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A mild method for regioselective de-O-methylation of saccharides by $Co_2(CO)_8/Et_3SiH/CO$ system

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ABSTRACT

A new method for cleaving methyl ethers off protected saccharides using $Co_2(CO)_8/Et_3SiH/CO$ system was developed. The method showed regioselectivity in different protected monosaccharides with various anomeric groups. The primary and equatorial secondary methyl ethers were preferentially removed. This method was successfully applied to the synthesis of the DEF trisaccharide segment of Idraparinux, which is highly methylated.

1. Introduction

Selective protection and deprotection of hydroxyl groups are critical transformations in carbohydrate chemistry. Among the many protecting groups, methyl ether is less frequently used than other ethers such as benzyl ether because of its harsh cleavage conditions, despite its simple installation and inherent stability. On the other hand, methyl group protected saccharides are widely found in various therapeutic agents and materials, such as idraparinux, cyclodextrin, and surfactants, because the protection of the hydroxyl group with a methyl group may enhance the stability of saccharides while also maintaining its solubility.[1] Comprehensive research on the formation and cleavage of methyl ethers is important for the synthesis of such complex oligosaccharides. In particular, several methods have been developed to remove methyl ethers, including acids (HCl, H_2SO_4, TFA), Lewis acids (BBr_3, BCl_3, $AlCl_3$, $SiCl_4$, $NbCl_5$, MgI, TMSI),[2] bases (LHDMS, PhSK, $Et_2NCH_2CH_2SH$),[3] reductive cleavage (LAH,[4] DIBAL-H and TIBAL[1-b,5a,b]), and ionic liquids.[6] However, these methods are sometimes too harsh for saccharide substrates such as thioglycosides and phenolic glycosides, or not able to remove the methyl ether regioselectively, which is essential for the synthesis of complex oligosaccharides. There are only a few reported conditions that are suitable for regioselective de-O-methylation of saccharides, such as MeS-$SiMe_3/ZnI_2/n$-Bu_4NI,[7] oxidation-based cleavage of DIB,[8] and engineered cytochrome $P450_{BM3}$ demethylases.[9] However, the substrate scope of these methods is limited, and development of a novel method for regioselective de-O-methylation is essential and a great challenge.

The most famous methylated oligosaccharide, idraparinux, is a derivative of fondaparinux, which is an efficient and safe anticoagulant drug used in the clinic.[10] With many hydroxyl groups protected by methyl ethers, the synthesis of idraparinux is simpler than that of fondaparinux. Moreover, it has better inhibitory activity and much longer half-life. In addition, the dosage and administration frequency of idraparinux are also less than those of fondaparinux. Because of these advantages, idraparinux has been extensively studied recently.[11] However, the synthesis of idraparinux is still a challenge, usually requiring 40 steps, with multiple protecting group transformations.[12] Considering the numerous methyl ethers in idraparinux, regioselective de-O-methylation may simplify the total synthesis.

In our previous study, the $Co_2(CO)_8/Et_3SiH/CO$ system was found to be efficient in the cleavage of benzyl and *p*-methoxybenzyl groups in saccharide and non-saccharide substrates.[13] This reactivity was mediated by the strong Lewis acidity and electrophilicity of the in situ generated $Et_3Si^+Co(CO)_4^-$ reagent. In this article, we report a novel method for the regioselective cleavage of methyl ethers in a wide variety of monosaccharides by the $Co_2(CO)_8/Et_3SiH/CO$ system (Scheme 1A). Furthermore, we explored the use

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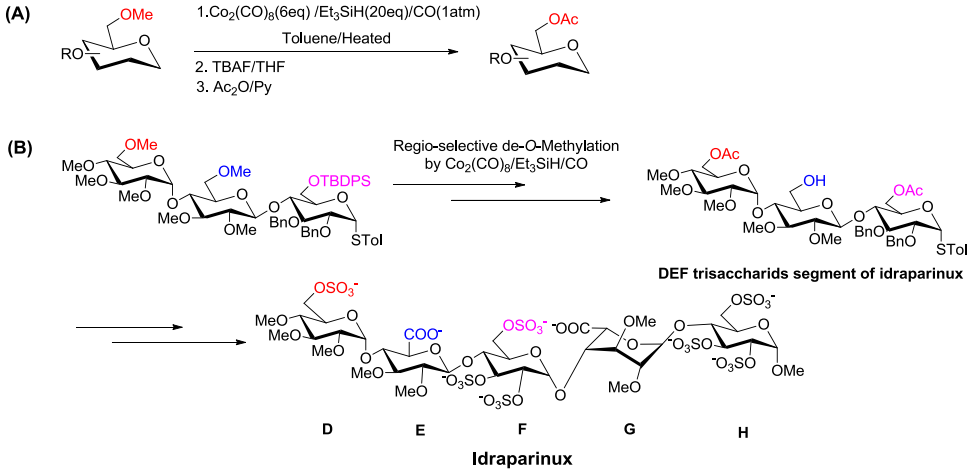
of regioselective de-O-methylation by this system to the synthesis of the DEF trisaccharide segment of idraparinux, which could be used as an intermediate for the total synthesis of idraparinux (Scheme 1B).



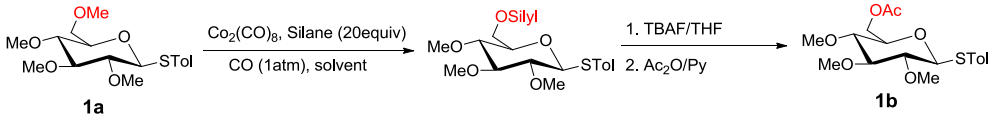
Scheme 1. (A)Regio-selective de-O-methylation of saccharides $Co_2(CO)_8/Et_3SiH/CO$ system; (B) Synthesis of DEF trisaccharides segment of idraparinux by regioselective de-O-methylation strategy.

2. Results and discussion

Recently, our laboratory extended the highly efficient and mild de-O-benzylation method with the $Co_2(CO)_8/Et_3SiH/CO$ system to the cleavage of *p*-methoxybenzyl ethers (PMB).[13] We found that except for the PMB group, a methyl group on PMB in per-*p*-methoxybenzylated glucoside was also removed when reacted at 80 °C. We were interested in this observation and hoped to find an efficient method for selective de-O-methylation of protected sugars. Therefore, we used per-methylated-β-thioglucoside **1a** as a model substrate to explore and optimize the reaction condition. To simplify the purification steps and identification of the products, we further transformed the generated silyl ether to an acetyl group by treating with TBAF/THF and Ac_2O/Py (Table 1).

With the fact that the actual catalytic reagent $Et_3Si^+Co(CO)_4^-$ generated by $Co_2(CO)_8/Et_3SiH/CO$ system *in situ* was sensitive to the steric hindrance and the hindrance of 6-OMe was smallest. Increasing the temperature to 70 °C or the reaction time to 72 h did not improve the conversion of **1a** (data not shown). With 6.0 equiv of $Co_2(CO)_8$, 85% of **1a** reacted, generating 52% **1b** and 18% de-2, 6-di-O-methylation product **1c** (the de-O-methylation site was confirmed by the chemical shifts and coupling constants of the hydrogen at the acetylation position, Table 1, Entry 2, and Table 2, Entry 1), indicating that enough amount of $Co_2(CO)_8$ is essential for sufficient conversion of **1a**. Lowering the temperature to room temperature gave no reaction of **1a** (Table 1, Entry 3), indicating that sufficiently high reaction temperatures were needed. If the solvent was changed to benzene, 40% of **1a** remained unreacted, and the products were a mixture of **1b** and de-2, 6-di-O-methylation products (Table 1, Entry 4). Changing the silane to $PhMe_2SiH$ and reducing the amount used, **1a** was reacted completely but the products were too complex to purify

Table 1
Condition screening of de-O-methylation with per-methylated-β-thioglucoside as model substrate

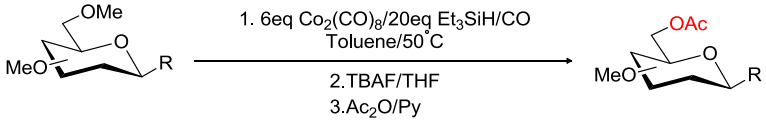


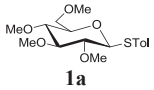
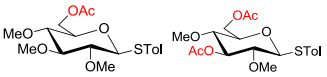
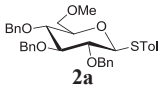
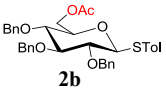
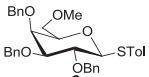
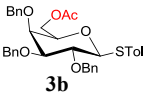
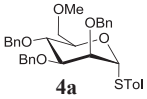
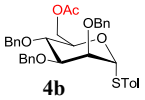
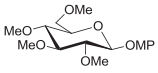
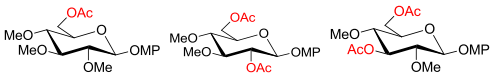
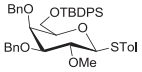
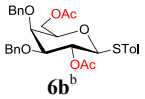
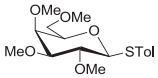
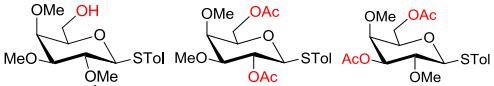
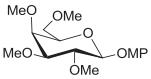
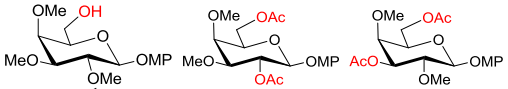
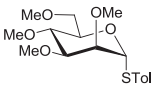
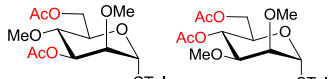
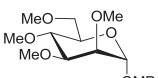
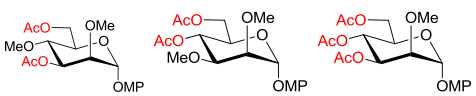
Entry	Silane	$Co_2(CO)_8$ (equiv)	Solvent	T (°C)	Time (h)	Yield (%)[a]
1	Et_3SiH	3.0	Toluene	50	48	63[b]
2	Et_3SiH	6.0	Toluene	50	42	52+18[c]
3	Et_3SiH	6.0	Toluene	rt.	48	0
4	Et_3SiH	6.0	Benzene	50	48	45+15[d]
5	$PhMe_2SiH$	1.0	Toluene	50	24	—[e]
6	$PhMe_2SiH$	0.5	Toluene	50	24	—[e]

[a] Yield of 3 steps.
[b] 37% of **1a** was unreacted.
[c] 52% of **1b** and 18% of de-2, 6-bi-O-methylation product **1c** were obtained, with 15% of **1a** unreacted (see Table 2, entry 1 for more details).
[d] 45% of **1b** and 15% of **1c** were obtained, with 40% of **1a** unreacted.
[e] **1a** was completely reacted but the products were rather complex.

As shown in Table 1, **1a** was treated with different equivalents of $Co_2(CO)_8$, silanes, solvents, and temperatures. When the reaction was carried out with 3.0 equiv of $Co_2(CO)_8$ and 20 equiv of Et_3SiH for 48 h at 50 °C in toluene, 63% of de-6-O-methyltion product was obtained with 37% of **1a** unreacted (Table 1, Entry 1). The de-O-methylation happened at 6-OMe was in accordance (Table 1, Entry 5 and 6), indicating that $PhMe_2SiH$ was too reactive and additional methyl ethers were removed. Consequently, our optimized reaction condition was 6.0 equiv of $Co_2(CO)_8$, 20 equiv of Et_3SiH, and CO (1 atm) in toluene at 50 °C, which could convert the starting materials adequately and gave sufficient product yield.

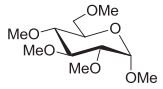
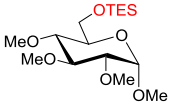
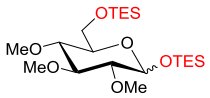
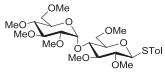
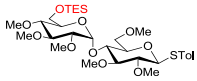
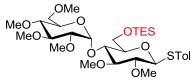
Table 2
Regioselective de-O-methylation of methylated saccarides by $Co_2(CO)_8/Et_3SiH/CO$ system



Entry	Substrates	Time (h)	Results
1	 **1a**	42	 **1b** 52% **1c** 18%
2[a]	 **2a**	48	 **2b** 84%
3[a]	 **3a**	48	 **3b** 85%
4[a]	 **4a**	48	 **4b** 87%
5	 **5a**	48	 **5b** 43% **5c** 18% **5d** 16%
6	 **6a**	48	 **6b**[b] 40%
7	 **7a**	28	 **7b**[b] 49% **7c** 28% **7d** 8%
8	 **8a**	48	 **8b**[b] 27% **8c** 41% **8d** 15%
9	 **9a**	48	 **9b** 42% **9c** 36%
10	 **10a**	48	 **10b** 30% **10c** 27% **10d** 8%

(*continued on next page*)

Table 2 (*continued*)

Entry	Substrates	Time (h)	Results
11[c]	 **11a**	18	 **11b** 55%  **11c** 43%
12[c]	 **12a**	48	 **12b** 30%  **12c** 30%

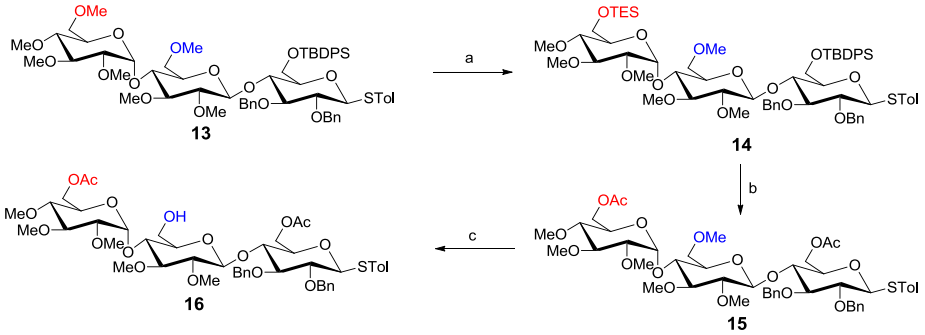
[a] The reaction was performed at 70 °C. [b] the removal of silly ether by TBAF/THF was performed at 50 °C for 2 h [c] No transformation of hydroxyl group to acetyl group was performed. [d] No transformation of silyl group to acetyl group was performed.

Under the established conditions, a wide variety of methylated saccharide substrates were treated with the $Co_2(CO)_8/Et_3SiH/CO$ system, and the results are summarized in Table 2. In these substrates, the 6-OMe was preferentially removed. For example, the per-methylated-β-thioglucoside **1a**, 2, 3, 4-tri-*O*-Bn- 6-*O*-Me-β-thioglucoside **2a**, 2, 3, 4-tri-*O*-Bn-6-*O*-Me-β-thiogalactoside **3a**, and 2, 3, 4-tri-*O*-Bn-6-*O*-Me-α-thiomannoside **4a**, all gave the de-6-*O*-Me products (entry1, 2, 3, 4) as the major product in high yield. This was attributed to the reduced steric hindrance at 6-O-position, where the methyl ether could be easily attacked by the $Et_3Si^+Co(CO)_4^-$ reagent.

In addition to the cleavage of 6-OMe, another methyl group was also removed. For **1a**, 18% of de-3, 6-di-*O*-Me product **1c** was obtained (Table 2, entry 1). Similar reactivity was observed in the de-O-methylation of per-methylated-β-phenolic glucoside **5a,** which yielded 18% of de-2, 6-di-*O*-Me product **5c** and 16% of de-4, 6-di-*O*-Me product **5d** (entry 5). For the substrates with only one secondary methyl ether at 2-*O*-position, such as 2-*O*-Me-3, 4-*O*-Bn-6-*O*-TBDPS-β-thioglucoside **6a**, the 2-OMe could also be removed with a yield of 40% (entry 6). These results indicated that unlike the benzyl ether system, secondary methyl ether may also be removed by $Co_2(CO)_8/Et_3SiH/CO$ system. This may be due to less steric hindrance of the secondary methyl ether compared to that of the analogous benzyl ether, allowing the $Et_3Si^+Co(CO)_4^-$ reagent to attack on these secondary methyl ethers.

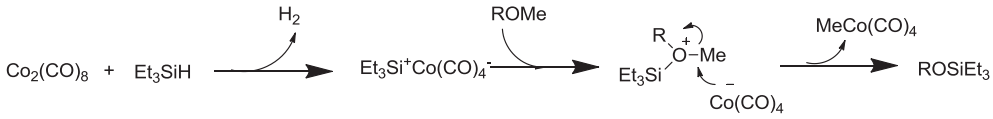
Among the 2-OMe, 3-OMe, 4-OMe groups, the equatorial methyl ethers were preferentially removed because the equatorial methyl ethers were less sterically hindered and more electron rich.[14] This could be demonstrated by the de-O-methylation of per-methylated-β-thiogalactoside **7a**, and per-methylated-β-phenolic galactoside **8a**, whose equatorial 2-OMe and 3-OMe groups were removed whereas the axial 4-OMe remained (entry 7, 8). The cleavage of the equatorial 3-OMe and 4-OMe groups and non-reactivity of the axial 2-OMe of the per-methylated-β-thiomannoside **9a** and per-methylated-β-phenolic mannoside **10a** (entry 9, 10) further confirmed our conclusion. In addition, because mannoses were more reactive, the main product of **9a** and **10a** were the de-4, 6-di-*O*-Me products (**9b, 9c, 10b and 10c**), and even the de-3, 4, 6-tri-*O*-Me product **10d** were obtained. Interestingly, the anomic methyl group could also be removed. Per-methylated glucose **11a** produced 43% of de-1, 6-bi-*O*-Me products **7c**, in addition to 55% of de-6-*O*-Me product **11b** (entry 11), suggesting that the anomic methyl group was sensitive to the reaction condition. The de-O-methylation reaction was also carried out with permethylated β-thiomaltoside **12a**, which has two 6-OMe groups, yielding the de-6-O-methylation product **12b** and de-6′-O-methylation product **12c** both in 30% yield (entry 12), suggesting that the hindrance of 6-OMe and 6′-OMe were similar.

After the successful application of the procedure to monosaccharides and disaccharides, we investigated the selective de-O-methylation of trisaccharide **13** in order to synthesize the DEF segment of Idraparinux. When compound **13** was treated with $Co_2(CO)_8$ (3.0 equiv) and Et_3SiH (20 equiv) at 50 °C in toluene for 24 h, the 6-*O*-Me on sugar D, whose steric hindrance was smaller the that on sugar E, was removed first and transformed to silyl ether (**14**, 48%). The silylated product **14** was then converted to acetylated compound **15** in 2 steps in 90% yield. When **15** was treated with $Co_2(CO)_8$ (6.0 equiv) and Et_3SiH (40 equiv) at 50 °C in toluene for 48 h, the 6-*O*-Me on sugar E was removed. Because of the high steric hindrance of 6-*O*-Me of sugar E, the yield of de-O-methylation is not very high. Then the TES group was removed by CSA quantitatively to produce compound **16** (Scheme 2), and the total yield of two steps is 20%. Compound **16** could be used as the key intermediate in the synthesis of Idraparinux.



Scheme 2. Reagents and conditions: (a) $Co_2(CO)_8$ (3.0 equiv)/Et_3SiH (20equiv)/CO(1 atm), toluene, 50 °C, 48%, 24 h. (b) 1. TBAF, THF, 50 °C, 15 h; 2. Ac_2O, Py, 3 h. 90% in 2 steps. (c) 1. $Co_2(CO)_8$ (6equiv)/Et_3SiH (40equiv)/CO(1 atm), toluene, 50 °C, 48 h; 2. CSA, CH_2Cl_2/CH_3OH (4/1), 20% in 2 steps.

The proposed mechanism for the deprotection of methyl ethers is shown in Scheme 3. $Co_2(CO)_8$ reacts with Et_3SiH, generating the active reagent $Et_3Si^+Co(CO)_4^-$ in situ. The Lewis acidic and electrophilic Et_3Si^+ combines adds to the oxygen atom and the $Co(CO)_4^-$ attacks the methyl group, leading to the cleavage of the methyl ether and generating the silyl ether.



Scheme 3. Proposed mechanism of de-O-methylation by $Co_2(CO)_8/Et_3SiH/CO$ system.

3. Conclusion

In conclusion, a novel regioselective method has been developed for the cleavage of methyl ethers of saccharides under mild conditions with the $Co_2(CO)_8/Et_3SiH/CO$ system. This system shows selectivity for primary and equatorial secondary methyl ether of various O-methylated saccharides. This de-O-methylation method provides a powerful tool for accessing an array of methylated saccharides with free primary and secondary hydroxyl groups, which could be used for further synthesis of more complex oligosaccharides. Using this regioselective de-O-methylation strategy, we achieved a concise synthesis of DEF trisaccharides segment of Idraparinux.

4. Experimental

4.1. General

All chemicals were purchased as reagent grade and used without further purification, unless otherwise noted. Dichloromethane was distilled over phosphorus pentoxide. Benzene, toluene, tetrahydrofuran, and pyridine were distilled over sodium. Analytical TLC was performed on precoated aluminum sheets with detection by fluorescence and/or by staining with 5% concentrated sulfuric acid in EtOH. Column chromatography was performed with silica gel (230–400 mesh, Merck). Optical rotation was measured using an Optical Activity AA-10R type polarimeter. ^1H NMR spectra were recorded on Advance DRX Bruker-400 spectrometers at 25 °C. Chemical shifts (in ppm) were referenced with tetramethylsilane (δ=0 ppm) in deuterated chloroform. ^{13}C NMR spectra were obtained using the same NMR spectrometers and were calibrated with $CDCl_3$ (δ=77.16 ppm).

4.2. General procedure A for de-O-methylation

$Co_2(CO)_8$ (3 equiv or 6 equiv, purchased from Alfa Aesar Chemicals Co. without further purification) was added to a flask under an atmosphere of CO. Et_3SiH (20 equiv, purchased from Alfa Aesar Chemicals Co. without further purification) was then added, and the mixture was stirred for 30 min at room temperature. A solution of permethylated saccharides in anhydrous toluene (2 mmol/5 ml) was degassed and then added using a syringe. The mixture was heated in an oil bath at 50 °C, and the reaction was monitored by TLC. After the disappearance of starting materials, the cobalt complex was precipitated by dropwise addition of pyridine and subsequent bubbling of oxygen through the solution for 20 min. The content of the flask was filtered through 5 cm of silica gel and eluted with ethyl acetate. The filtrate was evaporated and the residue was subjected to flash chromatography.

4.3. General procedure B for de-O-silylation and acylation

TBAF·$3H_2O$ (1.2 equiv) was added to a solution of the substrate in THF, and the mixture was stirred at room temperature for 30 min. The solvent was removed at reduced pressure and the residue was purified by flash chromatography.

4.4. General procedure C for acylation

For acetylation, the de-O-silylation product was dissolved in pyridine, acetic anhydride (4 equiv) was added slowly, and the mixture was stirred over 4 h. The reaction was stopped by the addition of CH_3OH in an ice bath. Evaporation of the solvent afforded a residue, which was purified by flash chromatography.

4.5. *p*-Methylphenyl 6-*O*-acetyl-2,3,4-tri-*O*-methyl-1-thio-β-D-glucopyranoside (1b)

General procedure A, B and C, white solid, 52%; ^1H NMR (400 MHz, $CDCl_3$) δ 7.44 (d, 2H, J=8.1 Hz), 7.10 (d, 2H, J=8.0 Hz), 4.42 (d, 1H, J=9.8 Hz), 4.35 (dd, 1H, J=2.1, 11.8 Hz), 4.19 (dd, 1H, J=6.1, 11.8 Hz), 3.65 (s, 3H), 3.61 (s, 3H), 3.52 (s, 3H), 3.36–3.40 (m, 1H), 3.22 (t, 1H, J=8.8 Hz), 2.99–3.08 (m, 2H), 2.33 (s, 3H), 2.09 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 138.0, 132.9, 129.7, 88.7, 87.5, 82.6, 79.8, 76.8, 63.6, 61.1, 61.0, 60.7, 21.3, 21.0.

4.6. *p*-Methylphenyl 3,6-di-*O*-acetyl-2,4-di-*O*-methyl-1-thio-β-D-glucopyranoside (1c)

General procedure A, B and C, white solid, 18%; ^1H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, 2H, J=8.1 Hz), 7.12 (d, 2H, J=8.0 Hz), 5.15 (t, 1H, J=9.2 Hz), 4.52 (d, 1H, J=9.8 Hz), 4.36 (dd, 1H, J=2.1, 11.9 Hz), 4.22 (dd, 1H, J=5.9, 11.9 Hz), 3.48–3.54 (m, 4H), 3.40 (s, 3H), 3.21 (t, 3H, J=9.5 Hz), 3.13 (t, 3H, J=9.5 Hz), 2.34 (s, 3H), 2.14 (s, 3H), 2.11 (s, 3H).

4.7. *p*-Methylphenyl 6-*O*-acetyl-2,3,4-tri-*O*-benzyl-1-thio-β-D-glucopyranoside (2b)

General procedure A, B and C, white solid, 85%; ^1H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, 2H, J=8.1 Hz), 7.50 (d, 2H, J=8.1 Hz), 7.44–7.33 (m, 13H), 7.19 (d, 2H, J=8.0 Hz), 5.03–5.00 (dd, 2H, J=10.3, 2.2 Hz), 4.95–4.92 (dd, 2H, J=10.8, 3.2 Hz), 4.84 (d, 1H, J=10.3 Hz), 4.69–4.65 (dd, 2H, J=9.8, 6.2 Hz), 4.47 (d, 1H, J=11.6 Hz), 4.32–4.28 (dd, 1H, J=11.8, 3.7 Hz), 3.82–3.78 (m, 1H), 3.61–3.54 (m, 3H), 2.41 (s, 3H), 2.13 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 138.0, 137.9, 137.7, 132.9, 129.7, 128.6, 128.5, 128.1, 128.0, 127.9, 87.8, 86.8, 80.9, 77.6, 76.9, 75.9, 75.5, 75.1, 63.3, 21.2, 21.0.

4.8. *p*-Methylphenyl 6-*O*-acetyl-2,3,4-tri-*O*-benzyl-1-thio-β-D-galactopyranoside (3b)

General procedure A, B and C, white solid, 85%; ^1H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, 2H, J=8.1 Hz), 7.47 (d, 2H, J=8.1 Hz), 7.45–7.28 (m, 13H), 7.08 (d, 2H, J=8.0 Hz), 5.05 (d, 1H, J=11.5 Hz), 4.90 (d, 1H, J=11.2 Hz), 4.84–4.78 (m, 3H), 4.7 (d, 1H, J=11.6 Hz), 4.63 (d, 1H, J=9.7 Hz), 4.34–4.30 (dd, 2H, J=11.2, 7.0 Hz), 4.18–4.14 (dd, 1H, J=11.3, 5.6 Hz), 3.99–3.95 (t, 1H, J=9.4 Hz), 3.81–3.77 (m,

1H), 3.66–3.60 (m, 2H), 2.35 (s, 3H), 2.04 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6, 138.3, 138.2, 137.4, 132.4, 130.2, 129.6, 128.4, 128.3, 128.1, 127.8, 127.7, 127.6, 88.1, 84.3, 76.0, 75.7, 74.3, 73.4, 73.2, 68.0, 63.5, 21.1, 20.9.

4.9. *p*-Methylphenyl 6-*O*-acetyl-2,3,4-tri-*O*-benzyl-1-thio-β-D-mannopyranoside (4b)

General procedure A, B and C, white solid, 85%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40–7.28 (m, 17H), 7.14 (d, 2H, *J*=8.0 Hz), 5.54 (d, 1H, *J*=1.4 Hz), 5.50 (d, 1H, *J*=5.50 Hz), 4.76–4.62 (m, 5H), 4.38–4.36 (m, 3H), 4.04–3.98 (m, 2H), 3.94–3.91 (dd, 1H, *J*=9.2, 3.0 Hz), 2.36 (s, 3H), 2.07 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 138.1, 138.0, 137.9, 132.3, 130.2, 129.8, 128.5, 128.4, 128.1, 127.9, 127.8, 85.9, 80.1, 76.0, 75.3, 74.7, 72.1, 71.9, 70.9, 63.6, 21.1, 20.9.

4.10. *p*-Methoxyphenyl 6-*O*-acetyl-2,3,4-tri-*O*-methyl-β-D-glucopyranoside (5b)

General procedure A, B and C, white solid, 43%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.99–7.05 (m, 4H), 4.79 (d, 1H, *J*=9.2 Hz), 4.34 (dd, 1H, *J*=2.2, 11.8 Hz), 4.23 (dd, 1H, *J*=6.1, 11.8 Hz), 3.66 (s, 3H), 3.65 (s, 3H), 3.54 (s, 3H), 3.50–3.53 (m, 1H), 3.24–3.31 (m, 2H), 3.16 (t, 1H, *J*=9.2 Hz), 2.28 (s, 3H), 2.07 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ155.0, 122.5, 118.0, 101.9, 86.5, 83.6, 79.6, 73.1, 63.4, 61.1, 60.8, 21.2, 21.0.

4.11. *p*-Methoxyphenyl 2,6-di-*O*-acetyl-3,4-di-*O*-methyl-β-D-glucopyranoside (5c)

General procedure A, B and C, white solid, 18%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.92–6.94 (m, 2H), 6.79–6.81 (m, 2H), 5.11 (dd, 1H, *J*=8.0, 9.2 Hz), 4.80 (d, 1H, *J*=7.9 Hz), 4.39 (dd, 1H, *J*=2.2, 11.8 Hz), 4.25 (dd, 1H, *J*=5.6, 11.9 Hz), 3.77 (s, 3H), 3.56 (s, 3H), 3.55 (s, 3H), 3.53–3.54 (m, 1H), 3.29–3.41 (m, 2H), 2.14 (s, 3H), 2.09 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 151.4, 118.6, 114.6, 100.4, 84.8, 79.4, 73.3, 72.9, 63.1, 60.8, 60.5, 55.8, 21.1, 21.0.

4.12. *p*-Methoxyphenyl 3,6-di-*O*-acetyl-2,4-di-*O*-methyl-β-D-glucopyranoside (5d)

General procedure A, B and C, white solid, 16%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.98–7.01 (m, 2H), 6.81–6.84 (m, 2H), 5.16 (t, 1H, *J*=9.3 Hz), 4.83 (d, 1H, *J*=7.7 Hz), 4.36 (dd, 1H, *J*=2.2, 11.9 Hz), 4.27 (dd, 1H, *J*=5.7, 11.9 Hz), 3.78 (s, 4H), 3.60 (s, 3H), 3.43 (s, 3H), 3.33 (t, 2H, *J*=9.2 Hz), 2.17 (s, 3H), 2.09 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 170.0, 155.5, 151.1, 118.6, 118.5, 114.5, 102.4, 83.4, 83.0, 81.2, 77.9, 75.5, 72.7, 63.0, 60.6, 60.0, 55.7, 21.1, 20.9, 20.8, 20.8.

4.13. *p*-Methylphenyl 2,6-di-*O*-acetyl-3, 4-di-*O*-benzyl-1-thio-β-D-glucopyranoside (6b)

General procedure A, B and C, white solid, 85%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43–7.28 (m, 12H), 7.09 (d, 2H, *J*=8.0 Hz), 5.45–5.40 (t, 1H, *J*=9.8 Hz), 5.0 (d, 1H, *J*=11.7 Hz), 4.74 (d, 1H, *J*=12.1 Hz), 4.63–4.54 (m, 3H), 4.31–4.26 (dd, 1H, *J*=11.2, 7.0 Hz), 4.14–4.10 (dd, 1H, *J*=11.3, 5.4 Hz), 3.88 (d, 1H, *J*=2.0 Hz), 3.64–3.57 (m, 2H), 2.33 (s, 3H), 2.09 (s, 3H), 2.01 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6, 169.5, 138.0, 137.7, 132.6, 129.7, 129.5, 128.5, 128.3, 128.2, 127.9, 127.7, 127.5, 87.0, 81.7, 76.2, 74.2, 72.5, 72.4, 69.7, 63.4, 21.1, 21.1, 20.8.

4.14. *p*-Methylphenyl 2,3,4-tri-*O*-methyl-1-thio-β-D-galactopyranoside (7b)

General procedure A and B, colorless oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (d, 2H, *J*=8.2 Hz), 7.10 (d, 2H, *J*=8.0 Hz), 4.46 (d, 1H, *J*=9.6 Hz), 3.88–3.93 (m, 1H), 3.65–3.71 (m, 1H), 3.63 (d, 1H, *J*=2.4 Hz), 3.60 (s, 3H), 3.54 (s, 3H), 3.53 (s, 3H), 3.38–3.43 (m, 2H), 3.20 (dd, 1H, *J*=3.0, 9.2 Hz), 2.32 (s, 3H), 2.06 (dd, 1H, *J*=3.0, 9.1 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.7, 132.5, 130.1, 129.7, 88.1, 86.1, 79.4, 78.9, 75.9, 62.4, 61.4, 61.3, 58.5, 21.2.

4.15. *p*-Methylphenyl 2,6-di-*O*-acetyl-3,4-di-*O*-methyl-1-thio-β-D-galactopyranoside (7c)

General procedure A, B and C, white solid, 28%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, 2H, *J*=8.1 Hz), 7.09 (d, 2H, *J*=8.1 Hz), 5.23 (t, 1H, *J*=9.8 Hz), 4.53 (d, 1H, *J*=10.0 Hz), 4.23–4.35 (m, 2H), 3.69 (d, 1H, *J*=2.6 Hz), 3.63 (t, 1H, *J*=6.3 Hz), 3.55 (s, 3H), 3.45 (s, 3H), 3.30 (dd, 1H, *J*=2.8, 9.6 Hz), 2.33 (s, 3H), 2.13 (s, 3H), 2.08 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 169.6, 137.7, 132.5, 130.1, 129.5, 87.3, 83.7, 76.2, 74.9, 69.7, 63.3, 61.3, 58.2, 21.1, 21.1, 20.8.

4.16. *p*-Methylphenyl 3,6-di-*O*-acetyl-2,4-di-*O*-methyl-1-thio-β-D-galactopyranoside (7d)

General procedure A, B and C, white solid, 8%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, 2H, *J*=8.1 Hz), 7.10 (d, 2H, *J*=8.0 Hz), 4.85 (dd, 1H, *J*=3.0, 9.7 Hz), 4.50 (d, 1H, *J*=9.7 Hz), 4.31 (dd, 1H, *J*=6.9, 11.2 Hz), 4.17 (dd, 1H, *J*=6.0, 11.2 Hz), 3.66 (m, 2H), 3.54 (s, 3H), 3.51 (d, 1H, 9.7 Hz), 3.48 (s, 3H), 2.33 (s, 3H), 2.16 (s, 3H), 2.06 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ170.7, 170.5, 137.9, 132.7, 130.0, 129.7, 88.3, 77.3, 77.3, 76.8, 75.7, 62.7, 61.5, 61.2, 21.3, 21.2, 20.9.

4.17. *p*-Methoxyphenyl 2,3,4-tri-*O*-methyl-β-D-galactopyranoside (8b)

General procedure A and B, colorless oil; ^{1}H NMR (400 MHz, DMSO) δ6.99–7.02 (m, 2H), 6.90–6.93 (m, 2H), 4.88 (d, 1H, *J*=5.2 Hz), 4.84 (d, 1H, *J*=7.2 Hz), 3.77 (d, 1H, *J*=2.1 Hz), 3.76 (s, 3H), 3.56–3.60 (m, 2H), 3.55 (s, 3H), 3.50 (s, 3H), 3.47 (s, 3H), 3.36 (d, 3H, *J*=14.0 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.3, 151.5, 118.5, 114.6, 102.9, 84.0, 80.6, 75.6, 75.2, 62.2, 61.4, 61.1, 58.7, 55.8.

4.18. *p*-Methoxyphenyl 2,6-di-*O*-acetyl-3,4-di-*O*-methyl-β-D-galactopyranoside (8c)

General procedure A, B and C, white solid, 41%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.94–6.96 (m, 2H), 6.78–6.81 (m, 2H), 5.43 (dd, 1H, *J*=7.9, 10.0 Hz), 4.79 (d, 1H, *J*=7.8 Hz), 4.27–4.39 (m, 2H), 3.77 (s, 3H), 3.71–3.73 (m, 2H), 3.61 (s, 3H), 3.49 (s, 3H), 3.36 (dd, 1H, *J*=2.8, 10.0 Hz), 2.11 (s, 3H), 2.10 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ170.8, 155.5, 151.6, 118.8, 114.5, 100.9, 82.5, 74.6, 72.7, 71.1, 63.1, 61.4, 58.4, 55.8, 21.1, 21.0.

4.19. *p*-Methoxyphenyl 3,6-di-*O*-acetyl-2,4-di-*O*-methyl-β-D-galactopyranoside (8d)

General procedure A, B and C, white solid, 15%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.00–7.02 (m, 2H), 6.80–6.82 (m, 2H), 4.87 (dd, 1H, *J*=3.1, 10.2 Hz), 4.78 (d, 1H, *J*=7.7 Hz), 4.35 (dd, 1H, *J*=6.7, 11.1 Hz), 4.20 (dd, 1H, *J*=6.3, 11.1 Hz), 3.77 (s, 3H), 3.67–3.75 (m, 2H), 3.63 (s, 3H), 3.53 (s, 3H), 2.18 (s, 3H), 2.08 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ170.7, 170.6, 155.6, 151.4, 118.9, 114.6, 103.0, 78.3, 76.3, 75.3, 72.1, 62.4, 61.6, 61.1, 55.8, 21.2, 20.9.

4.20. *p*-Methylphenyl 3,6-di-*O*-acetyl-2,4-di-*O*-methyl-1-thio-α-D-mannopyranoside (9b)

General procedure A, B and C, white solid, 42%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, 2H, J=8.1 Hz), 7.12 (d, 2H, J=8.0 Hz), 5.51 (d, 1H, J=1.8 Hz), 5.13 (dd, 1H, J=3.3, 9.5 Hz), 4.34 (m, 3H), 3.89 (dd, 1H, J=1.9, 3.2 Hz), 3.61 (t, 1H, J=9.2 Hz), 3.48 (s, 3H), 3.42 (s, 3H), 2.33 (s, 3H), 2.17 (s, 3H), 2.08 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 170.2, 138.0, 132.3, 129.9, 84.8, 79.5, 75.1, 73.9, 70.5, 63.5, 60.6, 58.4, 21.2, 21.2, 20.9.

4.21. *p*-Methylphenyl 4,6-di-*O*-acetyl-2,3-di-*O*-methyl-1-thio-α-D-mannopyranoside (9c)

General procedure A, B and C, white solid; ^{1}H NMR (400 MHz, CDCl3) δ 7.40 (d, 2H, J=8.1 Hz), 7.14 (d, 2H, J=8.0 Hz), 5.60 (d, 1H, J=1.4 Hz), 5.29 (t, 1H, J=9.8 Hz), 4.36–4.41 (m, 1H), 4.31 (t, 1H, J=6.7 Hz), 4.25 (dd, 1H, J=6.1, 12.2 Hz), 4.10 (dd, 1H, J=2.2, 12.1 Hz), 3.89 (dd, 1H, J=1.8, 2.9 Hz), 3.57 (dd, 1H, J=3.1, 9.4 Hz), 3.48 (s, 3H), 3.45 (s, 3H), 2.34 (s, 3H), 2.10 (s, 3H), 2.06 (s, 3H).

4.22. *p*-Methoxyphenyl 3,6-di-*O*-acetyl-2,4-di-*O*-methyl-α-D-mannopyranoside (10b)

General procedure A, B and C, white solid, 30%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.02–7.04 (m, 2H), 6.81–6.83 (m, 2H), 5.44 (d, 1H, J=1.8 Hz), 5.35 (dd, 1H, J=3.4, 9.5 Hz), 4.28–4.29 (m, 2H), 3.89–3.93 (m, 1H), 3.84 (dd, 1H, J=2.1, 3.3 Hz), 3.77 (s, 3H), 3.64 (t, 1H, J=9.7 Hz), 3.51 (s, 3H), 3.48 (s, 3H), 2.19 (s, 3H), 2.07 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 170.3, 155.2, 150.2, 117.9, 114.6, 96.3, 78.3, 74.8, 73.6, 70.2, 63.2, 60.5, 59.4, 55.7, 21.3, 20.9.

4.23. *p*-Methoxyphenyl 4,6-di-*O*-acetyl-2,3-di-*O*-methyl-α-D-mannopyranoside (10c)

General procedure A, B and C, white solid, 27%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.02–7.04 (m, 2H), 6.83–6.85 (m, 2H), 5.52 (d, 1H, J=1.7 Hz), 5.31 (t, 1H, J=9.8 Hz), 4.22 (dd, 1H, J=5.7, 12.2 Hz), 4.06 (dd, 1H, J=2.2, 12.2 Hz), 3.93–3.97 (m, 1H), 3.80–3.83 (m, 1H), 3.78 (s, 3H), 3.56 (s, 3H), 3.50 (s, 3H), 2.09 (s, 3H), 2.02 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9, 155.3, 150.3, 117.8, 114.8, 96.8, 78.8, 76.8, 69.6, 67.9, 62.8, 59.6, 58.1, 55.8, 21.0, 20.9.

4.24. *p*-Methoxyphenyl 3,4,6-tri-*O*-acetyl-2-*O*-methyl-α-D-mannopyranoside (10d)

General procedure A, B and C, white solid, 8%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.03–7.05 (m, 2H), 6.82–6.85 (m, 2H), 5.50 (d, 1H, J=1.9 Hz), 5.38–5.47 (m, 2H), 4.27 (dd, 1H, J=5.5, 12.6 Hz), 4.02–4.07 (m, 2H), 3.83 (dd, 1H, J=2.0, 2.8 Hz), 3.78 (s, 3H), 3.52 (s, 3H), 2.12 (s, 3H), 2.05 (s, 3H), 2.04 (s, 3H).

4.25. Methyl 2,3,4-tri-*O*-methyl-6-*O*-triethyl-silyl-α-D-glucopyranoside (11b)

General procedure A, colorless oil, 55%; ^{1}H NMR (400 MHz, $CDCl_3$) δ4.80 (d, 1H, J=3.6 Hz), 3.81 (d, 2H, J=3.1 Hz), 3.63 (s, 3H), 3.55 (s, 3H), 3.45–3.51 (m, 5H), 3.39 (s, 3H), 3.15–3.20 (m, 2H), 0.98 (t, 10H, J=8.0 Hz), 0.60–0.66 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 97.1, 83.6, 81.8, 79.0, 71.2, 61.7, 60.5, 60.1, 58.7, 54.6, 6.6, 4.3.

4.26. Triethyl-silyl 2,3,4-tri-*O*-methyl-6-*O*-triethyl-silyl-D-glucopyranoside (11c)

General procedure A, colorless oil, 43%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.84 (d, 1H, J=3.6 Hz), 4.56 (d, 1H, J=3.7 Hz), 3.79–3.86 (m, 5H), 3.61 (s, 3H), 3.40–3.57 (m, 13H), 3.37 (s, 3H), 3.36 (s, 3H), 3.04–3.15 (m, 3H), 0.96–1.00 (m, 36H), 0.60–0.70 (m, 24H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 100.2, 96.8, 84.4, 82.5, 80.5, 79.6, 74.3, 73.7, 71.5, 71.4, 62.2, 62.1, 61.3, 60.9, 60.4, 58.4, 55.0, 54.9, 7.0, 6.9, 6.8, 5.2, 4.9, 4.6, 4.6.

4.27. *p*-Methylphenyl (2,3,4-tri-*O*-methyl-6-*O*-triethyl-silyl-α-D-glucopyranosyl)-(1→4)-2,3,6-tri-*O*-methyl-1-thiol-β-D-glucopyranoside (12b)

General procedure A, colorless oil, 30%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44–7.42 (d, J=8.1 Hz, 1H), 7.11–7.09 (d, J=8.0 Hz, 1H), 5.59 (d, J=3.8 Hz, 1H), 4.48–4.46 (d, J=9.9 Hz, 1H), 3.85–3.75 (m, 4H), 3.65–3.53 (m, 19H), 3.45–3.40 (m, 5H), 3.32–3.24 (m, 5H), 3.19–3.16 (dd, J=9.8, 3.8 Hz, 1H), 2.33 (s, 3H), 0.98–0.95 (3, 10H), 0.64–0.58 (m, 7H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.3, 132.1, 130.3, 129.5, 96.4, 88.7, 87.7, 83.3, 83.1,81.8, 79.2, 79.1, 71.5, 70.8, 62.3, 60.7, 60.5, 60.3, 60.0, 59.7, 59.2, 21.1, 6.8, 4.6.

4.28. *p*-Methylphenyl (2,3,4,6-tetra-*O*-methyl-α-D-glucopyranosyl)-(1→4)-2,3-di-*O*-methyl-6-*O*-triethyl-silyl-1-thiol-β-D-glucopyranoside (12c)

General procedure A, colorless oil, 30%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44–7.42 (d, J=8.1 Hz, 1H), 7.11–7.09 (d, J=7.9 Hz, 1H), 5.53 (d, J=3.8 Hz, 1H), 4.45–4.43 (d, J=9.9 Hz, 1H), 3.85–3.74 (m, 4H), 3.64 (s, 3H), 3.62 (s, 3H), 3.60 (m, 4H), 3.56 (m, 7H), 3.53–3.46 (m, 2H), 3.44–3.36 (m, 5H), 3.33–3.25 (m, 5H), 3.16–3.08 (m, 2H), 2.33 (s, 3H), 0.99–0.95 (3, 10H), 0.65–0.60 (m, 7H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.5, 132.3, 131.9, 130.1, 129.6, 129.5, 96.6, 88.7, 87.8, 83.7, 83.1, 81.9, 78.9, 78.1, 72.0, 71.9, 71.3, 61.4, 60.7, 60.6, 60.4, 60.1, 59.7, 59.1, 21.1, 6.8, 4.5.

4.29. *p*-Methylphenyl (2,3,4-tri-*O*-methyl-6-*O*-triethyl-silyl-α-D-glucopyranosyl)-(1→4)-(2,3,6-tri-*O*-methyl-β-D-glucopyranosyl) -(1→4)-2,3-di-*O*-benzyl-6-*O*-*tert*-butyldiphenyl-silyl-1-thiol-β-D-glucopyranoside (14)

General procedure A, colorless oil, 48%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82–7.78 (m, 4H), 7.45–7.23 (m, 22H), 6.98 (d, J=8.0 Hz, 2H), 5.51 (d, J=4.0 Hz, 1H), 5.20 (d, J=11.2 Hz, 1H), 4.77–4.60 (m, 6H), 4.19–4.06 (m, 3H), 3.83–3.71 (m, 4H), 3.68–3.62 (m, 6H), 3.59 (s, 4H), 3.58–3.52 (m, 8H), 3.51–3.39 (m, 11H), 3.34–3.22 (m, 5H), 3.17–3.11 (m, 5H), 2.28 (s, 3H), 1.10 (s, 9H), 0.99–0.93 (t, 12H), 0.64–0.57 (m, 8H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.3, 138.4, 137.3, 136.0, 135.7, 133.8, 133.0, 132.3, 130.4, 129.6, 128.3, 128.1, 127.8, 127.7, 127.2, 102.9, 96.5, 87.9, 86.8, 85.5, 84.7, 83.5, 82.0, 80.1, 78.9, 76.9, 75.6, 75.3, 74.2, 72.4, 71.7, 70.8, 61.5, 60.7, 60.4, 60.3, 60.0, 59.2, 58.8, 26.9, 21.1, 19.5, 6.8, 4.5.

4.30. *p*-Methylphenyl (6-*O*-acetyl-2,3,4-tri-*O*-methyl-α-D-glucopyranosyl)-(1→4)-(2,3,6-tri-*O*-methyl-β-D-glucopyranosyl)-(1→4)-6-*O*-acetyl-2,3-di-*O*-benzyl-1-thiol-β-D-glucopyranoside (15)

TBFA·3H_2O (1.2 equiv) was added to a solution of **14** (240 mg, 0.2 mmol) in THF, and the mixture was stirred at room temperature for 1 h. Then the solvent was removed at reduced pressure and the residue was purified by column chromatography (PE/acetone=2/1).

Then the product was dissolved in pyridine (2 ml), then acetic anhydride (0.5 ml) was added and the mixture was stirred for 3 h. The reaction was stopped by the addition of CH_3OH in ice bath, and evaporation of the solvent afforded a residue which was purified by column chromatography, giving **15** as colorless oil (168 mg, 90% in 2 steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, J=81 Hz, 2H), 7.35–7.34 (d, J=8.4 Hz, 2H), 7.31–7.24 (m, 9H), 7.09 (d, J=8.0 Hz, 2H), 5.61 (d, J=3.8 Hz, 1H), 5.15 (d, J=11.4 Hz, 1H), 4.81 (d, J=10.2 Hz, 1H), 4.72–4.62 (m, 3H), 4.57 (d, J=9.8 Hz, 1H), 4.32–4.65 (m, 3H), 4.19–4.16(dd, J=11.9, 1.9 Hz, 1H), 3.83–3.77 (q, J=9.1 Hz, 2H), 3.67–3.60 (m, 5H), 3.56–3.49 (m, 14H), 3.46–3.30 (m, 6H), 3.18–3.15(dd, J=9.8, 3.7 Hz, 1H), 3.11–3.07 (m, 4H), 3.01–2.97 (t, J=8.0 Hz, 1H), 2.33 (s, 3H), 2.11 (s, 3H), 2.06 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 170.5, 139.1, 138.0, 137.9, 133.0, 129.6, 129.5, 128.3, 128.2, 127.8, 127.3, 127.2, 103.4, 95.9, 87.5, 86.8, 84.9, 84.5, 83.4, 81.8, 80.3, 79.5, 78.3, 77.1, 75.4, 75.3, 74.1, 71.4, 70.7, 69.1, 63.0, 62.8, 60.9, 60.6, 60.5, 59.8, 59.5, 58.9, 26.9, 21.0, 20.9.

4.31. *p*-Methylphenyl (6-*O*-acetyl-2,3,4-tri-*O*-methyl-α-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-methyl-β-D-glucopyranosyl)-(1→4)-6-*O*-acetyl-2,3-di-*O*-benzyl-1-thiol-β-D-glucopyranoside (16)

General procedure A and B, colorless oil, 20% in 2 steps. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, J=81 Hz, 2H), 7.35–7.34 (d, J=8.4 Hz, 2H), 7.31–7.24 (m, 10H), 7.09 (d, J=8.0 Hz, 2H), 5.62 (d, J=3.5 Hz, 1H), 5.15 (d, J=11.4 Hz, 1H), 4.81 (d, J=10.1 Hz, 1H), 4.73–4.62 (m, 3H), 4.58 (d, J=9.8 Hz, 1H), 4.32–4.21 (m, 4H), 3.88–3.76 (m, 3H), 3.69–3.65 (m, 3H), 3.56–3.52 (m, 14H), 3.49–3.26 (m, 6H), 3.18–3.10 (m, 5H),3.02–2.98 (t, J=8.0 Hz, 1H), 2.33 (s, 3H), 2.11 (s, 3H), 2.07 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 170.5, 139.1, 138.0, 137.9, 133.0, 129.6, 129.5, 128.3, 128.2, 127.8, 127.3, 127.2, 103.4, 95.4, 87.6, 86.5, 84.9, 84.4, 81.4, 80.3, 79.1, 78.4, 75.4, 75.3, 74.2, 72.9, 72.1, 70.7, 69.0, 63.1, 62.8, 60.7, 60.5, 59.8, 58.8, 26.9, 21.0, 20.9.

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Supplementary data

Supplementary data (Copies of ^{1}H, ^{13}C NMR spectra of relative compounds) associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2016.07.081.

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