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RESEARCH ARTICLE

The First Total Syntheses of the Diglycosides Virgaureoside A, of *Solidago virgaurea L.*, and its analogue iso-Virgaureoside A

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Abstract: The first syntheses of Virgaureoside A [2-(β-D-glucopyranosyloxy)benzyl 2-(β-D-glucopyranosyloxy) benzoate], a diglycoside of the *Solidago virgaurea* L. plant, and iso-Virgaureoside A [2-(β-D-glucopyranosyloxy) benzyl 4-(β-D-glucopyranosyloxy)benzoate], which is not found in nature and has not been described in the literature, have been accomplished. The key step involved selective acid catalyzed cleavage of acetyl esters in the presence of a substituted benzoyl ester and two glycosidic linkages.

Keywords: Diglycosides, Virgaureoside A, o-hydroxybenzyl salicylate, *Solidago virgaurea* L.

1. INTRODUCTION

The *Solidago virgaurea* L. (Goldenrod ordinary) plant is a well-known remedy in folk Chinese medicine and has diuretic, choleretic, and antiseptic effects [1, 2], as well as antioxidant [3] and antifungal activities [4], and cytotoxic activity on cancer cells [5]. *S. virgaurea* contains several phenolic glycosides [6], one of which is the diglycoside Virgaureoside A **1**. The availability of Virgaureoside A **1** by synthesis can provide an opportunity for any potential contribution of this diglycoside to the properties of the herbal remedy to be determined. As shown in Figure **1**, it contains 2-hydroxybenzyl salicylate as the aglycone, which is glycosylated by two glucose moieties.

The first reference to Virgaureoside A **1** is found in the studies by the German scientist Hiller [2,7], who reported its isolation from *S. virgaurea* in 0.008-0.141 % by weight. Only a few studies concerning the isolation of this diglycoside from natural sources have been reported, presumably because of its low content.

Thus, the second plant in which Virgaureoside A **1** was detected, *Prunus grayana* [1], contains only 0.04% by weight of this compound.

2. RESULTS AND DISCUSSION

In the present work, we report the first total synthesis of the diglycoside Virgaureoside A **1**, which allows the acquisition of this glycoside in any desired quantity and thereby permit an assessment of its potential biological properties.

Our synthetic approach also enables the acquisition of other diglycosides of similar structure. Thus, we report the synthesis of a structural analogue of Virgaureoside A **1** that is not found in plants, iso-Virgaureoside A **2** (Fig. **1**). The aglycone moiety of iso-Virgaureoside A **2** is an ester of salicylic alcohol and *p*-hydroxybenzoic acid. This latter acid is commonly found in plant extracts [8] so we speculate that *iso*-Virgaureoside A may also be present in plants extracts and that the availability of a synthetic standard and spectral characteristics may assist with its identification in future.

The phenolic acid esters **3** and **4** were used as the initial substrates in the synthesis of the intermediate glycosides **7** and **8** (Scheme **1**). Silver oxide assisted glycosylation with acetobromoglucose (ABG) provided the glycosides **5** and **6** in modest yields of 37 and 27%, respectively. The modest yields are due to competing formation of 3,4,6-tri-O-acetyl-D-glucal, levoglucosan triacetate, a 1,2-orthoester and glucose pentaacetate as side products as revealed by GC-MS analysis of the crude reaction product. However, this method was superior to previously reported syntheses of **5** and **6** in both yield and speed. Thus, glycoside **5** has been obtained in 30% yield using ABG in acetone with K_2CO_3 [9] but the reaction required 16 h compared to 1 hour in our case. Only a few examples of the synthesis of glycoside **6** or similar glycosides have been reported [10, 11].

Glycosides **5** and **6** were then saponified to release a carboxyl group for further reaction and re-acetylated to form glycosides **7** and **8**, respectively.

The synthesis of the intermediate glycoside **10** began with *o*-cresol, which was glycosylated using ABG under phase transfer conditions to give glycoside **9** in 30% yield. Radical bromination then yielded glycoside **10** (95%).

Condensation of glycosides **7** and **8** with bromide **10** was performed using sodium carbonate in DMF to give octaacetates **11** (57%) and **12** (59%), respectively.

The final, key reaction in the synthesis of **1** and **2** is the selective removal of the acetyl groups from **11** and **12** while leaving the benzyl benzoate ester linkages intact. This was successfully carried out using HCl-EtOH-$CHCl_3$, a system we previously demonstrated in related circumstances [12, 13]. Both β-glucosidic bonds in these substrates are stable in these acidic conditions.

The ^{1}H NMR spectral data for compound **1** measured here in DMSO-d_6 were in good agreement with those reported by Shimomura *et al*. [1] in pyridine-d_5, except for those protons that are over-

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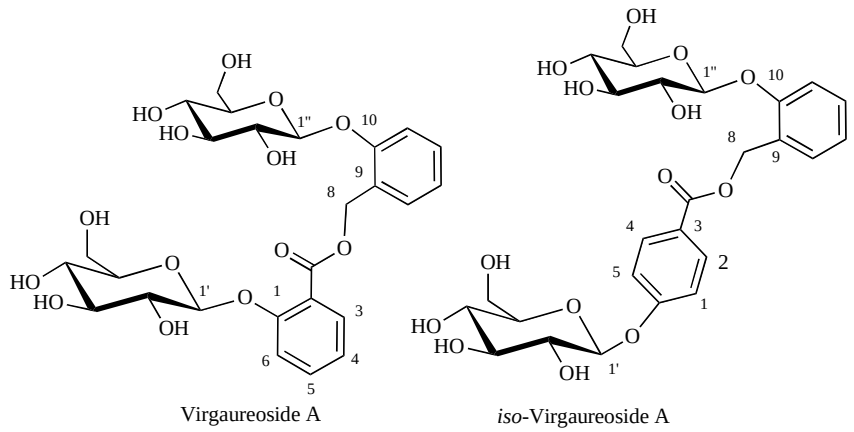
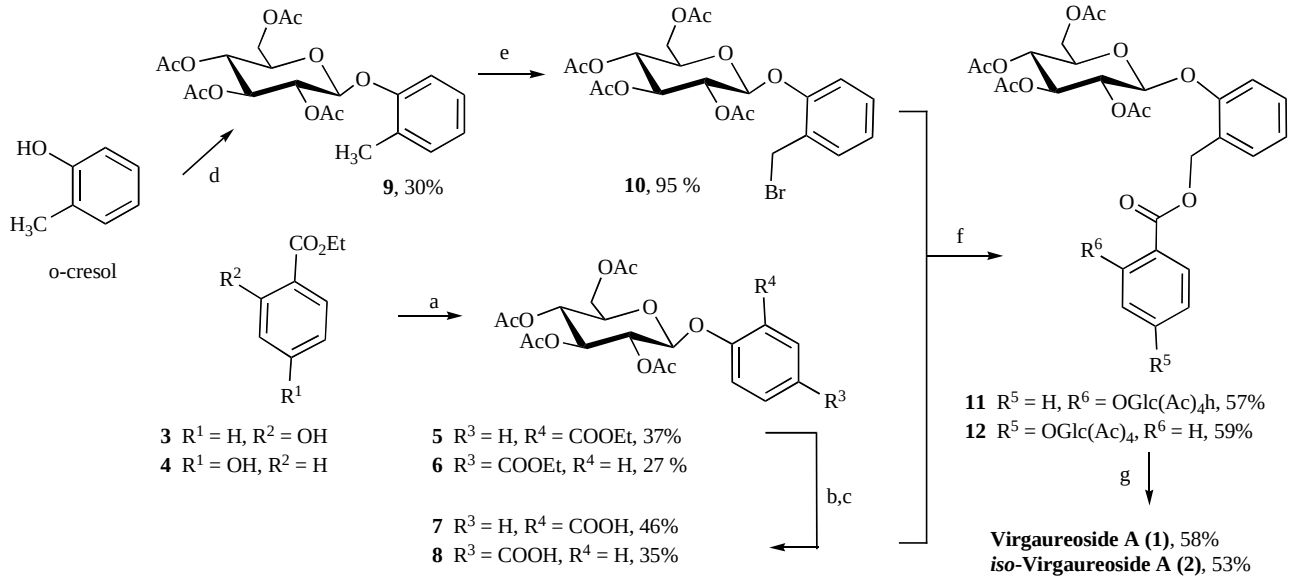


Fig. (1). Structures of Virgaureoside A and iso-Virgaureoside A.



Scheme 1. Synthesis of Virgaureoside A and iso-Virgaureoside A. Reagents and conditions: (a) ABG, Ag_2O, quinoline, 1 h, RT; (b) aq. NaOH, 100 °C, 1 h; (c) Ac_2O, Py, RT, 20 h; (d) ABG, TBAB, NaOH, $CHCl_3$, boiling, 4 h; (e) $NaHCO_3$, $CHCl_3$, Br_2, hν, 2 h; (f) $NaHCO_3$, DMF, 3 days; (g) HCl-$CHCl_3$-EtOH, RT, 48 h; (h) $Glc(Ac)_4$=2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl.

lapped by the pyridine peaks (near 7.6 and 7.2 ppm). In our ^{1}H NMR spectra, all the phenolic protons are distinguishable.

Thus, the first total syntheses of Virgaureoside A **1** and iso-Virgaureoside A **2** have been accomplished.

3. EXPERIMENTAL SECTION

3.1. General Experimental Procedures. The melting points, which are uncorrected, were determined using an MP50 melting point system (MettlerToledo). UV spectroscopic data were obtained with an SF-102 spectrophotometer. IR spectra were recorded with a Spectrum BX II Fourier IR spectrophotometer using KBr disks. The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker-300 MMX spectrometer at 300 and 75.5 MHz, respectively, and on Bruker AV-400 at 400 MHz for ^{1}H NMR in $CDCl_3$ and DMSO-d_6 with TMS as an internal standard. The chemical shifts are given in δ (ppm) and the spin−spin coupling constants (*J*) in Hertz. GC-MS analysis was performed using an Agilent 7890A/5975C GC/MSD instrument, with electron energy 70 eV, ion source temperature 230 °C, quadrupole temperature 150 °C and evaporator temperature 315 °C, and employing a 30 × 0.25 mm × 0.25 μm HP - 5MS fused-silica capillary column. Helium was used as carrier gas at a constant flow of 1 mL/min and an inlet temperature of 315 °C. The column temperature mode: 2 min at 150 °C, 150-315 °C (20°C/min), and 25 min at 315 °C. TLC was performed using Merck Silica gel 60 F254 and Sorbfil-UV 254 plates eluted with benzene-ethanol 9:1 (for acetylated glycosides) or chloroform-methanol 4:1 (for de-acetylated glycosides). HPLC analysis was carried out on an Agilent Compact LC with a 150 × 4.6 mm Exlips Plus C-18 (5 μm) column, eluted with a gradient of H_2O-CH_3CN containing 0.1% trifluoroacetic acid from 0% to 100 % CH_3CN in 20 min and a flow rate of 1 mL/min. Probe volume was 20 μL. UV detection was performed at 220 and 270 nm. Accurate mass measurement was performed on an Agilent 1200 series LC system coupled with micro TOF-6210 (Bruker) mass spectrometer with ESI detection. Silica gel MN Kieselgel 60 0.04 - 0.063 mm was used for column chromatography. Commercially available solvents were used after drying with $CaCl_2$. All yields are given after recrystallization and HPLC\GC-MS\TLC confirmation of sample purity.

3.2. Glycosylation of esters 3 and 4. Ag_2O (0.557 g, 2.4 mmol) was added to a suspension of ABG (1 g, 2.4 mmol) and ester **3** or **4** (0.480 g, 2.9 mmol) in quinoline (0.5 mL). The mixture was stirred thoroughly until it thickened, kept for 1 h at room temperature, then diluted with $CHCl_3$, filtered or centrifuged to remove

silver salts or subjected to flash chromatography if the solution was dark. The mother liquor was washed with 1N NaOH, 0.1 M H_2SO_4, and water, dried over sodium sulfate, and concentrated to give 0.640-0.660 g of crude product which was recrystallized from ethanol to give pure glycosides **5** (0.440 g) or **6** (0.320 g).

3.2.1. 2-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyloxy)-benzoic acid ethyl ester (5). White crystals from EtOH, yield 37%, mp 164-165 °C. (Lit.170-171 °C) [11].

3.2.2. 4-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyloxy)-benzoic acid ethyl ester (6). White crystals from EtOH, yield 27%, mp 127-129 °C Lit. 135.5-136°C [11] and 147-149 °C [14]. While we observe a lower but narrow melting range than reported in references [11, 14], our sample was a single peak on GC-MS and HPLC analyses, gave the MS fragmentation pattern seen with other glucosides tetraacetates [15], and the NMR data is consistent with the assigned structure (see support information).

3.3. 2-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyloxy)-toluene (9) was obtained according to a previously described procedure [16]. Yield 30%, mp 142-143 °C. (Lit. 141-142 °C) [17, 18].

3.4. 2-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyloxy)-benzyl bromide (10). Br_2 (23.5 µL, 0.45 mmol) was added to a solution of glycoside **5** (0.200 g, 0.45 mmol) in anhydrous chloroform (4 mL) and $NaHCO_3$ (0.380 g, 4.50 mmol) and the mixture was irradiated with 100 watt lamp for 2 h with vigorous stirring until the complete disappearance of the red colour. The reaction mixture was filtered to remove the inorganic products, the filter cake was washed with chloroform and the combined filtrate was concentrated. The residue was recrystallized from ethanol to give 0.220 g of glycoside **10**. Yield 95%, mp 150-151 °C, with the same spectral data is given in our previous work [12].

3.5. General procedure for the saponification and re-acetylation of glycosides 5 and 6. NaOH (0.245 g, 6.12 mmol) in water (4 mL) was added to glycoside **5** or **6 (**0.405 g, 0.82 mmol) and the mixture was heated under reflux for 1 h. The reaction mixture was treated with the acidic cation exchange resin KU-2-8 until a pH of 7 was reached, filtered, and concentrated under vacuum. Acetic anhydride (5 mL) and pyridine (1 mL) were added to the residue, and the reaction mixture was stirred for 20 h at room temperature. The reaction mixture was poured into 10 mL water and acidified with sulfuric acid. The precipitated crystals (0.300 and 0.320 g) were filtered and recrystallized from EtOH to give glycosides **7** (0.176 g) and **8** (0.135 g).

3.5.1 2-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyloxy)benzoic acid (7). Yield 81% of crude product with 46 % of pure material after a single recrystallization from EtOH. mp 163-164 °C (Lit. 164-165 °C) [19]. UV (EtOH) λ_{max} 282 nm. IR (KBr), ν_{max} 3438, 2975, 2343, 1725, 1604, 1496, 1376, 1232, 1069, 1042 cm^{-1}.^{1}H NMR (DMSO-d_6, 400 MHz) δ 1.98, 1.99, 2.00, 2.01 (12H, s, 8×CH_3); 4.03 (1H, dd, *J* = 2.0, 12.4 Hz, H-6'b); 4.21 (1H, dd, *J* = 4.4, 13.2 Hz, H-6'a); 429-4.34 (1H, m, H-5'); 5.04 (1H, t, *J* = 9.6 Hz, H-2'); 5.13 (1H, dd, *J* = 8.0, 10.0 Hz, H-4'); 5.55 (1H, t, *J* = 9.6 Hz, H-3'); 6.20 (1H, d, *J* = 8.4 Hz, H-1'); 6.95 (1H, t, *J* = 7.2 Hz, H-4); 7.00 (1H, d, *J* = 8.4 Hz, H-6); 7.53 (1H, m, H-3); 7.64 (1H, dd, *J* = 2.0, 8.0 Hz, H-5); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 20.5 (4×CH_3, Ac); 61.5 (CH_2, C-6'); 68.9 (CH, C-4'); 71.0 (CH, C-3'); 72,2 (CH, C-2', C-5'); 99.8 (CH, C-1'); 116.5 (CH, C-6); 120.2 (CH, C-2); 123.9 (C, C-4); 133.4 (CH, C-3); 134.8 (CH, C-5); 156.5 (C, C-1); 166.4 (C = O, C-7); 169.6; 169.8; 169.9; 170.3 (4 × C=O, Ac).

3.5.2 4-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyloxy)benzoic acid (8). Yield 78% of crude product, 35 % of pure material after a single recrystallization from EtOH. Colourless crystals, mp 185-186 °C (Lit. 178-180°C) [20]. UV (EtOH) λ_{max} 246 nm; IR (KBr), ν_{max} 3089, 2366, 1753, 1714, 1609, 1512, 1371, 1229, 1070, 1046, 775 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz), δ 2.05, 2.06, 2.062, 2.08 (12H, s, CH_3 × 4); 3.90-3.94 (1H, m, H-5'); 4.16 (1H, dd, *J* = 2.1, 12.0 Hz, H-6'b); 4.29 (1H, dd, *J* = 5.4, 12.3 Hz, H-6'a); 5.18-5.21 (2H, m, H-3', H-4'); 5.28-5.36 (2H, m, H-1', H-2'); 7.03 (2H, d, *J* = 9.0 Hz, H-2, H-4); 8.07 (2H, d, *J* = 9.0 Hz, H-1, H-5); ^{13}C NMR ($CDCl_3$, 75 MHz), δ 20.7 (4×CH_3, Ac); 62.0 (CH_2, C-6'); 68.2 (CH, C-4'); 71.1 (CH, C-2'); 72.3 (CH, C-3'); 72.6 (CH, C-5'); 98.2 (CH, C-1'); 116.3 (CH, C-2, C-4); 124.2 (C, C-6); 132.4 (CH, C-1, C-5); 160.9 (C, C-3); 169.5 (C = O, C-7); 170.3; 170.7 (4 × C = O, Ac).

3.6 Condensation of 7 or 8 with 10. $NaHCO_3$ (0.0756 g, 0.9 mmol) in 10 mL DMF was added to a mixture of glycoside **7** or **8** (0.220 g, 0.47 mmol) and **10 (**0.231 g, 0.45 mmol) and the suspension was vigorously stirred for 3 days at room temperature. The reaction mixture was slowly poured into 20 mL water with vigorous stirring. White crystals were precipitated and filtered to give 0.378 g (93%) and 0.370 g (91%) of crude product, which was recrystallized from ethanol to give **11** (0.232 g) and **12** (0.240 g), respectively.

3.6.1 Virgaureoside A, octaacetate (11). Colorless crystals from EtOH, yield 57%, mp 110-111 °C. The melting point given here is significantly different from that reported by Hiller et al (141 °C [7]). Yet the purity of our sample was confirmed using HPLC at 220 and 252 nm, and the structure was established by both ^{1}H and ^{13}C NMR data whereas in Hiller's work only ^{13}C NMR is given which is in good agreement with ours. UV (EtOH) λ_{max} 252 nm; IR (KBr), ν_{max} 3094, 2369, 1755, 1604, 1497, 1376, 1069, 1232, 1069, 1042 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.06, 2.07 (24H, s, 8×CH_3); 3.81-3.93 (2H, m, H-5', H-5''); 4.15-4.22 (2H, m, H-6'b, H-6''b); 4.28-4.32 (2H, m, H-6'a, H-6''a); 5.12-5.22 (4H, m, H-2', H-2'', H-3', H-3''); 5.27-5.33 (6H, m, H-1', H-1'', H-4', H-4'', H-8); 7.10-7.19 (4H, m, H-4, H-6, H-11, H-13); 7.28 (1H, t, *J* = 7.2 Hz, H-12); 7.43 (2H, m, H-5, H-14); 7.76 (1H, d, *J* = 6.9 Hz, H-3); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 20.1 (8 × CH_3, Ac); 60.8 (CH_2, C-8); 61.5 (2 × CH_2, C-6', C-6'); 67.8 (2 × CH, C-4', C-4''); 70.3 (2 × CH, C-2', C-2''); 71.5 (2 × CH, C-3', C-3''); 72.1 (2 × C, C-5', C-5''); 99.0 (CH, C-1'); 99.5 (CH, C-1''); 115.5 (CH, C-6); 117.5 (CH, C-11), 122.5 (C, C-2); 123.0 (CH, C-4); 122.1 (CH, C-13); 125.9 (CH, C-9); 128.7 (CH, C-5, C-12); 130.6 (CH, C-14); 133.8 (C, C-3); 153.8 (C, C-1); 155.1 (C, C-10); 164.5 (C=O, C-7); 168.9; 169.8; 170.0 (8 × C = O, Ac).

3.6.2 Iso-Virgaureoside A, octaacetate (12). Colourless crystals from EtOH, yield 59%, mp 176-177 °C. UV (EtOH) λ_{max} 248 nm; IR (KBr), ν_{max} 2356, 2330, 1752, 1609, 1489, 1377, 1271, 1238, 1058, 1046 cm^{-1}; ^{1}H NMR (DMSO-d_6, 400 MHz) δ 1.94, 1.96, 1.97, 2.00, 2.02, 2.03, 2.04 (24H, s, 8×CH_3, Ac); 4.05-4.11 (2H, m, H-5', H-5''); 4.17-4.33 (4H, m, H-6', H-6''); 4.98-5.04 (2H, m, H-4', H-4''); 5.09 (2H, t, *J* = 9.0 Hz, H-2', H-2''); 5.17 (1H, d, *J* = 12.0 Hz, H-8b); 5.25 (1H, d, *J* = 11.2 Hz, H-8a); 5.42 (2H, t, *J* = 9.6 Hz, H-3', H-3''); 5.56 (1H, d, *J* = 8.0 Hz, H-1''); 5.73 (1H,d, *J* = 8.0 Hz, H-1'); 7.01 (2H, d, *J* = 8.8 Hz, H-2, H-4); 7.12 (1H, t, *J* = 6.9 Hz, H-13); 7.17 (1H, d, *J* = 8.0 Hz, H-11); 7.38 (1H, t, *J* = 8.0 H-12); 7.43 (1H, d, *J* = 7.2 Hz, H-14); 7.97 (2H, d, *J* = 8.8 Hz, H-1, H-5); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 20.6 (8 × CH_3, Ac); 61.8 (CH_2, C-8); 61.9 (2 × CH_2, C-6', C-6''); 68.1 (2 × CH, C-4', C-4''); 68.6 (2 × CH, C-2', C-2''); 70.5 (2×CH, C-3', C-3''); 72.6 (2 × C, C-5', C-5''); 98.3 (CH, C-1'); 99.5 (CH, C-1''); 113.8 (CH, C-11); 116.1 (2 × C, C-2, C-4); 123.5 (CH, C-13); 123.6 (CH, C-6); 126.1 (CH, C-9); 129.5 (CH, C-12, C-14); 132.0 (2 × CH, C-1, C-5); 159.8 (C, C-3); 164.4 (C, C-10); 166.0 (C = O, C-7); 169.5; 169.8; 170.0 (8 × C = O, Ac). HRESIMS m/z 922.3018 (calcd for $C_{42}H_{50}O_{23}$ ($[M^+ + H_2O]^-$) 922.3025).

3.7. General procedure for the selective removal of the acetyl groups of diglycosides 11 and 12. Acetylated diglycoside **11** or **12** (0.200 g, 0.22 mmol) was treated with a mixture of hydrochloric acid (9.8 M, 0.250 mL), EtOH (0.750 mL), and $CHCl_3$ (0.250 mL). The reaction mixture was maintained at room temperature for 48 h. The mixture of solvents was distilled under vacuum (bath temperature not exceeding 45 °C), and the residue was subjected to column chromatography (chloroform - ethanol from 8:1 to 2:1). The resulting powdesr were recrystallized from aqueous ethanol to give pure digly-

coside Virgaureoside A **1** (0.073 g) and iso-Virgaureoside A **2** (0.066 g), respectively.

3.7.1. Virgaureoside A (1). White crystals from aq. EtOH, 58% yield, mp 180-181 °C (Lit. 180 °C) [1]. UV (EtOH) λ_{max} 247 nm; IR (KBr), ν_{max} 3398, 2401, 2303, 1707, 1693, 1605 cm^{-1}; ^{1}H NMR (DMSO-d_6, 300 MHz) δ: 3.19 (1H, m, H-5"); the 3.20-3.60 signals of glucose moieties are overlapped with the DMSO peak; 3.70 (1H, d, *J* = 11.4 Hz, H-6'a); 4.87 (1H, d, *J* = 6.9 Hz, H-1"); 5.03 (1H, m, H-1'); 5.43 (1H, d, *J* = 12.9 Hz, H-8b); 5.48 (1H, d, *J* = 12.9 Hz, H-8a); 6.94 (1H, t, *J* = 7.2 Hz, H-4); 6.99 (1H, d, *J* = 8.4 Hz, H-12); 7.05 (1H, t, *J* = 7.5 Hz, H-14); 7.20 (1H, d, *J* = 8.4 Hz, H-2) 7.34 (1H, t, *J* = 7.8 Hz, H-13); 7.43 (1H, d, *J* = 7.8 Hz, H-9); 7.53 (1H, t, *J* = 7.2 Hz, H-3); 7.83 (1H, d, *J* = 7.5 Hz, H-5); ^{13}C NMR (DMSO-d_6, 75 MHz) δ: 61.0 (CH_2, C-8); 62.3 (2 × CH_2, C-6', C-6"); 68.1 (CH, C-4"); 69.9 (CH, C-4'); 74.0 (2 × CH, C-2',C-2"); 76.0 (2 × CH, C-3',C-3"); 76.9 (2 × C,C-5', C-5"); 100.9 (2 × CH, C-1', C-1"); 113.1 (CH, C-6); 115.0 (C, C-11); 117.4 (CH, C-2); 119.9 (CH, C-4); 121.6 (C, C-13); 124.5 (C, C-9); 129.0 (CH, C-12); 129.5 (CH, C-14); 130.0 (CH, C-3); 135.2 (CH, C-5); 155.2 (C, C-1); 160.1 (C, C-11); 168.9 (C = O, C-7). The ^{13}C NMR spectrum is in good agreement with Hiller's work [7] except for C-5 (128.4 ppm) and C-14 (133.5 ppm) carbons, which we assigned conversely.

3.7.2 Iso-Virgaureoside A (2). White crystals from aq. EtOH, 53% yield, mp 194-195 °C. UV (EtOH) λ_{max} 251 nm; IR (KBr), ν_{max} 3366, 2377, 2346, 1707, 1607, 1406, 1376, 1286, 1244, 1078 cm^{-1}; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 3.18-3.42 (10H, m, H-2', 2", 3', 3", 4', 4", 5', 5", 6'b, 6"b); 3.66-3.72 (2H, m, H-6'a, H-6"a); 4.99-5.10 (2H, m, H-1', H-1"); 7.03-7.06 (2H, m, H-2, H-4); 7.11-7.20 (2H, m, H-11, H-13); 7.29-7.34 (1H, d, *J* = 7.5 Hz, H-14); 7.40 (1H, m, H-12); 8.02 (2H, d, *J* = 8.7 Hz, H-1, H-5); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 60.6 (CH_2, C-6"); 60.7 (CH_2, C-6'); 61.5 (CH_2, C-8); 69.6 (CH, C-4"); 69.7 (CH, C-4'); 73.2 (CH, C-2'); 73.4 (CH, C-2"); 76.6 (2 × CH, C-3', C-3"); 77.1 (2 × C, C-5', C-5"); 99.8 (CH, C-1'); 101.0 (CH, C-1"); 115.1 (CH, C-11); 116.1 (2 × C, C-2, C-4); 121.9 (CH, C-13); 123.6 (CH, C-6); 125.2 (CH, C-9); 128.6 (CH, C-14); 129.4 (CH, C-12), 131.3 (2 × CH, C-2, C-4); 155.2 (C, C-3); 161.2 (C, C-10); 165.3 (C = O, C-7). HRESIMS m/z 586.1966 (calcd for $C_{26}H_{34}O_{15}$ ([M-H^+]$^-$) 586.1898).

CONCLUSION

The desired products Virgaureoside A **1** and *iso*-Virgaureoside A **2** were synthesized in four steps in 5.6% and 3.0% overall yield, starting from phenolic acid esters **3** and **4**, respectively.

LIST OF ABBREVIATIONS

ABG = acetobromoglucose, 2,3,4,6-tetra-O-acetyl-α-D-glucopyranosyl bromide

CONFLICT OF INTEREST

The author(s) confirm that this article content has no conflict of interest.

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SUPPLEMENTARY MATERIAL

The NMR spectra of compounds **1, 2, 5-9, 11, 12** are provided.

Supplementary material is available on the publishers Web site along with the published article.

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