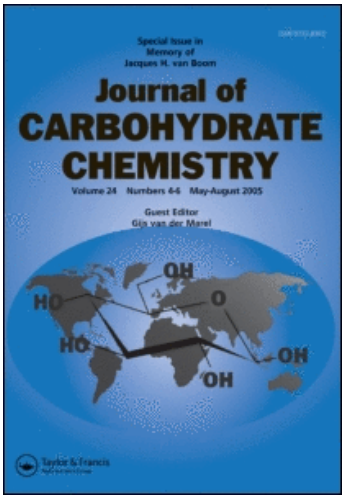

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THIOGLYCOSIDES AS POTENTIAL GLYCOSYL DONORS IN ELECTROCHEMICAL GLYCOSYLATION REACTIONS. PART 1: THEIR PREPARATION AND REACTIVITY TOWARD SIMPLE ALCOHOLS.

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ABSTRACT

Constant potential electrolysis of several glycosyl donors such as substituted phenyl 2,3,4,6-tetra-*O*-acetyl, benzoyl or benzyl-1-thio-β-D-gluco or galactopyranosides in dry acetonitrile in the presence of various primary, secondary or tertiary alcohols performed in an undivided cell, gave preferentially β-linked saccharides in moderate to good yields according to the nature of the protective groups on the sugar moiety. 2-Deoxy-2-phthalimido-1-thio-β-D-gluco derivatives gave the β-glucosides selectively in excellent yields. It was found, as expected, that substitution of the phenyl group with methoxy or methyl radicals facilitates the electrochemical glycosylation reaction by lowering the oxidation potentials of the corresponding thioglycosides.

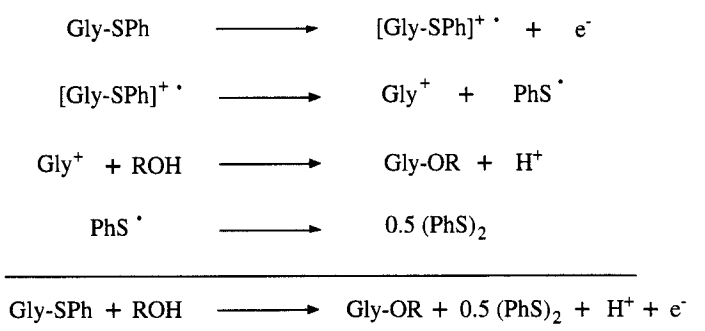
INTRODUCTION

Oligosaccharides are important constituents of glycoproteins, glycolipids and glycophospholipids and their preparations is a central problem in carbohydrate chemistry. Most of the reported[1] glycosylation processes rely on S_N1-type reactions at the anomeric center, i.e., the generation of a reactive intermediate oxocarbenium ion pair from an appropriate activated glycosyl donor. In this context S-glycosides have attracted considerable attention mainly due to their easy preparation and stability during various chemical transformations and their activation has been widely explored. Following the discovery by Noyori and Kurimoto[2] that one-electron anodic oxidation of aryl glycosides in the presence of alcohols resulted in glycosides formation and that, in other hands, alkyl phenyl sulfides (Ph-S-R) are easily anodically oxidised[3,4] to provide a radical cation $(Ph\text{-}S\text{-}R)^+$ which may undergo S-R bond cleavage to generate a thiyl radical (Ph-S$^\bullet$) and a cation (R^+), we[5] and others[6] found that electro-oxidative generation of oxocarbenium species from phenyl 1-thioglycosides resulted in electroglycosylation in the presence of alcohols (Scheme 1).

Moreover, phenyl or substituted phenyl 1-thioglycosides can be easily prepared in good yields and have lower oxidation potentials than aryl glycosides.[2] Following our preliminary communication[5] on this electroglycosylation, we now report full details and improvements of the original procedure.

RESULTS AND DISCUSSION

As described in our preliminary communication the glycosylation reactions were conducted first in dry acetonitrile (a suitable solvent for one-electron oxidation of sulfides[7]) at constant potentials in an undivided cell with a platinum anode and cathode using lithium perchlorate as the supporting electrolyte. The acid produced (Scheme 1) was not neutralized. In this way, we found that phenyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranoside (**1**)[8] reacted with methanol in very poor yield (16%) to give α and β methyl 2,3,4,6-tetra-*O*-acetyl-D-glucopyranoside[9] (**28**α) and (**28**β) (α/β : 13/87). In fact, under these conditions many side reactions occurred, giving complex mixtures in which compounds resulting from migration of acetyl groups to the anomeric position could be identified in large amount by ^1H NMR analysis on the crude reaction mixture. Moreover, several complications have been reported during the oxidation of phenyl sulfides which include the formation of a pseudodimer sulfonium salt after abstraction of the para

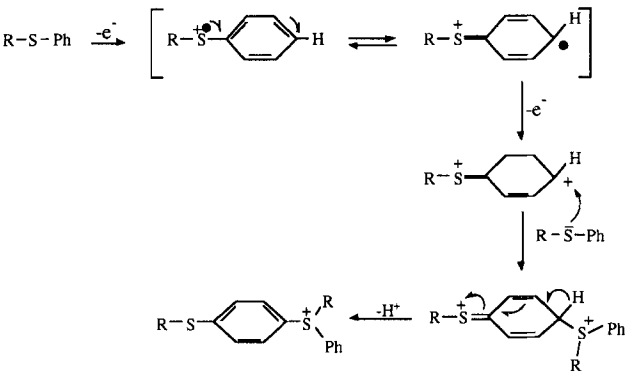


Scheme 1

hydrogen atom in the phenyl ring, and which could be in certain cases the major product of the reaction[4,10](Scheme 2).

For these reasons we decided first, to substitute the ortho and para positions in the phenyl ring by methyl or methoxy groups and second, to use directly unprotected thio glycosides or to replace acetyl protecting groups by benzoyl or benzyl groups. In addition, in order to extend the scope of the reaction, protected 2-acetamido and 2-phthalimido thioglucosides were also tested. Then, the acidity formed in the reaction was at least partially neutralized using molecular sieves and/or a nickel foam cathode which reduced protons under the reaction conditions. Finally, we modified the supporting electrolyte (changed to the less hazardous lithium tetrafluoroborate) and the anode (changed to vitrous or woven carbon).

The *p*-methyl or *p*-methoxy groups are expected to induce a greater stabilization of the intermediate cation radical through their electron releasing ability and reduce the chance for hydrogen atom abstraction. As a matter of fact, these groups considerably lower the oxidation potentials of the corresponding unsubstituted phenyl thioglycosides, as shown from the oxidation potentials of 2,4,6-trimethoxyphenyl thioglycosides (Table 1, entries 2 and 12 for example); therefore the oxidation potential of the glycosyl donor can be influenced by manipulating the substituent in the para or in both ortho and para positions in the phenyl ring (decreasing potential: Ph>*p*-CH3Ph>*p*-CH3OPh> (CH3O)3-Ph). For perbenzylated phenyl thioglucosides, the difference (0.5V) should be large enough that the trimethoxyphenyl thioglucoside could be selectively activated in the presence of the corresponding unsubstituted phenyl thioglucoside. This idea was exploited by Kahne et al.[11] who, investigating a glycosylation method that involves the chemical activation of anomeric phenyl sulfoxides with triflic anhydride, found that *p*-methoxyphenyl sulfoxides can be selectively activated in the presence of an



Scheme 2

TABLE 1: Oxidation potentials of some phenyl thio and selenoglycosides

Entry	glycosides	Eox[a](V)	Entry	glycosides	Eox[a](V)
1	**1**[8]	1.67	12	**12**	1.00
2	**2**[12]	1.50	13	**13**[16]	1.50
3	**3**[13,14]	1.45	14	**14**	1.52
4	**4**[14,15]	1.38	15	**15**[15]	1.34
5	**5**	1.50	16	**16**[15]	1.20
6	**6**	1.45	17	**17**	1.33
7	**7**[13]	1.34	18	**18**	1.28
8	**8**[15]	1.20	19	**21**	1.33
9	**9**	1.23	20	**22**[17]	1.35
10	**10**	1.20	21	**23**[17]	1.36
11	**11**	1.02			

a) See experimental part.

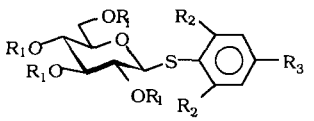
equimolecular amount of the corresponding unsubstituted phenyl sulfoxide. In the same context, we prepared also the known selenoglycosides **22** and **23** to lower even more the oxidation potential.

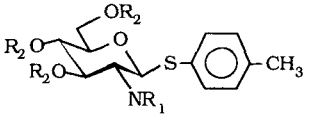
Preparation of thioglycosides.

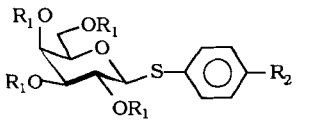
All new phenylthioglycosides **5**, **6**, **9**, **10**, **11**, **12**, **14**, **17**, **18**, and **21** were prepared conveniently on a large scale by the use of standard procedures. *p*-Methylphenyl 2,3,4,6-

tetra-*O*-benzoyl-1-thio-β-D-glucopyranoside (**5**) and *p*-methoxyphenyl 2,3,4,6-tetra-*O*-benzoyl-1-thio-β-D-galactopyranoside (**17**) were respectively prepared from the corresponding unprotected thioglycosides **4**[14,15] and **16**[15] by treatment with benzoyl chloride in pyridine. *p*-Methylphenyl 2,3,4,6-tetra-*O*-benzyl-1-thio-β-D-glucopyranoside (**6**), *p*-methoxyphenyl 2,3,4,6-tetra-*O*-benzyl-1-thio-β-D-glucopyranoside (**9**) and *p*-methoxyphenyl 2,3,4,6-tetra-*O*-benzyl-1-thio-β-D-galactopyranoside (**18**) were respectively prepared from the corresponding unprotected thioglycosides **4**,[14,15] **8**[15] and **16**.[15] 2',4',6'-Trimethoxyphenyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranoside (**10**) was prepared from the sodium salt of 2,4,6-trimethoxythiophenol (**41**)[18] and 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide[19] in DMF. Then, deacetylation of **10** using the classical Zemplen conditions afforded 2',4',6'-trimethoxyphenyl 1-thio-β-D-glucopyranoside (**11**). The preparation of **41** is described in the literature[18] in very low yield (6.5%). We improved its preparation by treating the commercially available 1, 3, 5-trimethoxybenzene with *n*-butyllithium in hexane in the presence of powdered sulfur and raised the yield up to 49%. 2',4',6'-Trimethoxyphenyl 2,3,4,6-tetra-*O*-benzyl-1-thio-β-D-glucopyranoside (**12**) was prepared by benzylation of **11** (benzyl bromide, NaH) in DMF.

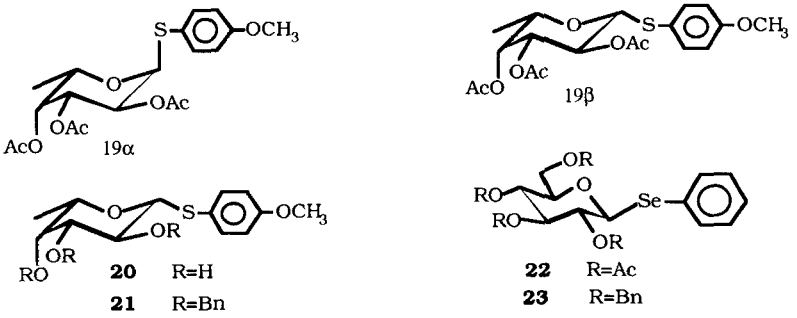
p-Methylphenyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (**14**) was prepared from 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranose[20] according to the procedure[8] described by Ferrier et al.







1:	R_1=Ac	R_2=H	R_3=H	**13:**R_1=HAc	R_2=Ac	**15:**R_1=Ac R_2=OMe
2:	R_1=Bn	R_2=H	R_3=H	**14:**R_1=Phth	R_2=Ac	**16:**R_1=H R_2=OMe
3:	R_1=Ac	R_2=H	R_3=Me			**17:**R_1=Bz R_2=OMe
4:	R_1=H	R_2=H	R_3=Me			**18:**R_1=Bn R_2=OMe
5:	R_1=Bz	R_2=H	R_3=Me			
6:	R_1=Bn	R_2=H	R_3=Me			
7:	R_1=Ac	R_2=H	R_3=OMe			
8:	R_1=H	R_2=H	R_3=OMe			
9:	R_1=Bn	R_2=H	R_3=OMe			
10:	R_1=Ac	R_2=OMe	R_3=OMe			
11:	R_1=H	R_2=OMe	R_3=OMe			
12:	R_1=Bn	R_2=OMe	R_3=OMe			



p-Methoxyphenyl 2, 3, 4-tri-*O*-acetyl-1-thio α and β-L-fucopyranosides **19α** and **19β** were prepared from the known tetra-*O*-acetyl-β-L-fucopyranose[21] and *p*-methoxy thiophenol by treatment with boron trifluoride-etherate in dichloromethane.[8] Classical deacetylation of **19β** afforded *p*-methoxyphenyl-1-thio-β-L-fucopyranoside **20** which was then perbenzylated to afford *p*-methoxyphenyl 2,3,4-tri-*O*-benzyl-1-thio-β-L-fucopyranoside **21**.

Electrochemical glycosylation.

Electrochemical glycosylations with the *p*-methoxyphenyl and trimethoxyphenyl peracetylated thioglucosides **7**[13] and **10** in acetonitrile in the presence of methanol (10 equiv) without molecular sieves using a woven carbon anode and a platinum cathode afforded, after reacetylation of the crude reaction mixture, an α:β mixture of the expected methyl glucosides **28α** and **28β** (25%). Additionally, α and β glucose peracetate **27α** and **27β** (40-44%) were formed as the major products coming from partially acetylated glucose formed in the reaction (Table 2, entries 7 and 8). On the other hand, when the peracetylated *p*-methylphenyl thioglucoside **3**[13,14] was electrolysed in the presence of methanol in acetonitrile containing 3Å molecular sieves using a woven carbon anode and a platinum or nickel foam cathode or a vitrous carbon anode and a platinum cathode, the glycosides **28α** and **28β** were formed along with the acetates **27α** and **27β** and the known[22] glucose 1,2-orthoester **25** (Table 2, entries 4,5 and 6). We found that large excess of methanol and the use of a vitrous carbon anode favors the formation of the orthester **25**, while the use under these conditions of only one equivalent of methanol increases the formation of the glucosides **28α** and **28β** and lowers the formation of **25**. The use of a woven carbon anode, which has a greater efficient surface than the corresponding vitrous carbon electrode, along with a nickel foam cathode also favors the formation of the methyl glucosides **28α** and **28β** but still in low yields. However, if 2-propanol is the nucleophile no orthoester is produced but the yields in the corresponding α and β glucosides **29α**[23] and **29β**[24] remain low (Table 2, entry 3). Thus, we can definitely conclude that use of acetyl as a hydroxyl protecting group should be avoided in electrochemical glycosylation reactions.

TABLE 2: Electrosynthesis of some simple monosaccharides and glucosyl fluorides

Entry	thioglycoside	E_{ox}[a] (V)	Electrodes Anode/Cathode	Nucleophile(eq)	product(s)	Yields[c]	α:β[b]
1	**4**	1.38	Pt/Pt	CH_3OH[d,f](2) CH_3OH[d,f](10)	**28α, 28β-**	85[e] 89[e]	36:64 36:64
2	**4**	1.38	Pt/Pt	C_6H_5OH (10)	**33α, 33β**	46[e]	30:70
3	**1**	1.67	Woven C/Ni foam	$(CH_3)_2CHOH$ (10)	**29α, 29β**	33	15:85
4	**3**	1.45	vitrous C/Pt	CH_3OH (10)	**28α, 28β** **+25**	11 48	3:16 -
5	**3**	1.45	vitrous C/Pt	CH_3OH (1)	**28α, 28β** **+25**	41 18	26:44 -
6	**3**	1.45	Woven C/Ni foam or Pt	CH_3OH (10)	**28α, 28β** **+25**	41 18	1:68 -
7	**7**	1.34	vitrous C/Pt	CH_3OH [d,f] (10)	**28α, 28β** **+27α , 27β**	29[e] 40[e]	12:88 55:45
8	**10**	1.20	vitrous C/Pt	CH_3OH [d,f] (10)	**28α, 28β** **+27α, 27β**	23[e] 44[e]	10:90 54:46
9	**14**	1.52	vitrous C/Pt	CH_3OH (10)	**35**	91	0:1
10	**14**	1.52	Woven C/Pt	$CH_3CH_2CH_2OH$ (10)	**36**	85	0:1
11	**14**	1.52	Woven C/Pt	$(CH_3)_2CHOH$ (10)	**37**	86	0:1
12	**14**	1.52	Woven C/Pt	$(CH_3)_3COH$ (10)	**38**	85	0:1
13	**14**	1.52	Woven C/Pt	$CH_3CH_2CH_2OH$ (5) $(CH_3)_2CHOH$ (5)	**36** **37**	45.5 40	0:1 0:1
14	**14**	1.52	Woven C/Pt	$CH_3CH_2CH_2OH$ (3.3) $(CH_3)_2CHOH$ (3.3) $(CH_3)_3COH$ (3.3)	**36** **37** **38**	35.5 32 18	0:1 0:1 0:1
15	**5**	1.50	vitrous C/Pt	CH_3OH (10)	**32** **+26**	46 37	0:1 -
16	**17**	1.33	Woven C/Ni foam	$(CH_3)_3COH$ (10)	**39**	67	0:1
17	**2**	1.50	Woven C/Ni foam	$(CH_3)_2CHOH$ (10)	**30α, 30β**	97	32:68
18	**6**	1.45	vitrous C/Pt	CH_3OH [d,f] (10)	**31α , 31β**	95	28:72
19	**9**	1.23	vitrous C/Pt	CH_3OH [d] (10)	**31α, 31β**	95	31:69
20	**12**	1.00	vitrous C/Pt	CH_3OH [d] (10)	**31α, 31β**	91	32:68
21	**23**	1.36	Woven C/Ni foam	$(CH_3)_2CHOH$ (10)	**30α 30β**	96	45:55
22	**22**	1.35	Woven C/Ni foam	$(CH_3)_2CHOH$ (10)	**29α, 29β**	34	1:9
23	**5**	1.50	Woven C/Ni foam	NaF (10)	**40**	59	1:0
24	**5**	1.50	Woven C/Ni foam	CsF (10)	**40**	52	1:0
25	**5**	1.50	Woven C/Ni foam	LiF (10)	**40**	53	1:0

a. Electrolyses were carried out on 1 mmol scale at room temperature in an undivided cell using square electrodes (4cm2) in anhydrous acetonitrile (32 mL) with lithium tetrafluoroborate (0.2M), unless otherwise stated, as supporting electrolyte. The reactions were performed at constant potential (1-1.67 vs a saturated calomel reference electrode) and monitored by TLC. Activated 3Å molecular sieve (1.7g) was added to the reaction mixture, unless otherwise stated. b. Determined by ^1H NMR. c. Isolated yield after chromatography. d. No molecular sieves was added. e. Isolated yield after reacetylation and chromatography. f. A 0.2M solution of lithium perchloratein acetonitrile was the supporting electrolyte.

Electrolysis of perbenzoylated *p*-methylphenyl thioglycosides showed that their behavior is similar to that observed for their corresponding peracetylated analogs (Table 2, entries 15 and 16) but the yields were uniformly more satisfactory and a total β-selectivity was observed. Thus, electrochemical glycosylation of *p*-methylphenyl 2,3,4,6-tetra-*O*-benzoyl-1-thio-β-D-glucopyranoside (**5**) with methanol in the presence of 3Å molecular sieves using a nickel foam cathode (Table 2, entry 15) gave the methyl β-D-glucoside **32**[25] selectively but in moderate yield (46%) and the known orthoester **26**[26] in 37% yield. As expected, when a more hindered alcohol was used no orthoester formation could be detected and the glycosylation yield was improved. Thus using a woven carbon anode and a nickel foam cathode, *p*-methoxyphenyl 2,3,4,6-tetra-*O*-benzoyl-1-thio-β-D-galactopyranoside (**17**) reacted with *t*-butyl alcohol to give the pure *t*-butyl β-D-galactoside **39**[27] in 67% yield (Table 2, entry 16).

Perbenzylated thioglycosides were also investigated and in contrast to acetylated or benzoylated derivatives, they react with primary and secondary alcohols in excellent yields (91-97%) with a marked β-selectivity. Furthermore, molecular sieves and a nickel foam cathode were not essential in this case. The yields were also shown to be independent of the substituents on the phenyl ring. Thus, perbenzylated phenyl-1-thio-β-D-glucopyranoside **2**[12] reacted with 2-propanol to give the glucosides **30**α and **30**β[28] in 97% yield (Table 2, entry 17) and perbenzylated *p*-methylphenyl, *p*-methoxyphenyl and 2', 4', 6'-trimethoxyphenyl-1-thio-β-D-glucopyranosides **6**, **9** and **12** reacted with methanol to afford the methyl glucosides **31**α[29] and **31**β[30] in more than 90% yields (Table 2, entries 18, 19, and 20).

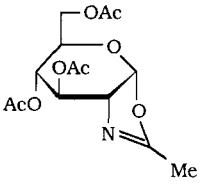
We then directed our attention to the unprotected thioglycosides. In fact, using our original conditions[5] (platinum anode and cathode, acetonitrile, $LiClO_4$ as supporting electrolyte), starting from the thioglycoside **4** we were able to prepare the methyl glycosides **28**α and **28**β (after acetylation of the reaction mixture) in 85% yield (α/β : 36/64) with two equivalents of methanol and in 89% yield with ten equivalents (Table 2, entry 1). In the case of cyclohexanol, the corresponding glycosides **33**α and **33**β[31] were obtained under the same conditions but in only 46% yield (α/β : 30/70) (Table2, entry 2). When we tried 2,2-dimethyl-1-propanol as the nucleophile no reaction occurred and the starting material remaining unaffected. We therefore conclude that unprotected thioglycosides are very sensitive to steric hindrance perhaps because they are adsorbed on the anode preventing reaction from occuring. Furthermore, subsequent addition of methanol to the reaction mixture, led to the formation of methyl glycoside but still, no trace of the expected 2,2-dimethyl-1-propyl glycoside could be detected.

We then investigated the behavior of two amino-protected derivatives of *p*-methylphenyl 2-amino-2-deoxy-1-thio-β-D-glucosides as glycosyl donors. When *p*-

methylphenyl 3,4,6-tri-*O*-acetyl-2-acetamido-2-deoxy-β-D-glucopyranoside (**13**)[16] was electrolysed in the presence of methanol (10 equiv) in acetonitrile containing 3Å molecular sieves and using a woven carbon anode and a platinum cathode, no trace of glycosides was formed. Rather, complete conversion of the starting material to the oxazoline **24**[32] occurred as proved by comparison with an authentic sample. Thus, 2-acetamido-2-deoxy-1-thio-β-D-glucosides were unsuitable for electrochemical glycosylation reactions. On the other hand, it turned out that *p*-methylphenyl 2-deoxy-2-phthalimido-1-thio-β-D-glucosides are outstanding glycosyl donors promoting exclusively β-selectivity. Thus the electrochemical glycosylation of *p*-methylphenyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (**14**) with methanol, 1-propanol, 2-propanol and even *t*-butyl alcohol (Table 2, entries 9, 10, 11 and 12) using either a vitrous carbon or woven carbon anode and a platinum cathode afforded the corresponding glycosides **35**,[33] **36**, **37**[34] and **38**[35] in good to excellent yields (85-91%). It is worth noting that the class of the alcohol seems to be of no importance on the yield of the glycosylation reactions and this was demonstrated by electrolysing **14** with mixtures of 1-propanol, 2-propanol or *t*-butyl alcohol (Table 2, entries 13 and 14). In the presence of equivalent amounts of 1-propanol (5 equiv) and 2-propanol (5 equiv) the corresponding β-glycosides **36** and **37** were produced in almost equal yields (45.5 and 40%). Electrolysis of **14** in the presence of 1-propanol (3.3 equiv), 2-propanol (3.3 equiv) and *t*-butyl alcohol (3.3 equiv) lead to the formation of equivalent amounts of the glycosides **36** and **37** (35.5 and 32%) and 18% of the *t*-butyl β-glycoside **38**[27] thus proving that there is almost no difference in reactivity between primary and secondary alcohols and that even tertiary alcohols react in their presence.

Finally, in order to lower even more the oxidation potentials of glycoside donors, which would allow the use of more oxidizible protective groups, we synthesized phenyl 2,3,4,6-tetra-*O*-acetyl-1-seleno-β-D-glucopyranoside (**22**)[17] and phenyl 2,3,4,6-tetra-*O*-benzyl-1-seleno-β-D-glucopyranoside (**23**)[17] and found that their oxidation potentials were respectively 1.35 and 1.36V (Table 1, entries 21 and 22). These values are similar to the oxidation potentials of *p*-methoxyphenyl thioglycosides and it can reasonably be predicted that *p*-methoxyphenyl and 2', 4', 6'-trimethoxyphenyl selenoglycosides will be oxidized at potentials lower than 1V. This would allow application of a substantial overvoltage during the electrolysis which would increase the rate of the reaction without damaging potentially oxidizible protective groups. The selenoglucosides **22** and **23** reacted with 2-propanol to give the corresponding glucosides in 34 and 96% yield respectively (Table 2, entries 22 and 21) thus confirming that peracetylated glycosides are unsuitable in electrochemical glycosylation reactions even as selenoglycosides.

It is worth noting that in all the reactions tested, β-anomers are preponderant in agreement with the fact that acetonitrile is known to promote β selectivity.[36]



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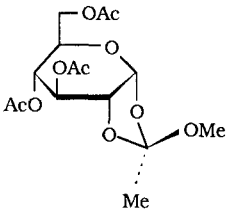

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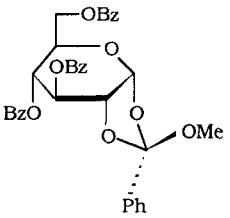

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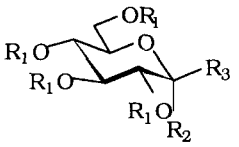
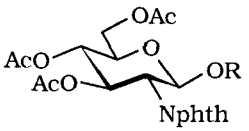
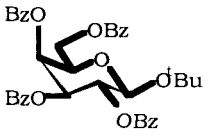




27α:	R_1=Ac	R_2=OAc	R_3=H
27β:	R_1=Ac	R_2=H	R_3=OAc
28α:	R_1=Ac	R_2=OMe	R_3=H
28β:	R_1=Ac	R_2=H	R_3=OMe
29α:	R_1=Ac	R_2=$OCH(CH_3)_2$	R_3=H
29β:	R_1=Ac	R_2=H	R_3=$OCH(CH_3)_2$
30α:	R_1=Bn	R_2=$OCH(CH_3)_2$	R_3=H
30β:	R_1=Bn	R_2=H	R_3=$OCH(CH_3)_2$
31α:	R_1=Bn	R_2=OMe	R_3=H
31β:	R_1=Bn	R_2=H	R_3=OMe
32:	R_1=Bz	R_2=H	R_3=OMe
33α:	R_1=Ac	R_2=OC_6H_{11}	R_3=H
33β:	R_1=Bn	R_2=H	R_3=OC_6H_{11}
34:	R_1=Bz	R_2=F	R_3=H

35:	R=Me
36:	R=$CH_2CH_2CH_3$
37:	R=$CH(CH_3)_2$
38:	R=$C(CH_3)_3$



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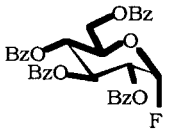

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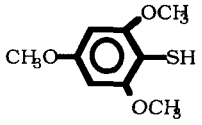

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Among the side products formed during electrochemical glycosylations of peracetylated or perbenzoylated phenyl thioglycosides we isolated small amounts of the corresponding α-glycosyl fluorides when lithium tetrafluoroborate was used as the supporting electrolyte, as already noted in ref. 6. Glycosyl fluorides were introduced as glycosyl donors by Mukaiyama[37] in 1981 and since that time interest in these compounds has continued to grow. Therefore we wanted to take advantage of this side reaction to prepare α-glycosyl fluorides electrochemically using the perbenzoylated *p*-methylphenyl thioglucoside **5** and various fluorides as nucleophiles (Table 2, entries 23, 24 and 25).

The best yield (59%) was obtained when sodium fluoride was the source of fluoride ions. We are currently trying to improve the yield in the preparation of glycosyl fluorides using other than benzoyl hydroxyl protecting groups.

EXPERIMENTAL

General Methods and Material. All solvents were distilled before use: THF from Na-benzophenone, alcohols from Mg, pyridine from CaH_2, dichloromethane from CaH_2, toluene from P_2O_5, acetonitrile from P_2O_5 and K_2CO_3. All reactions were performed under a constant stream of dry nitrogen. Solutions in organic solvents were concentrated on a rotary evaporator at 40 °C/15mm Hg (unless otherwise stated). Merck Silica-gel 60 F_{254} (0.2mm) was used for TLC, detection being carried out by spraying with an alcoholic solution (5%) of sulfuric acid, followed by heating. Melting points were determined on a Reichert apparatus and are uncorrected. IR spectra were recorded with a Brüker IFS 66 spectrophotometer fitted out with a Fourier transform system and are expressed in cm^{-1}. NMR spectra were recorded in $CDCl_3$ (unless otherwise specified) on Brüker AM250, AC250 or AC200 apparatus (250 MHz or 200 MHz for ^1H and 62.9 MHz or 50 MHz for ^{13}C). Chemical shifts are expressed in parts per million downfield from TMS. Coupling constants, checked by double irradiation, are in Hz and splitting pattern abbreviations are: s, singlet; d, doublet; q, quartet; m, multiplet. Optical rotations were determined with a Jasco DIP 370 electronic micropolarimeter at 20±2 °C. Flash column chromatography was performed on silica-gel SDS 6-35μ. Elemental analysis were performed by the "Service Central de Microanalyse du CNRS".

Electrochemical equipment. Cyclic voltammetry was performed in a three-electrode air-tight cell. The working microelectrode consisted of a vitrous carbon disc, with a surface area of 3 mm^2. The reference electrode was a standard calomel electrode (Tacussel) separated from the solution of lithium tetrafluoroborate in acetonitrile, identical to that used in the cell. The counter electrode was a platinum plate. The potentiostat used in cyclic voltammetry was an EG&G PAR Model 273. The cyclic voltammetry performed at a scan rate of 100 mV/s, allowed us to determine the oxidation potentials of different thioglycosides, necessary to carry out the preparative electrolysis. The preparative electrolyses were performed at constant potential using a PRT 100-1X (Tacussel) potentiostat fitted with an IG5-LN (Tacussel) coulometer.

Electroglycosylation. The preparative electroglycosylations were performed in a one compartment, three-electrode, air-tight, cell (60 mL capacity) under potentiostatic

control. The working electrode consisted of a woven carbon or vitrous carbon anode (6cm^2 in area), and the cathode consisted of a platinum foil or a nickel foam plate (MN 100) of a surface area comparable with that of the anode. The reference electrode was a standard calomel electrode separated from the solution by an electrolytic bridge filled with a solution of lithium tetrafluoroborate (0.2M) in acetonitrile. The electrolyser was charged with a solution of dry acetonitrile containing the glycosyl donor (1 mmol), the alcohol and activated 3Å molecular sieves (1.7 g). The mixture was stirred for 20 to 30 minutes and then the electrolyses were carried out at room temperature and at constant potential (the starting current was 15-20 mA depending on the substrate). The oxidation was monitored by TLC until complete disappearance of the starting materials. Complete reaction required about 2 Faradays per mole (1 Faraday per mole theoretically), probably due to the secondary oxidation of the disulfur products.

***p*-Methylphenyl 2, 3, 4, 6-Tetra-*O*-benzoyl-1-thio-β-D-glucopyranoside (5).** To a magnetically stirred solution of **4**[14,15] (4.3 g, 15 mmol) in pyridine (75 mL) was added benzoyl chloride (7.7 mL) and a catalytic amount of DMAP. After 15 h at room temperature the solvent was coevaporated with toluene. The residue was dissolved in dichloromethane (150 mL) and poured into a vigorously stirred saturated aqueous solution of potassium hydrogencarbonate. After 1 h the organic layer was separated, the aqueous phase extracted with dichloromethane (2×150 mL), the combined organic phases washed with water (2×250 mL) and dried (magnesium sulfate). Evaporation of the solvent afforded a solid which was crystallized from ethanol (9.48g, 90%): mp 186-188 °C, $[\alpha]_D^{20}$ +23° (*c* 1, chloroform); IR (KBr) 3067, 3033, 2965, 1726, 1601, 1583, 1492, 1451, 1376, 1269, 1177, 1110, 1026, 970, 937, 895, 858, 833, 806, 712; ^{1}H NMR δ 8.10-7.20 (m, 22H, aromatic), 6.93 (d, 2H, J=8.0, phenyl), 5.89 (t, 1H, $J_{3,4}$=$J_{3,2}$=10.0, H-3), 5.58 (t, 1H, $J_{4,5}$=10.0, H-4), 5.45 (t, 1H, $J_{2,1}$=10.0, H-2), 4.98 (d, 1H, H-1), 4.69 (dd, 1H, $J_{6,6'}$=12.0, $J_{6,5}$=2.5, H-6), 4.47 (dd, 1H, $J_{6',5}$=5.5, H-6'), 4.18 (m, 1H, H-5), 2.27 (s, 3H, methyl); ^{13}C NMR δ 165.93, 165.67, 165.07, 164.93 (4×CO benzoyl), 138.52 (C_{arom} phenyl), 133.78-127.38 (C_{arom} phenyl and benzoyl), 76.12, 74.10, 70.31, 69.20 (C-2, C-3, C-4 and C-5), 62.95 (C-6), 21.07 (methyl).

Anal. Calcd for $C_{41}H_{34}O_9S$ (702.78): C, 70.07; H, 4.88; O, 20.49; S, 4.56. Found: C, 69.86; H, 4.92; O, 20.32; S, 4.75.

***p*-Methylphenyl 2, 3, 4, 6-Tetra-*O*-benzyl-1-thio-β-D-glucopyranoside (6).** To a magnetically stirred solution of **4**[14,15] (10.0 g, 35 mmol) in DMF (350 mL) was slowly added sodium hydride (7.84 g). After 30 min benzyl bromide (23.3 mL) was added dropwise and the reaction mixture heated at 80 °C for 3.5 h before cooling to room temperature. Methanol (15 mL) was then added, the resulting solution was concentrated and the residue dissolved in ether (200 mL) and water (200 mL). After separation of the

organic phase the aqueous phase was extracted with ether (2×200 mL) The combined organic phases were washed with water (600 mL), dried (magnesium sulfate) and concentrated to give a solid which was chromatographed on silica gel using a mixture of pentane-ethyl acetate (9:1) as the eluent to give pure **6** (14.5 g, 64%). The analytical sample was recrystallized from ethanol: mp 80-81 °C, $[\alpha]_D^{20}$ +2° (*c* 2.5, chloroform); IR (KBr) 3031, 2901, 1947, 1873, 1806, 1598, 1494, 1452, 1357, 1284, 1214, 1065, 907, 808, 741, 696, 657; ^{1}H NMR δ 7.49 (d, 2H, J=8.0, phenyl), 7.44-7.15 (m, 20H, benzyl), 7.02 (d, 2H, phenyl), 4.95-4.78 (m, 4H, 2×OC$\underline{H}_2$Ph), 4.72 (d, 1H, J_{gem}=10.5, OC$\underline{H}_2$Ph), 4.66-4.55 (m, 2H, OC$\underline{H}_2$Ph), 4.60 (d, 1H, $J_{1,2}$=9.0, H-1), 4.52 (d, 1H, J_{gem}=12.0, OC$\underline{H}_2$Ph), 3.80 (dd, 1H, $J_{6,6'}$=11.0, $J_{6,5}$=2.0, H-6), 3.77-3.58 (m, 3H, H-3, H-4, H-6'), 3.48 (m, 2H, $J_{2,3}$=9.0, H-2, H-5), 2.30 (s, 3H, methyl); ^{13}C NMR δ 138.37–127.51 (aromatic), 87.62 (C-1), 86.75, 80.76, 79.04, 77.79 (C-2, C-3, C-4 and C-5), 75.81, 75.36, 75.03, 73.38, 69.01 (O$\underline{C}$H$_2$Ph, C-6), 21.10 (methyl).

Anal. Calcd for $C_{41}H_{42}O_5S$ (646.84): C, 76.13; H, 6.54; O, 12.37; S, 4.96. Found: C, 75.98; H, 6.58; O, 12.43; S, 5.22.

***p*-Methoxyphenyl 2, 3, 4, 6-Tetra-*O*-benzyl-1-thio-β-D-glucopyranoside (9).** To a magnetically stirred solution of **8**[15] (1.8 g, 6 mmol) in DMF (60 mL) was slowly added sodium hydride (1.44 g) and the resulting reaction mixture kept 15 min at room temperature. Benzyl bromide (4.3 mL) was then added dropwise and the reaction mixture heated at 80 °C for 22 h. After cooling at room temperature, methanol (5 mL) was added, the solution concentrated and the residue dissolved in ether (60 mL) and water (60 mL). After separation of the organic layer, the aqueous phase was extracted with ether (2×60 mL) and the combined organic phases dried (sodium sulfate) before being concentrated. The resulting solid was chromatographed on silica gel using a mixture of hexane-ethyl acetate (95:5) as the eluent to afford pure **9** (3.1 g, 78%). The analytical sample was recrystallized from ethanol: mp 79-80 °, $[\alpha]_D^{20}$ -6° (*c* 2.5, chloroform); IR (KBr) 3032, 2901, 1591, 1493, 1453, 1400, 1358, 1285, 1244, 1066, 908, 831, 744, 697, 659, 641; ^{1}H NMR δ 7.54 (d, 2H, phenyl), 7.45-7.17 (m, 20H, benzyl), 6.74 (d, 2H, phenyl), 4.94-4.78 (m, 4H, 2×OCH$_2$Ph), 4.73 (d, 1H, J_{gem}=10.5, OC$\underline{H}_2$Ph), 4.65-4.49 (m, 4H, $J_{1,2}$=9.5, H-1, OC$\underline{H}_2$Ph), 3.78 (dd, 1H, $J_{6,6'}$=11.0, $J_{6,5}$=2.0, H-6), 3.75 (s, 3H, OCH$_3$), 3.73-3.57 (m, 3H, H-3, H-4, H-6'), 3.45 (m, 2H, H-2, H-5); ^{13}C NMR δ 159.68 (phenyl), 138.36–138.09 and 128.41–127.51 (aromatic), 135.12 (phenyl), 123.42 (phenyl), 114.37 (phenyl), 87.85 (C-1), 86.73, 80.70, 78.95, 77.80 (C-2, C-3, C-4 and C-5), 75.79, 75.32, 75.01, 73.39, 69.05 (O$\underline{C}$H$_2$Ph, C-6), 55.25 (OCH$_3$).

Anal. Calcd for $C_{41}H_{42}O_6S$ (662.85): C, 74.29; H, 6.39; O, 14.48; S, 4.84. Found: C, 74.29; H, 6.31; O, 14.43; S, 4.87.

2, 4, 6-Trimethoxythiophenol (41). A 1M solution of *n*-butyllithium in hexane (40.5 mL) was added dropwise to a magnetically stirred solution of 1,3,5-trimethoxybenzene in hexane (120 mL) and freshly distilled *N,N,N',N'*-tetramethylenediamine (9.4 mL) heated under reflux. After 2 h sulfur powder (1.9 g) was added in three portions every 20 min and the reaction mixture refluxed for 3 more h. After cooling to room temperature, water (400 mL) was added and the resulting mixture stirred for 30 min before being filtered to afford a polysulfide (0.566 g). The two phases of the filtrate were separated and the organic phase extracted with a 5% aqueous solution of sodium hydroxyde (2×200 mL). The combined aqueous phases were acidified with hydrochloric acid and extracted with dichloromethane (3×250 mL). The dichloromethane extracts were dried (sodium sulfate) and concentrated to afford crude **41** (9.144 g). To a suspension of the previously isolated polysulfide (0.566 g) and zinc powder (1.31 g) in magnetically stirred toluene (11 mL) cooled to -15 °C was carefully added 12N hydrochloric acid (13.2 mL). The reaction mixture was stirred until complete dissolution of the zinc powder. The organic phase was separated, washed with water (3×25 mL), dried (sodium sulfate) and concentrated to afford another crop of **41** (0.537 g). Chromatography on silica gel of the combined two fractions using hexane-ether (95:5 v/v) as the eluent afforded pure **41** (5.78 g, 49%). The analytical sample was crystallized from cyclohexane: mp 59-60 °C (lit[18] mp 58-59 °C); IR (KBr) 2999, 2941, 2836, 2606, 1746, 1719, 1592, 1467, 1341, 1207, 1130, 1049, 952, 877, 804, 783, 711, 672, 624; ^{1}H NMR δ 6.17 (s, 2H, H-3, H-5), 3.88 (s, 6H, 2×OCH_3), 3.80 (s, 3H, *p*-OCH_3), 3.77 (s, 1H, SH); ^{13}C NMR δ 158.60 (C-4), 156.06 (C-2, C-6), 92.73 (C-1), 91.02 (C-3, C-5), 56.01 (2×OCH_3), 55.40 (p-OCH_3).

2', 4', 6'-Trimethoxyphenyl 2, 3, 4, 6-Tetra-*O*-acetyl-1-thio-β-D-glucopyranoside (10). Sodium hydride (0.320 g) was added to a stirred solution of **41**[18] (1.76 g, 8.8 mmol) in DMF (40 mL). After 10 min at room temperature, a solution of 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide[19] (3.3 g, 8 mmol) in DMF (10 mL) was added dropwise. After 3 h the reaction mixture was concentrated and the residue dissolved in ether (100 mL) and water (100 mL). The organic layer was separated and the aqueous phase extracted with ether (2×100 mL). The combined ethereal phases were dried (sodium sulfate), concentrated and the residual solid chromatographed on silica gel using toluene-ether (8:2, v/v) as the eluent to yield pure **10** (3.10 g, 73%):mp 102 °C, $[\alpha]_D^{20}$ -10° (*c* 2.5, chloroform); ^{1}H NMR δ 6.14 (s, 2H, phenyl), 5.17 (t, 1H, $J_{3,2}$=9.0, $J_{3,4}$=9.0, H-3), 5.05 (t, 1H, $J_{4,5}$=9.0, H-4), 4.97 (dd, 1H, $J_{2,1}$=10.0, H-2), 4.60 (d, 1H, H-1), 4.21 (dd, 1H, $J_{6,6'}$=12.0, $J_{6,5}$=4.5, H-6), 4.06 (dd, 1H, $J_{6',5}$=2.0, H-6'), 3.83 (s, 9H, 3×OCH_3), 3.58 (m, 1H, H-5), 2.07, 2.02, 1.98 and 1.97 (4s, 12H, 4×$COCH_3$); ^{13}C NMR δ 170.59-169.34 (C=O), 162.58 (C-4'), 162.35 (C-2', C-6'), 98.10 (C-1'), 91.02 (C-3',

C-5'), 85.67 (C-1), 75.56, 74.30, 70.86 and 68.25 (C-2, C-3, C-4, C-5), 62.32 (C-6), 56.07 (o-OCH_3), 55.35 (p-OCH_3), 20.70-20.67 ($CO\underline{C}H_3$).

Anal. Calcd for $C_{23}H_{30}O_{12}S$ (530.55): C, 52.07; H, 5.70; O, 36.19; S, 6,04. Found: C, 52.21; H, 5.83; O, 36.06; S, 5.79.

2', 4', 6'-Trimethoxyphenyl 1-Thio-β-D-glucopyranoside (11). A catalytic amount of sodium methoxide was added to a solution of compound **10** (2.98 g, 5.6 mmol) in methanol (30 mL). After 3 h at room temperature the solution was neutralized with Dowex 50×8 [H^+], filtered and concentrated to yield crude **11** which was crystallized from ethanol (1.9 g, 91%): mp 165-166 °C, $[\alpha]_D^{20}$ -20° (*c* 1, methanol); IR (KBr) 3384, 3002, 2935, 2836, 1580, 1465, 1408, 1331, 1224, 1158, 1127, 949, 874, 811, 781; ^1H NMR (CD_3OD) δ 6.14 (s, 2H, H-3', H-5'), 4.17 (d, 1H, $J_{1,2}$=9.5, H-1), 3.72 (s, 6H, 2× o-OCH_3), 3.69 (s, 3H, *p*-OCH_3), 3.62 (dd, 1H, $J_{6,6'}$=12.0, $J_{6,5}$=2.0, H-6), 3.41 (dd, 1H, $J_{6',5}$=5.5, H-6'), 3.26-3.11 (m, 2H, H-3, H-4), 3.04 (m, 1H, H-5), 2.92 (t, 1H, $J_{2,3}$=9.5, H-2); ^{13}C NMR (CD_4O) δ 164.40 (C-4'), 163.86 (C-2', C-6'), 98.42 (C-1'), 92.55 (C-3', C-5'), 89.36 (C-1), 82.15, 78.77, 74.24 and 71.36 (C-2, C-3, C-4, C-5), 63.08 (C-6), 56.74 (o-OCH_3), 55.95 (p-OCH_3).

Anal. Calcd for $C_{15}H_{22}O_8S$ (362.40): C, 49.71; H, 6.12; O, 35.32; S, 8.85. Found: C, 49.62; H, 6.10; O, 35.30; S, 8.78.

2', 4', 6'-Trimethoxyphenyl 2,3,4,6-Tetra-*O*-benzyl-1-thio-β-D-glucopyranoside (12). Sodium hydride (0.48 g) was slowly added to a solution of **11** (0.72 g, 2 mmol) in DMF (20 mL). After 10 min at room temperature benzyl bromide (1.43 mL) was added dropwise and the reaction mixture heated at 80 °C for 10 h. After cooling to room temperature and subsequent addition of methanol (5 mL), the solution was concentrated and the residue dissolved in ether (60 mL) and water (60 mL). The ethereal phase was separated and the aqueous phase extracted with ether (3×60 mL). The combined organic phase was dried (sodium sulfate), concentrated and the residual solid chromatographed on silica gel using a mixture of hexane-ethyl acetate (0.97 g, 67%). The analytical sample was crystallized from ethanol: mp 92-93 °C, $[\alpha]_D^{20}$ +14° (*c* 1, chloroform); IR (KBr) 3030, 2902, 1579, 1496, 1454, 1409, 1334, 1226, 1128, 910, 807, 740, 697, 658; ^1H NMR (CD_3OD) δ 7.52-7.15 (m, 20H, aromatic, H-1'), 6.10 (s, 2H, H-3', H-5'), 5.14 (d, 1H, J=10.5, $OC\underline{H}_2Ph$), 4.91 (d, 1H, J=11.0, $OC\underline{H}_2Ph$), 4.87-4.75 (m, 3H, $OC\underline{H}_2Ph$), 4.68 (d, 1H, $J_{1,2}$=9.5, H-1), 4.56 (d, 1H, J=11.0, $OC\underline{H}_2Ph$), 4.48-4.33 (m, 2H, $OC\underline{H}_2Ph$), 3.78 (s, 6H, 2× o-OCH_3), 3.75 (s, 3H, *p*-OCH_3), 3.72-3.47 (m, 5H, H-2, H-3, H-4, H-6, H-6'), 3.37 (ddd, 1H, $J_{5,4}$=9.5, $J_{5,6}$=5.0, $J_{5,6'}$=1.5, H-5); ^{13}C NMR δ 162.12 (C-2', C-6'), 161.94 (C-4'), 138.51-138.02 and 128.35-127.39 (aromatic), 110.28 (C-1'), 91.05 (C-3', C-5'), 86.78 (C-1), 86.70, 82.43, 79.74 and 78.03 (C-2, C-3, C-4, C-5), 75.73, 75.17, 74.90, 73.56 and 69.52 ($OC\underline{H}_2Ph$, C-6), 56.08 (o-OCH_3), 55.22 (p-OCH_3).

Anal. Calcd for $C_{43}H_{46}O_8S$ (722.90): C, 71.45; H, 6.41; O, 17.71; S, 4.43. Found: C, 71.32; H, 6.48; O, 17.98; S, 4.46.

***p*-Methylphenyl 3, 4, 6-Tri-*O*-acetyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (14). 14** was prepared from 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranose[20] according to the procedure[8] described by R. J. Ferrier et al. and crystallized from ethanol (77%): mp 161-163 °C, $[\alpha]_D^{20}$ +42° (*c* 1, chloroform); IR (KBr) 3027, 2953, 1742, 1713, 1612, 1498, 1474, 1431, 1388, 1220, 1152, 1120, 1075, 1041, 979, 917, 890, 828, 797, 725; ^{1}H NMR δ 7.9-7.7 (m, 4H, phthalimido), 7.30 (d, 2H, J=8.5, phenyl), 7.18 (d, 2H, J=8.5, phenyl), 5.78 (dd, 1H, $J_{3,2}$=10.0, $J_{3,4}$=9.0, H-3), 5.65 (d, 1H, $J_{1,2}$=10.0, H-1), 5.12 (dd, 1H, $J_{4,5}$=10.0, H-4), 4.32 (t, 1H, H-2), 4.30 (dd, 1H, $J_{6,6'}$=12.5, $J_{6,5}$=4.5, H-6), 4.20 (dd, 1H, $J_{6',5}$=2.5, H-6'), 3.88 (m, 1H, H-5), 2.33 (s, 3H, methyl), 2.12, 2.04 and 1.85 (3×s, 9H, 3×$COCH_3$); ^{13}C NMR δ 170.61-168.92 (C=O), 138.75 (phenyl), 134.88-123.67 (aromatic), 83.08 (C-1), 75.79, 71.61, 68.63 and 53.55 (C-2, C-3, C-4 and C-5), 62.15 (C-6), 21.16, 20.76, 20.60 and 20.40 ($CO\underline{C}H_3$ and CH_3).

Anal. Calcd for $C_{27}H_{27}NO_9S$ (541.58): C, 59.88; H, 5.02; O, 26.59; N, 2.59; S, 5.92. Found: C, 59.83; H, 5.01; O, 26.31; N, 2.59; S, 5.98.

***p*-Methoxyphenyl 2, 3, 4, 6-Tetra-*O*-benzoyl-1-thio-β-D-galactopyranoside (17).** To a solution of **16**[15] (1.67 g, 5.5 mmol) in pyridine (30 mL) containing a catalytic amount of DMAP was added benzoyl chloride (2.82 mL). After 12 h at room temperature, the reaction mixture was concentrated and the residue dissolved in dichloromethane (100 mL). The resulting solution was poured into a stirred aqueous solution saturated with potassium hydrogencarbonate. After one hour the organic phase was separated and the aqueous phase reextracted with dichloromethane (2×100 mL). The combined organic phases were washed with water, dried (magnesium sulfate) and concentrated to afford a solid which was crystallized from ethanol (3.45 g, 87%): mp 143-145°C, $[\alpha]_D^{20}$ +47° (*c* 1, chloroform); IR (KBr) 3061, 2956, 2837, 1724, 1599, 1494, 1451, 1396, 1346, 1314, 1258, 1174, 1095, 1025, 936, 912, 884, 855, 820, 718; ^{1}H NMR δ 8.08-7.35 (m, 20H, aromatic), 7.23 (d, 2H, J=8.5, phenyl), 6.85 (d, 2H, J=8.5, phenyl), 5.98 (d, 1H, $J_{4,3}$=3.5, H-4), 5.71 (t, 1H, $J_{2,1}$=10.0, $J_{2,3}$=10.0, H-2), 5.57 (dd, 1H, H-3), 4.90 (d, 1H, H-1), 4.65 (m, 1H, H-5), 4.38 (m, 2H, H-6, H-6'), 3.83 (s, 3H, OCH_3); ^{13}C NMR δ 165.49-165.23 (C=O), 160.44 ($\underline{C}$-OCH_3), 137.36-128.23 (aromatic), 133.22 (phenyl), 120.25 (phenyl), 114.27 (phenyl), 85.32 (C-1), 74.86, 73.09, 68.22 and 67.71 (C-2, C-3, C-4 and C-5), 62.38 (C-6), 55.21 (OCH_3).

Anal. Calcd for $C_{41}H_{34}O_{10}S$ (718.78): C, 68.51; H, 4.77; S, 4.46. Found: C, 68.04; H, 4.79; S, 4.82.

***p*-Methoxyphenyl 2, 3, 4, 6-Tetra-*O*-benzyl-1-thio-β-D-galactopyranoside (18).** Sodium hydride (3.84g) was progressively added at room temperature to a magnetically

stirred solution of **16**[15] (4.83 g, 16 mmol) in DMF (80 mL). After one hour at room temperature benzyl bromide (10.7 mL) was added dropwise and the reaction mixture kept for one night at room temperature. Methanol (10 mL) was then added, the reaction mixture was concentrated and the residue dissolved in ether (100 mL) and water (100 mL). The ethereal phase was separated and the aqueous solution washed with ether (2×100 mL). The combined organic extracts were washed with water (300 mL), dried (magnesium sulfate) and concentrated to yield a solid which crystallized from ethanol (8.7 g 82%): mp 109-110 °C, $[\alpha]_D^{20}$ -3° (*c* 1, chloroform); IR (KBr) 3031, 2861, 1588, 1493, 1455, 1242, 1085, 875, 830, 740, 699; ^{1}H NMR δ 7.52 (d, 2H, J=8.5, phenyl), 7.45-7.25 (m, 20H, aromatic), 6.72 (d, 2H, J=8.5, phenyl), 4.95 (d, 1H, J=11.5, OC$\underline{H}_2$Ph), 4.85-4.65 (m, 4H, OC$\underline{H}_2$Ph), 4.59 (d, 1H, OC$\underline{H}_2$Ph), 4.52 (d, 1H, $J_{1,2}$=9.5, H-1), 4.50-4.35 (m, 2H, OC$\underline{H}_2$Ph), 3.96 (d, 1H, $J_{4,3}$=2.5, H-4), 3.86 (t, 1H, $J_{2,3}$=9.5, H-2), 3.73 (s, 3H, OCH_3), 3.69-3.51 (m, 4H, H-3, H-5, H-6, H-6'); ^{13}C NMR δ 159.41 (C-OCH_3), 138.78-127.39 (aromatic), 134.61 (phenyl), 123.96 (phenyl), 114.29 (phenyl), 88.30 (C-1), 84.22, 77.26, 77.14 and 73.54 (C-2, C-3, C-4 and C-5), 75.58, 74.33, 73.54, 72.65 and 68.74 (O$\underline{C}H_2$Ph, C-6).

Anal. Calcd for $C_{41}H_{42}O_6S$ (662.85): C, 74.29; H, 6.39; O, 14.48; S, 4.84. Found: C, 74.16; H, 6.35; O, 14.20; S, 4.62.

***p*-Methoxyphenyl 2, 3, 4-Tri-*O*-acetyl-1-thio-α and β-L-fucopyranoside (19α) and (19β).** A mixture of compounds **19α** and **19β** were prepared from tetra-*O*-acetyl-β-L-fucopyranose[21] (5.06 g, 15 mmol) according to the procedure[8] described by Ferrier et al.. The resulting oily mixture was chromatographed on silica gel using a mixture of hexane-ethyl acetate (8:2 v/v) as the eluent to afford successively the β anomer **19β** (4.12 g, 66%) and the α anomer **19α** (0.92 g, 15%).

19α: oil, $[\alpha]_D^{20}$ -242° (*c* 1, dichloromethane); ^{1}H NMR δ 7.35 (d, 2H, J=8.5, phenyl), 6.84 (d, 2H, J=8.5, phenyl), 5.74 (d, 1H, $J_{1,2}$=3.5, H-1), 5.38-5.27 (m, 3H, H-2, H-3, H-4), 4.64 (m, 1H, J_{5,CH_3}=6.5, $J_{5,4}$=1.0, H-5), 3.79 (s, 3H, OCH_3), 2.16, 2.11 and 2.01 (3×s, 9H, 3×$COCH_3$), 1.13 (d, 3H, CH_3); ^{13}C NMR δ 170.38, 170.06 and 169.77 (C=O), 159.67 (phenyl), 134.88, 122.88 and 114.58 (phenyl), 86.39 (C-1), 70.82, 68.47, 68.15 and 65.11 (C-2, C-3, C-4 and C-5), 55.15 (OCH_3), 20.74, 20.54 and 20.46 ($CO\underline{C}H_3$), 15.69 (CH_3).

Anal. Calcd for $C_{19}H_{24}O_8S$ (412.46): C, 55.33; H, 5.87; S, 7.77. Found: C, 55.21; H, 5.60; S, 7.59.

19β: oil, $[\alpha]_D^{20}$ -8° (*c* 1, dichloromethane); IR (neat oil) 2985, 2940, 2838, 1754, 1745, 1593, 1494, 1463, 1442, 1369, 1286, 1246, 1224, 1174, 1159, 1084, 1056, 1031, 916, 830; ^{1}H NMR δ 7.48 (d, 2H, J=8.5, phenyl), 6.86 (d, 2H, J=8.5, phenyl), 5.23 (d, 1H, $J_{4,3}$=3.0, H-4), 5.16 (t, 1H, $J_{2,1}$=10.0, $J_{2,3}$=10.0, H-2), 5.02 (dd, 1H, H-3), 4.55 (d,

1H, H-1), 3.81 (s, 3H, OCH_3), 3.78 (q, 1H, J_{5,CH_3}=6.5, H-5), 2.12, 2.11 and 1.97 (3×s, 9H, 3×$COCH_3$), 1.21 (d, 3H, CH_3); ^{13}C NMR δ 170.56, 170.10 and 169.45 (C=O), 160.02, 135.59, 122.51 and 114.26 (phenyl), 86.90 (C-1), 72.99, 72.42, 70.28 and 67.33 (C-2, C-3, C-4 and C-5), 55.25 (OCH_3), 20.88 and 20.61 ($CO\underline{C}H_3$), 16.40 (CH_3).

Anal. Calcd for $C_{19}H_{24}O_8S$ (412.46): C, 55.33; H, 5.87; S, 7.77. Found: C, 55.84; H, 5.90; S, 7.65.

***p*-Methoxyphenyl 1-Thio-β-L-fucopyranoside (20).** To a methanolic solution of **19β** (3.51 g, 8.52 mmol) was added a catalytic amount of sodium methoxide After 1 hour at room temperature the solution was neutralized with Dowex 50×8 [H^+], filtered and concentrated. The resulting solid was crystallized from ethanol (2.07 g, 85%): mp 137-138°C, $[\alpha]_D^{20}$ +59° (*c* 1, methanol); ^1H NMR (CD_3OD) δ 7.50 (d, 2H, J=8.5, phenyl), 6.86 (d, 2H, J=8.5, phenyl), 4.36 (d, 1H, $J_{1,2}$=9.5, H-1), 3.77 (s, 3H, OCH_3), 3.62 (dd, 1H, $J_{4,3}$=3.0, $J_{4,5}$=1.0, H-4), 3.58 (dq, 1H, J_{5,CH_3}=6.5, H-5), 3.50 (t, 1H, $J_{2,3}$=9.0, H-2), 3.45 (dd, 1H, H-3), 1.24 (d, 3H, CH_3); ^{13}C NMR (CD_4O) δ 161.18, 135.89, 125.42 and 115.34 (phenyl), 90.96 (C-1), 76.46, 75.96, 73.10 and 70.79 (C-2, C-3, C-4 and C-5), 55.75 (OCH_3), 17.02 (CH_3).

Anal. Calcd for $C_{13}H_{18}O_5S$ (286.35): C, 54.53; H, 6.34; O, 27.94; S, 11.20. Found: C, 54.46; H, 6.39; O, 27.88; S, 11.01.

***p*-Methoxyphenyl 2, 3, 4-Tri-*O*-benzyl-1-thio-β-L-fucopyranoside (21).** To a solution of **20** (1.72 g, 6 mmol) in DMF (30 mL) was added sodium hydride (1.08 g). After 30 min at room temperature benzyl bromide (3 mL) was added dropwise and the resulting reaction mixture stirred for 4 h at room temperature. Methanol (5 mL) was then added, the solution concentrated and the residue dissolved in ether (50 mL) and water (50 mL). The organic phase was separated and the aqueous phase extracted with ether. The combined organic phases were washed with water (150 mL), dried (magnesium sulfate) and concentrated to afford a solid which was chromatographed on silica gel using a mixture of hexane-ethyl acetate (9:1, v/v) as the eluent. Pure **21** (3.0 g, 90%) was obtained as a white solid. The analytical sample was crystallized from hexane-ethyl acetate: mp 80-82 °C, $[\alpha]_D^{20}$ +3° (*c* 1, chloroform); IR (KBr) 3030, 2895, 1593, 1495, 1453, 1396, 1357, 1285, 1247, 1209, 1178, 1062, 1027, 1004, 875, 831, 798, 750; ^1H NMR δ 7.54 (d, 2H, J=8.5, phenyl), 7.45-7.26 (m, 15H, aromatic), 6.75 (d, 2H, phenyl), 4.99 (d, 1H, J=11.5, $OC\underline{H}_2Ph$), 4.84-4.61 (m, 5H, $OC\underline{H}_2Ph$), 4.48 (d, 1H, $J_{1,2}$=9.5, H-1), 3.85 (t, 1H, $J_{2,3}$=9.5, H-2), 3.76 (s, 3H, OCH_3), 3.62 (d, 1H, $J_{4,3}$=3.0, $J_{4,5}$=0, H-4), 3.58 (dd, 1H, H-3), 3.49 (q, 1H, J_{5,CH_3}=6.5, H-5), 1.25 (d, 3H, CH_3); ^{13}C NMR δ 159.37 (phenyl $\underline{C}$-OCH_3), 138.78-138.36 and 128.43-127.41 (aromatic), 134.64, 124.21 and 114.26 (phenyl), 88.14 (C-1), 84.59, 77.10, 76.54 and 74.49 (C-2, C-3, C-4 and C-5), 75.51, 74.98, 72.79 ($O\underline{C}H_2Ph$), 55.23 (OCH_3), 17.29 (CH_3).

Anal. Calcd for $C_{34}H_{36}O_5S$ (556.72): C, 73.35; H, 6.52; O, 14.37; S, 5.76. Found: C, 73.29; H, 6.76; O, 14.50; S, 5.62.

***n*-Propyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (36).** Compound **36** was electrochemically synthetized from compound **14** (0.542 g, 1 mmole) and 1-propanol (740 µL, 10 mmol). The reaction was performed at constant potential (1.55 V) using a woven carbon anode, a Pt cathode and lithium tetrafluoroborate as the supporting electrolyte in the presence of 3Å molecular sieves (1.7 g). After 4.5 h the reaction mixture was filtered, the filtrate concentrated and diluted with dichloromethane (50 mL). The organic phase was washed with an aqueous solution of potassium hydrogencarbonate (50 mL), water (50 mL), dried (magnesium sulfate) and concentrated. The residue was chromatographed on silica gel using a mixture of toluene-ether (8:2, v/v) as the eluent to afford pure **36** (0.404 g, 85%). The analytical sample was recrystallized from ethanol: mp 100-101 °C, $[\alpha]_D^{20}$ +22° (*c* 1, chloroform); IR (KBr) 2964, 1723, 1609, 1467, 1389, 1223, 1035, 900, 805, 727; ^{1}H NMR δ 7.90-7.70 (m, 4H, aromatic), 5.81 (dd, 1H, $J_{3,2}$=11.0, $J_{3,4}$=9.0, H-3), 5.39 (d, 1H, $J_{1,2}$=8.0, H-1), 5.20 (dd, 1H, $J_{4,5}$=10.0, H-4), 4.36 (dd, 1H, $J_{6,6'}$=12.0, $J_{6,5}$=4.5, H-6), 4.33 (dd, 1H, H-2), 4.17 (dd, 1H, $J_{6',5}$=2.5, H-6'), 3.88 (m, 1H, H-5), 3.80 (m, 1H, J=7.0 and 10.0, O-C<u>H</u>$_2$CH$_2$CH$_3$), 3.41 (m, 1H, O-C<u>H</u>$_2$CH$_2$CH$_3$), 2.20, 2.03 and 1.86 (3×s, 9H, 3×COCH$_3$), 1.45 (m, 2H, O-CH$_2$C<u>H</u>$_2$CH$_3$), 0.68 (t, 3H, J=7.0, O-CH$_2$CH$_2$C<u>H</u>$_3$); ^{13}C NMR δ 170.63, 170.05, 169.38 and 167.60 (C=O), 134.20, 131.18 and 123.43 (aromatic), 97.99 (C-1), 71.69, 70.65, 68.87 and 54.48 (C-2, C-3, C-4 and C-5), 71.60 (O-C<u>H</u>$_2$CH$_2$CH$_3$), 61.90 (C-6), 22.35 (O-CH$_2$C<u>H</u>$_2$CH$_3$), 20.62, 20.49 and 20.32 (CO<u>C</u>H3), 9.91 (O-CH$_2$CH$_2$C<u>H</u>$_3$).

Anal. Calcd for $C_{23}H_{27}O_{10}N$ (477.47): C, 57.86; H, 5.70; O, 33.51; N, 2.93. Found: C, 57.77; H, 5.48; O, 33.42; N, 2.71.

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