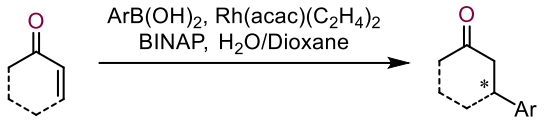
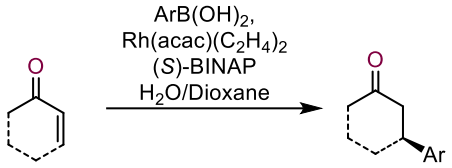
Hayashi Arylation

- Relatively stable toward oxygen and protic solvent.
- Organoboronic acid has very low reactivity toward enone without rhodium catalyst.
- Aryl and alkenyl group could be introduced in β-site of enone with high ee.



Hayashi, T. et al. Chem. Rev. 2003, *103*, 2829–2844. https://doi.org/10.1021/cr020022z

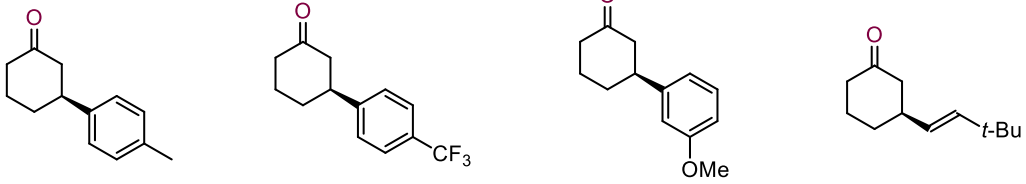
First Report of Rh-catalyzed Enantioselective Conjugate Addition of Aryl Boronic Acid to Enone



Optimization table

Temp.	Eq. of $ArB(OH)_2$	Yield(%)	ee (%)
100°C	1.4	64	97
40°C	1.4	<2	97
60°C	1.4	3	97
80°C	1.4	42	97
120°C	1.4	59	97
100°C*	2.5	15	43
100°C	5.0	93	97
100°C		>99	97

* Using $Rh(acac)(CO)_2$ instead

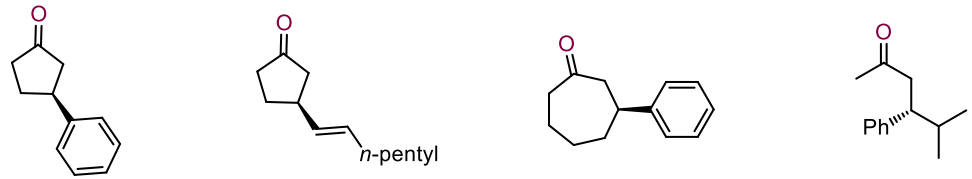


> 99%
97% ee

70%
99% ee

97%
96% ee

76%
91% ee



93%
97% ee

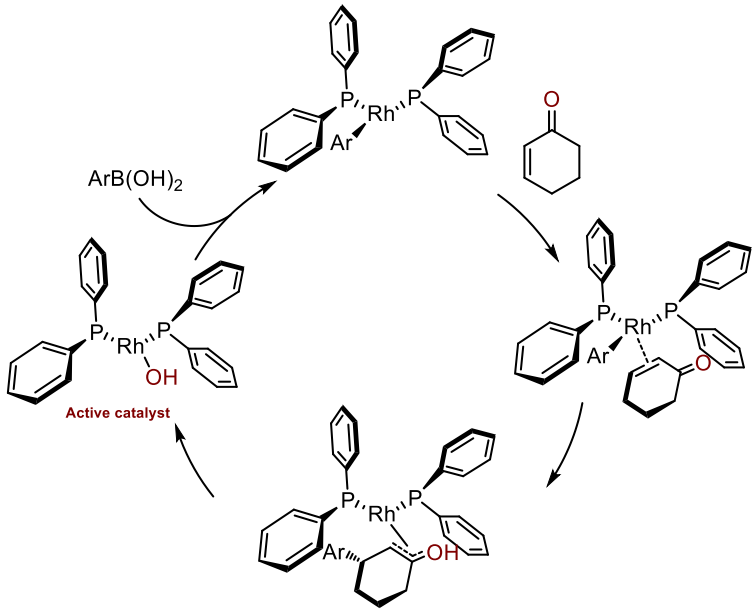
64%
96% ee

51%
93% ee

82%
97% ee

- ee is robust with respect to reaction temperature
- The [Rh] species is crucial to get good yield and ee
- Higher eq. of boronic acid prevents proto-deborylation

Mechanism (Binaphthylene omitted)

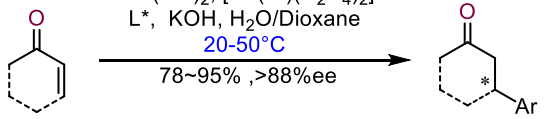


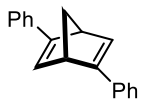
Hayashi, T., Miyaura, N. et al. J. Am. Chem. Soc. 1998, 120, 22, 5579–5580. https://doi.org/10.1021/ja980666h

Hayashi, T. et al. *J. Am. Chem. Soc.* 2002, 124, 18, 5052–5058. https://doi.org/10.1021/ja012711i

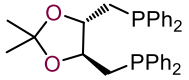
Hayashi Arylation

Diene-type Ligand

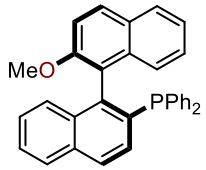




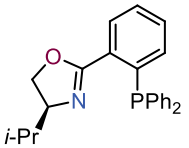
chiral diene ligand



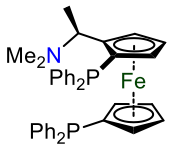
(*S*,*S*)-diop
30 %; 24% ee



(*R*)-MeO-mop
<2 %



(*S*)-*ip*-phox
5 %; 0% ee

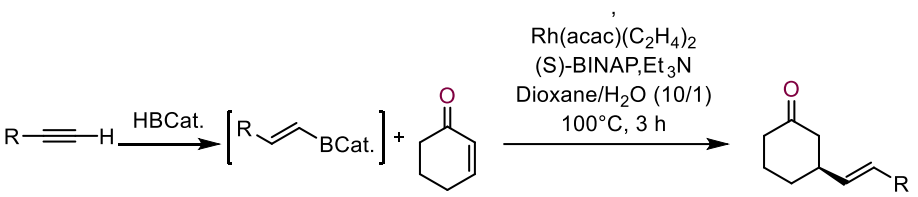


(*S*)-(*R*)-bppfa
5 %; 3% ee

- Diene type ligand provide milder condition with higher %yield and ee

Hayashi, T. et al. J. Am. Chem. Soc. 2003, 125, 38, 11508–11509. https://doi.org/10.1021/ja037367z
Hayashi, T. et al. Chirality 2000, 12, 469. https://doi.org/10.1002/(SICI)1520-636X(2000)12:5/6<469::AID-CHIR29>3.0.CO;2-H

One-pot Hydroboration/Alkenylation

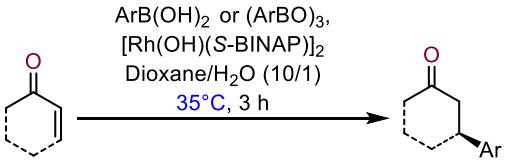


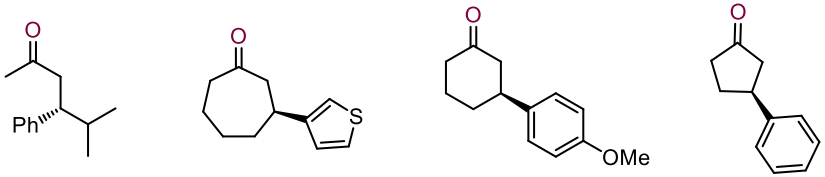
R= *n*-C_5H_{11}	92%, 96%ee
R= *t*-Bu	77%, 91%ee
R=CH_2OMe	83%, 98% ee

also work in cyclopentaone
acyclic enone

Hayashi, T., Tetrahedron Lett. 1998, 39, 8479. https://doi.org/10.1016/S0040-4039(98)01866-8.

$[Rh(OH)(S\text{-}BINAP)]_2$ as Catalyst

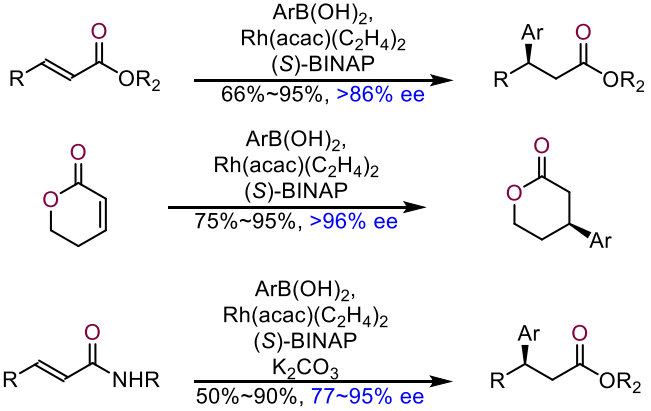


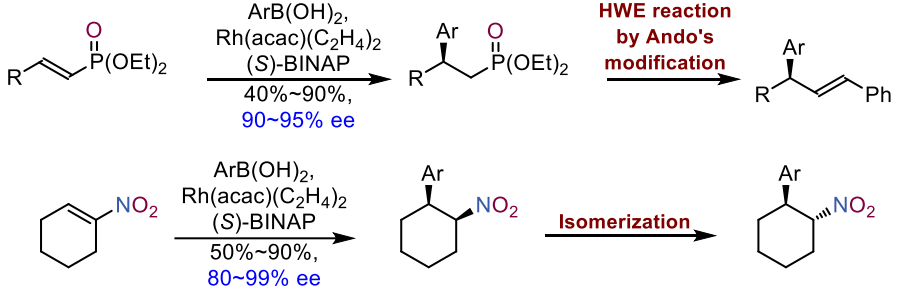


89%	81%	96%	95%
98% ee	99% ee	99.1% ee	98% ee

Hayashi, T. et al. J. Am. Chem. Soc. 2002, 124, 18, 5052–5058. https://doi.org/10.1021/ja012711i.

Other Activated Olefins

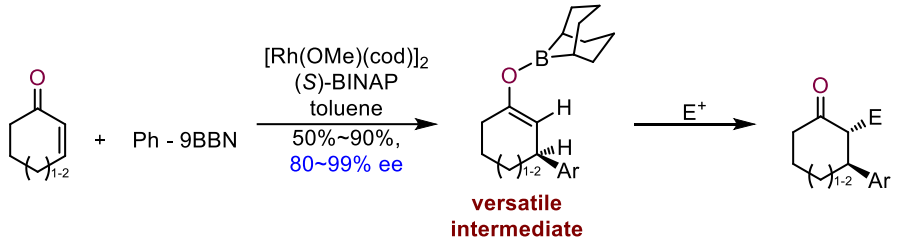


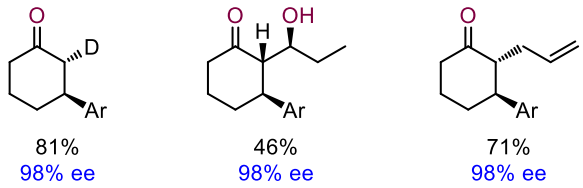


Hayashi, T., Tetrahedron: Asymmetry 1999, 10, 4047. https://doi.org/10.1016/S0957-4166(99)00417-6
Miyaura, N. et al. J. Org. Chem. 2001, 66, 26, 8944–8946. https://doi.org/10.1021/jo010747n
Hayashi, T., J. Am. Chem. Soc. 1999, 121, 49, 11591–11592. https://doi.org/10.1021/ja993184u
Hayashi, T., J. Am. Chem. Soc. 2000, 122, 43, 10716–10717. https://doi.org/10.1021/ja002805c
Hayashi, T., J. Am. Chem. Soc. 2000, 122, 43, 10716–10717 https://doi.org/10.1021/ja002805c

Hayashi Arylation

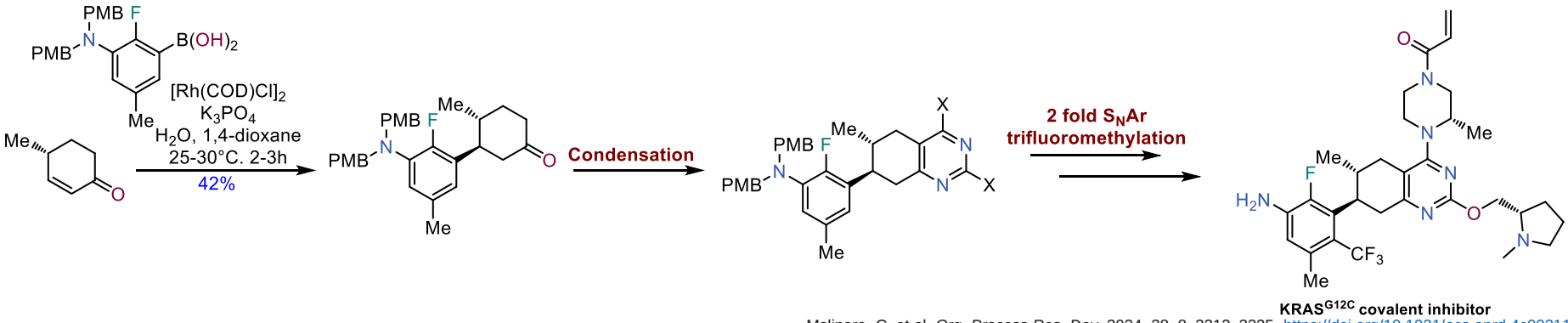
Tandem Reaction





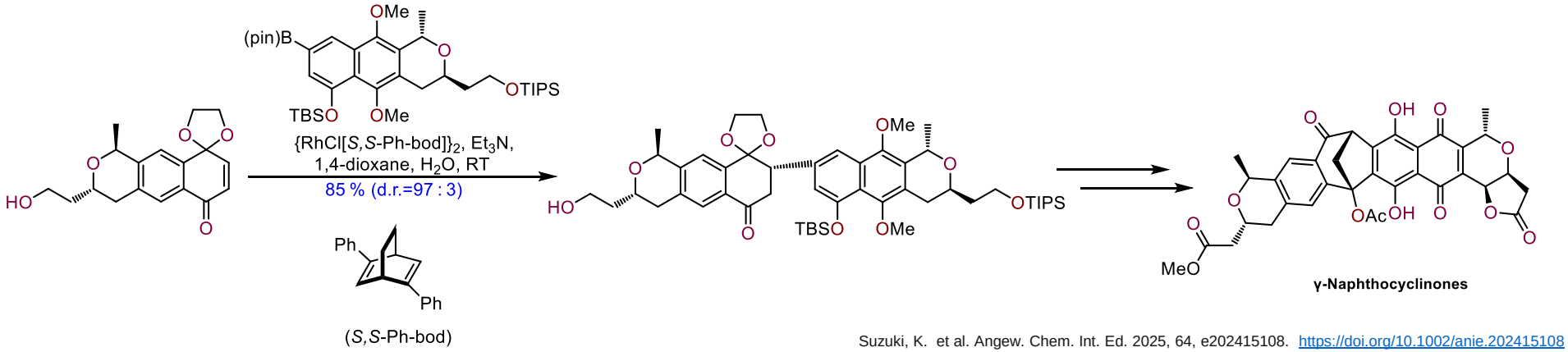
Hayashi, T. et al. J. Org. Chem. 2003, 68, 5, 1901–1905. https://doi.org/10.1021/jo020659i.

Synthetic Application – Drug Molecule



Molinaro, C. et al. *Org. Process Res. Dev.* 2024, 28, 8, 3313–3325. https://doi.org/10.1021/acs.oprd.4c00211

Synthetic Application – Total synthesis



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