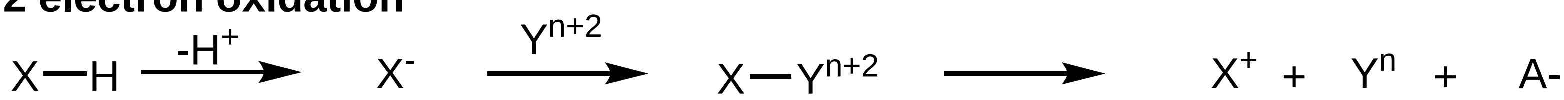
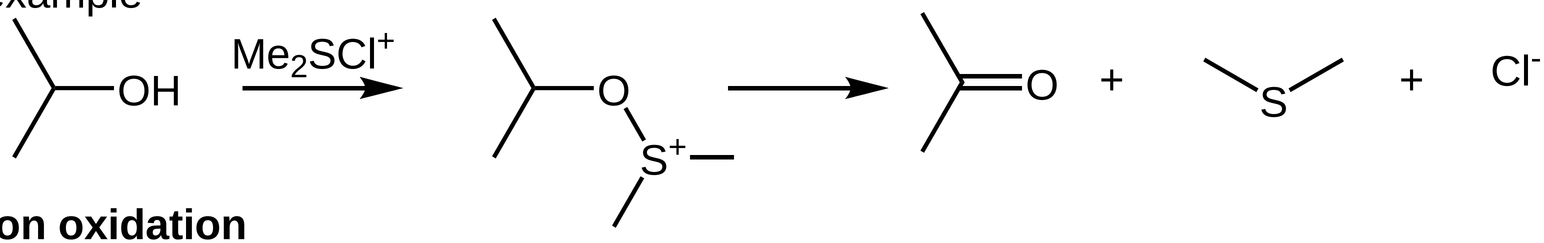
Oxidation of Unsaturated Systems

2 general reactivity patterns:

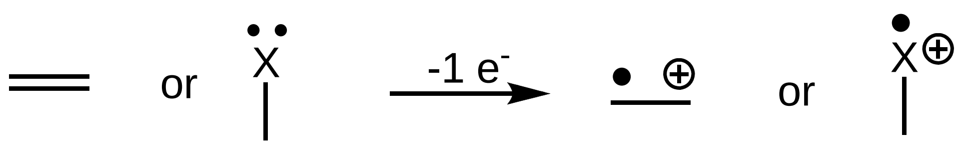
2 electron oxidation



simple example



1 electron oxidation



we will focus on oxidation of aromatic rings and enol/enolate systems

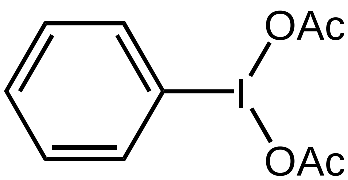
Reduction potentials of oxidants we will look at (bigger number = stronger [O]):

Couple			E^o
Cu(II) + e-	→	Cu(I)	0.16
Fe(III) + e-	→	Fe(II)	0.77
V(V) + e-	→	V(IV)	1.00
Tl(III) + 2 e-	→	Th(I)	1.25
Mn(III) + e-	→	Mn(II)	1.56
Ce(IV) + e-	→	Ce(III)	1.6
Pb(IV) + 2 e-	→	Pb(II)	1.6-1.7

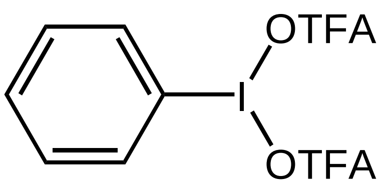
Oxidation of electron rich aromatic rings
Oxidation of phenols
2 e- processes
I(III) reagents

review: Pelter, Tet, 2001, 273

2 major reagents:

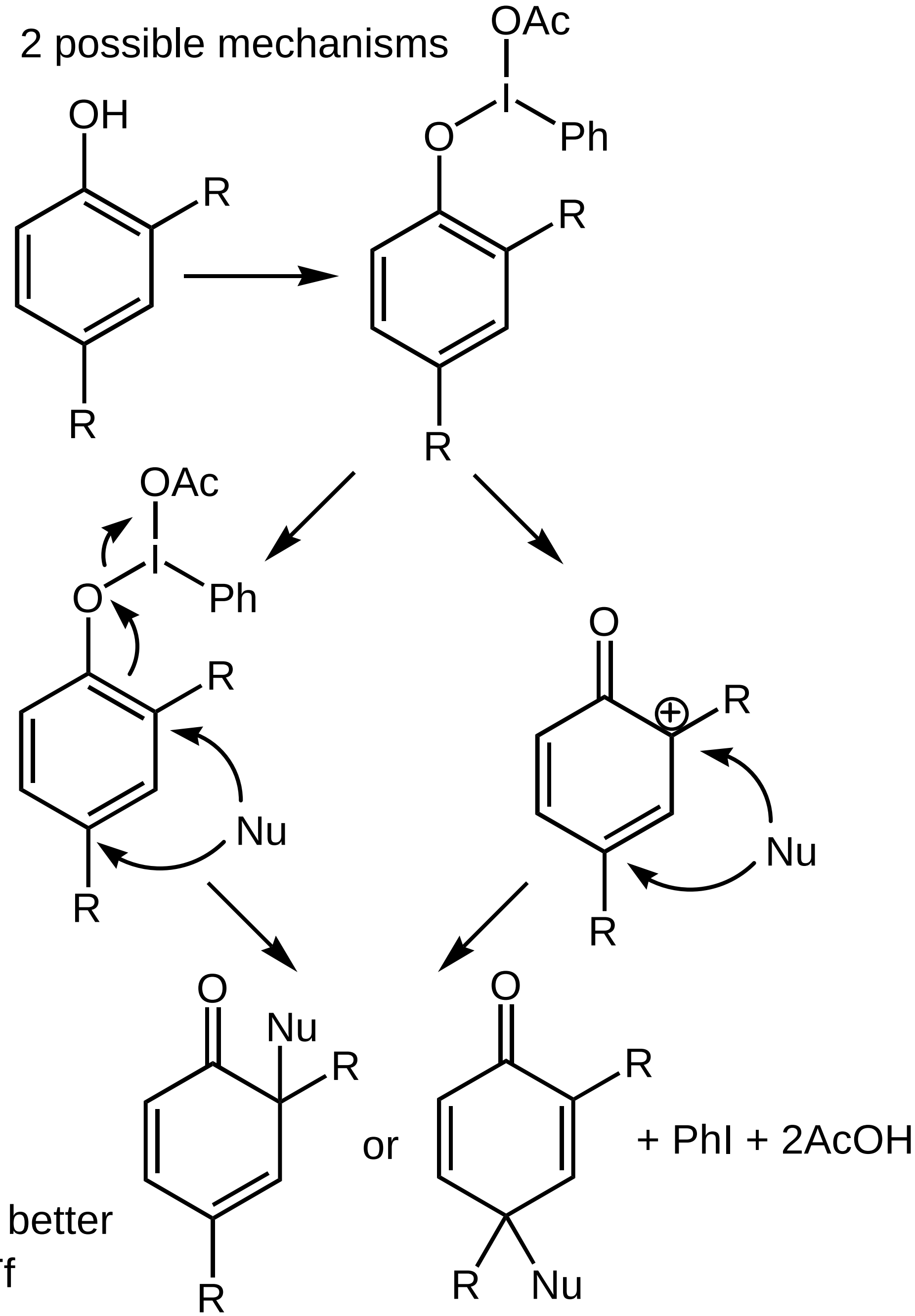


phenyl iodonium diacetate (PIDA)
AKA (diacetoxy) iodobenzene (DIB)
AKA iodobenzene diacetate



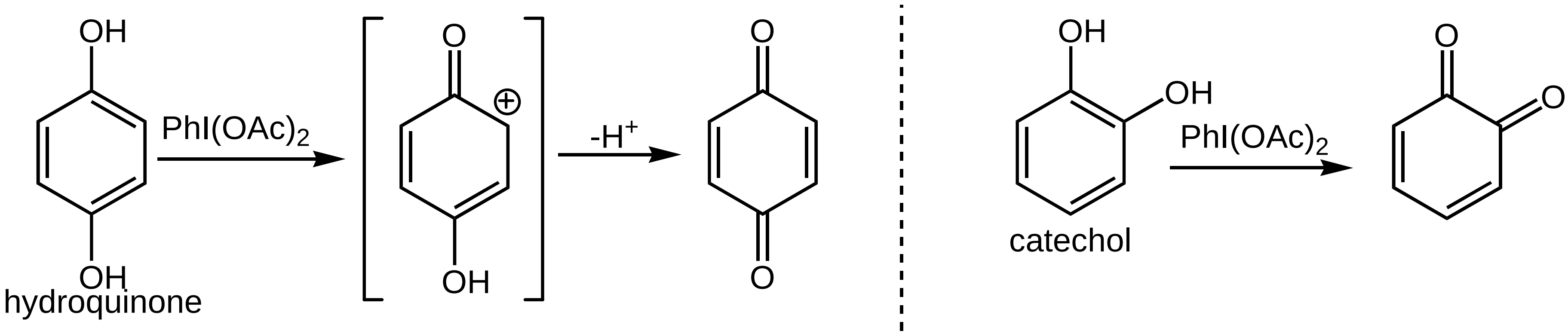
phenyl iodonium bis(trifluoroacetate) (PIFA)
aka bis(trifluoroacetoxy) iodobenzene (BTIB)
aka Iodobenzene bis(trifluoroacetate)

2 possible mechanisms

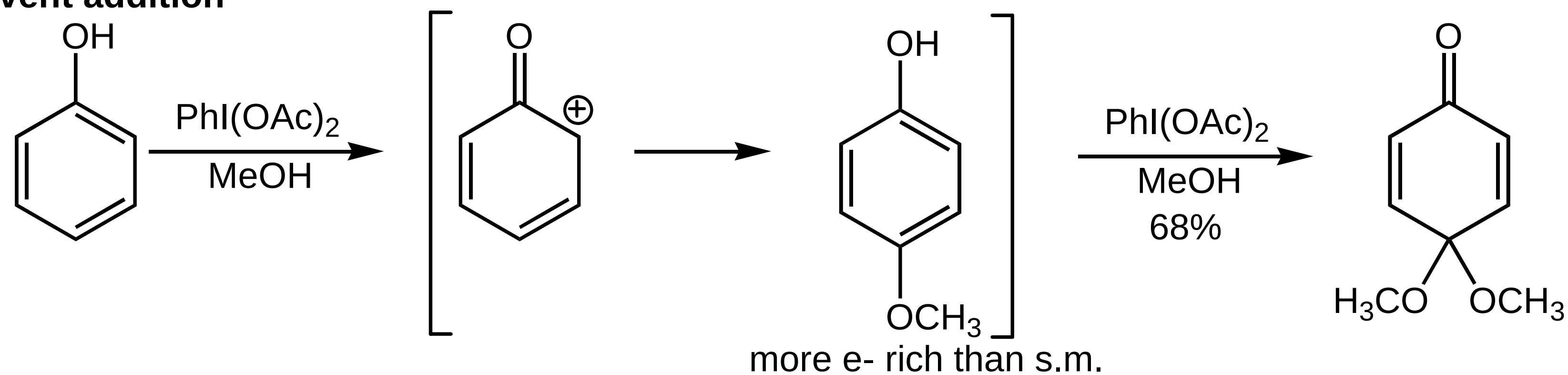


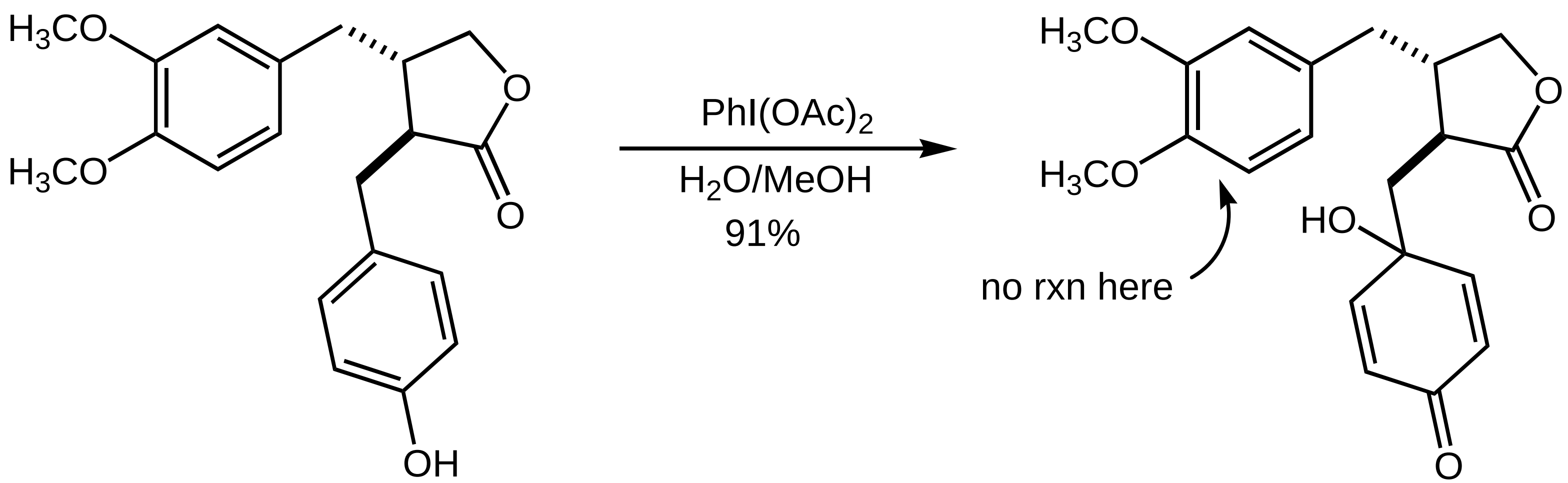
Note: PhI $8x10^5$ times better leaving group than OTf

Simplest case: hydroquinone to quinone

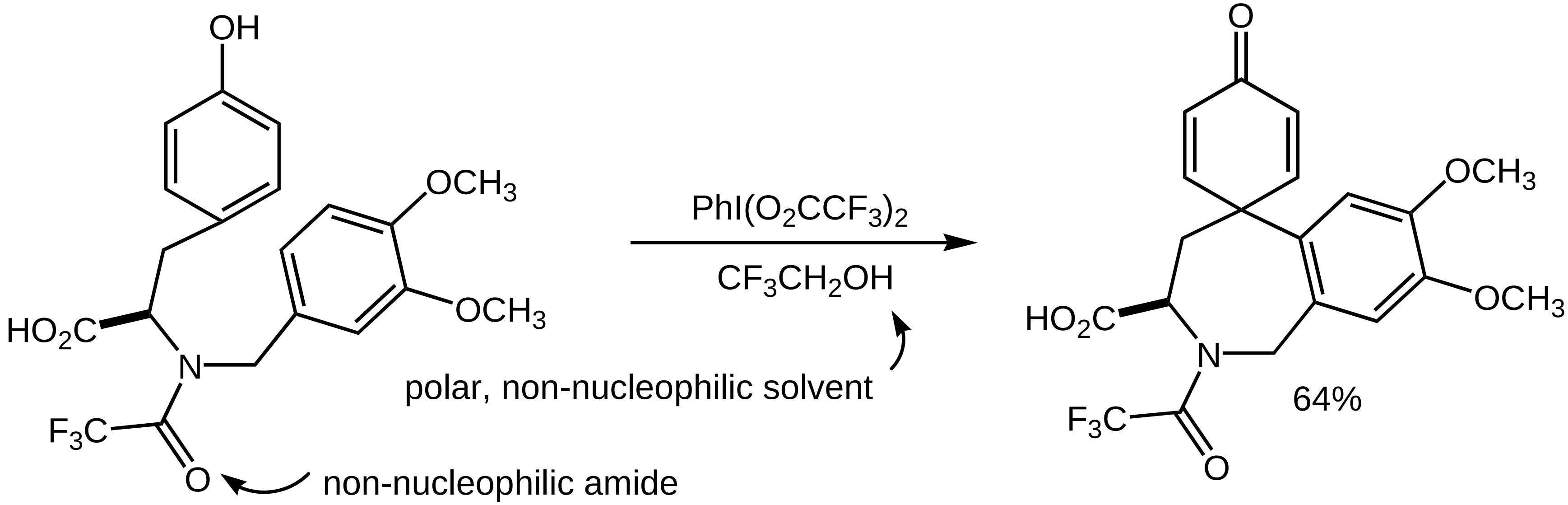


Solvent addition



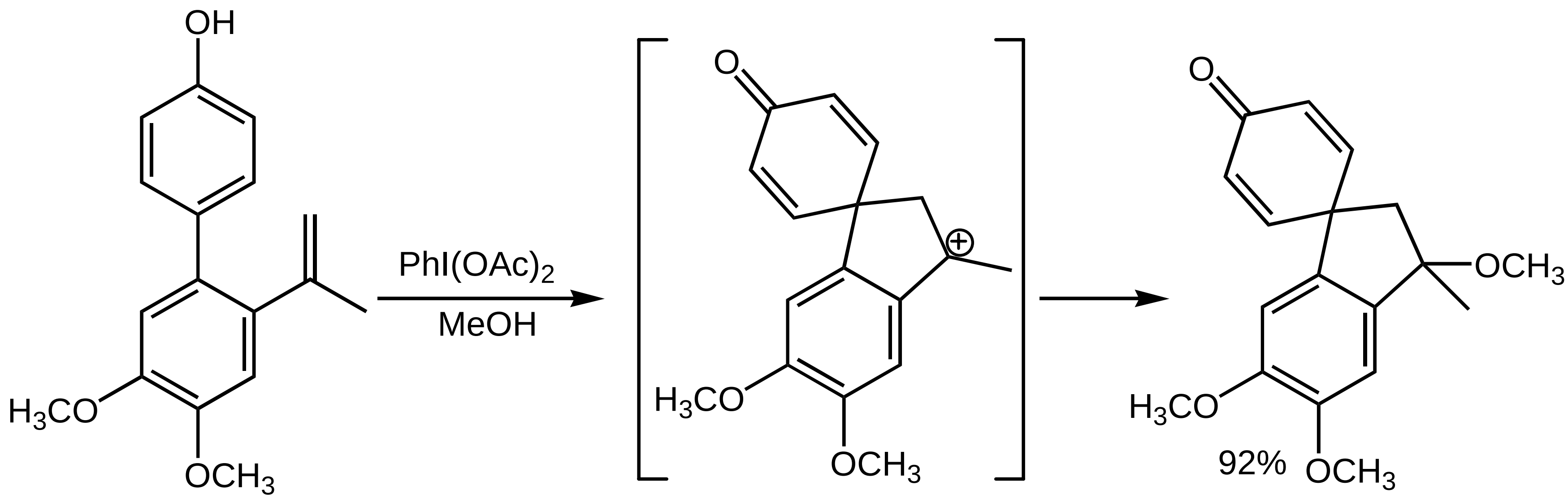


Addition of aromatic ring



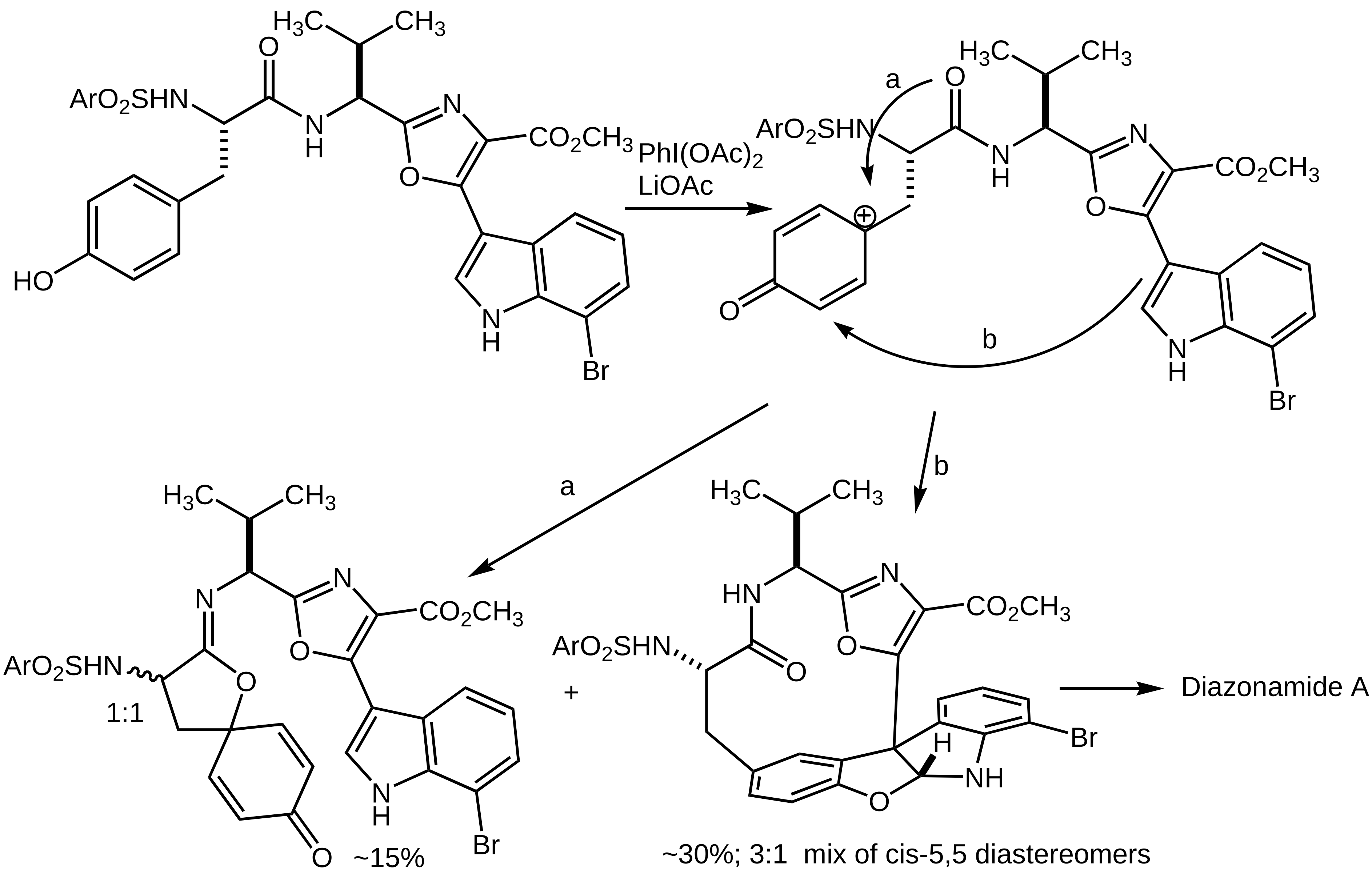
Kita, JOC, 1996, 5857

Addition of olefin



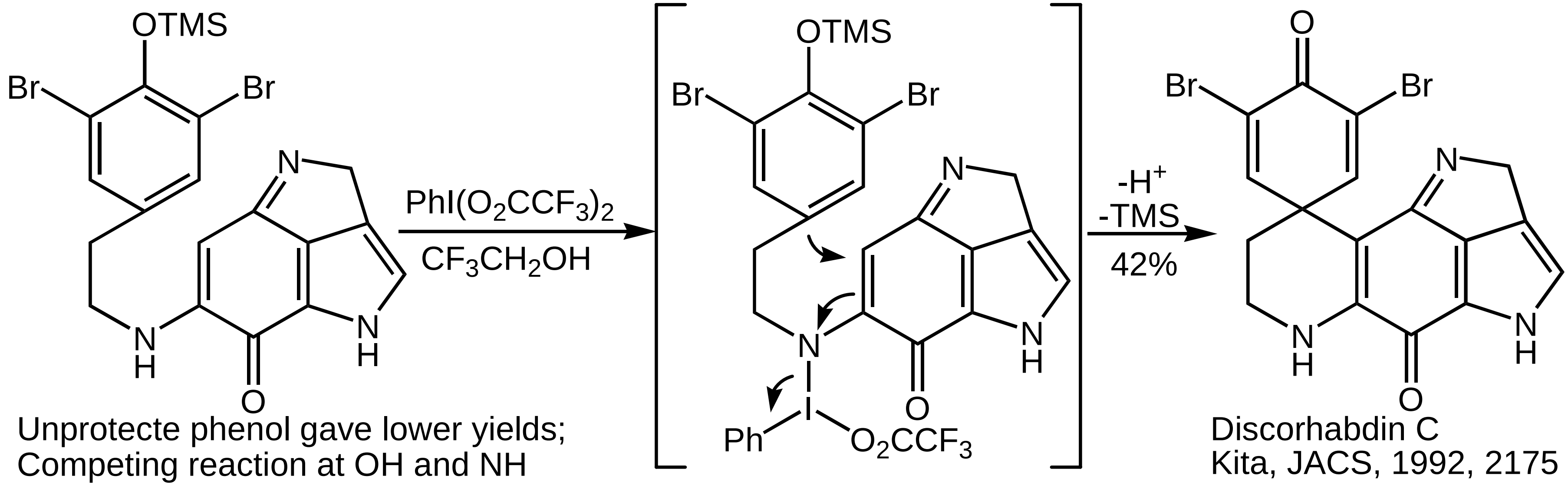
JOC, 1996, 1267

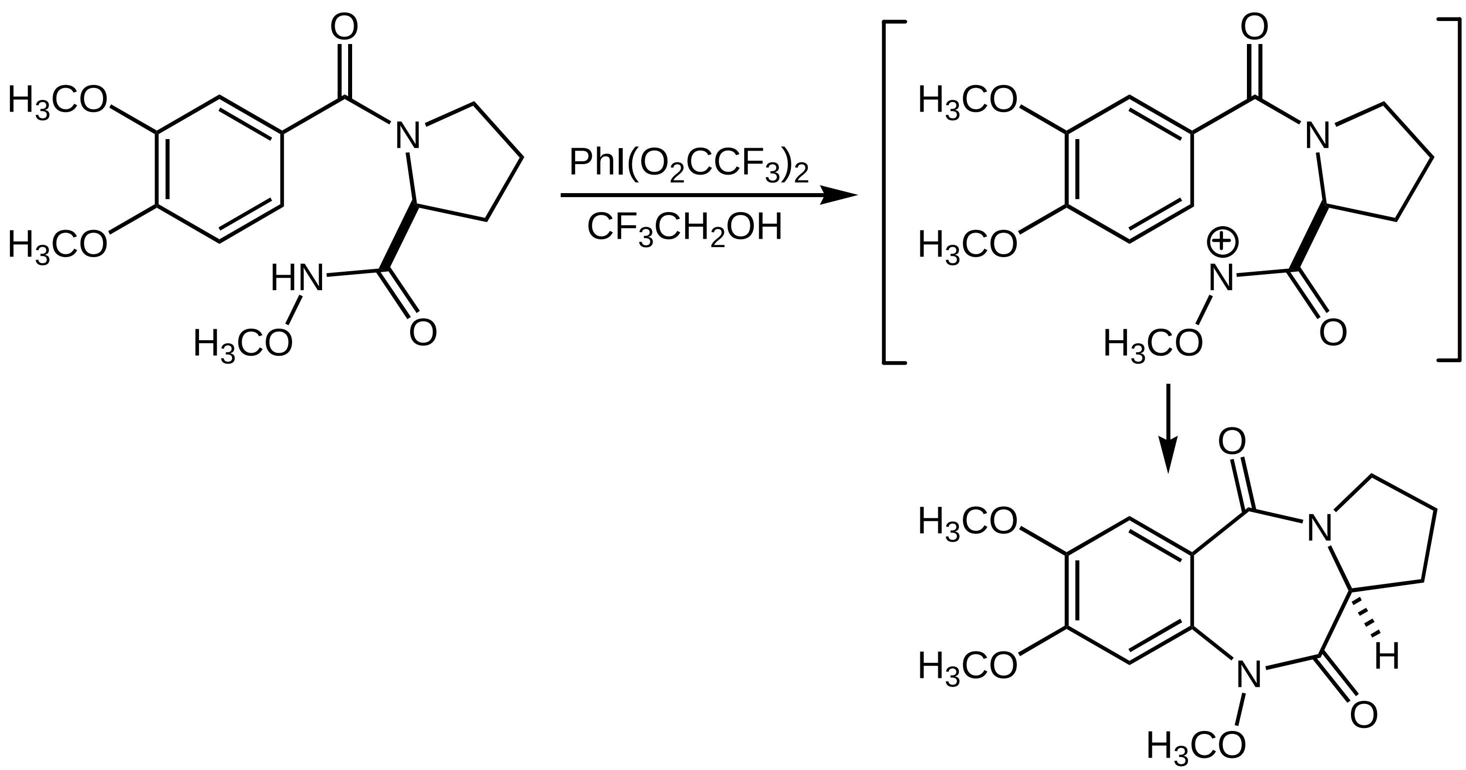
Addition of indole



~30%; 3:1 mix of cis-5,5 diastereomers
Harran, ACIEE, 2003, 4961

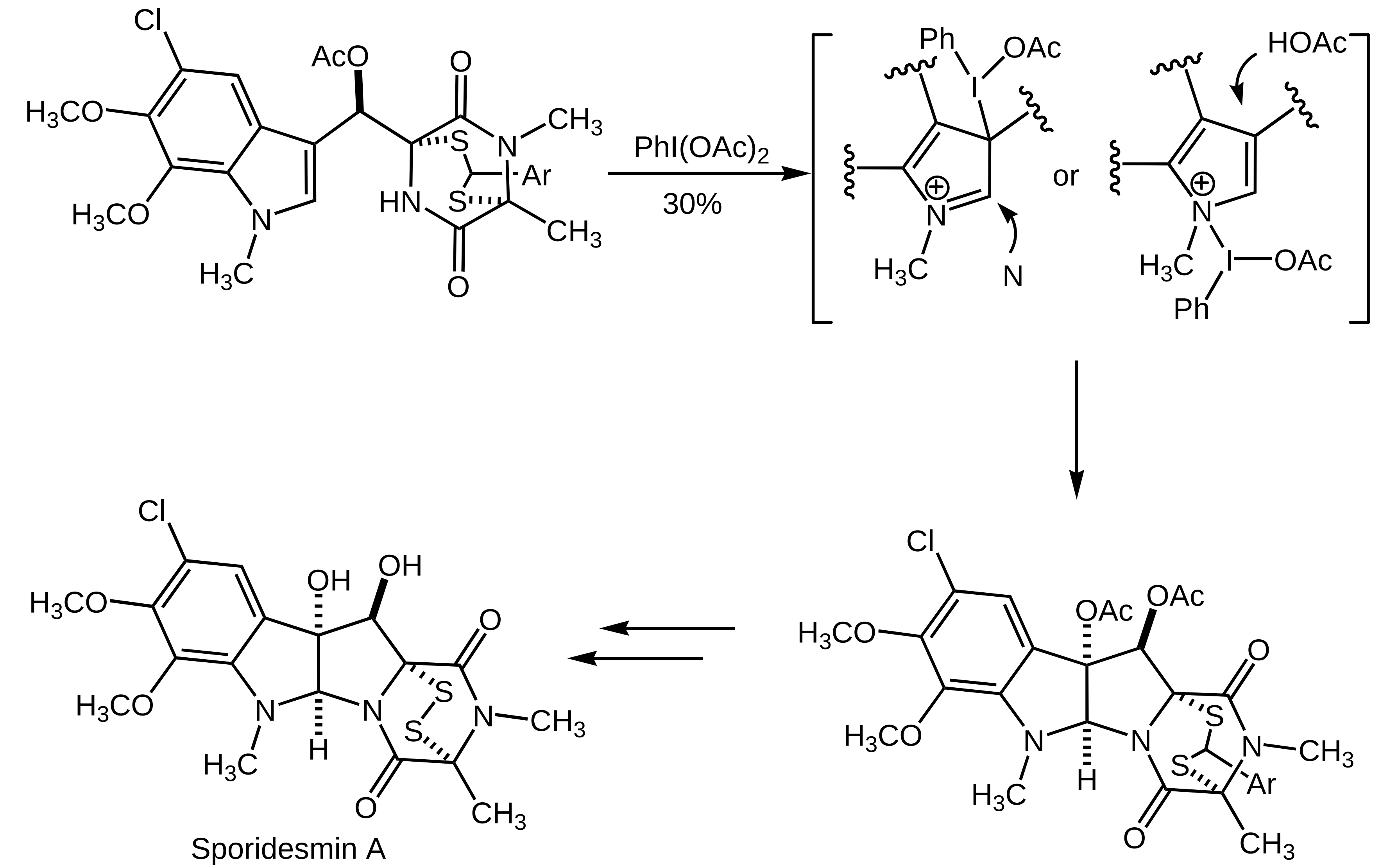
Oxidations involving Nitrogen





70%
JOC, 2005, 2256

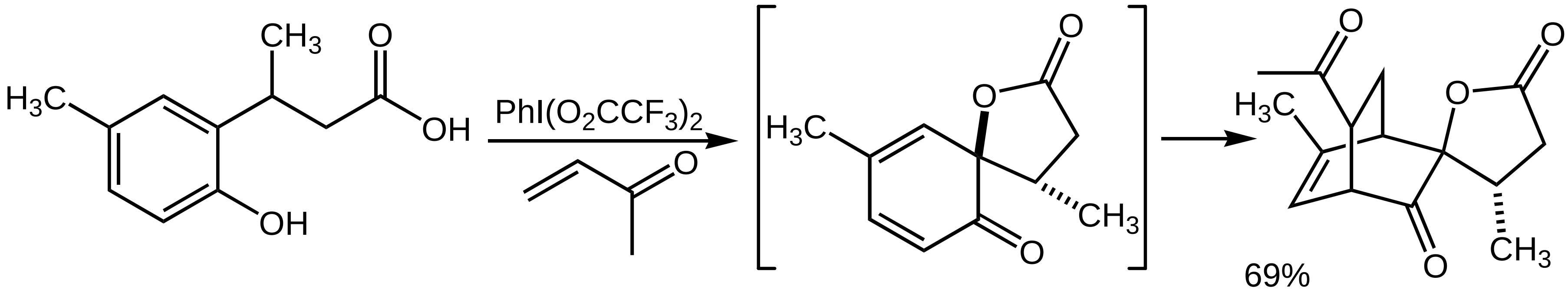
Indole oxidation



Sporidesmin A
Kishi, JACS, 1973, 6493

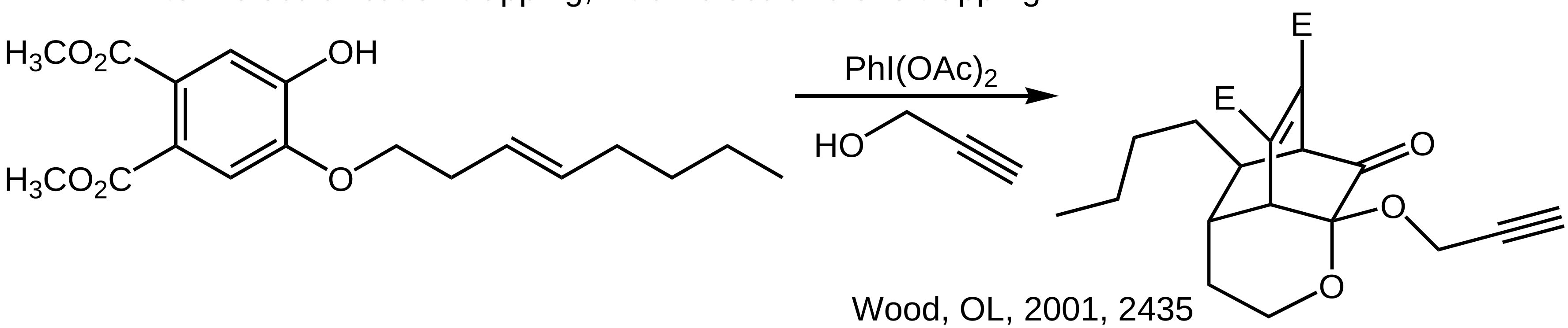
Trapping the dieneone from I(III) oxidations

intramolecular cation trapping; intermolecular diene trapping:



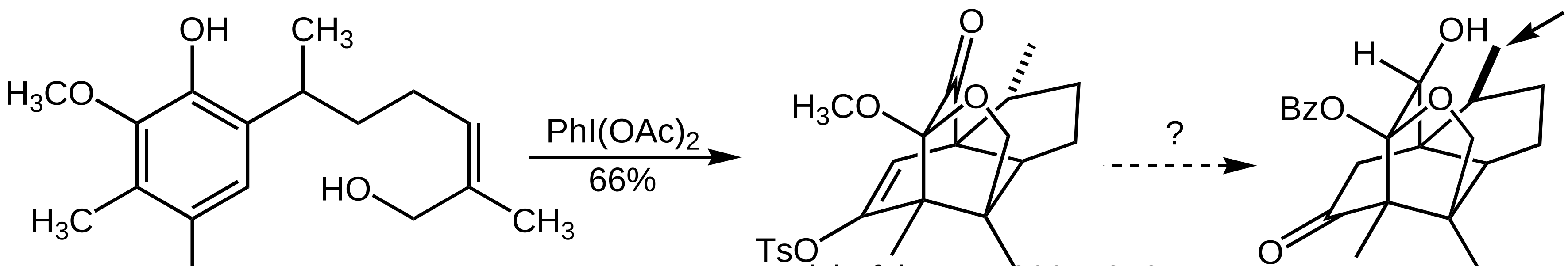
Wood, OL, 2002, 493

intermolecular cation trapping; intramolecular diene trapping



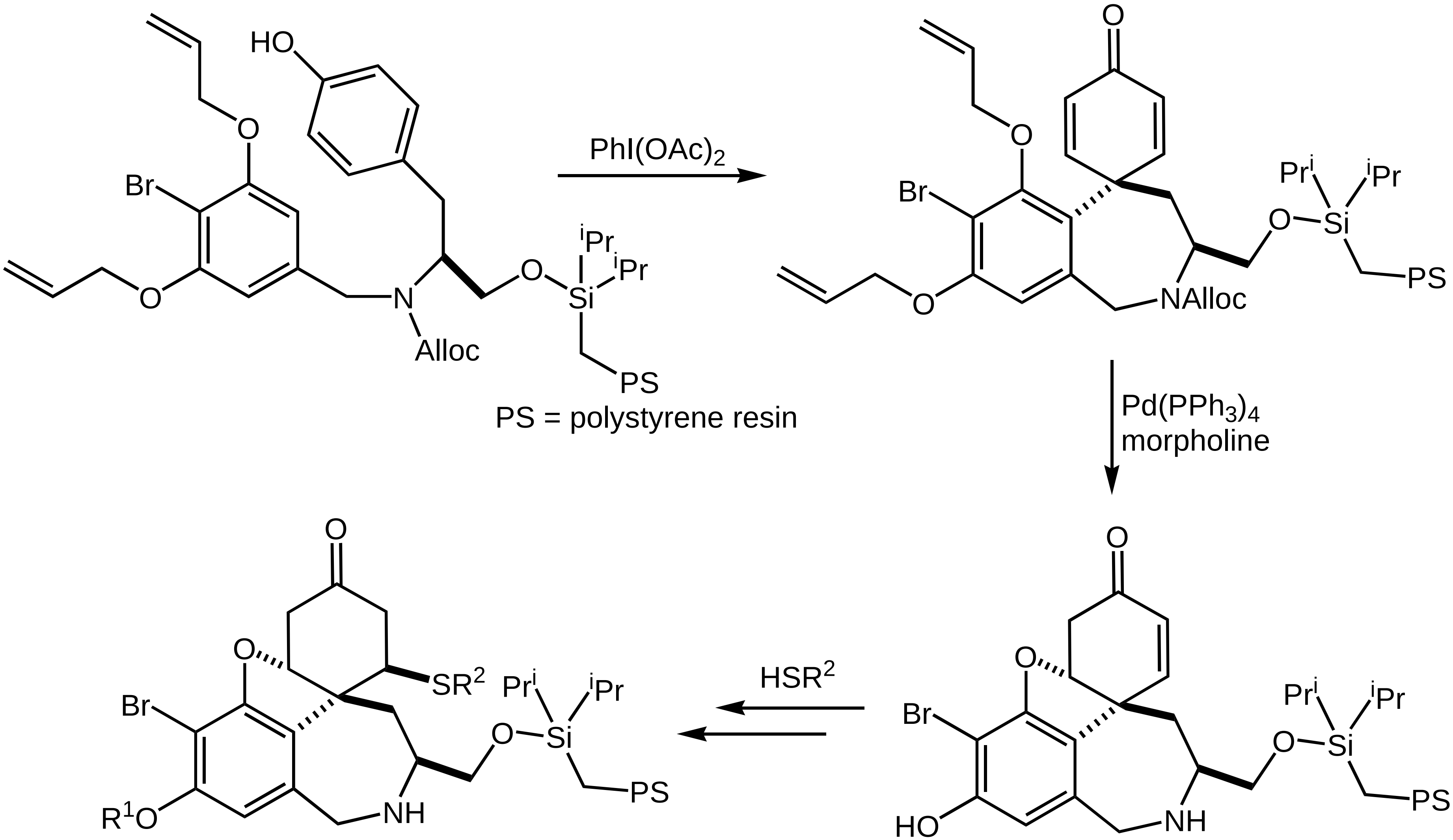
Wood, OL, 2001, 2435

intramolecular cation trapping; intramolecular diene trapping



Danishefsky, TL, 2005, 843

Trapping the dieneone from I(III) oxidations: Michael addition



PS = polystyrene resin

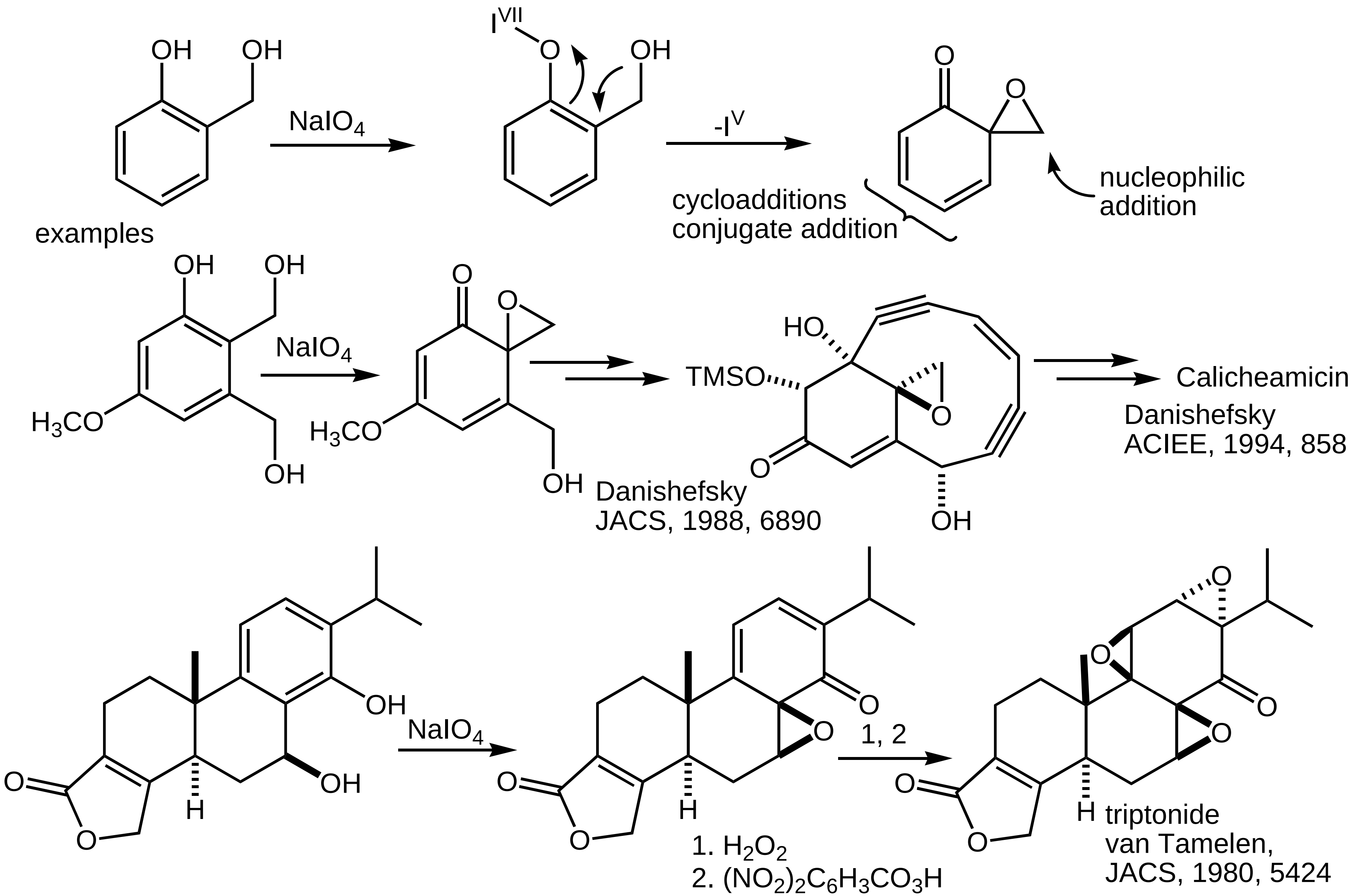
Shair, JACS, 2001, 6740

Oxidation of electron rich aromatic rings

Oxidation of phenols

2 e- processes

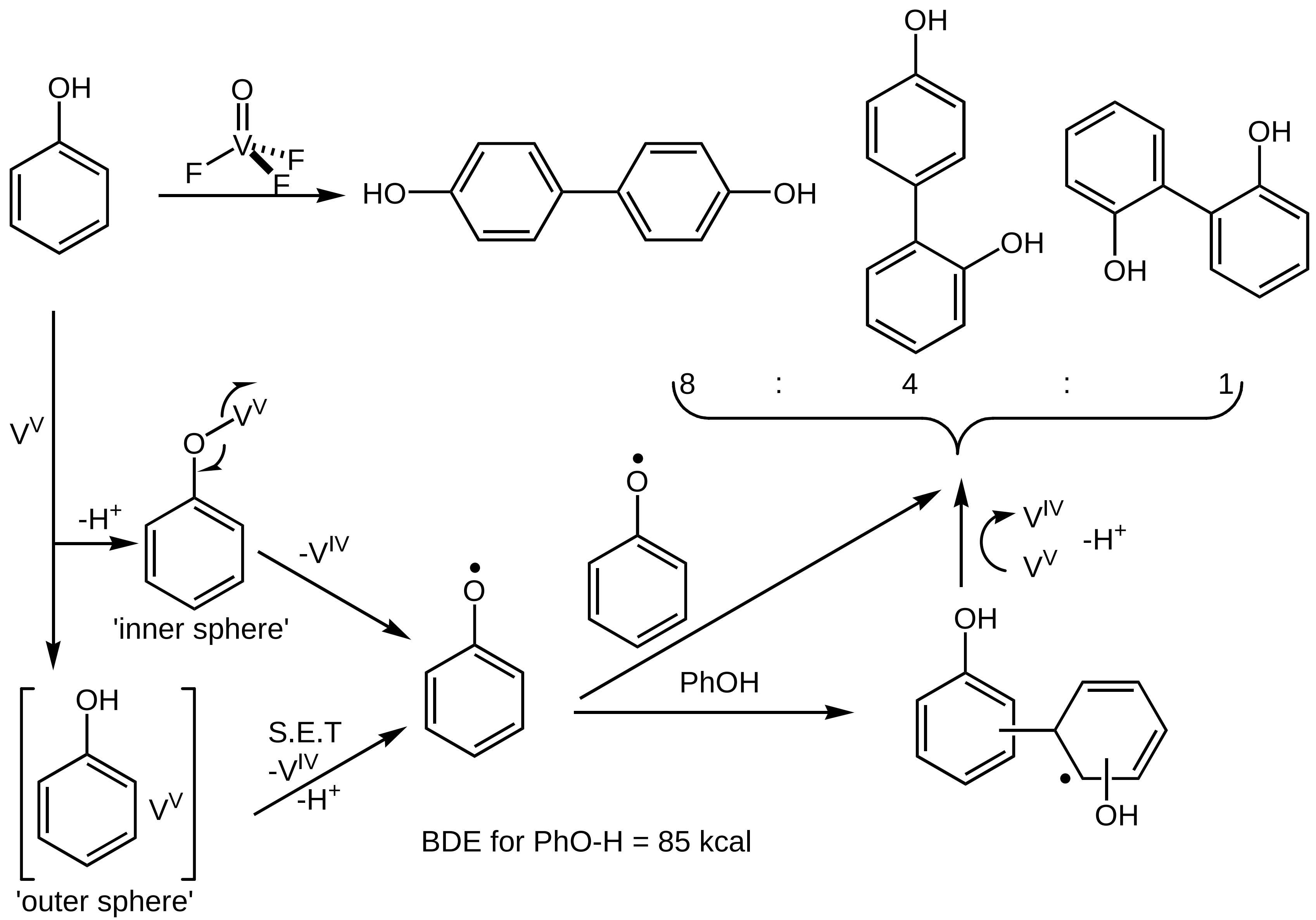
Special case of o-(hydroxymethyl)-phenols



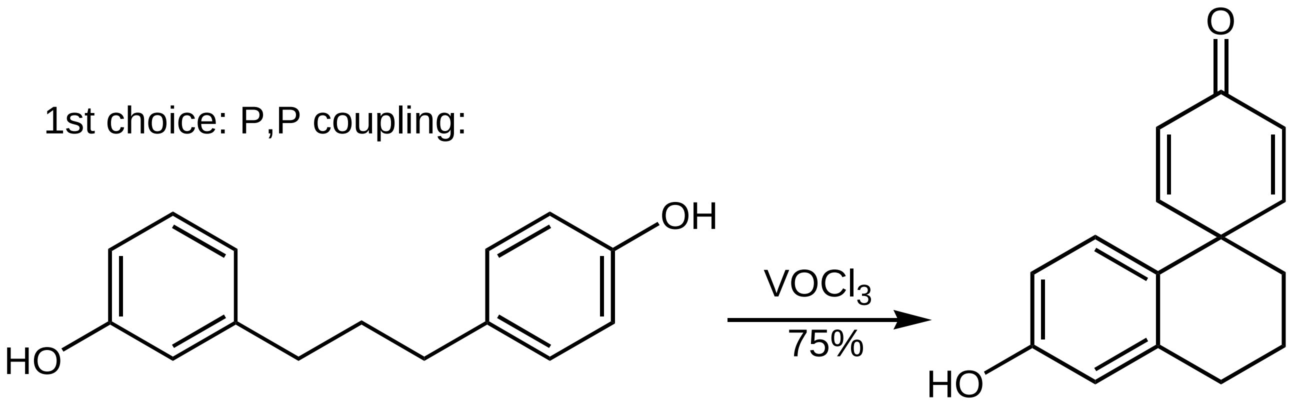
Oxidation of electron rich aromatic rings
Oxidation of phenols and phenolic ethers
1 e- processes
V reagents

Review: Hirao, Chem. Rev. 1997, 2707
Chem Rev. 1994, 519

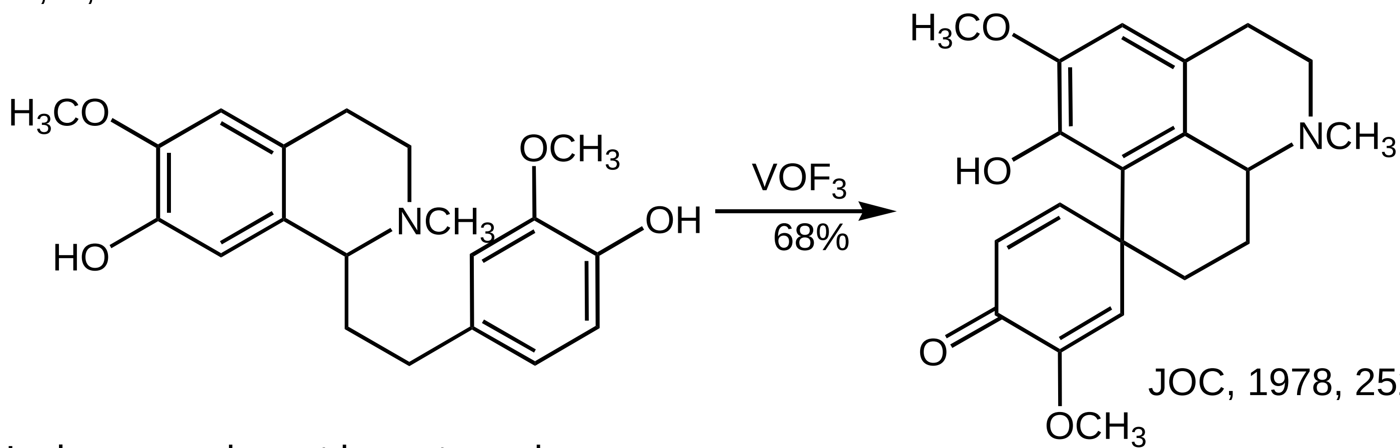
V can be V(-3) to V(+5)
Usually changes oxidation state in 1e- steps



1st choice: P,P coupling:

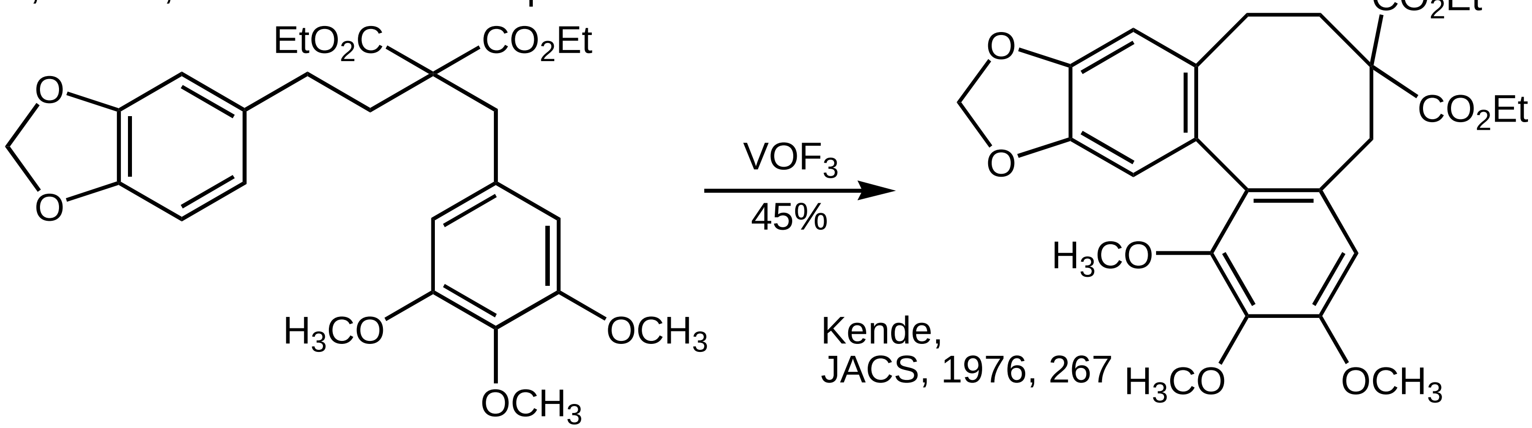


2nd choice, P,O



JOC, 1978, 2521

If no OH, slower, and must be outer sphere



Kende,
JACS, 1976, 267

Oxidation of electron rich aromatic rings

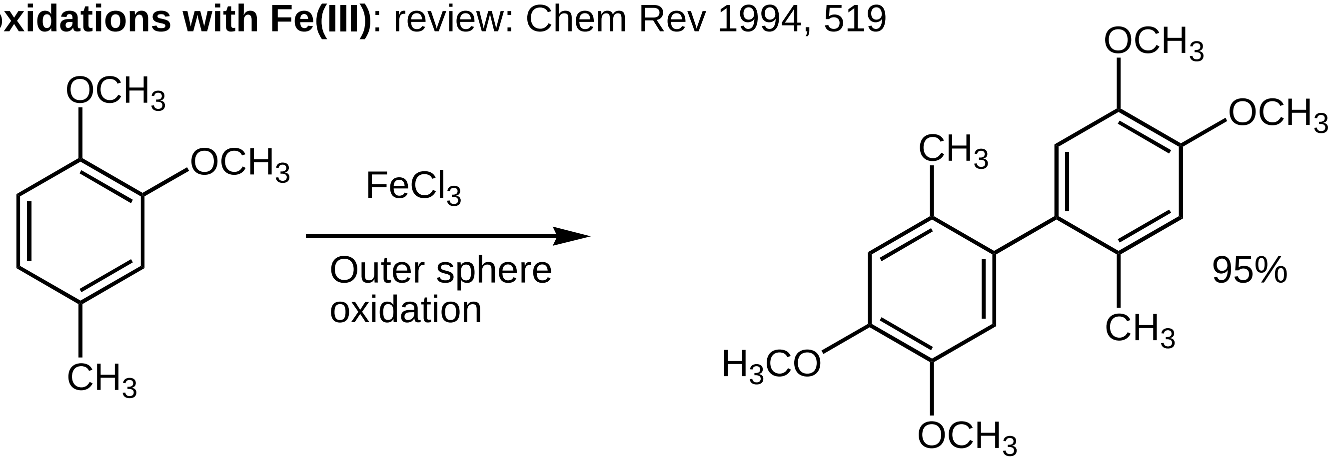
Oxidation of phenols and phenolic ethers

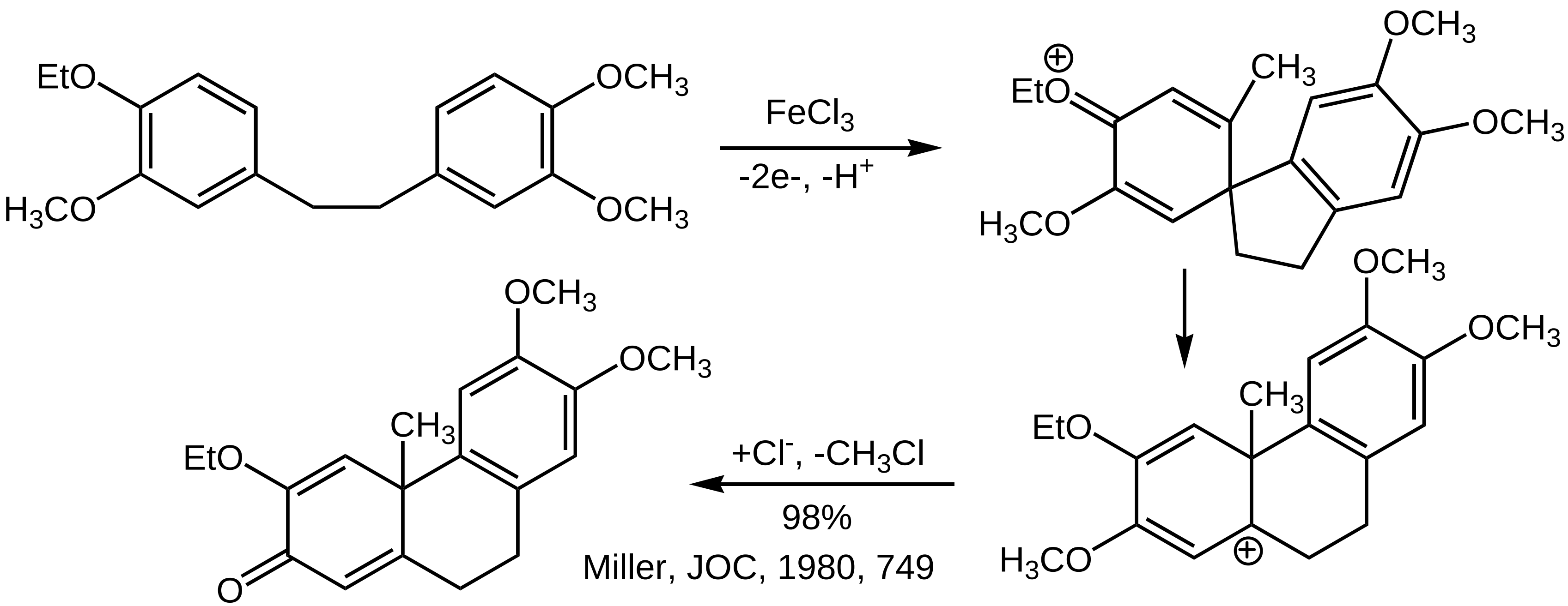
1 e- processes

Other metals

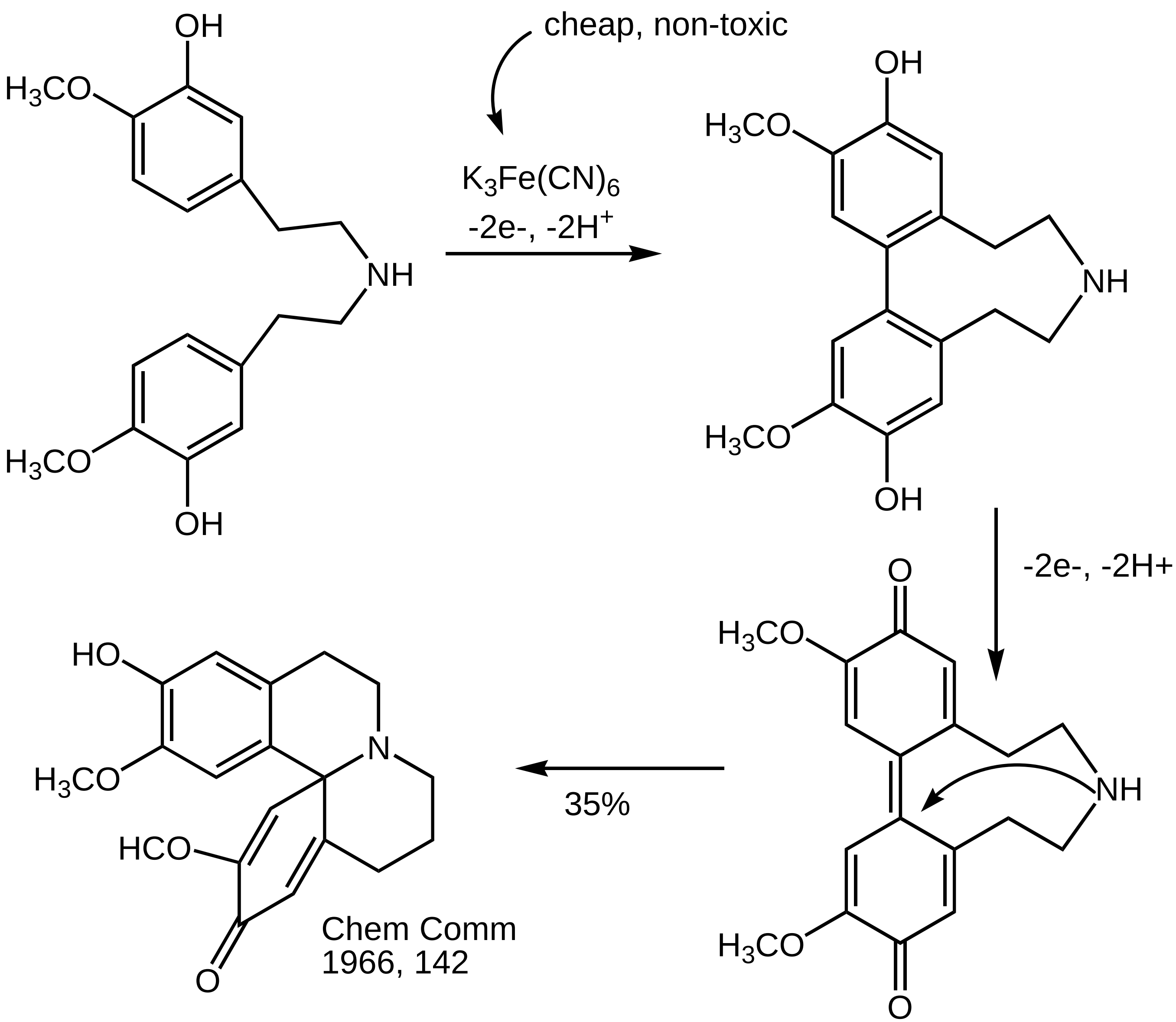
for 1e- oxidations of aromatic rings using $Tl(O_2CCF_3)$, see Taylor and McKillop, JACS, 1981, 6856

1 e- oxidations with Fe(III): review: Chem Rev 1994, 519



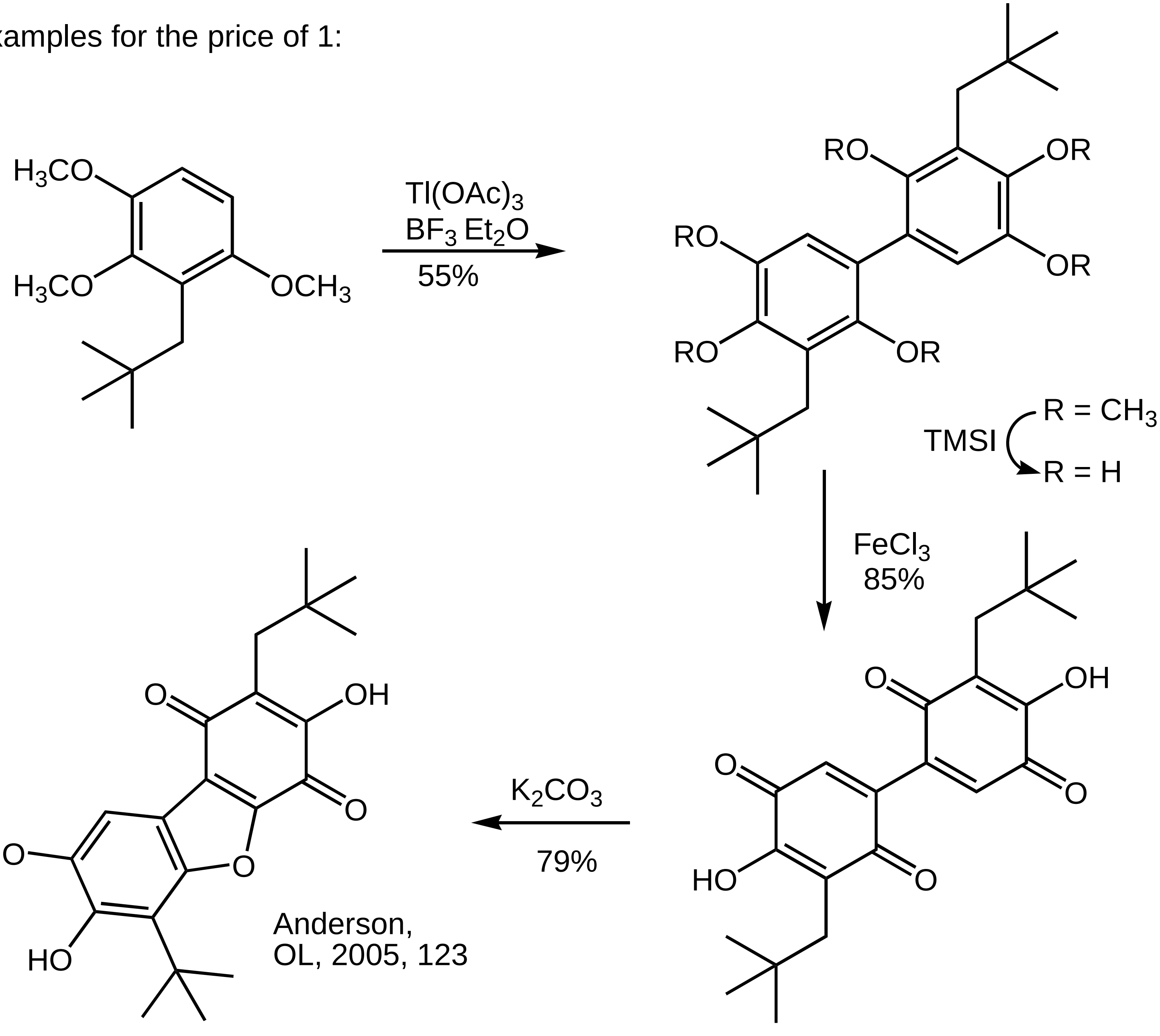


Oxidation with Fe(III), cont.



Chem Comm
1966, 142

2 examples for the price of 1:



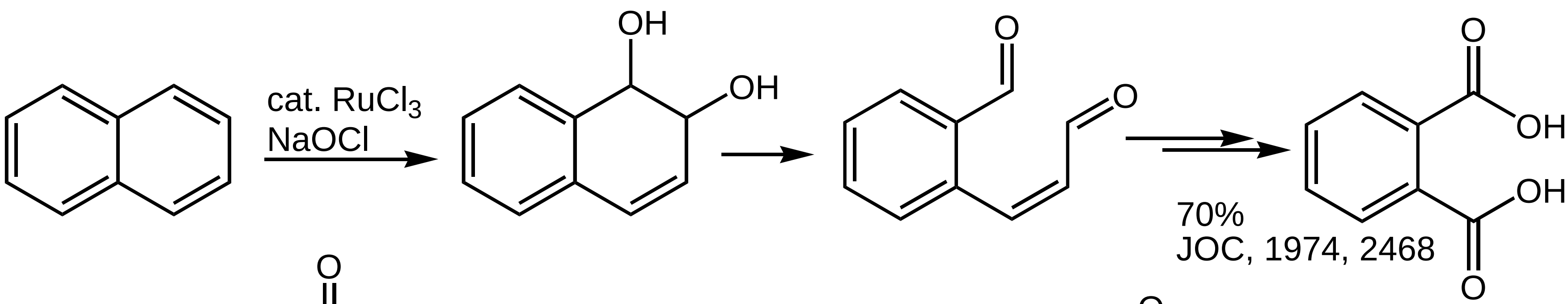
Oxidation of electron rich aromatic rings

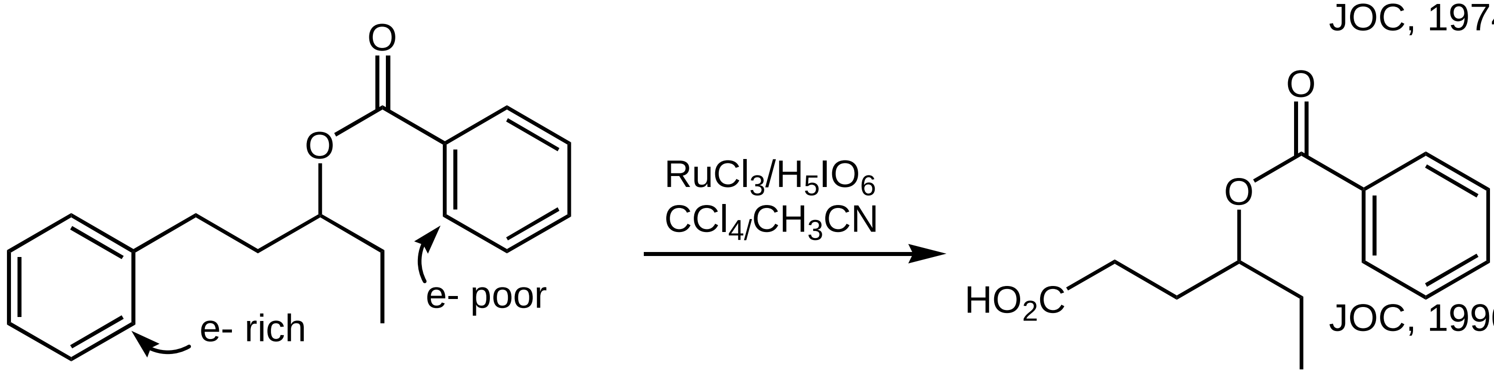
Oxidation of arenes

n x 2 e- processes

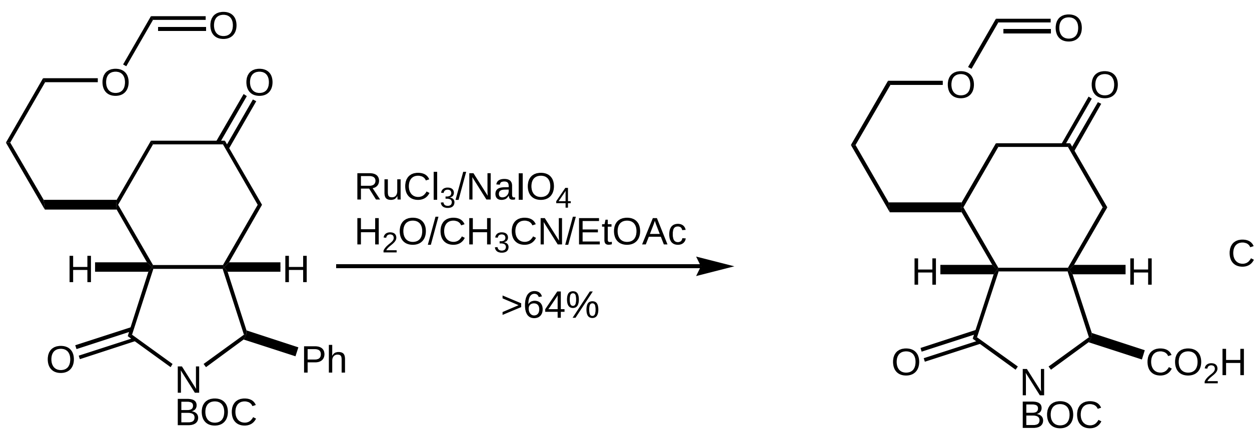
Ru(VIII) and oxidative cleavage

RuO_4 is very strong oxidizing agent, very expensive.
Usually use catalytic RuO_2 or $RuCl_3$ with stoichiometric cheap [O] e.g. $NaIO_4$, NaOCl
Review: Encylcopedia Reagents for Organic Synthesis





JOC, 1990, 1928



Clayden, JACS, 2005, 2412

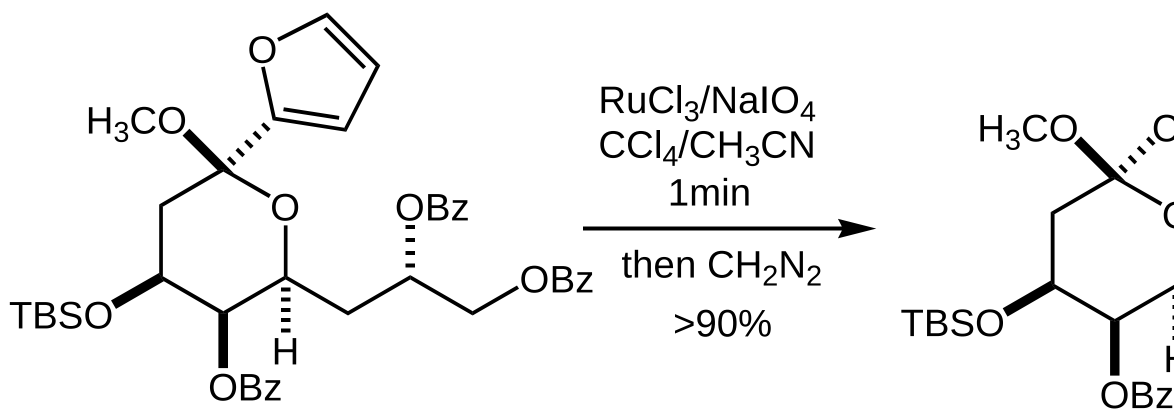
Oxidation of electron rich aromatic rings

Oxidation of arenes

n x 2 e- processes

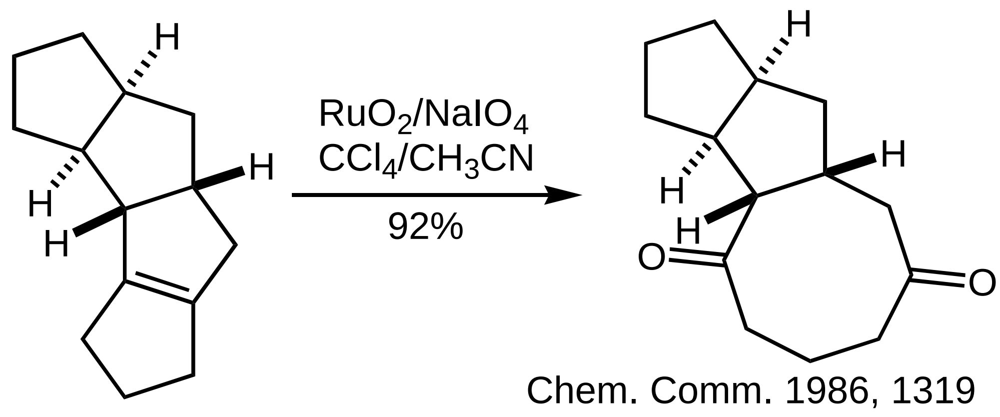
Ru(VIII) and oxidative cleavage

heteroaromatics



Jacs, 1988, 3929

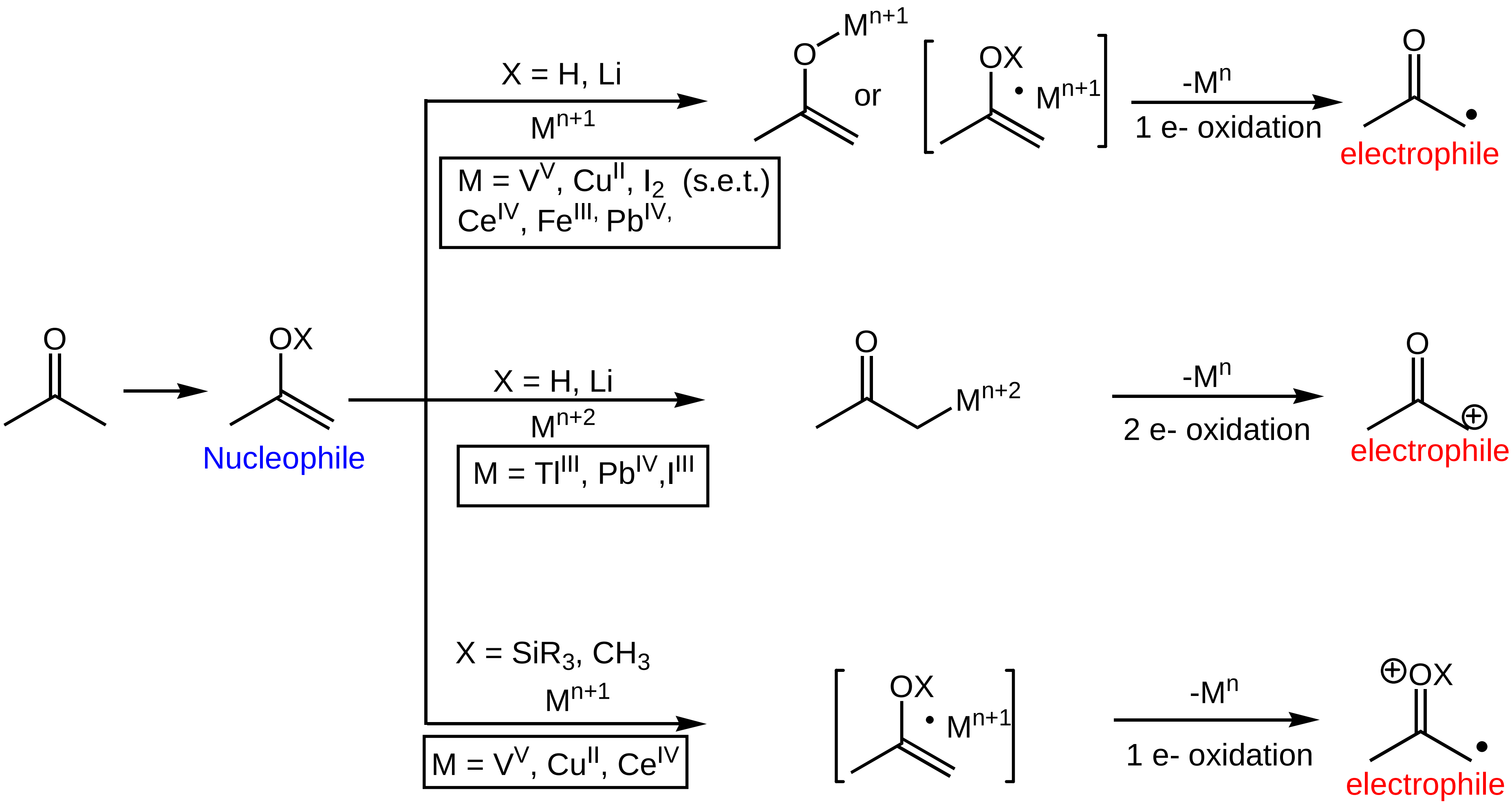
simple olefins work, too



Chem. Comm. 1986, 1319

Oxidation of enols
Introduction

Three general pathways for oxidation of enols and enolates:

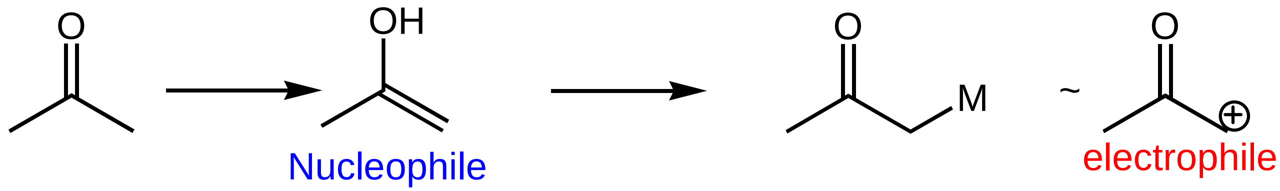


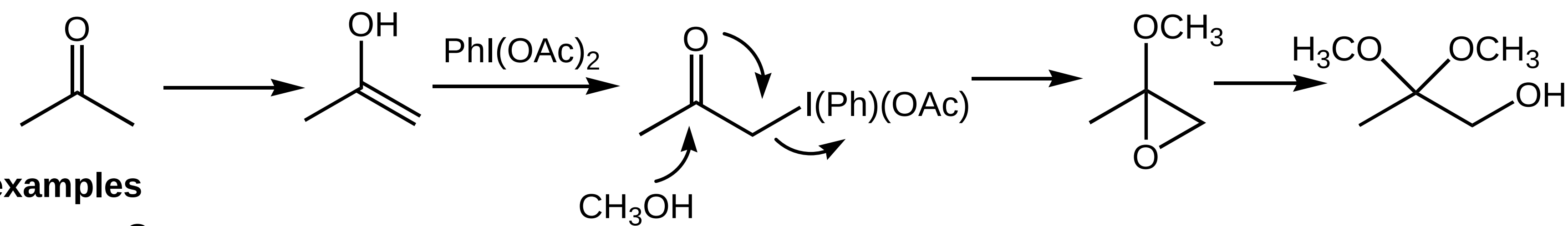
Oxidation of enols

2e- processes

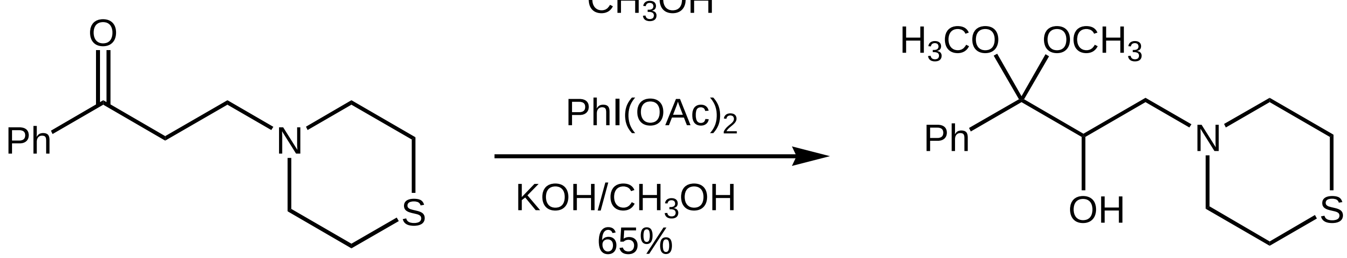
I^{III} and Tl^{III}

I^{III} and Tl^{III} react with enols to give α-metallo carbonyl intermediates
(recall I^{V} reagents convert enols to enones - see carbonyl oxidation class)



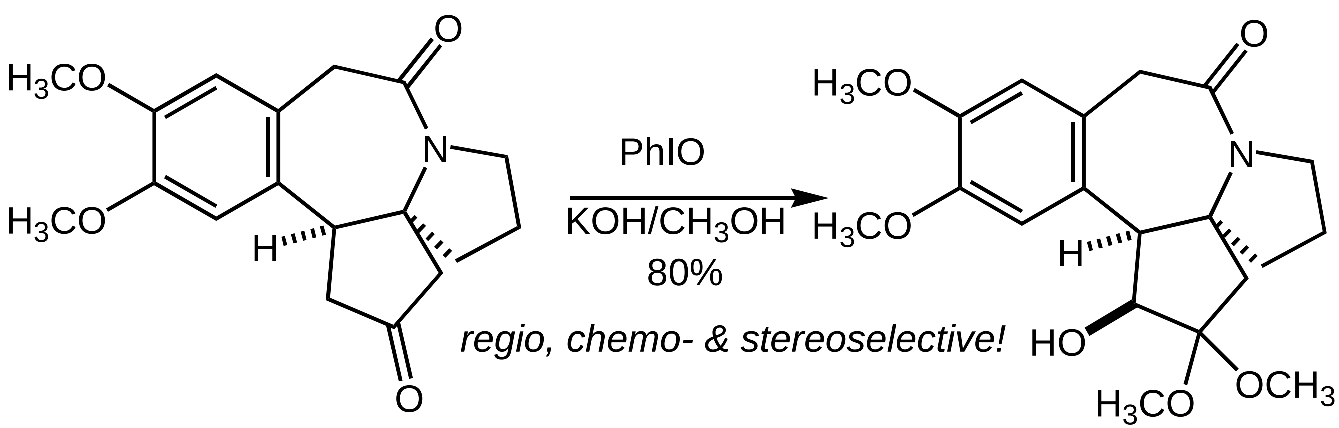


examples



no Ox at S!

TL, 1984, 4745



regio, chemo- & stereoselective!

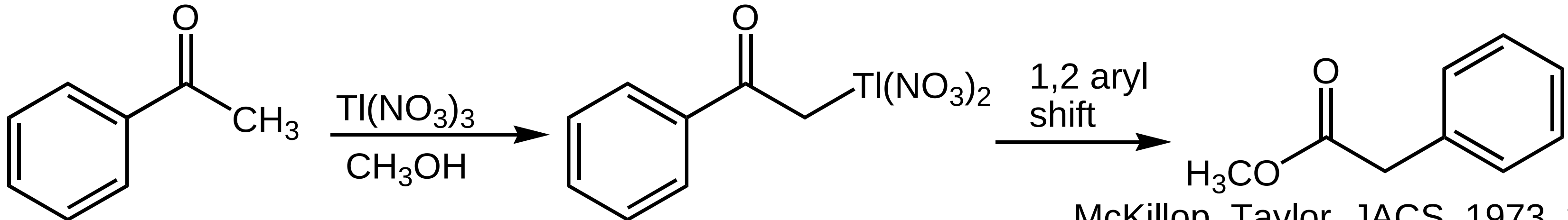
TL, 1986, 2023

Oxidation of enols

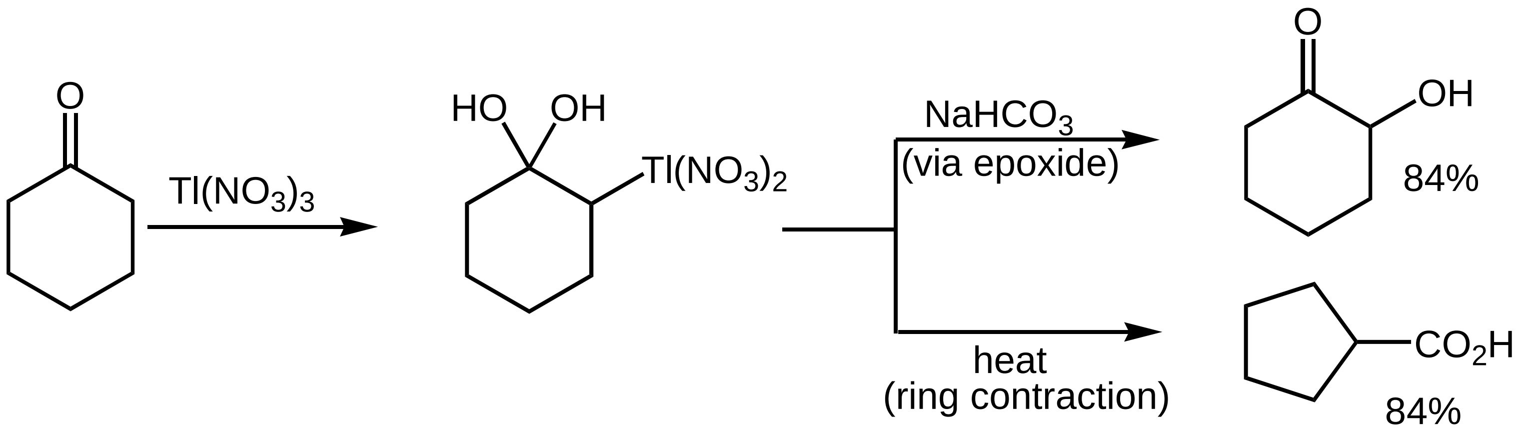
2e- processes

I^{III} and Tl^{III}

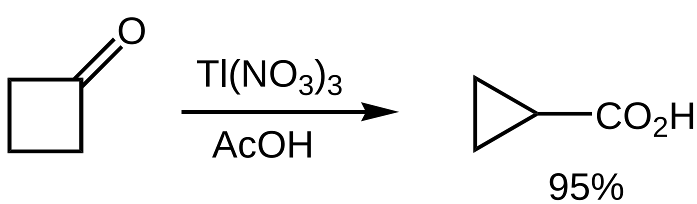
WIth Tl^{III}, often see ring contraction



McKillop, Taylor, JACS, 1973, 3340



McKillop, Taylor, JACS, 1973, 3381



Tet, 1974, 1423

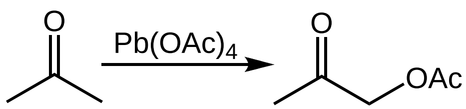
Oxidation of enols

2e- processes (except when it's 1e-)

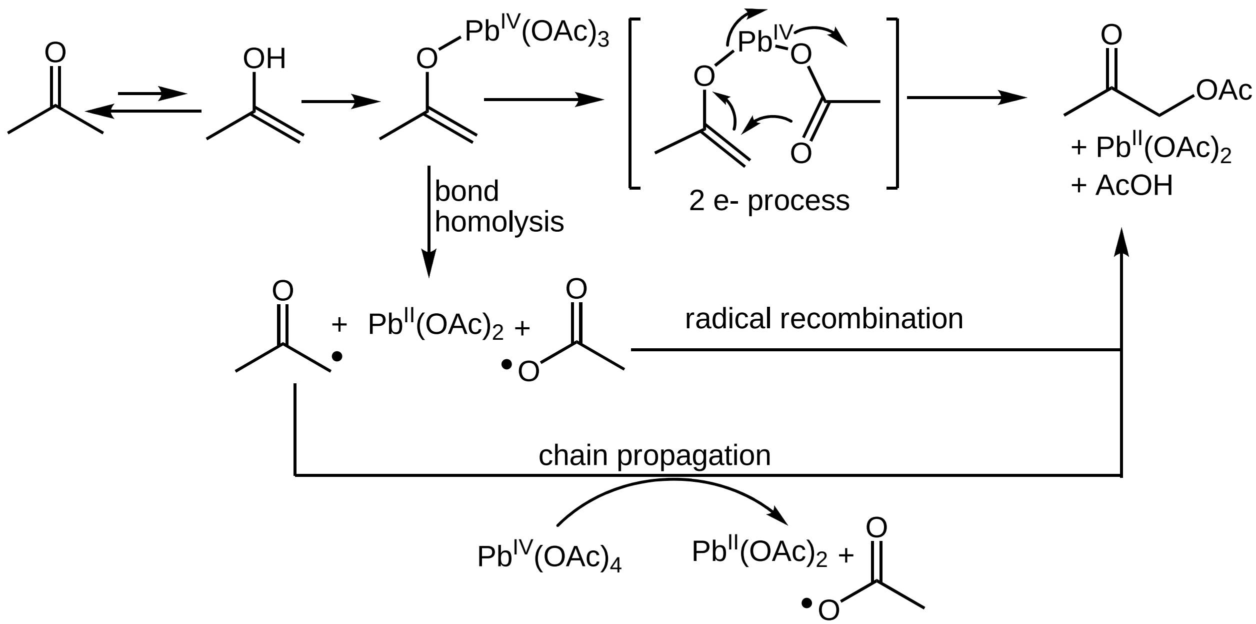
$Pb(OAc)_4$

$Pb(OAc)_4$ (aka LTA) is versitile, strong oxidant. Also used to oxidize aromatic rings [not usually as clean as $PhI(O_2CR)$]. Can cleave diols to dicarbonyl compounds (even trans diols!!)

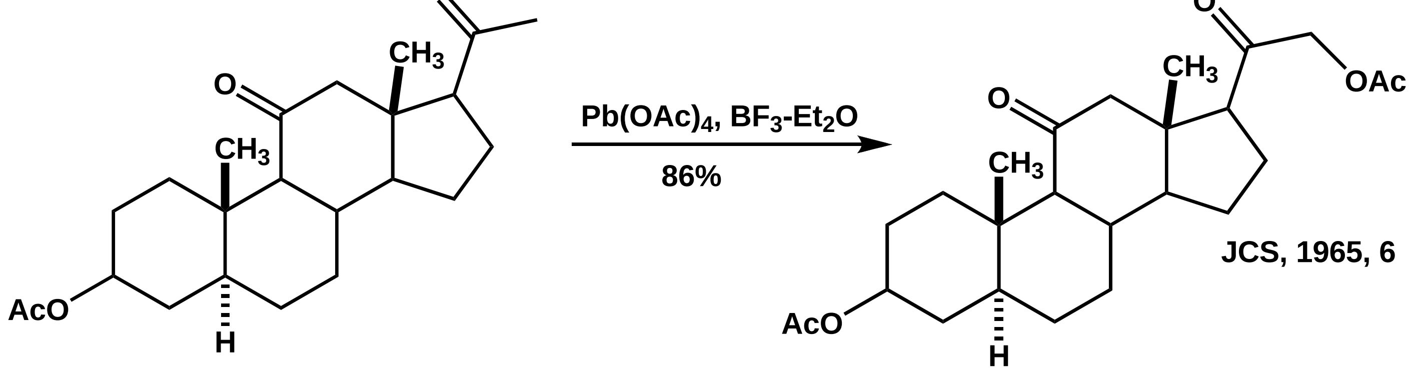
Overall transformation:



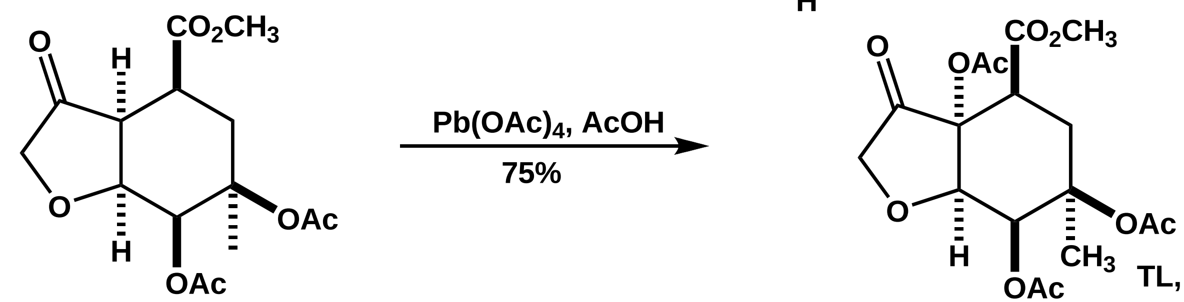
1e- and 2e- processes compete:



Pb(OAc)$_4$ examples

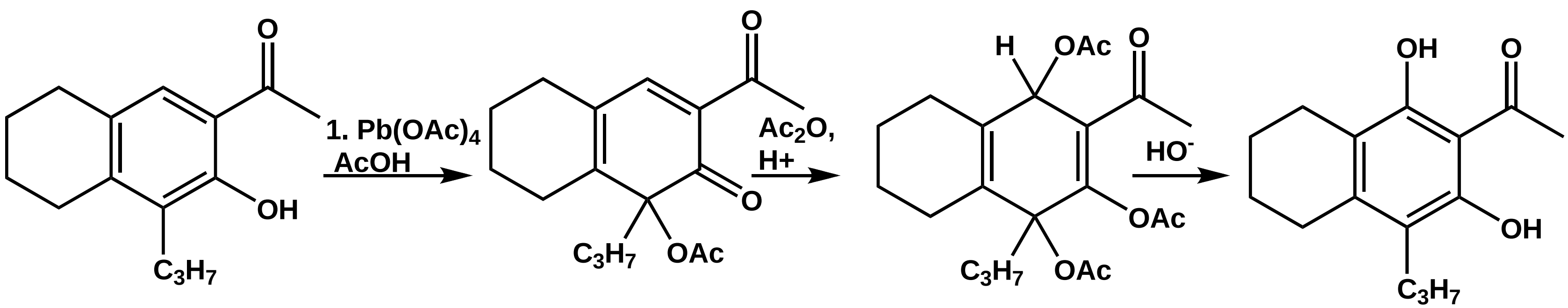


JCS, 1965, 6



TL, 1986, 5071

Phenols are similar to enols:



Pattenden, Perin 1, 1988, 1677

Oxidation of enols

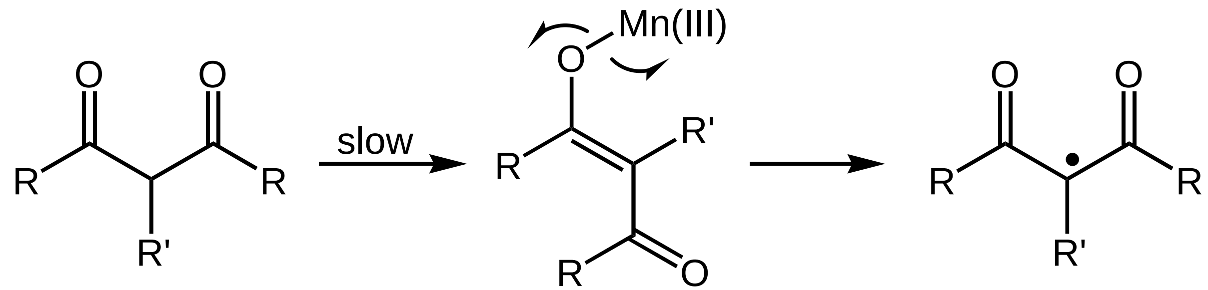
1e- processes

Oxidation of dicarbonyl compounds

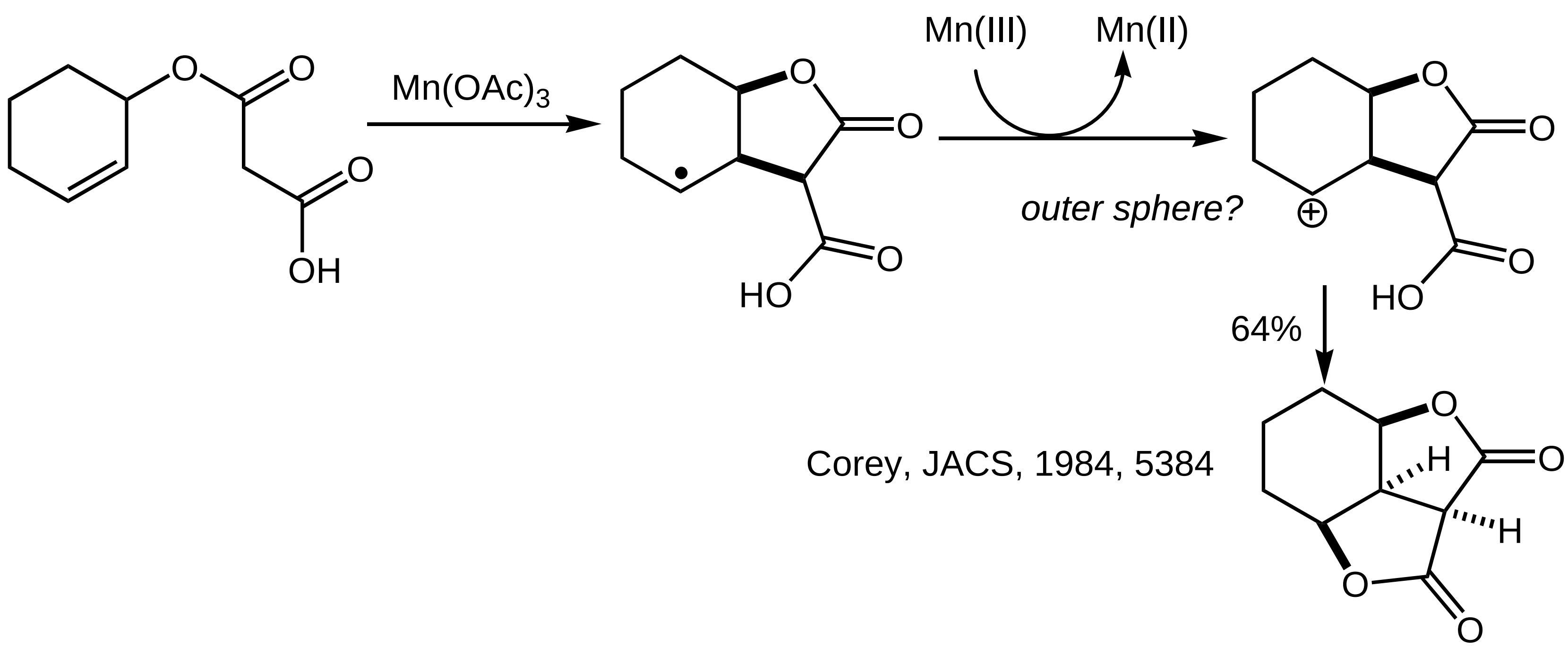
$Mn(OAc)_3$

Review: Snider, Chem Rev. 1996, 339

Mn(III) salts convert β-dicarbonyl compounds to electron-poor radicals:



usual application is cyclization onto tethered olefin



Corey, JACS, 1984, 5384

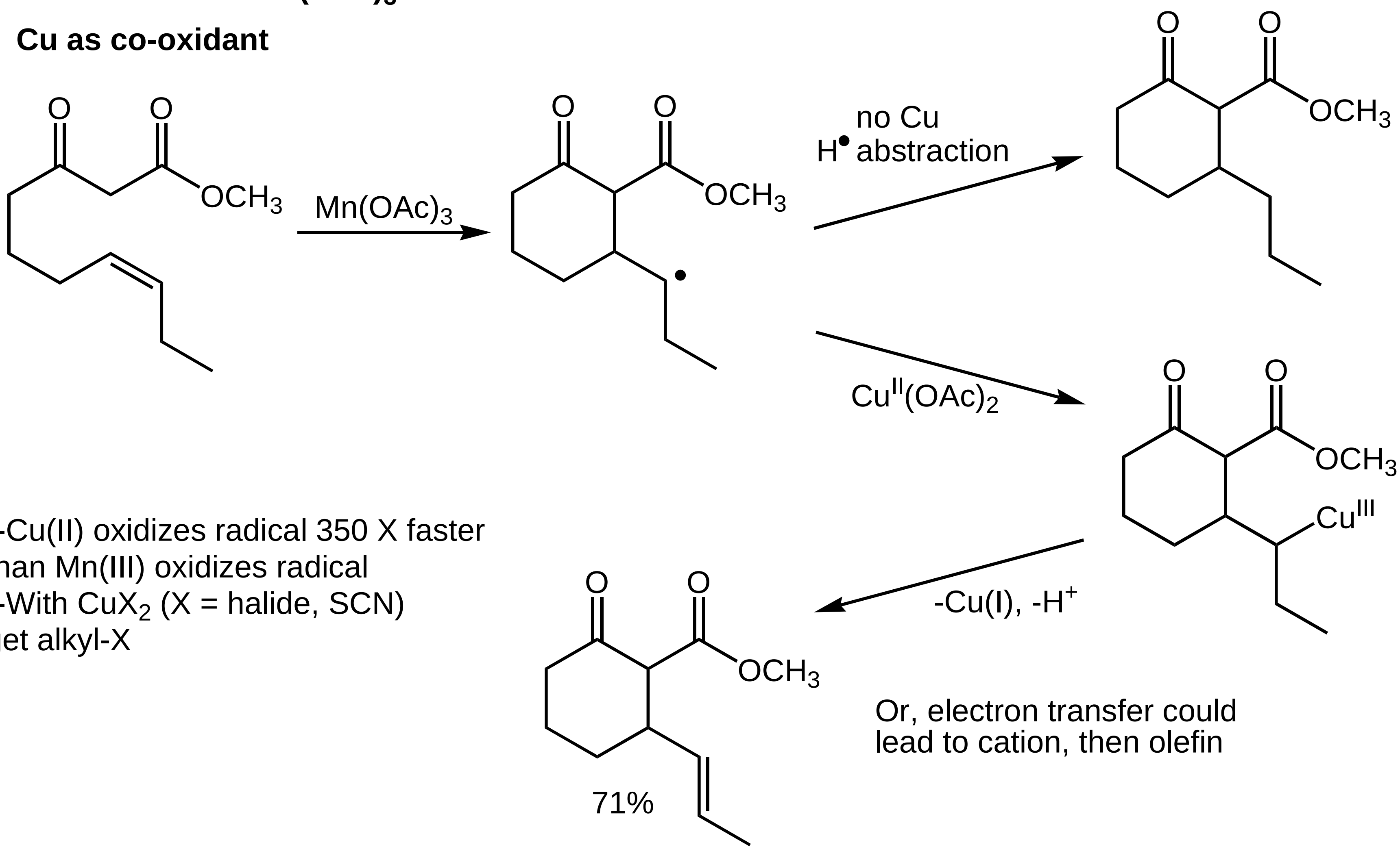
Oxidation of enols

1e- processes

Oxidation of dicarbonyl compounds

$Mn(OAc)_3$

Cu as co-oxidant



--Cu(II) oxidizes radical 350 X faster than Mn(III) oxidizes radical
--With CuX_2 (X = halide, SCN) get alkyl-X

Or, electron transfer could lead to cation, then olefin

Oxidation of enols

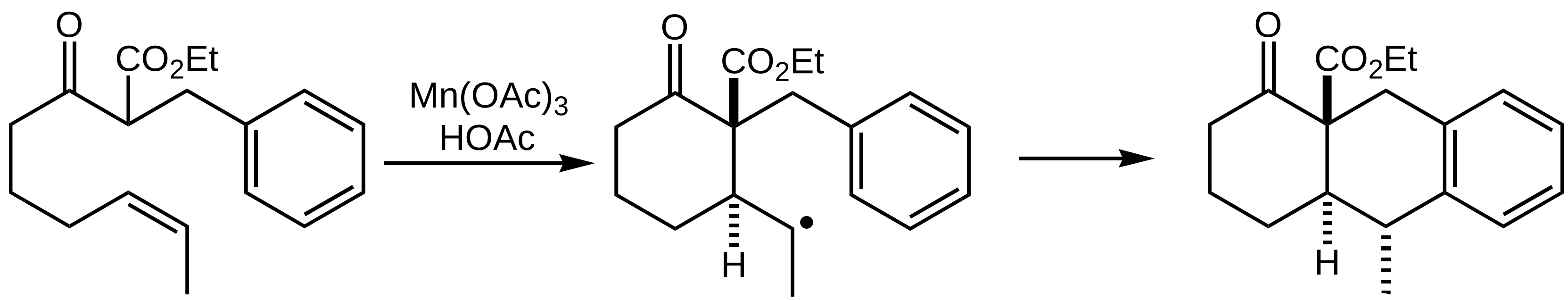
1e- processes

Oxidation of dicarbonyl compounds

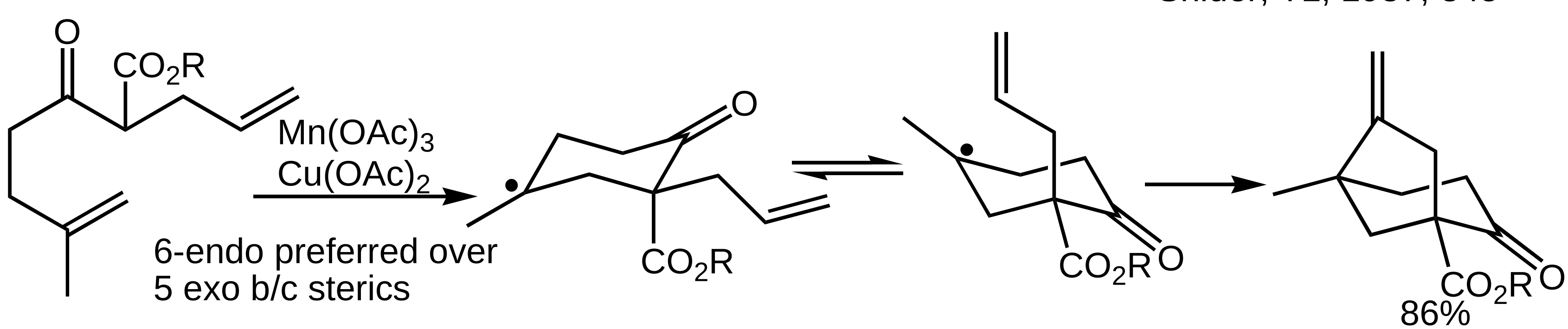
$Mn(OAc)_3$

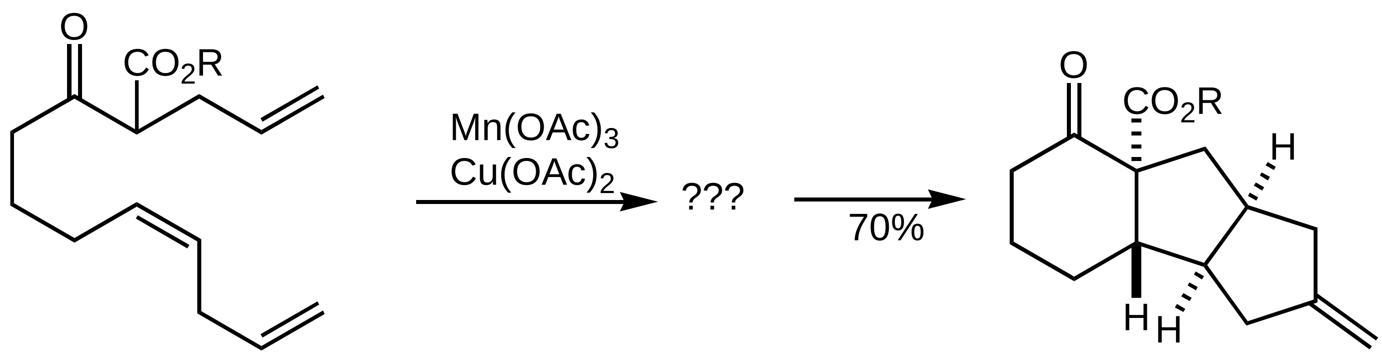
Examples

Tandem, with addition to aromatic ring



Snider, TL, 1987, 845





Oxidation of enols

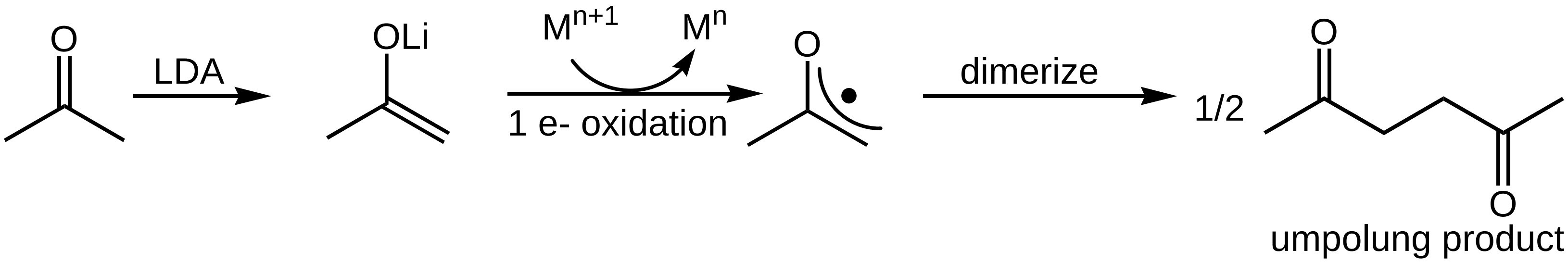
1e- processes

Oxidation of enolates

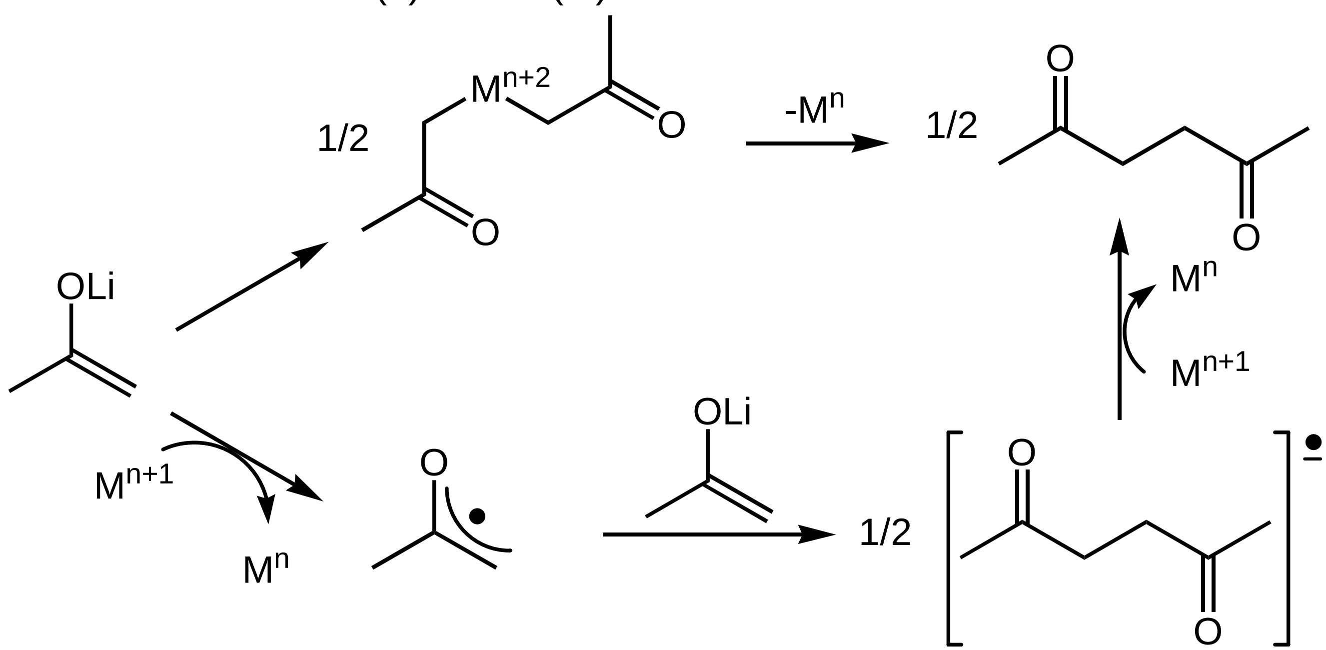
General information

Cu(II) [usually $Cu(OTf)_2$ or $CuCl_2$], Fe(III) [usually $FeCl_3$ in DMF], and I_2 promote enolate dimerization

Proposed mechanistic picture pretty similar for all three:

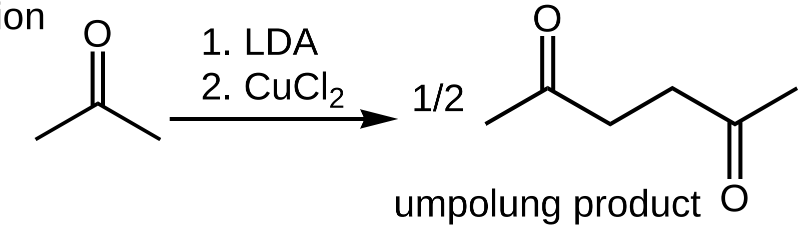


Other possibilities exist for Cu(II) and Fe(III)



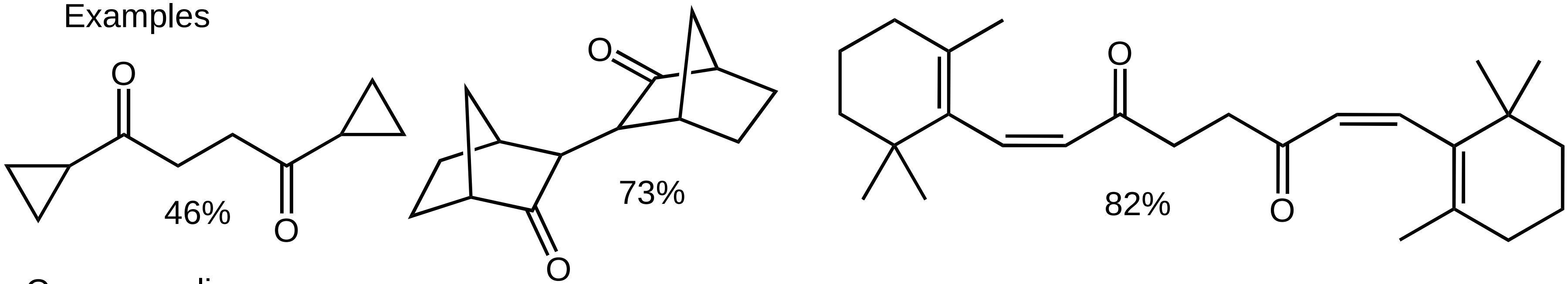
Oxidation of enols
1e- processes
Oxidation of enolates
Cu(II) examples

Generic reaction

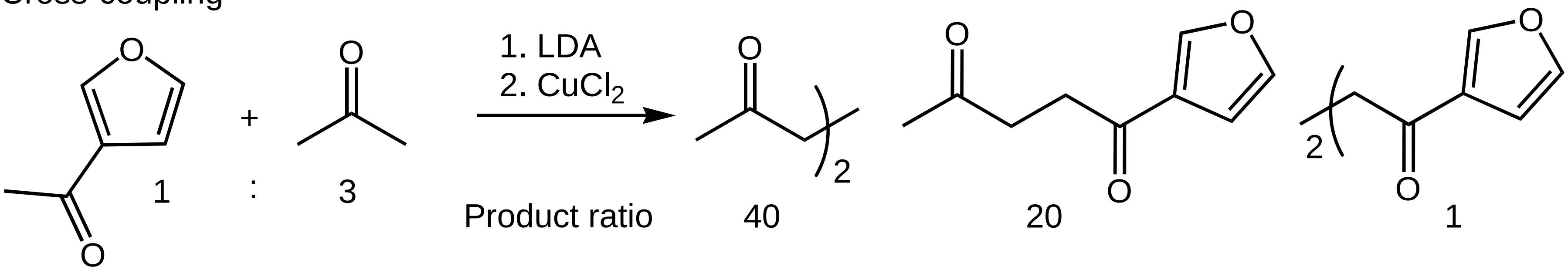


umpolung product
Saegusa, JACS, 1977, 1487

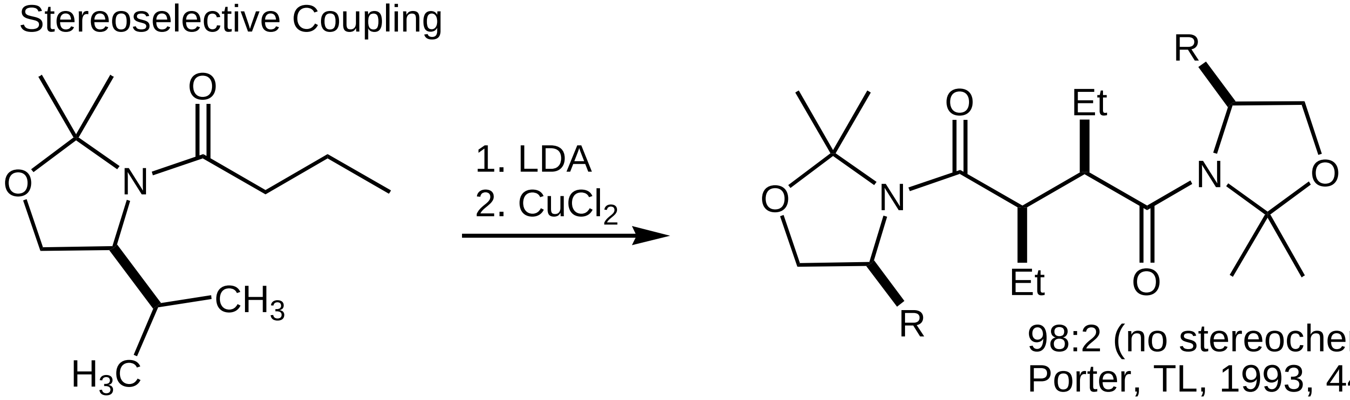
Examples



Cross-coupling



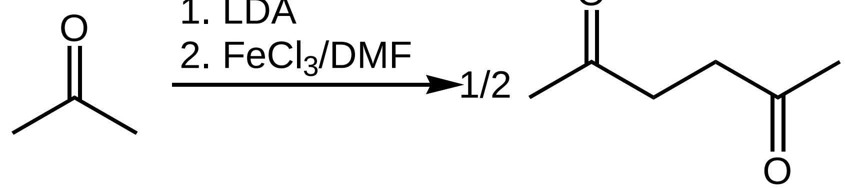
Stereoselective Coupling



98:2 (no stereochemical model given)
Porter, TL, 1993, 4457

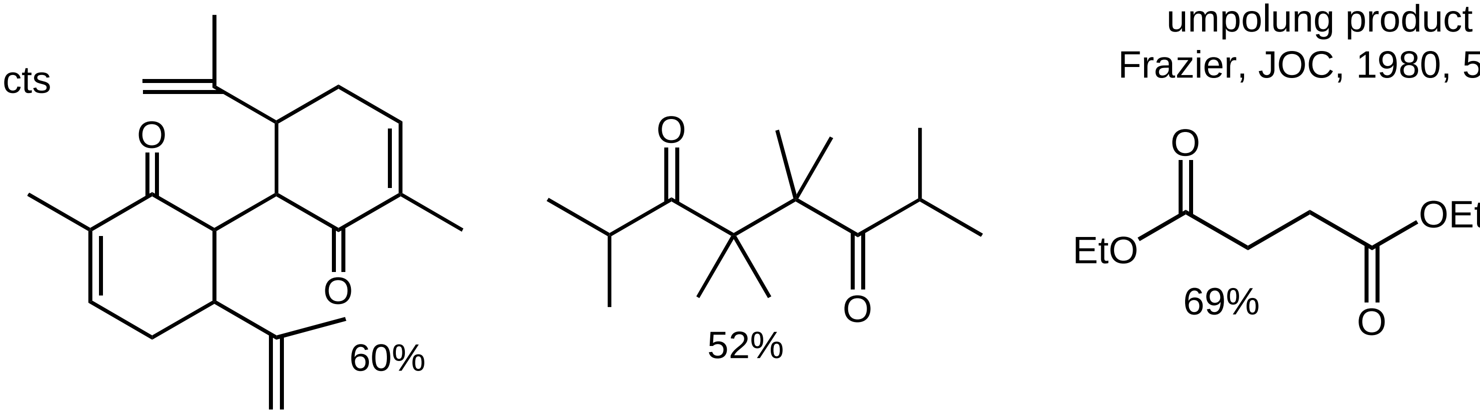
Oxidation of enols
1e- processes
Oxidation of enolates
Fe(III) examples

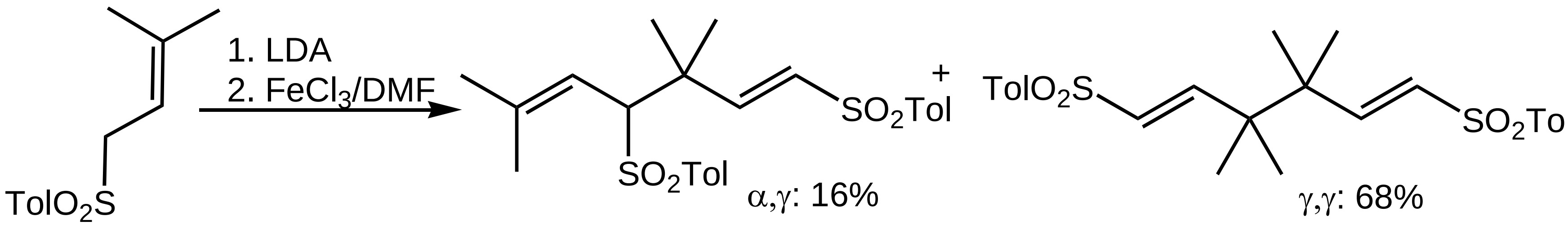
Generic reaction



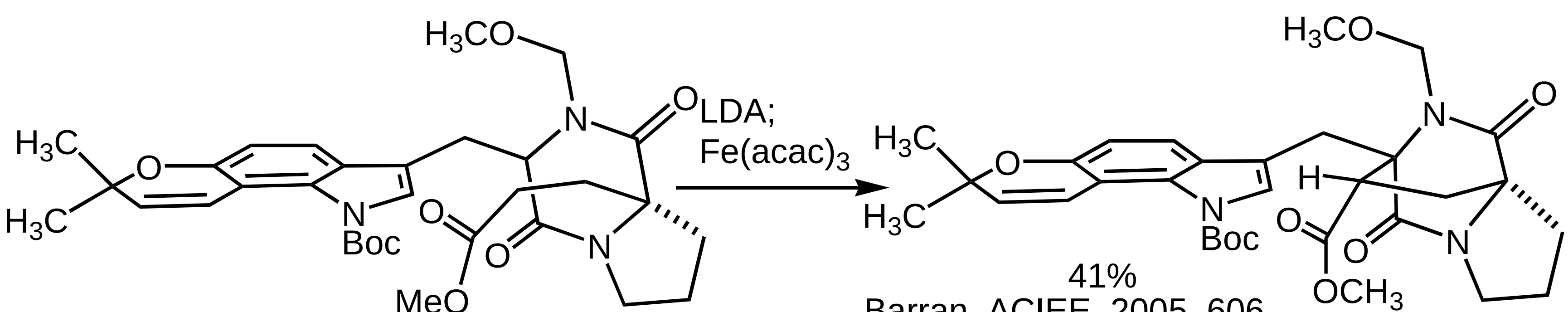
umpolung product
Frazier, JOC, 1980, 5408

Sample products





Kochi, JACS, 1974, 3332
TL, 1985, 5923

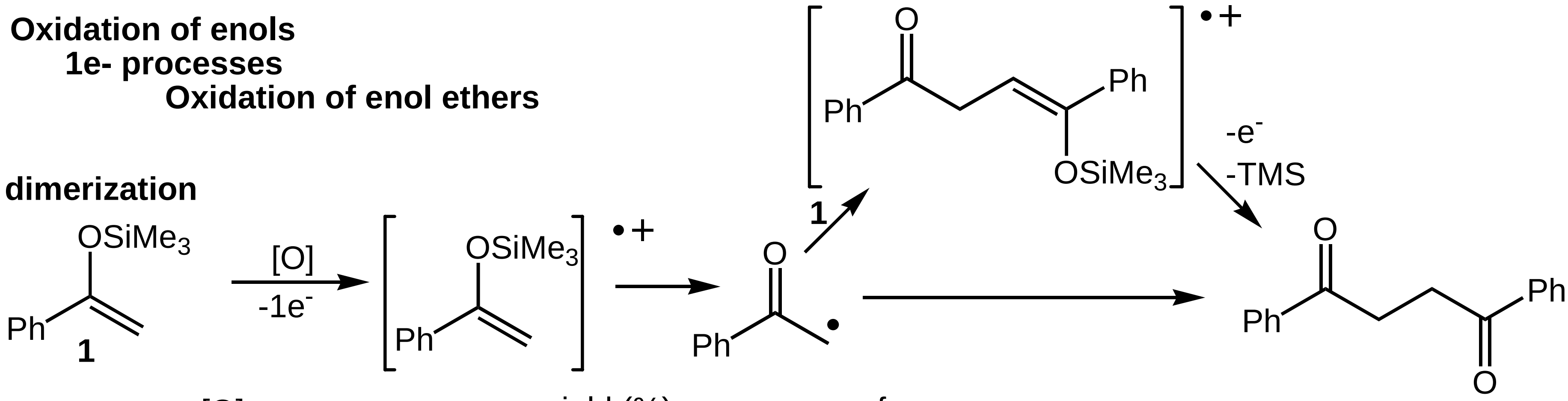


Oxidation of enols

1e- processes

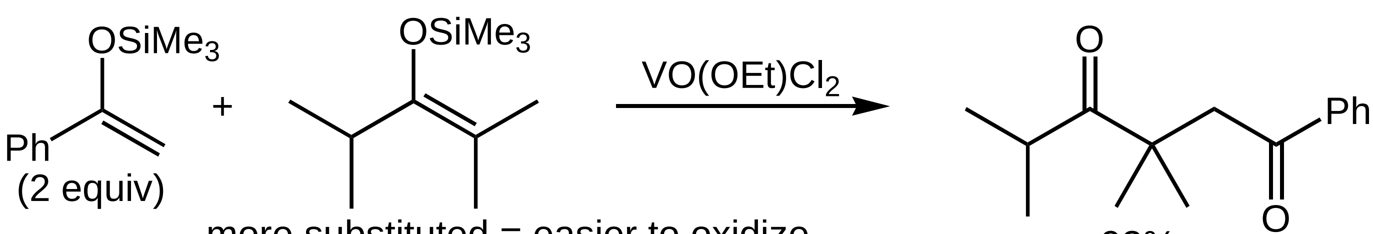
Oxidation of enol ethers

dimerization



[O]	yield (%)	ref
$Cu(OTf)_2/Cu_2O$	55	Kobayashi, Chem. Pharm Bull. 1980, 262
Ag_2O	73	Saegusa, JACS, 1975, 649
$Pb(OAc)_4$	45	Moriarty, TL, 1987, 873
$VO(OEt)Cl_2$	30	Ohshiro, TL, 1992, 5823

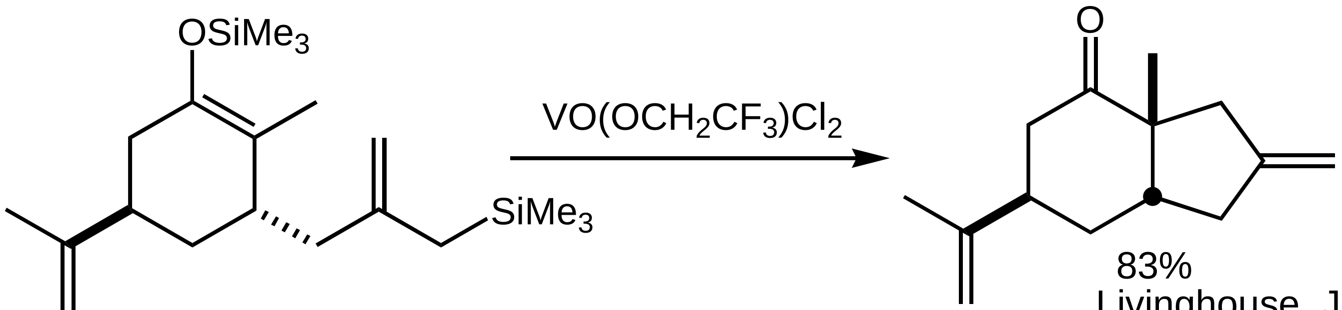
cross-coupling



93%

more substituted = easier to oxidize
more substituted = poorer nucleophile

cyclization



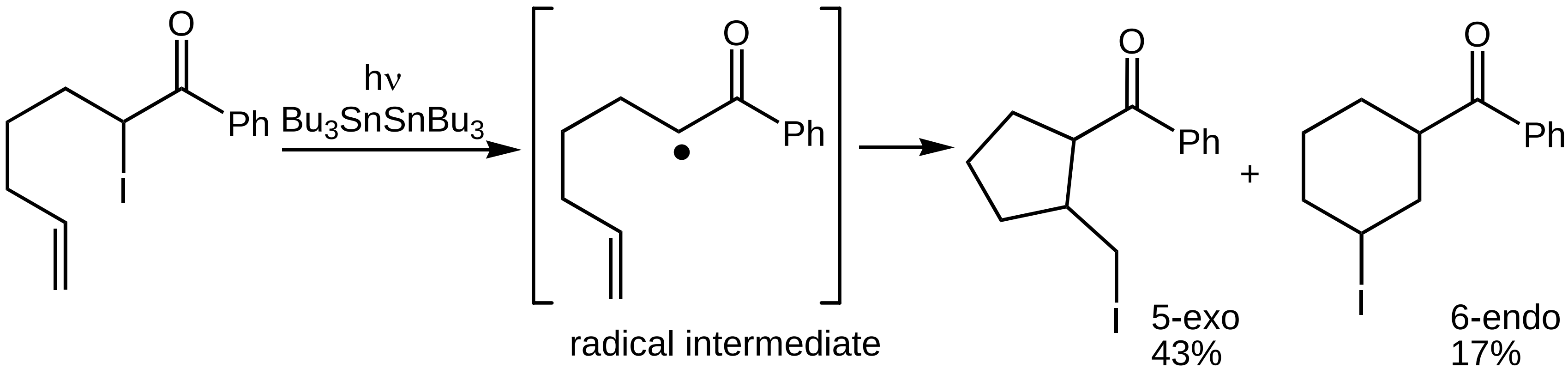
83%
Livinghouse, JACS, 1998, 2658

Oxidation of enols

1e- processes

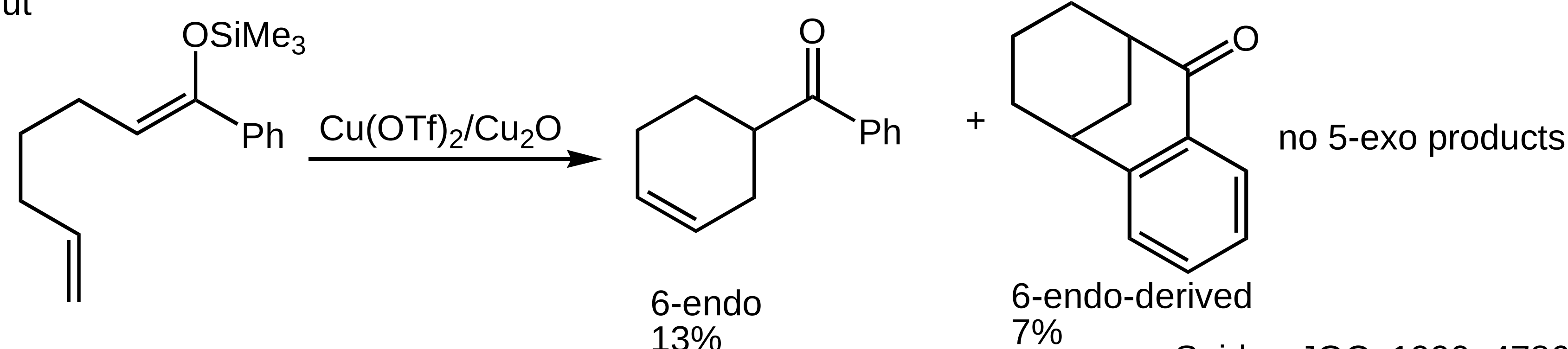
Oxidation of enol ethers

data in conflict with proposed mechanism:

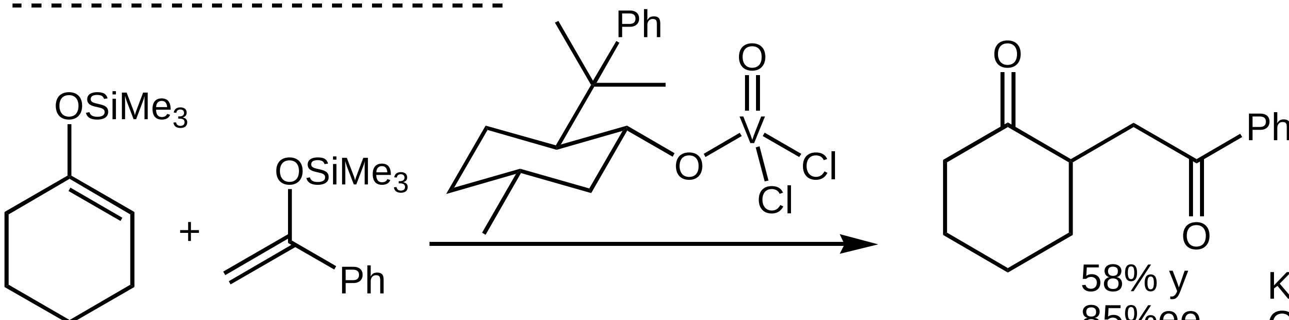


Curran, JOC, 1989, 3104

but



Snider, JOC, 1990, 4786



Kurihara,
Chem. Lett. 2001, 1324