Ruthenium(II)-Catalyzed C–H Bond Activation and Functionalization

Dixneuf, et al. *Chem. Rev*. **2012**, *112*, 5879.

Dr. Fanyang Mo

The Dong Group

Dec. 12, 2012

Why Ruthenium???

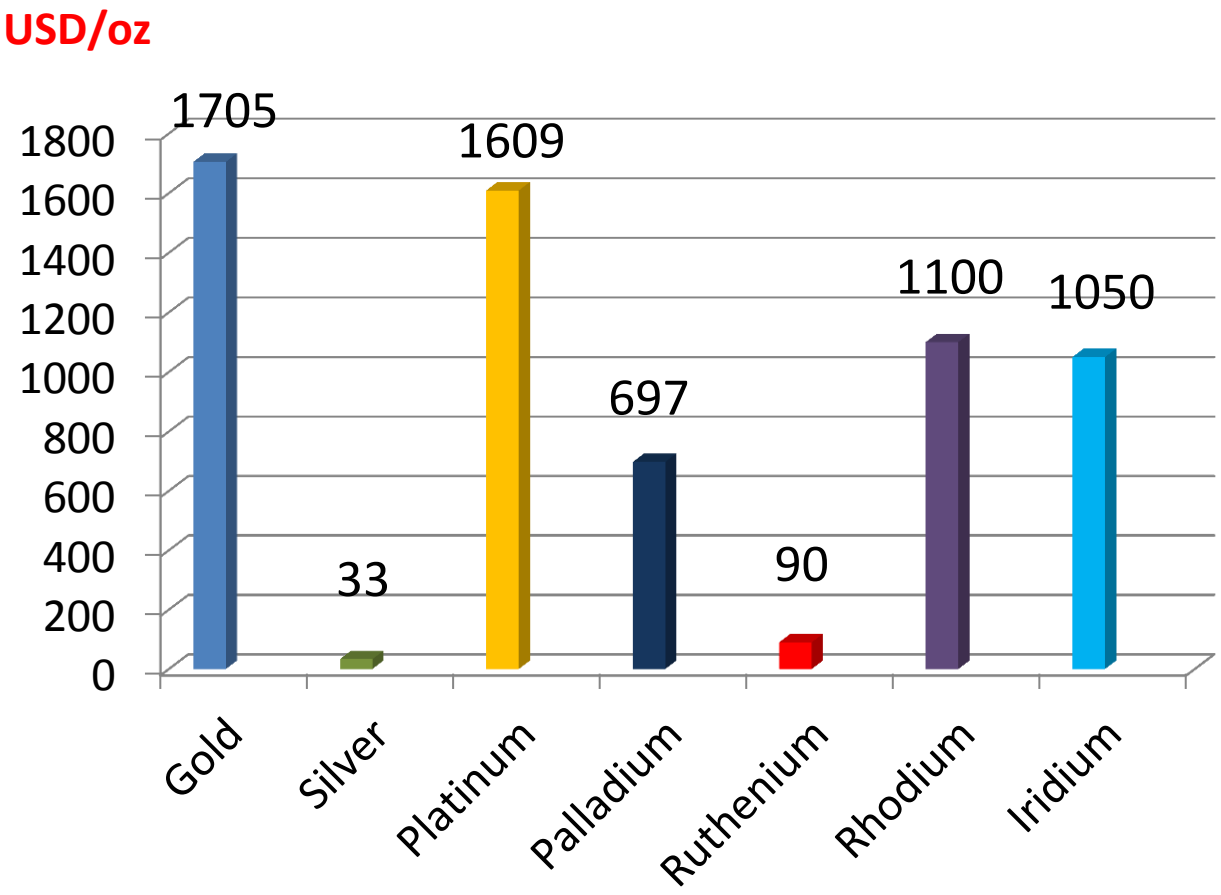
Reason 1: Previous group seminar topics.

Metal	Presenter
Pd	Zack, Tao and Momo
Rh	Alpay, Huang, Rachel, Brandon and Momo
Ir	Wallace, Hayemin and Momo

Reason 2: The papers we have published.

Metal	Papers published
Pd	1 JACS and 1 ACIE
Rh	2 JACS and 1 ACIE

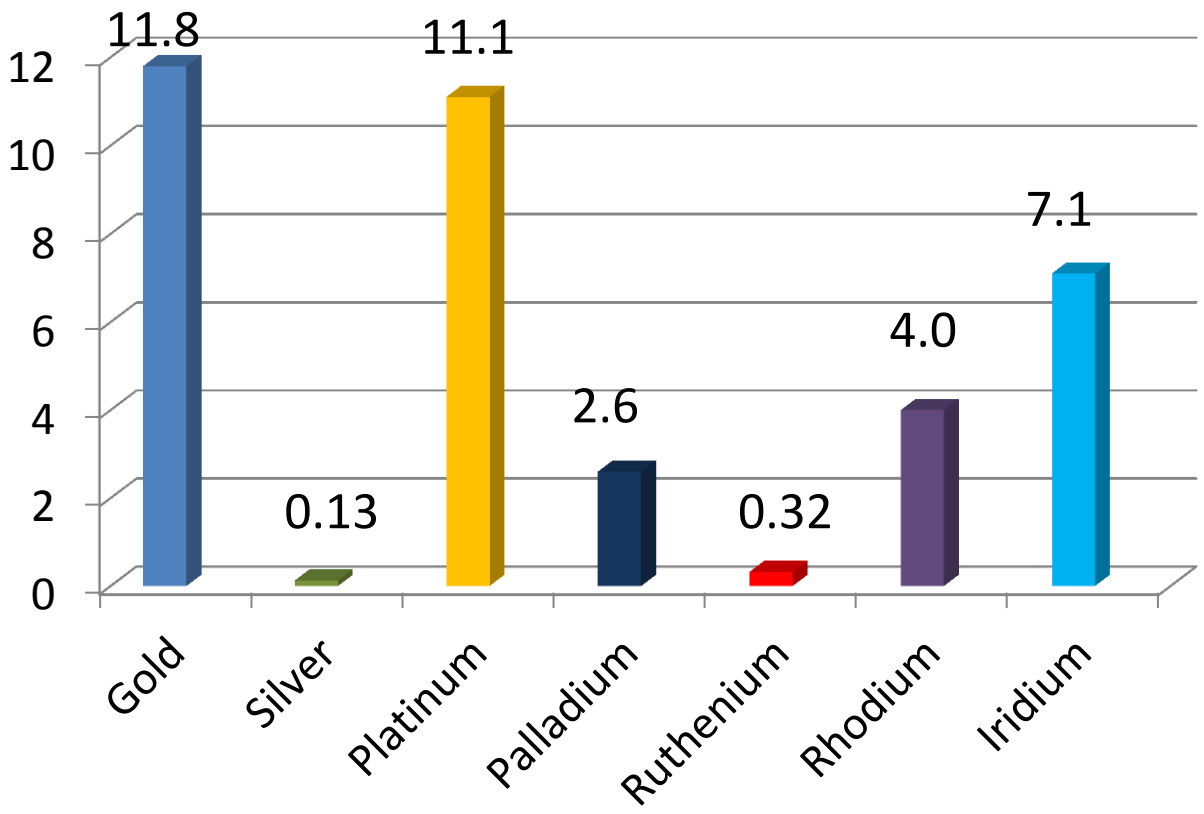
The price for metals on Dec. 7th, 2012



Source: http://www.infomine.com/investment/metal-prices/

The price for metals on Dec. 7, 2012

USD / mmol



Cobalt???

10.7 USD / lb

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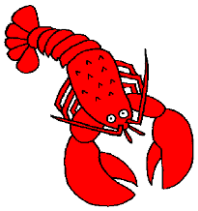

Source: http://www.infomine.com/investment/metal-prices/

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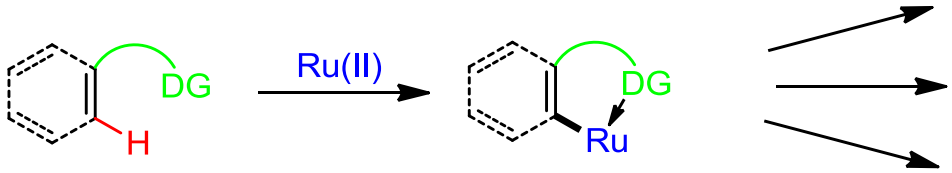
   - ➢ Acylation
   - ➢ Alkenylation
   - ➢ Others
3. Summary
4. Acknowledgement

Of (Hetero)Arenes and Alkene



☆ **Question 1**

Four different mechanisms for C–H activation

oxidative addition

(i) L_nM + H–R ⇌ $L_nM(H)(R)$ → $[L_nM(H)\cdots R]^{\ddagger}$ → $L_nM(H)(R)$

Low valent late-transition-metals

σ-bond metathesis

(ii) $L_nM(R')$ + H–R → $[L_nM(R')(H)\cdots R]^{\ddagger}$ → $L_nM(R)$ + R'–H

Early transition metals

electrophilic substitution

(iii) $L_nM^{\oplus}(X)$ + H–R → $L_nM(X)(H)(R)^{\oplus}$ → $L_nM^{\oplus}(R)$ + X–H

High valent late-transition-metals

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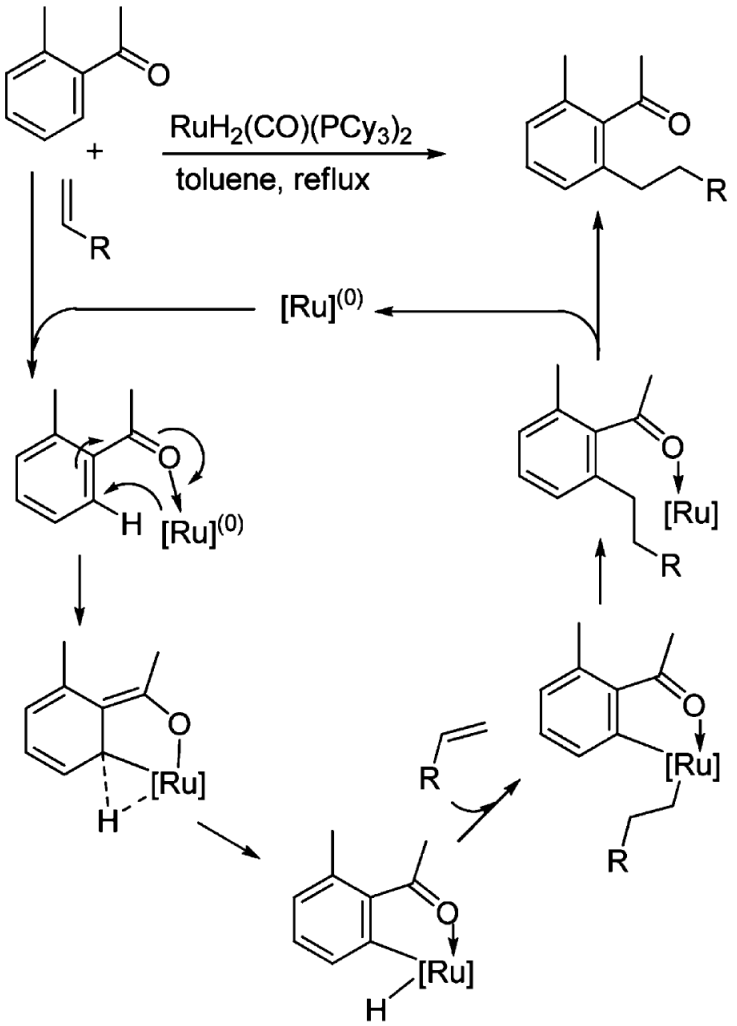
base-assisted metalation

(iv) $L_nM(O_2CR')$ + H–R → $[L_nM(O_2CR')\cdots H\cdots R]^{\ddagger}$ → $L_nM(R)(O_2CR'H)$

High valent late-transition-metals

Ru(0) catalyzed C−H activation (*1, 2, 3, 4*)

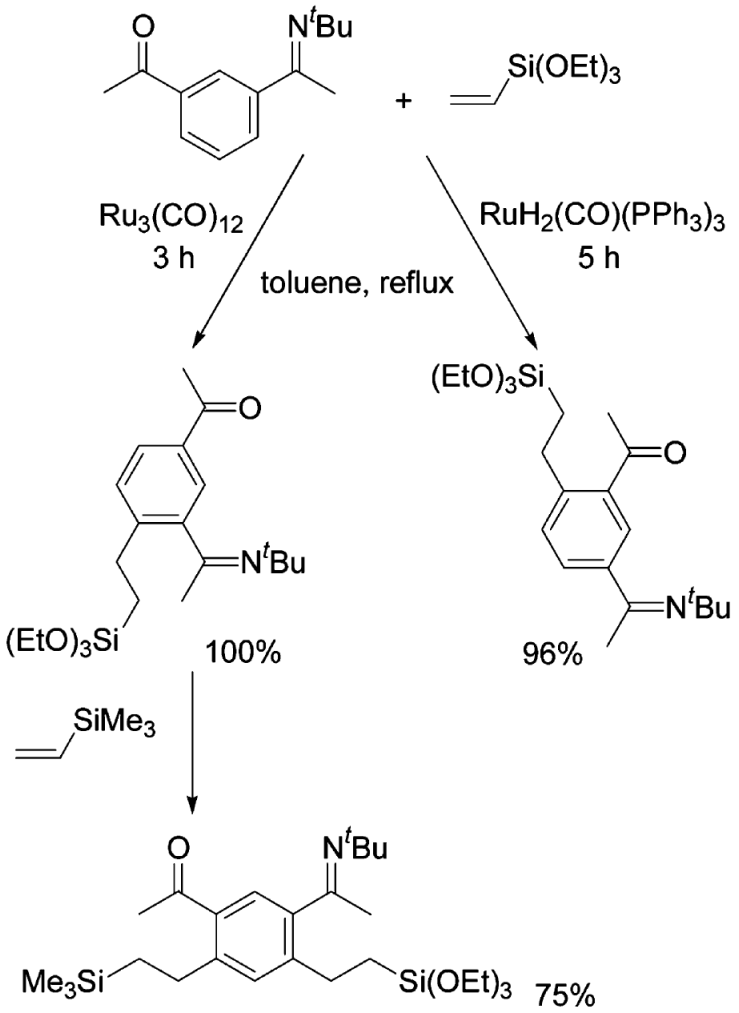
1. Seminal paper



Murai, S.; Kakiuchi, F.; Sekine, S.; Tanaka, Y.; Kamatani, A.; Sonoda, M.; Chatani, N. *Nature* **1993**, *366*, 529.

Ru(0) catalyzed C−H activation

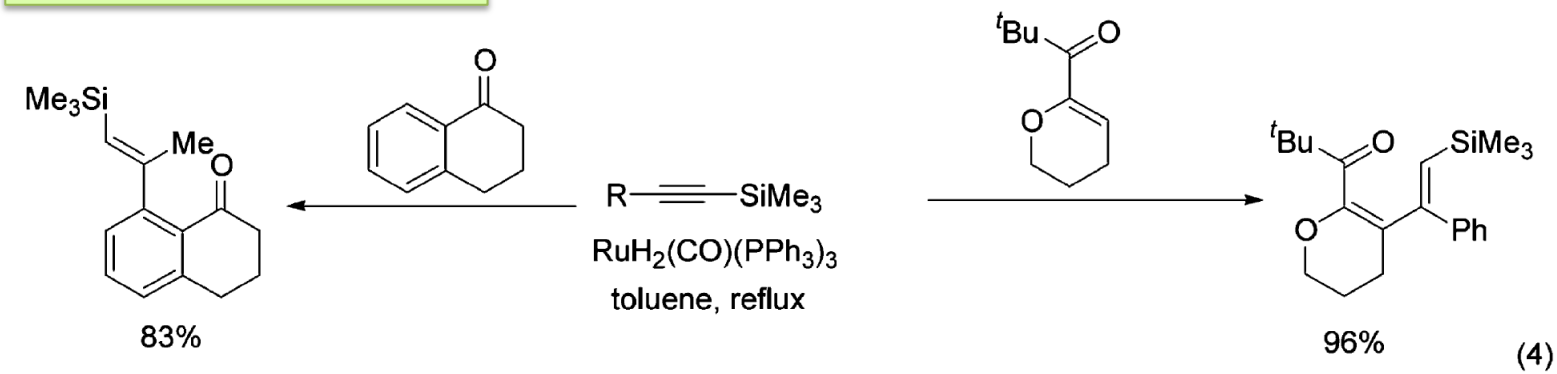
2. Catalysts prefer their own directing group.



Kakiuchi, F.; Sato, T.; Tsujimoto, T.; Yamauchi, M.; Chatani, N.; Murai, S. *Chem. Lett*. **1998**, *27*, 1053.

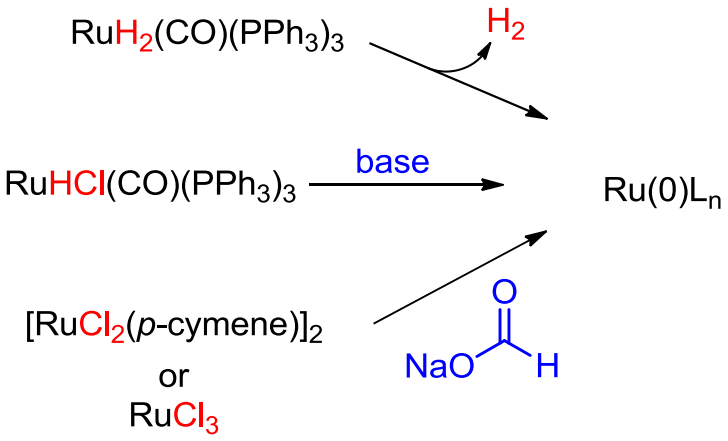
Ru(0) catalyzed C−H activation

3. Alkynes also work



a) Kakiuchi, F.; Uetsuhara, T.; Tanaka, Y.; Chatani, N.; Murai, S. *J. Mol. Catal. A: Chem*. **2002**, *182*, 511.
b) Kakiuchi, F.; Tanaka, Y.; Sato, T.; Chatani, N.; Murai, S. *Chem. Lett*. **1995**, 679.

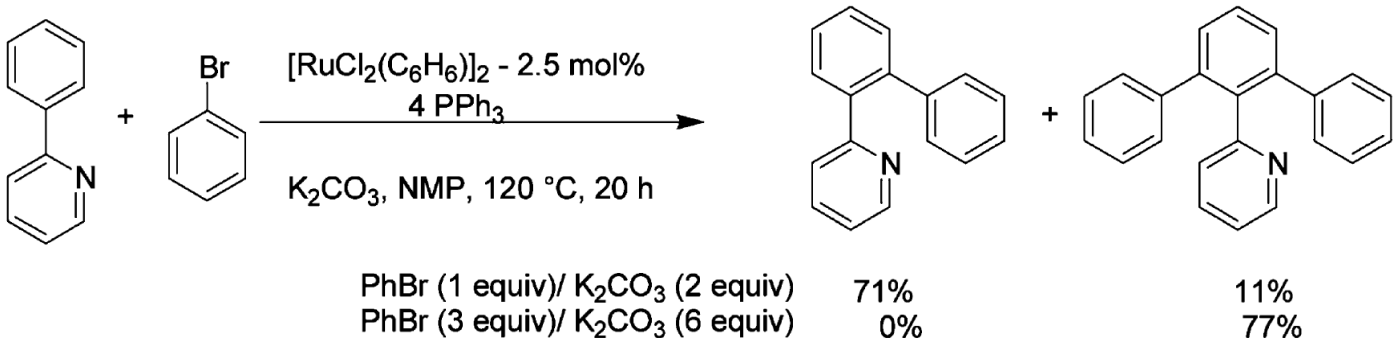
4. How to generate Ru(0)



Ru(II) catalyzed C−H activation

1) Arylation

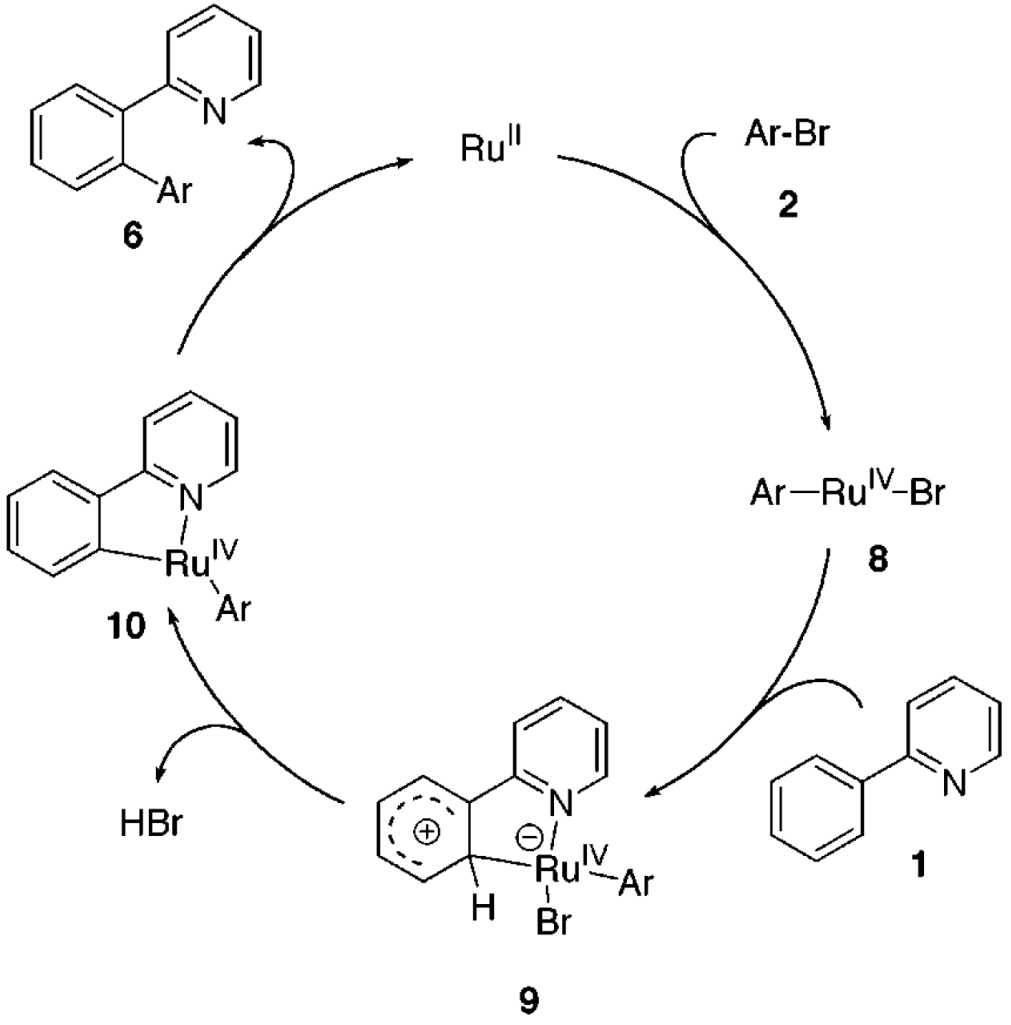
The first example was reported by Oi and Inoue in 2001. *Using aryl halides as both arylation reagents and oxidants.*



Oi, S.; Fukita, S.; Hirata, N.; Watanuki, N.; Miyano, S.; Inoue, Y. *Org. Lett*. **2001**, *3*, 2579.

Ru(II) catalyzed C−H activation

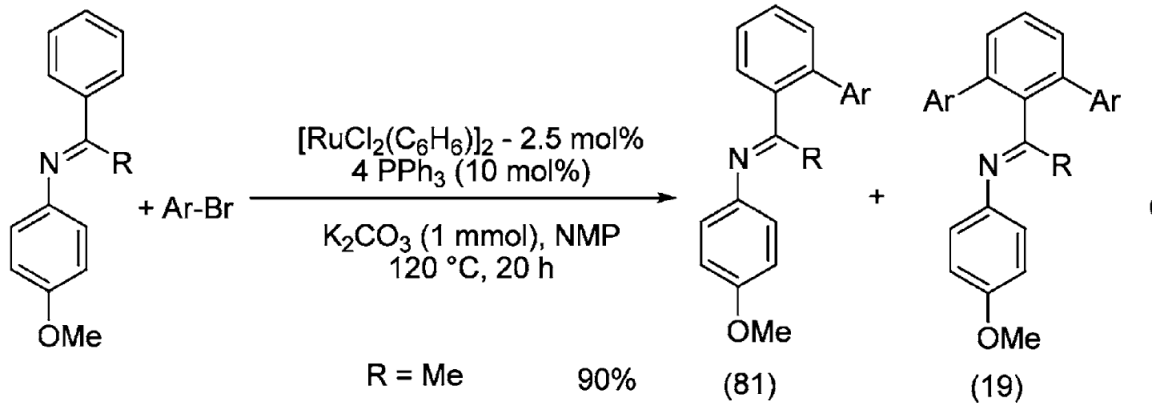
1) Arylation



Oi, S.; Fukita, S.; Hirata, N.; Watanuki, N.; Miyano, S.; Inoue, Y. *Org. Lett.* **2001**, *3*, 2579.

Ru(II) catalyzed C−H activation

1) Arylation



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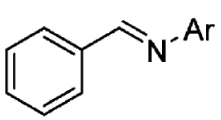	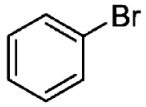	1.2 equiv	52%	10:90
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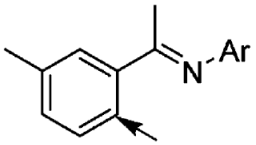
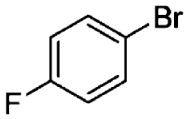
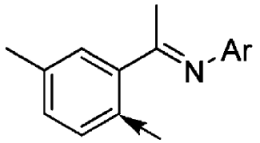
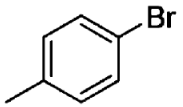
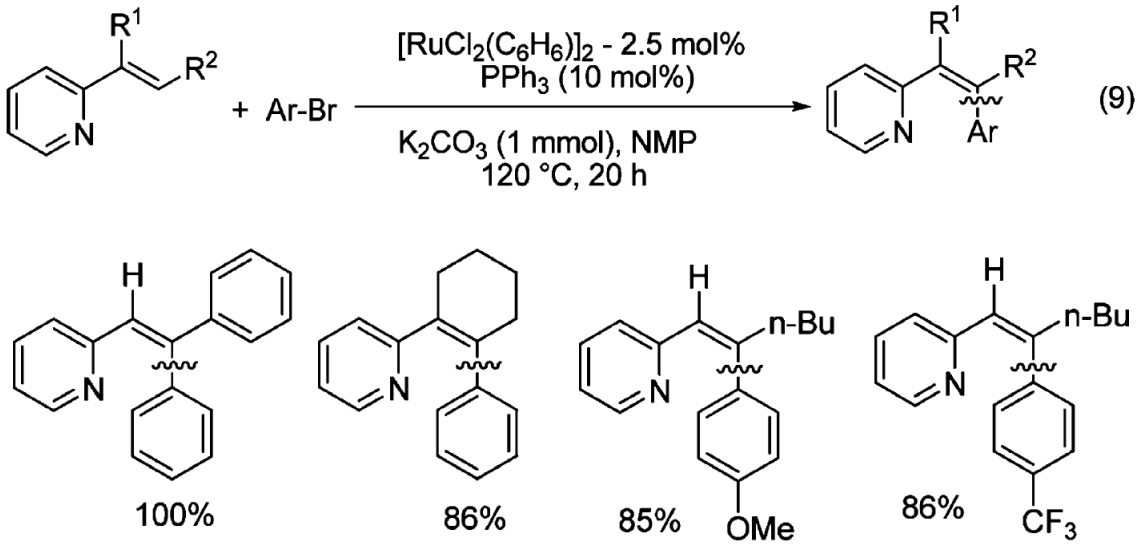
			85	100:0
			74	100:0

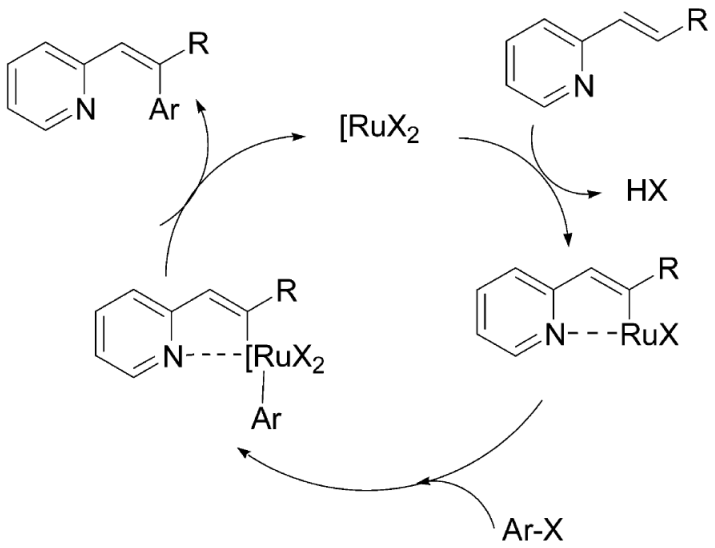
Ar = 4- MeO-C_6H_4

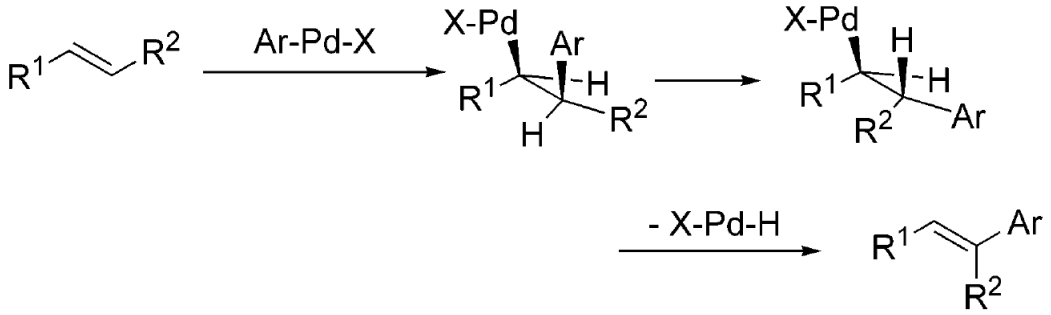
Oi, S.; Ogino, Y.; Fukita, S.; Inoue, Y. *Org. Lett*. **2002**, *4*, 1783.

Ru(II) catalyzed C−H activation

1) Arylation



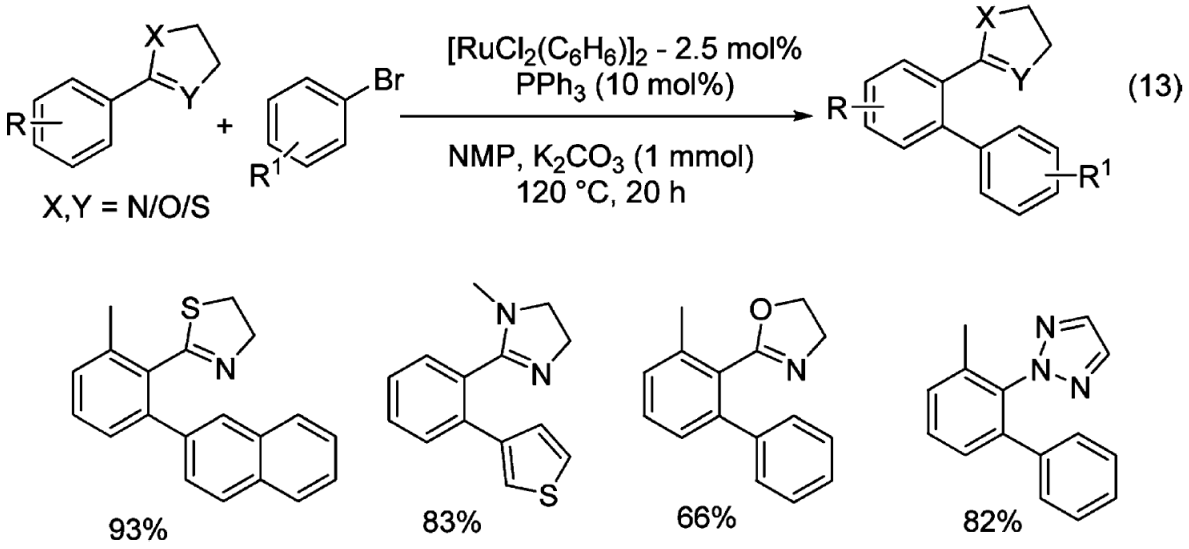




Oi, S.; Sakai, K.; Inoue, Y. *Org. Lett*. **2005**, *7*, 4009.

Ru(II) catalyzed C−H activation

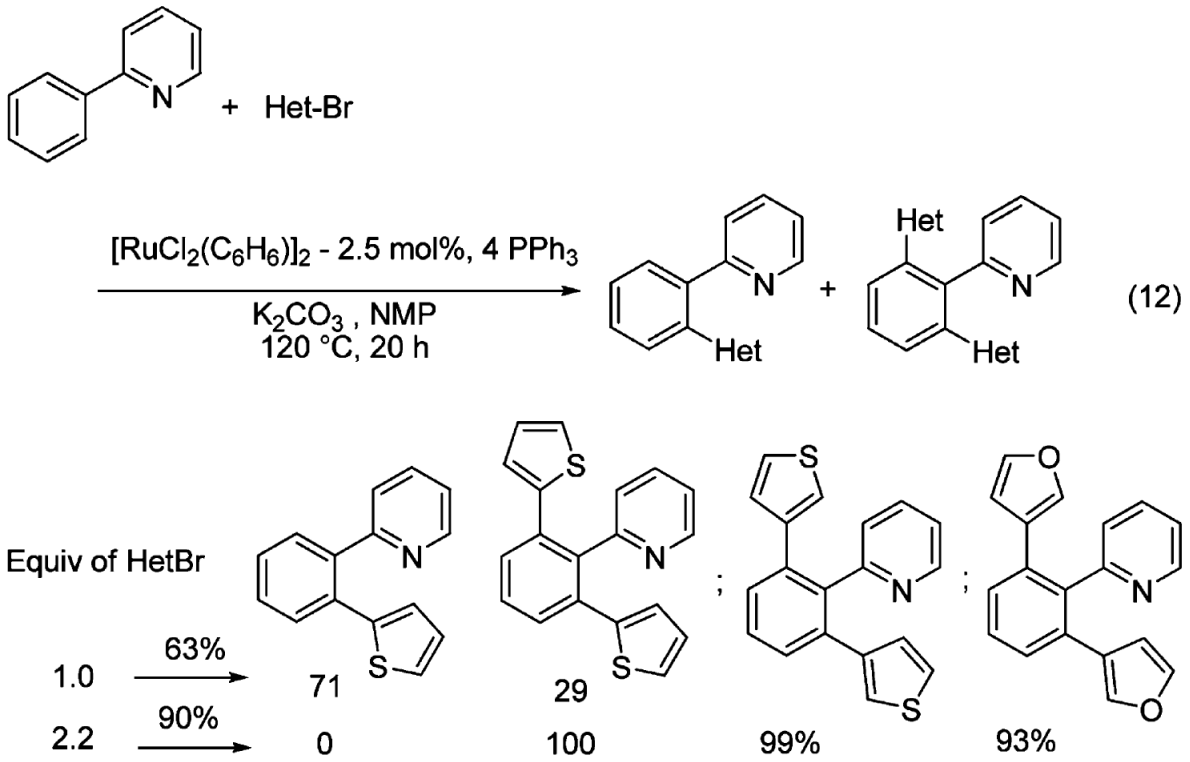
1) Arylation



Oi, S.; Sasamoto, H.; Funayama, R.; Inoue, Y. *Chem. Lett*. **2008**, *37*, 994.

Ru(II) catalyzed C−H activation

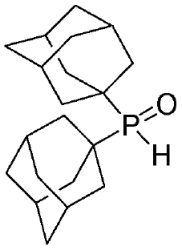
1) Arylation

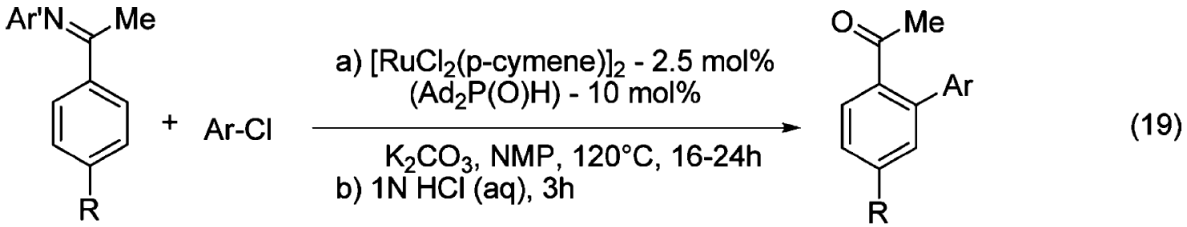


Oi, S.; Funayama, R.; Hattori, T.; Inoue, Y. *Tetrahedron* **2008**, *64*, 6051.

Ru(II) catalyzed C–H activation

1) Arylation





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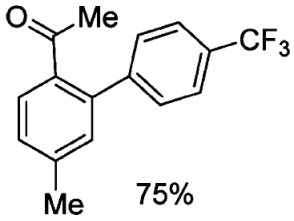

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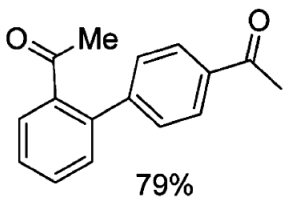

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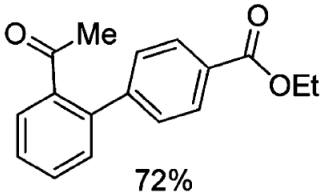

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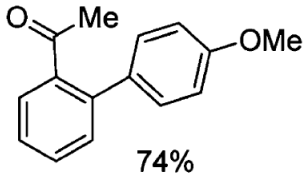

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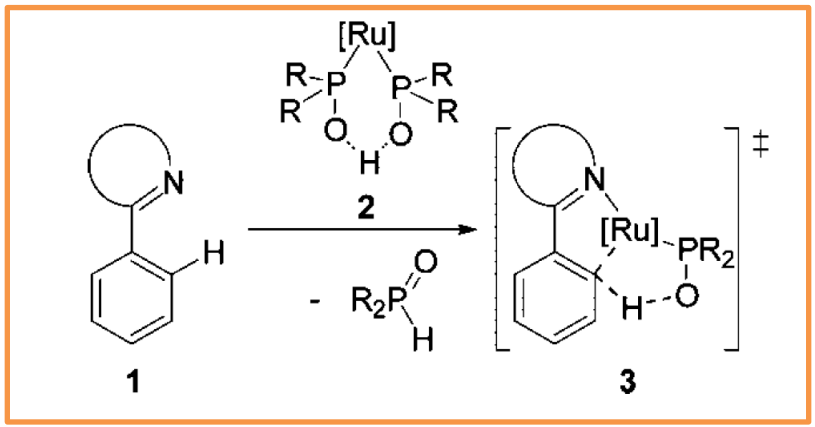
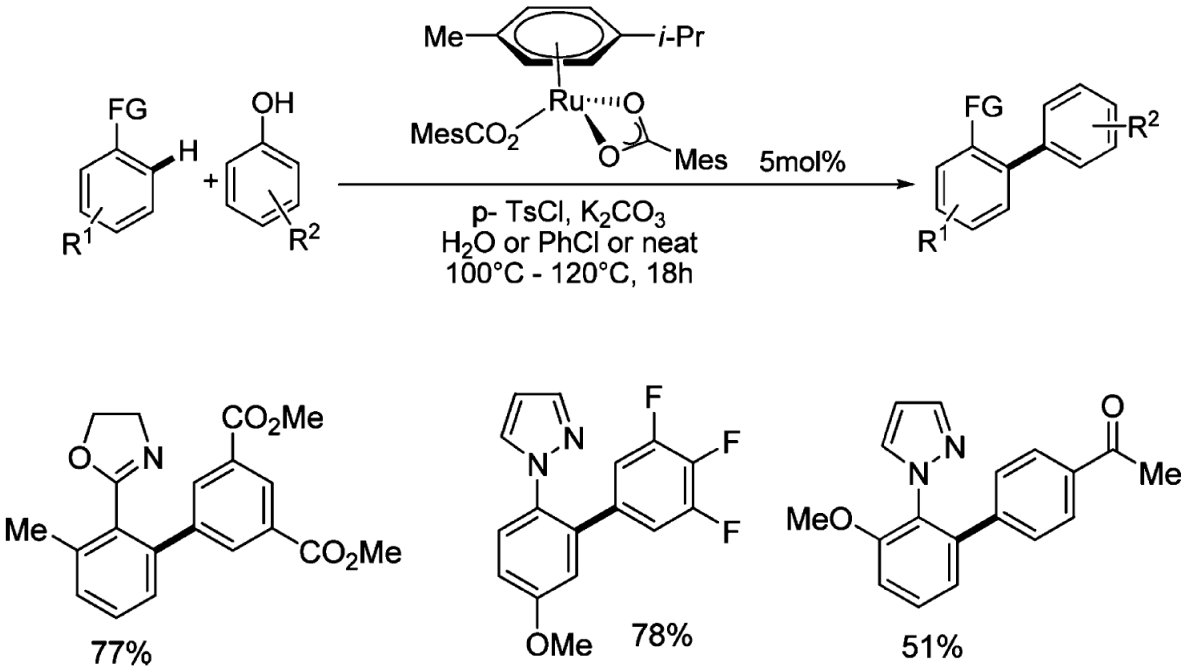


Ackermann, L. *Org. Lett*. **2005**, *7*, 3123.

Ru(II) catalyzed C−H activation

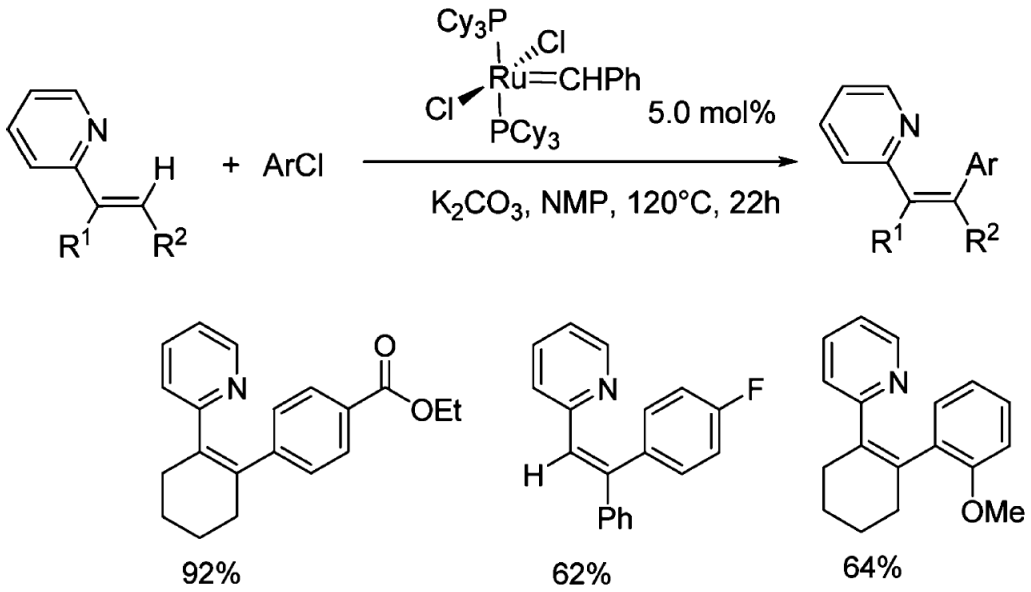
1) Arylation



Ackermann, L.; Pospech, J.; Potukuchi, H. K. *Org. Lett*. **2012**, *14*, 2146.

Ru(II) catalyzed C−H activation

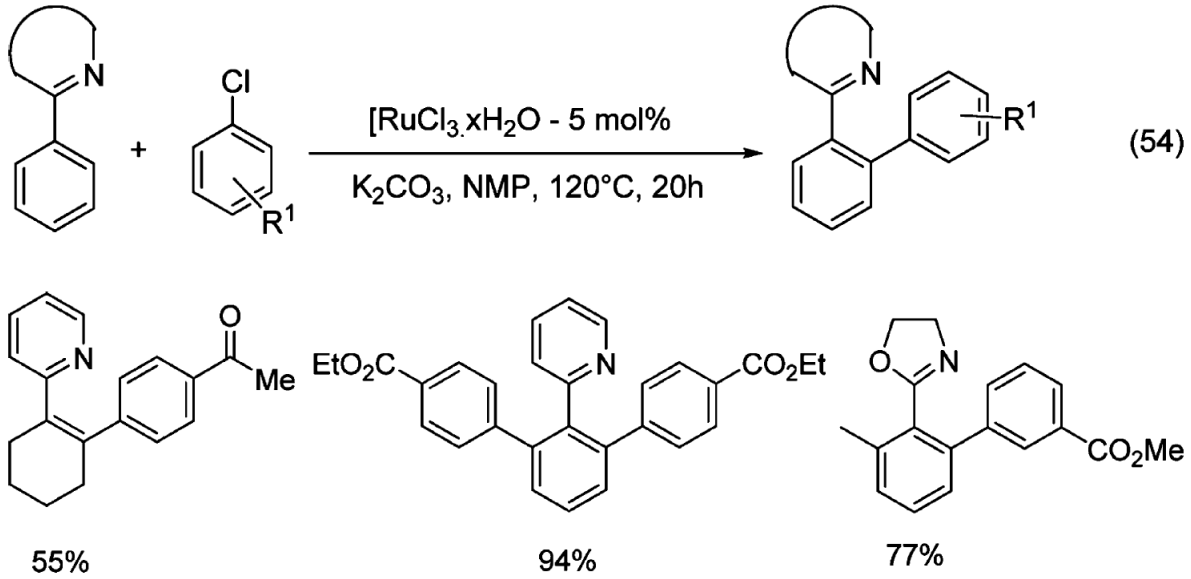
1) Arylation



Ackermann, L.; Born, R.; Alvarez-Bercedo, P. *Angew. Chem., Int. Ed*. **2007**, *46*, 6364.

Ru(II) catalyzed C−H activation

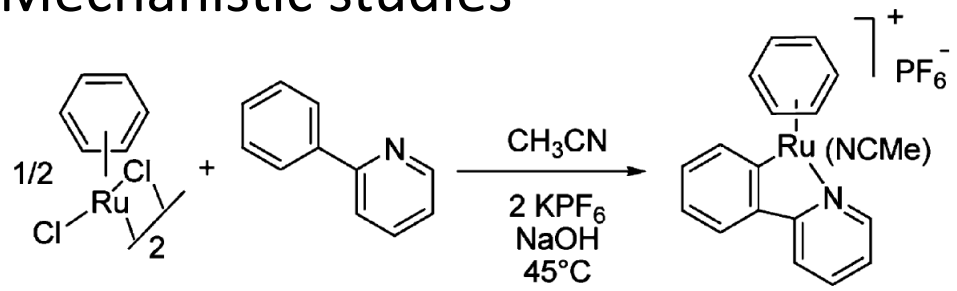
1) Arylation



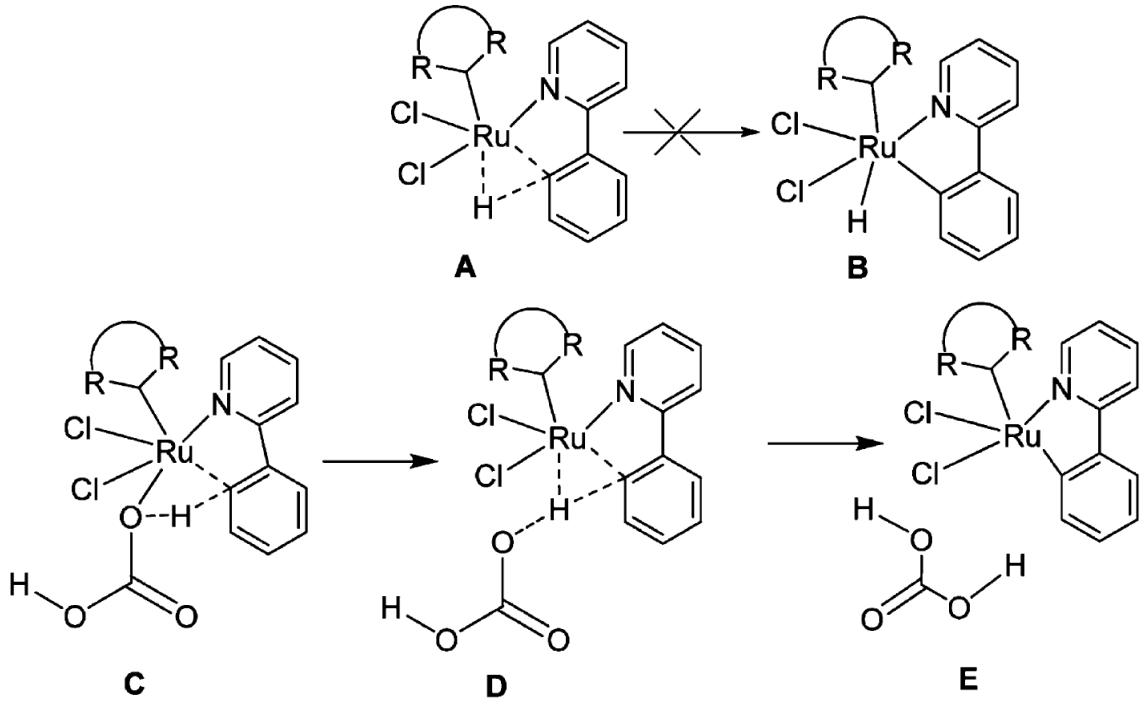
(a) Ackermann, L.; Althammer, A.; Born, R. *Tetrahedron* **2008**, *64*, 6115.
(b) Ackermann, L.; Althammer, A.; Born, R. *Synlett* **2007**, 2833.

Ru(II) catalyzed C−H activation

1) Arylation---Mechanistic studies



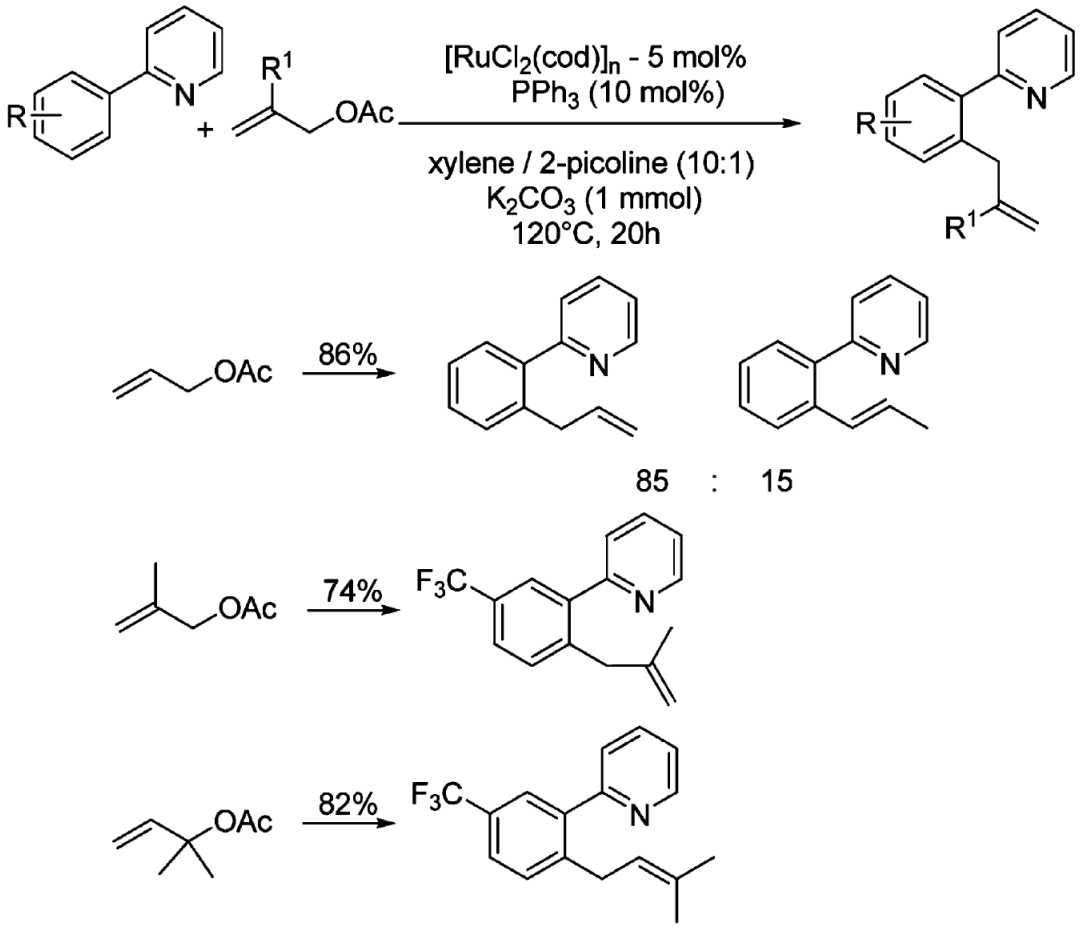
Fernandez, S.; Pfeffer, M.; Ritleng, V.; Sirlin, C. *Organometallics* **1999**, *18*, 2390.



Dixneuf, P. H. and *et al*. *J. Am. Chem. Soc*. **2008**, *130*, 1156.

Ru(II) catalyzed C−H activation

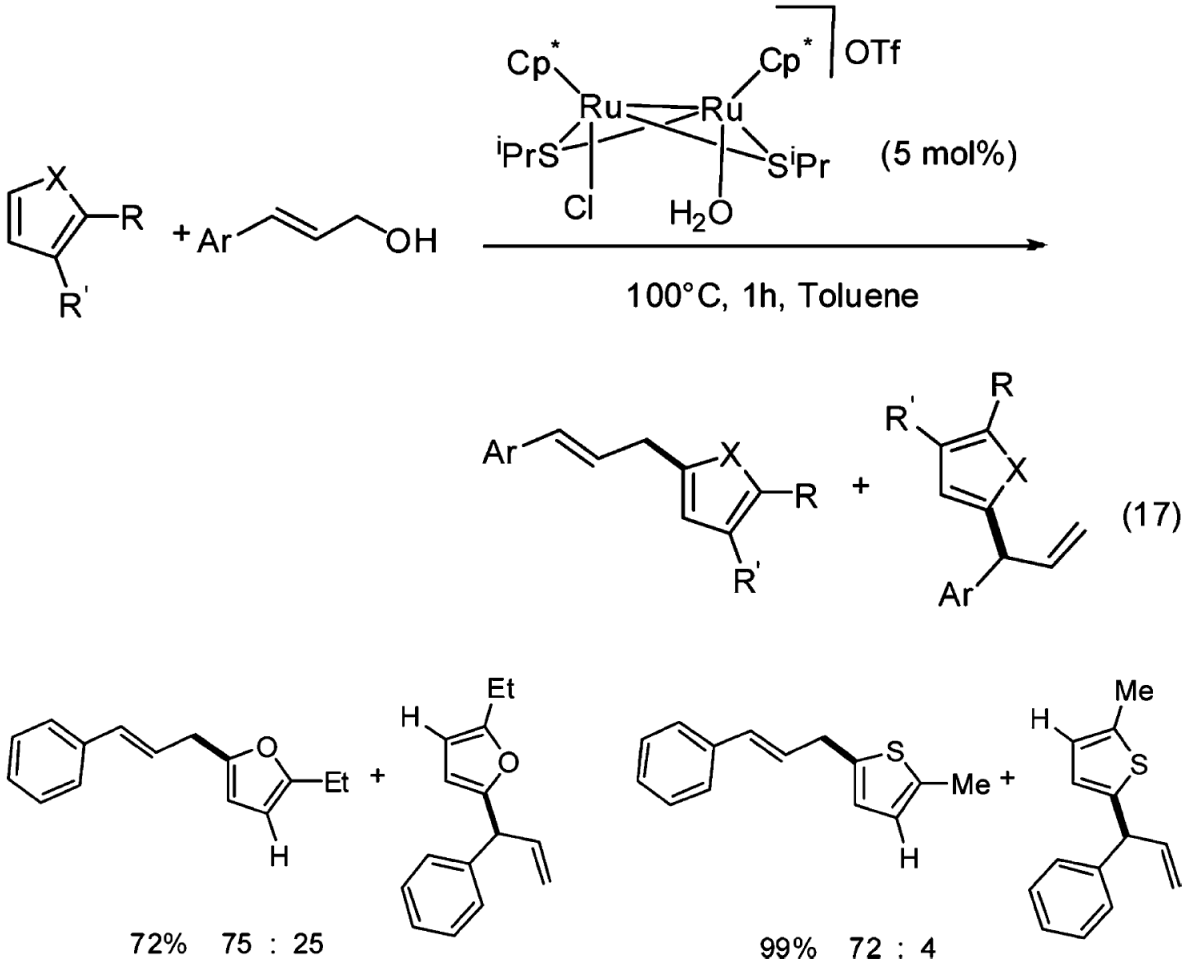
2) Allylation



Oi, S.; Tanaka, Y.; Inoue, Y. *Organometallics* **2006**, *25*, 4773.

Ru(II) catalyzed C−H activation

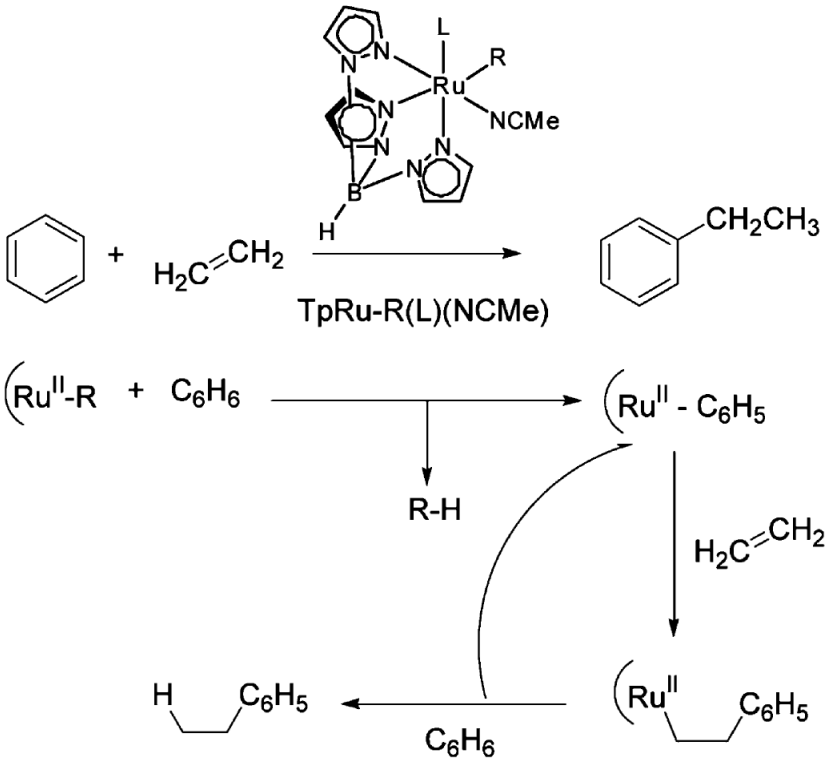
2) Allylation



Onodera, G.; Imajima, H.; Yamanashi, M.; Nishibayashi, Y.; Hidai, M.; Uemura, S. *Organometallics* **2004**, *23*, 5841.

Ru(II) catalyzed C−H activation

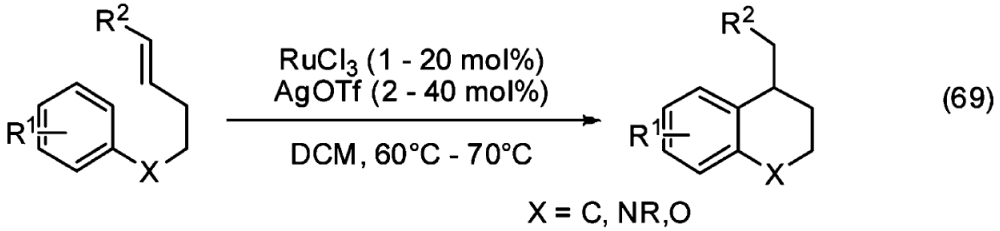
3) Alkylation with alkenes



Foley, N. A.; Lail, M.; Lee, J. P.; Gunnoe, T. B.; Cundari, T. R.; Petersen, J. L. *J. Am. Chem. Soc*. **2007**, *129*, 6765.

Ru(II) catalyzed C–H activation

3) Alkylation with alkenes



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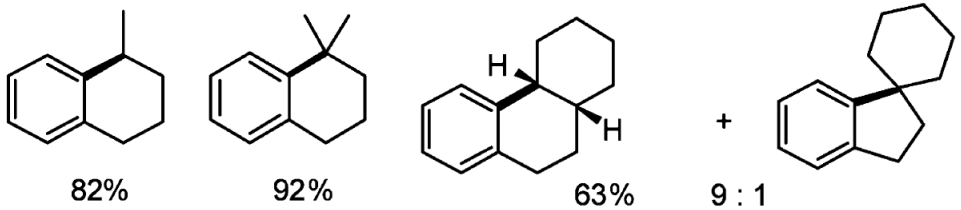
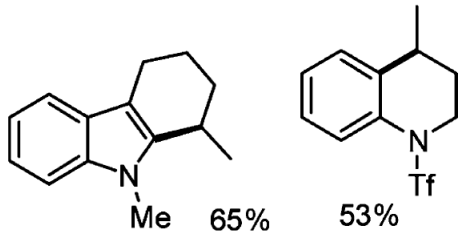
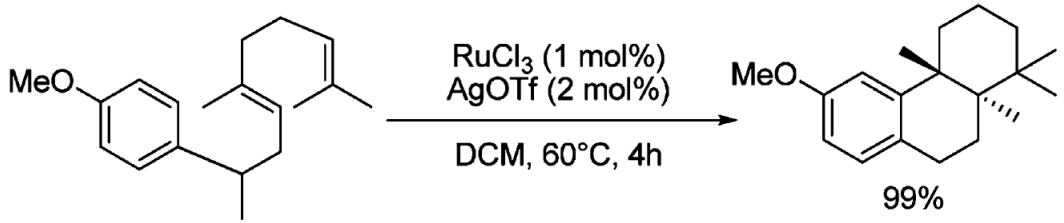


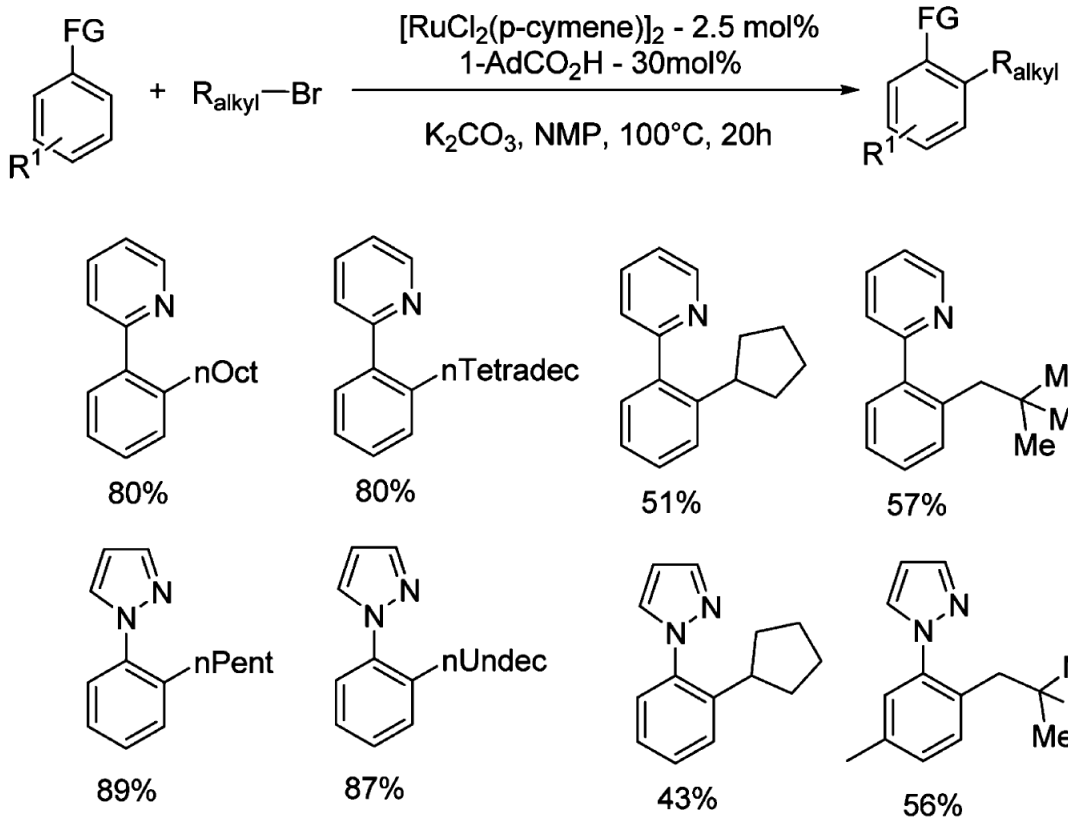




Youn, S. W.; Pastine, S. J.; Sames, D. *Org. Lett.* **2004**, *6*, 581.

Ru(II) catalyzed C−H activation

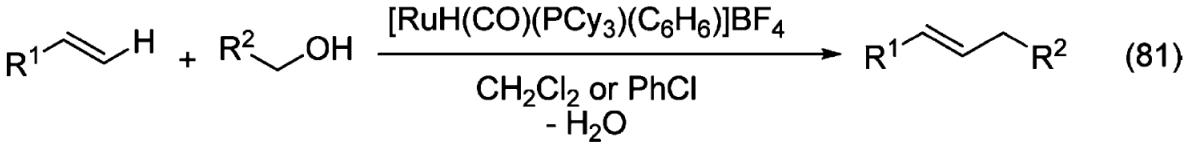
3) Alkylation with alkylhalides



Ackermann, L.; Novak, P.; Vicente, R.; Hofmann, N. *Angew. Chem., Int. Ed.* **2009**, *48*, 6045.

Ru(II) catalyzed C−H activation

3) Alkylation <u>with alcohols</u>



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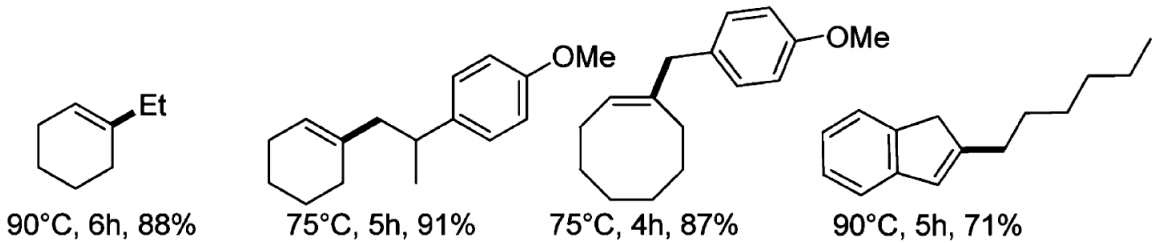
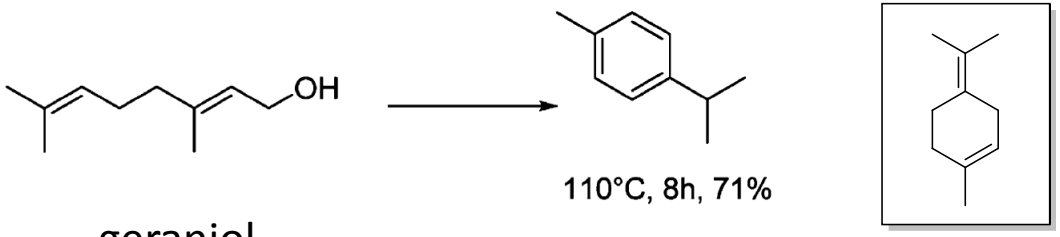


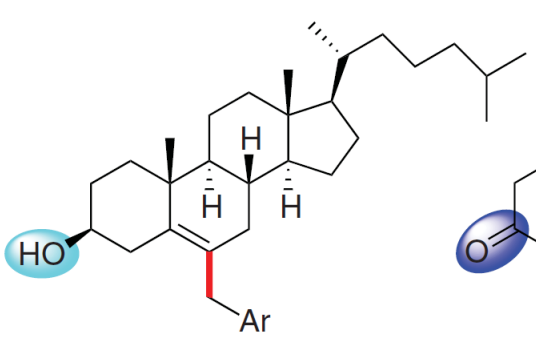


geraniol

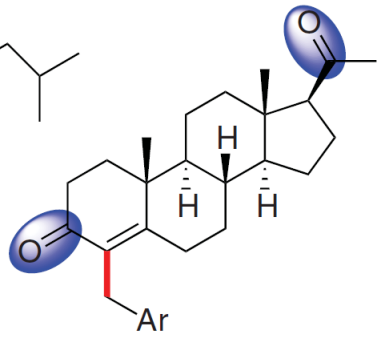
Lee, D.-H.; Kwon, K.-H.; Yi, C. S. *Science* **2011**, *333*, 1613.

Ru(II) catalyzed C–H activation

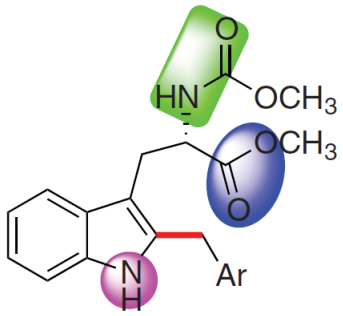
3) Alkylation <u>with alcohols</u>



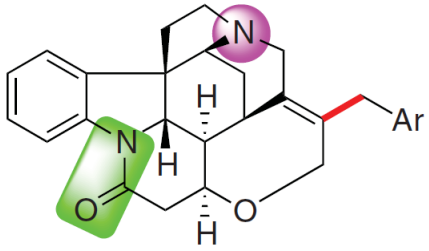
(-)-**16**, 57% (28% rsm)
conditions: 90 °C, 6 h



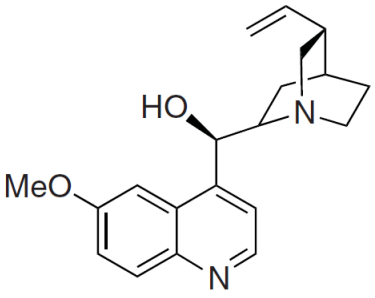
(+)-**17**, 81% (11% rsm)
conditions: 90 °C, 6 h



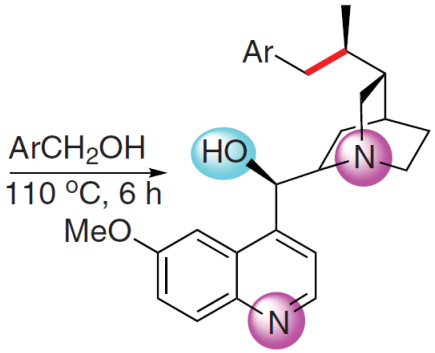
(-)-**18**, 84% (7% rsm)
conditions: 90 °C, 4 h



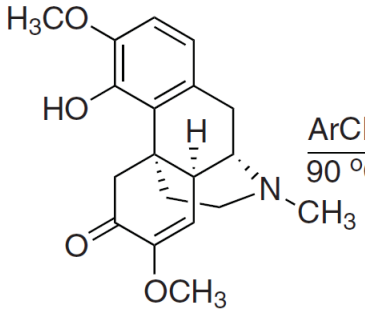
(-)-**19**, 73% (12% rsm)
conditions: 90 °C, 5 h



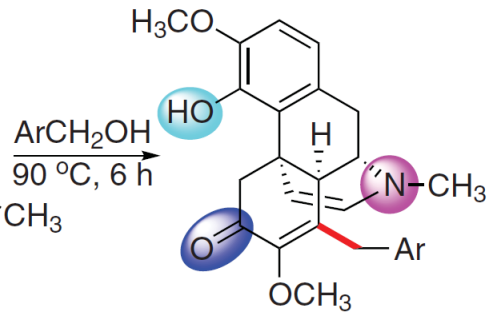
(-)-quinine



(-)-**20**, 58% (24% rsm)



(-)-sinomenine

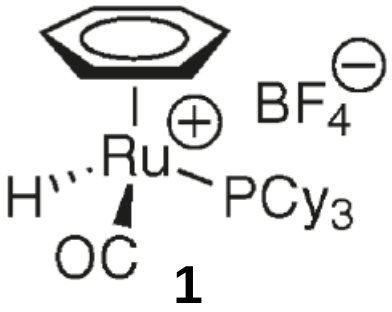


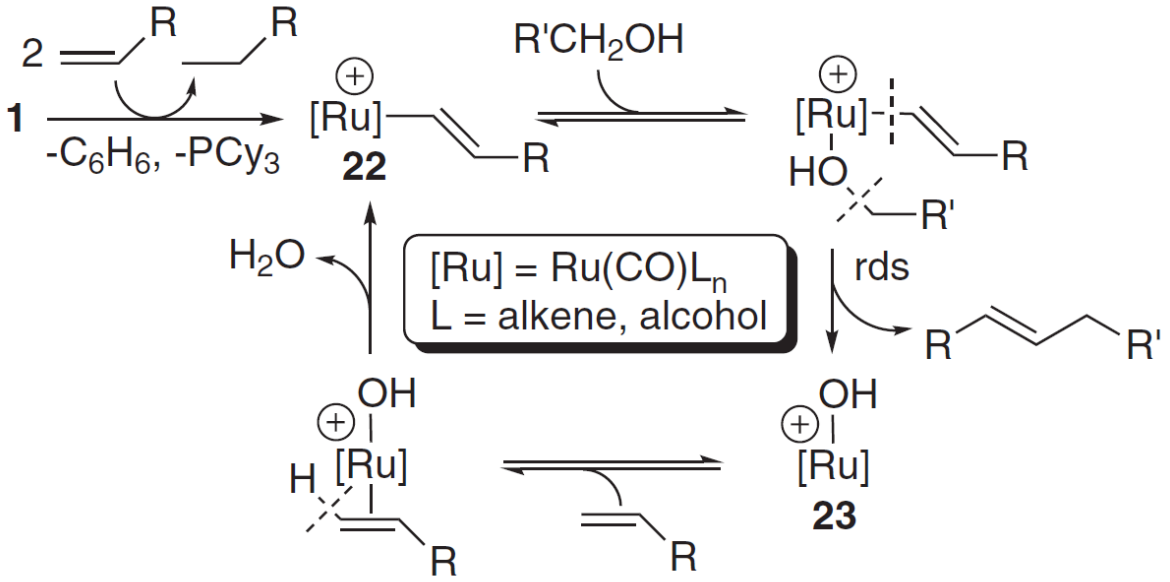
(-)-**21**, 62% (21% rsm)

Lee, D.-H.; Kwon, K.-H.; Yi, C. S. *Science* **2011**, *333*, 1613.

Ru(II) catalyzed C−H activation

3) Alkylation with alcohols

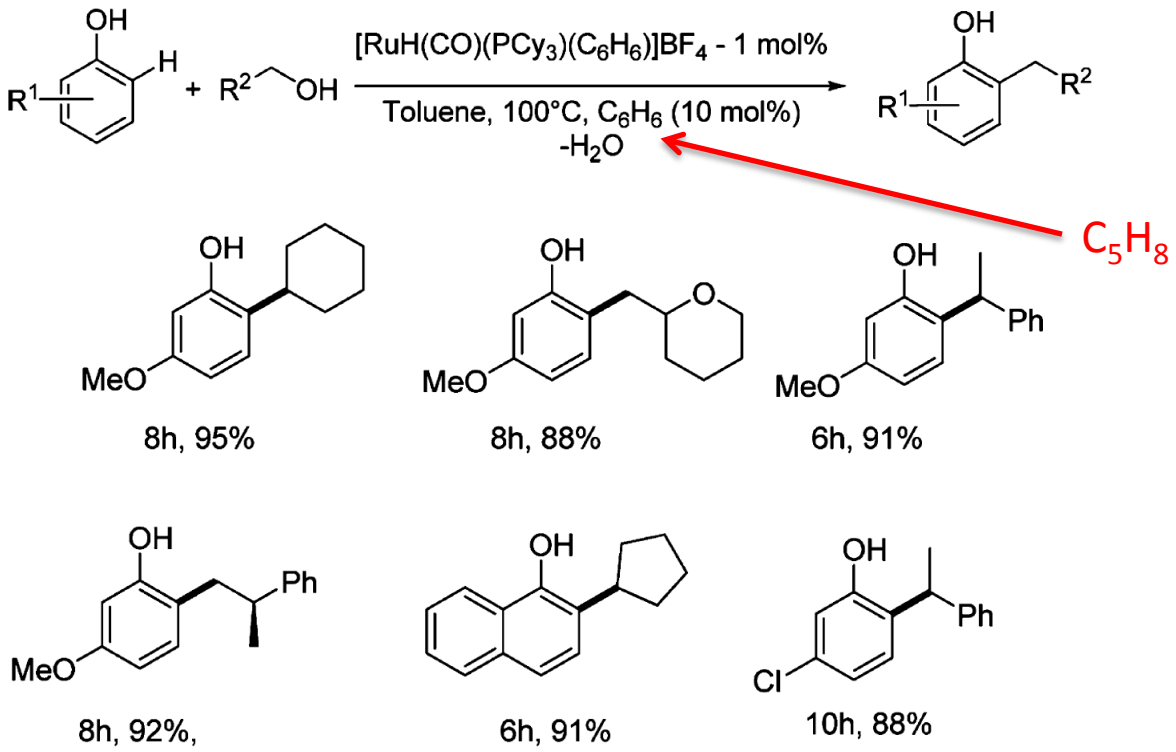




Lee, D.-H.; Kwon, K.-H.; Yi, C. S. *Science* **2011**, *333*, 1613.

Ru(II) catalyzed C–H activation

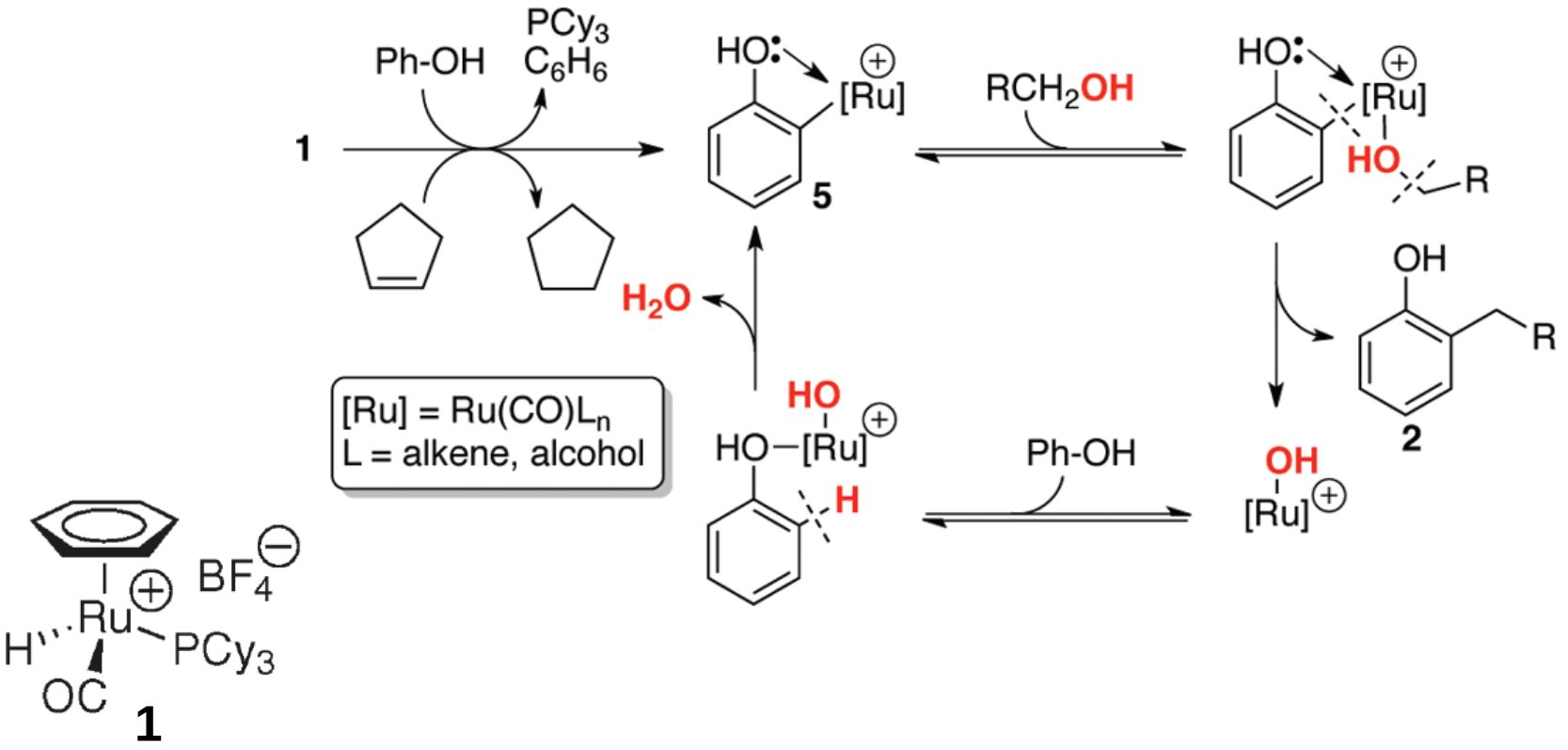
3) Alkylation with alcohols



Lee, D.-H.; Kwon, K.-H.; Yi, C. S. *J. Am. Chem. Soc*. **2012**, *134*, 7325.

Ru(II) catalyzed C−H activation

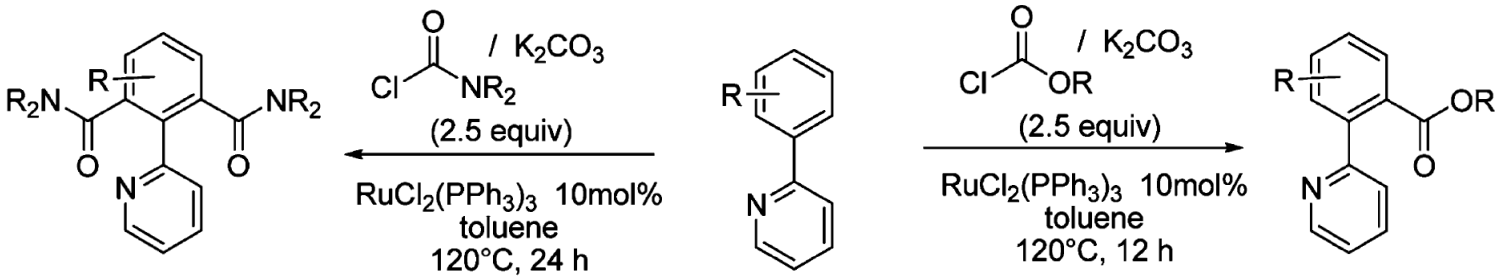
3) Alkylation with alcohols

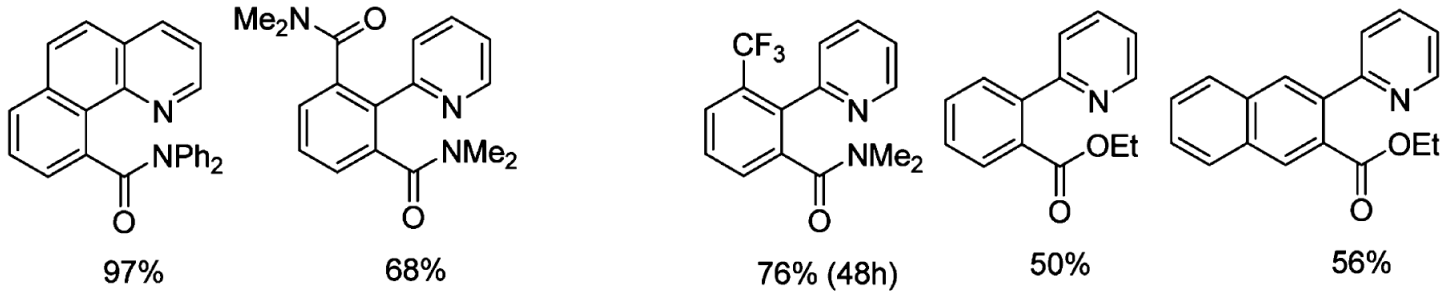


Lee, D.-H.; Kwon, K.-H.; Yi, C. S. *J. Am. Chem. Soc*. **2012**, *134*, 7325.

Ru(II) catalyzed C−H activation

4) Acylation

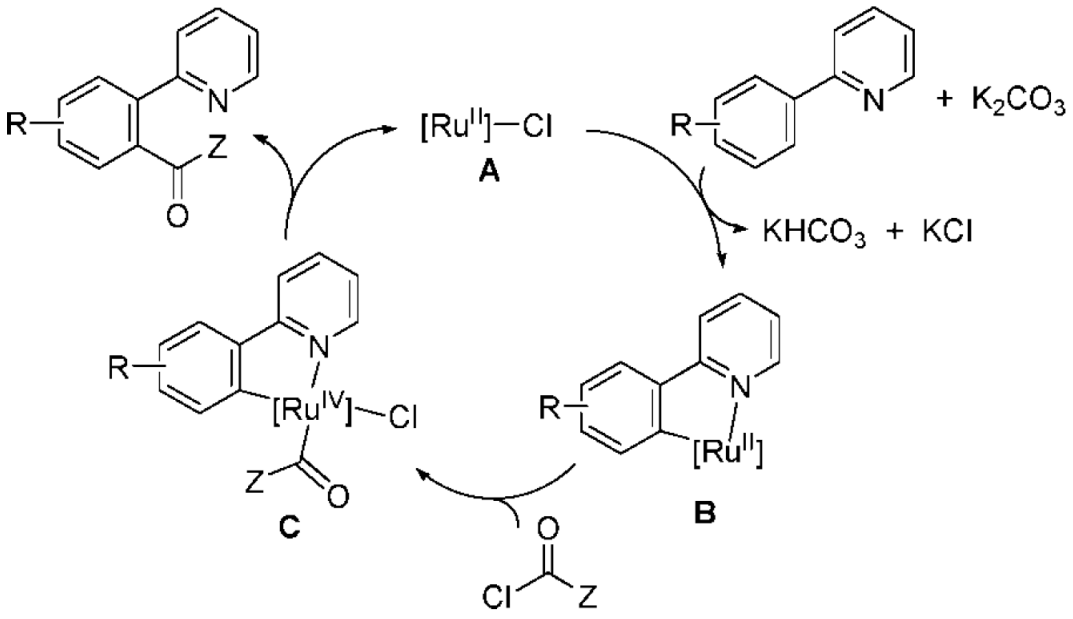




Kochi, T.; Urano, S.; Seki, H.; Mizushima, E.; Sato, M.; Kakiuchi, F. *J. Am. Chem. Soc*. **2009**, *131*, 2792.

Ru(II) catalyzed C−H activation

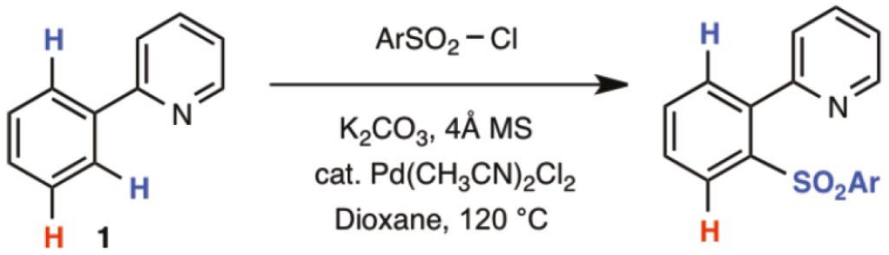
4) Acylation



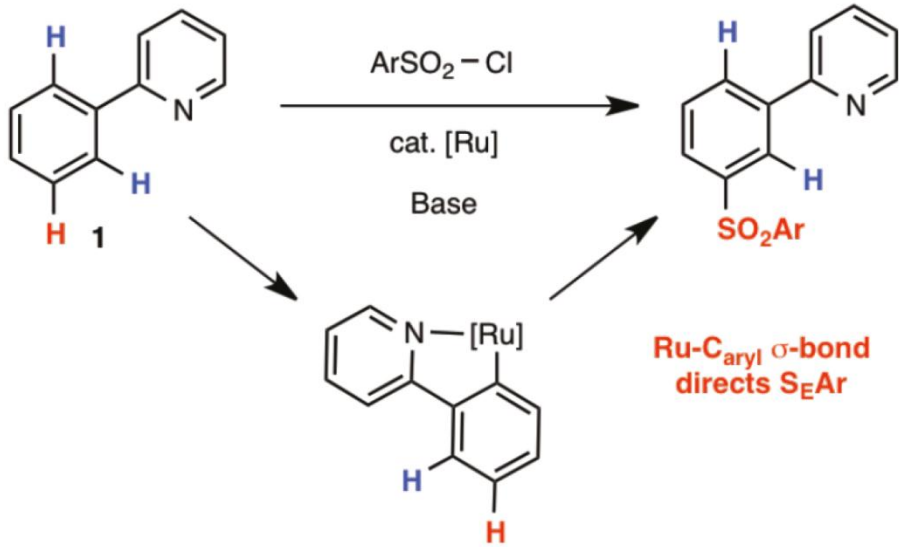
Kochi, T.; Urano, S.; Seki, H.; Mizushima, E.; Sato, M.; Kakiuchi, F. *J. Am. Chem. Soc*. **2009**, *131*, 2792.

Ru(II) catalyzed C−H activation

4) Acylation



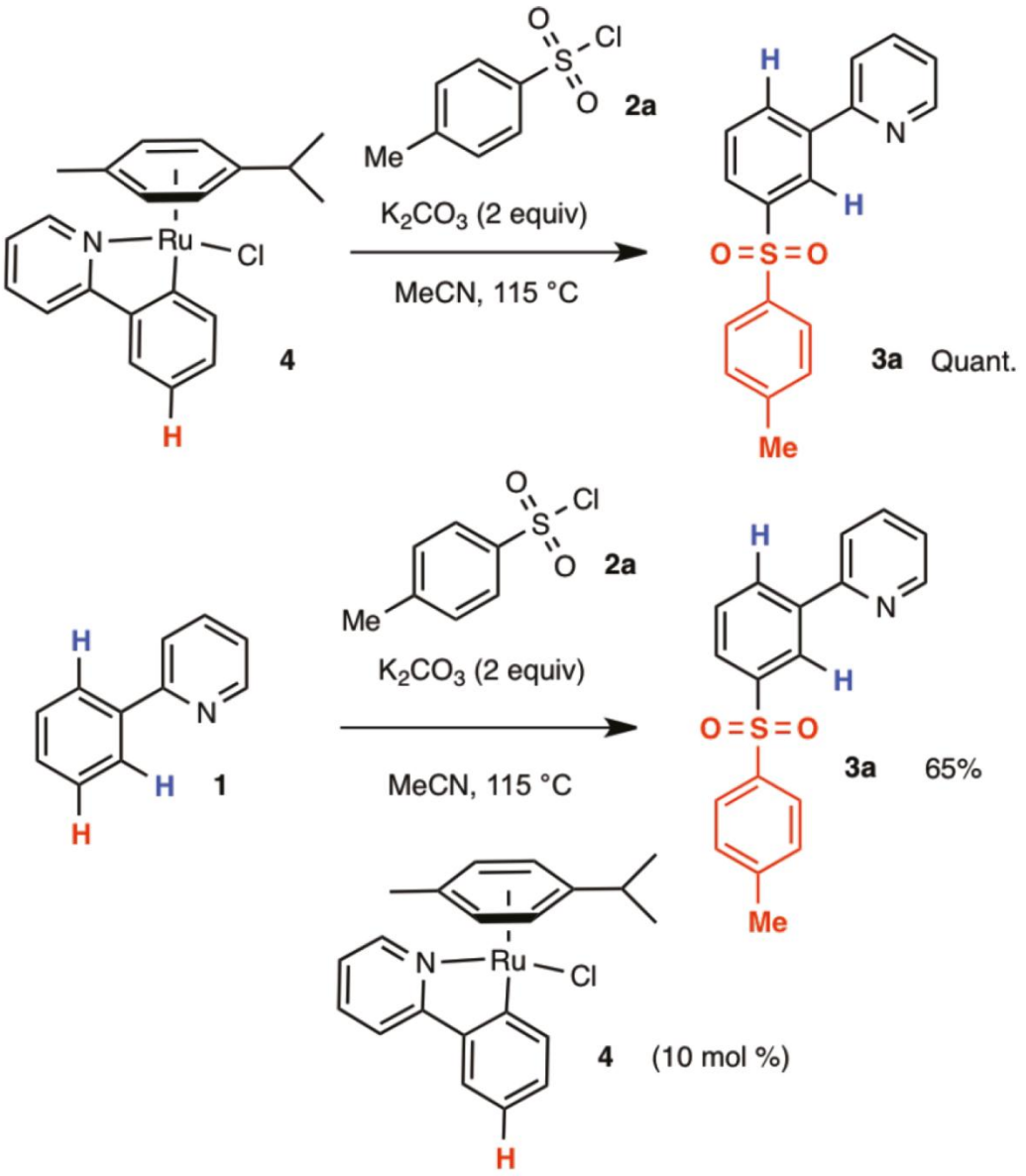
Zhao, X.; Dimitrijevic, E.; Dong, V. M. *J. Am. Chem. Soc*. **2009**, *131*, 3466.



Saidi, O.; Marafie, J.; Ledger, A. E. W.; Liu, P. M.; Mahon, M. F.; Kociok-Kohn, G.; Whittlesey, M. K.; Frost, C. G. *J. Am. Chem. Soc*. **2011**, *133*, 19298.

Ru(II) catalyzed C–H activation

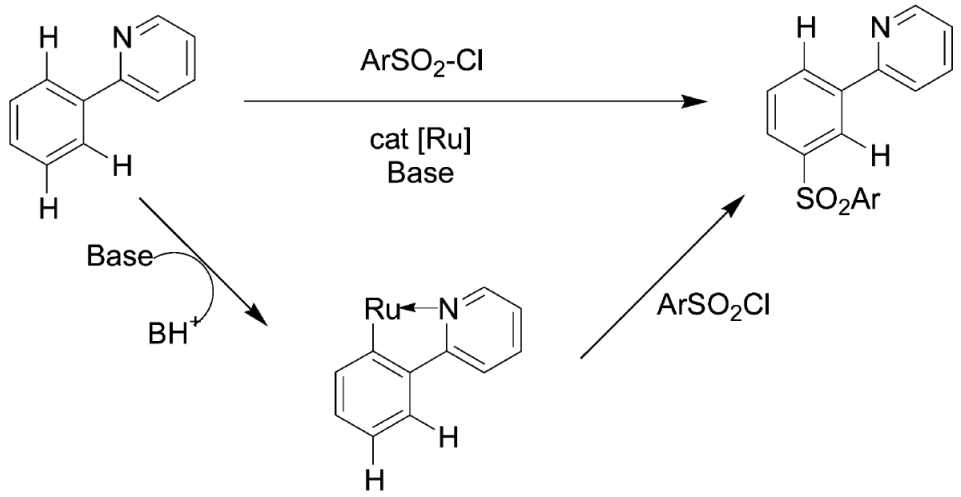
4) Acylation



Saidi, O.; Marafie, J.; Ledger, A. E. W.; Liu, P. M.; Mahon, M. F.; Kociok-Kohn, G.; Whittlesey, M. K.; Frost, C. G. *J. Am. Chem. Soc*. **2011**, *133*, 19298.

Ru(II) catalyzed C−H activation

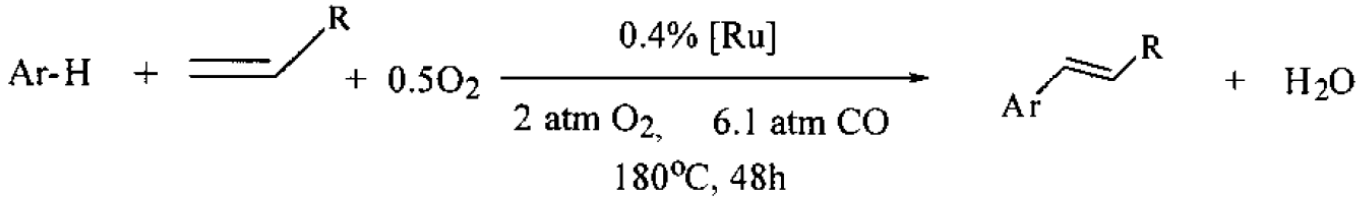
4) Acylation

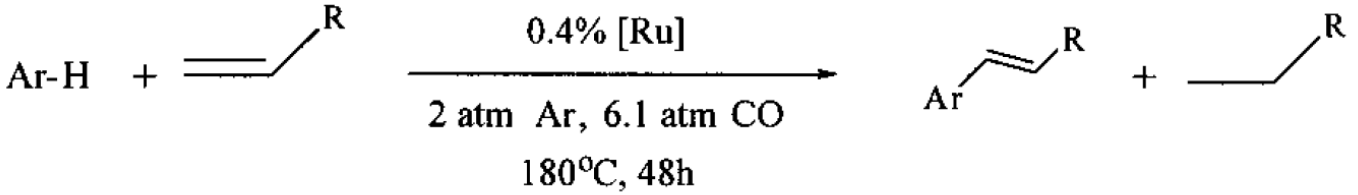


Saidi, O.; Marafie, J.; Ledger, A. E. W.; Liu, P. M.; Mahon, M. F.; Kociok-Kohn, G.; Whittlesey, M. K.; Frost, C. G. *J. Am. Chem. Soc*. **2011**, *133*, 19298.

Ru(II) catalyzed C−H activation

5) Alkenylation



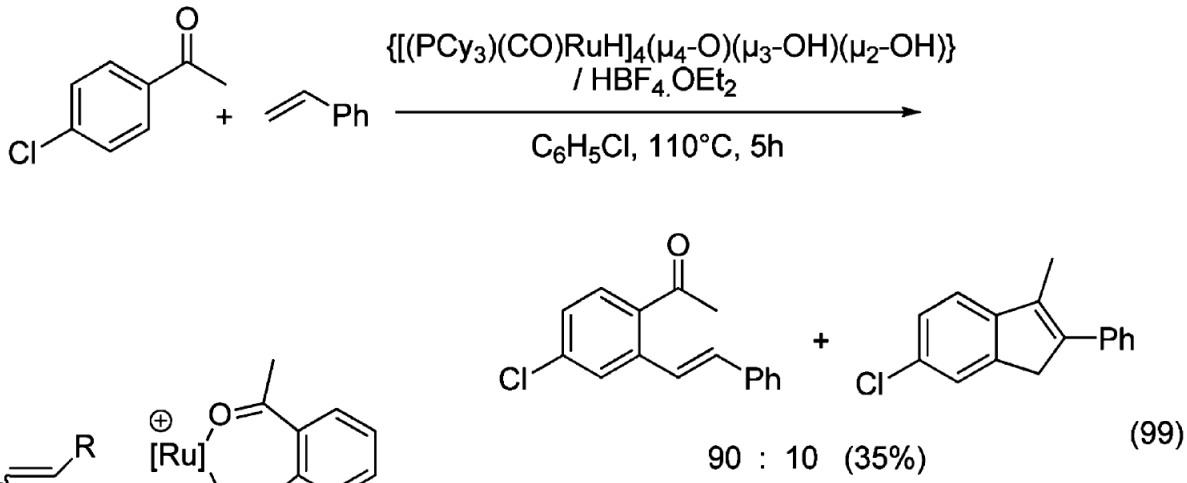


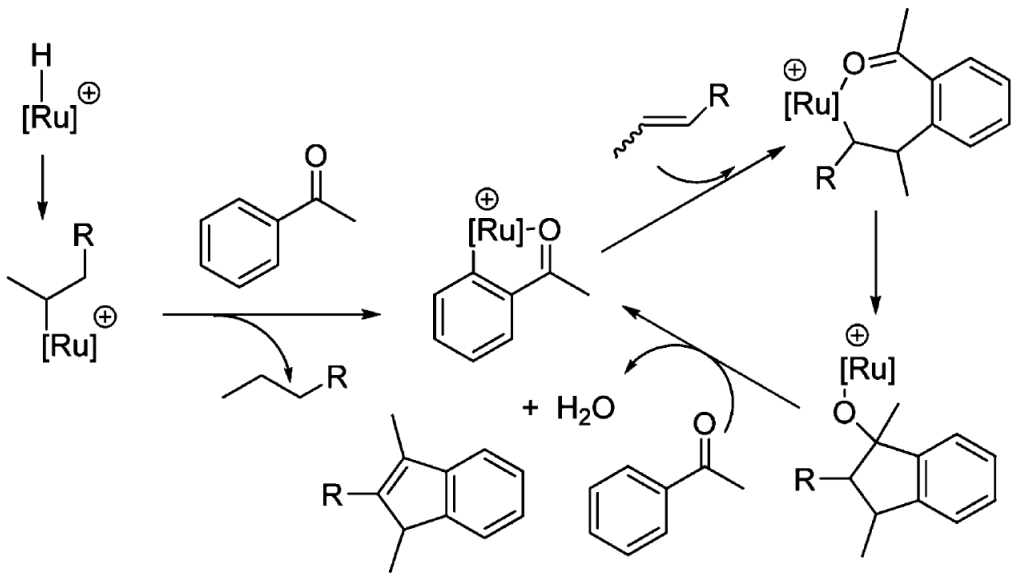
Yield 30-47%

Weissman, H.; Song, X. P.; Milstein, D. *J. Am. Chem. Soc*. **2001**, *123*, 337.

Ru(II) catalyzed C−H activation

5) Alkenylation

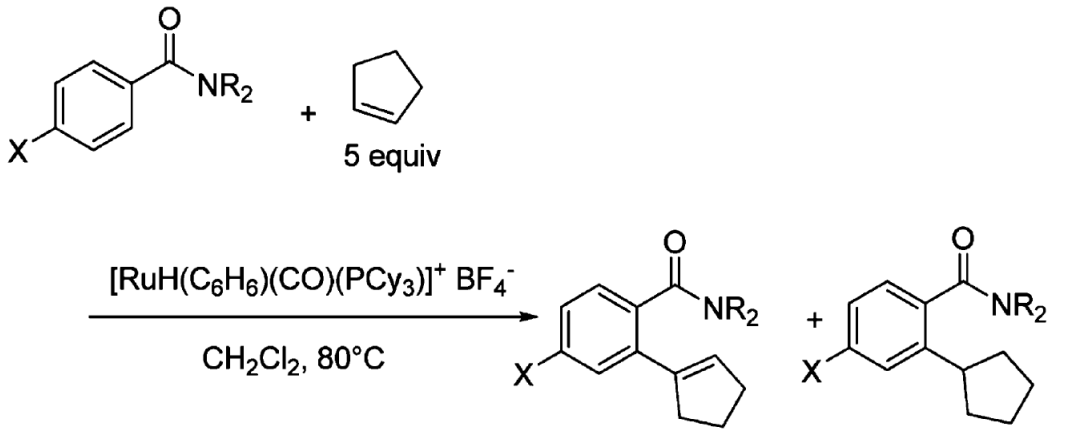




Yi, C. S.; Lee, D. W. *Organometallics* **2009**, *28*, 4266.

Ru(II) catalyzed C−H activation

5) Alkenylation



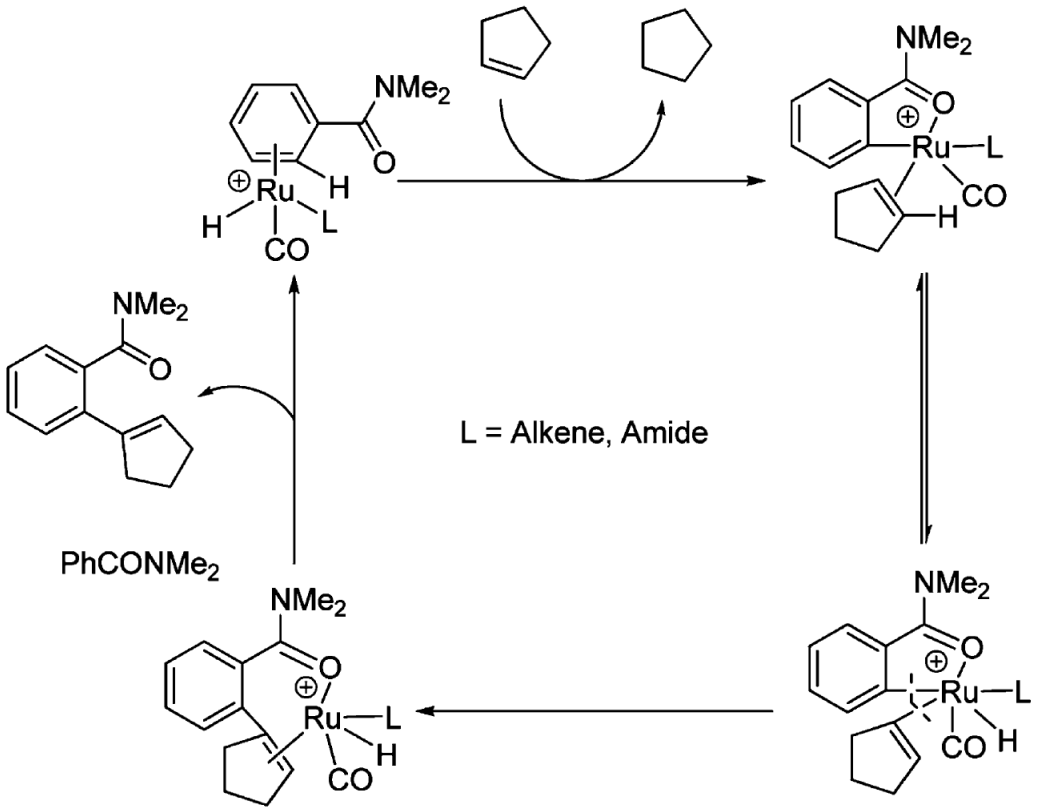
X = OMe,	R= Me, Me	91	:	9	(76%)
X = Cl,	R= Me, Me	88	:	12	(73%)
X = H,	R= H, Ph	100	:	0	(56%)
X = H,	R= H, p-OMe-C_6H_4	100	:	0	(57%)
X = H,	R= H, p-Cl-C_6H_4	100	:	0	(55%)

Kwon, K. H.; Lee, D. W.; Yi, C. S. *Organometallics* **2010**, *29*, 5748.

☆ Question 2

Ru(II) catalyzed C−H activation

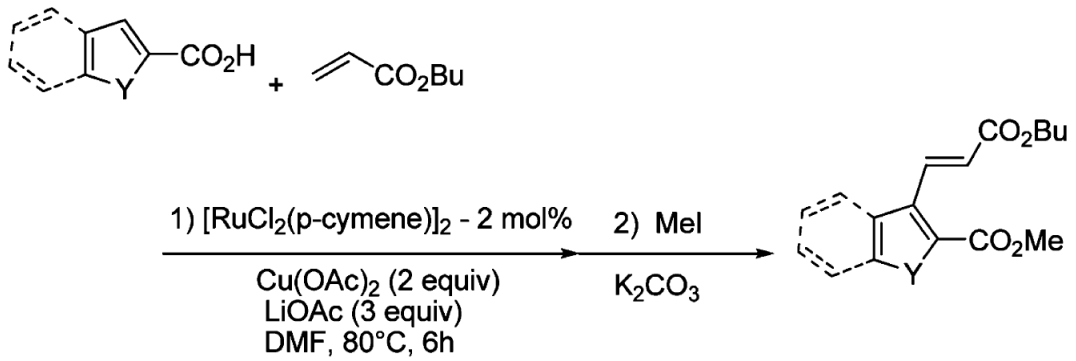
5) Alkenylation



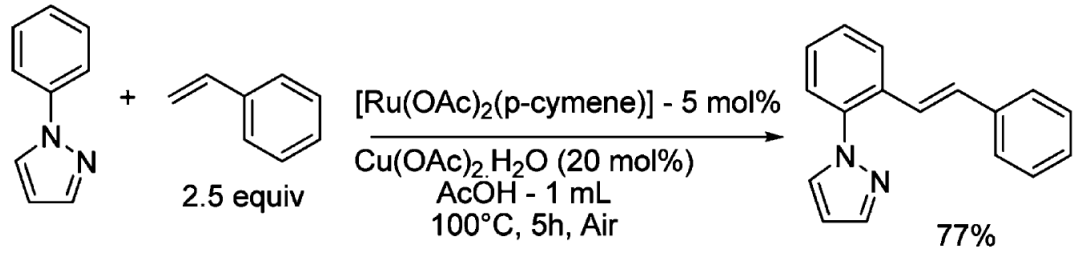
Kwon, K. H.; Lee, D. W.; Yi, C. S. *Organometallics* **2010**, *29*, 5748.

Ru(II) catalyzed C−H activation

5) Alkenylation



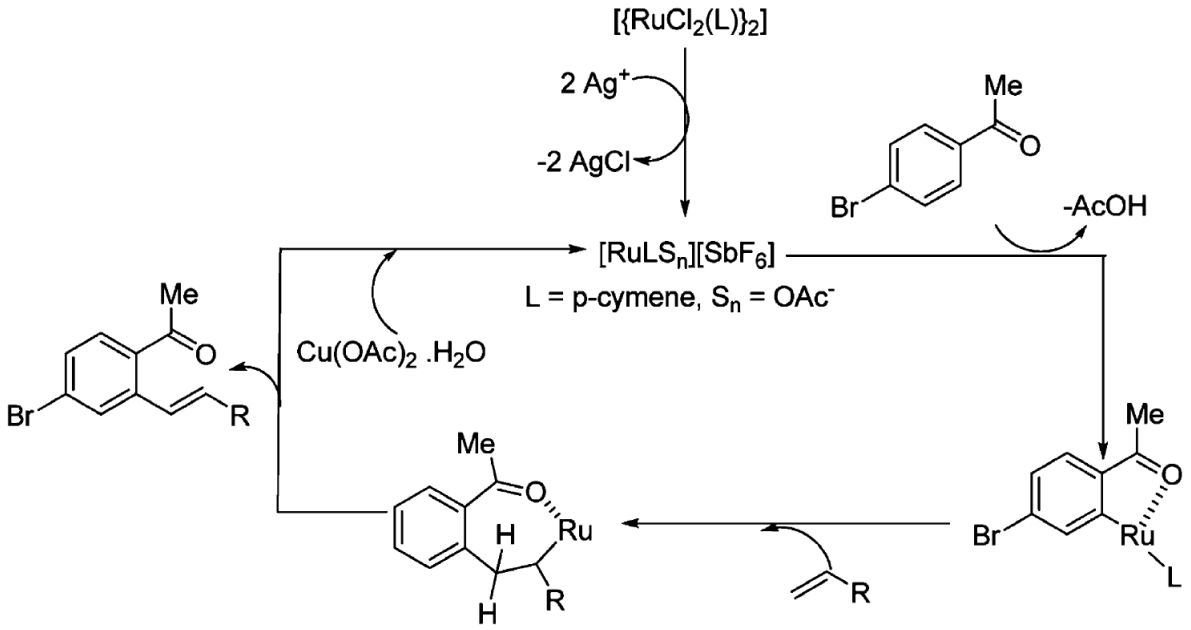
Ueyama, T.; Mochida, S.; Fukutani, T.; Hirano, K.; Satoh, T.; Miura, M. *Org. Lett*. **2011**, *13*, 706.



Arockiam, P. B.; Fischmeister, C.; Bruneau, C.; Dixneuf, P. H. *Green Chem*. **2011**, *13*, 3075.

Ru(II) catalyzed C−H activation

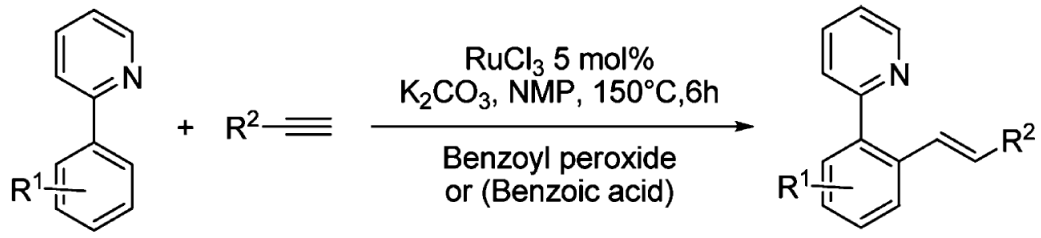
5) Alkenylation

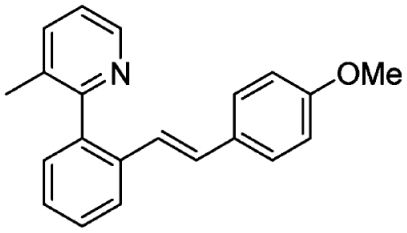


Padala, K.; Jeganmohan, M. *Org. Lett*. **2011**, *13*, 6144.

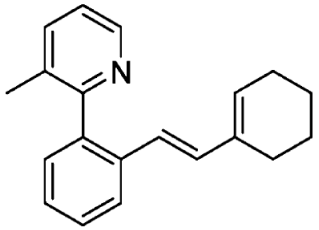
Ru(II) catalyzed C−H activation

5) Alkenylation





96% (79%)

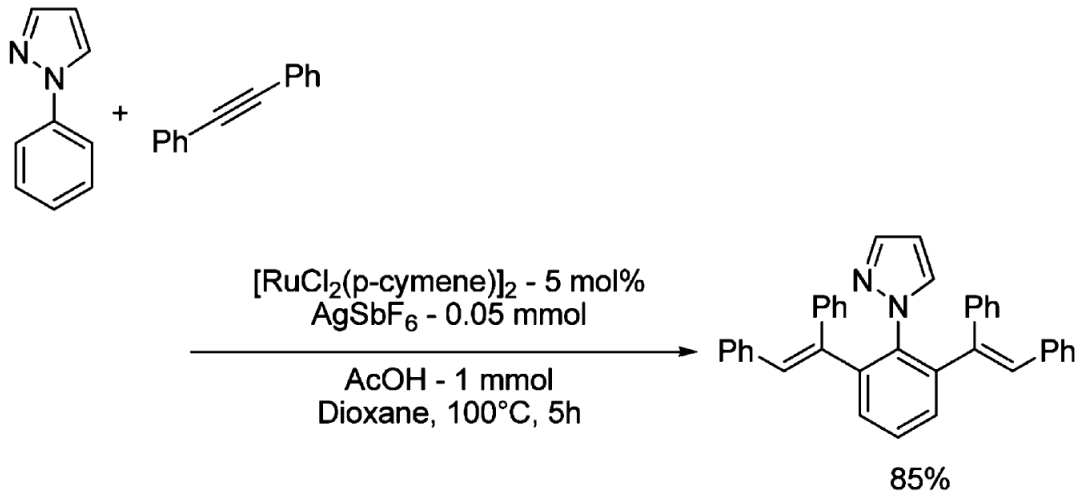


83% (66%)

Cheng, K.; Yao, B. B.; Zhao, J. L.; Zhang, Y. H. *Org. Lett*. **2008**, *10*, 5309.

Ru(II) catalyzed C−H activation

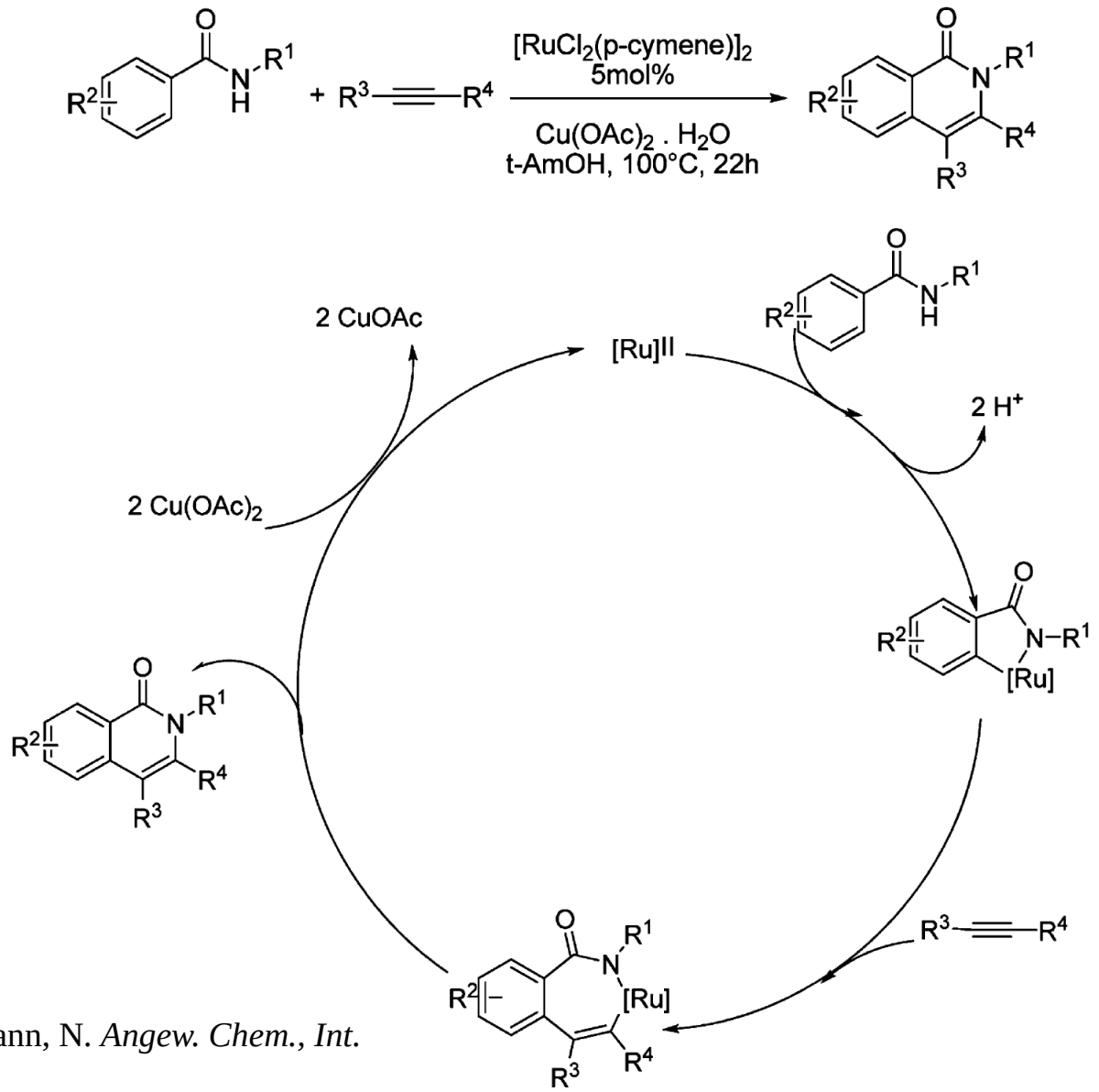
5) Alkenylation



Hashimoto, Y.; Hirano, K.; Satoh, T.; Kakiuchi, F.; Miura, M. *Org. Lett*. **2012**, *14*, 2058.

Ru(II) catalyzed C−H activation

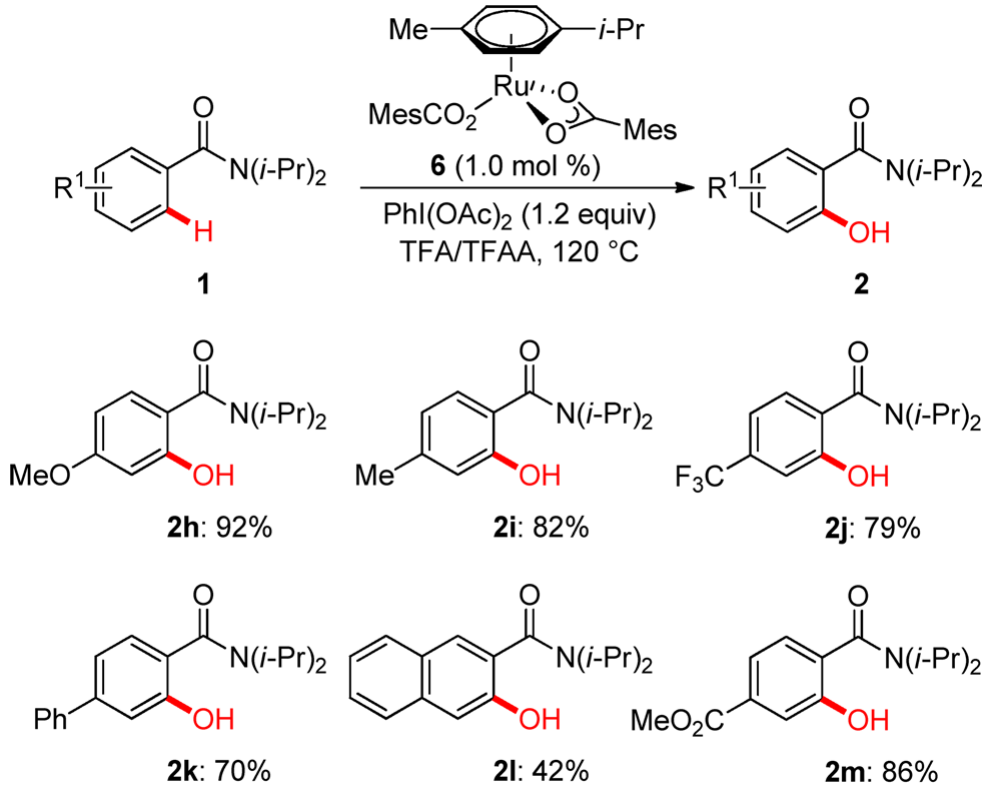
5) Alkenylation



Ackermann, L.; Lygin, A. V.; Hofmann, N. *Angew. Chem., Int. Ed*. **2011**, *50*, 6379.

Ru(II) catalyzed C−H activation

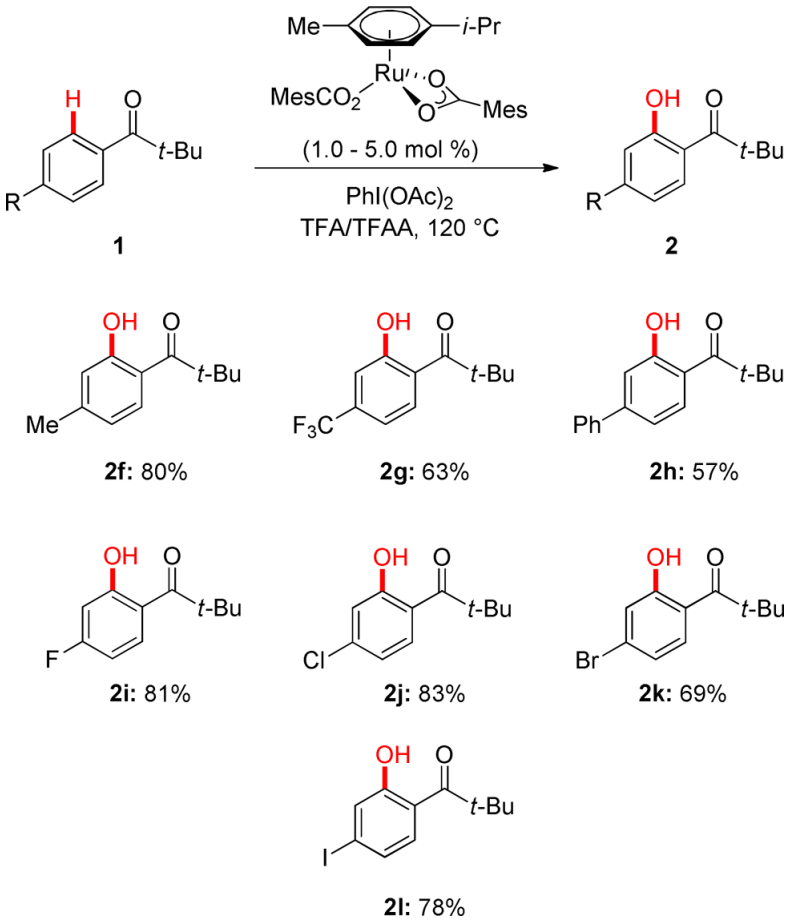
6) Others



Thirunavukkarasu, V. S.; Hubrich, J.; Ackermann, L. *Org. Lett*. **2012**, *14*, 4210.

Ru(II) catalyzed C–H activation

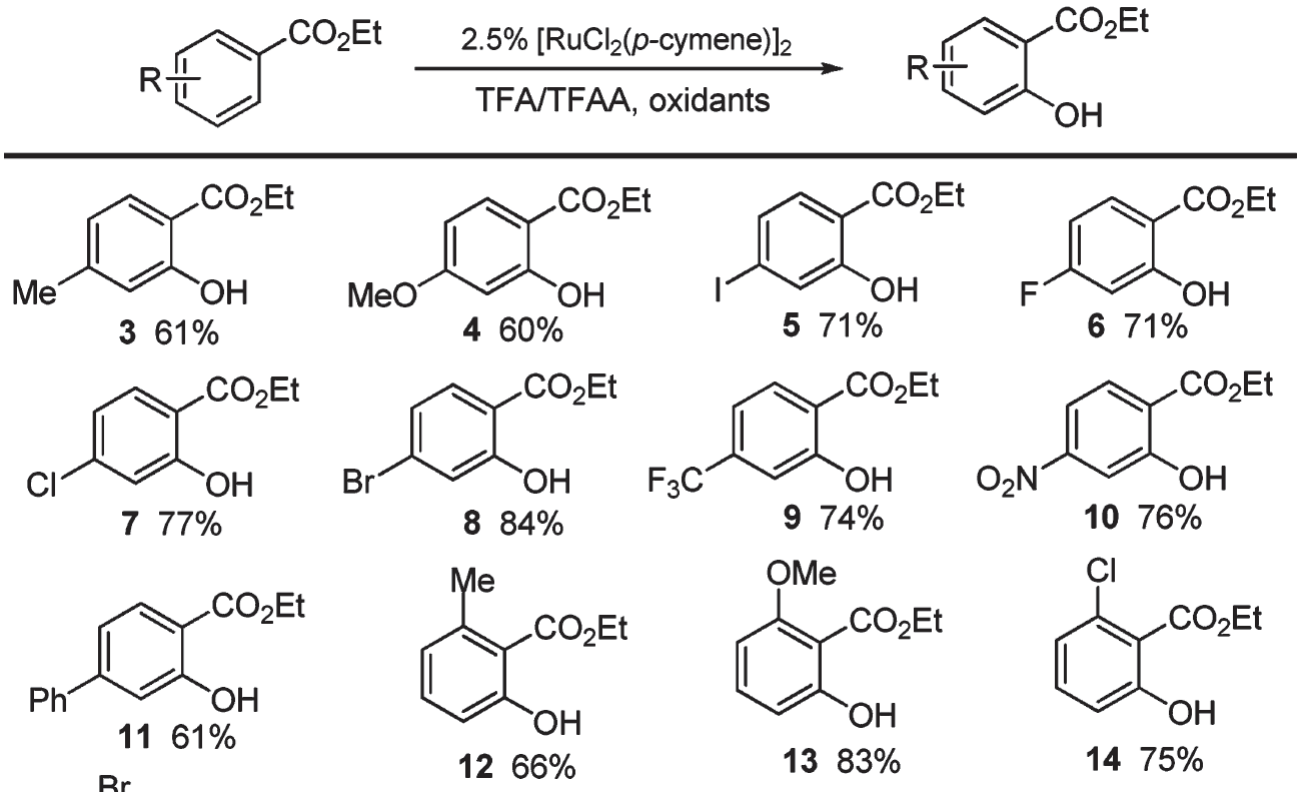
6) Others



Thirunavukkarasu, V. S.; Ackermann, L. *Org. Lett*. **2013**, 10.1021/ol302956s

Ru(II) catalyzed C−H activation

6) Others



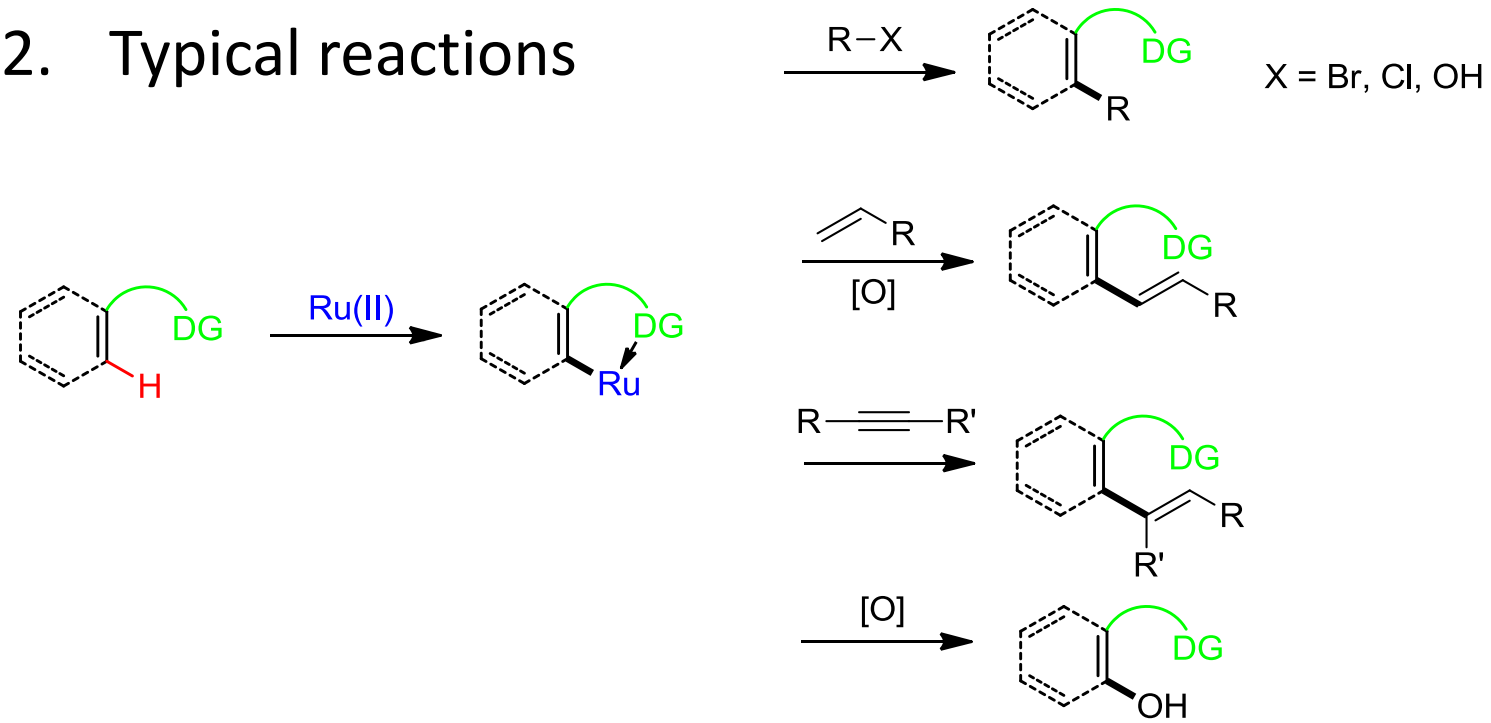
Yang, Y.; Lin, Y.; Rao, Y. *Org. Lett.* **2012**, *14*, 2874.

Summary

1. Frequently used Ru(II) catalysts:

$[RuCl_2(p\text{-cymene})]_2$	Ackermann's group
$[RuCl_2(C_6H_6)]_2$	Oi's group
$[RuH(CO)(PCy_3)(C_6H_6)]BF_4$	Yi's group

2. Typical reactions



Summary

- ✓ Inexpesive
- ✓ Stable
- ✓ Multiple valents
- ✓ Many reaction types

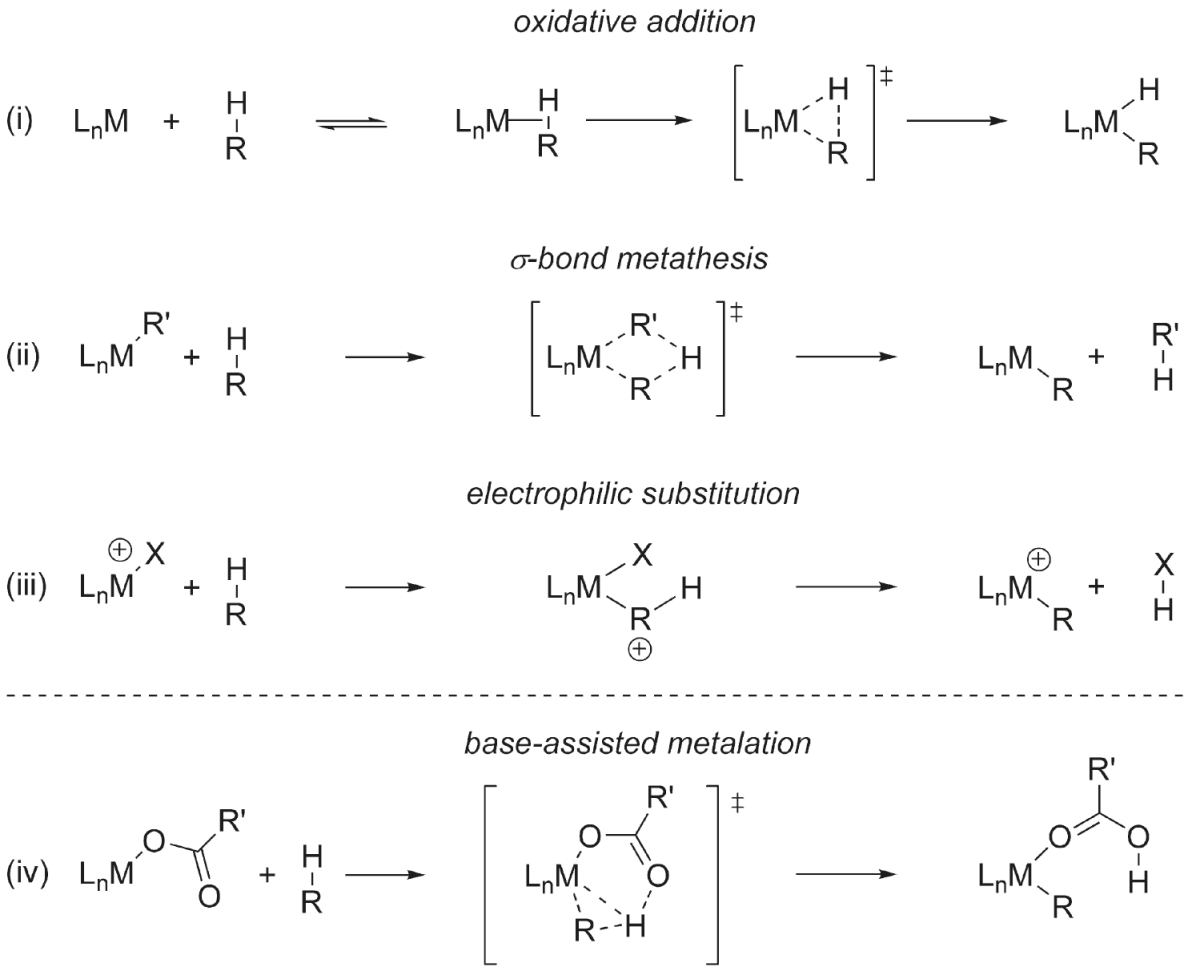
We have these Ru catalysts.
Having an idea? Try it! Good luck!!!

$RuCl_2(PPh_3)_3$	$[Cp^*RuCl_2]_n$	$CpRuCl(PPh_3)_2$
$RuH_2(CO)(PPh_3)_3$	$[RuCl_2(p\text{-cymene})]_2$	$RuCl_3 \cdot xH_2O$
$RuCl_2(bpy)_3$	$[RuCl_2(benzene)]_2$	$Ru(OAc)_3$
$RuH_2(PPh_3)_4$	$[RuCl_2(coe)_2]_2$	

Thank you for your attention!

☆ Question 1

Four different mechanisms for C–H activation



Ru(0), Rh(I)

Early transition metals

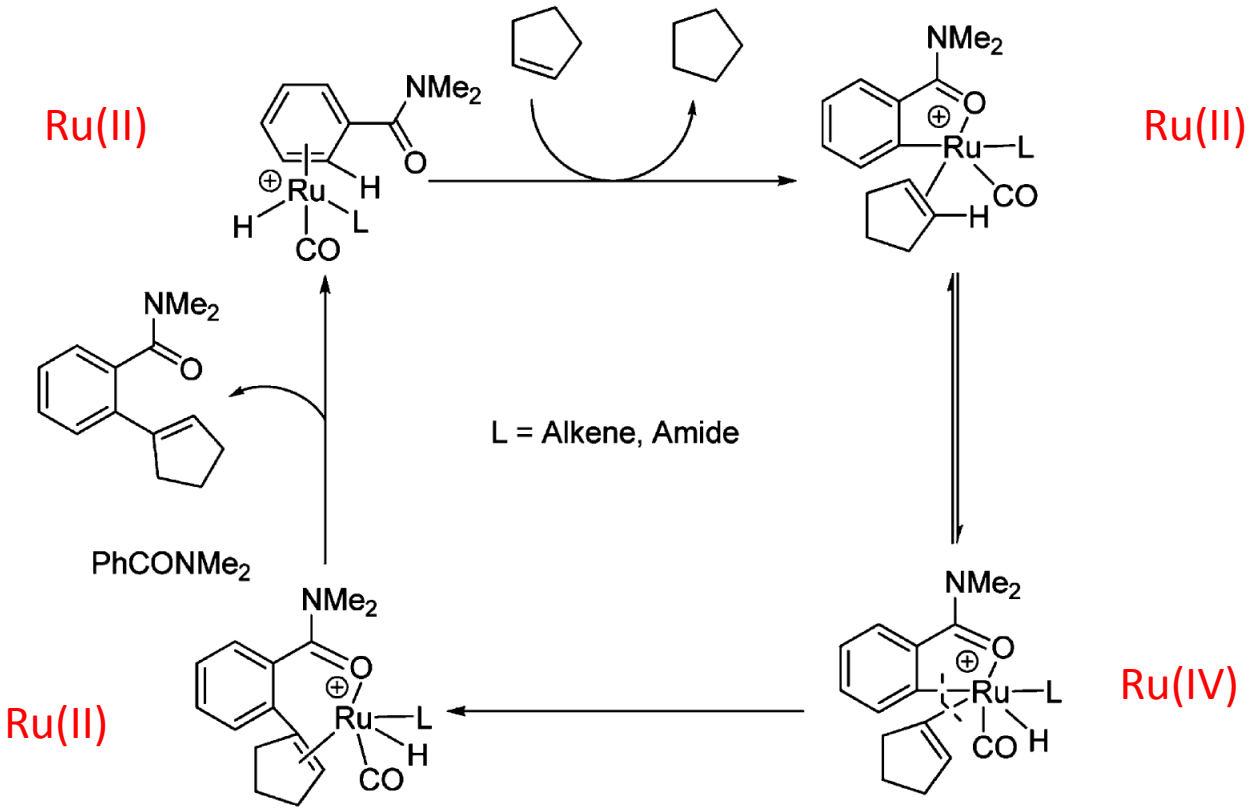
Pd(II), Pd(IV), Ru(II), Rh(III)

Pd(II), Ru(II)

☆ Question 2

Ru(II) catalyzed C−H activation

5) Alkenylation

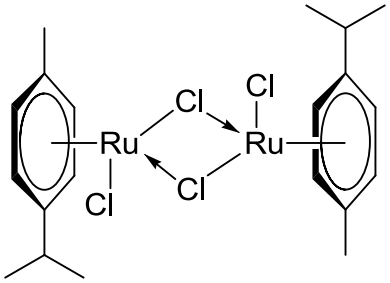


Kwon, K. H.; Lee, D. W.; Yi, C. S. *Organometallics* **2010**, *29*, 5748.

☆ Question 3

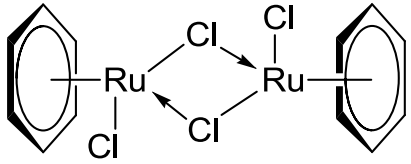
Conclusion

1. Frequently used Ru(II/III) catalysts:



$[RuCl_2(p\text{-cymene})]_2$

Ackermann's group



$[RuCl_2(C_6H_6)]_2$

Oi's group

$[RuH(CO)(PCy_3)(C_6H_6)]BF_4$

Yi's group