Formal Syntheses of Hepoxilin B_3, Trioxilin B_3 and Substances Effective against Rice Blast Disease and Total Syntheses of 11(*R*),12(*S*),13(*S*)-Trihydroxyoctadeca-9(*Z*),15(*Z*)-dienoic Acid

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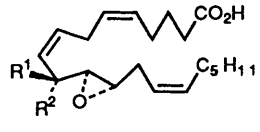
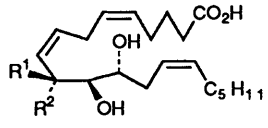
The stereoselective conversion of readily available tri-*O*-isopropylidene-D-mannitol into the known synthetic intermediates for preparation of oxygenated fatty acids **1a**, **1b**, **2a**, **2b** and **3a**, **3b** is described. Total synthesis of fatty acid **4a** and preparation of the known intermediate for producing another substance effective against rice blast disease, **4b**, from D-xylose are also reported. These syntheses are based on a strategy of selective cleavage of isopropylidene acetals and lactol-formation-induced epimerization.

Oxygenated metabolites of unsaturated fatty acids play various important roles in biological systems, either in animals or in plants.[1] For example, hepoxilin B_3 (**1a**, **1b**) and trioxilin B_3 (**2a**, **2b**), which arise from (12*S*)-12-hydroperoxyeicosatetraenoic acid [12(*S*)-HPETE], are found to be presynaptic messengers in *Aplysia* sensory cells[2] and pancreatic insulin secretagogues.[3] Both hepoxilin B_3 and trioxilin B_3 consist of two C_{10} diastereoisomers.[4] Several polyoxygenated C_{18} fatty acids, such as compounds **3a**, **3b** and **4a**, **4b**, have been isolated from rice plants suffering from rice blast disease, and proved to be self-defensive substances against the disease.[5]



1a R^1 = H, R^2 = OH
1b R^1 = OH, R^2 = H

Hepoxilin B_3



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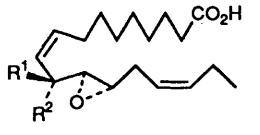
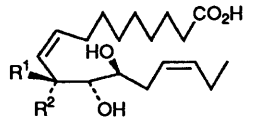
2b R^1 = OH, R^2 = H

Trioxilin B_3



3a R^1 = H, R^2 = OH
3b R^1 = OH, R^2 = H



4a R^1 = H, R^2 = OH
4b R^1 = OH, R^2 = H

Substances effective against rice blast disease

Owing to the need for biological evaluation and their limited availability from natural sources, syntheses of these compounds are of importance and have been realized independently by us[6-9] and by other groups.[2,10-15] Carbohydrates are widely used as chiral precursors for enantiomerically pure compounds.[16] Recently, we[17] have developed an efficient one-pot procedure for the selective hydrolysis of terminal isopropylidene acetal and subsequent oxidative cleavage of glycol. With the method in hand, we thought that isopropylidene derivatives of sugars would be of interest in the design of a general synthesis which would allow the preparation of all these structurally similar compounds.

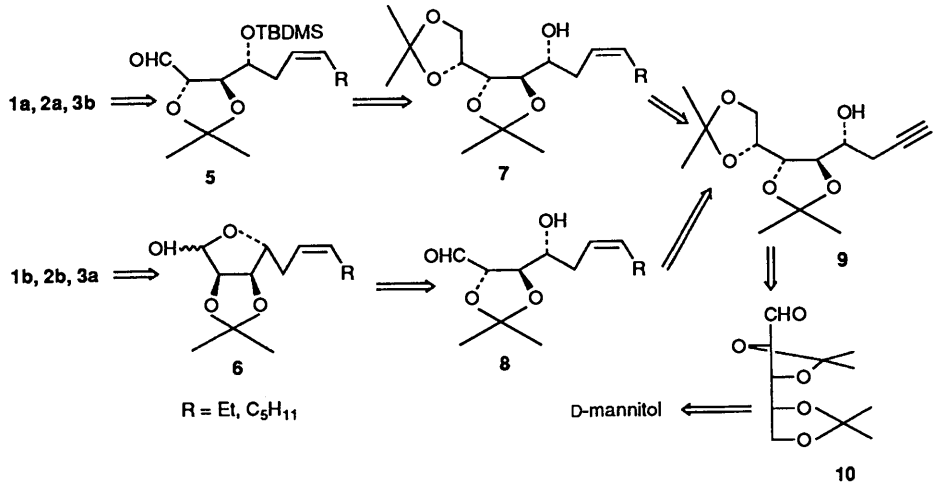
Syntheses of Compounds **1a**, **b**–**3a**, **b** *from* D-*Mannitol*.[18]—The synthesis of compounds **1a**, **1b**, **2a**, **2b**, **3a**, **3b** has already been achieved in our laboratory *via* intermediates **5** and **6** starting from D-(−)-tartaric acid and D-mannose respectively.[6-9] Retrosynthetic reasoning is depicted (Scheme 1) where **1a** (**2a**, **3b**) and **1b** (**2b**, **3a**) can be selectively obtained from compounds **5** and **6**, respectively, by a Wittig olefination followed by conventional transformations. The key aldehyde and lactol intermediates **5** and **6** in turn originate from a common chiral intermediate **9**. The two stereocentres, *i.e.* C-3 and C-4 in compound **9**, can be transferred from C-3 and C-4 of tri-*O*-isopropylidene-D-mannitol with a defined configuration. Access to the stereocentre present at C-5 in compound **9** can be obtained by a stereoselective reaction[6] by using aldehyde **10**.

The known aldehyde **10**,[19] readily prepared from 1,2:3,4:5,6-tri-*O*-isopropylidene-D-mannitol in an improved yield (58% + 31% recovered starting material) by exposure to periodic acid in diethyl ether,[17] was treated with prop-2-ynyl bromide in the presence of zinc dust[6] to give compound **9** as the sole product in 86% yield after chromatography. Substitution of terminal alkyne **9** with ethyl bromide (pentyl bromide) yielded compound **11a** (**11b**) in 87 (75%) yield. Partial hydrogenation of alkyne **11a** (**11b**) in the presence of Lindlar catalyst afforded alkene **7a** (**7b**) in 93 (94%) yield. After silylation of the free hydroxy group of alcohol **7a** (**7b**), selective hydrolysis and subsequent periodate cleavage using our one-pot reaction[17] afforded aldehyde **5a** (**5b**) in 86 (85%) in two steps (Scheme 2).

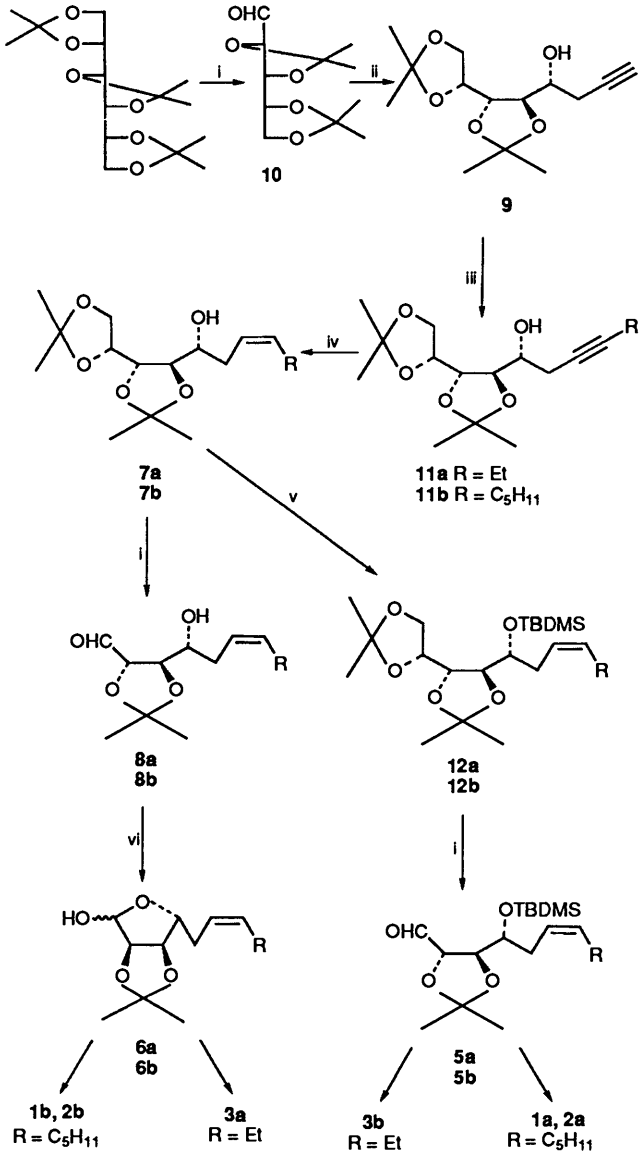
When ethereal periodic acid[17] was used, the transformation of alcohol **7a** (**7b**) into aldehyde **8a** (**8b**) *via* selective hydrolysis of the terminal isopropylidene ketal followed by glycol cleavage proceeded in one pot in 93 (89%) yield. Although epimerization of the acetonide of the *erythro*-2,3-dihydroxy aldehyde to the more stable *threo*-2,3-dihydroxy acetonide is known,[20] the reversed transformation has not yet appeared in the literature. It is clear that in the presence of a γ-OH group, the acetonide of the *threo*-2,3-dihydroxy aldehyde could be transformed into the *cis*-fused five-membered ring lactol with C-2 epimerization. Thus, treatment of **8a** (**8b**) with 3 mol equiv. of potassium carbonate in methanol at room temperature effected a smooth epimerization, providing the known lactol **6a** (**6b**)[8,9] in 84 (80%) yield.

Syntheses of Fatty Acids **4a** *and* **4b** *from* D-*Xylose*.—Synthesis of fatty acids **4a** and **4b** can be achieved in a similar way to that described above by using D-xylose as a chiral precursor (Scheme 3).

First, D-xylose was converted into the diethyl dithioacetal **13** according to the literature procedure.[21] Using the method



Scheme 1



Scheme 2 TBDMS = $SiMe_2Bu^t$. *Reagents:* i, H_5IO_6, Et_2O; ii, Zn, $BrCH_2C{\equiv}CH$; iii, BuLi, THF, HMPA, EtBr ($C_5H_{11}Br$); iv, H_2, Pd–Pb–$CaCO_3$; v, TBDMSCl, imidazole; vi, K_2CO_3, MeOH

developed by Fuchs,[22] the aldehyde **14** was obtained in almost quantitative yield. From aldehyde **14** on, the syntheses of acids **4a** and **4b** were pursued by analogy to the sequences for the preparation of epoxy acids **3a** and **3b** (Scheme 3).

The aldehyde **14** was treated with prop-2-ynyl bromide and zinc dust in dimethylformamide (DMF)–diethyl ether[6] to give the alkynylol **15** as an oil in 91% yield, which according to NMR spectroscopy still had a minor allene impurity (< 5%) inseparable by chromatography. The reaction was stereospecific and the *threo* product was not detected. Alkylation of compound **15** afforded compound **16** in 88% yield. Semihydrogenation of alkyne **16** gave the alkene **17** in 95% yield. After silylation of the free hydroxy group of compound **17**, hydrolytic cleavage with ethereal periodic acid furnished aldehyde **19** in 91% yield.

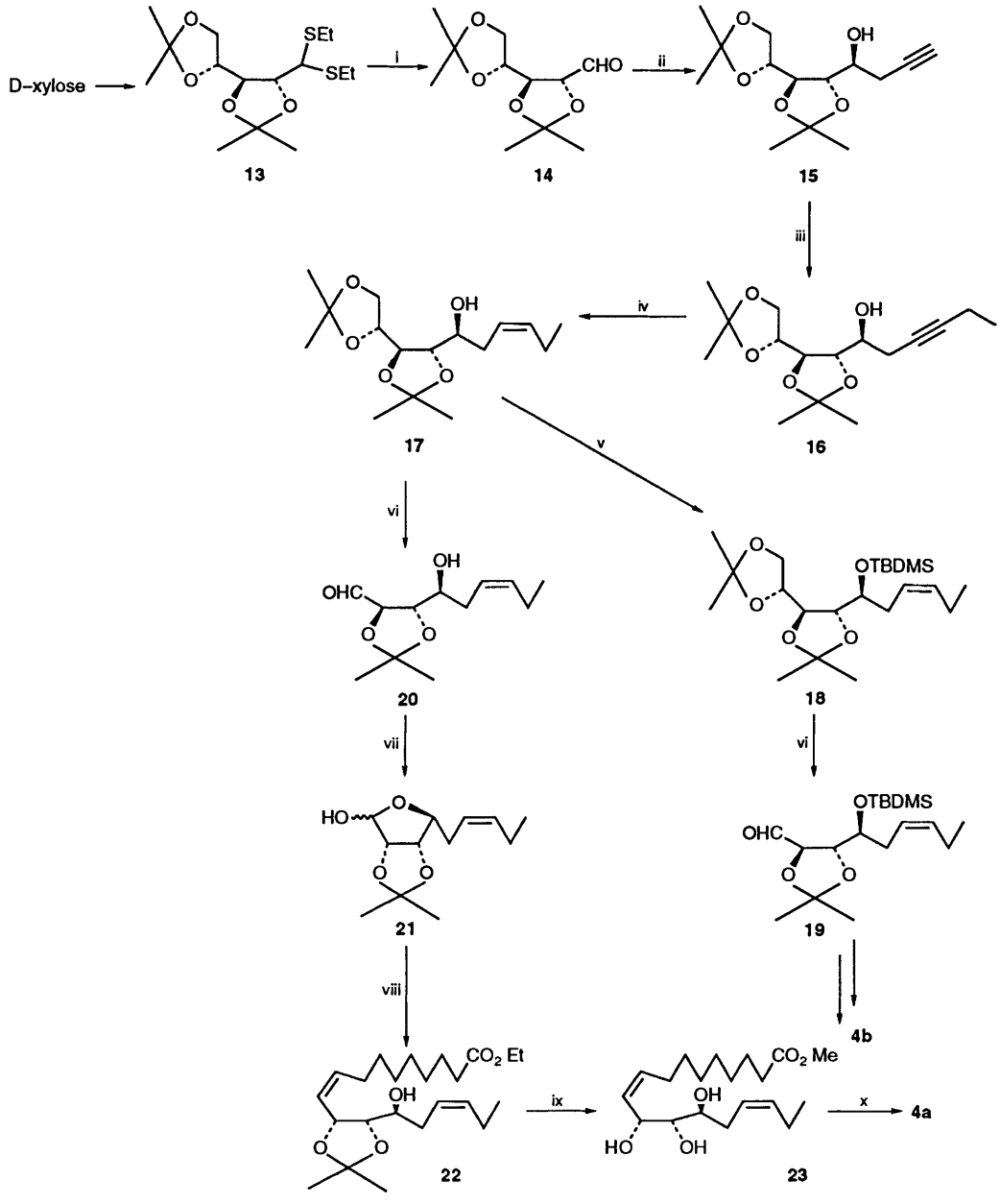
When diketal **17** was directly exposed to ethereal periodic acid,[17] aldehyde **20** was obtained and this was then treated with potassium carbonate in methanol to give lactol **21** following C-2 epimerization. Wittig reaction of lactol **21** with ethyl 9-(triphenylphosphorylidene)nonanoate under *cis*-olefination conditions led to the (*Z*,*Z*)-product **22** in 52% yield after chromatography. Deketalization of compound **22** accompanied with the ester exchange during treatment with toluene-*p*-sulfonic acid (PTSA) in MeOH afforded the known triol enoate **23**, whose ^1H NMR spectrum is in full accord with that reported in the literature.[11] Further saponification of methyl ester **23** with KOH in MeOH gave fatty acid **4a** in 80% yield.

The further reaction sequences of compounds **5a**, **5b**, **6a**, **6b** and **19** to acidic products **1a**, **1b**, **2a**, **2b**, **3a**, **3b** and **4b** have been established by us.[6–9] Thus, syntheses of aldehydes **5a** (**5b**), **19** and lactols **6a** (**6b**) formally constitute the syntheses of acids **1a**, **1b**, **2a**, **2b**, **3a**, **3b** and **4b**. These syntheses take advantage of conciseness, efficiency and high overall yield. Further exploitation of this strategy for the syntheses of other natural products is in progress in our laboratory.

Experimental

IR spectra were recorded with a Shimadzu 440 spectrometer. ^1H NMR spectra were recorded with $SiMe_4$ as internal standard at 200 MHz on a Varian XL-200 spectrometer or at 300 MHz on an AMX-300 MHz spectrometer. *J* Values are given in Hz. Mass spectra were obtained on a Finnigan 4201 spectrometer. Optical rotations were measured on a Perkin-Elmer 241 MS Autopol polarimeter, and $[\alpha]_D$ values are given in units of 10^{-1} deg cm^2 g^{-1}. Flash column chromatography was performed on silica gel H (10–40 μ), and with light petroleum (60–90 °C)–ethyl acetate system as eluent.

2,3:4,5-*Di*-O-*isopropylidene*-D-arabino-*pentose* **10**.—Tri-*O*-isopropylidene-D-mannitol (3.02 g, 10 mmol) was added at



Scheme 3 *Reagents:* i, HgO, BF_3; ii, Zn, prop-2-ynyl bromide; iii, BuLi, THF–HMPA, EtBr; iv, H_2, Pd–Pb–$CaCO_3$; v, TBDMSCl, imidazole; vi, H_5IO_6, Et_2O; vii, K_2CO_3, MeOH; viii, $Br^-Ph_3P^+[CH_2]_8CO_2Et$, $KN(SiMe_3)_2$; ix, PTSA, MeOH; x, KOH, MeOH

room temperature under nitrogen to a well stirred suspension of periodic acid (2.96 g, 13 mmol) in dry diethyl ether. The mixture was stirred overnight and the reaction mixture was worked up by simple filtration and evaporation of the solution. The residue was chromatographed to give aldehyde **10** (1.33 g, 58%) and the starting material (0.94 g, 31% recovery).

1,1,2,2-*Tetrahydro*-1,2,3-*trideoxy*-5,6:7,8-*di*-O-*isopropylidene*-D-manno-*octitol* **9**.—To a stirred mixture of aldehyde **10** (5.6 g, 24.3 mmol) and prop-2-ynyl bromide (4.2 g, 35 mmol) in DMF–Et_2O (1:1; 80 cm^3) was slowly added zinc dust (3.3 g, 50 mmol). An exothermic reaction started within a few minutes and the reflux was allowed to continue until most of compound **10** had been consumed. Then, the reaction mixture was poured into saturated aq. NH_4Cl. Usual work-up and chromatography yielded title compound **9** (5.64 g, 86%), $[\alpha]_D^{20}$ +10.7 (*c* 0.8, $CHCl_3$); ν_{max}(film)/cm^{-1} 3450 (OH), 3290 (≡CH), 1380 and 1370; δ_H(200 MHz; $CDCl_3$) 1.38 (6 H, s), 1.43 (3 H, s), 1.47 (3 H, s), 2.07 (1 H, t, *J* 2), 2.4–2.6 (2 H, m) and 3.70–4.25 (6 H, complex m); *m/z* 271 (M^+ + 1, 3.7%), 255 (M^+ − Me, 45.5), 253 (M^+ + 1 − H_2O, 2) and 43 (100) (Found: C, 62.4; H, 8.2%. Calc. for $C_{14}H_{22}O_5$: C, 62.20; H, 8.20).

3,3,4,4-*Tetrahydro*-1,2,3,4,5-*pentadeoxy*-7,8:9,10-*di*-O-*isopropylidene*-D-manno-*decitol* **11a**.—To a stirred solution of compound **9** (2.70 g, 10 mmol) in dry tetrahydrofuran (THF) (60 cm^3) was added BuLi (2.5 mol dm^{-3}; 23 mmol) dropwise at −50 °C. After being stirred for 30 min at −30 °C, the mixture was cooled to −50 °C and a solution of EtBr (1.6 g, 15 mmol) in hexamethylphosphoric triamide (HMPA) (8 cm^3) was added. The mixture was stirred for 1 h at −50 °C and warmed from −50 to 10 °C overnight. The reaction was quenched with saturated aq. NH_4Cl, and the aqueous layer was extracted with diethyl ether. The organic layers were combined, washed with brine, dried over Na_2SO_4, and evaporated. The residue was chromatographed to give compound **11a** (2.58 g, 87%), $[\alpha]_D^{20}$ +10.2 (*c* 0.4, $CHCl_3$); ν_{max}(film)/cm^{-1} 3450 (OH), 1380 and 1370; δ_H(200 MHz; $CDCl_3$) 1.14 (3 H, t, *J* 6), 1.38–1.50 (12 H, m,

4 × Me), 2.20 (2 H, m, 2.3–2.50 (2 H, m) and 3.70–4.25 (6 H, complex m); *m/z* 299 ($M^+ + 1$, 55%), 283 ($M^+ - Me$, 51) and 241 ($M^+ + 1 - H_2O - C_3H_4$, 100) (Found: C, 64.0; H, 8.5. Calc. for $C_{16}H_{26}O_5$: C, 64.40; H, 8.78%).

6,6,7,7-*Tetrahydro*-1,2,3,4,5,6,7,8-*octadeoxy*-10,11:12,13-*di*-O-*isopropylidene*-D-manno-*tridecitol* **11b**.—A procedure similar to that described above using pentyl bromide instead of EtBr, was followed, to give compound **11b** in 75% yield from terminal alkyne **9**; $[\alpha]_D^{20}$ +10.3 (*c* 0.3, $CHCl_3$); ν_{max}(film)/cm^{-1} 3450 (OH), 1380 and 1370; δ_H(200 MHz; $CDCl_3$) 0.89 (3 H, t, *J* 7), 1.25–1.60 (18 H, m with 4 s), 2.15 (2 H, m), 2.4–2.7 (2 H, m) and 3.65–4.20 (6 H, m); *m/z* 341 ($M^+ + 1$, 19%), 325 ($M^+ - Me$, 65), 323 ($M^+ + 1 - H_2O$, 1.5) and 173 (100) (Found: C, 67.25; H, 9.7. Calc. for $C_{19}H_{32}O_5$: C, 67.03; H, 9.47%).

(Z)-1,2,3,4,5-*Pentadeoxy*-7,8:9,10-*di*-O-*isopropylidene*-D-manno-*dec*-3-*enitol* **7a**.—The alkyne **11a** (2.09 g, 7 mmol) was hydrogenated under atmospheric pressure using Lindlar catalyst (0.3 g) in ethyl acetate (60 cm^3) in the presence of quinoline (0.1 g). After uptake of the theoretical amount of hydrogen, the mixture was filtered, and the filtrate was washed successively with 2 mol dm^{-3} HCl and aq. $NaHCO_3$, dried over Na_2SO_4, and evaporated. Chromatography of the residue produced the corresponding alkene compound **7a** (1.96 g, 93%), $[\alpha]_D^{20}$ +6.6 (*c* 0.6, $CHCl_3$); ν_{max}(film)/cm^{-1} 3450 (OH), 1380 and 1370; δ_H(200 MHz; $CDCl_3$) 0.98 (3 H, t, *J* 7.5), 1.36 (6 H, s), 1.38 (3 H, s), 1.44 (3 H, s), 2.10 (2 H, m), 2.26–2.55 (2 H, m), 3.65–3.74 (3 H, m), 4.0–4.35 (3 H, m) and 5.52 (2 H, m); *m/z* 301 ($M^+ + 1$, 10%), 285 ($M^+ - Me$, 27), 283 ($M^+ + 1 - H_2O$, 1) and 185 (100) (Found: C, 63.9; H, 9.5. Calc. for $C_{16}H_{28}O_5$: C, 63.98; H, 9.39%).

(Z)-1,2,3,4,5,6,7,8-*Octadeoxy*-10,11:12,13-*di*-O-*isopropylidene*-D-manno-*tridec*-6-*enitol* **7b**.—In the same way, compound **7b** was obtained in 94% yield from the alkyne derivative **11b**; $[\alpha]_D^{20}$ +5.6 (*c* 0.46, $CHCl_3$); ν_{max}(film)/cm^{-1} 3460 (OH), 1380 and 1370; δ_H(300 MHz; $CDCl_3$) 0.89 (3 H, t, *J* 6.8), 1.25–1.50 (18 H, m with 4 s), 2.04 (2 H, m), 2.25–2.56 (2 H, m), 3.70 (3 H, m), 3.9–4.20 (3 H, m) and 5.54 (2 H, m); *m/z* 342 (M^+, 1.4%), 328 ($M^+ + 1 - Me$, 35.2), 231 (61.8) and 173 (100) (Found: C, 66.3; H, 10.4. Calc. for $C_{19}H_{34}O_5$: C, 66.64; H, 10.00%),

(Z)-6-O-tert-*Butyldimethylsilyl*-1,2,3,4,5-*pentadeoxy*-7,8:9,10-*di*-O-*isopropylidene*-D-manno-*dec*-3-*enitol* **12a**.—A mixture of compound **7a** (0.45 g, 1.5 mmol), TBDMSCl (0.31 g, 1.95 mmol) and imidazole (0.41 g, 6 mmol) in DMF (8 cm^3) was stirred at room temperature overnight. The mixture was diluted with Et_2O (30 cm^3) and water (30 cm^3), and the aqueous layer was separated. The organic layer was washed successively with 5% aq. $NaHCO_3$ and brine, and dried with Na_2SO_4. After evaporation of the solvent under reduced pressure, the residue was purified by flash chromatography to give compound **12a** (0.575 g, 93%), $[\alpha]_D^{20}$ −3.1 (*c* 0.45, $CHCl_3$); ν_{max}(film)/cm^{-1} 2960, 1380 and 1370; δ_H(300 MHz; $CDCl_3$) 0.1 (6 H, s), 0.90 (9 H, s), 0.96 (3 H, *J* 7.5), 1.34 (3 H, s), 1.35 (3 H, s), 1.40 (3 H, s), 1.41 (3 H, s), 2.05 (2 H, m), 2.36 (2 H, m), 3.8–4.20 (6 H, m) and 5.43 (2 H, m); *m/z* 414 (M^+, 0.24%), 400 ($M^+ + 1 - Me$, 22.2), 240 (14.6) and 100 (100) (Found: C, 63.4; H, 10.4. Calc. for $C_{22}H_{42}O_5Si$: C, 63.73; H, 10.21%).

(Z)-9-O-tert-*Butyldimethylsilyl*-1,2,3,4,5,6,7,8-*octadeoxy*-10,11:12,13-*di*-O-*isopropylidene*-D-manno-*tridec*-6-*enitol* **12b**.—The same procedure for producing compound **12a** was followed, starting from the alcohol **7b** (0.45 g, 1.32 mmol). The crude product was purified by flash chromatography to give compound **12b** (0.55 g, 92%), $[\alpha]_D^{20}$ −2.8 (*c* 0.46, $CHCl_3$); ν_{max}(film)/cm^{-1} 2920, 1380 and 1370; δ_H(300 MHz; $CDCl_3$) 0.12 (6 H, s), 0.91 (3 H, t + 9 H, s), 1.3–1.50 (18 H), 2.07 (2 H, m), 2.39 (2 H, m), 3.80–4.20 (6 H, m) and 5.48 (2 H, m); *m/z* 456 (M^+, 0.22%), 441 ($M^+ - Me$, 7), 400 (4), 341 ($M^+ - SiMe_2Bu^t$, 59.6) and 73 (100) (Found: C, 65.4; H, 10.25. Calc. for $C_{25}H_{48}O_5Si$: C, 65.74; H, 10.60%).

(Z)-4-O-tert-*Butyldimethylsilyl*-5,6,7,8,9-*pentadeoxy*-2,3-O-*isopropylidene*-arabino-*non*-6-*enose* **5a**.—Compound **12a** (0.414 g, 1 mmol) was exposed to ethereal periodic acid (0.342 g 1.5 mmol) according to the procedure for producing substrate **10**, to yield title compound **5a** (0.31 g, 91%), $[\alpha]_D^{20}$ −29.2 (*c* 0.54, $CHCl_3$); ν_{max}(film)/cm^{-1} 2720, 1730, 1380 and 1370; δ_H(300 MHz; $CDCl_3$) 0.09 (6 H s), 0.90 (9 H, s), 0.96 (3 H, t, *J* 7.5), 1.34 (3 H, s), 1.49 (3 H, s), 2.05 (2 H, m), 2.15–2.45 (2 H, m), 3.92 (1 H, dt, *J* 4.4 and 6.3), 4.09 (1 H, dd, *J* 6.4 and 4.4), 4.42 (1 H, dd, *J* 7.1 and 1.7), 5.45 (2 H, m) and 9.76 (1 H, d, *J* 1.7); *m/z* 342 (M^+, 0.25%), 327 ($M^+ - Me$, 1.5), 273 ($M^+ - C_5H_9$, 35.6) and 227 ($M^+ - SiMe_2Bu^t$, 60) (Found: *m/z* 273.1550. Calc. for $C_{13}H_{25}O_4Si$: *m/z* 273.1522).

(Z)-4-O-tert-*Butyldimethylsilyl*-5,6,7,8,9,10,11,12-*octadeoxy*-2,3-O-*isopropylidene*-arabino-*dodec*-6-*enone* **5b**.—In the same way, compound **5b** was obtained from bisketal **12b** (0.456 g, 1 mmol) in 92% yield; $[\alpha]_D^{20}$ −29.6 (*c* 0.42, $CHCl_3$); ν_{max}(film)/cm^{-1} 2720, 1730, 1380 and 1370; δ_H(300 MHz; $CDCl_3$) 0.06 (6 H, s), 0.93 (12 H, t + s), 1.2–1.50 (6 H, m), 1.33 (3 H, s), 1.49 (3 H, s), 2.03 (2 H, m), 2.15–2.45 (2 H, m), 3.91 (1 H, dt, *J* 4.1 and 4.9), 4.09 (1 H, dd, *J* 6.7 and 4.1), 4.42 (1 H, dd, *J* 6.7 and 2), 5.45 (2 H, m) and 9.76 (1 H, d, *J* 1.5) (Found: *m/z* 287.1719. Calc. for $C_{14}H_{27}O_4Si$: *m/z* 287.1679).

(Z)-5,6,7,8,9-*Pentadeoxy*-2,3-O-*isopropylidene*-D-arabino-*non*-6-*enose* **8a**.—A procedure similar to that described for the hydrolytic cleavage of compound **10** with ethereal periodic acid was followed. Starting from bisketal **7a** (0.6 g, 2 mmol), compound **8a** (0.425, g, 93%) was isolated as an oil, $[\alpha]_D^{20}$ −8.9 (*c* 0.3, $CHCl_3$); ν_{max}(film)/cm^{-1} 3400br (OH), 1725, 1660, 1380 and 1370; δ_H(300 MHz; $CDCl_3$) 0.97 (3 H, t, *J* 7), 1.35–1.55 (6 H, 2 × Me), 2.05 (2 H, m), 2.2–2.55 (2 H, m), 3.5–4.2 (3 H, m), 4.7–5.2 (OH) and 5.50 (2 H, m); *m/z* 229 ($M^+ + 1$, 10.7%), 211 ($M^+ + 1 - H_2O$, 4.7), 171 (25) and 59 (100) (Found: M^+, 228.1354. Calc. for $C_{12}H_{20}O_4$: M, 1362).

(Z)-5,6,7,8,9,10,11,12-*Octadeoxy*-2,3-O-*isopropylidene*-D-arabino-*dodec*-6-*enone* **8b**.—In the same way, aldehyde **8b** was obtained in 89% yield from bisketal **7b** (0.342 g, 1 mmol), $[\alpha]_D^{20}$ −10.1 (*c* 0.5, $CHCl_3$); ν_{max}(film)/cm^{-1} 3400br (OH), 1730, 1380 and 1370; δ_H(300 MHz; $CDCl_3$) 0.89 (3 H, t, *J* 6.9), 1.2–1.52 (12 H), 2.06 (2 H, m), 2.2–2.54 (2 H, m), 3.5–4.2 (3 H, m), 4.7–5.2 (OH), 5.50 (2 H, m) and 9.80 (1 H, d, *J* 1.1); *m/z* 270 (M^+, 0.7%), 255 ($M^+ - Me$, 3) and 60 (100) (Found: M^+, 270.1909. Calc. for $C_{15}H_{26}O_4$: M, 270.1831).

(Z)-5,6,7,8,9-*Pentadeoxy*-2,3-O-*Isopropylidene*-D-ribo-*non*-6-*enofuranose* **6a**.—Compound **8a** (0.342 g, 1.5 mmol) was treated with K_2CO_3 (0.63 g, 4.5 mmol) under nitrogen for 24 h at room temperature. Usual work-up and purification by chromatography yielded the known lactol **6a** (0.287 g, 84%). The spectroscopic data are in full accord with those reported previously.[9]

(Z)-5,6,7,8,9,10,11,12-*Octadeoxy*-2,3-O-*isopropylidene*-D-ribo-*dodec*-6-*enofuranose* **6b**.—In the same way, aldehyde **8b** was converted into the known lactol **6b**[8] in 80% yield.

2,3:4,5-*Di*-O-*isopropylidene*-D-*xylose* **14**.—Red mercury(II) oxide (17.3 g, 80 mmol, 2 mol equiv.), boron trifluoride–diethyl

ether (9.77 g, 80 mmol, 2 mol equiv.) and 85% aq. THF (80 cm^3) were stirred vigorously in a flask. A solution of the dithioacetal **13** (13.5 g, 40 mmol) in THF (30 cm^3) was added over the course of 30 min under nitrogen. The mixture was stirred for 1 h after the addition was complete. During this time the red mercury(II) oxide gradually dissolved. Diethyl ether (450 cm^3) was added and the reaction mixture was neutralized with anhydrous sodium carbonate (28 g). The salts were removed by filtration, and the filtrate was concentrated to give title compound **14** as a syrup (9.0 g, 97%). This material was immediately used in the next step.

7,7,8,8-*Tetrahydro*-6,7,8-*trideoxy*-1,2:3,4-*di*-O-*isopropylidene*-L-gluco-*octitol* **15**.—A procedure similar to that described for compound **9** was followed. Starting from compound **14** (8.8 g, 38.3 mmol), the title product (9.4 g, 91% **15**; contaminated with a little of the isomeric allene compound) was obtained, ν_{max}(film)/cm^{-1} 3450, 3290, 2100, 1380 and 1370; δ_H(300 MHz; $CDCl_3$) 1.39 (6 H, s), 1.43 (3 H, s), 1.46 (3 H, s), 2.08 (1 H, t, *J* 2), 2.4–2.7 (2 H, m) and 3.7–4.4 (6 H, complex m); *m/z* 270 (M^+, 0.3%), 254 ($M^+ - 1 - Me$, 51.7), 201 (11.4) and 59 (100) (Found: *m/z* 255.1194. Calc. for $C_{13}H_{19}O_5$; *m/z* 255.1232).

7,7,8,8-*Tetradehydro*-6,7,8,9,10-*pentadeoxy*-1,2:3,4-*di*-O-*isopropylidene*-L-gluco-*decitol* **16**.—A procedure similar to that described for the preparation of compound **11a** was followed. Starting from compound **15** (5.4 g, 20 mmol), compound **16** (5.24 g, 88%) was obtained, $[\alpha]_D^{20}$ −17.3 (*c* 0.45, $CHCl_3$); ν_{max}(film)/cm^{-1} 3450, 1380 and 1370; δ_H(300 MHz; $CDCl_3$) 1.13 (3 H, t, *J* 7.6), 1.39 (6 H, s), 1.44 (3 H, s), 1.45 (3 H, s), 2.18 (2 H, m), 2.35–2.65 (2 H, m), 3.67 (1 H, m), 3.90 (2 H, m), 4.05 (2 H, m) and 4.24 (1 H, m); *m/z* 298 (M^+, 0.5%), 284 ($M^+ + 1 - Me$, 16.6), 282 ($M^+ - 1 - Me$, 38.5), 231 (19.7) and 50 (100) (Found: *m/z* 283.1503. Calc. for $C_{15}H_{23}O_5$; *m/z* 283.1545).

(Z)-6,7,8,9,10-*Pentadeoxy*-1,2:3,4-*di*-O-*isopropylidene*-L-gluco-*dec*-7-*enitol* **17**. Compound **16** (5.07 g, 17 mmol) was hydrogenated by the procedure described for compound **7a** to give compound **17** (4.86 g, 95%), $[\alpha]_D^{20}$ −15.1 (*c* 0.37, $CHCl_3$); ν_{max}(film)/cm^{-1} 3450, 1660w, 1380 and 1370; δ_H(300 MHz; $CDCl_3$) 0.99 (3 H, t, *J* 7.5), 1.39 (3 H, s), 1.41 (3 H, s), 1.44 (3 H, s), 1.45 (3 H, s), 2.06 (2 H, m) 2.2–2.5 (2 H, m), 3.64 (1 H, m), 3.80–4.10 (4 H, m), 4.26 (1 H, m), 5.43 (1 H, m) and 5.60 (1 H, m); *m/z* 300 (M^+, 2.84%), 285 (M^+, 31.54), 231 (41.66) and 42 (100) (Found: M^+, 300.1992. Calc. for $C_{16}H_{28}O_5$: M, 300.1947).

(Z)-5-O-tert-*Butyldimethylsilyl*-6,7,8,9,10-*pentadeoxy*-1,2:3,4-*di*-O-*isopropylidene*-L-gluco-*dec*-7-*enitol* **18**.—A similar procedure to that for the preparation of compound **12a** was followed. Starting from the alcohol **17** (0.60 g, 2 mmol), the silyl ether **18** (0.76 g, 92%) was obtained after purification by chromatography, $[\alpha]_D^{20}$ +9.0 (*c* 0.67, $CHCl_3$); ν_{max}(film)/cm^{-1} 1660w, 1380 and 1370; δ_H(300 MHz; $CDCl_3$) 0.1 (6 H, s), 0.89 (9 H, s), 0.95 (3 H, t, *J* 7.5), 1.37 (3 H, s), 1.40 (3 H, s), 1.41 (3 H, s), 1.43 (3 H, s), 2.03 (2 H, m), 2.2–2.5 (2 H, m), 3.76–4.20 (6 H, m) and 5.47 (2 H, m); *m/z* 415 ($M^+ + 1$, 1%), 399 ($M^+ - Me$, 18.9), 357 (12.8) and 101 (100) (Found: *m/z* 399.2550. Calc. for $C_{21}H_{39}O_5Si$; *m/z* 399.2567).

(Z)-4-O-tert-*Butyldimethylsilyl*-5,6,7,8,9-*pentadeoxy*-2,3-O-*isopropylidene*-L-arabino-*non*-6-*enose* **19**.—Compound **18** (0.54 g, 1.3 mmol) was treated with ethereal periodic acid according to the procedure for the preparation of compound **5a**, to give compound **19** in 91% yield, $[\alpha]_D^{20}$ +27.1 (*c* 0.56, $CHCl_3$); ν_{max}(film)/cm^{-1} 2720, 1720, 1380 and 1370; δ_H(300 MHz; $CDCl_3$) 0.10 (6 H, s), 0.90 (9 H, s), 0.96 (3 H, t, *J* 7.5), 1.34 (3 H, s), 1.49 (3 H, s), 2.05 (2 H, m), 2.15–2.42 (2 H, m), 3.91 (1 H, dt, *J* 6.2 and 4.7), 4.08 (1 H, m), 4.42 (1 H, dd, *J* 6.7 and 1.8), 5.3–5.5 (2 H, m) and 9.76 (1 H, d, *J* 1.8); *m/z* 343 ($M^+ + 1$, 1.3%), 327 ($M^+ - Me$, 3), 273 (5.5%) and 227 ($M^+ - SiMe_2$-Bu^t, 14.4) (Found: *m/z* 273.1502. Calc. for $C_{13}H_{25}O_4Si$; *m/z* 273.1522).

(Z)-5,6,7,8,9-*Pentadexoy*-2,3-O-*isopropylidene*-L-arabino-*non*-6-*enose* **20**.—In the same way as for **8**, title compound **20** was obtained in 93% yield from compound **17**, $[\alpha]_D^{20}$ +10.0 (*c* 0.38, $CHCl_3$); ν_{max}(film)/cm^{-1} 3400, 1730, 1380 and 1370; δ_H-(300 MHz; $CDCl_3$) 0.97 (3 H, t, *J* 7), 1.2–1.5 (12 H, m), 2.05 (2 H, m), 2.2–2.6 (2 H, m), 3.5–4.2 (3 H, m), 4.7–5.2 (OH), 5.50 (2 H, m) and 9.81 (1 H, d, *J* 1.4): *m/z* 228 (M^+, 0.82%), 213 ($M^+ - Me$, 3.9), 211 ($M^+ + 1 - H_2O$, 0.87), and 59 (100).

5,6,7,8,9-*Pentadeoxy*-2,3-O-*isopropylidene*-L-ribo-*non*-6-*eno*-*furanose* **21**.—A similar procedure to that used for the preparation of compound **6a** was followed. Starting from compound **20** (3.0 g, 13.2 mmol), title furanose **21** (2.27 g, 76%) was obtained, $[\alpha]_D^{20}$ +5.1 (*c* 0.45, $CHCl_3$); δ_H(300 MHz; $CDCl_3$) 0.97 (3 H, t, *J* 7.5, 1.3–1.56 (6 H, m), 2.0–2.5 (4 H, m), 4.17 (1 H, m), 4.4–4.70 (2 H, m) and 5.25–5.60 (3 H, m); *m/z* 229 ($M^+ + 1$, 1%), 213 ($M^+ - Me$, 13.8), 211 ($M^+ + 1 - H_2O$, 50) and 59 (100) (Found: *m/z* 213.1192. Calc. for $C_{11}H_{17}O_4$; *m/z* 213.1127).

Ethyl (11R,12S,13S)-11,12-*Isopropylidenedioxy*-13-*hydroxy*-*octadeca*-9(Z),15(Z)-*dienoate* **22**.—To a suspension of [8-(ethoxycarbonyl)octyl]triphenylphosphonium bromide (3.0 g, 6 mmol) in THF (50 cm^3) was added dropwise potassium bis(trimethylsilyl)amide [$KN(SiMe_3)_2$] (1 mol dm^{-3}; 6 mmol) at −20 °C. A red solution was obtained after the mixture had been stirred for an additional 1 h at the same temperature. After HMPA (6 cm^3) had been added, the solution was cooled to −70 °C, and a solution of lactol **21** (0.34 g, 1.5 mmol) in THF was added dropwise. The reaction mixture was stirred at between −70 and 15 °C overnight. After addition of saturated aq. NH_4Cl the mixture was extracted with diethyl ether–light petroleum (1:1). The combined extracts were washed with brine, dried over Na_2SO_4, and evaporated. The oily residue was chromatographed to give the title ester **22** (0.31 g, 52%), TLC [ethyl acetate–hexane (1:4)], R_f 0.72; $[\alpha]_D^{20}$ −19.3 (*c* 0.96, $CHCl_3$); ν_{max}(film)/cm^{-1} 3450, 1735 (CO_2Et), 1660w, 1380 and 1370; δ_H(300 MHz; $CDCl_3$) 0.96 (3 H, t, *J* 7.5), 1.27 (3 H, t, *J* 7.2), 1.3–1.70 (10 H, m), 1.44 (3 H, s), 1.47 (3 H, s), 2.0–2.5 (8 H, m), 3.70 (1 H, m), 3.97 (1 H, m), 4.15 (2 H, q, *J* 7.2), 5.01 (1 H, dd, *J* 8.5 and 5.8) and 5.3–5.70 (4 H, m, olefinic); *m/z* 381 ($M^+ - Me$, 0.4%), 321 (4), 268 (3.1) and 83 (100) (Found: *m/z* 268.2081. Calc. for $C_{16}H_{28}O_3$; *m/z*, 268.2038).

Methyl (11R,12S,13S)-11,12,13-*Trihydroxyoctadeca*-9(Z),15-(Z)-*dienoate* **23**.—To a stirred solution of partially protected ester **22** (0.26 g, 0.65 mmol) in MeOH (5 cm^3) was added PTSA (0.2 g). After being stirred for 24 h at room temperature, the reaction mixture was worked up as usual. Purification by flash chromatography gave unchanged ester **22** (0.032 g recovery) and product **23** (0.178 g, 76%), TLC [(ethyl acetate–hexane (1:1)], R_f 0.52; $[\alpha]_D^{20}$ −16.3 (*c* 0.56, $CHCl_3$) {lit.,[11] $[\alpha]_D^{20}$ −16 (*c*. 0.7, $CHCl_3$)}; ν_{max}(film)/cm^{-1} 3400, 1735 (CO_2Me) and 1660; δ_H(300 MHz; $CDCl_3$) 1.0 (3 H, t, *J* 7.4), 1.25–1.8 (12 H, m), 2.0–2.60 (8 H, m), 3.50 (1 H, dd, *J* 6.0 and 6.2, 12-H), 3.6–3.8 (4 H, m with methyl ester singlet at δ 3.67), 4.62 (1 H, dd, *J* 9.1 and 6.0, 11-H), 5.43 (1 H, dt, *J* 9.8 and 5.9), 5.51 (1 H, dd, *J* 9.1 and 10.6), 5.64 (1 H, dt, *J* 9.9 and 7.2) and 5.73 (1 H, dt, *J* 6.9 and 10.6); *m/z* 325 ($M^+ + 1 - H_2O$, 0.190), 307 ($M^+ + 1 - 2$ H_2O, 0.2), 223 (3.4), 213 (7.3) and 85 (100).

(11R,12S,13S)-11,12,13-*Trihydroxyoctadeca*-9(Z),15(Z)-*dienoic Acid* **4a**.—To a stirred solution of the methyl ester **23** (0.1 g, 0.28 mmol) in MeOH–water (4:1; 5 cm^3) was added KOH (0.28 g, 5 mmol). After being stirred for 24 h at room temperature, the reaction mixture was worked up as usual. Purfication by chromatography provided the acid **4a** (77 mg, 80%), $[\alpha]_D^{20}$ −16.4 (*c* 0.4, $CHCl_3$); ν_{max}(film)/cm^{-1} 3500–2500br (CO_2H), 1710 and 1660; δ_H(300 MHz; $CDCl_3$) 0.98 (3 H, t, *J* 7.5), 1.2–1.7 (12 H, m), 2.0–2.6 (8 H, m), 3.52 (dd, *J* 6.0 and 6.2, 12-H), 3.72 (1 H, m, 13-H), 4.63 (1 H, dd, *J* 9.1 and 6.0, 11-H), 5.42 (1 H, dt, *J* 9.9 and 5.9), 5.51 (1 H, dd, *J* 9.1 and 10.6), 5.63 (1 H, dt, *J* 9.9 and 7.3) and 5.73 (1 H, dt, *J* 6.9 and 10.6); *m/z* 311 ($M^+ + 1 - H_2O$), 293 ($M^+ + 1 - 2H_2O$), 275 ($M^+ + 1 - 3H_2O$) and 213.

Acknowledgements

We are grateful to the Chinese Academy of Sciences and the State Committee of Science and Technology of China for financial support.

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Paper 3/04284G
Received 21*st July* 1993
Accepted 26*th August* 1993