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Glycosylation and pyranose-furanose isomerization of carbohydrates using $HClO_4$-SiO_2: Synthesis of oligosaccharides containing galactofuranose [§]

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Abstract—A series of di- and trisaccharides containing galactofuranose were synthesized using $HClO_4$-SiO_2 catalyzed glycosylation and ring transformation for the conversion of galactopyranose to galactofuranose. Yields in glycosylations and ring transformation reactions were excellent.
Key words: Carbohydrate, galactofuranose, glycosylation, ring transformation, $HClO_4$-SiO_2.

Synthesis of oligosaccharides containing furanose units is a topic of increasing interest in the field of glycobiology. D-Galactofuranoside moieties are the constituents of many cell-wall polysaccharides of pathogenic bacterial[1] such as *Mycobacteria, Corynebacteria, Nocardia* and *Rhodococcus* and plants[2] such as *Aspergillus* and *Penicillium* as well as pathogenic protozoa such as *Trypanosoma cruzi* and certain *Leishmania* species and they were claimed to be immunodominant in many bacterial antigens[4]. Therefore, carbohydrate haptens containing furanosides moieties could be useful for designing bacterial cell-wall biosynthesis inhibitors as well as for the preparation of artificial carbohydrate antigens for vaccine generation. (1→6)-linked glycosyl galactofuranosides could be useful as cell-wall biosynthesis inhibitors of *Mycobacteria* and therefore can be evaluated for their potential as anti-mycobacterial agents. Although there are several reports on the synthesis of oligosaccharides having galactofuranose moiety, D-galactofuranose pentabenzoate[5] as donor has been utilized in most of cases. Synthesis of oligosaccharides containing galactofuranose has also been reported using acylic glycosyl donors[6] and *O*-pentenyl galactofuranoside derivatives.[7] We envisioned that $HClO_4$-SiO_2[8] catalyzed rearrangement of galactopyranose ring in the oligosaccharides into galactofuranose under acidic condition at elevated temperature could result the formation of oligosaccharides containing galactofuranose moiety.

Recently, we devoted a considerable effort towards the development of more environmentally benign catalyst for several important organic transformations.[8] Perchloric acid supported on silica ($HClO_4$-SiO_2)[9] has been successfully used by us and others in several carbohydrate transformation and glycosylation reactions.[8,10] In order to achieve biologically important carbohydrate haptens in a concise manner, we herein disclose a concise and practical approach for the synthesis of di- and trisaccharides containing galactofuranose at the reducing end applying $HClO_4$-SiO_2 as a versatile catalyst in the glycosylation reactions as well as ring transformations (Scheme 1).

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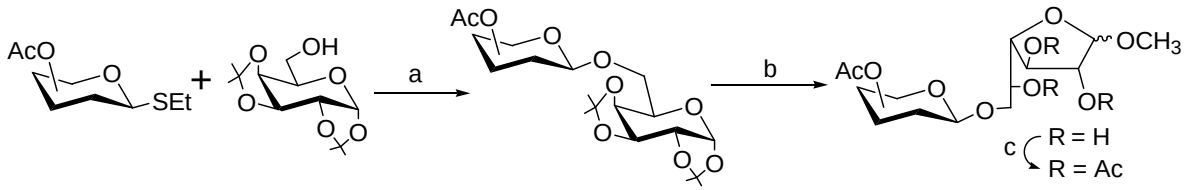
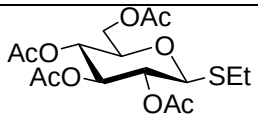
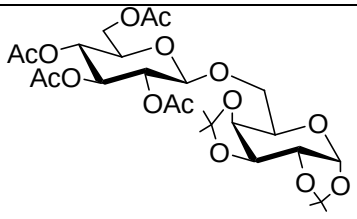
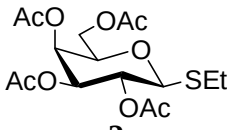
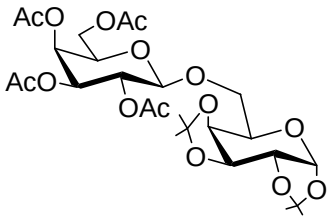
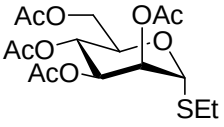
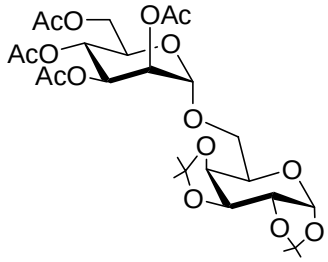
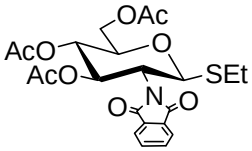
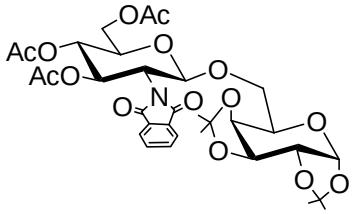
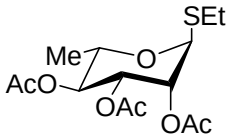
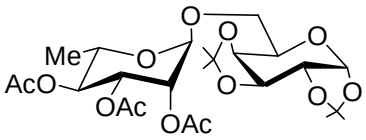
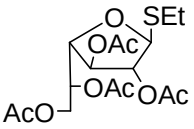
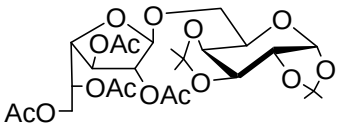
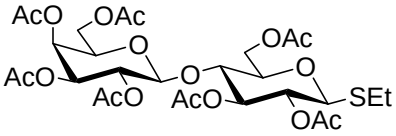
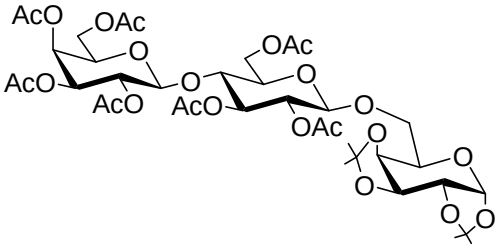
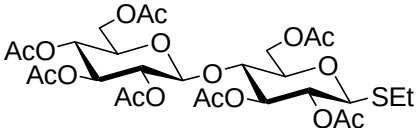
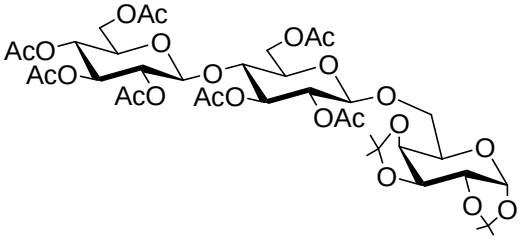


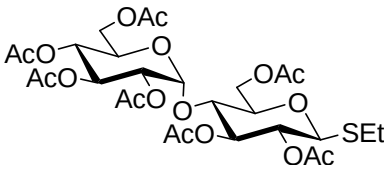
Scheme 1: Reagents: (a) *N*-iodosuccinimide, $HClO_4$-SiO_2, CH_2Cl_2, 0°C; (b) CH_3OH, $HClO_4$-SiO_2, CH_3CN, 70°C; (c) Acetic anhydride, $HClO_4$-SiO_2, CH_3CN, rt.

In order to synthesize a series of di- and trisaccharides containing D-galactopyranosyl moiety, 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose[11] was coupled with a series of mono- and disaccharide thioethylglycoside derivatives using a modified procedure involving *N*-iodosuccinimide (NIS) and $HClO_4$-SiO_2[10c] as glycosylation activator. The yields of glycosylated products were comparable with the products achieved following conventional NIS-TfOH procedure. The stereochemical outcome of the glycosylation reactions were confirmed by the NMR spectral data of the products (Table 1). Having achieved a number of (1→6)-linked di- and trisaccharides, several trials have been pursued for the next step to convert pyranose to furanose structure. As a model, 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (300 mg, 0.5 mmol) was treated with $HClO_4$-SiO_2 (100 mg) and methanol (1.0 mL) in acetonitrile (20 mL) at 70° C until full consumption of the starting material to a more polar product. The crude product was acetylated to furnish per-*O*-acetylated methyl 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl-(1→6)-D-galactofuranose in 77% yield. After a series of experimentation, it was observed that use of $HClO_4$-SiO_2 (50 mg/ mmol of substrate) and methanol (3.0 eqiv) in CH_3CN at 70° C furnished best results for the formation of required galactofuranose derivatives. Following similar reaction condition, a series of di- and trisaccharides containing di-*O*-isopropylidene-α-D-galactopyranose at the reducing end were converted to galactofuranose containing di- and trisaccharides as their methyl glycosides in excellent yield (Table 2). The formation of galactofuranose moiety in the products were unambigously confirmed from their NMR spectral data. In ^{13}C NMR spectra of compounds (**19-27**), signals appeared at δ 106-107 confirming the presence of galactofuranose moiety in the products (**19-27**), whereas in the case of compounds **10-18,** signals appeared in δ ~96-101 confirming the presence of galactopyrnose residue. Use of other commonly used apolar solvents, e.g. CH_2Cl_2, $CHCl_3$, THF, etc resulted no reaction or a very low yield of the formation of products. Interglycoside linkages remained unaffected under the reaction conditions. In most of the cases, a mixture of anomers were obtained, the ratio of which were determined from the NMR spectra. Pure products could be obtained by removal of the catalyst by simple filtration and evaporation of the solvent.

Table 1. Synthesis of di- and trisaccharides containing 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose using *N*-iodosuccinimide and $HClO_4$-SiO_2.

Entry	Donor	Product	Yield (%)
1	 **1**		85

2	 **2**	**10** 	80
3	 **3**	**11** 	82
4	 **4**	**12** 	85
5	 **5**	**13**  **14**	75
6	 **6**	 **15**	70
7	 **7**	 **16**	72
8	 **8**	 **17**	75

9  **9**

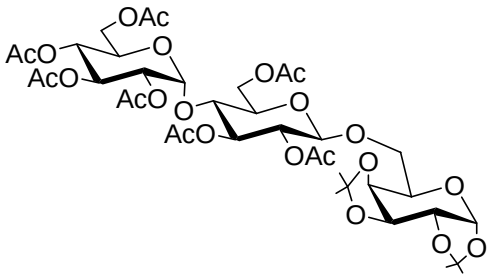
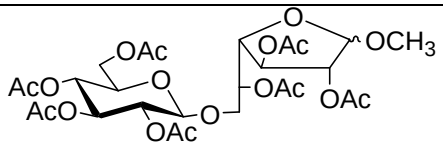
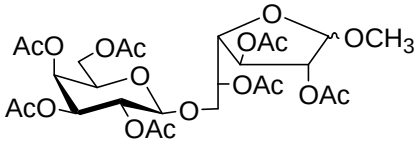
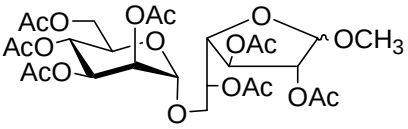
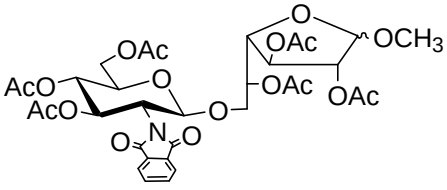
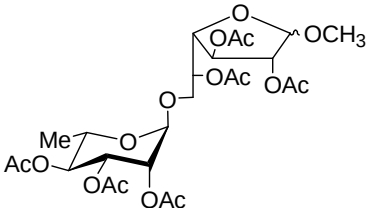
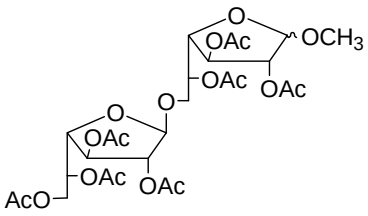
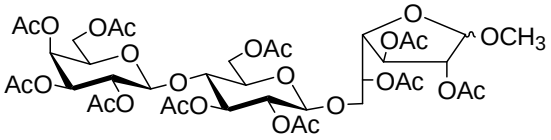
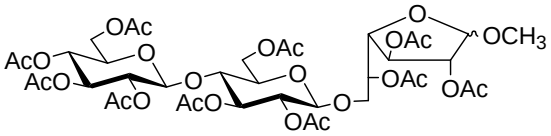
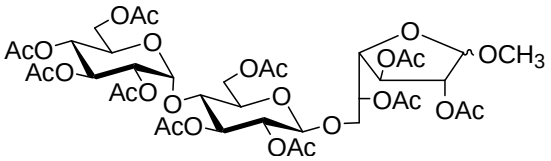
78  **18**

Table 2. Synthesis of methyl glycosides of di- and trisaccharides containing galactofuranose using $HClO_4$-SiO_2.

Entry	Substrate	Product	Yield (%)	(β/α)[a]
1	**10**	 **19**	75	3.5/1
2	**11**	 **20**	77	3.5/1
3	**12**	 **21**	75	2.6/1
4	**13**	 **22**	78	3.4/1
5	**14**	 **23**	70	5/1

6	**15**	 **24**	72	1/1
7	**16**	 **25**	75	3/1
8	**17**	 **26**	72	4.5/1
9	**18**	 **27**	75	3/1

[a] β/α ratio were calculated from the ^{1}H NMR spectra of the crude reaction products.

In summary, we have synthesized a series of di- and trisaccharides containing galactofuranosyl moiety at the reducing end in a concise manner applying $HClO_4$-SiO_2 in glycosylation reactions as well as in the ring transformation. This elegant reaction protocol can be scaled up for large scale preparation of (1→6)-linked glycosyl galactofuranosides for their biological evaluation. As these compounds (particularly compound **24**) are close analogs of the repeating unit of cell-wall oligosaccharide haptens found in *Mycobacteria*, these compounds could be potential cell-wall biosynthetic inhibitors of *Mycobacteria*.

1. Experimental

1.1. General Procedure: 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 2N H_2SO_4) sprayed plates in hot plate. Silica gel 230-400 mesh was used for column chromatography. ^{1}H and ^{13}C NMR was recorded on Brucker Advance DPX 200 MHz using $CDCl_3$ as solvent and TMS as internal reference. Chemical shift value is expressed in δ ppm. ESI-MS were recorded on a MICROMASS QUTTRO II triple quadrupole mass spectrometer. Elementary analysis was carried out on 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.

1.2. A typical experimental procedure for the glycosylation: To a solution of 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (260 mg, 1.0 mmol) and ethyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranoside (470 mg, 1.2 mmol) in anhydrous CH_2Cl_2 (10 mL) were added MS-4Å (1.0

g) and *N*-iodosuccinimide (315 mg, 1.4 mmol) and the reaction mixture was stirred under argon for 30 min at room temperature. After cooling the reaction mixture to 0° C, $HClO_4$-SiO_2 (50 mg) was added and the reaction mixture was stirred at 0° C for 45 min. After completion (TLC), the reaction mixture was filtered with CH_2Cl_2 (30 mL) and washed with 10% aq. $Na_2S_2O_3$, satd. aq. $NaHCO_3$ and water. The organic layer was dried (Na_2SO_4) and concentrated under reduced pressure. The crude mass was purified over SiO_2 using hexane-EtOAc (5:1) as eluant to afford pure 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galacto-pyranose (**10**) as a colourless oil (500 mg, 85%); Following similar reaction condition, a series of di- and trisaccharides (**11-18**) were prepared in excellent yield.

1.2.1. 2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galacto-pyranose (10): colourless oil; IR (neat): 1757, 1597, 1437, 1380, 1225, 1069, 1040, 1005, 900 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 5.45 (d, *J* = 4.9 Hz, 1H), 5.11 (t, *J* = 9.4 Hz, 1H), 5.00 (t, *J* = 8.4 Hz, 1H), 4.96 (t, *J* = 7.8 Hz, 1H), 4.57 (d, *J* = 7.7 Hz, 1H), 4.53 (dd, *J*= 7.4 and 2.3 Hz, 1H), 4.31-4.23 (m, 2H), 4.16-4.12 (m, 2H), 4.08-3.95 (m, 1H), 3.92-3.82 (m, 1H), 3.68-3.57 (m, 2H), 2.08, 2.06, 2.01, 1.99 (4s, 12H, 4 COCH_3), 1.49, 1.42 (2s, 6H, C(CH_3)$_2$), 1.30 (s, 6H, C(CH_3)$_2$); ^{13}C NMR (50 MHz, $CDCl_3$): δ 170.5, 170.1, 169.3 (2C), 111.7, 110.7, 101.8, 96.5, 73.1, 72.1, 71.6, 71.4, 71.0, 70.8, 69.8, 68.8, 68.2, 62.0, 26.4, 26.3, 25.5, 24.7, 20.9 (2C), 20.8 (2C); ESI-MS: *m/z* 613 [M+Na].

1.2.2. 2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galacto-pyranose (11): colourless oil; IR (neat):1750, 1374, 1263, 1224, 1159, 1070, 1043, 769 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 5.45 (d, *J* = 4.8 Hz, 1H), 5.33 (d, *J* = 2.8 Hz, 1H), 5.15 (dd, *J* = 10.5 and 7.8 Hz, 1H), 4.97 (dd, *J* = 10.5 and 3.3 Hz, 1H), 4.56 (d, *J* = 7.7 Hz, 1H), 4.53 (d, *J* = 7.8 Hz, 1H), 4.24 (dd, *J* = 4.8 and 2.4 Hz, 1H), 4.15-4.01 (m, 3H),, 3.91-3.84 (m, 3H), 3.65-3.56 (m, 1H), 2.16, 2.07, 2.04, 1.98, (4s, 12H, 4 COCH_3), 1.54, 1.43, 1.31, 1.30 (4s, 12H, 2C(CH_3)$_2$); ^{13}C NMR (50 MHz, $CDCl_3$): δ 170.2, 170.1, 170.0, 169.5, 109.6, 108.9, 100.9, 95.0, 70.2, 69.6, 69.5 (2C), 69.3, 68.5, 67.4, 66.8, 65.8, 59.8, 24.9 (2C), 24.0, 23.2, 19.6 (2C), 19.4 (2C); ESI-MS: *m/z* 613.3 [M+Na].

1.2.3. 2,3,4,6-Tetra-*O*-acetyl-α-D-mannopyranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galacto-pyranose (12): white solid; m.p. 58-60°C; IR (KBr): 1753, 1596, 1379, 1226, 1138, 1071, 1008 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 5.46 (d, *J* = 5.0 Hz, 1H), 5.32-5.10 (m, 3H), 4.82 (bs, 1H), 4.58 (dd, *J* = 7.8 and 2.3 Hz, 1H), 4.33-4.19 (m, 3H), 4.13-4.04 (m, 2H), 3.94 (ddd, *J* = 6.3, 4.8 and 1.4 Hz, 1H), 3.81-3.64 (m, 2H), 2.16, 2.09, 2.04, 1.98, (4s, 12H, 4 COCH_3), 1.54, 1.41, 1.32, 1.32 (4s, 12H, 2 C(CH_3)$_2$); ^{13}C NMR (50 MHz, $CDCl_3$): δ 171.0, 170.3, 170.2, 170.1, 109.7, 109.1, 98.2, 96.6, 71.2, 70.9 (2C),69.8, 69.5, 68.9, 67.4, 66.8, 66.4, 62.7, 26.5, 26.3, 25.3, 24.8, 21.2, 21.1, 21.0 (2C); ESI-MS: *m/z* 613.3 [M+Na].

1.2.4. 3,4,6-Tri-*O*-acetyl-2-deoxy-2-pthalimido-β-D-glucopyranosyl-(1→6)-1,2:3,4-di-*O*-isopropyli-dene-α-D-galactopyranose (13): white solid; m.p. 202°C; IR (KBr): 1753, 1720, 1598, 1436, 1385, 1231, 1168, 1070, 900, 721 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 7.84-7.80 (m, 2H), 7.70-7.69 (m, 2H), 5.82 (t, *J* = 9.2 Hz, 1H), 5.40 (d, *J* = 8.1 Hz, 1H), 5.18 (t, *J* = 9.6 Hz, 1H), 5.05 (d, *J* = 5.6 Hz, 1H), 4.38-4.26 (m, 3H), 4.21-4.04 (m, 2H), 3.98-3.84 (m, 3H), 3.71-3.64 (m, 2H), 2.11, 2.02, 1.85, (s, 9H, 3 COCH_3), 1.38, 1.22 (2s, 6H, C(CH_3)$_2$), 1.01 (s, 6H, C(CH_3)$_2$); ^{13}C NMR (50 MHz, $CDCl_3$): δ 170.5, 170.0, 169.4, 167 (2C), 133.8 (3C), 132.5, 123.7 (2C), 109.6, 108.2, 99.6, 96.2, 71.9, 71.2, 71.0 (2C), 70.4, 69.6, 69.2, 67.9, 62.2, 54.9, 26.3, 25.7, 25.0, 24.6, 21.0, 20.3, 20.7; ESI-MS: *m/z* 700.3 [M+Na].

1.2.5. 2,3,4-Tri-*O*-acetyl-α-D-rhamnopyranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galacto-pyranose (14): white solid; m.p. 60°C; IR (neat): 1751, 1596, 1378, 1224, 1073, 1007, 760 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 5.46 (d, *J* = 4.9 Hz, 1H), 5.26-5.20 (m, 2H), 4.99 (t, *J* = 9.7 Hz, 1H), 4.77 (bs, 1H), 4.60 (dd, *J* = 7.9 and 2.3 Hz, 1H), 4.29-4.25 (m, 2H), 4.00-3.93 (m, 2H), 3.82 (dd, *J* = 7.4 and 7.4 Hz, 1H), 3.56 (dd, *J* = 9.4 and 6.0 Hz, 1H), 2.15, 2.02, 1.98, (3s, 9H, 3 COCH_3), 1.54, 1.42 (2s, 6H, C(CH_3)$_2$), 1.32 (s, 6H, C(CH_3)$_2$), 1.19 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 169.8 (2C), 169.7, 109.3,108.9, 97.5, 96.4, 71.5, 71.2, 70.9 (2C), 70.1, 69.5, 66.6 (2C), 65.7, 26.5, 26.4, 25.3, 24.8, 21.1, 21.0 (2C), 17.6; ESI-MS: *m/z* 555.2 [M+Na].

1.2.6. 2,3,5,6-Tetra-*O*-acetyl-β-D-galactofuranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galacto-pyranose (15): colourless oil; IR (neat): 1749, 1594, 1371, 1228, 1070, 1005 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 5.47 (d, *J* = 4.7 Hz, 1H), 5.33 (dd, *J* = 7.6 and 4.0 Hz, 1H), 5.06-5.02 (m, 2H), 4.94 (d, *J* = 5.9 Hz, 1H), 4.57 (m, 1H), 4.41 (dd, *J* = 11.9 and 3.0 Hz, 1H), 4.27-4.03 (m, 4H), 3.96-3.82 (m, 2H), 3.65-3.52 (m, 1H), 2.12, 2.10, 2.07, 2.05 (4s, 12H, 4 COCH_3), 1.56, 1.43 (2s, 6H, C(CH_3)$_2$), 1.32 (s, 6H, C(CH_3)$_2$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.4, 169.9, 169.7, 169.4, 109.4, 108.7, 105.1, 96.5, 81.4, 80.3, 76.7, 71.2, 70.8 (2C), 69.5, 66.8, 65.2, 63.4, 26.4, 26.3, 25.3, 24.8, 21.1, 21.0 (2C), 20.9; ESI-MS: *m/z* 613 [M+Na].

1.2.7. 2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl-(1→4)-2,3,6-tri-*O*-acetyl-β-D-gluco-pyranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (16): White solid; m.p. 84° C ; IR (KBr): 1754, 1592, 1378, 1231, 1172, 1068, 899 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 5.41 (d, *J* = 5.1 Hz, 1H), 5.25 (d, *J* = 2.7 Hz, 1H), 5.13 (t, *J* = 9.3 Hz, 1H), 5.01 (dd, *J* = 10.2 and 7.8 Hz, 1H), 4.89 (dd, *J* = 6.9 and 3.3 Hz, 1H), 4.81 (dd, *J* = 9.3 and 7.8 Hz, 1H), 4.54 (d, *J* = 7.8 Hz, 1H), 4.51 (dd, *J* = 8.1 and 2.4 Hz, 1H), 4.46 (d, *J* = 7.5 Hz, 1H), 4.43-4.39 (m, 1H), 4.21 (dd, *J* = 4.8 and 2.4 Hz, 1H), 4.12-4.02 (m, 4H), 3.92-3.82 (m, 3H), 3.74 (t, *J* = 9.3 Hz, 1H), 3.61-3.55 (m, 2H), 2.15, 2.12, 2.02, 2.01, 2.00. 2.00, 1.92 (7s, 21H, 7 COCH_3), 1.45, 1.38 (2s, 6H, C(CH_3)$_2$), 1.27 (s, 6H, C(CH_3)$_2$); ^{13}C NMR (50 MHz, $CDCl_3$): δ 170.1, 169.9 (2C), 169.7, 169.6 (2C), 169.0, 109.6, 108.8, 101.4, 101.3, 96.5, 76.7, 73.1, 72.8, 71.8, 71.6, 71.3, 71.0, 70.9, 70.7, 69.5 (2C), 68.1, 66.9, 62.4, 61.0, 26.4, 26.3, 25.4, 24.7, 21.1 (3C), 20.9, 20.8 (2C), 20.7; ESI-MS: *m/z* 901.4 [M+Na].

1.2.8. 2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl-(1→4)-2,3,6-tri-*O*-acetyl-β-D-gluco-pyranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (17): colourless oil; IR (neat): 1748, 1592, 1435, 1380, 1230, 1171, 1135, 1071 1002 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 5.44 (d, *J* = 5.1 Hz, 1H), 5.14 (t, *J* = 9.6 Hz, 1H), 5.09 (t, *J* = 9.0 Hz, 1H), 5.02 (t, *J* = 10.8, 1H), 4.87 (t, *J* = 8.1 Hz, 1H), 4.85 (t, *J* = 7.8Hz, 1H), 4.57-4.45 (m, 4H), 4.36 (dd, *J* = 12.3 and 4.5 Hz, 1H), 4.24 (dd, *J* = 4.8 and 2.1 Hz, 1H), 4.12 (dd, *J* = 6.9 and 1.8 Hz, 1H), 4.07 (dd, *J* = 11.7 and 4.5 Hz, 1H), 4.00 (dd, *J* = 12.3 and 1.8 Hz, 1H), 3.93 (dd, *J* = 11.1 and 3.3 Hz, 1H), 3.88-3.85 (m, 1H), 3.74 (t, *J* = 9.3 Hz, 1H), 3.64-3.58 (m, 3H), 2.12, 2.08, 2.06, 2.04, 2.03, 2.02, 1.97 (7s, 21H, 7 COCH_3), 1.48, 1.41, 1.30, 1.28 (4s, 12H, 2C(CH_3)$_2$); ^{13}C NMR (50 MHz, $CDCl_3$): δ 170.4, 170.2 (2C), 169.7 (2C), 169.2, 168.9, 109.6, 108.8, 101.5, 101.1, 96.5, 76.9, 73.3, 72.9, 72.7, 72.3, 72.0, 71.7, 71.6, 71.0, 70.7, 69.5, 68.1 (2C), 62.3, 61.7, 26.4, 26.3, 25.4, 24.7, 21.1 (2C), 21.0, 20.9, 20.8 (3C); ESI-MS: *m/z* 901.4 [M+Na].

1.2.9. 2,3,4,6-Tetra-*O*-acetyl-α-D-glucopyranosyl-(1→4)-2,3,6-tri-*O*-acetyl-β-D-gluco-pyranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (18): White solid; m.p. 80°C; IR (KBr): 1754, 1594, 1437, 1378, 1235, 1171, 1042, 897 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ5.44 (d, *J* = 5.1 Hz, 1H), 5.38 (d, *J* = 4.2 Hz, 1H), 5.30 (t, *J* = 10.5 Hz, 1H), 5.21 (t, *J* =

9.3 Hz, 1H), 4.99 (t, *J* = 9.9 Hz, 1H), 4.81 (t, *J* = 2.4 Hz, 1H), 4.76 (dd, *J* = 8.4 and 3.9 Hz, 1H), 4.60 (d, *J* = 7.8 Hz, 1H), 4.54 (dd, *J* = 8.1 and 2.4 Hz, 1H), 4.43 (dd, *J* = 9.9 and 2.4 Hz, 1H), 4.26-4.23 (m, 2H), 4.20-4.18 (m, 1H), 4.14 (dd, *J* = 7.8 and 1.8 Hz, 1H), 4.10 (q, *J* = 7.2 Hz, 1H), 3.98-3.85 (m, 4H), 3.65-3.61 (m, 2H), 2.14, 2.09, 2.03, 2.03, 2.02, 2.02, 2.00, (7s, 21H, 7 COCH_3), 1.48, 1.42 (2s, 6H, C(CH_3)$_2$), 1.30 (s, 6H, C(CH_3)$_2$); ^{13}C NMR (50 MHz, $CDCl_3$): δ 170.5, 170.3 (2C), 170.1, 169.8 (2C), 169.3, 109.6, 108.8, 101.3, 96.4, 95.7, 76.0, 75.7, 73.0, 72.3, 71.6, 71.0, 70.7, 70.3, 69.7 (2C), 68.7, 68.4, 68.1, 63.2, 61.7, 26.4, 26.3, 25.4, 24.7, 21.2 (2C), 21.1, 20.9, 20.8 (3C); ESI-MS: *m/z* 901.4 [M+Na].

1.3. A typical experimental procedure for the conversion of galactopyranose to galactofuranose derivatives: To a solution of 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (**10**) (295 mg, 0.5 mmol) in anhydrous CH_3CN (5 mL) were added anhydrous MeOH (60 μL, 1.5 mmol) and $HClO_4$-SiO_2 (25 mg) and the reaction mixture was allowed to stir at 70° C for 3 h. After completion of the reaction (TLC), the reaction mixture was filtered through a Celite bed and concentrated under reduced pressure. Acetylation of the crude product using acetic anhydride and catalytic $HClO_4$-SiO_2 followed by purification over SiO_2 using hexane-EtOAc (2:1) as eluant furnished pure methyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl-(1→6)-2,3,5-tri-*O*-acetyl-β-D-galactofuranoside (**19**) together with its α-anomer (75%; β/α = 4:1); Following similar reaction condition, a series of di- and trisaccharides containing galactofuranose moiety as methyl glycosides (**20**-**27**) were synthesized in excellent yield.

1.3.1. Methyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl-(1→6)-2,3,5-tri-*O*-acetyl-β-D-galactofuranoside (19): colourless oil; IR (neat): 3023, 1752, 1372, 1221, 1043, 762 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.41 (d, *J* = 2.7 Hz, 1 H), 5.34 (dd, *J* = 10.8 and 3.6 Hz, 1 H), 5.18-5.15 (m, 1 H), 5.11-5.07 (m, 1 H), 5.03-4.91 (m, 2 H), 4.54 (d, *J* = 7.8 Hz, 1 H), 4.28-4.18 (m, 2 H), 4.17-4.09 (m, 2 H), 3.82-3.77 (m, 1 H), 3.71-3.56 (m, 2 H), 3.39 (s, 3 H), 2.13, 2.09, 2.08, 2.03, 2.02, 2.00, 1.97 (7 s, 21 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.8, 169.6, 169.5, 169.3, 169.1, 168.9, 168.7, 106.4, 100.5, 81.3, 79.4, 72.7 (2C), 71.9, 71.1, 68.2, 68.1, 61.6 (2 C), 54.7, 20.5 (2 C), 20.4 (3 C), 20.3 (2 C); ESI-MS: *m/z* 673 [M+Na]; Anal. Calcd. For $C_{27}H_{38}O_{18}$ (650): C, 49.85; H, 5.89%; Found: C, 49.6; H, 6.18%.

1.3.2. Methyl 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl-(1→6)-2,3,5-tri-*O*-acetyl-β-D-galactofuranoside (20): colourless oil; IR (neat): 2364, 1749, 1372, 1222, 1057, 769 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.39-5.37 (m, 1 H), 5.32-5.30 (m, 1 H), 5.18 (dd, *J* = 10.8 and 2.6 Hz, 1 H), 5.04-5.00 (m, 2 H), 4.98-4.95 (m, 1 H), 4.91 (bs, 1 H), 4.52 (d, *J* = 7.8 Hz, 1 H), 4.23-4.20 (dd, *J* = 6.0 and 3.3 Hz, 1 H), 4.17-4.10 (m, 2 H), 4.03-3.99 (dd, *J* = 10.8 and 5.1 Hz, 1 H), 3.93-3.90 (m, 1 H), 3.81-3.78 (m, 1 H), 3.38 (s, 3 H), 2.15, 2.13, 2.10, 2.09, 2.06, 2.05, 1.97 (7 s, 21 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.8 (2 C), 169.6 (2 C), 169.5, 169.1, 168.8, 106.4, 101.0, 81.4, 79.4, 76.5, 70.8 (2 C), 70.0, 68.6, 66.9 (2 C), 60.9, 54.7, 20.7 (2 C), 20.5 (2 C), 20.4 (3 C); ESI-MS: *m/z* 673 [M+Na]; Anal. Calcd. For $C_{27}H_{38}O_{18}$ (650): C, 49.85; H, 5.89%; Found: C, 49.58; H, 6.20%.

1.3.3. Methyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl-(1→6)-2,3,5-tri-*O*-acetyl-β-D-galactofuranoside (21): colourless oil; IR (neat): 2365, 1594, 1752, 1374, 1228, 1140, 1049 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.45-5.44 (m, 1 H), 5.19-5.15 (m, 3 H), 5.06-5.04 (m, 1 H), 5.02-5.00 (m, 1 H), 4.92 (bs, 1 H), 4.26-4.22 (m, 2 H), 4.20-4.18 (m, 2 H), 4.15-4.13 (m, 1 H), 3.84-3.80 (m, 1 H), 3.78-3.75 (m, 1 H), 3.39 (s, 3 H), 2.16, 2.14, 2.13, 2.12, 2.10, 1.98, 1.90 (7 s, 21 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.8, 169.6, 169.4, 169.3, 169.2, 168.9, 168.5, 106.5,

101.9, 81.4, 79.8, 76.3, 71.7, 70.9, 70.7, 69.7, 67.8, 62.2 (2 C), 54.8, 20.7 (2 C), 20.6 (3 C), 20.5 (2 C); ESI-MS: *m/z* 673 [M+Na]; Anal. Calcd. For $C_{27}H_{38}O_{18}$ (650): C, 49.85; H, 5.89%; Found: C, 49.56; H, 6.21%.

1.3.4. Methyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1→6)-2,3,5-tri-*O*-acetyl-β-D-galactofuranoside (22): colourless oil; IR (neat): 2365, 1594, 1751, 1720, 1596, 1387, 1231, 1142, 724 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.86-7.72 (m, 4 H, aromatic protons), 5.79-5.72 (m, 2 H), 5.41-5.36 (m, 2 H), 5.22-5.15 (m, 2 H), 4.92 (d, *J* = 2.6 Hz, 1 H), 4.35-4.26 (m, 2 H), 4.21-4.16 (m, 1 H), 4.07-4.03 (m, 1 H), 3.88-3.77 (m, 2 H), 3.76-3.30 (m, 1 H), 3.30 (s, 3 H), 2.12, 2.09, 2.04, 2.02, 2.01, 1.85 (6 s, 18 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.7, 169.6, 169.4, 169.2 (2 C), 168.9, 167.2 (2 C), 134.0-123.5 (aromatic carbons), 106.3, 97.7, 81.1, 79.3, 76.0, 71.9, 70.6, 69.5, 68.0, 61.7, 61.6, 54.8, 54.4, 20.5 (2 C), 20.4 (2 C), 20.2 (2 C); ESI-MS: *m/z* 760 [M+Na]; Anal. Calcd. For $C_{33}H_{39}NO_{18}$ (737): C, 53.73; H, 5.33%; Found: C, 53.45; H, 5.55%.

1.3.5. Methyl 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl-(1→6)-2,3,5-tri-*O*-acetyl-β-D-galactofuranoside (23): yellow oil; IR (neat): 2928, 2365, 1748, 1433, 1373, 1227, 1049, 761 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 5.39 (bs, 1 H), 5.34 (t, *J* = 4.2 Hz, 1 H), 5.30-5.28 (m, 1 H), 5.20-5.17 (m, 1 H), 4.99-4.98 (m, 1 H), 4.73 (bs, 1 H), 3.85-3.79 (m, 1 H), 3.74-3.72 (m, 1 H), 3.65-3.59 (m, 3 H), 3.52-3.47 (m, 1 H), 3.36 (s, 3 H), 2.09, 2.06, 2.04, 2.01, 2.00, 1.93 (6 s, 18 H), 1.17 (d, *J* = 6.2 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.8 (2 C), 170.6 (2 C), 170.4, 170.3, 106.6, 98.0, 71.1, 69.8, 69.3 (2 C), 61.1, 68.5, 68.0, 67.1, 66.9, 55.9, 21.2 (3 C), 21.0 (3 C), 17.7; ESI-MS: *m/z* 615 [M+Na]; Anal. Calcd. For $C_{25}H_{36}O_{16}$ (592): C, 50.67; H, 6.12 %; Found: C, 50.40; H, 6.40%.

1.3.6. Methyl 2,3,5,6-tetra-*O*-acetyl-β-D-galactofuranosyl-(1→6)-2,3,5-tri-*O*-acetyl-β-D-galactofuranoside (24): yellow oil; IR (neat): 1749, 1594, 1367, 1230, 1053 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 5.41 (dd, *J* = 10.3, 2.7 Hz, 1 H), 5.35-5.25 (m, 2 H), 5.14-5.05 (m, 1 H), 5.01-4.95 (m, 2 H), 4.93-4.90 (m, 1 H), 4.39-4.35 (m, 1 H), 4.31-4.28 (m, 1 H), 4.19-4.11 (m, 2 H), 4.09-4.06 (m, 1 H), 3.79-3.69 (m, 1 H), 3.66-3.64 (m, 1 H), 3.50 (s, 3 H), 2.16, 2.15, 2.14, 2.11, 2.07, 2.00, 1.98 (7 s, 21 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.0, 169.9, 169.8, 169.6, 169.4, 169.1, 169.0, 106.6, 105.4, 81.5, 80.9, 80.6, 76.3, 69.8, 68.1, 67.9, 66.7, 62.7, 62.5, 55.4, 20.7 (3 C), 20.6 (3 C), 20.5; ESI-MS: *m/z* 673 [M+Na]; Anal. Calcd. For $C_{27}H_{38}O_{18}$ (650): C, 49.85; H, 5.89 %; Found: C, 50.10; H, 6.20%.

1.3.7. Methyl 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl-(1→4)-2,3,6-tri-*O*-acetyl-β-D-glucopyranosyl-(1→6)-2,3,5-tri-*O*-acetyl-β-D-galactofuranoside (25): colourless oil; IR (neat): 2362, 1752, 1596, 1376, 1231, 1055 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 5.37 (dd, *J* = 8.1, 2.7 Hz, 1 H), 5.30 (d, *J* = 2.7 Hz, 1 H), 5.25 (dd, *J* = 7.8, 2.7 Hz, 1 H), 5.18-5.10 (m, 1 H), 5.08-5.06 (m, 1 H), 5.05-5.02 (m, 1 H), 4.95-4.88 (m, 2 H), 4.81 (t, *J* = 8.4 Hz, 1 H), 4.52-4.40 (m, 4 H), 4.14-4.05 (m, 4 H), 3.89-3.84 (m, 1 H), 3.79-3.70 (m, 2 H), 3.61-3.56 (m, 1 H), 3.38 (s, 3 H), 2.16, 2.14, 2.13, 2.10, 2.09, 2.07, 2.06, 2.04, 2.03, 1.97 (10 s, 30 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.8 (2 C), 169.6 (2 C), 169.3, 169.1 (2 C), 169.8, 169.7 (2 C), 105.9, 100.3, 97.1, 86.7, 79.5, 73.0, 72.6, 72.2, 71.6, 70.9, 70.7, 69.2, 68.6, 68.2, 67.6, 66.6, 62.1, 60.7, 55.3, 20.7 (4 C), 20.6 (3 C), 20.5 (3 C); ESI-MS: *m/z* 961.4 [M+Na]; Anal. Calcd. For $C_{39}H_{54}O_{26}$ (938): C, 49.89; H, 5.80 %; Found: C, 49.62; H, 6.10%.

1.3.8. Methyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl-(1→4)-2,3,6-tri-*O*-acetyl-β-D-glucopyranosyl-(1→6)-2,3,5-tri-*O*-acetyl-β-D-galactofuranoside (26): colourless oil; IR (neat): 2363, 1753, 1601, 1374, 1232, 1045 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 5.37 (dd, *J* =

9.3, 3.6 Hz, 1 H), 5.26 (dd, *J* = 9.3, 3.3 Hz, 1 H), 5.14 (dd, *J* = 9.0, 3.6 Hz, 1 H), 5.11-5.07 (m, 2 H), 5.04 (bs, 1 H), 5.01-4.97 (m, 1 H), 4.94-4.92 (m, 1 H), 4.89-4.80 (m, 3 H), 4.52-4.46 (m, 3 H), 4.41-4.32 (m, 1 H), 4.15-4.03 (m, 2 H), 4.02-3.91 (m, 2 H), 3.78-3.72 (m, 1 H), 3.66-3.58 (m, 1 H), 3.35 (s, 3 H), 2.15, 2.14, 2.13, 2.11, 2.10, 2.09, 2.07, 2.04, 2.03, 1.98 (10 s, 30 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.8, 169.6 (2 C), 169.4, 169.0, 168.8 (2 C), 168.6 (2 C), 167.9, 106.4, 97.6, 97.1, 81.3, 79.6, 73.0, 72.6, 72.0, 71.7, 71.5, 68.6, 68.1, 67.7, 67.5, 67.1, 61.5 (2 C), 61.2, 54.8, 20.7 (3 C), 20.5 (4 C), 20.4 (3 C); ESI-MS: *m/z* 961.4 [M+Na]; Anal. Calcd. For $C_{39}H_{54}O_{26}$ (938): C, 49.89; H, 5.80 %; Found: C, 49.60; H, 6.07%.

1.3.9. Methyl 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl-(1→4)-2,3,6-tri-*O*-acetyl-β-D-glucopyranosyl-(1→6)-2,3,5-tri-*O*-acetyl-β-D-galactofuranoside (27): colourless oil; IR (neat): 2928, 1752, 1596, 1437, 1377, 1235, 1040, 900 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.39-5.35 (m, 2 H), 5.30-5.25 (m, 1 H), 5.20-5.17 (m, 1 H), 5.09-4.94 (m, 2 H), 4.87-4.75 (m, 2 H), 4.58-4.54 (m, 1 H), 4.45 (dd, *J* = 9.0, 3.2 Hz, 1 H), 4.26-4.13 (m, 2 H), 4.13-4.10 (m, 1 H), 4.04-3.98 (m, 2 H), 3.95-3.92 (m, 2 H), 3.75-3.69 (m, 2 H), 3.68-3.60 (m, 2 H), 3.38 (s, 3 H), 2.17, 2.16, 2.15, 2.13, 2.11, 2.10, 2.08, 2.04, 2.01, 1.98 (10 s, 30 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.1 (2 C), 169.9 (3 C), 169.4 (2 C), 169.2, 168.9 (2 C), 104.1, 97.1, 95.5, 81.4, 79.4, 75.4, 72.8, 72.1, 72.0, 70.1, 69.4, 68.5, 68.2, 67.5, 67.3, 61.5 (2 C), 60.0, 55.3, 20.8 (3 C), 20.7 (4 C), 20.5 (3 C); ESI-MS: *m/z* 961.4 [M+Na]; Anal. Calcd. For $C_{39}H_{54}O_{26}$ (938): C, 49.89; H, 5.80%; Found: C, 49.65; H, 6.15%.

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9. **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.
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