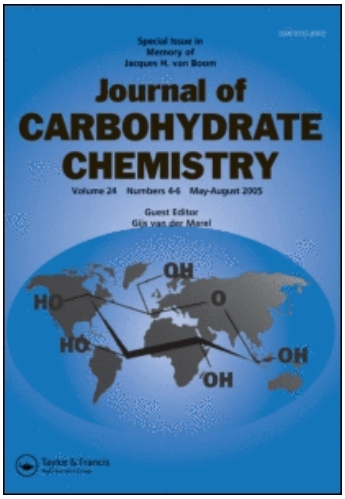

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PHASE TRANSFER CATALYZED ANOMERIC NUCLEOPHILIC SUBSTITUTIONS WITH D-XYLOPYRANOSYL HALIDES

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ABSTRACT

Anomeric pairs of per-*O*-acetylated-D-xylopyranosyl halides were individually treated with a wide variety of nucleophiles under mild PTC conditions. Thus, 2,3,4-tri-*O*-acetyl-α-D-xylopyranosyl bromide **1** provided exclusively the β-D-xylopyranosyl anomers **2-11** in good to excellent yields (65-95%). Alternatively, under the same PTC conditions, 2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl chloride **13** afforded solely the inverted α-D-anomers **15** (82%) and **16** (67%) upon treatment with thiophenol and sodium azide, respectively. Similarly, 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl chloride **19** provided the analogous products **20** (63%) and **21** (31%) upon treatment with thiophenol and sodium azide. In the presence of tetrabutylammonium chloride as PTC catalyst, β-xylopyranosyl chloride **13** was shown to slowly equilibrate to the α-chloride **14**. Therefore, care must be taken to avoid PTC catalyst for which counter anions can cause anomerization of the starting glycosyl halides.

INTRODUCTION

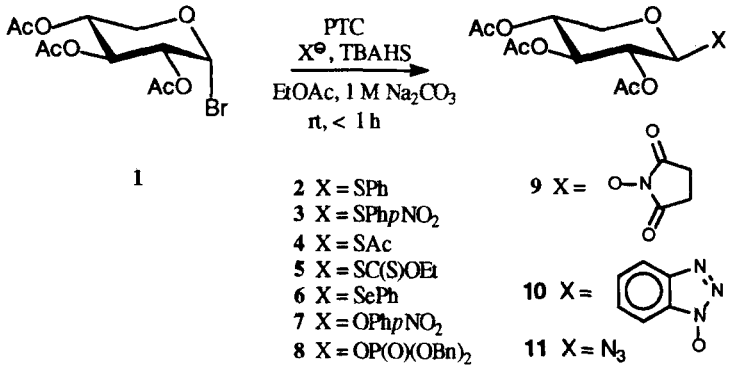
Phase transfer catalysis (PTC) has been extensively used in the field of carbohydrate chemistry.[1] Most recent applications of biphasic liquid-liquid PTC have dealt with anomeric nucleophilic substitutions of glycosyl halides using a wide variety of nucleophiles including: aryloxides,[2] alkyl- and arylthiolates,[3] thioacetates,[4] xanthates,[5] arylselenoxides,[6] azides,[7] phosphates,[8] and oxysuccinimides.[9] In most cases studied, 1,2-*cis* peracetylated glycosyl halides were used as starting materials. The resulting glycosyl derivatives usually had 1,2-*trans*-diequatorial arrangements. In a more recent study,[10] peracetylated glycopyranosyl bromides of L-fucose (1,2-*cis*, $^1C_4$), D-mannose (1,2-*trans*-diaxial, $^4C_1$), and L-rhamnose (1,2-*trans*-diaxial, $^1C_4$) were all shown to proceed with complete anomeric inversion (S_N2) using thiophenol and sodium azide as nucleophiles. Nucleophilic substitution of acetochloroneuramic acid having an axial chloride and no participating group, was also shown to occur with neat anomeric inversion under PTC conditions using a wide range of nucleophiles.[3-6] Therefore, in all cases, anomeric inversions occurred. It has been generally postulated that the anomeric inversions were due to anchimeric group participation from the neighboring 2-acyloxy group.[2f,g, 11] When non-participating benzyloxy substituents were used, the reactions gave mixtures of anomers.[12] However, in this last case, it is likely that the observed lack of stereoselectivity was due to the fact that anomeric mixtures of glycosyl halides were used as starting materials. As anticipated from these reactions, hydrolysis and elimination accounted for some of the by-products obtained.[13]

We report herein a case study of phase transfer catalyzed anomeric nucleophilic substitutions of peracetylated α-D-xylopyranosyl bromide (**1**) and α- and β-chlorides **13** and **14** having both 1,2-*cis*- or 1,2-*trans*-stereochemistry with a series of nucleophiles to further demonstrate that these anomeric substitutions occur with complete anomeric inversion. Although the reactions are likely to proceed by a direct inversion mechanism, anchimeric group participation cannot be totally ruled out. If the general trends hold, α- and β-glycosyl halides would provide β- and α-glycosyl derivatives respectively. Acyloxonium ions, if formed as intermediates, would result in orthoester-like products, while free oxonium ions would inevitably result in anomeric mixtures. As orthoesters are stable under basic conditions, it is unlikely that they would constitute transient intermediates. Under the basic PTC conditions used herein, it was hypothesized that the peracetylated β-D-xylopyranosyl chloride would provide α-xylopyranosyl derivatives exclusively.

RESULTS AND DISCUSSION

Treatment of 2,3,4-tri-*O*-acetyl-α-D-xylopyranosyl bromide (**1**)[14] with the respective nucleophiles, under improved liquid two phase PTC conditions[3a-c] (1 equiv of tetrabutylammonium hydrogen sulfate (TBAHS), EtOAc, 1 M Na_2CO_3, rt, < 1 h) afforded exclusively the inverted β-D-xylopyranosyl anomers **2-11** in good to excellent yields (65-95%) as judged from the ^{1}H NMR spectra of the crude reaction mixtures (Scheme 1, Table 1). No trace of orthoester-like products was observed. The only side reaction observed was the formation of small amount of hydrolysis product. The amount of hydrolyzed halide was dependent on the relative nucleophilicities of the incoming nucleophiles which appeared to be higher for *para*-nitrophenoxide (**7**), dibenzylphosphate (**8**), and oxysuccinimide (**9**). All anomeric configurations were clearly established from the $^3J_{1,2}$ coupling constants (4.1-8.3 Hz, Table 2) which indicated 1,2-*trans*-relationships between the nucleophiles and the 2-acyloxy groups. Interestingly, the smallest value for $^3J_{1,2}$ of 4.1 Hz was observed for compound **9**; the size of this coupling constant indicates that **9** largely exists in the $^1C_4$ chair conformation rather than the $^4C_1$ chair conformation.[15]

To unambiguously prove the stereochemical outcome of these PTC reactions, the opposite anomer, the β-halide was required. Owing to the high instability of the β-bromide, the more readily available 2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl chloride (**13**) was prepared instead. Slight modifications of published procedures (Scheme 2)[14-16] were used to prepare compound **13** and its corresponding α-anomer **14** from an anomeric mixture of 1,2,3,4-tetra-*O*-acetyl-D-xylopyranose (**12**) (α/β 1:6). However, β-anomer **13** is known to exist in its $^1C_4$ conformation in spite of severe 1,3-diaxial interactions between the four axially oriented substituents (Scheme 3),[14,16] as confirmed by the sizes of $J_{1,2}$ (3.0 Hz), $J_{4eq,5ax}$ (3.7 Hz) and $J_{4eq,5eq}$, (3.0 Hz). The structural integrity of **13** and **14** were clearly demonstrated by the differences in their ^{1}H NMR spectra which showed the anomeric proton of **13** as a doublet of doublets at 5.77 ppm ($J_{1,2}$ 3.0, $J_{1,3}$ 0.4 Hz, long range coupling) while that of the α-anomer **14** appeared as a well resolved doublet at 6.21 ppm ($J_{1,2}$ 4.0 Hz). More convincing perhaps were the coupling constants between the H-4 and H-5 protons. In **13**, the two coupling constants between H-4eq and both H-5eq/H-5ax were small ($J_{4eq,5eq}$ 3.0, $J_{4eq,5ax}$ 3.7 Hz) indicating gauche relationships in both cases. In **14**, a large $J_{4ax,5ax}$ *trans*-diaxial coupling constant (11.2 Hz) was observed, while that of $J_{4ax,5eq}$ was 6.1 Hz. Taken together these informations confirmed[14-16] the anomeric as well as the conformational identities of both β-anomer **13** ($^1C_4$) and α-anomer **14** ($^4C_1$).



Scheme 1

Table 1. Selected Physical Properties of Compounds **2-11, 15,16**

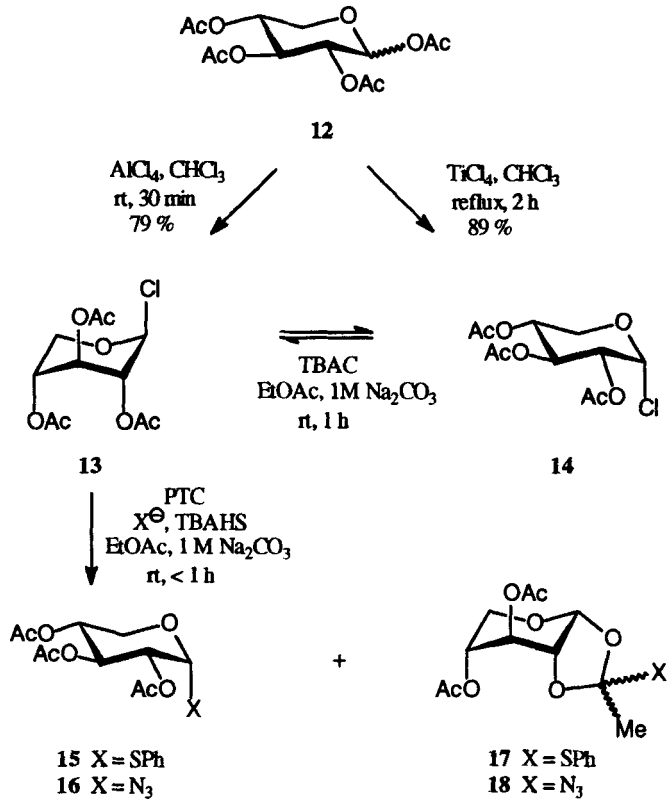
Cpd[a,ref]	Yield (%)	mp (°C)	$[\alpha]_D$	Formula	Combustion analyses Calculated (%) C/H/N	Found (%) C/H/N
2[18]	95	77.6-77.9	-54.9°	$C_{17}H_{20}O_7S$	55.42/5.48	55.55/5.43
3[19]	82	145.8-146.8	-60.1°	$C_{17}H_{19}NO_9S$	49.39/4.64/3.39	49.10/4.22/4.51
4	74	95.8-96.0	-7.5°	$C_{13}H_{18}O_8S$	46.70/5.43	46.64/5.21
5	84	103.4-103.7	+4.1°	$C_{14}H_{20}O_8S_2$	44.20/5.30	44.16/5.21
6	79	75.0-75.4	-90.3°	$C_{17}H_{20}O_7Se$	49.03/4.84	49.52/4.70
7[20]	67	136.6-136.7	-67.6°	$C_{17}H_{19}NO_{10}$	51.37/4.82/3.53	51.59/4.72/4.01
8	65	-	+40.8°	$C_{25}H_{29}O_{11}P$		
9	66	132.4-132.5	-148.6°	$C_{15}H_{19}NO_{10}$	48.24/5.13/3.75	48.34/5.00/3.80
10	78	-	-74.8°	$C_{17}H_{19}N_3O_8$	51.89/4.87/10.69	51.89/4.53/10.59
11	88	83.8-84.0	-80.5°	$C_{11}H_{15}N_3O_7$	43.84/5.02/13.95	43.58/4.67/13.93
15	82	-	+203.5°	$C_{17}H_{20}O_7S$		
16[21]	67	-	+170.5°	$C_{11}H_{15}N_3O_7$	43.84/5.02/13.95	44.06/4.95/13.58

a. Physical data of known compounds agreed with lit. values.

Table 2. ^{1}H NMR (500 MHz) Chemical Shifts δ (ppm) and Coupling Constants J (Hz) for Compounds **2-11, 15,16**

Cpd	H-1 ($J_{1,2}$)	H-2 ($J_{2,3}$)	H-3 ($J_{3,4}$)	H-4 ($J_{4,5e}$)	H-5e ($J_{5e,5a}$)	H-5a ($J_{5a,4}$)	OAc	Aglycon H's	
2	4.78	4.92	5.16	4.90	4.26	3.40	2.07(3H)	7.45	7.29
	(8.3)	(8.2)	(8.2)	(4.9)	(11.8)	(8.8)	2.02(6H)	(m, 2H)	(o, p, 3H)
3	5.05	4.97	5.18	4.92	4.32	3.53	2.01(3H)	8.14	7.54
	(7.4)	(7.3)	(7.4)	(4.5)	(12.0)	(7.7)	2.06(6H)	(m, 2H)	(o, 2H)
4	5.34	4.99	5.17	4.90	4.12	3.51	2.03(9H)	2.35 (CH_3)	
	(8.3)	(7.9)	(7.9)	(4.8)	(11.9)	(8.5)			
5	5.65	5.03	5.19	4.90	4.20	3.55	2.05(9H)	4.65	1.41
	(7.7)	(7.4)	(7.4)	(4.6)	(12.1)	(7.7)		(CH_2)	(CH_3)
6	5.16	5.01	5.10	4.85	4.33	3.51	2.06(6H)	7.56	7.28
	(6.6)	(6.7)	(6.8)	(4.2)	(12.2)	(6.9)	2.04(3H)	(m, 2H)	(o, p, 3H)
7	5.31	5.16	5.22	4.98	4.20	3.60	2.08(9H)	8.19	7.06
	(5.3)	(7.3)	(7.2)	(4.3)	(12.3)	(6.7)		(m,2H)	(o, 2H)
8	4.98	5.11	5.35	4.91	4.15	3.48	2.04(3H)	7.32	
	(7.8)	(7.6)	(6.6)	(4.6)	(12.4)	(7.8)	1.99(3H)	(m, 10H)	
	($^3J_{1,P}$ 5.9)						1.93(3H)		
9	5.22	5.12-5.13		4.93	4.58	3.59	2.05(3H)	2.70	
	(4.1)	(m)		(3.6)	(13.2)	(3.7)	2.10(6H)	(CH_2, 4H)	
10	5.52	5.25	5.32	5.03	4.44	3.57	2.18(3H)	7.99, 7.58 (o)	
	(5.5)	(7.4)	(5.5)	(4.3)	(12.5)	(6.4)	2.10(3H)	7.50, 7.37 (m)	
							2.00(3H)		
11	4.61	4.85	5.16	4.96	4.19	3.41	2.05(3H)	-	
	(8.1)	(8.9)	(8.9)	(5.3)	(11.7)	(9.6)	2.02(6H)		
15	5.75	5.01	5.37	4.94	3.84	4.11	2.08(3H)	7.41	7.27
	(5.3)	(9.6)	(9.2)	(5.5)	(11.5)	(11.4)	2.03(6H)	(m, 2H)	(o, p, 3H)
16	5.46	4.83	5.30	4.88	3.87	3.71	2.03(3H)	-	
	(4.1)	(9.8)	(9.5)	(5.8)	(11.3)	(11.0)	1.97(6H)		

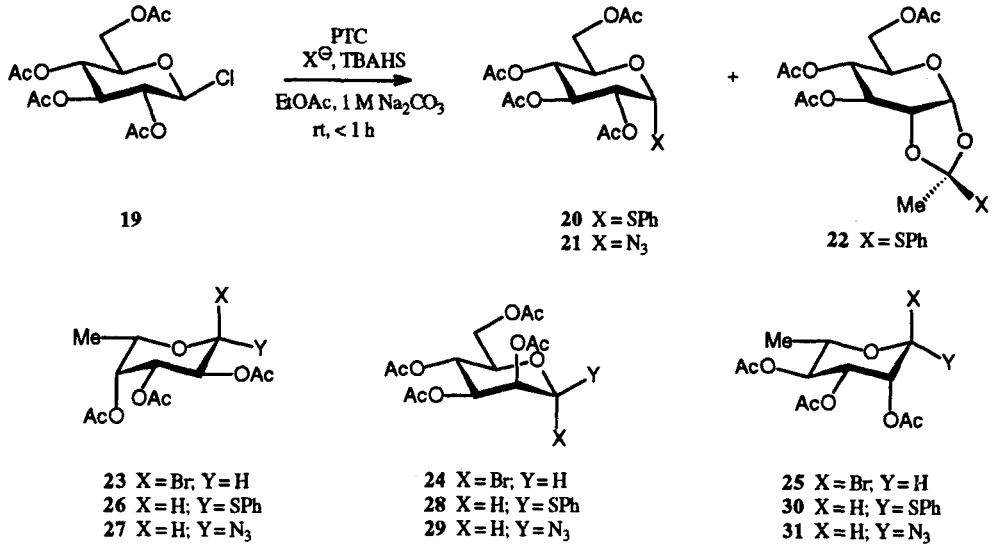
Treatment of the $^1C_4$ β-xylopyranosyl chloride **13**, having a 1,2-*trans*-diaxial stereochemistry, with either thiophenoxide or azide anions under exactly the same PTC conditions as described above for the α-bromo anomer **1** provided the corresponding α-D-xylopyranosyl derivatives **15** and **16** in 82% and 67% yields, respectively (Scheme 2). Again, in the ^{1}H NMR spectra of the crude reaction mixtures, no signals were observed in the regions of the spectra where the β-glycosyl derivatives (**2**, **11**) absorb, suggesting



Scheme 2

complete anomeric inversions. We did however obtain *ca.* <5% of side-products to which orthoester-like structures **17** and **18** were assigned (Scheme 2). Compounds **17** and **18** were purified by concentration of mixed fractions obtained during silica gel column chromatography of the crude products. The structural assignments for these minor by-products were based on the observed typical chemical shifts of their *endo*-methyl signals (1.80 ppm).

These by-products were derived from the nucleophilic attack of the nucleophiles (PhS^- and N_3^-) on the acyloxonium intermediates. Therefore, the 1,2-*trans*-xylopyranosyl chloride **13** appears to be slightly more prone to anchimeric group participation by its 2-acyloxy group than is its 1,2-*cis*-α-bromo analog **1**. However, this event constituted a very minor side reaction and was not unexpected owing to a favorable 1,2-*trans*-diaxial orientation of the anomeric chloride and the 2-acetoxy group in the preferred $^1C_4$



Scheme 3

conformation of **13**. When 1,2-*cis*-α-chloride **14** was used under the above PTC conditions, the reaction rates were dramatically reduced (not shown).

Since the β-D-xylopyranosyl chloride adopts a $^1C_4$ conformation, 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl chloride (**19**) having a fixed $^4C_1$ chair conformation was also investigated. The β-D-glucopyranosyl chloride **19** was similarly treated with thiophenol and sodium azide (Scheme 3). With the soft thiophenol nucleophile, 2,3,4,6-tetra-*O*-acetyl-1-thio-α-D-glucopyranoside(**20**) and its corresponding 1,2-*O*-thiophenoxyethylidene **22** were obtained as a 10.5:1 mixture (69 %). When the reaction was conducted with the more hydrophilic azide anion, the only substituted product 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl azide (**21**) was obtained (31%) without any detectable orthoester-like product. The poorer reactivity of the glycosyl chloride can be accounted for by the fact that more hydrolysis occurred in the case of azide anions.

In none of the above PTC reactions and the previously described situations[10] with acetobromo-L-fucose (**23**), acetobromo-D-mannose (**24**) and acetobromo-L-rhamnose (**25**) leading to **26-31** were both anomers formed. We can therefore conclude that these PTC catalyzed anomeric nucleophilic substitutions were stereospecific since each anomeric glycosyl halide gave its respective inverted glycosyl derivatives. It is, however, also

Table 3. ^{13}C NMR (500 MHz) Chemical Shifts δ (ppm) for Compounds **2-11, 15, 16**

Compound[a]	C_1	C_2	C_3	C_4	C_5	Aglycon C's Ci	Co	Cm	Cp
2	86.3	69.8	72.0	68.4	65.2	132.2	128.2	132.7	129.0
3	84.7	69.3	70.8	67.9	64.6	130.3	124.0	124.4	126.4
4	80.3	69.0	71.5	68.2	65.6	30.8(CH_3)		192.1(C=O)	
5	85.7	68.5	70.8	68.0	65.1	20.6 (CH_2),		13.7 (CH_3),	210.1(C=S)
6	82.3	70.2	70.3	67.9	64.8	128.4	128.2	134.4	129.1
7	97.5	69.4	69.8	68.0	61.8	161.0	116.5	125.8	143.1
8[b]	96.4	69.9	70.0	69.7	62.2	169.6	127.9	128.6	128.6
9	102.7	68.3	68.3	66.9	62.0	25.4(CH_2)		170.5(C=O)	
10	105.6	68.0	69.6	67.8	62.3	143.5, 128.3, 128.5, 124.8, 120.2, 109.1			
11	88.3	68.4	71.5	70.4	64.3	-			
15	85.4	69.6	70.8	69.0	60.0	133.0	127.7	131.7	129.1
16	86.4	68.5	70.1	68.9	60.5	-			

a. OAc: 20.6-20.7 ppm.

b. $^2J_{C1,P}$ 5.0 Hz.

possible to argue that double anomeric inversions might have occurred during the process. To examine this possibility further, we treated β-xylosyl chloride **13** with one equivalent of tetrabutylammonium chloride (TBAC) in the absence of any additional nucleophile under the same PTC conditions described above (Scheme 2). The anomerization process was rather slow as the reaction showed the formation of an anomeric mixture in a ratio of 1.2:1 in favor of the β-anomer **13** after one hour. These results suggest that in the presence of a large amount of phase transfer catalyst containing a halide anion which can compete with the added nucleophile, double inversions can occur. In the above set of experiments, we deliberately used TBAHS as catalyst to avoid this complication. This result also suggests that a nucleophile having a low partition coefficient between the organic and the aqueous

phases would face competitive hydrolysis and nucleophilic displacement by the halogen anion released from the glycosyl halide during reaction.

EXPERIMENTAL

General methods. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AMX 500 instrument in chloroform-d, unless stated otherwise. Chemical shifts are expressed in parts per million downfield from TMS. All assignments were based on COSY, NOESY, DEPT, and HMQC experiments. Optical rotations were measured on a Perkin Elmer 241 polarimeter at 23 °C in chloroform. Melting points were determined on a Gallenkamp apparatus and are uncorrected. Elemental analyses were performed at the University of Ottawa. HRMS (pos. FAB) were recorded on a Kratos Concept IIH spectrometer. Thin-layer chromatography (TLC) was performed on pre-coated silica gel 60 F-254 plates and column chromatography on silica gel 60 (230-400 mesh, Merck No. 9385).

Typical PTC reactions for the syntheses of compounds 2-11 and 15, 16. To a solution of 2,3,4-tri-*O*-acetyl-α-D-xylopyranosyl bromide (**1**)[14] (1 equiv) and tetrabutyl-ammonium hydrogen sulfate (1 equiv) in ethyl acetate (1.0 mL/100 mg of sugar) were added the nucleophiles (1.2-3 equiv) and 1M sodium carbonate (1.0 mL/100 mg of sugar). The reaction mixture was vigorously stirred at room temperature for 1 h until the starting material was completely consumed as judged by TLC monitoring using a mixture of ethyl acetate and hexane (4/6 v/v) as eluent. Then, the solution was diluted with ethyl acetate and the organic phase was separated from the aqueous phase. The organic solution was washed with saturated sodium bicarbonate (2 × 20 mL), water (1 × 20 mL), and brine (20 mL). It was then dried over anhydrous sodium sulfate and concentrated. The crude compounds were purified by silica gel column chromatography using a mixture of ethyl acetate and hexane (3/7 v/v) as eluent. The solid residues obtained after column chromatography were recrystallised from ethanol (Table 1).

PTC equilibration between 13 and 14. 2,3,4-Tri-*O*-acetyl-β-D-xylopyranosyl chloride (**13**)[22] (50 mg, 0.17 mmol) was dissolved in ethyl acetate (0.5 mL). To this solution, tetrabutylammonium chloride (47 mg, 0.17 mmol) in 1M aqueous Na_2CO_3 (0.5 mL) was added. The reaction mixture was stirred for 1 hour at room temperature. TLC indicated a mixture of α- and β-anomers ($R_{F,\alpha} = 0.46$, $R_{F,\beta} = 0.37$, hexane/ethyl acetate 7:3 v/v). The reaction mixture was diluted with ethyl acetate (5 mL) and the separated organic

phase was washed with saturated $NaHCO_3$ (5 mL), water (5 mL), and then brine. The organic solution was dried over anhydrous Na_2SO_4 and concentrated. The ^1H NMR spectrum of the crude product showed the anomeric ratio of α- (**14**) and β- (**13**) anomers to be: α:β = 1:1.2, as judged from the relative integration of their anomeric proton at 6.21 and 5.77 ppm, respectively.

3,4-Di-*O*-acetyl-1,2-*O*-thiophenoxyethylidene-α-D-xylopyranose (17). Compound **17** was partially purified from the crude reaction mixture resulting from the treatment of **13** and thiophenol under the general PTC conditions described above. The following ^1H NMR data were extracted from an enriched ≈1:1 mixture of **15** and **17**: 7.51-7.56 (m, 2H, Ar), 7.31-7.34 (m, 3H, Ar), 5.62 (d, 1H, $J_{1,2}$ = 4.8 Hz, H-1), 5.25 (dd, 1H, $J_{2,3}$ = 2.7 Hz, H-3), 4.86-4.89 (m, 1H, H-4), 4.43 (ddd, 1H, long range J 1.1 Hz, H-2), 3.92 (dd, 1H, $J_{4,5e}$ = 6.3 Hz, H-5e), 3.59 (dd, 1H, $J_{4,5a}$ = 8.5, $J_{5a,5e}$ = 11.9 Hz, H-5a), 2.12 (s, 3H, OAc), 2.04 (s, 3H, OAc), 1.80 (s, 3H, *endo*-Me). These spectroscopic data are similar to those previously observed for an analogous *p*-methylthiophenoxy thio ortho ester.[17]

Thiophenyl 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranoside (20). This compound was prepared by PTC using penta-*O*-acetyl-β-D-glucopyranosyl chloride (**19**).[22] However, the reaction time to consume the starting material was longer than the case of β-D-xylopyranosyl chloride (6 h); yield 63%; mp 84.7-85.3 °C; $[\alpha]_D$ = +193.0 (c 1.0, $CHCl_3$); ^1H NMR δ 7.42-7.40 (m, 2H, Ar), 7.29-7.24 (m, 3H, Ar), 5.89 (d, 1H, $J_{1,2}$ = 5.7 Hz, H-1), 5.41 (t, 1H, $J_{3,4}$ = 10.0 Hz, H-3), 5.08 (dd, 1H, $J_{2,3}$ = 10.3 Hz, H-2), 5.05 (dd, 1H, $J_{4,5}$ = 10.2 Hz, H-4), 4.54 (ddd, 1H, $J_{5,6a}$ = 5.2 Hz, $J_{5,6b}$ = 2.2 Hz, H-5), 4.25 (dd, 1H, $J_{6a,6b}$ = 12.3 Hz, H-6a), 4.01 (dd, 1H, H-6b), 2.07, 2.03, 2.01, 1.99 (4s, 3H×4, OAc); ^{13}C NMR δ 171.1, 170.5, 170.4, 170.2 (C=O), 132.4 (*m*-Ar), 129.7 (*o*-Ar), 129.5 (*ipso*-Ar), 128.4 (*p*-Ar), 85.5 (C-1), 71.3 (C-3), 71.0 (C-2), 69.1 (C-4), 68.7 (C-5), 62.5 (C-6), 21.3 (3 × Me), 21.2 (Me). HRMS (pos. FAB): *m/z* calcd for $C_{20}H_{24}O_9S$ [441.1219, $(M)H^+$]; found: *m/z* 441.1210.

2,3,4,6-Tetra-*O*-acetyl-α-D-glucopyranosyl azide (21). For this reaction the reaction rate was very slow and it took 19 h to consume the starting material; yield 31%; mp 102.7-103.2 °C; $[\alpha]_D$ = +155.6 (c 1.0, $CHCl_3$); ^1H NMR δ 5.58 (d, 1H, $J_{1,2}$ = 4.4 Hz, H-1), 5.36 (t, 1H, $J_{3,4}$ = 9.7 Hz, H-3), 5.02 (t, 1H, $J_{4,5}$ = 9.9 Hz, H-4), 4.92 (dd, 1H, $J_{2,3}$ = 10.1 Hz, H-2), 4.07-4.26 (m, 3H, H-5, H-6's), 2.07×2, 2.00, 1.98 (3s, 12H, OAc); ^{13}C NMR δ 171.2, 170.5, 170.1 (C=O), 86.8 (C-1), 70.7 (C-3), 70.2 (C-4), 70.1 (C-2), 68.4 (C-5), 62.1 (C-6), 21.3, 21.2, 21.2 (Me). HRMS (pos. FAB): *m/z* calcd for $C_{14}H_{19}N_3O_9$ [374.1199, $(M)H^+$]; found: *m/z* 374.1450.

3,4,6-Tri-*O*-acetyl-1,2-thiophenoxyethylidene-α-D-glucopyranose (22). This compound was a by-product from the PTC reaction using β-D-glucopyranosyl chloride and thiophenol as a nucleophile. This compound was purified from the column and its NMR was obtained; yield 6 %; ^{1}H NMR δ 7.50-7.53 (m, 2H, Ar), 7.30-7.36 (m, 3H, Ar), 5.75 (d, 1H, $J_{1,2}$ = 5.3 Hz, H-1), 5.22 (t, 1H, $J_{3,4}$ = 2.5 Hz, H-3), 4.89 (ddd, 1H, $J_{4,5}$ = 9.7 Hz, long range J = 1.0 Hz, H-4), 4.58 (ddd, 1H, $J_{2,3}$ = 2.7 Hz, long range J = 1.0 Hz, H-2), 4.17, 4.16, 4.16 (3s, 2H, H-6's), 3.93 (ddd, 1H, $J_{5,6a}$ = 4.14 Hz, $J_{5,6b}$ = 3.9 Hz, H-5), 2.12, 2.06, 2.05 (3s, 9H, OAc), 1.80 (s, 3H, *endo*-Me).

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