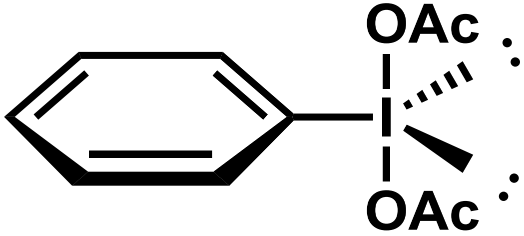
Aryl-λ3-iodane

~focusing on nucleophilic addition~

うがい薬や消毒薬
千葉県が世界第二の産地
ヨウ素デンプン反応：青紫色
甲状腺に集まる

ヨウ素 126.9
53 Iodine

Literature Seminar
2015/8/8 (Sat.)
Hideoki NAGAI (M2)



Contents

1. Introduction

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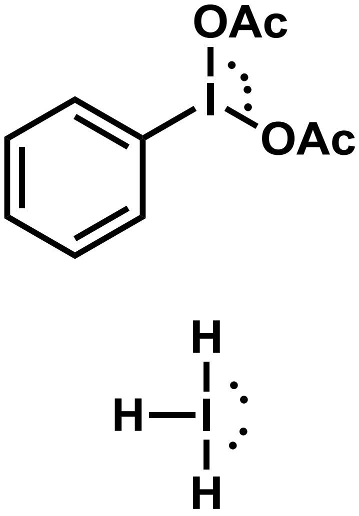
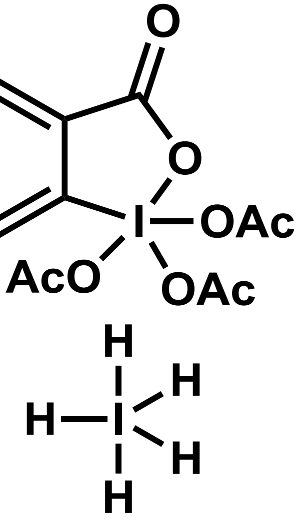
1-1. Hypervalent?

"Molecules containing elements of Group 15 - 18 bearing more electrons than the octet in the valence shell are described as hypervalent molecules."

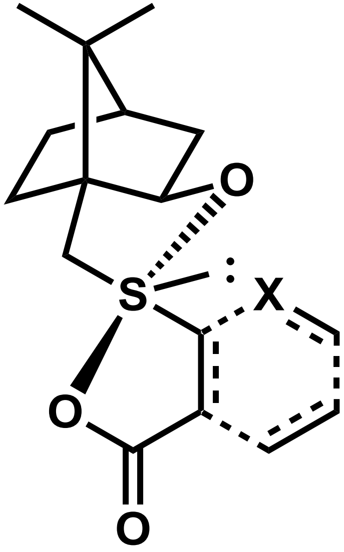
λ^3-iodane



λ^5-iodane



λ^4-sulforane



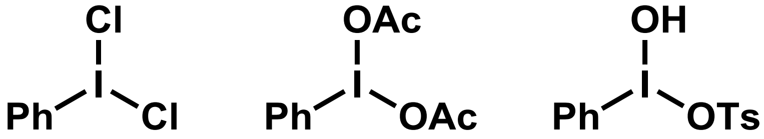
λ^{o} = the bonding number to an atom.

D.B. Dess, J.C. Martin, *J. Org. Chem.* **1983**, *48*. 4156.
J. Zhang, *et al.*, *J. Am. Chem. Soc.* **1998**, *120*, 1631.
Mr. Kojima, B4 literature seminar.

1-2. Features

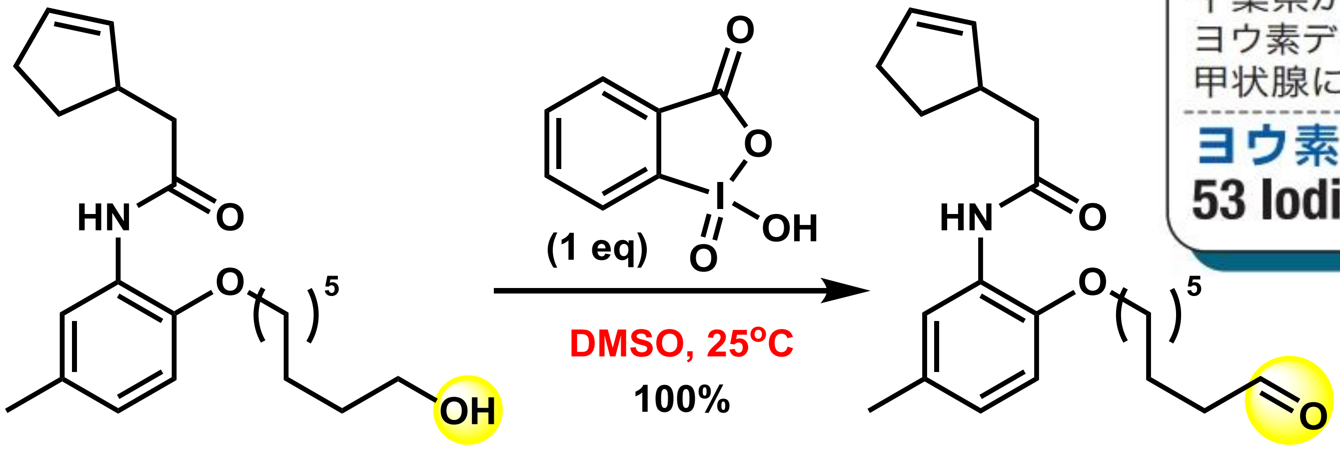
The important and significant factors of multivalent organoiodine compounds;

1) are made from relatively inexpensive commercial precursors.



2) tend to be selective in their reaction.

3) can be used under mild reaction condition.

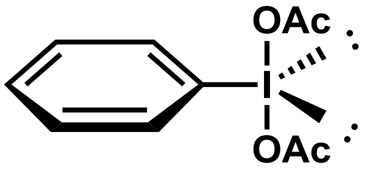


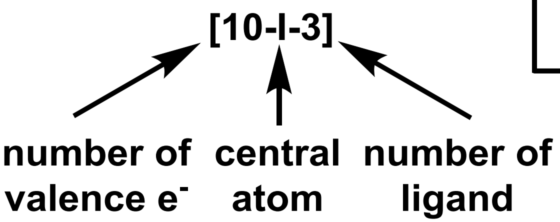
4) I(III) resenbles the reactivitiy characteristics of Hg(II), Tl(III) and Pb(IV) without the toxic and environmental problems.

Peter J. Stang, *J. Org. Chem.* **2003**, *68*, 2997.
Thomas Wirth, *Angew. Chem. Int. Ed.* **2001**, *40*, 2812.
K. C. Nicolaou, *J. Am. Chem. Soc.* **2002**, *124*, 2245.

1-3. Structure

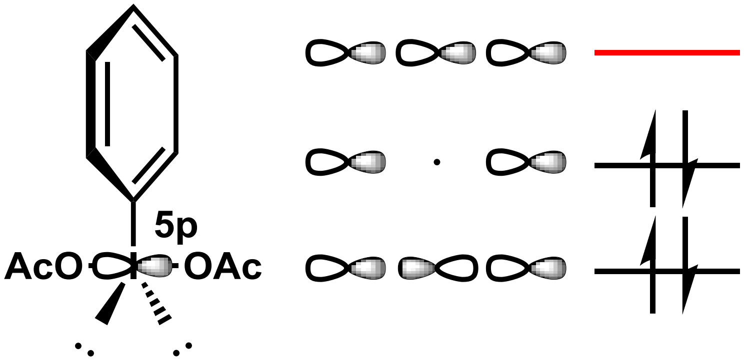
Aryl-λ^3-iodanes ($ArIL_2$)





- Ar-I bond is a typycal bond with sp^2 hybridization.
- I-L bonds are the hypervalent bonds.
- The most electronegative ligands reside in the apical positions.

The hypervalent molecular orbitals



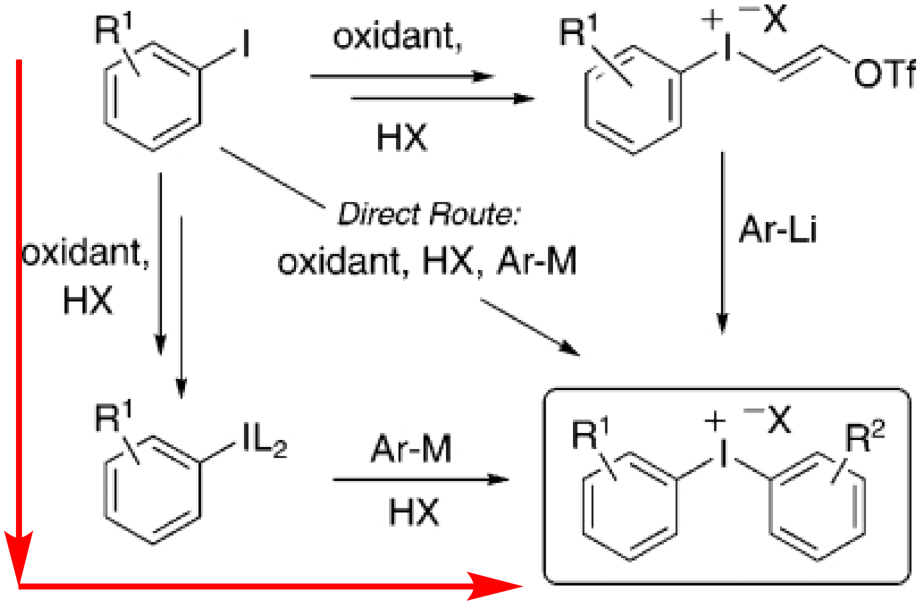
electrophilicity at iodine

2 e^- come from iodine and 1 e^- comes from each L, creating a 4 e^-, 3 center bond.

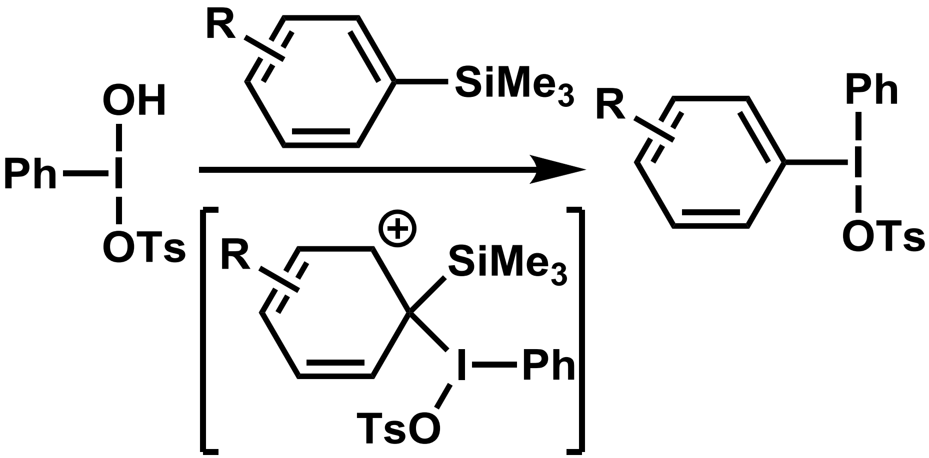
Mr. Kojima, B4 literature seminar.

1-4. Synthesis

3 routes for synthesis iodonium salt



HX = (Lewis) acid M = $B(OH)_2$, $SiMe_3$, $SnBu_3$



G.F. Koser, *et al.*, *J. Org. Chem.* **1980**, *45*, 1543.

1-5. Reactivity

1) Reaction with various nucleophiles

by initial Nu-I bond formation and release of one of ligands.

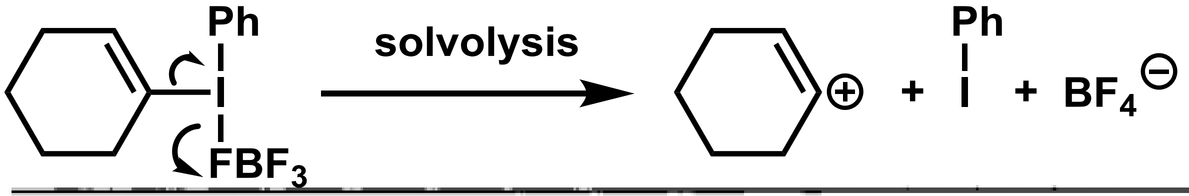
$$Nu^- + Ar\text{-}IL_2 \xrightarrow[- L^-]{} Ar\text{-}I(Nu)L \xrightarrow[\textit{reductive elimination}]{} Nu\text{-}L + Ar\text{-}I$$

2) Reaction with catalytic metal

$$M + Ar_2\text{-}IX \xrightarrow[\textit{oxidative addition}]{} M(Ar)X$$

more reactive version of aryl iodides

∗ The nucleofugality of trivalent iodine compounds



nucleofuge	relative leaving ability	
$-I^+Ph$	8×10^5	5×10^{17}
$-OTf$	1	6×10^{11}
$-OTs$	$1/(9 \times 10^5)$	7×10^5
$-S^+Me_2$	$1/(6 \times 10^{11})$	1

Eleanor A. Merritt, Berit Olofsson, *Angew. Chem. Int. Ed.* **2009**, *48*, 9052.
M. Ochiai, *et al.*, *J. Am. Chem. Soc.* **1995**, *127*, 3360.

2. Reaction with iodanes

2-1. Oxygenation

2-2. Nitrogenation

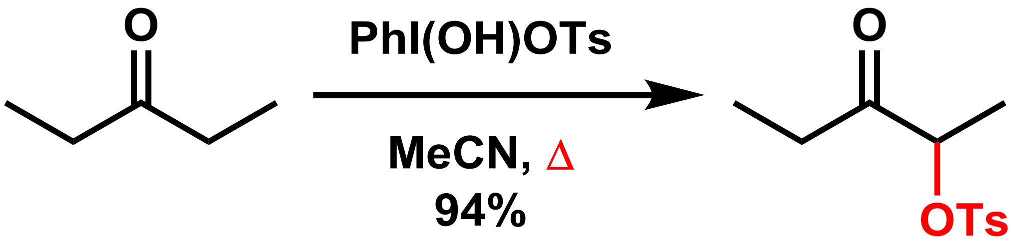
2-3. Alkynyl-iodane

2-4. Alkenyl-iodane

2-1. Oxygenation

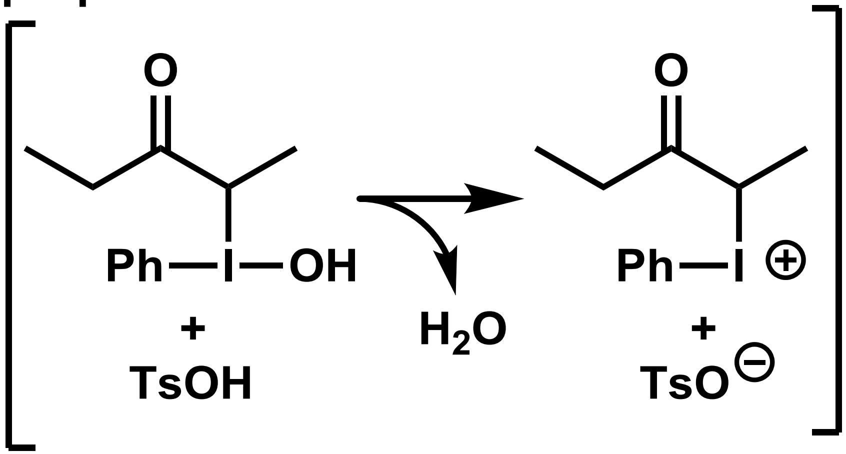
2-1-1. Basic reaction

Direct α-oxytosylation of ketones.

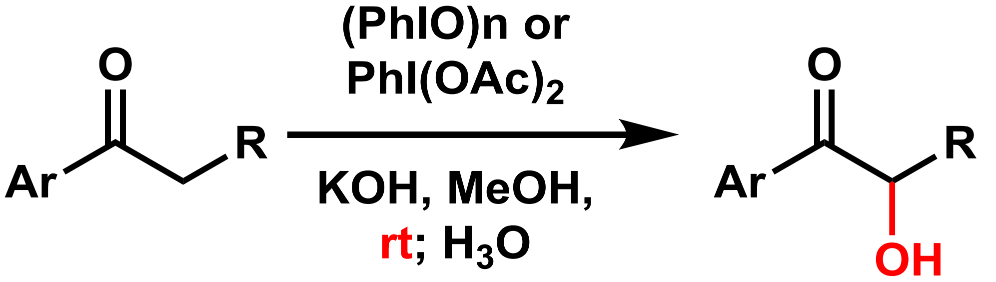


G.F. Koser, *et al.*, *J. Org. Chem.* **1982**, *47*, 2487.

proposed mechanism



Direct α-hydroxylation of ketones.

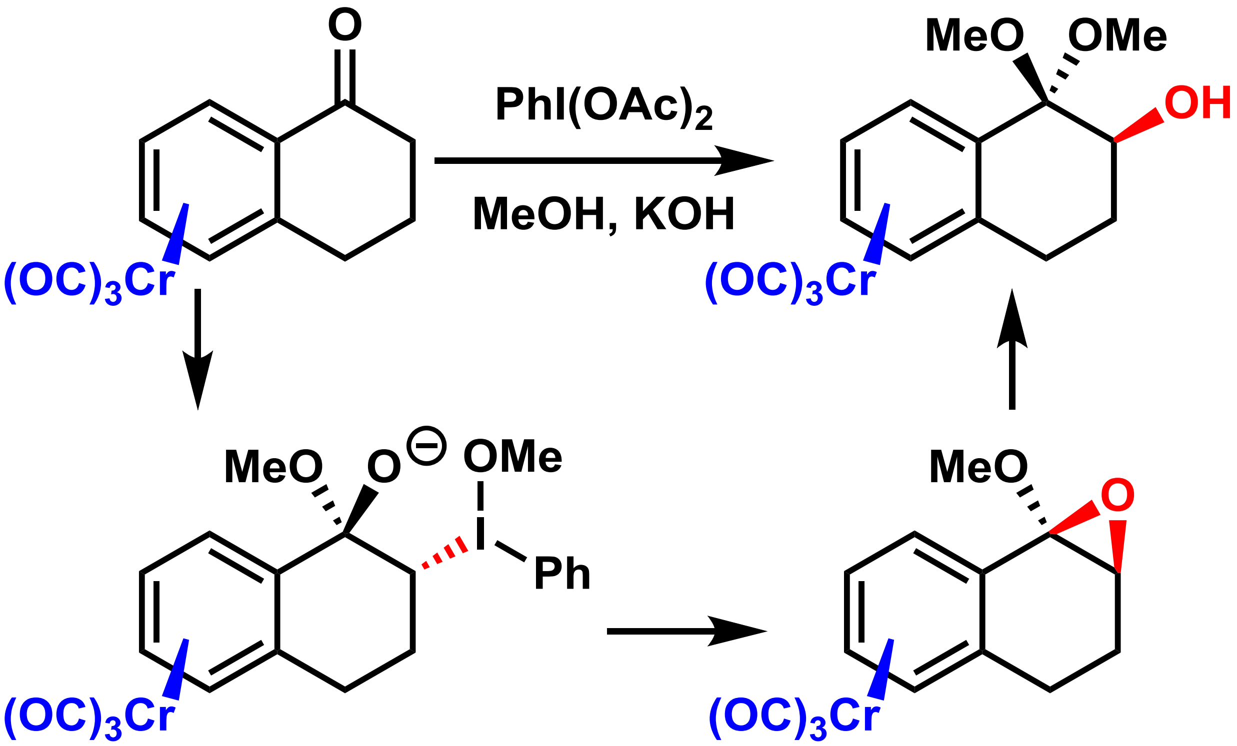


Robert M. Moriarty, *et al.*, *Tetrahedron Lett.* **1981**, 1283.

2-1. Oxygenation

2-1-1. Basic reaction

Oxygenation at hindered face.

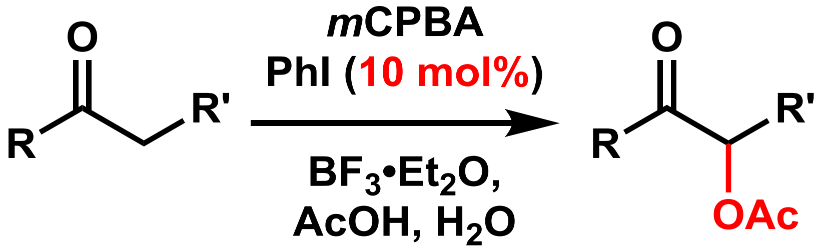


Robert M. Moriarty, *et al.*, *J. Org. Chem.* **1987**, 153.

2-1. Oxygenation

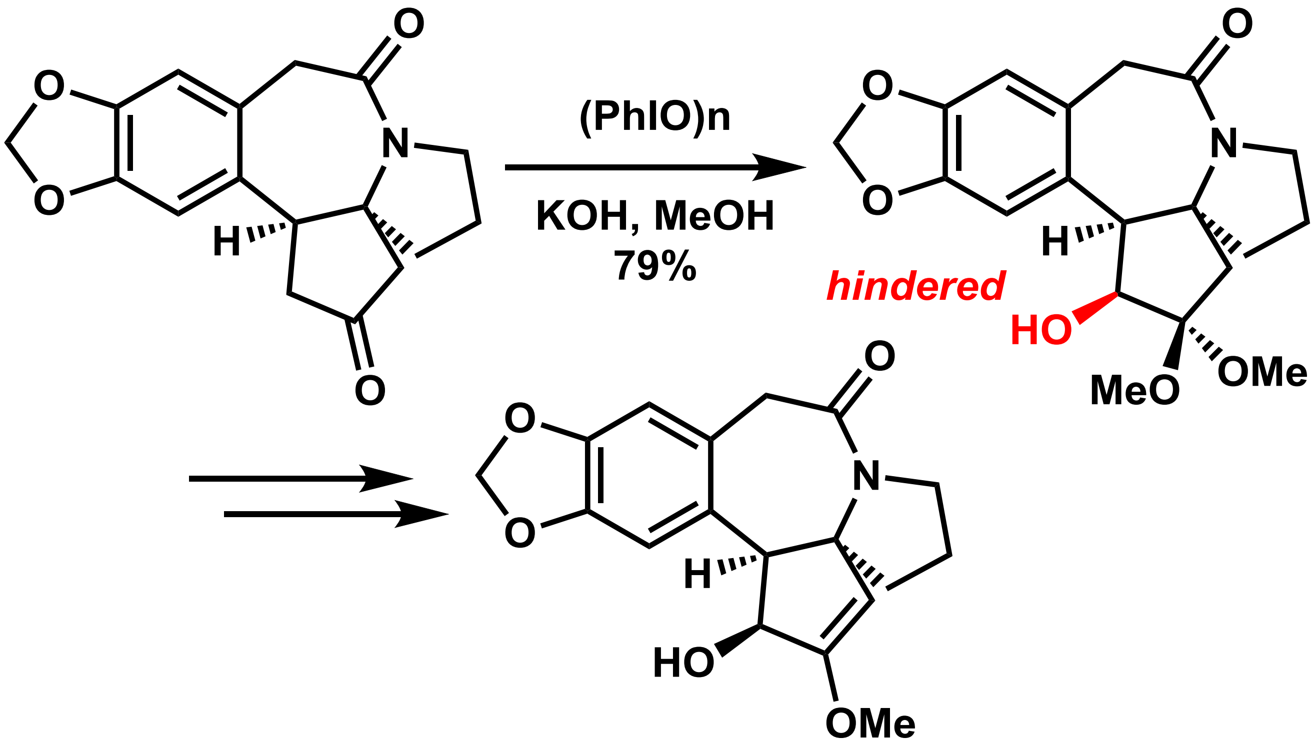
2-1-2. Application

α-Oxygenation under catalytic condition.



M. Ochiai, *et al.*, *J. Am. Chem. Soc.* **2005**, 12244.

The total synthesis of cephalotaxine.

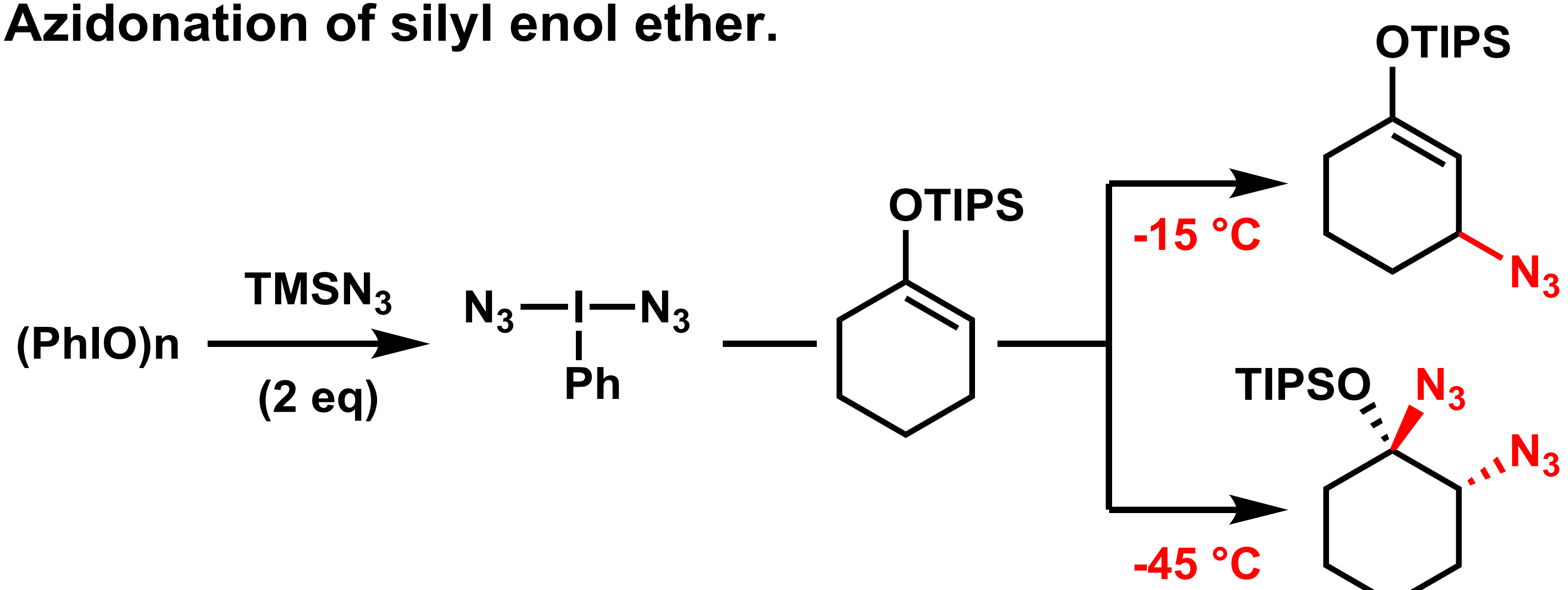


Robert M. Moriarty, *et al.*, *J. Org. Chem.* **1987**, 153.

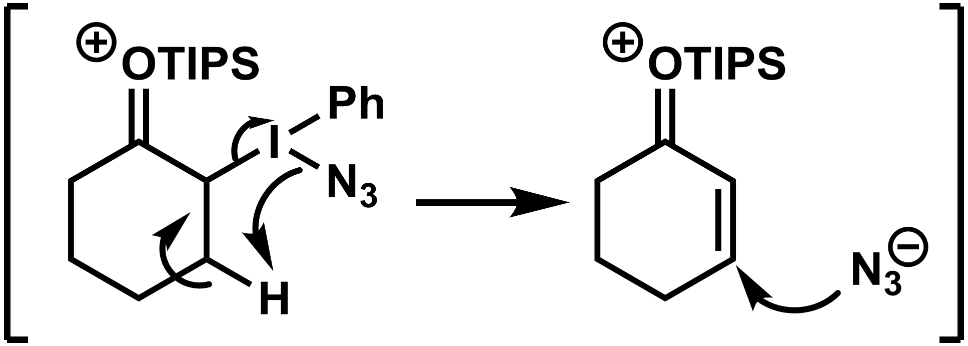
2-2. Nitrogenation

2-2-1. Azidonation

Azidonation of silyl enol ether.



β-Azidonation pathway

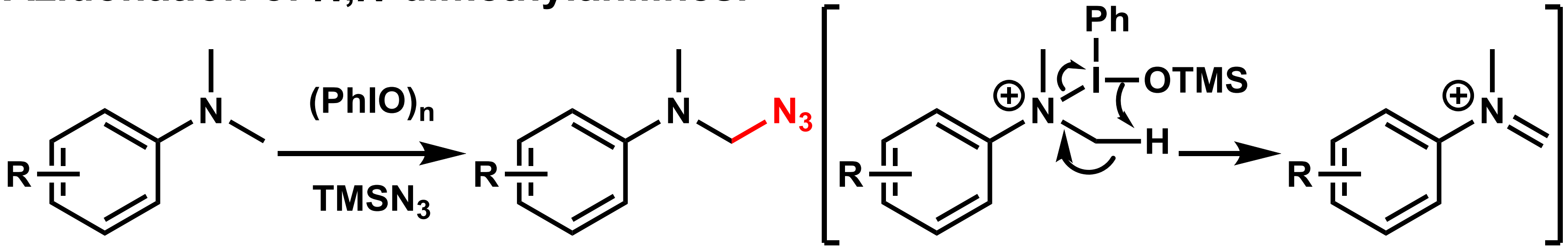


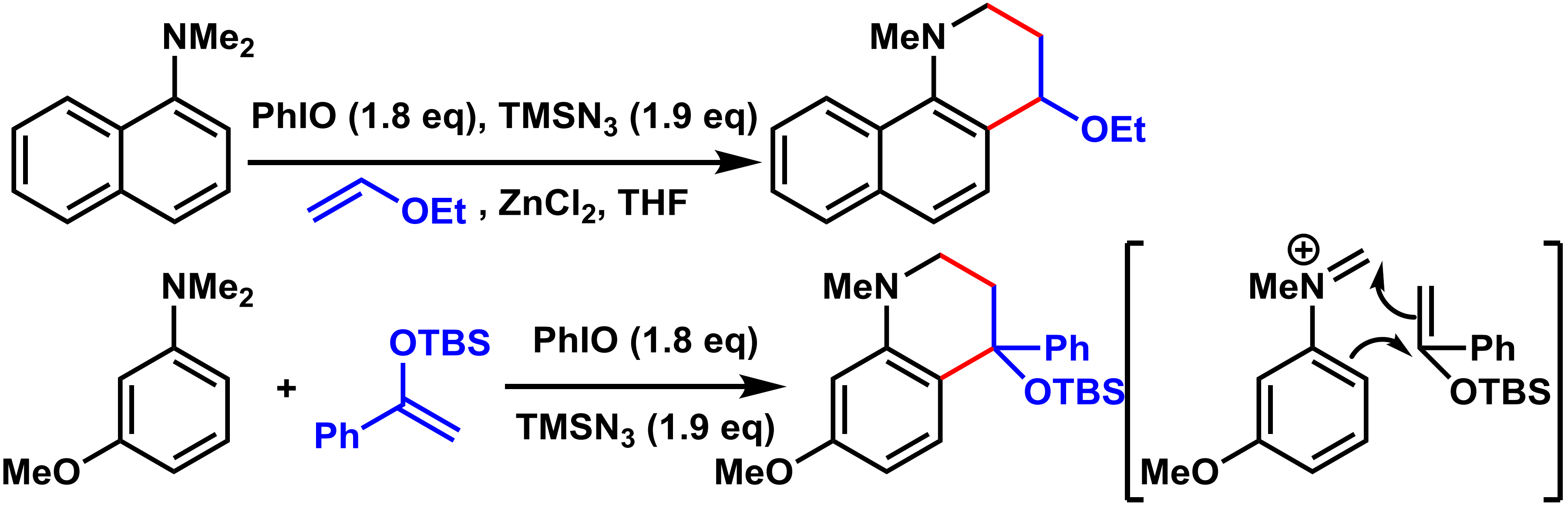
P. Magnus, et al., *J. Am. Chem. Soc.* **1992**, *114*, 767.

2-2. Nitrogenation

2-2-1. Azidonation (application)

Azidonation of *N*,*N*-dimethylanilines.



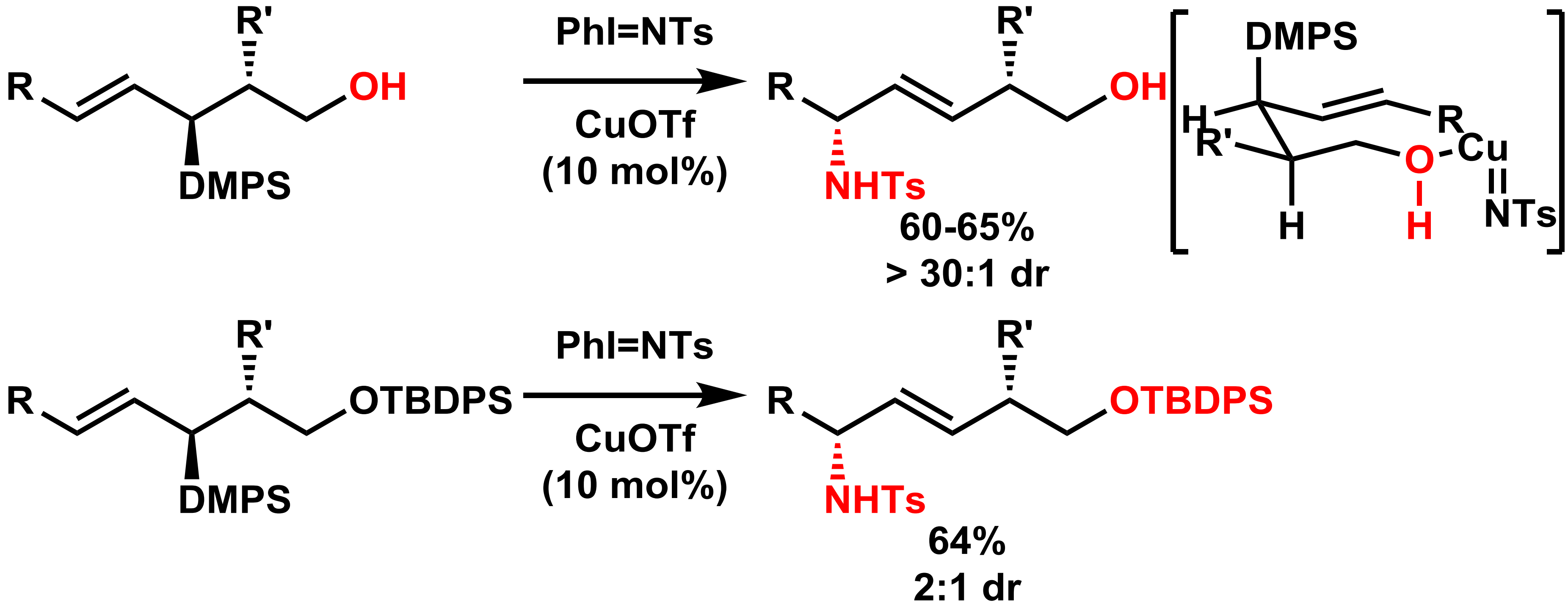


P. Magnus, *et al.*, *Synthesis* **1998**, 547.

2-2. Nitrogenation

2-2-2. Aziridination

Substrate controlled

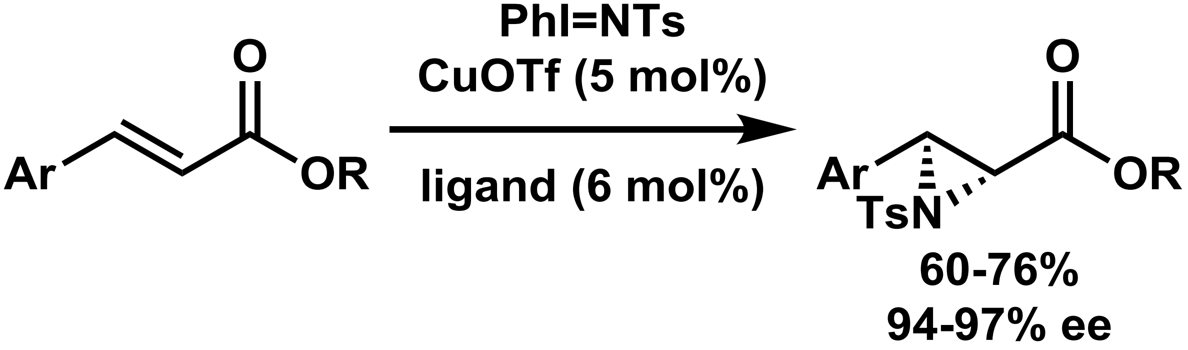


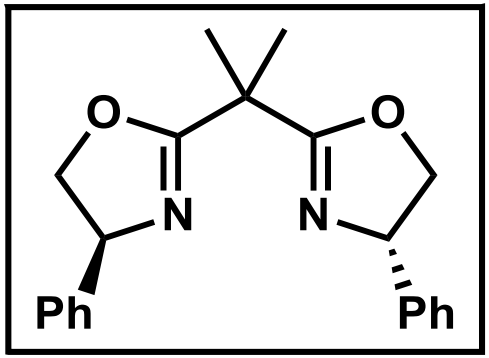
J.S. Panek, *et al.*, *J. Am. Chem. Soc.* **1997**, *119*, 6040.

2-2. Nitrogenation

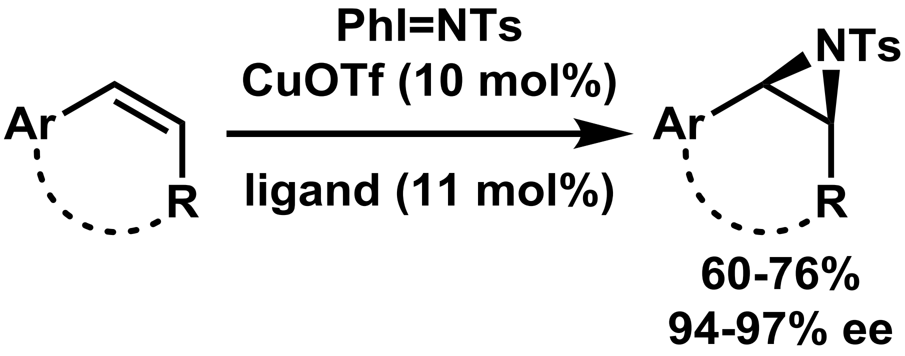
2-2-2. Aziridination

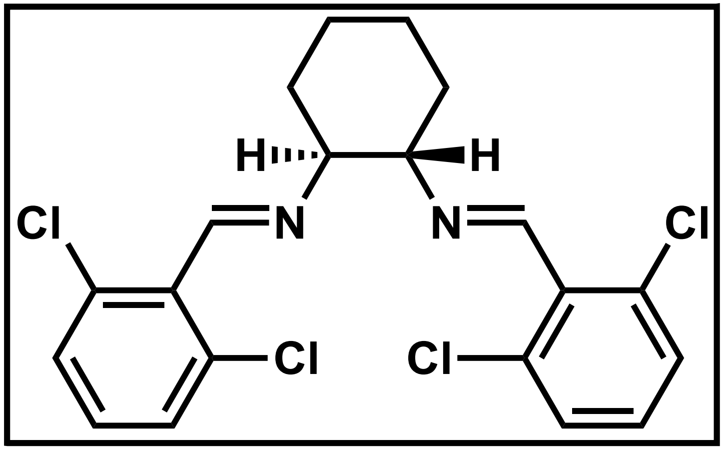
Enantioselective





D.A. Evans, *et al.*, *J. Am. Chem. Soc.* **1993**, *115*, 5328.
D.A. Evans, *et al.*, *J. Am. Chem. Soc.* **1994**, *116*, 2742.



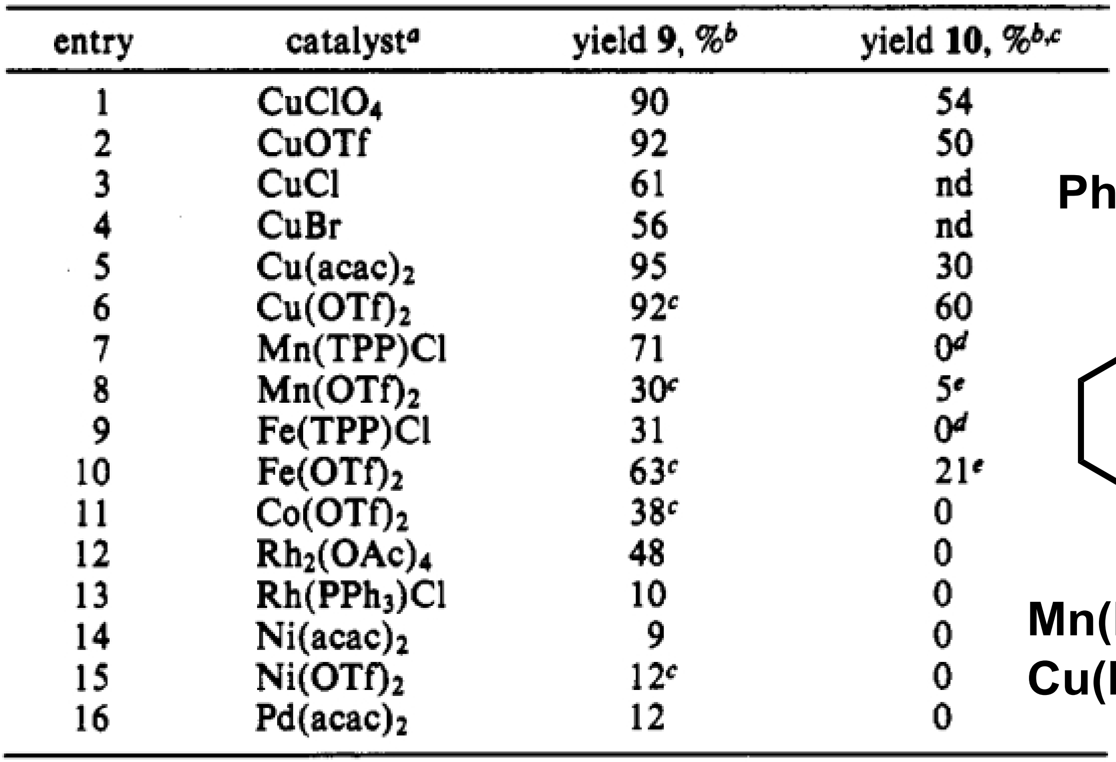


E.N. Jacobsen, *et al.*, *J. Am. Chem. Soc.* **1993**, *115*, 5326.

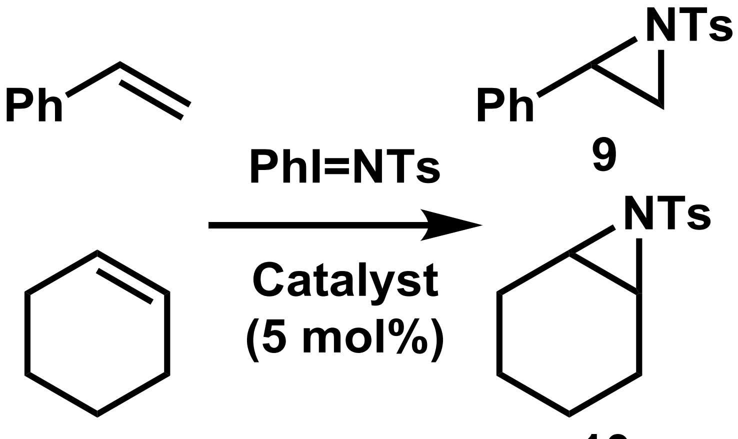
2-2. Nitrogenation

2-2-2. Aziridination

Transition-Metal catalysts in the Aziridination



entry	catalyst[a]	yield **9**, %[b]	yield **10**, %[b,c]
1	$CuClO_4$	90	54
2	CuOTf	92	50
3	CuCl	61	nd
4	CuBr	56	nd
5	$Cu(acac)_2$	95	30
6	$Cu(OTf)_2$	92[c]	60
7	Mn(TPP)Cl	71	0[d]
8	$Mn(OTf)_2$	30[c]	5[e]
9	Fe(TPP)Cl	31	0[d]
10	$Fe(OTf)_2$	63[c]	21[e]
11	$Co(OTf)_2$	38[c]	0
12	$Rh_2(OAc)_4$	48	0
13	$Rh(PPh_3)Cl$	10	0
14	$Ni(acac)_2$	9	0
15	$Ni(OTf)_2$	12[c]	0
16	$Pd(acac)_2$	12	0



9

10

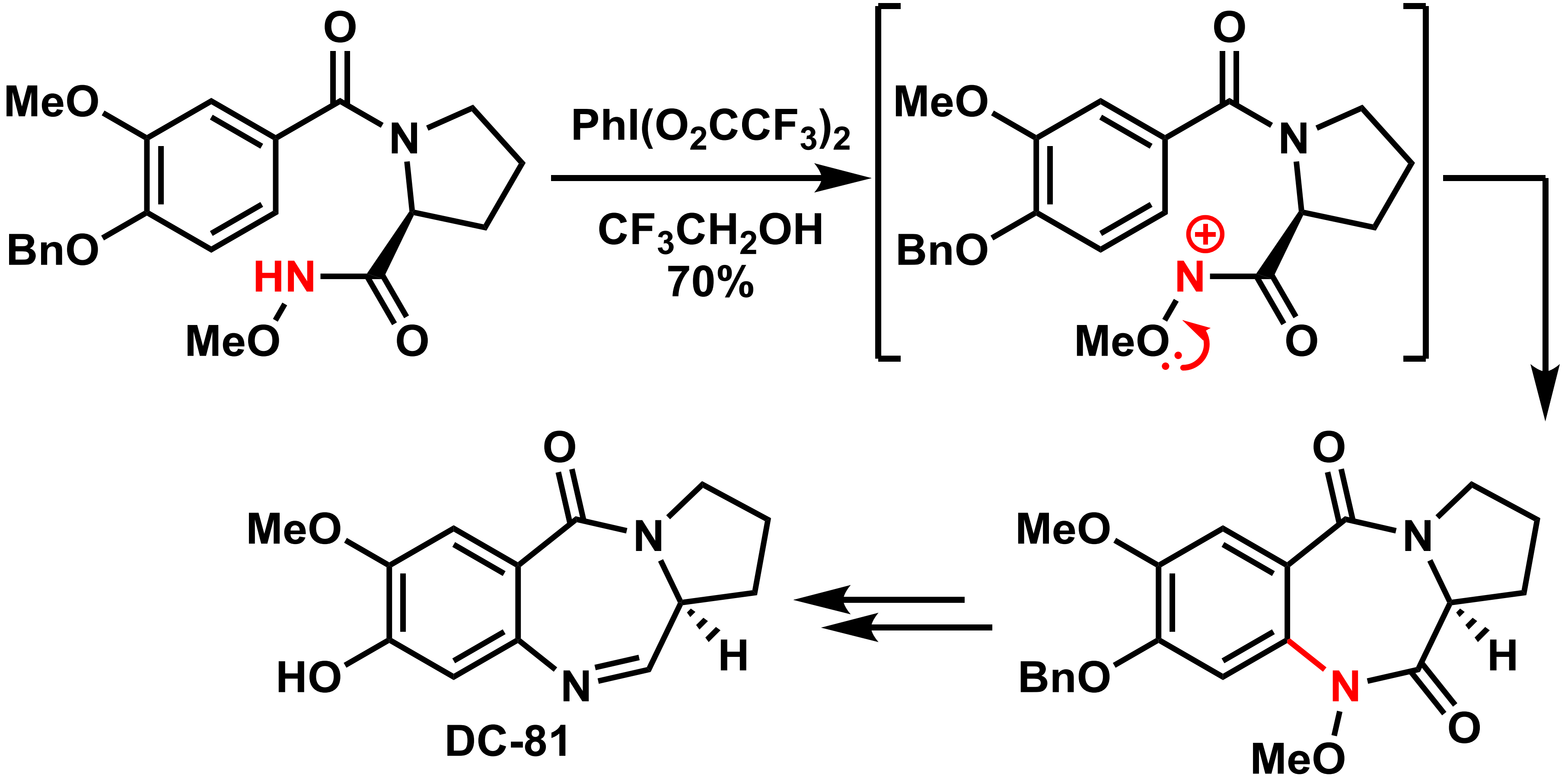
Mn(III), Fe(III) → olefin epoxidation
Cu(I), Rh(II) → cyclopropanation

D.A. Evans, *et al.*, *J. Am. Chem. Soc.* **1994**, *116*, 2742.

2-2. Nitrogenation

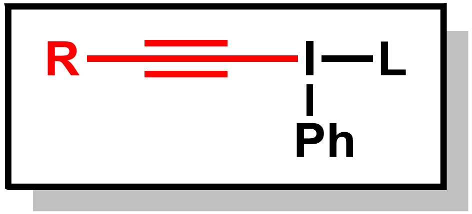
2-2-3. An advantageous access to the antitumor antibiotic DC-81

The total synthesis of DC-81.



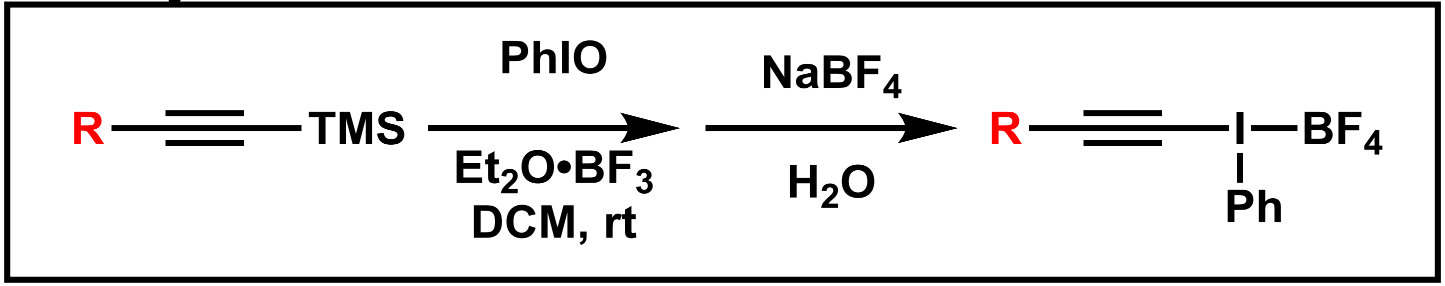
I. Tellitu, *J. Org. Chem.* **2005**, *70*, 2256.

2-3. Alkynyl-iodane



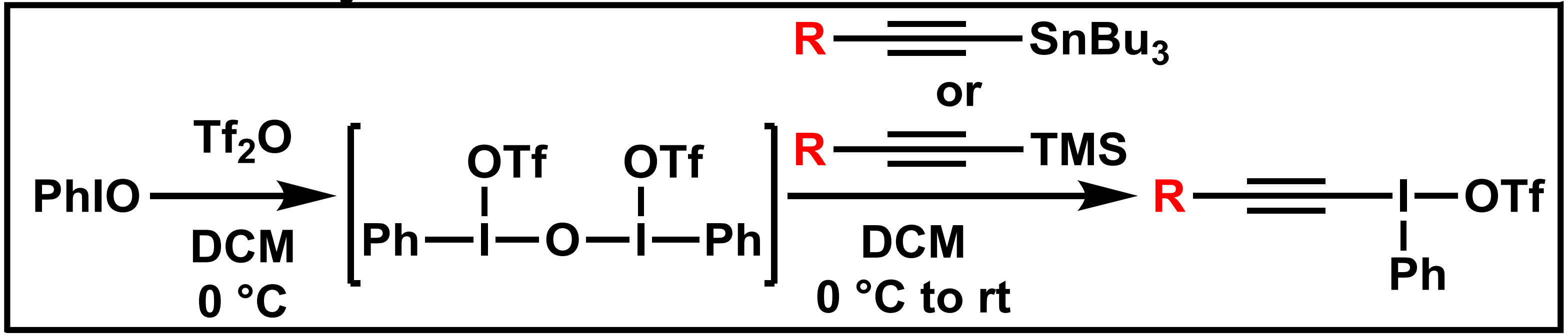
2-3-1. Synthesis

R = alkyl or Ph.



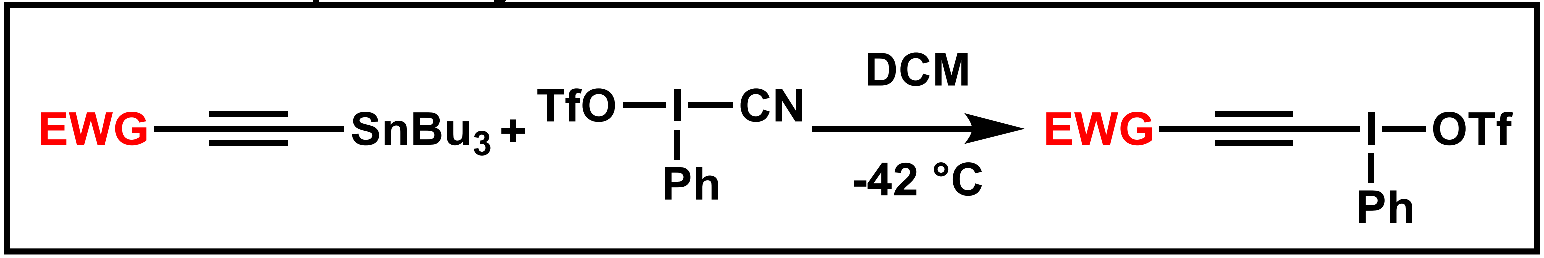
M. Ochiai, *et al.*, *Tetrahedron Lett.* **1985**, *26*, 4501.

R = TMS or alkyl.



P.J. Stang., *et al.*, *J. Org. Chem.* **1991**, *56*, 3912.

R = electrom poor alkynes.

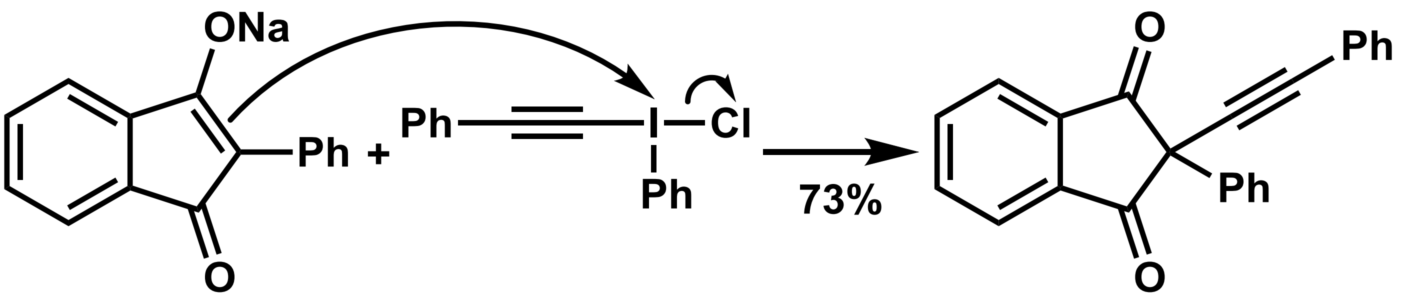


P.J. Stang., *et al.*, *J. Am. Chem. Soc.* **1994**, *116*, 93.

2-3. Alkynyl-iodane

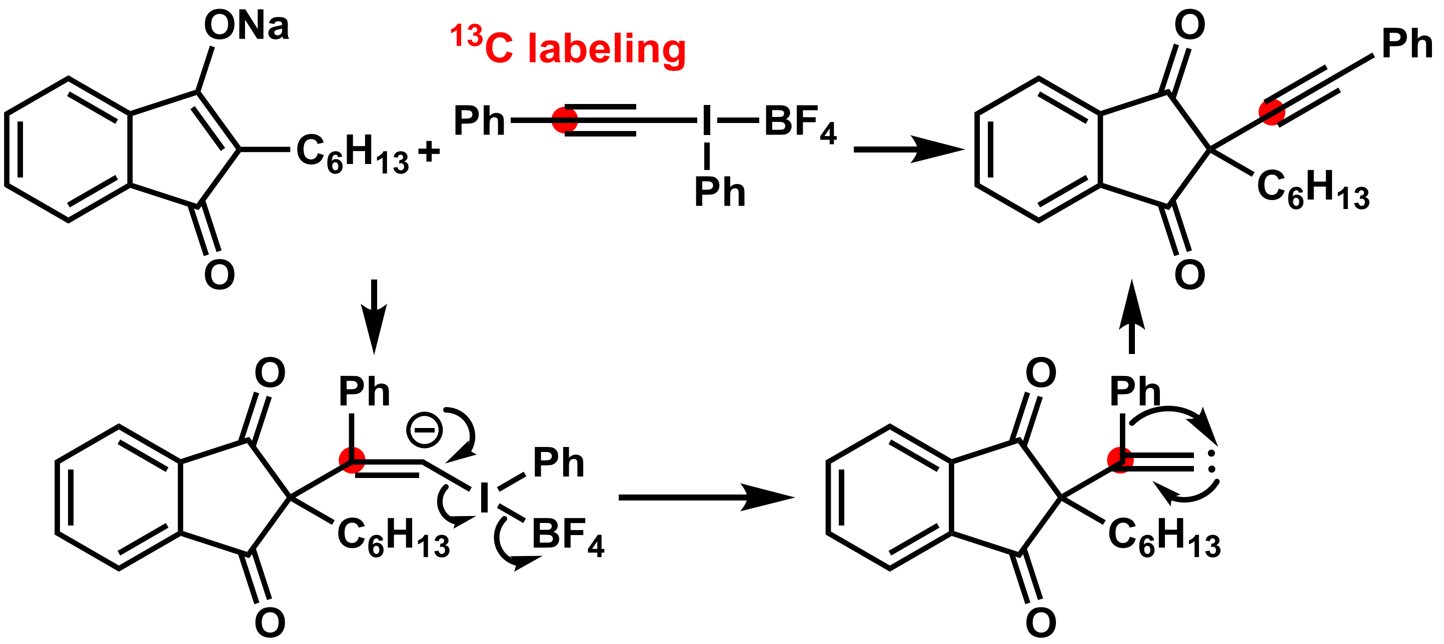
2-3-2. Mechanism

The originally proposed mechanism



F.M. Beringer., *et al.*, *J. Org. Chem.* **1965**, *30*, 1930.

The new proposed mechanism

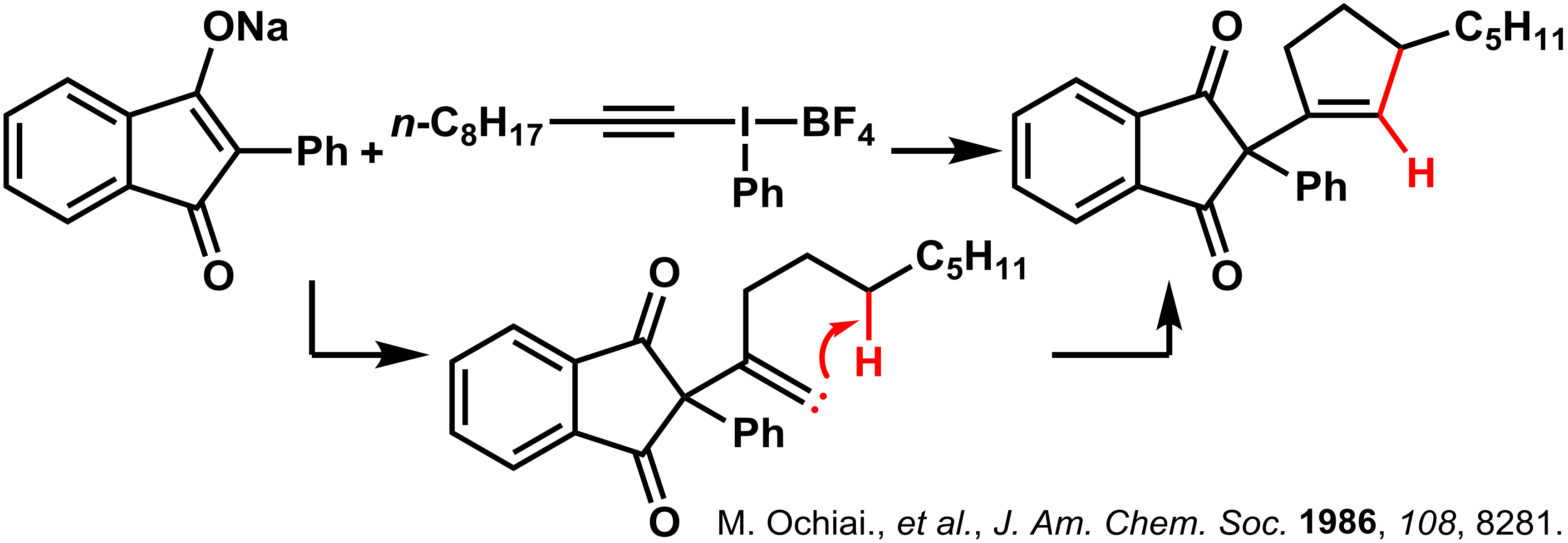


M. Ochiai., *et al.*, *J. Am. Chem. Soc.* **1986**, *108*, 8281.

2-3. Alkynyl-iodane

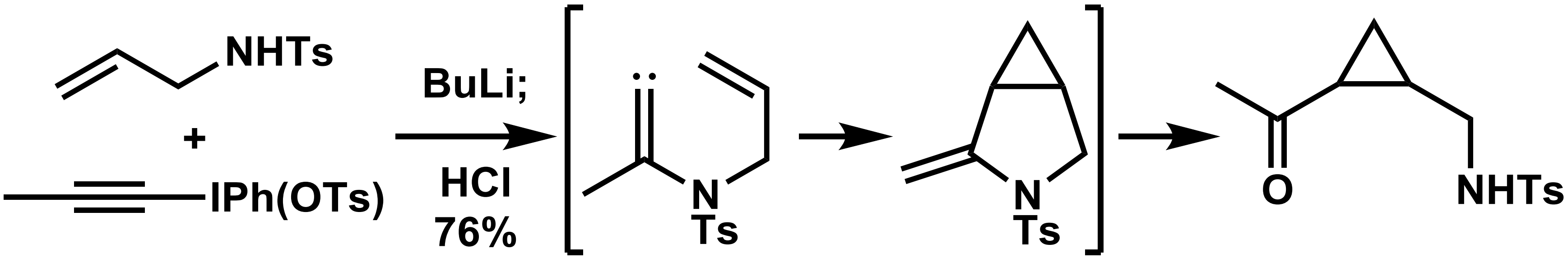
2-3-3. Reactions

Carbene insertion



M. Ochiai., *et al.*, *J. Am. Chem. Soc.* **1986**, *108*, 8281.

Cyclopropanation

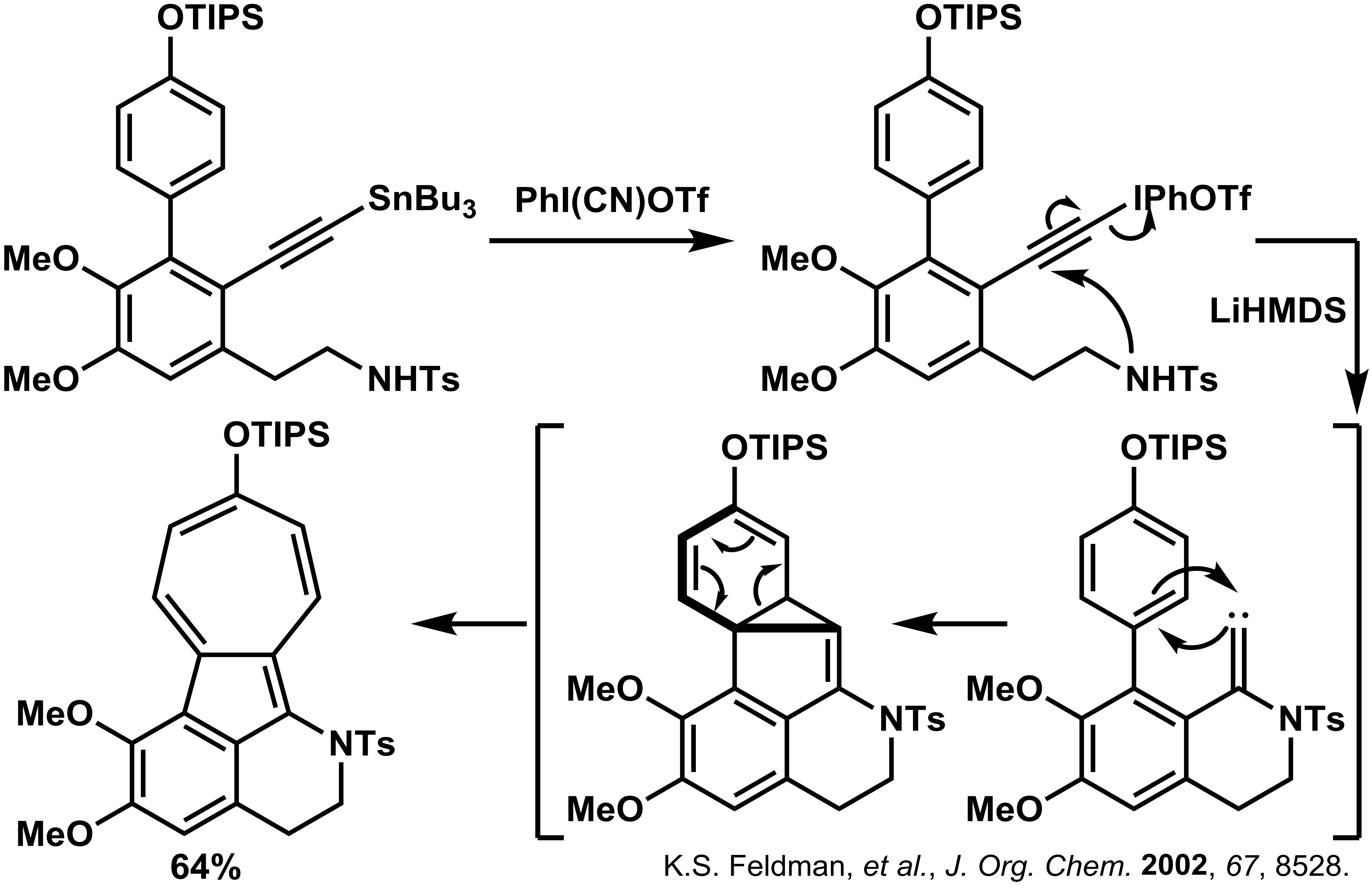


H.Y. Lee, *et al.*, *Synlett* **2001**, 1656.

2-3. Alkynyl-iodane

2-3-3. Reactions

The total synthesis of the Tropoloisoquinoline Alkaloid Pareitropone.

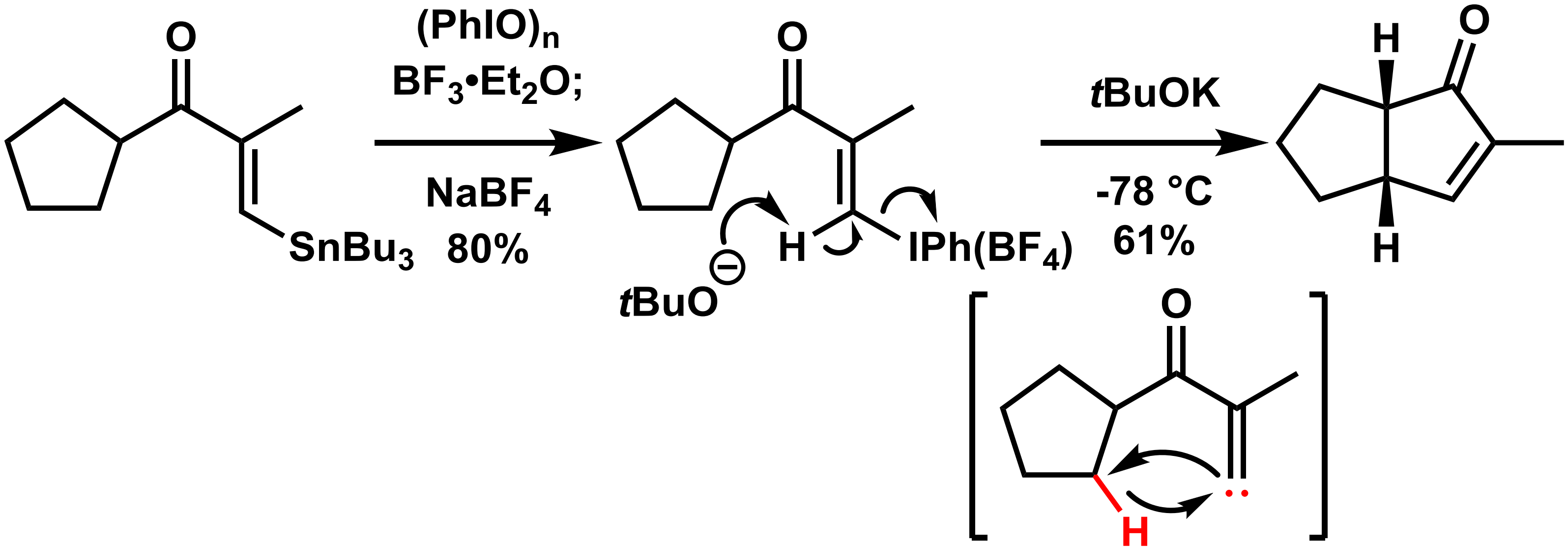


K.S. Feldman, *et al.*, *J. Org. Chem.* **2002**, *67*, 8528.

2-4. Alkenyl-iodane

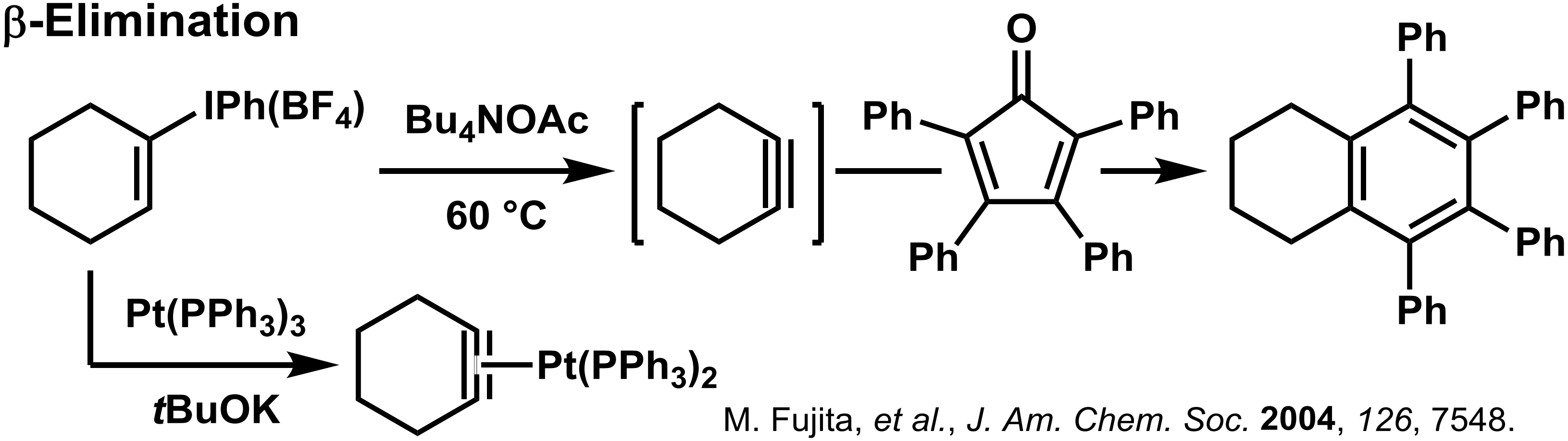
2-4. Reaction pattern

α-Elimination



M. Ochiai, *et al.*, *J. Am. Chem. Soc.* **1988**, *110*, 6565.

β-Elimination

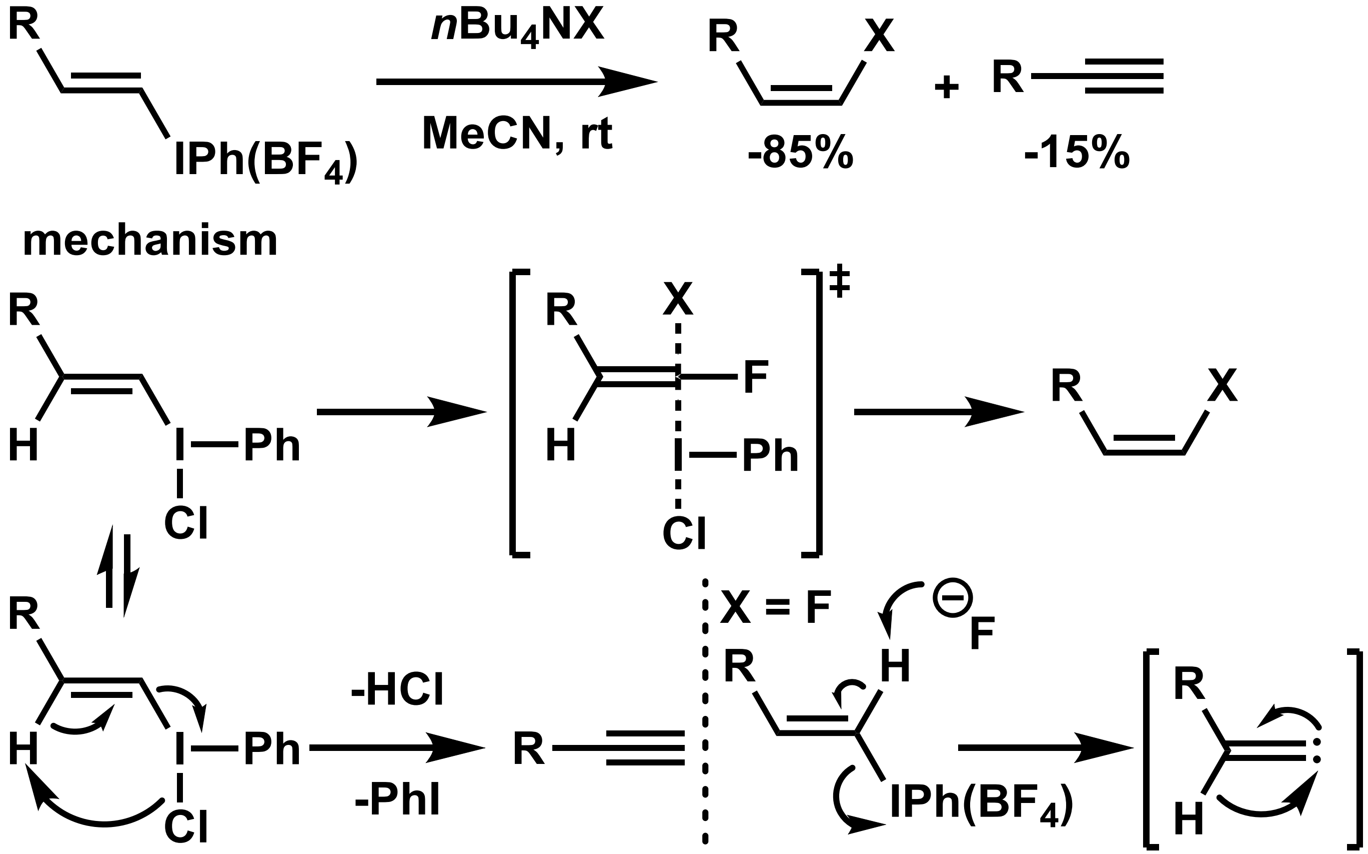


M. Fujita, *et al.*, *J. Am. Chem. Soc.* **2004**, *126*, 7548.

2-4. Alkenyl-iodane

2-4. Reaction pattern

Direct S_N2 reaction



M. Ochiai, *et al.*, *J. Am. Chem. Soc.* **1991**, *113*, 7059.

3. Current study

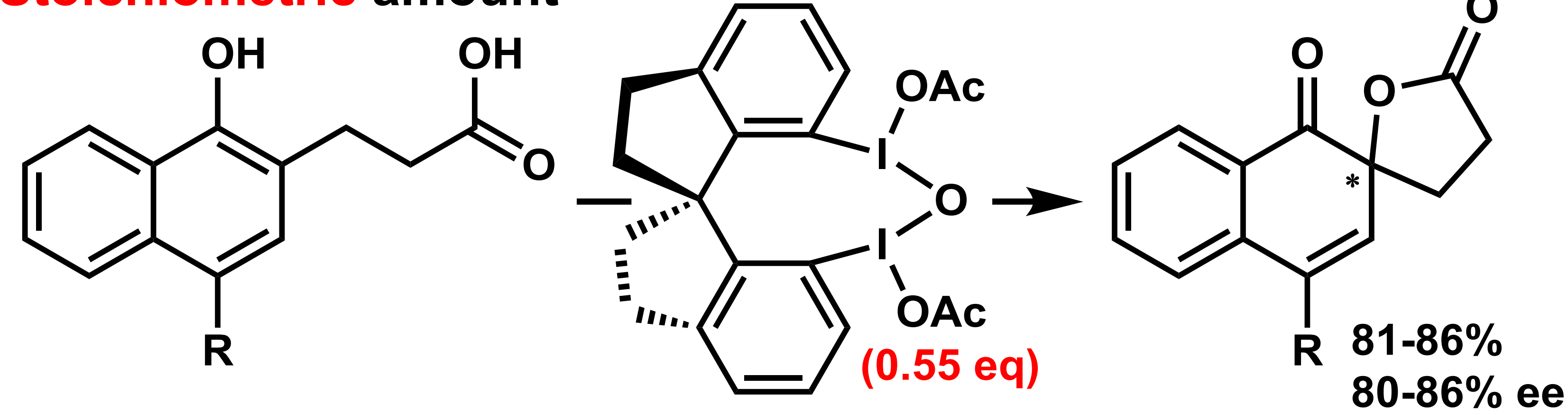
3-1. Chiral iodanes

3-2. Arylation by Prof. M. Gaunt

3-1. Chiral iodanes

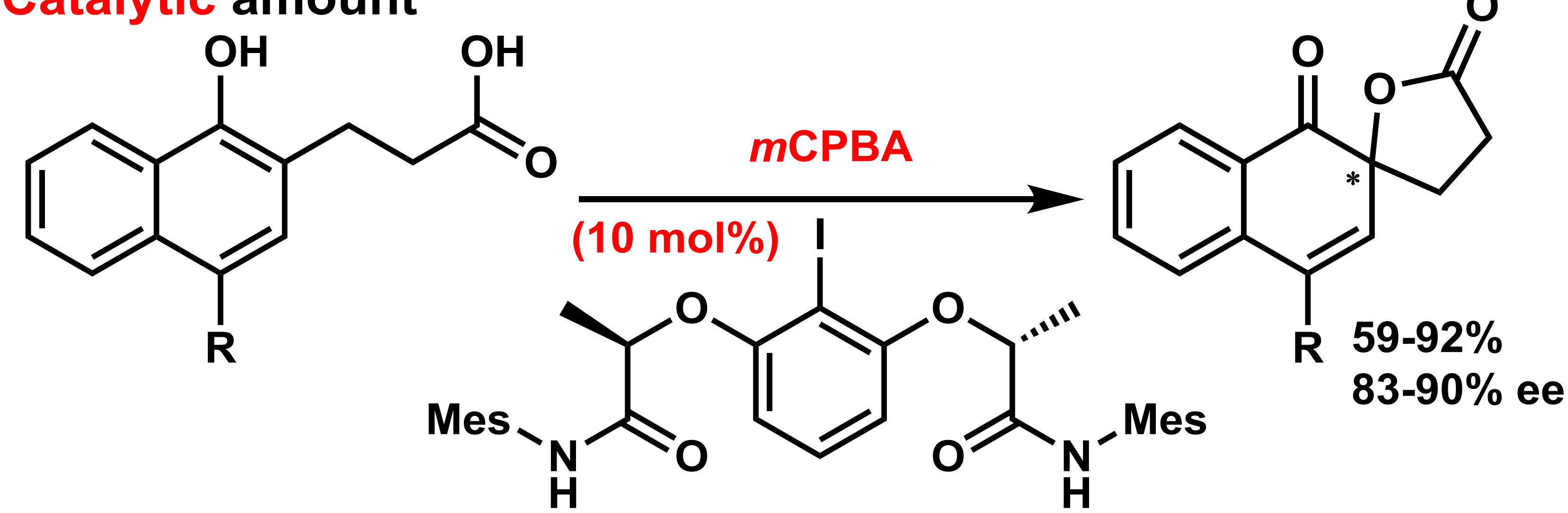
3-1-1. Enantioselective dearomatization

Stoichiometric amount



Y. Kita, *et al.*, *Angew. Chem. Int. Ed.* **2008**, *47*, 3787.

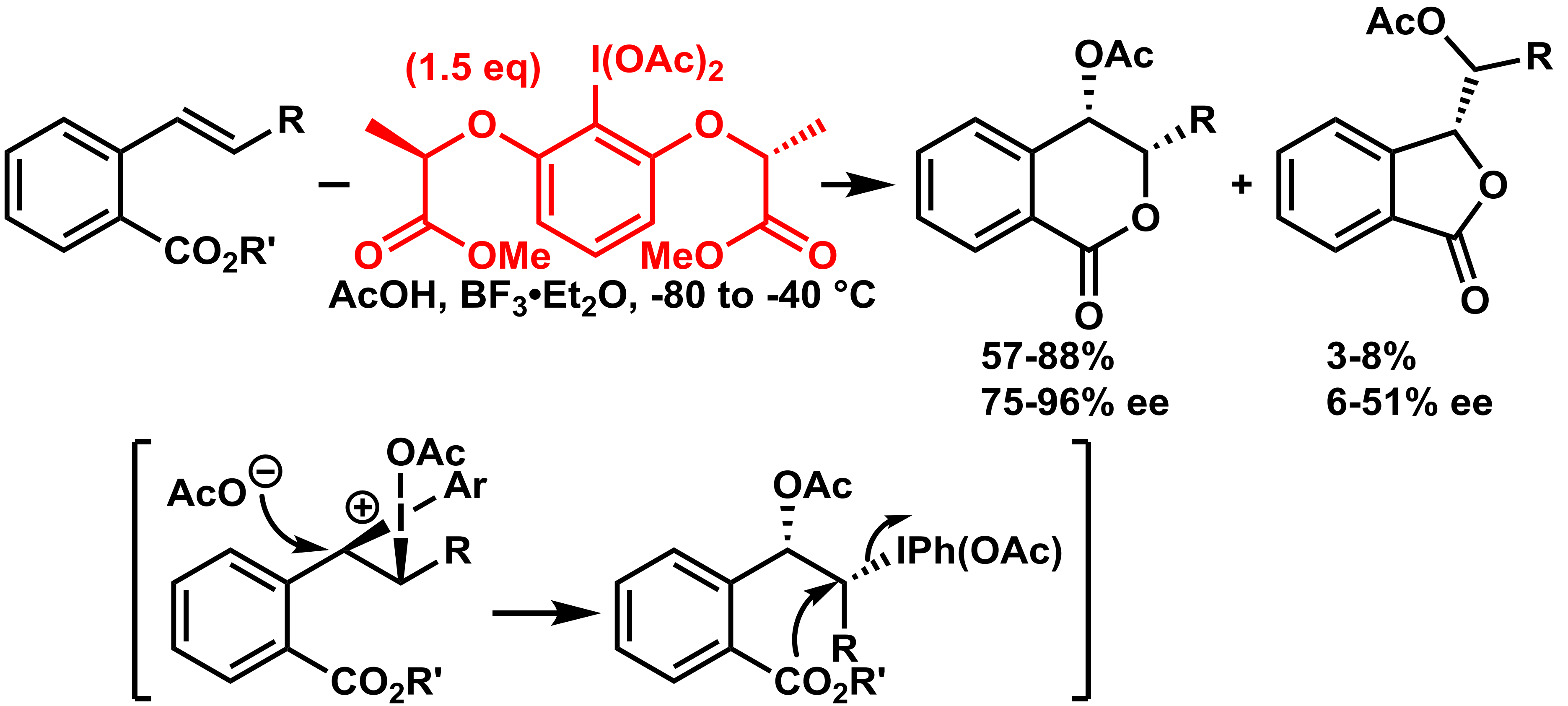
Catalytic amount



K. Ishihara, *et al.*, *Angew. Chem. Int. Ed.* **2010**, *49*, 2175.

3-1. Chiral iodanes

3-1-2. Enantioselective oxylactonization



M. Fujita, *et al.*, *Angew. Chem. Int. Ed.* **2010**, *49*, 7068.

3-2. Arylation by Prof. M. Gaunt

3-2-1. Introduction of Prof. M. Gaunt

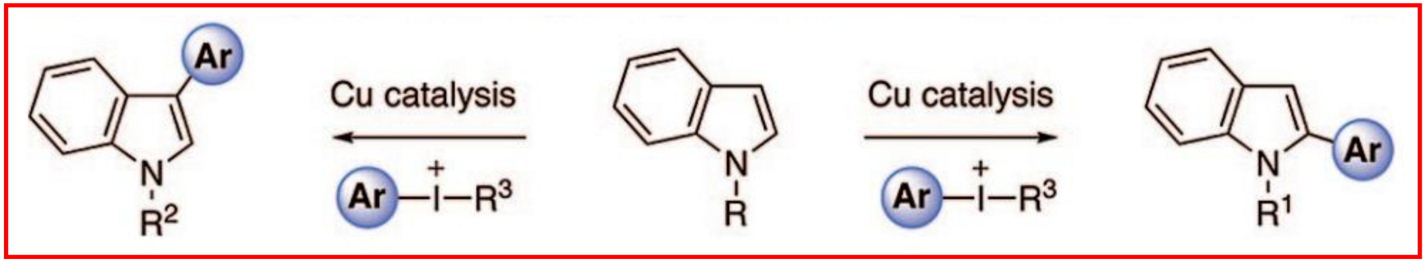
M.J. Gaunt, *et al.*, *Science* **2009**, *323*, 159.

1995 Graduated from the University of Birmingham with 1st Class Honors for Chemisty.
1999 Got Ph.D at the University of Cambridge. (Prof. J.B.Spencer)
1999-2001 Worked as a Postdoctoral fellow at the University of Pennsylvania. (Prof. A.B. Smith)
2001-2003 Worked as a Junior Reseach Fellow at the College of Saint Mary Magdalene. (Prof. S.V. Ley)
2003 Bagan his independent research career at the University of Cambridge.
2006 Was promoted to Lecturer in Organic Chemistry.
2010 Was promoted to Reader in Chemical Synthesis.
2012 Was promoted to Professor.
Recent 3 years; JACS **5**, ACIE **5**, Nature **1**, Chemical Sci **1**

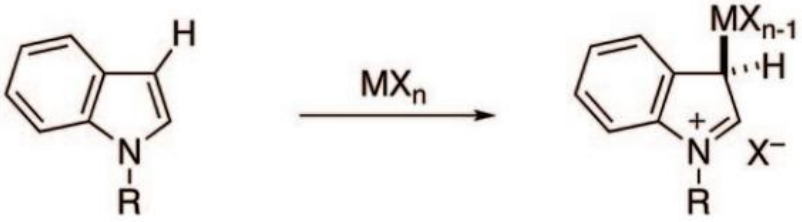
3-2. Arylation by Prof. M. Gaunt

3-2-2. Site-Selective Arylation of Indoles

Regioselective Cu(II) catalyzed C-H bond arylation



New catalysis mode for electrophilic metalation

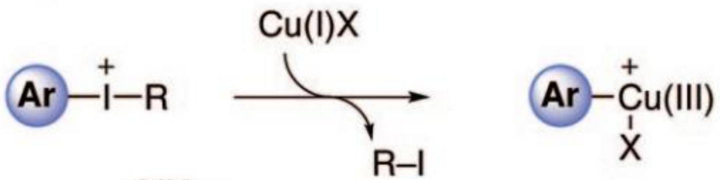


Pd(II) is a d^8 metal and is electrophilic

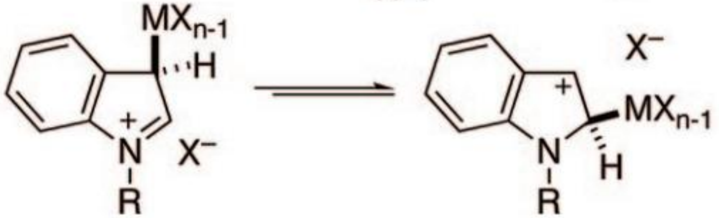
⇩

Cu (III) is a d^8 metal and should be highly electrophilic

- A more electrophilic metal catalyst should facilitate the metalation process [Pd(II) to Cu(III)]
- Iodine(III) reagents could oxidize Cu(I) to Cu(III)Ar. These intermediates should be highly electrophilic



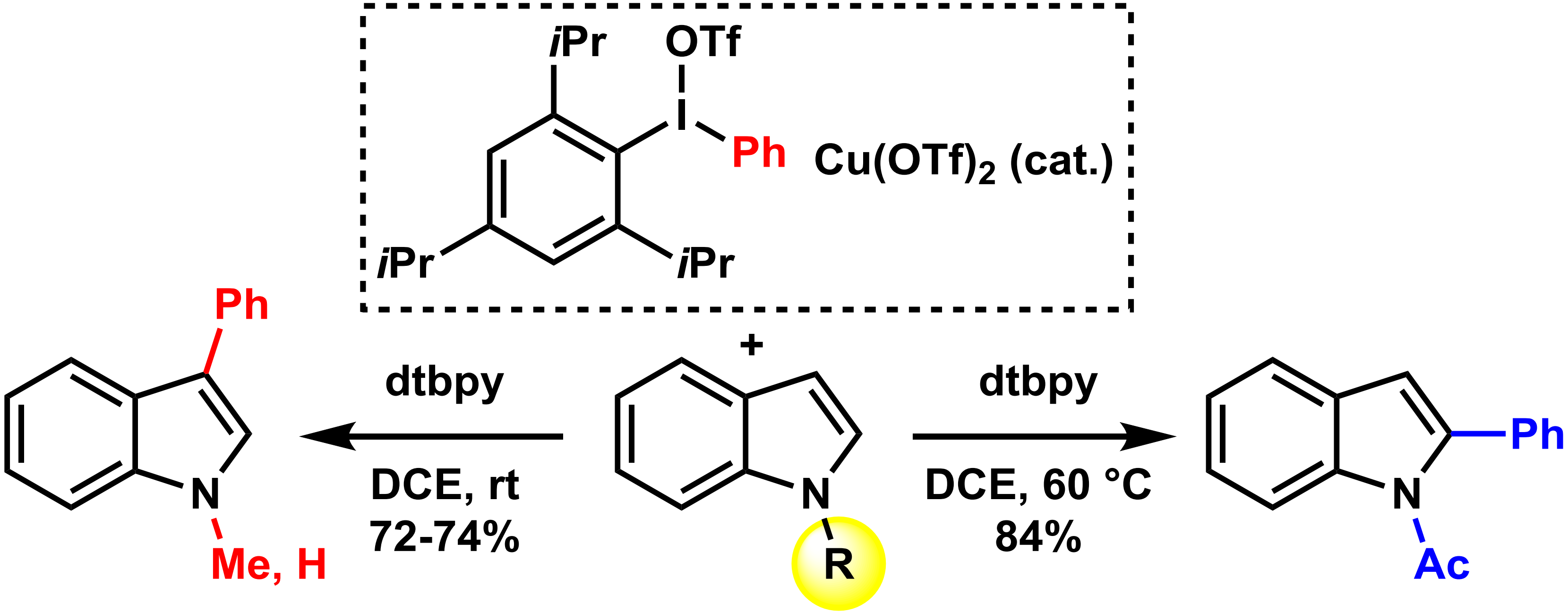
- Can a C3 to C2 migration of the C–Cu bond be controlled to in order to determine the site selectivity?



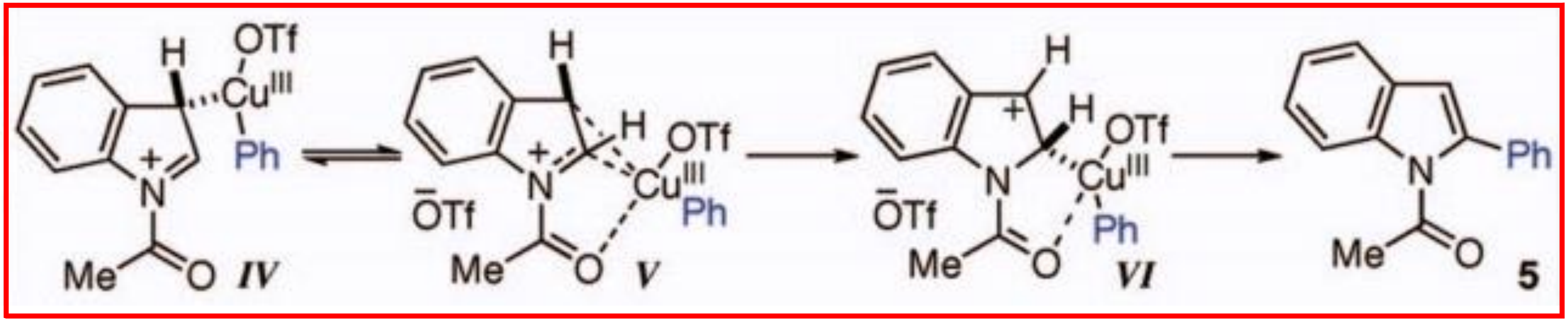
M.J. Gaunt, *et al.*, *J. Am. Chem. Soc.* **2008**, *130*, 8172.

3-2. Arylation by Prof. M. Gaunt

3-2-2. Site-Selective Arylation of Indoles



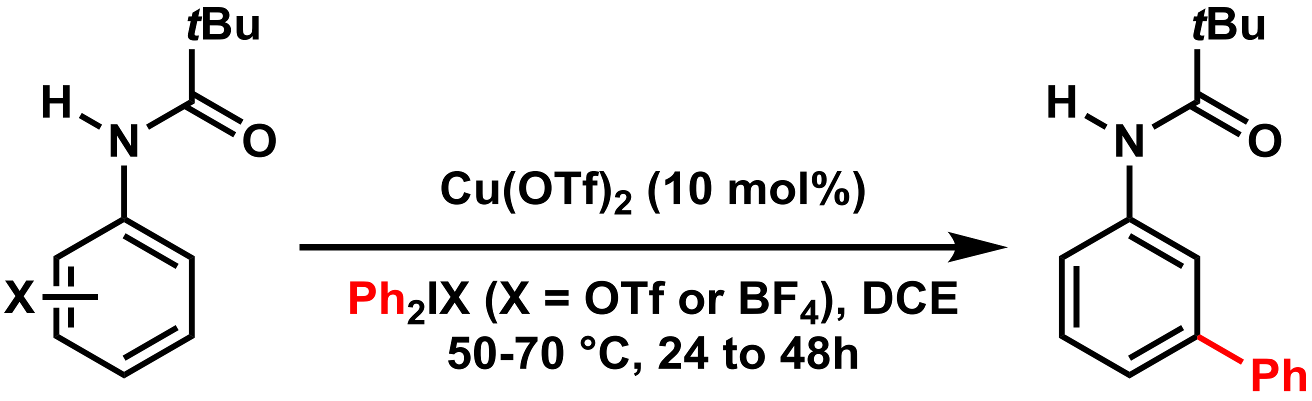
Proposed C3 to C2 migration of C-Cu bond



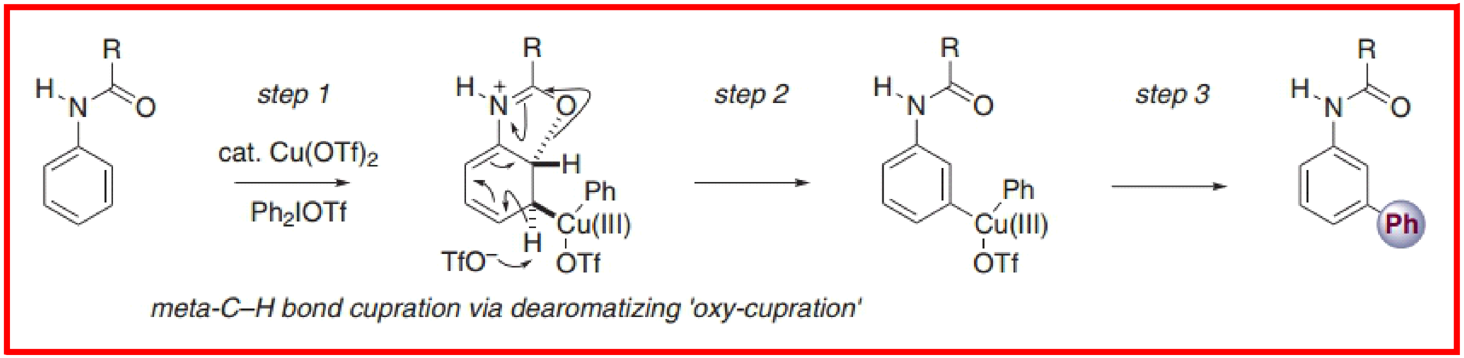
M.J. Gaunt, *et al.*, *J. Am. Chem. Soc.* **2008**, *130*, 8172.

3-2. Arylation by Prof. M. Gaunt

3-2-3. Meta-selective copper-catalyzed C-H bond arylation



Proposed mechanistic hypothesis



meta-C–H bond cupration via dearomatizing 'oxy-cupration'

Discussion

- Ortho position is electron rich.

- Copper shifts electron deficient meta position.

M.J. Gaunt, *et al.*, *Science* **2009**, *323*, 159.