SUPPORTING INFORMATION FOR:

Enantioselective Synthesis Of Syn- and Anti-1,3-Diols Via Allyltitanation Of Unprotected β-Hydroxyaldehydes

Samir BouzBouz*, Janine Cossy*

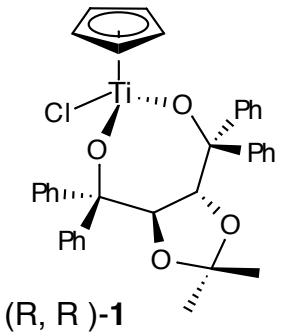
Laboratoire de Chimie Organique associé au CNRS, ESPCI,
10, rueVauquelin 75231 - Paris Cedex 05 - France

General experimental:

All the reactions were carried out under an argon atmosphere. Solvents, reagents were purified beyond reagent grade as follows: diethyl ether was distilled from Na/benzophenone. Thin layer chromatography was performed on Merck Kieselgel 60 F_{254} plates eluting with the solvents indicated, visualized by a 254 nm UV lamp, and stained with ethanolic solution of *p*-anisaldehyde. Nuclear magnetic resonnance spectra were acquiered on unity 300 spectrometer at 300 MHz for ^{1}H, and 75 MHz for ^{13}C. Optical rotations were obtained on a Perkin Elmer 241 mc polarimeter using a microcell with a 1 dm path length. Concentration are reported in g/100 mL.

Representative procedure for the preparation of 1,3-diols:

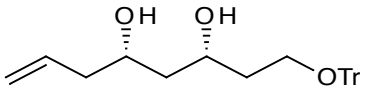
The hydroxy olefin **5** (0.09 g, 0.25 mmol) was dissolved in ether:H_2O (1:1; 6 mL), OsO_4 (0.5 mL, solution in *t*-BuOH, 20 mol %, 2.5 % by weight) was added at 0 °C and the mixture was vigourously stirred for 10 min at 25 °C. $NaIO_4$ (0.215 g, 1 mmol) was then added portionwise over 40 min, and the mixture was vigorously stirred at 25 °C. After completion of the reaction (indicated by TLC), the solution was diluted with ether. The organic phase was separated, dried ($MgSO_4$), and concentrated to furnished the crude hydroxy aldehyde **10** (0.075 g). The crude hydroxy aldehyde was used immediately for the preparation of the diols. Allylmagnesium chloride in THF (0.11 mL, 2M solution, 0.22 mmol) was added dropwise over 3 min at 0° C to a solution of (*R*, *R*)-**1** (0.16 g, 0.27 mmol) in ether (5 mL). After stirring for 2 h at 0 °C, the slightly orange suspension was cooled at – 78 °C, and the crude aldehyde dissolved in ether (3 ml), was added over 5 min. After 4 h at -78 °C, the reaction mixture was then treated with water (10 mL) stirred for 14 h, filtrered trough Celite, and extracted with ether (2x20 mL) and then with ethyl acetate (10 mL). The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated. Purification of the residue by flash chromatography on silica gel (AcOEt/hexanes: 3/7) gave diol **15** (0.066 g 0.16 mmol, 79%).



(R, R)-**1**

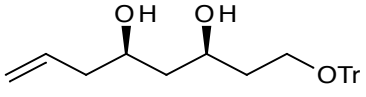
Representative procedure for the preparation of the acetonide:

To a solution of diol **15** (0.06 g, 0.15 mmol) in acetone (1mL) was added sequentielly 2,2-dimethoxypropane (1mL) and CSA (5 mg, 0.07 mmol). After 30 min at 25 °C. The reaction mixture was quenched with Et_3N (0.05mL) and then concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (AcOEt/hexanes: 3/7) to give acetonide **23** (0.061; g 93 %) as a colorless oil .



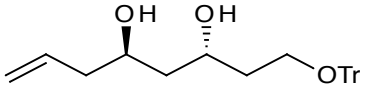
(-)-(3*R*,5*S*)-1-(trityloxy)oct-7-ene-3,5-diol **15**

Colorless solid: mp 98-100 °C. $[\alpha]^{22}_{D}$ = -12.1 (*c* 3, $CHCl_3$). R_f 0.3 (EtOAc/hexanes: 3/7); IR: 3301, 2950 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) *δ*: 7.48-7.30 (m, 15H), 5.90-5.75 (m, 1H), 5.12-5.05 (m, 2H), 4.05 (m, 1H), 3.90 (m, 1H), 3.61 (br s, 1H, OH), 3.52 (br s, 1H, OH), 3.39-3.21 (m, 2H), 2.23 (m, 2H), 1.90-1.71 (m, 2H), 1.54 (m, 2H); ^{13}C NMR (75MHz, $CDCl_3$) *δ*: 143.6 (s), 134.6 (d), 128.4 (d), 127.8 (d), 127.0 (d), 117.5 (t), 87.2 (s), 72.0 (d), 71.4 (d), 61.9 (t), 42.2 (t), 42.1 (t), 37.1 (t); HRMS (FAB$^+$-NBA+Na) calcd for $C_{27}H_{30}O_3Na$, 425.2093. Found 425.2087.



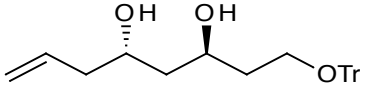
(+)-(3*S*,5*R*)-1-(trityloxy)oct-7-ene-3,5-diol **17**

Colorless solid: mp 98-100 °C. $[\alpha]^{22}_{D}$ = +12.3 (*c* 3, $CHCl_3$). R_f 0.3 (EtOAc/hexanes: 3/7); IR: 3301, 2950 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) *δ*: 7.48-7.30 (m, 15H), 5.90-5.75 (m, 1H), 5.12-5.05 (m, 2H), 4.05 (m, 1H), 3.90 (m, 1H), 3.61 (br s, 1H, OH), 3.52 (br s, 1H, OH), 3.39-3.21 (m, 2H), 2.23 (m, 2H), 1.90-1.71 (m, 2H), 1.54 (m, 2H); ^{13}C NMR (75MHz, $CDCl_3$) *δ*: 143.6 (s), 134.6 (d), 128.4 (d), 127.8 (d), 127.0 (d), 117.5 (t), 87.2 (s), 72.0 (d), 71.4 (d), 61.9 (t), 42.2 (t), 42.1 (t), 37.1 (t); Anal. Calcd for $C_{27}H_{30}O_3$: C, 80.56; H, 7.67. Found: C, 80.48; H, 7.66.



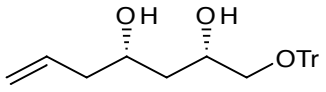
(-)-(3*R*,5*R*)-1-(trityloxy)oct-7-ene-3,5-diol **16**

Colorless oil. $[\alpha]^{22}_{D}$ = -24 (*c* 1.97, $CHCl_3$). R_f 0.31 (EtOAc/hexanes: 3/7); IR: 3301, 2950 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) *δ*: 7.45-7.22 (m, 15H), 5.90-5.75 (m, 1H), 5.15-5.07 (m, 2H), 4.12 (m, 1H), 4.01 (m, 1H), 3.45 (br s, 1H, OH), 3.48-3.20 (m, 2H), 2.71 (br s, 1H, OH), 2.25 (m, 2H), 1.93 (m, 1H), 1.75-1.55 (m, 3H); ^{13}C NMR (75MHz, $CDCl_3$) *δ*: 143.6 (s), 134.7 (d), 128.4 (d), 127.8 (d), 127.0 (d), 117.6 (t), 87.3 (s), 68.9 (d), 67.9 (d), 62.6 (t), 42.0 (t), 41.9 (t), 36.5 (t); HRMS (FAB$^+$-NBA+Na) calcd for $C_{27}H_{30}O_3Na$ (M+Na) 425.2093. Found 425.2079.



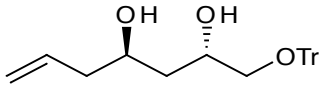
(+)-(3*S*,5*S*)-1-(trityloxy)oct-7-ene-3,5-diol **18**

Colorless oil. $[\alpha]^{22}_{D}$ = +21 (*c* 0.81, $CHCl_3$). R_f 0.31 (EtOAc/hexanes: 3/7); IR: 3301, 2950 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) *δ*: 7.45-7.22 (m, 15H), 5.90-5.75 (m, 1H), 5.15-5.07 (m, 2H), 4.12 (m, 1H), 4.01 (m, 1H), 3.45 (br s, 1H, OH), 3.48-3.20 (m, 2H), 2.71 (br s, 1H, OH), 2.25 (m, 2H), 1.93 (m, 1H), 1.75-1.55 (m, 3H); ^{13}C NMR (75MHz, $CDCl_3$) *δ*: 143.6 (s), 134.7 (d), 128.4 (d), 127.8 (d), 127.0 (d), 117.6 (t), 87.3 (s), 68.9 (d), 67.9 (d), 62.6 (t), 42.0 (t), 41.9 (t), 36.5 (t); HRMS (FAB$^+$-NBA+Na) calcd for $C_{27}H_{30}O_3Na$ 425.2093. Found 425.2101.



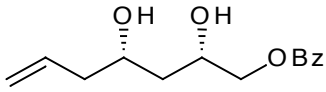
(+)-(2*S*,4*S*)-1-(trityloxy)hept-6-ene-2,4-diol **19**

Colorless oil. $[\alpha]^{22}_{D}$ = +5.2 (*c* 0.7, $CHCl_3$). R_f 0.26 (EtOAc/hexanes: 3/7); IR: 3301, 2950 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) *δ*: 7.50-7.25 (m, 15H), 5.90-5.75 (m, 1H), 5.14-5.04 (m, 2H), 4.08 (m, 1H), 3.92 (m, 1H), 3.25 (br s, 1H, OH), 3.15 (m, 2H), 3.07 (br s, 1H, OH), 2.25 (m, 2H), 1.57 (m, 2H); ^{13}C NMR (75MHz, $CDCl_3$) *δ*: 143.6 (s), 134.4 (d), 128.5 (d), 127.6 (d), 127.0 (d), 117.7 (t), 86.6 (s), 71.6 (d), 71.1 (d), 67.5 (t), 42.0 (t), 38.7 (t); HRMS (FAB^+-NBA+Na) calcd for $C_{26}H_{28}O_3Na$ 411.1936. Found 411.1956.



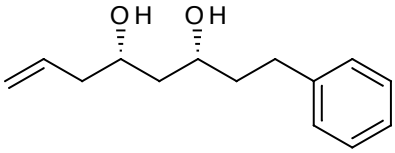
(+)-(2*S*,4*R*)-1-(trityloxy)hept-6-ene-2,4-diol **20**

Colorless oil. $[\alpha]^{22}_{D}$ = +4 (*c* 1.7, $CHCl_3$). R_f 0.28 (EtOAc/hexanes: 3/7); IR: 3301, 2950 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) *δ*: 7.45-7.20 (m, 15H), 5.90-5.72 (m, 1H), 5.14-5.04 (m, 2H), 4.12 (m, 1H), 3.90 (m, 1H), 3.20-3.08 (m, 2H), 2.81 (br s, 1H, OH), 2.43 (br s, 1H, OH), 2.23 (m, 2H), 1.65-1.51 (m, 2H); ^{13}C NMR (75MHz, $CDCl_3$) *δ*: 143.7 (s), 134.6 (d), 128.6 (d), 127.8 (d), 127.1 (d), 117.9 (t), 86.7 (s), 68.2 (d), 67.6 (d), 67.4 (t), 41.9 (t), 38.6 (t); HRMS (FAB^+-NBA+Na) calcd for $C_{26}H_{28}O_3Na$ 411.1936. Found 411.1931.



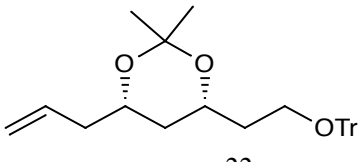
(+)-(3*R*,5*S*)-1-(trityloxy)hept-6-ene-1,2,4-triol-1-benzoate **21**

Colorless oil. $[\alpha]^{22}_{D}$ = +6.2 (*c* 1, $CHCl_3$). R_f 0.25 (EtOAc/hexanes: 3/7); IR: 3301, 2935, 1715 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) *δ*: 8.10-7.81 (m, 5H), 5.90-5.72 (m, 1H), 5.16-5.04 (m, 2H), 4.42-4.20 (m, 3H, $C\underline{H}_2OBz$ and $C\underline{H}OH$), 3.98 (m, 1H), 3.85 (br s, 1H, OH), 3.32 (br s, 1H, OH), 2.33 (m, 2H), 1.80-1.62 (m, 2H); ^{13}C NMR (75MHz, $CDCl_3$) *δ*: 166.6(s), 133.9 (d), 133.0 (d), 129.7(s), 129.52 (d), 128.3 (d), 118.3 (t), 71.0 (d), 70.4 (d), 68.7 (t), 42.2 (t), 38.6 (t); HRMS (CI^+) calcd for $C_{14}H_{19}O_4$ (M+1) 251.1283. Found 251.1281; Anal. Calcd for $C_{14}H_{18}O_4$: C, 67.18; H, 7.25 . Found: C, 67.12; H, 7.19.



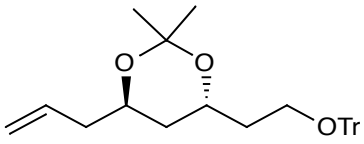
(+)-(4*S*,6*R*)-8-(Phenyloxy)oct-1-ene-4,6-diol **22**

Colorless oil. $[\alpha]^{22}_{D}$ = +16.4 (*c* 1.1, $CHCl_3$), Lit[1] ($[\alpha]^{25}_{D}$ = +17.2 (*c* 1.23, $CHCl_3$)). R_f 0.26 (EtOAc/hexanes: 3/7); IR: 3350, 2935 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) *δ*: 7.30-7.12 (m, 5H), 5.90-5.75 (m, 1H), 5.18-5.12 (m, 2H), 3.89 (m, 1H), 3.50 (br s, 1H, OH), 3.20 (br s, 1H, OH), 2.85-2.65 (m, 2H), 2.25 (m, 2H), 1.89-1.50 (m, 4H); ^{13}C NMR (75MHz, $CDCl_3$) *δ*: 141.9(s), 134.2 (d), 128.4 (d), 128.4 (d), 125.9 (d), 118.3 (t), 72.8 (d), 71.8 (d), 42.6 (t), 42.4 (t), 39.6 (t), 31.6 (t); HRMS (CI^+) calcd for $C_{14}H_{21}O_2$ (M+1) 221.1542. Found 221.1535.



(-)-(4*S*,6R)-4-allyl-2,2-dimethyl-6-[2-(trityloxy)ethyl]-1,3-dioxane **23**

Colorless oil. $[\alpha]^{22}_{D}$ = -4.1 (*c* 0.84, $CHCl_3$). R_f 0.45 (EtOAc/hexanes: 1/9); IR: 2935 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 7.45-7.20 (m, 15H), 5.85-5.75 (m, 1H), 5.11-5.01 (m, 2H), 4.12 (m, 1H), 3.85 (m, 1H), 3.32-3.01 (m, 2H), 2.40-2.14 (m, 2H), 1.75 (m, 2H), 1.45 (s, 3H), 1.37 (s, 3H), 1.52-1.21 (m, 2H); ^{13}C NMR (75MHz, $CDCl_3$) δ: 144.2 (s), 134.1 (d), 128.5 (d), 127.5 (d), 126.7 (d), 116.7 (t), 98.3 (s), 86.2 (s), 68.5 (d), 66.1 (d), 59.0 (t), 40.7 (t), 36.8 (t), 36.5 (t), 30.1 (q), 19.6 (q); MS *m/z* 442 (M, 0.1) 427 (6), 243 (100), 165 (25), 141 (5), 105 (10); Anal. Calcd for $C_{30}H_{34}O_3$: C, 81.41; H, 7.74 . Found: C, 81.40; H, 7.71.



(-)-(4*R*,6*R*)-4-allyl-2,2-dimethyl-6-[2-(trityloxy)ethyl]-1,3-dioxane **24**

Colorless oil. $[\alpha]^{22}_{D}$ = -6.3 (*c* 2.2, $CHCl_3$). R_f 0.43 (EtOAc/hexanes: 1/9); IR: 2935 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 7.49-7.22 (m, 15H), 5.85-5.70 (m, 1H), 5.12-5.01 (m, 2H), 4.05 (m, 1H), 3.85 (m, 1H), 3.12-3.08 (m, 2H), 2.35-2.12 (m, 2H), 1.75 (m, 2H), 1.65-1.52 (m, 2H), 1.25 (s, 6H); ^{13}C NMR (75MHz, $CDCl_3$) δ: 144.2 (s), 134.3 (d), 128.5 (d), 127.6 (d), 126.7 (d), 116.6 (t), 100.1 (s), 86.2 (s), 66.1 (d), 65.9 (d), 59.5 (t), 40.0 (t), 37.9 (t), 36.2 (t), 24.8 (q), 24.7 (q); Anal. Calcd for $C_{30}H_{34}O_3$: C, 81.4; H, 7.74 . Found: C, 81.34; H, 7.81.

Reference

1- Rychnovsky, S. D.; Griesgraber, G.; Zeller, S.; Skalitzky, D. J. *J. Org. Chem.* **1991**, *56*, 5161.