Stereoselective Synthesis of Alcohols, XLVII[1]

Application of Chiral *Z*-Pentenylboronates to the Synthesis of Erythronolide Building Blocks

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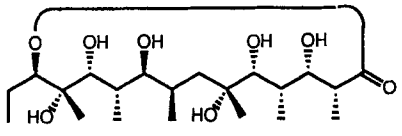
The chiral pentenylboronate **3** was the key reagent in the stereoselective construction of two erythronolide building blocks **6** and **7**. Addition of **3** to achiral aldehydes furnished homoallylic alcohols **21** and **26** with >98% e.e. Addition of **3** to chiral aldehydes **8** or **11** generated homoallylic alcohols with >95% d.e. In the mismatched case of addition to the aldehyde **29** diastereoselectivity reached merely 80%.

Erythronolide A, or more precisely its immediate synthetic precursor[2] (9*S*)-dihydro-erythronolide A (**1**), has been a very popular[3] target for research groups active in stereoselective synthesis. This may be ascribed to the sequences of contiguous stereocenters at C1–C7 and C7–C14, which still pose[4] a challenge to stereoselective synthesis and provide an established testing ground for evaluating the reliability of new stereoselective transformations.



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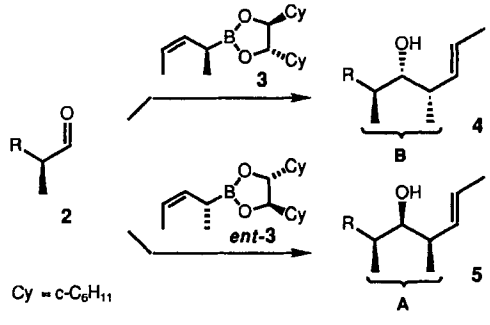
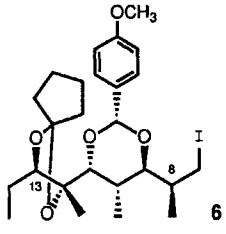
We developed lately[5] a highly enantioselective variant of the allylboration reaction with the aim to apply it to the synthesis of polyketide natural products. Obviously we turned to erythronolide A. The major task with respect to the synthesis of erythronolide A is, to develop a reagent which allows the conversion of a given chiral aldehyde **2** into each of the stereotriads[6] **4** and **5** with full (reagent) control of stereoselectivity.



The chiral pentenylboronate previously developed by us[5] promised to be a strongly stereodirecting agent for these transformations. To verify this, we applied **3** and *ent*-**3** to the synthesis of the subunits **6** and **7** of (9*S*)-dihydro-erythronolide A[7]. These subunits are of representative complexity with six and five adjacent stereocenters each.



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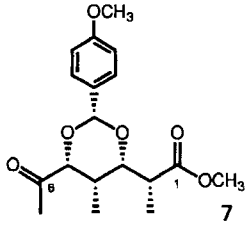

7

The C-7/C-15 Fragment 6

The general scheme used by us[6,7] for the synthesis of polypropionate natural products requires three steps for one chain elongation cycle: Crotylboration of an aldehyde, followed by protection of the new alcohol function and oxidative cleavage of the double bond to generate a new aldehyde. In our earlier investigations[5] exploratory studies of the reaction between the aldehyde **8**[8] and the chiral pentenyl boronate **3** had already be carried out. This led to the alcohol **9** in 71% yield. By refluxing the reactants in benzene for 2d the yield could be increased to 81%. Compound **9** was generated as a single diastereomer. Since the newly formed double bond had an E configuration, we have good reason[5] to assume that the newly formed stereocenters have the configuration indicated.

According to our general scheme[6,7], the alcohol **9** was protected as the *p*-methoxybenzyl ether **10** and then the double bond was ozonized to give the aldehyde **11**.

The next chain extension aimed at the generation of the stereotriad B with (8*R*,9*S*) configuration, cf. **12**. To this end, the enantiomeric reagent *ent*-**3** had to be applied. Reaction of **11** with *ent*-**3** at room temperature in petroleum ether furnished 79% of the alcohol **12** as a single diastereomer. Again we take from the fact, that the newly formed double bond has an *E* configuration, that the new stereocenters

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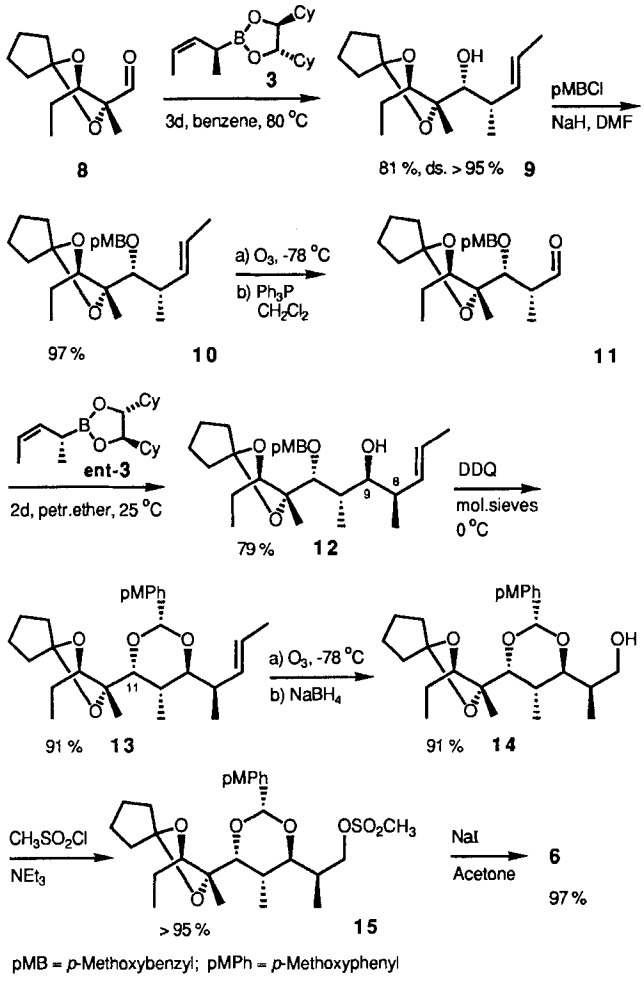
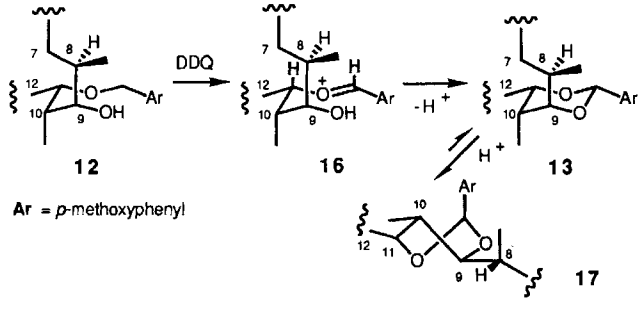


have been generated under reagent control of diastereoselectivity, i.e. in the desired (8*R*,9*S*) configuration. This, in fact, was substantiated by the ultimate conversion of **12** into (9*S*)-dihydroerythronolide[9]. The next step, the protection of the C-9 hydroxyl group appears trivial: DDQ oxidation[10] of the methoxybenzyl ether led in 91% yield to the *p*-methoxybenzylidene acetal **13**. In this reaction a single stereoisomer at the acetal center is formed, with the *p*-methoxyphenyl group in equatorial arrangement. This follows from a NOE contact between 11-H and the acetal H. This diastereomer arises, if the oxonium ion **16** is generated in the conformation shown, which minimizes 1,3-allylic strain[11], and if the oxonium ion **16** cyclizes more rapidly to **13** than it undergoes conformational relaxation.

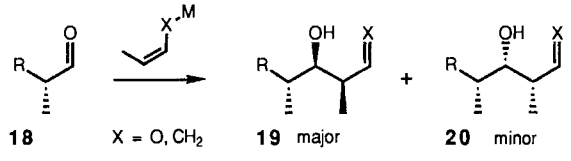


The dioxane diastereomer **13** obtained should populate a chair conformation[12] of the dioxane ring as has been discussed in detail by Yonemitsu[13]. The chair conformation of **13** is evident from the coupling constants of the dioxane ring: $J_{9,10}$ = 0.0 Hz, $J_{10,11}$ = 1.9 Hz. These coupling constants agree well with the data reported for a related erythronolide building block[13]. The dioxane **13** is formed under kinetic control and tends to epimerize under acidic conditions to **17** with a twist boat conformation and characteristically different coupling constants[13,14]. Since it is only the former diastereomer **13** that allows a later macrolactonisation to erythronolide[15], we were pleased that the isomer **13** was obtained directly and in good yield.

The conversion of **13** into the iodo compound **6** was essentially routine: Ozonolysis of **13** followed by reductive workup provided the alcohol **14**, which was converted to the iodo compound via the mesylate **15**. This two-step route gave slightly higher yields than the direct route using tributylphosphane, imidazole and iodine[16].

The C-1/C-6 Fragment

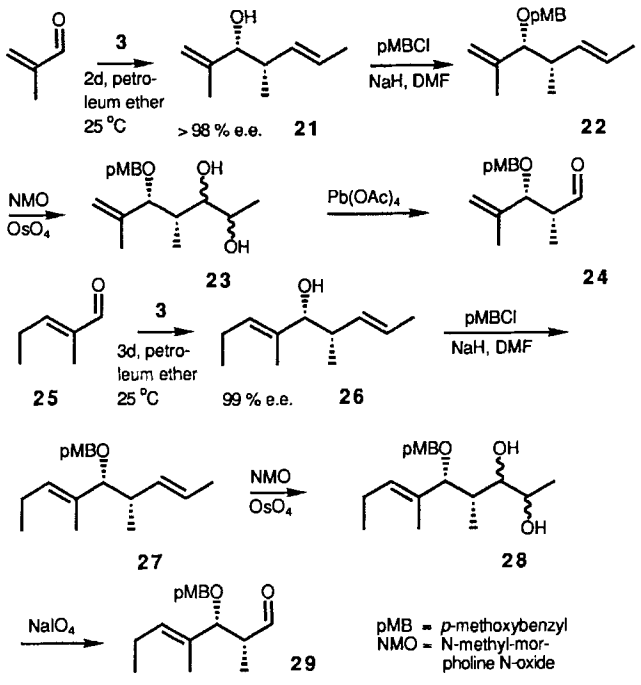
The synthesis of the C-1/C-6 fragment of erythronolide adresses a different problem: Chiral aldehydes such as **18** have a pronounced tendency to generate the *anti*-Cram product **19** on chain extension, be it by the aldol addition[17] or by allyl metalation sequences[18] with good to high selectivity[19] whereas for erythronolide the Cram product[20], stereotriad A, is required. Due to this situation reagent control of diastereoselectivity is absolutely necessary.

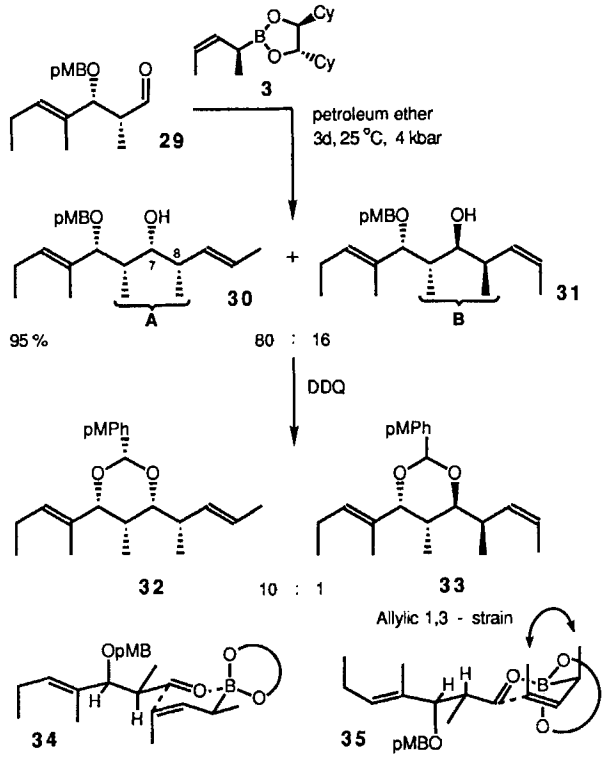


Our previous exposure to this problem[21] foreshadowed major difficulties in this chain extension, which therefore provides a good test for the capability of our chiral pentenylboronate **3** to exert reagent control of diastereoselectivity.

The synthesis of the C-1/C-6 segment was initiated by an enantioselective addition of **3** to methacrolein. The alcohol **21** obtained in 82% yield was protected as the *p*-methoxybenzyl ether. Selective oxidative cleavage of the 1,2-disubstituted double bond could be effected by osmylation (76%) followed by periodate cleavage (>90%). However, differentiation of the two double bonds of **22** in the osmylation step was not sufficiently reproducible. Especially when the reaction was carried out with more than 10 mmol of the reagent, overoxidation became the rule. S. Rychnovsky recently reported for a related system that a bulky triethylsilyl group on the hydroxyl group leads to a better differentiation[22] between the two double bonds.

We hoped that a *di*- and a *tri*-substituted double bond could be more readily differentiated and started anew from the aldehyde **25**. Its reaction with **3** furnished the homoallyl alcohol **26** in 81% yield. Protection with p-methoxybenzyl



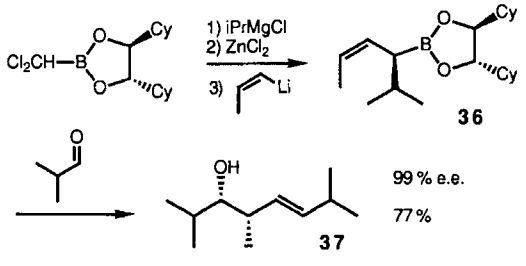


chloride led to the diene **27**. Osmylation of the latter was again not fully regioselective. Nevertheless, the desired diol was obtained in 75% yield as a 3:2 diastereomer mixture. This allowed satisfactory access to the aldehyde **29**.

At this stage the stereoselectivity in the critical chain elongation step could be addressed. Reagent control of diastereoselectivity forces a substrate to react via an otherwise unfavorable high-energy transition state, necessarily leading to a slow reaction. In the case of the reaction of the aldehyde **29** with the pentenylboronate **3** the reaction had to be run at 4 kbar pressure in order to achieve a satisfactory conversion. In this way a 95% yield of a 80:16:4 product mixture was obtained.

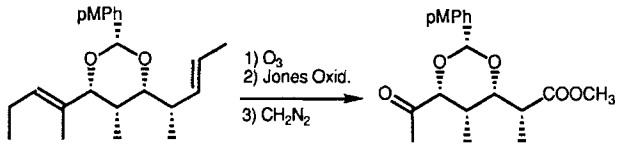
The major isomer has an *E* double bond (15.1 Hz coupling between the olefinic hydrogens in the ^{1}H-NMR spectrum). It should therefore be the isomer **30** with the desired (7*R*,8*S*) configuration formed via transition state **34**. The second abundant isomer could not be identified at this stage. The mixture of alcohols obtained was subjected to DDQ oxidation affording a 10:1 mixture of *p*-methoxybenzylidene acetals in 66% yield. The structure of the major isomer could readily be assigned as **32**. The ^{13}C-NMR signals of the second isomer were of low intensity. If small signals at δ = 15.0 and 34.5 were attributed to the second isomer this would suggest the presence of a *Z* double bond and hence a (7*S*,8*R*) configuration.

The formation of the diastereomer **30** as the predominant product shows that the chiral *Z*-pentenylboronate dictated the stereochemical outcome of the chain extension reaction of **29** to ca. 80%. Apparently the transition state **34** with a very hindered approach to the aldehyde[20] is still lower in energy than the transition state **35**, in which the approach to the aldehyde is optimal[20] but the pentenylboronate has to adopt a conformation destabilized by 1,3-allylic strain[5]. Perhaps, the selectivity could be improved further by a boronate reagent, in which a larger α-substituent would be even more reluctant to occupy an axial position in the transition state **35**. For this reason, we generated the chiral allylboronate **36** according to a standard procedure.



Its reaction with isobutylaldehyde led to the homoallylic alcohol **37** with 99% e.e. In the reaction of **36** with the aldehyde **29**, however, the selectivity reached just the same 80% level as before. In fact, trying to force the stereoselectivity up against the predisposition of the aldehyde **29** by more and more steric congestion is basically the wrong approach. It would be much more wise to use a different type of reaction. Thus, in earlier studies directed at erythronolide fragments other groups reached selectivities of up to 97% by reaction of aldehydes related to **29** with crotylstannanes under Lewis acid assistance[23]. In our hands, however, reaction of the aldehyde **29** with *Z*-crotyl-tributyl-stannane in the presence of either $MgBr_2$, $Et_2O \cdot BF_3$, or $SnCl_4$ led to the desired alcohol **3** but only in lower yields and lower selectivities than with the pentenylboronate **3**. This convinced us, that higher selectivites, in the chain extension **29** → **30** could not readily be obtained. We therefore continued

our efforts to prepare the desired erythronolide building block **7** by starting from **32**.



32 82% **7**

Ozonolysis of **32** was followed by Jones oxidation of the intermediate keto aldehyde to the keto acid which was immediately esterified with diazomethane. This route, although more laborious, was more reliable than the direct cleavage of **32** with RuO_4 followed by diazomethane esterification (78%).

With the building blocks **6** and **7** in hand, it was obvious to attempt their combination in a convergent synthesis of (9*S*)-dihydroerythronolide A (**1**) by converting **6** to a Grignard or related organometallic reagent and adding it to the carbonyl group of **7**. Such an assembly of the erythronolide A skeleton has been accomplished by Stork[15b] in its synthesis of (9*S*)-dihydro-erythronolide A (**1**). While we could convert **6** to a lithium, magnesium, or cerium reagent, which could be added to acetone[24], addition to the ketoester **7** remained unsuccessful. In view of the completion of our linear synthesis of (9*S*)-dihydro-erythronolide A, which was only two steps longer than the convergent synthesis based on **6** and **7** could be at best, we discontinued our efforts along these lines.

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Experimental

All temperatures quoted are not corrected. – ^1H NMR, ^{13}C NMR: Bruker AC-300, AM-400, AMX-500. – Boiling range of petroleum ether: 40–60°C. – Flash chromatography: Silica gel Si 60, E. Merck AG, Darmstadt, 40–63 μm. – Analytical gas chromatography: Siemens Sichromat 3 with a 30 m × 0.3 mm quartz capillary column with SE 52, 0.9 bar He.

1. *(2R,3S)-2-Ethyl-3-[(1R,2S,3E)-1-hydroxy-2-methyl-3-pentenyl]-3-methyl-1,4-dioxaspiro[4.4]nonane* (**9**): To a solution of 1.98 g (10.0 mmol) of (2*R*,3*R*)-3-ethyl-2-methyl-1,4-dioxaspiro[4.4]-nonane-2-carbaldehyde (**8**) in 80 ml of benzene was added 3.04 g (10.0 mmol) of (4*S*,5*S*)-4,5-dicyclohexyl-2-[(1*S*,2*Z*)-1-methyl-2-butenyl]-1,3,2-dioxaborolane (**3**). After heating to reflux for 2 d, 1.49 g (10.0 mmol) of triethanolamine was added and refluxing was continued for 1 h. Then 30 ml of saturated aqueous NH_4Cl solution was added, the phases were separated and the aqueous phase was extracted three times with 50 ml of ether. The combined organic phases were dried with $MgSO_4$ and concentrated. Flash chromatography of the residue with petroleum ether/ether (10:1) furnished 2.17 g (81%) of **9** as a colorless oil. – ^1H NMR (400 MHz, $CDCl_3$): δ = 0.99 (t, *J* = 7.4 Hz, 3H), 1.02 (d, *J* = 6.8 Hz, 3H), 1.21 (s, 3H), 1.7–1.9 (m, 10H), 1.65 (dd, *J* = 6.2 and 1.3 Hz, 3H), 2.30 (qd, *J* = 7.0 and 2.9 Hz, 1H), 2.35 (d, *J* = 5.6 Hz, 1H), 3.42 (dd, *J* = 5.5 and 3.0 Hz, 1H), 3.55 (dd, *J* = 9.5 and 4.1 Hz, 1H), 5.42 (dqd, *J* = 15.3, 6.0, and 0.8 Hz, 1H), 5.53 (ddq, *J* = 15.3, 6.1, and 1.4 Hz, 1H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.6, 14.2, 17.9, 22.2, 22.3, 23.1, 24.1, 37.2, 37.7, 38.8, 75.2, 83.2, 87.7, 117.1, 123.6, 136.1. – $C_{16}H_{28}O_3$ (268.4): calcd. C 71.60, H 10.51; found C 71.55, H 10.54.

2. *(2R,3S)-2-Ethyl-2-[(1S,2S,3E)-1-(4-methoxybenzyloxy)-2-methyl-3-pentenyl]-3-methyl-1,4-dioxaspiro[4.4]nonane* (**10**): 1.50 g (5.59 mmol) of **9** was added dropwise to a suspension of 0.70 g (22 mmol) of sodium hydride (80% in white oil) in 40 ml of dimethylformamide. After stirring for 10 min, 2.62 g (16.8 mmol) of 4-methoxybenzyl chloride was added. After stirring for ca. 12 h, 10 ml of water was added, the mixture was stirred for 1 h and extracted with 200 ml of ether. The aqueous phase was extracted three times with 50 ml each of ether and the combined organic phases were dried with $MgSO_4$ and concentrated. Flash chromatography of the residue with petroleum ether/ethyl acetate (10:1) furnished 2.10 g (97%) of **10** as a colorless oil. – ^1H NMR (300 MHz, $CDCl_3$): δ = 0.98 (t, *J* = 7.3 Hz, 3H), 1.08 (d, *J* = 6.8 Hz, 3H), 1.29 (s, 3H), 1.60–1.82 (m, 10H), 1.62 (d, *J* = 5.1 Hz, 3H), 2.32 (m, 1H), 3.29 (d, *J* = 5.4 Hz, 1H), 3.57 (dd, *J* = 9.3 and 4.3 Hz, 1H), 3.79 (s, 3H), 4.48 and 4.71 (AB system, *J* = 10.9 Hz, 1H each), 5.35 (m, 2H), 6.85 and 7.32 (AB system, *J* = 8.7 Hz, 2H each). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.3, 16.8, 18.0, 21.1, 22.5 (several signals), 23.7, 23.9, 39.2, 39.3, 55.3, 74.3, 84.7, 85.9, 113.6, 117.0, 124.0, 129.3, 131.7, 135.9, 158.9. – $[\alpha]_D^{20}$ = 34.2 (*c* = 0.8, $CHCl_3$). – $C_{24}H_{36}O_4$ (388.5): calcd. C 74.19, H 9.34; found C 74.23, H 9.26.

3. *(2R,3S)-2-Ethyl-3-[(1S,2R)-1-(4-methoxybenzyloxy)-2-methyl-3-oxopropyl]-3-methyl-1,4-dioxaspiro[4.4]nonane* (**11**): Into a solution of 6.00 g (15.4 mmol) of **10** in 150 ml of CH_2Cl_2 was introduced at −78°C a stream of ozone in oxygen until the blue color persisted. Excess ozone was purged by a stream of nitrogen. Then 7.86 g (30.0 mmol) of triphenylphosphane was added and the mixture was allowed to reach 0°C. The mixture was concentrated and residual solvent was removed at 10^{-3} Torr. A small aliquot was purified by flash chromatography with petroleum ether/ether (10:1) to give **11**. – ^1H NMR (400 MHz, $CDCl_3$): δ = 1.00 (t, *J* = 7.4 Hz, 3H), 1.23 (d, *J* = 7.5 Hz, 3H), 1.31 (s, 3H), 1.6–1.8 (m, 10H), 2.86 (ddq, *J* = 7.3, 4.6, and 1.4 Hz, 1H), 3.63 (dd, *J* = 8.2 and 5.2 Hz, 1H), 3.78 (s, 3H), 3.85 (d, *J* = 4.6 Hz, 1H), 4.36 and 4.39 (AB system, *J* = 11.2 Hz, 1H each), 6.85 and 7.26 (AB system, *J* = 8.5 Hz, 2H each), 9.3 (d, *J* = 1.5 Hz, 1H). – ^{13}C NMR (75 MHz, C_6D_6): δ = 10.1, 12.3, 22.3, 23.4, 24.2, 24.7, 37.2, 38.2, 47.8, 54.7, 73.9, 80.6, 83.6, 87.1, 114.0, 117.9, 129.0, 130.8, 159.6, 202.9. – $[\alpha]_D^{20}$ = 26.5 (*c* = 45, $CHCl_3$). – $C_{22}H_{32}O_5$ (376.5): calcd. C 70.18, H 8.56; found C 70.12, H 8.59.

4. *(2R,3S)-2-Ethyl-3-[(1S,2S,3S,4R,5E)-3-hydroxy-1-(4-methoxybenzyloxy)-2,4-dimethyl-5-heptenyl]-3-methyl-1,4-dioxaspiro[4.4]nonane* (**12**): The crude aldehyde obtained under 3. was taken up in 200 ml of petroleum ether. Then 6.08 g (20.0 mmol) of (4*R*,5*R*)-4,5-dicyclohexyl-2-[(1*R*,2*Z*)-1-methyl-2-butenyl]-1,3,2-dioxaborolane (*ent*-**3**) and 5 g of molecular sieves (3 Å) were added to the solution. After 2 d 2.98 g (20.0 mmol) of triethanolamine and 50 ml of a saturated aqueous NH_4Cl solution were added, the phases were separated and the aqueous phase was extracted three times with 100 ml each of ether. The combined organic phases were dried with $MgSO_4$ and concentrated. Flash chromatography of the residue with petroleum ether/ether (16:1) furnished 5.44 g (79%) of **12** as a colorless oil. – ^1H NMR (300 MHz, $CDCl_3$): δ = 0.87 (d, *J* = 6.9 Hz, 3H), 0.93 (t, *J* = 7.3 Hz, 3H), 0.98 (d, *J* = 7.1 Hz, 3H), 1.29 (s, 3H), 1.5–1.8 (m, 10H), 1.62 (d, *J* = 5.1 Hz, 3H), 1.92 (m, 1H), 2.28 (m, 1H), 2.96 (d, *J* = 3.6 Hz, 1H), 3.25 (dd,

J = 10.0 and 3.6 Hz, 1H), 3.55 (dd, J = 10.0 and 3.5 Hz, 1H), 3.68 (d, J = 2.9 Hz, 1H), 3.75 (s, 3H), 4.46 and 4.52 (AB system, J = 11.0 Hz, 1H each), 5.46 (m, with J = 15.4 and 5.3 Hz, 2H), 6.82 and 7.24 (AB system, J = 9.7 Hz, 2H each). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.6, 12.2 (two signals), 18.1, 22.1, 23.2, 24.0, 25.2, 36.5, 37.3, 38.0, 38.4, 55.3, 74.4, 79.4, 82.6, 84.5, 87.0, 113.6, 117.5, 124.6, 128.9, 131.2, 135.7, 159.0. – $[\alpha]_D^{20}$ = 35.8 (c = 0.800, $CHCl_3$). – $C_{27}H_{42}O_5$ (446.6): calcd. C 72.61, H 9.47; found C 72.83, H 9.40.

5. *(2R,3S)-2-Ethyl-3-{[(2R,4S,5S,6R)-2-(4-methoxyphenyl)-5-methyl-4-((1R,2E)-1-methyl-2-butenyl)]-1,3-dioxan-6-yl}-3-methyl-1,4-dioxaspiro[4.4]nonane* (**13**): A solution of 2.00 g (4.47 mmol) of **12** in 50 ml of CH_2Cl_2 was stirred for 30 min with 4 g of molecular sieves (3 Å). It was cooled to 0°C and 1.06 g (4.70 mmol) of freshly crystallized 2,3-dichloro-4,5-dicyanobenzoquinone was added. TLC indicated a complete reaction after 6 h at 0°C. The mixture was filtered and 30 ml of a saturated $NaHCO_3$ solution was added to the filtrate. The phases were separated and the aqueous phase was extracted three times with 50 ml each of ether. The combined organic phases were dried with $MgSO_4$ and concentrated. Flash chromatography of the residue with petroleum ether/ether/triethylamine (8:1:0.01) furnished 1.81 g (91%) of **13** as a colorless oil. The material crystallized after standing in the refrigerator. After recrystallization from pentane: m.p. 82–83°C. – ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.97 (t, J = 7.4 Hz, 3H), 1.04 (d, J = 6.6 Hz, 3H), 1.06 (s, 3H), 1.25 (d, J = 6.9 Hz, 3H), 1.55–1.80 (m, 10H), 1.60 (dd, J = 6.5 and 1.6 Hz, 3H), 1.93 (m, 1H), 2.92 (m, 1H), 3.30 (d, J = 11.0 Hz, 1H), 3.49 (dd, J = 8.8 and 4.3 Hz, 1H), 3.72 (s, 3H), 3.74 (d, J = 1.9 Hz, 1H), 5.12 (ddq, J = 15.2 and 8.4 Hz, 1H), 5.40 (dq, J = 15.2 and 6.5 Hz, 1H), 5.59 (s, 1H), 6.81 (d, J = 8.7 Hz, 2H), 7.40 (d, J = 8.7 Hz, 2H). – ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.9, 15.4, 17.8, 18.0, 22.0, 22.3, 23.2, 24.0, 29.7, 36.6, 36.7, 38.3, 55.3, 75.0, 81.6, 85.4, 87.7, 94.7, 113.3, 117.8, 125.9, 127.2, 132.0, 134.0, 159.6. – $[\alpha]_D^{20}$ = 23.3 (c = 1.24, $CHCl_3$). – $C_{27}H_{40}O_5$ (444.6): calcd. C 72.94, H 9.07; found C 72.84, H 8.86.

6. *(2R,3S)-2-Ethyl-3-{[(2R,4S,5S,6R)-4-((1R)-2-hydroxy-1-methylethyl)]-2-(4-methoxyphenyl)-5-methyl-1,3-dioxan-6-yl}-3-methyl-1,4-dioxaspiro[4.4]nonane* (**14**): 0.151 g (0.33 mmol) of **13** was ozonized as described under 5. After addition of 0.170 g (0.67 mmol) of triphenylphosphane the mixture was warmed to 0°C and concentrated. The crude aldehyde was taken up in 10 ml of methanol, then 25 mg (0.67 mmol) of $NaBH_4$ was added. After stirring for 10 h 10 ml of water and 30 ml of ethyl acetate were added to the solution. The phases were separated and the aqueous phase was extracted three times with 30 ml each of ethyl acetate. The combined organic phases were dried with $MgSO_4$ and concentrated. Flash chromatography of the residue with petroleum ether/ethyl acetate/triethylamine (8:1:0.01) furnished 0.131 g (91%) of **14** as a colorless foam. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.99 (t, J = 7.4, Hz, 3H), 1.02 (d, J = 6.8 Hz, 3H), 1.10 (s, 3H), 1.24 (d, J = 6.8 Hz, 3H), 1.49–2.00 (m, 12H), 2.32 (m, 1H), 3.42 (broad d, J = 10.5 Hz, 2H), 3.49 (d, J = 4.5 Hz, 1H), 3.53 (d, J = 3.9 Hz, 1H), 3.72 (s, 3H), 3.78 (d, J = 2.4 Hz, 1H), 5.61 (s, 1H), 6.82 (d, J = 8.7 Hz, 2H), 7.40 (d, J = 8.7 Hz, 2H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.9, 13.7, 15.3, 22.1, 22.2, 23.1, 24.0, 31.1, 34.6, 36.7, 38.2, 55.2, 65.8, 75.1, 81.6, 82.9, 87.7, 95.2, 113.4, 117.8, 127.2, 131.8, 159.5. – $[\alpha]_D^{20}$ = 1.5 (c = 1.0, $CHCl_3$). – $C_{25}H_{38}O_6$ (434.6): calcd. C 69.09, H 8.81; found C 68.99, H 8.79.

7. *(2R,3S)-2-Ethyl-3-{[(2R,4S,5S,6R)-2-(4-methoxyphenyl)-5-methyl-4-((1R)-1-methyl-2-(methylsulfonyloxy)ethyl)]-1,3-dioxan-6-yl}-3-methyl-1,4-dioxaspiro[4.4]nonane* (**15**): To a solution of 0.100 g (0.23 mmol) of **14** in 10 ml of CH_2Cl_2 were added at 0°C 46 mg (0.46 mmol) of triethylamine and 42 mg (0.37 mmol) of freshly distilled methanesulfonyl chloride. After stirring at 0°C for 6 h 5 ml of ice-cold brine was added, the phases were separated and the aqueous phase was extracted three times with 10 ml each of CH_2Cl_2. The combined organic phases were dried with $MgSO_4$ and concentrated. Flash chromatography of the residue with petroleum ether/ethyl acetate/triethylamine (8:1:0.01) furnished 0.118 g (100%) of **15** as a viscous oil. – ^{1}H NMR (300 MHz, C_6D_6): δ = 0.79 (t, J = 7.4 Hz, 3H), 0.82 (d, J = 7.4 Hz, 3H), 0.94 (s, 3H), 1.05 (d, J = 6.7 Hz, 3H), 1.49 (s, 3H), 1.52–1.64 (m, 4H), 1.76 (m, 4H), 2.00–2.30 (m, 4H), 3.00 (m, J = 11.1 and 5.6 Hz, 1H), 3.07 (m, J = 11.1 and 5.2 Hz, 1H), 3.21 (s, 3H), 3.44 (d, J = 2.6 Hz, 1H), 3.50 (d, J = 2.5 Hz, 1H), 3.58 (d, J = 2.3 Hz, 1H), 5.55 (s, 1H), 6.79 (d, J = 8.5 Hz, 2H), 7.63 (d, J = 8.5 Hz, 2H). – ^{13}C NMR (100 MHz, C_6D_6): δ = 12.3, 15.0, 15.6, 22.1, 22.8, 23.5, 24.4, 31.1, 34.7, 37.3, 38.6, 48.5, 54.7, 75.4 (2 C), 81.9, 82.2, 88.1, 95.6, 113.8, 118.4, 127.8, 132.2, 160.3. – $C_{26}H_{40}OS_8$ (512.7): calcd. C 60.91, H 7.86; found C 60.66, H 7.68.

8. *(2R,3S)-2-Ethyl-3-{[(2R,4S,5S,6R)-4-((1R)-2-iodo-1-methylethyl)]-2-(4-methoxyphenyl)-5-methyl-1,3-dioxan-6-yl}-3-methyl-1,4-dioxaspiro[4.4]nonane* (**6**): A solution of 0.100 g (0.19 mmol) of **15** and 0.690 g (4.60 mmol) of NaI in 5 ml of acetone was held for 30 min under reflux. The mixture was poured into 5 ml of ice/water. Then 20 ml of ether was added and the phases were separated. The aqueous phase was extracted three times with 20 ml each of ether. The combined organic phases were dried with $MgSO_4$ and concentrated leaving 0.10 g (97%) of **6** as an oil which rapidly darkened. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.97 (t, J = 7.4 Hz, 3H), 1.01 (s, 3H), 1.04 (d, J = 6.4 Hz, 3H), 1.31 (d, J = 6.8 Hz, 3H), 1.53–1.79 (m, 10H), 1.95 (m, 1H), 2.54 (m, 1H), 3.26 (m, J = 10.4 and 5.5 Hz, 1H), 3.38 (m, J = 10.4 and 6.3 Hz, 1H), 3.50 (m, 2H), 3.68 (d, J = 2.3 Hz, 1H), 3.74 (s, 3H), 5.57 (s, 1H), 6.80 (d, J = 8.5 Hz, 2H), 7.41 (d, J = 8.5 Hz, 2H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.1, 15.4, 16.0, 22.4, 22.5, 23.3, 24.2, 30.7, 34.0, 36.9, 38.2, 38.4, 55.4, 75.3, 81.7, 83.2, 87.9, 95.7, 113.3, 118.1, 127.4, 131.7, 159.8. – $[\alpha]_D^{20}$ = 4.8 (c = 2.8, $CHCl_3$). – $C_{25}H_{37}IO_5$ (544.5): calcd. C 55.15, H 6.85; found C 55.59, H 6.97; calcd. 544.1686, found 544.1703 (MS).

9. *(4R,4S,5E)-3-Hydroxy-2,4-dimethylhepta-1,5-diene* (**21**): A solution of 1.12 g (16.1 mmol) of methacrolein in 50 ml of petroleum ether was stirred for 30 min with 3 g of molecular sieves (3 Å). After cooling to 0°C 4.89 g (16.1 mmol) of **3a** was added. The mixture was stirred for 2 d at room temperature. Then 2.39 g (16.1 mmol) of triethanolamine was added and the mixture was heated at reflux for 1 h. 50 ml of a saturated aqueous NH_4Cl solution was added, the phases were separated and the aqueous phase was extracted three times with 100 ml each of ether. The combined organic phases were dried with $MgSO_4$ and concentrated. Flash chromatography of the residue with petroleum ether/ether (8:1) furnished 1.66 g (74%) of **21** as a colorless oil. The enantiomeric excess was determined by derivatization[25] with (*S*)-1-phenylethyl isocyanate to be 98%. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.94 (d, J = 6.7 Hz, 3H), 1.63 (d, J = 6.0 Hz, 3H), 1.69 (s, 3H), 2.32 (dq, J = 6.8 and 0.8 Hz, 1H), 3.84 (broad dd, J = 4.5 Hz, 1H), 4.82 (q, J = 1.5 Hz, 1H), 4.89 (q, J = 0.8 Hz, 1H), 5.34 (ddq, J = 15.4, 6.7, and 1.4 Hz, 1H), 5.45 (dqd, J = 15.4, 6.0, and 0.9 Hz, 1H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.3, 17.1, 18.0, 39.8, 80.4, 111.6, 125.2, 133.6, 146.0. – $[\alpha]_D^{20}$ = 3.6 (c = 6.5, $CHCl_3$). – $C_9H_{16}O$ (140.2): calcd. C 77.09, H 11.50; found C 76.78, H 11.40.

10. *(3R,4S,5E)-3-(4-Methoxybenzyloxy)-2,4-dimethylhepta-1,5-diene* (**22**): 0.25 g (1.78 mmol) of **21** was converted into the pMB ether as described under 2. Flash chromatography with petroleum

ether/ether (15:1) furnished 0.46 g (quantitative) of **22** as a colorless oil. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.04 (d, *J* = 6.6 Hz, 3H), 1.59 (dd, *J* = 5.7 and 0.6 Hz, 3H), 1.64 (s, 3H), 2.24 (m, 1H), 3.32 (d, *J* = 8.8 Hz, 1H), 3.78 (s, 3H), 4.14 and 4.42 (AB system, *J* = 11.5 Hz, 1H each), 4.82 (broad s, 1H), 4.95 (broad s, 1H), 5.18 (ddq, *J* = 15.3 and 7.8 Hz, 1H), 5.40 (dqd, *J* = 15.3 and 6.3 Hz, 1H), 6.85 (d, *J* = 8.6 Hz, 2H), 7.24 (d, *J* = 8.6 Hz, 2H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.1, 17.3, 17.9, 39.5, 55.2, 69.6, 87.4, 113.6, 114.5, 124.1, 129.3, 130.1, 133.4, 143.7, 159.5. – $[\alpha]_D^{20}$ = 56.7 (*c* = 0.7, $CHCl_3$). – $C_{17}H_{24}O_2$ (260.4): calcd. C 78.42, H 9.29; found C 78.38, H 9.44.

11. *(2S*,3S*,4S,5R)-2,3-Dihydroxy-5-(4-methoxybenzyloxy)-4,6-dimethyl-6-heptene* (**23**): To a solution of 0.26 g (1.0 mmol) of **22** in 3 ml of dioxane and 3 ml of water were added sequentially 0.49 g (3.0 mmol) of a 60% aqueous solution of *N*-methylmorpholine *N*-oxide, 0.31 g (0.05 mmol) of a 4% solution of OsO_4 in *tert*-butyl alcohol, and one drop of pyridine. After stirring for 10 h at room temperature 2.00 g of Na_2SO_3 and 50 ml of ethyl acetate were added. The phases were separated and the aqueous phase was extracted three times with 20 ml each of ethyl acetate. The combined organic extracts were dried with $MgSO_4$ and concentrated. Flash chromatography of the residue with petroleum ether/ethyl acetate (3:1) furnished 0.25 g (85%) of **23** as a colorless oil. – $C_{17}H_{26}O_4$ (294.4): calcd. C 69.36, H 8.90; found C 69.15, H 8.98.

Major diastereomer: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.94 (d, *J* = 6.3 Hz, 3H), 1.15 (d, *J* = 6.4 Hz, 3H), 1.68 (broad s, 3H), 1.88 (m, 1H), 2.60 (broad m, 1H), 3.24 (m, 1H), 3.46 (broad m, 1H), 3.68 (m, 1H), 3.76 (s, 3H), 4.03 (broad d, *J* = 4.2 Hz, 1H), 4.18 and 4.52 (AB system, *J* = 11.1 Hz, 1H each), 5.00 (s, 1H), 5.06 (broad s, 1H), 6.84 (d, *J* = 8.6 Hz, 2H), 7.20 (d, *J* = 8.6 Hz, 2H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.6, 19.7, 20.0, 36.7, 55.1, 68.5, 70.6, 79.0, 82.5, 112.7, 114.0, 129.6, 130.2, 141.7, 159.4.

The following signals of the minor diastereomer could be recorded: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.89 (d, *J* = 6.6 Hz, 3H), 1.07 (d, *J* = 6.3 Hz, 3H), 1.66 (broad s, 3H), 3.28 (dd, *J* = 7.9 and 1.9 Hz, 1H), 3.75 (s, 3H), 4.16 and 4.45 (AB system, *J* = 11.1 Hz, 1H each). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 7.9, 18.2, 18.8, 36.7, 55.3, 68.9, 70.4, 78.1, 86.2, 113.9, 114.9, 129.6, 130.0, 142.3, 159.3.

12. *(2R,3R)-3-(4-Methoxybenzyloxy)-2,4-dimethyl-4-pentenal* (**24**): To a solution of 100 mg (0.34 mmol) of **23** in 10 ml of CH_2Cl_2 was added at 0°C 150 mg (0.34 mmol) of lead tetraacetate in four portions. After stirring for 4 min the mixture was filtered over a 2 cm layer of Kieselgur with dichloromethane. The filtrate was concentrated at 0°C to give 74 mg (87%) of **24** a colorless oil which darkened rapidly. – ^{1}H NMR (300 MHz, C_6D_6): δ = 0.86 (d, *J* = 6.9 Hz, 3H), 1.59 (broad s, 3H), 2.18 (d quint., *J* = 7.5 and 1.5 Hz, 1H), 3.30 (s, 3H), 3.70 (d, *J* = 6.1 Hz, 1H), 3.90 and 4.24 (AB system, *J* = 11.4 Hz, 1H each), 4.78 (broad s, 2H), 6.60 (d, *J* = 8.6 Hz, 2H), 6.96 (d, *J* = 8.6 Hz, 2H), 9.25 (d, *J* = 1.6 Hz, 1H). – ^{13}C NMR (75 MHz, C_6D_6): δ = 9.3, 18.3, 49.3, 55.1, 70.2, 81.6, 114.1, 114.7, 129.6, 130.5, 142.1, 159.7, 203.0.

13. *(3E,5R,6S,7E)-5-Hydroxy-4,6-dimethyl-3,7-nonadiene:* 2.94 g (30.0 mmol) of (*E*)-2-methyl-2-pentenal, 150 ml of petroleum ether, 9.12 g (30.0 mmol) of **3**, 5 g of molecular sieves (3 Å) and 4.47 g (30.0 mmol) of triethanolamine were allowed to react as described under 9. to give 4.09 g (81%) of **26** as a colorless oil. The enantiomeric excess was determined by derivatization[25] with (*S*)-1-phenylethyl isocyanate to be 99%. – ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.93 (t, *J* = 7.2 Hz, 3H), 0.97 (d, *J* = 6.4 Hz, 3H), 1.50 (broad s, 1H), 1.54 (broad s, 3H), 1.62 (broad s, 3H), 2.01 (m, 2H), 2.33 (m, 1H), 3.74 (dd, *J* = 8.0 and 3.4 Hz, 1H), 5.30 (ddq, *J* = 15.6, 6.8, and 1.6 Hz, 1H), 5.34 (t quint., *J* = 7.2 and 1.2 Hz, 1H), 5.44 (dqd, *J* = 15.6, 6.3, and 0.9 Hz, 1H). – ^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.1, 14.6, 16.8, 18.0, 20.7, 40.7, 81.1, 124.7, 128.9, 133.8, 135.1. – $C_{11}H_{20}O$ (168.3): calcd. C 78.51, H 11.98; found C 78.20, H 11.71.

14. *(3E,5R,6S,7E)-5-(4-Methoxybenzyloxy)-4,6-dimethyl-3,7-nonadiene* (**27**): 1.87 g (62.4 mmol) of sodium hydride (80% in white oil), 100 ml of DMF, and 3.50 g (20.8 mmol) of **26** in 20 ml of DMF were allowed to react as described under 2. Flash chromatography with petroleum ether/ether (16:1) furnished 5.70 g (95%) of **27** as a colorless oil. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.95 (t, *J* = 7.5 Hz, 3H), 1.02 (d, *J* = 6.6 Hz, 3H), 1.50 (broad s, 3H), 1.56 (broad d, *J* = 5.5 Hz, 3H), 2.04 (broad quint., *J* = 7.5 Hz, 2H), 2.30 (broad quint., *J* = 7.3 Hz, 1H), 3.22 (d, *J* = 9.0 Hz, 1H), 3.78 (s, 3H), 4.12 and 4.39 (AB system, *J* = 11.6 Hz, 1H each), 5.16 (ddq, *J* = 15.3 and 6.2 Hz, 1H), 5.28 (m, 1H), 5.36 (dq, *J* = 15.3 and 6.5 Hz, 1H), 6.82 (d, *J* = 8.5 Hz, 2H), 7.22 (d, *J* = 8.5 Hz, 2H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 10.9, 14.1, 17.5, 17.8, 20.7, 39.6, 55.2, 69.2, 89.2, 113.6, 123.5, 129.2, 131.2, 131.5, 132.7, 133.7, 158.6. – $[\alpha]_D^{20}$ = 48.6 (*c* = 1.60, $CHCl_3$). – $C_{19}H_{28}O_2$ (288.4): calcd. C 79.12, H 9.78; found C 79.27, H 9.95.

15. *(3E,5R,6S,7R*,8R*)-7,8-Dihydroxy-5-(4-methoxybenzyloxy)-4,6-dimethyl-3-nonene* (**28**): 4.50 g (15.6 mmol) of **27**, 6.40 g (32.8 mmol) of a 60% aqueous solution of *N*-methylmorpholine *N*-oxide, and 0.95 g of a 4% solution of OsO_4 in *tert*-butyl alcohol were allowed to react as described under 11. to give 3.77 g (75%) of the diols **28** as a diastereomeric mixture. – $C_{19}H_{30}O_4$ (322.4): calcd. C 70.77, H 9.38; found C 70.60, H 9.19.

Major diastereomer: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.87 (d, *J* = 6.8 Hz, 3H), 0.92 (t, *J* = 7.4 Hz, 3H), 1.06 (d, *J* = 6.3 Hz, 3H), 1.52 (broad s, 3H), 1.82 (m, 1H), 2.06 (m, 2H), 2.50 (broad s, 20H), 3.26 (broad d, *J* = 9.5 Hz, 1H), 3.62 (m, 1H), 3.76 (s, 3H), 3.91 (d, *J* = 3.1 Hz, 1H), 4.12 and 4.41 (AB system, *J* = 11.0 Hz, 1H each), 5.40 (broad q, *J* = 7.2 Hz, 1H), 6.80 (d, *J* = 8.5 Hz, 2H), 7.18 (d, *J* = 8.5 Hz, 2H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 7.9, 11.9, 14.1, 18.5, 20.8, 37.0, 55.2, 68.7, 69.9, 78.1, 87.6, 113.8, 129.5, 129.8, 130.4, 131.3, 159.6.

The following signals of the minor diastereomer could be recorded: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.89 (d, *J* = 6.8 Hz, 3H), 0.96 (t, *J* = 7.3 Hz, 3H), 1.11 (d, *J* = 6.3 Hz, 3H), 1.54 (broad s, 3H), 1.80 (m, 1H), 2.08 (m, 2H), 2.64 (broad s, 20H), 3.65 (m, 2H), 3.79 (s, 3H), 3.84 (m, 1H), 4.12 and 4.46 (AB system, *J* = 10.8 Hz, 1H each), 5.40 (broad q, *J* = 7.2 Hz, 1H), 6.84 (d, *J* = 8.5 Hz, 2H), 7.20 (d, *J* = 8.5 Hz, 2H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 7.9, 12.0, 13.6, 19.6, 20.8, 37.3, 55.2, 68.4, 70.1, 79.2, 84.2, 113.9, 129.5, 129.7, 130.6, 131.5, 159.5.

Flash chromatography also provided 0.44 g (8%) of a tetraol which was converted into a tetraacetate. – $C_{27}H_{40}O_{10}$ (524.6): calcd. C 61.81, H 7.68; found C 61.65, H 7.90.

16. *(2R,3R,3E)-3-(4-Methoxybenzyloxy)-2,4-dimethyl-4-heptenal* (**29**): 1.99 g (9.30 mmol) of $NaIO_4$ was added at 0°C with vigorous stirring to a solution of 1.00 g (3.10 mmol) of the diastereomeric diols **28** in 20 ml of water and 20 ml of THF. The resulting suspension was stirred for 2 h. Then 30 ml of ether was added, the phases were separated and the aqueous phase was extracted with 100 ml of ether. The combined organic phases were dried with $MgSO_4$ and concentrated to leave 0.79 g (92%) of the aldehyde **29** as a colorless liquid. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.01 (t, *J* = 7.6 Hz, 3H), 1.10 (d, *J* = 6.9 Hz, 3H), 1.61 (broad s, 3H), 2.12 (m, 2H), 2.62 (quint. d, *J* = 6.8 and 2.2 Hz, 1H), 3.82 (s, 3H), 3.85 (d, *J* = 7.5 Hz, 1H), 4.18 and 4.48 (AB system, *J* = 11.4 Hz, 1H each), 5.44 (m, 1H), 6.90 (d, *J* = 8.5 Hz, 2H), 7.24 (d, *J* = 8.5 Hz, 2H),

9.58 (d, J = 2.2 Hz, 1H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 10.1, 11.8, 14.4, 20.9, 49.6, 55.3, 69.5, 83.8, 113.8, 129.4, 130.5, 131.3, 132.3, 159.3, 203.8. – $C_{17}H_{24}O_3$ (276.3): calcd. C 73.88, H 8.75; found C 73.53, H 8.65.

17. *(3E,5R,6S,7R,8S,9E)-7-hydroxy-5-(4-methoxybenzyloxy)-4,6,8-trimethyl-3,9-undecadiene* (**30**): A solution of 0.55 g (2.0 mmol) of the aldehyde **29** and 0.91 g (3.0 mmol) of **3** in 6 ml of petroleum ether was pressurized for 3 d to 4 kbar. Then 0.44 g (3.0 mmol) of triethanolamine was added and the mixture was held under reflux for 1 h. Subsequently, 10 ml of a saturated aqueous NH_4Cl solution was added, the phases were separated, and the aqueous phase was extracted three times with 20 ml each of ether. The combined organic extracts were dried with $MgSO_4$ and concentrated. Flash chromatography of the residue with petroleum ether/ether/triethylamine (10:1:0.01) furnished 0.65 g (95%) of a diastereomeric mixture of alcohols. The diastereomer ratio was estimated from the ^{13}C-NMR spectrum to be 80:16:4. – $C_{22}H_{34}O_3$ (346.5): calcd. C 76.29, H 9.89; found C 76.59, H 9.78.

Major diastereomer: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.84 (t, J = 6.9 Hz, 3H), 0.88 (d, J = 6.9 Hz, 3H), 0.94 (d, J = 7.1 Hz, 3H), 1.46 (broad s, 3H), 1.54 (dd, J = 6.2 and 1.5 Hz, 3H), 1.65 (m, 1H), 2.06 (m, 3H), 3.18 (broad m, OH), 3.59 (d, J = 6.5 Hz, 1H), 3.74 (s, 3H), 3.86 (dd, J = 6.8 and 3.5 Hz, 1H), 4.12 and 4.38 (AB system, J = 11.4 Hz, 1H each), 5.08 (ddq, J = 15.1, 6.4, and 1.5 Hz, 1H), 5.40 (m, 2H), 6.80 (d, J = 8.7 Hz, 2H), 7.18 (d, J = 8.7 Hz, 2H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 7.0, 12.0, 14.1 (two signals), 17.9, 20.8, 27.3, 40.9, 55.1, 69.9, 77.5, 88.4, 113.7, 125.0, 129.3, 129.7, 130.5, 131.8, 133.6, 159.0.

18. *(2R,4R,5S,6R)-2-(4-Methoxyphenyl)-5-methyl-4-((1S,2E)-1-methyl-2-butenyl)-6-((1E)-1-methyl-1-butenyl)-1,3-dioxane* (**32**): A solution of 0.45 g (1.29 mmol) of **30** in 20 ml of CH_2Cl_2 was stirred for 30 min with 1 g molecular sieves (3 Å). The mixtures was cooled to 0°C and 0.31 g (1.36 mmol) of freshly crystallized 2,3-dichloro-4,5-dicyanobenzoquinone was added. After 12 h at 0°C 1 ml of triethylamine was added and the mixture was concentrated. Flash chromatography of the residue with petroleum ether/ether/triethylamine (10:1:0.01) furnished 0.29 g (66%) of **32** as a ca. 9:1 diastereomeric mixture (^{13}C NMR). – ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.83 (d, J = 6.8 Hz, 3H), 1.01 (t, J = 7.5 Hz, 3H), 1.12 (d, J = 6.5 Hz, 3H), 1.61 (broad s, 3H), 1.69 (dd, J = 6.4 and 1.5 Hz, 3H), 1.77 (m, 1H), 2.10 (m, 2H), 2.40 (m, 1H), 3.47 (dd, J = 10.0 and 1.95 Hz, 1H), 3.81 (s, 3H), 4.17 (broad s, 1H), 5.27 (ddq, J = 15.2, 8.7, and 1.6 Hz, 1H), 5.54 (s, 1H), 5.56 (m, 2H), 6.90 (d, J = 8.8 Hz, 2H), 7.48 (d, J = 8.8 Hz, 2H). – ^{13}C NMR (125 MHz, $CDCl_3$): δ = 5.6, 13.2, 14.2, 18.0, 18.1, 20.7, 32.2, 39.0, 55.2, 83.4, 84.9, 101.0, 113.4, 125.8, 127.4, 127.5, 131.3, 131.9, 132.0, 159.7. – $[\alpha]_D^{20}$ = 14 (c = 0.40, $CHCl_3$). – $C_{22}H_{32}O_3$ (344.5): calcd. C 76.70, H 9.36; found C 76.63, H 9.41.

19. *(2R,4S,5S,6R)-4-((1R)-1-Methoxycarbonylethyl)-2-(4-methoxyphenyl)-5-methyl-6-(1-oxoethyl)-1,3-dioxane* (**7**): Into a solution of 0.10 g (0.29 mmol) of **32** in 10 ml of CH_2Cl_2 was introduced at −78°C a stream of ozone in oxygen until the blue color persisted. Excess ozone was purged by a stream of nitrogen. Then 0.152 g (0.58 mmol) of triphenylphosphane was added and the mixture was allowed to reach 0°C. The mixture was concentrated in vacuo and the residue was taken up in 10 ml of acetone. At −10°C 8 M Jones reagent (prepared from 6.68 g of CrO_3, 20 ml of water and 5.6 ml of concentrated sulfuric acid) was added dropwise to the solution until the orange color persisted. Then 1 ml of 2-propanol and 10 ml of water were added. The phases were separated and the aqueous phase was extracted with 30 ml of ether. The combined organic phases were dried with $MgSO_4$ and concentrated to 20 ml. At 0°C an ethereal diazomethane solution was added until the yellow color persisted. Excess diazomethane was destroyed by addition of a few drops of acetic acid. 10 ml of water was added, the phases were separated and the aqueous phase was extracted three times with 30 ml each of ether. The combined organic phases were dried with $MgSO_4$ and concentrated. Flash chromatography of the residue with petroleum ether/ether (10:1) furnished 80 mg (82%) of **7** as a viscous oil. – ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.93 (d, J = 6.8 Hz, 3H), 1.29 (d, J = 6.8 Hz, 3H), 2.13 (ddq, J = 6.7, 2.6, and 2.1 Hz, 1H), 2.23 (s, 3H), 2.73 (dq, J = 10.2 and 6.8 Hz, 1H), 3.69 (s, 3H), 3.80 (s, 3H), 3.90 (dd, J = 10.2 and 1.9 Hz, 1H), 4.25 (d, J = 2.6 Hz, 1H), 5.52 (s, 1H), 6.90 (d, J = 8.7 Hz, 2H), 7.45 (d, J = 8.7 Hz, 2H). – ^{13}C NMR (125 MHz, $CDCl_3$): δ = 7.1, 14.9, 27.5, 32.5, 41.9, 51.9, 55.3, 81.7, 85.4, 101.3, 113.6, 127.4, 130.5, 160.1, 174.2, 208.9. – $[\alpha]_D^{20}$ = 58.6 (c = 0.35, $CHCl_3$). – $C_{18}H_{24}O_6$ (336.4): calcd. C 64.27, H 7.19; found C 64.23, H 7.24.

20. *(4S,5S)-4,5-Dicyclohexyl-2-((1S,2Z)-1-(1-methylethyl)-2-butenyl)-1,3,2-dioxaborolane* (**36**): 9.00 mmol (9.00 mmol) of a 1 M solution of isopropylmagnesium chloride in THF was added at −78°C dropwise to a solution of 2.87 g (9.00 mmol) of (4*S*,5*S*)-2-dichloromethyl-4,5-dicyclohexyl-1,3,2-dioxaborolane in 70 ml of THF. After stirring for 30 min, a solution of 1.04 g (7.7 mmol) of anhydrous $ZnCl_2$ in 10 ml of THF was added dropwise. Stirring was continued at −78°C for 1 h and room temperature for 3 h. The mixture was cooled to −78°C again and 11.4 ml (9.0 mmol) of a 0.79 M solution of (*Z*)-1-lithiopropene in ether was added dropwise. The mixture was allowed to reach room temperature during 12 h. Then 20 ml of saturated aqueous NH_4Cl solution was added, the phases were separated and the aqueous phase was extracted three times with 30 ml each of ether. The combined organic phases were dried with $MgSO_4$ and concentrated. The residue was filtered with ether over a 20 × 6 cm column of silica gel. The solvents were removed in vacuo to give 2.90 g (97%) of **36** as a colorless oil. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.81 (d, J = 6.5 Hz, 3H), 0.85 (d, J = 6.5 Hz, 3H), 0.75–1.16 (m, 14H), 1.52 (dd, J = 6.3 and 1.0 Hz, 3H), 1.28–1.80 (m, 10H), 1.91 (m, 1H), 3.81 (m, 2H), 5.35 (m, J = 11.0 and 6.4 Hz, 2H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.2, 21.9, 22.7, 25.9, 26.1, 26.6, 27.7, 28.6, 30.0, 43.2, 83.3, 123.3, 130.9. – $C_{21}H_{37}BO_2$ (332.3): calcd. C 75.89, H 11.22; found C 75.61, H 11.17.

21. *(3S,4S,5E)-3-Hydroxy-2,4,7-trimethyl-5-octene* (**37**): A solution of 1.33 g (4.0 mmol) of the boronate **36** and 0.29 g (4.0 mmol) of isobutyraldehyde in 10 ml of petroleum ether was allowed to react for 3 d. Then 0.59 g (4.0 mmol) of triethanolamine were added, the mixture was stirred for 30 min, 20 ml of water and 20 ml of ether were added. The phases were separated and the aqueous phase was extracted three times with 30 ml each of ether. The combined organic extracts were dried with $MgSO_4$ and concentrated. Flash chromatography of the residue with petroleum ether/ether (10:1) furnished 0.53 g (77%) of **37** as a colorless oil. The enantiomeric purity was determined by derivatization[25] with (*S*)-1-phenylethyl isocyanate to be >99%. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.82 (d, J = 6.9 Hz, 3H), 0.84 (d, J = 6.8 Hz, 3H), 0.88 (d, J = 6.7 Hz, 3H), 0.91 (d, J = 6.8 Hz, 3H), 0.92 (d, J = 6.9 Hz, 3H), 1.38 (broad s, 1H), 1.66 (m, 2H), 2.19 (m, 1H), 3.04 (broad t, J = 5.8 Hz, 1H), 5.20 (dd, J = 15.5 and 7.3 Hz, 1H), 5.38 (dd, J = 15.5 and 6.3 Hz, 1H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.3, 16.9, 19.6, 22.5, 22.5, 30.3, 31.0, 39.4, 79.8, 130.0, 137.8. – $[\alpha]_D^{20}$ = −48.3 (c = 1.5, $CHCl_3$). – $C_{11}H_{22}O$ (170.3): calcd. C 77.58, H 13.02; found C 77.62, H 13.00.

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