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Asymmetric Reduction of Monoketo Hexadecanoic Acid Methyl Esters

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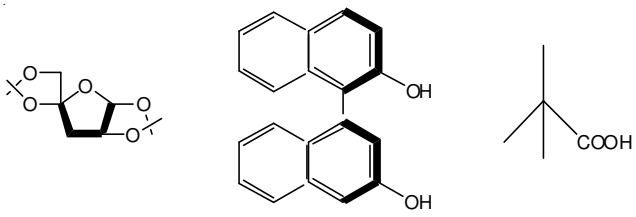
Methyl 2-,3-,6-,8-,14- and 15-keto hexadecanoates were reduced by using $NaBH_4$ in presence of 1,2;5,6-di-O-isopropilydene-D-glucofuranose [DIPGH], R(+)-1,1'-binaphthyl-2,2'-diol [RBND] and pivalic acid [PA]. The reduction of 2- and 3-keto esters in the presence of (+)-1,1'-binaphthyl-2,2'-diol results in considerably higher stereoselectivities (95 % ee). Enantiometric excess (ee %) was determined by ^1H and ^{13}C NMR analyses using a shift reagent, $Eu(tfc)_3$.

Key Words: Reduction, Enantiometric excess, Keto hexadecanoates.

INTRODUCTION

Long chain hydroxy fatty acid methyl esters are widely distributed in nature, since they have been investigated as components of animals, plants and microorganism and more recently, they have gained a great deal of attention because of their uses in food, medicinal and cosmetics areas[1-3]. Among them, chiral hydroxy aliphatic acid methyl esters are more valuable by possessing at least one stereogenic carbon atom. Most of the naturally occurring hydroxy acid methyl esters are optically active and they are essential biological molecules as well as intermediates for organic synthesis[4]. Monohydroxy hexadecanoic acid methyl ester isomers bearing a hydroxy group in various positions are important compounds amongst them. It has been well documented that 2- and 6-hydroxy hexadecanoic acids are shown that antitumor effect of Ehrlich tumor, Gardner leukemia cancer and TA_3 mamma cancer[5]. 14-and 15-hydroxy hexadecanoic acid methyl esters were isolated from bees wax using chromatographic and spectroscopic methods[6]. It has been reported that R-enantiomer of methyl 2-hydroxy hexadecanoate was obtained with a 97 % enantiomeric excess by HPLC measurements[7]. To our best of knowledge, there is no data about the asymmetric synthesis of methyl 3-,6-,8-,14- and 15-hydroxy hexadecanoates in the literature. Therefore, methyl 2-,3-,6-,8-,14- and 15-monohydroxy hexadecanoates were selected for this study. Auxiliaries used in this paper were 1,2;5,6-di-O-isopropylidene-D-glucofuranose [DIPGH], **1**, R(+)-1,1'-binaphtyl-2,2'-diol [RBND], **2** and pivalic acid [PA], **3** (**Scheme-I**). The optimal reduction conditions giving the highest enantiomeric purity were also determined.



1 **2** **3**

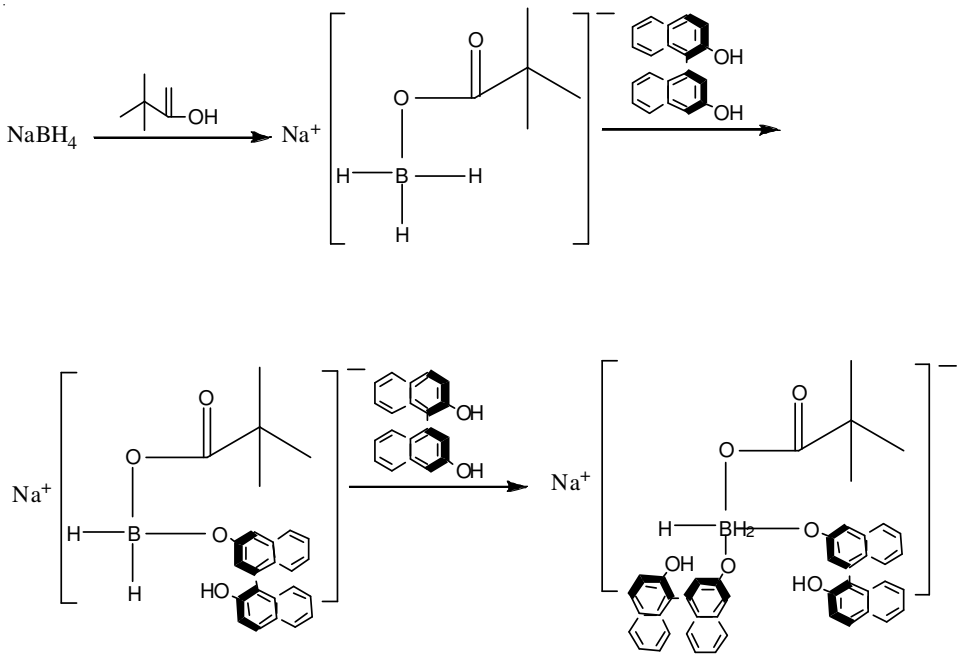
Scheme-I: Auxiliaries used for the asymmetric reduction

We also aimed to synthesize the enantiomers of methyl 2-,3-,6-,8-,14- and 15-keto hexadecanoates with high enantiomeric excess at atmospheric pressure using chirally modified $NaBH_4$ (**Schemes II-IV**).

These reductions at atmospheric pressure together with inexpensive auxiliaries make it competitive with other reduction methods. In the literature no study was found for the synthesis of these enantiomers by our presented manners. In previous studies, several aromatic ketones were reduced in presence of modified $NaBH_4$, 1,2:5,6-di-O-isopropylidene-D-glucofuranose, S(-)-1-(2 chlorophenyl)-2,2-dimethylpropane-1,3-diol and nonchiral acids[8,9]. Due to the lack in the literature of the spectroscopic analysis to determine these enantiomeric methyl monohydroxy hexadecanoate isomers, the synthesized enantiomers were analyzed by means of chiral ^1H NMR and chiral ^{13}C NMR-shift studies and pure reference compounds.

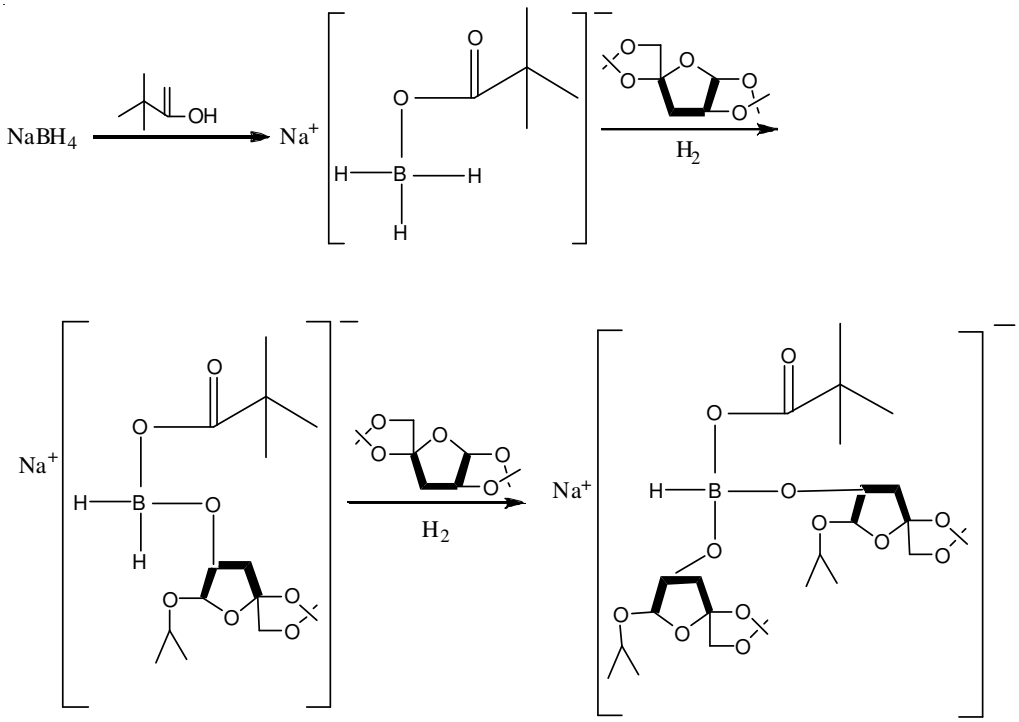
EXPERIMENTAL

The monoketohexadecanoic acid methyl esters used in the asymmetric reduction reactions, 2-ketohexadecanoic acid



I

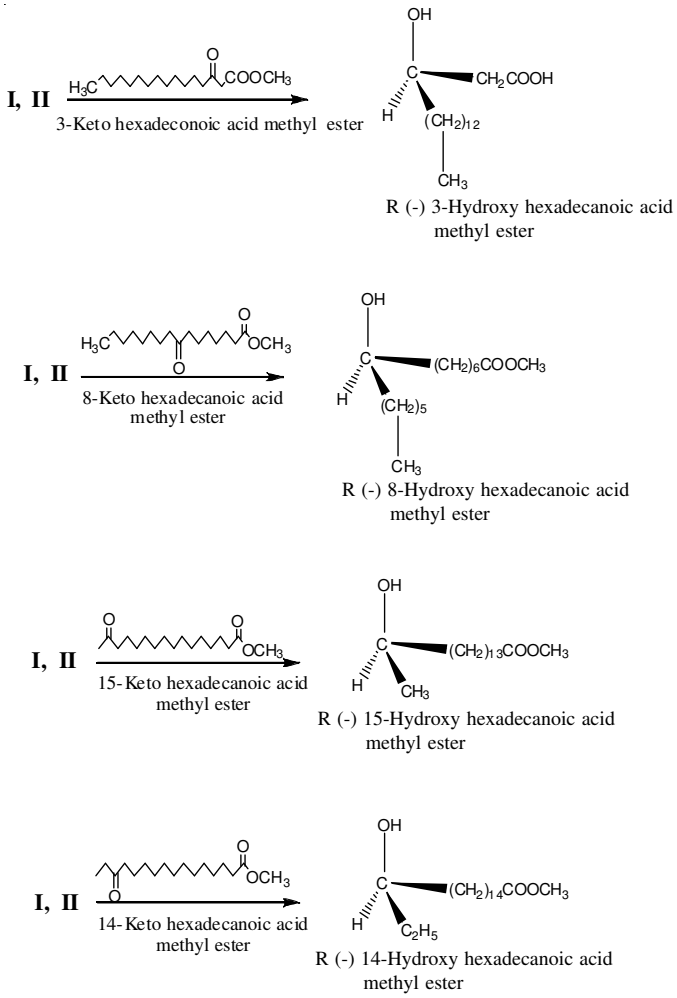
Scheme-II: Reduction agent with RBND using $NaBH_4$ (agent compound: **I**)



II

Scheme-III: Reduction agent with DIPGH using $NaBH_4$ (agent compound: **II**)

methyl esters were synthesized by the oxidation of 2-hdroxy hexadecanoic acid methyl esters which was obtained by *via* Hell-Volhard-Zelinsky reaction[13]; 6-,8-,14-monoketo hexadecanoic acid methyl ester isomers by Blaise reaction[14]; 3- and 15-monoketo hexadecanoic acid methyl ester isomers by ethyl acetoacetat reaction method[15,16], respectively. The richness of obtained keto- and hydroxy hexadecanoic acid methyl ester were controlled by thin layer chromatography. Their melting points were determined with Gallenkamp model melting point apparatus and were corrected. Refractive indices were measured with 60/70 Model Abbe refractometer. The optical rotations were measured with a AA-10 Automatic Polarimeter. IR was run on Mattson 1000 series FT-IR (as 1 % KBr tablets). All asymmetric reduction reactions were carried out at room temperature. The enantiomeric purity was checked by ^1H NMR-shift method as methyl esters. ^1H NMR spectrometer



Scheme-IV: Asymmetric reductions of monoketo hexadecanoates by DIPGH/RBND using $NaBH_4$

Mercury Pulls 300 Magnet Frequency: 300 MHZ, chemical shifts were given in ppm relative to internal standards TMS (σ = 0 ppm). Eu (tfc) 3 = Tris [3-(trifluoromethyl-hydroxy-methylene)-d-camfphorato] europium(III) was use as shift reactive in ^{1}H NMR method.

General procedure for asymmetric reduction of prochiral keto esters by chiral modified $NaBH_4$: To a stirred suspension of $NaBH_4$ (0.5 mmol) in THF (5 mL) was added a solution of the pivalin acid (0.5 mmol) in THF (5 mL).The solution was stirred 0.5 h. And evolution of H_2 was observed. The chiral alcohol [R(+)- 1,1'-binaphthyl-2,2-diol and 1,2:5,6-di-O-isopropylidene-α-D-glucofuranose] (1 mmol) in THF (10 mL) was added. After stirring 4 h, the keto ester (0.5 mmol) was added to the reaction solution all at once. The mixture was stirred for 4 days. The end of the reaction was controlled by TLC (developeding solvent: acetone/petroleum = 1:9). The reaction mixture was hydrolyzed by 1 N HCl solution. The solution was extracted with ether. Ether phase was separated and washed with distilled water. After drying over anhydrous Na_2SO_4, the unreacted keto ester, chiral alcohol and enantiomeric pure hydroxy esters were purified by column chromatography (developing solvent: acetone/petroleum =1:9). The enantiomeric excesses were measured by ^{1}H NMR.

Spectral data of methyl 2-,3-,6-,8-,14- and 15-hydroxy hexadecanoates

R(-)Methyl 2-hydroxy hexadecanoate obtained by using $NaBH_4$ in DIPGH, 1: m.p. 55 ºC; n_D^{20} = 1.4330; yield 90 %; R_f 0.40 (petroleum ether/acetone, 3/7); anal. calcd. (%) for $C_{17}H_{13}O_3$: C, 71.28; H, 11.96; Found (%): C, 71.86; H, 13.03; IR (KBr, ν_{max}, cm^{-1}); 3461 b, (-OH), 1727 s , (C=O), 1158 s, (C-O); ^{1}H NMR ($CDCl_3$, 300 MHz, ppm): δ 0.87 (t, J = 7 Hz, 3H, 16- CH_3), 1.25 (m, 24H, 4-, 5-, 6, 7-, 8-, 9-, 10-, 11-, 12-, 13-, 14-, 15- CH_2), 1.53 (s, 1H, OH), 1.65 (m, 1H, 3-CH_aH_b), 1.78 (m, 1H, 3-CH_aH_b), 3.79 (s, 3H, -OCH_3), 4.19 (s, 1H, 2- CHOH); ^{13}C NMR ($CDCl_3$, 300 MHz, ppm) δ: 14.578 (C-16), 22.724, 25.434, 29.327, -29.843, 32.923, 34.042, 37.863, 40.070, 40.909 (3,4,5,6,7,8,9,10,11,12,13,14,15-C), 51.803 ($COOCH_3$), 70,094 (2-C), 174 (1-C); $[\alpha]_D^{20}$ = -30 (c 1, $CHCl_3$ for ee 98 %).

R(-)Methyl 2-hydroxy hexadecanoate obtained by using $NaBH_4$ in RBND, 2: m.p. 56 ºC; n_D^{20} = 1.4332; yield 95 %; R_f 0.40 (petroleum ether/acetone, 3/7); Anal. calcd. (%) for C17H13O3: C, 71.28; H, 11.96; Found: C, 71.90; H, 12.77; IR (KBr, ν_{max}, cm^{-1}); 3461 b, (-OH), 1727 s , (C=O), 1158 s, (C-O); ^{1}H NMR ($CDCl_3$, 300 MHz, ppm): δ 0.87 (t, J = 7 Hz, 3H, 16-CH_3), 1.25 (m, 24H, 4-, 5-, 6, 7-, 8-, 9-, 10-, 11-, 12-, 13-, 14-, 15-CH_2), 1.53 (s, 1H, OH), 1.65 (m, 1H, 3-CH_aH_b), 1.78 (m, 1H, 3-CH_aH_b), 3.79 (s, 3H, -OCH_3), 4.19 (s, 1H, 2-CHOH); ^{13}C NMR ($CDCl_3$, 300 MHz, ppm) δ: 14.578 (C-16), 22.724, 25.434, 29.327, -29.843, 32.923, 34.042, 37.863, 40.070, 40.909 (3,4,5,6,7,8,9,10,11,12,13,14,15-C), 51.803 ($COOCH_3$), 70,094 (2-C), 174 (1-C); $[\alpha]_D^{20}$ = -25 (c 1, $CHCl_3$ for ee 82.5 %).

R(-) Methyl 3-hydroxy hexadecanoate obtained by using $NaBH_4$ in DIPGH, 3: m.p. 48 ºC; n_D^{20} = 1.4335; yield 85 %; R_f 0.40 (petroleum ether/acetone, 3/7); anal. calcd. (%) for $C_{17}H_{13}O_3$: C, 71.28; H, 11.96; found (%); C, 71.68; H, 9.96; IR (KBr, ν_{max}, cm^{-1}); 1754 s, (C=O, ester), 1712 s, (C=O, keton), 1179 s, (C-O); ^{1}H NMR ($CDCl_3$, 300 MHz, ppm): δ 0.88 (t, J = 6.9 Hz, 3H, 16-CH_3), 1.2-1.6 (m, 24H, 4-, 5-, 6-, 7-, 8-, 9-, 10-, 11-, 12-, 13-, 14-, 15- CH_2), 2.25 - 2.56 (ddd, J = 16, 9 ve 3.3 Hz, 2H, 2-CH_2), 3.6 (s, 3H,-OCH_3), 3.8(s, 1H, -OH), 4.1 (m, 1H, 3-CHOH); ^{13}C NMR ($CDCl_3$, 300 MHz, ppm) δ: 14.880 (C-16), 22.819, 29.789, 32.53 (2,4,5,6,7,8,9,10,11,12, 13,14,15-C), 76.717 ($COOCH_3$), 77.560 (3-C), 175.025 (1-C); $[\alpha]_D^{20}$ = -25 (c 1, $CHCl_3$ for ee 85 %).

R(-) Methyl 3-hydroxy hexadecanoate obtained by using $NaBH_4$ in RBND, 4: m.p. 51 ºC; n_D^{20} = 1.4336; yield 85 %; R_f 0.40 (petroleum ether/acetone, 3/7); anal. calcd. (%) for $C_{17}H_{13}O_3$: C, 71.28; H, 11.96; found (%): C, 71.358; H, 13.11; IR (KBr, ν_{max}, cm^{-1}); 1754 s, (C=O, ester), 1712 s, (C=O, keton), 1179 s, (C-O); ^{1}H NMR ($CDCl_3$, 300 MHz, ppm): δ 0.88 (t, J = 6.9 Hz, 3H, 16-CH_3), 1.2-1.6 (m, 24H, 4-, 5-, 6-, 7-, 8-, 9-, 10-, 11-, 12-, 13-, 14-, 15- CH_2), 2.25-2.56 (ddd, J = 16, 9 ve 3.3 Hz, 2H, 2-CH_2), 3.6 (s, 3H, -OCH_3), 3.8(s, 1H, -OH), 4.1 (m, 1H, 3-CHOH); ^{13}C NMR ($CDCl_3$, 300 MHz, ppm) δ: 14.880 (C-16), 22.819, 29.789, 32.53 (2,4,5,6,7,8,9,10,11, 12,13,14,15-C), 76.717 ($COOCH_3$), 77.560 (3-C), 175.025 (1-C); $[\alpha]_D^{20}$ = -15 (c 1, $CHCl_3$ for ee 87 %).

R(-) Methyl 6-hydroxy hexadecanoate obtained by using $NaBH_4$ in DIPGH, 5: m.p. 406 ºC; n_D^{20} = 1.4340; yield

90 %; R_f 0.40 (petroleum ether/acetone, 3/7); anal. calcd. (%) for $C_{17}H_{13}O_3$: C, 71.28; H, 11.96; found (%): C, 71.72.73; H, 11.56; IR (KBr, ν_{max}, cm^{-1}); 1732 s, (C=O, ester), 1713 s, (C=O, keton), 1180 s, (C-O); ^{1}H NMR ($CDCl_3$, 300 MHz, ppm): δ 0.87 (t, *J* = 6.4 Hz, 3H, 16-CH_3), 1.4 (m, 24H, 3-, 4-, 5- 7-, 8-, 9-, 10-, 11-, 12-, 13-, 14-, 15-CH_2), 1.5 (s, 1H, 6-CHOH), 2.2 (t, *J* = 7.2 Hz, 2H, 2-CH_2), 3.52(m, 1H, 6-CHOH), 3.65 (s, 3H, -OCH_3); ^{13}C NMR ($CDCl_3$, 300 MHz, ppm) δ: 14.578 (C-16), 22.724, 25.120- 25.98, 29.843-30.923, 32.120, 34.042, 37.980 (2,3,4,5,7,8,9,10,11,12,13,14,15-C), 50.878 ($COOCH_3$), 72,094 (6-C), 174.1 (1-C); $[\alpha]_D^{20}$ = -5 (c 1, $CHCl_3$ for ee 61 %).

R(-) Methyl 6-hydroxy hexadecanoate obtained by using $NaBH_4$ in RBND, 6: m.p. 43 ºC; n_D^{20} = 1.4342; yield 95 %; R_f 0.40 (petroleum ether/acetone, 3/7); anal. calcd. (%) for $C_{17}H_{13}O_3$: C, 71.28; H, 11.96; found (%): C, 71.78.; H, 11.59; IR (KBr, ν_{max}, cm^{-1}); 1732 s, (C=O, ester), 1713 s, (C=O, keton), 1180 s, (C-O); ^{1}H NMR ($CDCl_3$, 300 MHz, ppm): δ: 0.87 (t, *J* = 6.4 Hz, 3H, 16-CH_3), 1.4 (m, 24H, 3-, 4-, 5- 7-, 8-, 9-, 10-, 11-, 12-, 13-, 14-, 15- CH2), 1.5(s, 1H, 6-CHOH), 2.2 (t, *J* = 7.2 Hz, 2H, 2-CH_2), 3.52 (m, 1H, 6-CHOH), 3.65 (s, 3H, -OCH_3); ^{13}C NMR ($CDCl_3$, 300 MHz, ppm) δ: 14.578 (C-16), 22.724, 25.120- 25.98, 29.843-30.923, 32.120, 34.042, 37.980 (2,3,4,5,7,8,9,10,11,12,13,14,15-C), 50.878 ($COOCH_3$), 72,094 (6-C), 174.1 (1-C); $[\alpha]_D^{20}$ = -20 (c 1, $CHCl_3$ for ee 81 %).

R(-) Methyl 8-hydroxy hexadecanoate obtained by using $NaBH_4$ in DIPGH, 7: m.p. 44 ºC; n_D^{20} = 1.4355; yield 95 %; R_f 0.40 (petroleum ether/acetone, 3/7); anal. calcd. (%) for $C_{17}H_{13}O_3$: C, 71.86; H, 13.03; found (%): C, 71.28.65; H, 11.96; IR (KBr, ν_{max}, cm^{-1}); 3407 b, (-OH), 1754 s , (C=O), 1185 s, (C-O); ^{1}H NMR ($CDCl_3$, 300 MHz, ppm): δ 0.89 (t, *J* = 6.9 Hz, 3H, 16-CH_3), 1.2-1.7 (m, 24H, 3-, 4-, 5-, 6-, 7-, 9-, 10-, 11-, 12-, 13-, 14-, 15- CH_2), 1.58 (s, 1H, 8-CHOH), 2.39 (m, 2H, 2-CH_2), 3.6 (m, 1H, 8-CHOH), 3.75 (s, 3H, -OCH_3); ^{13}C NMR ($CDCl_3$, 300 MHz, ppm) δ: 14.58 (C-16), 22.910, 25.410, 25.870-25.970, 29.780- 30.120, 32.010, 34.120, 37.980 (2,3,4,5,6,7,9,10,11,12,13,14,15-C), 51.803 ($COOCH_3$), 72,120 (8-C), 178 (1-C); $[\alpha]_D^{20}$ = -20 (c 1, $CHCl_3$ for ee 91 %).

R(-) Methyl 8-hydroxy hexadecanoate obtained by using $NaBH_4$ in RBND, 8: m.p. 45.5 ºC; n_D^{20} = 1.4358; yield 98 %; R_f 0.40 (petroleum ether/acetone, 3/7); anal. calcd. (%) for $C_{17}H_{13}O_3$: C, 71.28; H, 11.96; found (%): C, 71.56; H, 11.70; IR (KBr, ν_{max}, cm^{-1}); 3407 b, (-OH), 1754 s , (C=O), 1185 s, (C-O); ^{1}H NMR ($CDCl_3$, 300 MHz, ppm): δ 0.89 (t, *J* = 6.9 Hz, 3H, 16-CH_3), 1.2-1.7 (m, 24H, 3-, 4-, 5-, 6-, 7-, 9-, 10-, 11-, 12-, 13-, 14-, 15-CH_2), 1.58 (s, 1H, 8-CHOH), 2.39 (m, 2H, 2-CH_2), 3.6 (m, 1H, 8-CHOH), 3.75 (s, 3H, -OCH_3); ^{13}C NMR ($CDCl_3$, 300 MHz, ppm) δ: 14.58 (C-16), 22.910, 25.410, 25.870-25.970, 29.780- 30.120, 32.010, 34.120, 37.980 (2,3,4,5,6,7,9,10,11,12,13,14,15-C), 51.803 ($COOCH_3$), 72,120 (8-C), 178 (1-C); $[\alpha]_D^{20}$ = -20 (c 1, $CHCl_3$ for ee 91 %).

R(-) Methyl 14-hydroxy hexadecanoate obtained by using $NaBH_4$ in DIPGH, 9: m.p. 46.5 ºC; n_D^{20} = 1.4370; yield 95 %; R_f 0.40 (petroleum ether /acetone, 3/7); anal. calcd. (%) for $C_{17}H_{13}O_3$: C, 71.28; H, 11.96; found (%): C,67.77; H, 10.99; IR (KBr, ν_{max}, cm^{-1}); 3434 b, (-OH), 1754 s, (C=O), 1212 s, (C-O); ^{1}H NMR ($CDCl_3$, 300 MHz, ppm): δ 0.9 (t, *J* = 8.5 Hz, 3H, 16- CH_3), 1.2-1.6 (m, 25H, 3-, 4-, 5-, 6- 7-, 8-, 9-, 10-, 11-, 12-, 13-, 15- CH_2, OH), 2.23 (t, *J* = 7.1 Hz, 2H, 2- CH_2), 3.58 (m, 1H, 14-CHOH), 3.7 (s, 3H, -OCH_3); ^{13}C NMR ($CDCl_3$, 300 MHz, ppm) δ: 10.090 (C-16), 24.434, 25.634, 29.890, 30.020, 34.120, 37.748 (2,3,4,5,6,7,8,9,10,11,12,13,15-C), 51.978 ($COOCH_3$), 73.786 (14-C), 174.2 (1-C); $[\alpha]_D^{20}$ = -20 (c 1, $CHCl_3$ for ee -%).

R(-) Methyl 15-hydroxy hexadecanoate obtained by using $NaBH_4$ in DIPGH, 10: m.p. 58 ºC; n_D^{20} = 1.4378; yield 95 %; R_f 0.40 (petroleum ether/acetone, 3/7); anal. calcd. (%) for $C_{17}H_{13}O_3$: C, 71.28; H, 11.96; found (%): C, 72.00; H, 11.60; IR (KBr, ν_{max}, cm^{-1}); 3407b, (-OH), 1754 s, (C=O), 1185 s, (C-O); ^{1}H NMR ($CDCl_3$, 300 MHz, ppm): δ 00.79 (t, *J* = 6.9 Hz, 3H, 16-CH_3), 1.26-1.72 (m, 25H, 3-, 4-, 5-, 6- 7-, 8-, 9-, 10-, 11-, 12-, 13-, 14- CH_2, OH), 2.23 (t, *J* = 7.1 Hz, 2H, 2-CH_2), 3.6 (s, 3H, -OCH_3), 3.8 (m, 1H, 15-CHOH); ^{13}C NMR ($CDCl_3$, 300 MHz, ppm) δ: 23.79 (C-16), 24.20, 25.8, 29.12-29.85, 33.9, 39.35 (2,3,4,5,6,7,8,9,10,11,12,13,14-C), 51.30 ($COOCH_3$), 67.98 (15-C), 175 (1-C); $[\alpha]_D^{20}$ = -20 (c 1, $CHCl_3$ for ee-%).

RESULTS AND DISCUSSION

2-,3-,6-,8-,14-,15-Monoketo hexadecanoic acid methyl esters carrying keto group at the end and the middle of the chain with 16 carbon atoms were chosen as prochiral compounds in order to determine the effect of keto position on the asymmetric reduction and enantiomeric excess. Chirally modified $NaBH_4$ was used as the reducing agent and it was prepared from chiral alcohols having at least one hydroxyl group and branched carboxylic acids. Naturally occurring **1** and sterically bulky (**2** and **3**) were used as auxiliaries. According to the previous study[9], 1 mol of $NaBH_4$ was sufficient for the reduction of 1 mol of keto ester. Two and four moles of chiral monoalcohols **1** and **2** and 1 mol of carboxylic acid **3** were taken for the preparation of **1** mol chiral $NaBH_4$. The increasing yield of $NaBH_4$ reduction in acidic medium has been established in the previous study[9]. In other reports[8-11] on $NaBH_4$ reductions by different acids were studied too, where the formation of a sodium carboxyborohydride was reported. The induction effects of the chiral alcohol **1** and **2** and the carboxylic acid **3** were examined in different mole ratios. In here, the asymmetric reductions were investigated in terms of the positional effect, reduction yield and it was also shown that the yield of the asymmetric reductions and the enantiomeric excess were changed by chiral alcohols. For the reduction yield of 2- and 3-keto esters, **2** was more dominant effective than **1**. The reduction of 2- and 3-keto esters, in the presence of **2** results in considerable higher streoselectivities (90-95 % ee). **1** had together with **3**, an e.e. value of 85-90 %, respectively. Compound **2** being less sterically hindered showed appositive reduction effect and **1** being more sterically hindered had a positive induction effect. 14- and 15-keto esters having its keto groups at the end of the chain gave a reduction yield (95 %). 6- and 8-keto esters isomers with a keto positions on the middle of the chain gave high reduction but 6- and 8- keto isomers exhibited lower enantiomeric excess, because on the middle of the chain has got asymmetry. This work demonstrates

the importance of the positional effect. At the position of lower steric hinderance the highest enantiomeric excess and asymmetric reduction yields were observed, namely the prochiral 14-15-keto isomers colloborates these, being located at the end of the carbon chain at the (ω-2) positions. 2- and 3-keto isomers carrying keto groups at the head, between the ester and long chained methylene groups and are more sterically hindered than 14- and 15-keto isomers. Therefore reduction yields and enantiomeric excess obtained are lower for the head of the carbon chain. 6- and 8-keto isomers have keto groups close to the middle of the chain and are more hindered from one side by the ester group carrying four and six methylene and the other side by nine and seven methylene with a methyl group at the end. These positions no caused lower reduction yield, but caused lower enantiomeric excess. Because of steric hinderance from both sides and on the middle of the chain has got asymmetry. The configuration of the mentioned enantiomeric hydroxy hexadecanoic acid methyl esters were assigned as R configuration from the literature values[12] of 2-hydroxy methyl hexadecanoate where negative rotation was measured for the (R)-configuration. In this present study the optical rotations sings for all enantiomeric 3-,6-,8-,14- and 15- monohydroxy methyl hexadecanoates are negative, therefore they were assigned the (R)- configuration. In the literature there are no data on the optical rotation of the 3-,6-,8-,14- and 15-monohydroxy methyl hexadecanoates. The specific rotations of the mentioned isomers from different enantiomeric excesses are determined for the first time in this study. The enantiomeric excesses were determined by the ^{1}H NMR-shift and ^{13}C NMR methods with Eu(tfc)$_3$. The difference in the chemical shift of methoxy singlet was distinguishable for the enantiomeric methyl esters in the presence of the chiral shift reagent, which produced a difference of 9-25 Hz for enantiomeric pairs of (R)- and (S)-configurations. Based on the intensity of each signals, the value of e.e. % was calculated. The methoxy signals of 14-and 15-hydroxy methyl hexadecanoates isomers could not be split by ^{1}H NMR shift, therefore its e.e. % was guessed optical rotations. The enantiomeric 2-,3-,6- and 8-hydroxy methyl hexadecanoate isomers gave also positive results with ^{1}H NMR shift.

Conclusion

The asymmetric reductions were examined in terms of positional effect, reduction yield and it was also found that chiral alcohols is an affective agent on the yield of the symmetric reductions and the enantiomeric excess. To auxiliaries used for the asymmetric reductions, while, in the presence of **2** together with **3**, the reduction of 2- 3-14-and 15-keto esters gave the higher stereoselectivities, in the presence of **1** stereoselectivities excess was more less than **2**.

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