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# Chiral Sulfoxides in Asymmetric Synthesis : Enantioselective Synthesis of (-)-(5S,7R)-Tarchonanthuslactone

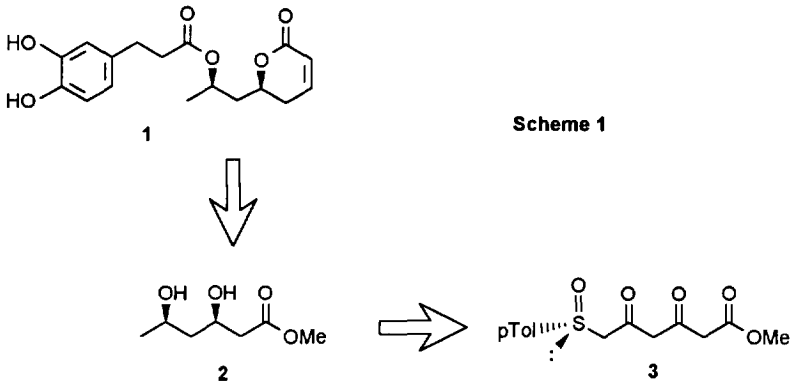
**Guy Solladié* and Laurence Gressot-Kempf**

Université Louis Pasteur (ECPM), Laboratoire de Stéréochimie associé au CNRS 1 Rue B. Pascal, 67008 - Strasbourg, France.

**Abstract :** The enantioselective synthesis of (-)-(5S,7R)-Tarchonanthuslactone, a substituted δ-lactone isolated from a compositae, is described. The main feature of this short synthesis is the stereoselective reduction of a β,δ-diketosulfoxide affording in 6 steps the chiral central part of the molecule, a syn-1,3-diol unit. Copyright © 1996 Elsevier Science Ltd

Tarchonanthuslactone **1** was isolated from a compositae, *tarchonanthus trilobus*,[1] and its absolute configuration was established by synthesis.[2] The basic structure of this compound is a syn 1,3-diol unit with one hydroxyl group involved in an α,β-unsaturated δ-lactone and the other esterified with 3,4-dihydroxyhydrocinnamic acid. Three total syntheses of this molecule have already been published. The first of Nakata[2] started from (-)-(R)-1,3-butanediol (80% ee) and was used to establish the absolute configuration of the two stereogenic centers. The two others from Mori started from (-)-(2S)-methyl malate[3] and (R)-3,4-isopropylidene dioxybutanal.[4] All these syntheses are in 16 steps and in all the cases the starting molecules already contained one stereogenic center and the conjugated double bond was obtained by dehydration We report in this paper an efficient enantioselective synthesis of **1**, induced by a chiral sulfoxide group in only twelve steps.

As shown on the retrosynthetic scheme 1, our strategy was to prepare the 1,3-diol unit by stereoselective reduction of the diketosulfoxide **3**,[5] an approach related to the presumed biological formation of 1,3-polyols by NAD(P)H reduction of the corresponding polyketide precursors. The chiral sulfoxide on the polyketide unit will control the stereoselectivity of the carbonyl reduction in this biomimetic synthesis of 1,3-diols. The diketoester **4** was obtained in one step from commercially available dehydroacetic acid by a known procedure.[6] Condensation of the trianion of **4**, prepared in THF with one equivalent of NaH and two equivalents of t-BuLi at 0°C, to (-)-menthyl (S)-p-toluene sulfinate[7] afforded in high yield the (R)-diketosulfoxide **3** (scheme 2). As expected from previous results,[5] the δ-carbonyl only was entirely enolized (one vinylic hydrogen at 5.64 ppm) and reduction with DIBAL gave only one diastereomer **5**. The relatively low yield of isolated product is due to some decomposition during the chromatographic purification. The absolute configuration (3R, SR) of compound **5** was deduced from our previous results[5] and will be confirmed by correlation with the known compound **1**.



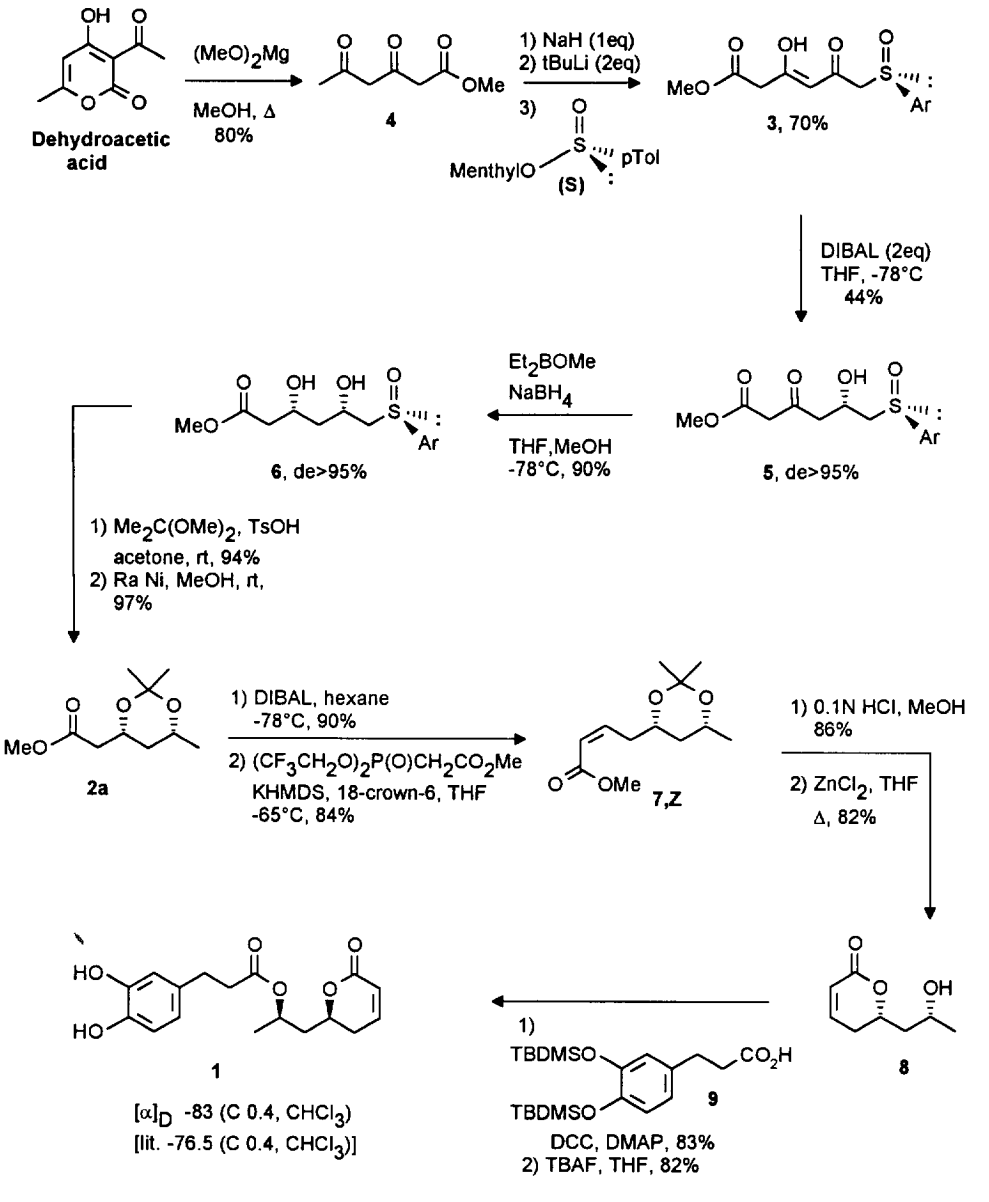

**Scheme 1**

In the next step, the δ-carbonyl was reduced to the syn diol **6** with $Et_2BOMe/NaBH_4$[8] in high yield and de > 95% (only one stereomer detected by $^1H$ NMR). Finally diol protection with 2,2-dimethoxypropane and desulfurization with Raney Nickel afforded the ester **2a**. The methyl ester was then reduced with DIBAL to the corresponding aldehyde. Horner-Emmons type reaction with methyl bis-(trifluoroethyl)-phosphono acetate[9] in the presence of potassium hexamethyldisilyl amide and 18-crown-6 ether, gave mainly the Z isomer (Z/E = 9/1) which was isolated in 84% yield after chromatography. After hydrolyzing the acetonide with dilute acid, the lactonisation of the hydroxyester was carried out with $ZnCl_2$ and molecular sieves in refluxing THF. Lactone **8** was isolated by chromatography in 82% yield. A small amount (14%) of the bicyclic lactone, resulting from 1,4-addition of OH to the lactone double bond, was also isolated. Classical esterification with **9** in presence of DCC/DMAP and removal of the phenol protecting groups afforded tarchonanthuslactone **1** showing all the spectral characteristics identical with the reported data[1,2b,4] but a higher specific rotation.

**Experimental Part**

**Methyl 3,5-dioxohexanoate, 4.**

To a magnetically stirred solution of magnesium methylate [prepared from Mg turnings (7.8 g, 0.32 mol) and MeOH (1.5 L)] were added dehydroacetic acid (36 g, 0.21 mol) and MeOH (300 mL). The reaction mixture was heated under reflux for 10 h, and the solvent evaporated under reduced pressure. The residue was dissolved in AcOEt and acidified with 1N HCl (650 mL). After extracting with AcOEt (5 x 200 mL), the combined organic layers were washed with brine, dried ($MgSO_4$) and evaporated. Distillation of the residue (85°C / 0.65 mmHg) gave 27 g (80%) of **4** as a colourless liquid : Rf 0.82 ($AcOEt/CH_2Cl_2$ = 1/1); $^1H$ NMR ($CDCl_3$, 200 MHz) : enol form : δ: 2 (s, 3H, H-6), 3.27 (s, 2H, H-2), 3.66 (s, 3H, $OCH_3$), 5.54 (s, 1H, H-4): ketone form: δ: 2.17 (s, 3H, H-6), 3.5 (s, 2H, H-2), 3.66 (s, 3H, $OCH_3$), 3.68 (s, 2H, H-4) ; $^{13}C$ NMR ($CDCl_3$) : enol form : δ: 23.4 (C-6), 44.1 (C-2), 51.5 ($OCH_3$), 99.9 (C-4), 167.3 (C-1), 186.9 (C-5), 189.5 (C-3) : ketone form : δ: 29.9 (C-6), 48.5 (C-2), 51.5 ($OCH_3$), 56.4 (C-4), 166.8 (C-1), 196.7 (C-3), 201.4 (C-5).




Scheme 2

**(+)-[S(R)] methyl 3,5-dioxo-6-(p-tolylsulfinyl) hexanoate, 3.**

To a cold (0°C) suspension of NaH (1.82 g, 75.8 mmol) in THF (250 mL) was dropwise added a solution of diketoester **4** (11.86 g, 75 mmol) in THF (50 mL). After stirring for 15 min at 0°C, a 1.5 M solution of t- at butyllithium in pentane (100 mL, 0.15 mol) was dropwise added. A solution of (-)-(S)-menthyl-p-toluene sulfinate (11.04 g, 37.5 mmol) in THF (45 mL) was then added to the red-black solution. After stirring for 2 h

0°C, the mixture was hydrolyzed with sat. $NH_4Cl$ (120 mL) and diluted with AcOEt (100mL). After adjusting the pH to 3 with 10% $H_2SO_4$, the aqueous layer was extracted with AcOEt (4 x 200 mL). The combined organic layers were washed with brine, dried ($MgSO_4$) and the solvents evaporated to give a brown oil. The crude product was purified by column chromatography on metal free silica gel[10] (hexane/$CH_2Cl_2$ gradient to elute menthol and diketoester in excess ; $CH_2Cl_2$/AcOEt gradient to elute diketosulfoxide) and by recrystallisation in ether to provide the diketosulfoxide **3** as a pale yellow solid (7.8 g, 70%) : mp 51-52°C ; Rf 0.42 (AcOEt/$CH_2Cl_2$ : 1/1) ; $[\alpha]_D$ = +262 (c 1, $CHCl_3$) ; $^1H$ NMR ($CDCl_3$, 200 MHz) : δ : 2.39 (s, 3H, Me ptol), 3.34 (s, 2H, H-2), 3.62 (AB, 2H, H-6, $J_{AB}$ = 13Hz, Δν = 17Hz), 3.71 (s, 3H, OMe), 5.64 (s, 1H, H-4), 7.40 [$(AB)_2$, 4H, H arom, $J_{AB}$ = 8Hz, Δν = 39Hz], 14.4 (bs, 1H, H enol) ; $^{13}C$ NMR ($CDCl_3$) : δ : 21.4 (Me ptol), 45.1 (C-2), 52.5 (OMe), 64.7 (C-6), 102.7 (C-4), 123.9 and 130.0 (CH arom), 139.5 and 142.3 (Cq arom), 167.3 (C-1), 179.5 (C-3), 188.8 (C-5). IR ($CHCl_3$) : 3080-2900, 1730, 1600 $cm^{-1}$. Anal. calc. for $C_{14}H_{16}O_5S$ : C, 56.74 ; H, 5.44. Found : C, 56.67 ; H, 5.53.

**(+)-[5(S), S(R)] methyl 3-oxo-5-hydroxy-6-(p-tolylsulfinyl) hexanoate, 5.**

To a cooled (30 min. at -78°C) solution of diketosulfoxide **3** (6.8 g, 0.23 mmol) in THF (340 mL) was dropwise added a cooled (30 min. at -60°C) 1M solution of DIBAL in toluene (0.46 mmol). After 30 min. at -78°C, the mixture was hydrolysed with methanol (200 mL), allowed to reach room temperature and the solvents were evaporated. The residue was diluted with AcOEt (200 mL) and hydrolyzed with sat. sodium tartrate (200 mL). After stirring for one night a clear phase-separation occured. Then after adjusting the pH to 4 with 10% $H_2SO_4$, the aqueous layer was extracted with AcOEt (3 x 200 mL). The combined organic layers were washed with brine, dried ($MgSO_4$) and the solvent evaporated. The crude product was purified by column chromatography on metal free silica gel (hexane/$CH_2Cl_2$ gradient and $CH_2Cl_2$/ACOEt gradient) and by recrystallisation in a ether/ $CH_2Cl_2$ mixture to give the β-hydroxy δ-ketosulfoxide **5** as a white solid (3 g, 44%) : mp 118°C ; Rf 0.44 (AcOEt) ; $[\alpha]_D$ = +211 (c 1, $CHCl_3$), de > 95% (only one diastereomer observed by $^1H$ NMR) ; $^1H$ NMR ($CDCl_3$, 200 MHz) : δ : 2.42 (s, 3H, Me ptol), 2.80 (AB of ABX, 2H, H-4, $J_{AB}$ = 17Hz), 2.90 (AB of ABX, 2H, H-6, $J_{AB}$ = 13.5Hz, $J_{AX}$ = 9.5Hz, $J_{BX}$ = 2.5Hz, Δν = 66Hz), 3.48 (s, 2H, H-2), 3.71 (s, 3H, OMe), 4.27 (d, 1H, OH, J = 3.5Hz), 4.63 (m, 1H, H-5), 7.43 [$(AB)_2$, 4H, H arom, $J_{AB}$ = 8Hz, Δν = 34Hz] ; $^{13}C$ NMR ($CDCl_3$) : δ : 21.4 (Me ptol), 49.0 (C-4), 49.6 (C-2), 52.5 (OMe), 60.6 (C-6), 63.4 (C-5), 124.0 and 130.1 (CH arom), 139.2 and 141.8 (Cq arom), 167.2 (C-1), 201.5 (C-3). IR ($CHCl_3$) : 3400, 3100-2900, 1730-1710 $cm^{-1}$. Anal. calc. for $C_{14}H_{18}O_5S$ : C, 56.36 ; H, 6.08. Found : C, 56.3 ; H, 5.98.

**(+)-[3(R), 5(S), S(R)] methyl 3,5-dihydroxy-6-(p-tolylsulfinyl) hexanoate, 6.**

To a cold (-78°C) solution of β-hydroxy δ-ketosulfoxide **5** (2.11 g, 7.07 mmol) in THF (67 mL) and methanol (16 mL), was added a 1M solution of diethylmethoxyborane in THF (7.78 mmol). After 45 min. at -78°C,

sodium borohydride (295 mg, 7.78 mmol) was added in two portions. The mixture was stirred for 5 h at -78°C and hydrolyzed with 1M AcOH (50 mL). After 15 min. the organic layer was diluted with AcOEt (50 mL) and sat. sodium bicarbonate (85 mL) was added. After stirring for 30 min., the aqueous layer was adjusted to pH 4 with 10% $H_2SO_4$ and extracted with AcOEt (3 x 100 mL). The combined organic layers were washed with brine, dried ($MgSO_4$) and solvents evaporated. Methanol was added and the crude oily product was heated at atmospheric pressure to distillate the azeotrope MeOH/$Et_2BOMe$. This operation was repeated 4 times before purifying the crude diol by column chromatography on metal free silica gel (AcOEt) to provide the β,δ-dihydroxysulfoxide **6** as a white solid (1.9 g, 90%) : mp 91°C ; Rf 0.29 (AcOEt) ; $[\alpha]_D$ = +227 (c 1.1, $CHCl_3$), de > 95% (only one diastereomer observed by $^1H$ NMR) ; $^1H$ NMR ($CDCl_3$, 200 MHz) : δ : 1.49-1.75 (m, 2H, H-4), 2.29 (s, 3H, Me ptol), 2.42 (AB of ABX, 2H, H-2, $J_{AB}$ = 16Hz), 2.80 (AB of ABX, 2H, H-6, $J_{AB}$ = 13Hz, $J_{AX}$ = 9.5Hz, $J_{BX}$ = 3Hz, Δν = 26Hz), 3.56 (s, 3H, OMe), 4.22 (m, 1H, H-3), 4.39 (m, 1H, H-5), 4.39 (bs, 1H, OH), 5.12 (bs, 1H, OH), 7.32 [$(AB)_2$, 4H, H arom, $J_{AB}$ = 8Hz, Δν = 42Hz] ; $^{13}C$ NMR ($CDCl_3$) : δ : 21.1 (Me ptol), 41.5 (C-4), 42.1 (C-2), 51.4 (OMe), 64.1 (C-6), 65.1 (C-3), 67.0 (C-5), 123.7 and 129.8 (CH arom), 139.7 and 141.3 (Cq arom), 172.0 (C-1). IR ($CHCl_3$) : 3400, 3060-2930, 1700 $cm^{-1}$. Anal. calc. for $C_{14}H_{20}O_5S$ : C, 55.98 ; H, 6.71. Found : C, 56.23 ; H, 6.72.

**(+)-[3(R), 5(R)] methyl 3,5-(isopropylidenedioxy) hexanoate, 2a.**

1). To a magnetically stirred solution of the β,δ-dihydroxysulfoxide **6** (1.9 g, 6.3 mmol) in dry acetone (95 mL) and 2,2-dimethoxypropane (9.5 mL) was added p-toluenesulfonic acid (195 mg, 0.1 mmol). After 12 h at room temperature, solvents were evaporated. The residue was diluted with AcOEt (50 mL) and sat. sodium bicarbonate (100 mL) was added. The aqueous layer was extracted with AcOEt (3 x 50 mL) and the combined organic layers were washed with brine, dried ($MgSO_4$) and the solvent was evaporated. The crude product was purified by column chromatography on silica gel ($CH_2Cl_2$/AcOEt = 8/2) to afford the diol acetonide as a white solid (2.3 g, 94%) : mp 103°C ; Rf 0.28 ($CH_2Cl_2$/AcOEt = 8/2) ; $[\alpha]_D$ = +189.5 (c 1.1, $CHCl_3$) ; $^1H$ NMR ($CDCl_3$, 200 MHz) : δ : 1.16 (q, 1H, H-4ax, $J_{4ax-4eq} = J_{4ax-3} = J_{4ax-5}$ = 13Hz), 1.51 (dt, 1H, H-4eq, $J_{4eq-4ax}$ = 13Hz, $J_{4eq-3} = J_{4eq-5}$ = 2Hz), 1.30 and 1.43 (2s, 2 x 3H, H-8), 2.28 (s, 3H, Me ptol), 2.35 (AB of ABX, 2H, H-2, $J_{AB}$ = 16Hz, $J_{AX}$ = 7Hz, $J_{BX}$ = 6Hz, Δν = 35Hz), 2.64 (AB of ABX, 2H, H-6, $J_{AB}$ = 13Hz), 3.55 (s, 3H, OMe), 4.26 (m, 1H, H-3), 4.41 (m, 1H, H-5), 7.30 [$(AB)_2$, 4H, H arom, $J_{AB}$ = 8Hz, Δν = 42Hz] ; $^{13}C$ NMR ($CDCl_3$) : δ : 19.4 and 29.6 (C-8), 21.1 (Me ptol), 35.6 (C-4), 40.7 (C-2), 51.4 (OMe), 63.1 (C-3), 64.4 (C-6), 65.4 (C-5), 99.2 (C-7), 123.5 and 129.7 (CH arom), 141.08 and 141.14 (Cq arom), 170.8 (C-1). IR ($CHCl_3$) : 3050-2900, 1720 $cm^{-1}$. Anal. Calcd. for $C_{17}H_{24}O_5S$ : C, 59.98 ; H, 7.11. Found : C, 59.83 ; H, 7.35. 2). A solution of the preceding acetonide (1.04 g, 3 mmol) in methanol (16 mL) was treated with Raney Nickel

until no more starting material was detected by TLC ($CH_2Cl_2$/AcOEt = 8/2). The catalyst was filtered on celite, washed with methanol, the solvent evaporated without heating and the crude product purified by silica gel chromatography (hexane/ether = 9/1) to provide the diol-ester **2a** (607 mg, 97%) as a pale yellow liquid : Rf 0.2 (hexane/ether = 9/1) ; $[\alpha]_D$ = +1 (c 2.5, $CHCl_3$) ; $^1H$ NMR ($CDCl_3$, 200 MHz) : δ : 1.05 (d, 3H, H-6, $J_{6-5}$ = 6Hz), 1.25 and 1.34 (2s, 2 x 3H, H-8), 1.05 (q, 1H, H-4ax, $J_{4ax-4eq} = J_{4ax-3} = J_{4ax-5}$ = 13Hz), 1.49 (dt, 1H, H-4eq, $J_{4eq-4ax}$ = 13Hz, $J_{4eq-3} = J_{4eq-5}$ = 2.5Hz), 2.34 (AB of ABX, 2H, H-2, $J_{AB}$ = 15.5Hz, $J_{AX}$ = 7Hz, $J_{BX}$ = 6Hz, Δν = 40Hz), 3.56 (s, 3H, OMe), 3.89 (qdd, 1H, H-5, $J_{5-6}$ = 6Hz, $J_{5-4ax}$ = 13Hz, $J_{5-4eq}$ = 2.5Hz), 4.18 (m, 1H, H-3) ; $^{13}C$ NMR ($CDCl_3$) : δ : 19.5 and 29.9 (C-8), 21.9 (C-6), 38.0 (C-4), 40.9 (C-2), 51.3 (OMe), 64.7 (C-5), 65.6 (C-3), 98.5 (C-7), 171.1 (C-1). IR ($CHCl_3$) : 3000-2900, 1725 $cm^{-1}$ . Anal. Calcd for $C_{10}H_{18}O_4$ : C, 59.38 ; H, 8.97. Found : C, 59.25 ; H, 9.19.

**(-)-[5(S), 7(R), 2Z] methyl 5,7-(isopropylidenedioxy) octenoate, 7.**

1). To a cooled (45 min. at -78°C) solution of ester **2a** (414 mg, 2.05 mmol) in dry hexane (36 mL) was dropwise added a cooled (1 hour at -60°C) 1M solution of DIBAL in toluene (2.15 mmol). After 30 min. at -78°C, the mixture was decomposed with methanol (4 mL) and allowed to reach room temperature. Then pentane (10 mL) and sat. sodium tartrate (20 mL) were added. The mixture was stirred until a clear phase-separation occured (30 min.). The aqueous layer was extracted with pentane (3 x 50 mL), the combined organic layers were dried ($MgSO_4$) and the solvents evaporated without heating. The crude product was purified by column chromatography on silica gel (hexane/ether = 1/1) to provide the corresponding aldehyde (318.6 mg, 90%) as a pale yellow liquid : Rf 0.37 (hexane/ether = 1/1) ; $^1H$ NMR ($CDCl_3$, 200 MHz) : δ : 1.12 (d, 3H, H-6, $J_{6-5}$ = 6Hz), 1.15 (dt, 1H, H-4ax, $J_{4ax-4eq}$ = 13Hz, $J_{4ax-3} = J_{4ax-5}$ = 12Hz), 1.33 and 1.42 (2s, 2 x 3H, H-8), 1.53 (dt, 1H, H-4eq, $J_{4eq-4ax}$ = 13Hz, $J_{4eq-3} = J_{4eq-5}$ = 2.5Hz), 2.49 (AB of ABMX, 2H, H-2, $J_{AB}$ = 17Hz, $J_{AX}$ = 7Hz, $J_{BX}$ = 5Hz, $J_{AM} = J_{BM}$ = 2Hz, Δν = 34Hz), 3.98 (qdd, 1H, H-5, $J_{5-6}$ = 6Hz, $J_{5-4eq}$ = 2.5Hz, $J_{5-4ax}$ = 12Hz), 4.35 (m, 1H, H-3), 9.72 (t, 1H, H-1, $J_{1-A} = J_{1-B}$ = 2Hz) ; $^{13}C$ NMR ($CDCl_3$) : δ : 19.6 and 30.0 (C-8), 22.0 (C-6), 38.2 (C-4), 49.7 (C-2), 64.5 (C-5), 64.8 (C-3), 98.6 (C-7), 200.9 (C-1).

2). A solution of methyl bis-(trifluoroethyl)-phosphonoacetate (1.16 g, 3.66 mmol) and 18-crown-6 ether (1.93 g, 7.33 mmol) (recrystallized in $CH_3CN$) in anhydrous THF (65 mL) was cooled under argon to -65°C and treated with 0.5M KHMDS solution in toluene (3.7 mmol). After 15 min. at -65°C a solution of the preceding aldehyde (601 mg, 349 mmol) in THF (8 mL) was dropwise added and the resulting mixture was stirred 1.5 h at -65°C. The mixture was then hydrolysed with sat. $NH_4Cl$ (35 mL) and diluted with ether. The aqueous layer was extracted with ether (3 x 30 mL), the combined organic layers were dried ($MgSO_4$) and the solvents evaporated without heating. The Z-isomer was purified from the mixture of isomers (Z/E = 9/1, from $^1H$ NMR) by two column chromatographies on silica gel (pentane/ether = 9/1 to pentane/ether = 8/2) to give the less polar Z-alkene 7 as a pale yellow liquid (668.5 mg, 84%) : Rf 0.29 (pentane/ether = 9/1) ; $[\alpha]_D$ = -23 (c 1.1, $CHCl_3$)

; $^1$H NMR ($CDCl_3$, 200 MHz) : δ : 1.09 (d, 3H, H-8, $J_{8-7}$ = 6Hz), 1.13 (dt, 1H, H-6ax, $J_{6ax-6eq}$ = 13Hz, $J_{6ax-5}$ = $J_{6ax-7}$ = 11.5Hz), 1.32 and 1.37 (2s, 2 x 3H, H-10), 1.44 (dt, 1H, H-6eq, $J_{6eq-6ax}$ = 13Hz, $J_{6eq-5}$ = $J_{6eq-7}$ = 2.5 Hz), 2.76 (AB of ABX coupled with H-2 and H-3, 2H, H-4, $J_{AB}$ = 16Hz, $J_{AX}$ = 5Hz, $J_{BX}$ = 7Hz, $J_{A-2}$ = $J_{B-2}$ = 2Hz, $J_{A-3}$ = $J_{B-3}$ = 7Hz, Δν = 43Hz), 3.63 (s, 3H, OMe), 3.91 (m, 2H, H-5 + H-7), 5.79 (dt, 1H, H-2, $J_{2-3}$ = 11.5Hz, $J_{2-A}$ = $J_{2-B}$ = 2Hz), 6.31 (dt, 1H, H-3, $J_{3-2}$ = 11.5Hz, $J_{3-A}$ = $J_{3-B}$ = 7Hz) ; $^{13}$C NMR ($CDCl_3$) : δ : 19.7 and 30.1 (C-10), 22.0 (C-8), 35.4 (C-6), 38.1 (C-4), 50.9 (OMe), 64.9 (C-7), 68.2 (C-5), 98.4 (C-9), 120.5 (C-2), 146.1 (C-3), 166.9 (C-1). IR ($CHCl_3$) 3080 - 2860, 1720, 1650 cm$^{-1}$. Anal. Calcd for $C_{12}H_{20}O_4$ : C, 63.14 ; H, 8.83. Found : C, 63.10 ; H, 8.99.

**(-)-[5(S), 7(R)]-7-hydroxy-5-(oct-2-enolide), 8.**

1). To a cold (0°C) solution of the acetonide **7** (672.8 mg, 2.95 mmol) in methanol (28 mL) was added 0.1N HCl (6 mL) and the resulting mixture was stirred 13 h at room temperature. The acid mixture was then neutralized with sat. sodium bicarbonate (6 mL) and methanol evaporated. Ether was then added to the residue, the aqueous layer was adjusted to pH 5 with 10% HCl and extracted with ether (4 x 20 mL). The combined organic layers were dried ($MgSO_4$) and the solvent evaporated. The resulting pale yellow oil was used in the next step without further purification (475 mg, 86%).

2). To an activated mixture of zinc chloride (282 mg, 2.07 mmol) and molecular sieve 4Å was added, under argon, a solution of the preceding diol (390 mg, 2.07 mmol) in THF (46 mL). The resulting mixture was heated at reflux during 3.5 h. The molecular sieves were then filtrated and the solvent evaporated. Ether (30 mL) and sat. NaCl (50 mL) were added to the residue. The aqueous layer was extracted with ether (4 x 30 mL). The combined organic layers were dried ($MgSO_4$) and the solvent evaporated. The crude product was purified by column chromatography on silica gel (ether/pentane = 8/2 to ether) to give the hydroxy lactone **8** (265 mg, 82%) as a pale yellow oily liquid : Rf 0.35 (AcOEt) ; $[\alpha]_D$ = -111 (c 1, $CHCl_3$) ; $^1$H NMR ($CDCl_3$, 200 MHz) : δ : 1.24 (d, 3H, H-8, $J_{8-7}$ = 6Hz), 1.88 (AB of ABX coupled with H-5, 2H, H-6, $J_{AB}$ = 14Hz, $J_{AX}$ = 8Hz, $J_{BX}$ = 5Hz, $J_{A-5}$ = 8Hz, $J_{B-5}$ = 4Hz, Δν = 57.5Hz), 2.28 - 2.49 (m, 2H, H-4), 4.07 (m, 1H, H-7), 4.63 (m, 1H, H-5), 6.0 (dt, 1H, H-2, $J_{2-3}$ = 10Hz, $J_{2-4}$ = 2Hz), 6.9 (1H, H-3, $J_{3-2}$ = 10Hz, $J_{3-4ax}$ = 8.5Hz, $J_{3-4eq}$ = 4Hz) ; $^{13}$C NMR ($CDCl_3$) : δ : 23.6 (C-8), 30.2 (C-4), 43.5 (C-6), 65.0 (C-7), 76.8 (C-5), 121.1 (C-2), 145.4 (C-3), 164.2 (C-1). IR ($CHCl_3$) 3600 - 3500, 3000 - 2860, 1750 - 1680 cm$^{-1}$. Anal. Calcd for $C_8H_{12}O_3$ : C, 61.52 ; H, 7.74. Found : C, 62.77 ; H, 7.89.

**3', 4'-(t-butyldimethylsilyldioxy) hydrocinnamic acid, 9.**

1). To a magnetically stirred solution of 3', 4'-dihydroxyhydrocinnamic acid (451.7 mg, 1.1 mmol) in dry DMF (4 mL) were added imidazole (674 mg, 9.9 mmol) and t-butyldimethylsilyl chloride (746 mg, 4.95 mmol). After 49 h at room temperature, the mixture was diluted with ether (20 mL) and water (5 ml).. The mixture was stirred until a clear phase-separation occured and extracted with ether (4 x 30 mL). The combined organic

layers were washed with sat. $NH_4Cl$ (3 x 100 mL) and brine (2 x 100 mL), dried ($MgSO_4$) and solvents evaporated to give the crude TBDMS ester of **9**.

2). An aqueous (0.7 mmol/L) potassium carbonate solution (4.7 mL) was dropwise added to a solution of the dried preceding oily ester in THF (5 mL) and methanol (14 mL). The resulting orange solution was stirred 20 min. at room temperature and the solvents evaporated. Ether (30 mL) and sat. NaCl (14 mL) were added to the residue. At 0°C the aqueous layer was acidified with 10% HCl to pH 6 and extracted with ether (3 x 100 mL). The combined organic layers were washed with brine (2 x 100 mL), dried ($MgSO_4$) and solvent evaporated. Silica gel column chromatography of the residue (hexane/AcOEt = 8/2) gave the acid **9** as a white solid (423 mg, 94%) : mp 88°C ; Rf 0.2 (hexane/AcOEt = 8/2) ; $^1H$ NMR ($CDCl_3$, 200 MHz) : δ : 0.18 (s, 12H, MeSi), 0.98 (s, 18H, t-BuSi), 2.62 (t, 2H, H-2, $J_{2-3}$ = 7.5Hz), 2.84 (t, 2H, H-3, $J_{3-2}$ = 7.5Hz), 6.63 (dd, 1H, H-6', $J_{6'-5'}$ = 8Hz, $J_{6'-2'}$ = 2Hz), 6.67 (d, 1H, H-2', $J_{2'-6'}$ = 2Hz), 6.74 (d, 1H, H-5', $J_{5'-6'}$ = 8Hz) ; $^{13}C$ NMR ($CDCl_3$) : δ : -4.1 (MeSi), 18.4 ($Me_3C$-Si), 25.9 ($(CH_3)_3CSi$), 29.9 (C-2), 35.9 (C-3), 121.0 and 121.2 (C-2', C-5', C-6'), 133.3 (C-1'), 145.3 and 146.7 (C-3', C-4'), 179.6 (C-1). IR ($CHCl_3$) 3060 - 2840, 1710, 1600 - 1575, 1500 - 1450 $cm^{-1}$. Anal. Calcd for $C_{21}H_{38}O_4Si_2$ : C, 61.41 ; H, 9.33. Found : C, 61.68 ; H, 9.49.

**(-)-[5(S), 7(R)]-7-[5-(oct-2-enolide)-3', 4'-(t-butyldimethylsilyldioxy)]-dihydrocinnamate, 10.**

Solutions in $CH_2Cl_2$ (8 mL) of the acid **9** (616 mg, 1.5 mmol) and of DCC (310 mg, 1.5 mmol) were added to a solution of the hydroxylactone **8** (213.1 mg, 1.36 mmol) in $CH_2Cl_2$ (40 mL). After 10 min. DCU precipitated and DMAP (83 mg, 0.68 mmol) was added. The mixture was stirred 15 h ar room temperature. DCU was filtrated and solvent evaporated. The crude product was purified by column chromatography on silica gel (hexane/AcOEt = 75/25) to provide the compound **10** (624.4 mg, 83%) as a colorless oil : Rf 0.26 (hexane/AcOEt = 75/25) ; $[\alpha]_D$ = -44 (c 1, $CHCl_3$) (lit.[4] : -44.74 (c 0.7, $CHCl_3$)) ; $^1H$ NMR ($CDCl_3$, 200 MHz) : δ : 0.14 and 0.16 (s, 12H, MeSi), 0.94 and 0.95 (s, 18H, t-BuSi), 1.22 (d, 3H, H-8, $J_{8-7}$ = 6Hz), 1.94 (AB of ABX coupled with H-5, 2H, H-6, $J_{AB}$ = 14.5Hz, $J_{AX}$ = 8Hz, $J_{BX}$ = 6.5Hz, $J_{A-5}$ = 6.5Hz, $J_{B-5}$ = 4.5Hz, Δν = 76Hz), 2.21 - 2.40 (m, 2H, H-4), 2.52 (t, 2H, H-8', $J_{8'-7'}$ = 7.5Hz), 2.78 (t, 2H, H-7', $J_{7'-8'}$ = 7.5Hz), 4.39 (tdd, 1H, H-5, $J_{5-A}$ = 6.5Hz, $J_{5-B}$ = 4.5Hz, $J_{5-4ax}$ = 11Hz, $J_{5-4eq}$ = 6.5Hz), 5.07 (qdd, 1H, H-7, $J_{7-8}$ = 6Hz, $J_{7-A}$ = 8Hz, $J_{7-B}$ = 6.5Hz), 5.96 (ddd, 1H, H-2, $J_{2-3}$ = 10Hz, $J_{2-4}$ = 2Hz, $J_{2-4}$ = 1Hz), 6.58 (dd, 1H, H-6', $J_{6'-2'}$ = 2Hz, $J_{6'-5'}$ = 8Hz), 6.63 (d, 1H, H-2', $J_{2'-6'}$ = 2Hz), 6.68 (d, 1H, H-5', $J_{5'-6'}$ = 8Hz), 6.81 (ddd, 1H, H-3, $J_{3-2}$ = 10Hz, $J_{3-4}$ = 3Hz, $J_{3-4}$ = 5.5Hz) ; $^{13}C$ NMR ($CDCl_3$) : δ : -4.2 (MeSi), 18.3 ($Me_3CSi$), 20.2 (C-8), 25.8 ($(CH_3)_3CSi$), 29.0 (C-4), 30.1 (C-8'), 36.1 (C-7'), 40.7 (C-6), 67.0 (C-5), 74.8 (C-7), 120.76, 120.97, 121.02, 121.17 (C-2, C-2', C-5', C-6'), 133.3 (C-1'), 144.7 (C-3), 145.1 and 146.5 (C-3', C-4'), 163.8 (C-1), 172.3 (C-9'). IR ($CHCl_3$) 2960 - 2860, 1740 - 1690, 1600 - 1575, 1500 - 1450 $cm^{-1}$. Anal. Calcd for $C_{29}H_{48}O_6Si_2$ : C, 63.46 ; H, 8.81. Found : C, 63.33 ; H, 8.97.

**(-)-Tarchonantuslactone, 1.**

A solution of the compound **10** (544mg, 0.99 mmol) in THF (38 mL) was treated with benzoïc acid (363 mg, 2.97 mmol) (recrystallised in a mixture hexane/ethanol), and with a 1.1M solution of TBAF in THF (2.25 mL, 2.5 mmol) and then stirred at room temperature for 1 h. The solvent was evaporated and AcOEt (15 mL) and water (15 mL) were added to the residue. The aqueous layer was saturated with sodium chloride and extracted with AcOEt (4 x 30 mL). The combined organic layers were washed with water (2 x 50 mL), brine (2 x 50 mL), dried ($MgSO_4$) and the solvent evaporated. The crude product was purified by column chromatography on silica gel (ether) to give Tarchonantuslactone (261.3 mg, 82%) as a white solid : mp 89-90°C ; Rf = 0.32 (ether) ; $[\alpha]_D$ = -83 (c 0.4 $CHCl_3$) (lit.[4] : -76.5 (c 0.4, $CHCl_3$)) ; $^1H$ NMR ($CDCl_3$, 200 MHz) : δ : 1.21 (d, 3H, H-8, $J_{8-7}$ = 6.5Hz), 1.89 (AB of ABX coupled with H-5, 2H, H-6, $J_{AB}$ = 14.5Hz, $J_{AX}$ = 8Hz, $J_{BX}$ = 7Hz, $J_{A-5}$ = 6.5Hz, $J_{B-5}$ = 4.5Hz, Δν = 74Hz), 2.13 - 2.34 (m, 2H, H-4), 2.57 (t, 2H, H-8', $J_{8'-7'}$ = 7Hz), 2.79 (t, 2H, H-7', $J_{7'-8'}$ = 7Hz), 4.21 (dddd, 1H, H-5, $J_{5-A}$ = 6.5Hz, $J_{5-B}$ = 4.5Hz, $J_{5-4ax}$ = 11Hz, $J_{5-4eq}$ = 6Hz), 5.04 (qdd, 1H, H-7, $J_{7-8}$ = 6.5Hz, $J_{7-A}$ = 8Hz, $J_{7-B}$ = 7Hz), 5.96 (ddd, 1H, H-2, $J_{2-3}$ = 10Hz, $J_{2-4}$ = 2Hz, $J_{2-4}$ = 1Hz), 6.53 (dd, 1H, H-6', $J_{6'-2'}$ = 2Hz, $J_{6'-5'}$ = 8Hz), 6.53 (bs, 2H, OH), 6.7 (d, 1H, H-2', $J_{2'-6'}$ = 2Hz), 6.73 (d, 1H, H-5', $J_{5'-6'}$ = 8Hz), 6.80 (ddd, 1H, H-3, $J_{3-2}$ = 10Hz, $J_{3-4}$ = 3Hz, $J_{3-4}$ = 6Hz) ; $^{13}C$ NMR ($CDCl_3$) : δ : 20.2 (C-8), 28.8 (C-4), 30.1 (C-8'), 36.0 (C-7'), 40.5 (C-6), 67.2 (C-5), 75.2 (C-7), 115.2 and 120.1 (C-2', C-5', C-6'), 120.5 (C-2), 132.4 (C-1'), 142.4 and 144.0 (C-3', C-4'), 146.0 (C-3), 165.3 (C-1), 173.0 (C-9'). IR ($CHCl_3$) 3540 - 3100, 3100 - 2840, 1750 - 1680, 1610, 1510, 1440 $cm^{-1}$. Anal. Calcd for $C_{17}H_{20}O_6$ : C, 63.74; H, 6.291. Found : C, 63.87 ; H, 6.27.

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