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Selective removal of anomeric O-acetate groups in carbohydrates using HCl04-Si02-tr

Pallavi Tiwari and Anup Kumar Misra.

Medicinal and Process Chemistry Division. Central Drug Research Institute, Chattar Manzil Palace, Lucknow
226 *00l, UP, India*

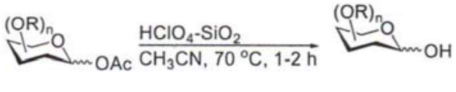
Abstract-A convenient methodology has been developed for the selective removal of the anomeric acyl group of carbohydrate derivatives using HCI04-Si02 under acidic reaction conditions. Anomeric benzoyl groups can also be removed selectively following similar reaction conditions. The yields were excellent in all cases.

Suitably protected I-hydroxy sugars or glycosyl hemiacetals are useful synthetic intermediates for the preparation of several glycosyl donors such as glycosyl trichloroacetimidates, I glycosyl l1uorides2 and iodides3 and glycosylation reactions towards the preparation of several bioactive molecules.4 Glycosyl hemiacetals have successfully been used in dehydrative glycosylations for the synthesis of several complex oligosaccharides.5 In general, protected glycosyl hemiacetals can be prepared by (a) deacetylation of glycosyl-I-O-acetates;6 (b) acid hydrolysis of alkyl glycosides;1 (c) hydrolysis of thioglycosides,8 etc. Conventional methods for anomeric O-deafetylation of per-O-acetylated carbohydrate derivatives suffer from several shortcomings, which include, the use of highly toxic reagents, for example, hydrazine acetate,6a and heavy metal salts, for example, bis(tributyltin)oxide,6b tributyltin methoxide6c and mercuric chloride/mercuric oxide.6d Although there are a number of environmentally benipn reagents (e.g., benz ylamine,6e sodium methoxide,6 ammonium salts,6g,h piperidine,6i Aho3,6j MgO,6k etc.) available for this transformation, most require longer reaction times leading to non selective de-O-acetylation and time-consuming purification steps. Therefore, the development of a metal-free, less-toxic reaction protocol, avoiding purification steps, would extend the scope of this transformation.

Recently, we have applied considerable effort towards the development of more environmentally benign catalysts for several important organic transformations.9

During our study on the Helferich glycosylation of per-O-acetylated sugars using HCI04 adsorbed on Si02,9b we observed that clean removal of the anomeric acetate group was taking place in each case instead of glycosylation. Taking cue from this observation, we explored the use of HCI04-Si02 for the anomeric deacetylation of I-O-acetylated carbohydrate derivatives. We herein disclose our findings on the anomeric de-O-acetylation of carbohydrates under acidic reaction conditions using HCI04-Si02 (Scheme I).

As a model system, per-O-acetylated ~-D-glucose was treated with HCI04-Si02 varying the quantity of catalyst and reaction solvent at 70°C. It was observed that use of 25 mg of HCI04-Si02 (0.012 mmol of HCI04) per mmol of per-O-acetylated ~-D-glucose in acetonitrile at 70°C resulted in clean formation of the hemiacetal in excellent yield without affecting other functional groups present in the substrate. In order to establish the reaction protocol, a series of protected mono- and disaccharides



Scheme I.

Keywords: Carbohydrate; Deacetylation; Acetates; HCIO~Si02; Hemiacetals.

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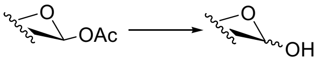
• Corresponding author. Tel.: +91 522 2612411 18; fax: +91 522 2623938; e-mail: akmisra69@redilfmail.com

Table 1. Anomeric de-O-acylation of carbohydrate derivatives using $HClO_4$–SiO_2



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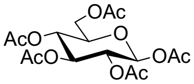
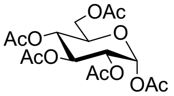
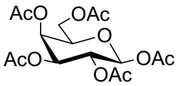
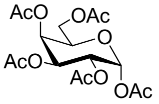
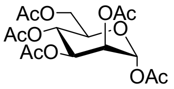
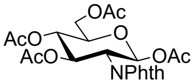
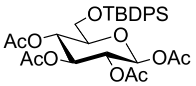
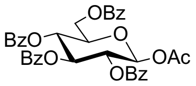
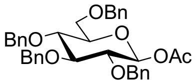
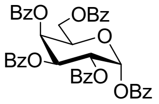
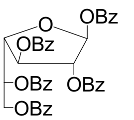
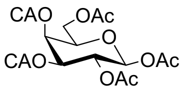
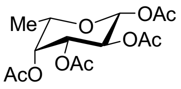
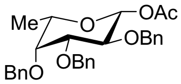
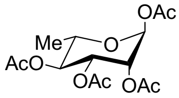
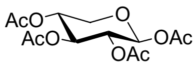
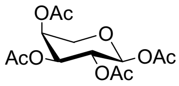
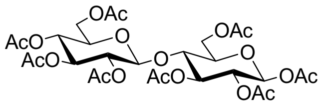
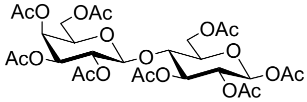
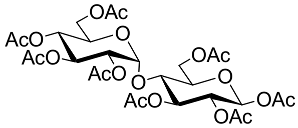
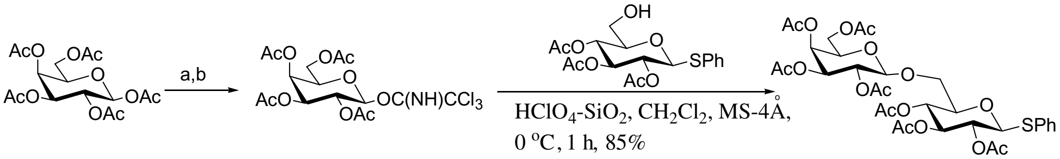
1		1.5	92	2:1
2		1.5	90	2:1
3		1.5	95	5:2
4		1.5	92	2:1
5		1.0	92	1:0
6		1.5	90	1:2
7		1.5	90	2:1
8		1.5	95	1:1
9		1.5	80	2:1
10		2.5	90	5:2
11		2.5	85	1:0
12		1.5	85	5:2
13		1.0	90	1:1
14		1.0	82	2:1
15		1.0	92	1:0
16		1.0	90	5:3
17		1.0	90	5:2
18		2.0	92	2:1
19		2.0	95	2:1
20		2.0	90	5:2

CAO: chloroacetyl group. All known compounds gave acceptable ^1H NMR spectra, which matched the data reported in the literature.

were subjected to the deacetylation conditions and the results are presented in Table 1. The reaction was equally effective for the removal of both α- and β-acetates. Anomeric benzoyl groups could also be removed in excellent yield using similar reaction conditions. Interglycoside linkages remained unaffected. Pure products could be obtained by removal of the catalyst by simple filtration and evaporation of the solvent. In order to justify the role of moisture present in the solvent in the anomeric deacylation, a parallel reaction was performed using distilled CH_3CN in place of commercial CH_3CN. In both cases the yields of the product and reaction times were almost similar indicating that the presence of moisture in the solvent did not have any effect on the reaction time and yield. No reaction or only very low yields of the product were obtained using other common apolar solvents, for example, CH_2Cl_2, $CHCl_3$, THF, etc. A typical experimental procedure is as follows: To a solution of 1-*O*-acetyl carbohydrate derivative (1.0 mmol) in CH_3CN (5 mL) was added $HClO_4$–SiO_2 (25 mg) and the reaction mixture was stirred at 70 °C for the appropriate time as mentioned in Table 1. After completion of the reaction (TLC), the reaction mixture was filtered through a Celite bed and washed with CH_2Cl_2 and the filtrate evaporated under reduced pressure to furnish the pure glycosyl hemiacetal. Although, the crude product was sufficiently pure, analytical samples were prepared by passing the crude reaction product through a short column of SiO_2. **Caution**: Although no explosions were reported under these conditions, extreme care has to be exercised for large-scale reactions using $HClO_4$–SiO_2. The generation of the catalyst should be performed with special care and in a safe environment.



Scheme 2. Reagents and conditions: (a) $HClO_4$–SiO_2, CH_3CN, 70 °C, 2 h, 95%; (b) CCl_3CN, K_2CO_3, CH_2Cl_2, 80%.

In order to verify the synthetic utility of our method in comparison to other reported protocols, peracetylated galactose was transformed into its hemiacetal, which was then converted to the trichloroacetimidate derivative using trichloroacetonitrile and K_2CO_3. The peracetylated galactosyltrichloroacetimidate thus obtained was further used in the glycosylation reaction using $HClO_4$–SiO_2 as the glycosylation activator[10] to prepare a novel disaccharide thioglycoside, which can be used as a disaccharide donor for the preparation of several oligosaccharides (Scheme 2).[11]

In summary, we have introduced a new method for the selective anomeric deacetylation or debenzoylation of carbohydrate derivatives under acidic reaction conditions. As the reaction does not require any toxic reagents and chromatographic purification, this environmentally benign reaction protocol should find application in synthetic organic chemistry.

Acknowledgements

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11. 1,2,3,4,6-Penta-*O*-acetyl-β-D-galactose (585 mg, 1.5 mmol) and $HClO_4$–SiO_2 (35 mg) were mixed in CH_3CN (5 mL) and stirred at 70 °C for 1.5 h. The reaction mixture was filtered through Celite, rinsed with CH_2Cl_2 and concentrated. To a mixture of the crude product (496 mg, 1.42 mmol) and CCl_3CN (570 μL, 5.68 mmol) in CH_2Cl_2 (5 mL) was added anhydrous K_2CO_3 (1.0 g) and the reaction mixture was stirred at room temperature for 3 h. After completion (TLC), the reaction mixture was filtered, rinsed with CH_2Cl_2, concentrated and passed through a short pad of SiO_2 to give per-*O*-acetylated galactosyl trichloroacetimidate (560 mg). To a mixture of per-*O*-acetylated galactosyl trichloroacetimidate (560 mg, 1.1 mmol) and phenyl 2,3,4-tri-*O*-acetyl-1-thio-β-D-glucopyranoside (398 mg, 1.0 mmol) in CH_2Cl_2 (5 mL) was added powdered MS-4 Å (500 mg) and the reaction mixture was stirred under Ar for 30 min at 0 °C. To the cooled reaction mixture was added $HClO_4$–SiO_2 (30 mg) and the reaction mixture was stirred at 0 °C for 1 h. After completion of the reaction (TLC), the reaction mixture was filtered through a Celite bed and washed with CH_2Cl_2. The organic layer was washed with satd aq $NaHCO_3$ and water, dried (Na_2SO_4) and concentrated. Column chromatography of the crude product over SiO_2 using hexane–EtOAc (3:1) furnished phenyl (2,3,4,6-tetra-*O*-acetyl-β-D-galacto-pyranosyl)-(1→6)-2,3,4-tri-*O*-acetyl-1-thio-β-D-glucopyranoside (618 mg, 85%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.48–7.32 (m, 5H, aromatic protons), 5.39–5.33 (dd, $J = 9.5$ and 2.4 Hz, 1H), 5.28 (d, $J = 7.9$ Hz, 1H), 5.21–5.17 (m, 1H), 5.15–5.02 (m, 1H),

5.00–4.80 (m, 3H), 4.73–4.65 (t, $J = 8.7$ Hz each, 1H), 4.54–4.48 (dd, $J = 8.8$ Hz, 8.8 Hz, 1H), 4.17–4.06 (m, 2H), 3.89–3.82 (m, 1H), 3.74–3.67 (m, 2H), 2.10, 2.08, 2.07, 2.06, 2.03, 1.98, 1.96 (7s, 21H, 7COCH_3); ^{13}C NMR (75 MHz, CDCl$_3$): δ 171.2, 170.6, 170.4, 170.0, 169.4 (2C), 168.9, 132.9–128.1 (aromatic carbons), 100.9, 85.4, 77.3, 76.6, 76.0, 73.7, 70.6, 69.0, 68.5, 68.3, 61.1, 60.7, 20.6 (2C), 20.5 (2C), 20.3 (2C), 20.0.