Enantio- and Diastereoselective Protonation of Photodienols: Total Synthesis of (*R*)-(−)-Lavandulol

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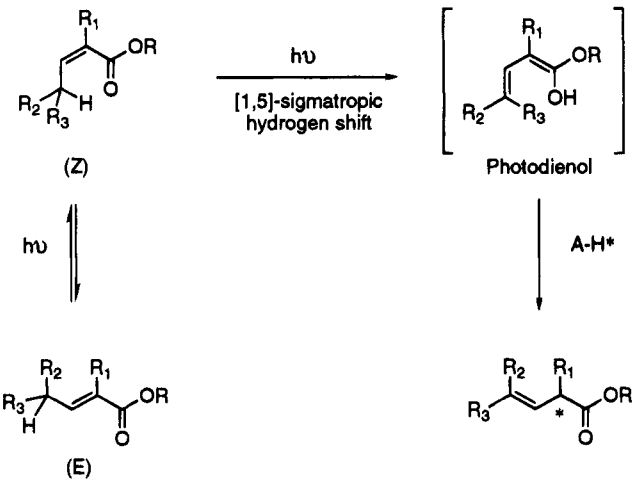
The total synthesis of (*R*)-(−)-lavandulol **1** has been achieved by asymmetric protonation of photodienols obtained from the irradiation of prochiral α,β-unsaturated esters. The photodeconjugation of ethyl 5-methyl-2-(1′-methylethylidene)-4-hexenoate (**3a**), carried out in the presence of catalytic amounts of a β-amino alcohol prepared from (+)-camphor, gives the β,γ-unsaturated isomer **2a** in good yields but with moderate enantioselectivities (40% ee). In contrast, irradiation of the corresponding ester **3b**, bearing the 1,2:5,6-di-*O*-isopropylidene-D-glucose group as a chiral alkoxy moiety, affords the deconjugated product **2b** in high de (>95%). Simple reduction of the ester function with $LiAlH_4$ gives (*R*)-(−)-lavandulol (**1**) without loss of optical purity.

Introduction

The asymmetric protonation of prochiral enols or enolates can be considered as one of the most efficient methods to create a chiral center in the α-position of an enolizable functionality, especially a carbonyl or a carboxylic group. During the past years, numerous efforts have been devoted to this field and high selectivities superior to 90% have been recently reported by chemical reactions[1-3] using enzymes[4] or antibodies.[5] By these means, asymmetric protonation appears to be an alternative route to the well established methods for the creation of chiral centers (e.g. asymmetric alkylations).

Scheme 1



The photodeconjugation of α,β-unsaturated esters and lactones is a convenient process to prepare the corresponding β,γ-unsaturated isomers, and the formation of a photodienol has been unambiguously demonstrated[6] (Scheme 1).

This intermediate constitutes a prochiral entity (when $R^1 \neq H$) and we have already shown that under appropriate conditions asymmetric protonation on one of the two stereotopic faces can be performed. Two alternative procedures have been thus considered. First, the enantioselective protonation of the photodienol has been carried out and high excesses (up to 91%) have been reached with catalytic amounts of *endo,endo*-aminobor-

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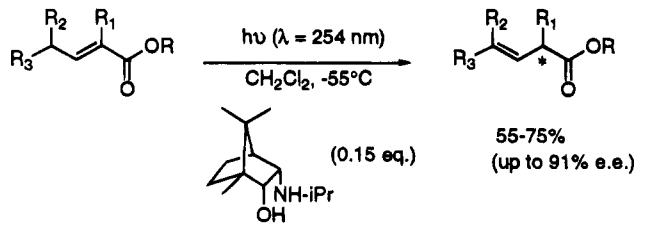
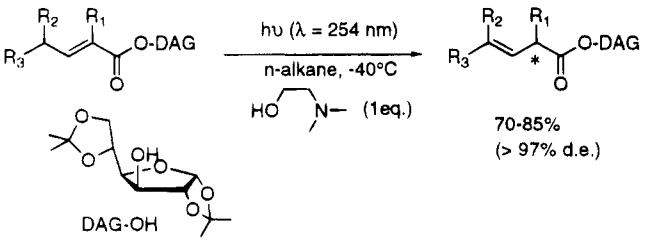
Scheme 2



Scheme 3

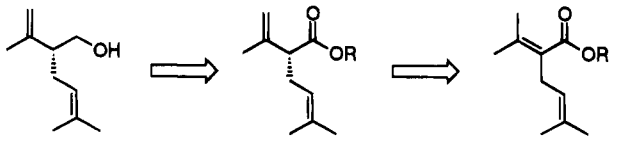


nanols,[7] readily prepared from (+)-camphor[8] (Scheme 2). A similar level of induction has been recently observed in this laboratory, with the same β-amino alcohols during the protonation of simple enols, obtained via a Norrish type II process.[9]

Diastereoselective photodeconjugation has been also studied. In this case, the chiral induction is produced owing to the presence of an optically active alkoxy group fixed on the ester moiety. High diastereoselectivities of up to 88% were initially obtained with Oppolzer's alcohols[10] or with 8-phenylmenthol derivatives[11] but required the use of stoichiometric amounts of these expensive compounds.[12] We have reinvestigated this reaction using the cheap and commercially available 1,2:5,6-di-*O*-isopropylidene-D-glucose, a reagent which has been used successfully in the creation of chiral centers in numerous applications.[13,14] The diastereoselectivities observed for the deconjugation process have reached up to 96%[15] (Scheme 3). Furthermore, these values were not dependent on the nature of the acid chain, and the reaction appears sufficiently efficient to be applied to the synthesis of natural products.

Our choice fell on lavandulol (**1**), a constituent of lavender oil,[16] which possesses an unusual monoterpene skeleton. This compound is an important additive in the perfume industry and has been also isolated as a defensive pheromone of the red-lined carrion beetle.[17] Due to its importance, many efforts have been devoted to its synthesis in racemic[18] and optically active form,[19] but previously reported syntheses have involved numerous steps[19a] or an expensive chiral reagent.[19c] The strategy of our synthesis based on the photodeconjugation of the α,β-unsaturated esters **3a** (R = ethyl) and **3b** (R = DAG) is depicted on Scheme 4. The crucial photochemical step allows both the formation of the double bond in the required position and also the creation of the chiral center.

Scheme 4



Results and Discussion

Preparation of the α,β-Unsaturated Esters. Ethyl ester **3a** has been prepared according to the procedure already described by Wolf and Pfander, from ethyl acetoacetate.[20] Transesterification of the ester **3a** into **3b** was tried under various conditions but led to disappointing results. For example, heating of **3a** in the presence of 1,2:5,6-di-*O*-isopropylidene-D-glucose and DMAP[21] or titanium tetraisopropylate[22] gives in both cases, a mixture of the two esters, difficult to separate on a preparative scale. We hoped to achieve the cleavage of the ester into the corresponding conjugate acid, which could be esterified using DCC activation as already published for the synthesis of other unsaturated DAG esters.[15] Unfortunately, alkaline hydrolysis[23] of **3a** leads directly to the racemic β,γ-unsaturated acid **4**. To avoid basic conditions, starting ester **3a** was then submitted

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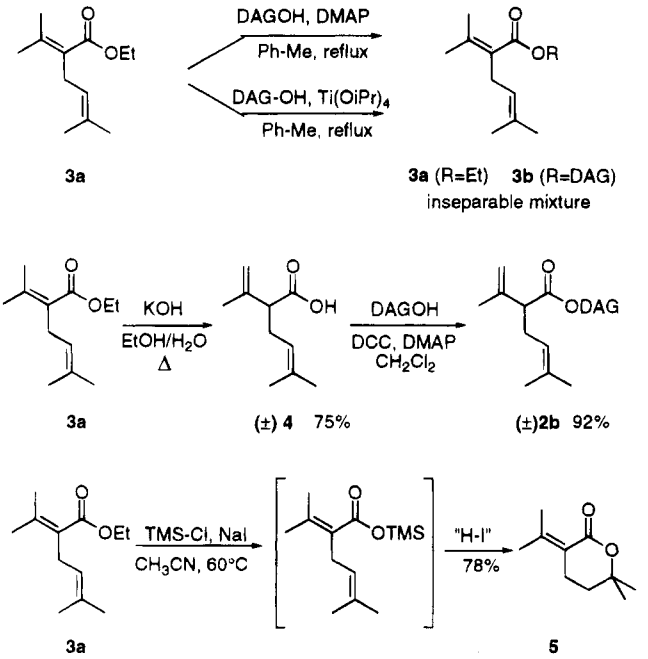
Scheme 5

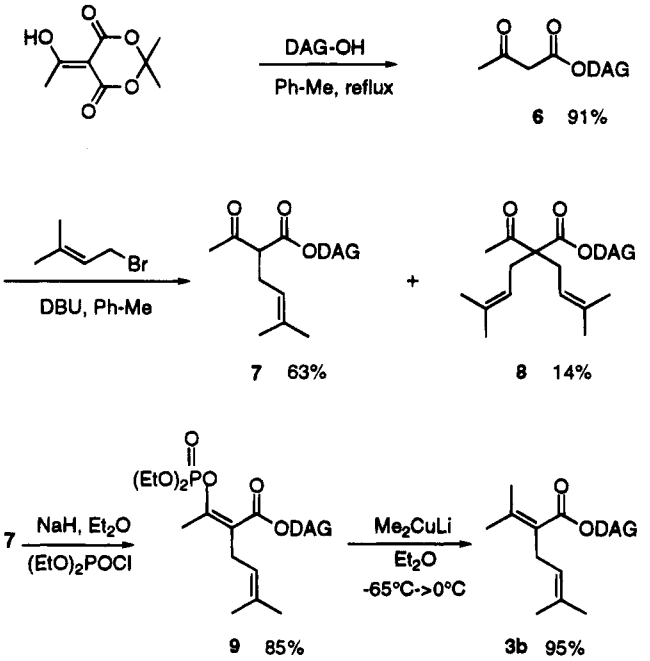


to the action of TMS-I, which is well known to allow easy deprotection of the ester function.[24,25] Under these conditions, the expected cleavage occurs but is followed by a lactonization process leading to the formation of the alkylidene lactone **5** in 78% yield. This new cyclization procedure is probably induced by traces of hydriodic acid generated from TMS-I itself[26] (Scheme 5) and has been generalized to other substrates.[27]

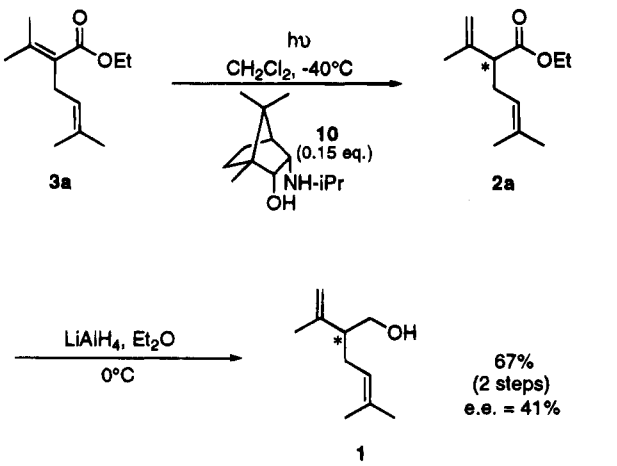
Finally, compound **3b** has been prepared from DAG acetylacetate **6**, according a multistep procedure, following the same strategy as the approach for **3a**. Acetyl Meldrum's acid[28] is converted into **6** by heating at reflux in toluene with 1,2:5,6-di-*O*-isopropylidene-D-glucose. Selective C-alkylation is performed by mixing **6**, 3,3-dimethylallylic bromide, and DBU at room temperature in toluene.[29] Compound **7**, readily separated by flash-chromatography[30] from the minor dialkylated product **8**, is transformed into phosphate enol ester **9**, which is directly treated with dimethylcuprate in ether, leading finally to the expected ester **3b** (Scheme 6).

Enantio- and Diastereoselective Photodeconjugation of the Unsaturated Esters. Ester **3a** was first submitted to the enantioselective irradiation conditions, at 254 nm, in methylene chloride, at low temperature (−40 °C) and in the presence of catalytic amounts of *endo,endo*-3-(isopropylamino)-2-hydroxybornane (**10**), prepared by reductive alkylation[31] of the free amino alcohol.[8] The reaction is followed by TLC and NMR control. As expected, the photodeconjugation occurs and gives in a few hours, the β,γ-unsaturated ester **2a**. After concentration and removal of the inductor by simple filtration

Scheme 6



Scheme 7



on silica gel, **2a** was reduced by action of lithium aluminum hydride in ether. The compound thus obtained in good yields has been fully characterized as lavandulol (**1**) (Scheme 7). The optical rotation has been measured and the enantioselectivity has been determined by GC using a chiral stationary phase. The relatively low value (ee = 41%) shows the considerable importance of the nature of the substituent in the α-position on the acid chain on the induction of chirality as already reported.[7]

To obtain lavandulol in higher ee, we turned to the diastereoselective process using ester **3b** (R = DAG) as starting material. Its irradiation in pentane at 254 nm, in the presence of an achiral β-amino alcohol, such as (*N,N*-dimethylamino)ethanol, gives efficiently the β,γ-unsaturated ester **2b** (Scheme 8). The diastereoselectivities were measured by NMR on the crude mixture. The spectrum was compared to that of the mixture of the two epimers (2*R*)-**2b** and (2*S*)-**2b** prepared by esterification of the racemic unsaturated acid **4** and the de was estimated to be greater than 96% (limits of detection). After purification by flash-chromatography, the chiral ester **2b** was reduced quantitatively into lavandulol. The enantiomeric purity was measured by GC and reached up to 95% and shows thus that no epimerization occurred

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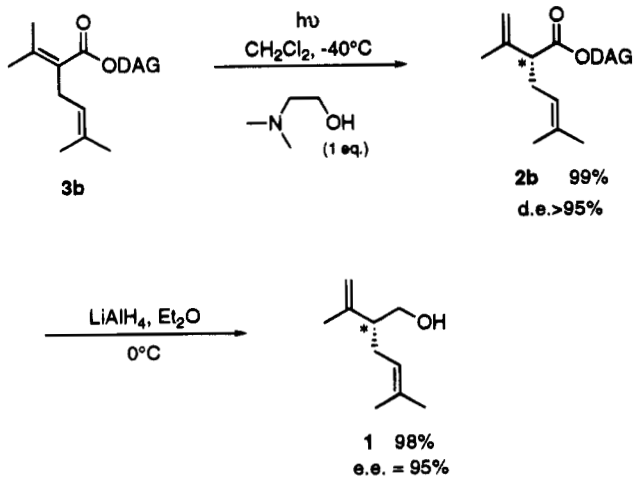
Scheme 8



during the reduction step. The absolute configuration of the product was established as (*R*) by comparison with the optical rotation of the natural product.[16,19]

Conclusions

We have developed a novel procedure to synthesize in good yields and high ee the natural enantiomer of lavandulol. This sequence represents the first application of asymmetric photodeconjugation to the synthesis of a natural product. Work is now in progress to apply this reaction to the synthesis of other molecules which possess a chiral center in an allylic position, especially in the field of pheromones.

Experimental Section

General. Solvents were distilled before use, under an argon atmosphere: THF, toluene, and diethyl ether over sodium/benzophenone; methylene chloride, pentane, and acetonitrile over calcium hydride. ^1H and ^{13}C NMR spectra were obtained at 250 and 75 MHz, respectively, with tetramethylsilane as internal standard. Chemical shifts are reported in parts per million. Measure of the enantioselectivities by GC were obtained using a capillary Chrompack WCOT-silica CP-cyclodextrin B-236-M-19. Elemental analyses were performed on a CHN 2400 Perkin-Elmer apparatus or obtained from the Service Central d'Analyse, CNRS, Vernaison, France.

Preparation of α,β-Unsaturated Esters 3a and 3b. Ethyl 5-Methyl-2-(1′-methylethylidene)-4-hexenoate (3a). Prepared from ethyl acetoacetate[20] 62% (three steps). ^1H NMR: 1.28 (t, 7.0 Hz, 3H); 1.65 (s, 3H); 1.67 (d, 1.1 Hz, 3H); 3.00 (d, 7.0 Hz, 2H); 4.17 (q, 7.0 Hz, 2H); 5.04 (tq, 7.0 Hz, 1.4 Hz, 1H). ^{13}C NMR: 14.27; 17.72; 21.74; 22.88; 25.66; 28.90; 59.97; 121.67; 127.22; 131.97; 141.51; 169.59. IR υ_{max} cm^{-1} (neat): 2980, 1680. MS (*m*/*z*): 196 ($M^{\bullet+}$, 35); 107 (100); 95 (35). UV (EtOH): ϵ_{212}: 8600.

2-Isopropenyl-5-methyl-5-hexenoic Acid (4). Ester **3a** (2.00 g, 10.2 mmol) diluted in ethanol (5 mL) is added to a solution of potassium hydroxide (0.860 g, 15.30 mmol) in ethanol (100 mL) and water (2 mL). The mixture is heated for 6 h at reflux, cooled to rt, concentrated under vacuum, and acidified with 2 N sulfuric acid. After extraction with hexanes, the organic phase is dried over $MgSO_4$, filtered, and concentrated. A rapid chromatography over silica gives compound **4** (1.28 g, 7.65 mmol), 75%. ^1H NMR: 1.62 (s, 3H); 1.68 (s, 3H); 1.77 (s, 3H); 2.28 (ddd, 7.1 Hz, 7.6 Hz, 14.6 Hz, 1H); 2.31 (dt, 14.6 Hz, 7.1 Hz, 1H); 3.02 (t, 7.6 Hz, 1H); 4.92 (s, 2H); 5.05 (tq, 7.1 Hz, 1.3 Hz, 1H). ^{13}C NMR: 17.81; 20.42; 25.72; 28.81; 53.08; 114.26; 120.85; 133.80; 141.91; 179.45). IR υ_{max} cm^{-1} (neat): 3600–3000; 2970; 1705; 1655. MS (*m*/*z*): 168 ($M^{\bullet+}$, 9); 125 (26); 107 (41); 91 (36). Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.58. Found: C, 71.34; H, 9.95.

2-(1′-Methylethylidene)-5,5-dimethylhexanolide (5). Trimethylsilyl chloride (6 mmol) is added under argon to a suspension of anhydrous sodium iodide (6 mmol) in freshly distilled acetonitrile (10 mL). After stirring for 10 min at room temperature, ethyl ester **3a** (0.980 g, 5 mmol) in acetonitrile (2 mL) is added and the resulting mixture is heated at 60 °C overnight. After cooling, the solution is hydrolyzed with brine, extracted with CH_2Cl_2, and washed with an aqueous thiosulfate solution. After drying with $MgSO_4$, the crude mixture is purified by flash-chromatography[30] giving **5** (0.655 g, 3.90 mmol), 78%. ^1H NMR: 1.35 (s, 6H); 1.83 (t, 7.1 Hz, 2H); 1.86 (s, 3H); 2.23 (t, 1.9 Hz, 3H); 2.50 (tq, 7.0 Hz, 1.9 Hz, 2H). ^{13}C NMR: 22.26; 23.80; 27.32; 33.42; 79.31; 118.98; 151.69; 166.31. IR υ_{max} cm^{-1} (neat): 1710; 1615; 1365; 1210; 1165; 1110. MS (*m*/*z*): 168 ($M^{\bullet+}$, 63); 153 (34); 125 (38); 111 (79); 94 (55). Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.58. Found: C, 71.34; H, 9.29.

(1,2:5,6-Di-*O*-isopropylidene-α-D-glucofuranos-3-*O*-yl)-3-oxobutanoate (6). A solution of acetyl Meldrum's acid (9.30 g, 50 mmol) and 1,2:5,6-di-*O*-isopropylidene-D-glucose (12.48 g, 48 mmol) in toluene is heated 6 h at reflux. After complete disappearance of the alcohol (TLC control), the solvent is removed by evaporation, and the compound **6** (15.02 g, 43.7 mmol) is purified by flash-chromatography (eluent AcOEt/hexanes: 30/70), 91%. ^1H NMR: 1.30 (s, 6H); 1.40 (s, 3H); 1.51 (s, 3H); 2.26 (s, 3H); 3.49 (d, 1.5 Hz, 2H); 3.96–4.14 (m, 2H); 4.18 (t, 3.3 Hz, 2H); 4.56 (d, 3.7 Hz, 1H); 5.31 (sl, 1H); 5.86 (d, 3.7 Hz, 1H). ^{13}C NMR: 25.22; 26.22; 26.73; 26.87; 30.08; 49.95; 67.41; 72.32; 76.94; 79.95; 83.22; 105.13; 109.46; 112.36; 165.75; 199.76. IR υ_{max} cm^{-1} (neat): 1755; 1720; 1645; 1265; 1165. MS (*m*/*z*): 345 ($M^{\bullet+}$ + 1, <5); 329 (35); 175 (15); 101 (10); 85 (63). $[\alpha]_D$ = −29.1 (*c* 1.2, MeOH). Anal. Calcd for $C_{16}H_{24}O_8$: C, 55.80; H, 7.02. Found: C, 55.45; H, 7.25.

Alkylation of Oxo Ester 6. DBU (3.05 mL, 20.35 mmol) and 1-bromo-3-methyl-3-butene (2.37 mL, 20.35 mmol) are successively added to a solution of ester **6** (6.35 g, 18.45 mmol) in toluene. The mixture is stirred for 72 h at rt. After concentration, the crude product is purified by flash-chromatography (AcOEt/hexanes: 20/80) giving the monoalkylated compound **7** (4.78 g, 11.62 mmol) and the dialkylated product **8** (1.24 g, 2.57 mmol).

(1,2:5,6-Di-*O*-isopropylidene-α-D-glucofuranos-3-*O*-yl)-2-acetyl-5-methyl-4-hexenoate (7), 63%. ^1H NMR (mixture of two diastereoisomers): 1.30 (s, 12H); 1.40 (s, 6H); 1.52 (s, 6H); 1.63 (s, 6H); 1.69 (s, 6H); 2.22 (s, 3H); 2.24 (s, 3H); 2.56 (t, 7.3 Hz, 4H); 3.42 (t, 7.5 Hz, 1H); 3.48 (t, 7.4 Hz, 1H); 3.96–4.17 (m, 8H); 4.42 (d, 2.0 Hz, 1H); 4.44 (d, 2.0 Hz, 1H); 5.02 (tq, 7.3 Hz, 1.3 Hz, 2H); 5.29 (d, 2.3 Hz, 1H); 5.31 (d, 2.2 Hz, 1H); 5.82 (d, 3.7 Hz, 1H); 5.86 (d, 3.7 Hz, 1H). ^{13}C NMR (mixture of two diastereoisomers): 17.68; 25.01; 5.09; 25.58; 26.07; 26.63; 26.71; 26.92; 28.48; 29.04; 59.48; 59.72; 67.32; 67.54; 72.18; 72.24; 76.68; 76.74; 79.76; 79.99; 83.03; 83.23; 105.40; 109.33; 112.27; 119.43; 134.91; 168.13; 168.30; 201.87; 202.23. IR υ_{max} cm^{-1} (neat): 1755; 1720; 1455; 1380; 1250; 1220; 1165. MS (*m*/*z*): 412 ($M^{\bullet+}$, 5); 411 (13); 378 (28); 352 (54); 176 (46); 150 (96); 101 (100). $[\alpha]_D$ = −27.8 (*c* 1.1, MeOH). Anal. Calcd for $C_{21}H_{32}O_8$: C, 61.15; H, 7.82. Found: C, 60.81; H, 7.69.

(1,2:5,6-Di-*O*-isopropylidene-α-D-glucofuranos-3-*O*-yl)-2-acetyl-2-(3′-methylbutenyl)-5-methyl-4-hexenoate (8), 14%. ^1H NMR: 1.20 (s, 3H); 1.23 (s, 3H); 1.32 (s, 3H); 1.44 (s, 3H); 1.52 (s, 6H); 1.61 (s, 6H); 2.07 (s, 3H); 2.47 (d, 7.1 Hz, 2H); 2.53 (d, 7.2 Hz, 2H); 3.88–4.06 (m, 4H); 4.3 (d, 3.6 Hz, 1H); 4.80 (t, 7.2 Hz, 1H); 4.83 (t, 7.2 Hz, 1H); 5.18 (d, 2.7 Hz, 1H); 5.70 (d, 3.6 Hz, 1H). ^{13}C NMR: 17.90; 25.00; 25.89; 26.09; 26.67; 26.79; 30.00; 30.37; 63.42; 67.66; 72.08; 76.87; 80.04; 83.01; 105.08; 109.40; 112.32; 117.45; 117.82; 135.25; 135.55; 171.00; 204.27. IR υ_{max} cm^{-1} (neat): 1745; 1720; 1620; 1455; 1380. MS (*m*/*z*): 481 ($M^{\bullet+}$ + 1, 7); 465 (62); 379 (54); 353 (72); 295 (34); 193 (35); 177 (59); 153 (55); 151 (89); 101 (100); 81 (49). $[\alpha]_D$ = −31.8 (*c* 1.1, MeOH). Anal. Calcd for $C_{26}H_{40}O_8$: C, 64.97; H, 8.38. Found: C, 64.59; H, 8.50.

(1,2:5,6-Di-*O*-isopropylidene-α-D-glucofuranos-3-*O*-yl)-2-[1′-(diethoxyphosphoryloxy)ethylidene]-5-methyl-4-hexenoate (9). Compound **7** (3.59 g, 8.71 mmol) in ether (25 mL) is added at 0 °C to a suspension of NaH (0.420 g, 10.45 mmol) in the same solvent (75 mL). After 1 h, diethyl phosphorochloridate (1.51 mL, 10.45 mmol) is added. The reaction mixture is stirred at rt overnight. Hydrolysis is then performed with an aqueous saturated solution of ammonium

chloride. After separation of the organic layer, the aqueous phase is extracted three times with ether. Finally, the organic phases are washed successively with a saturated solution of $NaHCO_3$ and brine and dried over $MgSO_4$. The crude product is purified by flash-chromatography (AcOEt/hexanes 30/70), and **9** (4.86 g, 8.89 mmol) is isolated, 85%. ^{1}H NMR: 1.30 (s, 6H); 1.32−1.38 (m, 6H); 1.40 (s, 3H); 1.52 (s, 3H); 1.64 (s, 3H); 1.68 (s, 3H); 2.13 (d, 1.9 Hz, 3H); 2.94 (m, 2H); 4.01−4.16 (m, 2H); 4.18−4.27 (m, 6H); 4.60 (d, 3.7 Hz,1H); 5.04 (t, 6.6 Hz, 1H); 5.29 (d, 2.5 Hz,1H); 5.88 (d, 3.7 Hz, 1H). ^{13}C NMR: 15.90; 16.01; 17.75; 25.16; 25.47; 26.12; 26.69; 27.64; 64.39; 64.48; 67.01; 72.38; 76.14; 79.79; 83.10; 105.08; 109.06; 111.95; 117.83; 117.95; 120.27; 133.28; 150.05; 150.18; 164.04. IR υ_{max} cm^{-1} (neat): 1770; 1730; 1450; 1375; 1260; 1220. MS (*m*/*z*): 548 (M$^{\bullet+}$, <5); 307 (95); 289 (27); 245 (20); 155 (100); 127 (60); 101 (78).

(1,2:5,6-Di-*O*-isopropylidene-α-D-glucofuranos-3-*O*-yl)-2-(1′-methylethylidene)-5-methyl-4-hexenoate (3b). Methyllithium (5.8 mL, 8.97 mol) in ether is added dropwise at 0 °C to a supension of CuI (0.856 g, 4.49 mmol) in dried ether (50 mL). The milky solution is cooled to −65 °C, and compound **9** (2.20 g, 4.01 mmol) in ether (10 mL) is slowly added. The solution is stirred for 2 h at this temperature and subsequently quenched with an aqueous saturated solution of ammonium chloride. After extraction three times with ether, the combined organic layers are dried over $MgSO_4$ and concentrated under vacuum. The product **3b** (1.56 g, 3.80 mmol) is obtained pure after flash-chromatography (AcOEt/hexanes: 10/90), 95%. ^{1}H NMR: 1.30 (s, 3H); 1.1 (s, 3H); 1.41 (s, 3H); 1.52 (s, 3H); 1.64 (s, 3H); 1.68 (s, 3H); 1.82 (s, 3H); 2.00 (s, 3H); 2.98 (d, 6.6 Hz, 2H); 4.01−4.12 (m, 2H); 4.22 (t, 2.4 Hz, 2H); 4.48 (d, 3.7 Hz, 1H); 5.02 (tq, 6.7 Hz, 1.5 Hz, 1H); 5.29 (d, 2.4 Hz, 1H); 5.83 (d, 3.7 Hz, 1H). ^{13}C NMR: 17.77; 22.06; 23.09; 25.19; 25.60; 26.16; 26.74; 28.75; 67.38; 72.39; 75.87; 80.10; 83.45; 105.04; 109.24; 112.17; 121.73; 126.26; 132.08; 144.27; 167.83. IR υ_{max} cm^{-1} (neat): 1720; 1630; 1455; 1365; 1215. MS (*m*/*z*): 411 (M$^{\bullet+}$ + 1, 13); 378 (28); 352 (54); 176 (46); 152 (48); 150 (96); 101 (100). UV (EtOH): ϵ_{215}: 9200. $[\alpha]_D = -31.9$ (*c* 1.0, MeOH). Anal. Calcd for $C_{22}H_{34}O_7$: C, 64.37; H, 8.35. Found: C, 64.15; H, 8.51.

Enantioselective Synthesis of Lavandulol from Ester 3a. A solution of ester **3a** (0.315 g, 1.60 mmol) and amino alcohol **10** (0.050 g, 0.24 mmol) in methylene chloride (180 mL) in quartz tubes is bubbled with argon. The tubes are placed around a quartz Dewar containing an Osram 254 lamp. The system is cooled to −40 °C with an external cooling cryostat, and the irradiation is performed for 8 h. After complete transformation of the starting material (NMR control), the solvent is removed. The crude compound dissolved in THF (15 mL) is directly treated by a slight excess of lithium aluminum hydride (0.073 g, 1.92 mmol) at 0 °C. After stirring for 2 h, the mixture is hydrolyzed with brine, extracted four times with ether, and after drying and concentration, lavandulol **1** (0.165 g, 1.07 mmol) is purified by preparative thin-layer chromatography, 67% (two steps). ^{1}H NMR: 1.20 (br, 1H); 1.61 (s, 3H); 1.70 (s, 6H); 1.90−2.15 (m, 2H); 2.28 (quint, 5.6 Hz, 1H); 3.45−3.60 (m, 2H); 4.81 (s, 1H); 4.92 (s, 1H); 5.08 (tq, 7.0 Hz, 1.3 Hz, 1H). ^{13}C NMR: 17.78; 19.52; 5.69; 28.39; 49.96; 63.67; 113.02; 122.04; 132.71; 145.44. IR υ_{max} cm^{-1} (neat): 3380; 3380; 3080; 1650; 1445; 1375; 1050. $[\alpha]_D = -3.8$ (*c* 1.0, MeOH), (ee = 41%, measured by GC).

Diastereoselective Synthesis of Lavandulol: (1,2:5,6-Di-*O*-isopropylidene-α-D-glucofuranos-3-*O*-yl)-2-isopropenyl-5-methyl-4-hexenoate (2b). Photodeconjugation of Ester 3b. A solution of ester **3b** (0.550 g, 1.34 mmol) and (*N*,*N*-dimethylamino)ethanol (0.120 g, 1.34 mmol) in *n*-pentane (135 mL) in quartz tubes is bubbled with argon. The tubes are arranged as described above. The system is cooled to −40 °C, and the irradiation is performed for 6 h. After complete transformation of the starting material, the solvent is removed. Flash-chromatography (AcOEt/hexanes: 10/90) gives the pure chiral deconjugated ester (2*R*)-**2b** (0.545 g, 1.33 mmol), 99%. ^{1}H NMR: 1.28 (s, 3H); 1.30 (s, 3H); 1.39 (s, 3H); 1.51 (s, 3H); 1.62 (s, 3H); 1.68 (s, 3H); 1.74 (d, 0.6 Hz, 3H); 2.28 (ddd, 7.0 Hz, 7.6 Hz, 14.6 Hz, 1H); 2.52 (ddd, 7.0 Hz, 7.6 Hz, 14.6 Hz, 1H); 3.04 (t, 7.6 Hz, 1H); 3.92−3.98 (m, 1H); 4.05−4.13 (m, 2H); 4.17 (t, 3.7 Hz,1H); 4.40 (d, 3.7 Hz, 1H); 4.90 (d, 1.0 Hz, 2H); 5.04 (tq, 7.0 Hz, 1.3 Hz, 1H); 5.29 (sl, 1H); 5.85 (d, 3.6 Hz, 1H). ^{13}C NMR: 17.81; 20.24; 25.09; 25.71; 26.19; 26.70; 28.88; 30.61; 53.30; 67.45; 72.18; 75.90; 80.32; 83.41; 105.12; 109.26; 112.30; 114.06; 120.90; 133.72; 141.88; 172.00. IR υ_{max} cm^{-1} (neat): 1745; 1655; 1455; 1380; 1215. MS (*m*/*z*): 410 (M$^{\bullet+}$, <5); 390 (19); 352 (21); 284 (14); 123 (76); 122 (47); 107 (28); 101 (100);. $[\alpha]_D = -47.7$ (*c* 1.0, CH_2Cl_2), (de > 97% by ^{1}H-NMR). Anal. Calcd for $C_{22}H_{34}O_7$: C, 64.37; H, 8.35. Found: C, 64.74; H, 8.55.

Esterification of Acid 4. DMAP (0.110 g, 0.9 mmol) and DAG-OH (0.832 g, 3.2 mmol) in methylene chloride (2 mL) are added successively to a solution of the racemic acid **4** (0.510 g, 3.0 mmol) in the same solvent (10 mL) containing 4 Å molecular sieves, under argon. After cooling to 0 °C, dicyclohexylcarbodiimide (0.66 g, 3.2 mmol) dissolved in the same solvent (2 mL) is added. The reaction mixture is stirred overnight, filtered, and concentrated in vacuum. A 50/50 mixture of the two esters (2*R*)-**2b** and (2*S*)-**2b** (1.14 g, 2.78 mmol) is isolated after flash-chromatography on silica (AcOEt/hexanes: 8/92), 92%. ^{1}H NMR: 1.28 (s, 6H); 1.30 (s,6H); 1.39 (s, 3H); 1.40 (s, 3H); 1.50 (s, 3H); 1.51 (s, 3H); 1.62 (s, 6H); 1.68 (s, 6H); 1.74 (sl, 3H); 1.77 (sl, 3H); 2.28 (ddd, 7.0 Hz, 7.6 Hz, 14.6 Hz, 2H); 2.52 (ddd, 7.0 Hz, 7.6 Hz, 14.6 Hz, 2H); 3.04 (t, 7.6 Hz, 2H); 3.90−4.20 (m, 8H); 4.38 (d, 3.6 Hz, 1H); 4.40 (d, 3.6 Hz, 1H); 4.90 (sl, 4H); 5.04 (t, 7.0 Hz, 2H); 5.26 (sl, 1H); 5.29 (sl, 1H); 5.83 (d, 3.6 Hz, 1H); 5.85 (d, 3.6 Hz,1H). ^{13}C NMR: 17.81 (2*R* and 2*S*); 20.25 (2*R*); 20.67 (2*S*); 24.75 (2*S*); 25.11 (2*R*); 25.25 (2*S*); 25.72 (2*R*); 26.22 (2*R* and 2*S*); 26.76 (2*R* and 2*S*); 28.91 (2*R* and 2*S*); 30.90 (2*R*); 32.82 (2*S*); 53.31 (2*R* and 2*S*); 67.25 (2*S*); 67.45 (2*R*); 72.18 (2*R*); 72.50 (2*S*); 75.90 (2*R*); 75.99 (2*S*); 79.97 (2*S*); 80.35 (2*R*); 83.24 (2*S*); 83.41 (2*R*); 105.12 (2*R* and 2*S*); 109.26 (2*R* and 2*S*); 112.30 (2*R*); 113.81 (2*S*); 114.06 (2*R* and 2*S*); 120.90 (2*R* and 2*S*); 133.75 (2*R* and 2*S*); 141.86 (2*R* and 2*S*); 172.00 (2*R* and 2*S*). IR υ_{max} cm^{-1} (neat): 1745; 1655; 1455; 1380; 1215. Anal. Calcd for $C_{22}H_{34}O_7$: C, 64.37; H, 8.35. Found: C, 64.98; H, 8.61.

(*R*)-Lavandulol (1). Ester **2b** (0.521 g, 1.27 mmol) in THF (5 mL) is added to a suspension of $LiAlH_4$ (0.072 g, 1.9 mmol) in THF (20 mL) at 0 °C. The resulting mixture is stirred for 4 h at rt and carefully hydrolyzed with brine. After extraction four times with ether, the organic phases are dried over $MgSO_4$ and the solvent is removed by distillation at atmospheric pressure. Preparative thin layer chromatography on silica allows the purification of (*R*)-lavandulol (**1**) (0.193 g, 1.25 mmol), 98%. Data is identical to that given above: $[\alpha]_D = -10.05$ (*c* 1.1, MeOH). Literature[19] (*S*): $[\alpha]_D = +10.8$ (*c* 0.94, MeOH), ee = 95% (determined by GC).

***endo,endo*-3-(Isopropylamino)-2-hydroxybornane (10).** *endo,endo*-3-Amino-2-hydroxybornane (1.69 g, 10 mmol) in absolute ethanol (10 mL) was stirred with acetone (1.1 mL, 15 mmol) at room temperature. After 30 min, the solution was cooled to 0 °C and sodium borohydride was added (0.69 g, 18 mmol). The solution was stirred for 1 h and quenched with water (0.5 mL). After addition of methylene chloride, the solution was filtered. After concentration under reduced pressure, the crude product was recrystallized from hexane to give **10** (1.94 g, 9.20 mmol), 92%. ^{1}H NMR: 0.86 (s, 3H); 0.89 (s, 3H); 0.92 (s, 3H); 1.02 (d, 6.4 Hz, 3H); 1.07 (d, 6.3 Hz, 3H); 1.15−1.30 (br, 2H); 1.39−1.46 (m, 1H); 1.72 (t, Hz, 1H); 1.73−1.82 (ma, 1H); 2.75 (sept, 6.4 Hz,1H); 3.13 (ddd, 1.3 Hz, 4.5 Hz, 9.0 Hz, 1H); 3.52 (dd, 1.7 Hz, 9.0 Hz, 1H). ^{13}C NMR: 14.61; 18.36; 19.08; 19.91; 23.49; 25.45; 28.87; 45.24; 48.76; 49.38. 49.55; 54.85; 72.20. IR υ_{max} cm^{-1} (neat): 3360; 3300; 3100; 1590; 1465; 1380; 1165; 1065. MS (*m*/*z*): 211 (M$^{\bullet+}$, 5); 196 (18); 182 (22); 140 (50); 126 (100); 98 (22). $[\alpha]_D = +30.9$ (*c* 1.0, EtOH). Anal. Calcd for $C_{13}H_{25}NO$: C, 73.88; H, 11.92; N, 6.62. Found: C, 73.47; H, 12.15; N, 6.57.

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