# Stereoselective Syntheses of (−)-Goniotriol and (−)-8-Acetylgoniotriol from D-*glycero*-D-*gulo*-Heptono-γ-lactone

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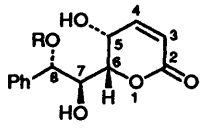
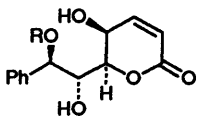
1-*O*-Acetyl-2,4:5,6-di-*O*-isopropylidene-1-*C*-phenyl-D-*glycero*-D-*ido*-hexitol **6** has been converted by three consecutive reactions (selective deacetonation, glycol cleavage oxidation, and Wittig reaction) into (*Z*)-methyl 7-*O*-acetyl-4,6-*O*-isopropylidene-7-*C*-phenyl-D-*ido*-hept-2-enote **9** which with basic methanol gave 2-deoxy-4,6-*O*-isopropylidene-3-*O*-methyl-7-*C*-phenyl-D-*glycero*-L-*ido*-heptono-δ-lactone **10**. The structure of **10** has been confirmed by X-ray crystallographic analysis. 1,3-Di-*O*-acetyl-2,4:5,6-di-*O*-isopropylidene-1-*C*-phenyl-D-*glycero*-D-*gulo*-hexitol **11** has been transformed *via* a sequence involving selective hydrolysis, deacetylation, glycol cleavage oxidation, and Wittig reaction into (*Z*)-methyl 4,6-*O*-isopropylidene-7-*C*-phenyl-L-*gluco*-hept-2-enonate **14** which with DBU provided (*Z*)-5,7-*O*-isopropylidene-8-*C*-phenyl-L-*gluco*-hept-3-enono-δ-lactone **16** from which (−)-goniotriol **1** and (−)-8-acetylgoniotriol **2** can be obtained readily. Absolute configurations 8-*C*-phenyl-L-*gluco*-hept-3-enono-δ-lactone **3** and 8-*O*-acetyl-8-*C*-phenyl-L-*gluco*-hept-3-enono-δ-lactone **4** are assigned to natural goniotriol and 8-acetylgoniotriol respectively.

Two styryl-pyrones, goniotriol and 8-acetylgoniotriol, which are cytotoxic to human tumour cells,[1,2] have been isolated from the ethanolic extracts of the stem bark of *Goniothalamus giganteus* Hook. f., Thomas (Annonaceae)[1,2] whereas goniotriol was also isolated from the leaves and twigs of *Goniothalamus sesquipedalis* Wall (Annonaceae).[3] Based on NMR spectral studies[1,2] and X-ray crystallographic analysis,[1] the structures of goniotriol and 8-acetylgoniotriol were established as **1** and **2** respectively, or their enantiomers **3** and **4**. As part



**1** R = H
**2** R = Ac

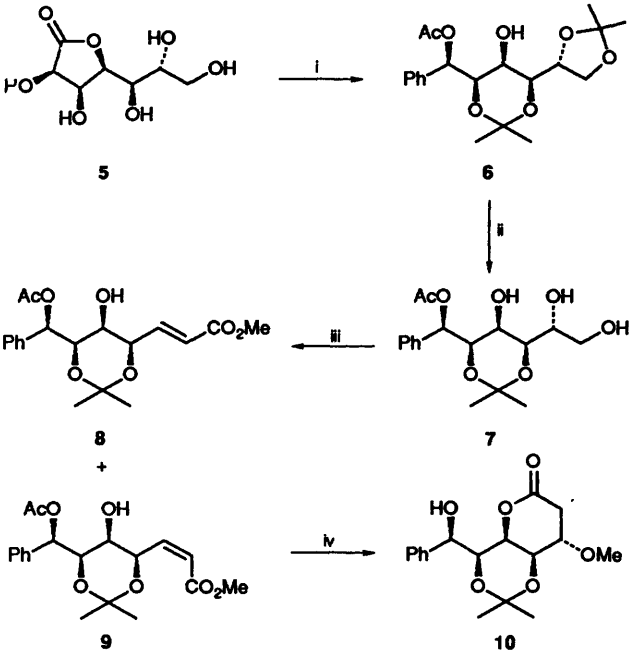


**3** R = H
**4** R = Ac

of our on-going programme in the syntheses of heavily oxygenated lactones as potential antitumour agents from sugars, we recently disclosed the enantiospecific synthesis of a related cytotoxic styryl-lactone, (+)-altholactone, from D-gulonolactone.[4] We also reported a synthesis of the (6*R*,7*S*)-diastereoisomer of the antitumour antibiotic asperlin from D-glucose.[5] This paper describes, starting from commercially available D-*glycero*-D-*gulo*-heptono-γ-lactone **5** (D-glucoheptono-γ-lactone), unambiguous syntheses of compounds **1** and **2** which are identical with the natural goniotriol and 8-acetylgoniotriol respectively except for the signs of the optical rotation, thereby enabling the assignments of the absolute configurations **3** and **4** to the respective natural materials. A preliminary account on part of this work has appeared.[6]

## Results and Discussion

Our initial approach towards compounds **1** and **2** is depicted in Scheme 1 in which we used the readily available acetate **6** to test our synthetic strategy. Our previous work has shown that D-glucoheptono-γ-lactone **5** could be readily transformed into compound **6** in five steps with an overall yield of 33%.[7] Selective hydrolysis of the terminal acetone group in **6** with aqueous acetic acid afforded the triol **7** in 67% yield. The vicinal diol



**Scheme 1** *Reagents:* i, 5 steps, see ref. 7; ii, 75% aq. AcOH; iii, $NaIO_4$, $MeOH–H_2O$, then $Ph_3P{=}CHCO_2Me$, MeOH or $CH_2Cl_2$; iv, MeOH, cat. $K_2CO_3$

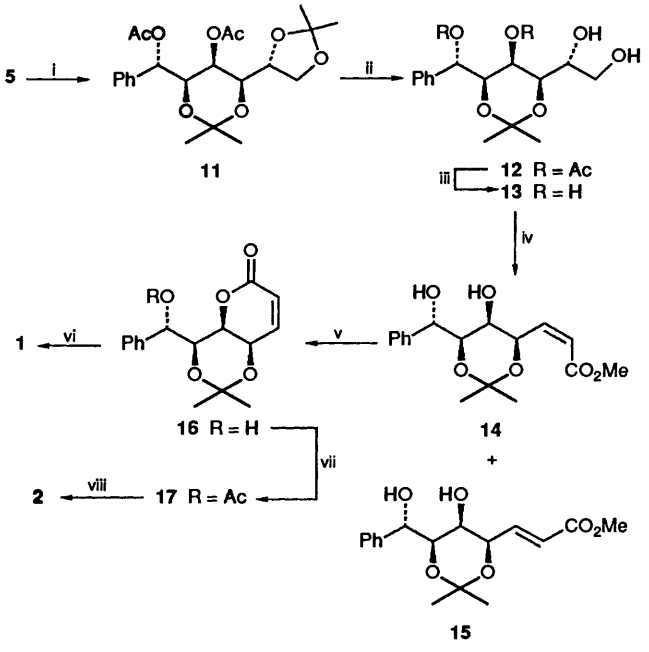
moiety in **7** was oxidatively cleaved[8] with sodium metaperiodate in aqueous methanol, forming the corresponding aldehyde which underwent immediate Wittig alkenation to give stereoselectively[9] the *Z*-alkene **9** (*Z*:*E* ratio 11:1 in methanol; *Z*:*E* ratio 2:3 in dichloromethane). Treatment of **9** with basic methanol proceeded with not only deacetylation and lactonisation, but also with the undesirable Michael reaction, to give the Michael adduct **10** in 85% yield. The structure of the methyl ether **10** was confirmed by X-ray (Table 1) analysis (Fig. 1).† In order to avoid the undesirable Michael reaction,

† *Supplementary data available:* (see Instructions for Authors, January issue). Tables of bond lengths, thermal parameters and H-atom coordinates have been deposited at the Cambridge Crystallographic Data Centre.

**Table 1** Atomic coordinates ( × $10^4$) for compound **10**

| Atom | *x* | *y* | *z* |
|---|---|---|---|
| O(1) | 2534(5) | 2499 | 4088(5) |
| O(2) | 2641(5) | 1298(8) | 5957(6) |
| O(4) | −932(5) | 1498(9) | 2205(6) |
| O(5) | 599(4) | 5470(8) | 3119(4) |
| O(7) | 2835(4) | 5703(8) | 3089(4) |
| O(8) | 4848(5) | 4687(8) | 2178(5) |
| C(2) | 1908(8) | 2070(11) | 4900(9) |
| C(3) | 396(7) | 2680(11) | 4521(7) |
| C(4) | −560(7) | 2969(12) | 2983(7) |
| C(5) | 297(7) | 3938(11) | 2427(7) |
| C(6) | 1677(7) | 3094(11) | 2642(7) |
| C(7) | 2654(7) | 4219(10) | 2353(7) |
| C(8) | 4189(7) | 3584(10) | 2744(7) |
| C(9) | −2196(8) | 738(14) | 2090(8) |
| C(10) | 1519(8) | 6514(11) | 2793(7) |
| C(11) | 1937(9) | 7904(11) | 3826(8) |
| C(12) | 706(8) | 7117(11) | 1287(7) |
| C(1′) | 4170(7) | 1934(10) | 2146(7) |
| C(2′) | 4578(8) | 593(11) | 3002(8) |
| C(3′) | 4567(9) | −936(12) | 2492(9) |
| C(4′) | 4161(8) | −1097(13) | 1093(8) |
| C(5′) | 3762(8) | 204(12) | 217(8) |
| C(6′) | 3744(7) | 1750(11) | 714(7) |

deacetylation should precede the Wittig olefination and a non-nucleophilic base should be used to induce lactonisation. This change of strategy gratifyingly led to the successful syntheses of compounds **1** and **2**; the routes are illustrated in Scheme 2.




**Scheme 2** *Reagents:* i, 5 steps, see ref. 7; ii, 75% aq. AcOH; iii, MeOH, cat. NaOMe; iv, $NaIO_4$, MeOH–$H_2O$, then $Ph_3P{=}CHCO_2Me$, MeOH; v, THF, cat. DBU; vi, 75% aq. AcOH; vii, $Ac_2O$, pyridine; viii, 75% aq. AcOH

Our previous work has also indicated that the lactone **5** could be converted into the diacetate **11** in five steps with an overall yield of 23%.[7] The terminal isopropylidene group in compound **11** was selectively removed with aqueous acetic acid to give the diol **12** in 81% yield. Deacetylation of **12** with a catalytic amount of NaOMe in dry methanol at room temperature led to the tetraol **13** in 93% yield. Glycol cleavage oxidation[8] of the vicinal diol moiety in compound **13** with sodium metaperiodate in aqueous methanol followed by immediate Wittig alkenation with (methoxycarbonyl)methylenetriphenylphosphorane in

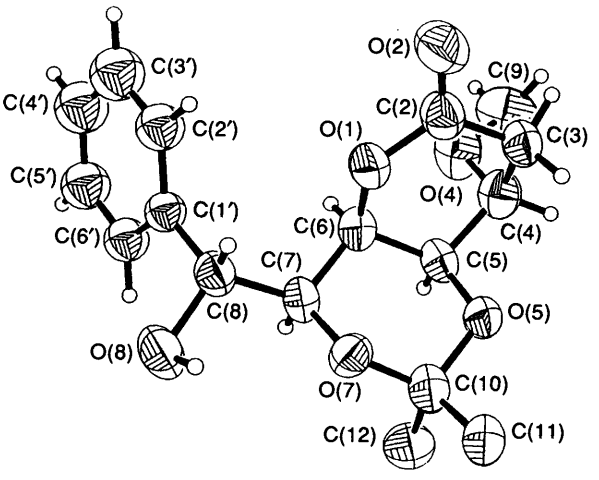



**Fig. 1** Perspective view of the molecular structure of compound **10**. The thermal ellipsoids are drawn at the 50% probability level.

methanol at room temperature, afforded stereoselectively[9] the *Z*-alkene **14** (*Z*:*E* ratio 5:1, estimated by TLC) in an overall yield of 92%. The *Z*-geometry of the double bond in compound **14** was evident from the $^1H$ NMR spectrum ($J_{2,3}$ 12 Hz). The *E*-isomer **15** was also isolated ($J_{2,3}$ 16 Hz). The *Z*-alkene **14** was induced to lactonise by a catalytic amount of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in boiling tetrahydrofuran (THF), furnishing the crystalline styryl-2-pyrone **16** in 83% yield. Acid hydrolysis of the acetone protecting group in compound **16** with aqueous acetic acid gave the target molecule **1** as prisms in 90% yield, m.p. 170–171 °C; $[\alpha]_D^{20}$ −119 (*c* 1.1, MeOH). The spectroscopic data of the synthetic goniotriol **1** are in accord with those reported,[1,2] and since the reported $[\alpha]_D$ value of goniotriol (m.p. 170 °C) is +121 (MeOH),[1] the absolute configuration of natural goniotriol must be **3**.

On the other hand, esterification of compound **16** with acetic anhydride gave the acetate **17** in 90% yield. The acetone blocking group was finally removed with aqueous acetic acid to form the other target molecule **2** in 88% yield, m.p. 158–159 °C; $[\alpha]_D^{20}$ −30 (*c* 0.85, EtOH). The spectroscopic data of the synthetic 8-acetylgoniotriol **2** are also in conformity with those reported,[2] but the reported m.p. had 158–159 °C and $[\alpha]_D^{20}$ had +30 (*c* 0.4, EtOH).[2] The absolute configuration of natural 8-acetylgoniotriol must be **4**.

In summary, we have synthesised stereoselectively, from D-*glycero*-D-*gulo*-heptono-γ-lactone **5**, (−)-goniotriol **1** and (−)-8-acetylgoniotriol **2** in 11 steps (8.2% overall yield) and 12 steps (7.4% overall yield) respectively and assigned the absolute configurations **3** and **4** to the respective natural materials.

## Experimental

For experimental generalisation, see ref. 7. *J*-Values in Hz. Optical rotations were measured in ethyl acetate unless stated otherwise.

1-O-*Acetyl*-2,4-O-*isopropylidene*-1-C-*phenyl*-D-glycero-D-ido-*hexitol* **7**.—An aqueous acetic acid solution (20 $cm^3$, 75% v/v) of compound **6**[7] (2.0 g, 5.3 mmol) was stirred at room temp. for 8 h. The solvents were removed under reduced pressure and the residual syrup was flash chromatographed [ethyl acetate–hexane (3:1 v/v)] and recrystallised (ethyl acetate–hexane) to afford the *triol* **7** (1.2 g, 67%) as a white solid, m.p. 140–141 °C (Found: C, 59.9; H, 7.1. $C_{17}H_{24}O_7$ requires C, 59.99; H, 7.11%); $[\alpha]_D$ −17.0 (*c* 1.0); $\nu_{max}$(film)/$cm^{-1}$ 3450 (OH) and 1737 (ester C=O); $\delta_H$(250 MHz, $CDCl_3$ + $D_2O$) 1.45 (3 H, s, Me), 1.47 (3 H,

s, Me), 2.05 (3 H, s, Ac), 3.47 (1 H, dd, *J* 6.0, 11.6, 6-$H_a$), 3.59 (1 H, dd, *J* 1.2, 8.3, 4-H), 3.69 (1 H, dd, *J* 3.1, 11.6, 6-$H_b$), 3.72 (1 H, dd, *J* 1.0, 1.2, 3-H), 4.01 (1 H, dd, *J* 1.0, 9.1, 2-H), 4.13 (1 H, ddd, *J* 3.7, 6.0, 8.3, 5-H), 5.99 (1 H, d, *J* 9.0, 1-H) and 7.27–7.44 (5 H, m, Ph); *m/z* (EI), 324 (1.2%, $M^+$ − Me).

5-O-*Acetyl*-2,4-O-*isopropylidene*-5-C-*phenyl*-D-ido-*pentose*.—A solution of **7** (0.50 g, 1.5 mmol) in methanol (10 $cm^3$) was treated with a solution of sodium metaperiodate (0.32 g, 1.5 mmol) in water (10 $cm^3$) for 1 h at room temp. The mixture was filtered through celite and the filtrate concentrated to dryness. The residue was extracted with chloroform (3 × 20 $cm^3$). Concentration of the dried ($MgSO_4$) extracts afforded the aldehyde as a white solid (0.45 g, 100%). This compound was used in the next step without further purification.

(E)- *and* (Z)-*Methyl* 7-O-*Acetyl*-4,6-O-*isopropylidene*-7-C-*phenyl*-D-ido-*hept*-2-*enonate* **8** *and* **9**.—The above aldehyde (0.45 g, 1.5 mmol) was dissolved in methanol (10 $cm^3$) and reacted with methoxycarbonylmethylenetriphenylphosphorane (0.50 g, 1.5 mmol) at room temp. for 2 h. The solvent was evaporated under reduced pressure and the residue was triturated with diethyl ether. The precipitated triphenylphosphine oxide was filtered off. The filtrate was concentrated and the residue flash chromatographed to give successively the *Z*-alkene **9** (0.41 g, 76%) and the *E*-alkene **8** (40 mg, 7.4%).

Recrystallisation of *Z*-alkene **9** (diethyl ether–hexane) gave colourless *plates* m.p. 125–126 °C (Found: C, 62.3; H, 6.3. $C_{19}H_{24}O_7$ requires C, 62.6; H, 6.6%); $[\alpha]_D$ −157 (*c* 0.85); $\nu_{max}$(film)/$cm^{-1}$ 3507 (OH), 1739 (ester C=O) and 1721 (α,β-unsaturated ester C=O); $\delta_H$(250 MHz) 1.42 (3 H, s, Me), 1.47 (3 H, s, Me), 2.00 (3 H, s, Ac), 2.60 (1 H, d, *J* 12.3, 5-OH), 3.01 (1 H, dd, *J* 0.5, 12.3, 5-H), 3.53 (3 H, s, $CO_2Me$), 4.07 (1 H, d, *J* 8.8, 6-H), 5.33 (1 H, dd, *J* 0.5, 7.3, 4-H), 5.76 (1 H, d, *J* 11.7, 2-H), 5.90 (1 H, d, *J* 8.8, 7-H), 6.16 (1 H, dd, *J* 11.7, 7.3, 3-H) and 7.23–7.38 (5 H, m, Ph); *m/z* (EI), 349 (0.5%, $M^+$ − Me).

The isomeric E-*alkene* **8** had m.p. 141.5–142.5 °C (Found: C, 62.5; H, 6.7. $C_{19}H_{24}O_7$ requires C, 62.64; H, 6.64%); $[\alpha]_D$ + 7.3 (*c* 0.60); $\nu_{max}$(film)/$cm^{-1}$ 3496 (OH), 1735 (ester C=O) and 1729 (α,β-unsaturated ester C=O); $\delta_H$(250 MHz) 1.67 (3 H, s, Me), 1.78 (3 H, s, Me), 2.01 (3 H, s, Ac), 2.61 (1 H, d, *J* 11.9, 5-OH), 3.11 (1 H, ddd, *J* 0.5, 0.9, 11.9, 5-H), 3.86 (3 H, s, $CO_2Me$), 4.21 (1 H, dd, *J* 0.9, 9.0, 6-H), 4.58 (1 H, ddd, *J* 0.5, 1.8, 4.0, 4-H), 6.15 (1 H, d, *J* 9.0, 7-H), 6.20 (1 H, dd, *J* 1.8, 15.7, 2-H), 6.70 (1 H, dd, *J* 4.0, 15.7, 3-H) and 7.48–7.63 (5 H, m, Ph); *m/z* (EI), 349 (1.3%, $M^+$ − Me).

Likewise, Wittig reaction of the aldehyde in dichloromethane gave the ratio of *E*-alkene **8** to *Z*-alkene **9** as 3:2.

2-*Deoxy*-4,6-O-*isopropylidene*-3-O-*methyl*-7-C-*phenyl*-D-glycero-L-ido-*heptono*-δ-*lactone* **10**.—To a solution of the *Z*-alkene **9** (89 mg, 0.27 mmol) in dry methanol (5.0 $cm^3$) was added a catalytic amount of potassium carbonate. The reaction gave two products after 10 min (both slower than the *Z*-alkene **9** by TLC). The IR spectra showed that the less polar product was an α,β-unsaturated ester and the more polar was a δ-lactone. After 1 h, the ester was all converted into the δ-lactone **10**. Concentration of the reaction mixture followed by flash chromatography [diethyl ether–hexane (2:1 v/v)] gave **10** as transparent *prisms* (75 mg, 85%), m.p. 189–190 °C (Found: C, 63.4; H, 6.9. $C_{17}H_{22}O_6$ requires C, 63.3; H, 6.9%); $[\alpha]_D$ +91.0 (*c* 0.80); $\nu_{max}$(film)/$cm^{-1}$ 3492 (OH) and 1724 (δ-lactone); $\delta_H$(250 MHz) 1.49 (3 H, s, Me), 1.55 (3 H, s, Me), 2.64 (1 H, dd, *J* 2.7, 17.7, 2-$H_a$), 2.81 (1 H, d, *J* 1.5, 8-OH), 2.83 (1 H, dd, *J* 4.4, 17.7, 2-$H_b$), 3.30 (3 H, s, OMe), 3.62 (1 H, ddd, *J* 2.7, 3.8, 4.4, 3-H), 3.81 (1 H, dd, *J* 1.3, 8.7, 6-H), 3.86 (1 H, dd, *J* 1.5, 1.6, 5-H), 3.94 (1 H, dd, *J* 1.6, 3.8, 4-H), 5.07 (1 H, dd, *J* 1.5, 8.7, 8-H) and 7.33–7.54 (5 H, m, Ph); *m/z* (EI), 307 (2.5%, $M^+$ − Me).

*Crystal data*. $C_{17}H_{22}O_6$, *M* = 322.39, monoclinic, space group $P2_1$ (No. 4); *a* = 10.327(3), *b* = 8.270(2), *c* = 10.745(4) Å, β = 117.85(2)°, *Z* = 2, $D_x$ = 1.32 g $cm^{-3}$, *F*(000) = 344, Mo-Kα radiation (λ = 0.710 73 Å), crystal dimensions: 0.10 × 0.10 × 0.08 $mm^3$, μ(Mo-Kα) = 12.89 $cm^{-1}$.

*Data collection and processing*. Intensities (818 unique reflections, $2\theta_{max}$ 40°) collected on a Nicolet R3m/V diffractometer were processed with the profile-fitting procedure of Diamond[10] and collected for absorption using ψ-scan data.[11] A total of 725 reflections with $I > 3\sigma(I)$ were considered to be observed and used in the structure analysis.

*Structure analysis and refinement*. The structure was solved by direct phase determination and refined with anisotropic temperature factors for all non-hydrogen atoms. The hydrogen atom of the hydroxy group was located from a difference map, and the other hydrogen atoms in the molecule were generated geometrically (C–H bond fixed at 0.96 Å). All hydrogen atoms were assigned the same isotropic temperature factor of *U* = 0.08 Å. Final *R* and $R_w$ are 0.044 and 0.059, respectively, with $w = [\sigma 2|F_0| + 0.0002\ |F^2|]^{-1}$. Computations were performed using the SHELXTXL-PLUS program package[12] on a DEC Micro VAX-II computer. Analytical expressions of neutral-atom scattering factors were used, and anomalous dispersion corrections were incorporated.[13]

1,3-*Di*-O-*acetyl*-2,4-O-*isopropylidene*-1-C-*phenyl*-D-glycero-D-gulo-*hexitol* **12**.—To a stirred solution of the diacetate **11**[7] (0.50 g, 1.2 mmol) in acetic acid (20 $cm^3$) was added water (20 $cm^3$). The reaction mixture was stirred at room temp. for 15 h and the solvents were removed by azeotropic distillation with toluene under reduced pressure to give a yellow syrupy residue. Purification by flash chromatography [ethyl acetate–hexane (1:1 v/v)] afforded **12** (367 mg, 81%) as a white *foam* (Found: C, 59.7; H, 6.8. $C_{19}H_{26}O_8$ requires C, 59.68; H, 6.85%); $[\alpha]_D^{24}$ +19 (*c* 1.0); $\nu_{max}$(film)/$cm^{-1}$ 3450 (OH), 1750 (ester C=O); $\delta_H$(250 MHz) 1.29 (3 H, s, Me), 1.34 (3 H, s, Me), 2.02 (3 H, s, Ac), 2.23 (3 H s, Ac), 3.40–3.49 (1 H, m, 5-H), 3.64 (1 H, br dd, *J* 5.0, 11, 6-$H_a$), 3.82 (1 H, br dd, *J* 3.2, 11, 6-$H_b$), 3.92 (1 H, dd, *J* 1.1, 9.4, 4-H), 4.25 (1 H, dd, *J* 1.5, 9.4, 2-H), 5.09 (1 H, br t, *J* 1.4, 3-H), 5.83 (1 H, d, *J* 9.4, 1-H) and 7.31–7.38 (5 H, m, Ph); *m/z* (EI) 325 ($M^+$ − Me − $C_2H_2O$, 100%).

2,4-O-*Isopropylidene*-1-C-*phenyl*-D-glycero-D-gulo-*hexitol* **13**.—To a stirred solution of **12** (0.51 g, 1.3 mmol) in methanol (10 $cm^3$) was added a catalytic amount of sodium methoxide. After being stirred at room temp. for 2 h, the solution was filtered through a short column of silica gel topped with Celite. Removal of solvent from the filtrate under reduced pressure gave a solid residue which was flash chromatographed (diethyl ether) to give compound **13** (0.37 mg, 93%) as a colourless solid. Recrystallisation from diethyl ether–hexane gave colourless *needles*, m.p. 169–172 °C (Found: C, 60.2; H, 7.2. $C_{15}H_{22}O_6$ requires C, 60.39; H, 7.43%); $[\alpha]_D^{24}$ +6.0 (*c* 0.53, EtOH); $\nu_{max}$(film)/$cm^{-1}$ 3400 (OH); $\delta_H$(250 MHz) 1.27 (3 H, s, Me), 1.30 (3 H, s, Me), 3.47–3.96 (5 H, m), 4.80 (1 H, d, *J* 7.5, 1-H) and 7.23–7.44 (5 H, m, Ph); *m/z* (EI) 107 ($PhCHOH^+$, 41%), 191 ($M^+$ − PhCHOH, 4%).

2,4-O-*Isopropylidene*-5-C-*phenyl*-L-gluco-*pentose*.—To a stirred solution of compound **13** (0.30 g, 1.0 mmol) in methanol (20 $cm^3$) and water (10 $cm^3$) was added sodium metaperiodate (0.30 g, 1.4 mmol). After being stirred at room temp. for 30 min, the mixture was filtered through a pad of silica. Methanol in the filtrate was then removed under reduced pressure. The residue was partitioned between $CHCl_3$ (20 $cm^3$) and saturated aqueous $NH_4Cl$ (10 $cm^3$). The aqueous solution was further extracted with $CHCl_3$ (7 × 10 $cm^3$). The combined organic extracts were dried ($MgSO_4$), filtered and evaporated to give

the aldehyde as a colourless syrup. It was used in the next step without further purification.

(Z)- *and* (*E*)-*Methyl* 4,6-O-*Isopropylidene*-7-C-*phenyl*-L-gluco-*hept*-2-*enonate* **14** *and* **15**.—To a stirred solution of the above aldehyde in methanol (20 $cm^3$) was added methoxycarbonylmethylenetriphenylphosphorane (0.40 g, 1.2 mmol) in one portion. After being stirred at room temp. for 2 h, the reaction mixture was concentrated under reduced pressure.

Fractionation of the residue by flash chromatography [diethyl ether–hexane (2:3 v/v)] gave first the *Z*-alkene **14** (0.25 g, 76%) as a colourless solid. Recrystallisation from diethyl ether–hexane gave colourless *needles*, m.p. 135–136 °C (Found: C, 63.1; H, 6.9. $C_{17}H_{22}O_6$ requires C, 63.34; H, 6.88%); $[\alpha]_D^{24}$ −65 (*c* 0.89, EtOH); $\nu_{max}$(film)/$cm^{-1}$ 3475 (OH), 1650 and 1719 (α,β-unsaturated ester C=O); $\delta_H$(250 MHz) 1.29 (3 H, s, Me), 1.33 (3 H, s, Me), 3.69 (3 H, s, $CO_2Me$), 3.91 (1 H, br s, 5-H), 4.00 (1 H, dd, *J* 1.4, 7.8, 6-H), 4.78 (1 H, br d, *J* 7.8, 7-H), 5.48 (1 H, m, 4-H), 5.91 (1 H, dd, *J* 1.4, 12, 2-H), 6.37 (1 H, dd, *J* 7.0, 12, 3-H) and 7.24–7.45 (5 H, m, Ph); *m*/*z* (EI) 307 ($M^+$ + Me, 6.0%).

The more polar *E*-alkene **15** was also obtained as a white solid (50 mg, 16%). Recrystallisation from diethyl ether–hexane also gave colourless *needles*, m.p. 114–115 °C (Found: C, 63.3; H, 6.8. $C_{17}H_{22}O_6$ requires C, 63.34; H, 6.88%); $[\alpha]_D^{22}$ −20 (*c* 0.58, EtOH); $\nu_{max}$(film)/cm 3433 (OH) and 1725 (α,β-unsaturated ester C=O); $\delta_H$(250 MHz) 1.34 (6 H, s, 2 × Me), 3.70 (3 H, s, $CO_2Me$), 3.84 (1 H, br s, 5-H), 4.00 (1 H, dd, *J* 1.2, 7.8, 6-H), 4.71 (1 H, m, 4-H), 4.79 (1 H, br d, *J* 7.8, 7-H), 6.07 (1 H, dd, *J* 1.9, 16, 2-H), 6.96 (1 H, dd, *J* 4.2, 16, 3-H) and 7.24–7.44 (5 H, m, Ph); *m*/*z* (EI) 307 ($M^+$ − Me, 5.81%). The ratio of **14**:**15** (5:1) was estimated by TLC.

(Z)-5,7-O-*Isopropylidene*-8-C-*phenyl*-L-gluco-*hept*-3-*enono*-δ-*lactone* **16**.—The *Z*-alkene **14** (0.20 g, 0.62 mmol) was dissolved in THF (20 $cm^3$) containing 0.05% (v/v) DBU. The resulting solution was refluxed at 70–80° C for 12 h. Then the cooled reaction mixture was passed through a short column of silica gel to eliminate the DBU. Removal of THF from the filtrate under reduced pressure gave a white solid which was flash chromatographed (diethyl ether) to give the 2-*pyrone* **16** (0.15 g, 83%) as colourless needles, m.p. 191–192 °C (Found: C, 65.8; H, 6.0. $C_{16}H_{18}O_5$ requires: C, 66.2; H, 6.2%); $[\alpha]_D^{20}$ −130 (*c* 1.0, MeOH); $\nu_{max}$(film)/$cm^{-1}$ 3396 (OH), 1633 and 1694 (α,β-unsaturated δ-lactone); $\delta_H$(250 MHz) 1.27 (3 H, s, Me), 1.27 (3 H, s, Me), 2.87 (1 H, d, *J* 0.8, 7-OH), 3.98 (1 H, dd, *J* 1.6, 8.4, 6-H), 4.28 (1 H, dd, *J* 2.0, 6.0, 4-H), 4.43 (1 H, dd, *J* 1.6, 2.0, 5-H), 5.03 (1 H, d, *J* 8.4, 7-H), 6.18 (1 H, d, *J* 9.6, 2-H), 6.82 (1 H, dd, *J* 6.0, 9.6, 3-H) and 7.22–7.38 (5 H, m, Ph); *m*/*z* (EI) 275 ($M^+$ − Me, 5.7%).

(−)-*Goniotriol* **1**.—A solution of the 2-pyrone **16** (100 mg, 0.34 mmol) in aqueous acetic acid (20 $cm^3$, 75% v/v) was heated at 70–80 °C for 4 h. The solvents were removed under reduced pressure and the residual syrup was flash chromatographed (diethyl ether) to afford **1** (78 mg, 90%) as *prisms*, m.p. 170–171 °C (Found: C, 62.0; H, 5.48. $C_{13}H_{14}O_5$ requires C, 62.4; H, 5.64%); $[\alpha]_D^{20}$ −119 (*c* 1.1, MeOH); $\nu_{max}$(film)/$cm^{-1}$ 3390 (OH) and 1718 (α,β-unsaturated δ-lactone); $\delta_H$(250 MHz) 4.17 (1 H, dd, *J* 3.7, 8.0, 6-H), 4.42 (1 H, dd, *J* 2.9, 5.7, 4-H), 4.59 (1 H, dd, *J* 3.2, 3.8, 5-H), 4.74 (1 H, d, *J* 7.9, 7-H), 6.08 (1 H, d, *J* 9.6, 2-H), 7.00 (1 H, dd, *J* 5.8, 9.6, 3-H) and 7.26–7.46 (5 H, m, Ph); *m*/*z* (EI) 251 ($MH^+$, 0.6%).

(Z)-8-O-*Acetyl*-5,7-O-*isopropylidene*-8-C-*phenyl*-L-gluco-*hept*-3-*enono*-δ-*lactone* **17**.—The 2-pyrone **16** (50 mg, 0.17 mmol) was acetylated by acetic anhydride and pyridine [10 $cm^3$, (5:4 v/v)] for 12 h. The reaction mixture was concentrated under reduced pressure by adding toluene. The residue was flash chromatographed [diethyl ether–hexane (3:1 v/v)] to give *monoacetate* **17** (51 mg, 92%) as a white solid, m.p. 190–191 °C (Found: C, 64.7; H, 5.94. $C_{18}H_{20}O_6$ requires C, 65.0; H, 6.06%); $[\alpha]_D^{20}$ −13 (*c* 0.06, EtOH); $\nu_{max}$(film)/$cm^{-1}$ 1724 (ester C=O) and 1701 (α,β-unsaturated δ-lactone); $\delta_H$(250 MHz) 1.49 (3 H, s, Me), 1.52 (3 H, s, Me), 1.98 (3 H, s, $CO_2Me$), 4.21 (1 H, dd, *J* 1.6, 9.3, 6-H), 4.28 (1 H, dd, *J* 1.6, 2.0, 5-H), 4.30 (1 H, dd, *J* 2.0, 5.8, 4-H), 5.92 (1 H, d, *J* 9.3, 7-H), 6.21 (1 H, d, *J* 9.6, 2-H), 6.83 (1 H, dd, *J* 5.8, 9.6, 3-H) and 7.23–7.33 (5 H, m, Ph); *m*/*z* (EI) 317 ($M^+$ − Me, 11.7%).

(−)-8-*Acetylgoniotriol* **2**.—An aqueous acetic acid solution (75% v/v; 10 $cm^3$) of the monoacetate **17** (50 mg, 0.15 mmol) was heated at 70–80 °C for 4 h. The reaction mixture was concentrated to dryness under reduced pressure. The residue was flash chromatographed (diethyl ether) to give (−)-acetylgoniotriol **2** (39 mg, 88%) as a white *solid*, m.p. 158–159 °C (Found: C, 61.3; H, 5.6. $C_{15}H_{16}O_6$ requires C, 61.6; H, 5.5%); $[\alpha]_D^{20}$ −30 (*c* 0.90, EtOH); $\nu_{max}$(film)/$cm^{-1}$ 3508 (OH), 1718 (ester C=O) 1684 and 1654 (α,β-unsaturated δ-lactone); $\delta_H$(250 MHz) 2.03 (3 H, s, $CO_2Me$), 4.45 (1 H, dd, *J* 3.5, 7.2, 6-H), 4.49 (1 H, dd, *J* 2.9, 3.9, 5-H), 4.57 (1 H, dd, *J* 2.9, 5.6, 4-H), 5.87 (1 H, d, *J* 7.1, 7-H), 6.03 (1 H, d, *J* 9.8, 2-H), 7.04 (1 H, dd, *J* 5.8, 9.8, 3-H) and 7.27–7.52 (5 H, m, Ph); *m*/*z* (EI) 293 ($MH^+$, 0.5%), 275 ($MH^+$ − $H_2O$, 2.4) and 233 ($MH^+$ − HOAc, 10.2).

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## References

1 A. Alkofahi, W.-W. Ma, A. T. Mckenzie, S. R. Byrn and J. L. McLaughlin, *J. Nat. Prod.*, 1989, **52**, 1371.
2 X. P. Fang, J. E. Anderson, P. E. Fanwick and J. L. McLaughlin, *J. Chem. Soc., Perkin Trans. 1*, 1990, 1655.
3 S. K. Talapatra, D. Basu, T. Deb, S. Goswami and B. Talapatra, *Indian J. Chem., Sect. B*, 1985, **24**, 29.
4 T. K. M. Shing and J. G. Guilhouley, *J. Chem. Soc., Chem. Commun.*, 1988, 976.
5 T. K. M. Shing and M. Aloui, *J. Chem. Soc., Chem. Commun.*, 1988, 1526; *Can. J. Chem.*, 1990, **68**, 1035.
6 T. K. M. Shing and Z.-H. Zhou, *Tetrahedron Lett.*, 1992, in the press.
7 T. K. M. Shing, Z.-H. Zhou, H.-C. Tsui and T. C. W. Mak, *J. Chem. Soc., Perkin Trans. 1*, 1992, 887.
8 For a recent review, see T. K. M. Shing, in *Comprehensive Organic Synthesis*, eds. B. M. Trost and I. Fleming, Pergamon, Oxford, 1991, vol. 7, p. 703.
9 J. M. J. Tronchet and B. Gentile, *Helv. Chim. Acta*, 1979, **62**, 2091.
10 R. Diamond, *Acta Crystallogr., Sect. A*, 1969, **25**, 43.
11 G. Kopfmann and R. Hubber, *Acta Crystallogr., Sect. A*, 1968, **24**, 348.
12 G. M. Sheldrick, in *Crystallographic Computing 3: Data Collection, Structure Determination, Proteins, and Databases*, eds. G. M. Sheldrick, C. Krüger and R. Goddard, Oxford University Press, New York, 1985, pp. 175–189.
13 *International Tables for X-ray Crystallography*, Kynoch Press, Birmingham, 1974, vol. IV, pp. 55, 99, 149 (now distributed by Kluwer Academic publishers, Dordrecht).

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