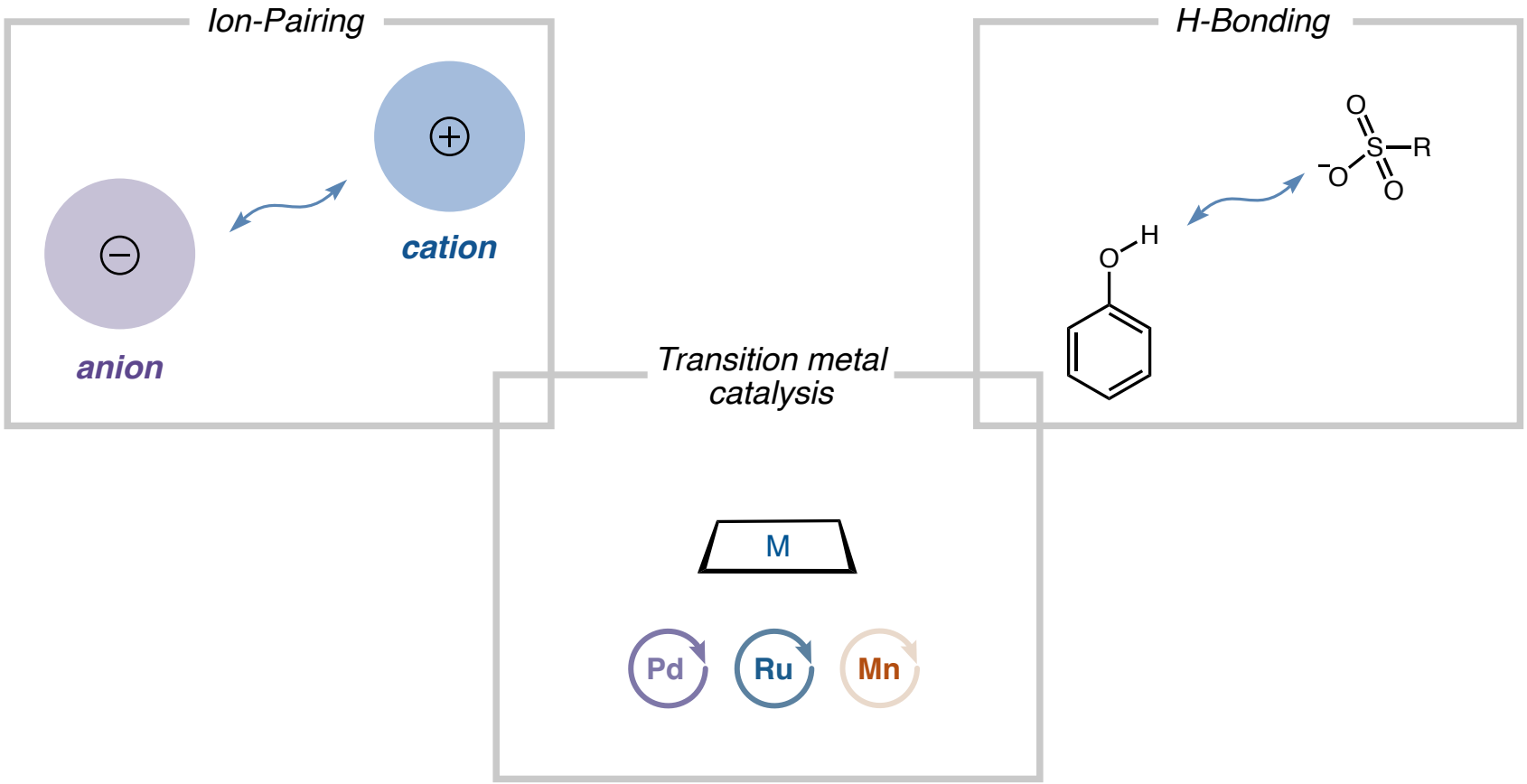
Selective Reactivity through Electrostatic Interactions in Transition Metal Catalysis

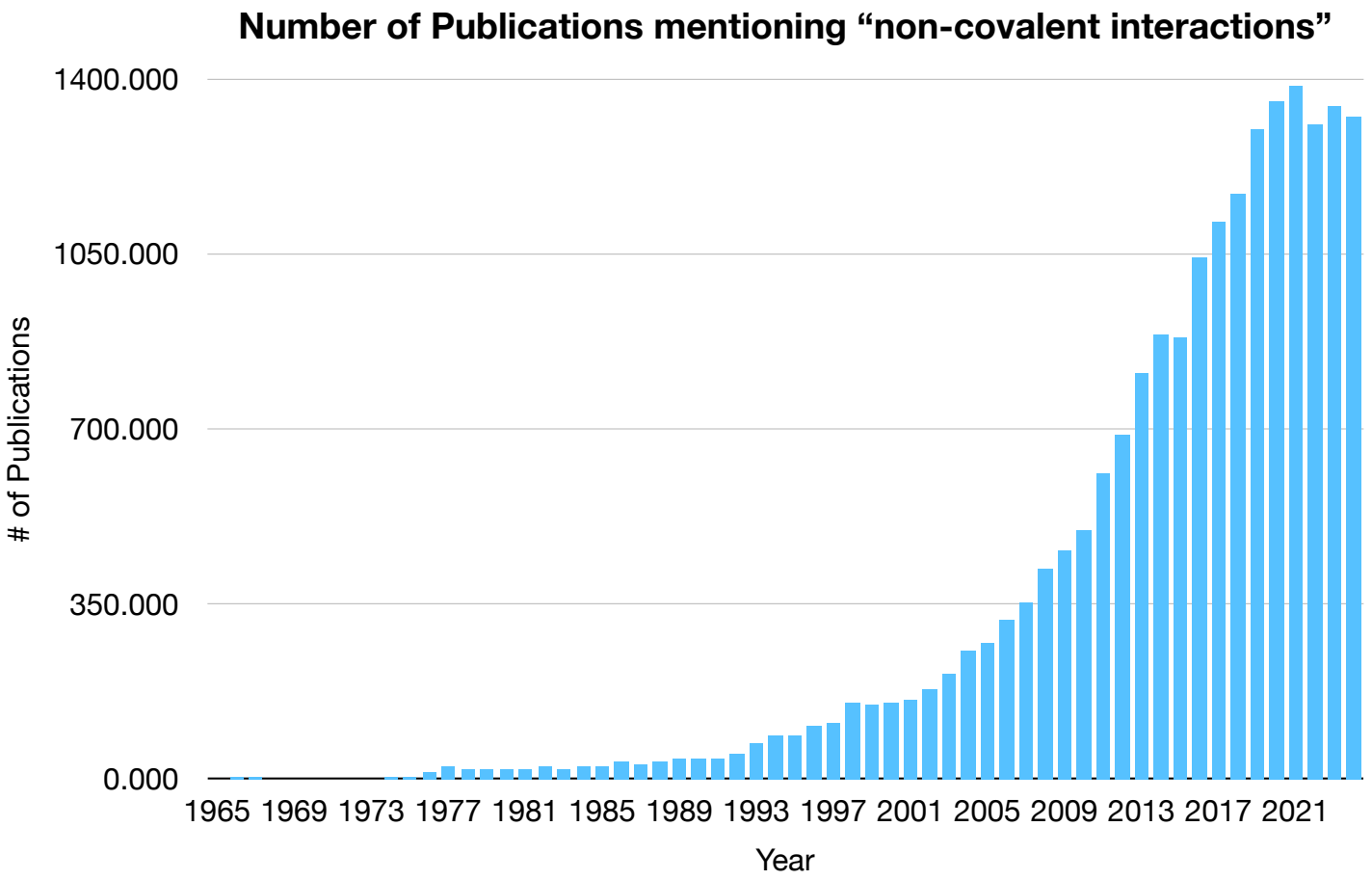


MacMillan Lab Group Meeting

Sven H. M. Kaster

12/13/2024

Prevalence of Non-covalent interactions



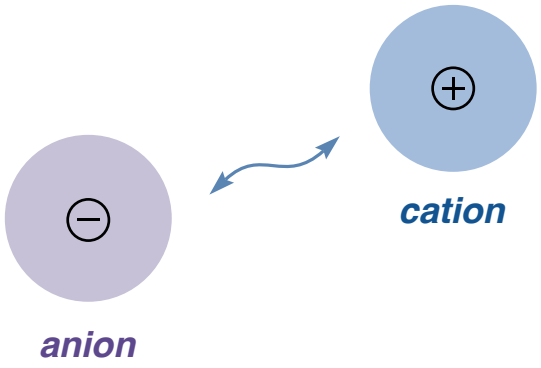
Increasing utilization of non-covalent interactions in reaction design

From *Web of Science*

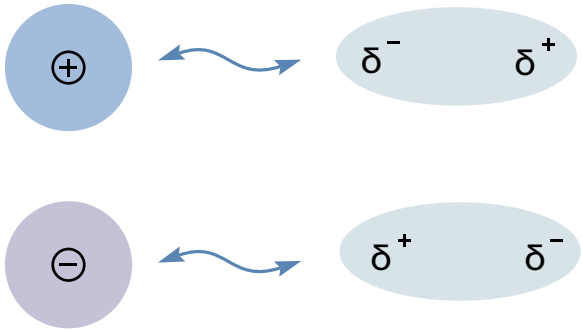
What are non-covalent interactions?

What are non-covalent interactions?

Ion-Pairing

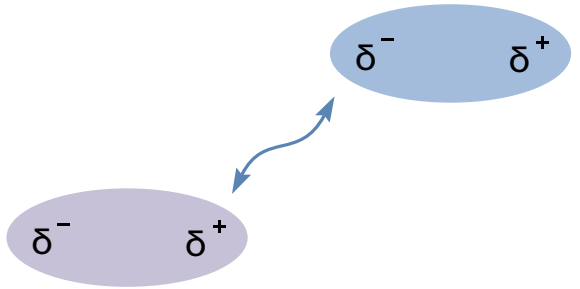


Ion-Dipole



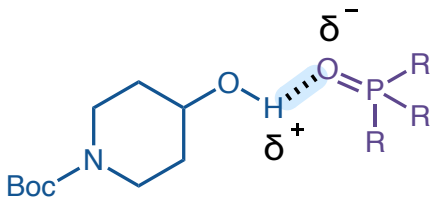
Induced or permanent dipoles

Dipole-Dipole



Induced or permanent dipoles

Hydrogen-Bonding

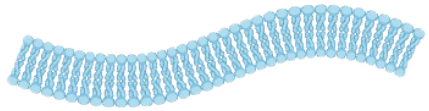


Pi-interactions

π—π

cation—π

Hydrophobic



Schneider, H. *J. Phys Org. Chem.* **2022**, *35*, e4340

What are non-covalent interactions?

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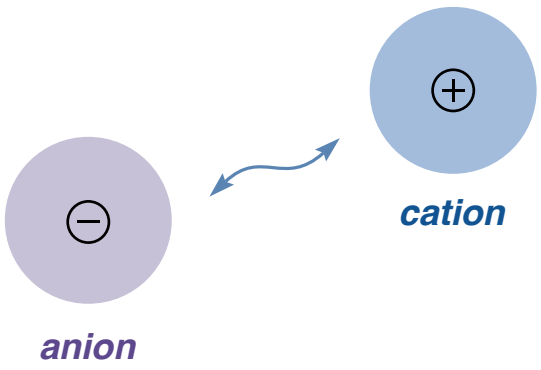

Ion-Dipole

Dipole-Dipole

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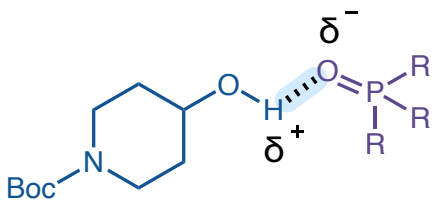

Pi-interactions

Electrostatic interactions

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Electrostatic interactions

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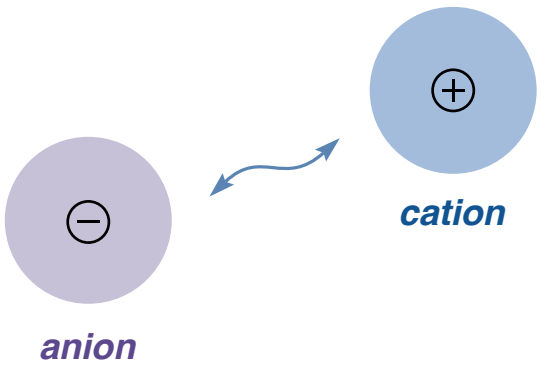

Electrostatics - Coulombic attraction or repulsion between partial charges that existed prior to the interaction

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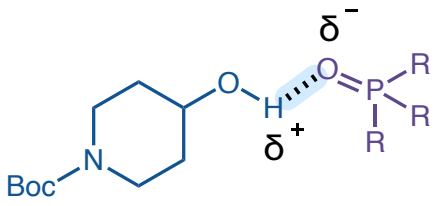

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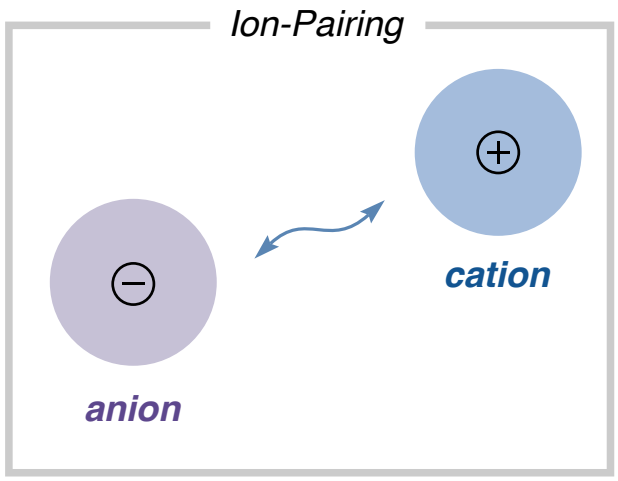
Electrostatic interactions



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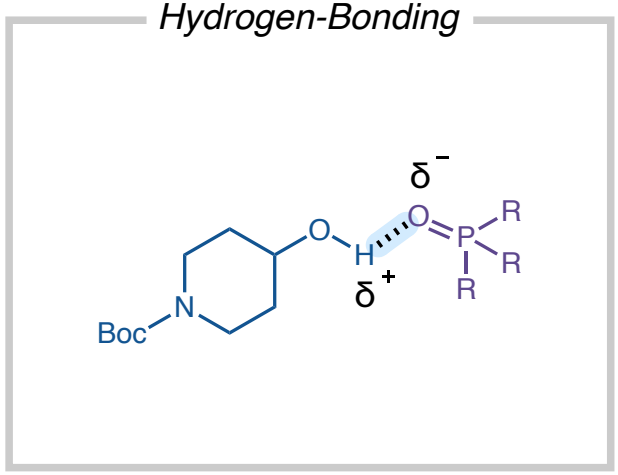

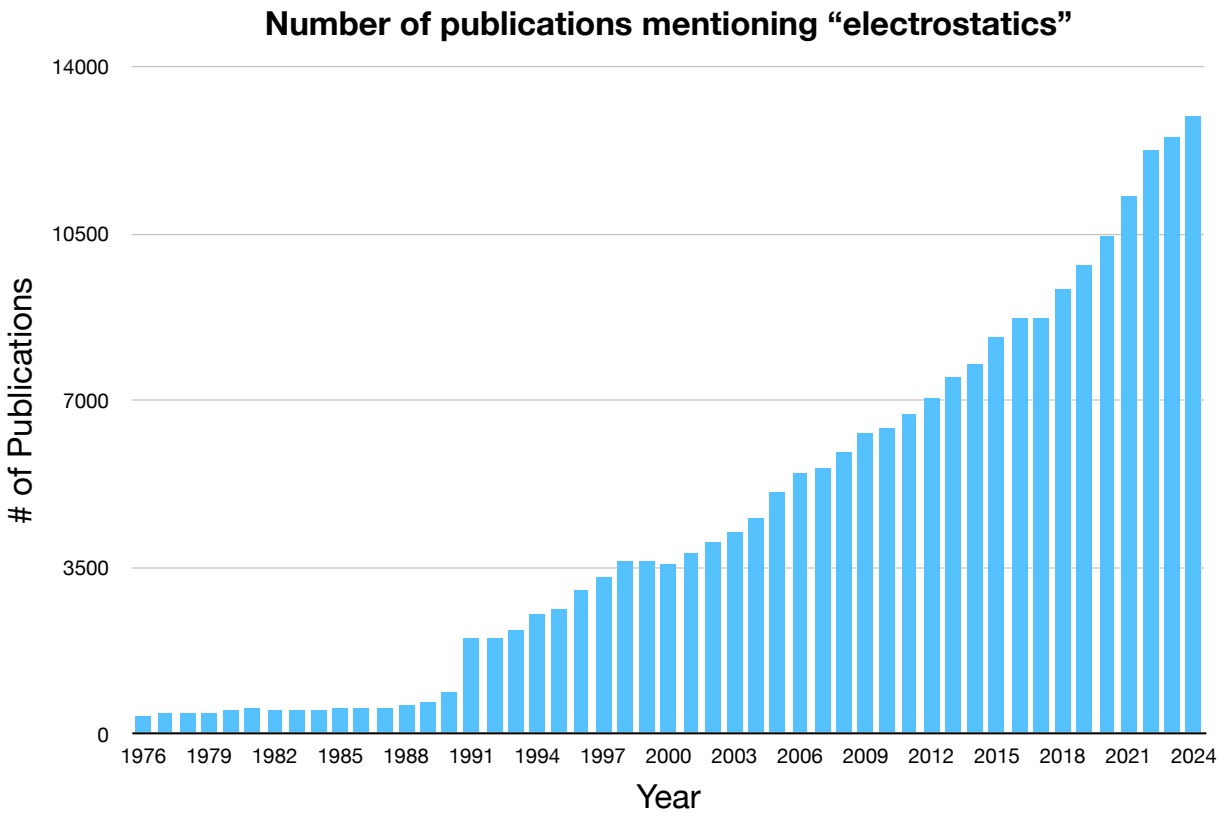

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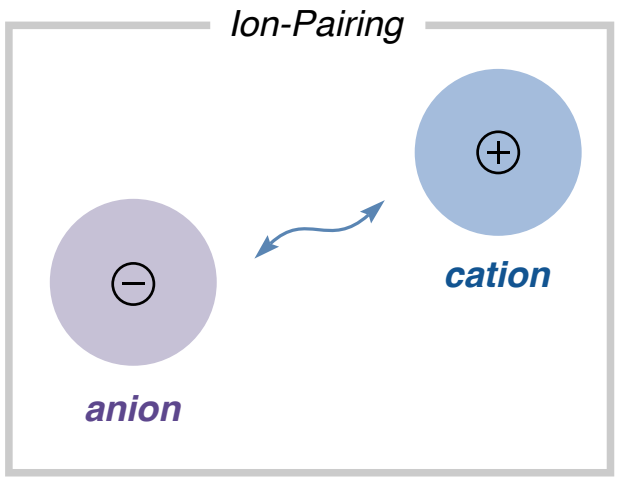
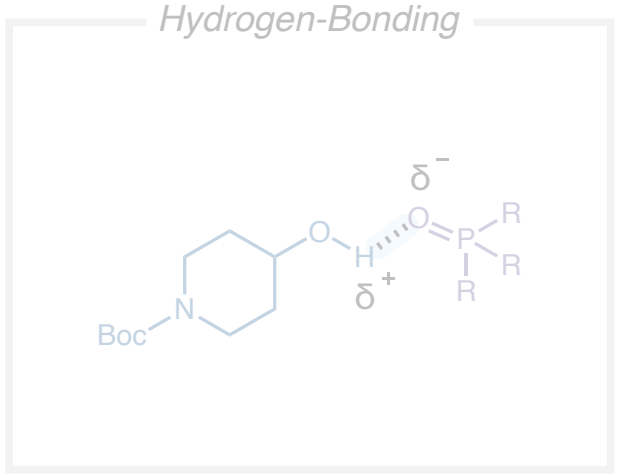


"An ion pair is defined to exist when a cation and anion are close enough in space that the energy associated with their electrostatic attraction is larger than the thermal energy (RT) available to separate them."



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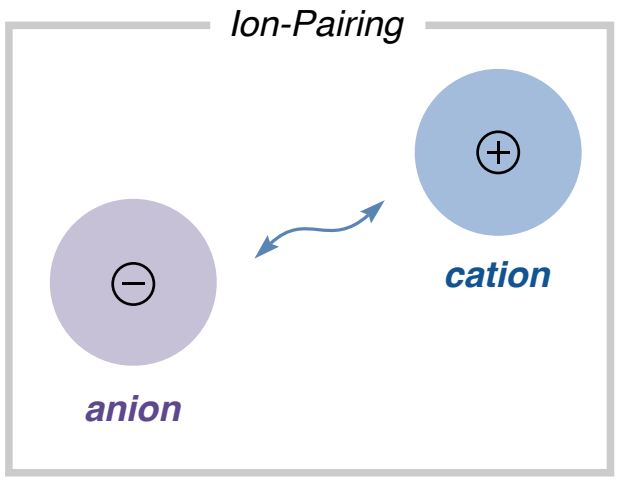

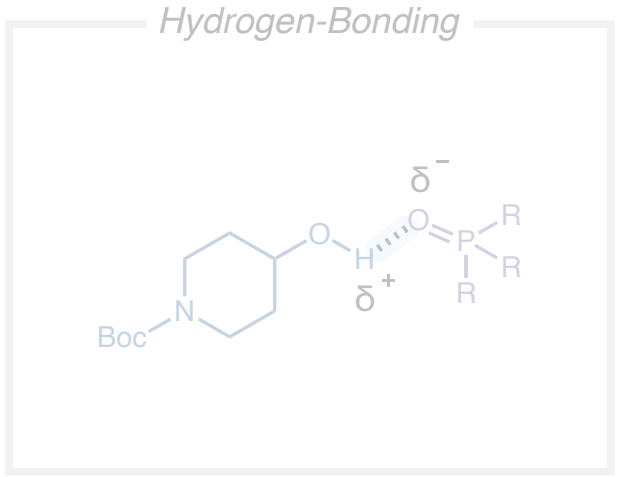

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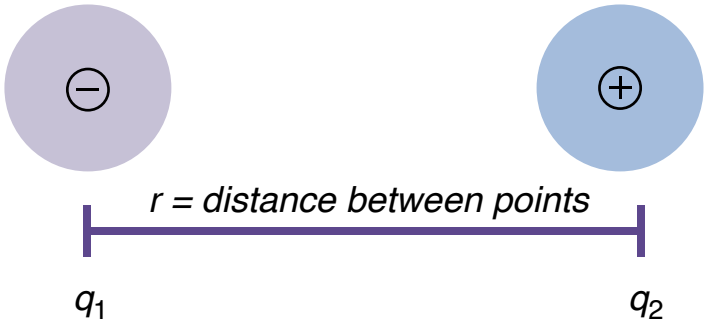
$$E = \frac{q_1 q_2}{4\pi\epsilon\epsilon_0 r}$$



E = attractive potential energy between two points

ε - dielectric constant

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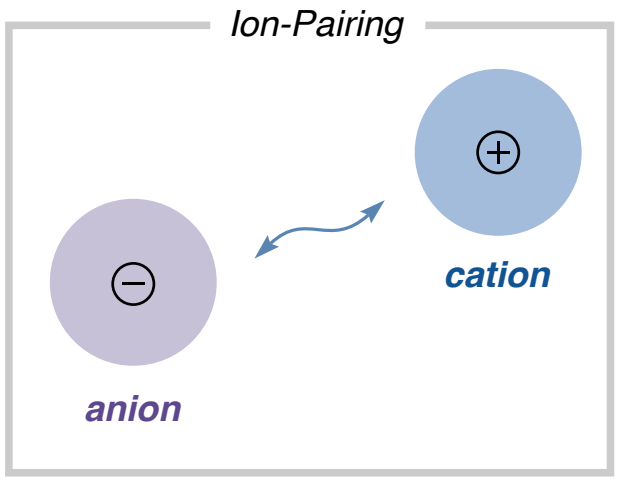

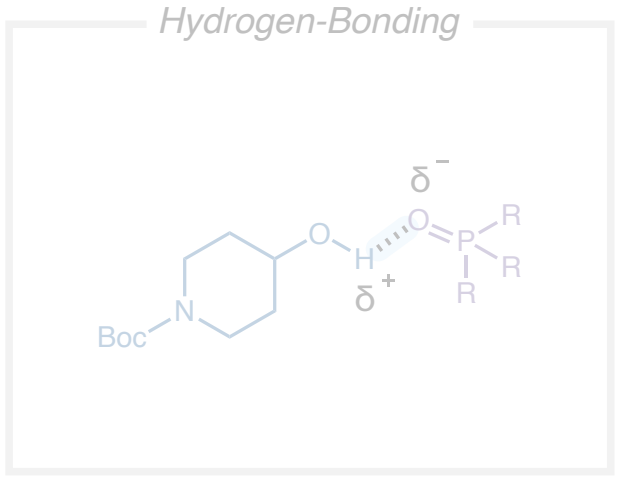

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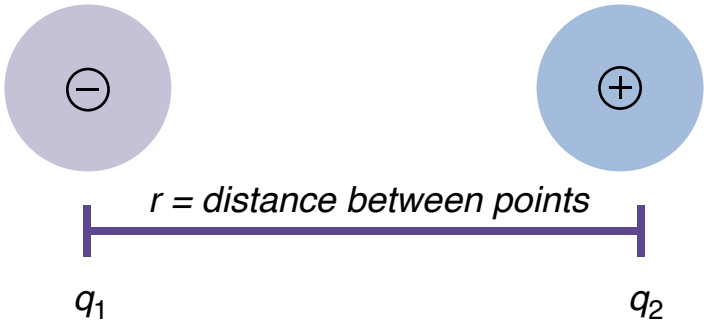

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Ion-pairing highly dependent upon solvent

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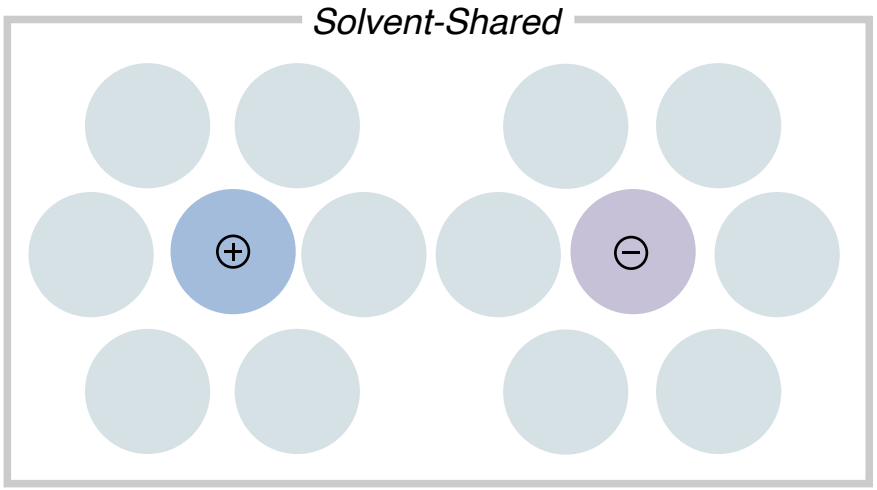
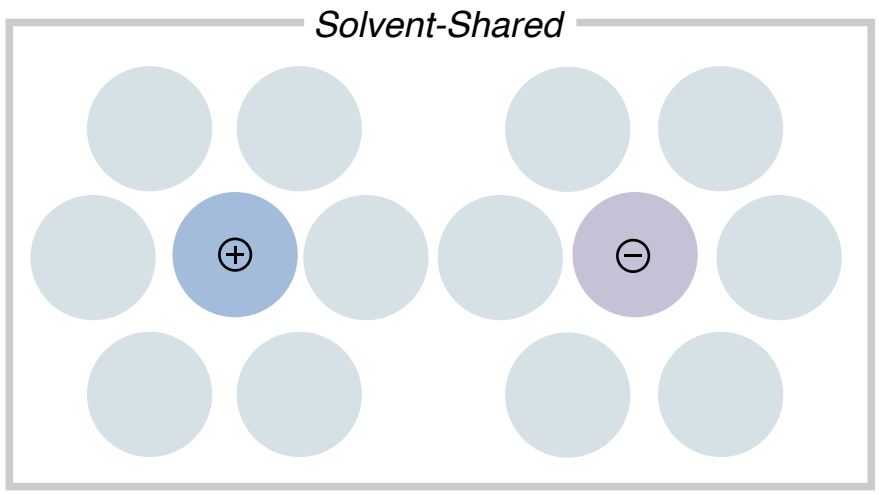
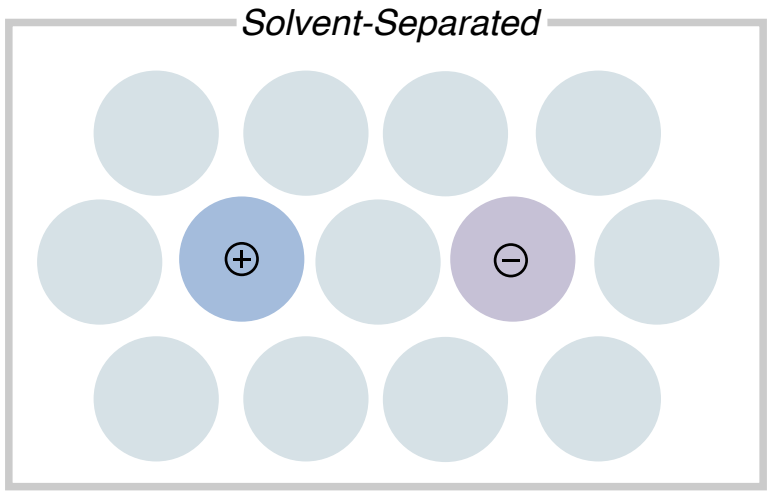
Types of Ion-Pairing



Brak, K. & Jacobsen, E. N. *Angew. Chem. Int. Ed.* **2013**, *52,* 534

Types of Ion-Pairing





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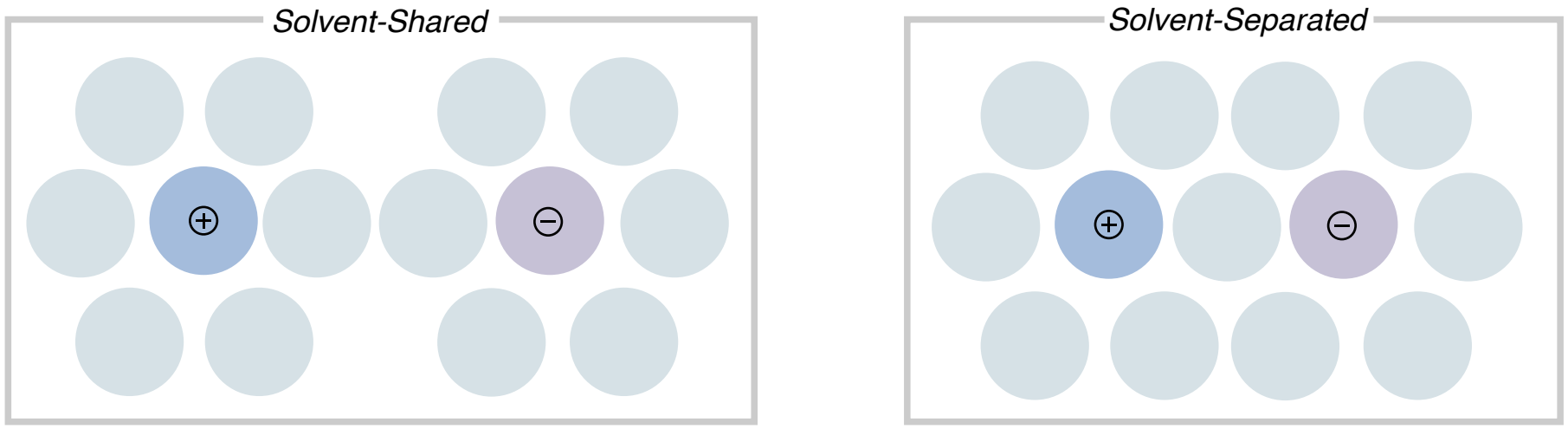

Solvents with high dielectric constants

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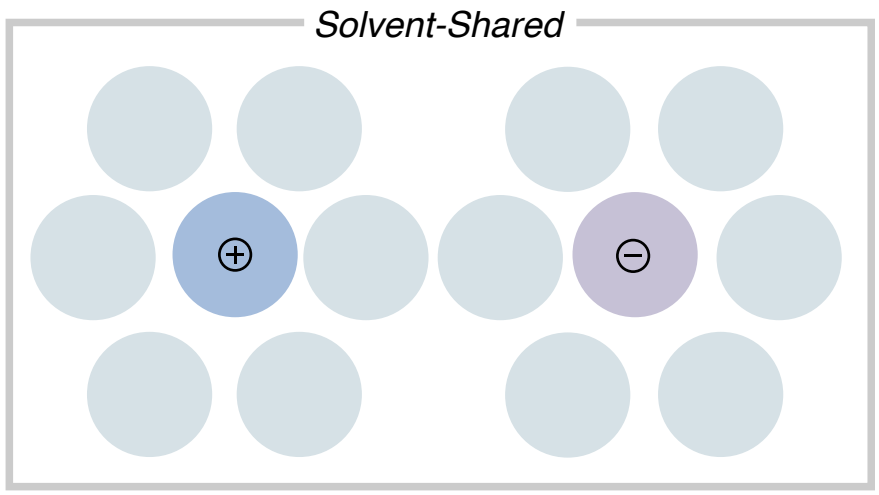

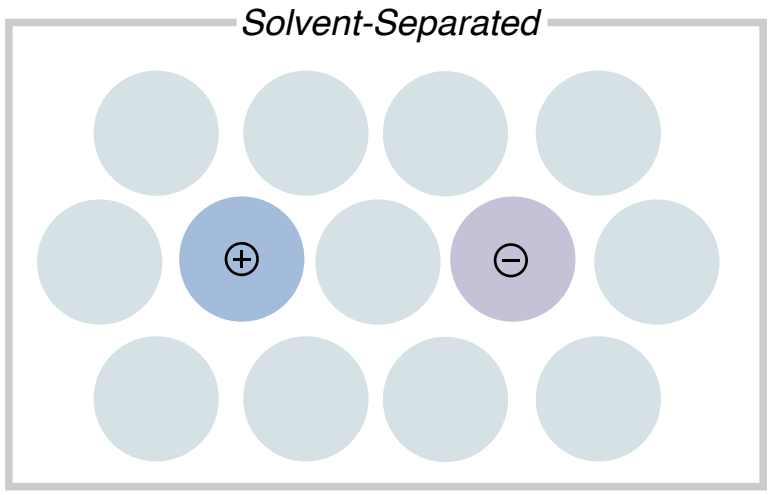

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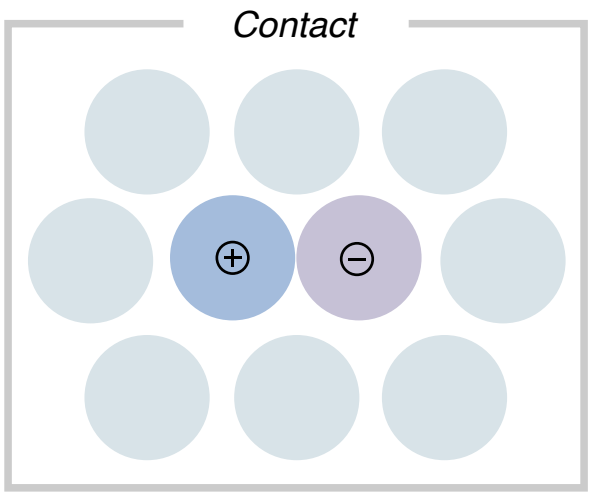
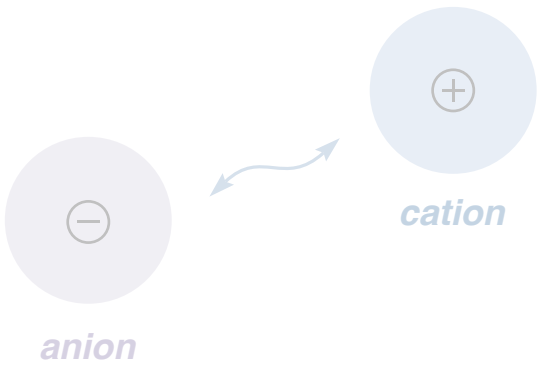


Favored in low dielectric solvents

Brak, K. & Jacobsen, E. N. *Angew. Chem. Int. Ed.* **2013**, *52,* 534

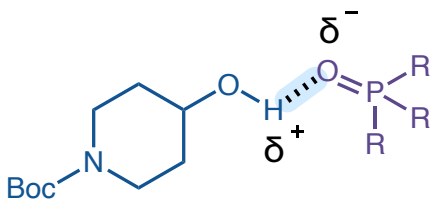
Hydrogen Bonding

Ion-Pairing



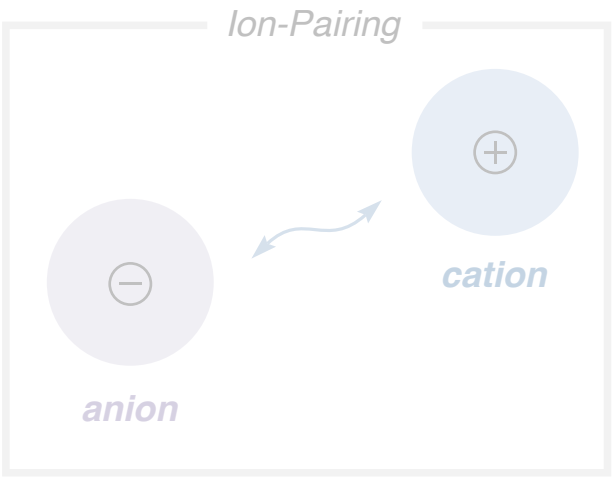
An X—H - A interaction is called a "hydrogen bond", if
1. it constitutes a local bond
2. X—H acts as proton donor to A

Hydrogen-Bonding



Taylor, M. S. & Jacobsen, E. N. *Angew. Chem. Int. Ed.* **2006**, 45, *1520*

Hydrogen Bonding



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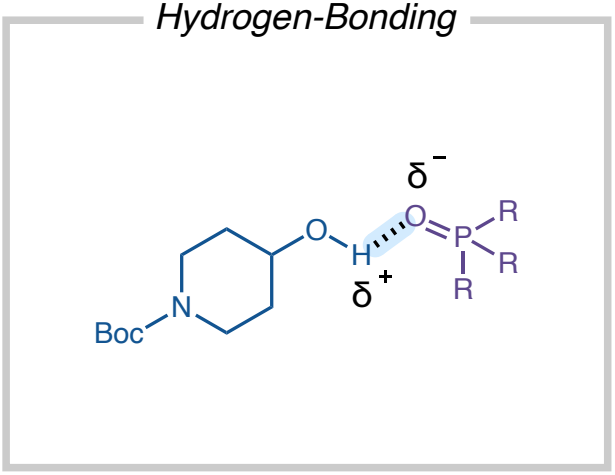

	Strong	Moderate	Weak
type of bonding	Mostly covalent	Mostly electrostatic	Electrostatic
Length of H-bond (Å)	1.2-1.5	1.5-2.2	2.2-3.2
Bond angles (°)	175-180	130-180	90-150
Bond energy (kcal/mol)	14-40	4-15	< 4
Typical example	NH—N in conjugate acid of proton sponge	NH—O=C in peptide helices and sheets	Bonds involving C—H donors to N or O acceptors

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What molecules can act as H-bond Acceptors/Donors?

Important contributions from Taft, Abraham, Franz, Kozlowski, Hunter and others

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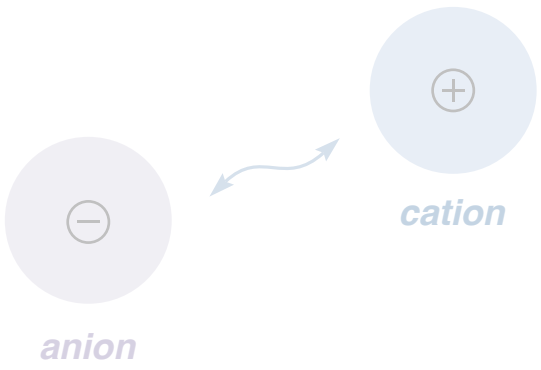

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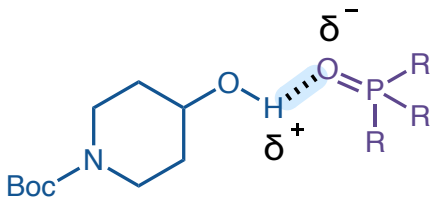

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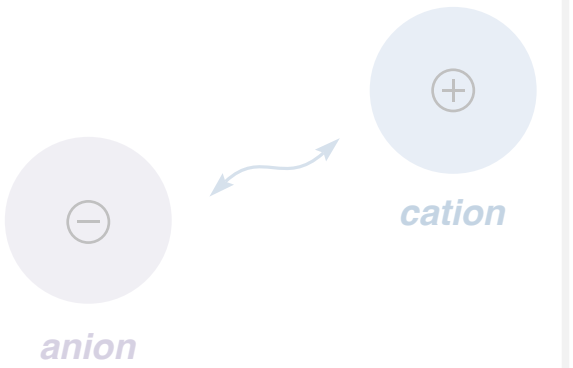

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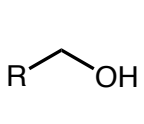

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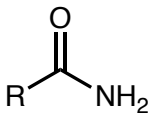

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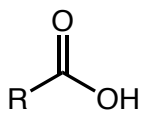

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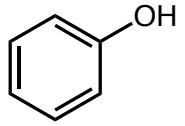

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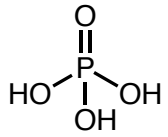

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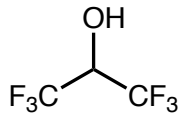
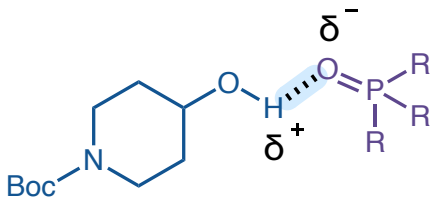


4.5

Kamlett-Taft α parameter - ability to act as an H-bond donor

Hydrogen-Bonding



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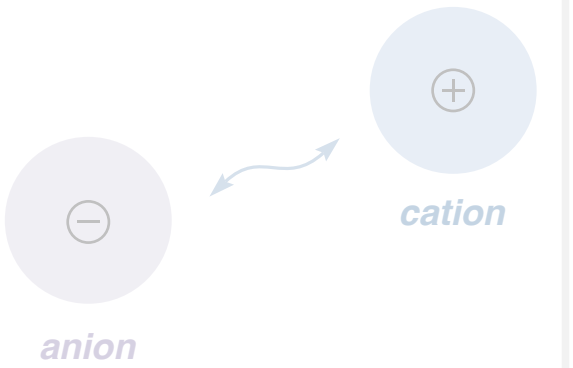

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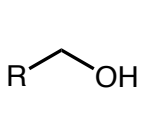

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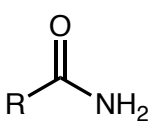

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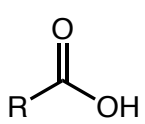

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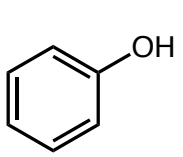

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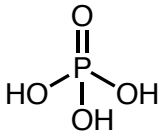

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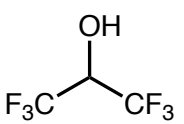

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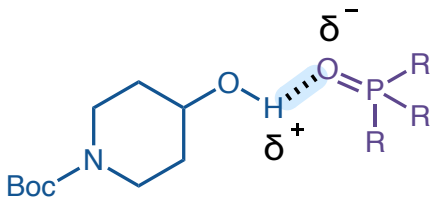
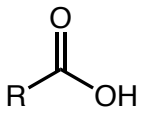
Hydrogen-Bonding





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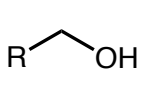

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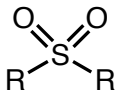

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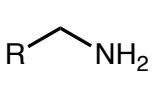

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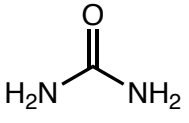

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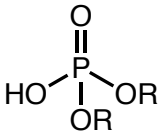


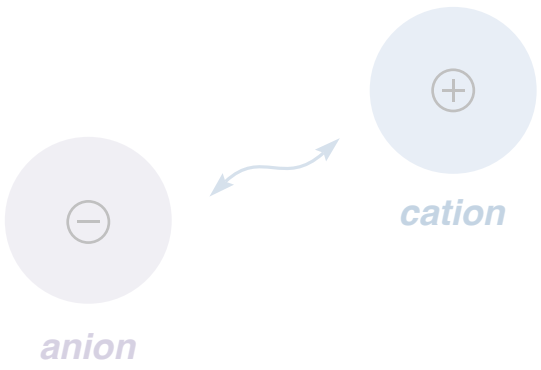
8.9

Kamlett-Taft β parameter - ability to act as an H-bond acceptor

Hunter, C. A. *Angew. Chem. Int. Ed.* **2004**, 43, *5310*

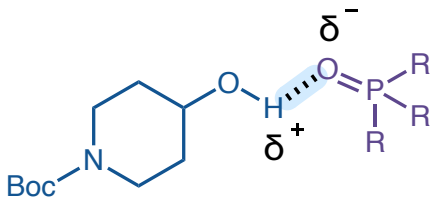
2-Point H-Bond Donors

Ion-Pairing



2-point hydrogen bonding leads to rigidity

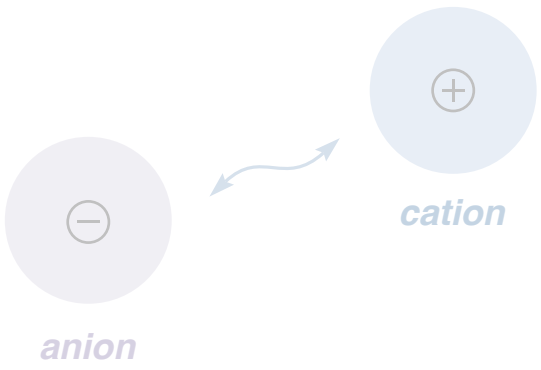
Hydrogen-Bonding



Doyle, A. G. & Jacobsen, E. N. *Chem. Rev.* **2007**, *107*, 5713

2-Point H-Bond Donors

Ion-Pairing



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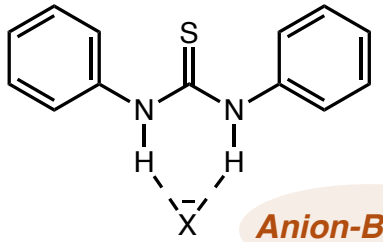
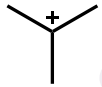


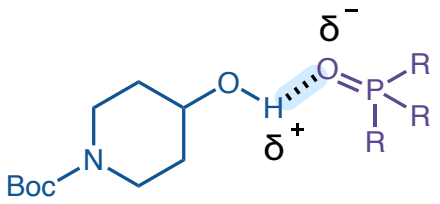
H-Bonding

Anion-Binding



Ion-Pairing

Hydrogen-Bonding



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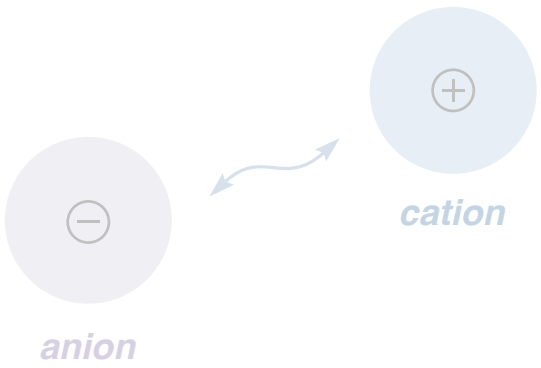
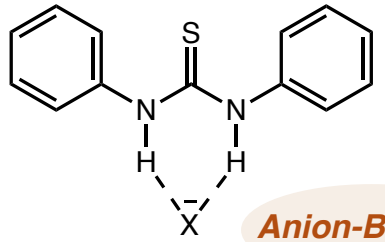
2-Point H-Bond Donors

Ion-Pairing

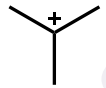


2-point hydrogen bonding leads to rigidity



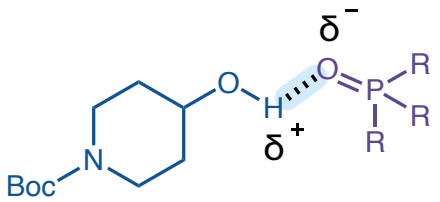
H-Bonding

Anion-Binding

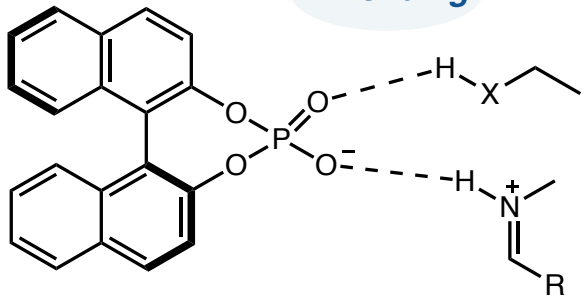


Ion-Pairing

Hydrogen-Bonding



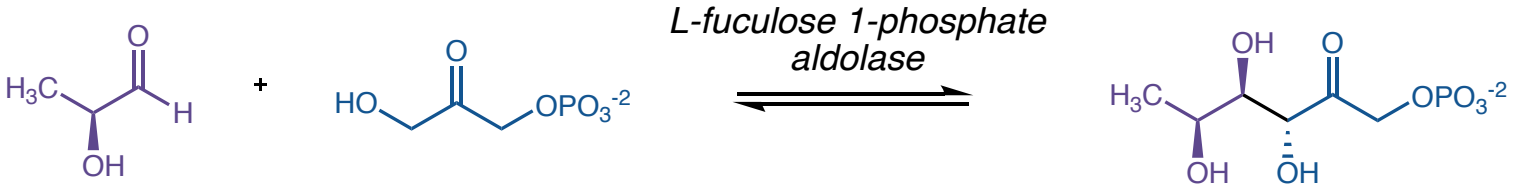
H-Bonding



Doyle, A. G. & Jacobsen, E. N. *Chem. Rev.* **2007**, *107*, 5713

Enzymes are the inspiration

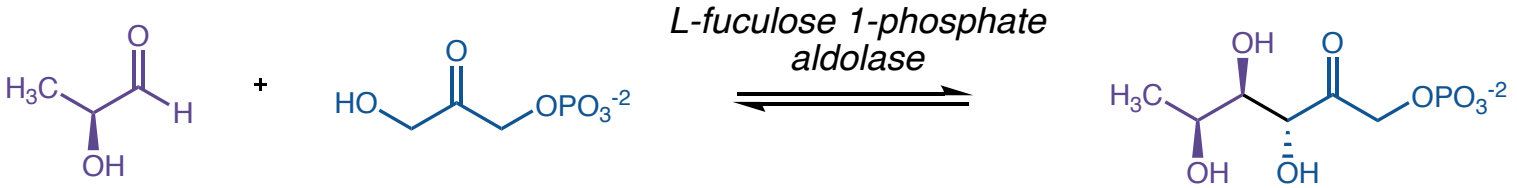
Enzymatic case study



Taylor, M. S.. & Jacobsen, E. N. *Angew. Chem. Int. Ed.* **2006**, 45*, 1520*

Enzymes are the inspiration

Enzymatic case study

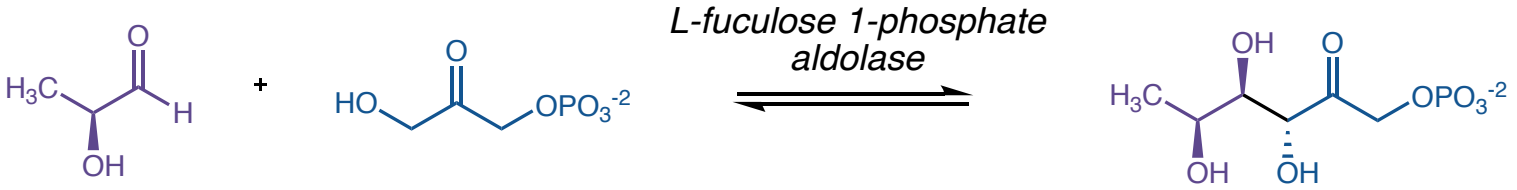


Enzymes use electrostatic interactions in their active sites

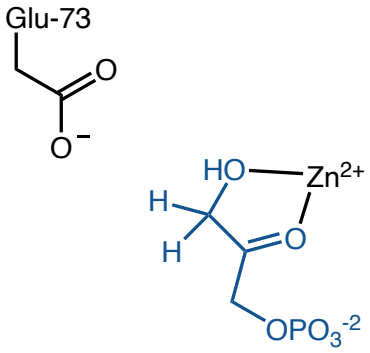
Taylor, M. S.. & Jacobsen, E. N. *Angew. Chem. Int. Ed.* **2006**, 45*, 1520*

Enzymes are the inspiration

Enzymatic case study



Enzymes use electrostatic interactions in their active sites



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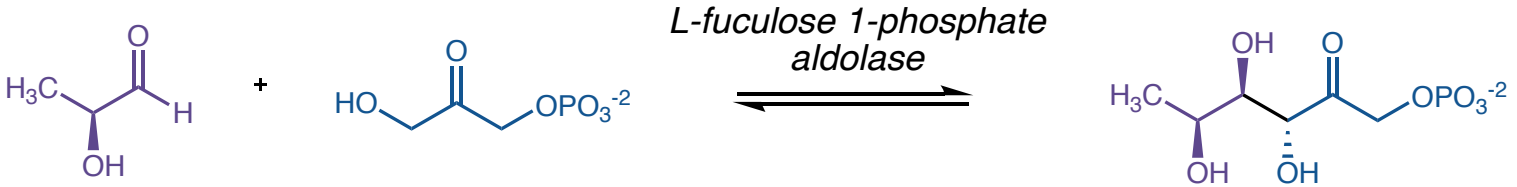
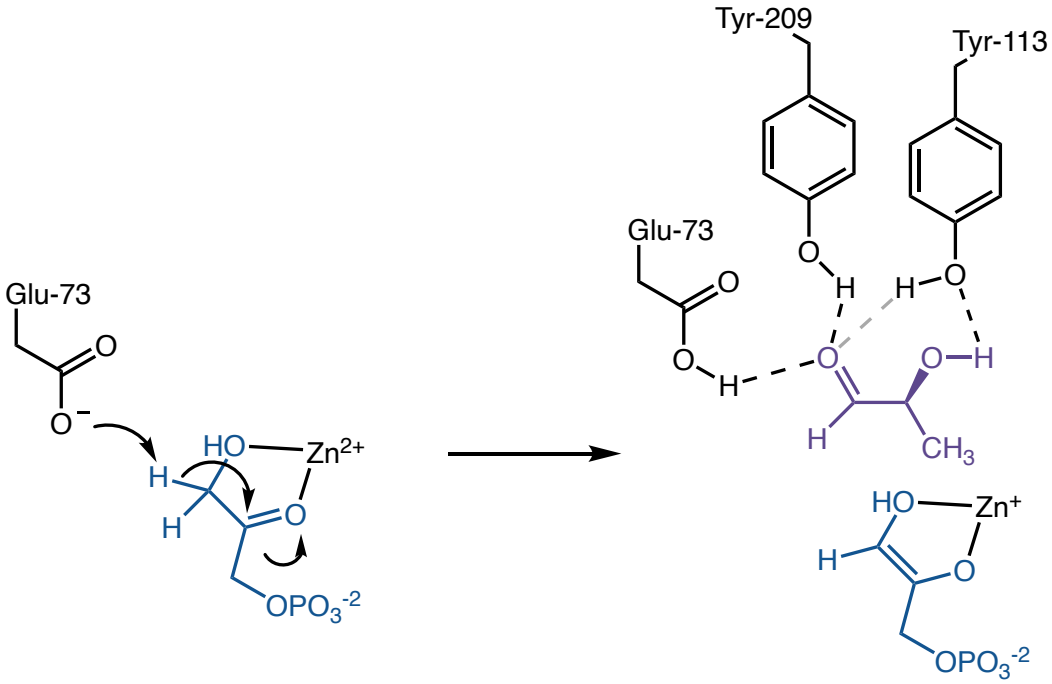


Enzymes use electrostatic interactions in their active sites



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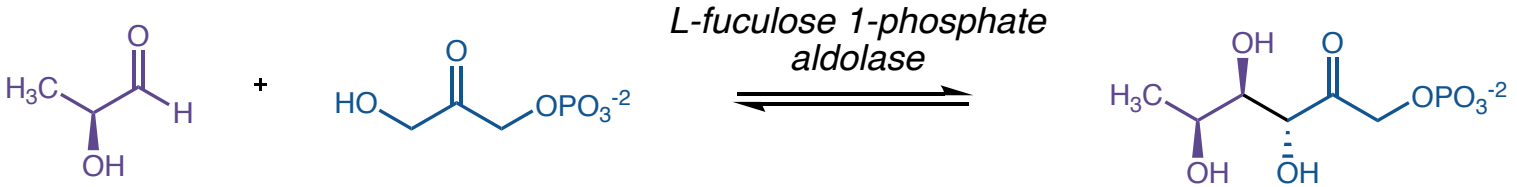

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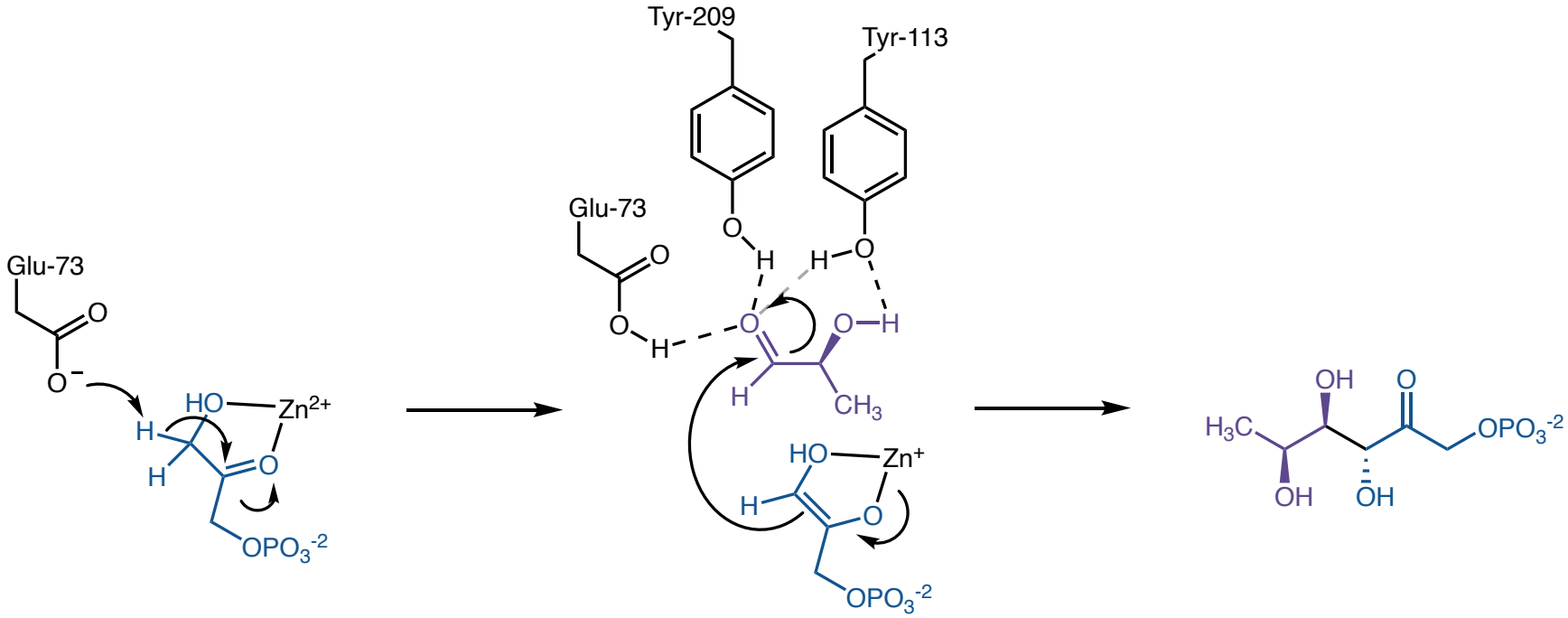

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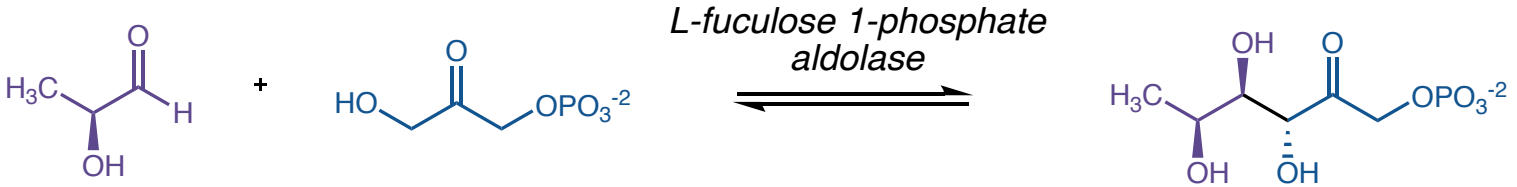
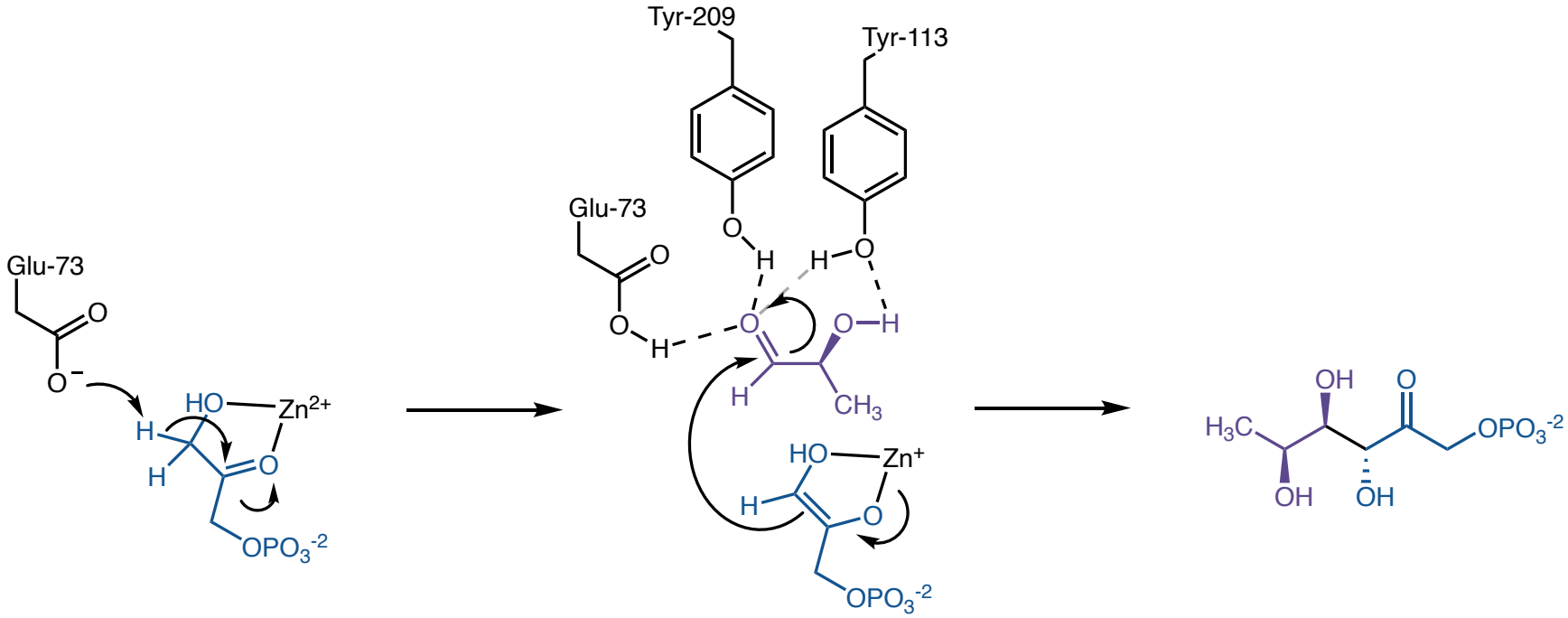
Enzymes are the inspiration

Enzymatic case study



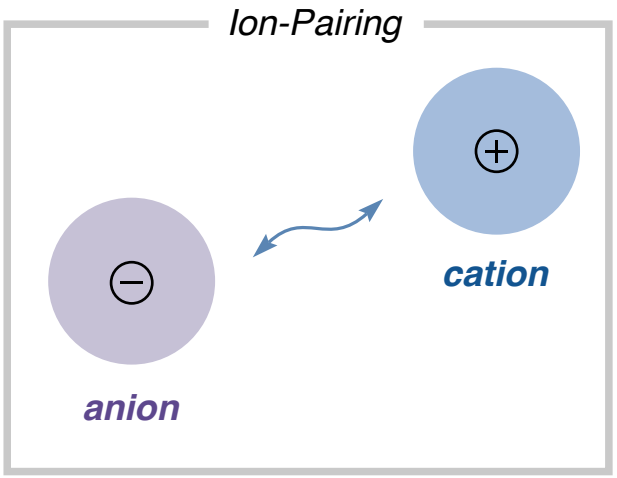
Enzymes use electrostatic interactions in their active sites



Multiple electrostatic interactions control the selectivity

Taylor, M. S.. & Jacobsen, E. N. *Angew. Chem. Int. Ed.* **2006**, 45, *1520*

Can we use electrostatic interactions in T.M. catalysis?



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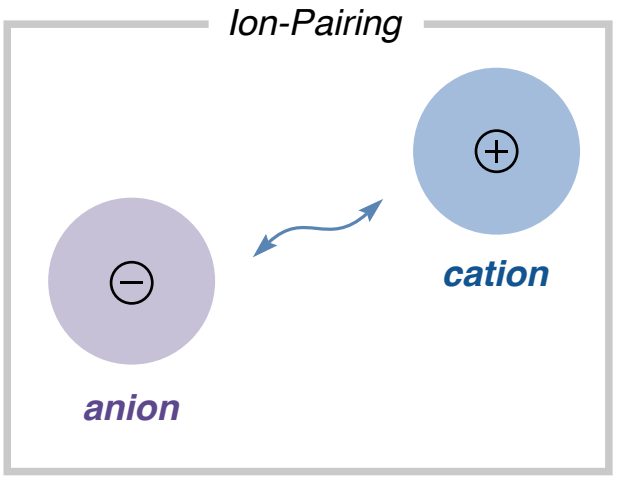

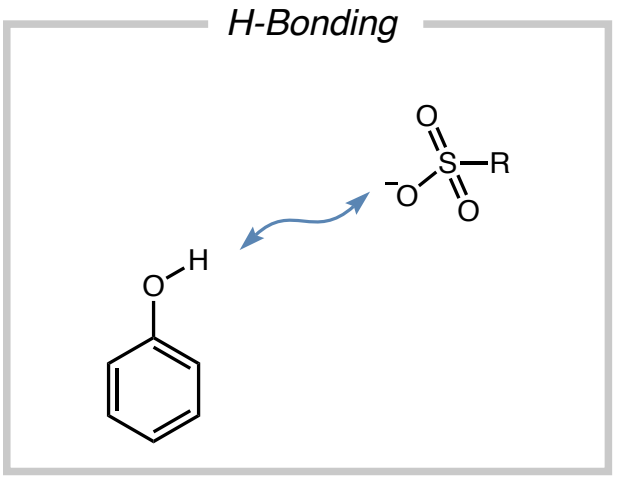

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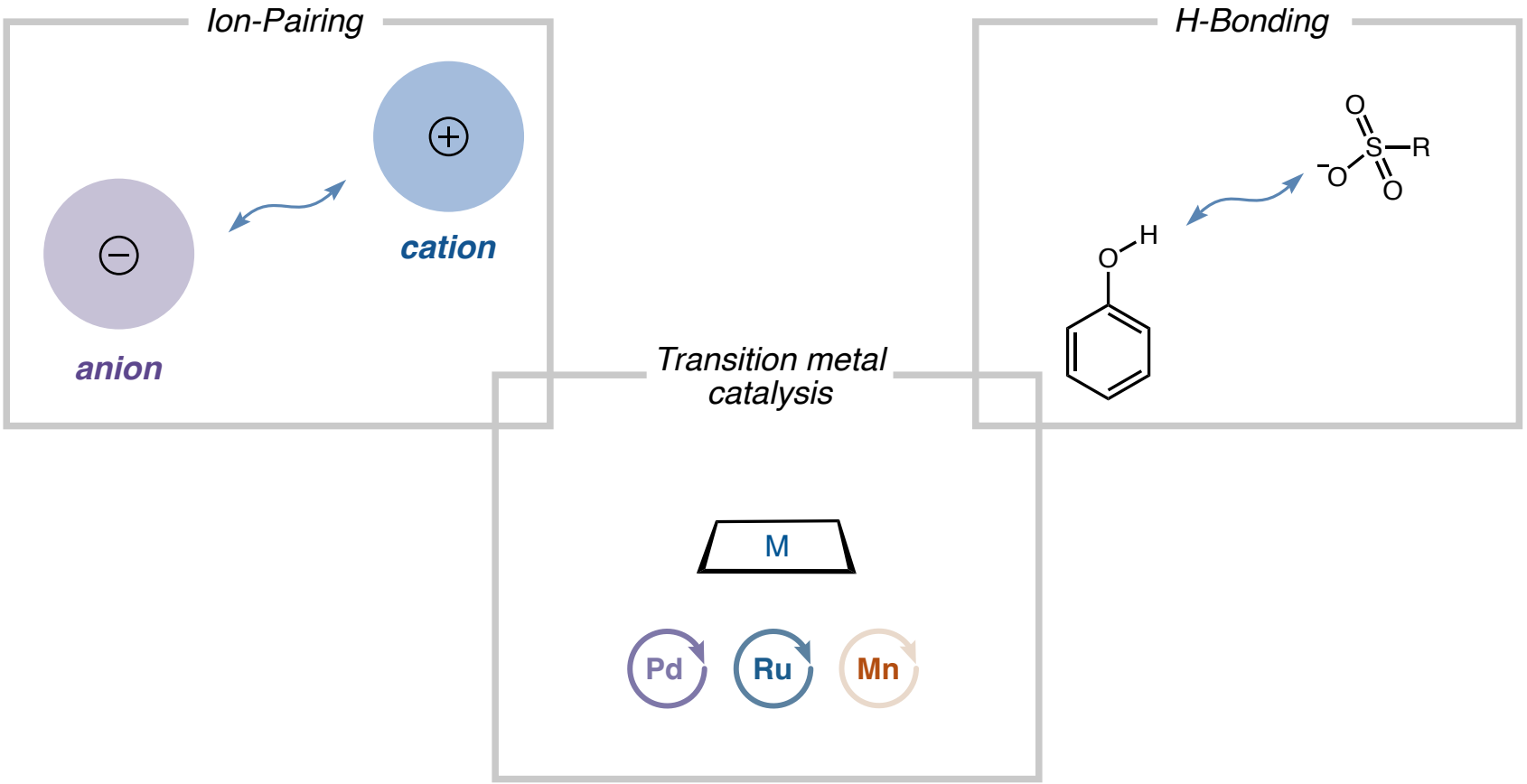
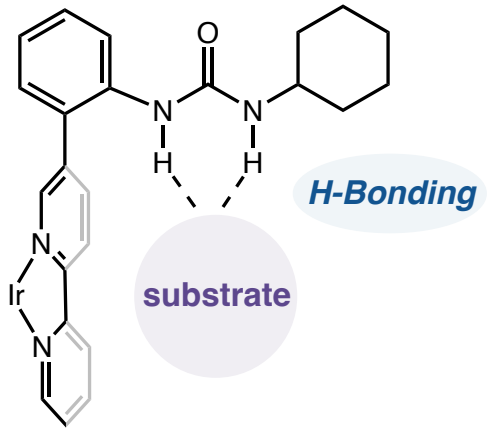


What will be covered

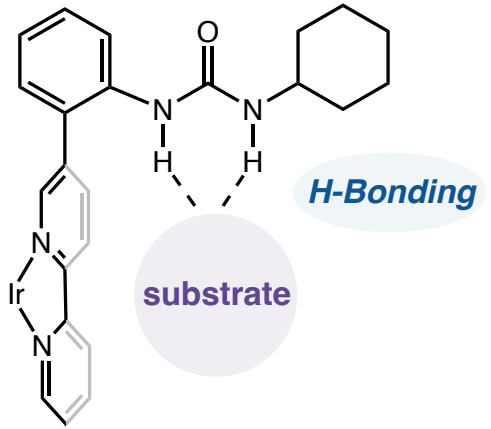
What will be covered

Hydrogen-bonding

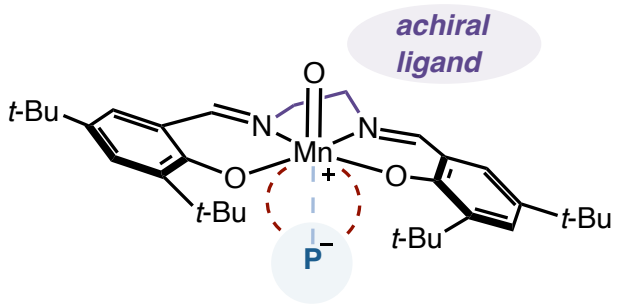


What will be covered

Hydrogen-bonding

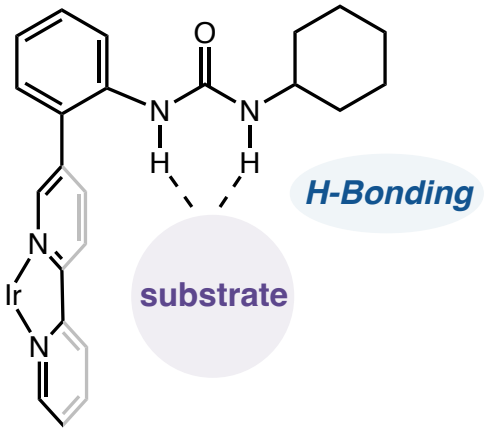


Ion-pairing

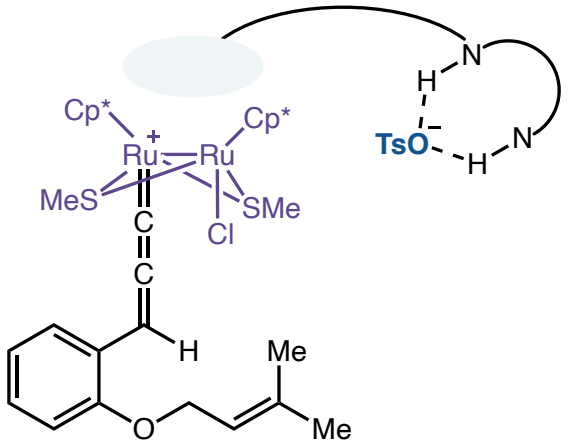


What will be covered

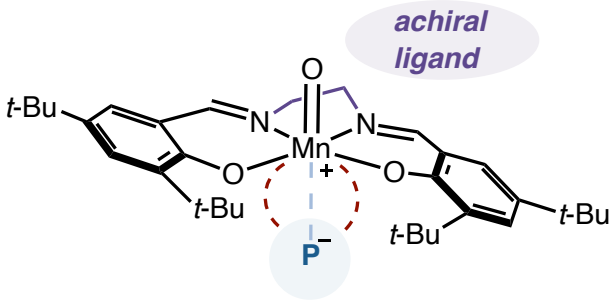
Hydrogen-bonding



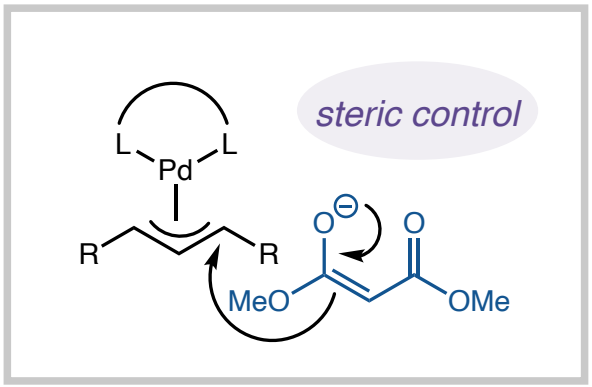
Ion-pairing & H-Bonding



Ion-pairing

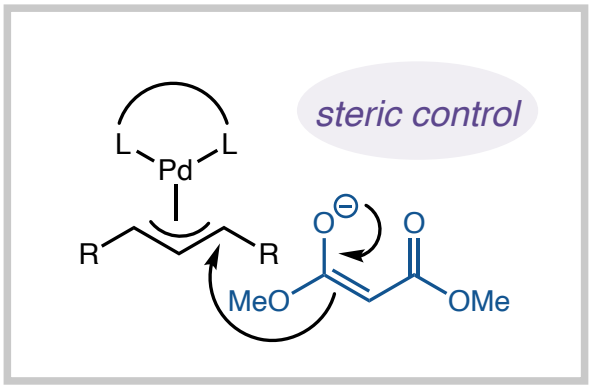


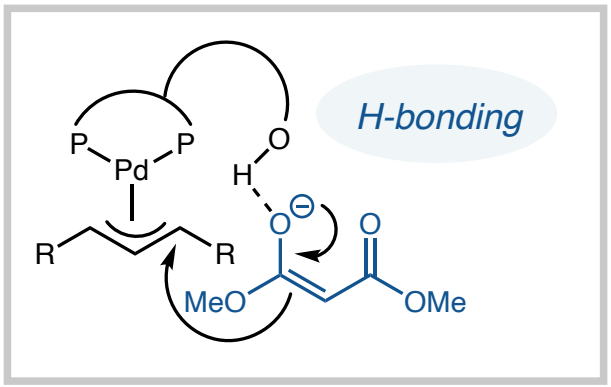
Hayashi H-bonding ligands



Ito, Y., Hagihara, T., Yamamotom A., & Hayashi, T. *Tet. Lett.* **1986**, *27,* 191

Hayashi H-bonding ligands





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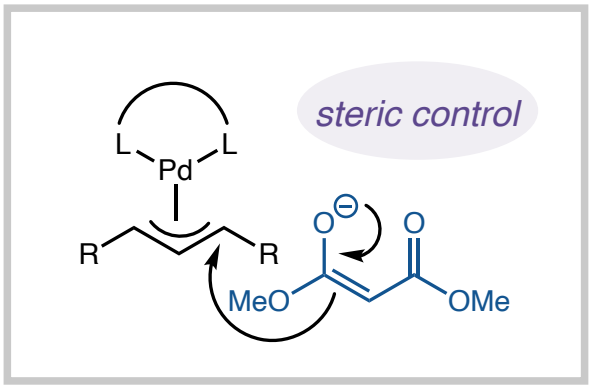
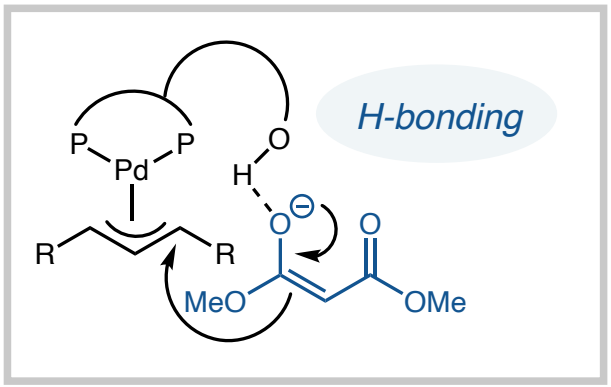
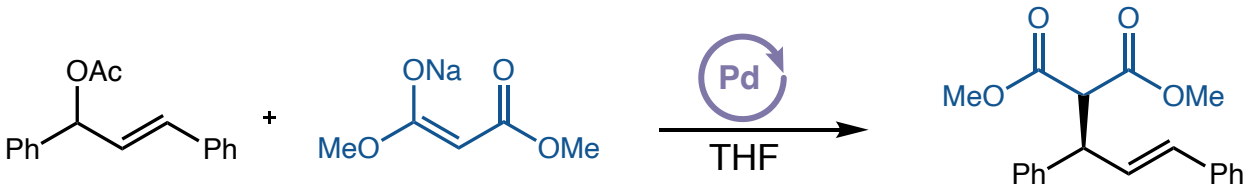
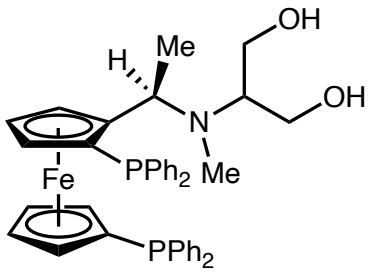


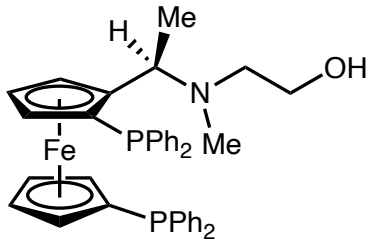






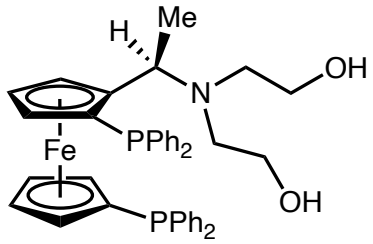
Ligand "A"

97% yield, 90% ee



Ligand "B"

86% yield, 81% ee

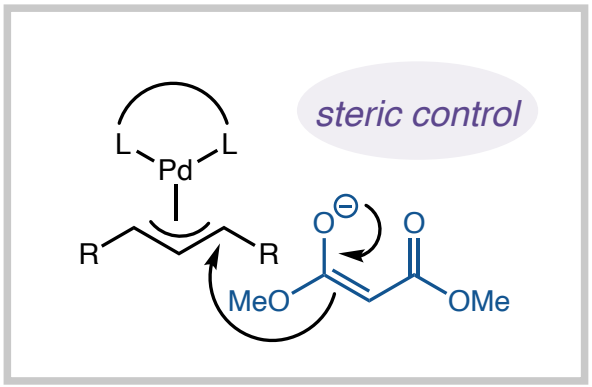


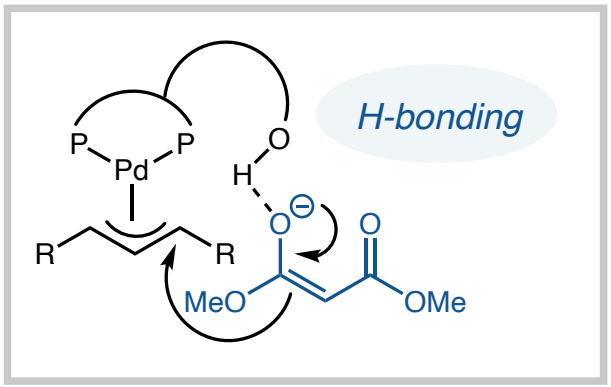
Ligand "C"

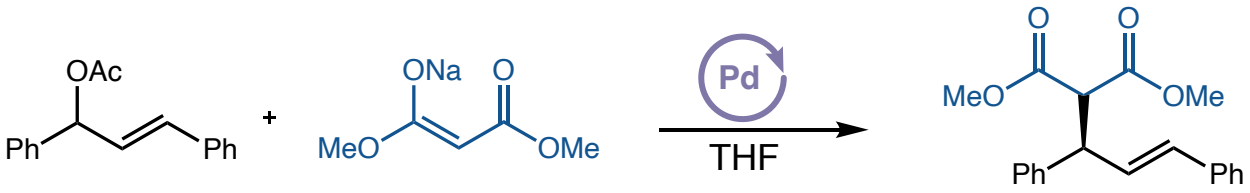
86% yield, 71% ee

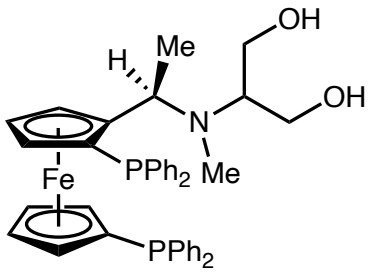
Ito, Y., Hagihara, T., Yamamotom A., & Hayashi, T. *Tet. Lett.* **1986**, *27,* 191

Hayashi H-bonding ligands









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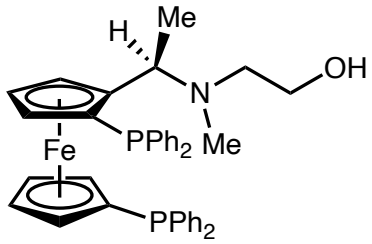
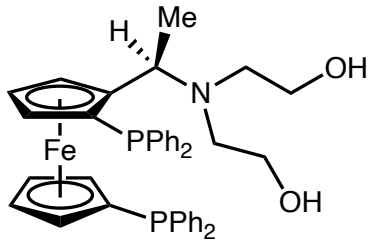
97% yield, 90% ee



Ligand "B"

86% yield, 81% ee



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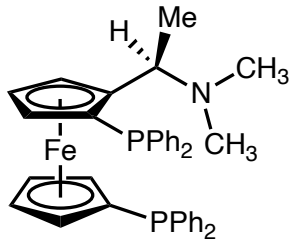
86% yield, 71% ee



Ligand "D"

51% yield, 62% ee

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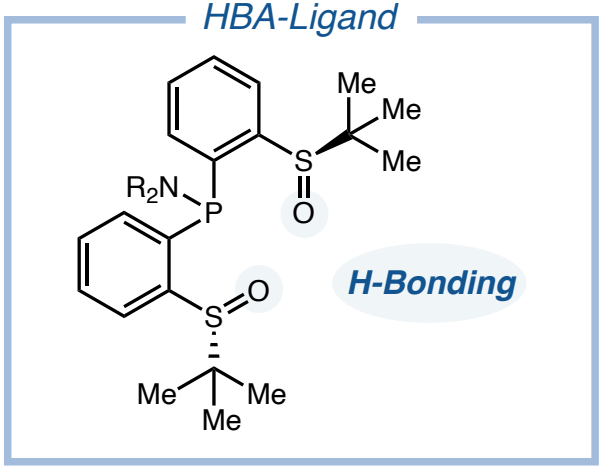
Indole H-bonding

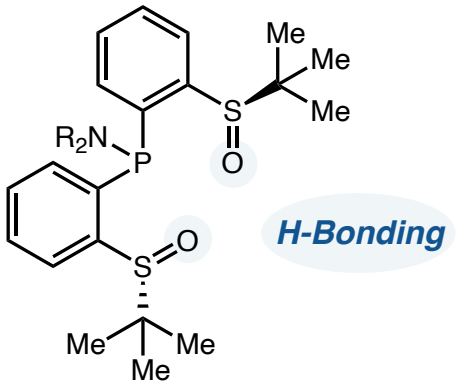
HBA-Ligand



Du, L. *et. al. Angew. Chem. Int. Ed.* **2013**, 52, 4207

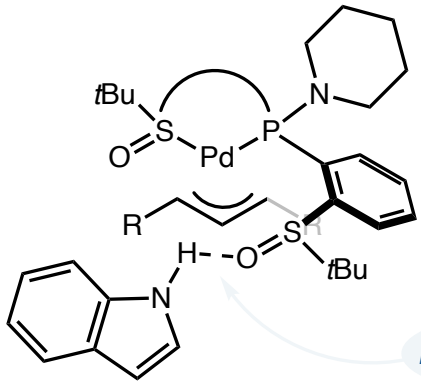
Indole H-bonding

HBA-Ligand



H-Bonding

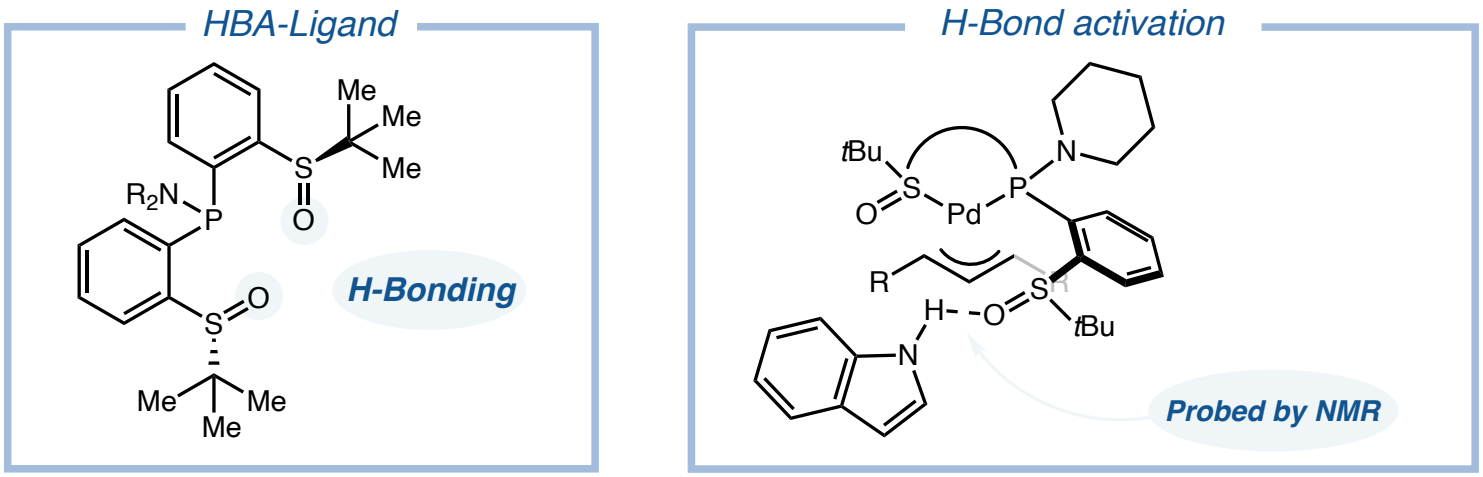
H-Bond activation

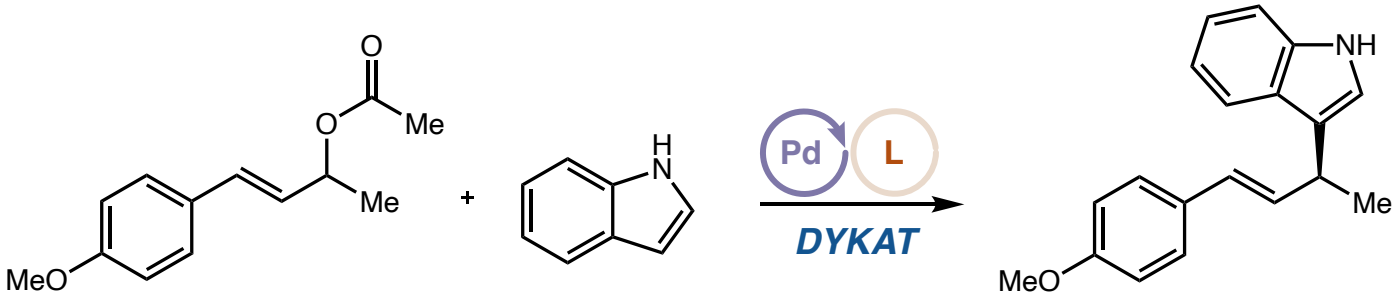


Probed by NMR

Du, L. *et. al. Angew. Chem. Int. Ed.* **2013**, 52, 4207

Indole H-bonding

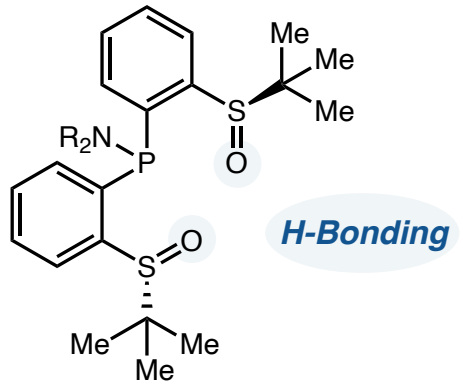




Du, L. *et. al. Angew. Chem. Int. Ed.* **2013**, 52, 4207

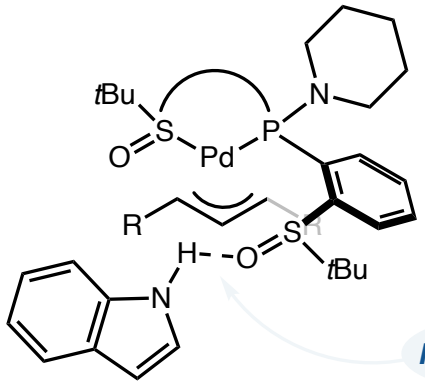
Indole H-bonding

HBA-Ligand

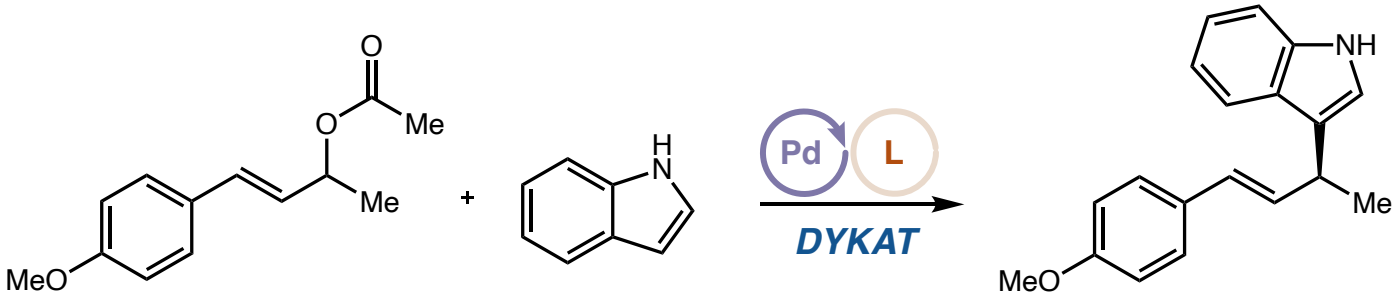


H-Bonding

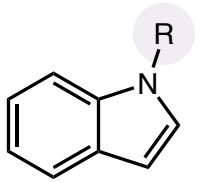
H-Bond activation



Probed by NMR



Mechanistic probe



R = Me, Bn or Boc
no reaction

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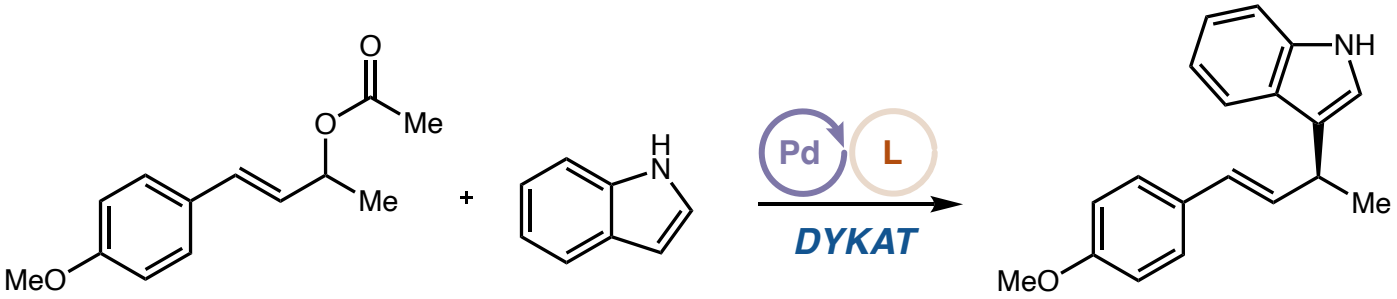
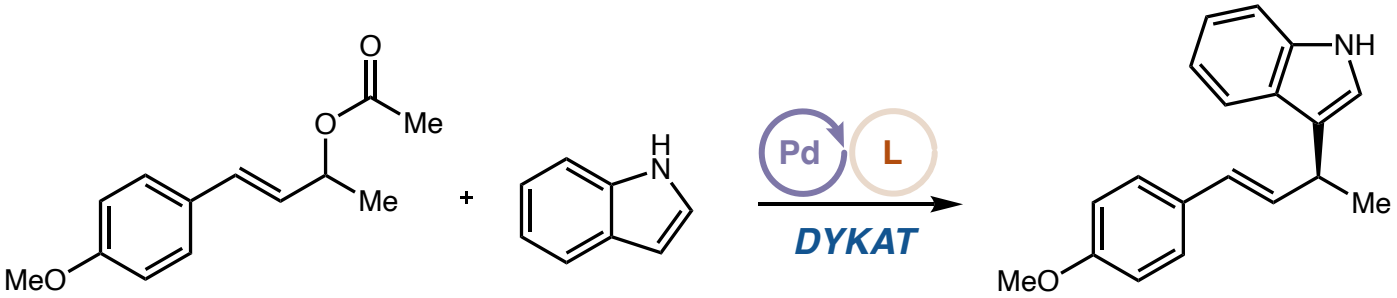
Indole H-bonding



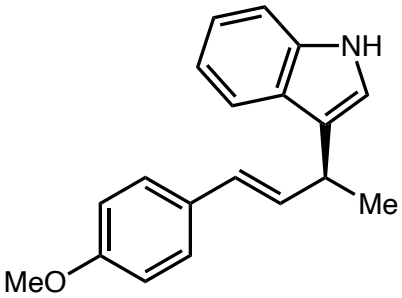
H-bonding allows for DYKAT indole allylation

Du, L. *et. al. Angew. Chem. Int. Ed.* **2013**, 52, 4207

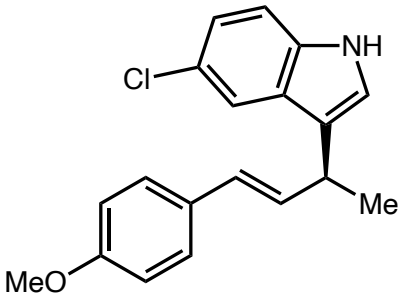
Indole H-bonding



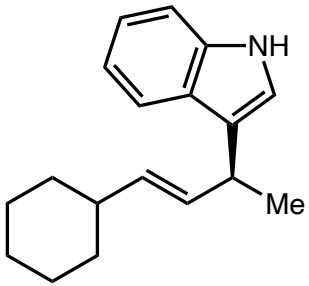
H-bonding allows for DYKAT indole allylation



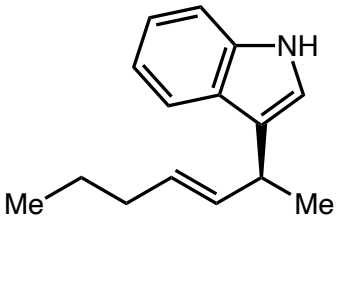
84% yield
94% ee



75% yield
93% ee



65% yield
88% ee



67% yield
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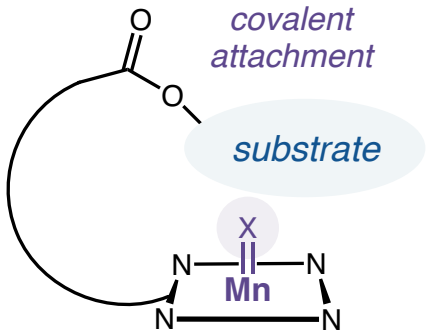
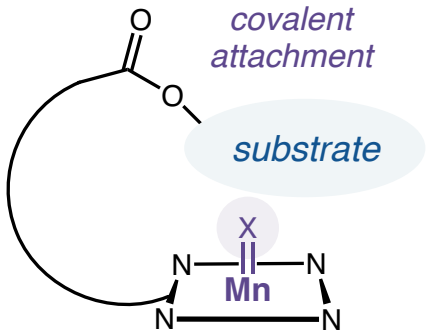
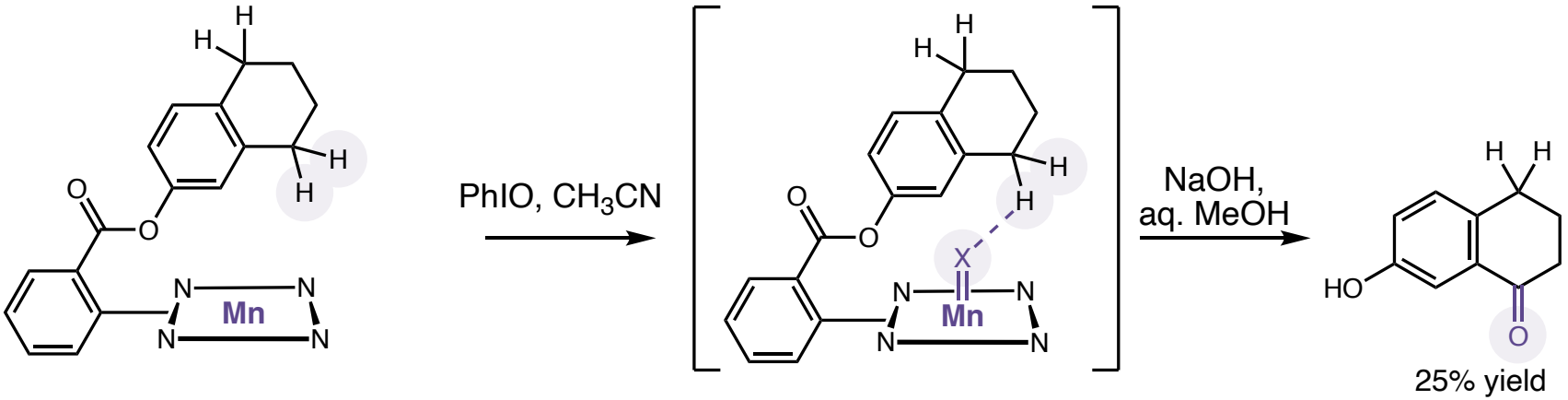


Covalent binding strategy

Moreira, R. F., Wehn, P. M., Sames, D. *Angew. Chem. Int. Ed.* **2000**, *39,* 1618

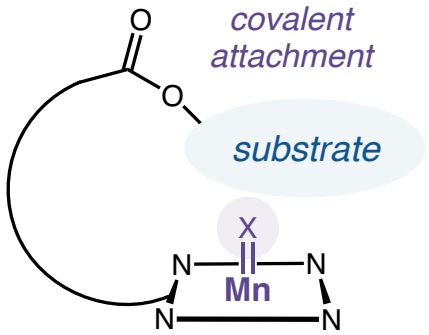


Covalent binding strategy

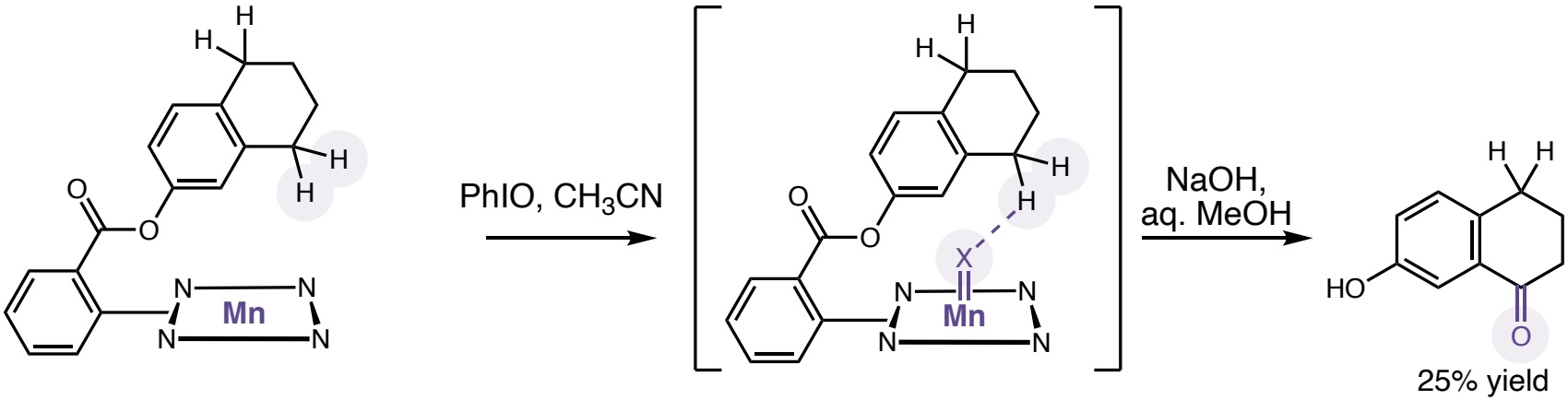


25% yield

Moreira, R. F., Wehn, P. M., Sames, D. *Angew. Chem. Int. Ed.* **2000**, *39,* 1618



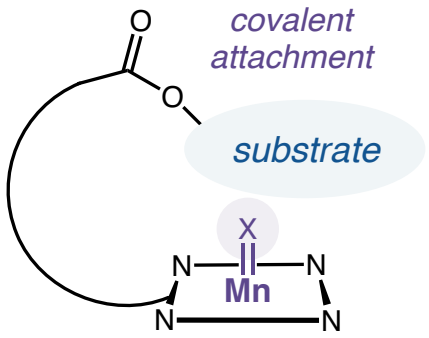
Covalent binding strategy

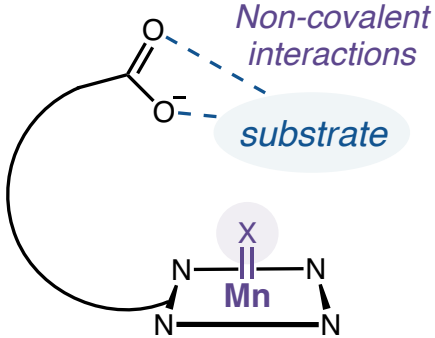


Highly selective but not catalytic

Moreira, R. F., Wehn, P. M., Sames, D. *Angew. Chem. Int. Ed.* **2000**, *39,* 1618

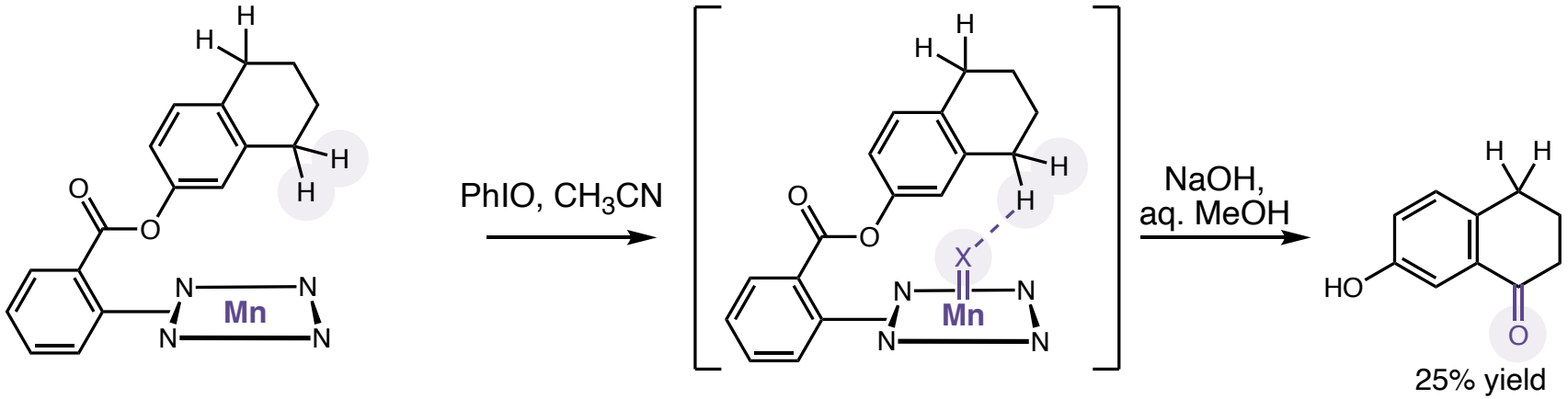
Crabtree - Molecular recognition





Covalent binding strategy

Templated strategy for C—H oxidation



Highly selective but not catalytic

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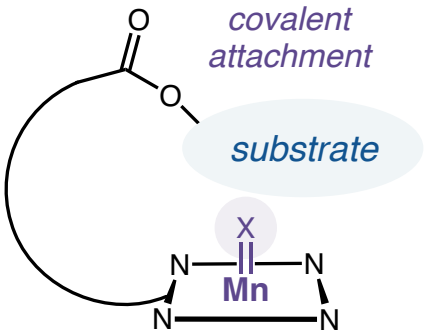
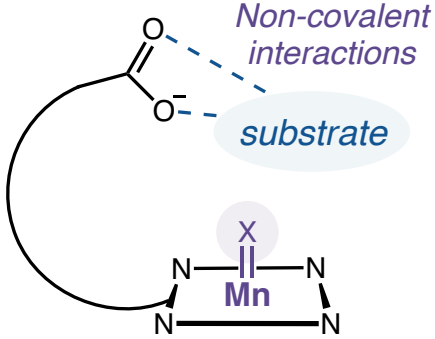
Crabtree - Molecular recognition

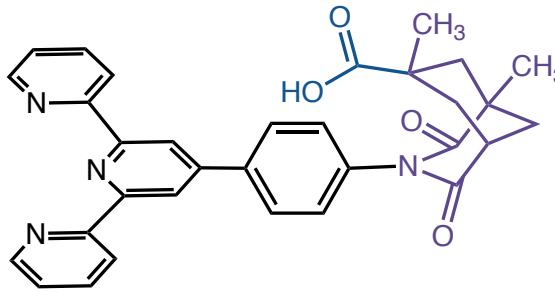


Covalent binding strategy



Templated strategy for C—H oxidation

H-bond donor & acceptor

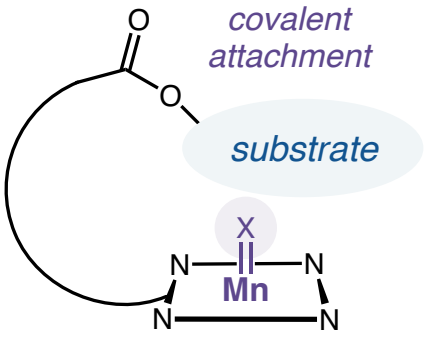


"U-turn motif"

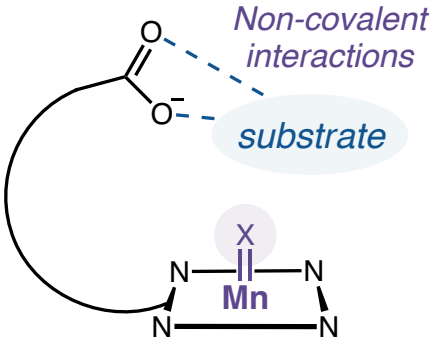
can promote Mn oxidation

Das, S., Incarvito, C. D., Crabtree, R. H., & Brudvig, G. W. *Science* **2006**, *312*, 1941

Crabtree - Molecular recognition

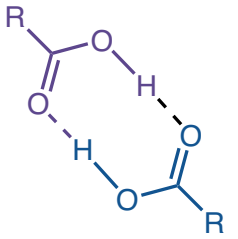


Covalent binding strategy



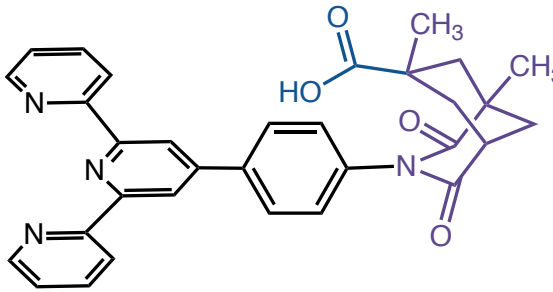
Templated strategy for C—H oxidation

substrate CO_2H



ligand CO_2H

H-bond donor & acceptor



"U-turn motif"

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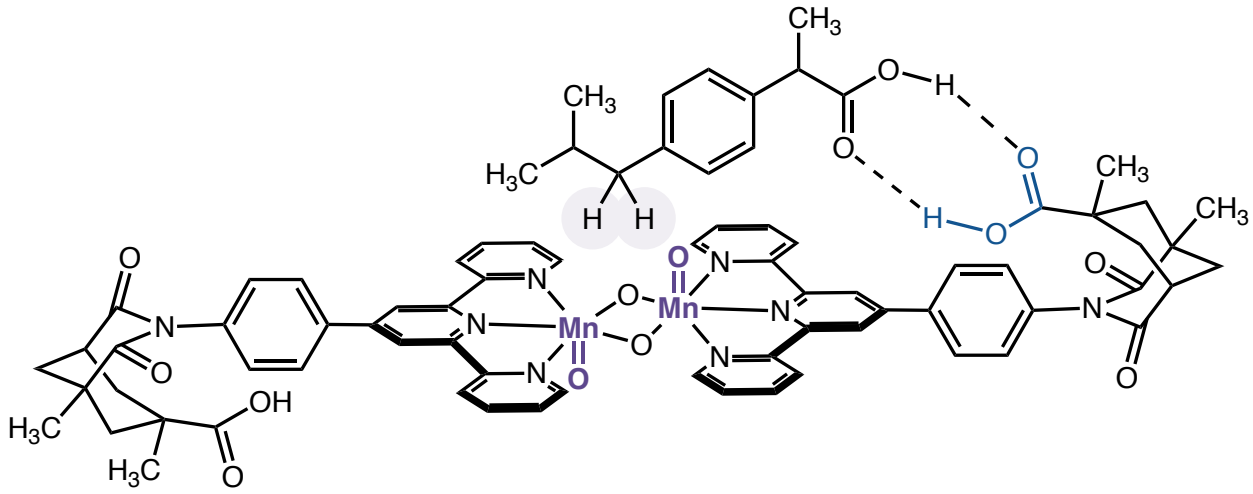
Das, S., Incarvito, C. D., Crabtree, R. H., & Brudvig, G. W. *Science* **2006**, *312*, 1941

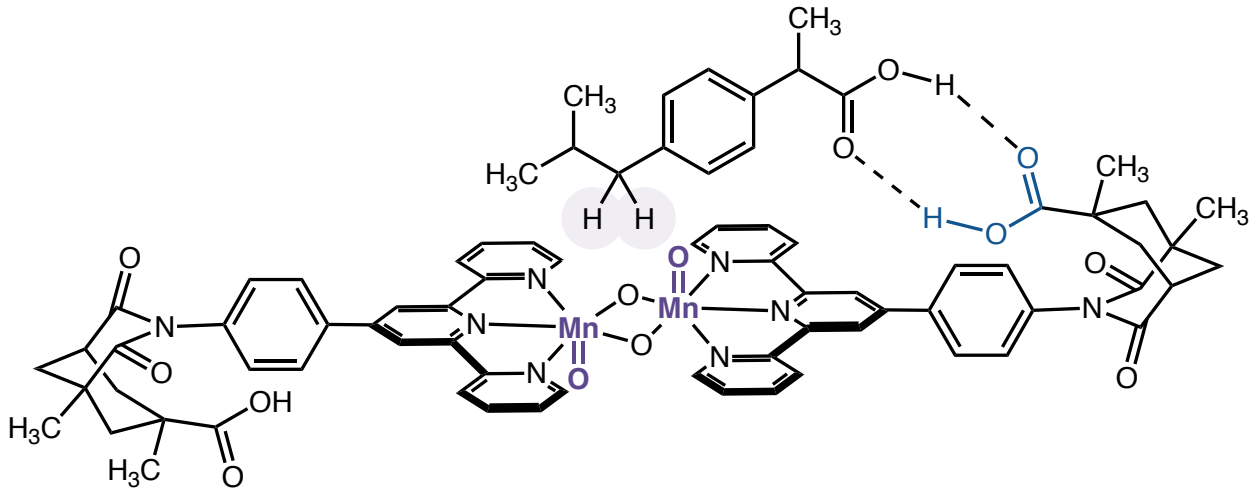
Crabtree - Molecular recognition



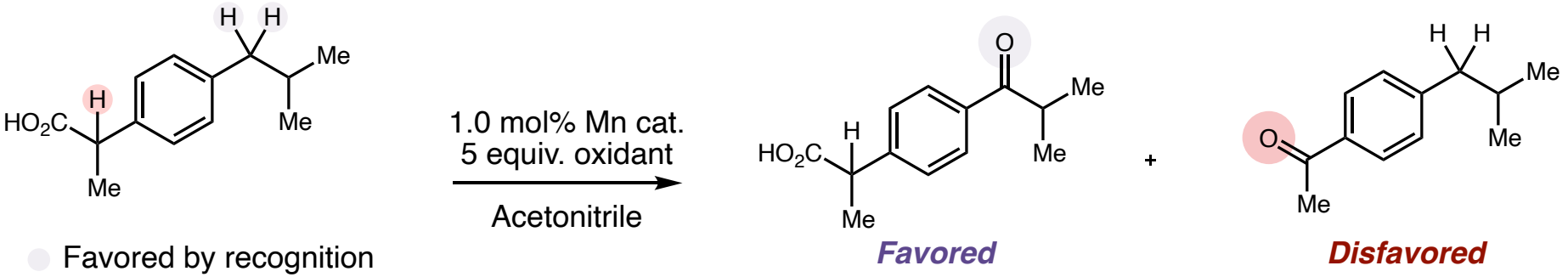
Can substrate recognition afford selective oxidation?

Das, S., Incarvito, C. D., Crabtree, R. H., & Brudvig, G. W. *Science* **2006**, *312*, 1941

Crabtree - Molecular recognition



Can substrate recognition afford selective oxidation?

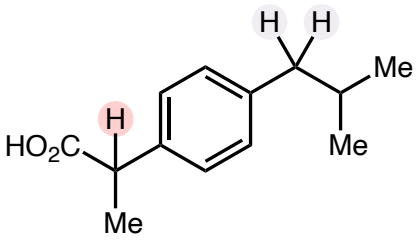


Favored by recognition

Disfavored by recognition

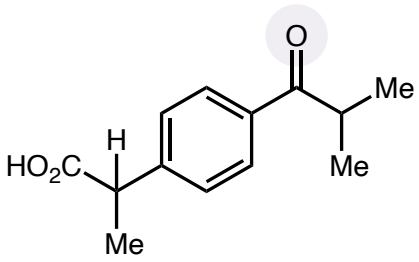
Das, S., Incarvito, C. D., Crabtree, R. H., & Brudvig, G. W. *Science* **2006**, *312*, 1941

Crabtree - Molecular recognition



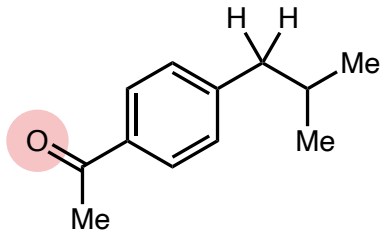
1.0 mol% Mn cat.
5 equiv. oxidant

Acetonitrile



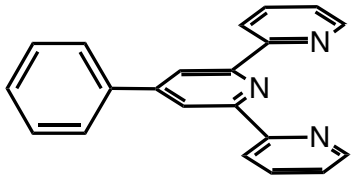
Favored

+



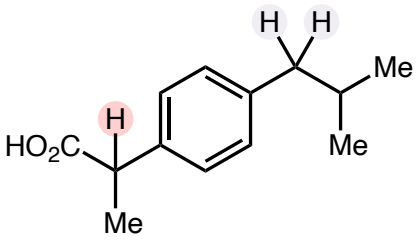
Disfavored

- Favored by recognition
- Disfavored by recognition



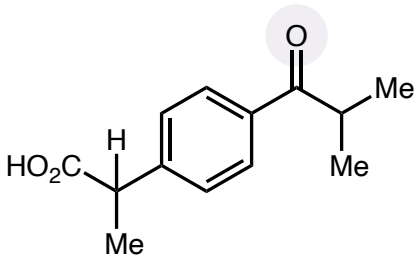
Das, S., Incarvito, C. D., Crabtree, R. H., & Brudvig, G. W. *Science*, **2006**, *312*, 1941

Crabtree - Molecular recognition



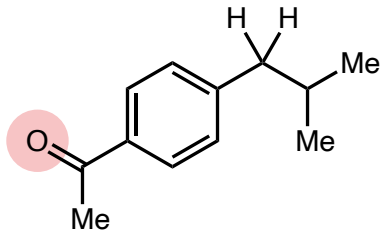
1.0 mol% Mn cat.
5 equiv. oxidant

Acetonitrile



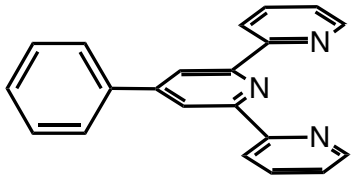
Favored

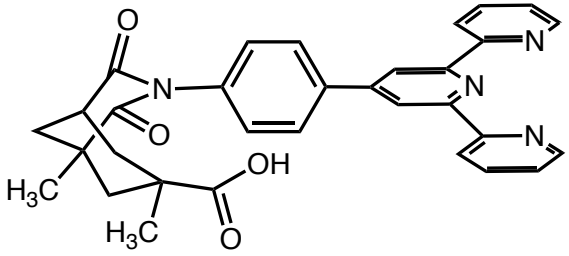
\+



Disfavored

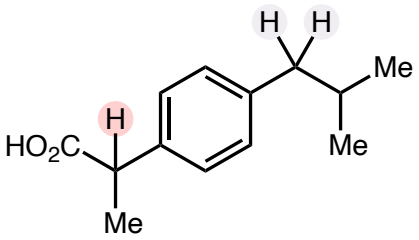
- Favored by recognition
- Disfavored by recognition





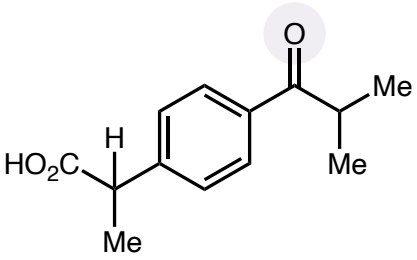
Das, S., Incarvito, C. D., Crabtree, R. H., & Brudvig, G. W. *Science*, **2006**, *312*, 1941

Crabtree - Molecular recognition



1.0 mol% Mn cat.
5 equiv. oxidant

Acetonitrile



Favored

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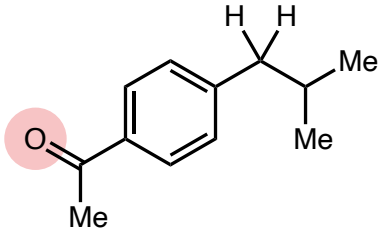
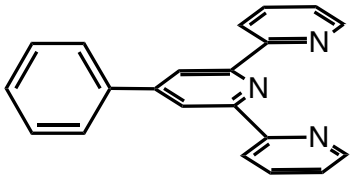
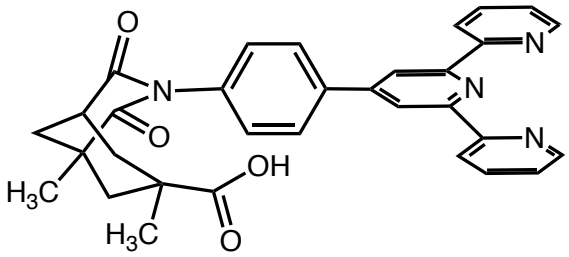


Disfavored

- Favored by recognition
- Disfavored by recognition



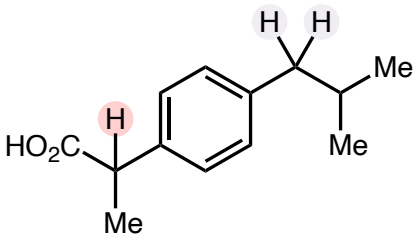


Conversion	Yield (A)	Yield (B)	Selectivity
53%	77%	23%	3:1
53%	98.5%	1.5%	67:1

Significant increase in selectivity using templated strategy

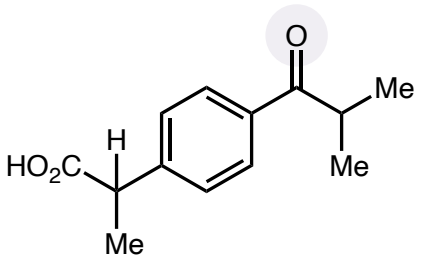
Das, S., Incarvito, C. D., Crabtree, R. H., & Brudvig, G. W. *Science*, **2006**, *312*, 1941

Crabtree - Molecular recognition



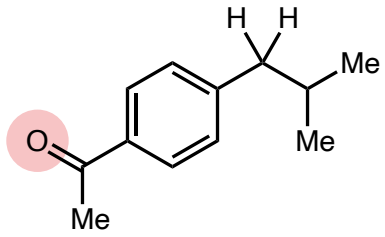
1.0 mol% Mn cat.
5 equiv. oxidant

Acetonitrile



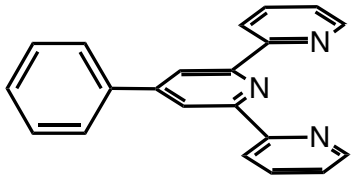
Favored

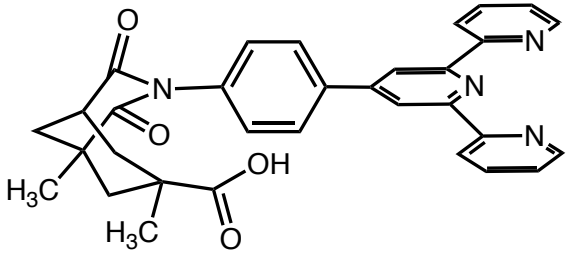
+



Disfavored

- Favored by recognition
- Disfavored by recognition



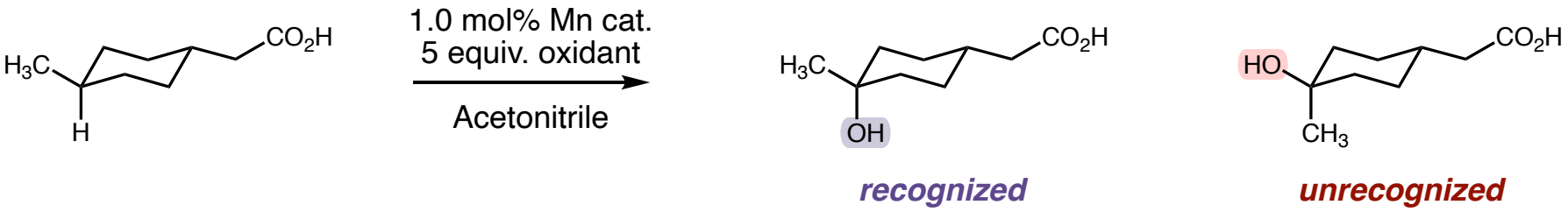


Conversion	Yield (A)	Yield (B)	Selectivity
56%	75%	25%	3:1
58%	77%	23%	3:1

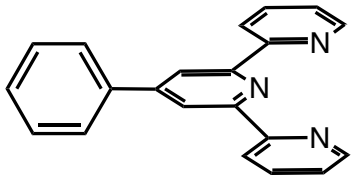
Adding 4.0 equiv. of Acetic Acid causes loss of selectivity

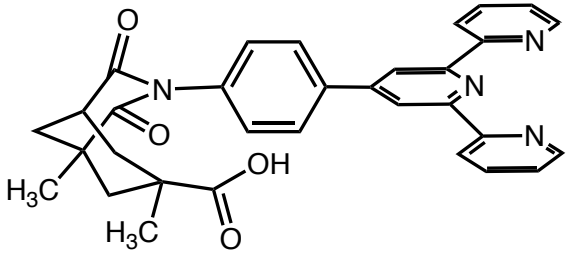
Das, S., Incarvito, C. D., Crabtree, R. H., & Brudvig, G. W. *Science*, **2006**, *312*, 1941

Crabtree - Molecular recognition



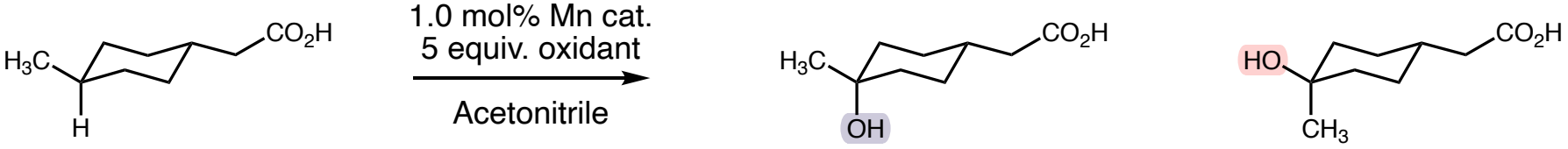
recognized ***unrecognized***





Das, S., Incarvito, C. D., Crabtree, R. H., & Brudvig, G. W. *Science*, **2006**, *312*, 1941

Crabtree - Molecular recognition



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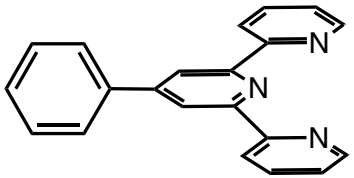
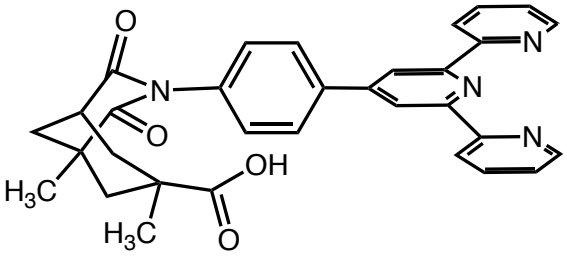


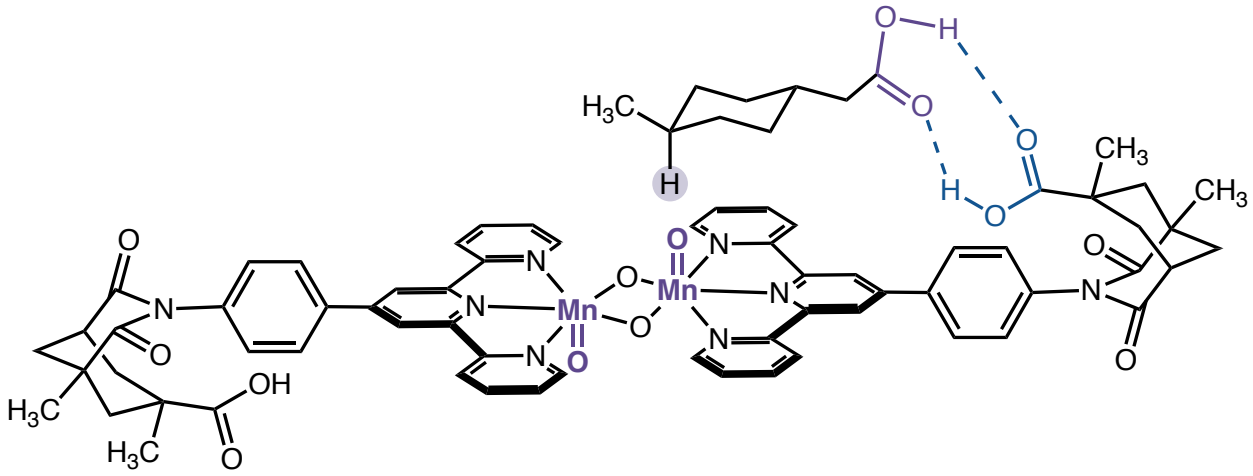
Conversion	Yield (A)	Yield (B)	Selectivity
19%	30%	30% (+other products)	Not selective



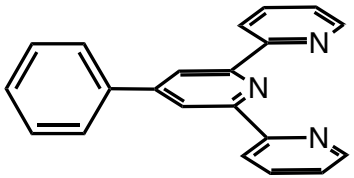
13%	>99%	<1%	>99:1

Das, S., Incarvito, C. D., Crabtree, R. H., & Brudvig, G. W. *Science*, **2006**, *312*, 1941

Crabtree - Molecular recognition



Selectivity due to the rapid rebound from Mn-Oxo



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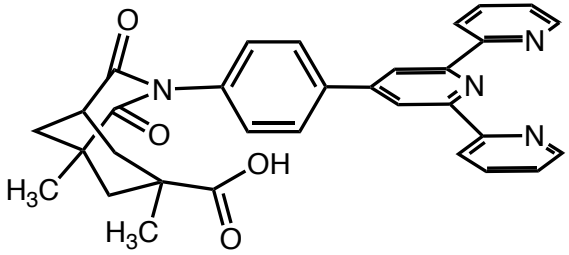

13%	>99%	<1%	>99:1

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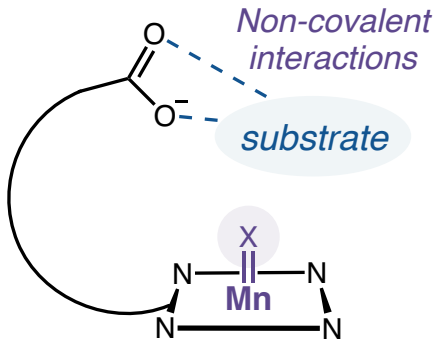
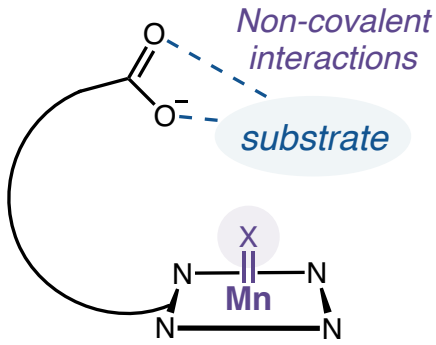
Templated Strategy for C—H Oxidation



Templated strategy for C—H oxidation

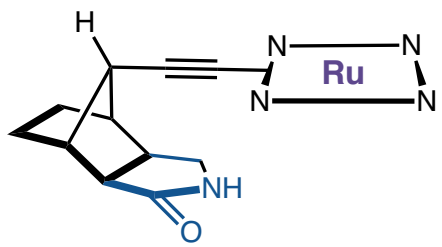
Fackler, P., Huber, S. M., & Bach, T. *JACS* **2012**, 12869, Frost, J. R. *et al*. *Angew. Chem. Int. Ed.* **2015**, *54*, 691, Annapureddy, R. R., Jandl, C., & Bach, T. *JACS* **2020**, *142*, 7374

Templated Strategy for C—H Oxidation

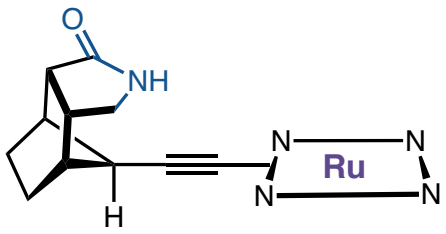


Templated strategy for C—H oxidation

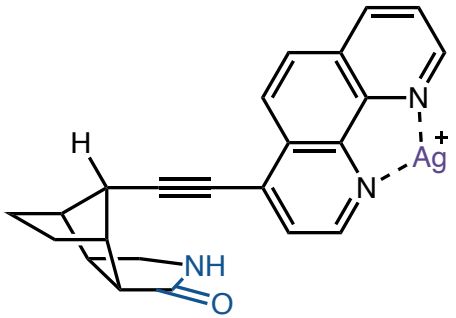
Epoxidation



Oxidation



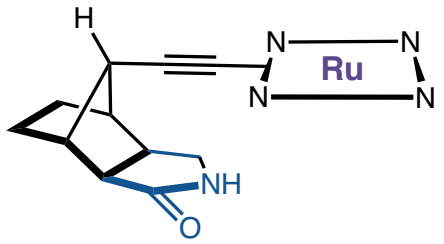
Amination

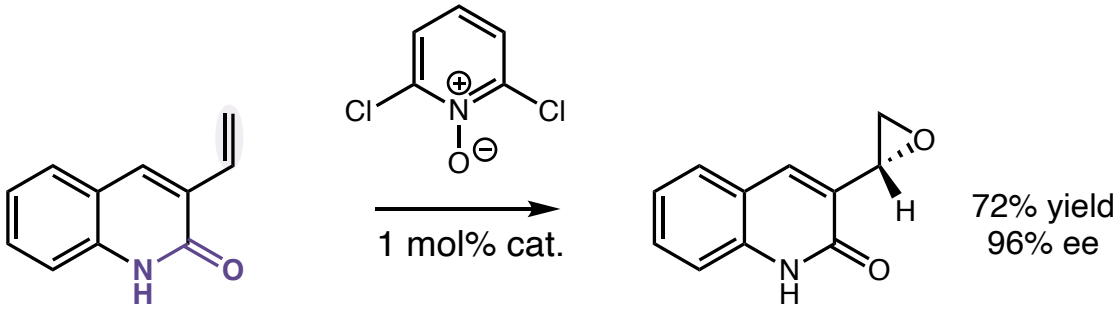


Fackler, P., Huber, S. M., & Bach, T. *JACS* **2012**, 12869, Frost, J. R. *et al*. *Angew. Chem. Int. Ed.* **2015**, *54*, 691, Annapureddy, R. R., Jandl, C., & Bach, T. *JACS* **2020**, *142*, 7374

Bach - Templated Strategy for C—H Oxidation

Epoxidation



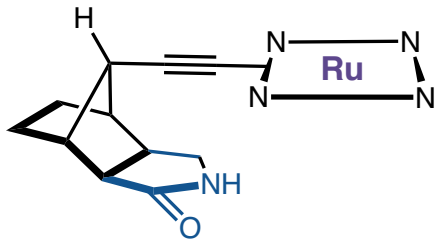


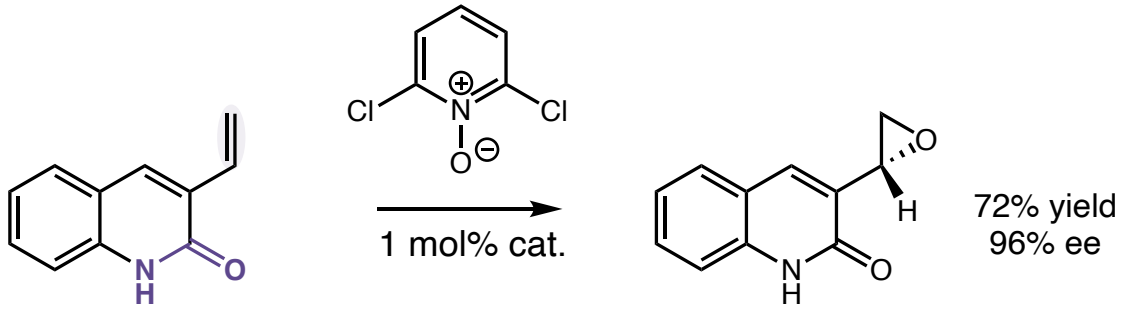
72% yield
96% ee

Fackler, P., Huber, S. M., & Bach, T. *JACS* **2012**, 12869, Frost, J. R. *et al*. *Angew. Chem. Int. Ed.* **2015**, *54*, 691, Annapureddy, R. R., Jandl, C., & Bach, T. *JACS* **2020**, *142*, 7374

Bach - Templated Strategy for C—H Oxidation

Epoxidation





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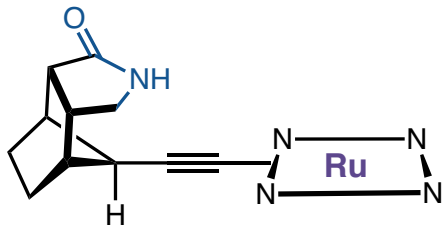
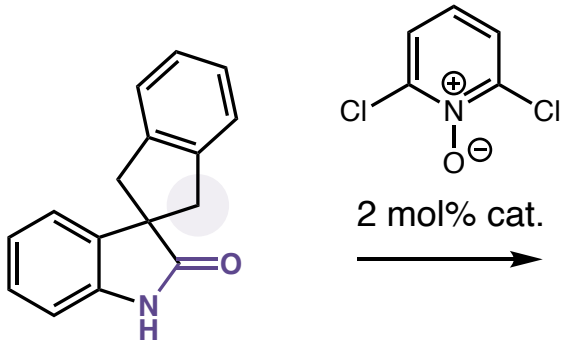
96% ee

Oxidation





70% yield
80% ee

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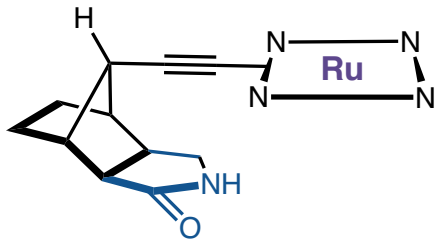
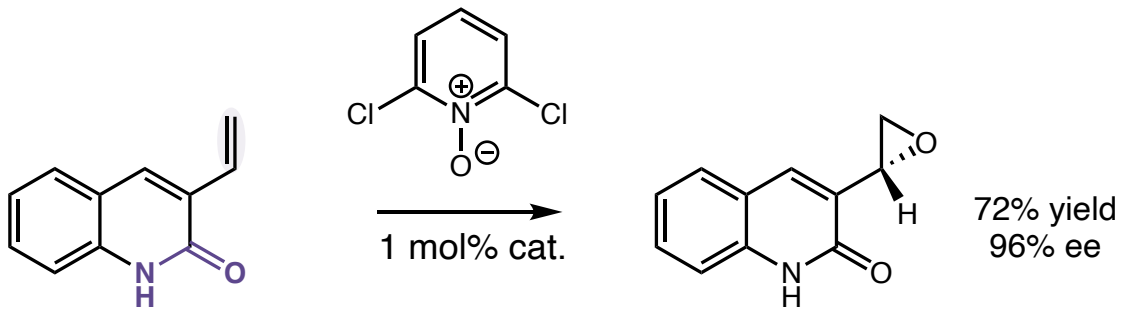
Bach - Templated Strategy for C—H Oxidation

Epoxidation





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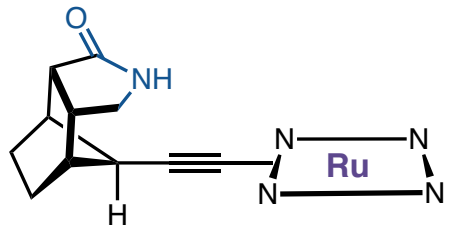
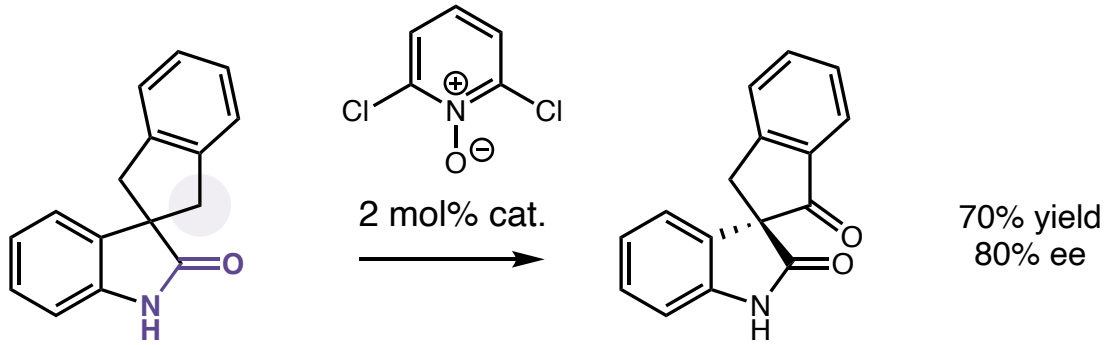
Oxidation





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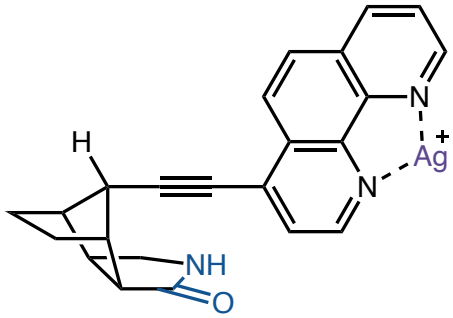
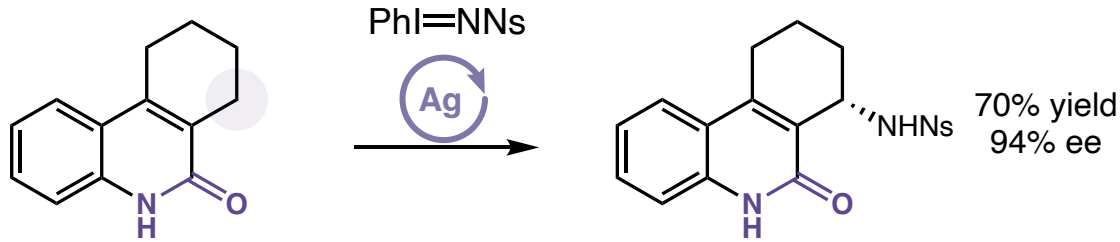
Amination





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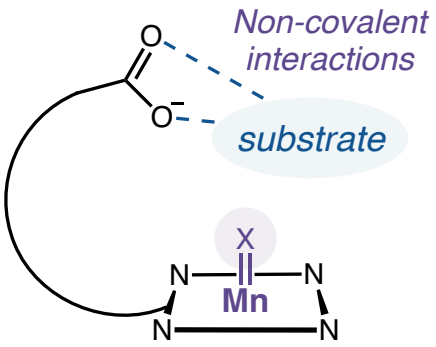
Costas - H-bond recognition



Specific binding motif
High selectivity

Olivo, G. *et al*. *Angew. Chem. Int. Ed.* **2017**, *56*, 16565

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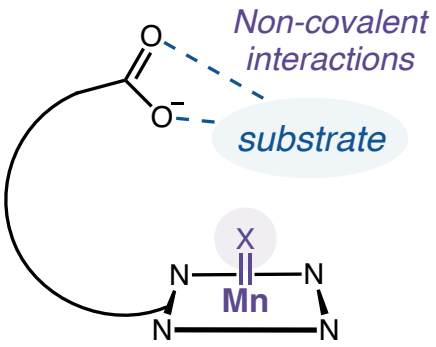

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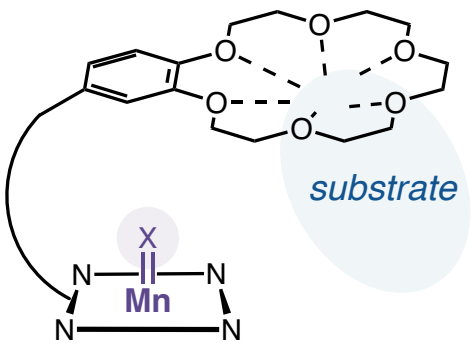
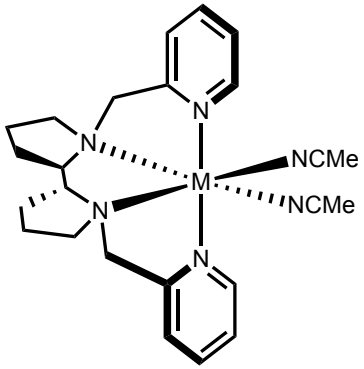


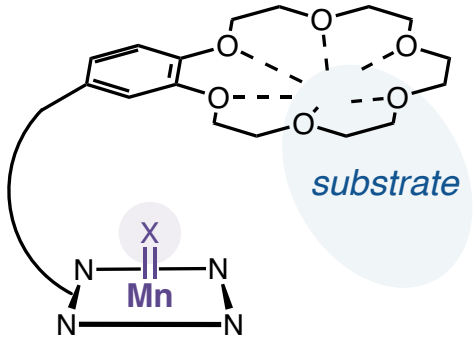
Less specific motif
More generality?

Olivo, G. *et al*. *Angew. Chem. Int. Ed.* **2017**, *56*, 16565

Costas - H-bond recognition

Metal Catalyst





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Costas - H-bond recognition

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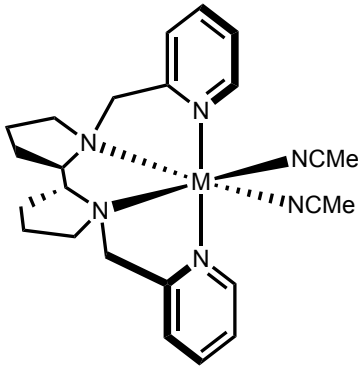

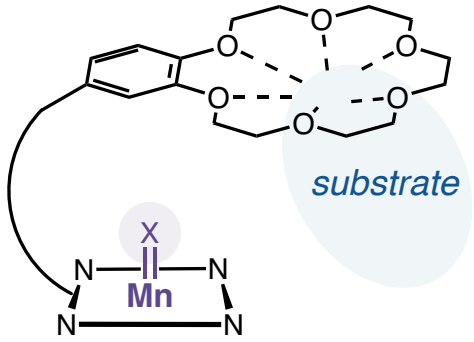

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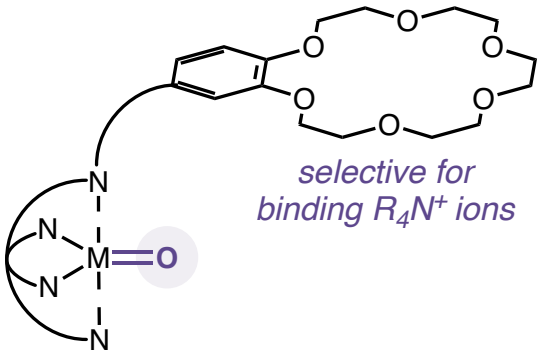

selective for
binding R_4N^+ ions

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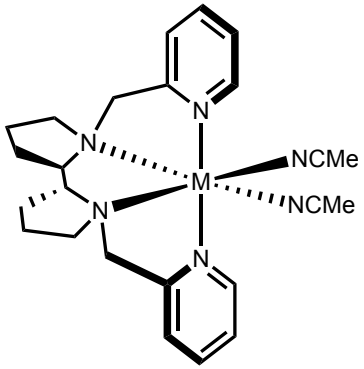
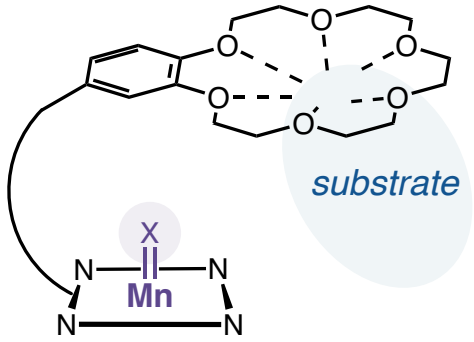
Costas - H-bond recognition

Metal Catalyst





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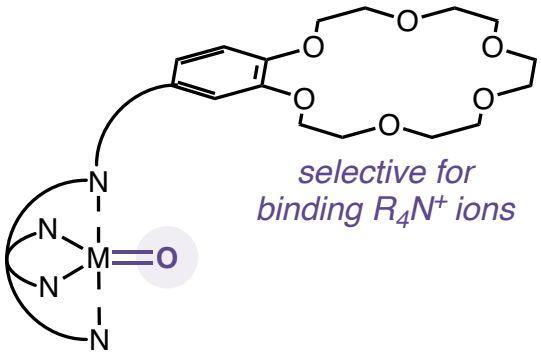

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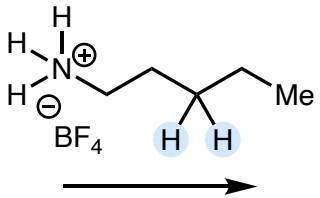
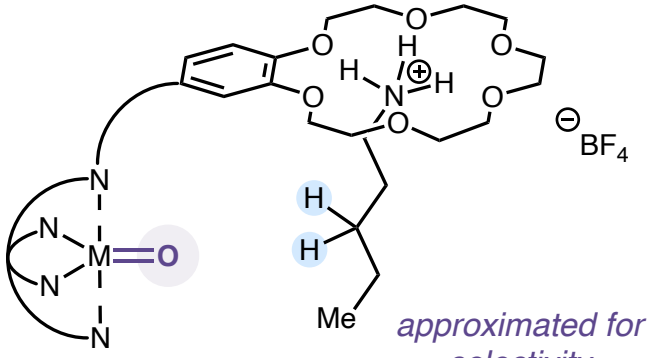
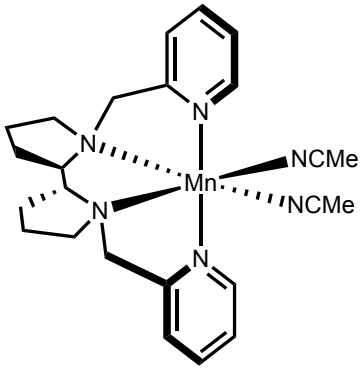




approximated for selectivity

Olivo, G. *et al*. *Angew. Chem. Int. Ed.* **2017**, *56*, 16565



Cat. 1

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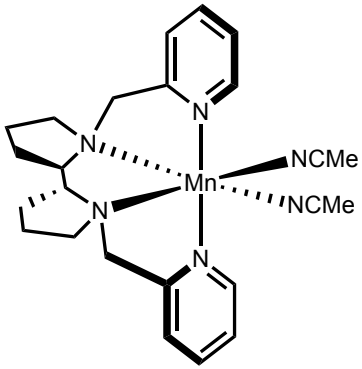
Costas - H-bond recognition



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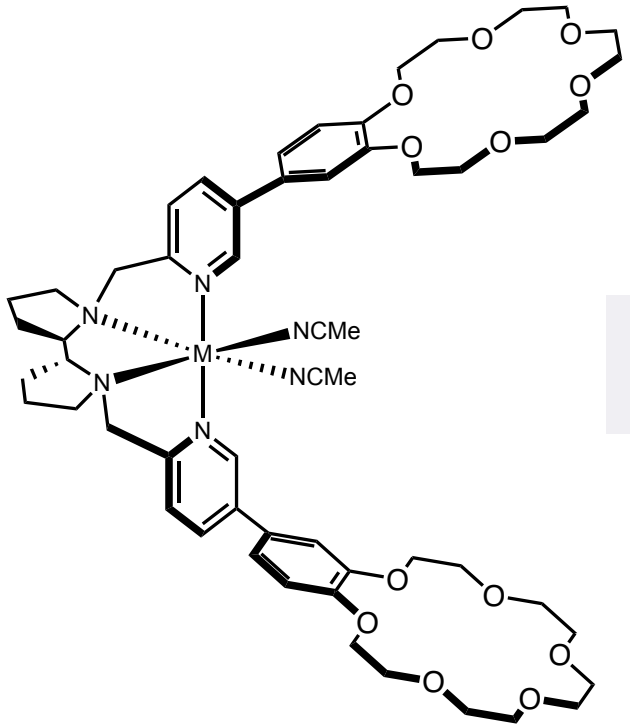
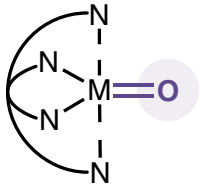


Cat. 2

Olivo, G. *et al*. *Angew. Chem. Int. Ed.* **2017**, *56*, 16565



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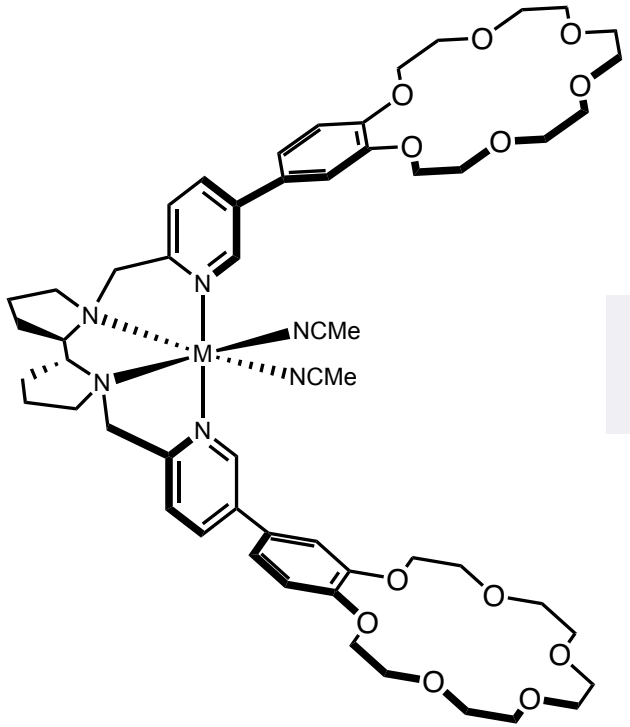

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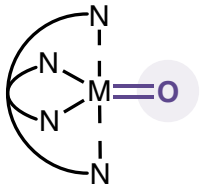

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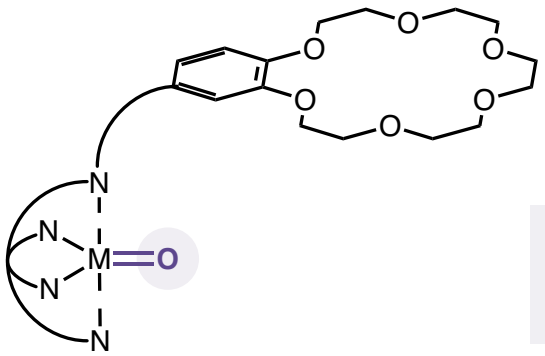
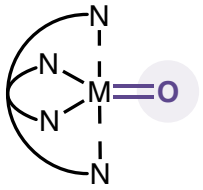


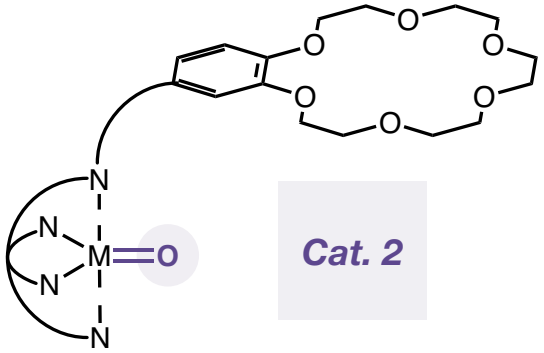
Cat. 2

Olivo, G. *et al*. *Angew. Chem. Int. Ed.* **2017**, *56*, 16565

Costas - H-bond recognition

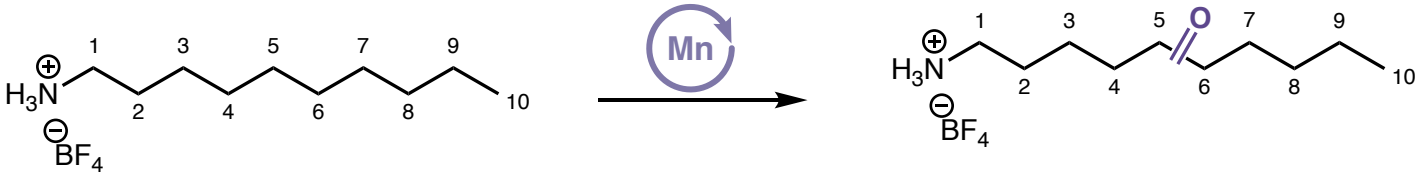


Cat. 1



Cat. 2

Evaluation of effect on site-selectivity



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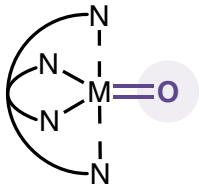
Costas - H-bond recognition



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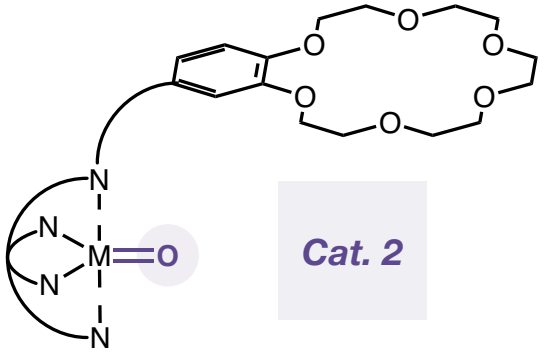
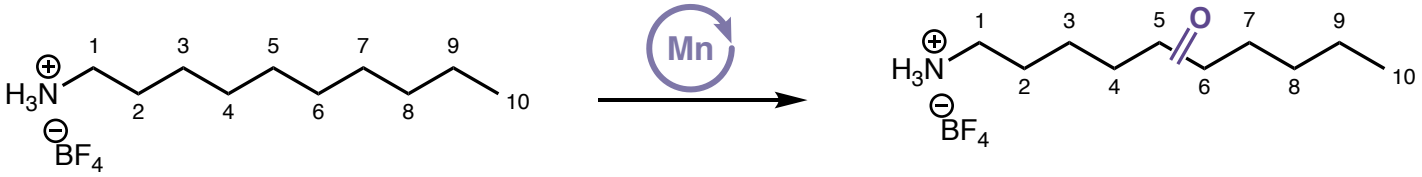


Cat. 2

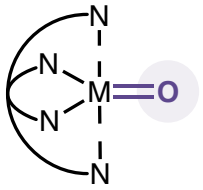
Evaluation of effect on site-selectivity



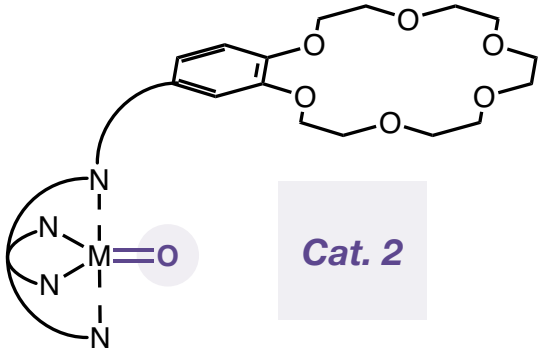
	Total Yield (%)	K3	K4	K5	K6	K7	K8	K9	Selectivity (C8+C)/Total
Cat. 1	34	0.5	2	2.5	5.5	5.5	8	10	**53%**
Cat. 2	36	-	-	0.5	1.5	5	13	16	**81%**

Olivo, G. *et al*. *Angew. Chem. Int. Ed.* **2017**, *56*, 16565

Costas - H-bond recognition

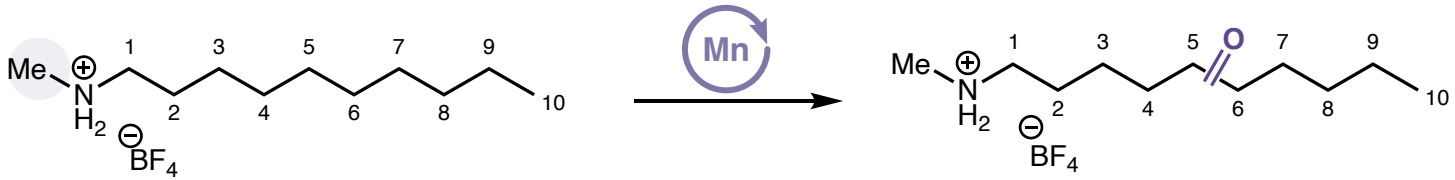


Cat. 1



Cat. 2

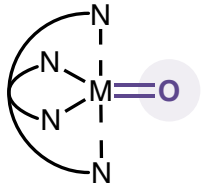
Methylation hinders reactivity and selectivity for Cat. 2 but not Cat. 1



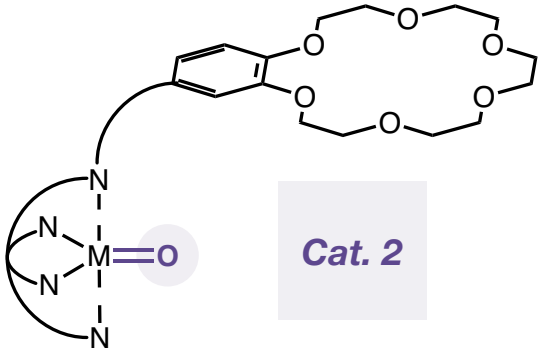
	Total Yield (%)	K3	K4	K5	K6	K7	K8	K9	Selectivity (C8+C)/Total
Cat. 1	34	0.5	2	2.5	5.5	5.5	8	10	**53%**
Cat. 2	36	-	-	0.5	1.5	5	13	16	**81%**
Cat. 1	28	0.5	1	3	4.5	4.5	5	7.5	49%
Cat. 2	9	trace	0.5	0.5	1.5	1.5	2	2	50%

Olivo, G. *et al*. *Angew. Chem. Int. Ed.* **2017**, *56*, 16565

Costas - H-bond recognition



Cat. 1



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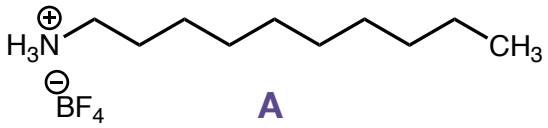
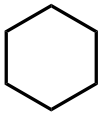


A

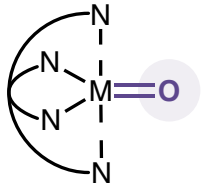
vs.



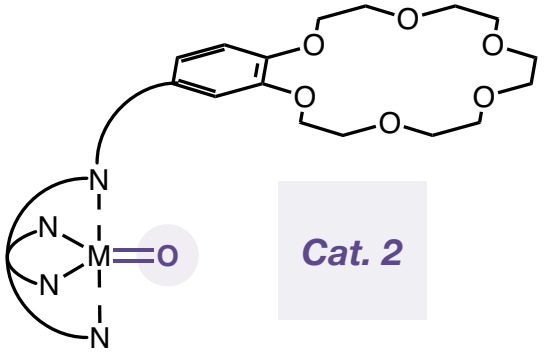
B

Olivo, G. *et al*. *Angew. Chem. Int. Ed.* **2017**, *56*, 16565

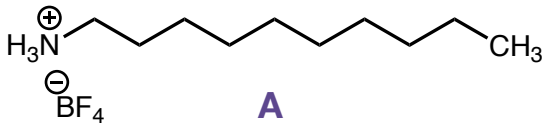
Costas - H-bond recognition



Cat. 1

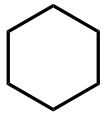


Cat. 2



A

vs.



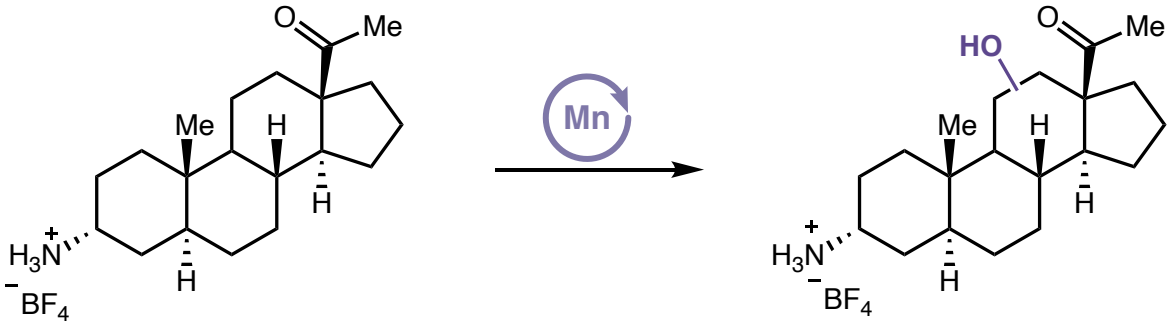
B

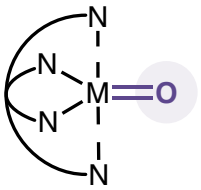
	Ratio (**A** Ox : **B** Ox)	Yield **A** Ox	Yield **B** Ox
Cat. 1	**1:3.5**	**4%**	**14%**
Cat. 2 + $Ba(ClO_4)_2$	**1:4**	**4%**	**16%**
Cat. 2	**9:1**	**18%**	**2%**

Cat. 2 selectively oxidizes amine substrate due to H-bonding

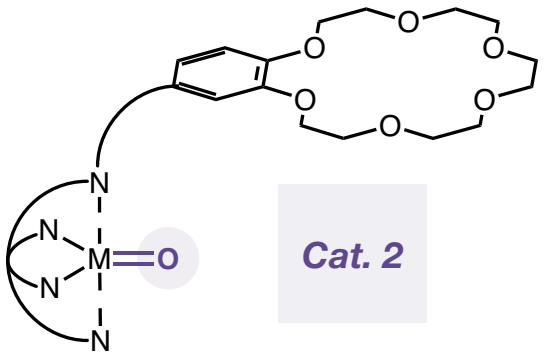
Olivo, G. *et al*. *Angew. Chem. Int. Ed.* **2017**, *56*, 16565

Costas - H-bond recognition





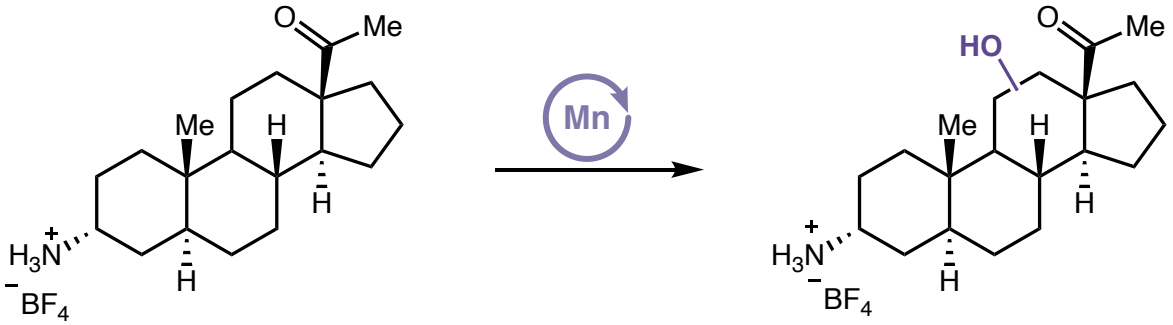
Cat. 1

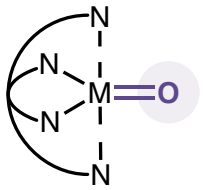


Cat. 2

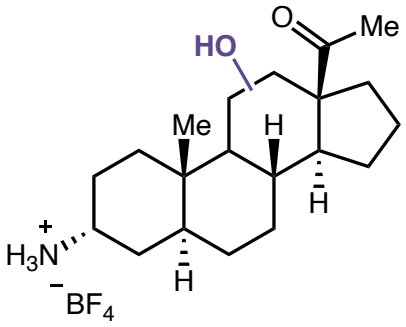
Olivo, G. *et al*. *Angew. Chem. Int. Ed.* **2020**, *59*, 12703

Costas - H-bond recognition



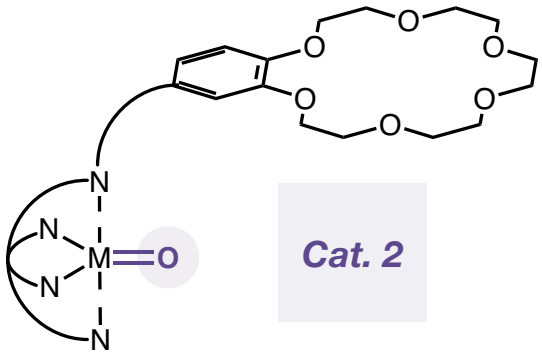


Cat. 1



10 products

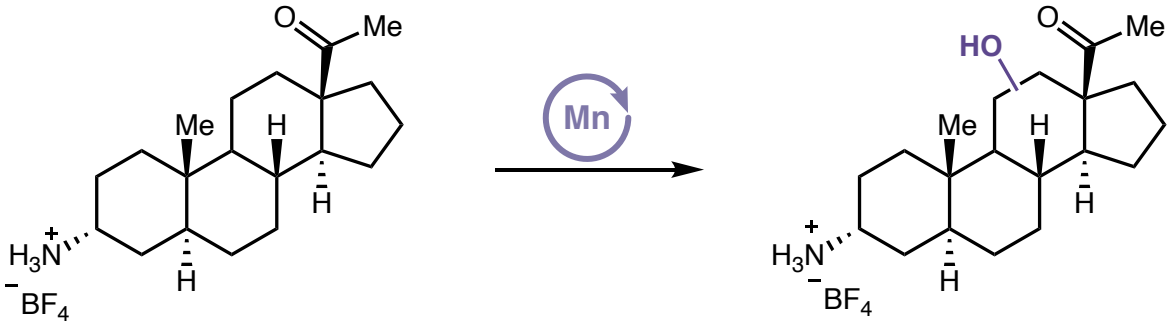
11% total yield

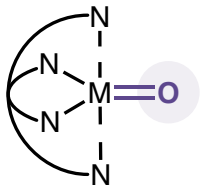


Cat. 2

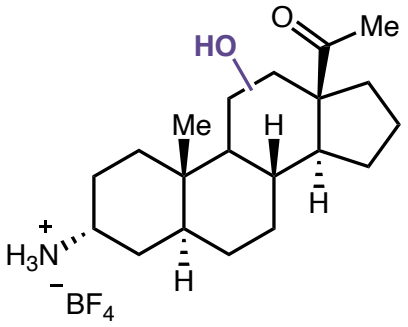
Olivo, G. *et al*. *Angew. Chem. Int. Ed.* **2020**, *59*, 12703

Costas - H-bond recognition

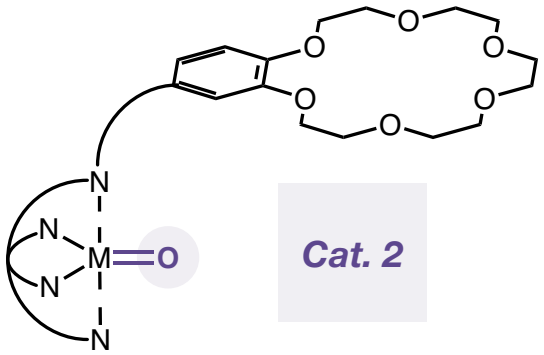




Cat. 1



10 products
11% total yield



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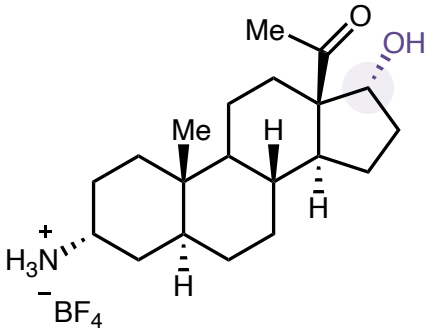
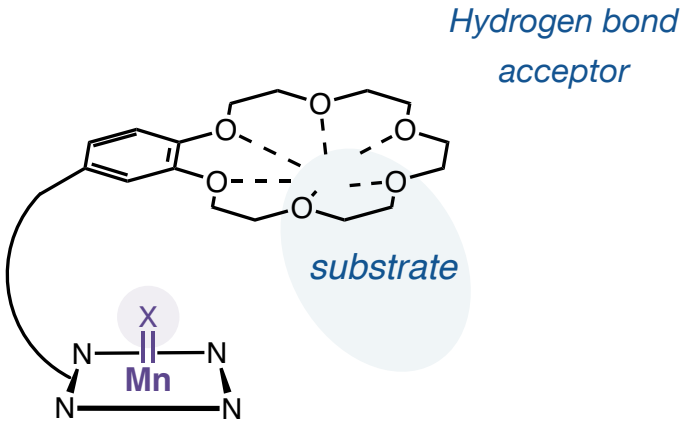


Main product
25% yield

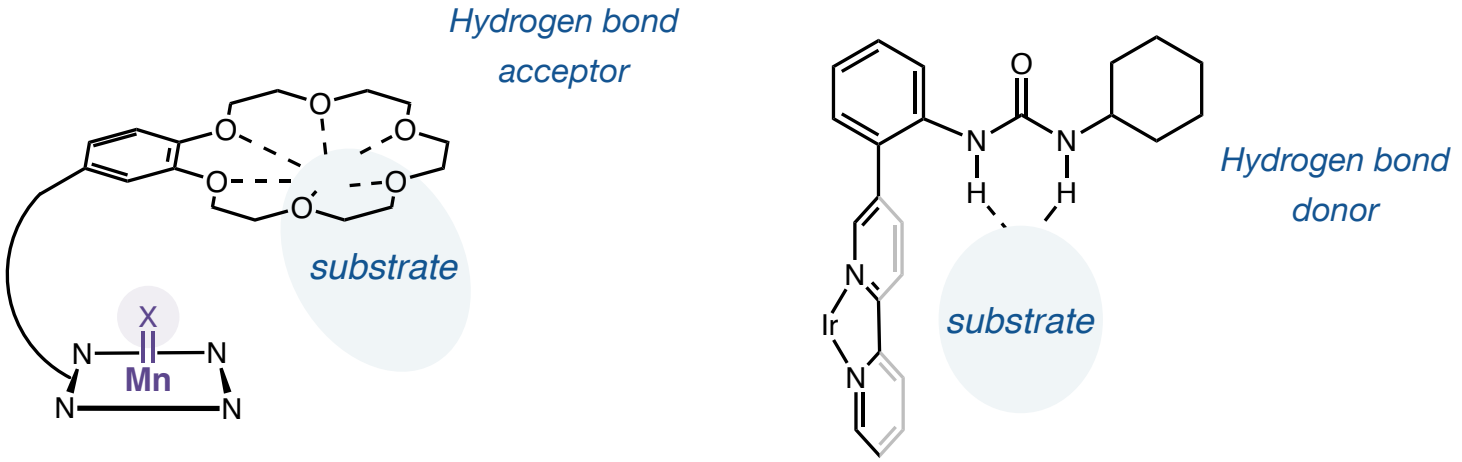
Olivo, G. *et al*. *Angew. Chem. Int. Ed.* **2020**, *59*, 12703

Ir C—H Borylation



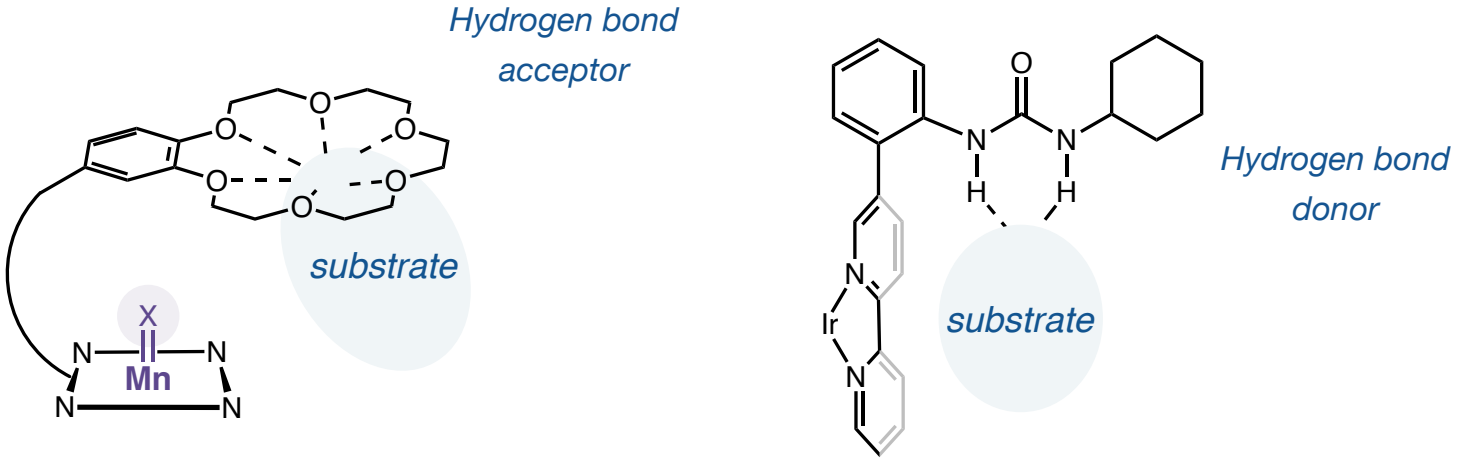
Cho, J.-Y., Tse, M.K., Holmes, D., Maleczka, R. E. & Smith, M. R. *Science* **2001**, *295*, 305

Ir C—H Borylation



Cho, J.-Y., Tse, M.K., Holmes, D., Maleczka, R. E. & Smith, M. R. *Science* **2001**, *295*, 305

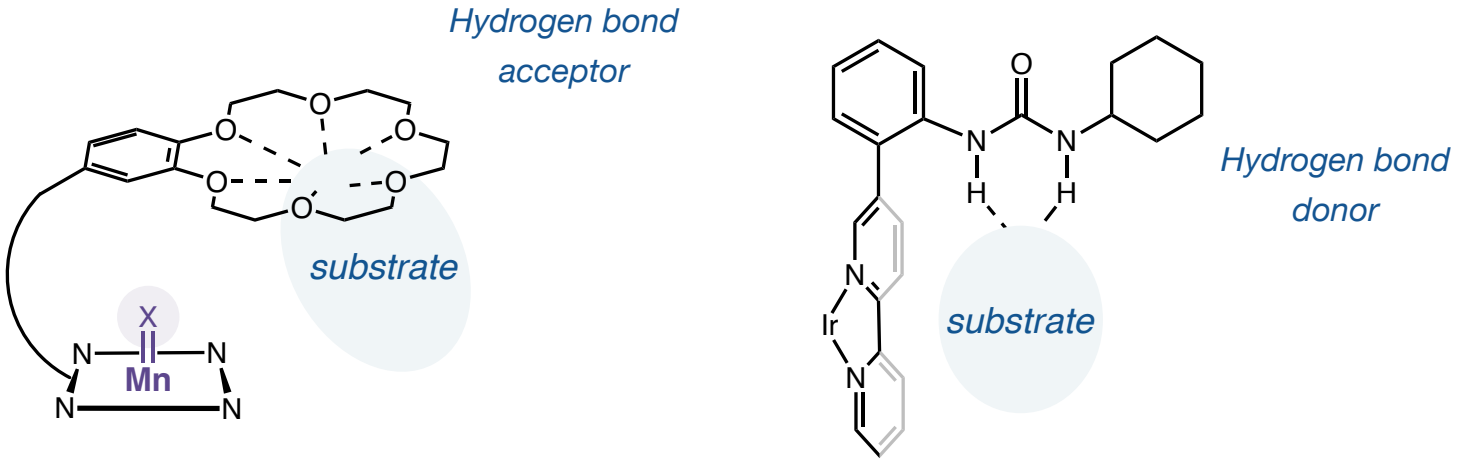
Ir C—H Borylation



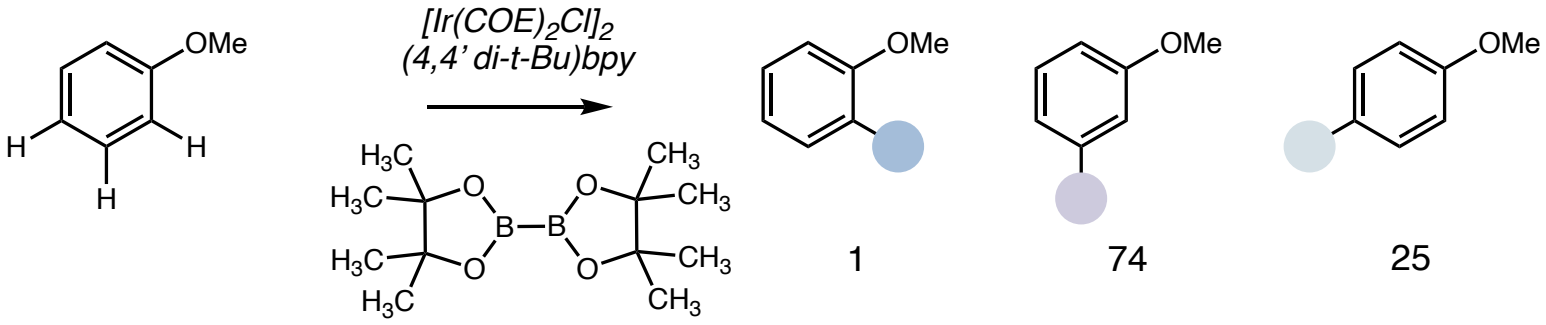
Ir catalyzed C-H borylation

Cho, J.-Y., Tse, M.K., Holmes, D., Maleczka, R. E. & Smith, M. R. *Science* **2001**, *295*, 305

Ir C—H Borylation



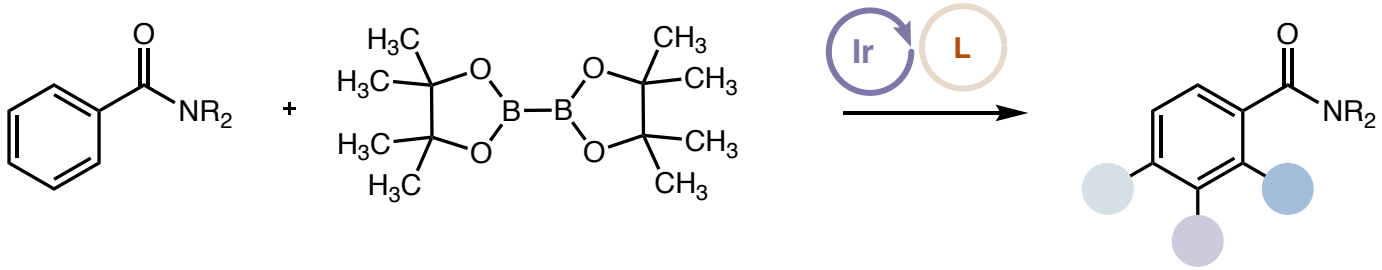
Ir catalyzed C-H borylation

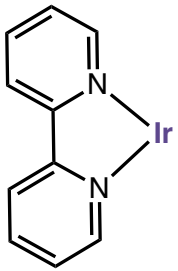


Can ligands change selectivity?

Cho, J.-Y., Tse, M.K., Holmes, D., Maleczka, R. E. & Smith, M. R. *Science* **2001**, *295*, 305

Kanai - C—H Borylation

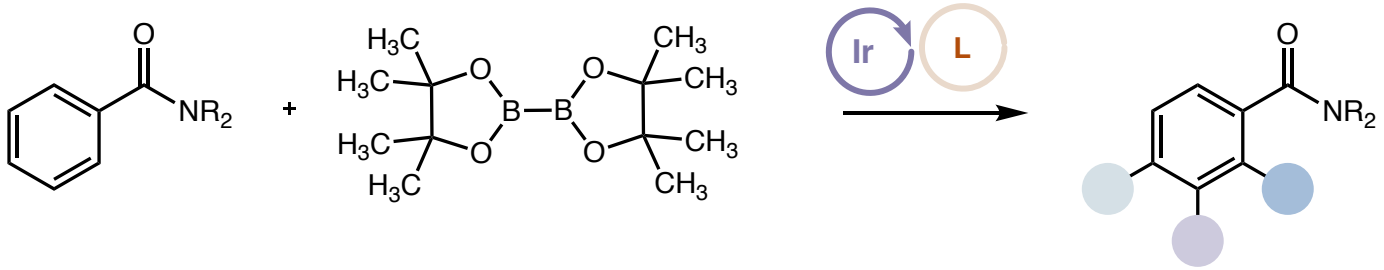


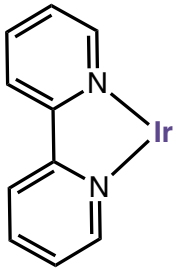


common ligand for C—H borylation

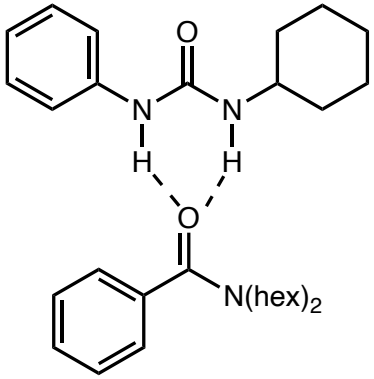
Kuninobu, Y., Ida, H., Nishi, M. & Kanai, M. *Nat. Chem.* **2015**, *7*, 712

Kanai - C—H Borylation





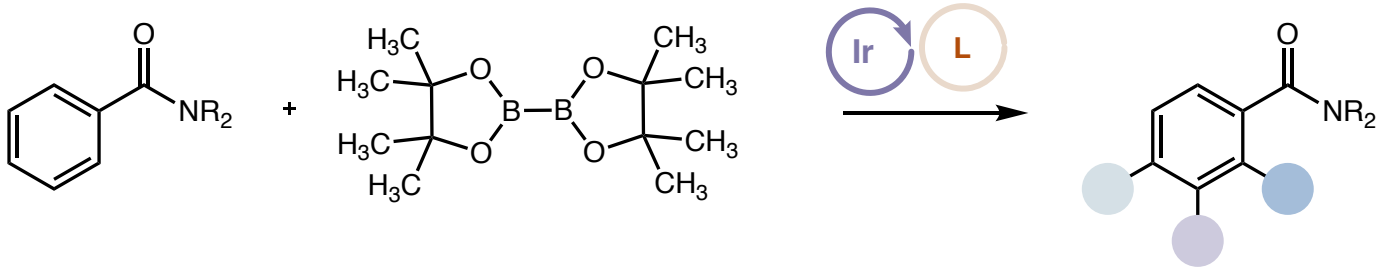
common ligand for C—H borylation

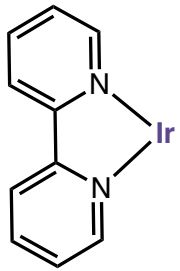


H-bond accepting motif

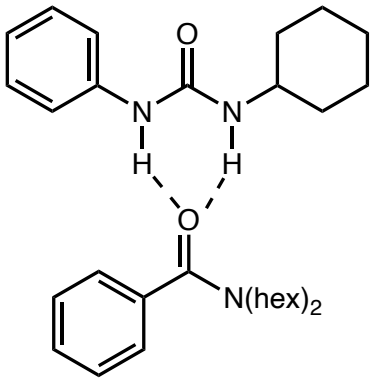
Kuninobu, Y., Ida, H., Nishi, M. & Kanai, M. *Nat. Chem.* **2015**, *7*, 712

Kanai - C—H Borylation

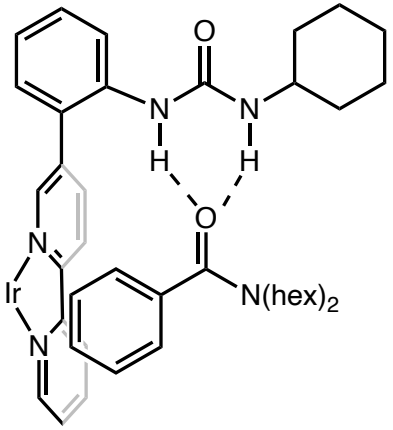




common ligand for C—H borylation



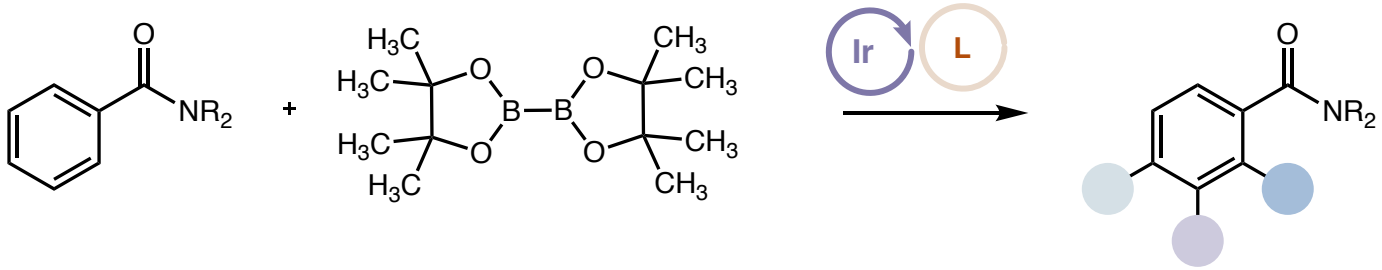
H-bond accepting motif



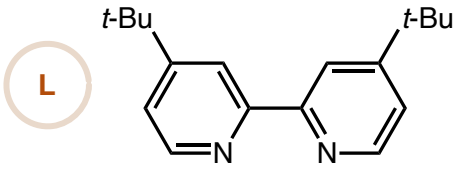
New catalyst for selectivity

Kuninobu, Y., Ida, H., Nishi, M. & Kanai, M. *Nat. Chem.* **2015**, *7*, 712

Kanai - C—H Borylation



Cond. A.



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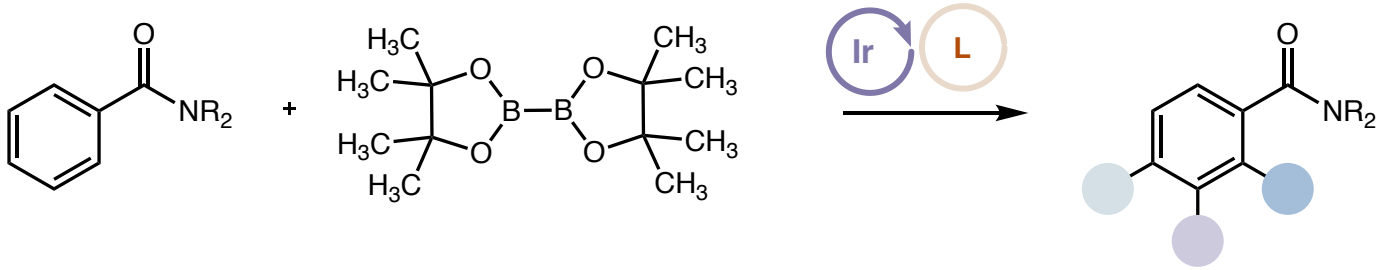
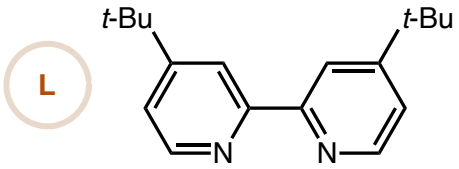
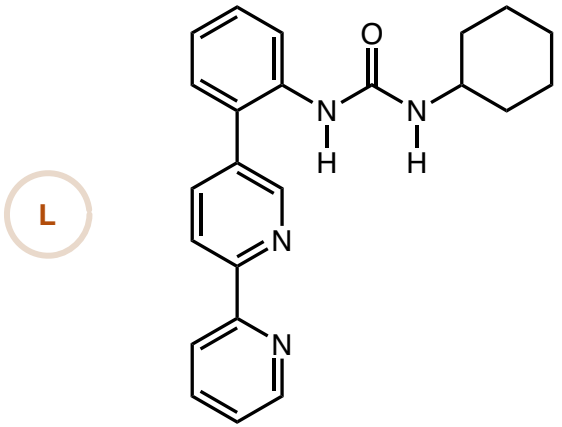
Kanai - C—H Borylation



Cond. A.



Cond. B.



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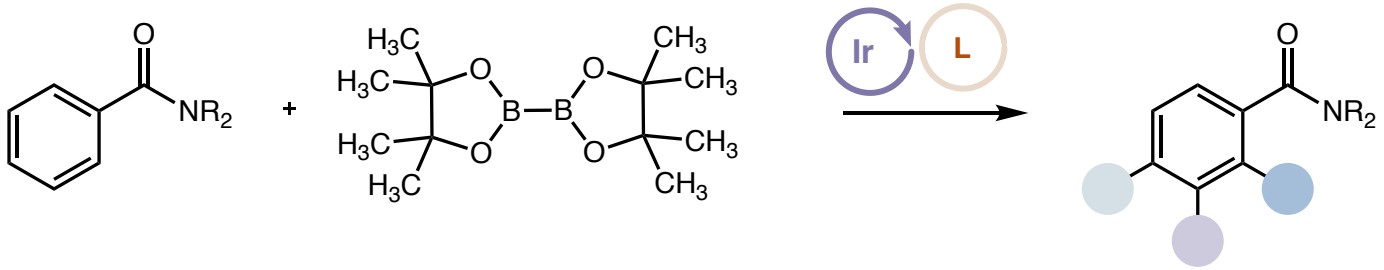
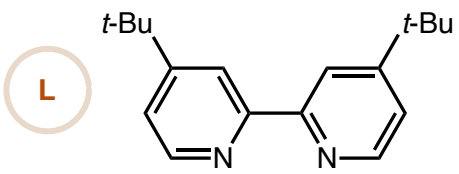
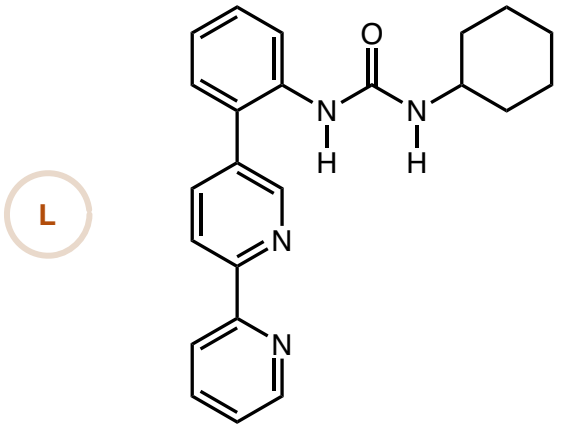
Kanai - C—H Borylation

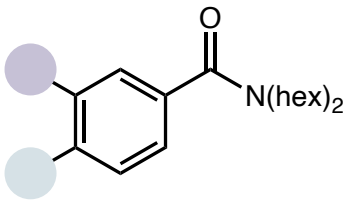


Cond. A.

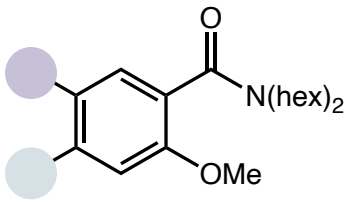


Cond. B.

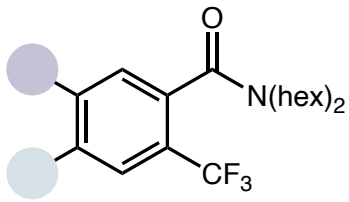




Cond. A. 57% yield (1:2 *m*:*p*)
Cond. B. 51% yield (17:1 *m*:*p*)



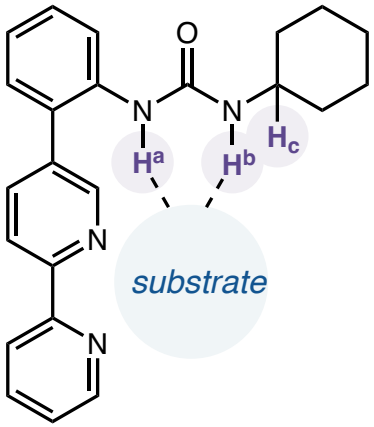
Cond. A. 40% yield (1:2 *m*:*p*)
Cond. B. 59% yield (7.8:1 *m*:*p*)



Cond. A. >99% yield (1:1.1 *m*:*p*)
Cond. B. >99% yield (30:1 *m*:*p*)

Kuninobu, Y., Ida, H., Nishi, M. & Kanai, M. *Nat. Chem.* **2015**, *7*, 712

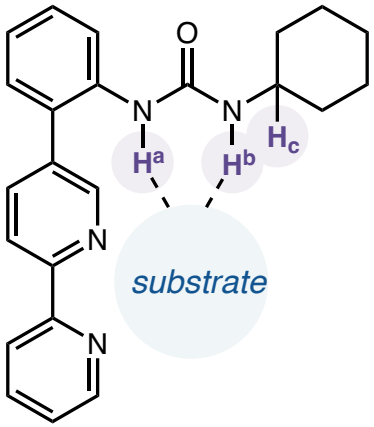
Importance of H-bonding



Entry	Cat.	Substrate	H_a	H_b	H_c
1	2.5 mM	0	5.65	3.60	3.63
2	2.5 mM	2.5 mM	5.78	3.74	3.65
3	2.5 mM	160 mM	~7.00	5.88	3.89

Kuninobu, Y., Ida, H., Nishi, M. & Kanai, M. *Nat. Chem.* **2015**, *7*, 712

Importance of H-bonding

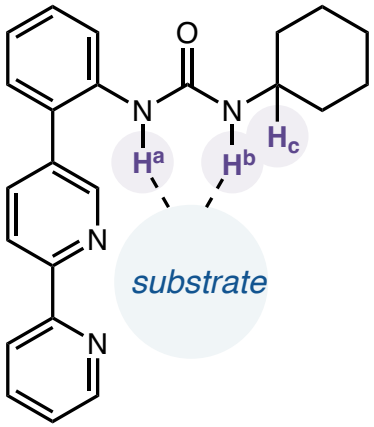


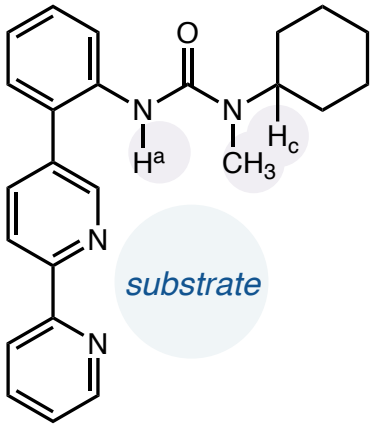
Entry	Cat.	Substrate	H_a	H_b	H_c
1	2.5 mM	0	5.65	3.60	3.63
2	2.5 mM	2.5 mM	5.78	3.74	3.65
3	2.5 mM	160 mM	~7.00	5.88	3.89

H-Bonding titration shows substrate—catalyst binding

Kuninobu, Y., Ida, H., Nishi, M. & Kanai, M. *Nat. Chem.* **2015**, *7*, 712

Importance of H-bonding





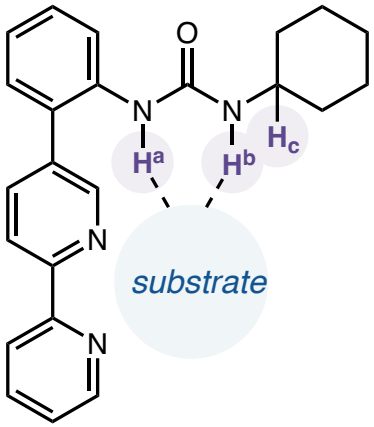
Entry	Cat.	Substrate	H_a	H_b	H_c
1	2.5 mM	0	5.65	3.60	3.63
2	2.5 mM	2.5 mM	5.78	3.74	3.65
3	2.5 mM	160 mM	~7.00	5.88	3.89

Entry	Cat.	Substrate	H_a	H_c
1	2.5 mM	0	6.26	3.91
2	2.5 mM	2.5 mM	6.26	3.91
3	2.5 mM	160 mM	6.37	3.92

H-Bonding titration shows substrate—catalyst binding

Kuninobu, Y., Ida, H., Nishi, M. & Kanai, M. *Nat. Chem.* **2015**, *7*, 712

Importance of H-bonding



Entry	Cat.	Substrate	H_a	H_b	H_c
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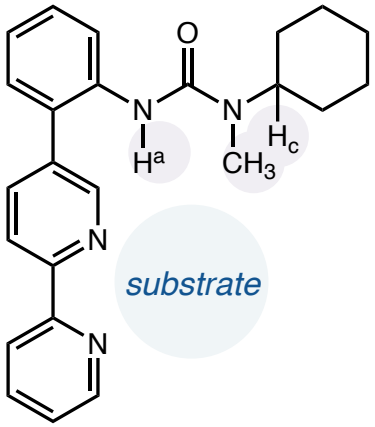
2	2.5 mM	2.5 mM	5.78	3.74	3.65
3	2.5 mM	160 mM	~7.00	5.88	3.89

H-Bonding titration shows substrate—catalyst binding

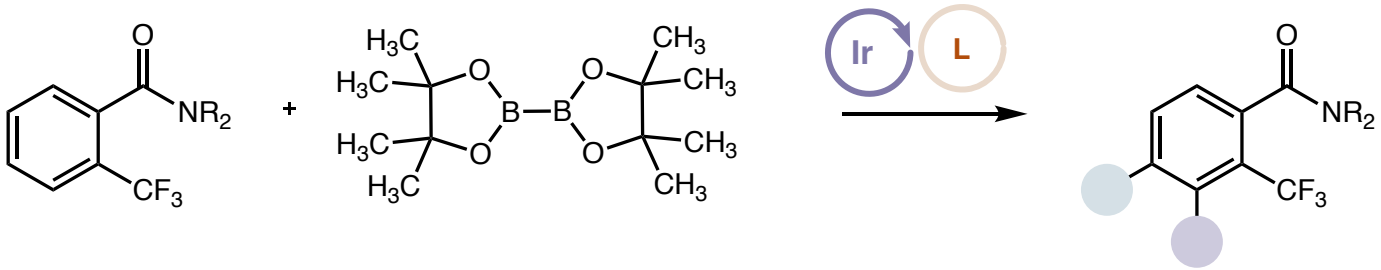


Entry	Cat.	Substrate	H_a	H_c
1	2.5 mM	0	6.26	3.91
2	2.5 mM	2.5 mM	6.26	3.91
3	2.5 mM	160 mM	6.37	3.92

Methylation disrupts catalyst—substrate binding

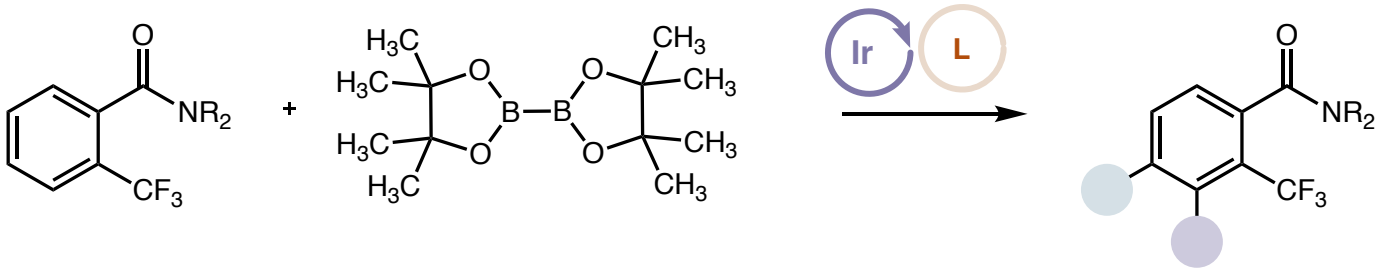
Kuninobu, Y., Ida, H., Nishi, M. & Kanai, M. *Nat. Chem.* **2015**, *7*, 712

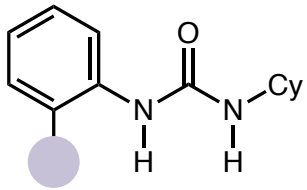
Kanai - C—H Borylation



Kuninobu, Y., Ida, H., Nishi, M. & Kanai, M. *Nat. Chem.* **2015**, *7*, 712

Kanai - C—H Borylation





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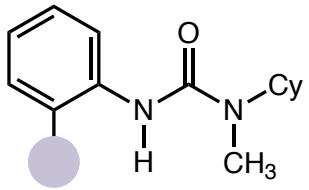

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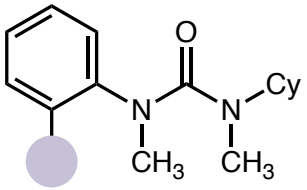
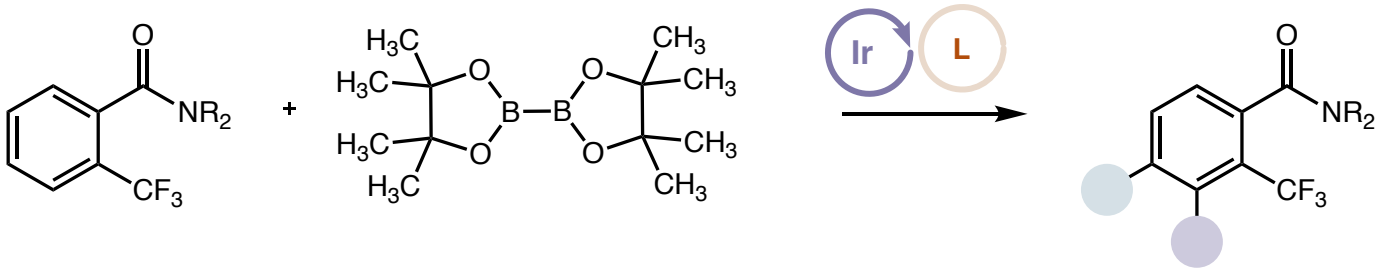


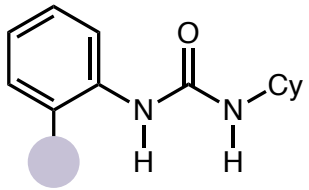
(3)

L	Yield	*meta*:*para*
1	95%	18
2	90%	1.6
3	90%	0.84

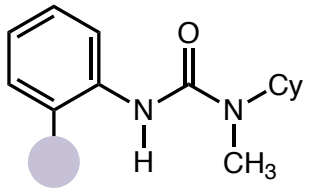
Kuninobu, Y., Ida, H., Nishi, M. & Kanai, M. *Nat. Chem.* **2015**, *7*, 712

Kanai - C—H Borylation





(1)



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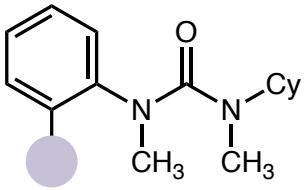

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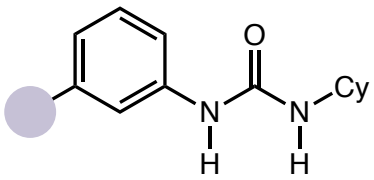

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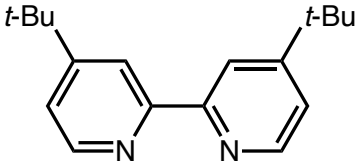

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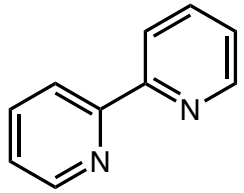
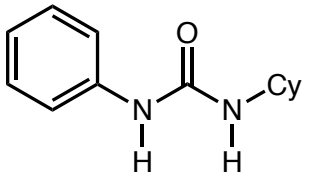


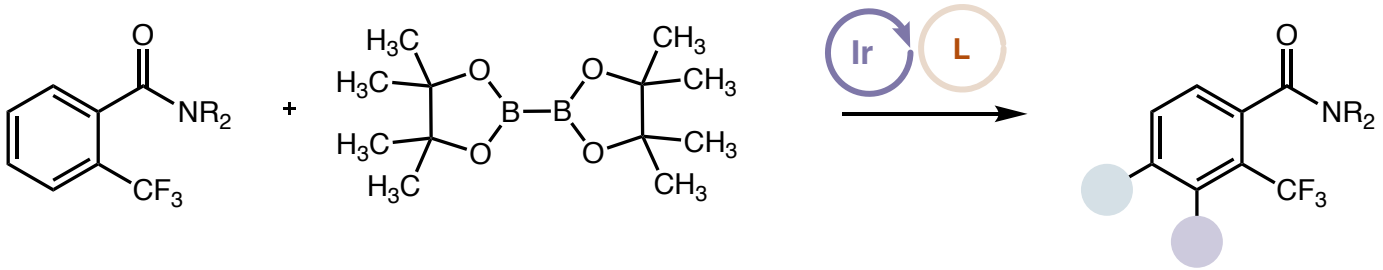


(6)

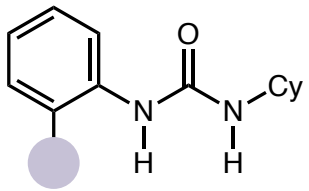
L	Yield	*meta*:*para*
1	95%	18
2	90%	1.6
3	90%	0.84
4	99%	1.0
5	98%	0.96
6	99%	1.1

Kuninobu, Y., Ida, H., Nishi, M. & Kanai, M. *Nat. Chem.* **2015**, *7*, 712

Kanai - C—H Borylation



Ligand is responsible for selectivity in reaction



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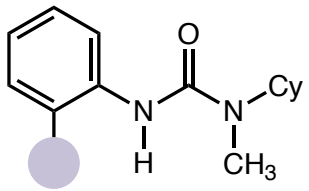

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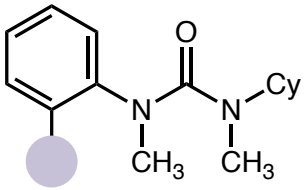

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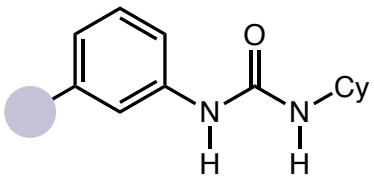

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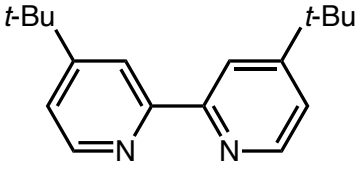

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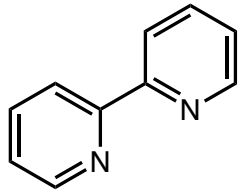

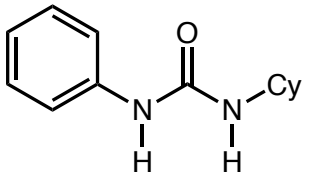

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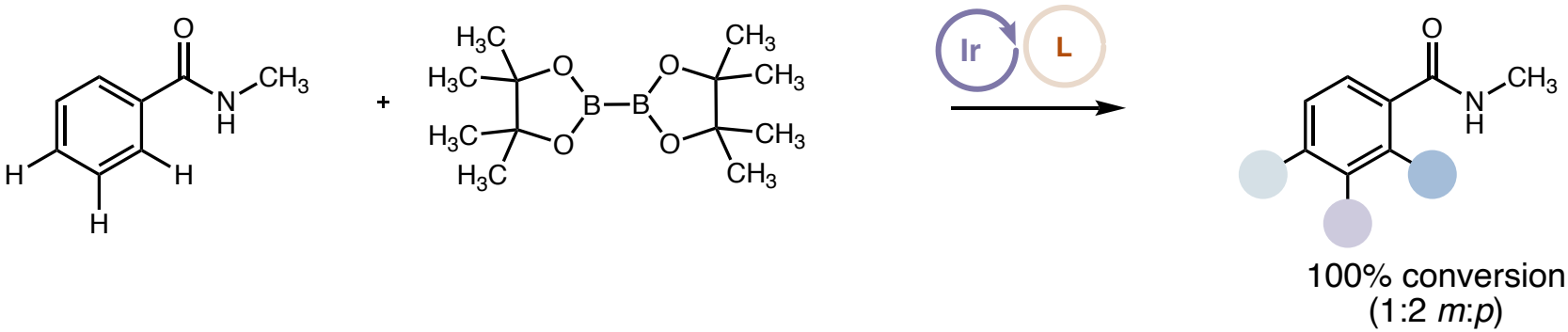
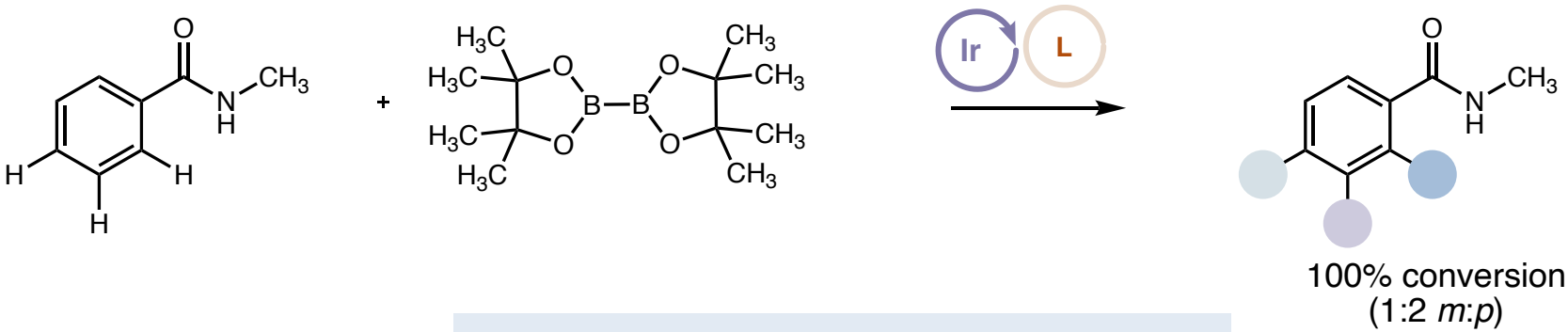
Reek - Ortho C—H borylation



100% conversion
(1:2 *m*:*p*)

Bai, S.T., Bheeter, C. B., & Reek, J. N. H. *Angew. Chem. Int, Ed.* **2019**, *58*, 13039

Reek - Ortho C—H borylation



100% conversion
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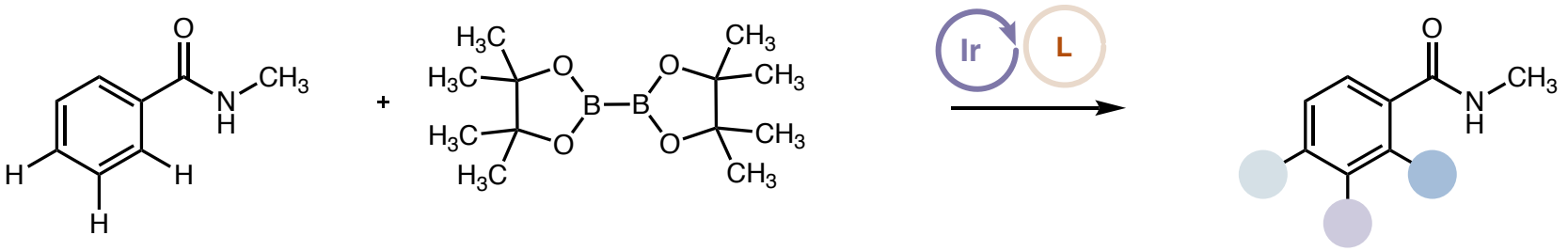
How do we achieve ortho- without directing groups?

Bai, S.T., Bheeter, C. B., & Reek, J. N. H. *Angew. Chem. Int, Ed.* **2019**, *58*, 13039

Reek - Ortho C—H borylation



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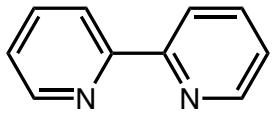

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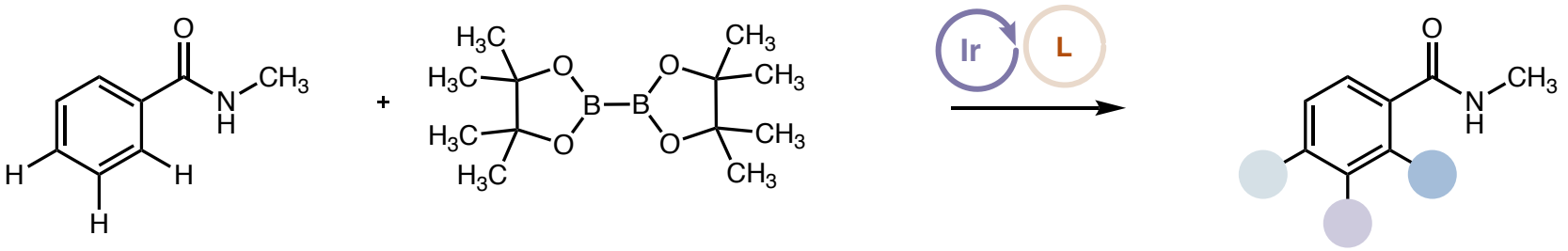

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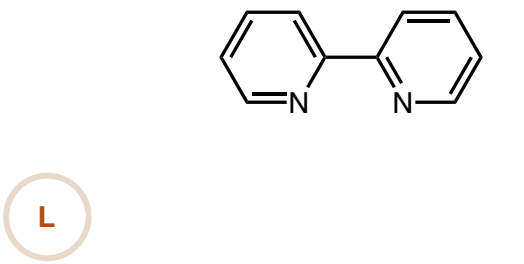

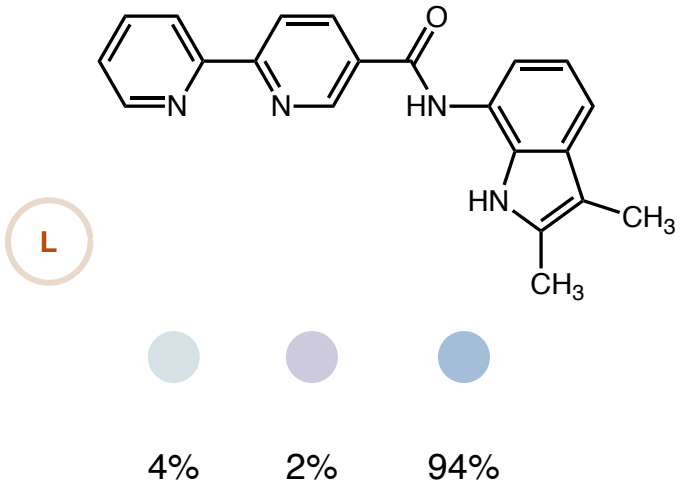

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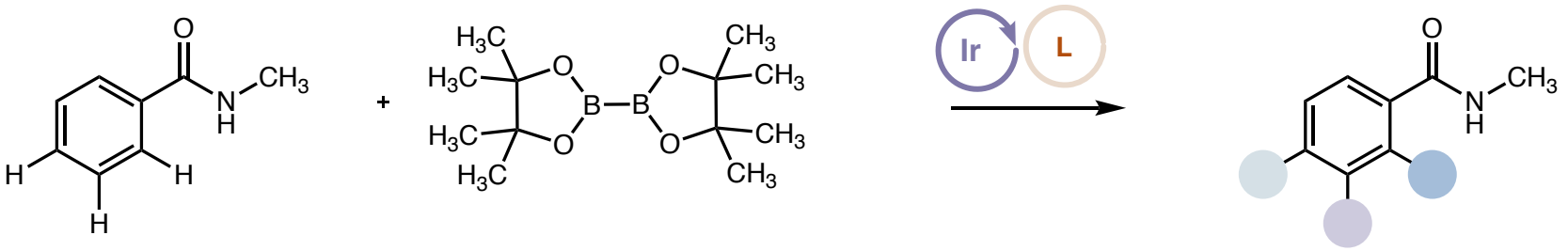
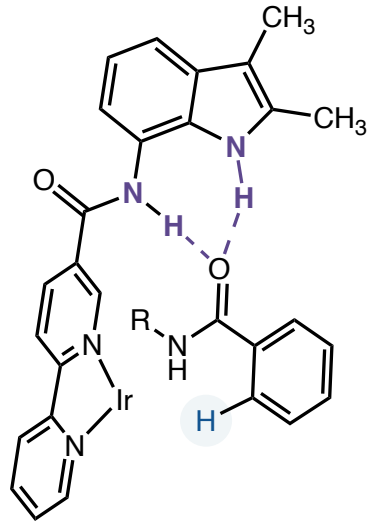
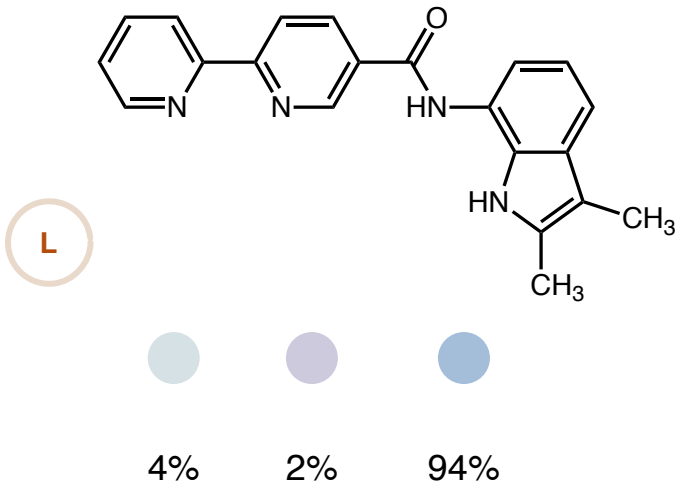
Reek - Ortho C—H borylation



How do we achieve ortho- without directing groups?

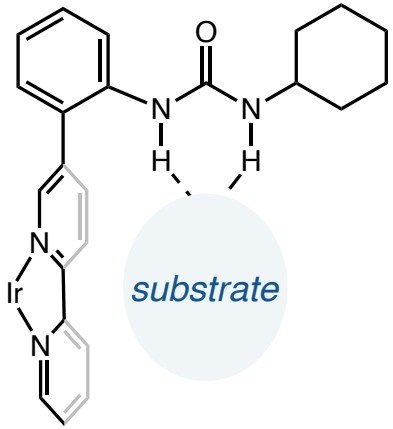
BAIPy-Ir catalyst





Bai, S.T., Bheeter, C. B., & Reek, J. N. H. *Angew. Chem. Int, Ed.* **2019**, *58*, 13039

Enantioselective Suzuki-Miyaura

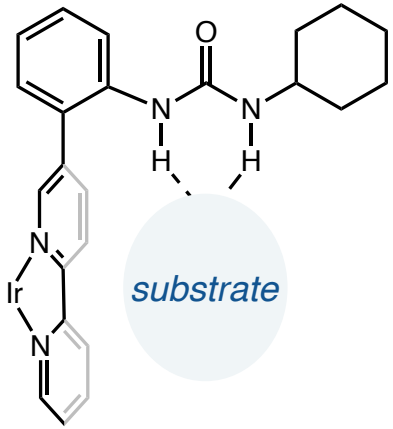


Hydrogen bond donor

Organizing catalyst—substrate for C—H activation

Pearce-Higgins, R. *et al. JACS* **2022**, *144*, 15026

Enantioselective Suzuki-Miyaura



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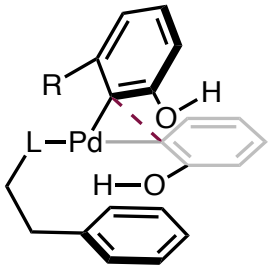
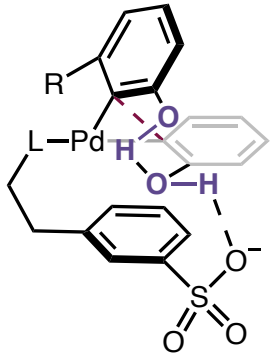


vs.

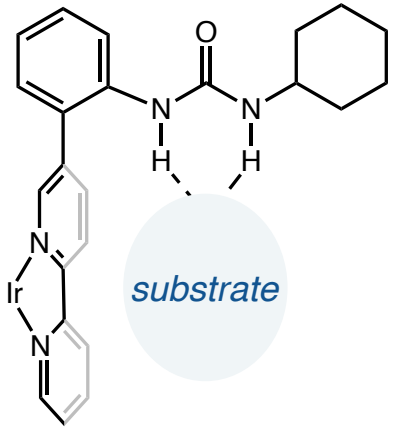


Organizing catalyst—substrate for C—H activation

H-bonding for selective reductive elimination

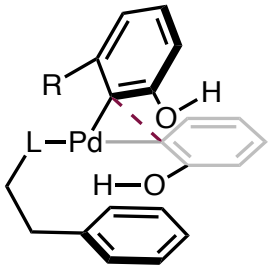
Pearce-Higgins, R. *et al. JACS* **2022**, *144*, 15026

Enantioselective Suzuki-Miyaura

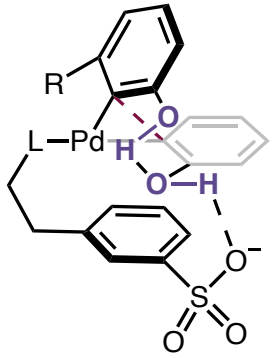


Hydrogen bond donor

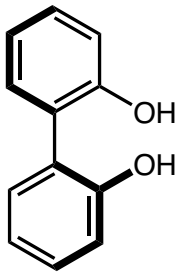
Organizing catalyst—substrate for C—H activation



vs.



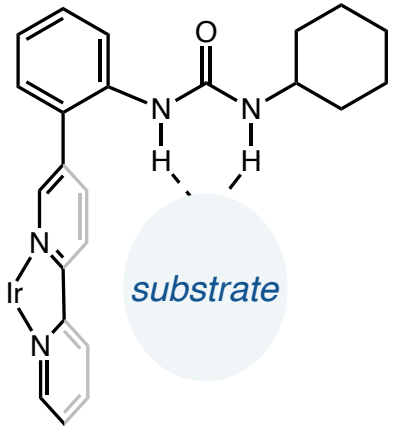
H-bonding for selective reductive elimination



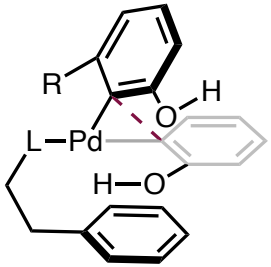
Hard to synthesize in high selectivity

Pearce-Higgins, R. *et al. JACS* **2022**, *144*, 15026

Enantioselective Suzuki-Miyaura



Hydrogen bond donor



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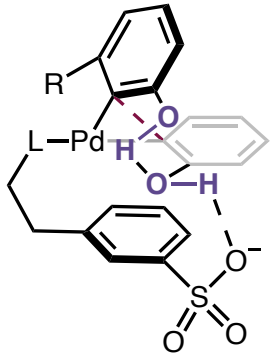
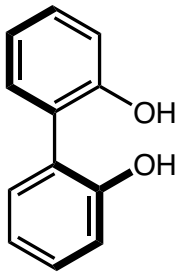
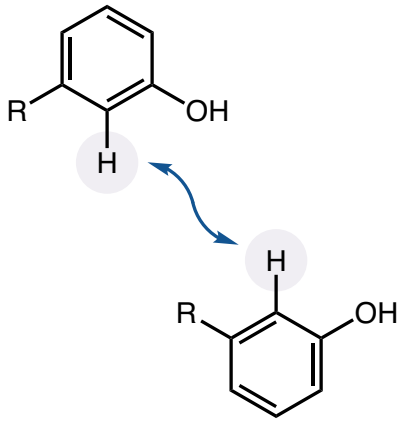


Organizing catalyst—substrate for C—H activation

H-bonding for selective reductive elimination



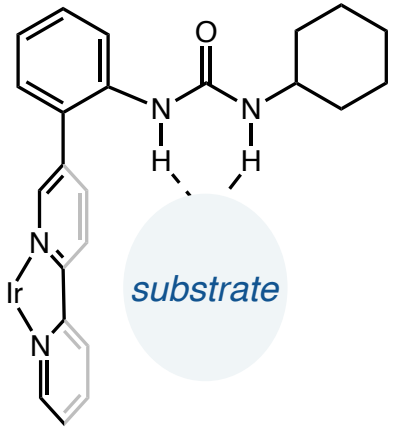


Hard to synthesize in high selectivity

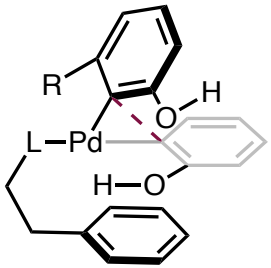
Challenging for simple substrates

Pearce-Higgins, R. *et al. JACS* **2022**, *144*, 15026

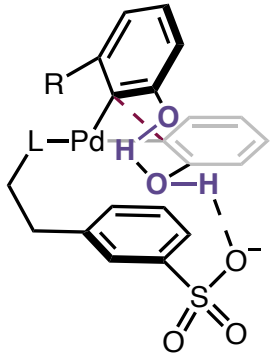
Enantioselective Suzuki-Miyaura



Hydrogen bond donor

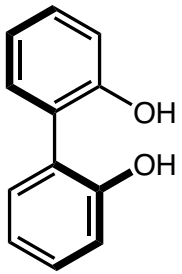


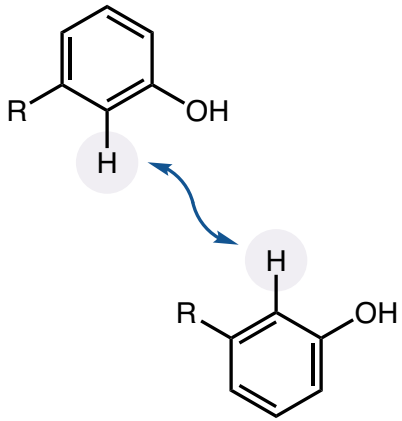
vs.

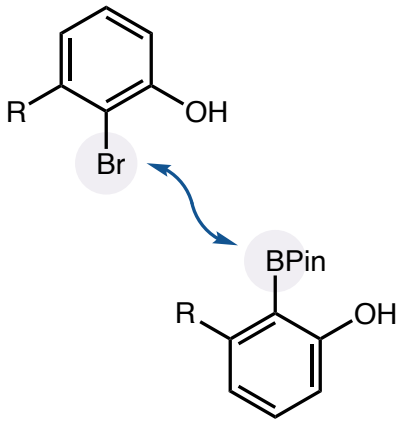


Organizing catalyst—substrate for C—H activation

H-bonding for selective reductive elimination







Hard to synthesize in high selectivity

Challenging for simple substrates

Can H-bonding control reductive elimination for selectivity?

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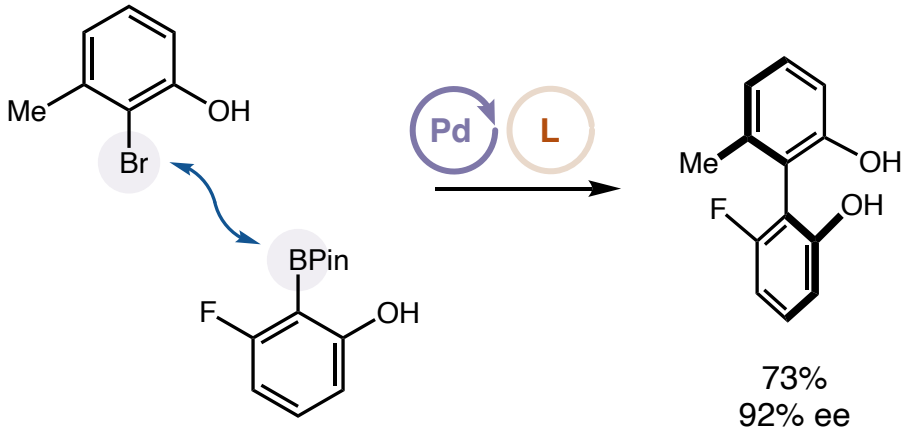
Enantioselective Suzuki-Miyaura



73%
92% ee

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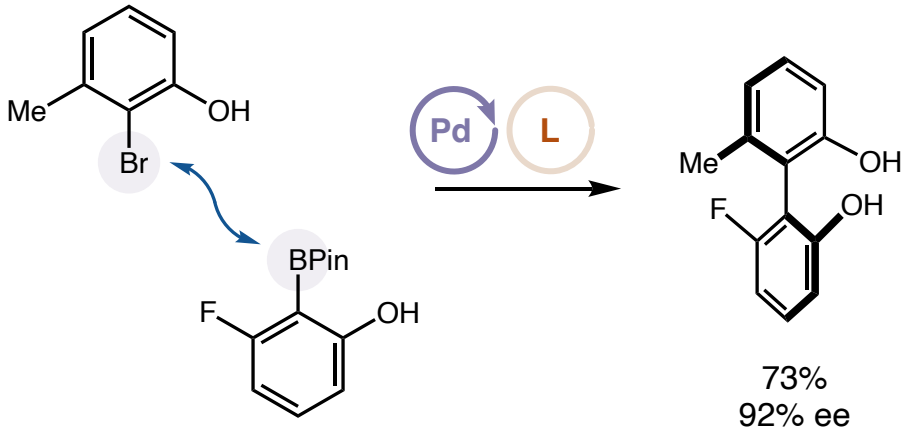
Enantioselective Suzuki-Miyaura



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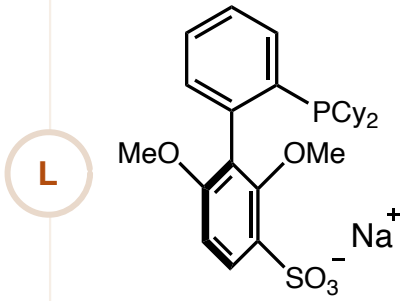

(R)-sSPhos

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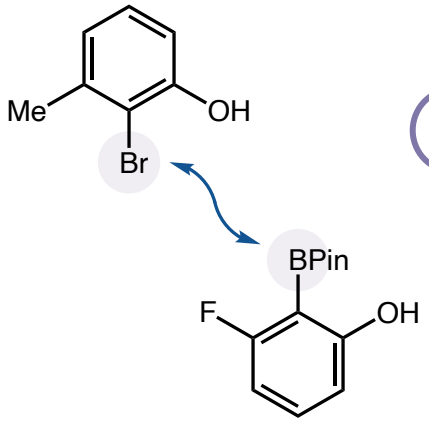
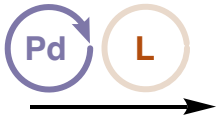
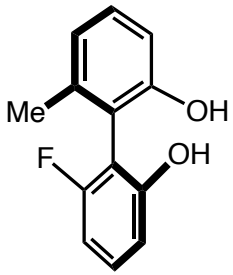
Enantioselective Suzuki-Miyaura







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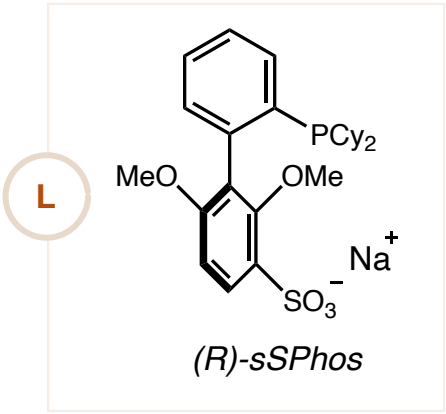

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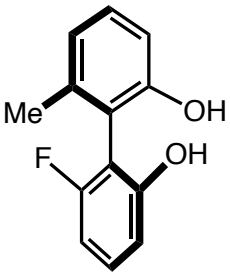

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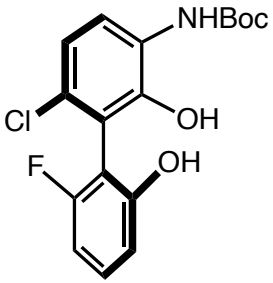

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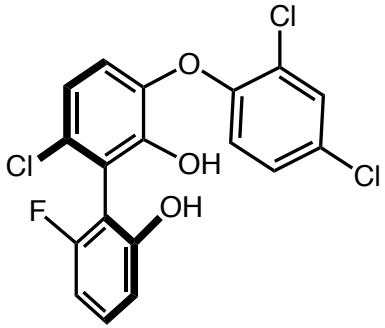

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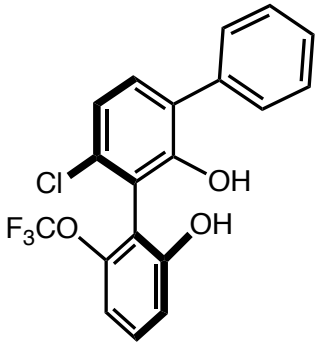

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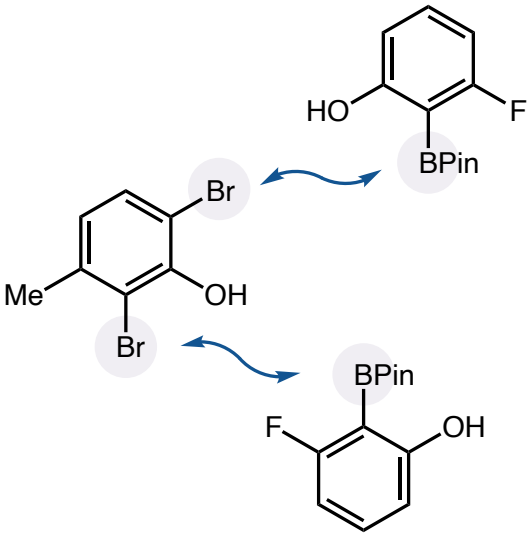
Enantioselective Suzuki-Miyaura



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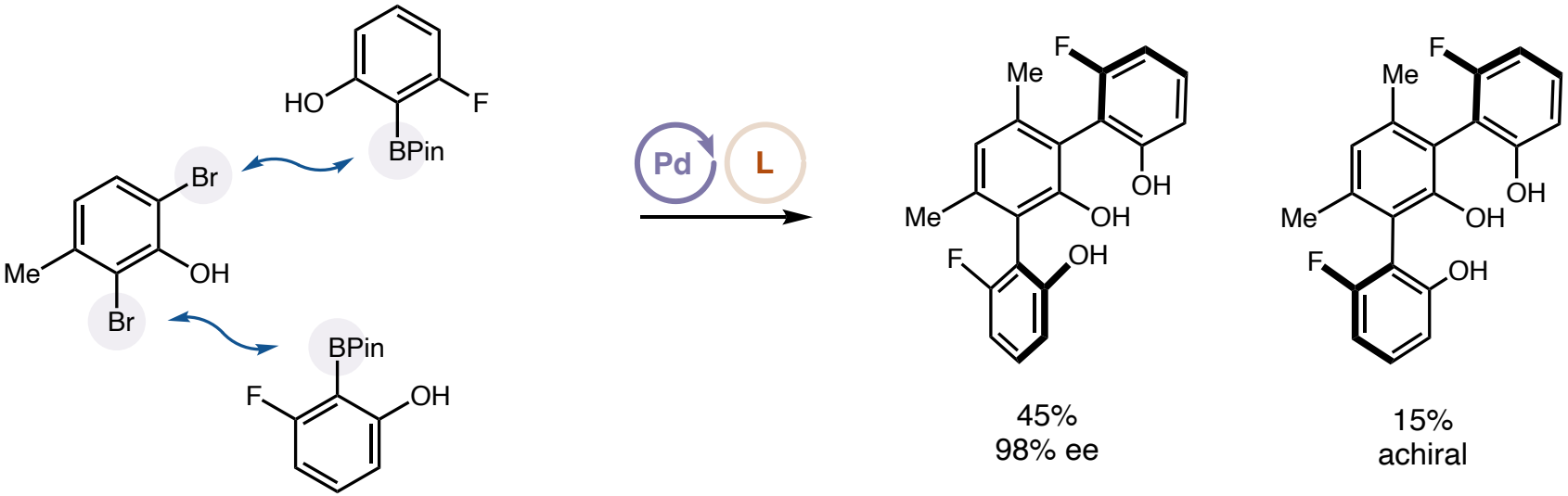
Enantioselective Suzuki-Miyaura



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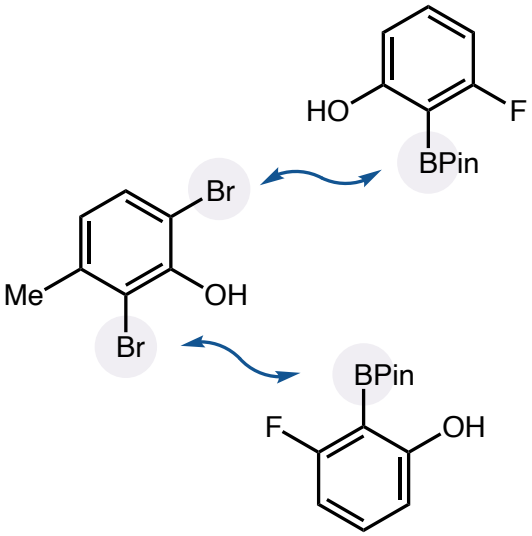

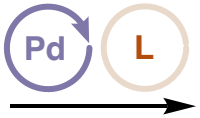

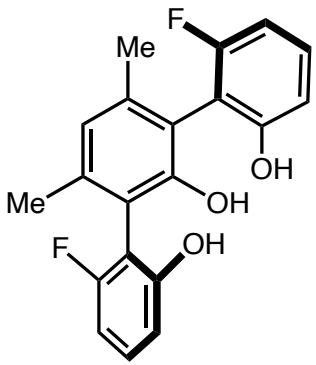

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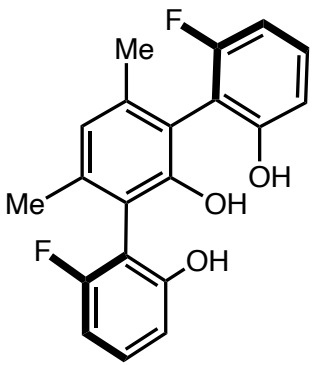

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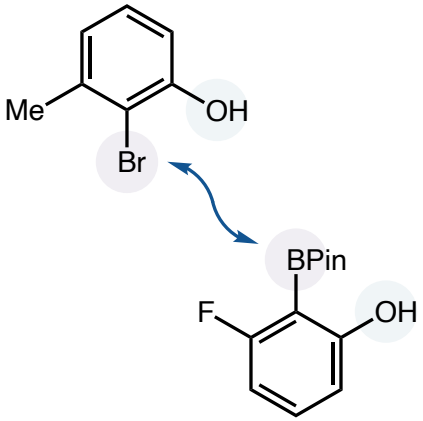
Effect of blocking the H-bond donors



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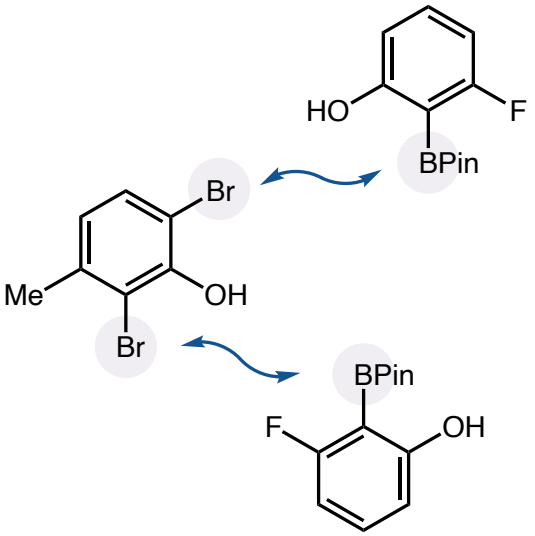
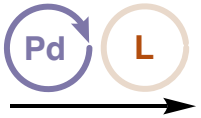
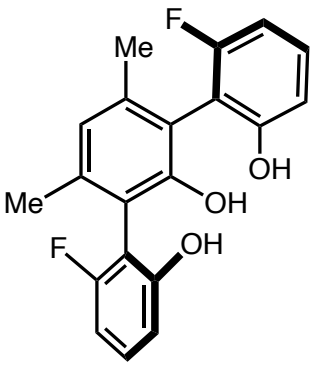
Enantioselective Suzuki-Miyaura







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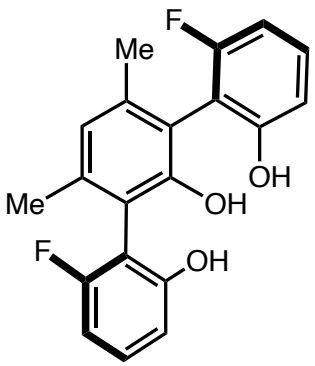

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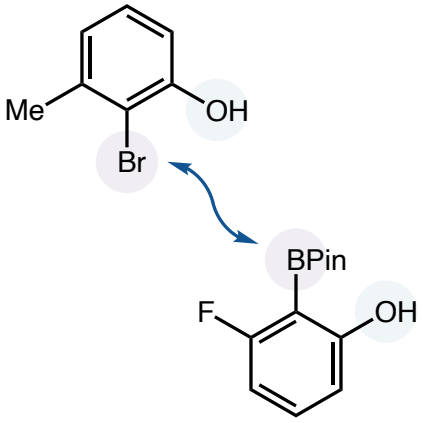
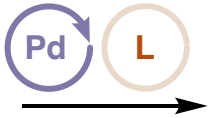
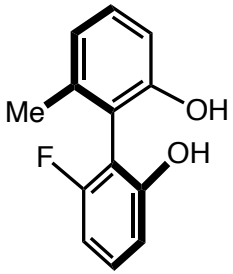
Effect of blocking the H-bond donors







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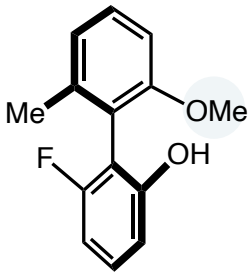

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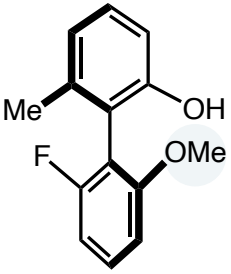

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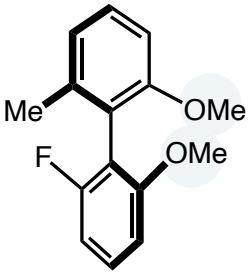

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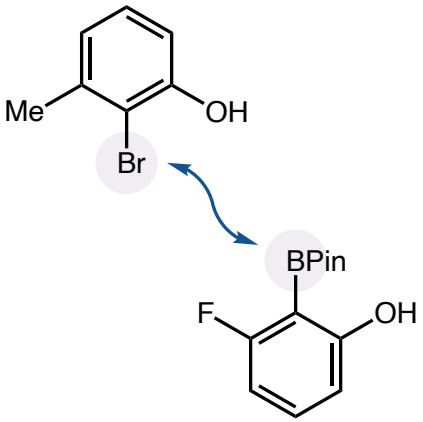
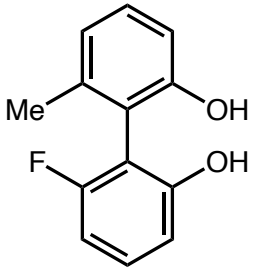
Enantioselective Suzuki-Miyaura





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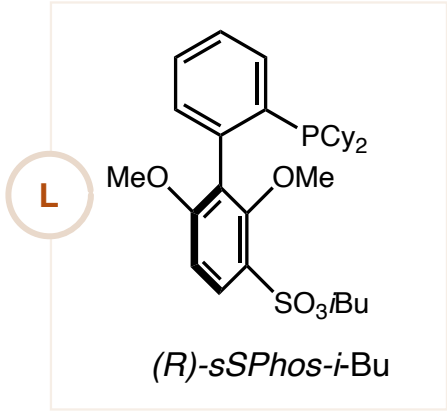

(R)-sSPhos-i-Bu

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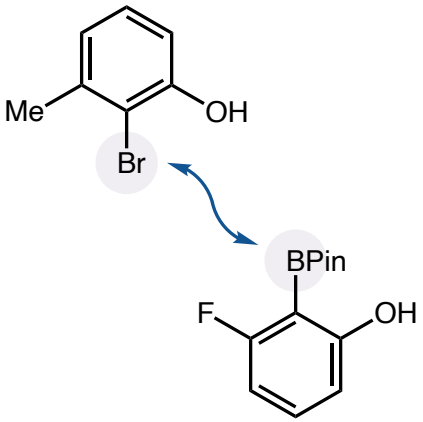
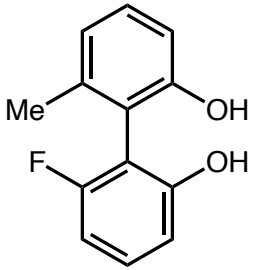
Enantioselective Suzuki-Miyaura





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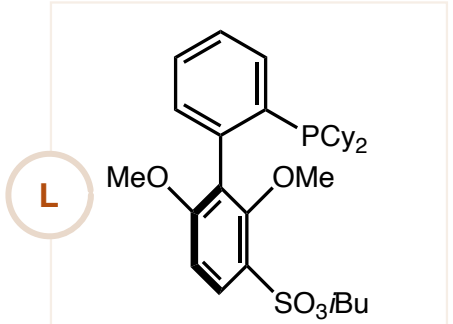
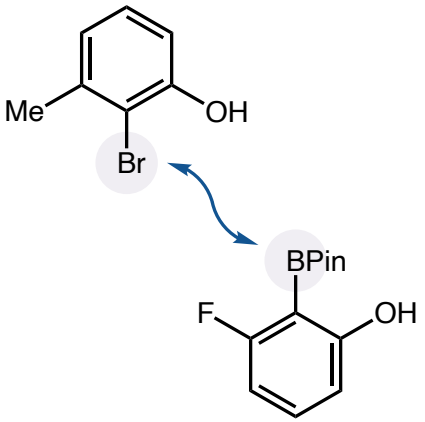


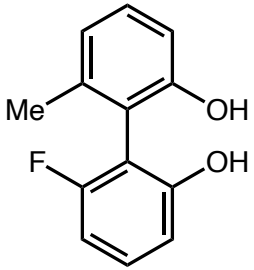
*(R)-sSPhos-i-*Bu

Use of alkylated ligand leads to poor ee

Pearce-Higgins, R. *et al. JACS* **2022**, *144*, 15026

Enantioselective Suzuki-Miyaura





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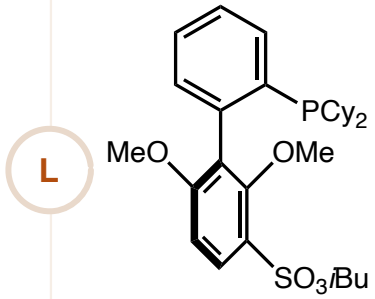
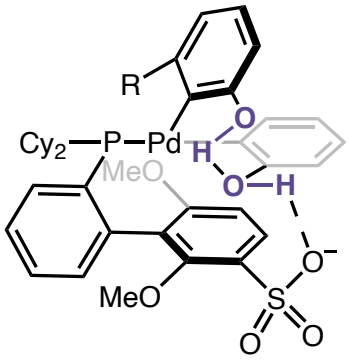


*(R)-sSPhos-i-*Bu

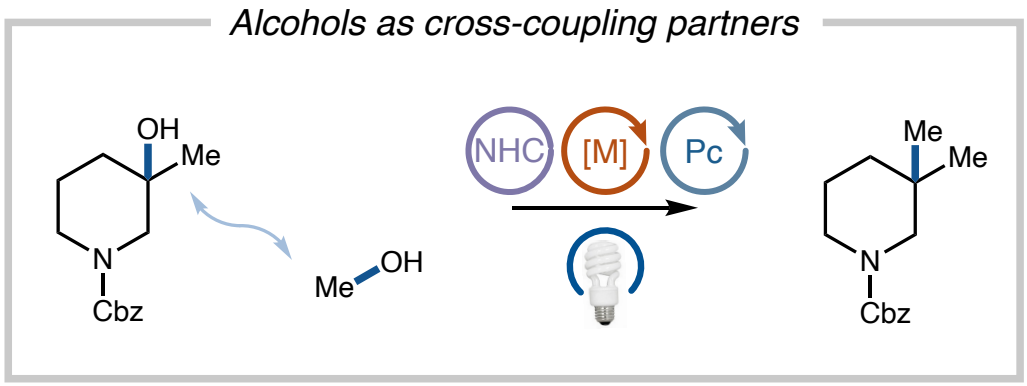
Use of alkylated ligand leads to poor ee

H-bonding controls enantioselectivity



Pearce-Higgins, R. *et al. JACS* **2022**, *144*, 15026

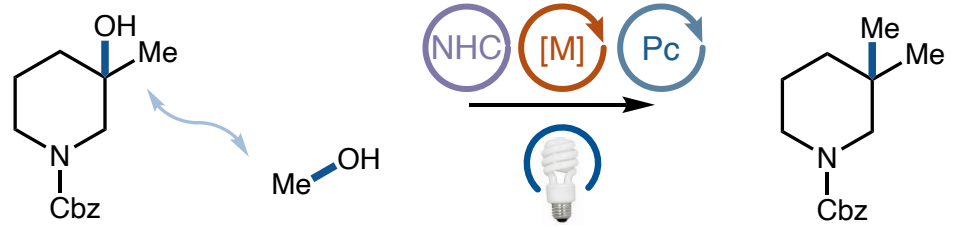
Alcohols as H-bond directing groups



Chen, R., Intermaggio, N. E., Xie, J., Ross-Ashton, J. A., Gould, C. A., Martin, R. T., Alcázar, J. & MacMillan, D. W. C. *Science* **2024**, *383*, 1350

Alcohols as H-bond directing groups

Alcohols as cross-coupling partners

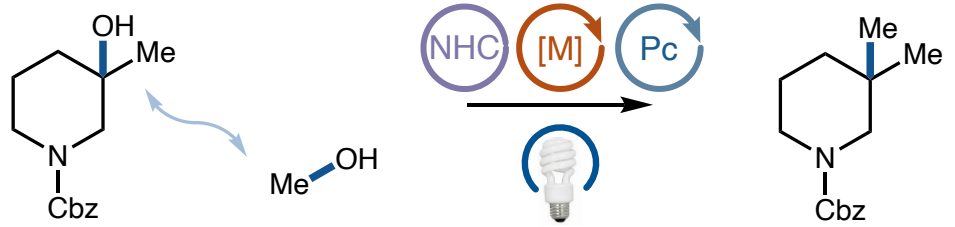


Can the ability of alcohols to engage in H-bonding control site-selectivity?

Chen, R., Intermaggio, N. E., Xie, J., Ross-Ashton, J. A., Gould, C. A., Martin, R. T., Alcázar, J. & MacMillan, D. W. C. *Science* **2024**, *383*, 1350

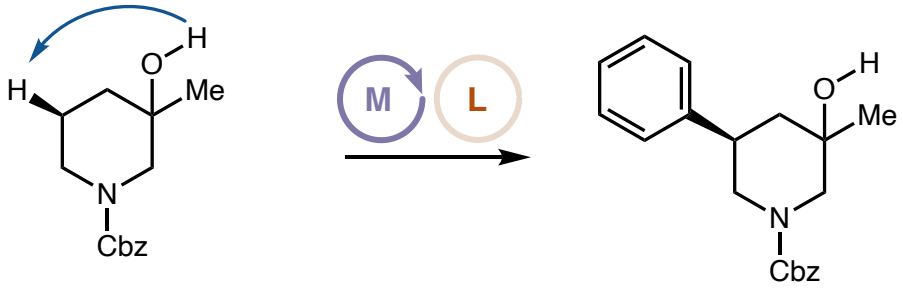
Alcohols as H-bond directing groups

Alcohols as cross-coupling partners



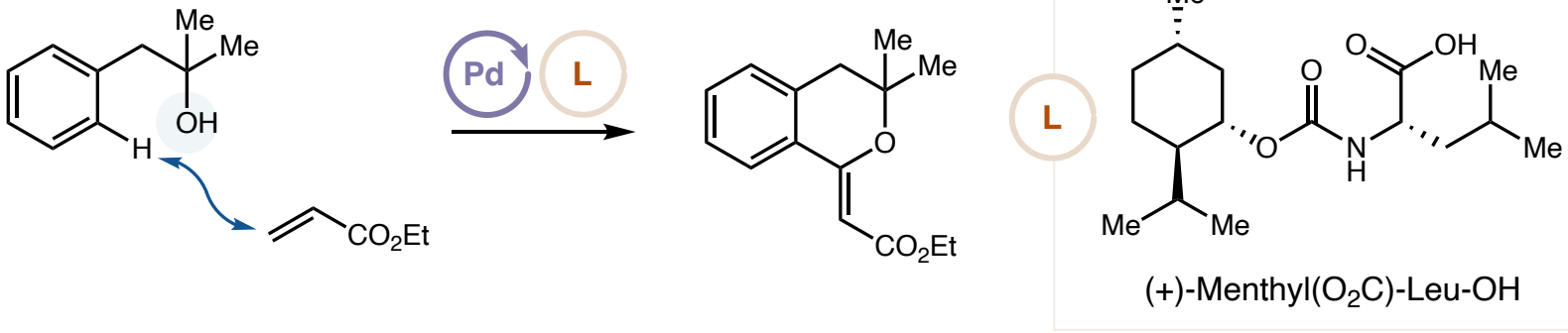
Can the ability of alcohols to engage in H-bonding control site-selectivity?

H-bond directed



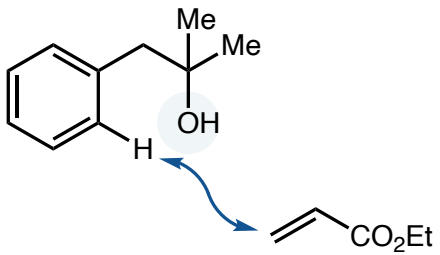
Chen, R., Intermaggio, N. E., Xie, J., Ross-Ashton, J. A., Gould, C. A., Martin, R. T., Alcázar, J. & MacMillan, D. W. C. *Science* **2024**, *383*, 1350

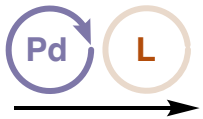
Alcohols as Lewis Basic directing groups

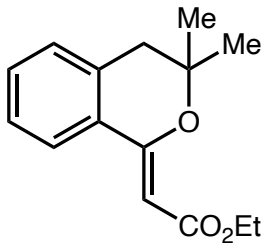


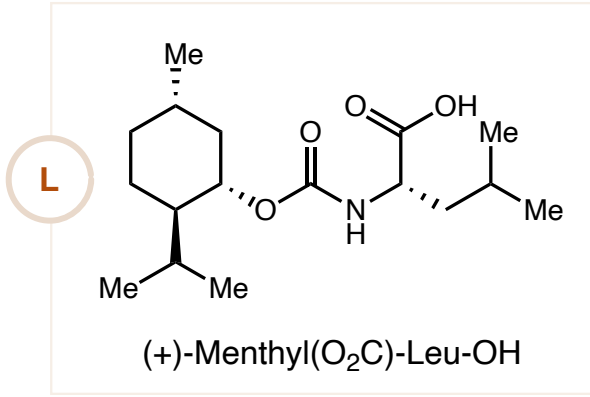
Lu, Y., Wang, D. H., Engle, K. & Yu, J.-Q. *JACS* **2010**, *132*, 5916

Alcohols as Lewis Basic directing groups

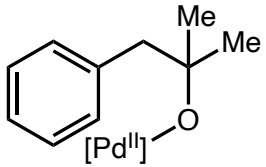




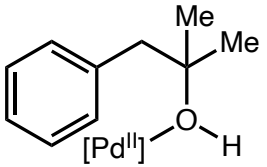




(+)-Menthyl(O_2C)-Leu-OH



anionic
X-type ligand

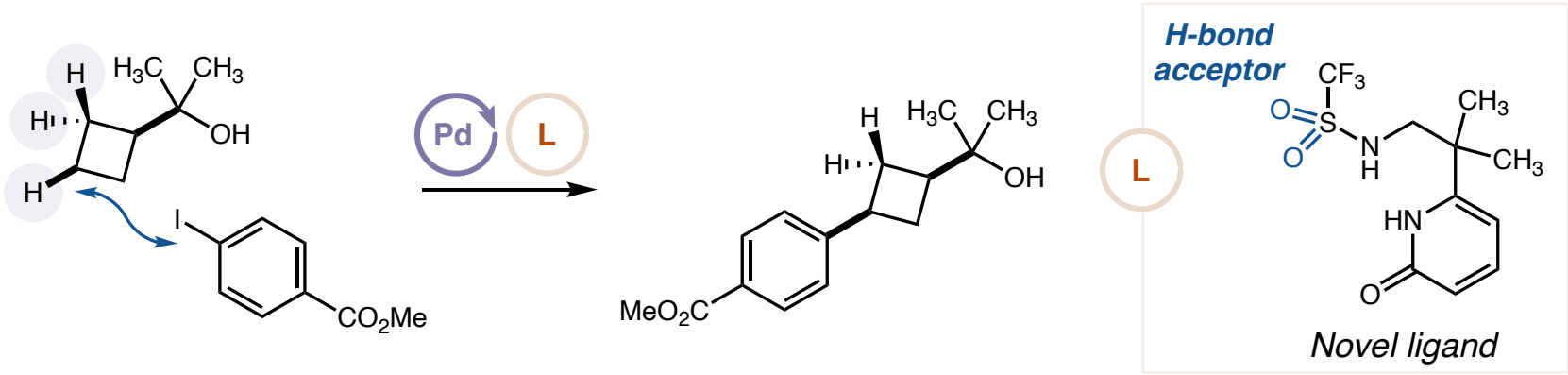


neutral
L-type ligand

Limited to Csp^2 functionalization

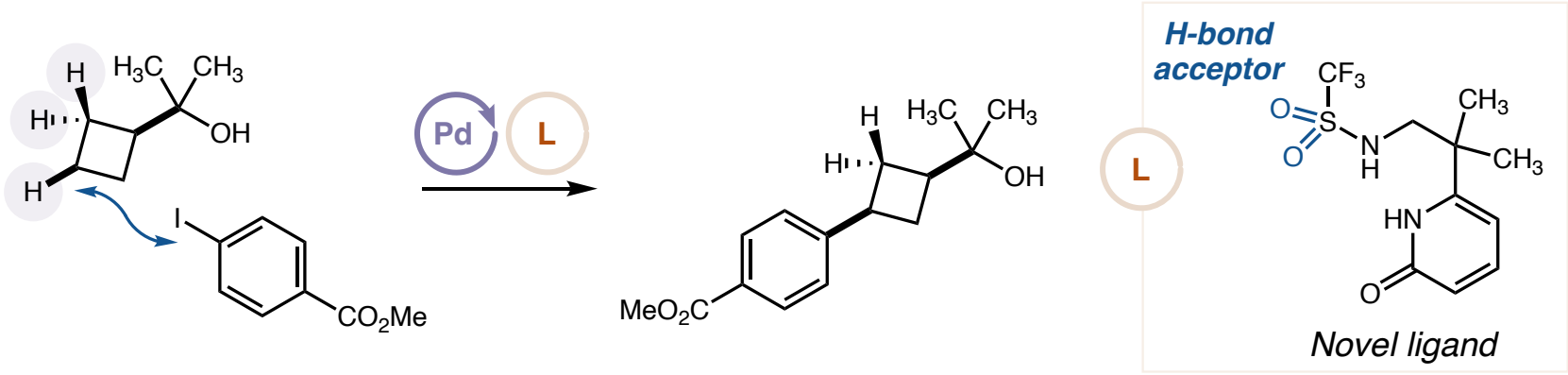
Lu, Y., Wang, D. H., Engle, K. & Yu, J.-Q. *JACS* **2010**, *132*, 5916

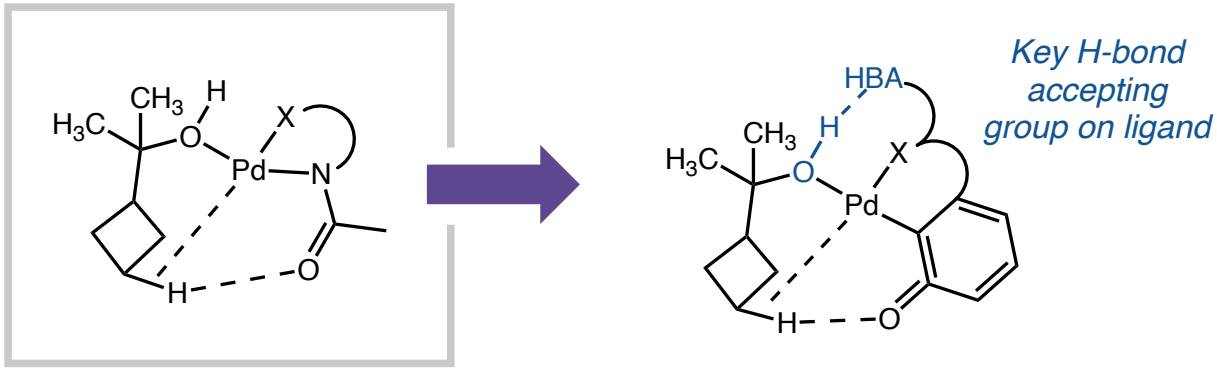
Distal Alcohol Functionalization



Strassfeld, D. A., Chen, C.-Y., Park, H. S., Phan, D. Q. & Yu, J.-Q. *Nature* **2023**, *622*, 80

Distal Alcohol Functionalization

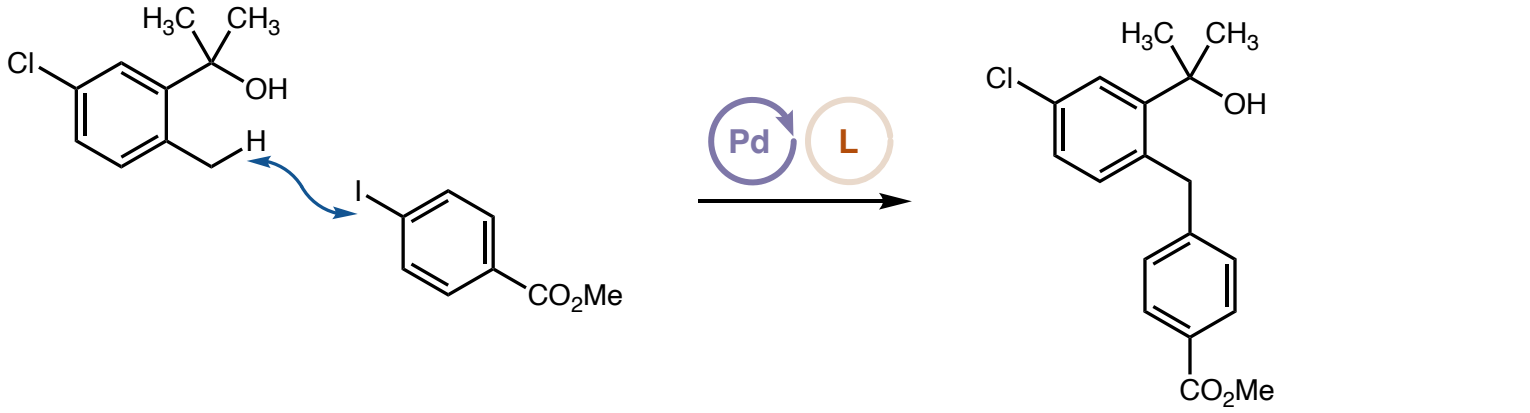


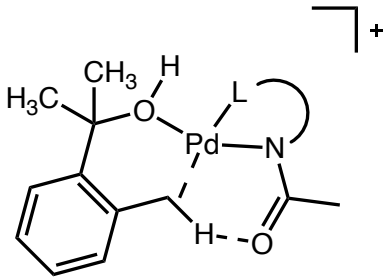


Enables alcohol directed C—H arylation

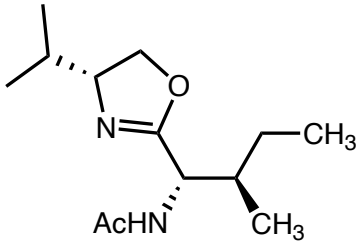
Strassfeld, D. A., Chen, C.-Y., Park, H. S., Phan, D. Q. & Yu, J.-Q. *Nature* **2023**, *622*, 80

Distal Alcohol Functionalization





Coulombic destabilization



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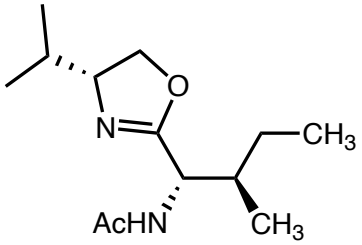

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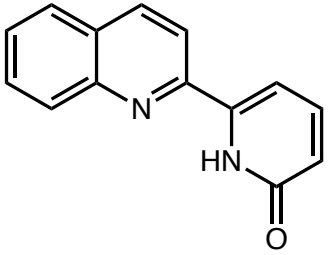

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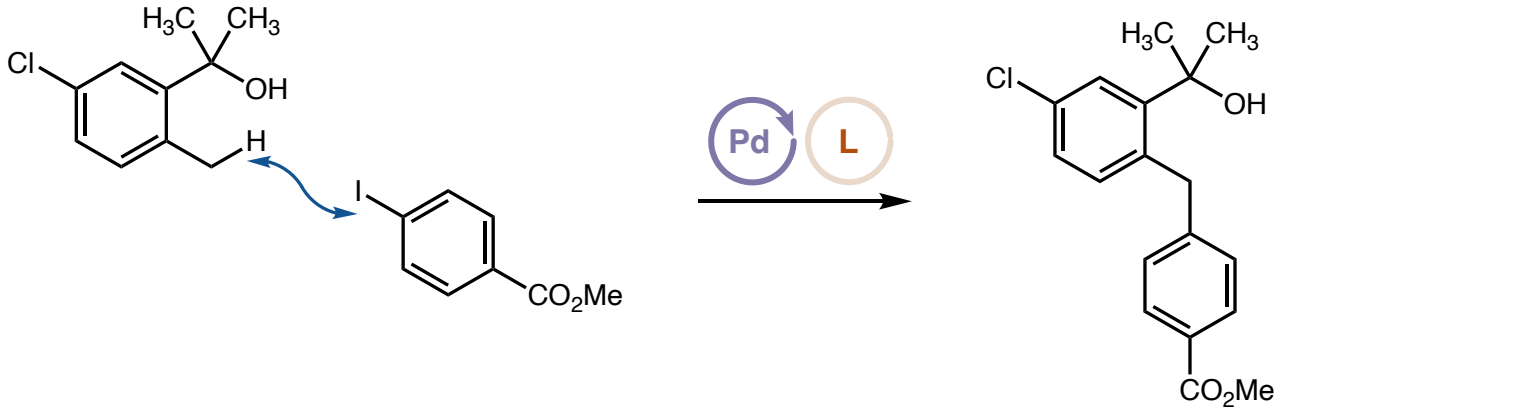
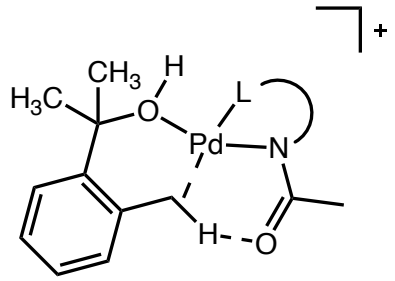
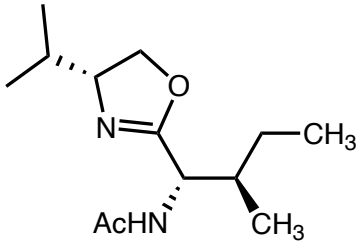
Strassfeld, D. A., Chen, C.-Y., Park, H. S., Phan, D. Q. & Yu, J.-Q. *Nature* **2023**, *622*, 80

Distal Alcohol Functionalization





Coulombic destabilization



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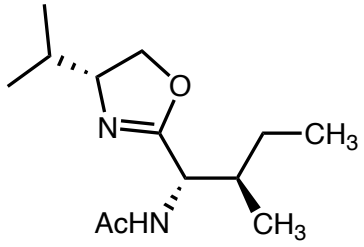

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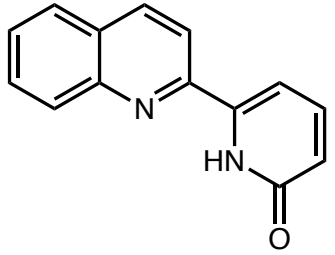

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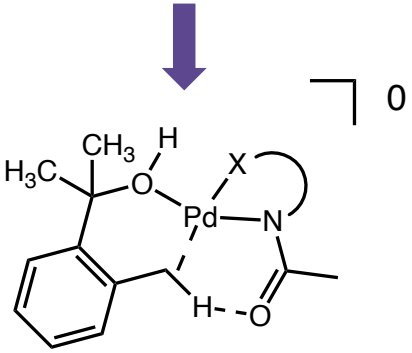
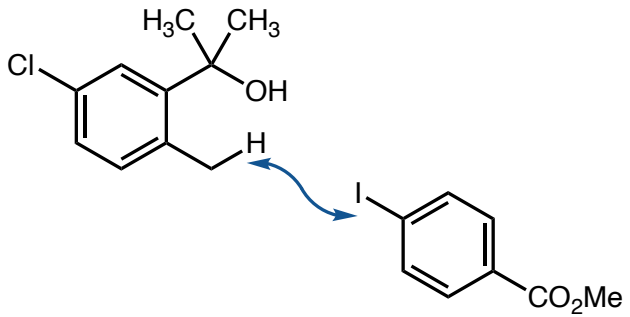
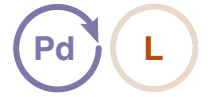


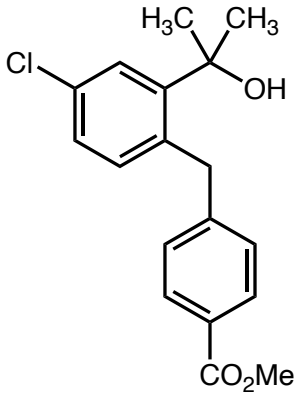
Increased stabilization?

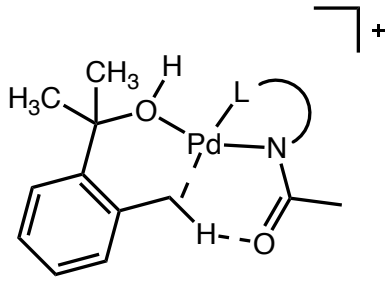
Strassfeld, D. A., Chen, C.-Y., Park, H. S., Phan, D. Q. & Yu, J.-Q. *Nature* **2023**, *622*, 80

Distal Alcohol Functionalization

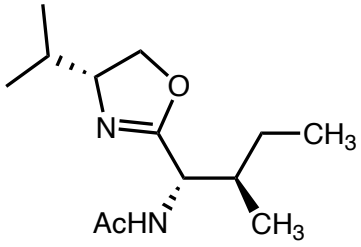








Coulombic destabilization



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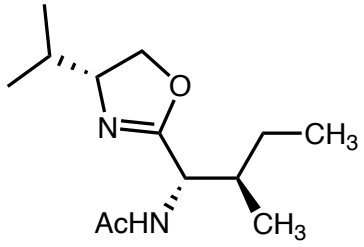

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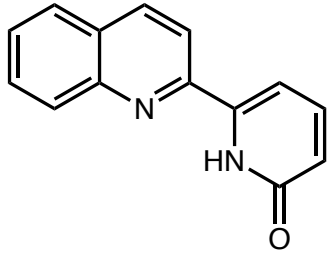

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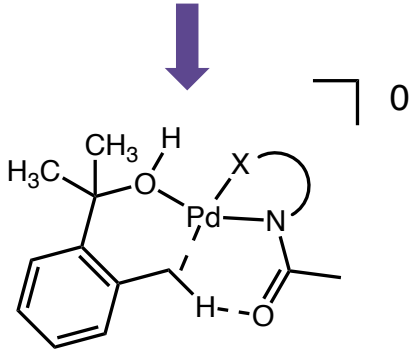
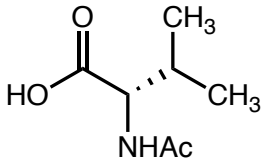


Increased stabilization?



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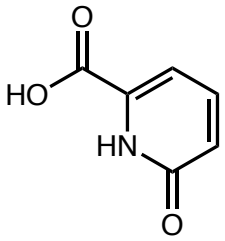

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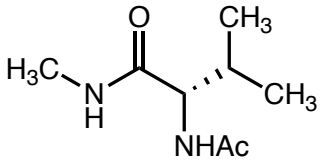

6% yield

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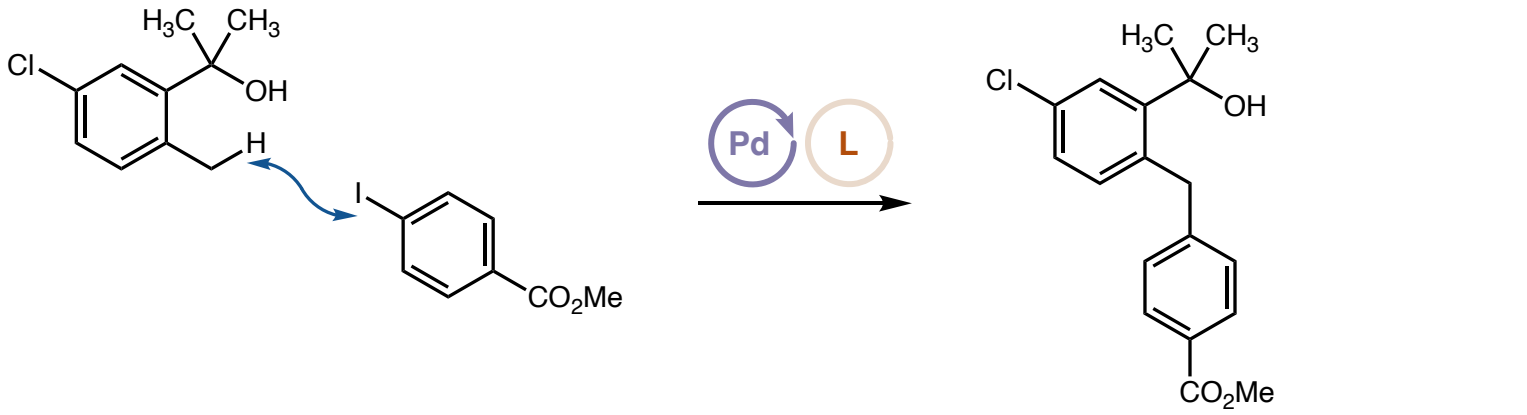
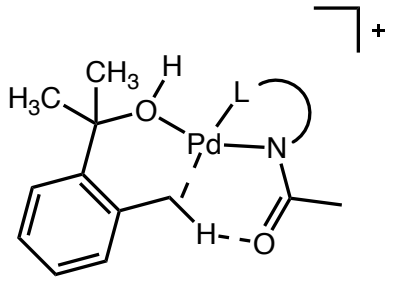
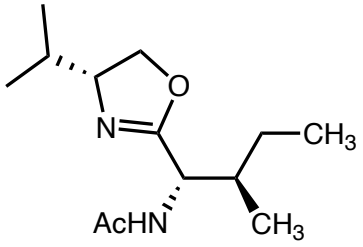
Distal Alcohol Functionalization





Coulombic destabilization



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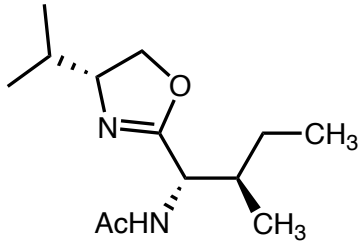

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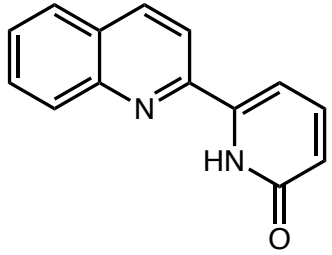

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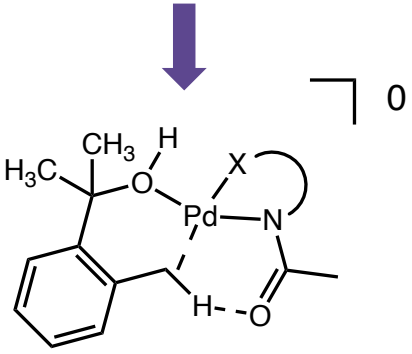
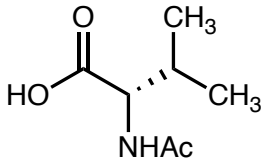


Increased stabilization?



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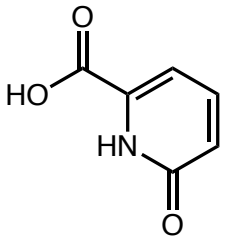

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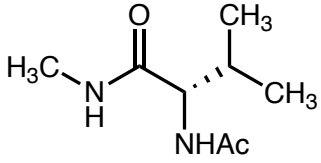

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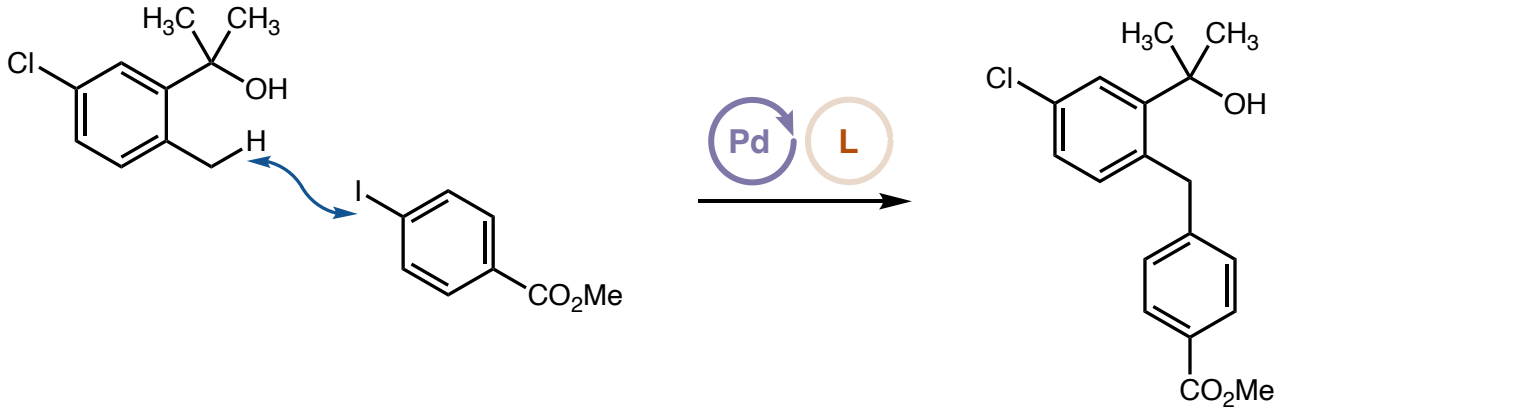
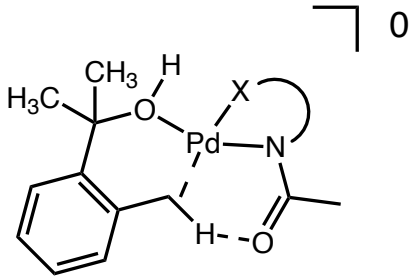
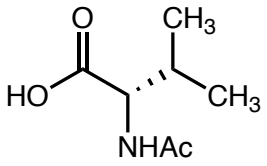
Distal Alcohol Functionalization







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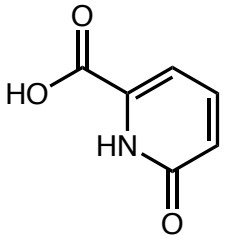

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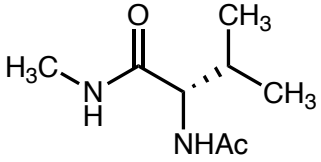

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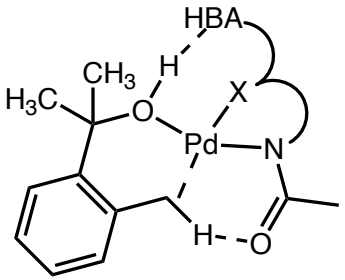
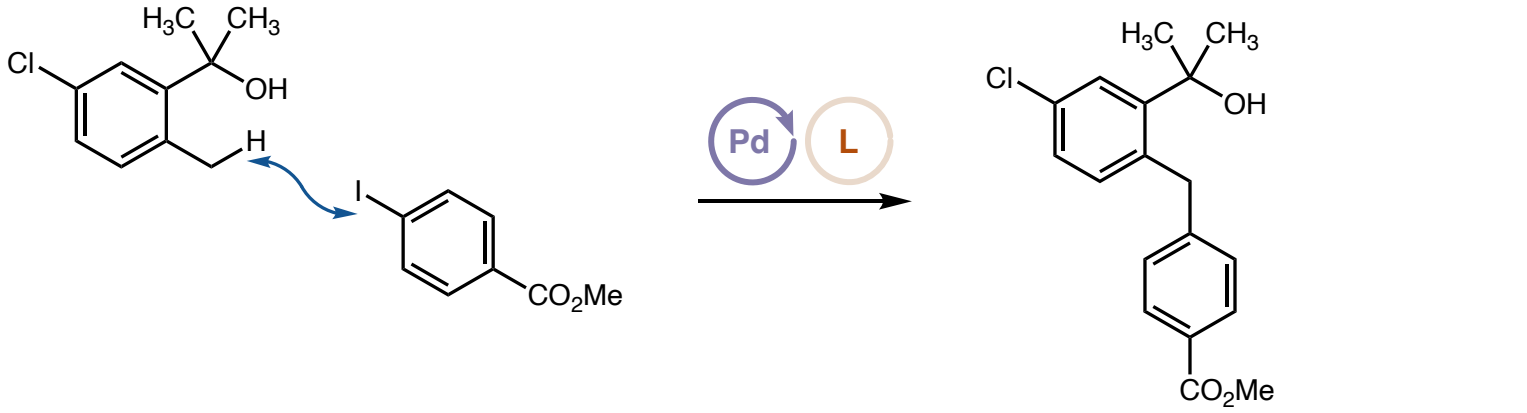
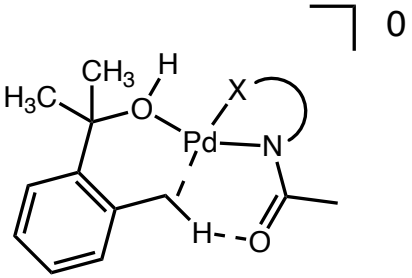


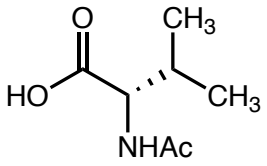
Internal H-Bond acceptor?

Strassfeld, D. A., Chen, C.-Y., Park, H. S., Phan, D. Q. & Yu, J.-Q. *Nature* **2023**, *622*, 80

Distal Alcohol Functionalization







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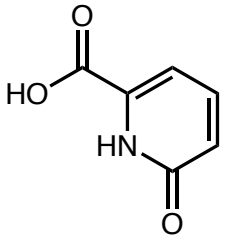

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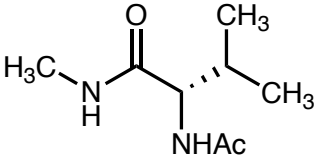

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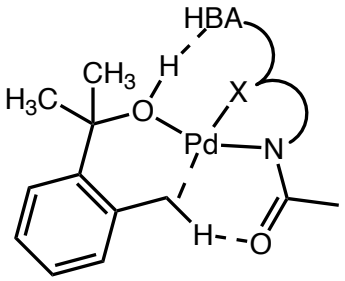

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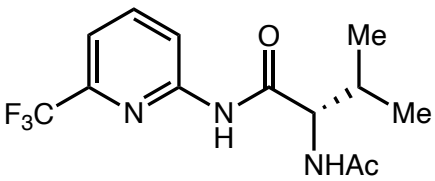

14% yield

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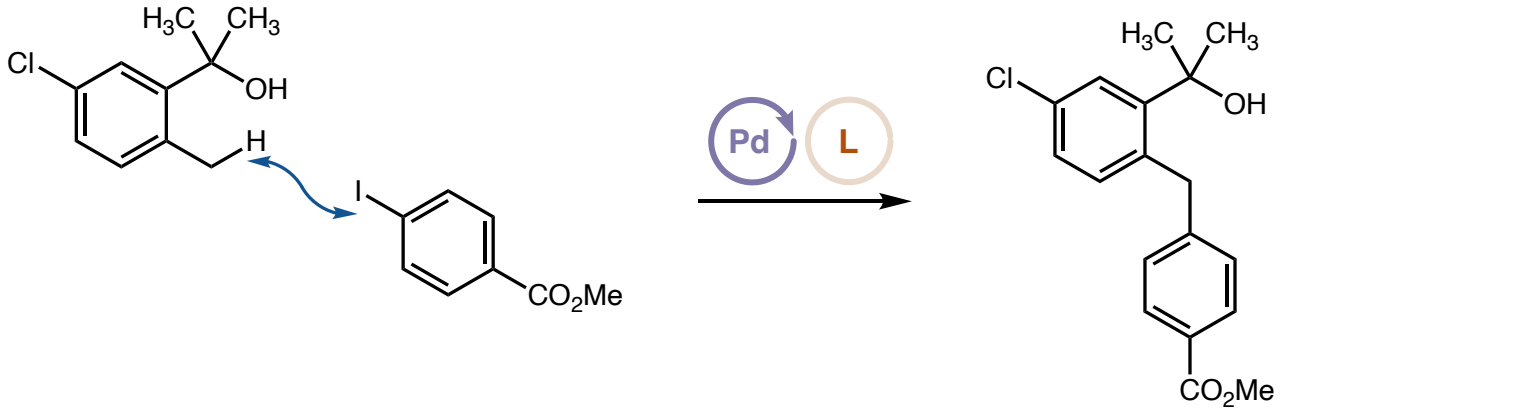
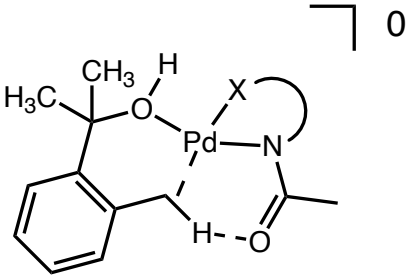
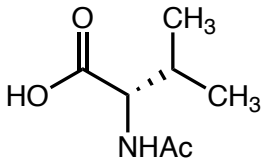
Distal Alcohol Functionalization







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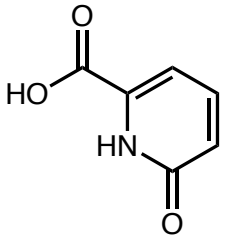

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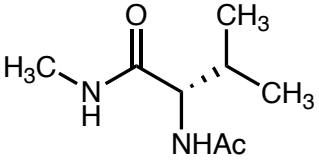

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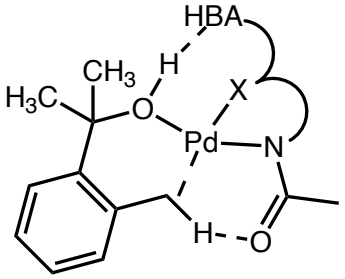
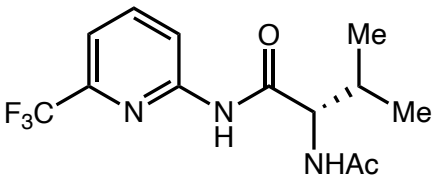


Internal H-Bond acceptor?



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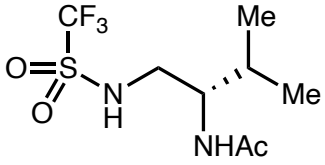

53% yield

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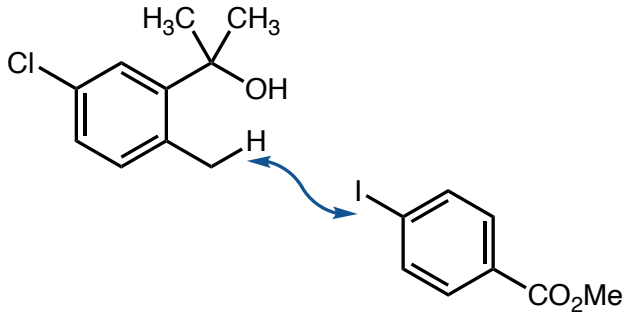
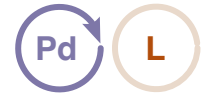
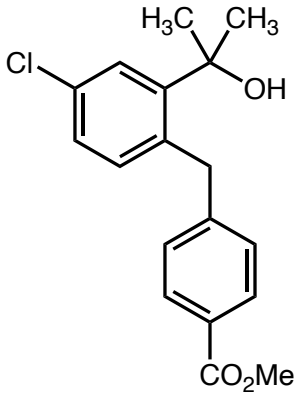
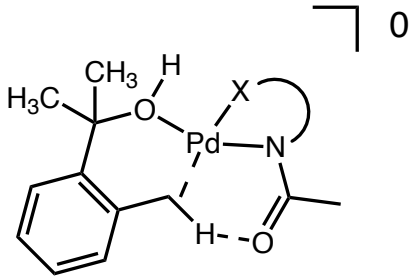
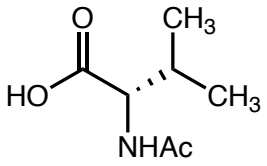
Distal Alcohol Functionalization



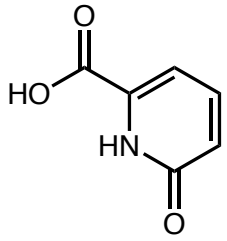




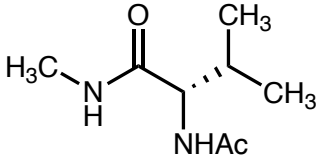




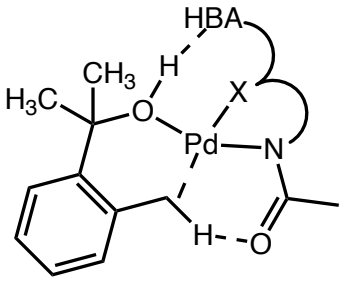
3% yield



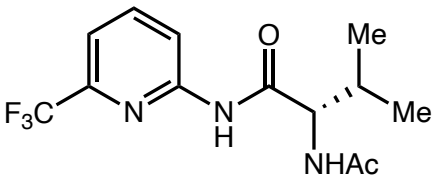
3% yield



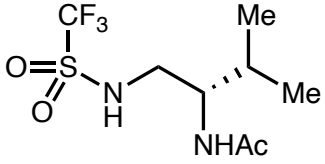
6% yield



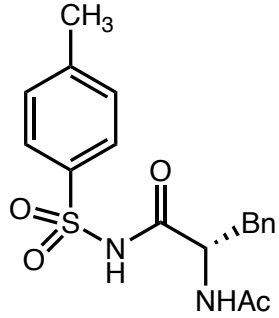
Internal H-Bond acceptor?



14% yield



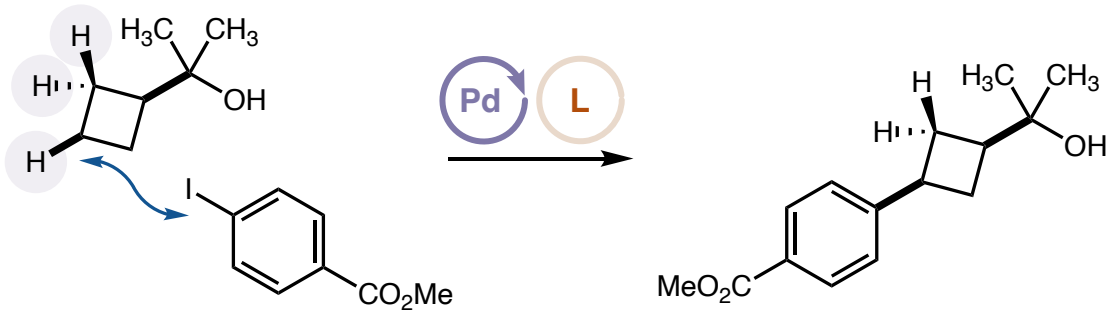
53% yield



86% yield

Strassfeld, D. A., Chen, C.-Y., Park, H. S., Phan, D. Q. & Yu, J.-Q. *Nature* **2023**, *622*, 80

Distal Alcohol Functionalization



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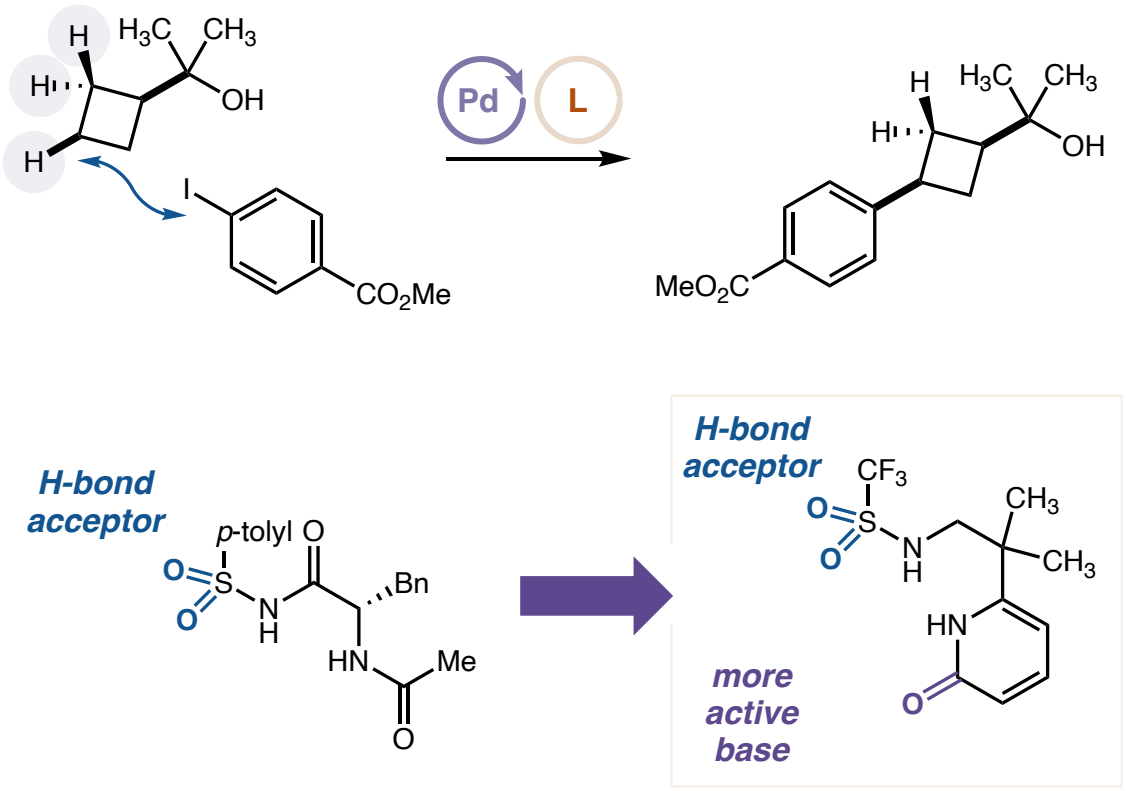
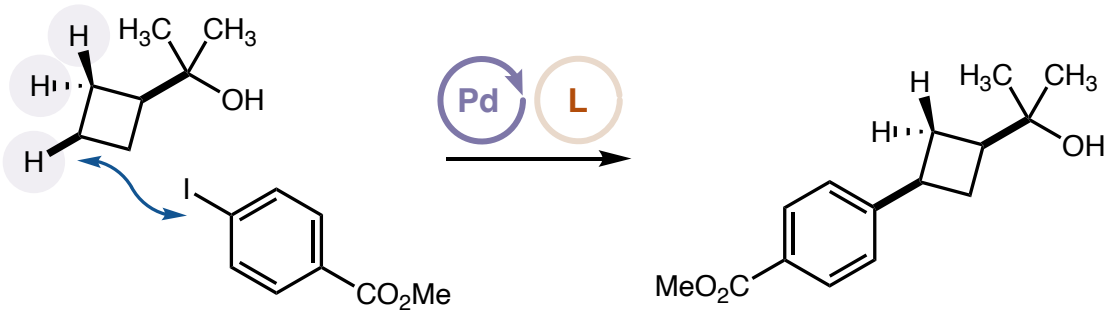
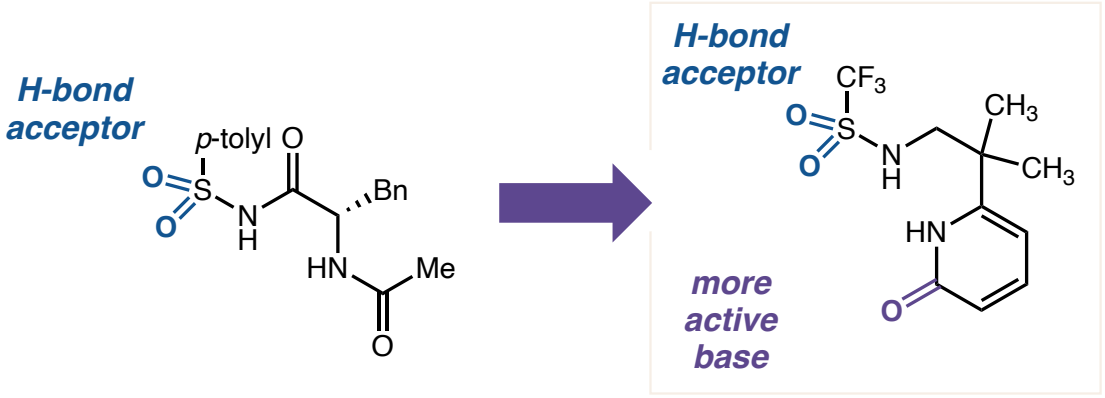
Distal Alcohol Functionalization

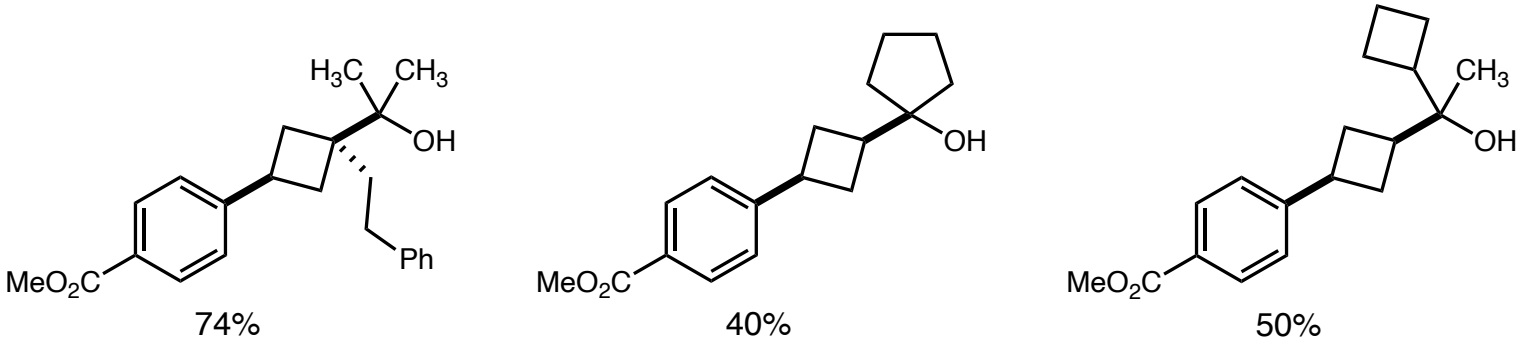


Strassfeld, D. A., Chen, C.-Y., Park, H. S., Phan, D. Q. & Yu, J.-Q. *Nature* **2023**, *622*, 80

Distal Alcohol Functionalization







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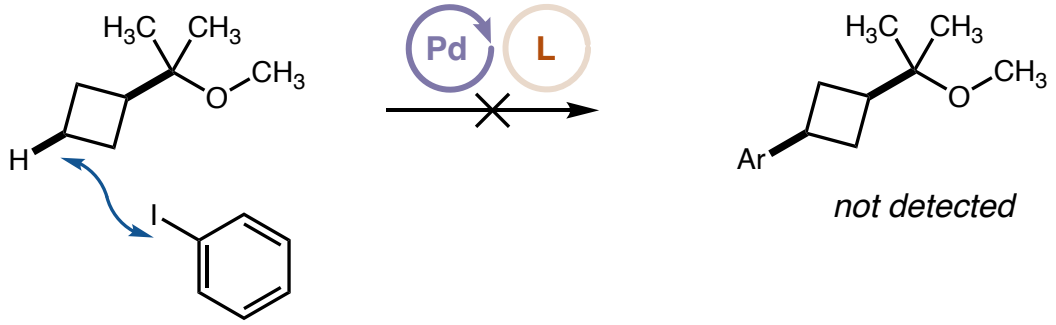
Distal Alcohol Functionalization



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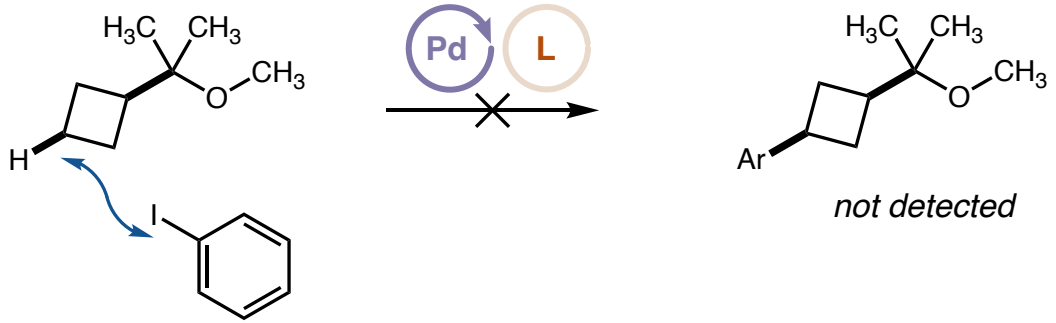
Distal Alcohol Functionalization

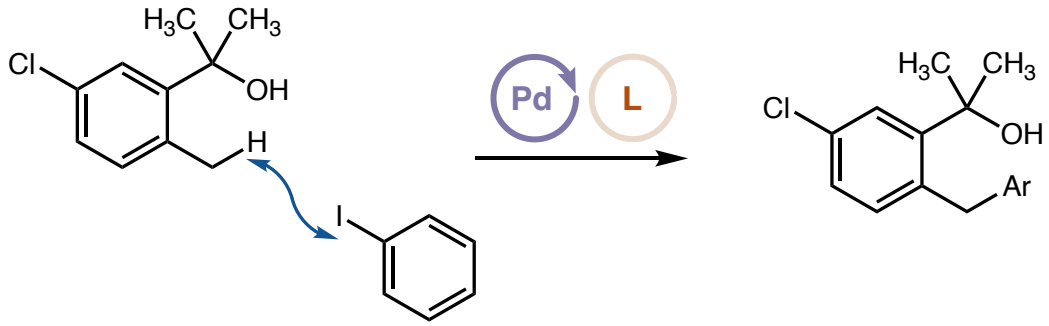


not detected

Alcohol is crucial for reaction

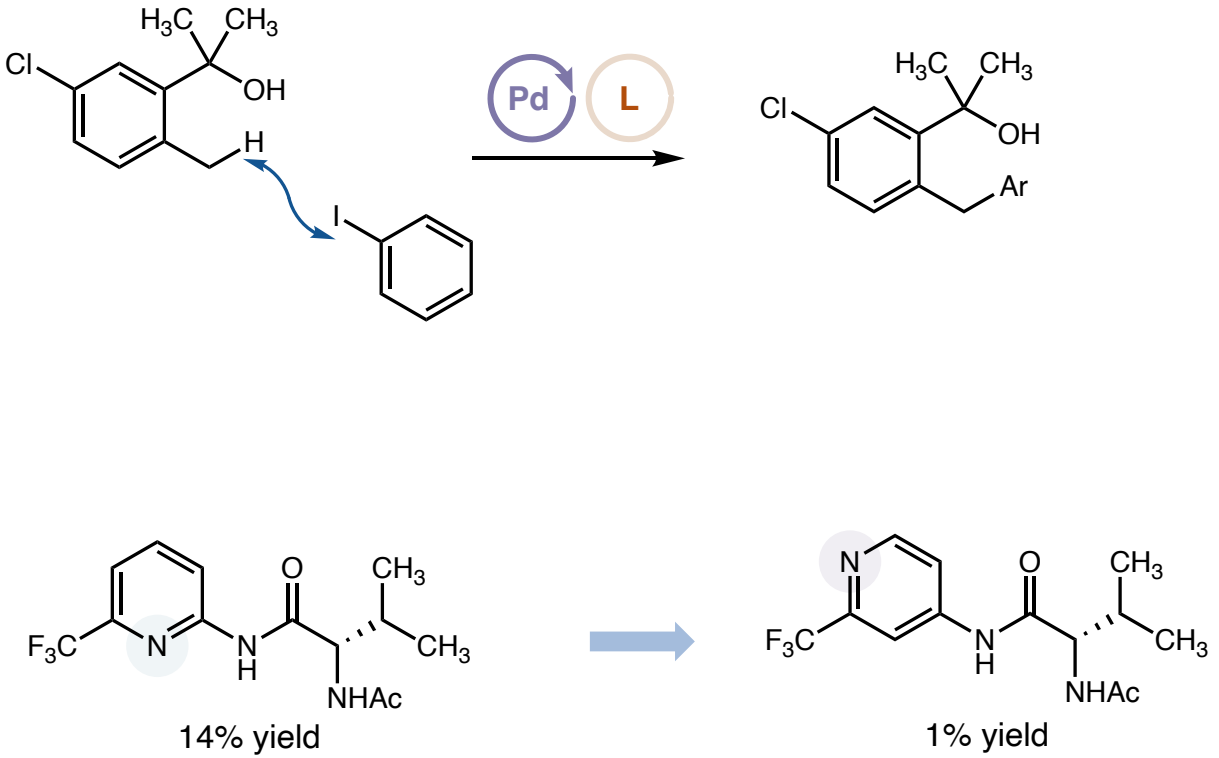
Strassfeld, D. A., Chen, C.-Y., Park, H. S., Phan, D. Q. & Yu, J.-Q. *Nature* **2023**, *622*, 80

Distal Alcohol Functionalization



Strassfeld, D. A., Chen, C.-Y., Park, H. S., Phan, D. Q. & Yu, J.-Q. *Nature* **2023**, *622*, 80

Distal Alcohol Functionalization



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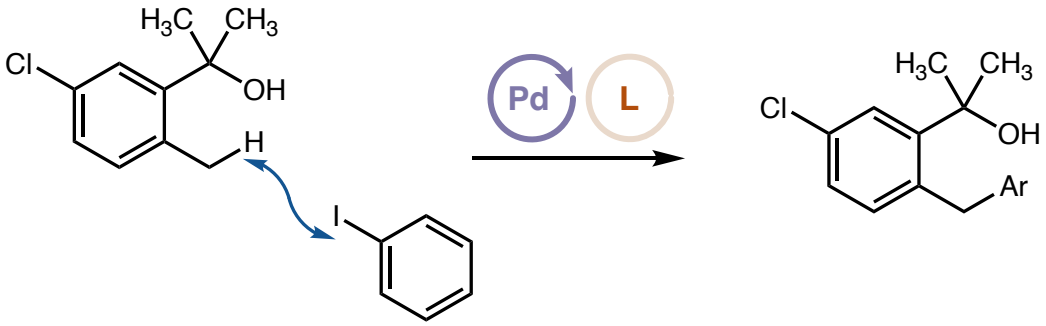
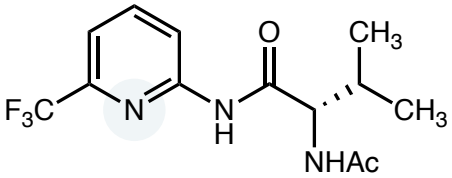
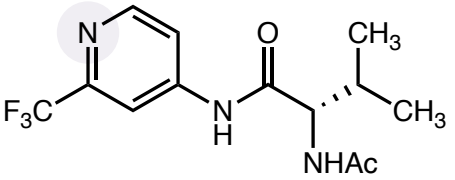
Distal Alcohol Functionalization

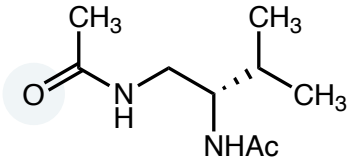




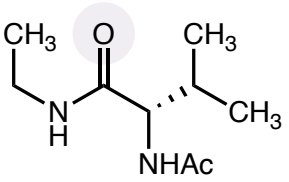
14% yield



1% yield



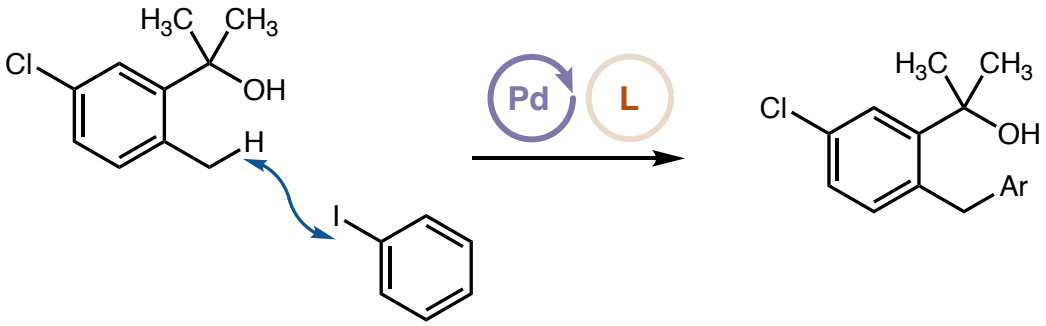
16% yield

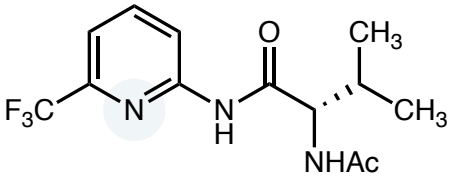


4% yield

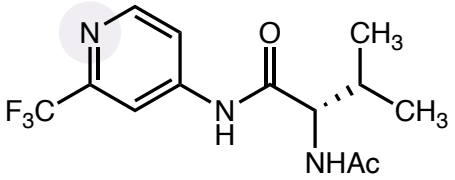
Strassfeld, D. A., Chen, C.-Y., Park, H. S., Phan, D. Q. & Yu, J.-Q. *Nature* **2023**, *622*, 80

Distal Alcohol Functionalization

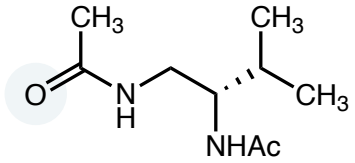




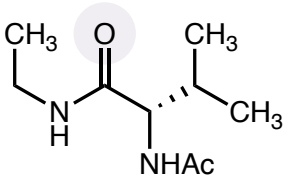
14% yield



1% yield



16% yield



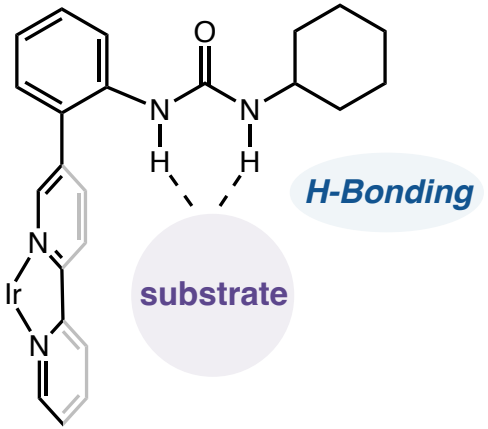
4% yield

Ligand isomers not competent

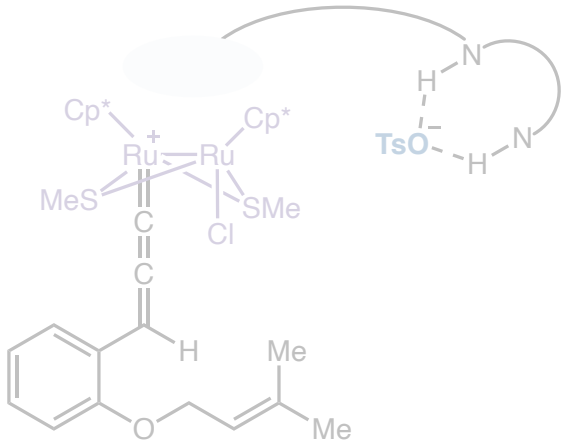
Strassfeld, D. A., Chen, C.-Y., Park, H. S., Phan, D. Q. & Yu, J.-Q. *Nature* **2023**, *622*, 80

Ion-Pairing

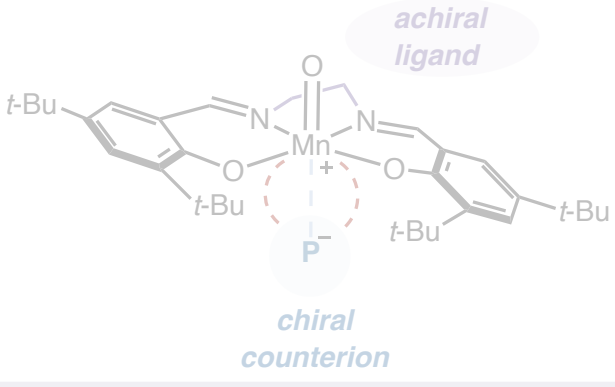
Hydrogen-bonding



Ion-pairing & H-Bonding

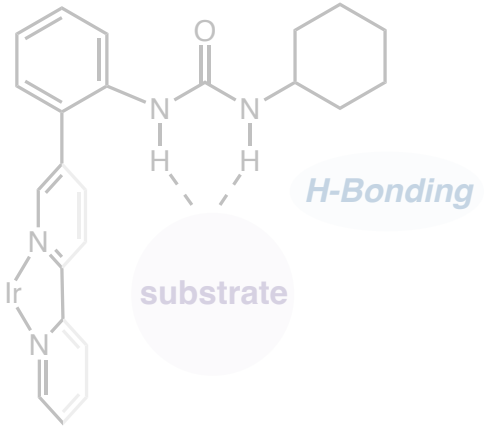


Ion-pairing

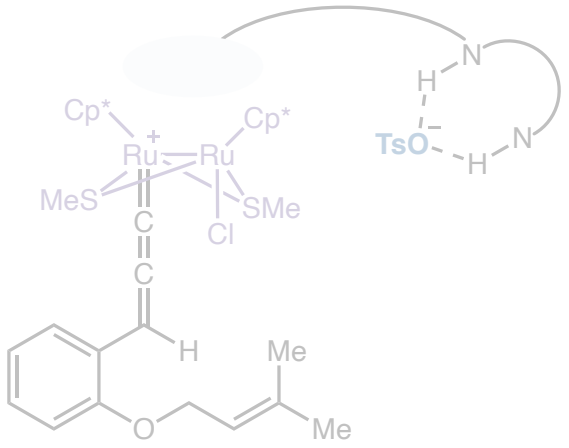


Ion-Pairing

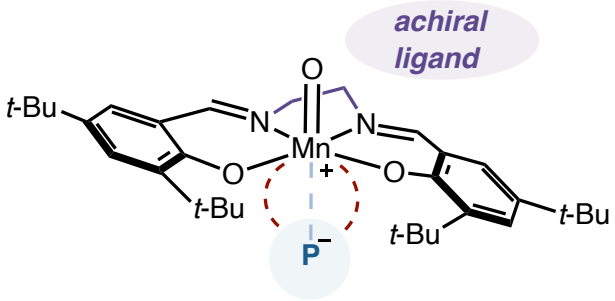
Hydrogen-bonding

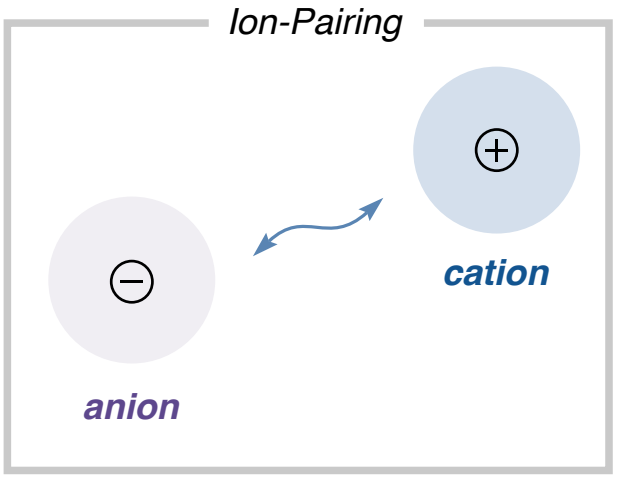


Ion-pairing & H-Bonding

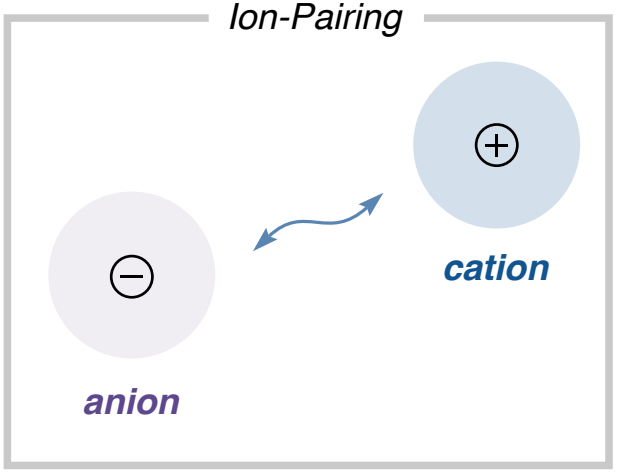


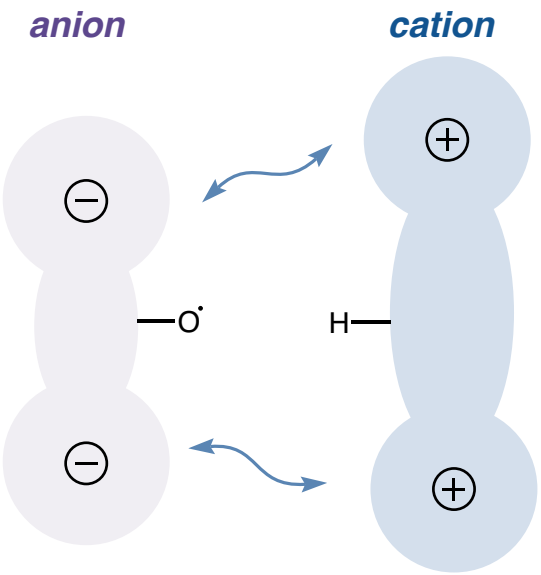
Ion-pairing



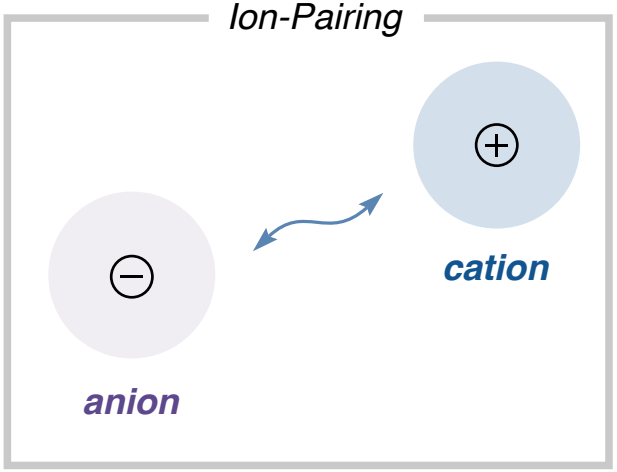

Ion-Pairing
cation
anion

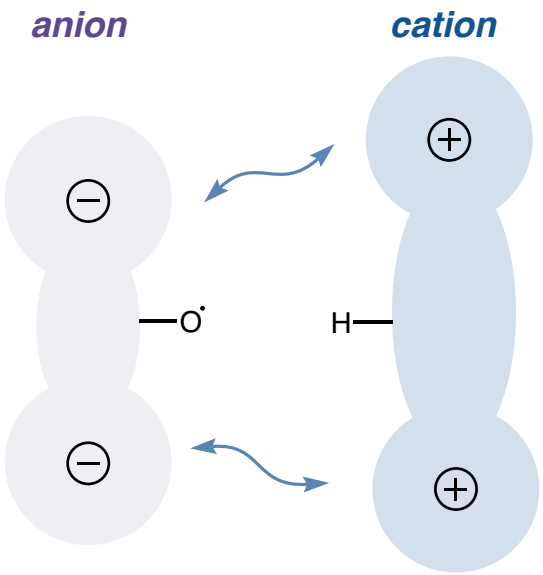
Ion-Pairing - Breslow





Ion-Pairing - Breslow





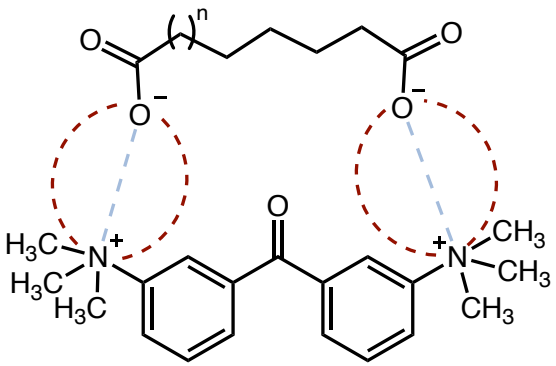
Ronald Breslow

(1931-2017)

Columbia University

Breslow - Ion-Pairing oxidation

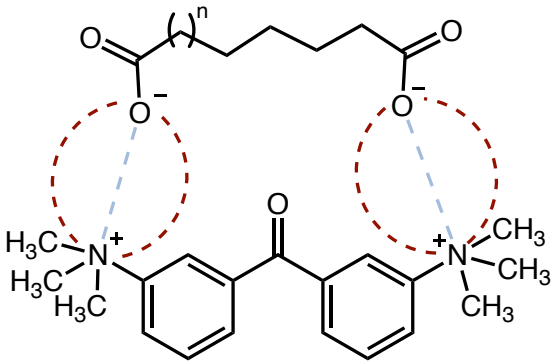
2 point binding

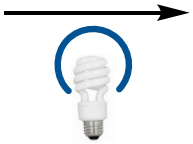


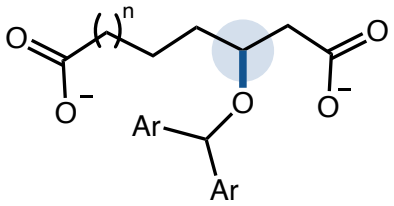
Rajagopalan, R., Schwarz, J., & Breslow, R. *JACS* **1981**, *103*, 2905

Breslow - Ion-Pairing oxidation

2 point binding







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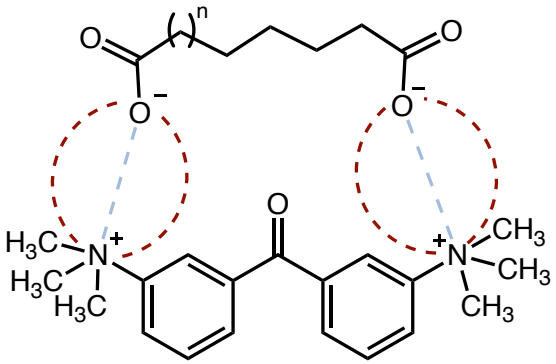
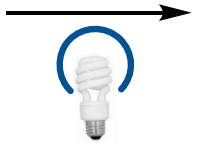
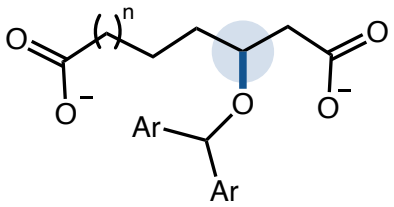
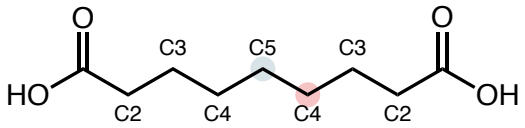
Breslow - Ion-Pairing oxidation

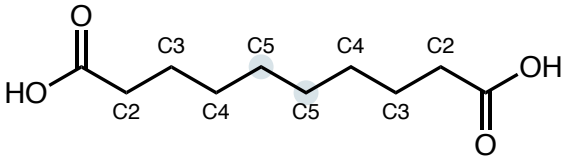
2 point binding

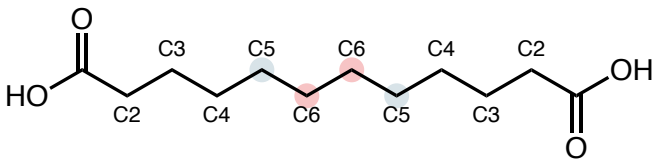










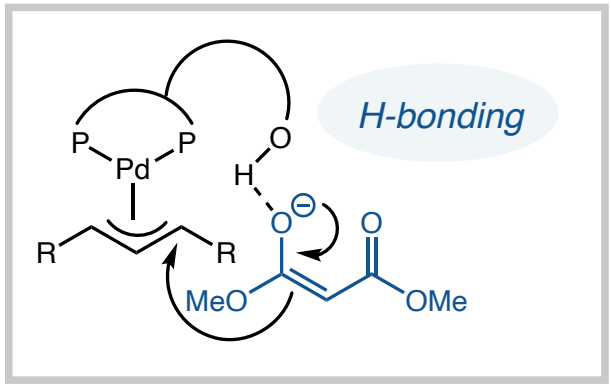


	C-2	C-3	C-4	C-5	C-6
	2.6%	**1.4%**	**22%**	**74%**	
	2.7%	**1.7%**	**2.7%**	**93%**	
	1%	**0.2%**	**3.6%**	**62%**	**34%**

Good selectivity, not really practical

Rajagopalan, R., Schwarz, J., & Breslow, R. *JACS* **1981**, *103*, 2905

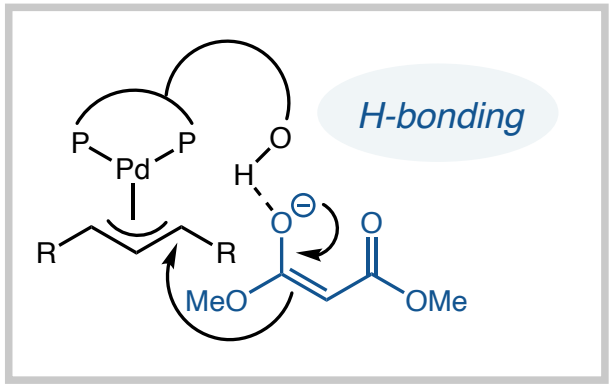
Sawamura - Ion-Pairing π-allyl



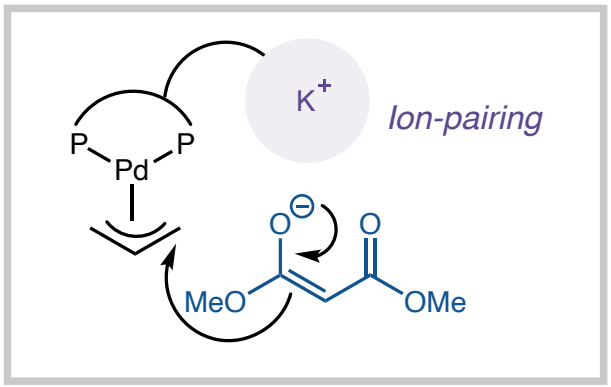
Hayashi - H-bonding

Ito, Y., Hagihara, T., Yamamotom A., & Hayashi, T. *Tet. Lett.* **1986**, *27,* 191; Sawamura, M., Nagata, H., Sakamoto, H., & Ito, Y. *JACS* **1992**, *114*, 2586

Sawamura - Ion-Pairing π-allyl



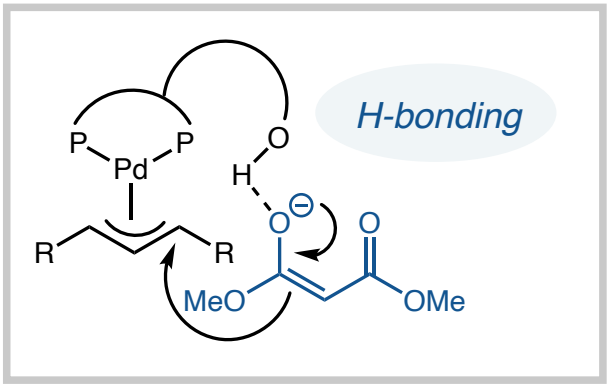
Hayashi - H-bonding

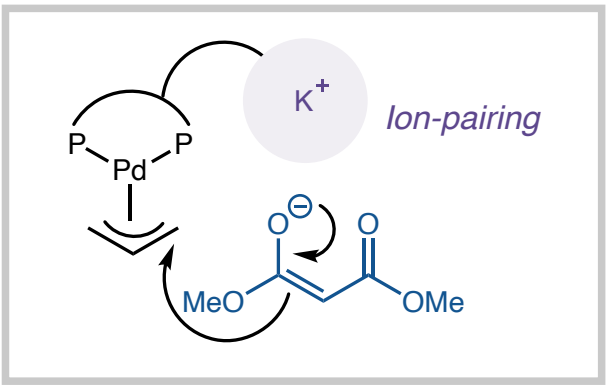


Sawamura - Ion-pairing

Ito, Y., Hagihara, T., Yamamotom A., & Hayashi, T. *Tet. Lett.* **1986**, *27,* 191; Sawamura, M., Nagata, H., Sakamoto, H., & Ito, Y. *JACS* **1992**, *114*, 2586

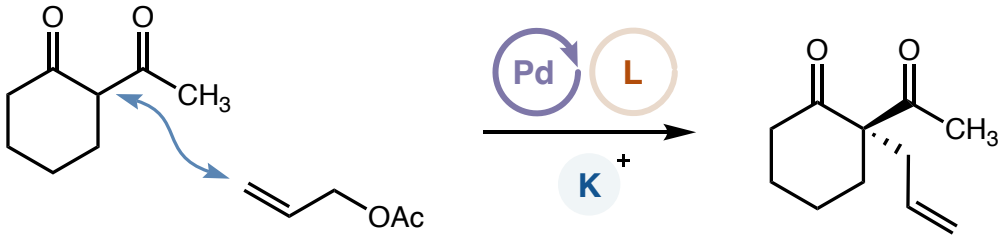
Sawamura - Ion-Pairing π-allyl

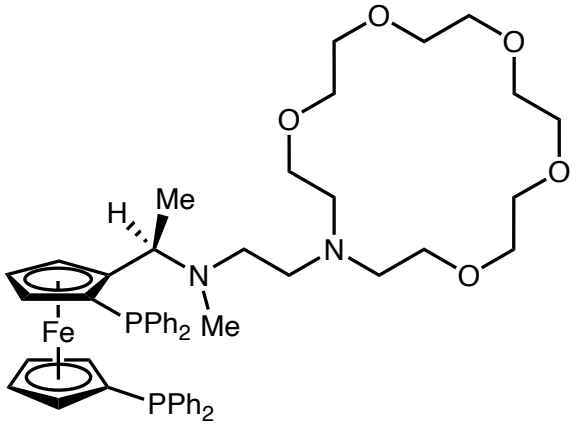




Hayashi - H-bonding

Sawamura - Ion-pairing

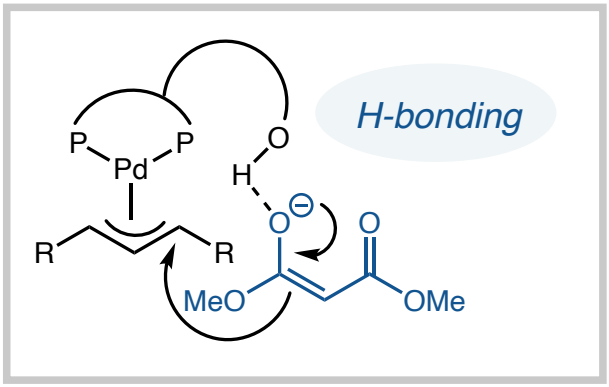


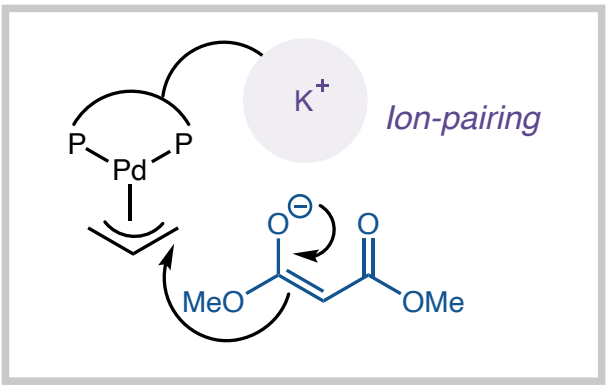


L

Ito, Y., Hagihara, T., Yamamotom A., & Hayashi, T. *Tet. Lett.* **1986**, *27,* 191; Sawamura, M., Nagata, H., Sakamoto, H., & Ito, Y. *JACS* **1992**, *114*, 2586

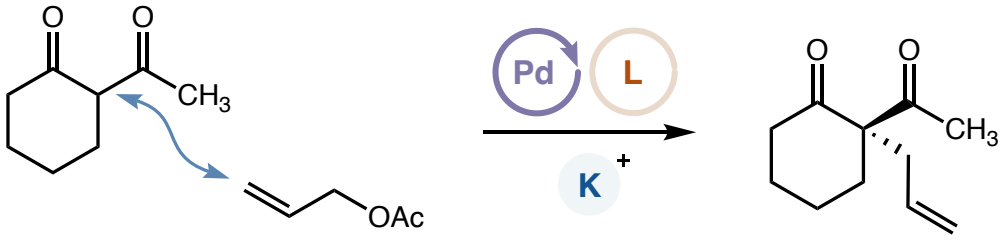
Sawamura - Ion-Pairing π-allyl

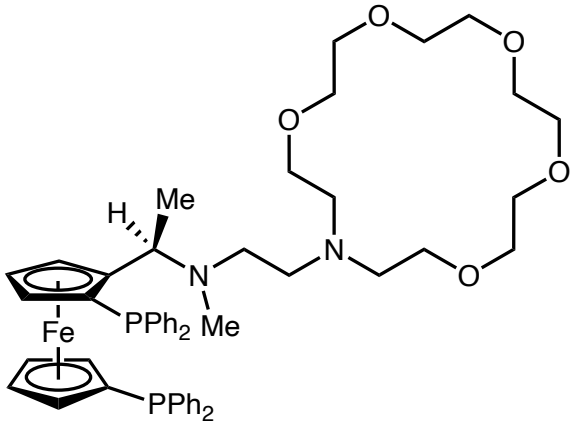




Hayashi - H-bonding

Sawamura - Ion-pairing





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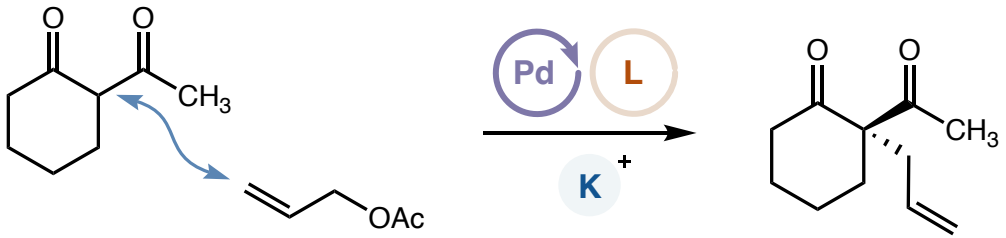
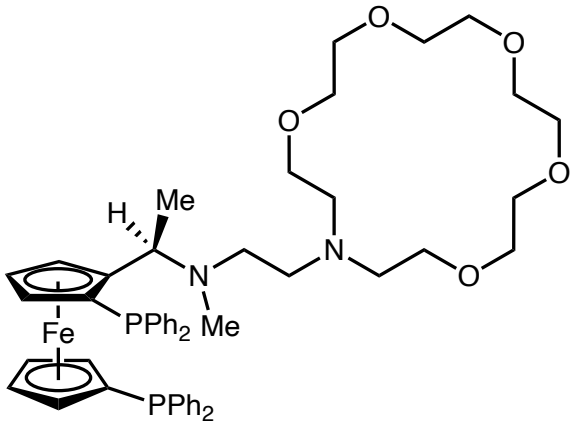
Sawamura - Ion-Pairing π-allyl





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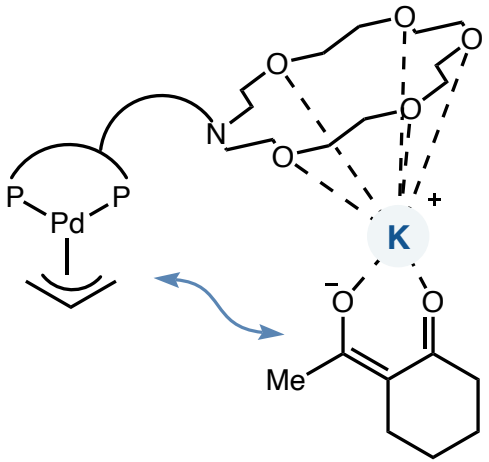

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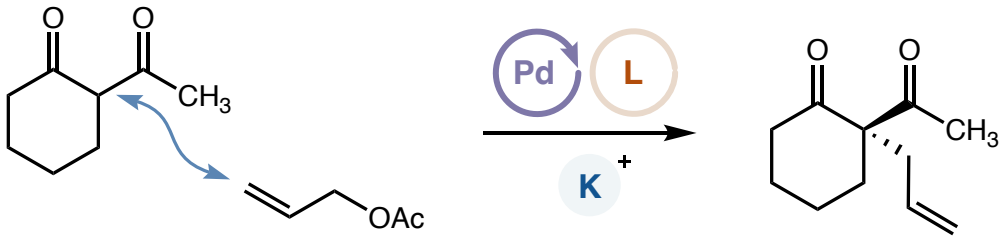
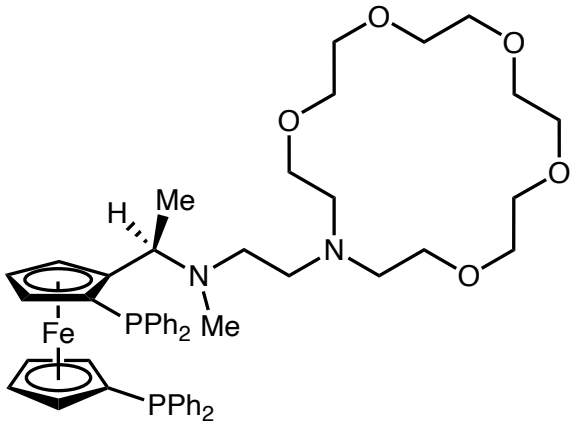
Sawamura - Ion-Pairing π-allyl





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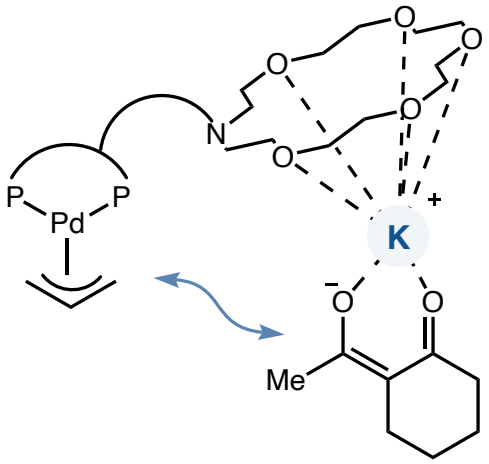
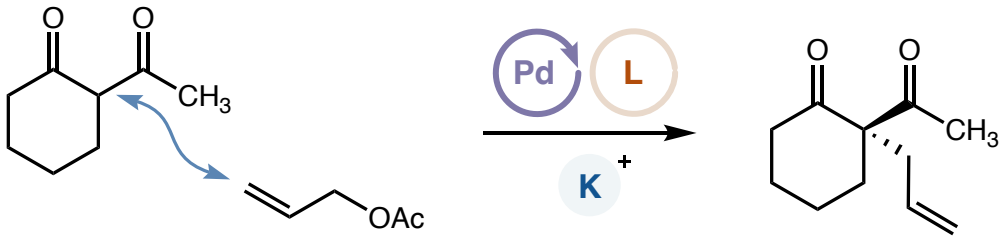
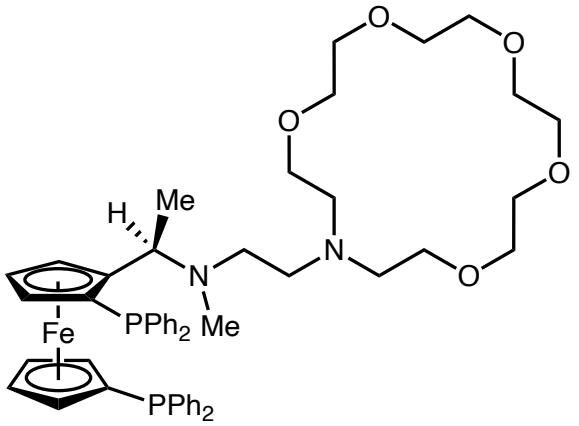


Solvent	%conv.	%ee
Mesitylene	100	60
Toluene	90	52
THF	90	41
CH_3CN	42	28
CH_2Cl_2	81	21
MeOH	0	-

Ito, Y., Hagihara, T., Yamamotom A., & Hayashi, T. *Tet. Lett.* **1986**, *27,* 191; Sawamura, M., Nagata, H., Sakamoto, H., & Ito, Y. *JACS* **1992**, *114*, 2586

Sawamura - Ion-Pairing π-allyl





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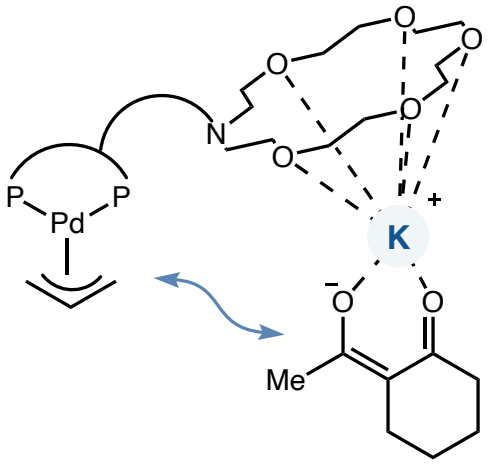

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MeOH	0	-

Solvent dependence suggests Ion-pairing

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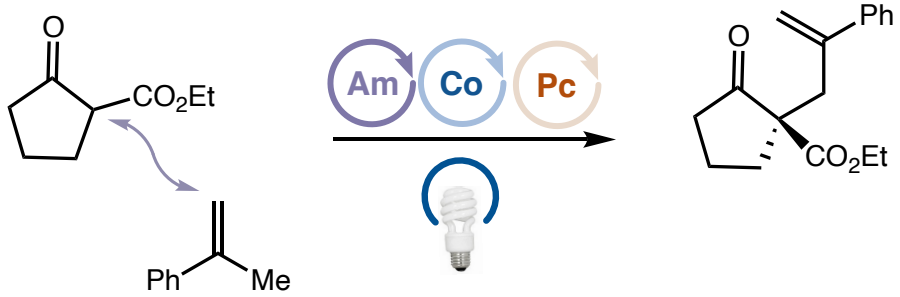
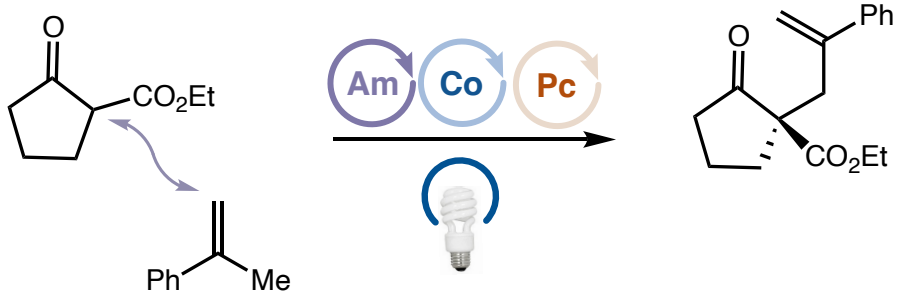
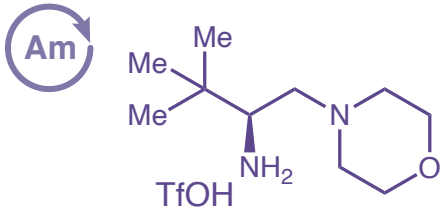
Luo - Photoredox Ion-Pairing



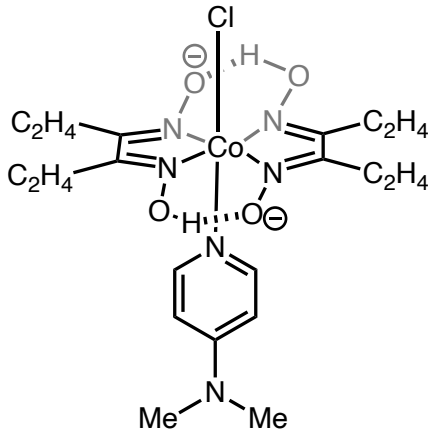
Jia, Z. Zhang, L. & Luo, S. *JACS* **2022**, *144*, 10705

Luo - Photoredox Ion-Pairing



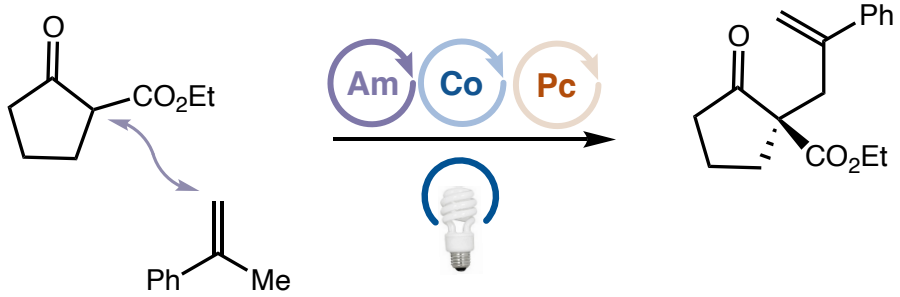


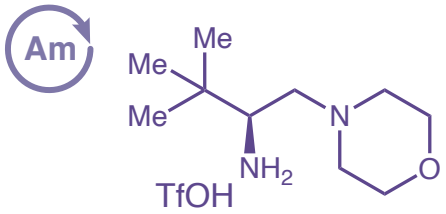
$Ir(ppy)_2(dtbbpy)(PF_6)$

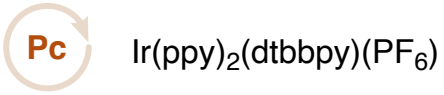


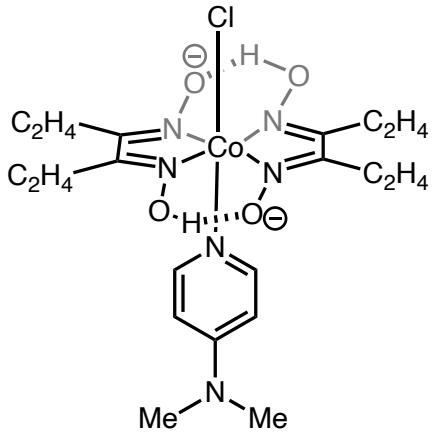
Jia, Z. Zhang, L. & Luo, S. *JACS* **2022**, *144*, 10705

Luo - Photoredox Ion-Pairing

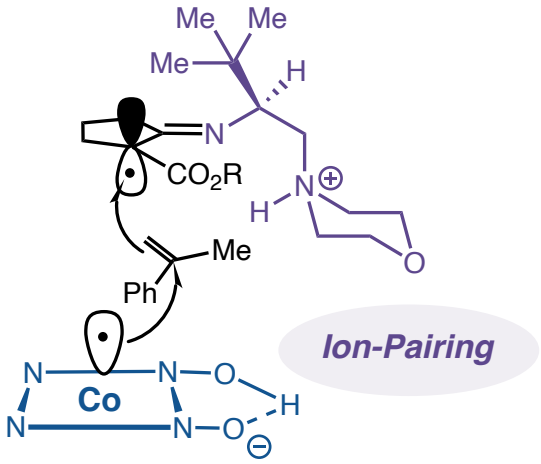






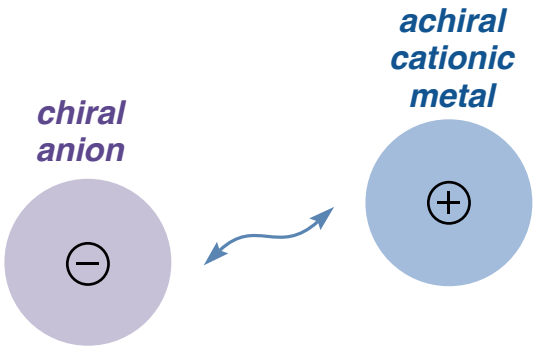


Ion-Paring interaction probed by 1H-NMR titration



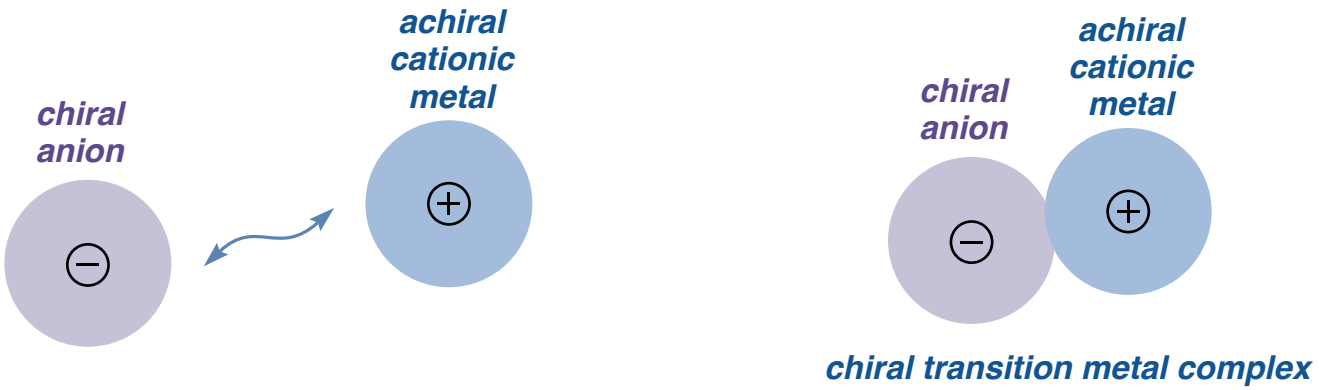
Jia, Z. Zhang, L. & Luo, S. *JACS* **2022**, *144*, 10705

Ion-Pairing Induced Enantioselectivity



Llewellyn, D. B., Adamson, D. & Arndtsen, B. A. *Org. Lett.* **2000**, *2*, 4165

Ion-Pairing Induced Enantioselectivity



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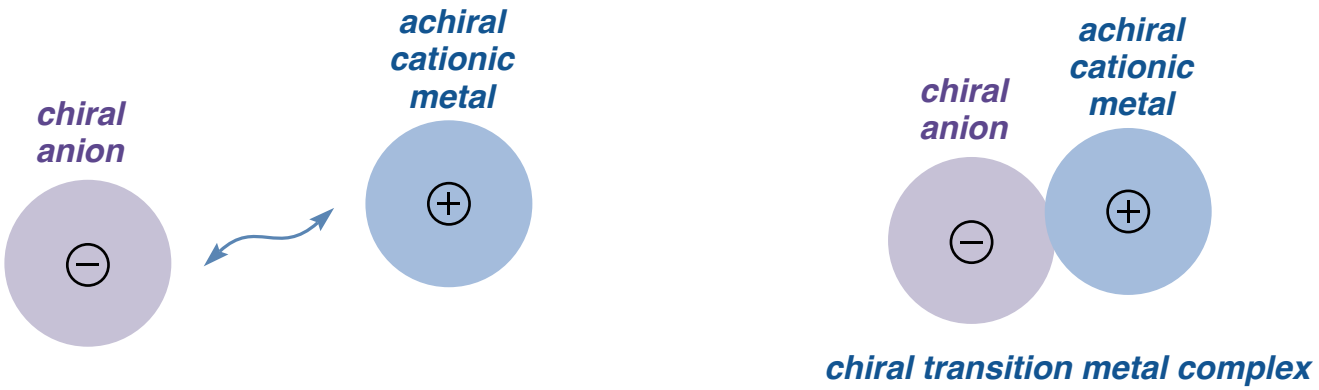

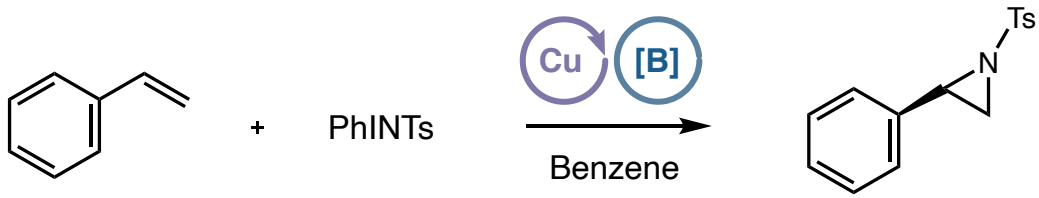

Use of chiral anion with achiral metal to give selectivity

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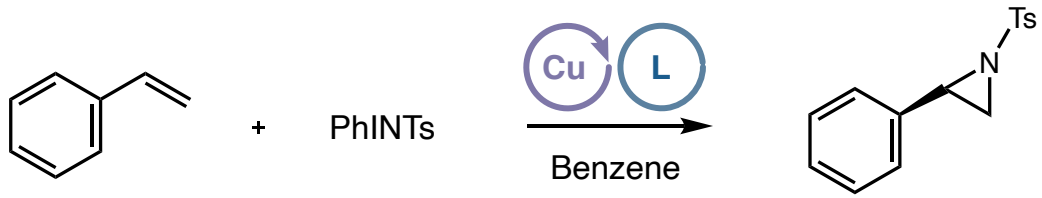
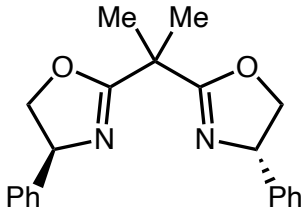
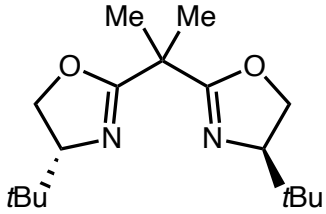
Arndtsen - Ion-Pairing







Copper source	%ee	%ee
CuOTf		
$CuClO_4$		
CuCl		
$CuPF_6$		

Copper source	%ee	%ee
CuOTf		
$CuClO_4$		
CuCl		
$CuPF_6$		

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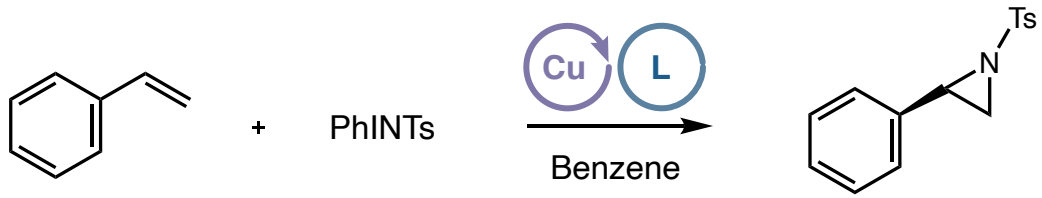
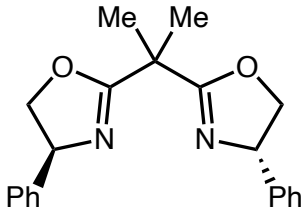
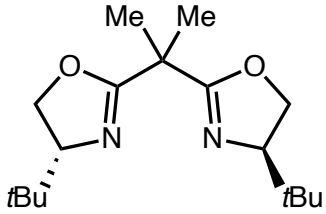
Arndtsen - Ion-Pairing







Copper source	%ee	%ee
CuOTf	**1**	
$CuClO_4$	**5**	
CuCl	**17**	
$CuPF_6$	**33**	

Copper source	%ee	%ee
CuOTf	**66**	
$CuClO_4$	**57**	
CuCl	**26**	
$CuPF_6$	**33**	

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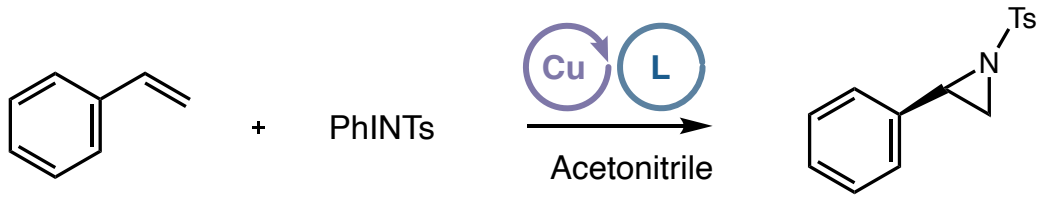
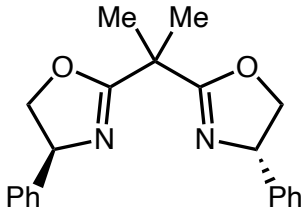
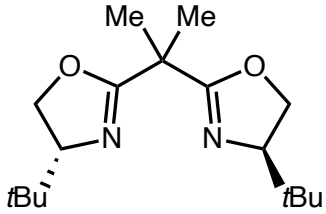
Arndtsen - Ion-Pairing







Copper source	%ee	%ee
CuOTf	**1**	**28**
$CuClO_4$	**5**	**28**
CuCl	**17**	**28**
$CuPF_6$	**33**	**28**

Copper source	%ee	%ee
CuOTf	**66**	**2**
$CuClO_4$	**57**	**2**
CuCl	**26**	**2**
$CuPF_6$	**33**	**2**

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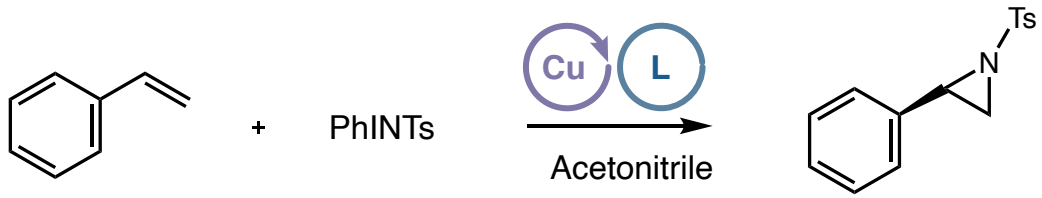
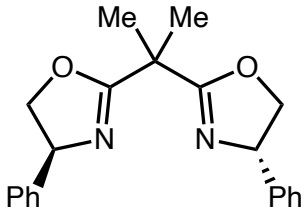
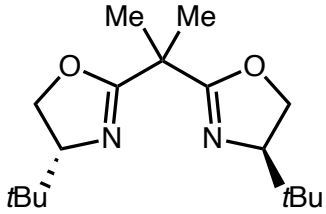
Arndtsen - Ion-Pairing







Copper source	%ee	%ee
CuOTf	**1**	**28**
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CuCl	**17**	**28**
$CuPF_6$	**33**	**28**

Copper source	%ee	%ee
CuOTf	**66**	**2**
$CuClO_4$	**57**	**2**
CuCl	**26**	**2**
$CuPF_6$	**33**	**2**

High %ee dependence on counterion and solvent suggests ion-pairing playing a role

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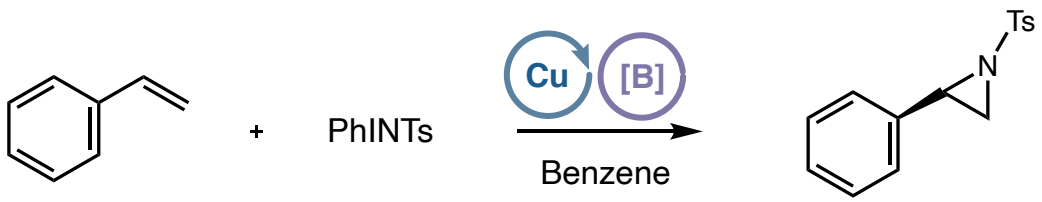
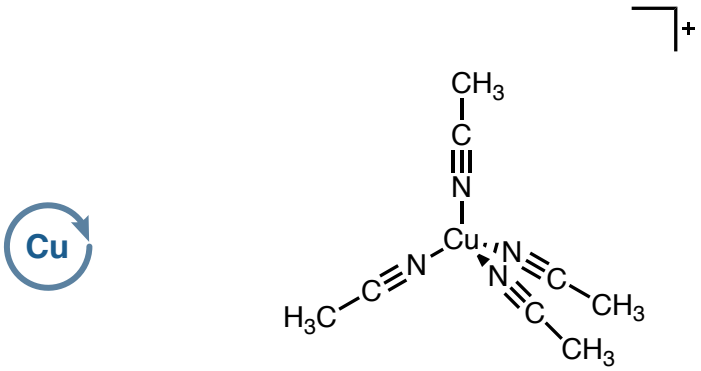
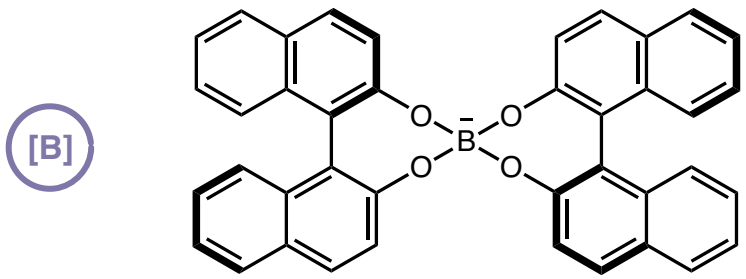
Arndtsen - Ion-Pairing







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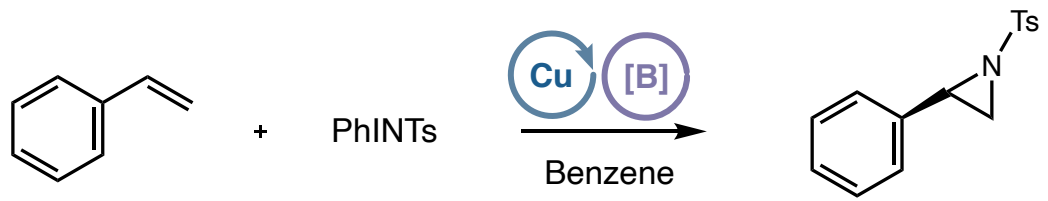
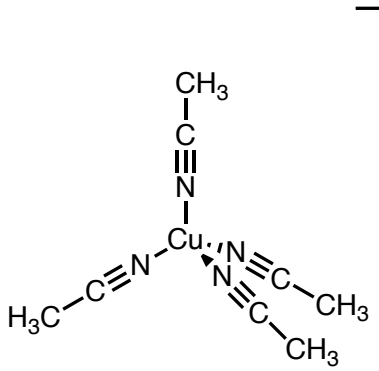
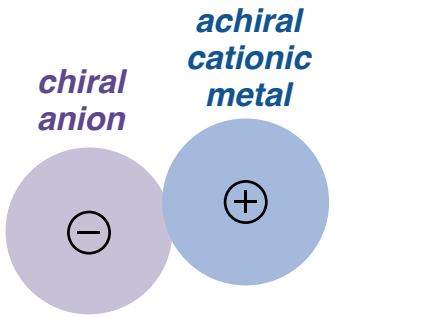
Arndtsen - Ion-Pairing



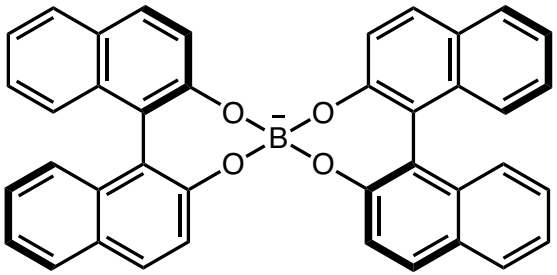
Cu





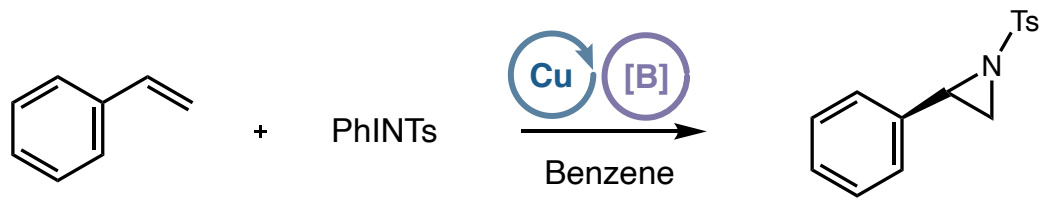
chiral transition metal complex

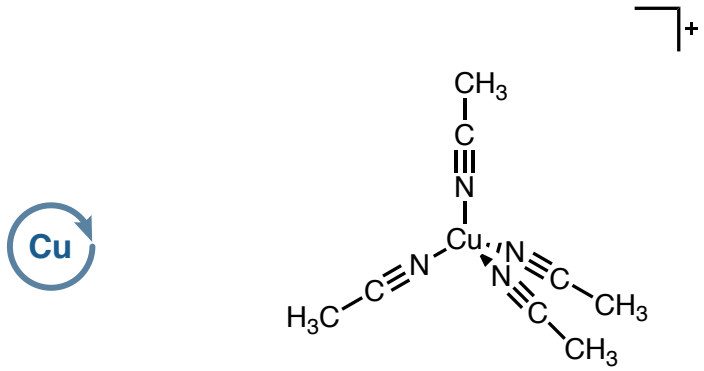
[B]

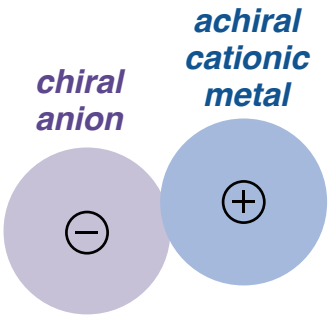


Llewellyn, D. B., Adamson, D. & Arndtsen, B. A. *Org. Lett.* **2000**, *2*, 4165

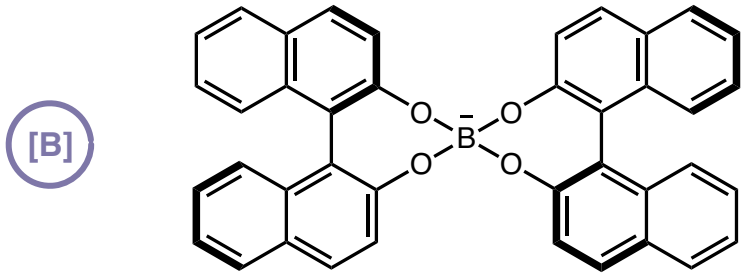
Arndtsen - Ion-Pairing







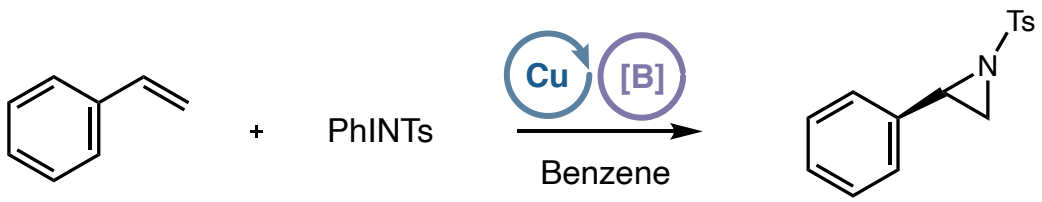
chiral transition metal complex

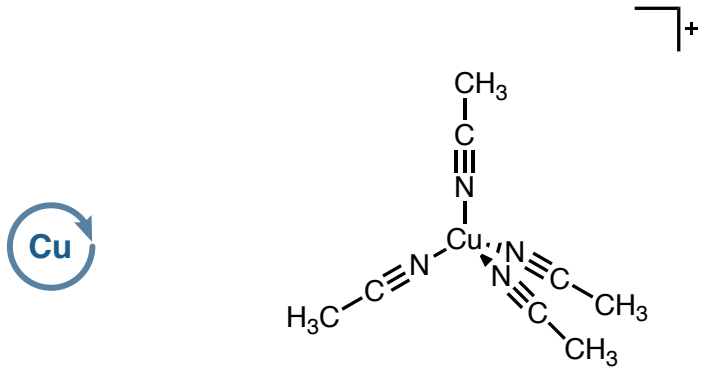


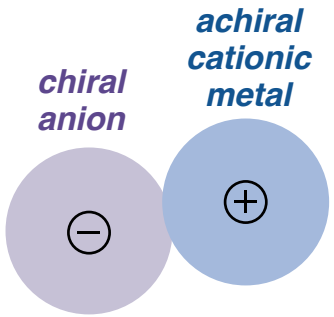
Ligand	[B]	Solvent	%Yield	%ee
none	*R*	C_6H_6	86	+7
none	*S*	C_6H_6	88	-7

Llewellyn, D. B., Adamson, D. & Arndtsen, B. A. *Org. Lett.* **2000**, *2*, 4165

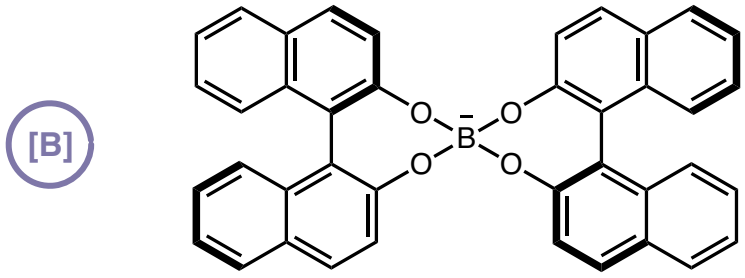
Arndtsen - Ion-Pairing







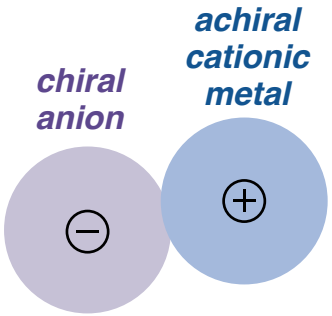
chiral transition metal complex



Ligand	[B]	Solvent	%Yield	%ee
none	*R*	C_6H_6	86	+7
none	*S*	C_6H_6	88	-7
none	R	CH_2Cl_2	97	+4
none	R	CH_3CN	87	+1

Llewellyn, D. B., Adamson, D. & Arndtsen, B. A. *Org. Lett.* **2000**, *2*, 4165

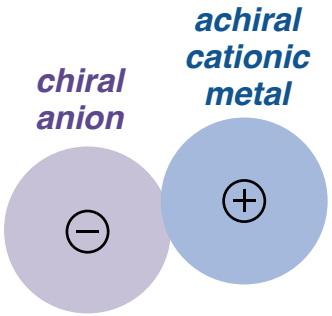
List - Ion-Pairing Oxidation



chiral transition metal complex

Liao, S. & List, B. *Angew. Chem . Int. Ed.* **2010**, *49*, 628

List - Ion-Pairing Oxidation



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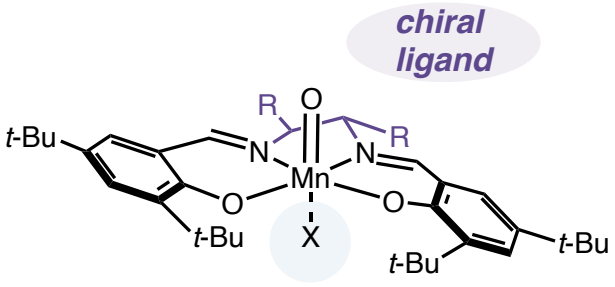

achiral counterion

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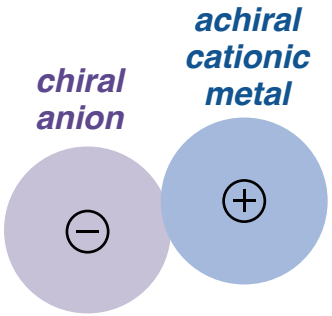
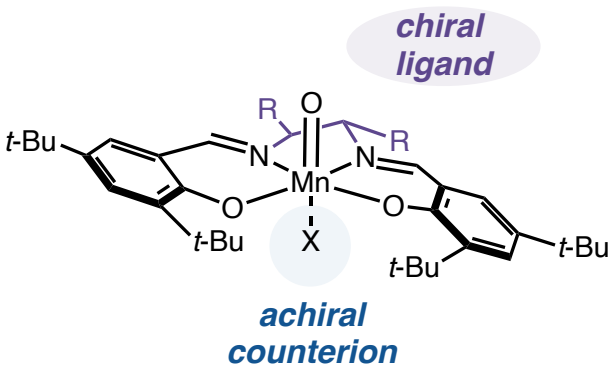
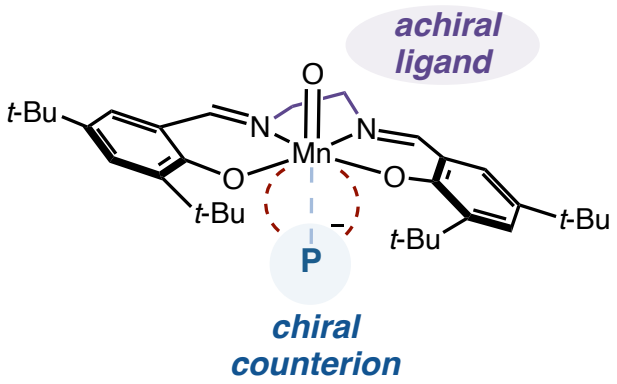
List - Ion-Pairing Oxidation



chiral transition metal complex



achiral counterion



chiral counterion

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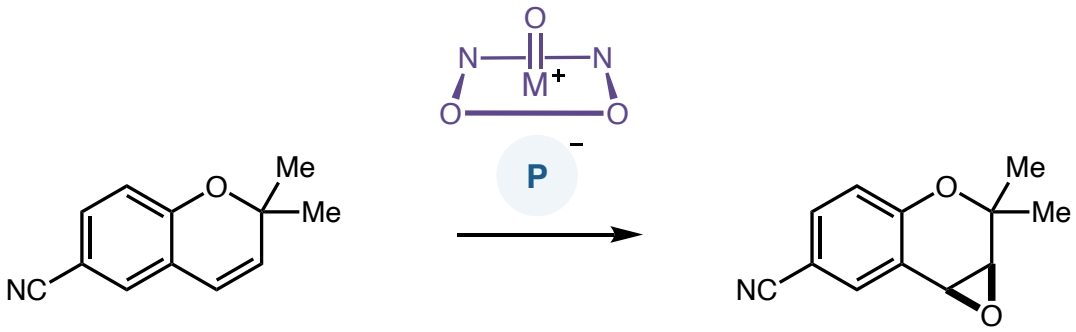
List - Ion-Pairing Oxidation



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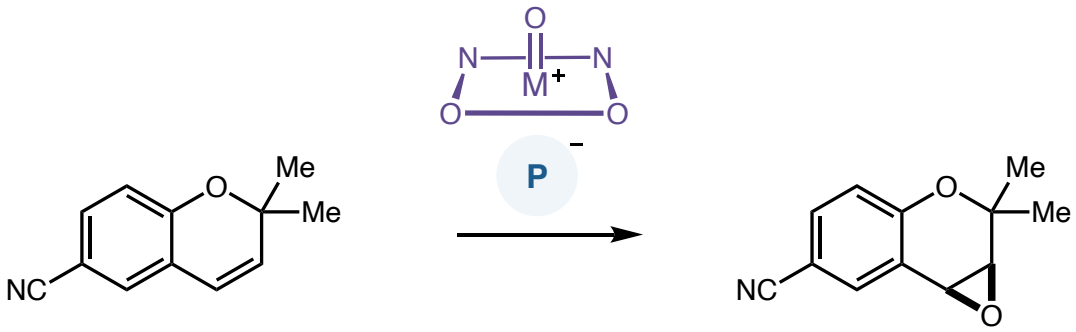
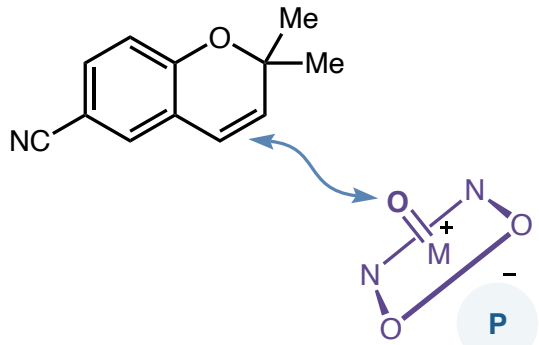
List - Ion-Pairing Oxidation



Counterion induced enantioselectivity



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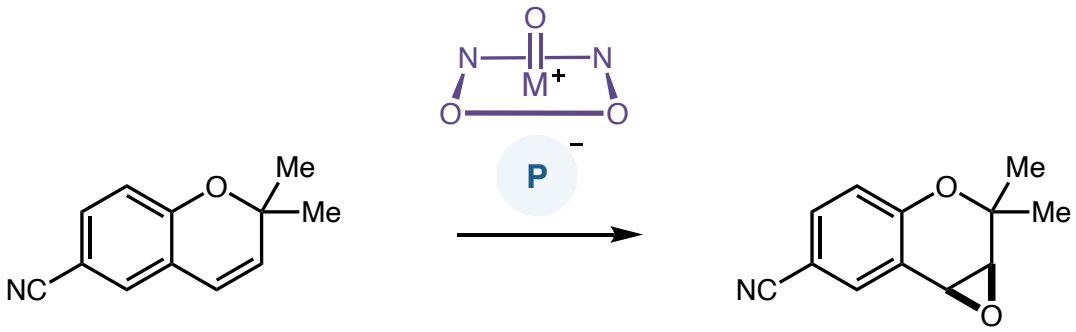
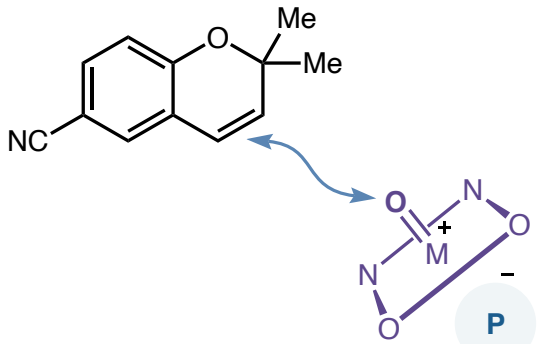
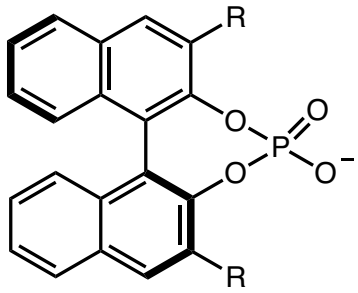
List - Ion-Pairing Oxidation



Counterion induced enantioselectivity





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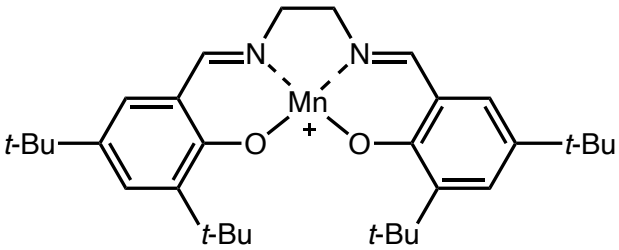

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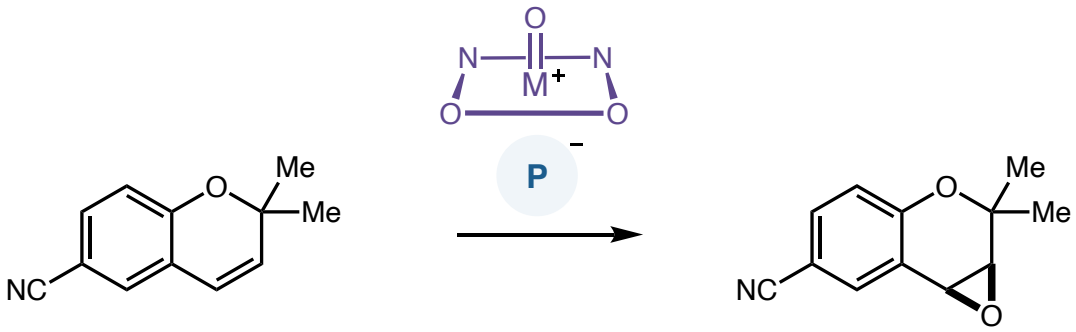
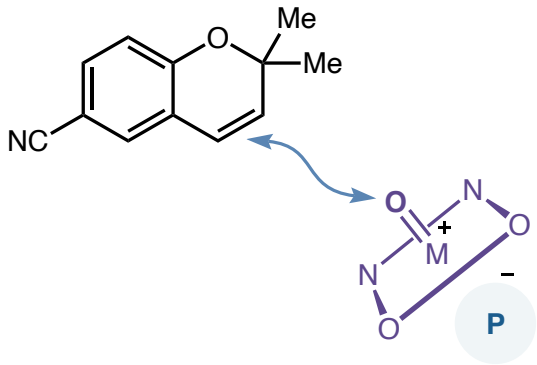
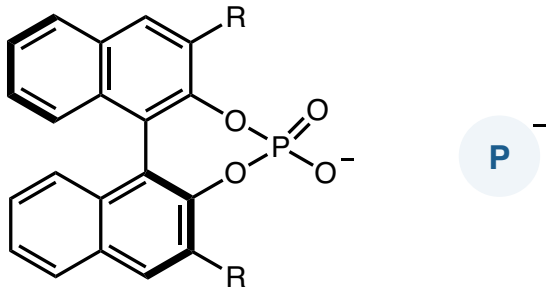
List - Ion-Pairing Oxidation

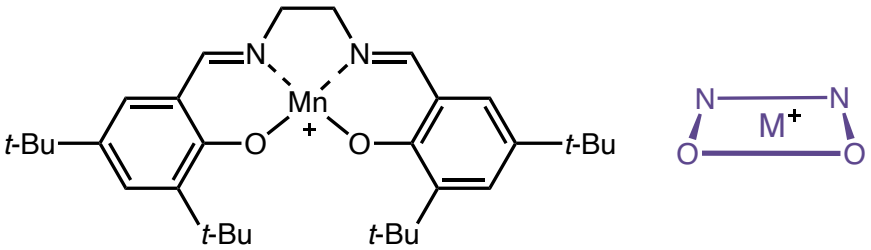


Counterion induced enantioselectivity





R	%Yield	%ee
Ph	**89**	**8**
4-biphenyl	**87**	**58**
9-anthryl	**83**	**12**
4-*t*Bu-C$_6$H$_4$	**99**	**90**



Lowered concentration led to 99% conversion and 94%ee

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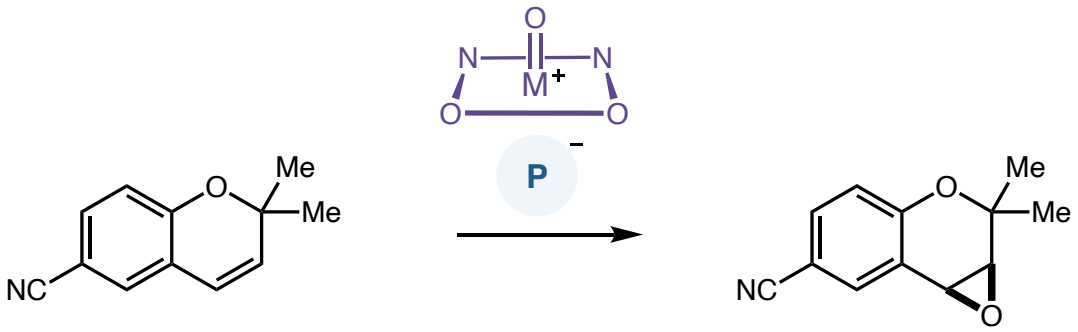
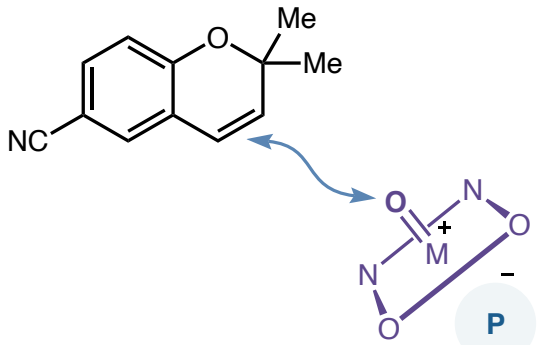
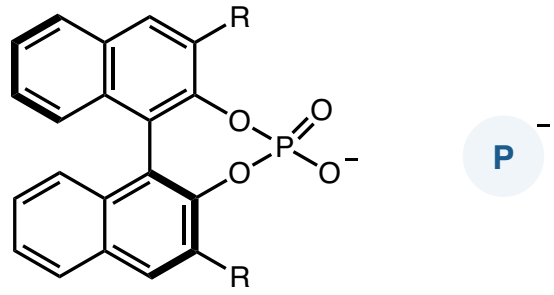
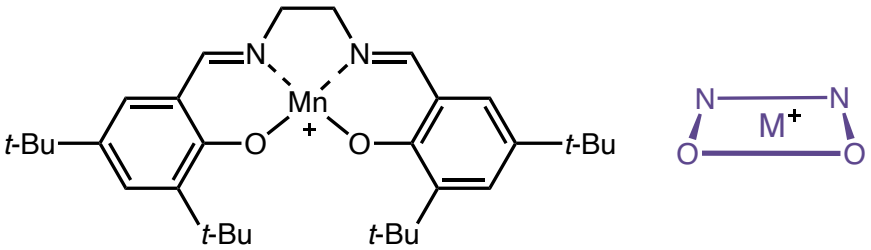
List - Ion-Pairing Oxidation

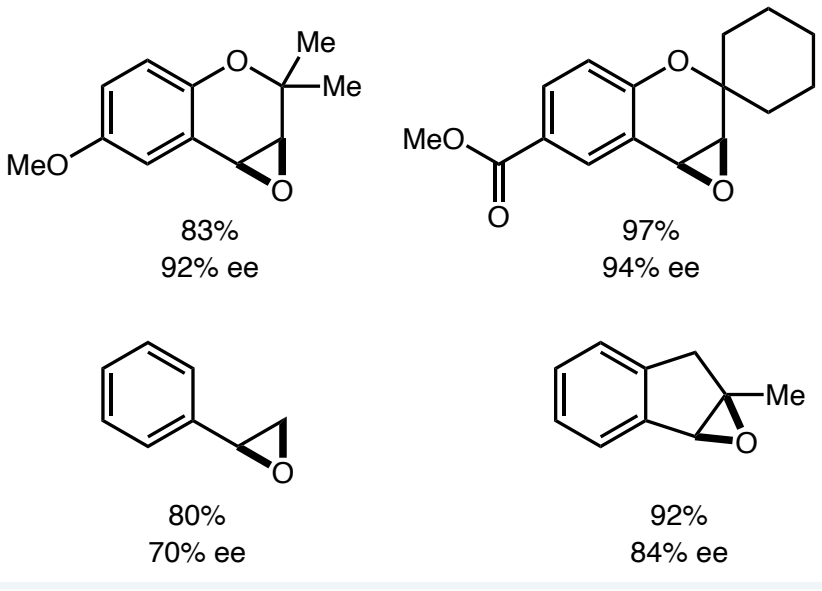


Counterion induced enantioselectivity









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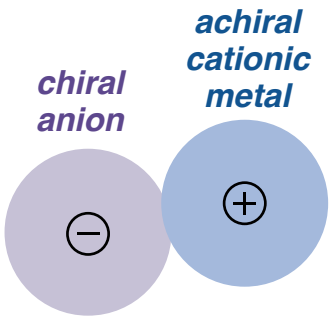

chiral transition metal complex

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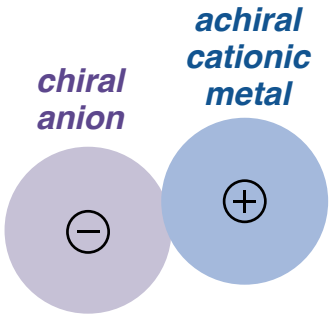
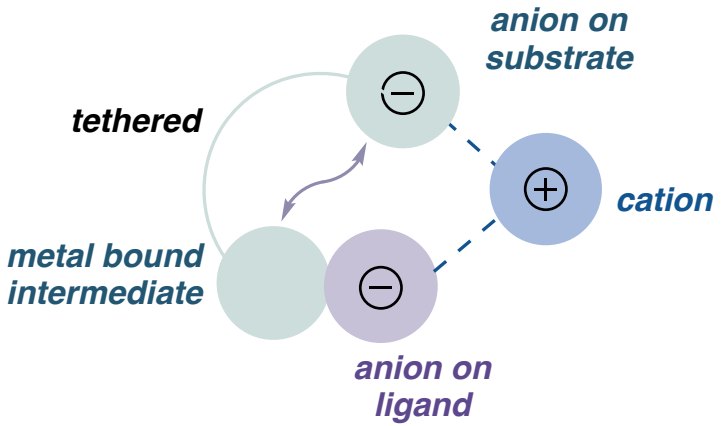
Phipps - Ion Pairing Enantioselectivity



chiral transition metal complex



electrostatic association

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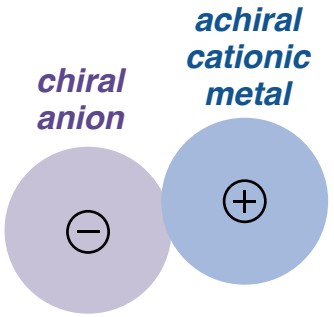
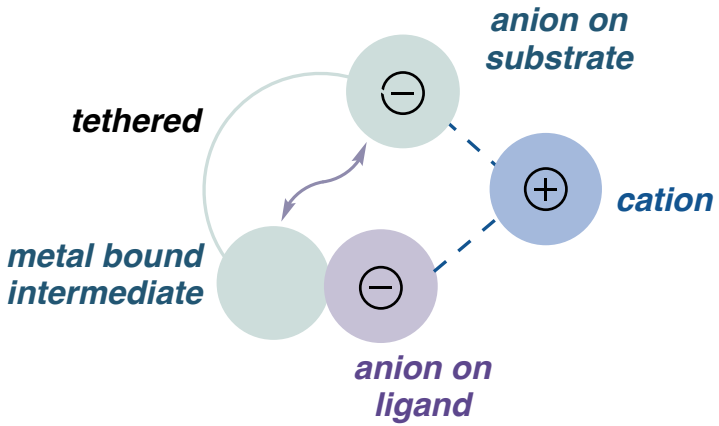
Phipps - Ion Pairing Enantioselectivity

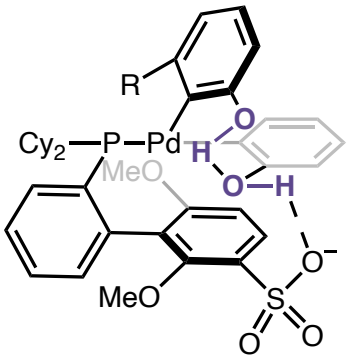


chiral transition metal complex



electrostatic association

H-bonding controls enantioselectivity



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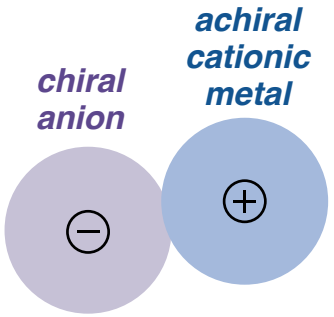
Phipps - Ion Pairing Enantioselectivity



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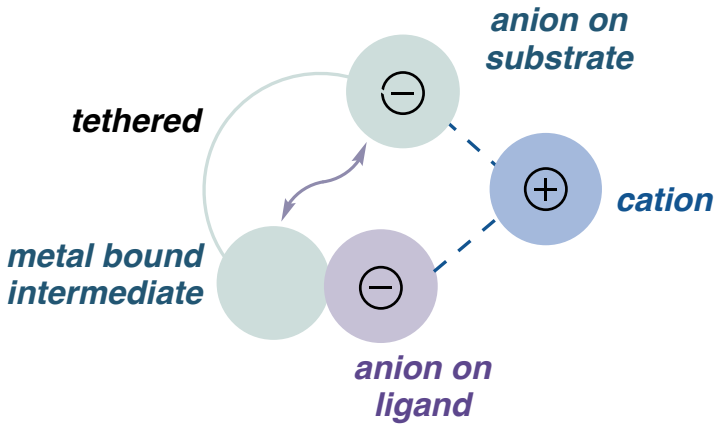

electrostatic association

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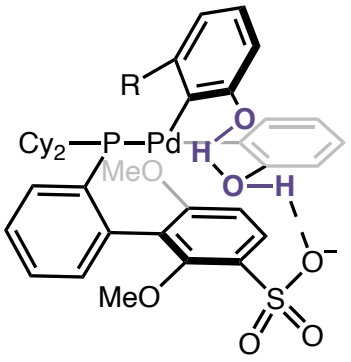
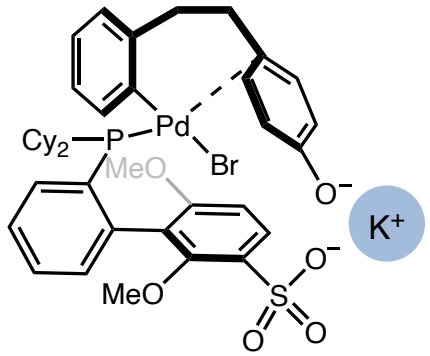


Ion-pairing controlled enantioselectivity



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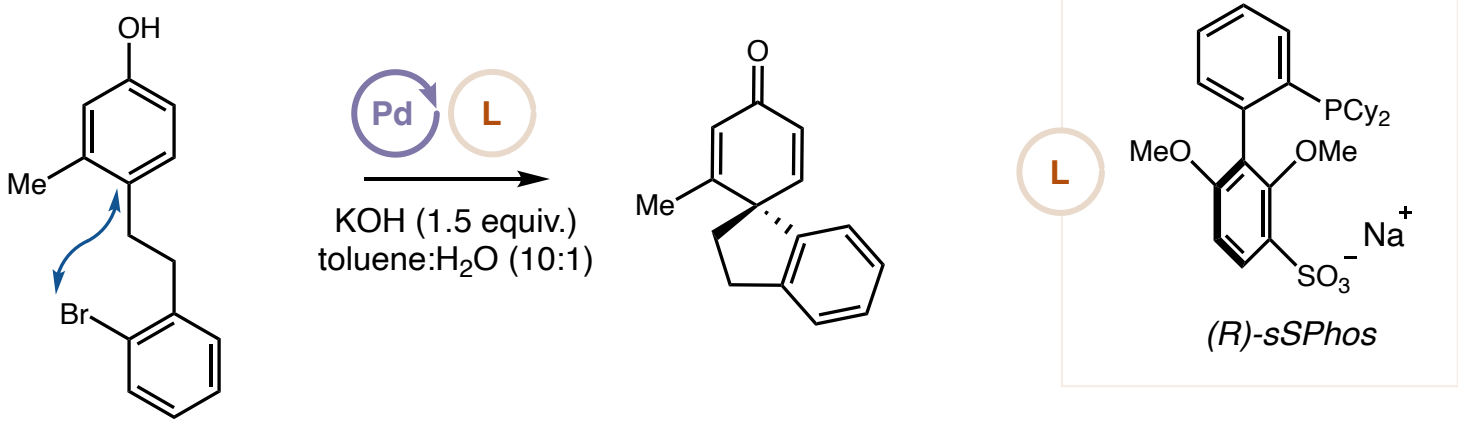
Phipps - Ion Pairing Enantioselectivity



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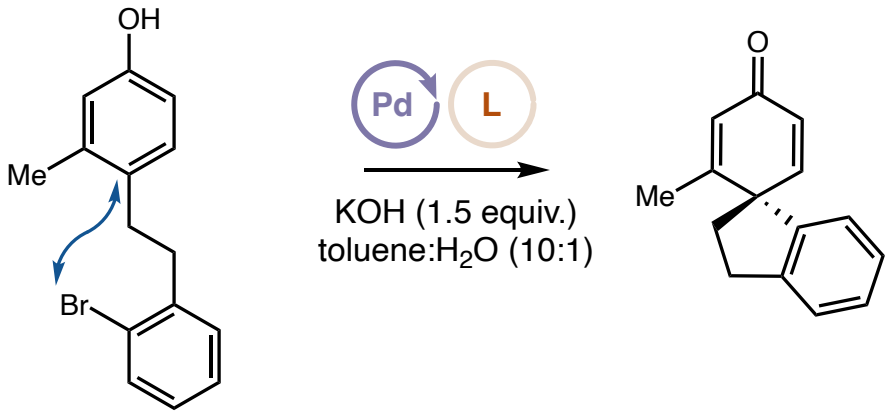
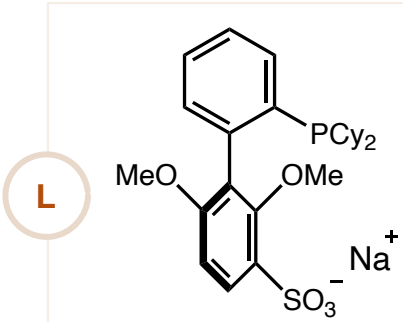
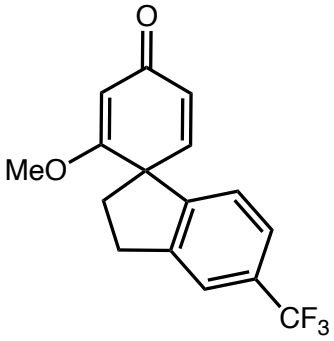


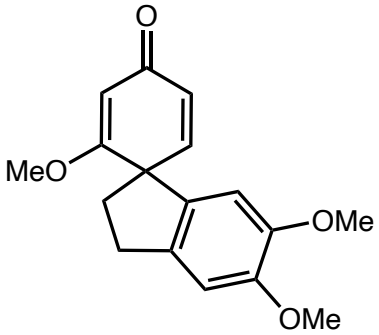


(R)-sSPhos

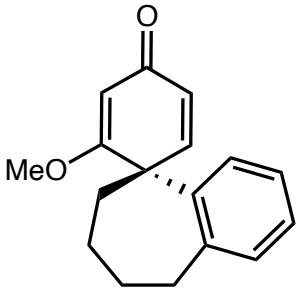
Excellent enantioselectivity for dearomatized products



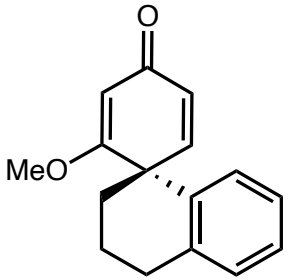
69% yield
88% ee



55% yield
90% ee



13% yield
88% ee



77% yield
93% ee

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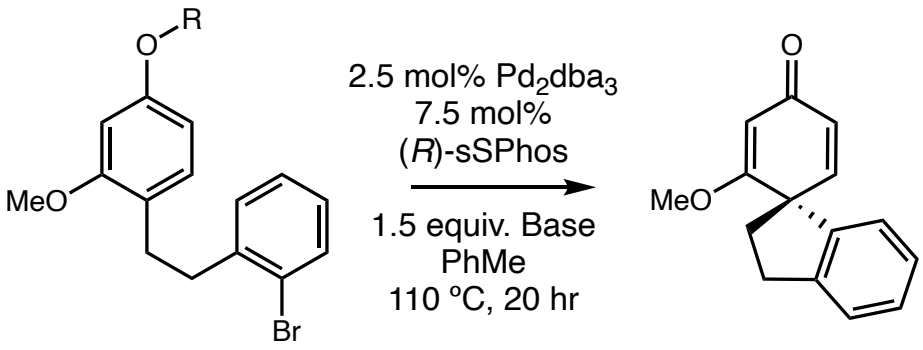
Phipps - Ion Pairing Enantioselectivity



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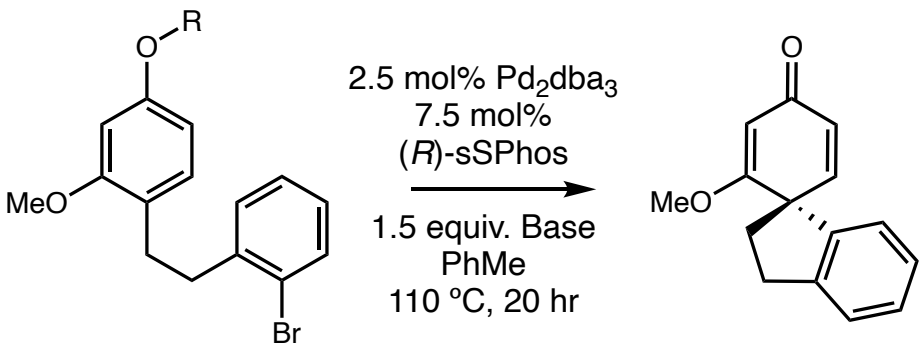

R	Yield	%ee
H	60	83
TMS	**46**	**83**
K	**53**	**92**

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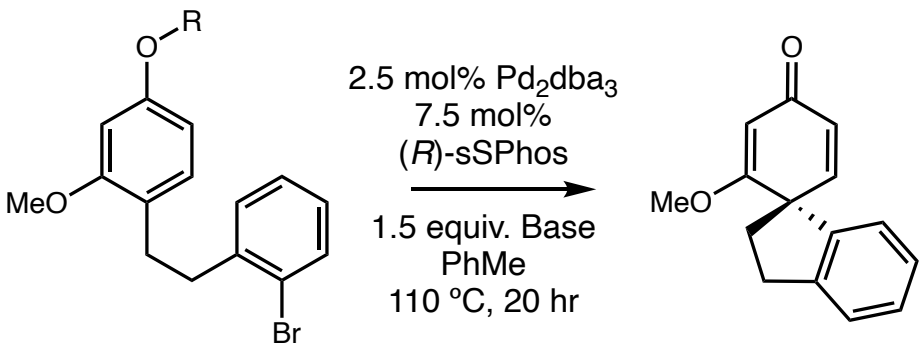
Phipps - Ion Pairing Enantioselectivity



R	Yield	%ee
H	60	83
TMS	**46**	**83**
K	**53**	**92**

Blocking ion pairing moiety leads to decrease in %ee

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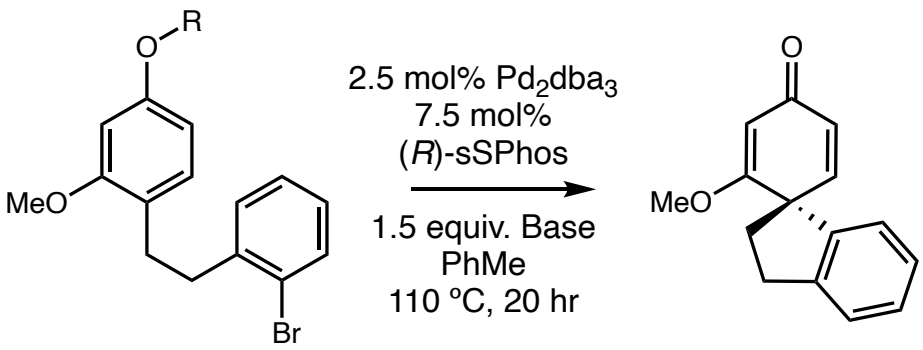
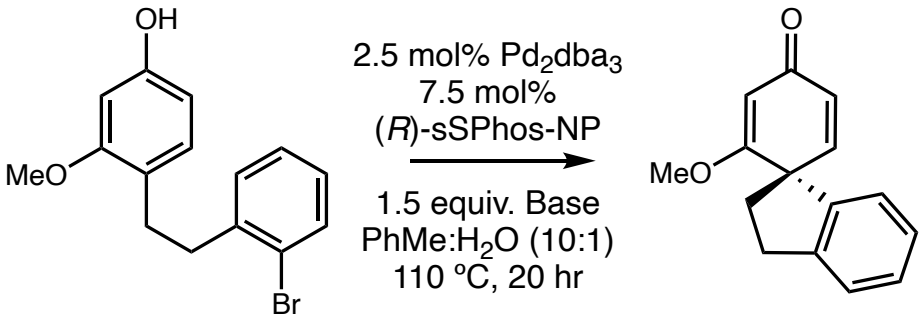
Phipps - Ion Pairing Enantioselectivity



R	Yield	%ee
H	60	83
TMS	**46**	**83**
K	**53**	**92**

Blocking ion pairing moiety leads to decrease in %ee

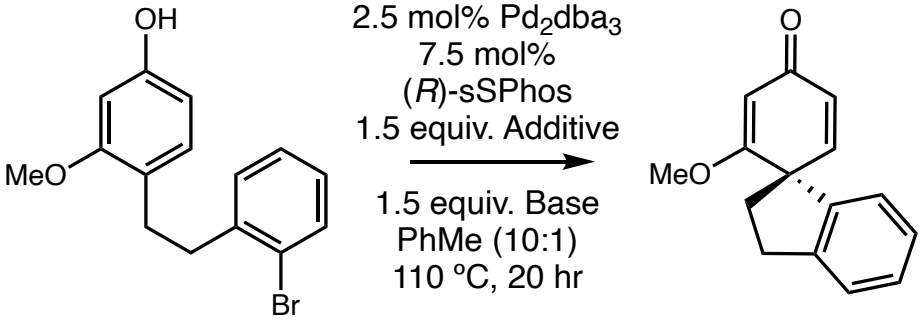


R	Yield	%ee
KOH	**99**	**92**
Bu_4NOH	**11**	**57**
Bu_4POH	**11**	**70**
Me_4NOH	**82**	**88**

Identity of cation crucial for selectivity

Kadarauch, M., Whalley, D. M., & Phipps, R. J. *JACS* **2023**, *145*, 25553

Phipps - Ion Pairing Enantioselectivity



Additive	%ee
None	**83**
12-Crown-4	**81**
15-Crown-5	**61**
18-Crown-6	**70**

K+ selective crown-ethers diminish %ee

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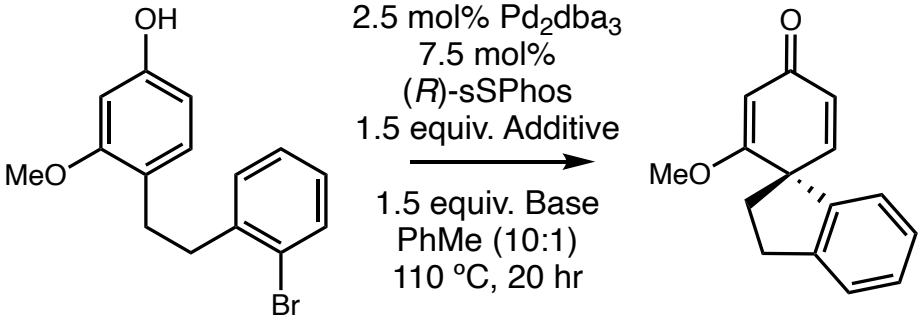
Phipps - Ion Pairing Enantioselectivity



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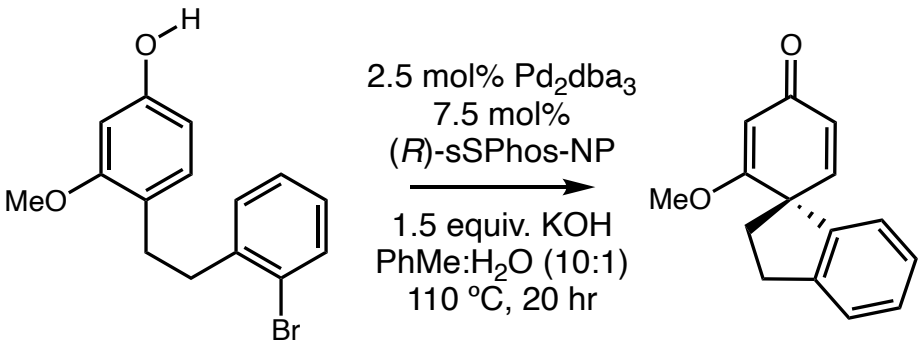
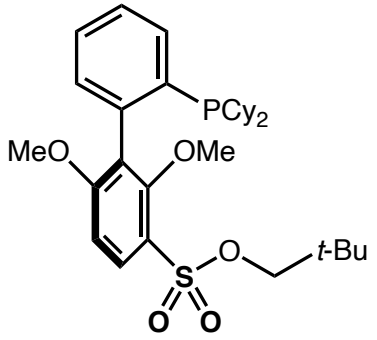


89%
-6% ee



(R)-sSPhos

Neutral ligand gives little selectivity

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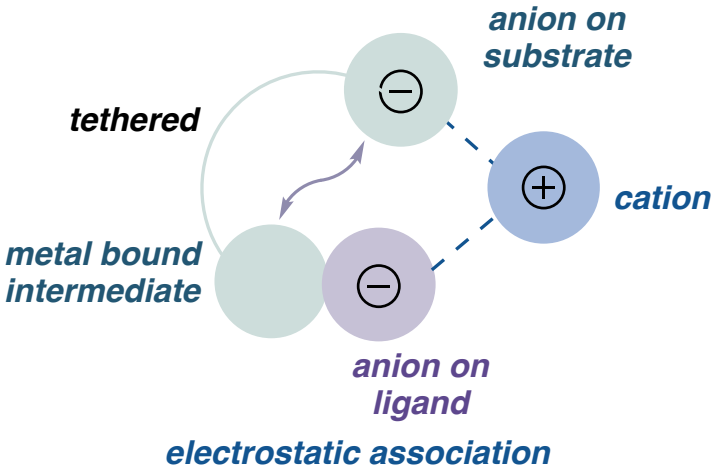
Phipps - Intermolecular Ion-Pairing



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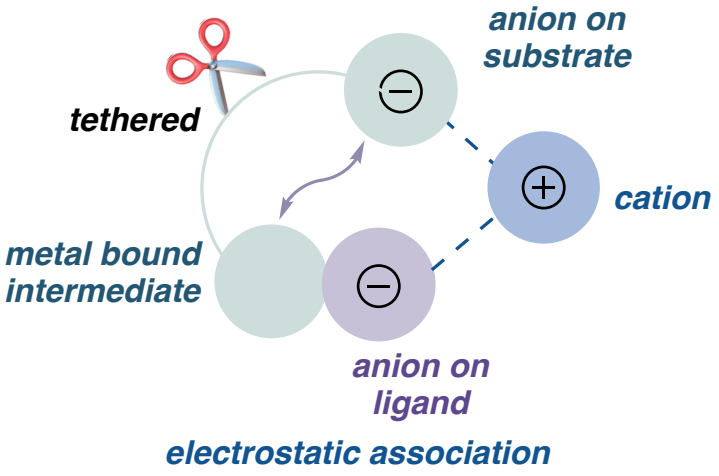

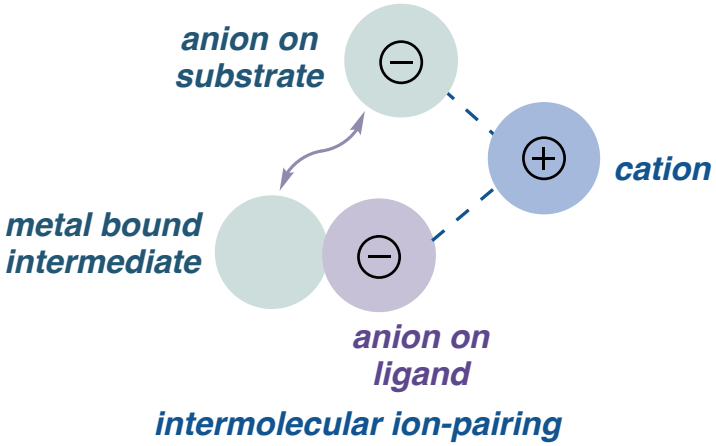

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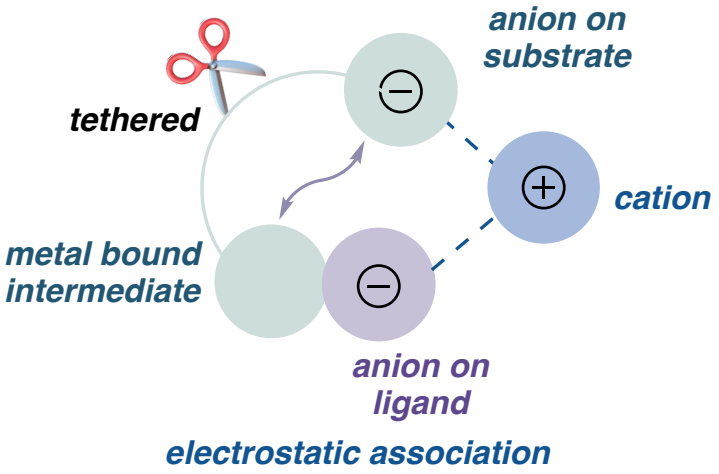
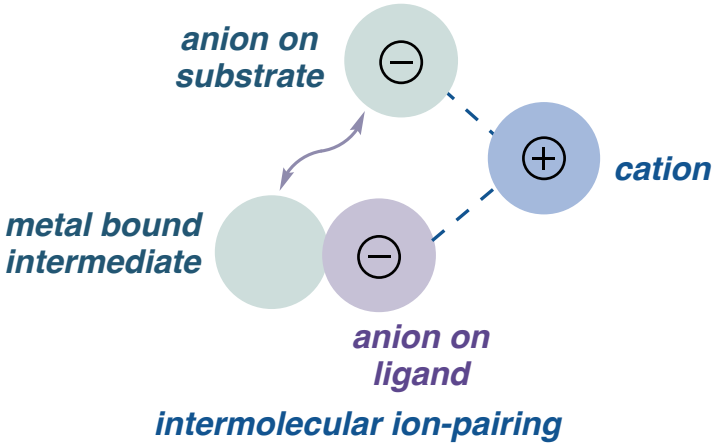
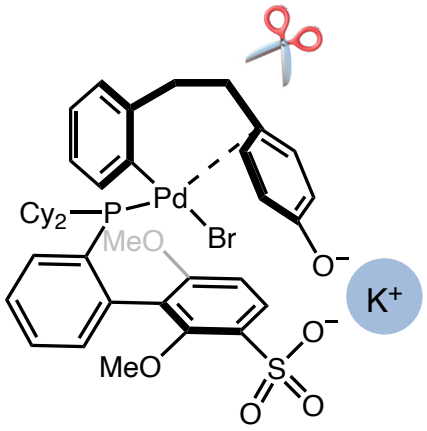
Phipps - Intermolecular Ion-Pairing







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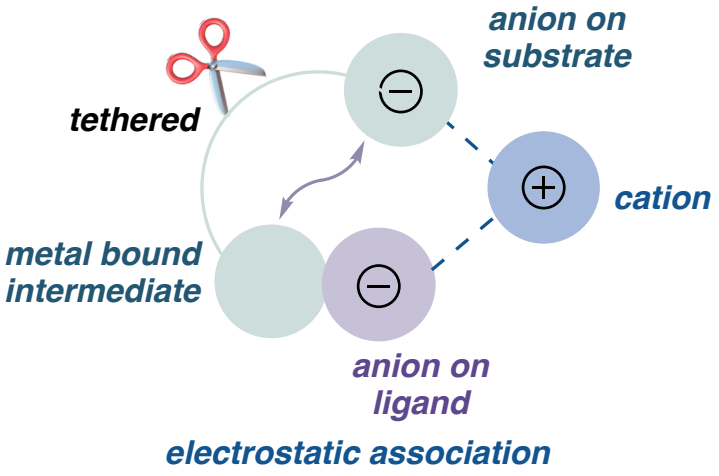
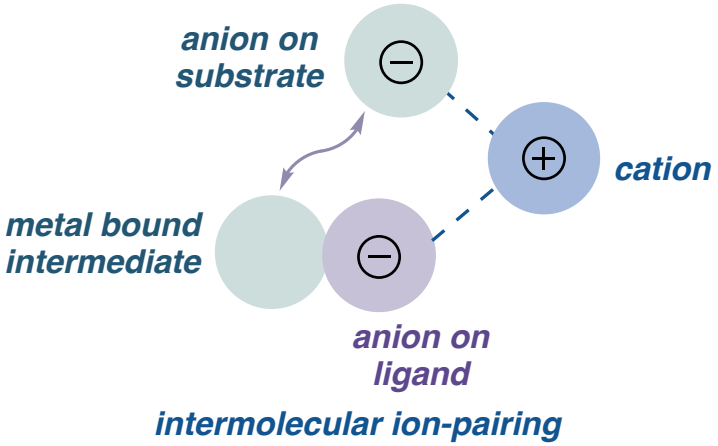
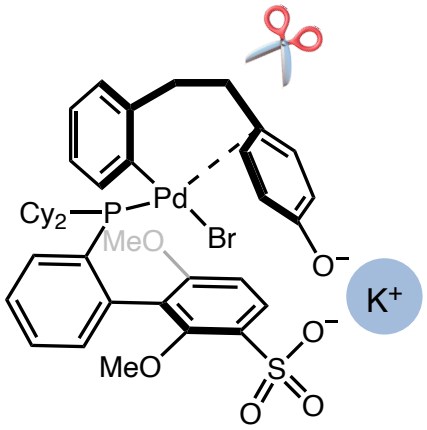
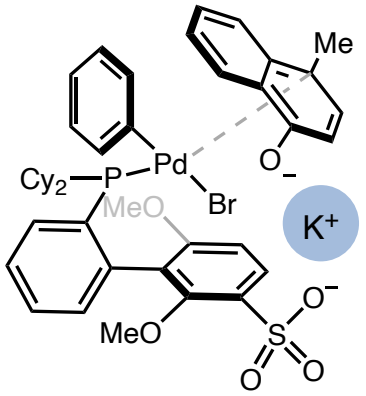
Phipps - Intermolecular Ion-Pairing









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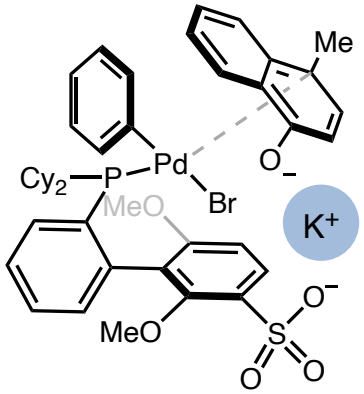
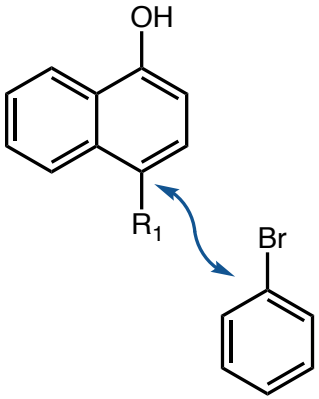
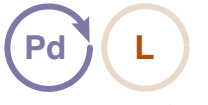
Phipps - Intermolecular Ion-Pairing

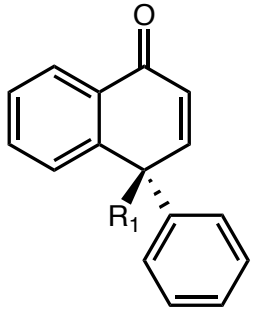


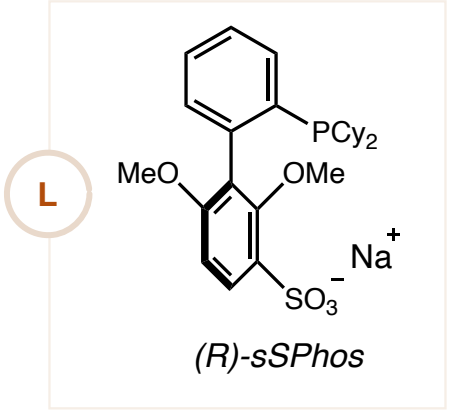
Dearomatization of 1-Napthols via ion-pairing





KOH (1.5 equiv.)
toluene:H_2O (10:1)





(R)-sSPhos

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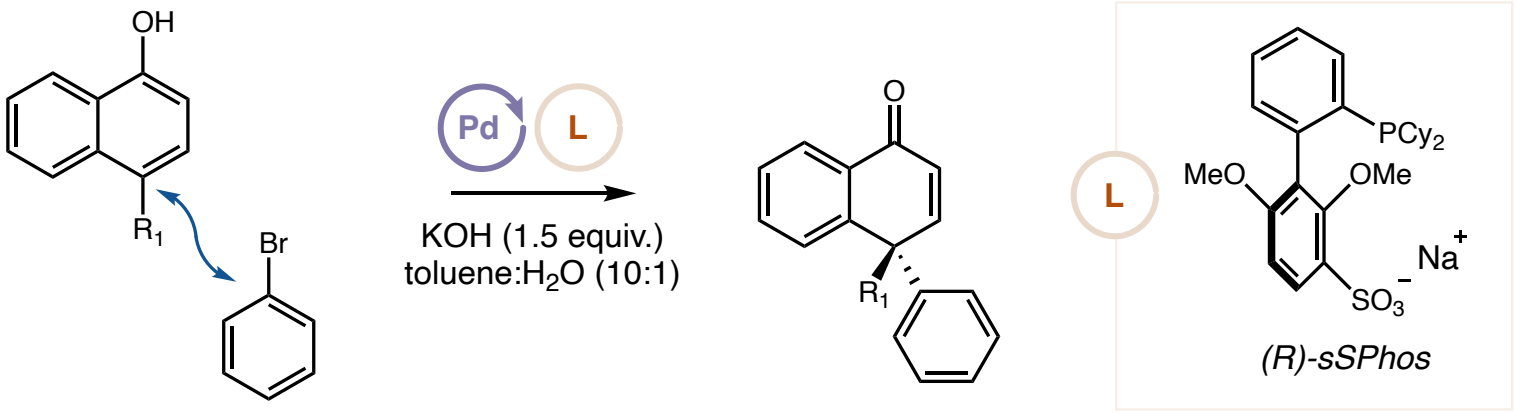
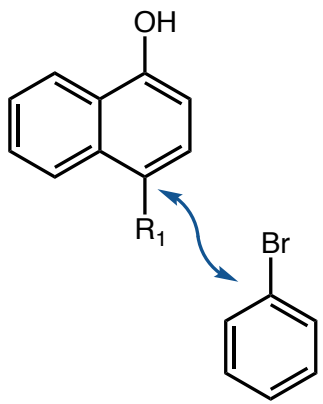
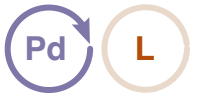
Phipps - Intermolecular Ion-Pairing



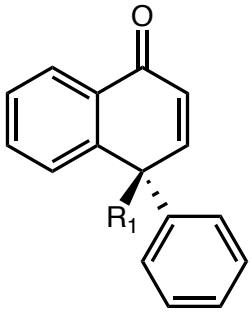
Kadarauch, M., Moss, T. A., & Phipps, R. J. *JACS* **2024**, *ASAP*

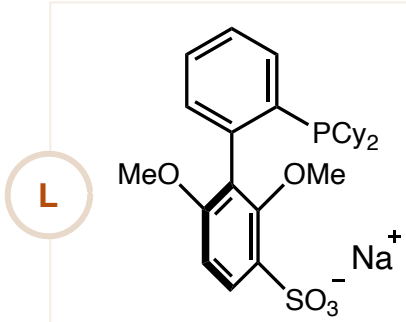
Phipps - Intermolecular Ion-Pairing



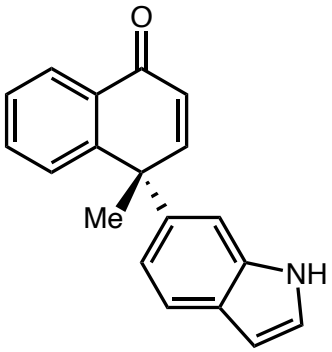


KOH (1.5 equiv.)
toluene:H_2O (10:1)

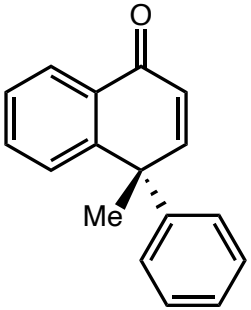




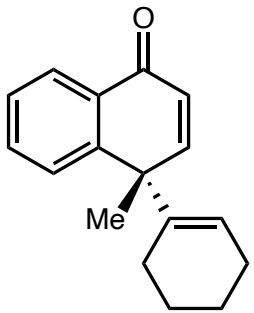
(R)-sSPhos



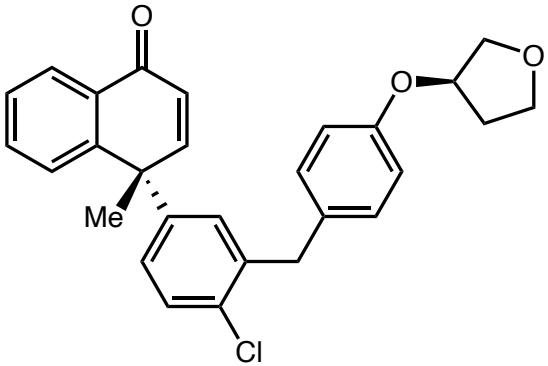
73%
85% ee



63%
97% ee



19%
98% ee



60%
25:1 dr

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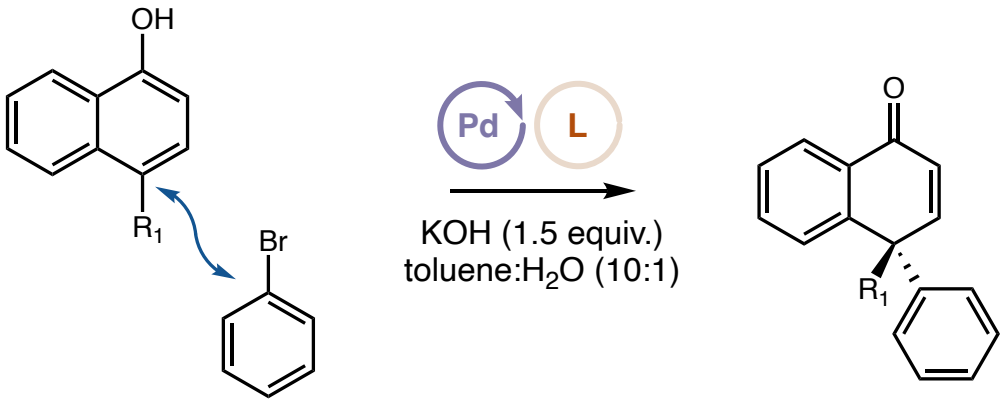
Phipps - Intermolecular Ion-Pairing



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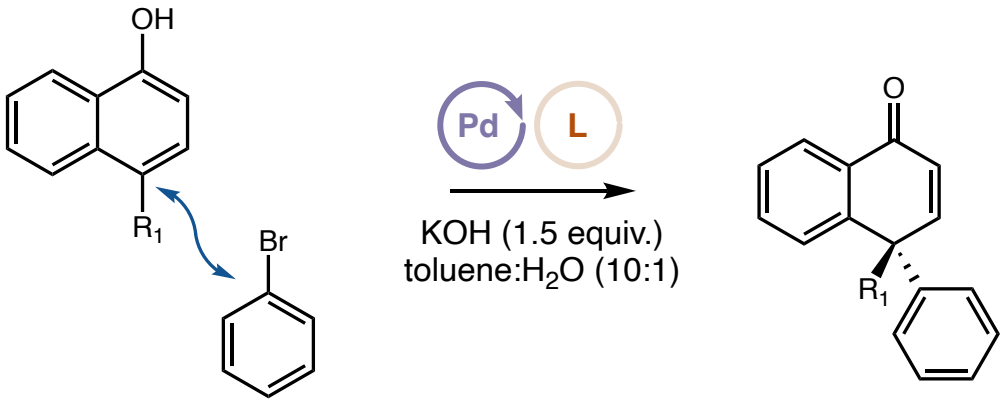
Phipps - Intermolecular Ion-Pairing



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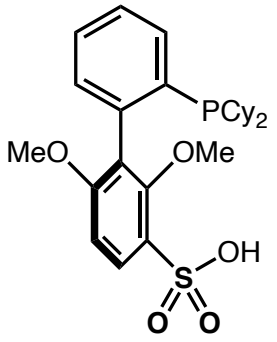
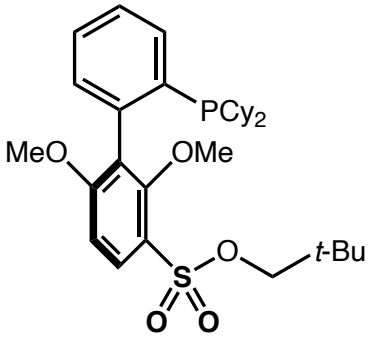
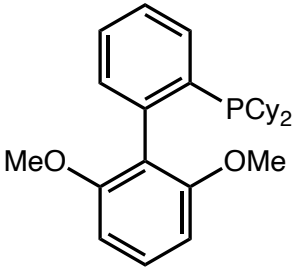


(R)-sSPhos



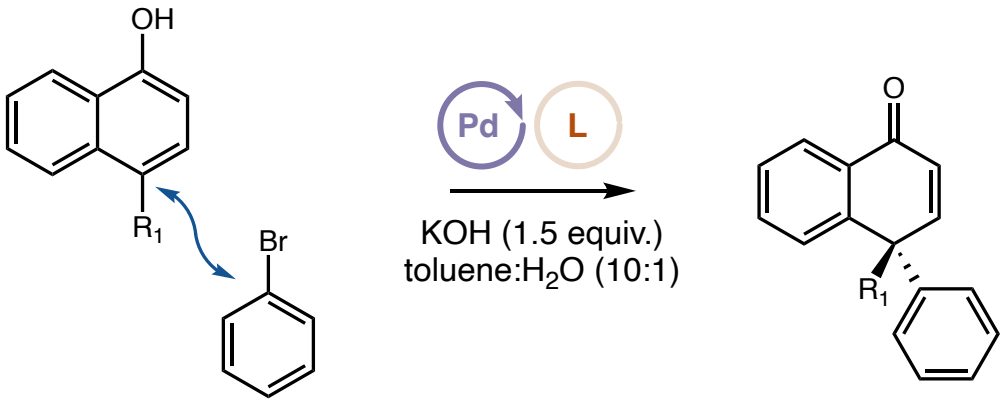
(R)-sSPhos-Np

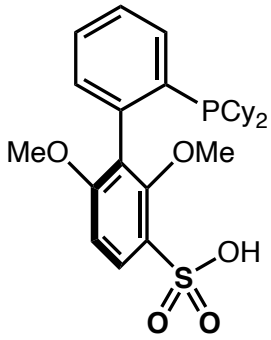


SPhos

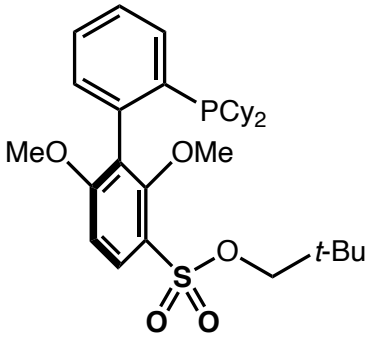
Kadarauch, M., Moss, T. A., & Phipps, R. J. *JACS* **2024**, *ASAP*

Phipps - Intermolecular Ion-Pairing



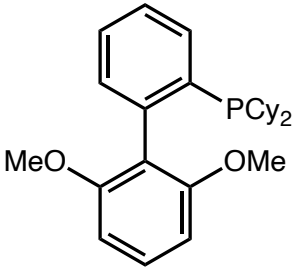


(R)-sSPhos



(R)-sSPhos-Np

L



SPhos

L	Yield	%ee
(*R*)-sSPhos	**62**	**97**
(*R*)-sSPhos-NP	**13**	**-19**
SPhos	**11**	**N.A.**

(rac)-sSPhos was 60x faster than SPhos

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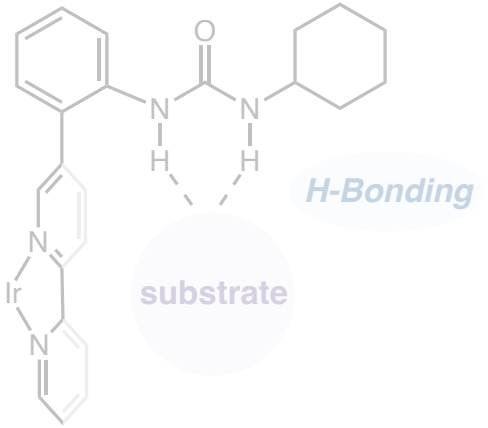
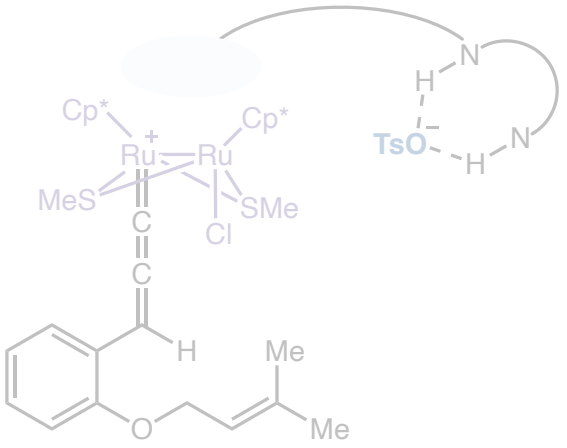
Ion-Pairing and H-bonding

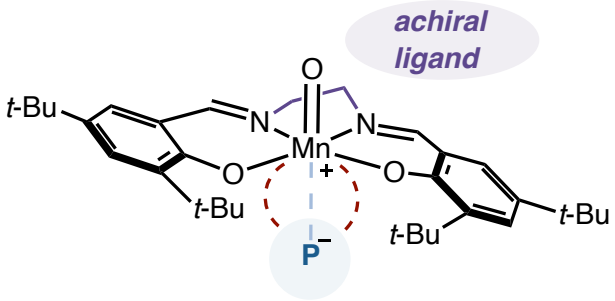
Hydrogen-bonding



Ion-pairing & H-Bonding

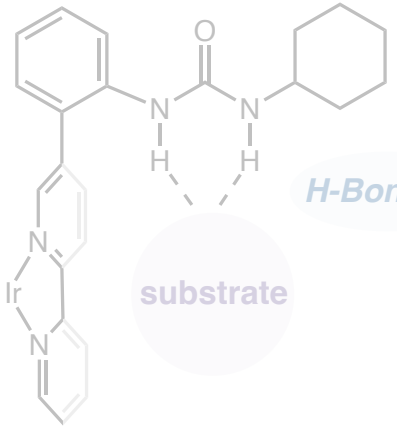


Ion-pairing

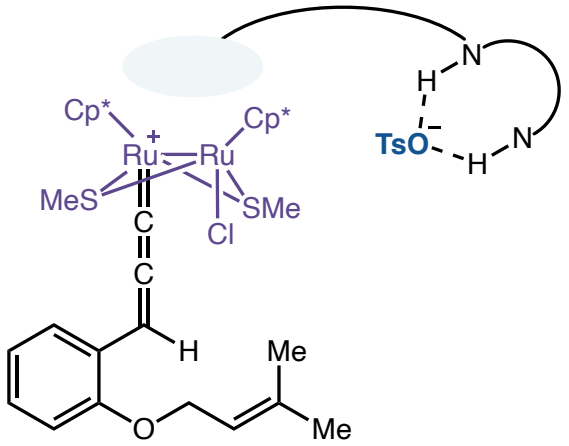


Ion-Pairing and H-bonding

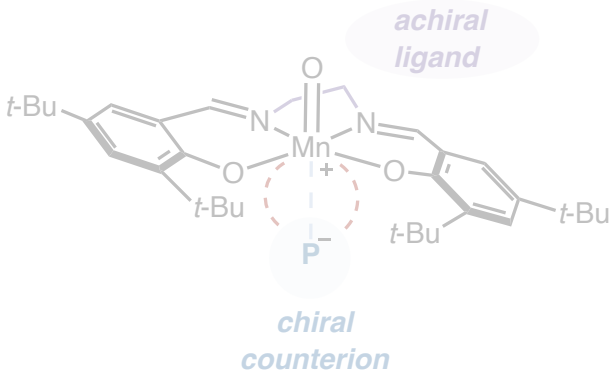
Hydrogen-bonding



Ion-pairing & H-Bonding

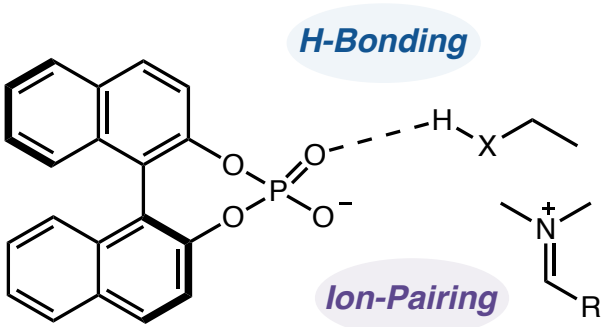


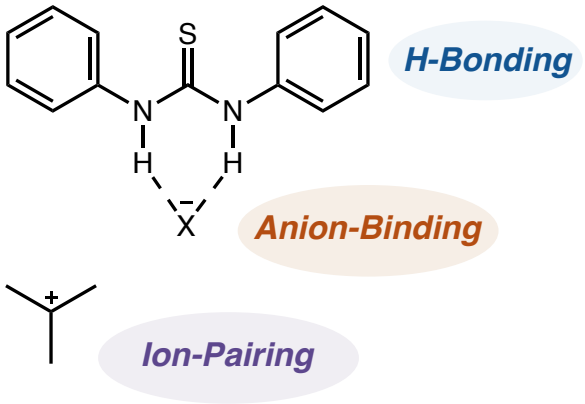
Ion-pairing



Ion-Pairing Merged with Transition Metal Catalysis

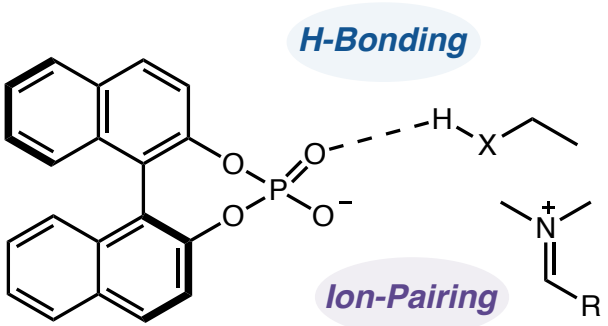
Ion-pairing with organic molecules

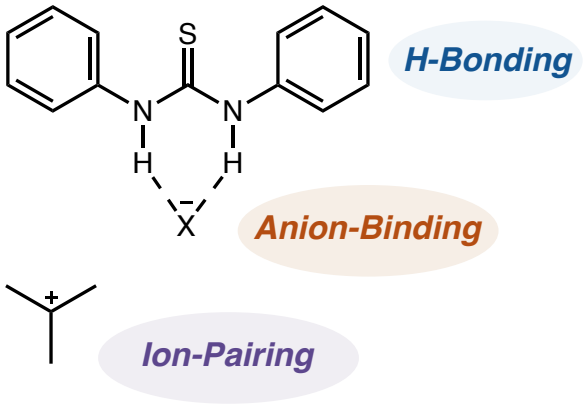




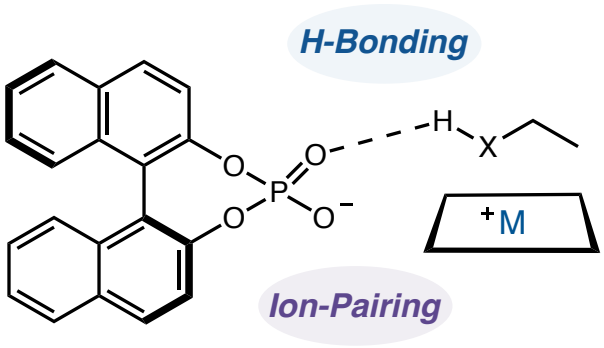
Ion-Pairing Merged with Transition Metal Catalysis

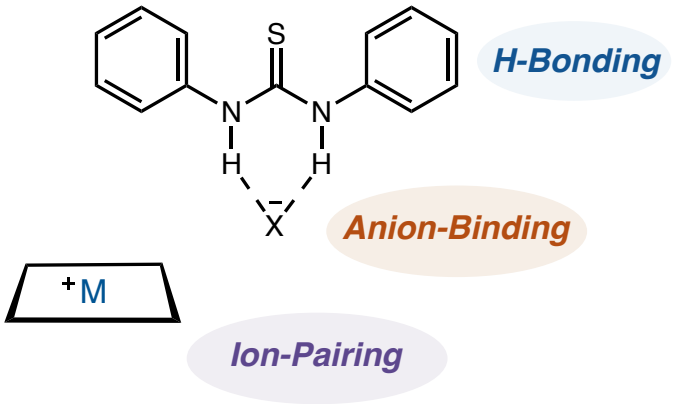
Ion-pairing with organic molecules





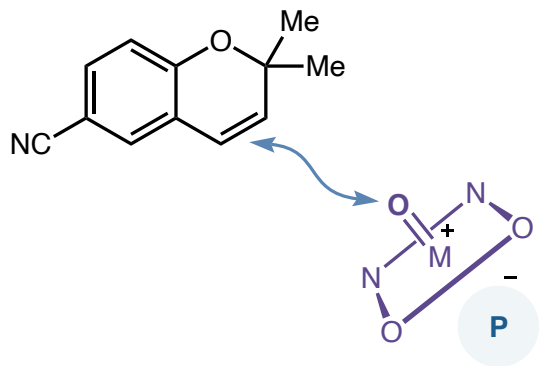
Ion-pairing with metals





Development of ACDC

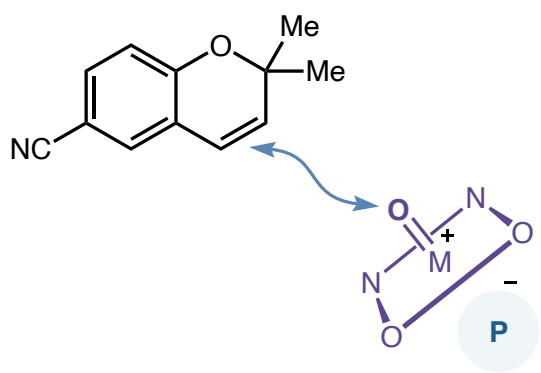
Counterion induced enantioselectivity

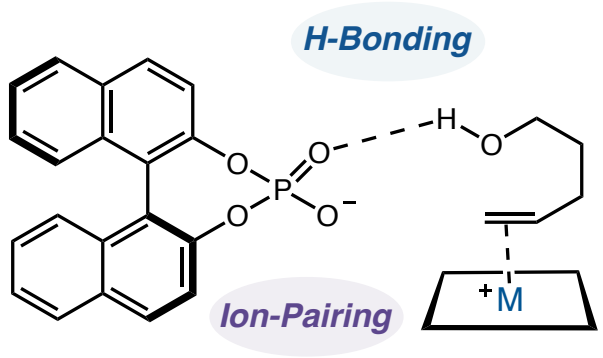


Hamilton, G. L., Kang, E. J., Mba, M. & Toste, F. D. *Science* **2007**, *317*, 496

Development of ACDC

Counterion induced enantioselectivity





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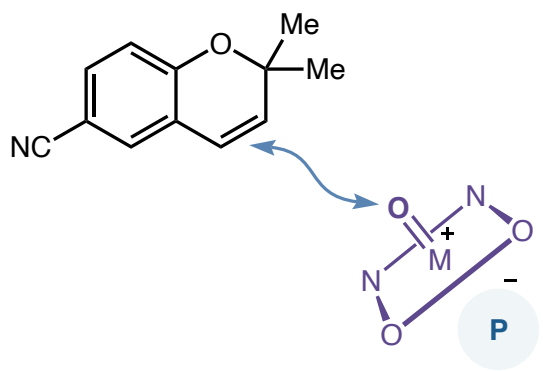
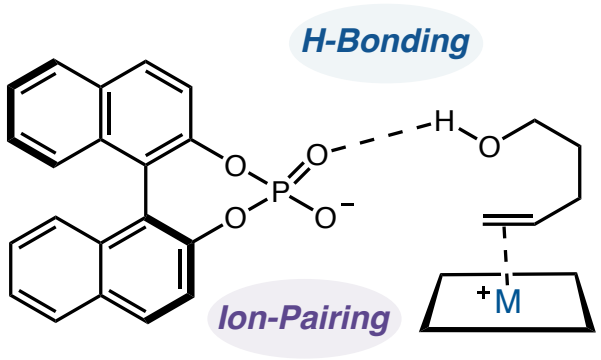
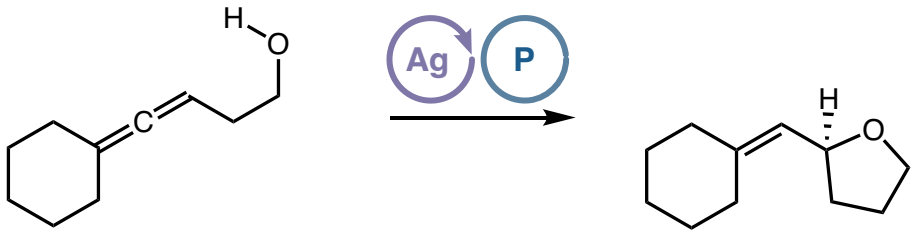
Development of ACDC

Counterion induced enantioselectivity

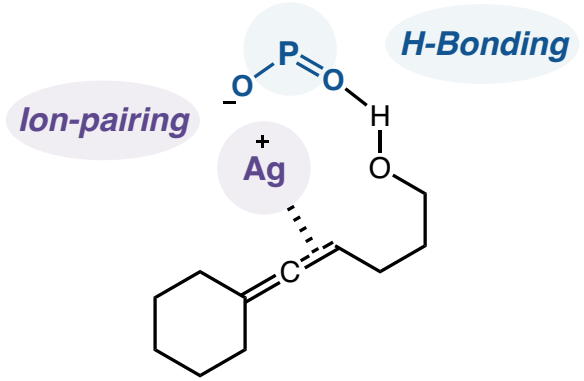




Initiated field of asymmetric countering directed catalysis (ACDC)



Proposed interactions



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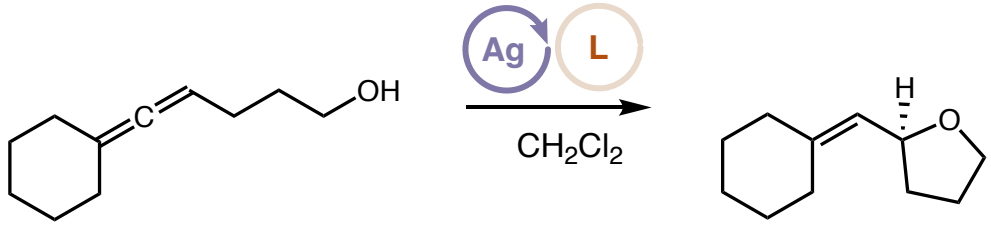
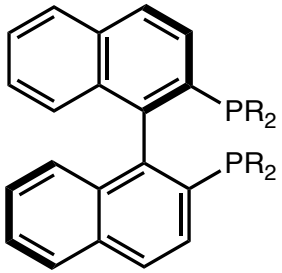
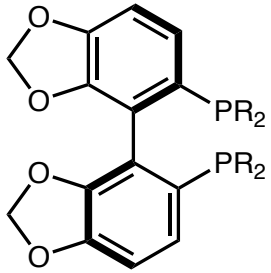
Toste - Gold—Phosphate Ion-Pairing



L



L1 R = Ph
L2 R = 3,5-DiMePh



L3 R = 3,5 Di*t*Bu-4-OMe-Ph

Ligand	X	%Yield	%ee
L1	**$^-BF_4$**	**52**	**6**
L2	**$^-BF_4$**	**68**	**0**
L3	**$^-BF_4$**	**79**	**2**

Ligand does not promote enantioselective reaction

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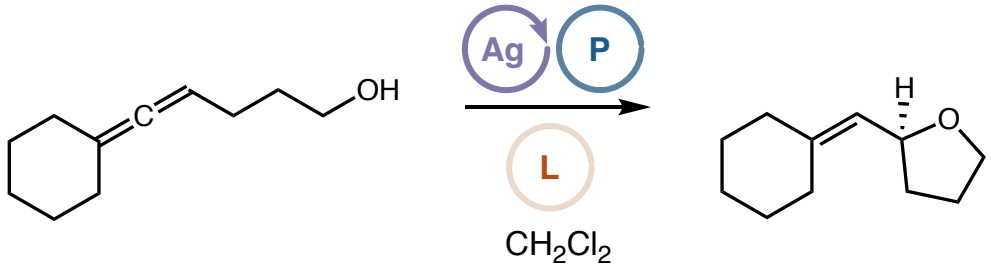
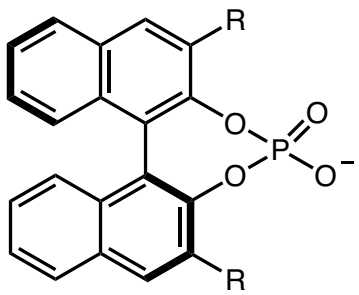


P



L	%Yield	%ee
PPh_3	89	48
dppm	76	65

Phosphoric acid promotes enantioselectivity

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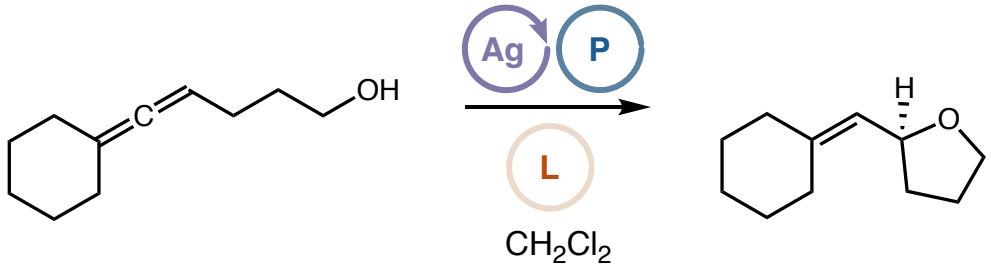
Toste - Gold—Phosphate Ion-Pairing



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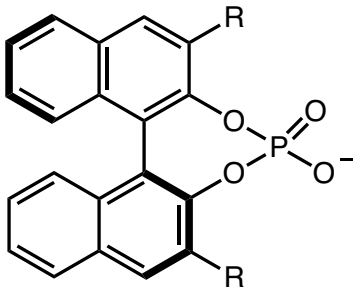

Solvent	ε	%Yield	%ee
CH_3NO_2	35.9	60	18
Acetone	20.7	71	37
DCM	8.9	76	65
THF	7.6	83	76
Benzene	2.3	90	97

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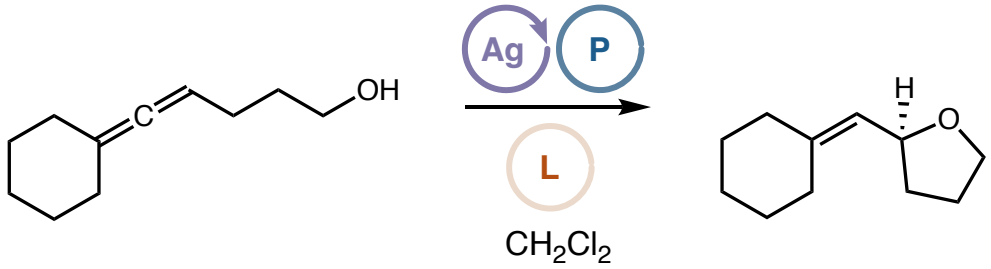
Toste - Gold—Phosphate Ion-Pairing



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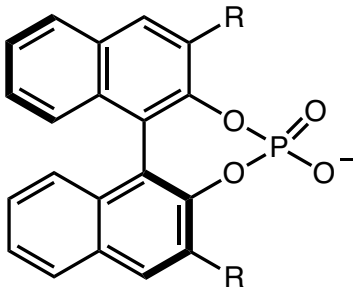

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Highly solvent dependent ee - Ion-pairing

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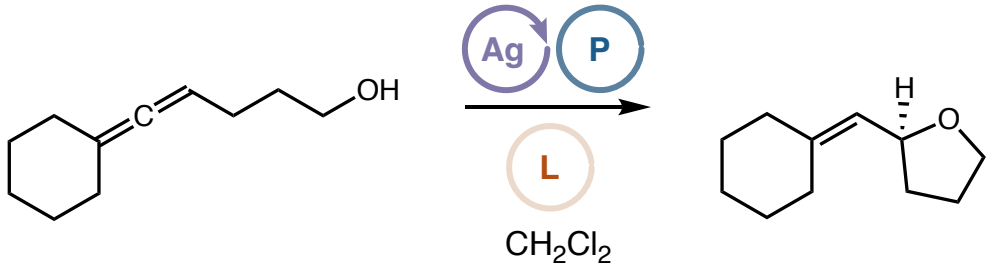
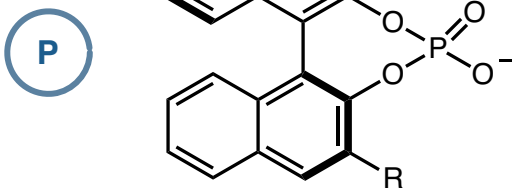
Toste - Gold—Phosphate Ion-Pairing





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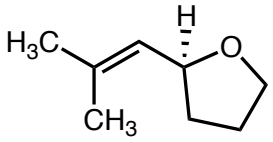
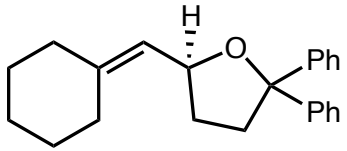
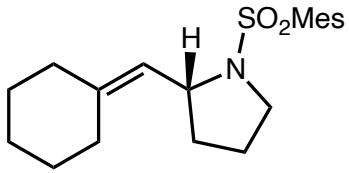
Highly solvent dependent ee - Ion-pairing



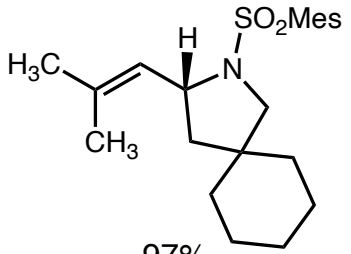
91%
95% ee



86%
92% ee



97%
96% ee



97%
96% ee

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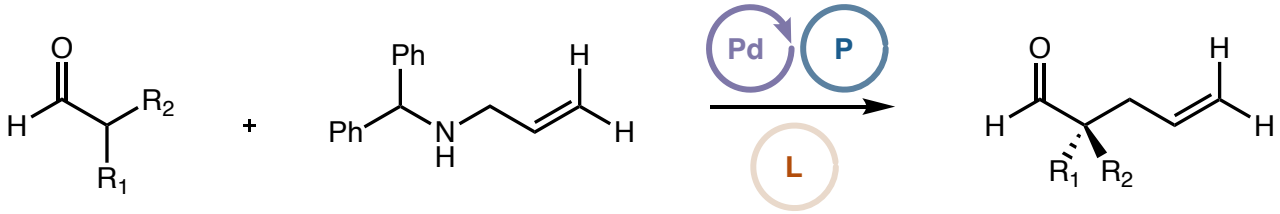
List - Pd-π-allyl Ion-Pairing



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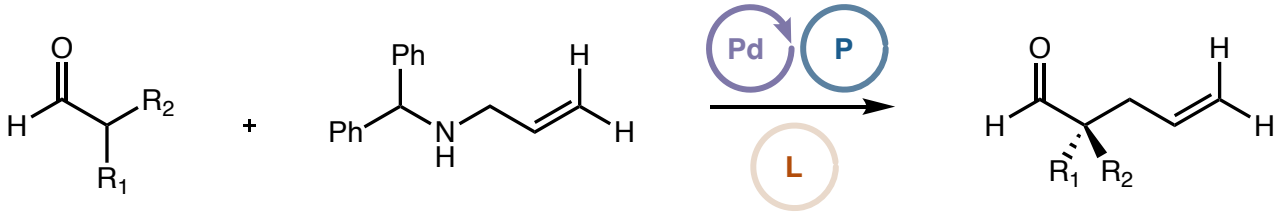
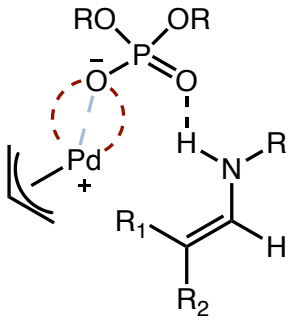
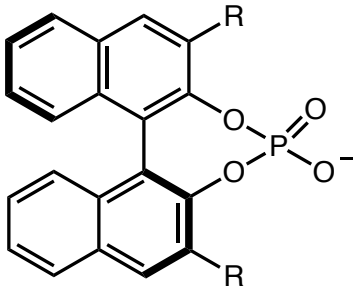
List - Pd-π-allyl Ion-Pairing



Key intermediate





P

R = 2,4,6-*i*-Pr_3-C_6H_2

Counterion controlled enantioselectivity

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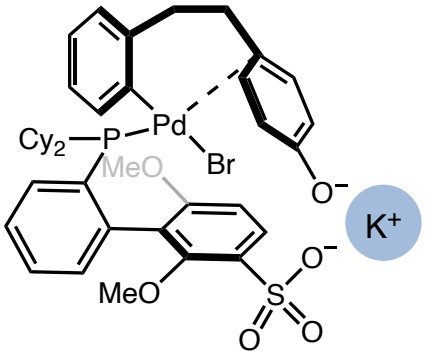
Phipps - Chiral Cation Controlled Enantioselectivity

Ion-pairing controlled enantioselectivity



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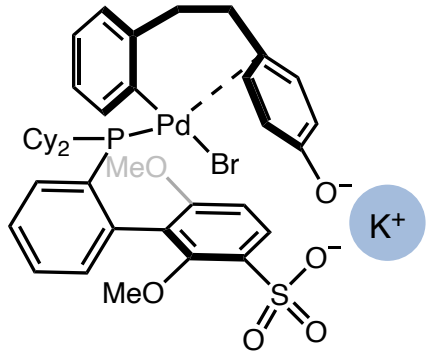
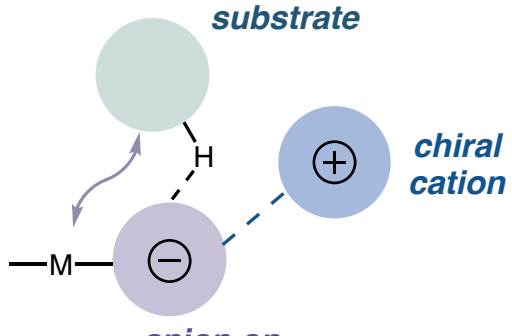
Phipps - Chiral Cation Controlled Enantioselectivity

Ion-pairing controlled enantioselectivity





chiral cation controlled enantioselectivity

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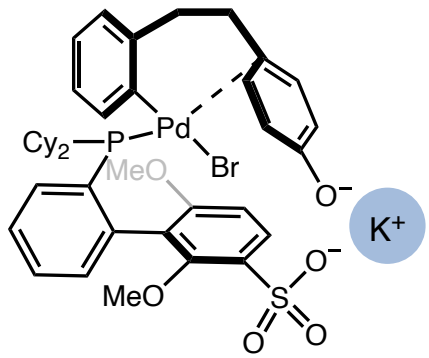
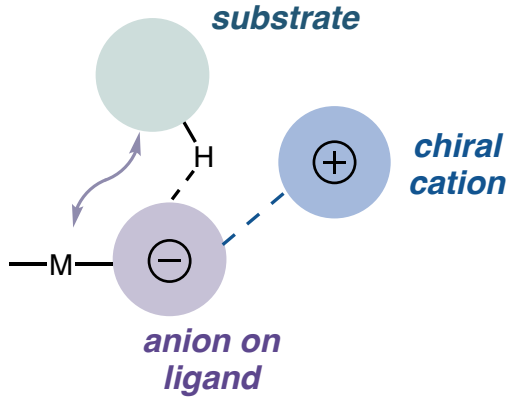
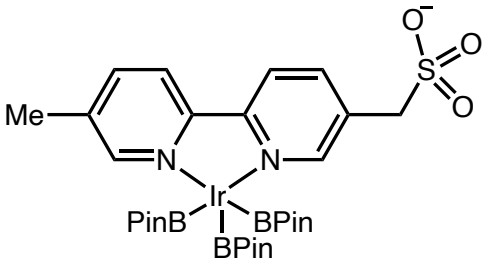
Phipps - Chiral Cation Controlled Enantioselectivity

Ion-pairing controlled enantioselectivity





chiral cation controlled enantioselectivity



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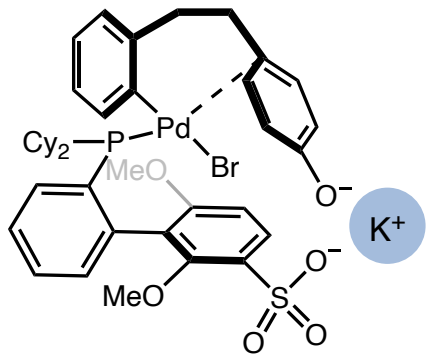
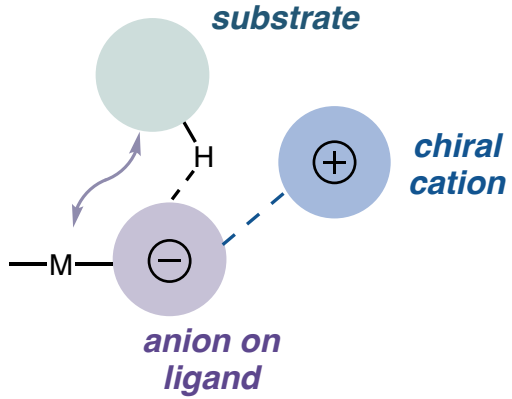
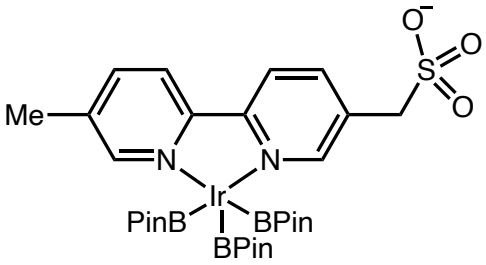
Phipps - Chiral Cation Controlled Enantioselectivity

Ion-pairing controlled enantioselectivity

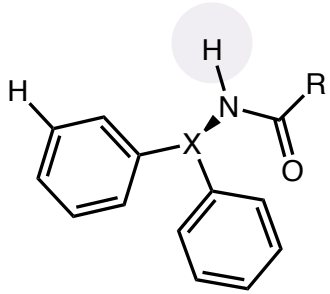




chiral cation controlled enantioselectivity



H-bonding



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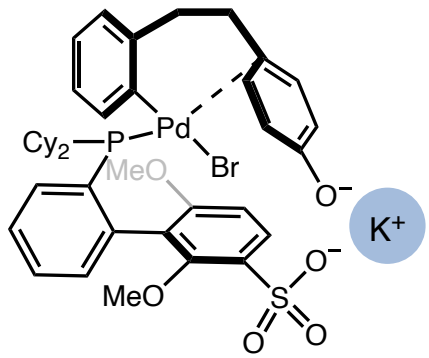
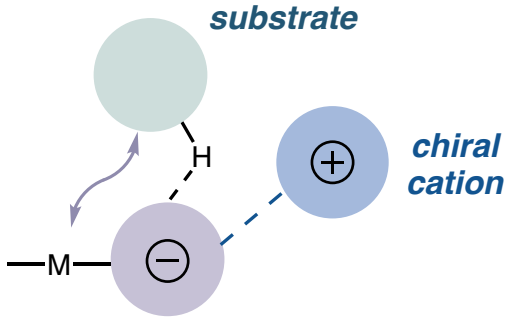
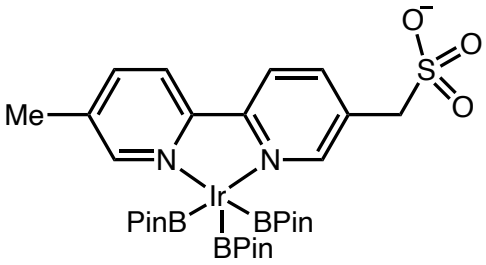
Phipps - Chiral Cation Controlled Enantioselectivity

Ion-pairing controlled enantioselectivity





chiral cation controlled enantioselectivity



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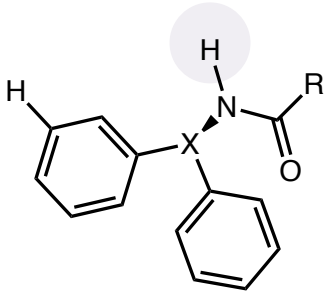

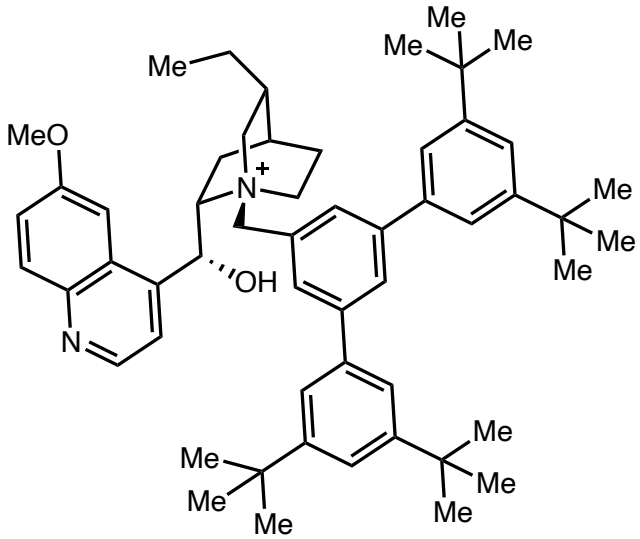

chiral cation

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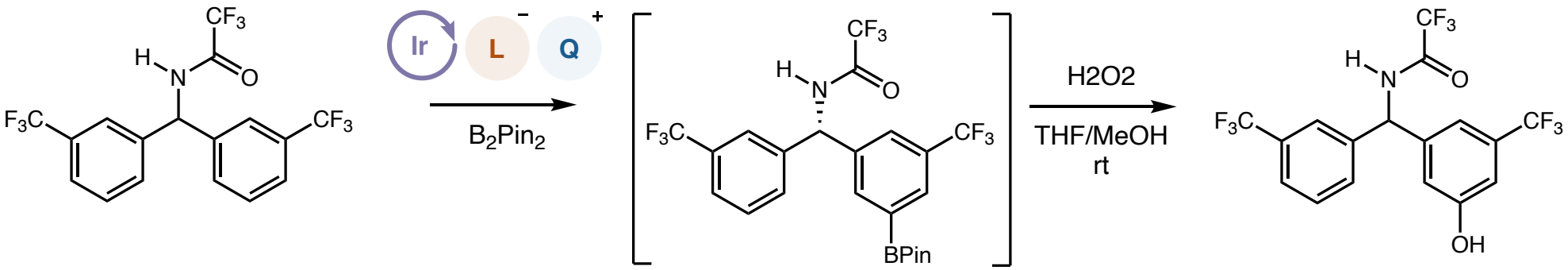

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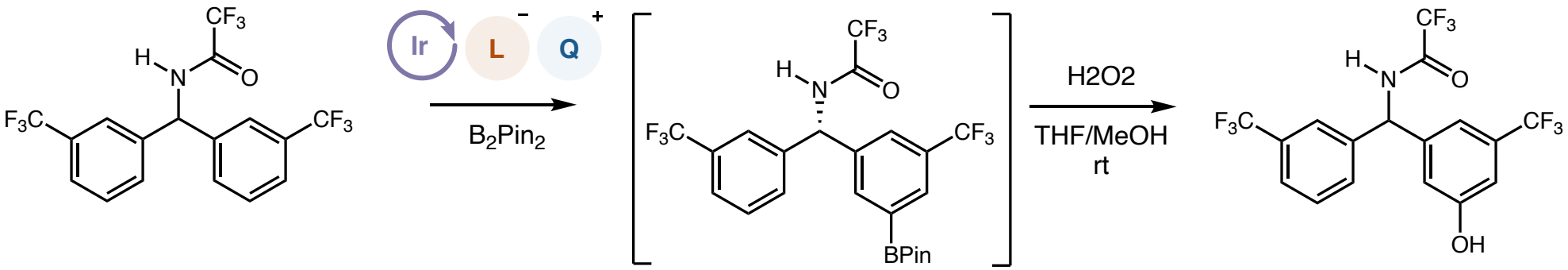

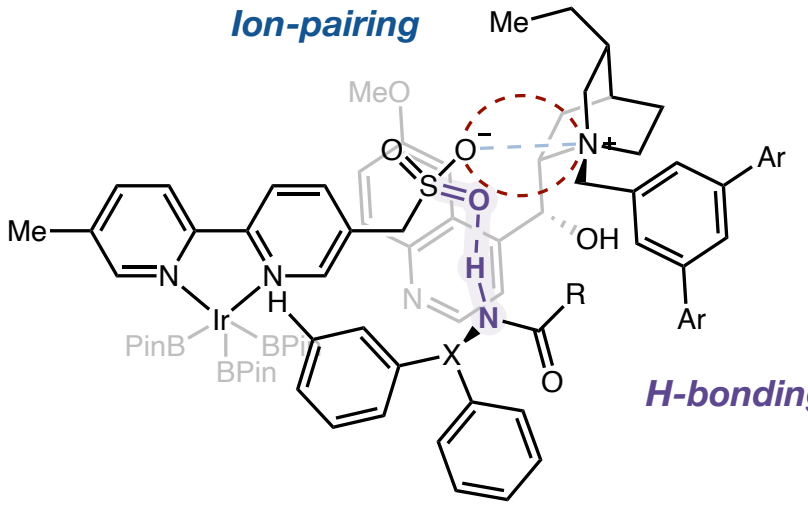

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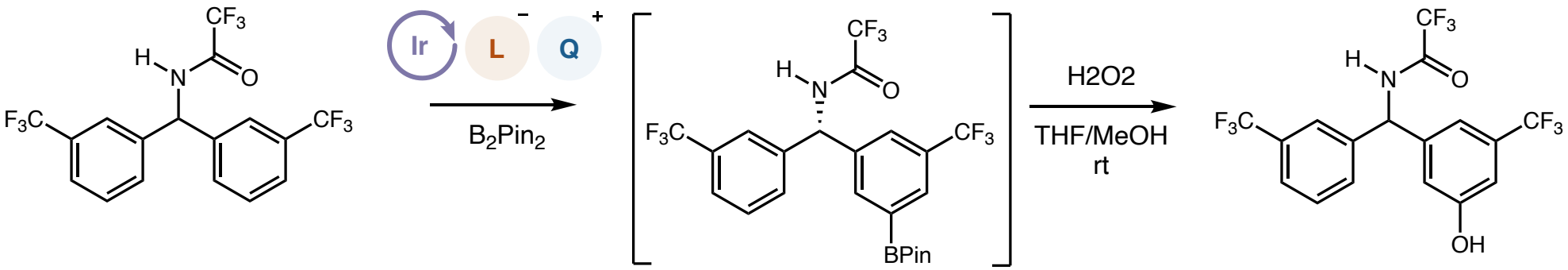

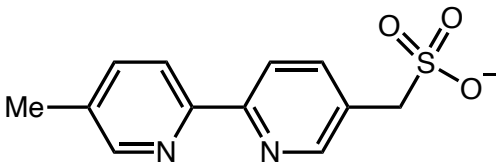

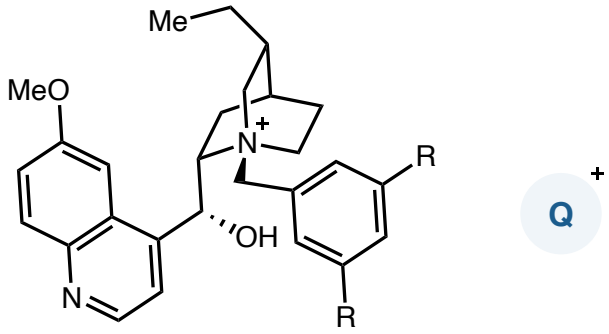

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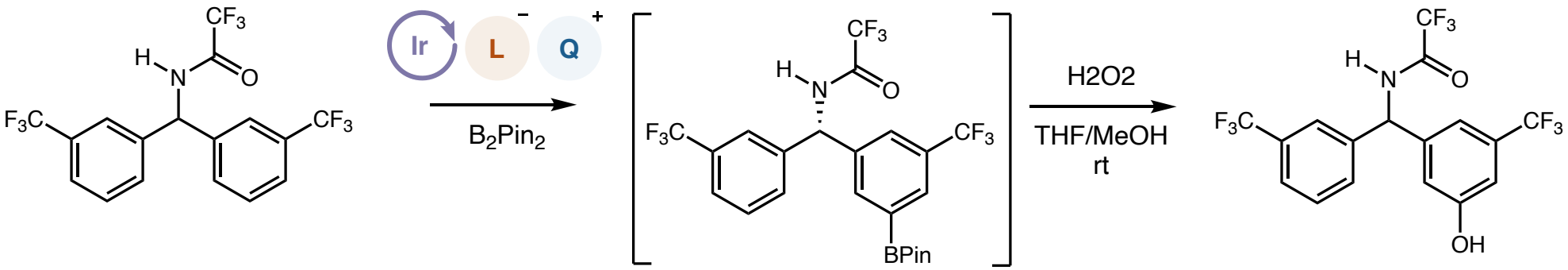
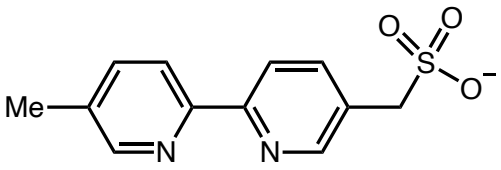
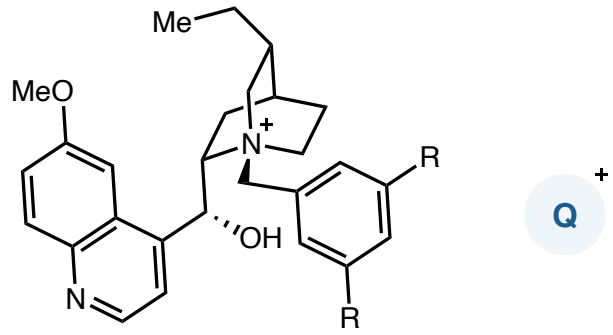
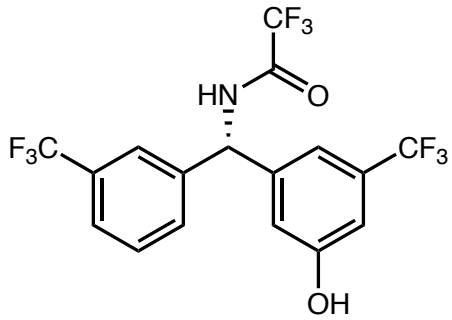
Phipps - Chiral Cation Controlled Enantioselectivity

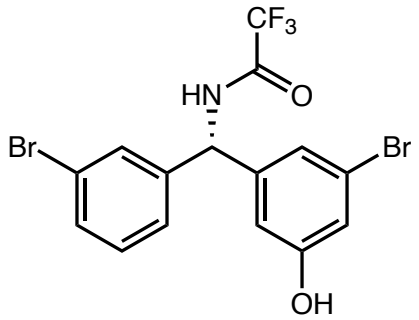




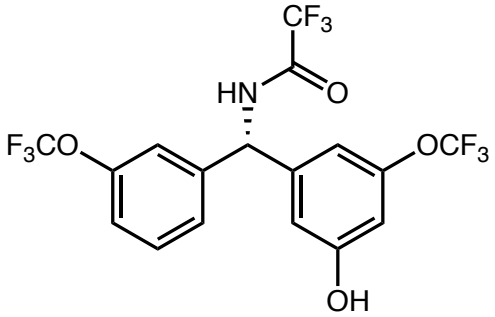




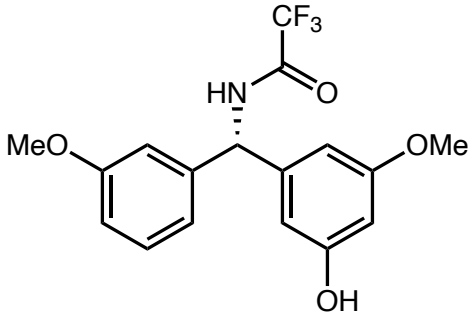
72%
96% ee



84%
91% ee



59%
95% ee



29%
45% ee

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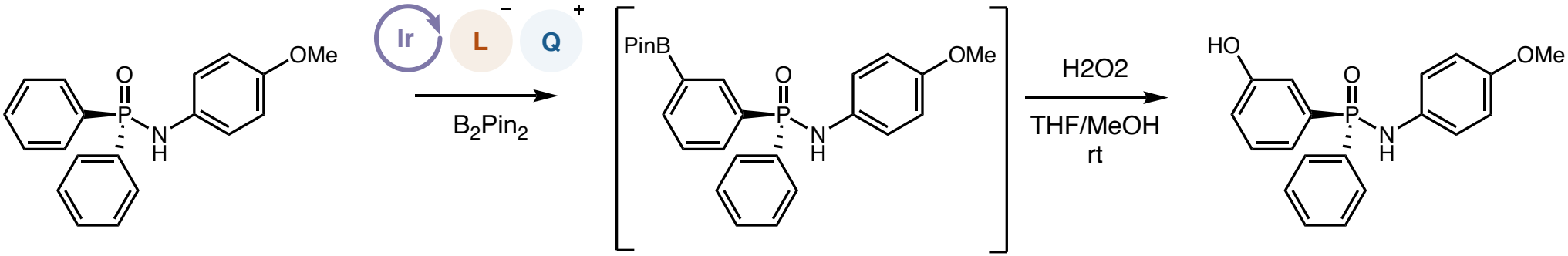
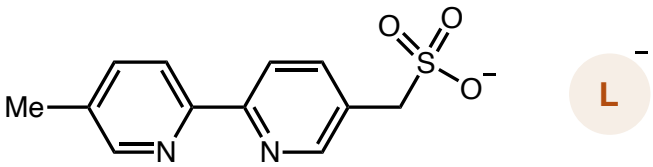
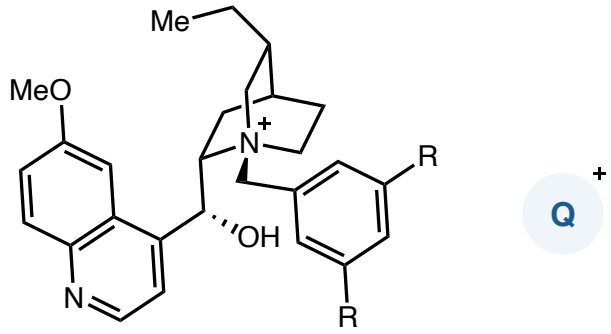
Phipps - Chiral Cation Controlled Enantioselectivity







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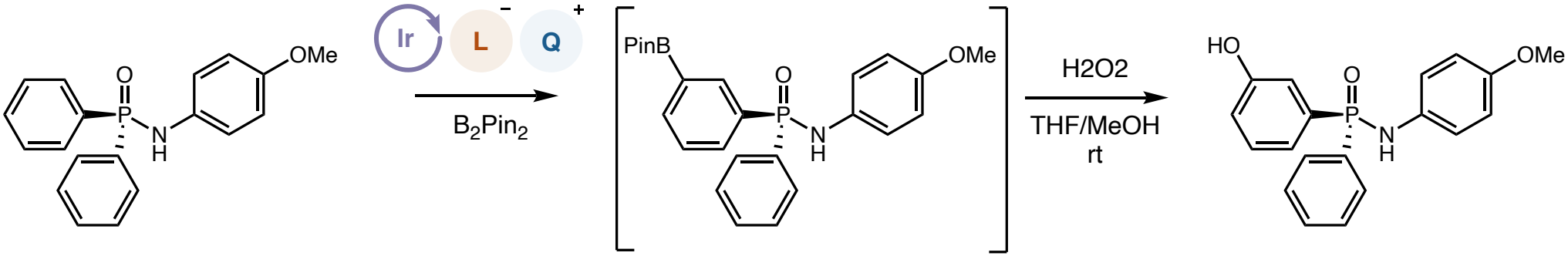
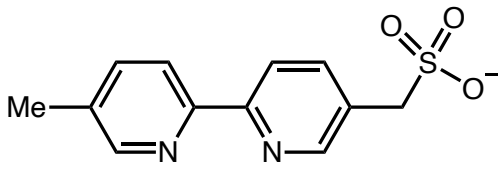
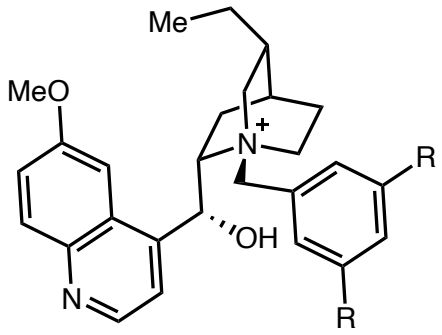
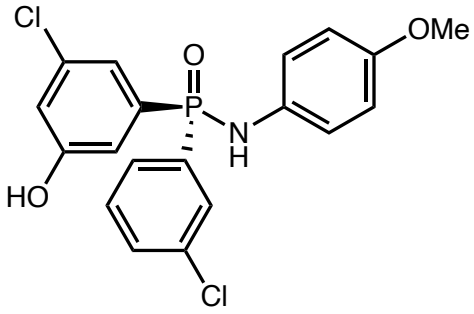
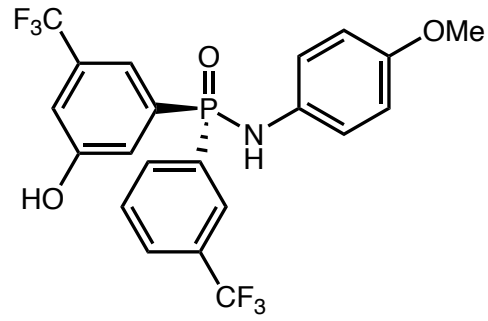








66%
90% ee



78%
89% ee

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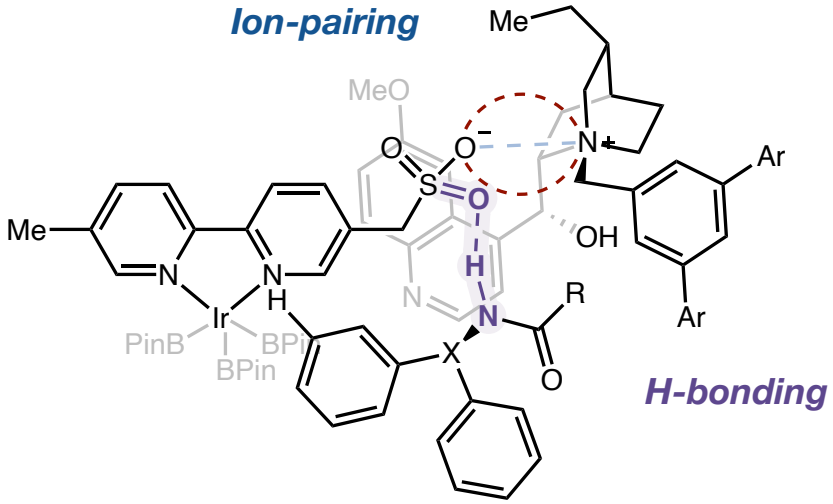

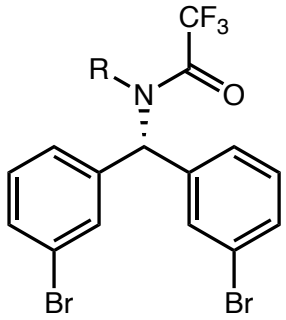

Ion-pairing highly dependent upon solvent

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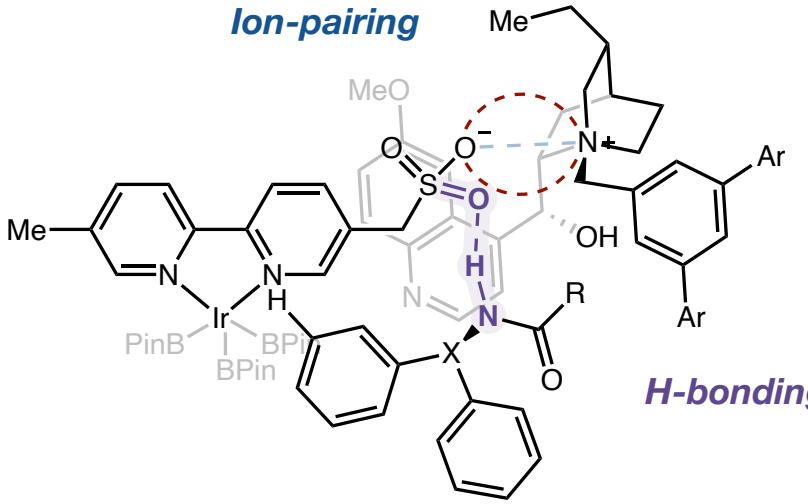
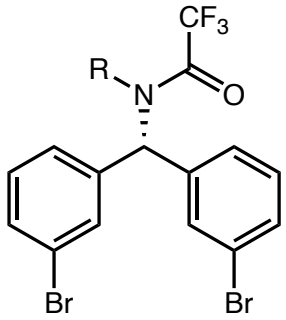
Phipps - Chiral Cation Controlled Enantioselectivity





Solvent	ε	NMR yield	%ee
Acetone	20.7	6	14
THF	7.6	100	73
Ethyl acetate	6.0	87	73
CPME	**4.8**	**>99**	**83**
Et_2O	**4.3**	**>99**	**86**
p-Xylene	2.6	82	76
Dioxane	2.3	97	66

Ion-pairing highly dependent upon solvent

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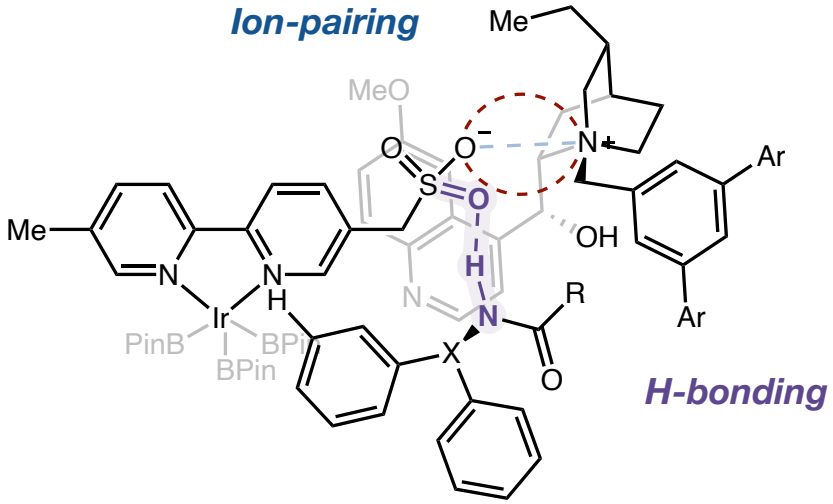

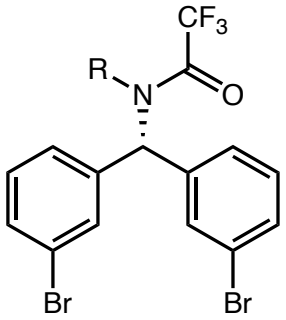

R	Temp.	%Conv.	%ee
H	**-10**	**91**	**91**
Me	**-10**	**0**	**-**

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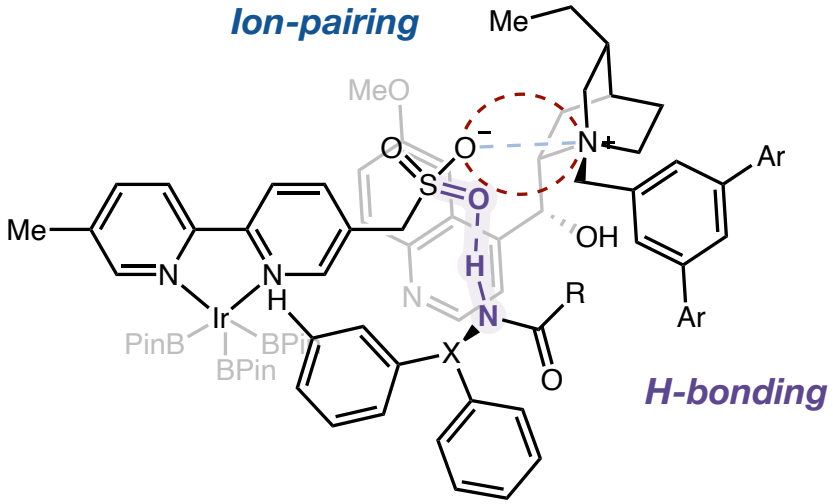

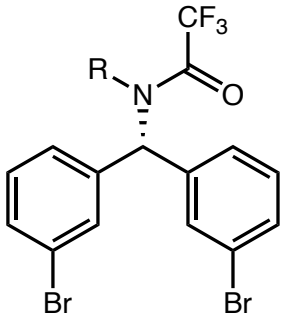

R	Temp.	%Conv.	%ee
H	**-10**	**91**	**91**
Me	**-10**	**0**	**-**
H	**10**	**>95**	**73**
Me	**10**	**>95**	**8**

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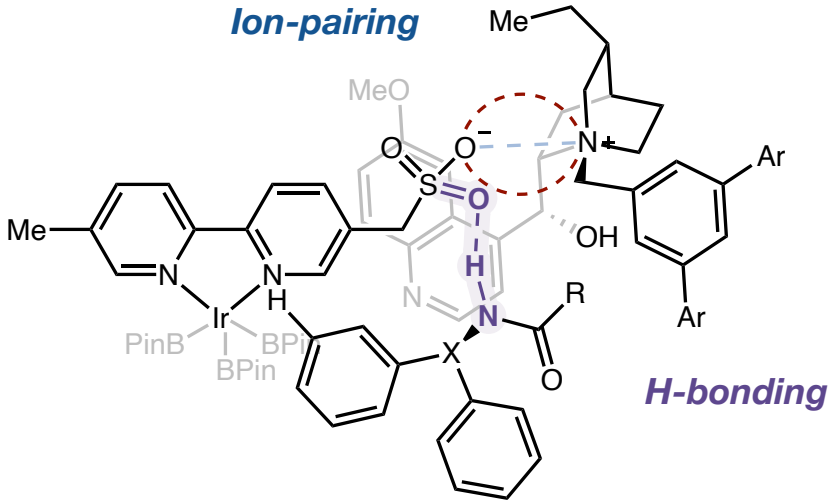
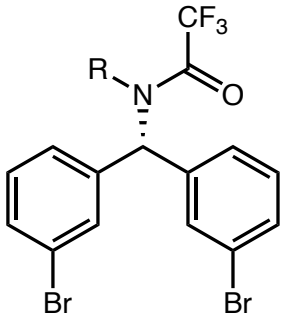
Phipps - Chiral Cation Controlled Enantioselectivity





R	Temp.	%Conv.	%ee
H	**-10**	**91**	**91**
Me	**-10**	**0**	**-**
H	**10**	**>95**	**73**
Me	**10**	**>95**	**8**

H-bonding crucial for enantioselectivity

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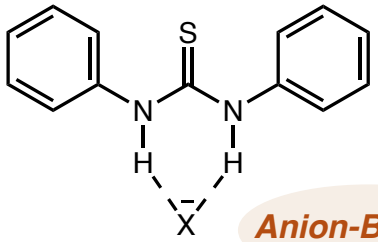
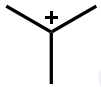
Anion Binding in T.M. Catalysis



H-Bonding

Anion-Binding



Ion-Pairing

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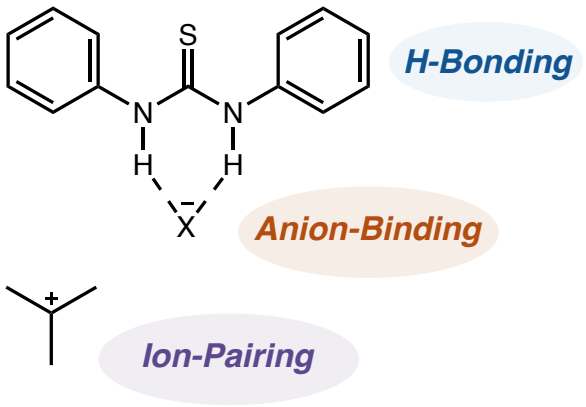
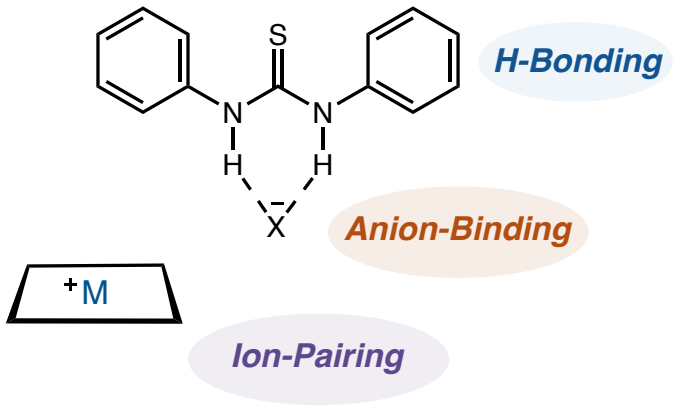
Anion Binding in T.M. Catalysis





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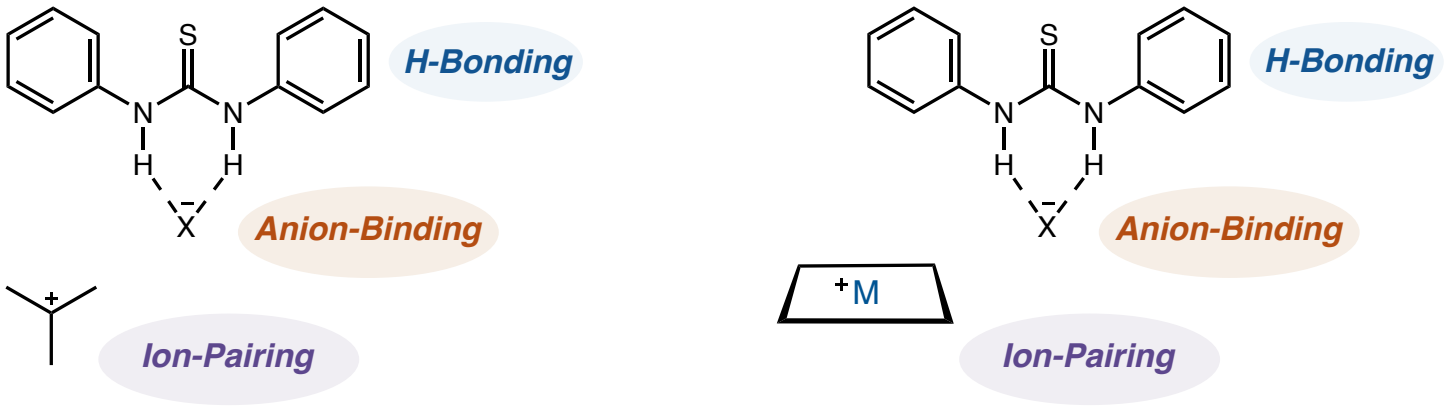

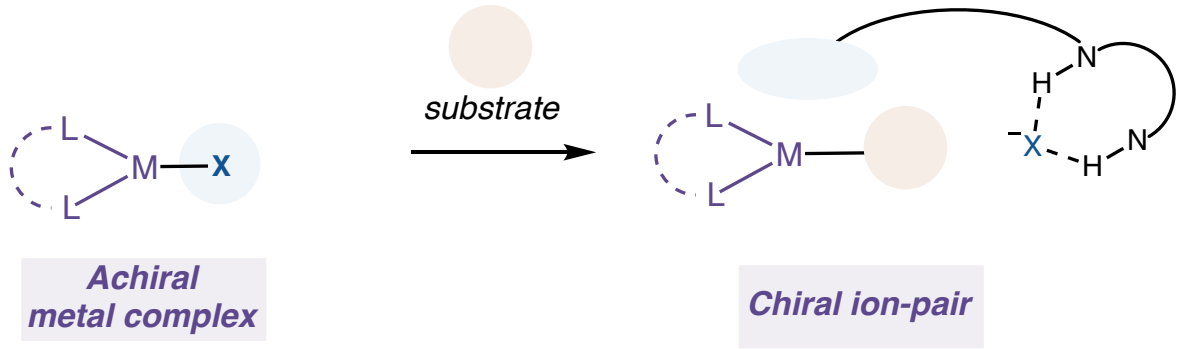

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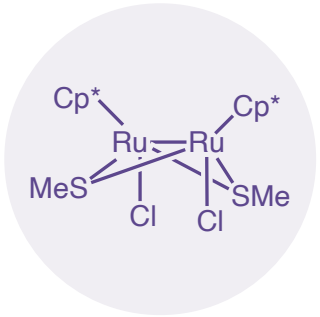
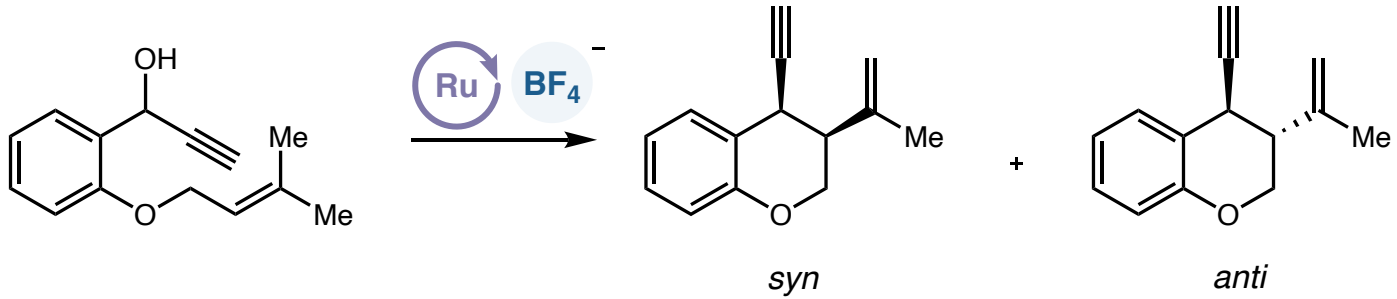
Ruthenium Cylcization

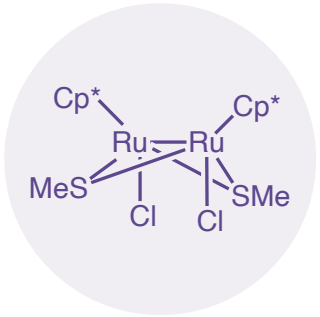


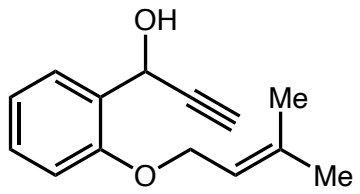


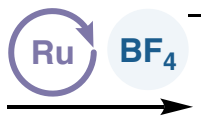
syn *anti*

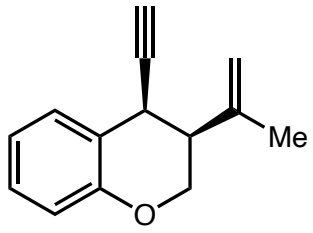
Nishibayashi, Y., Inada, Y. Hidai, M. & Uemura, S. *JACS* **2003**, *125*, 6060

Ruthenium Cylcization









syn

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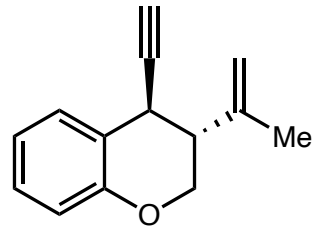

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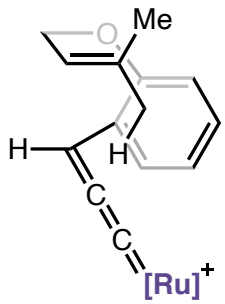

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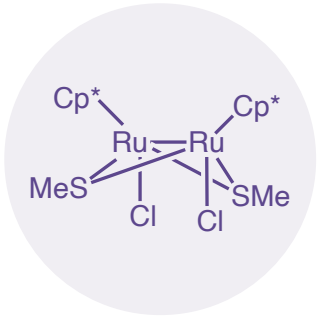
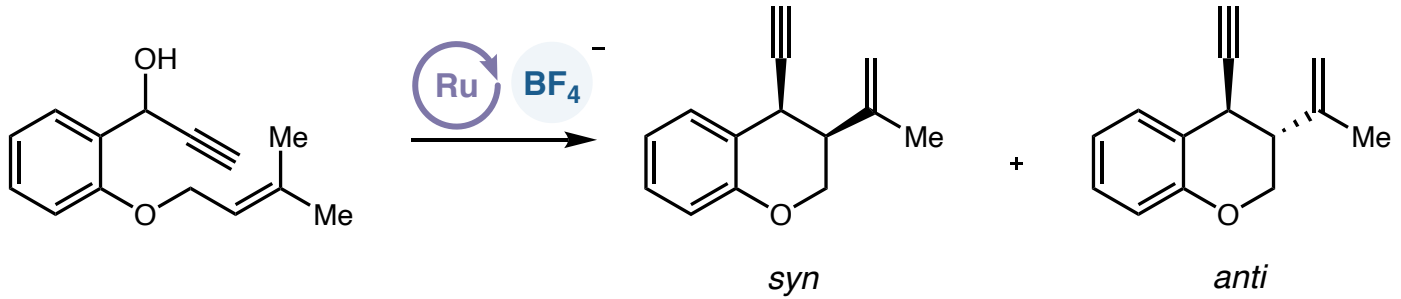
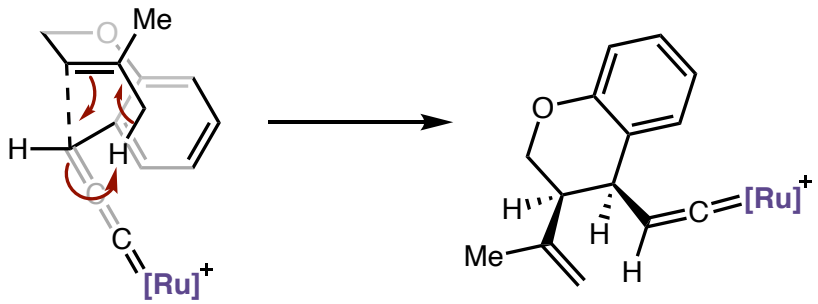
Ruthenium Cylcization





syn *anti*



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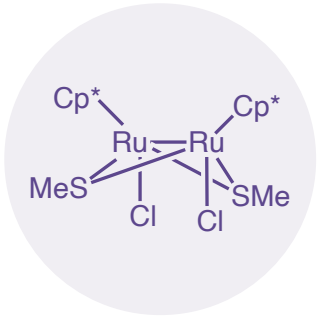

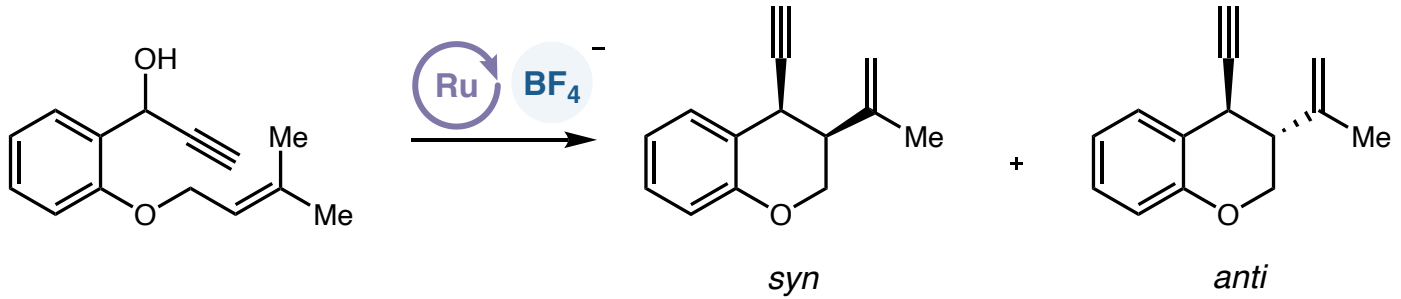

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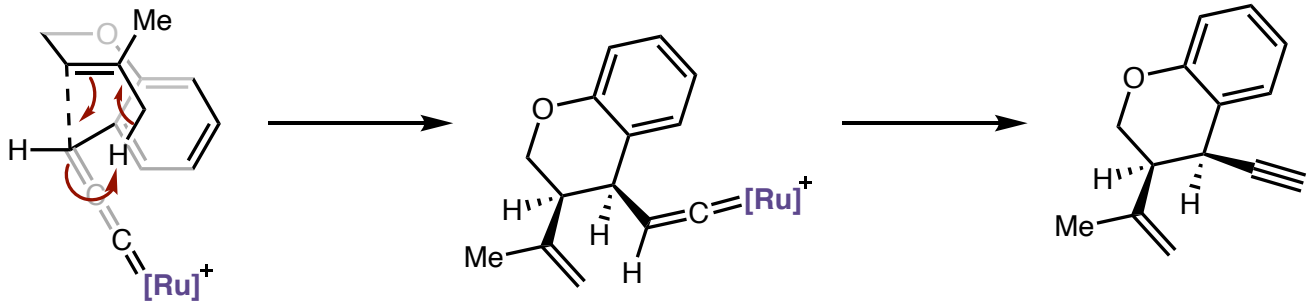

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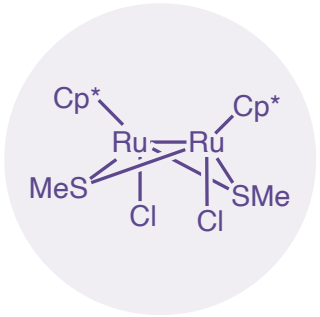
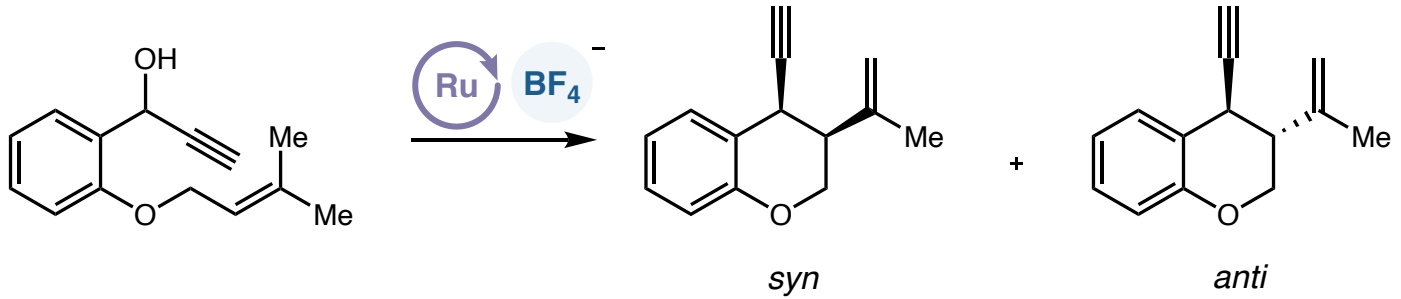
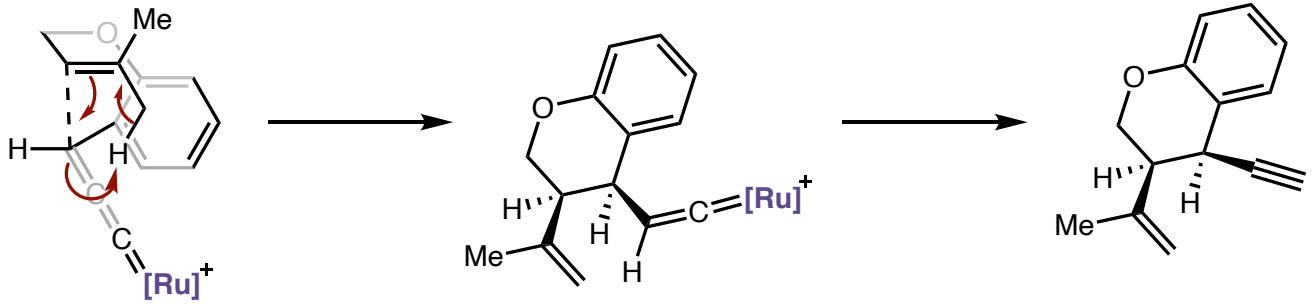
Ruthenium Cylcization







Cationic Ruthenium implicated in reaction

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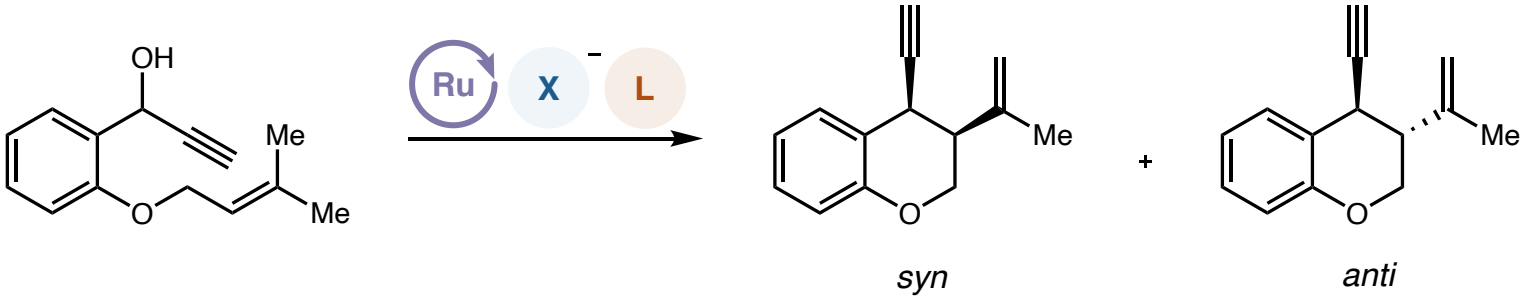
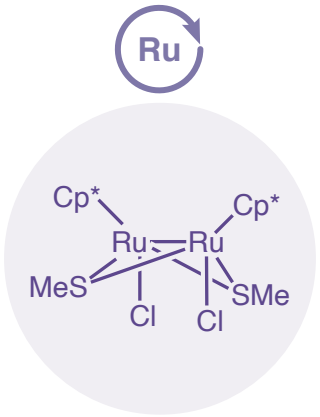
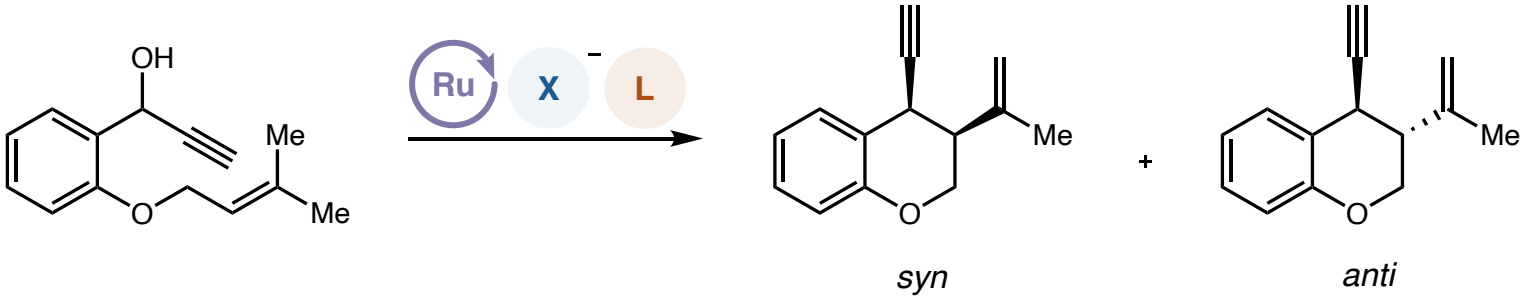




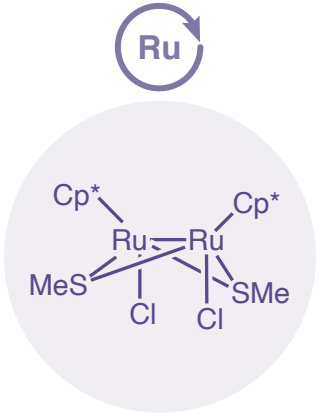
Ru-1

Ovian, J., Vojáčková, P. & Jacobsen, E. *Nature* **2023**, *616*, 84-89

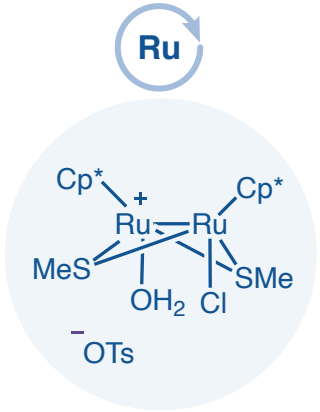
Jacobsen - Anion-Binding Catalysis



syn *anti*



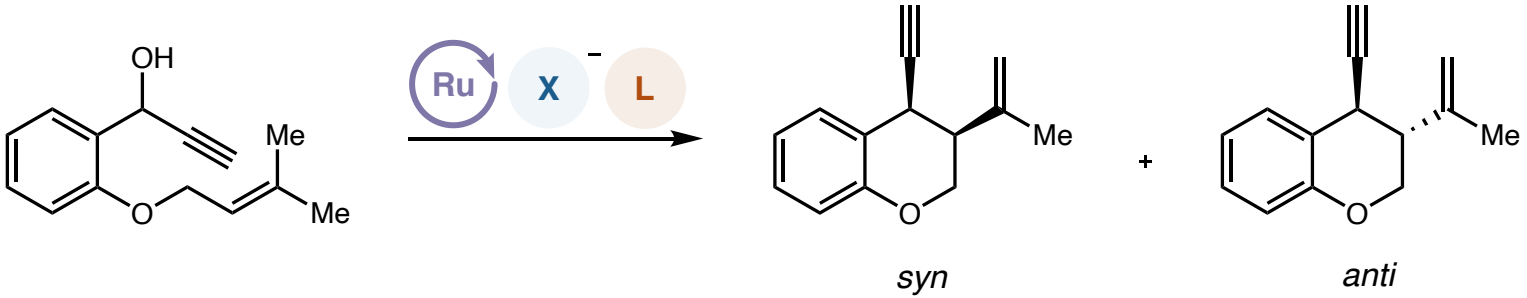
Ru-1

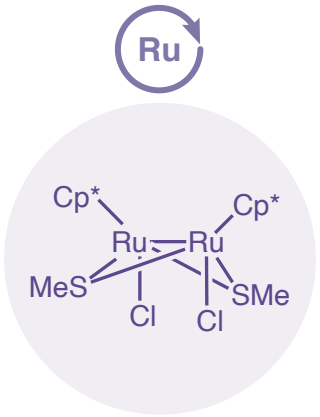


Ru-2

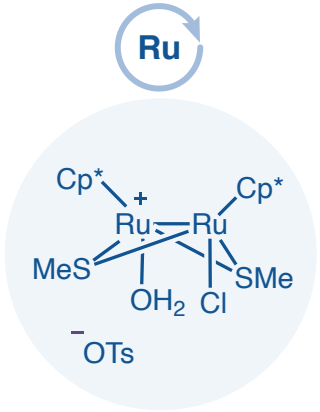
Ovian, J., Vojáčková, P. & Jacobsen, E. *Nature* **2023**, *616*, 84-89

Jacobsen - Anion-Binding Catalysis

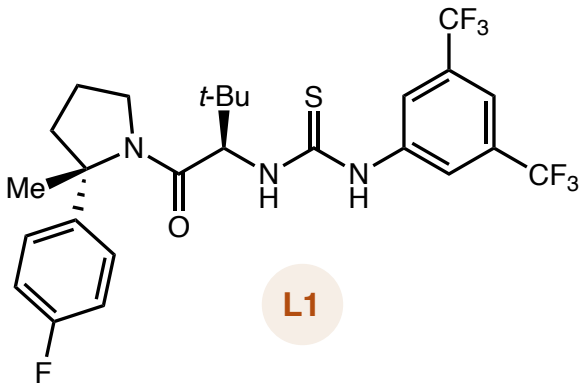




Ru-1



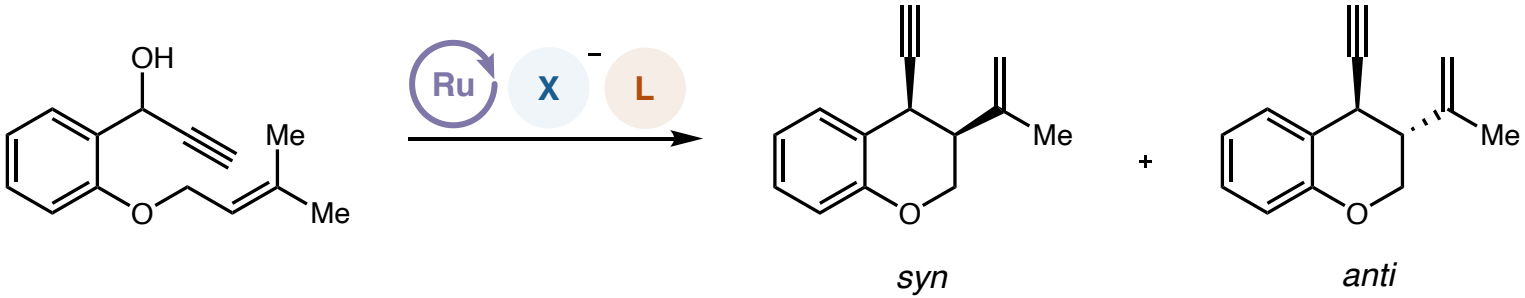
Ru-2



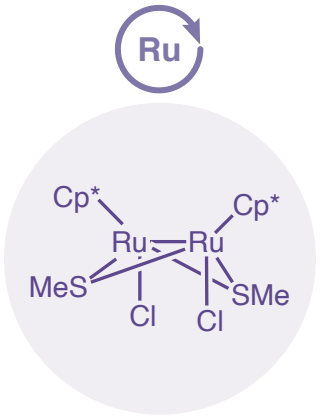
L1

Ovian, J., Vojáčková, P. & Jacobsen, E. *Nature* **2023**, *616*, 84-89

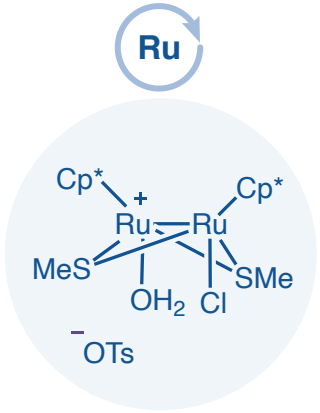
Jacobsen - Anion-Binding Catalysis



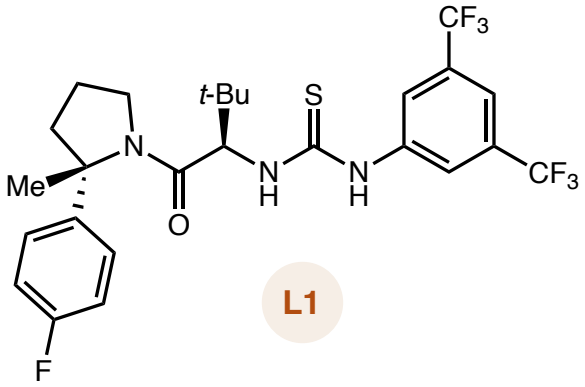
syn *anti*



Ru-1



Ru-2

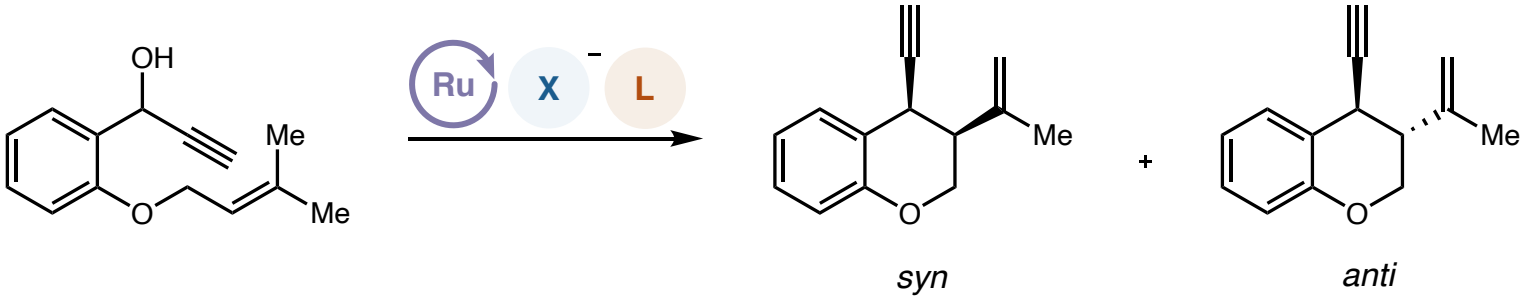


L1

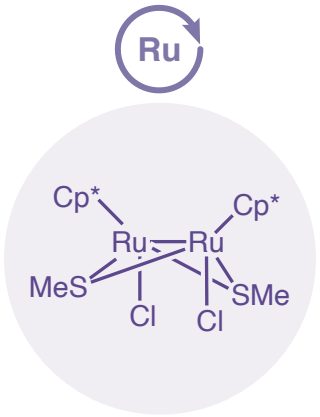
Ru	L	Yield	d.r.	%ee
Ru-1	**L1**	**13**	**6:1**	**3**
Ru-2	**L1**	**29**	**7:1**	**73**

Ovian, J., Vojáčková, P. & Jacobsen, E. *Nature* **2023**, *616*, 84-89

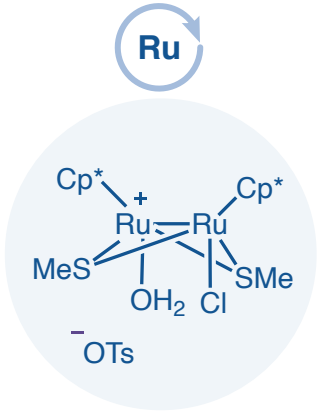
Jacobsen - Anion-Binding Catalysis



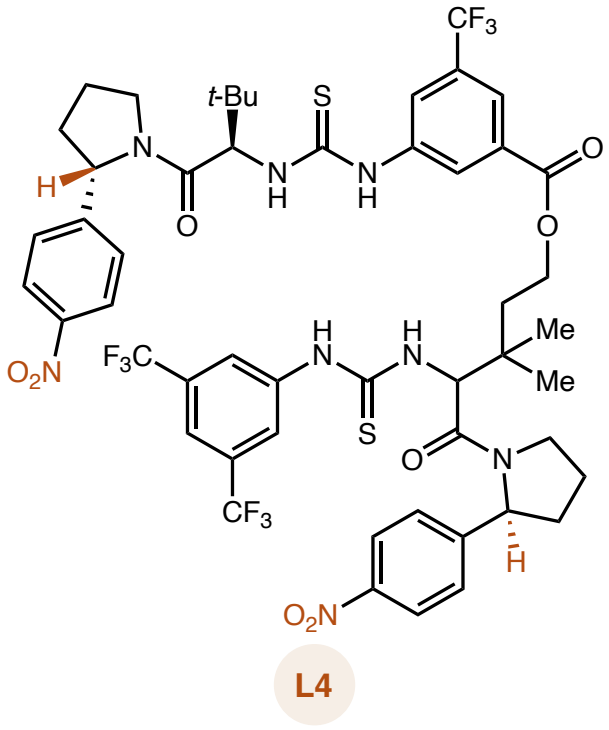
syn *anti*



Ru-1



Ru-2

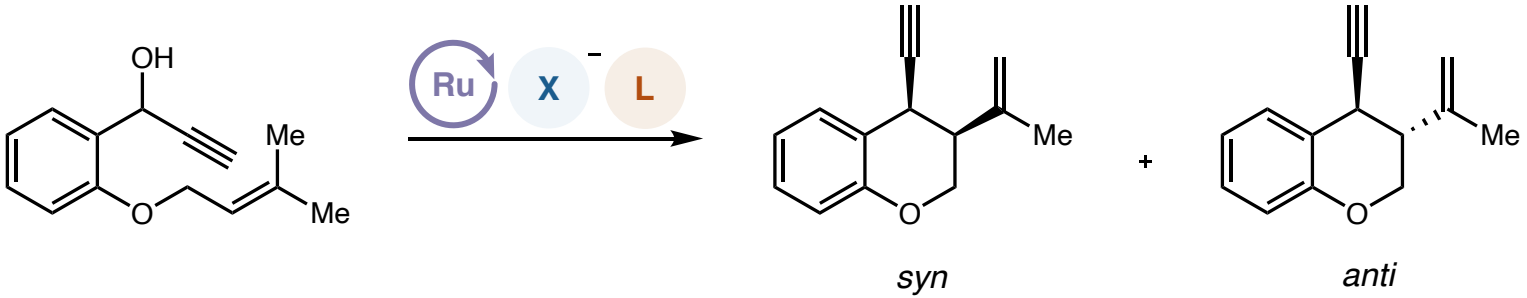


L4

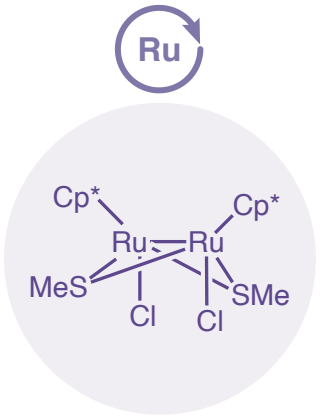
Ru	L	Yield	d.r.	%ee
Ru-1	L1	13	6:1	3
Ru-2	L1	29	7:1	73

Ovian, J., Vojáčková, P. & Jacobsen, E. *Nature* **2023**, *616*, 84-89

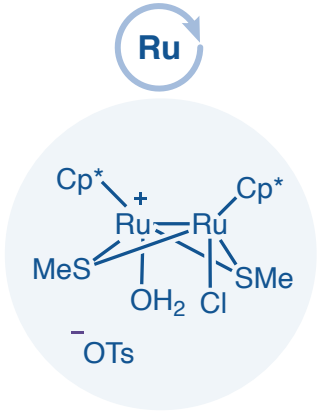
Jacobsen - Anion-Binding Catalysis



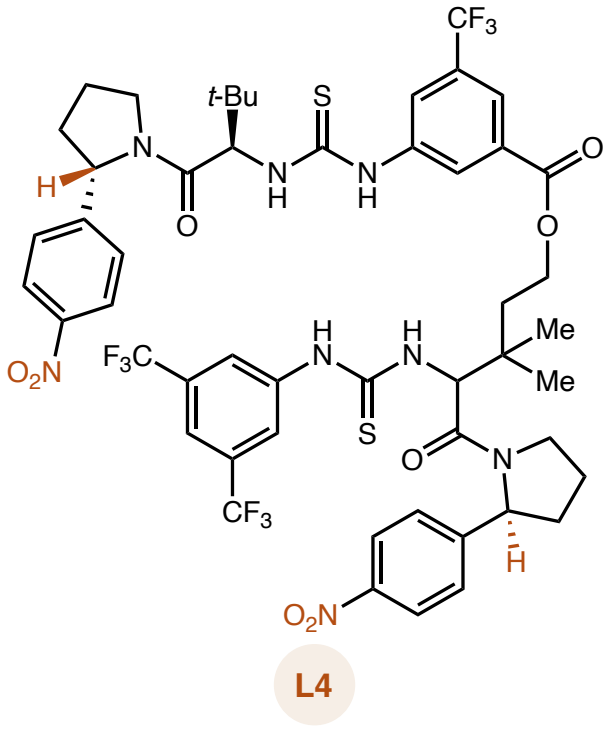
syn *anti*



Ru-1



Ru-2

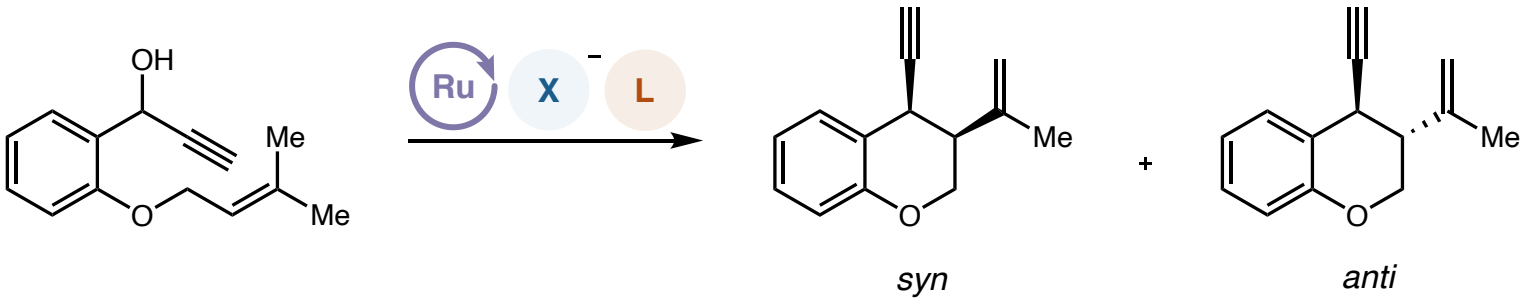


L4

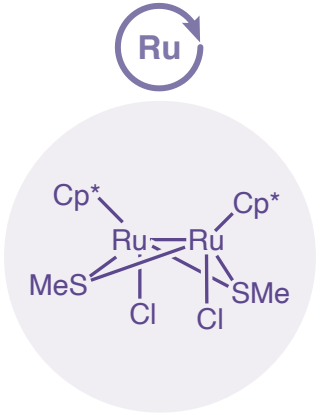
Ru	L	Yield	d.r.	%ee
Ru-1	L1	13	6:1	3
Ru-2	L1	29	7:1	73
Ru-2	L4	>99	36:1	95

Ovian, J., Vojáčková, P. & Jacobsen, E. *Nature* **2023**, *616*, 84-89

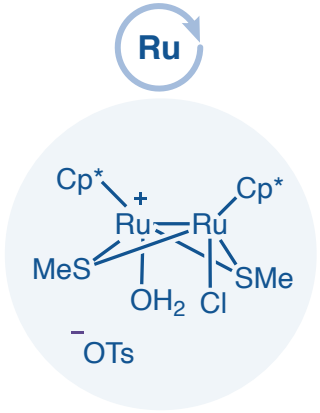
Jacobsen - Anion-Binding Catalysis



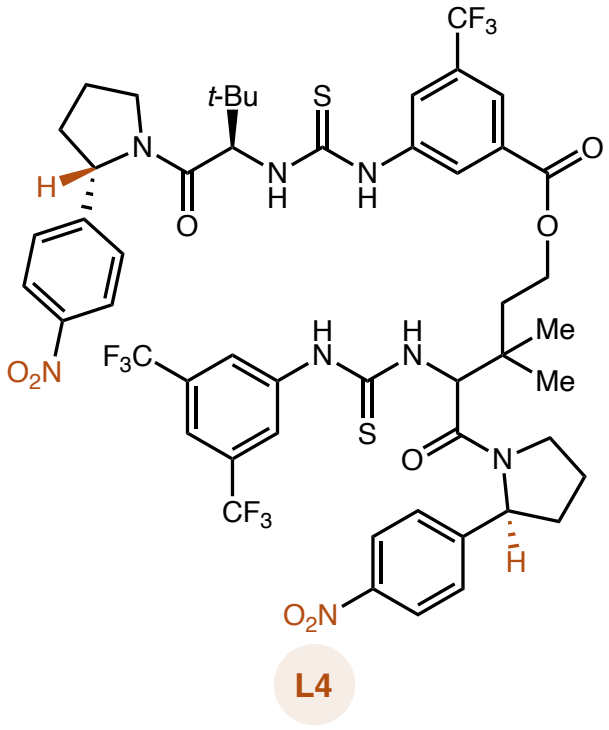
syn *anti*



Ru-1



Ru-2

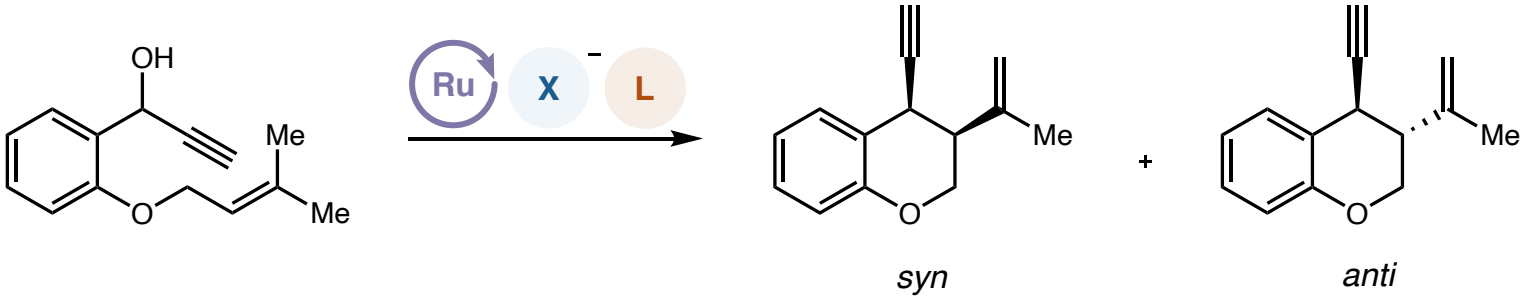


L4

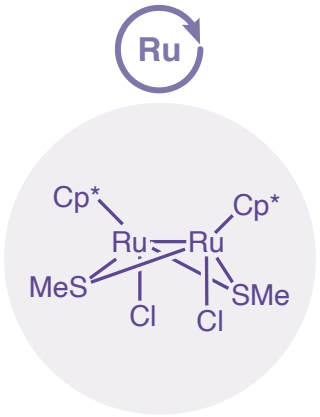
Ru	L	Yield	d.r.	%ee
Ru-1	L1	13	6:1	3
Ru-2	L1	29	7:1	73
Ru-2	L4	>99	36:1	95
Ru-1	-	<1	-	-
Ru-2	-	8	5:1	-

Ovian, J., Vojáčková, P. & Jacobsen, E. *Nature* **2023**, *616*, 84-89

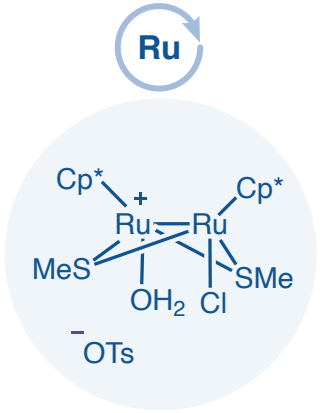
Jacobsen - Anion-Binding Catalysis



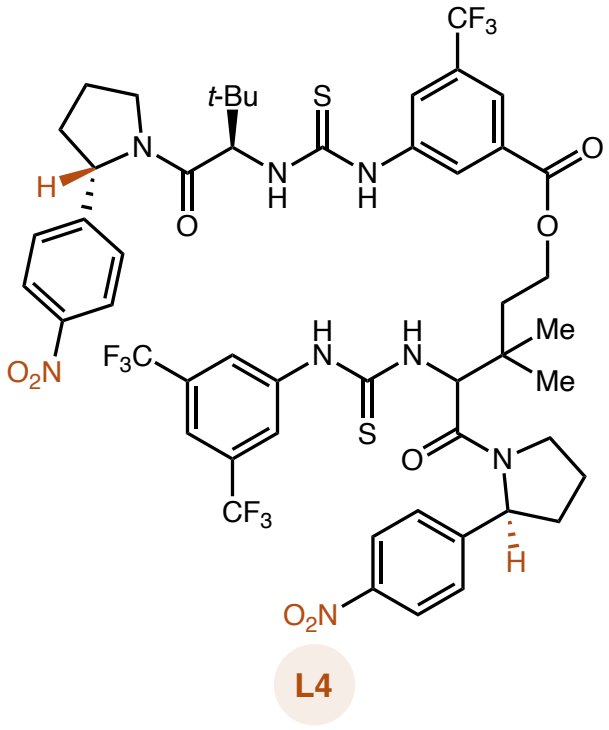
syn *anti*



Ru-1



Ru-2

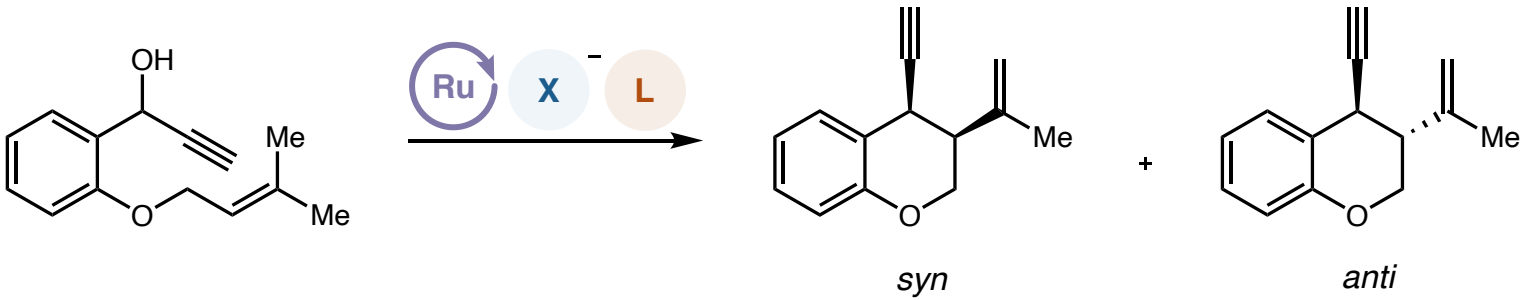


L4

Ru	L	Yield	d.r.	%ee
Ru-1	L1	13	6:1	3
Ru-2	L1	29	7:1	73
Ru-2	L4	>99	36:1	95
Ru-1	-	<1	-	-
Ru-2	-	8	5:1	-
-	L4	<1	-	-

Ovian, J., Vojáčková, P. & Jacobsen, E. *Nature* **2023**, *616*, 84-89

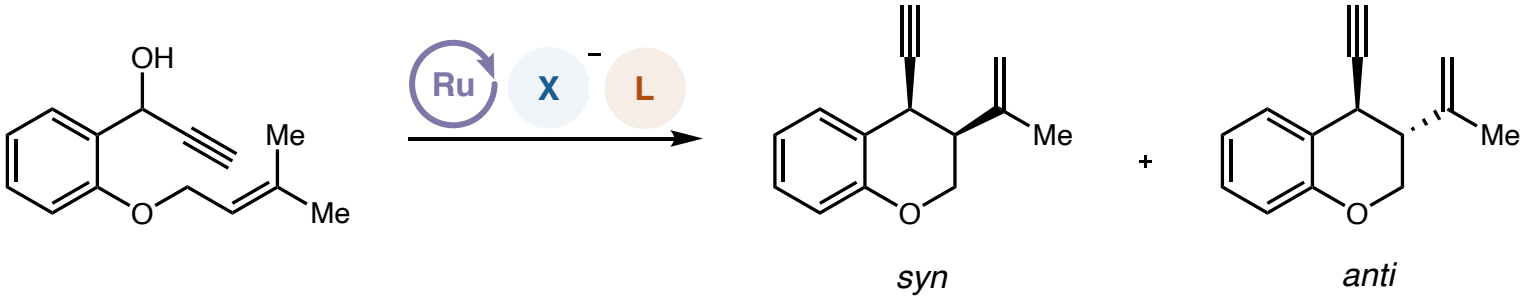
Jacobsen - Anion-Binding Catalysis



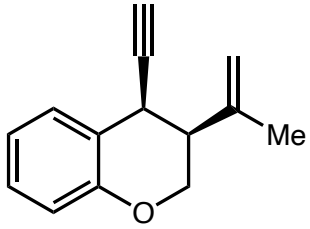
syn *anti*

Ovian, J., Vojáčková, P. & Jacobsen, E. *Nature* **2023**, *616*, 84-89

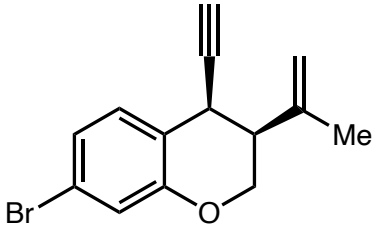
Jacobsen - Anion-Binding Catalysis



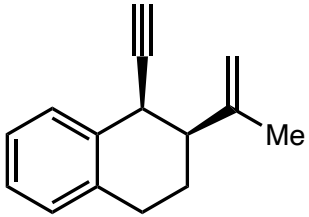
syn *anti*



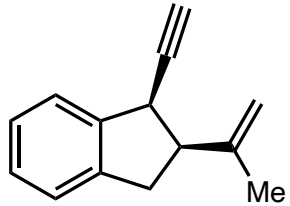
94%, 63:1 d.r.
97% ee



90%, 39:1 d.r.
97% ee



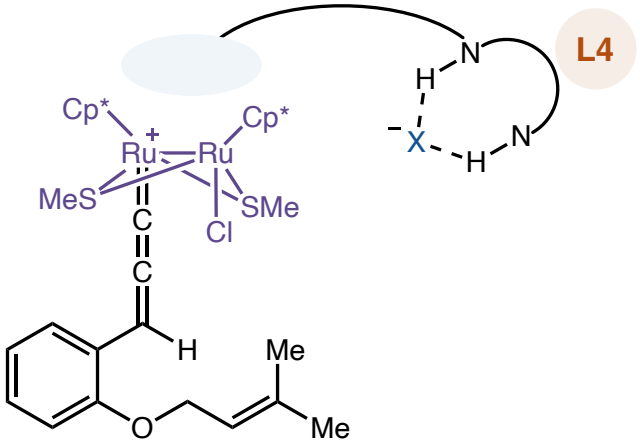
64%, 22:1 d.r.
87% ee



90%, >100:1 d.r.
98% ee

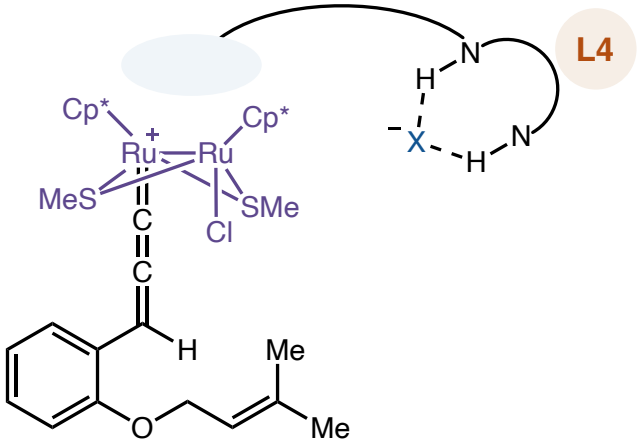
Scope shows high enantioselectivity

Ovian, J., Vojáčková, P. & Jacobsen, E. *Nature* **2023**, *616*, 84-89



Ovian, J., Vojáčková, P. & Jacobsen, E. *Nature* **2023**, *616*, 84-89

Jacobsen - Anion-Binding Catalysis

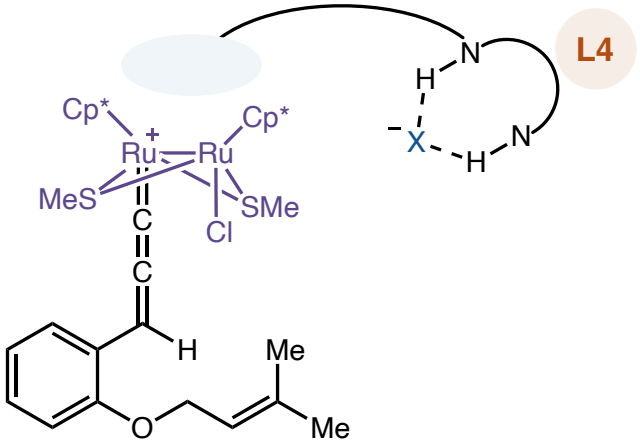


X	d.r.	e.e.%
OTs	**36:1**	**95**
OMs	**44:1**	**95**
OTf	**28:1**	**87**
PF_6	24:1	85
BF_4	12:1	75
Cl	8:1	66
$BAr^F{}_4$	**5:1**	**0**

Counterions play a role in selectivity

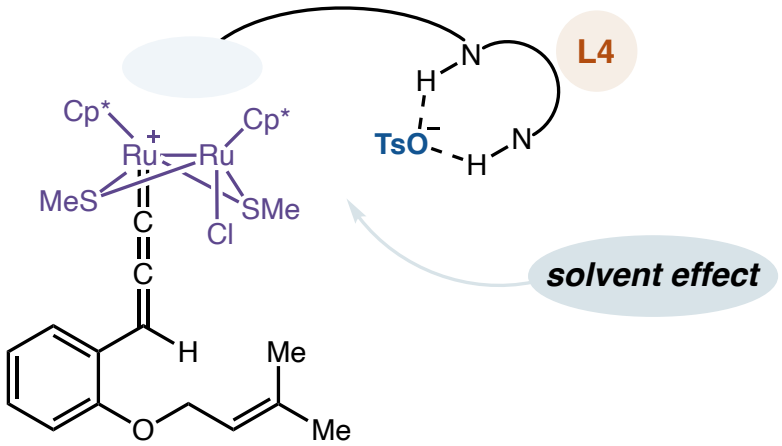
Ovian, J., Vojáčková, P. & Jacobsen, E. *Nature* **2023**, *616*, 84-89

Jacobsen - Anion-Binding Catalysis



X	d.r.	e.e.%
OTs	**36:1**	**95**
OMs	**44:1**	**95**
OTf	**28:1**	**87**
PF_6	24:1	85
BF_4	12:1	75
Cl	8:1	66
BAr^F_4	**5:1**	**0**

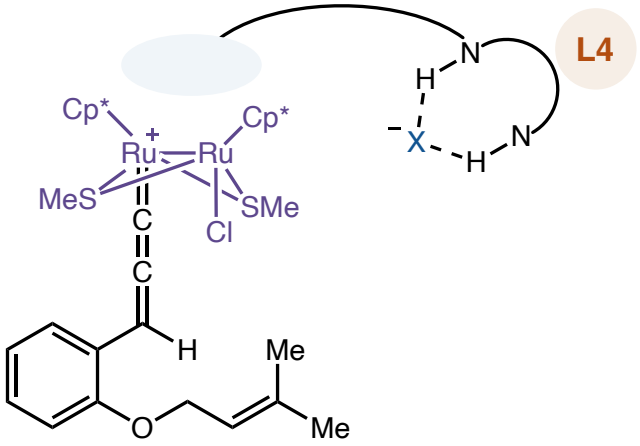
Counterions play a role in selectivity



Solvent	ε	d.r.	e.e.%
CCl_4	**2.2**	**35:1**	**95**
Benzene	**2.3**	**12:1**	**86**
Et_2O	**4.3**	**36:1**	**95**
TBME	**4.5**	**31:1**	**91**

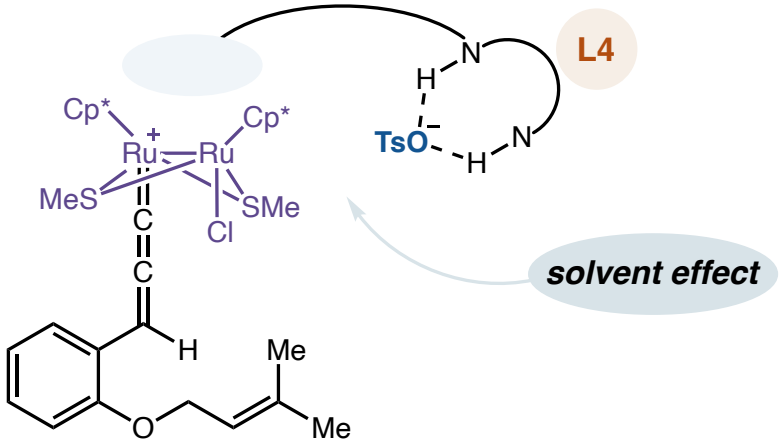
Ovian, J., Vojáčková, P. & Jacobsen, E. *Nature* **2023**, *616*, 84-89

Jacobsen - Anion-Binding Catalysis



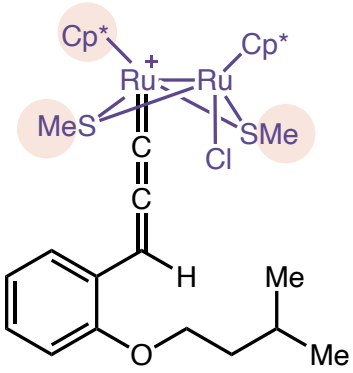
X	d.r.	e.e.%
OTs	**36:1**	**95**
OMs	**44:1**	**95**
OTf	**28:1**	**87**
PF_6	24:1	85
BF_4	12:1	75
Cl	8:1	66
BAr^F_4	**5:1**	**0**

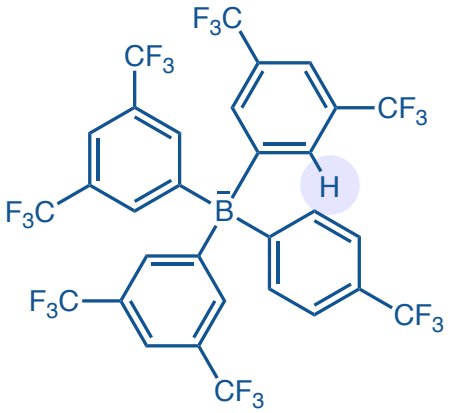
Counterions play a role in selectivity



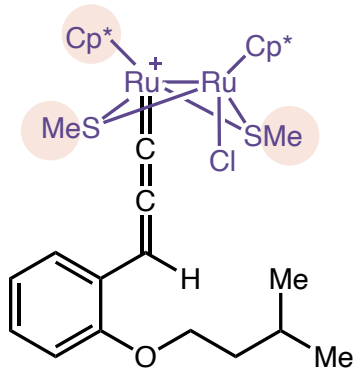
Solvent	ε	d.r.	e.e.%
CCl_4	**2.2**	**35:1**	**95**
Benzene	**2.3**	**12:1**	**86**
Et_2O	**4.3**	**36:1**	**95**
TBME	**4.5**	**31:1**	**91**
EtOAc	6.0	12:1	81
THF	7.5	6:1	63
DCM	9.1	5:1	10
1,2-DCE	10.4	4:1	8

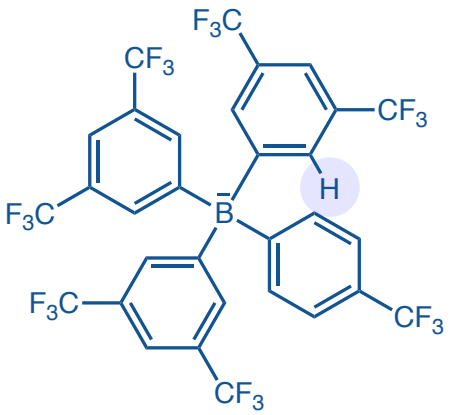
Ovian, J., Vojáčková, P. & Jacobsen, E. *Nature* **2023**, *616*, 84-89



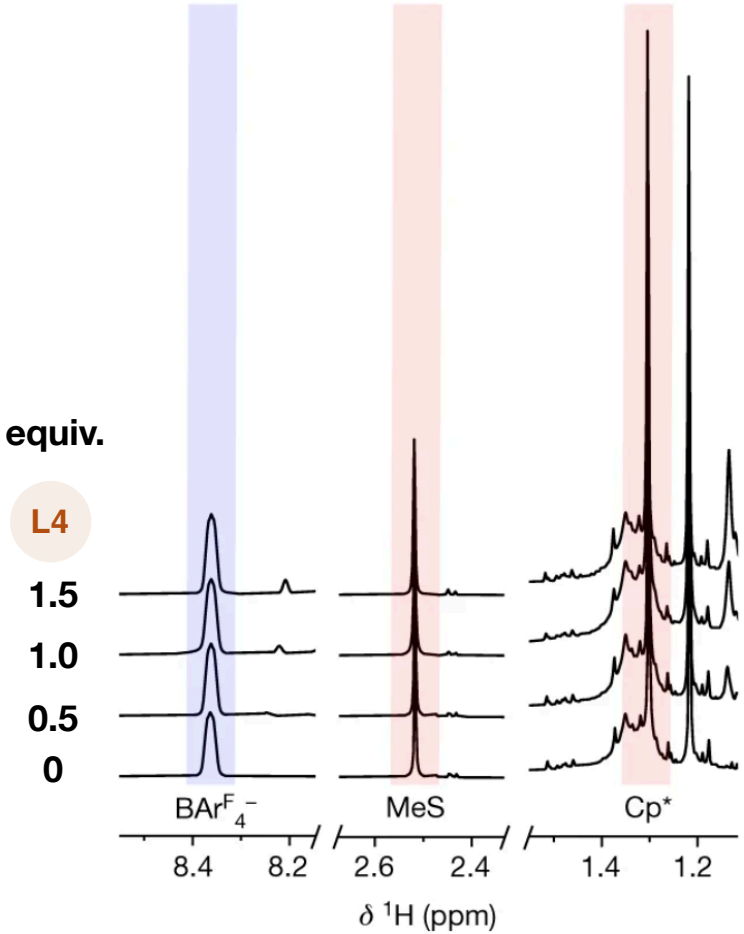


$BAr^{F}_{4}{}^{-}$

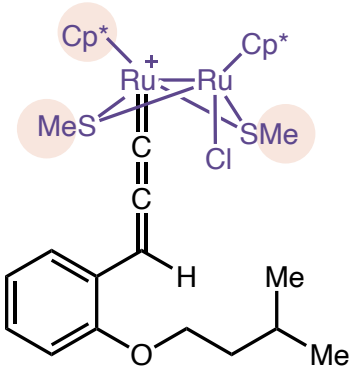

Cp*
Ru
Ru
Cp*
MeS
SMe
Cl
C
C
H
Me
O
Me

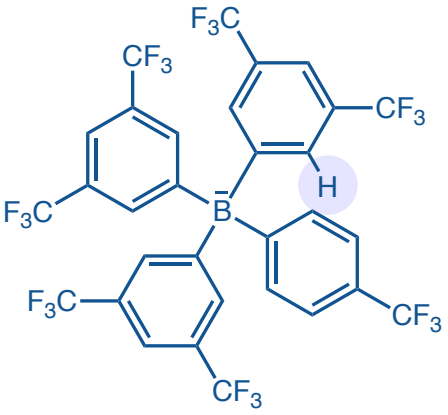

F3C
CF3
CF3
H
F3C
B
F3C
CF3
CF3

$BAr^{F}_{4}^{-}$

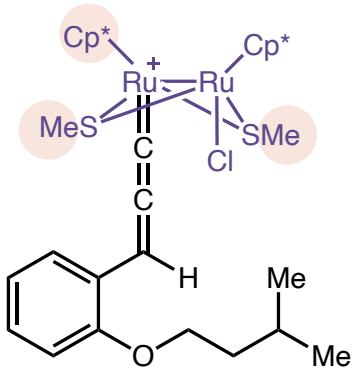

equiv.
L4
1.5
1.0
0.5
0
BArF4−
MeS
Cp*
8.4
8.2
2.6
2.4
1.4
1.2
δ 1H (ppm)

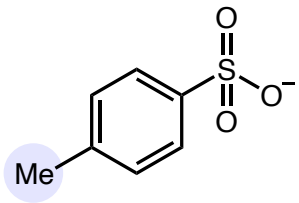
Jacobsen - Anion-Binding Catalysis

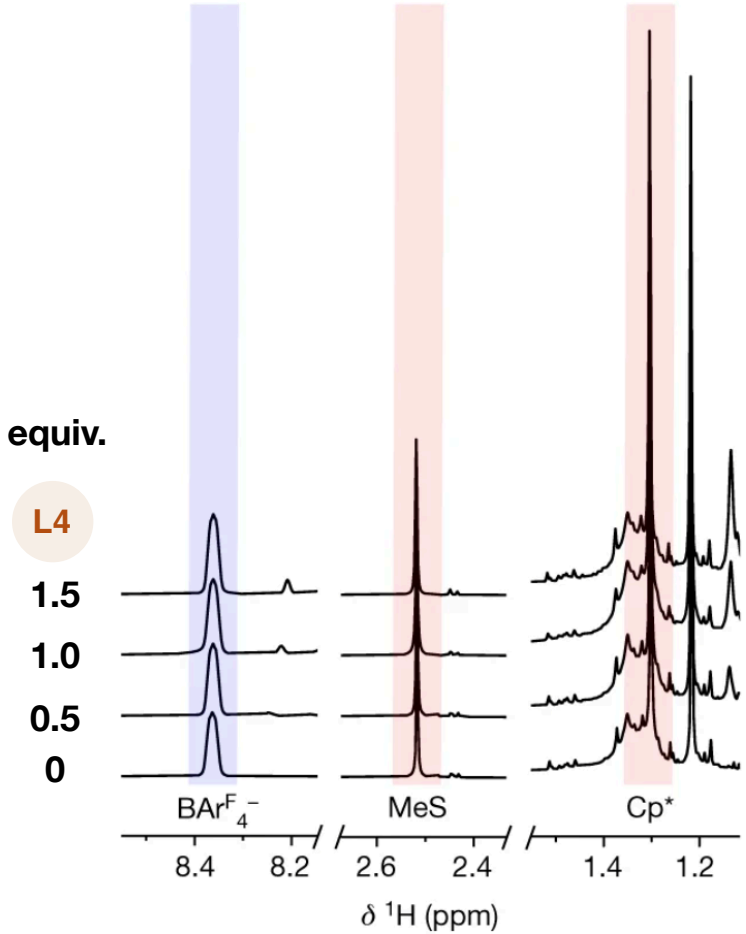


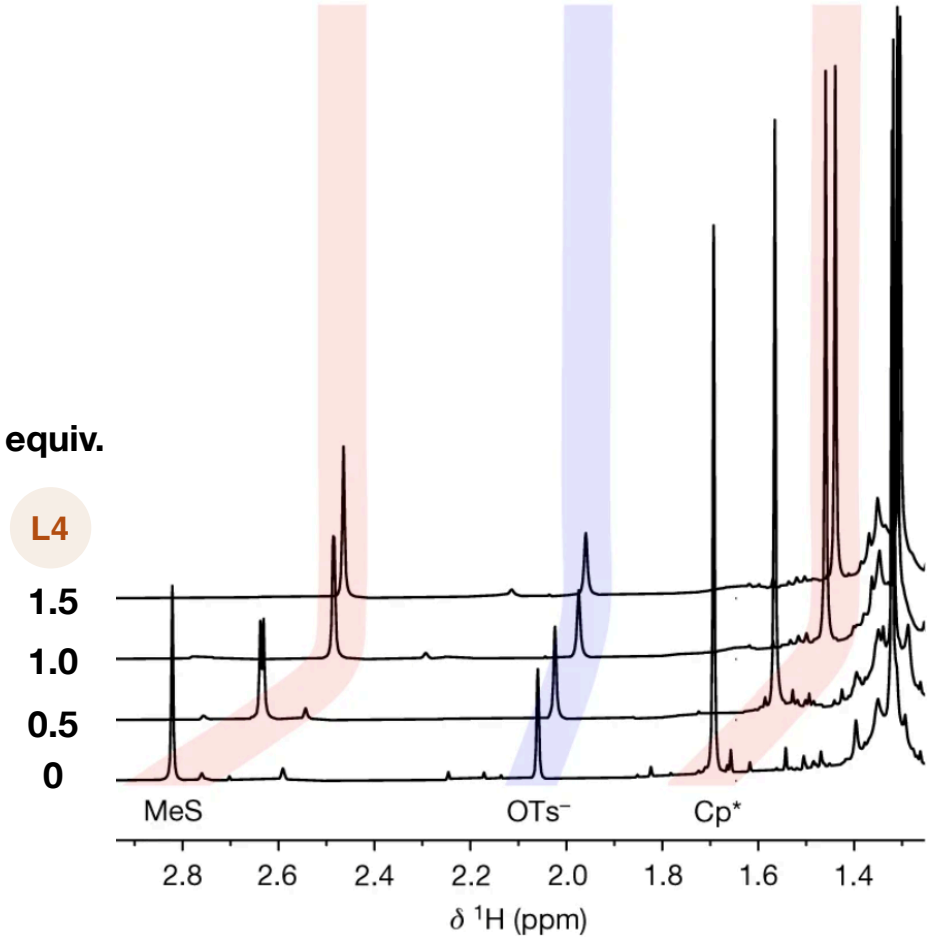


$BAr^F_4^-$









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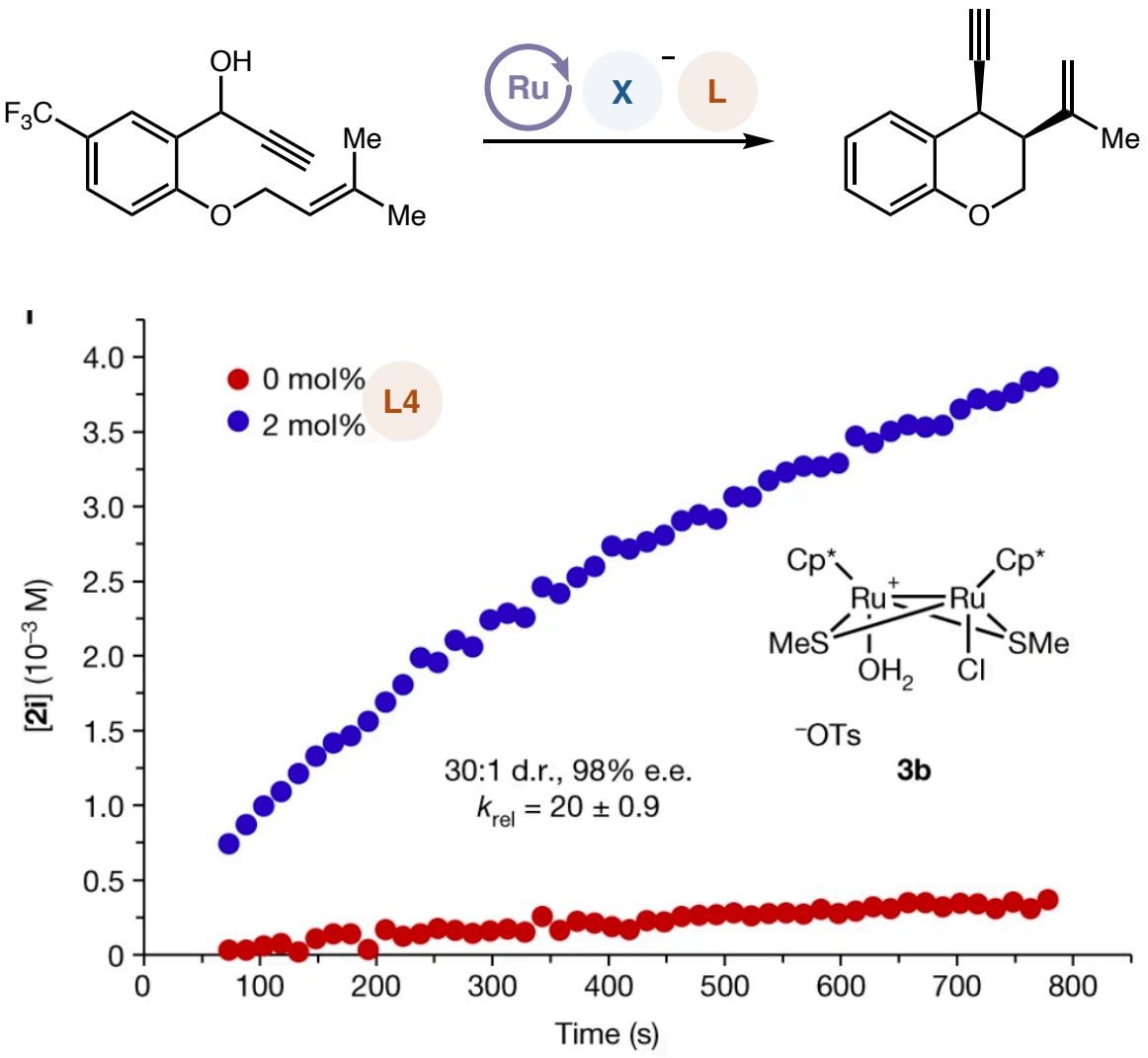
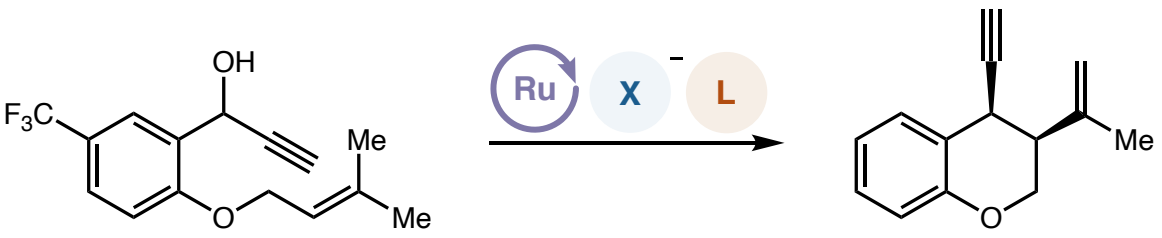
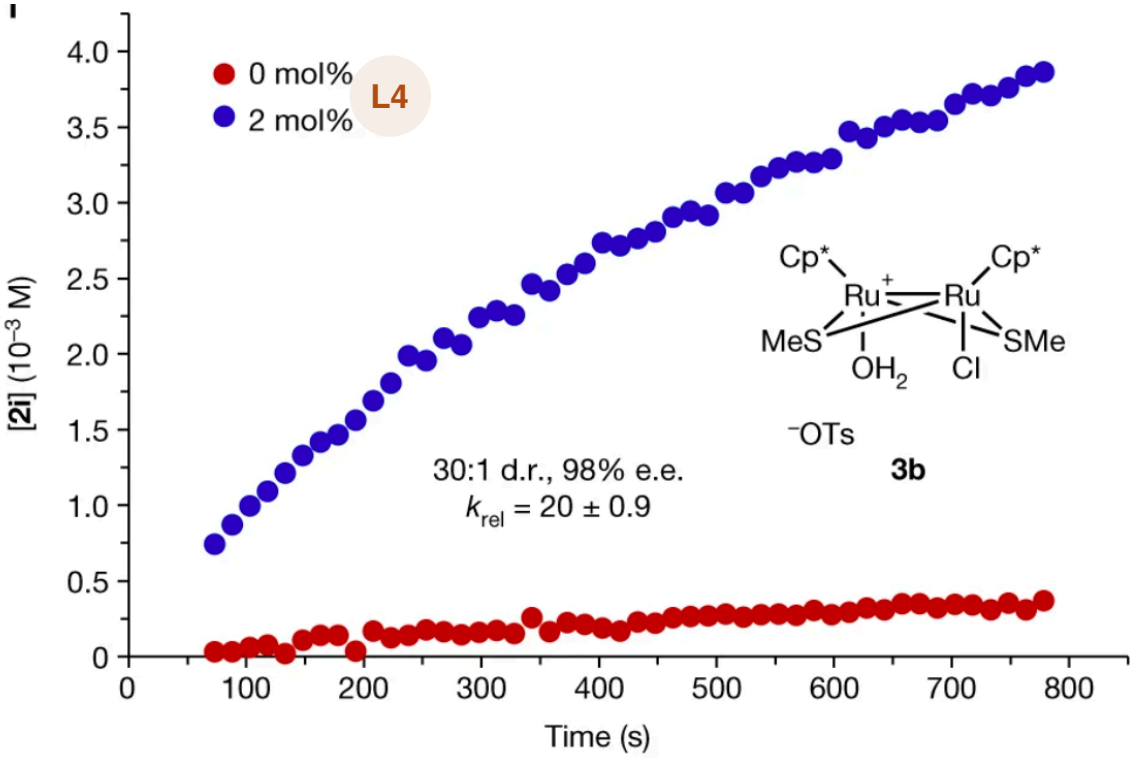


Ovian, J., Vojáčková, P. & Jacobsen, E. *Nature* **2023**, *616*, 84-89

Jacobsen - Anion-Binding Catalysis





Ligand increases rate 20x

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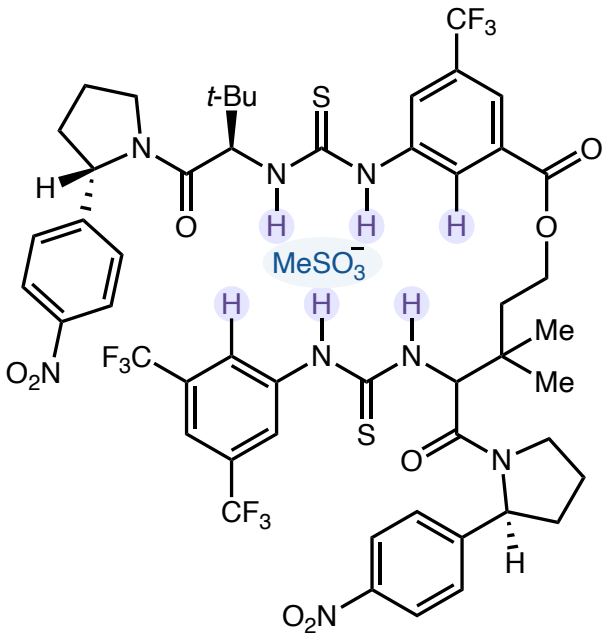
Jacobsen - Anion-Binding Catalysis



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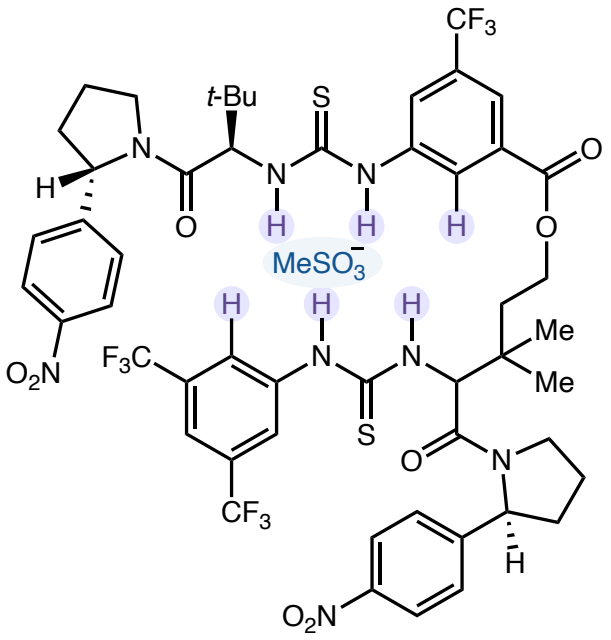

ROESY - Ion-pairing contacts

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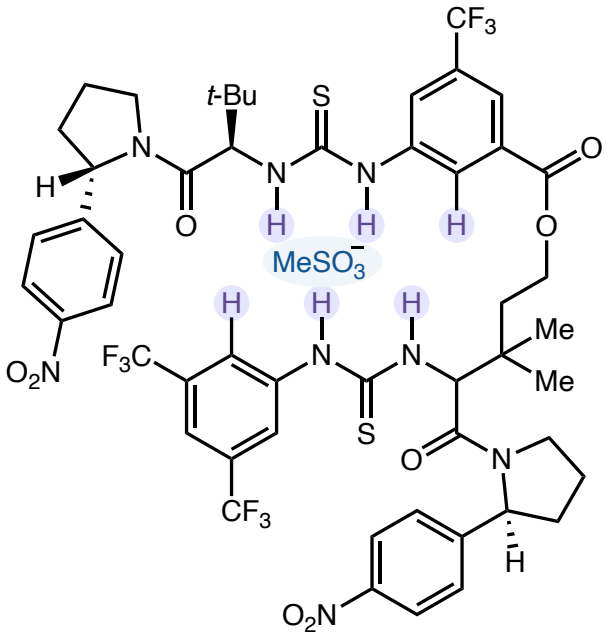
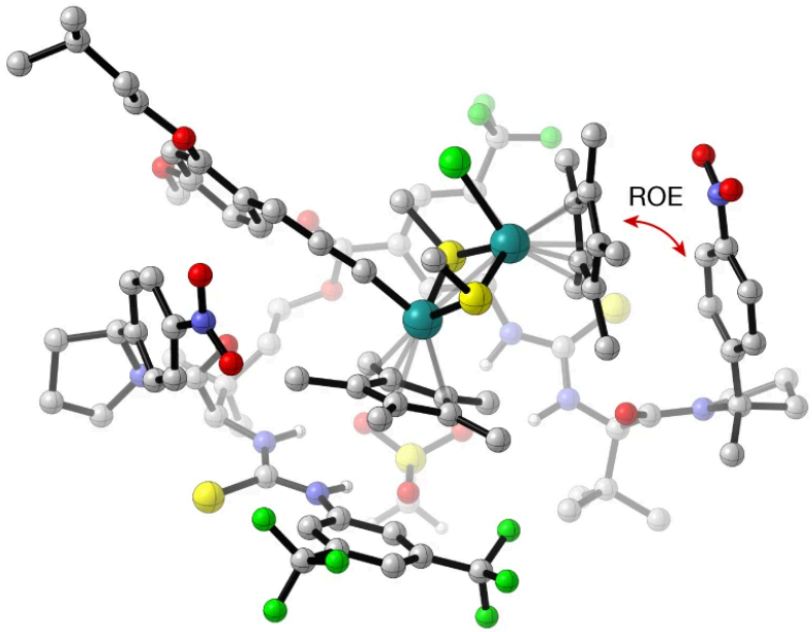
Jacobsen - Anion-Binding Catalysis





ROESY - Ion-pairing contacts

ROESY shows attractive interaction between Aryl and Cp* ligand

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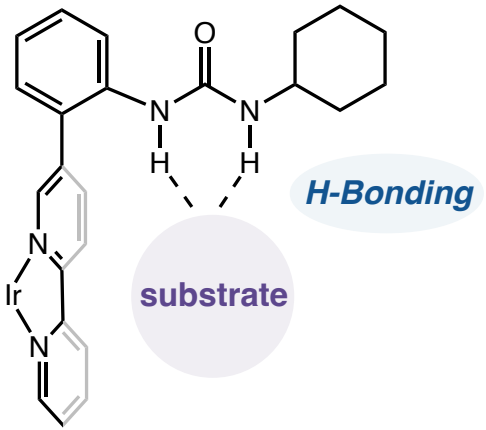
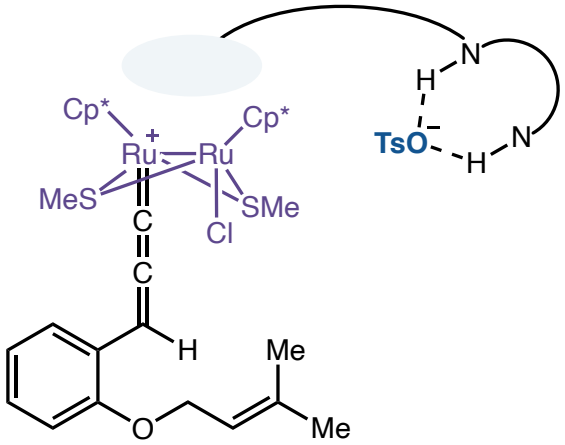
Conclusion

Conclusion

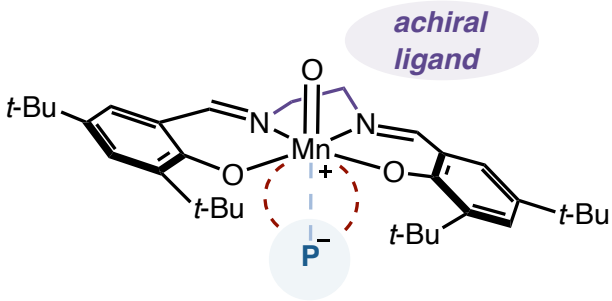
Hydrogen-bonding



Ion-pairing & H-Bonding

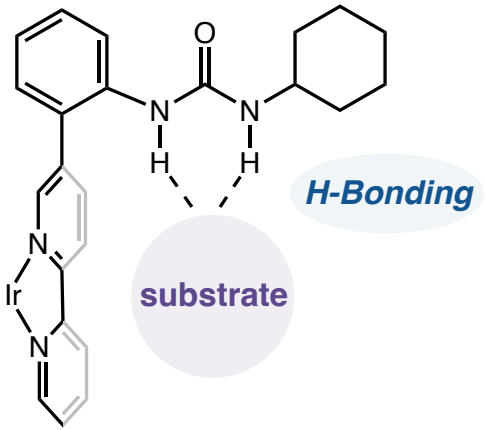


Ion-pairing

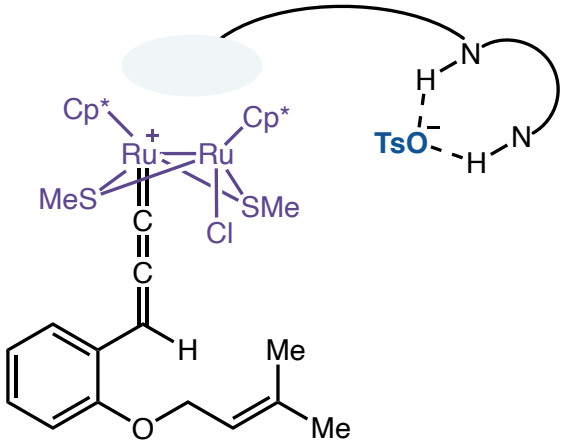


Conclusion

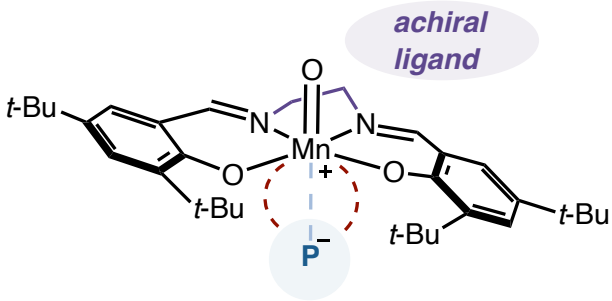
Hydrogen-bonding



Ion-pairing & H-Bonding



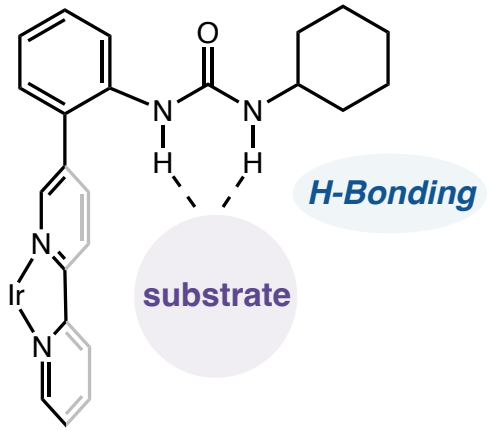
Ion-pairing



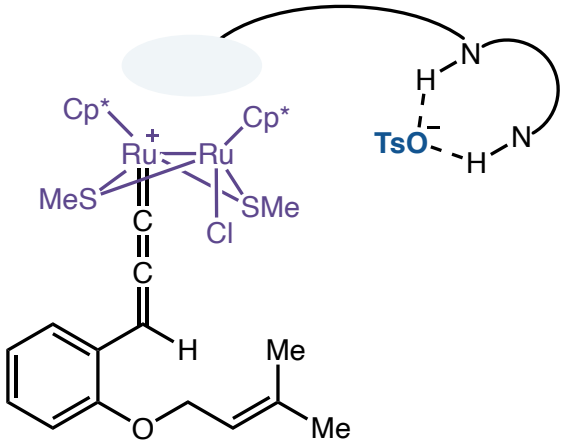
Strategy possesses potential for promoting reactivity and achieving selectivity

Conclusion

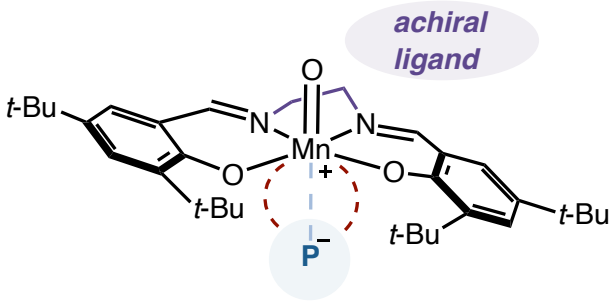
Hydrogen-bonding



Ion-pairing & H-Bonding



Ion-pairing

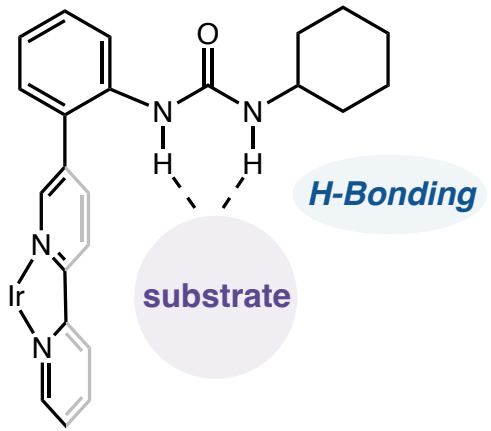


Strategy possesses potential for promoting reactivity and achieving selectivity

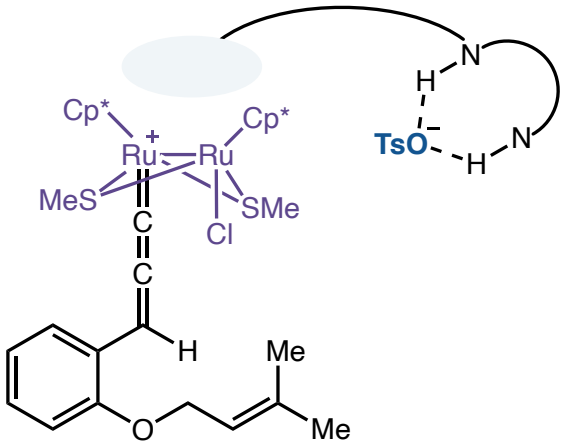
Methods are highly specific, lacking generality

Conclusion

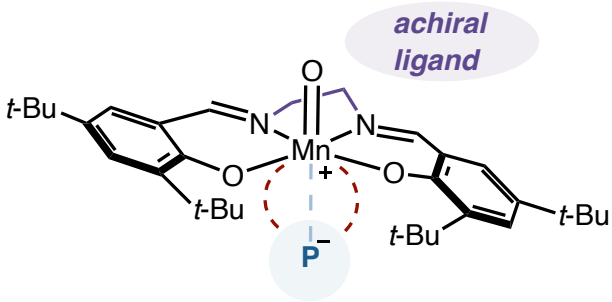
Hydrogen-bonding



Ion-pairing & H-Bonding



Ion-pairing



Strategy possesses potential for promoting reactivity and achieving selectivity

Methods are highly specific, lacking generality

Curious lack of Metallaphotoredox methods utilizing these interactions for selective catalysis

Thanks