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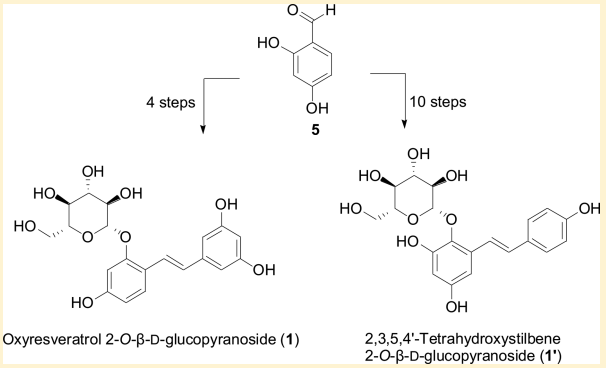
Total Synthesis of Two Glycosylated Stilbenes, Oxyresveratrol 2-*O*-*β*-D-Glucopyranoside and 2,3,5,4′-Tetrahydroxystilbene 2-*O*-*β*-D-Glucopyranoside

Sunil Kumar, Hsueh-Yun Lee, and Jing-Ping Liou*

School of Pharmacy, College of Pharmacy, Taipei Medical University, Taipei 11031, Taiwan

Supporting Information

ABSTRACT: Glycosylated stilbenes are biologically active secondary metabolites of plants and have the potential to alleviate a broad range of human diseases. However, some of these compounds are not naturally abundant, and thus the synthesis of such molecules is desirable. This paper reports the first synthesis of oxyresveratrol 2-*O*-*β*-D-glucopyranoside (**1**) and 2,3,5,4′-tetrahydroxystilbene 2-*O*-*β*-D-glucopyranoside (**1′**), which are stilbene glycosides obtained from the rhizomes of *Schoenocaulon officinale* and *Polygonum multiflorum*, respectively. A facile four-step synthesis of **1** involved selective protection of the hydroxy groups and Wittig olefination to generate the compound in 8% overall yield. For compound **1′**, a 10-step synthesis utilized selective protection of the hydroxy groups, Baeyer−Villiger oxidation, modified Duff formylation, and Wittig olefination to generate the compound in 6.9% overall yield.



Glycosylated stilbenes are congeners of resveratrol and fall under the broad category of phenolic substances, also known as phytoalexins.[1] Over the past several decades, significant research attention has been directed to the investigation of these compounds, which constitute members of a large class of secondary metabolites in plants,[2] especially of spermatophytes. These compounds are abundant in plants and plant-derived foods including grapes and some berries and nuts. A large chemical class of (poly)phenolic compounds, monomers, oligomers, and glycosylated derivatives of the stilbenoids have been isolated and broadly studied. Perhaps the best known examples are resveratrol[3] and astringin,[4] which are shown in Figure 1. Oxyresveratrol 2-*O*-*β*-D-glucopyranoside (**1**) has been isolated from the rhizome of *Schoenocaulon officinale* A. Gray (Melanthiaceae), an ornamental plant growing in the Sinai region of Egypt.[5] It has also been obtained from the root bark of *Morus alba* var. *multicaulis*[6] and the roots of *Morus nigra*.[7] According to the *Chinese Pharmacopeia*, compound **1** is derived from the root bark of *M. alba*, which is used as a well-known traditional Chinese herbal medicine.[8] A decoction has been used traditionally as an antitussive and antiasthmatic agent.[9] Compound **1** has been identified as an inhibitor of tyrosinase, which is a key enzyme responsible for enzymatic browning of many plant-derived food products. Enzymatic browning in most fresh fruits and vegetables usually leads to deterioration of the nutritional quality, and consequently, the use of tyrosinase inhibitors is one of a number of possible methods with which to suppress undesirable browning reactions and maintain the quality of the food products.[7]

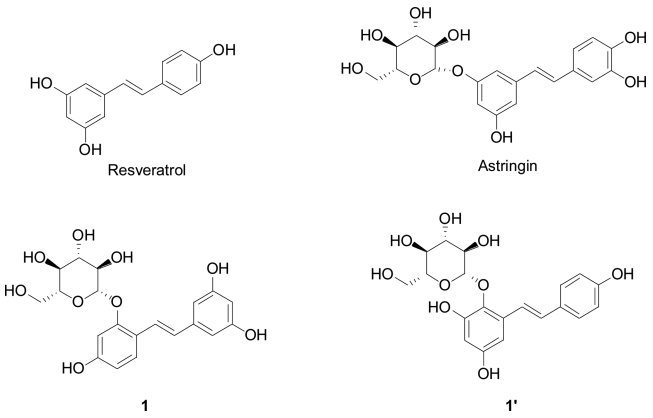


Figure 1. Structure of hydroxystilbenes.

2,3,5,4′-Tetrahydroxystilbene 2-*O*-*β*-D-glucopyranoside (**1′**) was first isolated in 1975 by Hata et al. from the traditional Chinese herb *Polygonum multiflorum* Thunb. (Polygonaceae).[10−12] To date, this compound has attracted scientific attention as a result of its diverse biological activities, which include antitumor,[13] antioxidant,[11] promotion of hair growth,[14] antimelanogenic activity,[15] neuron protection,[16] amelioration of vascular dysfunction,[17] antiaggregation,[18] antiatherosclerosis,[19] improvement of age-related cognitive impairment,[20] and anti-

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inflammatory effects.[21] However, detailed pharmacological study of these compounds so far has been minimal. Compound **1** has been isolated in low yield (0.006% w/w) from a natural source. Although compound **1′** is commercially available in satisfactory yield from natural sources, the synthetic routes required to synthesize various analogues and explore their bioactivity and medicinal potential are lengthy and difficult. The potential of these compounds as lead compounds has been hampered by the lack of appropriate synthetic methodology. In view of the diverse medicinal attributes of these phytoconstituents, the present study is important in the fields of medicinal chemistry and natural products research. Construction of multisubstituted arenes remains a challenge in natural product synthesis, and, on the basis of retrosynthetic analysis, we became intrigued with the possibility of synthesizing the multisubstituted arenes **1** and **1′**. Syntheses of such valuable bioactive molecules from a natural source are very important and can be applied for the synthesis of diverse analogues of these molecules in the future.

Figure 2 outlines the retrosynthetic methodology aimed at the desired structure **1**. It was envisaged that deprotection of

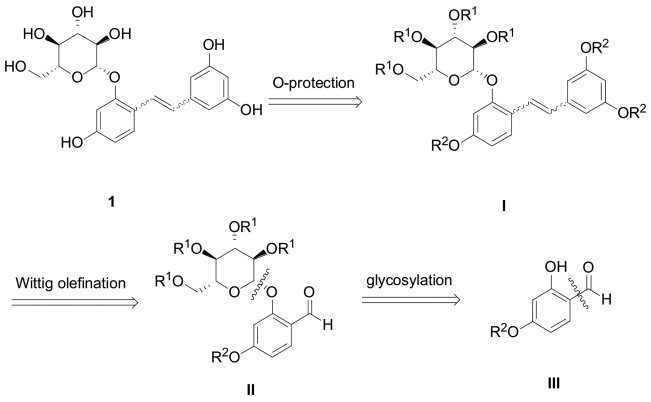

Figure 2. Retrosynthetic analysis of oxyresveratrol 2-*O*-*β*-D-glucopyranoside (**1**).

various hydroxy groups, which are masked by appropriate protecting groups (**I**) to minimize their influence on the synthetic process, would give **1**. Structure **I**, containing a stilbene moiety, could be constructed by Wittig olefination of the corresponding O-protected glycoside benzaldehyde (**II**). Compound **II** could then be synthesized from the selectively protected, readily available, and cost-effective reagent 2,4-dihydroxybenzaldehyde (**III**). Selective protection and deprotection are the crucial steps in this synthetic route.

Figure 3 outlines retrosynthetic methodologies aimed at the desired structure **1′**. Tamura et al. failed to achieve the synthesis of 2,3,5,4′-tetrahydroxystilbene 2-*O*-*β*-D-glucopyranoside (**1′**), although their synthesis of 2,3,5,4′-tetrahydroxystilbene was successful.[22] One encounters the problem of selective *O*-glycosylation of the many phenolic hydroxy groups. Therefore, these various hydroxy groups were masked by appropriate protecting groups (**I′**) to minimize their influence on the synthetic process. The C=C double bond was envisioned as being formed by Wittig olefination, which uses the corresponding O-protected benzaldehyde (**II′**) and phosphonium ylide. The glycoside **II′** can be synthesized by reaction of 2-hydroxybenzaldehyde (**III′**) with the corresponding glucosyl bromide. Compound **III′** can then synthesized by Duff formylation, which specifically introduces a formyl group at the *ortho*-position of the phenol (**IV′**). This in turn can be synthesized from compound **V′** under Baeyer−Villiger oxidation conditions.

There are no published synthetic routes to oxyresveratrol 2-*O*-*β*-D-glucopyranoside (**1**) or 2,3,5,4′-tetrahydroxystilbene 2-*O*-*β*-D-glucopyranoside (**1′**), but compound **1** has been constructed in four steps (Scheme 2) using conventional reactions such as glycosylation and Wittig olefination, based on the retrosynthetic analysis depicted in Figure 2. Phosphonium ylide (**9**) was synthesized as shown in Scheme 1 and used subsequently in a Wittig olefination (Scheme 2). As shown in Scheme 1, the hydroxy group of compound **6** was masked by a *tert*-butyldimethylsilyl (TBDMS) group, and the aldehyde was reduced using $NaBH_4$ to afford compound **7**. The hydroxy group of compound **7** was replaced by bromine using CBr_4 and PPh_3 under milder Appel reaction conditions,[23] and the resulting product was reacted with PPh_3 in the presence of refluxing toluene, generating the phosphonium ylide **9**.

The synthesis of compound **1** shown in Scheme 2 began with readily available 2,4-dihydroxybenzaldehyde (**5**), in which the hydroxy group at the *para*-position was selectively protected with a TBDMS group. Glycosylation of compound **4** with 2,3,4,6-tetra-*O*-acetyl-*α*-D-glucopyranosyl bromide under basic conditions, in the presence of the phase transfer catalyst tetra-*n*-butylammonium bromide (TBAB), yielded compound **3** in 75% yield. Reaction of the benzaldehyde **3** with the phosphonium ylide **9** under conditions of the Wittig reaction generated the *trans*-stilbenoid isomer (**2a**, 50%) and its *cis*-stilbenoid isomer (**2b**, 20%), which were separated by column chromatography. The *trans* double bond of compound **2a** was confirmed by the large coupling constant (J = 16.5 Hz) in its NMR spectrum. The TBDMS group of the isomers (**2a**) was removed by treatment with tetra-*n*-butylammonium fluoride (TBAF) followed by deacetylation in the presence of sodium methoxide and Dowex resin to afford **1**. The spectra of this synthetic compound (**1**) matched the published data.[5]

The phosphonium ylide (**14**) was synthesized as shown in Scheme 3 for use in the Wittig olefination (Scheme 4). The hydroxy group of compound **11** was masked by TBDMS, and the aldehyde was reduced using $NaBH_4$ to produce compound **13**. The hydroxy group of compound **13** was replaced by bromine using CBr_4 and PPh_3 under milder Appel reaction conditions,[23] and the resulting product was reacted with PPh_3 in refluxing toluene, generating the phosphonium ylide **14**.

Scheme 4 shows the synthesis of 2,3,5,4′-tetrahydroxystilbene 2-*O*-*β*-D-glucopyranoside (**1′**) based on the retrosynthesis procedure depicted in Figure 3. Compound **5** reacted with benzyl bromide in the presence of K_2CO_3 to afford compound **10** in 98% yield. The formyl group of compound **10** was converted into a hydroxy group under the conditions of Baeyer−Villiger oxidation, yielding the corresponding phenol (**9′**) in 95% yield.[24] This resorcinol can be protected by groups such as acetyl (Ac), methoxymethyl (MOM), and TBDMS, but such groups fail to survive the acidic conditions of the Baeyer−Villiger oxidation. The Duff formylation of compound **9′** was first carried out by hexamethylenetetramine (HMTA) in the presence of refluxing acetic acid, generating compound **8′**, a critical building block, but in only 20% yield.[25] To improve this yield, a mixture of HMTA and acetic acid was prepared prior to the addition of compound **9′** (see Experimental Section). This modified procedure led to an increase in the yield from 20% to 55%. Glycosylation of compound **8′** with 2,3,4,6-tetra-*O*-acetyl-*α*-D-glucopyranosyl bromide under basic conditions, in the

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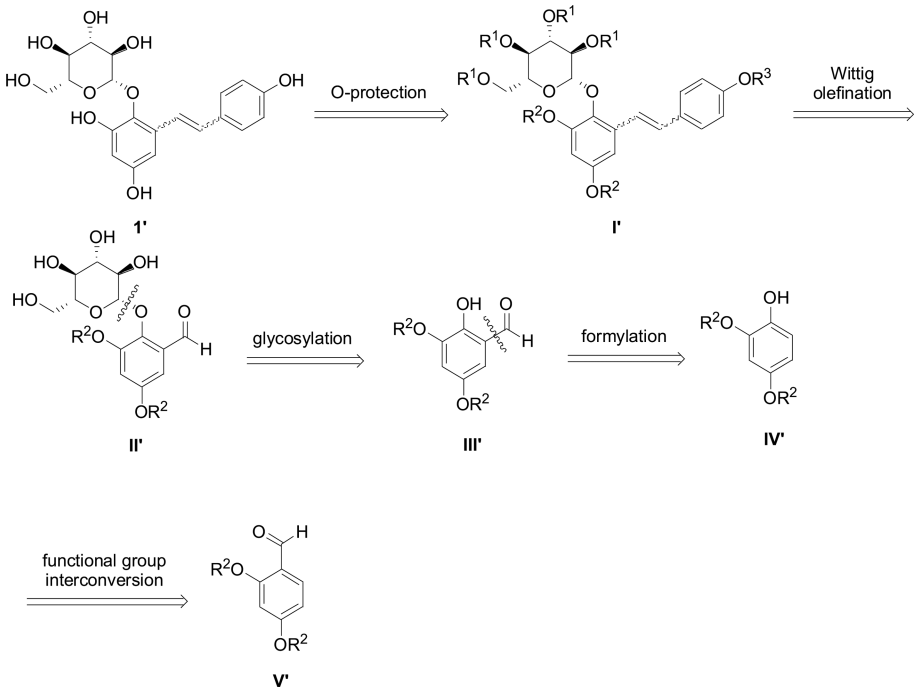
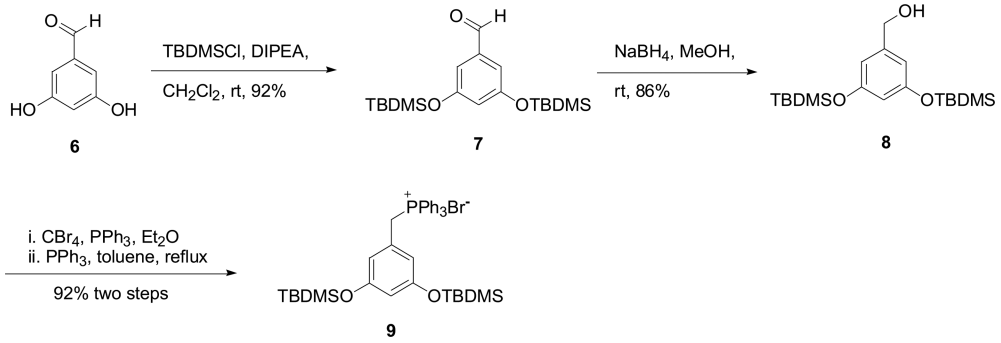


Figure 3. Retrosynthetic analysis of 2,3,5,4′-tetrahydroxystilbene 2-*O*-*β*-D-glucopyranoside (**1′**).

Scheme 1. Synthesis of Phosphonium Ylide 9



presence of the phase-transfer catalyst TBAB, yielded compound **7′** in 75% yield. To avoid the difficult task of selective debenzylation, the benzyl groups in **7′** were all removed and replaced by the protecting group TBDMS. Compound **7′** underwent hydrogenolysis of the benzyl moieties, together with the reduction of the formyl group, to yield compound **6′**. This unexpected reduction of benzaldehyde to benzyl alcohol was also observed in some studies, and the resulting product may be confirmed by instrumental analysis methods such as HRMS, ^{1}H NMR, and ^{13}C NMR.[26,27] This benzyl alcohol was oxidized by pyridinium dichromate (PDC) to afford the corresponding benzaldehyde (**5′**), which was subsequently reacted with TBDMS-Cl to obtain compound **4′**.

The reaction of the benzaldehyde **4′** with the phosphonium ylide **14** under conditions of the Wittig reaction generated the *trans*-stilbenoid isomer (**3′a**, 20%) and its *cis*-stilbenoid isomer (**3′b**, 40%), which were purified by column chromatography. The *trans* double bond of compound **3′a** gave a doublet (J = 16.5 Hz) in its NMR spectrum. The TBDMS of compounds **3′a** and **3′b** was removed by TBAF to afford the corresponding compounds **2′a** and **2′b**. Both **2′a** and **2′b** were converted into *trans*-2,3,5,4′-tetrahydroxystilbene 2-*O*-*β*-D-glucopyranoside (**1′**) by treating with KOH in EtOH. The spectra of synthetic **1′** matched the published spectra.[12]

The unexpected conversion of compound **2′b** to **1′**, which was also observed in the study by Ren and co-workers,[28] triggered an attempt to simplify the synthetic route without the complicated process for the resolution of the geometric isomers **3′a** and **3′b**. The mixture of geometric products produced by Wittig olefination was directly deprotected by tetra-*n*-butylammonium fluoride, yielding a mixture of **2′a** and **2′b**. This mixture was treated subsequently with KOH in EtOH to afford the desired compound **1′**. The *β*-D-glucopyranoside configuration of these compounds was confirmed by the coupling constant (J = 8.0 Hz) of the anomeric proton, which served to distinguish this compound from the *α*-anomer (J = 3.8 Hz).[25]

In summary, the first total syntheses of the naturally occurring and biologically interesting oxyresveratrol 2-*O*-*β*-D-glucopyranoside (**1**) and 2,3,5,4′-tetrahydroxystilbene 2-*O*-*β*-D-glucopyranoside (**1′**) have been achieved. Synthesis of **1** utilized a four-step synthesis from the commercially available 2,4-dihydroxybenzaldehyde (**5**) and gave compound **1** in an overall yield of 8%. However, 10 steps were required to produce **1′** in an overall yield of 6.9% from the same starting

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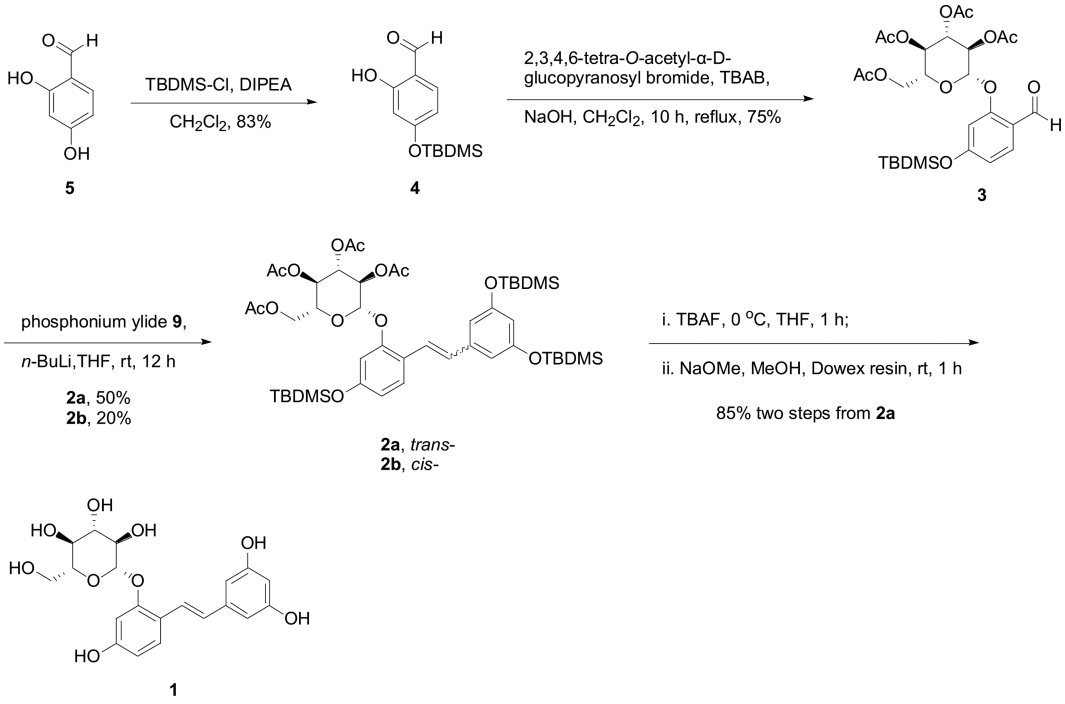
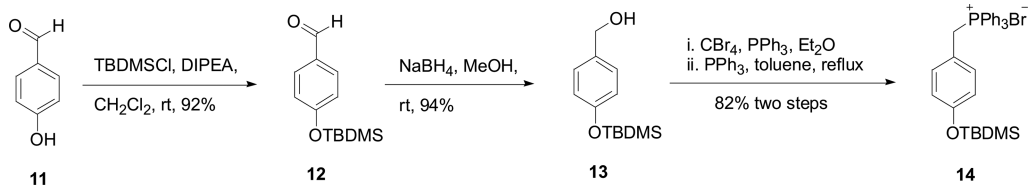
Scheme 2. Synthetic Approach to Compound 1



Scheme 3. Synthesis of Phosphonium Ylide 14



material **3**. The presently described synthesis of compound **1** features (a) selective glycosylation of a molecule with two hydroxy groups (**5** → **4** → **3**) and (b) Wittig olefination at room temperature (rt) using a nonpolar solvent to obtain more of the *trans* isomer than the *cis* isomer for compound **1′**. Application of reactions in the synthesis of the trihydroxybenzene ring demonstrated herein was not trivial. The final product (**1′**) was produced as a single isomer without purification of two isomeric mixtures formed during Wittig olefination. The total synthesis of these compounds thus provides an efficient synthetic route to diverse stilbene glycosides that can be used in further investigations.

EXPERIMENTAL SECTION

General Experimental Procedures. Unless otherwise specified, all reactions were performed under a nitrogen atmosphere with dry solvents under anhydrous conditions. Anhydrous toluene, tetrahydrofuran (THF), MeOH, Me_2CO, and Et_2O were obtained by passing the commercially available, oxygen-free solvents through activated alumina columns from Glass Contour. CH_2Cl_2 was distilled over calcium hydride under a nitrogen atmosphere. Yields refer to materials purified using silica gel column chromatography (Merck Kieselgel 60, no. 9385, 230−400 mesh ASTM). Optical rotations were recorded with a P-2000 digital polarimeter (JASCO, Tokyo, Japan). Melting points were measured with a Fargo melting point apparatus, MP-1D. ^{1}H NMR and ^{13}C NMR spectra were obtained with a Bruker DRX-500 NMR spectrometer (operating at 500 and 125 MHz) and a Bruker DRX-300 NMR spectrometer (operating at 300 and 75 MHz, respectively). Chemical shifts are reported in parts per million (ppm, δ) downfield from tetramethylsilane as an internal standard. High-resolution mass spectra (HRMS) were measured with a JEOL (JMS-700) electron-impact (ESI) mass spectrometer.

Oxyreveratrol 2-*O*-β-D-Glucopyranoside (1). A mixture of compound **2a** (1.0 g, 1.51 mmol), anhydrous THF (20 mL), and TBAF (1.0 M solution in THF, 4.25 mL) was stirred at 0 °C for 15 min. The reaction was quenched with ice-cold 6 N HCl (6.77 mL), and the mixture was extracted with EtOAc (4 × 50 mL). The combined organic layer was dried over $MgSO_4$ and evaporated in vacuo to give a residue (500 mg, 80% yield), which was used directly for the next step without further purification.

Sodium methoxide (0.094 g, 2 equiv) in MeOH was stirred in a flask at rt. In a separate flask, the residue obtained from the above reaction (0.50 g, 0.87 mmol) was dissolved in dry MeOH and added to a sodium methoxide solution, stirring continually for 1 h. After completion of the reaction, Dowex resin was added to neutralize the reaction mixture and a slurry was made in silica gel and purified by flash column chromatography (20:1 EtOAc−MeOH) to afford compound **1** (0.30 g, 85%) as an amorphous powder: $[\alpha]^{24.5}_D$ −59.1 (*c* 2.1, MeOH); ^{1}H NMR (500 MHz, MeOD) δ 7.41 (1H, *J* = 9.5 Hz, d), 7.28 (1H, *J* = 16.5 Hz, d), 6.88 (1H, *J* = 16.5 Hz, d), 6.60 (1H, *J* = 2.5 Hz, d), 6.58 (1H, *J* = 8.5, 2.5 Hz, dd), 6.46 (2H, *J* = 2.0 Hz, d), 6.16 (1H, *J* = 2.0 Hz, t), 4.88 (1H, *J* = 7.5 Hz, d), 3.93 (1H, *J* = 12.0, 2.0 Hz, dd), 3.72 (1H, *J* = 12.0, 5.0 Hz, dd), 3.47−3.30 (4H, m); ^{13}C NMR (125 MHz, MeOD) δ 159.7, 159.6, 157.2, 141.9, 130.9, 128.4, 128.1, 124.5, 120.5, 109.5, 105.9, 105.1, 102.7, 102.2, 78.3, 78.1, 74.9, 71.5, 62.6, 61.7; HRESIMS *m*/*z* 407.1339 $[M + H]^+$ (calcd for $C_{20}H_{22}O_9$, 407.1264).

2-Hydroxy-4-(*tert*-butyldimethylsilanyloxy)benzaldehyde (4). Di-isopropylethylamine (2.6 mL, 1.1 equiv) was added dropwise to a solution of 2,4-dihydroxybenzaldehyde (2.0 g, 14.5 mmol) and

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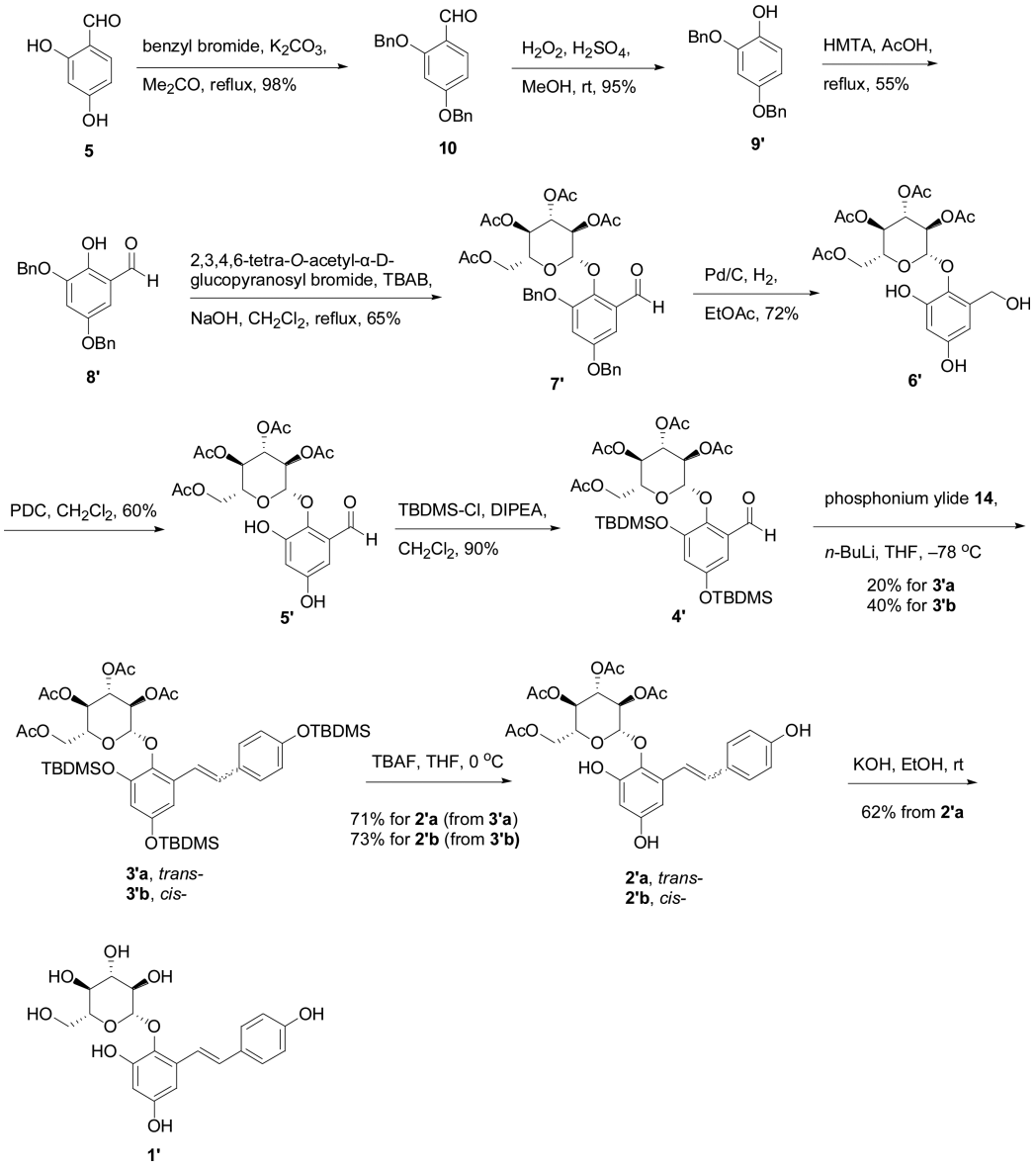
Scheme 4. Synthetic Approach to Compound 1′



tert-butyldimethylsilyl chloride (2.4 g, 1.1 equiv) in dry CH_2Cl_2 (20 mL), and the mixture was stirred for 3 h. The reaction was quenched with H_2O (50 mL) and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layer was evaporated under reduced pressure to give a crude product, which was purified by flash chromatography (1:3 EtOAc–*n*-hexanes) to afford **4** (3 g, 83.3%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.75 (1H, s), 7.43 (1H, J = 9.6 Hz, d), 6.50 (1H, J = 8.7, 2.1 Hz, dd), 6.41 (1H, J = 2.1 Hz, d), 1.02 (9H, s), 0.29 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 191.4, 161.5, 161.2, 132.8, 113.2, 110.5, 105.0, 23.0, 22.9, −6.2; HRESIMS m/z 253.1261 $[M + H]^+$ (calcd for $C_{13}H_{20}O_3Si$, 253.1181).

2-Hydroxy-4-(*tert*-butyldimethylsilanyloxy)benzaldehyde 2-*O*-*β*-D-Glucoside Acetate (3). Tetrabutylammonium bromide (1.2 g, 0.2 equiv) and 2,3,4,6-tetra-*O*-acetyl-*α*-D-glucopyranosyl bromide (5.4 g, 1.2 equiv) were added to a solution of compound **4** (3.0 g, 11.9 mmol), in aqueous NaOH (0.48 g, 1 equiv) and CH_2Cl_2 (100 mL). The mixture was stirred vigorously at 65–70 °C for 12 h, then quenched with H_2O and extracted with CH_2Cl_2, dried over $MgSO_4$, and evaporated in vacuo to yield the crude product, which was purified by column chromatography over silica gel to give **3** (5.0 g, 72.5%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.32 (1H, s), 7.78 (1H, J = 9.0, 1.2 Hz, dd), 6.65 (1H, J = 3.6, 1.2 Hz, dd), 6.45 (1H, J = 2.1 Hz, d), 5.33–5.16 (4H, m), 4.32 (1H, J = 5.1, 12.6 Hz, dd), 4.16 (1H, J = 2.1, 9.9 Hz, dd), 3.91 (1H, octet), 2.08 (3H, s), 2.07 (3H, s), 2.06 (3H, s), 2.05 (3H, s), 1.03 (9H, s), 0.29 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 185.9, 167.8, 167.5, 166.7, 159.6, 157.8, 127.5, 120.5, 106.9, 105.4, 95.4, 69.9, 68.3, 65.3, 59.1, 22.9, 18.0, 17.9, 15.7, −6.2, −6.9, −7.0; HRESIMS m/z 583.2216 $[M + H]^+$ (calcd for $C_{27}H_{38}O_{12}Si$, 583.2133).

2-Hydroxy-4,3′,5′-tris(*tert*-butyldimethylsilanyloxy) 2-*O*-*β*-D-Glucoside Acetate (2a, 2b). *n*-BuLi (1.6 M in hexane, 3.2 mL) was added dropwise to a suspension of compound **9** (2.68 g, 3.86 mmol) in toluene (20 mL), and the resulting mixture was stirred at rt for 30 min. Then, a solution of compound **3** (1.5 g, 2.57 mmol) in toluene (5 mL) was added, and stirring was continued at rt for 8 h. The reaction was quenched with cold H_2O (30 mL), and the product extracted with EtOAc (3 × 10 mL). The combined organic layer was dried over $MgSO_4$ and evaporated in vacuo to give a residue, which was purified by flash column chromatography over silica gel (1:10 EtOAc–*n*-hexane) to afford **2a** (1.18 g, 50%) and **2b** (0.47 g, 20%) as white solids. For **2a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.54 (1H, J = 8.4 Hz, d), 7.33 (1H, J = 16.2 Hz, d), 7.29 (1H, s), 6.84 (1H, J = 16.2 Hz, d), 6.65 (2H, J = 8.1 Hz, d), 6.51 (1H, J = 2.1 Hz, d), 6.27 (1H, J = 1.5 Hz, d), 5.34–5.22 (3H, m), 5.09 (1H, J = 6.6 Hz, d), 4.35 (1H, J = 4.2,

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4.5 Hz, dd), 4.19 (1H, J = 11.4 Hz, d), 3.88 (1H, J = 7.5 Hz, d), 2.13 (3H, s), 2.12 (3H, s), 2.11 (3H, s), 2.08 (3H, s), 1.08 (9H, s), 1.03 (9H, s), 1.02 (9H, s), 0.27 (6H, s), 0.24 (6H, s), 0.23 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.0, 167.7, 166.8, 166.7, 154.5, 154.4, 154.0, 151.3, 137.3, 136.9, 124.8, 124.2, 124.0, 121.7, 120.6, 120.3, 108.9, 108.7, 107.4, 106.1, 96.6, 70.1, 69.5, 68.5, 65.5, 59.2, 33.9, 27.1, 23.2, 23.1, 22.0, 18.1, 17.9, 16.9, 15.7, 15.6, 10.9, −1.6, −6.7, −6.8, −6.9, −7.0; HRESIMS m/z 916.4286 $[M + H]^+$ (calcd for $C_{46}H_{72}O_{13}Si_3$, 916.4281).

For **2b**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.09 (1H, J = 8.7 Hz, d), 6.56 (1H, J = 12 Hz, d), 6.49−6.46 (2H, m), 6.42 (1H, J = 2.7, 2.1 Hz, dd), 6.37 (2H, J = 1.8 Hz, d), 6.20 (1H, J = 2.1 Hz, d), 5.31−5.17 (3H, m), 5.01 (1H, J = 7.5 Hz, d), 4.36 (1H, J = 4.8, 4.8 Hz, dd), 4.14 (1H, J = 10.5 Hz, d), 3.82 (1H, octet), 2.08 (3H, s), 2.07 (3H, s), 2.06 (3H, s), 2.05 (3H, s), 1.03 (9H, s), 0.95 (18H, s), 0.25 (6H, s), 0.11 (12H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.9, 167.6, 166.7, 166.6, 154.3, 153.7, 151.8, 136.4, 128.4, 126.7, 123.5, 121.7, 111.2, 108.5, 106.7, 106.1, 96.5, 70.1, 69.4, 68.4, 65.5, 59.2, 27.1, 23.1, 23.0, 22.8, 18.1, 18.0, 17.9, 15.6, 15.5, −1.6, −6.7, −6.8, −7.1; HRESIMS m/z 916.4278 $[M + H]^+$ (calcd for $C_{46}H_{72}O_{13}Si_3$, 916.4281).

3,5-Di(*tert*-butyldimethylsilanyloxy)benzaldehyde (7). A solution of 3,5-dihydroxybenzaldehyde (2.0 g, 14.5 mmol) and diisopropylethylamine (6 mL, 2.2 equiv) in dry CH_2Cl_2 (50 mL) was stirred for 10 min at rt. To the solution was added *tert*-butyldimethylsilyl chloride (5.46 g, 2.2 equiv) in portions, and the mixture was stirred for 12 h. The reaction was quenched with H_2O and extracted with CH_2Cl_2 (3 × 30 mL), and the combined organic layer was evaporated under reduced pressure to give a pale yellow oil, which was purified by flash chromatography (1:3 EtOAc−*n*-hexane) to afford **7** (4.88 g, 92%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.89 (1H, s), 6.99 (2H, J = 2.4 Hz, d), 6.62 (1H, J = 2.4 Hz, t), 1.02 (18H, s), 0.25 (12H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 189.2, 154.6, 115.8, 111.7, 22.9, 15.6, −7.1.

[3,5-Di(*tert*-butyldimethylsilanyloxy)phenyl]methanol (8). A mixture of compound **7** (4.5 g, 12.27 mmol), $NaBH_4$ (0.510 g, 13.50 mmol), and MeOH (25 mL) was stirred at room temperature for 30 min. The reaction was quenched with dilute aqueous HCl and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layer was dried over anhydrous $MgSO_4$ and then evaporated in vacuo to give a residue, which was purified by flash column chromatography over silica gel (1:3 EtOAc−*n*-hexane) to afford **8** (3.89 g, 86%) as a colorless liquid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.50 (2H, J = 2.1 Hz, d), 6.29 (2H, J = 2.4 Hz, t), 4.58 (2H, s), 2.04 (1H, s, D_2O exchangeable), 1.02 (18H, s), 0.24 (12H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.0, 140.5, 109.1, 108.5, 62.4, 23.1, 15.6, −7.0; HRESIMS m/z 368.2205 $[M]^+$ (calcd for $C_{19}H_{36}O_3Si_2$, 368.2203).

[3,5-Di(*tert*-butyldimethylsilanyloxy)phenyl]methyl Triphenylphosphonium Bromide (9). Compound **8** (3.5 g, 9.49 mmol) was treated with PPh_3 (2.2 equiv) and CBr_4 (4.4 equiv) in Et_2O to afford the crude corresponding benzyl bromide (80% yield), which was used for the next step without further purification. The product was dissolved in dry toluene (35 mL), and Ph_3P (3.3 g, 4.72 mmol) was added, and the reaction mixture was refluxed for 12 h under N_2. The corresponding phosphonium salt (**9**) precipitated as a white solid during the reaction and was collected by filtration (4.88 g, 92% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.72−7.53 (15H, m), 6.13 (1H, J = 1.8 Hz, d), 6.03 (2H, s), 5.03 (2H, J = 14.4 Hz, d), 0.77 (18H, s), 0.08 (12H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.3, 154.2, 132.4, 132.3, 131.6, 131.4, 127.6, 127.5, 126.1, 125.9, 115.6, 114.5, 113.4, 113.3, 109.7, 109.6, 22.8, 15.3, −7.2.

***trans*-2,3,5,4′-Tetrahydroxystilbene 2-*O*-β-D-Glucopyranoside (1′).** A mixture of **2′a** (0.55 g, 0.96 mmol), EtOH (10 mL), and KOH (0.27 g, 4.7 mmol) was stirred at rt for 40 min. The reaction mixture was quenched with H_2O (10 mL) and extracted with $CHCl_3$ (3 × 10 mL). The combined organic layers were dried over $MgSO_4$ and evaporated in vacuo to give a residue, which was purified by flash column chromatography on silica gel (4:1 EtOAc−*n*-hexanes) to afford compound **1** (0.24 g, 62%) as a pale yellow powder: mp 167−169 °C; $[\alpha]^{24.5}_D$ +73.0 (c 0.63, Me_2CO); ^{1}H NMR (300 MHz, MeOD) δ 7.76 (1H, J = 16.5 Hz, d), 7.51 (2H, J = 8.7 Hz, d), 6.98 (1H, J = 16.5 Hz, d), 6.82 (2H, J = 8.4 Hz, d), 6.67 (1H, J = 3.0 Hz, d), 6.30 (1H, J = 2.7 Hz, d), 4.56 (1H, J = 8.1 Hz, d) 3.35−3.87 (6H, m); ^{13}C NMR (75 MHz, MeOD) δ 156.9, 154.5, 150.6, 136.5, 132.3, 129.4, 128.6, 127.8, 120.3, 115.0, 106.8, 102.2, 101.3, 76.8, 76.5, 74.1, 69.3, 60.7; HRESIMS m/z 405.1176 $[M - H]^-$ (calcd for $C_{20}H_{21}O_9$, 405.1180).

2,4-Bis(benzyloxy)benzaldehyde (10). The preparation of the title compound followed the published procedure:[29] yield 98%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.43 (1H, s), 7.88 (1H, J = 8.4 Hz, d), 7.47−7.38 (10H, m), 6.68 (1H, J = 2.1 Hz, d), 6.64 (1H, J = 2.1 Hz, d), 5.15 (2H, s), 5.12 (2H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 188.3, 165.2, 135.9, 130.5, 128.8, 128.4, 128.3, 127.6, 127.3, 119.5, 107.1, 100.1, 70.4, 70.4; HRESIMS m/z 341.1144 $[M + Na]^+$ (calcd for $C_{21}H_{18}O_3Na$, 341.1148).

2,4-Bisbenzyloxyphenol (9′). The reported method[30] gave the title compound in 21% yield. In the present case, the reaction procedure was modified to improve the reaction yield to 95%. A solution of compound **10** (22 g, 69.2 mmol) in MeOH (200 mL) was placed in a wide-mouth tube and stirred at 40 °C for 5 min. Then, H_2O_2 (16 mL, 35% w/v in H_2O) and concentrated H_2SO_4 (2−3 drops) were added simultaneously, and the mixture was stirred at rt for 2 h. The reaction was quenched with H_2O and filtered to give compound **9′** (20.1 g, 95%) as a white powder: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47−7.35 (10H, m), 6.90 (1H, J = 8.7 Hz, d), 6.68 (1H, J = 2.7 Hz, d), 6.54 (1H, J = 3.0, 2.7 Hz, dd), 5.36 (1H, s, D_2O exchangeable), 5.08 (2H, s), 5.02 (2H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.6, 146.2, 140.3, 137.2, 136.2, 128.8, 128.6, 128.5, 127.9, 127.8, 127.6, 114.4, 106.2, 101.8, 71.1, 70.8; HRESIMS m/z 307.1330 $[M + H]^+$ (calcd for $C_{20}H_{19}O_3$, 307.1329).

3,5-Bis(benzyloxy)-2-hydroxybenzaldehyde (8′). A mixture of HMTA (9.15 g, 65.4 mmol) and AcOH (20 mL) was stirred for 5 min in a round-bottomed flask. To this mixture was added a solution of compound **9′** (20 g, 65.4 mmol) and AcOH (4−5 drops) in dimethylformamide (40 mL), and the solution was then heated at reflux for 3 h. The reaction was quenched with H_2O and extracted with CH_2Cl_2 (6 × 100 mL). The combined organic phase was washed with brine (3 × 10 mL), dried over $MgSO_4$, and concentrated in vacuo to furnish a pale yellow oil. The resulting residue was purified by column chromatography over silica gel (1:10 EtOAc−*n*-hexanes) to afford compound **8′** (12 g, 55%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.62 (1H, s), 9.88 (1H, s, D_2O exchangeable), 7.47−7.34 (10H, m), 6.87 (1H, J = 2.7 Hz, d), 6.71 (1H, J = 2.7 Hz, d), 5.17 (2H, s), 5.02 (2H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.9, 151.7, 148.1, 147.3, 136.4, 136.2, 128.7, 128.3, 128.2, 127.6, 127.4, 119.9, 110.9, 106.6, 71.3, 70.8; HRESIMS m/z 333.1118 $[M - H]^-$ (calcd for $C_{21}H_{17}O_4$, 333.1121).

3,5-Bis(benzyloxy)benzaldehyde-2-*O*-β-D-glucoside Acetate (7′). Tetrabutylammonium bromide (1.2 equiv) and 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (1.2 equiv) were added to a mixture of compound **8′** (11.9 g, 35.6 mmol), aqueous NaOH (1 equiv), and CH_2Cl_2, and the mixture was stirred vigorously at 65−70 °C for 12 h. The reaction was quenched with H_2O, extracted with CH_2Cl_2, dried over $MgSO_4$, and evaporated in vacuo to yield a crude product, which was purified by column chromatography over silica gel to give **7′** (15.37 g, 65%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.33 (1H, s), 7.44−7.34 (10H, m), 7.01 (1H, J = 3.0 Hz, d), 6.90 (1H, J = 3.0 Hz, d), 5.30−5.05 (8H, m), 4.18 (1H, J = 4.8, 4.8 Hz, dd), 3.96 (1H, J = 2.4, 2.4 Hz, dd), 3.59 (1H, octet), 2.03 (3H, s), 2.02 (3H, s), 2.00 (3H, s), 1.71 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 190.4, 170.6, 170.2, 169.6, 169.4, 156.3, 151.9, 141.7, 136.2, 135.7, 131.6, 128.8, 128.7, 128.5, 128.3, 127.7, 108.4, 101.0, 100.6, 72.6, 71.7, 71.2, 71.0, 70.5, 68.4, 61.4, 20.6, 20.1; HRESIMS m/z 687.2045 $[M + Na]^+$ (calcd for $C_{35}H_{36}O_{13}Na$, 687.2048).

6-Hydroxymethyl-1,2,4-trihydroxybenzene 2-*O*-β-D-Glucoside Acetate (6′). A mixture of compound **7′** (15 g, 22.59 mmol), 10% Pd/C (1.0 g), and EtOAc (150 mL) was shaken under hydrogen in a Parr apparatus at 45 psi for 16 h. The reaction mixture was filtered through a pad of Celite, and the filtrate was purified by column chromatography over silica gel (1:2 EtOAc−*n*-hexanes) to afford **6′** (8.1 g, 72%): ^{1}H NMR (300 MHz, DMSO) δ 9.04 (1H, s), 8.95 (1H, s), 6.30 (1H, J = 3.0 Hz, d), 6.19 (1H, J = 3.0 Hz, d), 5.36−3.93 (7H,

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m), 2.03 (3H, s), 1.98 (3H, s), 1.97 (3H, s), 1.96 (3H, s); ^{13}C NMR (75 MHz, DMSO) δ 170.5, 170.0, 169.8, 169.7, 154.8, 150.0, 137.9, 133.8, 104.6, 102.2, 101.6, 72.2, 71.6, 70.8, 68.7, 62.3, 58.5, 21.0, 20.9, 20.8, 20.7; HRESIMS m/z 509.1267 $[M + Na]^+$ (calcd for $C_{21}H_{26}O_{13}Na$, 509.1266).

2,3,5-Trihydroxybenzaldehyde 1-*O*-β-D-Glucoside Acetate (5′). A mixture of compound **6′** (8.0 g, 16.4 mmol), pyridinium dichromate (4.26 g, 1.5 equiv), and anhydrous CH_2Cl_2 (150 mL) was stirred at room temperature for 12 h. To the resulting mixture was added a sufficient amount of Celite to absorb the reaction mixture, which then was vigorously stirred until the reaction was complete. The resulting paste was transferred directly to the top of a column of silica gel and subsequently purified by flash column chromatography (1:3 EtOAc−*n*-hexanes) to afford **5′** (4.78 g, 60%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.18 (1H, s), 7.27 (1H, s, D_2O exchangeable), 6.81 (1H, J = 3.0 Hz, d), 6.75 (1H, J = 3.0 Hz, d), 5.38−3.79 (8H, m, 1H D_2O exchangeable), 2.15 (3H, s), 2.11 (3H, s), 2.05 (3H, s), 2.04 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 190.3, 170.9, 170.4, 170.3, 169.8, 169.5, 169.4, 154.6, 150.9, 139.9, 130.0, 110.5, 105.6, 103.4, 72.5, 72.4, 71.5, 67.9, 61.4, 20.7, 20.6, 20.5, 20.5; HRESIMS m/z 483.1126 $[M + H]^+$ (calcd for $C_{21}H_{23}O_{13}$, 483.1133).

2-Hydroxy-3,5-bis(*tert*-butyldimethylsilanyloxy)-benzaldehyde 1-*O*-β-D-Glucoside Acetate (4′). A solution of compound **5′** (4.7 g, 9.7 mmol) and diisopropylethylamine (4.82 mL, 3 equiv) in dry CH_2Cl_2 (100 mL) was stirred at room temperature for 10 min. Then *tert*-butyldimethylsilyl chloride (4.39 g, 3 equiv) was added in portions, and the mixture was stirred for an additional 15 h. The reaction was quenched with H_2O (50 mL) and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layer was evaporated under reduced pressure to give a crude product, which was purified by flash chromatography (1:3 EtOAc−*n*-hexanes) to afford **4′** (6.2 g, 90%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.27 (1H, s), 6.90 (1H, J = 2.7 Hz, d), 6.60 (1H, J = 2.7 Hz, d), 5.34−3.60 (7H, m), 2.07 (3H, s), 2.03(3H, s), 2.01 (3H, s), 1.99 (3H, s), 1.03 (9H, s), 0.97 (9H, s), 0.28 (6H, s), 0.19 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 190.0, 170.6, 170.3, 169.3, 169.2, 152.8, 148.9, 142.3, 131.9, 118.4, 110.4, 99.1, 72.9, 71.9, 71.6, 68.3, 61.25, 25.9, 25.6, 20.8, 20.6, 20.5, 20.5, 18.1, 17.4, −4.0, −4.2, −4.5; HRESIMS m/z 735.2835 $[M + Na]^+$ (calcd for $C_{33}H_{52}O_{13}NaSi_2$, 735.2839).

2-Hydroxy-3,5,4′-tris(*tert*-butyldimethylsilanyloxy) 1-*O*-β-D-Glucoside Acetate (3′a, 3′b). To a suspension of compound **14** (3.56 g, 6.3 mmol) in THF (50 mL) was added dropwise *n*-BuLi (1.6 M in hexane, 8.1 mL) at −78 °C, and the resulting mixture was stirred at the same temperature for 30 min. The reaction was then warmed to rt and stirred for an additional 1 h. The reaction mixture was recooled to −78 °C and then was added to a solution of compound **4′** (3.0 g, 4.2 mmol) in THF (20 mL). Stirring was continued at −78 °C for 1 h, then at rt for 18 h. The reaction was quenched with cold H_2O (30 mL) and extracted with EtOAc (3 × 10 mL). The combined organic layer was dried over $MgSO_4$ and evaporated in vacuo to give a residue, which was purified by flash column chromatography over silica gel (1:10 EtOAc−*n*-hexane) to afford **3′a** (750 mg, 20%) as a pale yellow solid and **3′b** (1.5 g, 40%) as a pale yellow solid. For **3′a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40 (2H, J = 8.7 Hz, d), 7.21 (1H, J = 16.5 Hz, d), 6.88 (1H, J = 16.5 Hz, d), 6.81 (2H, J = 8.7 Hz, d), 6.67 (1H, J = 2.7 Hz, d), 6.25 (1H, J = 2.7 Hz, d), 5.34−3.56 (7H, m), 2.02 (3H, s), 2.01 (3H, s), 1.99 (3H, s), 1.90 (3H, s), 1.01 (9H, s), 0.99 (9H, s), 0.98 (9H, s), 0.26 (6H, s), 0.21 (6H, s), 0.19 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.0, 170.7, 169.8, 169.7, 156.0, 152.6, 149.2, 138.6, 133.3, 131.3, 129.8, 128.3, 121.8, 120.7, 112.1, 109.7, 100.4, 73.7, 72.4, 72.2, 68.7, 61.9, 30.1, 26.3, 26.1, 26.0, 23.7, 21.2, 21.0, 20.9, 20.8, 18.8, 18.6, 18.5, 14.5, −3.8, −3.8, −3.9, −3.9; HRESIMS m/z 917.4344 $[M + H]^+$ (calcd for $C_{46}H_{73}O_{13}Si_3$, 917.4353).

For **3′b**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.00 (2H, J = 6.3 Hz, d), 6.64 (2H, J = 6.3 Hz, d), 6.52 (1H, J = 12.3 Hz, d), 6.47 (1H, J = 12.3 Hz, d), 6.50 (2H, J = 3.6 Hz, d), 5.28−5.10 (4H, m), 4.20 (1H, J = 4.2, 3.9 Hz, dd), 4.11 (1H, J = 2.4, 2.4 Hz, dd), 3.53 (1H, octet), 2.05 (3H, s), 2.02 (3H, s), 1.99 (3H, s), 1.95 (3H, s), 1.03 (9H, s), 0.97 (9H, s), 0.89 (9H, s), 0.22 (6H, s), 0.18 (6H, s), 0.02 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.6, 170.4, 169.4, 169.3, 154.8, 152.0, 148.9, 138.5, 132.9, 130.4, 130.2, 129.8, 124.5, 119.7, 113.7, 112.1, 99.9, 73.2, 71.9, 71.7, 68.4, 61.7, 60.4, 29.7, 25.9, 25.6, 20.8, 20.6, 20.5, 20.5, 18.4, 18.2, 18.1, −3.8, −4.3, −4.4, −4.5; HRESIMS m/z 917.4344 $[M + H]^+$ (calcd for $C_{46}H_{73}O_{13}Si_3$, 917.4353).

***trans*-2,3,5,4′-Tetrahydroxystilbene 2-*O*-β-D-Glucoside Acetate (2′a).** A mixture of compound **3′a** (1.0 g, 1.51 mmol), anhydrous THF (20 mL), and TBAF (1.0 M solution in THF, 4.25 mL) was stirred at 0 °C for 1.5 h. The reaction was quenched with ice cold 6 N HCl (6.77 mL), and the mixture was extracted with EtOAc (4 × 50 mL). The combined organic layer was dried over $MgSO_4$ and evaporated in vacuo to give a residue, which was purified by column chromatography (1:1 EtOAc−*n*-hexanes) to give compound **2′a** (0.62 g, 71%) as a solid: ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.55 (1H, s, D_2O exchangeable), 9.21 (1H, s, D_2O exchangeable), 9.11 (s, 1H, D_2O exchangeable), 7.35 (d, J = 8.7 Hz, 2H), 7.32 (d, J = 16.5 Hz, 1H), 6.87 (1H, J = 16.5 Hz, d), 6.75 (2H, J = 8.7 Hz, d), 6.50 (1H, J = 2.7 Hz, d), 6.30 (1H, J = 2.7 Hz, d), 5.42−5.02 (4H, m), 4.19 (1H, J = 5.1, 4.8 Hz, dd), 4.04 (1H, J = 2.4, 2.4 Hz, dd), 3.80 (1H, m), 2.03 (3H, s), 1.99 (3H, s), 1.99 (3H, s), 1.89 (3H, s); ^{13}C NMR (75 MHz, DMSO-d_6) δ 167.7, 167.4, 167.2, 167.1, 154.9, 152.2, 148.4, 132.6, 130.2, 126.3, 126.1, 125.5, 118.6, 113.3, 100.6, 99.2, 98.8, 69.7, 69.2, 68.1, 65.9, 59.7, 57.6, 18.4, 18.2, 18.1, 11.9; HRESIMS m/z 597.1580 $[M + Na]^+$ (calcd for $C_{28}H_{30}O_{13}Na$, 597.1579).

***cis*-2,3,5,4′-Tetrahydroxystilbene 2-*O*-β-D-Glucoside Acetate (2′b).** The title compound was obtained in 73% overall yield from compound **3′b** in a manner similar to that described for the preparation of **2′b**: ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.46, 9.00, 8.96 (1H, s each, D_2O exchangeable), 7.04 (2H, J = 8.7 Hz, d), 6.62 (2H, J = 8.7 Hz, d), 6.46 (1H, J = 12.3 Hz, d), 6.41 (1H, J = 12.3 Hz, d), 6.23 (1H, J = 2.7 Hz, d), 6.00 (1H, J = 2.7 Hz, d), 5.38−4.94 (4H, m), 4.16−3.93 (3H, m), 2.54 (3H, s), 2.53 (3H, s), 2.52 (3H, s), 2.51 (3H, s); ^{13}C NMR (75 MHz, DMSO-d_6) δ 170.9, 170.2, 170.0, 169.9, 156.5, 154.2, 150.5, 134.8, 132.7, 130.4, 130.1, 128.1, 123.3, 114.5, 106.8, 102.3, 101.9, 72.8, 71.7, 68.4, 61.5, 19.5, 19.2, 19.1, 13.1; HRESIMS m/z 597.1580 $[M + Na]^+$ (calcd for $C_{28}H_{30}O_{13}Na$, 597.1579).

4-(*tert*-Butyldimethylsilanyloxy)benzaldehyde (12). A solution of 4-hydroxybenzaldehyde (5.0 g, 40.9 mmol) and diisopropylethylamine (10 mL, 1.5 equiv) in dry CH_2Cl_2 (100 mL) was stirred for 10 min at room temperature. To the solution was added *tert*-butyldimethylsilyl chloride (9.2 g, 1.5 equiv) in portions, and stirring continued for 12 h. The reaction was quenched with H_2O and extracted with CH_2Cl_2 (3 × 30 mL), and the combined organic layer was evaporated under reduced pressure to give a pale yellow oil, which was purified by flash chromatography (1:3 EtOAc−*n*-hexane) to afford **12** (8.8 g, 92%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.90 (1H, s), 7.80 (2H, J = 8.7 Hz, d), 6.96 (2H, J = 8.7 Hz, d), 1.00 (9H, s), 0.26 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 191.0, 161.6, 132.3, 131.9, 130.4, 120.5, 115.6, 25.6, 25.5, 18.2, −4.4; HRESIMS m/z 237.1294 $[M + H]^+$ (calcd for $C_{13}H_{20}O_2Si$, 237.1305).

[4-(*tert*-Butyldimethylsilanyloxy)phenyl]methanol (13). A mixture of compound **12** (5.0 g, 21.15 mmol), $NaBH_4$ (800 mg, 21.15 mmol), and MeOH (100 mL) was stirred at rt for 30 min. The reaction was quenched with dilute aqueous HCl and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layer was dried over anhydrous $MgSO_4$ and then evaporated in vacuo to give a residue, which was purified by flash column chromatography over silica gel (1:3 EtOAc−*n*-hexane) to afford **13** (4.73 g, 94%) as a colorless liquid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.22 (2H, J = 8.4 Hz, d), 6.84 (2H, J = 8.4 Hz, d), 4.58 (2H, s), 2.19 (1H, s, D_2O exchangeable), 1.00 (9H, s), 0.21 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.2, 133.7, 128.6, 120.1, 64.96, 25.7, −4.4.

[4-(*tert*-Butyldimethylsilanyloxy)phenyl]methyltriphenylphosphonium Bromide (14). Compound **13** (4.5 g, 18.87 mmol) was treated with PPh_3 (2.2 equiv) and CBr_4 (4.4 equiv) in Et_2O to afford the crude benzyl bromide (82% yield), which was used for the next step without further purification. The product was dissolved in toluene (35 mL), Ph_3P (6.97 g, 26.56 mmol) was added, and the reaction mixture was refluxed for 12 h under N_2. The corresponding phosphonium salt (**14**) precipitated as a white solid during the

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reaction and was collected by filtration (89% yield): ^{1}H NMR (300 MHz, DMSO) δ 7.93−7.88 (3H, m), 7.77−7.62 (12H, m), 6.86 (2H, J = 2.7 Hz, d), 6.70 (2H, J = 8.1 Hz, d), 5.13 (2H, J = 15.0 Hz, d), 0.90 (9H, s), 0.14 (6H, s); ^{13}C NMR (75 MHz, DMSO) δ 155.7, 143.8, 135.5, 134.6, 134.4, 132.6, 132.5, 130.6, 130.4, 120.9, 120.8, 120.7, 118.9, 117.8, 25.9, 18.4, −4.2.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.jnatprod.6b00861.

^{1}H NMR, ^{13}C NMR, and HRMS spectra of all synthetic products (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*Tel: 886-2-2736-1661, ext 6130. Fax: 886-2-2739-0671. E-mail: jpl@tmu.edu.tw.

ORCID

Jing-Ping Liou: 0000-0002-3775-6405

Notes

The authors declare no competing financial interest.

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