[Chem. Pharm. Bull. 36(9)3632—3637(1988)]

Syntheses of Unsaturated Trihydroxy C-18 Fatty Acids Isolated from Rice Plants Suffering from Rice Blast Disease

HIROSHI SUEMUNE, TETSUJI HARABE, and KIYOSHI SAKAI*

Faculty of Pharmaceutical Sciences, Kyushu University, Fukuoka 812, Japan

(Received February 24, 1988)

Two trihydroxy unsaturated C-18 fatty acids [(9*S*,12*S*,13*S*)-trihydroxyoctadeca-10*E*,15*Z*-dienoic acid (methyl ester) and (9*S*,12*S*,13*S*)-trihydroxy-10*E*-octadecenoic acid (methyl ester)] isolated from rice plants as agents with activity against blast disease were synthesized from (+)-dimethyl tartrate.

Keywords——methyl (9*S*,12*S*,13*S*)-trihydroxyoctadeca-10*E*,15*Z*-dienoate; methyl (9*S*,12*S*,13*S*)-trihydroxy-10*E*-octadecenoate; rice blast disease; fetal calf aorta; (+)-dimethyl tartrate; Wittig–Horner reaction

Unsaturated fatty acids are well known to possess a wide spectrum of biological activities in not only animals,[1] but also plants.[2] In particular, unsaturated C-18 fatty acids such as 9, 12, 13-trihydroxy-10-octadecenoic acid have attracted considerable attention. For example, linoleic acid (18:2) could be converted to monohydroxy unsaturated fatty acids (*e.g.*, 9-hydroxy-10,12-octadecadienoic acid and 13-hydroxy-9,11-octadecadienoic acid) and trihydroxy unsaturated fatty acids (9, 10, 11-trihydroxy-12-octadecenoic acid, 9, 10, 13-trihydroxy-11-octadecenoic acid and 9, 12, 13-trihydroxy-10-octadecenoic acid (**1a**)) by particular fractions from fetal calf aorta.[3] However, the physiological significance of these oxygenated metabolites has not yet been investigated, because of the low natural abundance. Kato *et al.* isolated a monohydroxy unsaturated C-18 fatty acid (coriolic acid)[4] and two trihydroxy unsaturated C-18 fatty acids (9*S*, 12*S*, 13*S*-trihydroxyoctadeca-10*E*, 15*Z*-dienoic acid (**1b**) and 9*S*, 12*S*, 13*S*-trihydroxy-10*E*-octadecenoic acid (**1a**))[5,6] from a resistant cultivar of rice plant, and demonstrated their activity against rice blast disease.

To evaluate correctly the biological activities of such compounds in animals and plants, we have undertaken the synthesis of **1**. Previously, we succeeded in the synthesis[7] of (*S*)-13-hydroxy-9*Z*,11*E*-octadecadienoic acid using microbial reduction. Now, we wish to describe the synthesis of natural **1a**, **b**, in addition to the unnatural forms, **1c** and **2a**—**c**. The designed

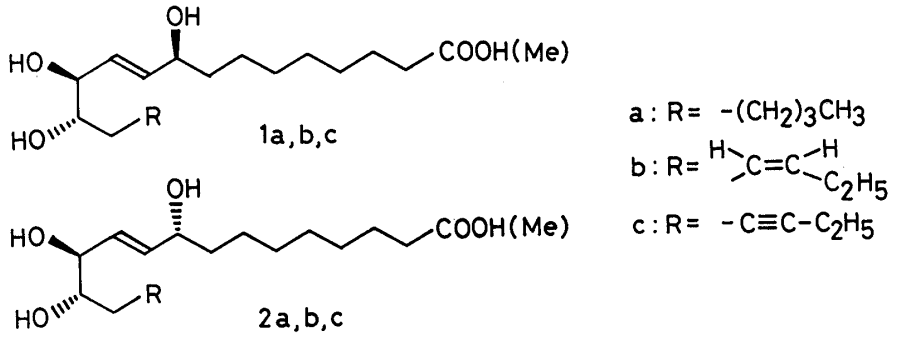


Chart 1

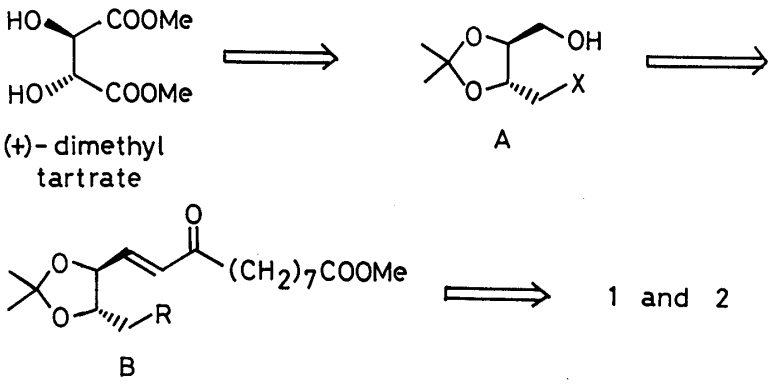
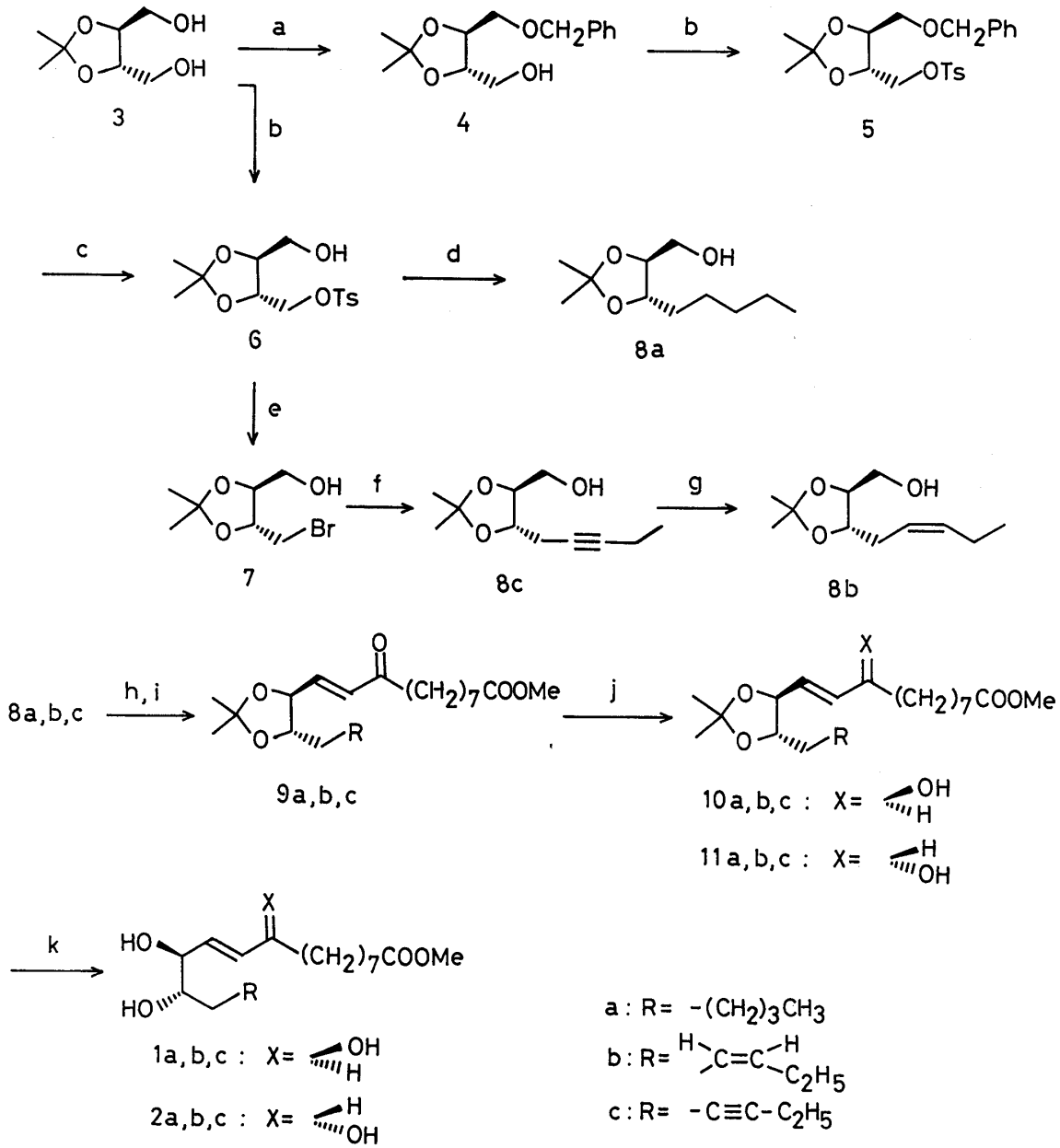


Chart 2



a) $PhCH_2Cl$, NaOH. b) *p*-TsCl, pyridine. c) H_2/Pd–C. d) *n*-BuLi, CuI. e) LiBr. f) $LiC{\equiv}CEt$. g) H_2/Lindlar cat. h) Collins oxid. i) $(MeO)_2P(O)CH_2CO(CH_2)_7COOMe$, LiCl, DBU. j) $NaBH_4$. k) *p*-TsOH, MeOH.

Chart 3

sequence starts with (+)-dimethyl tartrate (Chart 2); the *trans* double bond (10*E*) may be introduced by Wittig–Horner reaction of the corresponding aldehyde with dimethyl 9-methoxycarbonyl-2-oxononylphosphonate.[7] Introduction of an R-substituent may be accomplished by replacing the halide in A with alkyl or alkynyl lithium. Each step should proceed with retention of the original configuration

The diol (**3**) was easily prepared from dimethyl tartrate through protection of the diol as the acetonide by treatment with 2,2-dimethoxypropane in the presence of *p*-toluenesulfonic acid (*p*-TsOH), and subsequent reduction with $LiAlH_4$. Attempted monotosylation of **3** using *p*-toluenesulfonyl chloride (*p*-TsCl)/pyridine resulted in a poor yield (38%) (Chart 3). Monobenzylation (**4**, 92%) of **3** with benzyl chloride/NaOH/dimethyl sulfoxide (DMSO) followed by tosylation (**5**, 92%) with *p*-TsCl/pyridine and subsequent catalytic hydrogenation (**6**, 93%) with H_2/5% Pd–C/MeOH afforded a better yield than the direct monotosylation. An attempted substitution of the tosyl function in **5** with lithium 1-butylide failed, in accordance with the result observed in the substitution of the ditosylate by Takano *et al.*[8] However, direct substitution of the monotosylate (**6**) with BuLi/CuI gave **8a** in 74% yield. Similarly, the monobromide (**7**) derived from **6** by treatment with LiBr/*N*,*N*-dimethylformamide (DMF) could be converted to the ethylacetylene (**8c**, 90%) by treatment with lithium 1-butylide/tetrahydrofuran (THF)–hexamethylphosphoric triamide (HMPA). Partial reduction of **8c** to the ethylolefin (**8b**, 89%) was accomplished by use of the Lindlar catalyst. Compound **8** was converted to the enone (**9**) in 52—56% yield *via* Collins oxidation followed by Wittig–Horner reaction using dimethyl 9-methoxycarbonyl-2-oxononylphosphonate/LiCl/1,8-diazabicyclo[5.4.0]-7-undecene (DBU)/CH_3CN.[7] Reduction of **9** with $NaBH_4$ afforded a mixture of epimeric alcohols (**10** and **11**), which could be separated to the less polar fraction (**10a**, **11b**, and **11c**) and more polar fraction (**10b**, **10c**, and **11a**) in the ratio of 1 to 1 by preparative thin layer chromatography (TLC). This finding suggests that the protected chiral alcohol had no effect on the enantioselectivity in the reduction of the carbonyl function. Deprotection of **10** and **11** with *p*-TsOH/MeOH afforded **1** and **2**, respectively. The absolute stereochemistry of C-9 in the compounds of the less polar fraction, **10a**, **11b**, and **11c** was determined to be 9*S*, 9*R*, and 9*R* by the exciton chirality method[9] based on the circular dichroism (CD) spectra of the benzoates. Thus, **1** and **2** were determined as 9*S*, 12*S*, and 13*S*,[10] (natural form) and 9*R*, 12*S*, 13*S* (unnatural form), respectively. The biological activities of **1** and **2** are under investigation.

Experimental

Infrared (IR) spectra were measured with a JASCO A-202 spectrometer. Proton nuclear magnetic resonance (^{1}H-NMR) spectra were measured on JEOL JNM-FX-100 and GX-270 spectrometers. Mass spectra (MS) were taken on a JEOL JMS-D 300 spectrometer. Optical rotations were measured on a JASCO DIP-4 polarimeter. For column chromatography, silica gel (Merck, Kieselgel 60, 70—230 mesh) was used. TLC was performed on Silica gel F_{254} plates (Merck). All organic solvent extracts were washed with brine and dried over anhydrous sodium sulfate.

(4*S*,5*S*)-4-Benzyloxymethyl-5-hydroxymethyl-2,2-dimethyl-1,3-dioxolane (4)——The diol (**3**) (3.86 g, 23.8 mmol) in DMSO (10 ml) was added dropwise to a stirred solution of NaOH (1.35 g, 41.7 mmol) in DMSO (10 ml) at room temperature, and the whole was stirred for 1 h, then benzyl chloride (3.62 g, 28.6 mmol) in DMSO (10 ml) was added. After being stirred for 2 h, the reaction mixture was diluted with brine, and extracted with ether. The ether extract was washed and dried. The solvent was removed *in vacuo* to afford an oily residue, which was purified by column chromatography on silica gel. The fraction eluted with 20% AcOEt in hexane (v/v) afforded **4** (5.11 g, 86%) as a colorless oil. $[\alpha]_D^{28}$ +7.57° (c=2.96, $CHCl_3$). IR (neat): 3440, 1450, 1090 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.43 (6H, s, $(CH_3)_2C$), 3.46—3.76 (4H, m, $CH_2O \times 2$), 4.58 (2H, s, OCH_2Ph), 7.33 (5H, s, aromatic-H).

(4*S*,5*S*)-4-Benzyloxymethyl-2,2-dimethyl-5-tosyloxymethyl-1,3-dioxolane (5)——*p*-TsCl (1.0 g, 14.1 mmol) was added portionwise to a stirred solution of **4** (1.02 g, 4.02 mmol) in pyridine (11 ml) under ice-water cooling. After 3 h, the reaction mixture was diluted with H_2O, and extracted with AcOEt. The AcOEt extract was washed, and dried, then removal of the solvent *in vacuo* afforded an oily residue, which was chromatographed on silica gel (15 g). The fraction eluted with 10% AcOEt in hexane (v/v) gave **5** (1.61 g, 98%) as a colorless oil. $[\alpha]_D^{26}$ −9.26° (c=2.50, $CHCl_3$).

IR (neat): 1590, 1500, 1170 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.43 (3H, s, aromatic-CH_3), 3.50—3.70 (2H, m, CH_2OBn), 4.53 (2H, s, OCH_2Ph).

(4*S*,5*S*)-4-Hydroxymethyl-2,2-dimethyl-5-tosyloxymethyl-1,3-dioxolane (6)——A solution of **5** (4.07 g, 10 mmol) in MeOH (150 ml) was hydrogenated in the presence of 5% Pd–C under an H_2 atmosphere at room temperature for 1.5 h. The catalyst was filtered off, and the filtrate was concentrated *in vacuo* to afford an oily residue, which was subjected to column chromatography on silica gel (40 g). The fraction eluted with 25% AcOEt in hexane (v/v) gave **6** (2.68 g, 85%) as a colorless oil. $[\alpha]_D^{28}$ $-10.82°$ ($c=3.40$, $CHCl_3$). IR (neat): 3450, 1595, 1170 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.37 (6H, s, $(CH_3)_2C$), 2.47 (3H, s, aromatic-CH_3), 3.67 (2H, d, $J=5.1$ Hz, CH_2O).

(4*R*,5*S*)-4-Bromomethyl-5-hydroxymethyl-2,2-dimethyl-1,3-dioxolane (7)——A mixture of LiBr (548 mg, 5.2 mmol) and **6** (500 mg, 1.58 mmol) in acetone (5 ml) containing DMF (2 ml) was heated under reflux for 3 h. The reaction mixture was diluted with brine, and extracted with AcOEt. The AcOEt extract was washed, and dried, then concentrated *in vacuo* to leave an oily residue, which was purified by silica-gel column chromatography (15 g). The fraction eluted with 12% AcOEt in hexane (v/v) gave **7** (381 mg, 85%) as an oily residue. $[\alpha]_D^{25}$ $+0.82°$ ($c=4.52$, $CHCl_3$). IR (neat): 3630, 1390, 1160 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.45 (6H, s, $(CH_3)_2C$), 3.50 (2H, d, $J=4.9$ Hz, CH_2O), 3.75—3.85 (2H, m, CH_2Br).

(2*S*,3*S*)-2,3-*O*-Isopropylidenedioxyoctanol (8a)——BuLi (1.5 M in hexane) (118 ml, 177.6 mmol) was added dropwise with stirring to a suspension of CuI (16.8 g, 87.0 mmol) in ether (180 ml) at -30 °C under an N_2 atmosphere. The whole was stirred for 0.5 h, and **6** (4.65 g, 14.7 mmol) in ether (10 ml) was added dropwise at -30 °C, then stirring was continued for 1 h. The reaction mixture was diluted with 10% aqueous NH_4Cl (50 ml), and extracted with ether. The ether extract was washed, and dried, then concentrated *in vacuo* to leave an oily residue, which was purified by column chromatography on silica gel (60 g). The fraction eluted with 15% AcOEt in hexane (v/v) afforded **8a** (2.19 g, 74%) as a colorless oil. $[\alpha]_D^{28}$ $-25.36°$ ($c=2.32$, $CHCl_3$). IR (neat): 3330, 1446, 1365 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.89 (3H, t, $J=7.0$ Hz, CH_3), 1.42 (6H, s, $(CH_3)_2C$), 3.66—3.84 (4H, m, CH_2O, CHO–$\times 2$). MS *m/z*: 187 (M^+-CH_3), 171.

(2*S*,3*S*)-2,3-*O*-Isopropylidenedioxy-5-octyn-1-ol (8c)——BuLi (1.5 M in hexane) (63 ml, 93.8 mmol) was added to a stirred solution of 1-butyne (1 ml) in THF (25 ml) at -78 °C under an N_2 atmosphere. The mixture was stirred for 0.5 h at room temperature, then **7** (3.02 g, 11.9 mmol) in a mixture of THF (5 ml) and HMPA (40 ml) was added dropwise at -20 °C, and the whole was stirred for 3.5 h at 0 °C, and for 4 h at room temperature. The reaction mixture was diluted with 10% aqueous NH_4Cl, and extracted with ether. The ether extract was washed and dried. The solvent was removed *in vacuo* to afford an oily residue, which was subjected to column chromatography on silica gel (50 g). The fraction eluted with 15% AcOEt in hexane (v/v) gave **8c** (2.12 g, 90%) as a colorless oil. $[\alpha]_D^{20}$ $-3.65°$ ($c=3.40$, $CHCl_3$). IR (neat): 3450, 1445, 1375 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.04 (3H, t, $J=7.5$ Hz, CH_3), 1.31 (6H, s, $(CH_3)_2C$), 3.52—3.81 (4H, m, CH_2O, CHO–$\times 2$). MS *m/z*: 198 (M^+), 183, 180.

(5*Z*,2*S*,3*S*)-2,3-*O*-Isopropylidenedioxy-5-octen-1-ol (8b)——A solution of **8c** (630 mg) in hexane (120 ml) containing pyridine (1 ml) was hydrogenated in the presence of Lindlar catalyst at 0 °C under an H_2 atmosphere. Usual work-up afforded an oily residue, which was purified by column chromatography on silica gel (20 g). The fraction eluted with 15% AcOEt in hexane (v/v) afforded **8b** (576 mg, 90%) as a colorless oil. $[\alpha]_D^{20}$ $-16.12°$ ($c=0.67$, $CHCl_3$). IR (neat): 3400, 1440, 1375 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.97 (3H, t, $J=7.4$ Hz, CH_3), 1.41 (6H, s, $(CH_3)_2C$), 5.22—5.65 (2H, m, olefinic-H). MS *m/z*: 200 (M^+), 185, 169.

Methyl (10*E*,12*S*,13*S*)-12,13-*O*-Isopropylidenedioxy-9-oxo-10-octadecenoate (9a), Methyl (10*E*,15*Z*,12*S*,13*S*)-12,13-*O*-Isopropylidenedioxy-9-oxo-10,15-octadecadienoate (9b), and Methyl (10*E*,12*S*,13*S*)-12,13-*O*-Isopropylidenedioxy-9-oxo-10-octadecen-15-ynoate (9c)——**8a** (1.043 g, 5.10 mmol) in CH_2Cl_2 (15 ml) was added to the Collins reagent [prepared from CrO_3 (5.16 g, 51.6 mmol), pyridine (8.2 g, 103.2 mmol), and CH_2Cl_2 (160 ml)] with stirring under ice-water cooling. After 0.5 h, the reaction mixture was diluted with ether (50 ml), and the resulting precipitate was filtered off. The filtrate was successively washed with cold 2% aqueous HCl, 5% aqueous $NaHCO_3$, and brine, then dried. Removal of the solvent *in vacuo* afforded a crude aldehyde (686 mg), which was subjected to the Wittig–Horner reaction without being purified.

The aldehyde in MeCN (2.5 ml) was added to a stirred solution of dimethyl 9-methoxycarbonyl-2-oxononylphosphonate (1.57 g, 5.1 mmol), LiCl (214 mg, 5.1 mmol), and DBU (777 mg, 5.1 mmol) in MeCN (5 ml) at room temperature. After being stirred for 0.5 h, the reaction mixture was diluted with ether (200 ml). The ether layer was successively washed with cold 2% aqueous HCl, 5% aqueous $NaHCO_3$, and brine, then dried. Removal of the solvent *in vacuo* afforded an oily residue, which was purified by column chromatography on silica gel (15 g). The fraction eluted with 10% AcOEt in hexane (v/v) afforded **9a** (1.012 g, 56%) as a colorless oil.

In a similar manner, **9b** and **9c** were obtained in 52% and 54% yields from **8b** and **8c**, respectively.

9a: $[\alpha]_D^{26}$ $-9.76°$ ($c=1.27$, $CHCl_3$). IR (neat): 1730, 1712, 1665 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.89 (3H, t, $J=7.5$ Hz, CH_3), 1.42 (6H, s, $(CH_3)_2C$), 3.65 (3H, s, OCH_3), 6.32 (1H, d, $J=15.9$ Hz, CH=), 6.70 (1H, dd, $J=15.9$, 5.5 Hz, CH=). MS *m/z*: 382 (M^+), 367, 293. **9b**: $[\alpha]_D^{20}$ $-22.35°$ ($c=0.95$, $CHCl_3$). IR (neat): 1735, 1675, 1635 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.97 (3H, t, $J=7.4$ Hz, CH_3), 5.22—5.67 (2H, m, olefinic-H), 6.32 (1H, d, $J=15.9$ Hz, CH=), 6.69 (1H, dd, $J=15.9$, 5.3 Hz, CH=). MS *m/z*: 380 (M^+), 365, 321. **9c**: $[\alpha]_D^{20}$ $-21.03°$ ($c=0.84$, $CHCl_3$). IR (neat): 1735, 1675, 1630 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.00 (3H, t, $J=7.5$ Hz, CH_3), 3.65 (3H, s, OCH_3), 6.37 (1H, d,

J=15.8 Hz, CH=), 6.81 (1H, dd, J=15.8, 5.1 Hz, CH=). MS m/z: 378 (M^+), 363, 311.

Methyl (10*E*,9*R*,12*S*,13*S*)- and (10*E*,9*S*,12*S*,13*S*)-12,13-*O*-Isopropylidenedioxy-9-hydroxy-10-octadecenoate (10a and 11a), Methyl (10*E*,15*Z*,9*R*,12*S*,13*S*)- and (10*E*,15*Z*,9*S*,12*S*,13*S*)-12,13-*O*-Isopropylidenedioxy-9-hydroxy-10,15-octadecadienoate (10 b and 11b), and Methyl (10*E*,9*R*,12*S*,13*S*)- and (10*E*,9*S*,12*S*,13*S*)-12,13-*O*-Isopropylidenedioxy-9-hydroxy-10-octadecen-15-ynoate (10c and 11c)——$NaBH_4$ (7 mg) was added portionwise to a stirred solution of **9a** (65 mg) in MeOH (2 ml). Usual work-up and subsequent preparative TLC afforded **10a** (27 mg, less polar fraction in a solvent system of 15% AcOEt in hexane (v/v)) and **11a** as colorless oils.

In a similar manner, **9b** and **9c** afforded **10b** and **11b**, and **10c** and **11c**, as colorless oils, respectively. **11b** and **11c** were obtained as less polar fractions than **10b** and **10c** (15% AcOEt in hexane (v/v)).

10a: $[\alpha]_D^{25}$ −1.60° (c=1.25, $CHCl_3$). IR ($CHCl_3$): 3590, 1725, 1200 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.89 (3H, t, J=7.4 Hz, CH_3), 1.40 (6H, s, $(CH_3)_2C$), 3.67 (3H, s, OCH_3), 3.56—3.75 (1H, m, C_{13}-H), 3.93—4.13 (2H, m, C_9- and C_{12}-H), 5.72 (1H, dd, J=15.5, 5.7 Hz, CH=), 5.82 (1H, dd, J=15.5, 5.7 Hz, CH=). High-MS for $C_{22}H_{40}O_5$ (M^+): Calcd m/z 384.2873. Found 384.2885.

11a: $[\alpha]_D^{25}$ −9.21° (c=1.52, $CHCl_3$). IR ($CHCl_3$): 3590, 1725, 1200 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.89 (3H, t, J=7.4 Hz, CH_3), 1.40 (6H, s, $(CH_3)_2C$), 3.67 (3H, s, OCH_3), 3.55—3.75 (1H, m, C_{13}-H), 3.95—4.14 (2H, m, C_9- and C_{12}-H), 5.72 (1H, dd, J=15.5, 5.7 Hz, CH=), 5.82 (1H, dd, J=15.5, 5.7 Hz, CH=).

10b: $[\alpha]_D^{25}$ −6.64° (c=1.19, $CHCl_3$). IR (neat): 3420, 1735, 1430 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.42 (6H, s, $(CH_3)_2C$), 3.66 (3H, s, OCH_3), 3.70—3.77 (1H, m, C_{13}-H), 4.03—4.16 (2H, m, C_9- and C_{12}-H), 5.37—5.53 (2H, m, C_{15}- and C_{16}-H), 5.65 (1H, dd, J=15.6, 7.2 Hz, CH=), 5.84 (1H, dd, J=15.6, 5.6 Hz, CH=). High-MS for $C_{22}H_{38}O_5$ (M^+): Calcd m/z 382.2717. Found 382.2701. **11b**: $[\alpha]_D^{25}$ −8.60° (c=1.04, $CHCl_3$). IR (neat): 3420, 1735, 1430 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.42 (6H, s, $(CH_3)_2C$), 3.66 (3H, s, OCH_3), 3.71—3.77 (1H, m, C_{13}-H), 4.05—4.17 (2H, m, C_9- and C_{12}-H), 5.37—5.53 (2H, m, C_{15}- and C_{16}-H), 5.66 (1H, dd, J=15.6, 7.2 Hz, CH=), 5.84 (1H, dd, J=15.6, 5.4 Hz, CH=).

10c: $[\alpha]_D^{25}$ −2.40° (c=0.82, $CHCl_3$). IR (neat): 3440, 1730, 1160 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.44 (6H, s, $(CH_3)_2C$), 3.65 (3H, s, OCH_3), 3.76 (1H, dt, J=8.2, 5.1 Hz, C_{13}-H), 4.05—4.20 (1H, m, C_9-H), 4.27 (1H, dd, J=8.2, 6.4 Hz, C_{12}-H), 5.67 (1H, dd, J=15.5, 6.4 Hz, CH=), 5.91 (1H, dd, J=15.5, 5.4 Hz, CH=). High-MS for $C_{22}H_{36}O_5$ (M^+): Calcd m/z 380.2560. Found 380.2545. **11c**: $[\alpha]_D^{25}$ −7.25° (c=0.87, $CHCl_3$). IR (neat): 3440, 1730, 1160 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.44 (6H, s, $(CH_3)_2C$), 3.65 (3H, s, OCH_3), 3.76 (1H, dt, J=8.2, 5.1 Hz, C_{13}-H), 4.06—4.20 (1H, m, C_9-H), 4.27 (1H, dd, J=8.2, 6.6 Hz, C_{12}-H), 5.67 (1H, dd, J=15.5, 6.6 Hz, CH=), 5.91 (1H, dd, J=15.5, 5.3 Hz, CH=).

CD spectra of benzoates of **10a**, **11b**, and **11c**; **10a**: Δ_ε^{25}: +13.9 (223.0 nm, $c=1.28\times10^{-4}$, MeOH), **11b**: Δ_ε^{25}: −3.05 (223.0 nm, $c=1.43\times10^{-4}$, MeOH), **11c**: Δ_ε^{25}: −0.96 (223.0 nm, $c=1.26\times10^{-4}$, MeOH).

Methyl (10*E*,9*R*,12*S*,13*S*)- and (10*E*,9*S*,12*S*,13*S*)-9,12,13-Trihydroxy-10-octadecenoate (1a and 2a), Methyl (10*E*,15*Z*,9*R*,12*S*,13*S*)- and (10*E*,15*Z*,9*S*,12*S*,13*S*)-9,12,13-Trihydroxy-10,15-octadecadienoate (1b and 2b), and Methyl (10*E*,9*R*,12*S*,13*S*)- and (10*E*,9*S*,12*S*,13*S*)-9,12,13-Trihydroxy-10-octadecen-15-ynoate (1c and 2c)——A solution of **10a** (26 mg) in MeOH (2 ml) was stirred in the presence of *p*-TsOH (trace). After 20 h, triethylamine (1 drop) was added, and the solvent was removed *in vacuo* to leave an oily residue, which was purified by column chromatography on silica gel (1.5 g). The fraction eluted with 40% AcOEt in hexane afforded **1a** (18 mg) as a colorless oil. In a similar manner, **1b**, **1c**, and **2a**, **2b**, **2c** were obtained as colorless oils.

1a: $[\alpha]_D^{25}$ −7.03° (c=1.28, $CHCl_3$). IR ($CHCl_3$): 3590, 3010, 1730, 1600, 1360, 1210 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.89 (3H, t, J=6.5 Hz, CH_3), 3.47 (1H, m, C_{13}-H), 3.67 (3H, s, OCH_3), 3.94 (1H, dd, J=5.9, 5.9 Hz, C_{12}-H), 4.39 (1H, dt, J=5.7, 5.7 Hz, C_9-H), 5.70 (1H, dd, J=15.5, 5.9 Hz, CH=), 5.82 (1H, dd, J=15.5, 5.7 Hz, CH=). MS m/z: 345 (M^++1), 327, 309, 273. **2a**: $[\alpha]_D^{25}$ −18.25° (c=0.90, $CHCl_3$). IR ($CHCl_3$): 3590, 3010, 1730, 1600, 1365, 1215 cm^1. ^{1}H-NMR ($CDCl_3$) δ: 0.89 (3H, t, J=6.5 Hz, CH_3), 3.47 (1H, m, C_{13}-H), 3.67 (3H, s, OCH_3), 3.94 (1H, dd, J=5.9, 5.9 Hz, C_{12}-H), 4.40 (1H, dt, J=5.7, 5.7 Hz, C_9-H), 5.71 (1H, dd, J=15.7, 5.9 Hz, CH=), 5.85 (1H, dd, J=15.7, 5.7 Hz, CH=).

1b: $[\alpha]_D^{25}$ −10.90° (c=1.01, $CHCl_3$). IR (neat): 3420, 1730, 1600 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.97 (3H, t, J=7.4 Hz, CH_3), 3.52 (1H, m, C_{13}-H), 3.67 (3H, s, OCH_3), 4.01 (1H, br s, C_{12}-H), 4.14 (1H, dt, J=5.8, 5.9 Hz, C_9-H), 5.35—5.62 (2H, m, C_{16}- and C_{17}-H), 5.72 (1H, dd, J=15.5, 5.8 Hz, CH=), 5.83 (1H, dd, J=15.5, 5.9 Hz, CH=). MS m/z: 343 (M^++1), 325, 307. **2b**: $[\alpha]_D^{25}$ −13.35° (c=0.51, $CHCl_3$). IR (neat): 3420, 1730, 1600 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.97 (3H, t, J=7.4 Hz, CH_3), 3.52 (1H, m, C_{13}-H), 3.67 (3H, s, OCH_3), 4.01 (1H, br s, C_{12}-H), 4.15 (1H, dt, J=5.9, 5.9 Hz, C_9-H), 5.33—5.60 (2H, m, C_{16}- and C_{17}-H), 5.72 (1H, dd, J=15.5, 6.0 Hz, CH=), 5.84 (1H, dd, J=15.5, 5.9 Hz, CH=).

1c: $[\alpha]_D^{25}$ −16.83° (c=1.83, $CHCl_3$). IR ($CHCl_3$): 3590, 3010, 1730, 1600 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.13 (3H, t, J=7.4 Hz, CH_3), 3.60 (1H, br s, C_{13}-H), 3.67 (3H, s, OCH_3), 4.11—4.15 (2H, m, C_9- and C_{12}-H), 5.71 (1H, dd, J=15.7, 5.8 Hz, CH=), 5.86 (1H, dd, J=15.7, 5.8 Hz, CH=). MS m/z: 341 (M^++1), 323. **2c**: $[\alpha]_D^{25}$ −18.97° (c=0.93, $CHCl_3$). IR ($CHCl_3$): 3590, 3010, 1730, 1600 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.13 (3H, t, J=7.4 Hz, CH_3), 3.60 (1H, br s, C_{13}-H), 3.67 (3H, s, OCH_3), 4.10—4.16 (2H, m, C_9- and C_{12}-H), 5.72 (1H, dd, J=15.7, 5.8 Hz, CH=), 5.87 (1H, dd, J=15.7, 5.9 Hz, CH=).

References and Notes

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10) $[\alpha]_D$ Values of the natural products (ref. 5) were not described. Comparison of reported[5] ^{1}H-NMR (400 MHz) data with those (270 MHz, $CDCl_3$) of **1** and **2** supported the proposed structures.