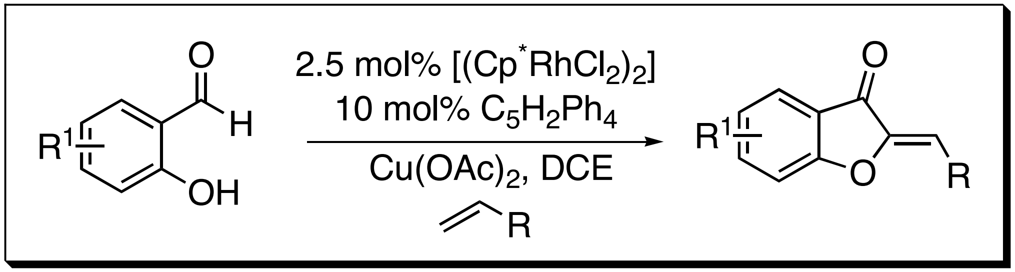
Rhodium(III)-Catalyzed Dehydrogenative Heck Reaction of Salicylaldehydes

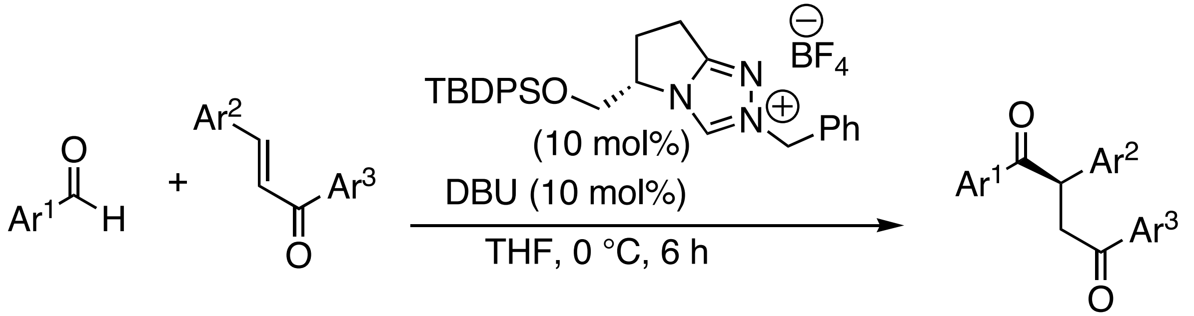
Shi, Z.; Schröder, N.; Glorius, F. *Angew. Chem. Int. Ed.* **2012,** *Early View,* DOI 10.1002/anie.201203224



Current Literature
Presented by Melissa Sprachman
July 28, 2012

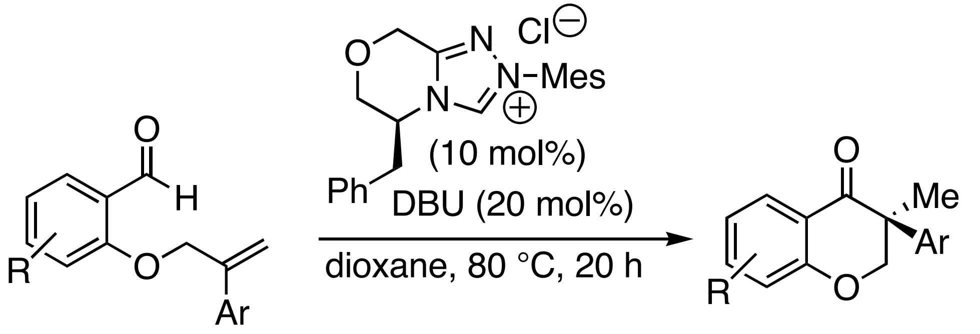
Functionalization of Aldehyde C-H Bonds

Umpolung of Aldehydes with N-Heterocyclic Carbenes (NHCs):



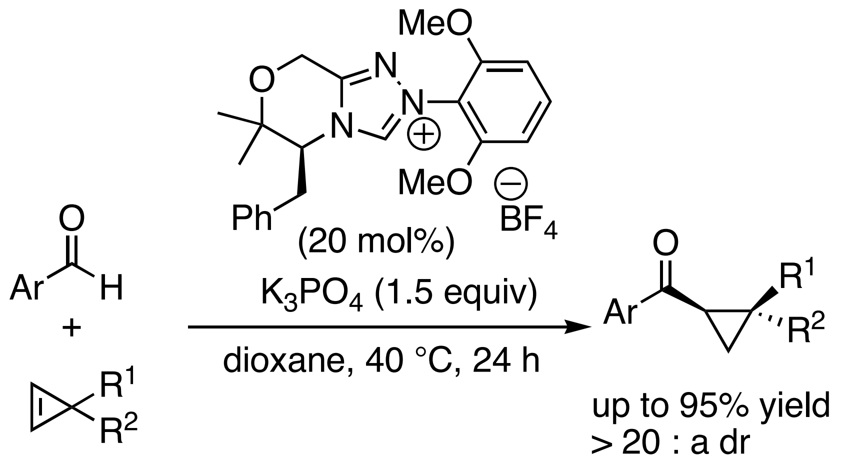
43-98%; 56-78% ee

Bugaut, X.; Glorius, F. *Chem. Soc. Rev.* **2012,** *41,* 3511-3522.



8-99%; 96-99% ee

Piel, I.; Steinmetz, K.; Hirano, R.; Fröhlich, R.; Grimme, S.; Glorius, F. *Angew. Chem. Int. Ed.* **2011,** *50,* 4983-4987.

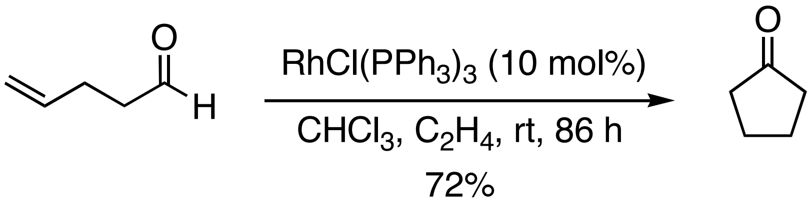


up to 95% yield
> 20 : a dr
up to 96% ee

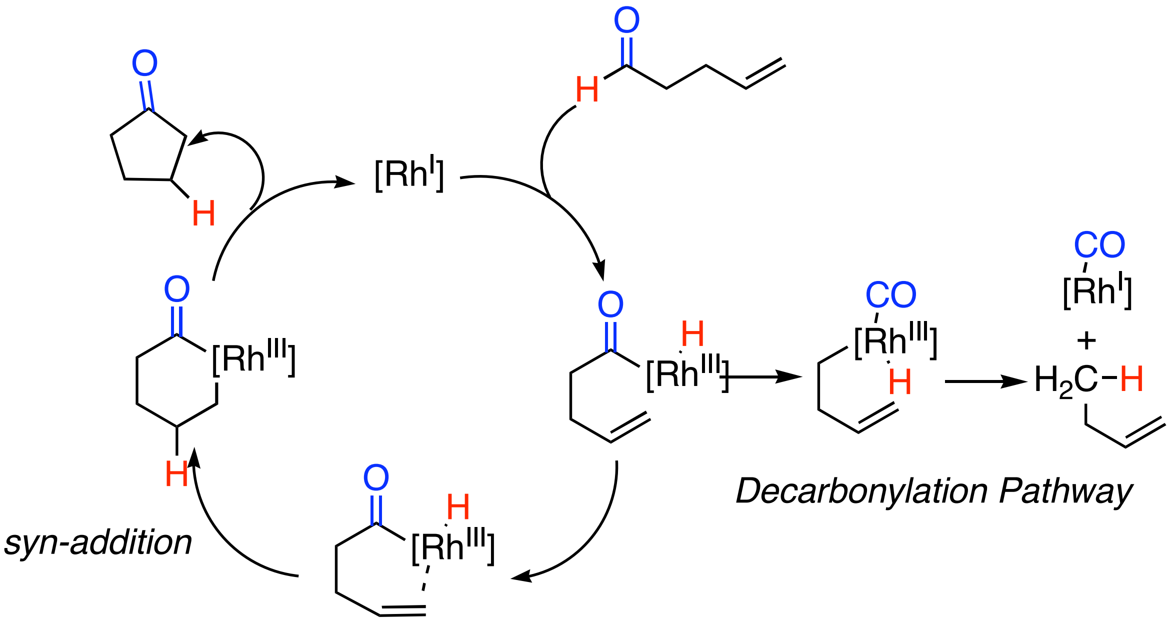
Liu, F.; Bugaut, X.; Schedler, M.; ; Fröhlich, R.; Glorius, F. *Angew. Chem. Int. Ed.* **2011,** *50,* 12626-12630.

Functionalization of Aldehyde C-H Bonds

Starting Point: Intramolecular Alkene Hydroacylation:

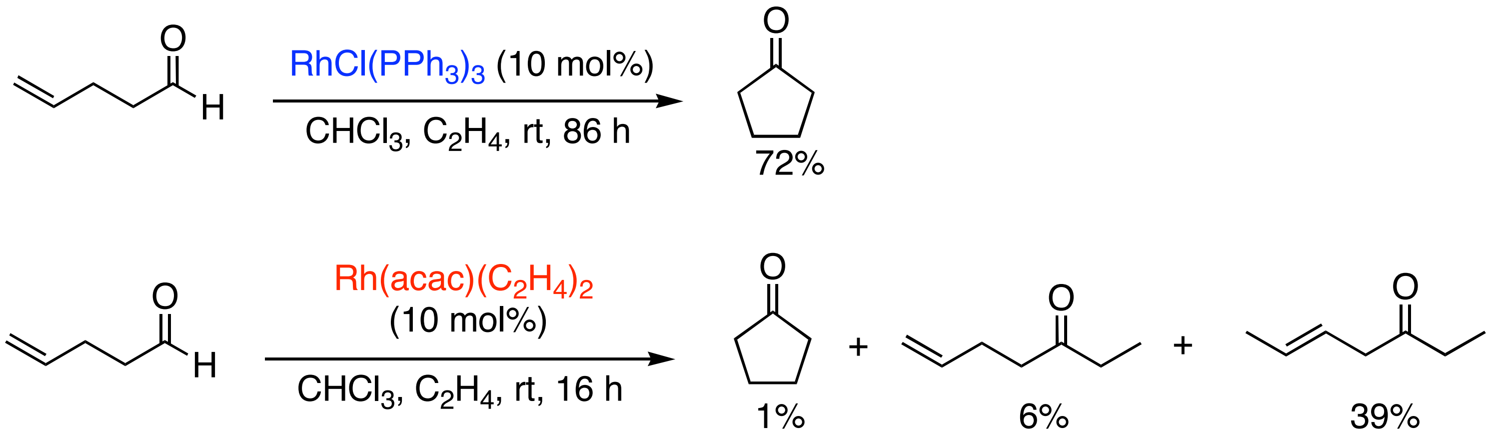


Lochow, C. F.; Miller, R. G. *J. Am. Chem. Soc.* **1976,** *98,* 1281-1283



Willis, M. C. *Chem Rev.* **2010,** *110,* 725-748.

Intermolecular Alkene Hydroacylation



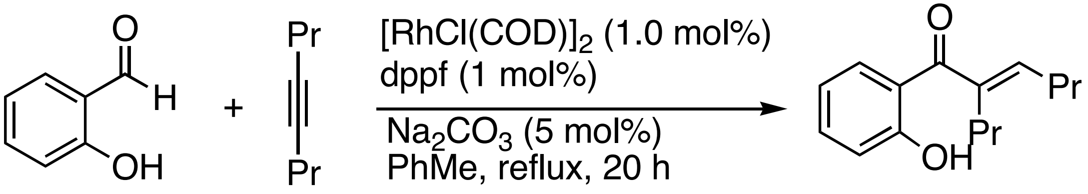
No hydroacylation products were formed when *saturated* aldehydes were used as substrates.

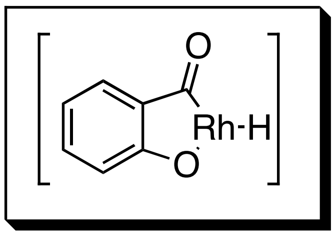
It was hypothesized that internal alkene coordination was required for reactivity.

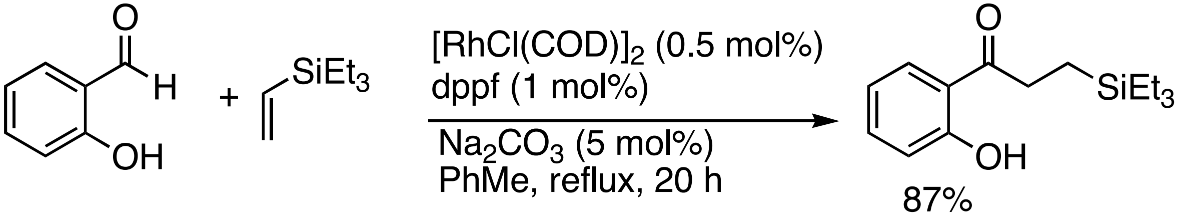
→ Use of *heteroatom* chelation as a strategy for intermolecular hydroacylation

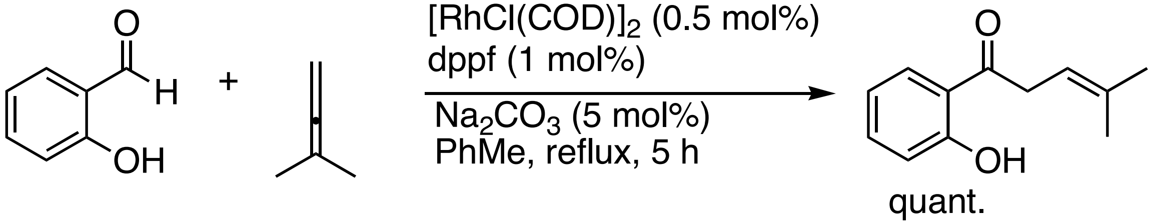
Lochow, C. F.; Miller, R. G. *J. Am. Chem. Soc.* **1976,** *98,* 1281-1283.
Vora, K. P.; Lochow, C. F.; Miller, R. G. *J. Organomet. Chem.* **1980,** *192,* 257-264.

Hydroacylation via Heteroatom Chelation





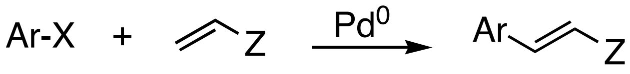


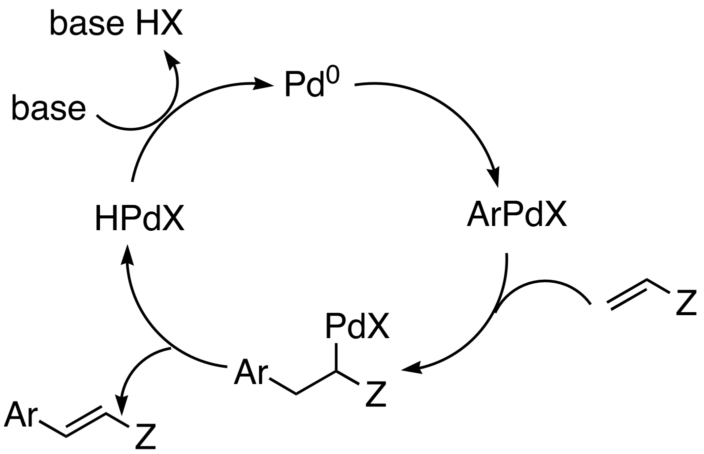


Kokobu, K.; Matsumasa, K.; Nishinaka, Y.; Miura, M.; Nomura, M. *Bull. Chem. Soc. Jpn.* **1999,** *72,* 303-311.

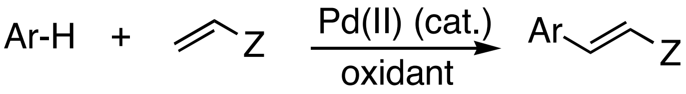
Dehydrogenative Heck Reaction (DHR)

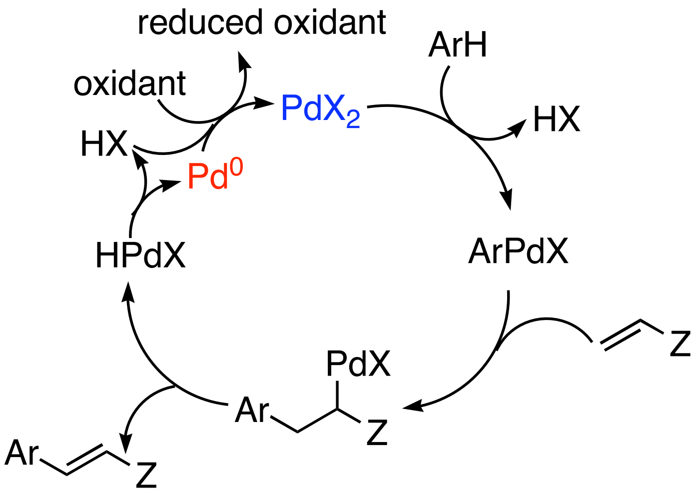
Traditional Mizoroki-Heck Reaction:





Dehydrogenative Heck Reaction:

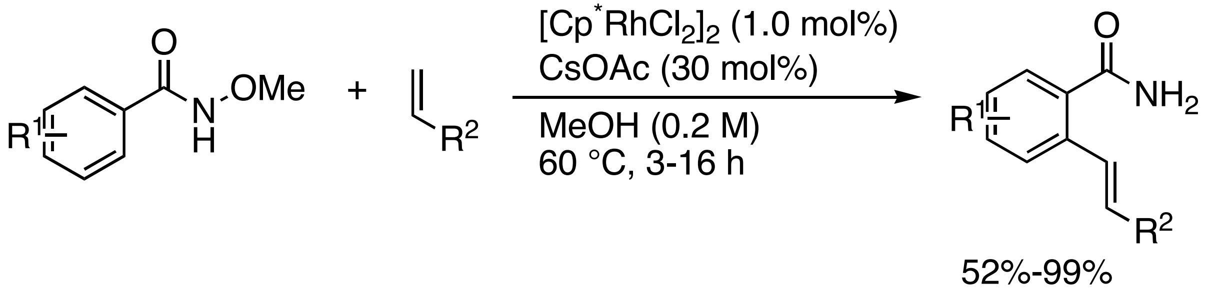




Bras, J. L.; Muzart, J. *Chem. Rev.* **2011,** *111,* 1170-1214.

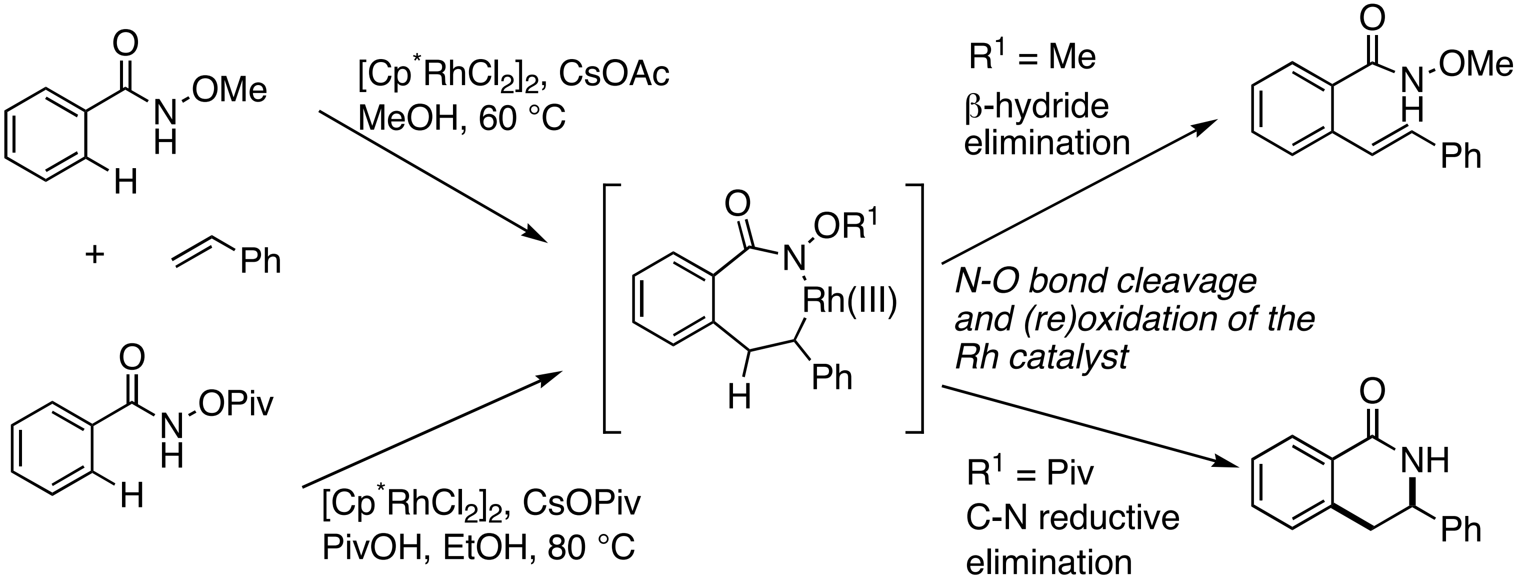
Rh(III)-Mediated C-H Olefination

Use of an oxidizing directing group:



$[Cp^*RhCl_2]_2$ (1.0 mol%)
CsOAc (30 mol%)
MeOH (0.2 M)
60 °C, 3-16 h

52%-99%



$[Cp^*RhCl_2]_2$, CsOAc
MeOH, 60 °C

$[Cp^*RhCl_2]_2$, CsOPiv
PivOH, EtOH, 80 °C

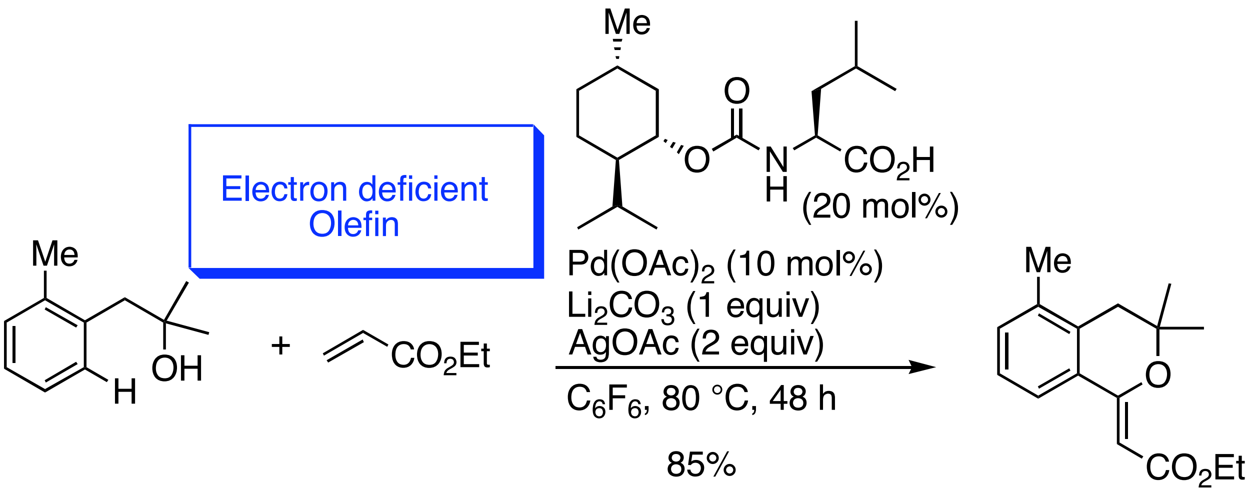
R^1 = Me
β-hydride
elimination

N-O bond cleavage
and (re)oxidation of the
Rh catalyst

R^1 = Piv
C-N reductive
elimination

Rakshit, S.; Grohmann, C.; Besset, T.; Glorius, F. *J. Am. Chem. Soc.* **2011,** *133,* 2350-2353.

Inspiration for the Title Paper

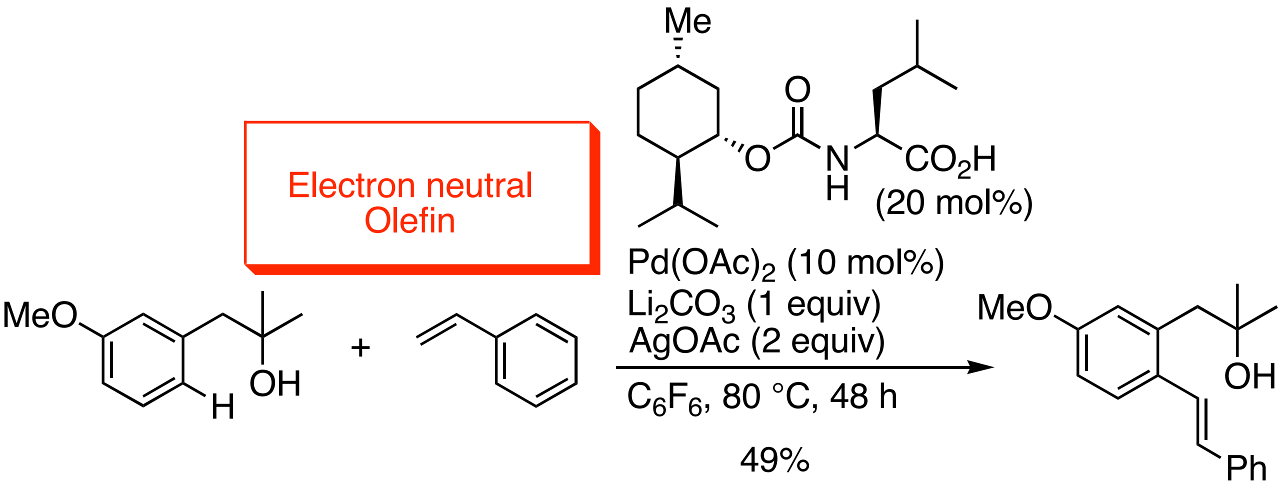


Electron deficient Olefin

(20 mol%)

$Pd(OAc)_2$ (10 mol%)
Li_2CO_3 (1 equiv)
AgOAc (2 equiv)
C_6F_6, 80 °C, 48 h

85%



Electron neutral Olefin

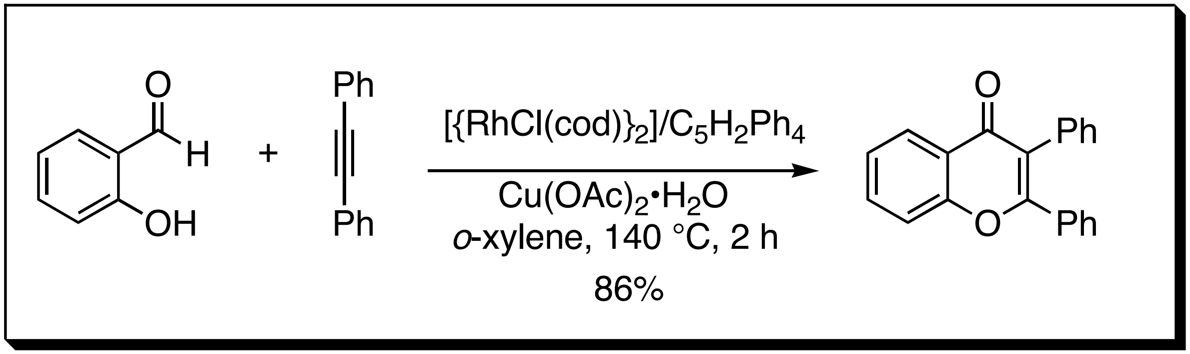
(20 mol%)

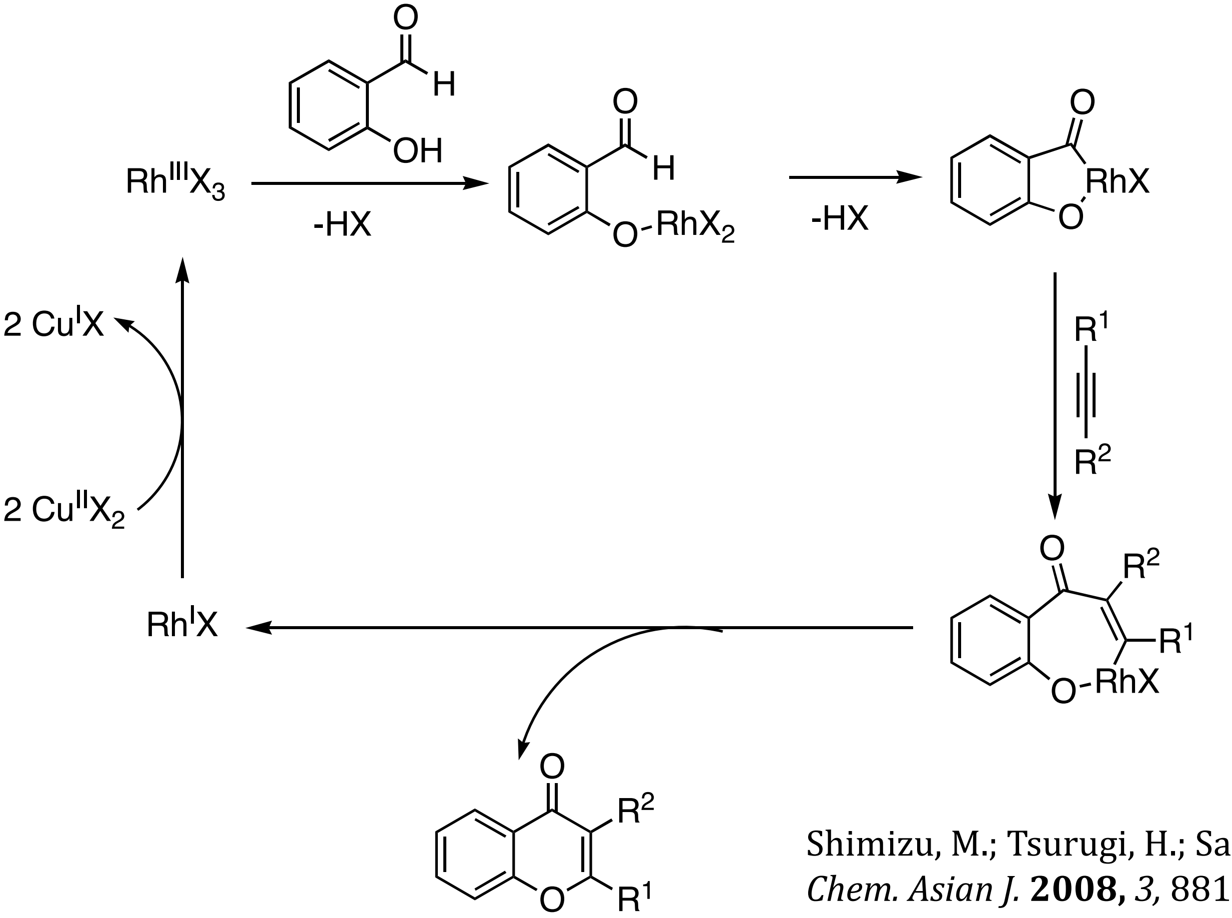
$Pd(OAc)_2$ (10 mol%)
Li_2CO_3 (1 equiv)
AgOAc (2 equiv)
C_6F_6, 80 °C, 48 h

49%

Lu, Y.; Wang, D.-H.; Engle, K. M.; Yu, J.-Q. *J. Am. Chem. Soc.* **2010,** *132,* 5916-5921

Rh-Catalyzed Synthesis of Chromones

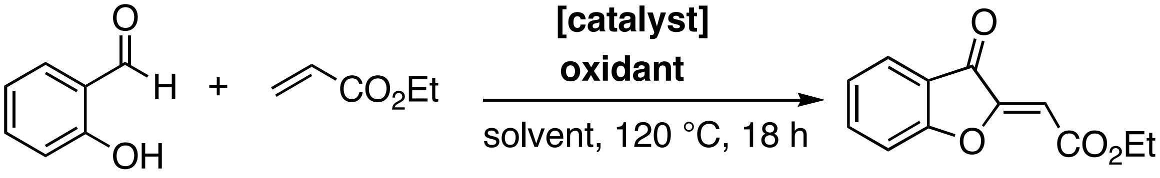




Shimizu, M.; Tsurugi, H.; Satoh, T.; Miura, M.
Chem. Asian J. **2008,** *3,* 881-886.

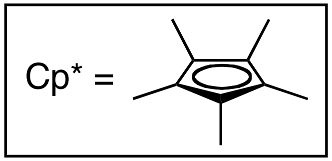
Rh(III)-Catalyzed DHR of Salicylaldehydes

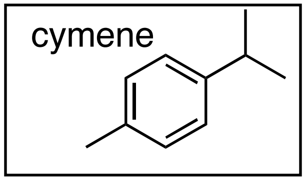
Catalyst and Oxidant Optimization:



Entry	Catalyst (mol%)	Oxidant (equiv)	Solvent	Yield
1	$[RuCl_2(p\text{-cymene})]_2$ (2.5)	$Cu(OAc)_2$ (2)	*t*-amylOH	0%
2	$[Cp^*RhCl_2]_2$ (2.5)	$Cu(OAc)_2$ (2)	*t*-amylOH	12%
3	$[Cp^*RhCl_2]_2$ (2.5)	$Cu(OAc)_2$ (4)	*t*-amylOH	48%
4[a]	$[Cp^*RhCl_2]_2$ (2.5)	$Cu(OAc)_2$ (4)	DCE	76%

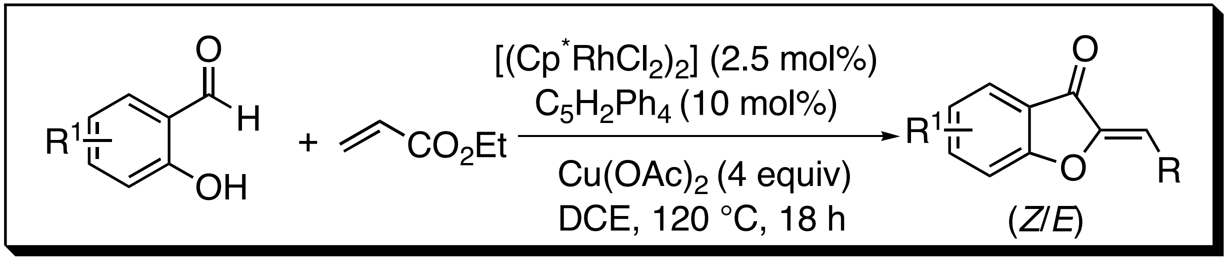
[A] 10 mol% 1,2,3,4-tetraphenyl-1,3-cyclpentadiene was used as a ligand

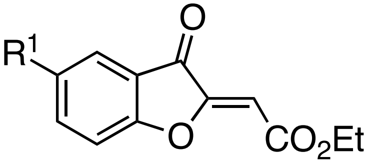




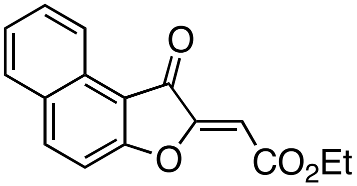
Selected examples from the SI from the Title paper.

Salicylaldehyde Substrate Scope

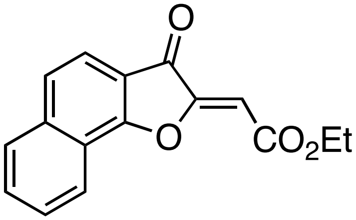




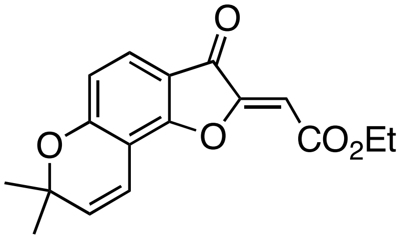
R^1	Yield	*Z/E ratio*	R^1	Yield	*Z/E ratio*
H	76%	98:2	F	70%	98:2
Me	80%	98:2	Cl	62%	96:4
OMe	82%	95:5	Br	70%	95:5
SMe	85%	100:0	I	33%	95:5
NO_2	44%	100:0			
Ph	71%	99:1			
CO_2Me	68%	99:1			



63% (97:3)

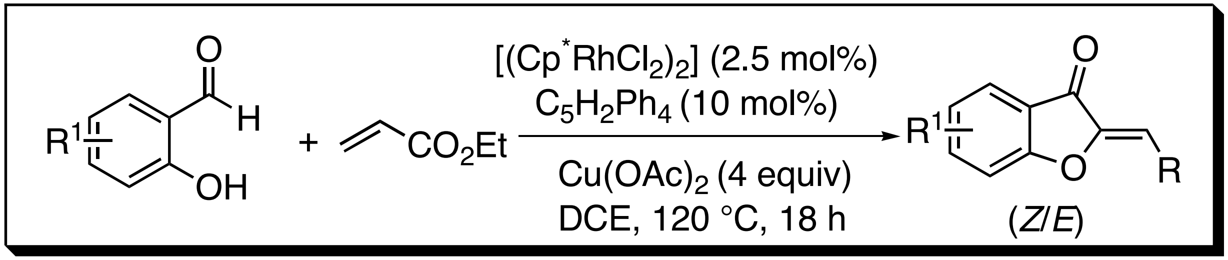


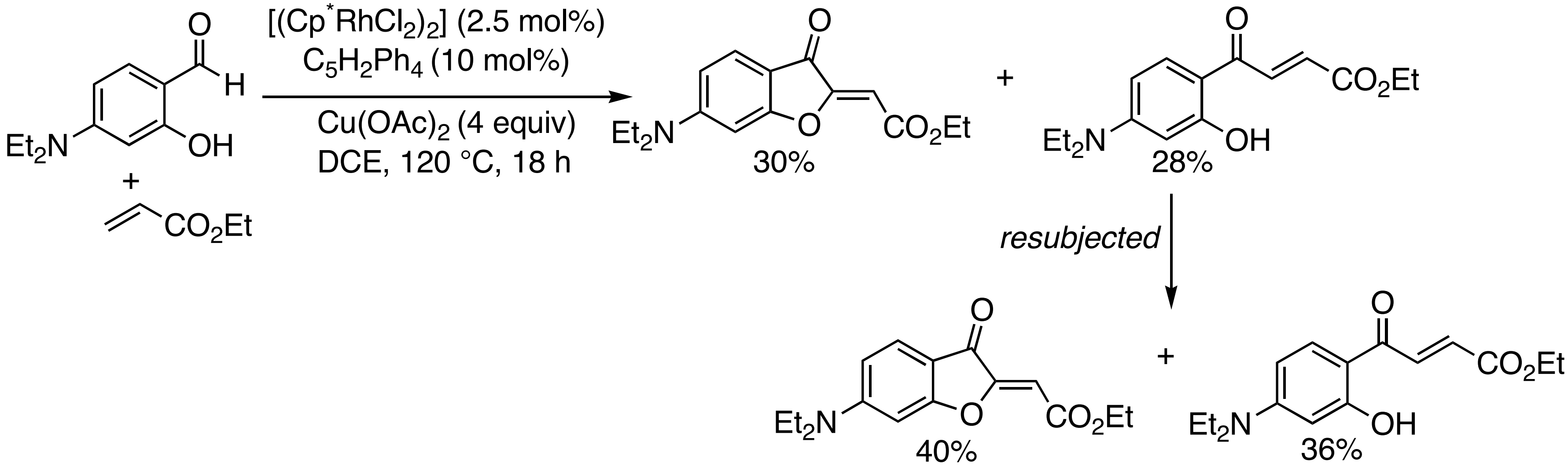
75% (100:0)



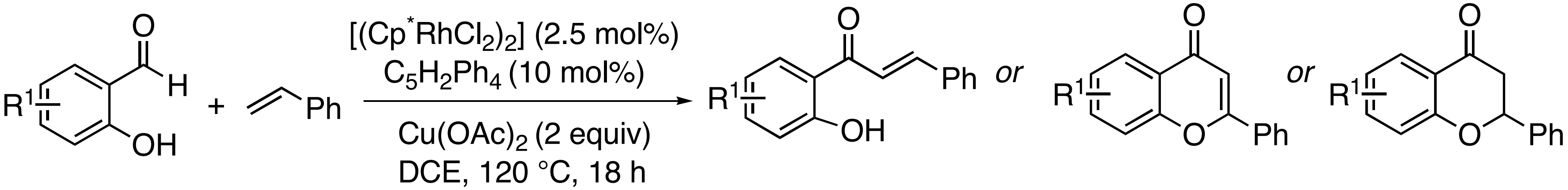
76% (93:7)

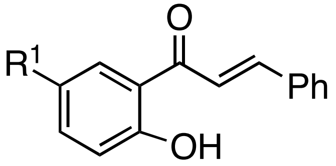
Salicylaldehyde Substrate Scope



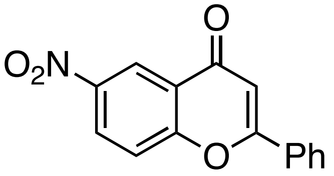


Olefin Substrate Scope

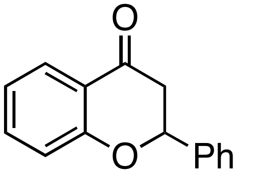




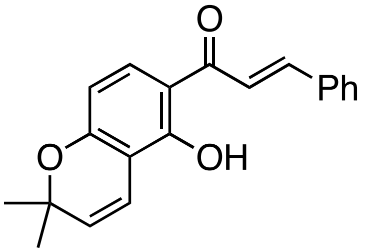
R^1	Yield	
H	66%	
Me	71%	
F	47%	+ < 10% chromone
Cl	43%	+ < 10% chromone
CO_2Me	64%	+ < 10% chromone



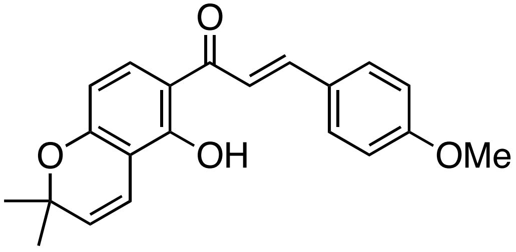
44% (4 equiv $Cu(OAc)_2$



34% (2 equiv Ag_2CO_3 was used as the oxidant)

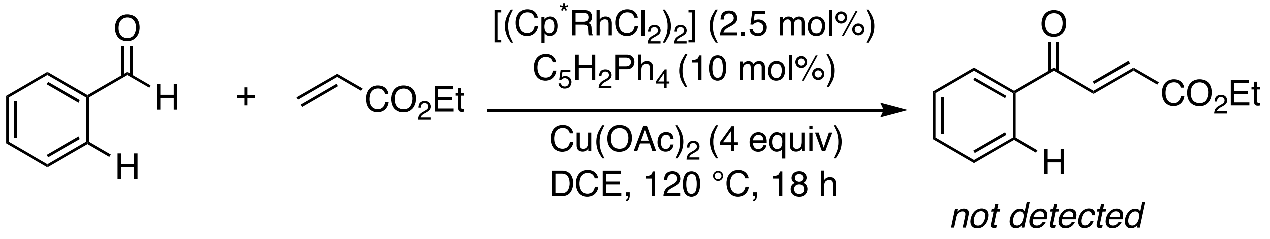


57% (lonchocarpin)



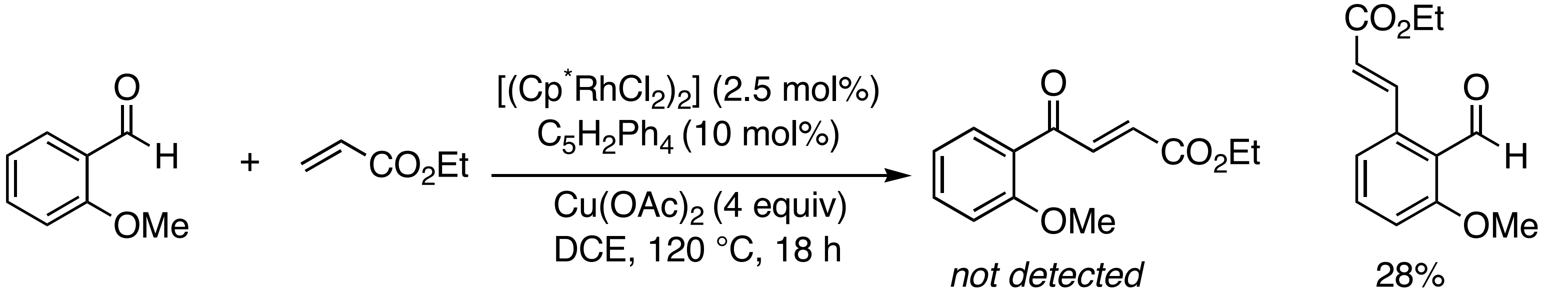
54% (4-methoxylonchocarpin)

Mechanistic Insights



$[(Cp^*RhCl_2)_2]$ (2.5 mol%)
$C_5H_2Ph_4$ (10 mol%)
$Cu(OAc)_2$ (4 equiv)
DCE, 120 °C, 18 h

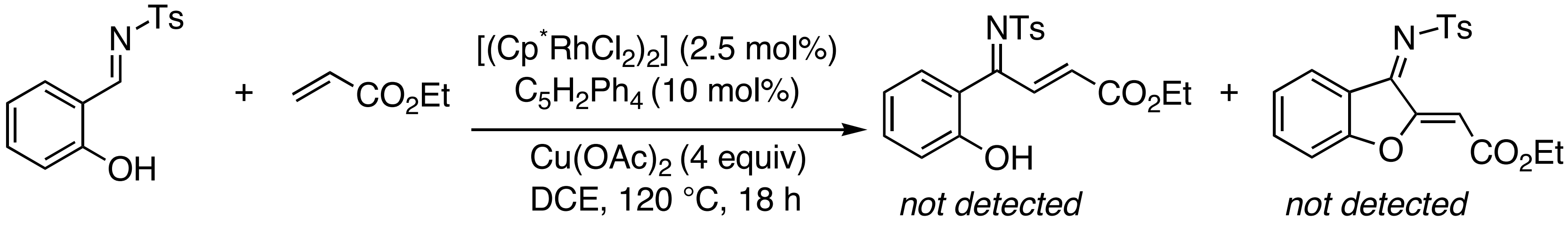
not detected



$[(Cp^*RhCl_2)_2]$ (2.5 mol%)
$C_5H_2Ph_4$ (10 mol%)
$Cu(OAc)_2$ (4 equiv)
DCE, 120 °C, 18 h

not detected

28%

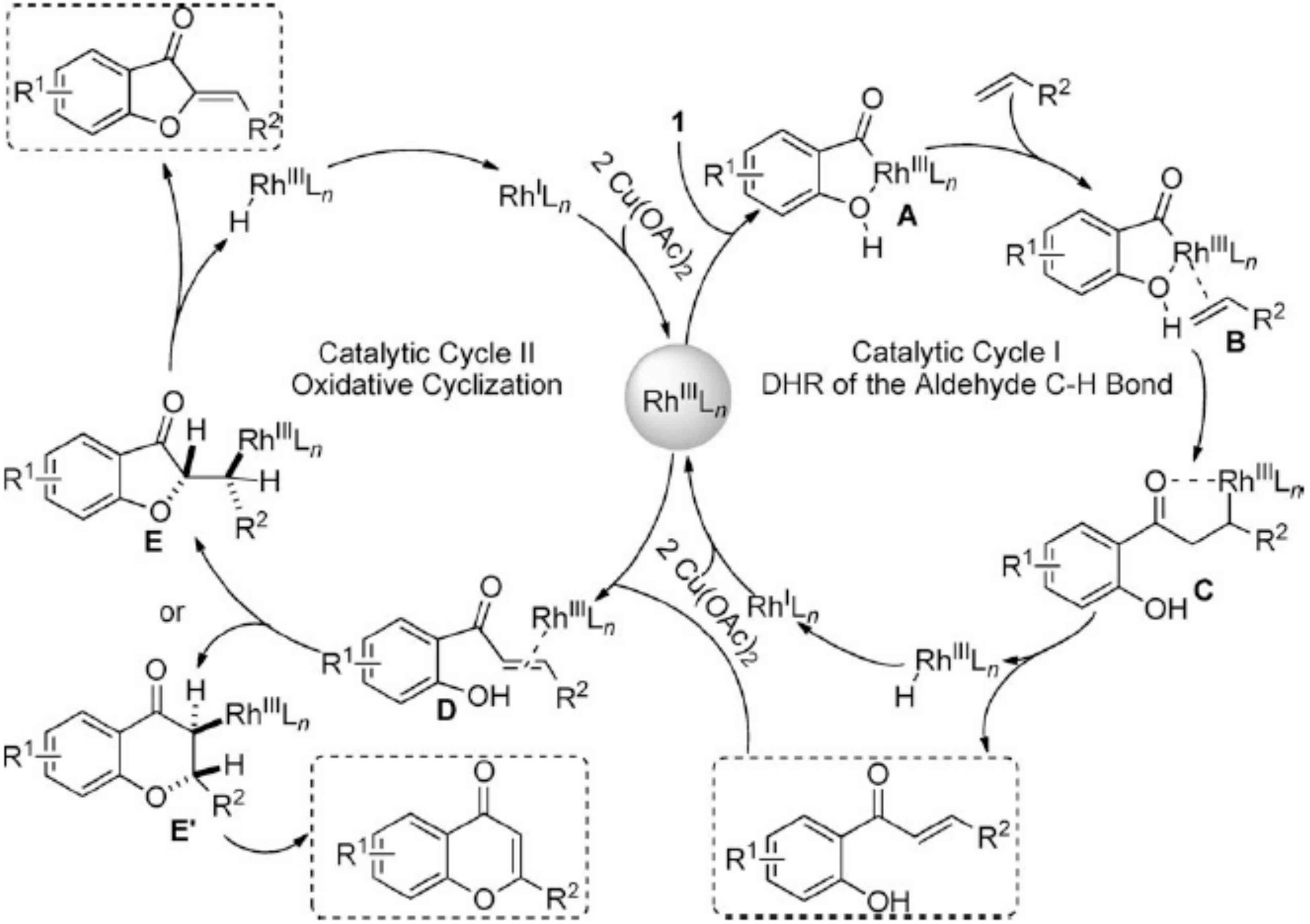


$[(Cp^*RhCl_2)_2]$ (2.5 mol%)
$C_5H_2Ph_4$ (10 mol%)
$Cu(OAc)_2$ (4 equiv)
DCE, 120 °C, 18 h

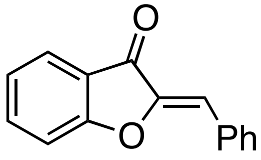
not detected

not detected

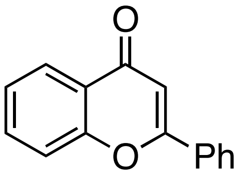
Proposed Mechanism



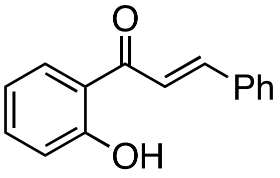
Salicylaldehyde-Based Natural Products



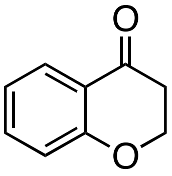
aurone



flavone

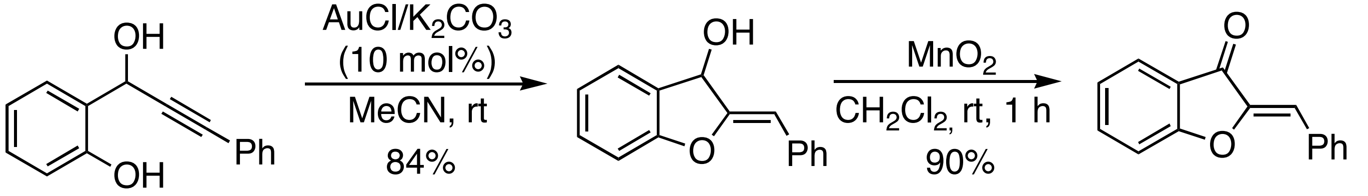


2'-hydroxychalcone

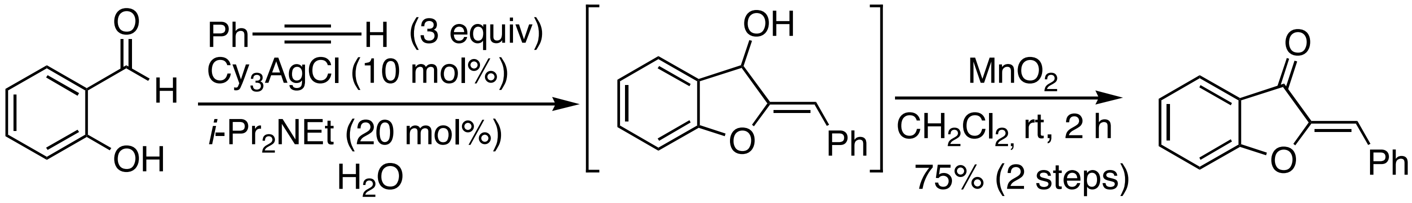


flavanone

Alternative synthesis of aurones:



Harkat, H.; Blanc, A.; Weibel, J.-M.; Pale, P. *J. Org. Chem.* **2008,** *73,* 1620-1623.



Yu, M.; Skouta, R.; Zhou, L.; Jiang, H.-f.; Yao, X.; Li, C.-J. *J. Org. Chem.* **2009,** *74,* 3378-3383.

Summary and Outlook

A catalytic DHR reaction using salicylaldehydes has been developed.

The methodology for forming aurone derivatives may be limited to cases where electron-deficient olefins are used as substrates.

The authors demonstrated the necessity of heteroatom chelation for the reaction to proceed.