# Hypervalent Iodine(III) Reagents as Safe Alternatives to α-Nitro-α-diazocarbonyls

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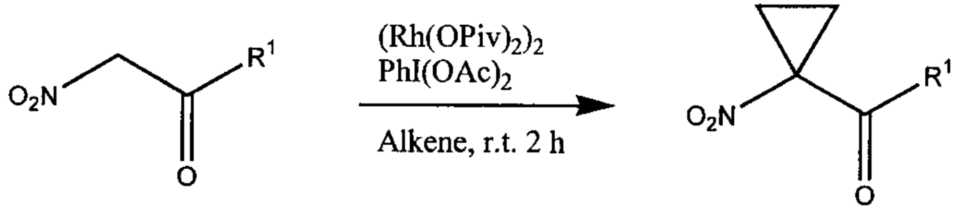
*Org. Lett.* **2003**, *13*, 2327



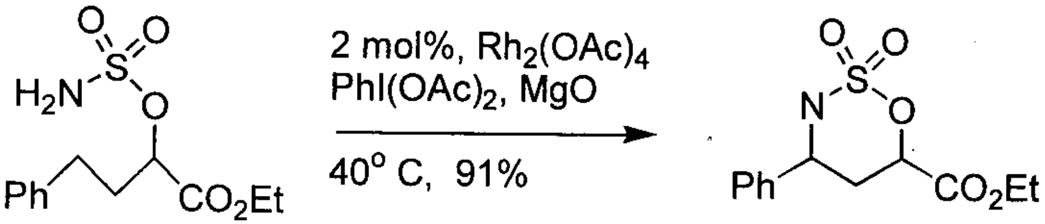
# Some Properties of Polyvalent Iodine Compounds:

- The first polyvalent iodine compound ((dichloroiodo)benzene) was discovered in 1886 by Willgerodt. There has been increasing interest in these compounds within the past two decades.
- The most common polyvalent iodine reagents contain **I(III)** or I(V)
- The chemistry of I(III) resembles that of Hg(II), Tl(III) and Pb(IV) without the negative environmental and health hazards.
- Many of the common I(III) reagents can be readily prepared or are available commercially (ex. Phenyliodine(III)diacetate is available from Aldrich for 2.40/g)

*Synthesis*,**1999**, 1271

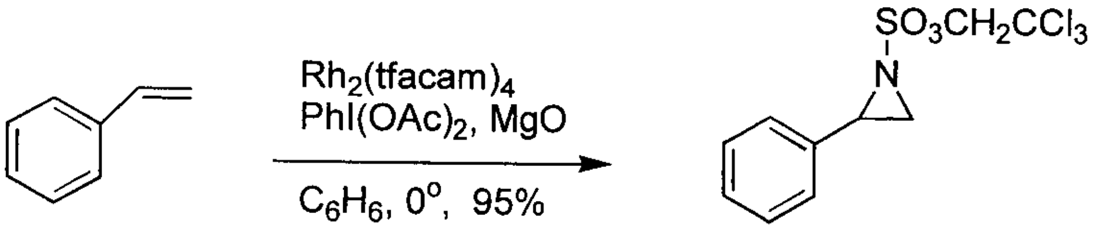
# Examples of Reactions involving I(III) Reagents:

**C-H Bond Activation:**



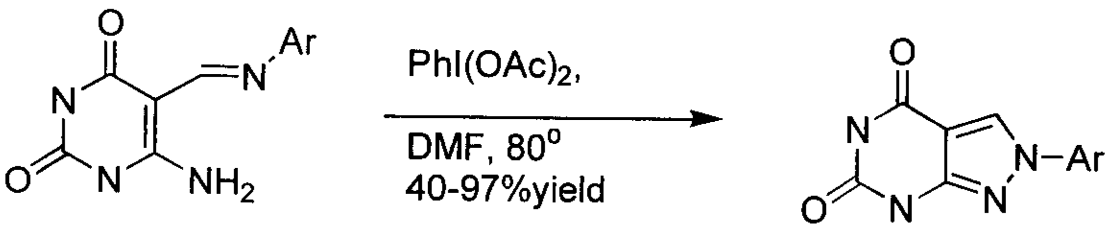
Du Bois, *J.A.C.S.* **2001**,*123*, 6935

**Aziridine Formation:**



Du Bois, *J.A.C.S.* **2002**, *124*, 13672

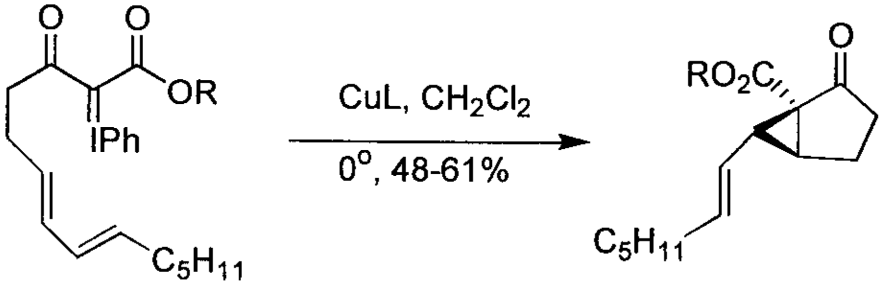
**Heterocycle Formation:**



Hirota, *SynLett.* **1997**,1409

# Example of Reactions Involving I(III) Reagents (cont.)

**Cyclopropanation:**

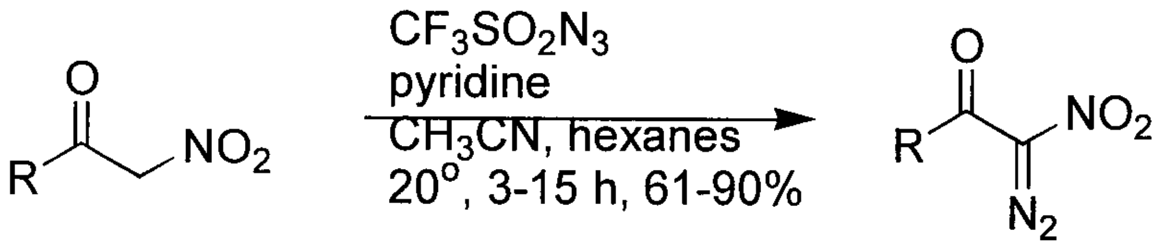


Müller, *Synlett.* **2000**,*6*, 826

This starting material gave yields between 48-61%. When the phenyliodonium functionality was replaced with the diazo moiety, no product was obtained.

# Research by Charette and coworkers

- The Charette group has been working on the synthesis of unnatural amino acids
- They developed a methodology for producing α-nitro-α-diazocarbonyl compounds

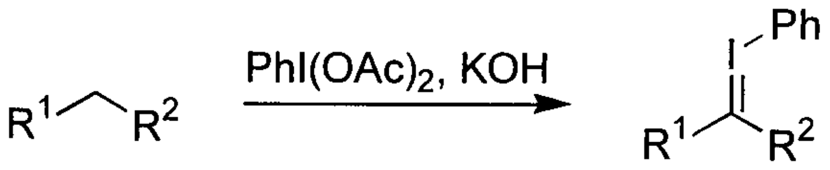


*J.Org.Chem.* **2000**, *26*, 9252

Because of the potentially explosive nature of the products, large scale reactions could not be utilized.

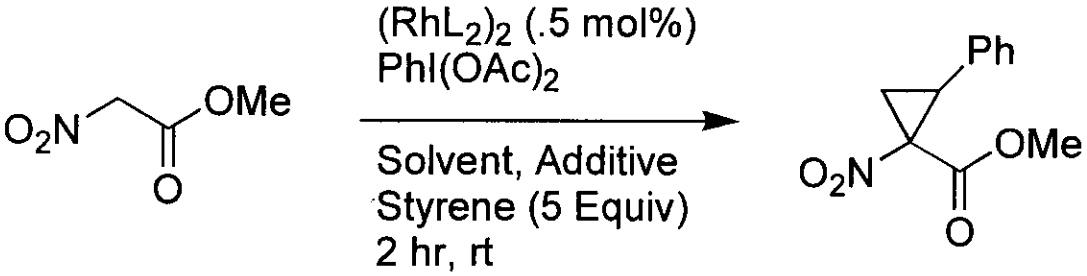
# Alternative Route:

- Hypervalent Iodine(III) reagents can be used as diazo equivalents without the explosion hazard.
- The group initially tried synthesizing the iodonium ylide. However, due to solubility problems and decomposition, the product was never isolated.



$R^1$=$R^2$=$CO_2R$
$R^1$=$R^2$=$NO_2$
$R^1$=$R^2$=$SO_2Ar$

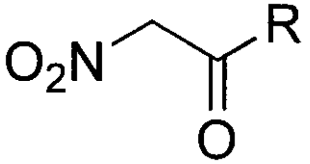
# In Situ Generation of Iodonium Ylide:



| Solvent | Catalyst (L=) | Additive | yield | E/Z |
|---|---|---|---|---|
| DCM | O.Ac | MS | 20 | 92/8 |
| DCM | O.Ac | MgO | 52 | 92/8 |
| DCM | O.Ac | Sodium Bicarb. | 32 | 90/10 |
| water | O.Piv | Sodium Bicarb. | 86 | 93/7 |
| none | Oac | none | 41 | 90/10 |
| none | C7H15CO2 | none | 71 | 91/9 |
| none | O.Piv | none | 83 | 92/8 |
| none | O.Piv | none | 67 | 92/8 |

# Scope of reaction:

- To test the versatility of this reaction, various R groups were tested.

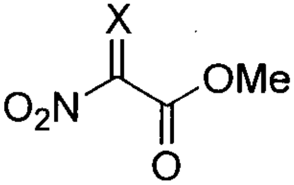


- O-Allyl, OBn, O *i*-Pr, Ph and propane as R groups gave 61-83% yield

- The α-nitro keto substituents give predominantly Z products while the ester substituents give predominantly E

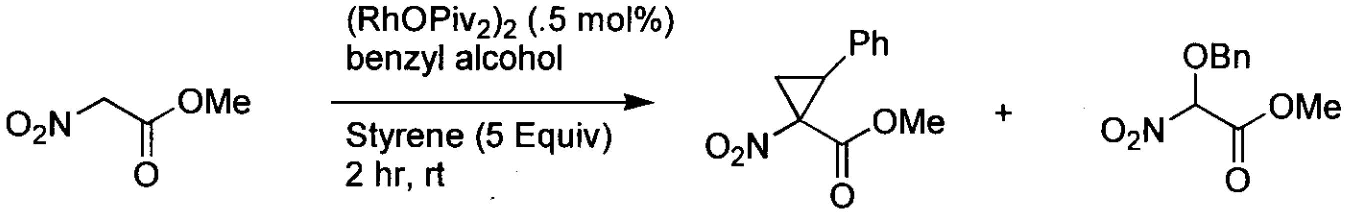
# Iodonium Ylide vs. Diazo Cyclopropanation

Indene, para styrenes and α-methyl styrene, when used as the alkene reactant, all gave similar results. (75-90%yield)



1,1diphenylethylene and Methylenecyclopentene gave 0%yield with the iodonium ylide and 60-90% with the diazo compound.

# Competition experiment



- The diazo compounds are known to undergo O-H insertion products. Under the above conditions, there was a 1.7:1 ratio of products
- Surprisingly, the iodonium ylide did not give any of the O-H bond insertion. Mechanistic reasons are unknown, but currently being explored.

# Conclusions

- Polyvalent iodine reagents can be used for a variety of transformations
- These reagents can give comparable results to the diazo analogues without the explosion hazard
- Iodonium ylides can be potentially advantageous to diazo compounds by not undergoing O-H bond insertion