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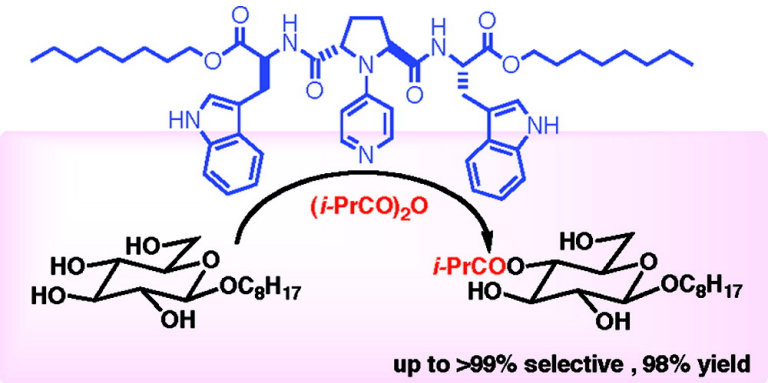

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A Catalytic One-Step Process for the Chemo- and Regioselective Acylation of Monosaccharides

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Abstract: An organocatalytic method for the chemo- and regioselective acylation of monosaccharides has been developed. Treatment of octyl β-D-glucopyranoside with isobutyric anhydride in the presence of 10 mol % of a C_2-symmetric chiral 4-pyrrolidinopyridine catalyst (**1**) at −50 °C gave the 4-*O*-isobutyryl derivative as the sole product in 98% yield. Thus, chemoselective acylation, favoring a secondary hydroxyl group in the presence of a free primary hydroxyl group, and regioselective acylation, favoring one of three secondary hydroxyl groups, took place with perfect selectivity. A competitive acylation between octyl β-D-glucopyranoside and a primary alcohol (2-phenylethanol) with 1.1 equiv of isobutyric anhydride in the presence of **1** gave the 4-*O*-isobutyrate of octyl β-D-glucopyranoside with 99% regioselectivity in 98% yield, which indicates that acylation of the secondary hydroxyl group at C(4) of the carbohydrate proceeds in an accelerative manner. A possible mechanism, involving multiple hydrogen-bonding between **1** and the monosaccharide, is proposed for the chemo- and regioselective acylation.

Introduction

Carbohydrates play key roles in intercellular processes, including infection, metastasis, differentiation, regulation of signaling, and so on.[1] In order to clarify the mechanisms of these events and to develop new therapeutics, chemical synthesis of carbohydrates is indispensable. However, synthetic methods leading to carbohydrates have been relatively unexplored. Multistep protection/deprotection procedures are usually required for their synthesis because of the lack of a direct method for the chemo- and regioselective manipulation of one of the multiple hydroxyl groups of carbohydrates.[2] Selective acylation of a primary hydroxyl group in the presence of three secondary hydroxyl groups of octyl β-D-glucopyranoside has been achieved with ∼100% chemoselectivity by enzymatic processes; however, concomitant diacylation was unavoidable.[3,4] Recently, Kattnig and Albert reported a convenient method for the selective monoacylation of octyl β-D-glucopyranoside with a typical acylation catalyst, 4-(dimethylamino)pyridine (DMAP), and acetyl chloride to give the 6-*O*-acetate with 85% selectivity in 73% yield.[5] Since the primary hydroxyl group at C(6) has the highest intrinsic reactivity, the selective introduction of an acyl group at C(6)−OH of carbohydrates is a reasonable consequence. On the other hand, chemoselective acylation of a secondary hydroxyl group in the presence of a primary hydroxyl group is much more difficult. Yoshida and co-workers reported the chemoselective acylation of a secondary hydroxyl group at C(4) of octyl α-D-glucopyranoside with 61% selectivity with an acetic anhydride−DMAP system, where diacylation was minimized by the use of less (0.70 equiv) acetic anhydride.[6] Recently, Griswold and Miller reported an excellent approach to the selective introduction of an acetyl group at a secondary hydroxyl group of octyl β-D-glucopyranoside using peptide-based chiral catalysts.[7] Moderately selective 4-*O*-acylation has been achieved in a ratio of 22:58:11:9 for 6-*O*-, 4-*O*-, 3-*O*-, and 2-*O*-acylate, respectively, without the formation of diacylates. Here we report an organocatalytic one-step procedure for the chemo- and regioselective acylation of a secondary hydroxyl group of monosaccharides.[8] With an organocatalyst, acylation of the secondary hydroxyl group at C(4) of octyl β-D-glucopyranoside proceeded with up to >99% selectivity in the presence of a primary hydroxyl group at C(6) and two other secondary hydroxyl groups at C(2) and C(3) (Figure 1a). Competitive acylation between the primary and secondary hydroxyl groups usually takes place chemoselectively at the primary one.[9] On the other hand, with the present catalyst, chemoselective acylation, favoring of a secondary hydroxyl group, and regioselective acylation, favoring one of three secondary hydroxyl groups, took place with perfect selectivity. The same molecular transformation could be achieved alterna-

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(7) Griswold, K. S.; Miller, S. J. *Tetrahedron* **2003**, *59*, 8869.
(8) Site-selective acylation of erythromycin has recently been developed. See: Lewis, C. A.; Miller, S. J. *Angew. Chem., Int. Ed.* **2006**, *45*, 5616.
(9) We recently reported regioselective acylation of 6-*O*-protected octyl β-D-glucopyranosides by DMAP catalysis. See: Muramatsu, W.; Kawabata, T. *Tetrahedron Lett.* **2007**, *48*, 5031.

10.1021/ja074882e CCC: $37.00

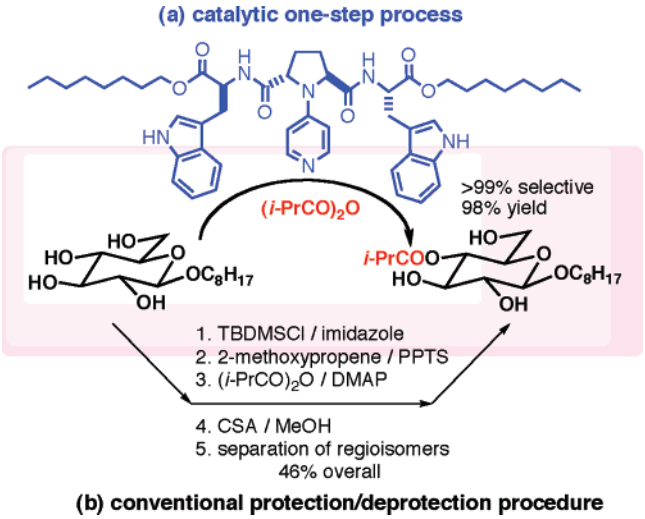

Figure 1. (a) Catalytic one-step process and (b) conventional protection/deprotection procedure for the preparation of octyl 4-*O*-isobutyryl-β-D-glucopyranoside.

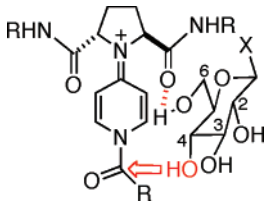

Figure 2. Working hypothesis for selective acylation of a secondary hydroxyl group in the presence of a primary hydroxyl group of a glucose derivative.

tively by a conventional protection/deprotection procedure involving five steps in 46% overall yield (Figure 1b).

Results and Discussion

We chose 4-pyrrolidinopyridine (PPY) as a catalytic center for acylation because PPY is known to be one of the most powerful catalysts for acylation of alcohols.[10] It has been well established that the reactive intermediates generated from PPY and acid anhydrides are acylpyridinium ions.[11] Figure 2 shows a hypothetical picture of transition state molecular assembly between an acylpyridinium ion and a carbohydrate substrate, which enables the selective acylation of a secondary hydroxyl group in the presence of a primary hydroxyl group. Since the primary hydroxyl group at C(6) of carbohydrates is the most reactive, it would preferentially form a H-bond with a H-bond acceptor (e.g., an amide carbonyl group) of the catalyst. If additional interactions of the hydroxyl groups at C(2) and/or C(3) with functionality R of the catalyst are operative, the combined effects of these attractive interactions would fix the conformation of the carbohydrate, where the hydroxyl group at C(4) is in close proximity to the reactive acyl group of the acylpyridinium ion, so that it would be acylated selectively. We chose tryptophan as a functional side chain of the catalyst because its indole substructure is expected to be suitable for H-bonding as well as for CH-π interaction with carbohydrates. It has also been reported that pyrrole units (similar to indole units) were used effectively as recognition sites for carbohydrates.[12] The notion that tryptophan can be used as a carbohydrate recognition site is also suggested by the fact that two tryptophan moieties are highly preserved in the substrate-recognition site of a family of β-glucosidases.[13] On the basis of this hypothesis, we designed C_2-symmetric chiral PPYs **1** and **2**, each having two identical side chains, consisting of L- and D-tryptophan, respectively (Figure 3).[14] Octyl esters in **1** and **2** are employed to enhance the solubility of the catalysts in nonpolar solvents, where H-bonding effects are stronger. In addition to **1** and **2**, catalysts **3** and **4**, consisting of L- and D-tyrosine, respectively, were also prepared because the phenol substructure in tyrosine is expected to have properties similar to those of the indole substructure in tryptophan.

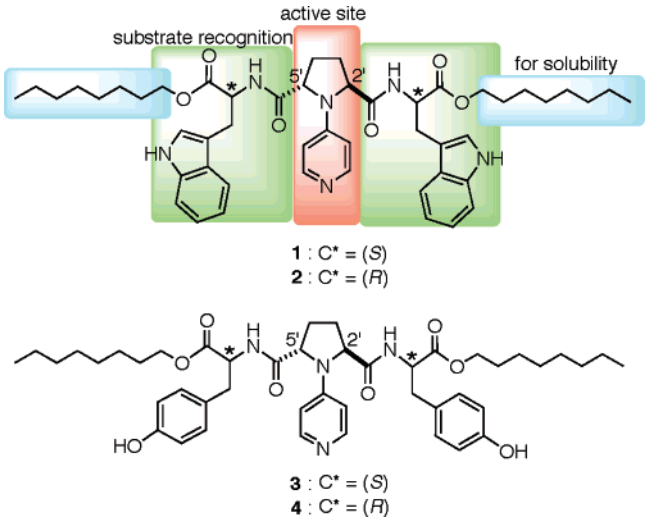

Figure 3. Design and structure of catalysts.

Catalysts **1**−**4** were prepared from L-pyroglutamic acid in six steps (see Supporting Information). The acylation of octyl β-D-glucopyranoside was investigated with 10 mol % of catalyst and 1.1 mol equiv of isobutyric anhydride in the presence of 1.5 mol equiv of collidine in toluene at 20 °C (Table 1). Isobutyric anhydride was chosen as an acylating agent because it shows high selectivity in the kinetic resolution of racemic

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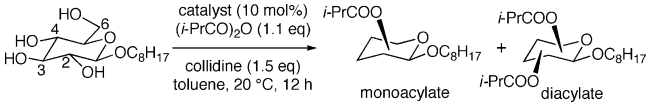
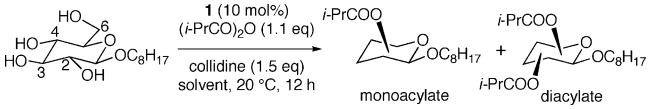
Table 1. Effects of Catalysts on Regioselectivity of Acylation of Octyl β-D-Glucopyranoside[a]



entry	catalyst	monoacylate (%)	regioselectivity[b] 6-*O*:4-*O*:3-*O*:2-*O*	diacylate (%)	recovery (%)
1	DMAP	47	36:26:26:12	22	31
2	**1**	84	11:86:3:0	12	2
3	**2**	71	20:73:7:0	17	9
4	**3**	60	23:58:19:0	21	14
5	**4**	80	24:59:16:1	13	6

[a] The reactions were carried out with a substrate concentration of 0.08 M. [b] Regioselectivity (%) among four monoacylates.

Table 2. Effects of Solvents on Regioselectivity of Acylation of Octyl β-D-Glucopyranoside with **1**[a]



entry	solvent	monoacylate (%)	regioselectivity[b] 6-*O*:4-*O*:3-*O*:2-*O*	diacylate (%)	recovery (%)
1	toluene	84	11:86:3:0	12	2
2	$CHCl_3$	90	4:91:5:0	4	3
3	THF	51	27:51:22:0	28	16
4	DMF	46	63:12:24:1	26	21

[a] The reaction in entry 1 and the reactions in entries 2−4 were carried out with a substrate concentration of 0.08 and 0.1 M, respectively. [b] Regioselectivity (%) among four monoacylates.

alcohols[15] and also has a high k_{cat}/k_{uncat} ratio.[16] Analysis of the products was unambiguously performed by comparison with authentic samples of octyl 6-*O*-, 4-*O*-, 3-*O*-, and 2-*O*-isobutyryl-β-D-glucopyranosides, which were independently prepared via conventional protection/deprotection sequences (see Supporting Information). With DMAP as catalyst, four monoacylates, the 6-*O*-, 4-*O*-, 3-*O*-, and 2-*O*-isobutyrates, were obtained in a ratio of 36:26:26:12 in a combined yield of 47%, together with 22% of diacylates and 31% recovery of starting material (entry 1). Thus, totally random acylation took place by DMAP catalysis. On the other hand, with C_2-symmetric chiral PPYs **1**−**4**, the secondary hydroxyl group at C(4) was preferentially acylated (58−86% regioselectivity among monoacylates) in the presence of a free primary hydroxyl group at C(6) (entries 2−5). The highest selectivity (86%) for 4-*O*-acylation was observed with **1**, consisting of L-tryptophan.

We then investigated the solvent effects on the regioselectivity of acylation with catalyst **1** (Table 2). $CHCl_3$, THF, and DMF were investigated in addition to toluene. The polarity of the solvents roughly correlated with the chemo- and regioselectivity of acylation. The highest selectivity (91%) for 4-*O*-acylation was observed in a less-polar solvent, $CHCl_3$ (entry 2), whereas acylation of the primary hydroxyl group was predominant (63%) in polar solvent, DMF (entry 4). The observed solvent effects indicate that the driving force for selective 4-*O*-acylation may involve H-bonding between a substrate and a catalyst and may not significantly involve CH-π interaction. Another interesting phenomenon is that a higher ratio of 4-*O*-acylation is associated with a higher yield for monoacylation (entries 1−4). This implies that acylation of the secondary hydroxyl group at C(4) would proceed in an accelerative manner (cf. Scheme 1c, below).

Having obtained promising results in the regioselective acylation with **1** in $CHCl_3$, we then investigated the temperature effects (Table 3). A decrease in the reaction temperature to 0 °C increased the regioselectivity for 4-*O*-acylation to 98% (entry 2). With a decrease in catalyst loading to 1 mol % in the reaction at 0 °C, the regioselectivity for 4-*O*-acylation decreased slightly to 96% (entry 3). On the other hand, 1 mol % of catalyst was effective for controlling the regioselectivity of acylation at −20 °C and gave the 4-*O*-acylate and the 3-*O*-acylate in a 99:1 ratio in a combined yield of 98% (entry 5).[17] The reaction at −50 °C with 10 mol % of **1** showed perfect chemo- and regioselectivity and gave the 4-*O*-acylate as the sole product in 98% yield (entry 6). These strong temperature effects may indicate the contribution of a large negative $\Delta S^{\ddagger}$ term for regioselective acylation, which suggests multiple H-bonding in the transition state of acylation (cf. Figure 5). Use of acetic anhydride instead of isobutyric anhydride gave the 4-*O*-acetate in slightly diminished regioselectivity of 96% (entry 7). On the other hand, use of isobutyryl chloride gave totally different results. The acylation was sluggish (47% yield for monoacylation after 48 h at 0 °C), and the major product was the 6-*O*-acylate with 60% regioselectivity (entry 2 vs 8). The results indicate that the counteranion of the acylpyridinium ion should significantly affect the selectivity of acylation.

Next, we investigated the scope of the regioselective acylation of various monosaccharides catalyzed by **1**. The results are summarized in Figure 4. Acetylation (R = CH_3) of octyl β-D-glucopyranoside with 1 mol % of **1** at −20 °C for 24 h gave the 4-*O*-acetyl surrogate with 96% regioselectivity in 96% yield for monoacylation (Figure 4a). Acylation of octyl β-D-thioglucopyranoside with isobutyric anhydride or acetic anhydride at −60 °C gave the 4-isobutyryl derivative with 97% regioselectivity (92% yield for monoacylation) or the 4-acetyl derivative with 95% regioselectivity (99% yield for monoacylation), respectively (Figure 4b). The acylated thioglycosides are expected to be used directly for glycosylation because thioglycosides can be used as glycosyl donors.[18] Acylation of octyl α-D-glucopyranoside with isobutyric anhydride at 20 °C gave the 4-*O*-isobutyryl surrogate as a major product but with a largely diminished selectivity (54% regioselectivity and 75% yield for monoacylation, Figure 4c). Acylation of octyl β-D-mannopyranoside with isobutyric anhydride at −50 °C gave the 4-isobutyryl surrogate with 85% regioselectivity in 61% yield for monoacylation (Figure 4d). Preferable acylation of the secondary hydroxyl group at C(4) was observed in glucopyranosides and in a mannopyranoside in which C(4)−OH is

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(17) Experimental procedure for Table 3, entry 5: Octyl β-D-glucopyranoside (58.5 mg, 0.20 mmol), **1** (1.7 mg, 2.0 μmol), and 2,4,6-collidine (40 μL, 0.30 mmol) were dissolved in $CHCl_3$ (2.0 mL) at 20 °C. After the solution was cooled at −20 °C, isobutyric anhydride (36 μL, 0.22 mmol) was added. The resulting mixture was stirred at −20 °C for 24 h. The reaction mixture was quenched with saturated aqueous NH_4Cl solution and extracted with ethyl acetate. The organic layer was washed with H_2O and brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by SiO_2 column chromatography (ethyl acetate/hexane = 30:70 to 100:0) to give a 99:1 mixture of octyl 4-*O*-isobutyryl-β-D-glucopyranoside and octyl 3-*O*-isobutyryl-β-D-glucopyranoside in a combined yield of 98% (71 mg). Identification of the regioisomeric products was unambiguously performed by the comparison with pure regioisomers prepared independently by a conventional protection/deprotection procedure (see Supporting Information).
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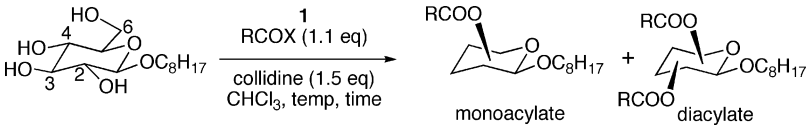
Table 3. Effects of Temperature and Acylating Agents on Regioselectivity of Acylation of Octyl β-D-Glucopyranoside with **1** in $CHCl_3$[a]



entry	mol % of **1**	temp (°C)	RCOX	time (h)	monoacylate (%)	regioselectivity[b] 6-*O*:4-*O*:3-*O*:2-*O*	diacylate (%)	recovery (%)
1	10	20	$(i\text{-PrCO})_2O$	12	90	4:91:5:0	4	3
2	10	0	$(i\text{-PrCO})_2O$	12	97	0:98:2:0	2	0
3	1	0	$(i\text{-PrCO})_2O$	12	97	2:96:2:0	2	1
4	10	−20	$(i\text{-PrCO})_2O$	12	98	0:99:1:0	0	0
5	1	−20	$(i\text{-PrCO})_2O$	24	98	0:99:1:0	0	0
6	10	−50	$(i\text{-PrCO})_2O$	38	98	0:>99:<1:0	0	0
7	1	−20	Ac_2O	24	96	0:96:4:0	4	0
8	10	0	*i*-PrCOCl	48	47	60:35:5:0	13	19

[a] The reactions were carried out with a substrate concentration of 0.1 M. [b] Regioselectivity (%) among four monoacylates.

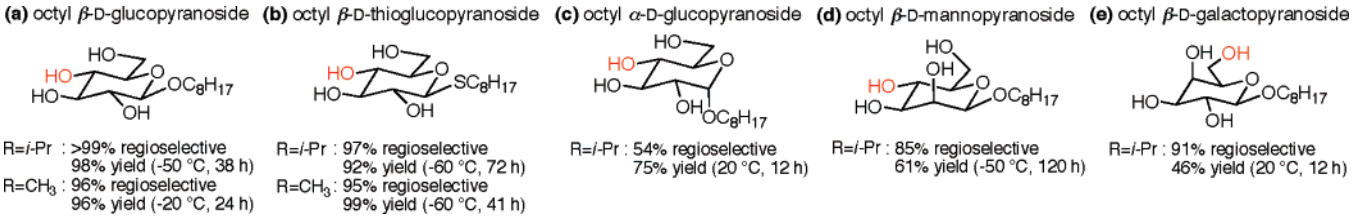
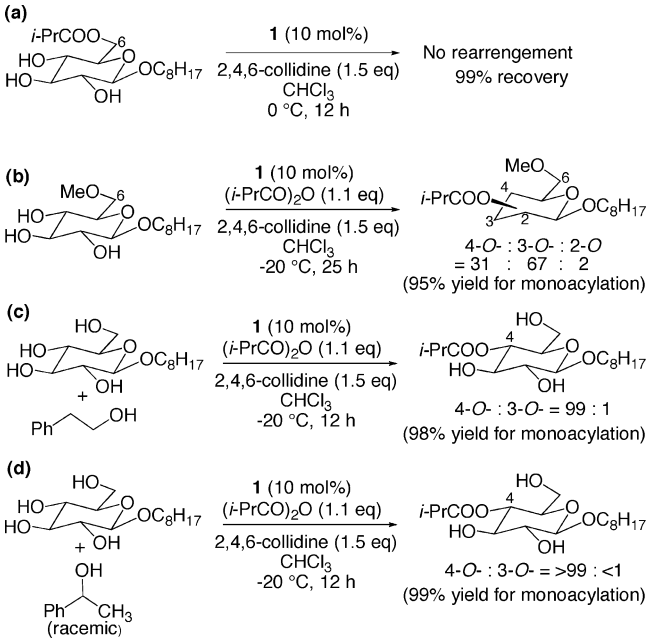


Figure 4. Regioselectivity profiles in acylation of carbohydrates with 10 mol % of **1**/$(RCO)_2O$/collidine/$CHCl_3$ (1 Mol % of **1** was employed for (a), R═CH_3). R originates in the anhydride, $(RCO)_2O$. The hydroxyl group predominantly acylated is shown as red colored OH, and the regioselectivity is shown as a percentage among the four monoacylates. Yields shown are those for monoacylation. The reactions were carried out at the temperature and for the time indicated in the parentheses.

equatorially oriented. On the other hand, acylation of octyl β-D-galactopyranoside, whose C(4)−OH is axially oriented, took place predominantly at the primary hydroxyl group at C(6) (Figure 4e). This indicates that equatorial orientation is crucial for the selective acylation of C(4)−OH.

We then investigated the mechanistic aspects to determine the origin of the regioselectivity of acylation catalyzed by **1**. It might be supposed that the acylation of C(4)−OH is the result of migration of the 6-*O*-acylate into the 4-*O*-acylate. To examine this possibility, the 6-*O*-isobutyrate of octyl β-D-glucopyranoside was independently prepared (see Supporting Information),# and was treated under reaction conditions similar to those in entry 2 in Table 3, except that isobutyric anhydride was absent (Scheme 1a). The 6-*O*-isobutyrate was recovered in 99% yield, and no migration to the 4-*O*-isobutyrate was detected. This clearly indicates that acylation of a secondary hydroxyl group at C(4) took place directly under the influence of the catalyst. Since we hypothesized that H-bonding between the primary hydroxyl group at C(6) of the carbohydrate and the catalyst is critical for regioselective acylation, the 6-OMe derivative was prepared and treated under reaction conditions similar to those in entry 4 in Table 3 (Scheme 1b). The 4-*O*-, 3-*O*-, and 2-*O*-isobutyrates were obtained in a ratio of 31:67:2 in a combined yield of 95%. Upon treatment of octyl β-D-glucopyranoside with isobutyric anhydride in the presence of 10 mol % of DMAP in $CHCl_3$ at −20 °C, nonselective acylation took place to give 6-*O*-, 4-*O*-, 3-*O*-, and 2-isobutyrate in a ratio of 38:23:38:1 in a combined yield of 69%. Accordingly, **1** behaves like a nonselective catalyst, such as DMAP, when the primary hydroxyl group at C(6) is protected. These results indicate that H-bonding between the primary hydroxyl group at C(6) and the catalyst is critical for the regioselectivity caused by **1** (cf. Figure 5).

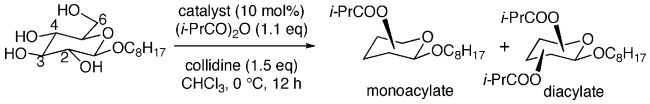
Scheme 1. Mechanistic Investigation into Regioselectivity of Acylation of Octyl β-D-Glucopyranoside[a]



[a] (a) Rearrangement of octyl 6-*O*-isobutyryl-β-D-glucopyranoside into the 4-*O*-isobutyrate in the presence of **1** was not observed at all. (b) Nonselective acylation of the 6-OMe derivative took place with **1**. (c) Competitive acylation between octyl β-D-glucopyranoside and 2-phenylethanol in the presence of **1** gave the 4-*O*-isobutyrate of octyl β-D-glucopyranoside with 99% regioselectivity. (d) Competitive acylation between octyl β-D-glucopyranoside and racemic 1-phenyethanol in the presence of **1** gave the 4-*O*-isobutyrate of octyl β-D-glucopyranoside with >99% regioselectivity.

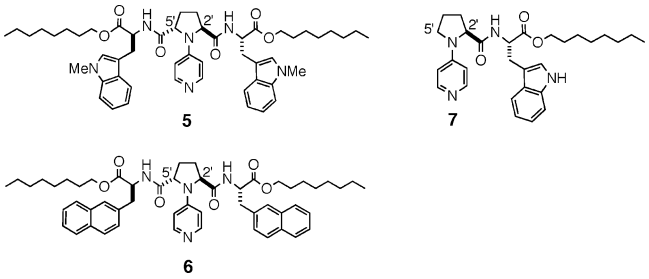
The effects of the functionality of the catalysts on the regioselectivity of the acylation were investigated (Table 4).

Table 4. Effects of Catalysts on Regioselectivity of Acylation of Octyl β-D-Glucopyranoside[a]



entry	catalyst	monoacylate (%)	regioselectivity[b] 6-*O*:4-*O*:3-*O*:2-*O*	diacylate (%)	recovery (%)
1	**1**	97	0:98:2:0	2	0
2	**5**[c]	69	14:60:26:0	20	8
3	**6**[c]	74	7:65:28:0	15	4
4	**7**[c]	62	13:66:20:1	13	22
5	DMAP	61	33:24:43:0	21	14

[a] The reactions were carried out with a substrate concentration of 0.1 M. [b] Regioselectivity (%) among four monoacylates. [c] Catalyst structures:



With catalyst **5** or **6**, in which an indole substructure of **1** was replaced by an *N*-methylindole or by 2-naphthyl, respectively, acylation at the secondary hydroxyl group at C(4) was still predominant, but with decreased regioselectivity (entries 2 and 3). 4-*O*-Acylation took place predominantly throughout the reactions with catalysts **1**−**6**, which suggests that two amide carbonyl groups at C(2′) and C(5′), common functionality in these catalysts, seems essential for the selective acylation at C(4)−OH. Comparison of the regioselectivity of acylation catalyzed by **1** with that of acylation catalyzed by **5** indicates that the indole NH of **1** seems to participate in increasing the regioselectivity of acylation at C(4)−OH. On the basis of all of these observations, we propose a possible transition state assembly for the regioselective acylation of octyl β-D-glucopyranoside with **1** (Figure 5). Since the primary hydroxyl group at C(6) is the most reactive in the carbohydrate substrate, it would preferentially form a H-bond with an amide carbonyl that is likely to be the strongest H-bond accepter in the acylpyridinium ion. As the result of the H-bonding, the indole NH of the catalyst locates near C(3)−OH of the carbohydrate, resulting in the formation of an additional H-bond between them. The cooperative effects of the multiple H-bonding would fix the conformation of the substrate at the transition state for acylation, where the hydroxyl group at C(4) is in close proximity to the reactive carbonyl group of the acylpyridinium ion, resulting in the selective acylation of C(4)−OH in an accelerative manner. The notion of accelerative acylation is supported experimentally by the competitive acylation between octyl β-D-glucopyranoside and a primary alcohol or a secondary alcohol (Scheme 1c,d). When a 1:1 mixture of octyl β-D-glucopyranoside and 2-phenylethanol was treated under conditions similar to those in entry 4 in Table 3, the 4-*O*-isobutyrate of octyl β-D-glucopyranoside was obtained with 99% regioselectivity in 98% yield for monoacylation. Similary, competitive acylation between octyl β-D-glucopyranoside and racemic 1-phenylethanol gave the 4-*O*-isobutyrate of octyl β-D-glucopyranoside with

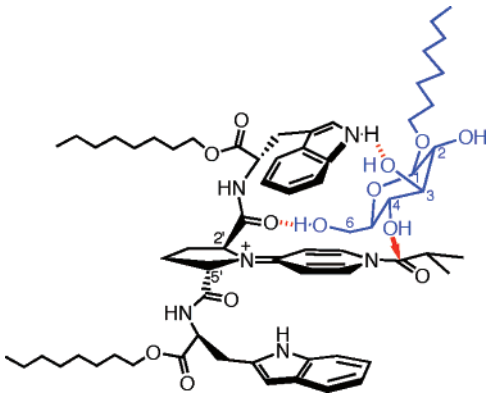


Figure 5. Proposed transition state model for the chemo- and regioselective acylation of octyl β-D-glycopyranoside catalyzed by **1**.

>99% regioselectivity in 99% yield for monoacylation. The existence of the primary or secondary alcohol did not affect the selective acylation of the carbohydrate at all, indicating that acylation of the secondary hydroxyl group at C(4) of the carbohydrate with **1** proceeds in an accelerative manner. The C_2-symmetric structure of catalyst **1** seems to be important, since approach of the carbohydrate substrate from the face of the C(2′) side chain of the catalyst would lead to the transition state structure shown in Figure 5, which is supposed to be identical with that caused by the substrate approach from the face of the C(5′) side chain. This notion was supported by the results of the corresponding reaction with non-C_2-symmetric catalyst **7** (Table 4, entry 4). Acylation of octyl β-D-glucopyranoside with **7** gave the 4-*O*-acylate as the major product but with decreased regioselectivity of 66% (entry 1 vs 4). A substrate approaching from the β-face (the face of the C(2′) side chain) of the acylpyridinium ion generated from **7** would undergo selective acylation at C(4)−OH, while a substrate approaching from the less-hindered α-face (the C(5′) side chain is absent in **7**) would undergo nonselective acylation. As the result, the 4-*O*-acylate was obtained as the major product but with diminished regioselectivity in the acylation catalyzed by **7**.

The transition state assembly shown in Figure 5 may reasonably explain the difference in the regioselectivity profiles of acylation of monosaccharides. In the case of octyl α-D-glucopyranoside (Figure 4c), a transition state assembly as shown in Figure 5 may be possible; however, it is somewhat disfavored by the unfavorable interaction between an α-octyloxy substituent at C(1) of the carbohydrate and the acylpyridinium ion. Therefore, acylation of C(4)−OH of octyl α-D-glucopyranoside took place predominantly but with the diminished regioselectivity of 54%. One difference between octyl β-D-glucopyranoside (Figure 4a) and octyl β-D-mannopyranoside (Figure 4d) is the orientation of the hydroxyl group at C(2). Since the orientation of the hydroxyl group at C(2) does not seem to significantly affect the transition state assembly, selective 4-*O*-acylation is also expected for the mannose derivative. On the other hand, a transition state assembly as shown in Figure 5 is not possible with carbohydrates that have an axial hydroxyl group at C(4). Accordingly, acylation of the galactose derivative proceeded in a totally different manner and gave the 6-*O*-acylate as a major product (Figure 4e), because of the intrinsically high reactivity of the primary hydroxyl group of the carbohydrate.

Conclusions

Organocatalytic chemo- and regioselective acylation of monosaccharides has been developed. The present method enables direct functionalization of one of the multiple hydroxyl groups of octyl β-D-glucopyranosides with >99% selectivity and in 98% yield. Accordingly, the development of the present process greatly reduces the synthetic steps toward carbohydrates. It also provides a novel strategy for the preferential functionalization of a secondary hydroxyl group in the presence of a free primary hydroxyl group.

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Supporting Information Available: Preparation and characterization of **1**−**7** and of octyl 6-*O*-, 4-*O*-, 3-*O*-, and 2-*O*-isobutyryl-β-D-glucopyranosides. This material is available free of charge via the Internet at http://pubs.acs.org.

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