苯的去芳构化反应

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2019.4.19

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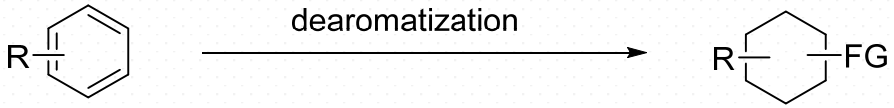
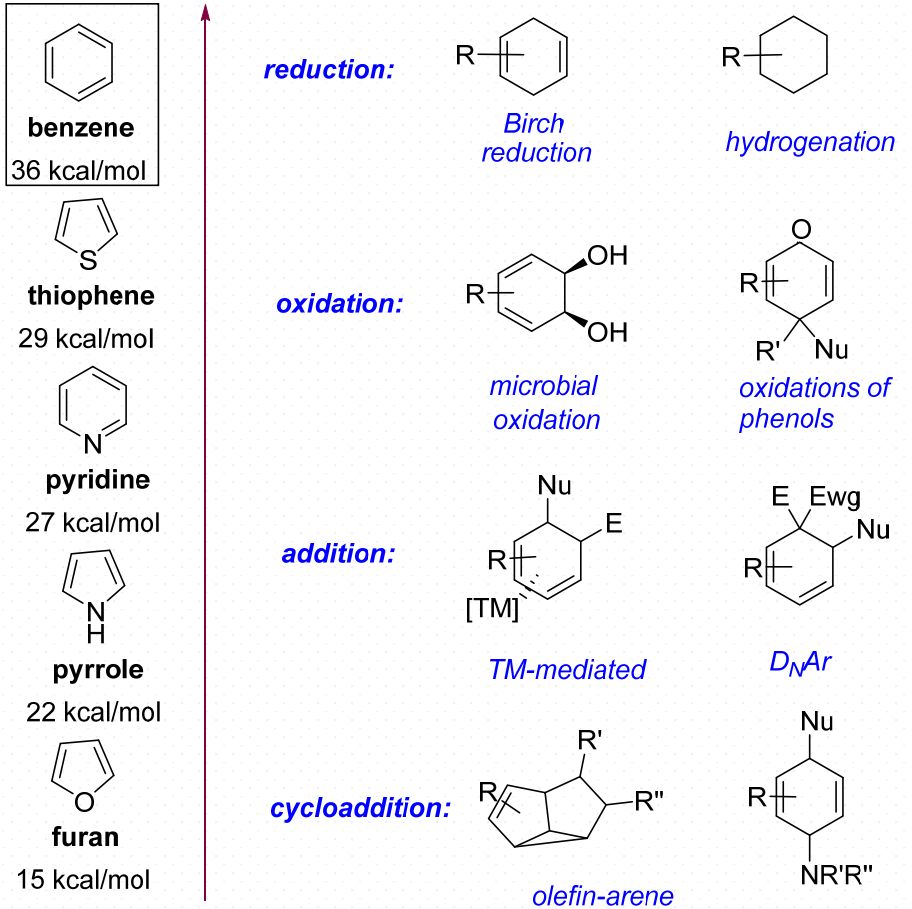
前言



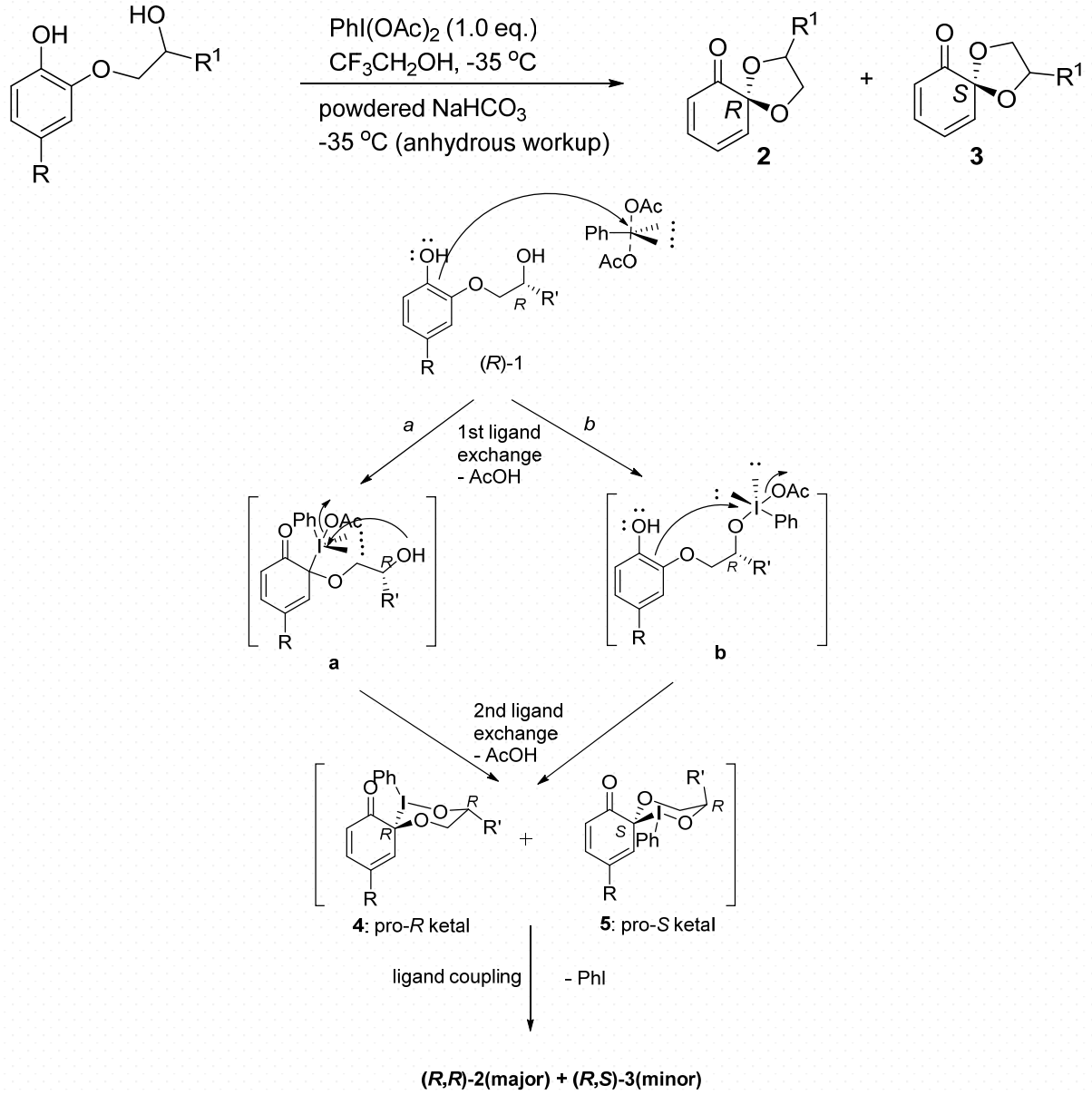
便宜，相对易得，稳定，平面

高度官能团化，丰富三维立体结构，
构建桥环、并环，广泛存在于天然产物中



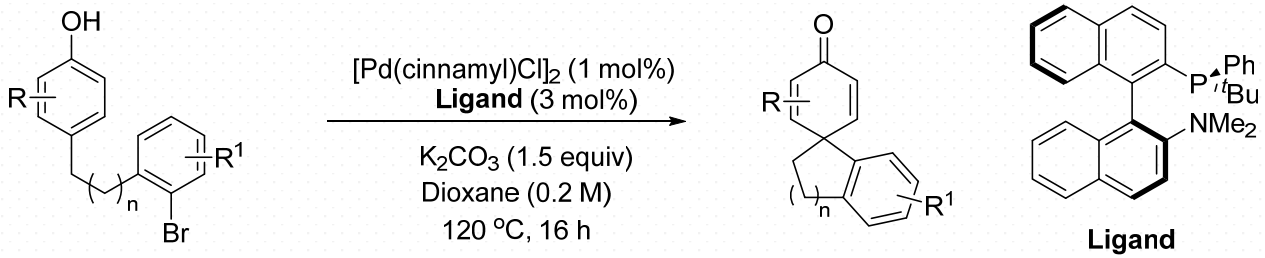
02 活化苯环的去芳构化

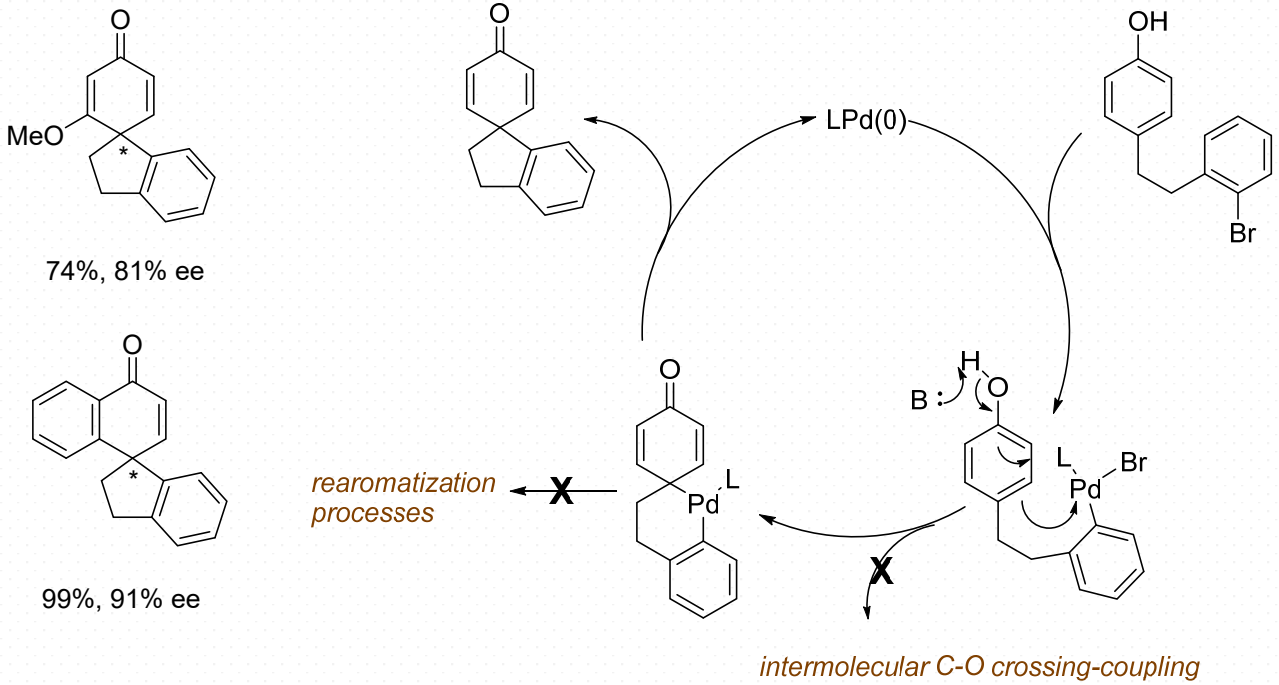
hypervalent iodine involved reactions



Pouysgu, L.; Chassaing, S.; Quideau, S. *Angew. Chem. Int. Ed.* **2008**, *47*, 3552

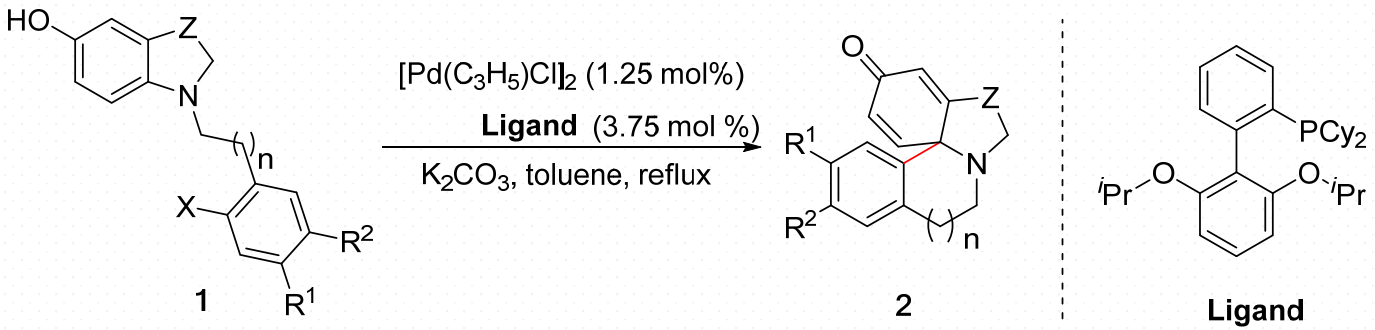
Arylative dearomatization reactions

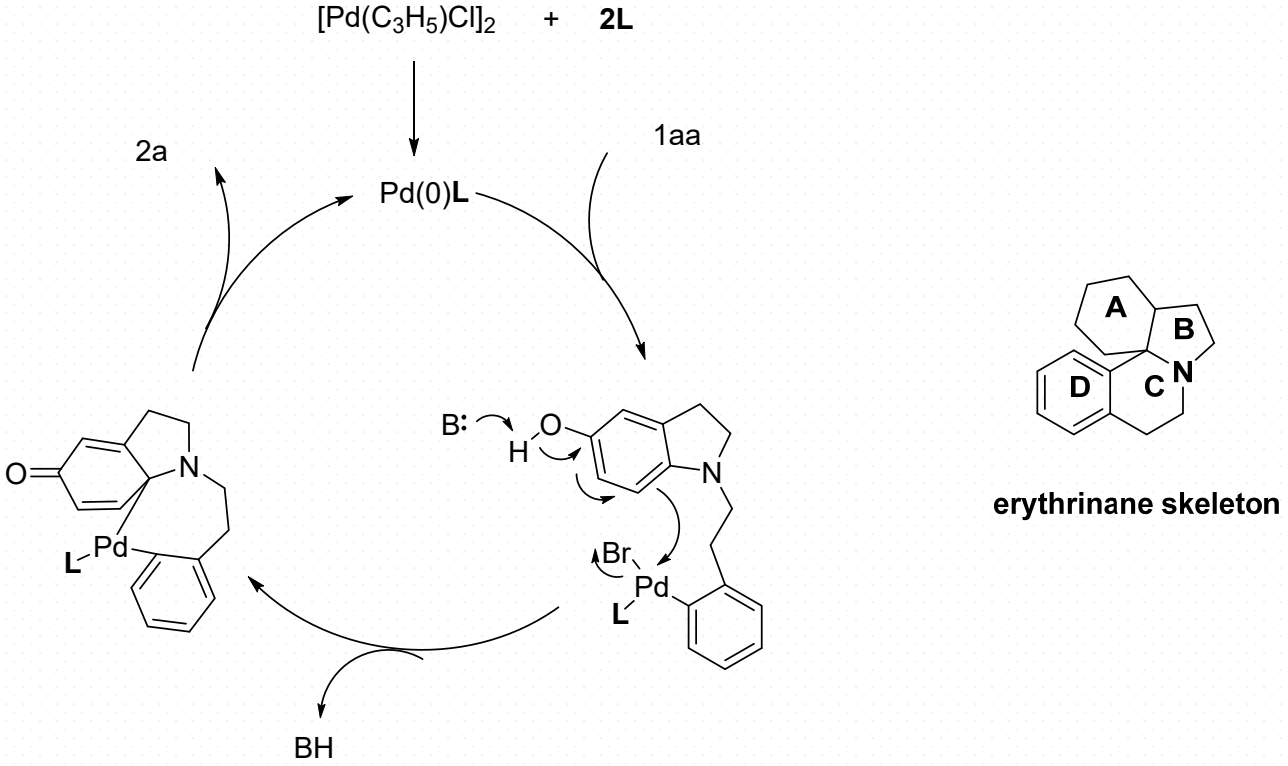




Rousseaux, S.; García-Fortanet, J.; Buchwald, S. *J. Am. Chem. Soc*. **2011**, *133*, 9282

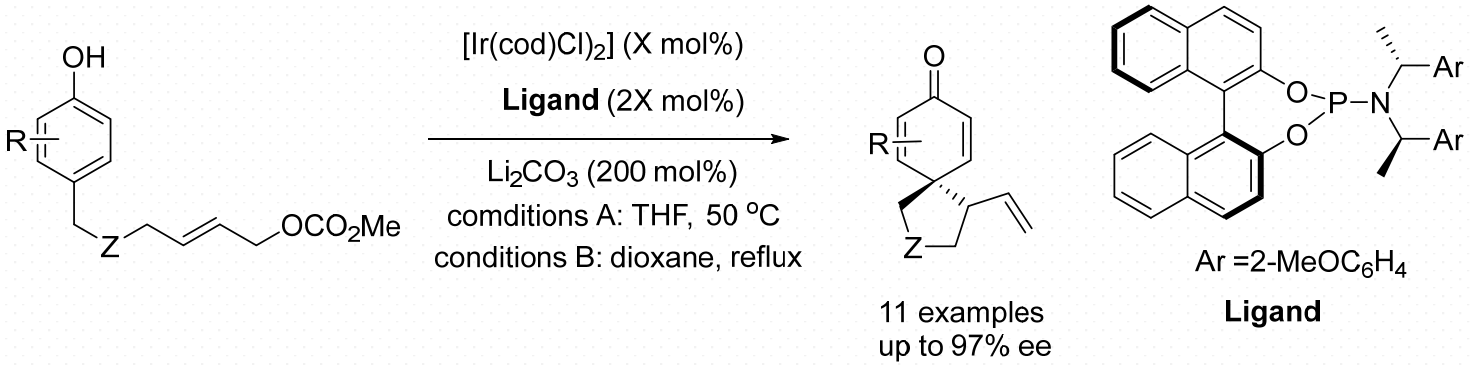
Arylative dearomatization reactions

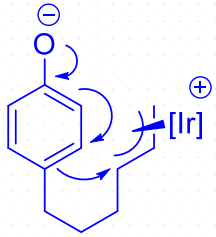




Xu, R.; Gu, Q.; Wu, W.; You, S. *J. Am. Chem. Soc*. **2014**, *136*, 15469

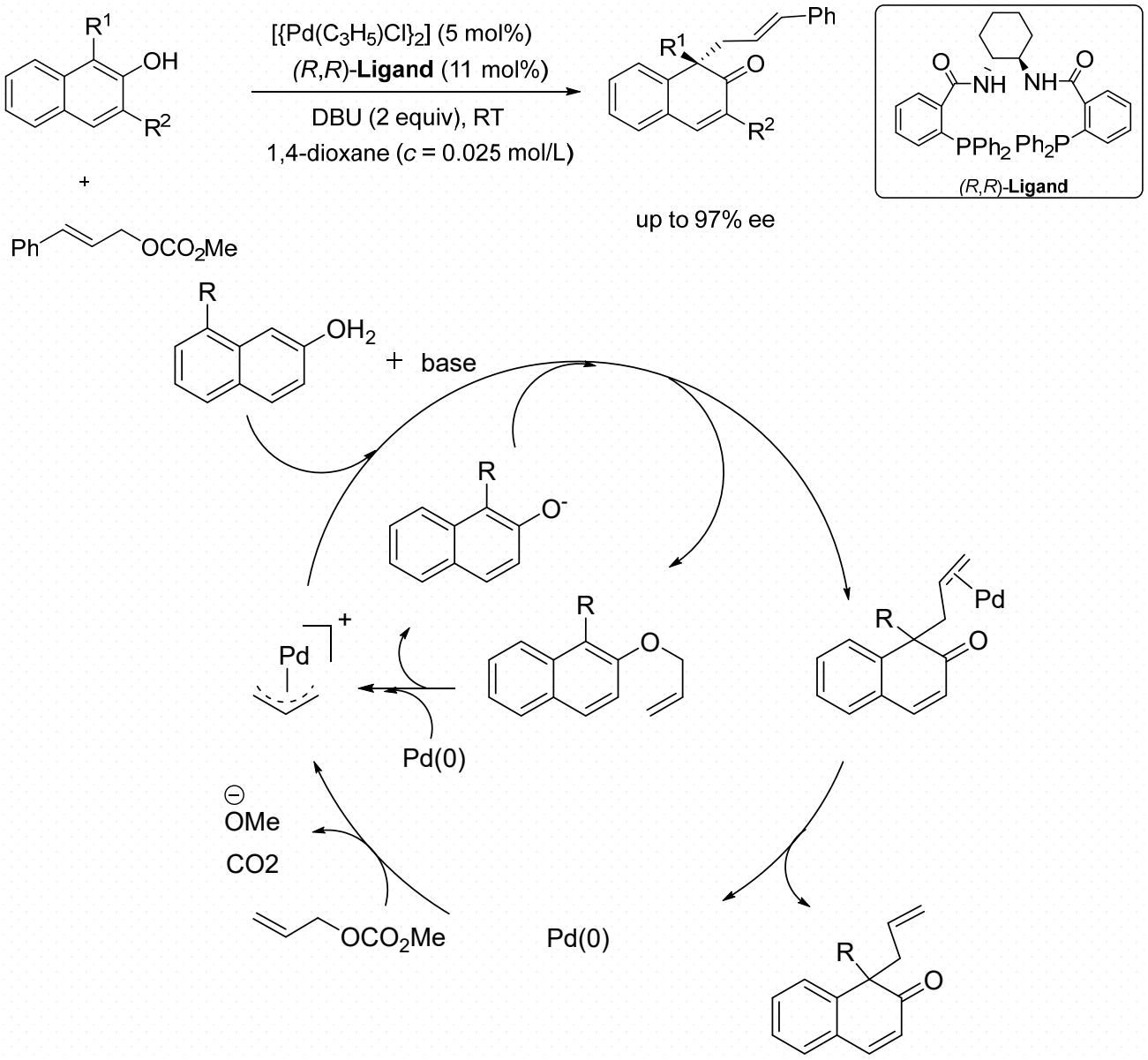
Allylative dearomatization reactions





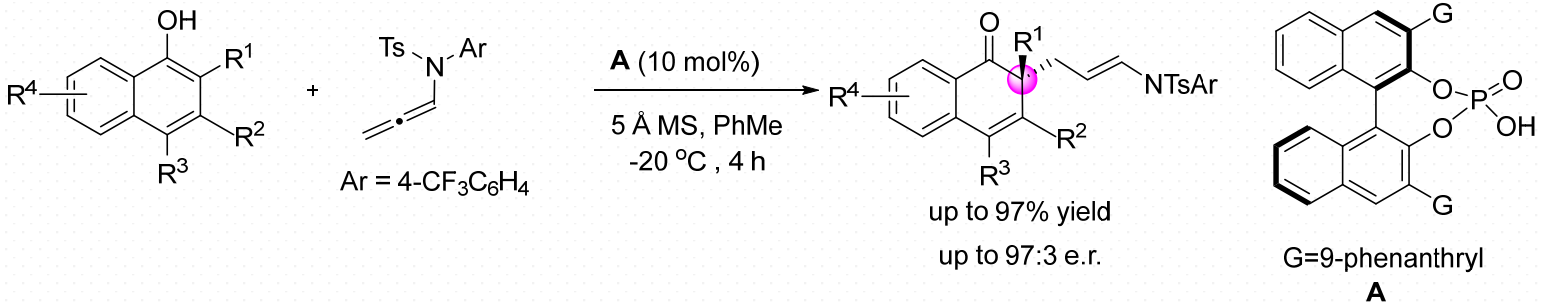
Wu, Q.; Liu, W.; Zhuo, C.; Rong, Z.; You, S. *Angew. Chem. Int. Ed*. **2011**, *50*, 4455

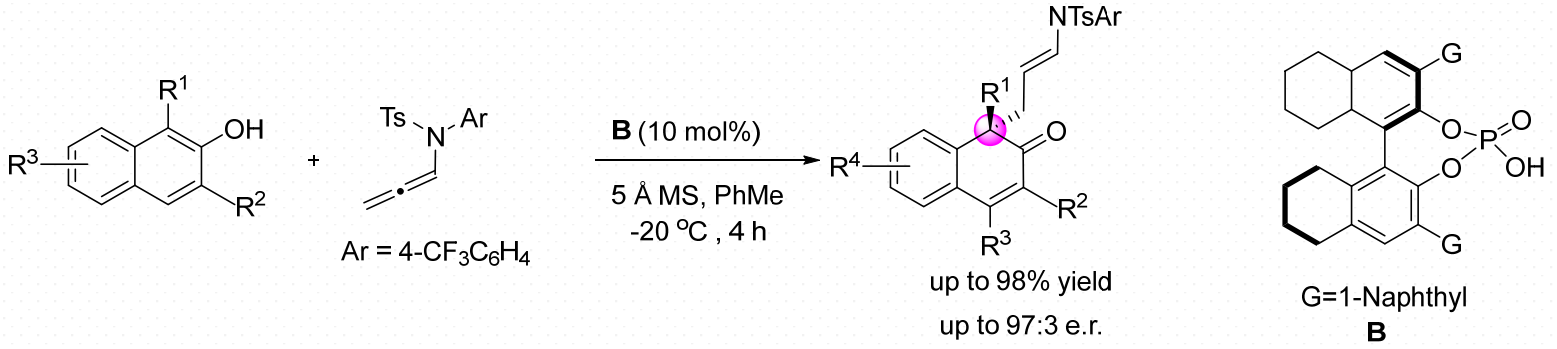
Allylative dearomatization reactions

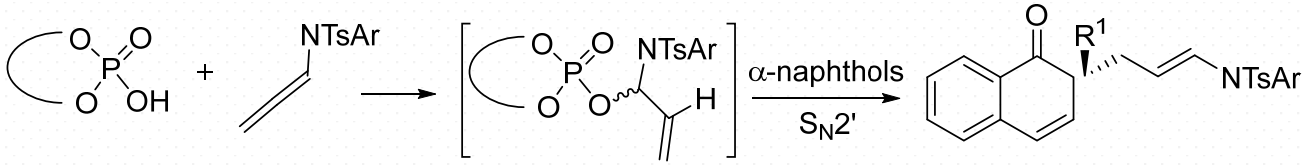


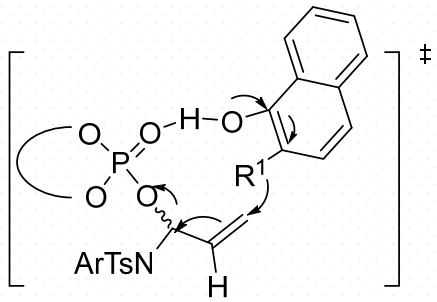
Zhuo, C.; You, S. *Angew. Chem. Int. Ed*. **2013**, *52*, 10056

Allylative dearomatization reactions



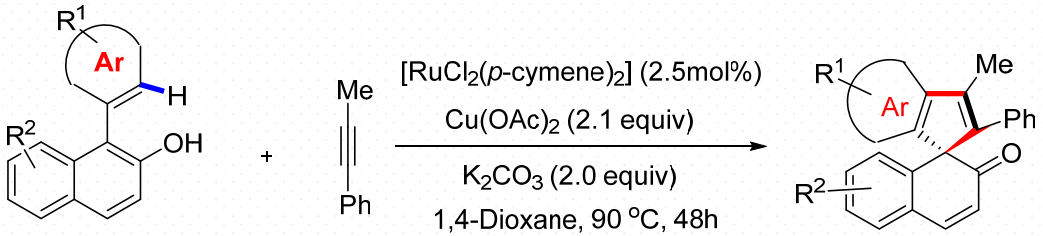




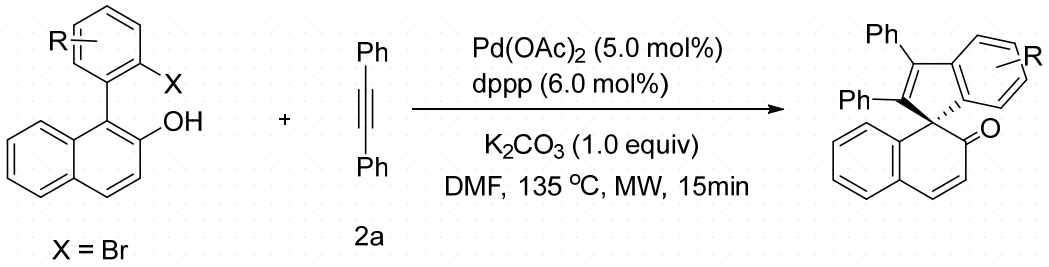


Yang, B.; Zhai, X.; Feng, S.; Hu, D.; Deng, Y.; Shao, Z. *Org. Lett*. **2019**, *21*, 330−334

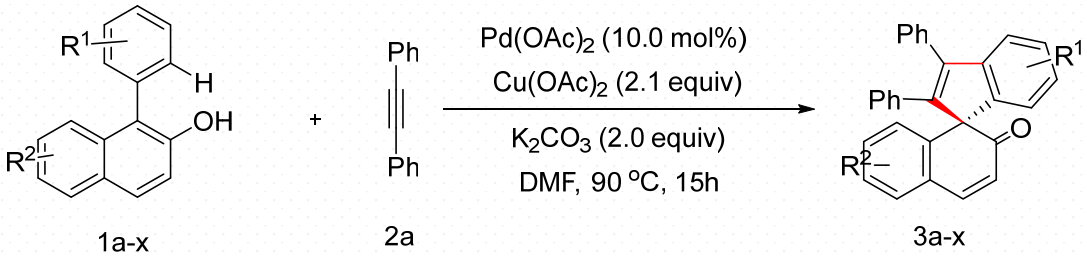
Alkenylative dearomatization reactions



Nan, J.; Zuo, Z.; Luo, L.; Bai, L.; Liu, J.; Luan, X. *J. Am. Chem. Soc.* **2013**, *135*, 17306

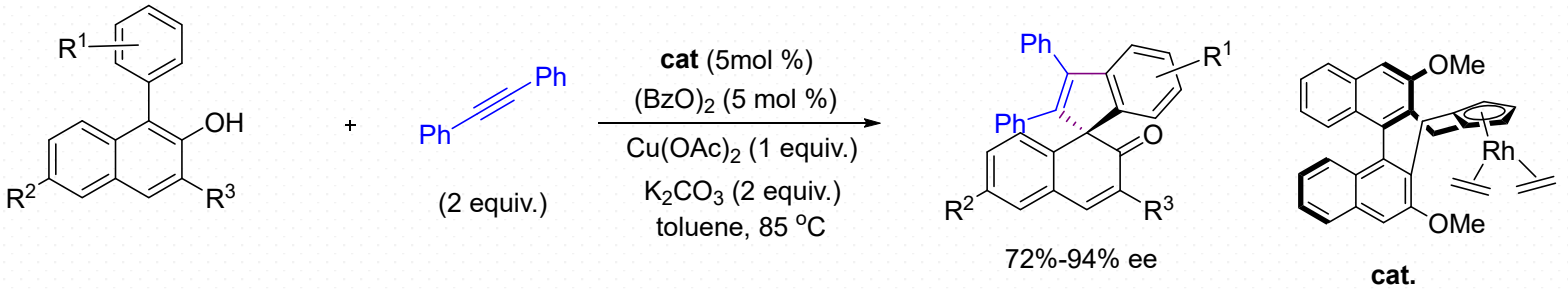


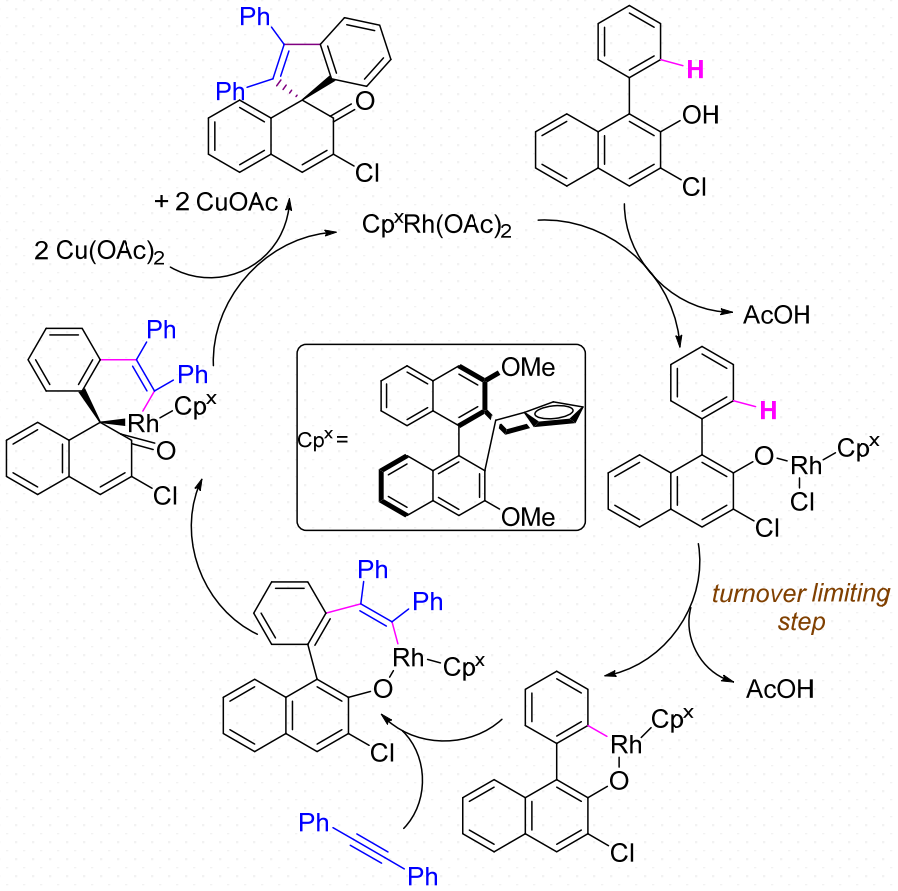
Zheng, H.; Bai, L.; Liu, J.; Luan, X. *Chem. Commun.*, **2015**, *51*, 3061



Han, L.; Wang, H.; Luan, X. *Org. Chem. Front.*, **2018**, *5*, 2453

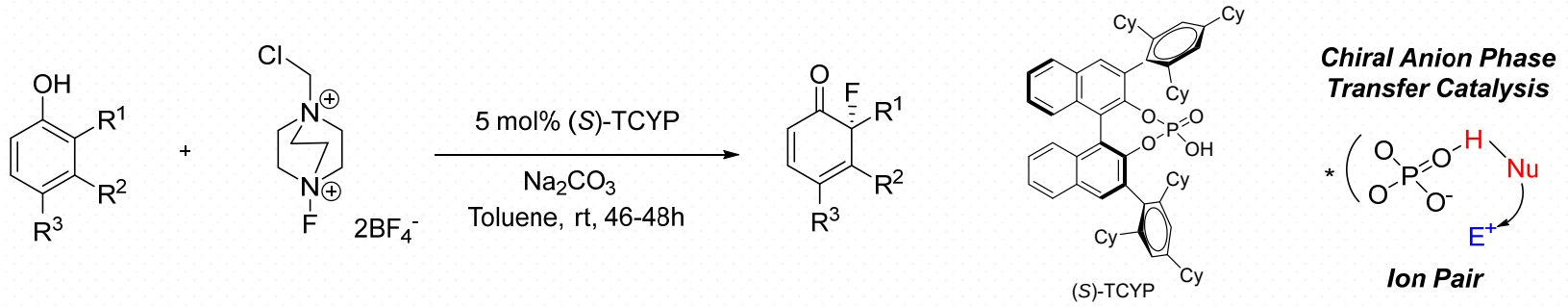
Alkenylative dearomatization reactions



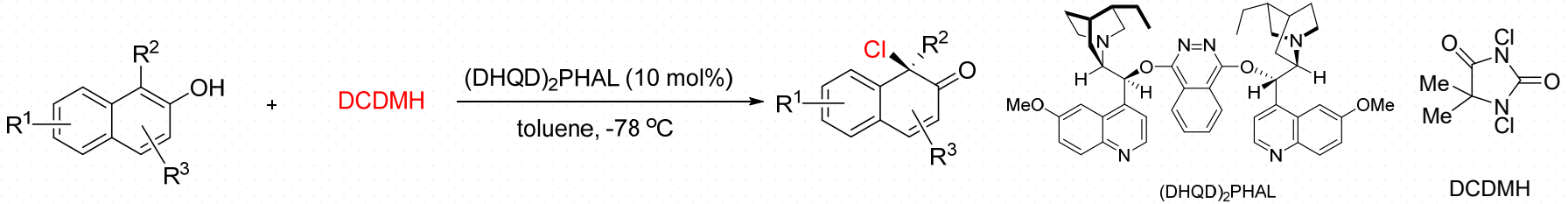


Zheng, J.; Wang, S.; Zheng, C.; You, S. *J. Am. Chem. Soc*. **2015**, *137*, 4880

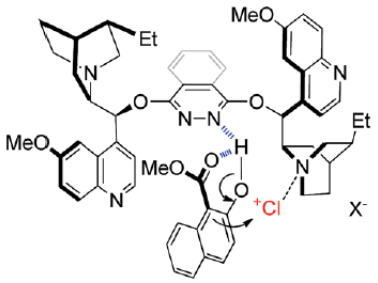
Halogenative dearomatization reactions



Phipps, R.; Toste, F. D. *J. Am. Chem. Soc*. **2013**, *135*, 1268



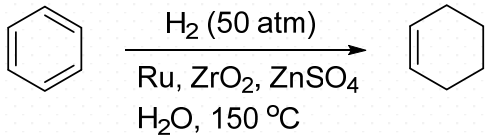
Yin, Q.; Wang, S.; Liang, X.; Gao, D.; You, S. *Chem. Sci*., **2015**, *6*, 4179



Proposed working model.

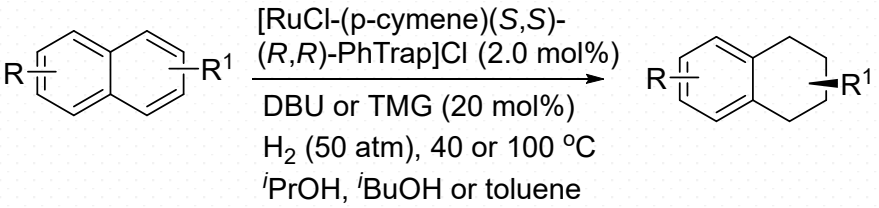
03 非活化苯环去芳构化

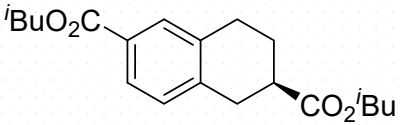
Dearomative hydrogenations



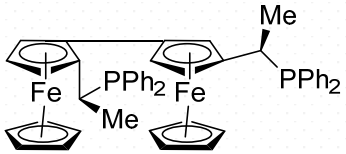
60% selective
at >90% conversion
50,000 tons/year

Asahi Chemical Co. chemoselective hydrogenation of benzene

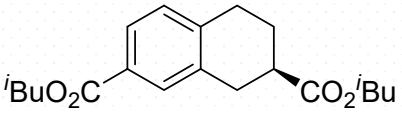




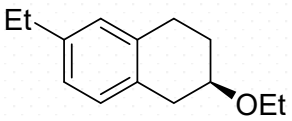
98%, 93:7 er



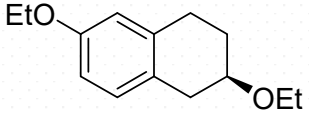
(*S*,*S*)-(*R*,*R*)-PhTrap



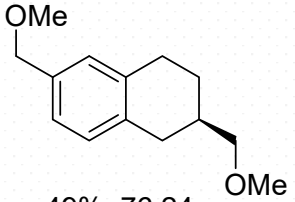
91%, 80.5:19.5 er



61%, 95.5:4.5 er



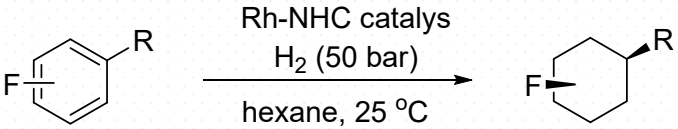
87%, 95:5 er

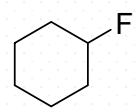


49%, 76:24 er

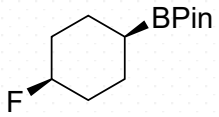
Kuwano, R.; Morioka, R.; Kashiwabara M.; Kameyama, N. *Angew. Chem., Int. Ed.*, **2012**, *51*, 4136

Dearomative hydrogenations

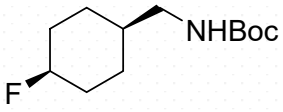




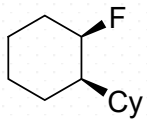
90%



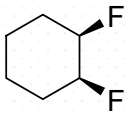
88%, 9:1 dr



90%, 7:1 dr



91%, >20:1 dr



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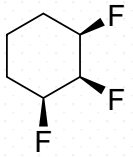
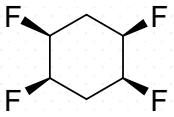
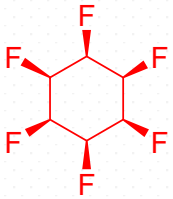


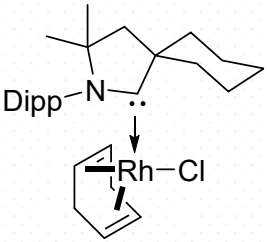
91%, 6:1 dr



60%, >20:1 dr

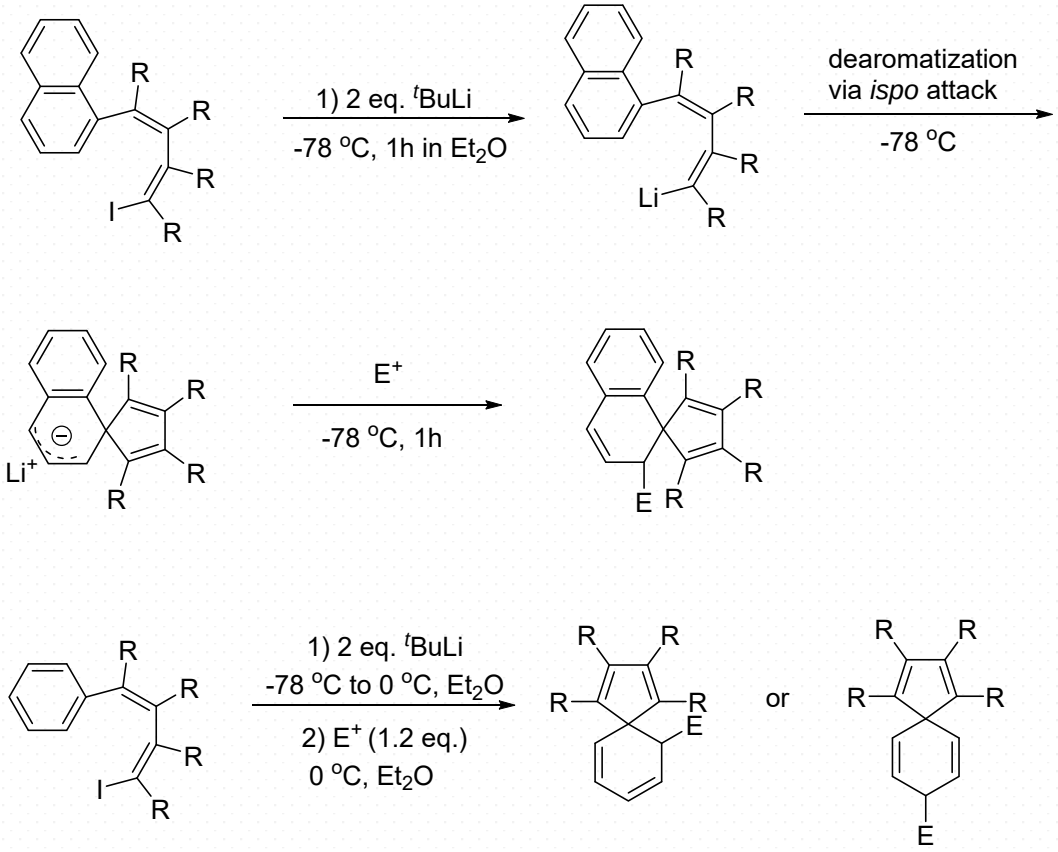


34%, >20:1 dr



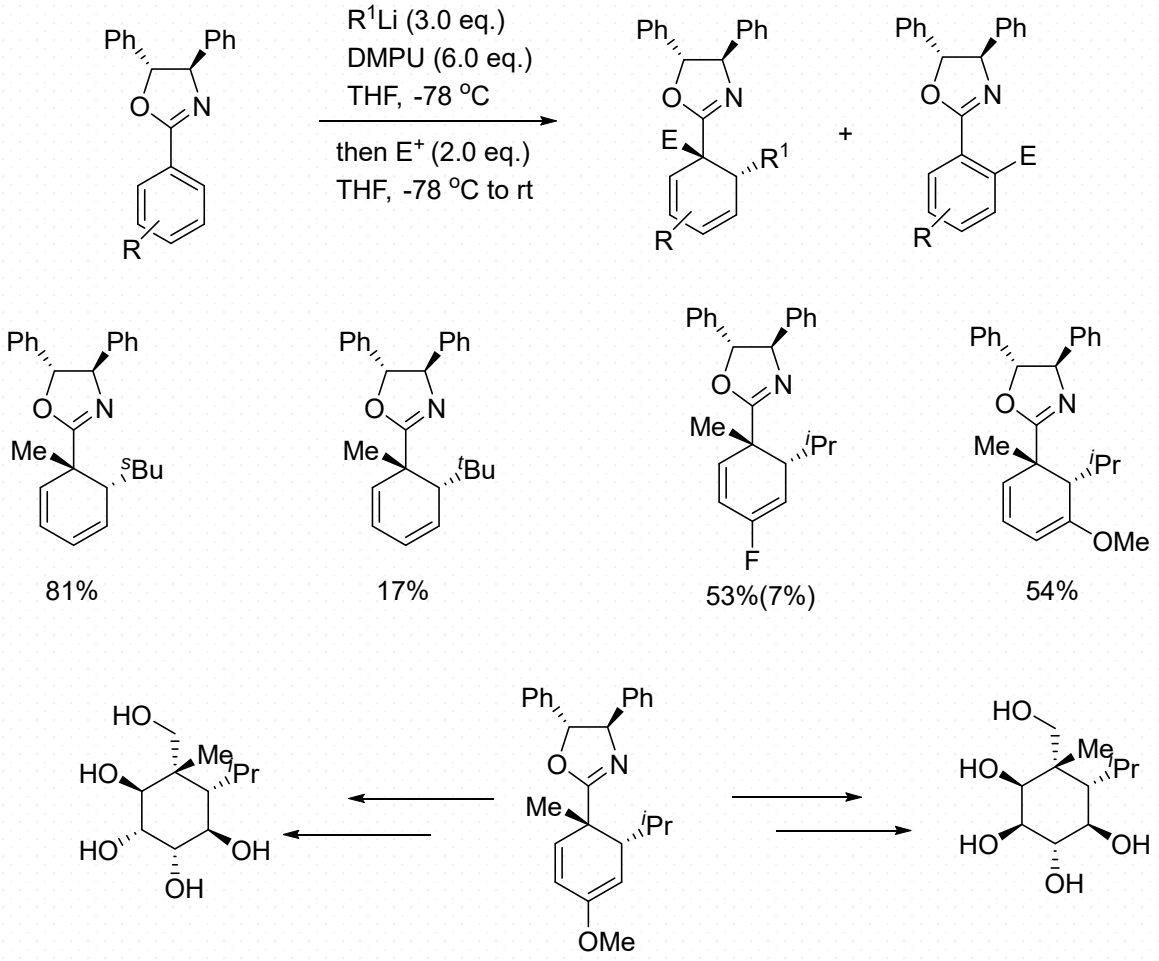
Wiesenfeldt, M. P.; Nairoukh, Z.; Li, W.; Glorius, F. *Science*, **2017**, *357*, 908

Nucleophilic dearomatizing reactions



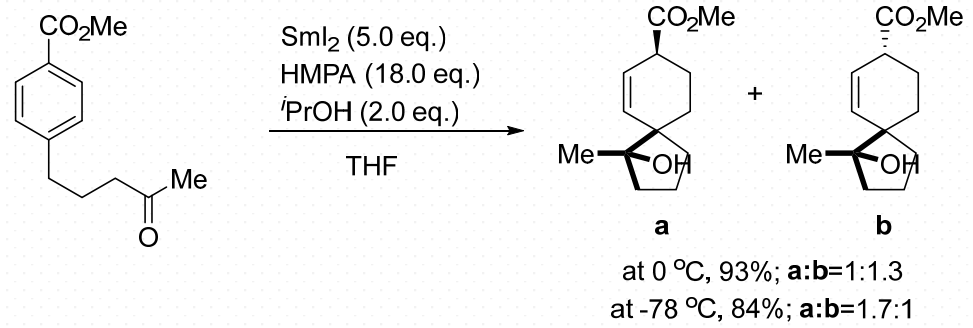
Liu, L.; Wang, Z.; Zhao, F.; Xi, Z. *J. Org. Chem*., **2007**, *72*, 3484

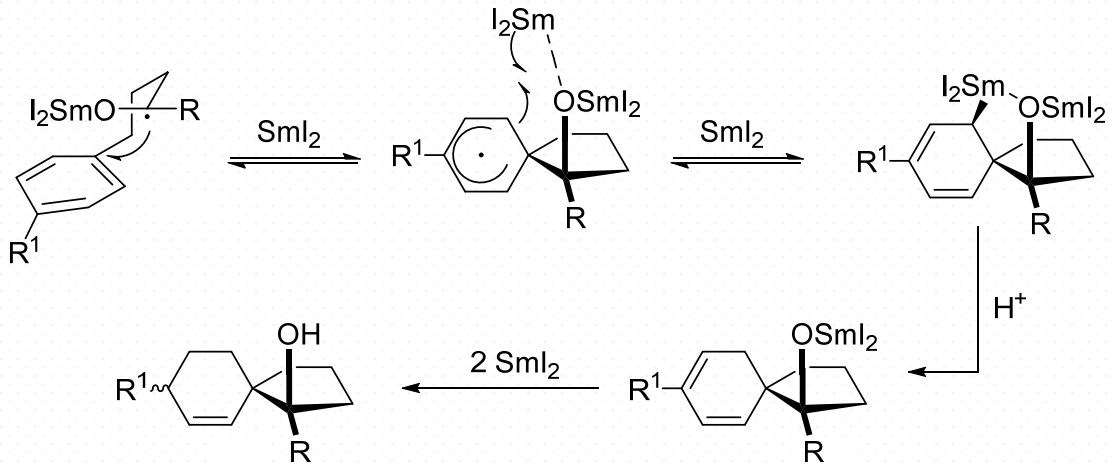
Nucleophilic dearomatizing reactions



Clayden, J.; Parris, S.; Cabedo, N.; Payne, A.H. *Angew. Chem.Int. Ed*., **2008**, *47*, 5060

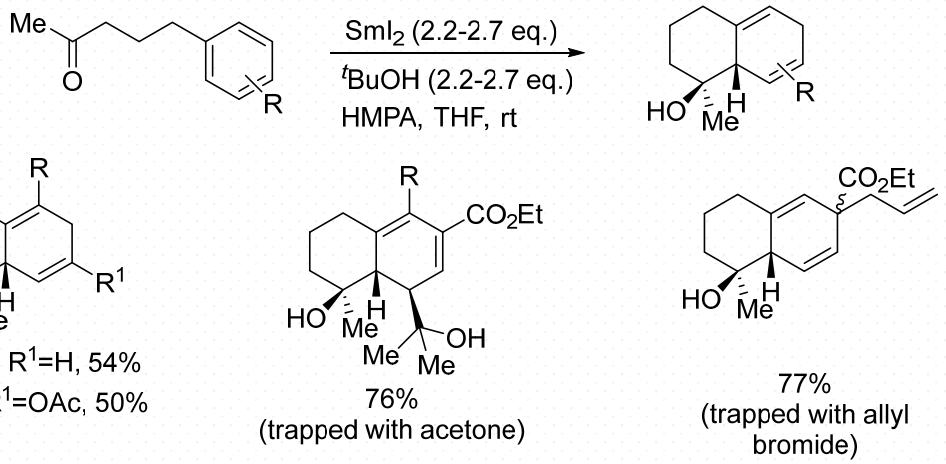
Radical dearomatizations

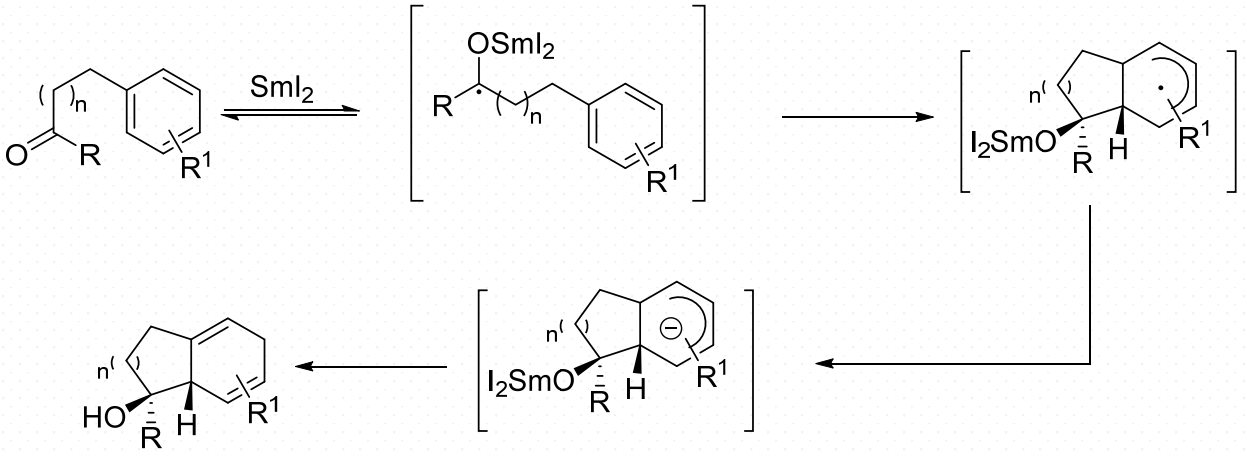




Ohno, H.; Okumura, M.; Maeda, S.; Iwasaki, H.; Wakayama, R.; Tanaka, T. *J. Org. Chem*., **2003**, *68*, 7722

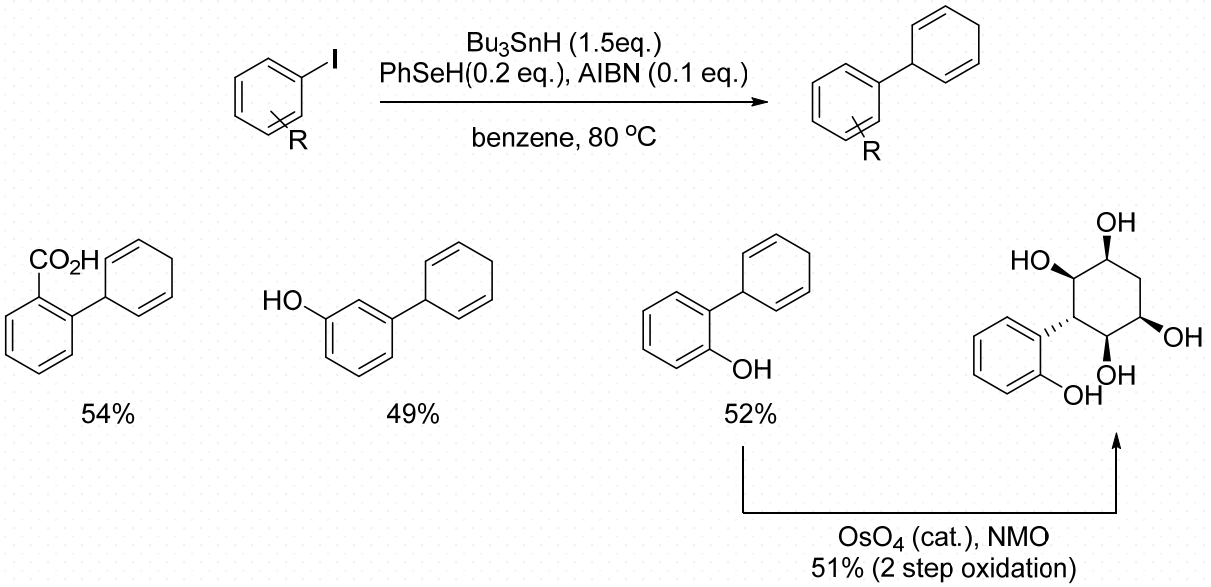
Radical dearomatizations

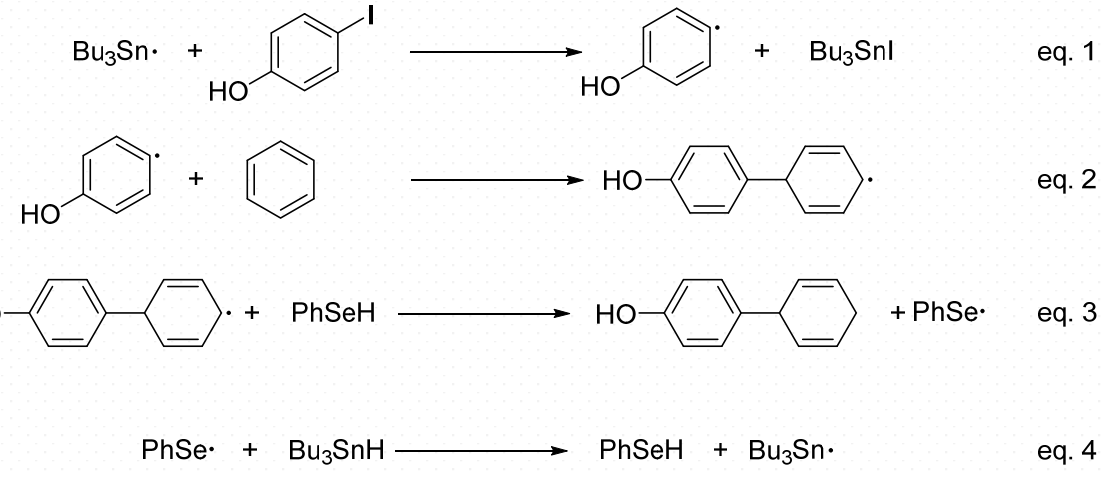




Wefelscheid, U. K.; Berndt, M.; Reissig, H. *Eur. J. Org. Chem.*, **2008**, 3635

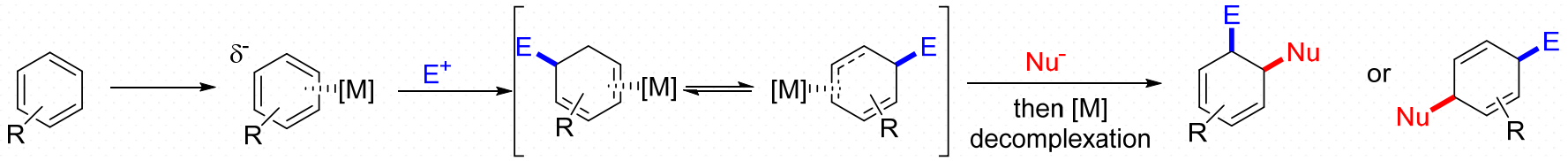
Radical dearomatizations

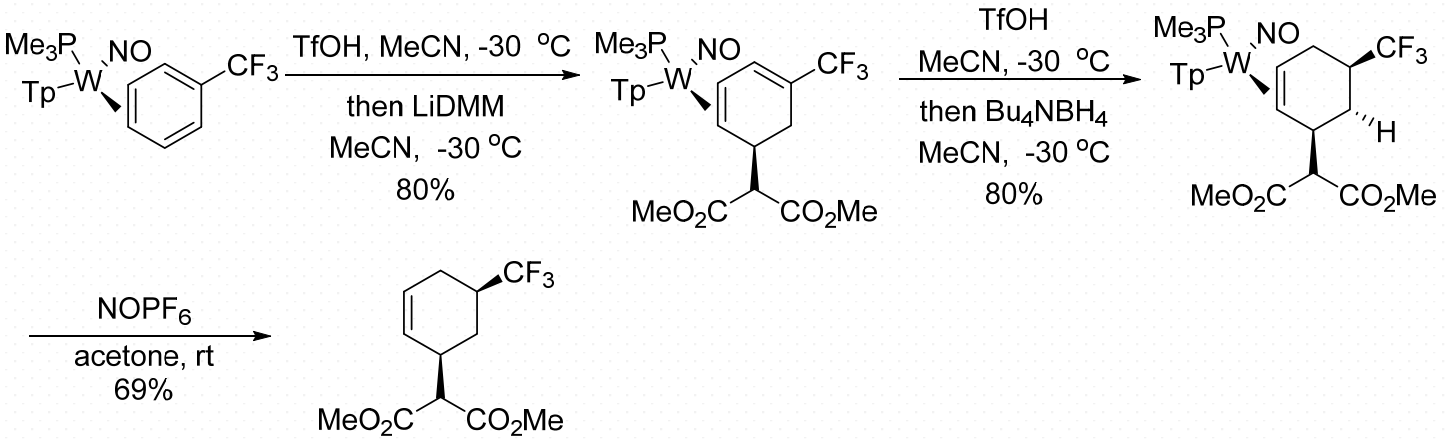




Crich, D.; Grant, D.; Wink, D. J. *J. Org. Chem.*, **2006**, *71*, 4521

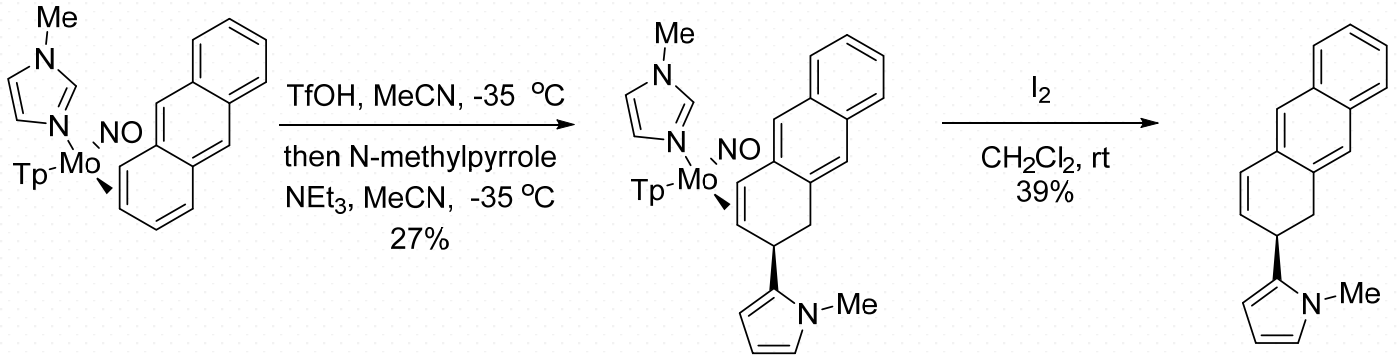
Transition-metal-mediated dearomatizations



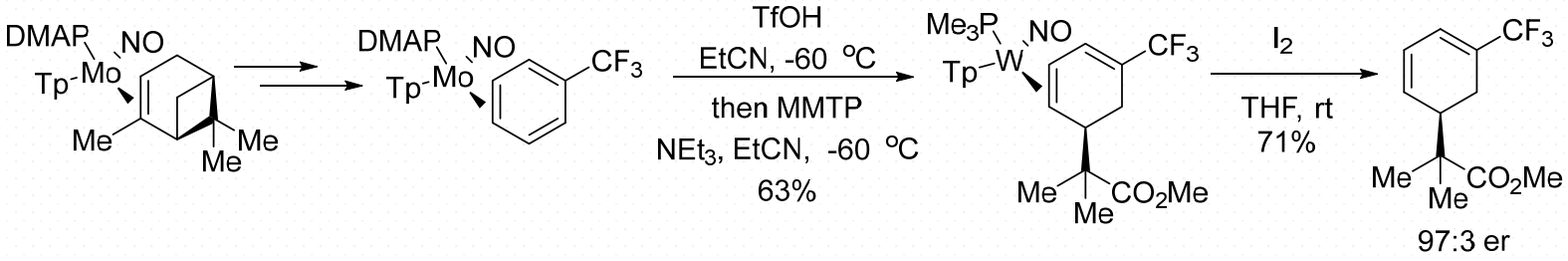


Wilson, K. B,; Harman, W. D. *J. Am. Chem. Soc.*, **2017**, *139*,11401

Transition-metal-mediated dearomatizations

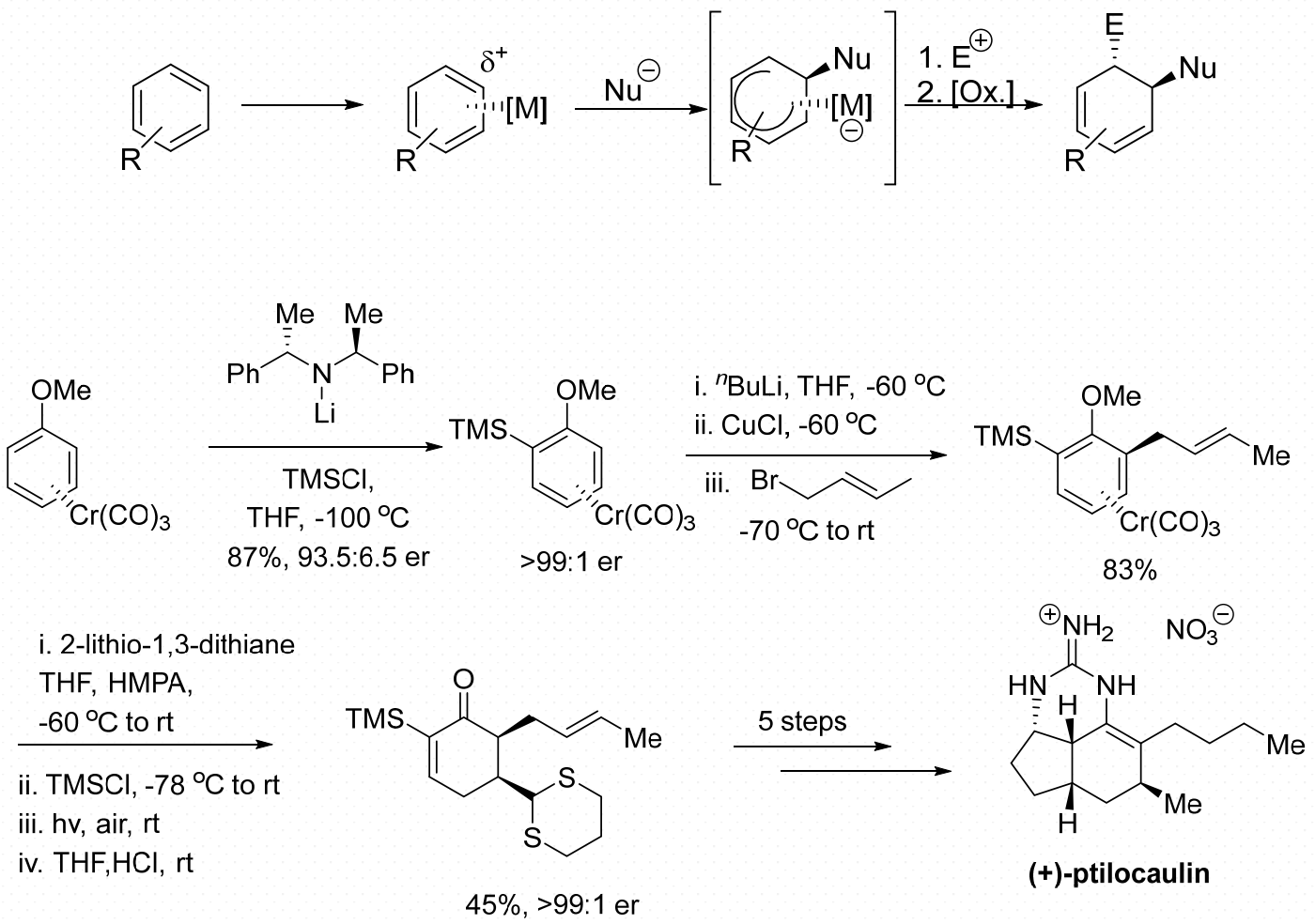


Myers, J. T.; Harman, W. D. *Organometallics*, **2015**, *34*, 3648



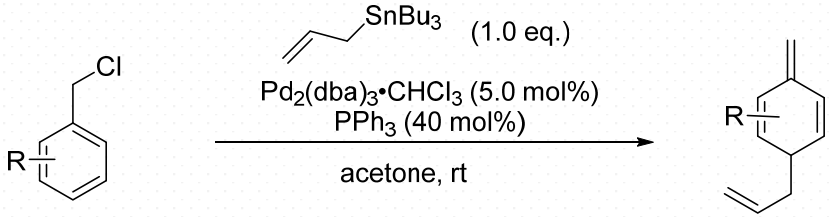
Shivokevich, P. J.; Harman, W. D. *Organometallics*, **2018**, *37,* 4446

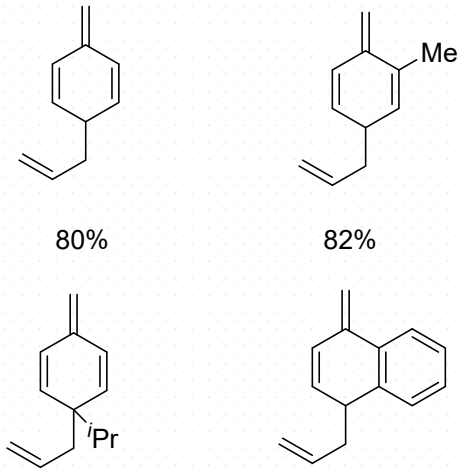
Transition-metal-mediated dearomatizations

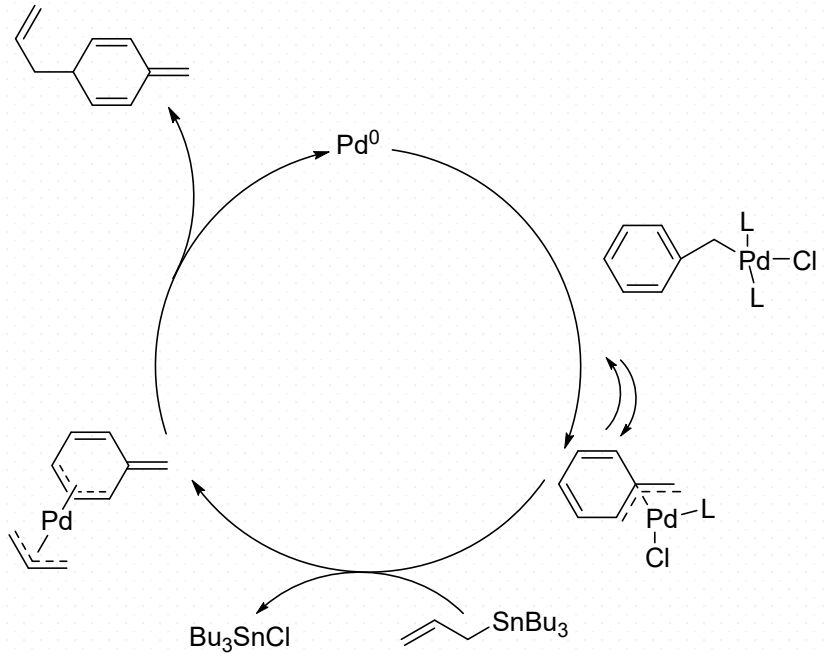


Schellhaas, K.; Schmalz, H.-G.; Bats, J. W. *Chem. Eur. J.*,**1998**, *4*, 5

Transition-metal-catalyzed dearomatizations

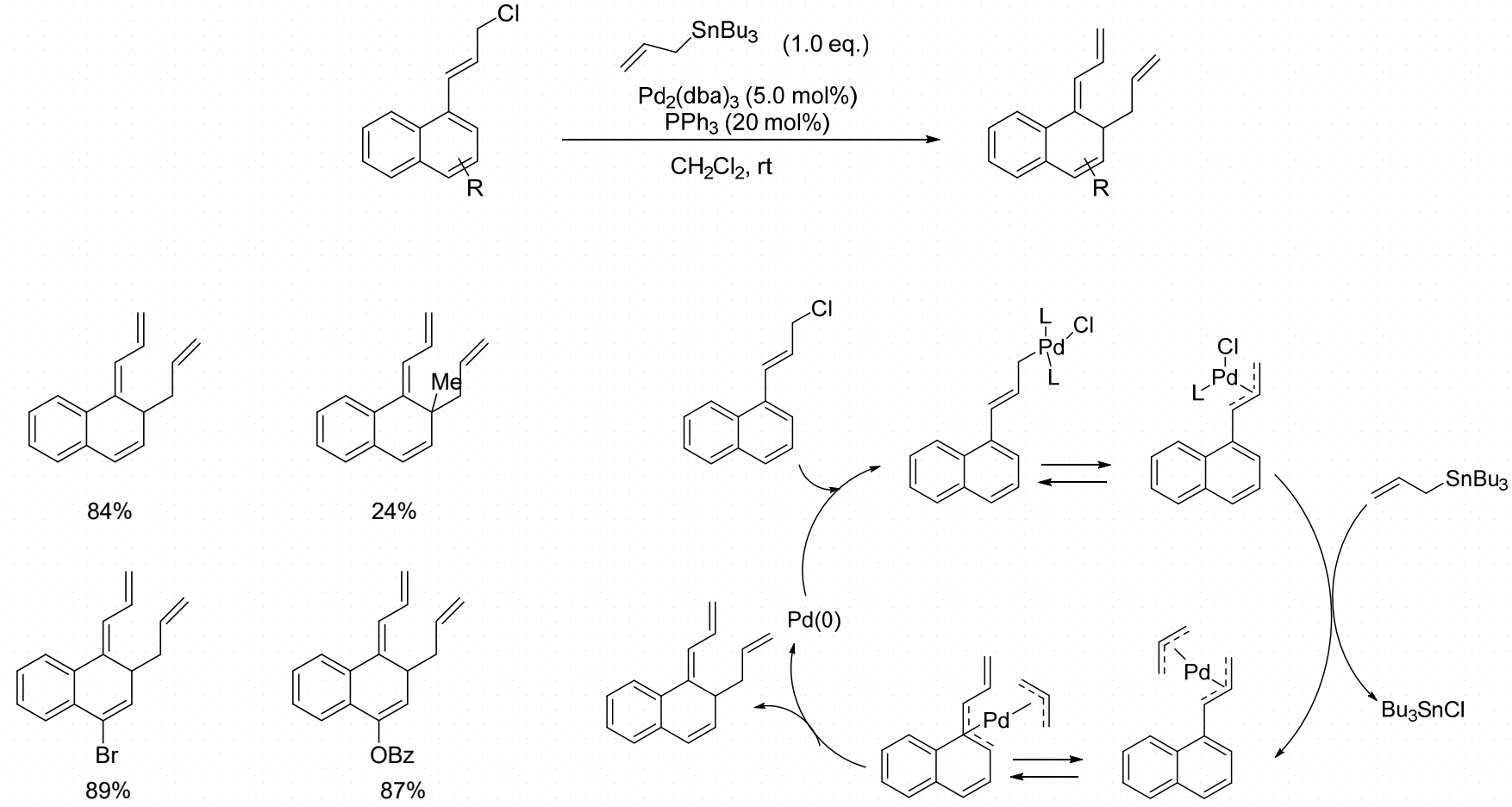






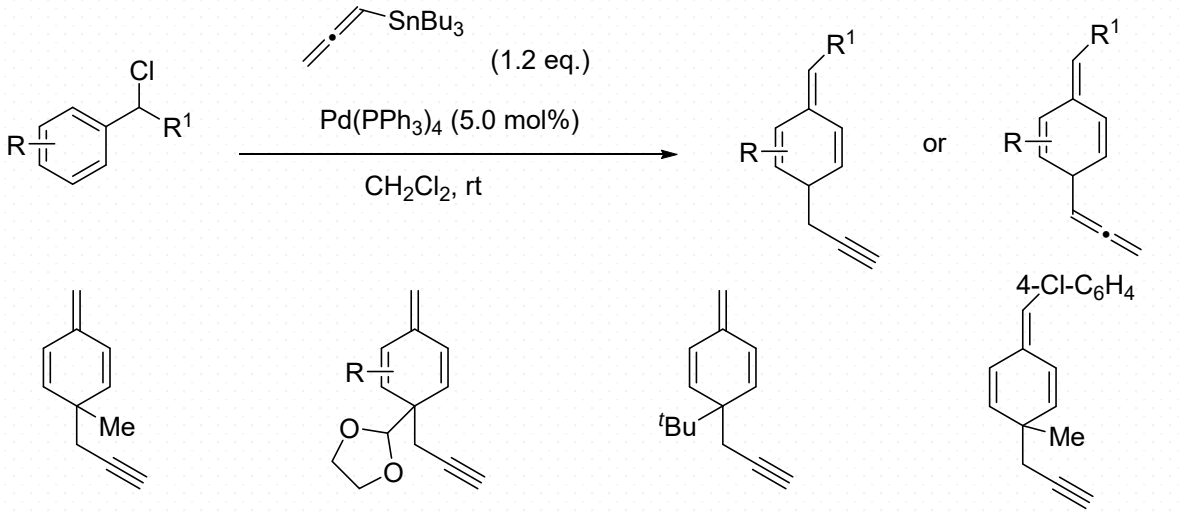
Bao, M.; Nakamura, H.; Yamamoto, Y. *J. Am. Chem. Soc.*, **2001,** *123*, 759

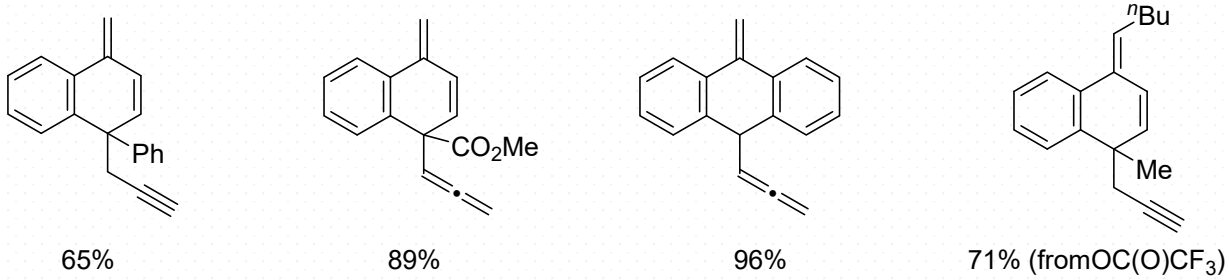
Transition-metal-catalyzed dearomatizations



Lu, S.; Xu, Z.; Bao, M.; Yamamoto, Y. *Angew. Chem., Int. Ed.*, **2008,** *47*, 4366

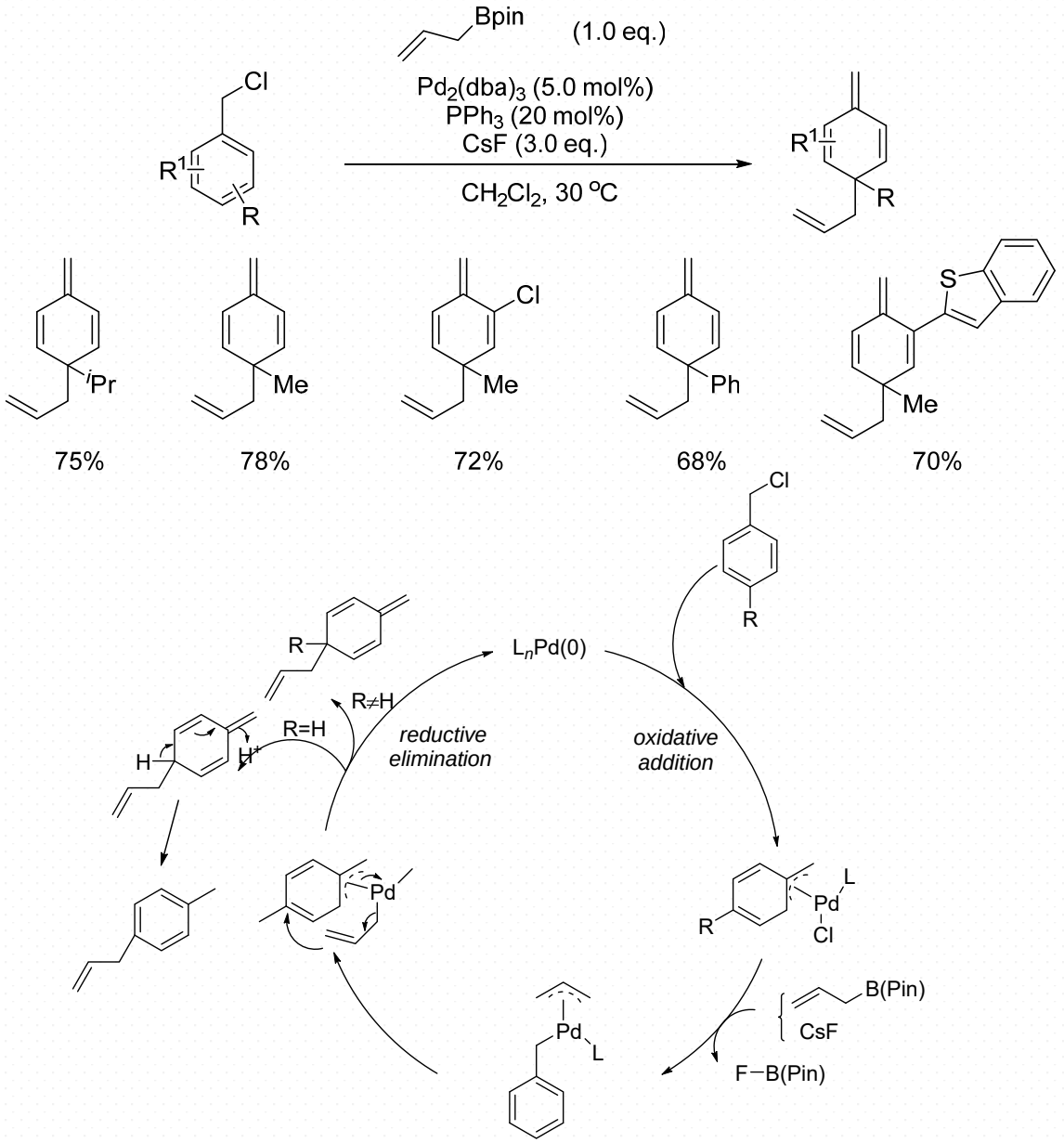
Transition-metal-catalyzed dearomatizations





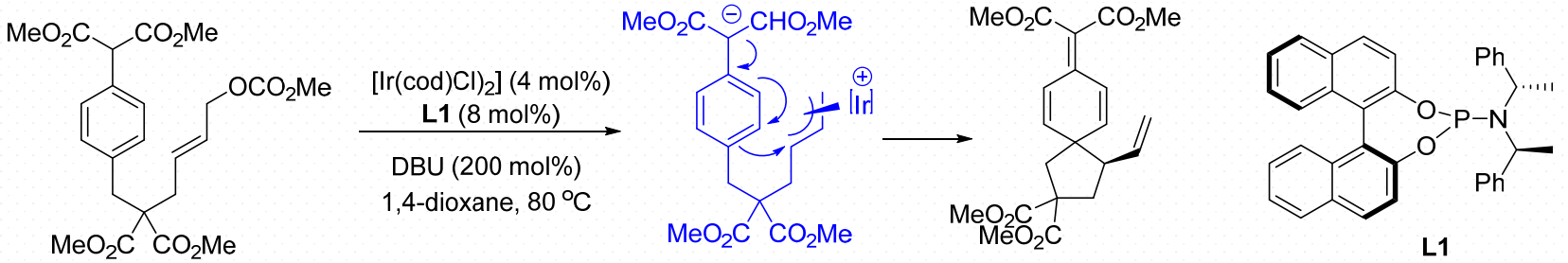
Peng, B.; Feng, X.; Zhang, X.; Bao, M. *J. Org. Chem.*, **2010,** *75*, 2619

Transition-metal-catalyzed dearomatizations

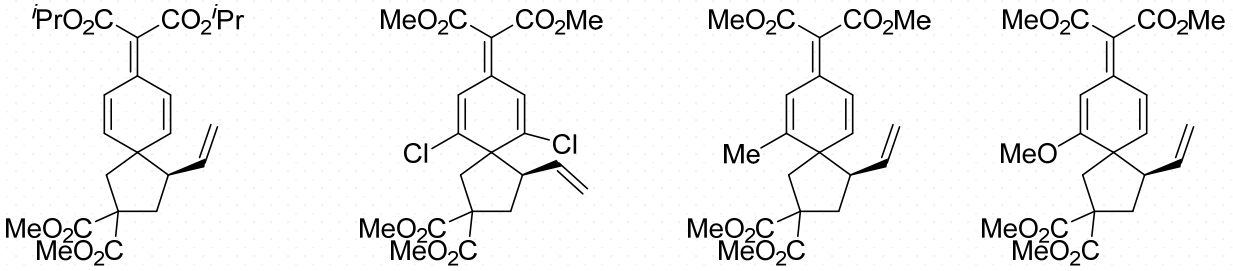


Zhang, S.; Ullah, A.; Yamamoto, Y.; Bao, M. *Adv. Synth. Catal.*, **2017,** *359*, 2723

Transition-metal-catalyzed dearomatizations



53%, 93% ee



31%, 95% ee

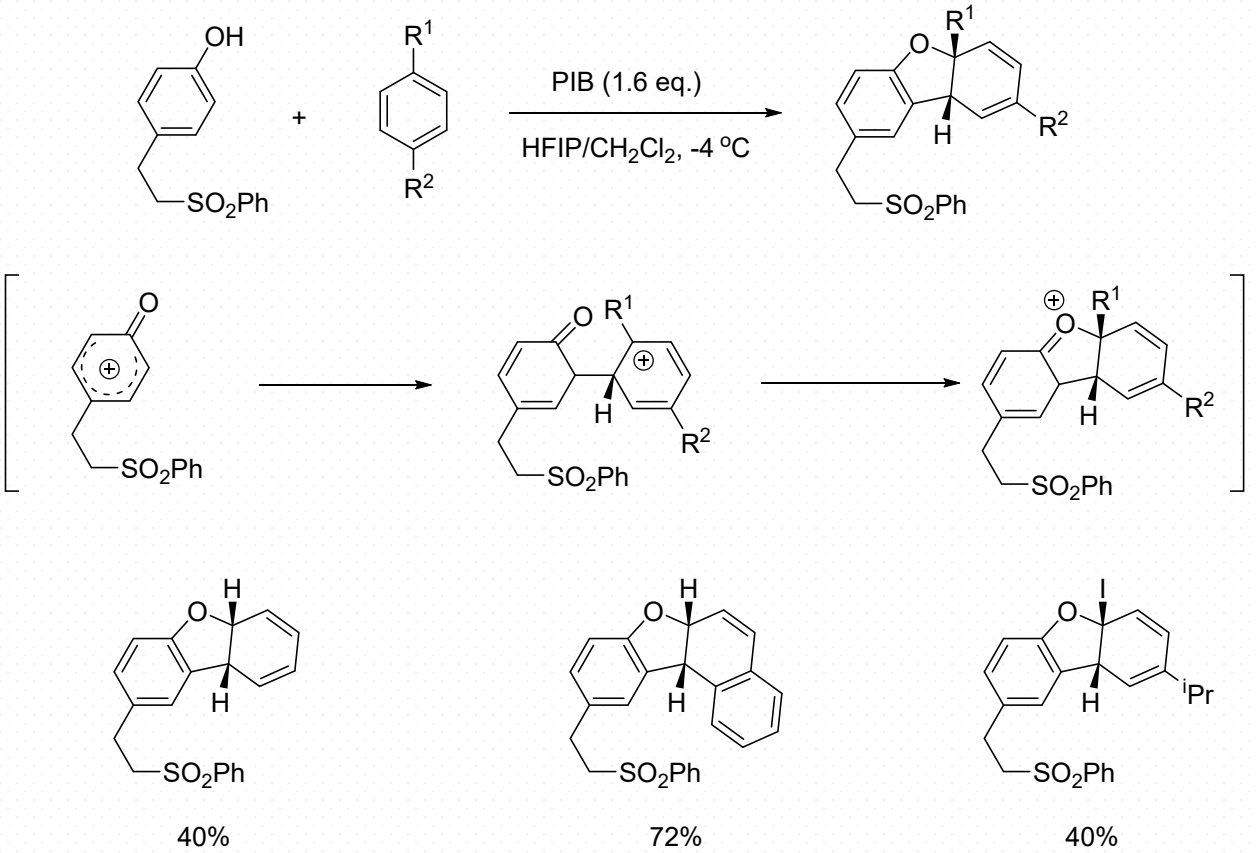
61%, 94% ee

37%, 98% ee
dr >20/1

79%, 94% ee
dr=1.4/1

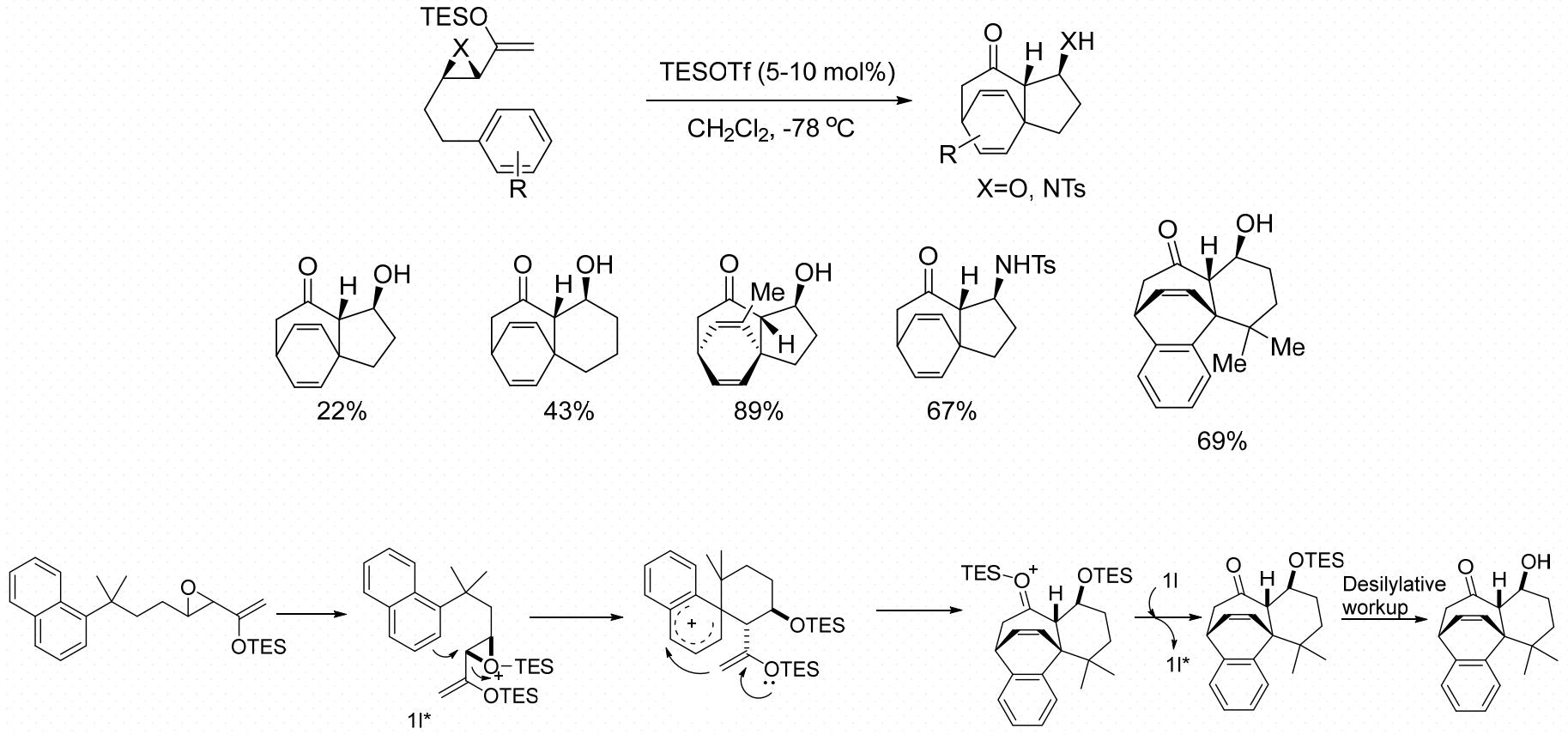
Yang, Z.; Jiang, R.; Wu, Q.; Zheng, C.; You, S. *Angew. Chem. Int. Ed*. **2018**, *57*, 16190

Dearomative cycloadditions



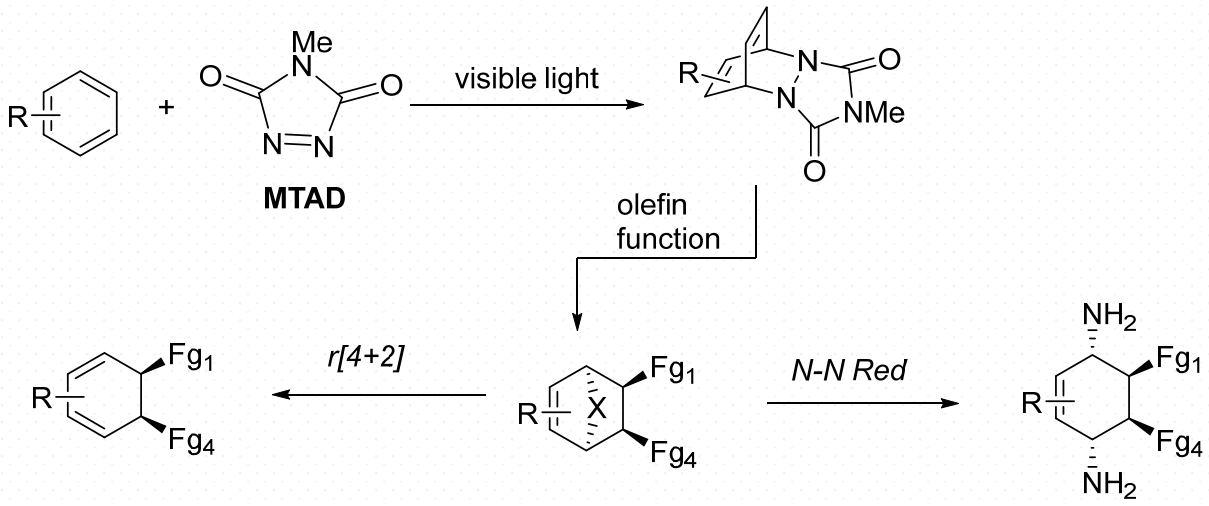
Jacquemot, G.; Me´nard, M.-A.; L'Homme, C.; Canesi, S. *Chem. Sci*., **2013**, *4*, 1287

Dearomative cycloadditions

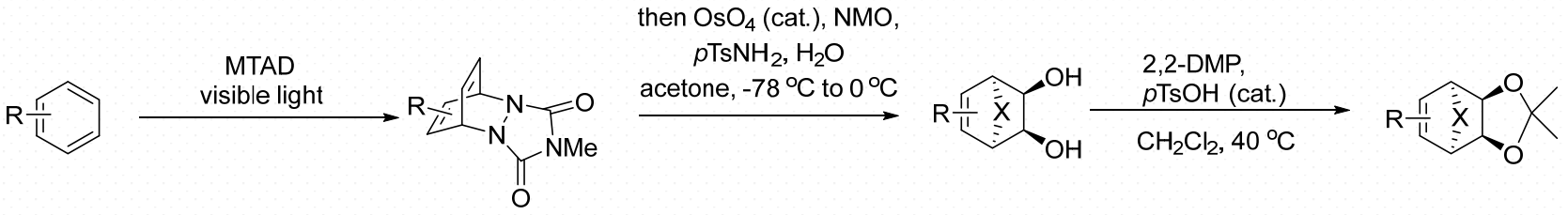


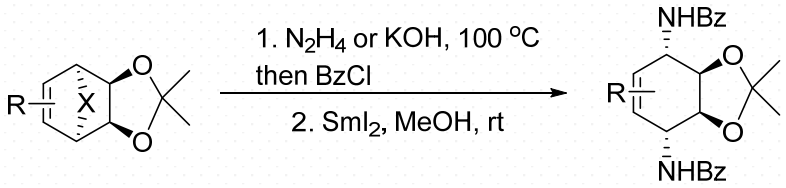
Ling, J.; Lam, S.; Low, K.-H.; Chiu, P. *Angew. Chem., Int. Ed.*, **2017**, *56*, 8879

Arenophile-mediated dearomatizations

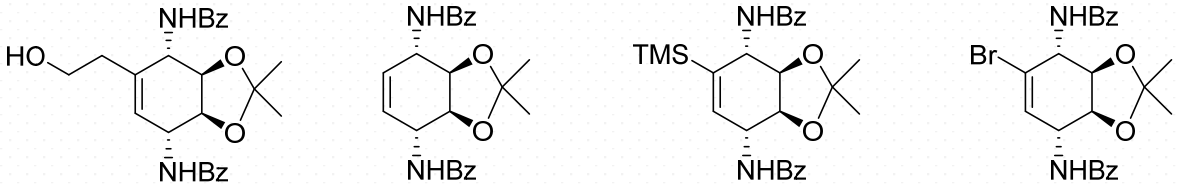


Arenophile-mediated dearomatizations



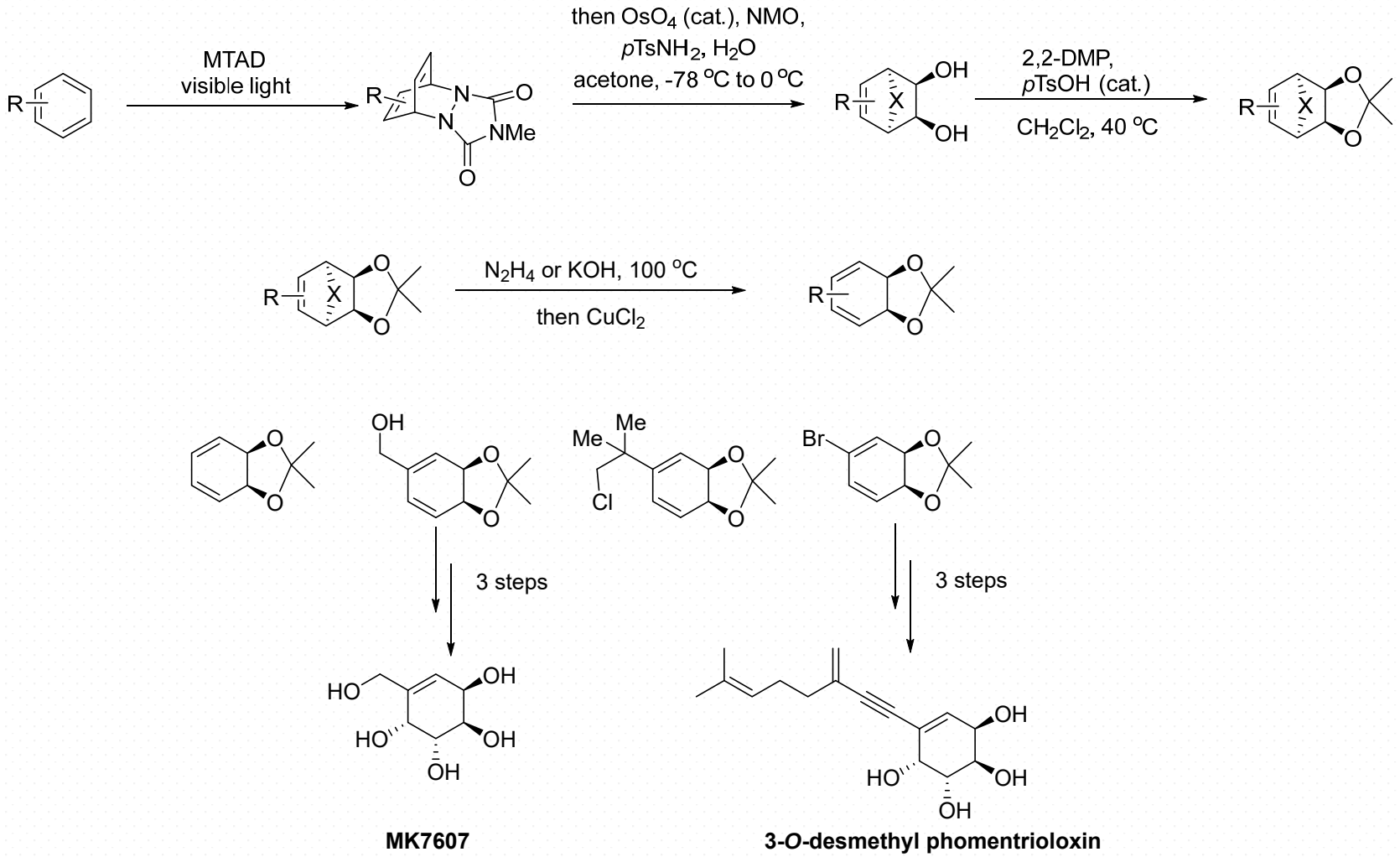


dearomative diaminodihydroxylation 13%-32% over four steps



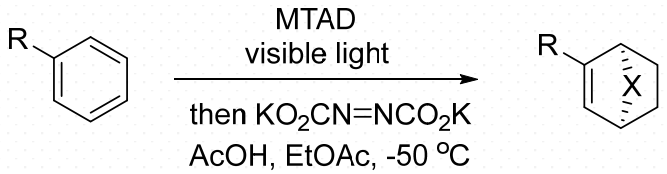
Southgate, E. H.; Pospech, J.; Fu, J.; Holycross, D. R.; Sarlah, D. *Nat. Chem.*, **2016**, 8, 922

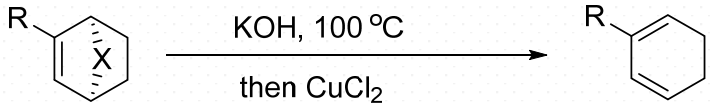
Arenophile-mediated dearomatizations



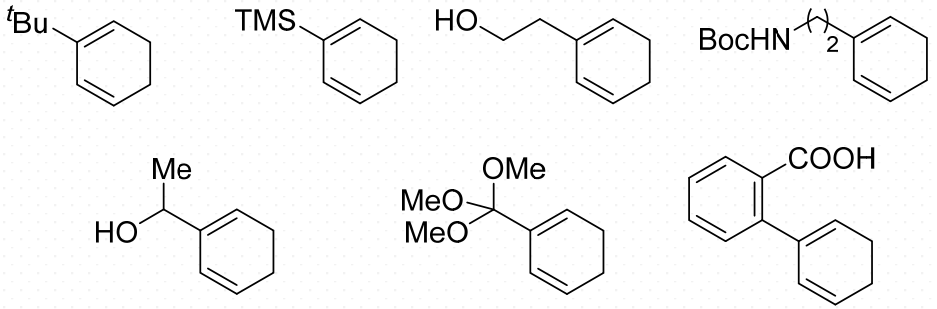
Southgate, E. H.; Pospech, J.; Fu, J.; Holycross, D. R.; Sarlah, D. *Nat. Chem.*, **2016**, 8, 922

Arenophile-mediated dearomatizations



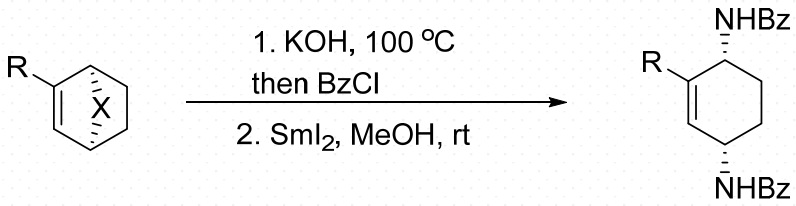


dearomative reduction 35%-67% over two steps

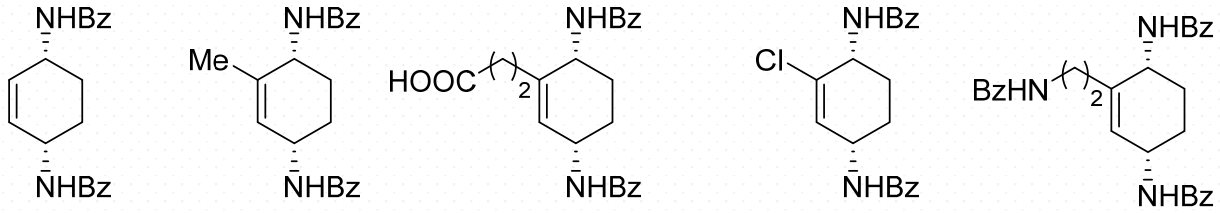


Okumura, M.; Nakamata Huynh, S. M.; Pospech, J.; Sarlah, D. *Angew. Chem., Int. Ed.*, **2016**, *55*, 15910

Arenophile-mediated dearomatizations

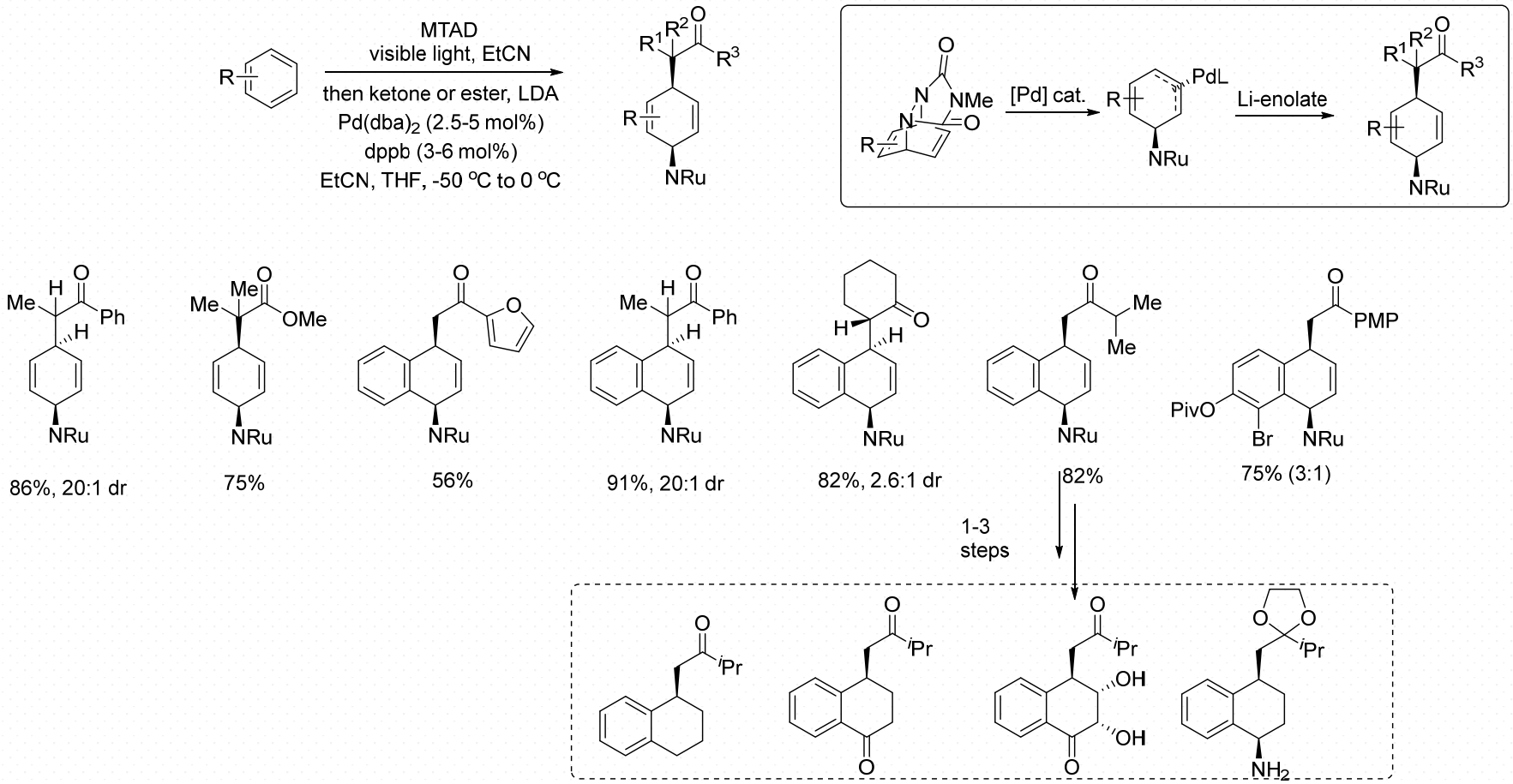


14%-39% over three steps



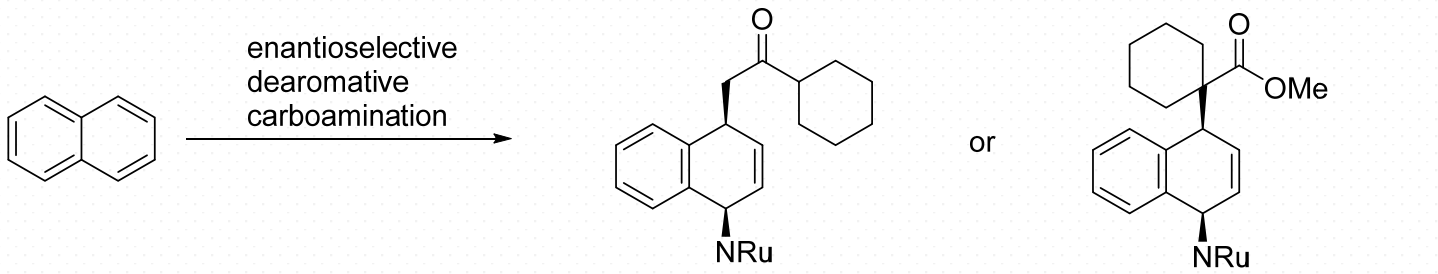
Okumura, M.; Nakamata Huynh, S. M.; Pospech, J.; Sarlah, D. *Angew. Chem., Int. Ed*., **2016**, *55*, 15910

Arenophile-mediated dearomatizations



Okumura, M.; Shved, A. S.; Sarlah, D. *J. Am. Chem. Soc.*, **2017**, *139*, 17787

Arenophile-mediated dearomatizations

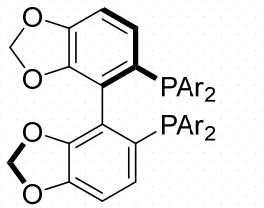


68%, 97:3 er

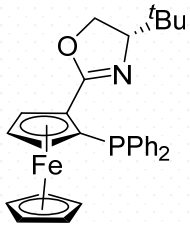
with $Pd(dba)_2$ (5 mol%),
(*S,Sp*)-^{t}Bu-Phosferrox (6 mol%)

72%, 95:5 er

with $[Pd(allyl)Cl]_2$ (5 mol%),
(*R*)-DTBM-SEGPHOS (6 mol%)



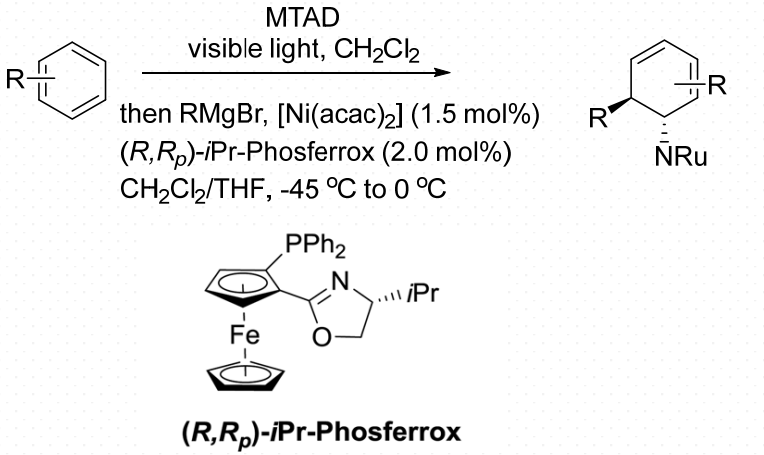
(*R*)-DTBM-SEGPHOS
Ar=3,5-di-^{t}Bu-4-OMe-C_6H_2



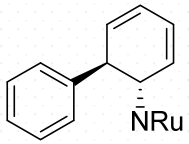
(*S*,S_p)-^{t}Bu-Phosferrox

Okumura, M.; Shved, A. S.; Sarlah, D. *J. Am. Chem. Soc*., **2017**, *139*, 17787

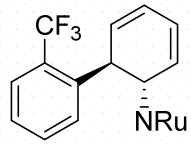
Arenophile-mediated dearomatizations



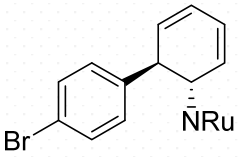
(R,R_p)-*i*Pr-Phosferrox



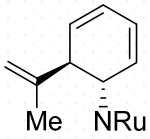
70%, 97:3 er



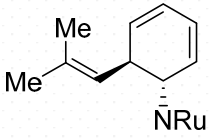
55%, 91:9 er



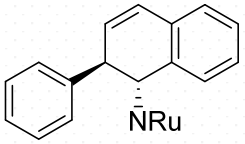
66%, 96.5:3.5 er



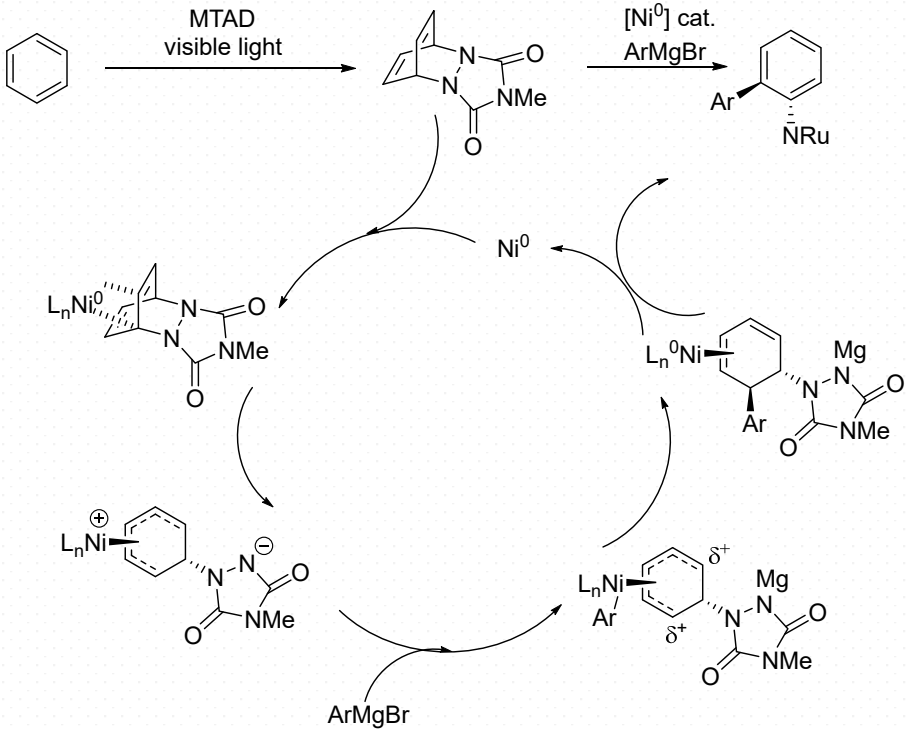
55%, 89:11 er



55%, 97.5:2.5 er

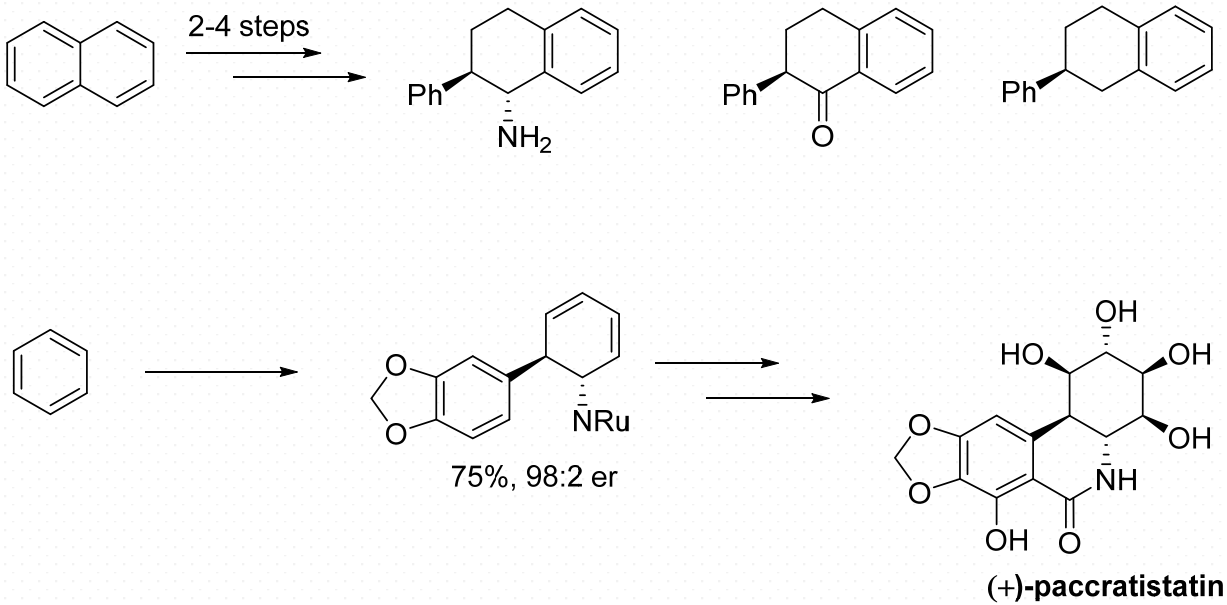


63%, 94.5:5.5 er



Hernandez, L. W.; Klockner, U.; Pospech, J.; Hauss, L.; Sarlah, D. , *J. Am. Chem. Soc*., **2018**, *140*, 4503

Arenophile-mediated dearomatizations



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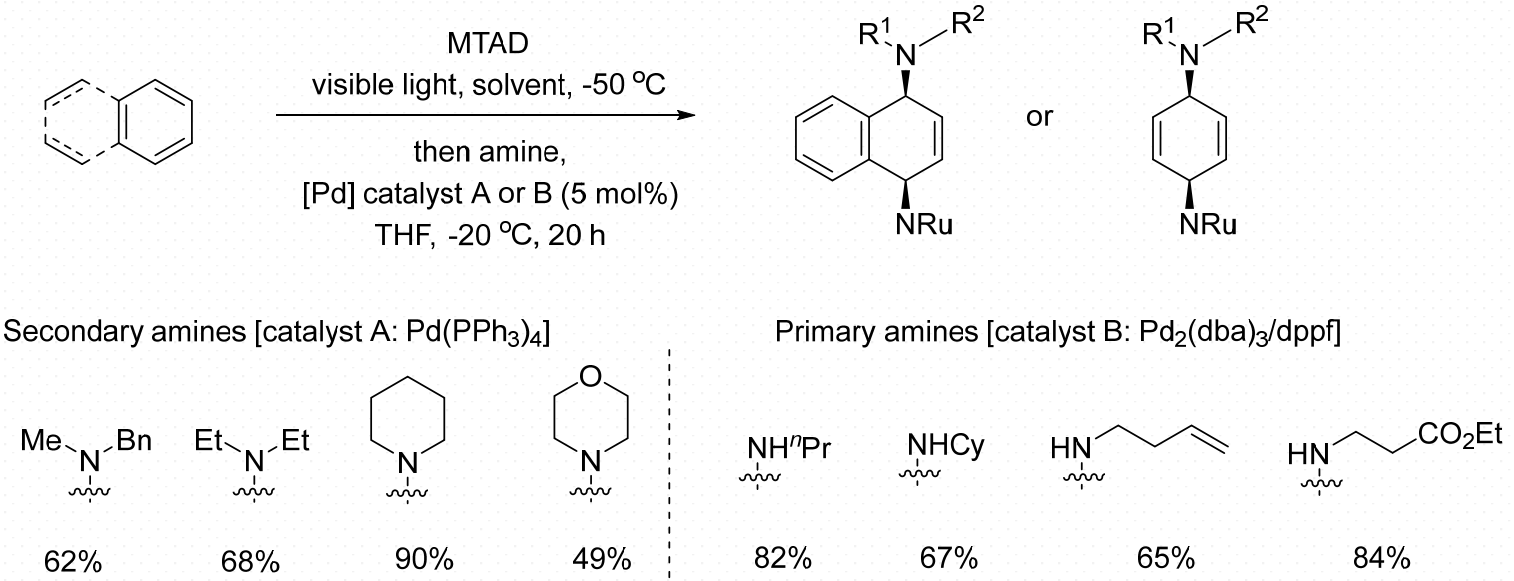
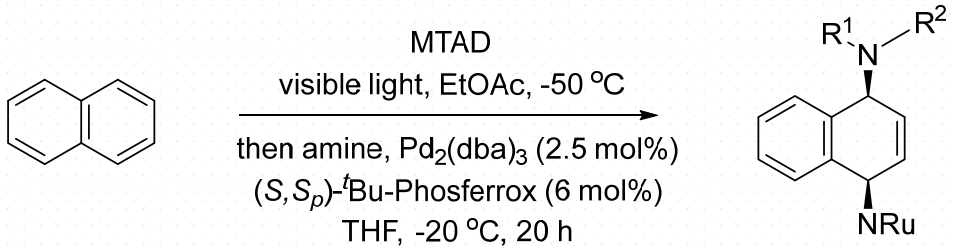
Arenophile-mediated dearomatizations

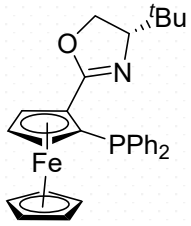


Wertjes, W. C.; Okumura, M.; Sarlah, D. *J. Am. Chem. Soc.*, **2019**, *141*, 163

Arenophile-mediated dearomatizations



66%, 97:3 er | 53%, 99:1 er | 93%, 97:3 er | 88%, 99:1 er | 84%, 97:3 er



(*S*,*S*$_p$)-^{t}Bu-Phosferrox

Wertjes, W. C.; Okumura, M.; Sarlah, D. *J. Am. Chem. Soc.*, **2019**, *141*, 163

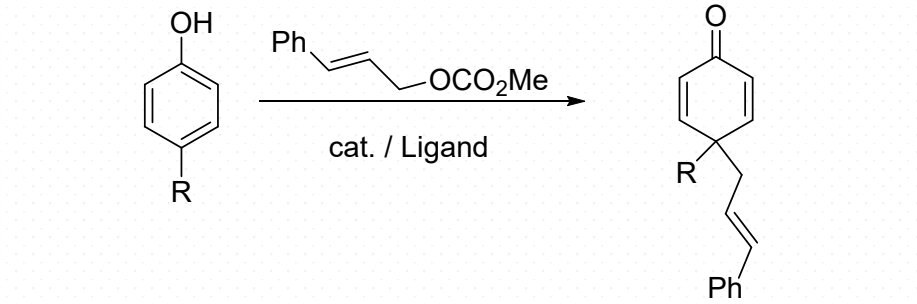
04

总结

苯环去芳构化

- 从苯环出发，原料来源广泛，成本低
- 构建季碳中心
- 简便地构建螺环、桥环等复杂多环体系
- 天然产物及药物分子合成

总结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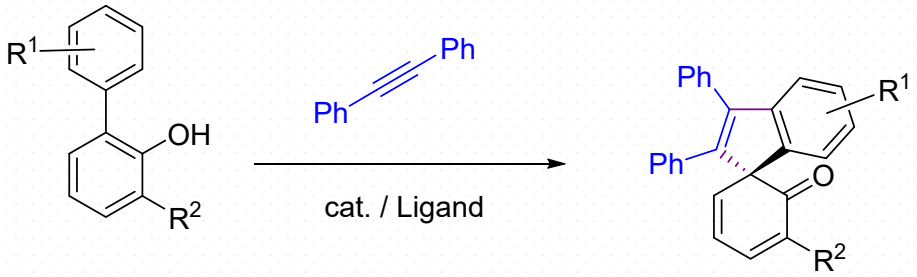
R
Ph
OCO2Me
cat. / Ligand
O
R
Ph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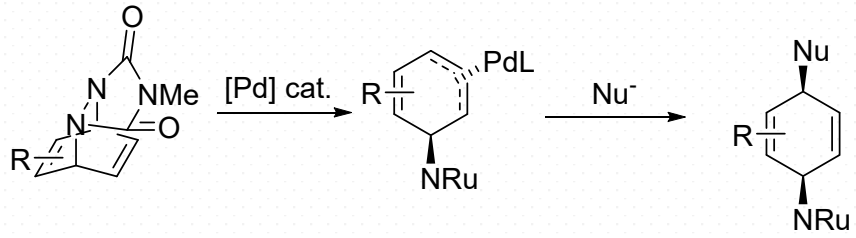
OH
R2
Ph
Ph
cat. / Ligand
Ph
Ph
R1
O
R2


O
N
NMe
N
O
R
[Pd] cat.
R
PdL
NRu
Nu-
Nu
R
NRu

Thanks for your attention