

# The Chemistry of Hypervalent Iodine



MacMillan Group Meeting  
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## Key References:

T. Wirth, M. Ochiai, A. Varvoglis, V. V. Zhdankin, G. F. Koser, H. Tohma, Y. Kita, *Topics in Current Chemistry: Hypervalent Iodine Chemistry -/- Modern Developments in Organic Synthesis*, pp. 1-248, 224. Springer-Verlag, Berlin, 2002.

A. Varvoglis, *Hypervalent Iodine in Organic Synthesis*, pp. 1-223, Academic Press, London, 1997.

P. Stang, V. V. Zhdankin, *Chem. Rev.* **96**, 1123-1178 (1996)

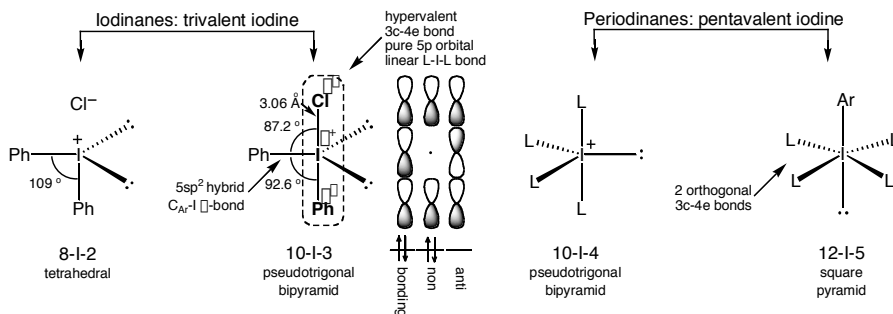
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## Background and Introduction

- Iodine is most commonly in monovalent compounds with an oxidation state of -1, however, because it is the largest, most polarizable, and most electropositive of the group 17 elements, it also forms stable polycoordinate, multivalent compounds.
- First polyvalent organic iodine complex, (dichloroiodo)benzene or  $\text{PhICl}_2$ , was prepared was by German chemist C. Willgerodt in 1886. Although its oxidizing properties were known since 1893, a renaissance in the field of polyvalent iodine has occurred only in the past 20 years.
- Factors leading to resurgence of interest:
  - (1) Chemical properties and reactivity is similar to the heavy metal reagents such as  $\text{Hg(III)}$ ,  $\text{Tl(III)}$ ,  $\text{Pb(IV)}$  but without the toxicity & environmental issues.
  - (2) Mild reaction conditions and easy handling of hypervalent iodine compounds
  - (3) Commercial availability of key precursors such as  $\text{PhI(OAc)}_2$ .
- Topics to be covered in this talk:
  - Nomenclature, Structures, and Properties*
  - Reactivity Pattern and Mechanisms of Organo- $\text{I}^{\text{III}}$ -Iodanes:  $\text{RIL}_2$  and  $\text{R}_2\text{IL}$*
  - Survey of Reactive Transformations Using Hypervalent Iodine Reagents*
  - Selected Applications in Total Synthesis*
- Topics that are NOT covered in this talk: Transition Metal Mediated Reactions and Polymer Supported Reagents

## Nomenclature for Hypervalent Iodine

- The term hypervalent was established in 1969 for molecules with elements of groups 15-18 bearing more electrons than an octet in their valence shell.
- IUPAC rules designate  $\square$  as non-standard bonding; thus,  $\text{H}_3\text{I}$  is  $\square^3$ -iodane and  $\text{H}_3\text{I}$  is  $\square^3$ -iodane. Most common decet structure is aryl- $\square^3$ -iodane  $\text{ArIL}_2$  (L = heteroatom) and for dodecet structure is aryl- $\square^5$ -iodane  $\text{ArIL}_4$ .
- Polyvalent iodine species differ in Martin-Arduengo designation [N-X-L] where N = # of valence electrons on central atom, X = central atom, L = # of ligands on central atom.



- Diphenyliodonium chloride vs. Chloro(diphenyl)- $\square^3$ -Iodane?

Onium salts (such as ammonium, phosphonium, oxonium, etc.) refers to a tetrahedral geometry with an octet in the valence shell of a positively charged atom and are not hypervalent compounds. Also, X-ray structural data of iodine(III) compounds with a coordination of 2 (as in iodonium salts) have never been observed.

## Classes of Hypervalent Iodine

- Traditional classification is based on the # of carbon ligands on central iodine.

### For Iodinanones

- 1 C-bond: **iodosyl/iodoso** compounds (RIO) and their derivatives ( $\text{RIX}_2$ , where X = non-carbon ligands and R = aryl or  $\text{CF}_3$ )
- 2 C-bonds: **iodonium salts** ( $\text{R}_2\text{I}^+\text{X}^-$ )
- 3 C-bonds: (Iodanes with 3 C-I bonds are thermally unstable and not synthetically useful)

### For Periodinanones

- 1 C-bond: **iodyl/iodoxy** compounds ( $\text{RIO}_2$ ) and their derivatives ( $\text{RIX}_4$  or  $\text{RIX}_2\text{O}$ )
- 2 C-bonds: **iodyl salts** ( $\text{R}_2\text{IO}^+\text{X}^-$ )

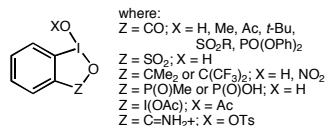
- Compounds with more than one formal carbon bond to iodine:

*Alkenyliodonium* ( $\text{PhI}^+\text{C}=\text{CHR X}^-$ ) and *Alkynyliodonium* ( $\text{PhI}^+\text{C}\equiv\text{CR X}^-$ ) Salts

*Iodonium Ylides* ( $\text{PhI}=\text{CXY}$ , where X, Y = electron acceptors)

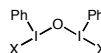
- Cyclic Iodinanones:

$\square^3$ -Iodinanones: Benziodoxazoles based on *o*-iodosobenzoic acid.



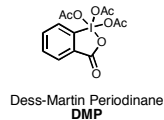
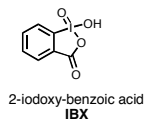
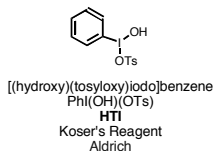
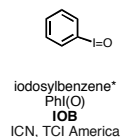
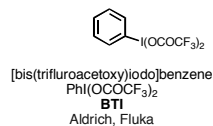
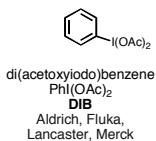
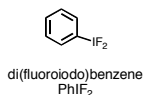
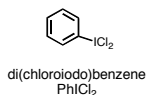
$\square^5$ -Iodinanones: Benziodoxazoles based on *o*-iodoxybenzoic acid. (ie. IBX and Dess-Martin Reagent)

- $\square$ -Oxo-bridged Iodanes ( $\text{PhI}(\text{X})\text{OI}(\text{X})\text{Ph}$ , where X = OTf,  $\text{ClO}_4$ ,  $\text{BF}_4$ ,  $\text{PF}_6$ ,  $\text{SbF}_6$ )

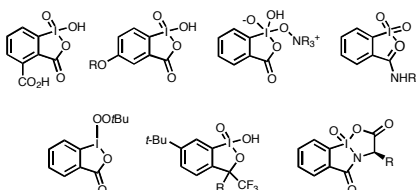


## Established Hypervalent Iodide Reagents

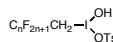
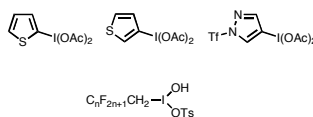
### Most Frequently Used Reagents



### IBX Related Reagents

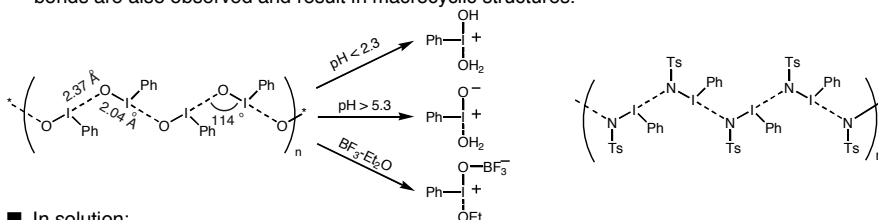


### Newer Iodine(III) Reagents



## Physical Aspects of I<sup>III</sup>-Iodanes

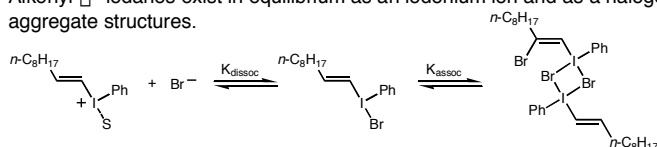
- Most hypervalent iodine reagents are solid (amorphous or crystalline) and are stable to atmospheric oxygen and moisture. Certain iodonium salts are less stable and should be generated *in situ*. A mild explosion will occur if heated in the absence of solvent for PhI(OMe)<sub>2</sub>, PhIO, PhIO<sub>2</sub>, (PhI<sup>+</sup>)<sub>2</sub>O 2BF<sub>4</sub><sup>-</sup>, and *o*-iodylbenzoic acid.
- In the solid state: Iodosylbenzene and (tosyliminoiodo)benzene are polymeric structures terminated by water: HO(PhIO)<sub>n</sub>H. Monomeric species are generated in reactive solvents. Secondary I-O bonds are also observed and result in macrocyclic structures.



### In solution:

Diaryl-I<sup>III</sup>-iodanes (Ar<sub>2</sub>IL, where L = BF<sub>4</sub><sup>-</sup>, Cl, Br, OAc) in polar solvents show extensive dissociation into solvated iodonium ions (Ar<sub>2</sub>IS<sup>+</sup> where S = H<sub>2</sub>O, MeOH, and DMSO)

Alkenyl-I<sup>III</sup>-iodanes exist in equilibrium as an iodonium ion and as a halogen-bridged dimeric and aggregate structures.

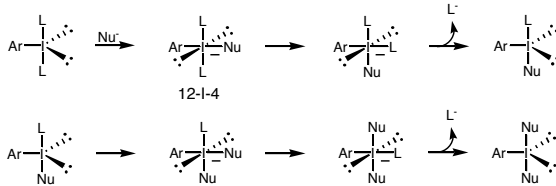


## General Reactivity of Hypervalent Iodine

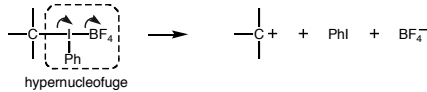
- Hypervalent iodine chemistry is based on the strongly electrophilic nature of the iodine making it susceptible to nucleophilic attack, in combination with the leaving group ability of phenyliodonio group -IPhX (~10<sup>6</sup> times greater than triflate!!!). The favorable reduction of the hypervalent iodide to normal valency by reductive elimination of iodobenzene is the key to its reactivity.
- Organo- $\lambda^3$ -iodanes have reactivity based on the number of carbon and heteroatom ligands. They generally fit in two classes:

(1) RIL<sub>2</sub>: Majority of reactions fit under this category. Performs oxidation of various functional groups. The two heteroatoms occupying the apical sites of the pseudo-trigonal bipyramid are essential – one is used in ligand exchange and the other in reductive elimination.

### Ligand Exchange

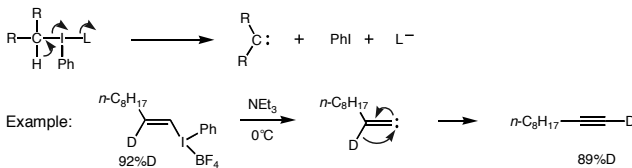


### Reductive Elimination of the Hypernucleofuge

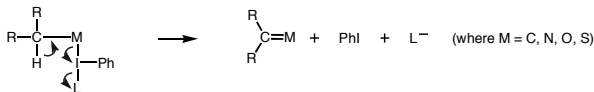


## Reductive $\alpha$ - and $\beta$ -Elimination of RIL<sub>2</sub> Organo- $\lambda^3$ -Iodanes

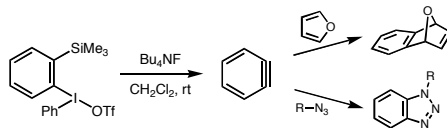
**Reductive  $\alpha$ -Elimination:** Provides a method for the generation of carbenes.



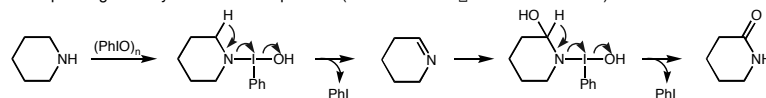
**Reductive  $\beta$ -Elimination**



On carbon atoms (M=C) produces C=C multiple bonds:

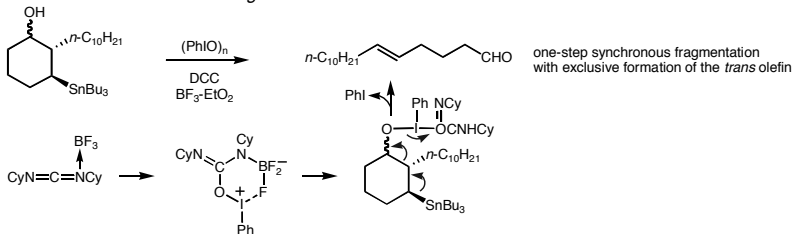


Oxygen and nitrogen atoms (M=O and N) provides oxidation of benzylic/allylic alcohols and amines to the corresponding carbonyl and imine compounds. (ie. Dess-Martin  $\lambda^3$ -iodane oxidations)

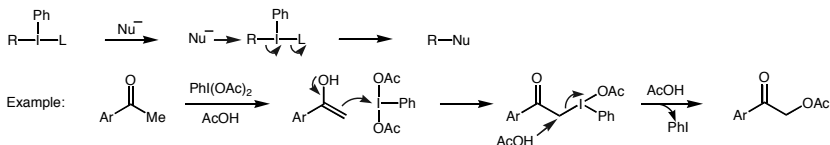


## More Reductive Eliminations of $RIL_2$ Organo- $\square^{\beta}$ -Iodanes

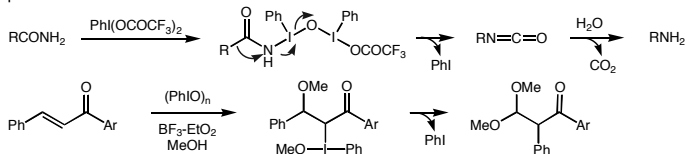
### Reductive Elimination with Fragmentation



**Reductive Elimination with Substitution:** Elimination of  $\square^{\beta}$ -iodanes with 2 carbon ligands with attack by a nucleophile on the carbon atom attached to the iodine(III) gives substitution products.

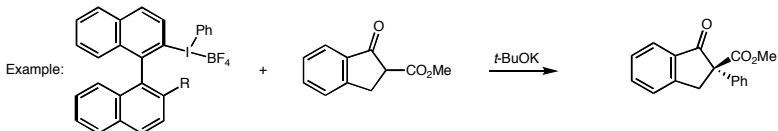
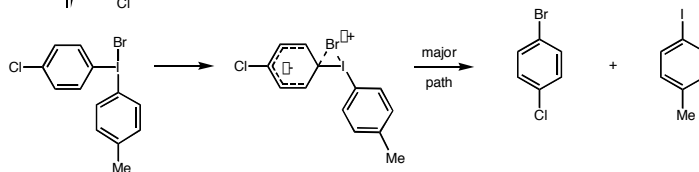
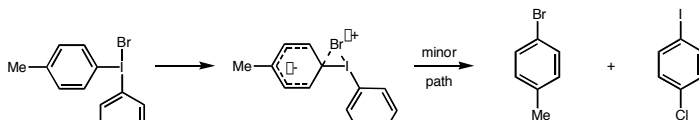


**Reductive Elimination with Rearrangement:** Elimination with concomitant 1,2-alkyl or aryl shift gives rearranged products.



## Reductive Elimination by Ligand Coupling of $RIL_2$ Organo- $\square^{\beta}$ -Iodanes

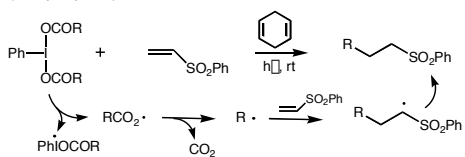
### Ligand Coupling



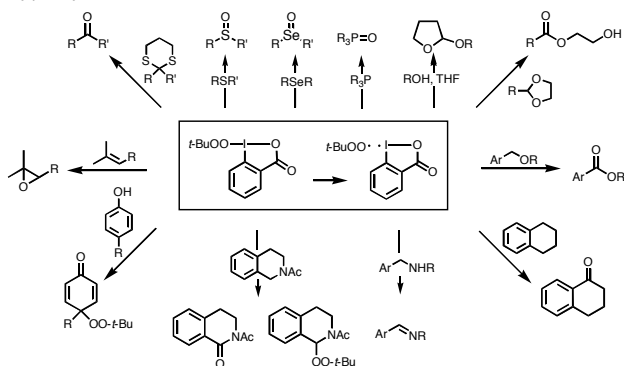
## Other Mechanisms of $RIL_2$ Organo- $\lambda^3$ -Iodanes

**Homolytic Cleavage:** Photochemical decomposition of a hypervalent I-O bond generates a reactive radical.

(Diacyloxyiodo)arenes



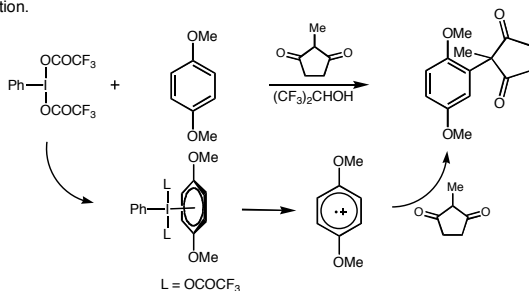
Alkylperoxy- $\lambda^3$ -iodanes



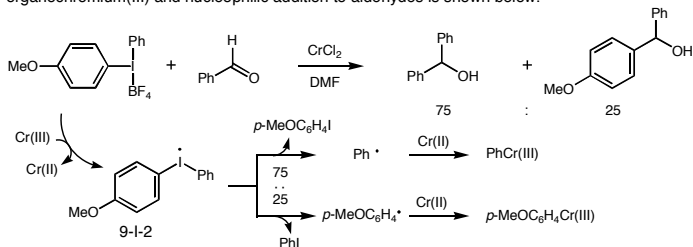
## Other Mechanisms of $RIL_2$ Organo- $\lambda^3$ -Iodanes (Continued)

**Single-Electron Transfer**

Single-electron transfer from phenol ethers to  $\lambda^3$ -iodanes generates an arene cation radical resulting in a direct nucleophilic substitution.



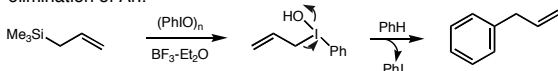
The method for reactivity umpolung of diaryl-, alkenyl(aryl)-, and alkynyl(aryl)- $\lambda^3$ -iodanes involves the generation of organochromium(III) and nucleophilic addition to aldehydes is shown below.



## Reactivity of $R_2IL$ Organo- $\Gamma^{\beta}$ -Iodanes

(2)  $R_2IL$ : Acts mainly to transfer a carbon ligand (R) to nucleophiles with reductive elimination of ArI. The nature of the carbon ligands are important in determining reactivity.

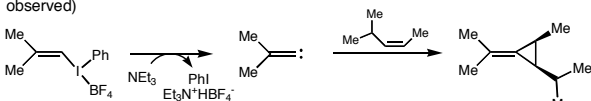
**Alkyl(aryl)- $\Gamma^{\beta}$ -Iodanes:** Generally labile and decompose readily by heterolysis of C-I bond and reductive elimination of ArI.



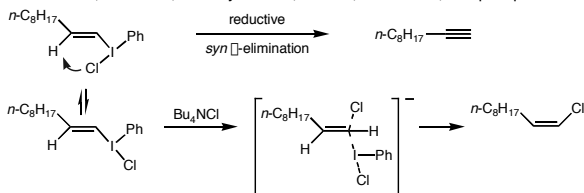
$BF_3$ -catalyzed ligand exchange of allylsilane, germane, or stannane with iodobenzene generates allyl- $\Gamma^{\beta}$ -iodane. This is a highly reactive species that is equivalent to an allyl cation. Also may serve as a perfluoroalkylating agent.

### Alkenyl(aryl)- $\Gamma^{\beta}$ -Iodanes

Progenitor of alkylidene carbene that are formed by base abstraction of an acidic  $\alpha$ -hydrogen of an alkenyl- $\Gamma^{\beta}$ -iodane. The free alkylidene carbene can form solvent-alkylidene carbene complexes (ie. in ethereal solvents an oxonium ylide is observed)



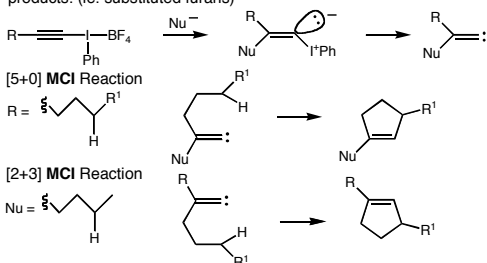
Performs nucleophilic vinylic substitutions by  $S_N2$  reaction with inversion of configuration. Nucleophiles that undergo vinylic  $S_N2$  reactions are sulfides, selenides, carboxylic acids, amides, thioamides, and phosphoroselenoates.



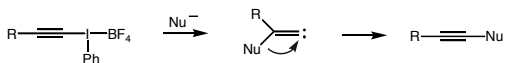
## Reactivity of $RIL_2$ Organo- $\Gamma^{\beta}$ -Iodanes (Continued)

### Alkynyl(aryl)- $\Gamma^{\beta}$ -Iodanes

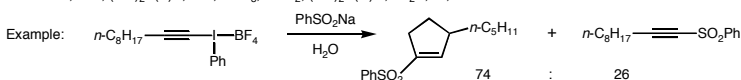
The highly electron-deficient nature of the  $\alpha$ -acetylenic carbon atom make these reagents good Michael acceptors towards soft nucleophiles (O, N, and S) and undergo tandem Michael-carbene insertion (**MCI**) to give cyclopentene annulation products. (ie. substituted furans)



Because the electron-deficient nature of the carbenic center of the alkylidene carbene, nucleophiles with high tendency to migrate undergo Michael-carbene rearrangements (**MCR**). When the migratory aptitude of a nucleophile is poor, the **MCI** pathway competes with the **MCR** reaction



Nu = NSC, TsS, (RO)<sub>2</sub>P(S)S, ArS, RSO<sub>3</sub>, RCO<sub>2</sub>, (RO)<sub>2</sub>P(O)O, Ph<sub>2</sub>N, Br, I



Other useful reactions include Diels-Alder reactions, 1,3-dipolar cycloadditions, and reactions with transition metal complexes.

## Transformations Enacted by Hypervalent Iodide Reagents

### ■ C-C Bond Forming Reactions

*Radical Decarboxylation of Organic Substrates*  
*Spirolactonization of para- and ortho-Substituted Phenols*  
*Intramolecular Oxidative Coupling of Phenol Ethers*  
*Reactions of Iodonium Salts and Ylides*

### ■ C-Heteroatom Bond Forming Reactions (N, O, P, S, Se, Te, X)

*Reactions of Aryl- $\lambda^3$ -Iodanes*  
*Arylations and Alkenylations of Nucleophiles*  
*Reactions of Alkynyl(aryl)iodonium Salt*  
*Cyanation with Cyanobenziodoxoles*  
*Aziridations and Amidations by Sulfonyliminoiodane*  
*Reactions of Iodonium Enolates*

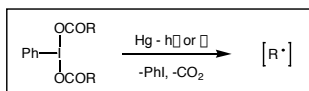
### ■ Heteroatom-Heteroatom Bond Forming Reactions

*Reactions of Aryl- $\lambda^3$ -Iodanes*  
*Reactions of Sulfonylimino(aryl)iodanes*

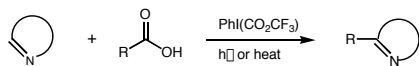
### ■ Oxidations and Rearrangements

*Sulfoxides from Sulfides*  
*Oxidations of Alcohols, Phenols, Heteroaromatic Compounds*  
*Functionalization of Carbonyl Compounds*  
*Functionalization in the  $\alpha$ -position*  
*Forming  $\alpha,\beta$ -Unsaturation*  
*Oxidation of C-H Bonds*  
*Rearrangements*

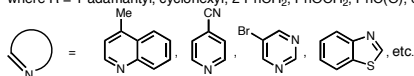
## C-C Bond Forming Rxns: Radical Decarboxylative Alkylation of [Bis(acyloxy)iodo]arenes



### ■ Alkylation of Nitrogen Heterocycles

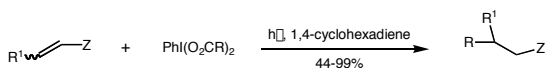


where R = 1-adamantyl, cyclohexyl, 2-PhCH<sub>2</sub>, PhOCH<sub>2</sub>, PhC(O), etc. and



### ■ Radical Alkylation of Electron-Deficient Alkenes

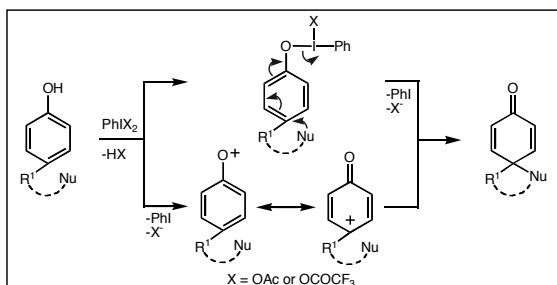
Yield of products depends on the stability and nucleophilicity of the alkyl radicals (tertiary > secondary > primary).



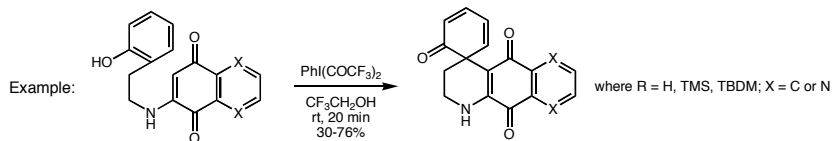
where Z = SO<sub>2</sub>Ph, SOPh, CO<sub>2</sub>Me, P(O)(OEt)<sub>2</sub>; R<sup>1</sup> = H, Me  
 R = 1-adamantyl, cyclohexyl, 2-PhCH<sub>2</sub>CH<sub>2</sub>, etc.



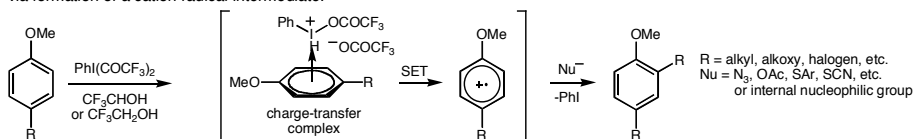
## C-C Bond Forming Rxns: Oxidative Cyclization of Phenols and Phenol Ethers



Important in constructing of various polycyclic systems from *p*- or *o*-substituted phenols with an external or internal nucleophile like alcohols, fluoride ions, amides, allylsilanes, and electron-rich aromatic rings.

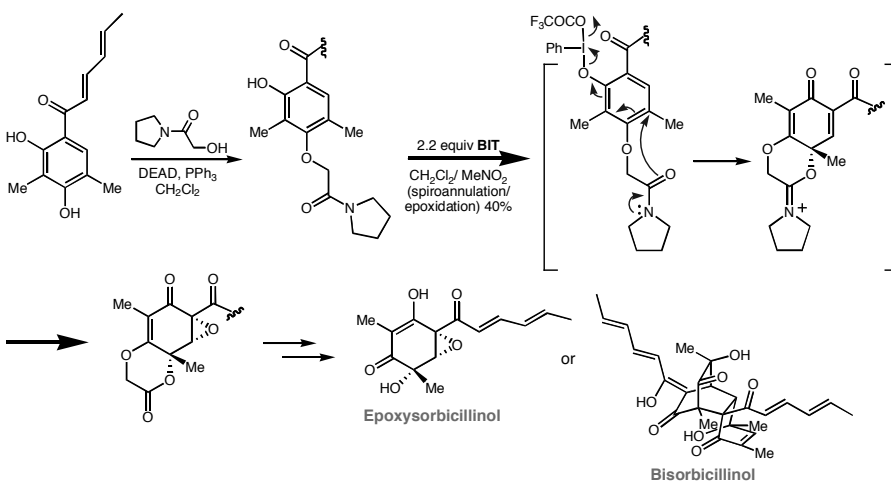


Oxidation of phenol ether in the presence of an external or internal nucleophile affords products of nucleophilic substitution via formation of a cation radical intermediate.



## Examples in Total Synthesis: Epoxysorbicillinol and Bisorbicillinol

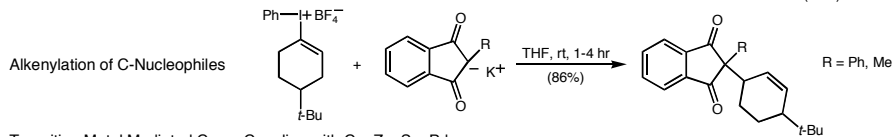
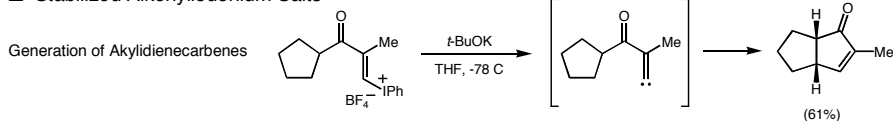
### ■ Hypervalent Iodide(III) Induced Oxidative Dearomatization





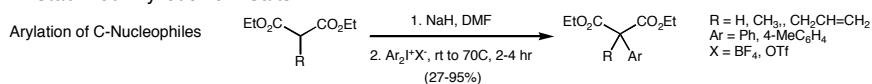
## C-C Bond Forming Rxns: Reactions of Iodonium Salts (Continued)

### ■ Stabilized Alkenyliodonium Salts

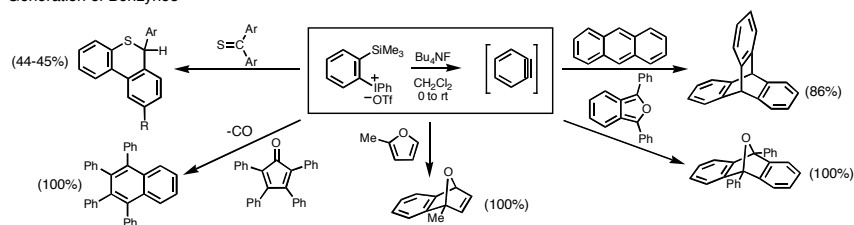


Transition Metal Mediated Cross-Coupling with Cu, Zn, Sn, Pd

### ■ Stabilized Aryliodonium Salts

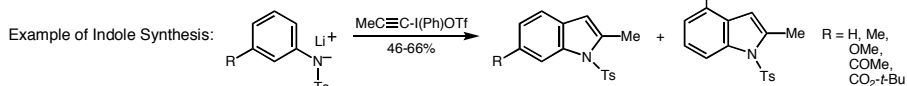
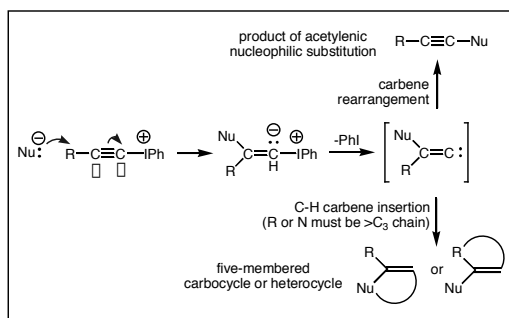


Generation of Benzynes

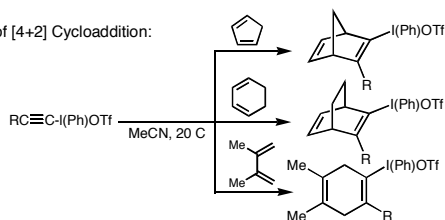


## C-C Bond Forming Rxns: Reactions of Iodonium Salts (Continued)

### ■ Alkynyliodonium Salts

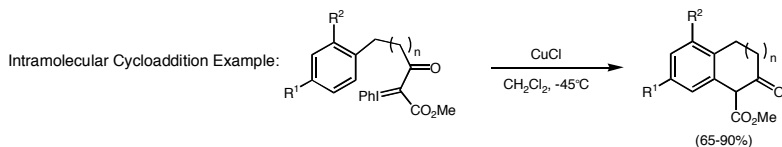
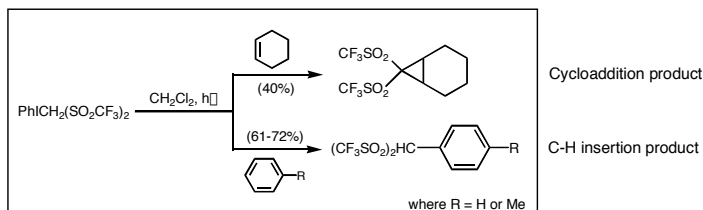


Example of [4+2] Cycloaddition:

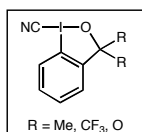


## C-C Bond Forming Rxns: Reactions with Iodonium Ylides and Cyanation

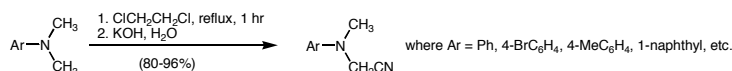
### ■ Reactions with Iodonium Ylides



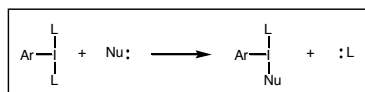
### ■ Cyanation with Cyanobenziodoxoles



Prepared in one step by cyanomethylsilane and hydroxybenziodoxoles and a stable radical precursor for an otherwise unstable I-CN bond. Efficient cyanating agents towards N,N-dialkylamines.

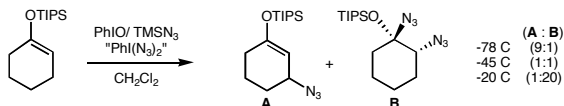


## C-Heteroatom Bond Forming Rxns: Aryl- $\beta$ -Iodanes



### ■ Azidation

Applications have been on TIPS enol ethers, glycols, dihydropyrans, aryl N,N-dialkylamines, cyclic amides, and cyclic sulfides.



### ■ Oxidative Addition of C,C-Multiple Bonds

*C,C-Double Bonds*: **DIB** with appropriate reagents results in co-introduction of equivalent/ non-equivalent heteroatom groups.

Dithiocyanation:  $\text{TMSNCS}$

Phenylselenyl-thiocyanation:  $\text{TMSNCS}$  and  $(\text{PhSe})_2$

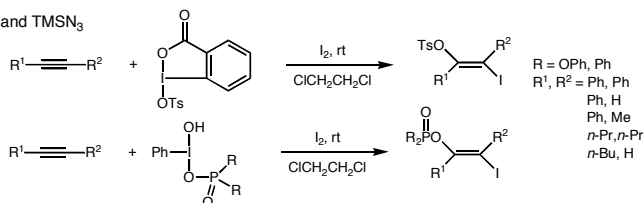
Phenylselenyl-acetoxylation:  $(\text{PhSe})_2$

Azido-phenylselenation:  $\text{NaN}_3$  and  $(\text{PhSe})_2$

Haloacetoxylation:  $\text{Ph}_4\text{P}^+\text{I}^-$

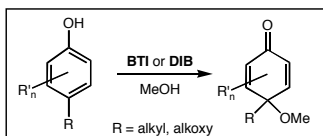
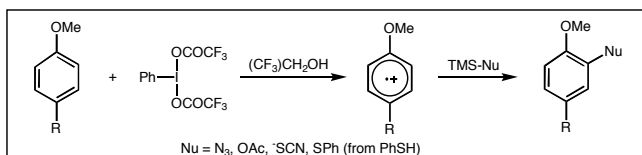
Haloazidation:  $\text{Et}_4\text{N}^+\text{X}^-$  and  $\text{TMSN}_3$

*C,C-Triple Bonds*

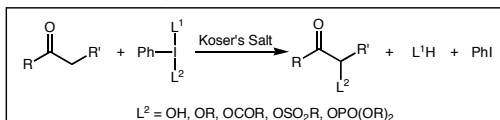


## C-Heteroatom Bond Forming Rxns: Aryl- $\text{I}^{\beta}$ -Iodanes (Continued)

### ■ Functionalization of Aromatic Compounds



### ■ $\text{I}^{\beta}$ -Functionalization of Carbonyl Compounds



### ■ C-Fluorine Bond Formations

*p*-(Difluoroiodo)toluene (**DFIT**) with appropriate reagents results in C-fluorine bond formation.

*vicinal*-difluorination of terminal alkynes:  $\text{Et}_3\text{N} \cdot 5\text{HF}$

*trans*-iodofluorination of terminal alkynes:  $\text{Et}_3\text{N} \cdot 5\text{HF}$  then  $\text{CuI}/\text{KI}$

monofluorination of  $\text{I}^{\beta}$ -dicarbonyl: (**DFIT** generated *in situ*)

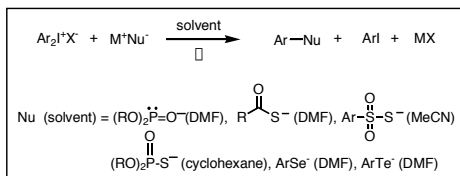
difluorination of dithioketals of benzophenone (to diarylfluoromethanes): (*in situ* generated *p*-(difluoroiodo)anisole)

fluorination of  $\text{I}^{\beta}$ -phenylsulfanyl esters and lactones: (DFIT-induced fluoro-Pummerer rxn)

alcohols to 1°- and 2°-alkyl fluorides: conversion to xanthate esters followed by **DFIT**

## C-Heteroatom Bond Forming Rxns: Diaryliodonium and Alkenyl(aryl)iodonium Salts

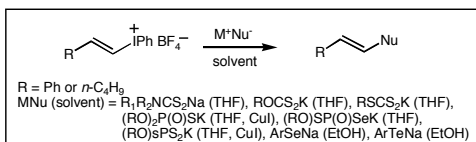
### ■ Diaryliodonium Salts



Arylations of weak organic nucleophiles are best with iodonium salts with nucleofugic anions and in some cases can be facilitated with transition metal catalysts (Cu, Pd)

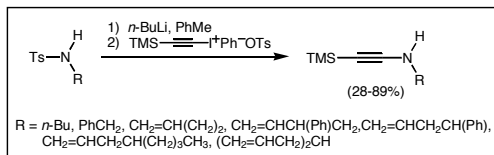
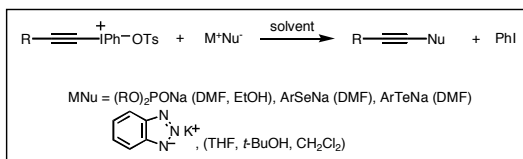
### ■ Alkenyl(aryl)iodonium Salts

Alkenylations of heteroatom nucleophiles occur by a variety of mechanisms;  $\text{S}_{\text{N}}1$ ,  $\text{S}_{\text{N}}2$ , alkyldiene carbene, and addition-elimination pathways.

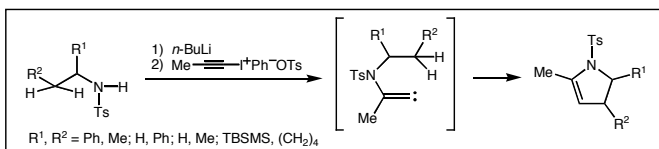


## C-Heteroatom Bond Forming Rxns: Alkynyl(aryl)iodonium Salts

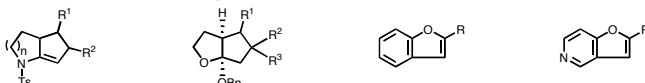
### Alkynylation



### C-H Bond Insertions

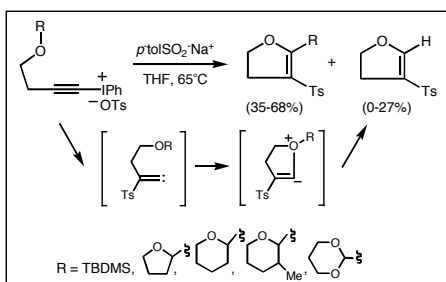


Intramolecular C-H bond insertions result in bicyclizations

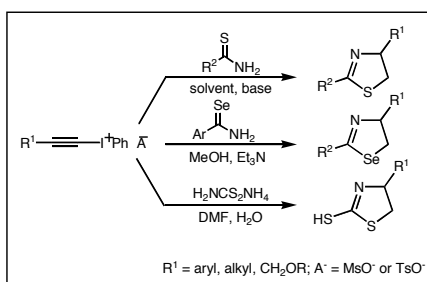


## C-Heteroatom Bond Forming Rxns: Alkynyl(aryl)iodonium Salts and Enolates

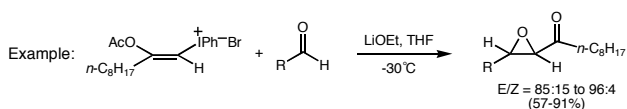
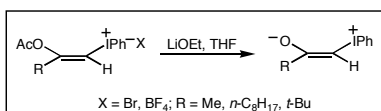
### C-Heteroatom Bond Insertions



### Cyclocondensations



### Iodonium Enolates

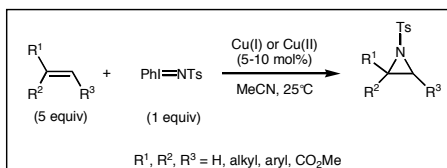


R = R'<sub>2</sub>CH (R' = H, 2-Me, 4-Me, 4-F, 4-Cl, 4-Br, 4-NO<sub>2</sub>), Et, *n*-C<sub>8</sub>H<sub>17</sub>, *i*-Pr, *t*-Bu, (E)-MeCH=CH

## C-Heteroatom Bond Forming Rxns: Sulfonylimino(aryl)iodanes

### ■ Aziridation

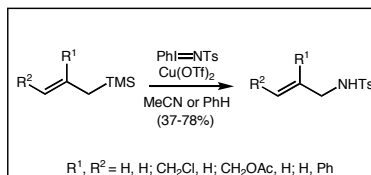
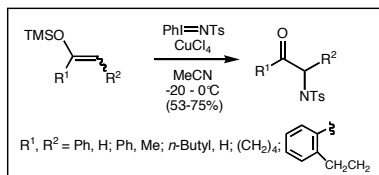
PhI=NTs as a nitrene transfer agents has been demonstrated with Mn(III)- and Fe(III) porphyrins and more generally with Cu(I)/Cu(II) salts (Evan's aziridation reaction) on cyclic/ acyclic alkenes, arylalkenes, and  $\alpha,\beta$ -unsaturated esters.



Product yields increase with substitution on the arenesulfonyl moiety ( $p$ -OMe >  $p$ -Me >  $p$ -NO<sub>2</sub>).

Chiral ligands (bis(oxazolines) and bis(benzylidene)diaminocyclohexanes) give asymmetric tosylaziridations (e.e. = 66%-94%). More reactive are [nosylimino]iodobenzene (**PhI=NNs**) and [(2-trimethylsilyl)ethanesulfonylimino]iodobenzene (**PhI=NSes**).

### ■ Amidations

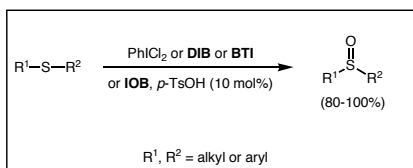


Chiral allylic and benzylic tosylamidations are performed with salen-Mn(III) complexes, Ru(II) and Mn(III)-porphyrins, and Ru(II)- and Ru(III)-amine complexes as catalysts. (e.e. = 41-67% for cyclic compounds and 12-53% for acyclic compounds)

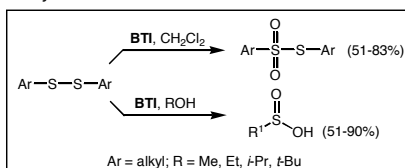
## Heteroatom-Heteroatom Bond Forming Rxns

### ■ Aryl- $\sigma^3$ -Iodanes: Oxidation of S, P, Se, Te, Sn, & Bi

#### Sulfide Oxidation

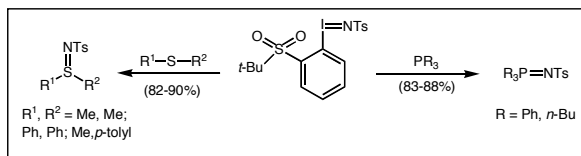
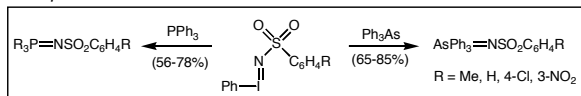


#### Diaryldisulfide Oxidation

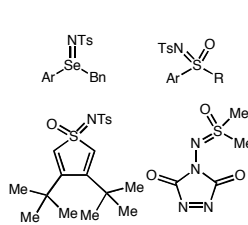


### ■ Sulfonylimino(aryl)iodanes: Constructing P-N, S-N, Se-N, As-N Bonds

#### Phosphorous and Arsenic Ylide Formation



#### PhI=NTs Reaction Products



## Summary of Oxidations with Hypervalent Iodine Compounds

### Chalcogen Oxidation

Sulfides to sulfoxides with **IOB** and **BTI**.  
 Disulfides to sulfinic esters or thiosulfonic S-esters.  
 Diselenides to selenosulfonates.  
 Ditellurides to mixed arenetellurinic anhydrides.

### Alcohols to Carbonyls

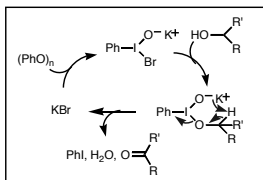
#### Iodine (V) Reagents

**DMP** or **IBX**: alcohol to aldehydes & ketones  
**IBX** + Wittig Ylides: benzylic, allylic, propargylic alcohol to  $\alpha,\beta$ -unsaturated ester  
 (water soluble reagent) benzylic, allylic, propargylic alc. oxidation



#### Iodine (III) Reagents

**DIB** + **TEMPO**: selective 1° alcohol to aldehyde  
**IOB** + cat. **KBr**: 1° alcohol to  $\text{RCO}_2\text{H}$ ,  
 2° alcohol to ketone  
**DIB** + **TMSN<sub>3</sub>**: desilylation and oxidation of glycols



### Oxidations of Phenols

#### Iodine (V) Reagents

**IBX**: Phenol to *ortho*-quinone only  
**DMP** + water: Anilides to *o*-imidoquinones and  
*p*-anilines to *para*-quinones



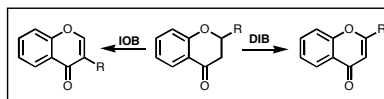
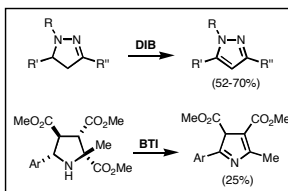
#### Iodine (III) Reagents

**BIT** or **DIB**: Phenols to quinones by oxidations at  
*o*- or *p*-position.  
**DIB** + water: Phenols or anilines to *p*-quinones



### Oxidations of Heteroaromatic Compounds

Aromatization of 5 and 6 membered rings using **BIT** or **DIB**



## Oxidations & Rearrangements Using Hypervalent Iodine Compounds

### $\alpha,\beta$ -Functionalization of Carbonyl Compds

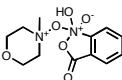
(Nucleophilic attack on phenyliodinated intermediate)

**IBX**/ **BID**/ **IOB** + base: Yields  $\alpha,\beta$ -hydroxylated acetals  
**HTI**:  $\alpha$ -tosylation of ketone (silyl enol ethers)



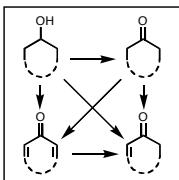
**HTI**:  $\alpha$ -tosylation with about 40% e.e.

### Introduction of $\alpha,\beta$ -Unsaturation



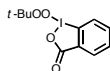
**HTI**: Dehydrogenation of enone via *in situ* formation of silyl enol ether

**IBX**: Dehydrogenation by single electron transfer process



### Oxidation of C-H Bonds

: Oxidation of benzylic, allylic, or propargylic ethers to esters by a radical process.

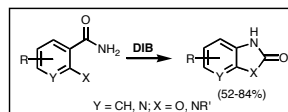


: Removal of benzyl ether protecting groups

### Rearrangements

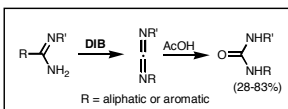
#### Hofmann-type Rearrangements

**BID**: Cyclizations of aromatic amides with a nucleophile in the *ortho*-position.

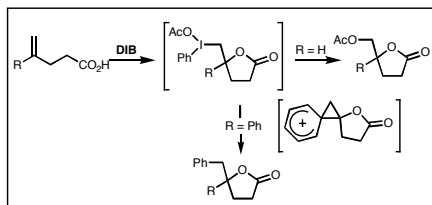


#### Rearrangement of Amidines

**BID**: Forms urea derivatives via carbodiimide intermediate.



#### Cyclization of Unsaturated Carboxylic Acids



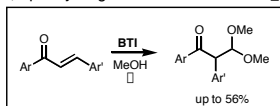


## Rearrangements Using Hypervalent Iodine Compounds

### ■ Rearrangements (Continued)

#### Rearrangement of Chalcones

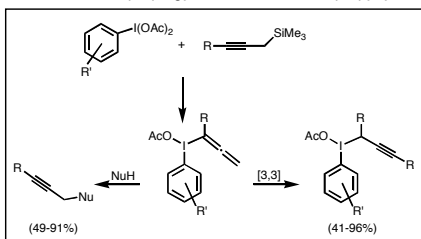
**BTI:** 1,2-phenyl migration and formation of  $\beta$ -acetal



#### Iodonio-Claisen Rearrangement

Alkenyl(phenyl)iodine(III) compounds or

**DIB** derivatives + propargyl silanes: Access to propynyl cmpds.



Alkynyl(phenyl)iodine(III) compounds:

Thioamides yield thiazoles

Furan derivative ring enlargements to yield pyrones

## Conclusions and Future Direction of the Hypervalent Iodine Chemistry

### ■ Future Goals

*Searching for newer reagents that will lead to new reaction transformations.*

*Recycleable polymer supported reagents*

*Broadening the scope of reactivity by studying transition metal-mediated reactions*

### ■ Conclusions

*The chemistry of hypervalent iodine reagents is cool because:*

- (1) Fundamental reactions with versatility have been developed
- (2) Mild reactivity with good yields
- (3) Readily available reagents that easy to work with
- (4) Non-toxic, enviromentally-friendly reagents