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Synthesis of Polyquinanes via Bicyclo [2.1.0] Pentane Intermediates. An easy access to optically pure Diquinane Alcohols of known absolute configuration.

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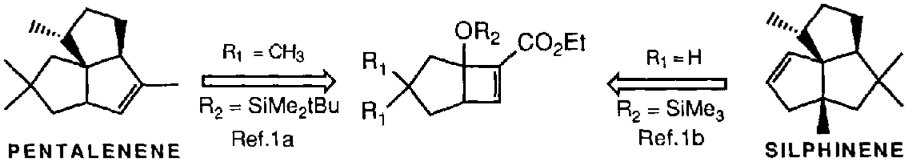
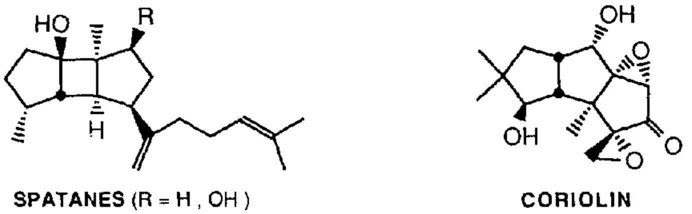
Abstract : The resolution of the cyclobutenic ester 1 using chiral lactols is described. After a stereospecific reaction sequence (cyclopropanation followed by an acidic solvolysis), the enantiomerically pure diquinanes 10 are obtained.

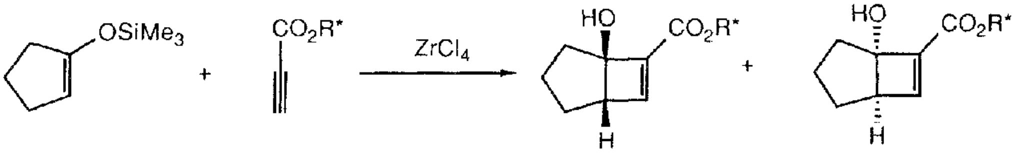
We have recently shown that cyclopentano-cyclobutene esters, which are readily available by a $ZrCl_4$ promoted cycloaddition of ethyl propynoate with adequately substituted silyl enol ethers of cyclopentanones, are useful starting materials for the synthesis of triquinanes[1].



Being currently involved in the synthesis of biologically active natural sesquiterpenes such as Spatanes[2] and Coriolin[3], we were searching for optically active starting cyclobutenes.



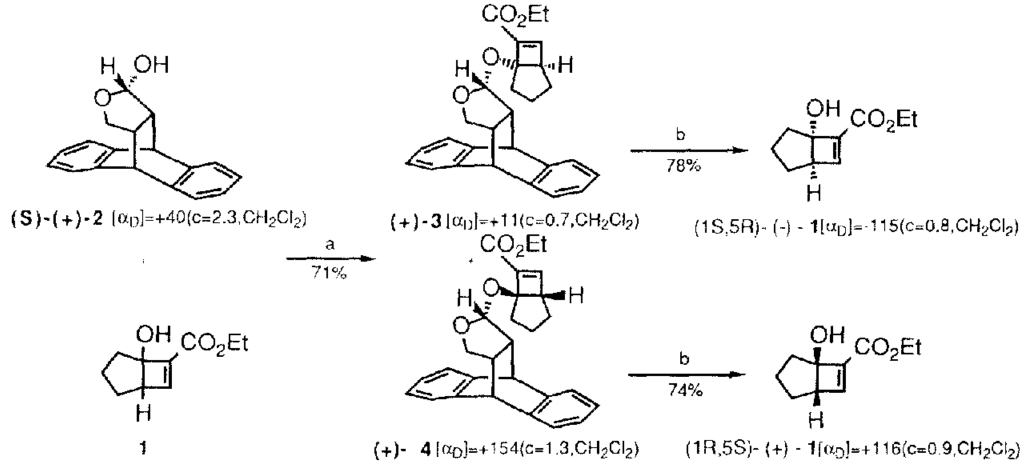
We tried therefore first to achieve the cycloaddition of the silyl enol ether of cyclopentanone with chiral propynoates.



R* = menthyl , bornyl

Inseparable mixture of diastereomers(ratio:1/1)

The cycloaddition reaction was successful with menthyl and bornyl propynoates[4], but we were unable to separate the diastereomeric cyclobutene esters obtained. The direct resolution of the cyclobutene ester **1** by formation of chiral derivatives of the alcohol function was then tried, using at first the lactol (S)-(+)-**2** as chiral auxiliary[5]. The mixture of the diastereomeric cyclobutene esters **3** (less polar) and **4** (more polar), obtained as acetals, could be separated by column chromatography on silica gel (overall yield 71 %, equal amounts of **3** and **4**). By removing the chiral auxiliary, the enantiomeric cyclobutene esters (-)-**1** and (+)-**1** were obtained with respectively 78 and 74 % yield. The ^{1}H-NMR spectra of these compounds showed no splitting of the peaks in the presence of chiral shift reagents (Eu(hfc)$_3$), so that they can be considered as enantiomerically pure to at least 95 % (limit of the method as checked with the racemic compound).



(S)-(+)-2 [α_D]=+40(c=2.3,CH$_2$Cl$_2$)

1

(+)-3 [α_D]=+11(c=0.7,CH$_2$Cl$_2$)

(+)- **4** [α_D]=+154(c=1.3,CH$_2$Cl$_2$)

(1S,5R)- (-) - **1**[α_D]=-115(c=0.8,CH$_2$Cl$_2$)

(1R,5S)- (+) - **1**[α_D]=+116(c=0.9,CH$_2$Cl$_2$)

a : pTsOH, CH$_2$Cl$_2$, MgSO$_4$(ratio**3**/**4** : 1/1) ; b : pTsOH, dioxane, H$_2$O

Their absolute configurations were determined by single crystal X-ray analysis of the less polar diastereomer **3**, the absolute configuration of the used resolving agent (S)-(+)-**2** being known[6].

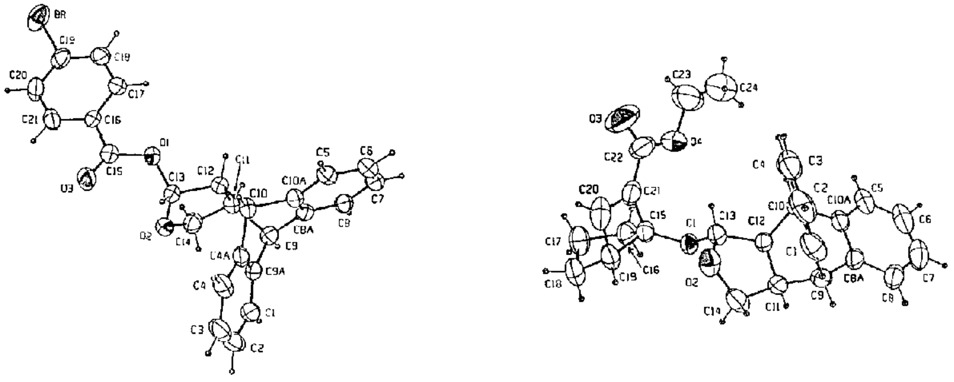
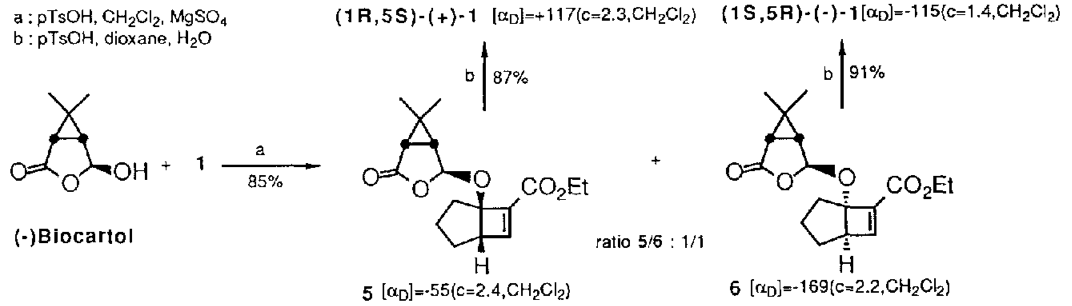
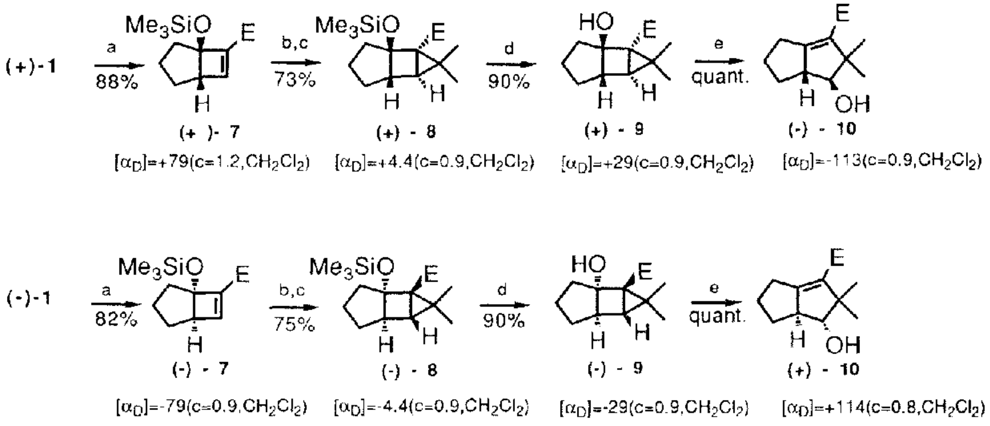


Fig. 1 : ORTEP views[7] of **11** (left) and (+)-**3** (right).

The lactol (S)-(+)-**2** used for the resolution must however itself be prepared by a multi-step synthesis[5]. This, and the fact that the chromatographic separation of the diastereomers **3** and **4** was rather tedious, induced us to try with another resolving lactol, the industrial synthetic intermediate "biocartol"[8] . The straightforward formation of the acetals **5** (less polar) and **6** (more polar) (dichloromethane reflux, pTsOH), very easily separated by a simple column chromatography on silica gel, followed by high yield deprotection (dioxane/water 80° C, pTsOH) of the tertiary alcohols, led to the cyclobutenes (+)-**1** and (-)-**1** of similar enantiomeric purity with more than 75 % overall yield .



The availability of the optically pure cyclobutene esters (+)-**1** and (-)-**1** could now be used to achieve the synthesis of non racemic diquinanic hydroxy-esters of known configuration, as a consequence of the high stereospecificity of the cyclopropanation reaction via 1,3-dipolar addition and of the bicyclo [2.1.0] pentan-2-ol to cyclopent-3-en-1-ol rearrangement already disclosed[1]. The (+)-**1** hydroxy-ester led thus after protection of the alcohol function as a silyl ether (+)-**7**, 1,3-dipolar cycloaddition with 2-diazopropane and sensitized photocleavage, to the tricyclic derivative (+)-**8**. After deprotection the bicyclo [2.1.0] pentan (+)-**9** was solvolyzed under acidic conditions to give the diquinane hydroxy-ester (-)-**10** (overall yield 68 %). Similarly the (-)-**1** cyclobutene ester led to the diquinane (+)-**10** with the same overall yield. No racemization occured during the whole reaction sequence as no splittings of the signals in the ^1H-NMR spectra could be detected in the presence of chiral shift reagents.



(+)-7 $[\alpha_D]$=+79(c=1.2,CH_2Cl_2)
(+)-8 $[\alpha_D]$=+4.4(c=0.9,CH_2Cl_2)
(+)-9 $[\alpha_D]$=+29(c=0.9,CH_2Cl_2)
(-)-10 $[\alpha_D]$=-113(c=0.9,CH_2Cl_2)

(-)-7 $[\alpha_D]$=-79(c=0.9,CH_2Cl_2)
(-)-8 $[\alpha_D]$=-4.4(c=0.9,CH_2Cl_2)
(-)-9 $[\alpha_D]$=-29(c=0.9,CH_2Cl_2)
(+)-10 $[\alpha_D]$=+114(c=0.8,CH_2Cl_2)

E = CO_2Et

a : $CF_3SO_3SiMe_3$,NEt_3,CH_2Cl_2 ; b : $(CH_3)_2CN_2$,Et_2O,-20°C ; c : hυ,acetone,benzophenone

d : TBAF,THF ; e : $H_2SO_4$10%,$C_6H_5CH_3$ reflux

The synthesis of chiral polyquinanes and related compounds starting from optically active electrophilic cyclobutenes is in consequence a reasonable proposal as high enantiomeric purities can be expected, with the advantage of an easy control of the absolute configurations.

Acknowledgments : We are grateful to the BASF for repeated gifts of ethyl propynoate and to Roussel-Uclaf for the gift of biocartol.

EXPERIMENTAL SECTION

General information :

IR spectra were recorded on a Perkin-Elmer IR-457 instrument (CCl_4 solution). ^1H-NMR spectra were recorded on a Bruker WSP 200 spectrometer at 200 MHz. Chemical shifts were measured in ppm relative to chloroform as internal standard unless otherwise stated and coupling constants (J values) are in Hertz (Hz). Multiplicities are designed as singlet (s), doublet (d), triplet (t), quartet (q) and multiplet (m). Optical rotations were determined with a Perkin-Elmer 241 MC polarimeter at the sodium D line. Concentrations were reported in g/100 ml. Analytical thin-layer chromatography (TLC) was performed on Merck silica gel (60F254) plates (0.25 mm). Visualization was effected with UV light and with ethanol-vanilline-H_2SO_4. Chromatography was carried out on Merck silica gel 60 (230-400 mesh ASTM) under low pressure (CFG pump). Melting points (mp) were determined with a Reichert melting point apparatus and are uncorrected. Elemental analyses were performed by "le Service de Microanalyse du Département de Chimie de l'ULP de Strasbourg" (values ± 0.3 %). Photolyses were carried in a Pyrex photoreactor with a Mazda 250 W lamp and stopped when the stoichiometric amount of nitrogen gas + 10 % was obtained.
Ether was distilled over CaH_2 before use ; CH_2Cl_2 was distilled over P_2O_5 before use ; THF was distilled over sodium/benzophenone before use.
All reactions were performed under an argon atmosphere in flame dried glasware.

Experimental :

*Formation of (+)-***3** *and (+)-***4** *:*

To a solution of cyclobutenic ester **1** (770 mg ; 4.22 mmol) in CH_2Cl_2 (25 ml) containing pTsOH (20 mg ; 0.10 mmol) and anhydrous $MgSO_4$ (3 g) was added at RT the lactol (S)-(+)-**2** (930 mg ; 3.51 mmol) in CH_2Cl_2 (25 ml). This mixture was refluxed for 3 h under an argon atmosphere. After cooling, the reaction mixture was diluted with CH_2Cl_2 (50 ml), washed with a $NaHCO_3$ saturated solution (50 ml), brine (50 ml), dried ($MgSO_4$) and concentrated in vacuo to give 1.76 g of crude material. This was chromatographed (SiO_2 : 80 g ; ether/toluene : 2/98) to give (+)-**3** as a white solid (532 mg ; 34 %) and (+)-**4** as a white solid (549 mg ; 37 %).

(+)-**3** : $C_{28}H_{28}O_4$; white solid ; F = 139-140° C ; Anal.: calc % C : 78.48, H : 6.58 ; found : C : 78.38, H : 6.36 ; $[\alpha]_D$ = + 11 (c = 0.74 ; CH_2Cl_2) ; IR : 1716 (C=O) cm^{-1} ; ^1H-NMR (C_6D_6) : 7.0-7.3 (8H, m), 6.41 (1H, s), 5.19 (1H, s), 4.46 (1H, d, J = 3 Hz), 4.17 (2H, q, J = 7 Hz), 3.97 (1H, tl, J = 8 Hz) , 3.71 (1H, d, J = 3 Hz), 3.42 (1H, dd, J = 2.5 Hz and J = 9 Hz), 3.15 (1H, d, J = 7 Hz), 3.06 (1H, dd, J = 3 Hz and 10 Hz), 2.50-2.68 (1H, m), 2.30 (1H, dd, J = 5 Hz and J = 12 Hz), 1.10-1.80 (5H, m), 1.13 (3H, t, J = 7 Hz).

(+)-**4** : $C_{28}H_{28}O_4$; white solid ; F = 115-117° C ; Anal.: calc % C : 78.48, H : 6.58 ; found : C : 78.50, H : 6.57 ; $[\alpha]_D$ = + 154 (c = 1.33 ; CH_2Cl_2) ; IR : 1717 (C=O) cm^{-1} ; ^1H-NMR (C_6D_6) : 7.45-6.98 (8H, m), 6.28 (1H, s), 5.19 (1H,s), 4.24 (1H, d, J = 3 Hz), 4.08 (2H, q, J = 7 Hz), 4.06 (1H, t, J = 8 Hz), 3.71 (1H, d, J = 3 Hz), 3.45 (1H, dd, J = 2.5 Hz and J = 9 Hz), 3.01 (1H, d, J = 7.0 Hz), 2.98 (1H, dd, J = 3 Hz and J = 10 Hz), 2.50-2.70 (1H, m), 2.33 (2H, dd, J = 5 Hz and J = 12 Hz), 1.05-1.80 (4H, m) ; 1.01 (3H, t, J = 7 Hz).

(1S,5R)-(-)-ethyl-1 hydroxybicyclo [3.2.0] hept-6-ene-7-carboxylate **1** *:*

To a solution of the less polar diastereomer (+)-**3** (124 mg ; 0.289 mmol) in a mixture dioxane/water (15 ml ; 2/1) was added pTsOH (25 mg ; 0.13 mmol). This mixture was refluxed during 1 h. After cooling, the reaction mixture was diluted with CH_2Cl_2 (10 ml), washed with a saturated $NaHCO_3$ solution (25 ml), brine (25 ml), dried ($MgSO_4$) and concentrated in vacuo to give 179 mg of crude material. This was chromatographed (SiO_2 : 10 g ; AcOEt/hexane : 10/90) to give (-)-**1** as a colorless oil (38 mg ; 78 %).

(1S,5R)-(-)-1 : $C_{10}H_{14}O_3$; colorless liquid ; Anal.: calc % C : 65.91, H : 7.74 ; found : C : 65.82, H : 7.88 ; $[\alpha]_D$ = - 115 (c = 0.77 ; CH_2Cl_2) ; IR (CCl_4) : 3560-3260 (OH), 3610 (OH), 1710 (C=O), 1606 (C=C) cm^{-1} ; ^1H-NMR ($CDCl_3$) : 6.72 (1H, s), 4.16 (2H, dd, J = 3 Hz and J = 7 Hz), 3.35-3.10 (1H, m), 2.81 (1H, d, J = 6.5 Hz), 2.10-2.95 (1H, m), 1.80-1.65 (1H, m), 1.60-1.35 (4H, m), 1.26 (3H, t, J = 7 Hz).

The same procedure was employed for the synthesis of (+)-**1**. (+)-**4** : 350 mg(0.81 mmol) ; dioxane/H_2O : 15ml (2/1) ; pTsOH : 50 mg (0.26 mmol). The crude material (386 mg) was chromatographed (15 g SiO_2 ; AcOEt/hexane : 10/90) yielding (+)-**1** as a colorless oil (109 mg ; 74 %).

(1R,5S)-(+)-1 : $C_{10}H_{14}O_3$; colorless liquid ; Anal.: calc % C : 65.91, H : 7.74 ; found : C : 65.70, H : 7.61 ; $[\alpha]_D$ = + 116 (c = 0.87 ; CH_2Cl_2).

X-ray structures of **11** *and (+)-***3**[9] *:*

Colorless transparent crystals were obtained by recrystallization from CH_2Cl_2-diethyl ether-hexane solutions of (+)-**3** and from 1:1 CH_2Cl_2-diethyl ether mixtures of **11**. Diffraction data were collected on an Enraf-Nonius CAD4 automated diffractometer with graphite monochromated CuKα radiation. Two selected crystals were sealed in glass capillaries ; their dimensions were 0.24 x 0.26 x 0.38 mm ((+)-**3**) and 0.10 x 0.20 x 0.34 mm

(**11**). Cell constants were obtained from least-squares refinements, using the setting angles of accurately centered reflections : 25 reflections for (+)-**3** in the range $20 < \theta < 27°$; 22 for **11** in the range $24 < \theta < 30°$. Intensity data were gathered by using the $\omega/2\theta$ scan technique ; 2595 reflections up to $2\theta = 146°$ for (+)-**3** and 2227 with $2\theta_{max} = 140°$ for **11**. No significant intensity variations were noticed during the collection of both data sets. Lorentz and polarization corrections were applied. Absorption corrections were made only in the case of **11** with transmission coefficients in the range 0.82-0.99. The number of reflections having $F_o^2 > 3\sigma(F_o^2)$ used in the subsequent determination and refinement of the structures was 2082 for (+)-**3** and 1761 for **11**.

Crystal data : i) (+)-**3** : $C_{28}H_{28}O_4$, fw = 428.53, orthorhombic space group P $2_12_12_1$, a = 9.234 (1), b = 11.010 (1) and c = 22.419 (2) Å ; V = 2279.2 Å^3, Z = 4, Dc = 1.25 g cm^{-3}, F(000) = 912, μ (CuKα) = 6.2 cm^{-1} ; ii) **11** : $C_{25}H_{19}BrO_3$, fw = 447.34, orthorhombic, P $2_12_12_1$, a = 7.069 (1), b = 9.718 (1), c = 28.998 (4) Å, V = 1992.0 (8) Å^3, Z = 4, Dc = 1.49 g cm^{-3}, μ(CuKα) = 30.1 cm^{-1}, F (000) = 912.

Multan calculations gave the positions of all non-hydrogen atoms in both (+)-3 and **11**. The hydrogen atoms were located from series of difference-Fourier syntheses and included as fixed contributions. The non-hydrogen atoms were refined anisotropically, using the full-matrix least-squares procedure. The function minimized was $\Sigma w(|Fo|-|Fc|)^2$, where the weights $w = 4F_o^2/\sigma^2(F_o^2)$ and $\sigma^2(F_o^2) = \sigma^2(I) + (pI)^2.\sigma(I)$ is based on counting statistics and p was assigned a value of 0.06. The final values of the residuals $R = \Sigma||Fo|-|Fc||/\Sigma|Fo|$ and $Rw = [\Sigma w(|Fo|-|Fc|)^2/\Sigma w(|Fo|)^2]^{1/2}$ are 0.053 and 0.067, respectively, for (+)-3, 0.041 and 0.054, respectively, for **11**. Scattering factors for neutral atoms and the values for Δf' and Δf'' were taken from the usual source[10]. Secondary extinction corrections were applied[11]. Final difference-Fourier map showed no significant features with the highest peak at 0.22 e Å^{-3} for (+)-3 and 0.43 e Å^{-3} for **11**[12].

For the determination of the absolute configuration, the models of (+)-3 and **11** were inverted and refined to convergence in identical fashions. In the case of (+)-**3**, the absolute configuration of (R) at C13, that expected from the enantiomer used in the compound synthesis, could not be confirmed by the resolution of the structure (the effects of anomalous dispersion are too weak). In the case of **11**, the refinement yielded R = 0.049 and Rw = 0.063, a significantly poorer result, as confirmed additionally by the Hamilton (1965) $\mathcal{R}$ test[13]. The absolute configuration (R) at C13 agrees with the configuration of the starting material used in the synthesis.

*Formation of (-)-**5** and (-)-**6** :*

The same procedure as for the formation of (+)-**3** and (+)-**4** was followed. (-) Biocartol : 1.10 g (6.64 mmol) ; **1** : 1.10 g (6.03 mmol) ; pTsOH : 100 mg (0.52 mmol) ; CH_2Cl_2 : 50 ml ; $MgSO_4$: 5 g. The crude material (2.08 g) was chromatographed (30 g SiO_2 ; Et_2O/hexane : 5/95) to give (-)-**5** as a white solid (779 mg ; 42 %) and (-)-**6** as a gum (794 mg ; 43 %).

(-)-**5** : $C_{17}H_{22}O_5$; white solid ; F = 111-113° C ; Anal.: calc % C : 66.65, H : 7.24 ; found : C : 66.65, H : 7.05 ; $[\alpha]_D$ = - 55 (c = 2.4 ; CH_2Cl_2) ; IR ($CHCl_3$) : 1762 (C=O), 1708 (C=O), 1602 (C = C) cm^{-1} ; ^{1}H-NMR ($CDCl_3$) : 6.84 (1H, s), 5.33 (1H, s), 4.27 (2H, dq, J = 7 Hz and J = 1 Hz), 3.30 (1H, m), δ_A = 2.12, δ_B = 2.02 (2H, AB, J_{AB} = 5.7 Hz), 2.05-2.15 (1H, m), 1.77 (1H, dd, J = 3.8 Hz and J = 12.0 Hz), 1.32 (3H, t, J = 7 Hz), 1.16 (6H, s), 1.15-1.70 (4H, m).

(-)-**6** : $C_{17}H_{22}O_5$; white gum ; Anal.: calc % C : 66.65, H : 7.24 ; found : C : 66.82, H : 7.07 ; $[\alpha]_D$ = - 169 (c = 2.2 ; CH_2Cl_2) ; IR ($CHCl_3$) : 1764 (C=O), 1708 (C=O), 1606 (C = C) cm^{-1} ; ^{1}H-NMR ($CDCl_3$) : 6.74 (1H, s), 5.51 (1H, s), 4.21 (2H, q, J = 7 Hz), 3.09 (1H, t, J = 2 Hz), δ_A = 2.06, δ_B = 2.00 (2H, AB, J_{AB} = 5.7 Hz), 1.30 (3H, t, J = 7 Hz), 1.17 (3H, s), 1.15 (3H, s), 1.15-2.15 (6H, m).

*(1S,5R)-(-) ethyl 1-(trimethylsilyloxy) bicyclo [3.2.0.] hept-6-ene-7 carboxylate **7** :*

At room temperature, to (-)-**1** (233 mg ; 1.28 mmol) in CH_2Cl_2 (10 ml) is added triethylamine (326 mg ; 3.20 mmol) and then TMSOTf (310 mg ; 1.40 mmol). After stirring 1h30 at room temperature, water (20 ml) was added. After extraction with Et_2O (2 x 10 ml), the organic layer was washed with water (20 ml), dried ($MgSO_4$) and evaporated in vacuo to give 312 mg of crude material. This was chromatographed (10 g SiO_2 ; Et_2O/hexane: 5/95) yielding (-)-**7** (266 mg ; 82 %) as a colorless oil.

(-)-**7** : $C_{13}H_{22}O_3Si$; colorless oil ; Anal.: calc % C : 61.37, H : 8.71 ; found : C : 61.77, H : 8.9 ; $[\alpha]_D$ = - 79 (c = 0.93 ; CH_2Cl_2) ; ^1H-NMR ($CDCl_3$) : 6.71 (1H, s), 4.21 (2H, dq, J = 7.0 Hz and J = 2.5 Hz), 2.90 (1H, d, J = 5.5 Hz), 2.05-2.20 (1H, m), 1.20-1.80 (5H, m), 1.31 (3H, t), 0.12 (9H, m).

The same procedure was employed for the formation of (+)-7. (+)-**1** : 382 mg (2.10 mmol) ; NEt_3 : 508 mg (5.24 mmol) ; TMSOTf : 517 mg (2.30 mmol); CH_2Cl_2 :15 ml. The crude material (524 mg) was chromatographed (15 g SiO_2 ; Et_2O/hexane : 5/95) yielding (+)-**7** as a colorless oil (471 mg ; 88 %) ;
(+)-7 : $[\alpha]_D$ = + 79 (c = 1.18 ; CH_2Cl_2).

(1S,5R,6S,8R)-(-) ethyl 1-(trimethylsilyloxy) 7,7-dimethyl tricyclo [3.3.0.0^{6,8}] octane 8-carboxylate **8** *:*

Diazo-2 propane 2.59 M in ether (0.70 ml ; 1.80 mmol) was added at -78° C to a solution of (-)-**7** (230 mg ; 0.90mmol) in ether (20 ml). The reaction mixture was then allowed to reach 15° C and the ether was evaporated. The crude oil was dissolved in acetone (400 ml) and acetophenone (5.60 g ; 47.00 mmol) was added. The photolysis was started and after 10 min the stoechiometric amount of nitrogen (40 ml) was evolved. After evaporation (15 mmHg and then 10^{-1} mmHg) the crude reaction mixture (270 mg) was chromatographed (15 g SiO_2 ; hexane) yielding (-)-**8** (203 mg ; 75 %) as a colorless oil.

(-)-**8** : $C_{16}H_{28}O_3Si$; colorless oil ; Anal.: calc % C : 64.81, H : 9.51 ; found : C : 64.72, H : 9.63 ; $[\alpha]_D$ = - 4.4 (c = 0.90 ; CH_2Cl_2) ; IR (CCl_4) : 1718 (C=O) cm^{-1} ; ^1H-NMR ($CDCl_3$) : 4.18 (2H, d, J = 7 Hz), 2.14-2.30 (1H, m), 2.130 (1H, dd, J = 6 Hz), 1.50-1.80 (4H, m), 1.49 (3H, s), 1.20-1.40 (2H, m) ; 1.29 (3H, t, J = 7 Hz) 1.16 (3H, s), 0.15 (9H, s).

The same procedure was employed for the synthesis of (+)-**8**. Diazo-2 propane 2.59 M (1.40 ml ; 3.50 mmol) ; (+)-7 : 444 mg(1.75 mmol) ; Et_2O : 30ml ; acetophenone : 5.60 g (47.00 mmol). The crude material (470 mg) was chromatographed (15g SiO_2 ; hexane) yielding (+)-**8** as a colorless oil (380 mg ; 73%). ; $[\alpha]_D$ = + 4.4 (c = 0.9 ; CH_2Cl_2).

(1S,5R,6S,8R)-(-) ethyl 1-(hydroxy) 7,7-dimethyl tricyclo [3.3.0.0^{6,8}] octane 8-carboxylate **9** *:*

To a solution of (-)-**8** (114 mg ; 0.38 mmole) in CH_2Cl_2 (20 ml) was added at room temperature TBAF (1 M in THF ; 8 ml ; 8 mmol). After stirring overnight, water (10 ml) was added. After extraction with ether (2 x 10 ml), the organic layer was washed with brine (2 x 10 ml) and dried ($MgSO_4$). After evaporation in vacuo, the crude material (134 mg) was chromatographed (10 g SiO_2 ; Et_2O/hexane : 15/85) yielding (-)-**9** (98 mg ; 89 %) as a colorless oil.

(-)-**9** : $C_{13}H_{20}O_3$; colorless oil ; Anal.: calc % C : 69.61, H : 8.98 ; found : C : 69.8, H : 9.1 ; $[\alpha]_D$ = - 29 (c = 0.95 ; CH_2Cl_2) ; IR (CCl_4) : 3610 (OH), 3420 (OH), 1730 (C=O) cm^{-1} ; ^1H-NMR ($CDCl_3$) : 4.24 and 4.20 (2H, ABX_3, J_{AB} = 10.5 Hz, J_{AX} = 7.0 Hz and J_{BX} = 7.0 Hz ; $\Delta\upsilon$ = 15.5 Hz), 2.19 (2H, m), 1.52-1.97 (6H, m), 1.52 (3H, s), 1.29 (3H, t, J = 7 Hz), 1.16 (3H, s).

The same procedure was employed for the formation of (+)-**9** . (+)-**8** : 145mg (0.49 mmol); TBAF (1 M/THF) : 10 ml (10.00 mmol), CH_2Cl_2 : 20 ml. The crude material (207 mg) was chromatographed (10 g SiO_2 ; Et_2O/hexane : 15/85) yielding (+)-**9** (96 mg ; 90 %). $[\alpha]_D$ =+ 29 (c = 0.88, CH_2Cl_2).

(5R,6S)-(+)-ethyl 6-hydroxy 7,7-dimethyl bicyclo [3.3.0] oct-8-ene-8 carboxylate **10** *:*

At room temperature, to a solution of (-)-**9** (54 mg ; 0.24 mmol) in ether (20 ml) was added H_2SO_4 20 % (10 ml). This reaction mixture was brought to reflux during 20 h. After cooling, the reaction mixture was extracted with ether (2 x 10 ml), washed with a saturated $NaHCO_3$ solution (2 x 10 ml), brine (2 x 10 ml) and dried ($MgSO_4$). After evaporation in vacuo, the crude material (61 mg) was chromatographed (3 g SiO_2 ; Et_2O/hexane: 20/80) yielding (+)-**10** (54 mg ; quant.) as a colorless oil.

(+)-**10** : $C_{13}H_{20}O_3$; colorless oil ; Anal.: calc % C : 69.61, H : 8.98 ; found : C : 69.5, H : 8.8 ; $[\alpha]_D$ = + 114 (c = 0.80 ; CH_2Cl_2) ; IR ($CHCl_3$) : 3610 (OH), 3400 (OH), 1696 (C=O) cm^{-1} ; ^1H-NMR ($CDCl_3$) : 4.18 (2H, dq, J = 7 Hz), 3.57 (1H, d, J = 8.4), 2.80-3.00 (1H, m), 2.40-2.80 (2H, m), 1.50-2.30 (4H, m), 1.29 (3H, t, J = 7 Hz), 1.27 (3H, s), 1.14 (3H, s).

The same procedure was employed for the synthesis of (-)-**10** . (+)-**9** : 75 mg (0.33 mmol); H_2SO_4 20 % : 10 ml ; Et_2O : 20 ml. The crude material (80 mg) was chromatographed (3 g SiO_2 ; Et_2O/hexane : 20/80) yielding (-)-**10** (75 mg ; quant.) as a colorless oil. $[\alpha]_D$ = - 113 (c = 0.97, CH_2Cl_2).

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