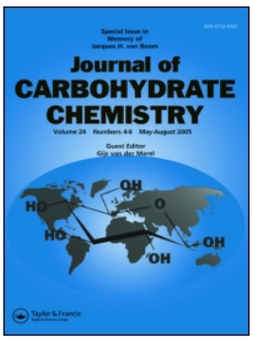

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Total synthesis of an isoflavone *C*-glycoside: 6-tert-butylpuerarin

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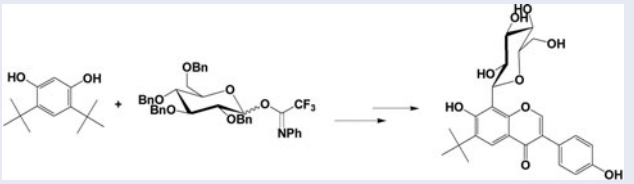
ABSTRACT

The first total synthesis of an isoflavone *C*-glycoside (6-*tert*-butylpuerarin) using commercially available 4,6-di-*tert*-butylbenzene-1,3-diol as starting material was achieved in five steps with an overall yield of 2.8%. The key intermediate **4** was obtained by de-*tert*-butylation of **2** with trifluoroacetic acid and Friedel-Crafts acetylation of 2-*C*-β-D-glucopyranoside **3**. Condensation of **4** with 4-(benzyloxy)benzaldehyde resulted in the formation of *C*-glucosylchalcone **5**, which was cyclized by oxidative rearrangement using (diacetoxyiodo)benzene (DIB) and p-toluenesulfonic acid to obtain the target molecule **6**. This environmentally friendly and concise synthetic pathway should be applicable to the large-scale synthesis of various isoflavone *C*-glycosides.

GRAPHICAL ABSTRACT



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C-glycoside; isoflavone; 6-*tert*-butylpuerarin; DIB

Introduction

Puerarin, an isoflavone *C*-glycoside isolated from *Pueraria radix*, was introduced in China in 1994 because of its benefits in the treatment of cardiovascular and neurological diseases.[1,2] The compound, which activated the endothelial nitric oxide synthase-mediated production of nitric oxide in EA.hy926 endothelial cells,[3] may be useful in the treatment or prevention of cardiovascular disorders and improved learning and memory impairment by suppressing the Aβ-induced inflammatory

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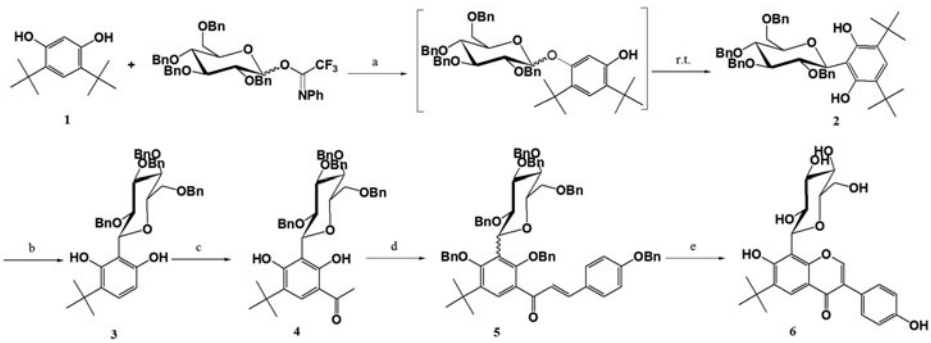
response.[4] To enhance the biological activities of puerarin, a 6-*tert*-butyl substituent, which prevented the 7-*O*-sulfate and 7-*O*-β-D-glucuronide formation of the compound to be metabolized in the liver, was introduced, thereby increasing the plasma concentration in the blood.

Recently, Koester et al.[5] reported the *C*-glycoside synthesis through Pd-catalyzed coupling of 1-iodo- or 1-triflato-glycals with alkynyl glycosides. Even more complex *C*-glycosidic bonds and α- and β-linked (1→2)-, (1→3)-, and (1idic*C*-disaccharides were prepared.[6,7] Unlike the synthesis of *C*-disaccharides, *C*-glycosyl isoflavones are usually synthesized through the O→C rearrangement of glycosyl donors with electron-rich aromatic compounds as glycosyl acceptors and the key oxidative rearrangement reaction employing the highly reactive thallium(III) nitrate.[8–10] However, although the highly toxic thallium trinitrate is widely used in the synthesis of isoflavone *C*-glycosides, scale-up preparation and control of toxic residues were difficult.

Lee and co-workers[11] succeeded in the first total synthesis of puerarin. The key intermediate was β-D-glucopyranosyl-2,6-dimethoxybenzene obtained by coupling the lithiated form of the appropriate aromatic reagent with 2,3,4,6-tetra-*O*-benzylpyranolactone. However, the synthetic route of the compound was unwieldy and required repeated protection and deprotection of the sugar moiety with the acetyl group. Herein, we carried out the total synthesis of 6-*tert*-butylpuerarin in five steps by developing cyclization method using (diacetoxyiodo)benzene (DIB), an environmentally friendly reagent, instead of thallium trinitrate for the oxidative rearrangement of chalcone.

Results and discussion

Our synthetic procedure for 6-*tert*-butylpuerarin is shown in Scheme 1. Coupling of 4,6-di-*tert*-butylbenzene-1,3-diol with 2,3,4,6-tetra-*O*-benzylglucopyranosyl

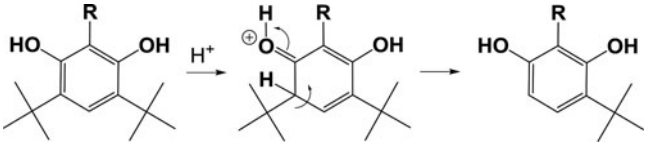


Scheme 1. Synthesis of 6-tert-butylpuerarin. *Reagents and conditions*: a) TMSOTf, CH_2Cl_2, 0°C to rt; 42.0%; b) CF_3COOH, rt, 90 min; 72.8%; c) $AlCl_3$, AcCl, Et_2O, overnight; 70.0%; d) (i) BnBr, K_2CO_3, DMF, rt, 14 h; (ii) 4-(benzyloxy)benzaldehyde, 28% NaOMe, 1,4-dioxane, rt, 20 h; 49.2% (from **4**); e) (i) DIB, *p*-TsOH, anhydrous MeOH, DCM, rt, 1 d, (ii) H_2, 10% Pd/C, MeOH, rt, 2 d, (iii) 6 M HCl, 1,4-dioxane-MeOH (0.4:0.3:1), reflux, 1 h, 26.8% (from **5**).

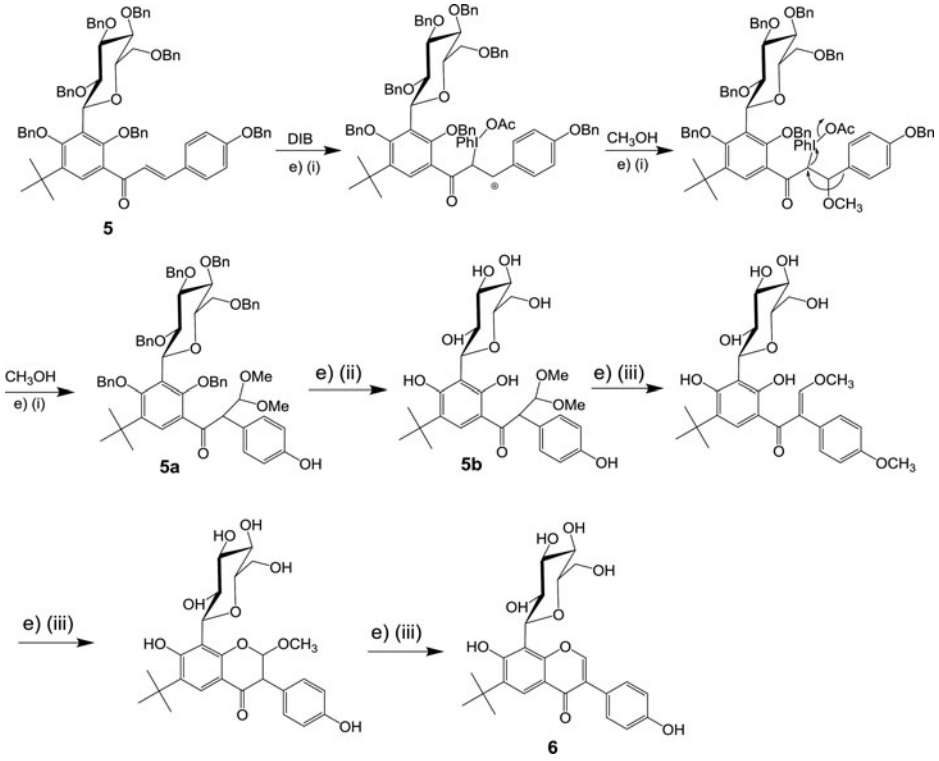
trifluoroacetimidate with trimetylsily triflate (TMSOTf) as the Lewis acid promoter yielded the desired 2-*C*-β-D-glucopyranoside **2** (Glc: $J_{H1,H2} = 10.1$ Hz) as a white solid obtained by recrystallization from petroleum ether and acid–base neutralization, which was proved to be purer than the product reported in literature.[12] The mechanism of the reaction may be as follows: After TMSOTf was added to reaction mixture, the corresponding *O*-glycoside was produced, which then underwent O→C rearrangement to yield the C-glycoside 2 in a regioselective manner. However, when we attempted the direct coupling of the glycosyl donor with resorcinol, the desired *C*-glycoside was not detected. Failure to detect *C*-glycoside from this reaction might have resulted from the mismatch between the reactivity of the glycosyl donor and the aromatic acceptor.[12] Moreover, when 4,6-dibromobenzene-1,3-diol was used as the phenol acceptor, only the corresponding α-*O*-glycoside [δ: 10.63 (s, 1H; OH-1), 7.66 (s, 1H; H-5), 6.91 (s, 1H; H-2), and 5.78 (d, $J = 3.2$ Hz, 1H; H-1′)] was isolated as the major product. The compound did not undergo O→C rearrangement to yield the ortho-hydroxyaryl C-glycoside because of the electron-withdrawing bromo groups at C-4 and C-6 in the O-glycoside.[13,14]

Through the successful de-butylation of the 6-*tert*-butyl group in compound **2** under the influence of trifluoroacetic acid (TFA), the desired compound **3** was obtained with a 72.8% yield,[15] which might proceed through a mechanism outlined in Scheme 2.[16] The reaction was examined using thin-layer chromatography every few minutes to prevent both *tert*-butyl groups from being removed at the same time. However, deprotection of the 4,6-di-*tert*-butyl groups in **2** by TFA obtained a poor yield (20%).[12] Moreover, the process required a longer reaction time (5 h) and produced complex mixtures, including de-benzylated products or the destruction of the sugar ring, as confirmed by ^{1}H NMR and TLC.

The reaction of glycoside **3** with acetyl chloride and anhydrous $AlCl_3$ in anhydrous ether resulted in the production of acetophenone **4**.[17] The large steric hindrance of the *tert*-butyl substituent allowed the acetyl group to be selectively attached to C-6 in the *C*-glycoside **3**. Following the procedure reported in literature,[18] benzylation of glycoside **4** was followed by condensation with 4-(benzyloxy)benzaldehyde to yield chalcone **5**. After two benzyl groups were introduced to the 4- and 6-*O*-positions of **4**, the ^{1}H NMR spectrum of the resultant **5** displayed two unequally populated sets of signals at r.t. (20°C), resulting from the chiral conformation of the glycosyl group in chalcone **5** rather than the conformational changes in the glucose ring. The crowdedness introduced by the two benzyl groups probably resulted in the restricted conformational motion around the C-3″–C-1‴ bond.[19]



Scheme 2. The de-butylation mechanism of 2-*C*-β-D-glucopyranoside 2.



Scheme 3. Proposed reactions and mechanisms for the conversion of chalcone **5** to 6-*tert*-butylpuerarin **6**.

Finally, **5** was converted into **6** via a series of transformations including oxidative methoxylation accompanied by rearrangement, catalytic hydrogenolysis to remove benzyl groups, and acid-catalyzed cyclization and elimination, as outlined in Scheme 3. It was proposed that the reaction between **5** and DIB led to the production of a phenyliodinated intermediate **5a**, which can be attacked by nucleophilic MeOH consecutively with 1,2-migration of the benzene ring to produce product **5b** (Sch. 3)[20] [major/minor (2:1): δ = 3.23 (s, 2H; OCH_{3Major}), 3.18 (s, 1H; OCH_{3Minor}), 3.03 (s, 2H; OCH_{3Major}), 2.96 (s, 1H; OCH_{3Minor})]. Compared to thallium(III) nitrate, oxidative rearrangement with DIB was safer and needed a shorter reaction time. The dimethyl acetal **5b** was then de-*O*-benzylated by hydrogenolysis using 10% Pd/C as the catalyst (room temperature for two days) to give a deprotected dimethyl acetal **5c**, which was cyclized after refluxing in aqueous 6 M HCl to obtain the desired 6-*tert*-butylpuerarin **6**.[21,22,23] The final product showed a single β-anomeric configuration (Glc H-1: $\delta = 5.19$ ppm; $J_{H1,H2} = 9.8$ Hz).

Experimental

General

The solvents used in these reactions were purified by distillation. Reactions were monitored by TLC on 0.20–0.25 mm silica gel F254 plates (Qingdao Marine

Chemistry Company, Qingdao, China) observed 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.

4,6-di-tert-Butyl-2-C-(2,3,4,6-tetra-O-benzyl-β-D-glucopyranosyl)-1,3-dihydroxybenzene (2)

A mixture of 2,3,4,6-tetra-*O*-benzylglucopyranosyl trifluoroacetimidate (25 g, 35.2 mmol), 4,6-di-tert-butylbenzene-1,3-diol **1**[24] (7.8 g, 35.2 mmol), and 4 Å MS (6.63 g) in anhydrous CH_2Cl_2 (310 mL) was stirred at 0°C for 30 min under an Ar atmosphere. Then, TMSOTf (7.13 mL, 35.2 mmol) was added. After stirring at 0°C for 2 h, the mixture was warmed to rt within 10 h. The above mixture was quenched by adding Et_3N (29.32 mL), stirred continuously for 30 min, and then filtered through a Celite pad. The filtrate was evaporated in vacuo to obtain a brown syrup, which was subjected to silica gel column chromatography (8:1, petroleum ether–EtOAc) and recrystallized from petroleum ether to obtain a white solid (18.47 g). The resulting white powder was stirred at 40°C for 30 min in 2 N NaOH (100 mL) and CH_2Cl_2 (100 mL). The DCM layer was separated from the mixture, and 70 mL of 2 N HCl was added. After stirring the mixture at 40°C for 30 min, the methylene chloride layer was then separated and dried to obtain **2** (10.99 g, 42.0%) as a white solid. m.p.138–141°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35–6.99 (m, 21H; C*H*-Ph, H-5), 5.00 (d, $J = 11.3$ Hz, 1H; CH_2Ph), 4.96 (d, $J = 10.1$ Hz, 1H; H-1′), 4.92 (d, $J = 11.3$ Hz, 1H; CH_2Ph), 4.86 (d, $J = 10.8$ Hz, 1H; CH_2Ph), 4.67 and 4.64 (d, $J = 10.7$ Hz, each 1H; CH_2Ph), 4.56 and 4.49 (d, $J = 12.1$ Hz, each 1H; CH_2Ph), 4.31 (d, $J = 10.8$ Hz, 1H; CH_2Ph), 3.97 (t, $J = 9.7$, 9.3Hz, 1H; H-2′), 3.92 (t, $J = 9.8$, 9.3Hz, 1H; H-4′), 3.82 (t, $J = 9.1$ Hz, 1H; H-3′), 3.75 (dd, $J = 10.3$, 2.1 Hz, 1H; H-6′b), 3.69 (dd, $J = 10.3$, 1.9 Hz, 1H; H-6′a), 3.58 (m, 1H; H-5′), 1.38 (s, 18H, $(CH_3)_3C$).^{13}C NMR (100 MHz, $CDCl_3$): δ 138.5, 138.0, 137.8, 136.4 (C, CH_2Ph), 128.6, 128.5, 128.4, 128.2, 128.0, 127.9, 127.9, 127.7, 127.5, 124.8 (C-5), 112.7 (C-2), 86.6 (C-3′), 81.5, 78.7, 77.3, 75.8, 75.5, 75.3, 73.4, 67.5 (C-6′), 34.7 (C, $(CH_3)_3C$), 30.2 (CH_3). ESI-MS *m/z*: 745.41 $[M+H]^+$, 767.39 $[M+Na]^+$.

4-tert-Butyl-2-C-(2,3,4,6-tetra-O-benzyl-β-D-glucopyranosyl)-1,3-dihydroxybenzene (3)

Sodium dithionite (110 mg, 0.63 mmol) and **2** (10.99 g, 15.97 mmol) in TFA (50 mL) were stirred at rt for 90 min. TFA was removed by a rotary evaporator to obtain a brown syrup, which was then subjected to silica gel column chromatography (15:1–12:1, petroleum ether–EtOAc) to obtain **3** (7.4 g, 72.8%) as brown syrup. ^{1}H NMR

(400 MHz, $CDCl_3$): δ 7.38–7.18 (m, 18H; C*H*-Ph), 7.13 (d, $J = 8.6$ Hz, 1H; H-5), 7.04 (d, $J = 6.5$ Hz, 2H; C*H*-Ph), 6.47 (d, $J = 8.6$ Hz, 1H; H-6), 5.03–4.93 (m, 3H; CH_2Ph, H-1′), 4.87 (d, $J = 10.8$ Hz, 1H; CH_2Ph), 4.68 (d, $J = 10.4$ Hz, 1H; CH_2Ph), 4.64–4.48 (m, 3H; CH_2Ph), 4.24 (d, $J = 10.4$ Hz, 1H; CH_2Ph), 4.00–3.81 (m, 3H; H-2′, H-3′, H-4′), 3.78 (dd, $J = 10.4$, 1.9 Hz, 1H; H-6′b), 3.71 (brd, $J = 10.4$ Hz, 1H; H-6′a), 3.61 (brd, $J = 9.7$ Hz, 1H; H-5′), 1.37 (s, 9H, $(CH_3)_3C$).^{13}C NMR (150 MHz, $CDCl_3$): δ 138.4 (C, CH_2Ph), 137.9 (C, CH_2Ph), 137.7 (C, CH_2Ph), 136.4 (C, CH_2Ph), 130.5, 128.5, 128.4, 128.3, 128.1, 128.0, 127.8, 127.8, 127.7, 127.6, 127.4, 127.1, 111.9 (C-2), 109.0 (C-6), 86.4 (C-3′), 82.0, 78.7, 77.2, 75.9, 75.6, 75.5, 75.2, 73.4, 67.5 (C-6′), 34.3 (C, $(CH_3)_3C$), 29.9(CH_3). ESI-MS *m/z*: 689.35 $[M+H]^+$, 711.33 $[M+Na]^+$.

5-tert-Butyl-2,4-hydroxy-3-C-(2,3,4,6-tetra-O-benzyl-β-D-glucopyranosyl)acetophenonoe (4)

A solution of anhydrous aluminum chloride (3.61 g, 27.10 mmol) in dry ether (15.01 mL) was added to a solution of the *C*-glycoside **3** (1.79 g, 2.6 mmol) in dry ether (15.01 mL). Acetyl chloride (2.69 mL, 30.87 mmol) was added dropwise with stirring. Afterward, the mixture was stirred overnight at rt. A brown oil was separated from the mixture after 1 h. The reaction mixture was decomposed by the dropwise addition of 2 N hydrochloric acid (60 mL) followed by water (50 mL). After the product was isolated with chloroform (3 × 20 mL), evaporation of the organic phase yielded a yellow oil (4 g), which was then subjected to silica gel column chromatography (25:1–20:1, petroleum ether–EtOAc) to obtain **4** (1.33g, 70.0%) as light yellow syrup. ^{1}H NMR (400 MHz, DMSO-d_6): δ 13.15 (s, 1H; OH-6), 9.30 (s, 1H; OH-4), 7.61 (s, 1H; H-8), 7.38–7.05 (m, 18H; C*H*-Ph), 6.82 (d, $J = 7.8$ Hz, 2H; C*H*-Ph), 5.07 (brs, 1H; H-1′), 4.81 and 4.76 (d, $J = 11.5$ Hz, each 1H; CH_2Ph), 4.72 and 4.51 (d, $J = 10.9$ Hz, each 1H; CH_2Ph), 4.47 (s, 2H; CH_2Ph), 4.34 and 3.82 (d, $J = 10.7$ Hz, 1H; CH_2Ph), 3.79–3.58 (m, 6H; H-2′, H-3′, H-4′, H-5′, H-6′a, H-6′b), 2.57 (s, 3H; H-1), 1.36 (s, 9H; $(CH_3)_3C$).^{13}C-NMR (150 MHz, DMSO-d_6): δ 203.6 (C-2), 162.2 (C-4), 160.2 (C-6), 138.6 (C, CH_2Ph), 138.1 (C, CH_2Ph), 138.0 (C, CH_2Ph), 137.5 (C, CH_2Ph), 129.4, 128.4, 128.2, 128.1, 128.1, 127.9, 127.9, 127.6, 127.4, 127.4, 127.4 (C-7), 127.3 (C-8), 111.9(C-5),110.8 (C-3), 85.0 (C-3′), 80.2, 77.8, 77.0, 74.5 (CH_2, CH_2Ph), 74.1 (CH_2, CH_2Ph), 74.0 (CH_2, CH_2Ph), 72.8, 72.1 (CH_2, CH_2Ph), 67.7 (C-6′), 34.1 (C-1), 29.4 (CH_3), 26.2 (C, $(CH_3)_3C$). ESI-MS *m/z*: 731.36 $[M+H]^+$, 753.34 $[M+Na]^+$.

5′-tert-Butyl-4,2′,4′-tribenzyloxy-3′-C-(2,3,4,6-tetra-O-benzyl-D-glucopyranosyl)chalcone (5)

$PhCH_2Br$ (0.96 mL, 8.12 mmol) and K_2CO_3 (1.13g, 8.18 mmol) were added to a solution of **4** (1.33 g, 3.34 mmol) in dry DMF (4.49 mL), and the resulting solution was stirred at rt for 14 h. After confirming the disappearance of **4** by TLC, the reaction mixture was poured into H_2O (50 mL) and extracted with EtOAc (3 × 40 mL). The organic extracts were concentrated and purified by silica gel column

chromatography (9:1, petroleum ether–EtOAc) to obtain a yellow syrup (1.56 g). Thereafter, 28% NaOMe in MeOH (10.52 mL) was added to a solution of the yellow syrup (1.37 g, 1.51 mmol) and 4-(benzyloxy)benzaldehyde (0.35 g, 1.66 mmol) in 1,4-dioxane (21.04 mL). After the resulting mixture was stirred at rt for 20 h, 24.5 mL of 2N HCl was added. The mixture was then extracted with EtOAc (3 × 20 mL), dried over Na_2SO_4, and concentrated. The residue was purified by silica gel column chromatography (20:1–10:1, petroleum ether–EtOAc) to obtain **5** (0.87 g, 49.2%) as light yellow oil. ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.60 (s, 0.75H; H-6″$_{Major}$), 7.57 (s, 0.25H; H-6″$_{Minor}$), 7.54–7.09 (m, 37H; C*H*-Ph, H-2, H-3, H-2′, H-6′), 7.03 (d, J = 8.8 Hz, 0.5H; H-3′$_{Minor}$, H-5′$_{Minor}$), 6.96 (d, J = 8.8 Hz, 1.5H; H-3′$_{Major}$, H-5′$_{Major}$), 6.74 (m, 2H; C*H*-Ph), 5.24–5.06 (m, 3H; CH_2Ph, H-1‴), 4.99 (d, J = 12.4 Hz, 0.75H; CH_2Ph_{Major}), 4.93 (d, J = 9.9 Hz, 0.25H; CH_2Ph_{Minor}), 4.82–4.68 (m, 3H; CH_2Ph), 4.64 (d, J = 10.9 Hz, 0.75H; CH_2Ph_{Major}), 4.60 (d, J = 10.9 Hz, 0.25H; CH_2Ph_{Minor}), 4.58–4.49 (m, 2H; CH_2Ph), 4.48–4.34 (m, 3H; CH_2Ph), 4.21 (d, J = 10.8 Hz, 0.25H; CH_2Ph_{Minor}), 4.15 (d, J = 10.8 Hz, 0.75H; CH_2Ph_{Major}), 3.68 (d, J = 10.0 Hz, 0.75H; CH_2Ph_{Major}), 3.62 (d, J = 10.0 Hz, 0.25H; CH_2Ph_{Minor}), 3.55–3.33 (m, 6H; H-2‴, H-3‴, H-4″, H-5‴, H-6‴a, H-6‴′b), 1.43 (s, 6.5H; $(CH_3)_3C_{Major}$), 1.38 (s, 2.5H; $(CH_3)_3C_{Minor}$). ^{13}C NMR (100 MHz, DMSO-d_6): δ 191.9 (C-1), 161.1 (C-4″), 160.4 (C-4′), 156.9 (C-2″), 144.1 (C-3), 142.6 (C-1′), 139.1 (C, CH_2Ph), 138.6 (C, CH_2Ph), 138.0 (C, CH_2Ph), 138.0 (C, CH_2Ph), 137.9 (C, CH_2Ph), 136.9 (C, CH_2Ph), 136.6 (C, CH_2Ph), 130.4, 128.7, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 128.0, 127.9.0, 127.8, 127.7, 127.7, 127.6, 127.5, 127.2, 126.9, 126.8, 126.7, 126.6, 126.4, 126.0, 124.4, 115.3 (C-3″$_{Minor}$), 115.2 (C-3″$_{Major}$), 86.6, 79.4, 79.2, 79.0, 77.8, 74.6, 74.4, 74.1, 73.8, 72.5, 69.4, 62.9, 54.9 (C-6‴), 35.1 (CH_{3Minor}), 34.9 (CH_{3Major}), 30.8 (C, $(CH_3)_3C_{Minor}$), 30.7 (C, $(CH_3)_3C_{Major}$). HRESI-MS (m/z): calcd for $C_{74}H_{73}O_9$ $[M + H]^+$ 1105.5249, found 1105.5252.

6-tert-Butylpuerarin (6)

A solution of **5** (870 mg, 0.79 mmol) in anhydrous MeOH (2.21 mL) and DCM (1.5 mL) was added dropwise to a solution of DIB (755 mg, 2.34 mmol) and p-TsOH·H_2O (599 mg, 3.15 mmol) in anhydrous MeOH (1.58 mL). After the mixture was stirred at r.t. for a day, aq 10% $Na_2S_2O_3$ (158.20 mL) was added to the reaction mixture. The resulting mixture was extracted with DCM (3 × 20 mL), dried over Na_2SO_4, and concentrated. The residue was purified by silica gel column chromatography (19:1–10:1, petroleum ether–EtOAc) to obtain **5b** (0.25 g) as colorless syrup. Subsequently, 10% Pd/C (74.02 mg) was added to a solution of **5b** in MeOH (18.4 mL). The mixture was then stirred at rt for 48 h under hydrogen atmosphere, filtered, and evaporated in vacuo to obtain **5c** (160 mg) as a colorless solid. Thereafter, 1,4-dioxane (0.49 mL) and 6 M HCl (0.65 mL) were added to a crude solution of **5c** in MeOH (1.63 mL), and the mixture was refluxed for 1 h. After removing the solvent in vacuo, EtOH (7 mL) was added to the residue and then evaporated. The residue was purified by silica gel column chromatography (9:1, DCM–MeOH) to obtain **6** (90 mg, 26.8%) as a colorless

solid. m.p.130–132°C. ^{1}H NMR (400 MHz, CD_3OD): δ 8.10 (s, 1H; H-5), 8.06 (s, 1H; H-2), 7.32 (d, J = 8.9 Hz, 2H; H-2′, H-6′), 6.80 (d, J = 8.9 Hz, 2H; H-3′, H-5′), 5.19 (d, J = 9.8 Hz, 1H; H-1″), 3.87 (dd, J = 12.2, 2.4 Hz, 1H; H-6″b), 3.83 (dd, J = 12.2, 4.1 Hz, 1H, H-6″a), 3.65 (t, J = 9.3 Hz, 1H; H-3″), 3.58(t, J = 9.8, 9.3 Hz, 1H; H-2″), 3.54–3.47 (m, 2H; H-4″, H-5″), 1.41 (s, 9H; $(CH_3)_3C$). ^{13}C NMR (150 MHz, CD_3OD): δ 178.5 (C-4), 162.0 (C-7), 158.7 (C-4′), 155.5 (C-8a), 154.2 (C-2), 138.2 (C-6), 131.4 (C-2′, C-6′), 125.6 (C-5), 124.4 (C-3), 124.3 (C-1′), 117.5 (C-4a), 116.2 (C-3′, C-5′), 112.7 (C-8), 83.0 (C-5″), 79.4 (C-3″), 77.1 (C-1″), 73.9 (C-2″), 70.9 (C-4″), 61.7 (C-6″), 36.2 (C, $(CH_3)_3C$), 30.0 (CH_3). ESI-MS *m/z*: 473.18 $[M+H]^+$.

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