

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

Thilo Berkenbusch and Reinhard Brückner*

Institut für Organische Chemie der Georg-August-Universität,
Tammannstr. 2, D-37077 Göttingen, Germany

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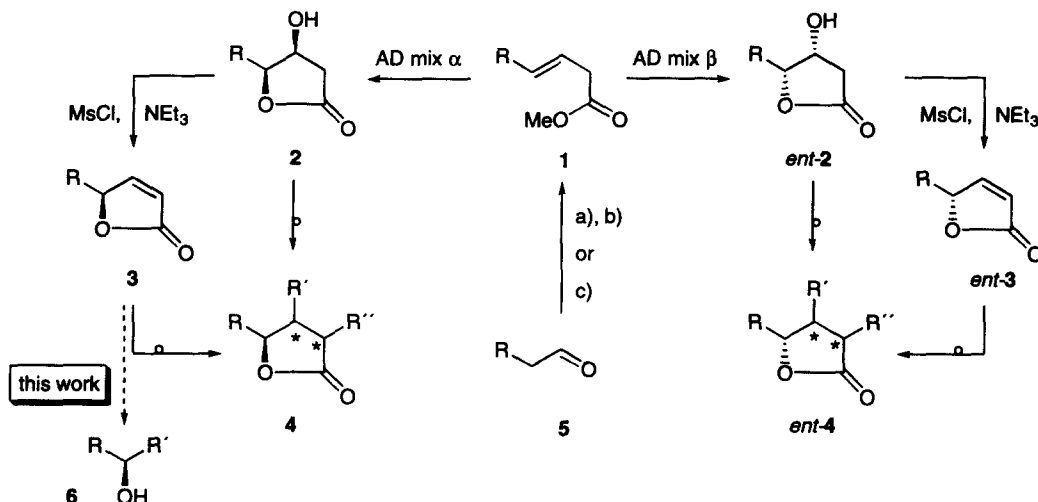
Abstract

An enantioselective synthesis of (+)-ginnol (**17**) illustrates how Sharpless' asymmetric dihydroxylation may be used for the asymmetric synthesis of monoalcohols. The dihydroxylation was performed 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**.
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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].

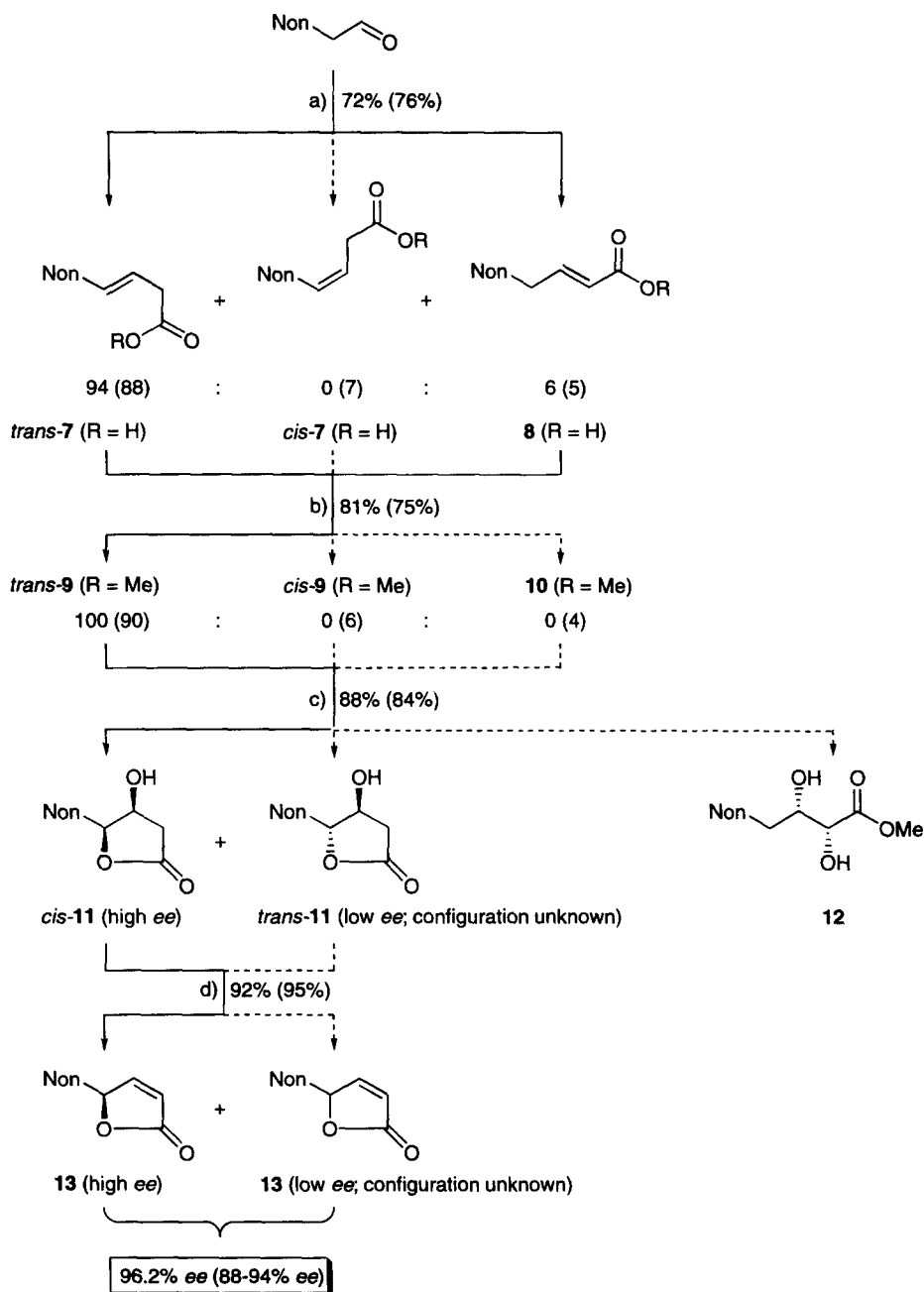
Fax: Int+49-551-392944
E-mail: rbrueck@gwdg.de



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 dihydroxylation ("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 lactone *cis*-**11** from *trans*-**11** chro-

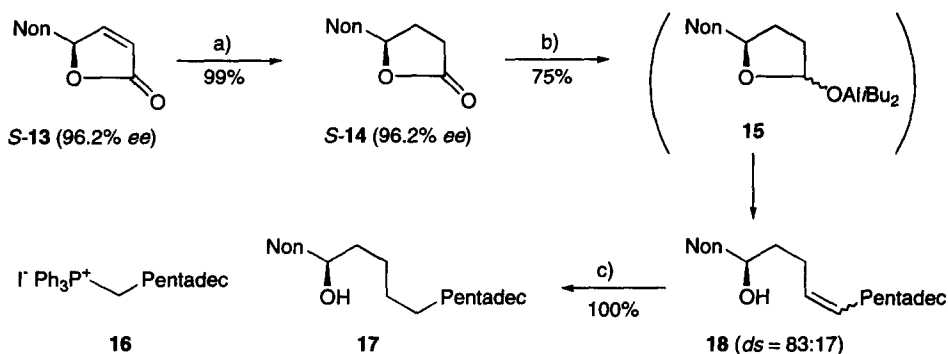


Scheme 2. a) Malonic acid (1.0 equiv.), NEt_3 (1.0 equiv.), reflux, 10.5 h; [alternative: addition of undecanal to refluxing solution of malonic acid (3.1 equiv.) and piperidine (0.5 mol-%) in xylene, azeotropic removal of H_2O , 5 h].– b) MeOH (3.7 equiv.), camphorsulfonic acid (1.5 mol-%), CHCl_3 , reflux, azeotropic removal of H_2O , 10 h.– c) AD mix a (1.40 g per mmol trans-9), methanesulfonamide (1.0 equiv.), $\text{tBuOH}/\text{H}_2\text{O}$ (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 $\leq 6\%$ 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 (\rightarrow 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 stoichiometric 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 ^1H 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 N₂. THF was freshly distilled from K, CH₂Cl₂ from CaH₂. Products were purified by flash chromatography on Merck silica gel 60 (eluents given in brackets). Yields refer to analytically pure samples. – ¹H NMR [300 MHz; CHCl₃ (7.26 ppm) as internal standard in CDCl₃] and ¹³C NMR [CDCl₃ (77.00 ppm) as internal standard in CDCl₃; APT ¹³C-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 ¹H- and ¹³C-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- β -cyclodextrin in 80% OV1701, 25 m, 70 kPa H₂, 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), NEt₃ (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 \times 60 ml). Drying of the combined organic extracts with MgSO₄, evaporation of the solvent, and distillation at 137–139°C / 0.3 torr yielded the title compound (18.6 g, 72%); ¹H 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-H₃), 1.26–1.40 (m, 6-H₂, 7-H₂, 8-H₂, 9-H₂, 10-H₂, 11-H₂, 12-H₂), 2.03 (dt, $J_{5,4}$ = $J_{5,6}$ = 6.7, 5-H₂), 3.06 (d, $J_{2,3}$ = 6.1, 2-H₂), 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, CO₂H); APT ¹³C-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 C₁₃H₂₄O₂ (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 CHCl₃ (130 ml) was refluxed under azeotropic removal of H₂O for 10 h. After cooling to room temp. the mixture was washed with satd. aqueous solutions of NaHCO₃ (2 × 40 ml) and NaCl (60 ml). Drying of the organic layer with MgSO₄, evaporation of the solvent, and distillation at 90-92°C / 0.2 Torr afforded the title compound (14.5 g, 81%); ¹H NMR: δ = 0.88 (t, *J*_{13,12} = 6.6, 13-H₃), 1.24-1.41 (m, 6-H₂, 7-H₂, 8-H₂, 9-H₂, 10-H₂, 11-H₂, 12-H₂), 2.02 (td, *J*_{5,6} = *J*_{5,4} = 6.4, 5-H₂), 3.03 (d, *J*_{5,6} = 5.2, 3-H₂), 3.68 (s, CO₂Me), 5.45-5.62 (m, 3-H, 4-H); ¹³C 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 C₁₄H₂₆O₂ (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 / H₂O (1:1, 110 ml). After 39 h the reaction was quenched by adding Na₂SO₃ (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 MgSO₄, 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; [α]_D²⁵ = -50.6 (*c* = 2.74 in CHCl₃); ¹H NMR: δ = 0.88 (t, *J*_{9,8} = 6.6, 9'-H₃), 1.22-1.58 (m, 2'-H₂, 3'-H₂, 4'-H₂, 5'-H₂, 6'-H₂, 7'-H₂, 8'-H₂), 1.65-1.78 (m, 1'-H¹), 1.81-1.94 (m, 1'-H²), 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-H₂), 4.37 (ddd, *J*_{4,5} = 8.2*, *J*_{4,3-H(B)} = 5.7*, *J*_{4,OH} = 3.7, 4-H), 4.48 (dddm, *J*_{5,1'-H(1)} ≈ *J*_{5,1'-H(2)} ≈ *J*_{5,4} ≈ 4.6, 5-H), *assignments interchangeable; APT ¹³C-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 $\text{C}_{13}\text{H}_{24}\text{O}_3$ (228.3), C 68.38, H 10.59; found C 68.65, H 10.89.

(5S)-5-Nonyl-2(5H)-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 \rightarrow 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); $^1\text{H NMR}$: $\delta = 0.86$ (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 $^{13}\text{C-NMR}$ (50 MHz): $\delta = 13.89$ (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 $\text{C}_{13}\text{H}_{22}\text{O}_2$ (210.3), C 74.24, H 10.54; found C 74.07, H 10.68.

(5S)-3,4-Dihydro-5-nonyl-2(5H)-furanone (S-14). At room temp. butenolide *S*-**13** (303 mg, 1.44 mmol) was hydrogenated in AcOEt (15 ml) for $2\frac{1}{2}$ 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); $^1\text{H NMR}$: $\delta = 0.88$ (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 ($\delta_A = 1.86$, $\delta_B = 2.32$, $J_{AB} = 13.4$, 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 $^{13}\text{C-NMR}$ (75 MHz): $\delta = 14.06$ (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 $\text{C}_{13}\text{H}_{24}\text{O}_2$ (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 H₂ 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 CHCl₃) {ref. [16] $[\alpha]_D^{20} = +0.33$ (in C₆H₆, c unknown)}; ¹H NMR: $\delta = 0.88$ (t, $J_{1,2} = J_{29,28} = 6.8$, 1-H₃, 29-H₃), 1.23 - ca. 1.59 (m, 2-H₂, 3-H₂, 4-H₂, 5-H₂, 6-H₂, 7-H₂, 8-H₂, 9-H₂, 11-H₂, 12-H₂, 13-H₂, 14-H₂, 15-H₂, 16-H₂, 17-H₂, 18-H₂, 19-H₂, 20-H₂, 21-H₂, 22-H₂, 23-H₂, 24-H₂, 25-H₂, 26-H₂, 27-H₂, 28-H₂, OH), 3.53-3.63 (10-H); ¹³C NMR (50 MHz): $\delta = 14.13$ (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 - H₂O), 297 (100%, C₁₉H₃₉CHOH⁺), 279 (14%, C₁₉H₃₉CHOH⁺ - H₂O), 157 (71%, C₉H₁₉CHOH⁺), 149 (31%); Anal calcd. for C₂₉H₆₀O (424.8), C 82.00, H 14.24; found C 81.70, H 13.96.

(10S)-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 **5-14** (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 H₂O (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 MgSO₄. 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; ¹H NMR: $\delta = 0.88$ (t, $J_{1,2} = J_{29,28} = 6.6$, 1-H₃, 29-H₃), 1.24 - ca. 1.56 (m, 2-H₂, 3-H₂, 4-H₂, 5-H₂, 6-H₂, 7-H₂, 8-H₂, 9-H₂, 11-H₂, 16-H₂, 17-H₂, 18-H₂, 19-H₂, 20-H₂, 21-H₂, 22-H₂, 23-H₂, 24-H₂, 25-H₂, 26-H₂, 27-H₂, 28-H₂, OH), 1.93-2.23 (m, 12-H₂, 15-H₂), 3.56-3.66 (m, 10-H), 5.32-5.46 (m, 13-H, 14-H); ¹³C NMR (50 MHz): *Major isomer*: $\delta = 14.03$ (rel. intensity = 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 $\text{C}_{29}\text{H}_{58}\text{O}$ (422.8), C 82.39, H 13.83; found C 82.50, H 13.77.

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