Enantiocontrolled synthesis of naturally occurring octadecadienoic acid derivatives, self-defensive substances against rice blast disease, by means of the Sharpless asymmetric epoxidation of unsymmetrical divinylmethanol[1]

Toshio Honda,* Mai Ohta and Hirotake Mizutani

Faculty of Pharmaceutical Sciences, Hoshi University, Ebara 2-4-41, Shinagawa-ku, Tokyo 142-8501, Japan

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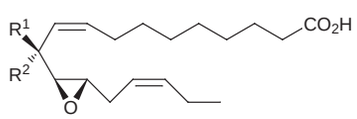
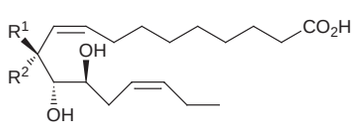
(11*S*,12*S*,13*S*)-(9*Z*,15*Z*)- and (11*R*,12*S*,13*S*)-(9*Z*,15*Z*)-11-hydroxy-12,13-epoxyoctadecadienoic acids and (11*R*,12*S*,13*S*)-(9*Z*,15*Z*)-11,12,13-trihydroxyoctadecadienoic acid, self-defensive substances against the rice blast disease, were synthesised enantioselectively by employing the Sharpless asymmetric epoxidation reaction of the unsymmetrical divinylmethanol, as a key step.

Introduction

Polyoxygenated metabolites of unsaturated fatty acids are becoming an increasingly interesting class of naturally occurring substances with regard to both biology and synthesis. Among them, several kinds of oxygenated unsaturated C_{18} fatty acids **1**–**4** have been isolated by Kato and his co-workers[2] from the



1: R^1 = OH, R^2 = H
2: R^1 = H, R^2 = OH



3: R^1 = H, R^2 = OH
4: R^1 = OH, R^2 = H

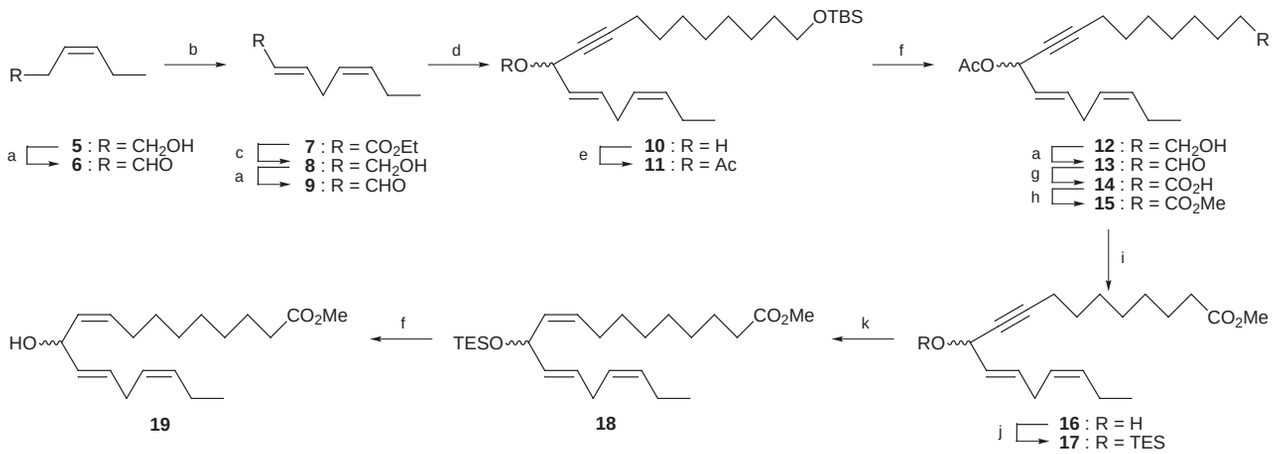
rice plants such as *Fukuyuki*, suffering from rice blast caused by the fungus *Pyricularia oryzae*. These fatty acids were shown to be self-defensive substances against the fungus. Owing to their interesting biological activity and also to their low abundance in natural sources, much effort has been devoted to develop an efficient procedure for their syntheses,[3] in which carbohydrates are widely employed as chiral precursors. Hatakeyama and his co-workers also reported[3h] the synthesis of (11*R*,12*S*,13*S*)-(9*Z*,15*Z*)-11,12,13-trihydroxyoctadeca-9,15-dienoic acid, where the Sharpless asymmetric epoxidation of symmetrical divinylmethanol was employed as a key reaction.

Recently we have developed the Sharpless asymmetric epoxidation reaction of racemic unsymmetrical divinylmethanols, where the kinetic resolution and subsequent epoxidation have proceeded in an entirely regio- and diastereoselective manner to give the corresponding epoxy alcohols with high enantiomeric excesses.[4,5] This procedure has already been successfully applied to the enantioselective synthesis of an antitumor antibiotic, (+)-asperlin.[4] As part of our program involving the study of the Sharpless asymmetric epoxidation of unsymmetrical divinylmethanols, we have begun to examine the utility of the process in an enantioselective synthesis of (11*S*,12*S*,13*S*)-(9*Z*,15*Z*)- and (11*R*,12*S*,13*S*)-(9*Z*,15*Z*)-11-hydroxy-12,13-epoxyoctadeca-9,15-dienoic acids, self-defensive substances against the rice blast disease. This report details our synthesis of the epoxy alcohols (**1** and **2**) and also the synthesis of trihydroxy acid (**3**), where the Sharpless asymmetric epoxidation of (9*Z*,12*E*,15*Z*)-11-hydroxyoctadeca-9,12,15-trienoic acid methyl ester and subsequent regioselective ring-opening reaction of the epoxide with tetramethylammonium triacetoxyborohydride [$Me_4NBH(OAc)_3$] were involved as key reactions.

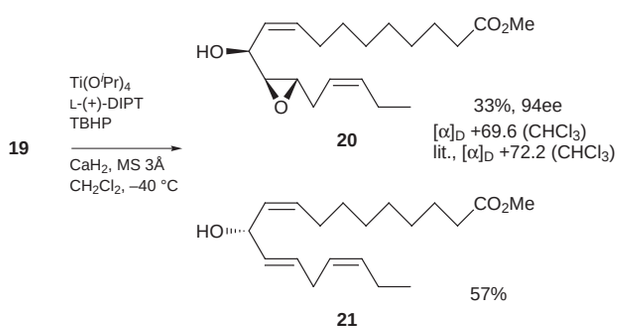
Results and discussion

The requisite racemic unsymmetrical divinylmethanol **19** was synthesised as shown in Scheme 1. Oxidation of (*Z*)-hex-3-en-1-ol **5** with Dess–Martin periodinane reagent[6] afforded (*Z*)-hex-3-enal **6**, which on Wittig–Horner reaction with triethyl phosphonoacetate gave the octadienoate **7**. Diisobutylaluminium hydride (DIBAL-H) reduction of the ester **7** and subsequent Dess–Martin periodinane oxidation of the alcohol **8** generated the dienal **9** in 69% yield from **7**. The lithiation of 10-(*tert*-butyldimethylsilyloxy)dec-1-yne[7] with *n*-butyllithium and subsequent addition to the aldehyde **9** gave the alcohol **10** in 83% yield. After protection of the secondary hydroxy group of **10** as the acetate **11**, the silyl group in **11** was removed by treatment with tetrabutylammonium fluoride (TBAF) to furnish the primary alcohol **12** in 92% yield from **10**. Oxidation of the alcohol **12** with Dess–Martin periodinane reagent gave the aldehyde **13**, which on oxidation with sodium chlorite[8] afforded the acid **14** in 89% yield from **12**. Esterification of the acid **14** with iodomethane and potassium carbonate in *N*,*N*-dimethylformamide afforded the ester **15**, which was further converted into the triethylsilyl ether **17** by two steps involving methanolysis giving the alcohol **16** and silylation of the secondary hydroxy group with triethylchlorosilane (TESCl). The formation of the *cis* olefin from the silyl ether **17** was achieved in the usual manner by using catalytic reduction with the Lindlar catalyst containing pyridine to give the triene **18**. Finally, deprotection of the silyl group in **18** with TBAF afforded the requisite racemic unsymmetrical divinylmethanol **19** in 89% yield from **14**.

The requisite unsymmetrical divinylmethanol in hand, the Sharpless kinetic resolution of **19** was carried out as follows



Scheme 1 *Reagents and conditions*: a, Dess–Martin oxidation; b, $(EtO)_2P(O)CH_2CO_2Et$, ″BuLi, THF, 0 °C; c, DIBAL-H, THF, 0 °C; d, 10-(*tert*-butyldimethylsilyloxy)decyne, ″BuLi, THF–HMPA, −40 °C; e, Ac_2O, pyridine, CH_2Cl_2; f, TBAF, THF, 0 °C; g, $NaClO_2$, 2-methylbut-2-ene, NaH_2PO_4, ′BuOH–H_2O (4:1); h, MeI, K_2CO_3, DMF; i, K_2CO_3, MeOH; j, TESCl, imidazole, CH_2Cl_2; k, Pd–$CaCO_3$, H_2, pyridine, hexane.



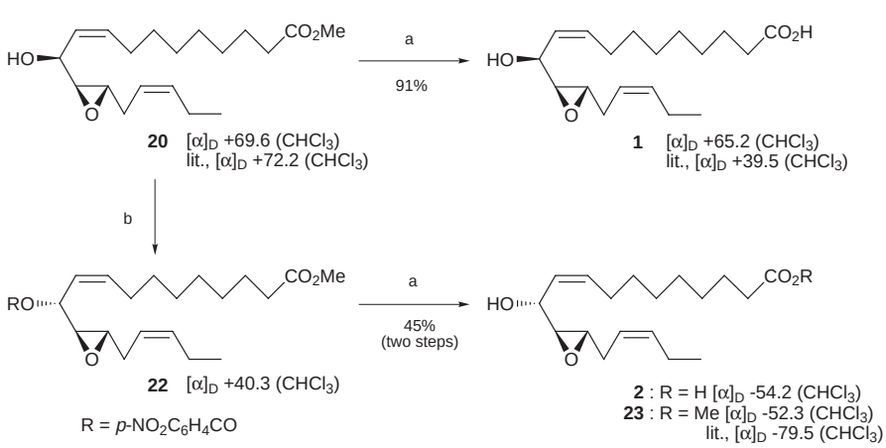
Scheme 2

(Scheme 2). The reaction of **19** with 0.4 equiv. of *tert*-butyl hydroperoxide (TBHP), 0.55 equiv. of L-(+)-diisopropyl tartrate (DIPT) and 0.5 equiv. of titanium(IV) tetraisopropoxide [Ti(O-^{i}Pr)$_4$] in dichloromethane in the presence of calcium hydride and activated molecular sieves 3 Å at −40 °C gave the epoxy alcohol **20** and the recovered (*R*)-secondary alcohol **21**, in 33 and 57% yields, respectively. None of the other oxidised products including the regioisomeric epoxide could be isolated in this reaction. The spectroscopic data including specific optical rotation, {$[\alpha]_D^{26}$ +69.6 ($CHCl_3$), lit.,[3f] $[\alpha]_D$ +72.2 ($CHCl_3$)}, of the former epoxide **20** were identical with those reported,[3f] suggesting its absolute configuration to be 11*S*, 12*S* and 13*S*. Its enantiomeric excess was also determined to be 94% by HPLC analysis of the corresponding *p*-bromobenzoate using the chiral column CHIRALPAK AD (Daicel Chemical Industries, Ltd.).

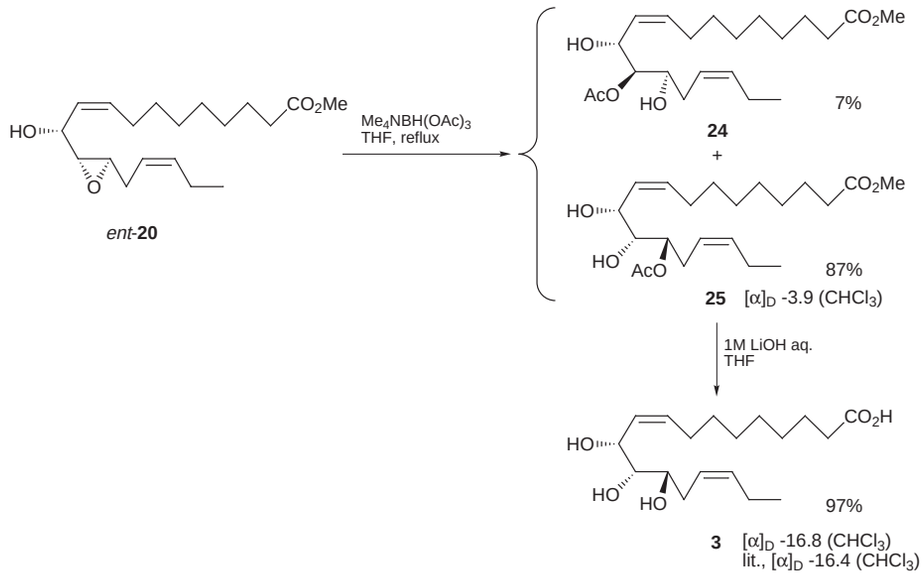
It should be noted again that the kinetic resolution and subsequent epoxidation of **19** under the Sharpless asymmetric epoxidation conditions proceeded in an entirely regio- and diastereoselective manner.

In order to complete the synthesis of natural compounds, the ester **20** was hydrolysed with 0.5 M aqueous lithium hydroxide to afford the desired acid **1**, {$[\alpha]_D^{27}$ +65.2 ($CHCl_3$), lit.,[3a] $[\alpha]_D$ +39.5 ($CHCl_3$)}, in 91% yield (Scheme 3). The reported value of optical rotation for the natural product[3a] was much smaller than that for our synthetic compound, which is probably due to sample contamination. Furthermore, (11*R*,12*S*,13*S*)-(9*Z*,15*Z*)-11-hydroxy-12,13-epoxyoctadeca-9,15-dienoic acid **2**, $[\alpha]_D^{29}$ −54.2 ($CHCl_3$), was synthesised from the epoxy alcohol **20** by two steps, including Mitsunobu reaction with *p*-nitrobenzoic acid, and hydrolysis of the resulting *p*-nitrobenzoate **22** with 0.5 M aqueous lithium hydroxide, in 45% overall yield. The partial hydrolysis of **22** under the above reaction conditions with a shorter reaction time gave the methyl ester **23**,[9] {$[\alpha]_D^{29}$ −52.3 ($CHCl_3$), lit.,[3d] $[\alpha]_D$ −79.5 ($CHCl_3$)}, which was also converted into the acid **2**.

Using *ent*-**20** prepared by the Sharpless epoxidation of **19** with D-(−)-DIPT, we next investigated the synthesis of (11*R*,12*S*,13*S*)-(9*Z*,15*Z*)-11,12,13-trihydroxyoctadeca-9,15-dienoic acid **3** as shown in Scheme 4. We have initially attempted the regioselective epoxide-opening reaction of *ent*-**20** with Ti(O^{i}Pr)$_4$ and benzoic acid under the reaction conditions developed by Sharpless,[10] however, none of the desired compound could be isolated unfortunately. Whereas, the treatment of *ent*-**20** with $Me_4NBH(OAc)_3$,[11] the reagent for a regioselective ring-opening of 2,3-epoxy alcohols, developed



Scheme 3 *Reagents and conditions*: a, 0.5 M LiOH, aqueous THF; b, DEAD, PPh_3, *p*-$NO_2C_6H_4CO_2H$, toluene.



Scheme 4

by us[12] recently, proceeded smoothly to provide the desired C-3 opening product **25** and C-2 opening isomer **24** in a ratio of *ca.* 13:1 based on the analysis of ^{1}H-NMR data. The pure **25** was isolated by column chromatography on silica gel, whereas the compound **24** was obtained as a mixture with **25**. Finally, hydrolysis of **25** with 1 M aqueous lithium hydroxide furnished (11*R*,12*S*,13*S*)-(9*Z*,15*Z*)-11,12,13-trihydroxyoctadeca-9,15-dienoic acid **3**, {[a]$_D^{24}$ −16.8 ($CHCl_3$), lit.,[3e] [a]$_D^{20}$ −16.4 ($CHCl_3$)}, in 97% yield. The synthetic substance exhibited spectral properties in good accord with those reported.[3e]

In conclusion, the present work illustrates a further application of the Sharpless asymmetric epoxidation of unsymmetrical divinylmethanols to the synthesis of biologically active C_{18} fatty acids **1** and **2** with high optical purity, and the synthesis of trihydroxy fatty acid **3** by means of the regioselective ring-opening reaction of epoxy alcohol with $Me_4NBH(OAc)_3$. This strategy should also be applicable to the synthesis of other stereoisomers and congeners of these oxygenated fatty acids with structural similarity.

Experimental

General methods

Mps were measured with a Yanagimoto MP apparatus and are uncorrected. IR spectra were recorded for thin films on a JASCO FT/IR-200 Fourier transform infrared spectrophotometer. ^{1}H- and ^{13}C-NMR spectra were obtained for solutions in $CDCl_3$ on a JEOL GSX-270, and chemical shifts are reported in ppm on the δ scale from internal Me_4Si. Mass spectra were measured with a JEOL HMS D-300 spectrometer. Elemental analyses were measured with a Yanako MT-5. Optical rotations were taken with a JASCO DIP-360 polarimeter using a commercial special grade of chloroform as a solvent, and are reported in units of 10^{-1} deg cm^2 g^{-1}. Column chromatography was carried out on BW-80S (Fuji silysia). Molecular sieves 3 Å were activated by heating at 250 °C *in vacuo* for 3 h.

(2*E*,5*Z*)-Octa-2,5-dienoic acid ethyl ester 7

To a stirred solution of (*Z*)-hex-3-en-1-ol **5** (10 g, 99.8 mmol) in dichloromethane (100 cm^3) was added portionwise Dess–Martin periodinane (63.5 g, 0.15 mol), and the resulting mixture was stirred for 30 min at 0 °C. After adding diethyl ether, followed by filtration of the mixture, the filtrate was washed with saturated aqueous sodium hydrogen carbonate and brine and dried over Na_2SO_4. Evaporation of the solvent gave a residue which, without further purification, was treated with triethyl phosphonoacetate (25.8 cm^3, 0.13 mol) and *n*-butyllithium (1.63 mol l^{-1} in *n*-hexane, 73.6 cm^3, 0.12 mol) in dry tetrahydrofuran (50 cm^3) for 2 h at 0 °C. After addition of saturated aqueous ammonium chloride, the mixture was extracted with diethyl ether. The extract was washed with brine, and dried over Na_2SO_4. Evaporation of the solvent gave a residue that was purified by column chromatography (*n*-pentane–diethyl ether, 30:1) to give **7** (14.96 g, 89%) as a colourless oil; ν_{max}(thin film)/cm^{-1} 900, 930, 993, 1047, 1096, 1120, 1165, 1208, 1234, 1272, 1308, 1325, 1368, 1400, 1464, 1652 and 1720; δ_H 0.97 (3H, t, *J* 7.5, 8-H_3), 1.28 (3H, t, *J* 7.2, OCH_2CH_3), 2.04 (2H, m, 7-H_2), 2.94 (2H, dd, *J* 6.3 and 7.1, 4-H_2), 4.18 (2H, q, *J* 7.2, OCH_2CH_3), 5.35 (1H, m, 6-H), 5.55 (1H, m, 5-H), 5.83 (1H, dt, *J* 1.7 and 15.5, 2-H) and 6.95 (1H, dt, *J* 6.3 and 15.5, 3-H); δ_C 13.9, 14.1, 20.4, 29.7, 60.1, 121.2, 123.5, 134.5, 147.2 and 166.6 (Found: M$^+$, 168.1145. Calc. for $C_{10}H_{16}O_2$: M$^+$, 168.1150).

(2*E*,5*Z*)-Octa-2,5-dien-1-ol 8

To a stirred solution of **7** (14.9 g, 89.0 mmol) in dry diethyl ether (150 cm^3) was added dropwise diisobutylaluminium hydride (206 cm^3, 0.19 mol), and the resulting mixture was stirred for 1 h at 0 °C. After adding dropwise methanol–H_2O (1:3), followed by filtration of the mixture, the solvent was removed to give a residue that was purified by column chromatography (*n*-pentane–diethyl ether, 2:1) to give **8** (10.1 g, 89%) as a colourless oil; ν_{max}(thin film)/cm^{-1} 986, 1005, 1072, 1090, 1225, 1268, 1304, 1374, 1400, 1432, 1462, 1652, 1670 and 3320; δ_H 0.97 (3H, t, *J* 7.4, 8-H_3), 1.34 (3H, br, OH), 2.05 (2H, dq, *J* 7.1 and 7.4, 7-H_2), 2.79 (2H, m, 4-H_2), 4.10 (2H, br, 1-H_2), 5.40 (2H, m, 5-H and 6-H) and 5.68 (2H, m, 2-H and 3-H); δ_C 14.0, 20.3, 29.8, 63.3, 126.0, 129.1, 131.0 and 132.6 (Found: M$^+$, 126.1057. Calc. for $C_8H_{14}O$: M$^+$, 126.1045).

(2*E*,5*Z*)-Octa-2,5-dienal 9

To a stirred solution of **8** (9.1 g, 72.2 mmol) in dichloromethane (90 cm^3) was added portionwise Dess–Martin periodinane (45.9 g, 0.11 mol), and the resulting mixture was stirred for 2 h at 0 °C. After adding diethyl ether, followed by filtration of the mixture, the filtrate was washed with saturated aqueous sodium hydrogen carbonate and brine, and dried over Na_2SO_4. Evaporation of the solvent *in vacuo* gave a residue, which was purified by column chromatography (*n*-pentane–diethyl ether,

3:1) to give **9** (7.8 g, 87%) as a colourless oil; ν_{max}(thin film)/cm^{-1} 906, 984, 1012, 1070, 1130, 1195, 1305, 1410, 1424, 1464, 1633, 1694, 2730, 2815, 2878, 2965 and 3012; δ_H 0.98 (3H, t, *J* 7.4, 8-H_3), 2.06 (2H, dq, *J* 6.3 and 7.4, 7-H_2), 3.08 (2H, dd, *J* 6.4 and 6.9, 4-H_2), 5.38 (1H, m, 6-H), 5.60 (1H, m, 5-H), 6.14 (1H, ddt, *J* 1.6, 7.7 and 15.7, 2-H), 6.84 (1H, dt, *J* 6.2 and 15.7, 3-H) and 9.53 (1H, d, *J* 7.7, CHO); δ_C 14.0, 20.5, 30.4, 122.6, 132.8, 135.1, 156.6 and 193.8 (Found: M$^+$, 275.2008. Calc. for $C_8H_{12}O$: M$^+$, 275.2010).

(3*Z*,6*E*)-18-(*tert*-Butyldimethylsilyloxy)octadeca-3,6-dien-9-yn-8-ol 10

To a stirred solution of 10-(*tert*-butyldimethylsilyloxy)dec-1-yne (5.09 g, 15.6 mmol) in dry tetrahydrofuran (50 cm^3) was added *n*-butyllithium (1.66 mol l^{-1} in *n*-hexane, 9.41 cm^3, 15.6 mmol) at −40 °C, and the resulting solution was stirred at 0 °C for 1 h under argon. Hexamethylphosphoric triamide (2.47 cm^3, 14.2 mmol) was then added to this mixture at the same temperature. After stirring for 5 min at the same temperature, a solution of aldehyde **9** (1.76 g, 14.2 mmol) in tetrahydrofuran (40 cm^3) was added, and the mixture was stirred at 0 °C for 1 h. After addition of saturated aqueous ammonium chloride solution, the organic solvent was evaporated to leave an oily product, which was extracted with ethyl acetate. The extract was washed with brine and dried over Na_2SO_4. Evaporation of the solvent gave a residue, which was purified by column chromatography (*n*-hexane–ethyl acetate, 8:1) to give **10** (4.60 g, 83%) as a colourless oil; ν_{max}(thin film)/cm^{-1} 836, 902, 940, 968, 1006, 1096, 1255, 1300, 1330, 1362, 1388, 1436, 1464, 1655, 1667, 2230 and 3420; δ_H 0.15 (6H, s, 2 × SiCH_3), 0.90 (9H, s, Si′Bu), 0.97 (3H, t, *J* 7.6, 18-H_3), 1.26–1.53 (12H, m, 12-H_2, 13-H_2, 14-H_2, 15-H_2, 16-H_2 and 17-H_2), 1.75 (1H, d, *J* 6.1, 8-OH), 2.00 (2H, dq, *J* 7.1 and 7.6, 2-H_2), 2.22 (2H, dt, *J* 2.0 and 6.9, 11-H_2), 2.76 (2H, br t, *J* 6.3, 5-H_2), 3.60 (2H, t, *J* 6.6, 18-H_2), 5.37 (1H, m, 8-H), 5.31–5.52 (2H, m, 3-H and 4-H), 5.62 (1H, ddt, *J* 1.5, 5.9 and 15.3, 7-H) and 5.86 (1H, ddt, *J* 1.0, 6.3 and 15.3, 6-H) (Found: M$^+$, 392.3116. Calc. for $C_{24}H_{44}O_2Si$: M$^+$, 392.3110).

(3*Z*,6*E*)-8-Acetoxy-18-(*tert*-butyldimethylsilyloxy)octadeca-3,6-dien-9-yne 11

To a stirred solution of **10** (4.3 g, 9.56 mmol) in dichloromethane (50 cm^3) were added pyridine (1.16 cm^3, 14.3 mmol), acetic anhydride (1.08 cm^3, 11.5 mmol) and a catalytic amount of 4-(dimethylamino)pyridine at 0 °C, and the resulting mixture was stirred for 2 h at the same temperature under argon. After addition of saturated aqueous ammonium chloride, the mixture was extracted with dichloromethane. The extract was washed with brine and dried over Na_2SO_4. Evaporation of the solvent gave a residue that was purified by column chromatography (*n*-hexane–ethyl acetate, 40:1) to give **11** (4.59 g, 96%) as a colourless oil; ν_{max}(thin film)/cm^{-1} 836, 916, 948, 964, 1013, 1096, 1158, 1230, 1255, 1298, 1350, 1370, 1388, 1434, 1464, 1472, 1655, 1668, 1742 and 2250; δ_H 0.46 (6H, s, 2 × SiCH_3), 0.89 (9H, s, Si′Bu), 0.96 (3H, t, *J* 7.4, 1-H_3), 1.23–1.43 (8H, m, 13-H_2, 14-H_2, 15-H_2 and 16-H_2), 1.44–1.57 (4H, m, 12-H_2 and 17-H_2), 1.97–2.12 (5H, m, 2-H_2 and COCH_3), 2.23 (2H, dt, *J* 1.8 and 7.1, 11-H_2), 2.82 (2H, br t, *J* 6.4, 5-H_2), 3.60 (2H, t, *J* 6.6, 18-H_2), 5.29–5.61 (3H, m, 3-H, 4-H and 7-H), 5.85 (1H, br d, *J* 6.1, 8-H) and 5.97 (1H, ddt, *J* 1.2, 6.4 and 15.3, 6-H); δ_C −5.5, 14.0, 18.1, 18.6, 20.3, 20.9, 25.6, 25.8, 28.3, 28.6, 28.9, 29.1, 29.4, 32.7, 63.0, 64.4, 76.0, 87.4, 125.0, 125.7, 133.1, 133.8 and 169.3 (Found: C, 71.56; H, 10.64. Calc. for $C_{26}H_{46}O_3Si$: C, 71.83; H, 10.67%).

(12*E*,15*Z*)-11-Acetoxyoctadeca-12,15-dien-9-yn-1-ol 12

To a stirred solution of **11** (4.74 g, 9.63 mmol) in tetrahydrofuran (50 cm^3) was added tetrabutylammonium fluoride (1.0 M solution in tetrahydrofuran, 3.07 cm^3, 11.0 mmol), and the resulting mixture was stirred for 2 h at 0 °C. After addition of saturated aqueous ammonium chloride, the organic solvent was evaporated to leave an oily product, which was extracted with ethyl acetate. The extract was washed with brine and dried over Na_2SO_4. Evaporation of the solvent gave a residue, which was purified by column chromatography (*n*-hexane–ethyl acetate, 3:1) to give **12** (2.97 g, 96%) as a colourless oil; ν_{max}(thin film)/cm^{-1} 790, 917, 950, 1016, 1055, 1160, 1230, 1300, 1348, 1370, 1436, 1462, 1664, 1740, 2250 and 3420; δ_H 0.97 (3H, t, *J* 7.4, 18-H_3), 1.23–1.44 (9H, m, 4-H_2, 5-H_2, 6-H_2, 7-H_2 and 1-OH), 1.46–1.62 (4H, m, 2-H_2 and 3-H_2), 1.99–2.10 (5H, m, 17-H_2 and COCH_3), 2.23 (2H, dt, *J* 2.0 and 7.1, 8-H_2), 2.82 (2H, br t, *J* 6.3, 14-H_2), 3.64 (2H, dt, *J* 5.6 and 6.4, 1-H_2), 5.34 (1H, ddt, *J* 1.5, 7.1 and 10.7, 15-H), 5.48 (1H, m, 16-H), 5.55 (1H, ddt, *J* 1.7, 6.1 and 15.3, 12-H), 5.84 (1H, m, 11-H) and 5.97 (1H, ddt, *J* 1.2, 6.3 and 15.3, 13-H); δ_C 13.7, 18.2, 20.0, 20.6, 25.3, 27.9, 28.2, 28.6, 28.8, 29.1, 32.2, 61.9, 64.2, 75.7, 87.1, 124.7, 125.3, 132.8, 133.6 and 169.3 (Found: C, 74.76; H, 10.10. Calc. for $C_{20}H_{32}O_3$: C, 74.96; H, 10.06%).

(12*E*,15*Z*)-11-Acetoxyoctadeca-12,15-dien-9-yn-1-al 13

To a stirred solution of **12** (80 mg, 0.25 mmol) in dichloromethane (1 cm^3) was added portionwise Dess–Martin periodinane (160 mg, 0.37 mmol), and the resulting mixture was stirred for 30 min at 0 °C. After the mixture was diluted with diethyl ether and then filtered through a pad of Celite, the filtrate was washed with saturated aqueous sodium hydrogen carbonate and brine, and dried over Na_2SO_4. Evaporation of the solvent gave a residue that was purified by column chromatography (*n*-hexane–ethyl acetate, 10:1) to give **13** (72 mg, 91%) as a colourless oil; ν_{max}(thin film)/cm^{-1} 916, 948, 964, 1015, 1046, 1068, 1158, 1230, 1298, 1348, 1370, 1432, 1464, 1668, 1730, 1740 and 2250; δ_H 0.97 (3H, t, *J* 7.6, 18-H_3), 1.27–1.44 (6H, m, 5-H_2, 6-H_2 and 7-H_2), 1.46–1.68 (4H, m, 3-H_2 and 4-H_2), 1.98–2.11 (5H, m, 17-H_2 and COCH_3), 2.23 (2H, dt, *J* 2.0 and 7.1, 8-H_2), 2.43 (2H, dt, *J* 1.8 and 7.4, 2-H_2), 2.82 (2H, br t, *J* 6.3, 14-H_2), 5.34 (1H, dtt, *J* 1.5, 7.3 and 10.7, 16-H), 5.48 (1H, dtt, *J* 1.5, 7.1 and 10.7, 15-H), 5.55 (1H, ddt, *J* 1.5, 6.1 and 15.3, 12-H), 5.84 (1H, m, 11-H), 5.97 (1H, ddt, *J* 1.0, 6.3 and 15.3, 13-H) and 9.77 (1H, t, *J* 1.8, CHO); δ_C 13.8, 18.2, 20.0, 20.6, 21.5, 27.9, 28.1, 28.4, 28.6, 29.2, 43.3, 64.1, 75.9, 124.8, 125.4, 132.8, 133.5, 169.0 and 201.7 [Found: (M$^+$ − 43), 275.2008. Calc. for $C_{18}H_{27}O_2$: (M$^+$ − 43), 275.2010].

(12*E*,15*Z*)-11-Acetoxyoctadeca-12,15-dien-9-ynoic acid 14

To a stirred solution of **13** (320 mg, 1.01 mmol) in *tert*-butyl alcohol–H_2O (4:1, 5 cm^3) were added 2-methylbut-2-ene (0.48 cm^3, 4.35 mmol), sodium dihydrogen phosphate (120 mg, 1.01 mmol) and sodium chlorite (320 mg, 3.52 mmol), and the resulting mixture was stirred for 1 h at room temperature. After addition of brine, the organic solvent was evaporated to leave an oily product, which was acidified (pH 2–3) with 1 M aqueous hydrochloric acid, and extracted with ethyl acetate. The extract was dried over Na_2SO_4. Evaporation of the solvent gave a residue, which was purified by column chromatography (*n*-hexane–ethyl acetate, 3:1) to give **14** (330 mg, 98%) as a colourless oil; ν_{max}(thin film)/cm^{-1} 917, 948, 1015, 1048, 1070, 1134, 1160, 1230, 1286, 1348, 1370, 1412, 1430, 1462, 1600, 1710, 1740, 2250 and 3000; δ_H 0.96 (3H, t, *J* 7.6, 18-H_3), 1.28–1.44 (6H, m, 5-H_2, 6-H_2 and 7-H_2), 1.47–1.68 (4H, m, 3-H_2 and 4-H_2), 1.98–2.10 (5H, m, 17-H_2 and COCH_3), 2.23 (2H, dt, *J* 1.8 and 7.1, 8-H_2), 2.35 (2H, t, *J* 7.4, 2-H_2), 2.82 (2H, br t, *J* 6.3, 14-H_2), 5.34 (1H, m, 11-H), 5.47 (1H, m, 15-H), 5.55 (1H, ddt, *J* 1.5, 6.3 and 15.2, 12-H), 5.84 (1H, m, 16-H) and 5.97 (1H, ddt, *J* 1.2, 6.3 and 15.2, 13-H); δ_C 13.9, 18.5, 20.2, 20.9, 24.3, 28.1, 28.3, 28.4, 28.6, 29.3, 33.8, 64.5, 75.9, 86.0, 125.0, 125.5, 133.1, 133.9, 169.6 and 179.8 (Found: M$^+$, 334.2147. Calc. for $C_{20}H_{30}O_4$: M$^+$, 334.2144).

(12*E*,15*Z*)-11-Acetoxyoctadeca-12,15-dien-9-ynoic acid methyl ester 15

Iodomethane (0.93 cm^3, 6.29 mmol) was added to a stirred solution of **14** (1.75 g, 5.24 mmol) in dry *N*,*N*-dimethylformamide (50 cm^3) containing potassium carbonate (0.87 g, 6.29 mmol) at room temperature. After 1 h, the mixture was diluted with ethyl acetate. The organic layer was washed with saturated aqueous ammonium chloride and brine, and dried over Na_2SO_4. Concentration of the solvent *in vacuo* gave a residue, which was purified by column chromatography (*n*-hexane–ethyl acetate, 12:1) to give **15** (1.8 g, 99%) as a colourless oil; ν_{max}(thin film)/cm^{-1} 916, 948, 1015, 1170, 1230, 1370, 1436, 1668, 1740 and 2250; δ_H 0.96 (3H, t, *J* 7.4, 18-H_3), 1.27–1.43 (4H, m, 6-H_2 and 7-H_2), 1.46–1.67 (6H, m, 3-H_2, 4-H_2 and 5-H_2), 1.98–2.12 (5H, m, 17-H_2 and $COCH_3$), 2.23 (2H, dt, *J* 2.0 and 7.1, 8-H_2), 2.31 (2H, dd, *J* 7.4 and 7.6, 2-H_2), 2.82 (2H, br t, *J* 6.3, 14-H_2), 3.67 (3H, s, CO_2CH_3), 5.28–5.52 (2H, m, 15-H and 16-H), 5.55 (1H, ddt, *J* 1.7, 6.3 and 15.3, 12-H), 5.84 (1H, m, 11-H) and 5.97 (1H, ddt, *J* 1.2, 6.3 and 15.2, 13-H); δ_C 13.7, 18.2, 20.0, 20.5, 24.4, 27.9, 28.1, 28.3, 28.5, 29.1, 33.4, 50.8, 64.1, 75.8, 86.9, 124.8, 125.4, 132.8, 133.5, 169.0 and 173.3 (Found: M^+, 348.2298. Calc. for $C_{21}H_{32}O_4$: M^+, 348.2299) (Found: C, 72.08; H, 9.30. Calc. for $C_{21}H_{32}O_4$: C, 72.38; H, 9.26%).

(12*E*,15*Z*)-11-Hydroxyoctadeca-12,15-dien-9-ynoic acid methyl ester 16

To a stirred solution of **15** (2.05 g, 5.87 mmol) in methanol (20 cm^3) was added potassium carbonate (0.81 g, 5.87 mmol) at 0 °C. After 4 h, the mixture was neutralized with 1 M aqueous hydrochloric acid, and concentrated. The residue was extracted with ethyl acetate. The organic layer was washed with water and brine, and dried over Na_2SO_4. Evaporation of the solvent gave a residue that was subjected to column chromatography (*n*-hexane–ethyl acetate, 6:1) to give **16** (1.77 g, 98%) as a colourless oil; ν_{max}(thin film)/cm^{-1} 968, 1084, 1174, 1190, 1248, 1330, 1368, 1437, 1462, 1664, 1740, 2240 and 3450; δ_H 0.97 (3H, t, *J* 7.6, 18-H_3), 1.28–1.68 (10H, m, 3-H_2, 4-H_2, 5-H_2, 6-H_2 and 7-H_2), 1.83 (1H, d, *J* 5.9, 11-OH), 2.05 (2H, m, 17-H_2), 2.23 (2H, dt, *J* 2.0 and 6.9, 8-H_2), 2.31 (2H, t, *J* 7.6, 2-H_2), 2.81 (2H, br t, *J* 6.3, 14-H_2), 3.68 (3H, s, CO_2CH_3), 4.83 (1H, m, 11-H), 5.30–5.52 (2H, m, 15-H and 16-H), 5.62 (1H, ddt, *J* 1.5, 5.9 and 15.3, 12-H) and 5.86 (1H, ddt, *J* 1.2, 6.3 and 15.3, 13-H); δ_C 13.8, 18.3, 20.0, 24.4, 28.1, 28.1, 28.2, 28.5, 29.1, 33.5, 51.0, 62.2, 79.6, 85.6, 125.4, 129.8, 130.4, 132.4 and 173.8 (Found: M^+, 306.2197. Calc. for $C_{19}H_{30}O_3$: M^+, 306.2195).

(12*E*,15*Z*)-11-(Triethylsilyloxy)octadeca-12,15-dien-9-ynoic acid methyl ester 17

Triethylchlorosilane (0.99 cm^3, 5.88 mmol) was added to a stirred solution of **16** (1.05 g, 4.90 mmol) in dry dichloromethane (10 cm^3) containing imidazole (670 mg, 9.80 mmol) at 0 °C under argon. After 1 h, the mixture was diluted with dichloromethane. The organic layer was washed with saturated aqueous ammonium chloride and brine, and dried over Na_2SO_4. Concentration of the solvent *in vacuo* gave a residue, which was purified by column chromatography (*n*-hexane–ethyl acetate, 20:1) to give **17** (2.04 g, 99%) as a colourless oil; ν_{max}(thin film)/cm^{-1} 848, 964, 1005, 1038, 1096, 1172, 1197, 1240, 1417, 1436, 1460, 1668, 1743 and 2240; δ_H 0.65 (6H, q, *J* 7.6, Si$CH_2$$CH_3$), 0.97 (12H, m, 18-$H_3$ and $SiCH_2CH_3$), 1.27–1.67 (10H, m, 3-H_2, 4-H_2, 5-H_2, 6-H_2 and 7-H_2), 2.04 (2H, m, 17-H_2), 2.20 (2H, dt, *J* 1.8 and 6.9, 8-H_2), 2.30 (2H, t, *J* 7.6, 2-H_2), 2.79 (2H, br t, *J* 6.3, 14-H_2), 3.67 (3H, s, CO_2CH_3), 4.84 (1H, m, 11-H), 5.40 (2H, m, 15-H and 16-H), 5.55 (1H, ddt, *J* 1.5, 5.6 and 15.2, 12-H) and 5.76 (1H, ddt, *J* 1.2, 6.3 and 15.2, 13-H); δ_C 4.5, 6.3, 13.8, 18.3, 20.1, 24.5, 28.1, 28.3, 28.4, 28.7, 29.1, 33.5, 50.8, 62.9, 79.9, 85.1, 125.5, 129.1, 130.4, 132.3 and 173.4 (Found: M^+, 420.3062. Calc. for $C_{25}H_{44}O_3Si$: M^+, 420.3060).

(9*Z*,12*E*,15*Z*)-11-(Triethylsilyloxy)octadeca-9,12,15-trienoic acid methyl ester 18

A mixture of **17** (50 mg, 0.12 mmol) and palladium on calcium carbonate (Lindlar catalyst, 10 mg) in *n*-hexane (2 cm^3) containing pyridine (0.05 cm^3, 0.6 mmol) was stirred for 7 h at room temperature under an atmosphere of hydrogen. The catalyst was filtered off, and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography (*n*-hexane–ethyl acetate, 30:1) to give **18** (48 mg, 96%) as a colourless oil; ν_{max}(thin film)/cm^{-1} 855, 969, 1006, 1068, 1098, 1172, 1196, 1240, 1362, 1416, 1436, 1460, 1655, 1665, 1745, 1880, 2935, 2958 and 3012; δ_H 0.59 (6H, q, *J* 7.8, Si$CH_2$$CH_3$), 0.94 (12H, m, 18-$H_3$ and $SiCH_2CH_3$), 1.28–1.40 (8H, m, 4-H_2, 5-H_2, 6-H_2 and 7-H_2), 1.54 (2H, m, 3-H_2), 2.04 (4H, m, 8-H_2 and 17-H_2), 2.31 (2H, t, *J* 7.4, 2-H_2), 2.75 (2H, br t, *J* 6.3, 14-H_2), 3.67 (3H, s, CO_2CH_3), 4.87 (1H, dd, *J* 5.8 and 6.1, 11-H), 5.27–5.48 (5H, m, 9-H, 10-H, 12-H, 15-H and 16-H) and 5.57 (1H, dt, *J* 6.3 and 15.3, 13-H) (Found: M^+, 422.3215. Calc. for $C_{25}H_{46}O_3Si$: M^+, 422.3215).

(9*Z*,12*E*,15*Z*)-11-Hydroxyoctadeca-9,12,15-trienoic acid methyl ester 19

Tetrabutylammonium fluoride (1.0 M solution in tetrahydrofuran, 1.28 cm^3, 4.41 mmol) was added dropwise to a stirred solution of **18** (1.68 g, 4.00 mmol) in tetrahydrofuran (50 cm^3) at 0 °C. After 1 h, the mixture was diluted with ethyl acetate. The organic layer was washed with brine and dried over Na_2SO_4. Concentration of the solvent *in vacuo* gave a residue, which was purified by column chromatography (*n*-hexane–ethyl acetate, 6:1) to give **19** (1.20 g, 97%) as a colourless oil; ν_{max}(thin film)/cm^{-1} 884, 970, 1020, 1085, 1174, 1198, 1250, 1364, 1437, 1460, 1649, 1655, 1740 and 3350; δ_H 0.96 (3H, t, *J* 7.4, 18-H_3), 1.25–1.44 (8H, m, 4-H_2, 5-H_2, 6-H_2 and 7-H_2), 1.47 (1H, d, *J* 3.6, 11-OH), 1.54–1.64 (2H, m, 3-H_2), 1.99–2.13 (4H, m, 8-H_2 and 17-H_2), 2.30 (2H, dd, *J* 7.4 and 7.6, 2-H_2), 2.78 (2H, br t, *J* 6.3, 14-H_2), 3.67 (3H, s, CO_2CH_3), 4.90 (1H, m, 11-H), 5.29–5.57 (5H, m, 9-H, 10-H, 12-H, 15-H and 16-H) and 5.67 (1H, dt, *J* 6.3 and 15.5, 13-H); δ_C 14.2, 20.4, 24.8, 27.5, 29.0, 29.0, 29.4, 29.8, 34.0, 51.4, 68.6, 125.9, 129.9, 130.8, 131.8, 131.9 and 174.2 [Found: (M^+ − 18), 290.2243. Calc. for $C_{19}H_{30}O_2$: (M^+ − 18), 290.2244].

(11*S*,12*S*,13*S*)-(9*Z*,15*Z*)-11-Hydroxy-12,13-epoxyoctadeca-9,15-dienoic acid methyl ester 20

To a stirred suspension of activated molecular sieves 3 Å (111 mg, 30 wt% based on the substrate) and calcium hydride (10 mg, 0.24 mmol) in dry dichloromethane (3 cm^3) was added titanium(IV) tetraisopropoxide (0.18 cm^3, 0.60 mmol) at room temperature. The stirred mixture was cooled to −20 °C, and treated with a solution of L-(+)-diisopropyl tartrate (155 mg, 0.66 mmol) in dry dichloromethane (3 cm^3). After stirring the mixture for 30 min at the same temperature, a solution of the alcohol **19** (370 mg, 1.20 mmol) in dry dichloromethane (4 cm^3) was added dropwise to the solution, and the mixture was stirred for a further 1 h. *tert*-Butyl hydroperoxide (5.28 M solution in 2,2,4-trimethylpentane, 0.091 cm^3, 0.48 mmol) was added dropwise to this mixture. After stirring of this mixture for 24 h at −20 °C, dimethyl sulfide (0.11 cm^3, 1.56 mmol) was slowly added and the mixture was stirred for 30 min at the same temperature. To this mixture were added 10% aqueous tartaric acid (0.11 cm^3, 0.30 mmol), diethyl ether (40 cm^3) and sodium fluoride (315 mg, 7.51 mmol), and the resulting mixture was vigorously stirred for 3 h at room temperature. The precipitate was filtered off through a pad of Celite. The filtrate was washed with saturated aqueous sodium hydrogen carbonate and brine.

Evaporation of the solvent gave a residue, which was purified by column chromatography (*n*-hexane–ethyl acetate, 10:1) to give the (*R*)-alcohol **21** (210 mg, 57%) as a colourless oil and the epoxy alcohol **20** (128 mg, 33%) also as a colourless oil. Epoxy alcohol **20**; $[\alpha]_D^{26}$ +69.6 (*c* 1.41, $CHCl_3$); ν_{max}(thin film)/cm^{-1} 725, 770, 822, 905, 940, 1018, 1090, 1105, 1172, 1200, 1250, 1375, 1437, 1455, 1464, 1660, 1740 and 3460; δ_H 0.97 (3H, t, *J* 7.6, 18-H_3), 1.25–1.45 (8H, m, 4-H_2, 5-H_2, 6-H_2 and 7-H_2), 1.54–1.68 (2H, m, 3-H_2), 1.88 (1H, d, *J* 2.5, 11-OH), 1.98–2.20 (4H, m, 8-H_2 and 17-H_2), 2.22–2.47 (4H, m, 2-H_2 and 14-H_2), 2.84 (1H, dd, *J* 2.3 and 2.8, 12-H), 3.05 (1H, dt, *J* 2.3 and 5.4, 13-H), 3.67 (3H, s, CO_2CH_3), 4.66 (1H, m, 11-H), 5.28–5.39 (2H, m, 10-H and 15-H), 5.54 (1H, m, 16-H) and 5.64 (1H, dt, *J* 7.4 and 11.0, 9-H); δ_C 14.0, 20.5, 24.7, 27.7, 28.8, 28.8, 28.9, 29.0, 29.4, 33.9, 51.3, 54.1, 59.7, 64.9, 122.2, 127.1, 134.5, 134.6 and 174.1 [Found: (M^+ − 18), 306.2199. Calc. for $C_{19}H_{30}O_3$: (M^+ − 18), 306.2194]. Its enantiomeric excess was determined to be 94% by HPLC analysis of the corresponding *p*-bromobenzoate, derived from **20** with *p*-bromobenzoyl chloride and pyridine, using the chiral column CHIRALPAK AD (Daicel Chemical Industries, Ltd.) (solvent: 3% propan-2-ol in hexane; retention time: 11.64 min; UV detection at 254 nm). (*R*)-alcohol **21**; its exhibited spectral properties (^{1}H-NMR, IR, MS) were identical with those of compound **19**.

(11*S*,12*S*,13*S*)-(9*Z*,15*Z*)-11-Hydroxy-12,13-epoxyoctadeca-9,15-dienoic acid 1

To a stirred solution of **20** (60 mg, 0.19 mmol) in tetrahydrofuran (2 cm^3) was added 0.5 M aqueous lithium hydroxide (2 cm^3) at room temperature, and the resulting mixture was stirred for 24 h. After addition of brine, the aqueous layer was acidified (pH 1–2) with 1 M aqueous hydrochloric acid, and extracted with a mixture of chloroform–methanol (9:1). The extract was dried over Na_2SO_4. Evaporation of the solvent *in vacuo* gave a residue, which was purified by column chromatography (chloroform–methanol, 30:1) to give **1** (52 mg, 91%) as a colourless oil; $[\alpha]_D^{27}$ +65.2 (*c* 0.81, $CHCl_3$); ν_{max}(thin film)/cm^{-1} 908, 938, 976, 1010, 1055, 1088, 1246, 1280, 1415, 1462, 1655, 1710, 2855, 2930, 3010 and 3420; δ_H 0.97 (3H, t, *J* 7.6, 18-H_3), 1.28–1.40 (8H, m, 4-H_2, 5-H_2, 6-H_2 and 7-H_2), 1.64 (2H, m, 3-H_2), 1.98–2.19 (4H, m, 8-H_2 and 17-H_2), 2.22–2.47 (4H, m, 2-H_2 and 14-H_2), 2.85 (1H, dd, *J* 2.4 and 2.8, 12-H), 3.07 (1H, dt, *J* 2.4 and 5.4, 13-H), 4.67 (1H, dd, *J* 2.8 and 8.6, 11-H), 5.34 (2H, m, 9-H and 10-H), 5.53 (1H, m, 16-H) and 5.65 (1H, dt, *J* 7.4 and 11.0, 15-H); δ_C 14.2, 20.7, 24.6, 27.9, 28.9, 29.0, 29.0, 29.2, 29.5, 34.0, 54.3, 59.9, 65.0, 122.3, 127.0, 135.0, 135.1 and 179.5 [Found: (M^+ − 18), 292.2035. Calc. for $C_{18}H_{28}O_3$: (M^+ − 18), 292.2037].

(11*R*,12*S*,13*S*)-(9*Z*,15*Z*)-11-(*p*-Nitrobenzoyloxy)-12,13-epoxyoctadeca-9,15-dienoic acid methyl ester 22

To a stirred solution of **20** (50 mg, 0.15 mmol), triphenylphosphine (200 mg, 0.77 mmol) and *p*-nitrobenzoic acid (129 mg, 0.77 mmol) in dry toluene (2 cm^3) was added dropwise diethyl azodicarboxylate (0.12 cm^3, 0.77 mmol) at −20 °C under argon. After 1 h, the solvent was concentrated to give a residue that was purified by column chromatography (*n*-hexane–ethyl acetate, 18:1) to give **22** (62 mg, 85%) as a colourless oil; $[\alpha]_D^{27}$ +40.3 (*c* 1.20, $CHCl_3$); ν_{max}(thin film)/cm^{-1} 832, 875, 934, 1001, 1015, 1115, 1171, 1198, 1268, 1320, 1350, 1410, 1437, 1460, 1528, 1608, 1655, 1730, 2858 and 2930; δ_H 0.97 (3H, t, *J* 7.6, 18-H_3), 1.25–1.44 (8H, m, 4-H_2, 5-H_2, 6-H_2 and 7-H_2), 1.52–1.66 (2H, m, 3-H_2), 2.05 (2H, dq, *J* 6.8 and 7.6, 17-H_2), 2.14–2.51 (6H, m, 2-H_2, 8-H_2 and 14-H_2), 2.96 (1H, dt, *J* 2.1 and 5.3, 13-H), 3.08 (1H, dd, *J* 2.1 and 6.4, 12-H), 3.67 (3H, s, CO_2CH_3), 5.31 (1H, m, 15-H), 5.47–5.64 (3H, m, 10-H, 11H and 16-H), 5.75 (1H, ddd, *J* 7.4, 7.6 and 10.7, 12-H), 8.22 and 8.29 (each 2H, each dt, *J* 2.1 and 8.9, *o*- and *m*-PhH) (Found: M^+, 473.2405. Calc. for $C_{26}H_{35}NO_7$: M^+, 473.2412).

(11*R*,12*S*,13*S*)-(9*Z*,15*Z*)-11-Hydroxy-12,13-epoxyoctadeca-9,15-dienoic acid 2

To a stirred solution of **22** (50 mg, 0.11 mmol) in tetrahydrofuran (2 cm^3) was added 0.5 M aqueous lithium hydroxide (2 cm^3) at room temperature, and the resulting mixture was stirred for 24 h. After addition of brine, the aqueous layer was acidified (pH 1–2) with 1 M aqueous hydrochloric acid, and extracted with a mixture of chloroform–methanol (9:1). The extract was dried over Na_2SO_4, and concentrated *in vacuo* to give a residue, which was purified by column chromatography (chloroform–methanol, 30:1) to give **2** (29 mg, 89%) as a colourless oil; $[\alpha]_D^{29}$ −54.2 (*c* 0.51, $CHCl_3$); ν_{max}(thin film)/cm^{-1} 862, 904, 932, 1024, 1080, 1244, 1282, 1412, 1464, 1655, 1710, 2858, 2930, 3050 and 3420; δ_H 0.97 (3H, t, *J* 7.6, 18-H_3), 1.25–1.42 (8H, m, 4-H_2, 5-H_2, 6-H_2 and 7-H_2), 1.57–1.68 (2H, m, 3-H_2), 1.98–2.15 (4H, m, 8-H_2 and 17-H_2), 2.23–2.47 (4H, m, 2-H_2 and 14-H_2), 2.85 (1H, dd, *J* 2.3 and 5.3, 12-H), 2.99 (1H, dt, *J* 2.3 and 5.4, 13-H), 4.29 (1H, dd, *J* 5.3 and 8.6, 11-H), 5.33 (1H, m, 10-H) and 5.43–5.66 (3H, m, 9-H, 15-H and 16-H); δ_C 14.2, 20.7, 24.9, 28.1, 29.0, 29.0, 29.1, 29.1, 29.3, 34.1, 55.4, 57.8, 69.6, 122.6, 131.7, 135.1, 137.3 and 174.4 [Found: (M^+ − 18), 292.2034. Calc. for $C_{18}H_{28}O_3$: (M^+ − 18), 292.2037].

(11*S*,12*R*,13*R*)-(9*Z*,15*Z*)-13-Acetoxy-11,12-dihydroxyoctadeca-9,15-dienoic acid methyl ester 25

Tetramethylammonium triacetoxyborohydride (45.6 mg, 0.17 mmol) was added to a stirred solution of *ent*-**20** (51 mg, 0.16 mmol) in dry tetrahydrofuran (5 cm^3) at room temperature, and the mixture was heated at reflux for 4 h. After cooling, saturated aqueous ammonium chloride was added, and the mixture was extracted with ethyl acetate. The combined extracts were washed with brine and dried over Na_2SO_4. Concentration of the solvent *in vacuo* gave a residue, which was purified by column chromatography (*n*-hexane–ethyl acetate, 2:1) to give **25** (52.6 mg, 87%) as a colourless oil; $[\alpha]_D^{23}$ −3.9 (*c* 0.936, $CHCl_3$); ν_{max}(thin film)/cm^{-1} 1028, 1048, 1175, 1205, 1240, 1372, 1437, 1462, 1740, 2858, 2930 and 3460; δ_H 0.96 (3H, t, *J* 7.6, 18-H_3), 1.26–1.40 (8H, m, 4-H_2, 5-H_2, 6-H_2 and 7-H_2), 1.61 (2H, m, 3-H_2), 1.77 (1H, br, 11-OH), 1.98–2.15 (7H, m, 8-H_2, 17-H_2 and $COCH_3$), 2.30 (2H, t, *J* 7.5, 2-H_2), 2.47 (1H, m, 12-OH), 2.51 (2H, dd, *J* 6.3 and 7.3, 14-H_2), 3.67 (3H, s, CO_2CH_3), 3.81 (1H, dt, *J* 4.4 and 5.9, 12-H), 4.51 (1H, dt, *J* 4.4 and 8.8, 11-H), 4.94 (1H, q, *J* 5.9, 13-H), 5.35 (1H, dtt, *J* 1.5, 7.3 and 10.9, 15-H), 5.51 (2H, m, 10-H and 16-H) and 5.67 (1H, dt, *J* 7.4 and 11.0, 9-H); δ_C 14.2, 20.6, 21.1, 24.8, 27.6, 27.8, 28.9, 29.0, 29.3, 34.0, 51.4, 68.0, 73.9, 74.3, 123.3, 126.8, 134.6, 135.5, 170.4 and 174.3 [Found: (M^+ − 60), 324.2303. Calc. for $C_{19}H_{32}O_4$: (M^+ − 60), 324.2301].

(11*S*,12*R*,13*R*)-(9*Z*,15*Z*)-11,12,13-Trihydroxyoctadeca-9,15-dienoic acid 3

To a stirred solution of **25** (47 mg, 0.12 mmol) in tetrahydrofuran (2 cm^3) was added 1 M aqueous lithium hydroxide (2 cm^3) at room temperature, and the resulting mixture was stirred for 6 h. After addition of brine, the aqueous layer was acidified (pH 1–2) with 1 M aqueous hydrochloric acid, and extracted with a mixture of chloroform–methanol (9:1). The extract was dried over Na_2SO_4. Evaporation of the solvent *in vacuo* gave a residue, which was purified by column chromatography (chloroform–methanol, 8:1) to give **3** (39 mg, 97%) as a colourless oil; $[\alpha]_D^{24}$ −16.8 (*c* 0.78, $CHCl_3$); ν_{max}(thin film)/cm^{-1} 874, 1025, 1066, 1216, 1248, 1280, 1408, 1460, 1655, 1710, 2848, 2930, 3010 and 3400; δ_H 0.97 (3H, t, *J* 7.6, 18-H_3), 1.24–1.42 (8H, m, 4-H_2, 5-H_2, 6-H_2 and 7-H_2), 1.62 (2H, m, 3-H_2), 2.05–2.22 (4H, m, 8-H_2 and 17-H_2), 2.33 (2H, t, *J* 7.3, 2-H_2), 2.38 (1H, m, 14-Ha), 2.49 (1H, m, 14-Hb), 3.53 (1H, dd, *J* 5.6 and 6.9, 12-H), 3.69 (1H, m, 13-H), 4.63 (1H, dd, *J* 5.6 and 9.1,

11-H), 5.47 (2H, m, 9-H and 10-H), 5.61 (1H, dt, *J* 7.3 and 11.0, 16-H) and 5.69 (1H, dt, *J* 7.4 and 11.0, 15-H); δ_C 14.1, 20.6, 24.5, 27.7, 28.7, 28.7, 28.7, 29.2, 31.2, 33.8, 69.6, 73.0, 75.3, 123.9, 127.5, 135.7, 135.7 and 178.8 [Found: $(M^+ - 18)$, 310.2145. Calc. for $C_{18}H_{30}O_4$: $(M^+ - 18)$, 310.2144].

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