

***Polyvalent Iodine in Synthesis
(more than just Dess-Martin)***

Matthew M. Kreilein
Wednesday, December 13th, 2006

General Notes:

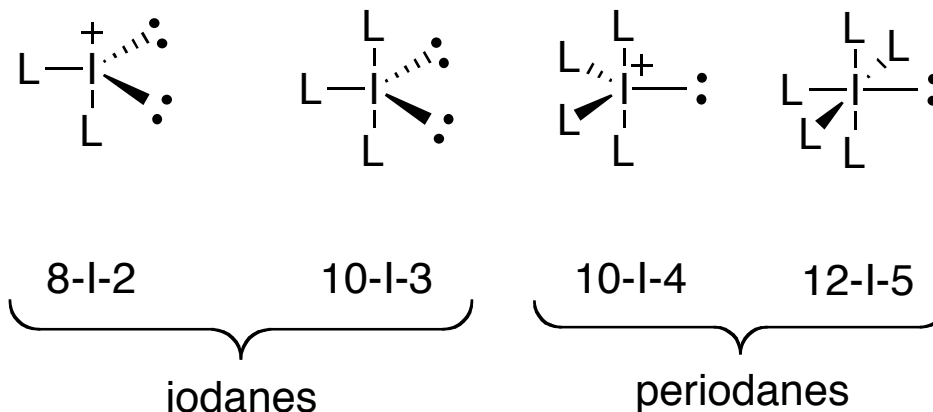
- + A LOT older than I though originally.
- + PhICl_2 was the first reported polyvalent iodine(III) compound prepared in 1886 by Willgerodt in Germany. PhIO_2 first iodine(V) compound, Willgerodt in 1900.
- + Chemical properties similar to Hg(II) , Tl(III) , Pb(IV) , without the nastiness. Also similar to organometallics to a certain extent (ligand exchange, reductive elimination, etc.)
- + Four most useful forms in organic chemistry are as follows:

N-X-L system

N = no. of valence electrons

X = heteroatom

L = no. of ligands



General Notes:

- + Further “classified” by number of carbon ligands. Number of carbon ligands affects the reactivity

Derivatives of Iodine(III) with one carbon ligand:

Iodosylarenes - ArIO

Iodoaryl halides - ArIX_2

[Bis(acyloxy)iodo]arenes - $\text{ArI}(\text{O}_2\text{CR})_2$

Strong acid derivatives - ArIX_2 ($\text{X} = \text{RSO}_3, \text{ClO}_4, \text{NO}_3, \text{etc.}$)

Five-membered Iodine(III) heterocycles (benziodoxoles and benziodazoles)

Derivatives with I-N bonds (amidodanes, iminiodanes, azidoiodanes)

Derivatives with I-“element” bonds

Iodine(III) species with one sp^3 -carbon ligand

Derivatives of Iodine(III) with two carbon ligands:

Cyano-, alkynyl-, alkenyl-, aryl-, heteroaryl-, alkyl-, and fluoroalkyliodonium salts

Iodonium ylides

Iodonium imides

Derivatives of Iodine(III) with three carbon ligands

Derivatives of Iodine(V):

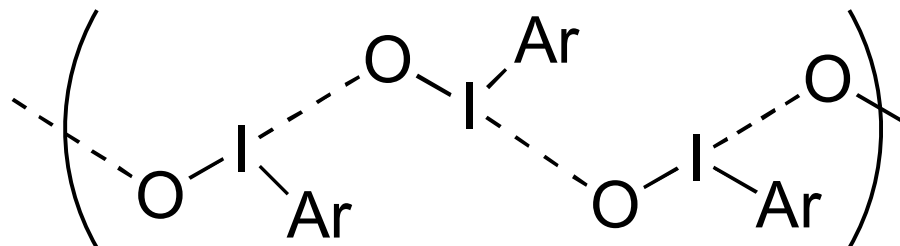
Iodyl compounds

Benziodoxole Oxides (IBX, DMP)

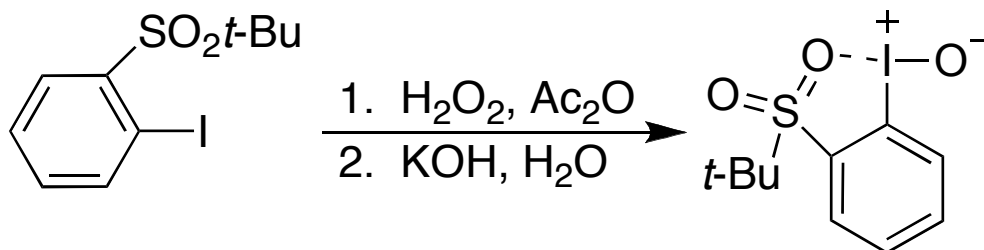
Derivatives of Iodine(III) with one carbon ligand

Iodosyl arenes - ArIO

- + polymeric in solution with secondary I-O bonds

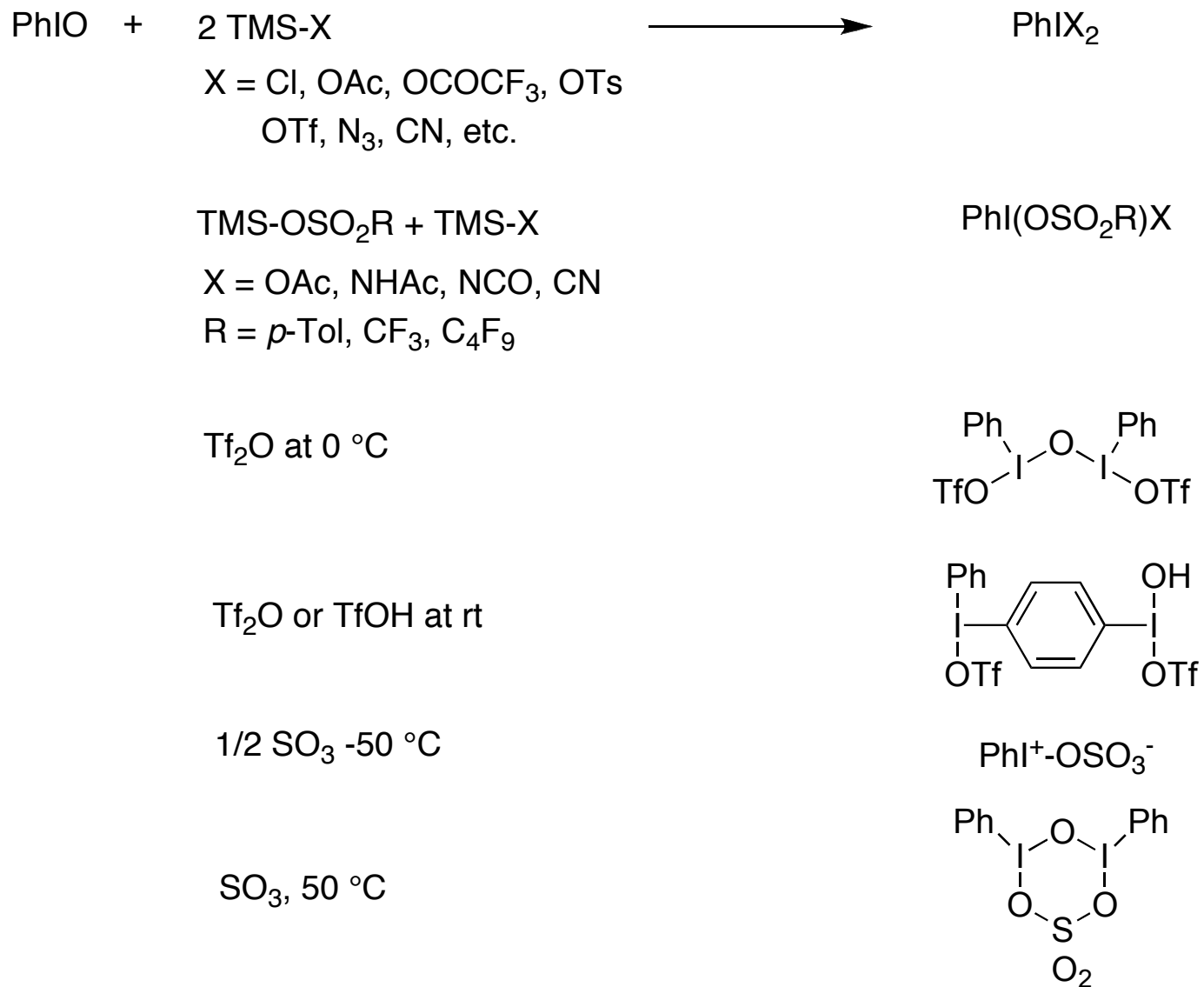


- + but some have been isolated as monomers (intramolecular stabilization):



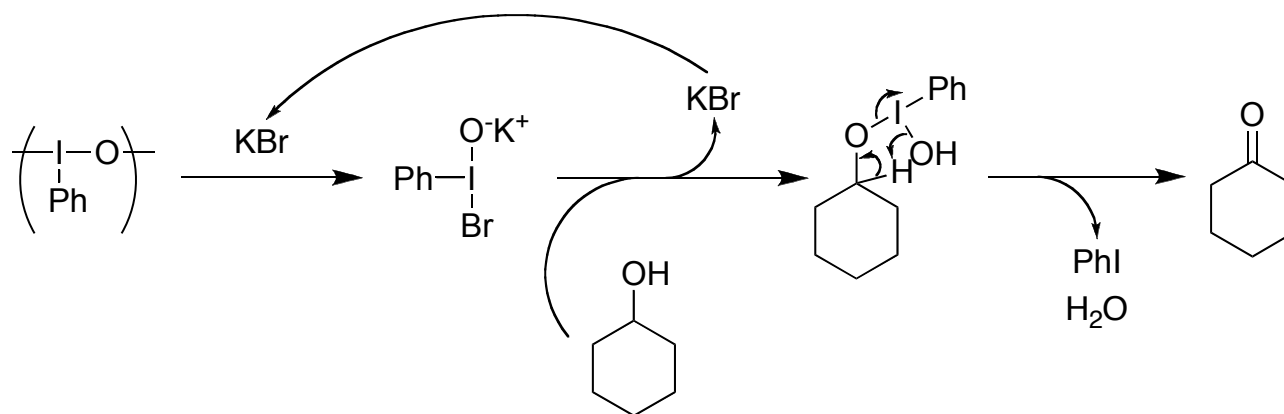
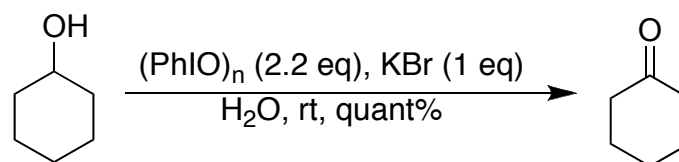
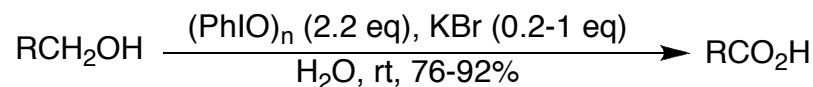
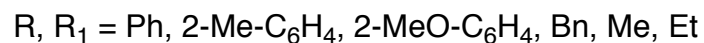
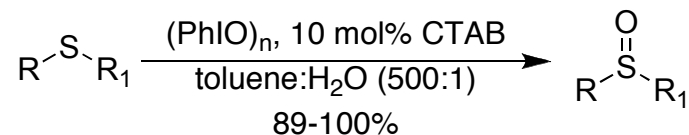
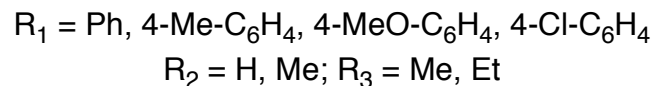
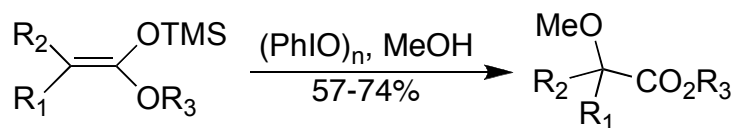
- + PhIO reactions usually carried out with a catalyst (Lewis acid, hydroxylic solvent, and others) in order to depolymerize.
- + PhIO can also be activated in solid state by pulverization (mortar/pestle) with natural clays, cation-exchange clays, and HCl-activated silica gel

+ Can be used as a precursor to a TON of other iodine(III) reagents:



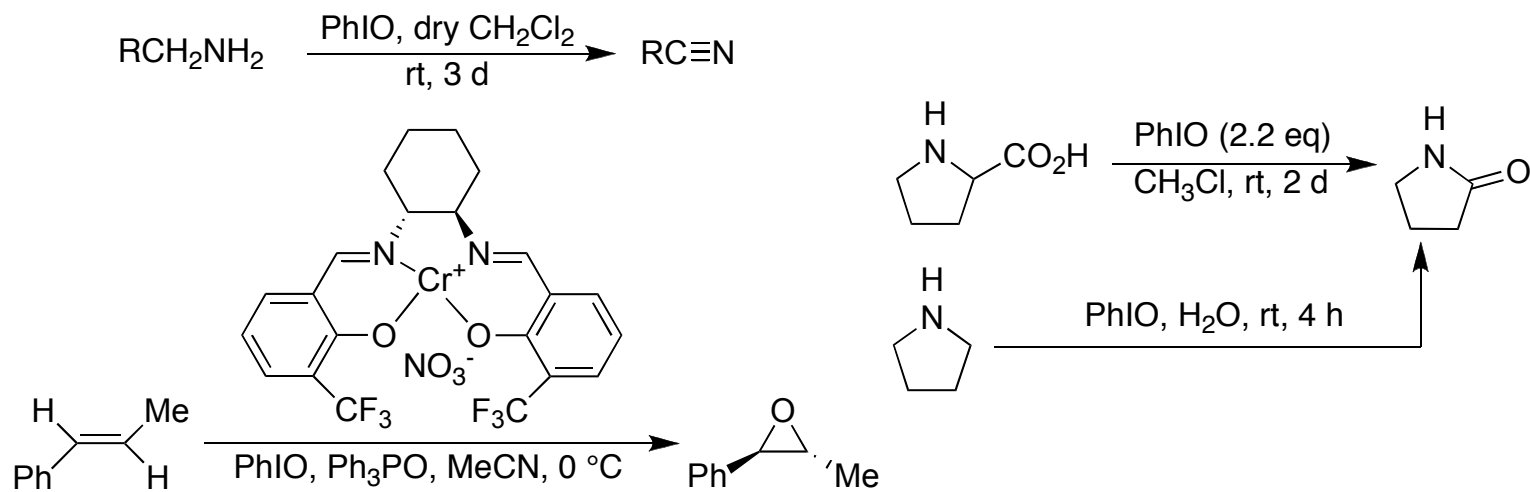
Iodosylbenzene - PhIO

- + α -methoxylation of silyl ketene acetals
- + oxidation of 1^o alcohols to carboxylic acids, 2^o alcohols to ketones, sulfides to sulfoxides
- + reaction tolerant of several functional groups

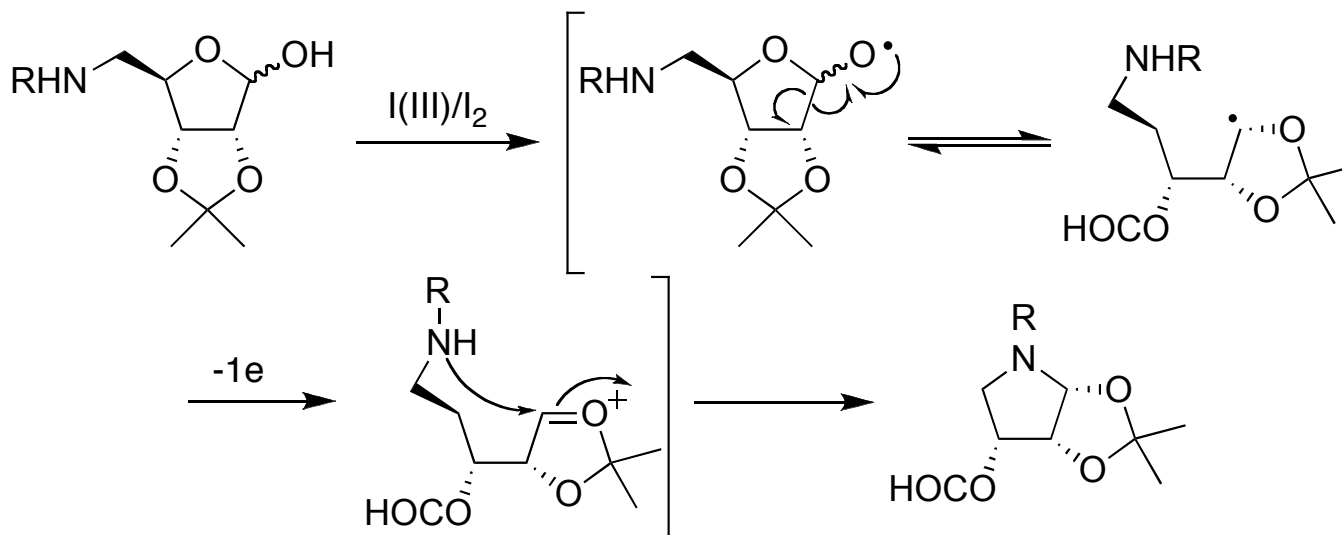


In MeOH, PhIO converted to $\text{PhI}(\text{OMe})_2$, in water, PhIO converted to $\text{PhI}(\text{OH})_2$

- + Other oxidations can be accomplished (very substrate dependent), asymmetric variants also known using chiral Cr, Mn(III), Ru(II)/(III) complexes

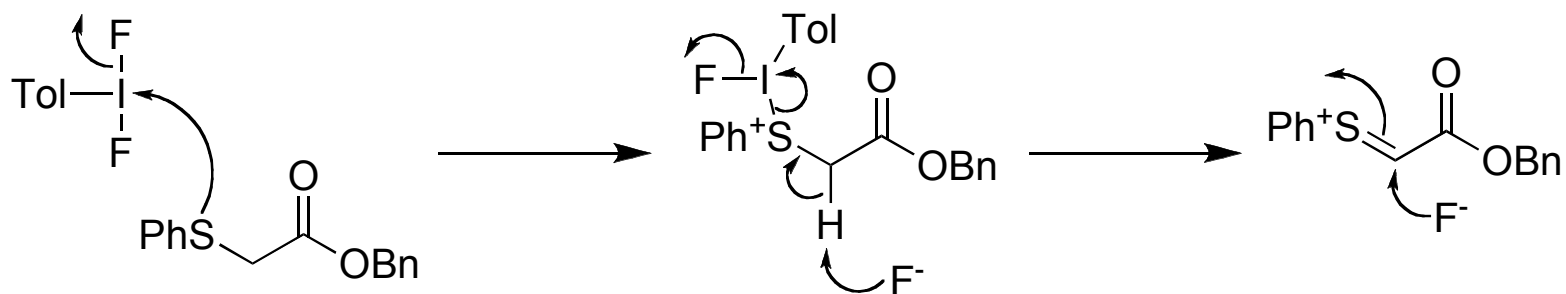
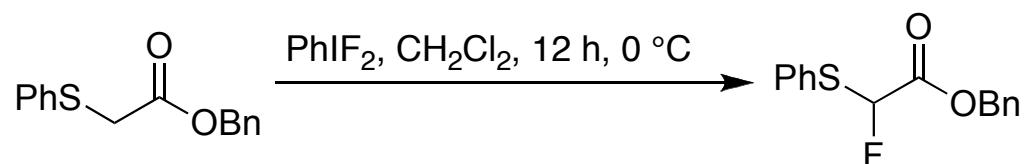
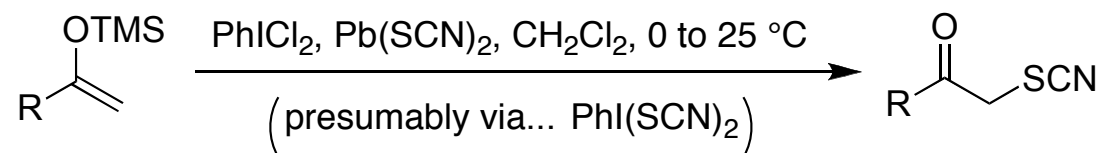


- + In concert with I_2 , initiates radical chemistry...



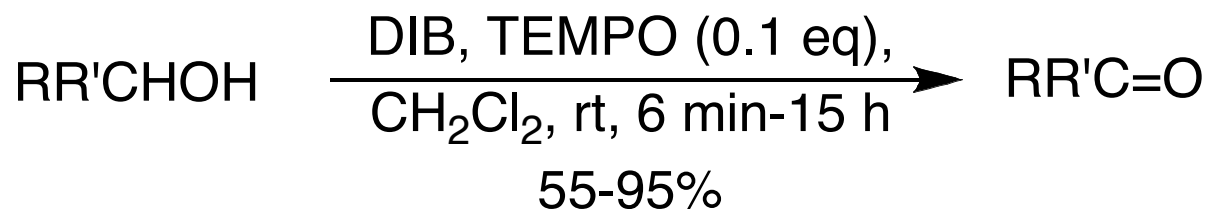
Iodoaryl halides - PhIX₂

- + Very powerful yet selective halogenating agents; however, they aren't that widely used due to...
 - difficult preparation (unless you like working with XeF₂, F₂, HF/HgO, etc. for example)
 - instability - PhIF₂ for example is VERY hygroscopic so using any aqueous methods is VERY clunky, bromides are unstable to the point that they can't be isolated as individual compounds.
- + Sometimes though, may be the best way to go...



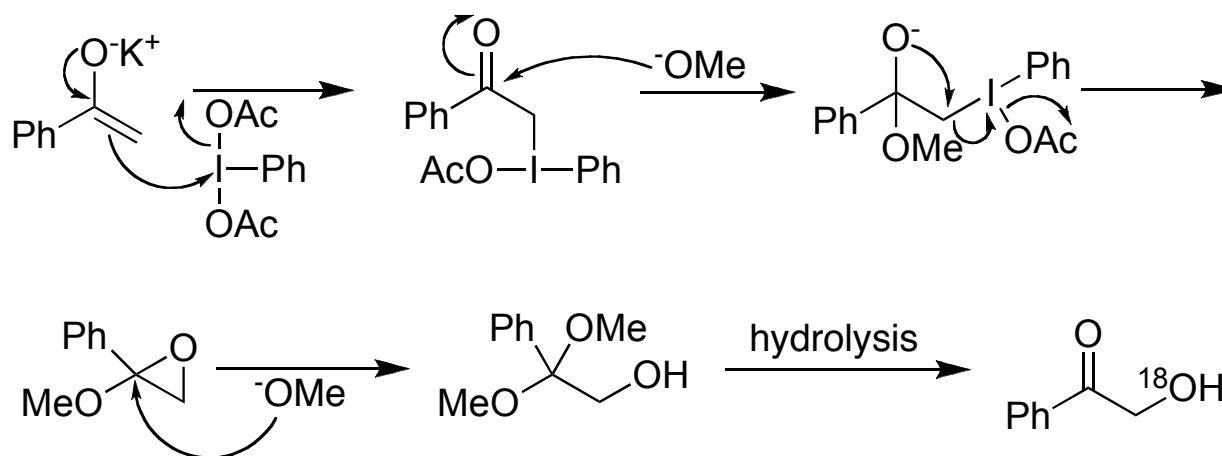
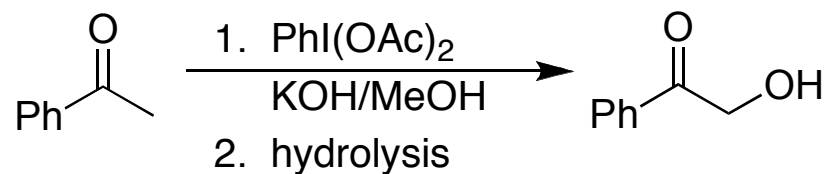
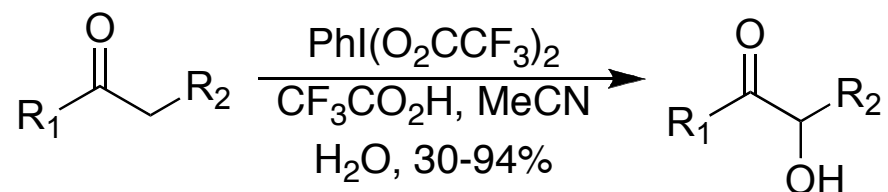
[Bis(acyloxy)iodo]arenes - ArI(O₂CR)₂

- + Probably the most well-known and well studied of the polyvalent iodine(III) compounds
- + Two are commercially available...
 - (diacetoxyiodo)benzene - DIB - PhI(OAc)₂ - 100g ~\$100
 - [bis(trifluoroacetoxy)iodo]benzene - BTI - PhI(OCOCF₃)₂ - 50g ~\$150
- + Also can be used to make a TRAINLOAD of other [bis(acyloxy)iodo]arenes (WAY too many to partially list).
- + Attachment to make polymer-supported variations has also been detailed.
- + Most useful as an oxidant for alkenes, heteroatoms, oxidative halogenation, phenols, phenolic ethers as well as a radical initiator at carbon, oxygen, and nitrogen.
- + Quite LOW reactivity for the oxidation of alcohols to aldehydes and ketones. Oxidation can be carried out under μ w or with addition of TEMPO. Useful if you need to oxidize another functional group with an alcohol or aldehyde present as oxidations with ArI(O₂CR)₂ do not give overoxidation to the acid.



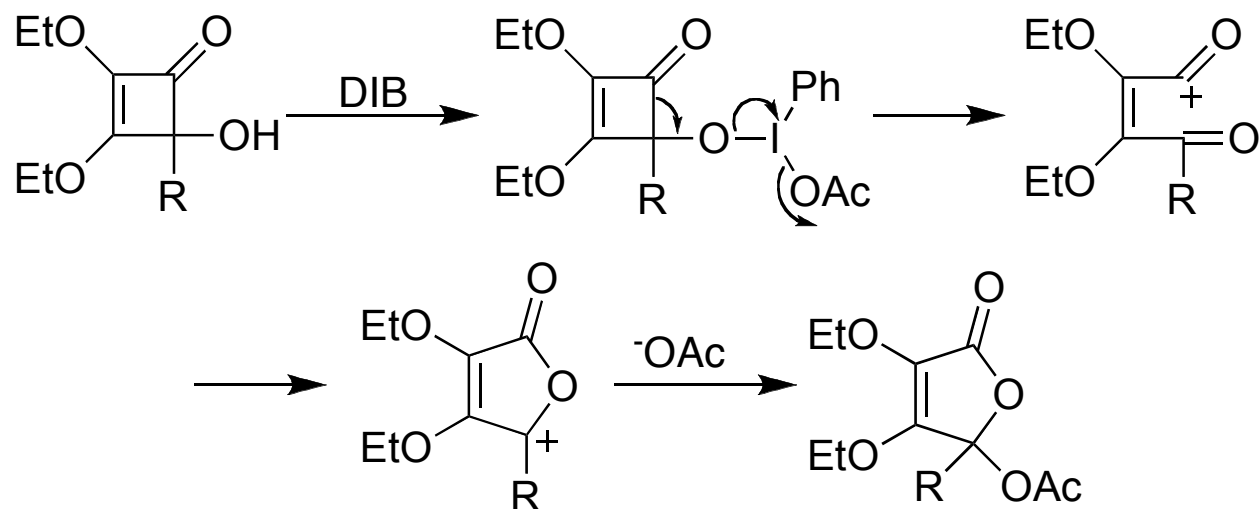
[Bis(acyloxy)iodo]arenes - $\text{ArI}(\text{O}_2\text{CR})_2$

+ α -hydroxylation of enolizable carbonyls

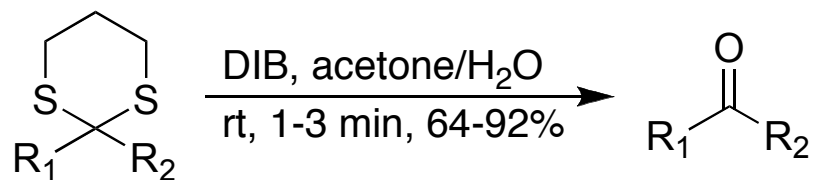
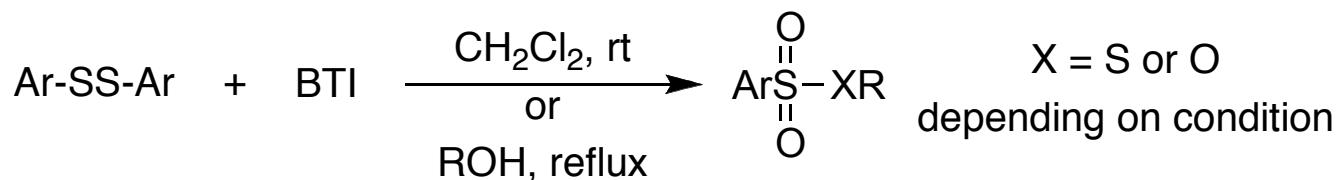


^{18}O label ends up here
if ^{18}O labelled acetophenone is used

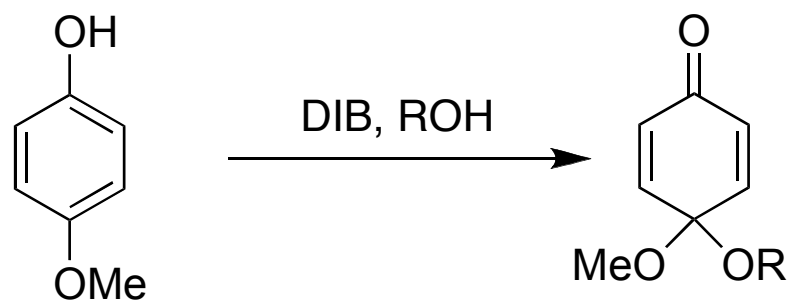
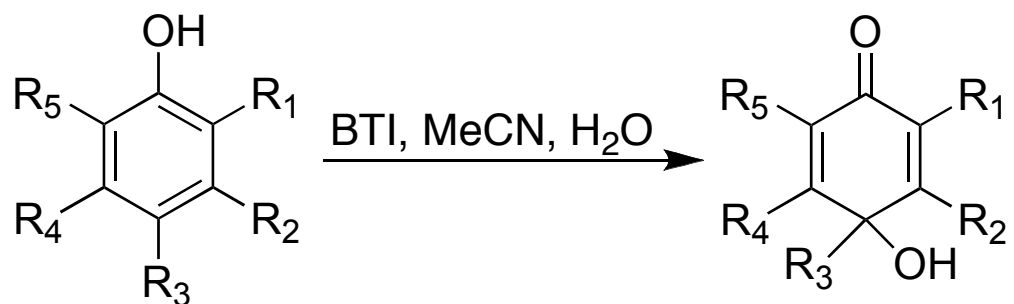
- + several fragmentations and rearrangements catalyzed by DIB and BTI especially at electron-deficient centers.



- + Also possible to oxidize sulfides to thiosulfonic S-esters or to arylsulfinic esters.
- + Notable use in sulfur oxidation is formation of carbonyls from monothioacetals or dithianes

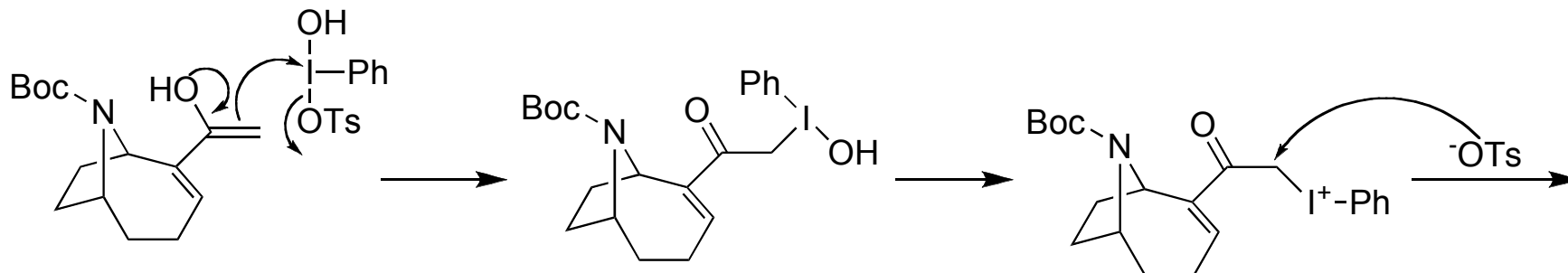
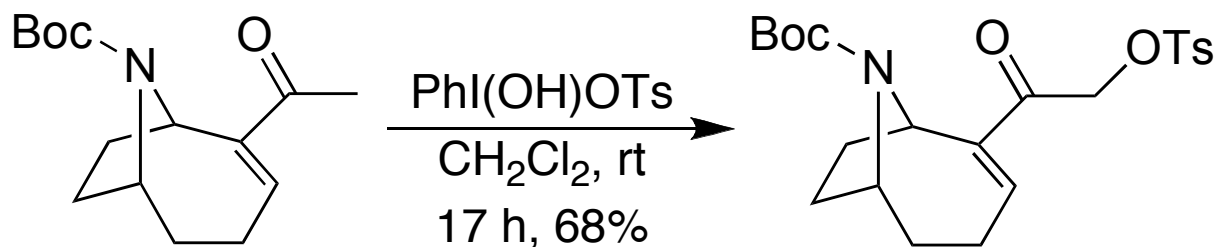


+ oxidation of phenols can be carried out using both DIB and BTI

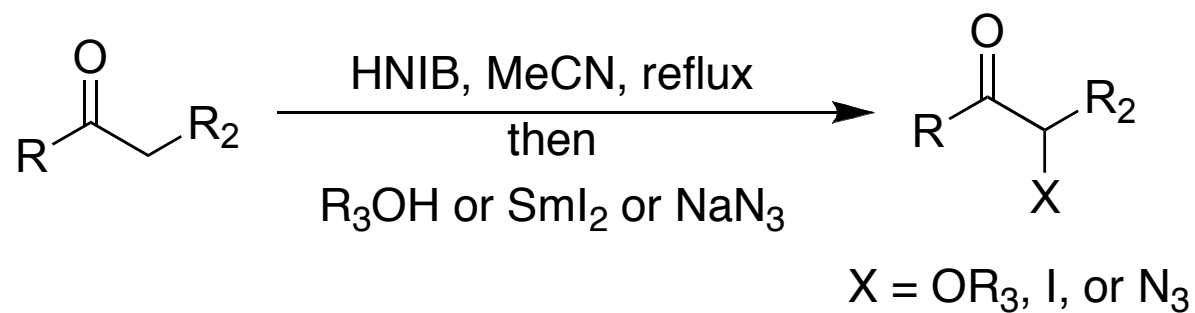


“Strong acid Derivatives” - ArI(OH)X

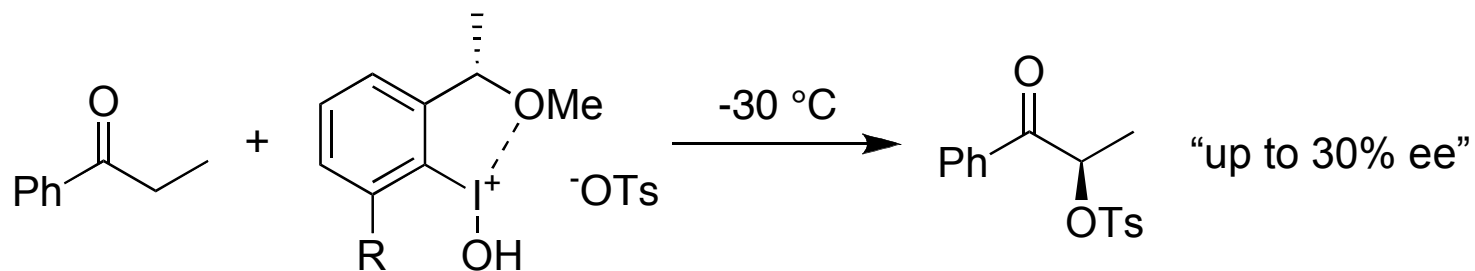
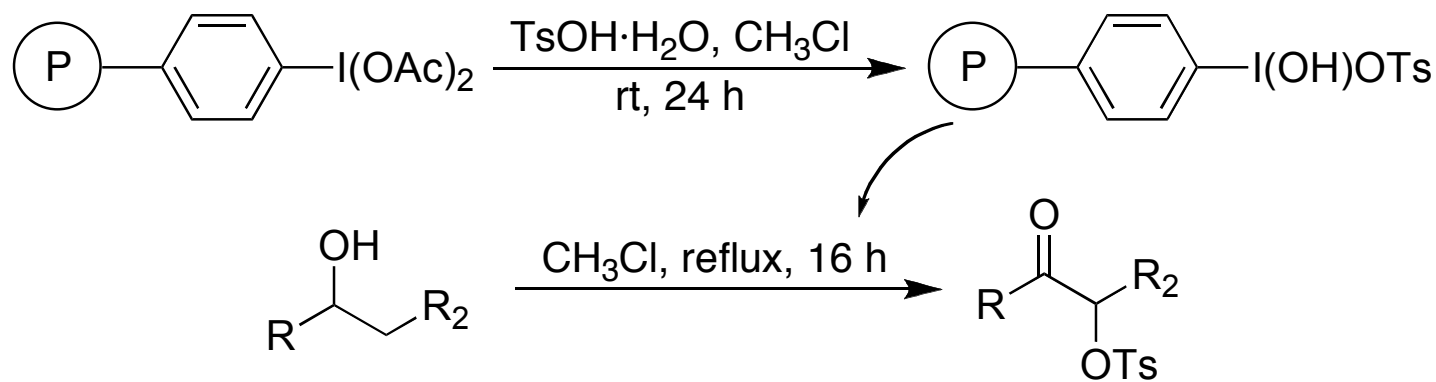
- + Most common is [hydroxy(tosyloxy)iodo]benzene - PhI(OH)OTs - HTIB also called “Koser’s Reagent”
- + The mesylate form of HTIB is also available PhI(OH)OMs as is the phosphoryl PhI(OH)OPO(OR)₂ and “nosyl” flavor PhI(OH)ONs
- + In solution, these tend to be fully dissociated into PhI⁺OH⁻OTs (for example).
- + Many uses for these, but the primary use is for the functionalization of carbonyl compounds by addition of the X group to the α-carbon, which is VERY handy for one step functionalization of carbonyls.



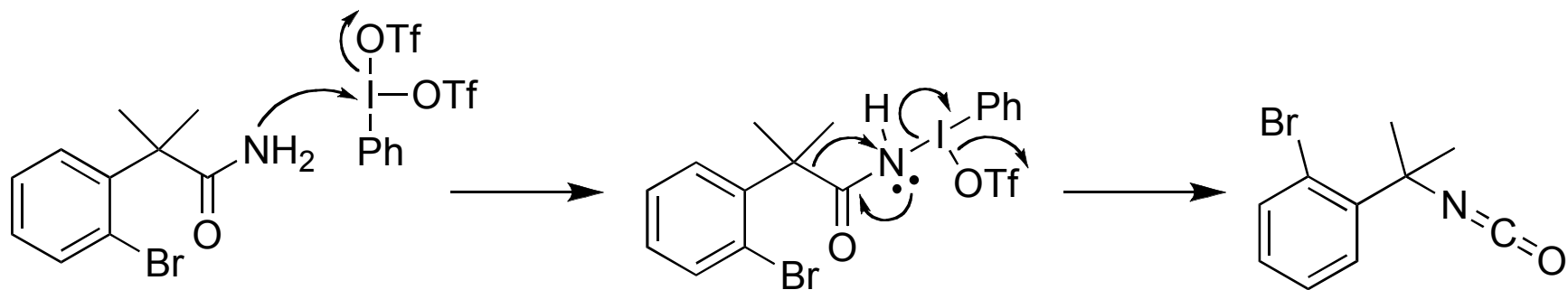
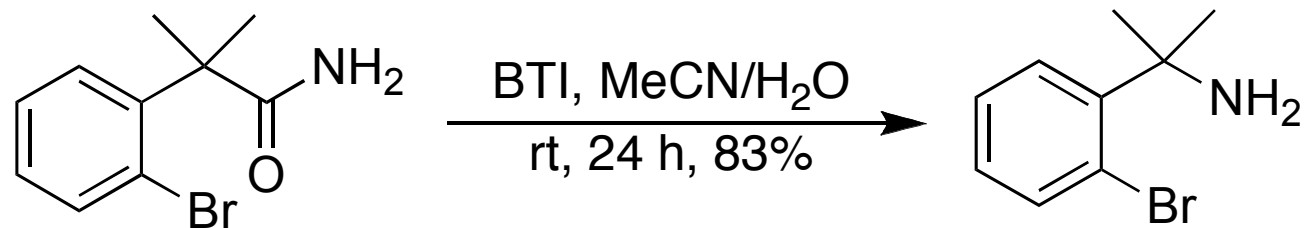
- + Functionalization of carbonyls in this manner can be followed by conversion to other functional groups. Very handy and some are one-pot two-step processes.



- + Always looking for improvements though...

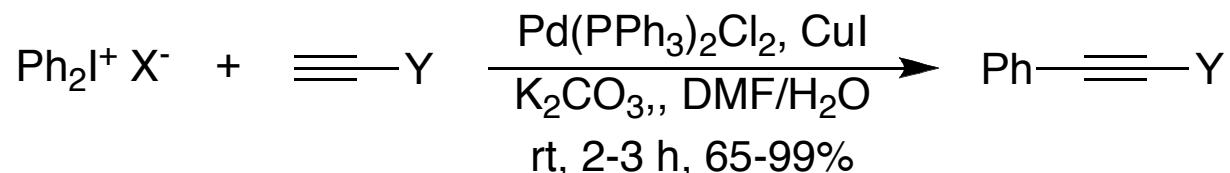


+ Can also catalyze the Hofmann Rearrangement:

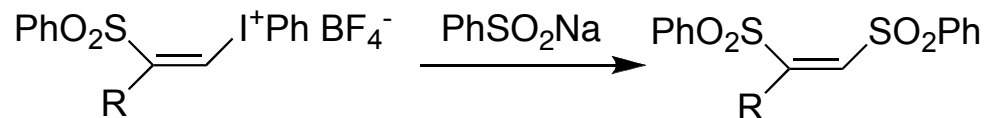
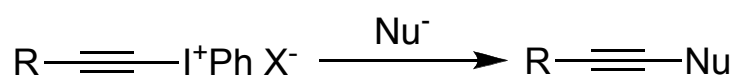


“Two carbon ligand derivatives” - translation...salts $R_2I^+ X^-$

- + These seem to have caught fire in a “random” manner.
- + No real set scale of stability, utility, etc. as it is all VERY dependent on the identity of the R and X groups. For example, several $X = CN$ variants decompose at rt in 2-5 min and explode when exposed to air; however, other $X = CN$ types (mainly the cyclic forms) are stable indefinitely.
- + Probably the most important research being done on them (synthetic organic chemist speaking) are couplings with palladium and other metals with amines, benzotriazoles, amidoximes, organoboron compounds, organostannanes, silanes, leads, zirconium compounds, phosphites, mercaptans, alcohols, allenes, substituted α,β -enones, Grignards, alkenes, alkynes, etc.

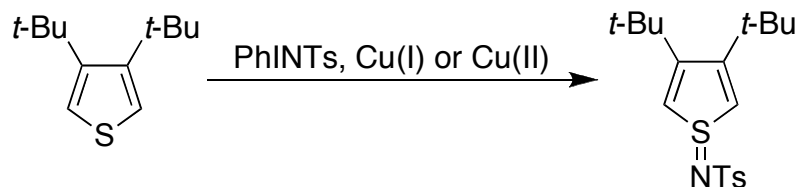
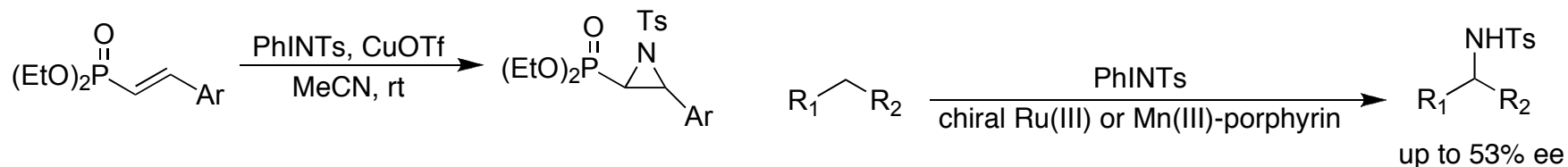
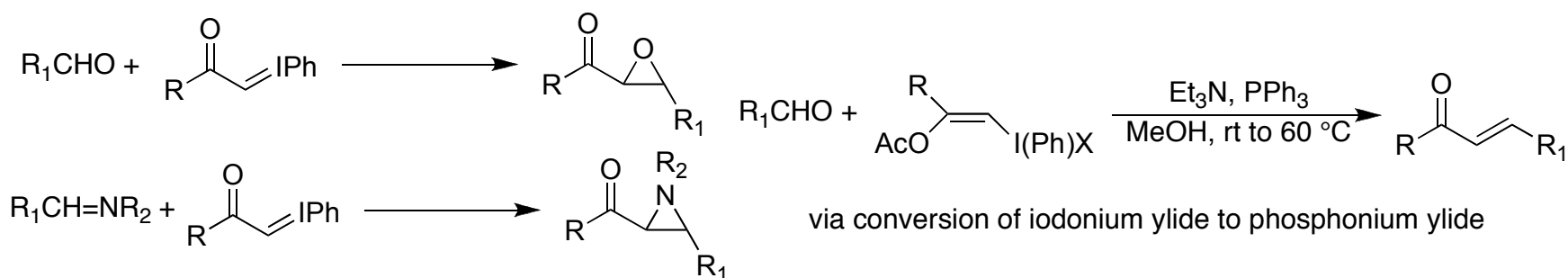
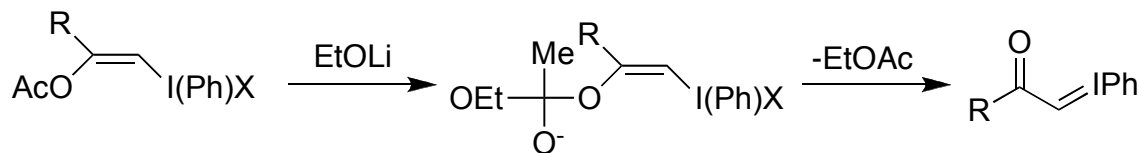


- + “Nucleophilic” substitutions are also known as well



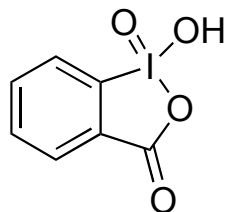
Iodonium ylides and imides ($R^1=IR^2$ and $ArI=NSO_2R$)

- + Again, getting a bit more attention.
- + Synthetically speaking, they have found application in epoxidations, aziridinations, Wittig olefination, amidation, and heteroatom imidation.
- + Again, asymmetric variations have been explored somewhat.

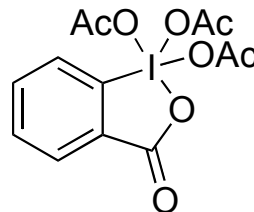


IBX and DMP

- + Varied applications in synthesis. Usually, what one can do the other can too (oxidize alcohols, C-H to C-OH, etc.)
- + One notable difference, IBX can oxidized diols to diketones or α -hydroxy ketones where as DMP usually leads to cleavage of the C-C diol bond. This has been studied by NMR and shown to result from the ability of the diol to bond twice with the iodine in DMP but not IBX.
- + IBX has also been show oxidize carbonyl compounds to α,β -unsaturated and cross-conjugated ketones.



2-iodoxybenzoic acid (IBX)



Dess-Martin periodinane (DMP)

Does IBX go BOOM!?!?!

I don't know 100%, but if I had heard of it happening, this is probably the LAST thing I'd do...

CAUTION Compound 1 was reported to be explosive by Meyer and more recently by J. B. Plumb and D. J. Harper, ICI Pharmaceuticals Group, in Chemical and Engineering News to be explosive similar to trinitrotoluene. The ICI preparation of 1, found to be explosive, had 43.5% iodine by elemental analysis (calculated 45.32% for 1) although none of the samples of 1 prepared by our method had any unexpected decrease in the percentage of iodine. They also had some bromine (4%) in 1 after washing with only water. We washed with water and ethanol to form a nonexplosive sample of 1. **Although we have been unable to induce an explosion of 1 that would break the glass container or an explosion upon hard impact of a steel hammer, we suggest that the synthesis of 1 be handled with care.** It is possible that some bromate or other impurity may be included in the samples found to be explosive

The Bottom Line (if there is one)

- + Polyvalent iodine compounds are more than just DMP
- + Have a wide array of synthetic utility
- + Drawbacks seem to be the need to prepare and instability of some of the reagents in storage

Leading References

Stang, P.J.; Zhdankin, V.V. *Chem. Rev.* **1996**, *96*, 1123-1178 (564 references cited)

Zhdankin, V.V.; Stang, P.J. *Chem. Rev.* **2002**, *102*, 2523-2584 (690 references cited)