Supporting Information

Regiospecific Glycosidation of Unprotected Sugars
via Arylboronic Activation

Kenji Oshima and Yasuhiro Aoyama

Department of BioEngineering, Nagaoka University of Technology,
Kamitomioka, Nagaoka, Niigata 940-2188, Japan and Institute for
Fundamental Research of Organic Chemistry, Kyushu University,
Hakozaki, Higashi-ku, Fukuoka 812-8581, Japan

Preparation and Characterization of Compound 3

Compound **3** was obtained in 49% yield as colorless crystals by the metalation of 2-(2-hydroxy-2-propyl)-1-bromobenzene (1 equiv) with BuLi (2 equiv) in ether-hexane followed by the reaction of the resulting dilithium species with $B(OCH_3)_3$ (2 equiv) in ether at -70 °C for 20 h and subsequent hydrolysis with dilute H_2SO_4: mp 182-184 °C; ^1H NMR ($CDCl_3$) 7.21-7.12 (6 H, m, Ar), 6.99 (2 H, d, Ar), 1.49 (12 H, s, CH_3); ^{13}C NMR (THF-d_8) 153.8, 130.4, 127.7, 127.2, 120.5, 84.3, 31.2; ^{11}B NMR ($CDCl_3$) -4.0. Anal. Calcd for $C_{18}H_{21}BO_2$: C, 77.17; H, 7.55. Found: C, 76.98; H, 7.55. Compound **3** in THF-d_8 showed a highly downfield shifted OH-proton resonance at $\delta_H = 11.7$. This, coupled with the significantly upfield shifted ^{11}B signal, provides the basis for the formulation of borinate **3** as a zwitterionic species. Treatment of **3** in THF with an equimolar amount of Ag_2CO_3 gave an intermediate **2c'** having two types of phenyl moieties and methyl groups. An acidic workup of the mixture afforded a 1:1 mixture of 2-phenyl-2-propanol and boronate **2c** in 70% yield as colorless crystals: mp ~78 °C; ^1H NMR ($CDCl_3$) 7.73 (1 H, d, Ar), 7.47 (1 H, t, Ar), 7.35 (1 H, t, Ar), 7.26 (1 H, d, Ar), 1.59 (6 H, s, CH3); ^{13}C NMR (THF-d_8) 163.4, 131.2, 131.1, 127.5, 121.1, 83.5, 29.7. Anal. Calcd for $C_9H_{11}BO_2$: C, 66.73; H, 6.84. Found: C, 67.06; H, 6.88.

Typical Glycosidation Procedure for Entry 2 of Table 1

A mixture of promoter **3** (0.46 mmol), acceptor **4a** (0.42 mmol), donor **5** (1.48 mmol), and MS 4A (1.5 g) in dry THF (20 mL) was refluxed for 1 h. $Et_4N^+I^-$ (0.48 mmol) was added at 0 °C and the mixture was stirred at room temperature for 30 min. Then, Ag_2CO_3 (0.87 mmol) was added at 0 °C to initiate the reaction. The mixture was stirred at room temperature for 48 h and at 50 °C for 20 h, diluted with dichloromethane, and filtered to remove insoluble salts.

Dichloromethane was evaporated and the residue was chromatographed on silica gel with acetone-dichloromethane (3/7) as eluent. Elution of donor **5** used in excess and 2-phenyl-2-propanol derived from promotor **3** was followed by that of product disaccharide **4b** (199 mg, 93 %). In every case, more than 80 % of excess amount of donor **5** was recovered. Glycosidation of other acceptors was carried out in essentially the same manner. The progress of the reactions was readily monitored by TLC. The TLC R_f values and the solvent systems used for both TLC and column chromatography are shown in Chart 2 in this Supporting Information.

Chart 2. Structures of Disaccharide and Trisaccharide Products and Their Peracetyl Derivatives. TLC R_f values on silica with eluent of acetone/dichloromethane = 3/7 (A), 1/1 (B), or 9/1 (C) are shown in parentheses.
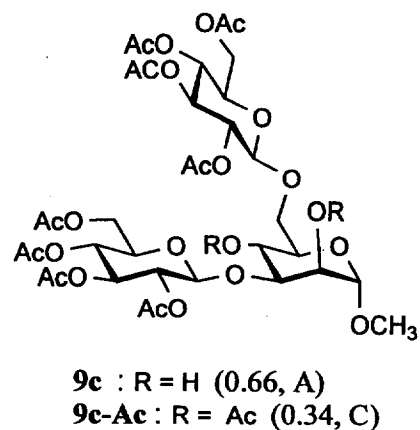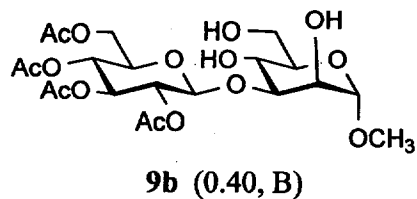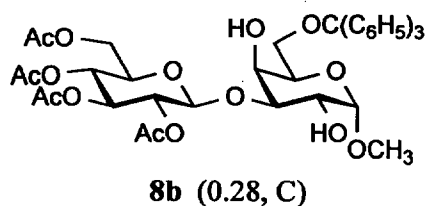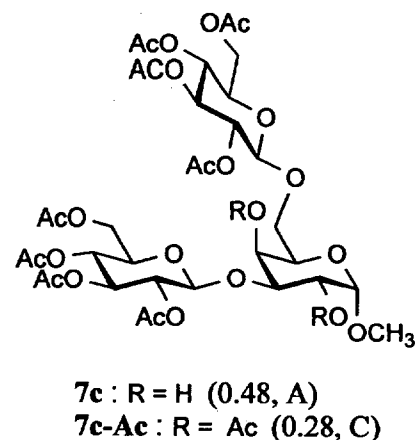

4b (0.43, A)

6b (0.39, B)

7b : R = H (0.17, B)
7b-Ac : R = Ac (0.53, C)

7c : R = H (0.48, A)
7c-Ac : R = Ac (0.28, C)

8b (0.28, C)

9b (0.40, B)

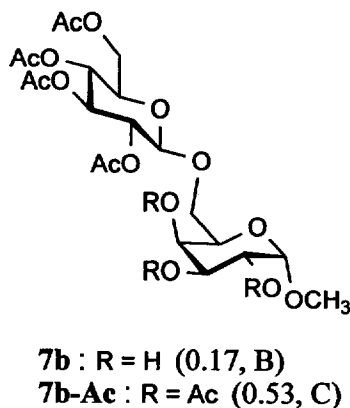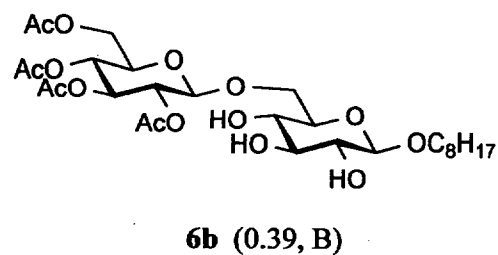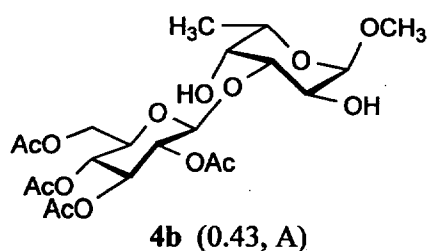**9c** : R = H (0.66, A)
9c-Ac : R = Ac (0.34, C)

Table 2. ^{1}H NMR Chemical Shifts for Disaccharide and Trisaccharide Products and Their Peracetyl Derivatives [a, b]

compound	solvent	H-1 ($J_{1,2}$) [c]	H-2	H-3	H-4	H-5	H-6	OCH$_3$
4b	CDCl$_3$	4.77 (3.9)	3.94	3.79	3.67	3.87	1.25	3.37
		4.65 (7.7)	4.99	5.18	5.03	3.72	4.19, 4.13	
6b	CDCl$_3$	4.23 (7.3)	3.33	3.50	3.43	3.43	4.09, 3.78	3.86, 3.50 [d]
		4.64 (7.8)	5.00	5.19	5.07	3.70	4.25, 4.16	
7b-Ac	CDCl$_3$	4.91 (3.4)	5.07	5.27	5.36	4.12	3.74, 3.60	3.34
		4.50 (7.8)	4.91	5.13	5.01	3.66	4.21, 4.08	
7c-Ac	CDCl$_3$	4.85 (3.9)	5.10	4.15	5.34	3.49	4.06, 3.87	3.34
		4.63 (7.8)	4.87	5.13	5.02	3.61	4.15-4.11	
		4.49 (7.8)	4.96	5.16	5.04	3.68	4.26, 4.08	
8b	CDCl$_3$	4.82 (3.4)	3.96	3.78	4.00	3.88	3.52-3.40, 3.27	3.49
		4.79 (8.3)	5.01	5.24	5.03	3.72	4.19, 4.09	
9b	CDCl$_3$	4.69 (1.5)	3.80	3.70	3.89	3.49	3.81	3.32
		4.60 (7.8)	4.98	5.18	5.00	3.76	4.14	
9c-Ac	C$_6$D$_6$	4.65 (1.5)	5.40	4.17	5.47	3.93	4.08, 3.59	3.11
		4.16 (7.8)	5.08	5.28	5.15	3.07	4.28, 3.84	
		4.34 (7.3)	5.35	5.41	5.24	3.22	4.24, 3.98	

[a] The disaccharide and trisaccharide products were isolated by chromatography and further converted to peracetyl derivatives when necessary. The glycosidation sites were assigned on the basis of ^{1}H-^{1}H and ^{1}H-^{13}C COSY spectra in reference to the glycosidation-induced shifts in δ_C (Usui, T.; Yamaoka, K.; Matsuda, K.; Tuzimura, K.; Sugiyama, H.; Seto, S. *J. Chem. Soc., Perkin Trans. I* 1973, 2425-2432) and the acetylation-induced shifts in δ_H (e.g. Lemieux, R. U.; Stevens, J. D. *Can. J. Chem.* 1965, *43*, 2059-2070. Casu, B.; Reggiani, M.; Gallo, G. G.; Vigevani, A. *Carbohydr. Res.* 1970, *12*, 157-170). The acetyl-proton resonances appear at $\delta_H \cong 2.1$. [b] For each saccharide, data for the glycosyl acceptor moiety are shown in the top line, followed by those for the donor (5) moiety in the lower line(s). [c] The coupling constant of $J \cong 8$ Hz for 1-H and 2-H in the donor (5) moiety of every product confirmed the β-configuration of the glycosidic linkage. [d] For OCH_2(CH$_2$)$_6$CH$_3$ in the octyl group.

Table 3. ^{13}C NMR Chemical Shifts for Disaccharide and Trisaccharide Products and Their Peracetyl Derivatives [a, b]

compound	solvent	C-1	C-2	C-3	C-4	C-5	C-6	OCH$_3$
4b	CDCl$_3$	99.33	66.96	82.23	70.75	65.13	15.86	55.20
		100.54	71.37	72.26	68.11	71.99	61.58	
6b	CDCl$_3$	102.44	73.58	76.27	70.87	74.73	69.08	70.16 [c]
		100.90	71.18	72.68	68.31	71.92	61.79	
7b-Ac	CDCl$_3$	96.97	68.11	67.51	68.61	67.40	67.98	55.26
		100.65	71.02	72.61	68.20	71.75	61.73	
7c-Ac	CDCl$_3$	96.86	70.21	72.23	70.29	69.17	68.44	55.11
		100.34	71.15	72.50	68.15	71.77	61.38	
		100.94	71.09	72.57	68.20	71.73	61.63	
8b	CDCl$_3$	99.17	67.90	80.90	68.95	69.01	63.41	55.11
		101.34	71.35	72.25	68.42	71.84	61.91	
9b	CDCl$_3$	100.41	69.58	83.58	65.41	71.68	61.80	54.76
		101.07	71.33	72.28	68.37	71.95	61.93	
9c-Ac	C$_6$D$_6$	98.58	73.25	75.88	67.01	70.30	68.73	54.70
		100.18	71.88	73.39	68.16	71.94	61.47	
		101.37	71.69	69.59	68.73	72.13	61.63	

[a] The disaccharide and trisaccharide products were isolated by chromatography and further converted to peracetyl derivatives when necessary. The glycosidation sites were assigned on the basis of ^{1}H-^{1}H and ^{1}H-^{13}C COSY spectra in reference to the glycosidation-induced shifts in δc (Usui, T.; Yamaoka, K.; Matsuda, K.; Tuzimura, K.; Sugiyama, H.; Seto, S. *J. Chem. Soc., Perkin Trans. I* 1973, 2425-2432) and the acetylation-induced shifts in δH (e.g. Lemieux, R. U.; Stevens, J. D. *Can. J. Chem.* 1965, *43*, 2059-2070. Casu, B.; Reggiani, M.; Gallo, G. G.; Vigevani, A. *Carbohydr. Res.* 1970, *12*, 157-170). The acetyl-carbon resonances appear at δc = 20-21 and 169-171. [b] For each saccharide, data for the glycosyl acceptor moiety are shown in the top line, followed by those for the donor (5) moiety in the lower line(s). [c] For O*C*H$_2$(CH$_2$)$_6$CH$_3$ in the octyl group.

Table 4. Elemental Analysis and HRMS Data for Disaccharide and Trisaccharide Products

compound	formula	elemental analysis				HRMS	
		calcd		found		calcd for $(M+Na)^+$	found
		C	H	C	H		
4b	$C_{21}H_{32}O_{14}$	49.61	6.34	50.42	6.50	531.1690	531.1689
6b	$C_{28}H_{46}O_{15}$	54.01	7.45	55.10	7.90	645.2734	645.2709
7b	$C_{21}H_{32}O_{15}$	48.09	6.15	48.14	6.21	547.1639	547.1627
7c	$C_{35}H_{50}O_{24}$	49.18	5.90	49.25	5.93	877.2590	877.2595
8b	$C_{40}H_{46}O_{15}$	62.66	6.05	62.87	6.21	789.2734	789.2722
9b	$C_{21}H_{32}O_{15}$	48.09	6.15	47.90	6.31	547.1639	547.1613
9c	$C_{35}H_{50}O_{24}$	49.18	5.90	49.20	6.05	877.2590	877.2592