EFFICIENT SYNTHESIS OF CHIRAL 1,3-DIOLS AND OF 1-SUBSTITUTED-PROPAN-1-OLS THROUGH ASYMMETRIC HYDROGENATION

Ridha Touati, Béchir Ben Hassine *

Laboratoire de Synthèse Organique Asymétrique et Catalyse Homogène (01UR1201), Faculté des Sciences de Monastir, 5019 Monastir, Tunisia

(Reçu le 31 Janvier 2008, accepté le 20 Novembre 2008)

Abstract: Asymmetric hydrogenations of an achiral β-keto ester using a chiral diphosphine-ruthenium catalyst to set the hydroxyl function in a stereo controlled manner were used in key-step towards the total synthesis of both enantiomers of secondary alcohols with excellent enantioselectivity (>99% ee) and high yields.

Keywords: Asymmetric hydrogenation, atmospheric pressure, β-hydroxy esters, 1,3-diols, monotosylate 1,3-diols, secondary alcohols.

INTRODUCTION

Optically active alcohols are among of many naturally-occurring compounds, biologically-active molecules and materials, such as liquid crystals. They are also important as synthetic intermediates for the preparation of various functionalities such as halides, amines, esters, ethers, etc [1]. Accordingly, the development of practical methods for the enantioselective synthesis of both enantiomers of secondary alcohols is of great interest.

For the synthesis of these compounds, many methods are used, including the chemical or enzymatic resolution of racemic secondary alcohols [2,3], and chemical or enzymatic asymmetric reduction of prochiral ketones [4,5].

However, enzymatic reactions have a disadvantage: it is difficult to obtain both enantiomers of an alcohol by using a single biocatalyst. Since the number of available enzymes is limited, it is usually impossible to find a suitable enzyme for an unnatural substrate.

Compared to optically active secondary aromatic alcohols, optically active secondary aliphatic alcohols are hard to synthesize. The number of secondary aliphatic alcohols that have been prepared by the asymmetric reduction of ketones [6] or by the asymmetric hydroboration of alkenes is somewhat limited [7].

On the other hand, the asymmetric reaction of dialkylzinc complexes with aldehydes has been demonstrated as a very useful method for the synthesis of optically active alcohols [8]. Since the first report of a highly-enantioselective amino alcohol catalyst by Noyori in 1986 [9], extensive studies have been carried out in this area and many good catalysts have been developed [10-12]. However, the general applicability of these catalysts is still restricted because most of these catalysts are active with aromatic aldehydes [10,11] and only few are fit for aliphatic aldehydes [12].

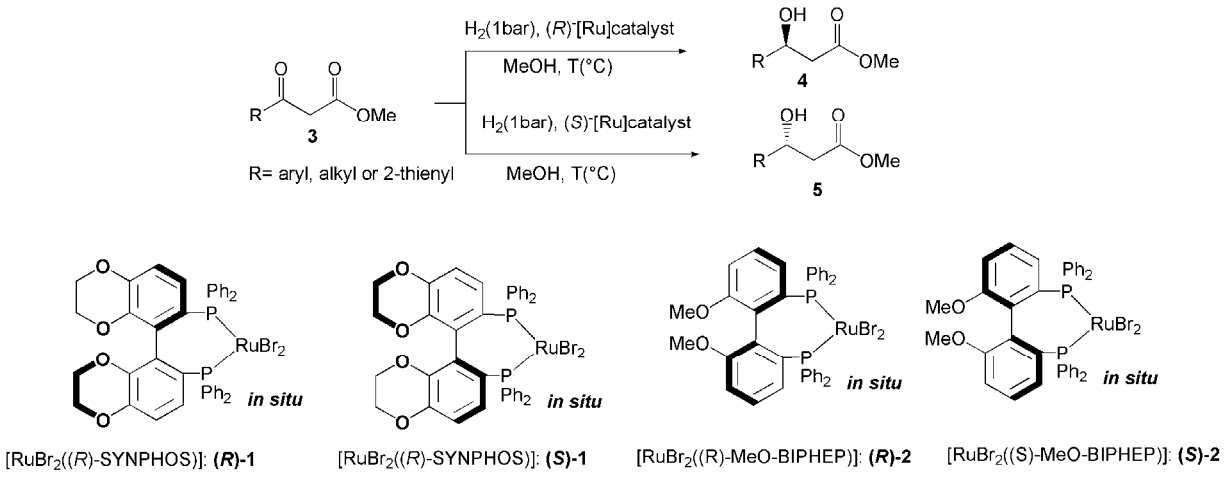
Thus, the development of a generally applicable catalytic enantioselective synthesis of optically active secondary aliphatic alcohols is a challenging problem. In this report, we would like to describe the enantioselective synthesis of both enantiomers of secondary aliphatic and aromatic alcohols in high optical purity.

* corresponding author, e-mail: bechirbenhassine@yahoo.fr

RESULTS AND DISCUSSION

In an earlier publication [13], we carried out an enantioselective hydrogenation of β-keto esters using chiral diphosphine-ruthenium complexes [14] **1**-**2** (Scheme 1).

As shown in table I, this method exhibited a wide scope and was applied to several alkyl- or aryl-substituted β-keto ester hydrogenations, giving access to multigram quantities of the corresponding β-hydroxy esters with high enantiomeric excesses. Excellent selectivities were conveniently (88<e.e.<99) obtained while working at atmospheric pressure for the ruthenium-promoted hydrogenation reaction of β-keto esters.

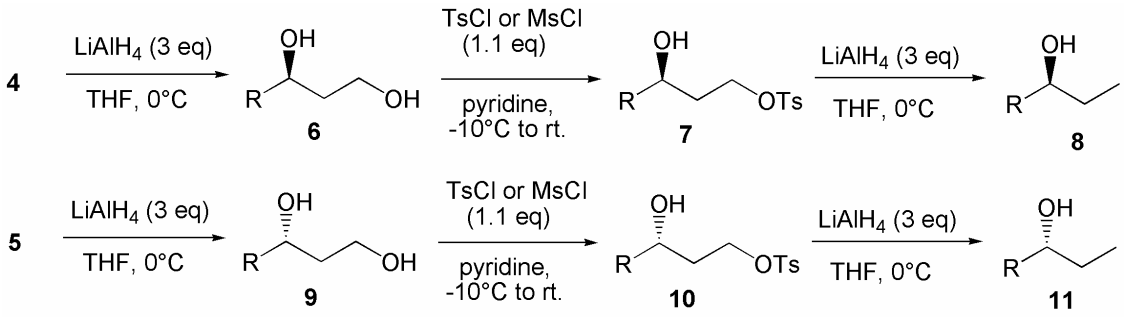


Scheme 1.

This procedure gives ready access to enantiomerically pure β-hydroxy esters **4** or **5** of various structures, without the need for special equipment. The method can thus be used in any laboratory in order to produce either pure enantiomer of the β-hydroxy esters in multigram quantities.

The absolute configuration of β-hydroxy esters 4 and 5 were assigned by considering the stereochemical model proposed for the hydrogenation reaction of functionalized ketones with ruthenium-arylphosphine catalysts [15].

To prepare non-racemic 1.3-diols **6** and **9**, (*R*)- or (*S*)-β-hydroxy esters previously obtained was treated with 3 equiv of $LiAlH_4$ in THF at 0°C for 2–3 h (Scheme 2). As shown in this scheme, all the reaction proceeded smoothly to give the desired products in high yields. The enantiomeric purities of **6** and **9**, (determined by HPLC analysis using Chiralcel OD or Chiralcel OD-H chiral columns) were very high, with near 99% e.e. for all the products bearing aryl, alkyl and 2-thienyl groups. The results indicate that no racemization occurred during the lithium aluminium hydride reduction.



Scheme 2.

The 1,3-diols **6** and **9** obtained were selectively tosylated (or mesylated) at the primary position yielding the monotosylate diols **7** and **10** in high yields (Scheme 2, 78%-91% yields).

Treatment of those products with lithium aluminium hydride afforded the secondary alcohols **8** and **11** in good yield. The specific rotation of these products (wich are summarized in experimental section), indicate that all products have high optical purity were found to be in agreement with the reported literature [9, 10(d),(i),(m)]. We confirmed these results by HPLC analysis (Figure 1)

Table I. Asymmetric hydrogenation of β-keto esters 3 at atmospheric pressure[a].

Hydroxy ester	R	Ru-catalyst[b]	T [°C]	time (h)[c]	Conv[d]	ee.[e] (configuration)
4a 5a	CH_3[f]	(*R*)-2 (*S*)-2	40	1	100	99 (*R*) 99 (*S*)
4b 5b	n-C_5H_{11}	(*R*)-1[T6] (*S*)-1	50	0.5	100	99 (*R*) 99 (*S*)
4c 5c	n-$C_{11}H_{23}$	(*R*)-2 (*S*)-2	50	24	100	97 (*R*) 97 (*S*)
4d 5d	n-$C_{13}H_{27}$	(*R*)-2 (*S*)-2	50	24	100	99 (*R*) 99 (*S*)
4e 5e	n-$C_{15}H_{31}$	(*R*)-2 (*S*)-2	50	24	100	99 (*R*) 99 (*S*)
4f 5f	Phenyl[f]	(*R*)-2 (*S*)-2	50	18	95	97 (*R*) 97 (*S*)
4g 5g	2-thienyl	(*R*)-2 (*S*)-2	25	72	100	90 (*R*) 90 (*S*)
4h 5h	4-Me-C_6H_4	(*R*)-1 (*S*)-1	65	20	100	97 (*R*) 97 (*S*)
4i 5i	4-MeO- C_6H_4	(*R*)-1 (*S*)-1	60	16	84	91 (*R*) 91 (*S*)
4j 5j	4-F- C_6H_4	(*R*)-1 (*S*)-1	65	18	87	89 (*R*) 89 (*S*)
4k 5k	4-Cl- C_6H_4	(*R*)-2 (*S*)-2	50	24	100	95 (*R*) 95 (*S*)
4l 5l	2-Cl- C_6H_4	(*R*)-1 (*S*)-1	50	24	95	94 (*R*) 94 (*S*)
4m 5m	1-naphtyl	(*R*)-2 (*S*)-2	65	24	100	94 (*R*) 94 (*S*)
4n 5n	2-naphtyl	(*R*)-1 (*S*)-1	65	24	100	88 (*R*) 88 (*S*)

[a] 2 mmol scale with MeOH as solvent (4 mL); [b] 2 mol% of the catalyst; [c] Not optimized; [d] Measured by ^{1}H NMR (300 MHz); [e] Enantiomeric excesses calculated by GC and HPLC analysis and/or ^{1}H NMR (300 MHz) with $Eu(tfc)_3$; [f] Ethyl ester.

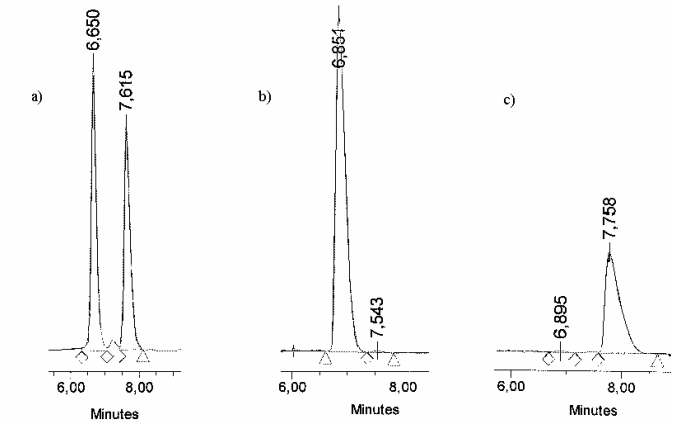


Figure 1: Chiral HPLC analysis, a) racemic-1-(4-chlorophényl)propan-1-ol, b) (*S*)-1-(4-chlorophényl)propan-1-ol, c) (*R*)-1-(4-chlorophényl)propan-1-ol For conditions, see Experimental Section.

3. Conclusion

We have developed a simple and highly efficient method for the asymmetric synthesis of both enantiomers of 1,3-diols and 1,3-diol monotosylates based upon catalytic asymmetric hydrogenation of an achiral β-keto ester by using atropisomeric diphosphine/ruthenium complexes to set the hydroxyl function in a stereo controlled manner with excellent enantioselectivity.

It is noteworthy that this method provides a convenient route to both enantiomers of 1-arylpropan-1-ols and 1-alkylpropan-1-ols in high synthetic yields and in high ee's (up to 99% ee) under mild reaction conditions.

EXPERIMENTAL SECTION

1. General Remarks

Melting points were determined with an Electrothermal-Engineering-LTD-9026 and are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AM 200 or 400 spectrometer. Spectra were obtained in deuteriated chloroform and Chemical shifts (δ) are reported in ppm downfield relative to internal Me_4Si. Coupling constants (*J*) are reported in Hz and refer to apparent peak multiplicities (recorded as s: singlet; d: doublet; t: triplet; q: quadruplet; m: multiplet; and br: broad). Mass spectra were determined on a Nermag R10-10C instrument. Ionization was obtained by chemical ionization with ammonia (DCI/NH_3) or by electrospray (on an API 3000 PE Sciex instrument). Optical rotations were measured on a Perkin-Elmer 241 polarimeter at 589 nm (sodium lamp). All solvents were freshly distilled, stored under argon and degassed by 3 purge cycles of vacuum/argon at room temperature prior to use. Optical purity (% ee) was determined by GC analysis on Lipodex A column, DB 1701 column [for (S)-O-acetyllactyl ester], HPLC Chiralcel OD-H or by ^{1}H-NMR spectroscopy in the presence of 10-20 mol % (+)-Eu(tfc)$_3$ at 300 MHz.

2. Synthesis of β-ketoesters

All β-ketoesters were prepared according to a literature procedure [13a].

3. Asymmetric hydrogenation reactions

4.3.1. *In situ* preparation [14] of dibromodiphosphine ruthenium (II) complexes [(P*P) $RuBr_2]_2$ (*R*)-MeO-biphep (30 mg, 0.048 mmol.) and (Cod)Ru(2-methylallyl)$_2$ (12.8 mg, 0.04 mmol) were placed in a 10 mL Schlenk tube and the vessel was purged with argon. Anhydrous acetone (2 mL degassed by 3 cycles of vacuum/argon at room temperature) was added. To this suspension was added 0.5 mL of a methanolic HBr solution (0.176 M, 8.8 mmol) and the suspension was stirred during 30 min at room temperature. A yellow solid precipitated. Subsequently, the solvent was thoroughly evaporated under vacuum and the catalyst was immediately used.

3.2. General procedure for hydrogenation reaction at atmospheric pressure:

A solution of substrate **3** (2 mmol) was diluted in degassed methanol (4 mL). This solution was canulated into a 10 mL Schlenk tube and degassed by 3 cycles of vacuum/argon. This mixture was added to the catalyst (2% mol) in a glass vessel and placed under argon. The argon atmosphere was replaced with hydrogen by 3 cycles of pressurizing. Hydrogenations were run under 1 atm of hydrogen. Conversion rate was determined by ^{1}H NMR analysis.

In the same manner as that described for the preparation of **4a-n**, **5a-n** were obtained by asymmetric hydrogenation reaction at atmospheric pressure using (*S*)-1or (*S*)-2. Its NMR and MS spectra were identical with those of **4a-n**

Ethyl (*S*)-3-hydroxybutanoate (4a): a colourless oil, Yield 95%, $[\alpha]^{25}_D$ = +32 (*c* 1, $CHCl_3$). ee> 99%. ^{1}H NMR ($CDCl_3$, 300 MHz, 27°C): δ= 3.98-4.11 (m, 1H), 3.78-3.84 (m, 2H), 2.9 (br, 1H), 2.41-2.56 (m, 2H), 1.44-1.52 (m, 2H), 1.27-1.35 (m, 3H), 0.96 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz, 27°C): δ= 171.5, 70.4, 69.1, 31.6, 25.1, 22.5.

Methyl (*R*)-(-)-3-hydroxyoctanoate (4b): a colourless oil, Yield 96%, $[\alpha]^{25}_D$ = -26 (*c* 1, $CHCl_3$).ee> 99%. ^{1}H NMR ($CDCl_3$, 300 MHz, 27°C): δ= 3.92-4.08 (m, 1H), 3.71 (s, 3H), 2.8 (br, 1H), 2.37-2.55 (m, 2H), 1.41-1.48 (m, 2H), 1.27-1.35 (m, 6H), 0.89 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz, 27°C): δ= 173.4, 68.1, 51.6, 41.1, 36.5, 31.6, 25.1, 22.5, 13.9. MS (DCI, NH_3): *m/z* 192 (100%, $[M+NH_4]^+$), 175 (50%, $[M+H]^+$), 157 (10%, $[M-H_2O+H]^+$). MS (EI, 70 eV): *m/z* 175 ($[M+H]^+$, 4%), 103 ($[M-C_5H_{11}]^+$, 100%), 71 ($[C_5H_{11}]^+$, 50%), 43 (60%).

Methyl (*R*)-3-hydroxytetradecanoate (4c): Yield 100%, as a white solid; mp 39-40°C; $[\alpha]_D$= -18.5 (*c* 1, $CHCl_3$). IR (KBr): ν= 3350 (νOH), 2950 (νCH_3), 2850 (νCH_2), 1745 (νCOO) cm^{-1} ^{1}H NMR ($CDCl_3$): δ = 3.99 (m, 1H), 3.68 (s, 3H), 3.03 (br, 1H), 2.31-2.55 (m, 2H), 1.63-1.65 (m, 2H), 1.20-1.42 (m, 18H), 0.87-0.93 (t, 3H, *J*= 6.1Hz); ^{13}C NMR ($CDCl_3$): δ = 173.5, 67.9, 52.1, 40.9, 36.4, 31.8, 29.5, 29.2, 25.3, 22.5, 13.9; MS (70 eV): m/z 258 (M^+, 5); 240 (4); 208 (19), 183 (17), 166 (16), 103 (100), 55 (41), 43 (64).

Methyl (*R*)-3-hydroxyhexadecanoate (4d): Yield: 98%, as a white solid, mp 52-53°C; $[\alpha]_D$= -16.6 (*c* 1, $CHCl_3$); IR (KBr): ν= 3500-3000 (νOH), 2980 (νCH_3), 2800 (νCH_2), 1760-1740 (ν COO) cm^{-1}; ^{1}H NMR ($CDCl_3$) : δ = 3.92-3.84 (m, 1H), 3.68 (s, 3H), 2.89 (br, 1H), 2.40-2.60 (m, 2H), 1.69-1.76 (m, 2H), 1.28-1.49 (m, 22H), 0.86-0.93 (t, 3H, *J*= 6.1Hz); ^{13}C NMR ($CDCl_3$): δ = 173.2, 67.8, 53.2, 41.1, 38.1, 31.7, 29.4, 29.1, 22.5, 25.3, 13.9; MS (70 eV): m/z =286 (M^+, 10), 268 (12), 236 (25), 211 (25), 111 (26), 103 (100), 75 (83), 55 (45), 43 (82).

Methyl (*R*)-3-hydroxyoctadecanoate (4e): Yield 98% , as a white solid; mp 55-56°C; $[\alpha]_D$= -15.5 (*c* 1, $CHCl_3$); IR (KBr) : ν= 3350 (νOH), 2950 (νCH_3), 2850 (νCH_2), 1745 (νCOO) cm^{-1}; ^{1}H NMR ($CDCl_3$) : δ = 3.99-4.12 (m,1H), 3.71 (s, 3H), 2.89 (s, 1H), 2.46-2.52 (m, 2H), 1.44 -1.54 (m, 2H), 1.25-1.34 (m, 26H), 0.87(t, 3H, *J*= 6.5Hz); ^{13}C NMR ($CDCl_3$): δ = 173.4, 67.9, 51.6, 41.0, 36.4, 31.8, 29.5, 25.4, 22.6, 14.0; MS (70 eV): m/z= 314 (M^+, 1), 296 (5), 103 (64), 43 (100).

Ethyl (*R*)-3-hydroxy-3-phenylpropanoate (5f): Yield 92%, as a colourless oil; $[\alpha]_D$= -52 (*c* 1, $CHCl_3$); IR (neat): ν= 3460 (νOH), 3040 (νCH_3), 2970 (νCH_2), 1716 (νCOO) cm^{-1}; ^{1}H NMR ($CDCl_3$) : δ = 7.25-7.42 (m, 5H), 5.11-5.19 (m, 1H), 4.17 (q, 2H, J= 7.1) 3.39-3.41 (br, 1H), 2.75 (t, 2H, *J*= 7.2), 1.24-1.31 (t, 3H, *J*= 7.1Hz); ^{13}C NMR ($CDCl_3$): δ = 172.2, 142.4, 128.4, 127.6, 125.5, 70.2, 60.7, 43.2, 14.0. MS (70 eV): m/z= 194 (M^+, 40), 177 (5), 120 (10), 107 (87), 79 (100), 77 (92).

Methyl (*S*)-3-hydroxy-3-thienylpropanoate (4g): Yield 96 %; as a colourless oil; IR (neat) : ν= 3350 (νOH), 2950 (νCH_3), 2850 (νCH_2), 1745 (νCOO) cm^{-1}; ^{1}H NMR ($CDCl_3$) : δ = 7.24-7.28 (m, 1H), 6.95-7.01 (m, 2H), 5.38 (t, 1H, *J*= 5,2Hz), 3.58 (br, 1H), 2.78 (d, 2H, *J*= 5.2 Hz), 3.72 (s, 3H); ^{13}C NMR ($CDCl_3$): δ = 172.1, 146.2, 126.6, 124.7, 123.5, 66.3, 51.8, 42.9; MS (70 eV): m/z 186 (M^+, 40); 113 (100); 85 (60); 45 (22). MS (CI / NH_3): m/z= 204 ($M+NH_4^+$, 90),186 ($M+NH_4^+$-H_2O, 100), 169 (MH^+-H_2O , 10).

Methyl (*R*)-3-Hydroxy-3-(4-methylphenyl)propanoate (5h): Yield 85%; as a white solid, mp 50-52°C; $[\alpha]_D$=-22 (*c*=1, $CHCl_3$); IR (KBr): ν= 3350 (νOH); 1730 (νCOO); 3045 (νCH_3); 2840 (νCH_2) cm^{-1}.^{1}H NMR ($CDCl_3$): δ = 2.30 (s, 3H), 2.63-2.80 (m, 2H), 3.15 (d, 1H, *J*= 14 Hz), 3.70 (s, 3H), 5.05-5.13 (m, 1H), 7.15 (d, 2H, *J*= 7.1 Hz), 7.28 (d, 2H, *J*= 7.1 Hz); ^{13}C NMR ($CDCl_3$): δ = 21.2, 43.3, 54.1, 72.5, 126.6, 131.6, 141.6, 144.1, 172.6; MS (70 eV): m/z= 194 (M^+, 22); 121 (100); 179 (11); 77 (33), 65 (20).

Methyl (*S*)-3-Hydroxy-3-(4-methoxyphenyl)propanoate (4i): Yield 80%; as a white solid, mp 29-31°C; $[\alpha]_D$= -29 (*c*=1, $CHCl_3$); IR (KBr): ν= 3433 (νOH); 1708 (νCOO); 2912 (νCH_3); 2850 (νCH_2) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 2.61-2.78 (m, 2H), 3.70(s, 3H), 3.80-3.82 (m, 3H), 5.02-5.16 (m, 1H), 6.77 (d, 2H, *J*= 7.2 Hz), 7.28-7.31(d, 2H); ^{13}C NMR ($CDCl_3$): δ = 43.2, 51.9, 55.3, 69.9, 113.9, 126.9, 134.7, 159.1, 172.7; MS (70 eV): m/z= 210(M^+, 9), 137 (100), 109 (23), 94 (14), 77 (15).

Methyl (*S*) –3-(4-fluorophenyl)-3-Hydroxypropanoate (4j): Yield 87 %; as a colourless oil; ^{1}H NMR ($CDCl_3$): δ = 2.62-2.,78 (m, 2H); 3.45-3.47(br, 1H); 3.70(s, 3H); 5.07-5.12 (m, 1H); 6.98-7.06 (m, 2H); 7.27-7.36(m, 2H); ^{13}C NMR ($CDCl_3$): δ = 42.6, 52.2, 70.0, 115.5, 127.7, 138.8, 164.3, 172.9. MS (70 eV): m/z= for $C_{13}H_{19}O_3FSi$, 270 (23%); 255(100%), 210(29%), 197(17%), 180(15%), 73(%).

Methyl (*S*)-3-(4-chlorophenyl)-3-hydroxypropanoate (4k) : Yield 74% ; as a white solid, mp 39-41°C; $[\alpha]_D$= -18 (*c*=1, EtOH); IR (KBr): ν= 3453 (νOH); 1717 (νCOO); 2998 (νCH_3); 2890 (νCH_2) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 2.70-2.72 (m, 2H), 3.32 (d, 1H, *J*= 2 Hz), 3.72(s, 3H), 5.08-5.14(m, 1H), 7.26-7.23 (m, 4H); ^{13}C NMR ($CDCl_3$): δ = 42.8, 51.8, 69.5,126.9, 128.6, 134.5, 140.8, 172.6. MS (70 eV): m/z= 214(M^+, 13), 141 (100), 113 (21), 77 (64), 43 (20).

Methyl (*S*) -3-(2-chlorophenyl) -3-Hydroxypropanoate (4l): Yield 77 %; as a colorless oil; $[\alpha]_D$= -20 (*c*=1, EtOH); IR (KBr): ν= 3453 (νOH); 1717 (νCOO); 2998 (νCH_3); 2890 (νCH_2) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ= 2.54-2.94 (m, 2H), 3.39 (br, 1H), 3.76 (m, 3H), 5.50-5.54 (m,1H), 7.19-7.67(m, 4H); ^{13}C NMR ($CDCl_3$): δ= 41.1, 51.8, 69.9, 126.9, 127.1, 128.6, 129.3, 131.2, 139.7, 172.7. MS (70 eV): m/z= 214(M^+, 6); 141 (100), 179 (30), 155(15), 77 (62), 49(55).

Methyl (*S*)-3-Hydroxy-3-(1-naphtyl)propanoate (4m): Yield 79%; as a white solid ; mp 50-52°C; $[\alpha]_D$= -38 (*c* 1, $CHCl_3$); IR (KBr): ν= 3422 (νOH); 1751 (νCOO); 2949 (νCH_3); 2830 (νCH_2) cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 2.79-2.97(m, 2H), 3.36(d, 1H, J= 2 Hz), 3.76(s, 3H), 5.30-5.38 (m, 1H), 7.48-7.87 (m, 7 H); ^{13}C NMR ($CDCl_3$): δ = 43.0, 51.8, 70.3, 123.5, 132.9, 172.5; MS (70 eV): m/z =230 (M^+, 99), 157 (100), 129 (83), 77 (16), 43 (21).

Methyl (*S*)-3-Hydroxy-3-(2-naphtyl)propanoate (4n): Yield : 75%; as a white solid ; mp 50-52°C; $[\alpha]_D$ = -44.6 (*c*=1, $CHCl_3$); IR (KBr): ν= 3422 (νOH); 1751 (νCOO); 2949 (νCH_3); 2830 (νCH_2) cm^{-1}. ^{1}H NMR ($CDCl_3$) : δ = 2.88-2.96 (m, 2H), 3.43 (d, 1H, *J*= 8 Hz), 3.91 (s, 3H), 5.22-5.30 (m, 1H), 7.57-8.27 (m, 7 H); ^{13}C NMR ($CDCl_3$): δ = 43.3, 52.8, 71.3, 122.5,123.3. 131.9, 173.5; MS (70 eV): m/z =230 (M^+, 99), 157 (100), 129 (83), 77 (16), 43 (21).

4. Synthesis of 1, 3-diols: General method

Ethyl-(*R*)-3–hydroxy-3-phenylepropanoate **5f** (0,265 g; 1,42 mmol) was dissolved in 10 mL of dry ether and the solution was added drop wise at 0°C to a stirred suspension of $LiAlH_4$ (0.115 g; 3 mmole; 2.1 eq.) in dry THF under argon. The mixture was allowed to warm to room temperature over 1.5 h and then was quenched by sequential addition of H_2O (0.25 mL), 10% NaOH (0.25 mL), and additional H_2O (0.50 mL). The product was extracted with ether and the organic phase was washed with brine, dried and evaporated. Column chromatography [SiO_2, Cyclohexane / AcOEt (50:50)] gave 185 mg of diol **9f**.

(*R*)-1-Phenylpropane-1, 3-diol (9f): Yield: 86%; as a colourless oil; $[\alpha]_D$= +64 (*c* 1, $CHCl_3$); IR(neat) : ν =3320 (ν_{OH}), 3020 (ν_{CH_3}), 2935 (ν_{CH_2}), 1595 ($\nu_{C=C}$) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ = 7.15-7.40 (m, 5H), 4.73-4.91 (m, 1H), 4,12-4,20 (br, 1H), 3,58-3,74 (m, 2H, +OH), 1.95-1.76 (m, 2H); ^{13}C NMR ($CDCl_3$) δ = 144.0, 128.1, 127.1, 125.4, 73.1, 60.4, 40.8; MS (70 eV): m/z= 152

(28); 133 (10); 107 (60); 91 (7), 79 (100), 77 (90); MS (CI / NH_3): m/z= 170 (MNH_4^+, 100), 152 (MH^+, 64).

(*R*)-butane-1,3-diol (6a): Yield: 85%, as a white oil; IR(neat) : ν= 3360 (ν_{OH}), 2994 (ν_{CH_3}), 2816 (ν_{CH_2}) cm^{-1}; ^1H NMR ($CDCl_3$) δ = 1.21 (d, 3H, *J*= 7.1Hz), 1.63 (m, 2H), 2.12 (br, 2H), 3.39 (m, 1H), 3.54 (t, 2H, *J*= 7.1Hz); ^{13}C NMR ($CDCl_3$) δ = 64.2, 56.4, 42.2, 25.5.

(*R*)-octane-1,3-diol (6b): Yield: 88%, as a colourless oil; IR(neat) : ν= 3400 (ν_{OH}), 2998 (ν_{CH_3}), 2825 (ν_{CH_2}) cm^{-1}; ^1H NMR ($CDCl_3$) δ = 0.96 (t, 3H, *J*= 7.3Hz), 1.29-1.44 (m,8H), 1.65 (m, 2H), 2.50 (br, 2H), 3.41 (m, 1H), 3.56 (m, 2H); ^{13}C NMR ($CDCl_3$) δ = 67.9, 56.7, 40.0, 36.9, 32.2, 23.2, 22.8, 14.1.

(*R*)-Tetradecane-1, 3-diol (6c): Yield: 87%; as a white solid, mp= 48-49°C; $[\alpha]_D$= -4.3 (*c* 1, EtOH); IR (KBr disk) : ν =3500-3100 (ν_{OH}), 2950(ν_{CH_3}), 2920, 2800 (ν_{CH2}) cm^{-1}; ^1H NMR ($CDCl_3$) δ = 0.88 (t, 3H, *J*= 7.1Hz), 1.27 (m, 18H), 1.48 (m, 2H), 1.73 (m, 2H), 2.94 (sl, 1H), 3.07 (br, 1H), 3.91 (m, 3H); ^{13}C NMR ($CDCl_3$) δ = 72.5, 61.9, 38.8, 37.7, 32.0, 29.9, 29.3, 25.5, 22.1, 14.0; MS (70 eV): m/z= 230 (M^+, 11); 214 (28); 213 (100); 183 (17), 111 (14), 97 (25); 83 (37).

(*R*)-Hexadecane-1,3-diol (6d): Yield : 88%; a white solid, mp= 60-63°C; $[\alpha]_D$= -3.7 (*c* 1, EtOH); IR (KBr disk) : ν= 3500-3100 (ν_{OH}), 2950(ν_{CH_3}), 2920, 2800 (ν_{CH2}) cm^{-1}; ^1H NMR ($CDCl_3$) δ = 0.86 (t, 3H, J= 7Hz), 1.23 (m, 22H), 1.42 (m, 2H), 1.70 (m, 2H), 2.91 (sl, 1H), 3.05 (br, 1H), 3.87 (m, 3H); ^{13}C NMR ($CDCl_3$) δ = 14.0, 22.6, 25.5, 29.3, 29.6, 31.8, 37.7, 38.2, 61.6, 72.1; MS (70 eV): m/z =258 (M^+, 11); 242 (30); 241 (100); 211 (19), 139 (16), 125 (26); 111 (40).

(*R*)-Octadecane-1,3-diol (6e): Yield : 84%; as a white solid, mp= 65-68°C; $[\alpha]_D$= -3.2 (*c* 1, EtOH); IR (KBr disk) : ν= 3500-3100 (ν_{OH}), 2950(ν_{CH_3}), 2920, 2800 (ν_{CH2}) cm^{-1}; ^1H NMR ($CDCl_3$) δ = 0.81 (t, 3H, *J*= 7Hz), 1.25 (m, 26H), 1.51 (m, 2H), 1.77 (m, 2H), 2.95 (sl, 1H), 3.14 (sl, 1H), 3.91 (m, 3H); ^{13}C NMR ($CDCl_3$) δ = 72.2, 62.4, 38.2, 36.5, 32.0, 29.5, 29.4, 25.2, 22.1, 14.1; MS (70 eV): m/z =286 (M^+, 13); 258 (100); 239 (16), 167 (17), 153 (25); 139 (41).

(*S*)-1-Thienylpropane-1,3-diol (6g): Yield: 83%, as a colourless oil; $[\alpha]_D$= -25 (*c* 1, $CHCl_3$) IR(neat) : ν= 3370 (ν_{OH}), 2964 (ν_{CH_3}), 2814 (ν_{CH_2}) cm^{-1}; ^1H NMR ($CDCl_3$) δ = 7.25-7.28 (m, 1H), 6.95-7.01 (m, 2H), 5.23-5.17 (t, 1H, *J*= 5.2Hz), 3.84-3.86 (m, 2H), 3,47 (br, OH), 2,84 (br, OH), 1.99-2.21 (m, 2H); ^{13}C NMR ($CDCl_3$) δ = 146.3, 126.5, 124.2, 123.3, 68.5, 59.9, 40.6; MS (70 eV): m/z =158 (M^+, 25); 140 (10); 113 (100); 85 (50) ; 45 (23). MS (CI / NH_3): m/z= 176 ($M+NH_4^+$, 15) ; 158 ($M+NH_4^+$-H_2O, 100) ; 141 (MH^+-H_2O, 10)

(*S*)-1-(4-Methylphenyl)-propane-1,3-diol (6h): yield: 85%, as a colorless oil; $[\alpha]_D$= -47 (*c*=1, $CHCl_3$); IR(neat) : ν cm^{-1} : 3320 (ν_{OH}), 3020 (ν_{CH_3}), 2935 (ν_{CH_2}), 1595 (($\nu_{C=C}$); ^1H NMR ($CDCl_3$) δ = 1.99-2.4 (m, 2H), 3.18 (s, 3H), 3.62-3.79 (m, 2H), 3.11-3.18 (br, 2H), 5.07-5.14 (m, 1H), 7.12-7.17 (d, 2H), 7.25-7.28 (d, 2H); ^{13}C NMR ($CDCl_3$) δ = 21.2, 43.3, 54.1, 72.5, 126.6, 131.6, 141.6, 144.1.

(*S*)-1-(4-Methoxyphenyl)-propane-1,3-diol (6i):Yield : 92%; a white solid, mp= 44-45°C; $[\alpha]_D$= -38 (*c* 1, $CHCl_3$); IR (KBr disk) : ν cm^{-1} : 3320 (ν_{OH}), 3020 (ν_{CH_3}), 2935 (ν_{CH_2}), 1595 (($\nu_{C=C}$); ^1H NMR ($CDCl_3$) δ = 1.90-2.10 (m, 2H), 3.65 (s, 3H), 4.80(m, 1H), 3.70-3.85 (m, 3H), 6.78-6.85. (d, 2H), 7.15-7.30 (d, 2H); ^{13}C NMR ($CDCl_3$) δ = 41.5, 55.9, 61.8, 74.1, 114.9, 127.5, 136.8, 160.0.

(*S*)-1-(4-fluorophenyl) propan-1,3-diol (6j): Yield: 95%, as a colourless oil; $[\alpha]_D$= -31 (*c* 1, MeOH)**;** RMN ^1H (MeOD, δ ppm): 1.80-2.05 (m, H); 3.54-3.80 (m, H); 4.81-4.89 (m, H); 7.02-7.1(m, 2H); 7.35-7.45 (m, 2H). ^{13}C NMR (CD_3OD) δ = 42.3, 59.6, 71.3, 128.7, 142.0, 161.4, 164.6; MS (70 eV): m/z = for $C_{12}H_{19}O_2ClSi$, 223 (32); 197 (100); 147 (42); 73 (76).

(*S*)-1-(4-Chlorophenyl)-propane-1,3-diol (6k): Yield : 84%; a white solid, mp= 45-46°C; $[\alpha]_D$= -27 (*c* 1, $CHCl_3$); IR (KBr disk) : ν cm^{-1} : 3320 (ν_{OH}), 3020 (ν_{CH_3}), 2935 (ν_{CH_2}), 1595 (($\nu_{C=C}$);^1H

NMR ($CDCl_3$) δ = 7.15-7.40 (m, 4H), 4.73-4.91 (m, 1H), 4,12-4,20 (br, OH), 3,58-3,74 (m, 2H, +OH), 1.95-1.76 (m, 2H); ^{13}C NMR ($CDCl_3$) δ = 144.0, 128.1, 127.1, 125.4, 73.1, 60.4, 40.8;

(*S*)-1-(2-chlorophenyl) propan-1,3-diol (6l): Yield : 84%; a white solid, mp= 67-68°C; $[\alpha]_D$= -32 (*c* 1, $CHCl_3$); IR (KBr disk) : ν cm^{-1} : 3320 (ν $_{OH}$), 3020 (ν $_{CH_3}$), 2935 (ν $_{CH_2}$), 1595 ((ν $_{C=C}$);^1H NMR ($CDCl_3$) δ = 7.00-7.49 (m, 4H), 5.15-5.22 (m, 1H), 3.65-3.79 (m, 1H),3.2 (br, 1H), 2.4 (br, 1H), 1.65-1.92 (m, 2H); ^{13}C NMR ($CDCl_3$) δ = 141.9, 131.8, 129.7, 128.8, 127.5, 127.4, 71.4, 62.0, 38.9.

(*S*)-1-(1-Naphtyl)-propane-1,3-diol (6m): yield: 80%, as a white solid; $[\alpha]_D$= -61 (*c* 1, $CHCl_3$); IR (KBr disk) : ν= 3320 (ν $_{OH}$), 3020 (ν $_{CH_3}$), 2935 (ν $_{CH_2}$), 1595 ((ν $_{C=C}$) cm^{-1} ; ^1H NMR ($CDCl_3$) δ = 2.90-3.10 (m, 2H), 3.65-3.90 (m, 1H+2 OH), 5.10-5.20 (m, 1H), 6.95-7.30 (m, 7H); ^{13}C NMR ($CDCl_3$) δ = 42.0, 58.8, 71.3, 124.8, 126.7, 128.7, 129.0, 130.5, 133.8, 134.0, 134.9.

(*S*)-1-(2-Naphtyl)-propane-1,3-diol (6n): yield: 85%, as a white solid; $[\alpha]_D$= -55 (*c* 1, $CHCl_3$); IR (KBr disk) : ν =3350 (ν $_{OH}$), 3010 (ν $_{CH_3}$), 2950 (ν $_{CH_2}$), 1596 (ν $_{C=C}$) cm^{-1}; ^1H NMR ($CDCl_3$) δ = 2.85-3.14 (m, 2H), 3.55-3.80 (m, 1H+2OH), 5.08-5.16 (m, 1H), 6.99-7.45 (m, 7H); ^{13}C NMR ($CDCl_3$) δ = 43.5, 60.1, 70.1, 121.5, 122.6, 126.5, 128.1, 128.9, 129.1, 129.8, 131.0, 132.4, 133.5, 135.9,

5. Preparation of (+)-(*S*)-l-(Tosyloxy)tetradecan-3-ol (10c).

A chilled solution of diol 9c (0.390 g, 1.70 mmol) in dry pyridine (1.5 mL) was added all at once via syringe to a -10 °C solution of tosyl chloride (0.355g, 1.86 mmol) also in dry pyridine (1.5 mL). The reaction mixture was allowed to warm to room temperature while stirring was continued under an atmosphere of N_2,. After being stirred at room temperature for 3 h, the reaction mixture was diluted with 50 mL of Et_20, washed with brine (10 mL), dried over Na_2S0_4, and concentrated in vacuo. The residual crude material (0.632 g) was chromatographed on 10 g of silica gel with 15% EtOAc/petroleum ether (160 mL) then concentrated in vacuo to give 10c as a white solid: 0.420 g (64%); $[\alpha]_D$= +10.4 (*c* 1, EtOH); ^1H NMR ($CDCl_3$) δ = 0.88 (t, *J* = 6.4 Hz, 3 H), 1.25 (m, 18 H), 1.37 (m, 2 H), 1.64 (m, 1 H), 1.81 (m, 1H), 2.23 (br, 1H), 2.42 (s, 3 H), 3.68 (m, 1 H), 4.18 (m,2H),7.35(d,J=7.5Hz,2H),7.78(d, J=7.5Hz,2H); ^{13}C NMR ($CDCl_3$) δ = 13.9, 21.4, 22.5, 25.3, 29.2, 29.4, 31.7, 36.0, 37.3, 67.5, 67.9, 127.7, 129.7, 132.8, 144.6; MS (70 eV): m/z =384 (M^+, 17), 230 (25), 213 (45), 212 (21), 196 (13), 195 (88), 139 (67), 125 (59), 111 (85).

(*R*)-3-Hydroxy-3-phenylpropyl methanesulfonate (10f): To a solution of (*R*)-1-phenylpropane-1,3-diol 9f (150 mg, 0.94 mmol) in ether (30 mL) was added drop wise 2 mL of distilled triethylamine (0.14 mmol, 1.5 eq.) and freshly distilled mesyl chloride (0.17 mmol, 1.1 eq.) under nitrogen at -10°C. After stirring at -10 to 0°C for 3 h, the mixture was poured into ice water (30 mL), washed with 20% H_2SO_4, saturated aqueous $NaHCO_3$, and brine, and dried over $MgSO_4$. The crude product was purified by column chromatography (SiO_2, CH_2Cl_2) to afford 20; yield: 238 mg (82%); colourless oil; $[\alpha]_D$: -25 (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ = 7.25-7.42 (m, 5H), 4.79-4.88 (m, 1H), 4.19-4.29 (m, 1H), 4.38-4.46 (m, 1H), 2.94 (s, 3H), 2.85 (br, OH), 2.06-2.15 (m, 2H); ^{13}C NMR ($CDCl_3$) δ =143.4, 128.5, 127.8,125.6, 70.0, 67.1, 38.0, 37.0; MS(70 eV): m/z_230 (M^+, 5), 134 (35), 107 (100), 105 (60), 79 (70), 77 (32).

(*S*)-l-(Tosyloxy)butan-3-ol (10a). yield: 86%, as a colorless oil; ^1H NMR ($CDCl_3$) δ = 1.21 (d, *J* = 7.2 Hz, 3 H), 2.25 (br, 1H),2.42 (s, 3 H), 3.54 (m, 1 H), 3.81-3.96 (m, 2 H), 7.40 (d, *J*=7.5Hz,2H),7.82 (d, *J*=7.5Hz,2H); ^{13}C NMR ($CDCl_3$) δ = 21.1, 24.3, 65.1, 74.8, 129.6, 131.0, 140.1, 146.3.

(*S*)-l-(Tosyloxy)octan-3-ol (10b). yield: 88%, as a white solid; $[\alpha]_D$: -33 (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$) δ = 0.91 (t, *J* = 6.4 Hz, 3 H), 1.32-1.44 (m, 8 H), 2.30 (br, 1H), 2.56 (s, 3 H), 3.36-3.85 (m, 1 H),4.18-4.25(m,2H),7.45(d, *J*=7.5Hz, 2H), 7.82(d, *J*=7.5Hz, 2H); ^{13}C NMR ($CDCl_3$) δ = 14.2, 22.9, 23.2, 24.5, 32.2, 33.5, 71.0, 73.5, 125.6, 128.6, 189.3, 146.3.

(*S*)-l-(Tosyloxy)hexadecan-3-ol (10d). yield: 90%, as a white solid; ^{1}H NMR ($CDCl_3$) δ = 0.94 (t, *J* = 6.4 Hz, 3 H), 1.33-1.48 (m, 18 H), 2.38 (br, 1H), 2.41 (s, 3 H), 3.58-3.85 (m, 1 H), 4.28-4.39(m, 2H), 7.45(d, *J*=7.5Hz, 2H),7.91(d, *J*=7.5Hz, 2H); ^{13}C NMR ($CDCl_3$) δ = 14.2, 22.8, 25.5, 29.7, 29.8, 31.4, 37.5, 38.6, 64.6, 70.1 126.4, 127.8, 137.2, 144.2.

(*S*)-l-(Tosyloxy)octadecan-3-ol (10e). yield: 91%, as a white solid; ^{1}H NMR ($CDCl_3$) δ = 0.86 (t, *J* = 6.4 Hz, 3 H), 1.33-1.48 (m, 28 H), 2.41 (br, 1H), 2.38 (s, 3 H), 3.56-3.95 (m, 1 H), 4.20-4.31(m,2H), 7.41 (d, *J*=7.5Hz, 2H),7.89 (d, *J*=7.5Hz, 2H); ^{13}C NMR ($CDCl_3$) δ = 14.0, 18.6, 20.4, 22.5, 22.7, 25.2, 27.5, 29.1, 31.6, 32.2, 33.4, 69.3, 73.5, 124.6, 127.5, 136.1, 144.2.

(*S*)-3-Hydroxy-3-(2-thienyl)propyl methanesulfonate (7g): yield: 78%, as a colorless oil; $[\alpha]_D$: -33 (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ = 7.23-7.28 (m, 1H), 6.93-7.01 (m, 2H), 5.05-5.14 (m, 1H), 4.51 (dt, 1H, *J*= 6.5 Hz; *J*= 10.1 Hz), 4.22 (dt, 1H, J= 6.5 Hz; *J*=10.1 Hz), 3.10 (br, 1H), 3.05 (s, 3H), 2.18 (m, 2H); ^{13}C NMR ($CDCl_3$) δ = 147.3, 126.7, 124.8, 123.9, 66.9, 65.7, 38.1, 37.0; MS(70 eV): m/z=236 (M^+, 20), 219 (4), 140 (40), 113 (89), 86 (100), 79 (50), 45 (60); MS(CI/NH_3): m/z= 254 ($M+NH_4^+$, 65), 236 ($M+NH_4^+$, H_2O, 100), 219 (MH^+- H_2O, 20).

(*S*)-1-(4-méthylphenyl)-3-(tosyloxy) propan-1-ol (7h): yield: 80%, as a colorless oil; $[\alpha]_D$: -33 (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ = 1.93(s, 3H); 2.1-2.15(m, 2H+ OH); 2.56 (s, 3H); 3.99-4.05(m, 1H); 4.12-4.21(m, 1H); 4.8-4.87(m, 1H); 6.89-7.20(m, 4H); 7.3-7.89(m, 4H).^{13}C NMR ($CDCl_3$) δ =21.1, 22.1, 38.3, 64.7, 67.4, 115.2, 128.3, 128.1, 129.0, 130.1, 132.9, 136.4, 137.2, 144.9.

(*S*)-1-(4-méthoxyphenyl)-3-(tosyloxy) propan-1-ol (7i): yield: 78%, as a colorless oil; $[\alpha]_D$: -28 (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ = 2.0-2.2 (m, 2H+ OH), 2.55(s, 3H), 3.79(s, 3H), 4.11-4.16 (m, 1H), 4.35-4.46 (m, 1H), 4.82-491 (m, 1H), 6.85-7.3(m, 4H), 7.4-7.9 (m, 4H). ^{13}C NMR ($CDCl_3$) δ =22.1, 38.5, 55.0, 69.5, 71.0, 114.9, 128.6, 129.1, 129.6, 130.5, 132.6, 137.4, 138.2, 160.1.

(*S*)-1-(4-fluorophenyl)-3-(tosyloxy) propan-1-ol (7j): yield: 85%, as a colorless oil; ^{1}H NMR ($CDCl_3$) δ =1.92-2.08 (m, 2H), 2.3 (br, OH), 2.45 (s, 3H), 3.96-4.03 (m, 1H), 4.20-4.28 (m, 1H), 4.73-4.77 (m, 1H), 6.90-6.3 (2d, 4H), 7.35-7.85 (2d, 4H). ^{13}C NMR ($CDCl_3$) δ = 22.0, 38.5, 68.1, 69.7, 115.2, 127.6, 128.1, 129.6, 134.5, 135.6, 137.4, 138.2, 164.1.

(*S*)-1-(4-chlorophenyl)-3-(tosyloxy) propan-1-ol (7k): yield: 81%, as a colorless oil; ^{1}H NMR ($CDCl_3$) δ =1.99-2.05(m, 1H), 2.11-2.18(m, 1H), 2.35(s, 3H), 4.05-4.21(m, 1H), 4.33-4.39(m, 1H), 5.1-5.23(m, 1H), 7.15-7.98 (m, 8H). ^{13}C NMR ($CDCl_3$) δ = 22.0, 39.5, 67.6, 68.0, 118.5, 128.6, 129.5, 129.5, 130.3, 132.6, 137.7, 138.6, 146.8.

(*S*)-1-(2-chlorophenyl)-3-(tosyloxy) propan-1-ol (7l): yield: 78%, as a colorless oil; ^{1}H NMR ($CDCl_3$) δ =1.95-2.06 (m, 1H), 2.20-2.30 (m, 1H), 2.39 (s, OH), 2.42 (s, 3H), 4.20-4.28 (m, 1H), 4.39-4.46 (m, 1H), 5.17-5.29 (m, 1H), 7.19-7.35(m, 4H), 7.52-7.95(m, 4H). ^{13}C NMR ($CDCl_3$) δ = 21.6, 36.3, 67.1, 67.6, 126.9, 128.6, 129.1, 129.6, 130.5, 132.6, 137.4, 138.2, 144.8. MS (70 eV): for $C_{18}H_{23}O_4ClSSi$; m/z 397(1%), 229(100%), 213(92%).

(*S*)-1-(1-naphtyl)-3-(tosyloxy) propan-1-ol (7m): yield: 82%, as a colorless oil; ^{1}H NMR ($CDCl_3$) δ = 2,02-2.24 (m, 1H), 2,25-2.36 (m, 1H+OH), 2,41 (s, 3H), 4,10-4.16 (m, 1H), 4,44-4.53(m, 1H), 5,5-5.68(m, 1H); 7,15-8,05(m, 11H arom). ^{13}C NMR ($CDCl_3$) δ = 22.5, 38.5, 67.7, 68.1, 122.8, 123.5, 125.8, 126.1, 126.4, 128.4, 129.6, 130.5, 131.5, 133.5, 138.2, 144.6.

(*S*)-1-(2-naphtyl)-3-(tosyloxy) propan-1-ol (7n): yield: 78%, as a colorless oil; ^{1}H NMR ($CDCl_3$) δ = 1.98-2.16 (m, 1H), 2,26-2.34 (m, 1H+OH), 2,36 (s, 3H), 4,16-4.25 (m, 1H), 4,42-4.56(m, 1H), 5,41-5.56(m, 1H); 7,14-7.82 (m, 11H arom). ^{13}C NMR ($CDCl_3$) δ = 23.5, 36.4, 68.4, 69.1, 123.1, 124.1, 125.6, 126.3, 126.5, 128.3, 130.1, 131.2, 133.5, 138.6, 144.8.

4.6. Synthesis of secondary alcohols: General method

(*R*)-1-(4-chlorophenyl)-3-(tosyloxy) propan-1-ol 10k (0,340g; 1 mmol) was dissolved in 10 mL of dry THF and the solution was added drop wise at 0°C to a stirred suspension of $LiAlH_4$ (0.115 g; 3 mmol ; 3 eq.) in dry THF under argon. The mixture was allowed to warm to room temperature over 2 h and then was quenched by sequential addition of H_2O (0.25 mL), 10% NaOH (0.25 mL), and additional H_2O (0.50 mL). The product was extracted with ether and the organic phase was

washed with brine, dried and evaporated. Column chromatography [SiO_2, Cyclohexane / AcOEt (50:50)] gave 141 mg of (*R*)-1-(4-chlorophenyl) propan-1-ol **11k** as colourless oil. Yield: 83%. $[\alpha]_D$: +25.5 (*c* = 1.0, $CHCl_3$) = 0.90 (t, 3H, *J* = 7.4 Hz), 1.64-1.86 (m, 2H + OH), 4.58 (t, 1H, *J* = 6.5 Hz), 7.25-7.33 (m, 5H, ArH). ^{13}C NMR ($CDCl_3$) δ = 10.5, 30.7, 68.2, 125.4, 128.1, 132.6, 141.9. Conditions for the analysis of the chiral secondary alcohol: chiral HPLC: Chiracel OD, 254 nm UV detector. The solvent used is (hexane/*iso*-propanol) 9/1 at 1.0 mL/min, Retention times: 6.65 min (*R*), 7.61 min (*S*).

(*R*)-butan-2-ol (8a): yield: 82%, as a white oil; $[\alpha]_D$: -12.4 (*c* 10, MeOH); ^1H NMR ($CDCl_3$) δ = 0.91 (t, 3H, *J* = 7.5 Hz), 1.17 (d, 3H, *J* = 3.6Hz,), 1.99 (s, OH), 3.68-3.74 (m, 1H). ^{13}C NMR ($CDCl_3$) δ = 10.3, 23.2, 32.3, 69.8.

(*S*)-octan-3-ol (8b): yield: 88%, as a white oil; $[\alpha]_D$:+10.5 (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$) δ = 1.09-1.14 (m, 6H), 1.24-1.53 (m, 10H), 2.03 (s, OH), 3.67-3.72 (m, 1H). ^{13}C NMR ($CDCl_3$) δ = 14.1, 18.5, 20.5, 22.6, 25.2, 29.1, 31.6, 69.4.

(*S*)-tetradecan-3-ol (8c): yield: 86%, as a white oil; $[\alpha]_D$: +9.7 (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$) δ = 0.86-1.10 (m, 6H), 1.29-1.56 (m, 22H), 2.34 (s, OH), 3.32-3.48 (m, 1H). ^{13}C NMR ($CDCl_3$) δ = 13.9, 22.5, 25.6, 23.5, 29.7, 32.5, 36.5, 40.9, 68.6.

(*S*)-hexadecan-3-ol (8d): yield: 85%, as a white oil; $[\alpha]_D$: +11.2(*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$) δ = 0.92-1.08 (m, 6H), 1.28-1.58 (m, 26H), 2.14 (s, OH), 3.36-3.52 (m, 1H). ^{13}C NMR ($CDCl_3$) δ = 13.9, 14.2, 22.6, 25.9, 24.5, 30.7, 31.4, 33.5, 37.5, 39.9, 70.3.

(*S*)-octadecan-3-ol (8e): yield: 83%, as a white oil; $[\alpha]_D$: +10.9 (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$) δ = 0.90-1.14 (m, 6H), 1.20-1.54 (m, 30H), 2.14 (s, OH), 3.69-3.73 (m, 1H). ^{13}C NMR ($CDCl_3$) δ = 14.0, 14.2, 18.6, 19.3, 20.4, 20.5, 22.5, 22.7, 25.2, 27.6, 29.0, 31.6, 32.0, 34.6, 36.1, 41.3, 69.4.

(*R*)-1-Phenyl-1-propanol (11f): yield: 82%, as a colourless oil; $[\alpha]_D$: +48.2 (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$) δ = 0.89 (t, 3H, *J* = 7.5 Hz), 1.74-1.83 (m, 2H, *J* = 13.6, 7.5, 7.0 Hz,), 2.46 (s, OH), 4.59 (t, 1H, *J* = 7.0 Hz), 7.29-7.37 (m, 5H, ArH). ^{13}C NMR ($CDCl_3$) δ = 14.1, 29.7, 61.9, 126.1, 128.6, 133.4, 145.5.

(*S*)-1-(1-Thienyl) propan-1-ol (8g): yield: 80%, as a colourless oil; $[\alpha]_D$: +22.5 (*c* = 1, $CHCl_3$). ^1H NMR ($CDCl_3$) δ = 0.91 (t, 3H, *J* = 7.4 Hz) 1.69-1.99 (m, 2H+OH), 4.55 (t, 1H, *J* = 6.7 Hz), 6.19 (d, 1H, *J* = 3.2 Hz, ArH), 6.28 (dd, 1H, *J* = 3.2, 1.8 Hz), 7.32 (dd, 1H, *J* = 1.8 Hz). ^{13}C NMR ($CDCl_3$) δ = 13.6, 30.1, 58.2, 75.5, 123.9, 125.8, 128.7, 142.3.

(*S*)-1-tolylpropan-1-ol (8h): yield: 76%, as a colourless oil; $[\alpha]_D$: -36.1 (*c* = 1, $CHCl_3$). ^1H NMR ($CDCl_3$) δ = 0,86 (t, 3H); 1.95 (s; H), 2.04-2.12 (m, 2H + OH), 4.52-4.57 (m, 1H), 7.01(d, 2H), 7.38(d, 2H). ^{13}C NMR ($CDCl_3$) δ = 10.5, 21.3, 29.8, 67.6, 123.4, 127.9, 137.6, 141.5.

(*R*)-1-(4-Methoxyphenyl)-1-propanol (11i): yield: 82%, as a colorless oil; $[\alpha]_D$: +34.0 (*c* = 1.01, $CHCl_3$) ^1H NMR ($CDCl_3$) δ = 0.89 (t, 3H, *J* = 7.4 Hz), 1.65-1.89 (m, 3H, 2H +OH), 3.80 (s, 3H), 4.54 (t, 1H, *J* = 6.6 Hz), 6.85-6.90 (m, 2H), 7.24-7.28 (m, 2H). ^{13}C NMR ($CDCl_3$) δ =10.6, 32.1, 55.7, 76.1, 114.2, 127.6, 137.1, 159.4.

(*S*)-1-(4-fluorophenyl) propan-1-ol (8j): yield: 84%, as a colourless oil; $[\alpha]_D$: -25.1 (*c* = 1, $CHCl_3$). ^1H NMR ($CDCl_3$) δ = 0.93 (t, 3H), 1.68-1.88 (m, 2H+OH), 4.56-4.60 (m, 1H), 7.00-7.05 (m, 2H), 7.26-7.39 (m, 2H). ^{13}C NMR ($CDCl_3$) δ = 10.0, 29.7, 75.4, 115.2, 126.6, 127.6, 128.5.

(S)-1-(2-chlorophenyl) propan-1-ol (8l): yield: 68%, as a colourless oil; $[\alpha]_D$: -22.2 (*c* = 1, $CHCl_3$). ^1H NMR ($CDCl_3$) δ = 1.17 (t, 3H, *J* = 7.4 Hz), 1.71-1,90 (m, 2H), 2.10 (br, OH), 5.04-5.08 (m, 1H), 7.16-7.53 (m, 3H), 7.55 (d, 1H). ^{13}C NMR ($CDCl_3$) δ = 10.1, 29.7, 72.0, 126.0, 127.2, 128.3, 129.4, 132.1, 142.0.

(*S*)-1-naphthyl propan-1-ol (8m): yield: 77%, as a colourless oil; $[\alpha]_D$: -19.1 (*c* = 1, $CHCl_3$). ^1H NMR ($CDCl_3$) δ = 0.95 (t, 3H, *J* = 7.1 Hz), 1.8-2.00(m, 2H), 2.25 (br, OH), 5.3(m, 1H), 7.30-8.19 (m, 7H arom). ^{13}C NMR ($CDCl_3$) δ = 10.9, 31.5, 72.9, 123.1, 125.1, 126.0, 127.5, 127.6, 127.3, 128.1, 131.2, 133.7

(*S*)-2-naphthyl propan-1-ol (8n): yield: 85%, as a colourless oil; $[\alpha]_D$: -16.6 (*c* = 1, $CHCl_3$). ^1H NMR ($CDCl_3$) δ = 0.98 (t, 3H, *J* = 7.2 Hz), 1.78-1.98 (m, 2H), 2.30 (br, OH), 5.20-5.24 (m, 1H), 7.20-8.28 (m, 7H arom). ^{13}C NMR ($CDCl_3$) δ = 14.9, 43.3, 71.3, 122.5, 123.8. 125.7, 126.1, 126.4, 128.4, 128.8, 131.2, 133.5, 139.5; MS (70 eV): for $C_{16}H_{22}OSi$; m/z = 258(13%), 229(100%), 153(22), 73(64%).

ACKNOWLEDGEMENTS

The authors are grateful to DGRSRT (Direction Générale de la Recherche Scientifique et de la Rénovation Technologique) of the Tunisian Ministry of Higher Education, Scientific Research and Technology for the financial support.

REFERENCES

(1) K. Soai, S. Niwa, *Chem. Rev*. *92* (1992) 833; (b) K.Ohno, S. Saito, K. Miyazawa, M. Ushioda, H. Inoue, N. Yoshida, *EP*270244, (1988) (*Chem. Abstr*. 110 (1988), 31528x); (c) Y. Koizumi, S. Matsui, H. Takeuchi, Y. Kubo, E. Nakagawa, *JP*2001114722, (2001) (*Chem. Abstr* 134. (2001) 318781f).

(2) A. R. Stein, R. D. Dawe, J. R. Sweet, *Can. J. Chem*. 63 (1985) 3442; (b) M. Pallavicini, E. Valoti, L. Villa, O. Piccolo, *Tetrahedron*: *Asymmetry* 5 (1994) 5; (c) X. B. Su, Q. H. Zhang, Y. Q. Wu, J. X. Xu, *Chin. J. Org. Chem*. 22 (2002) 496 and references cited therein.

(3) H. L. Holland, E. J. Bergen, P. C. Chenchaiah, S. H. Khan, B. Munoz, R. W. Ninniss, D. Richards, *Can. J. Chem*. 65 (1987) 502; (b) A. J. M. Janssen, A. J. H. Klunder, B. Zwanenburg, *Tetrahedron* 47 (1991) 7645.

(4] S. Wallbaum, J. Martens, *Tetrahedron*: *Asymmetry* 3 (1992) 1475; (b) V. K. Singh, *Synthesis* (1992) 605; (c) L. Deloux, M. Srebnik, *Chem. Rev*. 93 (1993) 763; (d) E. J.Corey, C. J. Helal, *Angew. Chem., Int. Ed. Engl*37. (1998) 1986; (e) J. X. Xu, X. B. Su, Q. H. Zhang, *Tetrahedron: Asymmetry* 14 (2003) 1781.

(5) R. Csuk, B. I. Glanzer, *Chem. Rev*. 91 (1991) 49; (b) J. S. Yadav, P. T. Reddy, S. Nanda, A. B. Rao, *Tetrahedron*: *Asymmetry* 12 (2001) 3381.

(6) Reetz, M. T.; Li, X. *J. Am. Chem. Soc*. 2006, *128*, 1044-1045; (b) T. Imai, T. Tamura, A. Yamamuro, T. Sato, T. A.Wollmann, R M. Kennedy, S. Messmune, *J. Am. Chem. Soc*. 108 (1986) 7402.

(7) A. Prlter, K. Smith, Brown, H. C. *Borane Reagents*; Academic Press: San Diego, (1988); (b). S. Masamme, B. M. Kim, J. S. Petereen, T. Sato, S. J Veemtra,. T. Imai, *J.* Am. *Chem. Soc*. 107 (1986) 4649; (c) U. Dhokte, P. M. Pathare, V. K. Mahindroo, H. C. Brown, *J. Org. Chem* 63.(1998) 8276.

(8) For general discussion and comprehensive reviews, see: R. Noyori, S. Suga, K. Kawai, S. Okada, M. Kitamura, N. Oguni, M. Hayashi, T. Kaneko, Y. Matsuda, *J. Organomet. Chem.* 381 (1990) 19; (b) R. Noyori, M. Kitamura, *Angew. Chem., Int. Ed. Engl*. 30 (1991) 49; (c) P. Knochel, R. D. Singer, *Chem. Rev*. 93 (1993) 2117; (d) L. Pu, H.-B. Yu, *Chem. Rev*. 101 (2001) 757 and references cited therein.

(9) M. Kitamura, S. Suga, K. Kawai, R. Noyori, *J. Am. Chem. Soc*. *108* (1986) 6071.

(10) For selected reports on diethylzinc additions, see: N. Oguni, T. Omi, Y. Yamamoto, A. Nakamura, *Chem. Lett*. (1983) 841; (b) N. Oguni, T. Omi, *Tetrahedron Lett.* 25 (1984) 2823; (c) P. A. Chaloner, S. A. R. Perera, *Tetrahedron Lett.* 28 (1987) 3013; (d) K. Soai, A. Ookawa, T. Kaba, K. Ogawa, *J. Am. Chem. Soc.* 109 (1987) 7111; (e) E. J. Corey, F. J. Hannon, *Tetrahedron Lett.* 28 (1987) 5233; (f) E. J Corey, F. J. Hannon, *Tetrahedron Lett*. 28 (1987) 5237; (g) K. Soai, M. Nishi, Y. Ito, *Chem. Lett.* (1987) 2405; (h) S. Itsuno, J. M. J. Fre´chet, *J. Org. Chem*. 52 (1987) 4140; (i) A. A. Smaardijk, H. Wynberg, *J. Org. Chem.* 52 (1987) 135; (j) N. Oguni, Y. Matsuda, T. Kaneko, *J. Am. Chem. Soc.* 110 (1988) 7877; (k) M. Kitamura, S. Okada, S. Suga, R. Noyori, *J. Am. Chem. Soc*. 111 (1989) 4028; (l) K. Soai,

H. Hori, S. Niwa, *Heterocycles* 29 (1989) 2065; (m) K. Soai, S. Yokoyama, T. Hayasaka, *J. Org. Chem*. 56 (1991) 4264; (n) M. Asami, S. Inoue, *Chem. Lett*. (1991) 685; (o) K. Kimura, E. Sugiyama, T. Ishizuka, T. Kunieda, *Tetrahedron Lett*. 33 (1992) 3147; (p) C. Anaya de Parrodi, E. Juraisti, L. Quintero-Cortes, P. Amador, *Tetrahedron: Asymmetry* 7 (1996) 1915; (q) W.-M. Dai, H.-J. Zhu, X.-J. Hao, *Tetrahedron: Asymmetry* 7 (1996) 1245; (r) J. Wilken, M. Kossenjans, H. Groger, J. Martens, *Tetrahedron: Asymmetry* 8 (1997) 2007; (s) G. Bringmann, M. Breuning, *Tetrahedron: Asymmetry* 9 (1998) 667; (t) B. T. Cho, Y. S. Chun, *Tetrahedron: Asymmetry* 9 (1998) 1489; (u) H. C. Hailes, J. Madden, *Synlett* (1999) 105; (v) Y.-J. Cherng, J.-M. Fang, T.-J. Lu, *J. Org. Chem*. 64 (1999) 3207; (v) S. Wassmann, J. Wilken, J. Martens, *Tetrahedron: Asymmetry* 10 (1999) 4437.

(11) For selected recent reports on diethylzinc additions, see: Y. Kawanami, T. Mitsuie, M. Miki, T. Sakamoto, K. Nishitani, *Tetrahedron* 56 (2000) 175; (b) K. S. Reddy, L. Sola`, A. Moyano, M. A. Perica`s, A. Riera, *Synthesis* (2000) 165; (c) M. Rita Paleo, I. Cabeza, F. J. Sardina, *J. Org. Chem*. 65 (2000) 2108; (d) W.-M. Dai, H.-J. Zhu, X.-J. Hao, *Tetrahedron: Asymmetry* 11 (2000) 2315; (e) Y. Wu, H. Yun, Y. Wu, K. Ding, Y. Zhou, *Tetrahedron: Asymmetry* 11 (2000) 3543; (f) T. Ohga, S. Umeda, Y. Kawanami, *Tetrahedron* 57 (2001) 4825; (g) M. Nevalainen, V.Nevalainen, Tetrahedron: Asymmetry 12 (2001) 1771; (h) V. Dimitrov, G. Dobrikov, M. Genov, *Tetrahedron: Asymmetry* 12 (2001) 1323; (i) G. Zhao, X.-G. Li, X.-R. Wang, *Tetrahedron: Asymmetry* 12 (2001) 399; (j) F. F. DiMauro, M. C. Kozlowski, *Org. Lett*. 3 (2001) 3053; (k) D.-X. Liu, L.-C. Zhang, Q. Wang, C.-S. Da, Z.-Q. Xin, R. Wang, M. C. K. Choi, A. S. C Chan,. *Org. Lett.* 3 (2001) 2733; (l) P. J. Hermsen, J. G. O. Cremers, L. Thijs, B. Zwanenburg, *Tetrahedron Lett* 42. (2001) 4243; (m) P. Wipf, X Wang,. *Org. Lett*. 4 (2002) 1197. (n) W. A. Nugent, Org. Lett. 4 (2002) 2133; (o) Q. Xu, G. Zhu, X. Pan, A. S. C. Chan, *Chirality* 14 (2002) 716; (p) J. Lu, X. Xu, C. Wang, J. He, Y. Hu, H. Hu, *Tetrahedron Lett*. 43 (2002) 8367; (q) D. Steiner, S. G. Sethofer, C. T. Goralski, B. Singaram, *Tetrahedron: Asymmetry* 13 (2002) 1477; (r) A. Garcia Martinez, E. Teso Vilar, A. Garcia Fraile, S. de la Moya Cerero, P. Martinez-Ruiz, *Tetrahedron: Asymmetry* 13 (2002) 1457; (s). D.-H. Ko, K. H. Kim, D.-C. Ha, *Org. Lett* 4.(2002) 3759; (t) R. D. Ionescu, A. Blom, T. Frejd, *Tetrahedron: Asymmetry* 14 (2003) 2369; (u) C. Jimeno, M. Pasto, A. Riera, M. A. Perica`s, *J. Org. Chem*. 68 (2003) 3130; (v) M. L. Richmond, C. T. Seto, *J. Org.Chem.* 68 (2003) 7505; (w) D. Scarpi, F. Lo Galbo, E. G. Occhiato, A. Guarna, *Tetrahedron: Asymmetry* 15 (2004) 1319; (x) B. Fu, D.-M. Du, J. Wang, *Tetrahedron: Asymmetry* 15 (2004) 119.

(12) A limited number of exceptions to this rule have been reported, see: K. Soai, S. Yokoyama, K. Ebihara, T. Hayasaka, *J. Chem. Soc., Chem. Commun*. (1987) 1690; (b) K. Soai, A. Ookawa, T. Kaba, K. Ogawa, *J. Am. Chem. Soc.* 108 (1987) 7111; (c) K. Sod, S. Yokoyama, T. Hayasaka, *J. Org. Chem.* 56 (1991) 4264; (d) W.-S. Huang, Q.-S. Hu, Zheng, L. Pu, *J. Org. Chem* 63.(1998) 1364; (e) K. S. Reddy, L. Sola, A. Moyano, M. A. Perica`s, A. Riera, *J. Org. Chem*. 64 (1999) 3969; (f) W. A. Nugent, *Chem. Commun.* (1999) 1360; (g) Y. Hari, T. Aoyama, *Synthesis* (2005) 583; (h) R. Roudeau, D. G. Pardo, J. Cossy, *Tetrahedron* 62 (2006) 2388.

(13) V. Ratovelomanana-Vidal, C. Girard, R. Touati, J. Tranchier, B. Ben Hassine, J.-P Genêt. *Advanced Synthesis & Catalysis* 345 (2003) 261; (b) C. Mordant, C. Cano de Andrade, R. Touati, V. Ratovelomanana-Vidal, B. Ben Hassine, J.-P. Genêt, *Synthesis* (2003) 2405; (c) R. Touati, V. Ratovelomanana-Vidal, B. Ben Hassine, J.-P Genêt, *Tetrahedron: Asymmetry*, 17 (2006) 3400.

(14) Genêt, J.-P.; Pinel, C.; Ratovelomanana-Vidal, V.; Mallart, S.; Pfister, X.; Caño de Andrade, M. C.; Laffitte, J. A. *Tetrahedron: Asymmetry* **1994**, *5*, 665.

(15) J.-P. Genêt, *Acc. Chem. Res.* 36 (2003) 908; (b) R. Noyori, *Asymmetric Catalysis in Organic Synthesis*; J. Wiley: NY, (1994).

(16) (a) Duprat de Paule, S.; Jeulin, S.; Ratovelomanana-Vidal, V.; Genêt, J.-P.; Champion, N.; Dellis, P. *Tetrahedron Lett.* **2003**, *44*, 823. (b) Duprat de Paule, S.; Jeulin, S.; Ratovelomanana-Vidal, V.; Genêt, J.-P.; Champion, N.; Dellis, P. *Eur. J. Org. Chem.* **2003**, 1931.