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Synthesis of 8-*C*-glucosylflavones

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Abstract

The syntheses of orientin, parkinsonin A, isoswertiajaponin, and parkinsonin B, which are 8-*C*-β-D-glucopyranosyl-3′,4′,5,7-tetrahydroxyflavone, 5-methyl orientin, 7-methyl orientin, and 5,7-dimethyl orientin, respectively, are reported herein. The *C*-glucosyl phloroacetophenone derivatives were obtained via a regio- and stereoselective O→C glycosyl rearrangement. Aldol condensation of the *C*-glucosyl phloroacetophenone derivatives with 3,4-bisbenzyloxybenzaldehyde afforded the corresponding *C*-glucosylchalcones. Construction of the flavone system by reaction with I_2–Me_2SO, followed by the elimination of the 5-benzyl protecting group in the flavone structure, yielded an orientin derivative and a isoswertiajaponin derivative. Methylation of the orientin derivatives with dimethyl sulfate afforded the parkinsonin A derivative, the isoswertiajaponin derivative, and the parkinsonin B derivative. Finally, hydrogenolysis of these *C*-glucosylflavone derivatives led to the four 8-*C*-glucosylflavones. The NMR spectra of these *C*-glucosylflavones showed a duplication of signals corresponding to a major rotamer, along with a minor one. Based on NOESY experiments in Me_2SO at ambient temperature, they adopted conformations in which the H-2″and H-4″ protons in the glucose moiety were oriented toward the B-ring in the flavone structure.

Keywords: *C*-glucosylflavone; Orientin; Isoswertiajaponin; Parkinsonin A; Parkinsonin B; Conformation

1. Introduction

A variety of plant constituents, *C*-Glycosylflavones, have been isolated to date. These compounds are used as natural dyestuffs, and some are biologically active.[1] Several studies on the synthesis of *C*-glycosylflavones have appeared. Following the successful total synthesis of 4′,7-di-*O*-methylbayin[2] (8-*C*-β-D-glucopyranosyl-4′,7-dimethoxyflavone), the synthesis of 4′,5,7-tri-*O*-methylvitexin (8-*C*-β-D-glucopyranosyl-4′,5,7-trimethoxyflavone) was also reported.[3] The C-glycosylation steps were performed via a zinc oxide-promoted coupling using tetra-*O*-acetyl-α-D-glucopyranosyl bromide as the glycosyl donor. The synthesis of 4′,7-di-*O*-methylisobayin (6-*C*-β-D-glucopyranosyl-4′,7-dimethoxyflavone) has also been described,[4] and the synthesis of 4′,5,7-tri-*O*-methylvitexin was reported later.[5] The C-glycosylation steps in these syntheses were carried out by arylation using a lithiated aromatic ring or an aromatic Grignard reagent as the glycosyl acceptor. Harborne and Mabry reported that the reaction of 5,7-dihydroxyflavones with glycosyl bromides afforded *C*-glycosylflavones in one step, but in

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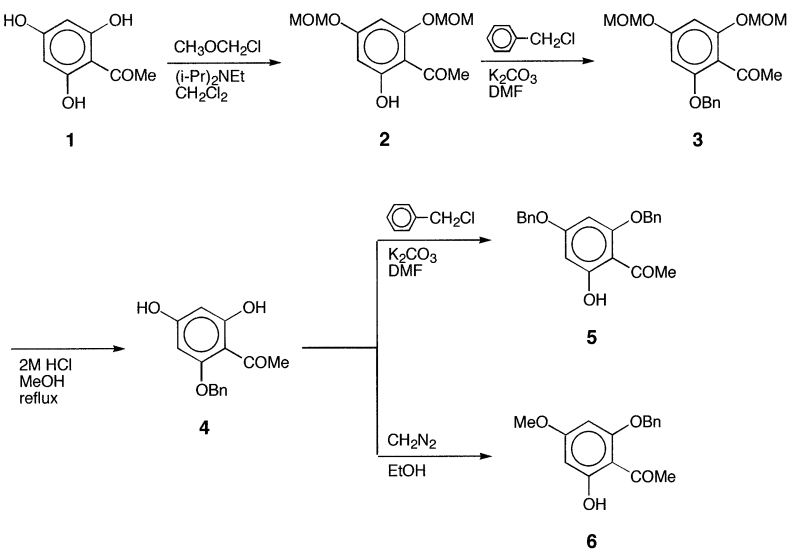
low yields.[6] Schmidt and co-workers reported on the synthesis of vitexin (8-*C*-β-D-glucopyranosyl-4′,5,7-trihydoxyflavone), isovitexin (6-*C*-β-D-glucopyranosyl-4′,5,7-trihydroxyflavone), and isoembigenin (8-*C*-β-D-glucopyranosyl-5-hydroxy-4′,7-dimethoxyflavone).[7] A Baker–Vankataraman-type rearrangement was employed to construct the flavone system. The C-glycosylation step in these syntheses was carried out via an O→C glycosyl rearrangement. We recently reported on the synthesis of isoorientin (6-*C*-β-D-glucopyranosyl-3′,4′,5,7-tetrahydroxyflavone).[8] In order to construct the 6-*C*-glucosyl substituted flavone system, a selective hydrogenolysis involving benzyl-protected and 2-methylbenzyl-protected derivatives was used.[9] The C-glycosylation step in this synthesis was carried out using boron trifluoride etherate as an activator via an O→C glycosyl rearrangement during the elevation of the reaction temperature, without the isolation of the *O*-glycoside intermediate.

We herein describe the facile synthesis of orientin **11**,[10] parkinsonin A **12**,[11,12] isoswertiajaponin **17**,[13] and parkinsonin B **18**,[11,12] all of which are 8-*C*-glucosylflavones. Orientin **11**, 8-*C*-β-D-glucopyranosyl-3′,4′,5,7-tetrahydroxyflavone, which is a regioisomer of isoorientin was mentioned above and parkinsonin A **12** is 5-methyl orientin, isoswertiajaponin **17** is 7-methyl orientin, and parkinsonin B **18** is 5,7-dimethyl orientin. The latter are either partially or fully methylated in the A-ring of the flavone, respectively. In order to achieve their synthesis, the selective methylation of the A-ring was necessary. While the synthesis of both parkinsonin A **12** and parkinsonin B **18** have not been reported, their isolation as natural products has been reported by Bhatia and co-workers.[11] The two compounds, however, have not been found in the extracts of the same source.[12]

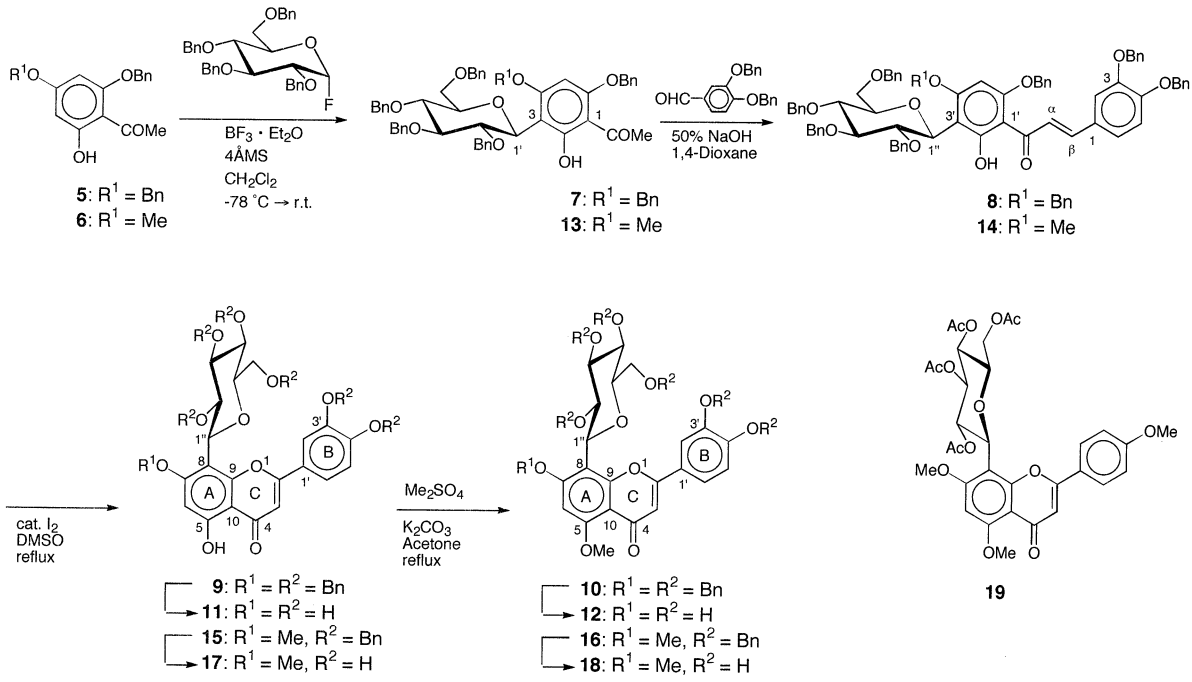
2. Results and discussion

Selective protection of the commercially available phloroacetophenone with methoxymethyl chloride (MOMCl) afforded the partially O-protected phloroacetophenone derivative **2**. After the protection of a chelated phenolic hydroxy group of compound **2** with benzyl chloride to afford compound **3**, the removal of both of the MOM groups of compound **3** with hydrochloric acid led to the benzyl-protected compound **4** in an overall yield of 71% in four steps (Scheme 1).[8]

For the synthesis of orientin **11** and parkinsonin A **12**, 2,4-dibenzylphloroacetophenone **5** was synthesized as the C-glucosylation acceptor via the regioselective benzylation of compound **4** with benzyl chloride in 89% yield (Scheme 1). Based on our previous method,[8,14] compound **5** was reacted with benzyl-pro-



Scheme 1.



Scheme 2.

tected glucopyranosyl fluoride[15] in the presence of boron trifluoride diethyl etherate as an activator at low temperature, and the temperature of the reaction mixture was then elevated gradually to ambient temperature. The desired synthetic intermediate **7**, having a β configuration, was obtained in nearly quantitative yield, via a highly regio- and stereoselective O→C glycosyl rearrangement. The aldol condensation of the *C*-glucosyl derivative **7** and 3,4-bis-benzyloxybenzaldehyde with sodium hydroxide afforded the chalcone derivative **8** in 84% yield. Selenium dioxide is the reagent that typically used for the oxidative cyclization of 2′-hydroxychalcone to the corresponding flavone. Because the 5-hydroxyflavone was produced as a synthetic intermediate, it was necessary to convert it to the 5-methoxy flavone. This was accomplished using a catalytic amount of iodine in Me_2SO,[16] which involved the elimination of a benzyl group. The chalcone derivative **8** was oxidized, followed by cleavage of a benzyl-protection group that was positioned ortho to the cinnamoyl group, to subsequently give the partial benzyl-protected orientin **9** in 84% yield. All benzyl-protection groups on the flavone derivative **9** were then removed by hydrogenolysis with 10% palladium-on-charcoal under an atmosphere of H_2 to afford orientin **11**, in quantitative yield. On the other hand, the flavone derivative **9** was methylated with dimethyl sulfate to afford the benzyl-protected parkinsonin A **10** in 85% yield. Deprotection by hydogenolysis of compound **10** under the conditions described above led to a quantitative yield of parkinsonin A **12**, which represents the desired 5-methyl orientin (Scheme 2).

Alternatively, for the synthesis of isoswertiajaponin **17** and parkinsonin B **18**, which contain a 7-methyl group in their orientin structure, 2-benzyl-4-methylphloroacetophenone **6**, a *C*-glucosylation acceptor was initially synthesized in 96% yield, via the regioselective methylation of compound **4** with diazomethane (Scheme 1). The *C*-glucoside **13** was synthesized regio- and stereoselectively under conditions identical to those mentioned above, in 81% yield. The aldol condensation of the *C*-glucosyl derivative **13** and 3,4-bis-benzyloxybenzaldehyde in the presence of sodium hydroxide gave the chalcone derivative **14** in 87% yield. The chalcone derivative **14** was oxidized with a catalytic amount of iodine in Me_2SO, followed by cleavage of the benzyl protection group, which was positioned ortho to the cinnamoyl group,

to subsequently give the flavone derivative **15** in 81% yield. Deprotection of all benzyl groups on compound **15** was carried out using 10% palladium-on-charcoal under H_2 at atmospheric pressure, to afford isoswertiajaponin **17**, in quantitative yield, which contains a 7-methyl group. The flavone derivative **15** was methylated with dimethyl sulfate to afford compound **16** in 96% yield. Compound **16** was subjected to hydrogenolysis to afford parkinsonin B **18** in quantitative yield, which represents the desired 5,7-dimethyl orientin (Scheme 2).

The individual structures of the compounds **7**–**18** were confirmed by their ^{1}H NMR spectra and ^{1}H–^{1}H COSY experiments at both ambient and elevated temperatures, as well as by their ^{13}C NMR and HMBC spectra at ambient temperature for compounds **11**, **12**, **17**, and **18**. ^{1}H NMR experiments were conducted at elevated temperature, because, when conducted at ambient temperature, the ^{1}H NMR spectra showed peaks representing the pairing of major and minor peaks. ^{13}C NMR spectra at ambient temperature also showed the pairing of individual peaks, and structural assignments using NMR spectroscopy at ambient temperature were hampered by the slow rotation around the C-1–aglycon bond.

^{1}H NMR spectra of orientin **11** at ambient temperature showed a duplication of signals reminiscent of the effects of dynamic rotational isomers and culminating in a ca. 4.7:1 ratio of rotamer populations, based on the H-3 peaks. The anomeric proton of the main rotamer appeared at 4.69 ppm (d, $J_{1'',2''}$ 9.9 Hz) and that corresponding to the minor rotamer appeared at 4.84 ppm (d, $J_{1'',2''}$ 9.6 Hz). In the case of the main rotamer, NOESY spectra of orientin **11** at ambient temperature indicated that the H-2″ signal in the glucose moiety was correlated to the H-2′ and H-6′ signals in the B-ring of the flavone structure, and also that the H-4″ signal was correlated to the H-2′ and H-6′ signals. The NOESY spectra also indicated a correlation between the C-ring H-3 signal and H-2′, as well as H-6′. ^{1}H NMR spectra of orientin **11** at 100 °C showed distinct signals, and the signal of the anomeric proton appeared at 4.80 ppm (d, $J_{1'',2''}$ 9.0 Hz).

^{1}H NMR spectra of parkinsonin A **12** at ambient temperature also showed a duplication of signals culminating in a ca. 4.0:1 ratio of rotamer populations, based on the H-3 peaks. The anomeric proton of the main rotamer appeared at 4.72 ppm (d, $J_{1'',2''}$ 9.8 Hz) and that of the minor rotamer was at 4.92 ppm (d, $J_{1'',2''}$ 9.8 Hz). In the case of the main rotamer of parkinsonin A **12**, NOESY spectra at ambient temperature also indicated that the H-2″ signal in the glucose moiety of the main rotamer was correlated to the H-2′ and H-6′ signals in the B-ring of the flavone structure and that the H-4″ signal was correlated to the H-2′ and H-6′ signals. In addition, NOESY spectra indicated a correlation between the C-ring H-3 signal and H-2′, as well as H-6′, as well as a correlation between the 5-methyl group and the H-6 aromatic proton. ^{1}H NMR spectra of parkinsonin A **12** at 140 °C showed distinct signals, and the signal of the anomeric proton appeared at 4.90 ppm (d, $J_{1'',2''}$ 9.8 Hz).

^{1}H NMR spectra of isoswertiajaponin **17** at ambient temperature also showed a duplication of signals culminating in a ca. 6.7:1 ratio of rotamer populations, based on the H-3 peaks. The anomeric proton of the main rotamer appeared at 4.72 ppm (d, $J_{1'',2''}$ 9.9 Hz) and that of the minor rotamer was at 4.79 ppm (d, $J_{1'',2''}$ 9.6 Hz). In the case of the main rotamer of isoswertiajaponin **17**, NOESY spectra at ambient temperature also indicated that the H-2″ signal was correlated to the H-2′ and H-6′ signals and also that the H-4″ signal was correlated to the H-2′ and H-6′ signals. In addition, the NOESY spectra indicated a correlation between the H-3 and H-2′, as well as H-6′, as well as a correlation between the 7-methyl group and the H-6 aromatic proton. ^{1}H NMR spectra of isoswertiajaponin **17** at 150 °C showed distinct signals, and the anomeric proton signal appeared at 4.82 ppm (d, $J_{1'',2''}$ 9.8 Hz).

^{1}H NMR spectra of parkinsonin B **18** at ambient temperature also showed a duplication of signals culminating in a ca. 7.7:1 ratio of rotamer populations, based on the H-3 peaks. The anomeric proton of the main rotamer appeared at 4.76 ppm (d, $J_{1'',2''}$ 9.9 Hz) and that of the minor rotamer at 4.85 ppm (d, $J_{1'',2''}$ 9.6 Hz). In the case of the main rotamer

of parkinsonin B **18**, NOESY spectra at ambient temperature also indicated that the H-2″ signal was correlated to the H-2′ and H-6′ signals and that the H-4″ signal was correlated to the H-2′ and H-6′ signals. In addition, the NOESY spectra indicated a correlation between the H-3 and H-2′, as well as H-6′, and a correlation between the H-6 aromatic proton and the 5-methyl group, as well as the 7-methyl group. ^{1}H NMR spectra of parkinsonin B **18** at 150 °C showed distinct signals, and the signal of the anomeric proton appeared at 4.86 ppm (d, $J_{1'',2''}$ 9.9 Hz).

These approaches provided proof for the position of the β-D-glucopyranosyl moiety at C-8 and, presumably, the preferred conformation for the main rotamer of the *C*-glucosylflavones **11**, **12**, **17**, **18** in Me_2SO at ambient temperature, in which, for the main rotamers, the H-2″and H-4″ protons in the glucose moiety were oriented toward the B-ring in the flavone structure, even though the 7-methyl group is absent in orientin **11** and parkinsonin A **12**. On the contrary, based on NOE experiments Rabe and co-workers determined the preferred conformation of 8-*C*-(2″,3″,4″,6″-tetra-*O*-acetyl-β-D-glucopyranosyl)-4′,5,7-tri-*O*-methoxyflavone in $CDCl_3$ at 23 °C, as being similar to that of **19**[17], in which, in the main rotamer, the H-1″ and H-3″ protons in the glucose moiety are oriented toward the B-ring in the flavone structure. Our NOESY studies are contradictory to their conclusions.

It is known that the methylation of the 5-hydroxyl group in apigenin (4′,5,7-trihydroxyflavone) produces an upfield shift of 1.6 ppm of the C-5 signal and a shift of −3.7, +4.3, and −6.1 ppm in the resonances of C-2, -3, and -4, respectively.[18] Similarly, ^{13}C NMR spectra show that glycosylation of the 5-hydroxy group in luteolin (3′,4′,5,7-tetrahydroxyflavone) has a marked effect on the resonances of the A- and C-ring carbons.[19] In this study, the effect of substituents on the ^{13}C NMR chemical shifts of parkinsonin A **12** and parkinsonin B **18**, respectively, were observed (Table 1). In a comparison of the ^{13}C NMR chemical shifts of orientin **11** with that of parkinsonin A **12**, the 5-methyl group of parkinsonin A **12** produced an upfield shift of −3.8 ppm for C-2 and − 6.0 ppm for C-4, and a downfield shift of +3.1 ppm for C-3 and +3.6 ppm for C-10. In a comparison of the ^{13}C NMR chemical shifts of orientin **11** with that of parkinsonin B **18**, the 5-methyl group of parkinsonin B **18** produced an upfield shift of −3.6 ppm for C-2, −6.0 ppm for C-4, and a downfield shift of +3.1 ppm for C-3 and +4.2 ppm for C-10. In contrast to the ^{13}C NMR chemical shifts mentioned above, effects of substituents on the ^{13}C NMR chemical shifts of isoswertiajaponin **17** were not observed. The hydrogen bond with the 4-keto function in orientin **11** and isoswertiajaponin **17** produces a downfield shift in C-4 of flavone structure. Alternatively, the 5-methyl group in parkinsonin A **12** and parkinsonin B **18** cause a disruption of hydrogen bonding with the 4-keto function. As the result, due to a conjugation effect in the C-ring, an upfield shift in C-2 and C-4 and a downfield shift in C-3 and C-10 are apparent.

In conclusion, orientin **11**, isoswertiajaponin **17**, parkinsonin A **12**, parkinsonin B **18** were synthesized in relatively high yield. Based on NOESY experiments in Me_2SO at ambient temperature, they were shown to adopt a conformation in which the H-2″and H-4″ protons in the glucose moiety are oriented toward the B-ring in the flavone structure.

3. Experimental

General methods.—All nonaqueous reactions were carried out under an atmosphere of dry Ar using freshly distilled solvents, unless otherwise noted. Reactions were monitored by TLC, which was carried out on 0.25 mm Silica Gel F_{254} plates (E. Merck) using either UV light, a 5% ethanolic solution of ferric chloride with heat as developing agents. Fuji Silysia BW-300 was used for silica-gel column chromatography. Optical rotations were recorded using either $CHCl_3$, MeOH or pyridine as the solvent on a JASCO DIP-370 digital polarimeter. IR spectra were recorded on a HORIBA FT-720 IR spectrometer in the form of 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 (NBA) or diethanolamine as the matrix. ^{1}H or ^{13}C NMR spectra were recorded on a VARIAN INOVA 500 instrument using Me_4Si as an internal reference.

2,4-Bis-benzyloxy-6-hydroxyacetophenone (**5**).—To a stirred solution of compound **4**[8] (14.07 g, 54.5 mmol) and anhyd K_2CO_3 (8.28 g, 59.9 mmol, 1.1 equiv)) in DMF (120 mL) at 0 °C, BnCl (6.58 mL, 57.4 mmol, 1.05 equiv) was added. After 5 min, the mixture was allowed to warm to 25 °C, followed by stirring for 24 h. The reaction mixture was then poured into 1 M HCl (750 ml) and extracted with EtOAc. The organic layer was washed with water and brine, dried over anhyd $MgSO_4$ and the resulting solution evaporated under reduced pressure. The residue was chromatographed on a silica gel column (8:1 hexane–EtOAc), followed by recrystallization from hexane–EtOAc to afford colorless prismatic crystals **5** (16.94 g, 89%): mp 108 – 109 °C; R_f 0.47 (5:1 hexane–EtOAc); IR (KBr): ν 3101, 3091, 3068, 3037, 3006, 2941, 2902, 2866, 1616, 1585, 1446, 1435, 1417, 1377, 1363, 1321, 1273, 1232, 1219, 1207, 1178, 1173, 1105, 1086, 1028, 978, 958, 904, 839, 812, 756, 734, 692 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 2.55 (s, 3 H, ArAc), 5.061 (s, 2 H, benzylic CH_2), 5.062 (s, 2 H, benzylic CH_2), 6.09 (d, 1 H, $J_{3,5}$ 2.4 Hz, ArH), 6.16 (d, 1 H, $J_{3,5}$ 2.4 Hz, ArH), 7.33–7.42 (m, 10 H, ArH), 14.03 (s, 1 H, ArOH); EIMS: m/z 348 $[M]^+$. Anal. Calcd for $C_{22}H_{20}O_4$: C, 75.85; H, 5.79. Found: C, 75.95; H, 5.79.

2-Benxyloxy-6-hydroxy-4-methoxyacetophenone (**6**).—Compound **4**[8] (7.00 g, 27.1 mmol) was dissolved in EtOH (500 mL) by refluxing, and the resulting solution was cooled at 0 °C. A diazomethane–ether solu-

Table 1
^{13}C NMR chemical shifts [a] of the major rotamers of 8-*C*-glucopyranosylflavones **11**, **12**, **17**, and **18**

Carbon	Orientin **11**	Parkinsonin A **12**	Isoswertiajaponin **17**	Parkinsonin B **18**
Aglycon				
2	164.0	160.2 (−3.8) [b]	164.4 (+0.4) [b]	160.4 (−3.6) [b]
3	102.3	105.4 (+3.1) [b]	102.3 (±0) [b]	105.4 (+3.1) [b]
4	181.9	175.9 (−6.0) [b]	182.1 (+0.2) [b]	175.9 (−6.0) [b]
5	160.3	159.2 (−1.1) [b]	161.2 (+0.9) [b]	156.0 (−4.3) [b]
6	98.0	95.4 (−2.6) [b]	94.9 (−3.1) [b]	92.1 (−5.9) [b]
7	162.4	160.7 (−1.7) [b]	163.2 (+0.8) [b]	161.6 (−0.8) [b]
8	104.4	105.3 (+0.9) [b]	105.5 (+1.1) [b]	106.7 (+2.3) [b]
9	155.9	157.8 (+1.9) [b]	155.0 (−0.9) [b]	157.0 (+1.1) [b]
10	103.9	107.5 (+3.6) [b]	104.3 (+0.4) [b]	108.1 (+4.2) [b]
1′	121.9	122.3	121.8	122.2
2′	114.0	113.5	114.0	113.6
3′	145.7	145.5	145.7	145.6
4′	149.5	148.5	149.6	148.7
5′	115.5	115.5	115.5	115.5
6′	119.3	118.6	119.4	118.7
C-Glucopyranose				
1″	73.3	73.6	73.0	73.3
2″	70.6	70.49 [c]	70.6	70.45 [c]
3″	78.6	78.9	78.6	78.8
4″	70.6	70.47 [c]	70.5	70.41 [c]
5″	81.9	82.0	82.0	82.1
6″	61.5	61.5	61.5	61.5
5-OMe		55.5		55.9
7-OMe			56.4	56.3

[a] δ in ppm from TMS, in Me_2SO-d_6 at rt.
[b] Substituent effects on the ^{13}C NMR chemical shifts of A- and C-ring in flavone structure.
[c] Assignments exchangeable.

tion was then added to the stirred solution. After TLC monitoring showed the disappearance of the starting material **4**, the reaction mixture was evaporated. The residue was recrystallized from hexane–EtOAc to afford colorless prismatic crystals **6** (7.11 g, 96%): mp 117 °C; R_f 0.54 (5:1 hexane–EtOAc); IR (KBr): *v* 3060, 3033, 3008, 2979, 2947, 2885, 1616, 1593, 1498, 1466, 1431, 1387, 1362, 1319, 1273, 1221, 1200, 1161, 1151, 1109, 1076, 1024, 1003, 954, 914, 899, 818, 802, 702, 692 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.56 (s, 3 H, ArAc), 3.81 (s, 3 H, –OMe), 5.08 (s, 2 H, benzylic CH_2), 6.01 (d, 1 H, $J_{3,5}$ 2.4 Hz, ArH), 6.08 (d, 1 H, $J_{3,5}$ 2.4 Hz, ArH), 7.35–7.44 (m, 5 H, ArH), 14.05 (s, 1 H, ArOH); EIMS: *m*/*z* 272 $[M]^+$. Anal. Calcd for $C_{16}H_{16}O_4$: C, 70.58; H, 5.92. Found: C, 70.48; H, 5.84.

*4,6-Bis-benzyloxy-3-*C*-(2,3,4,6-tetra-*O*-benzyl-β-*D*-glucopyranosyl)-2-hydroxyacetophenone* (**7**).—To a stirred mixture of compound **5** (6.05 g, 17.4 mmol, 3 equiv), 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl fluoride[15] (3.14 g, 5.79 mmol), and powdered 4 Å molecular sieves (6 g) in CH_2Cl_2 (60 mL) at −78 °C, $BF_3{\cdot}Et_2O$ (1.43 mL, 11.6 mmol, 2.0 equiv) was added dropwise, and the mixture was stirred for 30 min. The temperature was allowed to gradually increase to −42 °C, and the stirring was continued for 30 min, then for 30 min at −20 °C, for 30 min at 0 °C, and finally for 1 h at rt. After adding water, the resulting mixture was filtered through a Celite® pad. The filtrate was extracted with $CHCl_3$, and the organic layer was dried over anhyd $MgSO_4$. The solvent was evaporated under reduced pressure, and the resulting syrup was chromatographed on a silica gel column (5:1 hexane–EtOAc) to give compound **7** (4.84 g, 96%) as a pale yellowish–green highly viscous oil: $[\alpha]_D^{25}$ −19° (*c* 1.0, $CHCl_3$); R_f 0.47 (3:1 hexane–EtOAc); IR (KBr): *v* 3087, 3062, 3030, 3006, 2929, 2898, 2864, 1620, 1595, 1496, 1454, 1431, 1389, 1365, 1273, 1165, 1115, 1097, 1066, 1028, 1003, 910, 735, 696 cm^{-1}; ^1H NMR (DMSO-d_6 at 120 °C): δ 2.52 (s, 3 H, ArAc), 3.48–3.68 (m, 5 H, H-3′,4′,5′,6′a,6′b), 4.16 (d, 1 H, J_{gem} 11.4 Hz, benzylic CH_2), 4.31 (br. t, 1 H, *J* 9.0 Hz, H-2′), 4.43 (d, 1 H, J_{gem} 11.4 Hz, benzylic CH_2), 4.44 (d, 1 H, J_{gem} 12.2 Hz, benzylic CH_2), 4.50 (d, 1 H, J_{gem} 12.2 Hz, benzylic CH_2), 4.58 (d, 1 H J_{gem} 11.4 Hz, benzylic CH_2), 4.73 (d, 1 H J_{gem} 11.4 Hz, benzylic CH_2), 4.75 (d, 1 H J_{gem} 11.6 Hz, benzylic CH_2), 4.79 (d, 1 H J_{gem} 11.6 Hz, benzylic CH_2), 4.86 (d, 1 H, $J_{1',2'}$ 9.8 Hz, H-1′), 5.17 (s, 2 H, benzylic CH_2), 5.24 (d, 1 H J_{gem} 12.5 Hz, benzylic CH_2), 5.27 (d, 1 H J_{gem} 12.5 Hz, benzylic CH_2), 6.42 (s, 1 H, ArH), 6.88–7.48 (m, 30 H, ArH), 13.82 (br. s, 1 H, ArOH); FABMS (positive-ion mode, NBA matrix): *m*/*z* 871 $[M+H]^+$. Anal. Calcd for $C_{56}H_{54}O_9$: C, 77.22; H, 6.25. Found: C, 77.48; H, 6.23.

*3,4,4′,6′-Tetrakis-benzyloxy-3′-*C*-(2,3,4,6-tetra-*O*-benzyl-β-*D*-glucopyranosyl)-2′-hydroxychalcone* (**8**).—To a solution of compound **7** (3.48 g, 3.99 mmol) and 3,4-dibenzyloxybenzaldehyde (1.53 g, 4.79 mmol, 1.2 equiv) in 1,4-dioxane (60 mL), a 50 wt.% aq solution of NaOH (60 mL) was added. The mixture was then stirred vigorously at rt for 24 h. The mixture was poured into 1 M HCl, extracted with EtOAc, and then washed with water and brine. The organic layer was dried over anhyd $MgSO_4$ and then evaporated under reduced pressure. The residual orange syrup was chromatographed on a silica gel column (5:1 hexane–EtOAc) to afford compound **8** (3.92 g, 84%) as an orange-colored amorphous material: mp 50 °C; $[\alpha]_D^{25}$ −10° (*c* 1.0, $CHCl_3$); R_f 0.40 (3:1 hexane–EtOAc); IR (KBr): *v* 3088, 3062, 3030, 2929, 2901, 2861, 1624, 1580, 1555, 1509, 1453, 1430, 1331, 1260, 1235, 1210, 1151, 1135, 1101, 1065, 1027, 979, 910, 845, 806, 733, 695 cm^{-1}; ^1H NMR (DMSO-d_6 at 120 °C): δ 3.50–3.69 (m, 5 H, H-3″,4″,5″,6″a,6″b), 4.19 (d, 1 H, J_{gem} 11.4 Hz, benzylic CH_2), 4.33 (br. t, 1 H, $J_{1'',2''} = J_{2'',3''}$ 9.9 Hz, H-2″), 4.45 (d, 2 H, J_{gem} 12.4 Hz, benzylic CH_2), 4.51 (d, 1 H, J_{gem} 12.4 Hz, benzylic CH_2), 4.58 (d, 1 H, J_{gem} 11.4 Hz, benzylic CH_2), 4.73 (d, 1 H, J_{gem} 11.4 Hz, benzylic CH_2), 4.76 (d, 1 H, J_{gem} 11.6 Hz, benzylic CH_2), 4.80 (d, 1 H, J_{gem} 11.6 Hz, benzylic CH_2), 4.90 (d, 1 H, $J_{1'',2''}$ 9.9 Hz, H-1″), 5.04 (s, 2 H, benzylic CH_2), 5.18 (s, 2 H, benzylic CH_2), 5.21 (s, 2 H, benzylic CH_2), 5.24 (d, 1 H, J_{gem} 11.7 Hz, benzylic CH_2), 5.26 (d, 1 H, J_{gem} 11.7 Hz, benzylic CH_2), 6.49 (s, 1 H, ArH), 6.88–7.48 (m, 43 H, ArH), 7.57 (d, 1 H, $J_{\alpha,\beta}$ 15.6 Hz, trans-vinyl), 7.62 (d, 1 H,

$J_{\alpha,\beta}$ 15.6 Hz, trans-vinyl), 13.75 (br. s, 1 H, ArOH); FABMS (positive-ion mode, NBA matrix): m/z 1172 $[M+H]^+$; FABMS (negative-ion mode, NBA matrix): m/z 1170 $[M-H]^+$. Anal. Calcd for $C_{77}H_{70}O_{11}$: C, 78.95; H, 6.02. Found: C, 78.67; H, 6.01.

*2-(3,4-Bis-benzyloxyphenyl)-7-benzyloxy-8-*C*-(2,3,4,6-tetra-*O*-benzyl-β-*D*-glucopyranosyl)-5-hydroxy-4* H*-1-benzopyran-4-one* (**9**).—A solution of compound **8** (1.09 g, 0.93 mmol) and iodine (11 mg, 0.04 mmol, 0.05 equiv) in Me_2SO (10 mL) was refluxed for 30 min. The mixture was poured into water, and the resulting solution was extracted with EtOAc. The organic phase was then washed with sodium thiosulfate solution, water and brine. The organic layer was dried over anhyd $MgSO_4$, and the solvent was then evaporated under reduced pressure. The residual syrup was chromatographed on a silica gel column (5:1 hexane–EtOAc) to afford compound **9** (0.84 g, 84%) as a colorless amorphous powder: mp 55–56 °C; $[\alpha]_D^{25}$ −16° (*c* 1.0, $CHCl_3$); R_f 0.37 (3:1 hexane–EtOAc); IR (KBr): *v* 3087, 3062, 3030, 3006, 2924, 2902, 2864, 1653, 1603, 1591, 1512, 1496, 1454, 1437, 1375, 1362, 1325, 1293, 1259, 1205, 1180, 1142, 1113, 1066, 1028, 910, 847, 820, 808, 735, 696 cm^{-1}; ^1H NMR (DMSO-d_6 at 150 °C): δ 3.59–3.71 (m, 4 H, H-4″,5″,6″a,6″b), 3.67 (br. t, 1 H, *J* 8.4 Hz, H-3″), 4.11 (d, 1 H, J_{gem} 11.7 Hz, benzylic CH_2), 4.23 (br. t, 1 H, *J* 8.4 Hz, H-2″), 4.40 (s, 2 H, benzylic CH_2), 4.43 (d, 1 H, J_{gem} 11.7 Hz, benzylic CH_2), 4.57 (d, 1 H, J_{gem} 11.2 Hz, benzylic CH_2), 4.72 (d, 1 H, J_{gem} 11.2 Hz, benzylic CH_2), 4.78 (d, 1 H, J_{gem} 11.7 Hz, benzylic CH_2), 4.80 (d, 1 H, J_{gem} 11.7 Hz, benzylic CH_2), 5.05 (d, 1 H, $J_{1'',2''}$ 9.9 Hz, H-1″), 5.19 (s, 2 H, benzylic CH_2), 5.20 (d, 1 H, J_{gem} 12.5 Hz, benzylic CH_2), 5.21 (s, 2 H, benzylic CH_2), 5.24 (d, 1 H, J_{gem} 12.5 Hz, benzylic CH_2), 6.56–7.68 (m, 40 H, ArH and H-3), 13.02 (br. s, 1 H, ArOH); FABMS (positive-ion mode, NBA matrix): m/z 1180 $[M+H]^+$; FABMS (negative-ion mode, NBA matrix): m/z 1178 $[M-H]^+$. Anal. Calcd for $C_{70}H_{62}O_{11}$: C, 77.90; H, 5.79. Found: C, 77.60; H, 5.76.

*2-(3,4-Bis-benzyloxyphenyl)-7-benzyloxy-8-*C*-(2,3,4,6-tetra-*O*-benzyl-β-*D*-glucopyranosyl)-5-methoxy-4* H*-1-benzopyran-4-one* (**10**).—A mixture of compound **9** (692 mg, 0.64 mmol), Me_2SO_4 (152 μL, 1.60 mmol, 2.5 equiv), and K_2CO_3 (354 mg, 2.56 mmol, 4.0 equiv) in acetone (10 mL) was refluxed for 12 h. The reaction mixture was poured into water and then stirred for 6 h. The mixture was extracted with EtOAc, and washed with water and brine. The solvent was evaporated under reduced pressure, and the resulting syrup was chromatographed on a silica gel column (EtOAc) to give compound **10** (597 mg, 85%) as a colorless amorphous powder: mp 56–57 °C; $[\alpha]_D^{25}$ −17° (*c* 1.0, $CHCl_3$); R_f 0.37 (EtOAc); IR (KBr): *v* 3087, 3062, 3030, 3006, 2929, 2902, 2864, 1645, 1597, 1577, 1512, 1496, 1454, 1435, 1383, 1321, 1263, 1200, 1142, 1109, 1066, 1045, 1028, 1003, 910, 845, 808, 735, 696 cm^{-1}; ^1H NMR (DMSO-d_6 at 140 °C): δ 3.59–3.77 (m, 5 H, H-3″,4″,5″,6″a,6″b), 3.88 (s, 3 H, –OMe), 4.07 (d, 1 H, J_{gem} 11.5 Hz, benzylic CH_2), 4.28 (br. t, *J* 9.5 Hz, H-2″), 4.40 (d, 1 H, J_{gem} 11.5 Hz, benzylic CH_2), 4.41 (s, 2 H, benzylic CH_2), 4.57 (d, 1 H, J_{gem} 11.5 Hz, benzylic CH_2), 4.72 (d, 1 H, J_{gem} 11.5 Hz, benzylic CH_2), 4.74 (br. d, 1 H, J_{gem} 11.0 Hz, benzylic CH_2), 4.78 (br. d, 1 H, J_{gem} 11.0 Hz, benzylic CH_2), 5.11 (d, 1 H, $J_{1'',2''}$ 9.8 Hz, H-1″), 5.17 (s, 2 H, benzylic CH_2), 5.19 (s, 2 H, benzylic CH_2), 5.25 (br. d, 1 H, J_{gem} 12.0 Hz, benzylic CH_2), 5.28 (br. d, 1 H, J_{gem} 12.0 Hz, benzylic CH_2), 6.51–7.60 (m, 40 H, ArH and H-3); FABMS (positive-ion mode, NBA matrix): m/z 1094 $[M+H]^+$. Anal. Calcd for $C_{71}H_{64}O_{11}$: C, 78.00; H, 5.90. Found: C, 77.70; H, 6.08.

*8-*C*-β-*D*-Glucopyranosyl-2-(3,4-dihydroxyphenyl)-5,7-dihydroxy-4* H*-1-benzopyran-4-one; orientin* (**11**).—A solution of compound **9** (512 mg) and 10% Pd–C (250 mg) in EtOAc (20 mL) and EtOH (180 mL) was stirred at ambient temperature overnight under an atmosphere of H_2. After filtering, the filtrate was concentrated under reduced pressure to give orientin **11** (213 mg, quant) as a pale yellowish–green powder: mp (dec) 263–264 °C, lit.[12] 260 °C (dec); $[\alpha]_D^{25}$ −18° (*c* 0.50, pyridine), lit.[12] $[\alpha]_D^{20}$ −20° (*c* 0.41, pyridine); R_f 0.46 (25:35:5:1 Me_2CO–EtOAc–water–AcOH); IR (KBr): *v* 3514, 3381, 1655, 1612, 1593, 1577, 1552, 1514, 1423, 1371, 1323, 1292, 1250, 1194, 1132, 1117, 1105, 1045, 1009, 887, 848,

812, 791 cm^{-1}; ^1H NMR (DMSO-d_6 at 100 °C): δ 3.33–3.37 (m, 2 H, H-3″,5″), 3.42 (t, 1 H, $J_{3'',4''} = J_{4'',5''}$ 9.0 Hz, H-4″), 3.61 (dd, 1 H, $J_{5'',6''a}$ 5.5, J_{gem} 11.9 Hz, H-6″a), 3.77 (dd, 1 H, $J_{5'',6''b}$ 1.6, J_{gem} 11.9 Hz, H-6″b), 3.86 (t, 1 H, $J_{1'',2''} = J_{2'',3''}$ 9.0 Hz, H-2″), 4.26 (br. s, 1 H, –OH), 4.49 (br. s, 3 H, –OH), 4.80 (d, 1 H, $J_{1'',2''}$ 9.0 Hz, H-1″), 6.25 (s, 1 H, H-6), 6.54 (s, 1 H, H-3), 6.89 (d, 1 H, $J_{5',6'}$ 8.2 Hz, H-5′), 7.44 (d, 1 H, $J_{2',6'}$ 2.1 Hz, H-2′), 7.46 (dd, 1 H, $J_{2',6'}$ 2.1, $J_{5',6'}$ 8.2 Hz, H-6′), 9.38 (br. s, 3 H, ArOH), 13.02 (s, 1 H, ArOH); FABMS (negative-ion mode, diethanolamine matrix): m/z 447 $[M-H]^-$. Anal. Calcd for $C_{21}H_{20}O_{11}$: C, 56.25; H, 4.50. Found: C, 56.10; H, 4.60.

8-C-β-D-Glucopyranosyl-2-(3,4-dihydroxyphenyl)-7-hydroxy-5-methoxy-4H-1-benzopyran-4-one; parkisonin A (**12**).—The reaction using a compound **10** (404 mg), 10% Pd–C (200 mg), EtOAc (10 mL) and EtOH (50 mL) were carried out under identical conditions to those described above, and the post-treatment and isolation were also carried out in the same manner as described above. Parkinsonin A **12** was obtained (171 mg, quant) as an orange powder: mp (dec) 234–235 °C; $[\alpha]_D^{25}$ +5° (*c* 0.50, MeOH); R_f 0.12 (25:35:5:1 Me_2CO–EtOAc–water–AcOH); IR (KBr): ν 3284, 1643, 1601, 1502, 1446, 1390, 1336, 1294, 1271, 1203, 1111, 1084, 1041, 1026, 845, 822 cm^{-1}; ^1H NMR (DMSO-d_6 at 140 °C): δ 3.38–3.41 (m, 2 H, H-3″,5″), 3.46 (t, 1 H, $J_{3'',4''} = J_{4'',5''}$ 8.0 Hz, H-4″), 3.65 (dd, 1 H, $J_{5'',6''a}$ 5.2, J_{gem} 11.4 Hz, H-6″a), 3.77 (dd, 1 H, $J_{5'',6''b}$ 2.6, J_{gem} 11.4 Hz, H-6″b), 3.79 (s, 3 H, ArOMe), 3.86 (t, 1 H, $J_{1'',2''} = J_{2'',3''}$ 9.8 Hz, H-2″), 4.90 (d, 1 H, $J_{1'',2''}$ 9.8 Hz, H-1″), 6.27 (s, 1 H, H-3), 6.43 (s, 1 H, H-6), 6.87 (d, 1 H, $J_{5',6'}$ 8.0 Hz, H-5′), 7.35 (dd, 1 H, $J_{2',6'}$ 2.1, $J_{5',6'}$ 8.0 Hz, H-6′), 7.36 (d, 1 H, $J_{2',6'}$ 2.1 Hz, H-2′), 9.57 (br. s, 1 H, ArOH), Other phenolic –OH signals were very broad.; FABMS (positive-ion mode, NBA matrix): m/z 463 $[M+H]^+$; FABMS (negative-ion mode, NBA matrix): m/z 461 $[M-H]^-$. Anal. Calcd for $C_{22}H_{22}O_{11}$: C, 57.14; H, 4.80. Found: C, 57.24; H, 4.64.

6-Benzyloxy-3-C-(2,3,4,6-tetra-O-benzyl-β-D-glucopyranosyl)-2-hydroxy-4-methoxyacetophenone (**13**).—The reaction using compound **6** (5.58 g, 20.5 mmol, 3.0 equiv), 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl fluoride[15] (3.70 g, 6.83 mmol), $BF_3{\cdot}Et_2O$ (1.76 mL, 14.3 mmol, 2.0 equiv), CH_2Cl_2 (80 mL), and powdered 4 Å molecular sieves (6 g) were carried out, as described above for **7**, and the post-treatment and isolation were also carried out in the same manner. Compound **13** was obtained (4.39 g, 81%) as a pale yellowish–green highly viscous oil: $[\alpha]_D^{25}$ −12° (*c* 1.0, $CHCl_3$); R_f 0.34 (3:1 hexane–EtOAc); IR (KBr): ν 3087, 3062, 3030, 3006, 2929, 2902, 2860, 1622, 1595, 1496, 1466, 1454, 1429, 1367, 1273, 1234, 1201, 1163, 1119, 1097, 1065, 1028, 1001, 906, 800, 735, 696 cm^{-1}; ^1H NMR (DMSO-d_6 at 120 °C): δ 2.52 (s, 3 H, ArAc), 3.48 (dt, 1 H, $J_{5',6'}$ 3.1, $J_{4',5'}$ 9.5 Hz, H-5′), 3.57 (t, 1 H, $J_{3',4'} = J_{4',5'}$ 9.5 Hz, H-4′), 3.65–3.68 (m, 3 H, H-3′,6′a,6′b), 3.81 (s, 3 H, –OMe), 4.16 (d, 1 H, J_{gem} 11.3 Hz, benzylic CH_2), 4.29 (br. t, $J_{1',2'} = J_{2',3'}$ 9.4 Hz, H-2′), 4.45 (d, 1 H, J_{gem} 12.2 Hz, benzylic CH_2), 4.47 (d, 1 H, J_{gem} 11.3 Hz, benzylic CH_2), 4.55 (d, 1 H, J_{gem} 12.2 Hz, benzylic CH_2), 4.62 (d, 1 H, J_{gem} 11.4 Hz, benzylic CH_2), 4.77 (d, 1 H, J_{gem} 11.4 Hz, benzylic CH_2), 4.78 (d, 1 H, J_{gem} 11.6 Hz, benzylic CH_2 and H-1′), 4.83 (d, 1 H, J_{gem} 11.6 Hz, benzylic CH_2), 5.29 (s, 2 H, benzylic CH_2), 6.31 (s, 1 H, ArH), 6.89–7.50 (m, 25 H, ArH), 13.78 (br. s, 1 H, ArOH); FABMS (positive-ion mode, NBA matrix): m/z 795 $[M+H]^+$; FABMS (negative-ion mode, NBA matrix): m/z 793 $[M-H]^+$. Anal. Calcd for $C_{50}H_{50}O_9$: C, 75.55; H, 6.34. Found: C, 75.57; H, 6.36.

3,4,6′-Tris-benzyloxy-3′-C-(2,3,4,6-tetra-O-benzyl-β-D-glucopyranosyl)-2′-hydroxy-4′-methoxychalcone (**14**).—The reaction using compound **13** (3.98 g, 5.00 mmol), 3,4-dibenzyloxybenzaldehyde (1.91 g, 6.00 mmol, 1.2 equiv), 1,4-dioxane (60 mL), and a 50 wt.% aq solution of NaOH (60 mL), and the post-treatment and isolation were carried out as described above for **8**. Compound **14** was obtained (4.78 g, 87%) as an orange amorphous powder: mp 58–60 °C; $[\alpha]_D^{25}$ −9° (*c* 1.0, $CHCl_3$); R_f 0.28 (3:1 hexane–EtOAc); IR (KBr): ν 3087, 3062, 3030, 3006, 2935, 2900, 2860, 1624, 1579, 1558, 1508, 1496, 1454, 1429, 1383, 1360, 1331, 1261, 1209,

1136, 1117, 1103, 1066, 1028, 1005, 980, 908, 845, 806, 735, 696 cm^{-1}; ^1H NMR (DMSO-d_6 at 140 °C): δ 3.52 (dt, 1 H, $J_{5'',6''}$ 3.5, $J_{4'',5''}$ 9.5 Hz, H-5″), 3.61 (t, 1 H, $J_{3'',4''} = J_{4'',5''}$ 9.5 Hz, H-4″), 3.68–3.71 (m, 3 H, H-3″,6″a,6″b), 3.84 (s, 3 H, –OMe), 4.20 (d, 1 H, J_{gem} 11.4 Hz, benzylic CH_2), 4.31 (br. t, 1 H, J 9.3 Hz, H-2″), 4.46 (d, 1 H, J_{gem} 12.3 Hz, benzylic CH_2), 4.49 (d, 1 H, J_{gem} 11.4 Hz, benzylic CH_2), 4.55 (d, 1 H, J_{gem} 12.3 Hz, benzylic CH_2), 4.63 (d, 1 H, J 11.4 Hz, benzylic CH_2), 4.78 (d, 1 H, J_{gem} 11.4 Hz, benzylic CH_2), 4.80 (d, 1 H, J_{gem} 11.8 Hz, benzylic CH_2), 4.84 (d, 1 H, J_{gem} 11.8 Hz, benzylic CH_2), 4.85 (d, 1 H, $J_{1'',2''} = 9.8$ Hz, H-1″), 5.04 (s, 2 H, benzylic CH_2), 5.17 (s, 2 H, benzylic CH_2), 5.27 (s, 2 H, benzylic CH_2), 6.37 (s, 1 H, ArH), 6.89-7.46 (m, 38 H, ArH), 7.54 (d, 1 H, $J_{\alpha,\beta}$ 15.6 Hz, trans-vinyl), 7.59 (d, 1 H, $J_{\alpha,\beta}$ 15.6 Hz, trans-vinyl), 13.48 (br. s, 1 H, ArOH); FABMS (positive-ion mode, NBA matrix): m/z 1096 $[M+H]^+$. Anal. Calcd for $C_{71}H_{66}O_{11}$: C, 77.86; H, 6.07. Found: C, 77.73; H, 6.14.

2-(3,4-Bis-benzyloxyphenyl)-8-C-(2,3,4,6-tetra-O-benzyl-β-D-glucopyranosyl)-5-hydroxy-7-methoxy-4 H-*1-benzopyran-4-one* (**15**).—The reaction using a compound **14** (3.18 g, 2.91 mmol), iodine (37 mg, 0.14 mmol, 0.05 equiv), and Me_2SO (30 mL), and the post-treatment and isolation were carried out in the same manner as described above for **9**. Compound **15** was obtained (2.37 g, 81%) as a colorless amorphous powder: mp 57–58 °C; $[\alpha]_D^{25}$ −9° (*c* 1.0, $CHCl_3$); R_f 0.29 (3:1 hexane–EtOAc); IR (KBr): ν 3087, 3062, 3030, 3006, 2935, 2902, 2864, 1653, 1603, 1591, 1512, 1496, 1454, 1439, 1363, 1327, 1292, 1259, 1207, 1171, 1144, 1115, 1066, 1028, 1003, 912, 847, 822, 808, 735, 696 cm^{-1}; ^1H NMR (DMSO-d_6 at 140 °C): δ 3.61 (dt, 1 H, $J_{5'',6''}$ 3.2, $J_{4'',5''}$ 9.3 Hz, H-5″), 3.70 (d, 2 H, $J_{5'',6''}$ 3.2 Hz, H-6″a,6″b), 3.73 (t, 1 H, $J_{3'',4''} = J_{4'',5''}$ 9.3 Hz, H-4″), 3.80 (dd, 1 H, $J_{2'',3''}$ 8.5, $J_{3'',4''}$ 9.3 Hz, H-3″), 3.87 (s, 3 H, –OMe), 4.10 (d, 1 H, J_{gem} 11.6 Hz, benzylic CH_2), 4.19 (br. t, J 9.2 Hz, H-2″), 4.40 (d, 1 H, J_{gem} 11.6 Hz, benzylic CH_2), 4.44 (d, 2 H, J_{gem} 11.6 Hz, benzylic CH_2), 4.61 (d, 1 H, J_{gem} 11.4 Hz, benzylic CH_2), 4.75 (d, 1 H, J_{gem} 11.4 Hz, benzylic CH_2), 4.79 (d, 1 H, J_{gem} 11.5 Hz, benzylic CH_2), 4.83 (d, 1 H, J_{gem} 11.5 Hz, benzylic CH_2), 4.99 (d, 1 H, $J_{1'',2''} = 9.6$ Hz, H-1″), 5.19 (s, 2 H, benzylic CH_2), 5.21 (s, 2 H, benzylic CH_2), 6.47–7.71 (m, 35 H, ArH and H-3), 13.07 (br. s, 1 H, ArOH); FABMS (positive-ion mode, NBA matrix): m/z 1004 $[M+H]^+$. Anal. Calcd for $C_{64}H_{58}O_{11}$: C, 76.63; H, 5.83. Found: C, 76.56; H, 5.80.

2-(3,4-Bis-benzyloxyphenyl)-8-C-(2,3,4,6-tetra-O-benzyl-β-D-glucopyranosyl)-5,7-dimethoxy-4 H-*1-benzopyran-4-one* (**16**).—The reaction using a compound **15** (804 mg, 0.80 mmol), Me_2SO_4 (152 μL, 1.60 mmol, 2.0 equiv), K_2CO_3 (443 mg, 3.21 mmol, 4.0 equiv) and acetone (10 mL), and the post-treatment and isolation were carried out in the same manner as described above for **10**. Compound **16** was obtained (782 mg, 96%) as a colorless amorphous powder: mp 59–60 °C; $[\alpha]_D^{25}$ −9° (*c* 1.0, $CHCl_3$); R_f 0.26 (EtOAc); IR (KBr): ν 3087, 3062, 3030, 3006, 2933, 2906, 2864, 1645, 1599, 1576, 1512, 1496, 1454, 1435, 1383, 1336, 1323, 1265, 1209, 1144, 1109, 1066, 1045, 1028, 957, 912, 845, 810, 735, 696 cm^{-1}; ^1H NMR (DMSO-d_6 at 140 °C): δ 3.61 (dt, 1 H, $J_{5'',6''}$ 3.2, $J_{4'',5''}$ 9.3 Hz, H-5″), 3.71 (d, 2 H, $J_{5'',6''}$ 3.2 Hz, H-6″a,6″b), 3.73 (t, 1 H, $J_{3'',4''} = J_{4'',5''}$ 9.3 Hz, H-4″), 3.78 (dd, 1 H, $J_{2'',3''}$ 8.5, $J_{3'',4''}$ 9.3 Hz, H-3″), 3.906 (s, 3 H, –OMe), 3.909 (s, 3 H, –OMe), 4.06 (d, 1 H, J_{gem} 11.0 Hz, benzylic CH_2), 4.24 (br. t, 1 H, J 9.2 Hz, H-2″), 4.42 (br. m, 3 H, benzylic CH_2), 4.61 (d, 1 H, J_{gem} 11.5 Hz, benzylic CH_2), 4.75 (d, 1 H, J_{gem} 11.5 Hz, benzylic CH_2), 4.77 (d, 1 H, J_{gem} 11.7 Hz, benzylic CH_2), 4.81 (d, 1 H, J_{gem} 11.7 Hz, benzylic CH_2), 5.05 (d, 1 H, $J_{1'',2''}$ 9.8 Hz, H-1″), 5.16 (s, 2 H, benzylic CH_2), 5.19 (s, 2 H, benzylic CH_2), 6.50–7.65 (m, 35 H, ArH and H-3); FABMS (positive-ion mode, NBA matrix): m/z 1018 $[M+H]^+$. Anal. Calcd for $C_{65}H_{60}O_{11}$: C, 76.75; H, 5.95. Found: C, 76.70; H, 5.98.

8-C-β-D-Glucopyranosyl-2-(3,4-dihydroxyphenyl)-5-hydroxy-7-methoxy-4 H-*1-benzopyran-4-one; isoswertiajaponin* (**17**).—The reaction using compound **15** (489 mg), 10% Pd–C (240 mg), EtOAc (10 mL) and EtOH (50 mL) were carried out as described above for **11**. Isoswertiajaponin **17** was obtained (225 mg, quant) as a pale yellowish–green powder: mp (dec) 217–218 °C, lit.[13b] 252 °C (dec); $[\alpha]_D^{25}$ −15° (*c* 0.50, MeOH); R_f 0.47 (25:35:5:1 Me_2CO–EtOAc–water–AcOH); IR (KBr):

v 3392, 1655, 1601, 1520, 1498, 1448, 1429, 1367, 1329, 1263, 1207, 1120, 1084, 1024, 845, 822 cm^{-1}; ^1H NMR (DMSO-d_6 at 150 °C): δ 3.34 (m, 1 H, H-5″), 3.37 (t, 1 H, $J_{2'',3''} = J_{3'',4''}$ 8.8 Hz, H-3″), 3.45 (br. t, 1 H, $J_{3'',4''} = J_{4'',5''}$ 8.8 Hz, H-4″), 3.62 (dd, 1 H, $J_{5'',6''a}$ 5.6, J_{gem} 11.7 Hz, H-6″a), 3.79 (dd, 1 H, $J_{5'',6''b}$ 2.6, J_{gem} 11.7 Hz, H-6″b), 3.88 (s, 3 H, ArOMe), 3.97 (dd, 1 H, $J_{2'',3''}$ 8.8, $J_{1'',2''}$ 9.8 Hz, H-2″), 4.82 (d, 1 H, $J_{1'',2''}$ 9.8 Hz, H-1″), 6.45 (s, 1 H, H-6), 6.53 (s, 1 H, H-3), 6.91 (d, 1 H, $J_{5',6'}$ 8.7 Hz, H-5′), 7.447 (s, 1 H, H-2′), 7.452 (br. d, 1 H, $J_{5',6'}$ 8.7 Hz, H-6′), 8.50 (br. s, 1 H, ArOH), 9.00 (br. s, 1 H, ArOH), 13.09 (s, 1 H, ArOH); FABMS (positive-ion mode, NBA matrix): *m*/*z* 463 $[M+H]^+$; FABMS (negative-ion mode, NBA matrix): *m*/*z* 461 $[M-H]^-$. Anal. Calcd for $C_{22}H_{22}O_{11}\cdot 0.5\ H_2O$: C, 56.05; H, 4.92. Found: C, 56.43; H, 5.04.

8-C-β-D-Glucopyranosyl-2-(3,4-dihydroxyphenyl)-5,7-dimethoxy-4 H-*1-benzopyran-4-one; parkisonin B* (**18**).—The reaction using a compound **16** (617 mg), 10% Pd–C (300 mg), EtOAc (10 mL) and EtOH (50 mL) were carried out as described above for **11**. Parkinsonin B **18** was obtained (289 mg, quant) as a pale pink powder: mp (dec) 221–222 °C; $[\alpha]_D^{25}$ −11° (*c* 0.50, MeOH); R_f 0.04 (25:35:5:1 Me_2CO–EtOAc–water–AcOH); IR (KBr): *v* 3392, 1639, 1599, 1522, 1497, 1448, 1394, 1327, 1275, 1215, 1120, 1084, 1038, 847, 816 cm^{-1}; ^1H NMR (DMSO-d_6 at 150 °C): δ 3.34 (ddd, 1 H, $J_{5'',6''b}$ 2.4, $J_{5'',6''a}$ 5.2, $J_{4'',5''}$ 9.0 Hz, H-5″), 3.37 (t, 1 H, $J_{2'',3''} = J_{3'',4''}$ 8.7 Hz, H-3″), 3.46 (br. s, 1 H, H-4″), 3.63 (dd, 1 H, $J_{5'',6''a}$ 5.2, J_{gem} 11.6 Hz, H-6″a), 3.79 (dd, 1 H, $J_{5'',6''b}$ 2.4, J_{gem} 11.6 Hz, H-6″b), 3.89 (s, 3 H, 5-OMe), 3.92 (s, 3 H, 7-OMe), 4.02 (dd, 1 H, $J_{2'',3''}$ 8.7, $J_{1'',2''}$ 9.9 Hz, H-2″), 4.86 (d, 1 H, $J_{1'',2''}$ 9.9 Hz, H-1″), 6.30 (s, 1 H, H-3), 6.61 (s, 1 H, H-6), 6.88 (d, 1 H, $J_{5',6'}$ 8.9 Hz, H-5′), 7.39 (br. s, 2 H, H-2′,6′). phenolic –OH signals were very broad.; FABMS (positive-ion mode, NBA matrix): *m*/*z* 477 $[M+H]^+$; FABMS (negative-ion mode, NBA matrix): *m*/*z* 475 $[M-H]^-$. Anal. Calcd for $C_{23}H_{24}O_{11}\cdot 0.5\ H_2O$: C, 56.91; H, 5.19. Found: C, 57.05; H, 5.35.

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