c* = 4.72 in $CHCl_3$); ^{1}H NMR: δ = 0.86 (t, $J_{9',8'}$ = 6.6, 9′-H_3), 1.22-1.50 (m, 2′-H_2, 3′-H_2, 4′-H_2, 5′-H_2, 6′-H_2, 7′-H_2, 8′-H_2), 1.60-1.83 (m, 1′-H_2), 5.04 (dddd, $J_{5,1'\text{-H(1)}}$ = 7.2, $J_{5,1'\text{-H(2)}}$ = 5.7, $J_{5,4} \approx {}^4J_{5,3} \approx$ 1.8, 5-H), 6.11 (dd, $J_{3,4}$ = 5.6, $^4J_{3,5}$ = 1.9, 3-H), 7.46 (dd, $J_{4,3}$ = 5.8, $J_{4,5}$ = 1.3, 4-H); APT ^{13}C-NMR (50 MHz): δ = 13.89 (C-9′), 22.44, 24.76, 29.05, 29.09, 29.17, 29.23, 31.64, and 32.95 (C-1′, C-2′, C-3′, C-4′, C-5′, C-6′, C-7′, C-8′), 83.29 (C-5), 121.09 (C-3), 156.40 (C-4), 172.99 (C-2); IR (film): 2925, 2855, 1755, 1465, 1330, 1160, 1105, 1015, 900, 815 cm^{-1}; Anal calcd. for $C_{13}H_{22}O_2$ (210.3), C 74.24, H 10.54; found C 74.07, H 10.68.

(5*S*)-3,4-Dihydro-5-nonyl-2(5*H*)-furanone (*S*-**14**). At room temp. butenolide *S*-**13** (303 mg, 1.44 mmol) was hydrogenated in AcOEt (15 ml) for 2½ d at ca. 4 bar H_2 over Pd/C (82.2 mg with 10 weight-% Pd: 8.22 mg, 0.0772 mmol, 5.4 mol-%). Filtration through a frit filled with Celite and evaporation of the solvent yielded the title compound (302 mg, 99%) as a colorless liquid; chiral gas chromatography (120°C, R_T = 156.1 min for *S*-**14** and R_T = 153.2 min for *R*-**14**) revealed *ee* = 96.2%; $[\alpha]_D^{25}$ = -32.2 (*c* = 4.00 in $CHCl_3$); ^{1}H NMR: δ = 0.88 (t, $J_{9',8'}$ = 6.8, 9′-H_3), 1.22-1.51 (m, 2′-H_2, 3′-H_2, 4′-H_2, 5′-H_2, 6′-H_2, 7′-H_2, 8′-H_2), 1.53-1.65 (m, 1′-H^1), 1.68-1.79 (m, 1′-H^2), in part superimposed by AB signal (δ_A = 1.86, δ_B = 2.32, J_{AB} = 13.4, in addition split by $J_{A,3}$ = 9.5, $J_{A,5}$ = 8.2, $J_{B,3} = J_{B,5}$ = 6.7, 4-H_2), 2.53 (dd, $J_{3,4\text{-H(A)}}$ = 9.4, $J_{3,4\text{-H(B)}}$ = 6.8, 3-H_2), 4.49 (br. dddd, $J_{5,4\text{-H(A)}} \approx J_{5,4\text{-H(B)}} \approx J_{5,1'\text{-H(1)}} \approx J_{5,1'\text{-H(2)}} \approx$ 6.9, 5-H); APT ^{13}C-NMR (75 MHz): δ = 14.06 (C-9′), 22.63, 25.19, 27.98, 28.83, 29.24, 29.31, 29.43 (rel. intensity = 2), and 31.83 (C-4, C-1′, C-2′, C-3′, C-4′, C-5′, C-6′, C-7′, C-8′), 35.57 (C-3), 81.02 (C-5), 177.22 (C-2); IR (film): 2925, 2855, 1770, 1465, 1420, 1380, 1350, 1290, 1220, 1180, 1130, 1020, 985, 910, 725 cm^{-1}; Anal calcd. for $C_{13}H_{24}O_2$ (212.3), C 73.54, H 11.39; found C 73.40, H 11.56.

(+)-(*S*)-Nonacosan-10-ol [(+)-ginnol, 17]. At room temp. the unsaturated alcohol **18** (130 mg, 0.308 mmol) was hydrogenated in AcOEt (10 ml) for 2½ d at ca. 4 bar H_2 over Pd/C (24.0 mg; with 10 weight-% Pd: 2.40 mg, 0.0226 mmol, 7.3 mol-%). Filtration through a frit filled with Celite and evaporation of the solvent yielded the title compound (131 mg, 100%) as white crystals; mp 78-79°C (ref. [16] mp 81°C); $[\alpha]_D^{25}$ = +0.5 (*c* = 0.91 in $CHCl_3$) {ref. [16] $[\alpha]_D^{20}$ = +0.33 (in C_6H_6, *c* unknown)}; ^{1}H NMR: δ = 0.88 (t, $J_{1,2} = J_{29,28}$ = 6.8, 1-H_3, 29-H_3), 1.23 - ca. 1.59 (m, 2-H_2, 3-H_2, 4-H_2, 5-H_2, 6-H_2, 7-H_2, 8-H_2, 9-H_2, 11-H_2, 12-H_2, 13-H_2, 14-H_2, 15-H_2, 16-H_2, 17-H_2, 18-H_2, 19-H_2, 20-H_2, 21-H_2, 22-H_2, 23-H_2, 24-H_2, 25-H_2, 26-H_2, 27-H_2, 28-H_2, OH), 3.53-3.63 (10-H); ^{13}C NMR (50 MHz): δ = 14.13 (rel. intensity = 2; C-1, C-29), 22.70 (rel. intensity = 2), 25.66 (rel. intensity = 2), 29.33, 29.37, 29.58 (rel. intensity = 2), 29.70 (rel. intensity = 14), 31.90, 31.93, and 37.49 (rel. intensity = 2) (C-2, C-3, C-4, C-5, C-6, C-7, C-8, C-9, C-11, C-12, C-13, C-14, C-15, C-16, C-17, C-18, C-19, C-20, C-21, C-22, C-23, C-24, C-25, C-26, C-27, C-28), 72.02 (C-10); IR (KBr): 3135, 2915, 2850, 1720, 1620, 1470, 1400, 1260, 1130, 1090, 1040, 805, 720 cm^{-1}; MS (EI/70 eV): *m/z* = 407 (75%, M - H_2O), 297 (100%, $C_{19}H_{39}CHOH^{\oplus}$), 279 (14%, $C_{19}H_{39}CHOH^{\oplus}$ - H_2O), 157 (71%, $C_9H_{19}CHOH^{\oplus}$), 149 (31%); Anal calcd. for $C_{29}H_{60}O$ (424.8), C 82.00, H 14.24; found C 81.70, H 13.96.

(10*S*)-13-Nonacosen-10-ol (18; 83:17-mixture of unassigned stereoisomers). DIBAL (1.97 M in toluene, 0.60 ml, 1.2 mmol, 1.0 equiv.) was cooled to -78°C and added dropwise (5 min) to a solution of lactone *S*-**14** (246 mg, 1.16 mmol) in toluene (12 ml) at -78°C. Stirring was continued for 2¼ h. At room temp. nBuLi (1.51 M in cyclohexane, 2.60 ml, 3.93 mmol, 3.4 equiv.) was added to a solution of phosphonium iodide **16** (2.61 g, 4.25 mmol, 3.7 equiv.) in THF (80 ml). After having stirred for 30 min (→ red solution of the ylid) the -78°C cold lactolate (**15**) solution described above was added via cannula. After 1½ d the reaction was quenched by adding H_2O (50 ml). After extraction of the aqueous layer with petroleum ether / *tert*-butylmethyl ether (1:1, 3 × 40 ml) the combined organic extracts were washed with a satd. aqueous solution of NaCl (50 ml) and dried with $MgSO_4$. Evaporation of the solvent and flash chromatography on silica gel (eluent: petroleum ether / *tert*-butylmethyl ether 1:0 → 15:1 → 10:1) yielded the title compound (366 mg, 75%) as white crystals; mp 46-48°C; ^{1}H NMR: δ = 0.88 (t, $J_{1,2} = J_{29,28}$ = 6.6, 1-H_3, 29-H_3), 1.24 - ca. 1.56 (m, 2-H_2, 3-H_2, 4-H_2, 5-H_2, 6-H_2, 7-H_2, 8-H_2, 9-H_2, 11-H_2, 16-H_2, 17-H_2, 18-H_2, 19-H_2, 20-H_2, 21-H_2, 22-H_2, 23-H_2, 24-H_2, 25-H_2, 26-H_2, 27-H_2, 28-H_2, OH), 1.93-2.23 (m, 12-H_2, 15-H_2), 3.56-3.66 (m, 10-H), 5.32-5.46 (m, 13-H, 14-H); ^{13}C NMR (50 MHz): *Major isomer*: δ = 14.03 (rel. intensiy = 2; C-1, C-29), 22.62 (rel. intensity = 2), 23.53, 25.60, 27.18, 29.29 (rel. intensity = 2), 29.31, 29.53 (rel. intensity = 3),

29.61 (rel. intensity = 4), 29.66 (rel. intensity = 6), 31.85, 31.88, 37.25, and 37.44 (25 resonances –presumably because of superimposition by signals of the minor isomer – for 24 nuclei: C-2, C-3, C-4, C-5, C-6, C-7, C-8, C-9, C-11, C-12, C-15, C-16, C-17, C-18, C-19, C-20, C-21, C-22, C-23, C-24, C-25, C-26, C-27, C-28), 71.67 (C-10), 129.22 and 130.66 (C-13, C-14); *minor isomer*: δ = 28.90, 29.14, 29.38, 29.48 (rel. intensity = 3), 32.53, and 37.09 (8 resonances for C-2 - C-9, C-11, C-12, C-15 - C-28), 71.59 (C-10), 129.79 and 131.14 (C-13, C-14); **IR (KBr)**: 3135, 2920, 2850, 1635, 1465, 1400, 1130, 1090, 720 cm^{-1}; **Anal calcd. for** $C_{29}H_{58}O$ (422.8), C 82.39, H 13.83; found C 82.50, H 13.77.

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