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# OXIRANE RINGS: STUDIES AND APPLICATIONS OF A NEW CHEMO AND REGIO SELECTIVE REDUCTIVE OPENING OF EPOXIDES

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Summary:*the straightforward reductive opening of 1,2 epoxides to alcohols was studied and applied to several significant compounds. The reaction, which proceeds via the nucleophilic opening of the oxirane ring and the subsequent free radical dehalogenation, shows an excellent chemical yield as well as chemo and regioselectivity. This reaction was also applied to a chiral α,β-epoxyester.*

Among small rings in organic chemistry, the oxirane ring is one of the most versatile functional group. The strain and the polarity of the three membered ring allow many reactions with a large number of reagents such as electrophiles, nucleophiles, acids, bases and radicals[1]. Furthermore the increasing availability, thank to the Sharpless procedure[2], of a number of chiral epoxides makes them powerful intermediates in the synthesis of many natural products[3].

The simultaneous presence of other functional groups can limit the chemistry of oxiranes; this is still a problem in spite of the numerous efforts made in the search of chemoselective reagents, specific toward the oxirane ring and inactive toward other functional groups( i.e. carbonyl and carboxylic groups).

The reduction of epoxides to alcohols, expecially, has been accomplished by a variety of different reducing agents: the most useful method, until 1950, was the catalytic hydrogenolysis[4], but it was often complicated by the deoxygenation of the epoxide; this methodology has been almost completely replaced by the use of metal hydride reagents such as $LiAlH_4$ , boron derivatives and alkali metals[1].

Although hydride reagents have greatly improved the synthetic use of the reductive opening of epoxides, problems are still encountered in this transfor-

mation, especially with respect to the regio and chemoselectivity.

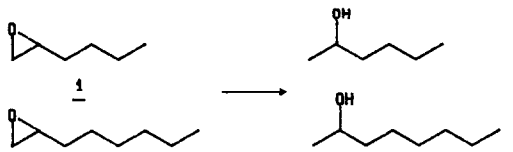
We wish to report our recent studies on the regio and chemoselective reductive opening of the oxirane ring ( mainly 1,2 epoxides) by different metal iodides and tributyltinhydride in a one pot procedure via a free radical process.

The use of radical reactions has greatly increased because of their high chemoselectivity and specificity[5]. Their many applications in the synthesis of complex natural products have shown a need for further studies along this way.

## Results and discussion

We have reported in a recent communication[6] that NaI,$nBu_3SnH$, AIBN refluxed in DME with 1,2 epoxides ( five examples) led to the corresponding secondary alcohols with excellent chemo and regioselectivity.

TABLE I



1



2

| entry | reaction conditions | yield * | regio selectivity * | reaction time |
|---|---|---|---|---|
| 1<br>2 | NaI,AIBN<br>n-$Bu_3SnH$<br>DME,reflux | 95%<br>95% | 93 : 7<br>99 : 1 | 3 h<br>2 h |
| 2 | LiI,AIBN<br>n-$Bu_3SnH$<br>DME,reflux | 95% | 99 : 1 | 1,5 h |
| 2 | $ZnI_2$,AIBN<br>n-$Bu_3SnH$<br>DME,reflux | 90% | 99 : 1 | 2 h |
| 1<br>2 | $MgI_2$,AIBN<br>n-$Bu_3SnH$<br>Toluene,reflux | 95%<br>95% | 93 : 7<br>90 : 10 | 1,5 h<br>1,5 h |
| 1,2 | $SrI_2$ or NaBr,AIBN<br>n-$Bu_3SnH$<br>DME,reflux | no reaction | | |

* yields are based on GLC

These preliminary results prompted us to test the reaction with two model terminal epoxides (1 and 2), selecting different reaction conditions

As described in Table I the reaction proceeded very well under all of these conditions. Some small selectivity differences did not allow us, at his point, to ascribe the latter to the nature of the salts: the only exceptions ( NaBr and $SrI_2$) seemed to be due the very low solubility of the salts in the solvent used. No attempts hade yet been made, at this stage, to isolate intermediates in the reaction. Monitoring by chromatography (TLC or GLC), revealed only the presence of the starting material and of the final product.

Using the data on model compounds, we have extensively studied the reaction on several different and significant substrates as shown in Table II. Some of these molecules were chosen because they also contained another functional group, and because they were important chiral synthons ( compounds 10, 13, 15 and 17 ). The reactions were carried out in three standard conditions: Condition A (NaI, $nBu_3SnH$, AIBN, in DME, reflux). Condition B (LiI, $nBu_3SnH$, AIBN, in DME, reflux). Condition C ($MgI_2$, $nBu_3SnH$, AIBN, in toluene, reflux).

Condition A proved to be satisfactory for compounds 13,15 and 17 so no other reaction conditions were employed for these. As shown, some of the tested compounds behave unlike the compounds 1 and 2 with respect to the used conditions and this deserves a deeper discussion.

Epoxystyrene 3 reacts differently according to the method used: the increase in regioselectivity from 6:1 to 9:1, in favour of 4,when LiI (B) is used instead of NaI (A), is noteworthy.

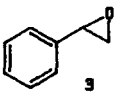
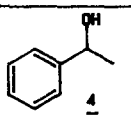
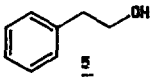
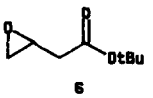
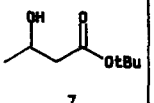
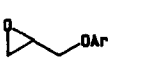
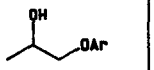
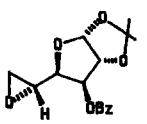
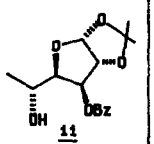
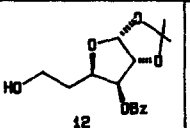
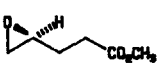
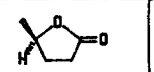
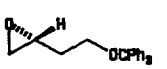
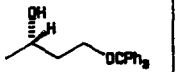
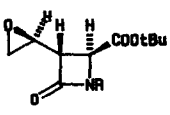
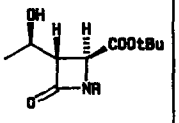
On the other hand, the use of $MgI_2$ (cond C), led to a complete reversal of the regioselectivity leading to 5 as the main product.

The case of the chiral epoxide 10 (easily obtained in four steps from acetone-D-glucose) was most significant: this important and useful synthon of several sugar derivatives, showed a significant increase in regioselectivity when LiI was used (cond. B) instead of the previously used conditions with NaI[6] ( from 5:1 to 15:1 in favour of 11). As in the case of epoxy styrene 3, the use of $MgI_2$ led to to the reversal of the regioselectivity in favour of the primary alcohol 12 (see below).

In the latter cases 13, 15 and 17 ( chiral compounds), the conditions used showed an excellent regio and chemoselectivity, with good chemical yields.

The reaction on compound 17, a useful intermediate in the synthesis of β-la-

TABLE II

| Entry | Products | Condition | Ratio[a] | Yield[b] | Time |
|---|---|---|---|---|---|
|  3 |  4 | A | 6 : 1 | 88% | 1 h |
| | | B | 9 : 1 | 90% | 1.5 h |
| |  5 | C | 1 : 20 | 80% | 1 h |
|  6 |  7 | A,C | 99 : 1 | 77% | 1 h |
|  8 |  9 | A,C | 99 : 1 | 91% | 2 h |
|  10 |  11 | A | 5 : 1 | 73% | 4 h |
| | | B | 15 : 1 | 65% | 2 h |
| |  12 | C | 1 : 5 | 65% | 2 h |
|  13 |  14 | A | 99 : 1 | 85% | 2 h |
|  15 |  16 | A | 15 : 1 | 95% | 6 h |
|  17 |  18 | A | 99 : 1 | 75% | 2 h |

Condition A (NaI,$nBu_3SnH$,AIBN, in DME reflux)

Condition B (LiI,$nBu_3SnH$,AIBN, in DME reflux)

Condition C ($MgI_2$,nBu$_3$SnH,AIBN, in toluene reflux)

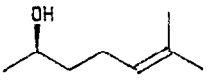
a)ratio secondary vs primary alcohol

b)yield referred to the isolated products

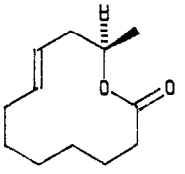
ctam antibiotics[7] , appears of particular importance: previously, an attempt at the reductive opening of the epoxy ring in a similar compound[8] by different hydride reagents did not give any result. With our method the transformation to the alcohol 18, which we strongly needed for the synthesis of useful 2-azetidinones, proceeds exceptionally well with no traces of the other regioisomer.

As in the other cases the reductive opening of the oxirane ring proceeds very well with the epoxy ester 13: this known chiral fragment, easily available (see experimental) from the "chiral pool", was cleanly reduced to the corresponding secondary alcohol affording directly (85% yield) the (R)-(+)-γ-methyl-γ-butyrolactone 14[9a,b].

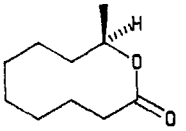
This transformation represents a new and easy way to prepare the chiral lactone 14, which was the key intermediate in the synthesis of natural products such as 2 (R)-(-)sulcatol[10]; in this way we obtained a substantial improvement ( overall yield 30%, from (S)-glutamic acid) in the preparation of 14[9a].




2 (R) - (-) -Sulcatol



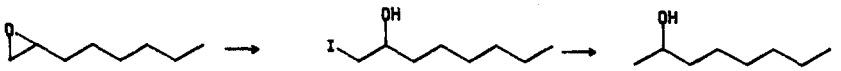

(R)-(-)-Recifeiolide




(R)-(-)-Phoracantholide

It is important to note that this type of chiral secondary alcohol unit is present in many naturally occurring macrocyclic lactones (mainly 10 or 12 membered ring) and work is in progress to synthesize by our procedure, (R)-(-) Recifeiolide, a macrolide from Cephalosporium recifei[11], and (R)-(-) Phorocantolide, a defensive secretion of the Eucarypt Lonficorn[12].

As for the mechanism of the reaction it seems possible that the first step involves the nucleophilic attack of the iodide ion on one side of the epoxy ring to give an intermediate iodohydrin, which is immediately reduced to the corresponding alcohol by means of $nBu_3SnH$. When the reaction was performed in the described conditions (A an B) no iodohydrine intermediate was observed . When we carried out the reaction on compound 2 with $MgI_2$ (cond. C), we were able to isolate the iodohydrine 19 , which was subsequently reduced to the corresponding 2-octanol in the standard radical conditions ($nBu_3SnH$, AIBN, in toluene, see experimental).




2 19

As already observed some of the substrates (3 and 10 ) showed a different behaviour in the regioselectivity of the reaction with the use of $MgI_2$ (cond C): that means that the nucleophilic attack of the iodide ion to form the intermediate iodohydrine is strongly depending on the nature of the cation ($Mg^{++}$) and of the solvent. While in the case of the epoxy 10 the reversal of the regioselectivity with the use of $MgI_2$ is hardly understandable, in the case of epoxystyrene 3 the nature of Lewis acid of the $MgI_2$ could explain the mostly favoured nucleophilic attack to the benzylic carbon.

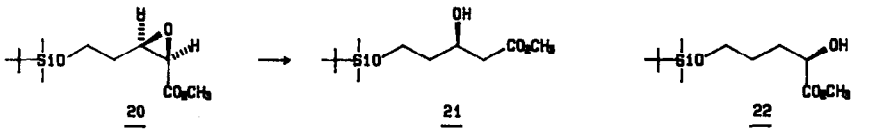
Since we needed, for our synthesis of inhibitors of HMGCoA reductase[13], to reduce regioselectively the chiral epoxyester 20 ( see experimental) to the corresponding β-hydroxy ester 21, we started to test the reactivity of this substrate in our reaction conditions. When we used the standard conditions A, B or C (see table III) we always obtained, as the main product, the β-hydroxyester 21, in different regio and chemical yields, yet to be optimized.

While our work was in progress, two excellent papers appeared on the reductive opening of α,β epoxyesters to α-hydroxyester[14] and to β-hydroxyester[15]. It is noteworthy that in the procedure to obtain the α-hydroxyesters, $MgI_2$ was used, at room temperature, to obtain regioselectively the corresponding iodohydrine which , after isolation, was reduced to the corresponding alcohol by $nBu_3SnH$. Then we applied this procedure to compound 20, adding in one pot, to the solution of 20 in ether, $MgI_2$ and $nBu_3SnH$ at room temperature. After one hour the reaction was completed affording the α-hydroxyester 22, with good regioselectivity, which demonstrates the possibility to perform this excellent reaction in a one pot procedure, without need to isolate the intermediate iodohydrine.

Since a possible kinetic control of the reaction by $MgI_2$ (in ether at room temp., for one minute) has been speculated by the authors, it seems evident that in our condition C (use of $MgI_2$, in toluene at reflux ,for two hours), other reasons, to be investigated, led to the reverse of the regioselectivity in the nucleophile attack to the epoxy ring.

Further studies will be needed to elucidate the role of $Mg^{++}$ in different conditions.

TABLE III




20 21 22

| reaction conditions | yield | ratio 21/22 | reaction time |
|---|---|---|---|
| A | 85% | 80 : 20 | 4 h |
| B | 25% | 96 : 4 | 5 h |
| C | 60% | 75 : 25 | 1 h |
| $MgI_2$, n-$Bu_3SnH$ Ether room temp. | 60% | 2 : 98 | 2 h |
| $SmI_2$, HMPA, DMAE THF, room temp. | 45% | 95 : 5 | 0,5 h |

Finally the epoxyester 20 was cleanly reduced to the β-hydroxy ester 21, by the use of the novel procedure with $SmI_2$ [15]; although the excellent observed observed regioselectivity, the fair chemical yield and the fastidious procedure in our hands[16] , will press us to try to extend and improve the use of our conditions for the reductive opening of α-β epoxyesters to the important class of β-hydroxyesters.

## EXPERIMENTAL SECTION

Column chromatography was carried out on silica gel 60, (70-230 mesh).TLC analysis were performed on Merck Kieselgel 60 F-254 plates. GLC measurements were performed utilizing a Carlo Erba 4100 and a H. P.5880A instruments, with either a 12 m capillary column ( OV101) or (SupelcoWax).

$^1$H-NMR spectra were recorded on a Varian XL 300 (300 MHz), a Varian 360 (60 MHz), and Bruker Wp 80 SV (80 MHz), with $Me_4Si$ as internal standard in $CDCl_3$ solution when needed. Mass spectral data were obtained on a Kratos MS-80 instrument. Infrared spectra were obtained on a Perkin-Elmer 457 instrument. Optical rotations were obtained using a Perkin-Elmer 241 polarimeter.

All new compounds gave satisfactory HR mass spectral data.

## PREPARATION OF THE STARTING EPOXIDES

Compounds 1,2,3 and 8 were all commercially available products.

Compound 6 was prepared according to S. G. Boots and M. R. Boots, J. Pharmacological Sciences, 64, 262 (1975).

Compound 10 : Diacetone-D-Glucose (Aldrich) was protected as 3-O-benzyl-diacetone-D-glucose as described ( S. Czernecki, C. Georgoulis and C. Provelenghio, Tetrahedron Lett., 3535 (1976). 4.0 gr of this benzyl derivative were dissolved in 20 ml of AcOH/$H_2O$ 4:1, and stirred with a magnetic apparatous for 24 h. The

AcOH was then evaporated by azeotropic distillation with toluene; the residue , dissolved in AcOEt (100 ml), was then extracted with satd. $NaHCO_3$ until neutrality and then washed with brine. The organic layer, dried over $Na_2SO_4$ and evaporated in vacuo, afforded 3.3 gr (93 %) of crude 1,2-O-isopropilydene,3-O benzyl-α-D-glucofuranose. This crude product (0.31 g, 1 meq) was dissolved in dry pyridine (4 ml) and then $NaPhSO_2Cl$ ( 0.25 g, 1.1 meq) was added at T=0° C under a nitrogen atmosphere. The mixture was magnetically stirred overnight and then AcOEt (30 ml) was added and the organic layer was extracted with 2N HCl (2 times with 10 ml) , with brine, then with satd. $NaHCO_3$ (10 ml) and finally with brine until neutrality. The organic layer, dried over $Na_2SO_4$ and evaporated in vacuo, afforded a residue which was dissolved in MeOH (5 ml). To this solution was then added ,at 0°C, powdered $K_2CO_3$ (2 eq) and the mixture was magnetically stirred for 2h. The reaction was quenched with satd. $NH_4Cl$ and extracted with AcOEt( 3 times). The organic layers were collected, dried over $Na_2SO_4$, and evaporated in vacuo. The residue was then chromatographed with silica gel column ( hexane/ether 1:1 as eluent) affording pure epoxide 10( 0.24 g, 81% overall yield) as a colourless oil. $^1$H-NMR (60 MHz): δ 1.25 ( s, 3H); 1.45 (s, 3H); 2.65-2.3 ( m, 2H); 3.0-3.4 (m, 1H)); 3.6-3.9 (q, 1H); 4.05 (d, J= 2Hz, 1H); 4.5-4.9 (m, 1H); 4.6 (s, 2H); 5.9 (d, J= 2Hz, 1H); 7.3 (s, 5H).

Compound 13 was prepared starting from S(+) glutamic acid according to J. Vigneron, R. Meric, M. Larcheveque, A. Debal, G. Kunesch, P. Zagatti and I Gallois, Tetrahedron Lett., 23, 5051, (1982).

Compound 15, was prepared according to R. Di Fabio and D. Misiti,Gazz.Chim. Ital., 118,209, (1988).

Compound 17 was prepared according to reference 7. 54 mg(0.9 meq) of 5β-hydroxy,6-naphtylsolphonyl derivative ( compound 11 in ref. 7), were dissolved in MeOH (3 ml); then powdered $K_2CO_3$ (28 mg) was added fractionwise at T= -35° C and the mixture was stirred ( magnetic apparatous) overnight at - 35° C. A TLC control showed the formation of the epoxide, with still some starting material( the reaction temperature must be mantained rigorously under -25° C, to avoid the formation of "ene" and other byproducts; on the other hand the use of DBU in dry THF at room temp. instead of $K_2CO_3$, only smoothly afforded the " ene" product). The reaction mixture was quenched with sat. $NH_4Cl$ (4 ml) and extracted with $Et_2O$ (3 times). The organic layers were then collected, dried over $Na_2SO_4$ and evaporated in vacuo. The crude mixture was purified by flash column chromatography ($Et_2O$/ hexane 1:1, then 8:2) affording 17 as a colourless oil ( 19 mg, 75 % based on the recovered starting material) and 12 mg of starting material. $^1$H-NMR (60 MHz): δ 1.4 s, 9H); 2.6-3.0 (m, 2H); 3.2-3.5 (m, 2H); 3.7 (s, 3H); 4.1 (m, 1H); 6.7-7.3 (dd, J= 8 Hz, 4H).

Compound 20 was prepared starting from the corresponding known chiral epoxy alcohol (ref. 13): the epoxyalcohol (100 mg) was dissolved in a round bottom flask equipped with a magnetic stirrer, with a mixture of $CH_3CN$ (1 ml), $H_2O$ (1.5 ml), $CCl_4$ (1 ml)( ref 17); to this heterogeneous mixture were then added $NaIO_4$ (0.6 gr), $RuCl_3$ (5 mg) and $NaHCO_3$ (0.6 g) to avoid the medium acidity to lower the yield by forming several bypoducts. After the usual work up the free acid was immediately methylated ($CH_2N_2$ in ether), affording crude epoxyester , which was purified by column chromatography ( hexane/ether 8:2 as eluent) affording 62 mg (60 overall yield) of pure 20.$^1$H-NMR (60 MHz): d 0.1, (s, 6H); 0.8 (s, 9H); 1.9 (q, 2H), 3.8 (s, 3H); 3,2-3.9 (m 4H). IR ($CHCl_3$), 1775 $cm^{-1}$ 1120, 1100 and 835.$[\alpha]_D$= - 6.4° (c= 1.25, $CHCl_3$).

GENERAL PROCEDURE FOR THE REDUCTIVE OPENING OF THE EPOXIDES WITH NaI AND LiI (Conditions A and B).

In a two necked round bottom flask, equipped with a condenser and a magnetic stirrer, was placed the epoxide (1 eq., $10^{-1}$M in dry DME) under a nitrogen atmosphere. To this solution were consequently added NaI or LiI (2.5 eq.), $nBu_3SnH$ (2.5 eq.) and a catalytic amount of AIBN. The mixture was then refluxed for 1-6 h. After the reaction is completed, DME was then evaporated under reduced pressure. MeOH was then added, followed by silica gel, and after evaporation the powder was poured on the top of a silica gel column ( in hexane) After elution first with hexane and then with hexane/ether 8:2 or 9:1 ( if not otherwise specified for particular compounds) the crude product was collected and then dissolved in $CH_3CN$ and washed with small portions of hexane (three times) obtaining the final product with less than 2% of the tin residues. When needed for spectroscopical and analytical porpouse the compound was further purified by column chromatography.

GENERAL PROCEDURE FOR THE REDUCTIVE OPENING OF THE EPOXIDES WITH $MgI_2$ (condition C).

In a two necked round bottom flask equipped with a condenser and a magnetic stirrer, was placed the epoxide (1 eq., $10^{-1}$M in dry toluene), under a nitrogen atmosphere. To the solution was then added $MgI_2$ in ether solution (1.5 eq.) and then $nBu_3SnH$( 2.5 eq.) and a catalytic amount of AIBN. The mixture was then refluxed for 1-3h until the reaction was completed. Most of the solvent was then evaporated, and the residue was diluted with ether and extracted with a KF aqueous solution. The organic layer, dried over anhydrous $Na_2SO_4$, was then evaporated under reduced pressure to a small volume and silica gel was added. After evaporation under vacuo of the solvent, the powder was poured on a silica gel column ( in hexane) and eluted first with hexane and then with hexane/ether 8:2 or 9:1( if not otherwise specified for particular compounds) The crude product was then collected , diluted with $CH_3CN$ and extracted with hexane. The final evaporation of $CH_3CN$ phase afforded almost pure compound. When needed a further purification ( to completely eliminate the tin residues) was effected with silica gel column chromatography.

Compound 7 : this compound was prepared from 6 according to condition A.$^1$H-NMR (60 MHz) : δ 1.2 (d, J=8 Hz, 3H), 1.4 (s, 9H); 2.4 (d, J=6 Hz, 2H); 3.3 (bd, 1H); 4.1 (m, 1H).

Compound 9 : prepared from 8 according to conditions A and C. $^1$H-NMR (60 MHz) : δ 1.2 (d, J= 6 Hz, 3H); 2.8 ( d, J= 3Hz, 1H); 3.8 (d, J= 8 Hz, 2H); 3.7-4.3 (m, 1H); 6.8 (bs, 5H).

Compound 11 : prepared from 10 according to conditions A and B; the product was purified by column chromatography, eluting with hexane/ether 4:6. $^1$H-NMR (200 MHz) : δ 1.24 (d, J= 6Hz, 3H); 1.30 (s, 3H); 1.46 (s, 3H); 2.20 (d, J= 6.4Hz, 1H); 3.88-3.94 ( dd, 1H); 4.06-4.08 (m, 2H); 4.62 (d, J= 4Hz, 2H); 4.45-4.75 (dd, J= 50HZ, J= 12Hz, 2H); 5.95 (d, J= 4Hz, 1H); 7.83 (bs, 5H). Anal.calcd. for $C_{16}H_{22}O_5$: C=65.29 ; H=7.3. Found :C=63.7; H=7.2.

Compound 12: prepared from 10 according to condition C; the product was purified by column chromatography eluting with hexane/ether 1:9. $^1$H-NMR ( 200 MHz) : δ 1.32 (s, 3H); 1.49 (s, 3H); 1.61-1.68 (m, 2H); 3.73-3.85 ( m, 1H); 4.0-4.10 ( m, 1H); 4.1-4.15 ( m, 2H); 4.63 (d, J= 3.6Hz, 1H); 4.76-4.53 (dd, J= 58Hz, J= 11.8Hz, 2H); 5.94 (d, J= 3.9Hz, 1H); 7.35 (bs, 5H).

Compound 14: prepared from 13 according to condition A. $^1$H-NMR (60 MHz): δ 1.4 (d, J= 7 Hz, 3H); 1.4-2.2 ( m, 2H); 2.3-2.6 (m, 2H); 4.6 (m, 1H).

Compound 16: prepared from 15 according to condition A. $^1$H-NMR (60 MHz): δ 1.1 (d, J= 8Hz, 3H); 1.4-1.8 (m, 2H); 3.8 (bs, 1H); 3.3 (m, 2H); 3.9 (m, 1H); 7.1-7.3 (bs, 15H).$[\alpha]_D$ = -15.5· ( c= 6.45, $CHCl_3$). Anal.calcd. for $C_{23}H_{24}O_2$: C=83.08; H=7.28). Found :C=82.5; H=7.9.

Compound 18: prepared from 17 according to condition A . $^1$H-NMR (80 MHz): δ 1.35 (d, J= 6Hz, 3H); 1.45 (s, 1H); 1.6 (bs, 1H); 3.3-3.4 ( dd, 1H); 3.80 (s, 3H); 4.35-4.45 (m, 1H); 4.45 (d, J= 2Hz, 1H); 6.8-7.4 (dd, J= 8Hz, 4H).$[\alpha]_D$ = -53.6· (c= 0.28, $CHCl_3$). IR ($CHCl_3$), 3600 $cm^{-1}$, 1755, 1150.

Compound 19: to a solution of 2 (30 mg, 0.23 meq) in dry ether in a two necked round bottom flask,with a magnetic stirrer, were added $MgI_2$, in ether solution (1.5 eq), under a nitrogen atmosphere. After 1 h, the solution was quenched with brine and the organic phase was dried over $Na_2SO_4$. After evaporation of the solvent the crude product was purified by silica gel chromatography (hexane/ether 9:1 as eluent) affording pure 19 as a single product (45mg, 80 %). $^1$H-NMR (80 MHz): δ 0.86 ( bt, 3H); 1.25 (bs, 8H); 1.45-1.7 (m, 2H); 1.85, (d, 1H); 3.1-3.5 (m, 3H).

Reduction of 19 : 2-octanol: to a solution of 19 (45 mg, 0.17 meq) in dry DME, in a two necked round bottom flask equipped with a magnetic stirrer and under a nitrogen atmosphere, $nBu_3SnH$ (2.5 eq) was added. After 30 min. at 60° C the reaction was completed and the DME was evaporated under reduced pressure. MeOH was then added with silica gel and, after evaporation of the solvent, the powder was poured on a silica gel column (in hexane) and then eluted first with hexane a then with hexane/ether 95:5. The purified product was collected (38 mg) and compared by GLC and $^1$H-NMR with an authentic sample of 2-octanol (Fluka).

Compound 21: prepared from 20 according to condition A, B or C. The reaction was monitored by GLC and the purification of the compound was also checked by GLC. $^1$H-NMR (200 MHz): δ 0.05 (s, 6H); 0.89 (s, 9H); 1.65 (cq, 2H); 2.40 (d, 7

Hz, 2H); 3.5 (bd, 1H); 3.65 (s, 3H); 3.75 (t, J= 6Hz, 2H); 4.21 (m, 1H). IR ($CHCl_3$) 3520 $cm^{-1}$, 3320, 1740 and 1200.$[\alpha]_D$ = - 4.9° (c= 1.8, $CHCl_3$). Anal.calcd. for $C_{12}H_{26}O_4Si$ : C=54.93; H=9.99. Found : C=53.97; H=10.21.

Compound 22: prepared from 20 according to reference 14. $^1$H-NMR (300 MHz): ∂ 0.05 ( s, 6H); 0.89 (s, 9H); 1.6-2.0 (m, 4H); 3.34 (d, 1H); 3.65 (t, J= 6 Hz, 2H); 3.77 (s, 3H); 4.25 (m, 1H). IR ($CHCl_3$): 3500 $cm^{-1}$, 1735 and 1180. $[\alpha]_D$ = - 3.9° (c= 1.3, $CHCl_3$).

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