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Cleavage of the C–C linkage between the sugar and the aglycon in *C*-glycosylphloroacetophenone, and the NMR spectral characteristics of the resulting di-*C*-glycosyl compound

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Abstract

The treatment of unprotected mono-*C*-β-D-glucopyranosylphloroacetophenone with a cation-exchange resin in anhydrous acetonitrile afforded both a phloroacetophenone and a di-*C*-β-D-glucopyranosylphloroacetophenone. Treatment of an unprotected mono-*C*-(2-deoxy-β-D-*arabino*-hexopyranosyl)phloroacetophenone (mono-*C*-2-deoxy-β-D-glucopyranosylphloroacetophenone) also afforded both the aglycon and di-*C*-(2-deoxy-β-D-*arabino*-hexopyranosyl)phloroacetophenone. The reaction mixtures were acetylated, and the structures of the isolated products were determined by NMR spectroscopy. This is the first demonstration of the formation of a di-*C*-glycosyl compound during the chemical cleavage of the C–C linkage between the sugar and the aglycon in an aryl *C*-glycosyl derivative.

Keywords: *C*-Glycosylflavonoid; *C*-Glycosyl compound; Di-*C*-Glycosyl compound; C–C linkage; Cation exchange resin

1. Introduction

Because of their biological activity, an efficient synthesis of aryl *C*-glycosylic compounds (aryl '*C*-glycosides') has been a subject of considerable interest, and several effective methods in this area have been reported to date.[1] The characteristic properties of aryl *C*-glycosyl compounds include resistance to acid hydrolysis, in contrast to *O*-glycosides. Therefore, these compounds have the potential for use as therapeutic agents for clinical use. *C*-glycosylflavonoids are plant constituents, some of which are biologically active.[2] Recently, we reported on the synthesis of *C*-glycosylphloroacetophenone derivatives,[3] which represent synthetic intermediates in the preparation of *C*-glycosylflavonoids, and for the regio- and stereoselective synthesis of isoorientin, 6-*C*-glucosylflavone.[4] In the field of *C*-glycosylflavonoid chemistry, three types of reactions are possible under hydrolytic conditions:[5] (1) the Wessely–Moser rearrangement of the aglycon moiety, but not the sugar; (2) the expected pyranose–furanose interconversion; and (3) the acid-catalyzed degradation of the *C*-glycosyl compound. In order to avoid

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the Wessely–Moser rearrangement of the aglycon moiety in the flavone during acid hydrolysis, *C*-glycosylphloroacetophenones were used, and it was shown that they could be converted into spiroketal compounds on treatment with a catalytic amount of *p*-toluenesulfonic acid in hot water.[6] However, Minamikawa and co-workers reported that bergenin, a *C*-glucoside derivative of 4-*O*-methylgallic acid, was transformed into a 4-*O*-methylgallic acid by a strain of soil bacteria.[7] Hattori and co-workers have showed that several *C*-glycosyl compounds, including *C*-glycosylflavonoids, were transformed into their corresponding aglycons by human intestinal bacteria on the course of a study of the metabolites of *C*-glycosyl compounds.[8] These results provide a clear demonstration of the enzymic hydrolysis of *C*-glycosyl compounds. On the other hand, treatment with a hydroiodic acid–phenol mixture readily yielded the corresponding isoflavones from *C*-glycosylisoflavones.[9] Ferric chloride oxidation also has been used to identify the *C*-glycosyl residue in *C*-glycosylisoflavones.[9,10] These chemical methods involve the cleavage of the C–C linkage in the aryl *C*-glycosyl compound and show that it is possible, using enzymic or chemical methods, to convert them to the corresponding aglycon and sugar. The present report shows that the C–C bond linkage between the sugar and the carbon atom of an aglycon in the *C*-glycosylphloroacetophenone can be cleaved using a strongly acidic cation-exchange resin in anhydrous acetonitrile, resulting in the production of the aglycon and di-*C*-glycosylphloroacetophenone. The formation of such a di-*C*-glycosyl compound under conditions of acidic hydrolysis has not previously been reported.

2. Results and discussion

Treatment of a solution of *C*-β-D-glucopyranosylphloroacetophenone (**1a**)[3a] with Dowex® 50W (H^+ form) at ambient temperature in anhydrous acetonitrile showed, by thin-layer chromatography (TLC), the presence of two new zones at the top and near the bottom of the plate that corresponded to phenolic substituents (red–brown with 5% ferric chloride spray), in addition to mono-*C*-glucosyl compound **1a** and a number of noncolored byproducts. Because of difficulties in the purification of these compounds, the reaction mixture was acetylated. After silica-gel column chromatography, acetylphloroacetophenone **2** was obtained in 31% yield, along with mono-*C*-β-D-glucosylphloroacetophenone acetate **3a** in 22% yield, and di-*C*-β-D-glucosylphloroacetophenone acetate **4a** in 9% yield (Entry 2). The structure of the aglycon acetate **2** was confirmed by a comparison of its ^{1}H NMR spectrum with an authentic sample. A ^{1}H NMR spectrum of the mono-*C*-glucosyl derivative **3a** was obtained at 50 °C in $CDCl_3$ because a structural assignment by NMR spectroscopy at ambient temperature was hampered by the slow rotation around the C-1–aglycon bond. The ^{13}C NMR spectrum of compound **3a** in $CDCl_3$ at ambient temperature showed that some of the peaks were broad and that the peaks that correspond to the aglycon represented the pairing of major and minor peaks. ^{1}H NMR spectra of the di-*C*-glucosyl derivative **4a** showed that the methine and methylene signals of each glucose moiety could be identified independently at ambient temperature in $CDCl_3$. The reason for this is mentioned above. To eliminate the rotational hindrance in compound **4a**, the ^{1}H NMR spectrum was obtained at an elevated temperature of 140 °C in Me_2SO-d_6. Although a slow decomposition of compound **4a** was observed during this ^{1}H NMR experiment at this temperature, the ^{1}H NMR spectra showed that the signals were sharpened, and that the chemical shift values for both the methine and methylene protons of the glucose moieties were clear and equivalent. Judging from $J_{1',2'} = J_{1'',2''} = 9.5$ Hz, the anomeric configuration of both of the glucose moieties of compound **4a** is β. We previously described the β stereoselective synthesis of mono-*C*-glucopyranosylphloroacetophenone using 2,4-dibenzyl-protected phloroacetophenone as a glycosyl acceptor, benzyl-protected glucosyl fluoride as a glycosyl donor, and boron trifluoride diethyl etherate as an activator, in CH_2Cl_2.[3a] In this study, the formation of the di-*C*-glucosyl compound **4a**, having a β

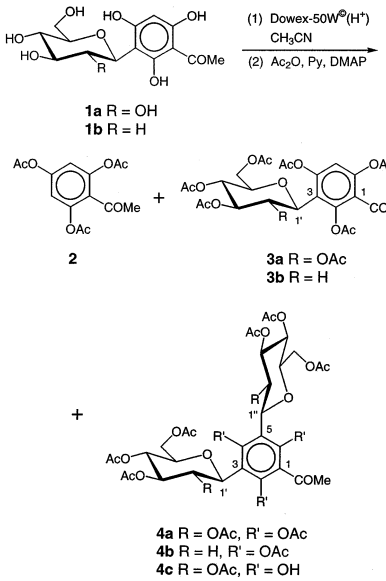
configuration for both of the glucose moieties, was verified when unprotected starting material **1a** was used. In relation to this fact, the glucose moieties in all natural di-*C*-glucosylflavonoids isolated thus far are of the β configuration. The ^{13}C NMR spectrum of compound **4a** at ambient temperature in $CDCl_3$ showed that the chemical shift values for C-3 and C-5 of the aromatic ring were not equivalent, and that the chemical shift values for the C-2 and C-6 were also not equivalent. We previously reported on the synthesis of 3,5-di-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)phloroacetophenone **4c**.[11] When the ^{13}C NMR spectra of the fully protected di-*C*-glucosyl compound **4a** was compared with that of compound **4c**, the data showed that the chemical shift values for the C-3 and C-5, as well as C-2 and C-6 of its aromatic ring, were equivalent. These differences result from the existence of acetyl groups on the phenolic hydroxy groups and are the result of the slow rotation around the C-1–aglycon bonds. HMBC spectra of the compound **4a** indicated that the H-1′ signal was correlated to the C-2, C-3, and the C-4 signals, and that the H-1″ signal was correlated to the C-4, C-5, and the C-6 signals. Therefore, all carbon signals in the aromatic ring could be assigned.

The cleavage of the C–C linkage of *C*-glucosylphloroacetophenone **1a** with Dowex® 50W (H^+) was examined under several conditions, and the results are summarized in Table 1. As a matter of course, when less cation-exchange resin was used, the yields of the aglycon acetate **2** and the di-*C*-glucosyl compound **4a** decreased, and when the reaction was carried out at the low temperature, their yields also decreased. Compound **1a** could be cleaved to generate an aglycon and a sugar oxonium ion by treatment with acid. The oxonium ion attacked the mono-*C*-glucosyl compound **1a** to give the unprotected di-*C*-glucosyl compound. The mechanism of the formation of the unprotected di-*C*-glucosyl compound is not clear. It is possible that the second *C*-glucosylation of the mono-*C*-glucosyl compound involved a Friedel–Crafts type reaction or underwent an O→C glycosylic rearrangement. To the contrary, it is also possible that the unprotected di-*C*-glucosyl compound was converted to the unprotected mono-*C*-glucosyl compound **1a** by acid, and was then converted to the aglycon. In addition, the decomposition of the oxonium ion is also possible during the reaction. Therefore, the yield of the di-*C*-glucosyl compound **4a** would not be expected to be over 10%. The possibility that a hydroxy group, positioned at C-2 of the glucose moiety of the mono-*C*-glucosyl compound **1a**, influences the formation of the di-*C*-glycosylation product also cannot be excluded.

We next examined the cleavage of an unprotected *C*-(2-deoxy-β-D-*arabino*-hexopyranosyl)phloroacetophenone **1b**[3a] [*C*-(2-deoxy-β-D-glucopyranosyl)phloroacetophenone], which does not contain a 2-OH group. The reaction was carried out under identical conditions, and the resulting mixture was acetylated. Acetylphloroacetophenone **2** in 31% yield, mono - *C* - (2-deoxy-β-D-*arabino*-hexopyranosyl)phloroacetophenone acetate **3b** in 22% yield, and di-*C*-(2-deoxy-β-D-*arabino*-hexopyranosyl)phloroacetophenone acetate **4b** in 9% yield were obtained, respectively. The yield of compound **4b** was less than 10%, by analogy with the di-*C*-glucosyl compound **4a**. We conclude from this experiment that the 2-OH group of the glucose moiety is not a factor in

Table 1
Cleavage of the C–C linkage of mono-*C*-glucosyl **1a** and formation of both the corresponding aglycon **2** and di-*C*-glucosyl **4a**

Entry	**1a** (mg)	Dowex®-50W (H^+) (g)	CH_3CN (mL)	Time (h)	Temperature (°C)	Yield **2** (%)	Yield **3a** (%)	Yield **4a** (%)
1	100	0.3	10	0.5	rt	15	50	8.2
2	100	1.5	50	0.5	rt	31	22	9.1
3	100	0.3	50	0.5	rt	17	53	5.0
4	100	1.5	50	5	0	32	27	9.3
5	100	7.5	100	5	−23	15	67	4.4



Scheme 1.

this reaction. Whereas the ^{1}H NMR spectrum of the compound **3b** was clear at ambient temperature, the ^{1}H NMR experiment of the di-*C*-2-deoxy-glucosyl compound **4b** had to be carried out at 50 °C in $CDCl_3$ because the structural assignment by NMR spectroscopy at ambient temperature was hampered by the slow rotation around the C-1–aglycon bond. Based on the fact that $J_{1',2'ax} = J_{1'',2''ax} = 9.5$ Hz, the anomeric configuration of both of the 2-deoxy-glucose moieties of compound **4b** can be assigned as β. The ^{13}C NMR spectrum of compound **4b** in $CDCl_3$ at ambient temperature showed that some of carbon peaks of the 2-deoxy-glucose moieties were broad. In particular, the carbon signals of C-1′ and C-1″ of the sugar moieties were broadened. The reason for this is mentioned above. Alternatively, the ^{13}C NMR spectrum of compound **4b** in acetone-d_6 at ambient temperature showed that the C-1′ and C-1″ signals were identified at 72.0 and 73.1 ppm, respectively, although these peaks may be interchanged.

In conclusion, the unprotected *C*-glycosylphloroacetophenones gives the aglycon and the di-*C*-glycosylphloroacetophenone on treatment with a cation-exchange resin in anhydrous acetonitrile. Alternatively, they give the spiroketal compounds on treatment with *p*-toluenesulfonic acid in hot water. This is the first demonstration of the formation of a di-*C*-glycosyl compound during the chemical cleavage of the C–C linkage between the sugar and the aglycon in the aryl *C*-glycosyl compound (Scheme 1).

3. Experimental

General methods.—All nonaqueous reactions were carried out under an atmosphere of dry Ar using freshly distilled solvent, unless otherwise noted. All reactions were monitored by TLC, which was carried out on 0.25 mm Silica Gel 60 F_{254} plates (E. Merck) using either UV light, a 5% ethanolic solution of ferric chloride or a 5% ethanolic solution of phosphomolybdic acid with heat as developing agents. Fuji Silysia BW-300 was used for silica-gel column chromatography. Optical rotations were recorded using $CHCl_3$ as the solvent on a JASCO DIP-370 digital polarimeter. IR spectra were recorded on a HORIBA FT-720 IR spectrometer as KBr pellets. Mass spectra were recorded on a JEOL JMS-AX-505-HA mass spectrometer under electron ionization (EI) conditions or under fast-atom bombardment (FAB) conditions using 3-nitrobenzyl alcohol as the matrix. ^{1}H NMR spectra were recorded on a VARIAN INOVA 500 instrument using Me_4Si as the internal reference.

2,4,6-Tri-acetoxyacetophenone (**2**), *2,4,6-tri-acetoxy-3-*C*-(2,3,4,6-tetra-*O*-acetyl-β-*D*-glucopyranosyl)acetophenone* (**3a**), *and 2,4,6-tri-acetoxy-3,5-bis-*C*-(2,3,4,6-tetra-*O*-acetyl-β-*D*-glucopyranosyl)acetophenone* (**4a**).—To a stirred solution of compound **1a**[3a] (100 mg), Dowex®-50W (H^+) which had been dried at 70 °C for 3 h under vacuo, was added. After 0.5 h, MeOH was added to the reaction mixture, and it was filtered to remove the resin. The solvent was evaporated under reduced pressure. The residual syrup was acetylated for 12 h at 0 °C using Ac_2O, pyridine, and a catalytic amount of 4,4-dimethylaminopyridine (DMAP). The reaction mixture was poured into 0.5 M HCl in ice and extracted with EtOAc. The organic layer was washed with water and brine, and the solvent was evaporated at reduced pressure. The residual syrup was purified by column chromatography on silica gel (1:1 → 1:2 hexane–EtOAc) to

give compound **2** (28 mg, 31%) as a colorless powder, compound **3a** (41 mg, 22%) as a colorless powder and compound **4a** (26 mg, 9%) as a crude syrup. Recrystallization of crude compound **4a** from hexane–Et_2O gave an analytically pure sample.

Physicochemical data for (**3a**): mp 191–193 °C; $[\alpha]_D^{25}$ −24° (*c* 1.0, $CHCl_3$); R_f 0.26 (1:1 hexane–EtOAc); IR (KBr): *v* 3107, 3066, 2979, 2943, 2895, 1774, 1755, 1701, 1612, 1429, 1371, 1238, 1213, 1182, 1151, 1101, 1055, 912, 901, 877, 839 cm^{-1}; ^1H NMR ($CDCl_3$ at 50 °C): δ 1.79 (s, 3 H, –OAc), 2.00 (s, 3 H, –OAc), 2.03 (s, 3 H, –OAc), 2.05 (s, 3 H, –OAc), 2.25 (s, 3 H, ArOAc), 2.31* (s, 3 H, ArOAc), 2.37* (s, 3 H, ArOAc), 2.41 (s, 3 H, ArAc), 3.75 (ddd, 1 H, $J_{5',6'a}$ 2.2, $J_{5',6'b}$ 4.6, $J_{4',5'}$ 10.1 Hz, H-5′), 3.99 (dd, 1 H, $J_{5',6'a}$ 2.2, J_{gem} 12.6 Hz, H-6′a), 4.37 (dd, 1 H, $J_{5',6'b}$ 4.6, J_{gem}12.6 Hz, H-6′b), 4.73* (br. d, 1 H, $J_{1',2'}$ 9.9 Hz, H-1′), 5.14 (dd, 1 H, $J_{3',4'}$ 9.3, $J_{4',5'}$ 10.1 Hz, H-4′), 5.25 (t, 1 H, $J_{2',3'} = J_{3',4'}$ 9.3 Hz, H-3′), 5.61* (dd, 1 H, $J_{2',3'}$ 9.3, $J_{1',2'}$ 9.9 Hz, H-2′), 7.01* (br. s, 1 H, ArH). The (*) indicates broad peaks. ^{13}C NMR ($CDCl_3$): δ 20.3, 20.59, 20.65, 20.7, 20.9*, 21.0, 21.2* (–OAc), 30.7*, 30.9* (ArAc), 61.9* (C-6′), 68.0 (C-4′), 69.7*, 70.0* (C-2′), 72.8 (C-1′), 74.5* (C-3′), 76.7* (C-5′), 115.4*, 116.9* (C-5), 118.8*, 119.2* (C-3), 125.7*, 127.2* (C-1), 146.5*, 147.8*, 148.0*, 148.2*, 149.8*, 151.3* (C-2,4,6), 167.6*, 167.7*, 167.8*, 168.0, 168.3, 169.3*, 169.5, 170.3, 170.5 (–OAc), 197.2*, 197.7*(ArAc). The (*) indicates broad peaks, and C-2, -4, and -6 may be interchanged. EIMS: *m/z* 624 $[M]^+$. Anal. Calcd for $C_{28}H_{32}O_{16}$: C, 53.85; H, 5.16. Found: C, 53.61; H, 5.16.

Physicochemical data for (**4a**): mp 137–139 °C; $[\alpha]_D^{25}$ −21° (*c* 1.0, $CHCl_3$); R_f 0.10 (1:1 hexane–EtOAc); IR (KBr): *v* 2943, 1784, 1759, 1707, 1597, 1435, 1371, 1230, 1171, 1142, 1090, 1055, 1036, 903, 874 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.73 (s, 3 H, –OAc), 1.93 (s, 3 H, –OAc), 2.01 (s, 3 H, –OAc), 2.032 (s, 6 H, –OAc), 2.038 (s, 3 H, –OAc), 2.043 (s, 3 H, –OAc), 2.09 (s, 3 H, –OAc), 2.30 (s, 3 H, –OAc), 2.37 (s, 3 H, –OAc), 2.41 (s, 3 H, ArAc), 2.46 (s, 3 H, –OAc), 3.62 (ddd, 1 H, $J_{5',6'a}$ 1.5, $J_{5',6'b}$ 4.9, $J_{4',5'}$ 9.8 Hz, H-5′), 3.78 (ddd, 1 H, $J_{5'',6''a}$ 1.5, $J_{5'',6''b}$ 4.9, $J_{4'',5''}$ 9.8 Hz, H-5″), 3.92 (dd, 1 H, $J_{5',6'a}$ 1.5, J_{gem} 13.5 Hz, H-6′a), 3.98 (dd, 1 H, $J_{5'',6''a}$ 1.5, J_{gem} 13.5 Hz, H-6″a), 4.34 (d, 1 H, $J_{1',2'}$ 10.0 Hz, H-1′), 4.40 (dd, 1 H, $J_{5',6'b}$ 4.9, J_{gem} 13.5 Hz, H-6′b), 4.42 (dd, 1 H, $J_{5'',6''b}$ 4.9, J_{gem} 13.5 Hz, H-6″b), 4.78 (d, 1 H, $J_{1'',2''}$ 10.0 Hz, H-1″), 5.130 (dd, 1 H, $J_{3',4'}$ 9.3, $J_{4',5'}$ 9.8 Hz, H-4′), 5.135 (dd, 1 H, $J_{3'',4''}$ 9.3, $J_{4'',5''}$ 9.8 Hz, H-4″), 5.22 (t, 1 H, $J_{2'',3''} = J_{3'',4''}$ 9.3 Hz, H-3″), 5.32 (t, 1 H, $J_{2',3'} = J_{3',4'}$ 9.3 Hz, H-3′), 5.57 (dd, 1 H, $J_{2'',3''}$ 9.3, $J_{1'',2''}$ 10.0 Hz, H-2″), 5.71 (dd, 1 H, $J_{2',3'}$ 9.3, $J_{1',2'}$ 10.0 Hz, H-2′); ^1H NMR (Me_2SO-d_6 at 140 °C): δ 1.73 (s, 6 H, –OAc), 1.92 (s, 6 H, –OAc), 1.96 (s, 6 H, –OAc), 1.98 (s, 6 H, –OAc), 2.27 (s, 6 H, –OAc), 2.30 (s, 3 H, –OAc), 2.38 (s, 3 H, ArAc), 3.95 (dd, 2 H, $J_{5',6'a} = J_{5'',6''a}$ 2.2, $J_{6'a,6'b} = J_{6''a,6''b}$ 12.5 Hz, H-6a′,6″a), 4.03 (ddd, 2 H, $J_{5',6'a} = J_{5'',6''a}$ 2.2, $J_{5',6'b} = J_{5'',6''b}$ 5.1, $J_{4',5'} = J_{4'',5''}$ 9.8 Hz, H-5′,5″), 4.14 (dd, 2 H, $J_{5',6'b} = J_{5'',6''b}$ 5.1, $J_{6'a,6'b} = J_{6''a,6''b}$ 12.5 Hz, H-6′b,6″b), 4.75* (d, 2 H, $J_{1',2'} = J_{1'',2''}$ 9.5Hz, H-1′,1″), 5.00 (t, 2 H, $J_{3',4'} = J_{3'',4''} = J_{4',5'} = J_{4'',5''}$ 9.8 Hz, H-4′,4″), 5.33 (dd, 2 H, $J_{2',3'} = J_{2'',3''}$ 9.5, $J_{3',4'} = J_{3'',4''}$ 9.8 Hz, H-3′,3″), 5.55 (t, 2 H, $J_{1',2'} = J_{1'',2''} = J_{2',3'} = J_{2'',3''}$ 9.5 Hz, H-2′,2″). The (*) indicates a broad peak. ^{13}C NMR ($CDCl_3$): δ 20.1, 20.3, 20.58, 20.62, 20.67, 20.68, 20.8, 20.9, 21.08, 21.13 (–OAc), 29.9 (ArAc), 61.6 (C-6′), 61.8 (C-6″), 68.0 (C-4′,4″), 69.4 (C-2″), 70.0 (C-2′), 73.0 (C-1″), 73.6 (C-1′), 74.4 (C-3′), 74.5 (C-3″), 76.9 (C-5′), 77.1 (C-5″), 119.6 (C-5), 121.7 (C-3), 128.7 (C-1), 146.4 (C-6) 148.4 (C-2), 150.8 (C-4) 167.3, 167.6, 168.1, 169.2, 169.5, 169.8, 170.22, 170.28, 170.41, 170.44 (–OAc), 197.4 (ArAc); FABMS (positive ion): *m/z* 955 $[M+H]^+$. Anal. Calcd for $C_{42}H_{50}O_{25}$: C, 52.83; H, 5.28. Found: C, 53.00; H, 5.31.

2,4,6-Tri-acetoxyacetophenone (**2**), *2,4,6-tri-acetoxy-3-*C*-(3,4,6-tri-*O*-acetyl-2-deoxy-β-*D*-*arabino*-hexopyranosyl)acetophenone* (**3b**), *and 2,4,6-tri-acetoxy-3,5-bis-*C*-(3,4,6-tri-*O*-acetyl-2-deoxy-β-*D*-*arabino*-hexopyranosyl)acetophenone* (**4b**).—The reaction conditions, post-treatment, and isolation were carried out in the same manner as described above. Recrystallization of crude compound **4b** from hexane–Et_2O gave an analytically pure sample.

Physicochemical data for (**3b**): mp 132–133 °C; $[\alpha]_D^{25}$ −14° (*c* 1.0, $CHCl_3$); R_f 0.29 (1:1 hexane–EtOAc); IR (KBr): *v* 3103, 3064,

3024, 2995, 2972, 2962, 2943, 2904, 2893, 1770, 1743, 1695, 1618, 1437, 1371, 1254, 1219, 1190, 1151, 1113, 1066, 1053, 1012, 920, 906, 881 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.03 (s, 3 H, –OAc), 2.04 (s, 3 H, –OAc), 2.06 (s, 3 H, 6′-OAc), 2.14 (ddd, 1 H, $J_{1',2'eq}$ 2.2, $J_{2'eq,3'}$ 5.4, J_{gem} 13.2 Hz, H-2′eq), 2.28 (s, 3 H, 6-OAc), 2.31 (s, 3 H, 2-OAc), 2.34 (ddd, 1 H, $J_{2'ax,3'}$ 11.2, $J_{1',2'ax}$ 12.0, J_{gem} 13.2 Hz, H-2′ax), 2.37 (s, 3 H, 4-OAc), 2.45 (s, 3 H, ArAc), 3.66 (ddd, 1 H, $J = J_{5',6'a}$ 2.0, $J_{5',6'b}$ 4.6, $J_{4',5'}$ 9.8 Hz, H-5′), 3.94 (dd, 1 H, $J_{5',6'a}$ 2.0, J_{gem} 12.5 Hz, H-6′a), 4.43 (dd, 1 H, $J_{5',6'b}$ 4.6, J_{gem} 12.5 Hz, H-6′b), 4.66 (dd, 1 H, $J_{1',2'eq}$ 2.2, $J_{1',2'ax}$ 12.0 Hz, H-1′), 5.03 (dd, 1 H, $J_{3',4'}$ 9.3, $J_{4',5'}$ 9.8 Hz, H-4′), 5.10 (ddd, 1 H, $J_{2'eq,3'}$ 5.4, $J_{3',4'}$ 9.3, $J_{2'ax,3'}$ 11.2 Hz, H-3′), 6.98 (s, 1 H, ArH); ^{13}C NMR ($CDCl_3$): δ 20.71, 20.79, 20.8, 20.9, 21.02, 21.03 (–OAc), 31.0 (ArAc), 34.4 (C-2′), 62.4 (C-6′), 68.9 (C-4′), 71.5 (C-1′), 71.9 (C-3′), 76.9 (C-5′), 116.3 (C-5), 122.9 (C-3), 126.6 (C-1), 146.2 (C-2), 147.4 (C-6), 149.8 (C-4), 167.8 (6-OAc), 168.2 (2-OAc), 168.5 (4-OAc), 169.9 (–OAc), 170.3 (–OAc), 170.5 (6′-OAc), 197.8 (ArAc); EIMS: m/z 566 $[M]^+$. Anal. Calcd for $C_{26}H_{30}O_{14}$: C, 55.12; H, 5.34. Found: C, 55.06; H, 5.34.

Physicochemical data for (**4b**): mp 113–115 °C; $[\alpha]_D^{25}$ −1° (*c* 0.5, $CHCl_3$); R_f 0.12 (1:1 hexane–EtOAc); IR (KBr): ν 2956, 2943, 2877, 1780, 1747, 1705, 1597, 1435, 1369, 1232, 1180, 1107, 1053, 962, 908, 883, 868 cm^{-1}; ^1H NMR ($CDCl_3$ at 50 °C): δ 2.02 (s, 6 H, –OAc), 2.03 (s, 6 H, –OAc), 2.05 (s, 6 H, –OAc), 2.14 (ddd, 2 H, $J_{1',2'eq} = J_{1'',2''eq}$ 2.0, $J_{2'eq,3'} = J_{2''eq,3''}$ 5.4, $J_{2'ax,2'eq} = J_{2''ax,2''eq}$ 13.3 Hz, H-2′eq, 2″eq), 2.30 (s, 6 H, –OAc), 2.304 (ddd, 2 H, $J_{2'ax,3'} = J_{2''ax,3''}$ 11.0, $J_{1',2'ax} = J_{1'',2''ax}$ 11.7, $J_{2'ax,2'eq} = J_{2''ax,2''eq}$ 13.3 Hz, H-2′ax, 2″ax), 2.411* (s, 3 H, ArAc), 2.412* (s, 3 H, –OAc), 3.61 (ddd, 2 H, $J_{5',6'a} = J_{5'',6''a}$ 2.0, $J_{5',6'b} = J_{5'',6''b}$ 4.9, $J_{4',5'} = J_{4'',5''}$ 9.5 Hz, H-5′,5″), 3.96 (dd, 2 H, $J_{5',6'a} = J_{5'',6''a}$ 2.0, $J_{6'a,6'b} = J_{6''a,6''b}$ 12.5 Hz, H-6′a,6″a), 4.40 (dd, 2 H, $J_{5',6'b} = J_{5'',6''b}$ 4.9, $J_{6'a,6'b} = J_{6''a,6''b}$ 12.5 Hz, H-6′b,6″b), 4.54 (dd, 2 H, $J_{1',2'eq} = J_{1'',2''eq}$ 2.0 $J_{1',2'ax} = J_{1'',2''ax}$ 11.7 Hz, H-1′,1″), 5.00 (t, 2 H, $J_{3',4'} = J_{3'',4''} = J_{4',5'} = J_{4'',5''}$ 9.5 Hz, H-4′,4″), 5.04 (ddd, 2 H, $J_{2'eq,3'} = J_{2''eq,3''}$ 5.4, $J_{3',4'} = J_{3'',4''}$ 9.5, $J_{2'ax,3'} = J_{2''ax,3''}$ 11.0 Hz, H-3′3″). The (*) indicates that these peaks may be interchanged. ^1H NMR (acetone-d_6): δ 1.98 (s, 6 H, –OAc), 1.997 (s, 6 H, –OAc), 2.003 (s, 6 H, –OAc), 2.37 (s, 6 H, –OAc), 2.40 (s, 3 H, ArAc), 2.50 (s, 3 H, –OAc), 3.88 (br. s, 2 H, H-5′,5″), 3.89 (dd, 2 H, $J_{5',6'a} = J_{5'',6''a}$ 2.0, $J_{6'a,6'b} = J_{6''a,6''b}$ 12.9 Hz, H-6′a,6″a), 4.36 (br. s, 2 H, H-6′b,6″b), 4.92 (m, 2 H, H-1′,1″), 5.01 (t, 2 H, $J_{3',4'} = J_{3'',4''} = J_{4',5'} = J_{4'',5''}$ 9.8 Hz, H-4′,4″), 5.19 (m, 2 H, H-3′,3″). The H-2′, and H-2″ peaks are very broad and not identified. ^{13}C NMR ($CDCl_3$): δ 20.7, 20.80, 20.84, 20.92, 20.94 (–OAc), 30.5 (ArAc), 34.1* (C-2′,2″), 62.2 (C-6′,6″), 68.7* (C-4′,4″), 71.9* (C-3′,3″), 77.2 (C-5′,5″), 124.2* (C-3,5), 129.6 (C-1), 145.8* (C-2,6), 147.8 (C-4), 168.2, 168.3, 169.8, 170.4, 170.5 (–OAc), 197.8 (ArAc). The (*) indicates broad peaks, and the C-1′ and C-1″ peaks appear broad around 73 ppm in $CDCl_3$. ^{13}C NMR (acetone-d_6): δ 20.71, 20.77, 20.85, 21.08, 21.12 (–OAc), 30.8 (ArAc), 35.0*, 35.3* (C-2′,2″), 63.2 (C-6′,6″), 69.9* (C-4′,4″), 72.3* (C-3′,3″), 72.0*, 73.1* (C-1′,1″), 77.3* (C-5′,5″), 125.6* (C-3,5), 130.7 (C-1), 146.8* (C-2, 6), 149.0 (C-4), 169.0, 169.4, 170.2, 170.4, 170.7 (–OAc), 197.6 (ArAc). The (*) indicates broad peaks, and the C-1′ and C-1″ peaks may be interchanged. FABMS (positive ion): m/z 839 $[M+H]^+$. Anal. Calcd for $C_{38}H_{46}O_{21}$: C, 54.42; H, 5.53. Found: C, 54.14; H, 5.61.

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