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SYNTHESIS OF (2*R*,3*S*)-3-[(BENZYLOXYCARBONYL)OXY]-2-FLUOROTETRADECANOIC ACID

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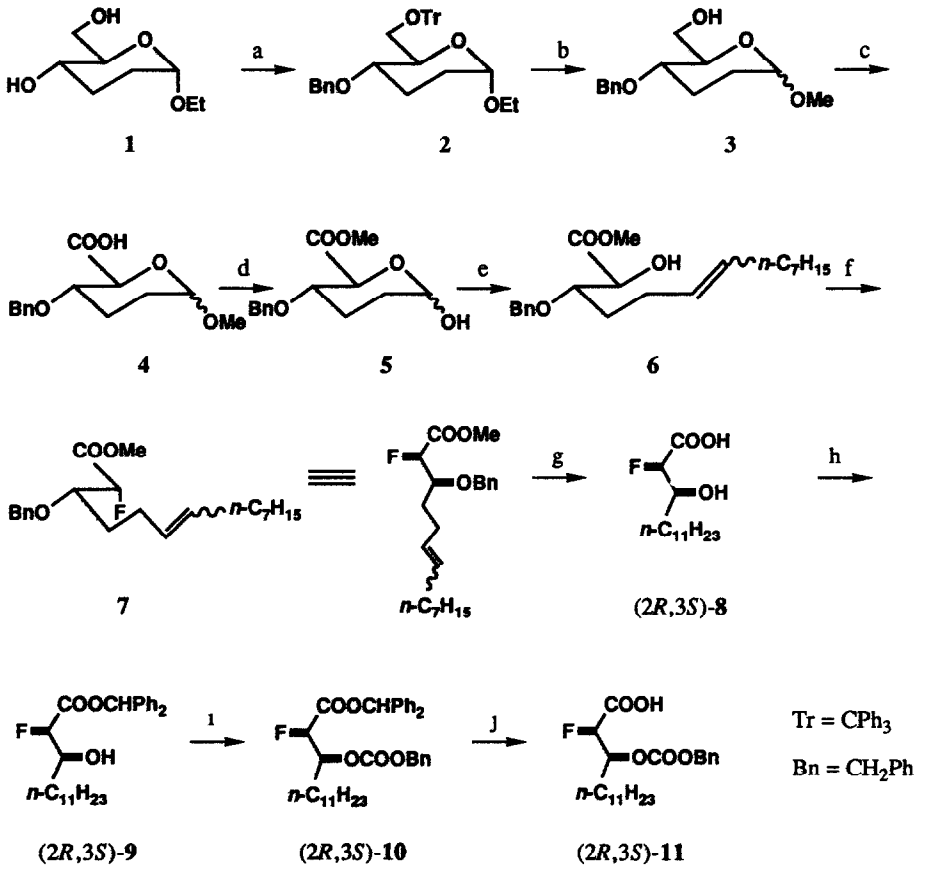
Abstract: Optically active *threo*-3-[(benzyloxycarbonyl)oxy]-2-fluorotetradecanoic acid, (2*R*,3*S*)-**11**, was synthesized from 3,4,6-tri-*O*-acetyl-D-glucal *via* methyl uronate derivative (**5**) Reaction of **5** with octylidene triphenylphosphorane followed by treatment with DAST yielded methyl 2-fluorotetradecenoate derivative (2*R*,3*S*)-**7**, from which (2*R*,3*S*)-**11** was achieved in four steps The enantiomer was obtained by the resolution of racemic **8**

Lipid A is a lipophilic part of lipopolysaccharide (LPS), which is a component of the outer membrane of Gram-negative bacteria, and shows most of the endotoxic activity of LPS [1] It has two (*R*)-3-hydroxytetradecanoyl groups at 2- and 3-positions of glucosamine, and also has (*R*)-acyloxytetradecanoyl groups at 2'- and 3'-positions of another glucosamine moiety Lipid X[2] is the reducing part of lipid A, and is one of the biosynthetic precursors of lipid A Hasegawa and Kiso showed that the non-reducing sugar part of lipid A (ex GLA-60) elicited some distinct and potential biological activity of lipid A and LPS.[3]

We are interested in the biological activity of the compounds related to lipid A, X or GLA-60, containing a fluorinated hydroxytetradecanoyl group. Therefore, we attempted to synthesize optically active *threo*-3-[(benzyloxycarbonyl)oxy]-2-fluorotetradecanoic acid, (2*R*,3*S*)-**11**, from 3,4,6-tri-*O*-acetyl-D-glucal. And the enantiomer was obtained by resolution of racemic **8**, which was prepared from 1-fluoro-3,3-dimethyl-2-butanone and dodecanal Here we describe the synthesis of (2*R*,3*S*)-3-[(benzyloxycarbonyl)oxy]-2-fluorotetradecanoic acid, (2*R*,3*S*)-**11**, (Scheme I), and the optical resolution of (±)-**8** [4]

The compound **1**, obtained from ethyl 2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside,[5] was converted to trityl ether by treatment with triphenylmethyl chloride in pyridine, and then to benzyl ether **2** by treatment with benzyl bromide in *N*,*N*-dimethylformamide (DMF) using sodium hydride (NaH) as a base Treatment of **2** with 4% sulfuric acid in methanol

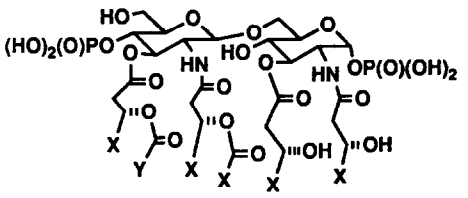


(a) TrCl-pyridine, room temperature, 16 h; and BnBr, NaH-DMF, room temperature, 18 h, 78%, (b) 4%-H_2SO_4-MeOH, room temperature, 1 5 h, 76%, (c) Jones oxidation, 0°C, 1 h, 63%, (d) CH_2N_2-Et_2O-EtOAc, room temperature, and dioxane-aq 0.5% H_2SO_4 (1.1), 70-75°C, 3 h, 88%, (e) *n*-$C_7H_{15}CH{=}PPh_3$-THF, room temperature, 15 min, 55%, (f) Et_2NSF_3-CH_2Cl_2, 0°C-room temperature, 2 h, 34%, (g) 1 M NaOH-EtOH (3.40), room temperature, 2 h, and H_2, Pd/C-AcOH, room temperature, (h) Ph_2CN_2-CH_2Cl_2, room temperature, 1 h, three steps, 53%; (i) ClCOOBn, DMAP-CH_2Cl_2, 0°C 30 min-room temperature 30 min, 95%, (j) CF_3COOH-CH_2Cl_2, room temperature, 1 h, 79%

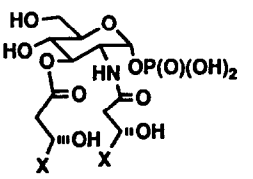
Scheme 1

gave the alcohol **3**[6]as an anomeric mixture. Treatment of **3** with Jones reagent gave an enantiomeric mixture of carboxylic acid **4**. Esterification of **4** with diazomethane, and deprotection of anomeric position with 5% sulfuric acid in dioxane gave **5**. Wittig reaction of **5** with *n*-octyl triphenylphosphonium bromide-lithium hexamethyldisilazide in THF gave **6**. Treatment of **6** with diethylaminosulfur trifluoride (DAST) gave **7** with the inversion of configuration. The *syn* configuration of **7** was confirmed by the comparison of physical data of **9** and **11** in the latter stage The compound **7** was found to have a smell similar to that of stinkbug Saponification of **7** with aqueous 1M sodium hydroxide in ethanol, and reduction of the double bond, followed by hydrogenolysis of the benzyl group using palladium on carbon as a catalyst in acetic acid gave (2*R*,3*S*)-**8** Esterification of thus resulted 2-fluoro-3-hydroxytetradecanoic acid with diphenyldiazomethane gave (2*R*,3*S*)-**9** Treatment of (2*R*,3*S*)-**9** with benzyl chloroformate-DMAP gave (2*R*,3*S*)-**10**, which was further converted to (2*R*,3*S*)-**11** using trifluoroacetic acid in dichloromethane.

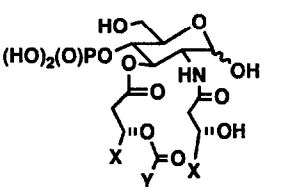
On the other hand, the optical resolution of racemic-**8** was achieved by treatment with dehydroabietylamine,[7] to get a crystalline salt of (2*S*,3*R*)-**8**, which was further converted to (2*S*,3*R*)-**11** by the same procedure as described for the preparation of (2*R*,3*S*)-**11** from (2*R*,3*S*)-**8**



X=*n*-$C_{11}H_{23}$
Y=*n*-$C_{13}H_{27}$
Lipid A of *E coli*



X=*n*-$C_{11}H_{23}$
Lipid X



X=*n*-$C_{11}H_{23}$
Y=*n*-$C_{13}H_{27}$
GLA-60

Figure 1

EXPERIMENTAL

Melting points are uncorrected ^{1}H NMR were recorded at 270 MHz using a JEOL JNN-270 with trimethylsilane as an internal standard The IR absorption spectra were determined on a Jasco IR A-2 spectrophotometer Mass spectra were obtained on a JMS-O1SG mass spectrometer Optical rotation was recorded Perkin-Elmer 241 polarimeter Column chromatography was carried out on silica gel-60 (Merck, 230-400 mesh ASTM), at slightly elevated pressure (1 2 atm) for elution

Ethyl 2,3-dideoxy-α-D-*erythro*-hexopyranoside (1). To a solution of ethyl 2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside[5] (18.0 g, 122 mmol) in EtOH (180 mL) was added 10% Pd on carbon (2 0 g). The mixture was stirred for 30 min under H_2 at room temperature. The catalyst was filtered off, and the filtrate was concentrated in *vacuo* to give 18 0 g of **1** (quantitatively) as a crystalline solid, mp 72.5-73 5°C (needles from EtOAc-cyclohexane), which was employed for the next reaction without purification. ^{1}H NMR ($CDCl_3$) δ 1.70-1.95 (4H, m), 3.41-3.82 (6H, m), 4.79-4.80 (1H, m, C1-H) IR ν_{max}(Nujol) 3400-3250 cm^{-1} MS *m/z* 175 (M^+-1), 145, 131, 116. Anal. Calcd. for $C_8H_{16}O_4$. C, 54 53, H, 9.15 Found: C, 54.38; H, 8 88

Ethyl 4-*O*-benzyl-6-*O*-triphenylmethyl-α-D-*erythro*-hexopyranoside (2). (i) To a solution of **1** (14 8 g, 84.0 mmol) in pyridine (150 mL) was added Ph_3CCl (23.4 g, 83 9 mmol) The mixture was stirred for 16 h at room temperature The precipitate was filtered off, and the filtrate was concentrated in *vacuo*, diluted with EtOAc, washed successively with dil. HCl, H_2O, sat $NaHCO_3$, and brine, dried over $MgSO_4$, and concentrated in *vacuo* to give 35 1 g of ethyl 6-*O*-triphenylmethyl-α-D-*erythro*-hexopyranoside, which was employed for the next reaction without purification (ii) To a solution of thus obtained trityl ether (35.1 g, 83.9 mmol) in DMF (200 mL) were added NaH (3 02 g, 126 mmol) and BnBr (21.5 g, 126 mmol) The mixture was stirred for 18 h at room temperature, and diluted with EtOAc, washed with ice-water, and brine, dried over $MgSO_4$, and concentrated in *vacuo* to give a mixture which was chromatographed on a silica gel column Elution with cyclohexane-EtOAc (9 1) gave 33 5 g of **2** (78 %) as a gum ^{1}H NMR ($CDCl_3$) δ 1 25 (3H, t, *J*=6 9-7 3 Hz), 1 74-2 06 (4H, m), 3 19 (1H, dd, *J*=5 4, 9 8 Hz), 3 41-3.58 (3H, m), 3 82-3 91 (2H, m, OCH_2), 4 25, 4 48 (2H, AB-q, *J*=11 5 Hz), 4 88 (1H, d, *J*=2 0 Hz), 6 99-7 03 (2H, m), 7 19-7.37 (13H, m), 7.48-7 52 (5H, m) IR ν_{max}(neat) 1595 (w) Anal Calcd for $C_{34}H_{36}O_4$ C, 80 28, H, 7 13 Found C, 79 95, H, 7 11

Methyl 4-*O*-benzyl-2,3-dideoxy-α,β-D-*erythro*-hexopyranoside (3). The mixture of **2** (33 0 g, 64 9 mmol) in 4% H_2SO_4 in MeOH (v/v %, 500 mL) was stirred for 1 5 h at room temperature To this solution Et_3N (56 mL) was added, and the mixture was concentrated in *vacuo* to give an oily mixture, which was diluted with EtOAc, washed successively with H_2O, sat. $NaHCO_3$, and brine, dried over $MgSO_4$, and concentrated in *vacuo* to give a mixture The mixture was chromatographed on a silica gel column Elution with cyclohexane-EtOAc (5 1, then 3 2) 12 4 g of **3** (76 %) as a gum ^{1}H NMR ($CDCl_3$) δ 1 45-2 15 (4H, m), 1.74-2.06 (4H, m), 3 35 (2 2H, s, α-OMe), 3 44 (1H, m), 3.49 (0 8H, s, β-OMe), 3 64-3 89 (4H, m), 4 48 (1H, d, *J*=11 7 Hz, OCHPh), 4 61-4 68 (2H, m, OCHPh and C1-H), 7 25-7 38 (5H, m) IR ν_{max}(neat) 3450 cm^{-1} Anal. Calcd for $C_{14}H_{20}O_4$ C, 66 64, H, 7 99 Found· C, 66 30, H, 8 33

Methyl 4-*O*-benzyl-2,3-dideoxy-α,β-D-*erythro*-hexopyranosiduronic acid (4). To a solution of **3** (11 0 g, 43 6 mmol) in acetone (270 mL) Jones reagent (21 mL) was added gradually at 0°C The mixture was stirred for 1 h at this temperature, diluted with EtOAc (2 L), and filtered The filtrate was washed with sat $NaHCO_3$ (500 mL x 3) The combined aqueous

layer was washed with EtOAc (800 mL), and acidified with conc HCl The acidic aqueous layer was extracted with EtOAc. The organic layer was washed with brine, dried over MgSO4, and concentrated to give 7.32 g of **4** (63%) as an oil ^{1}H NMR ($CDCl_3$) δ 1.60-1 97 (3H, m), 2.04-2 16 (1H, m), 3 40 (15/6H, s), 3 53 (3/6H, s), 3 68 (1H, dt, *J*=4 9, 9.8 Hz, C4-H), 4 26 (1H, d, *J*=9.8 Hz, C5-H), 4 56, 4 71 (2H, AB-q, *J*=11.2 Hz), 4.61 (1/6H, d, *J*=3.4 Hz, C1-Ha), 4 81-4 82 (5/6H, m, C1-He), 7.27-7 40 (5H, m) IR ν_{max}(neat) 3650-2400, 1715 cm^{-1} Anal Calcd for $C_{14}H_{18}O_5.1/2H_2O$: C, 61 31; H, 6 98 Found· C, 61 34, H, 6 54

Methyl 4-*O*-benzyl-2,3-dideoxy-α,β-D-*erythro*-hexopyranuronate (5) To a solution of **4** (7 31 g, 27 5 mmol) in EtOAc (200 mL) was added an excess solution of CH_2N_2 in Et_2O at room temperature with stirring The mixture was condensed in *vacuo* to give an oily residue, which was dissolved in dioxane-aqueous 0 5% H_2SO_4 (1:1, 500 mL). The solution was warmed to 70-75°C for 3 h with stirring, and cooled to room temperature using ice, diluted with EtOAc (1 5 L), washed with H_2O and brine, dried over $MgSO_4$, and concentrated in *vacuo* to give a mixture. The mixture was chromatographed on a silica gel column Elution with cyclohexane-EtOAc (1 1) to give 6 42 g of an anomeric mixture **5** (88%) as crystalls mp 111-113°C (from EtOAc-cyclohexane), ^{1}H NMR ($CDCl_3$) δ 1 8-2 2 (4H, m), 2 82 (1H, d, *J*=3.9 Hz, OH), 3 70 (2.2H, s, OCH_3), 3.76 (0 8H, s, OCH_3), 4 71 (1H, d, *J*=2 3 Hz, C5-H), 5.21-5.29 (1H, m, C4-H), 5.42 (1H, m, C1-H), 7.31-7 61 (3H, m), 8 01-8.06 (2H, m), IR ν_{max}(Nujol) 3410, 1742, 1705 cm^{-1}, MS *m/z* 248 (M$^+$-18) Anal. Calcd for $C_{14}H_{16}O_6$. C, 59 99; H, 5.75. Found: C, 60 10; H, 5 86.

(2*S*,3*S*)-Methyl 3-benzyloxy-2-hydroxytetradec-6-enoate (6) To a solution of **5** (996 mg, 3 74 mmol) in THF (20 mL) was added a solution of *n*-$C_7H_{15}CH$=PPh_3 in THF-hexane [prepared from a suspension of ($Ph_3P^+C_8H_{17}$)Br$^-$ (3 0 g) in THF (25 mL) and a solution of *n*-BuLi (1 6 M hexane solution, 6 mL) at room temperature for 15 min under nitrogen] After 15 min at room temperature, the reaction mixture was quenched with 4N-HCl, diluted with EtOAc, washed with sat. $NaHCO_3$, brine dried over $MgSO_4$, decolorized with activated charcoal, and concentrated in *vacuo* to give an oily residue, which was chromatographed on a silica gel column. Elution with cyclohexane-EtOAc (3 1) gave 739 mg of **6** (55%) as a gum The stereochemistry of this compound could not be established clearly ^{1}H NMR ($CDCl_3$) δ 0 88 (3H, t, *J*=6.3-6.9 Hz), 1.20-1.40 (10H, m), 1.40-1.52 (1H, m), 1.73-1 89 (1H, m), 1.90-2 21 (2H, m), 3.72 (1H, m), 3.80 (3H, s), 4.40 (1H, d, *J*=3.0 Hz) 4.58, 4 68 (2H, AB-q, *J*=11.6 Hz), 5.24-5 44 (2H, m, olefinic), 7.28-7.35 (5H, m), IR ν_{max}(neat) 3470, 1730 cm^{-1}; MS *m/z* 362 (M$^+$), 344, 273 Anal Calcd for $C_{22}H_{34}O_4$ C, 72 89; H, 9 45 Found· C, 72 69; H, 9 35

(2*R*,3*S*)-Methyl 3-benzyloxy-2-fluorotetradec-6-enoate (7). To a solution of **6** (362 mg, 1 0 mmol) in CH_2Cl_2 (6 mL) was added Et_2NSF_3 (450 mg, 2.79 mmol) at 0°C. The mixture was stirred for 2 h at room temperature The reaction mixture was quenched with ice-water, diluted with EtOAc, washed with sat. $NaHCO_3$, and brine, dried over $MgSO_4$, and concentrated in *vacuo* to give an oily residue, which was chromatographed on a silica gel

column Elution with cyclohexane-EtOAc (9:1) gave 51 mg of an unidentified product (Rf=0 421), and 124 mg of **7** (34%, Rf=0.368) as a gum. The stereochemistry of this compound could not be established clearly ^{1}H NMR ($CDCl_3$) δ 0.88 (3H, t, *J*=6 4-6.8 Hz), 1 27 (10H, m),1 70-1.90 (2H, m), 1 90-2.20 (4H, m), 3.76 (3H, s), 3.88 (1H, dm, J_{FH}=24.4 Hz, C3-H), 4.54, 4 61 (2H, AB-q , *J*=11 7 Hz, CH_2Ph), 4.94 (1H, dd, *J*=2.9-3.4, 48.4 Hz, C2-H), 5.27-5.47 (2H, m, olefinic), 7 27-7.37 (5H, m); IR ν_{max}(neat) 2930, 2850, 1745 cm^{-1}, MS *m/z* 364 (M^+), 273, 255, 235, 203, 175 Anal Calcd for $C_{22}H_{33}O_3F$: C, 72 49; H, 9.13, F, 5.21 Found. C, 72.29, H, 9.17, F, 4 85

(2*R*,3*S*)-Diphenylmethyl 2-fluoro-3-hydroxytetradecanoate [(2*R*,3*S*)-9]. To a solution of **7** (96 mg, 0 263 mmol) in EtOH (8 mL) was added a solution of 1M NaOH (0.6 mL). The mixture was stirred for 2 h at room temperature. The reaction mixture was acidified with dil HCl, and extracted with EtOAc. The organic layer was washed with sat. NaCl, dried over $MgSO_4$, and concentrated in *vacuo* to give 87 mg of 3-benzyloxy-2-fluorotetradec-6-enoic acid as a gum, which was reduced and hydrogenolyzed in AcOH (6 mL) containing 10% Pd on carbon (90 mg) at room temperature for 8 h. The catalyst was filtered off and the filtrate was concentrated in *vacuo* to give 71 mg of (2*R*,3*S*)-3-hydroxy-2-fluorotetradecanoic acid [(2*R*,3*S*)-**8**]. The acid in EtOAc (2 mL) was esterified with Ph_2CN_2 (70 mg) for 1 h at room temperature. The mixture was chromatographed on a silica gel column. Elution with cyclohexane-EtOAc (10·1) to give 60 mg of (2*R*,3*S*)-**9** (53%, Rf=0 420, cyclohexane:EtOAc=5·1) as crystalls mp 60-61°C (from hexane), $[\alpha]_D^{24}$ +4.5° (c 1.2, $CHCl_3$); ^{1}H NMR ($CDCl_3$+D_2O) δ 0 88 (3H, t, *J*=6.4-6 8 Hz), 1 25 (18H, m),1 40-1 64 (2H, m), 4 04 (1H, dtd, J=2.9, 6.0, 25.0 Hz, C3-H), 4.90 (1H, dd, *J*=2.9, 47.9 Hz, C2-H), 7.01 (1H, s), 7.28-7.38 (10H, m), IR ν_{max}(KBr) 3520, 1735 cm^{-1}. Anal Calcd. for $C_{27}H_{37}O_3F$· C, 75 67, H, 8 70, F, 4 43 Found. C, 75.78; H, 8 94, F, 4 56

(2*R*,3*S*)-Diphenylmethyl 3-[(benzyloxycarbonyl)oxy]-2-fluorotetradecanoate [(2*R*,3*S*)-10]. To a solution of (2*R*,3*S*)-**9** (24 mg, 0.056 mmol) in CH_2Cl_2 (1 mL) were added ClCOOBn (30 mg, 0.180 mmol) and DMAP (20 mg, 0 16 mmol). The mixture was stirred for 30 min at 0°C and then for 30 min at room temperature. The reaction mixture was chromatographed on a preparative TLC plate. Development with cyclohexane-EtOAc (9·1) gave 30 mg of (2*R*,3*S*)-**10** (95%) as a gum: ^{1}H NMR ($CDCl_3$) δ 0.88 (3H, t, *J*=6 4-6.8 Hz), 1.20-1.35 (18H, m),1.66-1.76 (2H, m), 4.90-5.20 (4H, m), 6.95 (1H, s), 7.25-7.40 (15H, m); IR ν_{max}(neat) 2925, 2860, 1750 cm^{-1}. Anal Calcd. for $C_{35}H_{43}O_5F$: C, 74.71; H, 7.70; F, 3.38. Found· C, 74 62, H, 7 79, F, 3 27

(2*R*,3*S*)-3-[(Benzyloxycarbonyl)oxy]-2-fluorotetradecanoic acid [(2*R*,3*S*)-11]. To a solution of (2*R*,3*S*)-**10** (20 mg, 0.036 mmol) in CH_2Cl_2 (1 mL) was added CF_3COOH (0.3 mL), and after 1 h at room temperature, the reaction mixture was concentrated in *vacuo* to give a residue, which was washed with hexane, leaving behind a deposit of 11 mg of (2*R*,3*S*)-**11** (79%) as a powder: mp 65°C. $[\alpha]_D^{24}$ - 8.0° (c 1.2, $CHCl_3$), ^{1}H NMR ($CDCl_3$) δ 0.88 (3H, t, *J*=6.4-6.8 Hz),

1.18 (18H, m), 1.68-1.90 (2H, m), 3.95 (1H, bs), 5.00 (1H, dd, J=2.9, 47.4 Hz), 5.09-5.24 (3H, m), 7 35 (5H, m); IR ν_{max}($CHCl_3$) 1770 cm^{-1}. Anal. Calcd. for $C_{27}H_{37}O_3F$: C, 66.85, H, 8.50, F, 4.82. Found: C, 66.70; H, 8.42; F, 4.71.

Optical Resolution of (±)-*threo*-3-[(Benzyloxycarbonyl)oxy]-2-fluoro-3-hydroxytetradecanoic acid, (±)-8, with dehydroabietylamine. To a suspension of the racemic carboxylic acid (±)-8[4](13.0 g, 49 6 mmol) in Et_2O (300 mL) was added dehydroabietylamine (14.9 g, 52.0 mmol) at room temperature. After 1 h the dehydroabietylamine salt of (2*S*,3*R*)-8 was precipitated from the resulted solution, and another 1 h stirring, the precipitated salt was collected by filtration. The precipitate was suspended in Et_2O (200 mL) and refluxed to dissolve the salt with gradual addition of MeOH (ca. 50 mL). The solution was allowed to stand at room temperature where upon a crystalline solid was obtained. This recrystallization process was repeated once more to obtain 2 1 g of dehydroabietylamine salt of (2*S*,3*R*)-8 as a powder, mp 163-171°C; $[\alpha]_D^{24}$ +20 8° (c 1.2, MeOH) ^1H NMR ($CDCl_3$) δ 0 86-2 07 [43H, m, containing at δ 1.08 (3H, s), 1.18 (3H, s), 1 20 (3H, s), 1.24 (3H, s)], 2 30-2 42 (1H, m), 2.70-2.97 (5H, m), 3.81-3.98 (1H, m), 4 58 (1H, dd, *J*=3.4, 50.3 Hz), 6 87 (1H, d, *J*=2 0 Hz), 6 95 (1H, dd, *J*=2.0, 8 3 Hz), 7.15 (1H, d, *J*=8.3 Hz) , IR ν_{max}(KBr) 3305, 2922, 2852, 1617, 1585, 1541, 1459, 1417, 14042 cm^{-1}. Anal Calcd for $C_{34}H_{58}NO_3F$: C, 74.54, H, 10 67; N, 2 56, F, 3 47 Found C, 74.45, H, 10 90, N, 2 42; F, 3 55

(2*S*,3*R*)-Diphenylmethyl 2-fluoro-3-hydroxytetradecanoate [(2*S*,3*R*)-9] To a suspension of dehydroabietylamine salt of (2*S*,3*R*)-8 (1.27 g, 2 32 mmol) in THF (20 mL) was added Ph_2CN_2 (495 mg, 2 55 mmol) The mixture was warmed at 50°C for 5 h, then quenched with AcOH, and concentrated in *vacuo* to give a residue, which was chromatographed on a silica gel column. Elution with cyclohexane-EtOAc (19 1) gave 900 mg of (2*S*,3*R*)-9, mp 59-60°C (from hexane), $[\alpha]_D^{24}$ - 4 4° (c 1 3, $CHCl_3$), ^1H NMR and IR data were identical with those of (2*R*,3*S*)-9 Anal Calcd for $C_{27}H_{37}O_3F$ C, 75 81, H, 8 85, F, 4 59 Found: C, 75 67, H, 8 70, F, 4 43

(2*S*,3*R*)-Diphenylmethyl 3-[(benzyloxycarbonyl)oxy]-2-fluorotetradecanoate [(2*S*,3*R*)-10]. Thus obtained (2*S*,3*R*)-9 (200 mg, 0 47 mmol) was esterified by the same procedure as described for the preparation of (2*R*,3*S*)-10 from (2*R*,3*S*)-9 Chromatography on a silica gel column gave 236 mg of (2*S*,3*R*)-10 (90%) $[\alpha]_D^{24}$ +2 3° (c 0.8, $CHCl_3$), ^1H NMR and IR data were identical with those of (2*R*,3*S*)-10 Anal Calcd for $C_{35}H_{43}O_5F$: C, 74 71, H, 7.70, F, 3 38 Found C, 74 95, H, 7 76, F, 3 27

(2*S*,3*R*)-3-[(Benzyloxycarbonyl)oxy]-2-fluorotetradecanoic acid [(2*S*,3*R*)-11]. Thus obtained (2*S*,3*R*)-10 (216 mg) was treated by the same procedure as described for the preparation of (2*R*,3*S*)-11 from (2*R*,3*S*)-10 to give 126 mg of (2*S*,3*R*)-2 (83%); mp 64 5-65 5°C $[\alpha]_D^{24}$ +7 9° (c 1 0, $CHCl_3$), ^1H NMR and IR data were identical with those of (2*R*,3*S*)-2. MS

m/z 395 (M^+-1), 351, 334, 245, 225, 180, 151, 107, 91 Anal. Calcd. for $C_{27}H_{37}O_3F$: C, 66.64; H, 8 39, F, 4 79 Found C, 66.85; H, 8.50; F, 4.82

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