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SYNTHESIS OF QUERCETIN-3-*O*-β-D-GLUCOPYRANOSYL-(1→2)-β-D-XYLOPYRANOSIDE VIA ORTHOESTER METHODOLOGY

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ABSTRACT.—The synthesis of quercetin-3-*O*-β-D-glucopyranosyl-(1→2)-β-D-xylopyranoside [10], a flavonoid recently isolated from *Kalanchoe prolifera*, has been carried out via orthoester methodology.

Synthetic oligosaccharides composed of glucose and xylose are important, particularly as model substances for the study of plant polysaccharides and organic natural substances which have variously linked oligosaccharides in their molecules (1,2). Until now, methyl 3,4-di-*O*-acetyl-β-D-xylopyranoside (3), benzyl 3,4-di-*O*-benzyl-β-D-xylopyranoside (2,4), and methyl 3,5-*O*-isopropylidene-α,β-D-xylofuranoside (5,6) have been used for the synthesis of (1→2)-linked disaccharides with D-xylopyranose at the reducing end, but their preparation is very laborious. More recently, the easily obtainable 1,3,4-tri-*O*-acetyl-α-D-xylopyranose has been proposed for glycosylation (7) but, in that case, the stereoselectivity of the coupling reaction with tetra-*O*-acetyl-2,3,4,6-α-D-glucopyranosyl bromide (1) is not satisfactory.

This paper deals with the synthesis of a flavonoid, quercetin-3-*O*-β-D-glucopyranosyl-(1→2)-β-D-xylopyranoside [10], that was recently isolated as a novel substance from *Kalanchoe prolifera* Raym.-Hamet (Crassulaceae) (1), via orthoester methodology. This synthetic procedure involves benzylation of 1,2-orthoesters to provide hexopyranose derivatives with blocking groups at all positions except C-1 and C-2 (8). To the best of our knowledge, the method has never been previously applied to xylose.

RESULTS AND DISCUSSION

Initially, *O-exo-*, and *O-endo-*3,4-di-*O*-acetyl-1,2-*O*-(methoxyethylidene)-α-D-xylopyranose ([2] and [3]) were prepared by reaction of tri-*O*-acetyl-α-D-xylopyranosyl bromide [4] (9) with dry MeOH in *sym*-collidine containing tetra-*n*-butylammonium bromide (10). The most abundant diastereoisomer formed had the methoxy group in the exo-orientation [2]. The orthoester mixture was deacetylated and benzylated to give *O-exo-* and *O-endo-*3,4-di-*O*-benzyl-1,2-*O*-(methoxyethylidene)-α-D-xylopyranose ([5] and [6]). These diastereoisomers were difficult to separate on a preparative scale. Therefore only small samples of compounds 2, 5, and 6 have been isolated from mixtures for analytical purposes. The di-*O*-benzyl orthoesters 5 and 6 were converted into methyl 3,4-di-*O*-benzyl-2-*O*-acetyl-β-D-xylopyranoside [7] (11), using standard orthoester rearrangement procedures (12). Conversion of the acetate 7 to the alcohol 8 followed by reaction with 2,3,4,6-tetra-*O*-acetylglucopyranosyl bromide using standard glycosidation procedures, afforded the desired β (1→2) disaccharide 2 in 56% yield. Debenzylation of the latter followed by acetylation afforded the intended methyl hexa-*O*-acetyl-2-*O*-(β-D-glucopyranosyl)-β-D-xylopyranoside [1]. ¹H- and ¹³C-nmr assignments of 1 (Table 1)
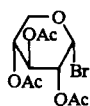
4
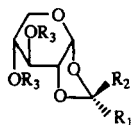
2 R_1=CH$_3$, R_2=OCH$_3$, R_3=Ac
3 R_1=OCH$_3$, R_2=CH$_3$, R_3=Ac
5 R_1=CH$_3$, R_2=OCH$_3$, R_3=Bn
6 R_1=OCH$_3$, R_2=CH$_3$, R_3=Bn
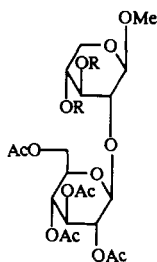
1 R=Ac
9 R=Bn
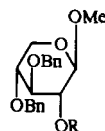
7 R=Ac
8 R=H
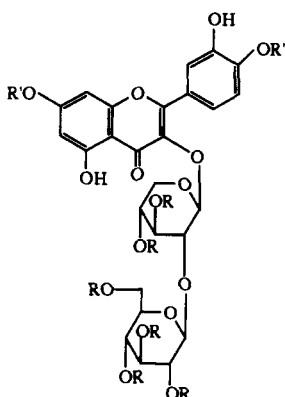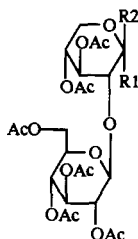
11a R_1=OAc, R_2=H
11b R_1=H, R_2=OAc
12 R_1=Br, R_2=H

10 R=R′=H
13 R=Ac, R′=Bn

were made, using 2D nmr experiments (^{1}H-^{1}H COSY 45°, ^{1}H-^{13}C HETCOR). The coupling constants, $J_{H_1-H_2}$=6 Hz and $J_{C_1-H_1}$=170 Hz (obtained by 2D-HMQC experiments)(13), suggested the predominance of the ^{4}C$_1$ conformer for the xylopyranoside ring (14–18) of **1**. Acetolysis of **1** by (CH$_3$CO)$_2$O in the presence of H$_2$SO$_4$ at room temperature followed by deacetylation with NaOMe in MeOH and acetylation, led to 2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl-(1→2)-1,3,4-tri-O-acetyl-α,β-D-xylopyranose [**11a,b**] (1), which was readily converted into the required bromide **12** by treatment with HBr in CH$_3$COOH (19). Condensation of 4′,7-di-O-benzylquercetin (20) with **12** under phase transfer-catalyzed conditions led to 4′,7-di-O-benzylquercetin-3-O-(2,3,4,6-tetra-O-acetyl)-β-D-glucopyranosyl-(1→2)-3,4-di-O-acetyl-β-D-xylopyranoside [**13**] in 40% yield. This latter product, after hydrogenolysis and deacetylation afforded **10** which was identical in all respects with the natural glycoside.

EXPERIMENTAL

TABLE 1. ^{1}H- and ^{13}C-Nmr Assignments for **1** in CDCl$_3$.[a]

Position	Xylose Moiety			Glucose Moiety		
	^{13}C	^{1}H			^{13}C	^{1}H
1	102.27	4.42 d, J=6	1'		100.95	4.68 d, J=8
2	77.72	3.57 dd, J=8, 6	2'		71.42	4.92 dd, J=9, 8
3	68.34	5.02 t, J=8	3'		72.98	5.11 t, J=9
4	69.13	4.80 td, J=8, 5	4'		72.41	5.04 t, J=9
5	61.86	4.01 dd, J=12, 5	5'		71.90	3.63 ddd, J=9, 5, 3
		3.35 dd, J=12, 8	6'		61.97	4.23 dd, J=12, 5
						4.20 dd, J=12, 3
OMe	56.55	3.48 s				
COCH$_3$×6 .	20.7–20.9	2–2.10 s				
COCH$_3$×6 .	169.2–170.3					

[a]Table entries are chemical shifts in ppm (multiplicity, J in Hz).

internal standard. Cidms were recorded with a Nermag R 10-10c spectrometer using NH$_3$ as reagent gas. Flash chromatography was performed on columns of Si gel (Merck, 0.04–0.06 mm).

*O-EXO- AND O-ENDO-*3,4-DI-*O*-ACETYL-1,2,-*O*-(METHOXYETHYLIDENE)-α-D-XYLOPYRANOSE ([**2**] AND [**3**]).—Tri-*O*-acetyl-α-D-xylopyranosyl bromide (3 g, 8.85 mmol) was dissolved in 7 ml of *sym*-collidine and 0.4 ml of dry MeOH. Tetra-*n*-butyl-ammonium bromide (0.6 g) was added and the mixture was vigorously stirred at 50° overnight. The almost solid reaction mixture was dissolved in a minimum of CHCl$_3$ and washed with just sufficient aqueous HCl (1 M) to neutralize the collidine, then with aqueous NaHCO$_3$ (10 ml), and finally H$_2$O (10 ml). The CHCl$_3$ layer was dried (Na$_2$SO$_4$) and evaporated under reduced pressure. Purification by flash chromatography (CH$_2$Cl$_2$-*n*-hexane, 9:1) afforded 2 g (87.5%) of an inseparable mixture of **2** and **3**. The ^{1}H-nmr spectrum of this mixture indicated that the ratio of exo and endo isomers was 90%:10%. Repeated cc (Si gel 60H, CH$_2$Cl$_2$-*n*-hexane, 9:1) of the above mixture gave the major component **2**: [α]^{20}D +1.9° (*c*=2, CHCl$_3$); cidms *m/z* 308 (M+NH$_4$$^+$), 276, 259; ^{1}H nmr (CDCl$_3$) δ 5.57 (1H, d, $J_{1,2}$=4 Hz, H-1), 5.26 (1H, t, $J_{3,4}$=3 Hz, H-3), 4.83 (1H, ddd, $J_{4,5ax}$=7 Hz, $J_{4,5eq}$=5 Hz, H-4), 4.22 (1H, dd, $J_{2,3}$=3 Hz, H-2), 3.93 (1H, dd, $J_{5eq,5ax}$=12 Hz, H-5eq), 3.73 (1H, dd, H-5ax), 3.28 (3H, s, OCH$_3$), 2.13, 2.08 (6H, 2s, 2×OAc), 1.73 (3H, s, CH$_3$); ^{13}C nmr (CDCl$_3$) δ 96.4 (C-1), 74.3 (C-2), 68.5 (C-3), 67.8 (C-4), 59.8 (C-5), 50.2 (OCH$_3$), 22.1 (CH$_3$), 20.8 (CH$_3$COO), 122.3 (OCH$_3$CCH$_3$), 169.9, 169.1 (CH$_3$COO). *Anal.* calcd for C$_{12}$H$_{18}$O$_8$: C, 49.65, H, 6.25, O, 44.10, found: C, 49.57, H, 6.32, O, 44.14.

*O-EXO- AND O-ENDO-*3,4-DI-*O*-BENZYL-1,2-*O*-(METHOXYETHYLIDENE)-α-D-XYLOPYRANOSE ([**5**] AND [**6**]).—To a solution of **2** and **3** (1.4 g, 5.4 mmol) in MeOH (3 ml) was added a 1 M solution of NaOMe in MeOH (8 ml) and the mixture was stirred at room temperature until tlc (*n*-hexane-EtOAc, 9:1) showed total conversion of starting material. After neutralization with an excess of Amberlite IR-50 (H$^+$) cation-exchange resin, filtration, and evaporation of the solvent, C$_6$H$_6$ (15 ml) portions were added and distilled three times from the residue. The residue was taken up in dry DMF (50 ml) and treated with NaH (1 g, 41.6 mmol). Benzyl bromide (2.5 ml, 21 mmol) was then added dropwise over 30 min with cooling to keep the reaction at approximately 20°. The solution was then left stirring for 16 h and worked up by addition of MeOH (20 ml). The solvent was evaporated under reduced pressure and the mixture was diluted with CH$_2$Cl$_2$ and washed with 2 M aqueous HCl (10 ml) and H$_2$O (15 ml). After drying (Na$_2$SO$_4$), the organic phase was evaporated under reduced pressure. Purification by flash chromatography (*n*-hexane/EtOAc) afforded 1.3 g of a mixture of **5** and **6** (62%). Repeated cc (Si gel 60H) of the above mixture permitted the isolation of analytical samples of **5** (exo-isomer) and **6** (endo-isomer).

Compound **5**.—[α]^{20}D +20.9° (*c*=1, CHCl$_3$); cidms *m/z* 387 (M+H$^+$), 355; ^{1}H nmr (CDCl$_3$) δ 7.30–7.15 (10H, m, 2×C$_6$H$_5$), 5.53 (1H, d, $J_{1,2}$=5 Hz, H-1), 4.67–4.46 (4H, m, 2×CH$_2$C$_6$H$_5$), 4.27 (1H, dd, $J_{2,3}$=4 Hz, H-2), 3.82 (1H, dd, $J_{3,4}$=3 Hz, H-3), 3.75 (1H, m, H-5$_{eq}$), 3.58 (2H, m, H-4, H-5$_{ax}$), 3.25 (3H, s, OCH$_3$), 1.66 (3H, s, CH$_3$). *Anal.*, calcd for C$_{22}$H$_{26}$O$_6$: C, 68.38, H, 6.78, O, 24.84; found: C, 68.31, H, 6.72, O, 24.89.

Compound **6**.—[α]^{20}D +29.6° (*c*=1, CHCl$_3$); cidms *m/z* 404 (M+NH$_4$$^+$), 387 (M+H$^+$), 355; ^{1}H nmr (CDCl$_3$) δ 7.34–7.23 (10H, m, 2×C$_6$H$_5$), 5.34 (1H, d, $J_{1,2}$=4 Hz, H-1), 4.77–4.55 (4H, m, 2×CH$_2$C$_6$H$_5$), 4.05 (1H, dd, $J_{2,3}$=8 Hz, H-2), 4.02 (1H, dd, $J_{3,4}$=4 Hz, H-3), 3.84 (1H, dd, $J_{5eq,5ax}$=12 Hz, H-5eq), 3.74 (1H, dd, H-5ax), 3.51 (1H, ddd, $J_{4,5ax}$=7 Hz, $J_{4,5eq}$=3 Hz, H-4), 3.34 (3H, s, OCH$_3$), 1.54 (3H, s, CH$_3$). *Anal.*, calcd for C$_{22}$H$_{26}$O$_6$: C, 68.38, H, 6.78, O, 24.84; found: C, 68.31, H, 6.72, O, 24.84.

METHYL 3,4-DI-*O*-BENZYL-2-ACETYL-β-D-XYLOPYRANOSIDE [7].—A solution of **5** and **6** (386 mg, 1 mmol) in dry CH_2Cl_2 (10 ml) was treated at 0° with 3 drops of $SnCl_4$. After stirring at 0° for 12 h, the solution was treated with aqueous NH_3 (2 ml) and washed with H_2O (3×100 ml). After drying (Na_2SO_4) and filtration, the organic phase was evaporated under reduced pressure. Purification by flash chromatography (EtOAc-*n*-hexane, 9:1) afforded 200 mg of **7** (52%). This compound exhibited: $[\alpha]^{20}D$ −27° (*c*=0.1, $CHCl_3$); cidms *m/z* 404 (M+NH_4^+), 355; ^1H nmr ($CDCl_3$) δ 7.35–7.26 (10H, m, 2×C_6H_5), 4.91 (1H, t, $J_{2,3}$=8 Hz, H-2), 4.86–4.57 (4H, m, 2×$CH_2C_6H_5$), 4.27 (1H, d, $J_{1,2}$=8 Hz, H-1), 3.99 (1H, dd, $J_{5eq,5ax}$=12 Hz, H-5eq), 3.69 (1H, ddd, $J_{4,5ax}$=9 Hz, $J_{4,5eq}$=5 Hz, H-4), 3.60 (1H, t, $J_{3,4}$=8 Hz, H-3), 3.45 (3H, s, OCH_3), 3.30 (1H, dd, H-5ax), 2.05 (3H, s, OAc). *Anal.*, calcd for $C_{22}H_{26}O_6$: C, 68.38, H, 6.78, O, 24.84; found: C, 68.38, H, 6.78, O, 24.84.

METHYL 3,4-DI-*O*-BENZYL-β-D-XYLOPYRANOSIDE [8].—To a solution of **7** (200 mg, 0.52 mmol) in MeOH (1 ml) was added a 2 M solution of NaOMe in MeOH (2.5 ml) and the mixture was stirred at room temperature until tlc showed the total conversion of the starting material. After neutralization with Amberlite IR-50 (H$^+$) cation-exchange resin, filtration and evaporation of the solvent, 150 mg of **8** was obtained (84%). This compound exhibited: $[\alpha]^{20}D$ −33.3° (*c*=0.6, $CHCl_3$); cidms *m/z* 362 (M+NH_4^+), 330; ^1H nmr ($CDCl_3$) δ 7.28–7.17 (10H, m, 2×C_6H_5), 4.82–4.55 (4H, m, 2×$CH_2C_6H_5$), 4.20 (1H, d, $J_{1,2}$=6 Hz, H-1), 3.95 (1H, dd, $J_{5eq,5ax}$=12 Hz, $J_{5eq,4}$=5 Hz, H-5eq), 3.55–3.46 (3H, m, H-2, 3, 4), 3.45 (3H, s, OCH_3), 3.27 (1H, dd, $J_{5ax,4}$=8 Hz, H-5ax). *Anal.*, calcd for $C_{20}H_{24}O_5$: C, 69.75, H, 7.02, O, 23.23; found: C, 69.70, H, 7.09, O, 23.29.

METHYL 3,4-DI-*O*-BENZYL-2-*O*-(β-D-2,3,4,6-TETRACETYL-GLUCOPYRANOSYL)-β-D-XYLOPYRANOSIDE [9].—To a solution of **8** (138 mg, 0.40 mmol) and anhydrous $HgCN_2$ (250 mg, 1.04 mmol) in dry MeCN (7 ml) was added tetraacetyl-α-D-glucopyranosyl bromide (411 mg, 1 mmol) with stirring; the stirring was continued for 5 h at room temperature. After filtration over Celite, the reaction mixture was diluted with CH_2Cl_2 (25 ml) washed with 1 N aqueous KBr (2×25 ml), aqueous $NaHCO_3$ (2×25 ml) and H_2O (2×30 ml), and dried over Na_2SO_4. The solvent was removed under reduced pressure and the remaining syrup was subjected to flash chromatography (CH_2Cl_2-MeOH, 99:1) to give 152 mg (56%) of **9**. This compound exhibited: $[\alpha]^{20}D$ −32° (*c*=1, $CHCl_3$); cidms *m/z* 692 (M+NH_4^+), 602, 331; ^1H nmr ($CDCl_3$) δ 7.29–7.14 (10H, m, 2×C_6H_5) 5.15–4.90 (4H, m, H-1′, -2′, -3′, -4′), 4.85–4.65 (4H, m, 2×$CH_2C_6H_5$), 4.25 (1H, d, $J_{1,2}$=3 Hz, H-1), 4.22 (1H, dd, $J_{6A',6B'}$=12 Hz, $J_{6A',5'}$=4 Hz, H-6A′), 4.07 (1H, dd, $J_{6B',5'}$=2 Hz, H-6B), 3.88 (1H, dd, $J_{5eq,5ax}$=12 Hz, $J_{5eq,4}$=5 Hz, H-5eq), 3.62–3.48 (4H, m, H-5′, H-4, -3, -2), 3.46 (3H, s, OCH_3), 3.17 (1H, dd, $J_{5ax,4}$=5 Hz, H-5ax), 2.05–1.78 (12H, 4s, 4×OAc). *Anal.*, calcd for $C_{34}H_{42}O_{14}$: C, 60.53, H, 6.27, O, 33.20; found: C, 60.58, H, 6.22, O, 33.12.

METHYL HEXA-*O*-ACETYL-2-*O*-(β-D-GLUCOPYRANOSYL)-β-D-XYLOPYRANOSIDE [1].—A solution of **9** (60 mg, 0.09 mmol) in MeOH (4 ml) was hydrogenolyzed (Pd-C, H_2) at 20° for 4 h. The catalyst was removed by filtration (Celite) and the solvent evaporated under reduced pressure. The residue was dissolved in dry pyridine (3 ml) and treated with Ac_2O (3 ml); after 24 h the reaction mixture was evaporated under reduced pressure. Purification by flash chromatography (CH_2Cl_2-MeOH, 99:1) afforded 40 mg of **1** (77%) which exhibited: $[\alpha]^{20}D$ −20° (*c*=0.5, $CHCl_3$); cidms *m/z* 596 (M+NH_4^+), 331; ^1H and ^{13}C nmr, see Table 1. *Anal.*, calcd for $C_{24}H_{34}O_{16}$: C, 49.83, H, 5.92, O, 44.25; found: C, 49.89, H, 5.97, O, 44.19.

2,3,4,6-TETRA-*O*-ACETYL-β-D-GLUCOPYRANOSYL-(1→2)-1,3,4-TRI-*O*-ACETYL-α,β-D-XYLOPYRANOSE [**11a,b**].—A solution of **1** (0.116 g, 0.2 mmol) in $(CH_3CO)_2O$ (0.4 ml, 4.2 mmol) was shaken with concentrated H_2SO_4 (0.012 ml, 0.2 mmol) in $(CH_3CO)_2O$ (0.6 ml, 6.3 mmol) for 6 h at 20°. The reaction mixture was diluted with CH_2Cl_2 (20 ml) and washed with H_2O (3×20 ml), saturated aqueous $NaHCO_3$ solution (2×20 ml), and again with H_2O (2×20 ml). The organic solution was dried over anhydrous Na_2SO_4, evaporated under reduced pressure, and gave a mixture (0.071 g, 56%) which was dissolved in MeOH (1 ml) and 1 N NaOMe in MeOH (2 ml) was added. The mixture was stirred for 12 h at 20°. After neutralization by addition of Amberlite IRC-50 H$^+$ ion exchange resin and filtration, the solvent was removed by evaporation and the residue was acetylated by $(CH_3CO_2)O$ (2 ml, 21 mmol) in dry pyridine (2 ml, 27 mmol) for 36 h at 20°. The reaction mixture was evaporated under reduced pressure. Purification by flash chromatography (CH_2Cl_2-MeOH, 98:2) afforded 0.042 g (69%) of an inseparable mixture of **11a** and **11b**.

2,3,4,6-TETRA-*O*-ACETYL-β-D-GLUCOPYRANOSYL-(1→2)-3,4-DI-*O*-ACETYL-α-D-XYLOPYRANOSYL BROMIDE [**12**].—To a solution of a mixture of **11a** and **b** (0.60 g, 1 mmol) in glacial CH_3COOH (0.6 ml) and dry $CHCl_3$ (0.6 ml), was added 33% HBr (6.7 mmol) in CH_3COOH (1.2 ml). The mixture was stirred for 3 h at 0°, diluted with $CHCl_3$ (20 ml), washed successively at 0° with H_2O (2×20 ml), saturated aqueous $NaHCO_3$ solution (30 ml) and H_2O (20 ml), and dried over anhydrous Na_2SO_4. Evaporation of the solvents under reduced pressure gave crude **12** (0.57 g, 91%) as a syrup which was used in the next step without further purification.

4',7-DI-*O*-BENZYLQUERCETIN-3-*O*-(2,3,4,6-TETRA-*O*-ACETYL)-β-D-GLUCOPYRANOSYL-(1→2)-3,4-DI-*O*-ACETYL-β-D-XYLOPYRANOSIDE[**13**].—A solution of **12** (0.140 g, 0.22 mmol) and 4',7-di-*O*-benzylquercetin (0.120 g, 0.25 mmol) (20) in CHCl₃ (5 ml) was stirred at reflux with benzyltriethylammonium bromide (0.055 g, 0.2 mmol) in 1.25 M aqueous KOH for 15 h. After dilution with H_2O (10 ml), the two phases were separated and the organic layer was washed with 1.25 M aqueous KOH (2×50 ml) and evaporated under reduced pressure.

Purification by cc (toluene-EtOAc, 90:10) afforded 0.103 g of **13** (40%). This compound exhibited $[\alpha]^{20}D$ −48° (c=0.25, CHCl₃); cidms m/z 1029 (M+H⁺); ¹H nmr (CDCl₃) δ 12.30 (1H, s, D₂O exchangeable, OH-5), 7.48–7.28 (10H, m, 2×CH₂C₆H₅), 7.17 (1H, d, $J_{2',6'}$=2 Hz, H-2'), 7.13 (1H, dd, $J_{6',5'}$=9 and 2 Hz, H-6'), 6.97 (1H, d, H-5'), 6.43 (1H, d, $J_{8,6}$=2 Hz, H-8), 6.36 (1H, d, H-6), 5.82 (1H, s, D₂O exchangeable, OH-3'), 5.43 (1H, d, $J_{1'',2''}$=4 Hz, H-1''), 5.21–5.05 (7H, m, H-3''', H-4''', H-2''', 2×CH₂C₆H₅), 5.02 (1H, t, $J_{3'',4''}$=6 Hz, H-3''), 4.77 (1H, d, $J_{1''',2'''}$=8 Hz, H-1'''), 4.71 (1H, ddd, $J_{4'',5''ax}$=5 Hz, $J_{4'',5''eq}$=4 Hz, H-4''), 4.33 (1H, dd, J=12 and 4 Hz, H$_a$-6'''), 4.10 (1H, dd, J=12 and 2 Hz, H$_b$-6'''), 4.07 (1H, dd, $J_{2'',3'}$=6 Hz, H-2''), 4.00 (1H, dd, J=12 Hz, H-5''$_{eq}$), 3.76 (1H, m, H-5'''), 3.33 (1H, dd, H-5''$_{ax}$), 2.17, 2.13, 2.08, 2.07, 2.02, 2.00 (18H, 6s, 6×OAc). *Anal.*, calcd for C₅₂H₅₂O₂₂: C, 60.70, H, 5.09; found: C, 60.64, H, 5.08.

DEBLOCKING OF GLYCOSIDE **13**.—A solution of **13** (0.075 g, 0.07 mmol) in MeOH (5 ml) was hydrogenolyzed (Pd-C, H₂) at 20° for 4 h. The catalyst was removed by filtration (Celite) and the solvent evaporated under reduced pressure. The residue was dissolved in 1 N NaOMe in MeOH (3 ml) and the mixture was stirred for 3 h at 20°. After neutralization by addition of Amberlite IRC-50 H⁺ ion exchange resin and filtration, the solvent was removed by evaporation to afford pure **10** as an amorphous solid (0.031 g, 71% overall yield from **13**), which was identical in all respects with the natural product (1).

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