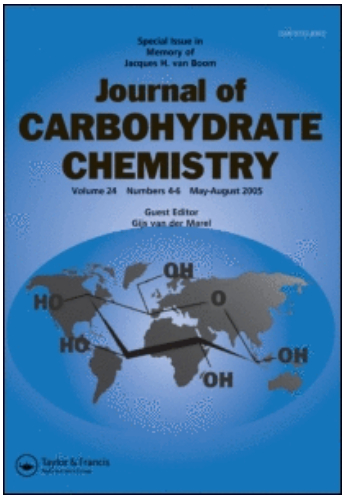

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Odorless Preparation of Thioglycosides and Thio-Michael Adducts of Carbohydrate Derivatives

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Odorless Preparation of Thioglycosides and Thio-Michael Adducts of Carbohydrate Derivatives

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A general, odorless, one-pot methodology has been developed for the preparation of 1,2-*trans*-thioglycosides and thio-Michael addition products of carbohydrate derivatives through triphenyl phosphine-mediated cleavage of disulfides and reaction of the thiolate formed *in situ* with glycosyl bromides and glycosyl conjugated alkenes.

Keywords Carbohydrate, Cleavage reactions, Thioglycosides, Conjugate addition, Triphenyl phosphine

INTRODUCTION

Glycosyl sulfides or thioglycosides have found versatile applications in the field of carbohydrate chemistry as very effective and stable glycosyl donors.[1] They are also useful intermediates for the preparation of glycosyl fluorides,[2] sulfoxides, and sulfones, which are used as glycosyl donors for *O*- and *C*-glycosylation.[3–5] There are a number of reports in the literature for the preparation of thioglycosides.[6] The most often employed protocol for thioglycoside preparation is the treatment of glycosyl acetates with alkyl/aryl thiols in the presence of a Lewis acid. These methods suffer from a number of drawbacks, such as the necessity of working with malodorous and toxic thiols and the formation of anomerized products.

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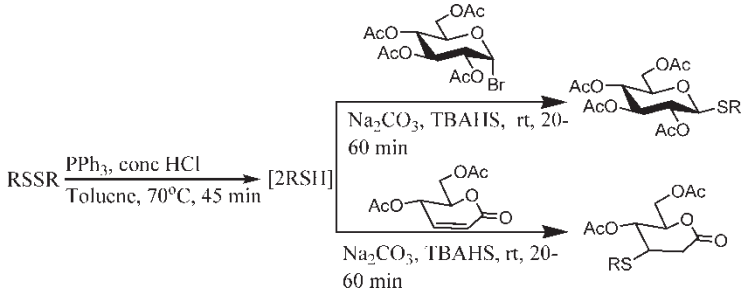
In another aspect, conjugate addition of thiols to the α,β-unsaturated carbonyl compounds derived from carbohydrates leads to various molecules of biological interest. In general, addition of thiols can be carried out either by activation of thiols with a base[7] or by activating the acceptor olefin with a Lewis acid.[8] In both cases, handling of toxic, malodorous thiols are major shortcomings.

Thus, there is a constant need to develop a suitable alternative reaction methodology in which toxic and malodorous thiols can be replaced by a less toxic and odorless thiolate source. The best alternative to the use of thiols is the cleavage of disulfides and subsequent reaction of thiolates with glycosyl halides or glycosyl conjugated carbonyl compounds. A few reports appeared for the cleavage of disulfides from our group and others, which include the use of $Zn/ZnCl_2$[9] or $RuCl_3$,[10] expensive and unstable indium(I) iodide,[11] reduction with $NaBH_4$,[12] or phosphines.[13] We wish to disclose here a facile cleavage of disulfides using triphenyl phosphine and subsequent reaction of thiolates with glycosyl halides to furnish thioglycosides and the addition of thiolates to the carbohydrate-derived conjugated alkenes in a one-pot reaction condition (Sch. 1).

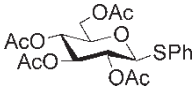
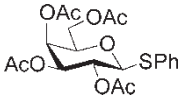
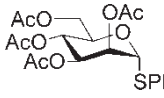
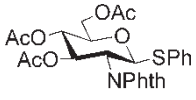
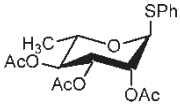
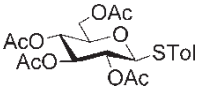
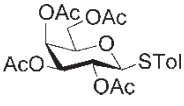
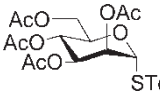
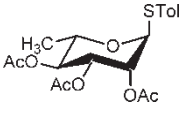
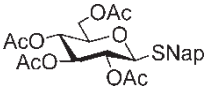
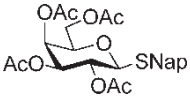
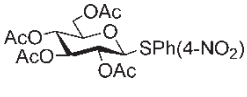
RESULTS AND DISCUSSION

In order to optimize the reaction conditions, an equimolar mixture of diphenyldisulfide and triphenylphosphine in toluene was stirred at 70°C in the presence of a few drops of conc. HCl. After complete consumption of disulfide in ca. 45 min, the reaction mixture cooled to rt and aq. satd. Na_2CO_3 solution was added followed by the addition of a catalytic amount of tetrabutylammonium hydrogen sulfate (TBAHS) and acetobromo-D-glucose (2.0 equiv). A clean formation of phenyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranoside was observed in 45 min by stirring the biphasic reaction mixture at rt. A series of experiments have revealed that a ratio of 1:1.1:2 (disulfide:triphenylphosphine: glycosyl halide) is ideal for the reaction to give high yield (Sch. 1, Table 1).



Scheme 1: PPh_3 promoted cleavage of disulfide and formation of thioglycosides and thio-Michael adducts.

Table 1: Triphenyl phosphine promoted cleavage of disulfides and preparation of thioglycosides in a one-pot reaction.

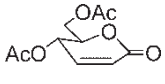
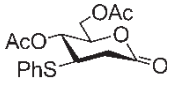
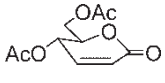
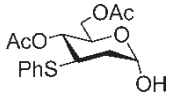
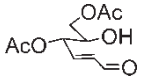
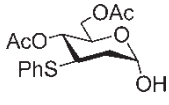
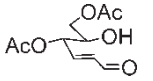
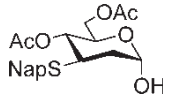
Entry	Disulfides	Substrate (a)	Product (b)	Yield (%)	Ref.
1	$(C_6H_5S)_2$	Acetobromo-D-glucose		90	(14)
2	$(C_6H_5S)_2$	Acetobromo-D-galactose		85	(15)
3	$(C_6H_5S)_2$	Acetobromo-D-mannose		88	(16)
4	$(C_6H_5S)_2$	Acetobromo-2-deoxy-2-phthalimido-D-glucose		85	(17)
5	$(C_6H_5S)_2$	Acetobromo-L-rhamnose		82	(18)
6	$((4\text{-}CH_3)C_6H_4S)_2$	Acetobromo-D-glucose		88	(19)
7	$((4\text{-}CH_3)C_6H_4S)_2$	Acetobromo-D-galactose		85	(19)
8	$((4\text{-}CH_3)C_6H_4S)_2$	Acetobromo-D-mannose		90	(19)
9	$((4\text{-}CH_3)C_6H_4S)_2$	Acetobromo-L-rhamnose		82	(19)
10	(2-Napthyl-S)$_2$	Acetobromo-D-glucose		85	—
11	(2-Napthyl-S)$_2$	Acetobromo-D-galactose		82	—
12	$((4\text{-}NO_2)C_6H_4S)_2$	Acetobromo-D-glucose		90	—

Following the generalized reaction condition, a series of thioglycosides were prepared in excellent yield. It is important to note that a scale-up reaction for the preparation of phenyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranoside has confirmed the applicability of this protocol on a 10-g scale without affecting the yield. It is also noteworthy that 1,2-*trans*-thioglycosides were formed exclusively, which were confirmed from the spectral studies of the crude products. Products of all known compounds gave acceptable ^{1}H NMR and ^{13}C NMR spectra that matched the data reported in the cited references.

After formation of the thiolates, 1,4-Michael addition was carried out adding a carbohydrate-derived conjugated ester or carbonyl compound to the reaction mixture. To our satisfaction, 1,4-thio adduct was formed in good yield in a few minutes using a ratio of 1:1.1:2.2 (disulfide:triphenylphosphine: glycosyl conjugated alkene). Following the protocol, a number of 3-thio-carbohydrate derivatives were prepared (Table 2).

In conclusion, a generalized efficient one-pot protocol has been demonstrated for the preparation of thioglycosides and thio-Michael addition products of carbohydrate-derived activated alkenes through triphenyl phosphine-mediated cleavage of disulfides. In contrast to the conventional use of obnoxious thiols for the preparation of thioglycosides and thio-Michael addition of thiols to conjugated alkene in the presence of strong alkali or at elevated temperature, where the yields are often lower due to disulfide formation of thiols, this protocol offers a novel alternative practical approach for the preparation of thioglycosides and β-keto sulfide derivatives of carbohydrates and have great promise for more useful applications in the carbohydrate synthesis.

Table 2: Triphenyl phosphine promoted cleavage of disulfides and conjugate addition to activated carbohydrate derivatives in a one-pot reaction.

Entry	Disulfides	Substrates (a)	Products (b)	Yield (%)
1	$(C_6H_5S)_2$			85
2	$((4\text{-}CH_3)C_6H_4S)_2$			82
3	$(C_6H_5S)_2$			78
4	(2-Napthyl-S)$_2$			80

EXPERIMENTAL

General Methods

All the reactions were monitored by thin-layer chromatography over silica gel-coated TLC plates. The spots on TLC were visualized by warming ceric sulphate (2% $Ce(SO_4)_2$ in 2 N H_2SO_4) sprayed plates in hot plate. Silica gel 230–400 mesh was used for column chromatography. ^1H and ^{13}C NMR were recorded on a Brucker Advance DPX 200 MHz using TMS as internal reference. Chemical shift value is expressed in δ ppm. Elementary analysis was carried out on a Carlo ERBA-1108 analyzer. Optical rotations were measured at 25°C on a Rudolf Autopol III polarimeter. Commercially available grades of organic solvents of adequate purity are used in many reactions.

Typical Reaction Protocol for the Preparation of Thioglycosides

To a solution of diaryl disulfide (1.0 mmol) and triphenyl phosphine (1.1 mmol) in toluene (3.0 mL) was added conc. HCl (three to four drops) and the reaction mixture was stirred at 70°C for 45 min. The reaction mixture was cooled to rt and satd. aq. Na_2CO_3 (2.0 mL) was added followed by TBAHS (0.1 mmol) and stirred at rt for 10 min. Glycosyl bromide (2.0 mmol) was added to the resulting biphasic reaction mixture and stirred for 45 min. After formation of thioglycosides (TLC), the reaction mixture was extracted with EtOAc (20 mL). The organic layer was washed with water, dried (Na_2SO_4), and concentrated under reduced pressure to furnish the crude product, which was further purified over SiO_2 using EtOAc-hexane (9:1 → 5:1) as eluant.

Typical Experimental Protocol for the Cleavage of Diaryl Disulfide and Subsequent Reaction with Activated Alkenes

Diaryl disulfide (1.0 mmol) was cleaved using triphenyl phosphine (1.1 mmol) as mentioned in the preparation of thioglycosides. After generation of thiolate, the reaction mixture was cooled and satd. aq. Na_2CO_3 (2.0 mL) was added followed by TBAHS (0.1 mmol) and stirred at rt for 10 min. Carbohydrate-derived activated alkene (2.2 mmol) was added to the resulting biphasic reaction mixture and stirred for 45 min. After formation of thioadduct (monitored by TLC), the reaction mixture was extracted with EtOAc (20 mL). The organic layer was washed with water, dried (Na_2SO_4), and concentrated under reduced pressure to furnish the crude product, which was further purified over SiO_2 using EtOAc-hexane (8:1) as eluant.

Spectral Data of Thioglycosides and Thio-Michael Adducts

Naphthyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranoside (entry 10, Table 1): White solid; m.p. 110–112°C; $[\alpha]_D$ −18.3 (*c* 1.2, $CHCl_3$); IR

(KBr): 1747, 1594, 1381, 1225, 1045 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 7.97 (bs, 1H), 7.82–7.73 (m, 3H), 7.56–7.45 (m, 3H), 5.19 (t, $J = 9.1$ Hz, 1H, H-2), 4.99 (t, $J = 9.6$ Hz each, 1H, H-3), 4.96 (t, $J = 9.5$ Hz each, 1H, H-4), 4.73 (d, $J = 9.9$ Hz, 1H, H-1), 4.21–4.10 (m, 2H, H-$6_{a,b}$), 3.73–3.65 (m, 1H, H-5), 2.10, 2.02, 2.0, 1.97 (4 s, 12H, 4 $COCH_3$); ^{13}C NMR (50 MHz, $CDCl_3$): δ 170.4, 170.1, 169.3, 169.1, 133.8, 133.3, 130.8, 129.0, 128.7, 128.1 (2C), 127.0 (2C), 126.9, 85.9, 76.3, 74.3, 70.4, 68.5, 62.3, 21.0, 20.9, 20.8 (2C); ESI-MS: m/z 513 $[M + Na]^+$; Anal. Calcd. for $C_{24}H_{26}O_9S$ (490): C, 58.77; H, 5.34; found C, 58.54; H, 5.58.

Naphthyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-galactopyranoside (entry 11, Table 1): White solid; m.p. 114–116°C; $[\alpha]_D$ +4.8 (c 1.2, $CHCl_3$); IR (KBr): 1743, 1592, 1375, 1224, 1043 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 7.99 (bs, 1 H), 7.82–7.74 (m, 3H), 7.57–7.44 (m, 3H), 5.36 (d, $J = 2.8$ Hz, 1H, H-4), 5.20 (t, $J = 9.8$ Hz each, 1H, H-2), 5.02 (dd, $J = 9.6$ and 3.2 Hz, 1H, H-3), 4.75 (d, $J = 9.7$ Hz, 1H, H-1), 4.19–4.06 (m, 2 H, H-$6_{a,b}$), 3.92–3.89 (m, 1H, H-5), 2.11, 2.03, 2.0, 1.96 (4 s, 12H, 4 $COCH_3$); ^{13}C NMR (50 MHz, $CDCl_3$): δ 170.7, 170.5, 170.4, 169.8, 133.8, 133.1, 132.3, 130.1, 129.9, 128.8, 128.1, 128.0, 127.0 (2C), 86.9, 74.9, 72.4, 67.7, 67.6, 62.1, 21.2, 21.0, 20.9 (2C); ESI-MS: m/z 513 $[M + Na]^+$; Anal. Calcd. for $C_{24}H_{26}O_9S$ (490): C, 58.77; H, 5.34; found C, 58.57; H, 5.55.

4-Nitrophenyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranoside (entry 12, Table 1): Yellow solid; m.p. 180–182°C; $[\alpha]_D$ −32.7 (c 1.2, $CHCl_3$); IR (KBr): 2923, 2368, 1753, 1344, 1220, 1042, 770 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 8.16 (d, $J = 8.9$ Hz, 2H), 7.59 (d, $J = 8.8$ Hz, 2H), 5.28 (t, $J = 9.2$ Hz, 1 H, H-3), 5.08 (t, $J = 9.7$ Hz, 1H, H-2), 5.04 (t, $J = 9.6$ Hz each, 1H, H-4), 4.89 (d, $J = 10.0$ Hz, 1H, H-1), 4.25–4.21 (m, 2H, H-$6_{a,b}$), 3.85–3.80 (m, 1H, H-5), 2.10, 2.08, 2.04, 2.0 (4 s, 12H, 4 $COCH_3$); ^{13}C NMR (50 MHz, $CDCl_3$): δ 170.2, 169.9, 169.2, 169.0, 147.6, 141.6, 131.7 (2C), 124.1 (2 C), 84.6, 76.6, 74.0, 70.0, 68.3, 62.2, 21.0, 20.9, 20.8 (2C); ESI-MS: m/z 508 $[M + Na]^+$; Anal. Calcd. for $C_{20}H_{23}NO_{11}S$ (485): C, 49.48; H, 4.78; found C, 49.25; H, 5.02.

4,6-Di-*O*-acetyl-2,3-dideoxy-3-thiophenyl-D-gluconolactone (entry 1, Table 2): Yellow oil; $[\alpha]_D$ +30 (c 1.2, $CHCl_3$); IR (Neat): 2929, 1747, 1669, 1372, 1224, 1048, 756 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 7.46–7.31 (m, 5 H, aromatic protons), 5.22–5.18 (dd, $J = 5.0$ and 3.2 Hz, 1H, H-4), 4.80–4.74 (dd, $J = 9.1$ and 4.2 Hz, 1H, H-5), 4.26–4.19 (m, 2H, H-$6_{a,b}$), 3.85–3.76 (m, 1H, H-3), 3.01–2.74 (m, 2H, H-$2_{a,b}$), 2.03 (s, 6H, 2 $COCH_3$); ^{13}C NMR (50 MHz, $CDCl_3$): δ 170.0, 169.7, 166.6, 133.7 (2C), 132.6, 129.8 (2C), 128.9, 77.6, 67.6, 63.2, 43.2, 33.9, 20.8 (2C); ESI-MS: m/z 361 $[M + Na]^+$; Anal. Calcd. for $C_{16}H_{18}O_6S$ (338): C, 56.79; H, 5.36; found: C, 56.60; H, 5.60.

4,6-Di-*O*-acetyl-2,3-dideoxy-3-thio-(4-methylphenyl)-D-gluconolactone (entry 2, Table 2): Yellow oil; $[\alpha]_D$ +32.7 (*c* 1.2, $CHCl_3$); IR (Neat): 3024, 2367, 1747, 1372, 1220, 1047, 763, 669 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 7.38–7.11 (m, 4H, aromatic protons), 5.20–5.16 (dd, $J = 5.0$ and 3.2 Hz, 1H, H-4), 4.78–4.72 (dd, $J = 9.1$ and 4.2 Hz, 1H, H-5), 4.24–4.20 (m, 2H, H-$6_{a,b}$), 3.76–3.67 (m, 1H, H-3), 2.94–2.70 (m, 2H, H-$2_{a,b}$), 2.35 (s, 3H, CH_3), 2.05, 2.03 (2 s, 6 H, 2 COCH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ 169.9, 169.7, 166.7, 135.2, 134.2 (2C), 130.5 (2C), 128.9, 77.6, 67.6, 63.2, 43.5, 33.8, 21.5, 20.9, 20.8; ESI-MS: *m/z* 375 $[M + Na]^+$; Anal. Calcd. for $C_{17}H_{20}O_6S$ (352): C, 57.94; H, 5.72; found: C, 57.70; H, 5.80.

4,6-Di-*O*-acetyl-2,3-dideoxy-3-thiophenyl-D-glucose (entry 3, Table 2): Yellow oil; $[\alpha]_D$ +31.5 (*c* 1.2, $CHCl_3$); IR (Neat): 2929, 1747, 1669, 1372, 1224, 1048, 756 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 7.44–7.25 (m, 5H, aromatic protons), 5.26 (bs, 1H, H-1), 4.96–4.83 (m, 1H, H-4), 4.18–3.95 (m, 3H, H-5, H-$6_{a,b}$), 3.65–3.57 (m, 1H, H-3), 2.22–1.77 (m, 2H, H-2), 2.05, 1.87 (2 s, 6 H, 2 COCH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ 170.9, 169.9, 143.4, 133.4 (2C), 129.2 (2C), 127.8, 91.38, 70.9, 69.4, 63.3, 43.7, 36.9, 21.1, 20.9; ESI-MS: *m/z* 363 $[M + Na]^+$; Anal. Calcd. for $C_{16}H_{20}O_6S$ (340): C, 56.46; H, 5.92; found: C, 56.70; H, 6.10.

4,6-Di-*O*-acetyl-2,3-dideoxy-3-(2-thionapthyl)-D-glucose (entry 4, Table 2): Yellow oil; $[\alpha]_D$ +35.4 (*c* 1.2, $CHCl_3$); IR (Neat): 2938, 2364, 1741, 1593, 1354, 1233, 1046, 749 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 7.98–7.47 (m, 7H, aromatic protons), 5.32 (bs, 1H, H-1), 5.07–5.0 (m, 1H, H-4), 4.25–4.10 (m, 2H, H-6a,b), 4.07–4.01 (m, 1H, H-5), 3.84–3.74 (m, 1H, H-3), 3.0 (bs, 1H, OH), 2.07–1.68 (m, 2H, H-2), 2.07, 1.82 (2 s, 6H, 2 COCH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ 171.0, 170.0, 133.9–126.7 (aromatic carbons), 91.3, 71.0, 69.4, 63.3, 43.7, 36.9, 21.1, 20.9; ESI-MS: *m/z* 413 $[M + Na]^+$; Anal. Calcd. for $C_{20}H_{22}O_6S$ (390): C, 61.52; H, 5.68; found: C, 61.35; H, 5.90.

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REFERENCES

[1] (a) Garegg, P.J. Thioglycosides as glycosyl donors in oligosaccharide synthesis. Adv. Carbohydr. Chem. Biochem. **1997**, *52*, 179–205; (b) Toshima, K.; Tatsuta, K. Recent progress in *O*-glycosylation methods and its application to natural products synthesis. Chem. Rev. **1993**, *93*, 1503–1531; (c) Kartha, K.P.R.; Field, R.A. Synthesis

and activation of carbohydrate donors: thioglycosides and sulfoxides. In *Best Synthetic Methods: Carbohydrates*; Osborn, H.M.I., Ed.; Academic Press: Oxford, UK, 2003, pp. 121–145.

[2] Nicolaou, K.C.; Dolle, R.E.; Papahatjis, D.P.; Randall, L.J. Reactions of glycosyl fluorides. Synthesis of *O*-, *S*-, and *N*-glycosides. J. Chem. Soc. Chem. Commun. **1984**, 1155–1156.

[3] Crich, D.; Sun, S. Direct synthesis of β-mannopyranosides by the sulfoxide method. J. Org. Chem. **1997**, *62*, 1198–1199.

[4] Yan, L.; Kahne, D. Generalizing glycosylation: synthesis of the blood group antigens Le^a, Le^b, and Le^x using a standard set of reaction conditions. J. Am. Chem. Soc. **1996**, *118*, 9239–9248.

[5] (a) Jaramillo, C.; Corrales, G.; Fernández-Mayoralas, A. Glycosyl phenyl sulfoxides as a source of glycosyl carbanions: stereoselective synthesis of C-fucosides-Tetrahedron Lett. **1998**, *39*, 7783–7786; (b) Vlahov, I.R.; Vlahova, P.I.; Linhardt, R.J. Diastereocontrolled synthesis of carbon glycosides of *N*-acetylneuraminic acid *via* glycosyl samarium(III) intermediates. J. Am. Chem. Soc. **1997**, *119*, 1480–1481.

[6] (a) Lönn, H. Synthesis of a tri- and a hepta-saccharide which contain α-L-fucopyranosyl groups and are part of the complex type of carbohydrate moiety of glycoproteins. Carbohydr. Res. **1985**, *139*, 105–114; (b) Pozsgay, V.; Jennings, H.J. A new, stereoselective synthesis of methyl 1,2-trans-1-thioglycosides. Tetrahedron Lett. **1987**, *28*, 1375–1376; (c) Driguez, H.; Szeja, W. Facile synthesis of 1,2-*trans*-nitrophenyl-1-thioglycopyranosides. Synthesis **1994**, 1413–1414; (d) Garcia-Lopez, J.J.; Hernandez-Mateo, F.; Isac-Garcia, J.; Kim, J.K.; Roy, R.; Santoyo-Gonzalez, F.; Vargas-Berenguel, A. Synthesis of perglycosylated β-cyclodextrins having enhanced lectin binding affinity. J. Org. Chem. **1999**, *64*, 522–531.

[7] (a) Perlmutter, P. *Conjugated Addition Reactions in Organic Synthesis*; Pergamon: Oxford, 1992, pp. 1–394; (b) Srivastava, N.; Banik, B.K. Bismuth nitrate-catalyzed versatile Michael reactions. J. Org. Chem. **2003**, *68*, 2109–2114; (c) Sebati, S.; Saber, A. Phosphate naturel et phosphate trisodique: nouveaux catalyseurs solides de la condensation de Knoevenagel en Milieu Hétérogène. Tetrahedron Lett. **1994**, *35*, 9399–9400.

[8] (a) da Silva, F.M.; Gomes, A.K.; Jones, J., Jr. Organic reaction in water. Part 2: Michael addition in water without phase transfer agents. Can. J. Chem. **1999**, *77*, 624–627; (b) Wabnitz, T.C.; Yu, J.-Q.; Spencer, J.B. A general, polymer-supported acid catalyzed hetero-Michael addition. Synlett **2003**, 1070–1072; (c) Bandini, M.; Cozzi, P.G.; Giacomini, M.; Melchiorre, P.; Selva, S.; Ronchi, A.U. Sequential one-pot $InBr_3$-catalyzed 1,4- then 1,2-nucleophilic addition to enones. J. Org. Chem. **2002**, *67*, 3700–3704.

[9] (a) Ranu, B.C.; Dey, S.S.; Hajra, A. Catalysis by an ionic liquid: efficient conjugate addition of thiols to electron deficient alkenes catalyzed by molten tetrabutylammonium bromide under solvent-free conditions. Tetrahedron **2003**, *59*, 2417–2421; (b) Yadav, J.S.; Reddy, B.V. S.; Baishya, G. Green protocol for conjugate addition of thiols to α/β-unsaturated ketones using a [Bmim]PF_6/H_2O system. J. Org. Chem. **2003**, *68*, 7098–7100.

[10] (a) Movassagh, B.; Shamsipoor, M. Zinc-mediated cleavage of diselenides: a novel synthesis of unsymmetrical diorganyl selenides in aqueous media. Synlett **2005**, 121–122; (b) Mukherjee, C.; Tiwari, P.; Misra, A.K. Synthesis of thio- and seleno-glycosides by cleavage of dichalconides in the presence of zinc/zinc chloride and reaction with glycosyl bromides. Tetrahedron Lett. **2006**, *47*, 441–445.

[11] Zhao, X.; Yu, Z.; Yan, S.; Wu, S.; Liu, R.; He, W.; Wang, L. Ruthenium(III) chloride catalyzed efficient synthesis of unsymmetrical diorganyl selenides via cleavage of dibenzyl and diphenyl diselenides in the presence of zinc. J. Org. Chem. **2005**, *70*, 7338–7341.

[12] Duane Brown, W. Reduction of protein disulfide bonds by sodium borohydride. Biochim. Biophys. Acta **1960**, *44*, 365–367.

[13] Overman, L.E.; Smoot, J.; Overman, J.D. The reduction of aryl disulfides with triphenylphosphine and water. Synthesis **1974**, 59–60.

[14] Agnihotri, G.; Tiwari, P.; Misra, A.K. One-pot synthesis of per-O-acetylated thioglycosides from unprotected reducing sugars. Carbohydr. Res. **2005**, *340*, 1393–1396.

[15] Khiar, N.; Martin-Lomas, M. A highly convergent synthesis of the tetragalactose moiety of the GPI anchor of the VSG of *Trypanosoma brucei*. J. Org. Chem. **1995**, *60*, 7017–7021.

[16] Martin-Lomas, M.; Khiar, N.; Garcia, S.; Koessler, J.-L.; Nieto, P.M.; Rademacher, T.W. Inositolphosphoglycan mediators structurally related to glycosyl phosphatidylinositol anchors: synthesis, structure and biological activity. Chem. Eur. J. **2000**, *6*, 3608–3621.

[17] Chowdhury, U.S. Synthesis of a versatile tetrasaccharide of sialyl Le^x and Le^x antigens. Tetrahedron **1996**, *52*, 12775–12782.

[18] Pozsgay, V.; Jennings, H.J. Synthetic oligosaccharides related to group B streptococcal polysaccharides. 3. Synthesis of oligosaccharides corresponding to the common polysaccharide antigen of group B streptococci. J. Org. Chem. **1988**, *53*, 4042–4052.

[19] Tai, A.-A.; Kulkarni, S.S.; Hung, S.-C. Facile $Cu(OTf)_2$-catalyzed preparation of per-*O*-acetylated hexopyranoses with stoichiometric acetic anhydride and sequential one-pot anomeric substitution to thioglycosides under solvent-free conditions. J. Org. Chem. **2003**, *68*, 8719–8722.