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Development of a Novel Method for Trimethylsilylation of Saccharides

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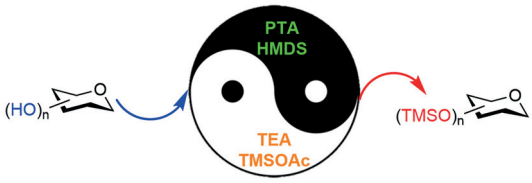

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Abstract The trimethylsilyl (TMS) group is widely used in carbohydrate synthesis, although this protecting group is unstable and its post-synthetic purification challenging. The successful trimethylsilylation of carbohydrates mediated by recyclable and efficient acidic catalyst PTA/HMDS and the novel reagent, TMSOAc (TEA/TMSOAc), under alkaline condition is reported. The advantages of these methods are that the reactions proceed in good to excellent yields without applying column chromatography for purification.

Key words phosphotungstic acid, trimethylsilyl acetate, trimethylsilylation, recover, reused, catalysis

Carbohydrates play diverse and essential roles in biomolecules,[1] including protein folding, viral and bacterial infections, masking immuno-responses, fertilization, embryogenesis, neural development, cell proliferation, cell growth, cell-cell communication, and the formation of specific tissues.[2] Because of its importance in biology, carbohydrate chemistry is a very active field of research.[3] As it is known, saccharides are soluble in water and poorly soluble in almost any other organic solvent except for a few exceptions. However, silyl protecting groups improve the solubility to solve this problem.[4]

The development of efficient methods for the silylation of carbohydrate is an important area of research in carbohydrate chemistry as the thermal stability and polarity can be significantly changed by silyl groups.[5,6] Silyl ethers and derivatives are widely applied as protecting groups in carbohydrate syntheses owing to their relative stability toward alkaline and acidic hydrolysis as well as high specificity for fluoride-mediated cleavage.[7] As of now, considerable progress has been made regarding the silylation of hydroxyl groups by using chlorosilanes,[8] hexamethyldisilazane (HMDS),[4c,9] or hydrosilanes[10] as silylating reagents in the past several decades.[11]

Among silyl ethers the most typically known one is the trimethylsilyl group (TMS), which is commonly used for the protection of functional groups in carbohydrates because its C–O–Si bonds can be easily cleaved at the O–Si bond. In particular, TMS groups also play a pivotal role in one-pot reactions.[12] While many TMS protecting reagents are known, HMDS is the most popular silylating agent because it is stable, commercially available, and inexpensive. Moreover, silylation with HMDS proceeds under almost nearly neutral conditions, requires no special precautions, and produces only ammonia (NH_3) as a reaction by-product.[13] However, in spite of all of its advantages, one prominent disadvantage of HMDS is its low silylating power in the absence of a suitable catalyst. Consequently, in order to increase the silylating efficiency of HMDS, a variety of catalysts have been reported.[14] Following the method of Firouzabadi et al., we applied a method on carbohydrate chemistry with phosphotungstic acid (PTA) as a catalyst, which yielded good results.[14c]

Recently, we reported on the phosphotungstic acid (PTA)-catalyzed protections along with the glycosylation of carbohydrates.[15] PTA is a heteropolyacid, which is a member of an increasingly important class of environmentally friendly catalysts for a variety of organic reactions.[16] PTA is frequently regarded as a green catalyst on account of its commercial availability, stability, non-toxicity, eco-friendliness, separability from liquid products, and most importantly, its recyclability.[14c,17]

In this paper, trimethylsilyl acetate, more often known as TMSOAc, was used as a TMS donor as well as acidic reagent in the trimethylsilylation of the starting material

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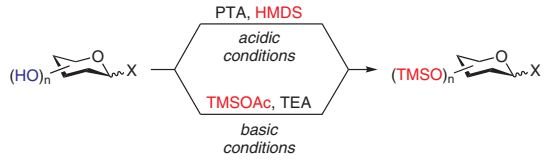
α-methyl-D-glucopyranoside (**1a**). Though TMSOAc is typically found as the by-product of reactions it serves as an even better carbohydrate silylation reagent. Among its many advantages, TMSOAc reduces the necessary purification process, while still providing a stable product in good yield.[18] Owing to the relatively polar nature of the acidic reagents, TMSOAc is easily separated from the other major product.[19] This property allows the pure product to be obtained without further purification.

In light of the advantages of both the acidic catalyst PTA and the novel reagent TMSOAc, our team used the new catalyst and reagent to explore their application in the traditionally reported trimethylsilylation procedures (Scheme 1). In this study, experiments are performed with different catalysts, reagents, and conditions to find the best reagent for TMS protecting of various carbohydrates while providing the highest yield in the shortest time. Additionally, the recycling potential of PTA is examined, and its repeated use is tested, providing favorable yields.

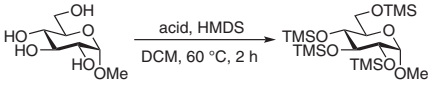


Scheme 1 Conception of trimethylsilylation under acidic and basic conditions

Various limitations exist with the traditionally reported reagents, such as their more expensive cost, strong corrosiveness, toxicity, and their ability to be easily destroyed under atmosphere. Following the method of Firouzabadi and co-workers,[14c] using PTA in the application of trimethylsilylation in carbohydrate synthesis, the catalytic activity of PTA was compared with the other acidic catalysts (Table 1).

First, trimethylsilylation of α-methyl-D-glucopyranoside (**1a**) was activated by HMDS (2.2 equiv) and the acid catalyst (0.20 equiv) to afford the product **2a** as shown in Table 1. The homogeneous acid catalysts TfOH and TMSOTf produced 94% and 98% of yield, respectively (Table 1, entries 1, 2). However, H_2SO_4 and *p*-toluenesulfonic acid (PTSA) afforded only 43% and 2% yield of the trimethylsilylated product due to the generation of massive tri-TMS side-products without regioselective protection (entries 3, 4). It should be noted that the $BF_3{\cdot}OEt_2$ afforded a very-low yield because the presence of F atoms is unfavorable with trimethylsilylation (entry 5). The reaction in heterogeneous acid catalysts such as silver trifluoromethanesulfonate (AgOTf), copper(II) trifluoromethanesulfonate [$Cu(OTf)_2$], camphorsulfonic acid (CSA), and PTA was also tested for the activation of HMDS. The lower yields from using AgOTf, $Cu(OTf)_2$, and CSA result from their poor heterogeneous catalytic efficiency (entries 6–8). Gratifyingly, PTA furnished a yield of up to

Table 1 Optimized Conditions for Trimethylsilylation with HMDS and Various Acids



1a **2a**

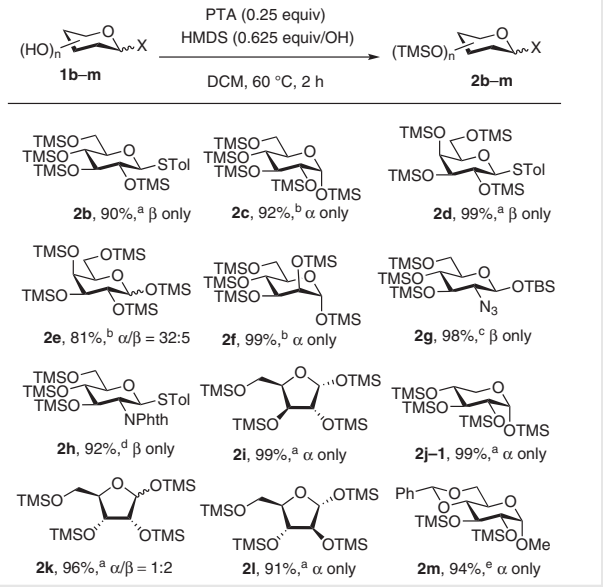
Entry	Acid (equiv)	HMDS (equiv)	Yield (%)
1	TfOH (0.2)	2.2	94
2	TMSOTf (0.2)	2.2	98
3[a]	H_2SO_4 (0.2)	2.2	43
4[a]	PTSA (0.2)	2.2	2
5	$BF_3{\cdot}OEt_2$ (0.2)	2.2	1
6[a]	AgOTf (0.2)	2.2	14
7[a]	$Cu(OTf)_2$ (0.2)	2.2	4
8[a]	CSA (0.2)	2.2	45
9	PTA (0.2)	2.2	95
10	PTA (0.25)	2.2	98
11	PTA (0.30)	2.2	95
12	PTA (0.25)	2.1	96
13	PTA (0.25)	2.5	99
14	PTA (0.25)	3.0	98
15[b]	PTA (0.25)	2.5	94
16[c]	PTA (0.25)	2.5	96

[a] Isolated yield.
[b] The reaction was performed at r.t.
[c] Starting material used: 1.0 g.

95% as the heterogeneous catalyst (entry 9). In addition, PTA also has many advantageous properties, many of which include its reusability, weak corrosiveness, and thermal stability. These results indicated that PTA is the favorable catalyst for this reaction. We further examined the effect of the best condition for protecting carbohydrates with trimethylsilyl groups catalyzed by PTA. The finding showed that raising the PTA to 0.25 equivalent would increase the yield to 98% (entry 10). Meanwhile when PTA was raised to 0.3 equivalent or when HMDS was lowered to 2.1 equivalents, the yields of product **2a** were lowered (entries 11, 12). Delightfully, the increase in the amount of HMDS to 2.5 equivalents, allowed the desired product **2a** to be obtained in a slightly higher yield of 99% (entry 13). However, the increase of HMDS to 3.0 equivalents, led to a decreased yield of 98% (entry 14). Decreasing the temperature gave lower yields, likely due to the fact that PTA was not thermally activated. This occurs since the reaction is heterogeneous (entry 15). Finally, a control experiment on an amplified scale to repeat the conditions of entry 15 resulted in the same yield of 96% (entry 16).

Under the optimal conditions, we studied the reaction ranging from pyranose to furanose (Scheme 2). The product **2b** was obtained in good yield (90%), when phenyl-1-thio-

β-D-glucoside (**1b**) was used as the starting material. The use of free-OH glucose **1c** afforded the desired product **2c** in 92% yield when HMDS was increased to 3.1 equivalents. On the other hand, 1-thiolcresol galactose reacted well to give the target product **2d** (99%), while free-OH galactose inhibited the formation of compound **2e** due to the increased steric hindrance at C4 position (81%). The use of mannose (**1f**) as starting material afforded the desired product **2f** in 99% yield. Furthermore, the reaction could be extended to N_3-protected glucosamine (**2g**). In addition, the product **2h** was formed from the glucosamine with *N*-phthalimide (NPhth) protecting group **1h**, thus demonstrating that NPhth protection was tolerated under the PTA. After the successful trimethylsilylation of pyranose substrates, our attention was then directed to furanose, which could also serve as important precursors in biochemistry and the synthesis such as ribose. At first, the substrate **1i** was subjected to the per-*O*-trimethylsilylation, which resulted in the desired product **2i** in 99% yield. Similarly, substrates **1j**, **1k**, and **1l** provided the desired trimethylsilyl protection products **2j–1**, **2k**, and **2l** in good yields (99%, 96%, and 91%). Notably, the benzylidene protecting group can also exist stably under this reaction environment, and the product **2m** with a yield of 94% was obtained. A plausible mechanism for the PTA trimethylsilylation of carbohydrates is presented in the Supporting Information.



Scheme 2 Trimethylsilylation of variety of saccharides by HMDS with PTA catalyst. [a] HMDS (2.5 equiv) was used; [b] HMDS (3.1 equiv) was used; [c] HMDS (1.9 equiv) was used; [d] HMDS (2.2 equiv) was used and stirred for 6 h; [e] HMDS (1.3 equiv) was used.

After the reactions were completed, the PTA was recycled via filtration. Several reagents were tested, and Amberlite® IR 120 H was found to be the best reagent in terms of acidification. Hence, the recycled PTA was again added to the same starting material **1a**. The reaction conducted under the same method of Table 1 gave the desired product **2a** in 97% to 99% yield and the recovered yield of PTA was over 80% (Figure 1). Furthermore, the catalyst could be recycled at least 6 times, while still maintaining the excellent yield. To our knowledge, this is the first time that catalytic trimethylation has been performed repeatedly with PTA.

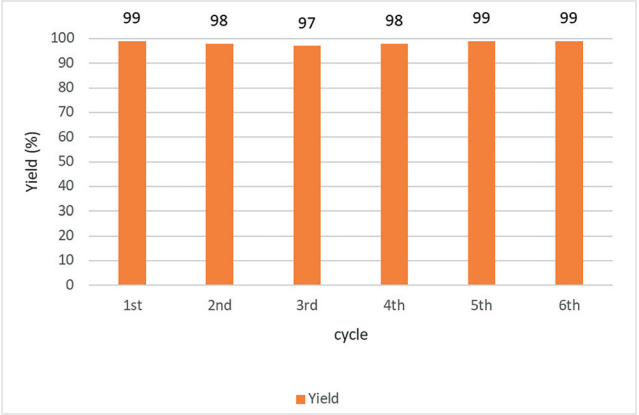
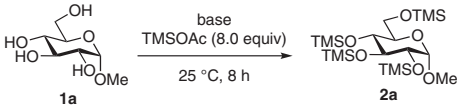


Figure 1 Reusing PTA for trimethylsilylation

Having established the trimethylsilyation with acid conditions by PTA and HMDS, we explored the same reaction under other conditions. To our excitement, the silyl ester TMSOAc could be a novel reagent for the trimethylsilylation. To demonstrate the application of TMSOAc, per-*O*-TMS protecting conditions were tested using α-methyl-D-glucopyranoside (**1a**) as the starting material (see Table 2). Initially, when the trimethylsilylation of **1a** was executed with only TMSOAc, the expected product was not found (Table 2, entry 1). Since the alkaline condition enhanced the reactivity, a series of organic bases were used. Solid bases such as 4-dimethylaminopyridine (DMAP) and imidazole were used to generate product **2a** in 33% and 50% yield, respectively (entries 2, 3). Then, the base was altered to pyridine, which is frequently used in the literature, but the result was the same as without base (entry 4). We also tested the base such as 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) and piperidine, and the change in base allowed the trimethylsilylated products to be isolated in better yields (83% and 88%, entries 5, 6). Altering the base to triethylamine (TEA) also considerably increased the yield (91%, entry 7). The optimal conditions had to be modulated to maximize the yield, so different equivalents of TEA were tested in the following entries. However, the yield of **2a** decreased while the amount of TEA was changed (76% and 82%, entries 8, 9). To sum up, entry 7 corresponded to a slightly better yield than all other entries, so TEA was chosen as the base reagent. We also examined different times and temperatures in the reaction but found that no changes benefited this reaction

(entries 10–13). Under the standard conditions, when the amount of TMSOAc was increased the reaction was less effective (entry 14).

Table 2 Different Conditions of Trimethylsilylation of **1a** with TMSOAc



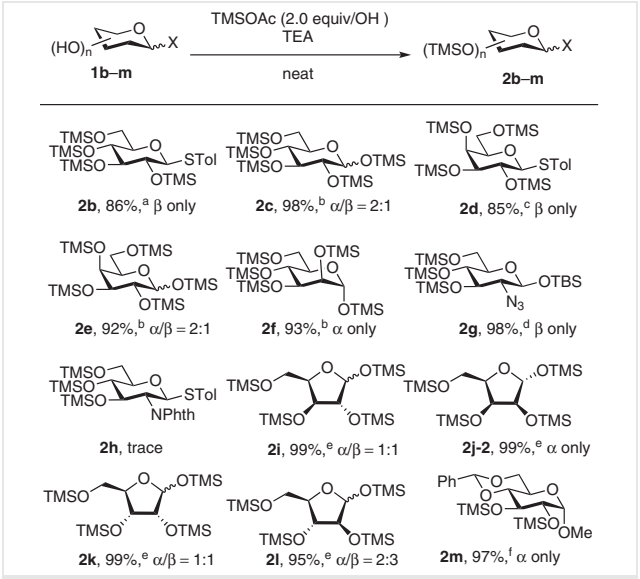
1a **2a**

Entry	Base (equiv)	Yield (%)
1	–	NR
2	DMAP (4.0)	33
3	imidazole (4.0)	50
4	pyridine (4.0)	NR
5	DBU (4.0)	83
6	piperidine (4.0)	88
7	TEA (4.0)	91
8	TEA (2.0)	76
9	TEA (6.0)	82
10[a]	TEA (4.0)	68
11[b]	TEA (4.0)	35
12[c]	TEA (4.0)	55
13[d]	TEA (4.0)	85
14[e]	TEA (4.0)	80

[a] Reaction time: 4 h.
[b] Reaction time: 12 h.
[c] Reaction temperature: 0 °C.
[d] Reaction temperature: 40 °C.
[e] TMSOAc (10.0 equiv) was used.

After optimizing the conditions of our proposed method, we next turned to screen the same compounds used in Scheme 2 (Scheme 3), which can also be easily trimethylsilylated with TMSOAc. Gratifyingly, TMS-protected general pyranoses could successfully afford the product in good to excellent yields (85–99%, **2b**–**g**). Unexpectedly, when the starting material was **1h**, the yield was not well. It is speculated that the oxygen anion activity is lower under alkaline conditions, which results in its poor activity, because NPhth is an electron-withdrawing group. To further demonstrate the efficiency of this new method for carbohydrates, we performed the reaction with several furanoses. Excellent yields were obtained for all of the examples (**2i**–**l**). Since TMSOAc will produce AcOH as a by-product, in order to test the tolerance of benzylidene to this reagent, we also tried **1m** for the reaction. To our delight, the reaction could smoothly produce a high yield of product **2m** (97%).

Finally, the saccharides with free OH and their different acid-base conditions can be adjusted according to experimental needs, the OH on the saccharides are protected by TMS to obtain the carbohydrate derivatives. Following an already described methodology that the product obtained



Scheme 3 Trimethylsilylation of a variety of saccharides with TEA and TMSOAc. [a] TMSOAc (10.0 equiv) and TEA (6.0 equiv) were used at 40 °C for 4 h; [b] TMSOAc (10.0 equiv) and TEA (5.0 equiv) were used at 25 °C for 8 h. [c] TMSOAc (8.0 equiv) and TEA (4.0 equiv) were used at 25 °C for 24 h; [d] TMSOAc (6.0 equiv) and TEA (3.0 equiv) were used at 25 °C for 8 h; [e] TMSOAc (8.0 equiv) and TEA (4.0 equiv) were used at 25 °C for 8 h; [f] TMSOAc (4.0 equiv) and TEA (2.0 equiv) were used at 25 °C for 8 h.

by the reaction of PTA and HMDS, or the protection by TMSOAc with base, only side-products of NH_3 or AcOH are formed, and these by-products can be removed easily by extraction or vacuum to acquire the desired product.

In conclusion, this study demonstrated the exceptionally well catalysis for the trimethylsilylation of a variety of pyranoses and furanoses by PTA with major advantages in the catalyst's mild reaction conditions and thermal stability. In addition, the PTA can also be recovered by simple filtration and reused in a high yield. We also found a novel reagent, TMSOAc, for the trimethylsilylation of carbohydrates under base conditions with the advantages of being commercially available and cheap. Most importantly, the acetic acid by-product can be removed by rotary evaporation. In summary, we believe that the two synthetic conditions for silyl ether formation of carbohydrates reported here would be friendly for the generation of their silylated products.

The reactions with TMSOAc were conducted in a flame-dried glassware under N_2 atmosphere. DCM, THF, toluene, MeOH, and DMF were purified and dried from a safe purification system containing activated Al_2O_3. All reagents were purchased from commercial sources and used without purification, unless otherwise mentioned. Flash column chromatography was carried out on Silica Gel 60. TLC was performed on pre-coated glass plates of Silica Gel 60 F_{254}; detection was executed by spraying with a solution of $Ce(NH_4)_2(NO_3)_6$ (0.5 g), $(NH_4)_6Mo_7O_{24}$ (24.0 g), and H_2SO_4 (28.0 mL) in H_2O (500.0 mL) and heating on a hot plate. Optical rotations were measured at 589 nm (Na). ^1H and ^{13}C NMR spectra were recorded with 400 MHz instruments. Chemical

shifts are in ppm from Me_4Si generated from the $CDCl_3$ lock signal at δ = 7.26. Mass spectra were analyzed on orbitrap instrument with an ESI source.

Trimethylsilylation of Sugars by PTA-Catalyzed HMDS; General Procedure 1

To a solution of **1a–m** (200 mg, 1.0 equiv) and PTA (0.25 equiv) in DCM (10 mL) were added HMDS (0.625 equiv/OH) and stirred at 60 °C for 2 h. After removal of the solvent by rotorary evaporation, PTA was filtered and recovered. The residue was diluted with hexane and the hexane layer was washed with sat. $NaHCO_3$ (3 ×). The hexane layer was dried (anhyd $MgSO_4$) and filtered. Evaporating the organic layer in vacuum furnished the desired product **2a–m** (Scheme 2).

Trimethylsilylation of Sugars with TEA and TMSOAc; General Procedure 2

To a solution of **1a–m** (200 mg, 1.0 equiv) and TEA (1.0 equiv/OH) were added TMSOAc (2.0 equiv/OH) and the mixture was stirred for 8 h under N_2 atmosphere. The mixture was diluted with hexane and the hexane layer was washed with sat. $NaHCO_3$ (3 ×) and brine (3 ×). The hexane layer was dried (anhyd $MgSO_4$) and filtered. Evaporating the organic layer in vacuum furnished the desired product **2a–m** (Scheme 3).

Reusable Procedure of PTA Catalyst

To further develop a reusability method of PTA catalyst, PTA was recovered from the reaction system by simple filtration after the completion of each run, and washed with EtOAc. Then PTA was dissolved in H_2O (10 mL, per gram of PTA) and stirred with Amberlite® IR 120 H (3.0 g, per gram of PTA) overnight, filtered, and dried under vacuum prior to its reuse for the next reaction cycle under the identical reaction conditions.

Methyl-2,3,4,6-tetra-*O*-trimethylsilyl-α-D-glucopyranoside (2a)

Prepared according to the general procedure 1; colorless oil; yield: 496.5 mg (99%); R_f = 0.52 (EtOAc/hexane 1:9); $[\alpha]_D^{29}$ +97.09 (*c* 1.1, DCM)

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 4.61 (d, *J* = 3.6 Hz, 1 H), 3.75 (t, *J* = 8.6 Hz, 2 H), 3.67 (dd, *J* = 11.6, 5.2 Hz, 1 H), 3.53–3.40 (m, 3 H), 3.34 (s, 3 H), 0.16 (s, 9 H), 0.15 (s, 9 H), 0.15 (s, 9 H), 0.12 (s, 9 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 99.5, 75.1, 73.8, 71.8, 71.6, 61.9, 54.3, 1.2, 0.7, 0.4, –0.4.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{46}O_6Si_4Na$: 505.2269; found: 505.2268.

p-Tolyl-2,3,4,6-tetra-*O*-trimethylsilyl-1-thio-β-D-glucopyranoside (2b)

Prepared according to the general procedure 1; white solid; yield: 359.1 mg (90%); mp 66–68 °C; R_f = 0.53 (EtOAc/hexane 1:22); $[\alpha]_D^{28}$ –44.50 (*c* 1.2, DCM).

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.43 (d, *J* = 8.0 Hz, 2 H), 7.07 (d, *J* = 8.0 Hz, 2 H), 4.58–4.53 (m, 1 H), 3.79 (dd, *J* = 11.0, 2.2 Hz, 1 H), 3.63 (dd, *J* = 11.2 , 6.4 Hz, 1 H), 3.44 (t, *J* = 5.4 Hz, 3 H), 3.28–3.23 (m, 1 H), 2.32 (s, 3 H), 0.24 (s, 9 H), 0.17 (s, 9 H), 0.16 (s, 9 H), 0.11 (s, 9 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 136.7, 131.9, 131.1, 129.4, 89.7, 81.1, 79.9, 75.2, 71.6, 62.6, 21.1, 1.7, 1.4, 0.9, –0.3.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{25}H_{50}O_5SSi_4Na$: 597.2354; found: 597.2351.

1,2,3,4,6-Penta-*O*-trimethylsilyl-α-D-glucopyranoside (2c)

Prepared according to the general procedure 1; colorless oil; yield: 553.6 mg (92%), α only; R_f = 0.50 (EtOAc/hexane 1:18); $[\alpha]_D^{29}$ +76.00 (*c* 1.2, DCM).

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.00 (d, *J* = 3.2 Hz, 1 H), 3.77 (t, *J* = 8.8 Hz, 1 H), 3.74–3.63 (m, 3 H), 3.40 (t, *J* = 8.8 Hz, 1 H), 3.33 (dd, *J* = 9.0, 3.0 Hz, 1 H), 0.17 (s, 9 H), 0.15 (s, 18 H), 0.13 (s, 9 H), 0.11 (s, 9 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 93.9, 74.2, 74.0, 72.5, 72.2, 62.3, 1.3, 0.9, 0.4, 0.2, –0.3.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{21}H_{52}O_6Si_5Na$: 563.2508; found: 563.2542.

4-Methylphenyl-2,3,4,6-tetra-*O*-trimethylsilyl-1-thio-β-D-galactopyranoside (2d)

Prepared according to the general procedure 1; colorless oil; yield: 401.5 mg (99%); R_f = 0.65 (EtOAc/hexane 1:11); $[\alpha]_D^{29}$ –31.8 (*c* 1.0, DCM).

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.41 (d, *J* = 8.2 Hz, 1 H), 7.07 (d, *J* = 8.0 Hz, 1 H), 4.51 (d, *J* = 9.2 Hz, 1 H), 3.94–3.89 (m, 1 H), 3.65 (d, *J* = 3.2 Hz, 1 H), 3.64 (d, *J* = 1.2 Hz, 1 H), 3.47–3.41 (m, 1 H), 2.31 (s, 3 H), 0.17 (s, 9 H), 0.16 (s, 9 H), 0.14 (s, 9 H), 0.10 (s, 9 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 136.4, 131.7, 130.8, 129.3, 89.9, 79.0, 77.1, 71.5, 70.6, 61.1, 21.0, 1.2, 0.7, 0.5, –0.5.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{25}H_{50}O_5SSi_4Na$: 597.2354; found: 597.2380.

1,2,3,4,6-Penta-*O*-trimethylsilyl-D-galactopyranoside (2e)

Prepared according to the general procedure 1; colorless oil; yield: 484.5 mg (81%); α/β = 32:5; R_f = 0.49 (EtOAc/hexane 1:30); $[\alpha]_D^{29}$ +76.9 (*c* 1.0, DCM).

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.04 (d, *J* = 2.0 Hz, 1 H), 4.40 (d, *J* = 7.2 Hz, 0.16 H), 3.90 (m 2 H), 3.81 (s, 2 H), 3.62 (t, *J* = 8.8 Hz, 1 H), 3.53 (dd, *J* = 9.6, 5.6 Hz, 1 H), 0.14 (s, 18 H), 0.13 (s, 9 H), 0.11 (s, 9 H), 0.10 (s, 9 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 94.5, 72.2, 71.1, 70.5, 69.9, 61.1, 0.5, 0.4, 0.2, 0.0, –0.6.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{21}H_{52}O_6Si_5Na$: 563.2508; found: 563.2610.

1,2,3,4,6-Penta-*O*-trimethylsilyl-α-D-mannopyranoside (2f)

Prepared according to the general procedure 1; colorless oil; yield: 597.7 mg (99%); α only; R_f = 0.57 (EtOAc/hexane 1:22).

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 4.85 (d, *J* = 1.6 Hz, 1 H), 3.84–3.76 (m, 2 H), 3.68 (d, *J* = 3.2 Hz, 2 H), 3.60 (t, *J* = 2.0 Hz, 1 H), 3.54–3.49 (m, 1 H), 0.10 (s, 9 H), 0.09 (s, 9 H), 0.06 (s, 9 H), 0.05 (s, 9 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 95.5, 75.2, 74.6, 72.1, 68.1, 62.3, 0.6, 0.5, 0.2, –0.3.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{21}H_{52}O_6Si_5Na$: 563.2508; found: 563.2542.

tert-Butyldimethylsilyl-2-azido-2-deoxy-3,4,6-tri-*O*-trimethylsilyl-β-D-glucopyranoside (2g)

Prepared according to the general procedure 1; white solid; yield: 329.6 mg (98%); mp 37–39 °C; R_f = 0.67 (EtOAc/hexane 1:22); $[\alpha]_D^{28}$ +8.545 (*c* 1.1, DCM)

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 4.48 (d, *J* = 7.6 Hz, 1 H), 3.72 (m, 2 H), 3.58 (dd, *J* = 9.4, 8.6 Hz, 1 H), 3.24 (dd, *J* = 9.8, 8.6 Hz, 1 H), 3.14–3.06 (m, 2 H), 0.93 (s, 9 H), 0.19 (s, 9 H), 0.15 (s, 6 H), 0.14 (s, 9 H), 0.10 (s, 9 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 97.3, 76.7, 76.5, 71.4, 69.9, 61.6, 25.6, 17.9, 0.9, 0.7, –0.4, –4.3, –5.3.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{21}H_{49}N_3O_5Si_4Na$: 558.2647; found: 558.2648.

2-Deoxyl-4-methylphenyl-2-phthalimido-1-thio-3,4,6-tri-*O*-trimethylsilyl-β-D-glucopyranoside (2h)

Prepared according to the general procedure 1; white solid; yield: 279.3 mg (92%); mp 123–125 °C; R_f = 0.35 (EtOAc/hexane 1:9); $[\alpha]_D^{29}$ +46.7 (*c* 1.0, DCM).

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.99 (d, *J* = 22.4 Hz, 2 H), 7.88 (s, 2 H), 7.42–7.37 (m, 2 H), 7.14 (d, *J* = 8 Hz, 2 H), 5.58 (d, *J* = 10 Hz, 1 H), 4.54 (t, *J* = 9.2 Hz, 1 H), 4.31 (t, *J* = 10.2 Hz, 1 H), 3.94 (dt, *J* = 11.6, 7.2 Hz, 3 H), 3.83 (t, *J* = 9.0 Hz, 1 H), 3.52 (d, *J* = 7.8 Hz, 1 H), 2.42 (s, 3 H), 0.32 (s, 9 H), 0.29 (s, 9 H), 0.01 (s, 9 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 137.7, 134.1, 132.8, 131.9, 129.4, 123.6, 123.12, 83.7, 80.7, 74.7, 72.5, 61.8, 56.8, 21.1, 0.84, 0.76, –0.2.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{30}H_{45}NO_6SSi_3Na$: 654.2173; found: 654.2177.

1,2,3,5-Tetra-*O*-trimethylsilyl-α-D-xylofuranoside (2i)

Prepared according to the general procedure 1; white solid; yield: 581.3 mg (99%); mp 36–38 °C; α only; R_f = 0.49 (EtOAc/hexane 1:22); $[\alpha]_D^{30}$ +69.8 (*c* 1.0, DCM).

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 4.93 (d, *J* = 3.2 Hz, 1 H), 3.69 (t, *J* = 8.4 Hz, 1 H), 3.64 (t, *J* = 10.0 Hz, 1 H), 3.53–3.46 (m, 1 H), 3.43 (dd, *J* = 10.2, 5.4 Hz, 1 H), 3.34 (dd, *J* = 9.0, 3.0 Hz, 1 H), 0.15 (s, 9 H), 0.13 (s, 9 H), 0.12 (s, 18 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 94.2, 74.12, 74.07, 71.9, 62.3, 0.9, 0.4, 0.3, 0.2.

HRMS (ESI): *m*/*z* [M]$^+$ calcd for $C_{17}H_{43}O_5Si_4$: 439.2188; found: 439.2183.

1,2,3,5-Tetra-*O*-trimethylsilyl-α-D-lyxopyranoside (2j-1)

Prepared according to the general procedure 1; colorless oil; yield: 577.5 mg (99%); α only; R_f = 0.44 (EtOAc/hexane 1:22); $[\alpha]_D^{29}$ +20.636 (*c* 1.1, DCM).

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 4.61 (s, 1 H), 3.91–3.84 (m, 1 H), 3.81 (dd, *J* = 11.2, 5.2 Hz, 1 H), 3.69–3.66 (m, 1 H), 3.36 (dd, *J* = 8.4, 2.8 Hz, 1 H), 3.06 (dd, *J* = 11.2, 9.6 Hz, 1 H), 0.14 (s, 9 H), 0.13 (s, 18 H), 0.10 (s, 9 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 95.7, 75.0, 74.6, 67.6, 66.1, 0.5, 0.3, 0.08, 0.02.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{17}H_{43}O_5Si_4Na$: 461.2007; found: 461.2011.

1,2,3,5-Tetra-*O*-trimethylsilyl-α-D-lyxofuranoside (2j-2)

Prepared according to the general procedure 2; colorless oil; yield: 577.7 mg (99%); α only; R_f = 0.81 (EtOAc/hexane 1:18); $[\alpha]_D^{29}$ +183.0 (*c* 1.0, DCM).

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 4.82 (d, *J* = 3.2 Hz, 1 H), 3.79 (m, 1 H), 3.74 (dd, *J* = 7.8, 2.6 Hz, 1 H), 3.61 (t, *J* = 2.8 Hz, 1 H), 3.60–3.56 (m, 1 H), 3.50 (dd, *J* = 11.2, 8.4 Hz, 1 H), 0.13 (s, 9 H), 0.12 (s, 18 H), 0.10 (s, 9 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 95.6, 74.3, 72.6, 68.5, 64.0, 0.4, 0.3, 0.02, –0.2.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{17}H_{43}O_5Si_4Na$: 461.2007; found: 461.2011.

1,2,3,5-Tetra-*O*-trimethylsilyl-D-ribofuranoside (2k)

Prepared according to the general procedure 1; colorless oil; yield: 582.5 mg (96%); α/β = 1:2; R_f = 0.65 (EtOAc/ hexane 1:22); $[\alpha]_D^{29}$ –16.833 (*c* 1.2, DCM).

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 4.85 (d, *J* = 3.6 Hz, 0.52 H), 4.75 (d, *J* = 7.2 Hz, 1 H), 3.99 (t, *J* = 10.4 Hz, 0.74 H), 3.87 (s, 0.54 H), 3.87 (s, 1 H), 3.68 (s, 0.68 H), 3.67 (d, *J* = 2.8 Hz, 1 H), 3.65–3.59 (m, 1 H), 3.52–3.44 (m, 1 H), 3.42–3.40 (t, *J* = 3.4 Hz, 0.55 H), 3.22 (dd, *J* = 7.2, 3.2 Hz, 1 H), 3.20–3.16 (m, 0.66 H), 0.14 (s, 9 H), 0.12 (s, 6 H), 0.12 (s, 9 H), 0.11 (s, 9 H), 0.10 (s, 9 H), 0.10 (s, 8 H), 0.09 (s, 4 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 94.7, 92.6, 74.9, 73.8, 73.6, 70.6, 63.8, 58.1, 0.5, 0.4, 0.3, –0.02, –0.06, –0.18.

HRMS (ESI): *m*/*z* [M]$^+$ calcd for $C_{17}H_{43}O_5Si_4$: 439.2188; found: 439.2187.

1,2,3,5-Tetra-*O*-trimethylsilyl-α-D-arabinofuranoside (2l)

Prepared according to the general procedure 1; colorless oil; yield: 531.2 mg (91%); α only; R_f = 0.45 (EtOAc/hexane 1:22); $[\alpha]_D^{29}$ –54.33 (*c* 1.0, DCM).

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 4.95 (d, *J* = 2.4 Hz, 1 H), 3.86–3.82 (m, 1 H), 3.73–3.63 (m, 3 H), 3.43 (dd, *J* = 11.2, 5.6 Hz, 1 H), 0.07 (s, 9 H), 0.06 (s, 9 H), 0.05 (s, 9 H), 0.05 (s, 9 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 94.0, 71.3, 70.0, 64.1, 0.2, 0.1, –0.1.

HRMS (ESI): *m*/*z* [M]$^+$ calcd for $C_{17}H_{43}O_5Si_4$: 439.2188; found: 439.2186.

Methyl-4,6-*O*-benzylidene-2,3-di-*O*-trimethylsilyl-α-D-glucopyranoside (2m)

Prepared according to the general procedure 1; colorless oil; yield: 285 mg (94%); R_f = 0.37 (EtOAc/hexane 1:9); $[\alpha]_D^{29}$ +44.5 (*c* 1.2, DCM).

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.51–7.47 (m, 2 H), 7.38–7.32 (m, 3 H), 5.51 (s, 1 H), 4.62 (d, *J* = 3.6 Hz, 1 H), 4.27 (dd, *J* = 10, 4.6 Hz, 1 H), 3.96 (t, *J* = 9.0 Hz, 1 H), 3.80 (dd, *J* = 10, 4.8 Hz, 1 H), 3.71 (t, *J* = 10.2 Hz, 1 H), 3.62 (dd, *J* = 8.8, 4.0 Hz, 1 H), 3.42 (s, 3 H), 0.18 (s, 9 H), 0.10 (s, 9 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 128.8, 128.1, 126.1, 101.7, 101.0, 82.1, 74.1, 71.7, 69.1, 62.3, 55.4, 0.7, 0.3.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{34}O_6Si_2Na$: 449.1792; found: 449.1779.

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J.-S.C. and S.-Y.L. designed the research. J.-S.C. and Y.-F.K. optimized conditions for the reactions listed in Table 1. Y.-F.K. and W.L. prepared compounds **2a–m** of Scheme 2. Y.-F.K. prepared the recovery and re-use of PTA for Figure 1. H.-Y.L. and Y.-F.K. optimized conditions for the reactions shown in Table 2. H.-Y.L. and W.-C.Y. prepared compounds **2a–m** of Scheme 3. H.R.W. analyzed the mass data. J.-S.C. wrote the manuscript with the help of S.-Y.L.

Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0040-1705990.

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