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First Asymmetric Synthesis of (+)- and (-)-Roccellaric Acid and Dihydroprotolichesterinic Acid

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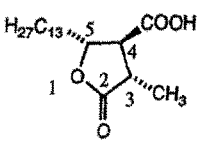
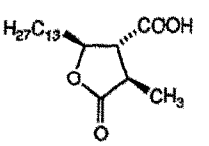
Abstract: Stereocontrolled syntheses of the title compounds from (R)-2,3-isopropylidene glyceraldehyde, (S)-O-THP-lactaldehyde and 1,2:5,6-Di-O-isopropylidene-α-D-glucofuranose ("diacetone-D-glucose") are described.

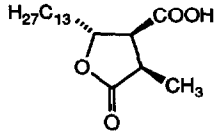
The total synthesis of naturally occurring chiral substituted γ-butyrolactones is of continuing interest for various reasons. For instance, about 10 % of all structurally elucidated natural products belong to this structural type, and many of these compounds are biologically significant[1]. Enantioselective approaches to γ-butyrolactones and in particular to their 4-carboxy-derivatives (paraconic acids) have been developed in a number of laboratories over the past decade[2]. We describe a convenient and general access to paraconic acids like roccellaric acid (**1**) and dihydroprotolichesterinic acid (**2**), which focuses on Claisen type rearrangements of chiral allylic alcohols[3]. **1** has been first isolated by Hesse from the chilenic lichen species Roccellaria mollis (HAMPE) ZAHLBR.[4].



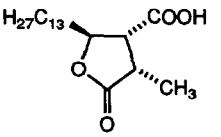
(+)-Roccellaric Acid ((+)-**1**)
(natural enantiomer)



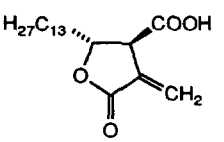
(-)-Roccellaric Acid ((-)-**1**)



(+)-Dihydroprotolichesterinic Acid ((+)-2)

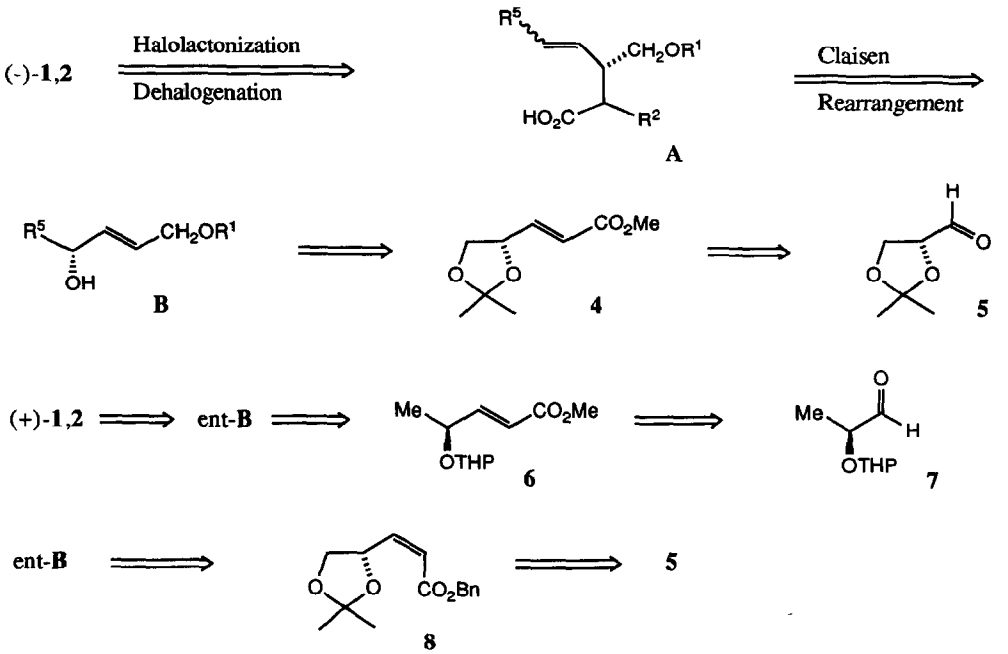


(-)-Dihydroprotolichesterinic Acid ((-)-2)



(+)-Protolichesterinic Acid (3)

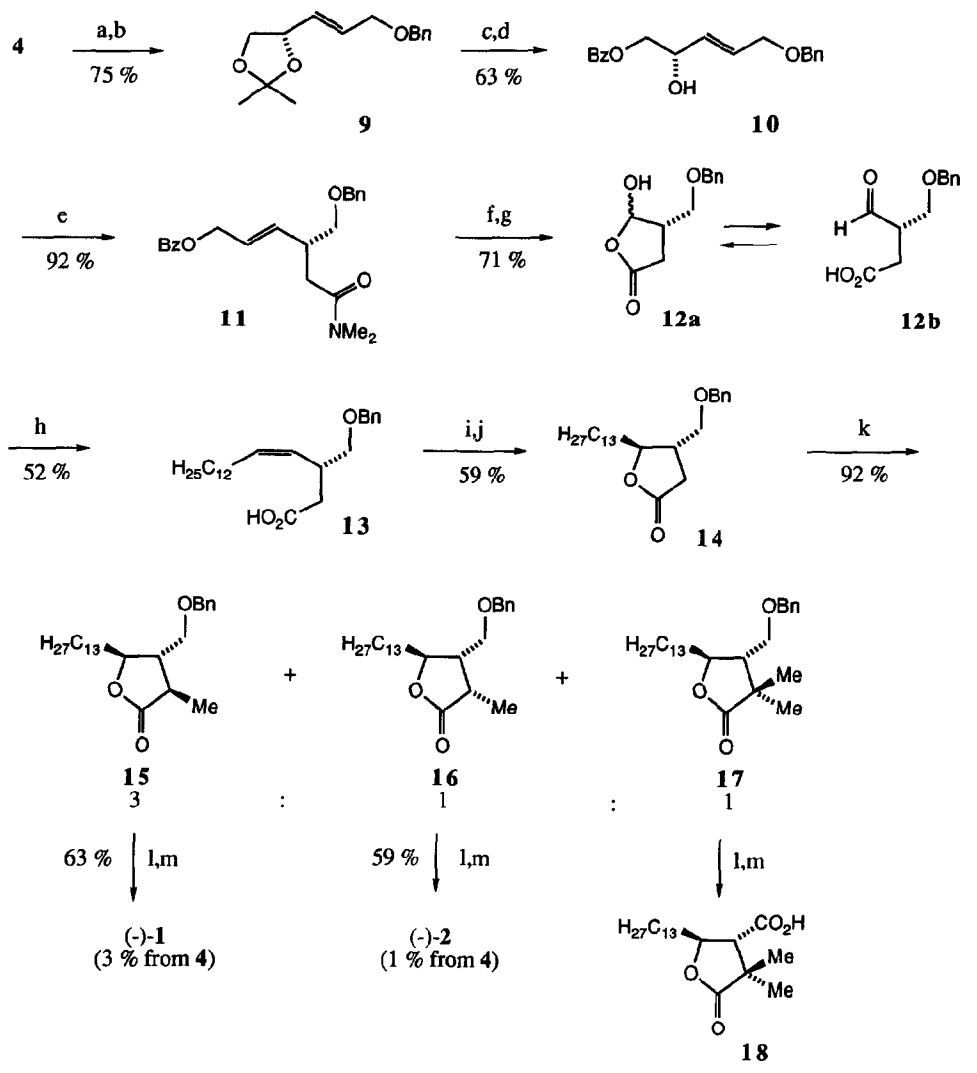
The structure was assigned by Huneck and Follmann on the basis of CD spectra[5]. **2** is not a natural product, but has been prepared from naturally occurring (+)-protolichesterinic acid (**3**) by catalytic hydrogenation[5,6]. So far only one synthesis has been reported of **1** (in racemic form)[7], whereas **2** has not yet been synthesized. Our synthesis was so planned as to provide substantial quantities of stereochemically pure **1** and **2** in both enantiomeric forms. The retrosynthetic analysis is shown in Scheme 1. The lactone ring in (-)-**1** and (-)-**2** was to be generated via a halolactonization-dehalogenation[8] sequence from precursor **A**, which in turn was a candidate for a Claisen rearrangement starting from **B**, easily available from (R)-2,3-isopropylidene glyceraldehyde (**5**) via **4**[9].



Scheme 1. Retrosynthetic Considerations

Analogously (+)-**1** and (+)-**2** are accessible from ent-**B**, which was to be prepared from known[13] (S)-O-THP-lactaldehyde (**7**) via ester **6**. Alternatively, ent-**B** could be prepared from **5** via the (Z)-ester **8**[11].

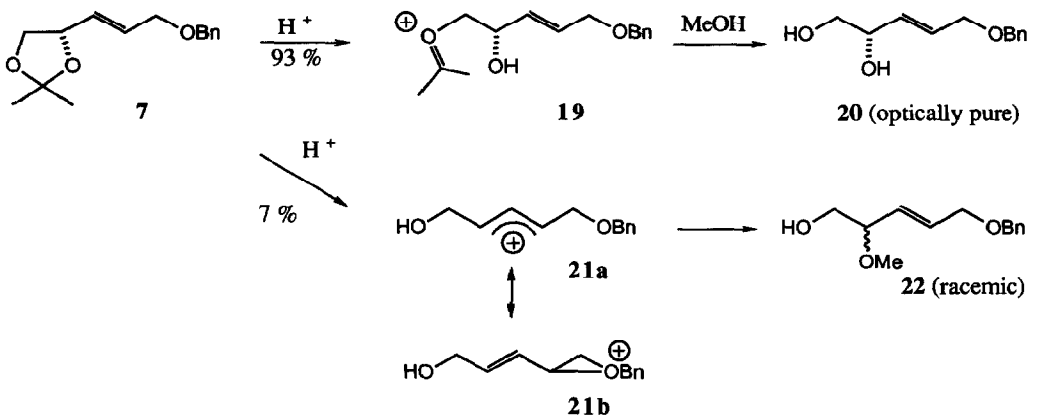
I. Synthesis of (-)-1 and (-)-2 from 4 (Scheme 2)



a. DIBAH, toluene, -78°C, 3h. b. NaH, DMF, 40°C, BnCl. c. MeOH, p-TsOH, 22°C, 24h. d. BzCl, pyridine, 0°C, (+ 10% di-benzoate). e. N,N-dimethylacetamide dimethyl acetal, toluene, reflux, 5h. f. MeOH, NaOH, 4h, 22°C. g. O_3, MeOH, -78°C, PPh_3-workup. h. $C_{12}H_{25}$-CH=PPh_3, THF, -78°C, 2h. i. I_2•KI, THF-H_2O, K_2CO_3, 22°C, 48h. j. Bu_3SnH, AIBN, toluene, reflux, 4h. k. LDA, -78°C, MeI. l. H_2/Pd, MeOH, 3 bar, 22°C. m. PDC, DMF, 22°C, 15h.

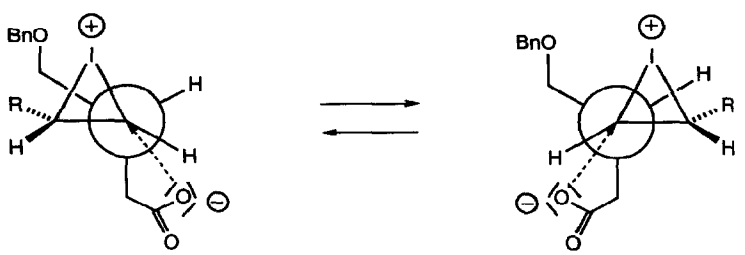
Scheme 2. Synthesis of (-)-1 and (-)-2 from 4

Ester **4** was reduced and benzylated to give **9**, whose deketalization met with some problems. Treatment with aqueous acid led to partial racemization, probably due to the formation of an allyl cation **21** (Scheme 3). This could be demonstrated by performing the deketalization in methanol. The pathway via **21** gave the racemic methyl ether **22** which could easily be separated from the diol **20** by chromatography.



Scheme 3. Acid catalyzed Deketalization of **7**

The optical purity of diol **20** (>95% ee) was confirmed by converting it into the Mosher ester[12]. **20** was selectively monobenzoylated to give **10** (10% of the di-benzoate was also formed) which was then submitted to an Eschenmoser-Claisen rearrangement[13], generating amide **11**. The lipophilic sidechain of **1/2** was introduced by ozonizing **11** to the crystalline acylal **12** which existed as a 99.5 : 0.5-mixture of **12a** and **b** in chloroform solution, according to the ^{1}H NMR spectrum. Wittig reaction furnished the isomerically pure (Z)-olefin **13**, which gave diastereomerically pure lactone **14** after iodolactonization-dehalogenation. The stereochemical outcome of the halolactonization may be interpreted in terms of an allylic 1,3-strain model **23**[14], which is based on the assumption that the carboxylate oxygen attacks the iodonium ring of the two diastereomers **23a** and **b** along a S_N2 trajectory.



23a (unfavorable) **23b** (favorable)

23a suffers from a R/CH_2OBn-interaction, whereas **23b** is essentially strain free. Obviously, the reaction is kinetically controlled as the product distribution does not change with prolonged reaction time. The high degree of stereoselectivity of the halolactonization hinges on the cis-geometry of olefin **13**[15], and hence

justifies the ozonolysis /Wittig olefination sequence described above. Additionally, the synthesis gains total flexibility with respect to the substituent of C-5, which is introduced via the ylid component.

Methylation of **14** yielded a 3:1:1-mixture of **15**, **16** and **17**, which were easily separated by chromatography. Debenzylation and oxidation furnished (-)-**1**, (-)-**2** and **18** in crystalline pure form. The relative configuration of **1** was secured by crystal structure analysis (Fig.1).

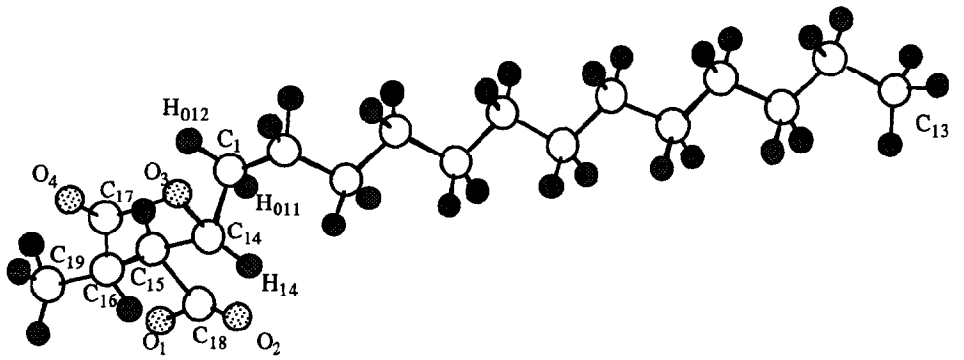
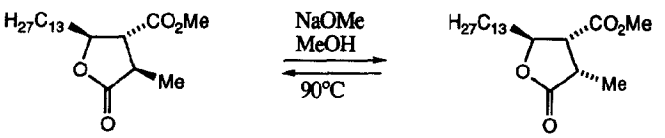


Figure 1. Crystal Structure of **1**

Conversion of 1 into 2.

1 was methylated with diazometane to give the ester **24**. Heating **24** with sodium methoxide in methanol led to an 1:1-equilibrium mixture of **24** and **25** (methyl ester of **2**)[16].



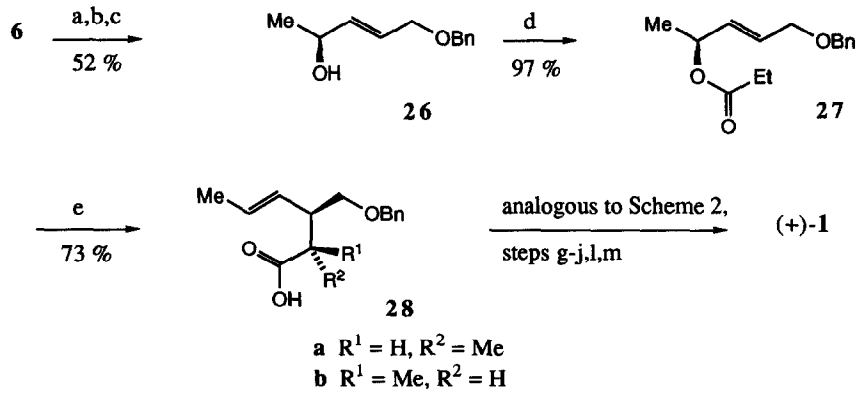
24 **25**

24 and **25** are readily separated by chromatography and saponified to **1** and **2**, respectively, so that a quantitative conversion of **1** into **2** and vice versa is possible.

II. Synthesis of (+)-1 and (+)-2 from 7 (Scheme 4)

The natural enantiomeric series could be accessed either by converting **5** into geometrically pure (Z)-ester **8** by Wittig olefination with carbobenzyloxymethylene triphenylphosphorane in methanol and reiterating the synthesis described in Scheme 2.

Alternatively, a sequence starting from **7** may be used (Scheme 4). **7** was transformed into pure (E)-ester **6** and then converted into **26** as described for **9**. In this case no methyl ether corresponding to **22** was found. Contrary to **10**, alcohol **26** is devoid of base labile functionality and could, hence, be submitted to Ireland-Claisen-rearrangement conditions[17]. In fact propionate **27** cleanly furnished a 85:15-mixture of the acids **28a** and **b** which was transformed into (+)-**1** as described for the conversion of **13** in (-)-**1** and **2**. The minor diastereomer was removed on the stage of the lactones **15/17** by crystallization. This route has the following advantages over the one described in Scheme 3: (1) it is suitable for both enantiomeric series, as (R)- and (S)-**7** are accessible equally well[18]. (2) it is shorter by two steps. (3) no racemization occurs during the deprotection of the THP-ether. (4) **1** is generated stereoselectively by applying the Ireland variation of the Claisen rearrangement; the yield of **1** is thus much higher than in synthesis I.

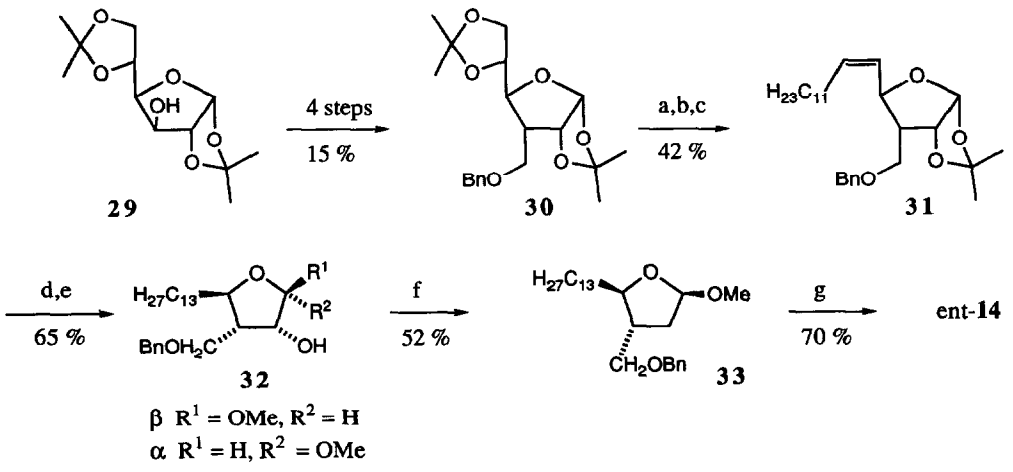


Steps a-c: see Scheme 2. d. propionic anhydride, DMAP, pyridine.
e. LDA, Me_3SiCl, -78°C, then 22°C, aqueous workup.

Scheme 4. Synthesis of (+)-**1** and (+)-**2** from **6**

III. Synthesis of (+)-1 and (+)-2 from Diacetone -D-glucose (Scheme 5).

To obtain **1** and **2** with undisputable optical purity, a synthesis starting from the "chiral pool" was also initiated. 1,2:5,6-Di-O-isopropylidene-α-D-glucofuranose ("diacetone-D-glucose") (**29**) was converted into **30** via oxidation, Wittig methylenation, hydroboration with 9-BBN and benzylation[19] (15 % overall yield). Selective removal of the exocyclic acetonide group followed by oxidative cleavage of the diol and cis-selective Wittig olefination of the resulting aldehyde generated **31**.



a. 50 % aq. HOAc. b. $Pb(OAc)_4$,CH_2Cl_2, 30min, 22°C. c. $H_{23}C_{11}CH{=}PPh_3$, THF. d. H_2/Pd/$BaSO_4$, 1 bar, 22°C, MeOH. e. pTsOH, MeOH. f. NaH, CS_2, MeI, THF; then toluene, Bu_3SnH, AIBN, reflux. g. Jones-oxidation: acetone, $Na_2Cr_2O_7$, 10%, aqu. H_2SO_4, 0°C.

Scheme 5. Synthesis of ent-**14** from **29**

Catalytic hydrogenation of the double bond and removal of the acetonide generated furanoside **32** as an 15:1-anomeric mixture of **32**β and α. Reductive removal of the 2-OH-group according to Barton and McCombie[20] led to **33** which was oxidized to ent-**4** with Jones' reagent. **14** and ent-**14** were identical in all respect except for the sense of the optical rotation. The rest of the synthesis was performed as shown in Scheme 2.

Conclusion

Three independent syntheses of roccellaric acid (**1**), dihydroprotolichesterinic acid (**2**) and their dimethyl derivative **18** have been described, leading to identical products from different chiral starting materials **5**, **7** and **29**. Two of the syntheses make use of the Claisen rearrangement to generate the chiral C,C-branching at C-4, whereas the third one utilizes the bicyclic structure of **29** in a highly stereoselective hydroboration reaction. From the comparison shown in Table 1 it can be seen that route II is clearly the most efficient one.

Synthesis	Starting Material	Number of steps	Products (mp, $[\alpha]_D^{20}$ in $CHCl_3$	overall yield (%)
I	**5**	14	(-)-**1**: 108°C, -26 (c=1.93) (-)-**2**: 103°C, -49.5 (c=1.75) (-)-**18**: 112°C -43 (c=2.0)	1.5 0.4 0.4
II	**7**	12	(+)-**1**: 109°C +27 (c=1.73)	5.2
III	Diacetone-D-glucose	14	(+)-**1**: 109°C +28.7 (c=1.58) (+)-**2**: 103°C +52.4 (c=1.29) (+)-**18**: 115°C +47.4 (c= 2.15)	0.5 0.5 0.2
Literature data			(+)-**1**: 110-111°C +35 (c=1.73)[5] (+)-**2**: 106°C +34.6 (c=2.54)[6b]	

Table 1. Comparison of the Syntheses I-III and Literature Data of **1** and **2**

The optical rotations of the synthetic products are the same within the limits of error. As D-glucose cannot but lead to optically pure material this means for the other two routes that no racemization has occured throughout the entire sequences. Moreover, the absolute and relative configurations of **1** and **2** have been unequivocally assigned for the first time. Surprisingly, our value of the optical rotation of **1** is considerably lower than the one reported in ref.[5] (Table 1), whereas our optical rotation of **2** is much higher than the literature value. Whereas the lower value for **2** can easily be explained by partial decomposition of the natural product during the isolation, the high value for **1** was alarming. We therefore contacted Dr. Huneck, who, in a letter of October 19, 1988, kindly informed us that the correct optical rotation of natural (+)-**1** is $[\alpha]_D^{24} = +24$

($CHCl_3$, c=1.37). This ensured us that our synthetic samples are at least as pure as the natural products. Tests concerning the biological properties of **1**, **2** and **18** are underway.

Experimental

Infrared spectra (IR) were obtained with a Perkin-Elmer IR 580 B spectrometer. Nuclear magnetic resonance spectra (NMR) were recorded with a Bruker WH 270 or AC 250 spectrometer in $CDCl_3$ (unless stated otherwise) and are reported in ppm downfield of internal tetramethylsilane (δ units). Optical rotations were determined in $CHCl_3$ (unless stated otherwise) with a Perkin-Elmer 121 polarimeter at 589 nm. HPLC separations were performed on 7μm nucleosil for preparative separations and on 5μm nucleosil 50 for analytical separations. All reactions were performed in dried and purified solvents and monitored by TLC plates (Merck 5554). Preparative column chromatography was performed on silica gel Merck 60, 230-400 mesh, with typically 20-30 g of silicagel per gram substance.

I. Synthesis of (-)-1, (-)-2 and 18 from 4

(2S,3E)-1,2-Isopropylidene-5-O-benzyl-3-pentene-1,2,5-triol ***9***.

Ester **4**[9] (40.0 g, 215 mmol) in ether (300 mL) was treated at -78°C with diisobutylaluminium hydride (1.2 M in toluene, 4 mL, 480 mmol) for 3h. The mixture was warmed to -40°C and solid sodium fluoride (122.0 g, 2.9 mol) and water (150mL) were added in succession and the mixture was stirred at 0°C for 1 h. Then magnesium sulfate (80 g) was added and the mixture was filtered. The filtrate was washed with brine, dried ($MgSO_4$) and distilled (110°C, 0.01 mbar) to give the alcohol (30.1g, 88%). For benzylation, the alcohol (25.0 g, 158 mmol) in DMF (60mL) was added dropwise at 22°C to a suspension of sodium hydride (9.0 g, of a 50% suspension in mineral oil was washed with hexane and dried in vacuo) in DMF (300mL). The mixture was stirred for 3h at 40°C, then benzyl chloride (18.6 mL, 162 mmol) in DMF (30mL) was added and the mixture was stirred at 25°C for 15h. The solvent was removed in vacuo, and the residue was diluted with ether, washed with brine dried ($MgSO_4$) and chromatographed (hexanes/ethyl acetate v/v 10:1) to give **9** (31.5 g, 80%) as a colorless oil.$[\alpha]_D^{20}$= +29.8 (c=2.20).
^{1}H-NMR: δ = 1.37 (s, 3H); 1.41 (s, 3H); 3.57 (t, 1H, J = 8 Hz); 4.01 (d, 2H, J = 5 Hz); 4.06 (dd, 1H, J = 8 Hz, 7 Hz); 4.48 (s, 2H,); 4.5 (q, 1H, J = 7 Hz); 5.71 (dd, 1H, J = 16 Hz, 7 Hz); 5.87 (dt, 1H, J = 16 Hz, 5 Hz); 7.3 (m, 5H). Anal. calcd. for $C_{15}H_{20}O_3$ (248.3): C 72.55, H 8.12. Found C 72.20, H 7.96

(2S,3E)-5-O-Benzyl-3-pentene-1.2.5-triol ***20***.

9 (30.0 g, 121 mmol) and p-TsOH (300 mg) were stirred in methanol (300 mL) at 22°C for 24h. The mixture was concentrated in vacuo, diluted with ether,washed with saturated aqueous sodium bicarbonate and brine, dried ($MgSO_4$) and purified by chromatography (ethyl acetate/hexanes v/v 1:1) to give **20** (18.6 g, 74%) along with the methyl ether **22** (1.5 g, 5 %). **20**: $[\alpha]_D^{20}$= +5.71 (c=2.11). ^{1}H-NMR: (270 MHz, $CDCl_3$) δ = 3.2 (s, 2H, OH); 3.44 (dd, ABX-system, A-part, 1H, J = 12 Hz, 7 Hz,); 3.6 (dd, ABX-system, B-part, 1H, J = 12 Hz, 4 Hz,); 4.0 (d, 2H, 5 Hz); 4.2 (m, 1H); 4.51 (s, 2H); 5.73 (dd, 1H, J = 17 Hz, 5 Hz); 5.9 (ddt, 1H, J = 17 Hz, 5.5 Hz); 7.32 (s, 5H). Anal. calcd. for $C_{12}H_{16}O_3$ (208.25): C 69.21 H 7.74. Found C 69.63 H 7.97.
22: $[\alpha]_D^{20}$= 0. ^{1}H-NMR: δ = 2.24 (br. OH); 3.34 (s, 3H); 3.52 (dd, 1H, J = 7 Hz); 3.56 (t, 1H, J = 7 Hz); 4.04 (m, 2H); 4.2 (m, 1H); 4.53 (s, 2H); 5.8 (m, 1H); 5.93 (m, 1H); 7.36 (s, 5H).

(2S,3E)-1-O-Benzoyl-5-O-benzyl-3-pentene-1.2.5-triol ***10***.

Alcohol **20** (20.0 g, 97 mmol) in pyridine (90 mL) was treated dropwise with benzoyl chloride (15.04 g 107 mmol) in pyridine (10 mL) at 0°C. The mixture was stirred 14 h at 20°C and concentrated under reduced pressure. The residue was diluted with ether (200 mL), washed with 2N H_2SO_4 and brine, dried ($MgSO_4$) and chromatographed (hexanes/ethyl acetate v/v 2:1) to furnish **10** (23.12 g, 77 %) along with the dibenzoate (7.81

g, 19 %). The dibenzoate was saponified with sodium methoxide in methanol to give **20**, which was recycled. In this way the overall yield of **10** was raised to 90 %. Colorless oil, $[\alpha]_D^{20}$= 2.81 (c=2.07).
^{1}H-NMR: δ = 2.60 (s, OH); 4.05 (d, 2H, J = 5 Hz); 4.28 (dd, ABX-system, A-part, 1H, J = 7 Hz, 12 Hz); 4.40 (dd, ABX-system, B-part, 1H, J = 12 Hz, 3.5 Hz); 5.52 (s, 2H); 5.54 (m, 1H); 5.84 (dd, 1H, J = 16.25 Hz, 5 Hz); 6 (dt, 1H, J = 16.25 Hz, 5 Hz); 7.32 (s, 5H); 7.42 (t, 2H, J = 7.5 Hz); 7.56 (d, 1H, J = 1.5 Hz); 8.02 (d, 2H, J = 7.5 Hz). Anal. calcd. for $C_{19}H_{20}O_4$ (312.36): C 73.06 H 6.45. Found C 72.93 H 6.71.

*(3R,4E)-6-O-Benzoyl-3-benzyloxymethyl-hexenoic Acid-N,N-Dimethylamide **11**.*
Alcohol **10** (25.0 g, 80 mmol) in a mixture of toluene and xylenes (200 mL, v/v 10:1) was treated dropwise with N,N-dimethyl-acetamide dimethylacetal (14 mL, 95 mmol) at 110 °C and refluxed for 5 h. To remove the methanol the reaction was performed in an extractor apparature whose thimble was filled with calcium chloride. The mixture was concentrated under reduced pressure, diluted with ether, washed with bride, dried ($MgSO_4$) and chromatographed to give **11** (28.1 g, 92 %) as a colorless oil with $[\alpha]_D^{20}$= -12.33 (c=2.19).
^{1}H-NMR: δ = 2.38 (ABX-system, A-part, 1H, J = 15.5 Hz, 8 Hz); 2.6 (ABX-system, B-part, 1H, J = 15 Hz, 6.5 Hz); 2.9 (s, 3H); 3.0 (s, 3H); 3.06 (sextet, 1H, J = 6.5 Hz); 3.53 (dd, 2H, J = 5.5 Hz); 5.8 (dt, 1H, J = 16 Hz, 5.5 Hz); 5.92 (dd, 1H, J = 16 Hz, 6.5 Hz); 7.32 (s, 5H); 7.42, 7.45 (2xd, 2H, J = 6.5 Hz); 7.56 (dd, 1H, J = 6.5 Hz); 8.06 (d, 2H, J = 6.5 Hz). IR (film) 3035 (m), 1715 (s), 1645 (s) 1600 (m), 1585 (m), 1495 (m), 1450 (s) 1395 (m), 1360 (m), 1315 (m), 1270 (s,br), 1175 (m), 1155 (m), 1110 (s,br), 1070 (s), 1027 (m) 975 (m), 740 (m), 715 (s), 100 (m) cm^{-1}. Anal. calcd. for $C_{23}H_{27}NO_4$ (381.47): C 72.42, H 7.13, N 3.67. Found: C 72.19, H 7.13, N 3.68.

*(4S,5RS)-4-Benzyloxy-5-hydroxy-oxolan-2-one **12**.*
The benzoyloxy-amide **11** was saponified in two steps to facilitate the removal of the benzoic acid. Thus **11** (22.0 g, 58 mmol) in methanol (100 mL) was treated with sodium hydroxide (5N in water, 40 mL) at 22°C for 4 h. The mixture was extracted with ether, and the etheral extract was washed with water, dried ($MgSO_4$) and purified by chromatography (ethyl acetate/hexanes v/v 15:1) to furnish (3R,4E)-3-benzyloxy-6-hydroxy-4-hexenoic acid (13.5 g, 84 %) as a colorless oil with $[\alpha]_D^{20}$= -15.9 (c=2.00) which was refluxed in methanol (90 mL) containing sodium hydroxide (10N in water, 22 mL) for 10 h. To remove the dimethylamine argon was bubbled through the mixture. After neutralizing the solution with 5N H_2SO_4 and extracting it with chloroform the organic extract was washed with brine, dried ($MgSO_4$) and evaporated under reduced pressure to give (3R,4E)-3-benzyloxy-6-hydroxy-4-hexenoic acid (110 g, 87 %) as colorless crystals of mp 65-66°C and $[\alpha]_D^{20}$= -19.6 (c=1.90). 10.0 g (40 mmol) of this acid were ozonized in methanol (200 mL) at -78°C until the solution was faintly blue. Triphenyl phosphine (8 g) was added and the mixture was stirred at 20°C for 2 h. The solvent was removed under reduced pressure, and ether was added to crystallize the phosphine oxide. The mother liquor was chromatographed (ethyl acetate/hexanes v/v 1:1) to give **12** (7.33 g, 85 %) as colorless crystals of mp 65°C and $[\alpha]_D^{20}$= +1.90 (c=2.60).
^{1}H-NMR: δ = 2.52 (m, 1H); 2.7 (s, br, 2H); 3.56 (s, 2H); 4.52 (s, 2H); 6.04-6.60 (m, 2H); 7.32 (m, 5H); 9.69 (d, 1H, ca. 5 % aldehyde). IR ($CHCl_3$) 3600 (m), 3040 (m), 2870 (m), 1780 (s, br)), 1720 (m), 1025 (m) 970 (s), 1365 (m), 1260 (m), 1240 (m) 1230 (m), 1225 (m), 1160 (s), 1110 (s), 1075 (m), 1025 (m), 970 (s, br), 770 (m), 765 (m), 760 (s), 750 (m), 725 (m), 715 (m), 700 (s) cm^{-1}. Anal. calcd. (222.24) : C 64.85, H 6.35. Found C 65.29, H 6.52.

*(3R,4Z)-3-Benzyloxymethyl-4-heptadecenoic Acid **13**.*
Tridecyl-triphenyl-phosphonium-bromide (12.14 g, 22.4 mmol) in THF (40 mL) was treated with n-butyl lithium (1.6 M in hexanes, 14.0 mL, 22.4 mmol) at 78°C. The precipitate was dissolved by removing the major part of the hexane under reduced pressure at -30°C and adding THF (20 mL). The dark red solution was cooled to -78°C and **12** (5.02 g, 22.4 mmol) in THF (20 mL) was added dropwise. The mixture was stirred at -78°C for 2 h and at 22°C for 3 h, concentrated under reduced pressure, diluted with water and extracted with ether. The ethereal extract was washed with brine, dried ($MgSO_4$) and chromatographed (hexanes/ethyl acetate v/v 3:1) to furnish **13** (4.6 g, 51 %) as a colorless oil with $[\alpha]_D^{20}$= -11.2 (c=2.6).

^{1}H-NMR: δ = 0.88 (t, 3H, J = 5.5 Hz); 1.28 (s, 20 H); 2.07 (q, 2H, J = 7 Hz); 2.28 (dd, ABX-system, A-part, 1H, J = 16 Hz, 8 Hz); 2.64 (dd, ABX-system, B-part, 1H, J = 16 Hz, 5.5 Hz); 3.22 (m, 1H); 3.28 (dd, ABX-system, A-part, 1H, J = 9 Hz, 5 Hz); 3.44 (dd, ABX-system, B-part, 1H, J = 9 Hz, 5.5 Hz); 4.51 (d, 2H, J = 3.5 Hz); 5.16 (dd, 1H, J = 11.5, 8 Hz); 5.48 (dt, 1H, J = 11.5 Hz, 7.5 Hz); 7.32 (m, 5H). Anal. calcd. for $C_{25}H_{40}O_3$ (388.58): C 77.27, H 10.38. Found C 77.40, H 10.70.

(4S,5S)-4-Benzyloxymethyl-5-tridecyl-oxolan-2-one ***14***.

13 (4.00 g, 12.9 mmol) in THF (20 mL) was treated with a solution of iodine (8.02 g, 31 mmol) and potassium iodide (21.7 g, 101 mmol) in aqueous sodium bicarbonate (0.5 M, 60 mL) for 48 h at 22°C. The mixture was extracted with ether, washed with sodium thiosulfate (10 % in water), dried ($MgSO_4$) and chromatographed (hexanes/ethyl acetate v/v 5:1) to give (4S, 5S, 1'R)-4-benzyloxymethyl-5-(1'-iodotridecyl)-oxolan-2-one (3.91 g, 76 %) as a yellowish oil with $[\alpha]_D^{20}$= -8.0 (c=1.91). This compound (3.80 g, 7.4 mmol) was refluxed in toluene (140 mL) with tributyltinhydride (3.62 mL, 13.7 mmol) and AIBN (20 mg) for 4 h. The solvent was evaporated under reduced pressure and the residue was purified by chromatography (hexanes/ethyl acetate v/v 3:1) to give **14** (2.14 g, 75 %) as a colorless oil with $[\alpha]_D^{20}$= -16.0 (c=2.30).
^{1}H-NMR (270 MHz, $CDCl_3$): δ = 0.88 (t, 3H, J = 5.5 Hz); 1.28 (m, 22H); 1.64 (m, 2H); 2.48 (m, 1H); 2.48 (dd, ABX-system, A-part, 1H, J = 20 Hz, 7 Hz); 2.64 (dd, ABX-system, B-part, 1H, J = 20 Hz, 10.5 Hz); 3.48 (d, 2H, 5.5 Hz); 4.34 (q, 1H, J = 6Hz); 4.52 (s, 2H); 7.32 (m, 5H). IR (film) 3070 (m), 3040 (m), 2930 (s,br), 2860 (s), 1775 (s,br), 1730 (s), 1495 (m), 1465 (s), 1455 (s), 1420 (m), 1365 (m), 1315 (m), 1270 (s), 1200 (s), 1175 (s), 1110 (s,br), 1075 (m), 1030 (m), 995 (m,br), 950 (m), 735 (m), 715 (m), 700 (m) cm^{-1}. ^{13}C-NMR ($CDCl_3$): δ = 14.03, 22.62, 25.37, 29.28, 29.40, 29.48, 29.59, 30.31, 31.84, 31.87, 35.16; 40.89; 70.24; 73.30; 83.08;127.54, 127.82, 128.45, 137.70, 176.19.

(3R,4S,5S)- and (3S,4S,5S)-4-Benzyloxymethyl-3-methyl-5-tridecyl-oxolan-2-one ***15*** *and* ***16***
(4S,5S)-4-Benzyloxymethyl-3,3-dimethyl-5-tridecyl-oxolan-2-one ***17***.

LDA was prepared from diisopropylamine (3.64 g, 25.6 mmol) and n-butyl lithium (1.6 M in hexanes, 12 mL, 14.4 mmol) in THF (20 mL) at -78°C. **14** (5.00 g, 12.8 mmol) in THF (10 mL) was added and the mixture was stirred for 3 h at -78°C. Methyl iodide (1.6 mL, 25.7 mmol) in THF (5 mL) was added and the mixture was stirred at 22°C for 15 h. The mixture was neutralized with 2N HCl, evaporated under reduced pressure, diluted with water and extracted with ether. The ethereal extract was washed with brine, dried ($MgSO_4$) and separated by HPLC (nucleosil 5 μm, hexanes/ ethyl acetate 95:5) to give with increasing R_f-values the following fractions. **17** (1.00 g, 19 %), **16** (1.05 g, 20 %), **15** (3.20 g, 60 %).
15: mp. 40°C, $[\alpha]_D^{20}$= -11.72 (c=1.92). ^{1}H-NMR: δ = 0.88 (t, 3H, J = 5.5 Hz); 1.2 (d, 3H, J = 5.5 Hz); 1.28 (m, 22H); 1.62 (m, 2H); 2.43 (m, 1H); 2.84 (dq, 1H, J = 9 Hz, 8 Hz); 3.44 (dd, ABX-system, A-part, 1H, J = 9 Hz, 7 Hz); 3.52 (dd, ABX-system, B-part, 1H, J = 9 Hz, 5.5 Hz); 4.36 (dq, 1H, J = 8 Hz, 5.5 Hz, 4 Hz); 4.52 (s, 2H); 7.32 (m, 5H). $C_{26}H_{42}O_3$ (402.65): C 77.56, H 10.52. Found C 77.67, H 10.62.
16: mp 39°C, $[\alpha]_D^{20}$= -8.37 (c=2.08). ^{1}H-NMR: δ = 0.88 (t, 3H, J = 5.5 Hz); 1.24 (d, 3H, J = 4.5 Hz); 1.32 (m, 22H); 1.62 (m, 2H); 1.96 (dq, 1H, J = 5 Hz, 16 Hz); 2.6 (dq, 1H, J = 11 Hz, 7 Hz); 3.51 (dd, ABX-system, A-part, 1H, J = 13.5 Hz, 5.5 Hz); 3.56 (dd, ABX-system, B-part, 1H, J = 13.5 Hz, 4 Hz); 4.24 (dt, 1H, J = 5.5 Hz, 3 Hz); 4.53 (s, 2H); 7.32 (m, 5H)
17 mp: 68°C, $[\alpha]_D^{20}$= -29.13 (c=2.46). ^{1}H-NMR: δ = 0.88 (t, 3H, J = 5.5 Hz); 1.12 (s, 3H); 1.24 (m, 22H); 1.32 (s, 3H); 1.57 (m, 2H); 2.18 (q, 1H, J = 5.5 Hz); 3.5 (ss, ABX-system, A-part, 1H, J = 10 Hz, 6 Hz); 3.56 (dd, ABX-system, B-part, 1H, J = 10 Hz, 7 Hz); 4.12 (dt, 1H, J = 9 Hz, 5.5 Hz); 4.52 (s, 2H); 7.32 (m, 5H). IR (KBr) : 3050 (s), 2920 (s), 2860 (s), 2820 (m), 1765 (s), 1720 (m), 1620 (m), 1600 (m), 1580 (m), 1500 (m), 1485 (m), 1470 (s), 1455 (s), 1420 (m), 1390 (m), 1385 (m), 1370 (m), 1340 (m), 1305 (m), 1285 (m), 1270 (m), 1245 (m), 1230 (m), 1215 (m), 1195 (m), 1150 (s), 1135 (m), 1120 (s), 1090 (m), 1070 (m), 1030 (m), 1020 (m), 1005 (m), 980 (m), 965 (m), 945 (m), 745 (s), 720 (m), 700 (s) cm^{-1}. Anal. calcd. for $C_{27}H_{44}O_3$ (416.65): C 77.84, H 10.65. Found C 76.87, H 9.95.

(3R,4S,5S)-4-Carboxy-3-methyl-5-tridecyl-oxolan-2-one (Roccellaric Acid) (-)-1.

15 (3.20 g, 4.0 mmol) in methanol (120 mL) and hexanes (40 mL) was hydrogenated over Pd/C (10 %) (100 mg) at 22°C under 3 bar for 2 h. The mixture was filtered and evaporated to give (3,R,4,S,5S)-4-hydroxymethyl-3-methyl-5-tridecyl-oxolan-2-one (2.44 g, 96 %) as colorless crystals of mp. 70°C and $[\alpha]_D^{20}$= -21.8 (c=1.96). For oxidation, this compound (2.00 g, 6.5 mmol) in DMF (20 mL) was added dropwise at 0°C to pyridinium dichromate (17.55 g, 46.5 mmol) in DMF (200 mL). The mixture was stirred at 22°C for 15 h, diluted with water (500 mL) and extracted with ether. The ethereal extract was washed with brine, dried ($MgSO_4$) and evaporated to give a solid residue which was dissolved in ether, triturated with $MgSO_4$, filtered and washed with ether. The combined filtrates were evaporated to dryness to furnish (-)-**1** (1.10 g, 53 5) as colorless crystals of mp. 108°C and $[\alpha]_D^{20}$= -26 (c=1.93).

^{1}H-NMR: δ = 0.88 (t, 3H, 5.5 Hz); 1.28 (m, 22H); 1.38 (d, 3H, J = 7 Hz); 1.52 (m, 2H); 1.76 (m, 2H); 2.7 (dd, 1H, J = 10 Hz, 9 Hz); 2.98 (dq, 1H, J = 10 Hz, 7 Hz); 4.48 (dt, 1H, J =9 Hz, 4.5 Hz). IR (KBr) 2920 (s), 2860 (s), 1750 (s,), 1715 (s), 1470 (m), 1455 (m), 1435 (m), 1425 (m), 1400 (m), 1380 (m), 1360 (m), 1340 (m), 1320 (m), 1265 (m), 1260 (s), 1240 (m), 1225 (m), 1210 (s) 1200 (m), 1172 (m), 1147 (m), 1130 (m), 1020 (m), 1010 (m), 975 (m), 945 (m), 910 (m), 895 (m), 865 (m), 835 (m), 815 (m), 735 (m), 720 (m), 700 (s), 675 (m), 640 (m), 600 (m) cm^{-1}. Anal. calcd. for $C_{19}H_{34}O_4$ (326.48): C 69.90, H 10.5. Found C 69.63, H 10.56.

Crystal Data and Experimental Details for the Structure Determination of (-)-1:

Formula $C_{19}H_{34}O_4$. Crystal system monoclinic, a 5.52 (2), b 32.57 (3), c 5.56 (2) Å. β (deg) 90. V (A^3) 999.6. Space group $P2_1$, Z = 2. Crystal size 0.53 x 0.22 x 0.04 mm. Radiation Cu Kα,. Ni-filter, data collection instrument STOE $2.5 < 2\theta < 42$. Absorption coefficient $\mu = 6.0$ cm^{-1}. Absorption factor 0.99 > A > 0.92, number of reflections: 1082, $995 < 2\sigma(I)$. Final R 0.058. R_w 0.068.

(3S,4R,5S)-4-Carboxy-3-methyl-5-tridecyl-oxolan-2-one (Dihydroprotolichesterinic Acid) (-)-2.

16 (1.00 g, 2.47 mmol) was hydrogenated as described for **15** to give (3S,4S,5S)-4-hydroxymethyl-3-methyl-5-tridecyl-oxolan-2-one (726 mg, 95 %) as colorless crystals with mp. 60°C and $[\alpha]_D^{20}$= -15.94 (c=2.02). This compound was treated as described above to give (-)-**2** (410 mg, 50 %) as colorless crystals with mp. 103°C and $[\alpha]_D^{20}$= -49.5 (c=1.75).

^{1}H-NMR (270 MHz, $CDCl_3$): δ = 0.88 (t, 3H, J = 5.5 Hz); 1.26 (m, 22H); 1.3 (d, 3H, J = 7 Hz); 1.68 (m, 2H); 3.02 (dq, 1H, J = 9.5 Hz, 7.5 Hz); 3.16 (dd, 1H, J = 9.5 Hz, 6 Hz); 4.68 (q, 1H, J = 6 Hz). IR (KBr) 2960 (m), 2920 (s), 2855 (s), 1760 (s), 1740 (s), 1710 (m), 1590 (w, br), 1555 (w, br), 1470 (m), 1430 (m), 1420 (m), 1410 (m), 1390 (m), 1380 (m), 1360 (m), 1340 (m), 1310 (m), 1290 (m), 1280 (m), 1235 (s), 1210 (m), 1195 (m), 1145 (m), 1125 (m), 1090 (m), 1070 (m), 1040 (m), 1025 (m), 1005 (m), 975 (m), 945 (m), 930 (w), 890 (m, br), 790 (w, br), 760 (w), 750 (w), 730 (m), 670 (m), 655 (m) cm^{-1}.

(4R,5S)-4-Carboxy-3,3-dimethyl-5-tridecyl-oxolan-2-one 18.

17 (1.00 g, 2.38 mmol) was converted into **18** as described for **15** and **16** to give **18** (315 mg, 41 %) as colorless crystals with mp. 112°C and $[\alpha]_D^{20}$ = -35 (c=2.0).

^{1}H-NMR: δ = 0.88 (t, 3H, J = 5.5 Hz); 1.24 (s, 3H); 1.26 (m, 22H); 1.44 (s, 3H); 1.70 (m, 2H); 2.82 (d 1H, J = 10 Hz); 4.64 (ddd, 1H, J = 10 Hz, 7.5 Hz, 4.5 Hz).

Conversion of 1 into 2 via the Methyl Esters 24 and 25.

(-)-**1** (80 mg, 0.25 mmol) was methylated with ethereal diazomethane in methanol to give (3S,4S,5R)-4-carbomethoxy-3-methyl-5-tridecyl-oxolan-2-one **24** as colorless crystals with mp. 39°C and $[\alpha]_D^{20}$= -22.5 (c=2.18) (ref.[5] mp. 40-41°C and $[\alpha]_D^{20}$= +23 (c=1.50) for (+)-**24**).

^{1}H-NMR (250 MHz, $CDCl_3$): δ = 0.88 (t, 3H, J = 5.5 Hz); 1.28 (m, 20H); 1.34 (d, 3H, J = 7 Hz); 1.49 (m, 2H); 1.74 (m, 2H); 2.66 (dd, 1H, J = 11.5 Hz, 8.75 Hz); 2.96 (dq, 1H, J = 11.5 Hz, 7 Hz); 3.78 (s, 3H); 4.44 (dt, 1H, J = 8.75 Hz).

Similarly, (-)-**2** was converted into (3R,4S,5R)-4-carbomethoxy-3-methyl-5-tridecyl-oxolan-2-one **25**. Colorless crystals with mp. 58-60°C and $[\alpha]_D^{20}$= -47 (c=0.64) (ref.[5] mp. 50-51°C and $[\alpha]_D^{20}$= +60 (c=1.76) for (+)-**25**).

^{1}H-NMR: δ = 0.88 (t, 3H, J = 5.5Hz); 1.22 (d, 3H, J = 7Hz); 1.27 (m, 20H); 1.54 (m, 2H); 1.66 (m, 2H); 2.98 (dq, 1H, J = 10 Hz, 7 Hz);3.12 (dd, 1H, J = 10 Hz, 6 Hz); 3.76 (s, 3H); 4.70 (q, 1H, J = 6 Hz).
24 (320 mg, 0.98 mmol) was heated with sodium (43 mg, 1.87 mmol) in methanol (1 mL) to 50°C for 3 h. The mixture was neutralized with 2N H_2SO_4 and extracted with ether. The ethereal extract was washed with brine, dried ($MgSO_4$) and evaporated to dryness to give a 1:1-mixture of **24** and **25** according to analytical HPLC.

II. Synthesis of (+)-1 from (S)-O-THP-Lactaldehyde 7

Methyl-(4S,2'RS,2E)-4-tetrahydropyran-2-yl)-oxy-2-pentenoate 6.
Sodium hydride (5.30 g, 177 mmol) (80 % suspension in mineral oil) was stirred in THF (50 mL) and carbomethoxymethane diethylphosphonate (40.0 g, 178 mmol) in THF (200 mL) was added dropwise at -10°C. The mixture was stirred at 22°C for 2 h, then (S)-O-THP-lactaldehyde[10] (23.5 g, 148.5 mmol) in THF (200 mL) was added at -20°C. The mixture was stirred at 22°C for 12 h. Water (50 mL) was added and the mixture was concentrated under reduced pressure. Ether (400 mL) was added and the organic layer was isolated, washed with brine, dried ($MgSO_4$) and chromatographed (hexanes/ethyl acetate v/v 7:1) to give **6** (23.0 g, 78 %) as a colorless oil.
^{1}H-NMR: δ = 1.28 (d, 3H, J = 7 Hz); 1.34 (d, 3H, J = 7 Hz); 1.56, 1.70, 1.84 (3 x mc, 3 x 6H); 3.49 (mc, each 1H); 3.75 (2 x s, 2 x 3H); 3.85 (mc, 2H); 4.20 (dq, 1H, J = 7 Hz 4.5 Hz); 4.46 (mc, 1H); 4.60 (t(dd), 1H, J = 3 Hz); 4.8 (t, 1H, J = 3.5 Hz); 5.96 (dd, 1H, J = 15.5 Hz, 1Hz); 6.08 (dd, 1H, J = 15.5 Hz, 2 Hz); 6.84 (dd, 1H, J = 15.5 Hz, 6.5 Hz); 7.7 (dd, 1H, J = 15.5 Hz, 4.5 Hz).

(4S,2E)-1-O-Benzyl-2-pentene-1,4-diol 26.
Ester **6** (21.0 g, 98 mmol) was reduced to the allylic alcohol as described for **4** to give the O-THP-alcohol (14.0 g, 77 %) after chromatography (hexanes/ethyl acetate 3:1) as a colorless oil, which was benzylated as described before to furnish the 1-benzyl-THP-diether (15.8 g, 79 %) after chromatography (hexanes/ethyl acetate 10:1) as a colorless liquid. For THP-removal, the compound (15.2 g, 55 mmol) was stirred in methanol (70 mL) with acidic ion exchange resin (DOWEX) (1-2 g) at 22°C for 20 h. The product was purified by chromatography (hexanes/ethyl acetate 3:1) to give **26** (8.90 g, 84 %) as a colorless oil with $[\alpha]_D^{20}$= +0.64 (c=2.48)
^{1}H-NMR: δ = 1.26 (d, 3H, J = 6.5 Hz); 2.02 (s, 1H, OH); 4.00 (d, 2H, J = 4.5 Hz); 4.30 (m, 1H); 4.50 (s, 2H); 5,80 (m, 2H); 7.32 (m, 5H).

(4S,2E)1-O-Benzyl-4-O-propionyl-2-pentene-1,4-diol 27.
26 (8.00 g, 41.6 mmol) in pyridine (60 mL) was treated dropwise with propionic anhydride (9.4 mL, 73 mmol) in pyridine (2 mL) at 0°C. The mixture was stirred at 22°C for 3 h and concentrated under reduced pressure. The residue was diluted with ether, washed with 2N H_2SO_4 and brine, dried ($MgSO_4$) and chromatographed (hexanes/ethyl acetate 8:1) to give **27** (10.4 g, 97 %) as a colorless oil with $[\alpha]_D^{20}$= -31 (c=2.56).
^{1}H-NMR: δ = 1.14 (t, 3H, J = 7Hz); 1.32 (d, 3H, J = 7 Hz); 2.32 (quint, 2H, J = 7 Hz); 4.02 (d, 2H, J = 4.5 Hz); 4.52 (s, 2H); 5.40 (dd, 1H, J = 15 Hz, 5 Hz); 5.84 (dd, 1H, J = 15 Hz, 5 Hz); 7.32 (m, 5H). Anal. calcd for $C_{15}H_{20}O_3$ (248.32): C 72.55, H 8.12. Found: C 72.46, H 8.30.

Methyl-(2RS,3R,4E)3-benzyloxymethyl-2-methyl-4-hexenoate 28.
LDA was prepared from diisopropylamine (0.41 mL, 2.90 mmol) and n-butyllithium (1.6 M in hexanes, 1.8 mL, 2.90 mmol) in THF (5 mL). **27** (1.40 g, 5.6 mmol) in THF (4 mL) was added at -78°C and the mixture was stirred for 5 min. Chlorotrimethylsilane (0.74 mL, 5.8 mmol) was added and the mixture was stirred at -78°C for 10 min, at 22°C for 3 h and at 70°C for 30 min. After cooling to 22°C methanol (1 mL) and then diazomethane in ether were added dropwise until the solution remained faintly yellow. The product was

isolated by chromatography (hexanes/ethyl acetate 3:1) to give **28** (910 mg, 62 %) as a 85:15-mixture of the 2S- and 2R-stereoisomers.
^{1}H-NMR-signals of **28a**: δ = 1.06 (d, 3H, J = 6.8 Hz); 1.66 (dd, 3H, J = 6 Hz,2 Hz); 2.70 (quint, 1H, J = 6.8 Hz); 3.34-3.48 (m, 2H); 3.58 (s, 3H); 4.48 (s, 2H); 5.22 (ddq, 1H, J = 16 Hz, 8 Hz, 2.5 Hz); 5.52 (dq, 1H, J = 16 Hz, 6 Hz); 7.36 (m, 5H). Additional signals of **28b** : δ = 1.1 (d, 3H, J = 7 Hz); 2.52 (quint, 1H, J = 6.8 Hz); 2.68 (quint, 1H); 3.6 (s, 3H); 5.36 (ddq, 1H, J = 16 Hz, 8 Hz, 2.5 Hz); 5.51 (ddq, 1H, J = 16 Hz, 6 Hz). Anal. calcd. for $C_{16}H_{22}O_3$ (262.35): C 73.25, H 8.45. Found: C 72.90, H 8.39.

*(3S,4R,5R)-4-Benzyloxymethyl-3-methyl-5-tridecyl-oxolan-2-one (+)-**15**.*
The mixture of **28a/b** (6.00 g, 22.8 mmol) was ozonized as described before to give the aldehyde which was olefinated without further purification to give the Wittig product as pure (Z)-olefin (3.90 g, 41 %). This olefinic ester (3.66 g, 9.3 mmol) was saponified with 3N NaOH in methanol to give the carboxylic acid (3.06 g, 89 %), which was iodolactonized and deiodinated as described to furnish after HPLC separation crystalline (+)-**15** (1.42 g, 46 %), identical in all respect with (-)-**15** except for the sense of the optical rotation $[\alpha]_D^{20}$= +12.22 (c=1.73).

*III. Synthesis of (+)-**1**, (+)-2 and **18** from 1,2:5,6-O-Diisopropylidene-α-D-glucofuranose ("Diacetone-D-glucose")*

*3-Benzyloxymethyl-3-deoxy-1,2:5,6-O-diisopropylidene-α-D-allofuranose **30**.*
Commercially available (Aldrich) 1,2:5,6-O-diisopropylidene-α-D-glucofuranose **29** (100 g, 380 mmol) was converted into **29** (33 g, 15 %) in altogether 4 steps[19]. $[\alpha]_D^{20}$= +42.7 (c=1.8).
^{1}H-NMR: δ = 1.32-1.36 (3 x s, 9H); 1.56 (s, 3H); 2.24 (m, 1H); 3.72-3.82 (m, 3H); 3.92 (m, 1H); 4.06 (m, 2H); 4.56 (s, 2H); 4.78 (t, 1H, J = 4 Hz); 5.79 (d, 1H, J = 4 Hz); 7.34 (m, 5H). IR (film) 2990 (s), 2940 (s), 2880 (s), 2810 (m), 1500 (m), 1480 (m), 1455 (s), 1415 (m), 1380 (s), 1370 (s), 1345 (m), 1310 (m), 1250 (s,br), 1215 (s), 1170 (s), 1145 (s), 1120 (s), 1100 (s), 1075 (s), 1045 (s), 1015 (s), 960 (m), 920 (m), 870 (s), 850 (s), 795 (m), 740 (s), 700 (s), 660 (m,br), 605 (m), 545 (m), 515 (m) cm^{-1}.

*3-Benzyloxymethyl-3-deoxy-1,2-O-isopropylidene-4-(17-tridec-1-enyl)-α-D-erythrofuranose **31**.*
30 (15.0 g, 41.2 mmol) was stirred in 60 % HOAc for 18 h at 22°C. The mixture was extracted three times with ether and the extract was washed with brine, dried ($MgSO_4$) and chromatographed (hexanes/ethyl acetate v/v 2:1) to give 3-benzyloxymethyl-3-deoxy-1,2-O-isopropylidene-α-D-allofuranose (11.5 g, 94 %) as a colorless oil with $[\alpha]_D^{20}$= +30.21 (c=2.8). This material (11.4 g, 39 mmol) in dichloromethane (300 mL) was treated in small portions with lead tetraacetate (19.0 g, 42.8 mmol). After 30 min solid potassium carbonate (6 g) was added, the mixture was stirred at 22°C for 15 min and filtered. The filtrate was evaporated to dryness in vacuo, diluted with ether, stirred with potassium carbonate for 5 min and filtered again. The filtrate was concentrated to give the aldehyde (9.51 g, 92 %) which was olefinated as described for **12** without purification. The crude olefin was purified by chromatography (hexanes/ethyl acetate v/v 10:1) to give **31** (7.60 g, 53 %) as a colorless oil with $[\alpha]_D^{20}$= +4.5 (c=2.0).
^{1}H-NMR: δ = 0.88 (t, 3H, J = 5.5 Hz); 1.28 (m, 18H); 1.34 (s, 3H); 1.52 (s, 3H); 1.96-2.14 (m, 3H); 3.4 (dd, 1H, J = 9 Hz, 5 Hz); 3.76 (t(dd), 1H, J = 9 Hz); 4.52-4.6 (m, 3H); 4.76 (t, 1H, J = 4 Hz); 5.32 (dd, 1H, J = 10.5 Hz, 9.5 Hz); 5.64 (dt, 1H, J = 10.5 Hz, 7.5 Hz); 5.84 (d, 1H, J = 4 Hz). Anal. calcd. for $C_{28}H_{44}O_4$: C 75.63, H 9.97. Found C 76.12, H 10.03.

*3-Benzyloxymethyl-3-deoxy-1-O-methyl-4-tridecyl-D-erythrofuranose **32**.*
31 (7.40 g, 16.6 mmol) in methanol (200 mL) was hydrogenated as described for the synthesis of **14** to furnish 3-benzyloxymethyl-3-deoxy-1,2-O-isopropylidene-4-tridecyl-erythrofuranose (6.30 g, 85 %) with $[\alpha]_D^{20}$= + 40.5 (c=2.0) as a colorless oil, which was stirred in methanol (70 mL) with p-toluenesulfonic acid (2.5 g) for 24 h at 22°C. After neutralization with potassium carbonate and usual workup including chromatography

(hexanes /ethyl acetate v/v 5:1) **32** (4.97 g, 85 %) was obtained as a 15:1 β/α-anomeric mixture which was separated by chromatography. The β-anomer has $[\alpha]_D^{20}$= -6 (c= 2.2) and the following ^{1}H-NMR-spectrum. ^{1}H-NMR: δ = 0.88 (t, 3H, J = 5.5 Hz); 1.28 (m, 22H); 1.52 (m, 2H); 2.28 (m, 1H); 3.0 (d, 1H, J = 5 Hz, OH); 3.33 (s, 3H); 3.72 (d, 2H, J = 5 Hz); 4.04 (m, 1H); 4.24 (t, 1H, J = 5 Hz); 4.54 (quint, 2H, J = 5.5 Hz); 4.76 (s, 1H); 7.35 (m, 5H).

3-Benzyloxymethyl-2,3-dideoxy-1-O-methyl-4-tridecyl-β-D-erythrofuranose ***33***.

32 (4.90 g, 11.6 mmol) in THF (50 mL) was added dropwise to a suspension of sodium hydride (1.2 g, 50 % in mineral oil) in THF (30 mL). The mixture was refluxed for 2 h, then carbon disulfide (5.0 mL, 83 mmol) was added and refluxing was continued for 1 h. Methyl iodide (10 mL) was added in three portions under reflux over 3 h. The mixture was cooled to 22°C, water (5 mL) was added and the mixture was concentrated under reduced pressure. The residue was diluted with ether and washed with water, dried ($MgSO_4$) and chromatographed (hexanes/ethyl acetate v/v 5:1) to give the xanthogenate (4.46 g, 75 %) as a colorless liquid, which was refluxed in toluene (120 mL) with tributyltinhydride (4.5 mL, 17 mmol) and AIBN (50 mg) for 30 min. The mixture was filtered, concentrated under reduced pressure and chromatographed to furnish **33** (2.90 g, 75 %) as the pure β-anomer with $[\alpha]_D^{20}$= +28.3 (c=2.26).
^{1}H-NMR: δ = 0.88 (t, 3H, J = 5.5 Hz); 1.28 (s, 22H); 1.6 (m, 2H); 1.8 (ddd, 1H, J = 12 Hz, 9 Hz, 5.5 Hz); 2.08 (dd, 1H, J = 12 Hz, 8 Hz); 2.4 (m, 1H); 3.32 (s, 3H); 3.44 (d, 2H, J = 6 Hz); 3.83 (q, 1H, J = 6.5 Hz); 4.52 (s, 2H); 4.96 (d, 1H, J = 5.5 Hz); 7.32 (m, 5H). IR (film) 3035 (m), 2980 (m), 2920 (s), 2850 (s), 2800 (m), 1495 (m), 1465 (m), 1450 (m), 1375 (m), 1360 (s), 1330 (m), 1320 (m), 1310 (m), 1285 (m), 1265 (m), 1250 (m), 1205 (m), 1115 (s), 1100 (s), 1080 (s), 1060 (s), 1030 (s), 975 (m,br) 950 (m), 935 (m), 905 (m), 855 (m), 845 (m), 735 (m), 700 (m), 605 (m) cm^{-1}. ^{13}C-NMR: δ = 14.07, 22.65, 26.42, 29.32, 29.59, 29.66, 31.89, 37.02, 37.33, 42.79, 54.26, 72.11, 72.94, 83.21, 104.76, 127.39, 127.49, 128.30, 138.35. Anal. calcd. for $C_{26}H_{44}O_3$ (404.54) C 77.17, H 10.96. Found C 76.98, H 10.94.

*(4S,5R)-4-Benzyloxymethyl-5-tridecyl-oxolan-2-one ent-***14**.

33 (2.75 g, 7.0 mmol) in acetone (20 mL9 was treated dropwise at 0°C with a solution of $Na_2Cr_2O_7$ (5 g) in conc. sulfuric acid (3.75 mL) and water (22 mL) in portions until the red color persisted for 15 min. This required altogether 10 h. 2-Propanol was added and the solvent was removed in vacuo. The residue was triturated with ether and $MgSO_4$, the ether was decanted, until the residue was grainy and could be removed by filtration. The ether extracts were washed with brine, dried ($MgSO_4$) and chromatographed to give ent-**14** (1.85 g, 70 %) with $[\alpha]_D^{20}$= +18.1 (c=2.26). All other data were identical with those of **14**.

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