Recent Developments in Aerobic Oxidation

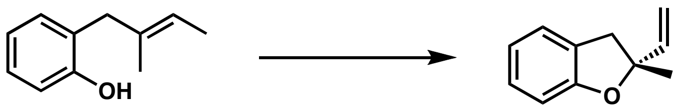
Stoltz Group Literature Talk

Monday, August 21, 2006

Brinton Seashore-Ludlow

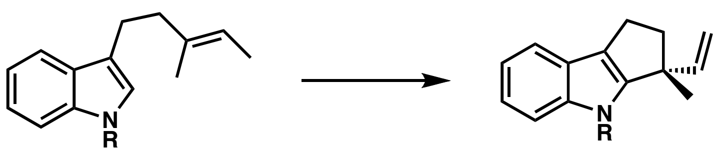
Stoltz Group Methodologies

Enantioselective Wacker Cyclization



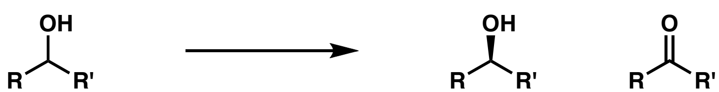
Trend, R. M.; Ramtohul, Y. K.; Ferreira, E. M.; Stoltz, B. M. *Angew. Chem., Int. Ed.* **2003,** *42*, 2892.

Aerobic Oxidative Annulation of Indoles



Ferriera, E. M.; Stoltz, B. M. *J. Am. Chem. Soc.* **2003**, *125*, 9578.

Aerobic Oxidative Kinetic Resolution of Secondary Alcohols



Ferreira, E. M.; Stoltz, B. M.; *J. Am Chem. Soc.* **2001**, *123*, 7725.
Bagdanoff, J. T.; Ferreira, E. M.; Stoltz, B. M. *Org. Lett.* **2003**, *5*, 835.
Bagdanoff, J. T.; Stoltz, B. M. *Angew. Chem., Int. Ed.* **2004**, *43,* 353.
Caspi, D. D.; Ebner, D. C.; Bagdanoff, J. T.; Stoltz, B. M. *Adv. Syn. Catal.* **2004**, *346*, 185.
Trend, R. M.; Stoltz, B. M. *J. Am. Chem. Soc.* **2004**, *126*, 4482.

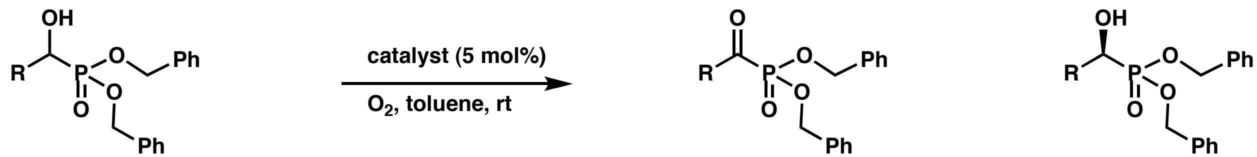
Jensen, D. R.; Pugsley, J. S.; Sigman, M. S. *J. Am. Chem. Soc.* **2001**, *123*, 7475.
Mandal, S. K.; Jensen, D. R.; Pugsley, J. S.; Sigman, M. S. *J. Org. Chem.* **2003**, *68*, 4600.
Mueller, J. A.; Sigman, M. S. *J. Am. Chem. Soc.* **2003**, *125*, 7005.

Aerobic Oxidation of Alcohols: Some Methods

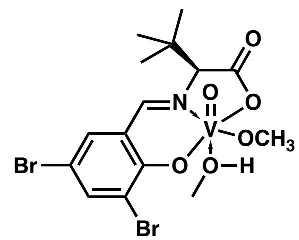
Additives	Catalyst	Types of Alcohols Oxidized	Converts to	Other
TEMPO	$Ru(PPh_3)_3Cl$	primary, secondary	aldehyde	substrates cannot contain: S, N, O
hydroquinone, K_2CO_3	$Ru(PPh_3)_3Cl$		aldehyde	
quinuclidine, Cu(II)	OsO_4	allylic, benzylic	aldehyde	
bathophenanthroline disulfonate	$Pd(OAc)_2$	secondary aliphatic, cyclic allylic and benzylic slow	aldehyde (TEMPO)	substrates cannot contain: S, N, O, C=C, H_2O solvent
sparteine	$Pd(nbd)Cl_2$ or $Pd(OAc)_2$	OKR		
NMO	polymer supported TPAP	unactivated primary, secondary	aldehyde	cyclohexanol and cyclohexenol were not oxidized
	molecular sieve supported TPAP	benzylic	aldehyde	
amine/ CuCl	polymer supported PIPO	benzylic, allylic	aldehyde	
	Silica supported TEMPO	primary, secondary, benzylic	aldehyde	can be recycled
	RuHAP (hydroxapatite)	activated and unactivated	aldehyde	can be recycled
	functionalized zeolites	unactivated	aldehyde	shape selectivity, no solvent
	PEG supported Pd	broad range		supercritial CO_2; can be recycled
	Au/CeO_2	broad range	benzylic aldehydes aliphatic esters	

Recent Developments in the Aerobic Oxidation of Alcohols: Zhan, B.-Z.; Thompson, A. *Tet.* **2004**, *60*, 2917-2935.
Palladium-catalyzed Oxidation of Primary and Secondary Alcohols: Muzart, J. *Tet.* **2003**, *59*, 5789-5816.
Palladium Oxidase Catalysis: Stahl, S. S. *Angew. Chem., Int. Ed.* **2004**, *43*, 3400-3420.
Zeolites: Zhan, B.-Z.; White, M. A.; Sham, T. K.; Pincock, J. A.; Doucet, R. J.; Rao, K. V. R.; Robertson, K. N.; Cameron, T. S. *J. Am. Chem. Soc.* **2003**, *125*, 2195-2199.
PEG Supported Pd: Hou, Z.; Theyssen, N.; Brinkmann, A.; Leitner, W. *Angew. Chem., Int. Ed.* **2005**, *44*, 1346-1349.
Gold: Abad, A.; Almela, C.; Corma, A.; García, H. *Tet.* **2006**, *62*, 6666-6672.

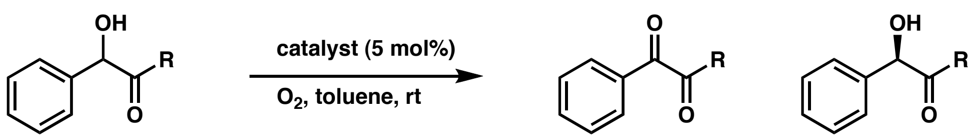
Oxidative Kinetic Resolution



R	% conversion	% ee (% yield)
C_6H_5	51	99 (47)
4-$CH_3C_6H_4$	49	96 (46)
4-$CH_3OC_6H_4$	50	99 (49)
4-$NO_2C_6H_4$	50	99 (49)
4-CNC_6H_4	51	95 (47)
3-HOC_6H_4	50	99 (46)
2-$CH_3OC_6H_4$	50	99 (49)
2-BrC_6H_4	50	33 (47)
2-furanyl	49	90 (47)
2-thiopheyl	50	99 (49)
trans-PhCHCH	49	95 (47)
PhCC	50	68 (49)
1-Np	50	99 (46)



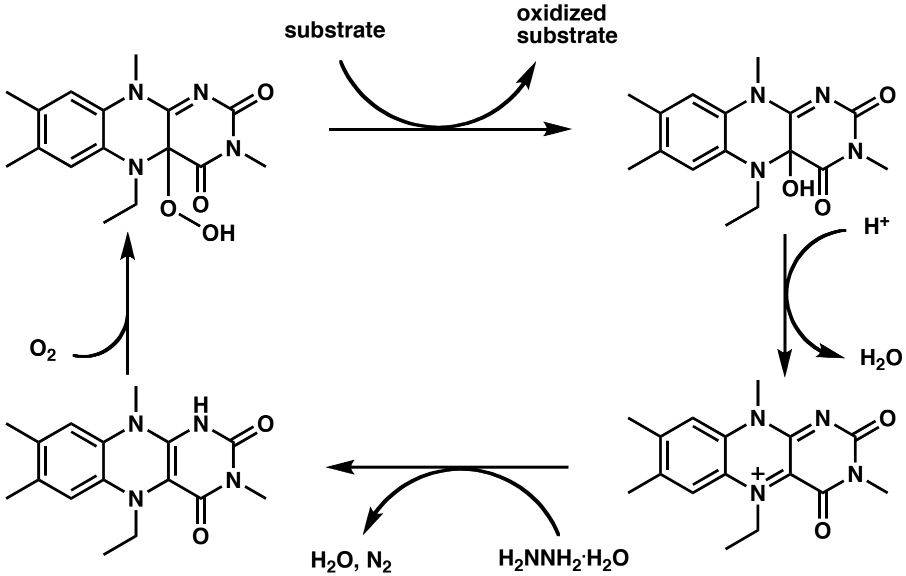
catalyst

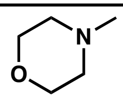
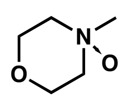
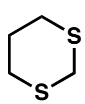
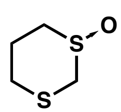
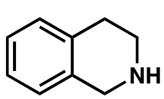
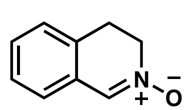


R	conversion	% ee (% yield)
OCH_3	54	93 (40)
$OCH(CH_3)_2$	49	88 (49)
OCH_2Ph	50	98 (46)
OPh	53	79 (45)
$NHCH(CH_3)_2$	50	7 (44)
$NHCH_2Ph$	50	99 (43)
NHPh	51	70 (46)

Pawar, V. D.; Bettingeri, S.; Weng, S.-S.; Kao, J.-Q.; Chen, C.-T. *J. Am. Chem. Soc.* **2006**, *128*, 6308 -6309.
Weng, S.-S.; Shen, M.-W.; Kao, J.-Q.; Munot, Y.; Chen, C.-T. *Proc. Nat. Acad. Sci.* **2006**, *103*, 3522-3527.
OKR of hydroxyesters using similar tetradentate salen ligands on vanadium see:
Radosevich, A. T.; Musich, C.; Toste, F. D. *J. Am. Chem. Soc.* **2005**, *127*, 1090-1091.

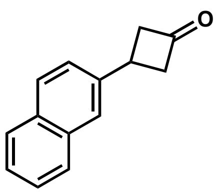
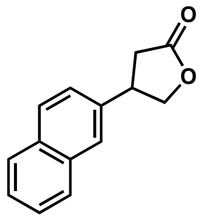
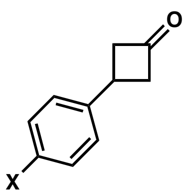
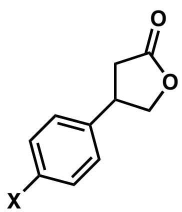
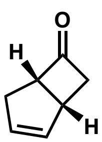
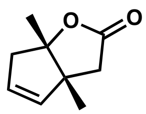
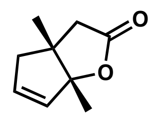
Flavin-Catalyzed Oxiation of Amines and Sulfides

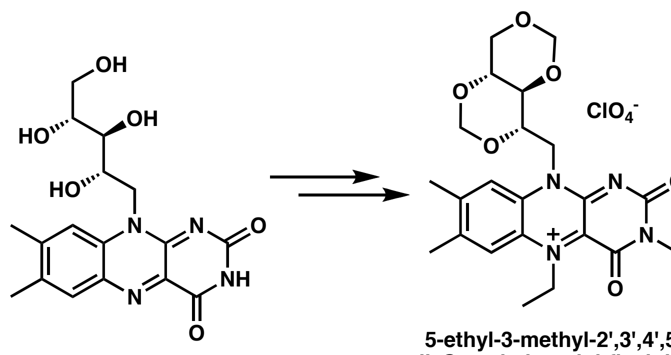


substrate	product	yield
		**97**
		**97**
		**85**

Imada, Y.; Iida, H.; Murahashi, S.-I. *J. Am. Chem. Soc.* **2003**,*125*, 2868-2869.
For autorecycling aerobic oxidation of some amines see:
Igarashi, K.; Yamaguchi, Y.; Mitsumoto, Y.; Naya, S.-I.; Nitta, M. *J. Org. Chem.* **2006**, *71*, 2690-2698.

Aerobic Baeyer-Villiger Oxidation of Ketones

substrate	product		yield
			94
			X= H 78, F 80, Cl 84
	 expected	 unexpected	83 (57:43)



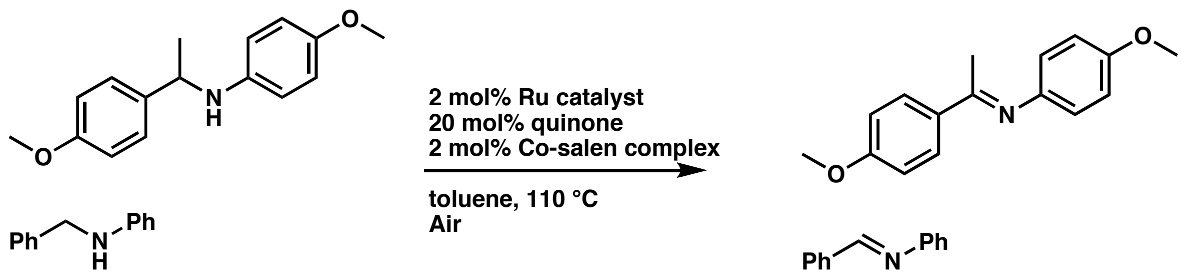
Vitamin B_2

5-ethyl-3-methyl-2',3',4',5'-di-*O*-methyleneriobflavinium perchlorate

Imada, Y.; Iida, Hiroki, Murahashi, S.-I.; Noata, T. *Angew. Chem. Int. Ed.* **2005,** *44*, 1704-1706**.**

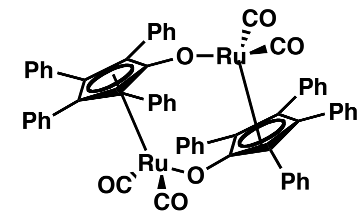
Biomimetic Aerobic Oxidation of Amines to Imines

Interception of Imines



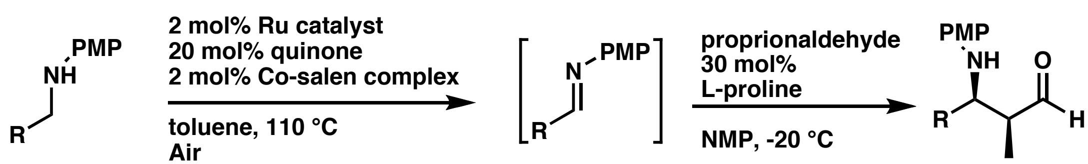
90

99



catalyst

Tandem aerobic oxidation and Mannich reaction

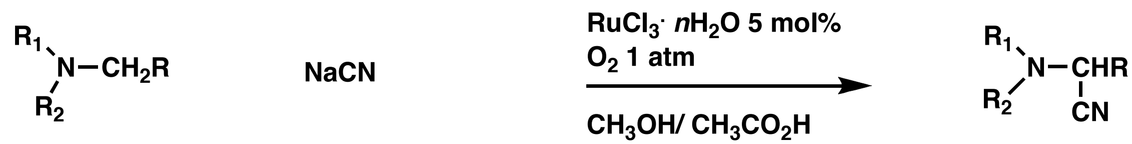


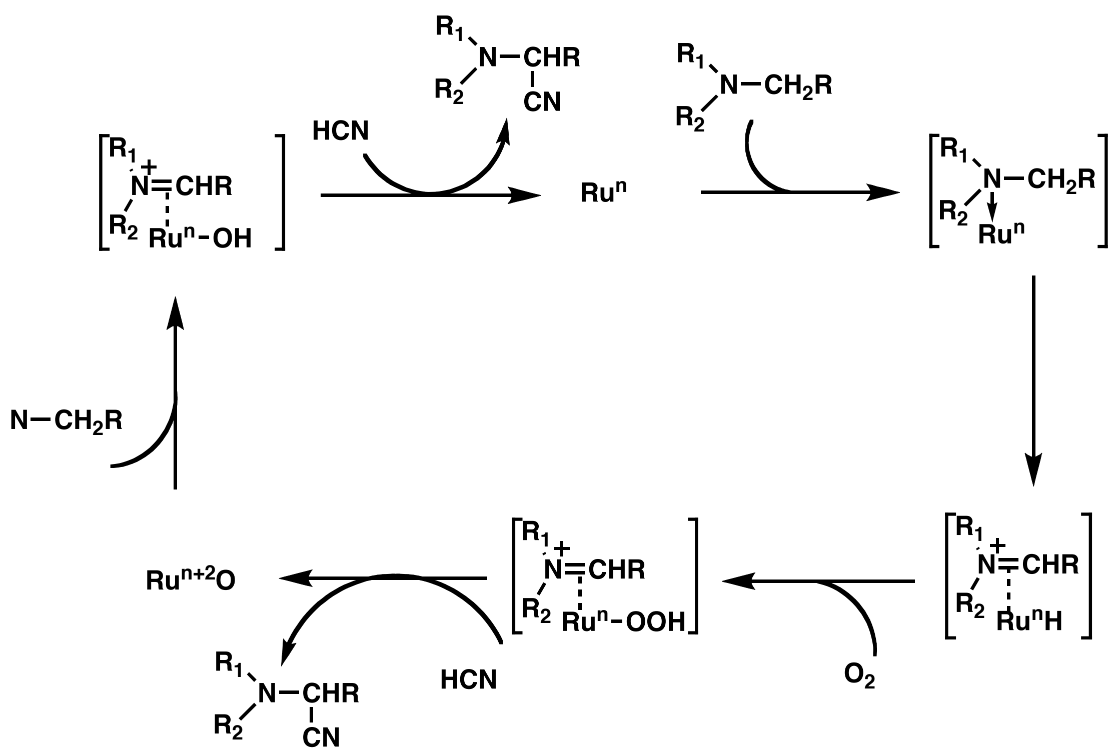
R =	Dr =	yield =	% ee =
Ph	19:1	> 95	> 99
CO_2Et	19:1	99	> 99
2-furyl	6:1	> 95	> 99
3-pyridyl	19:1	> 95	> 99

Ibrahem, I.; Samec, J. S. M.; Bäckvall, J.-E.; Córdova, A. *Tet. Lett.* **2005**, *46,* 3965-3968.

Interception of Imines

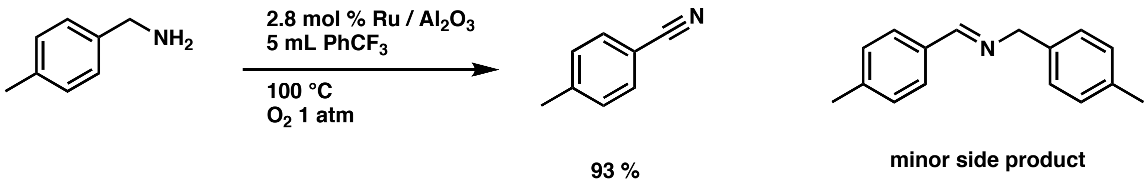
Trapping iminium ion intermediates with carbon nucleophiles: Oxidative cyanation

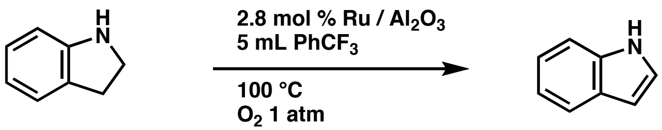




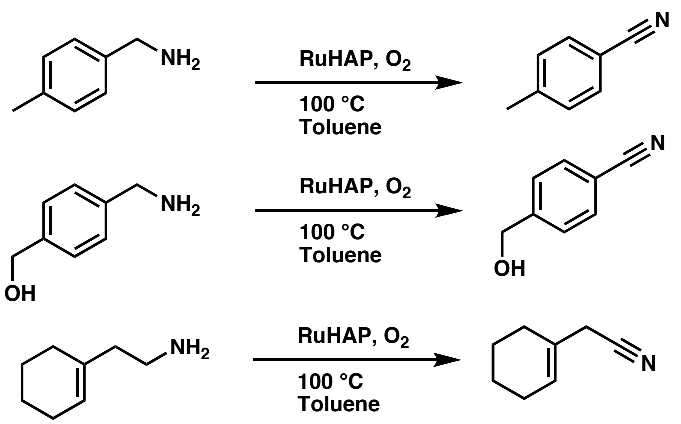
Murahashi, S.-I.; Komiya, N.; Terai, H.; Nakae, T. *J. Am. Chem. Soc.* **2003**, *125*, 15312.

Aerobic Oxidation of Amines to Nitriles





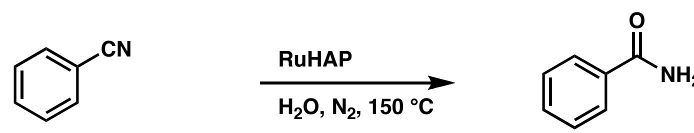
99 % new catalyst, 2h
99 % recycled catalyst, 2h

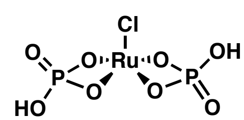


96 %

> 99 %

>99 %

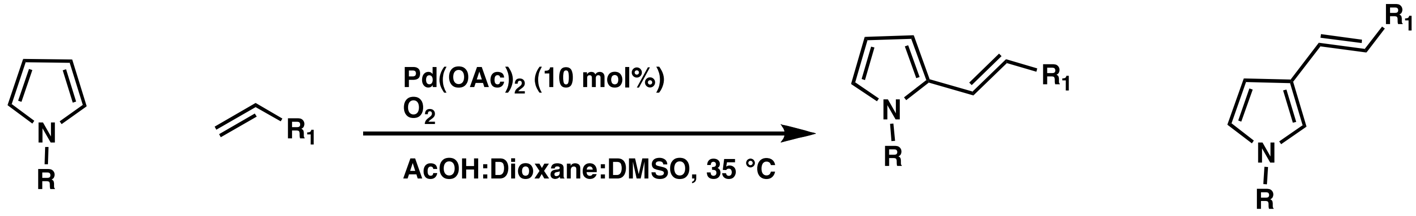




RuHAP
(calcium hydroxyapatite $Ca_{10}(PO_4)_6(OH)_2$ was stirred with $RuCl_3$)

Yamaguchi, K.; Mizuno, N. *Angew. Chem. Int. Ed.* **2003**, *42*, 1480.
Mori, K.; Yamaguchi, K.; Mizugaki, T.; Ebitani, K.; Kaneda, K. *Chem. Comm.* **2001**, 461-462.
Yamaguchi, K.; Mori, K.; Mizugaki, T.; Ebitani, K.; Kaneda, K. *J. Am. Chem. Soc.* **2000**, *122,* 7144.

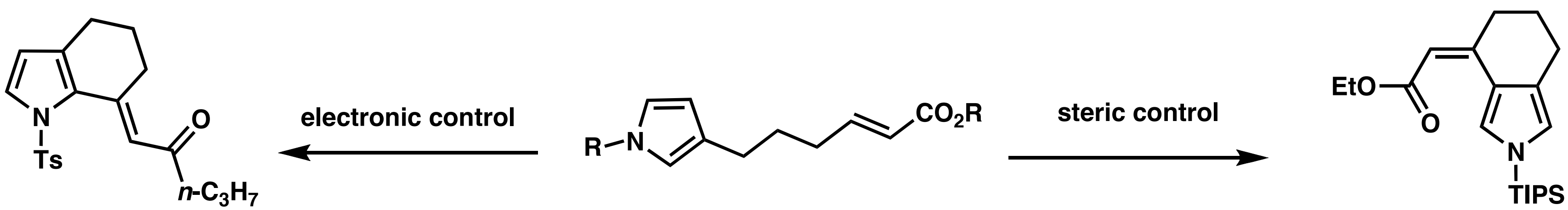
Alkenylation of Pyrroles



R = Boc | R = TIPS

R_1=	Yield of C 2	Yield of C 3
CO_2Bn	73 (73)	75 (78)
CO_2Bn (Air)	72	75
CO_2*n*-Bu	73 (75)	73 (81)
SO_2Me	38 (69)	45 (71)
4-(CO_2Me)Ph	53 (60)	58 (63)

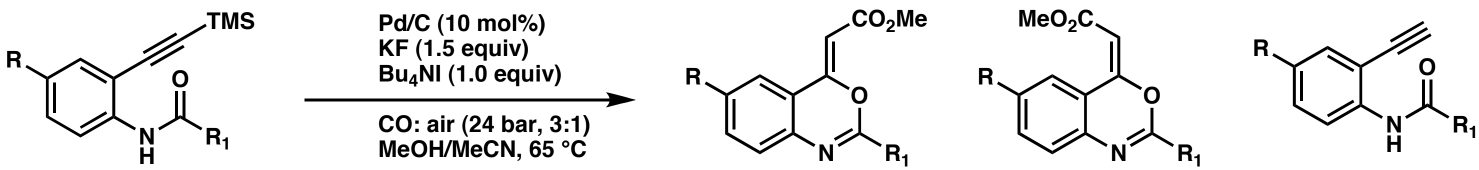
* yields listed in parentheses are from using *t*BuOOBz as a stoichiometric oxidant
using *t*BuOOBz as an oxidant trisubstituted alkenes could be generated in moderate yields (~ 60%)



60% 66%

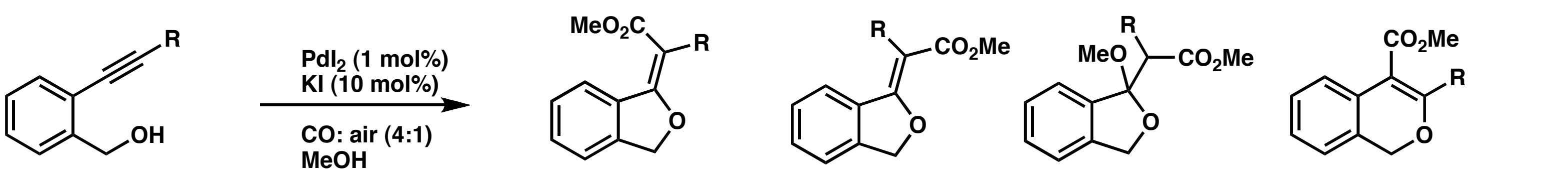
Beck, E.; Grimster, N.; Hatley, R.; Gaunt, M. J. *J. Am. Chem. Soc.* **2006**, *128*, 2528 - 2529.

Pd-Catalyzed Carbonylative Cyclization



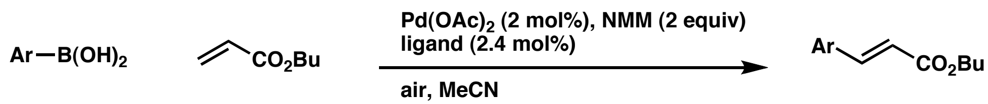
R_1	R_2	Z	E	desilylation
H	Ph	76	4	4
CO_2Me	Ph	53	0	23
CN	Ph	78	0	5
Cl	Ph	75	5	4
Me	Ph	64	5	12
H	-NHPh		74	
H	$-NHCH_2Ph$	68		

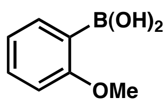
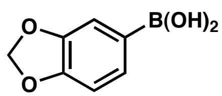
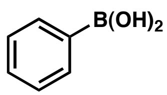
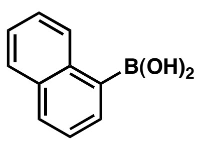
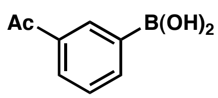
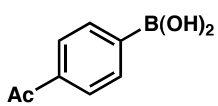
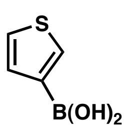
Costa, M.; Della Cà, N.; Gabriele, B.; Massera, C.; Salerno, G.; Soliani, M. *J. Org. Chem.* **2004**, *69*, 2469 - 2477.
Bacchi, A.; Costa, M.; Della Cà, N.; Fabbricatore, M.; Fazio, A.; Gabriele, B.; Nasi, C.; Salerno,G. *Eur. J. Org. Chem.* **2004**, 574-585.

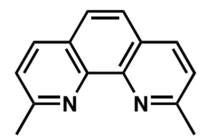


R				
H	19	17	7	
$SiMe_3$	7	44	10	
nBu	24			36
Ph	15	22		25

Heck Coupling….



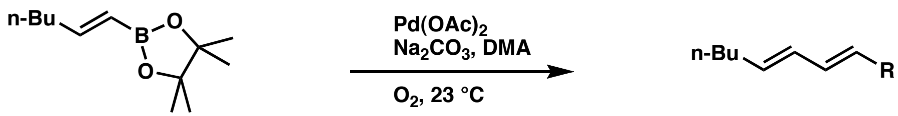
arylboronic acid	% yield	temp. (°C)
	82	80
	81	rt
	81	rt
	64	80
	67	rt
	61	80
	50	80

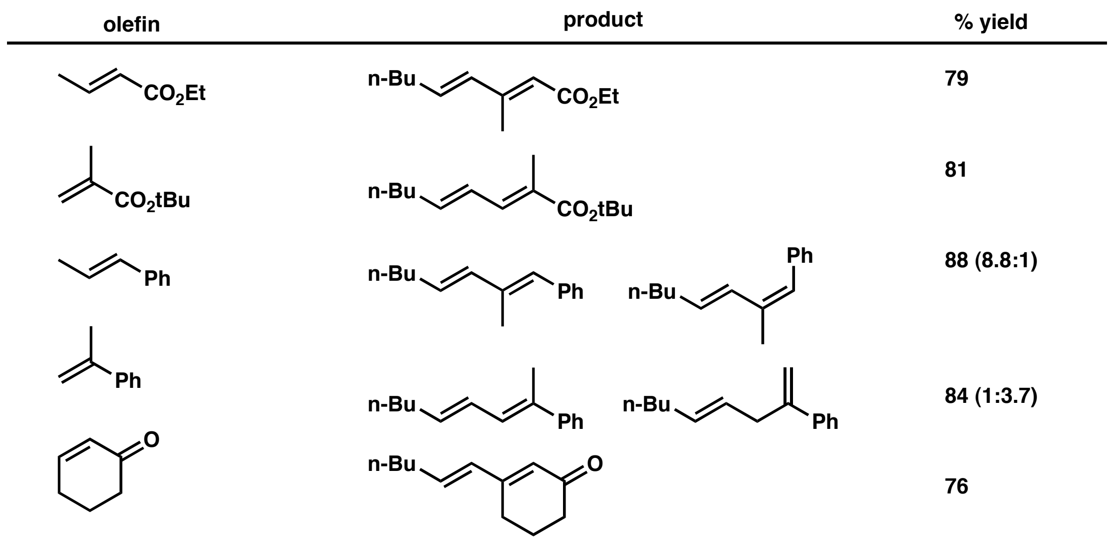


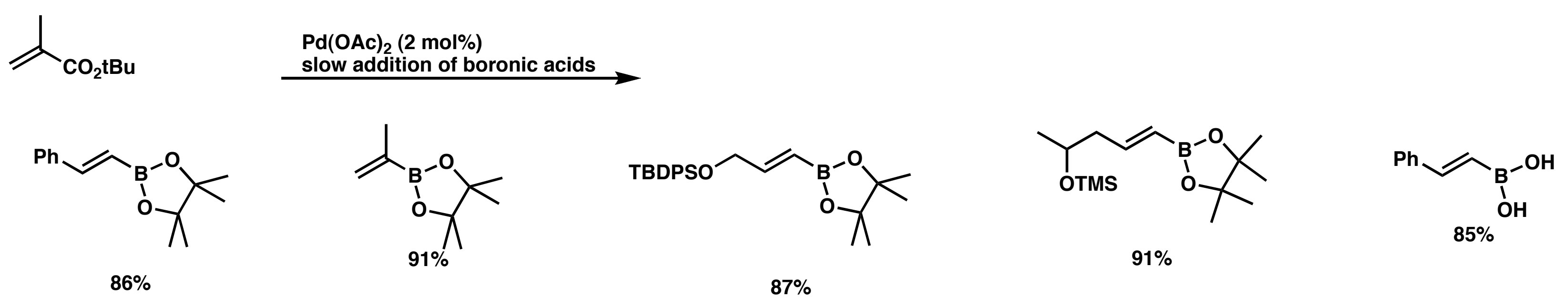
ligand

Enquist, P. E.; Lindh, J.; Nilsson, P.; Larhed, M. *Green Chem.*, **2006**, *8*, 338 - 343.

Oxidative Heck Reaction: Alkenyl Boronic Compounds

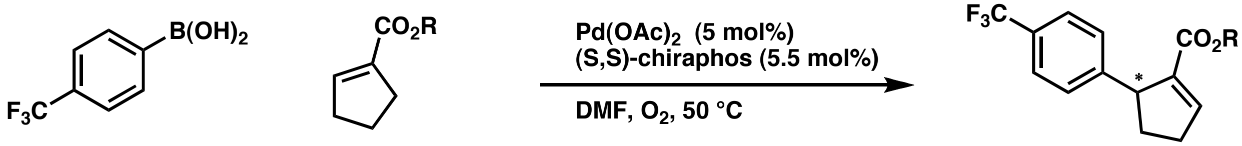






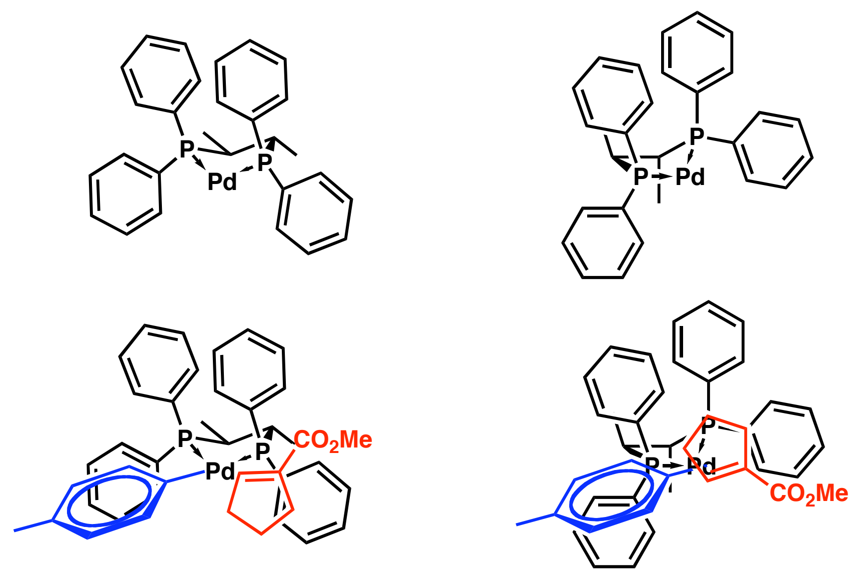
Yoon, C. H.; Yoo, K. S.; Yi, S. W.; Mishra, R. K.; Jung, K. W. *Org. Lett.,* **2004**, *6*, 4037 -4039.

Aerobic Enantioselective Heck-Type Reaction



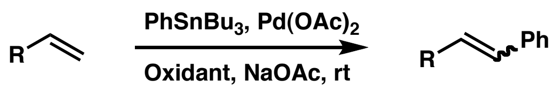
R	% yield	% ee
Me	73	46
Me[a]	25	59
Et	72	46
I-Pr	49	35
Ph	31	22
Bn	58	49

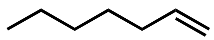
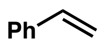
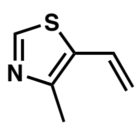
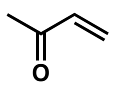
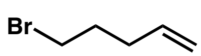
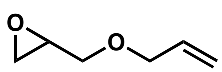
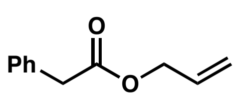
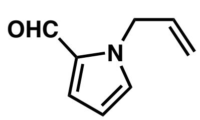
[a] run in MeOH

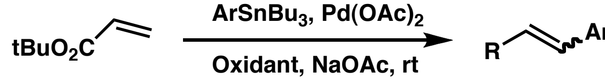


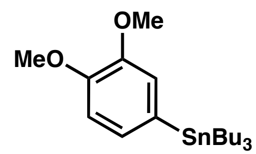
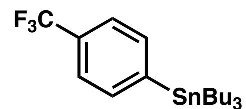
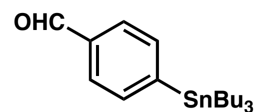
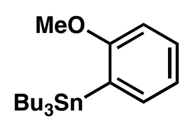
Akiyama, K.; Wakabayashi, K.; Mikami, K. *Adv. Synth. Catal.*, **2005**, *347*, 1569 -1575.

Cross-Coupling: Stannanes



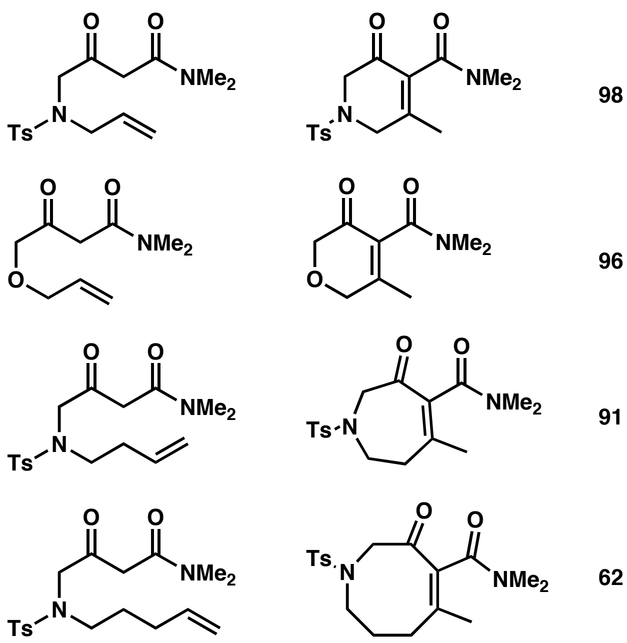
alkene	$CuCl_2$ THF	O_2 DMF
	0	82
	62	72
	0	51
	65	55
	0	80
	65	70
	81	67
	60	88



aryl	$CuCl_2$ THF	O_2 DMF
	96	98
	85	69
	60	60
	75	68

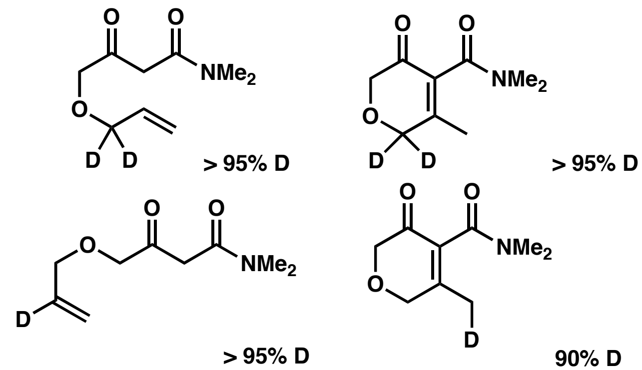
Parrish, J. P.; Jung, Y. C.; Shin, S. I.; Jung, K. W. *J. Org. Chem.* **2002**, *67*, 7127 -7130.

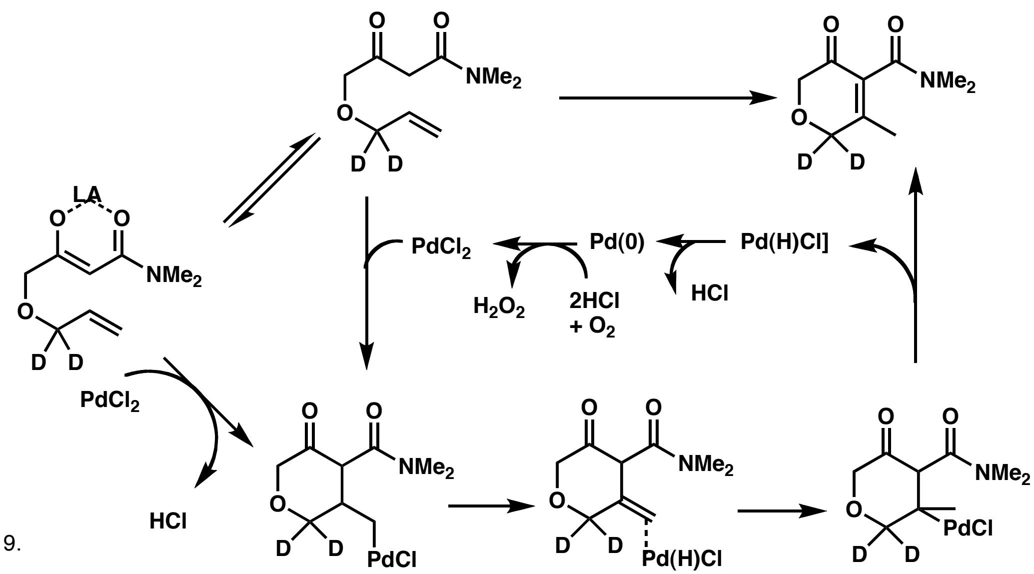
Generation of Heterocycles



Yb(OTf)$_3$ (1 equiv)
PdCl$_2$(MeCN)$_2$ (10 mol%)

THF, O$_2$ (1 atm), rt

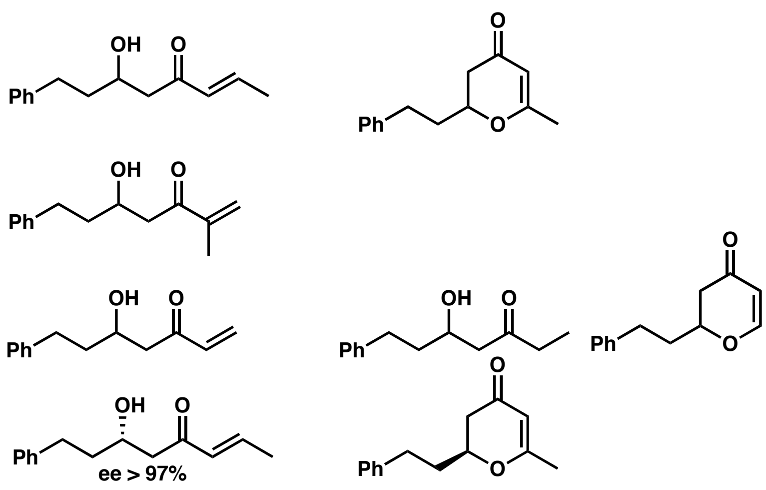




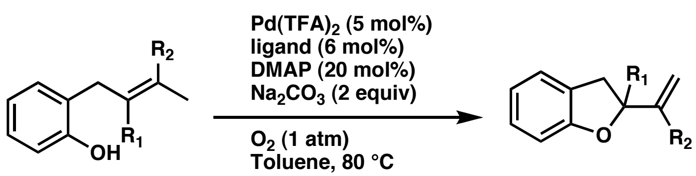
Yip, K.-T.; Li, J.-H.; Lee, O.-Y.; Yang, D. *Org. Lett.* **2005**, *7*, 5717-5719.

Oxidative Cyclization

substrate	product	yield
		79%
		0%
		60% 1:4 uncyclized: cyclized
		61% ee > 97%

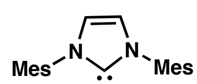


10 mol% $PdCl_2$, 1 atm O_2
10 mol% CuCl, 10 mol% Na_2HPO_4
DME, 50 °C



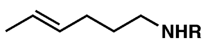
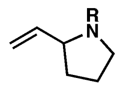
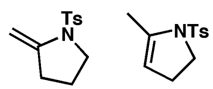
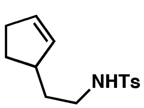
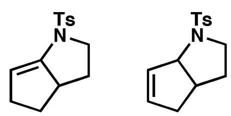
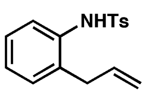
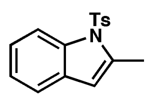
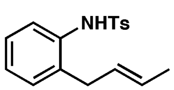
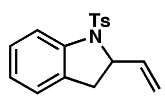
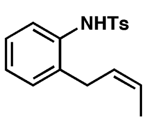
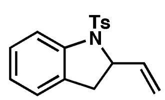
R_1	R_2	Yield
H	CH_3	91
CH_3	H	92
CH_3	CH_3	96
H	H	89
CH_3	H	87
CH_3	CH_3	88

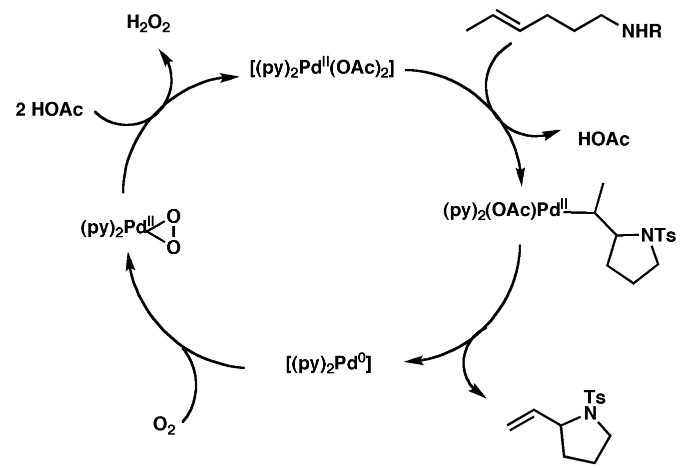
ligand:



Reiter, M.; Ropp, S.; Gouverneur, V. *Org. Lett.* **2004**, *6,* 91-94.
Muñiz, K. *Adv. Syn. Catal.* **2004**, *346*, 1425-1428.

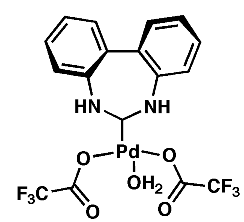
Oxidative Amination

substrate	product	yield	yield NHC catalyst
			
R = Ts		87	55
Ns		87	
Cbz		76	60 °C
		81 (7:3)	
		91 (91:0)	65 (85:15) 60 °C
		60	
		91	
			86 (O_2, 4h) 87 (in air, 15h)



reaction conditions:

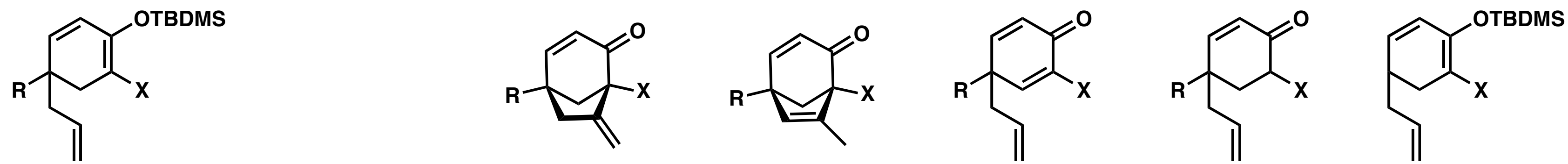
5 mol % $Pd(OAc)_2$
10 mol % pyridine
O_2
Toluene, 80 °C



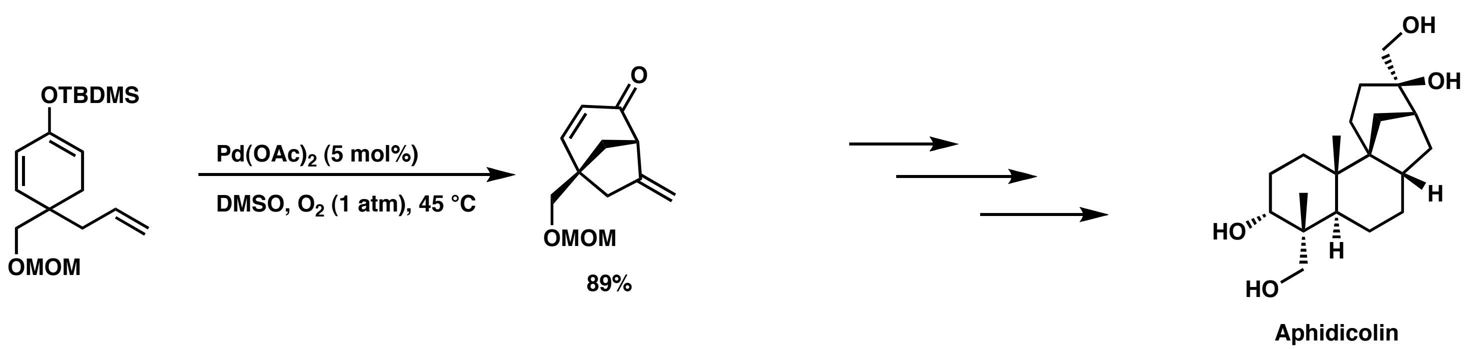
5 mol % NHC catalyst
20 mol % AcOH or PhCOOH
O_2 or Air
Toluene, 80 °C

Fix, S. R.; Brice, J. L.; Stahl, S. S. *Angew. Chem. Int. Ed.* **2002**, *41*, 164-166.
Rogers, M. M.; Wendlandt, J. E.; Guzei, I. A.; Stahl, S. S. *Org. Lett.* **2006**, *8*, 2257-2260.

C-C bond formation: Silylenolethers

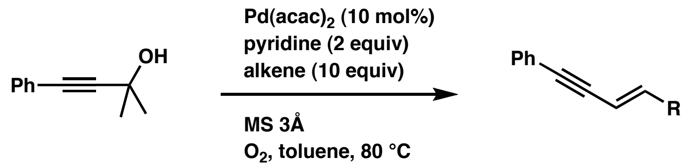


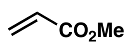
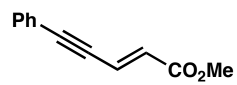
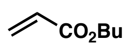
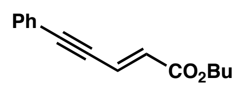
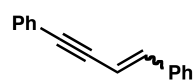
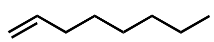
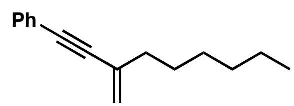
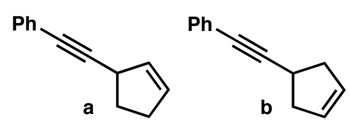
R	X					
Ph	H	87	1	4		
CH_2OMOM	H	80	6	4		
CH_2CH_2OMOM	Me	79	9			
CH_2OMOM	Me	79	9	2		
CH_2CH_2OMoM	OMe	46	9	10		
CH_2OBn	H	70	8	3		
OSEM	H	77	2	6		
OCH_2SMe	H					27
$CH_2CH_2CH_2OPv$	H	85	8	2		

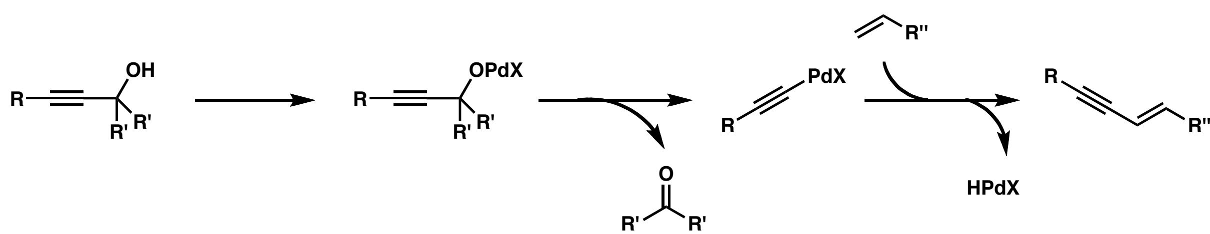


Toyota, M.; Rudyanto, M.; Ihara, M. *J. Org. Chem.* **2002**, *67*, 3374-3386.
Toyota, M.; Sasaki, M.; Ihara, M. *Org. Lett.* **2003**, *5*, 1193 -1195.

Aerobic Oxidative Cleavage of Alkynes: Generation of Enynes

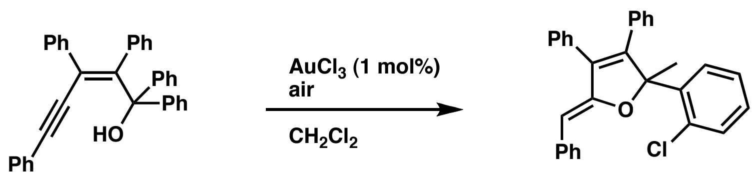


alkene	product	yield
		49
		57
		54 cis/trans = 1/ 4
		33
		40 a/b = 2/ 1

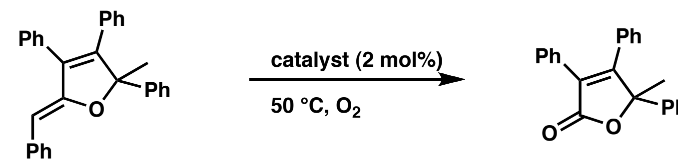


Nishimura, T.; Araki, H.; Maeda, Y.; Uemura, S. *Org. Lett.* **2003**, *5*, 2997 - 2999.

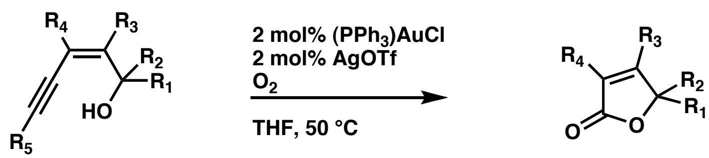
Tandem Cylcization and Oxidative Cleavage of Alkynes

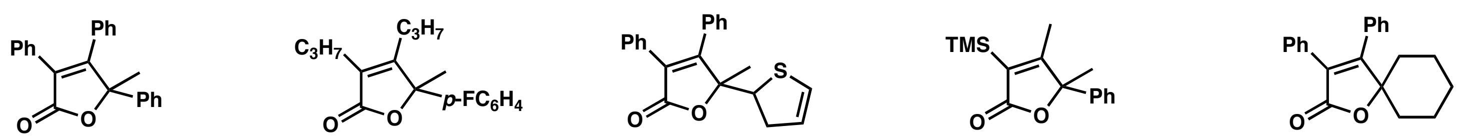


74



(PPh$_3$)AuOTf, THF	90% (21 h)
P(p-CF$_3$C$_6$H$_5$)$_3$AuOTF, THF	92% (14 h)
AuCl$_3$, CH$_2$Cl$_2$	6% (24 h)
(PPh$_3$)AuOTf, THF, air	99% (36 h)



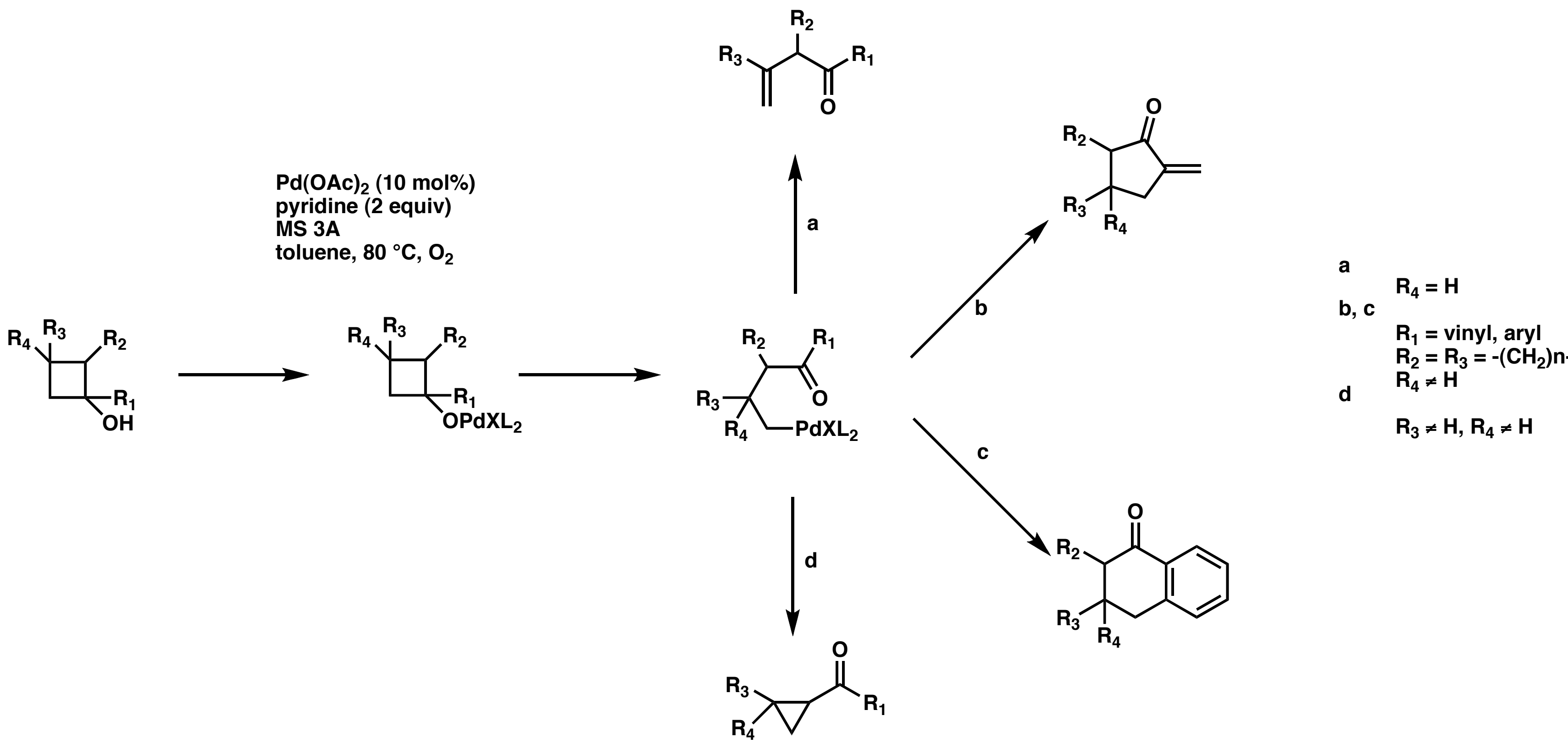


97%	80%	91%	41%	66%
R_5= Ph	R_5= Ph	R_5= Bu	R_5= Bu	R_5= Bu

- reaction is suppressed by the addition of TEMPO or 2,6-di-*tert*-butyl-*p*-cresol, which indicates that a radical species is involved
-AuCl(PPh$_3$) is stable under O$_2$ atm, but AuCl(PPh$_3$) and AgOTf in O$_2$ atm creates $(PPh_3)_2Au^+$

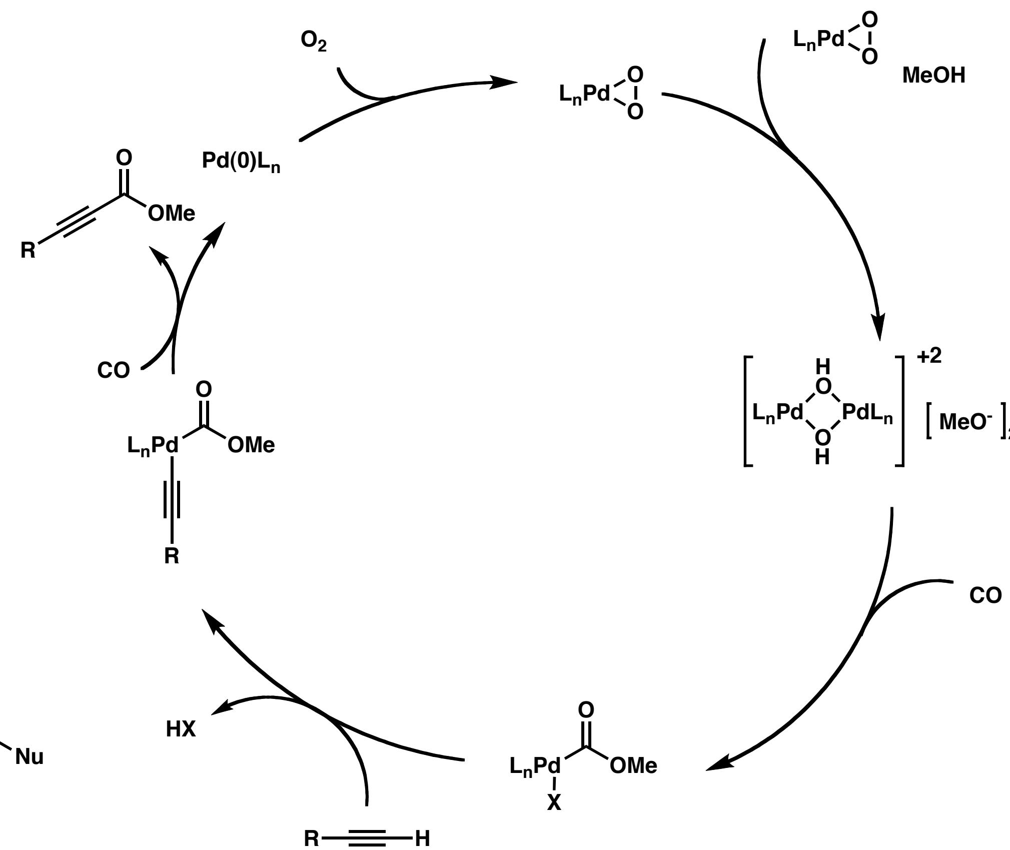
Liu, Y.; Guo, S. *J. Am. Chem. Soc.* **2006**, ASAP
Liu, Y.; Song, F.; Song, Z.; Liu, M.; Yan, B. *Org. Lett*, **2005**, *7*,5409 -5412.

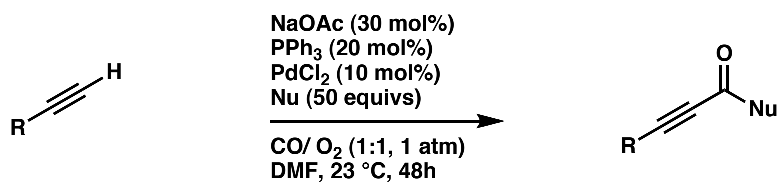
Oxidative Transformations of Cyclobutanols



Nishimura, T.; Ohe, K.; Uemura, S. *J. Org. Chem.* **2001**, *66*, 1455 - 1465.

Oxidative Carbonylation of Alkynes

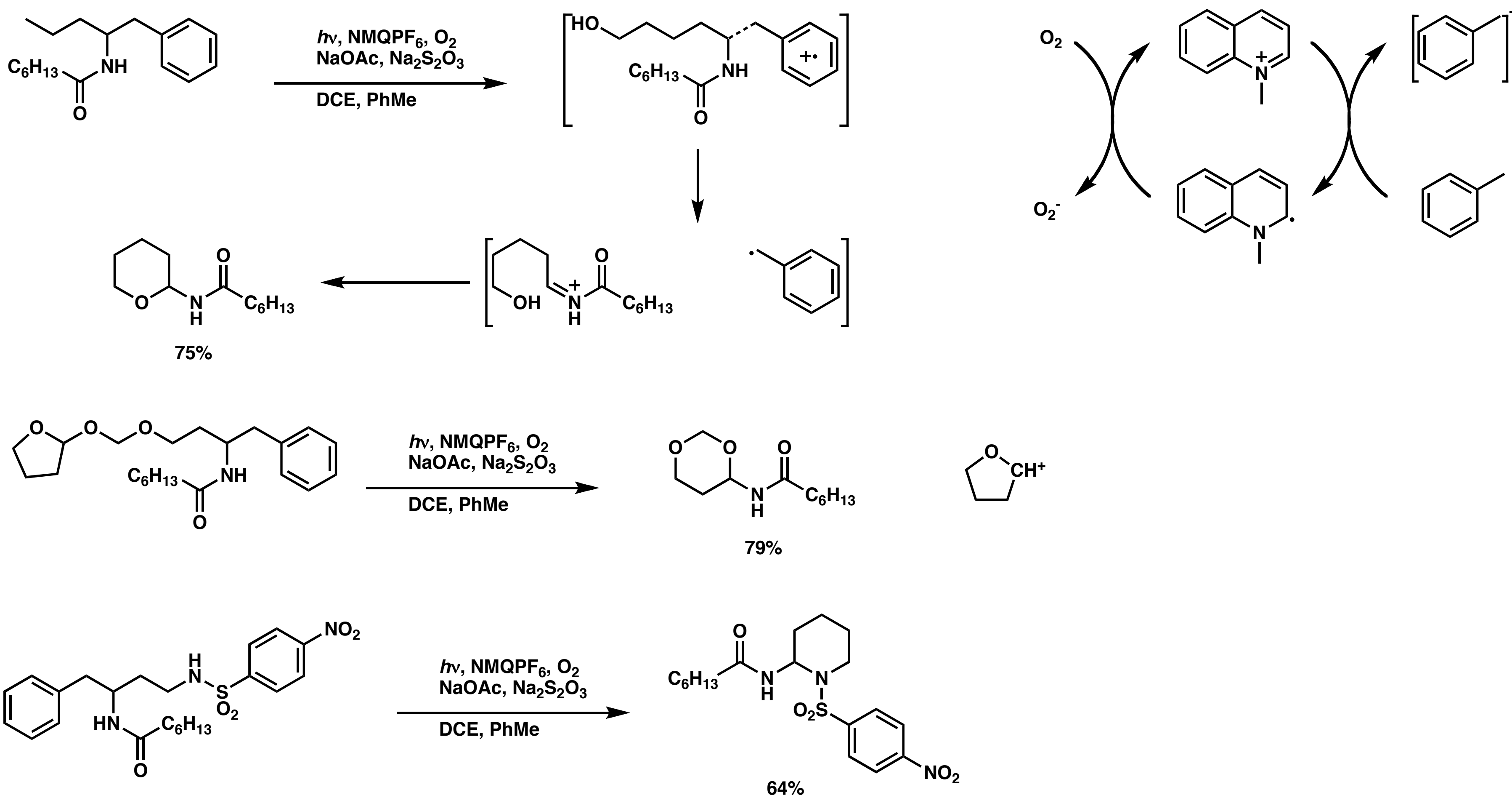




R	Nu	yield
Ph	MeOH	82
4-BrC$_6$H$_4$	MeOH	79
n-C$_5$C$_{11}$	MeOH	75
HO(CH$_2$)$_4$	MeOH	42
TBSO(CH$_2$)$_4$	MeOH	83
Ph	n-BuOH	86
Ph	HNEt$_2$	60

Izawa, Y.; Shimizu, I.; Yamamoto, A. *Bull. Chem. Soc. Jpn.* **2004**, *77*, 2033 -2045.

Aerobic Electron-Transfer-Initiated Cyclization



Aubele, D. L.; Recht, J. C.; Floreancig, P. E. *Adv. Syn. Catal.* **2004**, *346*, 359 -366.
For aerobic $NMQPF_6$ variant with oxonium intermediates see:
Kumar, V. S.; Aubele, D. L.; Floreancig, P. E. *Org. Lett.* **2001**, *3*, 4123.

Other Useful References….

Aerobic Sulfoxidation:

Polyoxometalate bridged by aquated Cu(II) unit:
Okun, N. M.; Anderson, T. M.; Hardcastle, K. I.; Hill, C. L. *Inorg. Chem*. **2003**, *42*, 6610 -6612.
Polyoxometalate Fe(II)/ hydrogen dinitrate:
Okun, N. M.; Tarr, J. C.; Hilleshiem, D. A.; Hardcastle, K. I.; Hill, C. L. *J. Mol. Catal. A. Chem.* **2006**, *246*, 11-17.

Aerobic Aryl Oxidation:

Parrish, J. P.; Jung, Y. C.; Floyd, R. J.; Jung, K. W. *Tet. Lett.* **2002**, *43,* 7899 -7902.
Yoshida, H.; Yamaryo, Y.; Oshita, J.; Kunai, A. *Tet. Lett*. **2003**, *44*, 1541 -1544.
Hossain, K. M.; Kameyama, T.; Shibata, T.; Takagi, K. *Bull. Chem. Soc. Jpn*. **2001**, *74*, 2415 -2420.

Aerobic Nazarov Reaction:

Bee, C.; Leclerc, E.; Tius, M. *Org. Lett*. **2003**, *5*, 4927-4930.

Epoxidation:

Ho, K. P.; Wong, K. Y.; Chan, T. H. *Tet*. **2006**, *62*, 6650-6658.
Lu, X.-H.; Xia, Q.-H.; Zhan, H.-J.; Yuan, H.-X.; Ye, C.-P. Su, K.-X.; Xu, G. *J. Mol. Catal. A: Chem*. **2006**, *250*, 62-69.

Radical Chain Promoter:

Baucherel, Y.; Gonsalvi, L.; Arends, I. W. C. E.; Ellwood, S.; Sheldon, R. A. *Adv. Syn. Catal.* **2004**, *346*, 286-296.

Summary

There are a number of aerobic oxidation methods that have been developed

- heterogenous
- homogenous
- biomimetic
- radical chain transfer

But there is still room for the development of enantioselective aerobic oxidations!!