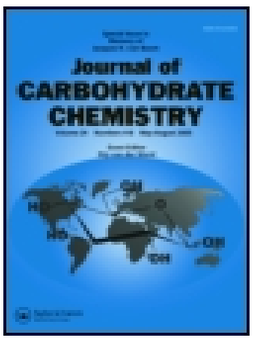

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A new strategy for isoflavone *C*-glycoside synthesis: The total synthesis of puerarin

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ABSTRACT

Given that *C*-glucosylisoflavones often possess promising biological activities, the development of an efficient synthetic method for this type of molecules is useful for drug discovery. Accordingly, a highly efficient five-step strategy was developed for the total synthesis of puerarin, an isoflavone *C*-glycoside. An alkyl substituent 4-$CH_3OC_6H_4CH_2CH_2$ with an electron-donating group on the aromatic ring was used to enhance the reactivity of phenol and the regioselectivity of O-C rearrangement of phenol glycoside. Thus, coupling of the ethylbenzene derivative of a phenol **1c** with glycosyl trifluoroacetimidate **2** resulted in *C*-glycoside **3c** in a 46.2% yield, which was easily de-*tert*-butylated with trifluoroacetic acid and oxidized with 2,3-dicyano-5,6-dichlorobenzoquinone to produce deoxybenzoin **5**. The ring closure reaction of **5** followed by deprotection gave puerarin. This new synthetic strategy is also suitable for the total synthesis of other *C*-glucosylisoflavones.

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C-glycoside; isoflavone; puerarin; total synthesis

Introduction

Pueraria lobate is a traditional Chinese herbal medicine that is extensively used for the treatment of fever,[1] diabetes,[2] hypertension,[3] and myocardial infarction.[4] It possesses a high content of flavonoid derivatives, such as puerarin, daidzin, daidzein, and genistein.[5] Puerarin, a *C*-glucosylisoflavone isolated from pueraria lobate, exhibits cardiovascular and neurological protective effects.[6,7] The compound, which protects against transverse aorta constriction-induced cardiac fibrosis associated with the inhibition of endothelial-to-mesenchymal transition,[8] provides neuroprotection against amyloid beta (Ab_{1-42}) toxicity by activating estrogen receptors.[9]

Previous syntheses of isoflavone *C*-glycosides in the literature[10–14] began from phenol acceptors containing an *o*-hydroxyacetophenone structure, which is critical for the construction of isofavone rings. However, phenol

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acceptors containing electron-withdrawing acyl groups often give low yields of *C*-glycoside in the O→C glycosyl rearrangement, except for methyl- or benzyl-protected 2,4,6-trihydroxyacetophenone,[15–22] which has limited the application to the synthesis of various isoflavone *C*-glycosides. The first total synthesis of puerarin was achieved by Lee et al.[10] in ten steps, starting from a lithiated aromatic reagent, which coupled with pyranolactone to produce *β*-D-glucopyranosyl-2,6-dimethoxybenzene in a 56.0% yield. However, the synthetic route employed the highly toxic thallium(III) nitrate in the oxidative rearrangement of *C*-glucosylchalcone and required repeated protection and deprotection of the sugar moiety with the acetyl group.

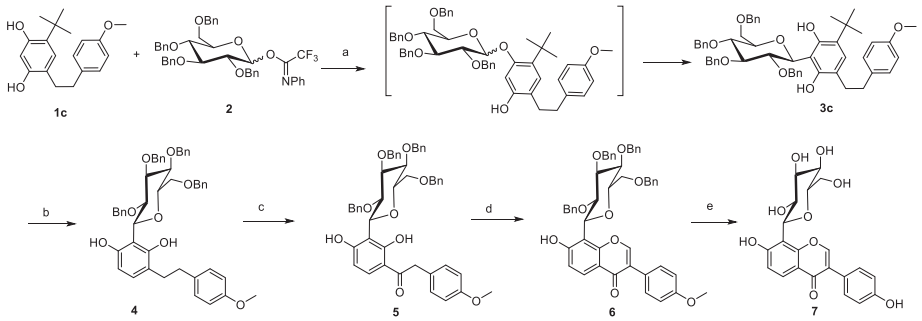
Although 6-*tert*-butyl puerarin was successfully synthesized in our previous studies,[23,24] it had limitations for the synthesis of other isoflavone *C*-glycosides containing puerarin. First, the large steric hindrance of the *tert*-butyl substituent allowed the acyl group to be easily attached to C-6 in *β*-D-glucopyranosyl-4-*tert*-butylresorcinol. When the *tert*-butyl substituent was removed from this *C*-glycoside, subsequent Friedel–Crafts acetylation could not occur. Second, the 6-*tert*-butyl group was difficult to be removed from other intermediates and 6-*tert*-butylpuerarin because of the existence of the electron-withdrawing acyl group. Therefore, a new synthetic strategy should be developed for isoflavone *C*-glycosides such as puerarin.

In this study, the total synthesis of puerarin was achieved through a new strategy and a highly efficient five-step sequence. A weak electron-donating alkyl substituent was introduced to the phenyl ring of a key intermediate to facilitate de-*tert*-butylation and *β*-*C*-glycoside oxidation. Remarkably, the *C*-glucoside invovled in this synthesis was also a key intermediate for the synthesis of related *C*-glucosylisoflavones. Thus, this new synthetic strategy was suitable for the total synthesis of other *C*-glucosylisoflavones.

Results and discussion

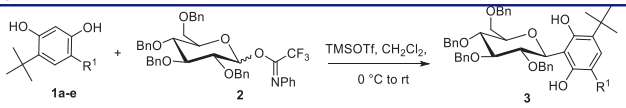
As shown in Scheme 1, our synthesis of puerarin began from coupling of glycosyl donor **2** with an ethylbenzene derivative **1c**. Upon treatment of **2** and **1c** with TMSOTf as the Lewis acid catalyst, the corresponding *O*-glycoside was rapidly produced and underwent O→C rearrangement to yield *C*-glycoside **3c** in a regioselective manner with a yield of 46.2%.[25]

Similarly, when **1a** and **1b** were used as glycosyl acceptors, the corresponding *C*-glycoside **3a** and **3b** were isolated as the major products with high yields (Table 1). In contrast, when acylbenzene derivatives **1d** and **1e** with electron-withdrawing acyl groups at the C-6 were employed as acceptors for *C*-glycosylation with trifluoroacetimidate **2**, the reactions led to complex mixtures. Clearly, the *C*-glycoside yields from O→C rearrangement were fully determined by the types of phenolic compound involved.



Scheme 1. Total synthesis of puerarin. *Reagents and conditions*: a) TMSOTf, CH_2Cl_2, 0 °C to rt, 46.2%; b) CF_3COOH, $Na_2S_2O_4$, rt, 30.7%; c) DDQ, H_2O, CH_3COOH, rt, 35.6%; d) $POCl_3$, DMF, 70 °C, 70.1%; e) BBr_3, CH_2Cl_2, −78 °C, 95.0%.

Table 1. Coupling of **2** with other phenol derivatives.

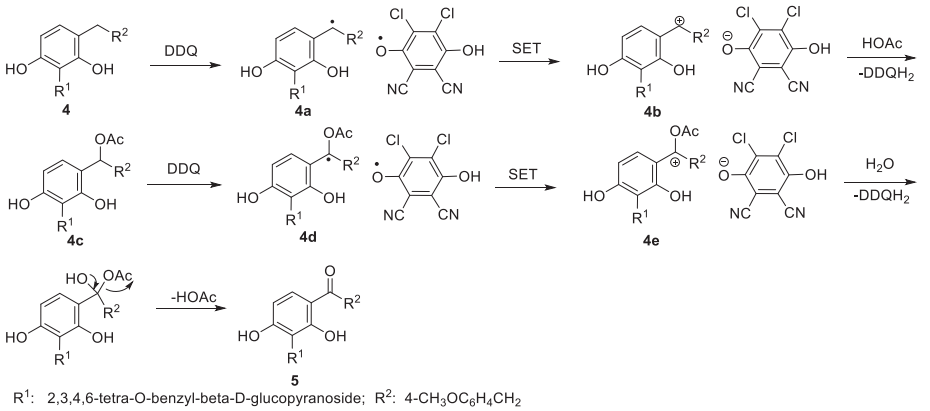


Entry	R^1	product, Yield (%)
1	*t*-butyl **1a**	**3a**, 51.6%
2	ethyl **1b**	**3b**, 63.7%
3	4-$CH_3OC_6H_4CH_2CH_2$ **1c**	**3c**, 46.2%
4	acetyl **1d**	**3d**, < 1.0%
5	4-$CH_3OC_6H_4COCH_2$ **1e**	-[a]

[a]The desired *C*-glycoside was not purified.

The weak electron-donating effect of the alkyl substituents on the phenyl rings enabled coupling of glycosyl trifluoroacetimidate **2** with phenolic compound **1c**. Thus, the high yields of *C*-glycosides from **2** and **1c** were probably a result of the efficient matching of their reactivity.

Notably, *C*-glucosyl ethylbenzene derivative **3b** was easily de-*tert*-butylated with trifluoroacetic acid (TFA) and oxidized with 2,3-dicyano-5, 6-dichlorobenzoquinone (DDQ) to produce *β*-D-glucopyranosyl-2,4-hydroxy-acetophenone, which is also a key intermediate for the total synthesis of related *C*-glucosylisoflavones. De-butylation of the 6-*tert*-butyl group of *C*-glucosyl ethylbenzene derivative **3c** was successfully achieved through stirring it at room temperature for 11 h in the presence of TFA to obtain the desired *C*-glycoside **4** in a yield of 30.7%.[26] However, subsequent oxidation encountered many difficulties. After attempt of several unsuccessful conditions of oxidation, such as treatment of **4** with DDQ in 10% HCl,[27] with CrO_3 and *t*-BuOOH in dichloromethane,[28] and with DDQ in benzene,[29] we observed that oxidation of **4** with the DDQ in $HOAc/H_2O$ could afford deoxybenzoin **5**.[30] The mechanism for this oxidative dehydrogenation was proposed in Scheme 2.[31–33] electron and hydrogen atom transfers from *C*-glycoside **4** to DDQ can form the benzyl radical **4a** followed by single electron transfer (SET) to form the benzyl



Scheme 2. Proposed mechanisms for converting *C*-glycoside **4** into ketone **5**.

cation **4b** and $DDQH^-$ anion. An abstraction of the proton of acetic acid by $DDQH^-$ generated the C–O coupled product **4c** and reduced hydroquinone $DDQH_2$. The subsequent oxidation to form the ketone **5** may be similar to the above oxidation process. An alkyl radical **4d**, which was generated by DDQ and **4c**, went through a single electron transfer process to form the alkyl cation **4e**, which reacted with H_2O to produce ketone **5**.

Moreover, we also examined an alternative procedure (Sch. 3). The oxidation of *β-C*-glycoside **3c** with DDQ in the presence of HOAc afforded deoxybenzoin **8**. However, the 5-*tert*-butyl group could not be removed from **8** with TFA. Failure to detect *β-C*-glycoside **5** from this reaction might have been resulted from the strong electron-withdrawing acyl group at C-1 in deoxybenzoin **8**.

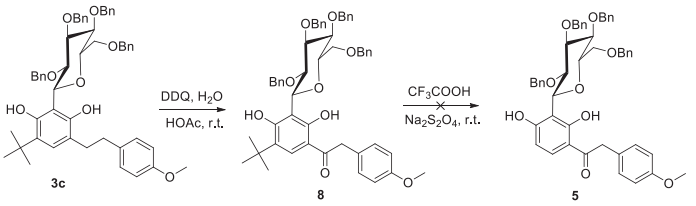
Glucosylisoflavone **6** was prepared by treatment of **5** with $POCl_3$ reagent in DMF at 70 °C for 6 h.[34] Detection under UV light at 365 nm revealed that **6** had bright blue fluorescence and deoxybenzoin **5** showed yellow fluorescence. The ^{1}H-NMR spectrum of **6** showed the appearance of a characteristic proton signal for the isoflavone ring with a chemical shift of δ 7.78 (s, 1H; H-2) and the disappearance of the proton signal of the methylene group in deoxybenzoin **5** at δ 4.16 (s, 2H; H-2). Finally, the debenzylation and demethylation of **6** with BBr_3 proceeded rapidly to yield puerarin **7** with a 95.0% yield.[19,35]

In conclusion, the total synthesis of puerarin was achieved by a highly efficient five-step sequence. This new synthetic strategy is suitable for the total synthesis of other related *C*-glucosylisoflavones.

Experimental

General experimental procedures

The solvents used in these reactions were purified by distillation. Reactions were monitored by TLC on 0.20–0.25 mm silica gel GF254 plates (Qingdao



Scheme 3. Attempted alternative route for converting **3c** into acetophenone **5**.

Marine Chemistry Company, Qingdao, China) using UV light and either a 5% ethanolic solution of $FeCl_3$ or a 5% ethanolic solution of sulfuric acid with heat as the coloration agent. Column chromatography was carried out on a silica gel (200–300 mesh, Qingdao Marine Chemistry Company, Qingdao, China). Melting points were recorded using an RY-1 melting point detector (Tianjin Tianfen Analysis Instrument Factory). NMR spectra were recorded on a Varian Inova 600 spectrometer. Mass spectral data were obtained by electron spray ionization on a Micromass ZabSpec high-resolution mass spectrometer.

*Typical procedure for the coupling of glycosyl N-phenyltrifluoroacetimidates with phenols [4-(4-methoxyphenethyl)-6-*tert*-butyl-2-C-(2,3,4,6-tetra-O-benzyl-β-D-glucopyranosyl)-1,3- dihydroxy-benzene (3c)].*

A mixture of 4-(4-methoxyphenethyl)-6-*tert*-butylbenzene-1,3-diol (**1c**) (13.60 g, 45.36 mmol), 4 Å MS (8.55 g) and **2** (32.26 g, 45.36 mmol) in anhydrous CH_2Cl_2 (400 mL) was stirred at 0 °C for 30 min under an Ar atmosphere. Then, TMSOTf (9.20 mL, 45.36 mmol) was added. After stirring at 0 °C for 2 h, the mixture was warmed to r.t. within 10 h. The above mixture was quenched by adding Et_3N (73 mL), stirred continuously for 30 min, and then filtered through a Celite pad. The filtrate was evaporated in vacuo to obtain a brown syrup (51 g), which was subjected to silica gel column chromatography (25:1-7:1, petroleum ether–EtOAc) to obtain another brown syrup **3c** (17.24 g, 46.2%). ^{1}H-NMR (400 MHz, DMSO-d_6): δ 8.29 (s, 1H; H-4″), 8.06 (s, 1H; H-2″), 7.36–7.09 (m, 18H; C*H*-Ph), 7.02 (d, $J = 7.6$ Hz, 2H; H-2′, H-6′), 7.09–6.92 (m, 2H; C*H*-Ph), 6.74 (brs, 2H; H-3′, H-5′), 6.69 (s, 1H; H-6″), 5.15 (s, 1H; H-1‴), 4.81 (d, $J = 11.4$ Hz, 1H; CH_2Ph), 4.78–4.68 (m, 2H; CH_2Ph), 4.56–4.43 (m, 3H; CH_2Ph), 4.25–4.12 (m, 1H; H-2‴), 3.92–3.55 (m, 10H; CH_2Ph, H-3‴, H-4‴, H-5‴, H-6‴a, H-6‴b, OCH_3), 2.84–2.56 (m, 4H; H-1, H-2), 1.25 (s, 9H; $(CH_3)_3C$). ^{13}C-NMR (150 MHz, DMSO-d_6): δ 157.3, 138.7 (C, CH_2Ph), 138.1 (C, CH_2Ph), 137.7 (C, CH_2Ph), 133.9 (C, CH_2Ph), 129.3, 128.2, 128.1, 128.0, 127.8, 127.5, 127.5, 127.4, 127.4, 127.3, 118.9, 113.4, 112.0 (C-3″), 85.1 (C-3‴), 80.0, 77.9, 77.1, 74.4, 74.1, 73.6, 72.1, 67.9 (C-6‴), 54.9 (OCH_3), 35.1 (C-1), 33.7 (C, $(CH_3)_3C$), 32.0 (C-2), 29.8 (CH_3, $(CH_3)_3C$). HRESI-MS (*m/z*): calcd for $C_{53}H_{58}O_8Na$ $[M + Na]^+$ 845.4029, found 845.4024.

4-*tert*-Butyl-6-ethyl-2-C-(2,3,4,6-tetra-O-benzyl-β-D-glucopyranosyl)-1,3-dihydroxy-benzene (3b, 63.7%) ^{1}H-NMR (400 MHz, DMSO-d_6): δ 8.14 (s, 1H; OH-1), 8.02 (s, 1H; OH-3), 7.35–7.08 (m, 18H; C*H*-Ph), 6.95–6.88 (m, 2H; C*H*-Ph), 6.86 (s, 1H; H-5), 5.10 (d, $J = 9.4$ Hz, 1H; H-1′), 4.80 (d, $J = 11.4$ Hz, 1H; CH_2Ph), 4.77–4.67 (m, 2H; CH_2Ph), 4.57–4.40 (m, 3H; CH_2Ph), 4.22–4.08 (m, 1H, H-2′), 3.86–3.54 (m, 7H; CH_2Ph, H-3′, H-4′, H-5′, H-6′a, H-6′b)), 2.50 (q, $J = 7.4$ Hz, 2H; CH_2), 1.30 (s, 9H; $(CH_3)_3C$), 1.05 (t, $J = 7.4$ Hz, 3H; CH_3). ^{13}C-NMR (100 MHz, DMSO-d_6): δ 138.8 (C, CH_2Ph), 138.1 (C, CH_2Ph), 137.7 (C, CH_2Ph), 128.3, 128.2, 128.2, 128.0, 127.7, 127.6, 127.5, 127.4, 126.5, 121.2 (C-5), 112.0 (C-2), 85.2 (C-3′), 80.1, 77.9, 77.2, 74.5, 74.4, 74.2, 73.8, 72.1, 67.9, 33.9 (C, $(CH_3)_3C$), 29.9 (CH_3, $(CH_3)_3C$), 23.0 (CH_2, CH_3CH_2), 15.0 (CH_3, CH_3CH_2). HRESI-MS (*m/z*): calcd for $C_{46}H_{53}O_7$ $[M + H]^+$ 717.3791, found 717.3786.

4-(4-Methoxyphenethyl)-2-C-(2,3,4,6-tetra-O-benzyl-β-D-glucopyranosyl)-1,3-dihydroxy benzene (4)

Sodium dithionite (112 mg, 0.64 mmol) and **3c** (12.24 g, 14.89 mmol) in TFA (67 mL) were stirred at r.t. for 11 h. The reaction mixture was decomposed by the dropwise addition of saturated $NaHCO_3$ solution (180 mL). The product was isolated with CH_2Cl_2 (3 × 70 mL) and evaporation of the organic phase to obtain a brown syrup, which was then subjected to silica gel column chromatography (7:1–5:1, petroleum ether–EtOAc) to obtain another brown syrup **4** (3.5 g, 30.7%). ^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.31 (s, 1H; H-2″), 8.01 (s, 1H; H-4″), 7.35–7.11 (m, 18H; C*H*-Ph), 7.04 (d, $J = 8.4$ Hz, 2H; H-2′, H-6′), 7.00–6.92 (m, 2H; C*H*-Ph), 6.77 (d, $J = 8.2$ Hz, 1H; H-6″), 6.70 (d, $J = 8.4$ Hz, 2H; H-3′, H-5′), 6.29 (d, $J = 8.2$ Hz, 1H; H-5″), 4.96 (d, $J = 9.7$ Hz, 1H; H-1‴), 4.81 (d, $J = 11.4$ Hz, 1H; CH_2Ph), 4.77–4.67 (m, 2H; CH_2Ph), 4.58–4.39 (m, 3H; CH_2Ph) 4.30–4.19 (m, 1H; H-2‴), 3.92–3.55 (m, 10H; CH_2Ph, H-3‴, H-4‴, H-5‴, H-6‴a, H-6‴b, OCH_3), 2.82–2.53 (m, 4H; H-1, H-2). ^{13}C-NMR (150 MHz, DMSO-d_6): δ 157.2, 154.4, 138.8 (C, CH_2Ph), 138.1 (C, CH_2Ph), 138.0 (C, CH_2Ph), 133.9 (C, CH_2Ph), 129.9, 129.2, 128.4, 128.2, 128.1, 128.1, 127.9, 127.8, 127.6, 127.5, 127.4, 127.4, 127.3, 119.3, 113.4 (C-3″), 85.3 (C-3‴), 80.1, 77.9, 77.4, 74.4, 74.0, 73.6, 73.5, 72.2, 68.3 (C-6‴), 54.8 (OCH_3), 34.7 (C-1), 31.6 (C-2). HRESI-MS (*m/z*): calcd for $C_{49}H_{50}O_8Na$ $[M + Na]^+$ 789.3403 found 789.3396.

2′,4′-Dihydroxy-4-methoxy-3′-C-(2,3,4,6-tetra-O-benzyl-β-D-glucopyranosyl)deoxy benzoin (5)

C-Glycoside **4** (650 mg, 0.85 mmol) was dissolved in acetic acid (70 mL), and 2.12 mL of water was added slowly to the mixture. As DDQ (578 mg,

2.55 mmol) was added, the solution initially became dark green. The reaction mixture was stirred at r.t. for 14 h, quenched with $NaHCO_3$ solution (200 mL), and extracted with CH_2Cl_2 (3 × 50 mL). The organic phases were combined, dried over anhydrous Na_2SO_4, concentrated under vacuum, and purified by silica gel column chromatography (11:1–6:1, petroleum ether–EtOAc) to obtain another brown syrup **5** (236 mg, 35.6%). ^{1}H-NMR (400 MHz, $CDCl_3$): δ 13.27 (s, 1H; OH-4″), 8.86 (s, 1H; OH-2″), 7.73 (d, J = 9.0 Hz, 1H; H-6″), 7.37–7.27 (m, 13H; C*H*-Ph), 7.23–7.07 (m, 7H; C*H*-Ph), 6.92 (d, J = 8.7 Hz, 2H; H-2′, H-6′), 6.86 (d, J = 8.7 Hz, 2H; H-3′, H-5′), 6.44 (d, J = 9.0 Hz, 1H; H-5″), 5.19 (d, J = 9.7 Hz, 1H; H-1‴), 4.96 (d, J = 10.9 Hz, 1H; CH_2Ph), 4.91–4.81 (m, 2H; CH_2Ph), 4.61–4.47 (m, 3H; CH_2Ph), 4.43 (d, J = 12.0 Hz, 1H; CH_2Ph), 4.16 (s, 2H; H-2), 4.03 (d, J = 10.4 Hz, 1H; CH_2Ph), 3.95–3.57 (m, 9H; H-2‴, H-3‴, H-4‴, H-5‴, H-6‴a, H-6‴b, CH_3). ^{13}C-NMR (150 MHz, $CDCl_3$): δ 202.6 (C-1), 163.8 (C-4″), 163.2 (C-2″), 158.8 (C-4'), 138.7 (C, CH_2Ph), 138.2 (C, CH_2Ph), 137.9 (C, CH_2Ph), 137.5 (C, CH_2Ph), 132.5, 130.4 (C-2′, C-6′), 128.6, 128.6, 128.6, 128.4, 128.3, 128.1, 128.0, 127.9, 127.9, 127.8, 127.8, 126.6, 114.4 (C-3′, C-5′), 112.6, 111.3 (C-3″), 109.7 (C-5″), 86.2 (C-5‴), 81.5 (C-3‴), 78.7, 77.3, 75.9, 75.8, 75.4, 74.1, 73.5, 67.8 (C-6‴), 55.4 (OCH_3), 44.1 (C-2). HRESI-MS (*m/z*): calcd for $C_{49}H_{48}O_9Na$ $[M + Na]^+$ 803.3191, found 803.3187.

7-Hydroxy-4′-methoxy-8-C-(2,3,4,6-tetra-O-benzyl-β-D-glucocopyranosyl) isoflavone (6)

$POCl_3$ (0.04 mL, 0.42 mmol) was added dropwise to anhydrous DMF (0.57 mL) and cooled to 10 °C. The mixture of DMF and $POCl_3$ was kept for 15 min at 10 °C, and deoxybenzoin **5** (0.2 g, 0.26 mmol) was then added. The solution was stirred at 70 °C for 6 h, cooled to room temperature, and poured into water (20 mL). The product was isolated with chloroform (3 × 10 mL) and evaporated in the organic phase to obtain a yellow oil (0.38 g), which was subjected to silica gel column chromatography (20:1 to 9:1, petroleum ether–EtOAc) to produce syrup **6** (0.14 g, 70.1%). ^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.81 (s, 1H; OH-7), 8.22 (d, J = 8.9 Hz, 1H; H-5), 7.78 (s, 1H; H-2), 7.43 (d, J = 8.8 Hz, 2H; H-2′, H-6′), 7.40–7.27 (m, 13H; C*H*-Ph), 7.22–7.06 (m, 5H; C*H*-Ph), 7.02 (d, J = 8.9 Hz, 1H; H-6), 6.98 (d, J = 8.8 Hz, 2H; H-3′, H-5′), 6.75–6.65 (m, 2H; C*H*-Ph), 5.25 (d, J = 9.3 Hz, 1H; H-1″), 5.04 and 4.96 (d, J = 11.0 Hz, each 1H; CH_2Ph), 4.89 (d, J = 10.8 Hz, 1H; CH_2Ph), 4.64–4.54 (m, 3H; CH_2Ph), 4.48 (d, J = 12.0 Hz, 1H; CH_2Ph), 4.01–3.67 (m, 10H; CH_2Ph, H-2″, H-3″, H-4″, H-5″, H-6″a, H-6″b, CH_3). ^{13}C-NMR (150 MHz, $CDCl_3$): δ 175.9 (C-4), 161.2 (C-7), 159.7 (C-4′), 154.9 (C-8a), 151.7 (C-2), 138.5 (C, CH_2Ph), 138.05 (C, CH_2Ph), 137.75 (C, CH_2Ph), 137.15 (C, CH_2Ph), 130.2 (C-2′, C-6′), 128.6,

128.5, 128.2, 128.1, 128.0, 128.0, 127.9, 127.7, 124.4, 124.3, 118.1, 116.7, 114.1 (C-3′, C-5′), 110.8 (C-3), 86.3 (C-5″), 81.9 (C-3″), 78.8 (C-1″), 77.2, 76.1, 75.9, 75.5, 74.4, 73.6, 67.7 (C-6″), 55.5 (OCH_3). HRESI-MS (*m/z*): calcd for $C_{50}H_{47}O_9$ $[M+H]^+$ 791.3215, found 791.3219.

Puerarin (7)

To achieve a solution of isoflavone **6** (53 mg, 67 μmol) in anhydrous CH_2Cl_2 (0.14 mL), a solution of BBr_3 (81.6 mg, 0.33 mmol) in anhydrous CH_2Cl_2 (0.31 mL) was added dropwise at −78 °C for 30 min under an Ar atmosphere. The cold bath was removed, and the mixture was stirred for 10 min. Methanol (3 mL) was added to the reaction mixture dropwise at 0 °C within 5 min. The solvent was evaporated under reduced pressure to yield a brown syrup (70 mg), which was subjected to silica gel column chromatography (20:1, dichloromethane methanol) to obtain a colorless solid **7** (26.5 mg, 95.0%). m.p.183–185 °C. ^{1}H-NMR (400 MHz, DMSO-d_6): δ 8.34 (s, 1H; H-2), 7.92 (d, $J=8.8$ Hz, 1H; H-5), 7.39 (d, $J=8.6$ Hz, 2H; H-2′, H-6′), 7.00 (d, $J=8.8$ Hz, 1H; H-6), 6.80 (d, $J=8.6$ Hz, 2H; H-3', H-5′), 4.80 (d, $J=9.8$ Hz, 1H; H-1″), 4.04 (dd, $J=9.8$ Hz, 8.6 Hz; H-2″), 3.71 (d, $J=10.9$ Hz, 1H; H-4″), 3.43 (dd, $J=11.6$, 5.4 Hz, 1H; H-6"a), 3.30–3.18 (m, 3H; H-3", H-5", H-6"b). ^{13}C-NMR (150 MHz, CD_3OD): δ 178.3 (C-4), 163.0 (C-7), 158.7 (C-4′), 154.4, 131.3 (C-2′, C-6′), 128.1, 125.6, 124.2, 118.5, 116.2 (C-3′, C-5′), 113.2 (C-8), 82.8 (C-5″), 80.0 (C-3″), 75.7 (C-1″), 73.0 (C-2″), 71.7 (C-4″), 62.8 (C-6″). HRESI-MS (*m/z*): calcd for $C_{21}H_{19}O_9$ $[M - H]^+$ 415.1035, found 415.1027.

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