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Note

Synthesis and biological activity of 4′,8-dihydroxyisoflavon-7-yl D-hexopyranosides

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Abstract

Four 4′,8-dihydroxyisoflavon-7-yl hexopyranoside derivatives having an aglycon part of A-76202 were synthesized, and their biological activities were evaluated toward rat liver α-glucosidase. However, the activities were disappointing. © 2001 Elsevier Science Ltd. All rights reserved.

Keywords: Glycosidation; Isoflavone; Stereoselective synthesis

Many phenolic isoflavone glycoconjugates are known in nature, and some of them have been synthesized. Recently, A-76202 (4′,8-dihydroxyisoflavon-7-yl α-D-arabinofuranoside) was isolated from *Rhodococcus* sp. SANK 61694,[1] and synthesized.[2] A-76202 is a strong inhibitor of α-glucosidase I and II existing in endoplasmic reticulum, and it also participates in the processing of secretory, cell membrane, and virus surface-glycoproteins. Although A-76202 has strong inhibitory activity for these enzymes in vitro, its activity is very weak in vivo. This is presumed difficult for A-76202 to penetrate through the cell membrane. We were interested in 4′,8-dihydroxyisoflavon-7-yl sugar derivatives having the exact aglycon of A-76202 to overcome this defect. Therefore, we tried to synthesize 4′,8-dihydroxyisoflavon-7-yl sugar derivatives such as hexopyranosides instead of the arabinofuranoside in order to examine their activities toward α-glucosidase (Fig. 1).

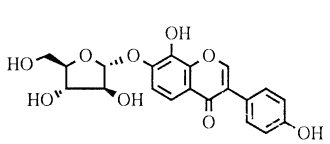

Fig. 1. A-76202.

First, we attempted a synthetic procedure reported in the synthesis of A-76202 for the glycosidation reaction of 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (**1**)[3] with 4′,8-diallyloxy-7-hydroxyisoflavone (**2**).[2] The reaction of bromide **1** with the lithium salt of **2** prepared in THF by addition of a hexane solution of BuLi at room temperature was carried out under various conditions. However, no glycosidation product was obtained as only the phenolic isoflavone **2** was recovered. Second, a mixture of bromide **1** and phenolic isoflavone **2** was treated with 1.2

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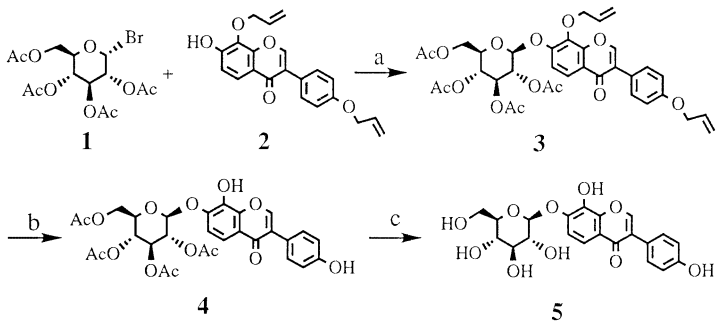


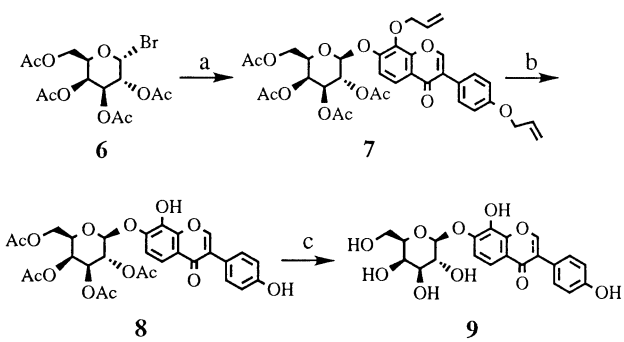
Scheme 1. Reagents and conditions: (a) Ag_2CO_3, pyridine, rt, 18 h, 13%; (b) $RhCl_3$, EtOH, reflux, 1.5 h, 73%; (c) ca. KOH, EtOH, rt, 4 h, 100%.

equivalents silver trifluoromethanesulfonate, 1.2 equivalents of bis(cyclopentadienyl)-hafnium dichloride and an excess of 4 Å molecular sieves in dichloromethane at 0–24 °C under nitrogen according to Suzuki's method.[4] However, this reaction also did not proceed. Finally, a glycosidation reaction of **2** with **1** using silver carbonate in pyridine[5] was carried out to yield β-D-glucoside **3** (13% yield), the recovered **2**, and 2,3,4,6-tetra-*O*-acetyl-D-glucopyranose derived from **1**. Although the yield of this glycosidation reaction was low, the reaction exclusively produced the 1,2-trans β anomer mainly due to the 2-OAc neighboring group effect. Deprotection of the two allyl groups of **3** by treatment with rhodium trichloride gave diphenol **4** in 73% yield. Deacetylation of **4** with a catalytic amount of KOH in EtOH quantitatively yielded **5** (Scheme 1).

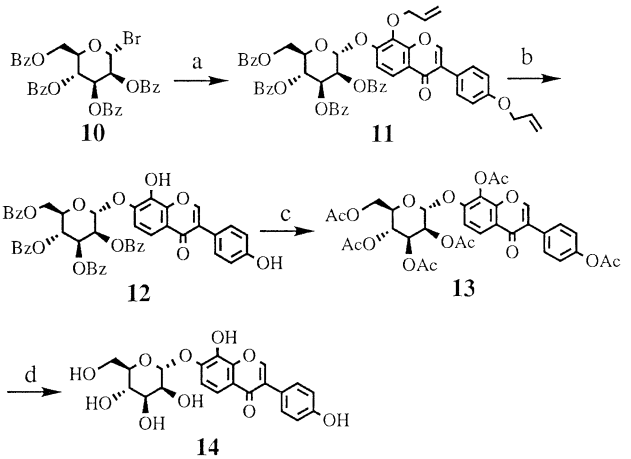
And also, glycosidation of **2** with 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide (**6**),[6] by the same procedure as for the formation of **3** from **1** and **2** using silver carbonate in pyridine, yielded β-D-galactoside **7** (55% yield), producing only the 1,2-trans β anomeric form. This should be also due to the 2-OAc neighboring group effect. Deprotection of the two allyl groups of **7** by treatment with rhodium trichloride gave diphenol **8** in 62% yield. Deacetylation of **8** with a catalytic amount of KOH in EtOH quantitatively yielded **9** (Scheme 2).

In addition, glycosidation of **2** with 2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl bromide (**10**),[7] by the same procedure used for the formation of **3** from **1** and **2** using silver carbonate in pyridine, yielded α-D-mannoside **11** (31% yield), exclusively producing the α anomeric form mainly due to the 2-OBz neighboring group effect. Deprotection of the two allyl groups of **11** by treatment with rhodium trichloride gave diphenol **12** in 67% yield. Debenzoylation of **12** with 0.2 M NaOH in MeOH gave **14**, which was contaminated with unidentified byproducts. Therefore, the mixture was acetylated with Ac_2O in pyridine to yield **13** in two steps 60% yield after chromatographic purification. Deacetylation of **13** with a catalytic amount of KOH in EtOH gave **14** in 97% yield (Scheme 3).

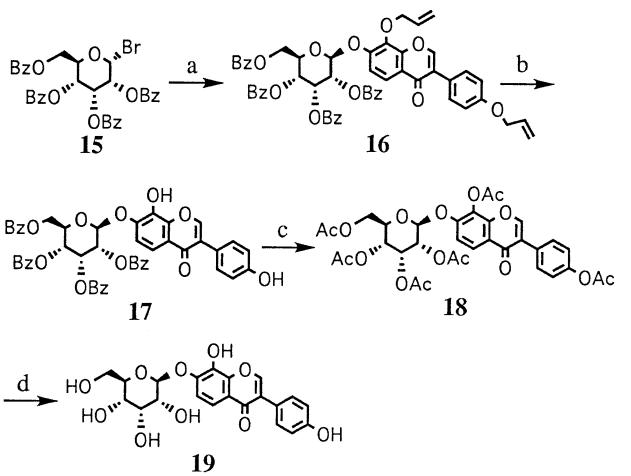
On addition, glycosidation of **2** with 2,3,4,6-tetra-*O*-benzoyl-α-D-allopyranosyl bromide (**15**), prepared from 1,2,3,4,6-penta-*O*-benzoyl-β-D-allopyranose according to the procedure described in the formation of 2,3,4,6-tetra-*O*-acetyl-α-D-allopyranosyl bromide,[8] by the same procedure used for the formation of **3** from **1** and **2** using silver carbonate in pyridine, yielded β-D-allopyranoside **16** (22% yield), producing only the β anomeric form also mainly due to the 2-OBz neighboring group effect. Deprotection of the two allyl groups of **16** by treatment with



Scheme 2. Reagents and conditions: (a) **2**, Ag_2CO_3, pyridine, rt, 18 h, 55%; (b) $RhCl_3$, EtOH, reflux, 1.5 h, 62%; (c) ca. KOH, EtOH, rt, 4 h, 100%.



Scheme 3. Reagents and conditions: (a) **2**, Ag_2CO_3, pyridine, rt, 18 h, 31%; (b) $RhCl_3$, EtOH, reflux, 1.5 h, 67%; (c) (1) 0.2 M NaOH in MeOH, rt, 18 h; (2) Ac_2O, pyridine, rt, 1 h, 2 steps 60%; (d) ca. KOH, EtOH, rt, 4 h, 100%.



Scheme 4. Reagents and conditions: (a) **2**, Ag_2CO_3, pyridine, rt, 18 h, 22%; (b) $RhCl_3$, EtOH, reflux, 1.5 h, 80%; (c) (1) 0.2 M NaOH in MeOH, rt, 18 h, (2) Ac_2O, pyridine, rt, 1 h, 2 steps 72%; (d) ca. KOH, EtOH, rt, 4 h, 100%.

rhodium trichloride gave diphenol **17** in 80% yield. Debenzoylation of **17** with 0.2 M NaOH in MeOH gave **19**, which was contaminated with unknown substances. Therefore, the mixture was also acetylated with Ac_2O in pyridine to give **18** in two steps after chromatographic purification (72% yield). Deacetylation of **18** with a catalytic amount of KOH in EtOH quantitatively gave **19** (Scheme 4).

The biological activities (IC_{50} values) toward rat liver microsome α-glucosidase of compounds **5** (β-D-glucopyranoside), **9** (β-D-galactopyranoside), **14** (α-D-mannopyranoside), **19** (β-D-allopyranoside) and A-76202 were 14.3, >100 μg/mL, 103.1 ng/mL, >100 μg/mL and 5.6 ng/mL, respectively. These four compounds synthesized and natural A-76202 have inhibitory activities as shown in Figs. 2 and 3; however, the activities of these compounds are much weaker than that of A-76202. Compound **14**, which has an α-mannose moiety as the glycan part, showed the most effective inhibitory activity among these four compounds except A-76202. Both A-76202 and **14** have the α-oriented aglycon part on arabinose and mannose, respectively. This may reveal that an α-oriented sugar-substrate may be mimicked as the part recognized by this α-glucosidase as a matter of course. Accordingly, compounds **5**, **9**, and **19** having β-oriented aglycon moieties may be less active than **14**. Among compounds **5**, **9**, and **19**, compound **5** was more active than the others. This may explain that the glucose moiety of **5** may be recognized as a better binding site

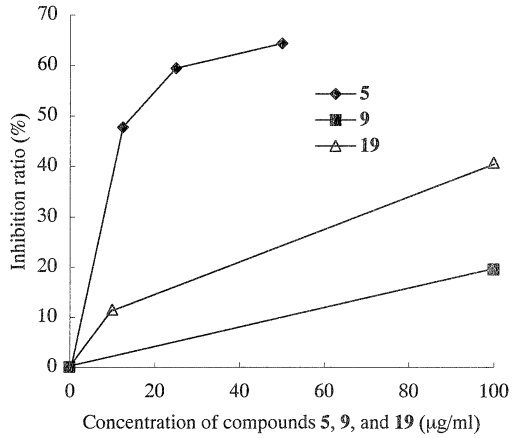


Fig. 2. Inhibition toward rat liver-α-D-glucosidase.

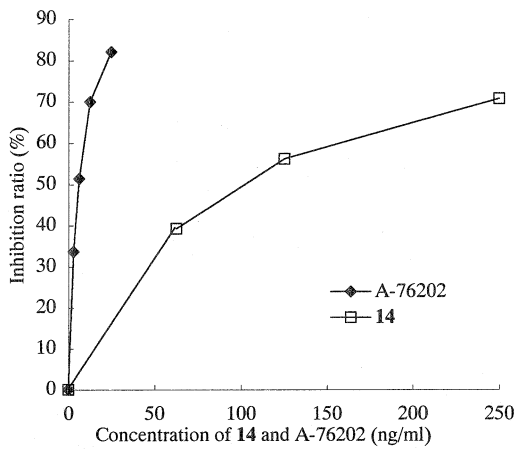


Fig. 3. Inhibition toward rat liver-α-D-glucosidase.

than those of either the galactose or allose moiety by this α-glucosidase. Nonetheless, the activities of these four compounds were disappointing.

Thus, 4′,8-dihydroxyisoflavon-7-yl D-glycosides (**5**, **9**, **14** and **19**), which were synthesized by the glycosidation reaction of glycosyl bromides (**1**, **6**, **10** and **15**) and 4′,8-diallyloxy-7-hydroxyisoflavone (**2**) using silver carbonate in pyridine and successive deprotection of the hydroxy groups, were less active than A-76202 toward rat liver microsome α-D-glucosidase.

1. Experimental

Melting points were determined on a Yanagimoto micro melting-point apparatus and are uncorrected. Optical rotations were obtained by the use of a JASCO P-1030 polarimeter. ^{1}H NMR (400 MHz) spectra were recorded with JEOL JNM-GSX 400 spectrometers using tetramethylsilane as the internal standard. IR absorption spectra were determined with an IR A-2 spectrophotometer, and mass spectra were obtained with a JMS-700 mass spectrometer. Elemental analyses were performed by the Institute of Science and Technology, Inc., Tokyo. Separation of the compounds by column chromatography was carried out with Silica Gel 60 (230–400 mesh ASTM, E. Merck) under a slightly elevated pressure (1.2–1.5 atm) for rapid elution. The quantity of silica gel used was 50–100 times the weight of material charged on the column. Detection involved spraying the chromatogram with a solution of 17% H_2SO_4 in water (w/w) containing ammonium molybdate (2.3%) and cerium(IV) sulfate (0.9%), and heating the plate for several minutes at ca. 180 °C. THF was distilled from sodium–benzophenone ketyl. DMF and pyridine were dried by storage over 4 Å molecular sieves.

4′,8-Diallyloxyisoflavon-7-yl 2,3,4,6-tetra-O-acetyl-β-D-glucopyranoside (**3**).—To a solution of 4′,8-diallyloxy-7-hydroxyisoflavone (**2**) (700 mg, 2.00 mmol) and 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (**1**) (1.30 g, 3.16 mmol) in pyridine (40 mL) was added Ag_2CO_3 (2.00 g, 7.25 mmol). The mixture was stirred for 18 h at rt, filtered, and concentrated in vacuo to give a mixture. This mixture was diluted with EtOAc, washed with aq 0.1 M HCl, water, satd aq $NaHCO_3$, and brine, dried over $MgSO_4$, filtered, concentrated in vacuo, and chromatographed on a silica gel column. Elution with 1:1 hexane–EtOAc gave **3** (175 mg, 13%) as a gum. $[\alpha]_D^{24}$ −17.3° (*c* 0.79, $CHCl_3$). IR ν_{max}($CHCl_3$) 1758, 1646, 1607, 1511 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 2.05 (3 H, s), 2.07 (3 H, s), 2.09 (3 H, s), 2.10 (3 H, s), 3.92 (1 H, m), 4.20 (1 H, dd, *J* 2.2, 12.5 Hz), 4.31 (1 H, dd, *J* 5.1, 12.5 Hz), 4.57 (1 H, ddt, *J* 1.5, 5.1, 11.7 Hz), 4.58 (2 H, dt, *J* 1.5, 5.1 Hz), 4.67 (1 H, ddt, *J* 1.5, 5.1, 11.7 Hz), 5.17–5.46 (8 H, m, containing 1 H, d, *J* 7.3 Hz, at 5.18 ppm), 6.03–6.16 (2 H, m), 6.99 (2 H, d, *J* 8.8 Hz), 8.00 (1 H, d, *J* 8.8 Hz), 8.01 (1 H, s). FABMS (positive-ion): *m*/*z* 703 $[M+Na]^+$, 681 $[M+H]^+$. HRFABMS, Calcd for $C_{35}H_{37}O_{14}$: 681.2183; Found: 681.2180.

4′,8-Dihydroxyisoflavon-7-yl 2,3,4,6-tetra-O-acetyl-β-D-glucopyranoside (**4**).—A solution of **3** (67.5 mg, 0.099 mmol) in anhyd EtOH (3 mL) containing $RhCl_3$ hydrate (13.1 mg, 0.050 mmol) was refluxed for 1.5 h under N_2. The mixture was concentrated in vacuo to give a residue, which was chromatographed on a silica gel column. Elution with 3:7 hexane–EtOAc gave **4** (43.5 mg, 73%). $[\alpha]_D^{24}$ −25.4° (*c* 0.84, $CHCl_3$). IR ν_{max}($CHCl_3$) 3595, 3482, 1758, 1613, 1579 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 2.07 (6 H, s), 2.12 (3 H, s), 2.14 (3 H, s), 3.91 (1 H, ddd, *J* 2.2, 5.1, 10.3 Hz), 4.21 (1 H, dd, *J* 2.2, 12.5 Hz), 4.33 (1 H, dd, *J* 5.9, 12.5 Hz), 5.09 (1 H, d, *J* 7.3 Hz), 5.19 (1 H, t, *J* 9.5 Hz), 5.29–5.38 (2 H, m), 5.88 (1 H, s, OH), 6.44 (1 H, s, OH), 6.87 (2 H, d, *J* 8.8 Hz), 7.07 (1 H, d, *J* 8.8 Hz), 7.39 (2 H, d, *J* 8.8 Hz), 7.80 (1 H, d, *J* 8.8 Hz), 8.02 (1 H, s). FABMS (positive-ion): *m*/*z* 601 $[M+H]^+$. HRFABMS, Calcd for $C_{29}H_{29}O_{14}$: 601.1557; Found: 601.1559.

4′,8-Dihydroxyisoflavon-7-yl β-D-glucopyranoside (**5**).—A solution of **4** (22.8 mg, 0.038 mmol) in EtOH (3 mL) containing KOH (4 mg) was stirred for 4 h at rt. The solution was concentrated in vacuo to give **5** (20.4 mg, 100%) as a yellow powder; mp 238.5–241.0 °C. $[\alpha]_D^{24}$ −55.9° (*c* 0.55, MeOH). IR

ν_{max}(KBr) 3201 (broad), 1666, 1595, 1559 cm^{-1}. ^1H NMR (CD_3OD): δ 3.40–3.58 (4 H, m), 3.73 (1 H, dd, *J* 5.1, 11.7 Hz), 3.93 (1 H, dd, *J* 2.2, 10.3 Hz), 4.80 (1 H, d, *J* 7.3 Hz), 6.69 (2 H, d, *J* 8.8 Hz), 7.16–7.22 (4 H, m), 8.16 (1 H, s). FABMS (positive-ion): *m*/*z* 433 $[M+H]^+$. FABMS (negative-ion): *m*/*z* 431 $[M-H]^-$. HRFABMS, Calcd for $C_{21}H_{19}O_{10}$: 431.0978; Found: 431.0985. Anal. Calcd for $C_{21}H_{20}O_{10}$: C, 58.33; H, 4.66. Found: C, 58.21; H, 4.70.

4′,8-Diallyloxyisoflavon-7-yl 2,3,4,6-tetra-O-acetyl-β-D-galactopyranoside (**7**).—2,3,4,6-Tetra-*O*-acetyl-α-D-galactopyranosyl bromide (**6**) (1.28 g, 3.11 mmol) was treated with **2** as described in the formation of **3** from **1** and **2** to give **7** (391 mg, 55%) as a gum. $[\alpha]_D^{23}$ −0.8° (*c* 1.05, $CHCl_3$). IR ν_{max}($CHCl_3$) 1753, 1646, 1607, 1570 cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.03 (3 H, s), 2.08 (3 H, s), 2.09 (3 H, s), 2.22 (3 H, s), 4.11–4.28 (3 H, m), 4.54–4.59 (3 H, m), 4.70 (1 H, dd, *J* 5.9, 11.7 Hz), 5.11–5.15 (2 H, m, containing 1 H, d, *J* 8.1 Hz, at 5.12 ppm), 5.26–5.49 (5 H, m), 5.61 (1 H, dd, *J* 8.1, 11.0 Hz), 6.03–6.17 (2 H, m), 6.99 (2 H, d, *J* 8.8 Hz), 7.21 (1 H, d, *J* 8.8 Hz), 7.49 (2 H, d, *J* 8.1 Hz), 7.99–8.01 (2 H, m). FABMS (positive-ion): *m*/*z* 681 $[M+H]^+$. HRFABMS, Calcd for $C_{35}H_{37}O_{14}$: 681.2183; Found: 681.2186.

4′,8-Dihydroxyisoflavon-7-yl 2,3,4,6-tetra-O-acetyl-β-D-galactopyranoside (**8**).—Compound **7** (265 mg, 0.390 mmol) was treated as described in the formation of **4** from **3** to give **8** (145 mg, 62%) as a gum. $[\alpha]_D^{24}$ −2.9° (*c* 0.90, $CHCl_3$). IR ν_{max}($CHCl_3$) 3691, 3598, 3483, 1752, 1647, 1612, 1579 cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.05 (2 H, s), 2.09 (3 H, s), 2.15 (3 H, s), 2.22 (3 H, s), 4.10–4.28 (3 H, m), 5.06 (1 H, d, *J* 7.3 Hz), 5.17 (1 H, dd, *J* 2.9, 10.3 Hz), 5.49–5.53 (2 H, m), 6.12 (1 H, s, OH), 6.45 (1 H, s, OH), 6.87 (2 H, d, *J* 8.8 Hz), 7.09 (1 H, d, *J* 8.8 Hz), 7.38 (2 H, d, *J* 8.8 Hz), 7.80 (1 H, d, *J* 8.8 Hz), 8.02 (1 H, s). FABMS (positive-ion): *m*/*z* 601 $[M+H]^+$. HRFABMS, Calcd for $C_{29}H_{29}O_{14}$: 601.1557; Found: 601.1564.

4′,8-Dihydroxyisoflavon-7-yl β-D-galactopyranoside (**9**).—Compound **8** (55.2 mg, 0.092 mmol) was treated as described in the formation of **5** from **4** to give **9** (48.2 mg, 100%) as a yellow powder; mp 237.0–239.5 °C. $[\alpha]_D^{23}$ −52.4° (*c* 0.43, MeOH). IR ν_{max}(KBr) 3394 (broad), 1558 cm^{-1}. ^1H NMR (CD_3OD): δ 3.59 (1 H, m), 3.70 (1 H, m), 3.76–3.91 (4 H, m), 4.74 (1 H, d, *J* 7.3 Hz), 6.72 (2 H, d, *J* 8.8 Hz), 7.16–7.25 (4 H, m), 8.17 (1 H, s). FABMS (positive-ion): *m*/*z* 433 $[M+H]^+$. HRFABMS, Calcd for $C_{21}H_{21}O_{10}$: 433.1135; Found: 433.1153.

4′,8-Diallyloxyisoflavon-7-yl 2,3,4,6-tetra-O-benzoyl-α-D-mannopyranoside (**11**).—To a solution of 2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl bromide (**10**) (2.01 g, 3.05 mmol) and **2** (352 mg, 1.00 mmol) in pyridine (20 mL) was added Ag_2CO_3 (2.18 g, 7.91 mmol). The mixture was stirred for 18 h at rt, filtered, and concentrated in vacuo to give a mixture. This mixture was diluted with EtOAc, washed with 0.1 M HCl, water, satd aq $NaHCO_3$, and brine, dried over $MgSO_4$, filtered, concentrated in vacuo, and chromatographed on a silica gel column. Elution with 3:2 cyclohexane–EtOAc gave a mixture (286 mg) of **11** and unknown byproducts that could not be separated. The crude product was employed for the next reaction without further purification.

4′,8-Dihydroxyisoflavon-7-yl 2,3,4,6-tetra-O-benzoyl-α-D-mannopyranoside (**12**).—The mixture of **11** and byproducts (154 mg) obtained above was treated as described in the formation of **4** from **3** to give **12** (63.9 mg, 67%) as a white powder; mp 270.7–272.0 °C. $[\alpha]_D^{24}$ +32.4° (*c* 0.80, $CHCl_3$). IR ν_{max}(KBr) 3392, 1730, 1269 cm^{-1}. ^1H NMR ($CDCl_3$): δ 4.53 (1 H, dd, *J* 5.9, 12.5 Hz), 4.66–4.69 (2 H, m), 5.95 (1 H, d, *J* 1.5 Hz), 6.09–6.13 (3 H, m, containing OH), 6.18 (1 H, t, *J* 9.5 Hz), 6.42 (1 H, s, OH), 6.88 (2 H, d, *J* 8.8 Hz), 7.25–8.09 (25 H, m). FABMS (positive-ion): *m*/*z* 849 $[M+H]^+$. HRFABMS, Calcd for $C_{49}H_{37}O_{14}$, 849.2183; Found: 849.2168.

4′,8-Diacetoxyisoflavon-7-yl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside (**13**).—Compound **12** (43.5 mg, 0.051 mmol) in 0.2 M NaOH MeOH solution (2 mL) was stirred for 18 h at rt. The solution was acidified with 1 M HCl (0.4 mL), and concentrated in vacuo to give a residue, which was chromatographed (Cosmosil 140 C18-OPN). Elution with 1:9 MeOH–water gave the product-containing fractions, which were concentrated in vacuo to

give a residue (18.3 mg). As the residue was not pure, it was purified again after the next acetylation of hydroxyl groups.

A solution of the residue (16.5 mg, 0.038 mmol) in Ac_2O (0.5 mL) and pyridine (1 mL) was stirred for 1 h at rt. The mixture was concentrated in vacuo, diluted with EtOAc, washed with water and brine, dried over $MgSO_4$, and chromatographed on a silica gel column. Elution with 2:3 cyclohexane–EtOAc gave **13** (19.8 mg, 60%) as a gum. $[\alpha]_D^{23}$ + 73.1° (*c* 0.95, $CHCl_3$). IR ν_{max}($CHCl_3$) 1753, 1652, 1625, 1508 cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.05 (6 H, s), 2.08 (3 H, s), 2.22 (3 H, s), 2.33 (3 H, s), 2.54 (3 H, s), 4.05–4.07 (2 H, m), 4.29 (1 H, dd, *J* 5.9, 12.5 Hz), 5.38–5.47 (3 H, m), 5.66 (1 H, s), 7.17 (2 H, d, *J* 8.1 Hz), 7.33 (1 H, d, *J* 8.8 Hz), 7.56 (2 H, d, *J* 8.1 Hz), 7.97 (1 H, s), 8.16 (1 H, d, *J* 9.5 Hz). FABMS (positive-ion): *m/z* 707 $[M + Na]^+$, 685 $[M + H]^+$. HRFABMS, Calcd for $C_{33}H_{32}NaO_{16}$, 707.1588; Found: 707.1559.

4′,8-Dihydroxyisoflavon-7-yl α-D-mannopyranoside (**14**).—Compound **13** (15.5 mg, 0.023 mmol) was treated as described in the formation of **5** from **4** to give **14** (10.8 mg, 100%) as a yellow powder; mp 174.5–177.0 °C. $[\alpha]_D^{23}$ + 85.8° (*c* 0.80, MeOH). IR ν_{max}(KBr) 3365 (broad), 1626, 1610, 1515 cm^{-1}. ^1H NMR (CD_3OD): δ 3.73–3.80 (4 H, m), 4.06 (1 H, m), 4.19 (1 H, m), 5.63 (1 H, s), 6.85 (2 H, d, *J* 8.8 Hz), 7.37–7.42 (3 H, m), 7.59 (1 H, d, *J* 8.8 Hz), 8.23 (1 H, s). FABMS (positive-ion): *m/z* 433 $[M + H]^+$. HRFABMS, Calcd for $C_{21}H_{21}O_{10}$, 433.1135; Found: 433.1096.

4′,8-Diallyloxyisoflavon-7-yl 2,3,4,6-tetra-O-benzoyl-β-D-allopyranoside (**16**).—2,3,4,6-Tetra-*O*-benzoyl-α-D-allopyranosyl bromide (**15**) (2.05 g, 3.11 mmol) was treated with **2** as described in the formation of **3** from **1** and **2** to give **16** (207 mg, 22%) as a gum. $[\alpha]_D^{23}$ + 20.1° (*c* 0.40, $CHCl_3$). IR ν_{max}($CHCl_3$) 1734, 1646, 1603 cm^{-1}. ^1H NMR ($CDCl_3$): δ 4.45–4.52 (3 H, m), 4.57–4.58 (2 H, m), 4.74–4.79 (2 H, m), 5.01–5.45 (4 H, m), 5.62 (1 H, dd, *J* 2.9, 10.3 Hz), 5.81 (1 H, dd, *J* 2.9, 8.1 Hz), 6.07 (1 H, m), 6.35 (1 H, t, *J* 2.9 Hz), 6.99 (2 H, d, *J* 8.8 Hz), 7.31–7.38 (5 H, m), 7.46–7.67 (10 H, m), 7.88–8.06 (10 H, m). FABMS (positive-ion): *m/z* 929 $[M + H]^+$. HR-FABMS, Calcd for $C_{55}H_{45}O_{14}$, 929.2809; Found: 929.2807.

4′,8-Dihydroxyisoflavon-7-yl 2,3,4,6-tetra-O-benzoyl-β-D-allopyranoside (**17**).—Compound **16** (163 mg, 0.176 mmol) was treated as described in the formation of **4** from **3** to give **17** (120 mg, 80%) as a white powder; mp 269.0–271.5 °C. $[\alpha]_D^{24}$ + 19.2° (*c* 0.78, $CHCl_3$). IR ν_{max}(KBr) 3420 (broad), 1731 cm^{-1}. ^1H NMR ($CDCl_3$): δ 4.51 (1 H, dd, *J* 5.9, 11.7 Hz), 4.75–4.83 (2 H, m), 5.62 (1 H, dd, *J* 2.9, 9.5 Hz), 5.70 (1 H, d, *J* 8.1 Hz), 5.72 (1 H, s, OH), 5.75 (1 H, dd, *J* 2.9, 8.1 Hz), 6.37 (1 H, t, *J* 2.9 Hz), 6.67 (1 H, s, OH), 6.87 (2 H, d, *J* 9.5 Hz), 7.18 (1 H, d, *J* 9.5 Hz), 7.33–7.72 (15 H, m), 7.88–8.10 (9 H, m). FABMS (positive-ion): *m/z* 849 $[M + H]^+$. HRFABMS, Calcd for $C_{49}H_{37}O_{14}$, 849.2183; Found: 849.2181.

4′,8-Diacetoxyisoflavon-7-yl 2,3,4,6-tetra-O-acetyl-β-D-allopyranoside (**18**).—Compound **17** (97.5 mg, 0.115 mmol) was treated as described in the formation of **13** from **12** to give **18** (55.8 mg, 72%) as a gum. $[\alpha]_D^{23}$ − 13.0° (*c* 0.40, $CHCl_3$). IR ν_{max}(KBr) 1754, 1654, 1624 cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.04 (3 H, s), 2.09 (3 H, s), 2.10 (3 H, s), 2.19 (3 H, s), 2.33 (3 H, s), 2.40 (3 H, s), 4.27–4.35 (3 H, m), 5.04 (1 H, dd, *J* 2.9, 10.3 Hz), 5.34 (1 H, dd, *J* 2.9, 8.1 Hz), 5.49 (1 H, d, *J* 8.1 Hz), 5.73 (1 H, t, *J* 2.9 Hz), 7.18 (2 H, d, *J* 8.8 Hz), 7.22 (1 H, d, *J* 8.8 Hz), 7.56 (2 H, d, *J* 8.8 Hz), 7.96 (1 H, s), 8.17 (1 H, d, *J* 8.8 Hz). FABMS (positive-ion): *m/z* 723 $[M + K]^+$ (on addition of aq NaI solution); 685 $[M + H]^+$. HR-FABMS, Calcd for $C_{33}H_{32}KO_{16}$, 723.1327; Found: 723.1323. Anal. Calcd for $C_{33}H_{32}O_{16}$ (684.6): C, 57.90; H, 4.71. Found: C, 57.67; H, 4.83.

4′,8-Dihydroxyisoflavon-7-yl β-D-allopyranoside (**19**).—Compound **18** (28.6 mg, 0.042 mmol) was treated as described in the formation of **5** from **4** to give **19** (23.6 mg, 100%) as a yellow powder; mp 249.0–251.5 °C. $[\alpha]_D^{24}$ − 64.1° (*c* 0.21, MeOH). IR ν_{max}(KBr) 3348 (broad), 1596, 1559 cm^{-1}. ^1H NMR (CD_3OD): δ 3.62 (1 H, dd, *J* 2.9, 9.5 Hz), 3.68 (1 H, dd, *J* 2.9, 8.1 Hz), 3.73 (1 H, dd, *J* 5.1, 11.7 Hz), 3.85–3.92 (2 H, m), 4.19 (1 H, t, *J* 2.9 Hz), 5.16 (1 H, d, *J* 8.1 Hz), 6.69 (2 H, d, *J* 8.1 Hz), 7.17–7.23 (4 H, m), 8.16 (1 H, s). FABMS (positive-ion): *m/z* 433 $[M + H]^+$. HRFABMS, Calcd for $C_{21}H_{21}O_{10}$, 433.1135;

Found: 433.1143. Anal. Calcd for $C_{21}H_{20}O_{10}$: C, 58.33; H, 4.66. Found: C, 58.12; H, 4.78.

Method for rat liver microsome α-D-glucosidase measurement.—For the measurement of α-glucosidase inhibition, rat liver microsome fraction solubilized with 25% Triton X-100 was used as an enzyme. The reaction was carried out at 37 °C for 20 min in a 96-well microtiter plate in a total volume of 150 μL consisting of 70 μL of phosphate buffer (100 mM potassium phosphate with 20 mM EDTA, pH 6.8), 10 μL of varying concentration of inhibitors, 50 μL of 10 mM 4-nitrophenyl α-D-glucopyranoside, and 20 μL of diluted enzyme solution (approximately 3×10^{-4} units), added finally. Then, 20 mL of 4 M sodium glycinate buffer (pH 10.4) was added to stop the reactions, and colorimetric changes at 415 nm being directly proportional to the amount of liberated 4-nitrophenol were measured by a microplate reader.

References

1. Takatsuki, A.; Nakajima, M.; Ando, O. *Jpn. Kokai Tokkyo Kouhou*, 96-134091 (May 28, 1996).
2. Shiozaki, M. *Tetrahedron: Asymmetry* **1999**, *10*, 1477–1482.
3. Redemann, C. E.; Niemann, C. *Org. Synth., Coll. Vol. 3* **1955**, 11–14.
4. Suzuki, K.; Maeta, H.; Suzuki, T.; Matsumoto, T. *Tetrahedron Lett.* **1989**, *30*, 6879–6882.
5. Wagner, M.; Bohringer, W.; Horhammer, L.; Farkas, L. *Chem. Ber.* **1968**, *101*, 1626–1629.
6. B-Martos, M.; Korosy, F. *Nature* **1950**, *165*, 369.
7. Ness, R. K.; Fletcher, Jr., H. G.; Hudson, C. S. *J. Am. Chem. Soc.* **1950**, *72*, 2200–2204.
8. Haga, M.; Tejima, S. *Carbohydr. Res.* **1974**, *34*, 214–218.