Site-selective acylation of complex molecules by 4-pyrrolidinopyridine catalyst

Literature seminar

M1 Yu Irie

2022/8/25 (Thu)

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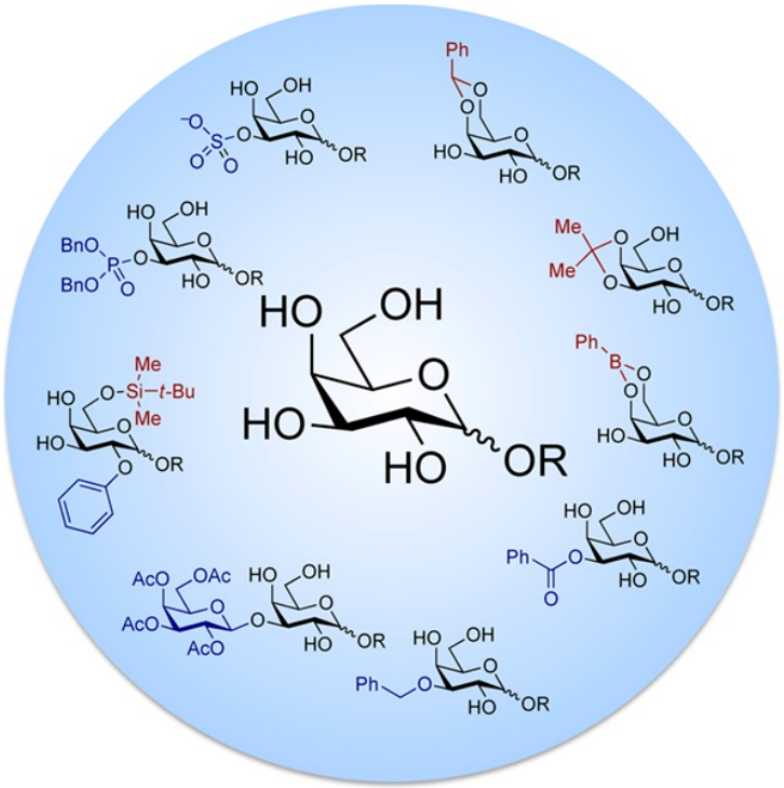
Modification of carbohydrates: Challenges

The key issue: Site-selectivity (several OH groups in one molecule)



Protecting-group strategies

- ✓ **Well developed**
- ✗ **Requires multi-step synthetic sequences**
- ✗ **May cause deactivation of the unprotected hydroxyl groups**

✓ **Site-selective modification with minimally protected substrates**

V. Dimakos, M. S. Taylor, *Chem. Rev.* **2018**, *118*, 11457–11517.

Modification of carbohydrates: Precedents

Sulfation

Phosphorylation

Formation of cyclic adducts from diol moieties

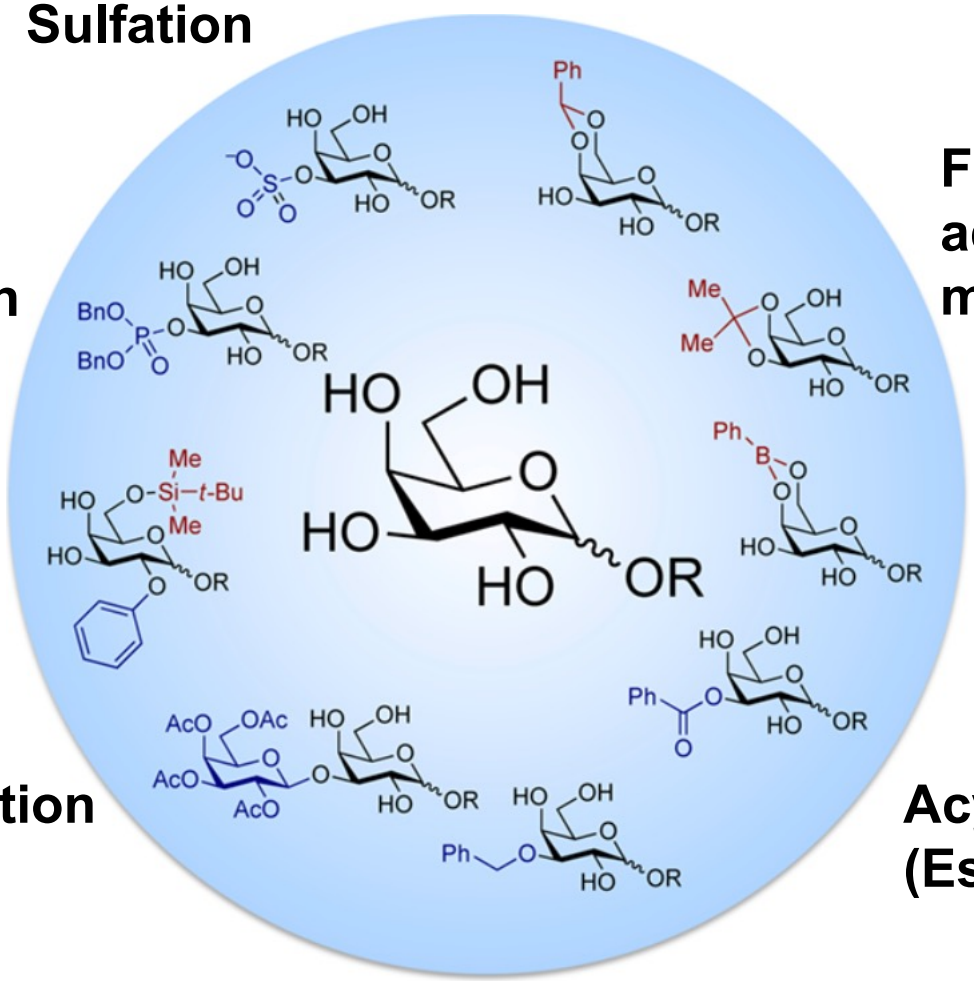
Silylation

Glycosylation

Acylation (Esterification)

…and so on

Alkylation



V. Dimakos, M. S. Taylor, *Chem. Rev.* **2018**, *118*, 11457–11517.

Modification of carbohydrates: Precedents

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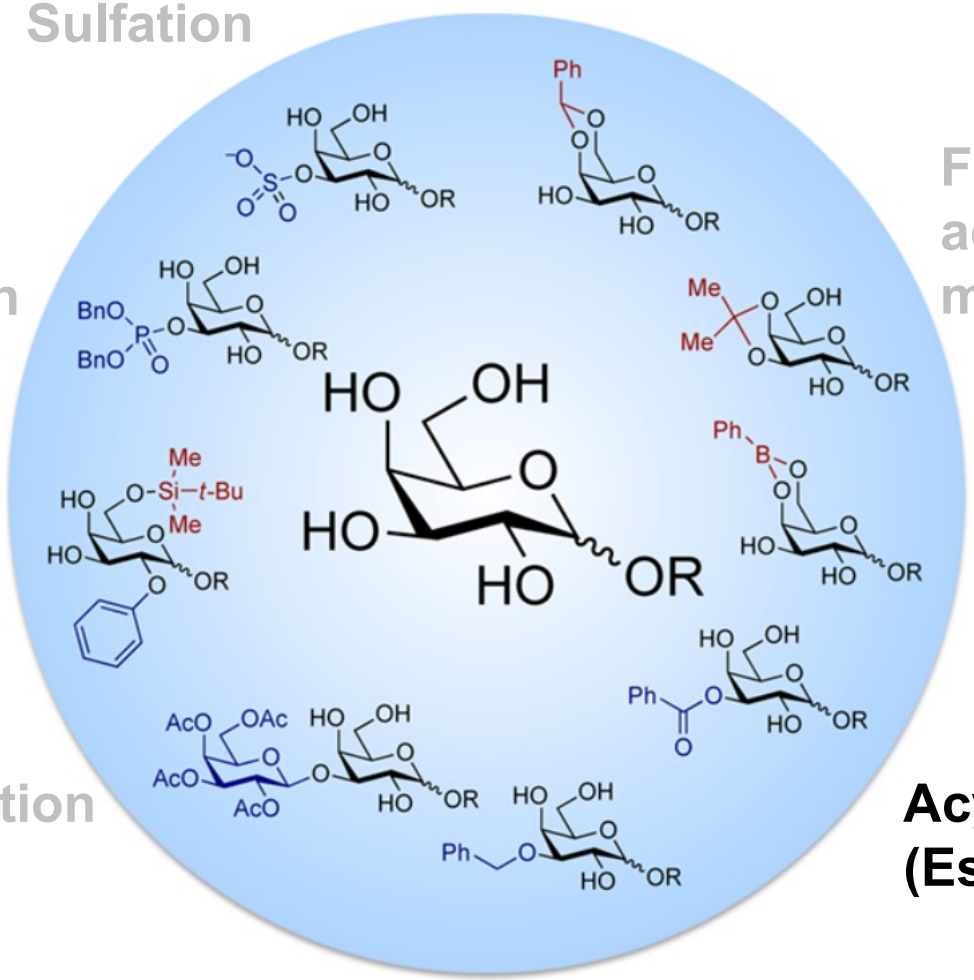
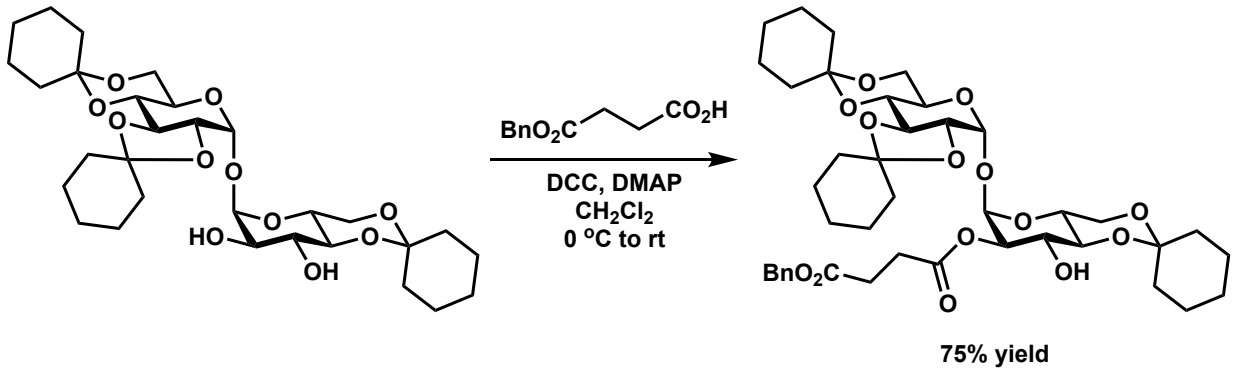


V. Dimakos, M. S. Taylor, *Chem. Rev.* **2018**, *118*, 11457–11517.

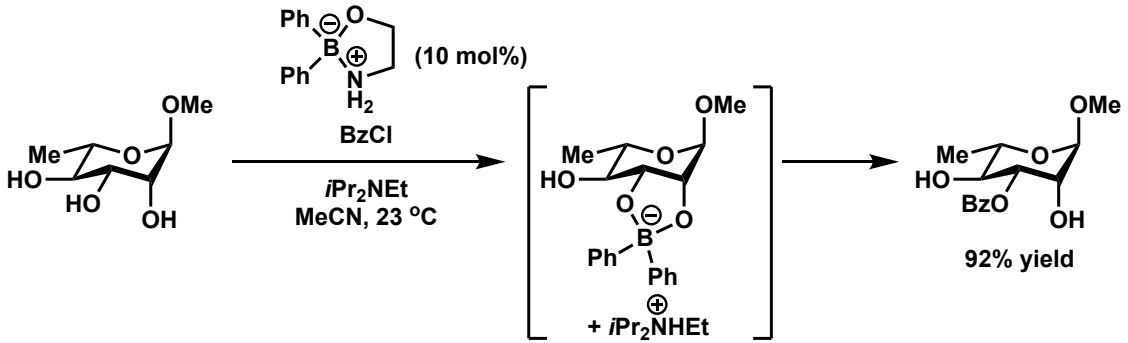
Examples of selective acylation of OH groups

- **Carbodiimide / Uronium Salt-Mediated Coupling**



S. Jana, S. Mondal, S. S. Kulkarni, *Org. Lett.* **2017**, *19*, 1784–1787.

- **Complexation of OH groups**



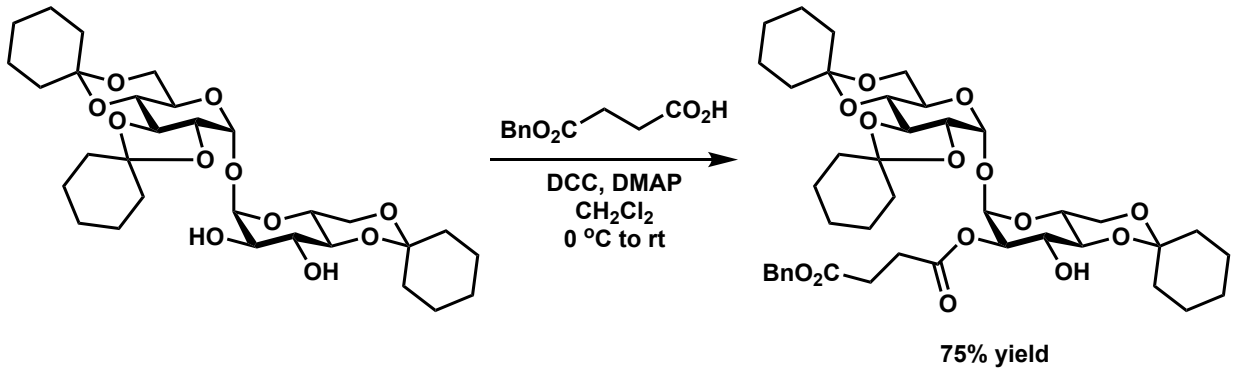
D. Lee, M. S. Taylor, *J. Am. Chem. Soc.* **2011**, *133*, 3724–3727.

- **Organocatalyzed acylations (using DMAP catalyst)**

…and so on

Examples of selective acylation of OH groups

- Carbodiimide- / Uronium Salt-Mediated Coupling



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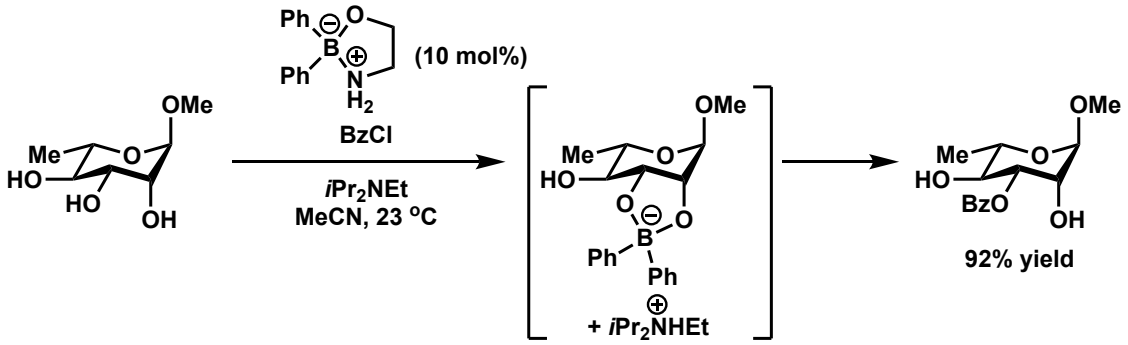


D. Lee, M. S. Taylor, *J. Am. Chem. Soc.* **2011**, *133*, 3724–3727.

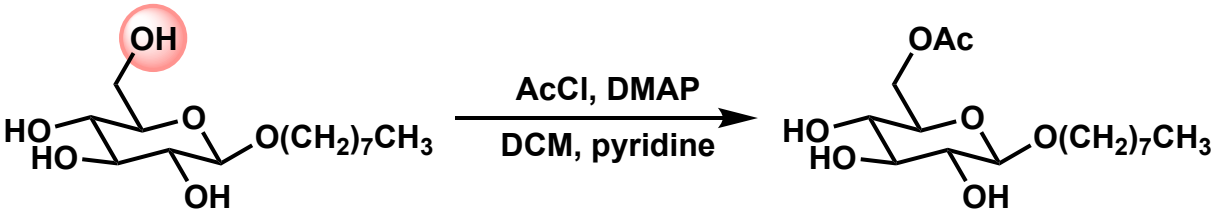
- **Organocatalyzed acylations (using DMAP catalyst)**

…and so on

Site-selective acylation using DMAP

Chemoselective acylation of a secondary hydroxyl group in the presence of a primary hydroxyl group

= Difficult because of the steric effects

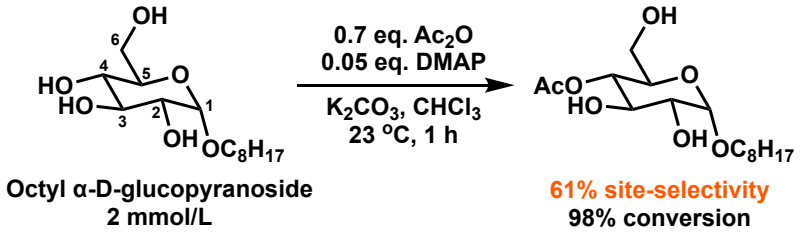


85% site-selectivity
73% yield

E. Kattnig, M. Albert, *Org. Lett.* **2004**, *6*, 945–948.

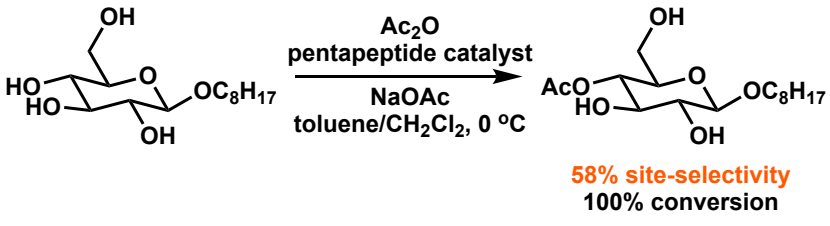
Site-selective acylation of C(4)-OH

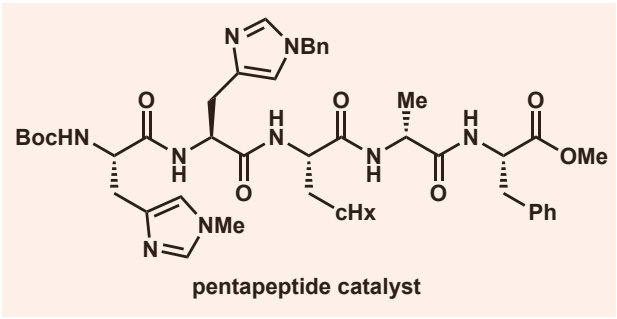
- **octyl α-D-glucopyranoside**



T. Kurahashi, T. Mizutani, J. Yoshida, *J. Chem. Soc. Perkin 1* **1999**, 465–474.

- **octyl β-D-glucopyranoside**





K. S. Griswold, S. J. Miller, *Tetrahedron* **2003**, *59*, 8869–8875.

✗ **Low selectivities**

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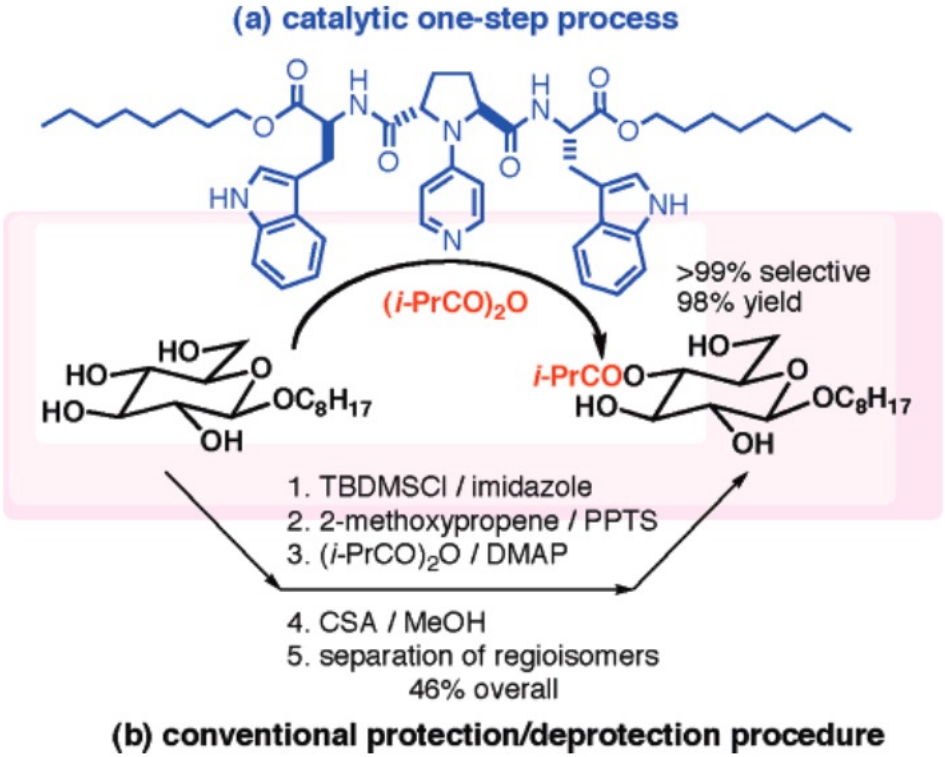
Catalytic site-selective single-step acylation



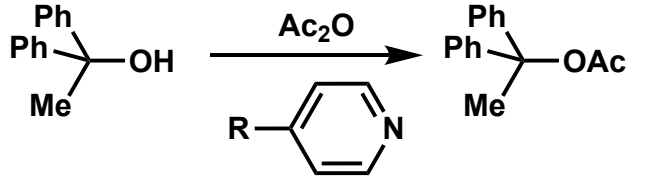
✓ **A newly developed catalyst** ✓ **High selectivity and high yield**
✓ **An extremely short method**

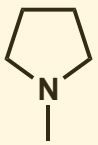
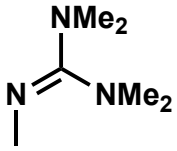
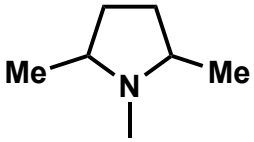
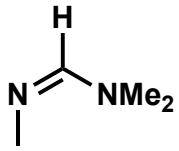
T. Kawabata, *et al. J. Am. Chem. Soc.* **2007**, *129*, 12890–12895.

Catalyst design: PPy as an active site

- **4-pyrrolidinopyridine (PPy): Powerful catalysts for acylation of alcohols**

Relative effects of the cataysts



R					
	1.0	0.9	0.63	0.5	0.3
	PPy		DMAP		

E. F. V. Scriven, *Chem. Soc. Rev.* **1983**, *12*, 129–161.

- **Reactive intermediate generated from PPy: acylpyridinium ions (such as in the reaction using DMAP).**

G. Höfle, W. Steglich, H. Vorbrüggen, *Angew. Chem. Int. Ed. Engl.* **1978**, *17*, 569–583.

Proposed transition state

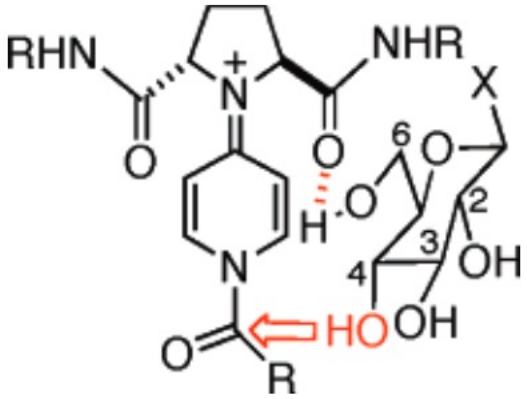


Figure 2. Working hypothesis for selective acylation of a secondary hydroxyl group in the presence of a primary hydroxyl group of a glucose derivative.

- **C(6)-OH: Preferentially form an H-bond with an acceptor (e.g. an amide carbonyl group) of the catalyst**
- **C(2)-OH, C(3)-OH: Additional interactions to fix the conformation of carbohydrate**

→ Selective acylation at C(4)-OH

T. Kawabata, *et al. J. Am. Chem. Soc.* **2007**, *129*, 12890–12895.

Catalyst design: Functional side chains

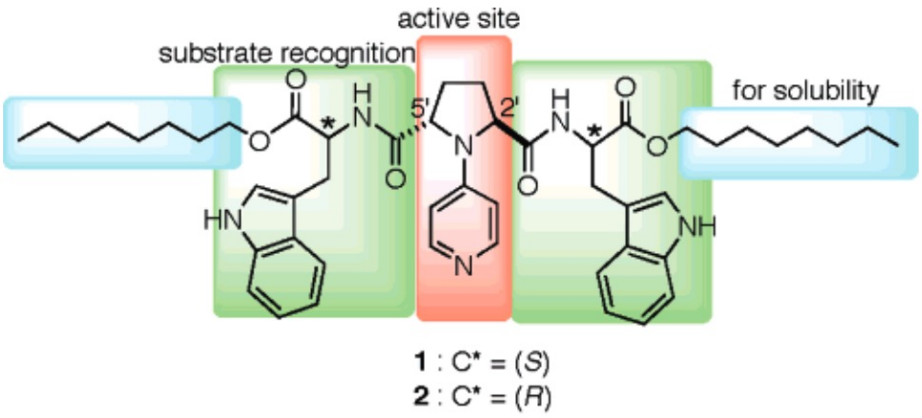


Figure 3. Design and structure of catalysts.

Indole substructure of tryptophan:
Suitable for H-bonding and CH-π interaction with carbohydrates

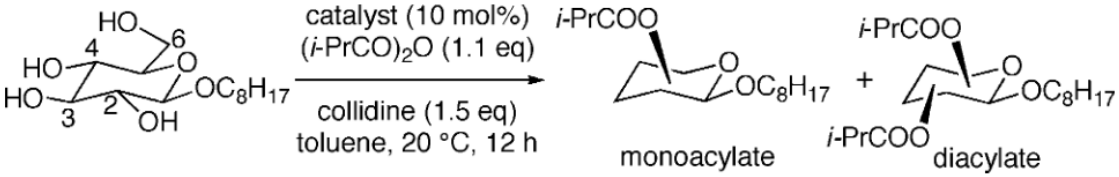
Octyl esters:
Enhance the solubility of the catalysts in nonpolar solvents

Catalysts 3 and 4:
Tyrosine instead of tryptophan

T. Kawabata, *et al. J. Am. Chem. Soc.* **2007**, *129*, 12890–12895.

Comparison of catalysts' activity

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.

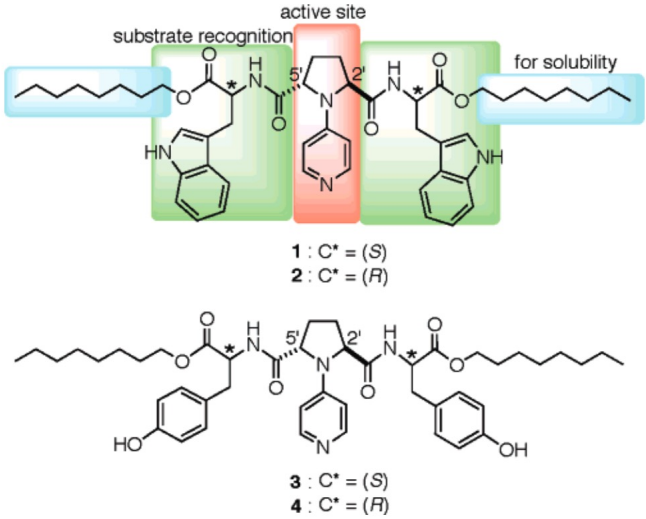


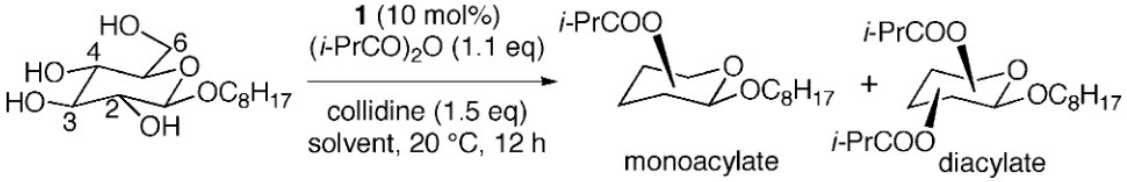
Figure 3. Design and structure of catalysts.

The highest selectivity for 4-*O*-acylation was observed by using catalyst 1.

T. Kawabata, *et al. J. Am. Chem. Soc.* **2007**, *129*, 12890–12895.

Solvent effects

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.

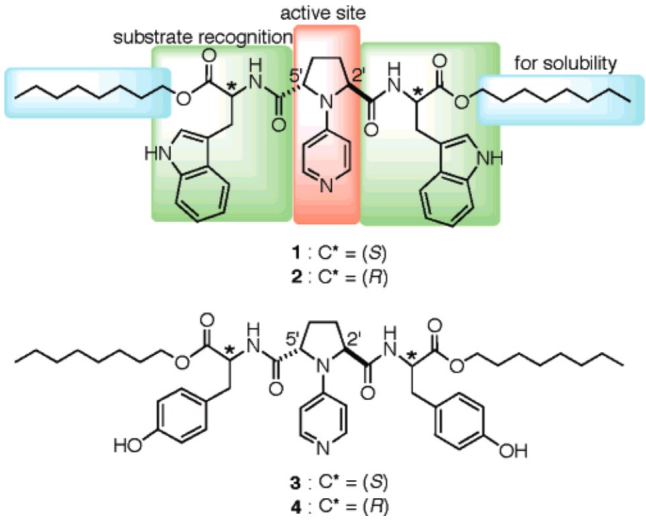


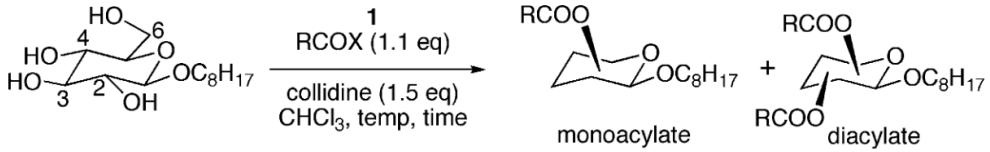
Figure 3. Design and structure of catalysts.

H-bonding > CH-π interaction

T. Kawabata, *et al. J. Am. Chem. Soc.* **2007**, *129*, 12890–12895.

Temperature effects and catalyst loading

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.

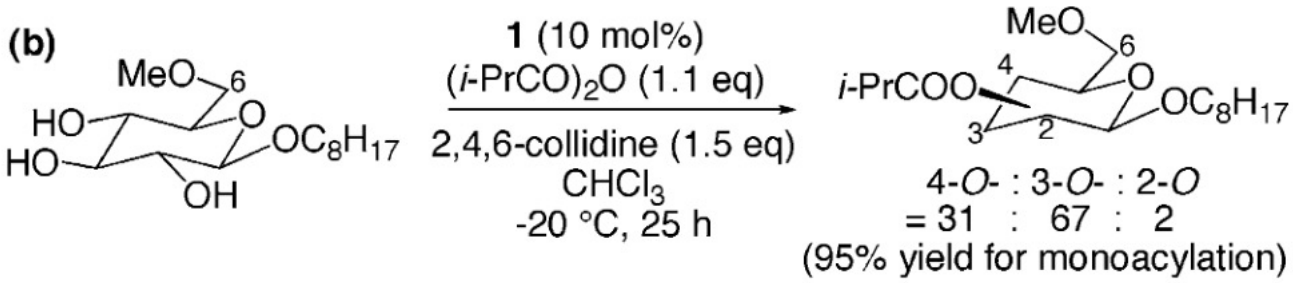
✓ **Low temperature and high catalyst loading**

T. Kawabata, *et al. J. Am. Chem. Soc.* **2007**, *129*, 12890–12895.

Mechanistic studies: Use of 6-OMe derivative

Confirmation of the effects of H-bonding between C(6)-OH and the catalyst to the regioselectivity

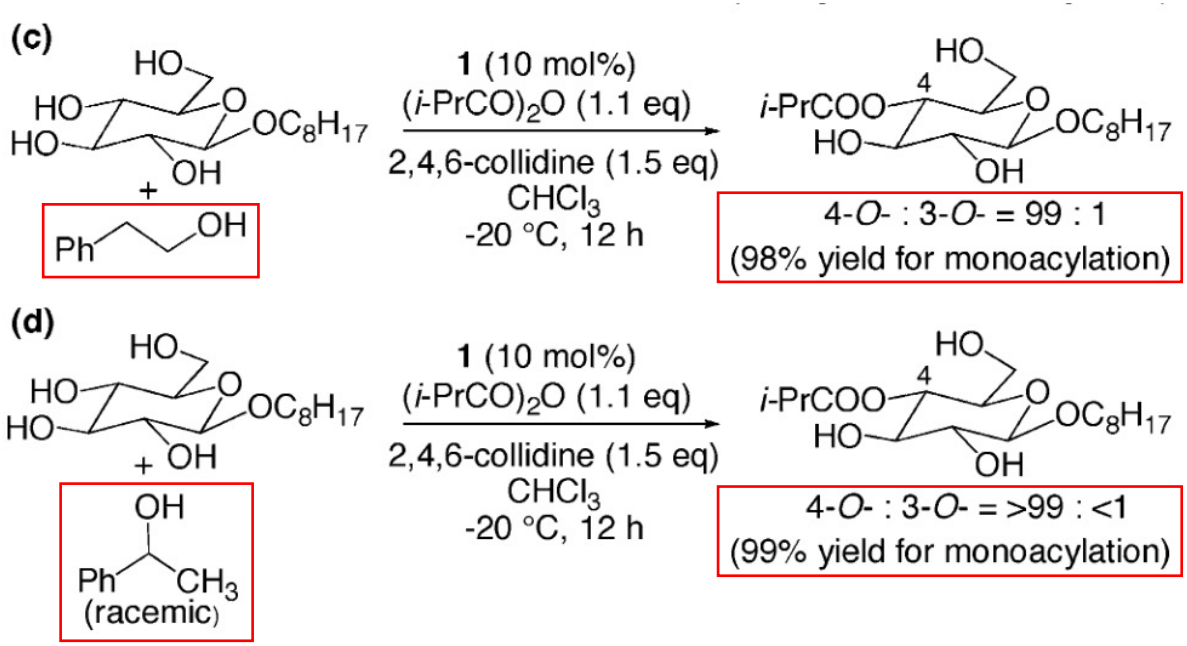
→ Use 6-OMe derivative



- **H-bonding between C(6)-OH and the catalyst is critical for the regioselective reaction.**

T. Kawabata, *et al. J. Am. Chem. Soc.* **2007**, *129*, 12890–12895.

Mechanistic studies: Competitive acylation

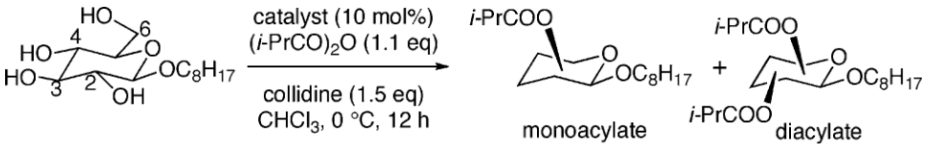


- **Site-selective acylation proceeds in an accelerative manner.**

T. Kawabata, *et al. J. Am. Chem. Soc.* **2007**, *129*, 12890–12895.

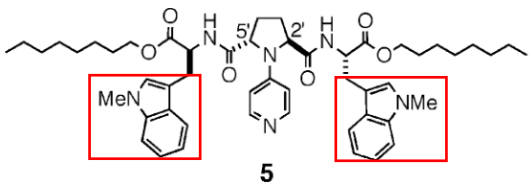
Effects of catalyst structures

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:



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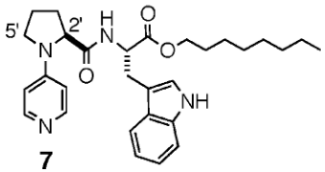

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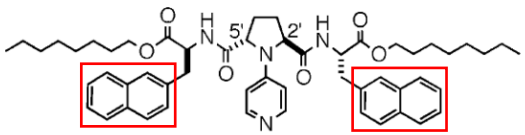


6

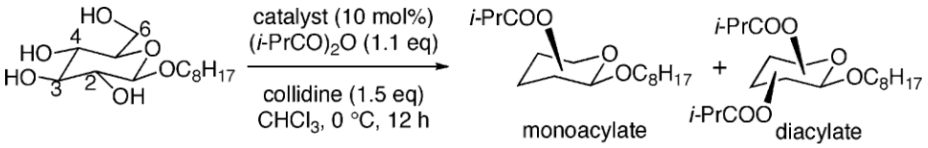
Indole substructure of catalyst 1:
→ N-methylindole (entry 2)
→ 2-naphthyl (entry 3)

Two amide carbonyl groups at C(2') and C(5') are essential for the selective acylation at C(4)-OH.

T. Kawabata, *et al. J. Am. Chem. Soc.* **2007**, *129*, 12890–12895.

C_2-symmetric structure of the catalyst

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



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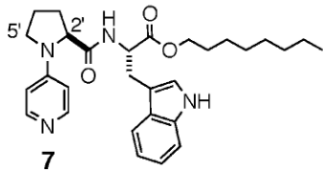
[a] The reactions were carried out with a substrate concentration of 0.1 M. [b] Regioselectivity (%) among four monoacylates. [c] Catalyst structures:



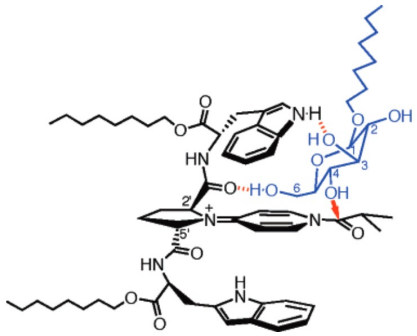


Figure 5. Proposed transition state model for the chemo- and regioselective acylation of octyl β-D-glycopyranoside catalyzed by **1**.

With C_2-symmetric structure, approach of the carbohydrate substrate from…
the face of the C(2') side chain = the face of the C(5') side chain

The low selectivity in entry 4 is caused by the nonselective acylation of carbohydrates which approaches from the C(5') side chain.

T. Kawabata, *et al. J. Am. Chem. Soc.* **2007**, *129*, 12890–12895.

Proposed transition state model

1) The primary hydroxyl group at C(6) (most reactive) forms H-bond with an amide carbonyl (strongest H-bond acceptor).

2) Indole NH located near C(3)-OH of the carbohydrate forms H-bond.

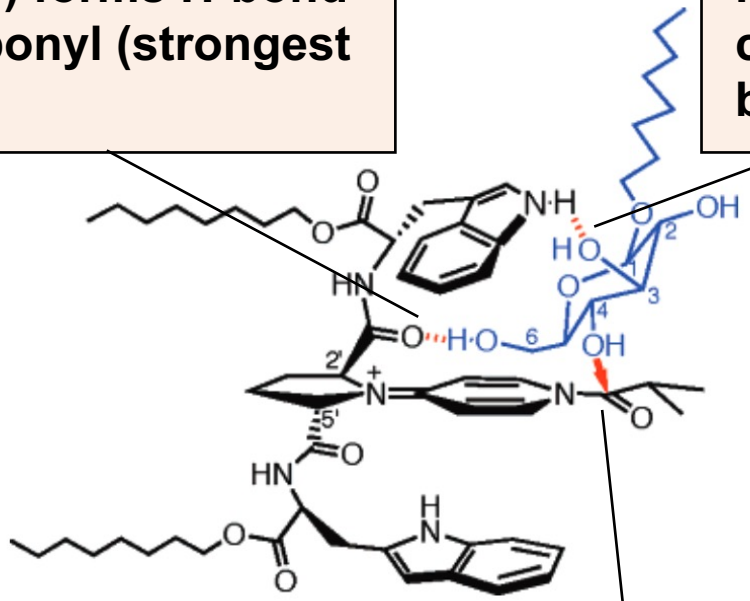
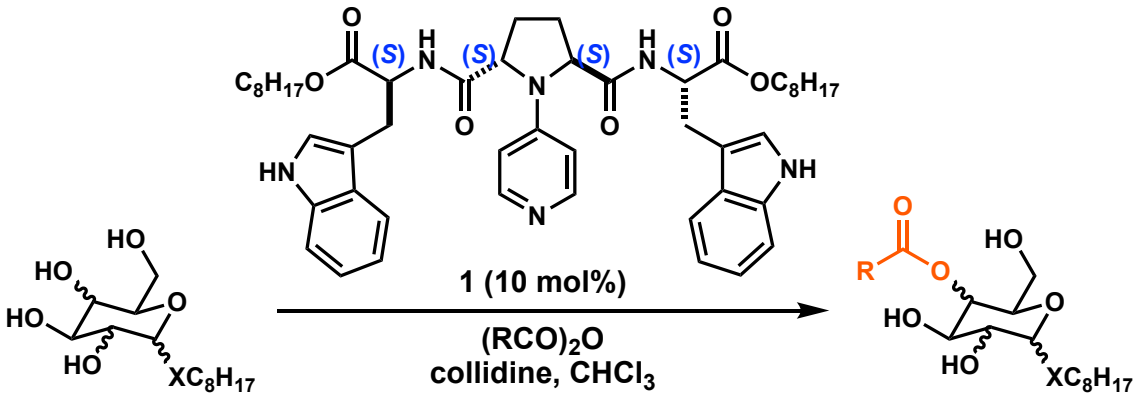


Figure 5. Proposed transition state model for the chemo- and regioselective acylation of octyl β-D-glycopyranoside catalyzed by **1**.

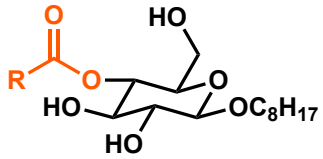
3) Substrate is fixed at this conformation via multiple H-bonding, and the acylation proceeds in an accelerative manner at C(4)-OH.

T. Kawabata, *et al. J. Am. Chem. Soc.* **2007**, *129*, 12890–12895.

Substrate scope

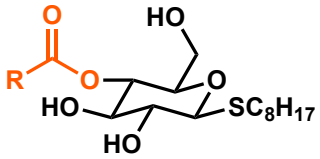


(a)



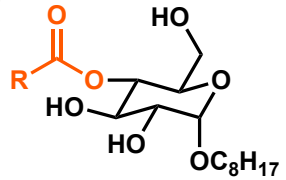
R = *i*Pr : >99% regioselective
98% yield (-50 °C, 38 h)
R = CH_3[a] : 96% regioselective
96% yield (-20 °C, 24 h)

(b)



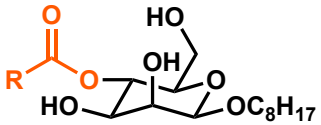
R = *i*Pr : 97% regioselective
92% yield (-60 °C, 72 h)
R = CH_3 : 95% regioselective
99% yield (-60 °C, 41 h)

(c)



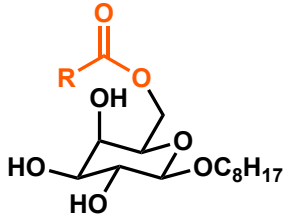
R = *i*Pr : 54% regioselective
75% yield (20 °C, 12 h)

(d)



R = *i*Pr : 85% regioselective
61% yield (-50 °C, 120 h)

(e)

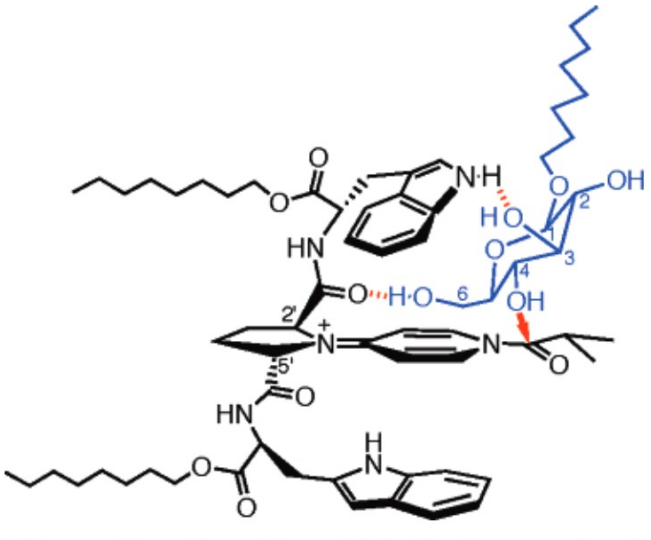


R = *i*Pr : 91% regioselective
46% yield (20 °C, 12 h)

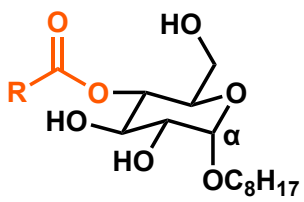
[a]1 mol% of 1 was used.

T. Kawabata, *et al. J. Am. Chem. Soc.* **2007**, *129*, 12890–12895.

Explanation of the substrate scope results



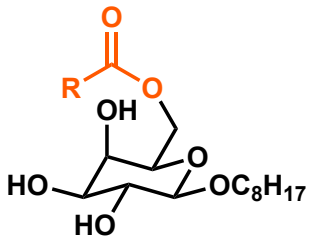
(c)



R = *i*Pr : 54% regioselective
75% yield (20 °C, 12 h)

Unfavorable interaction between an α-octyloxy substituent and the acylpyridinium ion

(e)



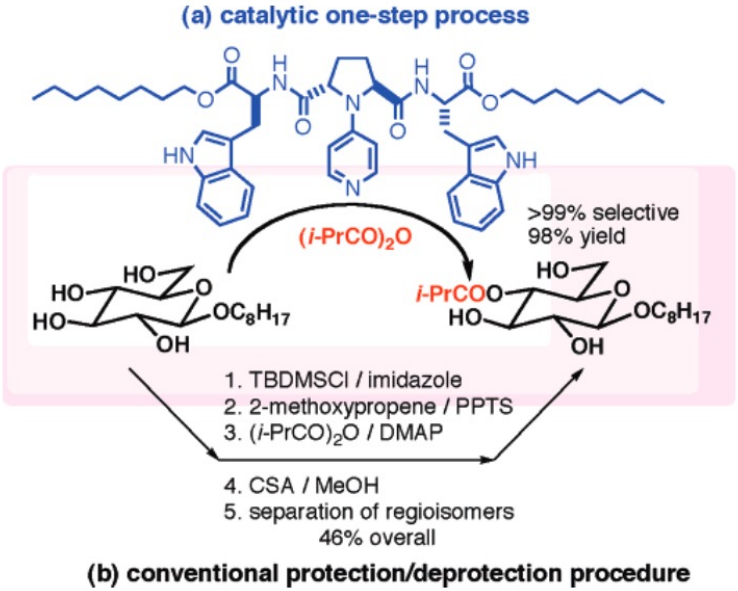
R = *i*Pr : 91% regioselective
46% yield (20 °C, 12 h)

Axial hydroxy group at C(4)

- **C(6)-OH selective reaction**

T. Kawabata, *et al. J. Am. Chem. Soc.* **2007**, *129*, 12890–12895.

Short summary



- ✓ **Organocatalytic site-selective acylation of monosaccharides**
- ✓ **Up to >99% selectivity, 98% yield**
- ✓ **Reduction of synthetic steps toward carbohydrates**

- ➢ **Application to various molecules**

T. Kawabata, *et al. J. Am. Chem. Soc.* **2007**, *129*, 12890–12895.

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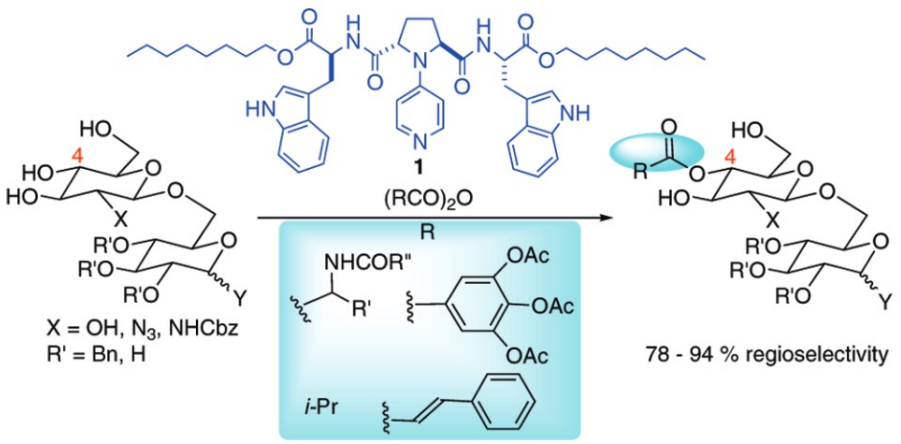
Expansion of substrate scope



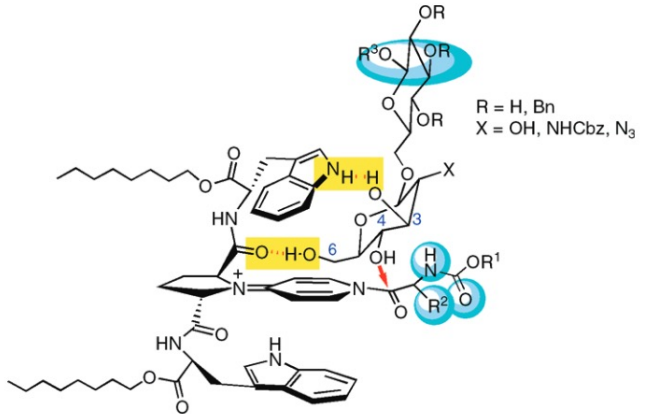


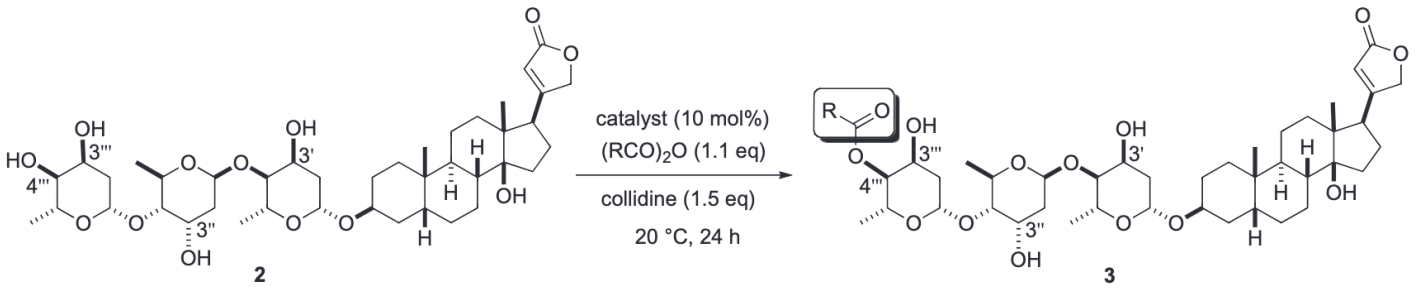
FIGURE 2. Functional group (blue circles) tolerance in molecular recognition via hydrogen bonding (yellow rectangles).

- ✓ **Various acid anhydrides (derived from α-amino acids, cinnamic acid, and gallic acid)**
- ✓ **Disaccharides with seven free hydroxy groups**

- ➢ **High functional group tolerance was confirmed.**

T. Kawabata, *et al. J. Org. Chem.* **2009**, *74*, 8802–8805.

Site-selective acylation of digitoxin



2 digitoxin 3

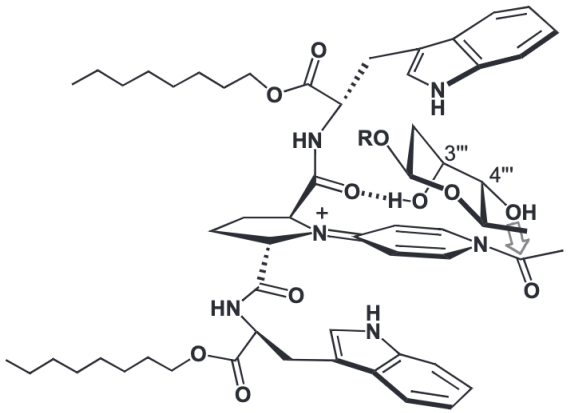
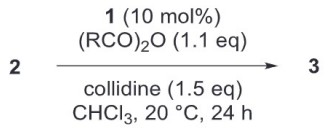


Figure 1. A hypothetical model of transition–state assembly for regioselective acylation of digitoxin (**2**) (the terminal digitoxose is shown) promoted by catalyst **1**.

Table 2
Regioselective acylation of **2** with various acid anhydride[a]



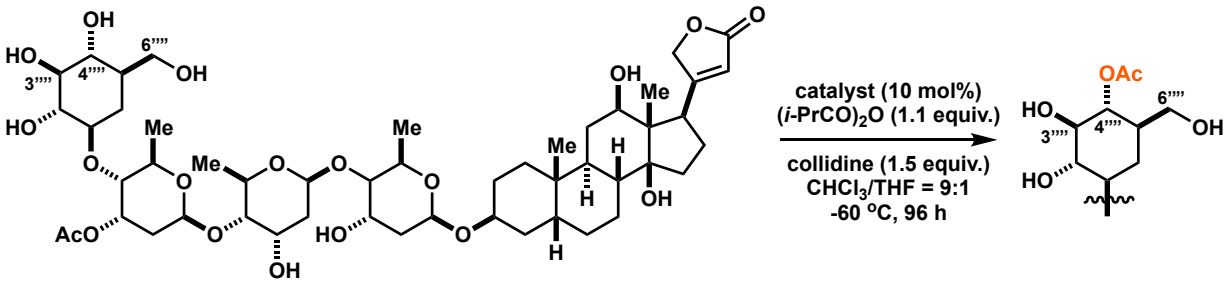
Entry	R	Regioselectivity[b] 4‴-*O*:3‴-*O*:3″-*O*:3′-*O*	Yield[c] (%)	Recovery (%)
1	$C_{11}H_{23}$	>99:0:0:0	92	7
2	$C_{15}H_{31}$	>99:0:0:0	90	8
3	$C_{21}H_{43}$	>99:0:0:0	96	2
4	CH_2=CH–$(CH_2)_2$	>99:0:0:0	90	7
5	2-Thiophene	>99:0:0:0	94	4
6	3-Furyl	>99:0:0:0	93	5
7	(*E*)-Ph-CH=CH	>99:0:0:0	90	6

[a] Reactions were carried out with a substrate concentration of 0.02 M.
[b] % Regioselectivity among four monoacylates.
[c] Formation of 3‴-*O*-, 4‴-*O*-diacylate was negligible in each run.

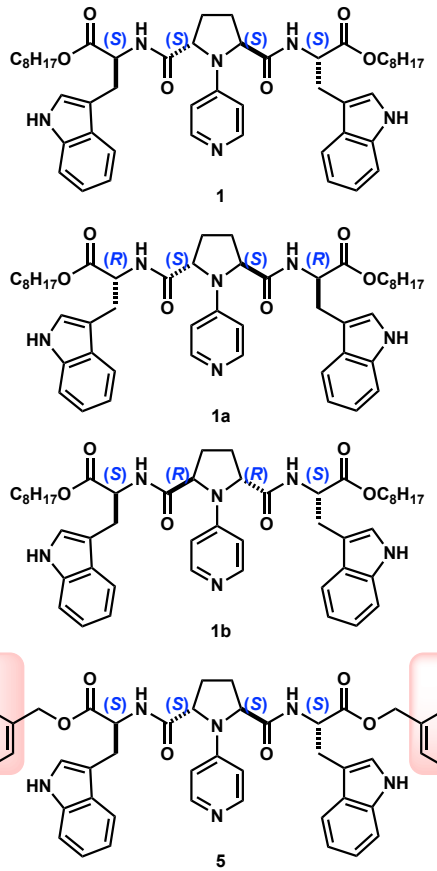
- ✓ **Various acid anhydrides (R = Me, *i*-Pr, Ph and so on)**
- ✓ **High C(4’’’) selectivity**

K. Yoshida, T. Furuta, T. Kawabata, *Tetrahedron Lett.* **2010**, *51*, 4830–4832.

Site-selective acylation of Lanatoside C



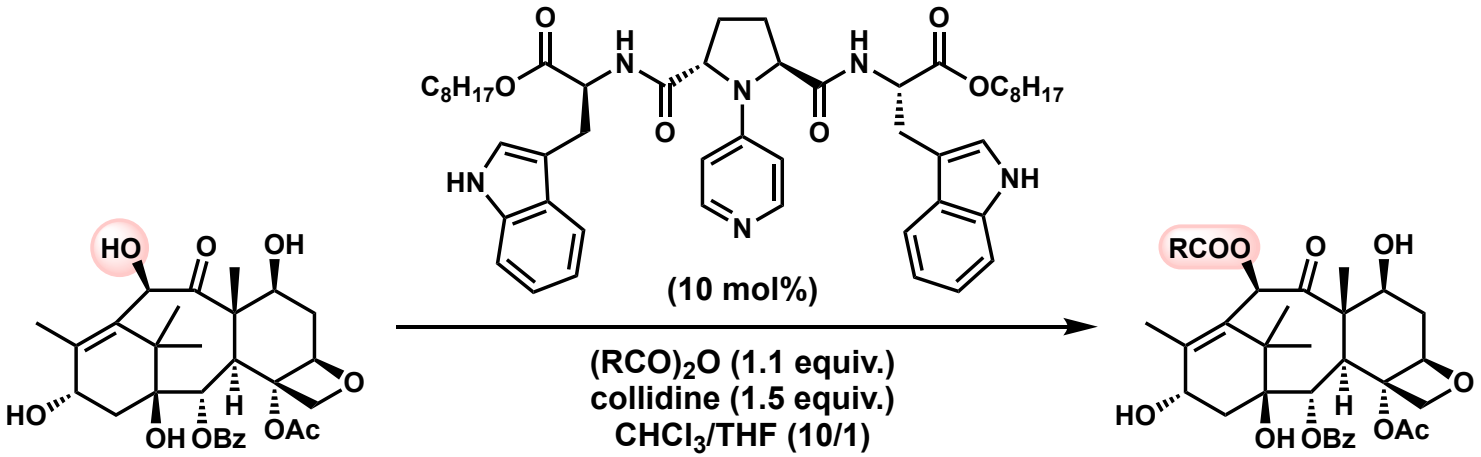
entry	catalyst	monoacylate	regioselectivity (6''''-O:4''''-O:3''''-O:others)
1	DMAP	85%	0:3:97:0
2	1	75%	0:86:14:0
3	1a	77%	0:73:27:0
4	1b	65%	7:13:80:0
5	*ent*-1	62%	25:13:62:0
6	5	87%	0:90:10:0



- ✓ **High C(4'''') selectivity with catalyst 5**
- ✓ **Confirmed significance of the chirality at the pyrrolidine ring**

Y. Ueda, K. Mishiro, K. Yoshida, T. Furuta, T. Kawabata, *J. Org. Chem.* **2012**, *77*, 7850–7857.

Site-selective acylation of 10-Deacetylbaccatin III



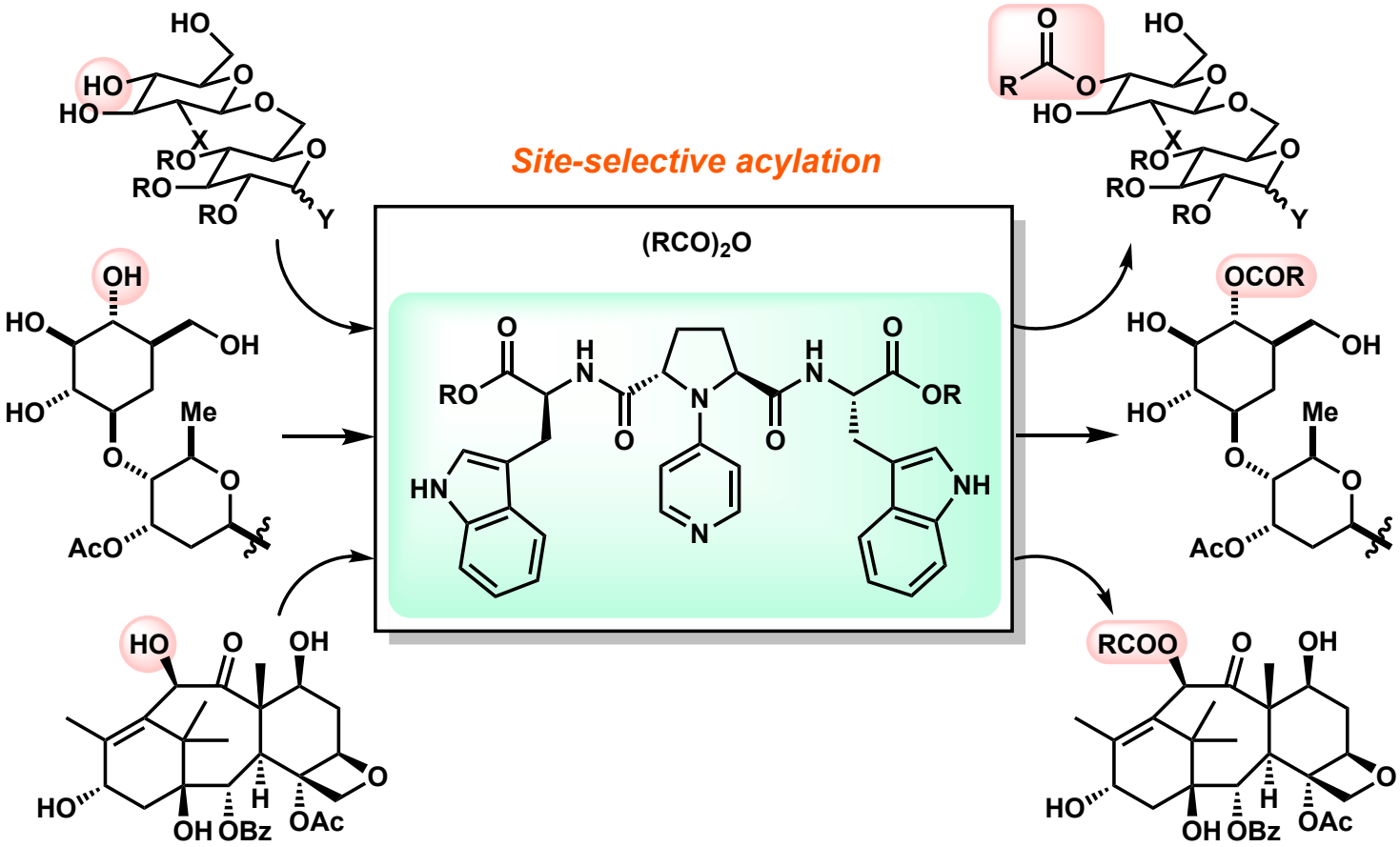
Entry	R	Temp.	Time (h)	Monoacylate (%)	Site-selectivity (%)
1[a]	*i*Pr	-20 °C	48	95	62
2	*i*Pr	-40 °C	48	89	95
3	Me	-20 °C	12	99	90
4	$C_{11}H_{23}$	-20 °C	120	75	95
5	C_6H_5	-20 °C	168	84	62

[a]DMAP was used as a catalyst.

✓ **Substrate without saccharide moiety**

T. Kawabata, *Chem. Pharm. Bull.* **2016**, *64*, 907–912.

Short summary



- ✓ **Site-selective acylation of complex molecules was achieved by using a similar PPy catalyst.**
- ➢ **Application to total synthesis**

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Total synthesis of Ellagitannins

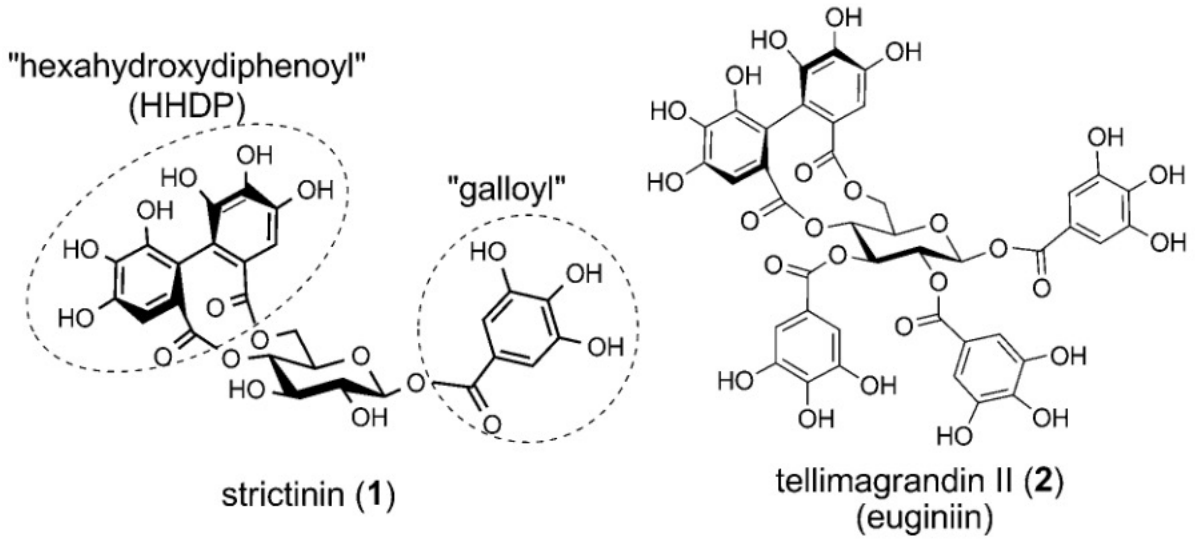
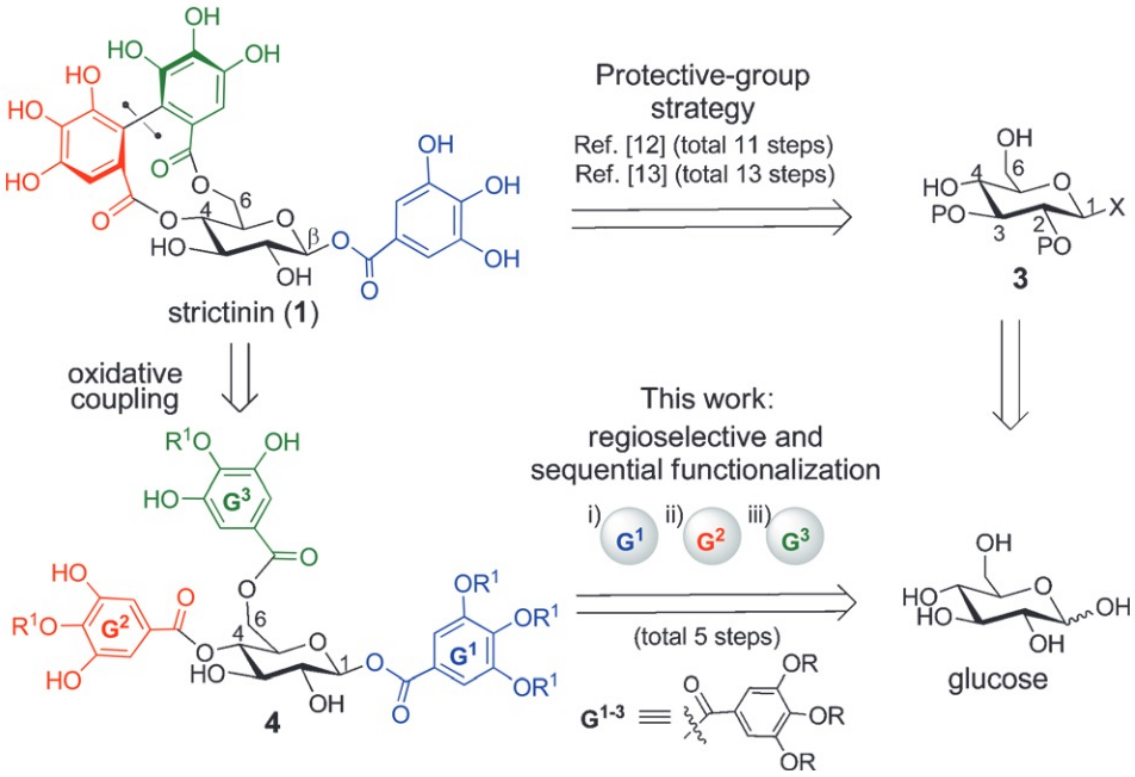


Figure 1. Target ellagitannins.

- **Ellagitannins: A large class of plant polyphenols with a wide variety of biological activities**
- **Strictinin (1) and tellimagrandin II (2): anti HSV, antitumor, anti-influenza virus, antiallergic activities**

T. Kawabata, *et al. Angew. Chem. Int. Ed. Engl.* **2015**, *54*, 6177–6180.

Retrosynthetic analysis

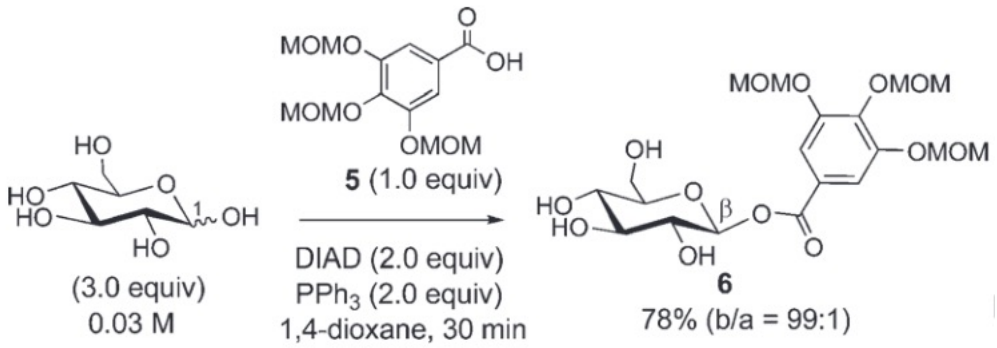


Scheme 1. Retrosynthetic analysis for strictinin (**1**). P = protective group. X = activating group for glycosylation.

- **Sequential and site-selective introduction of galloyl groups (G^1~G^3)**

T. Kawabata, *et al. Angew. Chem. Int. Ed. Engl.* **2015**, *54*, 6177–6180.

Stereoselective glycosidation



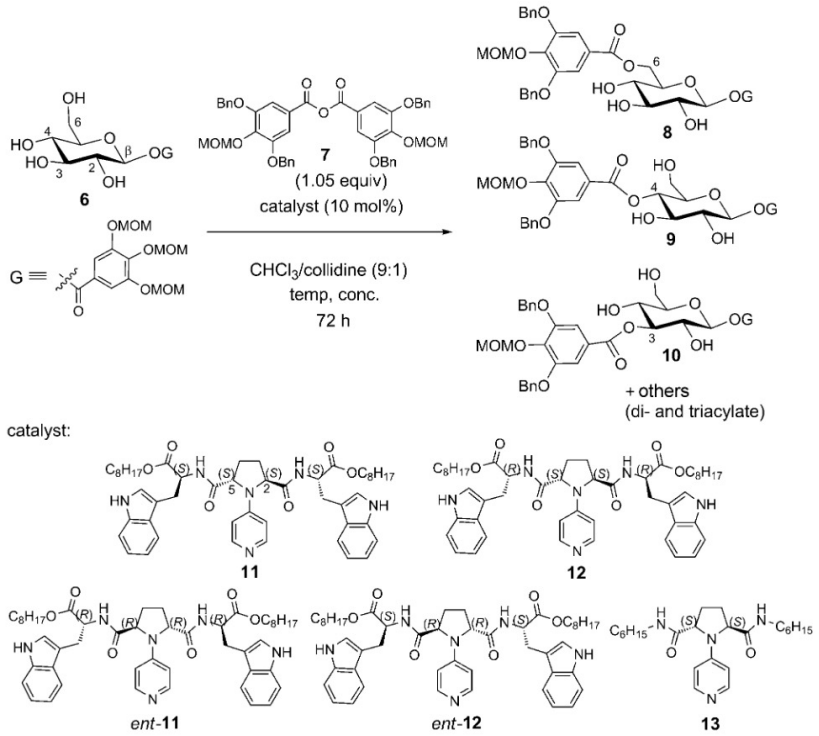
Scheme 2. Direct stereoselective glycosidation.

- **Highly stereoselective glycosidation under Mitsunobu conditions**

T. Kawabata, *et al. Angew. Chem. Int. Ed. Engl.* **2015**, *54*, 6177–6180.

C(4)-OH selective acylation

Table 1: Optimization of organocatalytic regioselective acylation of **6**.



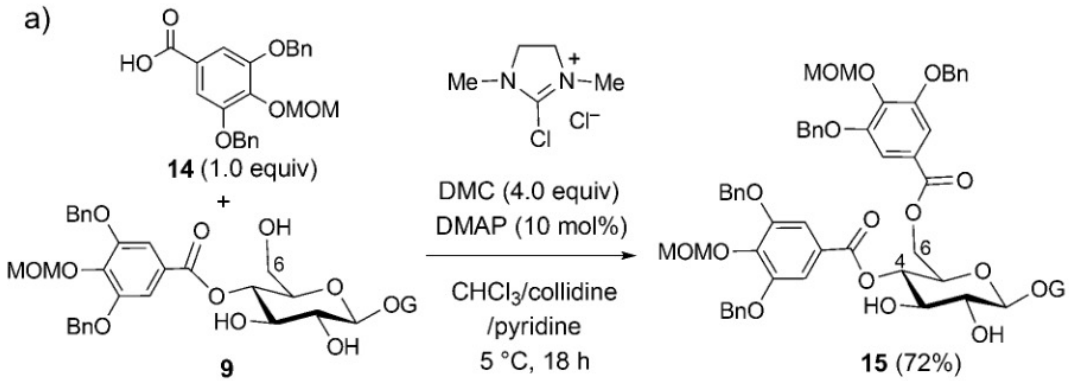
Entry	Catalyst	T [°C]	Conc. [M]	Product [%][a]			
				8	**9**	**10**	others
1[b]	**11**	−45	0.03	3	18	6	ca. 0[c]
2[d]	**11**	20	0.02	0	54	21	6
3	**11**	−40	0.02	1	83	4	3
4	**11**	−40	0.04	0	91	6	0
5	*ent*-**11**	−40	0.04	21	3	6	21
6	**12**	−40	0.04	15	35	10	16
7	*ent*-**12**	−40	0.04	11	14	4	16
8	**13**	−40	0.04	11	42	15	15

[a] Yields were determined by ^{1}H NMR with 1,3-dinitrobenzene as an internal standard. [b] Run in $CHCl_3$ in the presence of 1.5 equiv of 2,4,6-collidine. [c] 70% of the starting material was recovered. [d] Run for 24 h.

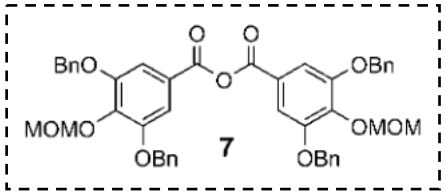
- **The chirality at the pyrrolidine ring is important.**

T. Kawabata, *et al. Angew. Chem. Int. Ed. Engl.* **2015**, *54*, 6177–6180.

Site-selective acylation of C(6)-OH



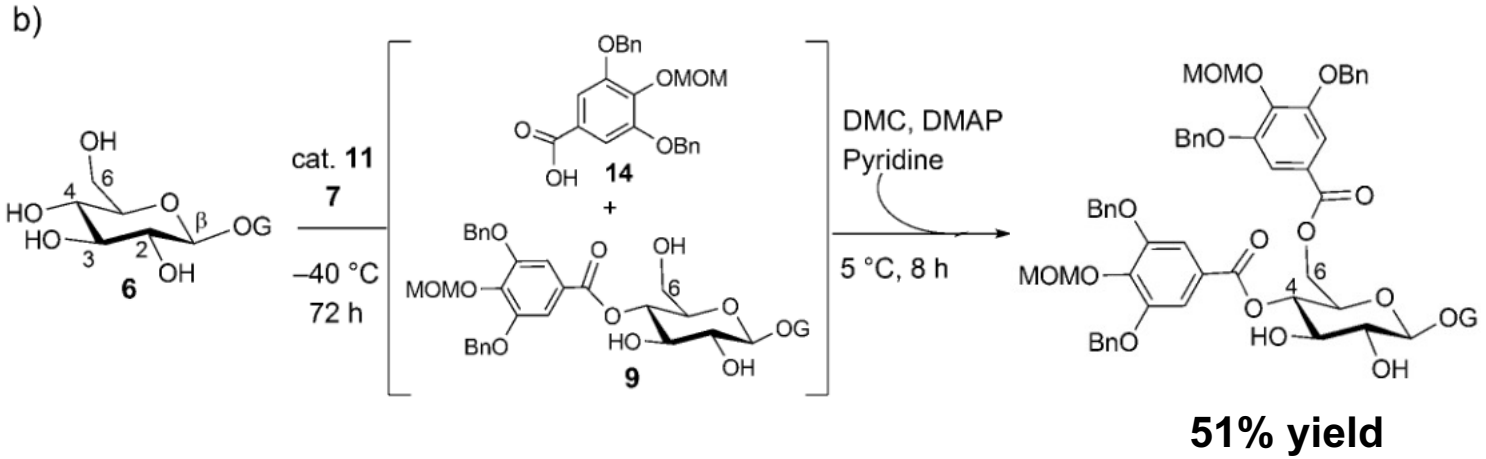
- **Site-selective introduction of a galloyl group to C(6)-OH of 9 (C(4)-OH acylated product)**
- **14 is generated from anhydride 7 and catalyst 11**

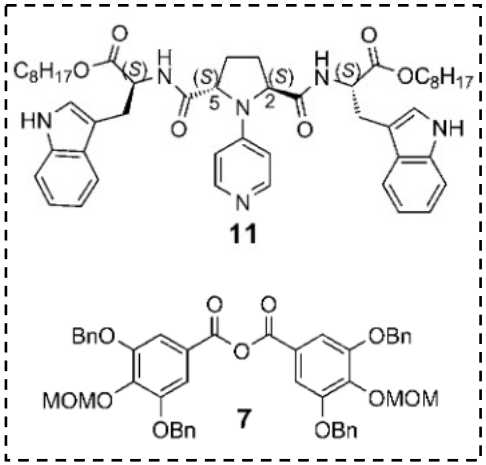


➢ **One-pot reaction**

T. Kawabata, *et al. Angew. Chem. Int. Ed. Engl.* **2015**, *54*, 6177–6180.

One-pot site-selective diacylation

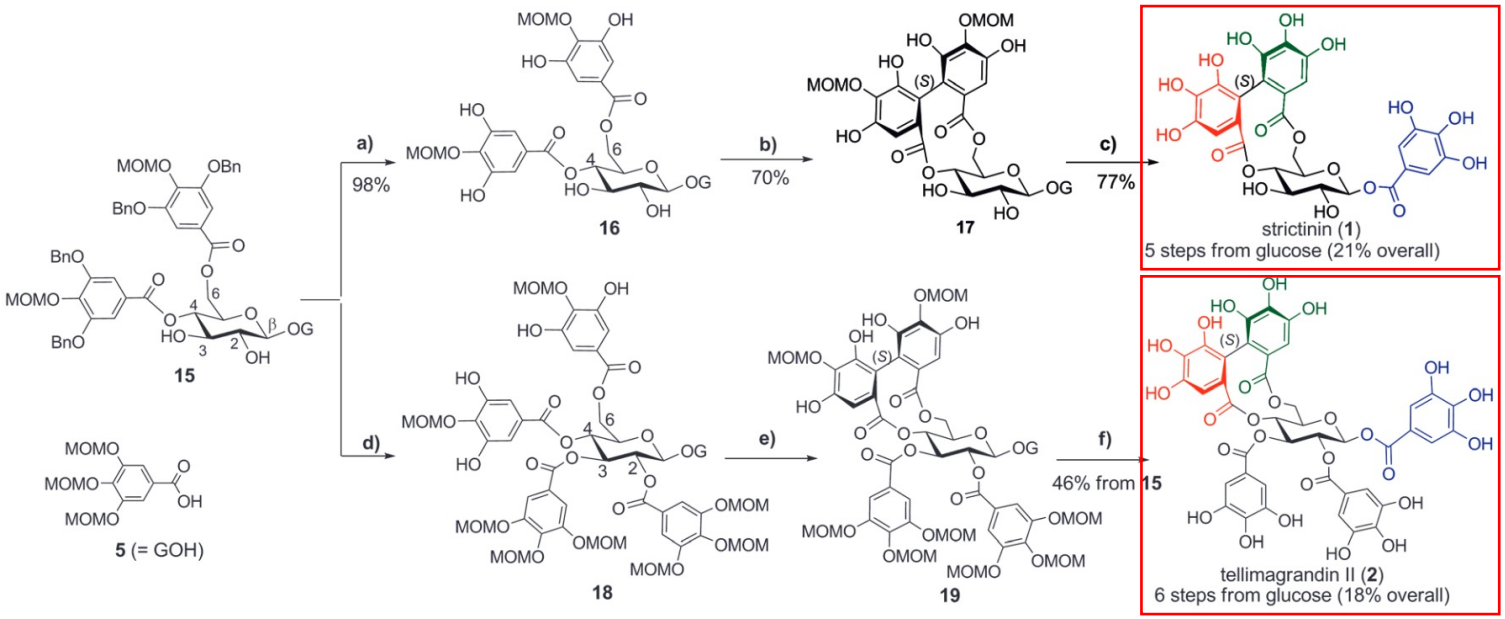




1) **Regioselective C(4)-*O*-galloylation**
2) **Substrate-controlled C(6)-*O*-galloylation**

T. Kawabata, *et al. Angew. Chem. Int. Ed. Engl.* **2015**, *54*, 6177–6180.

Final steps of the total synthesis

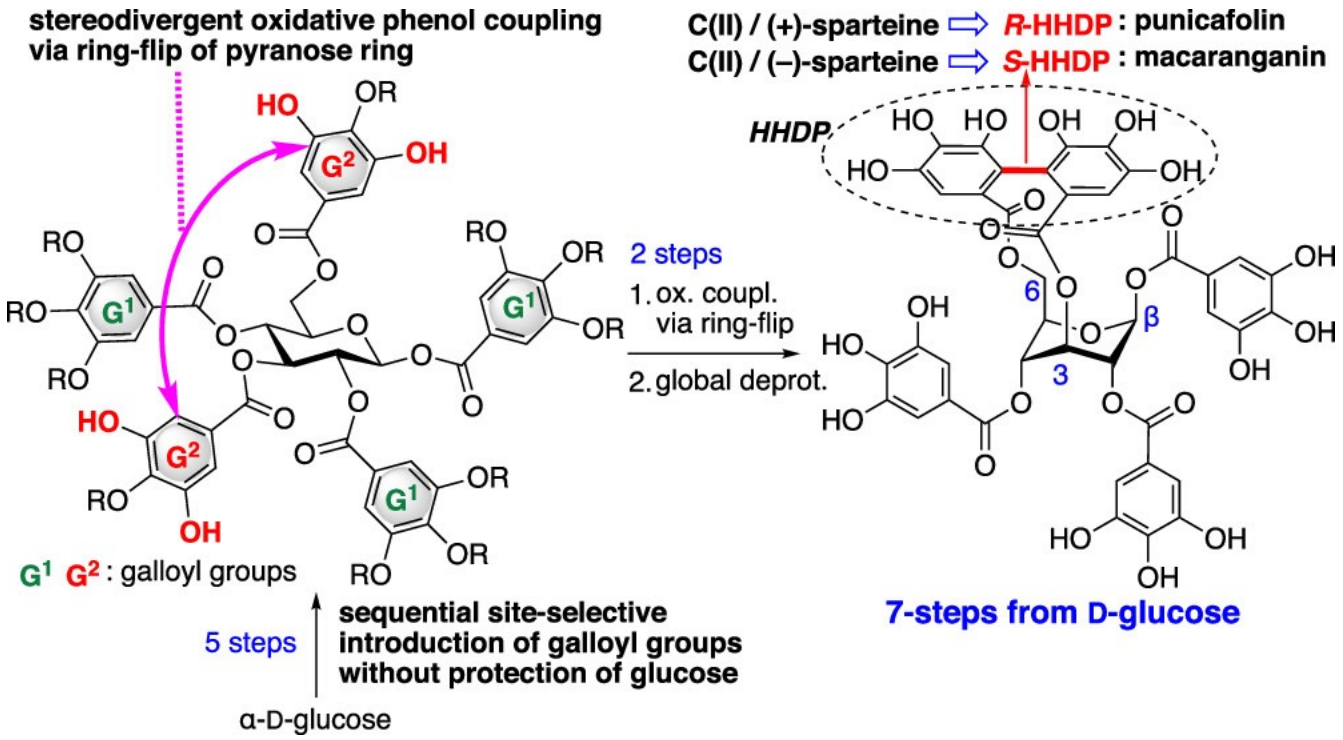


Scheme 4. Total syntheses of strictinin (**1**) and tellimagrandin II (**2**). Reagents and conditions: a) H_2, $Pd(OH)_2/C$, THF, RT; b) $CuCl_2$, nBuNH$_2$, MeOH/$CHCl_3$ (1:1), RT; c) conc. HCl/iPrOH/THF (1:50:50), RT; d) **5**, EDCI·HCl, DMAP, CH_2Cl_2, RT and then H_2, $Pd(OH)_2/C$, THF, RT; e) same as b); f) same as c). THF = tetrahydrofuran, EDCI = 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide.

- **Total syntheses achieved without using protecting groups for the glucose substrate**

T. Kawabata, *et al. Angew. Chem. Int. Ed. Engl.* **2015**, *54*, 6177–6180.

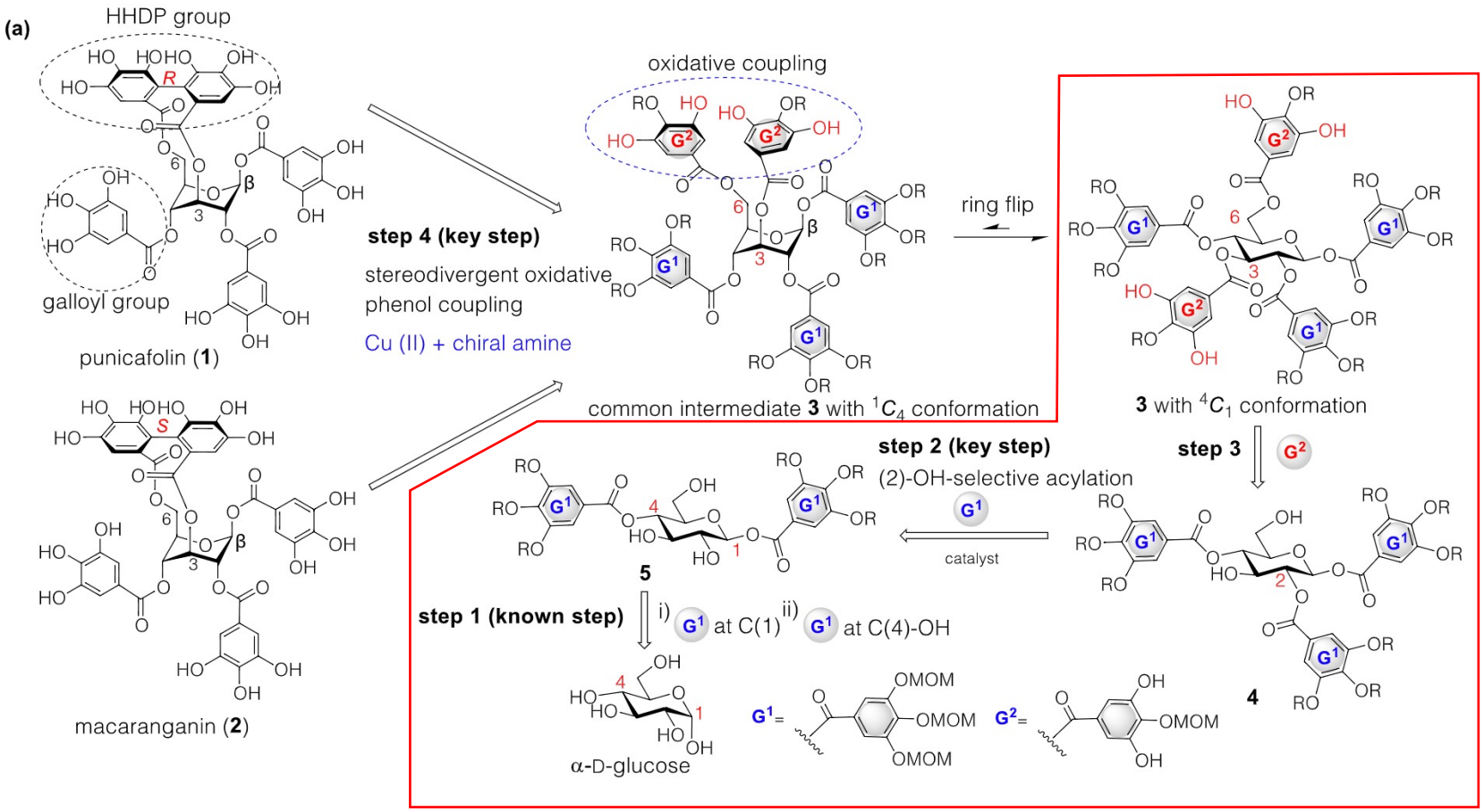
Total Syntheses of Punicafolin and Macaranganin



- ✓ **Sequential site-selective introduction of the galloyl groups into unprotected D-glucose**
- ✓ **Stereodivergent construction of the 3,6-HHDP bridge by oxidative phenol coupling**

H. Shibayama, Y. Ueda, T. Tanaka, T. Kawabata, *J. Am. Chem. Soc.* **2021**, *143*, 1428–1434.

Site-selective acylation by PPy catalyst

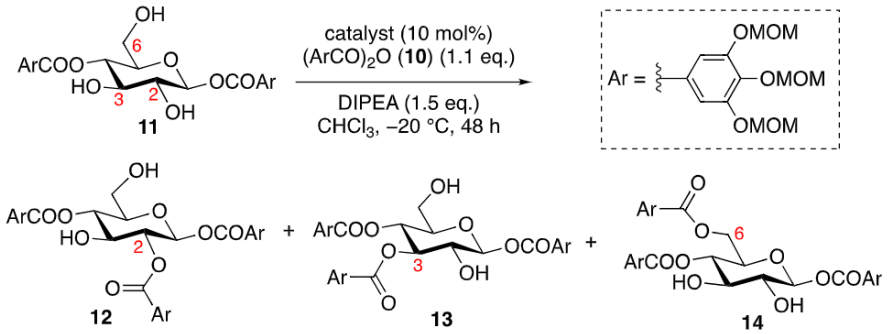


✓ **Key step:** ***(2)-OH selective acylation***

H. Shibayama, Y. Ueda, T. Tanaka, T. Kawabata, *J. Am. Chem. Soc.* **2021**, *143*, 1428–1434.

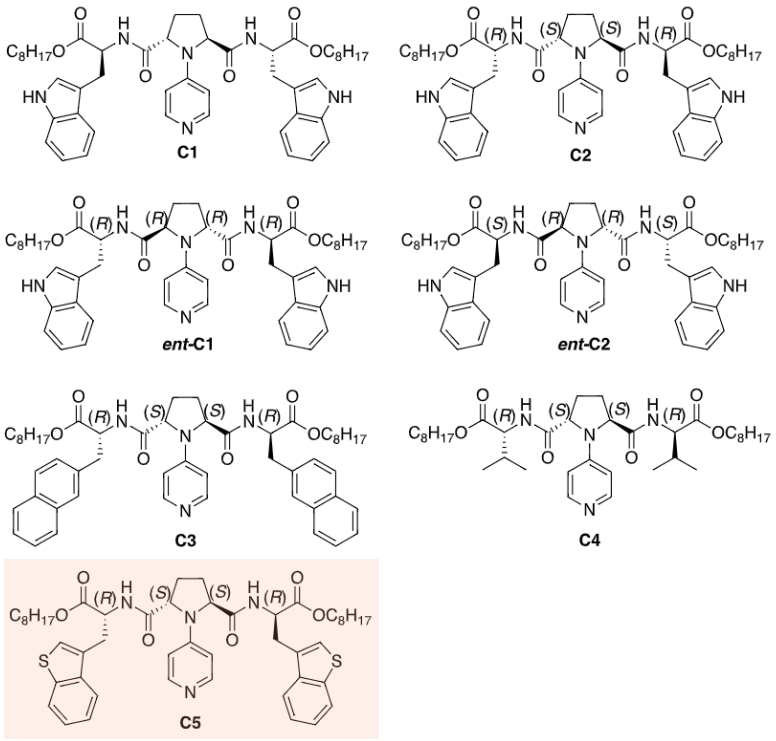
Catalyst screening for the C(2)-OH acylation

Table 1. Catalyst Screening for the C(2)—OH-Selective Introduction of the Third Galloyl Group into 1,4-Digallate 11



entry	catalyst	yield (%) 12	13	14	recovery (%) 11	site-selectivity (%) for C(2)—OH acylation 12/(12 + 13 + 14)
1	DMAP	44	36	0	10	55
2	**C1**	32	20	4	24	57
3	**C2**	23	9	1	48	70
4	***ent*-C1**	37	37	3	13	48
5	***ent*-C2**	21	19	3	36	49
6	**C3**	22	5	1	49	79
7	**C4**	13	7	4	37	54
8	**C5**	42	10	4	30	75
9[a]	**C5**	51	13	1	10	78

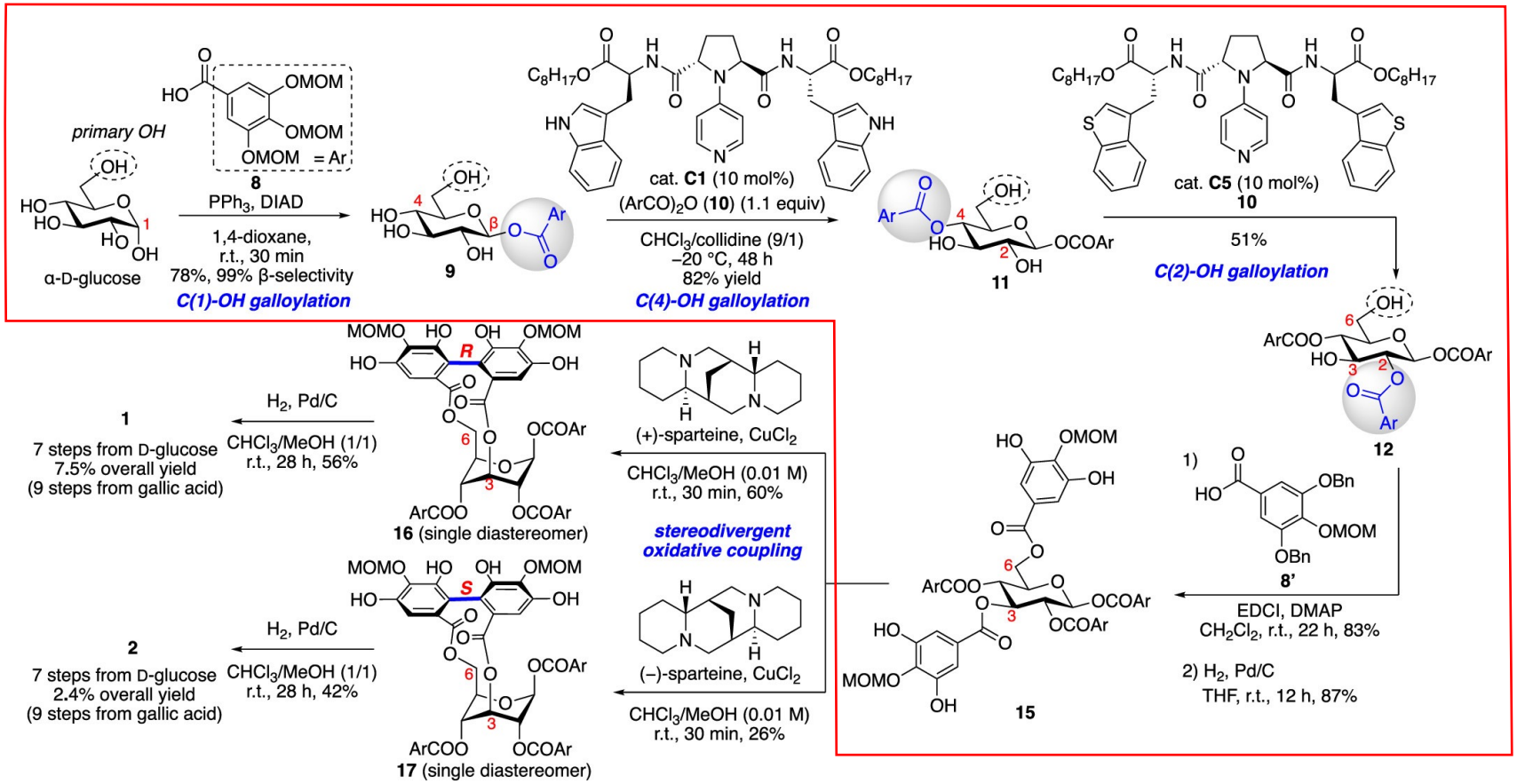
[a]Acid anhydride **10** (2.2 equiv) and DIPEA (3.0 equiv) were used.



✓ **A newly developed catalyst (C5) with a 3-benzothiophenyl group instead of the 3-indolyl group of C2**

H. Shibayama, Y. Ueda, T. Tanaka, T. Kawabata, *J. Am. Chem. Soc.* **2021**, *143*, 1428–1434.

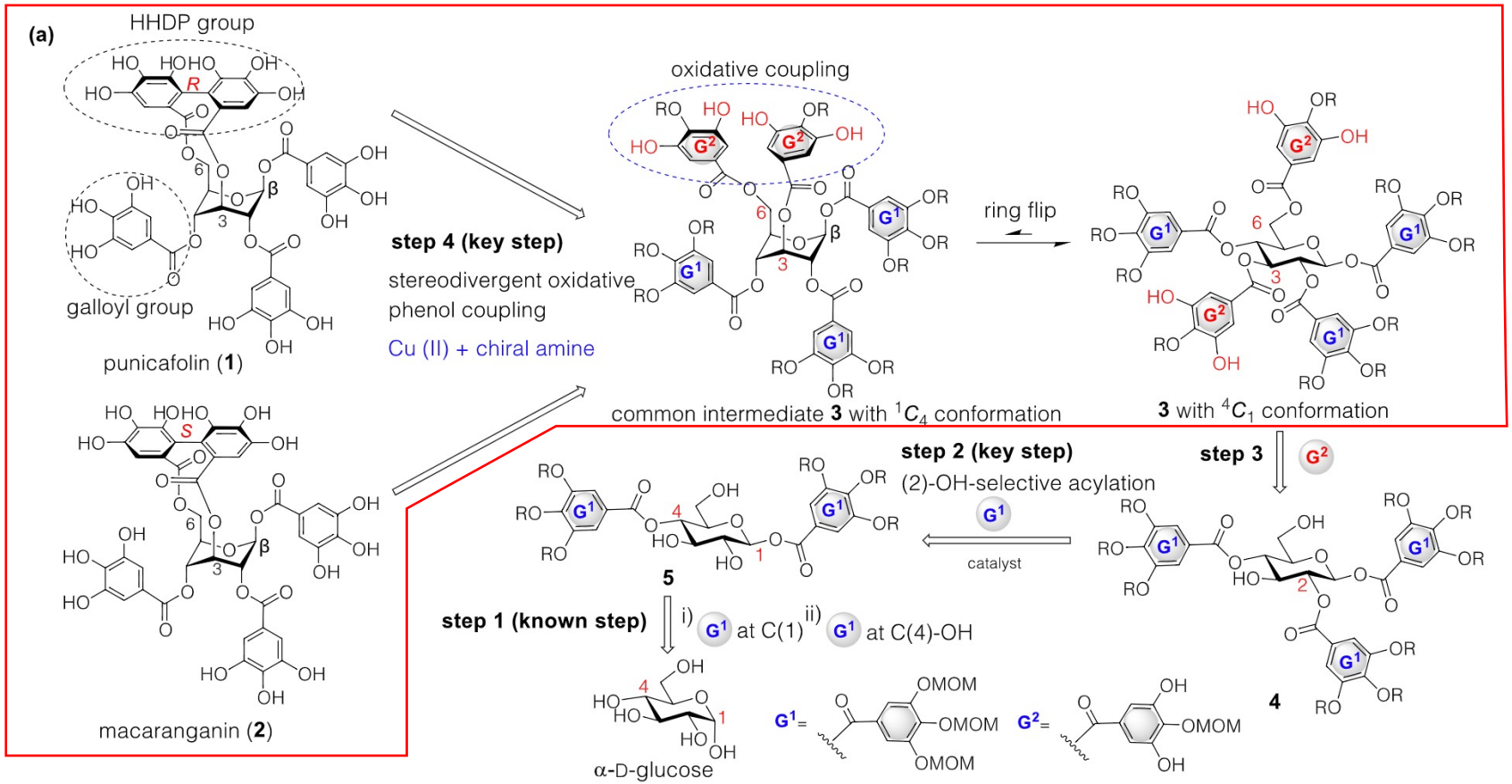
Sequential introduction of galloyl groups



- **12 was synthesized through sequential, site-selective reactions.**
- **Condensation of 12 with 8' gave an intermediate 15.**

H. Shibayama, Y. Ueda, T. Tanaka, T. Kawabata, *J. Am. Chem. Soc.* **2021**, *143*, 1428–1434.

Construction of the 3,6-HHDP bridge

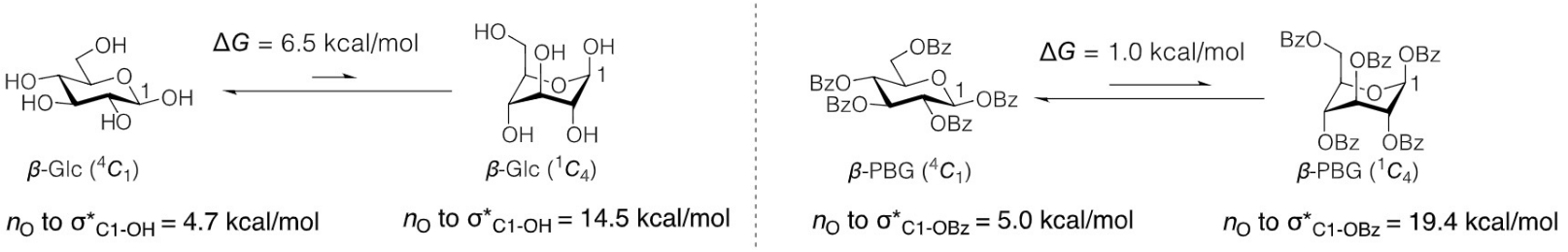


- **3,6-HHDP bridge: A less stable axial-rich conformer of the pyranose ring (3 with $^1C_4$ conformation) is required for the formation. = *difficult to synthesize***

H. Shibayama, Y. Ueda, T. Tanaka, T. Kawabata, *J. Am. Chem. Soc.* **2021**, *143*, 1428–1434.

Feasibility of using less stable intermediate

- **Conformational analysis of glucose (β-Glc) and the perbenzoylated derivative (β-PBG, a model for 3 (intermediate))**

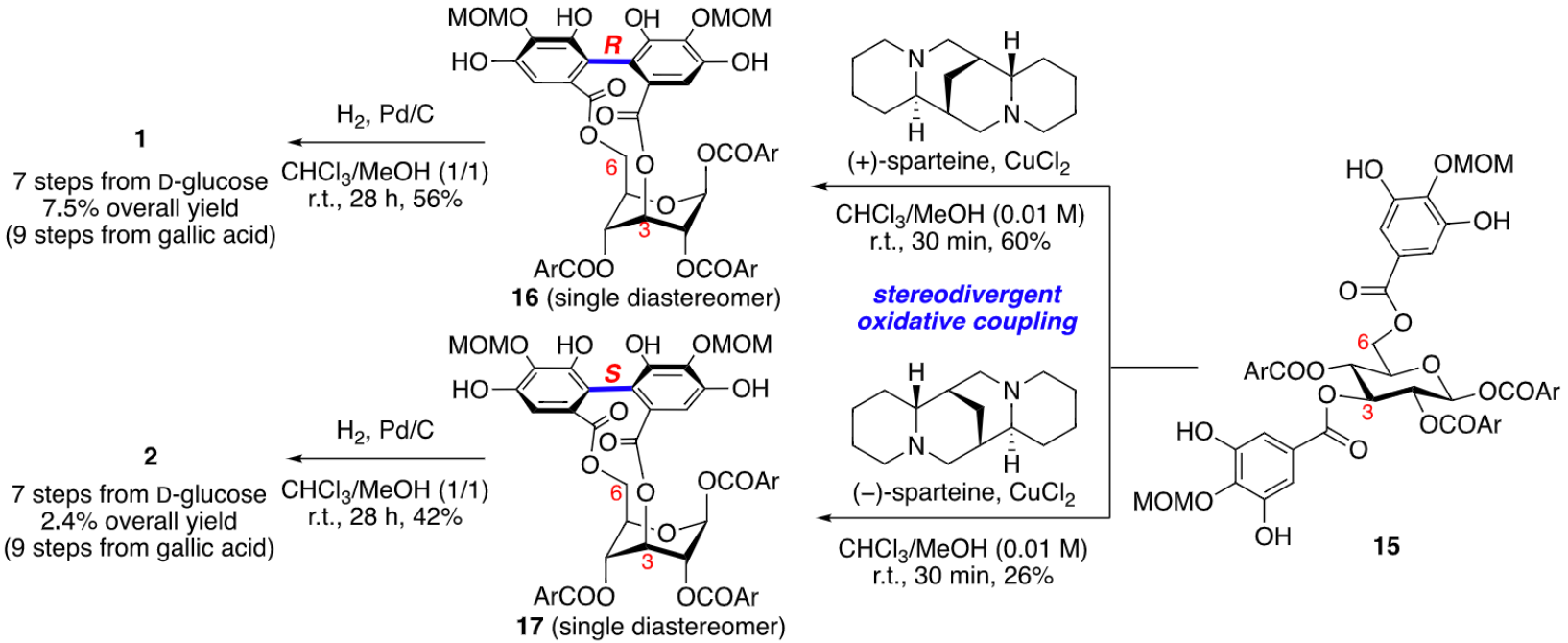


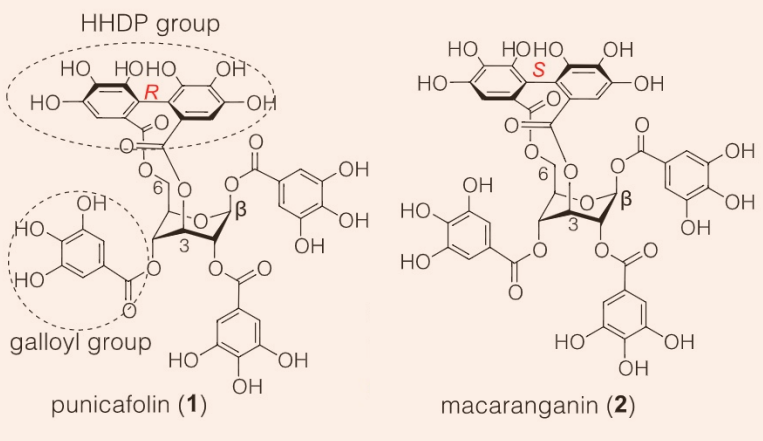
- **Stronger anomeric effect was suggested for β-PBG.**

➢ **Axial-rich conformations of 3 can exist to some extent via the ring-flip process of the stable $^4C_1$ conformer.**

H. Shibayama, Y. Ueda, T. Tanaka, T. Kawabata, *J. Am. Chem. Soc.* **2021**, *143*, 1428–1434.

Final steps of the syntheses

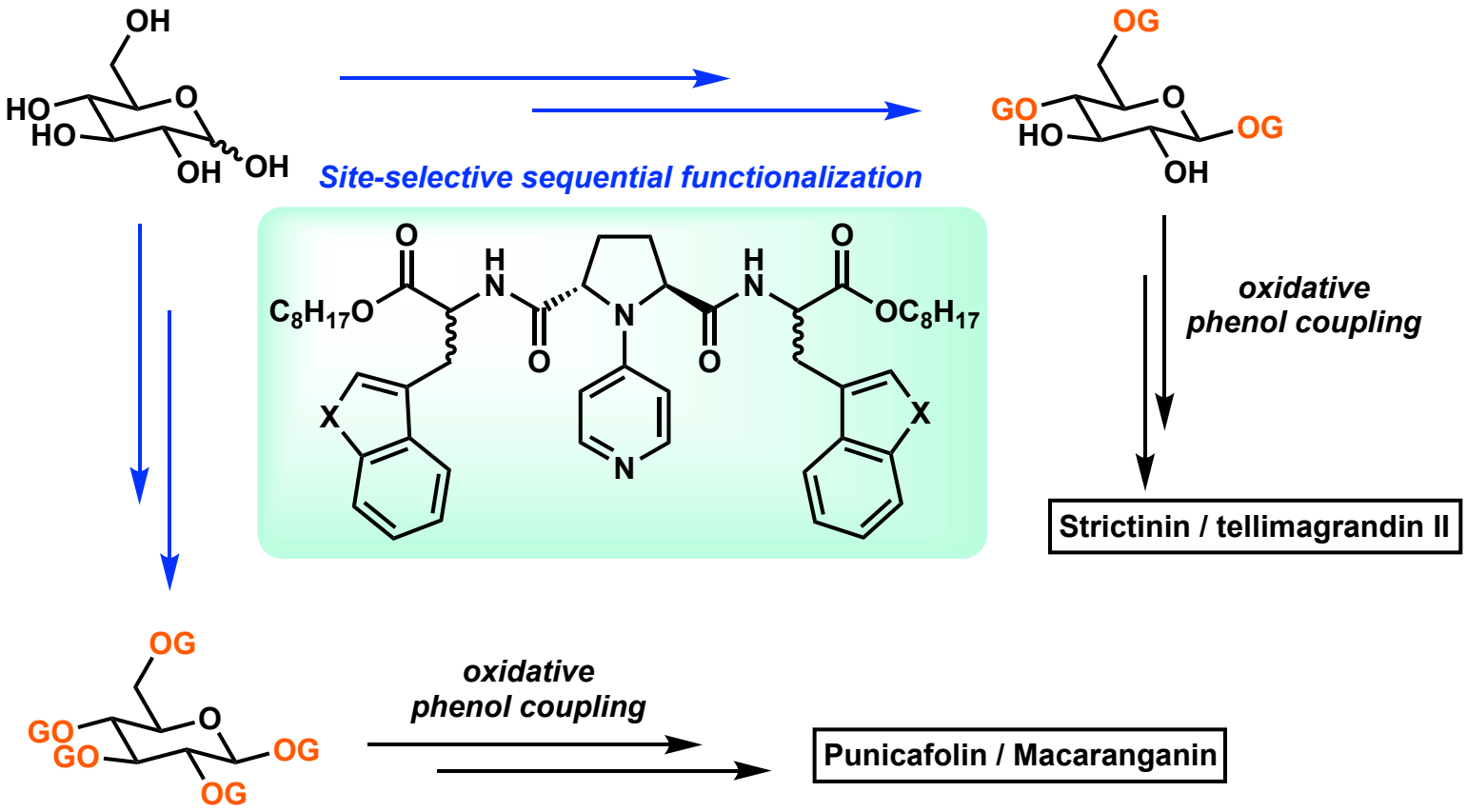




✓ **Construction of HHDP group: Oxidative phenol coupling using chiral amine catalyst**

H. Shibayama, Y. Ueda, T. Tanaka, T. Kawabata, *J. Am. Chem. Soc.* **2021**, *143*, 1428–1434.

Short summary



- ✓ **No protective groups used for glucose**
- ✓ **Extremely short-step total syntheses**

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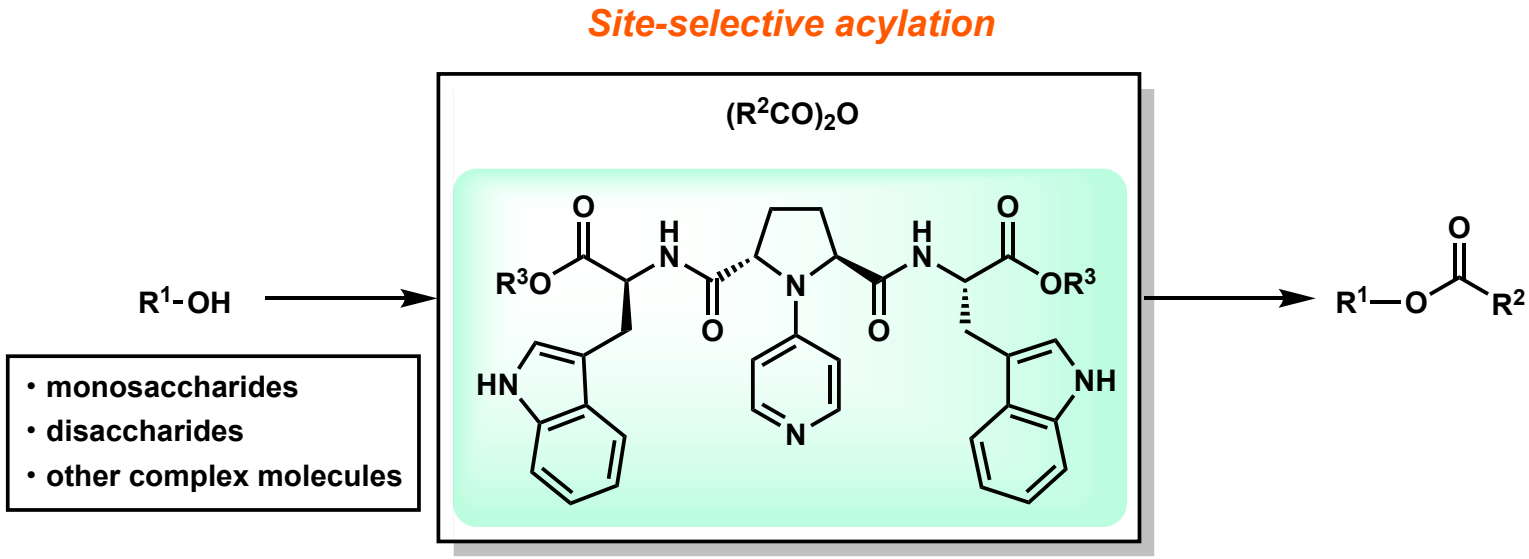
Site-selective acylation of complex molecules



✓ **A newly developed PPy catalyst** ✓ **High site-selectivity**
✓ **Minimally protected monosaccharides and complex molecules**
✓ **Key steps of total syntheses**

➢ **This catalyst can also be used for challenging kinetic resolution (an example for rotaxanes was reported recently:** *Nat. Commun.* **2021**, *12*, 404.**).**