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Stereocontrolled Syntheses of (-)-Goniofufurone and (-)-8-*epi*-Goniofufurone

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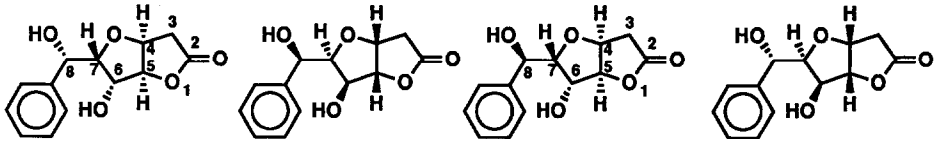
Abstract— The absolute configurations of natural goniofufurone and 8-*epi*-goniofufurone are shown to be **2** and **4** respectively by unambiguous syntheses of their enantiomers **1** and **3** from D-*glycero*-D-*gulo*-heptono-γ-lactone **7** involving an intramolecular Michael reaction as the key step. The diol **6**, readily available from D-*glycero*-D-*gulo*-heptono-γ-lactone, has been converted by six sequential reactions (acetylation, hydrolysis, deacetylation, glycol cleavage, Wittig reaction, and hydrolysis) into the γ-lactone **5** which underwent an intramolecular Michael reaction to yield (-)-goniofufurone **1**. Likewise reactions of the monoacetate **12** gave (-)-8-*epi*-goniofufurone **3**.

Goniofufurone and 8-*epi*-goniofufurone are novel styryl-lactones isolated from the ethanolic extracts of the stem bark of *Goniothalamus giganteus* Hook. f., Thomas (Annonaceae), obtainable in Thailand.[1,2] It is noteworthy that whereas goniofufurone shows significant cytotoxic activitites toward several human tumour cell lines, 8-*epi*-goniofufurone is only weakly bioactive.[1,2] The structures and the relative stereochemistry of goniofufurone and 8-*epi*-goniofufurone, which represent a new natural skeleton, were shown by *X*-ray crystallography to be **1** and **3** respectively or their enantiomers **2** and **4**.[1,2] As part of our long-term programme in the fabrication of highly oxygenated lactones as potential antitumour agents from carbohydrates, we recently described the enantiospecific synthesis of a related styryl-lactone, (+)-altholactone (syn: goniothalenol, a furano-2-pyrone), from D-gulonolactone.[3] We also disclosed an unambiguous synthesis of the (6*R*,7*S*)-diastereoisomer of the antitumour antibiotic asperlin (an epoxy-2-pyrone) from D-glucose.[4]

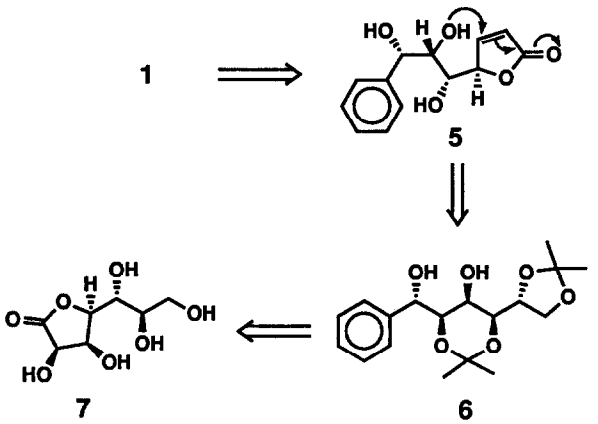


1 **2** **3** **4**

This paper reports, starting from commercially available D-*glycero*-D-*gulo*-heptono-γ-lactone **7** (D-glucoheptono-γ-lactone), an unambiguous synthesis of **1** which is identical to the natural goniofufurone except for the sign of the optical rotation, thereby enabling the assignment of the absolute configuration **2** to the natural material. A preliminary account on the synthesis of (-)-goniofufurone **1** has appeared.[5] The applicability of this stereoselective sequence has now been demonstrated by obtaining (-)-8-*epi*-goniofufurone **3** from the monoacetate **12** which could readily be derived from the lactone **7**. Since the synthetic 8-*epi*-goniofufurone **3** is also in accord to the natural material except for the sign of the optical rotation, the absolute stereochemistry of the

natural 8-*epi*-goniofufurone is assigned as **4**. After the completion of this work, we noticed that syntheses of **1** and **3** using a key palladium (II)-catalysed oxycarbonylation were recently reported by Jager and Gracza.[6]

Scheme I



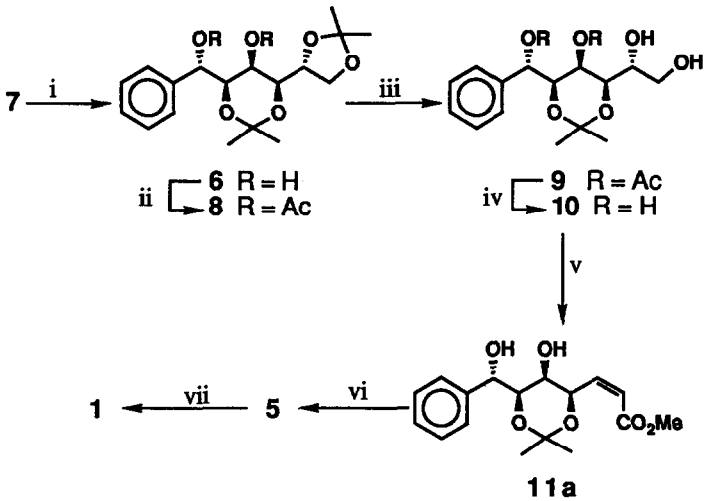
Retrosynthetic analysis of **1** shows that its [3.3.0] bicyclic ring system can be assembled *via* an intramolecular Michael protocol[7] on the γ-lactone **5** (Scheme I). We envisaged that the formation of the five-membered furanoid ring in **1** should be the most facile process and the resulting [3.3.0] bicycle should then be *cis*-fused; in this way, the desired stereochemistry at C-4 would be controlled by the preexisting chirality at C-5 of the α,β-unsaturated lactone **5**. Further disconnection of **5** shows that it can be derived from the known styryl-alcohol **6**[8] *via* sequential selective hydrolysis, glycol cleavage oxidation, and Wittig reaction. The alcohol **6** is then readily accessible from the abundant and affordable D-*glycero*-D-*gulo*-heptono-γ-lactone **7**.[8]

The route to goniofufurone **1** is illustrated in Scheme II. Esterification of **6**[8] with acetic anhydride in pyridine at room temperature gave the diacetate **8** from which the terminal acetonide protecting group was selectively hydrolyzed with aqueous acetic acid to form the diol **9** in an overall yield of 65%. Deacetylation of the diol **9** with a catalytic amount of NaOMe in dry methanol at room temperature led to the tetraol **10** in 93% yield. Attempted selective hydrolysis of the terminal isopropylidene ring in the diacetonide **6** to give **10** directly was unsuccessful; several by-products resulted from acetal isomerization were present in the reaction mixture and compound **10** was formed in low yields.

Glycol cleavage oxidation[9] of the vicinal diol moiety in **10** with sodium metaperiodate in aqueous methanol followed by immediate Wittig alkenation with (methoxycarbonyl)methylenetriphenylphosphorane in methanol at room temperature, afforded stereoselectively[10] the *Z*-alkene **11a** (*Z* : *E* ratio 5 : 1) in an overall yield of 92%. The *Z*-geometry of the double bond in **11a** was evident from the ^{1}H NMR spectrum ($J_{2,3}$ = 12 Hz). The *E*-isomer **11b** was also isolated and the ^{1}H coupling constant between H-2 and H-3 was 16 Hz.

Removal of the acetone protecting group in **11a** with aqueous acetic acid at room temperature occurred with concomitant lactonisation, providing the crystalline γ-lactone **5** in 83% yield. The most downfield methine proton in the ^{1}H NMR spectrum of **5**, centered at 5.24 ppm (ddd), was assigned as H-4 from the coupling constants. Since lactonization is an intramolecular acylation, the proton attached to the carbon bearing the *O*-acyl group is expected to be deshielded. The most downfield methine proton was H-4, hence compound **5** must be a γ-lactone.

Scheme II



11a

Reagents: i, 6 steps, see ref. 8; ii, Ac_2O, pyridine (80 %); iii, 50% aq. AcOH (81%); iv, MeOH, cat. NaOMe (93%); v, $NaIO_4$, MeOH, H_2O; then Ph_3P=CHCOOMe, MeOH (76% from **9**); vi, 80% aq. AcOH (83%); vii, THF, cat. DBU (71%).

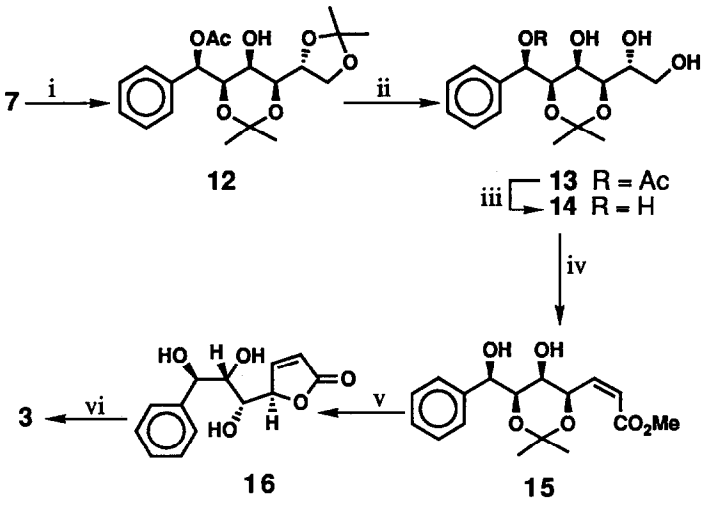
The intramolecular Michael addition reaction of **5**, mediated by a catalytic amount of DBU in THF, gratifyingly proceeded as planned to give the target molecule **1** as white plates, mp 152—154 °C; $[\alpha]_D^{24}$ - 8.5° (*c* 0.8, EtOH). The spectroscopic data of the synthetic goniofufurone **1** are in accord with those reported,[1] and since the natural goniofufurone had mp 152—154 °C and $[\alpha]_D^{22}$ + 9.0° (*c* 0.5, EtOH),[1] the absolute configuration of natural goniofufurone must be **2**.

The versatility of the above synthetic route is demonstrated by the facile construction of (-)-8-*epi*-goniofufurone **3** from the monoacetate **12** in a similar fashion. Our previous work has also shown compound **12** could readily be obtained from the lactone **7** in five steps with an overall yield of 33%.[8] Thus selective hydrolysis of **12** gave the triol **13** which was deacetylated to **14** in 67% yield. The tetraol **14** was then converted into the *Z*-enonate **15** *via* glycol cleavage oxidation and subsequent Wittig alkenation in an overall yield of 85%. In this case, the *E*-isomer was only present in trace amount and was not isolated. The methyl enonate **15** was then subjected to acid hydrolysis to give the lactone **16** which underwent the DBU-induced intramolecular Michael reaction in the same manner as described earlier for enonate **11a**, providing the crystalline (-)-8-*epi*-goniofufurone **3** in an overall yield of 63%, mp 208—209 °C, sinters at 190 °C; $[\alpha]_D^{24}$ - 92.5° (*c* 1.1, acetone). The spectroscopic data of the synthetic (-)-8-*epi*-goniofufurone **3** are also identical to those reported, but the reported mp and $[\alpha]_D^{22}$ value had 190—192 °C and + 108° (*c* 0.2, EtOH) respectively,[2] the absolute stereochemistry of natural 8-*epi*-goniofufurone was assigned as **4**.

In conclusion, this paper reports stereocontrolled syntheses of the enantiomers of the antitumour agents goniofufurone **1** and 8-*epi*-goniofufurone **3** *via* a key intramolecular Michael reaction, thereby allowing the assignment of the absolute configurations **2** and **4** to the respective natural materials. The synthesis is short, regio- and stereo-controlled and provides a rare example of using D-*glycero*-D-*gulo*-heptono-γ-lactone as a homochiral starting material.

The biological activities of all the new lactones will be reported elsewhere.

Scheme III



Reagents: i, 5 steps, see ref. 8; ii, 75% aq. AcOH (67%); iii, MeOH, cat. NaOMe (100%); iv, $NaIO_4$, MeOH, H_2O; then Ph_3P=CHCOOMe, MeOH (85%, from **14**); v, 75% aq. AcOH (90%); vi, THF, cat. DBU, 1 day (70%).

Experimental Section

Melting points were recorded on a Peichert apparatus and are uncorrected. ^1H NMR spectra were measured on a Brucker WM250 (250-MHz) spectrometer in acetone-d_6 with tetramethylsilane as an internal standard unless otherwise noted. IR spectra were recorded with a Nicolet 205 FT-IR spectrometer. Mass spectra were taken on a VG Micromass 7070F mass spectrometer. Specific rotations were measured with a JASCO DIP-300 digital polarimeter. Elemental analyses were carried out at Shanghai Institute of Organic Chemistry, Academic Sinica, China. TLC was performed on aluminium precoated with silica gel $60F_{254}$ and compounds were visualised with a spray of 5% w/v dodecamolybdophosphoric acid in ethanol and subsequent heating. Flash chromatography was performed on silica gel (230-400 mesh). THF was distilled from sodium and benzophenone under nitrogen.

1,3-Di-*O*-acetyl-2,4:5,6-di-*O*-isopropylidene-1-*C*-phenyl-D-*glycero*-D-*gulo*-hexitol 8. To a stirred solution of the diol 6[8] (325 mg, 0.96 mmol) in dichloromethane (15 mL) at room temp. was added pyridine (2.3 mL, 28 mmol), acetic anhydride (2.7 mL, 28 mmol) and a catalytic amount of DMAP. After being stirred at room temp. for 12 h, the mixture was then washed with water (20 mL). The aqueous layer was further extracted with $CHCl_3$ (5 × 10 mL). The combined organic extracts were dried ($MgSO_4$) and filtered. Concentration of the filtrate in *vacuo* followed by flash chromatography [ethyl acetate - hexane (1 : 4 v/v)] afforded **8** (325 mg, 80%) as white solids: mp 88—89°C; $[\alpha]_D$ -8.0° (c = 0.85); R_f 0.32 [ethyl acetate - hexane (1 : 4 v/v)]; IR (KBr) 1747 cm^{-1} (ester C=O); ^1H NMR ($CDCl_3$) δ 1.28 (s, 3 H, Me), 1.32 (s, 3 H, Me), 1.44 (s, 3 H, Me), 1.59 (s, 3 H, Me), 2.04 (s, 3 H, Ac), 2.15 (s, 3 H, Ac), 3.87-4.02 (m, 4 H), 4.26 (dd, J = 1.2, 9.5 Hz, 1 H, 2-H), 5.32 (dd, J = 0.5, 1.2 Hz, 1 H, 3-H), 5.63 (d, J = 9.5 Hz, 1 H, 1-H), 7.28-7.36 (m, 5 H, Ph); MS (EI) *m/e* 407 (M^+-Me, 10.6%). Anal. Calcd for $C_{22}H_{30}O_8$: C, 62.5; H, 7.2. Found: C, 62.2; H, 7.2.

1,3-Di-*O*-acetyl-2,4-*O*-isopropylidene-1-*C*-phenyl-D-*glycero*-D-*gulo*-hexitol 9.

To a stirred solution of **8** (500 mg, 1.18 mmol) in acetic acid (20 mL) at room temp. was added water (20 mL). The reaction mixture was stirred at room temp. for 15 h and the solvents were removed by azeotropic distillation with toluene *in vacuo* to give a yellow syrupy residue. Purification by flash chromatography [ethyl acetate - hexane (1 : 1 v/v)] afforded **9** (367 mg, 81%) as a white foam: $[\alpha]^{24}_D$ +19° (*c* =1.0, EtOAc); R_f 0.43 (diethyl ether); IR (KBr) 1750 (ester C=O), 3450 (OH) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.29 (s, 3 H, Me), 1.34 (s, 3 H, Me), 2.02 (s, 3 H, Ac), 2.23 (s, 3 H, Ac), 3.40-3.49 (m, 1 H, 5-H), 3.64 (br dd, *J* = 5.0, 11 Hz, 1 H, 6-H_a), 3.82 (br dd, *J* = 3.2, 11 Hz, 1 H, 6-H_b), 3.92 (dd, *J* = 1.1, 9.4 Hz, 1 H, 4-H), 4.25 (dd, *J* = 1.5, 9.4 Hz, 1 H, 2-H), 5.09 (br t, *J* = 1.4 Hz, 1 H, 3-H), 5.83 (d, *J* = 9.4 Hz, 1 H, 1-H), 7.31-7.38 (m, 5 H, Ph); MS (EI) *m/e* 310 (M^+-2×Me-C_3H_6, 5%), 325 (M^+-Me-C_3H_6, 100%). Anal. Calcd for $C_{19}H_{26}O_8$: C, 59.68; H, 6.85. Found: C, 59.66; H, 6.83.

2,4-*O*-Isopropylidene-1-*C*-phenyl-D-*glycero*-D-*gulo*-hexitol 10.

To a stirred solution of **9** (512 mg, 1.34 mmol) in methanol (10 mL) at room temp. 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 *in vacuo* gave a solid residue which was flash chromatographed (diethyl ether) to give **10** (370 mg, 93%) as colourless solids. Recrystallization from diethyl ether-hexane gave colourless needles: mp 169-172°C; $[\alpha]^{24}_D$ +6° (*c* = 0.53, EtOH); R_f 0.14 (diethyl ether); IR (KBr) 3400 cm^{-1} (OH); ^1H NMR δ 1.27 (s, 3 H, Me), 1.30 (s, 3 H, Me), 3.47-3.96 (m, 5 H), 4.80 (d, *J* = 7.5 Hz, 1 H, 1-H), 7.23-7.44 (m, 5 H, Ph); MS (EI) *m/e* 107 ($PhCHOH^+$, 41%), 191 (M^+-PhCHOH, 4%). Anal. Calcd for $C_{15}H_{22}O_6$: C, 60.39; H, 7.43. Found: C, 60.21; H, 7.24.

2,4-*O*-Isopropylidene-5-*C*-phenyl-L-*gluco*-pentose.

To a stirred solution of **10** (300 mg, 1.01 mmol) in methanol (20 mL) and water (10 mL) at room temp. was added sodium periodate (300 mg, 1.40 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 *in vacuo*. The residue was partitioned between $CHCl_3$ (20 mL) and saturated NH_4Cl (10 mL). The aqueous solution was further extracted with $CHCl_3$ (7 × 10 mL). The combined organic extracts were dried ($MgSO_4$) and filtered. Removal of solvent from the filtrate *in vacuo* gave the title compound as a colourless syrup. This compound was used in the next step without further purification.

***(Z)*-Methyl 4,6-*O*-isopropylidene-7-*C*-phenyl-L-*gluco*-hept-2-enonate 11a and *(E)*-methyl 4,6-*O*-isopropylidene-7-*C*-phenyl-L-*gluco*-hept-2-enonate 11b.**

To a stirred solution of the aldehyde obtained above in methanol (20 mL) at room temp. was added (methoxycarbonyl)methylenetriphenylphosphorane (405 mg, 1.21 mmol) in one portion. After being stirred at room temp. for 2 h, the reaction was concentrated under reduced pressure. Fractionation of the residue by flash chromatography [diethyl ether - hexane (2 : 3 v/v)] gave firstly **11a** (248 mg, 76%) as a colourless solid. Recrystallization from diethyl ether-hexane gave **11a** as colourless needles: mp 135-136°C; $[\alpha]^{24}_D$ -65° (*c* = 0.89, EtOH); R_f 0.20 [diethyl ether - hexane (1 : 1 v/v)]; IR (KBr) 1650, 1719 (α,β-unsaturated ester), 3475 cm^{-1} (OH); ^1H NMR δ 1.29 (s, 3 H, Me), 1.33 (s, 3 H, Me), 3.69 (s, 3 H, CO_2Me), 3.91 (br s, 1 H, 5-H), 4.00 (dd, *J* = 1.4, 7.8 Hz, 1 H, 6-H), 4.78 (br d, *J* = 7.8 Hz, 1 H, 7-H), 5.48 (m, 1 H, 4-H), 5.91 (dd, *J* =

1.4, 12 Hz, 1 H, 2-H), 6.37 (dd, J = 7.0, 12 Hz, 1 H, 3-H), 7.24-7.45 (m, 5 H, Ph); MS (EI) *m/e* 307 (M^+-Me, 6%). Anal. Calcd for $C_{17}H_{22}O_6$: C, 63.34; H, 6.88. Found: C, 63.13; H, 6.94.

The more polar compound **11b** was also obtained as a white solid (50 mg, 16%). Recrystallization from diethyl ether-hexane gave **11b** as colourless needles: mp 114-115 °C; $[\alpha]^{22}_D$ -20° (c = 0.58, EtOH); R_f 0.15 [diethyl ether - hexane (1 : 1 v/v)]; IR (KBr) 1725 (α,β-unsaturated ester), 3433 cm^{-1} (OH); ^1H NMR δ 1.34 (s, 6 H, 2×Me), 3.70 (s, 3 H, CO_2Me), 3.84 (br s, 1 H, 5-H), 4.00 (dd, J = 1.2, 7.8 Hz, 1 H, 6-H), 4.71 (m, 1 H, 4-H), 4.79 (br d, J = 7.8 Hz, 1 H, 7-H), 6.07 (dd, J = 1.9, 16 Hz, 1 H, 2-H), 6.96 (dd, J = 4.2, 16 Hz, 1 H, 3-H), 7.24-7.44 (m, 5 H, Ph); MS (EI) *m/e* 307 (M^+-Me, 5.81%). Anal. Calcd for $C_{17}H_{22}O_6$: C, 63.34; H, 6.88. Found: C, 63.34; H, 6.76.

(*Z*)-7-*C*-Phenyl-L-*gluco*-hept-2-enono-γ-lactone 5.

To a stirred solution of **11a** (101 mg, 0.31 mmol) in acetic acid (8 mL) at room temp. was added water (2 mL). The reaction mixture was stirred at room temp. for 2 d and the solvents were removed by azeotropic distillation with toluene *in vacuo* to give a white solid. Purification by flash chromatography [diethyl ether - hexane (1 : 1 v/v)] afforded **5** (65 mg, 83%) as colourless solids. Recrystallization from diethyl ether-hexane gave colourless needles: mp 109-111 °C; $[\alpha]^{22}_D$ +72° (c = 0.87, EtOH); R_f 0.20 [diethyl ether - hexane (1 : 1 v/v)]; IR (KBr) 1733 (α,β- unsaturated γ-lactone), 3400 cm^{-1} (OH); ^1H NMR δ 3.70 (br dd, J = 2.1, 7.7 Hz, 1 H, 6-H), 4.08 (br d, J = 2.1, 5.5 Hz, 1 H, 5-H), 4.77 (d, J = 7.7 Hz, 1 H, 7-H), 5.24 (ddd, J = 1.7, 1.9, 5.5 Hz, 1 H, 4-H), 6.13 (dd, J = 1.9, 5.8 Hz, 1 H, 2-H), 7.24-7.46 (m, 5 H, Ph), 7.80 (dd, J = 1.7, 5.8 Hz, 1 H, 3-H); MS (EI) *m/e* 107 ($PhCHOH^+$, 100%), 143 (M^+-PhCHOH, 1.17%). Anal. Calcd for $C_{13}H_{14}O_5$: C, 62.39; H, 5.64. Found: C, 61.63; H, 5.67.

(-)-Goniofufurone 1.

The unsaturated lactone **5** (75 mg, 0.3 mmol) was dissolved in THF (20 mL) containing 0.05% (v/v) DBU. The resulting solution was stirred at room temp. After being stirred at room temp. for 1 d, the reaction mixture was filtered through a short column of silica topped with Celite. Removal of solvent from the filtrate *in vacuo* gave a white solid which was flash chromatographed [diethyl ether] to give **1** (53mg, 71%) as colourless crystals. Recrystallization from ethyl acetate-hexane gave **1** as colourless plates: mp 152-154 °C; $[\alpha]^{24}_D$ -8° (c = 0.79, EtOH); R_f 0.24 (diethyl ether); IR (KBr) 1757(γ-lactone), 3406 cm^{-1} (OH); ^1H NMR ($CDCl_3$) δ 2.64-2.83 (m, 3 H, 3-H_a, 3-H_b, 8-OH), 4.10 (dd, J = 2.9, 4.5 Hz, 1 H, 7-H), 4.13 (d, J = 2.8 Hz, 1 H, 6-OH), 4.40 (m, 1 H, 6-H), 4.87 (br d, J = 4.3 Hz, 1 H, 5-H), 5.12 (dt, 1 H, J =1.3, 5.1 Hz, 1 H, 4-H), 5.21 (dd, J =3.3, 4.5 Hz, 1 H, 8-H), 7.33-7.43 (m, 5 H, Ph); MS (EI) *m/e* 107 ($PhCHOH^+$, 100%), 232 (M^+ - H_2O, 9.85%). Anal. Calcd for $C_{13}H_{14}O_5$: C, 62.39; H, 5.64. Found: C, 62.29; H, 5.53.

1-*O*-Acetyl-2,4-*O*-isopropylidene-1-*C*-phenyl-D-*glycero*-D-*ido*-hexitol 13.

A solution of the diacetonide **12**[8] (2.0 g, 5.3 mmol) in aqueous acetic acid (20 mL, 75% v/v) 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)] to afford the triol **13** (1.2 g, 67%) as white solids: mp 140-141°C; $[\alpha]_D$ -17.0° (c = 1.0); R_f 0.17 [ethyl acetate - hexane (3 : 1 v/v)]; IR (film) 1737 (ester C=O), 3450 cm^{-1} (OH), ; ^1H NMR ($CDCl_3$ + D_2O) δ 1.45 (s, 3 H, Me), 1.47 (s, 3 H, Me), 2.05 (s, 3 H, Ac), 3.47 (dd, J = 6.0, 11.6 Hz, 1 H, 6-H_a), 3.59 (dd, J = 1.2, 8.3 Hz, 1 H, 4-H), 3.69 (dd, J = 3.1, 11.6 Hz, 1 H, 6-H_b), 3.72 (dd, J = 1.0, 1.2 Hz, 1 H, 3-H), 4.01 (dd, J = 1.0, 9.1 Hz, 1 H, 2-H), 4.13 (ddd, J = 3.7, 6.0, 8.3 Hz, 1 H, 5-H),

5.99 (d, J = 9.0 Hz, 1 H, 1-H), 7.27-7.44 (m, 5 H, Ph); MS (EI) *m/e* 324 (M^+-Me, 1.2%). Anal. Calcd for $C_{17}H_{24}O_7$: C, 59.99; H, 7.11. Found: C, 59.88; H, 7.09.

2,4-*O*-Isopropylidene-1-*C*-phenyl-D-*glycero*-D-*ido*-hexitol 14.

A solution of **13** (1.0 g, 2.9 mmol) in methanol (10 mL) was treated with a catalytic amount of sodium methoxide at room temp. for 2 h. The mixture was then passed through a pad of silica gel. Concentration of the filtrate yielded the tetraol **14** (0.88 g, 100%) as hygroscopic white solids: mp 52-53°C; $[\alpha]_D$ +15.5° (c = 1.18, EtOH); R_f 0.26 (ethyl acetate); IR (film) 3420 cm^{-1} (OH); ^1H NMR ($CDCl_3$ + D_2O) δ 1.48 (s, 3 H, Me), 1.50 (s, 3 H, Me), 3.31 (dd, J = 1.1, 1.1 Hz, 1 H, 3-H), 3.77 (dd, J = 1.1, 8.2 Hz, 1 H, 2-H), 3.51-3.76 (m, 4 H ,4-H, 5-H, 6-H), 4.90 (d, J = 8.2 Hz, 1 H, 1-H), 7.31-7.49 (m, 5 H, Ph); MS (EI) *m/e* 283 (M^+-Me, 1.11%). Anal. Calcd for $C_{15}H_{22}O_6$: C, 60.4; H, 7.4. Found: C, 60.1; H, 7.1.

2,4-*O*-Isopropylidene-5-*C*-phenyl-D-*ido*-pentose.

A solution of **14** (0.50 g, 1.7 mmol) in methanol (10 mL) was treated with a solution of sodium metaperiodate (0.36 g, 1.7 mmol) in water (15 mL) 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 mL). Concentration of the dried ($MgSO_4$) extracts afforded the aldehyde as white solids (0.44 g, 100%). R_f 0.30 [ethyl acetate - hexane (3 : 1 v/v)]. This compound was used in the next step without further purification.

(*Z*)-Methyl 4,6-*O*-isopropylidene-7-*C*-phenyl-D-*ido*-hept-2-enonate 15.

The above aldehyde (0.44 g, 1.7 mmol) was dissolve in methanol (10 mL) and treated with (methoxycarbonyl)methylenetriphenylphosphorane (0.56 g, 1.7 mmol). The mixture was stirred for 2 h and concentrated to dryness. The residue was triturated with diethyl ether and filtered to eliminate triphenylphosphine oxide. The filtrate was concentrated and the residue flash chromatographed [ether - hexane (2 : 1 v/v)]. The *Z*-alkene **15** was obtained as white solids (0.45 g, 85%): mp 51-52°C; $[\alpha]_D$ -126° (c = 0.81, ethyl acetate); R_f 0.31 [diethyl ether - hexane (2 : 1 v/v)]; IR (film) 1721(α,β-unsaturated methyl acetate), 3508 cm^{-1} (OH); ^1H NMR ($CDCl_3$ + D_2O) δ 1.54 (s, 3 H, Me), 1.55 (s, 3 H, Me), 3.25 (dd, J = 1.0, 1.1 Hz, 1 H, 5-H), 3.71 (s, 3 H, CO_2Me), 3.89 (dd, J = 1.1, 8.0 Hz, 1 H, 6-H), 4.78 (d, J = 7.8 Hz, 1 H, 7-H), 5.48 (ddd, J = 1.0, 1.4, 7.0 Hz, 1 H, 4-H), 5.91 (dd, J = 1.4, 11.8 Hz, 1 H, 2-H), 6.37 (dd, J = 7.0, 11.8 Hz, 1 H, 3-H), 7.24-7.45 (m, 5 H, Ph); MS (EI) *m/e* 307 (M^+-Me, 3.1%). Anal. Calcd for $C_{17}H_{22}O_6$: C, 63.3; H, 6.9. Found: C, 63.6; H, 7.1.

(*Z*)-7-*C*-Phenyl-D-*ido*-hept-2-enono-γ-lactone 16.

The *Z*-Alkene **15** (200 mg, 0.62 mmol) was dissolved in aqueous acetic acid (10 mL, 75% v/v) and the solution stirred at room temp. for 12 h. The reaction mixture was concentrated to dryness *in vacuo* and the residue recrystallized from methanol and ether. γ-Lactone **16** was obtained as white solid (140 mg, 90%): mp 121-122°C; $[\alpha]_D$ +71.7° (c = 1.06, EtOH); R_f 0.25 (diethyl ether); IR (film) 1749 cm^{-1} (γ-lactone); ^1H NMR [$(CD_3)_2C$=O + D_2O] δ 3.41 (dd, J = 2.9, 5.1 Hz, 1 H, 6-H), 3.58 (dd, J = 2.9, 5.9 Hz, 1 H, 5-H), 4.77 (d, J = 5.1 Hz, 1 H, 7-H), 5.10 (ddd, J = 1.6, 2.1, 5.9 Hz, 1 H, 4-H), 5.96 (dd, J = 2.1, 5.8 Hz, 1 H, 2-H), 7.29-7.39 (m, 5 H, Ph), 7.64 (dd, J = 1.5, 5.8 Hz, 1 H, 3-H); MS (EI) *m/e* 251 (MH^+, 0.7%). Anal. Calcd for $C_{13}H_{14}O_5$: C, 62.4; H, 5.6. Found: C, 62.5; H, 5.8.

(-)-8-*epi*-Goniofufurone 3.

A solution of γ-lactone **16** (100 mg, 0.40 mmol) in THF (25 mL) containing 0.05% (v/v) DBU was stirred at room temp. for 12 h. The reaction mixture was then passed through a pad of silica gel and the filtrate concentrated to dryness. The residue was recrystallized from ethyl acetate and hexane. The (-)-8-epi-goniofufurone **3** was obtained as transparent tetragonal plates (70 mg, 70%): mp 208—209 °C, sinters at 190 °C; $[\alpha]_D^{24}$ - 92.5° (*c* 1.1, acetone); R_f 0.29 (diethyl ether); IR (film) 1758 cm^{-1} (γ-lactone), 3402 cm^{-1} (OH); ^1H NMR ($CDCl_3$ + D_2O) δ 2.65 (dd, *J* = 1.0, 18.8 Hz, 1 H, 3-H_a), 2.71 (dd, *J* = 5.0, 18.8 Hz, 1 H, 3-H_b), 4.24 (dd, *J* = 3.2, 3.8 Hz, 1 H, 7-H), 4.90 (dd, *J* = 0.5, 3.9 Hz, 1 H, 5-H), 5.08 (d, *J* = 3.9 Hz, 1 H, 8-H), 5.10 (ddd, *J* = 1.0, 4.2, 5.0 Hz, 1 H, 4-H), 7.35-7.41 (m, 5 H, Ph); MS (EI) *m/e* 232 (M^+-H_2O, 1.8%), 233 (MH^+-H_2O, 2.5%) and the other EIMS fragments were the same as that of natural goniofufurone. Anal. Calcd for $C_{13}H_{14}O_5$: C, 62.39; H, 5.64. Found: C, 62.51; H, 5.46.

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