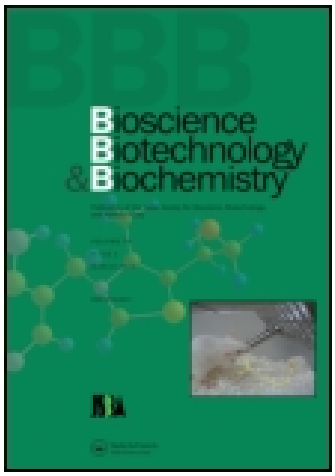


Bioscience, Biotechnology, and Biochemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/tbbb20

Synthesis of Both the Enantiomers of Aseanostatin P5 (Sarcinic Acid), an Inhibitor of Myeloperoxidase Release, and Four Diastereomers of Aggreceride A, a Platelet Aggregation Inhibitor

Takeshi Kitahara[a], Shigeru Aono[a] & Kenji Mori[a]
[a] Department of Applied Biological Chemistry, Division of Agriculture and Agricultural Life Sciences, The University of Tokyo, 1-1-1 Yayoi, Bunkyo-ku, Tokyo 113, Japan
Published online: 12 Jun 2014.

To cite this article: Takeshi Kitahara, Shigeru Aono & Kenji Mori (1995) Synthesis of Both the Enantiomers of Aseanostatin P5 (Sarcinic Acid), an Inhibitor of Myeloperoxidase Release, and Four Diastereomers of Aggreceride A, a Platelet Aggregation Inhibitor, Bioscience, Biotechnology, and Biochemistry, 59:1, 78-82, DOI: 10.1271/bbb.59.78

To link to this article: http://dx.doi.org/10.1271/bbb.59.78

Biosci. Biotech. Biochem., **59** (1), 78–82, 1995

Synthesis of Both the Enantiomers of Aseanostatin P5 (Sarcinic Acid), an Inhibitor of Myeloperoxidase Release, and Four Diastereomers of Aggreceride A, a Platelet Aggregation Inhibitor†

Takeshi KITAHARA, Shigeru AONO, and Kenji MORI

Department of Applied Biological Chemistry, Division of Agriculture and Agricultural Life Sciences, The University of Tokyo, 1-1-1 Yayoi, Bunkyo-ku, Tokyo 113, Japan

Received August 8, 1994

Both the enantiomers of aseanostatin P5 (sarcinic acid), an inhibitor of myeloperoxidase (MPO) release from human polymorphonuclear leukocytes (PMN), with high optical purity were synthesized by starting from (*S*)-2-methylbutanol and methyl (*S*)-3-hydroxy-2-methylpropanoate. They were converted to four diastereomers of aggreceride A, a platelet aggregation inhibitor.

Considerable attention has been paid to the isolation of modulators that regulate the function of polymorphonuclear leukocytes (PMN), which participate in the defence system against primary infection, in order to elucidate the mechanism and to find new clinically useful drugs.[1] During the course of a recent screening to obtain a new microbial modulator of the PMN function, branched fatty acids **1a**, **2**, and **3** were isolated from actinomycete strains from Thailand.[1] They inhibited the myeloperoxidase (MPO) release from PMN, but not the MPO activity itself not other PMN functions. It is remarkable that these fatty acids could possess such selective activity toward PMN functions and they promise to be a useful tool for studying this mechanism. Among them, aseanostatin P5 (**1a**) showed higher inhibitory effect than P1 (**2**) and P6 (**3**). Although P5, 12-methyltetradecanoic acid, has a chiral center in its molecule, the absolute configuration was not determined, and the chiroptical data for the natural product remain unknown.

This *anteiso* acid (**1a**) was originally isolated from degras (wool wax)[2] and then from bacteria.[3,4] In the latter case, these branched fatty acids are widely distributed in the bacterial world and are common substrates for phospholipid synthesis, the resulting lipids such as phosphatidylethanolamines and glycerols constituting the bacterial cell membrane and controling the mobility of the membrane.[5-7] This particular acid (**1a**) was named sarcinic acid, since it was discovered from the *Sarcina* species.[3] Interestingly, monoglycerides of branched fatty acids have been isolated from *Streptomyces* strain OM-3209 as platelet aggregation inhibitors and were named aggrecerides A (**1b**), B (**4**), and C (**5**).[8]

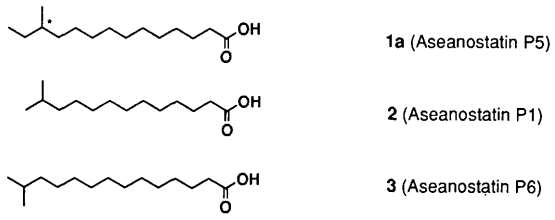


Fig. 1.

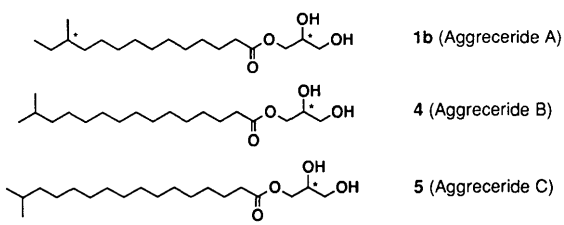


Fig. 2.

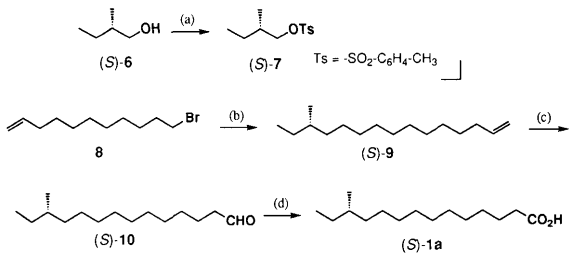
It is noteworthy that 1-monoglycerides of similar branched acids have an inhibitory effect against platelet aggregation. In the case of bacteria, both enantiomers of **1a** were available for phospholipid synthesis, although natural (*S*)-(+)-**1a** was incorporated more efficiently.[9] As for the inhibition of MPO release and platelet aggregation, however, the relationship between absolute configuration and activity is not known at all. Thus, we became interested in the synthesis of both the enantiomers of **1a** and their conversion to possible diastereomers **1b** to determine the absolute configurations of both inhibitors and to afford samples for a biological study. Described next is our simple synthesis of **1a** and **1b**, starting from readily available chiral building blocks.

Results and Discussion

Commercially available (*S*)-(−)-2-methyl-1-butanol [(*S*)-(−)-**6**] was treated with *p*-toluenesulfonyl chloride (*p*-TsCl) in pyridine to give tosylate (*S*)-**7**.[10] Grignard coupling of the tosylate with 10-undecenylmagnesium bromide[11] prepared from bromide **8**[11] in the presence of dilithium tetrachlorocuprate (Li_2CuCl_4)[12] gave branched alkene (*S*)-**9** in a 72% yield from **6**. Ozonolysis of (*S*)-**9** and a subsequent reductive workup with dimethyl sulfide (Me_2S) gave aldehyde (*S*)-**10**, which, without purification, was oxidized with Jones' chromic acid at 0°C to give crude acid (*S*)-(+)-**1a**.

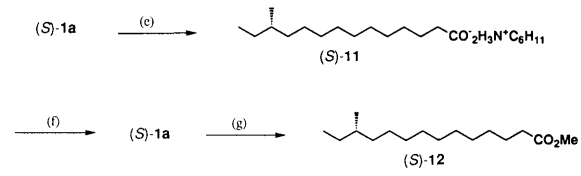
Purification of (*S*)-**1a** by repeated recrystallization of its cyclohexylamine salt (*S*)-**11** from acetone gave pure (*S*)-(+)-aseanostatin P5 [(*S*)-**1a**], $[\alpha]_D^{21} = +5.42°$ ($CHCl_3$)

† Synthetic Studies on Enzyme Inhibitors. Part 3. For Part 2, see T. Kitahara, N. Suzuki, K. Koseki, and K. Mori, *Biosci. Biotech. Biochem.*, **57**, 1906–1909 (1993).



(a) *p*-TsCl / pyridine; (b) (i) Mg / THF, (ii) **7** / THF, (iii) 0.5 M Li_2CuCl_4 / THF; (c) O_3, $(CH_3)_2S$; (d) CrO_3 / H_2SO_4 aq.

Scheme 1. Synthesis of (*S*)-**1a**.

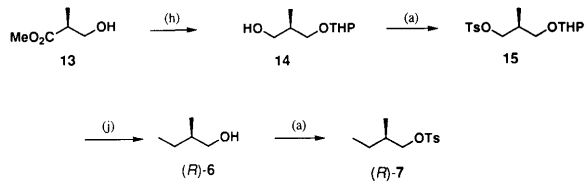


(e) (i) $C_6H_{11}NH_2$ / $(CH_3)_2CO$, (ii) recrystallization; (f) 2 N HCl aq; (g) CH_2N_2 / Et_2O

Scheme 2. Purification and Esterification of (*S*)-**1a**.

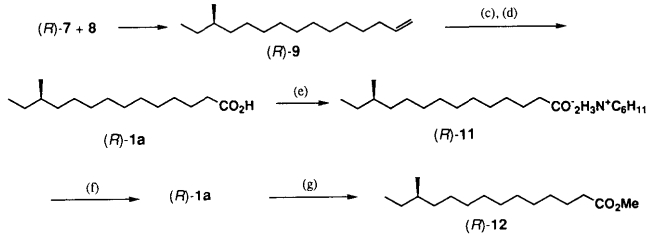
{lit.[3] $[\alpha]_D^{18} = +4.8°$} in a 70% yield from (*S*)-**9**. Diazomethane treatment of this acid gave methyl ester (*S*)-**12**, whose spectral data were identical with those of an authentic sample derived from natural aseanostatin P5. The homogeneity of (*S*)-**12** was confirmed by GLC giving a single peak.

In order to synthesize the antipode, it was necessary to obtain (*R*)-(+)-2-methyl-1-butanol [(*R*)-**6**],[13] which was commercially unavailable. Thus, we employed methyl (*S*)-(−)-3-hydroxy-2-methylpropanoate (**13**) of 99.6% *e.e.*[14] as the starting material. Treatment of **13** with dihydropyran and a catalytic amount of *p*-toluenesulfonic acid (*p*-TsOH), which was followed by the reduction with lithium aluminum hydride ($LiAlH_4$) afforded diol-mono tetrahydropyranyl (THP) ether **14**. Tosylation of **14** with *p*-TsCl in pyridine gave tosylate **15** in a 90% yield from **13**. Grignard coupling of tosylate **15** with methylmagnesium bromide in the presence of Li_2CuCl_4 and subsequent acidic methanolysis with *p*-TsOH-MeOH under reflux gave (*R*)-(+)-2-methyl-1-butanol [(*R*)-**6**]. As this alcohol was volatile, the crude product was directly converted to the (*R*)-tosylate [(*R*)-**7**] (*vide supra*).



(h) (i) DHP, *p*-TsOH, (ii) $LiAlH_4$; (j) (i) MeMgBr, Li_2CuCl_4 / THF, (ii) *p*-TsOH / MeOH

Scheme 3. Approach to (*R*)-**6**.

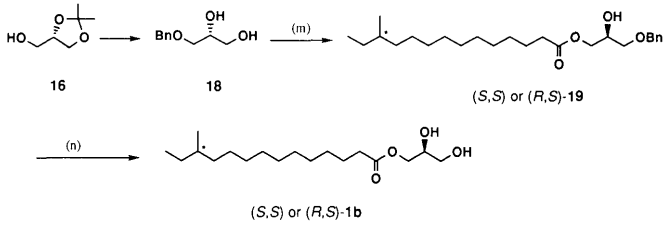


Scheme 4. Synthesis of (*R*)-**1a**.

Tosylate (*R*)-**7** was transformed to (*R*)-(−)-aseanostatin P5 [(*R*)-**1a**] in the same manner as that already described (45% overall yield from **7**), $[\alpha]_D^{21} = -5.84°$ ($CHCl_3$). The spectral data of its methyl ester (*R*)-**12** were identical with those of an authentic sample.

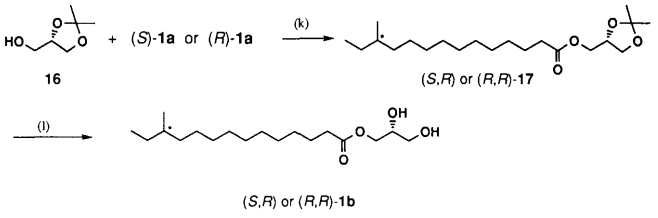
Next, two diastereomers of aggreceride A were synthesized by esterifying (*S*)-**1a** with D-1,2-*O*-isopropylidene-*sn*-glycerol (**16**),[15] $[\alpha]_D^{21} = +14.8°$ (neat) {lit.[15] $[\alpha]_D^{21} = +14.0°$}, using *N*,*N*′-dicyclohexylcarbodiimide (DCC) and 4-dimethylaminopyridine (DMAP) as condensing reagent, to afford protected monoglyceride (*S*,*R*)-**17** in a 91% yield. Deprotection of the acetonide was a cumbersome step; for instance, under a weak acid treatment for a relatively long period, 1,3-migration of the acyl chain resulted in a mixture of diastereomers at C-2 of glycerol. The optimum procedure to suppress randomization was by treating **17** with 35% perchloric acid ($HClO_4$)–ether (1 : 1) at 0°C for 10 min to give (12*S*,2′*R*)-aggreceride A [(*S*,*R*)-**1b**] in an 87% yield. Under these conditions, the chiral center at C-2 of the glycerol moiety was retained up to 94% *e.e.* In the same manner, (*R*)-(−)-**1a** was converted to (12*R*,2′*R*)-aggreceride [(*R*,*R*)-**1b**] in an 83% yield and 98% *e.e.* The enantiomeric purity of each at the C-2 position was determined by ^{1}H-NMR (300 MHz) of the respective bis MTPA ester of the monoglycerides.

Two other diastereomers, (*S*,*S*)- and (*R*,*S*)-**1b**, were



(m) (*S*) or (*R*)-**1a**, DCC, DMAP / CH_2Cl_2; (n) H_2, $Pd(OH)_2$ / MeOH

Scheme 5. Synthesis of (*S*, *R*)-**1b** and (*R*, *R*)-**1b**.



(k) DCC, DMAP / CH_2Cl_2; (l) 35% $HClO_4$, Et_2O

Scheme 6. Synthesis of (*S*, *S*)-**1b** and (*R*, *S*)-**1b**.

Table

Aggreceride A (**1b**)	Optical rotation ($CHCl_3$)
(12*S*, 2′*R*)-**1b**{(*S*, *R*)-**1b**}	+7.25°
(12*R*, 2′*R*)-**1b**{(*R*, *R*)-**1b**}	−4.49°
(12*S*, 2′*S*)-**1b**{(*S*, *S*)-**1b**}	+3.92°
(12*R*, 2′*S*)-**1b**{(*R*, *S*)-**1b**}	−6.39°
Natural **1b**[8]	+9.7°

prepared in two steps by esterifying (*S*)-**1a** and (*R*)-**1a** with 3-*O*-benzyl-*sn*-glycerol (**18**)[16] and subsequently debenzylating resulting esters (*S,S*)- and (*R,S*)-**19**. The enantiomeric purities at the C-2 position was satisfactory.

IR and ^{1}H-NMR spectra of the four synthetic diastereomers of **1b** were identical with those of natural aggreceride A, so it was impossible to determine the stereochemistry from the spectral data. However, as shown in the Table, the absolute configuration of aggreceride A was shown to be (12*S*,2′*R*) [(*S,R*)-**1b**] by comparing the optical rotation values of the four diastereomeric monoglycerides with that of the natural product. A bioassay of the four isomers of aggreceride A is now under investigation.

As chiroptical data for aseanostatin P5 were unavailable, a biological assay on both the enantiomers of synthetic samples was performed, and it was shown that the (*S*)-enantiomer was the more active inhibitor. Thus, the (*S*)-enantiomer must have been natural aseanostatin P5. Detailed biological data will be published in due course.

In conclusion, the syntheses of both enantiomers of aseanostatin P5, an inhibitor of MPO release from PMN, and four diastereomers of aggreceride A, a platelet aggregation inhibitor, both having been isolated from actinomycete strains, were accomplished, and the absolute configurations of both inhibitors were determined.

Experimental

IR spectra were recorded with a JASCO A-102 spectrometer. ^{1}H-NMR spectra were determined with a JEOL JNM EX-90 spectrometer (90 MHz) or a Bruker AC-300 spectrometer (300 MHz), using TMS as an internal standard. ^{13}C-NMR spectra were determined with a Bruker AC-300 spectrometer (75 MHz), using TMS as an internal standard. Optical rotation was determined with a JASCO DIP-371 polarimeter, and mass spectra were measured by a JEOL JMS-DX303 spectrometer. Column chromatography was performed on Merck Kieselgel 60, Art. No. 7734. Melting point (mp) and boiling point (bp) values are uncorrected.

(S)-2-Methylbutyl p-toluenesulfonate [(*S*)-**7**]. To a cooled solution (0°C) of (*S*)-2-methyl-1-butanol [(*S*)-**6**, 12.0 g, 0.136 mol] in pyridine (60 ml) was added *p*-TsCl (31.0 g, 0.163 mol), and the mixture was stirred at 4°C for 24 h. To the mixture was then added ice and water stirring, before the resulting mixture was extracted with Et_2O. The organic layer was sequentially washed with water, 2 N HCl, sat. $NaHCO_3$ and brine, dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. The residue was chromatographed over silica gel, and elution with hexane–EtOAc (15 : 1) gave (*S*)-**7** (32.4 g, 0.134 mol, 98.5%). $n_D^{22} = 1.5004$; $[\alpha]_D^{21} = +4.88°$ ($c = 2.02$, $CHCl_3$); IR (film) cm^{-1}: 1595 (m, aromatic C=C), 1355 (s, –O–SO_2–), 1175 (s, –O–SO_2–); ^{1}H-NMR (90 MHz, $CDCl_3$) δ: 0.83 (3H, t, $J = 7.7$ Hz, CH_3–CH_2–), 0.86 (3H, d, $J = 7.2$ Hz, CH_3–CH–), 1.00–1.90 (3H, m, –CH_2–CH–), 2.46 (3H, s, CH_3–Ph), 3.86 (2H, d, $J = 5.9$ Hz, –CH_2–O–), 7.35 (2H, d, $J = 8.1$ Hz, arom. *o*-H), 7.80 (2H, d, $J = 8.4$ Hz, arom. *m*-H).

Anal. Found: C, 59.74; H, 7.58%. Calcd. for $C_{12}H_{18}O_3S$: C, 59.48; H, 7.49%.

(S)-13-Methyl-1-pentadecene [(*S*)-**9**]. A catalytic amount of 1,2-dibromoethane was added under argon to a mixture of Mg (24.3 g, 0.1 mol) and a small amount of iodine. Bromide **8**[11] (18.6 g, 0.08 mol) in THF (70 ml) was then added dropwise to that mixture during the course of 30 min. After the addition was complete, the mixture was stirred for 10 min. To a solution of (*S*)-**7** (14.5 g, 0.06 mol) in THF (200 ml) was added dropwise the Grignard reagent at −70°C under argon, this being followed by the addition of a 0.1 M THF solution of Li_2CuCl_4 (7.2 ml). The mixture was stirred at room temperature for 15 h, and the resulting mixture was poured into ice-cooled NH_4Cl. The mixture was extracted with Et_2O, and the organic layer was washed with water, satd. $NaHCO_3$ and brine, dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. The residue was chromatographed over silica gel (pentane) to give an oil, which was distilled *in vacuo* to give (*S*)-**9** (9.68 g, 0.043 mol, 72.0%). bp 128–131°C at 8 Torr; $n_D^{22} = 1.4409$; $[\alpha]_D^{21} = +5.89°$ ($c = 2.00$, $CHCl_3$); IR (film) cm^{-1}: 3100 (w, =C–H), 1640 (m, C=C), 1000 (m, C=CH_2), 915 (s, C=CH_2); ^{1}H-NMR (90 MHz, $CDCl_3$) δ: 0.68–0.88 (6H, m, 2-CH_3–), 1.01–1.69 (21H, m), 1.85–2.20 (2H, br. m, –CH_2–C=C), 4.91 (1H, d, $J = 10.2$ Hz, –HC=CH*H*), 4.95 (1H, d, $J = 17.0$ Hz, –HC=C*H*H), 5.60–6.03 (1H, m, –*H*C=CH_2).

Anal. Found: C, 85.89; H, 14.31%. Calcd. for $C_{16}H_{32}$: C, 85.63; H, 14.37%.

(S)-12-Methyltetradecanal [(*S*)-**10**]. To a mixture of alkene (*S*)-**9** (9.33 g, 41.7 mmol) and $NaHCO_3$ (1.18 g, 14.0 mmol) in CH_2Cl_2 (50 ml) and MeOH (25 ml) was bubbled O_3 at −73°C until the mixture had changed into a blue suspension. After the excess O_3 had been flashed off with O_2, Me_2S (4.14 g, 66.7 mmol) was added to the suspension, and the mixture was stirred at ambient temperature for 15 h. The reaction mixture was concentrated *in vacuo*, and the residue was diluted with $NaHCO_3$ and extracted with Et_2O. The organic layer was sequentially washed with water (×2), satd. $NaHCO_3$ and brine, dried over anhydrous $MgSO_4$ and concentrated *in vacuo* to give crude (*S*)-**10** (9.35 g). This was used in the next step without further purification.

(S)-12-Methyltetradecanoic acid [*semi-pure* (*S*)-**1a**]. To a solution of crude aldehyde (*S*)-**10** (8.35 g) in acetone (200 ml) was added dropwise Jones' reagent (8 N, 16.7 ml) at 0°C until the reaction mixture became red brown. To this was added 2-propanol to decompose the excess Jones' reagent. The resulting mixture was concentrated *in vacuo* and the residue was diluted with water and extracted with Et_2O. The organic layer was sequentially washed with water (×2) and brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo* to give crude (*S*)-**1a** (9.44 g). This crude product was chromatographed over silica gel (hexane : EtOAc = 10 : 1) to give (*S*)-**1a** [8.28 g, 34.2 mmol, 82.0% from (*S*)-**9**]. The product was recrystallized as a cyclohexylamine salt for further purification.

Cyclohexylammonium (S)-12-methyltetradecanoate [(*S*)-**11**]. To a solution of (*S*)-**1a** (0.190 g, 0.785 mmol) in acetone (2 ml) was added dropwise cyclohexylamine (85.5 mg, 0.864 mmol) at 0°C, before an additional amount of acetone (0.5 ml) was added to the mixture. The resulting white precipitate was dissolved by refluxing, and the solution was left for 18 h at room temperature to recrystallize. The resulting white crystals were collected, dried, dissolved in acetone and treated by the same operation again to give colorless crystalline (*S*)-**11** (0.180 g, 0.528 mmol, 67.3%). mp 66–67°C; $[\alpha]_D^{22} = +4.74°$ ($c = 0.88$, $CHCl_3$); IR (KBr) cm^{-1}: 2210 (w, N^+–H), 1630 (m, C=O).

Anal. Found: C, 73.96; H, 12.67; N, 4.21%. Calcd. for $C_{21}H_{43}O_2N$: C, 73.84; H, 12.69; N, 4.10%.

(S)-12-Methyltetradecanoic acid [*pure* (*S*)-**1a**]. To a solution of amine salt (*S*)-**11** (0.180 g, 0.528 mmol) was added 2 N HCl until the solution reached pH 2–3. To this was added EtOAc and $(NH_4)_2SO_4$, and the mixture was stirred for 1 hour at room temperature. The organic layer was separated, dried over anhydrous Na_2SO_4 and concentrated *in vacuo* to give (*S*)-**1a** (0.128 g, 0.525 mmol, 99.4%). mp 23.5°C; $[\alpha]_D^{21} = +5.42°$ ($c = 0.93$, $CHCl_3$); IR (film) cm^{-1}: 3400–3000 (m, br., –OH), 1710 (s, C=O); ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 0.83–0.87 (3H, t, $J = 6.8$ Hz, CH_3–CH_2–CH–), 0.83–0.85 (3H, d, $J = 6.8$ Hz, CH_3–CH–), 1.05–1.21 (2H, br. m, CH_3–CH_2–CH–), 1.21–1.35 (17H, br.), 1.58–1.68 (2H, quint, $J = 7.2$ Hz, –CH_2CH_2–C=O), 2.32–2.37 (2H, t, $J = 7.5$ Hz, –CH_2–C=O); ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 179.9 (C=O), 36.7, 34.5, 34.1, 30.1, 29.7, 29.6, 29.5, 29.4, 29.2, 29.1, 27.2, 24.7, 19.3, 11.5.

Anal. Found: C, 74.45; H, 12.36%. Calcd. for $C_{15}H_{30}O_2$: C, 74.32; H, 12.48%.

Methyl (S)-12-methyltetradecanoate [(*S*)-**12**]. To a solution of (*S*)-**1a** (0.167 g, 0.690 mmol) in MeOH (15 ml) was added a solution of CH_2N_2 in Et_2O at 0°C until the mixture became yellow, acetic acid then being added to decompose the excess CH_2N_2. The resulting solution was neutralized with $NaHCO_3$, concentrated *in vacuo* and extracted with Et_2O. The organic layer was sequentially washed with water (×2) and brine (×2), dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. The residue was chromatographed over silica gel (hexane : EtOAc = 15 : 1) to give (*S*)-**12** (0.170 g, 0.664 mmol, 96.2%). bp 130°C at 3 Torr; $n_D^{22} = 1.4362$; $[\alpha]_D^{21} = +5.07°$ ($c = 2.08$, $CHCl_3$); IR (film) cm^{-1}: 1740 (s, C=O), 1170 (m, –C–O–), 1110 (w, –C–O–); ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 0.83–0.88 (3H, t, $J = 7.5$ Hz, CH_3–CH_2–CH–), 0.83–0.85 (3H, d, $J = 7.2$ Hz, CH_3–CH–), 1.07–1.16 (2H, br. m, CH_3–CH_2–CH–), 1.16–1.38 (17H, br.), 1.57–1.67 (2H, quint, $J = 7.5$ Hz, –CH_2–CH_2–C=O), 2.28–2.33 (2H, t,

J=7.5 Hz, $-CH_2-C=O$), 3.67 (3H, s, $CH_3-O-C=O$); ^{13}C-NMR (300 MHz, $CDCl_3$) δ: 174.5 (C=O), 51.4 (CH_3-O-), 36.7, 34.5, 34.2, 30.1, 29.8, 29.7, 29.6, 29.5, 29.3, 29.2, 27.1, 25.0, 19.4, 11.5.

Anal. Found: C, 74.77; H, 12.51%. Calcd for $C_{16}H_{32}O_2$: C, 74.94; H, 12.58%.

(R)-2-Methyl-1-butanol [(*R*)-**6**]. (*R*)-**6** was prepared from methyl (*S*)-3-hydroxy-2-methylpropanoate (**13**) in the same manner as that reported.[13] An analytical sample was purified by chromatography over silica gel (pentane : Et_2O = 10 : 1) and distillation, and the rest was used directly in the next step. bp 110°C; n_D^{21} = 1.4098; $[\alpha]_D^{21}$ = +5.72° (neat d_4^{21} = 0.819 g cm^{-3}) {lit.[13] n_D^{21} = 1.4037; $[\alpha]_D^{24}$ = +5.57° (neat, d_D^{23} = 0.823 g cm^{-3})}.

(R)-2-Methylbutyl p-toluenesulfonate [(*R*)-**7**]. Tosylate (*R*)-**7** was prepared in the same manner as that described for the preparation of (*S*)-**7** in a 49.3% overall yield through 6 steps from methyl (*S*)-3-hydroxy-2-methylpropanoate (**13**). n_D^{21} = 1.5006; $[\alpha]_D^{21}$ = −4.81° (c = 1.95, $CHCl_3$); IR (film) cm^{-1}: 1595 (m, aromatic C=C), 1355 (s, $-O-SO_2-$), 1175 (s, $-O-SO_2-$); ^{1}H-NMR (90 MHz, $CDCl_3$) δ: 0.75–1.00 (3H, br, CH_3-CH_2-), 0.87 (3H, d, J=7.2 Hz, CH_3-CH-), 1.10–1.90 (3H, m, $-CH_2-CH-$), 2.46 (3H, s, CH_3–Ph), 3.86 (2H, dd, J=6.3, 1.8 Hz, $-CH_2-O-$), 7.35 (2H, d, J=9.0 Hz, arom. *o*-H), 7.81 (2H, d, J=9.0 Hz, arom. *m*-H).

Anal. Found: C, 59.77; H, 7.50%. Calcd. for $C_{12}H_{18}O_3S$: C, 59.48; H, 7.49%.

(R)-13-Methyl-1-pentadecene [(*R*)-**9**]. With tosylate (*R*)-**7** (5.47 g, 22.6 mmol), crude (*R*)-**9** was prepared in the same manner as that described for the preparation of (*S*)-**9** and then distilled by a spinning-band column *in vacuo* to give pure (*R*)-**9** (2.82 g, 12.6 mmol, 55.8%). bp 134°C at 8 Torr; n_D^{21} = 1.4406; $[\alpha]_D^{21}$ = −6.50° (c = 2.00, $CHCl_3$); IR (film) cm^{-1}: 3060 (w, =C–H), 1635 (m, C=C), 990 (m, $C=CH_2$), 905 (s, $C=CH_2$); ^{1}H-NMR (90 MHz, $CDCl_3$) δ: 0.70–0.90 (6H, m, 2-CH_3–), 1.03–1.60 (21H, m), 1.87–2.20 (2H, br. m, $-CH_2-C=C$), 4.92 (1H, d, J = 10.8 Hz, $-HC=CH_2$), 4.97 (1H, d, J = 17.1 Hz, $-HC=CHH$), 5.60–6.07 (1H, m, $-HC=CH_2$).

(R)-12-Methyltetradecanoic acid [*semi-pure* (*R*)-**1a**]. Alkene (*R*)-**9** (1.50 g, 6.70 mmol) was converted to (*R*)-**1a** (1.33 g, 5.50 mmol, 82.1%). The product was recrystallized as a cyclohexylamine salt for further purification.

Cyclohexylammonium (R)-12-methyltetradecanoate [(*R*)-**11**]. With (*R*)-**1a** (2.01 g, 8.31 mmol), the same precedure as that used for the preparation of (*S*)-**11** gave pure (*R*)-**11** (1.28 g, 3.74 mmol, 44.5%). mp 65–67°C; $[\alpha]_D^{22}$ = −4.77° (c = 1.00, $CHCl_3$); IR (nujol) cm^{-1}: 2260 (w, N^+–H), 1645 (m, C=O).

Anal. Found: C, 73.56; H, 12.63; N, 3.91%. Calcd. for $C_{21}H_{43}O_2N$: C, 73.84; H, 12.69; N, 4.10%.

(R)-12-Methyltetradecanoic acid [*pure* (*R*)-**1a**]. Amine salt (*R*)-**11** (1.25 g, 3.67 mmol) was hydrolyzed and extracted in the same manner as that described for the preparation of (*S*)-**1a** to give (*R*)-**1a** (0.873 g, 3.61 mmol, 98.4%). mp 24.2°C; $[\alpha]_D^{22}$ = −5.84° (c = 2.01, $CHCl_3$); IR (film) cm^{-1}; 3400–3000 (m, br., –OH), 1710 (s, C=O); ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 0.83–0.88 (3H, t, J=7.2 Hz, CH_3-CH_2-), 0.83–0.85 (3H, d, J=6.4 Hz, CH_3-CH-), 1.05–1.21 (2H, br. m, CH_3-CH_2-CH-), 1.21–1.39 (17H, br.), 1.59–1.68 (2H, quint, J=7.3 Hz, $-CH_2-CH_2-C=O$), 2.32–2.37 (2H, t, J=7.4 Hz, $-CH_2-C=O$); ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 179.9 (C=O), 37.1, 34.8, 34.4, 30.4, 30.1, 30.0, 29.9, 29.8, 29.7, 29.5, 27.5, 25.1, 19.9, 11.8.

Anal. Found: C, 74.04; H, 12.61%. Calcd. for $C_{15}H_{30}O_2$: C, 74.32; H, 12.48%.

Methyl (R)-12-methyltetradecanoate [(*R*)-**12**]. With (*R*)-**1a** (0.297 g, 1.23 mmol), (*R*)-**12** (0.36 g, 1.20 mmol, 97.6%) was given in the same manner as that described for the preparation of (*S*)-**12**. bp 128°C at 4 Torr; n_D^{21} = 1.4396; $[\alpha]_D^{22}$ = −5.60° (c = 2.06, $CHCl_3$); IR (film) cm^{-1}: 1740 (s, C=O), 1170 (m, –C–O–), 1110 (w, –C–O–); ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 0.83–0.88 (3H, t, J=7.5 Hz, CH_3-CH_2-), 0.84 (3H, d, J=6.4 Hz, CH_3-CH-), 1.05–1.16 (2H, br. m, CH_3-CH_2-CH-), 1.16–1.38 (17H, br.), 1.57–1.67 (2H, br. quint, J=7.2 Hz, $-CH_2-CH_2-C=O$), 2.28–2.33 (2H, t, J=7.5 Hz, $-CH_2-C=O$), 3.66 (3H, s, $CH_3-O-C=O$); ^{13}C-NMR (300 MHz, $CDCl_3$) δ: 175.0 (C=O), 52.0 (CH_3-O-), 37.2, 34.9, 34.6, 30.5, 30.2, 30.1, 30.0, 29.9, 29.7, 29.6, 27.5, 25.4, 19.7, 11.9.

Anal. Found: C, 74.90; H, 12.56%. Calcd. for $C_{16}H_{32}O_2$: C, 74.94; H, 12.58%.

(R)-2,3-O-Isopropylidenedioxypropyl (S)-12-methyltetradecanoate [(*S,R*)-**17**]. To a stirred solution of the known optically active alcohol D-1,2-*O*-isopropylidene-*sn*-glycerol[15] (**16**, 0.167 g, 1.27 mmol) and DCC (0.288 g, 1.40 mmol) in dry CH_2Cl_2 (8 ml) was added a solution of (*S*)-**1a** (0.305 g, 1.26 mmol) and a catalytic amount of DMAP in dry CH_2Cl_2 (5 ml) under an argon atmosphere at 0°C. The mixture was stirred for 24 h at room temperature. To the resulting mixture was added a solution of hexane–Et_2O (1 : 1); (6 ml), and the mixture was stirred for 3 min at 0°C before the resulting white precipitate was filtered off. The filtrate was concentrated *in vacuo* and chromatographed over silica gel (hexane : Et_2O = 50 : 1) to give (*S,R*)-**17** (0.408 g, 1.15 mmol, 91.3%). bp 160–164°C at 5 Torr; n_D^{22} = 1.4476; $[\alpha]_D^{25}$ = +10.34° (c = 0.96, Et_2O); IR (film) cm^{-1}: 1740 (s, C=O), 1380, 1370, 1250, 1215, 1160, 1090, 1060 (m, –C–O–); ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 0.83–0.87 (3H, t, J=7.0 Hz, CH_3-CH_2-CH-), 0.83–0.85 (3H, d, J=6.9 Hz, CH_3-CH-), 1.05–1.19 (2H, br. m, CH_3-CH_2-CH-), 1.16–1.38 (17H, br.), 1.37 (3H, s, CH_3-C-), 1.44 (3H, s, CH_3-C-), 1.57–1.67 (2H, br., $-CH_2-CH_2-C=O$), 2.32–2.37 (2H, t, J=7.5 Hz, $-CH_2-C=O$), 3.72–3.76 (1H, dd, J=6.3, 8.4 Hz, $-O-CHH-CH-$), 4.06–4.20 (3H, m, $-O-CH_2-CH-$, $-O-CHH-CH-$), 4.28–4.36 (1H, m, –O–CH–).

Anal. Found: C, 70.65; H, 11.28%. Calcd. for $C_{21}H_{40}O_4$: C, 70.74; H, 11.31%.

(R)-2,3-Dihydroxypropyl (S)-12-methyltetradecanoate [(*S,R*)-*aggreceride A*; (*S,R*)-**1b**]. To acetonide (*S,R*)-**17** (46 mg, 0.129 mmol) was added a mixture of 35% $HClO_4$ (4 ml) and Et_2O (4 ml) at 0°C, and the mixture was stirred vigorously for 10 min. The resulting mixture was neutralized with NaOH and $NaHCO_3$, and extracted with Et_2O (×3). The organic layer was sequentially washed with water, satd. $NaHCO_3$ and brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was chromatographed over silica gel (hexane : EtOAC = 10 : 1) to give (*S,R*)-**1b** (35.5 mg, 0.112 mmol, 87.1%). mp 29–30°C; $[\alpha]_D^{21}$ = +7.25° (c = 0.30, $CHCl_3$); IR (film) cm^{-1}: 3600–3000 (s, br. shoulder, –OH), 1735 (s, C=O), 1380, 1180, 1110, 1100, 1060, 1040 (m, –C–O–); ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 0.83–0.87 (3H, t, J=6.8 Hz, CH_3-CH_2-CH-), 0.83–0.85 (3H, d, J=6.7 Hz, CH_3-CH-), 1.05–1.19 (2H, br. m, CH_3-CH_2-CH-), 1.16–1.37 (17H, br.), 1.57–1.67 (2H, br., $-CH_2-CH_2-C=O$), 2.33–2.38 (2H, t, J=7.5 Hz, $-CH_2-C=O$), 3.56–3.62 (1H, dd, J=11.4, 5.8 Hz, $HO-CHH-CH-$), 3.66–3.71 (1H, dd, J=11.4, 3.9 Hz, $HO-CHH-CH-$), 3.87–3.95 (1H, m, HO–CH–), 4.12–4.24 (2H, 2-dd, J=11.7, 5.9 Hz, J=11.7, 4.8 Hz, $O=C-O-CH_2-CH-$); ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 174.4 (C=O), 70.3 (–CH–O–), 65.2, 63.3 ($-CH_2-O-$), 36.6, 34.4, 34.2, 30.0, 29.7, 29.6, 29.5, 29.4, 29.2, 29.1, 27.1, 24.9, 19.2, 11.4.

HRMS m/z (M^+): found, 316.2645; calcd. for $C_{18}H_{36}O_4$, 316.2614.

(R)-2,3-O-Isopropylidenedioxypropyl (R)-12-methyltetradecanoate [(*R,R*)-**17**]. With (*R*)-**1a** (0.146 g, 0.603 mmol), the same procedure as that described for the preparation of (*S,R*)-**17** gave (*R,R*)-**17** (0.185 g, 0.520 mmol, 86.2%). bp 170–172°C at 3 Torr; n_D^{20} = 1.4489; $[\alpha]_D^{22}$ = +1.81° (c = 1.05, Et_2O); IR (film) cm^{-1}: 1740 (s, C=O), 1380, 1370 (m, –C–O–), 1250, 1215, 1160, 1090, 1060 (w, –C–O–); ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 0.83–0.87 (3H, t, J=7.2 Hz, CH_3-CH_2-CH-), 0.83–0.85 (3H, d, J=7.1 Hz, CH_3-CH-), 1.05–1.19 (2H, br. m, CH_3-CH_2-CH-), 1.18–1.38 (17H, br.), 1.37 (3H, s, CH_3-C-), 1.43 (3H, s, CH_3-C-), 1.57–1.67 (2H, br., $-CH_2-CH_2-C=O$), 2.31–2.36 (2H, t, J=7.5 Hz, $-CH_2-C=O$), 3.71–3.76 (1H, dd, J=8.5, 6.2 Hz, $-O-CHH-CH-$), 4.05–4.19 (3H, m, $-O-CH_2-CH-$, $-O-CHH-CH-$), 4.27–4.35 (1H, m, –OCH–).

Anal. Found: C, 70.45; H, 11.24%. Calcd. for $C_{21}H_{40}O_4$: C, 70.74; H, 11.31%.

(R)-2,3-Dihydroxypropyl (R)-12-methyltetradecanoate [(*R,R*)-*aggreceride A*; (*R,R*)-**1b**]. With acetonide (*R,R*)-**17** (33 mg, 0.0899 mmol), the same procedure as that described for the preparation of (*S,R*)-**1b** gave (*R,R*)-**1b** (27.5 mg, 0.0870 mmol, 96.8%). $[\alpha]_D^{22}$ = −4.49° (c = 0.39, $CHCl_3$); IR (film) cm^{-1}: 3700–3000 (s, br., –OH), 1735 (s, C=O), 1375, 1180, 1110, 1040 (w, –C–O–); ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 0.83–0.88 (3H, t, J=7.2 Hz, CH_3-CH_2-CH-), 0.83–0.85 (3H, d, J=6.4 Hz, CH_3-CH-), 1.05–1.19 (2H, br. m, CH_3-CH_2-CH-), 1.17–1.39 (17H, br.), 1.57–1.67 (2H, br., $-CH_2-CH_2-C=O$), 2.33–2.38 (2H, t, J=7.5 Hz, $-CH_2-C=O$), 3.56–3.61 (1H, dd, J=11.6, 5.8 Hz, $HO-CHH-CH-$), 3.66–3.71 (1H, dd, J=11.6, 4.0 Hz), $HO-CHH-CH-$), 3.87–3.96 (1H, m, HO–CH–), 4.12–4.24 (2H, 2-dd, J=11.7, 6.1 Hz, J=11.7, 4.7 Hz, $O=C-O-CH_2-CH-$); ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 175.0 (C=O), 71.0 (–CH–O–), 65.9, 64.0 ($-CH_2-O-$), 37.3, 35.1, 34.9, 30.7, 30.4, 30.3, 30.2, 30.1, 29.9, 29.8, 27.8, 25.6, 19.9, 12.1.

HRMS m/z (M^+): found, 316.2565; calcd. for $C_{18}H_{36}O_4$, 316.2614.

Bis-(R)-MTPA ester of (R,R)-**1b**. To a solution of (*R,R*)-**1b** (10 mg, 0.0316 mmol) in pyridine (0.2 ml) was added (*S*)-α-methoxy-α-(trifluoromethyl)-phenylacetyl chloride [(*S*)-MTPA chloride; 79 mg, 0.316 mmol] and a catalytic amount of DMAP, and the mixture was stirred at room temperature for 40 h. The mixture was poured into ice-cooled water and extracted with Et_2O. The organic layer was sequentially washed by satd. $CuSO_4$ (×2), water (×2) and brine, dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. The residue was analyzed by ^{1}H-NMR. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 0.83–0.87 (3H, t, J=7.2 Hz, CH_3–CH_2–CH–), 0.83–0.85 (3H, d, J=6.4 Hz, CH_3–CH–), 1.05–1.20 (2H, br. m, CH_3–CH_2–CH–), 1.18–1.40 (17H, br.), 1.52–1.63 (2H, br., –CH_2–CH_2–C=O), 2.24–2.29 (2H, t, J=7.5 Hz), –CH_2–C=O), 3.42 (3H, s, CH_3–O–), 3.48 (3H, s, CH_3–O–), 4.11–4.41 (2H, 2-dd, J=12.1, 7.1 Hz, J=12.2, 4.0 Hz, O=C–O–CH_2–CH–), 4.31–4.65 (2H, 2-dd, J=12.4, 4.7 Hz, J=12.4, 3.5 Hz, O=C–O–CH_2–CH–), 5.52–5.62 (1H, m, –O–CH–), 7.33–7.51 (10H, m, arom. H).

Bis-(S)-MTPA ester of (R,R)-**1b**. With (*R,R*)-**1b** and (*R*)-MTPA chloride, the same precedure as that described for preparing the bis-(*R*)-MTPA ester of (*R,R*)-**1b** gave the bis(*S*)-MTPA ester of (*R,R*)-**1b**, which was analyzed by ^{1}H-NMR. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 0.82–0.87 (3H, t, J=7.2 Hz, CH_3–CH_2–CH–), 0.83–0.85 (3H, d, J=7.1 Hz, CH_3CH–), 1.05–1.20 (2H, br. m, CH_3–CH_2–CH–), 1.18–1.39 (17H, br.), 1.50–1.62 (2H, br., –CH_2–CH_2–C=O), 2.19–2.24 (2H, t, J=7.6 Hz, –CH_2–C=O), 3.40 (3H, s, CH_3–O–), 3.48 (3H, s, CH_3–O–), 4.02–4.35 (2H, 2-dd, J=12.2, 6.1 Hz, J=12.2, 4.2 Hz, O=C–O–CH_2–CH–), 4.38–4.73 (2H, 2-dd, J=12.3, 6.2 Hz, J=12.3, 3.1 Hz, O=C–O–CH_2–CH–), 5.50–5.60 (1H, m, –O–CH–), 7.34–7.50 (10H, m, arom. H).

(S)-3-Benzyloxy-2-hydroxypropyl (S)-12-methyltetradecanoate [(*S,S*)-**19**]. To a stirred solution of 3-*O*-benzyl-*sn*-glycerol **18**[16] (127 mg, 0.698 mmol) and DCC (158 mg, 0.768 mmol) in dry CH_2Cl_2 (5 ml) was added a catalytic amount of DMAP and a solution of (*S*)-**1a** (169 mg, 0.698 mmol) in dry CH_2Cl_2 (3 ml) under an argon atmosphere at 0°C, the mixture then being stirred for 24 h at room temperature. To the resulting mixture was added a solution of hexane–Et_2O (1 : 1; 5 ml), and the mixture was stirred for 5 min at 0°C, before the resulting white precipitate was filtered off. The filtrate was concentrated *in vacuo* and chromatographed over silica gel (hexane : EtOAc = 100 : 1) to give (*S,S*)-**19** (180 mg, 0.433 mmol, 63.5%). n_D^{19} = 1.4850; $[\alpha]_D^{22}$ = +7.42° (c = 0.50, $CHCl_3$); IR (film) cm^{-1}: 3700–3100 (m, br., –OH), 1735 (s, C=O); ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 0.83–0.88 (3H, t, J=6.9 Hz, CH_3–CH_2–CH–), 0.83–0.85 (3H, d, J=6.8 Hz, CH_3–CH–), 1.05–1.20 (2H, br. m, CH_3–CH_2–CH–), 1.17–1.39 (17H, br.), 1.50–1.67 (2H, br., –CH_2–CH_2–C=O), 2.30–2.35 (2H, t, J=7.5 Hz, –CH_2–C=O), 2.40–2.60 (1H, br., –OH), 3.47–3.52 (1H, dd, J=9.7, 6.1 Hz, BnO–CHH–CH–), 3.54–3.58 (1H, dd, J=9.6, 4.4 Hz, BnO–CHH–CH–), 4.00–4.07 (1H, m, –O–CH–), 4.11–4.22 (2H, m, O=C–O–CH_2–CH–), 4.56 (2H, s, ph-CH_2–), 7.30–7.38 (5H, m, arom. H).

Anal. Found: C, 74.14; H, 10.46%. Calcd. for $C_{25}H_{42}O_4$: C, 73.85; H, 10.41%.

(S)-2,3-Dihydroxypropyl (S)-12-methyltetradecanoate [(*S,S*)-*aggreceride A*; (*S,S*)-**1b**]. To a stirred solution of (*S,S*)-**19** (180 mg, 0.443 mmol) in MeOH (7 ml) was added an excess amount of Pearlman's catalyst ($Pd(OH)_2$; 11 mg) under an H_2 atmosphere, and the mixture was stirred for 12 h at room temperature. The precipitate was filtered off over Celite, before the filtrate was concentrated *in vacuo* and chromatographed over silica gel (hexane : EtOAc = 5 : 1) to give (*S,S*)-**1b** (120 mg, 0.380 mmol, 86.3%). $[\alpha]_D^{22}$ = +3.92° (c = 0.37, $CHCl_3$); IR ($CHCl_3$) cm^{-1}: 3600–3000 (m, br. shoulder, –OH), 1735 (s, C=O), 1375, 1170, 1115, 1055 (m, –C–O–); ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 0.83–0.88 (3H, t, J=6.8 Hz, CH_3–CH_2–CH–), 0.83–0.85 (3H, d, J=7.0 Hz, CH_3–CH–), 1.05–1.19 (2H, br. m, CH_3–CH_2–CH–), 1.18–1.38 (17H, br.), 1.58–1.68 (2H, br. m, –CH_2–CH_2–C=O), 2.33–2.38 (2H, t, J=7.5 Hz, –CH_2–C=O), 3.57–3.63 (1H, dd, J=11.5 Hz, 5.8 Hz, HO–CHH–CH–), 3.67–3.73 (1H, dd, J=11.6 Hz, 4.0 Hz, HO–CHH–CH–), 3.90–3.97 (1H, m, HO—CH–), 4.12–4.24 (2H, 2-dd, J=11.7, 5.9 Hz, J=11.7, 4.8 Hz, O=C–O–CH_2–CH–); ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 174.3 (C=O), 70.3 (–CH–O–), 65.2, 63.4 (–CH_2–O–), 36.7, 34.4, 34.2, 30.0, 29.7, 29.6, 29.5, 29.4, 29.2, 29.1, 27.1, 24.9, 19.2, 11.4.

HRMS m/z (M^+): found, 316.2640; calcd. for $C_{18}H_{36}O_4$, 316.2614.

(S)-3-Benzyloxy-2-hydroxypropyl (R)-12-methyltetradecanoate [(*R,S*)-**19**]. With (*R*)-**1a** (137 mg, 0.566 mmol), **18** (103 mg, 0.566 mmol) and DCC (130 mg, 0.631 mmol), the same procedure as that described for the preparation of (*S,S*)-**19** gave (*R,S*)-**19** (162 mg, 0.399 mmol, 70.5%). n_D^{20} = 1.4849; $[\alpha]_D^{22}$ = +1.38° (c = 0.50, $CHCl_3$); IR (film) cm^{-1}: 3700–3100 (m, br., –OH), 1740 (s, C=O); ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 0.83–0.88 (3H, t, J=7.2 Hz, CH_3–CH_2–CH–), 0.83–0.86 (3H, d, J=7.0 Hz, CH_3–CH–), 1.05–1.21 (2H, br. m, CH_3–CH_2–CH–), 1.17–1.40 (17H, br.), 1.53–1.67 (2H, br., –CH_2–CH_2–C=O), 2.30–2.35 (2H, t, J=7.5 Hz, –CH_2C=O), 2.40–2.60 (1H, br., –OH), 3.47–3.52 (1H, dd, J=9.6 Hz, 6.0 Hz, BnO–CHH–CH–), 3.54–3.59 (1H, dd, J=9.6, 4.4 Hz, BnO–CHH–CH–), 4.01–4.07 (1H, m, HO–CH–), 4.11–4.23 (2H, m, O=C–O–CH_2–CH–), 4.56 (2H, s, ph-CH_2–), 7.30–7.36 (5H, m, arom. H).

(S)-2,3-Dihydroxypropyl (R)-12-methyltetradecanoate [(*R,S*)-*aggreceride A*; (*R,S*)-**1b**]. With (*R,S*)-**19** (152 mg, 0.374 mmol), the same procedure as that described for the preparation of (*S,S*)-**1b** gave (*R,S*)-**1b** (111 mg, 0.351 mmol, 93.9%). $[\alpha]_D^{22}$ = −6.39° (c = 0.35, $CHCl_3$); IR (film) cm^{-1}: 3700–3000 (s, br. shoulder, –OH), 1735 (s, C=O); ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 0.83–0.88 (3H, t, J=7.2 Hz, CH_3–CH_2–CH–), 0.83–0.85 (3H, d, J=7.3 Hz, CH_3–CH–), 1.04–1.20 (2H, br. m, CH_3–CH_2–CH–), 1.16–1.38 (17H, br.), 1.57–1.69 (2H, m, –CH_2–CH_2–C=O), 2.32–2.37 (2H, t, J=7.5 Hz, –CH_2–C=O), 3.57–3.63 (1H, dd, J=11.3 Hz, 5.8 Hz, HO–CHH–CH–), 3.67–3.72 (1H, dd, J=11.3, 4.0 Hz, HO–CHH–CH–), 3.88–3.97 (1H, m, HO–CH–), 4.11–4.24 (2H, 2-dd J=11.6, 6.0 Hz, J=11.6, 4.8 Hz, O=C–O–CH_2–CH–); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 174.3 (C=O), 70.3 (–CH–O–), 65.2, 63.4 (–CH_2–O–), 36.7, 34.4, 34.2, 30.0, 29.7, 29.6, 29.5, 29.4, 29.2, 29.2, 29.1, 27.1, 24.9, 19.2, 11.4.

Acknowledgments. We are greatly indebted to Dr. K. Suzuki of National Institute of Health in Japan, and K. Yazawa of Sagami Chemical Research Center for the bioassay of aseanostatin P5 and for generously providing the spectral data for the authentic sample. Our thanks are due to Professor S. Omura of Kitazato University for generously providing the spectral data of the authentic aggreceride A. Elemental analysis performed by Mrs. Y. Naito is gratefully acknowledged.

References

1) A. Ishida-Okawara, Y. Kimoto, K. Watanabe, K. Tokuda, M. Shibata, K. Masuda, Y. Takano, K. Kawaguchi, H. Akagawa, N. Nilubol, K. Hotta, K. Yazawa, S. Mizuno, and K. Suzuki, *J. Antibiot.*, **44**, 524–532 (1991).
2) A. W. Weitcamp, *J. Am. Chem. Soc.*, **67**, 447–454 (1945).
3) S. Akashi and K. Saito, *J. Biochem.*, **47**, 222–229 (1960).
4) K. Saito, *J. Biochemistry*, **47**, 710–719 (1960).
5) T. Kaneda, *Bioscience and Industry*, **48**, 229–235 (1990).
6) W. M. O'Leary and S. G. Wilkinson, in "Microbial Lipids," Vol. 1, ed. by C. Ratledge and S. G. Wilkinson, Academic Press, New York, 1988, p. 117.
7) T. Kaneda, *Biochim. Biophys. Acta*, **280**, 297–305 (1972).
8) S. Omura, A. Nakagawa, N. Fukamachi, K. Otaguro, and B. Kobayashi, *J. Antibiot.*, **39**, 1180–1181 (1986).
9) T. Kaneda, *Biochim. Biophys. Acta*, **960**, 10–18 (1988).
10) K. Mori and J. Wu, *Liebigs Ann. Chem.*, **1991**, 213–217.
11) R. R. Iyer and V. R. Mamdapar, *Indian J. Chem., Sect. B*, **28B**, 728–732 (1989).
12) G. Fouquet and M. Schlosser, *Angew. Chem. Int. Ed. Engl.*, **13**, 82–83 (1974).
13) K. Mori and H. Takikawa, *Liebigs Ann. Chem.*, **1991**, 497–500.
14) K. Mori, *Tetrahedron*, **39**, 3107–3109 (1983).
15) E. Baer, *Biochem. Prepn.*, **2**, 31–37 (1952).
16) R. I. Duclos, Jr. and A. Makriyannis, *J. Org. Chem.*, **57**, 6156–6163 (1992).