Article

Improved Synthesis of Glucosyl Esters

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Abstract: An improved synthesis of glucosyl esters was reported here, avoiding the use of expensive Ag reagent as well as the hydrolysis of instable glucosyl bromide. Notably, -configuration product was exclusively obtained in good yield.

Keywords: glucosyl esters; glucosyl bromide; aromatic acids; aliphatic acids.

1. Introduction

Much more glycosyl esters have been investigated because of the biologically activity. Such as tuliposide-A and tuliposide-B, showed bacteriotoxic and fungitoxic effects [1]. Some of saturated fatty glycosyl esters were examined for antitumor activity [2]. In addition, glycosyl esters have also been applied for cosmetics, detergents, oral-care products and medical supplies as the flavor precursors.

The fact that a few of glycosyl esters have been found in nature, forced various synthetic methods to be developed. The Koenigs-Knorr reaction using glucosyl bromide with acid is the most attractive. Several publications disclosed the glucosylation of carboxylic acid promoted by Ag catalysts through Koenigs-Knorr reaction [1a, 3]. However, the expensive Ag catalysts (at least one equivalent) limited its application. Therefore, other alternative methods have been reported, involving the compounds such as orthoesters [4], trifluoroacetates [5], TMSET glycosides [6], glucosyl fluoride [7], instead of glucosyl bromide. In addition, the Mitsunobu protocol was also explored [8]. But the added-steps and the cost for the preparation of these compounds, low yield and low selectivity of the product as well as the harsh condition make the reaction challenging.

2. Results and Discussion

The formation of the glucosyl esters by condensation of acid with glucosyl bromide in inorganic base aqueous/DCM seemed to be a good choice [9]. In our research, however, we found low yield results for most of the substrates when the reaction ran on larger sacle (1 g). The impurity **4** (mixture) was formed during the condensation. The reason was found to be the hydrolysis of the glucosyl bromide **1** in the presence of H_2O. Herein, we describe the improved synthesis of this reaction and a series of glucosyl esters were prepared.

We started to study this reaction with benzoic acid **2a**, which was reacted with -glucosyl bromide **1** in the presence of Aliquat 336® (CAS: 63393-96-4) as the phase transfer catalyst (PTC). From Table 1, we could see that the reaction was influenced largely by the water. The more water exists, the more compound **4** forms (Table 1, entries 1–3). When only DCM was used as the solvent, product **3a** was obtained in high yield, with less than 5% impurity **4** (Table 1, entry 4). Considering 0.5 equiv of water would form by the reaction itself with K_2CO_3, 4A molecular sieve (4A MS) was added, which made the yield increased by 6% (Table 1, entry 5). It was found that K_2CO_3 was the best base after the comparison of the bases according to the yield and the cost (Table 1, entries 6-10). The reaction was completely suppressed when NaOH or Et_3N was used as the base with compound **1** recycled, probably because of the instability of PTC in stronger base (Table 1, entry 9) or the quite weaker basicity of Et_3N (Table 1, entry 10).

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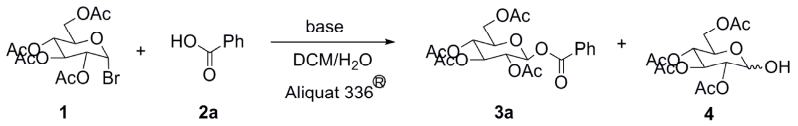
Table 1. The influence of water and the screening of base for the reaction of **1** with **2a**[a]

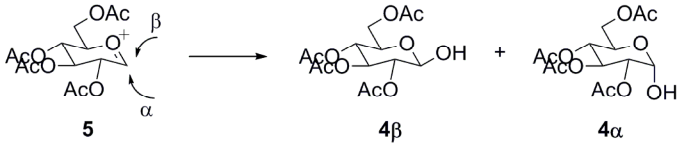


1 2a 3a 4

Entry	Base	H_2O	3a[b]	4[b]
1	K_2CO_3	5 mL (278 mmol)[c]	35%	55%
2	K_2CO_3	2.5 mL (139 mmol)	54%	35%
3	K_2CO_3	0.5 mL (27.8 mmol)	78%	12%
4	K_2CO_3	-	88%	4%
5	K_2CO_3	-[d]	94%	trace
6	Na_2CO_3	-[d]	80%	trace
7	$NaHCO_3$	-[d]	69%	trace
8	Cs_2CO_3	-[d]	90%	trace
9	NaOH	-[d]	NR	trace
10	Et_3N	-[d]	NR	trace

[a]The reaction was conducted with **1** (2.5 mmol), **2a** (5 mmol), base (5 mmol) and Aliquat 336 (0.25 mmol) in 35 mL DCM with or without H_2O. [b]Isolated yield. [c]About 115 equiv of H_2O to glucosyl bromide was used according to reference 9. [d]0.25 g 4A molecular sieve was added.

Notably, -configuration product was exclusively obtained through SN_2 substitution, compared with the known data [5–6, 10–11]. Unlike condensation product, the mixture of for impurity **4** was observed by ^1H NMR according to the known data [12], which implies that intermediate **5** might be involved (Scheme 1).

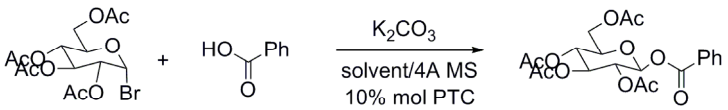


5 4β 4α

Scheme 1. mixture of compound **4** from intermediate **5**.

Next, PTC and the solvents were screened. In Table 2, it seemed that the reaction did not happen without PTC. Only 10% mol PTC, such as TBAB (Tetrabutyl ammonium bromide), TEAB (Tetraethyl ammonium bromide), BTEAC (Benzyl triethyl ammonium chloride), CTMAB (Hexadecyl trimethyl ammonium bromide) compelled the reaction to give the product in high yield (Table 2, entries 1–5). After comparison of the solvents, DCM proved to be the best solvent (Table 2, entries 6–8).

Table 2. Screening of PTC and the solvent[a]



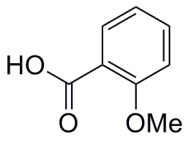
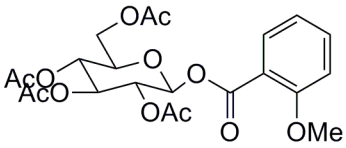
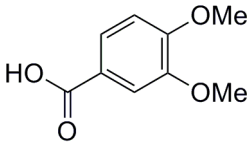
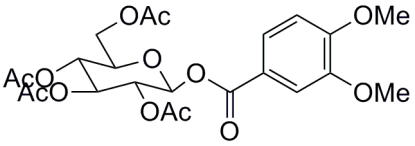
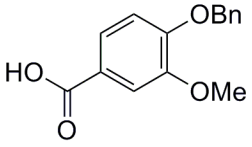
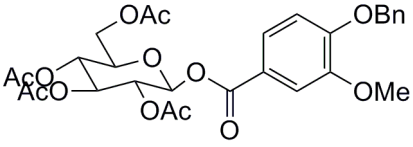
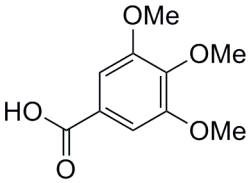
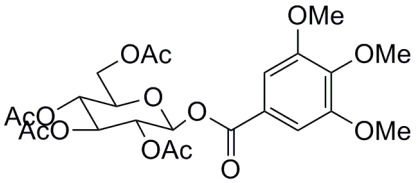
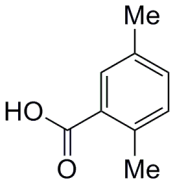
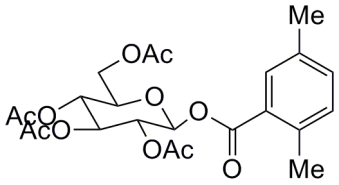
1 2a 3a

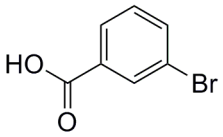
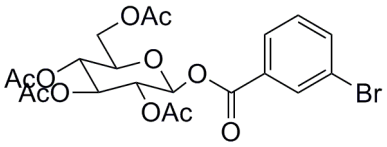
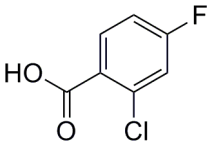
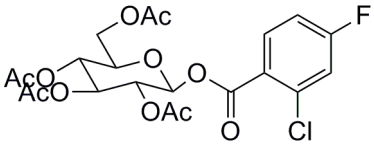
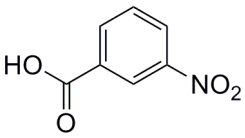
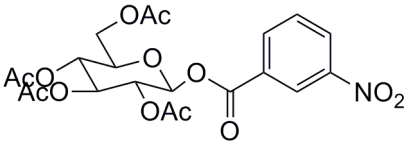
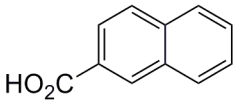
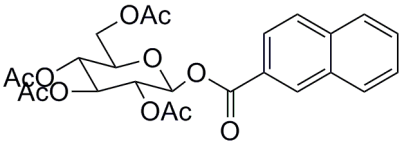
Entry	PTC	Solvent	3a[b]
1	TBAB	DCM	99%
2	TEAB	DCM	99%
3	BEAC	DCM	96%
4	CMAB	DCM	97%
5	-	DCM	NR
6	TEAB	THF	<10%
7	TEAB	CH_3CN	78%
8	TEAB	DMF	<10%

[a]The reaction was conducted with **1** (2.5 mmol), **2a** (5 mmol), K_2CO_3 (5 mmol), PTC (0.25 mmol) and 0.25 g 4A MS in 35 mL solvent. [b]Isolated yield.

Then, various acids were chosen to testify this reaction (Table 3 and 4). Aromatic acids with substituent group at different position on benzene ring, gave the desired product in good to high yield. For example, electron-donating groups, such as methoxy, benzyloxy or methyl all could make the reaction happen smoothly (Table 3, entries 1–5). Electron-withdrawing group also produced the corresponding products in good yield (Table 3, entries 6–8). Specially, different halogen groups probably make the structure much diverse through some coupling reaction. Similarly, -naphtoic acid gave product **3j** quantitatively (Table 3, entry 9). From Table 3, it was shown that these groups could exist either at ortho-, meta-, or para-position on benzene ring. Besides, mono-, di- or tri-substituted groups all exhibited good activities. In the comparison experiment, yield decreased evidently when the reaction was conducted in the presence of water within the expectation (Table 3, entry 1, 3, 7 and 9).

Table 3. The reaction of glucosyl bromide **1** with aromatic acids[a]

Entry	Aromatic acids 2	Product 3	Yield[b] (%)
1	 **2b**	 **3b**	95[c]
2	 **2c**	 **3c**	98
3	 **2d**	 **3d**	91[c]
4	 **2e**	 **3e**	80
5	 **2f**	 **3f**	96

6	 **2g**	 **3g**	99
7	 **2h**	 **3h**	85[c]
8	 **2i**	 **3i**	90
9	 **2j**	 **3j**	99[c]

[a]The reaction was conducted with **1** (2.5 mmol), **2** (5 mmol), K_2CO_3 (5 mmol), TEAB (0.25 mmol) and 0.25 g 4A MS in 35 mL DCM. [b]Isolated yield. [c]28–54% of yields for these compounds were obtained when 5 mL H_2O was added in the reaction.

Not only aromatic acids, but aliphatic acids could be applied to the reaction. The results were listed in Table 4. Phenylacetic acid **2k**, 2,4,5-trifluoro-phenylacetic acid **2l** offered the product in no less than 95% yield (Table 4, entries 1–2). Good results were also acquired by using other aliphatic acids without benzene ring. For example, isobutyric acid **2m**, isovaleric acid **2n** gave the product in more than 90% yield respectively. Lower yield was obtained for pivalic acid **2o**, probably due to the steric hindrance (Table 4, entries 3–5). In addition, long chain glucosyl ester was prepared in good yield from acid **2q** (Table 4, entry 6). Satisfactorily, this reaction could be well extended to the aliphatic acids with olefin and cyclic section (Table 4, entries 7–11). For the same reason, the result was not good when water was added in the comparison sample (Table 4, entry 1, 4, 6 and 10).

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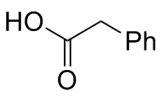
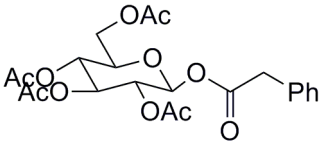
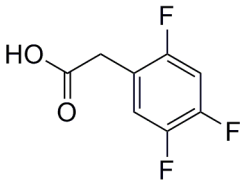
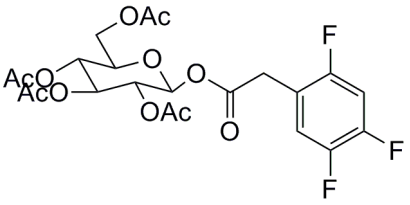
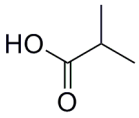
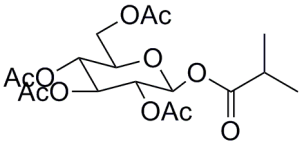
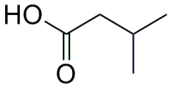
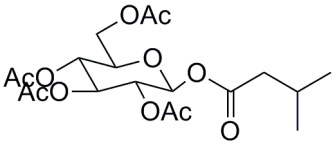
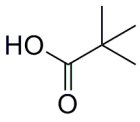
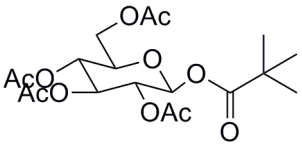
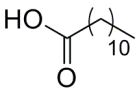
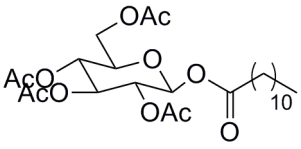
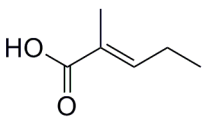
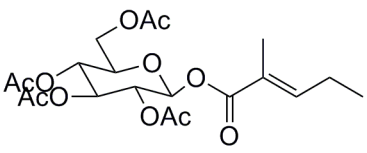
Table 4. The reaction of glucosyl bromide **1** with aliphatic acids[a]

Entry	Aliphatic acids 2	Product 3	Yield[b] (%)
1	 **2k**	 **3k**	95[c]
2	 **2l**	 **3l**	97
3	 **2m**	 **3m**	91
4	 **2n**	 **3n**	99[c]
5	 **2o**	 **3o**	72
6	 **2p**	 **3p**	92[c]
7	 **2q**	 **3q**	96

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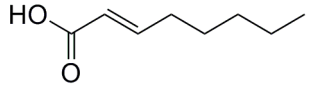
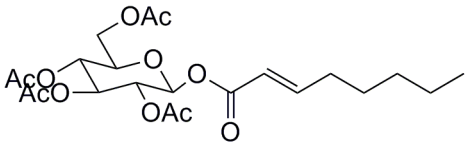
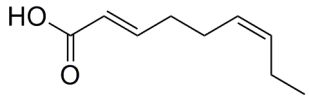
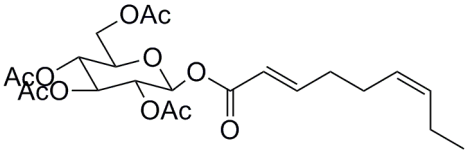
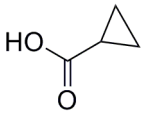
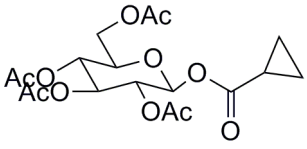
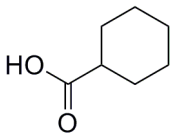
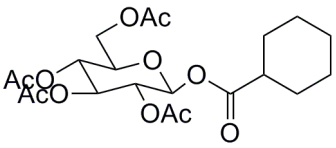
8		**2r**		**3r**	79
9		**2s**		**3s**	94
10		**2t**		**3t**	99[c]
11		**2u**		**3u**	78

[a]The reaction was conducted with **1** (2.5 mmol), **2** (5 mmol), K_2CO_3 (5 mmol), TEAB (0.25 mmol) and 0.25 g 4A MS in 35 mL DCM. [b]Isolated yield. [c]40–58% of yields for these compounds were obtained when 5 mL H_2O was added in the reaction.

It is noteworthy that one of the compounds was tried to be prepared on scale (**3a**, more than 100 g), and it was purified through simple manipulation, not by column chromatography. It seems that this method is possible to be applied in industrial manufacture due to the high yields generally. The scale-up synthesis of other compounds is now underway.

3. Materials and Methods

3.1. General Methods

^1H (400 MHz) and ^{13}C (100 MHz) NMR spectra were recorded on a Bruker Avance 400 spectrometer in $CDCl_3$ using tetramethylsilane (TMS) as internal standards. J values were given in hertz. Mass spectra & High resolution mass spectra were recorded on a Finnigan MAT mass spectrometer.

*3.2. General Procedure for the Synthesis of Compound **3***

The mixture of glucosyl bromide **1** (1.03 g, 2.5 mmol), acid (5.0 mmol), K_2CO_3 (0.69 g, 5.0 mmol), TEAB (0.05 g, 0.25 mmol) and 4A MS (0.25 g) in 35 mL DCM was stirred 24–48 h at room temperature. After filtration, water was added to the mixture, and separation. The organic layer was washed with 25% K_2CO_3 aq., dried over $MgSO_4$ and concentrated in vacuo. The residue was purified via silica gel column chromatography using EtOAc/hexane (1:10 to 1:1) as eluent to yield the desired product **3**.

*3.3. The Scale-up Synthesis of Compound **3a***

The mixture of glucosyl bromide **1** (150.0 g, 0.36 mol), benzoic acid **2a** (89.0 g, 0.73 mol), K_2CO_3 (100.7 g, 0.73 mol), TEAB (7.5 g, 36 mmol) and 4A MS (36.0 g) in 5 L DCM was stirred 24 h at room temperature. After filtration, water was added to the mixture, and separation. The organic layer was washed with 25% K_2CO_3 aq., dried over $MgSO_4$ and concentrated in vacuo to obtain solid crude. This crude was purified in refluxed EtOH to give **3a** as a white solid after cooling down in 89% yield.

2,3,4,6-Tetra-O-acetyl-1-O-benzoyl- -D-glucopyranosyl ester (3a). ^{1}H NMR($CDCl_3$, 400 MHz): = 1.99 (s, 3H), 2.04 (s, 3H), 2.05 (s, 3H), 2.07 (s, 3H), 3.93–3.97 (m, 1H), 4.14 (dd, *J* = 2.0, 12.8 Hz, 1H), 4.33 (dd, *J* = 4.4, 12.4 Hz, 1H), 5.18–5.23 (m, 1H), 5.34–5.37 (m, 2H), 5.93–5.95 (m, 1H) [13], 7.46 (t, *J* = 8.0 Hz, 1H), 7.61 (t, *J* = 7.2 Hz, 1H), 8.05 (dd, *J* = 1.2, 8.0 Hz, 2H); ^{13}C NMR($CDCl_3$, 100 MHz): = 20.45, 20.49, 20.51, 20.58, 61.4, 67.9, 70.1, 72.6, 72.7, 92.2 [14], 128.4, 128.6, 130.1, 133.9, 164.4, 169.3, 169.4, 170.0, 170.5; ESI-MS (*m*/*z*) 475 $[M + Na]^+$; HRMS calcd for $C_{21}H_{24}O_{11}$ 452.1330, found 452.1321.

2,3,4,6-Tetra-O-acetyl-1-O-(2-methoxybenzoyl)- -D-glucopyranosyl ester (3b). ^{1}H NMR($CDCl_3$, 400 MHz): = 2.01 (s, 3H), 2.04 (s, 3H), 2.05 (s, 3H), 2.07 (s, 3H), 3.91 (s, 3H), 3.91–3.94 (m, 1H), 4.14 (dd, *J* = 2.0, 12.8 Hz, 1H), 4.33 (dd, *J* = 4.4, 12.4 Hz, 1H), 5.17–5.22 (m, 1H), 5.31–5.33 (m, 2H), 5.95–5.97 (m, 1H), 6.97–7.01 (m, 2H), 7.50–7.55 (m, 1H), 7.87 (dd, *J* = 1.6, 8.0 Hz, 2H); ^{13}C NMR($CDCl_3$, 100 MHz): = 20.44, 20.46, 20.5, 20.6, 55.7, 61.5, 67.8, 70.2, 72.6, 72.8, 91.8, 112.0, 117.4, 120.1, 132.4, 134.8, 160.1, 163.2, 169.2, 169.3, 170.0, 170.4; ESI-MS (*m*/*z*) 505 $[M + Na]^+$.

2,3,4,6-Tetra-O-acetyl-1-O-(3,4-dimethoxybenzoyl)- -D-glucopyranosyl ester (3c). ^{1}H NMR($CDCl_3$, 400 MHz): = 1.99 (s, 3H), 2.04 (s, 3H), 2.06 (s, 3H), 2.08 (s, 3H), 3.94 (s, 3H), 3.95 (s, 3H), 3.96–3.98 (m, 1H), 4.14 (dd, *J* = 2.0, 12.4 Hz, 1H), 4.33 (dd, *J* = 4.4, 12.8 Hz, 1H), 5.18–5.23 (m, 1H), 5.34–5.36 (m, 2H), 5.88–5.90 (m, 1H), 6.91 (d, *J* = 8.4 Hz, 1H), 7.54 (d, *J* = 2.0 Hz, 1H), 7.70 (dd, *J* = 1.6, 8.0 Hz, 2H); ^{13}C NMR($CDCl_3$, 100 MHz): = 20.5, 20.6, 55.9, 56.0, 61.4, 67.9, 70.1, 72.5, 72.6, 92.2, 110.4, 112.2, 120.6, 124.5, 148.7, 153.8, 164.1, 169.3, 169.4, 170.0, 170.5; ESI-MS (*m*/*z*) 535 $[M + Na]^+$.

2,3,4,6-Tetra-O-acetyl-1-O-(4-benzyloxy-3-methoxybenzoyl)- -D-glucopyranosyl ester (3d). ^{1}H NMR($CDCl_3$, 400 MHz): = 1.98 (s, 3H), 2.04 (s, 3H), 2.05 (s, 3H), 2.07 (s, 3H), 3.92–3.96 (m, 1H), 3.94 (s, 3H), 4.14 (dd, *J* = 2.4, 12.4 Hz, 1H), 4.33 (dd, *J* = 4.4, 12.4 Hz, 1H), 5.17–5.21 (m, 1H), 5.2 (s, 3H), 5.33–5.35 (m, 2H), 5.87–5.89 (m, 1H), 6.91 (d, *J* = 8.8 Hz, 1H), 7.32–7.44 (m, 5H), 7.55 (d, *J* = 1.6 Hz, 1H), 7.62 (dd, *J* = 1.6, 8.4 Hz, 1H); ^{13}C NMR($CDCl_3$, 100 MHz): = 20.6, 20.7, 56.1, 61.5, 67.9, 70.2, 70.7, 72.5, 72.7, 92.2, 112.5, 112.7, 120.9, 124.3, 127.2, 128.1, 128.7, 136.1, 149.2, 152.9, 164.2, 169.3, 169.4, 170.0, 170.6; ESI-MS (*m*/*z*) 611 $[M + Na]^+$.

2,3,4,6-Tetra-O-acetyl-1-O-(3,4,5-trimethoxybenzoyl)- -D-glucopyranosyl ester (3e). ^{1}H NMR($CDCl_3$, 400 MHz): = 1.97 (s, 3H), 2.02 (s, 3H), 2.03 (s, 3H), 2.05 (s, 3H), 3.85–3.95 (m, 1H), 3.88 (s, 9H), 4.12 (d, *J* = 12.8 Hz, 1H), 4.32 (dd, *J* = 4.4, 12.8 Hz, 1H), 5.16–5.20 (m, 1H), 5.30–5.36 (m, 2H), 5.83–5.85 (m, 1H), 7.28 (s, 2H); ^{13}C NMR($CDCl_3$, 100 MHz): = 20.4, 20.5, 20.6, 56.2, 60.8, 61.4, 67.9, 70.2, 72.3, 72.6, 92.4, 107.3, 123.1, 142.9, 152.9, 164.0, 169.3, 169.4, 170.0, 170.5; ESI-MS (*m*/*z*) 565 $[M + Na]^+$.

2,3,4,6-Tetra-O-acetyl-1-O-(2,5-dimethylbenzoyl)- -D-glucopyranosyl ester (3f). ^{1}H NMR($CDCl_3$, 400 MHz): = 1.94 (s, 3H), 1.97 (s, 3H), 1.98 (s, 3H), 2.00 (s, 3H), 2.28 (s, 3H), 2.48 (s, 3H), 3.84–3.88 (m, 1H), 4.07 (dd, *J* = 2.4, 12.4 Hz, 1H), 4.26 (dd, *J* = 4.4, 12.4 Hz, 1H), 5.11–5.16 (m, 1H), 5.25–5.28 (m, 2H), 5.86–5.88 (m, 1H), 7.07 (d, *J* = 8.0 Hz, 1H), 7.18 (d, *J* = 8.0 Hz, 1H), 7.69 (s, 1H); ^{13}C NMR($CDCl_3$, 100 MHz): = 20.53, 20.56, 20.6, 20.7, 21.4, 21.5, 61.5, 67.9, 70.3, 72.7, 72.9, 91.9, 127.0, 131.7, 131.8, 133.9, 135.6, 138.4, 165.0, 169.3, 169.5, 170.2, 170.7; ESI-MS (*m*/*z*) 503 $[M + Na]^+$.

2,3,4,6-Tetra-O-acetyl-1-O-(3-bromobenzoyl)- -D-glucopyranosyl ester (3g). ^{1}H NMR($CDCl_3$, 400 MHz): = 2.00 (s, 3H), 2.05 (s, 3H), 2.06 (s, 3H), 2.08 (s, 3H), 3.92–3.97 (m, 1H), 4.14 (dd, *J* = 2.0, 12.8 Hz, 1H), 4.33 (dd, *J* = 4.4, 12.4 Hz, 1H), 5.17–5.22 (m, 1H), 5.33–5.35 (m, 2H), 5.92–5.94 (m, 1H), 7.35 (t, *J* = 8.0 Hz, 1H), 7.72–7.75 (m, 1H), 7.95–7.98 (m, 1H), 8.18 (t, *J* = 1.6 Hz, 1H); ^{13}C NMR($CDCl_3$, 100 MHz): = 20.50, 20.53, 20.55, 20.6, 61.4, 67.8, 70.1, 72.5, 72.7, 92.5, 122.6, 128.6, 130.2, 130.4, 133.0, 136.9, 163.2, 169.3, 169.4, 170.0, 170.5; ESI-MS (*m*/*z*) 553 $[M + Na]^+$.

2,3,4,6-Tetra-O-acetyl-1-O-(2-chloro-4-fluorobenzoyl)- -D-glucopyranosyl ester (3h). ^{1}H NMR($CDCl_3$, 400 MHz): = 2.00 (s, 3H), 2.03 (s, 3H), 2.04 (s, 3H), 2.07 (s, 3H), 3.90–3.94 (m, 1H), 4.13 (dd, *J* = 2.0, 12.0 Hz, 1H), 4.32 (dd, *J* = 4.8, 12.4 Hz, 1H), 5.15–5.20 (m, 1H), 5.30–5.33 (m, 2H), 5.92–5.93 (m, 1H), 7.03–7.08 (m, 1H), 7.21 (dd, *J* = 6.8, 8.4 Hz, 1H), 7.97 (dd, *J* = 2.0, 6.0 Hz, 1H); ^{13}C NMR($CDCl_3$, 100 MHz): = 20.5, 20.6, 61.4, 67.7, 70.1, 72.6, 72.8, 92.3, 114.4 (d, *J* = 21.7 Hz), 119.0 (d, *J* = 24.5 Hz), 123.6 (d, *J* = 3.4 Hz), 134.5 (d, *J* = 9.9 Hz), 137.1 (d, *J* = 10.7 Hz), 161.8, 164.7 (d, *J* =257.1 Hz), 169.2, 169.3, 170.0, 170.5; ESI-MS (*m*/*z*) 527 $[M + Na]^+$; HRMS calcd for $C_{21}H_{22}ClFO_{11}$ 504.0808, found 504.0805.

2,3,4,6-Tetra-O-acetyl-1-O-(3-nitrobenzoyl)- -D-glucopyranosyl ester (3i). ^{1}H NMR($CDCl_3$, 400 MHz): = 1.99 (s, 3H), 2.03 (s, 3H), 2.04 (s, 3H), 2.07 (s, 3H), 3.93–3.97 (m, 1H), 4.13 (dd, *J* = 2.0, 12.0 Hz, 1H), 4.31 (dd, *J* = 4.4, 12.8 Hz, 1H), 5.17–5.21 (m, 1H), 5.33–5.35 (m, 2H), 5.94–5.96 (m, 1H), 7.68 (t, *J* = 8.0 Hz, 1H), 8.32–8.35 (m, 1H), 8.44–8.46 (m, 1H), 8.86–8.87 (m, 1H); ^{13}C NMR($CDCl_3$, 100 MHz): = 20.4, 20.5, 20.6, 61.4, 67.8, 70.1, 72.3, 72.8, 92.8, 125.1, 128.2, 130.0, 130.2, 135.5, 148.3, 162.5, 169.2, 169.4, 170.0, 170.5; ESI-MS (*m*/*z*) 520 $[M + Na]^+$.

2,3,4,6-Tetra-O-acetyl-1-O-(2-naphthoyl)- -D-glucopyranosyl ester (3j). ^{1}H NMR($CDCl_3$, 400 MHz): = 1.99 (s, 3H), 2.01 (s, 3H), 2.07 (s, 3H), 2.08 (s, 3H), 3.97–4.00 (m, 1H), 4.16 (dd, *J* = 2.0, 12.8 Hz, 1H), 4.35 (dd, *J* = 4.4, 12.4 Hz, 1H), 5.24 (t, *J* = 9.6 Hz, 1H), 5.35–5.44 (m, 2H), 6.01 (d, *J* = 8.0 Hz, 1H), 7.55–7.59 (m, 1H), 7.60–7.64 (m, 1H), 7.88–7.91 (m, 2H), 7.98 (d, *J* = 7.2 Hz, 1H), 8.04 (dd, *J* = 2.0, 8.8 Hz, 1H), 8.63 (d, *J* = 0.8 Hz, 1H); ^{13}C NMR($CDCl_3$, 100 MHz): = 20.51, 20.56, 20.58, 20.6, 61.5, 67.9, 70.3, 72.7, 72.8, 92.4, 125.1, 125.6, 126.9, 127.8, 128.5, 128.8, 129.6, 132.2, 132.3, 135.9, 164.7, 169.4, 169.5, 170.1, 170.6; ESI-MS (*m*/*z*) 525 $[M + Na]^+$.

2,3,4,6-Tetra-O-acetyl-1-O-(2-phenylacetyl)- -D-glucopyranosyl ester (3k). ^{1}H NMR($CDCl_3$, 400 MHz): = 1.76 (s, 3H), 1.99 (s, 3H), 2.03 (s, 3H), 2.09 (s, 3H), 3.66 (s, 2H), 3.82–3.86 (m, 1H), 4.12 (dd, *J* = 2.0, 12.8 Hz, 1H), 4.30 (dd, *J* = 4.4, 12.4 Hz, 1H), 5.10–5.15 (m, 2H), 5.21 (t, *J* = 8.8 Hz, 1H), 5.69 (d, *J* = 7.6 Hz, 1H), 7.25–7.34 (m, 5H); ^{13}C NMR($CDCl_3$, 100 MHz): = 20.2, 20.5, 20.6, 41.1, 61.4, 67.7, 69.9, 72.6, 72.7, 91.8, 127.4, 128.7, 129.2, 132.9, 169.0, 169.3, 169.4, 170.0, 170.5; ESI-MS (*m*/*z*) 489 $[M + Na]^+$; HRMS calcd for $C_{22}H_{26}O_{11}$ 466.1481, found 466.1477.

2,3,4,6-Tetra-O-acetyl-1-O-(2-(2,4,5-trifluorophenyl)acetyl)- -D-glucopyranosyl ester (3l). ^{1}H NMR($CDCl_3$, 400 MHz): = 1.99 (s, 3H), 2.01 (s, 3H), 2.03 (s, 3H), 2.09 (s, 3H), 3.67 (s, 2H), 3.82–3.87 (m, 1H), 4.12 (dd, *J* = 2.0, 12.8 Hz, 1H), 4.30 (dd, *J* = 4.4, 12.4 Hz, 1H), 5.10–5.15 (m, 2H), 5.25 (t, *J* = 8.8 Hz, 1H), 5.73 (d, *J* = 8.8 Hz, 1H), 6.91–6.98 (m, 1H), 7.07–7.13 (m, 1H); ^{13}C NMR($CDCl_3$, 100 MHz): = 20.2, 20.4, 20.6, 33.5 (d, *J* = 1.9 Hz), 61.3, 67.6, 70.0, 72.5, 72.7, 92.2, 105.5 (dd, *J* = 20.5, 27.5 Hz), 116.5 (d, *J* = 17.5 Hz), 119.0 (dd, *J* = 5.6, 19.0 Hz), 146.6 (dd, *J* = 12.7, 243.1 Hz), 149.5 (d, *J* = 251.5 Hz), 156.0 (dd, *J* = 10.4, 243.5 Hz), 167.9, 169.0, 169.3, 170.0, 170.5; ESI-MS (*m*/*z*) 543 $[M + Na]^+$.

2,3,4,6-Tetra-O-acetyl-1-O-isobutyryl- -D-glucopyranosyl ester (3m). ^{1}H NMR($CDCl_3$, 400 MHz): = 1.16 (d, *J* = 7.2 Hz, 3H), 1.17 (d, *J* = 7.2 Hz, 3H), 2.02 (s, 6H), 2.04 (s, 3H), 2.09 (s, 3H), 2.57–2.64 (m, 1H), 3.83–3.87 (m, 1H), 4.12 (dd, *J* = 2.0, 12.4 Hz, 1H), 4.30 (dd, *J* = 4.4, 12.8 Hz, 1H), 5.12–5.19 (m, 2H), 5.26 (t, *J* = 8.8 Hz, 1H), 5.72 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR($CDCl_3$, 100 MHz): = 18.1, 18.7, 20.3, 20.4, 20.6, 33.7, 61.4, 67.8, 70.1, 72.6, 91.5, 169.0, 169.3, 169.9, 170.4, 174.9; ESI-MS (*m*/*z*) 441 $[M + Na]^+$.

2,3,4,6-Tetra-O-acetyl-1-O-(3-methylbutanoyl)- -D-glucopyranosyl ester (3n). ^{1}H NMR($CDCl_3$, 400 MHz): = 0.95 (d, *J* = 6.8 Hz, 6H), 2.02 (s, 6H), 2.04 (s, 3H), 2.08 (s, 3H), 2.10–2.12 (m, 1H), 2.25 (d, *J* = 6.4 Hz, 2H), 3.83–3.87 (m, 1H), 4.11 (dd, *J* = 2.0, 12.4 Hz, 1H), 4.30 (dd, *J* = 4.4, 12.8 Hz, 1H), 5.11–5.17 (m, 2H), 5.26 (t, *J* = 9.2 Hz, 1H), 5.74 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR($CDCl_3$, 100 MHz): = 20.3, 20.4, 20.5, 22.0, 25.4, 42.9, 61.4, 67.7, 70.1, 72.5, 72.7, 91.3, 168.9, 169.2, 169.9, 170.3, 170.8; ESI-MS (*m*/*z*) 455 $[M + Na]^+$.

2,3,4,6-Tetra-O-acetyl-1-O-pivaloyl- -D-glucopyranosyl ester (3o). ^{1}H NMR($CDCl_3$, 400 MHz): = 1.19 (s, 9H), 2.00 (s, 6H), 2.02 (s, 3H), 2.08 (s, 3H), 3.81–3.85 (m, 1H), 4.10 (dd, *J* = 2.4, 12.8 Hz, 1H), 4.29 (dd, *J* = 4.4, 12.0 Hz, 1H), 5.11–5.19 (m, 2H), 5.25 (t, *J* = 9.2 Hz, 1H), 5.66 (d, *J* = 8.8 Hz, 1H); ^{13}C NMR($CDCl_3$, 100 MHz): = 20.3, 20.47, 20.48, 20.6, 26.6, 38.7, 61.4, 67.9, 70.0, 72.5, 72.6, 91.7, 169.0, 169.3, 170.0, 170.5, 176.4; ESI-MS (*m*/*z*) 455 $[M + Na]^+$.

2,3,4,6-Tetra-O-acetyl-1-O-dodecanoyl- -D-glucopyranosyl ester (3p). ^{1}H NMR($CDCl_3$, 400 MHz): = 0.88 (t, *J* = 9.2 Hz, 3H), 1.25–1.30 (m, 16H), 1.57–1.62 (m, 2H), 2.01 (s, 3H), 2.02 (s, 3H), 2.03 (s, 3H), 2.09 (s, 3H), 2.34–2.38 (m, 2H), 3.82–3.87 (m, 1H), 4.11 (dd, *J* = 2.0, 12.0 Hz, 1H), 4.30 (dd, *J* = 4.4, 12.0 Hz, 1H), 5.11–5.16 (m, 2H), 5.26 (t, *J* = 9.2 Hz, 1H), 5.73 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR($CDCl_3$, 100 MHz): = 14.0, 20.42, 20.46, 20.58, 20.59, 22.6, 24.5, 28.8, 29.1, 29.2, 29.3, 29.5, 31.8, 33.9, 61.4, 67.8, 70.2, 72.6, 72.7, 91.5, 169.1, 169.4, 170.0, 170.5, 171.7; ESI-MS (*m*/*z*) 553 $[M + Na]^+$.

2,3,4,6-Tetra-O-acetyl-1-O-((E)-2-methylpent-2-enoyl)- -D-glucopyranosyl ester (3q). ^{1}H NMR($CDCl_3$, 400 MHz): = 1.05 (t, *J* = 8.0 Hz, 3H), 1.82 (s, 3H), 2.01 (s, 3H), 2.03 (s, 3H), 2.04 (s, 3H), 2.09 (s, 3H), 2.17–2.24 (m, 2H), 3.86–3.91 (m, 1H), 4.12 (dd, *J* = 2.0, 12.4 Hz, 1H), 4.31 (dd, *J* = 4.4, 12.4 Hz, 1H), 5.15 (t, *J* = 9.2 Hz, 1H), 5.21–5.32 (m, 2H), 5.75 (d, *J* = 8.0 Hz, 1H), 6.85 (dt, *J* = 1.2, 7.6 Hz, 1H); ^{13}C NMR($CDCl_3$, 100 MHz): = 11.9, 12.7, 20.43, 20.47, 20.48, 20.6, 22.1, 61.4, 67.9, 70.1, 72.5, 72.6, 91.9, 125.7, 147.2, 165.7, 169.1, 169.3, 170.0, 170.5; ESI-MS (*m*/*z*) 467 $[M + Na]^+$, HRMS calcd for $C_{20}H_{28}O_{11}$ 444.1614, found 444.1618.

2,3,4,6-Tetra-O-acetyl-1-O-((E)-oct-2-enoyl)- -D-glucopyranosyl ester (3r). ^{1}H NMR($CDCl_3$, 400 MHz): = 0.86 (t, *J* = 7.2 Hz, 3H), 1.22–1.28 (m, 4H), 1.39–1.47 (m, 2H), 1.98 (s, 3H), 1.99 (s, 3H), 2.00 (s, 3H), 2.05 (s, 3H), 2.16–2.21 (m, 2H), 3.83–3.87 (m, 1H), 4.08 (dd, *J* = 2.0, 12.4 Hz, 1H), 4.27 (dd, *J* = 4.4, 12.4 Hz, 1H), 5.10–5.18 (m, 2H), 5.25 (t, *J* = 9.2 Hz, 1H), 5.75 (d, *J* = 7.6 Hz, 1H), 5.76–5.80 (m, 1H), 7.01–7.09 (m, 1H); ^{13}C NMR($CDCl_3$, 100 MHz): = 13.8, 20.44, 20.48, 20.5, 20.6, 22.3, 27.4, 31.2, 32.3, 61.4, 67.8, 70.2, 72.6, 72.7, 91.6, 119.5, 153.1, 164.2, 169.2, 169.4, 170.0, 170.6; ESI-MS (*m*/*z*) 495 $[M + Na]^+$.

2,3,4,6-Tetra-O-acetyl-1-O-((2E,6Z)-nona-2,6-dienoyl)- -D-glucopyranosyl ester (3s). ^{1}H NMR($CDCl_3$, 400 MHz): = 0.96 (t, *J* = 8.0 Hz, 3H), 2.01 (s, 3H), 2.02 (s, 3H), 2.02–2.05 (m, 2H), 2.04 (s, 3H), 2.08 (s, 3H), 2.19–2.23 (m, 2H), 2.25–2.29 (m, 2H), 3.85–3.89 (m, 1H), 4.11 (dd, *J* = 2.0, 12.4 Hz, 1H), 4.30 (dd, *J* = 4.4, 12.4 Hz, 1H), 5.12–5.21 (m, 2H), 5.27 (t, *J* = 9.2 Hz, 1H), 5.27–5.32 (m, 1H), 5.78 (d, *J* = 8.0 Hz, 1H), 5.80–5.86 (m, 1H), 7.04–7.11 (m, 1H); ^{13}C NMR($CDCl_3$, 100 MHz): = 14.1, 20.4, 20.5, 20.6, 25.3, 32.4, 61.4, 67.8,70.2, 72.5, 72.7, 91.6, 120.0, 126.8, 133.0, 152.1, 164.0, 169.2, 169.3, 170.0, 170.5; ESI-MS (*m*/*z*) 507 $[M + Na]^+$.

2,3,4,6-Tetra-O-acetyl-1-O-(cyclopropanecarbonyl)- -D-glucopyranosyl ester (3t). ^{1}H NMR($CDCl_3$, 400 MHz): = 0.94–0.97 (m, 2H), 1.03–1.10 (m, 2H), 1.63–1.67 (m, 1H), 2.02 (s, 3H), 2.03 (s, 3H), 2.04 (s, 3H), 2.09 (s, 3H), 3.82–3.86 (m, 1H), 4.11 (dd, *J* = 2.0, 12.0 Hz, 1H), 4.30 (dd, *J* = 4.4, 12.4 Hz, 1H), 5.11–5.17 (m, 2H), 5.26 (t, *J* = 9.6 Hz, 1H), 5.72 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR($CDCl_3$, 100 MHz): = 9.3, 12.7, 20.4, 20.6, 61.4, 67.7, 70.2, 72.5, 72.6, 91.5, 169.1, 169.3, 169.9, 170.4, 172.8; ESI-MS (*m*/*z*) 439 $[M + Na]^+$.

2,3,4,6-Tetra-O-acetyl-1-O-(cyclohexanecarbonyl)- -D-glucopyranosyl ester (3u). ^{1}H NMR($CDCl_3$, 400 MHz): = 1.20–1.49 (m, 6H), 1.62–1.65 (m, 1H), 1.68–1.77 (m, 1H), 1.85–1.90 (m, 2H), 2.02 (s, 6H), 2.04 (s, 3H), 2.09 (s, 3H), 2.33–2.39 (m, 1H), 3.83–3.87 (m, 1H), 4.11 (dd, *J* = 2.0, 12.0 Hz, 1H), 4.30 (dd, *J* = 4.4, 12.4 Hz, 1H), 5.11–5.18 (m, 2H), 5.26 (t, *J* = 9.6 Hz, 1H), 5.72 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR($CDCl_3$, 100 MHz): = 20.3, 20.4, 20.6, 24.9, 25.3, 25.5, 28.1, 28.7, 42.5, 61.4, 67.8, 70.1, 72.5, 72.6, 91.4, 169.1, 169.3, 170.0, 170.5, 173.8; ESI-MS (*m*/*z*) 481 $[M + Na]^+$.

4. Conclusions

The formation of the glucosyl esters by condensation of acids with glucosyl bromide was developed on larger scale in DCM without water. A diverse array of glucosyl esters were prepared in good yields, which seemed that our reaction condition could be applied in a broad substrate scope. In addition, the scale-up preparation was also attempted.

Supplementary Materials: The following are available online at www.mdpi.com/link.

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supervision of Xianhua Pan who is the corresponding author. Hui Dai contributed part of the data analysis.

Conflicts of Interest: The authors declare no conflict of interest.

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14 Anomeric C shift for -configuration is located at = 92.3, please see reference 10.