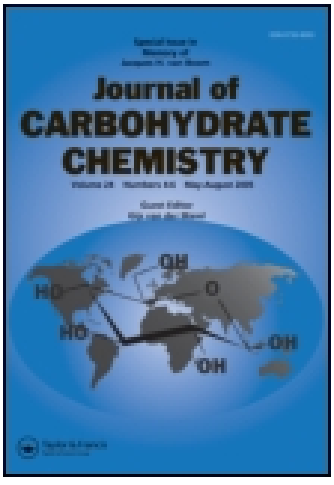

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Unprecedented Transformation of Thioglycosides to Their Corresponding 1-O-Acetates in the Presence of $HClO_4$-SiO_2

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Unprecedented Transformation of Thioglycosides to Their Corresponding 1-*O*-Acetates in the Presence of $HClO_4$-SiO_2[§]

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An unprecedented conversion of thioalkyl/aryl glycoside to the corresponding 1-*O*-acetates has been described using acetic anhydride and $HClO_4$-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, $HClO_4$-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.[1] Among several glycoside donors

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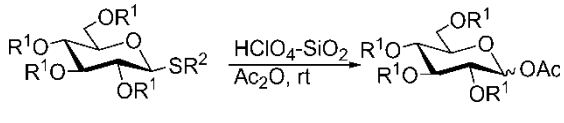
used in the oligosaccharide syntheses, thioglycosides are widely used because of their high degree of stability to many reaction conditions.[2] As in the case of thioglycosides, glycosyl-1-*O*-acetates[3] have also been used in several oligosaccharide syntheses. Besides their use as glycosyl donors under Lewis acid promoted glycosylation,[3] they find applications in the preparation of glycosyl halides.[4] Conventional method for the preparation of these compounds consists of a two-step reaction sequence, which includes removal of a temporary anomeric protecting group[5] (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.[6]

Recently we spent a considerable effort toward the development of more environmentally friendly catalysts for several important organic transformations.[7] During our study on the acetylation of carbohydrate derivatives using acetic anhydride and $HClO_4$ adsorbed on SiO_2 ($HClO_4$-SiO_2),[7a] 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 $HClO_4$-SiO_2 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 $HClO_4$-SiO_2 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 $HClO_4$-SiO_2 (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 $HClO_4$-SiO_2 (0.012 mmol of $HClO_4$) 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 occured 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 $HClO_4$-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

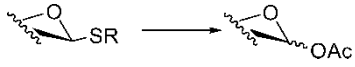
General methods: General methods are the same as used previously.[5d]

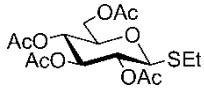
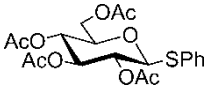
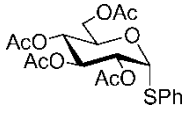
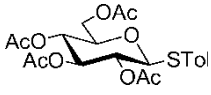
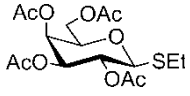
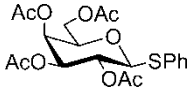
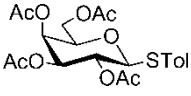
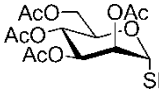
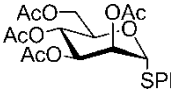
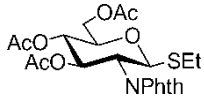
Preparation of $HClO_4$-SiO_2: $HClO_4$ (1.8 g, 12.5 mmol, as a 70% aq solution) was added to a suspension of SiO_2 (230–400 mesh, 23.7 g) in Et_2O (70.0 mL). The mixture was concentrated and the residue was heated at 100°C for 72 h under vacuum to furnish $HClO_4$-SiO_2 (0.5 mmol/g) as a free-flowing 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 $HClO_4$-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 CH_2Cl_2.The organic layer was washed with satd. aq. $NaHCO_3$ and water, and evaporated under reduced pressure to furnish crude glycosyl 1-*O*-acetates, which were further purified over SiO_2 using hexane-EtOAc (1 : 1) as eluent.

1,2-Di-*O*-acetyl-3,4,6-tri-*O*-benzoyl-α-D-glucopyranose (entry 14, Table 1): Yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 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,

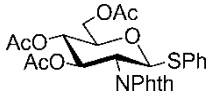
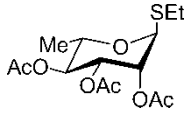
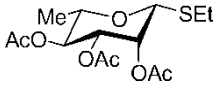
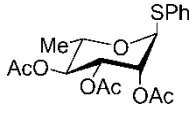
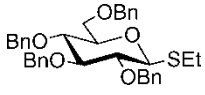
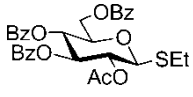
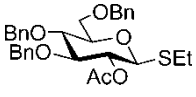
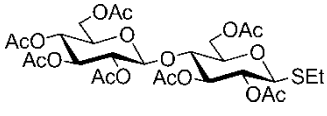
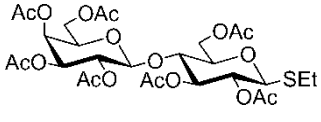
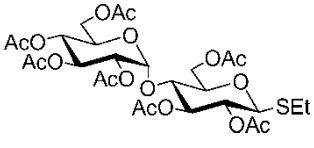
Table 1: Direct conversion of thioglycosides to corresponding glycosyl 1-*O*-acetates using acetic anhydride and $HClO_4$-SiO_2.



Entry	Substrates	Time (min)	Yield (%)	α/β	Ref
1		20	98	4:1	(8)
2		30	96	6:1	(8)
3		30	95	α	(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	α	(8)
10		20	96	1:4	(9)

(*continued*)

Table 1: Continued.

Entry	Substrates	Time (min)	Yield (%)	α/β	Ref
11		30	98	1:4	(9)
12		15	92	α	(8)
13		25	90	α	(8)
14		20	90	α	(8)
15		10	90	8:1	(10)
16		15	95	α	—
17		10	90	α	—
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}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_a), 4.49–4.38 (m, 2H, H-6_b and H-5), 2.27, 1.95 (2 s, 6H, 2 COCH_3). ^{13}C NMR (50 MHz, $CDCl_3$): δ 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^{-1}; $[\alpha]_D^{25}$ +107.4° (*c* 1.0, $CHCl_3$); ESI-MS: 599 [M + Na]; Anal. calcd. for $C_{31}H_{28}O_{11}$ (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-α-D-glucopyranose (entry 15, Table 1): Yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 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_2), 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_{ab}), 2.10, 2.07 (2 s, 6H, 2$COCH_3$). ^{13}C NMR (50 MHz, $CDCl_3$): δ 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^{-1}; $[\alpha]_D^{25}$ +164.1° (*c* 1.0, $CHCl_3$); ESI-MS: 557 [M + Na]; Anal. calcd. for $C_{31}H_{34}O_8$ (534): C, 69.65; H, 6.41; found C, 69.40; H, 6.60.

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