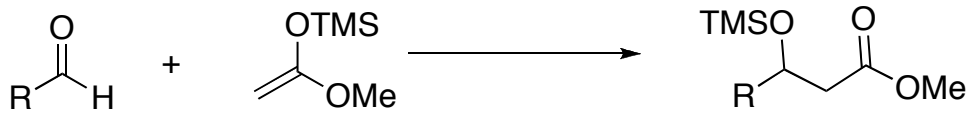
A Powerful Chiral Counteranion Motif for Asymmetric Catalysis

Li HUANG

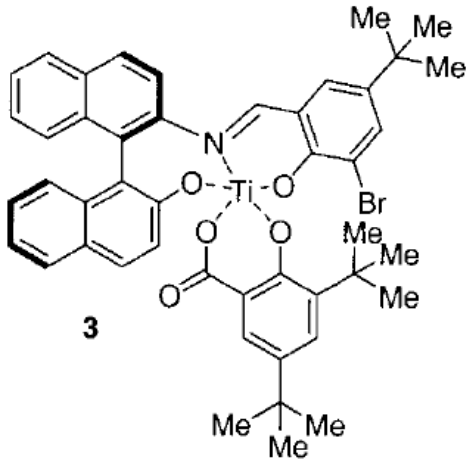
06/27/2009

Mukaiyama aldol reaction



up to 99%*ee*

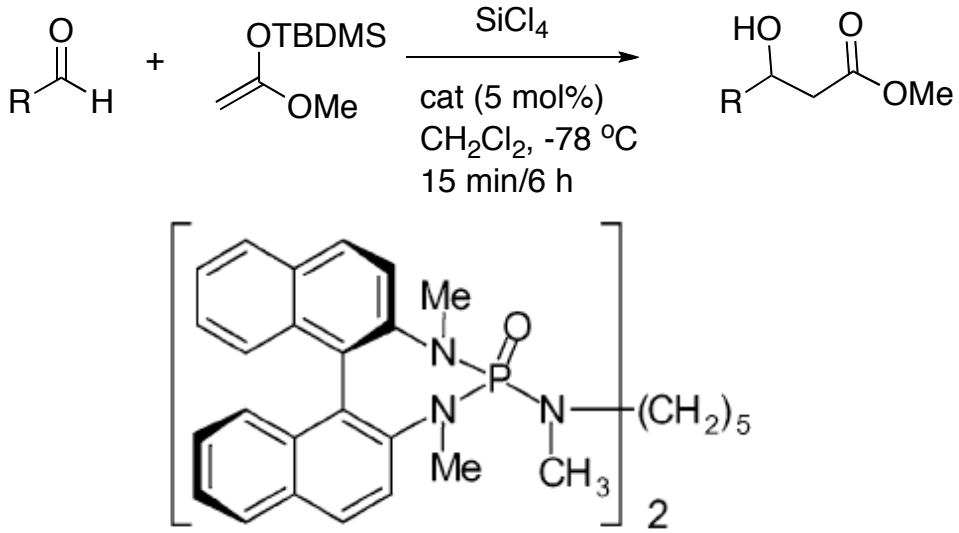
R = alkyl, alkenyl, alkynyl, aromatic

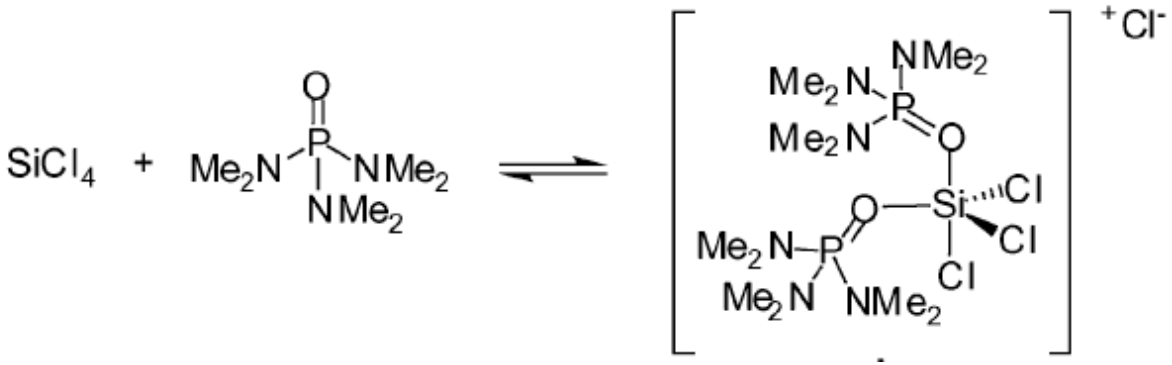


0.5-5 mol%

Singer, R.A.; Carreira, E. M. Helv. Acta. Chim. 2003, 86, 1040.

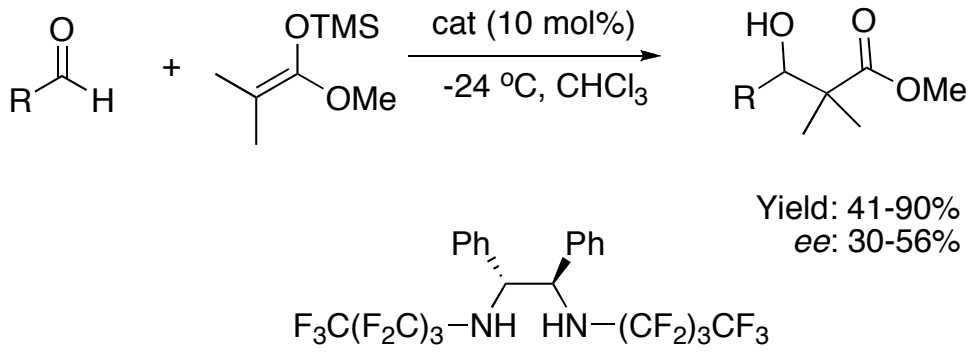
Mukaiyama aldol reaction





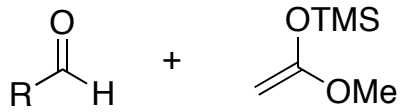
Denmark, S. E.; Wynn, T.; Beutner, G. L. J. Am. Chem. Soc. 2002, 124, 13405.

Mukaiyama aldol reaction



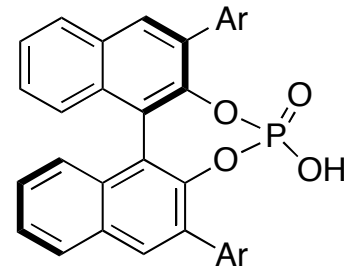
McGilvra, J.D.; Unni, A. K.; Rawal, V. H. Angew. Chem. Int. Ed. 2006, 45, 6130.

Mukaiyama aldol reaction



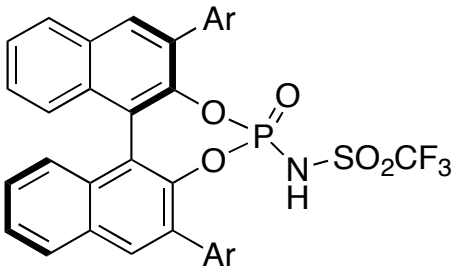
Activation of simples aldehydes

General Background



pKa 1 (water)

Activation of imines and functionalized aldehydes

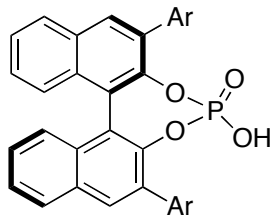


pKa -3 (water)

Activation of Imines and functionalized ketones

Garcia, P.; Lay, F.; Garcia, P.; Rabalakos, C.; List, B. Angew. Chem. Int. Ed. 2009, 48, 4363.

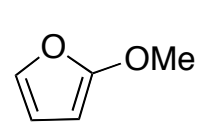
Imines as electrophiles

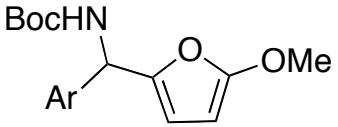


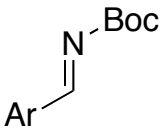
Electrophiles

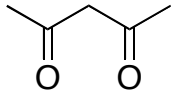
Nucleophiles

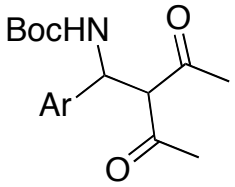
Product



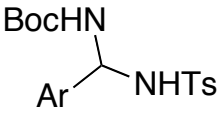


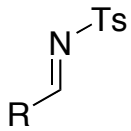


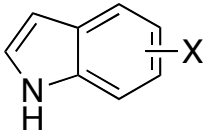


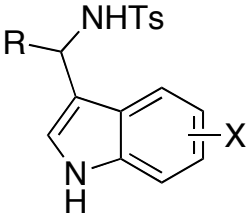


NH_2Ts



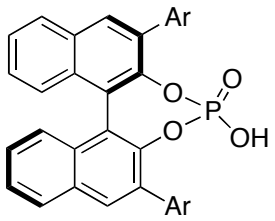


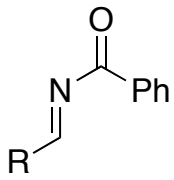


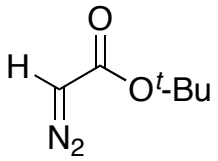


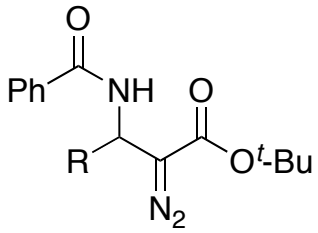
Akiyama, T. Chem. Rev. 2007, 107, 5744.

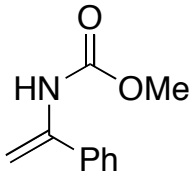
Imines as electrophiles

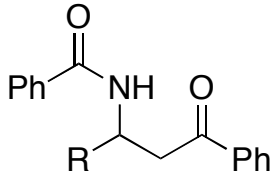


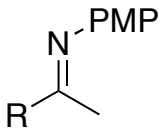


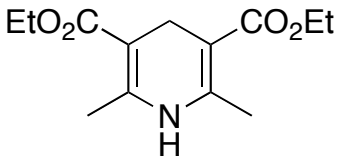


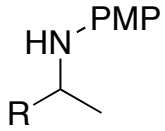






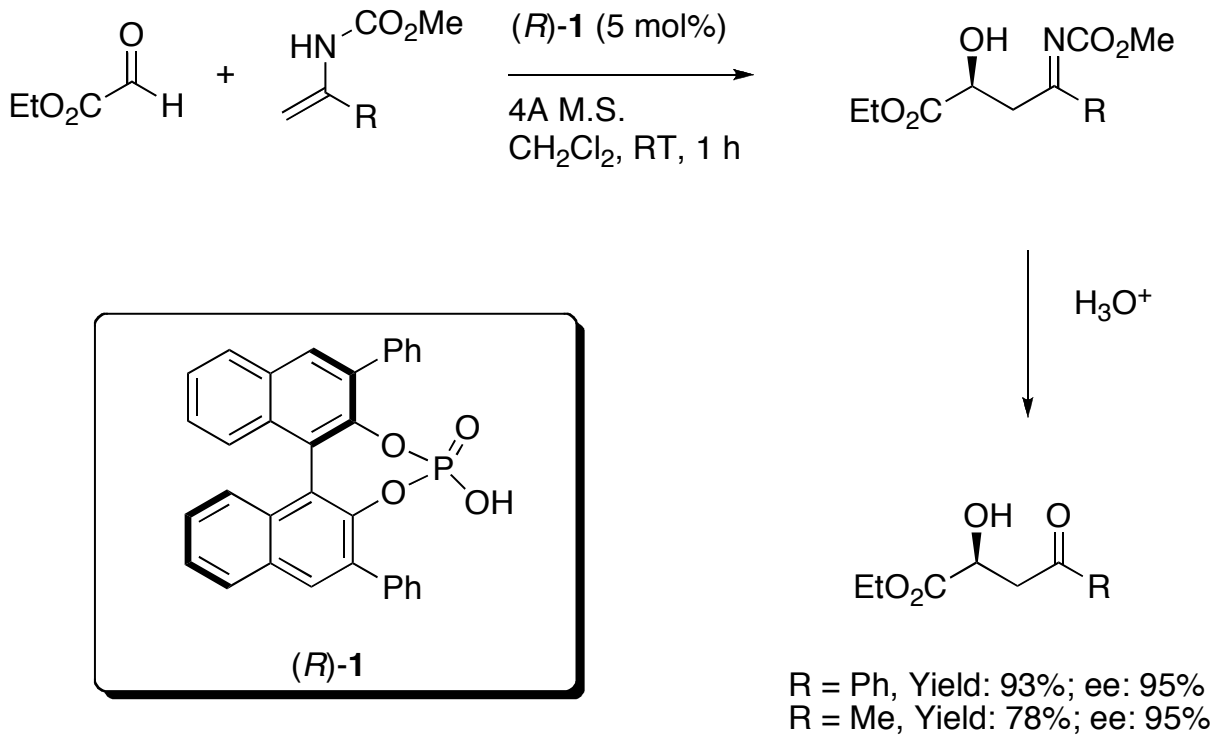






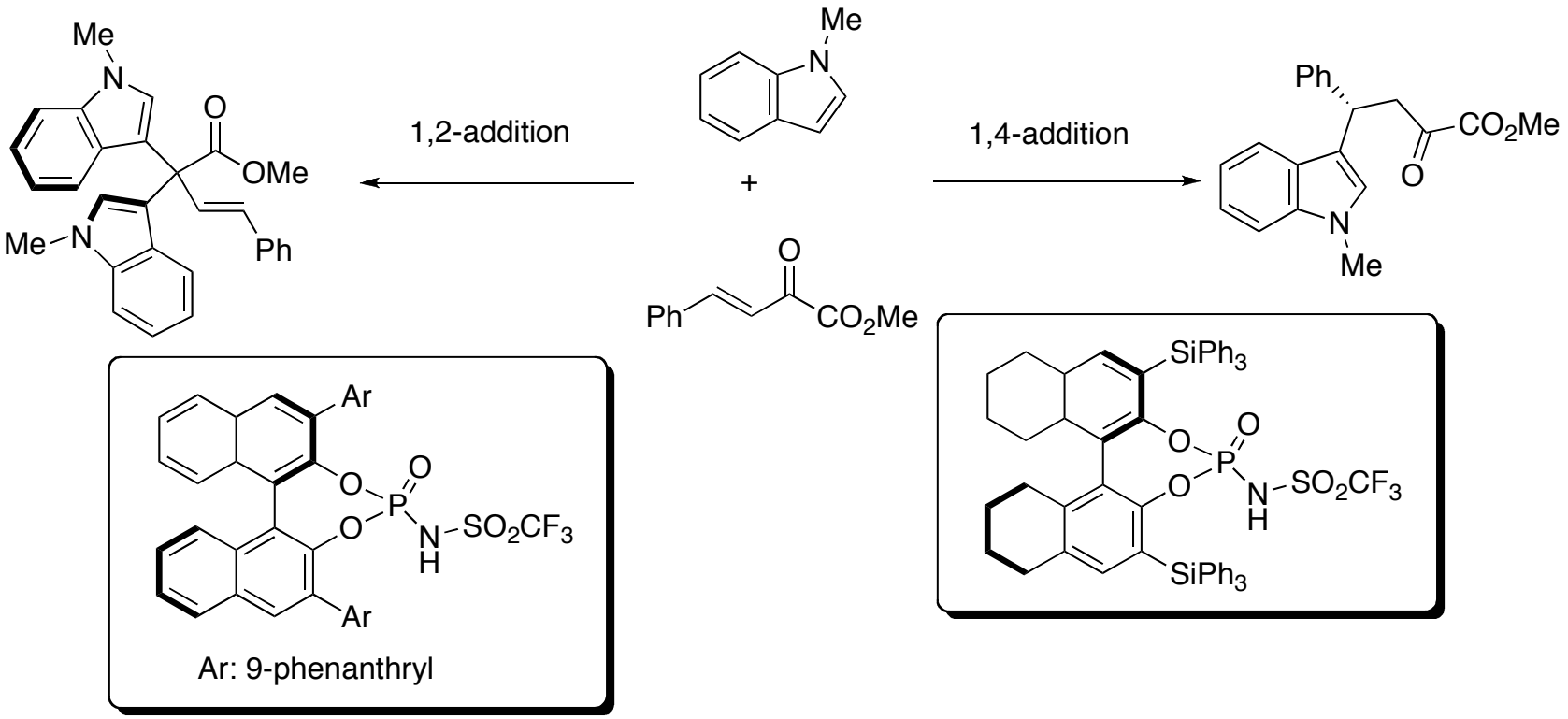
Akiyama, T. Chem. Rev. 2007, 107, 5744.

Functionalized aldehydes as electrophiles



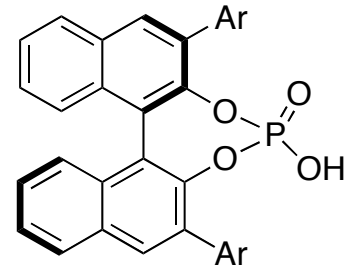
Terada, M.; Soga, K.; Momiyama, N. Angew. Chem. Int. Ed. 2008, 47, 4122.

Ketone as electrophiles



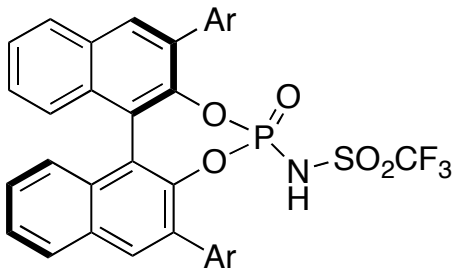
Rueping, M.; Nachtsheim, S. A. angew. Chem. Int. Ed. 2008, 47. 593.

General Background



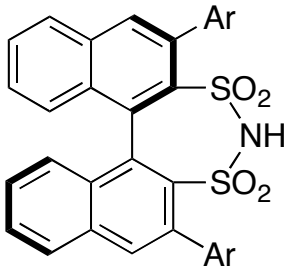
pKa 1 (water)

Activation of imines and functionalized aldehydes



pKa -3 (water)

Activation of Imines and functionalized ketones

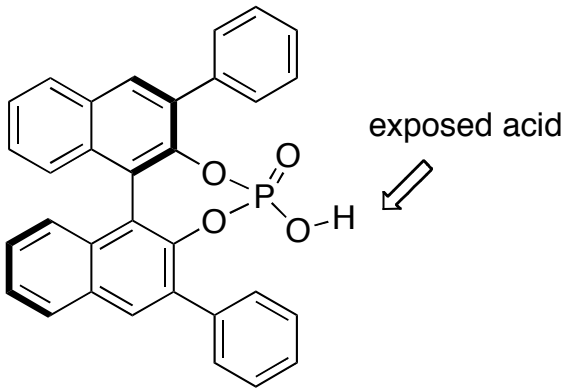


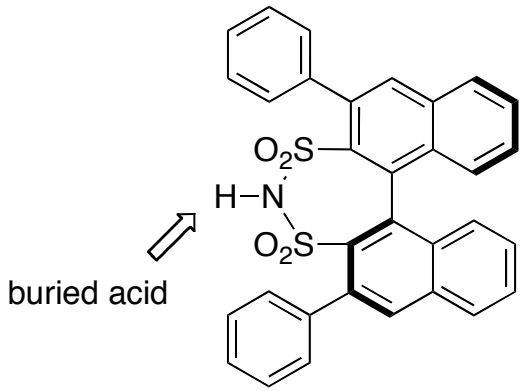
pKa ~ -5.9 (water)

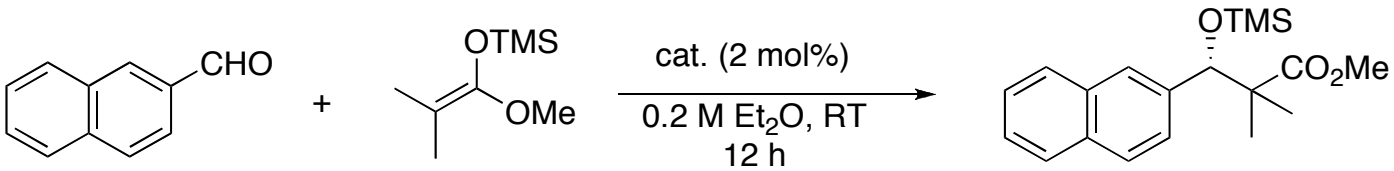
Activation of simple aldehydes

Garcia, P.; Lay, F.; Garcia, P.; Rabalakos, C.; List, B. Angew. Chem. Int. Ed. 2009, 48, 4363.

Different Acids

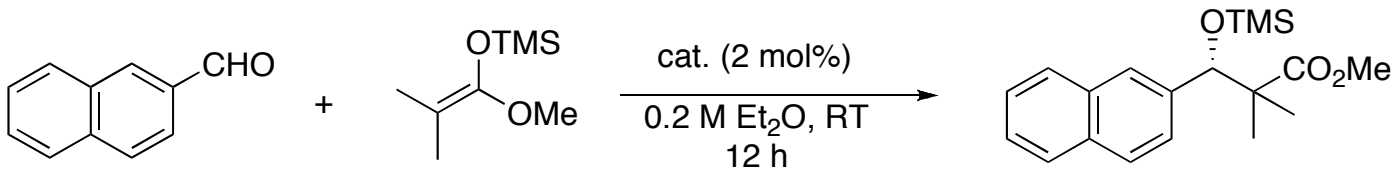


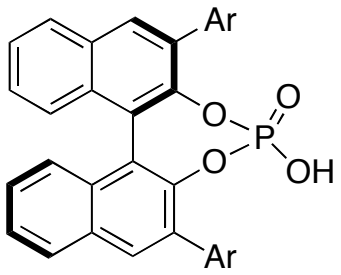




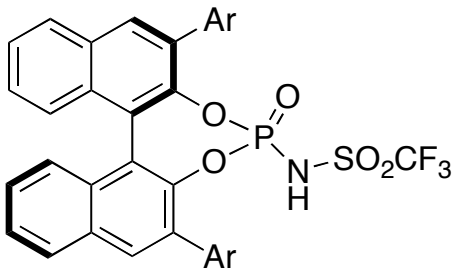
Garcia, P.; Lay, F.; Garcia, P.; Rabalakos, C.; List, B. Angew. Chem. Int. Ed. 2009, 48, 4363.

Simple aldehydes as electrophiles





Yield: <2%



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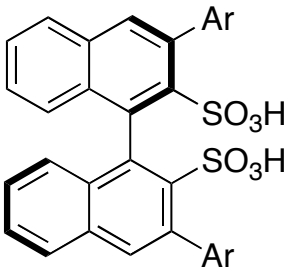

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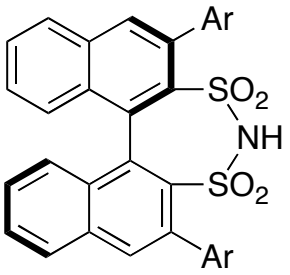
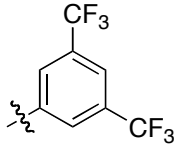
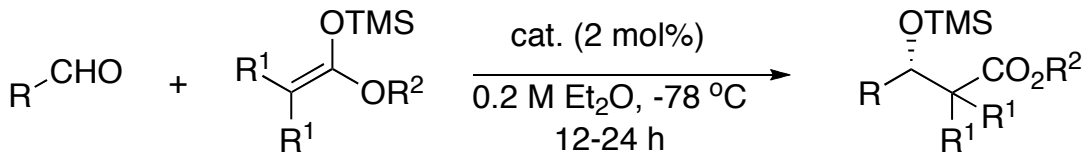


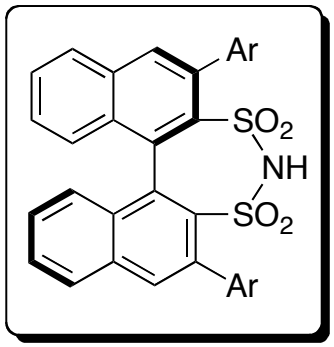
Yield: >99%
ee: 80%

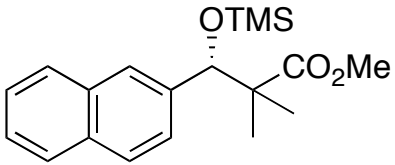
Ar:



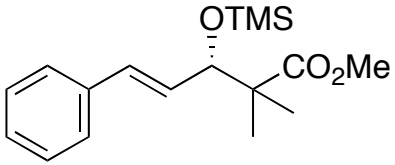
Substrate scope



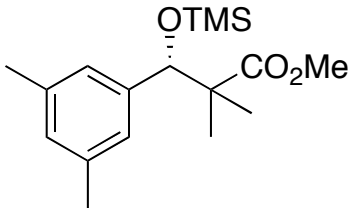




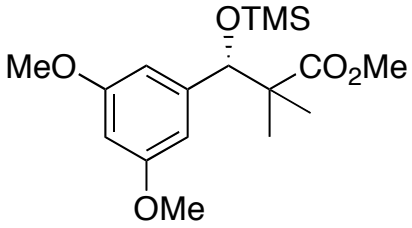
Yield: 98%
ee: 94%



Yield: 82%
ee: 94%

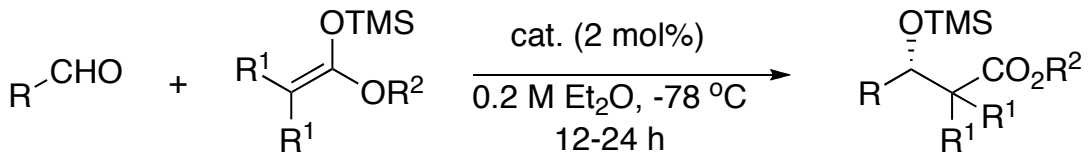


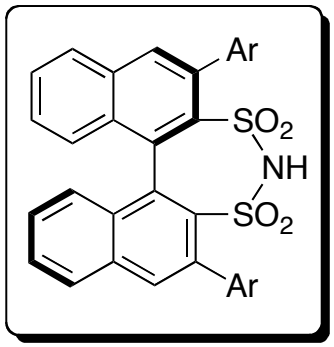
Yield: 78%
ee: 90%

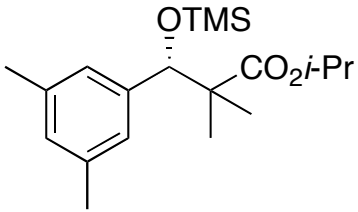


Yield: 98%
ee: 92%

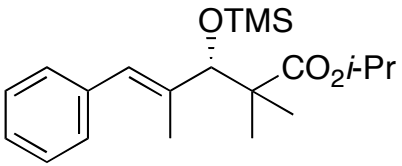
Substrate scope





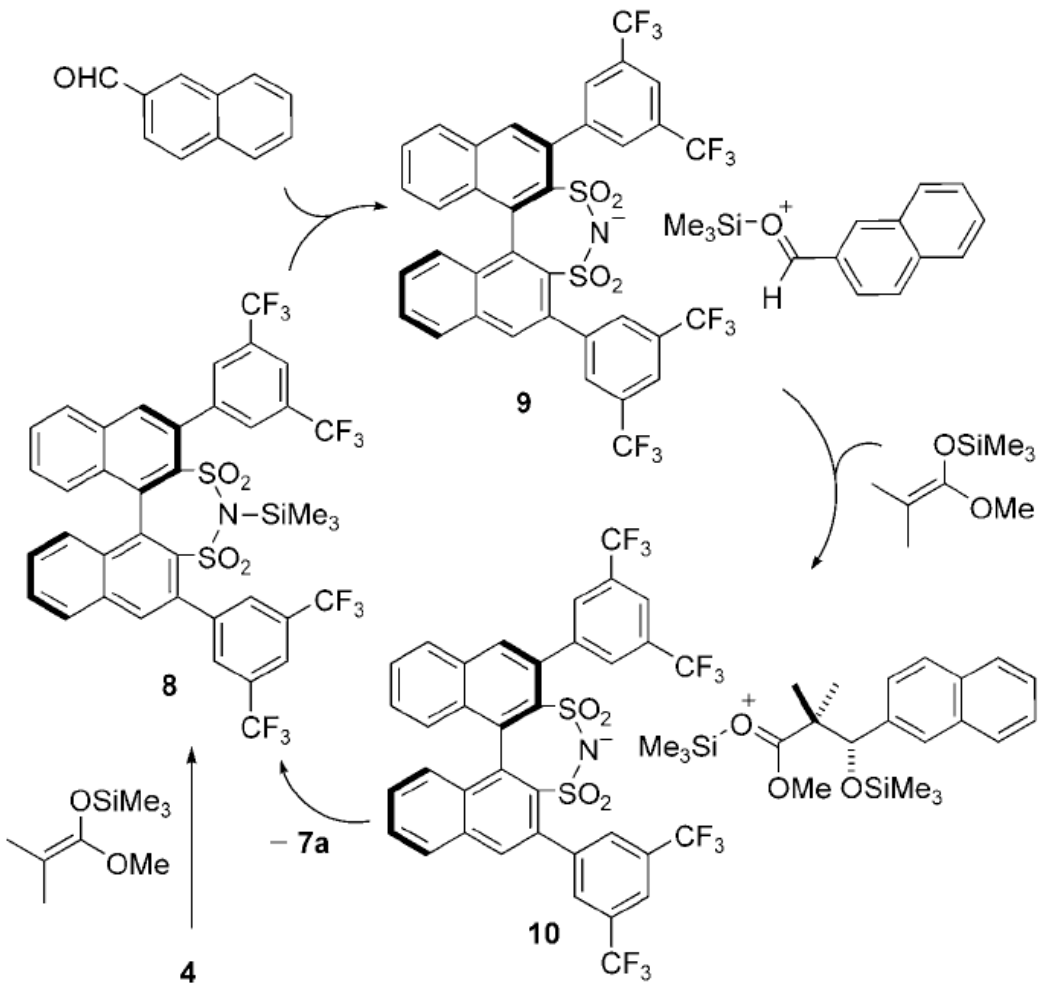


cat loading	T (°C)	Yield	*ee*
2	- 78 °C	93	84
0.1	- 45 °C	80	80
0.05	- 45 °C	70	80



2	- 78 °C	95	86
0.1	- 78 °C	90	86
0.05	- 78 °C	90	86
0.01	0 °C	88	76

Proposed catalytic cycle



Conclusion

- Activation of simple aldehydes
- High turn over was achieved in the reaction
- Potential counterion in ACDC