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ORIGINAL ARTICLE

Hidenori Tozuka · Michikazu Ota · Hisayoshi Kofujita
Kouetsu Takahashi

Synthesis of dihydroxyphenacyl glycosides for biological and medicinal study: β-oxoacteoside from *Paulownia tomentosa*

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Abstract The protected structure of β-oxoacteoside (tomentoside A), 2-oxo-2-(3,4-dihydroxyphenyl)ethyl 3-*O*-(2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl)-4-*O*-caffeoyl-β-D-glucopyranoside **14** was synthesized in 14% overall yield in 11 steps, starting from D-glucose for biological and medicinal studies of phenylpropanoid glycosides. The first step was the preparation of a 3-*O*-rhamnopyranosyl disaccharide sugar core **2** from a suitably protected rhamnosyl trichloroacetimidate **10** and glucose derivative (diacetone-D-glucose **1**) in 71% yield. To the glucose moiety of this sugar core, several protection/deprotection procedures were performed sequentially to obtain a fully acetylated sugar core **7** with a 4-OH group on the glucose moiety, in 57% yield in five steps. Thereafter, to the 4-OH group of the glucose moiety, selective 4-*O*-caffeoylation was achieved by proton-transfer esterification with 3,4-di-*O*-allylcaffeic acid **16** to give the caffeoyl disaccharide **11** in 97% yield. Then, it was converted to trichloroacetimidate **13** for a glycosylation donor in 90% in two steps. Finally, anomeric glycosylation was conducted with 2-oxo-2-(3,4-di-allyloxyphenyl)ethyl alcohol **19** with catalytic amounts of $BF_3{\cdot}Et_2O$ to give 2-oxo-2-(3,4-di-allyloxyphenyl)ethyl 2,6-di-*O*-acetyl-3-*O*-(2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl)-4-*O*-(3,4-di-allyloxycaffeoyl)-β-D-glucopyranoside **14** in 60% yield. Deprotected intermediates of compounds **2**, **11**, **14**, and **19** which were obtained in high yield would be useful for biological and medicinal studies of phenylpropanoid glycosides.

Key words Synthesis · Phenylpropanoid glycoside · 2,3′,4′-Trihydroxyacetophenone · Dihydroxyphenacyl glycoside · β-Oxoacteoside

H. Tozuka (✉) · M. Ota · H. Kofujita · K. Takahashi
The United Graduate School of Agricultural Science, Iwate University, Morioka 020-8550, Japan
Tel. +81-19-621-6173; Fax +81-19-621-6177
e-mail: u0299013@iwate-u.ac.jp

M. Ota · H. Kofujita
Faculty of Agriculture, Department of Environmental Sciences, Iwate University, Morioka 020-8550, Japan

K. Takahashi
Faculty of Agriculture, Department of Bioenvironment, Yamagata University, Tsuruoka 997-8555, Japan

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Introduction

Phenylpropanoid glycosides are widely distributed natural substances in plant species.[1] Their structures are functionalized with a variety of phenolic substituents, which are common components of secondary plant metabolites (the substituted phenylethyl and cinnamoyl moieties). Many phenylpropanoid glycosides have other sugar components attached to the sugar core; also, they are generally composed of more than one sugar.[2]

The acteoside family is shown in Fig. 1 (acteoside, isoacteoside, β-oxoacteoside, 2-hydroxyacteoside). The rhamnosyl group is attached via an α-L-type glycosidic linkage at the 3-hydroxyl position of the glucose moiety. In nature, the caffeoyl group is usually attached at the 4-hydroxyl position of the glucose moiety and less commonly so at the 6-hydroxyl position. Anomeric substituents are phenylethyl, 2-hydroxyphenylethyl and β-oxophenylethyl aglycons. The former two aglycon structures exist predominantly in plant materials in that order. In contrast, β-oxophenylethyl aglycon is quite rare.

In a previous study, β-oxoacteoside was isolated from ethanol extracts of *Paulownia tomentosa* with the unusual β-oxophenylethyl aglycon in phenylpropanoid glycosides, and was then named tomentoside A.[3] At that time, others named it β-oxoacteoside.[4] This compound has 3′,4′-dihydroxyphenacyl alcohol (2,3′,4′-trihydroxyacetophenone) as the glycoside aglycon, which was isolated from tamarind (*Tamarindus indica* L.) seeds and showed the same strong antioxidative activity as α-tocopherol.[5] It was also isolated from insect hard cuticle in another study.[6]

Recently, biological and particularly medicinal studies of phenylpropanoid glycosides have progressed. They have dealt widely with antioxidative,[7] antiproliferative,[8] neurosedative,[9] and radical scavenging[10] activity; effects on cyclic 3′,5′-adenosine monophosphate level,[11] endothelial NO production/release,[12] and relaxing;[13] telomerase modulatory,[14] immunomodulatory,[15] and HIV-1 integrase inhibitory[16] properties.

Structural elucidation of the disaccharide sugar core, the caffeoyl moiety, and the phenacyl alcohol glycoside moiety or the phenethyl alcohol glycoside moiety are required to provide insight into the activities referred to above, and hence, an efficient and useful synthetic procedure has been in demand. It would be convenient and advantageous to introduce caffeoyl and anomeric aglycon substituents at a step that is as late as possible in the synthetic scheme.[17–23] We therefore describe here such a synthetic approach for β-oxoacteoside, starting from the preparation of the disaccharide sugar core.

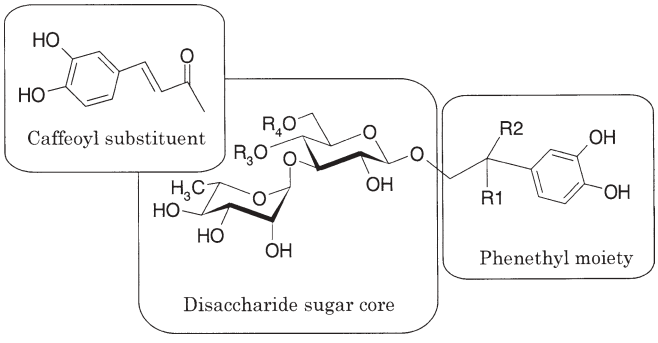

Fig. 1. Structure of acteoside family (phenylpropanoid glycosides). β-Oxoacteoside: R_1 = O, R_2 = none, R_3 = caffeoyl, R_4 = H; β-hydroxyacteoside: R_1 = OH, R_2 = H, R_3 = caffeoyl, R_4 = H; acteoside: R_1 = H, R_2 = H, R_3 = caffeoyl, R_4 = H; isoacteoside: R_1 = H, R_2 = H, R_3 = H, R_4 = caffeoyl

Results and discussion

Figures 2 and 3 show our strategy for synthesis of the title compound **14**. In our approach, we selected the acetyl group as a protecting group for sugar hydroxyl groups and allyl groups for phenolics because both protecting groups are stable under various reactions and facile protection/deprotection procedures have been developed.[24] Allyl protective groups were easily prepared by reaction of corresponding phenolics and allylbromide in the presence of weak bases (Figs. 4,5) and showed strong durability in the course of the transformations (Fig. 3). For formation of glycosidic linkages, we selected highly reactive trichloroacetimidates as glycosylation donors (compounds **10** and **13**) in the presence of catalytic amounts of $BF_3{\cdot}Et_2O$. For both 3-*O*-rhamnosylation (step b in Fig. 2) and anomeric glycosylation (step d in Fig. 3), C-2 acetate ester sugar protecting groups were expected to express a participating effect for increasing selectivity of certain anomeric configurations.[25] Incidentally, the Koenigs-Knorr method leads to the same effect as above, but it requires at least an equimolar amount of metal salt as promoter. Both imidates were easily prepared from corresponding anomeric hydroxyl derivatives (compounds **9** and **12**) under the mild conditions.

At first, the disaccharide sugar core **2** of β-oxoacteoside/acteoside/isoacteoside (step b in Fig. 2) was constructed. This step was carried out with the fully acetylated rhamnosyl trichloroacetimidate **10** as the glycosylation donor, diacetone-D-glucose **1** as the glycosyl acceptor and $BF_3{\cdot}Et_2O$ as catalyst in CH_2Cl_2. The acceptor **1** was prepared by the conventional procedure in 63% yield.[26] The donor **10** was prepared as shown in Fig. 6.[22] Commercially available rhamnose monohydrate was fully acetylated by Ac_2O in pyridine to give compound **8** in quantitative yield, followed by selective anomeric deacetylation by hydrazine

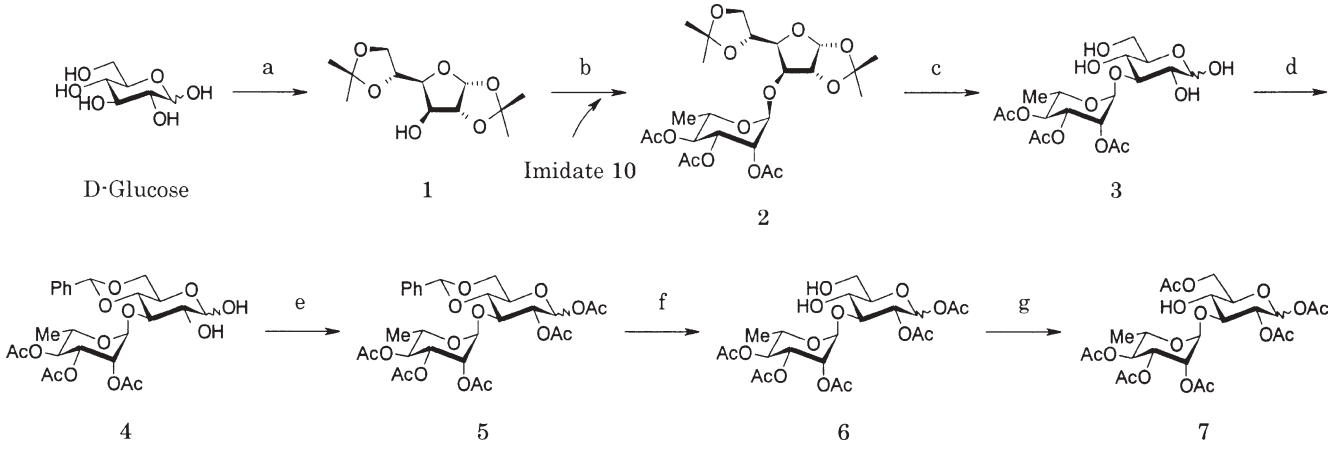

Fig. 2. Construction of ester precursor **7** from disaccharide sugar core **2**

Reagents and conditions:
(a) 85% H_3PO_4, $ZnCl_2$, acetone, room temperature (r.t.) 40 h, 63%;
(b) 1.2 equiv. of **10**, $BF_3{\cdot}Et_2O$, CH_2Cl_2, −20°C 4 h → r.t. 12 h, 71%;
(c) 80%–90% TFA, CH_2Cl_2, r.t., 65%–79%;
(d) PhCHO, $BF_3{\cdot}Et_2O$, CH_2Cl_2, r.t. 1 h, 81%;
(e) Ac_2O, pyridine, 90%;
(f) 80% TFA, r.t. 30 min, 100%;
(g) 1.4 equiv. of AcCl, collidine, −40°C 3 h → r.t. 1 h, 99%, (26%, seven steps)

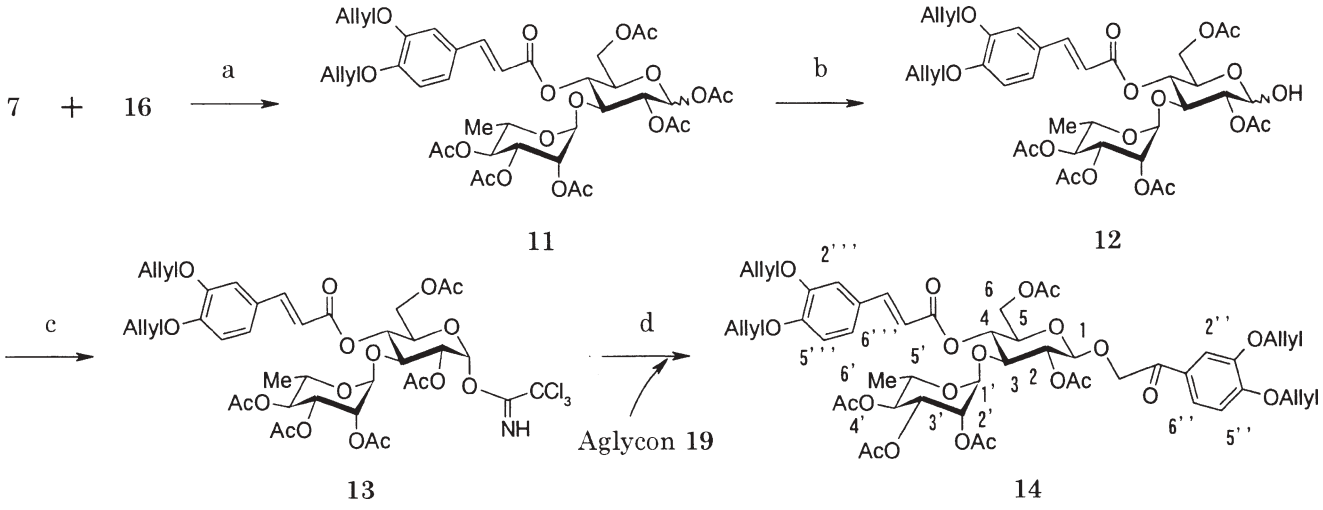

Fig. 3. Preparation of the protected β-oxoacteoside **14**
Reagents and conditions:
(a) 1.3 equiv. of acid **16**, DMAP, DMAP·HCl, DCC, CH_2Cl_2, reflux, 24 h, 97%;
(b) $H_2NNH_2{\cdot}CH_3COOH$, DMF, r.t. 1 h, 96%;
(c) CCl_3CN, DBU, CH_2Cl_2, −20°C;
(d) 1.3 equiv. of aglycon **19**, $BF_3{\cdot}Et_2O$, mol. sieves (0.3 nm), CH_2Cl_2, r.t. 2 h, 60%, (53%, four steps)

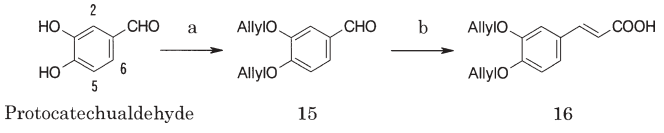

Fig. 4. Preparation of the protected caffeic acid **16**
Reagents and conditions:
(a) 2.4 equiv. of allylbromide, 2.4 equiv. of K_2CO_3, acetone, reflux, 2 h, 94%;
(b) 1.2 equiv. of $CH_2(COOH)_2$, 0.1 equiv. of piperidine, pyridine, 60°C 24 h, 87%, (82%, two steps)

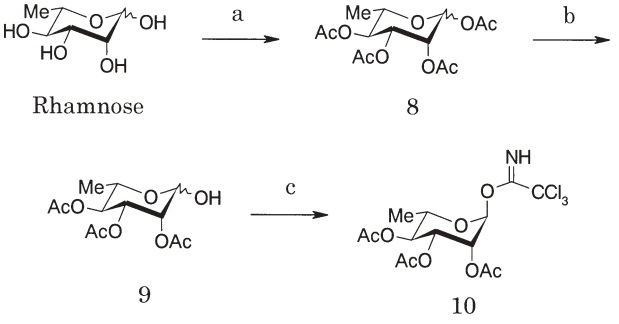

Fig. 6. Preparation of rhamnosyl trichloroacetimidate **10**
Reagents and conditions:
(a) Ac_2O, pyridine, 0°C 1 h → r.t. 16 h, quantitative;
(b) Hydrazine acetate, DMF, r.t. 2 h, 91%;
(c) 5 equiv. of CCl_3CN, 0.2 equiv. of DBU, CH_2Cl_2, −20°C 1 h → r.t. 2 h, 80%, (73%, three steps)

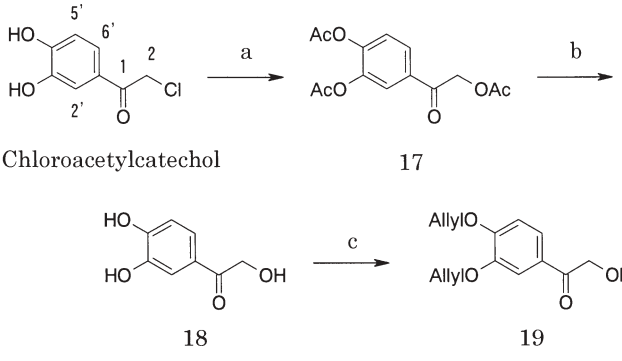

Fig. 5. Preparation of the protected aglycon **19**
Reagents and conditions:
(a) 1.5 equiv. of K_2CO_3, 9.8 equiv. of Ac_2O, r.t. 20 min → 140°C 10 min, 75%;
(b) MeOH, cat. HCl, r.t. 40 h, 86%;
(c) 2.4 equiv. of allylbromide, 2.4 equiv. of K_2CO_3, r.t. 4 h → 60°C 20 min, 80%, (52%, three steps)

acetate in *N*,*N*-dimethylformamide (DMF) to give compound **9** in 91% yield (α and β anomeric mixtures). Then, CCl_3CN (5.0 equivalents) was used for trichloroacetimidoylation of compound **9** in the presence of trace amounts of 1,8-diazabicyclo[5.4.0]-7-undecene (DBU) in CH_2Cl_2 to give exclusively α-type anomeric rhamnosyl trichloroacetimidate **10** in 80% yield.

Under ordinary conditions,[17,22,27] substrates **1** and **10** did not give the desired product in satisfactory yield. Therefore, a slight modification was adopted. Under conditions of high concentration (aglycon **1**, 290 μmol/ml), high dose of $BF_3{\cdot}Et_2O$ catalyst (0.2 equivalents) and prolonged reaction time (12 h), the reaction proceeded smoothly at room temperature. Before the reaction was stopped, thin-layer chromatography (TLC) showed complete consumption of the starting aglycon **1** with predominant formation of the desired sugar core **2** and a small spot of the unreacted imidate **10**. However, after workup procedures, the isolated yield of **2** was moderate (71%) and a considerable amount of the unexpected 5,6-*O*-acetonide deprotected product was obtained (29% yield).

After construction of the disaccharide **2**, acetonide protecting groups were cleaved. Treatment of compound **2** with aqueous trifluoroacetic acid[28] (TFA) provided the unprotected compound **3** in 45%–79% yield (methods A–C). This reaction proceeded almost quantitatively just before the reaction was stopped (methods A–C). However, the conventional workup procedure (method A) produced a considerable amount of an unidentified by-product in low yield (45%). Additionally, this by-product was readily converted to compound **3** by treatment with water (29%). When the reaction was stopped by adding aqueous 5% (w/v) $NaHCO_3$ (method B), it was difficult to separate highly water-soluble compound **3** from the TFA-Na salt by solvent extraction (water with EtOAc, CH_2Cl_2—EtOAc, EtOH—Et_2O, or *n*-BuOH). Therefore, gel chromatography was used to remove the large mass of TFA-Na. In the case of other TFA salts, treatments with $CaCO_3$, K_2CO_3, and triethylamine or pyridine also resulted in inseparable salts. Chromatography or filtration through silica gel did not separate compound **3** from the TFA salt (EtOAc, EtOH, Et_2O, CH_2Cl_2, or EtOAc/MeOH as eluent). Thus (method C), to remove most of the TFA, the reaction mixtures were subjected to short periods of vacuum concentration, and were then neutralized with ion-exchange resin, resulting in good yield (79%).

The deacetonated sugar core **3** was used in a series of protection and deprotection steps to yield compound **7** with free 4-OH group (steps d–g in Fig. 2). Benzylidenation of the 4,6-OH groups of the glucose moiety of compound **3** was achieved with benzaldehyde (10 equivalents) and catalytic amounts of $BF_3{\cdot}Et_2O$ (0.1 equivalents) in CH_2Cl_2 to give 4,6-*O*-benzylidene-protected glucose **4** in 81% yield. This combination of reagents for preparing the 4,6-*O*-benzylidene derivative of glucose is rare and interesting.[24] When used with 3-*O*-acetylglucose, which is rather insoluble in dichloromethane, this reaction showed poor conversion to the benzylidene. Thereafter, 1,2-OH groups of the glucose moiety of compound **4** were protected by ordinary acetylation with Ac_2O–pyridine to give compound **5** in 90% yield. Product **5** was obtained as an α,β-anomeric mixture (α:β, 51%:49%). Debenzylidenation was performed by exposure to 80% (v/v) TFA for short periods to give compound **6** in quantitative yield. In this reaction, the prolonged reaction time (more than 10–20 min) and workup procedures for removing TFA (concentration in vacuo) diminished the yield of compound **6**. The 6-OH group of compound **6** was then regioselectively protected with acetyl chloride (1.3–1.4 equivalents) in collidine at $-40°C$.[29] This acetylation proceeded exclusively at the primary hydroxyl group and afforded compound **7** with free 4-OH group in 99% yield {δ 4.23, 4.30, 4.51, and 4.55 [H-6(α/β)]}. This ester precursor **7** is considered to be a useful intermediate for synthesis of other phenylpropanoid glycosides.

The sequential transformation from D-glucose to compound **7** was successfully conducted in seven steps in 26% overall yield. The transformation from compound **2** to compound **7** was achieved with an overall yield 57% in five steps. During each reaction step, especially from step e to step g (Fig. 2), it appears that purification was not necessary because of near-quantitative conversion and the products were pure by TLC. It might also be viable to conduct deacetonation and benzylidenation without purification to improve the overall yield.[17]

The protected caffeic acid derivative **16** was prepared according to the details given in Fig. 4. Commercially available protocatechualdehyde was converted to 3,4-diallyloxy-protected aldehyde **15** with allylbromide and K_2CO_3 in acetone in 94% yield.[21] The Knoevenagel condensation was then adopted to give compound **16** in 87% yield.

Ester precursor **7** was used in 4-*O*-caffeoylation[18] with the protected acid **16** with *N*′,*N*′-dicyclohexylcarbodiimide (DCC). The proton-transfer condition mediated by equimolar amounts of 4-dimethyaminopyridine (DMAP) and DMAP·HCl[30] afforded the protected partial structure **11** of β-oxoacteoside in 97% yield. Reaction conditions were slightly modified from the reported ones[18] and were proven to be useful. The slight excess amount of acid **16** (1.2–1.3 equivalents), low catalyst concentration (DMAP and DMAP·HCl, 0.10 equivalents each), the elevated temperature (reflux), and the rather high concentration of alcohol **7** (100μmol/ml) were sufficient for quantitative conversion. Incidentally, this excellent yield is a great advantage for providing variously labeled caffeoyl derivatives for biological and medicinal studies. Caffeoyl incorporation was confirmed by nuclear magnetic resonance (NMR) analysis; its binding position was at the 4-OH of the glucose moiety: {δ 5.29 [1H, t, J = 9.5 Hz, H-4(β)] and δ 5.33 [1H, t, J = 9.3 Hz, H-4(α)]}.

From compound **11**, subsequent transformations to trichloroacetimidate **13** were conducted exactly as for the preparation of rhamnosyl trichloroacetimidate **10**. Selective anomeric deacetylation and trichloroacetimidoylation gave compound **12** in 96% yield and trichloroacetimidate **13** in 94% yield. During two steps, anomeric mixtures were converted gradually toward one anomer, then exclusively to give the α-type imidate **13**. {δ 6.60 [1H, d, J = 3.4 Hz, H-1(α)]}.

Preparation of di-*O*-allyl protected anomeric aglycon **19** is depicted in Fig. 5. Commercially available 4-chloroacetylcatechol was treated with CH_3COOK and Ac_2O at 140°C for 10–15 min,[31,32] resulting in triacetyl derivative **17** in 75% yield. In this step, the prolonged reaction time was disadvantageous for preparation of compound **17** because a by-product (Rf 0.55, Toluene/HCOOEt/HCOOH, 7/2/1) was formed in significant yield in 20–30 min.[31] Compound **17** was then subjected to methanolic solvolysis in the presence of a trace amount of aqueous HCl to give trihydroxy aglycon **18** in 86% yield.[31] As shown in Table 1, the ^1H and ^{13}C NMR data of the synthesized compound **18** are identical to those of the natural compound,[5] although there are small differences in the case of the spectrum run acetone-d_6 due to the existence of intermolecular hydrogen bonds between 3′,4′-OH substituents and acetone-d_6. Phenolic hydroxyl groups in compound **18** were then protected selectively by allyl groups with allylbromide and K_2CO_3 in DMF to give aglycon substituent **19** in 81% yield. In this reaction, DMF was used as a solvent instead of acetone (step a in Fig. 5) because of the low solubility of

Table 1. ^{1}H and ^{13}C NMR data for compound **18**

H and C positions	Synthetic compound				Natural compound[a]	
	CD_3OD		Acetone-d_6		Acetone-d_6	
	^{1}H	^{13}C	^{1}H	^{13}C	^{1}H	^{13}C
1		198.2		197.3		198.7
2	4.79 (s)	65.7	4.77 (d, 5.13)	65.4	4.73 (s)	65.3
1′		127.5		127.2		127.0
2′	7.40 (d, 1.7)	115.2	7.48 (d, 2.2)	115.0	7.29 (d, 2.0)	115.2
3′		146.4		145.7		145.7
4′		152.3		151.4		151.7
5′	6.84 (d, 8.1)	115.8	6.94 (d, 8.1)	115.7	6.82 (d, 8.0)	116.1
6′	7.38 (dd, 2.2, 8.1)	122.1	7.44 (dd, 2.2, 8.3)	121.9	7.31 (dd, 1.9, 8.3)	122.3
Hydroxyl group			3.79 (d, 5.13) 8.44 (br d, 3.9) 8.86 (br d, 3.6)			

Splitting patterns and *J* values (Hz) are given in parentheses. Chemical shifts given in ppm relative to tetramethylsilane. All ^{1}H data recorded at 400 MHz, ^{13}C data at 100 MHz
[a] These data were measured by Tsuda et al.[5]

compound **18** in acetone. Fortunately, phenolic hydroxyl groups were selectively allylated over phenacyl hydroxyl groups. Attempts at direct substitution from chloride to alcohol[33–35] were far from satisfactory in the present experiment; therefore, rather cumbersome acetylation–deacetylation steps were required.

Finally, the modified glycosylation of the protected aglycon **19** and trichloroacetimidate **13** proceeded at high concentrations (imidate **13**, 500 μmol/ml) in the presence of $BF_3{\cdot}Et_2O$ in CH_2Cl_2 to give title compound **14** in 60% yield. Introduction of anomeric aglycon was confirmed by NMR analysis and its configuration was β-type: {δ 4.62 [1H, d, J = 8.3 Hz, H-1(β)]}. The overall yield of the protected compound **14** was 14% in 11 steps starting from D-glucose.

Deprotection of acetyl groups from compound **14** with basic reagents could result in migration of the caffeoyl moiety to the 6-OH position of the glucose moiety in the present scheme; therefore, some modification would be required in the scheme adopted. Replacement of the acetyl group in the 6-OH position by a trityl or allyl group would overcome this problem.

In conclusion, the present results show that the synthetic approach adopted with the above modification would be applicable to construction of other members of phenylpropanoid glycosides. Deprotected intermediates of compounds **2**, **11**, **14**, and **19**, which were obtained in high yield, would be useful for biological and medicinal studies of phenylpropanoid glycosides.

Experimental

General methods

Melting point (mp) determinations were measured with a Yanagimoto MP-S2 and are uncorrected. Chromatographic separations were recorded with an ultraviolet (UV) detector (Eyela UV-D2; Tokyorikakikai, Japan) or a refractometer (Shodex RI-72; Showa Denko, Japan). Infrared (IR) spectra were recorded with a Jasco FT/IR-230 (Jasco, Japan). ^{1}H and ^{13}C NMR spectra were recorded with a Jeol AL-400 (400 and 100 MHz, respectively; Jeol, Japan). Mass spectra (MS) were recorded with a Jeol JMS-SX102A.

Reactions and chromatographic products were checked by TLC on Merck 60-G or Merck silica gel 60 F_{254}. Silica gel chromatography was performed on Wakogel C-300. 2-Chloro-3′,4′-dihydroxyacetophenone (4-chloroacetylcatechol), hydrazine acetate, and $BF_3{\cdot}Et_2O$ were purchased from Aldrich and were used without purification. α-D-Glucose, molecular sieves 0.3 or 0.4 nm, and DCC were purchased from Nacalai Tesque. Rhamnose monohydrate, protocatechualdehyde, trichloroacetonitrile (CCl_3CN), TFA, and 2,4,6-trimethylpyridine (collidine) were purchased from Wako and were used as received; 85% H_3PO_4 was purchased from Kanto Chemical. DMAP and DBU were purchased from Tokyo Kasei. Amberlite IR-410 (Cl form) was purchased from Organo and was regenerated to the OH form. To this dried resin was added an equal mass of water to maintain 50% w/w and the slurry was stored at 0°C before use. The resin (1.0 g) neutralized 100–130 mg of TFA. DMAP·HCl was prepared from DMAP by exposure to gaseous HCl in tetrahydrofuran (THF).

Dichloromethane (CH_2Cl_2), $CHCl_3$, and Ac_2O were dried over P_2O_5 and distilled before use. For glycosylation reaction, CH_2Cl_2 and $BF_3{\cdot}Et_2O$ were redistilled under N_2 just before use. Pyridine and DMF were dried over CaH_2 and distilled. Acetone was dried over pulverized Drielite (activated Ca_2SO_4) and distilled just before use. Each distilled solvent was properly stored over molecular sieves or suitable drying reagents.

1,2:5,6-Di-*O*-isopropylidene-D-glucofranoside **1**[26]

To a stirred suspension of finely pulverized dry α-D-glucose (76.8 g, 427 mmol) and pulverized molten $ZnCl_2$ (65.0 g, 477 mmol) in dry acetone (573 ml, 453 g, 7.80 mol) was

added 85% H_3PO_4 (3.95 g) at room temperature. The mixture was stirred for 48 h at room temperature. The mixture was filtered to remove unreacted glucose (21.2 g), which was then washed with acetone (total 295 ml). The combined filtered solution and washings were neutralized by adding 85.4 g of 50% (w/w) NaOH. The resulting inorganic precipitate was filtered off, the filtered solution was concentrated in vacuo, redissolved in $CHCl_3$ (75 ml) and washed with water (75 ml). The aqueous layer was re-extracted with $CHCl_3$ (25 ml × 3), the combined organic layer was dried over Na_2SO_4, filtered, and concentrated and dried in vacuo to give crude product (74.0 g, 92% based on consumed glucose, mp 92°–102°C). Successive recrystallization from hot *n*-hexane and $CHCl_3$ gave title compound **1** [white needles, 50.7 g, 63%, mp 111°–112°C, (Lit.[26] 110°–111°C)]: Rf 0.39 (*n*-hexane/ethyl acetate, 1.0/0.8 v/v); ^{1}H NMR ($CDCl_3$): δ 1.32, 1.37, 1.45, and 1.50 (each 3H, s, acetonide CH_3), 2.69 [1H, broad s, H-3(OH)], 3.99 (1H, dd, J = 5.3, 8.5, H-6), 4.07 (1H, dd, J = 2.6, 7.8, H-4), 4.17 (1H, dd, J = 6.1, 8.5, H-6), 4.32–4.37 (2H, m, H-3 and H-5), 4.53 (1H, d, J = 3.6, H-2), 5.94 (1H, d, J = 3.6, H-1); ^{13}C NMR ($CDCl_3$): δ 25.2, 26.2, 26.8, and 26.9 (acetonide CH_3), 67.6 (C-6), 73.4 (C-5 or C-3), 75.1 (C-3 or C-5), 81.1 (C-4), 85.0 (C-2), 105.1 (C-1), 109.5, and 111.6 (quaternary C).

1,2:5,6-Di-*O*-isopropylidene-3-*O*-(2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl)-glucofranoside **2**

The solution of rhamnosyl imidate **10** (82.7 g, 190 mmol), acceptor **1** (41.1 g, 158 mmol), and finely pulverized activated molecular sieves (0.3 nm) (80.1 g) in CH_2Cl_2 (492 ml) was degassed and purged three times with N_2, cooled to −20°C, and stirred for 2 h at that temperature. To this solution was added $BF_3{\cdot}Et_2O$ (2.24 g, 1.92 ml, 15.8 mmol) in CH_2Cl_2 (52.4 ml) and the mixture was vigorously stirred for 4 h at −20°C. At this point, TLC analysis showed incomplete reaction. An additional identical amount of $BF_3{\cdot}Et_2O$ solution was added and stirred for 2 h at −20°C and allowed to stand for 12 h at room temperature. After 12 h, TLC analysis indicated complete consumption of compound **1**, a small amount of remaining rhamnosyl imidate **10**, and trace amounts of hydrolyzed compound **9**. The mixture was diluted with CH_2Cl_2 (300 ml), filtered through a celite pad, washed with saturated $NaHCO_3$ solution (500 ml), H_2O (300 ml), saturated NaCl solution (300 ml), filtered, concentrated, and dried over Na_2SO_4 to yield crude yellow powder. Recrystallization from EtOH (50°C→−20°C) afforded a crystalline white powder of compound **2** (44.2 g, 53% based on compound **1**). To the filtered mother liquor, further recrystallization and chromatography (*n*-hexane/ethyl acetate, 1.0/0.5 v/v) were applied to give title compound **2** (15.0 g, 18%) and 5,6-OH deacetonated product as a pale yellow paste (22.7 g, 29%). Compound **2**: Rf 0.53 (*n*-hexane/ethyl acetate, 1.0/0.8 v/v); mp 148°–149°C; ^{1}H NMR ($CDCl_3$): δ 1.19 (3H, d, J = 6.3, H-6′), 1.31, 1.35, 1.40, and 1.50 (each 3H, s, acetonide CH_3), 1.99, 2.03, and 2.17 (each 3H, s, OAc), 3.95 (1H, dd, J = 5.8, 8.5, H-6), 4.10 (1H, dd, J = 3.1, 9.0, H-2 or H-5), 4.19 (1H, dd, J = 6.1, 8.5, H-6), 4.26–4.32 (1H, m, H-5′), 4.32–4.41 (2H, m, H-3 and H-5), 4.50 (1H, d, J = 3.9, H-2), 4.91 (1H, d, J = 1.4, H-1′), 5.09 (1H, t, J = 9.7, H-4′), 5.20 (1H, dd, J = 1.7, 3.4, H-2′), 5.23 (1H, dd, J = 3.4, 9.7, H-3′), 5.91 (1H, d, J = 3.9, H-1); ^{13}C NMR ($CDCl_3$): δ 17.1 (C-6′), 20.8, 20.8, and 21.0 (OAc), 25.3, 26.2, 26.8, and 26.9 (acetonide CH_3), 66.6 (C-5′), 68.2 (C-6), 69.0 (C-3′), 70.0 (C-2′), 70.8 (C-4′), 71.8 (C-5 or C-3), 77.0 (C-3 or C-5), 80.9 (C-4), 81.7 (C-2), 94.7 (C-1′), 105.2 (C-1), 109.1, and 111.9 (quaternary C), 169.6, 169.6, and 170.0 (OAc); electron impact-mass spectrometry (EI-MS): *m/z* 517 (M − 15); fast atom bombardment – mass spectrometry (FAB-MS): *m/z* 533 (M + 1), 517 (M − 15).

3-*O*-(2,3,4-Tri-*O*-acetyl-α-L-rhamnopyranosyl)-α,β-D-glucopyranose **3**

Method A[28]

To a stirred solution of compound **2** (12.0 g, 22.6 mol) in CH_2Cl_2 (118 ml) was added 90% v/v TFA (123 ml) at room temperature; it was then stirred for 1 h at that temperature. The mixture was concentrated in vacuo at 40°C for 10 min, and then at 50°C for 10 min, before being coevaporated with toluene (30 ml × 3), EtOH (30 ml × 2), and *n*-hexane (50 ml). The crude materials (12.8 g) obtained were purified by flash chromatography (ethyl acetate/MeOH, 1.0/0.05 v/v) to give title compound **3** (4.58 g, 45%, Rf 0.27) and unidentified by-products (7.71 g, Rf 0.28–0.70). The yield of by-products increased during concentration procedures. After the EtOH coevaporation steps, nearly half of the desired product was converted to the unidentified by-products.

The by-products (5.96 g) were treated with water (29 ml) and EtOH (29 ml). After 1 h at room temperature, TLC analysis showed that the by-products were completely converted to title compound **3**. Workup and purification procedures then gave title compound **3** (2.93 g, 29%) and partially deacetylated compound (0.78 g, Rf 0.11).

Method B

To a stirred solution of compound **2** (3.06 g, 5.76 mmol) in CH_2Cl_2 (22.5 ml) was added 90% w/w TFA (31.2 g) at 0°C and the mixture was stirred for 2 h and then at room temperature for 3 h. Then, to the mixture was added dropwise a solution of 5% w/v $NaHCO_3$ (430 ml) with stirring in a fume hood. The mixture was concentrated in vacuo to 100 ml, extracted with ethyl acetate (30 ml × 6), and the combined organic layer was washed with H_2O (20 ml). The aqueous layer was re-extracted with ethyl acetate (30 ml × 4) to recover the large loss of the desired product. The organic layer was combined and dried over Na_2SO_4, filtered, concentrated, and extensively dried to give crude product (16.0 g). The crude material was subjected to gel chromatography (Sephadex LH-20, 165 g, MeOH, 11.3 ml/min) to afford title compound **3** (1.69 g, 65%) and salt (13.3 g).

Method C

To a stirred solution of compound **2** (10.0 g, 18.8 mmol) in CH_2Cl_2 (50 ml) was added 80% v/v TFA (50 ml) at room temperature and the mixture was stirred for 2.5 h at that temperature. Then the mixture was concentrated in vacuo at 40°C for 20 min and coevaporated with toluene (20 ml) at 40°C for 20 min. To the resulting paste was added water (20 ml), and the mixture was rapidly neutralized with 50% w/w Amberlite IRA-410 (OH form) (62.4 g), filtered, and washed with EtOH (25 ml × 5). The crude white powder was purified by flash chromatography on silica gel (130 g, ethyl acetate/MeOH, 1.0/0.05) to give title compound **3** (6.22 g, 73%, Rf 0.27) and partially deacetylated compound (1.05 g, 14%, Rf 0.11). The filtered resin was washed successively with H_2O (50 ml × 2), EtOH (50 ml), and Et_2O (50 ml). The washings were purified as above, giving title compound **3** (0.471 g, 5.5%) and the partially deacetylated compound (0.084 g, 1.1%). Compound **3**: (α:β, 57%:43%); Rf 0.22 (ethyl acetate); mp 95°–110°C; ^{1}H NMR ($CDCl_3$): δ 1.21 (3H, m, H-6′), 1.99, 2.05, and 2.16 (each 3H, s, OAc), 3.41 (1H, t, J = 9.2), 3.53 (1H, t, J = 8.8), 3.61 (1H, t, J = 8.9), 3.67 (1H, m), 3.70–3.84 (m), 3.93 (m), 4.26 (2H, m), 4.65 (1H, d, J = 7.3), 5.08 (2H, t, J = 9.9), 5.15 (1H, broad s), 5.23 (1H, broad s), 5.26–5.33 (m), 5.37 (2H, broad s); ^{13}C NMR ($CDCl_3$): δ 17.2, 20.7, 20.9, 61.7, 62.1, 66.7 × 2, 68.9, 69.1, 69.3, 69.4, 69.6, 69.7, 70.6, 71.4, 71.7, 74.5, 75.7, 82.0, 83.3, 91.9, 96.0, 98.1, 98.2, 169.5 × 2, 170.2 × 2, 170.3, 170.5; FAB-MS: *m/z* 475 (M + Na), 491 (M + K).

4,6-*O*-Benzylidene-3-*O*-(2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl)-α,β-D-glucopyranose **4**

To a stirred solution of compound **3** (4.00 g, 8.85 mmol), freshly distilled benzaldehyde (9.00 ml, 88.5 mmol), and granulated activated molecular sieves (0.3 nm) (1.60 g) in CH_2Cl_2 (40.0 ml) was added $BF_3{\cdot}Et_2O$ (0.109 ml, 0.885 mmol) at room temperature. The mixture was stirred for 1 h at room temperature and 20 ml of pyridine was added for quenching. The quenched mixture was filtered and the residual molecular sieves were washed with CH_2Cl_2 (10 ml × 3); the filtrates and washings were combined and concentrated in vacuo and the residues were azeotropically distilled with H_2O (10 ml × 3), and co-evaporated successively with toluene (10 ml × 3), EtOH (10 ml × 3), and *n*-hexane (30 ml). The crude products were purified by flash chromatography to afford title compound **4** (3.87 g, 81%). Compound **4**: (α:β, 55%:45%); Rf 0.32–41 (ethyl acetate/*n*-hexane, 3.0/1.0 v/v); mp 103°–113°C; ^{1}H NMR ($CDCl_3$): δ 0.83 [3H, d, J = 6.1, H-6′(α/β)], 1.96, 1.97, 1.98, 1.99, 2.13, and 2.14 (each 3H, s, OAc), 3.50 [1H, dt, J = 4.4, 9.5, H-5(β)], 3.54 (1H, t, J = 9.2), 3.55 (1H, t, J = 9.5), 3.61 (1H, t, J = 9.2), 3.67 (1H, m), 3.72 [1H, t, J = 10.2, H-6(α)], 3.78 (1H, t, J = 10.2), 3.86 [1H, t, J = 9.2, H-6(β)], 3.72–3.81 (1–2H, m), 4.03 (1H, t, J = 9.2), 4.08 (1H, dt, J = 4.8, 10.0), 4.19 (1H, dd, J = 1.7, 10.0), 4.19 (1H, d, J = 10.2), 4.29 (1H, dd, J = 4.8, 10.2), 4.35 (1H, dd, J = 4.6, 10.2), 4.68 (1H, d, J = 7.8), 4.98 (1H × 2, t, J = 10.0), 5.18 (1H, d, J = 1.5), 5.19 (1H, d, J = 1.4), 5.25 (1H, d, J = 3.6), 5.27 (1H, d, J = 3.6), 5.29 (1H, d, J = 3.4), 5.34 (1H, dd, J = 1.7, 3.4), 5.36 (1H, dd, J = 1.7, 3.4), 5.55 [2H, s, PhCH(α and β)], 7.32–7.34 (3H × 2, m, Ph), 7.46–7.52 (2H × 2, m, Ph); ^{13}C NMR($CDCl_3$): δ 16.8, 16.8, 20.8, 20.9, 21.0, 21.1, 62.8, 66.1, 66.8, 68.6, 68.9, 69.3, 69.8, 69.8, 70.9, 73.5, 75.5, 78.9, 79.1, 93.2, 97.3, 97.6, 101.5, 101.6, 126.1 × 2, 127.8, 128.8, 128.8, 136.9, 137.0, 169.6, 170.1, 170.2, 170.4; FAB-MS: *m/z* 541 (M + 1), 539 (M − 1).

1,2-Di-*O*-acetyl-4,6-*O*-benzylidene-3-*O*-(2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl)-D-glucopyranoside **5**

To a solution of compound **4** (3.00 g, 5.56 mmol) in Ac_2O (6.02 ml, 63.5 mmol) was added pyridine (6.22 ml, 74.6 mmol) at room temperature and the mixture was stirred for 2 h. The mixture was concentrated in vacuo, and then dissolved in ethyl acetate (120 ml), washed with saturated $NaHCO_3$ solution (60 ml), H_2O (60 ml), saturated NaCl solution (60 ml), dried over Na_2SO_4 (30.4 g), filtered, washed with ethyl acetate (20 ml × 3), and concentrated in vacuo to obtain the crude products. Recrystallization from MeOH (reflux → −20°C) afforded title compound **5** (2.94 g, 85%). Recrystallization from the filtered mother liquor as above, gave the second crystal (0.181 g, 5.2%). Compound **5**: (α:β, 51%:49%); Rf 0.43–47 (*n*-hexane/ethyl acetate, 1.0/0.8 v/v); mp 210°–215°C; ^{1}H NMR ($CDCl_3$): δ 0.67 [3H, d, J = 6.3, H-6′(β)], 0.74 [3H, d, J = 6.1, H-6′(α)], 1.96, 1.97, 1.99, 2.00, 2.09, 2.10, 2.11, 2.11, 2.11, 2.11, and 2.16 [each 3H, s, OAc(α/β)], 3.62 [1H, dt, J = 4.6, 9.5, H-5(β)], 3.71 (1H, t, J = 9.5), 3.72 (1H, t, J = 9.2), 3.76 (1H, t, J = 10.2), 3.78 (1H, t, J = 10.0), 3.97 [1H, dt, J = 3.6, 9.0, H-5(α)], 3.98 [1H, t, J = 9.0, H-3(β)], 4.07 [1H, dd, J = 6.1, 9.7, H-5′(β)], 4.13 [1H, dd, J = 6.1, 9.7, H-5′(α)], 4.20 (1H, t, J = 9.5), 4.32 [1H, dd, J = 4.8, 10.4, H-6(β)], 4.39 [1H, dd, J = 4.6, 10.4, H-6(β)], 4.90–4.95 (2H, m), 4.98 (3H, m), 5.17 [1H, dd, J = 8.3, 9.0, H-2(β)], 5.30 [2H, dd, J = 3.4, 10.0, H-3′(α/β)], 5.56 [1H, s, PhCH(β)], 5.58 [1H, s, PhCH(α)], 5.69 [1H, d, J = 8.3, H-1(β)], 6.30 [1H, d, J = 3.6, H-1(α)], 7.33–7.36 (3H × 2, m), 7.46–7.50 (2H × 2, m); ^{13}C NMR ($CDCl_3$): δ 16.6, 16.7, 20.5, 20.7, 20.8 × 2, 20.9, 21.0, 65.3, 66.3, 66.4, 67.2, 68.4, 68.5, 68.6, 70.3, 70.4, 71.1, 71.2, 72.2, 72.4, 73.4, 78.6, 78.9, 89.7, 92.3, 97.4, 97.5, 101.9 × 2, 126.1, 126.2, 127.9 × 2, 129.0, 129.1, 136.6 × 2, 168.6, 168.8, 169.1, 169.6 × 2, 169.7, 169.8; FAB-MS: *m/z* 625 (M + 1).

1,2-Di-*O*-acetyl-3-*O*-(2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl)-D-glucopyranoside **6**

To a stirred solution of compound **5** (2.88 g, 4.62 mmol) in CH_2Cl_2 (35.0 ml) was added 80% v/v TFA (17.4 ml) in one portion at room temperature. After 5 min of stirring, $NaHCO_3$ (total 16.6 g, 1.05 equivalents/TFA) was carefully added within 5 min and stirred for 30 min. During this quenching, the mixture showed vigorous evolution of gas. The mixture was then poured into CH_2Cl_2 (90 ml) and washed with H_2O (60 ml). The aqueous layer was extracted with CH_2Cl_2 (30 ml × 2). The combined organic layer was then washed with saturated $NaHCO_3$ solution (60 ml), H_2O

(60 ml), and saturated NaCl solution (60 ml); dried over Na_2SO_4, filtered, washed, and concentrated in vacuo. The crude materials were purified by silica gel flash chromatography to give title compound **6** (2.47 g, 100%). Compound **6**: (α:β, 54%:46%); Rf 0.47 (*n*-hexane/ethyl acetate, 1/3 v/v); mp 92°C–105°C; ^{1}H NMR ($CDCl_3$): δ 1.25 [3H, d, J = 6.3, H-6′(α/β)], 1.99, 1.99, 2.06, 2.06, 2.11, 2.11, 2.14, 2.15 × 2, and 2.16 [each 3H, s, OAc(α/β)], 3.50 [1H, ddd, J = 3.4, 4.1, 9.0, H-5(β)], 3.53 (1H, broad s), 3.60 (1H, broad m), 3.66 (1H, t, J = 8.7), 3.69–3.79 (m), 3.82–3.89 (2H, broad m), 3.94 [1H, dd, J = 8.5, 10.0, H-3(α)], 4.10–4.20 [2H, m, H-5′(α/β)], 4.91 [1H, d, J = 1.9, H-1′(β)], 4.98 [1H, d, J = 1.9, H-1′(α)], 5.01 [1H, dd, J = 3.6, 10.0, H-2(α)], 5.09 [1H, dd, J = 8.3, 9.5, H-2(β)], 5.10 [1H, t, J = 9.7, H-4′(α or β)], 5.11 [1H, t, J = 9.5, H-4′(αorβ)], 5.13 [1H, dd, J = 1.7, 2.6, H-2′(α)], 5.17 [1H, dd, J = 1.9, 3.4, H-2′(β)], 5.21 [1H, dd, J = 3.4, 10.0, H-3′(β)], 5.23 [1H, dd, J = 3.4, 10.0, H-3′(α)], 5.66 [1H, d, J = 8.3, H-1(β)], 6.26 [1H, d, J = 3.6, H-1(α)]; ^{13}C NMR ($CDCl_3$): δ 17.6 × 2, 20.5, 20.6, 20.7, 20.8, 20.9, 21.0, 61.8, 67.7, 67.9, 68.5, 68.5, 69.4, 69.7, 69.8, 70.0, 70.3, 70.5, 70.6, 73.5, 76.1, 81.0, 85.0, 89.4, 91.8, 98.7, 98.9, 168.7, 168.9, 169.1, 169.4, 169.5, 169.6 × 2, 169.7 × 2, 169.8; FAB-MS: m/z 559 (M + 23).

1,2,6-Tri-*O*-acetyl-3-*O*-(2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl)-D-glucopyranoside **7**[29]

To a stirred solution of compound **6** (1.44 g, 2.69 mmol) in collidine (16.1 ml) was added acetylchloride (0.27 ml, 3.78 mmol) at −40°C. The mixture was stirred for 3 h at that temperature and then for 1 h at room temperature. Water (1.5 g) was added for quenching and the mixture was diluted with ethyl acetate (300 ml) and then washed with 1M HCl (150 ml × 2), saturated $NaHCO_3$ solution (150 ml), H_2O (150 ml), and saturated NaCl solution (150 ml). The organic layer was dried over Na_2SO_4, filtered, and concentrated in vacuo to give the crude products. Recrystallization from ethyl acetate and *n*-hexane (60°C → −20°C) afforded title compound **7** (1.10 g, 71%). The filtered mother liquor was treated by flash chromatography on silica gel (*n*-hexane/ethyl acetate, 1/2 v/v) to give title compound **7** (0.441 g, 28%). Compound **7**: (α:β, 55%:45%); Rf 0.47 (*n*-hexane/ethyl acetate, 1/2 v/v); mp 176°–187°C; ^{1}H NMR ($CDCl_3$): δ 1.23 [3H, d, J = 6.1, H-6′(α/β)], 2.00, 2.00, 2.05, 2.06, 2.09, 2.10, 2.12, 2.14, 2.14, 2.15, 2.16, 2.17, and 2.18 [each 3H, s, OAc(α/β)], 3.49–3.60 (4H, m), 3.69 [1H, dd, J = 8.5, 9.5, H-3(β)], 3.88 [1H, broad dt, J = 2.2, 3.4, 9.8, H-5(α)], 3.96 [1H, dd, J = 8.7, 10.0, H-3(α)], 4.19–4.28 [2H, m, H-5′(α/β)], 4.23 [1H, dd, J = 1.9, 12.4, H-6(α)], 4.30 [1H, dd, J = 1.9, 12.4, H-6(β)], 4.51 [1H, dd, J = 3.9, 12.4, H-6(β)], 4.55 [1H, dd, J = 3.6, 12.4, H-6(α)], 4.91 [1H, d, J = 1.9, H-1′(β)], 4.98 [1H, d, J = 1.2, H-1′(α)], 5.00 [1H, dd, J = 3.6, 10.2, H-2(α)], 5.07–5.13 [m, H-2(β), H-4(β), H-2′(β)], 5.10 [1H, t, J = 9.8, H-4′(α or β)], 5.26 [1H, dd, J = 3.4, 10.2, H-3′(β)], 5.27 [1H, dd, J = 3.4, 10.2, H-3′(α)], 5.62 [1H, d, J = 8.5, H-1(β)], 6.27 [1H, d, J = 3.6, H-1(α)]; ^{13}C NMR ($CDCl_3$): δ 17.4, 20.5, 20.6, 20.8, 20.9, 21.0, 62.5, 67.3, 67.5, 68.5, 68.6, 70.0, 70.5, 70.7 × 2, 72.3, 74.8, 78.9, 82.9, 89.4, 91.7, 98.4, 98.5, 168.5, 169.5, 169.6 × 2, 169.7 × 2, 171.5, 171.7; FAB-MS: m/z 578 (M), 600 (M + Na − 1).

1,2,3,4-Tetra-*O*-acetyl-L-rhamnopyranoside **8**[22]

To a stirred suspension of α-L-rhamnose monohydrate (49.4 g, 0.27 mmol) in acetic anhydride (201 ml, 2.0 mol) was added pyridine (201 ml, 2.5 mol) at 0°C over 10 min. The reaction mixture was allowed to warm to room temperature and was stirred for 16 h at that temperature. The mixture was concentrated in vacuo, diluted with the mixture of Et_2O (500 ml) and benzene (25 ml), and washed with H_2O (500 ml). The aqueous layer was re-extracted with Et_2O (150 ml × 3). The combined organic layers were washed with 10% v/v H_2SO_4 (300 ml × 3), saturated $NaHCO_3$ solution (150 ml), H_2O (150 ml), and saturated NaCl solution (150 ml); dried over Na_2SO_4 (429 g), filtered, concentrated in vacuo, coevaporated with benzene (50 g), and extensively dried to give **8** as a clear syrup (90.7 g). The crude product was experimentally pure by TLC analysis and was taken to the next reaction without further purification.

2,3,4-Tri-*O*-acetyl-L-rhamnopyranoside **9**[22]

To a stirred solution of the crude compound **8** (90.0 g, 0.27 mol) in DMF (649 ml) was added hydrazine acetate (37.7 g, 0.41 mol) at room temperature. The mixture was stirred at room temperature for 2 h. The mixture was diluted with ethyl acetate (2800 ml), washed with saturated NaCl solution (1200 ml × 3), dried over Na_2SO_4, filtered, and concentrated in vacuo to give the crude product. Recrystallization from hot ethyl acetate (145 ml) and *n*-hexane (198 ml) afforded pure compound **9** (66.0 g, 85%). The second crystal was recovered from the filtered mother liquor (4.44 g, 5.8%). Compound **9**: (α:β, 84%:16%): Rf 0.35 (*n*-hexane/ethyl acetate, 1.0/0.8 v/v); mp75°–82°C; ^{1}H NMR ($CDCl_3$): for an α form anomer, δ 1.22 (3H, d, J = 6.3, H-6′), 2.00, 2.06, and 2.16 (each 3H, s, OAc), 3.52 [1H, broad s, H-1′(OH)], 4.08–4.17 (1H, dd, J = 6.35, 9.77, H-5′), 5.08 (1H, t, J = 10.0, H-4′), 5.16 (1H, broad s, H-1′), 5.27 (1H, dd, J = 1.7, 3.4, H-2′), 5.37 (1H, dd, J = 3.4, 10.2, H-3′); ^{13}C NMR ($CDCl_3$): δ 17.5 (C-6′), 20.8, 20.9, and 21.0 (OAc), 66.3 (C-5′), 68.8 (C-3′), 70.2 (C-2′), 71.1 (C-4′), 92.0 (C-1′), 169.8, 169.9, and 170.0 (OAc).

2,3,4-Tri-*O*-acetyl-α-L-rhamnopyranosyl trichloroacetimidate **10**[22]

To a stirred solution of compound **9** (70.9 g, 0.24 mol) and CCl_3CN (175 g, 122 ml, 1.22 mol) in CH_2Cl_2 (504 ml) was added DBU (7.22 ml, 48.3 mmol) at −20°C over 15 min under N_2. The mixture was stirred at −20°C for 2 h and then concentrated under reduced pressure. The residual oil was purified by flash chromatography (*n*-hexane/ethyl acetate, 1.0/0.3) to give title compound **10** (84.6 g, 80%): Rf 0.53 (*n*-hexane/ethyl acetate, 1.0/0.8 v/v); ^{1}H NMR ($CDCl_3$): δ 1.27 (3H, d, J = 6.1, H-6′), 2.00, 2.07, and 2.19 (each 3H, s, OAc),

4.09 (1H, dd, J = 5.8, 9.5, H-5′), 5.18 (1H, t, J = 10.0, H-4′), 5.37 (1H, dd, J = 3.4, 10.0, H-3′), 5.46 (1H, dd, J = 1.9, 3.4, H-2′), 6.20 (1H, d, J = 1.9, H-1′), 8.73 [1H, s, C(N═H)Cl_3]; ^{13}C NMR ($CDCl_3$): δ 17.6 (C-6′), 20.7, and 20.9 × 2 (OAc), 68.1 (C-2′), 68.7 (C-3′), 69.3 (C-5′), 70.2 (C-4′), 90.6, 94.6 (C-1′), 159.7 [C(N═H)Cl_3], 169.5, and 169.6 × 2 (OAc).

4-*O*-(3,4-Di-allyloxycaffeoyl)-1,2,6-tri-*O*-acetyl-3-*O*-(2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl)-D-glucopyranoside **11**[18,30]

To a stirred solution of the ester precursor **7** (1.00 g, 1.73 mmol), the acid **16** (0.588 g, 2.26 mmol), DMAP (21.6 mg, 177 μmol), and DMAP·HCl (28.2 mg, 178 μmol) in CH_2Cl_2 (17.3 ml) was added DCC (0.536 g, 2.60 mmol) at room temperature, and the mixture was refluxed for 24 h. After complete consumption of the starting sugar **7**, the mixture were filtered, washed with CH_2Cl_2 (3 ml × 3), and purified by flash chromatography on silica gel (*n*-hexane/ethyl acetate, 1.0/1.2 v/v) to give title compound **11** (1.38 g, 97%). Compound **11**: (α:β, 68%:32%); Rf 0.44 (*n*-hexane/ethyl acetate, 1.0/1.2 v/v); mp 69°–81°C; ^{1}H NMR ($CDCl_3$): δ 1.05 [3H, d, J = 5.6, H-6′(β)], 1.07 [3H, d, J = 6.1, H-6′(α)], 1.83, 1.86, 1.96 × 2, 2.10, 2.10, 2.11, 2.11 × 2, 2.12, 2.13, and 2.18 [each 3H, s, OAc(α/β)], 3.80–3.89 [3H, m, H-3(α), H-4′(α/β)], 4.00 (1H, t, J = 9.2), 4.06–4.11 [1H, m, H-5(α)], 4.14–4.23 [5H, m, H-6(α/β)], 4.62–4.66 (4H, m, allyl), 4.91 [1H, d, J = 1.7, H-1′(β)], 4.96–5.01 (2H, dt, J = 1.2, 9.9), 4.97 [1H, t, J = 9.7, H-3(β)], 4.98 [1H, d, J = 1.7, H-1′(α)], 5.05 [1H, dd, J = 1.9, 3.4, H-2′(β)], 5.10 [1H, dd, J = 3.4, 10.0, H-2(α)], 5.11–5.15 (3H, m), 5.12 [1H, dd, J = 1.4, 3.1], 5.23 [1H, dd, J = 8.3, 9.2, H-2(β) or H-3(β)], 5.29 [1H, t, J = 9.5, H-4(β)], 5.33 [1H, t, J = 9.3, H-4(α)], 5.29–5.33 (m, allyl), 5.40–5.41 (1H, m, allyl), 5.44–5.45 (1H, m, allyl), 5.67 [1H, d, J = 8.3, H-1(β)], 6.03–6.13 (2H, m, allyl), 6.24 [1H, d, J = 15.8, H-2‴(β), CH═CH—COO], 6.25 [1H, d, J = 15.8, H-2‴ (α), CH═CH—COO], 6.36 [1H, d, J = 3.4, H-1(α)], 6.88 [1H × 2, d, J = 8.3, H-5‴ (α/β)], 7.06–7.10 [4H, m, H-2‴ and 6‴ (α/β)], 7.64 [1H, d, J = 15.9, H-1‴(β), CH═CH—COO], 7.67 [1H, d, J = 15.9, H-1‴(α), —CH═CH—COO—]; ^{13}C NMR ($CDCl_3$): δ 17.6, 17.7, 20.5, 20.6, 20.7 × 2, 20.8, 21.0, 61.9, 67.2, 67.3, 68.2, 68.5 × 2, 68.6, 69.7 × 2, 69.9, 70.0 × 3, 70.3, 70.6 × 2, 71.4, 71.5, 73.0, 80.0, 89.2, 91.7, 98.8, 112.7, 113.2, 114.0, 117.8, 117.9, 122.7, 126.8, 132.5, 132.7, 146.3, 148.4, 150.9, 165.1, 168.3, 169.3, 169.5, 169.6, 169.7, 170.4; FAB-MS: m/z 821 (M + 1), 781 (M − 41).

4-*O*-(3,4-Di-allyloxycaffeoyl)-2,6-di-*O*-acetyl-3-*O*-(2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl)-D-glucopyranose **12**

To a stirred solution of compound **11** (1.48 g, 1.80 mmol) in DMF (3.60 ml) was added hydrazine acetate (0.20 g, 2.17 mmol) at room temperature. The mixture was stirred for 1 h at room temperature, diluted with ethyl acetate (18 ml), and washed with saturated NaCl solution (6 ml × 3). The organic layer was dried over Na_2SO_4, filtered, and concentrated in vacuo to give a crude yellow paste. The crude material was purified by flash chromatography on silica gel (*n*-hexane/ethyl acetate, 1.0/1.2 v/v) to afford compound **12** (1.35 g, 96%): (α:β, 94%:6%); Rf 0.24 (*n*-hexane/ethyl acetate, 1.0/1.2 v/v); mp 72°–85°C; ^{1}H NMR ($CDCl_3$): for an α form anomer, δ 1.05 (3H, d, J = 6.3, H-6′), 1.85, 1.95, 2.11, 2.12, and 2.17 (each 3H, s, OAc), 3.33 [broad s, H-1(OH)], 3.82–3.87 (1H, dd, J = 6.1, 9.7, H-5′), 4.16–4.19 (2H, m, H-6), 4.23 (1H, dt, J = 3.1, 10.0, H-5), 4.29 (1H, t, J = 9.5, H-3), 4.62–4.66 (4H, m, allyl), 4.88 (1H, dd, J = 3.4, 10.0, H-2), 4.98 (1H, d, J = 1.2, H-1′), 4.98 (1H, t, J = 9.7, H-4′), 5.14 (1H, dd, J = 3.4, 10.0, H-3′), 5.18 (1H, dd, J = 1.9, 3.1, H-2′), 5.26 (1H, t, J = 9.7, H-4), 5.29–5.33 (2H, m, allyl), 5.40–5.41 (1H, m, allyl), 5.45–5.46 (1H, m, allyl), 5.53 (1H, broad d, J = 3.1, H-1), 6.02–6.13 (2H, m, allyl), 6.26 (1H, d, J = 15.8, CH═CH—COO), 6.88 (1H, d, J = 8.3, H-5‴), 7.06–7.10 (2H, m, H-2‴ and H-6‴), 7.65 (1H, d, J = 15.8, CH═CH—COO); ^{13}C NMR ($CDCl_3$): for an α form anomer, δ 17.7 (C-6′), 20.7 × 2, 20.8, 20.9 × 2 (OAc), 62.3 (C-6), 67.1 (C-5′), 67.8 (C-5), 68.8 (C-3′), 68.9 (C-4), 69.7 (allyl), 69.8 (C-2′), 70.0 (allyl), 70.7 (C-4′), 73.4 (C-2), 76.9 (C-3), 90.0 (C-1), 99.1 (C-1′), 112.7 (C-2‴), 113.2 (C-5‴), 114.3 (CH═CH—COO), 117.8 and 117.9 (allyl), 122.8 (C-6‴), 126.9 (C-1‴), 132.5 and 132.8 (allyl), 146.0 (CH═CH—COO), 148.3 (C-3‴), 150.8 (C-4‴), 165.3 (CH═CH—COO), 169.4, 169.7 × 2, 170.1, and 170.6 (OAc); FAB-MS: m/z 778(M), 761 (M − 17).

4-*O*-(3,4-Di-allyloxycaffeoyl)-2,6-di-*O*-acetyl-3-*O*-(2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl)-D-glucopyranosyl trichloroacetimidate **13**

To a stirred solution of compound **12** (1.32 g, 1.70 mmol), trichloroacetonitrile (1.23 g, 8.50 mmol) in CH_2Cl_2 (8.48 ml) was added DBU (50.7 μl, 343 μmol) at −20°C under N_2. The mixture was stirred for 1 h at that temperature, and then for 1 h at room temperature. Immediately after concentration in vacuo, the crude syrup obtained was directly chromatographed on silica gel (*n*-hexane/ethyl acetate, 1.0/0.8 v/v) to give title compound **13** (1.47 g, 94%): Rf 0.36 (*n*-hexane/ethyl acetate, 1.0/0.8 v/v); ^{1}H NMR ($CDCl_3$): δ 1.06 (3H, d, J = 6.1, H-6′), 1.83, 1.96, 2.09, 2.09, and 2.12 (each 3H, s, OAc), 3.84 (1H, m, J = 6.1, 9.7, H-5′), 4.16–4.19 (3H, m, H-5, H-6), 4.30 (1H, t, J = 9.7, H-3), 4.61–4.66 (4H, m, allyl), 4.99 (1H, t, J = 9.7, H-4′), 5.00 (1H, d, J = 1.4, H-1′), 5.12 (1H, dd, J = 3.6, 10.0, H-2), 5.13–5.16 (2H, m, H-2′ and H-3′), 5.29–5.33 (2H, m, allyl), 5.37 (1H, ddt, J = 2.4, 9.5, H-4), 5.40–5.41 (1H, m, allyl), 5.44–5.46 (1H, m, allyl), 6.02–6.12 (2H, m, allyl), 6.27 (1H, d, J = 15.8, CH═CH—COO), 6.60 (1H, d, J = 3.4, H-1), 6.88 (1H, d, J = 8.3, H-5‴), 7.07 (1H, d, J = 1.9, H-2‴), 7.09 (1H, dd, J = 1.9, 8.3, H-6‴), 7.67 (1H, d, J = 15.8, CH═CH—COO), 8.69 [1H, s, C(N═H)Cl_3]; ^{13}C NMR ($CDCl_3$): δ 17.7 (C-6′), 20.5, 20.6, 20.7, 20.8, and 21.0 (OAc), 61.8 (C-6), 67.2 (C-5′), 68.0 (C-4), 68.6 (C-3′ or C-2′), 69.7 (allyl), 69.9 (C-2′ or C-3′), 69.9 (allyl), 70.5 (C-5), 70.6 (C-4′), 72.2 (C-2), 76.8 (C-3), 90.7, 93.0 (C-1), 98.9 (C-1′), 112.6 (C-2‴), 113.2 (C-5‴), 113.9 (CH═CH—COO), 117.8 and 117.9 (allyl), 122.9 (C-6‴), 126.8 (C-1‴), 132.5 and 132.7 (allyl), 146.4 (CH═CH—COO), 148.4 (C-3‴), 150.9

(C-4‴), 160.4 [C(N=H)Cl_3], 165.2 (CH=CH—COO), 169.3, 169.6, 169.7 × 2, and 170.3 (OAc).

2-Oxo-2-(3,4-di-allyloxyphenyl)ethyl 2,6-di-*O*-acetyl-3-*O*-(2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl)-4-*O*-(3,4-di-allyloxycaffeoyl)-β-D-glucopyranoside **14** (protected β-oxoacteoside)

To a stirred solution of imidate **13** (0.756 g, 820 μmol), aglycon **19** (0.264 g, 1070 μmol), activated pulverized molecular sieves (0.4 nm) (0.181 g) in CH_2Cl_2 (1.62 ml) was added BF_3·Et_2O (20 μl, 163 μmol) at room temperature. After stirring for 2 h at room temperature, $NaHCO_3$ (0.139 g) was added. The mixture was diluted with CH_2Cl_2 (8 ml), passed through a celite pad, and washed with CH_2Cl_2 (1.5 ml × 3). The organic layer was washed with saturated $NaHCO_3$ solution, H_2O, and saturated NaCl solution (each 8 ml); dried over anhydrous Na_2SO_4, and concentrated in vacuo to yield a crude syrup. Purification by medium-pressure chromatography (*n*-hexane/ethyl acetate, 1.0/0.8 v/v) on silica gel afforded title compound **14** (paste, 0.495 g, 60%) and imidoyl-hydrolyzed product **12** (0.164 g, 25%). The products obtained were recrystallized from MeOH and a small amount of water (room temperature → −20°C) to give a white powder (0.427 g, 52%): Rf 0.19 (*n*-hexane/ethyl acetate, 1.0/0.8 v/v); mp 62°–89°C; ^{1}H NMR ($CDCl_3$): δ 1.04 (3H, d, *J* = 6.3, H-6′), 1.85, 1.95, 2.08, 2.10, and 2.11 (each 3H, s, OAc), 3.64 (1H, ddd, *J* = 3.4, 4.1, 9.7, H-5), 3.83 (1H, dq, *J* = 6.3, 9.8, H-5′), 3.96 (1H, t, *J* = 9.5, H-3), 4.15–4.17 (2H, m, H-6), 4.61–4.70 (8H, m, allyl), 4.62 (1H, d, *J* = 8.3, H-1), 4.80 (1H, d, *J* = 16, CO—$\underline{CH_2}$), 4.91 (1H, d, *J* = 1.9, H-1′), 4.92 (1H, d, *J* = 16, CO—$\underline{CH_2}$), 4.96 (1H, t, *J* = 10.0, H-4′), 5.06 (1H, dd, *J* = 1.9, 3.1, H-2′), 5.14 (1H, dd, *J* = 3.4, 10.0, H-3′), 5.18 (1H, dd, *J* = 8.3, 9.5, H-2), 5.25 (1H, t, *J* = 9.5, H-4), 5.29–5.34 (4H, m, allyl), 5.40–5.48 (4H, m, allyl), 6.02–6.14 (4H, m, allyl), 6.23 (1H, d, *J* = 15.8, CH=$\underline{CH}$—COO), 6.87 (1H, d, *J* = 8.3, H-5‴), 6.90 (1H, d, *J* = 8.5, H-5″), 7.05 (1H, d, *J* = 1.9, H-2‴), 7.07 (1H, dd, *J* = 1.9, 8.3, H-6‴), 7.50–7.53 (2H, m, H-2″ and H-6″), 7.63 (1H, d, *J* = 15.9, $\underline{CH}$=CH—COO); ^{13}C NMR ($CDCl_3$): δ 17.5 (C-6′), 20.5, 20.5, 20.7, 20.8, and 20.9 (OAc), 62.0 (C-6), 64.6, 67.0 (C-5′), 68.3 (C-3′), 68.8, 69.5, 69.6, 69.8, 69.9, 70.6 (C-4′), 72.0, 76.4, 76.8, 77.1, 79.9 (C-3), 98.7 (C-1′), 99.9 (C-1), 111.9 (C-5″), 112.3 (C-2‴), 112.5 (C-2″), 113.1 (C-5‴), 114.0 (C-2, CH=$\underline{CH}$—COO), 117.6, 117.7, 117.8, and 117.9 (allyl), 122.6 (C-6″), 122.6 (C-6‴), 126.7 (C-1‴), 127.5 (C-1″), 132.1, 132.4, 132.4, and 132.6 (allyl), 146.0 ($\underline{CH}$=CH—COO), 148.0 (C-3″ or C-3‴), 148.2 (C-3‴ or C-3″), 150.7 (C-4‴), 152.8 (C-4″), 165.0 (CH=CH—$\underline{COO}$), 168.5, 169.0, 169.4, 169.5, and 170.2 (OAc), 193.1 ($\underline{CO}$—CH_2).

3,4-Di-allyloxyprotocatechualdehyde **15**

To a stirred suspension of protocatechualdehyde (13.8 g, 0.1 mol), allylbromide (20.8 ml, 0.24 mol) in acetone (100 ml) was added powdered K_2CO_3 (33.2 g, 0.24 mol). The reaction mixture was stirred vigorously and refluxed for 2 h. The residual inorganic precipitates were filtered off, washed with acetone (25 ml × 3), and the filtrate was concentrated in vacuo. The residual yellow paste was diluted with Et_2O (200 ml), washed with 10% w/v NaOH solution (100 ml) for a short time, H_2O (100 ml × 2), and saturated NaCl solution (100 ml). The organic layer was dried over Na_2SO_4, filtered, and concentrated in vacuo to afford a crude paste. The crude materials were purified by flash chromatography on silica gel, giving title compound **15** (paste, 20.6 g, 94%): Rf 0.40 (*n*-hexane/ethyl acetate, 1.0/0.2 v/v); ^{1}H NMR ($CDCl_3$): 4.66–4.71 (4H, m, allyl), 5.30–5.35 (2H, m, allyl), 5.43–5.44 (1H, m, allyl), 5.47–5.48 (1H, m, allyl), 6.04–6.14 (2H, m, allyl), 6.98 (1H, d, *J* = 7.8, H-5), 7.41–7.45 (2H, m, H-2 and H-6), 9.83 (1H, s, CHO); ^{13}C NMR ($CDCl_3$): δ 69.6 and 69.7 (allyl), 111.4 (C-2), 112.2 (C-5), 117.9 and 118.1 (allyl), 126.3 (C-6′), 129.9 (C-1), 132.1 and 132.4 (allyl), 148.6 (C-3), 153.6 (C-4), 190.4 (CHO); FAB-MS: *m*/*z* 218 (M), 219 (M + 1).

3,4-Di-*O*-allylcaffeic acid **16**

To a solution of compound **15** (4.36 g, 20.0 mmol) and malonic acid (2.51 g, 24.0 mmol) in pyridine (10 ml) was added piperidine (116 μl, 1.99 mmol) at room temperature. The mixture was heated at 60°C for 24 h. After completion of the reaction, the mixture was poured into 2M HCl (70 ml) with stirring and allowed to stand overnight (−20°C). The residual crystals were filtered off, washed with cold water (10 ml × 3), and dried in vacuo. Recrystallization from MeOH at reflux gave title compound **16** (4.34 g, 84%). A second crop was recovered from the mother liquor (0.179 g, 3.4%): Rf 0.58 (toluene/HCOOEt/HCOOH, 5/4/1 v/v/v); mp 159°–160°C; ^{1}H NMR ($CDCl_3$): δ 4.64–4.66 (4H, m, allyl), 5.29–5.33 (2H, m, allyl), 5.40–5.43 (1H, m, allyl), 5.45–5.47 (1H, m, allyl), 6.03–6.14 (2H, m, allyl), 6.29 (1H, d, *J* = 15.8, CH=$\underline{CH}$—COOH), 6.89 (1H, d, *J* = 8.5, H-5), 7.10–7.13 (2H, m, H-2 and H-6), 7.71 (1H, d, *J* = 15.8, $\underline{CH}$=CH—COOH); ^{13}C NMR ($CDCl_3$): δ 69.7 and 69.9 (allyl), 112.7 (C-2), 113.2 (C-5), 114.8 (CH=$\underline{CH}$—COOH), 117.8 and 117.8 (allyl), 123.0 (C-6), 127.0 (C-1), 132.6 and 132.8 (allyl), 146.7 ($\underline{CH}$=CH—COOH), 148.3 (C-3), 150.8 (C-4), 172.4 (CH=CH—$\underline{CO}$OH); FAB-MS: *m*/*z* 260 (M), 283 (M + 23).

2,3′,4′-Triacetoxyacetophenone **17**[32]

A suspended solution containing 4-chloroacetylcatechol (43.6 g, 0.23 mol), pulverized molten CH_3COOK (34.3 g, 0.35 mol), and Ac_2O (218 ml, 2.30 mol) was stirred for 20 min at room temperature before it was heated at 140°C for 10 min. Charcoal (5 g) was added to this mixture and the flask was swirled for 5 min at 140°C, and then cooled in an ice bath. The mixture was filtered through a celite pad and washed with Ac_2O (50 ml × 3). The filtrate and washings were concentrated in vacuo, and poured into water (1800 ml); the resulting precipitate was filtered off, washed with cold water (100 ml × 3), and dried over anhydrous KOH in vacuo to give the crude products. The crude products were recrystallized from acetic acid (280 ml) and water (424 ml), standing at 40°C → −18°C, to afford pure compound **17** (51.5 g, 75%): Rf 0.49 (toluene/HCOOEt/

HCOOH, 7/2/1 v/v/v); mp 95°–96°C; ^{1}H NMR ($CDCl_3$): δ 2.22, 2.31, and 2.32 (3H, s, OAc), 5.28 (2H, CO—$\underline{CH_2}$—OAc), 7.34 (1H, d, J = 8.3, H-5′), 7.77 (1H, d, J = 1.9, H-2′), 7.82 (1H, dd, J = 1.9, 8.3, H-6′); ^{13}C NMR ($CDCl_3$): δ 20.6 × 2 and 20.7 (OAc), 65.8 (CO—$\underline{CH_2}$—OAc), 123.1 (C-2′), 123.8 (C-5′), 126.0 (C-6′), 132.3 (C-1′), 142.3 (C-3′), 146.4 (C-4′), 167.2, 167.5, and 169.9 (OAc), 190.0 ($\underline{CO}$—CH_2—OAc); FAB-MS: m/z 248 (M), 249 (M + 1).

2,3′,4′-Trihydroxyacetophenone **18**[31]

To a stirred suspension of compound **17** (44.8 g, 152 mmol) in MeOH (179 ml) was added concentrated HCl (5.01 ml, 50.1 mmol) under N_2 at room temperature. The mixture was stirred for 40 h at room temperature and then concentrated in vacuo and dried over anhydrous KOH in vacuo to afford the crude products. Recrystallization from hot EtOH (238 ml) and n-hexane (244 ml) (60°C → −18°C) gave title compound **18** (17.7 g, 69%). The second crystal was recovered from the filtered mother liquor by further recrystallization (4.34 g, 17%): Rf 0.29 (toluene/HCOOEt/HCOOH, 5/4/1 v/v/v); mp 161°–162°C; UV (CH_3OH): λ_{max} nm (log ε) 308 (3.89), 276 (3.98), 231 (4.14), 206 (4.22); ^{1}H NMR (DMSO-d_6): δ 3.65 (1H, broad d, J = 4.6, CO—CH_2—$\underline{OH}$), 4.64 (2H, s, CO—$\underline{CH_2}$—OH), 6.80 (1H, dd, J = 2.0, 8.1, H-5′), 7.30–7.31 (2H, m, H-2′ and H-6′), 9.54 (broad s, PhOH), 9.86 (broad s, PhOH); ^{1}H NMR (CD_3OD): δ 4.79 (2H, s, CO—$\underline{CH_2}$—OH), 6.84 (1H, d, J = 8.1, H-5′), 7.38 (1H, dd, J = 2.2, 8.1, H-6′), 7.40 (1H, d, J = 1.7, H-2′); ^{1}H NMR (Acetone-d_6): δ 3.79 (broad t, J = 5.13, CO—CH_2—$\underline{OH}$), 4.77 (2H, d, J = 5.13, CO—$\underline{CH_2}$—OH), 6.94 (1H, d, J = 8.3, H-5′), 7.44 (1H, dd, J = 2.2, 8.3, H-6′), 7.48 (1H, d, J = 2.2, H-2′), 8.44 (broad d, J = 3.9, PhOH), 8.86 (broad d, J = 3.6, PhOH); ^{13}C NMR (CD_3OD): δ 65.7 (CO—$\underline{CH_2}$—OH), 115.2 (C-2′), 115.8 (C-5′), 122.1 (C-6′), 127.5 (C-1′), 146.4 (C-3′), 152.3 (C-4′), 198.2 ($\underline{CO}$—CH_2—OH); ^{13}C NMR (Acetone-d_6): δ 65.4 (CO—$\underline{CH_2}$—OH), 115.0 (C-2′), 115.7 (C-5′), 121.9 (C-6′), 127.2 (C-1′), 145.7 (C-3′), 151.4 (C-4′), 197.3 ($\underline{CO}$—CH_2—OH); IR (KBr): 3502 cm^{-1} (82%), 3380 (27), 3116 (50), 1668 (4), 1608 (5), 1523 (33), 1425 (30), 1392 (45), 1340 (27), 1299 (4), 1261 (30), 1228 (47), 1197 (11), 1135 (40), 1089 (10), 1014 (43), 892 (43), 808 (31), 777 (29); FAB-MS: m/z 168 (M).

3′,4′-Di-allyloxy-2-hydroxyacetophenone **19**

To a solution of compound **18** (4.20 g, 25.0 mmol) and allylbromide (7.27 g, 60.1 mmol) in anhydrous DMF (12.5 ml) was added finely powdered K_2CO_3 (8.29 g, 60.0 mmol) at room temperature. The mixture was stirred for 4 h at room temperature, and then swirled at 60°C for 20 min. After completion of the reaction, the mixture was poured into cold water (63 ml), and allowed to stand overnight. The resulting precipitate was collected, washed with cold water (10 ml × 3), and dried in vacuo to give the crude products. Recrystallization from MeOH (7.0 ml, 70°C → −18°C) afforded title compound **19** (4.01 g, 65%). Further recrystallization from the filtered mother liquor gave crystals of compound **19** (0.978 g, 16%): Rf 0.50 (toluene/HCOOEt/HCOOH, 5/4/1 v/v/v); mp 72°–75°C; ^{1}H NMR ($CDCl_3$): δ 3.55 (1H, broad s, CO—CH_2—$\underline{OH}$), 4.66–4.70 (4H, allyl), 4.81 (2H, broad s, CO—$\underline{CH_2}$—OH), 5.30–5.35 (2H, m, allyl), 5.42–5.44 (1H, m, allyl), 5.46–5.48 (1H, m, allyl), 6.03–6.14 (2H, m, allyl), 6.92 (1H, d, J = 8.5, H-5′), 7.47 (1H, dd, J = 1.9, 8.3, H-6′), 7.52 (1H, d, J = 1.9, H-2′); ^{13}C NMR ($CDCl_3$): δ 64.9 (CO—$\underline{CH_2}$—OH), 69.6 and 69.9 (allyl), 112.2 (C-5′), 112.2 (C-2′), 118.0 and 118.1 (allyl), 122.1 (C-6′), 126.3 (C-1′), 132.1 and 132.5 (allyl), 148.3 (C-3′), 153.4 (C-4′), 196.4 ($\underline{CO}$—CH_2—OH); FAB-MS: m/z 248 (M), 249 (M + 1).

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