Chiral Phosphoric Acids as Catalysts

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DCB Group Renaud
Universität Bern

Topic Review
04/12/2014

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- Imine as substrate
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Generalities

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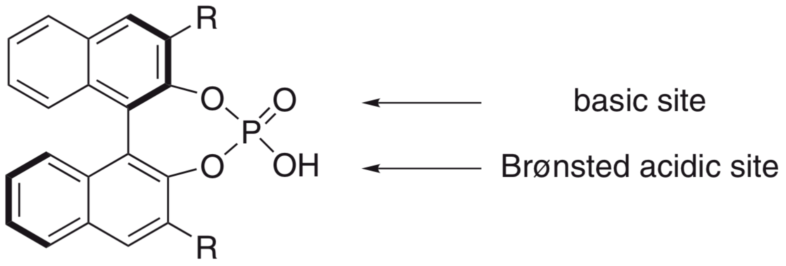
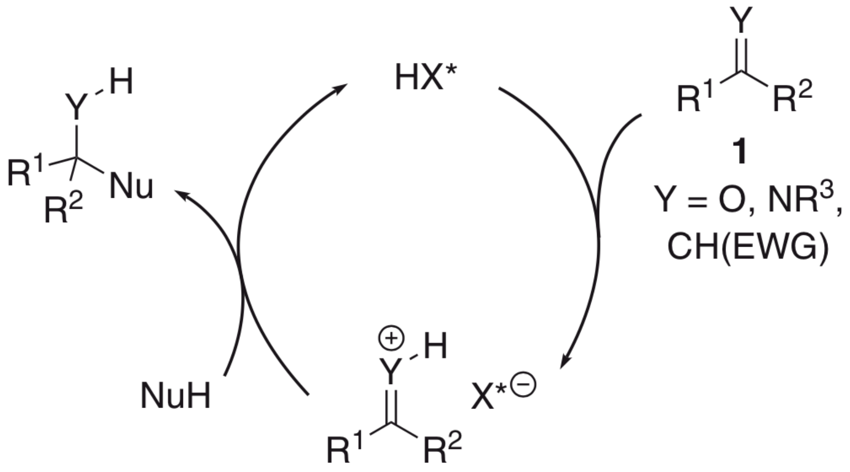
- Many different types of organocatalyst for bronsted acid catalysis (cf. Josephine's topic review last month)
  - Thioureas
  - TADDOL
  - BINOL
  - ….
- Beginning of 2000 : Focus on Chiral Phosphoric Acids



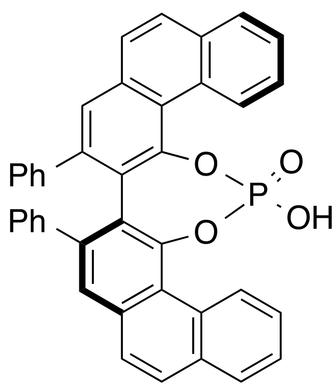
Generalities

> Mechanism

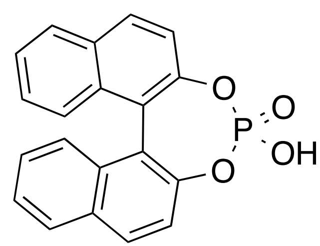


Generalities

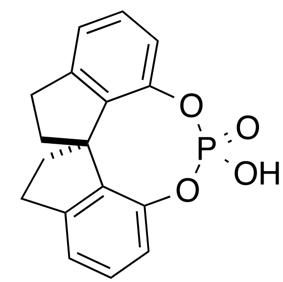
> Lower pKa → new scope of substrate



pKa = 1.98



pKa = 3.37



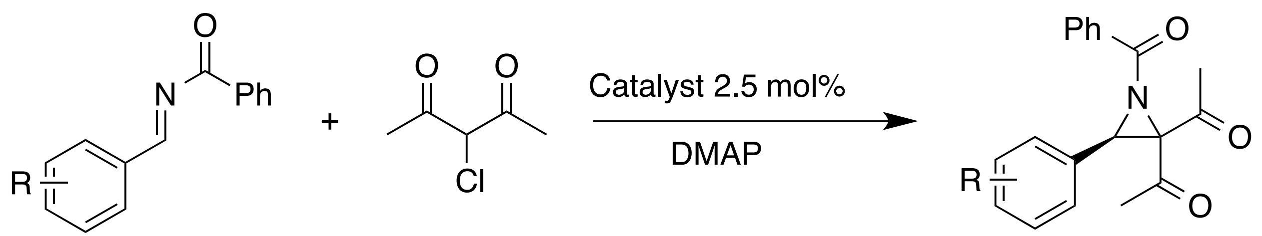
pKa = 4.20

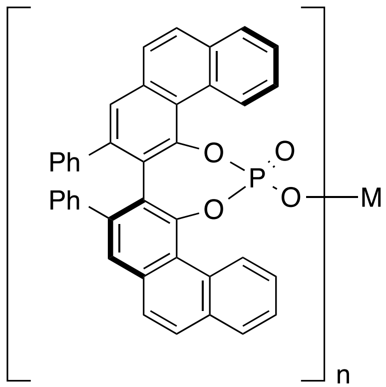
Yang, C.; Xue, X.-S.; Jin, J.-L.; Li, X.; Cheng, J.-P. *J. Org. Chem.* **2013**, *78*, 7076.

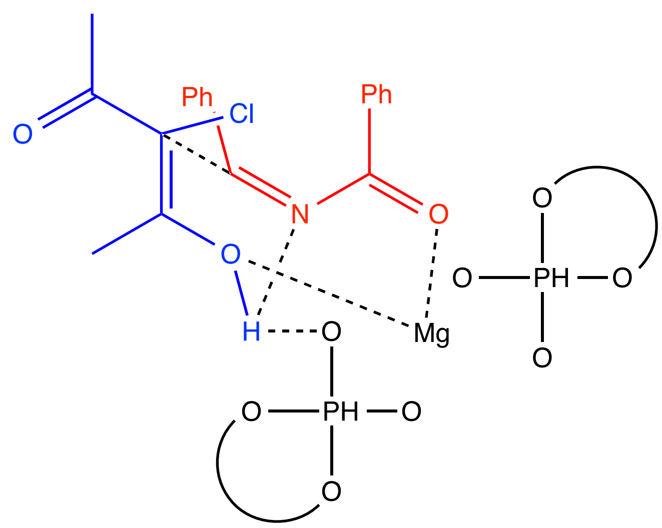
Imine as substrate

Imine as substrate

> Aziridine Formation



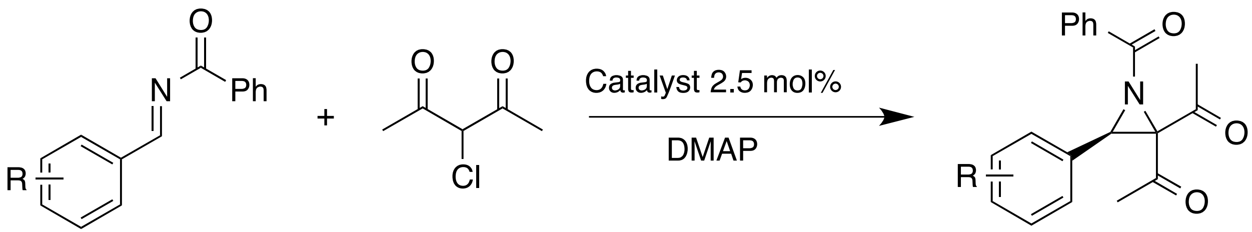


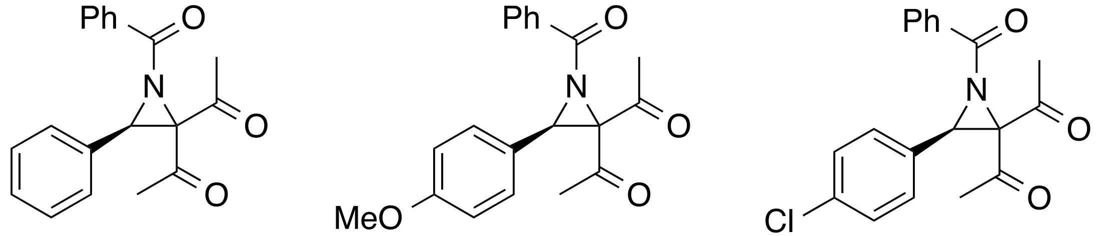


Larson, S. E.; Li, G.; Rowland, G. B.; Junge, D.; Huang, R.; Woodcock, H. L.; Antilla, J. C. *Org. Lett.* **2011**, *13*, 2188.

Imine as substrate

> Aziridine Formation



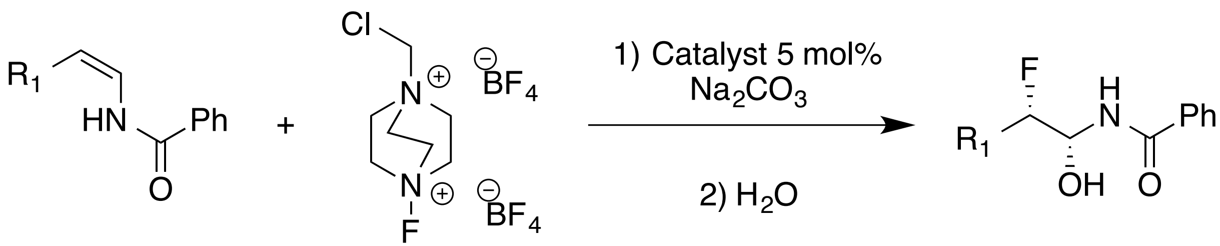


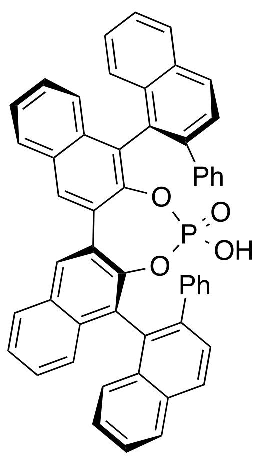
53%	71%	62%
ee 88%	ee 90%	ee 89%

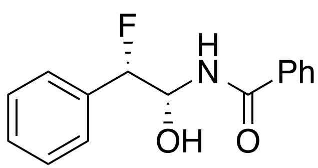
Larson, S. E.; Li, G.; Rowland, G. B.; Junge, D.; Huang, R.; Woodcock, H. L.; Antilla, J. C. *Org. Lett.* **2011**, *13*, 2188.

Imine as substrate

> Oxyfluorination







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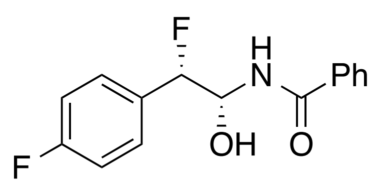

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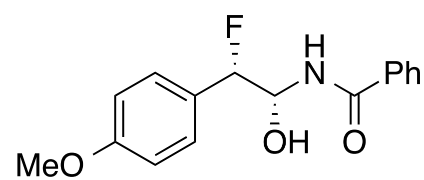
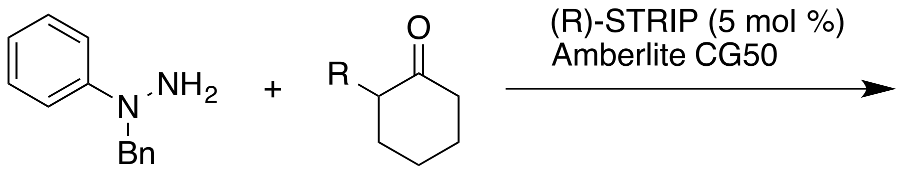


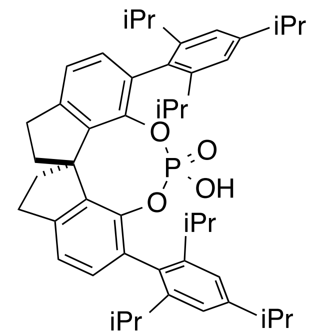
59%
ee 70%

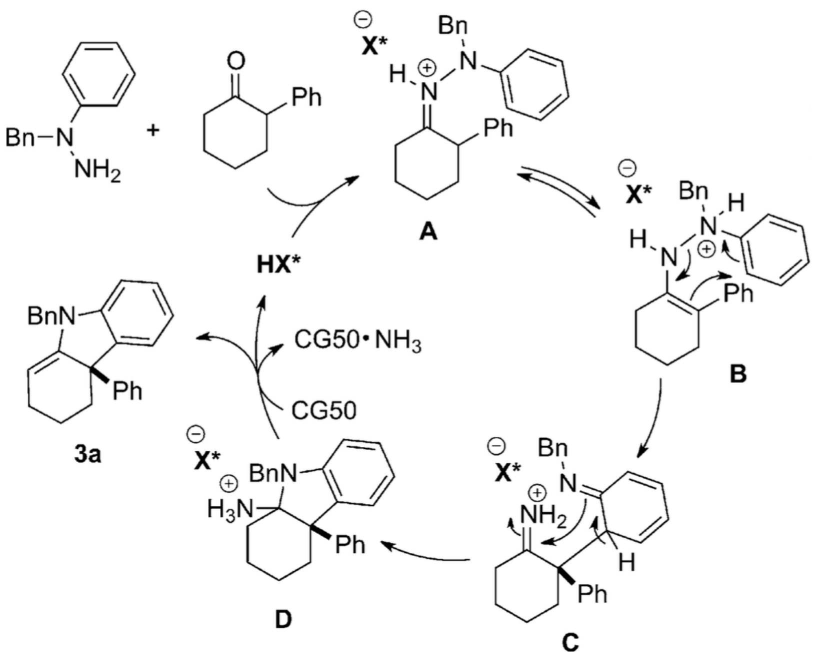
Honjo, T.; Phipps, R. J.; Rauniyar, V.; Toste, F. D. *Angew. Chem. Int. Ed. Engl.* **2012**, *51*, 9684.

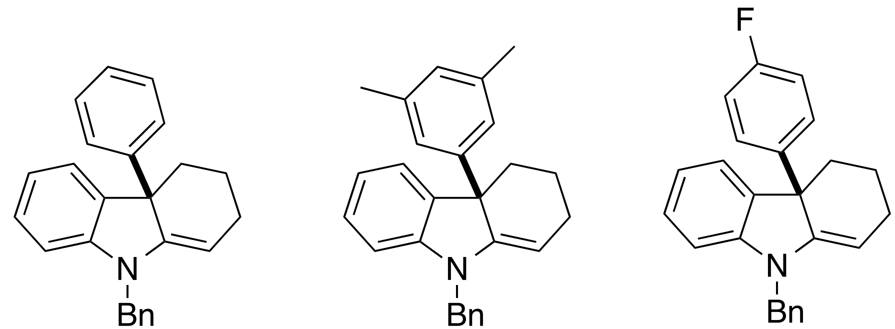
Imine as substrate

- Fischer indole









98%
ee 94.5:5.5

96%
ee 94.5:5.5

98%
ee 95.5:4.5

Martínez, A.; Webber, M. J.; Müller, S.; List, B. *Angew. Chem. Int. Ed. Engl.* **2013**, *52*, 9486.

Imine as substrate

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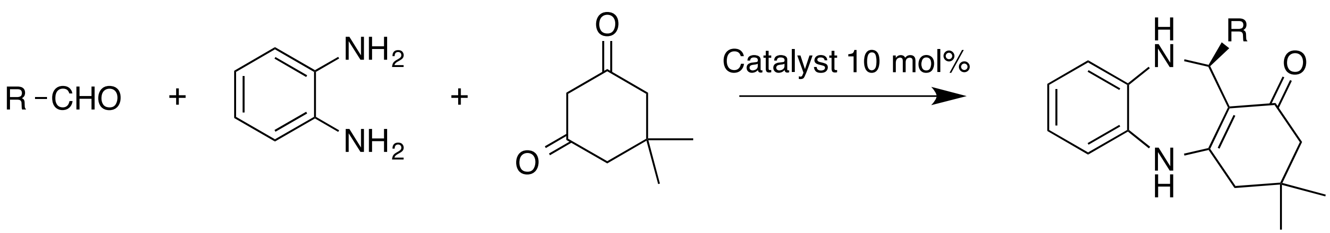
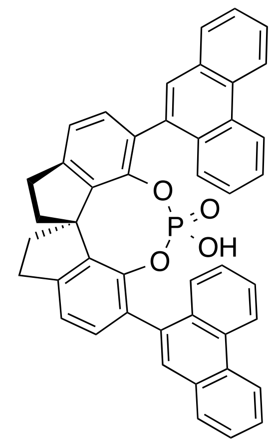
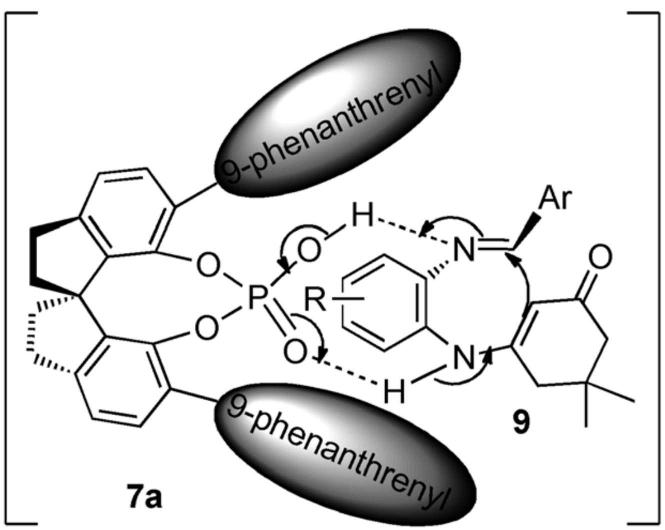
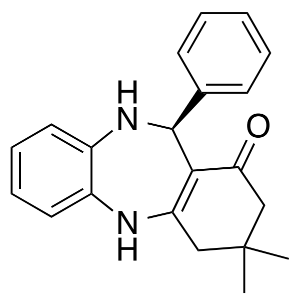
> Diazepine formation









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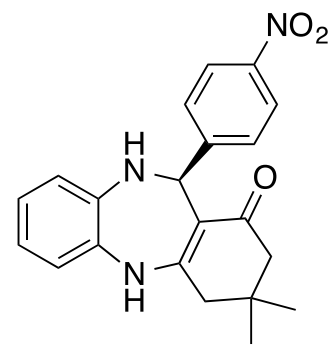

85%
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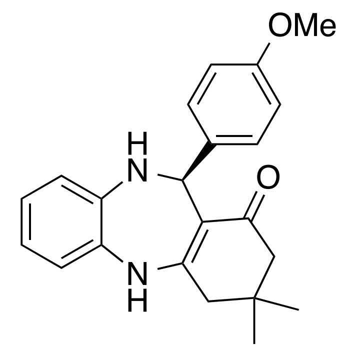
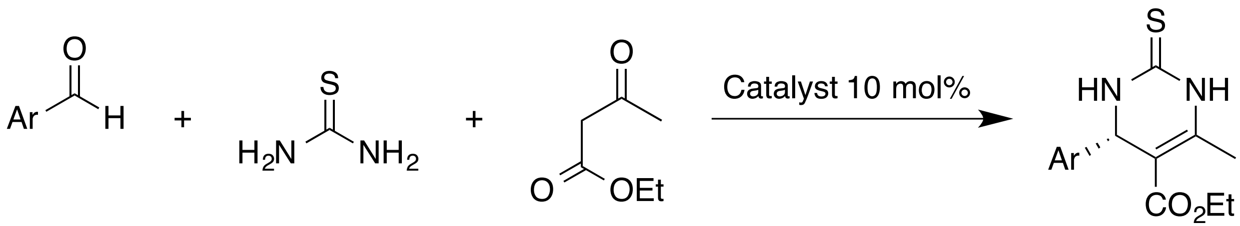


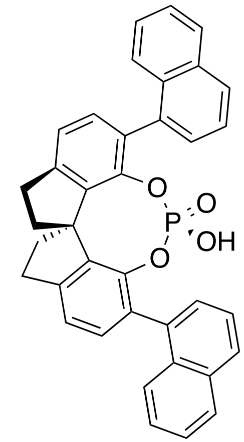
61%
ee 91:9

Wang, Y.; Tu, M. S.; Shi, F.; Tu, S. J. *Adv. Synth. Catal.* **2014**, *356*, 2009.

Imine as substrate

> Biginelli





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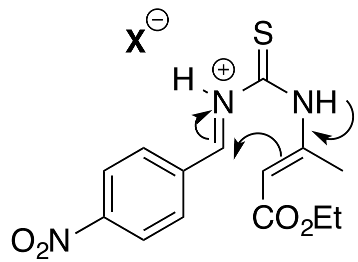

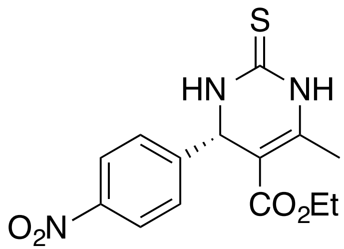

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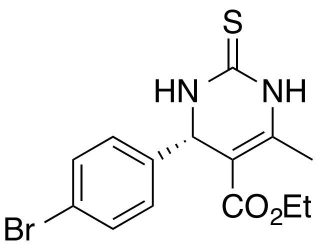

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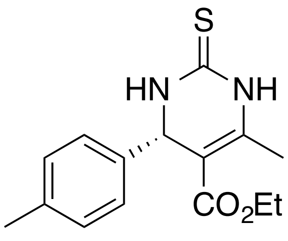
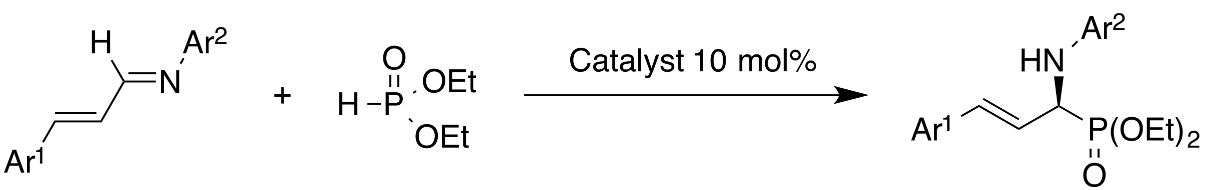


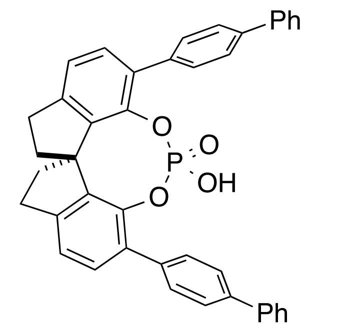
96%
ee 91%

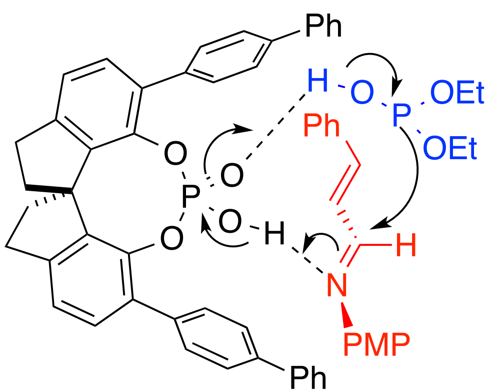
Xu, F.; Huang, D.; Lin, X.; Wang, Y. *Org. Biomol. Chem.* **2012**, *10*, 4467.

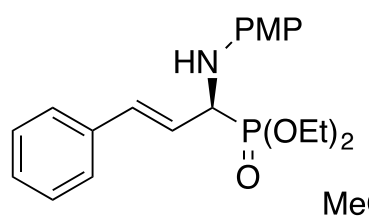
Imine as substrate

> Hydrophosphonylation









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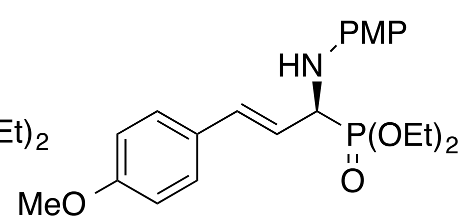

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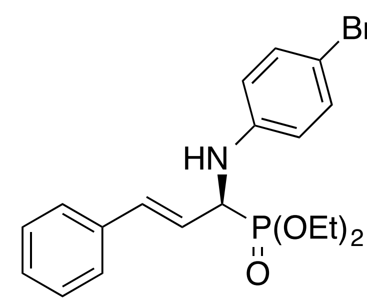


85%
ee 88%

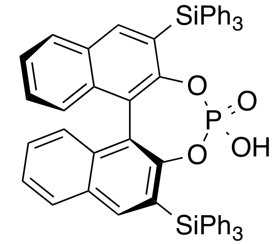
Zhao, Y.; Li, X.; Mo, F.; Li, L.; Lin, X. *RSC Advances* **2013**, *3*, 11895.

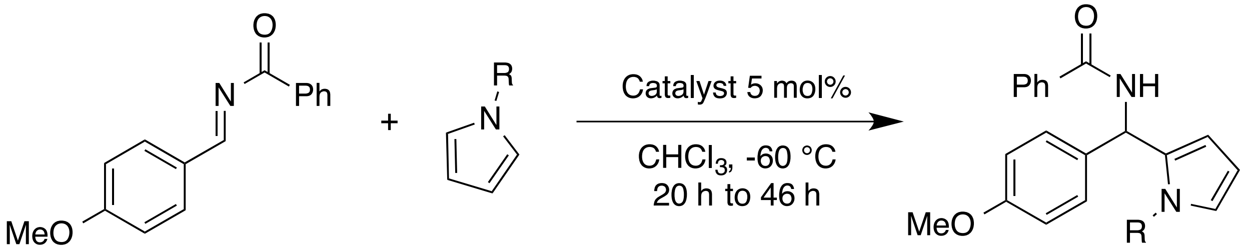
Imine as substrate

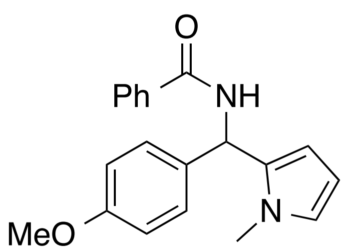
Aromatic electrophilic substitution

Imine as substrate

> Friedel-Crafts







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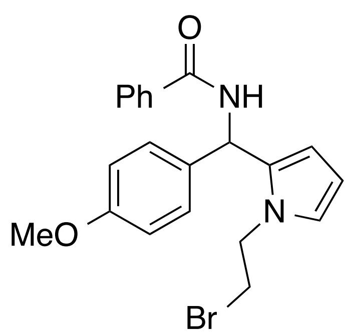

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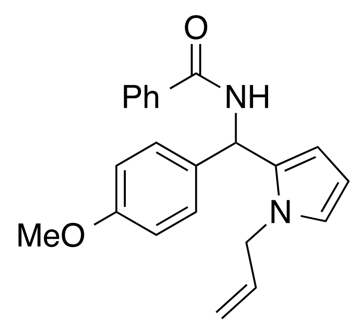
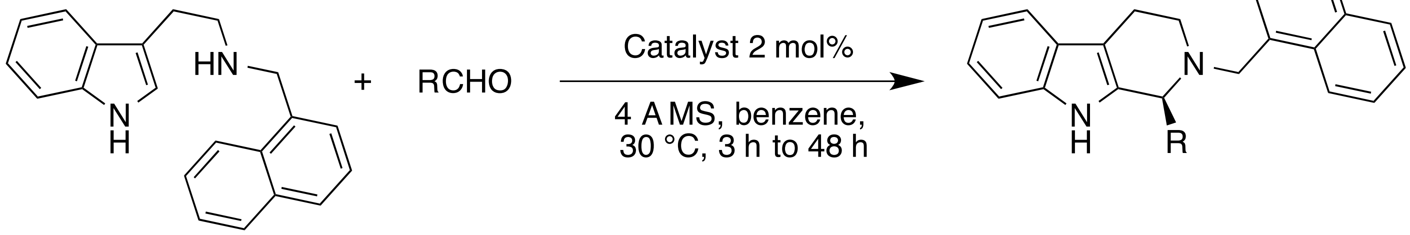


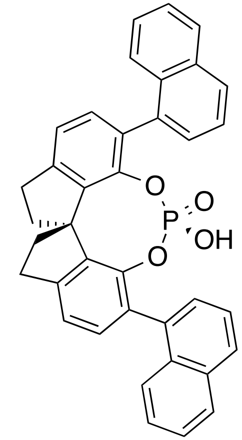
66%
ee 91%

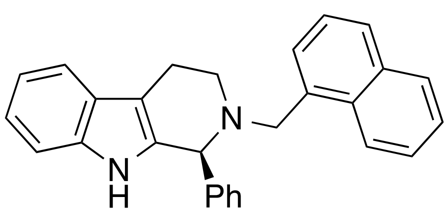
Li, G.; Rowland, G. B.; Rowland, E. B.; Antilla, J. C. *Org. Lett.* **2007**, *9*, 4065.

Imine as substrate

> Pictet Spengler







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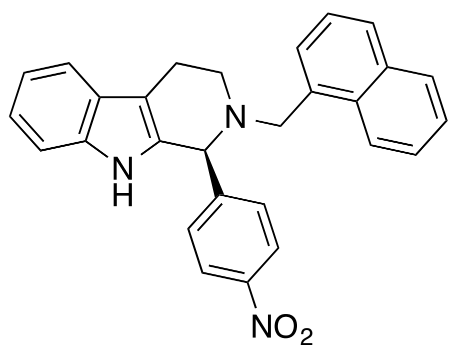
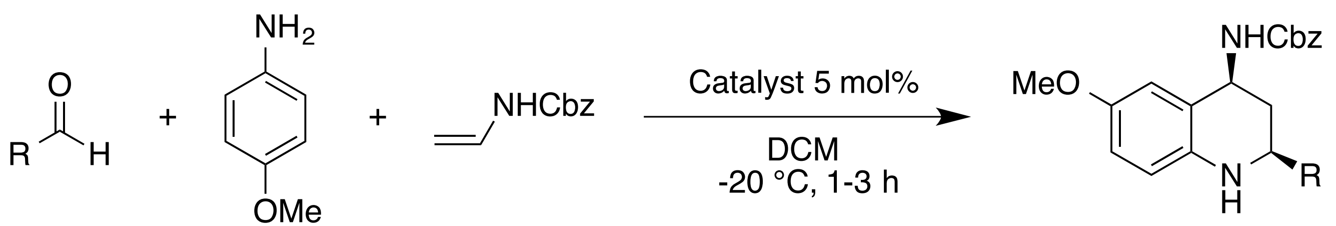


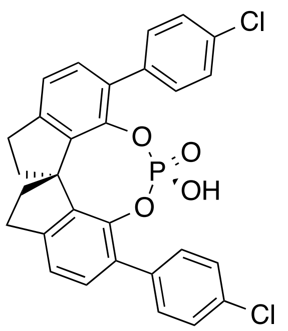
99%
ee 96%

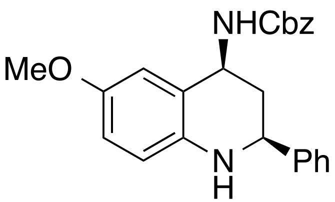
Huang, D.; Xu, F.; Lin, X.; Wang, Y. *Chemistry* **2012**, *18*, 3148.

Imine as substrate

> Povarov reaction







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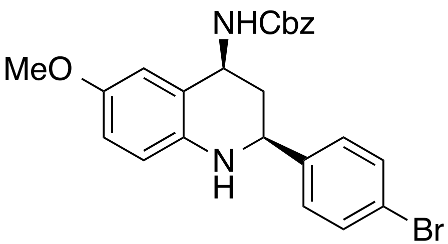

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Huang, D.; Xu, F.; Chen, T.; Wang, Y.; Lin, X. *RSC Advances* **2013**, *3*, 573.

Imine as substrate

Cycloaddition

Imine as substrate

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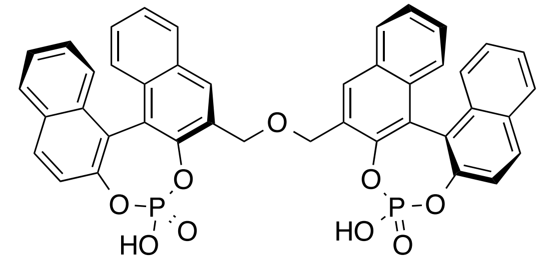
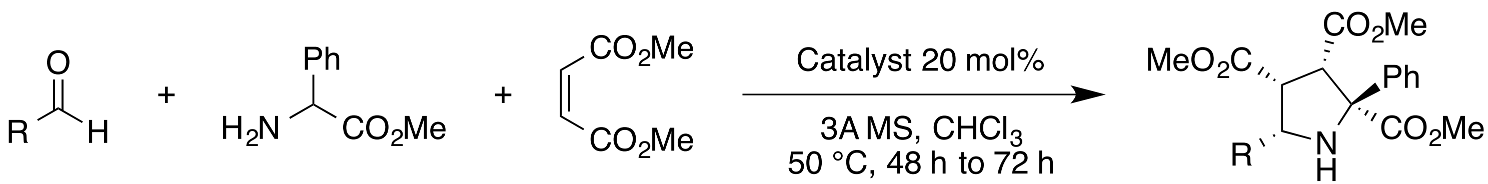
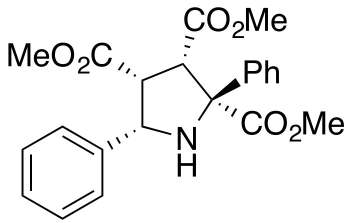
> 1,3 Dipolar







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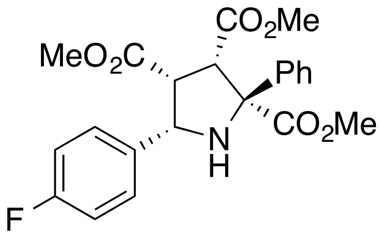

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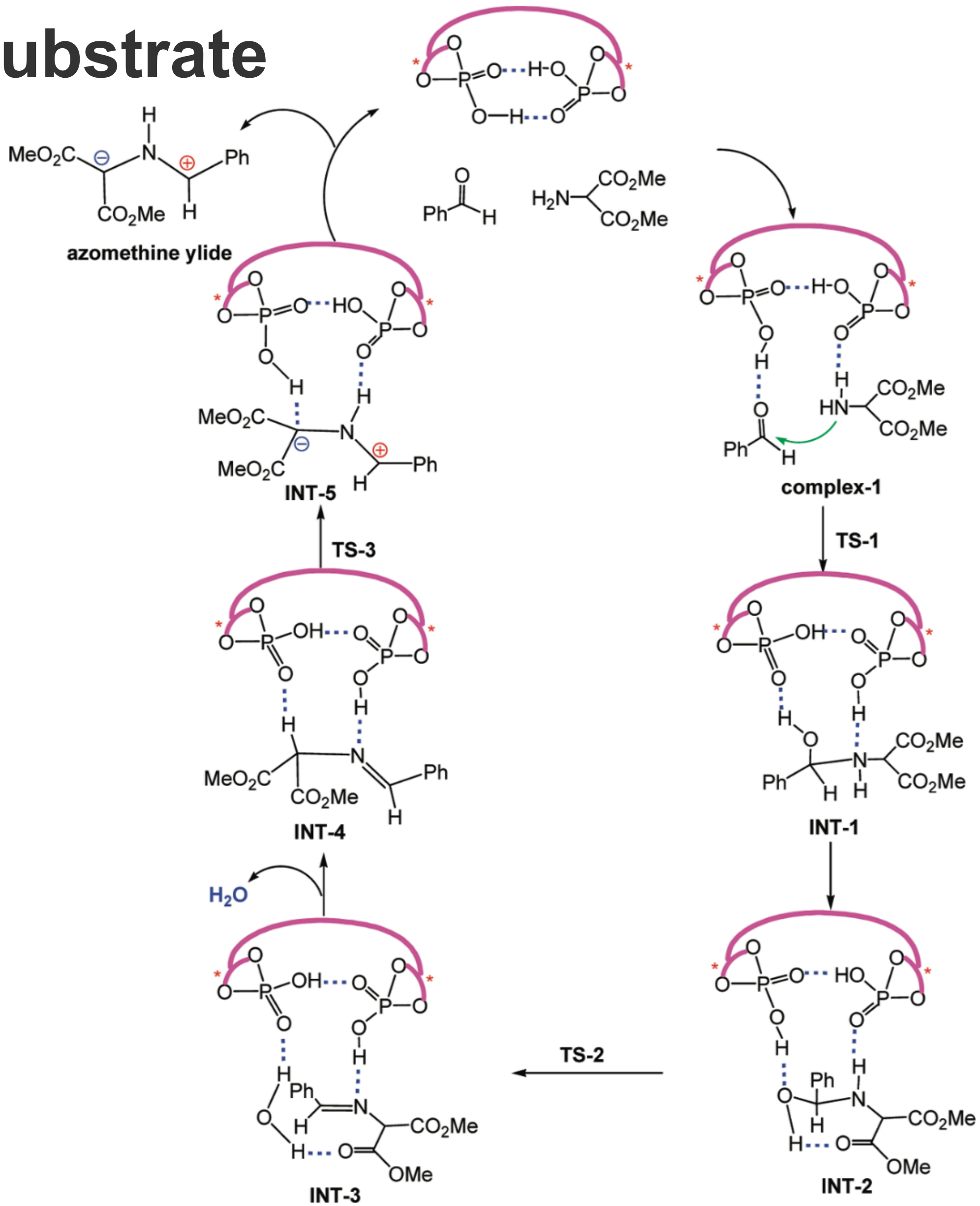
He, L.; Chen, X.-H.; Wang, D.-N.; Luo, S.-W.; Zhang, W.-Q.; Yu, J.; Ren, L.; Gong, L.-Z. *J. Am. Chem. Soc.* **2011**, *133*, 13504.

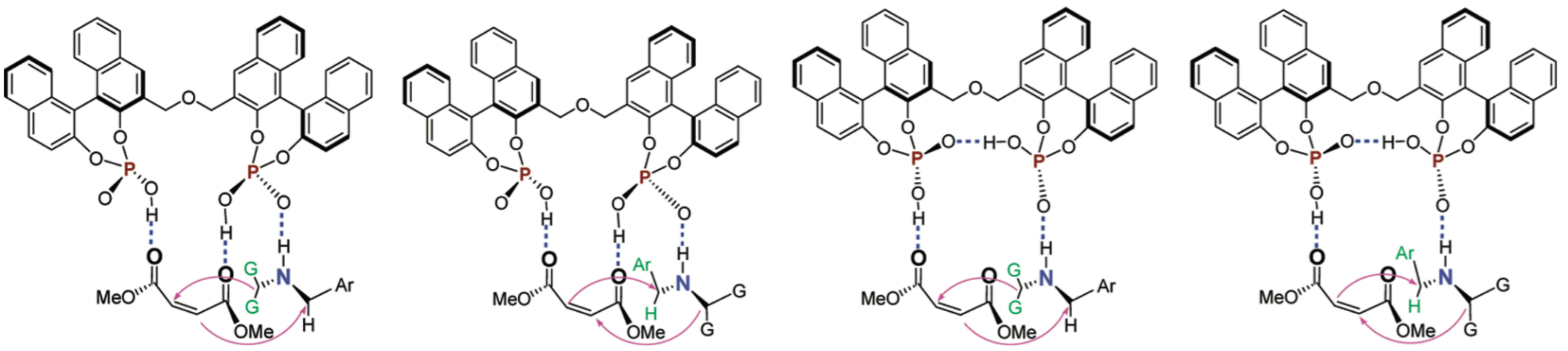
Imine as substrate



He, L.; Chen, X.-H.; Wang, D.-N.; Luo, S.-W.; Zhang, W.-Q.; Yu, J.; Ren, L.; Gong, L.-Z. *J. Am. Chem. Soc.* **2011**, *133*, 13504.

Imine as substrate

> 1,3 Dipolar

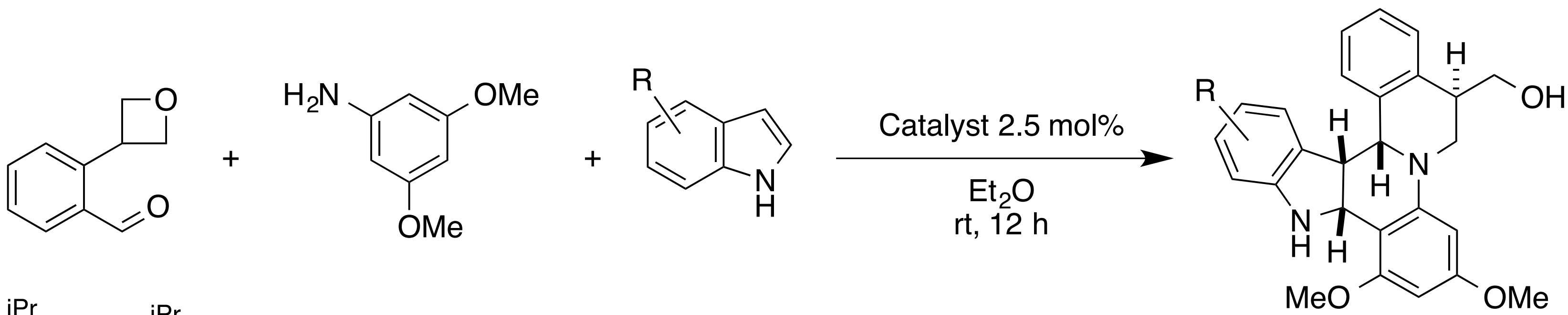


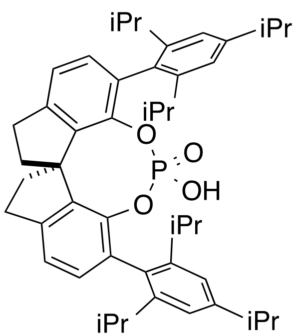
Model-I-Mi Model-I-Ma Model-II-Mi Model-II-Ma

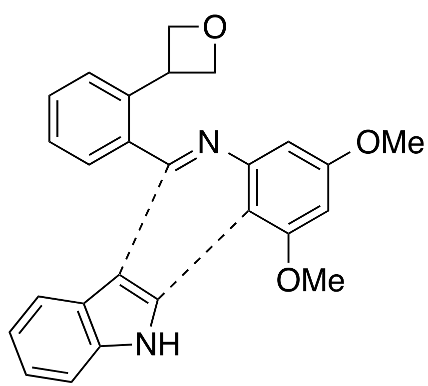
He, L.; Chen, X.-H.; Wang, D.-N.; Luo, S.-W.; Zhang, W.-Q.; Yu, J.; Ren, L.; Gong, L.-Z. *J. Am. Chem. Soc.* **2011**, *133*, 13504.

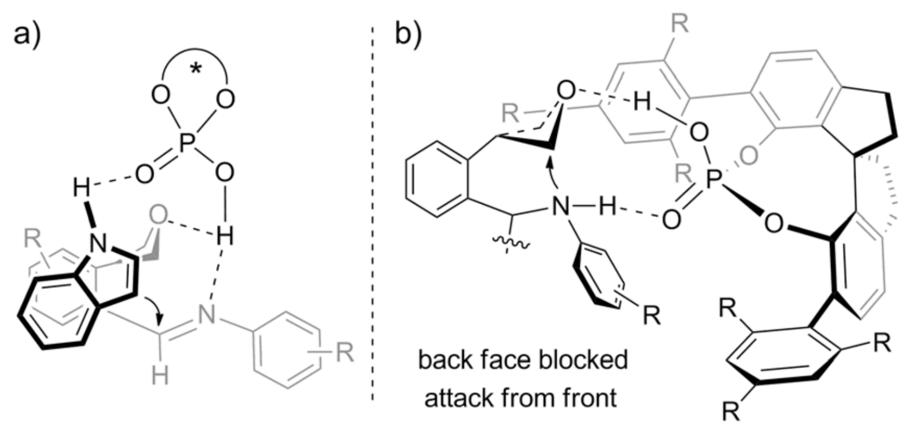
Imine as substrate

> Aza Diels Alder









Chen, Z.; Wang, B.; Wang, Z.; Zhu, G.; Sun, J. *Angew. Chem. Int. Ed. Engl.* **2013**, *52*, 2027.

Imine as substrate

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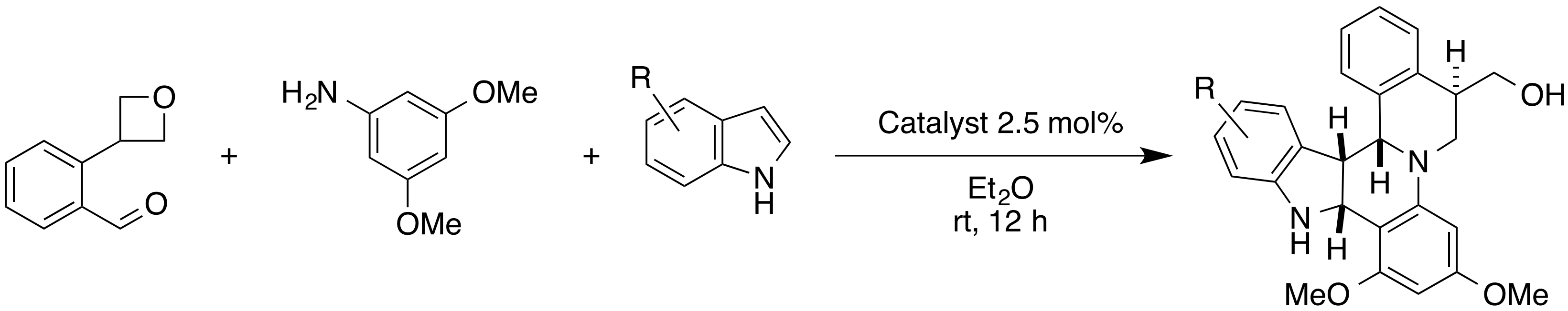
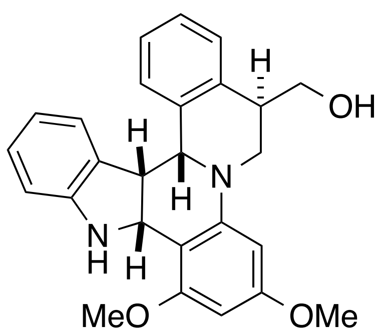
> Aza Diels Alder





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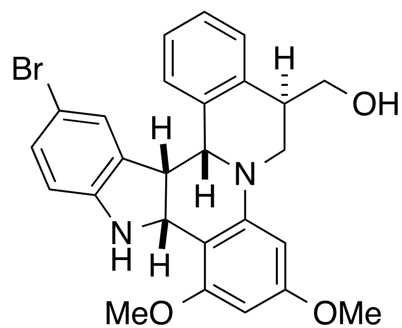
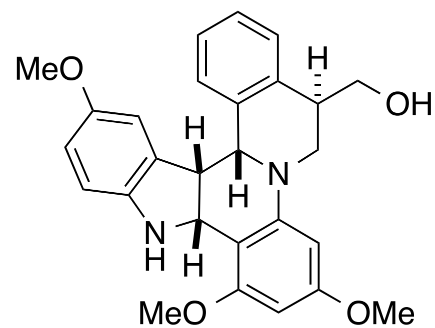


76%
dr 9:1
ee 86%



82%
dr 99:1
ee 96%

Chen, Z.; Wang, B.; Wang, Z.; Zhu, G.; Sun, J. *Angew. Chem. Int. Ed. Engl.* **2013**, *52*, 2027.

Imine as substrate

Reduction

Imine as substrate

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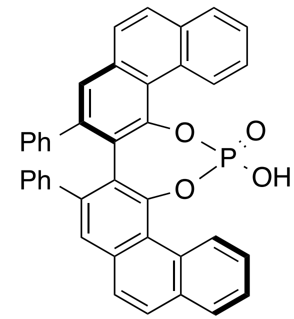
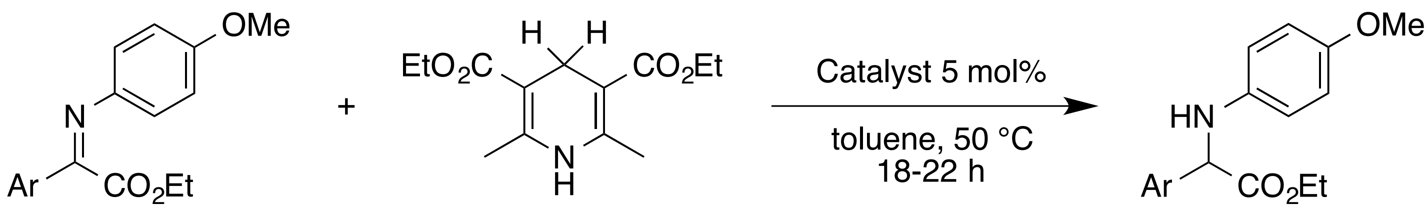
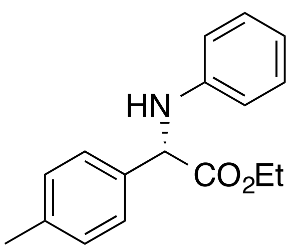
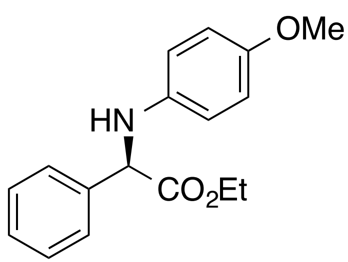
> Reduction using Hantzsch ester



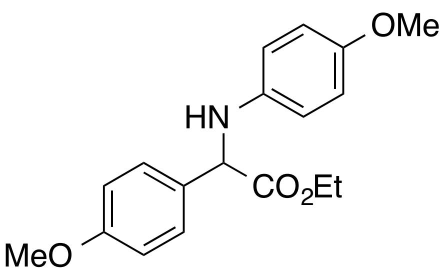




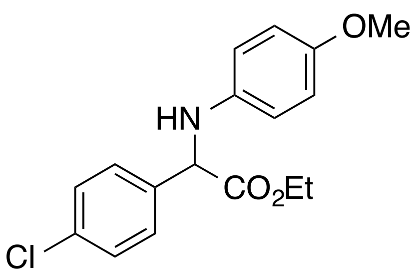
(*S*) 88%
ee 99%



(*R*) 93%
ee 96%



96%
ee 94%



95%
ee 98%

Li, G.; Liang, Y.; Antilla, J. C. *J. Am. Chem. Soc.* **2007**, *129*, 5830.

Imine as substrate

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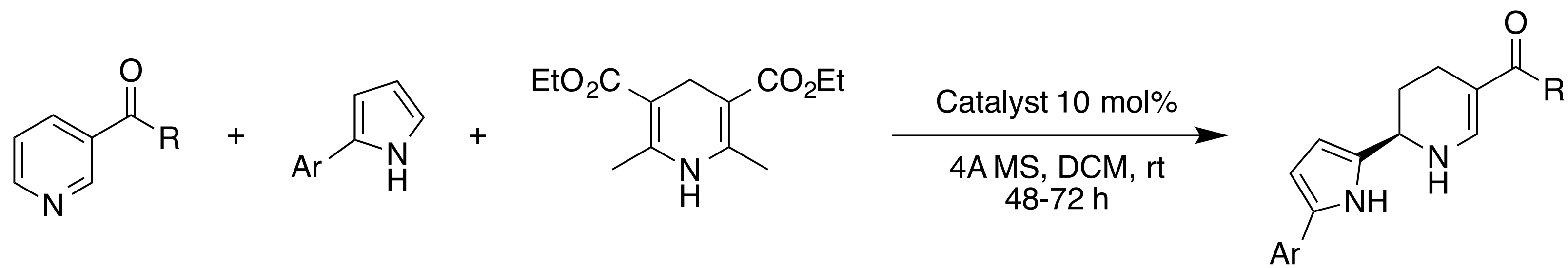
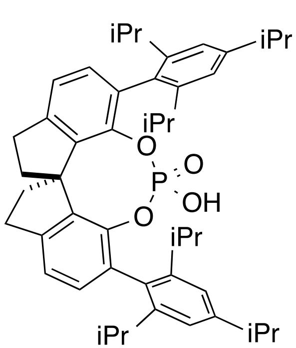
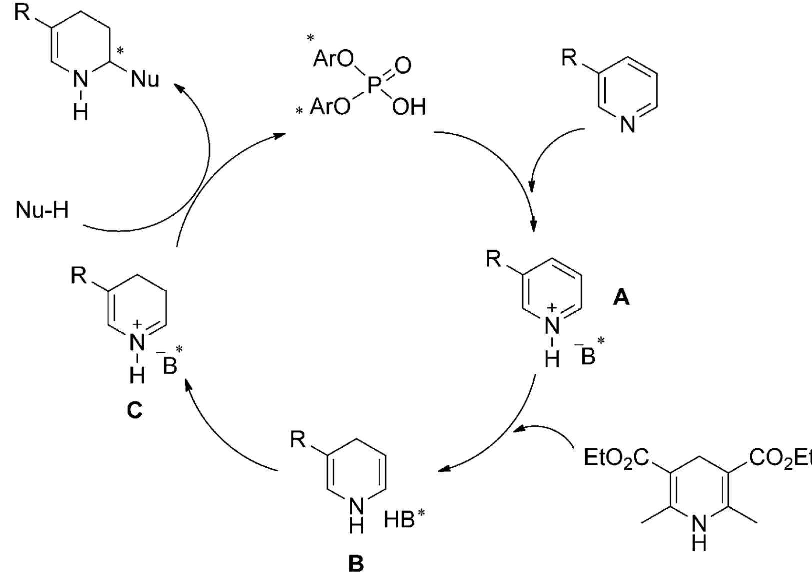
> Reduction



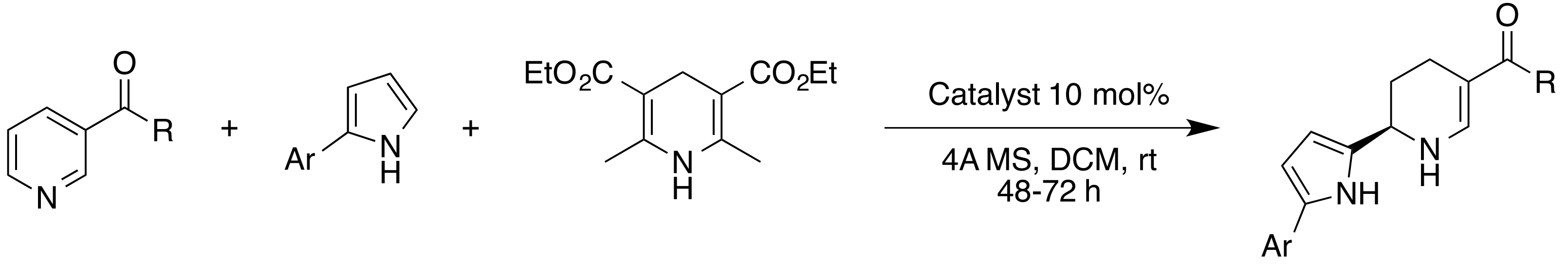


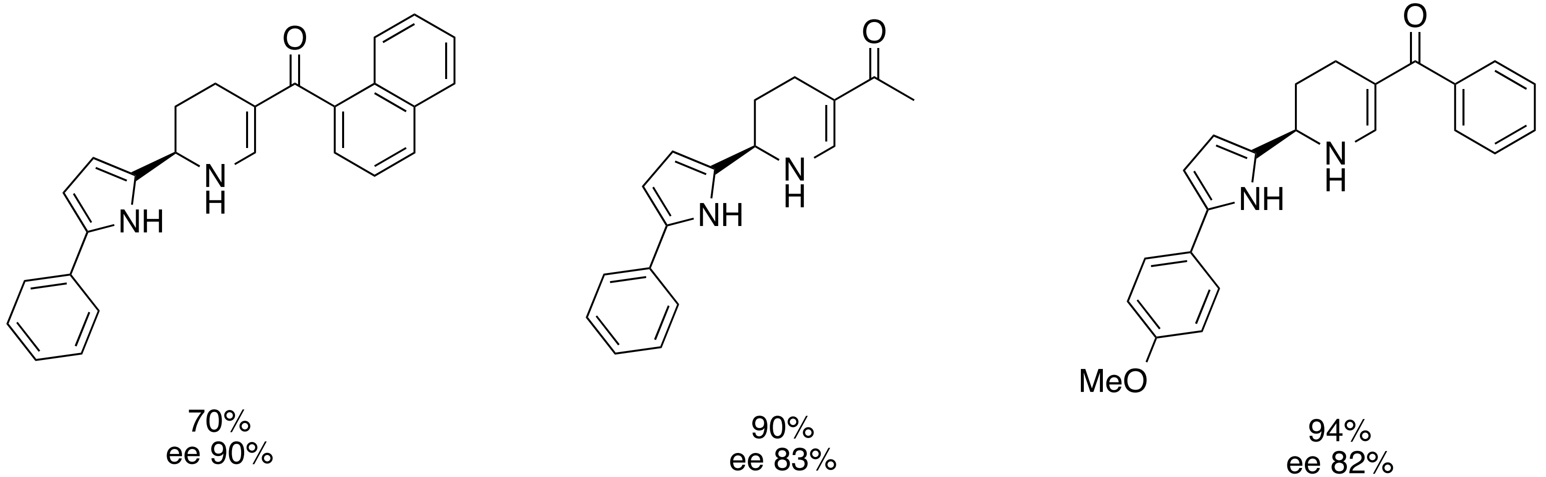


Wang, S.-G.; You, S.-L. *Angew. Chem. Int. Ed. Engl.* **2014**, *53*, 2194.

Imine as substrate

> Reduction





Wang, S.-G.; You, S.-L. *Angew. Chem. Int. Ed. Engl.* **2014**, *53*, 2194.

Ketone as substrate

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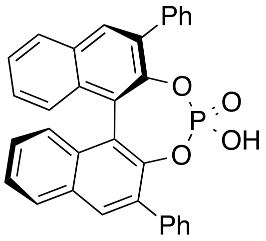
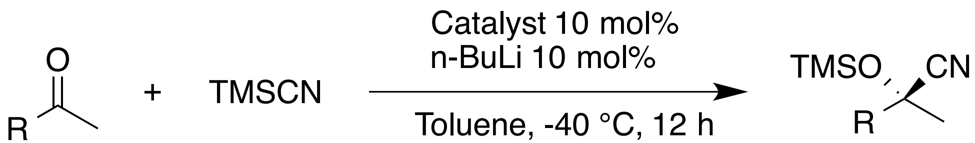
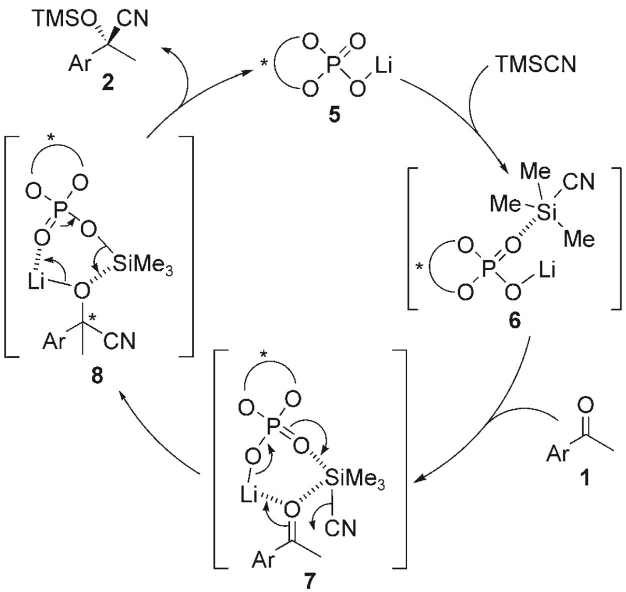
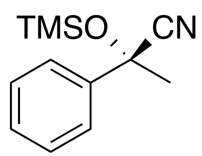
> Cyanosilylation

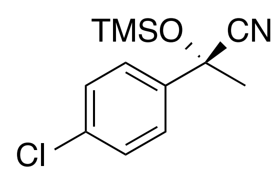




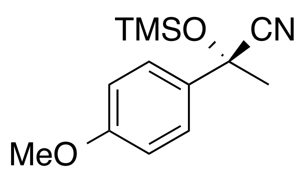




96%
ee 86%



95%
ee 68%

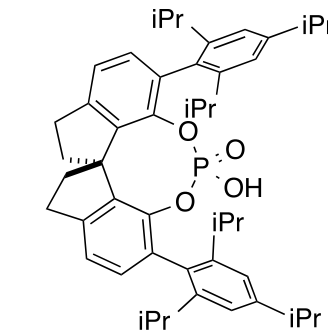


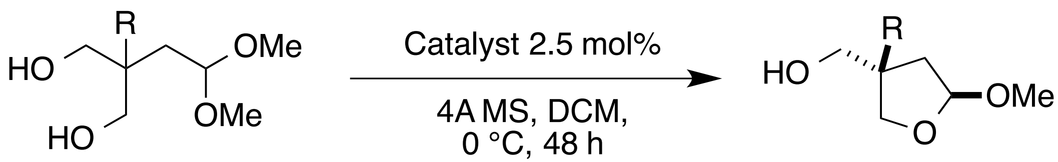
94%
ee 63%

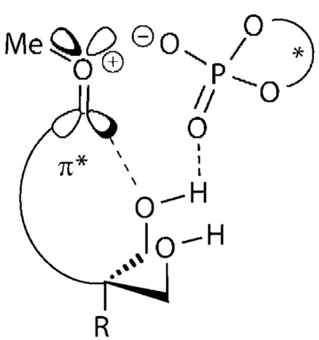
Hatano, M.; Ikeno, T.; Matsumura, T.; Torii, S.; Ishihara, K. *Adv. Synth. Catal.* **2008**, *350*, 1776.

Ketone or Hydroxyl as substrate

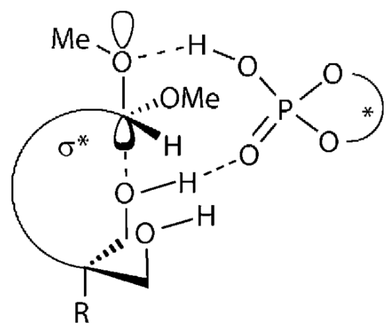
> THF formation



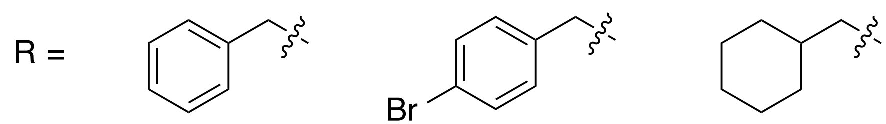




TS1 (S_N1-type)



TS2 (S_N2-type)



96%
ee 94%
dr 12:1

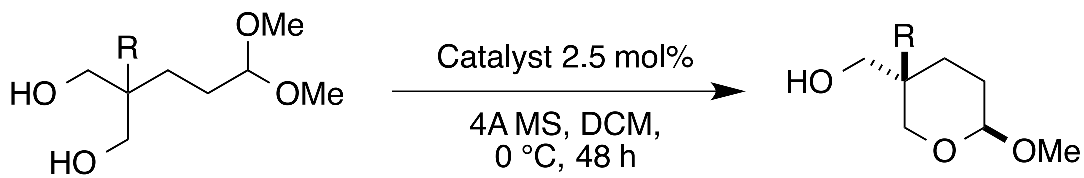
95%
ee 90%
dr 6:1

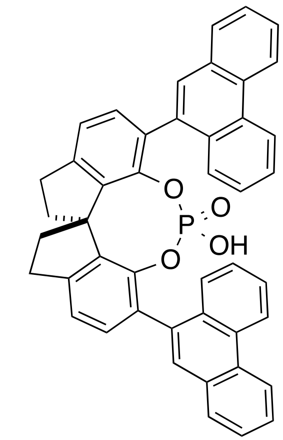
95%
ee 93%
dr 19:1

Chen, Z.; Sun, J. *Angew. Chem. Int. Ed. Engl.* **2013**, *52*, 13593.

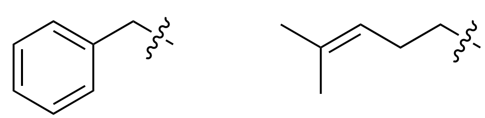
Ketone or Hydroxyl as substrate

> THP formation





R =



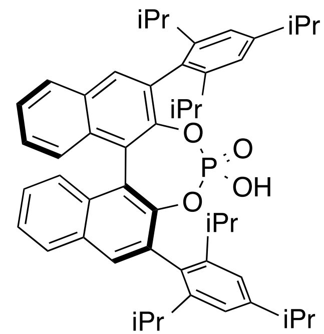
90%
ee 94%
dr 4:1

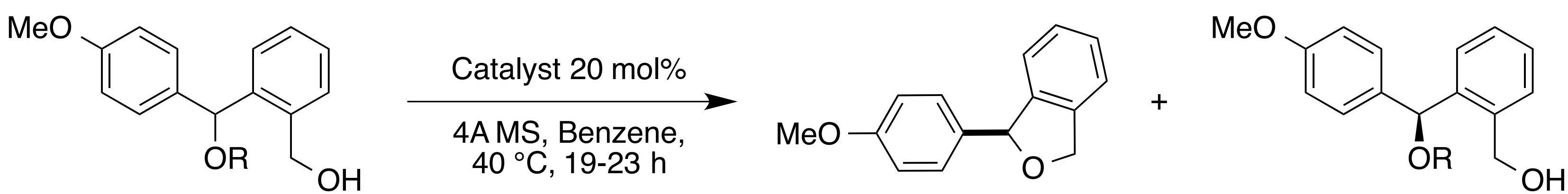
95%
ee 93%
dr 3:1

Chen, Z.; Sun, J. *Angew. Chem. Int. Ed. Engl.* **2013**, *52*, 13593.

Ketone or Hydroxyl as substrate

> S_N2 O-alkylation

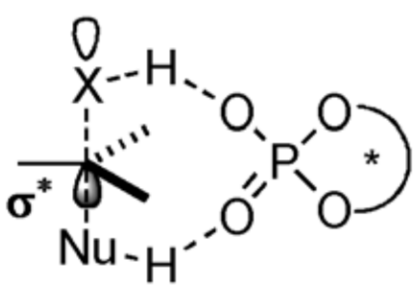




racemic

(*S*)

R =	H	Et	*i*Pr	*t*Bu
	Conv 32% er 63:37	Conv 26% er 81:19	Conv 35% er 87.5:12.5	Conv 49% er 93.5:6.5



Čorić, I.; Kim, J. H.; Vlaar, T.; Patil, M.; Thiel, W.; List, B. *Angew. Chem. Int. Ed. Engl.* **2013**, *52*, 3490.

Hydroxyl as substrate

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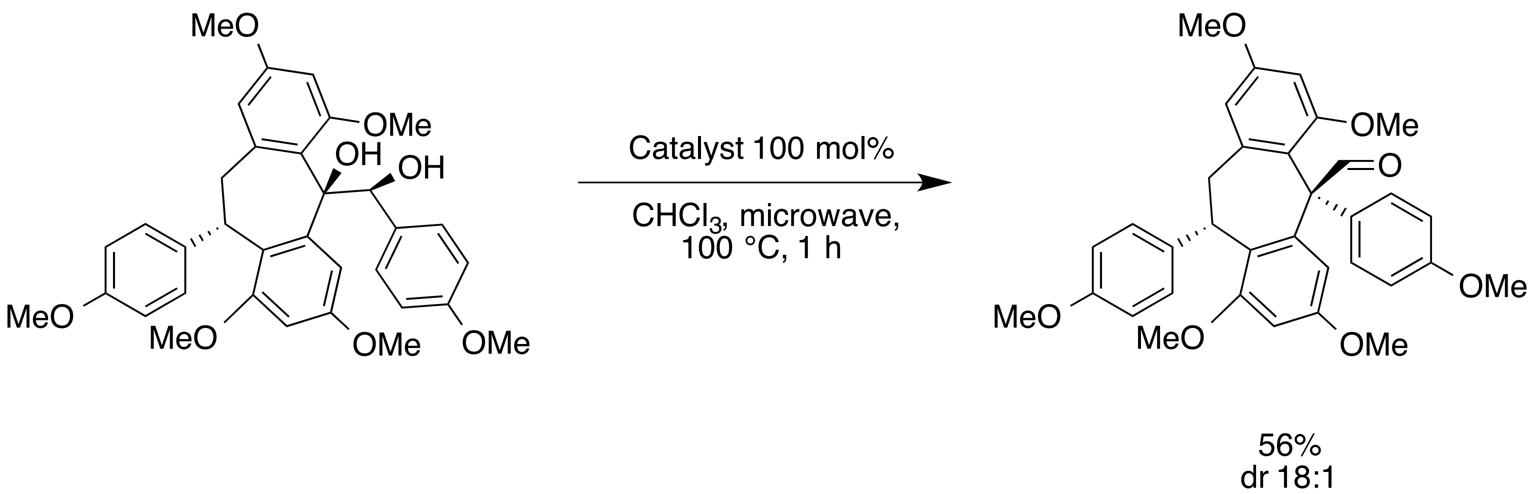
> Pinacol rearangement



Snyder, S. A.; Thomas, S. B.; Mayer, A. C.; Breazzano, S. P. *Angew. Chem. Int. Ed. Engl.* **2012**, *51*, 4080.

Aziridine as substrate

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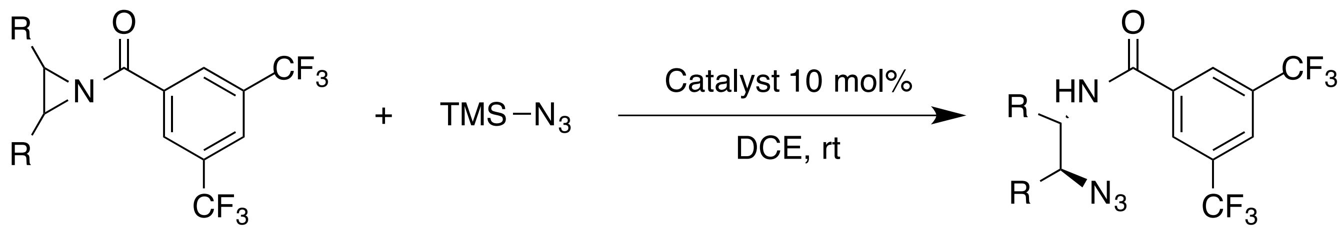
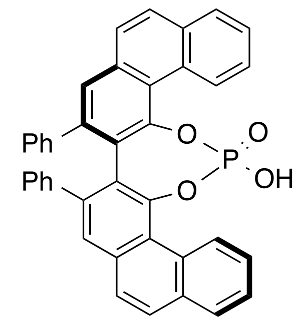
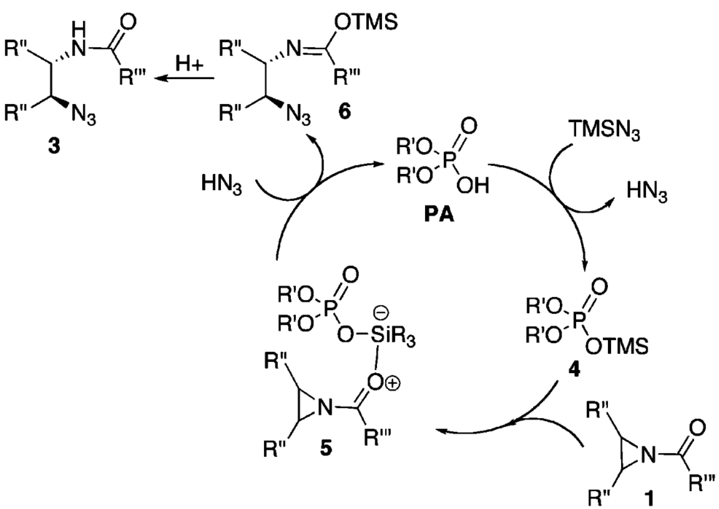
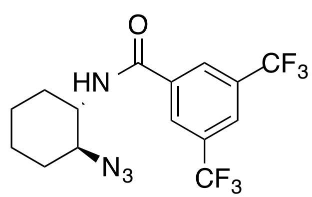
> Aziridine Desymetrization

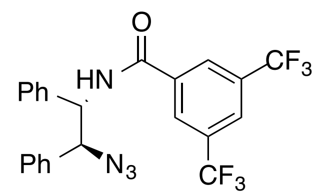




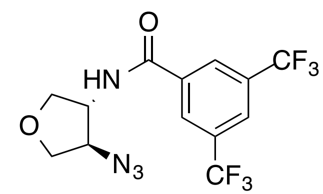




97%
ee 95%



95%
ee 83%

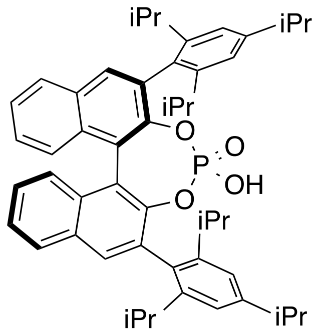


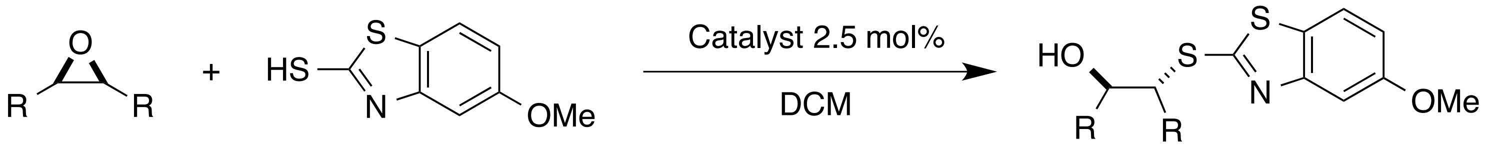
49%
ee 87%

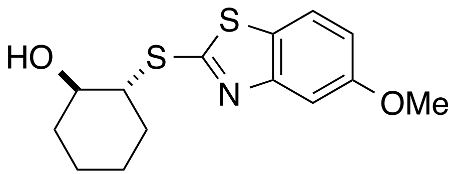
Rowland, E. B.; Rowland, G. B.; Rivera-Otero, E.; Antilla, J. C. *J. Am. Chem. Soc.* **2007**, *129*, 12084.

Epoxyde as Substrate

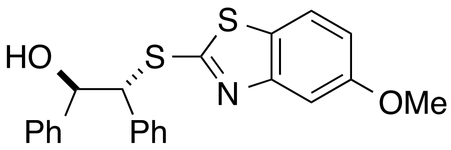
> Epoxyde Desymetrization







98%
ee 85%

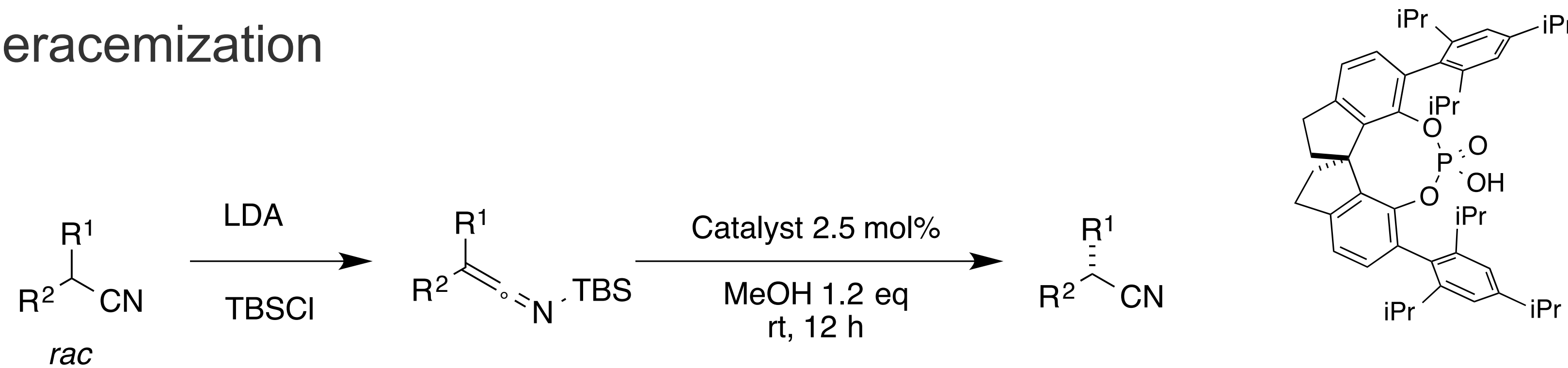


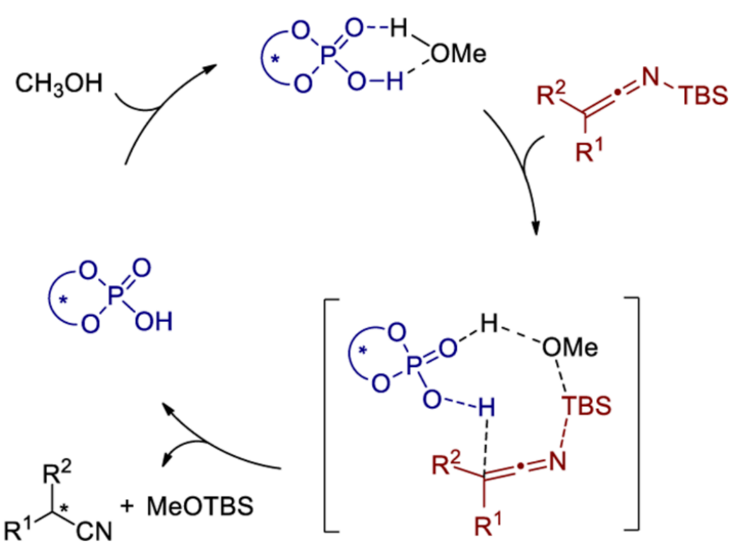
94%
ee 76%

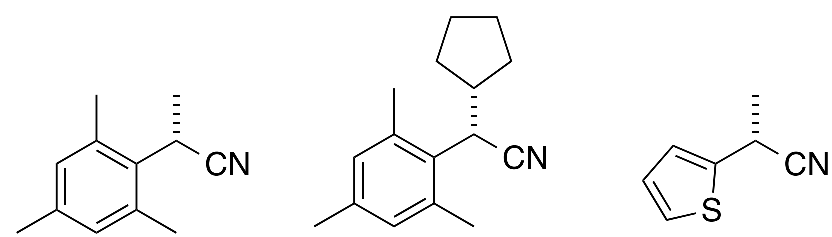
Wang, Z.; Law, W. K.; Sun, J. *Org. Lett.* **2013**, *15*, 5964.

Silyl ketene imine as Substrate

> Deracemization







95%
er 99:1

90%
er 98:2

82%
er 97:3

Guin, J.; Varseev, G.; List, B. *J. Am. Chem. Soc.* **2013**, *135*, 2100.

Conclusion

- The scope of substrate has been extended
- Catalyst tunable
- But still mainly used with imines
- Requires high loading of catalyst (5-10 mol% average)
- Still a lot of derivatives to develop (Acid (di)thiophosphoric,…)

Aknowledgments

Thank you for your attention !