DOI 10.1007/s10600-016-1721-5
Chemistry of Natural Compounds, Vol. 52, No. 4, July, 2016

SYNTHESIS OF GLYCOSYLATED CHRYSIN DERIVATIVES VIA ESTER LINKERS

Gaishun Fei, Xiaofei Fan, Huiping Ma, Pengchang Fan, Zhengping Jia, and Linlin Jing*

A series of glycosylated chrysin derivatives have been synthesized in good yields with simple procedures and mild reaction conditions. Six different kinds of sugar moieties were introduced through each ester linker.

Keywords: flavonoid, chrysin, glycosylated derivative, ester linker.

Natural flavonoids, which are the most widely distributed polyphenols in the plant kingdom, play an important role in treating a variety of modern diseases, including diabetes, cardiovascular diseases, and cancer [1]. To date, more than 15,000 flavonoids have been separated and identified from plants [2].

Chrysin (5,7-dihydroxyflavone), a natural flavonoid found in many plant extracts, honey, and propolis, presents only a small side effect and many different biological activities, including anti-oxidant [3], anti-inflammatory [4], anti-bacterial [5], anti-allergic [6], anti-diabetic [7], anxiolytic [8], anti-mutagenic [9], anti-cancer [10], anti-atherogenic [11], hepatoprotective [12], and neuroprotective [13] effects. However, there are some drawbacks, such as low solubility, relatively poor absorption in the intestines, and rapid metabolism of glycosylation, which significantly limit its clinical and therapeutic application. It is reported that most of the absorbed chrysin was detectable as glucuronic acid and sulfate acid conjugates with the unprotected hydroxyl at 5- and 7-positions of chrysin in the blood and vascular system [14, 15]. In order to obtain more pharmacologically active and more selective drugs with less adverse reactions for clinical use, a large number of studies have been performed via the synthesis of chrysin derivatives [16–20].

Carbohydrates are ubiquitous in nature and play a key role in a number of important biological processes, including fertilization, cell-cell recognition, immune response, hormone regulation, and inflammation. Sugar appendages add important features to the shape and the stereoelectronic properties of a molecule and thus wield remarkable influences. It is well known that the modification of a drug with sugar and its derivatives may yield big changes in water solubility, promote absorption, reduce toxicity and other side effects, and enhance the drug′s efficacy [21, 22].

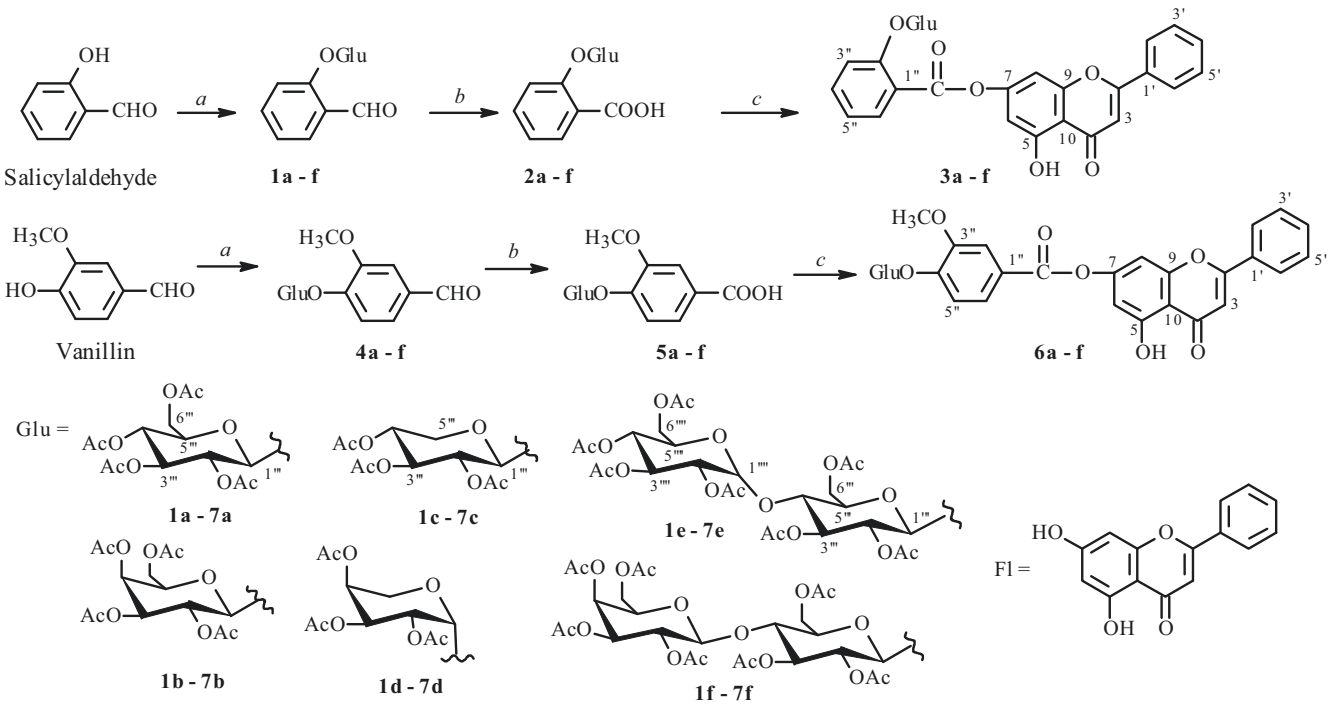
Considering the fact that most natural flavonoids exist as their glycosides and the glycosylated compound is 50 times more active than the aglycon, we reported earlier on the synthesis of glycosylated chrysin derivatives through coupling chrysin with sugar directly at 7-OH of chrysin [23]. In the present study, we design and synthesize a range of new glycosylated chrysin derivatives by introducing sugar moieties into chrysin via ester linkers for the first time.

More and more studies have revealed that linkers can modulate the physicochemical properties of the whole molecule and thereby affect the biological activities [24, 25]; so we chose two ester linkers (vanillate and salicylate) to design novel structures.

The glycosylated derivatives of chrysin modified with six sugars, including D-glucose, D-galactose, D-xylose, L-arabinose, maltose, and lactose, and two linkers were synthesized via three steps (Scheme 1). First, the direct *O*-glycosylation of salicylate was performed with peracetylglycosyl bromide **7** using tetrabutylammonium bromide (TBAB) as phase transfer catalyst and NaOH as a base, in biphasic media (CH_2Cl_2–H_2O), affording the desired glycosylated salicylate **1** in 73–87% yields. Subsequent oxidation with potassium permanganate in water and acetone afforded aromatic acid **2** in 90–94% yields. In the presence of *N*,*N*′-diisopropylcarbodiimide (DIC), chrysin smoothly underwent esterification with **2** catalyzed by 4-dimethylaminopyridine (DMAP), giving glycosylated chrysin derivatives **3** in 80–87% yields.

Department of Pharmacy, Lanzhou General Hospital, Lanzhou Command of CPLA, 730050, Lanzhou, P. R. China, fax: +86 931 8994950, e-mail: lfjinglinlin@163.com. Published in *Khimiya Prirodnykh Soedinenii*, No. 4, July–August, 2016, pp. 522–528. Original article submitted July 25, 2014.

 0009-3130/16/5204-0602 ©2016 Springer Science+Business Media New York



a. Glu-Br **7a - f**, TBAB–NaOH; *b*. $KMnO_4$; *c*. Fl, DIC–DMAP

Scheme 1

The introduction of sugar moieties using vanillate as a linker was conducted by a similar protocol to that for **3** using salicylate as a linker, furnishing glycosylated chrysin derivatives **6**.

The two hydroxyl groups of chrysin have different reactivities due to the different influence of electron donors, steric factors, and intramolecular H-bonds. So the 7-hydroxyl of chrysin is acylated exclusively by aromatic acid under mild conditions.

The structures of synthesized glycosylated chrysin derivatives were identified by FT-IR, NMR spectroscopy, and mass spectra. The IR spectrum of **3** and **6** contained absorption maxima for OH at 3430 $cm^{-1}$and for C=O at 1655 cm^{-1}. The PMR spectrum of **3** and **6** contained resonances for the flavone ring, the sugar moieties, and the linker. The ^1H NMR spectra of **3** and **6** showed the absence of the 7-OH proton, indicating esterification at the 7-OH position. The resonance of 5-OH in **3** and **6**, which was involved in an intramolecular H-bond, appeared in the range 12.76–12.79 ppm. The ^{13}C NMR data of **3** and **6** were in agreement with the ^1H NMR and FT-IR data for those derivatives. The C=O resonance for C-4 in chrysin appeared at 182 ppm. The *O*-acetyl CH_3 peaks of the sugar units are seen at 2.0 ppm in the ^1H NMR spectrum as well as at 20 ppm in the ^{13}C NMR spectrum. The chemical shifts of the proton and the carbon atoms in sugar varied in the range of 3.58–5.61 and 60.70–99.98 ppm, respectively, in the PMR spectrum. The anomeric hydrogen in sugar was observed at 5.20–5.60 ppm, and the anomeric carbon appeared at 99 ppm.

Thus, a series of new glycosylated chrysin derivatives containing chrysin and sugar connected by a linker was synthesized in good yields with simple procedures and mild reaction conditions.

EXPERIMENTAL

Reagents and starting materials were purchased from commercial sources and were used without further purification unless noted. Melting points (uncorrected) were determined on a micro-melting point apparatus X-4A (Shanghai Cany Precision Instrument Company, China). ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance III 400 spectrometer with $CDCl_3$ as a solvent. Chemical shifts are reported in δ values relative to TMS as an internal standard. Coupling constants are in units of Hz. Low-resolution mass spectra (ESI-MS) were obtained on an Applied Biosystems LCMS-API 3200 system. Optical rotations were measured using a PerkinElmer 341 spectropolarimeter. Elemental analyses of all compounds agreed with those calculated.

General Procedure for Synthesis of Peracetylglycosyl Bromide 7. Perchloric acid (0.5 mL) was added to acetic anhydride (20 mL) under ice water bath. Glucose (30 mmol) was added to the mixture for an hour at room temperature. The whole was stirred at room temperature for 3 h. Then the reaction mixture was cooled to 20°C, and amorphous phosphorus (50 mmol), bromine (56 mmol), and water (100 mmol) were added dropwise in turn. After a 3 h reaction at room temperature, dichloromethane (40 mL) was used to dilute the mixture. The organic layer was washed with cold water (2 × 20 mL) and stirred with sodium bicarbonate solution (30 mL) for 30 min. The organic layers was dried over Na_2SO_4 and concentrated. The residue was purified by recrystallization from diethyl ether or ethanol.

2,3,4,6-Tetra-*O*-acetyl-α-bromo-D-glucopyranose (7a), yield 83%, mp 86–88°C. $[\alpha]_D^{25}$ +73° (*c* 1.0, CH_2Cl_2).

2,3,4,6-Tetra-*O*-acetyl-α-bromo-D-galactopyranose (7b), yield 86%, mp 82–83°C. $[\alpha]_D^{25}$ +68° (*c* 1.0, CH_2Cl_2).

2,3,4-Tri-*O*-acetyl-α-bromo-D-xylopyranose (7c), yield 75%, mp 99–100°C. $[\alpha]_D^{25}$ –11° (*c* 1.0, CH_2Cl_2).

2,3,4-Tri-*O*-acetyl-α-bromo-L-arabinopyranose (7d), yield 77%, mp 137–138°C. $[\alpha]_D^{25}$ +48° (*c* 1.0, CH_2Cl_2).

2,3,6,2′,3′,4′,6′-Hepta-*O*-acetyl-α-bromo-maltose (7e), yield 61%, mp 110–112°C. $[\alpha]_D^{25}$ +86° (*c* 1.0, CH_2Cl_2).

2,3,6,2′,3′,4′,6′-Hepta-*O*-acetyl-α-bromo-lactose (7f), yield 63%, mp 141–143°C. $[\alpha]_D^{25}$ +99° (*c* 1.0, CH_2Cl_2).

General Procedure for Synthesis of Glycosides of 1a–f or 4 a–f. Acetylated glycosides of **1a–f** or **4a–f** were prepared by using salicylaldehyde or vanillin as a reactant. Vanillin (10 mmol), NaOH (1 g), and tetrabutylammonium bromide (3.2 g, 10 mmol) were added into water (20 mL) and stirred. A solution of peracetylglycosyl bromide (12.5 mmol) in dichloromethane (20 mL) was added, and the reaction mixture was refluxed for 8 h and monitored by TLC. After completion of the reaction, the mixture was cooled to room temperature and diluted with CH_2Cl_2 (20 mL). The organic layer was washed with cold 1 N HCl solution and brine and then dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give the crude products. Purification by column chromatography yielded products **1a–f** (72–85%) or **4a–f** (71–83%).

2-(2′,3′,4′,6′-Tetra-*O*-acetyl-β-D-glucopyranosyloxy)benzaldehyde (1a). Yield 78.1%, white solid, $C_{21}H_{24}O_{11}$, mp 137–138°C. $[\alpha]_D^{25}$ +43° (*c* 1.0, CH_2Cl_2). ESI-MS *m/z* 453 $[M + H]^+$. ^{1}H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 10.35 (1H, s, CHO), 7.87 (1H, d, J = 8.0, H-6), 7.59–7.55 (1H, m, H-4), 7.21–7.18 (1H, m, H-5), 7.12 (1H, d, J = 8.4, H-3), 5.41–5.31 (2H, m, H-1′, 3′), 5.23–5.18 (2H, m, H-2′, 4′), 4.30 (1H, dd, J = 4.8, 12.0, H-6′), 4.21–4.17 (1H, m, H-5′), 3.91(1H, dd, J = 4.4, 11.6, H-6′), 2.09, 2.08, 2.06, 2.02 (12H, 4s, 4 × $COCH_3$).

2-(2′,3′,4′,6′-Tetra-*O*-acetyl-β-D-galactopyranosyloxy)benzaldehyde (1b). Yield 85.9%, light yellow solid, $C_{21}H_{24}O_{11}$, mp 92–94°C. $[\alpha]_D^{25}$ +55° (*c* 1.0, CH_2Cl_2). ESI-MS *m/z* 453 $[M + H]^+$. ^{1}H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 10.37 (1H, s, CHO), 7.87 (1H, d, J = 7.6, H-6), 7.57–7.55 (1H, m, H-4), 7.21–7.17 (1H, m, H-5), 7.13 (1H, d, J = 8.0, H-3), 5.61 (1H, d, J = 8.0, H-1′), 5.50–5.49 (1H, m, H-3′), 5.15 (2H, d, J = 2.8, H-2′, 4′), 4.25 (1H, dd, J = 4.0, 10.0, H-6′), 4.18–4.14 (1H, m, H-5′), 4.13–4.09 (1H, dd, J = 4.2, 10.8, H-6′), 2.21, 2.10, 2.08, 2.03 (12H, 4s, 4 × $COCH_3$).

2-(2′,3′,4′-Tri-*O*-acetyl-β-D-xylopyranosyloxy)benzaldehyde (1c). Yield 82.4%, light yellow oil, $C_{18}H_{20}O_9$. $[\alpha]_D^{25}$ –72° (*c* 1.0, CH_2Cl_2). ESI-MS *m/z* 381 $[M + H]^+$. ^{1}H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 10.41 (1H, s, CHO), 7.86 (1H, d, J = 7.2, H-6), 7.59–7.55 (1H, t, J = 7.6, H-4), 7.19–7.17 (2H, m, H-3, 5), 5.35 (1H, d, J = 6.8, H-1′), 5.27–5.25 (2H, m, H-3′, 4′), 5.01–5.00 (1H, m, H-2′), 4.24 (1H, dd, J = 4.0, 12.0, H-5′), 3.60 (1H, dd, J = 3.6, 12.0, H-5′), 2.12, 2.10, 2.05 (9H, 3s, 3 × $COCH_3$).

2-(2′,3′,4′-Tri-*O*-acetyl-β-L-arabinopyranosyloxy)benzaldehyde (1d). Yield 81.9%, light yellow oil, $C_{18}H_{20}O_9$. $[\alpha]_D^{25}$ +47° (*c* 1.0, CH_2Cl_2). ESI-MS *m/z* 381 $[M + H]^+$. ^{1}H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 10.45 (1H, s, CHO), 7.87 (1H, d, J = 7.6, H-6), 7.59–7.57 (1H, m, H-4), 7.18–7.17 (2H, m, H-3, 5), 5.48 (1H, d, J = 7.2, H-1′), 5.45–5.43 (1H, m, H-3′), 5.26–5.23 (2H, m, H-2′, 4′), 4.12 (1H, dd, J = 4.8, 12.6, H-5′), 3.78 (1H, dd, J = 4.4, 12.6, H-5′), 2.10, 2.08, 2.04 (9H, 3s, 3 × $COCH_3$).

2-(2′,3′,6′,2″,3″,4″,6″-Hepta-*O*-acetyl-β-D-maltosyloxy)benzaldehyde (1e). Yield 74.8%, light yellow solid, $C_{33}H_{40}O_{19}$, mp 101–103°C. $[\alpha]_D^{25}$ +86°C (*c* 1.0, CH_2Cl_2). ESI-MS *m/z* 741 $[M + H]^+$. ^{1}H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 10.33 (1H, s, CHO), 7.86 (1H, d, J = 7.6, H-6), 7.60–7.57 (1H, m, H-4), 7.20 (1H, d, J = 7.6, H-5), 7.13 (1H, d, J = 8.0, H-3), 5.45 (1H, d, J = 8.0, H-1′), 5.42–5.36 (3H, m, H-2′, 3′, 1″), 5.23–5.21 (1H, m, H-3″), 5.08–5.06 (1H, m, H-4″), 4.87 (1H, dd, J = 3.6, 10.0, H-2″), 4.51 (1H, d, J = 11.6, H-6″), 4.26–4.23 (2H, m, H-5′, 6′), 4.13–4.06 (2H, m, H-4′, 6′), 4.02–3.94 (2H, m, H-5″, 6″), 2.15, 2.12, 2.11, 2.09, 2.08, 2.04, 2.02 (21H, 7s, 7 × $COCH_3$).

2-(2′,3′,6′,2″,3″,4″,6″-Hepta-*O*-acetyl-β-D-lactosyloxy)benzaldehyde (1f). Yield 72.7%, light yellow solid, $C_{33}H_{40}O_{19}$, mp 169–171°C. $[\alpha]_D^{25}$ +97°C (*c* 1.0, CH_2Cl_2). ESI-MS *m/z* 741 $[M + H]^+$. ^{1}H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 10.34 (1H, s, CHO), 7.86 (1H, d, J = 8.0, H-6), 7.58–7.56 (1H, m, H-4), 7.19–7.17 (1H, m, H-5), 7.10 (1H, d, J = 8.4, H-3), 5.36 (1H, d, J = 7.8, H-1′), 5.32–5.27 (2H, m, H-2′, 3′), 5.18–5.13 (2H, m, H-1″, 3″), 4.98 (1H, dd, J = 2.8, 10.4,

H-2″), 4.54–4.52 (2H, m, H-4″, 6′), 4.10–4.07 (3H, m, H-5′, 6′, 6″), 3.92–3.83 (3H, m, H-4′, 5″, 6″), 2.17, 2.13, 2.10, 2.08, 2.07, 2.06, 1.98 (21H, 7s, 7 × $COCH_3$).

3-Methoxy-4-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosyloxy)benzaldehyde (4a). Yield 80.3%, white solid, $C_{22}H_{26}O_{12}$, mp 141–142°C. $[\alpha]_D^{25}$ +37° (*c* 1.0, CH_2Cl_2). ESI-MS *m/z* 483 $[M + H]^+$. ^1H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 9.90 (1H, s, CHO), 7.44 (1H, d, J = 7.6, H-6), 7.41 (1H, s, H-2), 7.22 (1H, d, J =7.6, H-5), 5.33–5.31 (2H, m, H-1′, 3′), 5.21–5.18 (1H, m, H-2′), 5.12–5.10 (1H, m, H-4′), 4.28 (1H, dd, J = 5.2, 12.4, H-6′), 4.20–4.18 (1H, m, H-5′), 3.90 (3H, s, OCH_3), 3.85 (1H, dd, J = 4.8, 10.6, H-6′), 2.09, 2.08, 2.05, 2.03(12H, 4s, 4 × $COCH_3$).

3-Methoxy-4-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-galactopyranosyloxy)benzaldehyde (4b). Yield 87.5%, white solid, $C_{22}H_{26}O_{12}$, mp 127–129°C. $[\alpha]_D^{25}$ +28° (*c* 1.0, CH_2Cl_2). ESI-MS *m/z* 483 $[M + H]^+$. ^1H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 9.90 (1H, s, CHO), 7.44 (1H, d, J = 7.6, H-6), 7.41 (1H, s, H-2), 7.23 (1H, d, J = 7.6, H-5), 5.56 (1H, d, J = 8.8, H-1′), 5.47–5.45 (1H, m, H-3′), 5.16–5.12 (1H, m, H-2′), 5.06–5.04 (1H, m, H-4′), 4.27–4.22 (1H, m, H-6′), 4.19–4.15 (1H, m, H-5′), 4.04–4.08 (1H, m, H-6′), 3.90 (3H, s, OCH_3), 2.18, 2.08, 2.06, 2.03 (12H, 4s, 4 × $COCH_3$).

3-Methoxy-4-(2′,3′,4′-tri-*O*-acetyl-β-D-xylopyranosyloxy)benzaldehyde (4c). Yield 83.4%, white solid, $C_{19}H_{22}O_{10}$, mp 68–70°C. $[\alpha]_D^{25}$ –39° (*c* 1.0, CH_2Cl_2). ESI-MS *m/z* 411 $[M + H]^+$. ^1H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 9.89 (1H, s, CHO), 7.43 (1H, d, J = 8.4, H-6), 7.41 (1H, s, H-2), 7.21 (1H, d, J = 8.4, H-5), 5.30 (1H, d, J = 8.0, H-1′), 5.24–5.22 (2H, m, H-3′, 4′), 5.11–4.89 (1H, m, H-2′), 4.26 (1H, dd, J = 3.6, 12.0, H-5′), 3.89 (3H, s, OCH_3), 3.58 (dd, J = 6.8, 12.0, H-5′), 2.12, 2.10, 2.05 (9H, 3s, 3 × $COCH_3$).

3-Methoxy-4-(2′,3′,4′-tri-*O*-acetyl-β-L-arabinopyranosyloxy)benzaldehyde (4d). Yield 82.7%, yellow oil, $C_{19}H_{22}O_{10}$. $[\alpha]_D^{25}$ +69° (*c* 1.0, CH_2Cl_2). ESI-MS *m/z* 411 $[M + H]^+$. ^1H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 9.89 (1H, s, CHO), 7.44 (1H, d, J = 8.4, H-6), 7.41 (1H, s, H-2), 7.23 (1H, d, J = 8.4, H-5), 5.49 (1H, d, J = 6.8, H-1′), 5.34–5.33 (1H, m, H-4′), 5.18–5.15 (2H, m, H-2′, 3′), 4.14 (1H, dd, J = 4.8, 12.0, H-5′), 3.90 (3H, s, OCH_3), 3.74 (1H, dd, J = 4.0, 11.6, H-5′), 2.15, 2.12, 2.03 (9H, 3s, 3 × $COCH_3$).

3-Methoxy-4-(2′,3′,6′,2″,3″,4″,6″-hepta-*O*-acetyl-β-maltosyloxy)benzaldehyde (4e). Yield 71.4%, white solid, $C_{34}H_{42}O_{20}$, mp 134–136°C. $[\alpha]_D^{25}$ +51° (*c* 1.0, CH_2Cl_2). ESI-MS *m/z* 771 $[M + H]^+$. ^1H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 9.90 (1H, s, CHO), 7.44 (1H, d, J = 8.4, H-6), 7.41 (1H, s, H-2), 7.19 (1H, d, J = 8.4, H-5), 5.46 (1H, d, J = 6.8, H-1′), 5.40–5.37 (2H, m, H-2′, 3′), 5.19–5.16 (2H, m, H-1″, 3″), 5.06–5.05 (1H, m, H-4″), 4.88–4.86 (1H, m, H-2″), 4.51 (1H, d, J = 11.6, H-6″), 4.28–4.24 (2H, m, H-5′, 6′), 4.09–4.05 (2H, m, H-4′, 6′), 3.99–3.93 (2H, m, H-5″, 6″), 3.96 (3H, s, OCH_3), 2.13, 2.11, 2.10, 2.08, 2.06, 2.04, 2.02 (21H, 7s, 7 × $COCH_3$).

3-Methoxy-4-(2′,3′,6′,2″,3″,4″,6″-hepta-*O*-acetyl-β-lactosyloxy)benzaldehyde (4f). Yield 73.2%, $C_{34}H_{42}O_{20}$, mp 86–88°C. $[\alpha]_D^{25}$ +66° (*c* 1.0, CH_2Cl_2). ESI-MS *m/z* 771 $[M + H]^+$. ^1H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 9.88 (1H, s, CHO), 7.42 (1H, d, J = 8.0, H-6), 7.40 (1H, s, H-2), 7.18 (1H, d, J = 8.0, H-5), 5.36 (1H, d, J = 7.8, H-1′), 5.30–5.25 (1H, m, H-3′), 5.25–5.21 (1H, m, H-2′), 5.13–5.08 (2H, m, H-1″, 3″), 4.99–4.96 (1H, m, H-2″), 4.53–5.52 (2H, m, H-4″, 6′), 4.17–4.11 (3H, m, H-5′, 6′, 6″), 3.90–3.86 (3H, m, H-4′, 5″, 6″), 3.89 (3H, s, OCH_3), 2.17, 2.13, 2.10, 2.09, 2.07, 2.06, 1.98 (21H, 7s, 7 × $COCH_3$).

General Procedure for Synthesis of Glycosides 2a–f or 5a–f. To a stirred mixture of acetylated glycosides of salicylaldehyde **1a–f** or vanillin **4a–f** (5 mmol) in a mixture of water (10 mL) and acetone (10 mL) was added potassium permanganate (1.26 g, 6.0 mmol). The reaction mixture was stirred at 50°C for 1 h. The warm mixture was filtered, and the residue was washed with hot water (3 × 10 mL). The filtrate was concentrated so that approximately 5 mL water was left. After acidification with 2 N hydrochloric acid, a white precipitate formed immediately. The crude product was collected by filtration after cooling at 0°C overnight, washed with ice-cold water, and dried, affording the desired glycosides **2a–f** (90–93%) or **5a–f** (92–94%).

2-[(2′,3′,4′,6′-Tetra-*O*-acetyl-β-D-glucopyranosyl)oxy]benzoic Acid (2a). Yield 93.2%, $C_{21}H_{24}O_{11}$, mp 162–164°C. $[\alpha]_D^{25}$ +34° (*c* 1.0, CH_2Cl_2). ESI-MS *m/z* 469 $[M + H]^+$. ^1H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 8.17 (1H, d, J = 8.2, H-6), 7.63–7.59 (1H, m, H-4), 7.29–7.27 (1H, m, H-5), 7.24 (1H, d, J = 8.4, H-3), 5.42–5.40 (2H, m, H-1′, 3′), 5.37–5.35 (1H, t, H-2′), 5.29–5.27 (1H, m, H-4′), 4.34 (1H, dd, J = 5.2, 12.4, H-6′), 4.27–4.25 (1H, m, H-5′), 3.99 (1H, dd, J = 4.8, 11.6, H-6′), 2.16, 2.13, 2.12, 2.10 (12H, 4s, 4 × $COCH_3$).

2-[(2′,3′,4′,6′-Tetra-*O*-acetyl-β-D-galactopyranosyl)oxy]benzoic Acid (2b). Yield 91.3%, $C_{21}H_{24}O_{11}$, mp 69–71°C. $[\alpha]_D^{25}$ +42° (*c* 1.0, CH_2Cl_2). ESI-MS *m/z* 469 $[M + H]^+$. ^1H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 8.12 (1H, d, J = 8.0, H-6), 7.57–7.53 (1H, m, H-4), 7.25–7.22 (1H, m, H-5), 7.18 (1H, d, J = 8.4, H-3), 5.60 (1H, d, J = 8.0, H-1′), 5.56–5.55 (1H, m, H-3′), 5.50–5.49 (1H, m, H-2′), 5.25–5.24 (1H, m, H-4′), 5.16 (1H, dd, J = 3.2, 10.0, H-6′), 4.16 (2H, m, H-5′, 6′), 2.21, 2.11, 2.07, 2.03 (12H, 4s, 4 × $COCH_3$).

2-[(2′,3′,4′-Tri-*O*-acetyl-β-D-xylopyranosyl)oxy]benzoic Acid (2c). Yield 92.2%, $C_{18}H_{20}O_{10}$, mp 122–124°C. $[\alpha]_D^{25}$ –65° (*c* 1.0, CH_2Cl_2). ESI-MS *m/z* 397 $[M + H]^+$. ^1H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 8.19 (1H, d, J = 8.0, H-6), 7.57 (1H, t, J = 7.2, H-4), 7.23–7.20 (2H, m, H-3, 5), 5.24 (1H, d, J = 8.4, H-1′), 5.13 (2H, m, H-3′, 4′), 4.92–4.91 (1H, m, H-2′), 4.23 (1H, dd, J = 2.4, 12.8, H-5′), 3.77 (1H, m, H-5′), 2.12, 2.10, 2.03 (9H, 3s, 3 × $COCH_3$).

2-[(2′,3′,4′-Tri-*O*-acetyl-β-L-arabinopyranosyl)oxy]benzoic Acid (2d). Yield 93.5%, $C_{18}H_{20}O_{10}$, mp 52–54°C. $[\alpha]_D^{25}$ +27° (*c* 1.0, CH_2Cl_2). ESI-MS *m/z* 397 $[M + H]^+$. ^1H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 8.18 (1H, d, J = 7.2, H-6), 7.56 (1H, t, J = 7.2, H-4), 7.23–7.20 (2H, m, H-3, 5), 5.49 (1H, d, J = 7.2, H-1′), 5.43–5.41 (1H, m, H-3′), 5.35–5.32 (2H, m, H-2′, 4′), 4.07 (1H, dd, J = 3.8, 12.6, H-5′), 3.77 (1H, dd, J = 4.0, 12.4, H-5′), 2.12, 2.08, 2.04 (9H, 3s, 3 × $COCH_3$).

2-[(2′,3′,6′,2″,3″,4″,6″-Hepta-*O*-acetyl-β-D-maltosyl)oxy]benzoic Acid (2e). Yield 91.1%, $C_{33}H_{40}O_{19}$, mp 92–93°C. $[\alpha]_D^{25}$ +71° (*c* 1.0, CH_2Cl_2). ESI-MS *m/z* 757 $[M + H]^+$. ^1H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 8.11 (1H, d, J = 8.0, H-6), 7.54 (1H, t, J = 8.0, H-4), 7.22 (1H, t, J = 8.0, H-5), 7.17 (1H, d, J = 8.0, H-3), 5.36 (1H, d, J = 7.8, H-1′), 5.34–5.31 (2H, m, H-1″, 3′), 5.23 (1H, t, J = 6.8, H-3″), 5.17–5.12 (1H, m, H-4″), 4.98 (1H, dd, J = 2.8, 10.4, H-2″), 4.57–4.53 (2H, m, H-2′, 6″), 4.20–4.02 (4H, m, H-5′, 6′, 4′, 6′), 3.93–3.90 (2H, m, H-5″, 6″), 2.15, 2.10, 2.08, 2.06, 2.04, 2.02, 1.99 (21H, 7s, 7 × $COCH_3$).

2-[(2′,3′,6′,2″,3″,4″,6″-Hepta-*O*-acetyl-β-lactosyl)oxy]benzoic Acid (2f). Yield 90.3%, $C_{33}H_{40}O_{19}$, mp 100–102°C. $[\alpha]_D^{25}$ +88° (*c* 1.0, CH_2Cl_2). ESI-MS *m/z* 757 $[M + H]^+$. ^1H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 8.12 (1H, d, J = 8.0, H-6), 7.57 (1H, t, J = 7.2, H-4), 7.24 (1H, d, J = 7.2, H-5), 7.19 (1H, d, J = 8.0, H-3), 5.45 (1H, d, J = 8.4, H-1′), 5.38–5.32 (3H, m, H-2′, 3′, 1″), 5.17 (1H, t, J = 7.2, H-3″), 5.07 (1H, t, J = 9.6, H-4″), 4.87 (1H, dd, J = 3.6, 10.0, H-2″), 4.55–4.52 (1H, m, H-6′), 4.26 (2H, dd, J = 4.0, 8.8, H-6′, 6″), 4.18–4.16 (1H, m, H-5′), 4.07–4.05 (1H, m, H-4′), 3.98–3.96 (2H, m, H-5″, 6″), 2.15, 2.10, 2.08, 2.06, 2.04, 2.02, 1.99 (21H, 7s, 7 × $COCH_3$).

3-Methoxy-4-[(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosyl)oxy]benzoic Acid (5a). Yield 94.2%, $C_{22}H_{26}O_{13}$, mp 172–174°C. $[\alpha]_D^{25}$ +22° (c 1.0, CH_2Cl_2). ESI-MS *m/z* 499 $[M + H]^+$. ^1H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 7.70 (1H, d, J = 8.4, H-6), 7.63 (1H, s, H-2), 7.15 (1H, d, J = 8.4, H-5), 5.33–5.31 (2H, m, H-1′, 3′), 5.20–5.16 (1H, m, H-2′), 5.10–5.08 (1H, m, H-4′), 4.28 (1H, dd, J = 5.2, 12.0, H-6′), 4.20–4.18 (1H, m, H-5′), 3.89 (3H, s, OCH_3), 3.85 (1H, dd, J = 4.8, 10.6, H-6′), 2.12, 2.11, 2.08, 2.05 (12H, 4s, 4 × $COCH_3$).

3-Methoxy-4-[(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-galactopyranosyl)oxy]benzoic Acid (5b). Yield 93.4%, $C_{22}H_{26}O_{13}$, mp 91–93°C. $[\alpha]_D^{25}$ +42° (*c* 1.0, CH_2Cl_2). ESI-MS *m/z* 499 $[M + H]^+$. ^1H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 7.69 (1H, d, J = 8.0, H-6), 7.63 (1H, s, H-2), 7.16 (1H, d, J = 8.4, H-5), 5.56 (1H, d, J = 8.6, H-1′), 5.47–4.46 (1H, m, H-3′), 5.14–5.12 (1H, m, H-2′), 5.03–5.02 (1H, m, H-4′), 4.26–4.17 (2H, m, H-6′), 4.07–4.04 (1H, m, H-5′), 3.89 (3H, s, OCH_3), 2.18, 2.09, 2.06, 2.03 (12H, 4s, 4 × $COCH_3$).

3-Methoxy-4-[(2′,3′,4′-tri-*O*-acetyl-β-D-xylopyranosyl)oxy]benzoic Acid (5c). Yield 91.4%, $C_{19}H_{22}O_{11}$, mp 77–79°C. $[\alpha]_D^{25}$ –61° (*c* 1.0, CH_2Cl_2). ESI-MS *m/z* 427 $[M + H]^+$. ^1H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 7.71 (1H, d, J = 8.4, H-6), 7.63 (1H, s H-2), 7.14 (1H, d, J = 8.4, H-5), 5.28 (1H, d, J = 8.0, H-1′), 5.23 (2H, m, H-3′, 4″), 5.01–5.00 (1H, m, H-2′), 4.25 (1H, dd, J = 3.6, 12.0, H-5′), 3.89 (3H, s, OCH_3), 3.56 (1H, dd, J = 4.0, 12.0, H-5′), 2.15, 2.12, 2.10 (9H, 3s, 3 × $COCH_3$).

3-Methoxy-4-[(2′,3′,4′-tri-*O*-acetyl-β-L-arabinopyranosyl)oxy]benzoic Acid (5d). Yield 90.3%, $C_{19}H_{22}O_{11}$, mp 86–88°C. $[\alpha]_D^{25}$ +17° (*c* 1.0, CH_2Cl_2). ESI-MS *m/z* 427 $[M + H]^+$. ^1H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 7.71 (1H, d, J = 8.4, H-6), 7.62 (1H, s, H-2), 7.17 (1H, d, J = 8.4, H-5), 5.48 (1H, d, J = 6.8, H-1′), 5.34–5.33 (1H, m, H-3′), 5.19–5.16 (2H, m, H-2′, 4′), 4.14 (1H, dd, J = 3.6, 12.0, H-5′), 3.90 (3H, s, OCH_3), 3.75 (1H, dd, J = 4.0, 12.0, H-5′), 2.14, 2.12, 2.05 (9H, 3s, 3 × $COCH_3$).

3-Methoxy-4-[(2′,3′,6′,2″,3′,4″,6″-hepta-*O*-acetyl-β-maltosyl)oxy]benzoic Acid (5e). Yield 92.1%, $C_{34}H_{42}O_{21}$, mp 148–150°C. $[\alpha]_D^{25}$ +55° (*c* 1.0, CH_2Cl_2). ESI-MS *m/z* 787 $[M + H]^+$. ^1H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 7.68 (1H, d, J = 8.0, H-6), 7.61 (1H, s, H-2), 7.11 (1H, d, J = 8.0, H-5), 5.36 (1H, d, J = 7.2, H-1′), 5.29–5.27 (1H, m, H-2′), 5.23–5.21 (2H, m, H-3′, 1″), 5.12–5.11 (1H, m, H-3″), 5.07–5.05 (1H, m, H-4″), 4.97 (1H, dd, J = 2.8, 10.4, H-2″), 4.53–4.51 (2H, m, H-6″, 6′), 4.16–4.11 (3H, m, H-4′, 5′, 6′), 3.91 (2H, m, H-5″, 6″), 3.88 (3H, s, OCH_3), 2.18, 2.13, 2.09, 2.08, 2.07, 2.06, 1.98 (21H, 7s, 7 × $COCH_3$).

3-Methoxy-4-[(2′,3′,6′,2″,3″,4″,6″-hepta-*O*-acetyl-β-lactosyl)oxy]benzoic Acid (5f). Yield 91.3%, $C_{34}H_{42}O_{21}$, mp 111–113°C. $[\alpha]_D^{25}$ +83° (*c* 1.0, CH_2Cl_2). ESI-MS *m/z* 787 $[M + H]^+$. ^1H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 7.71 (1H, d, J = 8.4, H-6), 7.63 (1H, s, H-2), 7.13 (1H, d, J = 8.4, H-5), 5.45 (1H, d, J = 7.6, H-1′), 5.40–5.37 (2H, m H-3′, 2′), 5.16–5.15 (2H, m, H-1″, 3″), 4.87 (1H, dd, J = 4.0, 10.4, H-2″), 4.51 (2H, m, H-4″, 6′), 4.27–4.25 (3H, m, H-5′, 6′, 6″), 4.11–4.08 (3H, m, H-4′, 5″, 6″), 3.96 (3H, s, OCH_3), 2.15, 2.13, 2.11, 2.10, 2.08, 2.06, 2.04 (21H, 7s, 7 × $COCH_3$).

General Procedure for Synthesis of Glycosylated Chrysin Derivatives 3a–f or 6a–f. To a solution of **2a–f** or **5a–f** (1.0 mmol) and chrysin (254 mg, 1.0 mmol) in anhydrous CH_2Cl_2 (5 mL) was added 4-dimethylaminopyridine (0.05 g, 0.4 mmol) and a solution of *N*,*N*′-diisopropylcarbodiimide (0.15 g, 1.2 mmol) in anhydrous CH_2Cl_2 (5 mL) at 0°C. Then the reaction mixture was stirred at room temperature for another 24 h. After completion of the reaction, water (20 mL) was added to the mixture. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layers were washed with saturated aqueous brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give the crude products. Purification by column chromatography yielded products **3a–f** (80–87%) or **6a–f** (80–88%).

Glycosylated Chrysin Derivative 3a. Yield 85.7%, $C_{36}H_{32}O_{15}$, mp 143–146°C. $[\alpha]_D^{25}$ +59° (*c* 0.5, CH_2Cl_2). IR spectrum (KBr, cm^{-1}): 3437, 1753, 1654, 1619, 1370, 1239, 1133, 1040. ESI-MS *m/z* 705 $[M + H]^+$. ^1H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 12.76 (1H, s, 5-OH), 7.98 (1H, d, J = 0.8, H-6″), 7.96 (2H, d, J = 1.6, H-2′, 6′), 7.59–7.53 (4H, m, H-4″, 3′, 4′, 5′), 7.27–7.23 (2H, m, H-3″, 5″), 6.97 (1H, d, J = 2.0, H-8), 6.76 (1H, s, H-3), 6.68 (1H, d, J = 2.0, H-6), 5.39–5.32 (2H, m, H-1‴, 3″), 5.24–5.20 (2H, m, H-2‴, 4‴), 4.32 (1H, dd, J = 5.2, 12.0, H-6‴), 4.20 (1H, dd, J = 2.0, 12.0, H-6‴), 3.94–3.90 (1H, m, H-5‴), 2.09, 2.06, 2.01, 1.98 (12H, 4s, 4 × $COCH_3$). ^{13}C NMR spectrum (100 MHz, $CDCl_3$, δ, ppm): 182.90 (C-4), 170.51 (CH_3CO), 170.19 (CH_3CO), 169.29 (C=O), 164.69 (C-2), 162.94 (C-5), 161.78 (C-9), 156.72 (C-7), 156.12 (C-6″), 134.29 (C-4″), 132.10 (C-1′), 131.95 (C-2′, 6′), 130.96 (C-5″), 129.14 (C-3′, 5′), 126.42 (C-4′), 123.27 (C-2″), 120.75 (C-3″), 117.26 (C-1″), 108.93 (C-10), 106.10 (C-6), 105.66 (C-3), 101.32 (C-8), 99.24 (C-1‴), 72.61 (C-5‴), 72.14 (C-3‴), 70.83 (C-2‴), 68.08 (C-4‴), 61.84 (C-6‴), 20.61 (CH_3), 20.56 (CH_3).

Glycosylated Chrysin Derivative 3b. Yield 84.5%, $C_{36}H_{32}O_{15}$, mp 91–93°C. $[\alpha]_D^{25}$ +26° (*c* 0.5, CH_2Cl_2). IR spectrum (KBr, cm^{-1}): 3437, 1754, 1655, 1619, 1370, 1230, 1132, 1037. ESI-MS *m/z* 705 $[M + H]^+$. ^1H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 12.76 (1H, s, 5-OH), 7.97 (1H, m, H-6″), 7.92 (2H, d, J = 6.8, H-2′, 6′), 7.61–7.53 (4H, m, H-4″, 3′, 4′, 5′), 7.25–7.22 (2H, m, H-3″, 5″), 6.99 (1H, d, J = 2.0, H-8), 6.77 (1H, s, H-3), 6.70 (1H, d, J = 2.0, H-6), 5.60 (1H, d, J = 8.0, H-1‴), 5.48 (1H, d, J = 3.2, H-3‴), 5.17 (1H, d, J = 8.0, H-2‴), 5.13 (1H, dd, J = 3.2, 10.4, H-4‴), 4.28–4.26 (1H, m, H-6‴), 4.19–4.17 (1H, m, H-6‴), 4.12–4.09 (1H, m, H-5″), 2.20, 2.08, 2.05, 2.00 (12H, 4s, 4 × $COCH_3$). ^{13}C NMR spectrum (100 MHz, $CDCl_3$, δ, ppm): 182.95 (C-4), 170.32 (CH_3CO), 170.13 (CH_3CO), 169.27 (C=O), 164.72 (C-2), 163.02 (C-5), 161.82 (C-9), 156.76 (C-7), 156.24 (C-6″), 134.26 (C-4″), 132.12 (C-1′), 131.93 (C-2′, 6′), 131.04 (C-5″), 129.16 (C-3′, 5′), 126.43 (C-4′), 123.31 (C-2″), 120.95 (C-3″), 117.46 (C-1″), 108.94 (C-10), 106.17 (C-6), 105.74 (C-3), 101.38 (C-8), 99.98 (C-1‴), 71.21 (C-5‴), 70.85 (C-2‴), 68.19 (C-3‴), 66.79 (C-4‴), 61.28 (C-6‴), 20.71 (CH_3), 20.64 (CH_3), 20.54 (CH_3).

Glycosylated Chrysin Derivative 3c. Yield 86.7%, $C_{33}H_{28}O_{13}$, mp 162–164°C. $[\alpha]_D^{25}$ –30° (*c* 0.5, CH_2Cl_2). IR spectrum (KBr, cm^{-1}): 3438, 1756, 1657, 1619, 1368, 1230, 1135, 1036. ESI-MS *m/z* 633 $[M + H]^+$. ^1H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 12.76 (1H, s, 5-OH), 7.99 (1H, d, J = 7.6, H-6″), 7.92 (2H, d, J = 7.6, H-2′, 6′), 7.60–7.53 (4H, m, H-4″, 3′, 4′, 5′), 7.27–7.25 (1H, m, H-3″), 7.22–7.18 (1H, m, H-5″), 6.98 (1H, d, J = 1.2, H-8), 6.76 (1H, s, H-3), 6.69 (1H, d, J = 1.2, H-6), 5.36 (1H, d, J = 7.6, H-1‴), 5.24 (2H, m, H-3‴, 4‴), 5.02 (1H, m, H-2‴), 4.33 (1H, dd, J = 4.0, 12.0, H-5‴), 3.62 (1H, dd, J = 6.8, 12.0, H-5‴), 2.10, 2.08, 2.05 (9H, 3s, 3 × $COCH_3$). ^{13}C NMR spectrum (100 MHz, $CDCl_3$, δ, ppm): 182.91 (C-4), 169.97 (CH_3CO), 169.81 (CH_3CO), 169.31 (C=O), 164.69 (C-2), 162.63 (C-5), 161.82 (C-9), 156.74 (C-7), 156.41 (C-6″), 134.53 (C-4″), 132.11 (C-1′), 131.97 (C-2′, 6′), 130.94 (C-5″), 129.15 (C-3′, 5′), 126.41 (C-4′), 122.83 (C-2″), 120.20 (C-3″), 116.91 (C-1″), 108.86 (C-10), 106.11 (C-6), 105.64 (C-3), 101.27 (C-8), 98.49 (C-1‴), 69.89 (C-2‴), 69.46 (C-3‴), 68.20 (C-4‴), 61.66 (C-5‴), 20.67 (CH_3).

Glycosylated Chrysin Derivative 3d. Yield 82.7%, $C_{33}H_{28}O_{13}$, mp 67–69°C. $[\alpha]_D^{25}$ +19° (*c* 0.5, CH_2Cl_2). IR spectrum (KBr, cm^{-1}): 3434, 1750, 1654, 1619, 1371, 1231, 1132, 1039. ESI-MS *m/z* 633 $[M + H]^+$. ^1H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 12.76 (1H, s, 5-OH), 7.99 (1H, d, J = 7.2, H-6″), 7.97 (2H, d, J = 6.6, H-2′, 6′), 7.56 (4H, m, H-4″, 3′, 4′, 5′), 7.29–7.28 (1H, t, H-3″), 7.20 (1H, t, J = 7.2, H-5″), 6.99 (1H, s, H-3), 6.77 (1H, d, J = 2.0, H-8), 6.71 (1H, d, J = 2.0, H-6), 5.50 (1H, d, J = 8.0, H-1‴), 5.34–5.32 (1H, m, H-4‴), 5.23 (1H, d, J = 6.0, H-2‴), 5.18 (1H, dd, J = 3.6, 8.8, H-3‴), 4.19 (1H, dd, J = 4.4, 12.4, H-5‴), 3.83–3.81 (1H, m, H-5‴), 2.16, 2.05, 2.04 (9H, 3s, 3 × $COCH_3$). ^{13}C NMR spectrum (100 MHz, $CDCl_3$, δ, ppm): 182.93 (C-4), 170.24 (CH_3CO), 169.32 (C=O), 164.73 (C-2), 162.81 (C-5), 156.76 (C-7), 156.48 (C-6″), 134.47 (C-4″), 132.13 (C-1′), 131.92 (C-2′, 6′), 130.62 (C-5″), 129.16 (C-5″), 126.42 (C-4′), 122.89 (C-2″), 120.47 (C-3″), 117.04 (C-1″), 108.91 (C-10), 106.14 (C-6), 105.73 (C-3), 101.34 (C-8), 99.03 (C-1‴), 69.41 (C-2‴), 68.70 (C-3‴), 66.80 (C-4‴), 62.38 (C-5‴), 20.87 (CH_3), 20.78 (CH_3), 20.64 (CH_3).

Glycosylated Chrysin Derivative 3e. Yield 85.8%, $C_{48}H_{48}O_{23}$, mp 179–180°C. $[\alpha]_D^{25}$ +34° (*c* 0.5, CH_2Cl_2). IR spectrum (KBr, cm^{-1}): 3438, 1756, 1657, 1619, 1368, 1230, 1135, 1039. ESI-MS *m/z* 993 $[M + H]^+$. ^1H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 12.75 (1H, s, 5-OH), 7.97 (1H, d, J = 6.8, H-6″), 7.92 (2H, d, J = 6.8, H-2′, 6′), 7.61–7.53

(4H, m, H-4″, 3′, 4′, 5′), 7.24–7.21 (2H, m, H-3″, 5″), 6.95 (1H, s, H-3), 6.76 (1H, d, J = 1.6, H-8), 6.68 (1H, d, J = 1.6, H-6), 5.45 (1H, d, J = 6.8, H-1‴), 5.40–5.27 (3H, m, H-1⁗, 3⁗, 3‴), 5.21–5.17 (1H, m, H-4‴), 5.06 (1H, t, J = 9.6, H-2⁗), 4.86 (1H, dd, J = 4.0, 10.4, H-2‴), 4.55–4.52 (1H, m, H-6⁗), 4.31–4.24 (2H, m, H-5‴, 6‴), 4.17 (1H, t, J = 9.2, H-4″), 4.06 (1H, d, J = 11.6, H-6″), 3.96–3.93 (2H, m, H-5⁗, 6⁗), 2.10, 2.09, 2.07, 2.04, 2.01, 1.99, 1.98 (21H, 7s, 7 × $COCH_3$). ^{13}C NMR spectrum (100 MHz, $CDCl_3$, δ, ppm): 182.91 (C-4), 170.50 (CH_3CO), 170.21 (CH_3CO), 169.55 (CH_3CO), 169.40 (C=O), 164.70 (C-2), 162.76 (C-5), 161.84 (C-9), 156.76 (C-7), 156.17 (C-6″), 134.41 (C-4″), 132.14 (C-1′), 131.99 (C-2′, 6′), 129.16 (C-5″), 126.22 (C-4′), 123.14 (C-2″), 120.24 (C-3″), 116.93 (C-1″), 108.76 (C-10), 106.14 (C-6), 105.65 (C-3), 101.24 (C-8), 98.49 (C-1‴), 95.62 (C-1⁗), 75.17 (C-3⁗), 72.44 (C-5⁗), 71.76 (C-5‴), 69.99 (C-2⁗), 69.23 (C-2‴), 68.57 (C-3‴), 67.95 (C-4⁗), 62.68 (C-4‴), 61.48 (C-6‴, 6⁗), 20.82 (CH_3), 20.57 (CH_3).

Glycosylated Chrysin Derivative 3f. Yield 80.8%, $C_{48}H_{48}O_{23}$, mp 104–106°C. $[\alpha]_D^{25}$ +46° (*c* 0.5, CH_2Cl_2). IR spectrum (KBr, cm^{-1}): 3440, 1755, 1655, 1619, 1370, 1228, 1132, 1050. ESI-MS *m/z* 993 $[M + H]^+$. ^1H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 12.76 (1H, s, 5-OH), 7.97 (1H, t, H-6″), 7.92 (2H, d, J = 6.8, H-2′, 6′), 7.55 (4H, m, H-4″, 3′, 4′, 5′), 7.23–7.19 (2H, m, H-3″, 5″), 6.96 (1H, s, H-3), 6.77 (1H, d, J = 2.0, H-8), 6.68 (1H, d, J = 2.0, H-6), 5.36 (1H, d, J = 7.2, H-1‴), 5.26–5.22 (3H, m, H-2‴, 3‴, 1⁗), 5.16–5.13 (1H, m, H-3⁗), 4.97 (1H, dd, J = 3.2, 10.4, H-2⁗), 4.55–4.52 (2H, t, H-4⁗, 6‴), 4.14 (1H, dd, J = 5.6, 12.0, H-6⁗), 4.11–4.06 (2H, m, H-5‴, 6‴), 3.98 (1H, t, J = 9.2, H-4″), 3.88–3.83 (2H, m, H-5⁗, 6⁗), 2.16, 2.12, 2.11, 2.10, 2.08, 2.05, 1.98 (21H, 7s, 7 × $COCH_3$). ^{13}C NMR spectrum (100 MHz, $CDCl_3$, δ, ppm): 182.90 (C-4), 170.25 (CH_3CO), 170.10 (CH_3CO), 169.73 (CH_3CO), 169.52 (C=O), 164.70 (C-2), 163.12 (C-5), 161.78 (C-9), 156.73 (C-7), 156.17 (C-6″), 134.35 (C-4″), 132.13 (C-1′), 131.93 (C-2′, 6′), 129.15 (C-5″), 127.12 (C-4′), 123.11 (C-2″), 121.04 (C-3″), 116.91 (C-1″), 108.76 (C-10), 106.12 (C-6), 105.64 (C-3), 101.26 (C-8), 98.73 (C-1‴), 95.62 (C-1⁗), 76.04 (C-3⁗), 72.82 (C-5‴), 71.16 (C-5‴), 70.87 (C-2⁗), 70.68 (C-2‴), 69.02 (C-3‴), 66.50 (C-4⁗), 61.88 (C-4‴), 60.70 (C-6‴, 6⁗), 20.61 (CH_3), 20.48 (CH_3).

Glycosylated Chrysin Derivative 6a. Yield 84.2%, $C_{37}H_{34}O_{16}$, mp 175–176°C. $[\alpha]_D^{25}$ +32° (*c* 0.5, CH_2Cl_2). IR spectrum (KBr, cm^{-1}): 3436, 1741, 1654, 1619, 1367, 1214, 1132, 1036. ESI-MS *m/z* 735 $[M + H]^+$. ^1H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 12.78 (1H, s, 5-OH), 7.90 (2H, d, J = 2.8, H-2′, 6′), 7.80 (1H, d, J = 8.4, H-6″), 7.70 (1H, s, H-2″), 7.56 (3H, m, H-3′, 4′, 5′), 7.21 (1H, d, J = 8.8, H-5″), 6.98 (1H, d, J = 1.2, H-8), 6.76 (1H, s, H-3), 6.69 (1H, d, J = 1.2, H-6), 5.35–5.33 (2H, m, H-1‴, 3‴), 5.20–5.18 (1H, m, H-2‴), 5.14–5.12 (1H, m, H-4‴), 4.28 (1H, dd, J = 5.2, 12.0, H-6‴), 4.23–4.22 (1H, m, H-5‴), 3.92 (3H, s, OCH_3), 3.87–3.84 (1H, m, H-6‴), 2.10, 2.06, 2.05, 1.80 (12H, 4s, 4 × $COCH_3$). ^{13}C NMR spectrum (100 MHz, $CDCl_3$, δ, ppm): 182.81 (C-4), 170.51 (CH_3CO), 170.20 (CH_3CO), 169.37 (C=O), 164.70 (C-2), 163.56 (C-5), 161.91 (C-9), 156.76 (C-4″), 156.19 (C-7), 150.70 (C-3″), 132.15 (C-1′), 130.88 (C-2′, 6′), 129.15 (C-3′, 5′), 126.37 (C-4′), 124.48 (C-6″), 123.87 (C-1″), 118.11 (C-2″), 113.91 (C-5″), 108.95 (C-10), 106.11 (C-6), 105.59 (C-3), 101.16 (C-8), 99.77 (C-1‴), 72.34 (C-5‴), 72.20 (C-3‴), 70.96 (C-2‴), 68.08 (C-4‴), 61.82 (C-6‴), 56.20 (CH_3O), 20.61 (CH_3), 20.56 (CH_3).

Glycosylated Chrysin Derivative 6b. Yield 88.2%, $C_{37}H_{34}O_{16}$, mp 165–166°C. $[\alpha]_D^{25}$ +20° (*c* 0.5, CH_2Cl_2). IR spectrum (KBr, cm^{-1}): 3438, 1747, 1657, 1620, 1368, 1227, 1134, 1078. ESI-MS *m/z* 735 $[M + H]^+$. ^1H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 12.79 (1H, s, 5-OH), 7.91 (2H, d, J = 6.8, H-2′, 6′), 7.80 (1H, d, J = 8.4, H-6″), 7.70 (1H, s, H-2″), 7.58–7.53 (3H, m, H-3′, 4′, 5′), 7.23 (1H, d, J = 8.4, H-5″), 6.98 (1H, d, J = 1.6, H-8), 6.77 (1H, s, H-3), 6.70 (1H, d, J = 1.6, H-6), 5.61–5.58 (1H, d, J = 6.4, H-1‴), 5.48 (1H, d, J = 2.8, H-3‴), 5.14–5.12 (1H, m, H-2‴), 5.04–5.01 (1H, m, H-4‴), 4.29–4.25 (1H, m, H-6″), 4.23–4.19 (1H, m, H-6‴), 4.10–4.06 (1H, m, H-5‴), 3.89 (3H, s, OCH_3), 2.18, 2.09, 2.06, 2.03 (12H, 4s, 4 × $COCH_3$). ^{13}C NMR spectrum (100 MHz, $CDCl_3$, δ, ppm): 182.85 (C-4), 170.33 (CH_3CO), 170.12 (CH_3CO), 169.36 (C=O), 164.70 (C-2), 163.61 (C-5), 161.94 (C-9), 156.77 (C-4″), 156.18 (C-7), 150.89 (C-3″), 132.16 (C-1′), 130.93 (C-2′, 6′), 129.16 (C-3′, 5′), 126.37 (C-4′), 124.40 (C-6″), 123.90 (C-1″), 117.92 (C-2″), 113.89 (C-5″), 108.96 (C-10), 106.14 (C-6), 105.60 (C-3), 101.17 (C-8), 100.39 (C-1‴), 71.24 (C-5‴), 70.54 (C-2‴), 68.42 (C-3‴), 66.77 (C-4‴), 61.30 (C-6‴), 56.20 (CH_3O), 20.66 (CH_3), 20.62 (CH_3), 20.58 (CH_3).

Glycosylated Chrysin Derivative 6c. Yield 85.1%, $C_{34}H_{30}O_{14}$, mp 130–132°C. $[\alpha]_D^{25}$ –39° (*c* 0.5, CH_2Cl_2). IR spectrum (KBr, cm^{-1}): 3432, 1763, 1657, 1619, 1370, 1211, 1137, 1067. ESI-MS *m/z* 663 $[M + H]^+$. ^1H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 12.79 (1H, s, 5-OH), 7.91 (2H, d, J = 2.8, H-2′, 6′), 7.81 (1H, d, J = 8.4, H-6″), 7.69 (1H, s, H-2″), 7.58–7.54 (3H, m, H-3′, 4′, 5′), 7.19 (1H, d, J = 8.4, H-5″), 6.98 (1H, d, J = 1.6, H-8), 6.77 (1H, s, H-3), 6.70 (1H, d, J = 1.6, H-6), 5.32 (1H, d, J = 8.0, H-1‴), 5.27–5.21 (2H, m, H-3‴, 4‴), 5.03–5.00 (1H, m, H-2‴), 4.28 (1H, dd, J = 4.4, 12.4, H-5‴), 3.93 (3H, s, OCH_3), 3.59 (1H, dd, J = 4.8, 12.0, H-5‴), 2.13, 2.11, 2.05 (9H, 3s, 3 × $COCH_3$). ^{13}C NMR spectrum (100 MHz, $CDCl_3$, δ, ppm): 182.82 (C-4), 169.80 (CH_3CO), 169.27 (C=O), 164.63 (C-2), 163.61 (C-5), 161.89 (C-9), 156.73 (C-4″), 156.23 (C-7), 150.42 (C-3″), 132.32 (C-1′), 131.92 (C-2′, 6′), 130.88 (C-2′, 6′), 129.31 (C-3′, 5′), 128.94

(C-4′), 126.32 (C-6″), 123.89 (C-1″), 119.22 (C-2″), 115.11 (C-5″), 108.89 (C-10), 106.23 (C-6), 105.71 (C-3), 100.97 (C-8), 98.43 (C-1‴), 69.47 (C-2‴), 69.17 (C-3‴), 68.02 (C-4‴), 61.47 (C-5‴), 56.07 (CH_3O), 20.75 (CH_3), 20.67 (CH_3).

Glycosylated Chrysin Derivative 6d. Yield 80.9%, $C_{34}H_{30}O_{14}$, mp 159–161°C. $[\alpha]_D^{25}$ +13° (*c* 0.5, CH_2Cl_2). IR spectrum (KBr, cm^{-1}): 3438, 1744, 1654, 1619, 1370, 1227, 1137, 1048. ESI-MS *m/z* 663 $[M + H]^+$. ^1H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 12.79 (1H, s, 5-OH), 7.91 (2H, d, J = 2.8, H-2′, 6′), 7.82 (1H, d, J = 8.4, H-6″), 7.70 (1H, s, H-2″), 7.58–7.53 (3H, m, H-3′, 4′, 5′), 7.22 (1H, d, J = 8.4, H-5″), 6.98 (1H, d, J = 1.6, H-8), 6.77 (1H, s, H-3), 6.70 (1H, d, J = 1.6, H-6), 5.51 (1H, d, J = 7.2, H-1‴), 5.34 (1H, d, J = 2.4, H-3‴), 5.20–5.18 (2H, m, H-2‴, 4‴), 4.15 (1H, dd, J = 4.8, 12.4, H-5‴), 3.94 (3H, s, OCH_3), 3.75 (1H, dd, J = 2.0, 12.4, H-5‴), 2.15, 2.14, 2.13 (9H, 3s, 3 × $COCH_3$). ^{13}C NMR spectrum (100 MHz, $CDCl_3$, δ, ppm): 182.89 (C-4), 170.15 (CH_3CO), 169.33 (C=O), 164.71 (C-2), 163.69 (C-5), 161.96 (C-9), 156.77 (C-4″), 156.26 (C-7), 150.69 (C-3″), 132.16 (C-1′), 130.98 (C-2′, 6′), 129.17 (C-3′, 5′), 124.07 (C-4′, 6′), 123.89 (C-1″), 117.16 (C-2″), 113.71 (C-5″), 108.83 (C-10), 106.14 (C-6), 105.61 (C-3), 101.17 (C-8), 98.79 (C-1‴), 69.11 (C-2‴), 68.66 (C-3‴), 66.54 (C-4‴), 61.95 (C-5‴), 56.10 (CH_3O), 20.87 (CH_3), 20.74 (CH_3).

Glycosylated Chrysin Derivative 6e. Yield 84.1%, $C_{49}H_{50}O_{24}$, mp 171–173°C. $[\alpha]_D^{25}$ +16° (*c* 0.5, CH_2Cl_2). IR spectrum (KBr, cm^{-1}): 3437, 1747, 1656, 1623, 1371, 1240, 1131, 1037. ESI-MS *m/z* 1023 $[M + H]^+$. ^1H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 12.79 (1H, s, 5-OH), 7.91 (2H, d, J = 6.8, H-2′, 6′), 7.82 (1H, d, J = 8.0, H-6″), 7.69 (1H, s, H-2″), 7.58–7.53 (3H, m, H-3′, 4′, 5), 7.18 (1H, d, J = 8.4, H-5″), 6.98 (1H, s, H-3), 6.77 (1H, d, J = 2.0, H-8), 6.70 (1H, d, J = 2.0, H-6), 5.46 (1H, d, J = 7.2, H-1‴), 5.41–5.34 (2H, m, H-1⁗, 3⁗), 5.20–5.17 (2H, m, H-3‴, 4‴), 5.10–5.05 (1H, m, H-2⁗), 4.88 (1H, dd, J = 4.0, 10.4, H-2‴), 4.54 (1H, dd, J = 2.0, 12.0, H-6⁗), 4.26 (2H, dd, J = 4.0, 12.0, H-5‴, 6‴), 4.16–4.11 (1H, m, H-4‴), 4.08–4.06 (1H, m, H-6‴), 3.98 (1H, d, J = 10.4, H-6⁗), 3.92 (3H, s, OCH_3), 3.89–3.87 (1H, m), 2.13, 2.12, 2.08, 2.06, 2.05, 2.02 (21H, 7s, 7-$COCH_3$). ^{13}C NMR spectrum (100 MHz, $CDCl_3$, δ, ppm): 182.86 (C-4), 170.48 (CH_3CO), 170.15 (CH_3CO), 169.95 (CH_3CO), 169.51 (CH_3CO), 169.38 (C=O), 164.69 (C-2), 163.62 (C-5), 161.95 (C-9), 157.03 (C-4″), 156.20 (C-7), 150.56 (C-3″), 134.02 (C-1′), 132.16 (C-2′, 6′), 130.97 (C-2′, 6′), 129.93 (C-2′, 6′), 128.48 (C-4′), 126.37 (C-6″), 124.40 (C-1″), 117.94 (C-2″), 113.71 (C-5″), 109.23 (C-10), 106.14 (C-6), 105.60 (C-3), 101.19 (C-8), 99.04 (C-1‴), 95.65 (C-1⁗), 74.89 (C-3⁗), 72.54 (C-5⁗), 71.79 (C-5‴), 70.02 (C-2⁗), 69.23 (C-2‴), 68.57 (C-3‴), 67.96 (C-4⁗), 62.61 (C-4‴), 61.49 (C-6‴, 6⁗), 56.18 (CH_3O), 20.90 (CH_3), 20.73 (CH_3), 20.56 (CH_3).

Glycosylated Chrysin Derivative 6f. Yield 81.8%, $C_{49}H_{50}O_{24}$, mp 216–218°C. $[\alpha]_D^{25}$ +27° (*c* 0.5, CH_2Cl_2). IR spectrum (KBr, cm^{-1}): 3438, 1748, 1654, 1620, 1370, 1230, 1132, 1057. ESI-MS *m/z* 1023 $[M + H]^+$. ^1H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 12.79 (1H, s, 5-OH), 7.91 (2H, d, J = 6.8, H-2′, 6′), 7.79 (1H, d, J = 8.4, H-6″), 7.69 (1H, s, H-2″), 7.59–7.53 (3H, m, H-3′, 4′, 5), 7.17 (1H, d, J = 8.4, H-5″), 6.98 (1H, s, H-3), 6.77 (1H, d, J = 1.2, H-8), 6.69 (1H, d, J = 1.2, H-6), 5.37–5.30 (3H, m, H-1‴, 2‴, 3‴), 5.16–5.10 (2H, m, H-1⁗, 3⁗), 4.98 (1H, dd, J = 3.6, 10.4, H-2⁗), 4.56–4.52 (2H, m, H-4⁗, 6‴), 4.19–4.07 (3H, m, H-6⁗, 5‴, 6‴), 3.94–3.89 (5H, m, H-4‴, 6⁗, OCH_3), 3.81–3.78 (1H, m, H-5⁗), 2.17, 2.12, 2.10, 2.09, 2.08, 2.07, 1.98 (21H, 7s, 7 × $COCH_3$). ^{13}C NMR spectrum (100 MHz, $CDCl_3$, δ, ppm): 182.89 (C-4), 170.36 (CH_3CO), 170.23 (CH_3CO), 169.71 (CH_3CO), 169.53 (CH_3CO), 169.06 (C=O), 164.73 (C-2), 163.62 (C-5), 161.97 (C-9), 156.83 (C-4″), 156.23 (C-7), 150.76 (C-3″), 133.42 (C-1′), 132.18 (C-2′, 6′), 130.93 (C-2′, 6′), 129.88 (C-3′, 5′), 129.18 (C-4′), 126.40 (C-6″), 123.90 (C-1″), 117.87 (C-2″), 113.89 (C-5″), 108.99 (C-10), 106.17 (C-6), 105.63 (C-3), 101.14 (C-8), 99.45 (C-1⁗, 1‴), 76.08 (C-3⁗), 72.43 (C-5‴), 71.26 (C-5‴), 70.91 (C-2⁗), 70.70 (C-2‴), 69.06 (C-3‴), 66.54 (C-4⁗), 61.80 (C-4‴), 60.76 (C-6‴, 6⁗), 56.22 (CH_3O), 20.80 (CH_3), 20.62 (CH_3), 20.50 (CH_3).

ACKNOWLEDGMENT

Financial support from the National Natural Science Foundation of China (81202458), the China Postdoctoral Science Foundation (2012M521926), and the Scientific Research Foundation of Gansu Province (1308RJYA061) are gratefully acknowledged.

REFERENCES

1. J. B. Xiao, T. T Chen, and H. Cao, *Biotechnol. Adv*., **33**, 214 (2015).
2. M. Li and A. E. Hagerman, *Curr. Drug Metab.*, **14**, 432 (2013).
3. T. Lapidot, M. D. Walker, and J. Kanner, *J. Agric. Food. Chem.*, **50**, 7220 (2002).

4. N. Gresa-Arribas, J. Serratosa, J. Saura, and C. Sola, *J. Neurochem.*, **115**, 526 (2010).
5. J. Wang, J. Qiu, J. Dong, H. Li, M. Luo, X. Dai, Y. Zhang, B. Leng, X. Niu, S. Zhao, and X. Deng, *J. Appl. Microbiol.*, **111**, 1551 (2011).
6. P. G. Wadibhasme, M. M. Ghaisas, and P. A. Thakurdesai, *Pharm. Biol.*, **49**, 508 (2011).
7. M. Torres-Piedra, R. Ortiz-Andrade, R. Villalobos-Molina, N. Singh, J. L. Medina-Franco, S. P. Webster, M. Binnie, G. Navarrete-Vazquez, and S. Estrada-Soto, *Eur. J. Med. Chem.*, **45**, 2606 (2010).
8. E′. Brown, N. S. Hurd, S. McCall, and T. E. Ceremuga, *AANA J.*, **75**, 333 (2007).
9. G. A. Oliveira, E. R. Ferraz, A. O. Souza, R. A. Lourenco, D. P Oliveira, and D. J. Dorta, *J. Toxicol. Environ. Health. A*, **75**, 1000 (2012).
10. A. Pick, H. Muller, R. Mayer, B. Haenisch, I. K. Pajeva, M. Weigt, H. Bonisch, C. E. Muller, and M. Wiese, *Bioorg. Med. Chem.*, **19**, 2090 (2011).
11. R. Anandhi, P. A. Thomas, and P. Geraldine, *Mol. Cell. Biochem.*, **385**, 103 (2014).
12. G. Pushpavalli, P. Kalaiarasi, C. Veeramani, and K. V. Pugalendi, *Eur. J. Pharmacol.*, **631**, 36 (2010).
13. A. D. Kandhare, V. Shivakumar, A. Rajmane, P. Ghosh, and S. L. Bodhankar, *J. Nat. Med.*, **68**, 586 (2014).
14. P. A. Tsuji, R. N. Winn, and T. Walle, *Chem. Biol. Interact.*, **164**, 85 (2006).
15. U. K. Walle, A. Galijatovic, and T. Walle, *Biochem. Pharmacol.*, **58**, 431 (1999).
16. S. P. Bondarenko and M. S. Frasinyuk, *Chem. Nat. Compd.*, **49**, 841 (2013).
17. X. Zheng, W. D. Meng, Y. Y. Xu, J. G. Cao, and F. L Qing, *Bioorg. Med. Chem. Lett.*, **13**, 881 (2003).
18. H. A. Mohammed, L. A. Ba, T. Burkholz, E. Schumann, B. Diesel, J. Zapp, A. K. Kiemer, C. Ries, R. W. Hartmann, M. Hosny, and C. Jacob, *Nat. Prod. Commun.*, **6**, 31 (2011).
19. H. Che, H. Lim, H. P. Kim, and H. Park, *Eur. J. Med. Chem.*, **46**, 4657 (2011).
20. M. V. Veselovskaya, M. M. Garazd, A. S. Ogorodniichuk, Ya. L. Garazd, and V. P. Khilya, *Chem. Nat. Compd.*, **44**, 704 (2008).
21. C. R. Bertozzi and L. L. Kiessling, *Science*, **291**, 2357 (2001).
22. P. H. Seeberger and D. B. Werz, *Nat. Rev. Drug Discov.*, **4**, 751 (2005).
23. X. F. Fan, L. L. Jing, H. P. Ma, P. C. Fan, and Z. P. Jia, *Chem. Reagents*, **35**, 975 (2013).
24. F. F. Zhang, L. L. Gan, and C. H. Zhou, *Bioorg. Med. Chem. Lett.*, **20**, 1881 (2010).
25. Y. Luo, Y. H. Lu, L. L. Gan, C. H. Zhou, J. Wu, R. X. Geng, and Y. Y. Zhang, *Arch. Pharm. (Weinheim)*, **342**, 386 (2009).