ÉCOLE POLYTECHNIQUE
FÉDÉRALE DE LAUSANNE

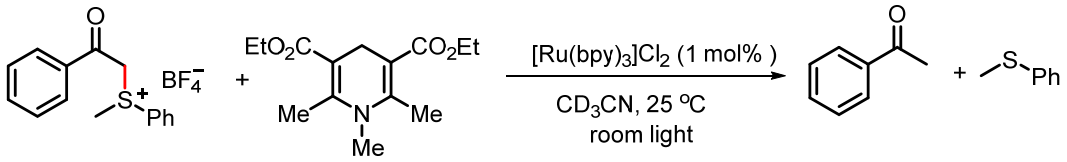
Visible Light Induced C(sp^3)-H Bonds Functionalization

LSPN Seminar
BAO, Xu
13. 09. 2018

1912. Light had the potential to serve as an inexpensive, abundant, renewable, and nonpolluting reagent for chemical synthesis.

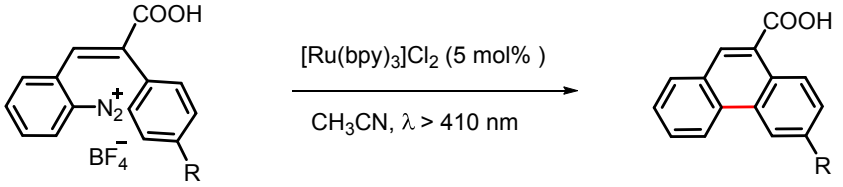
G. Ciamician, *Science*, **1912**, *36*, 385

1978.



D. M. Hedstrand, W. H. Kruizinga, R. M. Kellogg, *Tetrahedron Lett.* **1978**, *19*, 1255

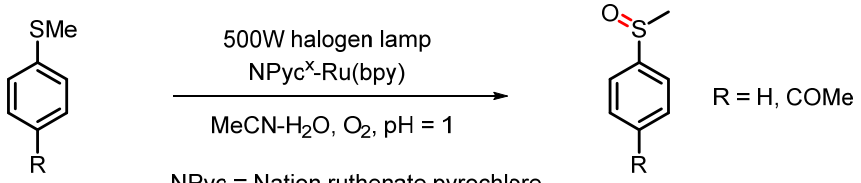
1984.



R = H, Br or OMe

H. Cano-Yelo, A. Deronzier, *J. Chem. Soc., Perkin Trans. 2,* **1984**, 1093.

2003.

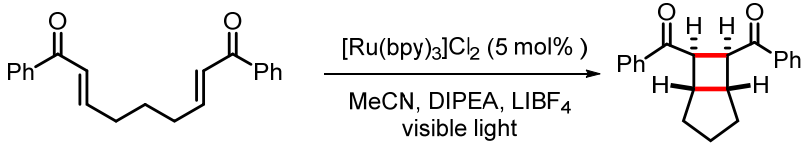


NPyc = Nation ruthenate pyrochlore

R = H, COMe

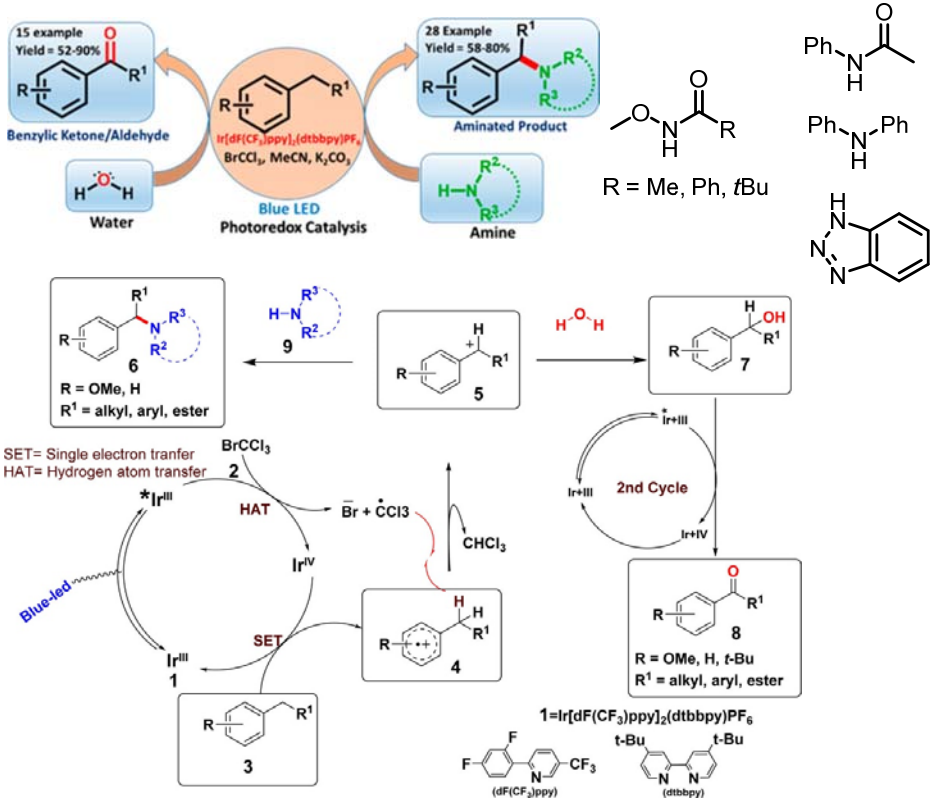
J. M. Zen, S. L. Liou, A. S. Kumar, M. S. Hsia, *Angew. Chem. Int. Ed.* **2003**, *42*, 577

2008.

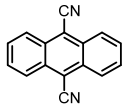


M. A. Ischay, M. E. Anzovino, J. Du, T. P. Yoon, *J. Am. Chem. Soc*. **2008**, *130*, 12886

Pandey's work: Oxidation and Amination



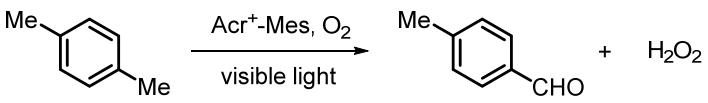
DCA



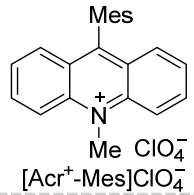
DCA could also serve as PC

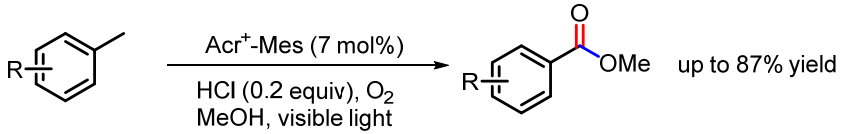
[a] Pandey, G.; Laha, R.; Singh, D., *J. Org. Chem.* **2016,** *81*, 7161;
[b] Pandey, G.; Laha, R., *Angew. Chem.Int. Ed.* **2015,** *54*, 14875.

Acridinium ion as PC

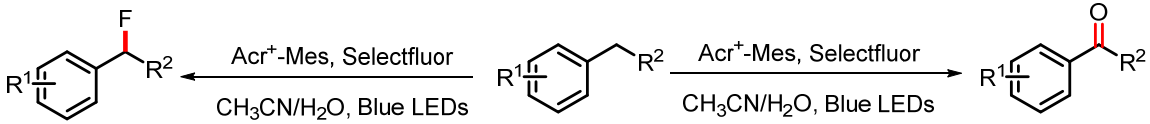


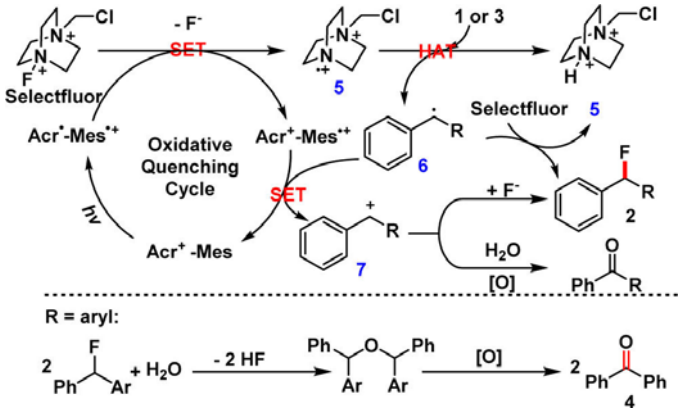
Fukuzumi, S. et al, *Chem. Commun.***2010,** *46*, 601





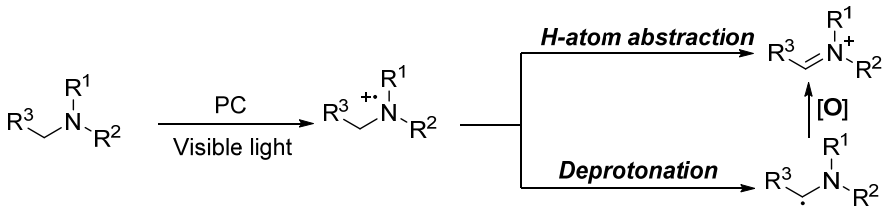
Zhang, L.; Yi, H.; Wang, J.; Lei, A., *Green Chem.* **2016,** *18*, 5122



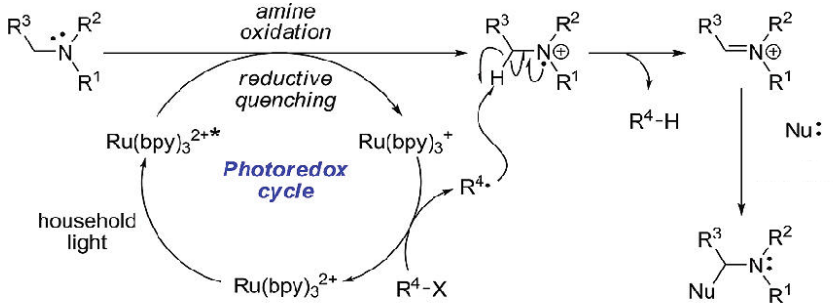


Xiang, M.; Xin, Z.-K.; Chen, B.; Tung, C.-H.; Wu, L.-Z., *Org. Lett.* **2017,** *19*, 3009.

Reactive Intermediate: Iminium ion & α-Aminoalkyl radical

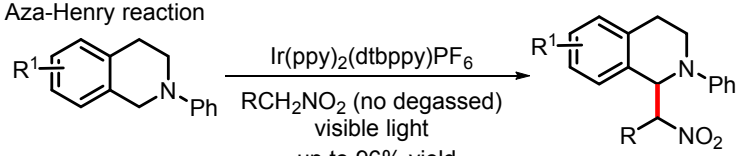


Mechanism for Iminium ion formation



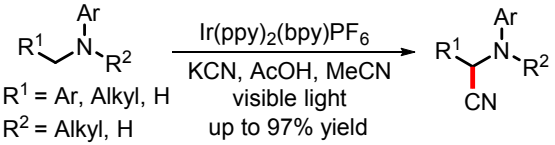
Stephenson, C. R. J. et al *J. Am. Chem. Soc*. **2010**, *132*, 1464.

Aza-Henry reaction



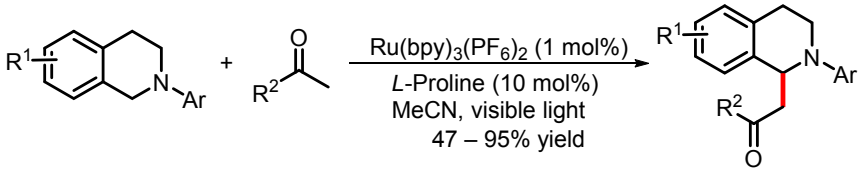
Stephenson, C. R. J. et al *J. Am. Chem. Soc.* **2010**, *132*, 1464.

Strecker reaction

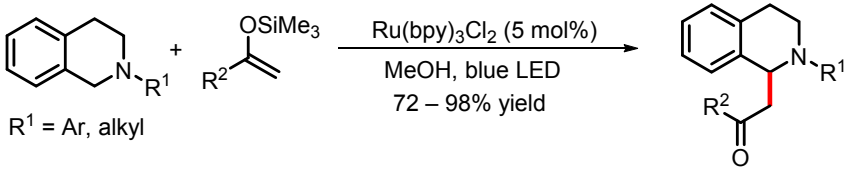


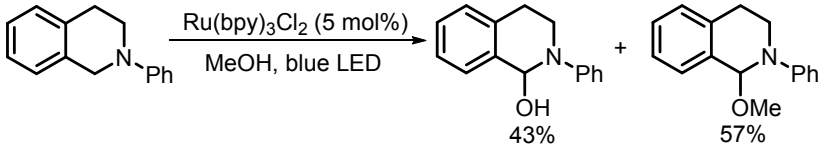
Rueping, M. et al *Chem Commun.* **2011**, *47*, 12709.

Mannich reaction



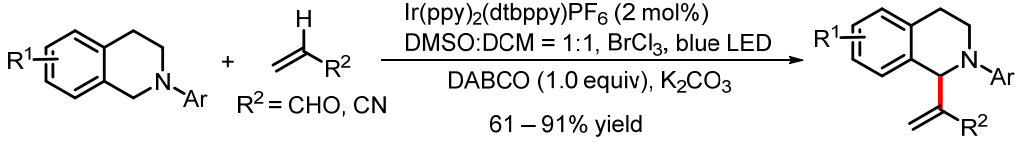
Rueping, M. et al *Chem Commun.* **2011**, *47*, 2360.





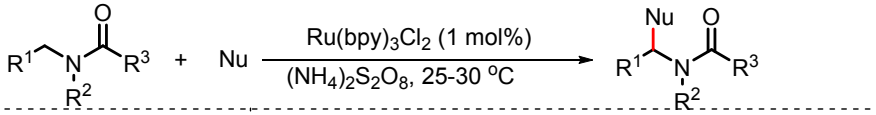
Xia, W. et al *Chem. Commun.* **2012**, *48*, 2337

Baylis-Hillman reaction

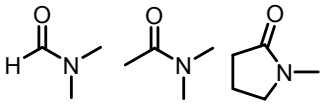


Xiao, W.-J. et al *Org. Bio. Chem.* **2014,** *12*, 2037

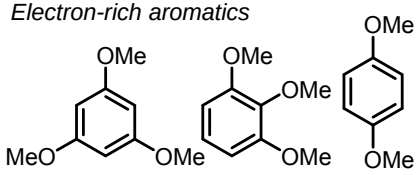
Friedel-Crafts amidoalkylation



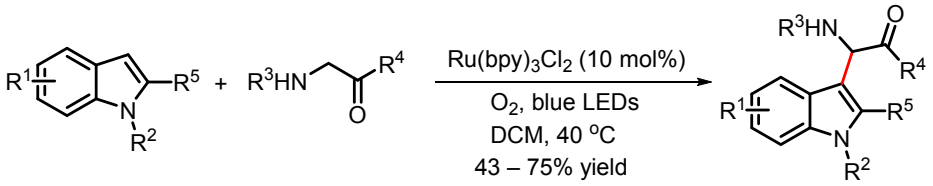
alkylamides:



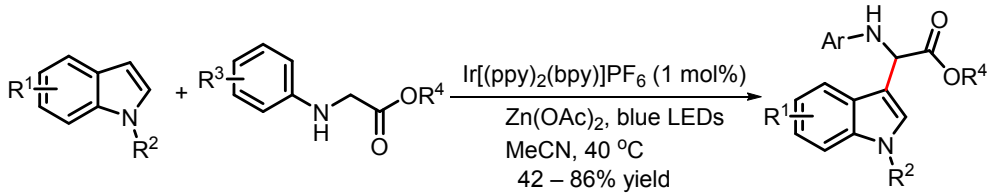
Electron-rich aromatics



Stephenson, C. R. J. *J. Org. Chem.* **2012**, *77*, 4425; *Org. Lett.* **2012**, *14*, 94



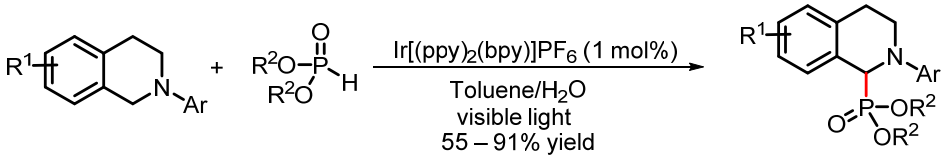
Li, J.-H. *J. Org. Chem.* **2012**, *77*, 8705.



Rueping, M. et al *Chem Commun.* **2012**, *48*, 11960.

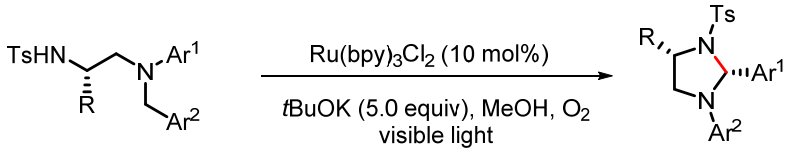
C–X bonds formation

C–P



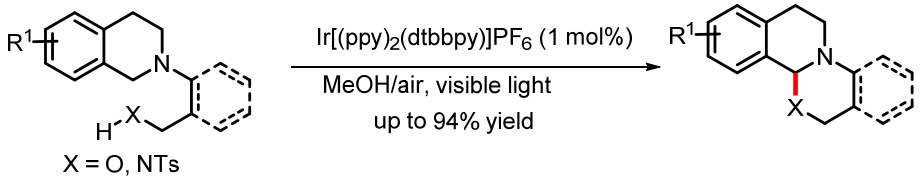
Rueping, M. et al *Chem. Commun.* **2011**, *47*, 8679.

C–N



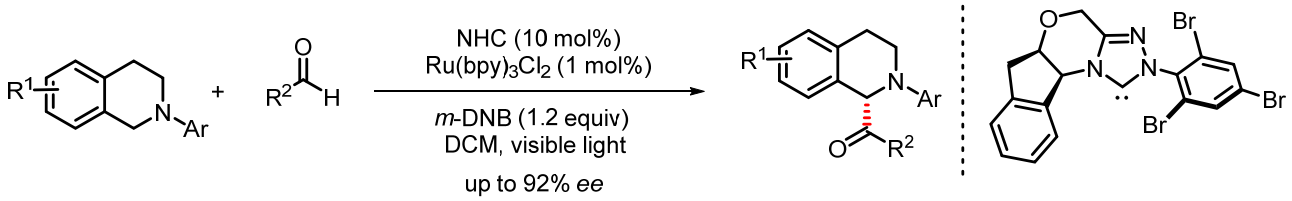
Xiao, W.-J. et al *Chem. Commun.* **2011**, *47*, 8337.

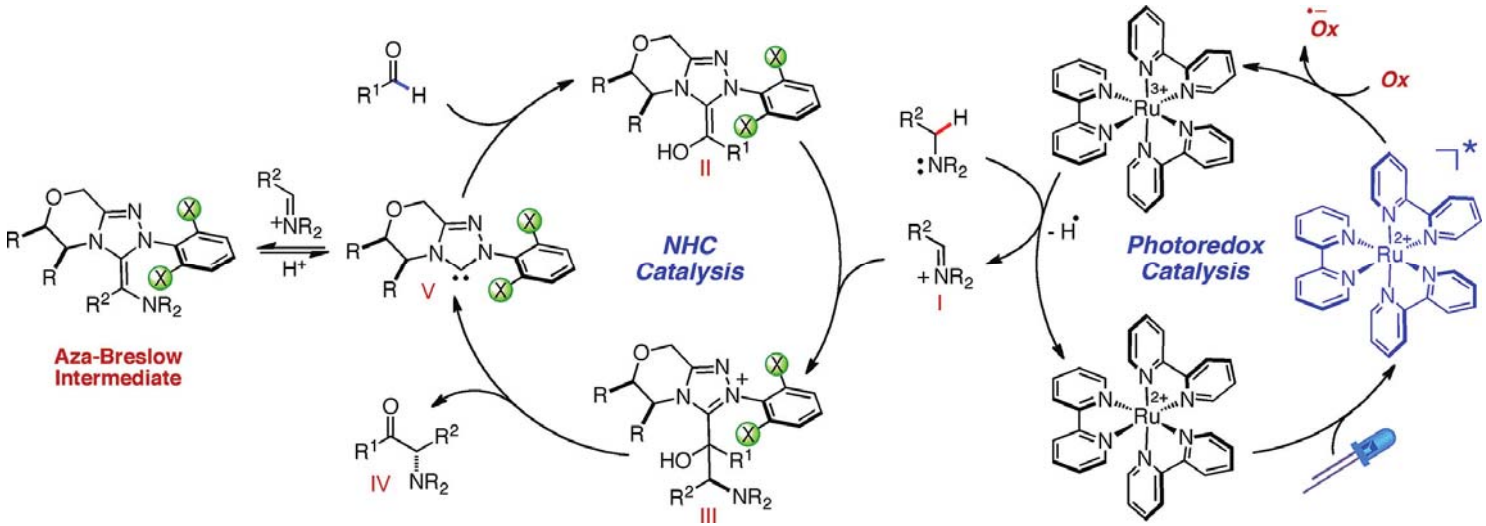
C–O



Xiao, W.-J. et al *RSC Adv.* **2012**, *2*, 4065.

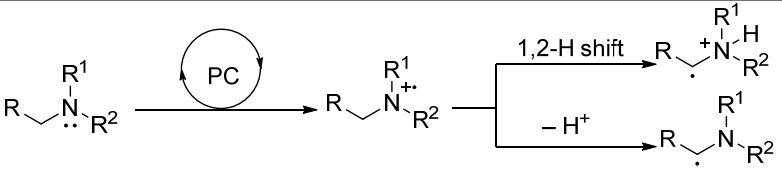
α-Acylation of Tertiary Amines

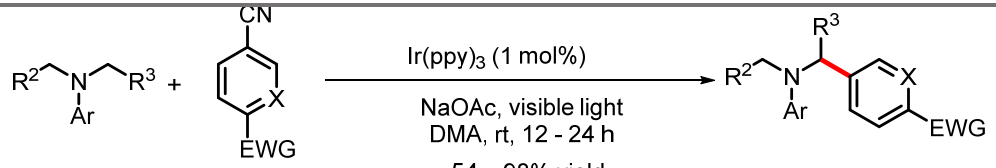




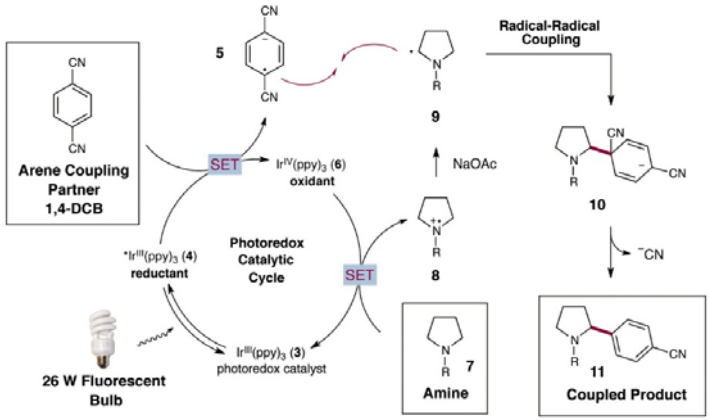
DiRocco, D. A.; Rovis, T., *J. Am. Chem. Soc.* **2012,** *134*, 8094

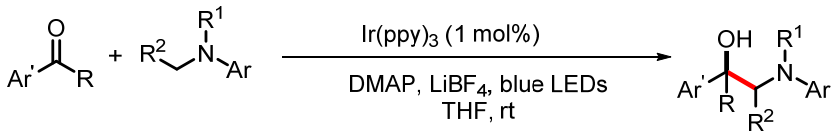
Mechanism for α-Aminoalkyl radical formation



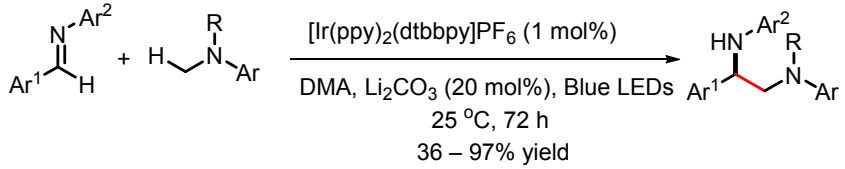


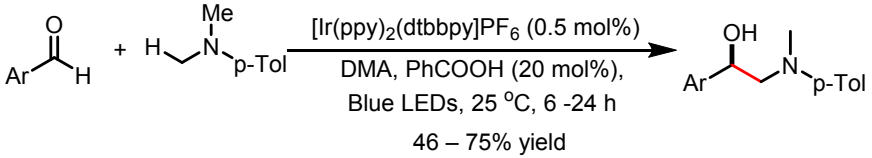
McNally, A.; Prier, C. K.; MacMillan, D. W. C., *Science* **2011**, *334*, 1114.



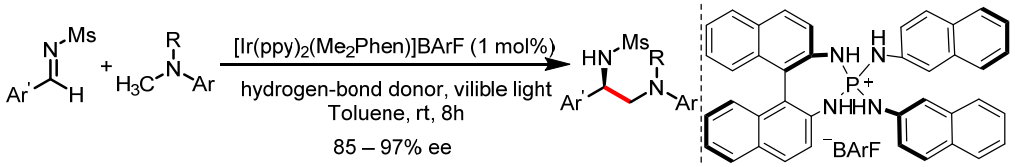


Xiao, W.-J. et al *J. Org. Chem.* **2016**, *81*, 7237.

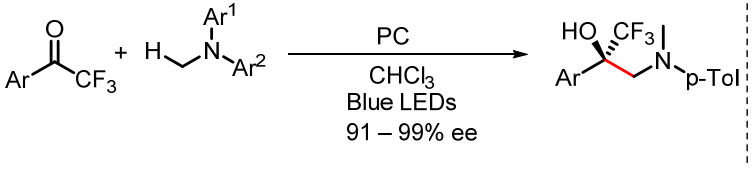


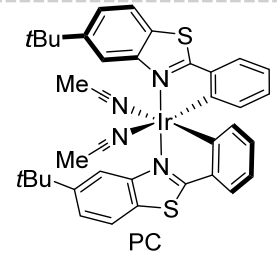


Rueping, M., et al *Angew. Chem. Int. Ed.* **2016**, *55*, 6776.

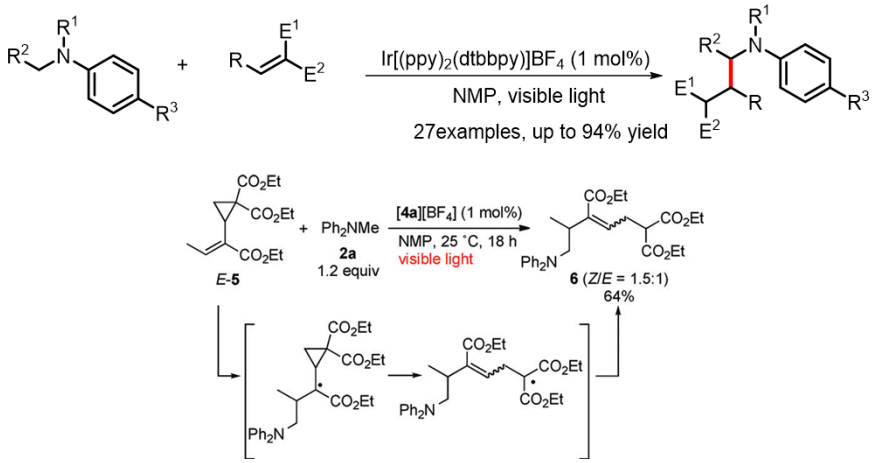


Ooi, T. et al *J. Am. Chem. Soc.* **2015**, *137*, 13768

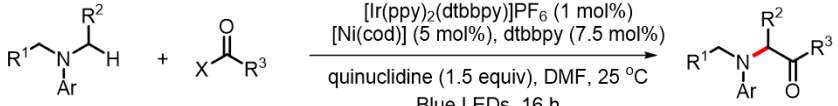




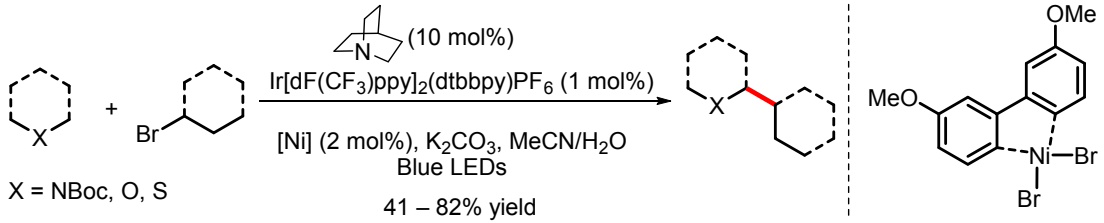
Meggers, E. et al *Angew. Chem. Int. Ed.* **2016**, *55*, 685



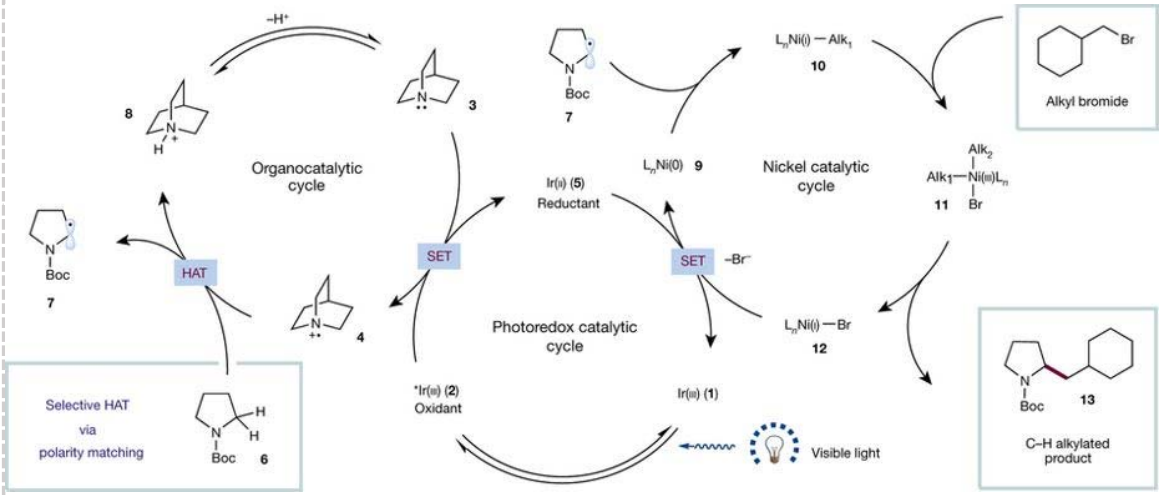
Miyake, Y.; Nakajima, K.; Nishibayashi, Y., *J. Am. Chem. Soc.* **2012**, *134*, 3338.

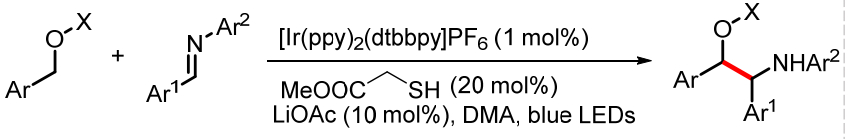


Joe, C. L.; Doyle, A. G., *Angew. Chem. Int. Ed.* **2016**, *55*, 4040.

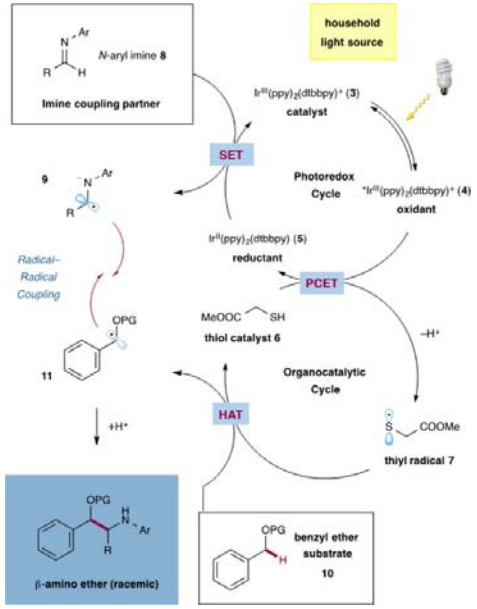


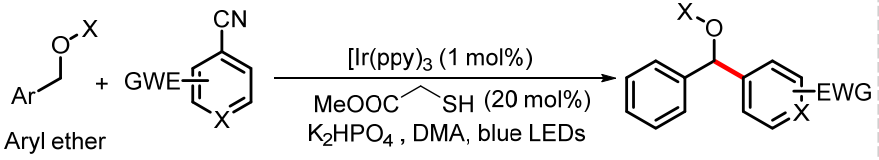
MacMillan, D. W. C.et al *Nature*, **2017**, *547*, 79.



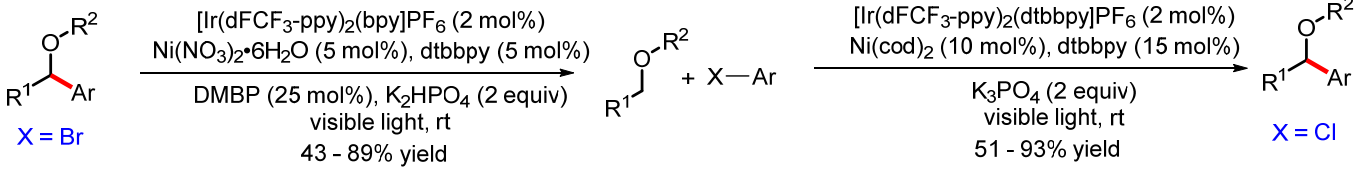


Hager, D.; MacMillan, D. W. C., *J. Am. Chem. Soc.* **2014**, *136*, 16986.





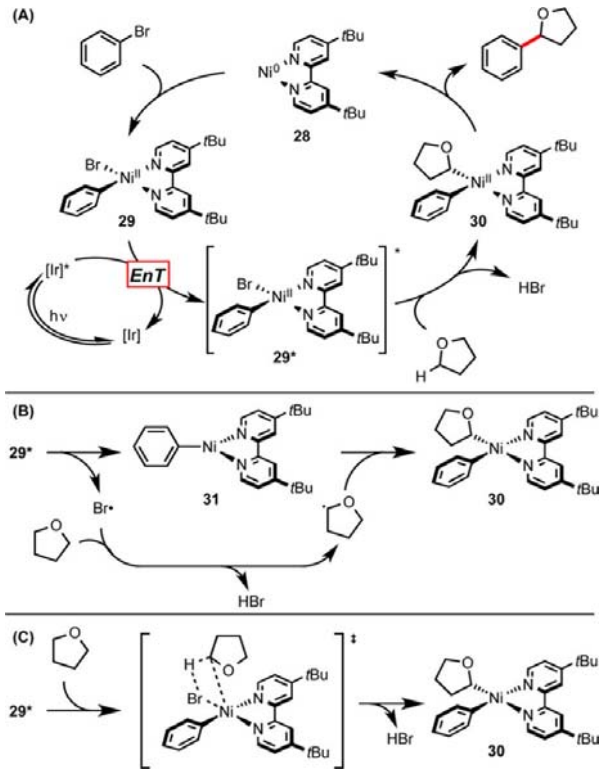
Qvortrup, K.; Rankic, D. A.; MacMillan, D. W. C., *J. Am. Chem. Soc.* **2014**, *136*, 626.



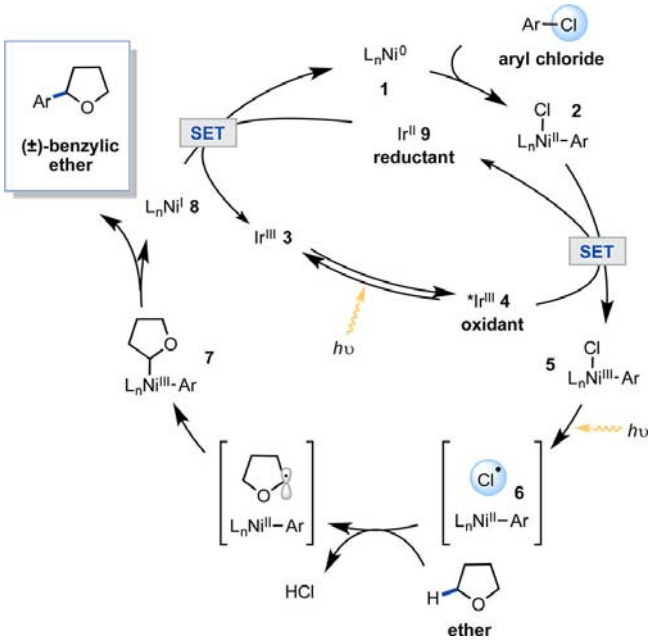
Molander, G. A. et al *J. Am. Chem. Soc.* **2016**, *138*, 12715.

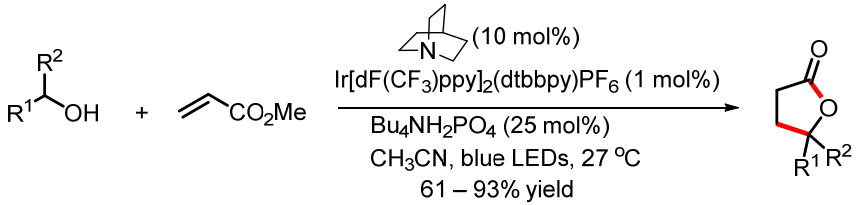
Doyle, A. G. et al *J. Am. Chem. Soc.* **2016**, *138*, 12719.

Molander's mechanism

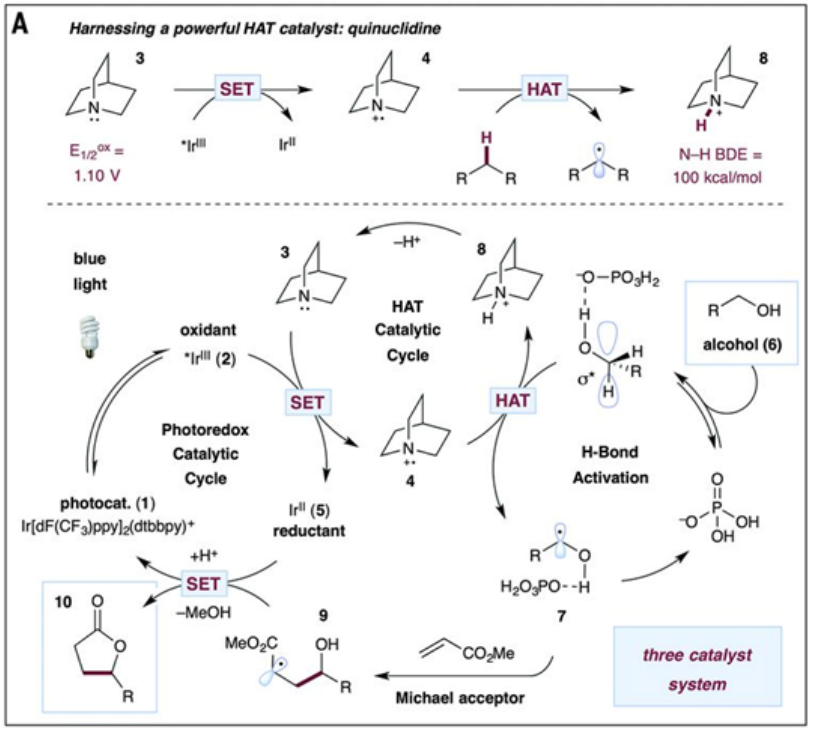


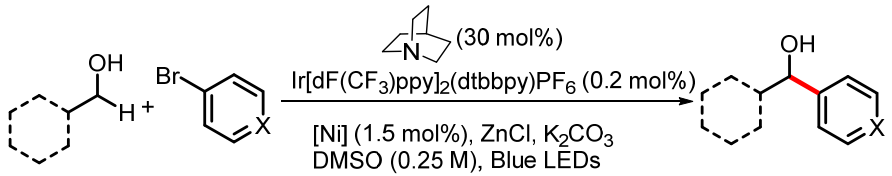
Doyle's mechanism

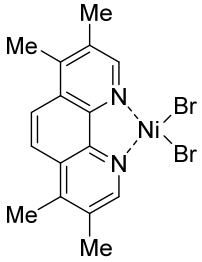




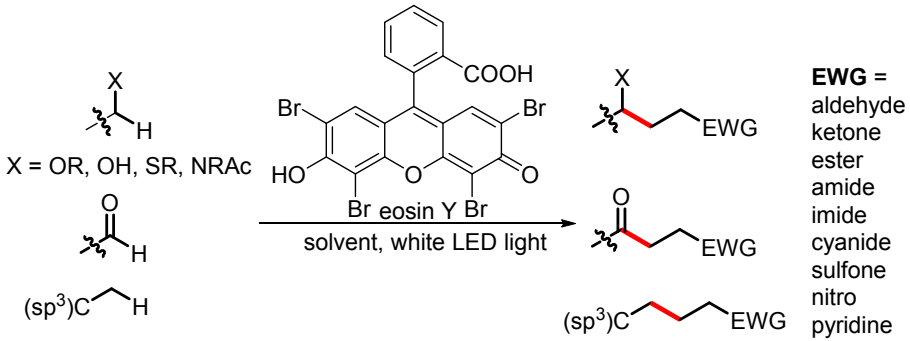
Jeffrey, J. L.; Terrett, J. A.; MacMillan, D. W. C., *Science* **2015**, *349*, 1532.





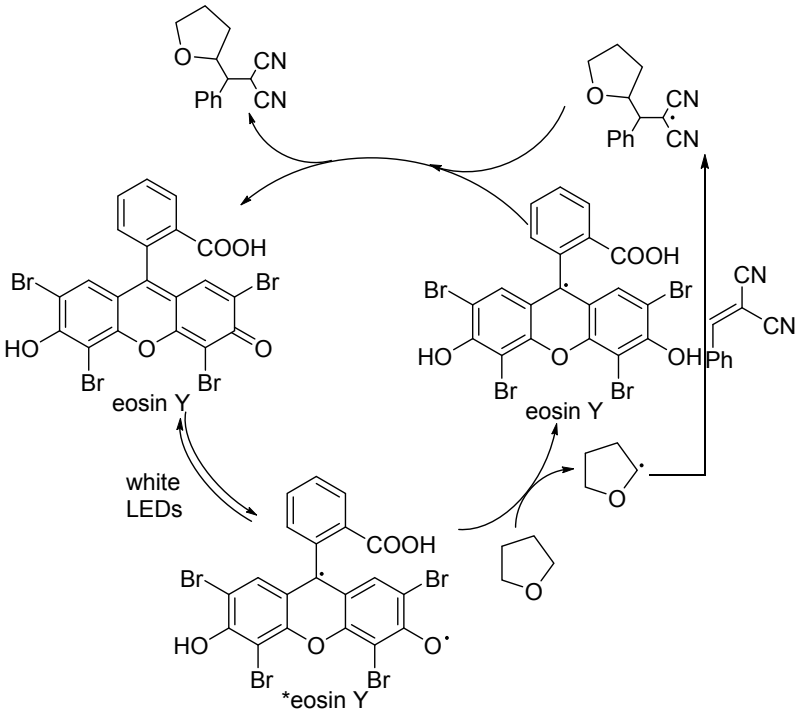


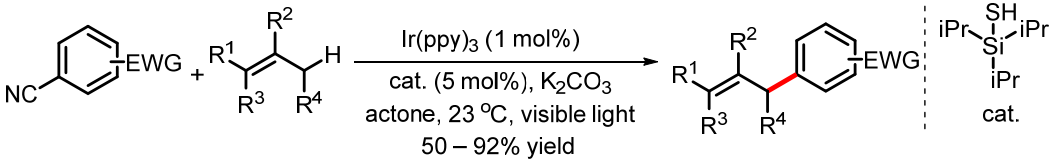
MacMillan, D. W. C. at al *Angew. Chem. Int. Ed.* **2018**, *57*, 5369.



EWG =
aldehyde
ketone
ester
amide
imide
cyanide
sulfone
nitro
pyridine

Wu, J. et al *Angew. Chem. Int. Ed.* **2018**, *57*, 8514.





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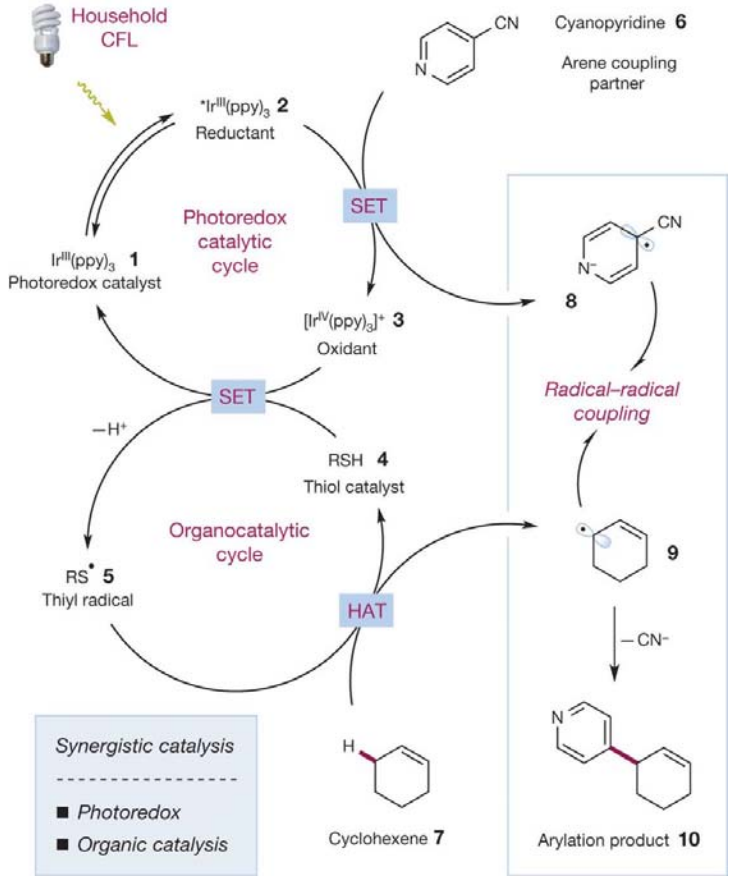
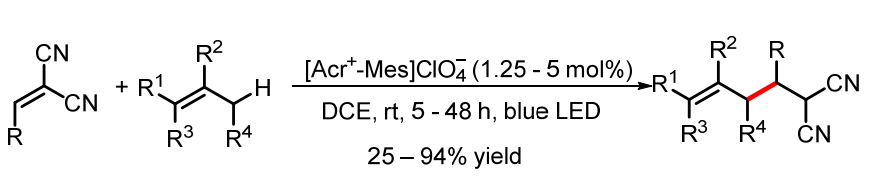
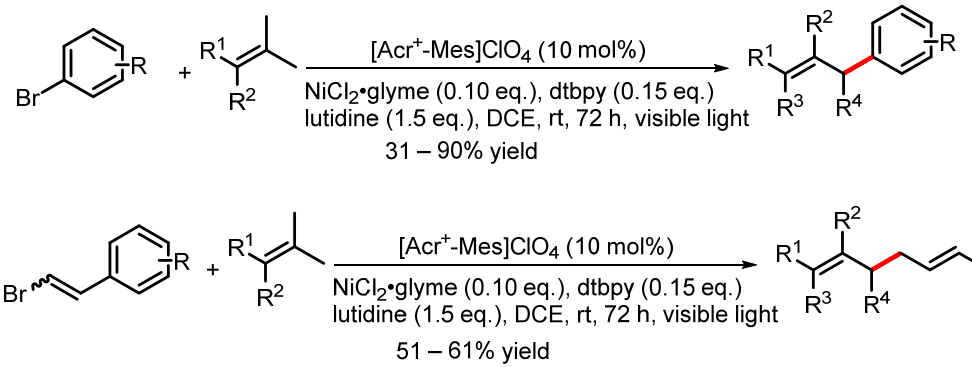
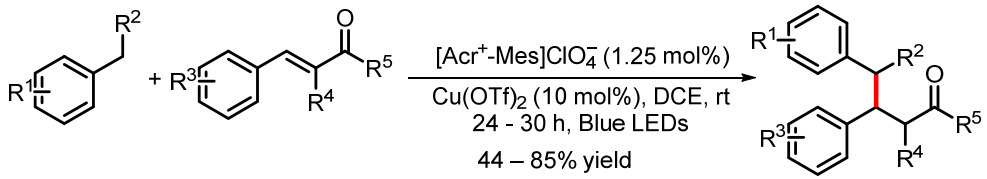




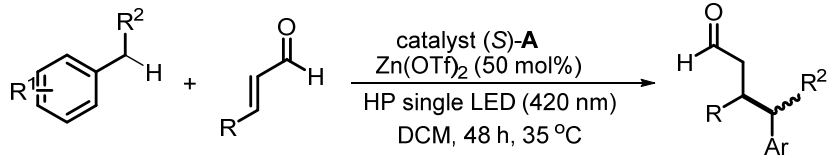
Zhou, R.; Liu, H.; Tao, H.; Yu, X.; Wu, J., *Chem. Sci.* **2017**, *8*, 4654.



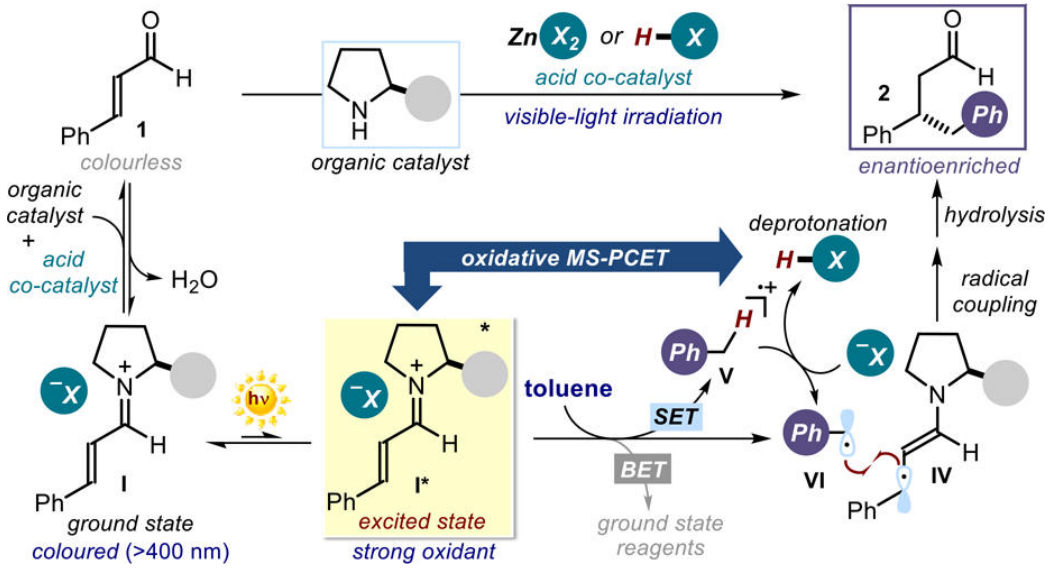
Huang, L.; Rueping, M., *Angew. Chem. Int. Ed.* **2018**, *57*, 10333.

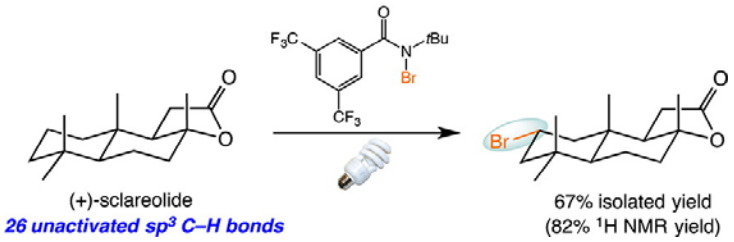


Liu, H.; Ma, L.; Zhou, R.; Chen, X.; Fang, W.; Wu, J., *ACS Catal.* **2018**, *8*, 6224.



Mazzarella, D.; Crisenza, G. E. M.; Melchiorre, P., *J. Am. Chem. Soc.* **2018**, *140*, 8439.





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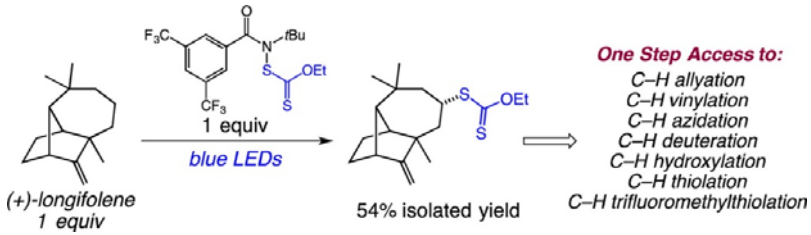

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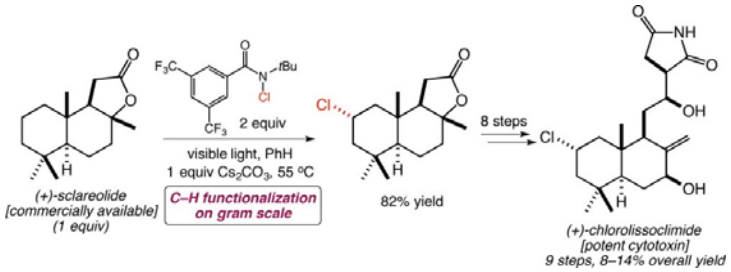

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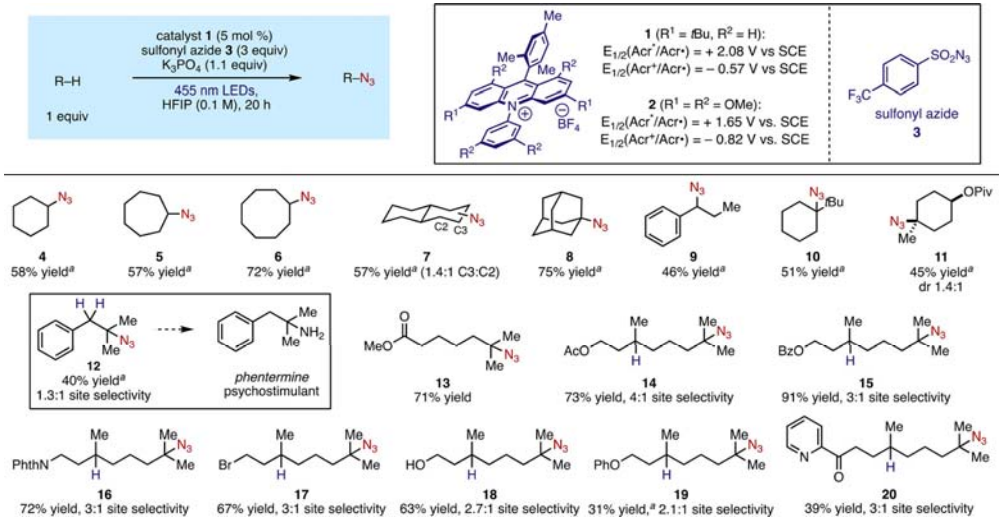
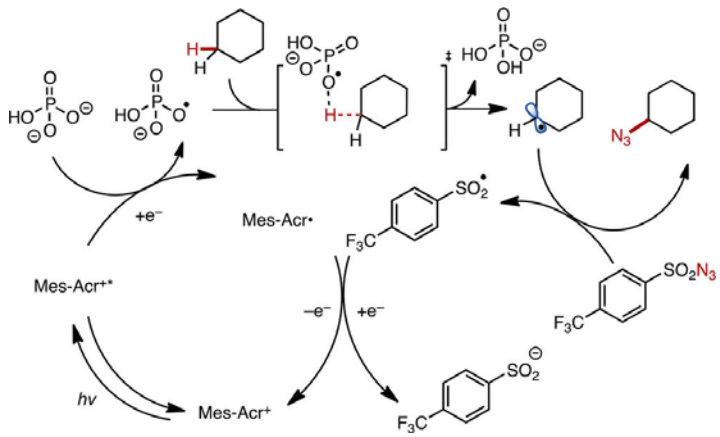
Alexanian, E. J. et al *Chem. Sci.* **2018**, *9*, 5360





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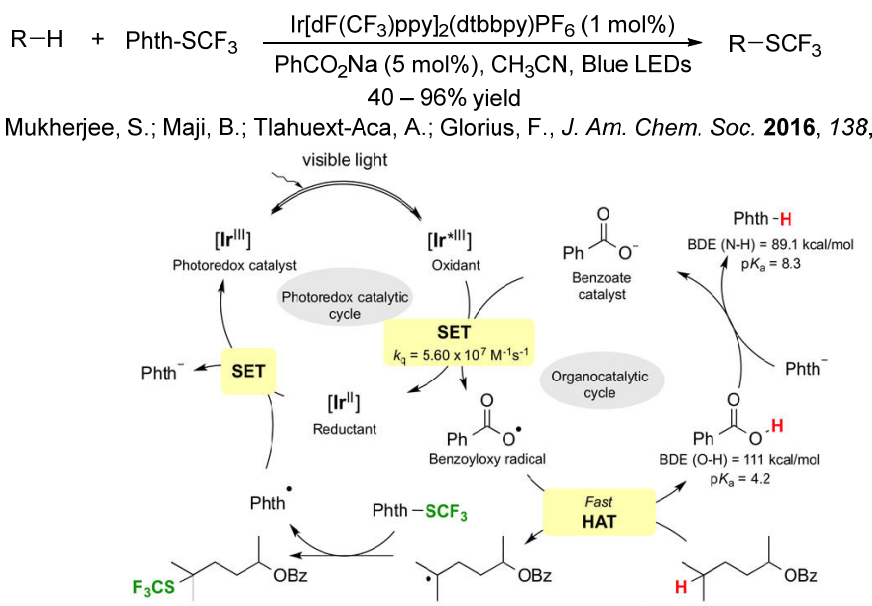
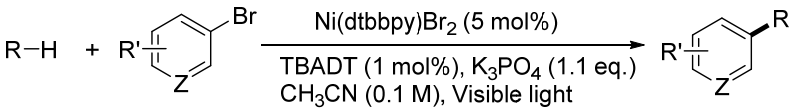
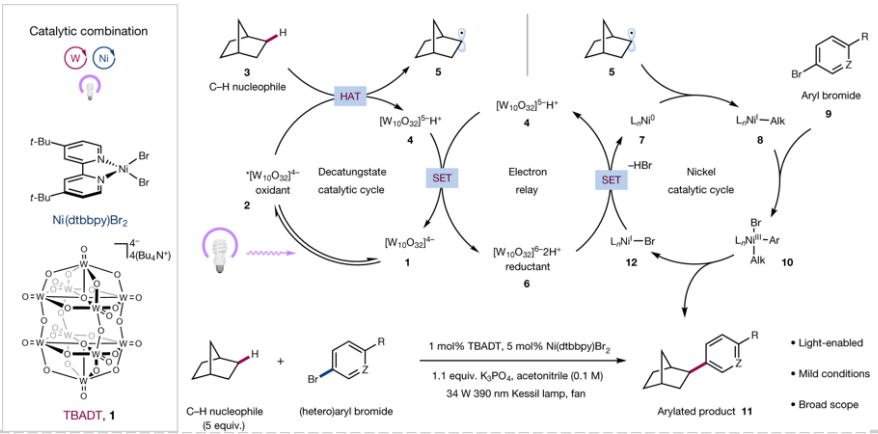
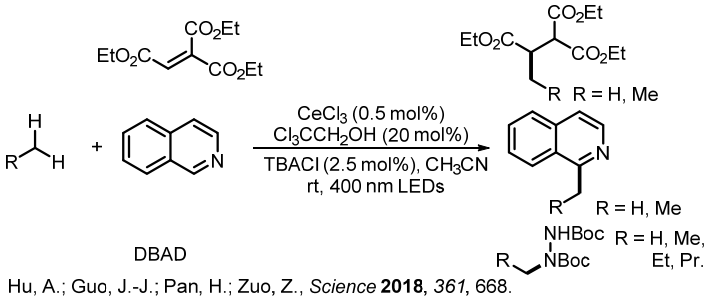
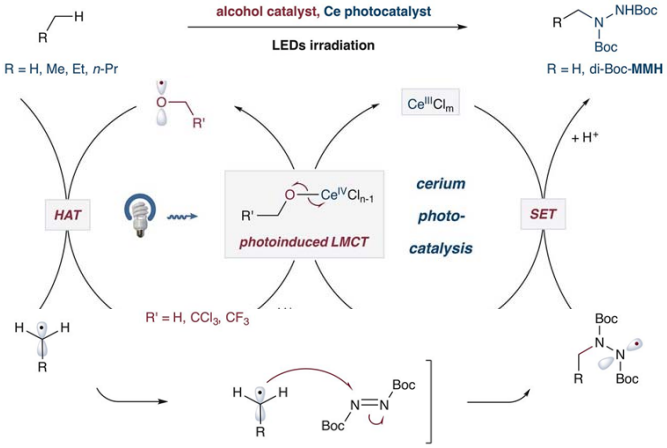
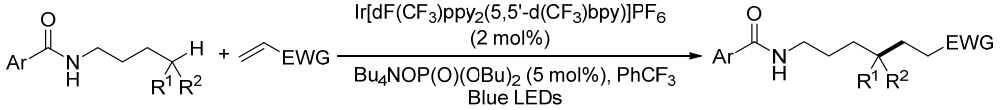

R–H + Phth-SCF3
Ir[dF(CF3)ppy]2(dtbbpy)PF6 (1 mol%)
PhCO2Na (5 mol%), CH3CN, Blue LEDs
R–SCF3
40 – 96% yield
Mukherjee, S.; Maji, B.; Tlahuext-Aca, A.; Glorius, F., J. Am. Chem. Soc. 2016, 138, 16200.
visible light
[IrIII]
Photoredox catalyst
[Ir*III]
Oxidant
Photoredox catalytic cycle
SET
kq = 5.60 x 10^7 M^-1s^-1
Benzoate catalyst
Phth-H
BDE (N-H) = 89.1 kcal/mol
pKa = 8.3
Phth−
SET
[IrII]
Reductant
Organocatalytic cycle
Benzoyloxy radical
BDE (O-H) = 111 kcal/mol
pKa = 4.2
Phth•
Phth–SCF3
Fast HAT
F3CS
OBz
H


R–H + R'
Br
Z
Ni(dtbbpy)Br2 (5 mol%)
TBADT (1 mol%), K3PO4 (1.1 eq.)
CH3CN (0.1 M), Visible light
R
31 – 94% yield
MacMillan, D. W. C. at al Nature 2018, 560, 70

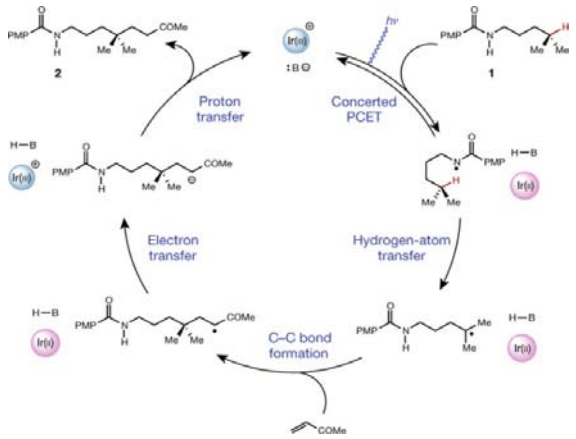

Catalytic combination
Ni(dtbbpy)Br2
TBADT, 1
C–H nucleophile
HAT
Decatungstate catalytic cycle
SET
Electron relay
Nickel catalytic cycle
Aryl bromide
reductant
C–H nucleophile (5 equiv.)
(hetero)aryl bromide
1 mol% TBADT, 5 mol% Ni(dtbbpy)Br2
1.1 equiv. K3PO4, acetonitrile (0.1 M)
34 W 390 nm Kessil lamp, fan
Arylated product 11
• Light-enabled
• Mild conditions
• Broad scope

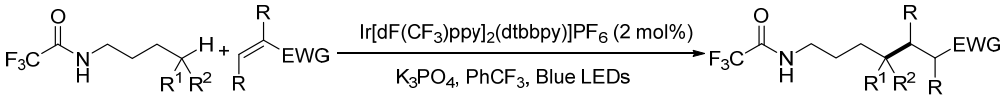

CO2Et
EtO2C
CO2Et
CeCl3 (0.5 mol%)
Cl3CCH2OH (20 mol%)
TBACl (2.5 mol%), CH3CN
rt, 400 nm LEDs
R = H, Me
NHBoc
NBoc
R = H, Me, Et, Pr.
DBAD
Hu, A.; Guo, J.-J.; Pan, H.; Zuo, Z., Science 2018, 361, 668.


alcohol catalyst, Ce photocatalyst
LEDs irradiation
R = H, Me, Et, n-Pr
R = H, di-Boc-MMH
HAT
SET
CeIIICln
CeIVCln-1
photoinduced LMCT
cerium photo-catalysis
R' = H, CCl3, CF3
+ H+

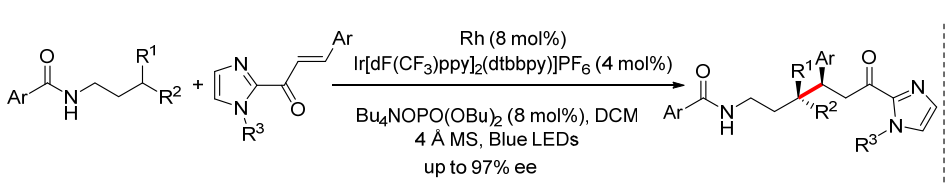


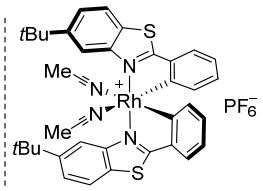
Choi, G. J.; Zhu, Q.; Miller, D. C.; Gu, C. J.; Knowles, R. R., *Nature* **2016**, *539*, 268.





Rovis, T. et al *Nature* **2016**, *539*, 272; *J. Am. Chem. Soc.* **2017**, *139*, 14897.





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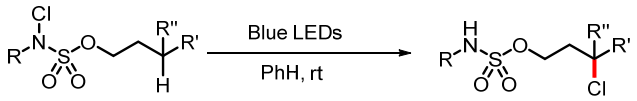
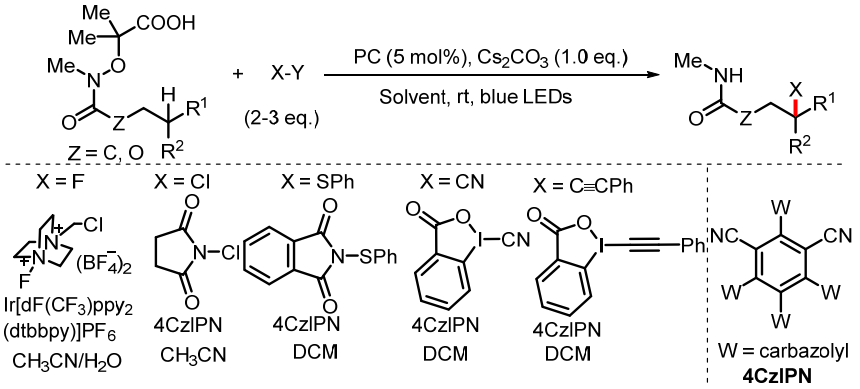
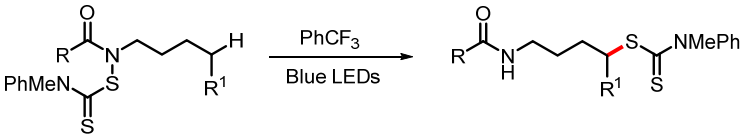
Yuan, W.; Zhou, Z.; Gong, L.; Meggers, E., Chem. Commun. **2017**, *53*, 8964.



Short, M. A.; Blackburn, J. M.; Roizen, J. L., *Angew. Chem. Int. Ed.* **2018**, *57*, 296.



Leonori, D. et al *Angew. Chem. Int. Ed.* **2018**, *27*, DOI: 10.1002/anie.201807941



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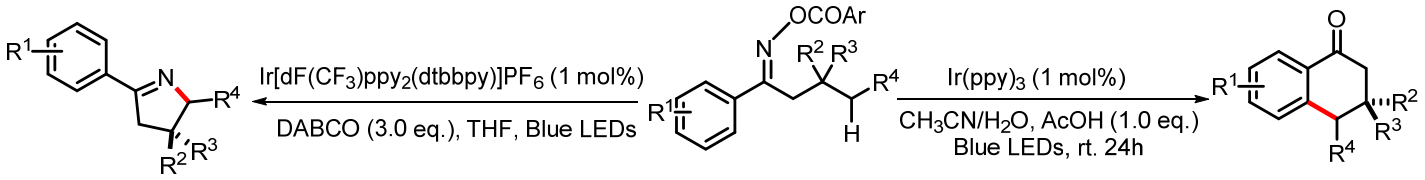

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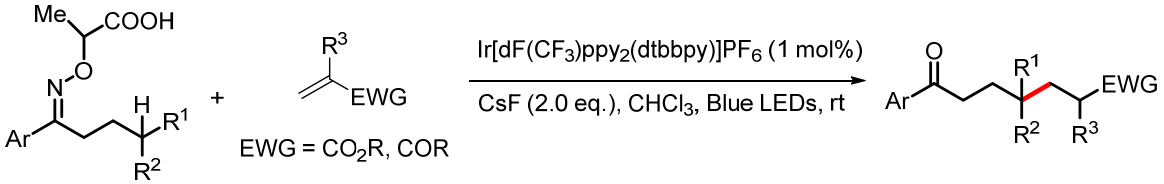

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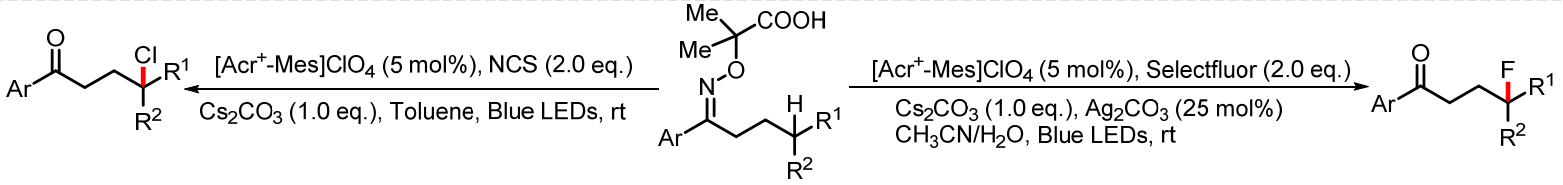

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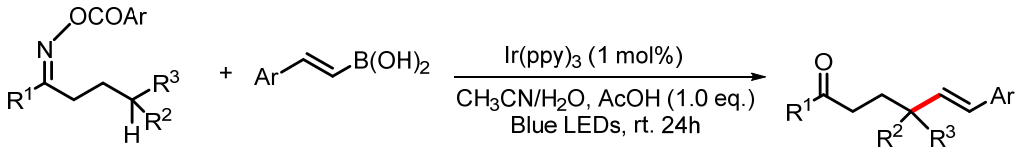
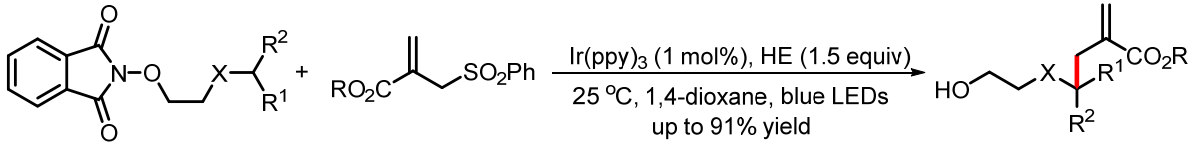


Shen, X.; Zhao, J.-J.; Yu, S., *Org. Lett.* **2018**, *20*, 5523.



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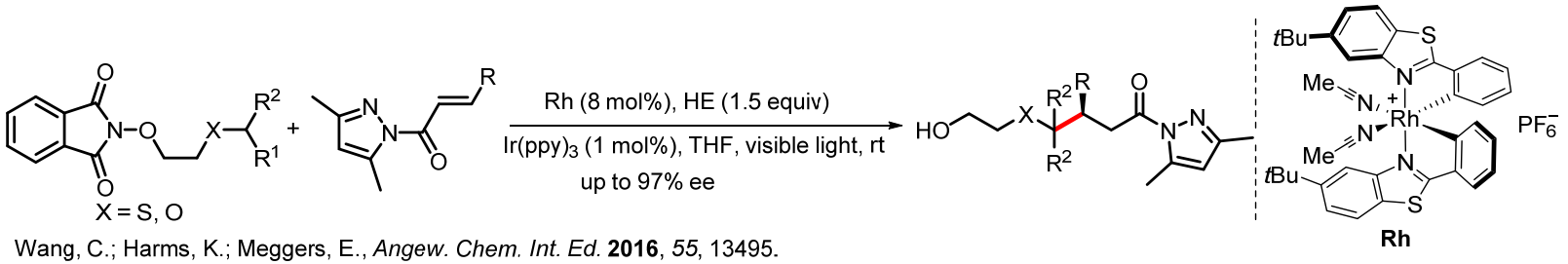
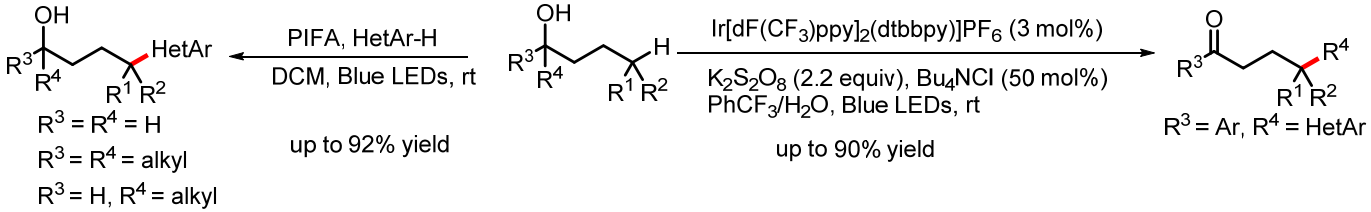


Wang, C.; Harms, K.; Meggers, E., *Angew. Chem. Int. Ed.* **2016**, *55*, 13495.



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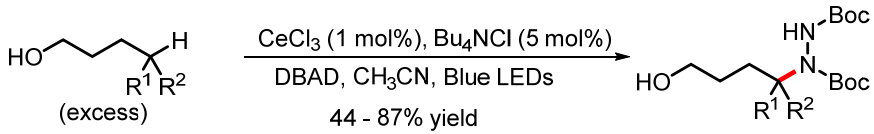

Hu, A.; Guo, J.-J.; Pan, H.; Tang, H.; Gao, Z.; Zuo, Z., *J. Am. Chem. Soc.* **2018**, *140*, 1612.

Advantage

- mild condition
- good compatibility with several functional group
- Formation of C-C and C-X bonds are possible

Disadvantage

- Poor regioselectivity
- Poor siteselectivity
- Enantioselectivity challenge

Many areas left to explore!