Pergamon

Tetrahedron, Vol. 52, No. 47, pp. 14877-14890, 1996

0040-4020/96 $15.00 + 0.00

PII: S0040-4020(96)00918-0

Enantioselective Synthesis of (+)-Goniodiol and of its Naturally Occurring Acetylated Analogs

Jean-Philippe Surivet, Jacques Goré and Jean-Michel Vatèle*

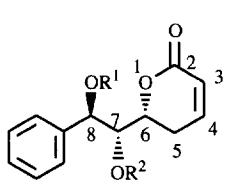
Laboratoire de Chimie Organique I, associé au CNRS, Université Claude Bernard CPE-Lyon, 43 Bd. du 11 Novembre 1918, 69622 Villeurbanne, France.
Fax (33) 72.43.12.14

Abstract : A novel route to enantioenriched (+)-goniodiol and its natural acetylated derivatives, potent cytotoxic compounds, is described. The main features of this synthesis are transfer of the asymmetric information of the scalemic allenic alcohol **5** to the α- and β- carbons through highly diastereoselective reactions and introduction of the α,β-unsaturated lactone moiety by the Ghosez' methodology. Copyright © 1996 Elsevier Science Ltd

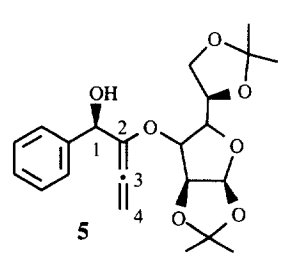
Introduction

Asian trees of the genus *Goniothalamus* have a wide variety of uses in folk medecine. Thus, the powder of dried leaves of *Goniothalamus sesquipedalis* Wall (Annonaceae) is taken by women during labor pain and the burning leaves are used as mosquito repellant.[1] Extracts of seeds of *Goniothalamus amuyon* have been used for the treatment of edema and rheumatism.[2] Bioactivity-directed studies on the constituents of these plants by McLaughlin and Coll.[3] and others[1,2,4] have led to the isolation of several classes of biologically active compounds (acetogenins, alkaloids, styryllactones).

Styryllactones **1-3** have been isolated from the petrol extract of powdered leaves and twigs of *Goniothalamus sesquipedalis* [5] whereas goniodiol-8-monoacetate **4** has been isolated from the leaves of *Goniothalamus amuyon*.[6]



1 $R^1 = R^2 = H$ **2** $R^1 = H$, $R^2 = Ac$
3 $R^1 = R^2 = Ac$ **4** $R^1 = Ac$, $R^2 = H$



5

Goniodiol **1** and its acetylated derivatives **2-4** have significant toxicity against several tumor cell lines,[2,5a,6] the former presenting the interesting feature of being selectively cytotoxic against A-549 human lung carcinoma.[5a] The structure and the relative configuration of compounds **1-4** were determined by NMR spectral and/or X-ray crytallographic analysis. These compounds contain a 6-substituted 5,6-dihydro-α-pyrone moiety, widely distributed in the plant kingdom. Natural products containing this lactone unit also possess a wide range of biological activity (insect antifeedants, antifungal, plant growth inhibitors,...).[7]

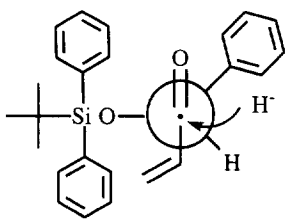
In the course of our program directed toward the enantioselective synthesis of styryllactones, we have recently reported in a preliminary account the total synthesis of scalemic goniodiol **1**.[8] We report herein details of this synthetic study and of its mono-and diacetylated derivatives starting from the allenic alcohol **5**. The chiral information carried by **5** was introduced by a diastereoselective addition[9] of the lithium salt of 3-O-allenyl diacetone-D-glucose[10] to benzaldehyde (de = 92%).

The key steps involved in the synthetic route of goniodiol **1** are (1) transfer of the chiral information contained in C-1 of **5** to C-2 and C-3 by three highly diastereoselective reactions (2) introduction of the α,β-insaturated δ-lactone unit using Ghosez' methodology.[11]

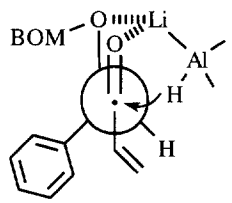
Results and Discussion

In the original synthetic strategy of compound **1**, we envisaged to introduce the chiral centre at C-6 by a $VO(acac)_2$-catalysed *erythro*-selective epoxidation of the double bond of the monoprotected diol **8** or **9** directed by the adjacent hydroxyl functionality (7-OH of **1**). In order to get this alcohol group in the proper configuration, we examined the reduction with various hydride agents of the two differently protected racemic α',β'-insatured α-ketol **7a** and **7b**, readily obtained from methoxyallene[12] (Scheme 1).

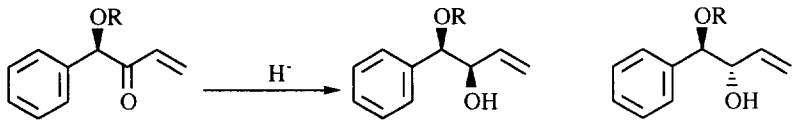
As seen in Table 1, the highest selectivity of the reduction (entry 7, de > 92%) was obtained from the enone **7b** under Luche conditions[13] and must proceed through conformer A (Felkin-Anh open-chain model)[14] where the steric interactions between allyl and phenyl groups are minimized. In the case of the reduction of the α-ketol **7a**, good *anti*-selectivity was observed using $LiAlH_4$ as reducing agent (entries 1 and 2) and can be explained by the Cram chelation model[15] involving a five membered chelated ring (conformer B).



A



B



7a R = CH_2OCH_2Ph (BOM) **8a** **8b**
7b R = $SitBuPh_2$ (TBDPS) **9a** **9b**

Scheme 1

Table 1 : Metal hydride reduction of α-alkoxy ketones **7a** and **7b**.

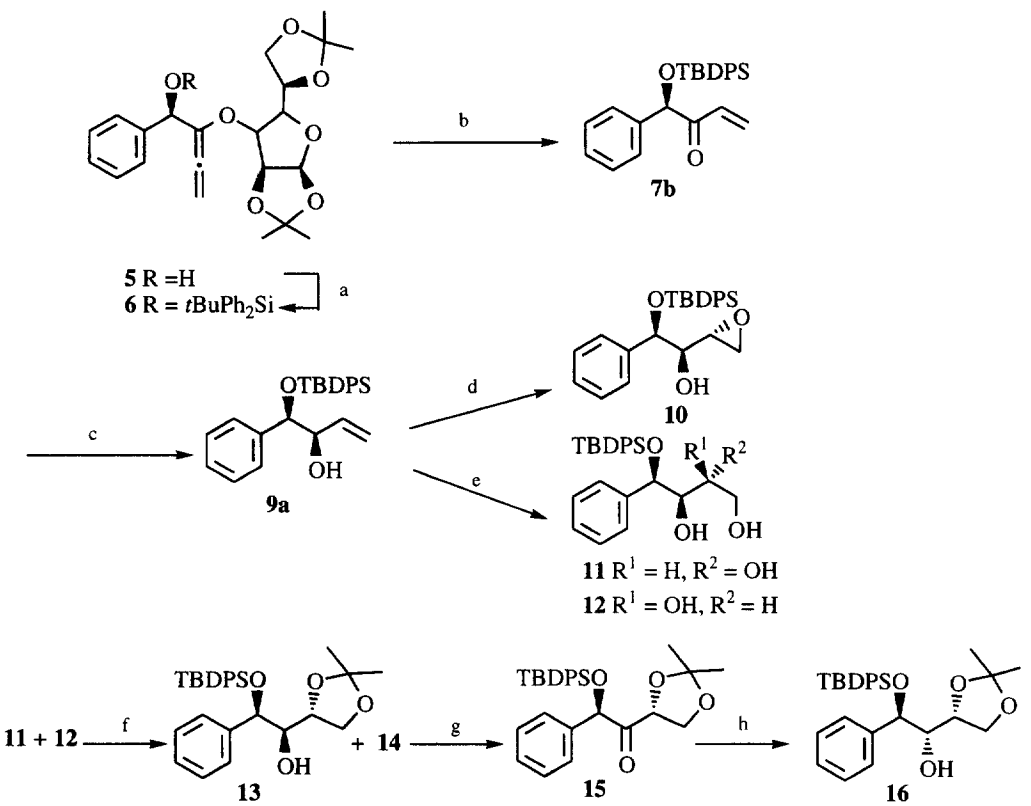
Entry	Substrate	Reagent	Solvent	Temp.	Ratio[a] (*syn* : *anti*)	Yield (%)
1	**7a**	$LiAlH_4$	Et_2O	- 78°C	25 : 75	60[b]
2		$LiAlH_4$	THF	"	23 : 77	-[c]
3		Red-Al®	Toluene	"	20 : 80	55
4		L-Selectride®	THF	"	86 : 14	68[b]
5		$NaBH_4$-$CeCl_3$	MeOH	"	88 : 12	92[b]
6	**7b**	$LiAlH_4$	Et_2O	"	83 : 17[d]	60
7		$NaBH_4$-$CeCl_3$	MeOH	"	96 : 4[e]	98

[a] Relative stereochemistry of diastereomers **8a,b** was established by ^1H NMR spectroscopy[16] and that of diastereomers **9a, b** by comparison of the spectral data of their corresponding diols with the published values.[16,17] [b] The diastereomeric ratio was determined by GLC analysis after acetylation. [c] In this case, the diastereomeric mixture of **8a, b** was not isolated. [d] Under the reaction conditions, **9a, b** was desilylated and the diastereomeric ratio was determined by GLC analysis of the corresponding diacetate derivative. [e] The diastereomeric ratio was determined by ^1H NMR analysis.

Having set up the reaction conditions to obtain highly diastereoselectively **9a** from **7b**, easily made in two steps from **5** by O-silylation and acidic hydrolysis[9] in 81% overall yield, we turned our attention to the epoxidation of the terminal double bond. Epoxidation of allylic alcohol **9a** with $VO(acac)_2$-*t*-BuOOH system[18a,b] in CH_2Cl_2 was not very successful providing, beside several by-products, the epoxy alcohol **10** in 30% yield after stirring for 3 days at 0°C (Scheme 2). The diastereoselectivity of this epoxidation was high in favor of the *erythro* isomer (dr 95 : 5) as determined by ^{13}C NMR spectroscopy. The assignment of the relative configuration of the major epoxide **10** (1,2-*syn*, 2,3-*anti*) by ^1H NMR analysis was based on the results of Mihelich[18b] who observed that the α-proton of the *erythro* epoxide was constantly downfield from that of its *threo* isomer (3.81ppm versus 3.62ppm) and the coupling constant of the *erythro* epoxide was invariably smaller from that of its *threo* isomer (J = 5.2Hz versus J = 6.4Hz).
Other epoxidizing agents gave either poor selectivity (MCPBA, 1:1) or reacted very sluggishly (H_2WO_4, H_2O_2[19] ; L-(+)-DIPT, Ti(O*i*Pr)4, *t*-BuOOH).

Fortunately, dihydroxylation of **9a** with osmium tetroxide in the presence of N-methylmorpholine N-oxide monohydrate (NMO)[20], gave an unseparable mixture of triols **11** and **12** with a good level of diastereoselectivity (dr 8 : 1) and in excellent yield (90%). Based on the empirical rule of Kishi[21], the relative configuration of the major isomer **11** was tentatively assigned to be 1,2-*syn*, 2,3-*anti*. After treatment of the

mixture **11 and 12** by 2-methoxypropene in the presence of camphorsulfonic acid, the resulting acetonides **13-14**, obtained in 92% yield, were easily separable by flash chromatography. The next stage of the synthesis, the configurational inversion of the stereocenter at C-2 of alcohol **13**, was effected by an oxidation-reduction sequence. Thus, oxidation of **13** by the TPAP catalytic system[22] [$Pr_4N^+RuO_4^-$(TPAP) 2 mole %, NMO (4 equiv.), 4Å molecular sieves] followed by L-Selectride®[23d] reduction of the ensuing ketone **15**, at -100°C, correctly set up the C-2 stereogenic center with 12 : 1 diastereoselection to afford alcohol **16** in 72% yield along with **13** (6% yield) and the starting ketone **15** (20%).



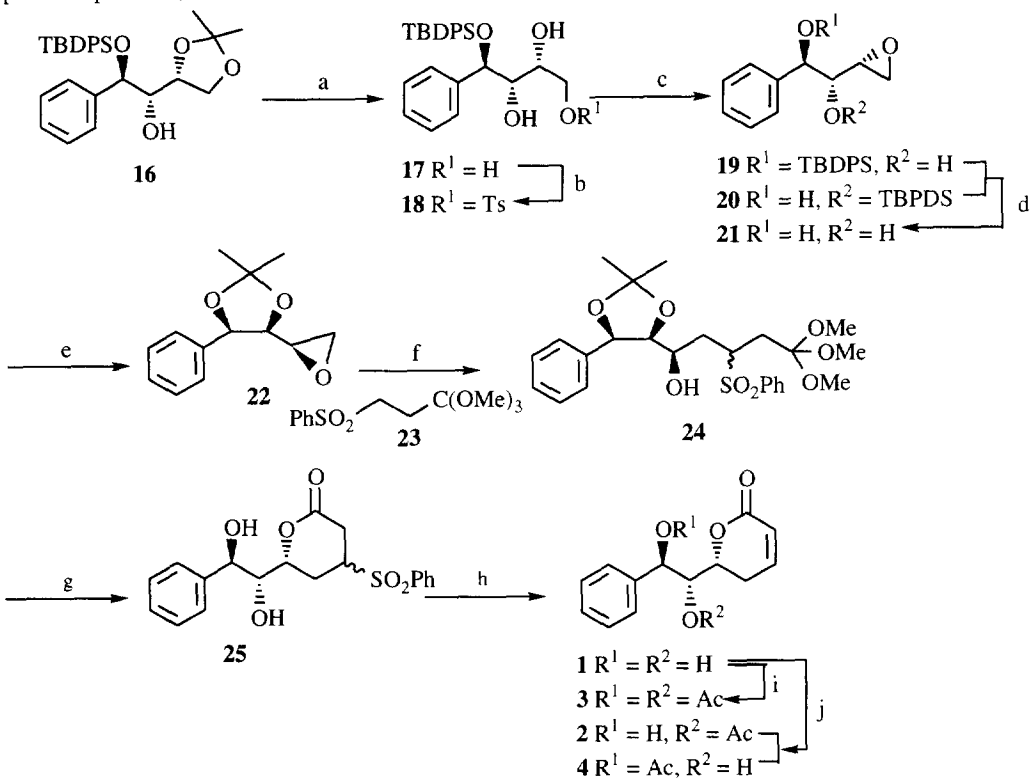
Scheme 2

Reagents and conditions : (a) *t*-$BuPh_2SiCl$, DMAP, CH_2Cl_2, 3 days ; (b) 50% CF_3CO_2H-CH_2Cl_2, 3 h (81% for the 2 steps) ; (c) $NaBH_4$, $CeCl_3.7H_2O$, MeOH, 1 h, -78°C (98%) ; (d) $VO(acac)_2$, TBHP, CH_2Cl_2, 0°C (30%) ; (e) cat. OsO_4, NMO, 5 h, RT, acetone (90%) ; (f) 2-methoxypropene, camphorsulfonic acid, CH_2Cl_2, RT, 10 min then separation by SiO_2 chromatography (83% yield for **13**) ; (g) cat. $Pr_4N^+RuO_4^-$, NMO, 4Å sieves, CH_2Cl_2, RT, 1 h ; (h) L-Selectride®, THF, -100°C, 1 h (72% for two steps).

Next, we focused our attention to the formation of epoxide **22** from the protected tetrol **16** (Scheme 3). After acidic hydrolysis of the acetal function of **16**, the resulting triol **17** was converted to the monotosylate **18** by reaction with 1 equivalent of p-toluenesulfonyl chloride, in the presence of 1 equivalent of 4-dimethylaminopyridine and an excess of triethylamine. Epoxide formation by treatment of the 1,2-tosyloxy

alcohol **18** with NaH in the presence of an catalytic amount of DMSO[24] occurred with partial 1,2-O-silyl group migration to yield a mixture of regioisomers **19** and **20** in 2 : 3 ratio and 57% yield. Desilylation of **19** and **20** effected by NBu4F in THF, followed by acid catalyzed ketalisation (2-methoxypropene, CSA) of the resulting diol **21** furnished the protected diol epoxide **22** in 68% overall yield.

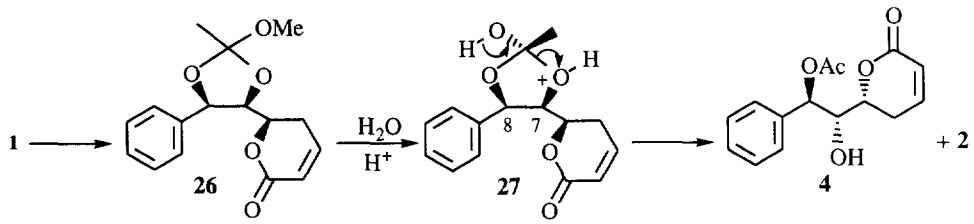
At this stage, the remaining task for the synthesis of (+)-goniodiol **1** was the installation of the α,β-unsaturated-δ-lactone fragment using the Ghosez' methodology.[12] Hence, addition of 2 equivalents of methyl 3-phenylsulfonyl orthopropionate **23**, easily prepared in three steps from acrylonitrile[25], in the presence of 2 equivalents of $BF_3.Et_2O$ followed by treatment of the crude γ-hydroxy sulfone **24** with 3M H_2SO_4 at 50°C yielded the β-sulfonyl lactone **25**. Finally, exposure of **25** to DBU in CH_2Cl_2 afforded scalemic (+)-goniodiol **1** in 60% yield from epoxide **22**. Its spectral and physical properties were in accord with the published data.[1,5a] Acetylation of (-)-**1** with acetic anhydride and pyridine gave diacetyl goniodiol **3** as needles mp 148-150°C; $[\alpha]_D^{20}$ + 78 (c 0,9, $CHCl_3$)] [lit.[1] mp 150°C, $[\alpha]_D^{30}$ + 84,5 ($CHCl_3$)]. Spectroscopic data (^1H and ^{13}C NMR, IR) were found identical with those of the natural product.[1,6]



Scheme 3

Reagents and Conditions : (a) 80% AcOH, 60°C, 2 h (77%) ; (b) p.TsCl, Et_3N, DMAP, CH_2Cl_2, -20°C, overnight (72%) ; (c) NaH, THF-DMSO (50:1), 0°C, 1 h (57%) ; (d) NBu4F, THF ; (e) 2-methoxypropene, camphorsulfonic acid, CH_2Cl_2, 10 min, RT (68% for the two steps) ; (f) **23**, n-BuLi, $BF_3.Et_2O$, THF, -78°C, 30 min ; then epoxide **22**, -78°C, RT, 2 h ; (g) 3M H_2SO_4, 50°C, 3 h ; (h) 3 equiv DBU, CH_2Cl_2, 1 h, 0°C (60% yield from the epoxide **22**). ; (i) Ac_2O, pyridine, RT, 12h (80%) ; (j) methyl orthoacetate, *p*-TsOH, CH_2Cl_2, RT, 10 min, then AcOH 80%, RT, 10 min (88%).

Monoacetylation of goniodiol **1** was accomplished by reaction with methyl orthoacetate in the presence of a catalytic amount of p-toluenesulfonic acid followed by treatment of the resulting orthoester **26** (Scheme 4) with aqueous acetic acid to afford mainly the 8-monoacetate **4** (72% yield) along with the 7-monoacetate **2** (16% yield). As suggested by Deslongchamps[26] and King[27] on five membered ring orthoester-derived from sugars, we assumed that the origin of the regioselectivity of the orthoester hydrolysis could be attributed to a combination of steric and stereoelectronic factors which must favor the preferential protonation of O-7 of the hemi-orthoester intermediate **27**[27] (Scheme 3).



Scheme 4

In summary, we have reported a new synthesis of enantioenriched (+)-goniodiol **1** and its acetylated derivatives **2-4** from the readily available benzaldehyde/ 3-O-allenyl diacetone-D-glucose adduct in 15 steps and 5% overall for **1**. Other synthetic applications of optically active alkoxyallenes are currently studied in our laboratory.

Experimental section

General. ^1H NMR spectra were recorded in $CDCl_3$ (δH = 7.25) at ambient probe temperature on a Bruker AC 200 (200MHz) spectrometer. Data are presented as follows : chemical shift (in ppm on the δ scale relative to δ_{TMS} = 0), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), integration, coupling constant and interpretation. ^{13}C NMR spectra were recorded at ambient probe temperatures on Bruker AC 200 (50.3 MHz) in $CDCl_3$ used as reference (δ_c 77.0). IR spectra were recorded on a Perkin-Elmer 298 spectrophotometer using 5mm sodium chloride plates. Mass spectra were carried out on a Nermag R10-10 H quadrupole mass spectrometer. Optical rotations were measured on a Perkin-Elmer 141 polarimeter at the sodium D line (589 mm). Combustion analyses were performed by the Service Central de Microanalyse, CNRS, Solaize.

Reagents and solvents were purified by standard means. Boron trifluoride-etherate, dichloromethane, pyridine, toluene and triethylamine were distilled from calcium hydride ; diethyl ether, tetrahydrofuran were distilled from sodium wire / benzophenone and stored under a nitrogen atmosphere. All other chemicals were used as received. Unless otherwise stated, all experiments were performed under anhydrous conditions in an atmosphere of nitrogen.

4-Benzyloxymethyl-4-phenylbut-1-en-3-one (7a). To a cooled (0°C) solution of 2-methoxy-2-phenylbuta-2,3-dien-1-ol[12] (1 g, 5.6 mmol) in CH_2Cl_2 (25 ml) were added diisopropylamine (4.6 ml, 24 mmol) followed by benzyloxymethyl chloride (1.7 ml, 12 mmol). After stirring for 4 days at room

temperature, the reaction mixture was diluted with CH_2Cl_2 (20 ml) and water (20 ml) and the mixture was acidified at pH 2 by 2N HCl solution. The aqueous phase was extracted with CH_2Cl_2 (3 x 20 ml) and the combined organic extracts were dried ($MgSO_4$) and evaporated to dryness. The crude mixture was diluted with CH_2Cl_2 (20 ml) and 6N HCl (5 ml) was added at 0°C. After stirring for 30 min at 0°C, the mixture was partitioned between CH_2Cl_2 (20 ml) and water (20 ml). The aqueous phase was extracted with CH_2Cl_2 (25 ml), dried over magnesium sulfate and concentrated *in vacuo*. The residue was purified by flash chromatography (Et_2O-petroleum ether, 3:7) to give **7a** as an oil (0.97g, 61% yield) : IR (neat) 3010, 1700, 1620, 1100, 700 cm^{-1} ; ^1H NMR : 4.61 (d, 1H, J=11.7Hz, C<u>H</u>$_2$Ph), 4.65 (d, 1H, J=11.7Hz, C<u>H</u>$_2$Ph), 4.85 (d, 1H, J=6.9Hz, C<u>H</u>$_2$Ph), 4.89 (d, 1H, J=6.9Hz, C<u>H</u>$_2$Ph), 5,37 (s, 1H, C<u>H</u>OBOM), 5,72 (dd, 1H J=1.8 and 10.3Hz, CH=C<u>H</u>$_2$), 6.38 (dd, 1H, J=1.8 and 17.4Hz, CH=C<u>H</u>$_2$), 6.63 (dd, 1H,J=10.3 and 17.4Hz, C<u>H</u>=CH$_2$), 7.2-7.5 (m, 10H, Ph) ; ^{13}C NMR : 70.7, 83.1, 93.8, 128.2 (2C), 128.3, 128.5 (2C), 129.0 (2C), 129.3, 129.5 (2C), 130.3, 132.2, 136.0, 138.1, 196.5 ; MS *m/z* (relative intensity) : 227 [(19) M^+-C_3H_3O], 197 (16), 91 (100), 55 (16).

(R)-4-(t-Butyldiphenylsilyloxy)-4-phenylbut-1-en-3-one (7b). To a solution of allenic alcohol[9,10] (5.8 g, 14.3mmol) in CH_2Cl_2 (50 ml) were successively added at 0°C 4-dimethylaminopyridine (0.52 g, 0.25 mmol), triethylamine (4 ml, 28.6 mmol) and finally *t*-butyldiphenylchlorosilane (4.5 ml, 17.6 mmol). After stirring the reaction mixture for 3 days at room temperature, CH_2Cl_2 (100 ml), water (50 ml) were added and the pH was adjusted to 2 by 2N HCl solution. The aqueous phase was extracted with CH_2Cl_2 (3 x 100 ml) and the combined organic phases were dried ($MgSO_4$) and concentrated *in vacuo*. The crude silyl ether **6** was dissolved in CH_2Cl_2 (100 ml) and at 0°C, 50% CF_3COOH solution (10 ml) was added. After stirring for 2h at 0°C, $NaHCO_3$ (6 g) was added by portions. The reaction mixture was partitioned between CH_2Cl_2 (75 ml) and water (50 ml). The aqueous phase was extracted with CH_2Cl_2 (2 x 75 ml) and the combined organic extracts were dried ($MgSO_4$) and evaporated to dryness. The residue was purified by flash chromatography (Et_2O-petroleum ether, 1:9 then 1:4) to afford the enone **7b** as an oil (4,65 g, 81% yield) : $[\alpha]_D^{20}$ -35 (c 2, $CHCl_3$) ; IR (neat) 3010, 1700, 1620, 1100 cm^{-1} ; ^1H NMR : 1.2 (s, 9H, $SiC(CH_3)_3$), 5.3 (s, 1H, C<u>H</u>OSi), 5,65 (dd, 1H,J=2 and 10Hz, CH=C<u>H</u>$_2$), 6.3 (dd, 1H, J=2 and 17Hz, CH=C<u>H</u>$_2$), 6.87 (dd, 1H, J=10 and 17Hz, C<u>H</u>=CH$_2$), 7.2-7.6 (m, 15H, 3Ph) ; ^{13}C NMR : 19.6, 27.1 (3C), 81.1, 126.7 (2C), 127.8 (2C), 127.9 (2C), 128.3, 128.8 (2C), 129.7, 130.0, 130.2, 130.8, 132.9, 133.0, 135.9 (2C), 136.0 (2C), 138.3, 197.4 ; Anal. Calcd for $C_{26}H_{28}O_2Si$: C, 77.95; H, 7.04. Found : C, 77.97; H, 7.07.

<u>Typical procedure for the reduction of 7a (Table 1, entry 1)</u>

To a well-stirred solution of **7a** (0.28 g, 1mmol) in Et_2O (5 ml) was added at -78°C lithium aluminium hydride (0.038g, 1mmol). After stirring the reaction mixture for 20 min at -78°C, 4 drops of saturated Na_2SO_4 solution was added. After warming up the mixture to room temperature, saturated Na_2SO_4 solution was added and the precipitate formed was filtered. After concentration *in vacuo* the residue was purified by flash chromatography (Et_2O-petroleum ether, 4:1) to give a mixture of **8a** and **8b** (dr 1:3) as a colourless oil (0.17 g, 60% yield) : ^1H NMR (*anti* isomer **8b**) : 2.75 (br s, 1H, OH), 4.32 (br t, 1H, C<u>H</u>OHCH=CH$_2$), 4.42-4.85 (m, 5H), 5.17 (dt, J=2 and 10Hz, CH=C<u>H</u>$_2$), 5.25 (dt, J=2 and 17Hz, CH=C<u>H</u>$_2$), 5.9 (ddd, 1H, J=6, 10 and 17Hz, C<u>H</u>=CH$_2$), 7.2-7.4 (m, 10H, 2Ph) ; ^{13}C NMR : 70.0, 75.7, 81.9, 93.1, 116.8, 127.8

(2C), 128.0 (3C), 128.3 (2C), 128.4, 128.5 (2C), 136.4, 137.5, 137.7 ; ^{1}H NMR (*syn* isomer **8a**) : 2.3 (br s, 1H, OH), 4.29 (br t, 1H, C<u>H</u>OHCH=CH_2), 4.42-4.85 (m, 5H), 5.09 (dt, 1H, J=2 and 10Hz, CH=C<u>H</u>$_2$), 5.25 (dt, 1H, J=2 and 17Hz, CH=C<u>H</u>$_2$), 5.65 (ddd, 1H, J=6, 10 and 17Hz, C<u>H</u>=CH_2), 7.2-7.4 (m, 10H, 2Ph) ; ^{13}C NMR : 70.0, 75.9, 82.5, 92.8, 116.9, 126.9 (2C), 128.0 (3C), 128.1 (2C), 128.2, 128.3 (2C), 135.9, 137.4, 137.9 ; Anal. Calcd for $C_{18}H_{20}O_3$ (mixture of diastereomers) : C, 76.03; H, 7.09. Found : C, 75.85; H, 7.46.

(1R,2R)-1-(t-Butyldiphenylsilyloxy)-1-phenylbut-3-en-2-ol (9a). To a cooled (0°C) solution of $CeCl_3.7H_2O$ (6.5 g, 17.4 mmol) in MeOH (80 ml) was added $NaBH_4$ (0.88 g, 23.2 mmol). The mixture was cooled to -78°C and a solution of **7b** (4.65 g, 11.6 mmol) in MeOH (17 ml) was added dropwise. The reaction mixture was stirred at -78°C for 1h and quenched with saturated NH_4Cl solution (16 ml). The mixture was warmed up to room temperature and was filtered on a pad of Celite. The filtrate was concentrated and diluted with Et_2O (200 ml). The ethereal solution was extracted with water (100 ml). The aqueous phase was extracted with Et_2O (3 x 150 ml) and the combined organic phases were washed with brine, dried ($MgSO_4$) and concentrated. Flash chromatography of the residue (Et_2O-petroleum ether, 1:9) gave **9a** as a colourless oil (4,65 g, 98% yield) : $[\alpha]_D^{20}$ -43 (c 2.5, $CHCl_3$) ; IR (neat) 3480, 3060, 2920, 1590, 1430, 1100, 700 cm^{-1} ; ^{1}H NMR : 1.05 (s, 9H, $SiC(CH_3)_3$), 2.45 (d, 1H, J=4Hz, OH), 4,2 (m, 1H, C<u>H</u>OH), 4.5 (d, 1H, J=6Hz, C<u>H</u>OSi), 5.0 (dt, 1H, J=1.8 and 10Hz, CH=C<u>H</u>$_2$), 5,1 (dt, 1H, J=1.8 and 17Hz, CH=C<u>H</u>$_2$), 5,65 (ddd, 1H, J=5.2, 10.5 and 17Hz, C<u>H</u>=CH_2), 7.2-7.7 (m, 15H, 3Ph) ; ^{13}C NMR : 19.5, 27.1 (3C), 77.0, 79.7, 116.6, 127.5 (2C), 127.7 (2C), 127.8 (3C), 127.9 (2C), 129.7, 129.9, 133.0, 133.7, 135.9 (2C), 136.0 (2C), 136.1, 140.2 ; Anal. Calcd for $C_{26}H_{30}O_2Si$: C, 77.56; H, 7.51. Found : C, 77.36; H, 7.60.

(1R,2R,3S)-1-(t-Butyldiphenylsilyloxy)-3,4-epoxy-1-phenylbutan-2-ol (10). To an ice-cooled solution of allylic alcohol **9a** (0.4 g, 1 mmol) in CH_2Cl_2 (5 ml) were added vanadyl acetylacetonate [$VO(acac)_2$] (0.135g, 0.5 mmol) and then dropwise *t*-BuOOH (5.6M in CH_2Cl_2), 0.5 ml, 2.8 mmol). After stirring for 3 days at 0°C, the reaction mixture was diluted with CH_2Cl_2 (10 ml) and water (3 ml) and sodium thiosulfate (1 g) was added. The aqueous phase was extracted with CH_2Cl_2 (3 x 10 ml), washed with brine, dried ($MgSO_4$) and concentrated *in vacuo*. Flash chromatography of the residue (Et_2O-petroleum ether, 3:7) gave a diastereomeric mixture of epoxide **10** (dr 95:5, determined by ^{13}C NMR spectroscopy) as a colourless oil (0.125 g, 30% yield) : IR (neat) 3480, 3080, 2920, 1590, 1430, 1100, 700 cm^{-1} ; ^{1}H NMR : 1.09 (s, 9H, $SiC(CH_3)_3$), 2.19 (d, 1H, J=3.9Hz, OH), 2.42-2.52 (m, 2H, C<u>H</u>$_2$), 2.9 (dt, 1H, J=2.8 and 3.9Hz, C<u>H</u>(epoxide)), 3.78 (dt, 1H, J=3.9 and 5.3Hz, C<u>H</u>OH), 4.78 (d, 1H, J=5.3Hz, C<u>H</u>OSi), 7.2-7.7 (m, 15H, 3Ph) ; ^{13}C NMR : 19.7, 27.3 (3C), 44.0, 51.6, 74.4, 77.5, 127.8 (2C), 128.0 (2C), 128.3 (3C), 128.5 (2C), 130.3, 130.5, 133. 4, 134.0, 136.4 (2C), 136.5 (2C), 140.6 ; Anal. Calcd for $C_{26}H_{30}O_3Si$: C, 74.6; H, 7.22. Found : C, 74.4; H, 7.08.

(1R,2R,3R and 3S)-1-(t-Butyldiphenylsilyloxy)-1-phenylbutane-2,3,4-triol (11) and (12). To a solution of allylic alcohol **9a** (4.65 g,11.5 mol) in acetone-water (4:1, 50 ml) were successively added N-methylmorpholine N-oxide.monohydrate (2.7 g, 23 mmol) and OsO_4 solution (2.5% wt. in BuOH, 2.2 ml, 0.174 mmol). After stirring at room temperature for 5h, the reaction mixture was concentrated *in vacuo*. The

residue was diluted with CH_2Cl_2 (100 ml) and water (50 ml) and the mixture was adjusted to pH 5 with 2N HCl. The aqueous phase was extracted with CH_2Cl_2 (2 x 50 ml) and the combined organic layers were dried ($MgSO_4$) and evaporated under reduced pressure. The residue was purified by flash chromatography on silica gel (Et_2O-petroleum ether, 1:1 then Et_2O) to give a 8:1 mixture of triols **11** and **12** (4.65 g, 90% yield) : IR (film) 3450, 3080, 2920, 1590, 1100, 700 cm^{-1} ; ^1H NMR of the major isomer **11** : 1.0 (s, 9H, $SiC(CH_3)_3$), 2.3 (br s, 2H, OH), 2.6 (br s, 1H, OH), 3.3 (dt, 1H, J=4.8 and 6.8Hz, C<u>H</u>OH-CH_2OH), 3.6 (m, 2H, C<u>H</u>$_2$OH), 3.7 (dd, 1H, J=4.6 and 6.8Hz, C<u>H</u>OH-CHOSi), 4.83 (d, 1H, J=4.8Hz, C<u>H</u>OSi), 7.2-7.8 (m, 15H, 3Ph) ; ^{13}C NMR of **11** : 19.4, 27.0 (3C), 63.5, 70.9, 76.0, 76.4, 127.1 (2C), 127.4 (2C), 127.8 (3C), 128.1 (2C), 129.8, 130.0, 132.5, 133.2, 135.8 (2C), 135.9 (2C), 140.3 ; Anal. Calcd for $C_{26}H_{32}O_4Si$: C, 71.52; H, 7.38. Found : C, 71.63; H, 7.45.

(1R,2R,3S)- and (1R,2R,3R)-1-(t-Butyldiphenylsilyloxy)-3,4-isopropylidenedioxy-1-phenylbutan-2-ol (13) and (14). To a solution containing **11** and **12** (4.5 g, 10.3 mmol) and camphorsulfonic acid (0.24 g, 1 mmol) in CH_2Cl_2 (65 ml) was added dropwise at room temperature 2-methoxypropene (1.55 ml, 15.5 mmol). After stirring for 10 min, the solution was filtered on a pad of silica gel, eluted with Et_2O and the filtrate was concentrated *in vacuo*. Flash chromatography of the residue (Et_2O-petroleum ether, 3:7) gave first **14** (0.44 g, 9% yield) : IR (film) 3480, 3060, 2980, 1590, 1430, 1380,1100, 700 cm^{-1} ; ^1H NMR : 1.05 (s, 9H, $SiC(CH_3)_3$), 1.06 (s, 3H, CH_3), 1.32 (s, 3H, CH_3), 3.0-3.3 (m, 3H, OH, C<u>H</u>$_2$OR), 3.68 (ddd, 1H, J=3.4, 4.8 and 8.3Hz, C<u>H</u>OR-CH_2OR), 4.0 (dd, 1H, J= 6.2 and 8.3Hz, C<u>H</u>OH-CHOSi), 4.76 (d, 1H, J=6.2Hz, C<u>H</u>OSi), 7.2-7.7 (m, 15H, 3Ph) ; ^{13}C NMR : 19.4, 26.6, 27.0 (3C), 27.2, 62.3, 76.9, 77.6, 80.6, 108.8, 127.3 (2C), 127.4 (2C), 127.5 (2C), 127.9, 128.0 (2C), 129.5, 129.6, 133.2, 133.5, 136.0 (2C), 136.1 (2C), 139.4 . The second fraction was constituted by pure **13** (4.1 g, 83% yield) obtained as an oil : $[\alpha]_D^{20}$ -31 (c 4.3 $CHCl_3$) ; IR (film) 3480, 3060, 2980, 1590, 1430, 1380, 1100, 700 cm^{-1} ; ^1H NMR : 1.05 (s, 9H, $SiC(CH_3)_3$), 1.2 (s, 3H, CH_3), 1.31 (s, 3H, CH_3), 2.62 (d, 1H, J=6.3Hz, OH), 3.62-3.89 (m, 4H, C<u>H</u>OH-C<u>H</u>OR-C<u>H</u>$_2$OR), 4.82 (d, 1H, J=3.8Hz, C<u>H</u>OSi), 7.2-7.7 (m, 15H, 3Ph) ; ^{13}C NMR : 19.4, 25.5, 26.3 (3C), 28.1, 61.1, 73.0, 77.0, 81.1, 108.4, 127.2 (2C), 127.8 (2C), 127.9 (2C), 128.1, 128.3 (2C), 128.4, 129.3, 133.7, 133.8, 135.0 (2C), 136.3 (2C), 139.8 ; Anal. Calcd for $C_{29}H_{36}O_4Si$: C, 73.07; H, 7.61. Found : C, 72.56; H, 7.63.

(1R,3R)-1-(t-Butyldiphenylsilyloxy)-3,4-isopropylidenedioxy-1-phenylbutan-2-one (15). A solution containing **13** (4 g, 8.4 mmol), 4Å molecular sieves (5 g) and N-methylmorpholine N-oxide (4.23 g, 36 mmol) in CH_2Cl_2 (40 ml) was stirred at room temperature for 30 min and tetrapropylammonium perruthenate (0.05 g, 0.168 mmol) was added. The reaction mixture was stirred for 90 min and filtered on a pad of silica gel. After concentration *in vacuo* of the filtrate, the crude mixture was purified by flash chromatography on silica gel (Et_2O-petroleum ether, 3:7) to yield pure ketone **15** as an oil (3.98 g, 100% yield) : $[\alpha]_D^{20}$ -31 (c 2.8, $CHCl_3$) ; IR (film) 3060, 2930, 1730, 1590, 1430, 1380,1100, 700 ; ^1H NMR : 1.08 (s, 9H, $SiC(CH_3)_3$), 1.1 (s, 6H, $2CH_3$), 3.6 (dd, 1H, H=6.9 and 8.2Hz, C<u>H</u>$_2$OR), 3.88 (dd, 1H, J=7.8 and 8.2Hz, C<u>H</u>$_2$OR), 4.4 (dd, 1H, J=6.9 and 7.8Hz, C<u>H</u>OR), 5.55 (s, 1H, C<u>H</u>OSi), 7.2-7.7 (m, 15H, 3Ph) ; ^{13}C NMR : 19.3, 25.3, 25.4, 26.9 (3C), 66.1, 77.6, 79.3, 110.5, 127.2 (2C), 127.6 (2C), 127.8 (2C), 128.3, 128.5 (2C), 129.9, 130.1, 132.5, 132.7, 135.7 (2C), 135.8 (2C), 137.3; 205.2 ; Anal. Calcd for $C_{29}H_{34}O_4Si$: C, 73.4; H, 7.22. Found : C, 73.4; H, 7.23.

(1R,2S,3S)-1-(t-Butyldiphenylsilyloxy)-3,4-isopropylidenedioxy-1-phenylbutan-2-ol (16)
To a solution of ketone **15** (3.9 g, 8.4 mmol) in THF (50 ml) was added at -100°C L-Selectride® (1M in THF, 16.4 ml, 16.4 mmol, 1.9 equiv). After stirring for 1h at -100°C, the reaction mixture was quenched with 2N HCl solution (5 ml). The reaction mixture was diluted with water (30 ml) and extracted with CH_2Cl_2 (3 x 100 ml). The combined organic phases were dried ($MgSO_4$) and concentrated *in vacuo*. Flash chromatography of the residue (Et_2O-petroleum ether, 1:4) gave first the starting ketone **15** (0.78 g, 20% yield) followed by **13** (0.22 g, 6% yield) and finally pure **16** obtained as an oil (2.81 g, 72% yield) : $[\alpha]_D^{20}$ -30 (c 4.3 $CHCl_3$) ; IR (film) 3480, 3060, 2980, 1590, 1400, 1380,1100, 700 cm^{-1} ; ^1H NMR : 1.06 (s, 9H, $SiC(CH_3)_3$), 1.3 (s, 3H, CH_3), 1.38 (s, 3H, CH_3), 2.27 (d, 1H, J=6.8Hz, OH), 3.58 (dd, 1H, J= 6.6 and 8Hz, $C\underline{H}_2OR$), 3.62-3.88 (m, 2H, $C\underline{H}_2OR$, $C\underline{H}OHCHOSi$), 4.23 (ddd, 1H, J=4.4, 6.2 and 6.6Hz, $C\underline{H}OR\text{-}CH_2OR$), 4.68 (d, 1H, J=6.1Hz, $C\underline{H}OSi$), 7.2-7.7 (m, 15H, 3Ph) ; ^{13}C NMR : 19.4, 25.4, 26.4, 27.4 (3C), 66.3, 74.2, 74.6, 77.3, 109.1, 127.3 (2C), 127.4 (2C), 127.5 (2C), 127.6, 128.0 (2C), 129.5, 129.7, 133.0, 133.6, 135.9 (2C), 136.0 (2C), 140.7 ; Anal. Calcd for $C_{29}H_{36}O_4Si$: C, 73.07; H, 7.61. Found : C, 72.74; H, 7.68.

(1R,2S,3R) -1-(t-Butyldiphenylsilyloxy)-1-phenylbutane-2,3,4-triol (17) . A solution of the acetonide alcohol **16** (2.8 g, 5.85 mmol) in a mixture of acetic acid-water (4:1) was refluxed for 3 h. After concentration *in vacuo*, the residue was purified by flash chromatography (Et_2O-petroleum ether, 7:3) to give **17** as an oil (2.17 g, 85% yield) : $[\alpha]_D^{20}$ -60 (c 2.6 $CHCl_3$) ; IR (film) 3400, 3080, 2920, 1590, 1100, 700 cm^{-1}; ^1H NMR (CD_3OD) : 1.0 (s, 9H, $SiC(CH_3)_3$), 3.52 (dd, 1H, J= 6.6 and 10.9Hz, $C\underline{H}_2OH$), 3.59 (dd, 1H, J= 6.6 and 10.9Hz, $C\underline{H}_2OH$), 3.89 (dd, 1H, J=2 and 7.6Hz, $C\underline{H}OHCHOSi$), 4.08 (dt, 1H, J=2 and 6.6Hz, $C\underline{H}OHCH_2OH$), 4.79 (d, 1H, J=7.6Hz, $C\underline{H}OSi$), 7.1-7.7 (m, 15H, 3Ph) ; ^{13}C NMR : 19.4, 27.4 (3C), 64.7, 69.5, 73.7, 75.8, 127.3 (2C), 127.5 (2C), 127.8 (2C), 127.9, 128.2 (2C), 129.8, 130.0, 132.9, 133.2, 136.0 (2C), 136.1 (2C), 140.4 ; Anal. Calcd for $C_{26}H_{32}O_4Si$: C, 71.52; H, 7.38. Found : C, 71.32; H, 7.65.

(1R,2S,3S)-1-(t-Butyldiphenylsilyloxy)-1-phenyl-4-(p-toluenesulfonyloxy)butane-2,3-diol (18) . To a solution of triol **17** (1.35 g, 3.1 mmol) and triethylamine (0.87 ml, 6.2 mmol) in CH_2Cl_2 (12 ml), cooled to -78°C, were successively added 4-dimethylaminopyridine (0.38 g, 3.1 mmol) and *p*-toluenesulfonyl chloride (0.7 g, 3.7 mmol). The reaction mixture was warmed up to -20°C and let overnight at this temperature in a freezer. The mixture was quenched at -20°C with 1N HCl solution (5 ml) and the aqueous phase was extracted with CH_2Cl_2 (2 x 20 ml). The combined organic phases were dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by flash chromatography (Et_2O-petroleum ether, 3:5) to afford **18** as an oil (1.32 g, 72% yield) : $[\alpha]_D^{20}$ -32 (c 1.5 $CHCl_3$) ; IR (film) 3450, 3080, 2920, 1600, 1590, 1180, 1100, 700 cm^{-1} ; ^1H NMR : 1.04 (s, 9H, $SiC(CH_3)_3$), 2.11 (br s, 1H, OH), 2.44 (s, 3H, $SO_2PhC\underline{H}_3$), 3.60 (dd, 1H, J=1.2 and 6.3Hz, $C\underline{H}OHCHOSi$), 3.87 (m, 2H, $C\underline{H}_2OTs$), 4.11 (ddd, 1H, J=1.2, 5.7 and 6.8Hz, $C\underline{H}OHCH_2OTs$), 4.8 (d, 1H, J=6.3Hz, $C\underline{H}OSi$), 7.2-7.7 (m, 19H, Ph) ; ^{13}C NMR : 19.4, 21.7, 27.1 (3C), 64.7, 67.5, 74.0, 76.9, 127.3, 127.5 (2C), 127.9 (2C), 128.0 (2C), 128.1 (2C),

128.4 (2C), 129.8, 129.9 (2C), 130.1, 132.6, 132.8, 133.1, 135.9 (2C), 136.0 (2C), 140.1, 144.9 ; Anal. Calcd for $C_{33}H_{38}O_6SSi$: C, 67.08; H, 6.48; S, 5.42. Found : C, 67.29; H, 6.59; S, 5.11.

(1R,2S,3S)-1-(t-Butyldiphenylsilyloxy)-3,4-epoxy-1-phenylbutan-2-ol (19) and (1R,2R,3R)-2-(t-butyldiphenylsilyloxy)-3,4-epoxy-1-phenylbutan-1-ol (20). To a well-stirred solution of tosylate **18** (1.3 g, 2.2 mmol) and DMSO (0.3 ml) in THF (15 ml) was added at 0°C, NaH (60% dispersion in mineral oil, 0.14 g, 1.5 equiv). After stirring for 15 min at 0°C, the reaction mixture was quenched with a NH_4Cl saturated solution (3 ml). The mixture was diluted with water (5 ml) and extracted with CH_2Cl_2 (3 x 20 ml). The combined organic extracts were dried ($MgSO_4$) and concentrated *in vacuo*. Flash chromatography of the residue (Et_2O-petroleum ether, 3:7) afford first **19** as an oil (0.22 g, 24% yield) : IR (film) 3480, 2920, 1590, 1430, 1100, 700 cm^{-1} ; ^1H NMR : 1.05 (s, 9H, $SiC(CH_3)_3$), 2.05 (d, 1H, J=6.7Hz, OH), 2.45 (dd, 1H, J=2.7 and 5Hz, CH_2(epoxide)), 2.6 (dd, 1H, 4.9 and 5Hz, CH_2(epoxide)), 3.05 (ddd, 1H, J=2.7, 4.9 and 5Hz, CH(epoxide)), 3.52 (dt, 1H, J=4.9 and 6.7Hz, C<u>H</u>OH), 4.85 (d, 1H, J=4.9Hz, C<u>H</u>OSi), 7.2-7.8 (m, 15H, 3Ph) ; ^{13}C NMR : 19.4, 27.1 (3C), 44.5, 51.7, 77.4, 77.8, 127.2 (2C), 127.6 (2C), 127.8 (2C), 127.9, 128.0 (2C), 128.3, 129.8, 133.0, 133.7, 136.0 (2C), 136.1 (2C), 140.3 ; Anal. Calcd for $C_{26}H_{30}O_3Si$: C, 74.6; H, 7.22. Found : C, 74.25; H, 7.18. The second fraction was constituted of pure **20** obtained as an oil (0.3 g, 33%) : IR (film) 3480, 3080, 2920, 1590, 1430, 1100, 700 cm^{-1} ; ^1H NMR 1.05 (s, 9H, $SiC(CH_3)_3$), 1.9 (dd, 1H, J=2.8 and 4.7Hz, CH_2(epoxide)), 2.35 (dd, 1H J=4.2 and 4.7Hz, CH_2(epoxide)), 2.9 (d, 1H, J=2.4Hz, OH), 3.1 (ddd, 1H, J=2.8, 4.2 and 6.6Hz, CH(epoxide)), 3.42 (dd, 1H, J=3.7 and 6.6Hz, C<u>H</u>OSi), 4.57 (br t, 1H, J= 2.9Hz, C<u>H</u>OH), 7-7.8 (m, 15H, 3Ph) ; ^{13}C NMR : 19.6, 27.1 (3C), 45.2, 52.1, 76.3, 79.1, 127.2 (2C), 127.6 (2C), 127.7 (2C), 128.0, 128.2 (2C), 130.0, 130.2, 131.1, 133.4, 136.0 (2C), 136.1 (2C), 139.6 ; Anal. Calcd for $C_{26}H_{30}O_3Si$: C, 74.6; H, 7.22. Found : C, 74.25; H, 7.18.

(1R,2R,3S)-3,4-Epoxy-1-phenylbutane-1,2-diol (21) . To a solution of mixture of regioisomers **19** and **20** (0.52 g, 2.2 mmol) in THF (10 ml) was added NBu_4F (1M in THF, 2 ml, 2 mmol). After stirring for 30 min at room temperature, the reaction mixture was quenched with HCl 1N solution (2 ml). The solution was diluted with water (10 ml) and extracted with CH_2Cl_2 (3 x 15 ml). The combined organic extracts were dried ($MgSO_4$) and evaporated to dryness. Flash chromatography of the residue (Et_2O-petroleum ether, 1:2) afforded the epoxydiol **21** as an oil (0.16 g, 71% yield) : $[\alpha]_D^{20}$ -52 (c 1.02 $CHCl_3$) ; IR (film) 3480, 2980, 1605, 1495, 1450 cm^{-1} ; ^1H NMR (CD_3OD) : 2.43 (dd, 1H, J=2.8 and 5Hz, CH_2(epoxide)), 2.65 (dd, 1H, J=4.3 and 5Hz, CH_2(epoxide)), 3.15 (ddd, 1H, J=2.8, 4.3 and 6Hz, CH(epoxide)), 3.4 (br t, 1H, J=6.2Hz, C<u>H</u>OHCHOHPh), 4.65 (d, 1H, J=6.3Hz, C<u>H</u>OHPh), 7.2-7.5 (m, 5H, Ph) ; ^{13}C NMR (CD_3OD) : 45.7, 53.3, 76.5, 76.8, 128.0 (2C), 128.5, 129.1 (2C), 143.3 ; Anal. Calcd for $C_{10}H_{12}O_3$: C, 66.65; H, 6.71; O, 26.6. Found : C, 66.67; H, 6.68; O, 26.46.

(1R,2S,3R)-3,4-Epoxy-1,2-isopropylidenedioxy-1-phenylbutane (22). To a solution of **21** (0.16 g, 0.89 mmol) in CH_2Cl_2 (4 ml) was added at room temperature camphorsulfonic acid (0.02 g, 0.09 mmol) followed by 2-methoxypropene (0.1 ml, 0.1 mmol). After stirring for 10 min, the solution was filtered on a pad of silica gel and concentrated *in vacuo*. The residue was purified by flash chromatography (Et_2O-petroleum ether, 1:4) to give **22** as an oil (0.19 g, 97% yield) : $[\alpha]_D^{20}$ -87.3 (c 1.1 $CHCl_3$) ; ^1H NMR : 1.46

(s, 3H, CH_3), 1.67 (s, 3H, CH_3), 2.35 (dd, 1H, J=4 and 5Hz, CH_2(epoxide)), 2.37 (dd, 1H, J=3 and 5Hz, CH_2(epoxide)), 2.5 (ddd, 1H, J=3, 4 and 6.8Hz, CH(epoxide)), 3.98 (dd, 1H, J=6.8 and 7.1Hz, CHOR-CHORPh), 5.3 (d, 1H, J=7.1Hz, PhCH), 7.2-7.4 (m, 5H, Ph) ; ^{13}C NMR : 24.9, 26.8, 43.5, 51.5, 78.8, 80.3, 109.5, 126.3 (2C), 127.9, 128.4 (2C), 136.6 ; Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32; O, 21.79. Found : C, 71.05; H, 7.33; O, 21.62.

(+)-Goniodiol (1). To a solution of methyl 3-phenylsulfonylorthopropionate **23** (0.42 g, 1.7 mmol) in THF (5 ml), cooled to -78°C, was added *n*-BuLi (2.2M in hexanes, 0.78 ml, 1.72mmol). After stirring for 30 min at -78°C, $BF_3.Et_2O$ (0.22 ml, 1.72 mmol) was added followed by epoxyde **22** (0.19 g, 0.86 mmol) 5 min later. After stirring for 1h at -78°C, the reaction mixture was allowed to warm up to room temperature (2 h) and 3M H_2SO_4 solution (2 ml) was added. The mixture was refluxed for 3h, cooled down to room temperature, diluted with water (10 ml) and extracted with CH_2Cl_2 (3 x 10 ml). The combined organic extracts were dried ($MgSO_4$) and concentrated *in vacuo*. The crude mixture was filtered on a pad of silica gel (Et_2O-petroleum ether, 3:1 then Et_2O-MeOH, 98:2). After concentration *in vacuo*, the resulting powder (compound **25**) was dissolved in CH_2Cl_2 (4 ml), cooled to 0°C, and DBU (0.21 ml, 1.4 mmol) was added. After stirring for 1h at 0°C, the solution was filtered on a pad of silica gel and concentrated. The residue was purified by flash chromatography (Et_2O-MeOH, 49:1) to give **1** as a colourless oil (0.12g, 60% yield from **22**) : $[\alpha]_D^{20}$ +70 (c 1.2 $CHCl_3$) (92% ee determined by polarimetry) [lit. $[\alpha]_D^{30}$ + 75.7 ($CHCl_3$)[1] and $[\alpha]_D^{30}$ + 74.4 ($CHCl_3$)[5a].; ^1H NMR : 2.16 (qd, 1H, J=3.7, 6.4 and 18.5Hz, CH_2-CH=CH), 2.6 (d, 1H, J=8Hz, 7-OH), 2.78 (m, 1H, CH_2-CH=CH), 3.1 (d, 1H, J=4.2Hz, 8-OH), 3.71 (t, 1H, J=7Hz, CHOH-CHOHPh), 4.77 (qd, 1H, J=2.2, 3.7, and 12.8Hz, CH-OCOR), 4.93 (dd, 1H, J=5 and 7Hz, PhCHOH), 5.98 (dd, 1H, J=2.9 and 9.8Hz, CH=CH-CO), 6.91 (ddd, 1H, J=2.3, 6.4 and 9.8Hz, CH=CH-CO), 7.2-7.4 (m, 5H, Ph) ; ^{13}C NMR : 26.0, 73.5, 75.2, 77.2, 120.5, 126.9 (2C), 128.2, 128.7 (2C), 141.2, 146.7, 164.4.

7,8-Di-O-acetylgoniodiol (3). A solution containing (+)-**1** (0.03 g, 0.128 mmol) and acetic anhydride (0.2 ml, 2.1 mmol) in pyridine (2 ml) was stirred at room temperature for 12 h. After concentration *in vacuo*, the residue was chromatographied on silica gel (Et_2O) to give the diacetate **3** as a solid (0.033 g, 80% yield) : mp 148-150°C ; $[\alpha]_D^{20}$ +78 (c 0.9 $CHCl_3$) (92% ee determined by polarimetry) [lit. mp 150°C $[\alpha]_D^{30}$+ 84.5 ($CHCl_3$)[1]; mp 152-154°C; $[\alpha]_D^{24}$+ 82.6 (c 0.1, $CHCl_3$)] ; ^1H NMR : 1.8 (s, 3H, CH_3CO), 2.07 (s, 3H, CH_3CO), 2.34 (m, 2H, CH_2-CH=CH), 4.75 (septuplet, 1H, J=2.6, 5.2 and 11Hz, CH-OCOR), 5.33 (dd, 1H, J=2.6 and 8.6Hz, PhCHOAc-CHOAc), 6.02 (d, 1H, J=9.8Hz, CH=CH-CO), 6.02 (d, 1H, J= 8.6Hz, PhCHOAc), 6.85 (ddd, 1H, J=2.9, 5.8 and 9.8Hz, CH=CH-CO), 7.2-7.4 (m, 5H, Ph) ; ^{13}C NMR : 20.3, 21.0, 26.0, 72.2, 73.4, 74.6, 121.5, 127.4 (2C), 128.4 (2C), 128.7, 136.5, 144.5, 162.9, 169.0, 169.6.

7-O-acetylgoniodiol (2) and 8-O-acetylgoniodiol (4). To a solution of goniodiol **1** (0.09 g, 0.038 mmol) in CH_2Cl_2 (9 ml) was added methyl orthoacetate (0.5 ml, 0.39 mmol) and *p*-toluenesulfonic acid (5 mg). After stirring for 10 min at room temperature, 80% acetic acid solution (2 ml) was added. The reaction mixture was stirred for 10 min at room temperature and concentrated *in vacuo*. The residue was purified by flash chromatography (Et_2O) to give first **2** as a white solid (0.018 g, 16% yield) : mp 141-143°C; $[\alpha]_D^{20}$ +132 (c 0.2 $CHCl_3$) (92% ee determined by polarimetry) [lit[1]. mp 140°C $[\alpha]_D^{30}$ + 145.6 ($CHCl_3$)] ; ^1H NMR : 1.82 (s, 3H, CH_3CO), 2.34 (m, 2H, CH_2-CH=CH), 3.12 (br s, 1H, 8-OH), 5.08 (ddd, 1H, J=1,

4.8 and 9.6Hz,CHOCOR), 5.12 (d, 1H, J=8Hz, PhCHOH), 5.16 (dd, 1H, J=4.8 and 8Hz, CHOAc), 6.02 (ddd, 1H, J=1, 2.2 and 9.6Hz, CH=CH-CO), 6.90 (ddd, 1H, J= 2.2, 4.8 and 9.6Hz, CH=CH-CO), 7.2-7.4 (m, 5H, Ph) ; ^{13}C NMR : 20.4, 26.2, 70.9, 75.1, 75.3, 121.1, 126.9 (2C), 128.3, 128.4 (2C), 140.5, 145.4, 163.9, 169.9. The next fraction was constituted of pure 8-O-monoacetate goniodiol **4** as an oil (0.076, 72%) : $[\alpha]_D^{20}$ +40.4 (c 0.37, $CHCl_3$) (92% ee) [lit[6]. $[\alpha]_D^{24}$ + 43 (c 0.1,$CHCl_3$)] ;. ^{1}H NMR : 2.02 (s, 3H, CH_3CO), 2.2 (dq, 1H, J=3.6, 6.2 and 18.4Hz, CH_2-CH=CH), 2.75 (m, 1H, CH_2-CH=CH), 2.85 (br s, 1H, 7-OH), 3.89 (dd, 1H, J= 2.1 and 18.4Hz, CHOH), 4.68 (dq, 1H, J=2.2, 3.6 and 12.6Hz, CHOCOR), 5.87 (d, 1H, J=8Hz, PhCHOAc), 5.96 (dd, 1H, J=2.2 and 9.6Hz, CH=CH-CO), 6.90 (ddd, 1H, J= 2, 6.2 and 9.6Hz, CH=CH-CO), 7.2-7.4 (m, 5H, Ph) ; ^{13}C NMR : 21.7, 26.5, 74.4, 75.0, 76.7, 121.4, 128.1 (2C), 129.1 (3C), 137.9, 146.1, 164.0, 170.3.

Acknowledgments : One of us (JPS) thanks the Ministère de l'Enseignement Supérieur et de la Recherche for a fellowship.

References and notes :

1. Talapatra, S.K. ; Basu, D. ; Goswami, S. ; Talapatra, B. *Indian J. Chem. Sect. B* **1985**, *24*, 29-34.
2. Wu, Y.C. ; Duh, C.Y. ; Chang, F.R. ; Chang, G.Y. ; Wang, S.K. ; Chang, J.J. ; McPhail, D.R. ; McPhail, A.T. ; Lee, K.H. *J. Nat. Prod.* **1991**, *54*, 1077-1081.
3. Fang, X.P. ; Anderson, J.E. ; Qiu, X.X. ; Kozlowski, J.F. ; Chang, C.J. ; Mc Laughlin, J.L. *Tetrahedron* **1993**, *49*, 1563-1570 and references cited therein.
4. (a) Hasan, C.M. ; Mia, M.Y. ; Rashid, M.A. ; Connoly, J.D. *Phytochemistry* **1994**, *37*, 1763-1764.
   (b) Goh, S.H. ; Ee, G.C.L. ; Chuah, C.H. ; Wei, C. *Aust. J. Chem.* **1995**, *48*, 199-205.
5. see ref.1. Goniodiol and its 7-monoacetate have been also isolated from other *Goniothalamus* species : for goniodiol see : (a) Fang, X.P. ; Anderson, J.E. ; Chang, C.J. ; Mc Laughlin, J.L. ; Fanwick, P.E *J. Nat. Prod.* **1991**, *54*, 1034-1043 and for its 7-monoacetate see ref.2.
6. Wu, Y.C. ; Chang, F.R. ; Duh, C.Y. ; Wang, S.K. ; Wu, T.S. *Phytochemistry* **1992**, *31*, 2851-2853.
7. Davies-Coleman, M.T. ; Rivett, D.E.A in *Progress in the Organic Chemistry of Natural Products* **1989**, *55*, 1-35.
8. Surivet, J.P.; Vatèle, J.M. ; Goré, J. *Tetrahedron Lett.* **1996**, *37*, 371-374.
9. Rochet, P. ; Vatèle, J.M. ; Goré, J. *Synlett* **1993**, 105-107
10. Rochet, P. ; Vatèle, J.M. ; Goré, J. *Synthesis* **1994**, 795-799.
11. (a) Carretero, J.C. ; Ghosez, L. *Tetrahedron Lett.* **1988**, *29*, 2059-2062 ; for a recent use of **23** see (b) Patron, A.P. ; Richter, P.K. ; Tomaszewski, M.J. ; Miller, R.A. ; Nicolaou, K.C. *J. Chem. Soc. Chem. Commun.* **1994**, 1147-1149.
12. Zimmer, R. ; Reissig, H.U. *Liebigs Ann. Chem.* **1991**, 553-567.
13. Gemal, A.L. ; Luche, J.L. *J. Am. Chem. Soc.* **1981**, *103*, 5454-5459.
14. (a) Cherest, M. ; Felkin, H. ; Prudent, N. *Tetrahedron Lett.* **1968**, 2199-2204;

(b) Anh, N.T. ; Eisenstein, O. *Nouv. J. Chim.* **1977**, 61-70.

15. Cram, D. ; Wilson, D.R. *J. Am. Chem. Soc.* **1963**, *85*, 1245-1249.
16. Dana, G. ; Chuche, J. ; Monot, M.R. *Bull. Soc. Chim. Fr.* **1967**, 3308-3316.
17. (a) Hafner,A. ; Duthaler, R.O. ; Marti, R. ; Rihs, G. ; Rothestreit, P. ; Schwarzenbach, F. *J. Am. Chem. Soc.* **1992**, *114*, 2321-2336
    (b) Kadota, I. ; Kobayashi, K. ; Okoono, H. ; Asao, N. ; Yamamoto, Y. *Bull. Soc. Chim. Fr.* **1995**, *132*, 615-623.
18. (a) Rossiter, B.E. ; Verhoeyen, T.R. ; Sharpless, K.B. *Tetrahedron Lett.* **1979**, 4733-4736 ;
    (b) Mihelich, E.D. *Tetrahedron Lett.* **1979**, 4729-4732.
19. Prat, D. ; Lett, R. *Tetrahedron Lett.* **1986**, *27*, 707-710.
20. Van Rheenen, V. ; Kelly, R.C. ; Cha, D.Y. *Tetrahedron Lett.* **1976**, 1973-1976.
21. (a) Cha, J.K. ; Christ, W.J. ; Kishi, Y. *Tetrahedron Lett.* **1983**, *24*, 3943-3946 ;
    (b) Cha, J.K. ; Christ, W.J. ; Kishi, Y. *Tetrahedron* **1984**, *40*, 2247-2255.
22. Ley, S.V. ; Norman, J. ; Griffith, W.P. ; Marsden, S.P. *Synthesis* **1994**, 639-666.
23. For other examples of stereoselective α-alkoxyketone reductions with L-Selectride® see :
    (a) Takahashi, T. ; Miyazawa, M. ; Tsuji, J. *Tetrahedron Lett.* **1985**, *26*, 5139-5142 ; (b) Mulzer, J. ; Dupré, S. ; Buschmann, J. ; Luger, P. *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 1452-1454 ; (c) Wei, A. ; Kishi, Y. *J. Org. Chem.* **1994**, *59*, 88-96 ; (d) for a review on the diastereoselective reduction of α-hydroxy or alkoxy ketones see : Oishi, T. ; Nakata, T. *Acc. Chem. Res.* **1994**, *17*, 338-344.
24. White, J.D. ; Kang, M.C. ; Sheldon, B.G. *Tetrahedron Lett.* **1983**, *24*, 4539-4542.
25. De Lombaert, S. ; Nemery, I. ; Rockens, B. ; Carretero, J.C. ; Kimmel, T. ; Ghosez, L. *Tetrahedron Lett.* **1986**, *27*, 5099-5102
26. Deslongchamps, P. in *Stereoelectronic Effects in Organic Chemistry*, J.E. Baldwin, Ed. Pergamon Press, **1983** pp 29-32 and 72-85.
27. King, J.F. ; Albutt, A.D. *Can. J. Chem.* **1970**, *48*, 1754-1769.

(*Received in Belgium* 25 *July* 1996; *accepted* 8 *October* 1996)