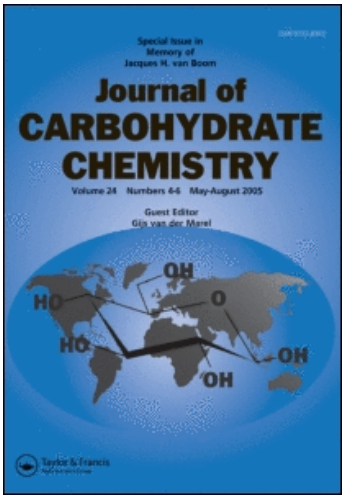

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C-Glycosylated Biphenyls: The Stille Coupling Reaction of *C*-Glycosylated Aryl Tins with Aryl Bromides

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C-GLYCOSYLATED BIPHENYLS: THE STILLE COUPLING REACTION OF *C*-GLYCOSYLATED ARYL TINS WITH ARYL BROMIDES

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ABSTRACT

C-glycosylated biphenyls were prepared by the palladium-mediated cross-coupling reaction of *C*-glycosylated aryl tins with variously substituted aryl bromides, which will provide physiologically stable glycomimetics of various glycoepitopes. A *C*-sialylated biphenyl, a glycomimetic of biologically significant sialosides, is also available by this method.

INTRODUCTION

In the preceding paper[1] we reported the facile preparation of *C*-glycosylated aryl tins as versatile building blocks for aryl *C*-glycosylated glycomimetics. The palladium-catalyzed cross-coupling of *C*-glycosylated aryl tins with a variety of electrophiles will provide a wide range of *C*-glycosides on different aromatic platforms; these glycosides are expected to possess novel bioactivities. Although the cross-coupling of organotin compounds with various electrophiles has been extensively studied and well documented,[2] nothing has been reported on specific stannyl compounds bearing *C*-glycosides.

In this communication, we wish to report on the synthesis of *C*-glycosylated biphenyls that will provide low molecular weight and physiologically stable glycomimetics of biologically important glycoepitopes.

RESULTS AND DISCUSSION

To begin with, tri-*n*-butyl[2,5-dimethoxy-4-(2,3,4,6-tetra-*O*-acetyl-β-D-galacto-pyranosyl)phenyl]stannane and methyl *p*-bromobenzoate were subjected to the reported Stille coupling reactions with various combinations of palladium catalysts and additives.

After several screenings, tetrakis(triphenylphosphine)palladium, triphenylphosphine, copper(I) bromide and a small amount of 2,6-di-*t*-butyl-*p*-cresol in refluxing DMF, a procedure reported by Saá and Martorell,[2e] turned out to be the method of choice for the coupling; a *C*-galactosylated biphenyl (**1**) was obtained in 84% (Table 1, entry 1). The coupling of a number of *C*-glycosylated aryl tins with methyl *p*-bromobenzoate was examined using this procedure. The results are summarized in Table 1.

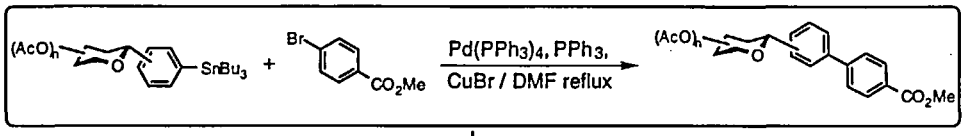
Table 1 shows that the procedure produced not only a 1,4-substituted *C*-galactosylated aryl tin but also a 1,3-substituted *C*-galactosylated aryl tin with methyl *p*-bromobenzoate and afforded the *C*-glycosylated biphenyls in yields of 84% and 72%, respectively (entries 1 and 2). Likewise, L-fucose-, D-glucose-, *N*-phthaloyl-D-glucosamine-, L-rhamnose- and D-xylose-derived *C*-glycosylated aryl tins were successfully applied to this synthetic method (entries 3-8). All the data indicated that the coupling yields were not affected by sugar moieties and substitution patterns on the *C*-glycosylated aryl tin.

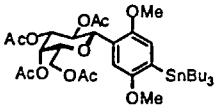
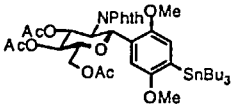
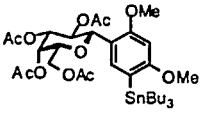
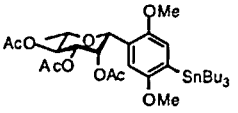
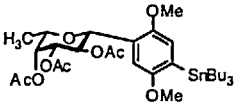
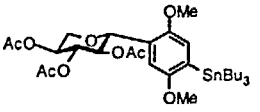
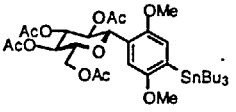
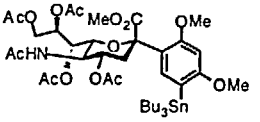
It is noteworthy that a *C*-sialylated aryl tin also reacted smoothly with methyl *p*-bromobenzoate and afforded a biphenyl *C*-sialoside (**8**) in 71% yield (entry 8). As sialylated oligosaccharides are involved in a large variety of biological events and as sialic acids are ideally positioned to participate in numerous carbohydrate-protein interactions as boundary residues,[3] a large number of sialyloligosaccharide mimetics have been reported. However, information on stable mimetics of sialyloligosaccharides such as aryl *C*-sialosides has not been published yet. To our knowledge, this is the first report of stable sialoside mimetics.

Next, we examined the effect of the position of substituents on aryl bromides. The procedure provided good yields in the cases of methyl *o*- and *m*-bromobenzoate, similar to the case of methyl *p*-bromobenzoate (Table 2, entries 1-3). Likewise, methyl 4-bromoisophthalate and methyl *o*-bromophenylacetate were coupled with the *C*-galactosylated aryl tin in 90% and in 51% yield, respectively (entries 4 and 5). Knowing that the yields were not affected by the position of substituents on the aryl bromides and on the *C*-glycosylated aryl tins, our attention was turned to investigate the effect on the coupling yields by functional groups on the aryl bromides.

The procedure allowed the *C*-galactosylated aryl tin to react with a number of aryl bromides with a cyano, nitro, aldehyde or ketone group, respectively, and afforded the *C*-

TABLE 1. The Stille Reaction of Various *C*-Glycosylated Aryl Tins with Methyl *p*-Bromobenzoate[a, b]



Entry	*C*-glycosylated aryl tin	Yield	Entry	*C*-glycosylated aryl tin	Yield
1.		1: 84%	5.		5: 74%
2.		2: 72%	6.		6: 59%
3.		3: 95%	7.		7: 72%
4.		4: 80%	8.		8: 71%

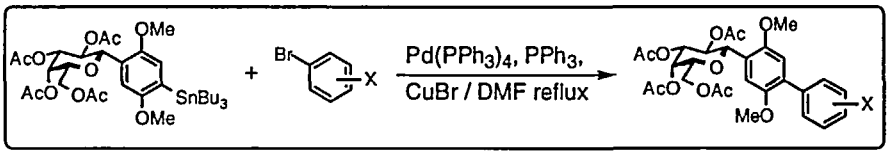
a. Only *C*-glycosylated aryl tins as starting materials are shown in Table 1 and yield indicates the coupling yield. b. These reactions were carried out in refluxing DMF by the following equivalency: *C*-glycosylated aryl tin / methyl *p*-bromobenzoate / $Pd(PPh_3)_4$ / PPh_3 / CuBr = 1 / 3 / 0.1 / 0.2 / 0.4 in the presence of a small amount of 2,6-di-*t*-butyl-*p*-cresol.

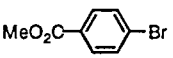
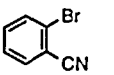
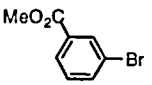
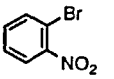
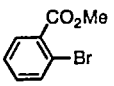
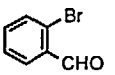
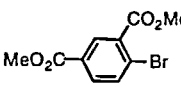
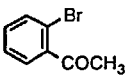
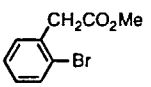
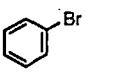
glycosylated biphenyls in good yields (entries 6-9). The functional groups on the aromatic ring will allow further transformations using general synthetic methods. Furthermore, a simple bromobenzene was used as a substrate in this reaction (entry 10).

CONCLUSION

As far as we examined, the *C*-glycosylated aryl tins afforded the *C*-glycosylated biphenyls without restrictions on the type of sugar moieties, of their position attachment to the aromatic ring, and the type of functional groups and their position on aryl bromides. Further synthetic applications using the *C*-glycosylated aryl tins and other electrophiles are going to be reported soon. The evaluation of the products, *C*-glycosylated biphenyls, as various glycoepitope mimetics such as sLe^X mimetics, will be presented elsewhere.

TABLE 2. Effect of Substituents on Aryl Bromides[a, b]



Entry	Substrate	Yield	Entry	Substrate	Yield
1.		**1**: 84%	6.		**13**: 79%
2.		**9**: 70%	7.		**14**: 85%
3.		**10**: 77%	8.		**15**: 85%
4.		**11**: 90%	9.		**16**: 75%
5.		**12**: 51%	10.		**17**: 55%

a. Only aryl bromides as starting materials are shown in Table 2 and yield indicates the coupling yield. b. These reactions were carried out in refluxing DMF by the following equivalency: *C*-galactosylated aryl tin / aryl bromide / $Pd(PPh_3)_4$ / PPh_3 / CuBr = 1 / 3 / 0.1 / 0.2 / 0.4 in the presence of a small amount of 2,6-di-*t*-butyl-*p*-cresol.

EXPERIMENTAL

General methods. Analytical TLC was done on E. Merck precoated (0.25 mm) silica gel 60 F254 plates. Column chromatography was conducted using silica gel 60 (E. Merck 9385, 230-400 mesh). Melting points were measured with a Yanaco MP-500D and were uncorrected. Infrared (IR) spectra were recorded on a JASCO FT-IR-8900 spectrometer. ^{1}H NMR spectra were measured on a JEOL-JNM-EX-270 (270 MHz) or a JEOL JNM-GX-270 (270 MHz) spectrometer. Chemical shifts from ^{1}H NMR spectra are reported relative to tetramethylsilane (δ 0). Splitting patterns are indicated as s, singlet; d,

doublet; t, triplet; q, quartet; m, multiplet; br, broad. Mass spectra were recorded with a JEOL HX-100, a SX-102A or a JMS-AX-505H mass spectrometer. Optical rotation was measured on a Perkins-Elmer 241 polarimeter. All experiments were carried out under a nitrogen atmosphere. In experiments requiring dry solvents, dry DMF was purchased from Kanto Chemica.

Methyl 4-[2,5-Dimethoxy-4-(2,3,4,6-tetra-*O*-acetyl-β-D-galacto-pyranosyl)phenyl]benzoate (1). A suspended solution of tri-*n*-butyl[2,5-dimethoxy-4-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)phenyl]stannane (149.1 mg, 0.197 mmol), methyl 4-bromobenzoate (128.5 mg, 0.598 mmol), tetrakis(triphenylphosphine)palladium (0) (22.2 mg, 0.0192 mmol), triphenylphosphine (15.0 mg, 0.0572 mmol), copper (I) bromide (12.5 mg, 0.0873 mmol) and a catalytic amount of 2,6-di-*t*-butyl-*p*-cresol in DMF was refluxed for 4 h under a nitrogen atmosphere. The resulting mixture was diluted with ethyl acetate, washed with a saturated aqueous KF solution, a saturated aqueous $NaHCO_3$ solution, and brine, dried over $MgSO_4$, and concentrated under reduced pressure. A purification of the resulting residue by column chromatography with ethyl acetae/hexane (1:3) provided the compound (99.2 mg, 0.165 mmol) in 84% yield: mp <30 °C; TLC R_f 0.36 (hexane/EtOAc 3:2); ^{1}H NMR (270 MHz, $CDCl_3$) δ 8.07 (d, 2H, J = 8.4 Hz, Ar), 8.37 (d, 2H, J = 8.4 Hz, Ar), 7.09 (s, 1H, Ar), 6.86 (s, 1H, Ar), 5.57 (t, 1H, J = 10.1 Hz, H_2), 5.55 (d, 1H, J = 3.4 Hz, H_4), 5.25 (dd, 1H, J = 10.1 Hz and 3.4 Hz, H_3), 4.98 (d, 1H, J = 10.1 Hz, H_1), 4.21-4.08 (m, 3H, H_5 and H_6), 3.94 (s, 3H, OMe), 3.84 (s, 3H, OMe), 3.79 (s, 3H, OMe), 2.23 (s, 3H, OAc), 2.05 (s, 3H, OAc), 2.01 (s, 3H, OAc), 1.85 (s, 3H, OAc); IR (KBr pellet) 2956, 2935, 2872, 2854, 1753, 1724 cm^{-1}; FABHRMS *m/z* 625.1914 (625.1897 Calcd for $C_{30}H_{34}O_{13}Na$ $[M+Na]^+$); $[\alpha]_D^{23}$ -11.8° (*c* 0.770 CH_2Cl_2).

Methyl 4-[2,4-Dimethoxy-5-(2,3,4,6-tetra-*O*-acetyl-β-D-galacto-pyranosyl)phenyl]benzoate (2). 72% yield; mp 68-70 °C; TLC R_f 0.36 (hexane/EtOAc 1:1); ^{1}H NMR (270 MHz, $CDCl_3$) δ 8.06 (d, 2H, J = 8.4 Hz, Ar), 7.58 (d, 2H, J = 8.4 Hz, Ar), 7.41 (s, 1H, Ar), 6.50 (s, 1H, Ar), 5.57 (t, 1H, J = 10.0 Hz, H_2), 5.51 (d, 1H, J = 3.3 Hz, H_4), 5.21 (dd, 1H, J = 10.0 Hz and 3.3 Hz, H_3), 4.88 (d, 1H, J = 10.1 Hz, H_1), 4.19-4.03 (m, 3H, H_5 and H_6), 3.93 (s, 3H, OMe), 3.92 (s, 3H, OMe), 3.83 (s, 3H, OMe), 2.18 (s, 3H, OAc), 2.03 (s, 3H, OAc), 1.99 (s, 3H, OAc), 1.82 (s, 3H, OAc); IR (KBr pellet) 3465, 2954, 2845, 1752, 1723, 1610, 1370 cm^{-1}; FABHRMS *m/z* 602.1973 (602.1999 Calcd for $C_{30}H_{34}O_{13}$ $[M]^+$); $[\alpha]_D^{23}$ -42° (*c* 0.47 CH_2Cl_2).

Methyl 4-[2,5-Dimethoxy-4-(2,3,4-tri-*O*-acetyl-β-L-fucopyranosyl)-phenyl]benzoate (3). 95% yield; TLC R_f 0.63 (hexane/EtOAc 1:1); ^{1}H NMR (270 MHz, $CDCl_3$) δ 8.07 (d, 2H, J = 8.4 Hz, Ar), 7.59 (d, 2H, J = 8.4 Hz, Ar), 7.11 (s, 1H, Ar),

6.85 (s, 1H, Ar), 5.57 (t, 1H, J = 10.0 Hz, H_2), 5.39 (d, 1H, J = 4.1 Hz, H_4), 5.25 (dd, 1H, J = 10.0 Hz and 4.1 Hz, H_3), 4.96 (d, 1H, J = 10.0 Hz, H_1), 4.00 (q, 1H, J = 6.3 Hz, H_5), 3.94 (s, 3H, OMe), 3.84 (s, 3H, OMe), 3.79 (s, 3H, OMe), 2.26 (s, 3H, OAc), 2.01 (s, 3H, OAc), 1.84 (s, 3H, OAc), 1.24 (d, 3H, J = 6.3 Hz, H_6); IR (KBr pellet) 3438, 2985, 2955, 2852, 1751, 1724 cm^{-1}; FABHRMS *m/z* 544.1968 (544.1945 Calcd for $C_{28}H_{32}O_{11}$ $[M]^+$); $[\alpha]_D^{23}$ +22° (*c* 0.36 CH_2Cl_2).

Methyl 4-[2,5-Dimethoxy-4-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)phenyl]benzoate (4). 80% yield; mp 58-60 °C; TLC R_f 0.29 (hexane/EtOAc 3:2); ^1H NMR (270 MHz, $CDCl_3$) δ 8.07 (d, 2H, J = 8.4 Hz, Ar), 7.58 (d, 2H, J = 8.4 Hz, Ar), 7.02 (s, 1H, Ar), 6.85 (s, 1H, Ar), 5.42-5.23 (m, 3H, H_3, H_4 and H_2), 5.01 (d, 1H, J = 9.8 Hz, H_1), 4.29 (dd, 1H, J = 12.4 Hz and 4.7 Hz, H_6), 4.17 (dd, 1H, J = 12.4 Hz and 2.2 Hz, H_6), 3.94 (s, 3H, OMe), 3.92-3.86 (m, 1H, H_5), 3.84 (s, 3H, OMe), 3.78 (s, 3H, OMe), 2.08 (s, 3H, OAc), 2.07 (s, 3H, OAc), 2.03 (s, 3H, OAc), 1.83 (s, 3H, OAc); IR (KBr pellet) 2998, 2954, 2847, 1754, 1723 cm^{-1}; FABHRMS *m/z* 602.2007 (602.1999 Calcd for $C_{30}H_{34}O_{13}$ $[M]^+$); $[\alpha]_D^{23}$ -30° (*c* 0.31 CH_2Cl_2).

Methyl 4-[2,5-Dimethoxy-4-(3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)phenyl]benzoate (5). 74% yield; TLC R_f 0.14 (hexane/EtOAc 3:2); ^1H NMR (270 MHz, $CDCl_3$) δ 8.02 (d, 2H, J = 8.4 Hz, Ar), 7.86 (d, 1H, J = 6.4 Hz, Ar), 7.83-7.63 (m, 3H, Ar), 7.50 (d, 2H, J = 8.4 Hz, Ar), 7.12 (s, 1H, Ar), 6.60 (s, 1H, Ar), 6.16 (t, 1H, J = 10.3 Hz, H_2), 5.74 (d, 1H, J = 10.3 Hz, H_1), 5.33 (t, 1H, J = 10.3 Hz, H_4), 4.68 (t, 1H, J = 10.3 Hz, H_3), 4.36 (dd, 1H, J = 12.4 Hz and 4.7 Hz, H_6), 4.23 (dd, 1H, J = 12.4 Hz and 2.0 Hz, H_6), 4.10-4.02 (m, 1H, H_5), 3.92 (s, 3H, OMe), 3.80 (s, 3H, OMe), 3.46 (s, 3H, OMe), 2.11 (s, 3H, OAc), 2.08 (s, 3H, OAc), 1.88 (s, 3H, OAc); IR (KBr pellet) 3470, 2997, 2954, 2847, 1752, 1721 cm^{-1}; FABHRMS *m/z* 689.2104 (689.2108 Calcd for $C_{36}H_{35}O_{13}N$ $[M]^+$); $[\alpha]_D^{23}$ -112° (*c* 0.49 CH_2Cl_2).

Methyl 4-[2,5-Dimethoxy-4-(2,3,4-tri-*O*-acetyl-β-L-rhamnopyranosyl)phenyl]benzoate (6). 59% yield; mp 167-168 °C; TLC R_f 0.49 (hexane/EtOAc 3:2); ^1H NMR (270 MHz, $CDCl_3$) δ 8.07 (d, 2H, J = 8.4 Hz, Ar), 7.59 (d, 2H, J = 8.4 Hz, Ar), 7.15 (s, 1H, Ar), 6.78 (s, 1H, Ar), 5.61 (d, 1H, J = 3.2 Hz, H_2), 5.29 (dd, 1H, J = 9.5 Hz and 3.2 Hz, H_4), 5.18 (t, 1H, J = 9.5 Hz, H_3), 5.07 (s, 1H, H_1), 3.93 (s, 3H, OMe), 3.82 (s, 3H, OMe), 3.77 (s, 3H, OMe), 3.74-3.69 (m, 1H, H_5), 2.09 (s, 3H, OAc), 2.00 (s, 3H, OAc), 1.95 (s, 3H, OAc), 1.36 (d, 3H, J = 6.1 Hz, H_6); IR (KBr pellet) 3473, 2987, 2943, 2847, 1749, 1721 cm^{-1}; FABHRMS *m/z* 545.2010 (545.2023 Calcd for $C_{28}H_{33}O_{11}$ $[M+H]^+$); $[\alpha]_D^{23}$ +38° (*c* 0.21 CH_2Cl_2).

Methyl 4-[2,5-Dimethoxy-4-(2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl)-phenyl]benzoate (7). 72% yield; TLC R_f 0.45 (hexane/EtOAc 3:2); ^1H NMR (270 MHz,

$CDCl_3$) δ 8.07 (d, 2H, *J* = 8.4 Hz, Ar), 7.59 (d, 2H, *J* = 8.4 Hz, Ar), 7.02 (s, 1H, Ar), 6.84 (s, 1H, Ar), 5.39 (t, 1H, *J* = 9.2 Hz, H_2), 5.33 (t, 1H, *J* = 9.2 Hz, H_3), 5.23-5.14 (m, 1H, H_4), 4.90 (d, 1H, *J* = 9.2 Hz, H_1), 4.24 (dd, 1H, *J* = 11.2 Hz and 5.6 Hz, H_5), 3.93 (s, 3H, OMe), 3.84 (s, 3H, OMe), 3.78 (s, 3H, OMe), 3.50 (t, 1H, *J* = 11.2 Hz, H_5), 2.07 (s, 3H, OAc), 2.05 (s, 3H, OAc), 1.83 (s, 3H, OAc); IR (KBr pellet) 2998, 2952, 2848, 1756, 1722, 1610 cm^{-1}; FABHRMS *m/z* 530.1794 (530.1788 Calcd for $C_{27}H_{30}O_{11}$ $[M]^+$); $[\alpha]_D^{23}$ -52° (*c* 0.30 CH_2Cl_2).

Methyl 4-[2,4-Dimethoxy-5-(methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-α-D-glycero-D-galacto-2-neuropyranosinate)phenyl]-benzoate (8). 71% yield; mp 110-115 °C; TLC R_f 0.11 (hexane/EtOAc 1:2); ^1H NMR (270 MHz, $CDCl_3$) δ 8.03 (d, 2H, *J* = 8.5 Hz, Ar), 7.64 (d, 2H, *J* = 8.5 Hz, Ar), 7.60 (s, 1H, Ar), 6.70 (s, 1H, Ar), 5.49 (dt, 1H, *J* = 10.0 Hz and 5.1 Hz, H_4), 5.36 (dd, 1H, *J* = 6.9 Hz and 1.8 Hz, H_7), 5.31 (dt, 1H, *J* = 6.7 Hz and 2.8 Hz, H_8), 4.44 (dd, 1H, *J* = 12.2 Hz and 2.8 Hz, H_6), 4.12 (dd, 1H, *J* = 12.2 Hz and 6.9 Hz, H_9), 4.03-3.71 (m, 2H, H_5 and H_9), 3.92 (s, 3H, OMe), 3.85 (s, 3H, OMe), 3.84 (s, 3H, OMe), 3.07 (dd, 1H, *J* = 13. Hz and 5.1 Hz, H_3), 2.06 (s, 3H, NAc), 1.99 (s, 3H, OAc), 1.99 (s, 3H, OAc), 1.97 (s, 3H, OAc), 1.97 (s, 3H, OAc), 1.96 (s, 3H, OAc), 1.85 (s, 3H, OAc), 1.66 (dd, 1H, *J* = 13.3 Hz and 10.0 Hz, H_3); IR (KBr pellet) 3372, 3065, 2998, 2953, 2842, 1756 cm^{-1}; FABHRMS *m/z* 746.2658 (746.2660 Calcd for $C_{36}H_{44}O_{16}N$ $[M+H]^+$); $[\alpha]_D^{23}$ +7.0° (*c* 0.29 CH_3OH).

Methyl 3-[2,5-Dimethoxy-4-(2,3,4,6-tetra-*O*-acetyl-β-D-galacto-pyranosyl)phenyl]benzoate (9). 70% yield; mp 144-146 °C; TLC R_f 0.25 (hexane/EtOAc 1:1); ^1H NMR (270 MHz, $CDCl_3$) δ 8.17 (s, 1H, Ar), 8.01 (d, 1H, *J* = 7.9 Hz, Ar), 7.73 (d, 1H, *J* = 7.9 Hz, Ar), 7.48 (t, 1H, *J* = 7.9 Hz, Ar), 7.08 (s, 1H, Ar), 6.86 (s, 1H, Ar), 5.58 (t, 1H, *J* = 10.0 Hz, H_2), 5.55 (d, 1H, *J* = 3.4 Hz, H_4), 5.25 (dd, 1H, *J* = 10.0 Hz and 3.4Hz, H_3), 4.98 (d, 1H, *J* = 10.0 Hz, H_1), 4.25-4.09 (m, 3H, H_5 and H_6), 3.94 (s, 3H, OMe), 3.85 (s, 3H, OMe), 3.79 (s, 3H, OMe), 2.23 (s, 3H, OAc), 2.05 (s, 3H, OAc), 2.01 (s, 3H, OAc), 1.85 (s, 3H, OAc); IR (KBr pellet) 3438, 2997, 2955, 2852, 1752, 1726 cm^{-1}; FABHRMS *m/z* 625.1884 (625.1898 Calcd for $C_{30}H_{34}O_{13}Na$ $[M+Na]^+$); $[\alpha]_D^{23}$ -9.87° (*c* 1.03 CH_2Cl_2).

Methyl 2-[2,5-Dimethoxy-4-(2,3,4,6-tetra-*O*-acetyl-β-D-galacto-pyranosyl)phenyl]benzoate (10). 77% yield; TLC R_f 0.50 (hexane/EtOAc 1:1); ^1H NMR (270 MHz, $CDCl_3$) δ 7.87 (dd, 1H, *J* = 7.8 Hz and 1.2 Hz, Ar), 7.56 (dt, 1H, *J* = 7.8 Hz and 1.2Hz, Ar), 7.41 (dt, 1H, *J* = 7.8 Hz and 1.2Hz, Ar), 7.31 (dd, 1H, *J* = 7.8 Hz and 1.2Hz, Ar), 6.98 (s, 1H, Ar), 6.81 (s, 1H, Ar), 5.55 (d, 1H, *J* = 3.4 Hz, H_4), 5.54 (t, 1H, *J* = 9.9 Hz, H_2), 5.25 (dd, 1H, *J* = 9.9 Hz and 3.4Hz, H_3), 4.98 (d, 1H, *J* = 9.9 Hz, H_1), 4.25-4.08 (m, 3H, H_5 and H_6), 3.83 (s, 3H, OMe), 3.69 (s, 3H, OMe),

3.64 (s, 3H, OMe), 2.22 (s, 3H, OAc), 2.05 (s, 3H, OAc), 2.00 (s, 3H, OAc), 1.84 (s, 3H, OAc); IR (KBr pellet) 3469, 2996, 2952, 2854, 1752 cm^{-1}; FABHRMS *m/z* 602.2006 (602.1999 Calcd for $C_{30}H_{34}O_{13}$ $[M]^+$); $[\alpha]_D^{23}$ -6.0° (*c* 0.40 CH_2Cl_2).

Dimetyl 4-[2,5-Dimethoxy-4-(2,3,4,6-tetra-*O*-acetyl-β-D-galacto-pyranosyl)phenyl]isophthalate (11). 90% yield; TLC R_f 0.19 (hexane/EtOAc 1:1); ^1H NMR (270 MHz, $CDCl_3$) δ 8.52 (d, 1H, *J* = 1.6 Hz, Ar), 8.19 (dd, 1H, *J* = 8.1 Hz and 1.6 Hz, Ar), 7.40 (d, 1H, *J* = 8.1 Hz, Ar), 6.99 (s, 1H, Ar), 6.81 (s, 1H, Ar), 5.55 (d, 1H, *J* = 3.6 Hz, H_4), 5.53 (t, 1H, *J* = 9.9 Hz, H_2), 5.25 (dd, 1H, *J* = 9.9 Hz and 3.6 Hz, H_3), 4.98 (d, 1H, *J* = 9.9 Hz, H_1), 4.25-4.08 (m, 3H, H_5 and H_6), 3.96 (s, 3H, OMe), 3.84 (s, 3H, OMe), 3.70 (s, 3H, OMe), 3.68 (s, 3H, OMe), 2.22 (s, 3H, OAc), 2.05 (s, 3H, OAc), 2.00 (s, 3H, OAc), 1.84 (s, 3H, OAc); IR (KBr pellet) 3434, 2998, 2954, 2855, 1752, 1729 cm^{-1}; FABHRMS *m/z* 683.1927 (683.1951 Calcd for $C_{32}H_{36}O_{15}Na$ $[M+Na]^+$); $[\alpha]_D^{23}$ -11° (*c* 0.38 CH_2Cl_2).

Methyl 2-[2',5'-Dimethoxy-4'-(2,3,4,6-tetra-*O*-acetyl-β-D-galacto-pyranosyl)biphenyl]acetate (12). 51% yield; TLC R_f 0.20 (hexane/EtOAc 3:2); ^1H NMR (270 MHz, $CDCl_3$) δ 7.43-7.07 (m, 4H, Ar), 7.03 (s, 1H, Ar), 6.73 (s, 1H, Ar), 5.56 (t, 1H, *J* = 9.9 Hz, H_2), 5.54 (d, 1H, *J* = 3.4 Hz, H_4), 5.25 (dd, 1H, *J* = 9.9 Hz and 3.4 Hz, H_3), 4.96 (d, 1H, *J* = 9.9 Hz, H_1), 4.23-4.08 (m, 3H, H_5 and H_6), 3.78 (s, 3H, OMe), 3.68 (s, 3H, OMe), 3.58 (s, 3H, OMe), 3.47 (s, 2H, CH_2), 2.20 (s, 3H, OAc), 2.04 (s, 3H, OAc), 1.99 (s, 3H, OAc), 1.82 (s, 3H, OAc). IR (KBr pellet) 3422, 2953, 2854, 1751 cm^{-1}; FABHRMS *m/z* 639.2044 (639.2054 Calcd for $C_{31}H_{36}O_{13}Na$ $[M+Na]^+$); $[\alpha]_D^{23}$ -4.4° (*c* 0.48 CH_2Cl_2).

2-[2,5-Dimethoxy-4-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-phenyl]benzonitrile (13). 78% yield; mp 86-87 °C; TLC R_f 0.70 (hexane/EtOAc 2:3); ^1H NMR (270 MHz, $CDCl_3$) δ 7.73 (d, 1H, *J* = 7.7 Hz, Ar), 7.62 (t, 1H, *J* = 7.7 Hz, Ar), 7.49 (d, 1H, *J* = 7.7 Hz, Ar), 7.43 (t, 1H, *J* = 7.7 Hz, Ar), 7.11 (s, 1H, Ar), 6.84 (s, 1H, Ar), 5.59 (t, 1H, *J* = 10.0 Hz, H_2), 5.55 (d, 1H, *J* = 3.6 Hz, H_4), 5.25 (dd, 1H, *J* = 10.0 Hz and 3.6 Hz, H_3), 4.98 (d, 1H, *J* = 10.0 Hz, H_1), 4.26-4.08 (m, 3H, H_5 and H_6), 3.84 (s, 3H, OMe), 3.81 (s, 3H, OMe), 2.23 (s, 3H, OMe), 2.06 (s, 3H, OAc), 2.01 (s, 3H, OAc), 1.85 (s, 3H, OAc); IR (KBr pellet) 2960, 2940, 2228, 1752 cm^{-1}; FABHRMS *m/z* 570.1987 (570.1975 Calcd for $C_{29}H_{32}O_{11}N$ $[M+H]^+$); $[\alpha]_D^{23}$ -12° (*c* 0.58 CH_2Cl_2).

2,5-Dimethoxy-2'-nitro-4-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyrano-syl)biphenyl (14). 85% yield; mp 73-75 °C; TLC R_f 0.36 (hexane/EtOAc 1:1); ^1H NMR (270 MHz, $CDCl_3$) δ 7.94 (dd, 1H, *J* = 7.8 Hz and 1.2 Hz, Ar), 7.64 (dt, 1H, *J* = 7.8 Hz and 1.2 Hz, Ar), 7.48 (dd, 1H, *J* = 7.8 Hz and 1.2 Hz, Ar), 7.39 (dt, 1H, *J* = 7.8 Hz and 1.2 Hz, Ar), 6.98 (s, 1H, Ar), 6.84 (s, 1H, Ar), 5.60 (t, 1H, *J* = 10.0 Hz, H_2), 5.54 (d, 1H, *J* = 3.4 Hz, H_4), 5.24 (dd, 1H, *J* = 10.0 Hz and 3.4 Hz, H_3), 4.95 (d, 1H, *J*

= 10.0 Hz, H_1), 4.25-4.08 (m, 3H, H_5 and H_6), 3.85 (s, 3H, OMe), 3.68 (s, 3H, OMe), 2.22 (s, 3H, OAc), 2.06 (s, 3H, OAc), 2.00 (s, 3H, OAc), 1.85 (s, 3H, OAc); IR (KBr pellet) 2960, 2940, 2857, 1752, 1531 cm^{-1}; FABHRMS *m/z* 590.1853 (590.1874 Calcd for $C_{28}H_{32}O_{13}N$ $[M+H]^+$); $[\alpha]_D^{23}$ -43° (*c* 0.56 CH_2Cl_2).

2-[2,5-Dimethoxy-4-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-phenyl]benzaldehyde (15). 85% yield; mp 70-73 °C; TLC R_f 0.67 (hexane/EtOAc 1:1); ^1H NMR (270 MHz, $CDCl_3$) δ 9.75 (s, 1H, CHO), 8.00 (dd, 1H, *J* = 7.9 Hz and 1.2 Hz, Ar), 7.65 (dt, 1H, *J* = 7.9 Hz and 1.2 Hz, Ar), 7.49 (t, 1H, *J* = 7.9 Hz, Ar), 7.35 (d, 1H, *J* = 7.9 Hz, Ar), 7.07 (s, 1H, Ar), 6.82 (s, 1H, Ar), 5.57 (t, 1H, *J* = 9.9 Hz, H_2), 5.55 (d, 1H, *J* = 3.4 Hz, H_4), 5.26 (dd, 1H, *J* = 9.9 Hz and 3.4 Hz, H_3), 4.99 (d, 1H, *J* = 9.9 Hz, H_1), 4.23-4.08 (m, 3H, H_5 and H_6), 3.83 (s, 3H, OMe), 3.72 (s, 3H, OMe), 2.23 (s, 3H, OAc), 2.17 (s, 3H, OAc), 2.05 (s, 3H, OAc), 2.01 (s, 3H, OAc); IR (KBr pellet) 2998, 2940, 2854, 1752, 1698, 1510 cm^{-1}; FABHRMS *m/z* 572.1899 (572.1893 Calcd for $C_{29}H_{32}O_{12}$ $[M]^+$); $[\alpha]_D^{23}$ -12° (*c* 0.65 CH_2Cl_2).

2-[2,5-Dimethoxy-4-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-phenyl]acetophenone (16). 75% yield; TLC R_f 0.47 (hexane/EtOAc 1:1); ^1H NMR (270 MHz, $CDCl_3$) δ 7.61 (dd, 1H, *J* = 6.7 Hz and 1.2 Hz, Ar), 7.52 (dt, 1H, *J* = 6.7 Hz and 1.2 Hz, Ar), 7.41 (dt, 1H, *J* = 6.7 Hz and 1.2 Hz, Ar), 7.32 (dd, 1H, *J* = 6.7 Hz and 1.2 Hz, Ar), 7.01 (s, 1H, Ar), 6.79 (s, 1H, Ar), 5.55 (d, 1H, *J* = 3.4 Hz, H_4), 5.54 (t, 1H, *J* = 10.0 Hz, H_2), 5.25 (dd, 1H, *J* = 10.0 Hz and 3.4 Hz, H_3), 4.97 (d, 1H, *J* = 10.0 Hz, H_1), 4.25-4.08 (m, 3H, H_5 and H_6), 3.82 (s, 3H, OMe), 3.72 (s, 3H, OMe), 2.22 (s, 3H, OAc), 2.14 (s, 3H, OAc), 2.05 (s, 3H, OAc), 2.00 (s, 3H, OAc), 1.82 (s, 3H, OAc); IR (KBr pellet) 3469, 3060, 2957, 2938, 2855, 1752, 1693 cm^{-1}; FABHRMS *m/z* 586.2052 (586.2050 Calcd for $C_{30}H_{34}O_{12}$ $[M]^+$); $[\alpha]_D^{23}$ -15° (*c* 0.64 CH_2Cl_2).

2,5-Dimethoxy-4-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-biphenyl (17). 55% yield; mp 65-67 °C; TLC R_f 0.77 (hexane/EtOAc 3:2); ^1H NMR (270 MHz, $CDCl_3$) δ 7.54-7.30 (m, 5H, Ar), 7.07 (s, 1H, Ar), 6.86 (s, 1H, Ar), 5.58 (t, 1H, *J* = 10.1 Hz, H_2), 5.54 (d, 1H, *J* = 3.0 Hz, H_4), 5.24 (dd, 1H, *J* = 10.1 Hz and 3.0 Hz, H_3), 4.98 (d, 1H, *J* = 10.1 Hz, H_1), 4.21-4.08 (m, 3H, H_5 and H_6), 3.83 (s, 3H, OMe), 3.78 (s, 3H, OMe), 2.23 (s, 3H, OAc), 2.04 (s, 3H, OAc), 2.01 (s, 3H, OAc), 1.84 (s, 3H, OAc); IR (KBr pellet) 2996, 2957, 2853, 1752, 1513 cm^{-1}; FABHRMS *m/z* 544.1939 (544.1945 Calcd for $C_{28}H_{32}O_{11}$ $[M]^+$); $[\alpha]_D^{23}$ -11° (*c* 0.55 CH_2Cl_2).

REFERENCES AND NOTES

1. T. Kuribayashi, Y. Mizuno, S. Gohya and S. Satoh, *J. Carbohydr. Chem.*, preceding paper in this issue.
2. (a) J. Tsuji, *Palladium Reagents and Catalysts: Innovations in Organic Synthesis*; Wiley: New York, 1995, p 228; (b) J. K. Stille, *Angew. Chem. Int. Ed. Engl.*, **25**,

508 (1986); (c) T. N. Mitchell, *Synthesis*, 803 (1992); (d) V. Farina, V. Krishnamurthy and W. J. Scott, in *Organic Reactions*; L. A. Paquette, Ed.; Wiley: New York, 1997, p 1; (e) J. M. Saá and G. Martorell, *J. Org. Chem.*, **58**, 1963 (1993); (f) K. Kato, H. Hayakawa, H. Tanaka, H. Kumamoto and T. Miyasaka, *Tetrahedron Lett.*, **36**, 6507 (1995).

3. R. Roy in *Carbohydrates in Drug Design*; Z. J. Witczak and K. A. Nieforth, Eds.; Marcel Dekker : New York, 1997, p 83.