Carbohydrate Research, 198 (1990) 223–234
Elsevier Science Publishers B.V., Amsterdam – Printed in The Netherlands

NEW SYNTHESES OF PLANT ARYL GLYCOSIDES AS POTENTIAL GENE INDUCERS

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(Received June 8th, 1989; accepted for publication, September 15th, 1989)

ABSTRACT

Aryl β-D-glycopyranosides have been synthesized by coupling acetovanillone (4-hydroxy-3-methoxyacetophenone) with D-glucose, D-galactose, and maltose; acetosyringone (4-hydroxy-3,5-dimethoxyacetophenone) with D-glucose and D-galactose; syringaldehyde (3-methoxyvanillin) with D-glucose; and syringic acid (4-hydroxy-3,5-dimethoxybenzoic acid) with D-glucose. The Mauthner's procedure using peracetylated glycosyl bromides and phenolates in aqueous acetone afforded the acetylated β-D-glycosides, which were deacetylated.

INTRODUCTION

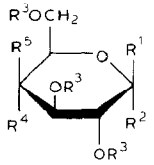
Aromatic compounds figure prominently among the natural products found in plants. They are very reactive and, hence, subject to oxidation, substitution, and coupling reactions. Phenols and flavonoids exhibit a wide variety of biochemical, physiological, and ecological activities which enable plants to meet the challenges of their environment. They are generally toxic compounds to protect the plant from pathogens and pests, yet because they are sequestered in the form of glycosides they are harmless to the plant. They are also important in plant–microorganism interrelationships. They may act as chemoattractants[1–4] and also induce *vir* genes on the Ti plasmid of *Agrobacterium tumefaciens*[5] and the *nod D* regulatory gene which is located on the Sym plasmid of *Rhizobium spp*[6–9].

In order to determine the chemotaxis and the specificity of *vir* gene induction in various *A. tumefaciens* strains, we needed a number of aromatic glycosides. This paper describes the synthesis of some β-D-glucopyranosides, β-D-galactopyranosides, and β-maltoside of acetovanillone (**18**) (4-hydroxy-3-methoxyacetophenone), acetosyringone (**20**) (4-hydroxy-3,5-dimethoxyacetophenone), syringaldehyde (**21**) (3-methoxyvanillin), and syringic acid (**22**) (4-hydroxy-3,5-dimethoxybenzoic acid). Some of these compounds have been previously identified in plants. Thus, androsin [3-methoxy-4-(β-D-glucopyranosyloxy)acetophenone] was isolated from the rhizome of *Apocynum androsaemifolium*[10]. It was also identified in high-moorland peat extracts[11], in cactus *Neolloydia texensis*[12,13], in the

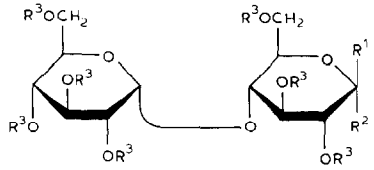
rhizome of *Iris tectorum*[14], in needles from some species of the *Pinaceae* family[15,16], and in *Penstemon pinifolius*[17], A β-D-glucoside of acetosyringone (3,5-dimethoxy-4-β-D-glucopyranosyloxyacetophenone) was found in *Ranzania japonica*[18], and a β-D-glucoside of syringic acid (3,5-dimethoxy-4-β-D-glucopyranosyloxybenzoic acid) was found in *Anodendron affine*[19].

RESULTS AND DISCUSSION

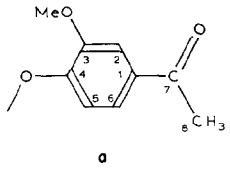
At the onset of this work, various glycosidation procedures were investigated for the preparation of the β-D-glucoside **3** of acetovanillone (**18**). The Helferich method[20] [fusion of 1,2,3,4,6-penta-*O*-acetyl-D-glucopyranose with acetovanillone (**18**) in the presence of zinc chloride] afforded the β-D-glucopyranoside **3** in a poor yield (14%) after purification. Similarly, the procedure of Zurabyan *et al.*[21] [using the phenolate **19** and 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (**1**) in *N,N*-dimethylformamide] also afforded a low yield (25%). Better results were obtained with the Mauthner procedure[22]; treatment of phenolate **19** with 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (**1**) in 1:1 acetone–water afforded the



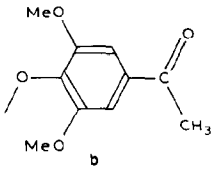
	R^1	R^2	R^3	R^4	R^5
1	H	Br	Ac	OAc	H
2	H	Br	Ac	H	OAc
3	a	H	Ac	OAc	H
4	a	H	Ac	H	OAc
5	a	H	H	OH	H
6	a	H	H	H	OH
7	b	H	Ac	OAc	H
8	b	H	Ac	H	OAc
9	b	H	H	OH	H
10	b	H	H	H	OH
11	c	H	Ac	OAc	H
12	c	H	H	OH	H
13	d	H	Ac	OAc	H
14	d	H	H	OH	H



15 $R^1 = H, R^2 = Br, R^3 = Ac$
16 $R^1 = \alpha, R^2 = H, R^3 = Ac$
17 $R^1 = \alpha, R^2 = R^3 = H$



a



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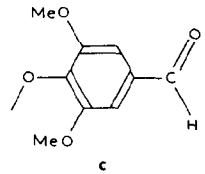

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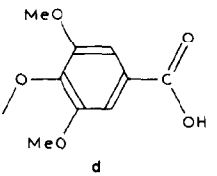
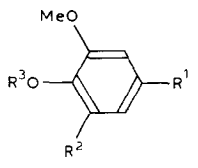


d



18 $R^1 = COMe, R^2 = R^3 = H$
19 $R^1 = COMe, R^2 = H, R^3 = Na$
20 $R^1 = COMe, R^2 = OMe, R^3 = H$
21 $R^1 = CHO, R^2 = OMe, R^3 = H$
22 $R^1 = CO_2H, R^2 = OMe, R^3 = H$

desired compound **3** in 71% yield. The reaction was stereoselective, affording only the β-D anomer. However, a partial deacetylation occurred during coupling, so the resulting mixture had to be acetylated with acetic anhydride in pyridine. By-products of this step were phenyl acetate from unreacted phenol and peracetylated sugars. These compounds were easily removed.

The structure of the prepared glycosides was established by n.m.r. spectroscopy, and i.r. and mass spectrometry. The β-D-anomeric configuration was usually determined by ^{1}H-n.m.r. spectroscopy of the peracetylated glycosides. In some

cases where the signals of the anomeric protons were not resolved, the *O*-deacetylated derivatives were used instead. The signals of the anomeric protons then appeared as easily identifiable sharp doublets. In the case of the peracetylated glycosides **3** and **16**, a 2D-n.m.r. experiment was needed to confirm the β-D-anomeric configuration.

All the deacetylated glycosides (**5**, **6**, **9**, **10**, **12**, **14**, **17**) and their parent phenols were analyzed by liquid chromatography (h.p.l.c.). An RP-18 column and an isocratic mobile phase (acetonitrile–acetic acid–water)[23] gave good separations (see Table I). Absorption spectra were generally not sensitive to pH variations between 5.2 and 9.5. Nevertheless, compound **17** showed a hypochromic effect at pH 7.4, and compound **9** a hyperchromic effect at pH 7.4. None of the glycosides exhibited an isosbestic point, unlike their parent phenol (Table II).

TABLE I

H.P.L.C.[a] OF DEACETYLATED GLYCOSIDES (**5**, **6**, **9**, **10**, **12**, **14**, **17**) AND RELATED PHENOLS (**18**, **20–22**)

Compound	*Retention time (min)*
14	3.07
6	4.07
17	4.14
5	4.47
12	4.48
10	4.81
9	5.30
22	7.43
21	12.85
18	14.51
20	15.63

[a]The isocratic mobile phase was 7:1:42 acetonitrile–acetic acid–water, the flow 1 mL.min^{-1}, and detection at 270 nm. The sample (1 mg) was dissolved in bidistilled water (1 mL) and 10 μL were injected.

TABLE II

ISOSBESTIC POINTS[a] OF PHENOLS (**18**, **20**, **21**)

Compound	λ_{max} *(nm), log* ε[b]		
18	238 (3.78)	257 (3.64)	309 (3.83)
20	237 (3.84)	262 (3.46)	320 (3.83)
21	238 (3.71)	265 (3.22)	327 (3.72)

[a]Determined in the following buffers: 0.1M sodium acetate, pH 5.2; 0.1M sodium phosphate, pH 7.4; and 0.05M sodium carbonate, pH 9.5. [b]In parentheses.

EXPERIMENTAL

General methods. — Melting points were determined with a Leitz hot-plate microscope and are uncorrected. Optical rotations were measured with a Perkin–Elmer spectropolarimeter model 141. Infrared spectra were recorded with a Perkin–Elmer 257 spectrometer for KBr pellets. N.m.r.spectra were recorded with an AM 300 WB Bruker spectrometer, m.s. data with a Nermag R-10-10C spectrometer in the chemical ionization mode using ammonia to generate ions, and u.v. and visible absorption spectra with an Uvikon 860 spectrophotometer. T.l.c. was performed on Silica Gel Merck 60 F_{254} and spots were detected by fluorescence and the phosphomolybdic–sulfuric acid $\{H_7[P(MO_2O_7)_6]$–$H_2SO_4\}$ reagent. H.p.l.c. was performed with a Spectra-Physics high performance liquid chromatograph, equipped with a SP 8700 ternary-solvent-delivery system, an SP 8440 spectrophotometric detector attached to an SP 4270 integrator, an ODS Spheri-5 analytical column (23 cm; Spectra-Physics), and an RP-18 guard column (7 μm × 2 cm) (Spectra-Physics). 2,3,4,6-Tetra-*O*-acetyl-α-D-glucopyranosyl bromide (**1**), 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide (**2**) and 2,3,6,2′,3′,4′,6′-hepta-*O*-acetyl-α-maltosyl bromide (**15**) were purchased from Sigma (La Verpillière, France). Acetovanillone (**18**), acetosyringone (**20**), syringaldehyde (**21**) and syringic acid (**22**) were from Aldrich (Strasbourg, France). Silica Gel 60 (0.04–0.06 mm, 230–400 mesh) and other chemical reagents were purchased from Merck (Nogent-sur-Marne, France).

General procedure for glycosylation[22]. — A stirred solution of the phenol (2.05 mmol) in 0.286M NaOH (7 mL, 2 mmol) was cooled to 14° and treated with a solution of per-*O*-acetylglycosyl bromide (1.95 mmol) in acetone (7 mL) added dropwise. The solution was stirred at room temperature for 3–5 h in the dark, and then concentrated to dryness. Examination of the syrupy residue by t.l.c. on silica gel revealed the presence of the desired glycoside as the major component, some excess phenolic compound, and some partially deacetylated glycosyl derivatives. The syrup was evaporated under vacuum and acetylated with acetic anhydride (2 mL) in pyridine (2 mL) for 50 min at 90°. The solution was then concentrated to dryness under reduced pressure. Purification was achieved by chromatography on a silica gel column using 1:1 chloroform–ethyl acetate as solvent.

General procedure for deacetylation. — To a solution of phenyl per-*O*-acetylglycoside (0.5 mmol) in anhydrous methanol (4–8 mL) was added dropwise a solution of M sodium methoxide in methanol (25 μL, 25 μmol). After being kept for 6 h at room temperature, the solution was rendered neutral with acetic acid, and the solvent removed by evaporation. The solid residue crystallized as described.

*3-Methoxy-4-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyloxy)acetophenone* (**3**). — The sodium salt of 4-hydroxy-3-methoxyacetophenone (**19**; sodium 4-acetyl-2-methoxyphenolate), obtained from acetovanillone (**18**; 340 mg, 2.05 mmol) with 0.286M NaOH (7 mL, 2 mmol), was subjected to the general glycosidation proce-

dure by coupling with 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (**1**; 805 mg, 1.95 mmol) to give **3** which spontaneously crystallized after being kept overnight at 4° (460 mg, 48%). The filtrate afforded an additional crop (23%). The crystals were homogeneous by t.l.c. in 1:1 chloroform–ethyl acetate (R_F 0.59) and 4:1 chloroform–methanol (R_F 0.95); m.p. 157–158° (lit.[24,13] m.p. 158.5–159.5°, 155–157°); $[\alpha]_D^{22}$ −40.5° (*c* 2, chloroform), $[\alpha]_{546}^{22}$ −50.5° (*c* 2, chloroform) {lit.[24,13] $[\alpha]_D^{20}$ −42° (*c* 2, chloroform), $[\alpha]_D$ −43.5° (*c* 0.01, pyridine)}; ν_{max}^{KBr} 1740 (OAc), 1680 (CO ketone), 1590, 1515, 1380, 1295, 1230 and 1045 (CO methoxy and sugar), 915, and 835 cm^{-1} (CH arom.); ^{1}H-n.m.r. ($CDCl_3$): δ 7.52 (d, 1 H, $J_{2,6}$ 2 Hz, H-2), 7.48 (dd, 1 H, $J_{2,6}$ 2, $J_{5,6}$ 8 Hz, H-6), 7.11 (d, 1 H, $J_{5,6}$ 8 Hz, H-5), 5.29 (m, 2 H, H-2′,3′), 5.16 (m, 1 H, $J_{4',5'}$ 10 Hz, H-4′), 5.06 (d, 1 H, $J_{1',2'}$ 7.5 Hz, H-1′β), 4.26 (dd, 1 H, $J_{5',6'a}$ 5, $J_{6'a,6'b}$ 12.5 Hz, H-6′a), 4.16 (dd, 1 H, $J_{5',6'b}$ 2.5, $J_{6'a,6'b}$ 12.5 Hz, H-6′b), 3.86 (s, 3 H, OCH_3), 3.80 (m, 1 H, H-5′), 2.55 (s, 3 H, CH_3-8), 2.06 (s, 3 H, OAc), 2.05 (s, 3 H, OAc), 2.03 (s, 3 H, OAc), and 2.02 (s, 3 H, OAc); m.s.: *m/z* (%) 514 (65, MNH_4^+), 331 (100, M^+ − **a**), 271 (30, 331 − CH_3CO_2H), and 167 (35, acetovanillone·H^+).

Anal. Calc. for $C_{23}H_{28}O_{12}$: C, 55.65; H, 5.65. Found: C, 55.75; H, 5.55.

3-Methoxy-4-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyloxy)acetophenone (**4**). — This compound was obtained by the general procedure for glycosylation from **18** (340 mg, 2.05 mmol) and 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide (**2**; 800 mg, 1.95 mmol). After acetylation and evaporation to dryness, t.l.c. on silica gel in 1:1 chloroform–ethyl acetate showed **4** (R_F 0.59) as the major component, some 4-acetoxy-3-methoxy-acetophenone (R_F 0.79), and some 1,2,3,4,6-penta-*O*-acetyl-D-galactopyranose (R_F 0.70). Compound **4** was isolated, by chromatography on a silica gel column (2.2 × 75 cm) using 1:1 chloroform–ethyl acetate as solvent (685 mg, 71%). It crystallized from ethanol–water, needles, m.p. 123–124°, $[\alpha]_D^{22}$ −24° (*c* 1.9, chloroform), $[\alpha]_{546}^{22}$ −31° (*c* 1.9, chloroform); ν_{max}^{KBr} 1740 (OAc), 1660 (CO ketone), 1585, 1505, 1415, 1370, 1220 (CO methoxy and sugar), 1070, 875, 805 (CH arom.), and 590 cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$): δ 7.51 (m, 2 H, H-2,6), 7.13 (d, 1 H, $J_{5,6}$ 8 Hz, H-5), 5.52 (dd, 1 H, $J_{1',2'}$ 8, $J_{2',3'}$ 10.5 Hz, H-2′), 5.44 (dd, 1 H, $J_{3',4'}$ 3.5, $J_{4',5'}$ 1 Hz, H-4′), 5.10 (dd, 1 H, $J_{2',3'}$ 10.5, $J_{3',4'}$ 3.5 Hz, H-3′), 5.00 (d, 1 H, $J_{1',2'}$ 8 Hz, H-1′β), 4.18 (m, 2 H, $J_{5',6'}$ 6.5, $J_{6',a,6'b}$ 11.5 Hz, H-6′a,6′b), 4.01 (dt, 1 H, $J_{4',5'}$ 1, $J_{5',6'}$ 6.5 Hz, H-5′), 3.86 (s, 3 H, OCH_3), 2.56 (s, 3 H, CH_3-8), 2.15 (s, 3 H, OAc), 2.05 (s, 3 H, OAc), 2.03 (s, 3 H, OAc), and 2.00 (s, 3 H, OAc); m.s.: *m/z* (%) 514 (70, MNH_4^+), 348 (5, MNH_4^+ − **18**), and 331 (100, M^+ − **a**).

Anal. Calc. for $C_{23}H_{28}O_{12}$: C, 55.65; H, 5.65. Found: C, 55.89; H, 5.75.

3-Methoxy-4-[O-(2,3,4,6-tetra-O-acetyl-α-D-glucopyranosyl-(1→4)-2,3,6-tri-O-acetyl-β-D-glucopyranosyloxy]acetophenone (**16**). — This compound was obtained from **18** (340 mg, 2.05 mmol) and 2,3,6,2′,3′,4′,6′-hepta-*O*-acetyl-α-maltosyl bromide (**15**; 1.365 g, 1.95 mmol) by use of the general procedure for glycosylation. After acetylation and concentration to dryness, chromatography on a silica gel column (2.2 × 75 cm) using 1:1 chloroform–ethyl acetate as solvent gave

16 (550 mg, 36%; R_F 0.45). It crystallized from methanol, m.p. 147.5–148.5°; $[\alpha]_D^{22}$ +31° (*c* 2, chloroform), $[\alpha]_{546}^{22}$ +31.5° (*c* 2, chloroform); ν_{max}^{KBr} 1740 (OAc), 1675 (CO ketone), 1590, 1505, 1415, 1370, 1270, 1240 (CO methoxy and sugar), 1030, 940, and 805 cm^{-1} (CH arom.); ^{1}H-n.m.r. ($CDCl_3$): δ 7.50 (m, 2 H, $J_{2,6}$ 2, $J_{5,6}$ 8 Hz, H-2,6), 7.08 (d, 1 H, $J_{5,6}$ 8 Hz, H-5), 5.43 (d, 1 H, $J_{1'',2''}$ 4 Hz, H-1''α), 5.35 (t, 1 H, $J_{2'',3''} = J_{3'',4''}$ 10 Hz, H-3''), 5.31 (m, 1 H, $J_{2',3'}$ 4.5, $J_{3',4'}$ 9 Hz, H-3'), 5.12 (m, 2 H, H-1',2'), 5.04 (t, 1 H, $J_{3'',4''} = J_{4'',5''}$ 10 Hz, H-4''), 4.85 (dd, 1 H, $J_{1'',2''}$ 4, $J_{2'',3''}$ 10.5 Hz, H-2''), 4.49 (dd, 1 H, $J_{5',6'a}$ 3, $J_{6'a,6'b}$ 12 Hz, H-6'a), 4.24 (dd, 2 H, $J_{5',6'b} = J_{5'',6''a}$ 4.5, $J_{6'a,6'b} = J_{6'a,6''b} = 12$ Hz, H-6'b,6''a), 4.09 (t, 1 H, $J_{3',4'} = J_{4',5'} = 9$ Hz, H-4'), 4.04 (dd, 1 H, $J_{5'',6''b}$ 2.5, $J_{6''a,6''b}$ 12.5 Hz, H-6''b), 3.96 (m, 1 H, $J_{4'',5''}$ 10, $J_{5'',6''a}$ 4, $J_{5'',6''b}$ 2.5 Hz, H-5''), 3.85 (s, 3 H, OCH_3), 3.81 (m, 1 H, $J_{4',5'}$ 9, $J_{5',6'a}$ 3, $J_{5',6'b}$ 4.5 Hz, H-5'), 2.56 (s, 3 H, CH_3-8), 2.08 (s, 3 H, OAc), 2.07 (s, 3 H, OAc), 2.03 (s, 9 H, 3 OAc), 2.01 (s, 3 H, OAc), and 1.99 (s, 3 H, OAc); m.s.: *m/z* (%) 802 (100, MNH_4^+), 619 (3, M^+ − **a**), and 559 (2, 619 − CH_3CO_2H).

Anal. Calc. for $C_{35}H_{44}O_{20} \cdot H_2O$: C, 52.37; H, 5.74. Found: C, 52.45; H, 5.67.

*3,5-Dimethoxy-4-(2,3,4,6-tetra-*O*-acetyl-β-*D*-glucopyranosyloxy)acetophenone* (**7**). — This compound was obtained by the general procedure for glycosylation from **20** (402 mg, 2.05 mmol) and **1** (805 mg, 1.95 mmol). After acetylation and concentration to dryness, t.l.c. in 1:1 chloroform–ethyl acetate showed **7** (R_F 0.48) as the major component and some 4-acetoxy-3,5-dimethoxyacetophenone (R_F 0.73) and 1,2,3,4,6-penta-*O*-acetyl-D-glucopyranose (R_F 0.67). Compound **7** was isolated by column chromatography as a colorless syrup (715 mg, 70%) that crystallized from methanol, needles, m.p. 122–123.5° (lit.[22,18] m.p. 119–120°, 120.5–121.5°); $[\alpha]_D^{22}$ −11° (*c* 1, chloroform), $[\alpha]_{546}^{22}$ −16.5° (*c* 1, chloroform); ν_{max}^{KBr} 1745 (OAc), 1670 (CO ketone), 1585, 1495, 1455, 1365, 1330, 1220 (CO methoxy and sugar), 1130, 1060, 1030, and 610 cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$): δ 7.18 (s, 2 H, H-2,6), 5.25 (m, 4 H, H-1',2',3',4'), 4.21 (dd, 1 H, $J_{5',6'a}$ 5, $J_{6'a,6'b}$ 12 Hz, H-6'a), 4.10 (dd, 1 H, $J_{5',6'b}$ 3, $J_{6'a,6'b}$ 12 Hz, H-6'b), 3.87 (s, 6 H, 2 OCH_3), 3.70 (m, 1 H, H-5'), 2.57 (s, 3 H, CH_3-8), and 2.01 (s, 12 H, 4 OAc); m.s.: *m/z* (%) 544 (100, MNH_4^+), 331 (80, M^+ − **b**), 271 (25, 331 − CH_3CO_2H), and 197 (15, **20**·H^+).

Anal. Calc. for $C_{24}H_{30}O_{13}$: C, 54.75; H, 5.70. Found: C, 54.46; H, 5.68.

*3,5-Dimethoxy-4-(2,3,4,6-tetra-*O*-acetyl-β-*D*-galactopyranosyloxy)acetophenone* (**8**). — This compound was obtained in the usual manner from **20** (402 mg, 2.05 mmol) and **2** (800 mg, 1.95 mmol). After acetylation and concentration to dryness, t.l.c. on silica gel in 1:1 chloroform–ethyl acetate showed **8** (R_F 0.52) as the major component and some 4-acetoxy-3,5-dimethoxyacetophenone (R_F 0.73) and 1,2,3,4,6-penta-*O*-acetyl-D-galactopyranose (R_F 0.70). Compound **8** was purified by chromatography on a silica gel column (2.2 × 75 cm) with 1:1 chloroform–ethyl acetate as solvent (677 mg, 66%). It crystallized from diethyl ether as needles, m.p. 113.5–114.5°, $[\alpha]_D^{22}$ −1.5° (*c* 1.9, chloroform), $[\alpha]_{546}^{22}$ −2.5° (*c* 1.9, chloroform); ν_{max}^{KBr} 1730 (OAc), 1680 (CO ketone), 1580, 1410, 1365, 1330, 1220 (CO methoxy and sugar), 1130, 1040, 850 and 830 (CH arom.), 605, and 590 cm^{-1};

^{1}H-n.m.r. ($CDCl_3$): δ 7.19 (s, 2 H, H-2,6), 5.51 (dd, 1 H, $J_{1',2'}$ 8, $J_{2',3'}$ 10.5 Hz, H-2'), 5.38 (dd, 1 H, $J_{3',4'}$ 3.5, $J_{4',5'}$ 1 Hz, H-4'), 5.06 (dd, 1 H, $J_{2',3'}$ 10.5, $J_{3',4'}$ 3.5 Hz, H-3'), 5.03 (d, 1 H, $J_{1',2'}$ 8 Hz, H-1'β), 4.14 (m, 2 H, $J_{5',6'}$ 6.5 and 7 Hz, $J_{6'a,6'b}$ 15.5 Hz, H-6'a,6'b), 3.87 (s, 6 H, 2 OCH_3), 3.86 (dt, 1 H, $J_{4',5'}$ 1, $J_{5',6'}$ 6.5 Hz, H-5'), 2.57 (s, 3 H, CH_3-8), 2.17 (s, 3 H, OAc), 2.01 (s, 3 H, OAc), 1.99 (s, 3 H, OAc), and 1.98 (s, 3 H, OAc); m.s.: *m/z* (%) 544 (100, MNH_4^+), 331 (35, M^+ − **b**), 197 (7, **20**·H^+), 181 (4, $\mathbf{b}^+ - CH_3$).

Anal. Calc. for $C_{24}H_{30}O_{13}$: C, 54.75; H, 5.70. Found: C, 55.04; H, 5.90.

*3,5-Dimethoxy-4-(2,3,4,6-tetra-*O*-acetyl-β-*D*-glucopyranosyloxy)benzaldehyde* (**11**). — This compound was obtained from syringaldehyde (**21**) and **1**. After acetylation, the mixture was concentrated to a syrup under reduced pressure and t.l.c. on silica gel in 1:1 chloroform–ethyl acetate showed three compounds having R_F values of 0.77, 0.67, and 0.52. The mixture was chromatographed on a silica gel column (2.2 × 75 cm) in the same eluting solvent to give 4-acetoxy-3,5-dimethoxybenzaldehyde (R_F 0.77), 1,2,3,4,6-penta-*O*-acetyl-D-glucopyranose (R_F 0.67), and **11** (R_F 0.52) as the major component (63%). This crystallized from methanol as colorless triclinic crystals, m.p. 160.5–161.5° (lit.[22] m.p. 158–159°), $[\alpha]_D^{22}$ −13° (*c* 2.1, chloroform), $[\alpha]_{546}^{22}$ −18° (*c* 2.1, chloroform); ν_{max}^{KBr} 1755 (OAc), 1685 (CO formyl), 1590, 1495, 1460, 1390, 1330, 1235 and 1215 (CO methoxy and sugar), 1120, 1080, 1030, 910, 845 (CH arom.), and 735 cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$): δ 9.86 (s, 1 H, H-7), 7.11 (s, 2 H, H-2,6), 5.27 (m, 4 H, H-1',2',3',4'), 4.22 (dd, 1 H, $J_{5',6'a}$ 5, $J_{6'a,6'b}$ 12 Hz, H-6'a), 4.11 (dd, 1 H, $J_{5',6'b}$ 3, $J_{6'a,6'b}$ 12 Hz, H-6'b), 3.89 (s, 6 H, 2 OCH_3), 3.71 (m, 1 H, H-5'), and 2.01 (s, 12 H, 4 OAc); m.s.: *m/z* (%) 530 (100, MNH_4^+), 331 (20, M^+ − **c**), and 271 (3, 331 − CH_3CO_2H).

Anal. Calc. for $C_{23}H_{28}O_{13}$: C, 53.91; H, 5.47. Found: C, 54.00; H, 5.46.

*3,5-Dimethoxy-4-(2,3,4,6-tetra-*O*-acetyl-β-*D*-glucopyranosyloxy)benzoic acid* (**13**). — 3,5-Dimethoxy-4-hydroxy-benzoic acid (**22**, syringic acid; 400 mg, 2.02 mmol) was dissolved in 0.571M NaOH (7 mL, 4 mmol) and subjected to glycosidation. The mixture was concentrated to dryness to afford a foam which was triturated in ethanol (20 mL) to give a suspension. Salts (sodium bromide and sodium syringate) were removed by filtration. The solution was concentrated to dryness and acetylated with acetic anhydride (4 mL) for 50 min at 90°. After evaporation to dryness, t.l.c. of the solid residue on silica gel in 10:10:1 chloroform–ethyl acetate–acetic acid showed **13** (R_F 0.57) as the major component and some 4-acetoxy-3,5-dimethoxybenzoic acid (R_F 0.76), 1,2,3,4,6-penta-*O*-acetyl-D-glucopyranose (R_F 0.67), and an unidentified compound (R_F 0.63). Compound **13** was isolated by column chromatography on silica gel as a yellowish foam (470 mg, 46%) that crystallized from diethyl ether to give a yellowish, semicrystalline solid, m.p. 153–156° (lit.[19] m.p. 164–166°), $[\alpha]_D^{22}$ −8.5° (*c* 1.9, chloroform), $[\alpha]_{546}^{22}$ −13° (*c* 1.9, chloroform); ν_{max}^{KBr} 1740 (OAc), 1690 (CO acid), 1585, 1460, 1415, 1370, 1225 (CO), 1130, 1035, 910, 775, 690, and 600 cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$): δ 7.32 (s, 2 H, H-2,6), 5.26 (m, 4 H, H-1',2',3',4'), 4.23 (dd, 1 H, $J_{5',6'a}$ 5, $J_{6'a,6'b}$ 12 Hz, H-6'a), 4.11 (dd, 1 H, $J_{5',6'b}$ 2.5, $J_{6'a,6'b}$ 12 Hz, H-6'b), 3.86 (s, 6 H, 2 OCH_3), 3.71 (m, 1 H, H-5'), and 2.01 (s, 12 H, 4 OAc); m.s.: *m/z* (%) 546 (100, MNH_4^+) and 331 (10, M^+ − **d**).

Anal. Calc. for $C_{23}H_{28}O_{14}$: C, 52.27; H, 5.30. Found: C, 52.18; H, 5.36.

4-β-D-Glucopyranosyloxy-3-methoxyacetophenone (androsin) (**5**). — This compound was obtained from **3** by the general procedure for deacetylation, and it crystallized from ethanol as needles, m.p. 228.5–229.5° (lit.[25,24,17] m.p. 223–224°, 226–227°, 219–222°). Compound **5** was homogeneous in t.l.c. (4:1 chloroform–methanol) R_F 0.40; $[\alpha]_D^{25}$ −48° (*c* 1, *N,N*-dimethylformamide), $[\alpha]_{546}^{25}$ −61° (*c* 1, *N,N*-dimethylformamide); λ_{max} 302 nm (log ε 3.80), λ_{max} 267 nm (log ε 4.07); ν_{max}^{KBr} 3490 and 3410 (OH), 3070 (CH arom.), 2980 and 2890 (CH), 1655 (CO ketone), 1585, 1510, 1415, 1280 (CO), 1215 (CO methoxy), 1080 (CO sugar), 1020, 895, 870 and 815 (CH arom.), 640, and 425 cm^{-1}; ^{1}H-n.m.r. (D_2O): δ 7.68 (dd, 1 H, $J_{2,6}$ 2, $J_{5,6}$ 8.5 Hz, H-6), 7.58 (d, 1 H, $J_{2,6}$ 2 Hz, H-2), 7.23 (d, 1 H, $J_{5,6}$ 8.5 Hz, H-5), 5.25 (d, 1 H, $J_{1',2'}$ 7.5 Hz, H-1′β), 3.93 (dd, 1 H, $J_{5',6'a}$ 2, $J_{6'a,6'b}$ 12.5 Hz, H-6′a), 3.93 (s, 3 H, OCH_3), 3.76 (dd, 1 H, $J_{5',6'b}$ 5.5, $J_{6'a,6'b}$ 12.5 Hz, H-6′b), 3.69–3.60 (m, 3 H, H-2′,3′,4′), 3.52 (m, 1 H, $J_{4',5'}$ 9, $J_{5',6'a}$ 2.5, $J_{5',6'b}$ 5.5 Hz, H-5′), and 2.62 (s, 3 H, CH_3-8); m.s.: *m/z* (%) 346 (2, MNH_4^+), 329 (2, MH^+), 180 (10, MNH_4^+ − **18**), 167 (100, **18**·H^+), and 151 (10, $\mathbf{18}^+$ − CH_3).

Anal. Calc. for $C_{15}H_{20}O_8$: C, 54.88; H, 6.10. Found: C, 54.81; H, 6.15.

4-β-D-Galactopyranosyloxy-3-methoxyacetophenone (**6**). — This compound was obtained from **4** by the general procedure for deacetylation. The progress of the reaction was monitored by t.l.c. on silica gel in 4:1 chloroform–methanol (R_F 0.96 (**4**), 0.35 (**6**). The deacetylation was quantitative and **6** was crystallized from ethanol, m.p. 189.5–192.5°, $[\alpha]_D^{22}$ −28° (*c* 1.1, *N,N*-dimethylformamide), $[\alpha]_{546}^{25}$ −35° (*c* 1.1, *N,N*-dimethylformamide); λ_{max} 301 nm (log ε 3.82), λ_{max} 267 nm (log ε 4.09); ν_{max}^{KBr} 3500 to 3350 (OH), 1660–1645 (CO ketone), 1585, 1505, 1415, 1275 (CO), 1215 (CO methoxy), 1140, 1090 (CO sugar), 1020, 890, 820 and 810 (CH arom.), 775, and 705 cm^{-1}; ^{1}H-n.m.r. (D_2O): δ 7.66 (dd, 1 H, $J_{2,6}$ 2, $J_{5,6}$ 8.5 Hz, H-6), 7.54 (d, 1 H, $J_{2,6}$ 2 Hz, H-2), 7.22 (d, 1 H, $J_{5,6}$ 8.5 Hz, H-5), 5.17 (d, 1 H, $J_{1',2'}$ 7.5 Hz, H-1′β), 4.02 (d, 1 H, $J_{3',4'}$ 3.5 Hz, H-4′), 3.91 (s, 3 H, OCH_3), 3.94–3.86 (m, 2 H, H-2′,3′), 3.82–3.77 (m, 3 H, H-5′,6′a,6′b), and 2.60 (s, 3 H, CH_3-8); m.s.: *m/z* (%) 346 (30, MNH_4^+), 184 (70, **18**·NH_4^+), 180 (30, MNH_4^+ − **18**), 167 (100, **18**·H^+), and 151 (8, $\mathbf{18}^+$ − CH_3).

Anal. Calc. for $C_{15}H_{20}O_8 \cdot H_2O$: C, 52.02; H, 6.36. Found: C, 51.92; H, 6.29.

4-[O-α-D-Glucopyranosyl-(1→4)-β-D-glucopyranosyloxy]-3-methoxyacetophenone (**17**). — This compound was obtained from **16** by the usual procedure of deacetylation. The progress of the reaction was monitored by t.l.c. (silica gel, 4:1 chloroform–methanol) R_F 0.91 (**16**), 0.15 (**17**). Compound **17** crystallized from 2-propanol, m.p. 142–144°, $[\alpha]_D^{22}$ +33° (*c* 0.9, *N,N*-dimethylformamide), $[\alpha]_{546}^{22}$ +37° (*c* 0.9, *N,N*-dimethylformamide); λ_{max} 302 nm (log ε 3.62), λ_{max} 267 nm (log ε 3.89); ν_{max}^{KBr} 3350 (OH), 1655 (CO ketone), 1585, 1505, 1415, 1355, 1270 (CO), 1215 (CO methoxy), 1180, 1140, 1070 (CO sugar), 1045, and 805 cm^{-1} (CH arom.); ^{1}H-n.m.r. (D_2O): δ 7.67 (d, 1 H, $J_{5,6}$ 8.5 Hz, H-6), 7.56 (s, 1 H, H-2), 7.22 (d, 1 H, $J_{5,6}$ 8.5 Hz, H-5), 5.44 (d, 1 H, $J_{1'',2''}$ 4 Hz, H-1α), 5.25 (d, 1 H, $J_{1',2'}$ 8 Hz, H-1′β), 3.92 (s, 3 H, OCH_3), 3.96–3.58 (m, 11 H, H-2′,3′,4′,6′a,6′b,2″,3″,4″,5″,6″a,6″b), 3.43 (t, 1 H, $J_{4',5'}$ 9.5 Hz, H-5′), and 2.61 (s, 3 H, CH_3-8); m.s.: *m/z* (%) 508 (3,

MNH_4^+), 342 (17, MNH_4^+ − **18**), 180 (30, MNH_4^+ − **5**), 167 (100, **18**·H^+), and 151 (20, **18**$^+$ − CH_3).

Anal. Calc. for $C_{21}H_{30}O_{13}\cdot H_2O$: C, 49.61; H, 6.30. Found: C, 49.47; H, 6.26.

4-β-D-Glucopyranosyloxy-3,5-dimethoxyacetophenone (**9**). — This compound was obtained from **7** by deacetylation in the usual manner; t.l.c. (4:1 chloroform–methanol) R_F 0.45; it crystallized from ethanol, m.p. 221.5–222.5° (lit.[22] m.p. 208–209°), $[\alpha]_D^{22}$ −17° (*c* 1, *N,N*-dimethylformamide), $[\alpha]_{546}^{22}$ −19° (*c* 1, *N,N*-dimethylformamide); λ_{max} 277 nm (log ε 3.98); ν_{max}^{KBr} 3400 (OH), 2940 (CH), 1665 (CO ketone), 1580, 1495, 1460, 1415, 1360, 1330, 1220 (CO methoxy), 1190, 1130, 1095 and 1065 (CO sugar), 1020, 985, 895, 850 (CH arom.), 810, and 610 cm^{-1}; ^{1}H-n.m.r. (D_2O): δ 7.30 (s, 2 H, H-2,6), 5.15 (d, 1 H, $J_{1',2'}$ 7.5 Hz, H-1′β), 3.90 (s, 6 H, 2 OCH_3), 3.80 (dd, 1 H, $J_{5',6'a}$ 2.5, $J_{6'a,6'b}$ 12.5 Hz, H-6′a), 3.69 (dd, 1 H, $J_{5',6'b}$ 5, $J_{6'a,6'b}$ 12.5 Hz, H-6′b), 3.61–3.45 (m, 3 H, H-2′,3′,4′), 3.35 (m, 1 H, $J_{4',5'}$ 9, $J_{5',6'a}$ 2, $J_{5',6'b}$ 5 Hz, H-5′), and 2.62 (s, 3 H, CH_3-8); m.s. *m/z* (%) 376 (10, MNH_4^+), 214 (7, **20**·NH_4^+), 197 (100, **20**·H^+), and 180 (30, MNH_4^+ − **20**).

Anal. Calc. for $C_{16}H_{22}O_9$: C, 53.63; H, 6.15. Found: C, 53.65; H, 5.87.

4-β-D-Galactopyranosyloxy-3,5-dimethoxyacetophenone (**10**). — This compound was obtained from **8** by deacetylation in the usual manner; t.l.c. (4:1 chloroform–methanol) R_F 0.36. It crystallized from ethanol as needles, m.p. 222–223°, $[\alpha]_D^{22}$ −12° (*c* 1, *N,N*-dimethylformamide), $[\alpha]_{546}^{22}$ −14° (*c* 1, *N,N*-dimethylformamide); λ_{max} 277 nm (log ε 3.95); ν_{max}^{KBr} 3510–3330 (OH), 2930 (CH), 1665 (CO ketone), 1580, 1495, 1460, 1415, 1360, 1330, 1220 (CO methoxy), 1190, 1130, 1070 (CO sugar), 1015, 890, 860, 785 (CH arom.), 700, and 610 cm^{-1}; ^{1}H-n.m.r. (D_2O): δ 7.29 (s, 2 H, H-2,6), 5.13 (d, 1 H, $J_{1',2'}$ 7.5 Hz, H-1′β), 3.94 (d, 1 H, $J_{3',4'}$ 3.5 Hz, H-4′), 3.91 (s, 6 H, 2 OCH_3), 3.82 (dd, 1 H, $J_{1',2'}$ 7.5, $J_{2',3'}$ 10 Hz, H-2′), 3.70 (m, 3 H, H-3′,6′a,6′b), 3.61 (t, 1 H, $J_{5',6'}$ 6 Hz, H-5′), and 2.62 (s, 3 H, CH_3-8); m.s.: *m/z* (%) 376 (4, MNH_4^+), 214 (3, **20**·NH_4^+), 197 (100, **20**·H^+), 181 (7, **20**$^+$ − CH_3), and 180 (5, MNH_4^+ − **20**).

Anal. Calc. for $C_{16}H_{22}O_9$: C, 53.63; H, 6.15. Found: C, 53.66; H, 6.00.

4-β-D-Glucopyranosyloxy-3,5-dimethoxybenzaldehyde (**12**). — This compound was obtained from **11** by the general procedure of deacetylation; t.l.c. (4:1 chloroform–methanol) R_F 0.44. It crystallized from ethanol as needles, m.p. 214–216° (lit.[22] m.p. 210–211°), $[\alpha]_D^{25}$ −16° (*c* 1, *N,N*-dimethylformamide), $[\alpha]_{546}^{22}$ −19° (*c* 1, *N,N*-dimethylformamide), {lit.[22] $[\alpha]_D^{20}$ −12.8° (*c* 1.3, water)}; λ_{max} 284 nm (log ε 4.05); ν_{max}^{KBr} 3350 (OH), 2900 (CH), 1685 (CO formyl), 1585, 1495, 1460, 1415, 1380, 1335, 1235, 1125, 1070 (CO sugar), 1020, 830 (CH arom.), 740, and 630 cm^{-1}; ^{1}H-n.m.r. (D_2O): δ 9.79 (s, 1 H, H-7), 7.31 (s, 2 H, H-2,6), 5.18 (d, 1 H, $J_{1',2'}$ 7.5 Hz, H-1′β), 3.93 (s, 6 H, 2 OCH_3), 3.81 (dd, 1 H, $J_{5',6'a}$ 2, $J_{6'a,6'b}$ 12.5 Hz, H-6′a), and 3.70 (dd, 1 H, $J_{5',6'b}$ 5, $J_{6'a,6'b}$ 12.5 Hz, H-6′b), 3.62–3.46 (m, 3 H, H-2′,3′,4′), 3.37 (m, 1 H, $J_{4',5'}$ 9, $J_{5',6'a}$ 2, $J_{5',6'b}$ 5 Hz, H-5′); m.s.: *m/z* (%) 362 (15, MNH_4^+), 200 (30, **21**·NH_4^+), 183 (100, **21**·H^+), and 180 (70, MNH_4^+ − **21**).

Anal. Calc. for $C_{15}H_{20}O_9$: C, 52.32; H, 5.81. Found: C, 52.34; H, 5.91.

4-β-D-Glucopyranosyloxy-3,5-dimethoxybenzoic acid (**14**). — To a solution

of **13** (264 mg, 0.5 mmol) in anhydrous methanol (3 mL) was added dropwise a M solution of sodium methoxide in methanol (525 μL, 525 μmol). The progress of the reaction was monitored by t.l.c. on silica gel in 20:5:1 chloroform–methanol–acetic acid: R_F 0.82 (**13**), 0.30 (**14**). The solution was stirred for 5 h at room temperature and concentrated to dryness. The residue was dissolved in water (2 mL) and to this solution was added a solution of $KHSO_4$ (75 mg, 551 μmol) in water (2 mL). The gel formed was solidified by trituration and isolated by filtration (135 mg, 75%). Compound **14** crystallized from methanol as needles, m.p. 227–228° (dec.) (lit.[19] m.p. 209–210°), $[\alpha]_D^{22}$ −20° (*c* 1, *N,N*-dimethylformamide), $[\alpha]_{546}^{22}$ −24° (*c* 1, *N,N*-dimethylformamide); λ_{max} 251 nm (log ε 3.96); ν_{max}^{KBr} 3510 (OH acid), 3440 (OH), 2920 (CH), 2590 (OH acid), 1660 (CO acid), 1590, 1495, 1455, 1415, 1325, 1265 (OH acid), 1225 (CO), 1185, 1130, 1065 (CO sugar), 1005, 910, 860 (CH arom.), 815, 765, 745, 715, 615, 525, and 355 cm^{-1}; ^{1}H-n.m.r. (D_2O): δ 7.38 (s, 2 H, H-2,6), 5.14 (d, 1 H, $J_{1',2'}$ 7.5 Hz, H-1′β), 3.91 (s, 6 H, 2 OCH_3), 3.81 (dd, 1 H, $J_{5',6'a}$ 2.5, $J_{6'a,6'b}$ 12.5 Hz, H-6′a), 3.71 (dd, 1 H, $J_{5',6'b}$ 5, $J_{6'a,6'b}$ 12.5 Hz, H-6′b), 3.62–3.46 (m, 3 H, H-2′,3′,4′), 3.36 (m, 1 H, $J_{4',5'}$ 9, $J_{5',6'a}$ 2.5, $J_{5',6'b}$ 5 Hz, H-5′); m.s.: *m/z* (%) 378 (50, MNH_4^+), 361 (7, MH^+), 216 (100, **22**·NH_4^+), 198 (80, **22**$^+$), and 180 (40, MNH_4^+ − **22**).

Anal. Calc. for $C_{15}H_{20}O_{10}$: C, 50.00; H, 5.56. Found: C, 49.85; H, 5.52.

ACKNOWLEDGMENTS

The authors thank Mrs. A. Caille for helpful technical assistance in n.m.r. experiments and Mr. G. Keravis for providing the mass spectra (Centre de Mesures Physiques, Université d'Orléans). They are grateful to Prof. M. Monsigny for encouragement.

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