Pergamon

Tetrahedron 57 (2001) 5377–5384

TETRAHEDRON

Syntheses of β-resorcylic acid derivatives, novel potato micro-tuber inducing substances isolated from *Lasiodiplodia theobromae*

Qing Yang, Hiroaki Toshima and Teruhiko Yoshihara*

Division of Applied Bioscience, Graduate School of Agriculture, Hokkaido University, Sapporo, 060-8589, Japan

Received 21 March 2001; accepted 27 April 2001

Abstract—The syntheses of β-resorcylic acid derivatives **1** and **2**, isolated from fungus *Lasiodiplodia theobromae*, and their dimethyl ethers were accomplished. (*R*)-(−)-1,3-Butanediol was used as a chiral source of the side chain C_6-synthon. The dianion of the benzoic acid moiety was alkylated with C_6-bromide to give the desired skeleton. Several β-resorcylic acid derivatives including **1** and **2** were synthesized via hydrogenation, lactonization, demethylation and esterification. The (*R*)-configuration of the stereogenic center in the side chain was proved by this synthesis. It is confirmed that two phenolic hydroxy groups are required for **1** and **2** to exhibit potato micro-tuber inducing activity. © 2001 Elsevier Science Ltd. All rights reserved.

1. Introduction

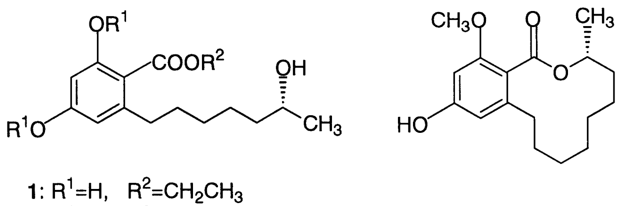
In our ongoing screening program for potato micro-tuber inducing substances from fungus *Lasiodiplodia theobromae* IFO 31059, novel β-resorcylic acid derivatives **1** and **2** were isolated in addition to lasiodiplodin **7** and others (Fig. 1).[1–3] The isolation and the structural elucidation of **1** and **2** have been previously reported,[4] in which the absolute configuration of the sole stereogenic center in the side chain was determined to be *R* by the advanced Mosher method.[5] While both **1** and **2** possessing a 6-hydroxyheptyl side chain at the C_6-position occur as the ester structure, lasiodiplodins possessing a corresponding 8-hydroxynonyl side chain occur as the 12-membered macrolactone structure.[6] There is a possibility that both **1** and **2** might be artifacts derived from the corresponding hydroxy acid **3**. In order to confirm the absolute configuration of C-6′ and investigate the structure–activity relationship of such β-resorcylic acid derivatives, **1–6** (Fig. 1) were synthesized.

In our approach to **1** and **2**, the corresponding dimethyl ethers **4–6** were supposed and retrosynthesized as shown in Fig. 2, because several successful syntheses of lasiodiplodin using an analogous route had been reported.[7] Alkylation of a stabilized dianion **8** derived from the known carboxylic acid **10** with a C_6-chiral halide **9** or its equivalent would provide the desired carbon skeleton.[7] (*R*)-(−)-1,3-Butanediol was selected as the chiral starting material to introduce the requisite stereogenic center.[7]

2. Results and discussion

2.1. Synthesis of chiral bromide 16

Selective protection of the secondary hydroxy group of (*R*)-(−)-1,3-butanediol **11** (99.4% *e.e.*) was achieved via acetalization and subsequent regioselective reduction. Treatment of **11** with benzaldehyde dimethyl acetal and *p*-toluenesulfonic acid in refluxing dichloromethane gave *p*-methoxybenzylidene acetal **12** in 98% yield. DIBAL-H reduction of **12** in toluene alone gave primary alcohol **13** in 91% yield because **12** was regioselectively reduced from the less-hindered site. Swern oxidation of **13** and subsequent Wittig reaction with (methoxycarbonylmethylene)triphenylphosphorane in one-pot gave (*E*)-unsaturated ester **14** in 77% yield. DIBAL-H reduction of **14** gave alcohol **15** in 98% yield. Treatment of **15** with carbon tetrabromide and triphenylphosphine in dichloromethane gave bromide **16** in 93% yield. After coupling **8** and **16**, both benzyl group and



1: R^1=H, R^2=CH_2CH_3
2: R^1=H, R^2=$CH_2CH(CH_3)_2$
3: R^1=H, R^2=H
4: R^1=Me, R^2=CH_2CH_3
5: R^1=Me, R^2=$CH_2CH(CH_3)_2$
6: R^1=Me, R^2=H

7: lasiodiplodin

Figure 1. Structures of β-resorcylic acid derivatives (**1–6**) and lasiodiplodin (**7**).

Keywords: β-resorcylic acid derivatives; micro-tuber inducing substance; demethylation; structure–activity relationship.

* Corresponding author. Tel.: +81-11-706-3349; fax: +81-11-706-2505; e-mail: yoshihara@chem.agr.hokudai.ac.jp

0040–4020/01/$ - see front matter © 2001 Elsevier Science Ltd. All rights reserved.
PII: S0040-4020(01)00455-0

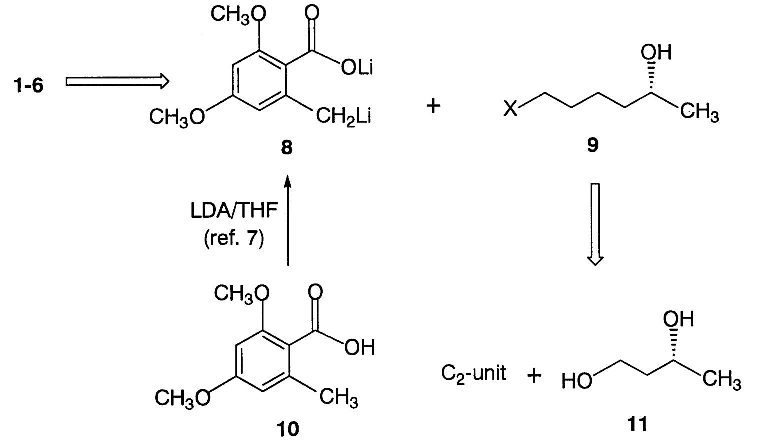


Figure 2. Retrosynthetic analysis of β-resorcylic acid derivatives **1–6**.

olefin originated from **16** would be reduced at the same time under the conventional catalytic hydrogenolysis or hydrogenation conditions. Thus, the synthesis of C_6-chiral bromide **16** corresponding to **9** in the retrosynthesis was completed (Scheme 1).

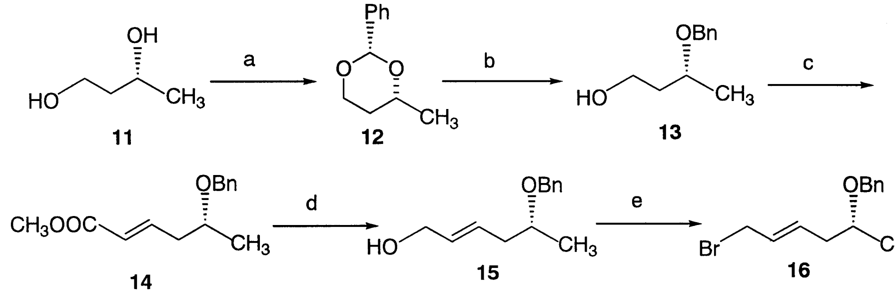
2.2. Synthesis of dimethyl ether derivatives of 4, 5 and 6

Carboxylic acid **10** was treated with LDA in THF to give dianion **8**, which was alkylated with **16**. After chromatographic purification with silica gel column, the desired product **17** was obtained in 52% yield without the contamination of unreacted **10**. Hydrogenolysis of **17** was carried out in the presence of palladium hydroxide on carbon at the atmospheric pressure to give hydroxy acid **6** in 90% yield. As we expected, deprotection of the benzyl group and hydrogenation of olefin proceeded smoothly in one step. Esterification of **6** with iodoethane and potassium carbonate gave ethyl ester **4** in 75% yield, and with isobutyl bromide gave **5** in 71% yield (Scheme 2). The optical purity of **4** was determined to be >99% *e.e.* as judged by integration of the ^{1}H NMR signals of the corresponding (*R*)-MTPA ester. The optical purity of **5** would be same as that of **4**.

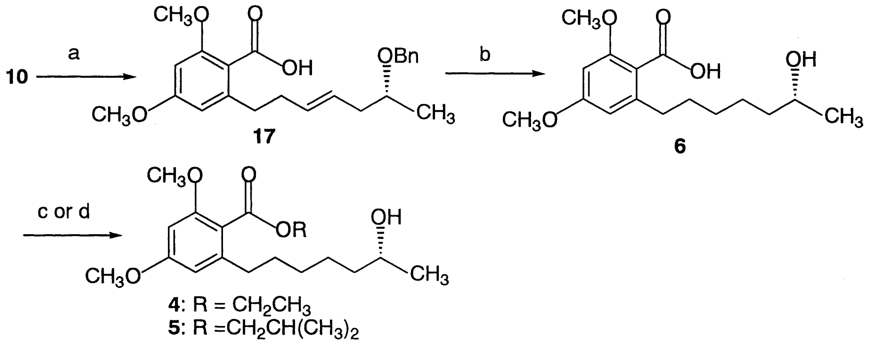
2.3. Synthesis of 1, 2 and 3

Out of our expectation, the resulting dimethyl ethers **4**, **5** and **6** could not be demethylated without substitution of the hydroxy group in the side chain or decarboxylation. We failed in all our attempts to deprotect directly the methyl ethers in **4**, **5** and **6**, though a lot of ether cleavage reagents were employed.[8] Treatment of **4** with boron tribromide in dichloromethane at −78°C resulted in only one methyl ether cleaved, accompanying substitution of the hydroxyl group in the side chain by bromine, giving ethyl 2-(6-bromoheptyl)-6-hydroxy-4-methoxybenzoate (HR-MS: calcd. for $C_{17}H_{25}O_4{}^{79}Br$ (M^+) *m/z* 372.0937, found 372.0945) as a major product. The modifications of reaction condition did not affect the result.[9] When hydrobromic acid[10] was used for **6**, demethylation and decarboxylation occurred together to give 1-(6-bromoheptyl)-3,5-dihydroxybenzene. Pyridine hydrochloride[11] did not cleave the methyl ether, but removed the carboxyl group of **6** to give 1-(6-chloroheptyl)-3,5-dimethoxybenzene (HR-MS: calcd. for $C_{15}H_{23}O_2{}^{35}Cl$ (M^+) *m/z* 270.1388, found 270.1424). The reaction using iodotrimethylsilane[12] failed to cleave the methyl ethers even if excess reagent was used for prolonged time. Aluminum chloride/ethanethiol system[13] completely cleaved the methyl ethers of **6**, but substitution of hydroxyl group with ethylsulfanyl group was not avoided. The product was confirmed to be 2,4-dihydroxy-6-(6-ethylsulfanylheptyl)benzoic acid (HR-MS: calcd. for $C_{16}H_{24}O_4S$ (M^+) *m/z* 312.1396, found 312.1364).

Therefore, a suitable protection of the hydroxy group may be required fundamentally to prevent substitution for our substrates under the conventional deprotection conditions of phenolic methyl ethers. Lactonization corresponds to intramolecular protection by the own acyl group and might fill our objectives preventing not only substitution, but also decarboxylation, because demethylation in some successful syntheses of lasiodiplodins was conducted



Scheme 1. (a) Benzaldehyde dimethyl acetal *p*-toluenesulfonic acid/CH_2Cl_2, 98%; (b) DIBAL-H/CH_2Cl_2, 91%; (c) Swerm oxid. then $Ph_3P{=}CHCOOMe$, 77%; (d) DIBAL-H/THF, 98%; (e) CBr_4, Ph_3P/CH_2Cl_2, 93%.



Scheme 2. (a) LDA/THF, then **16**, 52%; (b) H_2, $Pd(OH)_2$/EtOH, 90%; (c) EtI, K_2CO_3/acetone, 75%; (d) $ICH_2CH(CH_3)_2$, K_2CO_3/DMF, 70%.

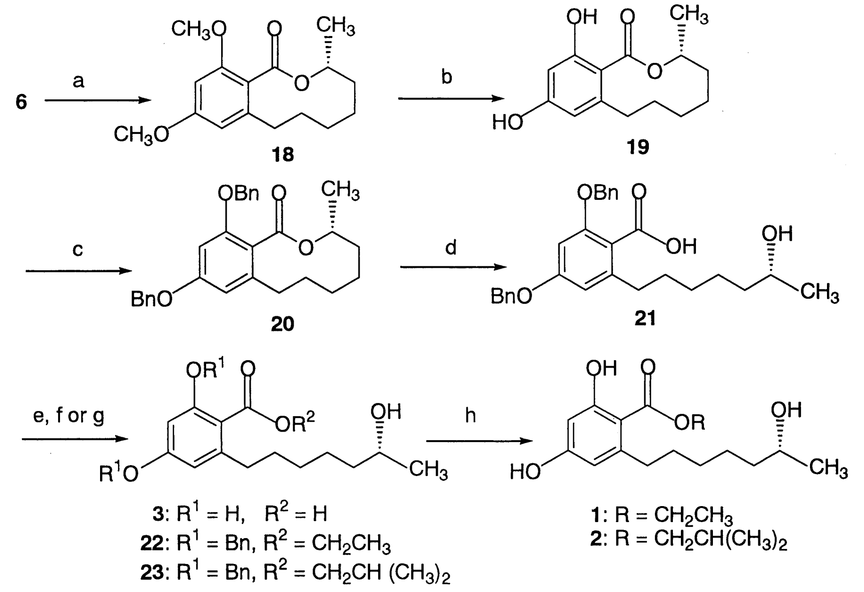
smoothly in this way.[14] Treatment of **6** with di-(2-pyridyl) disulfide and triphenylphosphine gave the corresponding 2-pyridylthiol ester which was then treated with silver perchlorate.[15] The desired lactone **18**, which corresponds to the C_2-shortened homologue of lasiodiplodin, was obtained in 50% yield. Demethylation of **18** was achieved with excess boron tribromide at room temperature to yield phenolic lactone **19** in 25% yield.[14] Although the yield is not high, our experimental hypothesis has been proved by this improvement. Optimization of this reaction is in progress (Scheme 3).

Anyway, the alkaline hydrolysis of **19** cleaved the lactone ring but in that case decarboxylation also occurred to give 1,3-dihydroxy-5-(6-hydroxyheptyl)benzene. The IR spectrum of the product showed no absorption for carboxyl group. Therefore, the two phenolic functions of **19** were protected again by benzyl group to give **20** in 88% yield. Under strong alkaline conditions, **20** was successfully hydrolyzed to give carboxylic acid **21** in 65% yield.[16] Hydrogenolysis of **21** gave hydroxy acid **3**, the probable precursor of **1** and **2** in 90% yield. Esterification of **21** with iodoethane and potassium carbonate gave ethyl ester **22** in 87% yield, and with isobutyl bromide gave isobutyl ester **23** in 95% yield. Hydrogenolysis of **22** and **23** was carried out in the presence of palladium hydroxide on carbon at the atmospheric pressure to give **1** in 87% yield and **2** in 75% yield, respectively. Synthetic **1** was methylated then converted into (*R*)-MTPA ester. The ^1H NMR spectrum of the corresponding (*R*)-MTPA ester showed the existence of a single diastereomer. Thus. the optical purity of synthetic **1** was confirmed to be >99% *e.e.* The optical purity of **2** would be same as that of **1**.

The spectral data (^1H , ^{13}C NMR, IR, MS) of synthetic **1** and **2** were completely identical with those of natural **1** and **2**. The sign of the specific rotation of synthetic **1** and **2** was similar to that of natural **1** and **2**. From this result, the absolute configuration of C-6′ in **1** and **2** was unambiguously determined as *R*.

3. Conclusion

The asymmetric total syntheses of **1** and **2** were accomplished and confirmed the absolute configuration of stereogenic center in the side chain to be *R*. The crucial step, demethylation could be overcame via lactonization



Scheme 3. (a) (1) Pyr_2S_2, Ph_3P, PhH, (2) $AgClO_4$, CH_3CN, 50%; (b) BBr_3/CH_2Cl_2, 25%, (c) BnCl, K_2CO_3/DMSO, 88%; (d) NaOH/H_2O/DMSO, 65%; (e) H_2, Pd/EtOH, 90%; (f) EtI, K_2CO_3/DMF, 87%; (g) $ICH_2CH(CH_3)_2$, K_2CO_3/DMF, 95%; (h) H_2, $Pd(OH)_2$/EtOH, 87% for **1**, 75% for **2**.

corresponding to intramolecular protection. The syntheses of **1–6** made it possible to examine the biological activity of such β-resorcylic acid derivatives.

Using bioassay of potato single-node stem segment cultures, methyl ether derivatives **4**, **5** and **6** did not show potato micro-tuber inducing activity at the same concentration (10^{-4} M) as that of natural **1** and **2**. Dimethyl ether **4** exhibited weak activity at 10^{-3} M. This result implied that the phenolic group is required for the potato micro-tuber inducing activity of β-resorcylic acid derivatives. The bioassay of **3** and other lasiodiplodin related compounds is in progress.

4. Experimental

4.1. General methods

^{1}H and ^{13}C NMR spectra were recorded with a JEOL JNM-EX-270 spectrometer (^{1}H: 270 MHz, ^{13}C: 67.8 MHz). IR spectra were measured with a Perkin Elmer System 2000 FT–IR spectrometer. Mass spectra were recorded with a JEOL JMS-AX500 spectrometer or a JEOL JMS-SX102A spectrometer. Melting point values were obtained with a Yanaco micro-melting point apparatus MP-30 and are uncorrected. Specific rotation values were recorded with a JASCO DIP-370 digital polarimeter. Column chromatography was carried out with Silica gel 60 (spherical, 70–140 mesh ASTM, Kanto Chemicals). Silica gel 60 F_{254} precoated plates were used for analytical TLC (catalog no. 5715, Merck). (*R*)-(−)-1,3-Butanediol (99.4% *e.e.*) was purchased from Wako Pure Chemical Industries Ltd.

4.1.1. (2*S*,4*R*)-4-Methyl-2-phenyl-1,3-dioxane (12). A mixture of **11** (1.00 g, 11.1 mmol), benzaldehyde dimethyl acetal (2.50 ml, 16.7 mmol) and *p*-toluenesulfonic acid (94.6 mg, 0.55 mmol) in CH_2Cl_2 (23 ml) was refluxed for 3 h. After addition of $NaHCO_3$ (46.2 mg, 0.55 mmol), the reaction mixture was concentrated under reduced pressure. The residue was purified by column chromatography (silica gel 60 g, hexane: EtOAc=20:1) to give **12** (1.93 g, 98%) as a pale yellow oil. $[\alpha]_D^{25}+2.0°$(*c* 7.1, $CHCl_3$); IR (film) 2973, 2853, 1454, 1375, 1311, 1247, 1166, 1110, 1061, 1026, 968, 853, 820 and 664 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.30 (3H, d, *J*=6.2 Hz), 1.54 (1H, br. d, *J*=12.5 Hz), 1.78 (1H, dq, *J*=12.5, 5.3 Hz), 3.98 (2H, m), 4.24 (1H, br. dd, *J*=12.5, 5.3 Hz), 5.50 (1H, s), 7.30–7.50 (5H, m); ^{13}C NMR (67.8 MHz, $CDCl_3$): 21.8, 33.0, 67.1, 73.4, 101.3, 126.1, 128.2, 128.7, 138.7; EI-MS *m/z* 178 (M^+, 15), 177 (M^+-H, 25), 105 (100), 91 (21), 77 (54), 55 (38); HR-MS calcd. for $C_{11}H_{14}O_2$ (M^+) *m/z* 178.0994, found 178.0966.

4.1.2. (*R*)-3-Benzyloxy-butan-1-ol (13). To a solution of **12** (1.82 g, 10.2 mmol) in dry CH_2Cl_2 (50 ml) was added dropwise DIBAL-H (31.9 ml, 30.6 mmol, 0.96 M solution in hexane) at −78°C under argon atmosphere. The mixture was gradually allowed to warm to room temperature and stirring was continued overnight. To the reaction mixture cooled to 0°C was added sat. aq. Rochelle salt (15 ml) in three portions. After being stirred for 1 h at room temperature, the mixture was filtered through a Celite pad. The filtrate was dried over anhydrous magnesium sulfate and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel 60 g, hexane: EtOAc=3:1) to give **13** (1.67 g, 91%) as a colorless oil: $[\alpha]_D^{25}-48.1°$(*c* 8.3, $CHCl_3$); IR (film) 3398, 3031, 2969, 2932, 1719, 1496, 1453, 1375, 1277, 1206, 737 and 698 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ1.16 (3H, d, *J*=6.1 Hz), 1.68 (2H, m), 2.28 (1H, br s, OH), 3.71 (3H, m), 4.39 (1H, d, *J*=11.5 Hz), 4.54 (1H, d, *J*=11.5 Hz), 7.25 (5H, m); ^{13}C NMR (67.8 MHz, $CDCl_3$): 19.3, 38.7, 60.9, 70.4, 74.6, 127.6, 127.7, 128.3, 138.4; EI–MS *m/z* 180 (M^+, 0.27), 162 (2.3), 161 (1.4), 145 (0.25), 123 (0.61), 105 (13.4), 91 (100), 77 (44), 51 (43), 43 (90); HR-MS calcd. for $C_{11}H_{16}O_2$ (M^+) *m/z* 180.1151, found 180.1179.

4.1.3. Methyl (2*E*,5*R*)-5-benzyloxy-2-hexenoate (14). To a stirred solution of oxalyl chloride (1.10 ml, 12.5 mmol) in CH_2Cl_2 (50 ml) was added dropwise dimethyl sulfoxide (1.20 ml, 16.6 mmol) at −78°C under argon atomsphere. After 5 min, to this solution was added dropwise a solution of **13** (1.50 g, 8.33 mmol) in dry CH_2Cl_2 (15 ml) at −78°C. The mixture was stirred for 30 min at the same temperature. After the addition of triethylamine (5.80 ml, 41.5 mmol), the temperature was gradually allowed to warm to room temperature to give a crude aldehyde which was used for the next Wittig reaction in one-pot. To the mixture containing a crude aldehyde was added (methoxycarbonylmethylene)triphenylphosphorane (13.8 g, 41.5 mmol) at room temperature and the mixture was stirred overnight. Hexane (60 ml) was added to the reaction mixture and the resulting insoluble materials were filtered off. The filtrate was diluted with EtOAc (100 ml), washed with 1 M HCl (50 ml) and brine (50 ml), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel 100 g, hexane:EtOAc=15:1) to give **14** (1.50 g, 77%) as a colorless oil: $[\alpha]_D^{25}-4.1°$(*c* 6.1, $CHCl_3$); IR (film) 2972, 1724, 1658, 1436, 1322, 1272, 1174, 1091, 980, 737 and 697 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ1.14 (3H, d, *J*=6.3 Hz), 2.35 (2H, m), 3.61 (1H, m), 3.64 (3H, s), 4.42 (1H, d, *J*=11.7 Hz), 4.44 (1H, d, *J*=11.7 Hz), 5.80 (1H, dt, *J*=15.7, 1.5 Hz), 6.90 (1H, dt, *J*=15.7, 7.4 Hz), 7.25 (5H, m); ^{13}C NMR (67.8 MHz, $CDCl_3$): 19.7, 39.3, 51.4, 70.5, 73.5, 123.0, 127.5, 127.6, 128.4, 138.5, 145.6, 166.8; EI-MS *m/z* 234 (M^+, 0.11), 216 (0.12), 190 (0.39), 174 (0.78), 158 (0.84), 135 (5.8), 128 (3.5), 105 (1.2), 91 (100); HR-MS calcd. for $C_{14}H_{18}O_3$ (M^+) *m/z* 234.1256, found 234.1237.

4.1.4. (2*E*,5*R*)-5-Benzyloxy-2-hexen-1-ol (15). To a solution of **14** (1.50 g, 6.41 mmol) in dry THF (40 ml) was added dropwise DIBAL-H (20.0 ml, 19.2 mmol, 0.96 M solution in hexane) at −78°C under argon atmosphere. The mixture was gradually allowed to warm to room temperature and stirring was continued overnight. To the reaction mixture cooled to 0°C was added sat. aq. Rochelle salt (15 ml) in three portion. After being stirred for 2 h at room temperature, the mixture was filtered through a Celite pad. The filtrate was dried over anhydrous magnesium sulfate and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel 60 g, hexane:EtOAc=3:1) to give **15** (1.30 g, 98%) as a colorless oil: $[\alpha]_D^{25}-12.0°$(*c* 2.4, $CHCl_3$); IR (film) 3389, 3031, 2970, 2866, 1670, 1496, 1454, 1375, 1342, 1206, 1090, 972, 923, 737 and 697 cm^{-1}; ^{1}H NMR (270 MHz,

$CDCl_3$) δ1.13 (3H, d, *J*=6.1 Hz), 1.68 (1H, br. s, OH), 2.24 (2H, m), 3.50 (1H, m), 4.03 (2H, br. s), 4.44 (1H, d, *J*=11.8 Hz), 4.46 (1H, d, *J*=11.8 Hz), 5.64 (2H, m), 7.27 (5H, m); ^{13}C NMR (67.8 MHz, $CDCl_3$): 19.5, 39.1, 63.7, 70.3, 74.4, 127.4, 127.6, 128.3, 129.0, 131.4, 138.8; EI-MS *m/z* 206 (M^+, 1.2), 188 (1.7), 135 (20.4), 91 (100); HR-MS calcd. for $C_{13}H_{18}O_2$ (M^+) *m/z* 206.1307, found 206.1344.

4.1.5. (2*E*,5*R*)-5-Benzyloxy-1-bromo-2-hexene (16). To a stirred solution of **15** (1.25 g, 6.10 mmol) in CH_2Cl_2 (40 ml) was added triphenylphosphine (2.40 g, 9.15 mmol) and carbon tetrabromide (3.03 g, 9.15 mmol) at 4°C. After being stirred for 30 min at room temperature, the reaction mixture was concentrated under reduced pressure. The residue was purified by column chromatography (silica gel 50 g, hexane:EtOAc=30:1) to give **16** (1.53 g, 93%) as a colorless oil: $[\alpha]_D^{25}-8.7°$(*c* 9.8, $CHCl_3$); IR (film) 2969, 1453, 1375, 1203, 1092, 966, 772, 735 and 697 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ1.10 (3H, d, *J*=6.1 Hz), 2.24 (2H, m), 3.50 (1H, m), 3.85 (2H, d, *J*=6.1 Hz), 4.44 (1H, d, *J*=11.7 Hz), 4.46 (1H, d, *J*=11.7 Hz), 5.69 (2H, m), 7.26 (5H, m); ^{13}C NMR (67.8 MHz, $CDCl_3$): 19.5, 33.2, 39.1, 70.4, 74.2, 127.5, 127.6, 128.3, 128.6, 132.5, 138.7; FD–MS *m/z* 270 (M^+ for ^{81}Br, 0.90), 268 (M^+ for ^{79}Br, 0.94); EI-MS *m/z* 189 (M^+-Br, 3.8), 172 (1.7), 145 (2.6), 135 (16.2), 91 (100); HR-MS calcd. for $C_{13}H_{17}O$ (M^+-Br) *m/z* 189.1280, found 189.1298.

4.1.6. (3′*E*,6′*R*)-2,4-Dimethoxy-6-(6′-benzyloxy-hept-3′-enyl)benzoic acid (17). To a solution of diisopropylamine (2.97 ml, 21.0 mmol) in dry THF (25 ml) was added dropwise *n*-butyllithium (14.0 ml, 21.0 mmol, 1.50 M solution in hexane) at −78°C under argon atmosphere. The reaction mixture was slowly warmed up to 0°C and stirred for 30 min to give a LDA solution (0.50 M). To a solution of **10** (1.12 g, 5.69 mmol) in dry THF (15 ml) was added dropwise the above LDA solution (23.8 ml, 11.9 mmol) at −78°C under argon atmosphere. The reaction mixture was stirred in the range from −15 to −10°C for 3 h then cooled to −30°C. To the resulting dianion solution, bromide **16** (1.53 g, 5.69 mmol) in 10 ml THF was added. The stirring was continued for 12 h and the temperature was gradually increased from −30 to 20°C. The reaction mixture was poured into saturated aq. NH_4Cl solution (100 ml) and subsequently acidified by 2 M HCl to pH 2. After evaporation of the organic solvent, the aq. layer was extracted with EtOAc (100 ml×3). The combined EtOAc layers were concentrated, and the residue was subjected to column chromatography (silica gel 50 g, $CHCl_3$: EtOAc:AcOH=12:1:0.02) to give **17** (1.14 g, 52%) as a colorless oil: $[\alpha]_D^{25}-7.3°$(*c* 3.3, $CHCl_3$); IR (film) 3400–2600 (br.), 2934, 1715, 1603, 1455, 1277, 1203, 1161 and 772 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 1.05 (3H, d, *J*=6.1 Hz), 2.08 (2H, m), 2.25 (2H, m), 2.88 (2H, t, *J*=7.6 Hz), 3.43 (1H, m), 3.74 (3H, s), 3.80 (3H, s), 4.43 (1H, d, *J*=12.2 Hz), 4.45 (1H, d, *J*=12.2 Hz), 5.30 (1H, dt, *J*=15.2, 8.3 Hz), 5.45 (1H, dt, *J*=15.2, 8.3 Hz), 6.26 (1H, d, *J*=2.2 Hz), 6.34 (1H, d, *J*=2.2 Hz), 7.25 (5H, m), the ^1H signal of COOH could not be observed clearly due to broadening; ^{13}C NMR (67.8 MHz, $CDCl_3$): 19.2, 34.4, 34.8, 39.5, 55.4, 56.3, 70.1, 74.5, 96.6, 108.1, 113.2, 127.1, 127.4, 127.6, 128.2, 131.9, 138.7, 146.6, 158.9, 162.1, 167.9; EI-MS *m/z* 384 (M^+, 0.45), 383 (M^+-H, 0.45), 366 (M^+-18, 0.99), 252 (14), 236 (8.9), 219 (7.1), 178 (7.6), 105 (18), 91 (35), 77 (23.5); HR-MS calcd. for $C_{23}H_{28}O_5$ (M^+) *m/z* 384.1937, found 384.1937.

4.1.7. (*R*)-2,4-Dimethoxy-6-(6-hydroxyheptyl)benzoic acid (6). A mixture of **17** (224 mg, 0.58 mmol) and palladium hydroxide on carbon (71.6 mg) in ethanol (6.0 ml) was stirred under hydrogen atmosphere for 3 h at room temperature. The reaction mixture was filtered through a Celite pad, and the filtrate was concentrated under reduced pressure. Purification of the crude product with column chromatography (silica gel 50 g, $CHCl_3$: EtOAc:AcOH=1:1:0.01) gave **6** (155 mg, 90%) as a colorless oil: $[\alpha]_D^{25}-6.8°$(*c* 4.5, $CHCl_3$); IR (film) 3400–2600 (br.), 2935, 1699, 1604, 1463, 1423, 1324, 1203, 1162, 1114, 1047, 945, 833, 758 and 601 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 1.16 (3H, d, *J*=6.1 Hz), 1.40 (6H, m), 1.60 (2H, m), 2.87 (2H, t, *J*=7.8 Hz), 3.57 (1H, br. s, OH), 3.77 (1H, m), 3.82 (3H, s), 3.88 (3H, s), 6.35 (1H, d, *J*=2.2 Hz), 6.40 (1H, d, *J*=2.2 Hz), the ^1H signal of COOH could not be observed clearly due to broadening; ^{13}C NMR (67.8 MHz, $CDCl_3$): 23.3, 25.0, 29.2, 31.1, 34.6, 38.9, 55.4, 56.3, 68.3, 96.4, 107.6, 113.3, 146.9, 159, 162.0, 168.7; EI-MS *m/z* 296 (M^+, 34.6), 278 (M^+-18, 14.8), 263 (26.5), 261 (12.2), 233 (5.2), 207 (30.2), 196 (100), 191 (41.4), 152 (54.1), 151 (20.0), 137 (14.8), 120 (14.2), 91 (9.1), 77 (8.6), 45 (16.4), 44 (15.2); HR-MS calcd. for $C_{16}H_{24}O_5$ (M^+) *m/z* 296.1624, found 296.1613.

4.1.8. Ethyl (*R*)-2,4-dimethoxy-6-(6-hydroxyheptyl)benzoate (4). A mixture of **6** (20.0 mg, 0.07 mmol), dry K_2CO_3 (28.2 mg, 0.20 mmol) and iodoethane (21.8 μl, 0.27 mmol) in dry acetone (1.0 ml) was stirred at room temperature overnight. The reaction mixture was concentrated and subjected to column chromatography (silica gel 5 g, hexane: EtOAc=3:2) to give **4** (16.5 mg, 75%) as a colorless oil: $[\alpha]_D^{25}-6.2°$(*c* 1.5, $CHCl_3$); IR (film) 3419, 2934, 1723, 1605, 1436, 1268, 1203, 1159 and 1097 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 1.15 (3H, d, *J*=6.2 Hz), 1.32 (3H, t, *J*=7.1 Hz), 1.24–1.44 (7H, m), 1.58 (2H, m), 2.54 (2H, t, *J*=7.6 Hz), 3.70 (1H, m), 3.77 (3H, s), 3.78 (3H, s), 4.34 (2H, q, *J*=7.3 Hz), 6.30 (2H, s); ^{13}C NMR (67.8 MHz, CD_3COCD_3): 14.5, 24.0, 26.3, 29.2, 32.1, 34.3, 40.1, 55.2, 56.4, 67.1, 67.8, 97.0, 106.9, 117.8, 143.1, 158.8, 162.2, 168.4; EI-MS *m/z* 324 (M^+, 48.7), 279 (32), 263 (33.4), 251 (23.7), 224 (100), 211 (27.1), 191 (46), 165 (13), 151 (50.9), 91 (9), 77 (8.3), 45 (23.9), 43 (8.6); HR-MS calcd. for $C_{18}H_{28}O_5$ (M^+) *m/z* 324.1937, found 324.1950.

4.1.9. Isobutyl (*R*)-2,4-dimethoxy-6-(6-hydroxyheptyl)-benzoate (5). A mixture of **6** (10.0 mg, 0.03 mmol), dry K_2CO_3 (14.0 mg, 0.10 mmol) and isobutyl iodide (3.90 μl, 0.03 mmol) in DMF (1.0 ml) was stirred at room temperature overnight. The reaction mixture was partitioned between water (10 ml) and EtOAc (3 ml) and the aqueous layer was further extracted with EtOAc (5 ml×2). The combined extracts were washed with water and brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel 5 g, hexane:EtOAc=2:1) to give **5** (8.40 mg, 70%) as a colorless oil: $[\alpha]_D^{25}-15.9°$(*c* 1.0, $CHCl_3$); IR (film) 3429, 2931, 2857, 1722, 1604, 1463, 1422, 1374, 1265, 1203, 1159, 1098, 1048, 946 and 831 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.97 (6H, d, J=6.6 Hz), 1.15 (3H, d, J=6.3 Hz), 1.32–1.41 (7H, m), 1.55 (2H, m), 2.03 (1H, m), 2.55 (2H, t, J=7.6 Hz), 3.75 (1H, m), 3.77 (3H, s), 3.78 (3H, s), 4.05 (2H, d, J=6.6 Hz), 6.30 (2H, s); ^{13}C NMR (67.8 MHz, $CDCl_3$): 19.2, 23.5, 25.5, 27.8, 29.7, 31.2, 33.8, 39.2, 55.3, 55.9, 68.1, 71.3, 96.1, 105.7, 116.8, 142.7, 158.0, 161.2, 168.6; EI-MS *m/z* 352 (M^+, 66.4), 279 (76), 252 (100), 251 (52), 196 (61.4), 191 (55.7), 152 (63), 151 (38.6), 99 (14.5), 91 (9.6), 85 (18), 77 (6.8), 57 (62), 43 (37.7); HR-MS calcd. for $C_{20}H_{32}O_5$ (M^+) *m/z* 352.2251, found 352.2267.

4.1.10. (*R*)-2,4-Dimethoxy-7-methyl-7,8,9,10,11,12-hexahydro-6-oxa-benzocyclodecen-5-one (18). To a solution of **6** (92.0 mg, 0.31 mmol) in benzene (2.8 ml) was added di-(2-pyridyl) disulfide (97.0 mg, 0.44 mmol) and triphenylphosphine (115 mg, 0.44 mmol). After stirring for 1 h, dry acetonitrile (25 ml) was added. The resulting yellow solution was added with an automatic syringe over 5 h to a boiling solution of silver perchlorate (322 mg, 1.55 mmol) in acetonitrile (28 ml). After heating the mixture at 160°C for 30 min, the solvent was evaporated. The residue was dissolved in EtOAc, and the insoluble materials were filtered off. The filtrate was concentrated, and the residue was subjected to column chromatography (silica gel 75 g, hexane:EtOAc=10:1) to give **18** (43.2 mg, 50%) as colorless crystals: $[\alpha]_D^{25}+38.7°$(c 2.3, $CHCl_3$); mp 138–140°C; IR (film) 2930, 1719, 1605, 1465, 1330, 1261, 1204, 1159, 1095, 1046, 962, 843 and 730 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.32 (3H, d, J=6.5 Hz), 1.42 (4H, m), 1.60–1.77 (4H, m), 2.54 (2H, t, J=7.2 Hz), 3.79 (3H, s), 3.80 (3H, s), 5.17 (1H, m), 6.31 (2H, s); ^{13}C NMR (67.8 MHz, $CDCl_3$): 20.7, 21.8, 28.8, 30.7, 34.1, 34.9, 55.3, 55.8, 74.0, 96.2, 106.3, 117.2, 143.4, 152.0, 157.7, 161.3; EI-MS *m/z* 278 (M^+, 76.1), 250 (14.8), 234 (14.6), 205 (23.6), 191 (75.2), 165 (32.1), 152 (100), 151 (28.6), 127 (12.8), 99 (15.3), 91 (17), 83 (23.2), 77 (13.1), 57 (50), 40 (51.1); HR-MS calcd. for $C_{16}H_{22}O_4$ (M^+) *m/z* 278.1518, found 278.1489.

4.1.11. (*R*)-2,4-Dihydroxy-7-methyl-7,8,9,10,11,12-hexahydro-6-oxa-benzocyclodecen-5-one (19). To a solution of **18** (156 mg, 0.56 mmol) in methylene chloride (10 ml) under argon atmosphere at 0°C, was added a cooled 1.26 M solution of BBr_3 in methylene chloride (7.40 ml, 8.40 mmol). The reaction mixture was stirred for 30 min between 0°C and room temperature. After addition of saturated aqueous $NaHCO_3$ (10 ml), the mixture was acidified with 3 M HCl, and then extracted with $CHCl_3$. The combined extracts were dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified with column chromatography (silica gel 100 g, hexane:EtOAc:AcOH=7:1:0.02) to give **19** (35.0 mg, 25%) as a white powder: $[\alpha]_D^{25}+52.0°$(c 1.0, $CHCl_3$); mp 94–96°C; IR (film) 3357, 2938, 1653, 1457, 1362, 1312, 1261, 1156, 1005, 772 and 669 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.36 (3H, d, J=6.2 Hz), 1.43 (3H, m), 1.64–1.84 (5H, m), 2.30 (1H, m), 3.30 (1H, t, J=9.9 Hz), 5.07 (1H, s, OH), 5.28 (1H, m), 6.21 (1H, d, J=2.3 Hz), 6.24 (1H, d, J=2.3 Hz), 11.5 (1H, s, OH); ^{13}C NMR (67.8 MHz, $CDCl_3$): 19.4, 19.8, 28.0, 29.0, 32.7, 34.8, 71.7, 101.3, 105.8, 110.8, 149.5, 160.1, 165.2, 170.5; EI-MS *m/z* 250 (M^+, 26.4), 232 (7.0), 203 (5.1), 182 (10.8), 168 (59.4), 71 (14.3), 57 (19.1), 55 (13.7), 43 (13.1); HR-MS calcd. for $C_{14}H_{18}O_4$ (M^+) *m/z* 250.1205, found 250.1189.

4.1.12. (*R*)-2,4-Dibenzyloxy-7-methyl-7,8,9,10,11,12-hexahydro-6-oxa-benzocyclodecen-5-one (20). A mixture of **19** (33.0 mg, 0.13 mmol), benzyl chloride (52.0 μl, 0.45 mmol) and anhydrous potassium carbonate (82.0 mg, 0.59 mmol) in dimethyl sulfoxide (4.0 ml) was stirred at 100°C for 2 h. The reaction mixture was cooled to room temperature, diluted with water (2 ml), and extracted three times with $CHCl_3$. The combined organic layers were washed with brine, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure. The residue was purified with column chromatography (silica gel 40 g, hexane:EtOAc:AcOH=10:1:0.01) to give **20** (49.9 mg, 88%) as an oil. Crystallization from ether/hexane gave pure **20** as a white powder: $[\alpha]_D^{25}+8.6°$(c 1.0, $CHCl_3$); mp 118–119°C; IR (film) 2933, 1717, 1653, 1603, 1498, 1456, 1375, 1266, 1159, 1041, 736, 696 and 669 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.30 (3H, d, J=6.2 Hz), 1.42 (3H, m), 1.53 (1H, m), 1.72 (4H, m), 2.60 (2H, m), 5.00 (2H, s), 5.05 (2H, s), 5.25 (1H, m), 6.42 (2H, s), 7.36–7.37 (10H, m); ^{13}C NMR (67.8 MHz, $CDCl_3$): 20.8, 21.9, 26.2, 29.1, 30.4, 34.3, 70.1, 70.3, 73.9, 98.5, 107.9, 118.7, 126.8, 127.5, 127.7, 128.1, 128.4, 128.6, 136.6, 136.8, 143.0, 156.4, 160.3, 168.2; EI-MS *m/z* 430 (M^+, 23.1), 386 (1.9), 355 (3.59), 321 (3.89), 279 (2.35), 253 (1.37), 221 (3.25), 181 (14.1), 149 (11.3), 147 (2.77), 91 (100), 57 (6.38), 43 (4.17); HR-MS calcd. for $C_{28}H_{30}O_4$ (M^+) *m/z* 430.2145, found 430.2156.

4.1.13. (*R*)-2,4-Dibenzyloxy-6-(6-hydroxyheptyl)benzoic acid (21). A solution of **20** (15.2 mg, 0.04 mmol) in 40% sodium hydroxide (1.0 ml) and dimethyl sulfoxide (3.0 ml) was heated at reflux overnight. The cooled solution was acidified with concentrated HCl. After the addition of water (3 ml), the mixture was extracted with EtOAc (10 ml×3). The combined extracts were washed with water, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure. Purification of the crude product with preparative TLC (hexane:EtOAc:AcOH=15:10:0.1, double development) provided **21** as a white solid (10.3 mg, 65%). $[\alpha]_D^{25}+8.7°$(c 1.2, $CHCl_3$); mp 130–131°;C IR (film) 3421 (br.), 2927, 1699, 1602, 1541, 1457, 1376, 1312, 1162, 1028, and 802 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.15 (3H, d, J=6.0 Hz), 1.24–1.41 (6H, m), 1.57–1.62 (2H, m), 2.81 (2H, t, J=7.2 Hz), 3.79 (1H, m), 4.20 (1H, br. s, OH), 5.02 (2H, s), 5.11 (2H, s), 6.48 (2H, br. s), 7.30–7.67 (10H, m), the ^{1}H signal of COOH could not be observed clearly due to broadening; ^{13}C NMR (67.8 MHz, $CDCl_3$): 23.5, 25.1, 29.3, 31.1, 34.8, 38.9, 68.2, 70.2, 71.6, 98.7, 109.5, 113.2, 127.4, 127.5, 128.3, 128.5, 128.7, 128.8, 135.7, 136.5, 147.8, 158.3, 161.1, 167.5; EI-MS *m/z* 448 (M^+, 3.7), 430 (M^+-18, 1.05), 415 (1.52), 404 (0.93), 357 (0.77), 339 (21.03), 321 (6.88), 258 (4.09), 251 (1.88), 181 (6.79), 180 (3.02), 149 (1.90), 91 (100), 44 (2.91); HR-MS calcd. for $C_{28}H_{32}O_5$ (M^+) *m/z* 448.2251, found 448.2296.

4.1.14. (*R*)-2,4-Dihydroxy-6-(6-hydroxyheptyl)benzoic acid (3). A mixture of **21** (10.0 mg, 0.02 mmol) and 5% palladium on carbon (11.5 mg) in ethanol (2.0 ml) was vigorously stirred for 4 h at room temperature under hydrogen atmosphere. The catalyst was filtered through a Celite pad and the filtrate was concentrated under reduced pressure. The residue was purified with column chromatography (silica gel 5 g, hexane:EtOAc:AcOH=1:1:0.02) to give **3** (5.10 mg, 90%) as a powder. $[\alpha]_D^{25}-103.6°$(*c* 1.0, MeOH); mp 98–101°C; IR (film) 3400–2600 (br.), 2925, 2854, 1732, 1601, 1464, 1260, 1091 and 802 cm^{-1}; ^{1}H NMR (270 MHz, CD_3OD) δ 1.04 (3H, d, *J*=6.1 Hz), 1.20–1.40 (6H, m), 1.40–1.60 (2H, m), 2.87 (2H, t, *J*=7.2 Hz), 3.55 (1H, m), 6.03 (2H, d, *J*=6.1 Hz); ^{13}C NMR (67.8 MHz, CD_3OD): 23.4, 26.8, 31.0, 33.1, 37.0, 40.2, 68.6, 101.4, 110.9 129.8, 133.8, 149.8, 151.5, 161.9; FD–MS *m/z* 269 (M^+ + H, 28.1), 291 (M^+ + Na, 92.6); FAB *m/z* 267 (M^+−H), 291 (M^++Na), 313 (M^++2Na); FAB–HR-MS calcd. for $C_{14}H_{19}O_5$ (M^+−H) *m/z* 267.1233, found 267.1223.

4.1.15. Ethyl (*R*)-2,4-dibenzyloxy-6-(6-hydroxyheptyl)-benzoate (22). A mixture of **21** (14.8 mg, 0.03 mmol), dry K_2CO_3 (13.8 mg, 0.10 mmol) and iodoethane (2.70 μl, 0.03 mmol) in DMF (1.0 ml) was stirred at room temperature overnight. The reaction mixture was partitioned between water (10 ml) and EtOAc (3 ml), and the aqueous layer was further extracted with EtOAc (5 ml×3). The combined organic layers were washed with water and brine, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure. The residue was subjected to column chromatography (silica gel 5 g, hexane:EtOAc=2:1) to give **22** (13.8 mg, 87%) as a colorless oil: $[\alpha]_D^{25}+15.0°$(*c* 2.3, $CHCl_3$); IR (film) 3418, 2930, 2858, 1722, 1603, 1498, 1455, 1263, 1161, 1096, 1028, 804, 736 and 697 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.15 (3H, d, *J*=6.1 Hz), 1.27 (3H, t, *J*=7.2 Hz), 1.25–1.40 (5H, m), 1.52–1.58 (4H, m), 2.60 (2H, t, *J*=7.4 Hz), 3.76 (1H, m), 4.30 (2H, q, *J*=7.1 Hz), 5.01 (4H, s), 6.41 (2H, d, *J*=1.8 Hz), 7.27–7.37 (10H, m); ^{13}C NMR (67.8 MHz, $CDCl_3$): 14.2, 23.5, 25.5, 29.4, 31.0, 33.7, 39.2, 61.0, 68.1, 70.1, 70.4, 98.4, 107.3, 117.4, 127.1, 127.5, 127.8, 128.1, 128.4, 128.6, 136.6, 136.7, 142.8, 157.0, 160.3, 168.3; EI-MS *m/z* 476 (M^+, 7.40), 431 (2.79), 385 (4.77), 339 (17.67), 321 (6.11), 286 (2.75), 181 (13.41), 180 (6.94), 91 (100); HR-MS calcd. for $C_{30}H_{36}O_5$ (M^+) *m/z* 476.2564, found 476.2519.

4.1.16. Isobutyl (*R*)-2,4-dibenzyloxy-6-(6-hydroxyheptyl)-benzoate (23). A mixture of **21** (14.8 mg, 0.03 mmol), dry K_2CO_3 (13.8 mg, 0.10 mmol) and isobutyl iodide (3.80 μl, 0.03 mmol) in DMF (1.5 ml) was stirred at room temperature overnight. The reaction mixture was partitioned between water (10 ml) and EtOAc (3 ml) and the aqueous layer was further extracted with EtOAc (5 ml×3). The combined organic layers were washed with water and brine, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure. The residue was subjected to column chromatography (silica gel 5 g, hexane:EtOAc=3:1) to give **23** (15.8 mg, 95%) as a colorless oil: $[\alpha]_D^{25}+10.4°$(*c* 2.0, $CHCl_3$); IR (film) 3384, 2928, 1723, 1603, 1455, 1376, 1262, 1160, 1038, 803, 736 and 697 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.90 (6H, d, *J*=6.7 Hz), 1.16 (3H, d, *J*=6.3 Hz), 1.22–1.42 (7H, m), 1.58 (2H, m), 1.96 (1H, m), 2.56 (2H, t, *J*=7.6), 3.76 (1H, m), 4.03 (2H, d, *J*=6.6 Hz), 5.00 (2H, s), 5.02 (2H, s), 6.41 (2H, br. s), 7.27–7.37 (10H, m); ^{13}C NMR (67.8 MHz, $CDCl_3$): 19.2, 23.5, 25.5, 27.8, 29.4, 31.1, 33.7, 39.2, 68.0, 70.1, 70.4, 71.3, 98.4, 107.3, 117.6, 127.1, 127.5, 127.8, 128.1, 128.4, 128.6, 136.6, 136.7, 142.7, 157.0, 160.3, 168.5; EI-MS *m/z* 504 (M^+, 7.44), 431 (4.41), 413 (4.71), 339 (26.88), 321 (5.90), 181 (12.02), 180 (6.69), 91 (100); HR-MS calcd. for $C_{32}H_{40}O_5$ (M^+) *m/z* 504.2877, found 504.2898.

4.1.17. Ethyl (*R*)-2,4-dihydroxy-6-(6-hydroxyheptyl)-benzoate (1). A mixture of **22** (10.0 mg, 0.02 mmol) and palladium hydroxide on carbon (2.60 mg) in ethanol (2.0 ml) was vigorous stirred for 3 h at room temperature under hydrogen atmosphere. The catalyst was filtered through a Celite pad and the filtrate was concentrated under reduced pressure. The residue was purified with column chromatography (silica gel 5 g, MeOH:$CHCl_3$=4:96) to give **1** (5.50 mg, 87%) as a colorless oil. $[\alpha]_D^{25}$ $-10.3°$(*c* 1.6, MeOH), lit.[4] $[\alpha]_D^{25}-9.1°$(*c* 0.9, MeOH); EI-MS *m/z* 296 (M^+, 47.6), 249 (14.2), 232 (32.2), 203 (9.9), 196 (100), 168 (52.6), 150 (80.7), 123 (18.6), 121 (11.9), 81 (5.9), 69 (14.4), 45 (14.8); HR-MS calcd. for $C_{16}H_{24}O_5$ (M^+) *m/z* 296.1624, found 296.1583. Other spectral data were completely identical with those of natural **1**.

4.1.18. Isobutyl (*R*)-2,4-dihydroxy-6-(6-hydroxyheptyl)-benzoate (2). A mixture of **23** (14.0 mg, 0.02 mmol) and palladium hydroxide on carbon (3.40 mg) in ethanol (3.0 ml) was vigorous stirred for 5 h at room temperature under hydrogen atmosphere. The catalyst was filtered through a Celite pad and the filtrate was concentrated under reduced pressure. The residue was purified with column chromatography (silica gel 5 g, MeOH:$CHCl_3$=4:96) to give **2** (6.81 mg, 75%) as a colorless oil. $[\alpha]_D^{25}-22.0°$(*c* 1.0, $CHCl_3$), lit.[4] $[\alpha]_D^{25}-15.5°$(*c* 0.6, $CHCl_3$); EI-MS *m/z* 324 (M^+, 35.7), 250 (13.9), 224 (50.7), 211 (28.2), 177 (10.0), 168 (100), 150 (52.3), 124 (11.4), 69 (8.8), 57 (14.9), 41 (14.2); HR-MS calcd. for $C_{18}H_{28}O_5$ (M^+) *m/z* 324.1937, found 324.1914. Other spectral data were completely identical with those of natural **2**.

Acknowledgements

We are grateful to Mr K. Watanabe and Dr E. Fukushi in our faculty for measuring the MS spectra.

References

1. Nakamori, K.; Matsuura, H.; Yoshihara, T.; Ichihara, A.; Koda, Y. *Phytochemistry* **1994**, *35*, 835–839.
2. Matsuura, H.; Nakamori, K.; Omer, E. A.; Hatakeyama, C.; Yoshihara, T.; Ichihara, A. *Phytochemistry* **1998**, *49*, 579–584.
3. Yang, Q.; Asai, M.; Matsuura, H.; Yoshihara, T. *Phytochemistry* **2000**, *54*, 489–494.
4. Yang, Q.; Asai, M.; Yoshihara, T. *Z. für Naturforschung* **2000**, *55c*, 546–551.
5. Ohtani, I.; Kusumi, T.; Kashman, Y.; Kakisawa, H. *J. Am. Chem. Soc.* **1991**, *113*, 4092–4096.
6. Aldridge, D. C.; Galt, S.; Giles, D.; Turner, W. B. *J. Chem. Soc. (C).* **1971**, 1623–1627.

7. Braun, M.; Mahler, U.; Houben, S. *Liebigs Ann. Chem.* **1990**, 513–517.
8. Bhatt, M. V.; Kulkarni, S. U. *Synthesis* **1983**, 249–282.
9. Hitchcock, S. A.; Pattenden, G. *J. Chem. Soc., Perkin Trans. 1* **1992**, 1323–1328.
10. Birch, A. J.; Mani, N. S.; Rao, G. S. R. S. *J. Chem. Soc., Perkin Trans. 1* **1990**, 1423–1427.
11. Taub, D.; Girotra, N. N.; Hoffsommer, R. D.; Kuo, C. H.; Slates, H. L.; Weber, S.; Wendler, N. L. *Tetrahedron* **1968**, *24*, 2443–2461.
12. Jung, M. E.; Lyster, M. A. *J. Org. Chem.* **1977**, *42*, 3761–3763.
13. Node, M.; Nishide, K.; Fuji, K.; Fujita, E. *J. Org. Chem.* **1980**, *45*, 4275–4277.
14. Solladié, G.; Rubio, A.; Carreño, M. C.; Ruano, J. L. G. *Tetrahedron: Asymmetry* **1990**, *1*, 187–198.
15. Jones, G. B.; Huber, R. S.; Chapman, B. J. *Tetrahedron: Asymmetry* **1997**, *8*, 1797–1809.
16. Peters, A. C.; Hurd, N. R. United States Patent, 3,997,568.