# A General Method for the Synthesis of Both Enantiomers of Optically Pure β-Hydroxy Esters from (*S*)-(*p*-Chlorophenylsulfinyl)acetone Easily Obtainable by Kinetic Resolution with Bakers' Yeast

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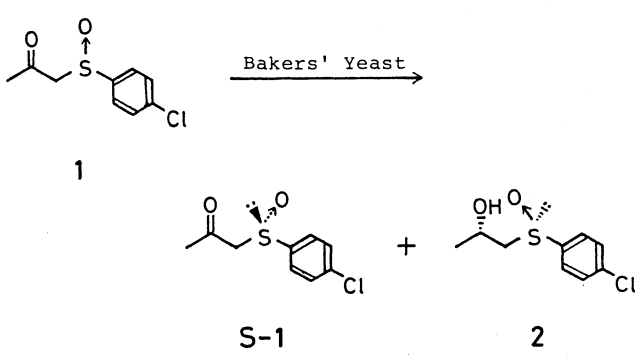
Both enantiomers of various optically pure (*R*)- and (*S*)-β-hydroxy esters were generally synthesized from (*S*)-(*p*-chlorophenylsulfinyl)acetone obtained by kinetic resolution with bakers' yeast, followed by γ-alkylation, diastereoselective reduction, subsequent introduction of ester group and reductive elimination of the sulfinyl group. The key step of the diastereoselective reduction of (*S*)-β-keto sulfoxides was performed with diisobutylaluminum hydride to give (*R*)c-(*S*)s-β-hydroxy sulfoxides or after complexation with zinc chloride followed by addition of diisobutylaluminum hydride to give (*S*)c-(*S*)s-β-hydroxy sulfoxides which were easily separated in an optically pure form by easy crystallization or separation by silica-gel chromatography due to the *p*-chlorophenyl moiety in the β-hydroxy sulfoxides. The utility of the present method could be successfully demonstrated in the synthesis of both (+)- and (−)-corynomycolic acids from optically pure methyl esters of (*R*)- and (*S*)-3-hydroxyoctadecanoic acid by alkylation with tetradecyl iodide at α-position and hydrolysis.

Optically active β-hydroxy esters are well-known as important intermediates for the synthesis of various natural products. They are prepared by a number of procedures; for example, asymmetric aldol reaction[1] by use of chiral α-sulfinyl esters,[2] lithium enolates,[3] zirconium enolates,[4] boron enolates,[5] tin enolates, and chiral diamines,[6] the Reformatsky reaction using sparteine,[7] regioselective epoxide ring opening,[8] cleavage of oxetanones,[9] and asymmetric reduction of β-keto ester with bakers' yeast.[10] Most of them give optically active β-hydroxy esters in high yields with very high optical purity, but they can not give both of the enantiomers from the same starting material. We report here a general method for the synthesis of both enantiomers of optically pure β-hydroxy ester **6** starting from (*S*)-(*p*-chlorophenylsulfinyl)acetone (**S-1**), which is easily obtainable by kinetic resolution of the corresponding racemic sulfinylacetone **1**, followed by γ-alkylation, diastereoselective reduction, subsequent introduction of ester group, and reductive elimination of the sulfinyl group. By use of the present method, both (+)- and (−)-corynomycolic acids **10** were synthesized in optically pure state.

Recently diastereoselective reduction of chiral β-keto tolyl sulfoxides with diisobutylaluminum hydride has been reported to give both diastereomers of β-hydroxy sulfoxides.[11] In spite of many attempts, we have found that it is quite difficult to isolate each diastereomer. In the case of *p*-chlorophenyl group combined to sulfinyl group, however, each diastereomer of the corresponding β-hydroxy sulfoxide was found to be easily isolated in an optically pure state, which could apply to the synthesis of optically pure β-hydroxy esters (vide infra).

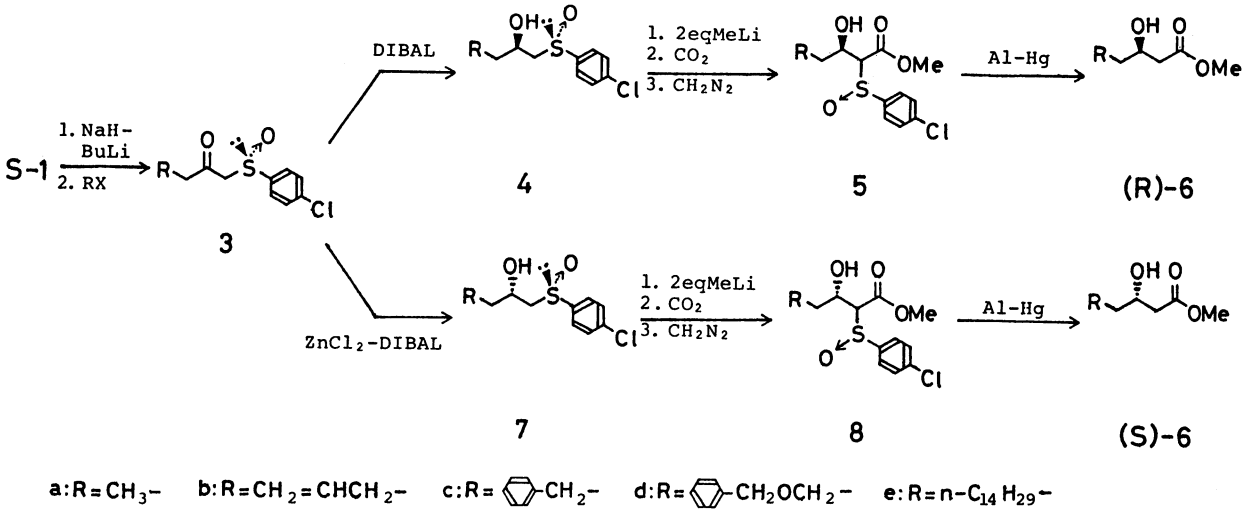


Scheme 1.

Racemic (phenylsulfinyl)acetone is known to be resolved to (*S*)-(phenylsulfinyl)acetone by bakers' yeast.[12] In the reduction of racemic (*p*-chlorophenylsulfinyl)acetone (**1**) with bakers' yeast, one enantiomer was reduced to (*S*)c-(*R*)s-2-hydroxypropyl *p*-chlorophenyl sulfoxide (**2**) and (*S*)-(*p*-chlorophenylsulfinyl)-acetone (**S-1**) remained intact. This keto sulfoxide **S-1** could be separated from the hydroxy sulfoxide by silica-gel chromatography more easily than (phenylsulfinyl)acetone is separated from the corresponding alcohol. The optically pure acetone derivative **S-1** was easily obtained by recrystallization from benzene-hexane in a yield of 38% from the racemate. Methylation at γ-position of **S-1** was carried out by use of sodium hydride and butyllithium in THF to generate the dianion, followed by addition of methyl iodide at 0 °C to yield 2-oxobutyl sulfoxide **3a**(R=$CH_3$) in 67% yield.[13] The β-keto sulfoxide **3a** was reduced with diisobutylaluminum hydride at −90 °C in THF to give optically active (*R*)c-(*S*)s-alcohol **4a** in 80% yield, which was easily recrystallized from benzene-hexane to give optically pure (*R*)c-(*S*)s-alcohol **4a** in 50% yield. Various β-hydroxy sulfoxides **4** were obtained by alkylation of **S-1**, with allyl bromide, benzyl bromide, benzyloxymethyl chloride, and tetradecyl iodide, respectively, followed by diastereoselective reduction with diisobutylaluminum hydride. All of these β-hydroxy sulfoxides except **4e**(R=$C_{14}H_{29}$), which was recrystallized from methanol, were recrystallized from benzene-hexane to give optically pure ones in 50—58% yields. Then carboxylation at α-position by treatment of **4a** with two

equivalents of methyllithium in THF at 0 °C to produce the dianion of **4a**, followed by pouring them into powdered Dry Ice, then esterification with diazomethane in methanol gave ester **5a**. Elimination of the sulfinyl group from **5a** by treatment with aluminum amalgam[14] in THF-water furnished optically pure methyl (*R*)-3-hydroxypentanoate (**R-6a**). Yields and values of physical properties of various optically pure methyl ester of (*R*)-β-hydroxy acids **R-6**, synthesized by the present method, were listed in Table 1.

On the other hand, when the β-keto sulfoxide **3** was reduced with diisobutylaluminum hydride in the presence of zinc chloride in THF, (*S*)c-(*S*)s-β-hydroxy sulfoxide **7** was mainly obtained. In the case of the diastereomeric mixtures of methyl- and allyl-substituted hydroxy sulfoxides **7a** and **7b**, which are oily and not crystallized, each diastereomers of them were isolated by use of silica-gel chromatography to give optically pure **7**. The (*S*)c-(*S*)s-isomers of β-hydroxy sulfoxides substituted with benzyl, and benzyloxymethyl group, **7c** and **7d**, were easily recrystallized from benzene-hexane, and substituted one with tetradecyl group **7e** was recrystallized from methanol in an optically pure state. Then introduction of ester group to prepare **8**




Scheme 2.

Table 1. Synthesis of (*R*)-β-Hydroxy Esters **R-6**

| R | **4** | | Optically pure **4** | | | **R-6** | |
|---|---|---|---|---|---|---|---|
| | Yield/% | *SS*/*RS*[a] | Yield/% | Mp $\theta_m$/°C | $[\alpha]_D^{23}$/°[b] | Yield/%[c] | $[\alpha]_D^{23}$/°[d] |
| $CH_3$ | 80 | 8/92 | 50[e] | 96—98 | −233 | 38 | −37.0[g] |
| $CH_2$=$CHCH_2$ | 85 | 6/94 | 58[e] | 77—79 | −237 | 50 | −22.3[h] |
| -$CH_2$ | 80 | 3/97 | 56[e] | 69—71 | −192 | 56 | −12.2 |
| -$CH_2OCH_2$ | 87 | 5/95 | 54[e] | 74—75 | −174 | 54 | −11.5 |
| *n*-$C_{14}H_{29}$ | 81 | 11/89 | 58[f] | 76—77 | −146 | 48 | −15.1[i] |

a) Determined by HPLC (Finepak SIL $C_{18}$). b) *c* ca. 1.0, MeOH. c) Yield from **4** via **5**. d) *c* ca. 0.5, $CHCl_3$. e) Recrystallized from benzene-hexane. f) Recrystallized from methanol. g) Lit,[15] $[\alpha]_D$ −36.9° ($CHCl_3$). h) Lit,[16] $[\alpha]_D$ −22.1° ($CHCl_3$). i) Lit,[17] $[\alpha]_D$ −15° ($CHCl_3$).

Table 2. Synthesis of (*S*)-β-Hydroxy Esters **S-6**

| R | **7** | | Optically pure **7** | | | **S-6** | |
|---|---|---|---|---|---|---|---|
| | Yield/% | *SS*/*RS*[a] | Yield/% | Mp $\theta_m$/°C | $[\alpha]_D^{23}$/°[b] | Yield/%[c] | $[\alpha]_D^{23}$/°[d] |
| $CH_3$ | 91 | 96/4 | 87[e] | — | −137 | 54 | +36.7 |
| $CH_2$=$CHCH_2$ | 94 | 95/5 | 89[e] | — | −135 | 49 | +22.1 |
| -$CH_2$ | 87 | 98/2 | 42[f] | 59—61 | −91.0 | 55 | +12.2 |
| -$CH_2OCH_2$ | 83 | 96/4 | 60[f] | 66—67 | −73.6 | 50 | +11.6 |
| *n*-$C_{14}H_{29}$ | 87 | 92/8 | 55[g] | 84—85 | −71.7 | 37 | +14.8 |

a) Determined by HPLC (Finepak SIL $C_{18}$). b) *c* ca. 1.0, MeOH. c) Yield from **7** via **8**. d) *c* ca. 0.5, $CHCl_3$. e) Isolated by silica-gel chromatography. f) Recrystallized from benzene-hexane. g) Recrystallized from methanol.

and elimination of the sulfinyl group in the same manner as above gave methyl esters of (*S*)-β-hydroxy acids **S-6** (Table 2).

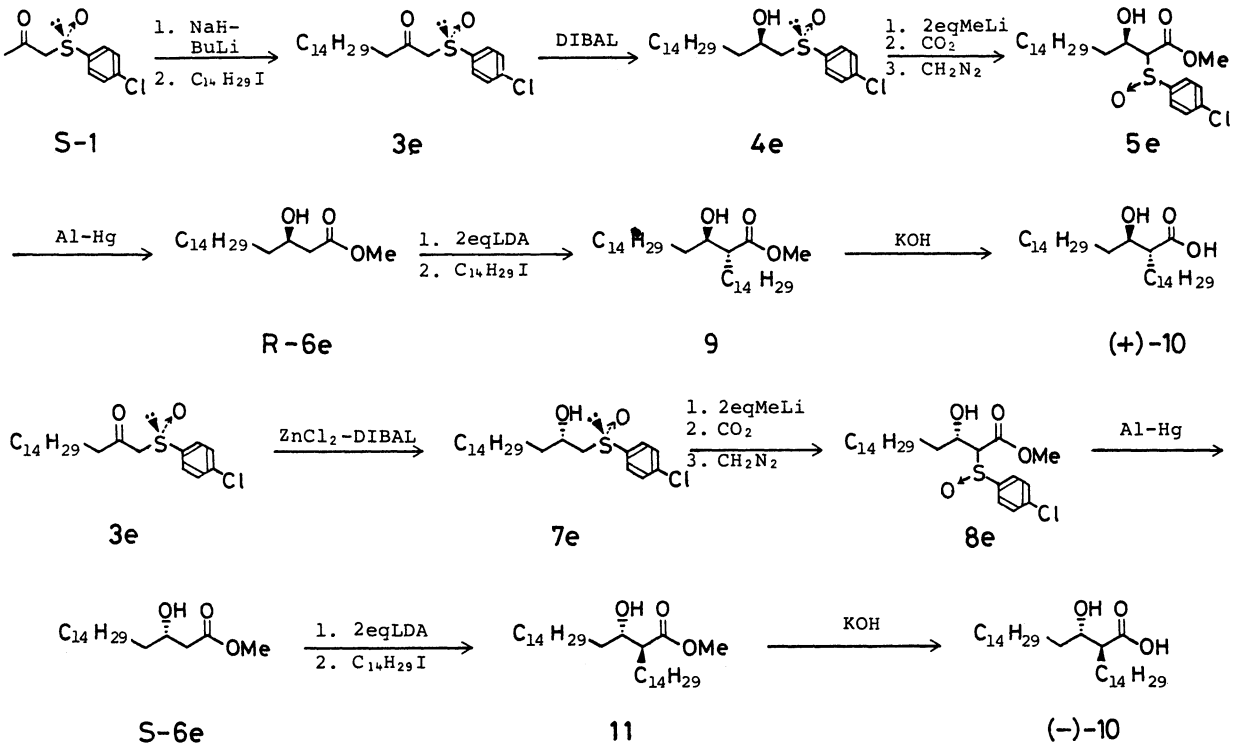
Corynomycolic acid **10** is one of the mycolic acids produced from coryne bacteria and its trehalose 6,6′-diester has various biological activities such as adjuvant, antibacterial, antitumor, and antiparasitic.[18] Optically active (+)-corynomycolic acid has been prepared in one report,[19] but (−)-comycolic acid has not been synthesized so far. The precursor of both enantiomers of corynomycolic acids is methyl 2-hydroxyoctadecanoate which can be easily prepared by the present method. Tetradecyl iodide was added to the dianion of β-keto sulfoxide **S-1** to furnish β-keto sulfoxide **3e** (R=$C_{14}H_{29}$) in 61% yield and reduction with diisobutylaluminum hydride afforded (*R*)c-(*S*)s-alcohol **4e** in 81% yield. Recrystallization from methanol gave optically pure **4e**. Subsequent carboxylation and esterification afforded ester **5e** and elimination of sulfinyl group gave methyl (*R*)-3-hydroxyoctadecanoate (**6e**). Then alkylation at α-position with tetradecyl iodide by Fráter's method[20] gave (2*R*,3*R*)-β-hydroxy ester **9** in 67% yield with (2*R*,3*R*):(2*S*,3*R*) ratio of 92:8, which was determined by HPLC of the corresponding β-benzoyloxy esters. After hydrolysis and recrystallization from methanol-hexane, optically pure (+)-corynomycolic acid (+)-**10** was obtained in 85% yield. Similarly the reduction of β-keto sulfoxide **3e** (R=$C_{14}H_{29}$) with diisobutylaluminum hydride in the presence of zinc chloride gave (*S*)c-(*S*)s-alcohol **7e** in 87% yield, and recrystallization from methanol afforded optically pure alcohol **7e**. In the same manner as above, (2*S*,3*S*)-β-hydroxy ester **11** with a (2*S*,3*S*):(2*R*,3*S*) ratio of 91:9 was hydrolyzed and recrystallized to give optically pure (−)-corynomycolic acid (−)-**10**.

In conclusion, each diastereomer of β-hydroxyalkyl *p*-chlorophenyl sulfoxides obtained by kinetic resolution of (*p*-chlorophenylsulfinyl)acetone with bakers' yeast followed by γ-alkylation and diastereoselective reduction, was easily separated to an optically pure form, and both enantiomers of optically pure (*R*)- and (*S*)-β-hydroxy esters were conveniently synthesized by using the present method.

## Experimental

Melting points were uncorrected. The IR spectra were recorded on JASCO IR 810. The $^1$H NMR spectra were recorded on JEOL JNM-PMX60si. High-pressure liquid chromatography was performed on Finepak SIL or Finepak SIL $C_{18}$ using JASCO UVIDEC-100V. Elemental analyses were carried out by Yanaco CHN CORDER MT-3. Optical rotations were determined at ambient temperature with Union PM-101. Tetrahydrofuran (THF) was freshly distilled on sodium benzophenone ketyl.

**(*S*)-(*p*-Chlorophenylsulfinyl)acetone (S-1).** To a mixture of 450 ml of water and 70 g of sucrose with rapid stirring was added 45 g of bakers' yeast (Oriental Yeast Co.). After stirring for 0.5 h at ambient temperature, the solution of 4.4 g (20 mmol) of racemic (*p*-chlorophenylsulfinyl)acetone (**1**) in 40 ml of ethanol was added dropwise. After the mixture was stirred vigorously for 12 h, 200 ml of ethyl acetate was added. Stirring was continued for 0.5 h, then 40 g of celite was added, and the mixture was filtered. The solids were washed




Scheme 3.

with ethyl acetate, and the combined filtrate was extracted with ethyl acetate. The organic layer was dried with sodium sulfate and concentrated. The crude material was purified by chromatography on silica gel (eluent; ethyl acetate : hexane=1 : 3) to give 1.73 g (8.0 mmol) of **S-1** (40% yield) $[\alpha]_D^{23}$ −219 ° (*c* 1.00, MeOH). Recrystallization of **S-1** from benzene-hexane afforded 1.65 g (7.6 mmol) of optically pure **S-1** (38% yield); mp 109—110 °C; $[\alpha]_D^{23}$ −231 ° (*c* 1.16, MeOH).

**General Procedure for the Preparation of (*S*)-β-Keto Sulfoxide (3).**[13] To a suspension of sodium hydride (1.1 mmol) in THF (2 ml) at 0 °C was added 216 mg (1 mmol) of (*S*)-(*p*-chlorophenylsulfinyl)acetone (**S-1**) in THF (3 ml). Then 1.57 mol dm$^{-3}$ hexane solution of butyllithium (0.7 ml) was added to the reaction mixture. After stirring for 30 min at the same temperature, alkyl halide (1.1 mmol) in THF (3 ml) was added to the reaction mixture. After stirring for 3 h at 0 °C, saturated aqueous $NH_4Cl$ was added to the reaction mixture and extracted with ethyl acetate. The organic layer was dried over sodium sulfate and the solvent was evaporated. The crude material was purified by chromatography on silica gel (eluent; ethyl acetate : hexane=1 : 3) to give (*S*)-β-keto sulfoxide.

**(*S*)-1-(*p*-Chlorophenylsulfinyl)-2-butanone (3a):** 67% yield; $[\alpha]_D^{23}$ −201° (*c* 0.99, MeOH); mp 96—98 °C; IR ($CHCl_3$) 1010, 1050, 1090, 1390, 1470, 1710, and 2970 cm$^{-1}$; $^1$H NMR ($CDCl_3$) δ=1.04 (t, *J*=7.2 Hz, 3H), 2.55 (q, *J*=7.1 Hz, 2H), 3.83 (s, 2H), and 7.55 (s, 4H). Found: C, 52.14; H, 4.80%. Calcd for $C_{10}H_{11}SO_2Cl$: C, 52.11; H, 4.77%.

**(*S*)-1-(*p*-Chlorophenylsulfinyl)-5-hexen-2-one (3b):** 63% yield; $[\alpha]_D^{23}$ −206° (*c* 0.34, MeOH); mp 104—105 °C; IR ($CHCl_3$) 1090, 1385, 1470, 1705, 2900, and 3000 cm$^{-1}$. $^1$H NMR ($CDCl_3$) δ=2.03—2.91 (m, 4H), 3.85 (s, 2H), 4.73—5.26 (m, 2H), 5.34—6.06 (m, 1H), and 7.57 (s, 4H). Found: C, 56.33; H, 5.25%. Calcd for $C_{12}H_{13}SO_2Cl$: C, 56.20; H, 5.07%.

**(*S*)-1-(*p*-Chlorophenylsulfinyl)-4-phenyl-2-butanone (3c):** 52% yield; $[\alpha]_D^{23}$ −168° (*c* 1.01, $CHCl_3$); mp 119—120 °C; IR ($CHCl_3$) 1000, 1095, 1470, 1720, 2925, and 3000 cm$^{-1}$; $^1$H NMR ($CDCl_3$) δ=2.84(s, 4H), 3.78(s, 2H), and 6.81—7.80(m, 9H). Found: C, 62.60; H, 5.17%. Calcd for $C_{16}H_{15}SO_2Cl$: C, 62.68; H, 4.89%.

**(*S*)-1-(*p*-Chlorophenylsulfinyl)-4-benzyloxy-2-butanone (3d):** 54% yield; $[\alpha]_D^{23}$ −111° (*c* 1.08, $CHCl_3$); mp 56—58 °C; IR ($CHCl_3$) 1005, 1025, 1050, 1090, 1360, 1390, 1480, 1700, 2900, 3025, and 3050 cm$^{-1}$; $^1$H NMR ($CDCl_3$) δ=2.72 (t, *J*=6.0 Hz, 2H), 3.71(t, *J*=5.9 Hz, 2H), 3.84(s, 2H), 4.45(s, 2H), 7.11(s, 5H), and 7.71(s, 4H). Found: C, 60.98; H, 5.17%. Calcd for $C_{17}H_{17}SO_3Cl$: C, 60.68; H, 5.05%.

**(*S*)-1-(*p*-Chlorophenylsulfinyl)-2-heptadecanone (3e):** 61% yield; $[\alpha]_D^{23}$ −121° (*c* 1.04, $CHCl_3$); mp 95—97°C; IR ($CHCl_3$) 1005, 1040, 1705, 2850, and 2950 cm$^{-1}$; $^1$H NMR ($CDCl_3$) δ=0.61—1.90 (m, 29H), 2.47 (t, *J*=6.0 Hz, 2H), 3.80 (s, 2H), and 7.25—7.81 (m, 4H). Found: C, 66.90; H, 9.10%. Calcd for $C_{23}H_{37}SO_2Cl$: C, 66.98; H, 8.98%.

**General Procedure for the Preparation of (*R*)c-(*S*)s-β-Hydroxy Sulfoxides 4.** To a solution of (*S*)-β-keto sulfoxide **3** (1 mmol) in THF (4 ml) was dropwise added 1.4 ml of a 1.5 mol dm$^{-3}$ solution of diisobutylaluminum hydride in hexane at −90 °C. After stirring for 5 h at −90 °C, 2 mol dm$^{-3}$ HCl solution (3 ml) was added to the reaction mixture and the products were extracted with ethyl acetate. The organic layer was dried over sodium sulfate and the solvent was evaporated. The crude material was purified by chromatography on silica gel (eluent; $CH_2Cl_2$) to give (*R*)c-(*S*)s-β-hydroxy sulfoxide **4**. The yields, the diastereomeric ratios and the yields of optically pure **4** recrystallized from benzene-hexane were listed in Table 1.

**(2*R*)-1-[(*S*)-*p*-Chlorophenylsulfinyl]-2-butanol (4a):** $[\alpha]_D^{23}$ −233° (*c* 1.02, MeOH); mp 96—98 °C; IR ($CHCl_3$) 1020, 1090, 1120, 1450, 2950, 3000, and 3400 cm$^{-1}$; $^1$H NMR ($CDCl_3$) δ=0.94 (t, *J*=6.6 Hz, 3H), 1.58 (m, 2H) 2.70 (dd, *J*=3.2, 13.2 Hz, 1H) 3.06 (dd, *J*=9.6, 13.2 Hz, 1H), 3.79—4.40 (m, 2H), and 7.62(s, 4H). Found: C, 51.43; H, 5.56%. Calcd for $C_{10}H_{13}SO_2Cl$: C, 51.66; H, 5.59%.

**(2*R*)-1-[(*S*)-*p*-Chlorophenylsulfinyl]-5-hexen-2-ol (4b):** $[\alpha]_D^{23}$ −237° (*c* 1.03, MeOH); mp 77—79 °C; IR ($CHCl_3$) 1005, 1020, 1090, 1475, 2950, and 3350 cm$^{-1}$; $^1$H NMR ($CDCl_3$) δ=1.38—1.87 (m, 2H), 1.95—2.47 (m, 2H), 2.80 (dd, *J*=4.0, 13.4 Hz, 1H), 3.04 (dd, *J*=8.4, 13.4 Hz, 1H), 4.26 (m, 2H), 4.77—5.28 (m, 2H), 5.46—6.26 (m, 1H), and 7.64 (s, 4H). Found: C, 55.67; H, 6.04%. Calcd for $C_{12}H_{15}SO_2Cl$: C, 55.77; H, 5.80%.

**(2*R*)-1-[(*S*)-*p*-Chlorophenylsulfinyl]-4-phenyl-2-butanol (4c):** $[\alpha]_D^{23}$ −192° (*c* 1.02, MeOH); mp 69—71 °C; IR ($CHCl_3$) 1005, 1040, 1090, 1260, 1390, 1450, 1480, 2900, 3000, and 3400 cm$^{-1}$; $^1$H NMR ($CDCl_3$) δ=1.92 (t, *J*=6.0 Hz, 2H), 2.49—3.18 (m, 4H), 3.94—4.45 (m, 2H), and 7.19 (s, 5H), 7.44 (s, 4H). Found: C, 62.51; H, 5.71%. Calcd for $C_{16}H_{17}SO_2Cl$: C, 62.28; H, 5.51%.

**(2*R*)-1-[(*S*)-*p*-Chlorophenylsulfinyl]-4-benzyloxy-2-butanol (4d):** $[\alpha]_D^{23}$ −174° (*c* 0.92, MeOH); mp 74—75 °C; IR ($CHCl_3$) 1000, 1090, 1470, 2850, 3000, and 3450 cm$^{-1}$; $^1$H NMR ($CDCl_3$) δ=1.9 (t, *J*=6.0 Hz, 2H), 2.76 (dd, *J*=3.6, 13.6 Hz, 1H), 3.07 (dd, *J*=7.2, 13.6 Hz, 1H), 3.65 (t, *J*=5.7 Hz, 2H), 4.16—4.70 (m, 2H), 4.53 (s, 2H), 7.08 (s, 5H), and 7.73 (s, 4H). Found: C, 60.40; H, 5.57%. Calcd for $C_{17}H_{19}SO_3Cl$: C, 60.32; 5.61%.

**(2*R*)-1-[(*S*)-*p*-Chlorophenylsulfinyl]-2-heptadecanol (4e):** $[\alpha]_D^{23}$ −146° (*c* 0.52, MeOH); mp 76—77 °C; IR ($CHCl_3$) 1000, 1040, 1095, 1390, 1460, 2850, 2900, and 3400 cm$^{-1}$; $^1$H NMR ($CDCl_3$) δ=0.65—1.80 (m, 31H), 2.70 (dd, *J*=3.2, 13.6 Hz, 1H), 3.03 (dd, *J*=8.8, 13.6 Hz, 1H), 3.94—4.50 (m, 2H), and 7.73 (s, 4H). Found: C, 66.70; H, 9.54%. Calcd for $C_{23}H_{39}SO_2Cl$: C, 66.66; H, 9.41%.

**General Procedure for the Preparation of (*S*)c-(*S*)s-β-Hydroxy Sulfoxides 7.**[11] To a suspension of anhydrous zinc chloride (1.1 mmol) in THF (2 ml) was added (*S*)-β-keto sulfoxide **3** (1 mmol) in THF (4 ml). After stirring for 30 min at room temperature, the reaction mixture was cooled to −90 °C, and 1.4 ml of 1.5 mol dm$^{-3}$ solution of diisobutylaluminum hydride in hexane was added. After stirring for 5 h at −90 °C, the reaction mixture was treated with 2 mol dm$^{-3}$ HCl solution and extracted with ethyl acetate. The organic layer was dried with sodium sulfate and the solvent was evaporated. The crude material was purified by chromatography on silica gel (eluent; $CH_2Cl_2$) to give (*S*)c-(*S*)s-β-hydroxy sulfoxide. The yields, the diastereomeric ratio and the yields of optically pure **7** were listed in Table 2.

**(2*S*)-1-[(*S*)-*p*-Chlorophenylsulfinyl]-2-butanol (7a):** $[\alpha]_D^{23}$ −137° (*c* 0.87, MeOH); IR (neat) 1020, 1090, 1120, 1450, 2950, 3000, and 3400 cm$^{-1}$; $^1$H NMR ($CDCl_3$) δ=0.96 (t, 7.4 Hz, 3H), 1.72 (m, *J*=7.4 Hz, 2H), 2.77 (dd, *J*=4.0, 12.8 Hz, 1H), 3.10 (dd, *J*=8.0, 12.8 Hz, 1H), 3.58—4.39 (m, 2H), and 7.63 (s, 4H). Found: C, 51.37; H, 5.59%. Calcd for $C_{10}H_{13}SO_2Cl$: C, 51.66; H, 5.59%.

**(2*S*)-1-[(*S*)-*p*-Chlorophenylsulfinyl]-5-hexene-2-ol (7b):** $[\alpha]_D^{23}$ −135° (*c* 1.03, MeOH); IR (neat) 1005, 1070, 1090, 1475, 2950, and 3350 cm$^{-1}$: $^1$H NMR ($CDCl_3$) δ=1.23—1.92 (m,

2H), 1.92—2.44 (m, 2H), 2.78 (dd, $J$=4, 12.6 Hz, 1H), 3.02 (dd, $J$=7.6, 12.6 Hz, 1H), 3.80—4.51 (m, 2H), 4.79—5.28 (m, 2H), 5.46—6.19 (m, 1H), and 7.63 (s, 4H). Found: C, 55.69; H, 5.70%. Calcd for $C_{12}H_{15}SO_2Cl$: C, 55.77; H, 5.80%.

**(2*S*)-1-[(*S*)-*p*-Chlorophenylsulfinyl]-4-phenyl-2-butanol (7c):** $[\alpha]_D^{23}$ −91.0° ($c$ 1.01, MeOH); mp 59—61 °C; IR ($CHCl_3$) 1005, 1040, 1090, 1260, 1390, 1450, 1480, 2900, 3000, and 3400 $cm^{-1}$. $^1H$ NMR ($CDCl_3$) $\delta$=1.93 (t, $J$=6.1 Hz, 2H), 2.56—3.11 (m, 3H), 3.67 (s, 1H), 4.08—4.49 (m, 2H), 7.23 (s, 5H), and 7.53 (s, 4H). Found: C, 62.42; H, 5.41%. Calcd for $C_{16}H_{17}SO_2Cl$: C, 62.28; H, 5.51%.

**(2*S*)-1-[(*S*)-*p*-Chlorophenylsulfinyl]-4-benzyloxy-2-butanol (7d):** $[\alpha]_D^{23}$ −73.6° ($c$ 1.02, MeOH); mp 66—67 °C; IR ($CHCl_3$) 1000, 1090, 1470, 2850, 3000, and 3450 $cm^{-1}$, $^1H$ NMR ($CDCl_3$) $\delta$=1.83 (t, $J$=5.6 Hz, 2H), 2.83 (dd, $J$=4.8, 13.2 Hz, 1H), 3.14 (dd, $J$=7.2, 13.2 Hz, 1H), 3.65 (t, $J$=5.4 Hz, 2H), 3.90—4.60 (m, 2H), 4.46 (s, 2H), 7.10 (s, 5H), and 7.53 (s, 4H). Found: C, 60.59; H, 5.45%. Calcd for $C_{17}H_{19}SO_3Cl$: C, 60.32; H, 5.61%.

**(2*S*)-1-[(*S*)-*p*-Chlorophenylsulfinyl]-2-heptadecanol (7e):** $[\alpha]_D^{23}$ −71.7° ($c$ 0.51, MeOH); mp 84—85 °C; IR ($CHCl_3$) 1000, 1040, 1095, 1390, 1460, 2850, 2900, and 3400 $cm^{-1}$, $^1H$ NMR ($CDCl_3$) $\delta$=0.67—1.79 (m, 31H), 2.77 (dd, $J$=3.6, 12.8 Hz, 1H), 3.03 (dd, $J$=7.6, 12.8 Hz, 1H), 3.94—4.58 (m, 2H), and 7.75 (s, 4H). Found: C, 66.48; H, 9.59%. Calcd for $C_{23}H_{39}SO_2Cl$: C, 66.66; H, 9.41%.

**General Procedure for the Preparation of Esters.** To a solution of β-hydroxy sulfoxide **4** or **7** (1 mmol) in THF (2 ml) at −5 °C was added 1.48 ml (2 mmol) of a 1.35 mol $dm^{-3}$ solution of methyllithium in ether. After stirring for 1 h at 0 °C, the reaction mixture was cooled to −70 °C, then poured onto 20 g of powdered Dry Ice, and shaken for 15 min. The reaction mixture was acidified with 5 ml of 2 mol $dm^{-3}$ HCl solution and extracted with ethyl acetate. The organic layer was dried over sodium sulfate and the solvent was evaporated. The residue was dissolved in 5 ml of methanol and 0.3 mol $dm^{-3}$ diazomethane solution in ether was added until the yellow color of the solution did not fade. After removal of the solvent, the crude material was purified by chromatography on silica gel (eluent; ethyl acetate : hexane=1 : 2) to give 3-hydroxy-2-sulfinyl ester **5** or **8**.

**Methyl (3*R*)-2-[(*S*)-*p*-Chlorophenylsulfinyl]-3-hydroxypentanoate (5a):** 50% yield; $[\alpha]_D^{23}$ −180.9° ($c$ 1.06, MeOH); mp 110—111 °C; IR ($CHCl_3$) 1040, 1090, 1380, 1450, 1740, 2950, 2975, and 3300 $cm^{-1}$: $^1H$ NMR ($CDCl_3$) $\delta$=0.73—1.23 (m, 3H), 1.25—2.67 (m, 2H), 3.23—4.03 (m, 5H), 4.29 (s. 1H), and 7.64 (m, 4H). Found: C, 49.64; H, 5.24%. Calcd for $C_{12}H_{15}SO_4Cl$: C, 49.62; H, 5.16%.

**Methyl (3*R*)-2-[(*S*)-*p*-Chlorophenylsulfinyl]-3-hydroxy-6-heptenoate (5b):** 68% yield; $[\alpha]_D^{23}$ −134° ($c$ 1.26, MeOH); mp 85—87 °C; IR ($CHCl_3$) 1010, 1090, 1300, 1730, 2950, and 3400 $cm^{-1}$: $^1H$ NMR ($CDCl_3$) $\delta$=1.34—1.91 (m, 2H), 2.01—2.56 (m, 2H), 3.29—3.87 (m, 4H), 4.28 (s, 2H), 4.76—5.40 (m, 2H), 5.44—6.26 (m, 1H), and 7.04—7.94 (m, 4H). Found: C, 52.96; H, 5.54%. Calcd for $C_{14}H_{17}SO_4Cl$: C, 53.13; H, 5.37%.

**Methyl (3*R*)-2-[(*S*)-*p*-Chlorophenylsulfinyl]-3-hydroxy-5-phenylpentanoate (5c):** 70% yield; $[\alpha]_D^{23}$ −119 ° ($c$ 1.15, MeOH); mp 82—83 °C; IR ($CHCl_3$) 1010, 1090, 1300, 1350, 1730, 2850, 2940, and 3450$^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$=1.67—2.17 (m, 2H), 2.58—3.07 (m, 2H), 3.16—4.43 (m, 6H), 7.20 (s, 5H), and 7.50 (s, 4H). Found: C, 59.22; H, 5.28%. Calcd for $C_{18}H_{19}SO_4Cl$: C, 58.98; H, 5.18%.

**Methyl (3*R*)-2-[(*S*)-*p*-Chlorophenylsulfinyl]-3-hydroxy-5-(benzyloxy)pentanoate (5d):** 69% yield; $[\alpha]_D^{23}$ −98° ($c$ 1.16, MeOH); mp 82—84 °C; IR ($CHCl_3$) 1005, 1095, 1485, 1730, 2350, 3000, and 3450 $cm^{-1}$. $^1H$ NMR ($CDCl_3$) $\delta$=1.57—2.10 (m, 2H), 3.33—3.93 (m, 8H), 4.57 (s, 2H), and 7.00—7.76 (m, 9H). Found: C, 57.81; H, 5.33%. Calcd for $C_{19}H_{21}SO_5Cl$: C, 57.56; H 5.30%.

**Methyl (3*R*)-2-[(*S*)-*p*-Chlorophenylsulfinyl]-3-hydroxyoctadecanoate (5e):** 65% yield; $[\alpha]_D^{23}$ −146.7° ($c$ 0.51, MeOH); mp 76—79 °C; IR ($CHCl_3$) 1095, 1310, 1460, 1718, 2850, 2950, and 3400 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$=0.64—1.78 (m, 31H), 3.25—4.19 (m, 6H), and 7.53 (s, 4H). Found: C, 63.55; H, 8.52%. Calcd for $C_{25}H_{41}SO_4Cl$: C, 63.69; H, 8.70%.

**Methyl (3*S*)-2-[(*S*)-*p*-Chlorophenylsulfinyl]-3-hydroxypentanoate (8a):** 69% yield; $[\alpha]_D^{23}$ −164° ($c$ 0.96, MeOH); mp 53—55 °C; IR ($CHCl_3$) 1040, 1090, 1380, 1450, 1740, 2950, 2975, and 3300 $cm^{-1}$. $^1H$ NMR ($CDCl_3$) $\delta$=0.93—1.21 (m, 3H), 1.25—2.23 (m, 2H), 3.44—4.71 (m, 6H), and 7.61 (m, 4H). Found: C, 49.73; H, 5.43%. Calcd for $C_{12}H_{15}SO_4Cl$: C, 49.62; H, 5.16%.

**Methyl (3*S*)-2-[(*S*)-*p*-Chlorophenylsulfinyl]-3-hydroxy-6-heptenoate (8b):** 62% yield; $[\alpha]_D^{23}$ −102° ($c$ 1.54, MeOH); mp 42—43 °C; IR ($CHCl_3$) 1010, 1090, 1300, 1730, 2950, and 3400 $cm^{-1}$: $^1H$ NMR ($CDCl_3$) $\delta$=1.39—1.94 (m, 2H), 2.03—2.60 (m, 2H), 3.31—4.04 (m, 3H), 4.47 (s, 1H), 4.79—5.41 (m, 2H), 5.46-6.31 (m, 1H), 7.07—7.82 (m, 4H). Found: C, 53.32; H, 5.39%. Calcd for $C_{12}H_{15}SO_4Cl$: C, 53.13; H, 5.37%.

**Methyl (3*S*)-2-[(*S*)-*p*-Chlorophenylsulfinyl]-3-hydroxy-5-phenylpentanoate (8c):** 70% yield; $[\alpha]_D^{23}$ −102° ($c$ 1.02, MeOH); mp 68—70 °C; IR ($CHCl_3$) 1010, 1090, 1300, 1350, 1730, 2850, 2940, and 3450 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$=1.82—2.13 (m, 2H), 2.61—3.15 (m, 2H), 3.20—4.48 (m, 5H), 7.31 (s, 5H), and 7.61 (s, 4H). Found: C, 58.71; H, 5.35%. Calcd for $C_{18}H_{19}SO_4Cl$: C, 58.98; H, 5.18%.

**Methyl (3*S*)-2-[(*S*)-*p*-Chlorophenylsulfinyl]-3-hydroxy-5-(benzyloxy)pentanoate (8d):** 65% yield; $[\alpha]_D^{23}$ −85 ° ($c$ 1.2, MeOH); mp 76—78 °C; IR ($CHCl_3$) 1005, 1095, 1485, 1730, 2350, 3000, and 3450 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$=1.68—2.23 (m, 2H), 3.47—3.93 (m, 8H), 4.57 (s, 2H), 7.17—7.80 (m, 9H). Found: C, 57.60; H, 5.22%. Calcd for $C_{19}H_{21}SO_5Cl$: C, 57.56; H, 5.30%.

**Methyl (3*S*)-2-[(*S*)-*p*-Chlorophenylsulfinyl]-3-hydroxyoctadecanoate (8e):** 60% yield; $[\alpha]_D^{23}$ −83.2 ° ($c$ 0.59, MeOH); mp 95—97 °C; IR ($CHCl_3$) 1095, 1310, 1460, 1718, 2850, 2950, and 3400 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$=0.65—2.07 (m, 31H), 3.27—4.72 (m, 6H), and 7.54 (s, 4H). Found: C, 63.63; H, 8.61%. Calcd for $C_{25}H_{41}SO_4Cl$: C, 63.69; H, 8.70%.

**General Procedure for the Preparation of β-Hydroxy Esters 6.**[14] To a solution of 3-hydroxy-2-sulfinyl ester (1 mmol) in 10% aqueous THF (10 ml) was added 0.2 g of aluminum amalgam at 0 °C. The reaction mixture was stirred at room temperature in hydrogen atmosphere. After stirring for 3 h, the reaction mixture was filtered and washed with ether, and the product was extracted with ether. The organic layer was dried over sodium sulfate, and the solvent was evaporated. The crude material was purified by chromatography on silica gel (eluent; ethyl acetate : hexane=1 : 4) to give methyl β-hydroxy ester **6**.

**Methyl (*R*)-3-Hydroxypentanoate (*R*-6a):** 75% yield; $[\alpha]_D^{23}$ −37.0° ($c$ 2.00, $CHCl_3$) (lit,[15] $[\alpha]_D$ −36.9°).

**Methyl (*R*)-3-Hydroxy-6-heptenoate (*R*-6b):** 74% yield; $[\alpha]_D^{23}$ −22.3° ($c$ 0.7, $CHCl_3$) (lit,[16] $[\alpha]_D$ −22.1°); IR (neat) 1100, 1285, 1640, 1740, 2900, and 3500 $cm^{-1}$; $^1H$ NMR ($CCl_4$) $\delta$=1.19—2.56 (m, 6H), 3.69 (s, 3H), 4.24 (m, 2H),

4.77—5.33 (m, 2H), and 5.59—5.95 (m, 6H). Found: C, 45.52; H, 6.58%. Calcd for $C_{18}H_{14}O_3$: C, 45.61; H, 6.33%.

**Methyl (*R*)-3-Hydroxy-5-phenylpentanoate (*R*-6c):** 80% yield; $[\alpha]_D^{23}$ −12.2° (*c* 1.16, $CHCl_3$); IR (neat) 1100, 1280, 1310, 1720, 2900, and 3500 $cm^{-1}$; $^1H$ NMR ($CCl_4$) δ=1.43—1.82 (m, 2H), 2.34—3.03 (m, 4H), 3.67 (s, 3H), 3.81—3.97 (m, 2H), and 6.97 (s, 5H). Found: C, 69.06; H, 7.65%. Calcd for $C_{12}H_{16}O_3$: C, 69.26; H, 7.67%.

**Methyl (*R*)-3-Hydroxy-5-(benzyloxy)pentanoate (*R*-6d):** 78% yield; $[\alpha]_D^{23}$ −11.5° (*c* 2.5, $CHCl_3$). The $^1H$ NMR and IR spectra were in agreement with the literature.[21]

**Methyl (*R*)-3-Hydroxyoctadecanoate (*R*-6e):** 74% yield; $[\alpha]_D^{23}$ −15.1° (*c* 0.56, $CHCl_3$) (lit,[17] $[\alpha]_D$ −15°).

**Methyl (*S*)-3-Hydroxypentanoate (*S*-6a):** 78% yield; $[\alpha]_D^{23}$ +36.7° (*c* 0.60, $CHCl_3$).

**Methyl (*S*)-3-Hydroxyheptenoate (*S*-6b):** 79% yield; $[\alpha]_D^{23}$ +22.1° (*c* 0.60, $CHCl_3$); IR (neat) 1100, 1285, 1640, 1740, 2900, and 3500 $cm^{-1}$; $^1H$ NMR ($CCl_4$) δ=1.18—2.58 (m, 6H), 3.68 (s, 3H), 4.33 (m, 2H), 4.91—5.36 (m, 2H), and 5.43—5.97 (m, 1H). Found: C, 45.44; H, 6.58%. Calcd for $C_{18}H_{14}O_3$: C, 45.61; H, 6.33%.

**Methyl (*S*)-3-Hydroxy-5-phenylpentanoate (*S*-6c):** 79% yield; $[\alpha]_D^{23}$ +12.2° (*c* 0.98, $CHCl_3$). IR (neat) 1100, 1280, 1310, 1720, 2900, and 3500 $cm^{-1}$; $^1H$ NMR ($CCl_4$) δ=1.43—1.96 (m, 2H), 2.36—3.04 (m, 4H), 3.59 (s, 3H), 3.75—4.05 (m, 2H), 7.07 (s, 5H). Found: C, 69.33; H, 7.71%. Calcd for $C_{12}H_{16}O_3$: C, 69.26; H, 7.67%.

**Methyl (*S*)-3-Hydroxy-5-(benzyloxy)pentanoate (*S*-6d):** 77% yield; $[\alpha]_D^{23}$ +11.6° (*c* 2.6, $CHCl_3$). The $^1H$ NMR and IR spectra were in agreement with the literature.[21]

**Methyl (*S*)-3-Hydroxyoctadecanoate (*S*-6e):** 62% yield; $[\alpha]_D^{23}$ +14.8° (*c* 0.55, $CHCl_3$).

**Corynomycolic Acids ((+)- and (−)-10).** To a solution of diisopropylamine (100 mg, 1 mmol) in THF (0.5 ml) was added 0.65 ml of an 1.54 mol $dm^{-3}$ solution of butyllithium in hexane at 0 °C. The solution of lithium diisopropylamide was cooled to −50 °C, and 150 mg (0.48 mmol) of methyl 3-hydroxyoctadecanoate (**6e**) in THF (2 ml) was added. After stirring for 1 h at the same temperature, a solution of tetradecyl iodide (162 mg, 0.5 mmol) in 1 g of HMPA was added, and the mixture was stirred for 3 h at −30 °C. The mixture was poured on ice-water and extracted with ether. The ethereal layer was dried over sodium sulfate, and the solvent was evaporated. The crude material was purified by chromatography on silica gel (eluent; ethyl acetate: hexane=1 : 3) to give methyl corynomycolate **9** or **11**.

**Methyl (2*R*,3*R*)-3-Hydroxy-2-tetradecyloctadecanoate (9):** 67% yield; $[\alpha]_D^{23}$ +4.2° (*c* 0.53, $CHCl_3$); mp 58—60 °C.

**Methyl (2*S*,3*S*)-3-Hydroxy-2-tetradecyloctadecanoate (11):** 65% yield; $[\alpha]_D^{23}$ −4.0° (*c* 0.52, $CHCl_3$); mp 58—60 °C.

To a solution of methyl corynomycolate **9** or **11** (510 mg, 1 mmol) in 50 ml of methanol was added 5 ml of an 1 mol $dm^{-3}$ solution of potassium hydroxide in methanol at 30 °C. After stirring for 5 h, the solvent was evaporated. The residue was dissolved into water (20 ml) and washed with ether. After acidification with 2 mol $dm^{-3}$ HCl solution (10 ml), the acid was extracted with ether. The organic layer was dried over sodium sulfate and the solvent was evaporated. The residue was recrystallized from methanol-petroleum ether to give optically pure corynomycolic acid (**10**).

**(+)-Corynomycolic Acid ((+)-10):** 85% yield; $[\alpha]_D^{23}$ +7.2° (*c* 0.40, $CHCl_3$) (lit,[18] $[\alpha]_D$ +7.2°); mp 68—70 °C (lit,[18] mp 70 °C).

**(−)-Corynomycolic Acid ((−)-10):** 83% yield; $[\alpha]_D^{23}$ −7.3° (*c* 0.50, $CHCl_3$); mp 68—69 °C.

**Methyl 2-Tetradecyl-3-(benzoyloxy)octadecanoate.** To a solution of **9** or **11** (51 mg, 0.1 mmol) and catalytic amount of 4-dimethylaminopyridine (2 mg) in pyridine (2 ml) was added benzoylchloride (30 mg, 0.2 mmol) at room temperature. After stirring for 15 h, 2 mol $dm^{-3}$ HCl solution (2 ml) was added to the reaction mixture. The products were extracted with dichloromethane, dried over sodium sulfate and evaporated. The crude material was purified by chromatography on silica gel (eluent; ethyl acetate : hexane=5 : 1) to give methyl 2-tetradecyl-3-(benzoyloxy)octadecanoate.

**Methyl (2*R*,3*R*)-2-Tetradecyl-3-(benzoyloxy)octadecanoate;** 85% yield. The ratio of (2*R*,3*R*) : (2*S*,3*R*) was determined to be 92 : 8 by HPLC on a Finepak SIL column using hexane : 2-propanol=600 : 1. IR (neat) 1275, 1460, 1720, 2850, and 2925 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ=0.95—1.35 (m, 60H), 2.20 (m, 1H), 3.65 (m, 4H), and 7.30 (m, 5H).

**Methyl (2*S*,3*S*)-2-Tetradecyl-3-(benzoyloxy)octadecanoate;** 90% yield. The ratio of (2*S*,3*S*) : (2*R*,3*S*) was determined to be 91 : 9 by HPLC on a Finepak SIL column using hexane : 2-propanol=600 : 1. IR (neat) 1260, 1500, 1720, 2850, and 2920 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ=0.98—1.35 (m, 60H), 2.21 (m, 1H), 3.70 (m, 4H), and 7.38 (m, 5H).

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