

XU GROUP  
*Department of Chemistry, Peking University*

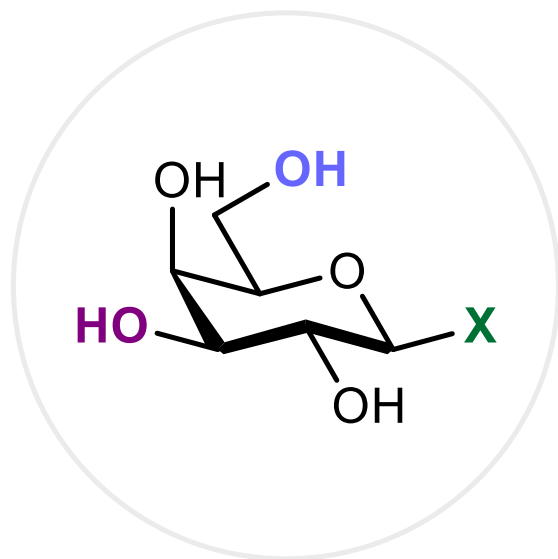
# *Selected Weekly Literature Presentations*

*Disclaimer:*

*These slides contain personal interpretations and may include errors or subjective views.*

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# Catalytic Approaches to Chemo- and Site-Selective Transformation of Carbohydrates



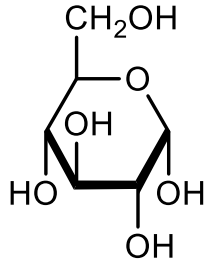
*Reporter: Qingrui Zeng*

*Adviser: Yan Xu*

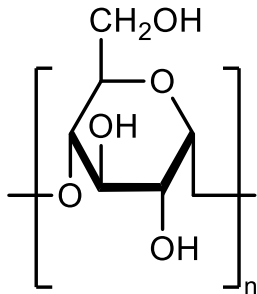
*2023.11.18*

# Background

*Provide energy*



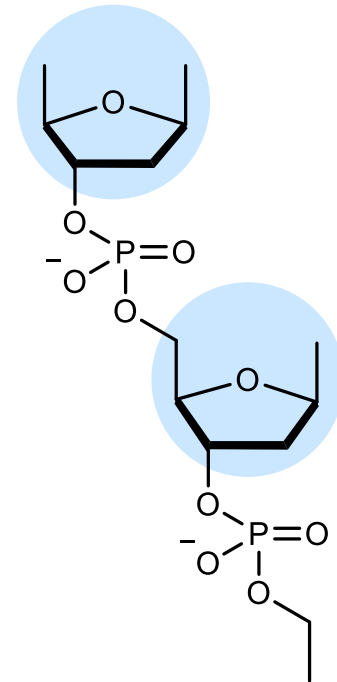
*Store energy*



*Supply carbon*



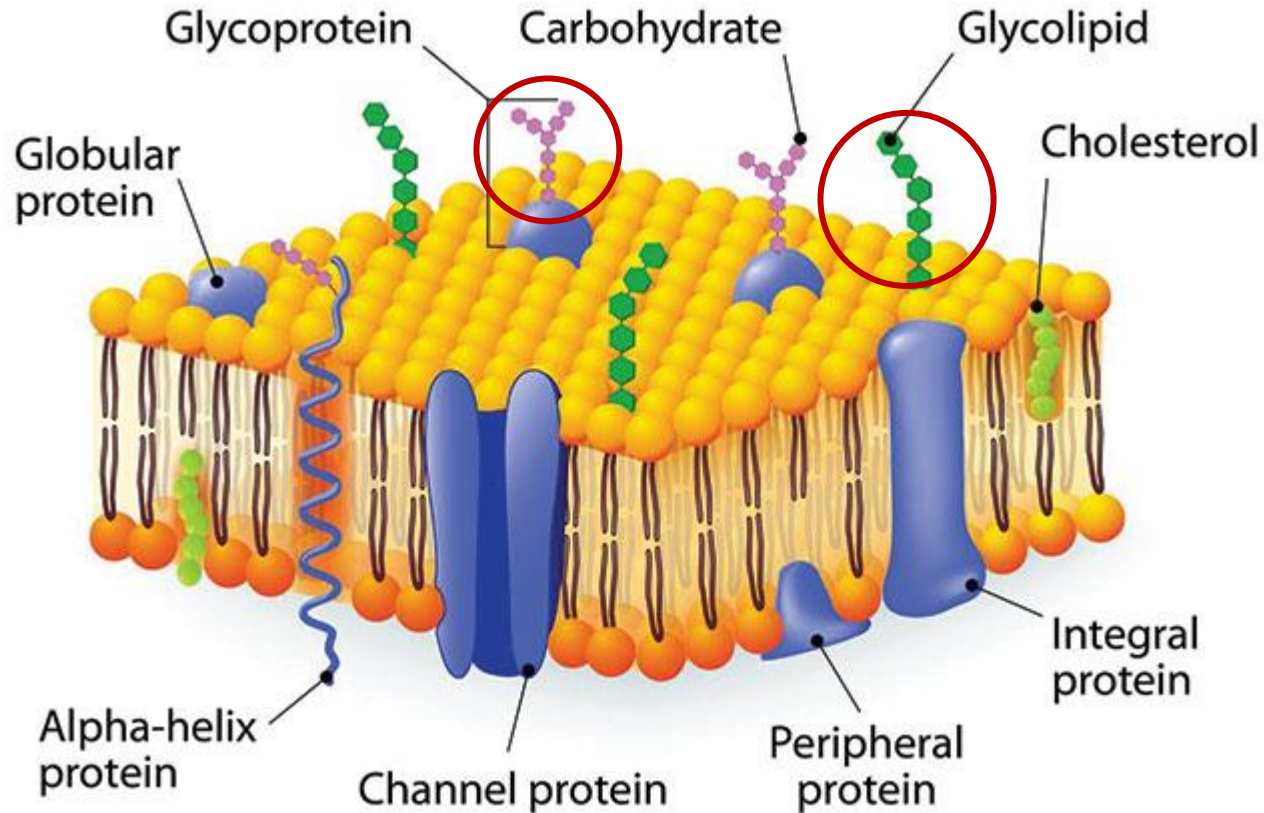
*Form structural components*



Watson, J. D.; Crick, F. H. C. *Nature* **1953**, *171*, 737–738.

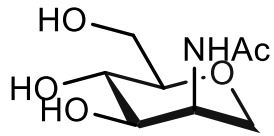
# Background

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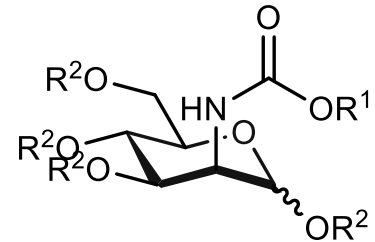
*The oligomer is not only a **building block** but also an **important metabolite** and a **coenzyme**.*

# Background



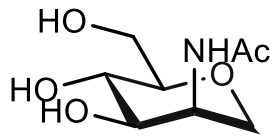
**ManNAc**  
natural sugar

*replace by*



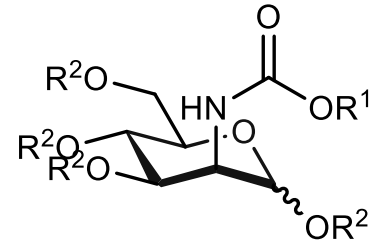
**ManNAc analogs**  
unnatural sugar

*How to do?*



**ManNAc**  
natural sugar

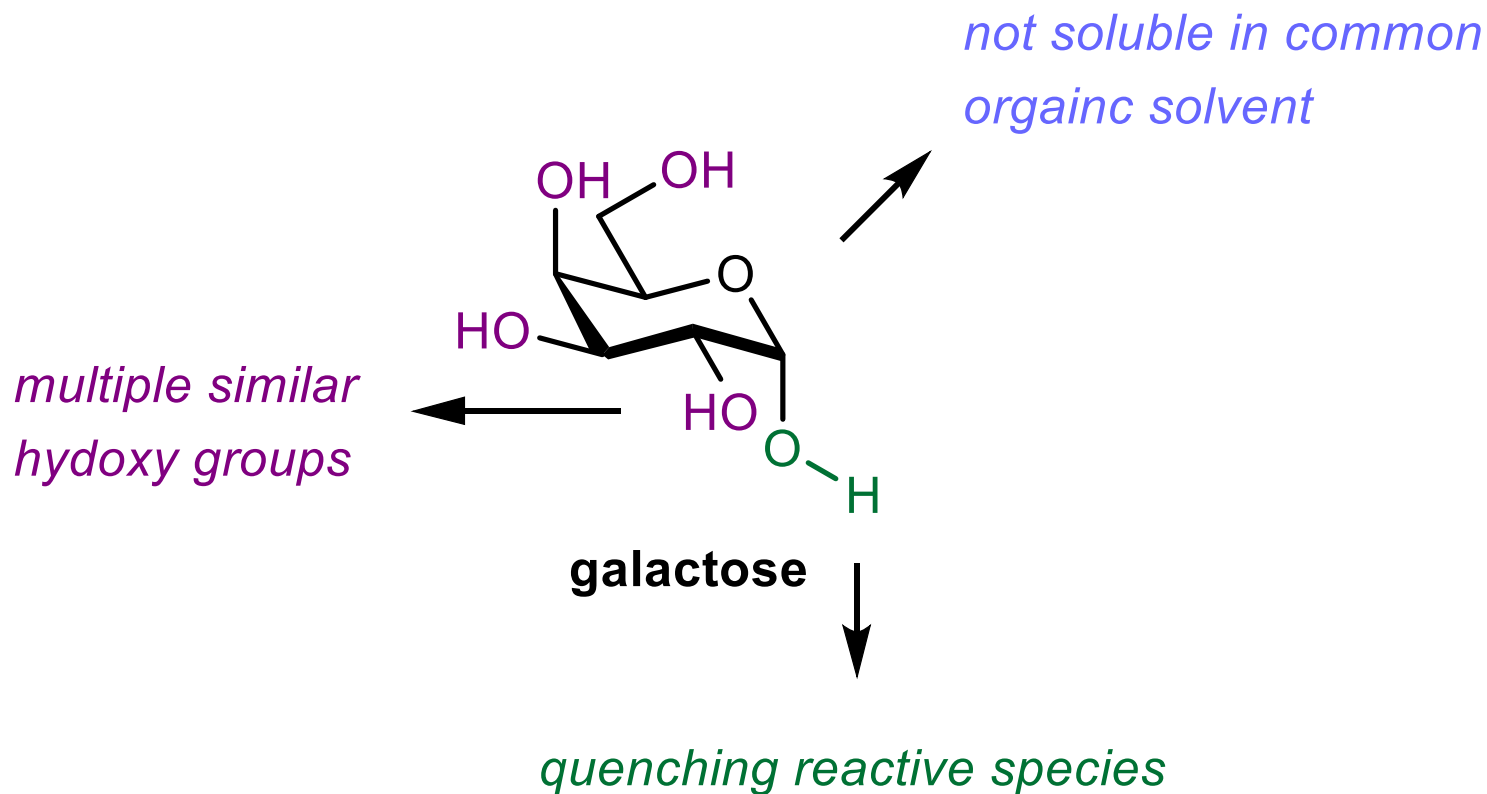
?



**ManNAc analogs**  
unnatural sugar

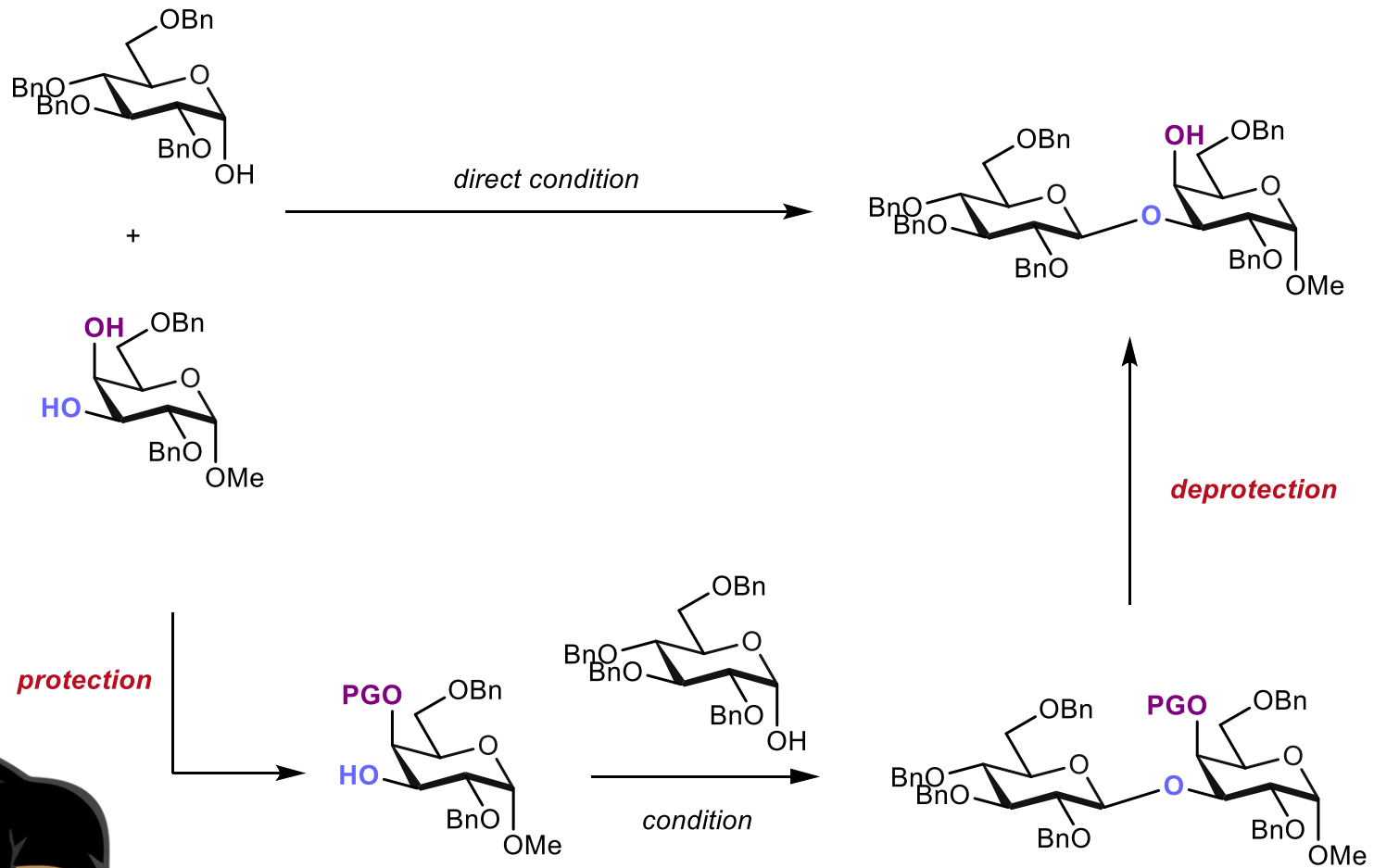
# Molecular Complexity

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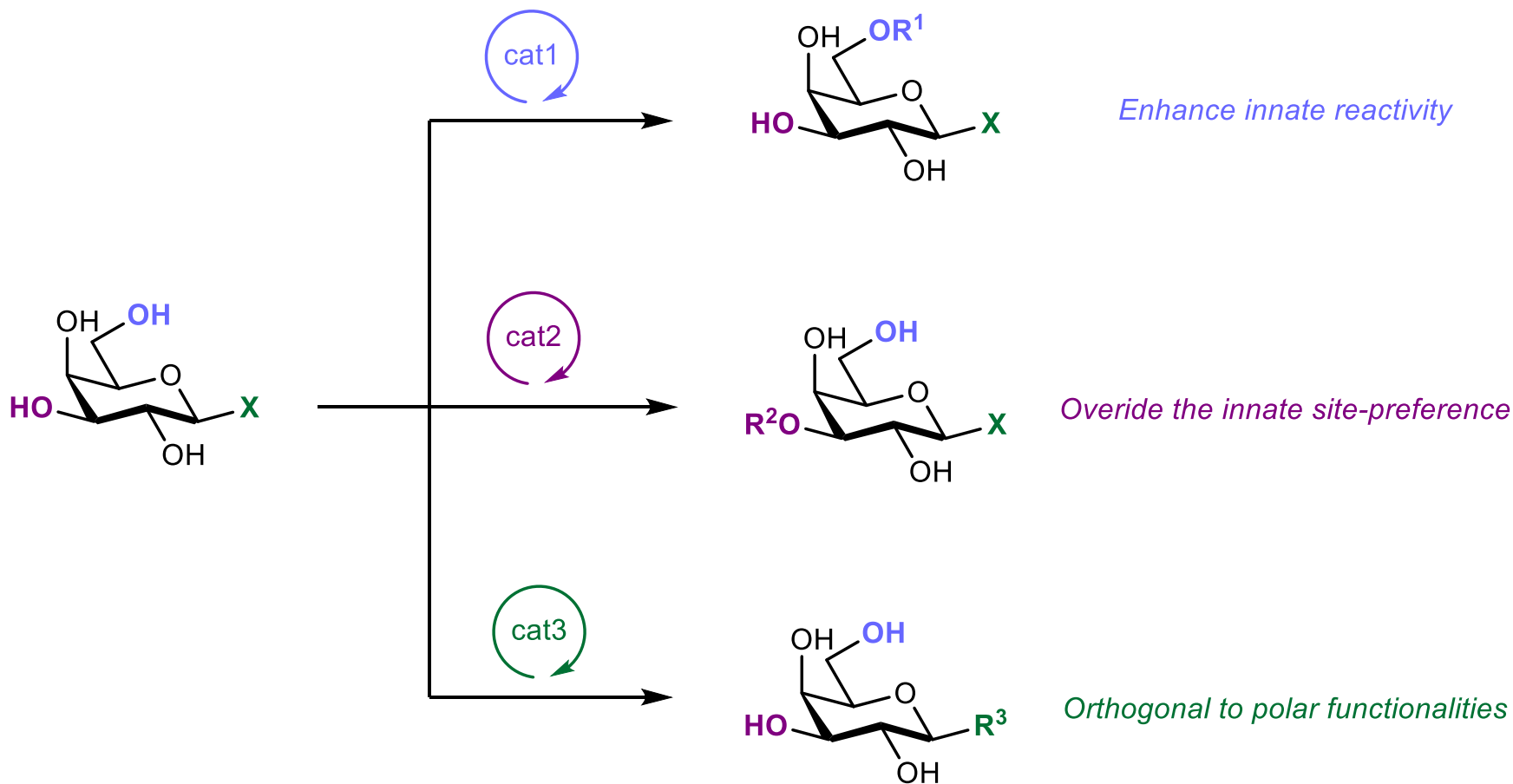
Motomu, K. *et al. Chem. Rev.* **2023**, *123*, 6793–6838

# Background



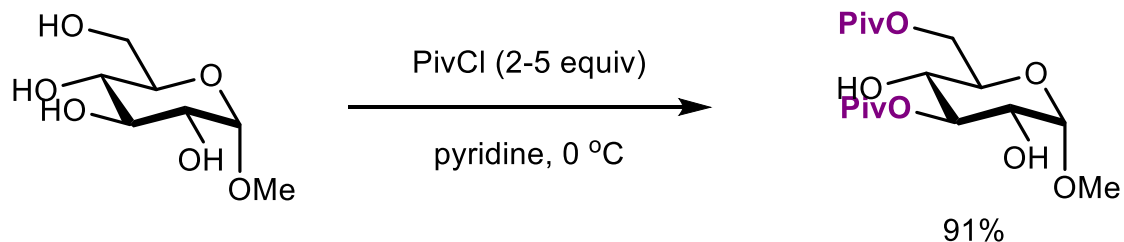
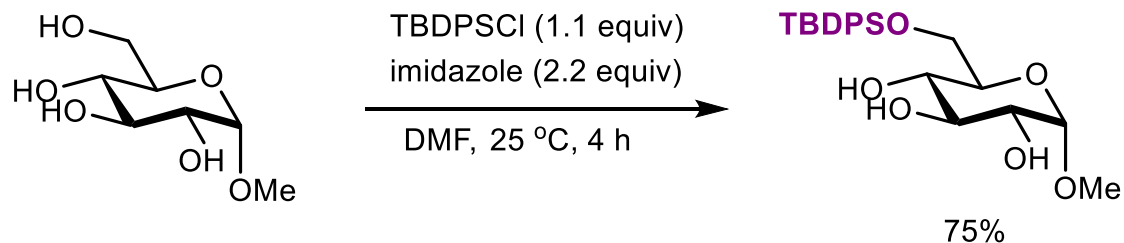
*Selectivity!*

# Classification

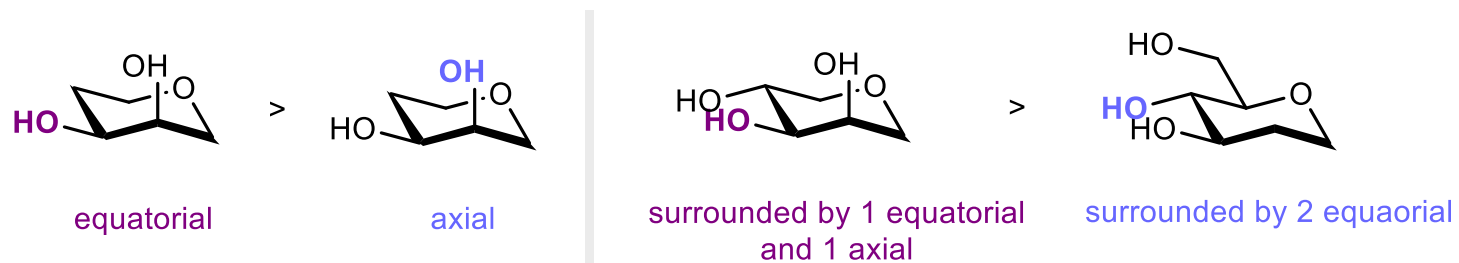


Motomu, K. *et al. Chem. Rev.* **2023**, *123*, 6793–6838

# Steric Effects

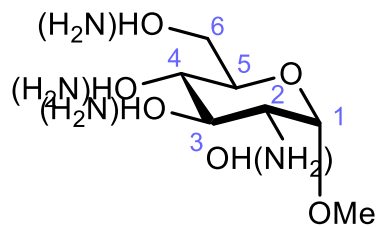
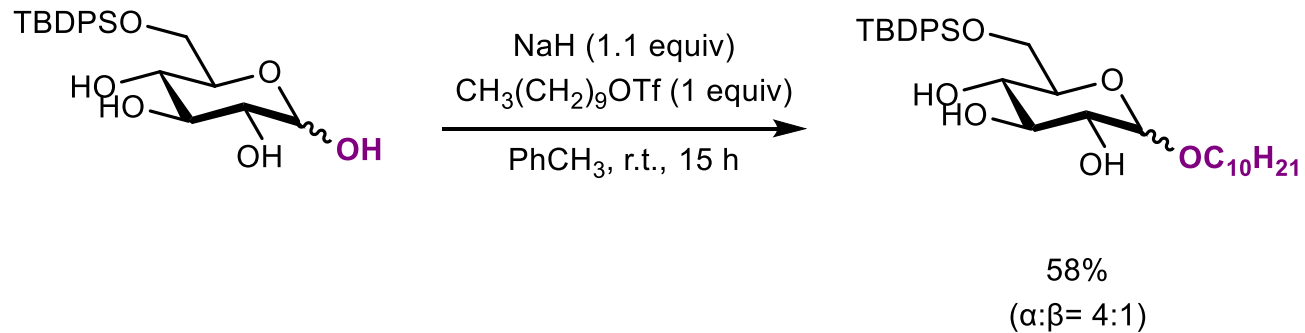


*general reactivity trend*

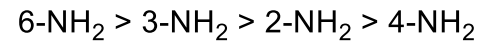


# Electron Density

*acidity*

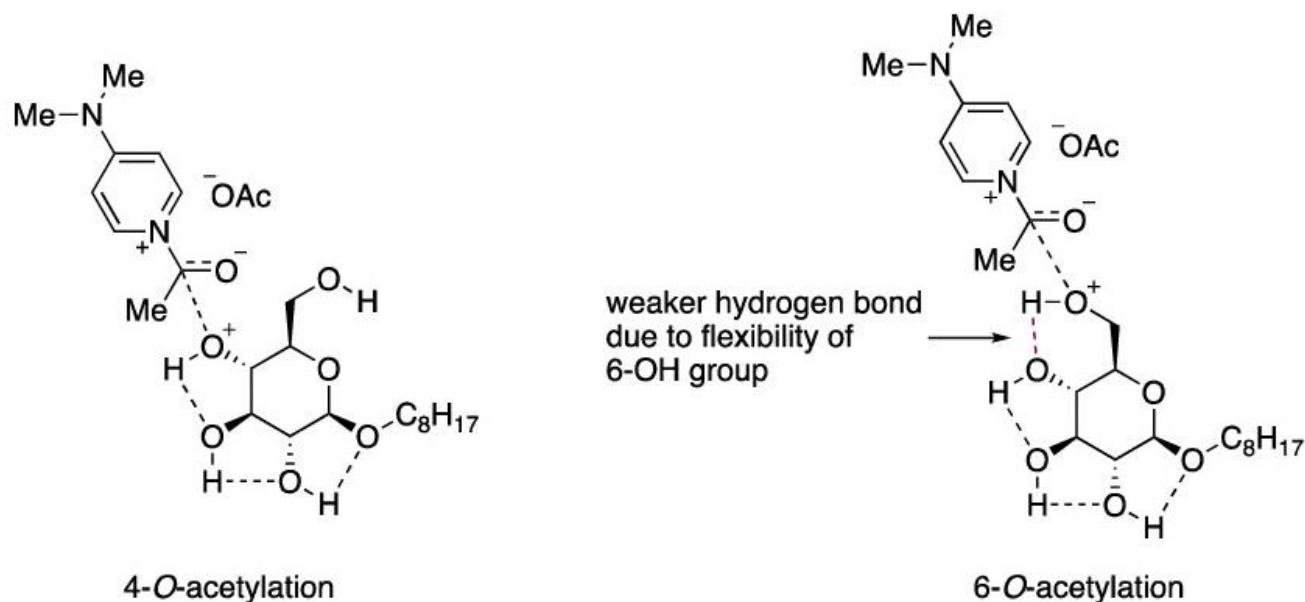
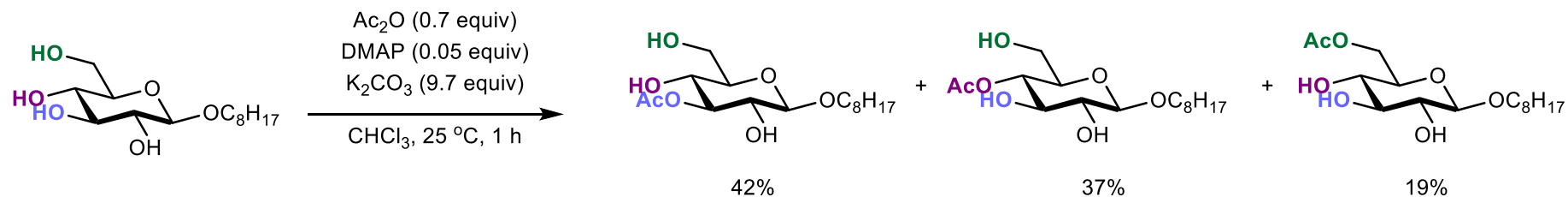


*basicity of amino group*



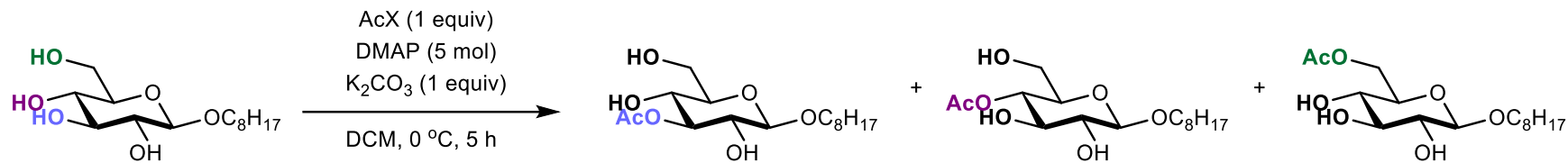
Pedersen, C. M. *et al. Chem. -Eur. J.* **2011**, 17, 7080–7086.

# Hydrogen Bond Network

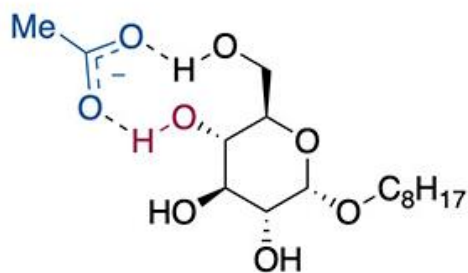


Kurahashi, T. *et al. J. Chem. Soc., Perkin Trans. 1* **1999**, 465–474.

# Anion Effect

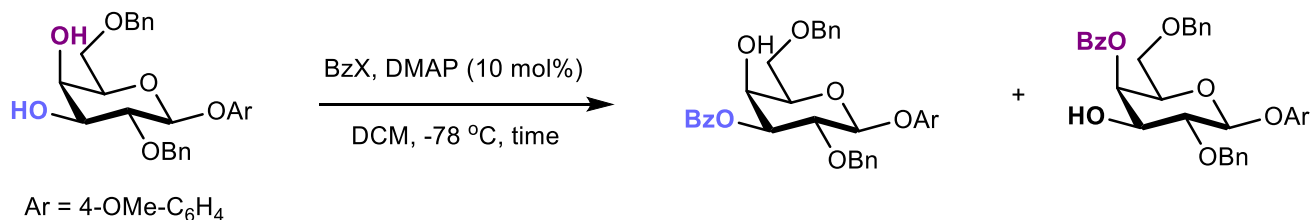


Entry	AcX	Yield (%)	Ratio		
			3-O	4-O	6-O
1	Ac <sub>2</sub> O	47	0.50	0.46	0.04
2	AcCl	44	0.17	0.03	0.74
3	AcCN	44	0.15	0.08	0.76

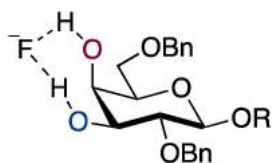
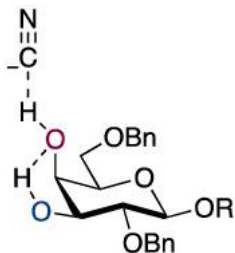
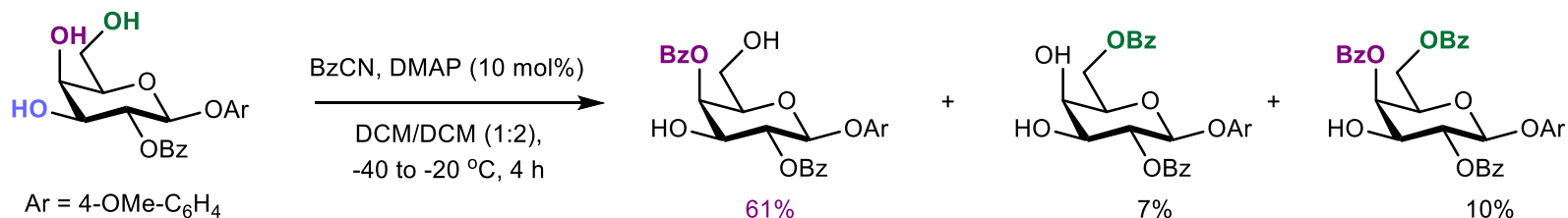


Albert, M. *et al. Org. Lett.* **2004**, *6*, 945– 948.

# Cyanide Effect

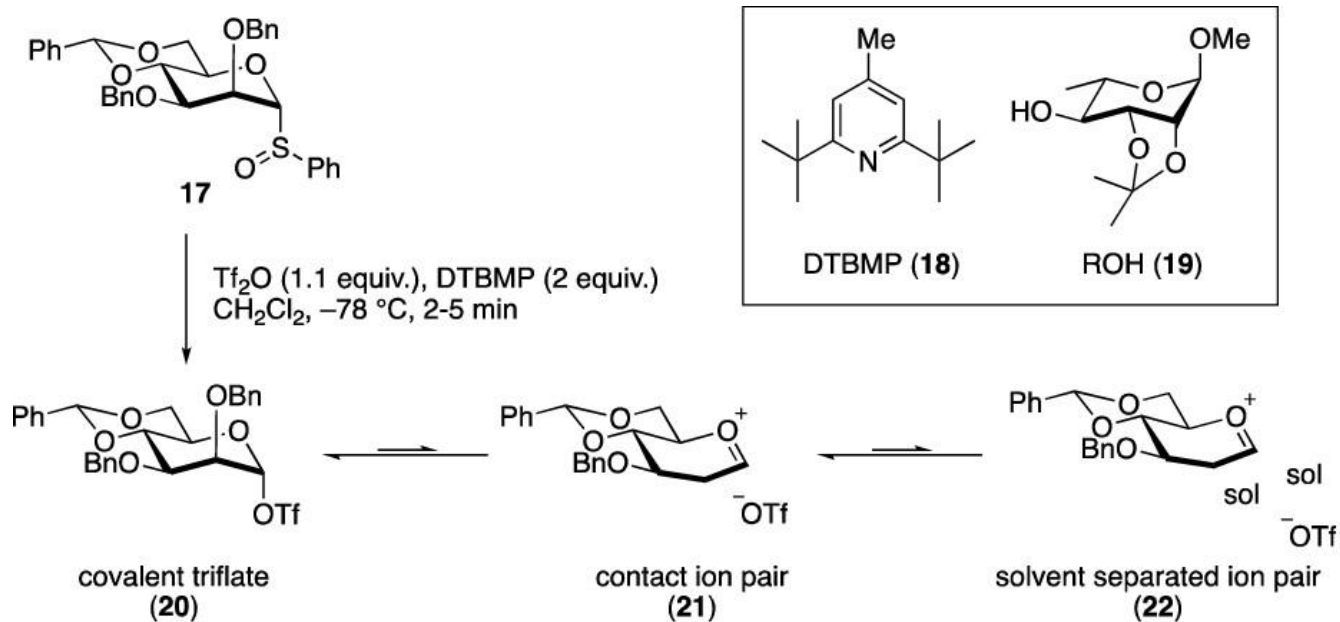


Entry	BzX	Time (h)	3-O (%)	4-O (%)
1	BzCN	4	< 3	90
2	BzCl	4	0	0
3	Bz <sub>2</sub> O	10	90	< 3
4	BzF	1	57	6



Schmidt, R. R. *et al. J. Am. Chem. Soc.* **2016**, *138*, 6002–6009.

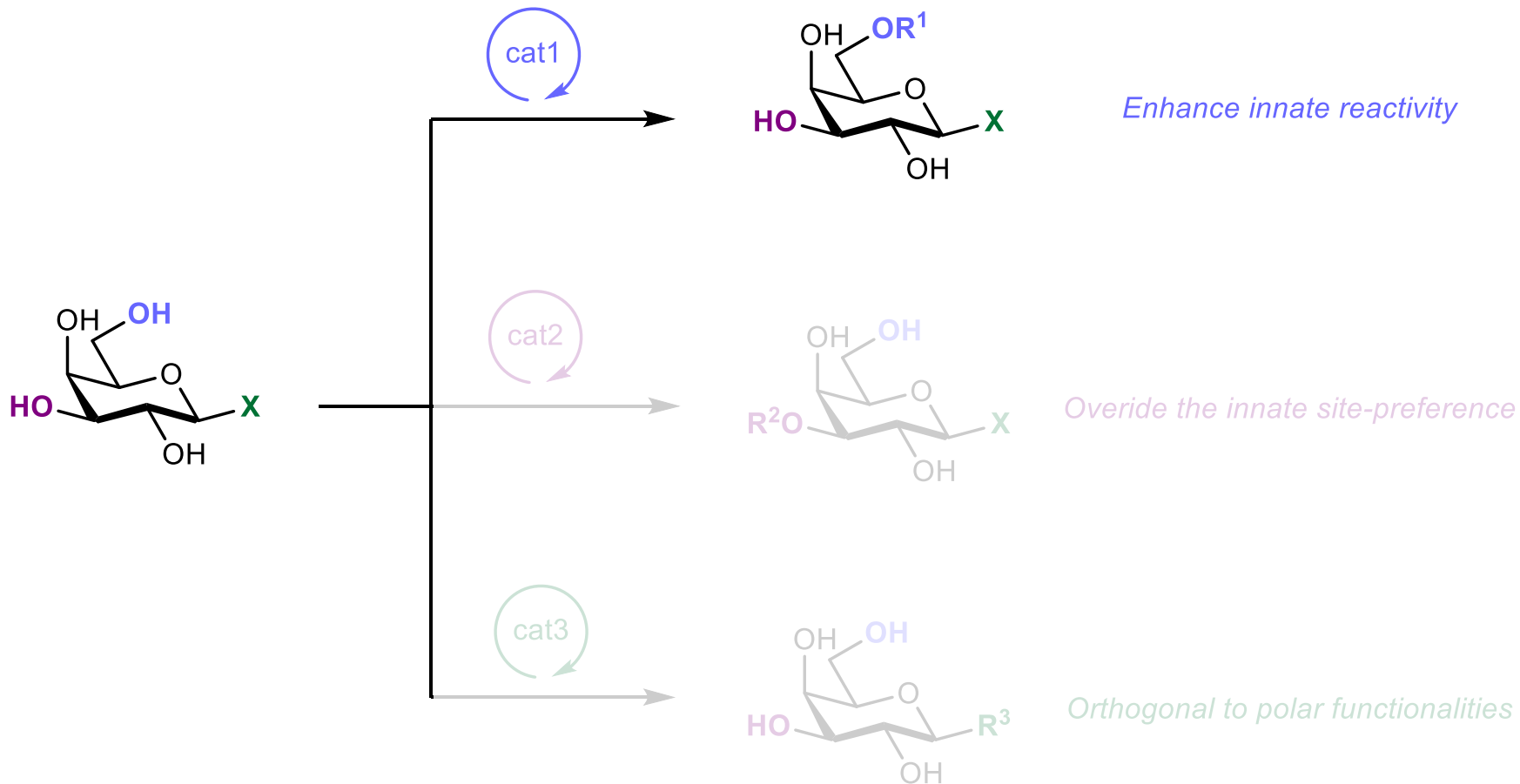
# Protecting Group Effects



Crich, D. *et al. J. Org. Chem.* **1996**, *61*, 4506–4507

Crich, D. *et al. J. Org. Chem.* **1997**, *62*, 1198–1199.

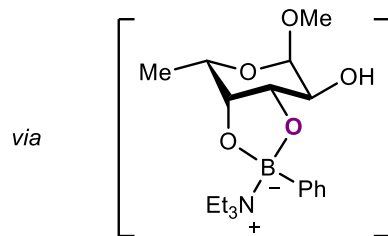
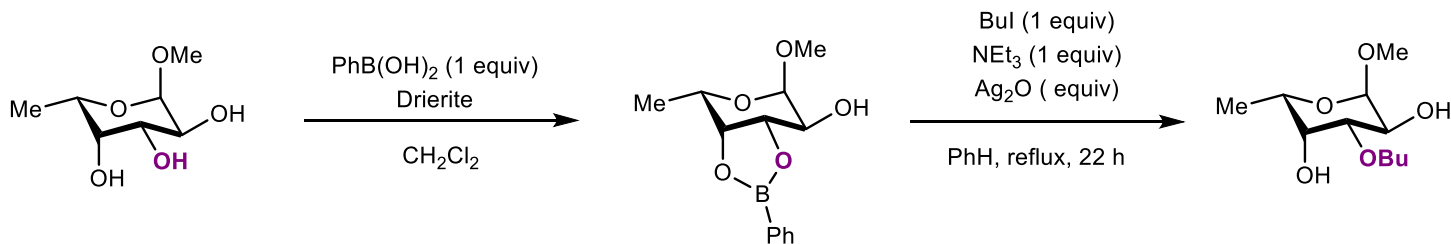
# Enhance Innate Reactivity





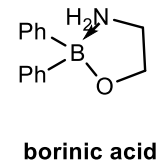
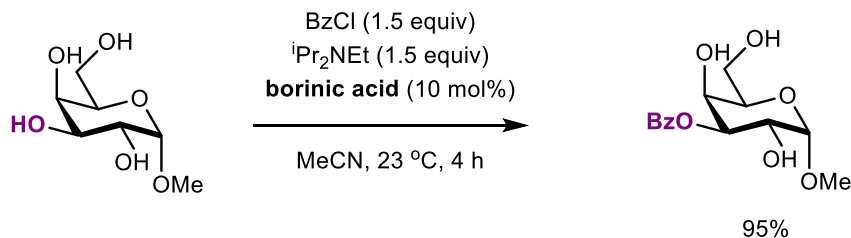
# Borinate Ester

1997, Aoyama



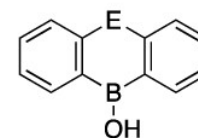
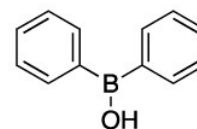
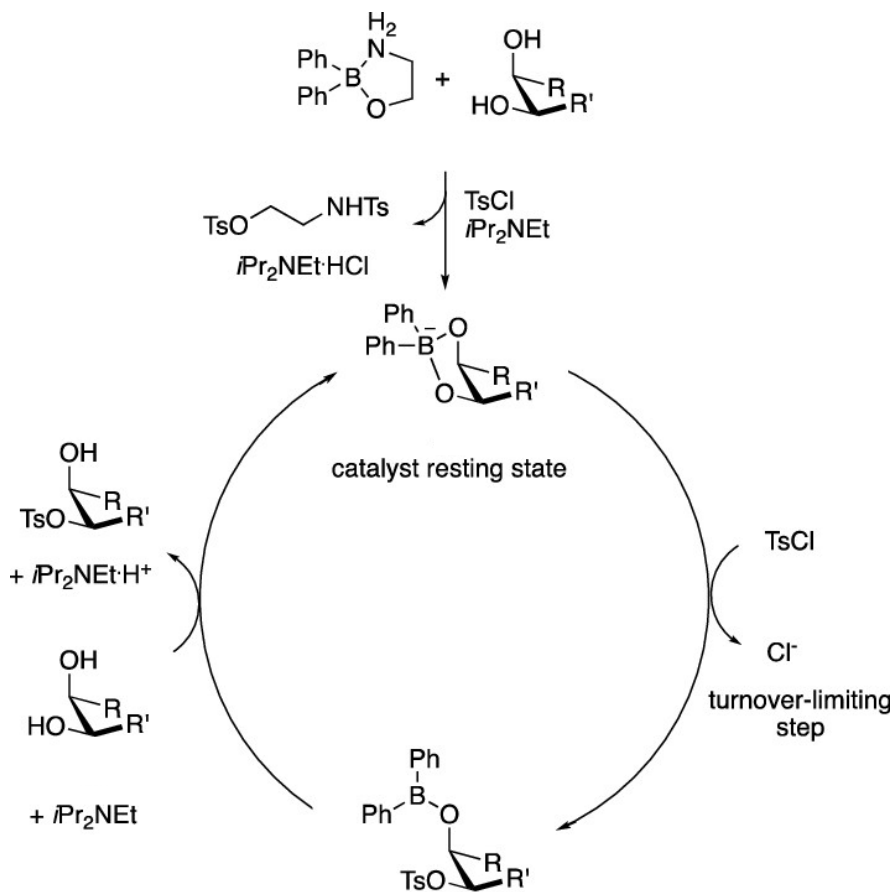
Aoyama, Y. *et al. Tetrahedron Lett.* **1997**, 38, 5001–5004.

2011, Taylor



Taylor, M.S. *et al. J. Am. Chem. Soc.* **2011**, 133, 3724–3727.

# Borinate Ester



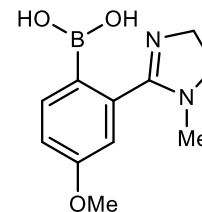
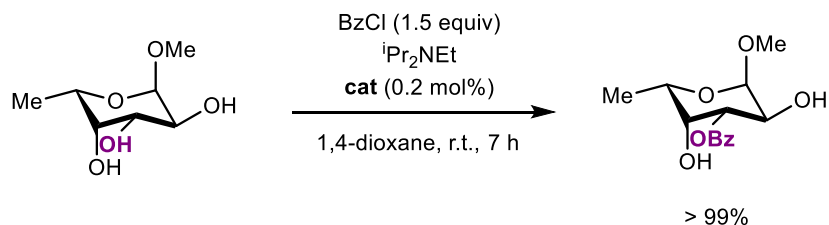
E = O or NMe

affinity to diols	Higher	Lower
nucleophilicity of borinate	Lower	Higher
Catalytic activity	Lower	Higher

Dimitrijević, E. *et al. Chem. Sci.* **2013**, *4*, 3298.

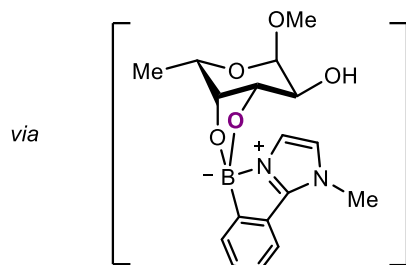
# Boronate Ester

## 1,2-cis diol



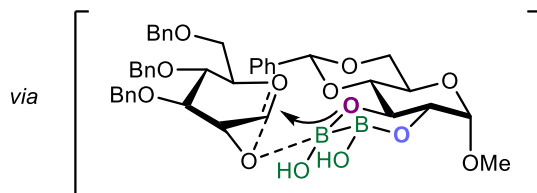
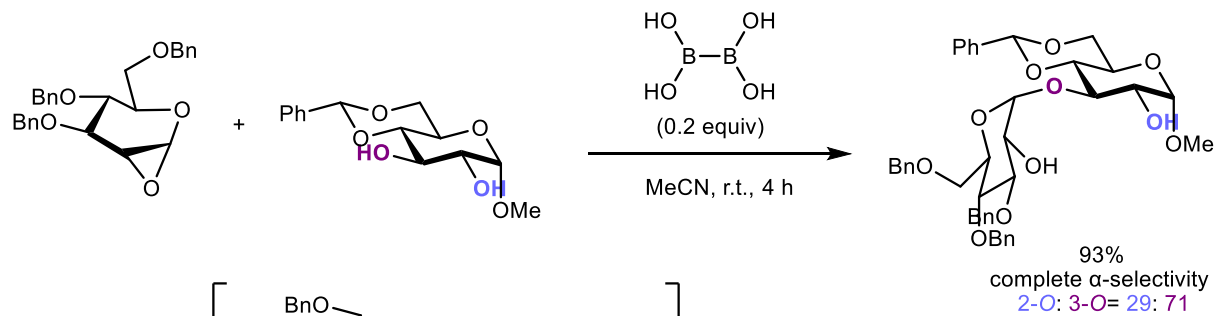
**cat**

DMAP instead of **cat**:  
87% (2-O: 3-O: 2,3-bis=5:44:38)



Makino, K. *et al. Org. Lett.* **2019**, *21*, 3789–3794.

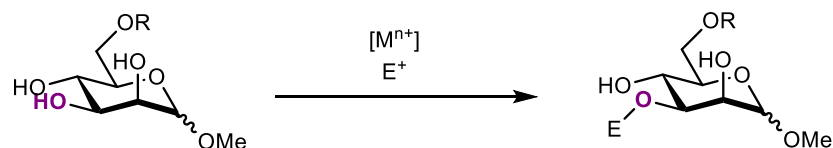
## 1,2-trans diol



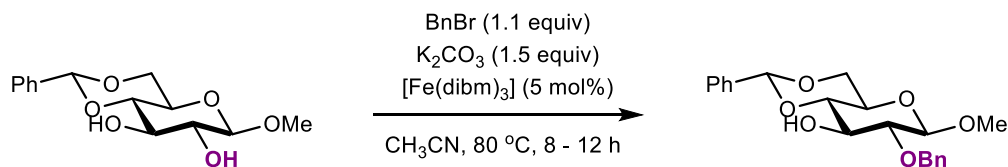
Toshima, K. *et al. J. Org. Chem.* **2020**, *85*, 16254–16262.

# Metal Salts Coordinated by Diols

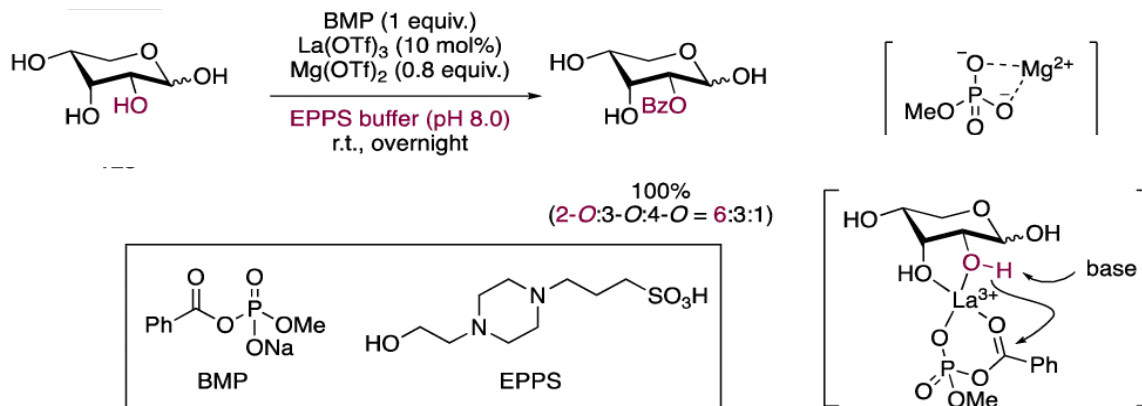
$Zn^{2+}$  (Nishino, Ishido),  $Mo_3^+$  (Evtushenko),  $Fe^{3+}$  (Dong)



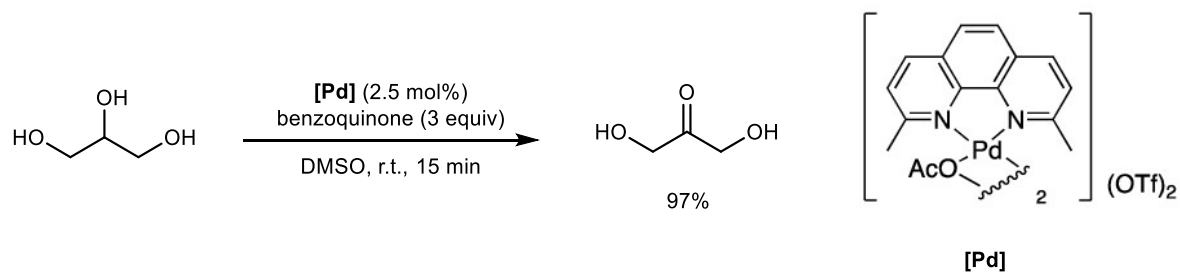
**1,2-trans-diol**



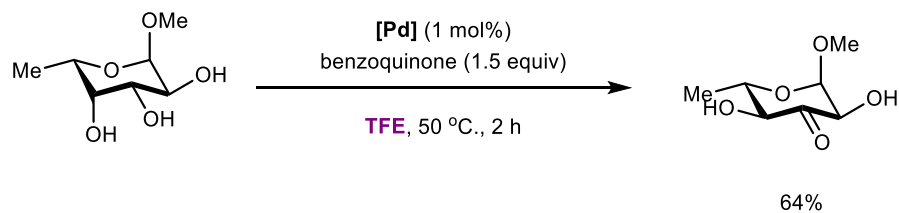
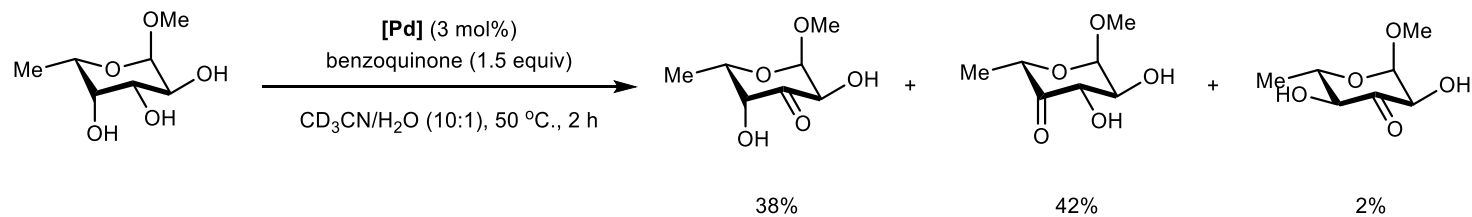
**$La^{3+}$  (Kluger)**



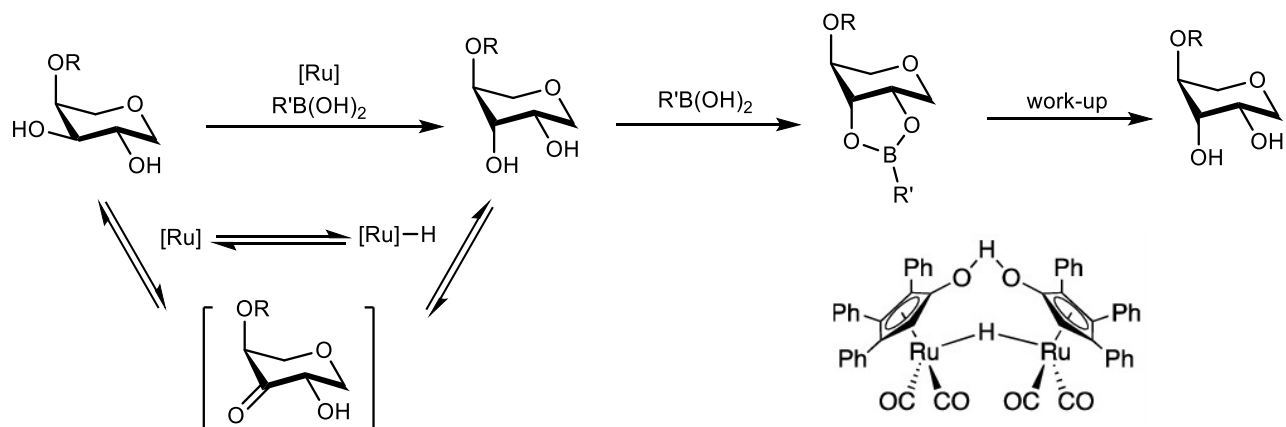
# Oxidation by Metal Catalysts



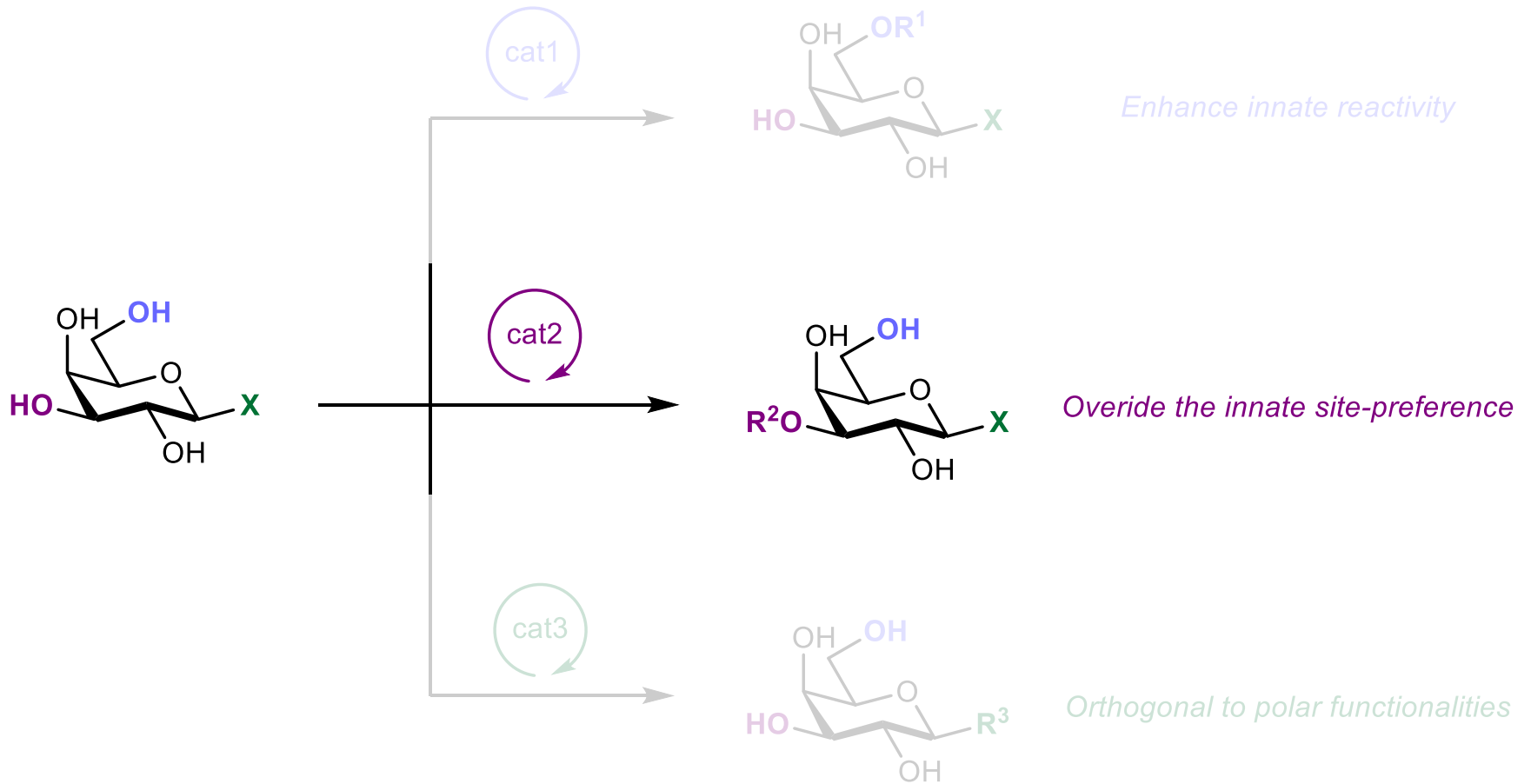
## 3-oxidation and 4-epimerization



# Epimerization

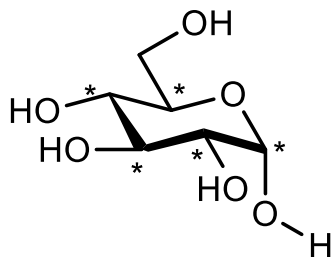


# Enhance Innate Reactivity



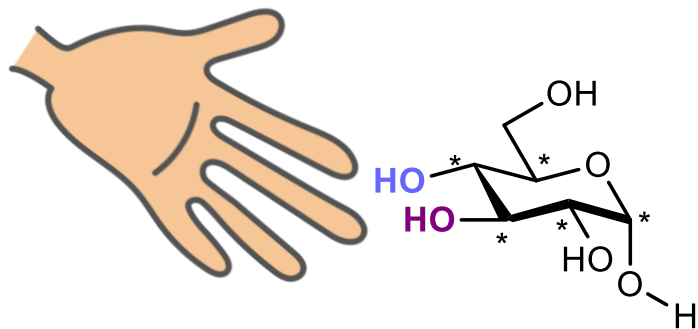
# Asymmetric Catalyst

*Carbohydrates have many chiral centers*



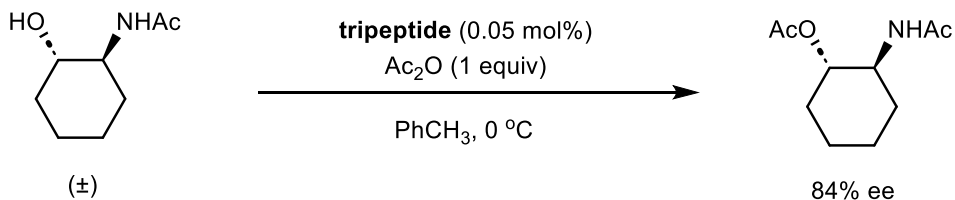
*Achiral reagents are hard to distinguish similar steric space*

*Asymmetric catalysts can!*

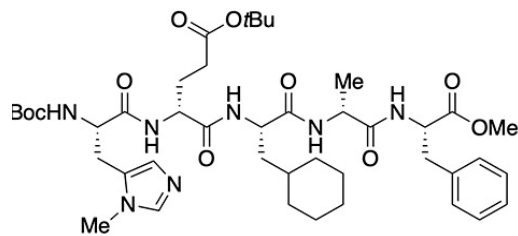
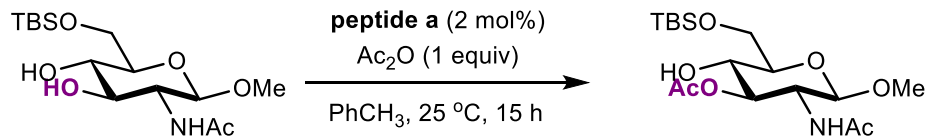


# Peptide Catalysts

1997, Miller



2003, Miller

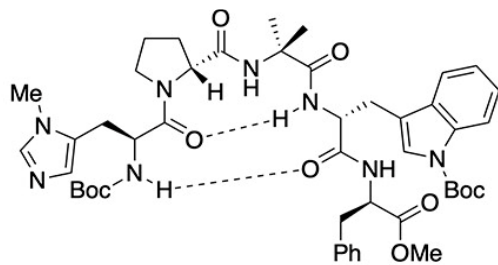
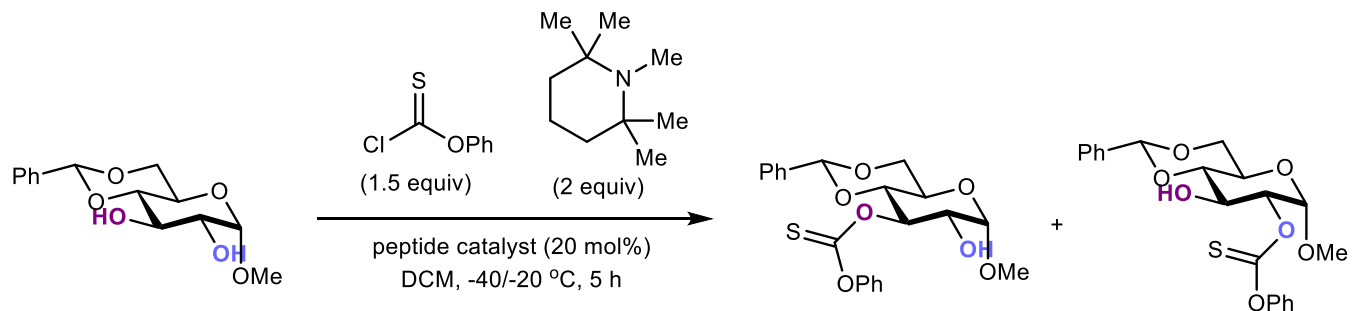


peptide a

Miller, S. J. *et al. J. Am. Chem. Soc.* **1998**, *120*, 1629–1630.

Miller, S. J. *et al. Tetrahedron* **2003**, *59*, 8869–8875.

# Peptide Catalysts



peptide b

w/ peptide b  
( $-40$  °C)

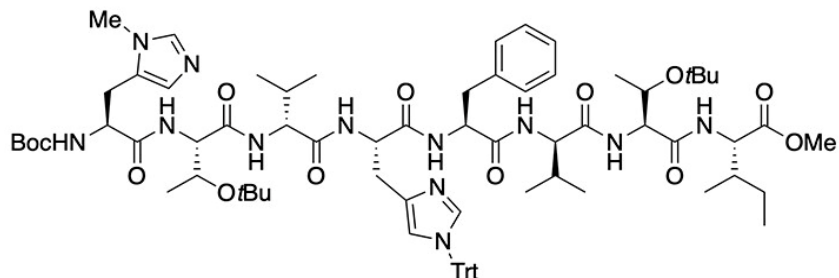
67%

3%

w/ peptide c  
w/  $\text{FeCl}_3$  (15 mol%)  
( $-20$  °C)

8%

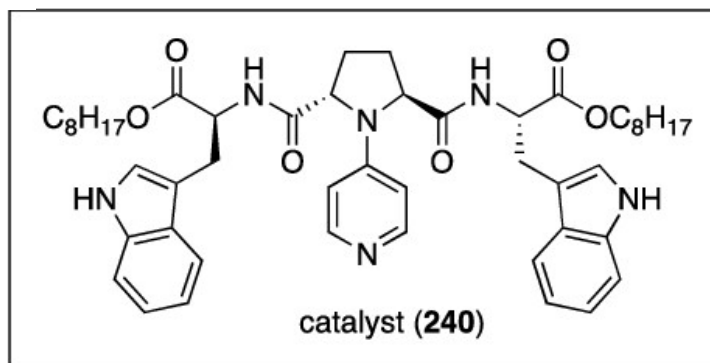
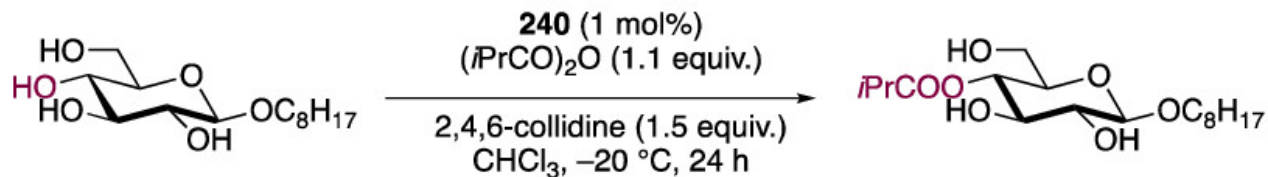
53%



peptide c

Sanchez-Rosello, M. *et al.* *J. Org. Chem.* **2008**, *73*, 1774–1782.

# Chiral 4-Pyrrolidinopyridine Catalysts



98%

6-*O*:4-*O*:3-*O*:2-*O*

0:99:1:0

cf. with DMAP

47%

6-*O*:4-*O*:3-*O*:2-*O*

36:26:26:12



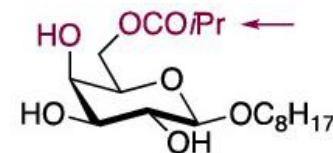
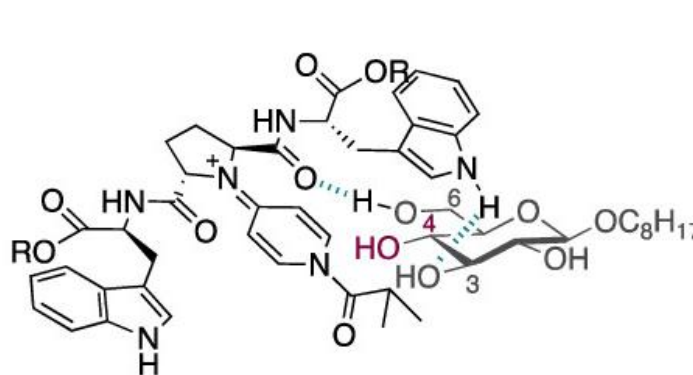
$\beta$ -D-glucopyranoside

R = *i*Pr : y. 98%

>99% 4-*O*-selec

R = Me : y. 96%

96% 4-*O*-selective



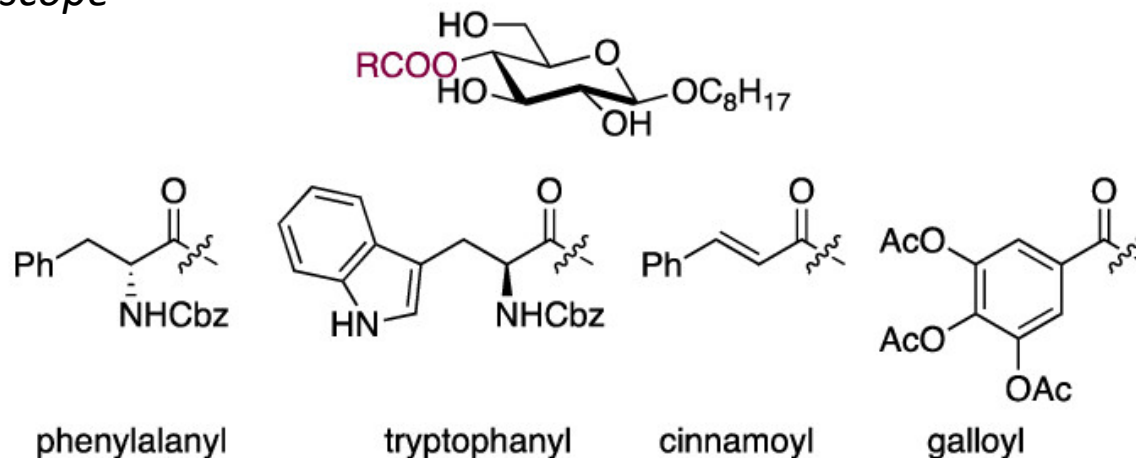
$\beta$ -D-galactopyranoside

y. 46%

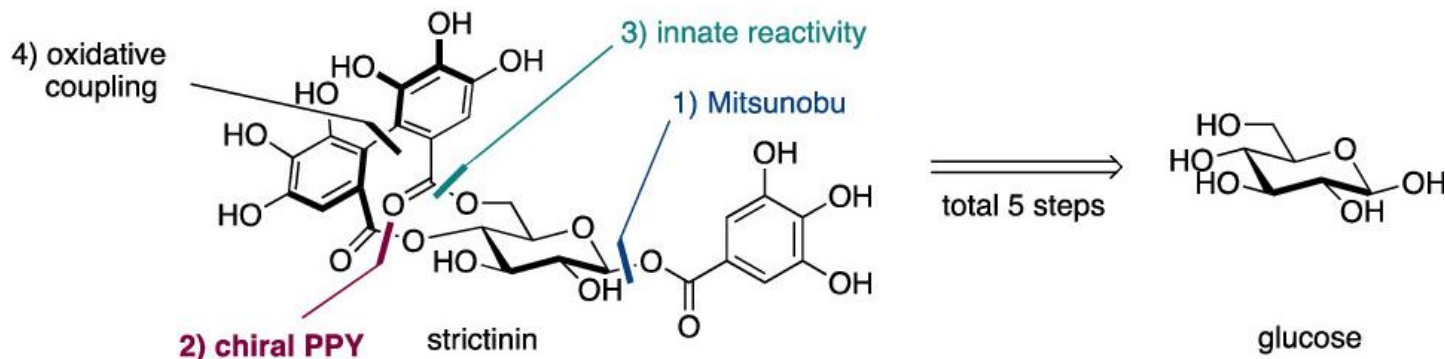
91% 6-*O*-selective

# Chiral 4-Pyrrolidinopyridine Catalysts

## Acyl group scope

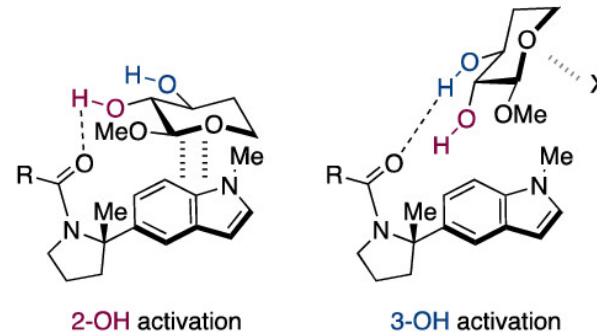
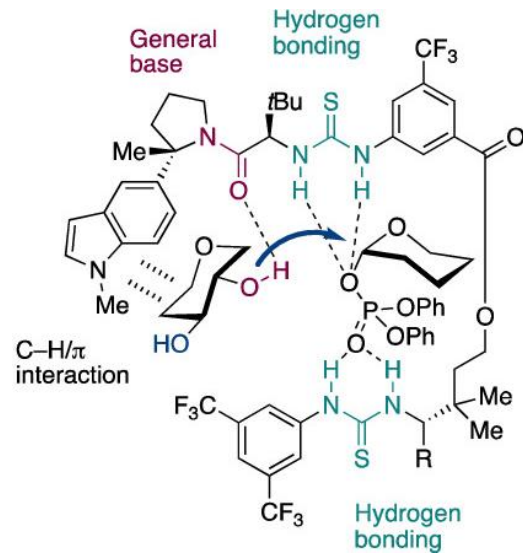


## Application

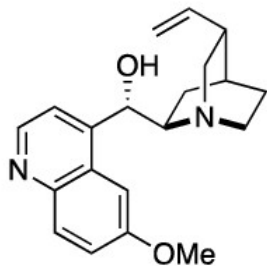


# Other Asymmetric Catalyst

## Chiral Thiourea Catalysts



## Cinchona Alkaloid-Boron Catalysts



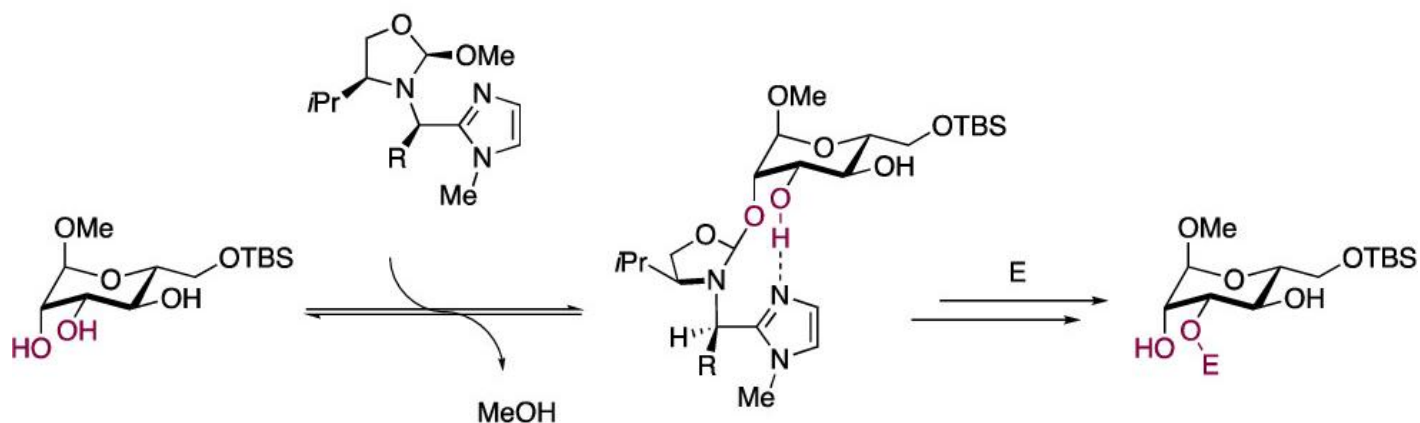
- *desymmetrization*
- *acylation*

## Chiral Copper Catalysts



- *desymmetrization*
- *acylation*

# Reversible Covalent Bond-Forming Catalysts

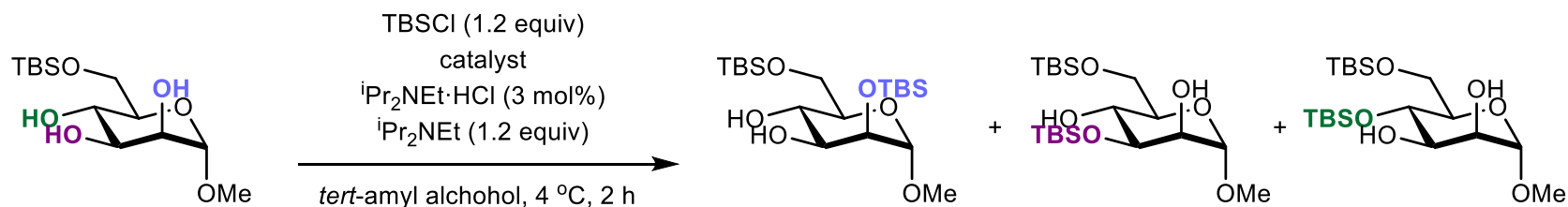


Tan, K. L. *et al. J. Am. Chem. Soc.* **2008**, *130*, 9210–9211.

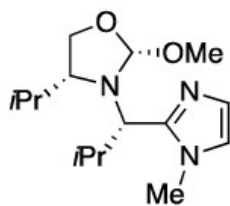
Tan, K. L. *et al. J. Am. Chem. Soc.* **2012**, *134*, 7321–7324.

Tan, K. L. *et al. Org. Lett.* **2013**, *15*, 4710–4713.

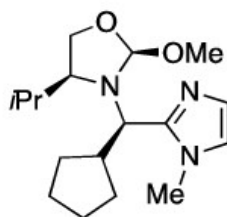
# Reversible Covalent Bond-Forming Catalysts



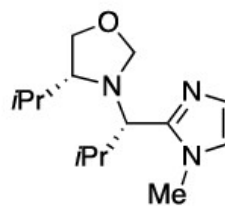
entry	Catalyst	Yield (%)	2-O	:	3-O	:	4-O
1	NMI (20 mol%)	77			5: <b>78</b> : 17		
2	<b>(+)-cat 1</b> (20 mol%)	84			<b>90</b> : 10: -		
3	<b>(-)-cat 2</b> (20 mol%)	>98			-: <b>100</b> : -		
4	<b>(+)-cat 1'</b> (20 mol%)	7			3: <b>92</b> : 5		
5	<b>(-)-cat 2'</b> (20 mol%)	9			2: <b>92</b> : 6		



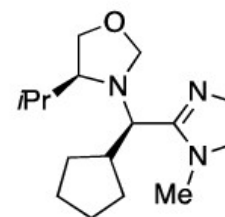
**(+)-cat 1**



**(-)-cat 2**



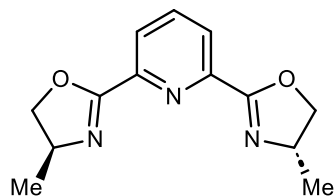
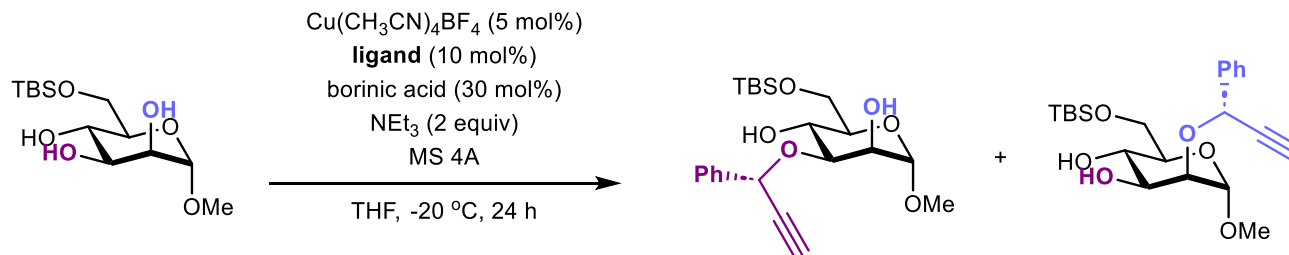
**(+)-cat 1'**



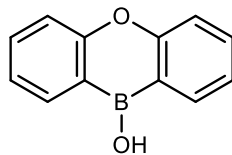
**(-)-cat 2'**

# Hybrid Catalysis

2017, Niu



ligand



borinic acid

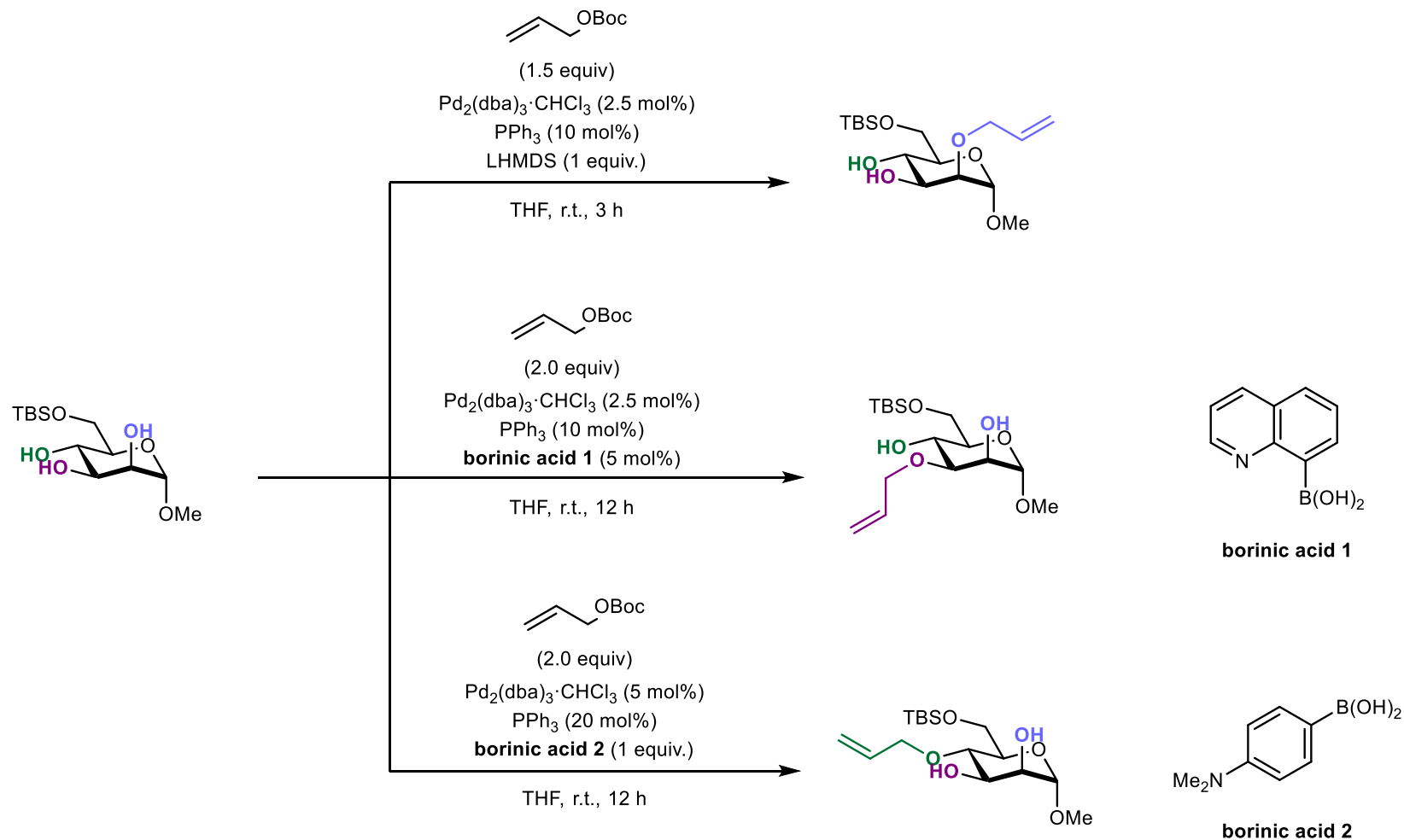
entry	Catalyst	Yield (%)	3-O : 2-O
1	<b>ligand</b>	82	13:1
2	<b>ent-ligand</b>	63	1:11
3	<b>(+/-) ligand</b>	40	2.8:1

*Mechanism*

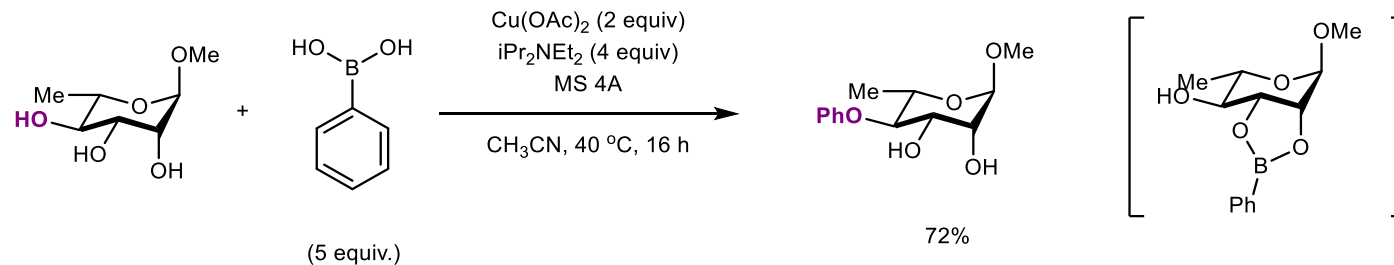


Niu, D. *et al. Chem.* **2017**, *3*, 834–845.

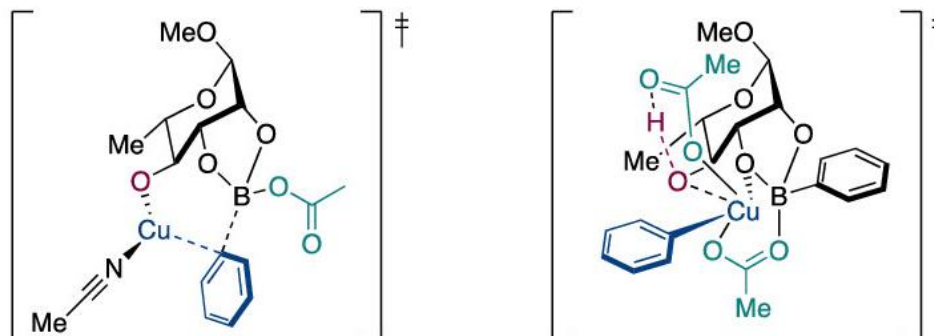
# Regiodivergent O-allylation



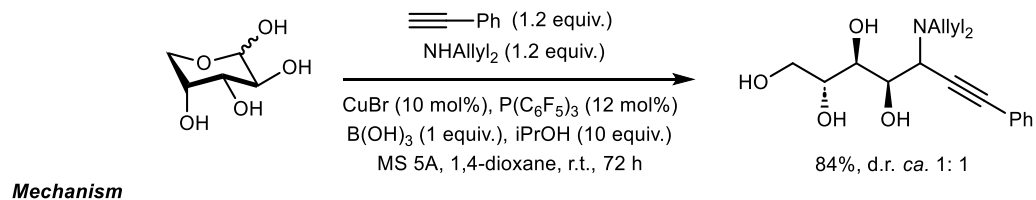
# Hybrid Catalysis



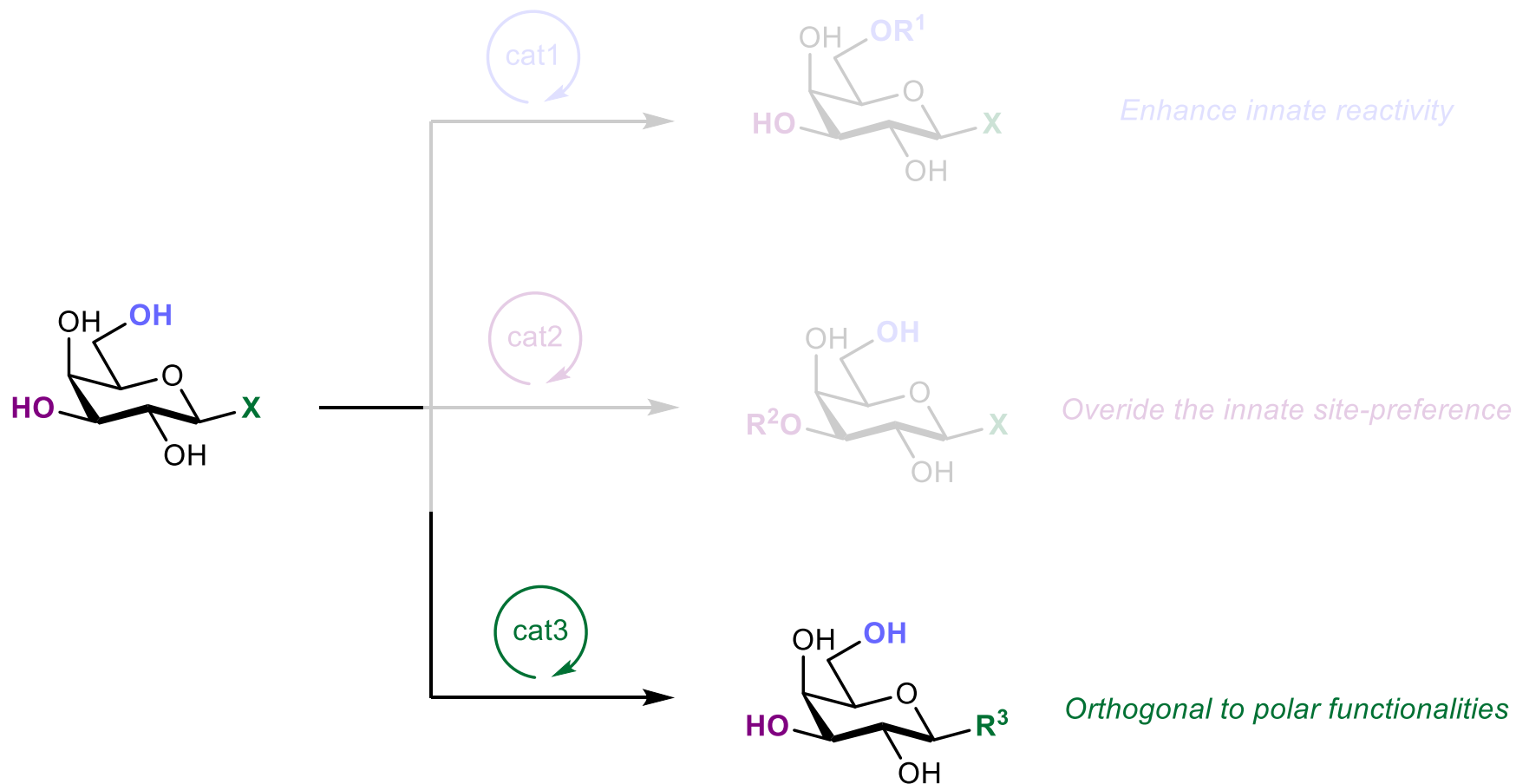
*Mechanism studies*



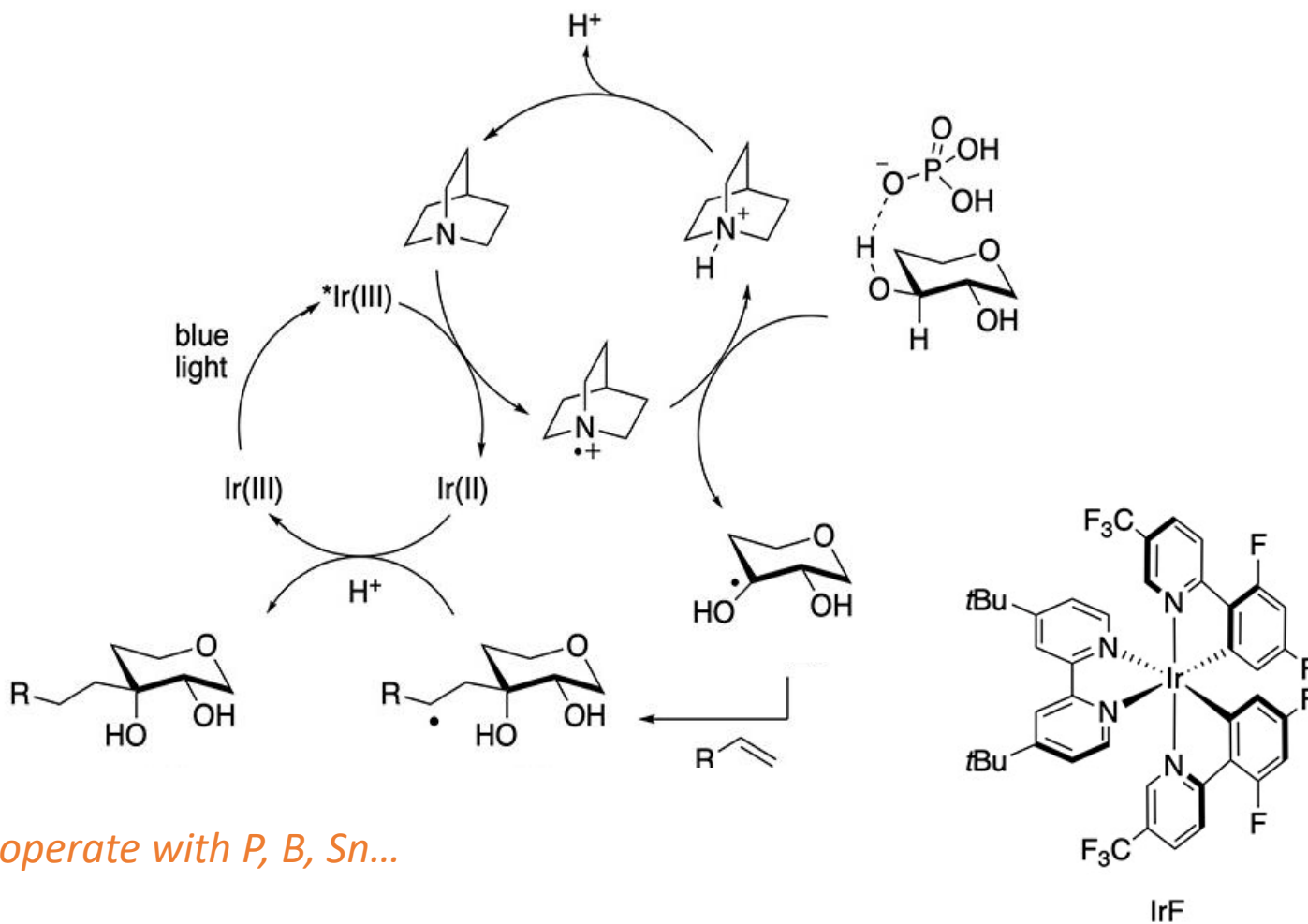
# Soft-Metal Hard-Anion Cooperative Catalysts



# Radical Catalysis Approaches

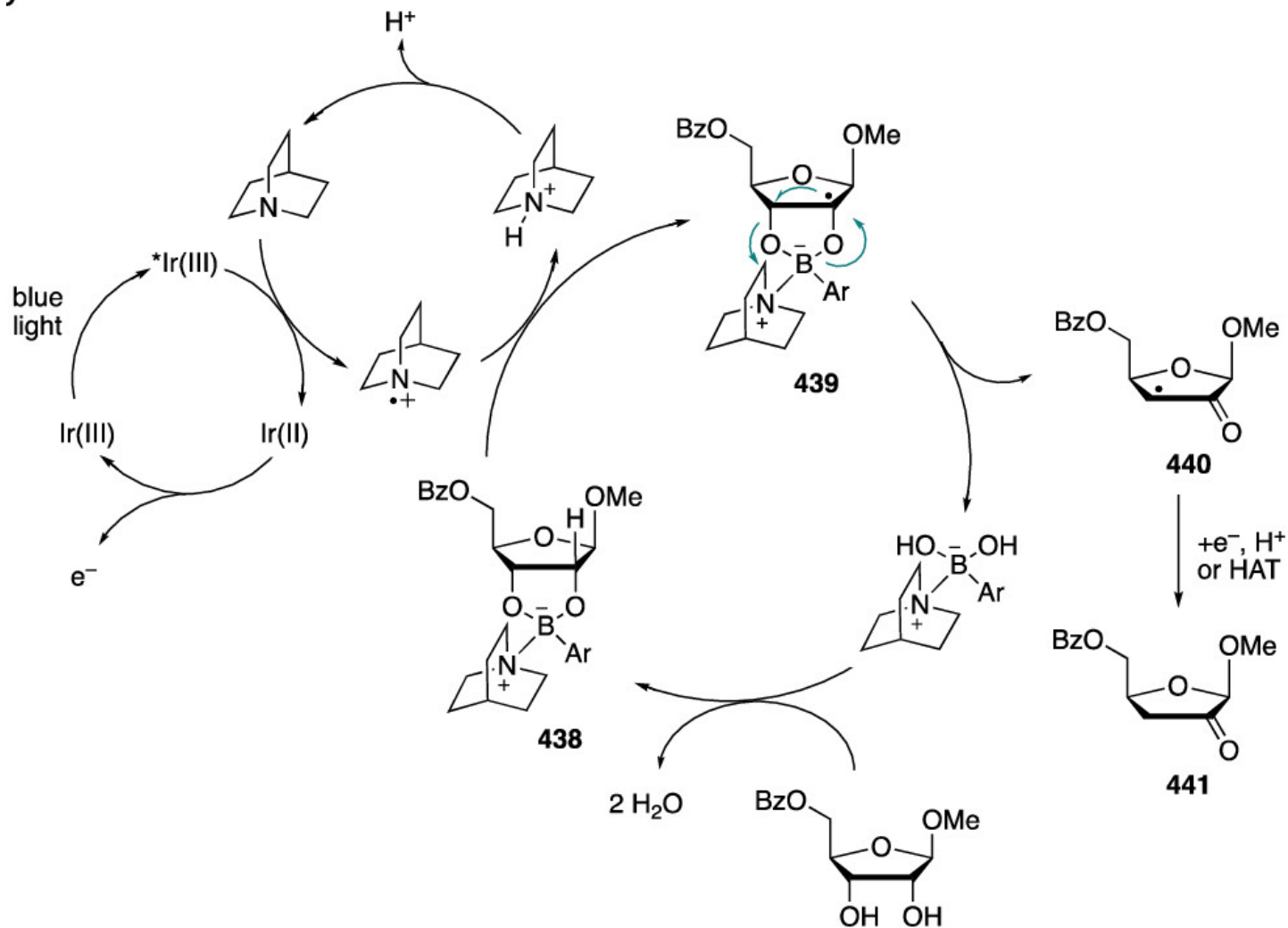


# Classic System



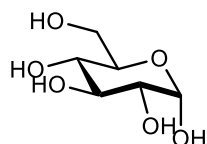
MacMillan, D. W. *et al. Science* **2015**, *349*, 1532–1536.

# Redox Isomerization



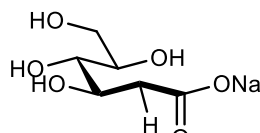
# Redox Isomerization

2020, Murakami

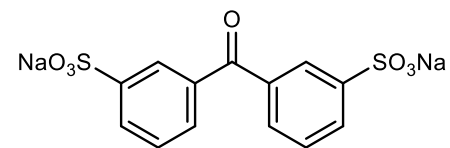


BPSS (50 mol%)  
NaOH (1.5 equiv.)

H<sub>2</sub>O, r.t., 2.5 h  
365 nm light

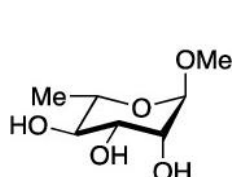


48%



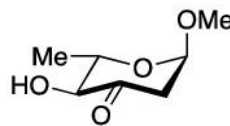
BPSS

2021, Wendlandt

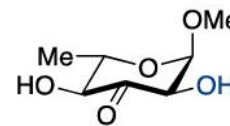


4-CzIPN (2 mol%)  
quinuclidine (5 mol%)  
Bu<sub>4</sub>NOAc (5 mol%)  
additive

MeCN/DMSO (95:5)  
25 °C, 18 h, blue LED

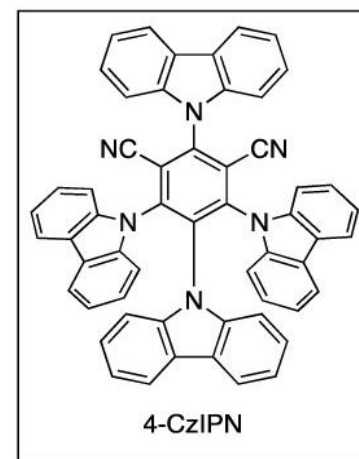


1



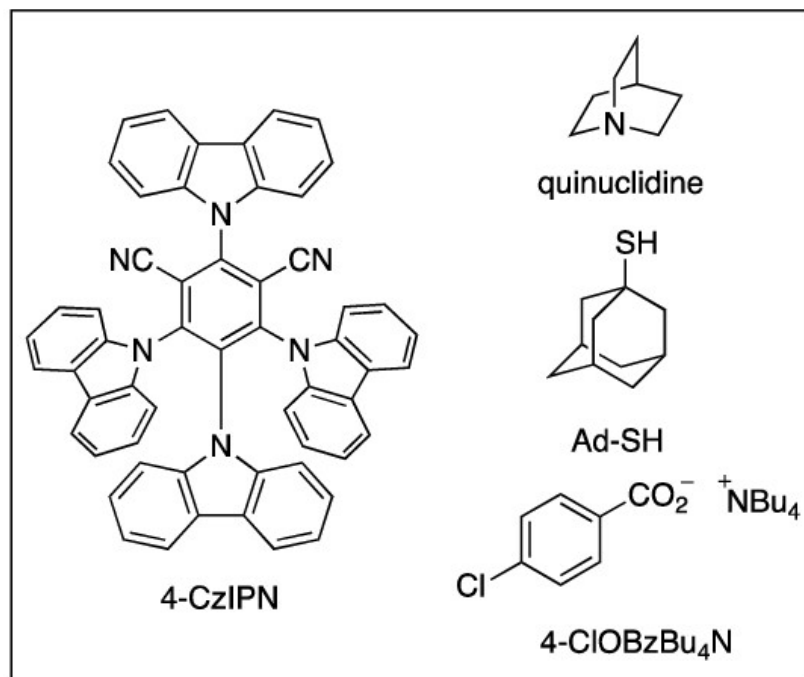
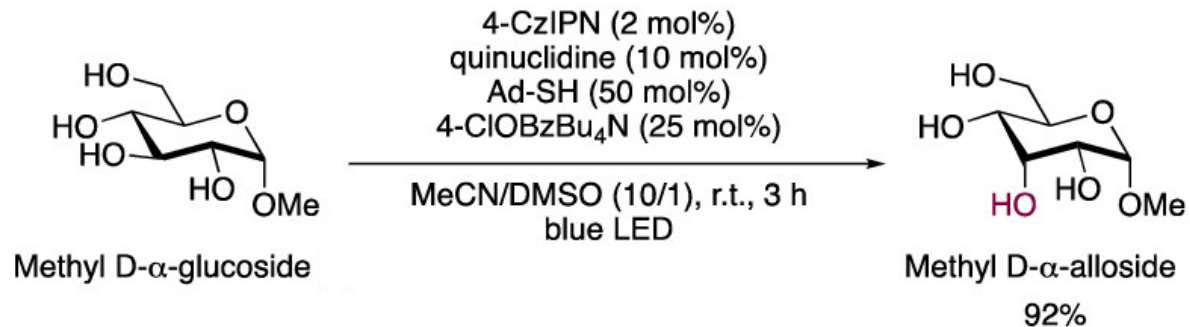
2

Entry	Additive	Yield 1	Yield 2
1	none	2%	9%
2	Brønsted base or acid	< 3%	< 10%
3	C <sub>6</sub> F <sub>5</sub> B(OH) <sub>2</sub> (5 mol%)	1%	7%
4	Cu(OAc) <sub>2</sub> (5 mol%)	5%	38%
5	Mn(OAc) <sub>2</sub> ·4H <sub>2</sub> O (10 mol%)	50%	0%

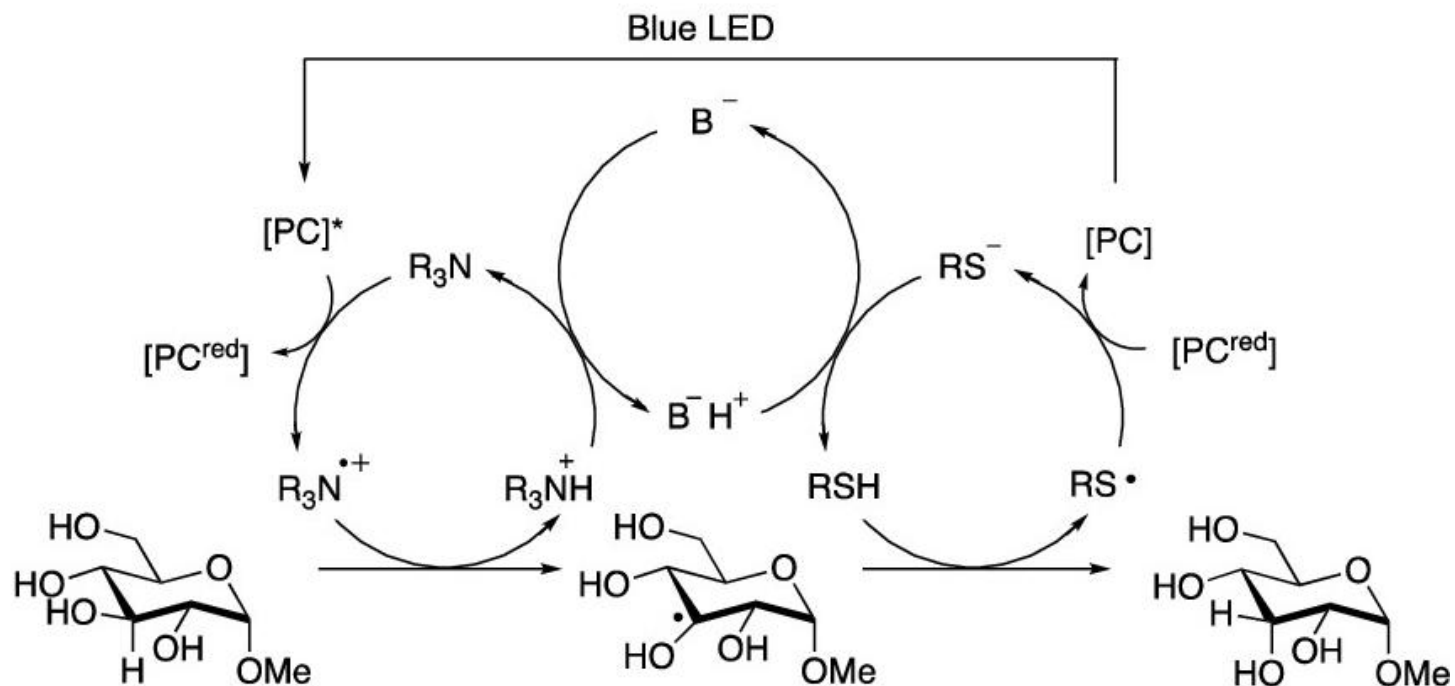


# Site-Selective Epimerization

2020, Wendlandt

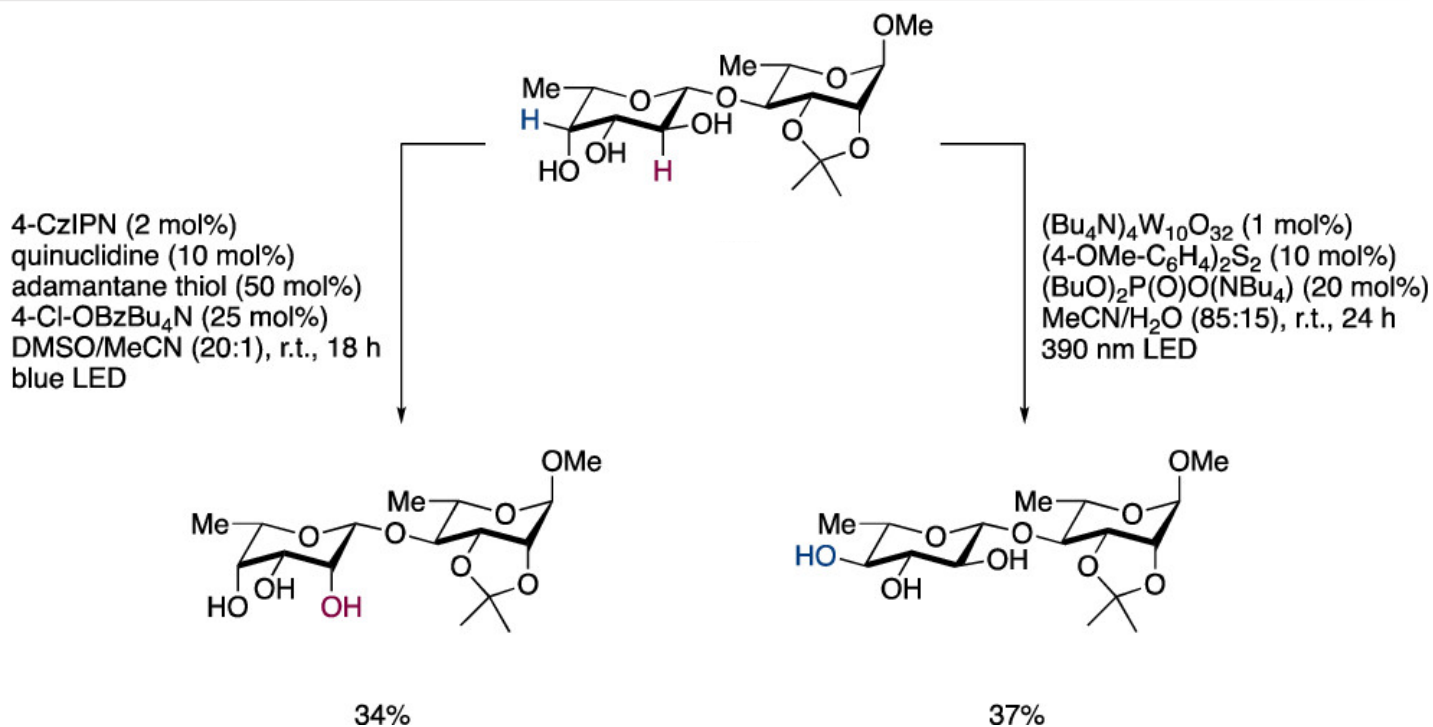
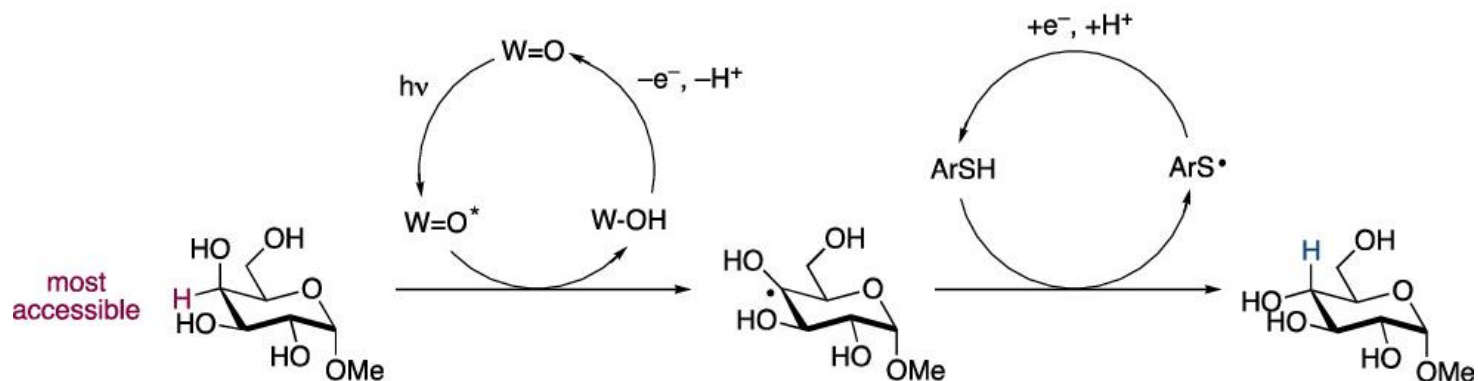


# Site-Selective Epimerization

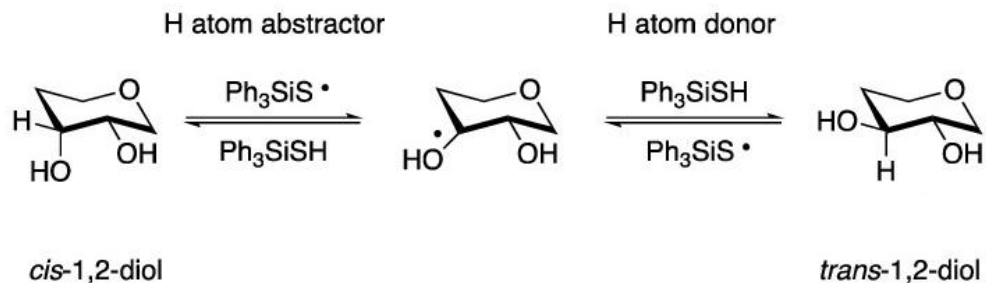


Wendlandt, A. E. *et al. Nature* **2020**, 578, 403–408.

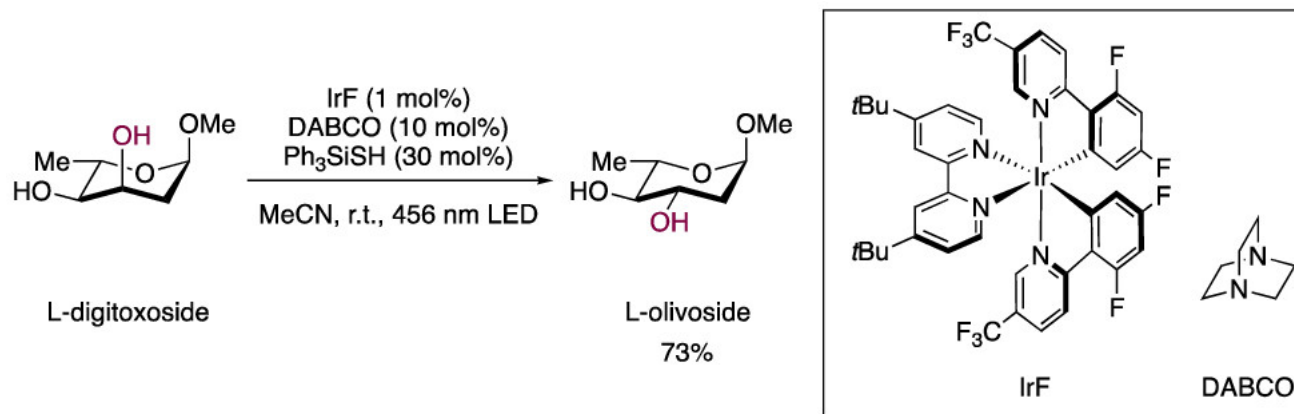
# Site-Selective Epimerization



# Epimerization with Thermodynamic Control

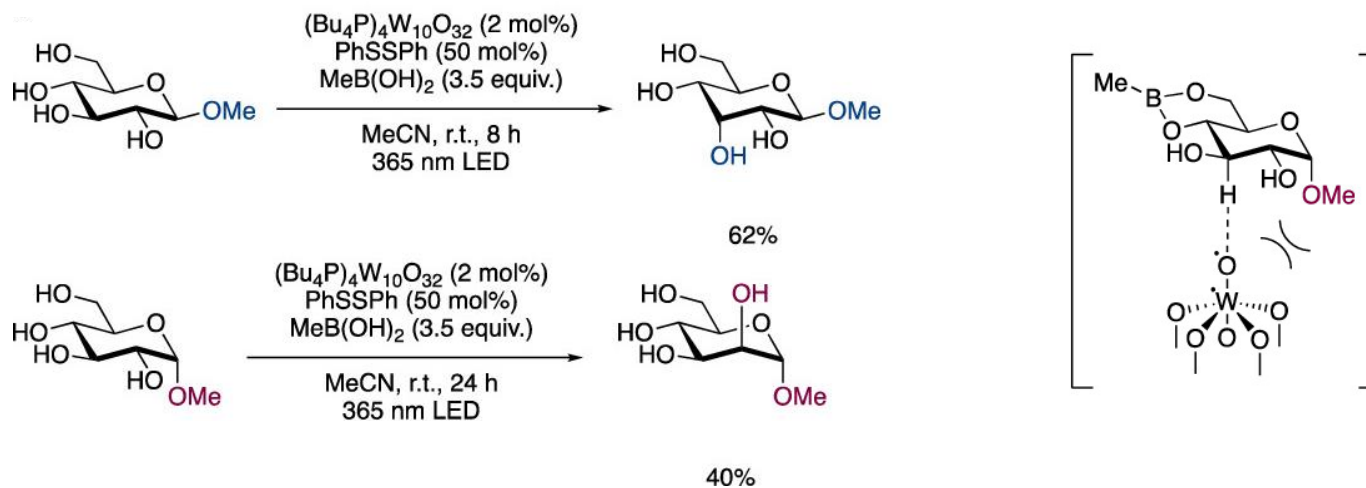
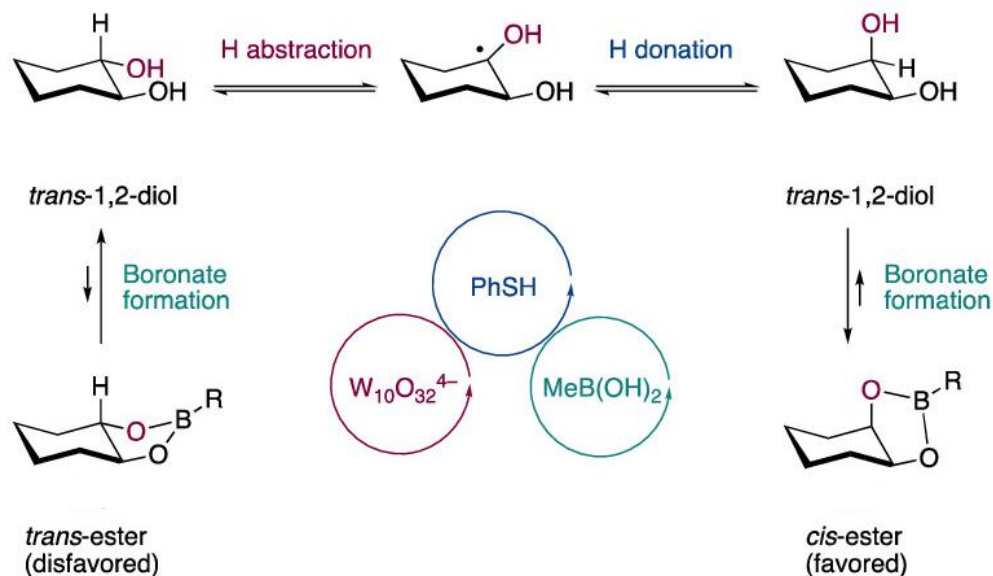


## Example

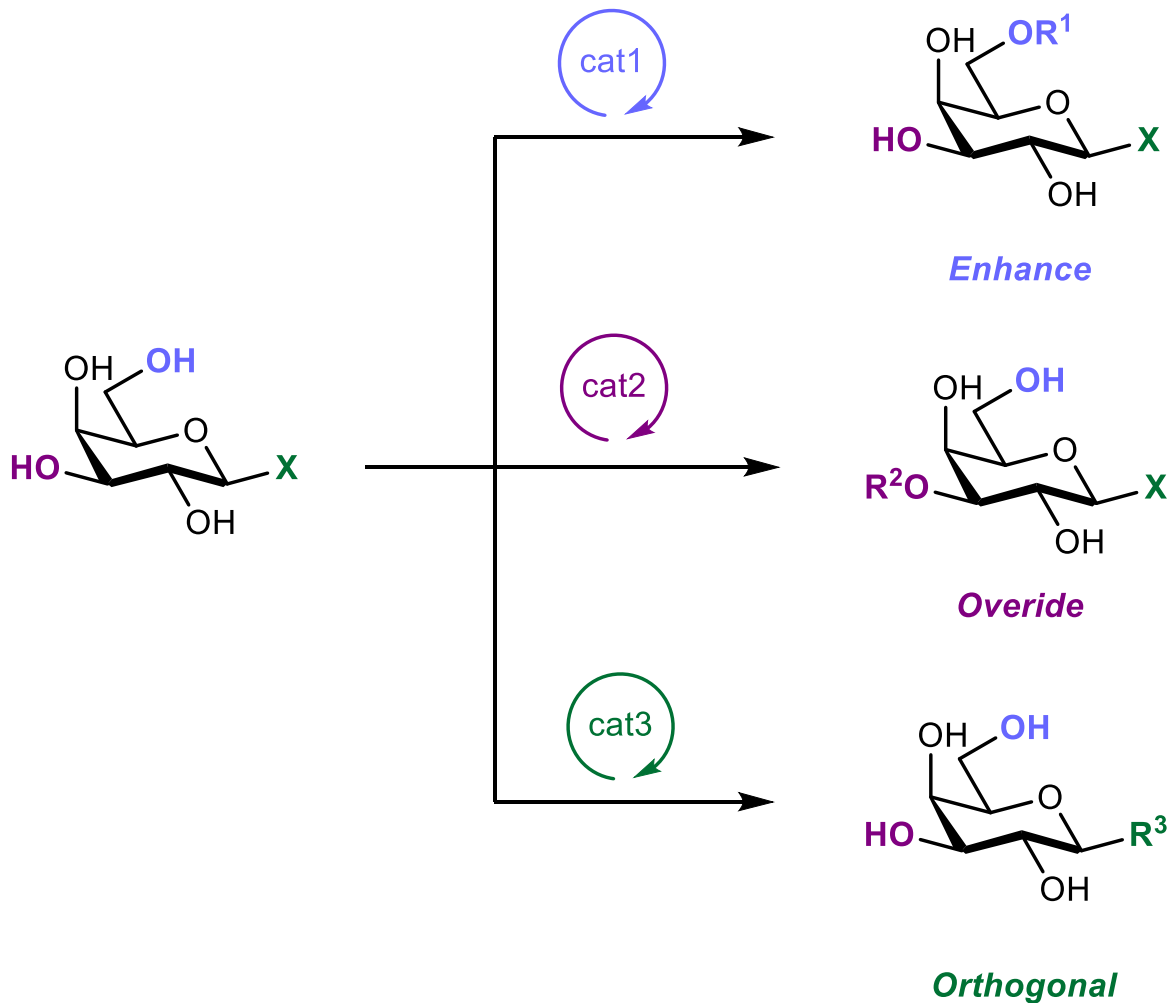


Wendlandt, A. E. *et al. J. Am. Chem. Soc.* **2022**, *144*, 599–605.

# Epimerization with Thermodynamic Control



# Conclusion



*Protection: borinic acid,  
boronic acid, Sn<sup>4+</sup>, Fe<sup>3+</sup>,  
Ca<sup>2+</sup>, etc.  
Oxidation, Epimerization*

*Enhance*

*Asymmetric catalysts*

*Override*

*Radical catalysis approaches:  
isomerization, epimerization*

*Orthogonal*