Available online at www.sciencedirect.com
SCIENCE DIRECT
Carbohydrate Research 341 (2006) 1091–1095
Carbohydrate RESEARCH

Total synthesis of two isoflavone *C*-glycosides: genistein and orobol 8-*C*-β-D-glucopyranosides

Shingo Sato,* Kaoru Hiroe, Toshihiro Kumazawa and Onodera Jun-ichi

Department of Chemistry and Chemical Engineering, Faculty of Engineering, Yamagata University, 4-3-16 Jonan, Yonezawa-shi, Yamagata 992-8510, Japan

Received 20 February 2006; received in revised form 21 March 2006; accepted 27 March 2006
Available online 27 April 2006

Abstract—Genistein and orobol 8-*C*-β-D-glucopyranosides (**1** and **3**) were firstly synthesized in overall yields of 39% and 41% from 2,4-di-*O*-benzylphloroacetophenone (**4**), as follows: (1) the formation of the chalcone (**6**, **7**) by aldol condensation of the benzyl-protected *C*-glycosylphloroacetophenone (**5**), a key intermediate of the total synthesis of **1** and **3** and synthesized by a C-glycosylation method involving the O→C glycoside rearrangement of **4** in 96% yield; (2) the formation of isoflavones (**10**, **11** and **12**, **13**) by the formation of acetals by oxidative rearrangement of the protected chalcones (**8** and **9**) using $Tl(NO_3)_3$, followed by acid-catalyzed cyclization; (3) a final debenzylation by hydrogenolysis.

Keywords: Isoflavone *C*-glycosides; Total synthesis; C-Glycosylation; Oxidative rearrangement; O-Debenzylation

1. Introduction

Genistein 8-*C*-glucoside (**1**), a naturally occurring isoflavone *C*-glycoside, has been isolated together with puerarin (**2**) from *Pueraria lobota*, a popular Chinese herbal medicine,[1] and from *Lupinus luteus* L.,[2] or from the bark of *Dalbergia nitidula* Welw. *ex* Bak.[3] Genistein 8-*C*-glucoside (**1**) inhibits HOCl-induced damage to human erythrocytes[4] and would be expected to be useful as an antioxidant and a radioprotective agent, since it prevents the destruction of cytochrome P-450 in a dose-dependent manner and exerts a protective effect against gamma irradiation in rats.[5] Orobol 8-*C*-glucoside (**3**) is also a naturally occurring isoflavone *C*-glycoside and has been isolated from the bark of *D. monetaria* as a major constituent[6] and from the bark of *D. nitidula* Welw. *ex* Bak.[3] The fact that **3** shows strong mitogenic and colony-stimulating, factor-inducing activities, suggests that it might act on hematopoietic system.[6] Thus, both isoflavone *C*-glycosides have some important biological activities, which are different from isoflavone aglycones that show biological activities[7] analogous to the female hormone, estrogen. Both are prominent bioflavonoid-type compounds.

The total synthesis of some *C*-glycosylflavonoids has been reported; however, most were involved in the synthesis of *C*-glycosylflavone.[8] In spite of these various bioactivities of isoflavone *C*-glycosides, the total synthesis of **2** has only been reported by Lee et al., in which β-D-glucopyranosyl-2,6-dimethoxybenzene, a key intermediate in the synthesis of 8-*C*-glucosyl-7,4′-dihydroxyisoflavone (puerarin **2**) was synthesized by coupling a lithiated aromatic reagent with pyranolactone in 56% yield.[9b] This synthetic method is sophisticated, but it is tedious, and the overall yield is low. In previous studies, we reported on the synthesis of the *C*-glycosylflavones, orientin and its methyl derivatives (isoswertiajaponin, parkinsonin A, and B),[10] and isoorientin[11] using 2,6-di-*O*-benzyl-3-*C*-β-D-(2,3,4,6-tetra-*O*-benzyl)glucopyranosylphloroacetophenone (**5**) as the key intermediate. The *C*-Glycoside **5** was synthesized by the glycosylation of 3,5-benzyl protected phloroacetophenone **4** with benzyl-protected glucosyl fluoride in the presence of catalytic amount of $BF_3{\cdot}OEt_2$ in a yield of 96%.[12] In this report, we propose **5** as a candidate for a key intermediate in

* Corresponding author. Tel./fax: +81 238 26 3121; e-mail: shingo-s@yz.yamagata-u.ac.jp

0008-6215/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.carres.2006.03.038

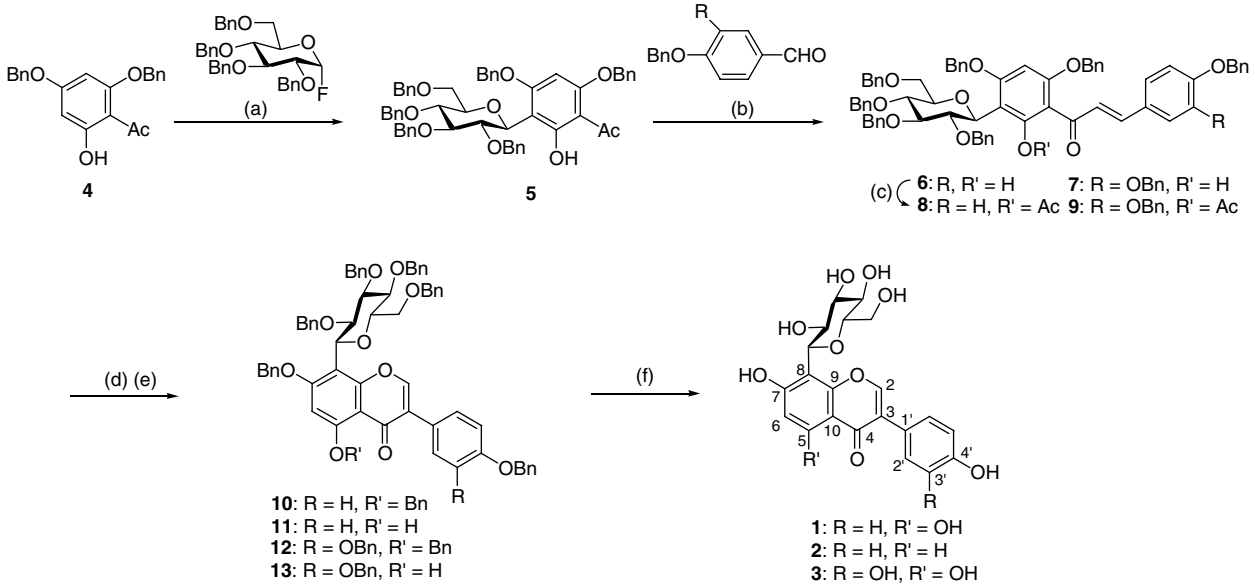
the total synthesis of 5,7,4′-trihydroxy- and 5,7,3′,4′-tetrahydroxy-8-*C*-β-D-glucosylisoflavones, namely genistein and orobol 8-*C*-glucosides, which have not yet been synthesized. Since the final demethylation step was difficult and gave a poor yield in the total synthesis of **2**,[9] our approach employs the benzyl group, which can be deprotected readily under mild hydrogenation conditions, as a protecting group for all hydroxyl groups. In the synthesis of **1** and **3** starting from **5**, the synthesis of the chalcone by aldol condensation with benzyl-protected hydroxybenzaldehydes, followed by the formation of acetals by oxidative rearrangement of the chalcones and synthesis of isoflavones by a subsequent acid-catalyzed cyclization of the acetals, as was employed in the synthesis of **2**,[9] were employed. Although thallium(III) nitrate (TTN) was used here as a oxidant in the key oxidative rearrangement based on the reports of Eade et al.[9a] and Lee et al.,[9b] it might be possible to use environmentally benign and recently developed diacetoxyiodobenzene (DIB) as an alternative reagent.[13] As a further final deprotecting step, debenzylation involves much milder conditions than those required for demethylation. We describe here the first and effective total synthesis of two isoflavone *C*-glycosides, namely genistein 8-*C*-β-D-glucoside (**1**) and orobol 8-*C*-β-D-glucoside (**3**) (Scheme 1).

2. Results and discussion

The aldol condensation of **5** with 4-benzyloxy- and 3,4-dibenzyloxybenzaldehyde in 1,4-dioxane at room temperature in the presence of sodium methoxide (NaOMe) gave chalcones **6** and **7** in 98% and 92% yields, respectively. After acetylation of the 2-hydroxyl group of **6** and **7** (94% and 90%), oxidative rearrangement, by treatment with 2 equiv of TTN in dimethoxymethane and methanol gave the dimethyl acetals (δ 3.11, 3.35, OMe × 2; 2.99, 3.23, OMe × 2), respectively, which were refluxed without further purification in the presence of a 10% HCl–methanol solution in 1,4-dioxane for 1 day,[9b] to afford the desired isoflavones **10** and **12** and their 4-O-debenzylated products **11** and **13** in a total yield of 47% and 60% from **8** and **9**, respectively. No influence of the benzyl protecting group was observed in the oxidative rearrangement reaction or the acid-catalyzed cyclization. The subsequent debenzylation of **10** and **11** and **12** and **13** was performed by hydrogenolysis using 20 wt % of $Pd(OH)_2/C$[14,8e] in EtOAc and MeOH under an H_2 atmosphere to yield **1** and **3** in 94% and 86% yield, respectively, without the reduction of the olefin. Under hydrogenolysis using 10% Pd–C in the presence of aqueous HCl, the yield in either case was low, 41% and 38%, respectively. Since this debenzylation reaction proceeded in good yield, as a consequence, the total synthesis of **1** and **3** starting from **4** was accomplished in relatively good overall yields of 39% and 41%, respectively. The ^{13}C NMR spectral data for the compounds were in agreement with data obtained for the natural products (see Table 1).

3. Conclusion

Two naturally occurring isoflavone *C*-glycosides, genistein, and orobol 8-*C*-glucosides, were effectively



Scheme 1. Total synthesis of genistein and orobol *C*-β-D-glucosides (**1**, **3**). Reagents and conditions: (a) $BF_3{\cdot}OEt_2$, −78 °C to rt, **5**: *Y* 96%; (b) MeONa in 1,4-dioxane, reflux for 20 h, **6**: *Y* 98%, **7**: *Y* 92%; (c) Ac_2O–pyridine–DMAP, rt, 6 h, **8**: *Y* 94%, **9**: *Y* 90%; (d) TTN (2 equiv) in MeOH–$CHCl_3$, reflux for 26 h; (e) 10% HCl in MeOH–1,4-dioxane, reflux for 22 h, *Y* 47% (**10**:**11** = 70:30), *Y* 60% (**12**:**13** = 50:50); (f) H_2–20% $Pd(OH)_2/C$, in EtOAc–MeOH, rt for 5 h, **1**: *Y* 94%, **3**: *Y* 86%.

Table 1. ^{13}C NMR spectral data for genistein and orobol 8-*C*-glycosides (**1** and **3**)

Compound	1		3	
Carbon	Natural[1] (DMSO-d_6)	Synthetic (CD_3OD)	Natural[3b] (CD_3OD)	Synthetic (CD_3OD)
2	153.6	154.7	154.6	154.7
3	122.0	124.4	124.2	124.6
4	180.4	182.5	182.3	182.6
5	160.7	163.4	163.2	163.5
6	98.7	100.4	100.2	100.4
7	162.9	164.7	164.4	164.8
8	103.9	106.5	106.3	106.5
9	156.2	158.0	157.7	158.0
10	104.5	104.4	104.1	104.6
1′	121.2	123.1	123.5	123.7
2′	130.1	131.3	116.3	116.4
3′	115.1	116.1	145.9	146.3
4′	157.0	158.8	146.5	146.9
5′			117.3	117.4
6′			121.6	121.7
G1	73.1	75.4	75.2	75.5
G2	70.5	72.8	72.7	72.9
G3	78.4	80.1	79.9	80.1
G4	70.2	71.8	71.6	71.8
G5	81.3	82.6	82.3	82.7
G6	61.2	62.9	62.7	62.9

synthesized by aldol condensation of the benzyl-protected *C*-β-D-glucopyranosylphloroacetophenone, oxidative rearrangement using TTN, followed by acid-catalyzed cyclization and a final deprotection.

4. Experimental

The solvents used in this reaction were all prepared by distillation. Separation and purification involved the use of flash-column chromatography using silica gel (230–400 mesh, Fuji-Silysia Co. Ltd, BW-300), and column chromatography using Sephadex LH-20 gel. Melting points were determined on a Shibayama micro-melting point apparatus and are uncorrected. Optical rotations were recorded on a JASCO DIP-370 polarimeter. Absorption spectra were measured using a Hitachi U-3000 spectrophotometer. IR measurements were achieved using a Horiba FT-720 IR spectrometer. NMR spectra were recorded on a Varian Inova 500 spectrometer using Me_4Si as the internal standard. Mass spectra were obtained by the fast-atom bombardment (FAB) method using 3-nitrobenzyl alcohol (NBA) as a matrix on a JEOL JMS-AX505HA. Elemental analyses were performed on a Perkin–Elmer PE 2400 II instrument.

4.1. Preparation of 5

Preparation of **5** was carried out according to previously published reports.[12a,b]

4.2. Aldol condensation

4.2.1. 4,4′,6′-Tribenzyloxy-2′-hydroxy-3′-*C*-(2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosyl)chalcone (6). To a solution of **5** (1.24 g, 1.43 mmol) and *p*-benzyloxybenzaldehyde (0.33 g, 1.57 mmol) in 1,4-dioxane (20 mL), was added 10 mL of a 28% NaOMe–MeOH (solution), followed by stirring at room temperature for 20 h. The reaction mixture was poured into 100 mL of a 2 M HCl solution and extracted twice with EtOAc. The combined extracts were washed with water and brine, dried over $MgSO_4$, and then evaporated in vacuo. The residue was purified by flash-column chromatography on silica gel (7:1 hexane–EtOAc) to give **6** (1.49 g, 98%) as a viscous yellow oil: $[\alpha]_D^{22}$ −1.58 (*c* 1.015, $CHCl_3$); IR (KBr) *ν* 3060, 3030, 2868, 1622, 1579 cm^{-1}; ^1H NMR ($CDCl_3$) *δ* 3.50–3.68 (m, 5H, H-3″, -4″, -5″, -6″ab), 4.35 (br t, 1H, *J* 9.8 Hz, H-2″), 4.90 (d, 1H, *J* 9.8 Hz, H-1″), 6.50 (s, 1H, ArH), 6.91–7.51 (m, 39H, ArH), 7.61 (d, 1H, *J* 15.4 Hz, *trans*-vinyl H), 7.65 (d, 1H, *J* 15.4 Hz, *trans*-vinyl H), 14.01 (br s, 1H, OH); FABMS (*m*/*z*) 1065 $(M+H)^+$. Anal. Calcd for $C_{70}H_{64}O_{10}$: C, 78.92; H, 6.06. Found: C, 78.54; H, 6.02.

4.2.2. 3,4,4′,6′-Tetrabenzyloxy-2′-hydroxy-3′-*C*-(2″,3″,4″,6″-tetra-*O*-benzyl-β-D-glucopyranosyl)chalcone (7). Chalcone **7** was produced in a yield of 88% (2.60 g) as a viscous yellow oil from **5** (2.20 g, 2.53 mmol) and 3,4-dibenzyloxybenzaldehyde (0.97 g, 3.05 mmol) in the same manner as for the synthesis of **6**. Data for **7**: $[\alpha]_D^{21}$ −5.42 (*c* 0.775, $CHCl_3$); IR (KBr) *ν* 3062, 3030, 2861, 1624, 1580, 1558, 1508, 1454, 1429, 1260, 1151, 1136, 1066, 1028 cm^{-1}; ^1H NMR ($CDCl_3$) *δ* 3.50–3.69 (m, 5H, H-3″, -4″, -5″, -6″ab), 4.33 (br t, 1H, *J* 9.9 Hz, H-2″), 4.90 (d, 1H, *J* 9.9 Hz, H-1″), 6.49 (s, 1H, ArH), 6.88–7.48 (m, 43H, ArH), 7.57 (d, 1H, *J* 15.6 Hz, *trans*-vinyl H), 7.62 (d, 1H, *J* 15.6 Hz, *trans*-vinyl H), 13.75 (br s, 1H, OH); FABMS (*m*/*z*) 1171 $(M+H)^+$. Anal. Calcd for $C_{77}H_{70}O_{11}$: C, 78.95; H, 6.02. Found: C, 78.76; H, 6.04.

4.3. Acetylation of chalcone

4.3.1. 2′-Acetoxy-4,4′,6′-tribenzyloxy-3′-*C*-(2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosyl)chalcone (8). Chalcone **6** (2.69 g, 2.30 mmol) and DMAP (30 mg) were dissolved in Ac_2O (50 mL) and pyridine (18 mL) and stirred at room temperature for 20 h. The reaction mixture was poured into water and extracted twice with EtOAc. The combined extracts were washed with 1 M HCl, water, and brine, and then dried over $MgSO_4$, followed by evaporation. The residue was purified by flash-column chromatography on silica gel (3:1 hexane–EtOAc) to give **8** (2.5 g, 90%) as a pale-yellow oil: $[\alpha]_D^{21}$ −23.4 (*c* 0.76, $CHCl_3$); IR (KBr) *ν* 3062, 3032, 2923, 2862, 1774, 1603 cm^{-1}; ^1H NMR ($CDCl_3$) *δ* 2.04

(s, 3H, ArOAc), 3.47–4.13 (m, 5H, H-3″, -4″, -5″, -6″ab), 4.65 (dd, 1H, *J* 9.2, 9.8 Hz, H-2″), 4.82 (d, 1H, *J* 9.8 Hz, H-1″), 6.41 (s, 1H, ArH), 6.82 (d, 1H, *J* 16.1 Hz, *trans*-vinyl H), 6.86–7.45 (m, 44H, ArH and *trans*-vinyl H); FABMS (*m*/*z*) 1107 $(M+H)^+$. Anal. Calcd for $C_{72}H_{66}O_{11}$: C, 78.10; H, 6.01. Found: C, 77.77; H, 5.84.

4.3.2. 2′-Acetoxy-3,4,4′,6′-tetrabenzyloxy-3′-*C*-(2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosyl)chalcone (9). The acetylation of **7** was carried out in the same manner as for **6** to give **9** as a pale-yellow viscous oil in a yield of 90%: $[\alpha]_D^{22}$ −25.6 (*c* 1.000, $CHCl_3$); IR (KBr) *ν* 3062, 3030, 2913, 2868, 1774, 1604 cm^{-1}; ^1H NMR ($CDCl_3$) *δ* 2.03 (s, 3H, ArOAc), 3.45–4.10 (m, 5H, H-3″, -4″, -5″, -6″ab), 4.97 (dd, 1H, *J* 9.2, 9.8 Hz, H-2″), 4.97 (d, 1H, *J* 9.8 Hz, H-1″), 6.37 (s, 1H, ArH), 6.79 (d, 1H, *J* 16.1 Hz, *trans*-vinyl H), 6.86–7.45 (m, 44H, ArH and *trans*-vinyl H); FABMS (*m*/*z*) 1215 $(M+H)^+$. Anal. Calcd for $C_{79}H_{72}O_{12}$: C, 78.19; H, 5.98. Found: C, 78.15; H, 5.83.

4.4. Synthesis of the isoflavone system in the genistein series

TTN (0.33 g, 0.74 mmol) was added to a solution of **8** (0.41 g, 0.37 mmol) in $(MeO)_3CH$ (10 mL) and MeOH (10 mL). The mixed solution was stirred at 40 °C for 23 h and then poured into water (100 mL) and extracted twice with toluene. The combined extracts were washed with water and brine and then dried over anhyd $MgSO_4$, and evaporated in vacuo to give pale-brown solids as the oxidative-rearrangement product that was used without purification in the next reaction. A solution of the residue in 1,4-dioxane (1 mL), MeOH (5 mL) and 10% HCl (0.5 mL) was refluxed for 20 h. The reaction mixture was extracted twice with toluene. The combined extracts were washed with water and brine and then dried over anhyd Na_2SO_4, and the solution evaporated in vacuo. The residue was separated by flash-column chromatography on silica gel (5:1 hexane–EtOAc) to give the fraction including **10**, which was further recrystallized from Et_2O–EtOAc to give **10** (0.12 g, 33%) as pale-yellow prisms, and **11** (0.05 g, 14%) as a pale-yellow oil.

4.4.1. 5,7,4′-Tribenzyloxy-8-*C*-(2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosyl)isoflavone (10). Pale-yellow prisms: mp 148–149 °C; $[\alpha]_D^{21}$ −33.9 (*c* 0.985, $CHCl_3$); IR (KBr) *ν* 3062, 3030, 2897, 2864, 1653, 1608, 1568, 735, 696 cm^{-1}; ^1H NMR ($CDCl_3$) *δ* 3.56–4.25 (m, 5H, H-3″,4″,5″,6″ab), 4.23 (br t, 1H, *J* 9.5, 9.3 Hz, H-2″), 4.50 (d, 1H, *J* 9.5 Hz, H-1″), 6.39, 6.40 (each s, 1H, ArH),* 6.73–7.57 (m, 39H, ArH), 7.80 (s, 1H, H-2),* two peaks were observed, corresponding to rotamers; FABMS (*m*/*z*) 1063 $(M+H)^+$. Anal. Calcd for $C_{70}H_{62}O_{10}$: C, 79.07; H, 5.88. Found: C, 78.90; H, 5.67.

4.4.2. 7,4′-Dibenzyloxy-5-hydroxy-8-*C*-(2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosyl)isoflavone (11). Pale-yellow viscous oil: $[\alpha]_D^{21}$ −35.6 (*c* 1.280, $CHCl_3$); IR (KBr) *ν* 3062, 3030, 2906, 2866, 1649, 1608, 1581, 737, 696 cm^{-1}; ^1H NMR ($CDCl_3$) *δ* 6.41, 6.42 (each s, 1H, ArH),* 6.76–7.52 (m, 34H, ArH), 7.90 (s, 1H, H-2), 13.19, 13.24 (each s, 1H, ArOH);* FABMS (*m*/*z*) 973 $(M+H)^+$. Anal. Calcd for $C_{63}H_{56}O_{10}$: C, 77.76; H, 5.80. Found: C, 77.43; H, 5.51.

4.5. Synthesis of isoflavone system in the orobol series

The oxidative rearrangement of **9** (0.37 g) was carried out in the same manner as for **8**. A solution of the crude oxidative-rearrangement products of **9** in 1,4-dioxane (1 mL), MeOH (5 mL), and 10% HCl (0.5 mL) was refluxed for 22 h. The reaction mixture was extracted twice with toluene. The combined extracts were washed with water and brine, then dried over anhyd Na_2SO_4, and evaporated in vacuo. The residue was separated by flash-column chromatography on silica gel (2:1 hexane–EtOAc) to give **12** (0.12 g, 30%) and **13** (0.14 g, 30%) as a pale-yellow oil, respectively.

4.5.1. 5,7,3′,4′-Tetrabenzyloxy-8-*C*-(2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosyl)isoflavone (12). Pale-yellow viscous oil: $[\alpha]_D^{21}$ −28.3 (*c* 1.04, $CHCl_3$); IR (KBr) *ν* 3062, 3030, 2904, 2866, 1649, 1599, 1510, 737, 696 cm^{-1}; ^1H NMR ($CDCl_3$ at 140 °C) *δ* 3.50–3.75 (m, 5H, H-3″,4″,5″,6″ab), 4.23 (br t, 1H, *J* 9.5, 8.9 Hz, H-2″), 5.02 (d, 1H, *J* 9.6 Hz, H-1″), 6.80, 6.81 (s, 1H, ArH),* 6.94–7.58 (m, 43H, ArH), 8.00 (s, 1H, H-2); FABMS (*m*/*z*) 1169 $(M+H)^+$. Anal. Calcd for $C_{77}H_{68}O_{11}$: C, 79.09; H, 5.86. Found: C, 79.05; H, 6.04.

4.5.2. 7,3′,4′-Tribenzyloxy-5-hydroxy-8-*C*-(2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosyl)isoflavone (13). Pale-yellow oil: $[\alpha]_D^{21}$ −22.7 (*c* 1.04, $CHCl_3$); IR (KBr) *ν* 3062, 3030, 2927, 2864, 1651, 1581, 1508, 737, 696 cm^{-1}; ^1H NMR ($CDCl_3$) *δ* 6.40, 6.42 (each s, 1H, ArH),* 6.85–7.50 (m, 38H, ArH), 7.80 (s, 1H, H-2), 13.19, 13.22 (each s, 1H, ArOH);* FABMS (*m*/*z*) 1063 $(M+H)^+$. Anal. Calcd for $C_{70}H_{62}O_{11}$: C, 77.90; H, 5.79. Found: C, 77.63; H, 5.89.

4.6. Synthesis of genistein-8-*C*-glucoside (1)

To a solution of **10** (0.15 g, 0.14 mmol) and **11** (0.05 g, 0.05 mmol) in MeOH (3 mL) and EtOAc (3 mL) was added 20 wt % of $Pd(OH)_2/C$ (20 mg). The suspension was stirred vigorously under an H_2 atmosphere for 5 h at room temperature. The catalyst was then removed by filtration through Celite, followed by washing with MeOH. The filtrate was evaporated in vacuo and purified by flash-column chromatography on silica gel

(15:55:2:1 acetone–EtOAc–H_2O–AcOH) and subsequent column chromatography on Sephadex LH-20 gel (8:2 MeOH–H_2O) to give **1** (57.2 mg, 94%) as a pale-yellow amorphous powder.

Data for **1**: $[\alpha]_D^{21}$ +17.9 (*c* 1.005, MeOH) [$[\alpha]_D^{30}$ +13.0 (*c* 0.5, DMSO),[1] $[\alpha]_D^{25}$ +4.7 (*c* 0.52, DMSO)[2]]; R_f 0.38 (15:30:2:1 acetone–EtOAc–H_2O–HOAc); UV λ_{max}^{MeOH} ($\log\varepsilon$) 263.5 nm (4.57) [λ_{max}^{MeOH} ($\log\varepsilon$) 265 nm (4.46);[1] 264 nm (4.47)[2]]; IR (KBr) *v* 3400, 2897, 2933, 1653, 1616, 1585 cm^{-1}; ^{13}C NMR (Table 1); FABMS (*m*/*z*) 433 $(M+H)^+$. Anal. Calcd for $C_{21}H_{20}O_{10}\cdot H_2O$: C, 56.00; H, 4.92. Found: C, 55.86; H, 5.10.

4.7. Synthesis of orobol-8-*C*-glucoside (3)

Debenzylation of **12** (0.12 g, 0.10 mmol) and **13** (0.14 g, 0.13 mmol) was carried out in the same manner as for **10** and **11**, and **3** was obtained in 86% yield (88.6 mg) as a pale-yellow amorphous powder: $[\alpha]_D^{21}$ +14.2 (*c* 0.790, MeOH), R_f 0.32 (15:30:2:1 acetone–EtOAc–H_2O–HOAc); UV λ_{max}^{MeOH} ($\log\varepsilon$) 264.5 nm (4.47) (λ_{max}^{MeOH} 264 nm[3b]). IR (KBr) *v* 3367, 2931, 1655, 1616, 1577 cm^{-1}; ^{13}C NMR (Table 1); FABMS (*m*/*z*) 449 $(M+H)^+$. Anal. Calcd for $C_{21}H_{20}O_{11}\cdot 0.5H_2O$: C, 55.14; H, 4.63. Found: C, 55.46; H, 4.92.

Acknowledgement

The authors gratefully acknowledge the technical assistance of Mr. Hiroaki Nishizawa.

References

1. Kinjo, J.; Furusawa, J.; Baba, J.; Takeshita, T.; Yamasaki, M.; Nohara, T. *Chem. Pharm. Bull.* **1987**, *35*, 4846–4850.
2. Watanabe, K.; Kinjo, J.; Nohara, T. *Chem. Pharm. Bull.* **1993**, *41*, 394–396.
3. (a) Heerden, F. R.; Brandt, E. V.; Roux, D. G. *J. Chem. Soc., Perkin Trans. 1* **1980**, 2463–2469; (b) Nunes, D. S.; Haag, A.; Bestmann, H. J. *Liebigs Ann. Chem.* **1989**, 331–335.
4. Zavodnik, L. B.; Zavodnik, I. B.; Lapshina, E. A.; Shkodich, A. P.; Bryszewska, M.; Unko, V. U. *Biochemistry (Moscow)* **2000**, *65*, 946–951.
5. Zavodnik, L. B. *Radiat. Biol. Radioecol.* **2003**, *43*, 432–438.
6. Kawaguchi, K.; Melloalves, S.; Watanabe, T.; Kikuchi, S.; Satake, M.; Kumazawa, Y. *Planta Med.* **1998**, *329*, 855–859.
7. (a) Ricketts, M.-L.; Moore, D. D.; Banz, W. J.; Mezei, O.; Shay, N. F. *J. Nutr. Biochem.* **2005**, *16*, 321–330; (b) Kulling, S. E.; Lehmann, L.; Metzler, M. *J. Chromatgr. B* **2002**, *777*, 211–218.
8. (a) Chopin, J.; Dellamonica, G. *C*-Glycosylflavonoids. In *The Flavonoids*; Harborne, J. B., Ed.; Chapman and Hall: London, 1988; pp 63–97; (b) Chopin, J.; Durix, A.; Bouillant, M. L. *Tetrahedron Lett.* **1966**, 3657–3661; (c) Mahling, J.-A.; Jung, K.-H.; Schmidt, R. R. *Liebigs Ann. Chem.* **1995**, 461–466; (d) Frick, W.; Schmidt, R. R. *Liebigs Ann. Chem.* **1989**, 565–570; (e) Oyama, K.-i.; Kondo, T. *J. Org. Chem.* **2004**, *69*, 5240–5246; (f) Nakatsuka, T.; Tomimori, Y.; Fukuda, Y.; Nukada, H. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 3201–3203; (g) Furuta, T.; Kimura, T.; Kondo, S.; Mihara, H.; Wakimoto, T.; Nukada, H.; Tsuji, K.; Tanaka, K. *Tetrahedron* **2004**, *60*, 9375–9379.
9. (a) Eade, R. A.; McDonald, F. J.; Pham, H.-P. *Aust. J. Chem.* **1978**, *31*, 2699–2706; (b) Lee, D. Y. W.; Zhang, W.-Y.; Karnati, V. V. R. *Tetrahedron Lett.* **2003**, *44*, 6857–6859.
10. Kumazawa, T.; Kimura, T.; Matsuba, S.; Sato, S.; Onodera, J.-i. *Carbohydr. Res.* **2001**, *324*, 183–193.
11. Kumazawa, T.; Minatogawa, T.; Matsuba, S.; Sato, S.; Onodera, J.-i. *Carbohydr. Res.* **2000**, *329*, 507–513.
12. (a) Kumazawa, T.; Ohki, K.; Ishida, M.; Sato, S.; Onodera, J.-i.; Matsuba, S. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 1379–1384; (b) Kumazawa, T.; Kimura, T.; Matsuba, S.; Sato, S.; Onodera, J.-i. *Carbohydr. Res.* **2001**, *334*, 183–193; (c) Kumazawa, T.; Akutsu, Y.; Matsuba, S.; Sato, S.; Onodera, J.-i. *Carbohydr. Res.* **1999**, *320*, 129–137; (d) Kumazawa, T.; Saito, T.; Matsuba, S.; Sato, S.; Onodera, J.-i. *Carbohydr. Res.* **2000**, *329*, 855–859; (e) Kumazawa, T.; Sato, S.; Matsuba, S.; Onodera, J.-i. *Carbohydr. Res.* **2001**, *322*, 103–108; (f) Kometani, T.; Kondo, H.; Fujimori, Y. *Synthesis* **1988**, 1005; (g) Matsumoto, T.; Katsuki, M.; Suzuki, K. *Tetrahedron Lett.* **1988**, *29*, 6935–6938.
13. Kawamura, Y.; Maruyama, M.; Tokuoka, T.; Tsukayama, M. *Synthesis* **2002**, *17*, 2490–2496.
14. Tückmantel, W.; Kozikowski, A. P.; Romanczyk, L. J., Jr. *J. Am. Chem. Soc.* **1999**, *121*, 12073–12081.