

This article was downloaded by:

On: 22 January 2011

Access details: *Access Details: Free Access*

Publisher *Taylor & Francis*

Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



## Journal of Carbohydrate Chemistry

Publication details, including instructions for authors and subscription information:

<http://www.informaworld.com/smpp/title~content=t713617200>

### Unprecedented Transformation of Thioglycosides to Their Corresponding 1-O-Acetates in the Presence of $\text{HClO}_4\text{-SiO}_2$

Geetanjali Agnihotri<sup>a</sup>; Pallavi Tiwari<sup>a</sup>; Anup Kumar Misra<sup>a</sup>

<sup>a</sup> Medicinal and Process Chemistry Division, Central Drug Research Institute, Lucknow, UP, India

**To cite this Article** Agnihotri, Geetanjali, Tiwari, Pallavi and Misra, Anup Kumar (2006) 'Unprecedented Transformation of Thioglycosides to Their Corresponding 1-O-Acetates in the Presence of  $\text{HClO}_4\text{-SiO}_2$ ', *Journal of Carbohydrate Chemistry*, 25: 6, 491 – 498

**To link to this Article:** DOI: 10.1080/07328300600860153

**URL:** <http://dx.doi.org/10.1080/07328300600860153>

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: <http://www.informaworld.com/terms-and-conditions-of-access.pdf>

This article may be used for research, teaching and private study purposes. Any substantial or systematic reproduction, re-distribution, re-selling, loan or sub-licensing, systematic supply or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

# Unprecedented Transformation of Thioglycosides to Their Corresponding 1-O-Acetates in the Presence of $\text{HClO}_4\text{-SiO}_2$ <sup>§</sup>

Geetanjali Agnihotri, Pallavi Tiwari, and Anup Kumar Misra

Medicinal and Process Chemistry Division, Central Drug Research Institute, Lucknow, UP, India

An unprecedented conversion of thioalkyl/aryl glycoside to the corresponding 1-O-acetates has been described using acetic anhydride and  $\text{HClO}_4\text{-SiO}_2$  at rt. Although this transformation does not play an important role in the oligosaccharide synthesis in comparison to its reverse transformation, this gives useful information in selecting the reaction condition for the synthesis of oligosaccharides. The yields were excellent in all cases.

**Keywords** Carbohydrate, Thioglycosides, Acetates, One-pot,  $\text{HClO}_4\text{-SiO}_2$

## INTRODUCTION

The role of carbohydrates in several biological processes is now well established. Although carbohydrates are naturally abundant, the limited supply of complex carbohydrates forced us to synthesize them chemically. A plethora of glycosylation techniques is now available in the literature using a wide range of glycosyl donors used in the glycosylation reactions.<sup>[1]</sup> Among several glycoside donors

---

Received March 23, 2006; accepted June 5, 2006.

<sup>§</sup>C.D.R.I. communication no. 6979.

Authors contributed equally to this work.

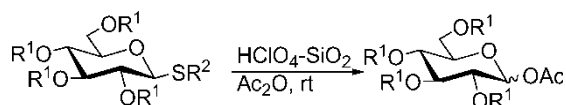
Address correspondence to Anup Kumar Misra, Medicinal and Process Chemistry Division, Central Drug Research Institute, Chattar Manzil Palace, Lucknow 226001, UP, India. E-mail: akmisra69@rediffmail.com

used in the oligosaccharide syntheses, thioglycosides are widely used because of their high degree of stability to many reaction conditions.<sup>[2]</sup> As in the case of thioglycosides, glycosyl-1-*O*-acetates<sup>[3]</sup> have also been used in several oligosaccharide syntheses. Besides their use as glycosyl donors under Lewis acid promoted glycosylation,<sup>[3]</sup> they find applications in the preparation of glycosyl halides.<sup>[4]</sup> Conventional method for the preparation of these compounds consists of a two-step reaction sequence, which includes removal of a temporary anomeric protecting group<sup>[5]</sup> (methyl, benzyl, allyl, trimethylsilylethyl, thioalkyl, thioaryl, etc.) followed by acetylation of the anomeric hydroxyl group. Although thioglycosides have widely been used as glycosyl donors for the successful outcome of several complex oligosaccharides, there are few reports on the unusual behavior of thioglycosides, which results in intermolecular aglycon transfer instead of formation of any glycosylated products.<sup>[6]</sup>

Recently we spent a considerable effort toward the development of more environmentally friendly catalysts for several important organic transformations.<sup>[7]</sup> During our study on the acetylation of carbohydrate derivatives using acetic anhydride and HClO<sub>4</sub> adsorbed on SiO<sub>2</sub> (HClO<sub>4</sub>-SiO<sub>2</sub>),<sup>[7a]</sup> we observed that in the case of thioglycosides, a clean substitution of anomeric thioalkyl or thioaryl group by an acetate group was taking place with time. In several circumstances, use of thioglycosides in the glycosylation reactions did not produce the expected glycosides in our hands although both donor and acceptor have been consumed during the reaction conditions. In order to add information about some unusual behaviors of thioglycosides, we sought to explore the use of HClO<sub>4</sub>-SiO<sub>2</sub> for the direct conversion of thioglycosides to the corresponding 1-*O*-acetylated carbohydrate derivatives. We herein disclose our finding on the direct conversion of thioglycoside to the glycosyl anomeric acetates using HClO<sub>4</sub>-SiO<sub>2</sub> without using any solvent.

## RESULTS AND DISCUSSION

As a model system, ethyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranoside was treated with acetic anhydride (1 mL/mmol of substrate) in the presence of HClO<sub>4</sub>-SiO<sub>2</sub> (50 mg/mmol of the substrate) at rt. An exothermic reaction started immediately and a quantitative yield of D-glucosepentaacetate was obtained in 20 min. After a series of experimentation, it was observed that use of 25 mg of HClO<sub>4</sub>-SiO<sub>2</sub> (0.012 mmol of HClO<sub>4</sub>) per mmol of thioglycoside in acetic anhydride (1 mL/mmol) at rt could result a clean formation of



**Scheme 1**

glycosyl 1-*O*-acetate in excellent yield (Sch. 1). In order to establish the reaction protocol, a series of differentially protected mono- and disaccharides have been treated under this reaction condition and the results are presented in Table 1. The reaction condition is equally effective for the replacement of thioaryl groups. It is noteworthy that 1,2-*cis* thioglycosides (entries 3 and 13, Table 1) also resulted in anomeric acetates in a similar fashion as it occurred in the case of 1,2-*trans* thioglycosides. Interglycoside linkages remain unaffected under the reaction condition. Pure product can be obtained by removal of the catalyst through filtration and evaporation of the solvent.

In summary, we are disclosing an unprecedented transformation of thioglycosides to their corresponding glycosyl 1-*O*-acetates using  $\text{HClO}_4\text{-SiO}_2$  very rapidly. Although this transformation is less important to the oligosaccharide synthesis as the glycosyl acetate is a less reactive donor than its thioglycoside counterpart, this could justify the failure of many glycosylation reactions using thioglycosides as donors. Above all, the reaction is very fast and proceeds well without requirement of any added solvent. This transformation will be considered to explain the unusual behavior of thioglycosides in the synthetic carbohydrate chemistry.

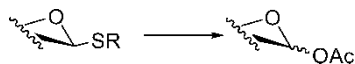
## EXPERIMENTAL

**General methods:** General methods are the same as used previously.<sup>[5d]</sup>

**Preparation of  $\text{HClO}_4\text{-SiO}_2$ :**  $\text{HClO}_4$  (1.8 g, 12.5 mmol, as a 70% aq solution) was added to a suspension of  $\text{SiO}_2$  (230–400 mesh, 23.7 g) in  $\text{Et}_2\text{O}$  (70.0 mL). The mixture was concentrated and the residue was heated at 100°C for 72 h under vacuum to furnish  $\text{HClO}_4\text{-SiO}_2$  (0.5 mmol/g) as a free-flowing powder. Caution!: Although no explosions were reported under these conditions, extreme care has to be exercised for large-scale reactions.

**Typical experimental procedure is as follows:** To a solution of thioglycosides (1.0 mmol) in acetic anhydride (1.0 mL) was added  $\text{HClO}_4\text{-SiO}_2$  (25 mg) and the reaction mixture was stirred at rt for an appropriate time (Table 1). After completion of the reaction (TLC), the reaction mixture was filtered through a celite bed and diluted with  $\text{CH}_2\text{Cl}_2$ . The organic layer was washed with satd. aq.  $\text{NaHCO}_3$  and water, and evaporated under reduced pressure to furnish crude glycosyl 1-*O*-acetates, which were further purified over  $\text{SiO}_2$  using hexane-EtOAc (1:1) as eluent.

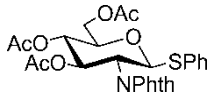
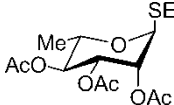
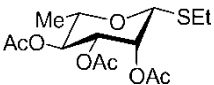
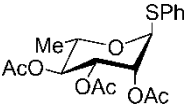
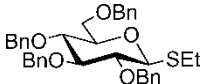
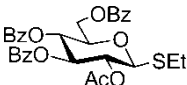
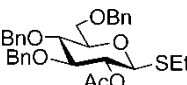
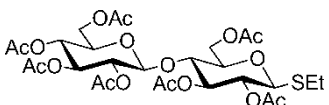
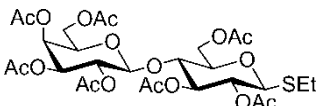
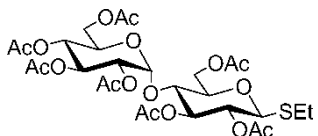
**1,2-Di-*O*-acetyl-3,4,6-tri-*O*-benzoyl- $\alpha$ -D-glucopyranose (entry 14, Table 1):** Yellow oil;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  8.04–7.90 (m, 6H, aromatic protons), 7.58–7.33 (m, 9H, aromatic protons), 6.46 (d,  $J = 3.3$  Hz, 1H, H-1), 6.01–5.95 (dd,  $J = 10.2$  and 9.9 Hz, 1H, H-3), 5.73–5.66 (dd,  $J = 9.9$  and 3.6 Hz, 1H,

**Table 1:** Direct conversion of thioglycosides to corresponding glycosyl 1-O-acetates using acetic anhydride and  $\text{HClO}_4\text{-SiO}_2$ .

Entry	Substrates	Time (min)	Yield (%)	$\alpha/\beta$	Ref
1		20	98	4:1	(8)
2		30	96	6:1	(8)
3		30	95	$\alpha$	(8)
4		30	96	5:1	(8)
5		20	96	6:1	(8)
6		30	95	6:1	(8)
7		30	95	5:1	(8)
8		15	95	6:1	(8)
9		20	92	$\alpha$	(8)
10		20	96	1:4	(9)

(continued)

Table 1: Continued.

Entry	Substrates	Time (min)	Yield (%)	$\alpha/\beta$	Ref
11		30	98	1:4	(9)
12		15	92	$\alpha$	(8)
13		25	90	$\alpha$	(8)
14		20	90	$\alpha$	(8)
15		10	90	8:1	(10)
16		15	95	$\alpha$	—
17		10	90	$\alpha$	—
18		30	96	5:1	(11)
19		30	95	4:1	(12)
20		30	96	4:1	(13)

Products of all known compounds gave acceptable  $^1\text{H}$  NMR spectra that matched data reported in the literature.

H-2), 5.41–5.36 (dd,  $J = 9.9$  and  $9.6$  Hz, 1H, H-4), 4.65 (d,  $J = 11.4$  Hz, 1H, H-6<sub>a</sub>), 4.49–4.38 (m, 2H, H-6<sub>b</sub> and H-5), 2.27, 1.95 (2 s, 6H, 2 COCH<sub>3</sub>). <sup>13</sup>C NMR (50 MHz, CDCl<sub>3</sub>):  $\delta$  169.6, 168.7, 166.0, 165.8, 165.2, 133.7–128.7 (aromatic carbons), 89.7, 70.7, 70.5, 69.8, 69.3, 62.8, 21.8, 20.7; IR (neat): 2961, 1756, 1724, 1648, 1599, 1451, 1376, 1271, 1231, 1097, 1067, 1026, 710 cm<sup>-1</sup>;  $[\alpha]_D^{25} +107.4^\circ$  (c 1.0, CHCl<sub>3</sub>); ESI-MS: 599 [M + Na]; Anal. calcd. for C<sub>31</sub>H<sub>28</sub>O<sub>11</sub> (576): C, 64.58; H, 4.90; found C, 64.35 H, 5.12.

**1,2-Di-O-acetyl-3,4,6-tri-O-benzyl- $\alpha$ -D-glucopyranose (entry 15, Table 1):**

Yellow oil; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  7.32–7.14 (m, 15 H, aromatic protons), 6.29 (d,  $J = 3.6$  Hz, 1H, H-1), 5.07–5.02 (dd,  $J = 9.3$  and  $3.6$  Hz, 1H, H-2), 4.85–4.78 (m, 6H, PhCH<sub>2</sub>), 4.01–3.95 (dd,  $J = 9.6$  and  $9.3$  Hz, 1H, H-3), 3.83–3.80 (m, 1H, H-4), 3.78–3.53 (m, 3H, H-5, H-6<sub>ab</sub>), 2.10, 2.07 (2 s, 6H, 2COCH<sub>3</sub>). <sup>13</sup>C NMR (50 MHz, CDCl<sub>3</sub>):  $\delta$  169.6, 169.3, 138.7–127.8 (aromatic carbons), 90.3, 80.3, 77.6, 77.5, 76.2, 75.6, 75.3, 72.5, 68.4, 21.2, 21.0; IR (neat): 2923, 2341, 1751, 1596, 1355, 1228, 1062, 754 cm<sup>-1</sup>;  $[\alpha]_D^{25} +164.1^\circ$  (c 1.0, CHCl<sub>3</sub>); ESI-MS: 557 [M + Na]; Anal. calcd. for C<sub>31</sub>H<sub>34</sub>O<sub>8</sub> (534): C, 69.65; H, 6.41; found C, 69.40; H, 6.60.

## ACKNOWLEDGEMENTS

Instrumentation facilities from SAIF, CDRI are gratefully acknowledged. G.A. and P.T. thank CSIR, New Delhi, for providing Senior Research Fellowships. This project was partly funded by Department of Science and Technology (DST), New Delhi (SR/FTP/CSA-10/2002), India.

## REFERENCES

- [1] (a) Dwek, R.A. Glycobiology: towards understanding the function of sugar. *Chem. Rev.* **1996**, *96*, 683–720; (b) Hanessian, S. *Preparative Carbohydrate Chemistry*; Hanessian, S., Ed.; Marcel Dekker: New York, **1996**, pp. 1–636.
- [2] (a) Norberg, T. In *Modern Methods in Carbohydrate Synthesis*; Khan, S.H., O'Neill, R.A., Eds.; *Frontiers in Natural Product Research Series*; Harwood Academic, **1995**; Vol. 1, Chapter 4, pp. 82–106; (b) Garegg, P.J. Thioglycosides as glycosyl donors in oligosaccharide synthesis. *Adv. Carbohydr. Chem. Biochem.* **1997**, *52*, 179–205.
- [3] (a) Kiso, M.; Anderson, L. The synthesis of disaccharides by the ferric chloride-catalyzed coupling of 2-acylamido-2-deoxy- $\beta$ -D-glucopyranose 1-acetates to protect sugar acceptors. *Carbohydr. Res.* **1979**, *72*, C15–C17; (b) Dahmen, J.; Frejd, T.; Magnusson, G.; Noori, G. Boron trifluoride etherate-induced glycosidation: formation of alkyl glycosides and thioglycosides of 2-deoxy-2-phthalimidoglycopyranoses. *Carbohydr. Res.* **1983**, *114*, 328–330; (c) Paulsen, H.; Paal, M. Lewissäure-katalysierte synthesen von di- und trisaccharid-sequenzen der O- und N-glycoproteine. Anwendung von trimethylsilyltrifluoromethanesulfonat. *Carbohydr. Res.* **1984**, *135*, 53–69.

- [4] (a) Scheurer, P.G.; Smith, F. Synthesis of acetobromo sugars. *J. Am. Chem. Soc.* **1954**, *76*, 3224–3224; (b) Jain, R.K.; Piskorz, C.F.; Chandrasekharan, E.V.; Matta, K.L. Synthesis of benzyl-*O*-(3-*O*-methyl- $\beta$ -D-galactopyranosyl)-(1  $\rightarrow$  3)-2-acetamido-2-deoxy- $\alpha$ -D-galactopyranoside and benzyl *O*-( $\beta$ -D-galactopyranosyl)-(1  $\rightarrow$  3)-2-acetamido-2-deoxy-6-*O*-methyl- $\alpha$ -D-galactopyranoside as specific acceptors for sialyltransferases. *Carbohydr. Res.* **1995**, *271*, 247–251; (c) Nishimura, S.I.; Kuzuhara, H. Synthesis of a peripheral trisaccharide sequence of lutropin, a pituitary glycoprotein hormone; use of chitobiose as a key starting material. *Carbohydr. Res.* **1990**, *206*, 207–217.
- [5] (a) Misra, A.K.; Basu, S.; Roy, N. Synthesis of the immunodominant trisaccharide related to the antigen from *E. coli* O126. *Synth. Commun.* **1996**, *26*, 2857–2862; (b) Zhang, Z.; Magnusson, G. Conversion of *p*-methoxyphenyl glycosides into the corresponding glycosyl chlorides and bromides, and into thiophenyl glycosides. *Carbohydr. Res.* **1996**, *295*, 41–55; (c) Jansson, K.; Frejd, T.; Kihlberg, J.; Magnusson, G. Boron trifluoride etherate as an effective reagent for the stereoselective one-pot conversion of acetylated 2-trimethylsilylethyl glycosides into sugar 1,2-*trans*-acetates. *Tetrahedron Lett.* **1986**, *27*, 753–756; (d) Misra, A.K.; Agnihotri, G. Chloramine-T-mediated chemoselective hydrolysis of thioglycosides into glycosyl hemiacetals under neutral conditions. *Carbohydr. Res.* **2004**, *339*, 885–890, and references cited therein.
- [6] (a) Leigh, D.A.; Smart, J.P.; Truscello, A.M. Intermolecular aglycon transfer of ethyl 1-thiorhamnopyranosides under Koenigs-Knorr and Helferich glycosylation conditions. *Carbohydr. Res.* **1995**, *276*, 417–424; (b) Belot, F.; Jacquinet, J. Intermolecular aglycon transfer of a phenyl 1-thiogalactosaminide derivative under trichloroacetimidate glycosylation conditions. *Carbohydr. Res.* **1996**, *290*, 79–86; (c) Yu, H.; Yu, B.; Wu, X.; Hui, Y.; Han, X. Synthesis of a group of diosgenyl saponins with combined use of glycosyl trichloroacetimidate and thioglycoside donors. *J. Chem. Soc., Perkin Trans. 1*, **2000**, 1445–1453; (d) Zhu, T.; Boons, G.-J. Intermolecular aglycon transfer of ethyl thioglycosides can be prevented by judicious choice of protecting groups. *Carbohydr. Res.* **2000**, *329*, 709–715.
- [7] (a) Misra, A.K.; Tiwari, P.; Madhusudan, S.K.  $\text{HClO}_4$ - $\text{SiO}_2$  catalyzed per-*O*-acetylation of carbohydrates. *Carbohydr. Res.* **2005**, *340*, 325–329; (b) Misra, A.K.; Tiwari, P.; Agnihotri, G. Ferrier rearrangement catalyzed by  $\text{HClO}_4$ - $\text{SiO}_2$ : synthesis of 2,3-unsaturated glycopyranosides. *Synthesis* **2005**, *2*, 260–266; (c) Tiwari, P.; Agnihotri, G.; Misra, A.K. Synthesis of 2,3-unsaturated C-glycosides by  $\text{HClO}_4$ - $\text{SiO}_2$  catalyzed Ferrier rearrangement of glycols. *Carbohydr. Res.* **2005**, *340*, 749–752; (d) Kumar, R.; Tiwari, P.; Maulik, P.R.; Misra, A.K.  $\text{HClO}_4$ - $\text{SiO}_2$  catalyzed chemoselective synthesis of acylals from aldehydes under solvent-free conditions. *J. Mol. Cat. A: Chemical* **2005**, *247*, 27–30; (e) Tiwari, P.; Misra, A.K. Selective removal of anomeric *O*-acetate groups in carbohydrates using  $\text{HClO}_4$ - $\text{SiO}_2$ . *Tetrahedron Lett.* **2006**, *47*, 3573–3576.
- [8] Tai, A.-A.; Kulkarni, S.S.; Hung, S.-C. Facile  $\text{Cu}(\text{OTf})_2$ -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.
- [9] Lemieux, R.U.; Takeda, T.; Chung, B.Y. In *Synthetic Methods for Carbohydrates*; El Khadem, H.S., Ed.; ACS Symposium Series, American Chemical Society, 1976; Vol. 39, 90–115.
- [10] Austin, P.W.; Hardy, F.E.; Buchanan, J.G.; Baddiley, J. 2,3,4,6-Tetra-*O*-benzyl-D-galactosyl chloride and its use in the synthesis of  $\alpha$  and  $\beta$ -D-galactopyranosides. *J. Chem. Soc.* **1965**, 1419–1424.



- [11] Bhaskar, P.M.; Loganathan, D. Per-*O*-acetylation of sugars catalysed by montmorillonite K-10. *Tetrahedron Lett.* **1998**, *39*, 2215–2218.
- [12] Chen, C.-T.; Kuo, J.-H.; Li, C.-H.; Barhate, N.B.; Hon, S.-W.; Li, T.-W.; Chao, S.-D.; Liu, C.-C.; Li, Y.-C.; Chang, I.-H.; Lin, J.-S.; Liu, C.-J.; Chou, Y.-C. Catalytic nucleophilic acyl substitution of anhydrides by amphoteric vanadyl triflate. *Org. Lett.* **2001**, *3*, 3729–3732.
- [13] Das, S.K.; Reddy, K.A.; Krovvidi, V.L.N.R.; Mukkanti, K. InCl<sub>3</sub> as a powerful catalyst for the acetylation of carbohydrate alcohols under microwave irradiation. *Carbohydr. Res.* **2005**, *340*, 1387–1392.