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Isoflavone Glycosides: Synthesis and Evaluation as α-Glucosidase Inhibitors

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On the basis of the structure of 4′,7,8-trihydroxyisoflavone 7-*O*-α-D-arabinofuranoside (namely A-76202, **1**), a Rhodococcus metabolite showing potent inhibitory activities against the α-glucosidases of rat liver microsome (IC_{50} = 0.46 ng/mL), 26 analogs, each with minor variations at the sugar moiety and the isoflavone A and B rings, were readily synthesized. Notably, a new and efficient method was developed for the divergent synthesis of the B-ring congeners of the isoflavone glycosides by using Suzuki–Miyaura coupling as the final step. Modifications at the sugar moiety and the isoflavone A ring significantly diminish the activity, whereas variations at the B ring are largely tolerated for retaining the potent α-glucosidase inhibitory activity.

Introduction

The generation of glycoproteins involves the cotranslational transference of the tetradecaoligosaccharide $Glc_3Man_9GlcNAc_2$ from the dolichyl diphosphate to the *N*-asparagine of the nascent protein, by the action of the oligosaccharyltransferase in the lumen of the reticulum endoplasmatic membrane.[1] Then, the processing enzymes α-glucosidase I and II cleave the Glc(1→2)Glc and Glc(1→3)-Glc linkages, respectively, in this N-linked oligosaccharide to liberate the three terminal glucose residues.[2] This immature glycoprotein is further processed by the concomitant action of glycosidases and transferases to give specific glycoconjugates, which play fundamental roles in the biological processes, such as the immune response, intercellular recognition, cellular differentiation, the stability and solubility of proteins, and in pathological processes, such as inflammation and cancer.[3] Tremendous efforts have been made in the development of glucosidase inhibitors that are potentially useful for the treatment of diabetes,[4] obesity,[5] glycosphingolipid lysosomal storage disease,[6] HIV infections,[7] and tumors.[8] Potent inhibitors with IC_{50} values at the nM level are largely structural mimics of the transition state of the hydrolyses of the glucosidic linkage.[9] In this regard, 4′,7,8-trihydroxyisoflavone 7-*O*-α-D-arabinofuranoside (**1**, Figure 1) is an exception that shows potent inhibitory activity (against the α-glucosidases of rat liver microsome) with an IC_{50} value of 0.46 ng/mL.[10] This isoflavone glycoside, named A-76202, was isolated by Takatsuki et al. in 1996 from Rhodococcus sp. SANK 61694. Shiozaki et al. synthesized this compound along with several hexopyranoside analogs (**2**) and evaluated their α-glucosidase inhibitory activities.[11] However, these hexose analogs were found to be inactive. We developed a general approach to the synthesis of flavone 7-*O*-glycosides such as A-76202 (**1**).[12] Here we report the synthesis of a series of analogs of **1**, each with minor variations at the sugar moiety and the isoflavone A and B rings, and the evaluation of their α-glucosidase inhibitory activities.

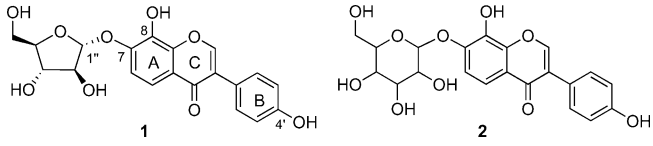

Figure 1. A-76202 (**1**) and hexose analogues **2**.

Results and Discussion

Synthesis

Adopting a modified version of our previous method for the synthesis of flavone 7-*O*-glycosides,[12] desired pentosides **9a**–**d** and natural product **1** were readily prepared by glycosylation of the ready available isoflavone derivative **8**[12] with the corresponding imidates **3**–**7**[13–17] under the promotion of $BF_3{\cdot}OEt_2$ and subsequent removal of the acyl groups with K_2CO_3 in a mixed solvent of MeOH/THF/H_2O (Scheme 1). The yields (over two steps) are only moderate (26–76%); partial migration of the 8-*O*-hexanoyl group to the neighboring 7-OH group under the glycosylation conditions was observed.

To synthesize the A- and B-ring congeners of A-76202 (**1**), a divergent approach by using Suzuki–Miyaura coupling[18] of bromide **15** or **21** with a panel of commercially

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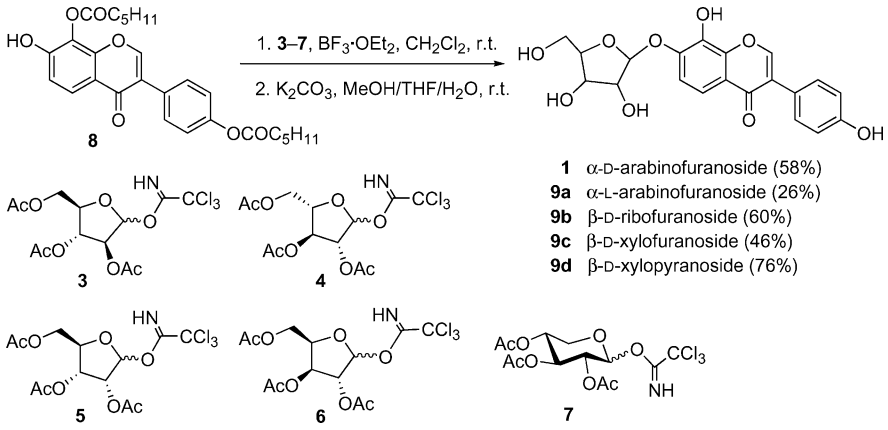
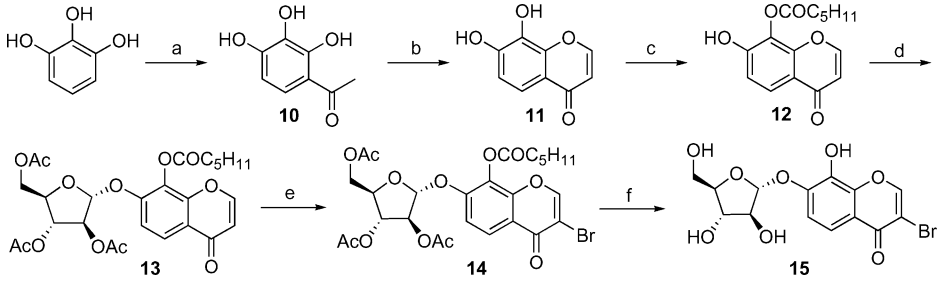


Scheme 1. Synthesis of pentosides **9a**–**d**.

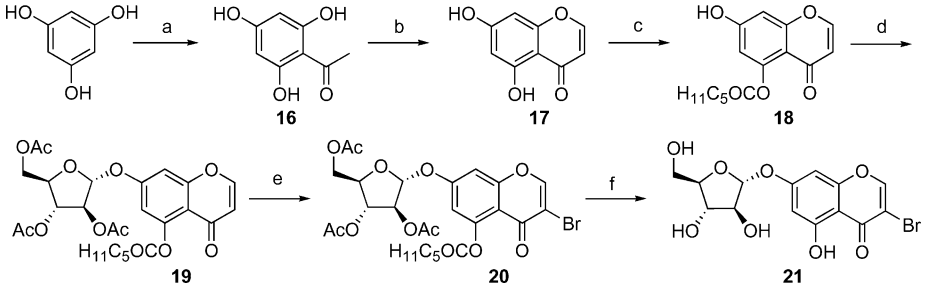
available aryl boronic acids as the final step was envisioned. Required bromides **15** and **21** were prepared as shown in Schemes 2 and 3.

Thus, acylation of pyrogallol with glacial acetic acid under the action of $BF_3{\cdot}OEt_2$ at 90–100 °C provided ketone **10**, which was treated with triethyl orthoformate in the presence of 70% $HClO_4$ to afford chromone **11** (Scheme 2). Selective protection of the 7-OH group in diol **11** was achieved by 7,8-di-*O*-hexanoate formation and subsequent removal of the 7-*O*-acyl group,[12] which is *para* to the electron-withdrawing pyrone carbonyl functionality, with PhSH and imidazole in *N*-methyl pyrolidinone (NMP) to give **12** (70% over two steps). Glycosylation of phenol **12** with imidate **3** under the promotion of $BF_3{\cdot}OEt_2$ led to α-glycoside **13** in 62% yield. Bromination of compound **13** was achieved with $PhI(OAc)_2$ and TMSBr at room temperature with pyridine as a base,[19] affording chromone **14** (67%). Removal of the acyl protecting groups in **14** with K_2CO_3 in a mixed solvent of MeOH/THF/H_2O to compromise the solubility of the reactants provided desired **15** (77%).

Employing a similar procedure to that described above, A-ring isomer **21** was synthesized from phloroglucinol as the starting material (Scheme 3). It is worth noting that the glycosylation of 5-*O*-hexanoyl-7-ol **18** with **3** gave glycoside

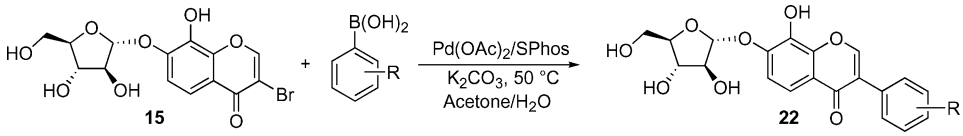


Scheme 2. Synthesis of bromide **15**. Reagents and conditions: (a) AcOH, $BF_3{\cdot}OEt_2$, 90–100 °C, 4 h, 96%; (b) $HC(OEt)_3$, 70% $HClO_4$, 85 °C, 12 h, 82%; (c) i) $CH_3(CH_2)_4COCl$, pyridine, 0 °C to r.t., 16 h; ii) PhSH, imidazole, NMP, 0 °C to r.t., 3 h, 70%; (d) **3**, $BF_3{\cdot}OEt_2$, CH_2Cl_2, 4 Å MS, r.t., 62%; (e) $PhI(OAc)_2$, TMSBr, CH_2Cl_2, pyridine, 0 °C to r.t., 67%; f) K_2CO_3, MeOH/THF/H_2O (2:1:0.2), r.t., 77%.



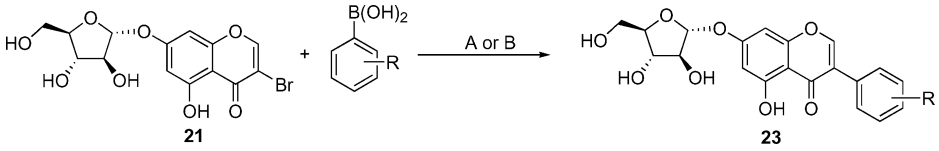
Scheme 3. Synthesis of bromide **21**. Reagents and conditions: (a) Ac_2O, $BF_3{\cdot}OEt_2$, r.t., 34 h; (b) MsCl, DMF, $BF_3{\cdot}OEt_2$, 50 °C, 4 h, 37%; (c) i) $CH_3(CH_2)_4COCl$, pyridine, 0 °C to r.t., 16 h; ii) PhSH, imidazole, NMP, 0 °C to r.t., 3 h, 64%; (d) **3**, $BF_3{\cdot}OEt_2$, CH_2Cl_2, 4 Å MS, r.t., 89%; (e) $PhI(OAc)_2$, TMSBr, CH_2Cl_2, pyridine, 0 °C to r.t., 63%; (f) K_2CO_3, MeOH/THF/H_2O (2:1:0.2), r.t., 42%.

Table 1. Synthesis of B-ring congeners **22** by Suzuki–Miyaura coupling of **15**.



Product	R	Yield [%]	Product	R	Yield [%]
22a	H	65	**22h**(1)	4-OH	48
22b	4-OMe	54	**22i**	3-OH	35
22c	2-OMe	50	**22j**	4-F	31
22d	3-OMe	75	**22k**	4-NMe_2	36
22e	4-Me	45	**22l**	4-NHBoc	39
22f	2-Me	34	**22m**	4-CF_3	41
22g	3-Me	58	**22n**	4-$SiMe_3$	30

Table 2. Synthesis of A,B-ring congeners **23** by Suzuki–Miyaura coupling of **21**.



Product	R	Conditions[a]	Yield [%]	Product	R	Conditions[a]	Yield [%]
23a	H	A	28	**23e**	4-Me	B	39
23a	H	B	16	**23f**	3-Me	A	16
23b	4-OMe	A	43	**23g**	4-OH	A	39
23c	2-OMe	A	39	**23g**	4-OH	B	12
23d	3-OMe	A	37	**23h**	3-OH	B	35

[a] Conditions A: $Pd(OAc)_2$ (0.05 equiv.), SPhos (0.15 equiv.), K_2CO_3 (3.0 equiv.), acetone/H_2O, 50 °C. Conditions B: $Pd(OAc)_2$ (0.05 equiv.), NaOAc (3.0 equiv.), MeOH, reflux.

19 in a much better 89% yield than that obtained for the glycosylation of 8-*O*-hexanoyl-7-ol **12** with imidate **3** (and that of the glycosylation of isoflavone derivative **8**, Scheme 1) under similar conditions (62%). The latter reaction suffered from migration of the 8-*O*-hexanoyl group to the neighboring 7-OH group under the glycosylation conditions as mentioned.

Although Suzuki–Miyaura reaction has been widely used as one of the most efficient methods for C–C bond formation,[18] in only a few examples have flavonoid iodides or *O*-triflates been employed as the coupling partners.[20] In fact, the instability of the 4*H*-pyranones under basic conditions limited the choice of bases in the Suzuki–Miyaura coupling of bromides **15** and **21** with boronic acids. Under the optimized conditions with 2-(2,6-dimethoxybiphenyl)dicyclohexylphosphane (SPhos) as a ligand, as introduced by Buchwald et al.,[21] in the presence of $Pd(OAc)_2$ and K_2CO_3, coupling of bromide **15** with a variety of aryl boronic acids provided the corresponding isoflavone glycosides **22a**–**n** in moderate yields (Table 1). Reduction of the bromide and degradation of the chromone B ring are the major side reactions.

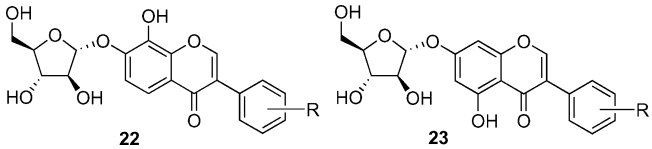
Under similar conditions, the couplings with bromide **21** gave lower yields of the desired products (Table 2), because **21** was found to be more vulnerable to basic degradation than its regioisomer **15**. An alternative procedure applied here for the coupling was in the absence of ligand and with NaOAc as a base, but the coupling yields were generally even lower.

Inhibitory Activities Against α-Glucosidases

Synthetic natural product **1** exhibited potent inhibitory activity against the α-glucosidases of rat liver microsome, with IC_{50} = 18 nM, that is comparable to the literature value of 14 nM.[11b] However, stereoisomers **9a**–**d** did not show remarkable activities at concentrations up to 10 μM. Gratifyingly, all the B-ring analogs of **1** (i.e., **22a**–**n**) exhibited activities at a concentration of 10 nM (Table 3). The 4-OH group in the B ring of **1** could be replaced by -OMe, -H, -F, -Me, and -CF_3 without considerably affecting the activity. Their regioisomers, that is, the 3-OH, 2-OMe, 3-OMe, 2-Me, and 3-Me derivatives, were similarly potent. Especially, the 3-OMe and 4-NMe_2 derivatives (**22d** and **22k**) were about threefold more potent that the 4′-OH natural product (**1**). However, the 5-OH (on the A ring) derivatives (i.e., **23a**–**h**), which are regioisomers of the above 8-OH iso-

flavone glycosides **22a**–**i** were 1000 times less potent inhibitors. It is worth noting that all these compounds, including natural isoflavone glycoside **1**, were found inert towards the α-glucosidase from bakers yeast.

Table 3. Inhibitory activities of α-D-arabinofuranosides **22** and **23** against the α-glucosidases of rat liver microsome.



22 **23**

R	Compound (IC_{50}, μM)	
H	**22a** (0.040)	**23a** (10)
4-OMe	**22b** (0.022)	**23b** (8)
2-OMe	**22c** (0.015)	**23c** (10)
3-OMe	**22d** (0.006)	**23d** (10)
4-Me	**22e** (0.035)	**23e** (7)
2-Me	**22f** (0.020)	–
3-Me	**22g** (0.050)	**23f** (5)
4-OH	**1** (0.018)	**23g** (15)
3-OH	**22i** (0.017)	**23h** (33% at 50)
4-F	**22j** (0.015)	–
4-NMe_2	**22k** (0.008)	–
4-NHBoc	**22l** (0.020)	–
4-CF_3	**22m** (0.030)	–
4-$SiMe_3$	**22n** (35% at 0.050)	–

Conclusions

A concise approach to the synthesis of isoflavone glycosides was developed, in which the Suzuki–Miyaura coupling between glycosyloxy bromide **15** or **21** and aryl boronic acids was employed as the final step. Although there remains room for increasing the coupling and glycosylation yields, the present method provides quick and divergent access to this type of common natural product. In total, 26 isoflavone glycosides (**9a**–**d**, **22a**–**n**, and **23a**–**h**) were readily synthesized, and they are all analogs of the potent α-glucosidase inhibitor A-76202 that posses minor variations at the sugar moiety and the A and B rings. Evaluation of the inhibitory activities of these compounds against the α-glucosidases of rat liver microsome led to a preliminary and clear structure–activity relationship conclusion: the stereochemistry of the sugar moiety (the α-D-arabinofuranosyl unit) and the 8-hydroxy group in the A ring are crucial to the activity, whereas variations at the B ring of the isoflavone 7-*O*-glycosides are largely tolerated to retain the potent α-glucosidase inhibitory activities.

Experimental Section

General Methods: See ref.[12]

General Procedure for Assay of the α-Glucosidase Inhibitory Activity: IC_{50} values were determined at 37 °C in 0.1 M K_2HPO_4/KH_2PO_4/0.15 M KCl buffer (pH 6.8) with *p*-nitrophenyl α-D-glucopyranoside (Sigma Chemical Co.) as the substrate. Rat liver microsome fraction solubilized with 25% Triton X-100 was used as enzyme. The inhibitor (5 μL, in DMSO), diluted enzyme solution (20 μL), and buffer solution (105 μL) were added to a 96-well microtiter plate, and preincubated for 10 min at 37 °C. The enzymatic reaction was started by the addition of 20 μL of the substrate solution (20 mM). The absorption at 400 nm was measured immediately. The increase in absorption per min at 400 nm was taken as the relative rate for the hydrolysis of the substrate. The increase was linear during all measurements (30 min). IC_{50} values were determined by plotting the relative rate of the substrate hydrolysis versus the inhibitor concentration. The inhibitor concentration corresponding to half of the relative rate measured in the absence of the inhibitor gave the appropriate IC_{50} value. All the experiments were carried out in triplicate.

General Procedure for the Synthesis of 4′,7,8-Trihydroxyisoflavone 7-*O*-Pentosides (9a–d): $BF_3{\cdot}OEt_2$ (0.1 M in CH_2Cl_2, 0.4 mL) was added slowly to a solution of **8** (100 mg, 0.214 mmol) and the pentosyl trichloroacetimidate (250 mg, 0.612 mmol) in dry CH_2Cl_2 (8 mL) in the presence of freshly activated 4-Å molecular sieves at 0 °C. The mixture was warmed to room temperature and stirred until TLC indicated the completion of the reaction. The solid in the mixture was filtered off by passing it through a pad of Celite, and the filtrate was concentrated in vacuo. The residue was dissolved in MeOH/THF/H_2O (2:1:0.2, 5 mL) and K_2CO_3 (119 mg, 0.856 mmol) was added. The mixture was stirred at room temperature until TLC indicated the completion of the reaction. Dowex-50 (H^+) resin was used to neutralize the reaction mixture. The solution was filtered, and the filtrate was concentrated. The residue was purified by silica-gel column chromatography (CH_2Cl_2/MeOH, 10:1) to yield **1** or **9** as a white solid.

4′,7,8-Trihydroxyisoflavone 7-*O*-α-L-Arabinofuranoside (9a): Yield: 22 mg, 26%. R_f = 0.38 (CH_2Cl_2/MeOH, 10:1). $[\alpha]_D^{22}$ = –106.2 (*c* = 0.56, MeOH). ^{1}H NMR (300 MHz, CD_3OD): δ = 8.21 (s, 1 H), 7.85 (d, *J* = 9.0 Hz, 1 H), 7.37 (d, *J* = 8.7 Hz, 2 H), 7.00 (d, *J* = 9.0 Hz, 1 H), 6.84 (d, *J* = 8.7 Hz, 2 H), 5.90 (s, 1 H), 4.40 (s, 1 H), 4.30 (dd, *J* = 7.8, 4.5 Hz, 1 H), 4.10 (br. s, 1 H), 3.67–3.62 (m, 2 H) ppm. MS (ESI): *m*/*z* = 403.1 [M + H]$^+$. HRMS (ESI): calcd. for $C_{20}H_{19}O_9^+$ 403.1024; found 403.1024.

4′,7,8-Trihydroxyisoflavone 7-*O*-β-D-Ribofuranoside (9b): Yield: 52 mg, 60%. R_f = 0.14 (CH_2Cl_2/MeOH, 10:1). $[\alpha]_D^{23}$ = –107.6 (*c* = 0.24, MeOH). ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 9.59 (br. s, 1 H), 8.41 (s, 1 H), 7.55 (d, *J* = 9.0 Hz, 1 H), 7.41 (d, *J* = 8.7 Hz, 2 H), 7.24 (d, *J* = 9.0 Hz, 1 H), 6.83 (d, *J* = 8.7 Hz, 2 H), 5.52 (s, 1 H), 5.05 (d, *J* = 6.0 Hz, 1 H), 4.30–4.10 (m, 2 H), 3.94 (br. s, 1 H), 3.61 (dd, *J* = 12.0, 1.8 Hz, 1 H), 3.44 (dd, *J* = 12.0, 6.0 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 175.4, 157.4, 153.4, 148.1, 146.3, 136.4, 130.4, 123.5, 122.7, 120.0, 115.3, 115.2, 115.16, 115.10, 107.2, 84.9, 74.7, 70.2, 62.2 ppm. MS (ESI): *m*/*z* = 403.2 [M + H]$^+$. HRMS (ESI): calcd. for $C_{20}H_{19}O_9^+$ 403.1024; found 403.1023.

4′,7,8-Trihydroxyisoflavone 7-*O*-β-D-Xylofuranoside (9c): Yield: 40 mg, 46%. R_f = 0.20 (CH_2Cl_2/MeOH, 10:1). $[\alpha]_D^{22}$ = –100.2 (*c* = 0.21, MeOH). ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 9.45 (br. s, 1 H), 8.38 (s, 1 H), 7.55 (d, *J* = 9.0 Hz, 1 H), 7.41 (d, *J* = 8.4 Hz, 2 H), 7.28 (d, *J* = 9.0 Hz, 1 H), 6.82 (d, *J* = 8.4 Hz, 2 H), 5.57 (s, 1 H), 4.31 (s, 1 H), 4.21 (m, 1 H), 4.07 (dd, *J* = 4.5, 1.5 Hz, 1 H), 3.70 (dd, *J* = 11.7, 4.8 Hz, 1 H), 3.53 (dd, *J* = 11.7, 6.6 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 175.2, 157.2, 153.1, 147.2, 145.9, 137.3, 130.1, 123.4, 122.6, 120.1, 115.6, 115.0, 107.7, 84.6, 80.3, 75.0, 60.1 ppm. MS (ESI): *m*/*z* = 401.3 [M – H]$^+$. HRMS (ESI): calcd. for $C_{20}H_{19}O_9^+$ 403.1024; found 403.1023.

4′,7,8-Trihydroxyisoflavone 7-*O*-β-D-Xylopyranoside (9d): Yield: 65 mg, 76%. R_f = 0.20 (CH_2Cl_2/MeOH, 10:1). $[\alpha]_D^{21}$ = –33.8 (*c* = 0.29, MeOH); ^{1}H NMR (300 MHz, CD_3OD): δ = 8.21 (s, 1 H), 7.63 (d, *J* = 8.7 Hz, 1 H), 7.37 (d, *J* = 7.8 Hz, 2 H), 7.25 (d, *J* = 8.7 Hz, 1 H), 6.84 (d, *J* = 7.8 Hz, 2 H), 4.96 (d, *J* = 7.8 Hz, 1 H), 3.90 (dd, *J* = 11.1, 4.8 Hz, 1 H), 3.60–3.36 (m, 4 H) ppm. ^{13}C NMR (75 MHz, CD_3OD): δ = 178.7, 159.0, 155.2, 150.2, 148.3, 137.6, 131.7, 126.0, 124.4, 121.8, 117.0, 116.5, 115.8, 104.2, 77.5, 74.8, 71.2, 67.3 ppm. MS (ESI): *m*/*z* = 401.1 [M – H]$^+$. HRMS (ESI): calcd. for $C_{20}H_{18}O_9Na^+$ 425.0843; found 425.0813.

1-(2,3,4-Trihydroxyphenyl)ethanone (10): A solution of pyrogallol (12.61 g, 100 mmol) and glacial acetic acid (64 mL, 110.9 mmol) in BF_3·OEt_2 (37 mL) was heated at 90–100 °C for 4 h under an atmosphere of argon, and it was then cooled, poured into 10% NaOAc (600 mL), and stirred overnight. The resulting dark solution was extracted with diethyl ether (3 × 300 mL). The organic layer was washed with saturated NaCl and dried with anhydrous Na_2SO_4. Removal of the solvent gave **10** (16.1 g, 96%) as a yellow solid. R_f = 0.69 (CH_2Cl_2/MeOH, 10:1).

7,8-Dihydroxy-4*H*-chromen-4-one (11): Compound **10** (10.0 g, 59.47 mmol) was suspended in ethyl orthoformate (50 mL, 300 mmol) and treated with 70% $HClO_4$ (6 mL) slowly. The mixture was heated in an oil bath at 85 °C for 12 h, and it was then cooled and ether (200 mL) was added. The precipitate was filtered off, washed with water, and dried to give crude **11** (8.72 g, 82%) as yellow solid. R_f = 0.45 (CH_2Cl_2/MeOH, 10:1).

7-Hydroxy-4-oxo-4*H*-chromen-8-yl Hexanoate (12): Hexanoyl chloride (27 mL, 195.6 mmol) was added to a stirring solution of **11** (6.8 g, 38.2 mmol) in pyridine at 0 °C, and the mixture was warmed up to room temperature. After stirring for an additional 16 h, the solution was diluted with CH_2Cl_2 and then washed with aqueous HCl (1 N) and brine. The organic layer was dried with anhydrous Na_2SO_4 and then concentrated in vacuo. The resulting residue was dissolved into dried NMP (60 mL). Imidazole (1.10 g, 15.84 mmol) was added, and the solution was cooled to 0 °C by an ice–water bath, followed by the addition of PhSH (5.8 mL, 56.94 mmol). The reaction mixture was stirred and warmed up to room temperature naturally. When TLC indicated the completion of the reaction, CH_2Cl_2 (300 mL) was added, and the resulting mixture was washed with aqueous HCl (1 N), water, and brine sequentially. The organic layer was dried with anhydrous Na_2SO_4 and concentrated in vacuo. The residue was purified by silica-gel column chromatography (petroleum ether/EtOAc, 2:1) to yield **12** as a yellow solid (7.64 g, 70% over two steps). R_f = 0.17 (petroleum ether/EtOAc, 2:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.28 (br. s, 1 H), 7.98 (d, *J* = 9.0 Hz, 1 H), 7.79 (d, *J* = 5.7 Hz, 1 H), 7.11 (d, *J* = 9.0 Hz, 1 H), 6.32 (d, *J* = 5.7 Hz, 1 H), 2.71 (t, *J* = 7.5 Hz, 2 H), 1.82 (p, *J* = 7.2 Hz, 2 H), 1.48–1.35 (m, 4 H), 0.93 (t, *J* = 6.9 Hz, 3 H) ppm.

8-(Hexanoyloxy)-7-hydroxy4-oxo-4*H*-chromene 7-*O*-2,3,5-Tri-*O*-acetyl-α-D-arabinofuranoside (13): A solution of **12** (7.64 g, 27.65 mmol) and glycosyl imidate **3** (17.86 g, 42.46 mmol) in dry CH_2Cl_2 (200 mL) was treated with freshly activated 4-Å MS and stirred at room temperature for 15 min. BF_3·OEt_2 (2.8 mL, 2.80 mmol) was added dropwise to the solution at 0 °C, and the reaction mixture was stirred at room temperature for 3 h, and then Et_3N (5 mL) was added to quench the reaction. The solid was filtered off by passing the reaction mixture through a pad of Celite, and the solvent was removed in vacuo. The residue was purified by silica-gel column chromatography (petroleum ether/EtOAc, 2:1) to yield **13** as a yellow syrup (9.1 g, 62%). R_f = 0.53 (petroleum/EtOAc, 1:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.05 (d, *J* = 9.0 Hz, 1 H), 7.78 (d, *J* = 6.3 Hz, 1 H), 7.31 (d, *J* = 9.0 Hz, 1 H), 6.30 (d, *J* = 6.3 Hz, 1 H), 5.79 (s, 1 H), 5.38 (s, 1 H), 5.11 (br. s, 1 H), 4.47–4.35 (m, 2 H), 4.28 (dd, *J* = 11.7, 4.5 Hz, 1 H), 2.68 (t, *J* = 7.8 Hz, 2 H), 2.16 (s, 3 H), 2.14 (s, 3 H), 2.11 (s, 3 H), 1.84 (q, *J* = 7.5 Hz, 2 H), 1.51–1.30 (m, 4 H), 0.96 (t, *J* = 6.6 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 176.4, 170.5, 170.4, 169.9, 169.4, 154.8, 152.0, 149.9, 128.8, 123.6, 120.7, 113.8, 113.0, 104.5, 82.0, 81.1, 76.7, 62.7, 33.7, 31.2, 24.6, 22.2, 20.7, 20.6, 13.9 ppm. MS (ESI): *m*/*z* = 535.3 [M + H]$^+$, 557.3 [M + Na]$^+$. HRMS (MALDI): calcd. for $C_{26}H_{30}O_{12}Na^+$ 557.1630; found 557.1638.

3-Bromo-8-hexanoyloxy-7-hydroxy-4-oxo-4*H*-chromene 7-*O*-2,3,5-Tri-*O*-acetyl-α-D-arabinofuranoside (14): TMSBr (8.6 mL, 64.96 mmol) was added slowly to a solution of $PhI(OAc)_2$ (10.6 g, 32.71 mmol) in dry CH_2Cl_2 (50 mL) at 0 °C, and the solution was stirred in an ice bath for 45 min before the addition of **13** (5.8 g, 10.85 mmol) in CH_2Cl_2 (25 mL). The ice bath was removed, and the reaction mixture was warmed up to room temperature and left for 2 h. Pyridine (5.7 mL, 66.47 mmol) was then added, and the stirring was continued for an additional 1 h. The resulting mixture was diluted with CH_2Cl_2 and washed with saturated $Na_2S_2O_3$ and brine. The organic layer was dried with anhydrous Na_2SO_4 and concentrated in vacuo. The residue was purified by silica-gel column chromatography (petroleum ether/EtOAc, 3:1 to 5:2) to yield **14** as a yellow syrup (4.5 g, 67%). R_f = 0.85 (petroleum ether/EtOAc, 1:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.15 (s, 1 H), 8.11 (d, *J* = 9.0 Hz, 1 H), 7.35 (d, *J* = 9.0 Hz, 1 H), 5.80 (s, 1 H), 5.38 (s, 1 H), 5.12 (d, *J* = 3.6 Hz, 1 H), 4.47–4.36 (m, 2 H), 4.28 (dd, *J* = 11.1, 4.5 Hz, 1 H), 2.68 (t, *J* = 7.5 Hz, 2 H), 2.16 (s, 3 H), 2.14 (s, 3 H), 2.11 (s, 3 H), 1.83 (q, *J* = 7.2 Hz, 2 H), 1.48–1.35 (m, 4 H), 0.96 (t, *J* = 6.6 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.2, 170.4, 170.38, 169.9, 169.4, 153.2, 152.3, 149.6, 128.6, 124.2, 118.8, 114.5, 110.9, 104.5, 82.2, 81.1, 76.7, 62.7, 33.7, 31.2, 24.6, 22.2, 20.7, 20.62, 20.60, 13.9 ppm. MS (ESI): *m*/*z* = 613.1 [M + H]$^+$, 635.2 [M + Na]$^+$. HRMS (MALDI): calcd. for $C_{26}H_{29}O_{12}BrNa^+$ 635.0735; found 635.0721.

3-Bromo-7,8-dihydroxy-4-oxo-4*H*-chromene 7-*O*-α-D-Arabinofuranoside (15): Chromone derivative **14** (585 mg, 0.954 mmol) in MeOH/THF/H_2O (2:1:0.2, 50 mL) was treated with K_2CO_3 (527 mg, 3.82 mmol) at room temperature, and the reaction was stirred for 10 h. TLC indicated the completion of the reaction. Dowex-50 (H^+) was added to neutralize the mixture. The solvent was removed in vacuo. Flash chromatography of the residue on silica gel yielded **15** as a yellow solid (287 mg, 77%). R_f = 0.41 (CH_2Cl_2/MeOH, 10:1). $[\alpha]_D^{24}$ = 74.7 (*c* = 0.20, MeOH). ^{1}H NMR (300 MHz, CD_3OD): δ = 8.57 (s, 1 H), 7.56 (d, *J* = 9.0 Hz, 1 H), 7.33 (d, *J* = 9.0 Hz, 1 H), 5.72 (s, 1 H), 4.36 (d, *J* = 2.1 Hz, 1 H), 4.13 (dd, *J* = 9.0, 4.5 Hz, 1 H), 4.08 (m, 1 H), 3.75 (dd, *J* = 11.7, 3.6 Hz, 1 H), 3.70 (dd, *J* = 11.7, 5.1 Hz, 1 H) ppm. MS (ESI): *m*/*z* = 410.8 [M + Na]$^+$.

1-(2,4,6-Trihydroxyphenyl)ethanone (16): A solution of phloroglucinol (25.0 g, 198 mmol) and Ac_2O (190 mL, 199.5 mmol) in BF_3·OEt_2 (75 mL) was stirred at room temperature for 34 h before it was poured into 10% NaOAc (700 mL) and stirred overnight. The precipitate was filtered off, washed with water, and dried to give crude **16** (24 g) as a yellow solid. R_f = 0.74 (CH_2Cl_2/MeOH, 5:1).

5,7-Dihydroxy-4*H*-chromen-4-one (17): Freshly distilled BF_3·OEt_2 (50 mL, 0.54 mol) was added slowly to a solution of **16** (20.2 g, 0.12 mmol) in dry DMF (180 mL) over 1 h at room temperature. The reaction was then transferred to an oil bath of 50 °C before the addition of a solution of MsCl (32 mL, 0.4 mol) in dried DMF (72 mL, 0.9 mol). The mixture was stirred at 50 °C for 4 h, and then cooled and poured into ice–water (2 L). The black solid was

filtered off, and the filtrate was extracted with EtOAc. Evaporation of the solvent and purification of the residue by silica-gel column chromatography (CH_2Cl_2/MeOH, 10:1) yielded yellow solid **17** (8.0 g, 37% over two steps). R_f = 0.90 ($CHCl_3$/MeOH, 10:1). ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 12.07 (br. s, 1 H), 10.92 (br. s, 1 H), 8.18 (d, J = 6.0 Hz, 1 H), 6.38 (d, J = 2.1 Hz, 1 H), 6.28 (d, J = 6.0 Hz, 1 H), 6.21 (d, J = 2.1 Hz, 1 H) ppm.

5-Hexanoyloxy-7-hydroxy-4-oxo-4*H*-chromene (18): A procedure similar to that described for the synthesis of **12** was employed (7.7 g, 64% over two steps). R_f = 0.21 (petroleum ether/EtOAc, 3:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 10.97 (br. s, 1 H), 7.67 (d, J = 9.0 Hz, 1 H), 7.78 (d, J = 2.4 Hz, 1 H), 6.59 (d, J = 2.4 Hz, 1 H), 6.09 (d, J = 9.0 Hz, 1 H), 2.71 (t, J = 7.5 Hz, 2 H), 1.80 (m, 2 H), 1.50–1.33 (m, 4 H), 0.94 (t, J = 6.9 Hz, 3 H) ppm.

5-Hexanoyloxy-7-hydroxy-4-oxo-4*H*-chromene 7-*O*-2,3,5-Tri-*O*-acetyl-α-D-arabinofuranoside (19): A procedure similar to that described for the synthesis of **13** was employed (14.0 g, 72%). R_f = 0.38 (petroleum ether/EtOAc, 2:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.70 (d, J = 6.0 Hz, 1 H), 7.00 (d, J = 2.1 Hz, 1 H), 6.72 (d, J = 2.1 Hz, 1 H), 6.16 (d, J = 6.0 Hz, 1 H), 5.77 (s, 1 H), 5.37 (s, 1 H), 5.11 (d, J = 4.5 Hz, 1 H), 4.47–4.35 (m, 2 H), 4.29 (dd, J = 11.4, 4.8 Hz, 1 H), 2.71 (t, J = 7.8 Hz, 2 H), 2.16 (s, 3 H), 2.15 (s, 3 H), 2.12 (s, 3 H), 1.80–1.70 (m, 2 H), 1.45–1.30 (m, 4 H), 0.93 (t, J = 6.6 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 175.7, 172.3, 170.5, 170.1, 169.5, 159.5, 158.7, 153.9, 150.8, 113.9, 113.5, 109.9, 103.8, 102.1, 82.2, 81.1, 76.7, 62.8, 34.2, 31.3, 24.1, 22.4, 20.73, 20.68, 20.65, 13.9 ppm. MS (ESI): m/z = 557.3 [M + Na]$^+$. HRMS (MALDI): calcd. for $C_{26}H_{30}O_{12}Na^+$ 557.1630; found 557.1638.

3-Bromo-5-hexanoyloxy-7-hydroxy-4-oxo-4*H*-chromene 7-*O*-2,3,5-Tri-*O*-acetyl-α-D-arabinofuranoside (20): A procedure similar to that described for the synthesis of **14** was employed (7.5 g, 63%). R_f = 0.55 (petroleum ether/EtOAc, 2:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.10 (s, 1 H), 7.02 (d, J = 1.2 Hz, 1 H), 6.77 (d, J = 1.2 Hz, 1 H), 5.77 (s, 1 H), 5.38 (s, 1 H), 5.12 (d, J = 4.5 Hz, 1 H), 4.48–4.35 (m, 2 H), 4.27 (dd, J = 11.4, 4.8 Hz, 1 H), 2.75 (t, J = 7.5 Hz, 2 H), 2.16 (s, 3 H), 2.15 (s, 3 H), 2.12 (s, 3 H), 1.77 (q, J = 6.9 Hz, 2 H), 1.45–1.30 (m, 4 H), 0.93 (t, J = 6.6 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.3, 170.5, 170.1, 169.9, 169.5, 159.8, 158.3, 152.5, 150.9, 111.6, 110.6, 103.9, 102.0, 82.3, 81.1, 76.6, 62.8, 57.9, 34.1, 31.3, 24.1, 22.4, 20.75, 20.70, 20.66, 13.9 ppm. MS (ESI): m/z = 635.2 [M + Na]$^+$. HRMS (MALDI): calcd. for $C_{26}H_{29}O_{12}BrNa^+$ 635.0735; found 635.0720.

3-Bromo-5,7-dihydroxy-4-oxo-4*H*-chromene 7-*O*-α-D-Arabinofuranoside (21): A procedure similar to that described for the synthesis of **15** was employed (1.0 g, 42%). R_f = 0.47 (CH_2Cl_2/MeOH, 10:1). $[\alpha]_D^{24}$ = 117.6 (c = 0.28, MeOH). ^{1}H NMR (300 MHz, CD_3OD): δ = 8.47 (s, 1 H), 6.70 (d, J = 1.8 Hz, 1 H), 6.54 (d, J = 1.8 Hz, 1 H), 5.65 (d, J = 1.5 Hz, 1 H), 4.30 (dd, J = 3.9, 1.5 Hz, 1 H), 4.08 (m, 1 H), 4.03 (dd, J = 6.0, 3.9 Hz, 1 H), 3.80 (dd, J = 12.0, 2.7 Hz, 1 H), 3.70 (dd, J = 12.0, 4.8 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, CD_3OD): δ = 178.2, 165.0, 163.0, 159.3, 157.3, 108.9, 108.2, 107.2, 102.0, 96.5, 87.4, 83.9, 78.5, 63.0 ppm. MS (ESI): m/z = 410.8 [M + Na]$^+$.

General Method for the Suzuki–Miyaura Coupling

Procedure A: $Pd(OAc)_2$ (1.5 mg, 0.0067 mmol), SPhos (8.0 mg, 0.0195 mmol), and K_2CO_3 (54 mg, 0.390 mmol) were added to a solution of bromide **15** or **21** (50 mg, 0.129 mmol) and aryl boronic acid (0.195 mmol) in acetone/H_2O (1:1, 1.0 mL) under an atmosphere of argon. The mixture was stirred in an oil bath at 50 °C until TLC indicated the disappearance of the starting material (**15** or **21**). The reaction solution was then filtered through a pad of silica gel (300–400 mesh). The filtrate was concentrated in vacuo to give a residue, which was purified by preparative TLC (CH_2Cl_2/MeOH, 8:1) to yield the coupling products. The yields are given in Tables 1 and 2.

Procedure B: $Pd(OAc)_2$ (1.5 mg, 0.0067 mmol) and NaOAc (32 mg, 0.390 mmol) were added to a solution of bromide **21** (50 mg, 0.129 mmol) and aryl boronic acid (0.195 mmol) in methanol (0.5 mL) under an atmosphere of argon. The mixture was heated at reflux in an oil bath until TLC indicated the disappearance of **21**. Similar workup procedure as that given in procedure A provided the coupling products. The yields are given in Table 2.

7,8-Dihydroxyisoflavone 7-*O*-α-D-Arabinofuranoside (22a): Yield: 32 mg, 65%. R_f = 0.29 ($CHCl_3$/MeOH, 10:1). $[\alpha]_D^{24}$ = 31.8 (c = 0.11, MeOH). ^{1}H NMR (300 MHz, CD_3OD): δ = 8.26 (s, 1 H), 7.62 (d, J = 9.0 Hz, 1 H), 7.52 (d, J = 6.3 Hz, 2 H), 7.43–7.35 (m, 3 H), 7.31 (d, J = 9.0 Hz, 1 H), 5.73 (s, 1 H), 4.37 (br. s, 1 H), 4.16 (dd, J = 8.7, 4.5 Hz, 1 H), 4.06 (m, 1 H), 3.73 (dd, J = 11.7, 3.6 Hz, 1 H), 3.68 (dd, J = 11.7, 5.4 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, CD_3OD): δ = 178.5, 155.9, 149.7, 148.3, 138.0, 133.6, 130.6, 129.7, 129.4, 126.1, 121.4, 116.8, 115.8, 109.1, 88.7, 83.0, 78.9, 63.3 ppm. MS (ESI): m/z = 387.2 [M + H]$^+$, 409.2 [M + Na]$^+$, 425.0 [M + K]$^+$. HRMS (MALDI): calcd. for $C_{20}H_{18}O_8Na^+$ 409.0894; found 409.0902.

7,8-Dihydroxy-4′-methoxyisoflavone 7-*O*-α-D-Arabinofuranoside (22b): Yield: 29 mg, 54%. R_f = 0.29 ($CHCl_3$/MeOH, 10:1). $[\alpha]_D^{24}$ = 142.4 (c = 0.10, MeOH). ^{1}H NMR (300 MHz, CD_3OD): δ = 8.29 (s, 1 H), 7.66 (d, J = 8.7 Hz, 1 H), 7.50 (d, J = 8.4 Hz, 2 H), 7.35 (d, J = 8.7 Hz, 1 H), 7.01 (d, J = 8.4 Hz, 2 H), 5.77 (s, 1 H), 4.41 (br. s, 1 H), 4.18 (dd, J = 8.7, 4.5 Hz, 1 H), 4.10 (m, 1 H), 3.85 (br. s, 3 H), 3.77 (dd, J = 11.7, 3.6 Hz, 1 H), 3.73 (dd, J = 11.7, 5.1 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, CD_3OD): δ = 178.8, 161.5, 155.4, 149.6, 148.4, 138.1, 131.7, 125.74, 125.71, 121.4, 116.7, 115.8, 115.2, 109.1, 88.8, 83.0, 78.9, 63.3, 56.1 ppm. MS (ESI): m/z = 417.0 [M + H]$^+$, 439.0 [M + Na]$^+$, 455.0 [M + K]$^+$. HRMS (MALDI): calcd. for $C_{21}H_{20}O_9Na^+$ 439.1000; found 439.0999.

7,8-Dihydroxy-2′-methoxyisoflavone 7-*O*-α-D-Arabinofuranoside (22c): Yield: 27 mg, 50%. R_f = 0.29 ($CHCl_3$/MeOH, 10:1). $[\alpha]_D^{24}$ = 74.2 (c = 0.12, MeOH). ^{1}H NMR (300 MHz, CD_3OD): δ = 8.54 (br. s, 1 H), 8.13 (s, 1 H), 7.37 (t, J = 7.8 Hz, 1 H), 7.33 (d, J = 8.7 Hz, 1 H), 7.28–7.19 (m, 2 H), 7.05 (d, J = 8.7 Hz, 1 H), 6.99 (t, J = 7.8 Hz, 1 H), 5.68 (s, 1 H), 4.39 (br. s, 1 H), 4.19 (dd, J = 8.7, 4.5 Hz, 1 H), 4.00 (m, 1 H), 3.77 (br. s, 4 H), 3.70 (dd, J = 11.7, 5.4 Hz, 1 H) ppm. MS (ESI): m/z = 439.0 [M + Na]$^+$. HRMS (MALDI): calcd. for $C_{21}H_{20}O_9Na^+$ 439.1000; found 439.0990.

7,8-Dihydroxy-3′-methoxyisoflavone 7-*O*-α-D-Arabinofuranoside (22d): Yield: 40 mg, 75%. R_f = 0.29 ($CHCl_3$/MeOH, 10:1). $[\alpha]_D^{24}$ = 27.6 (c = 0.13, MeOH). ^{1}H NMR (300 MHz, CD_3OD): δ = 8.33 (s, 1 H), 7.54 (d, J = 9.0 Hz, 1 H), 7.36 (t, J = 7.2 Hz, 1 H), 7.31 (d, J = 9 Hz, 1 H), 7.16 (br. s, 1 H), 7.12 (d, J = 7.5 Hz, 1 H), 6.97 (br. d, J = 7.2 Hz, 1 H), 5.73 (s, 1 H), 4.40 (br. s, 1 H), 4.19 (dd, J = 8.7, 4.5 Hz, 1 H), 4.05 (m, 1 H), 3.85 (s, 3 H), 3.83–3.65 (m, 2 H) ppm. ^{13}C NMR (75 MHz, CD_3OD): δ = 179.1, 161.4, 156.1, 150.5, 145.9, 144.5, 135.2, 130.7, 125.6, 122.8, 121.7, 116.4, 116.2, 115.0, 113.8, 109.1, 88.5, 83.0, 78.9, 63.3, 56.1 ppm. MS (ESI): m/z = 417.2 [M + H]$^+$, 439.2 [M + Na]$^+$, 455.2 [M + K]$^+$. HRMS (MALDI): calcd. for $C_{21}H_{21}O_9^+$ 417.1180; found 417.1188.

7,8-Dihydroxy-4′-methylisoflavone 7-*O*-α-D-Arabinofuranoside (22e): Yield: 23 mg, 45%. R_f = 0.27 ($CHCl_3$/MeOH, 10:1). $[\alpha]_D^{24}$ = 37.1 (c = 0.17, MeOH). ^{1}H NMR (300 MHz, CD_3OD): δ = 8.18 (s, 1 H), 7.54 (d, J = 9.0 Hz, 1 H), 7.34 (d, J = 7.5 Hz, 2 H), 7.24

(d, J = 9.0 Hz, 1 H), 7.15 (d, J = 7.5 Hz, 2 H), 5.66 (s, 1 H), 4.30 (br. s, 1 H), 4.08 (dd, J = 8.7, 4.5 Hz, 1 H), 3.98 (br. s, 1 H), 3.66 (dd, J = 11.7, 3.9 Hz, 1 H), 3.62 (dd, J = 11.7, 4.8 Hz, 1 H), 2.28 (s, 3 H) ppm. MS (ESI): m/z = 401.0 $[M + H]^+$, 423.0 $[M + Na]^+$. HRMS (MALDI): calcd. for $C_{21}H_{21}O_8^+$ 401.1231; found 401.1235.

7,8-Dihydroxy-2′-methylisoflavone 7-*O*-α-D-Arabinofuranoside (22f): Yield: 18 mg, 34%. R_f = 0.39 ($CHCl_3$/MeOH, 10:1). $[\alpha]_D^{24}$ = 52.1 (c = 0.10, MeOH). ^{1}H NMR (300 MHz, CD_3OD): δ = 8.13 (s, 1 H), 7.40 (d, J = 8.7 Hz, 1 H), 7.34–7.16 (m, 5 H), 5.71 (s, 1 H), 4.39 (br. s, 1 H), 4.20 (dd, J = 8.7, 4.5 Hz, 1 H), 4.03 (m, 1 H), 3.76 (dd, J = 11.7, 3.9 Hz, 1 H), 3.67 (dd, J = 11.7, 5.1 Hz, 1 H), 2.21 (s, 3 H) ppm. MS (ESI): m/z = 401.2 $[M + H]^+$, 423.2 $[M + Na]^+$, 439.0 $[M + K]^+$. HRMS (MALDI): calcd. for $C_{21}H_{20}O_8Na^+$ 423.1050; found 423.1058.

7,8-Dihydroxy-3′-methylisoflavone 7-*O*-α-D-Arabinofuranoside (22g): Yield: 30 mg, 58%. R_f = 0.35 ($CHCl_3$/MeOH, 10:1). $[\alpha]_D^{24}$ = 17.7 (c = 0.13, MeOH). ^{1}H NMR (300 MHz, CD_3O D): δ = 8.32 (s, 1 H), 7.78–7.63 (m, 2 H), 7.42–7.29 (m, 3 H), 7.22 (br. s, 1 H), 5.79 (s, 1 H), 4.43 (br. s, 1 H), 4.21 (dd, J = 8.7, 4.5 Hz, 1 H), 4.10 (m, 1 H), 3.78 (dd, J = 11.7, 3.9 Hz, 1 H), 3.71 (dd, J = 11.7, 5.1 Hz, 1 H), 2.41 (s, 3 H) ppm. MS (ESI): m/z = 401.2 $[M + H]^+$, 423.2 $[M + Na]^+$, 439.2 $[M + K]^+$. HRMS (ESI): calcd. for $C_{21}H_{20}O_8Na^+$ 423.1050; found 423.1051.

4′,7,8-Trihydroxyisoflavone 7-*O*-α-D-Arabinofuranoside (22h, A-76202):[11,12] Yield: 25 mg, 48%.

3′,7,8-Trihydroxyisoflavone 7-*O*-α-D-Arabinofuranoside (22i): Yield: 18 mg, 35%. R_f = 0.23 ($CHCl_3$/MeOH, 8:1). $[\alpha]_D^{24}$ = 99.7 (c = 0.08, MeOH). ^{1}H NMR (300 MHz, CD_3OD): δ = 8.31 (s, 1 H), 7.67 (d, J = 8.7 Hz, 1 H), 7.37 (d, J = 8.7 Hz, 1 H), 7.28 (t, J = 7.5 Hz, 1 H), 7.05 (br. s, 1 H), 7.03 (d, J = 8.1 Hz, 1 H), 6.85 (br. d, J = 6.6 Hz, 1 H), 5.79 (s, 1 H), 4.43 (br. s, 1 H), 4.22 (dd, J = 8.7, 4.5 Hz, 1 H), 4.11 (m, 1 H), 3.79 (dd, J = 11.7, 3.9 Hz, 1 H), 3.74 (dd, J = 11.7, 5.1 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, CD_3OD): δ = 178.6, 158.8, 155.7, 150.0, 148.7, 138.9, 134.9, 130.7, 126.2, 121.7, 117.7, 116.5, 116.4, 116.2, 109.4, 88.9, 83.0, 79.0, 63.4 ppm. MS (ESI): m/z = 403.0 $[M + H]^+$, 425.0 $[M + Na]^+$. HRMS (MALDI): calcd. for $C_{20}H_{19}O_9^+$ 403.1024; found 403.1028.

4′-Fluoro-7,8-dihydroxyisoflavone 7-*O*-α-D-Arabinofuranoside (22j): Yield: 16 mg, 31%. R_f = 0.42 ($CHCl_3$/MeOH, 8:1). $[\alpha]_D^{24}$ = 31.6 (c = 0.16, MeOH). ^{1}H NMR (300 MHz, CD_3OD): δ = 8.34 (s, 1 H), 7.65–7.56 (m, 3 H), 7.34 (d, J = 9.0 Hz, 1 H), 7.19 (t, J = 8.4 Hz, 2 H), 5.77 (s, 1 H), 4.41 (br. s, 1 H), 4.21 (dd, J = 8.7, 4.5 Hz, 1 H), 4.09 (m, 1 H), 3.78 (dd, J = 11.7, 3.9 Hz, 1 H), 3.73 (dd, J = 11.7, 5.1 Hz, 1 H) ppm. MS (ESI): m/z = 405.2 $[M + H]^+$, 427.2 $[M + Na]^+$. HRMS (ESI): calcd. for $C_{20}H_{17}O_8FNa^+$ 427.0800; found 427.0795.

4′-Dimethylamino-7,8-dihydroxyisoflavone 7-*O*-α-D-Arabinofuranoside (22k): Yield: 20 mg, 36%. R_f = 0.30 ($CHCl_3$/MeOH, 10:1). $[\alpha]_D^{24}$ = 104.6 (c = 0.10, MeOH). ^{1}H NMR (300 MHz, CD_3OD): δ = 8.22 (s, 1 H), 7.43 (d, J = 8.4 Hz, 3 H), 7.25 (d, J = 9.0 Hz, 1 H), 6.84 (d, J = 8.4 Hz, 2 H), 5.69 (s, 1 H), 4.40 (br. s, 1 H), 4.20 (dd, J = 8.7, 4.5 Hz, 1 H), 4.02 (m, 1 H), 3.77 (dd, J = 11.7, 3.0 Hz, 1 H), 3.71 (dd, J = 11.7, 5.1 Hz, 1 H), 2.96 (br. s, 6 H) ppm. ^{13}C NMR (75 MHz, CD_3OD): δ = 180.0, 155.0, 152.3, 150.6, 144.4, 131.1, 125.6, 122.1, 116.7, 124.0, 112.1, 109.1, 88.3, 83.0, 79.0, 63.4, 41.1 ppm. MS (ESI): m/z = 430.0 $[M + H]^+$. HRMS (ESI): calcd. for $C_{22}H_{23}O_8NNa^+$ 452.1316; found 452.1320.

4′-*tert*-Butoxycarbonylamino-7,8-dihydroxyisoflavone 7-*O*-α-D-Arabinofuranoside (22l): Yield: 25 mg, 39%. R_f = 0.42 ($CHCl_3$/MeOH, 10:1). $[\alpha]_D^{24}$ = 45.6 (c = 0.10, MeOH). ^{1}H NMR (300 MHz, CD_3OD): δ = 8.57 (s, 1 H), 8.28 (s, 1 H), 7.60 (d, J = 9.0 Hz, 1 H), 7.48 (br. s, 4 H), 7.31 (d, J = 9.0 Hz, 1 H), 5.75 (s, 1 H), 4.40 (br. s, 1 H), 4.17 (dd, J = 8.7, 4.5 Hz, 1 H), 4.07 (m, 1 H), 3.79 (dd, J = 11.7, 3.9 Hz, 1 H), 3.71 (dd, J = 11.7, 5.1 Hz, 1 H), 1.53 (s, 9 H) ppm. MS (ESI): m/z = 502.0 $[M + H]^+$, 524.0 $[M + Na]^+$. HRMS (MALDI): calcd. for $C_{25}H_{27}O_{10}NNa^+$ 524.1527; found 524.1532.

7,8-Dihydroxy-4′-trifluoromethylisoflavone 7-*O*-α-D-Arabinofuranoside (22m): Yield: 24 mg, 41%. R_f = 0.43 ($CHCl_3$/MeOH, 10:1). $[\alpha]_D^{24}$ = 37.5 (c = 0.23, MeOH). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.41 (s, 1 H), 7.83–7.65 (m, 4 H), 7.57 (d, J = 8.4 Hz, 1 H), 7.32 (d, J = 7.8 Hz, 1 H), 5.77 (s, 1 H), 4.42 (br. s, 1 H), 4.21 (dd, J = 7.8, 4.5 Hz, 1 H), 4.09 (m, 1 H), 3.82–3.74 (m, 2 H) ppm. ^{13}C NMR (75 MHz, CD_3OD): δ = 178.3, 156.4, 150.3, 149.1, 140.6, 138.1, 131.1, 126.4, 124.6, 121.7, 116.4, 115.1, 109.3, 88.9, 82.8, 79.0, 63.4, 31.0 ppm. MS (ESI): m/z = 455.0 $[M + H]^+$, 477.0 $[M + Na]^+$. HRMS (ESI): calcd. for $C_{21}H_{17}O_8F_3Na^+$ 477.0768; found 477.0768.

7,8-Dihydroxy-4′-trimethylsilylisoflavone 7-*O*-α-D-Arabinofuranoside (22n): Yield: 18 mg, 30%. R_f = 0.58 (CH_2Cl_2/MeOH, 8:1). $[\alpha]_D^{24}$ = 49.1 (c = 0.12, MeOH). ^{1}H NMR (300 MHz, CD_3OD): δ = 8.32 (s, 1 H), 7.71–7.46 (m, 5 H), 7.32 (d, J = 8.7 Hz, 1 H), 5.76 (s, 1 H), 4.42 (br. s, 1 H), 4.21 (dd, J = 8.7, 4.5 Hz, 1 H), 4.07 (br. s, 1 H), 3.86–3.64 (m, 2 H), 0.30 (s, 9 H) ppm. MS (ESI): m/z = 459.0 $[M + H]^+$.

5,7-Dihydroxyisoflavone 7-*O*-α-D-Arabinofuranoside (23a): Yield: 14 mg, 28%, procedure A; 8 mg, 16%, procedure B. R_f = 0.42 (CH_2Cl_2/MeOH, 10:1). $[\alpha]_D^{24}$ = 86.7 (c = 0.15, MeOH). ^{1}H NMR (300 MHz, CD_3OD): δ = 8.20 (s, 1 H), 7.56 (d, J = 6.6 Hz, 2 H), 7.48–7.34 (m, 3 H), 6.70 (br. s, 1 H), 6.50 (br. s, 1 H), 5.65 (s, 1 H), 4.29 (br. s, 1 H), 4.13–3.96 (m, 2 H), 3.78 (dd, J = 12.0, 2.4 Hz, 1 H), 3.69 (dd, J = 12.0, 4.5 Hz, 1 H) ppm. MS (ESI): m/z = 387.0 $[M + H]^+$, 409.0 $[M + Na]^+$. HRMS (ESI): calcd. for $C_{20}H_{19}O_8^+$ 387.1074; found 387.1075.

5,7-Dihydroxy-4′-methoxyisoflavone 7-*O*-α-D-Arabinofuranoside (23b): Yield: 23 mg, 43%, procedure A. R_f = 0.48 (CH_2Cl_2/MeOH, 10:1). $[\alpha]_D^{24}$ = 68.6 (c = 0.19, MeOH). ^{1}H NMR (300 MHz, CD_3OD): δ = 8.17 (s, 1 H), 7.50 (d, J = 7.2 Hz, 2 H), 6.99 (d, J = 7.2 Hz, 2 H), 6.69 (br. s, 1 H), 6.50 (br. s, 1 H), 5.67 (s, 1 H), 4.31 (br. s, 1 H), 4.13–4.02 (m, 2 H), 3.84 (s, 3 H), 3.80 (dd, J = 12.0, 3.0 Hz, 1 H), 3.73 (dd, J = 12.0, 4.5 Hz, 1 H) ppm. MS (ESI): m/z = 417.0 $[M + H]^+$, 439.0 $[M + Na]^+$. HRMS (MALDI): calcd. for $C_{21}H_{21}O_9^+$ 417.1180; found 417.1186.

5,7-Dihydroxy-2′-methoxyisoflavone 7-*O*-α-D-Arabinofuranoside (23c): Yield: 21 mg, 39%, procedure A. R_f = 0.49 (CH_2Cl_2/MeOH, 10:1). $[\alpha]_D^{24}$ = 74.6 (c = 0.19, MeOH). ^{1}H NMR (300 MHz, CD_3OD): δ = 8.28 (s, 1 H), 7.63 (t, J = 8.4 Hz, 1 H), 7.50 (d, J = 7.2 Hz, 1 H), 7.30 (d, J = 8.4 Hz, 1 H), 7.24 (t, J = 7.2 Hz, 1 H), 6.93 (d, J = 1.8 Hz, 1 H), 6.74 (d, J = 1.8 Hz, 1 H), 5.89 (s, 1 H), 4.53 (d, J = 2.1 Hz, 1 H), 4.35–4.22 (m, 2 H), 4.04 (dd, J = 12.0, 3.0 Hz, 1 H), 4.03 (s, 3 H), 3.93 (dd, J = 12.0, 4.5 Hz, 1 H) ppm. MS (ESI): m/z = 417.2 $[M + H]^+$. HRMS (ESI): calcd. for $C_{21}H_{21}O_9^+$ 417.1180; found 417.1190.

5,7-Dihydroxy-3′-methoxyisoflavone 7-*O*-α-D-Arabinofuranoside (23d): Yield: 20 mg, 37%, procedure A. R_f = 0.47 (CH_2Cl_2/MeOH, 10:1). $[\alpha]_D^{24}$ = 89.2 (c = 0.08, MeOH). ^{1}H NMR (300 MHz, CD_3OD): δ = 8.22 (br. s, 1 H), 7.34 (t, J = 7.5 Hz, 1 H), 7.15 (br. s, 1 H), 7.11 (d, J = 7.5 Hz, 1 H), 6.96 (d, J = 7.5 Hz, 1 H), 6.70 (d, J = 1.5 Hz, 1 H), 6.51 (d, J = 1.5 Hz, 1 H), 5.65 (br. s, 1 H), 4.29 (d, J = 3.6 Hz, 1 H), 4.10–3.98 (m, 2 H), 3.82 (s, 3 H), 3.78 (dd, J = 12.0, 3.0 Hz, 1 H), 3.70 (dd, J = 12.0, 4.5 Hz) ppm. MS (ESI): m/z = 417.2 $[M + H]^+$, 439.2 $[M + Na]^+$. HRMS (ESI): calcd. for $C_{21}H_{21}O_9^+$ 417.1180; found 417.1178.

5,7-Dihydroxy-4′-methylisoflavone 7-*O*-α-D-Arabinofuranoside (23e): Yield: 20 mg, 39%, procedure B. R_f = 0.50 (CH_2Cl_2/MeOH, 10:1). $[\alpha]_D^{24}$ = 136.7 (*c* = 0.13, MeOH). ^{1}H NMR (300 MHz, CD_3OD): δ = 8.16 (s, 1 H), 7.43 (d, *J* = 7.8 Hz, 2 H), 7.24 (d, *J* = 7.8 Hz, 2 H), 6.68 (br. s, 1 H), 6.49 (br. s, 1 H), 5.64 (s, 1 H), 4.29 (br. s, 1 H), 4.13–3.98 (m, 2 H), 4.06 (dd, *J* = 12.0, 3.0 Hz, 1 H), 3.98 (dd, *J* = 12.0, 4.5 Hz, 1 H), 2.37 (s, 3 H) ppm. MS (ESI): *m*/*z* = 401.1 $[M + H]^+$, 423.1 $[M + Na]^+$. HRMS (ESI): calcd. for $C_{21}H_{21}O_8^+$ 401.1231; found 401.1232.

5,7-Dihydroxy-3′-methylisoflavone 7-*O*-α-D-Arabinofuranoside (23f): Yield: 8 mg, 16%, procedure A. R_f = 0.49 (CH_2Cl_2/MeOH, 10:1). $[\alpha]_D^{24}$ = 97.6 (*c* = 0.10, MeOH). ^{1}H NMR (300 MHz, CD_3OD): δ = 8.16 (s, 1 H), 7.40–7.30 (m, 3 H), 7.22–7.18 (d, *J* = 7.2 Hz, 1 H), 6.69 (br. s, 1 H), 6.51 (br. s, 1 H), 5.64 (br. s, 1 H), 4.28 (br. s, 1 H), 4.12–3.98 (m, 2 H), 3.84–3.63 (m, 2 H), 2.39 (s, 3 H) ppm. MS (ESI): *m*/*z* = 401.1 $[M + H]^+$, 423.0 $[M + Na]^+$. HRMS (ESI): calcd. for $C_{21}H_{20}O_8Na^+$ 423.1050; found 423.1050.

4′,5,7-Trihydroxyisoflavone 7-*O*-α-D-Arabinofuranoside (23g): Yield: 30 mg, 39%, procedure A; 6 mg, 12%, procedure B. R_f = 0.28 (CH_2Cl_2/MeOH, 10:1). $[\alpha]_D^{24}$ = 37.1 (*c* = 0.15, MeOH). ^{1}H NMR (300 MHz, CD_3OD): δ = 8.15 (s, 1 H), 7.39 (d, *J* = 8.4 Hz, 2 H), 6.85 (d, *J* = 8.4 Hz, 2 H), 6.69 (d, *J* = 1.5 Hz, 1 H), 6.50 (d, *J* = 1.5 Hz, 1 H), 5.65 (br. s, 1 H), 4.29 (d, *J* = 3.6 Hz, 1 H), 4.07 (m, 1 H), 4.02 (dd, *J* = 6.6, 3.9 Hz, 1 H), 3.78 (dd, *J* = 12.0, 2.7 Hz, 1 H), 3.70 (dd, *J* = 12.0, 4.5 Hz, 1 H) ppm. MS (ESI): *m*/*z* = 403.1 $[M + H]^+$, 425.2 $[M + Na]^+$. HRMS (ESI): calcd. for $C_{20}H_{19}O_9^+$ 403.1024; found 403.1025.

3′,5,7-Trihydroxyisoflavone 7-*O*-α-D-Arabinofuranoside (23h): Yield: 18 mg, 35%, procedure B. R_f = 0.29 (CH_2Cl_2/MeOH, 10:1). $[\alpha]_D^{24}$ = 49.2 (*c* = 0.17, MeOH). ^{1}H NMR (300 MHz, CD_3OD): δ = 8.18 (s, 1 H), 7.24 (t, *J* = 7.8 Hz, 1 H), 7.02 (br. s, 1 H), 7.00 (d, *J* = 7.8 Hz, 1 H), 6.82 (d, *J* = 7.8 Hz, 1 H), 6.69 (br. s, 1 H), 6.50 (br. s, 1 H), 5.65 (s, 1 H), 4.29 (d, *J* = 3.0 Hz, 1 H), 4.07 (m, 1 H), 4.03 (dd, *J* = 6.6, 3.9 Hz, 1 H), 3.79 (dd, *J* = 12.0, 2.7 Hz, 1 H), 3.69 (dd, *J* = 12.0, 4.8 Hz, 1 H) ppm. MS (ESI): *m*/*z* = 403.1 $[M + H]^+$. HRMS (MALDI): calcd. for $C_{20}H_{19}O_9^+$ 403.1024; found 403.1030.

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