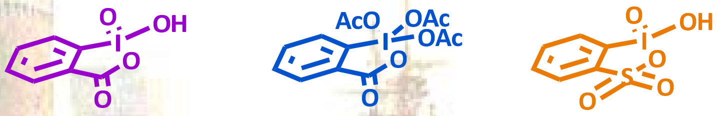
Hypervalent Iodine(V) compounds: an oxidative journey from IBX to DMP and IBS



Damien Mailhol, 1st year Ph.D.
May 19th 2009

Iodine

A historic review

- I_2 is a **dark purple solid.**

53
I
126.9

- Halide of atomic number 53.
- Naturally-occurring iodine is a single isotope with 74 neutrons.

- Discovered by Courtois[1] in 1811 from seaweed ashes.

- Named by Gay-Lussac[2] from greek « *iodes* » means *violet.*

- Iodine and its compounds are primarily used in **medicine, photography**, and **dyes**.

(1) (a) Courtois B. *Annales de chimie* **1813**, *88*, 304.
(b) Swain P. A. *Bulletin for the History of Chemistry* **2005**, *30*, 2, 103.
"Bernard Courtois (1777-1838) famed for discovering iodine (1811), and his life in Paris from 1798”
http://www.scs.uiuc.edu/~mainzv/HIST/awards/OPA%20Papers/2007-Swain.pdf.
(2) Gay-Lussac J. *Annales de chimie* **1814**, *91*, 5.

Hypervalent Iodine

- The term **hypervalent**[3] was established in 1969 for molecules with elements of groups 15-18 bearing **more electrons than an octet in their valence shell**.

- All known organic polyvalent iodine derivatives belong to 2 general structural types:
  - **iodine (III)** compounds (or **λ^3-iodanes** (IUPAC name))
  - **iodine (V)** compounds (or **λ^5-iodanes**(IUPAC name))

- *Old chemistry…*
  - **$PhICl_2$: 1st reported** hypervalent **iodine(III)** compound prepared by Willgerodt, Germany, **1886**.
  - **$PhIO_2$: 1st reported** hypervalent **iodine(V)** compound, prepared by Willgerodt, Germany, **1900**.

- *Dusted* in the **early 1990s**. Since, the chemistry of polyvalent iodine organic compounds has experienced an explosive development (4 books and several reviews[4]).

(3) Jensen, W. B. *J. Chem. Educ.* **2006**, *83*, 1751

(4) (a) Varvoglis, A. Hypervalent Iodine in Organic Synthesis, *Academic Press, London* **1997,** 1-223

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

(c) Stang, P. J.; Zhdankin, V. V. *Chem. Rev.* **1996**, *96*, 1123

(d) Zhdankin, V. V.; Stang, P. J. *Chem. Rev.* **2002**, *102*, 2523

(e) Zhdankin, V. V.; Stang, P. J. *Chem. Rev.* **2008**, *108*, 5299

Polyvalent Iodine

- Due to:
  - useful oxidizing properties

    Chemical properties similar to Hg(II), Tl(III), Pb(IV), without the nastiness !
  - benign environmental character
  - commercial availability

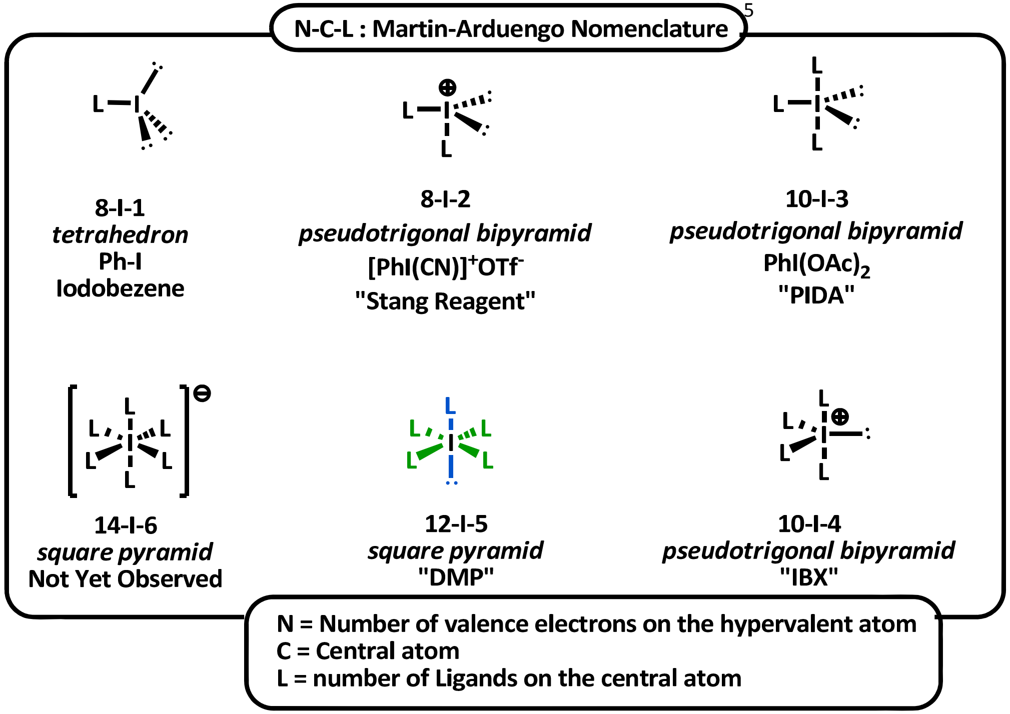
- Also similar to organometallics to a certain extent *(ligand exchange, reductive elimination, etc.)*

- Hypervalent organoiodine chemistry areas of current interest:
  - **synthetic applications** of IBX and analogs
  - development and synthetic use of **polymer-supported and recyclable reagents**
  - **catalytic applications**
  - **structural studies** of complexes and supramolecular assemblies

Outline

1. Structure & Bonding: the Martin-Arduengo Notation
2. Iodine(V) Compounds
    1. **Non-cyclic Iodylarenes**
    2. **Cyclic Iodylarenes**
        1. **IBX**
        2. **DMP**
        3. **IBX analogs**
        4. **IBS cat.**
3. Conclusion

Structure and Bonding



N-C-L : Martin-Arduengo Nomenclature[5]

8-I-1
tetrahedron
Ph-I
Iodobezene

8-I-2
pseudotrigonal bipyramid
$[PhI(CN)]^+OTf^-$
"Stang Reagent"

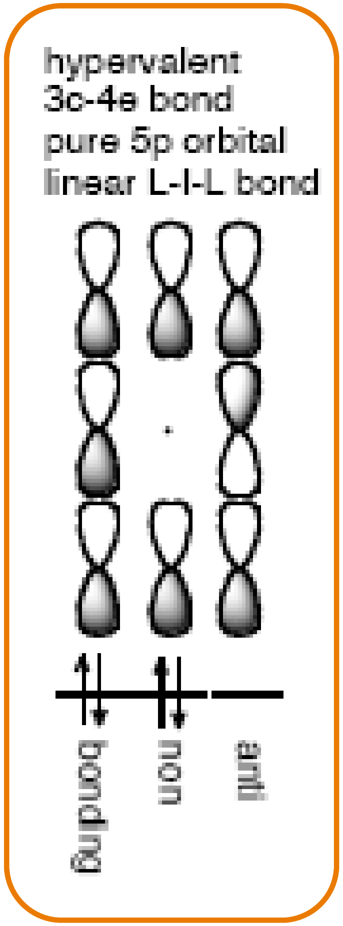
10-I-3
pseudotrigonal bipyramid
$PhI(OAc)_2$
"PIDA"

14-I-6
square pyramid
Not Yet Observed

12-I-5
square pyramid
"DMP"

10-I-4
pseudotrigonal bipyramid
"IBX"

N = Number of valence electrons on the hypervalent atom
C = Central atom
L = number of Ligands on the central atom



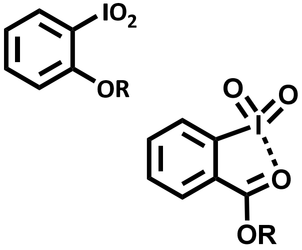
hypervalent
3c-4e bond
pure 5p orbital
linear L-I-L bond

- **C_{Ar}** and the **electron pair** in **apical positions**
  - normal covalent bond using 5sp-hybridized orbital
- **4 heteroatoms** ligands X in **basal positions**
  - 2 ⊥ hypervalent **3c-4e bonds**
- **3c-4e bond** has a both ionic & covalent character.

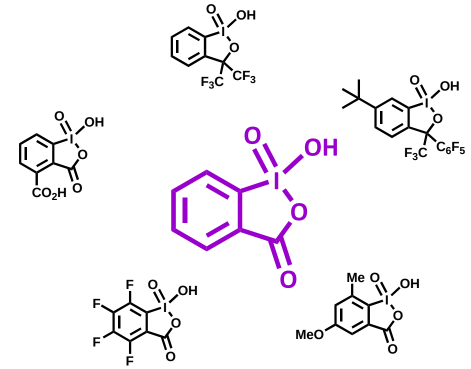
- *In general only λ^3- and λ^5-iodanes with aromatic group have suffcient stability and can be isolated.*

(5) Perkins, C. W.; Martin, J. C.; Arduengo, A. J.; Lau, W.; Alegria, A.; Kochi, J. K. *J. Am. Chem. Soc.* **1980**, *102,* 7753.

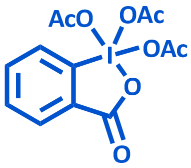
Iodine(V) compounds



Noncyclic (pseudocyclic) iodylarenes



IBX and analogs

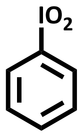


DMP

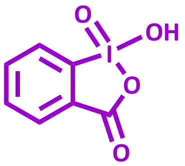
- I(V) compounds have been less developped than I(III)
- Significant recent interest in I(V) compounds, mainly in IBX, DMP and IBX analogs.

Iodine(V) Compounds

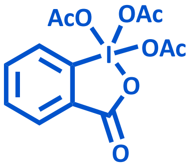
Chronology



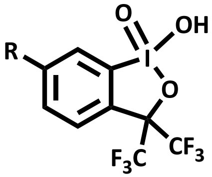
(1886)



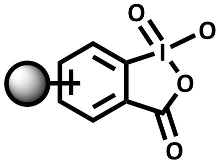
IBX
(1893)



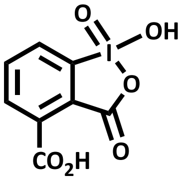
DMP
(1983)



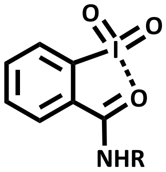
(1991)



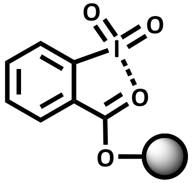
(2001)



mIBX
(2002)



IBX-amides
(2003)



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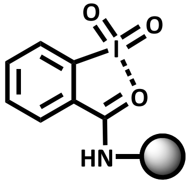

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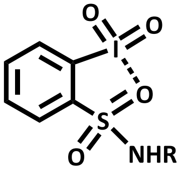

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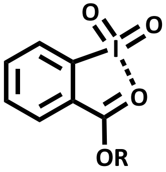
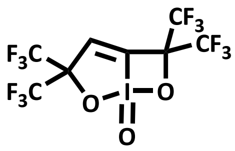


IBX-esters
(2004)



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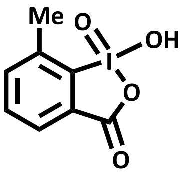

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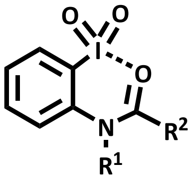
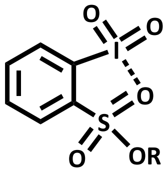
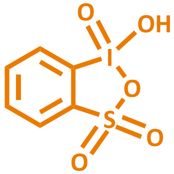


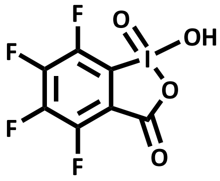
NIPA
(2005)



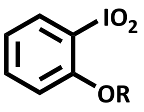
(2005)



IBS
(2006)



FIBX
(2007)



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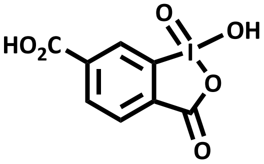
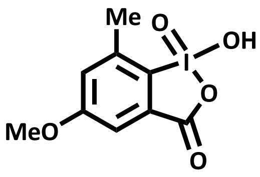
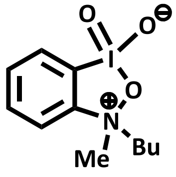


(2008)



MeIBX
(2008)



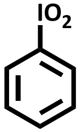
(2008)

(6) Uyanik, M.; Ishihara, K. *Chem. Commun.* **2009**, 2086

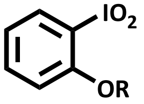
Iodine(V) Compounds

Functional Evolution

Noncyclic

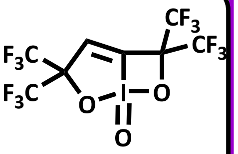


(1886)



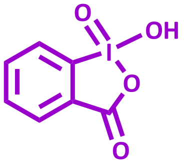
(2007)

Nonaromatic

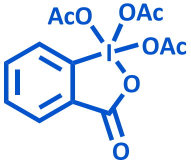


(2004)

IBX analogs

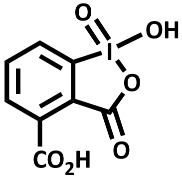


IBX
(1893)

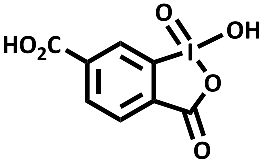


DMP
(1983)

Arene-modified



mIBX
(2002)



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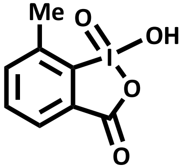

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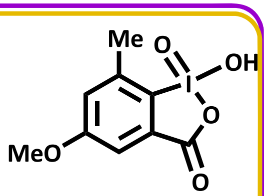
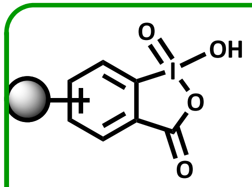


MeIBX
(2008)

Polymer-supported



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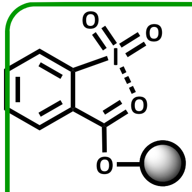

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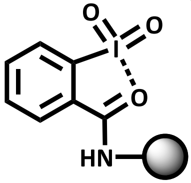

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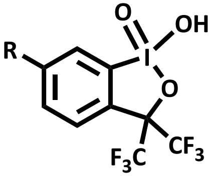
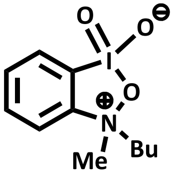


(1991)



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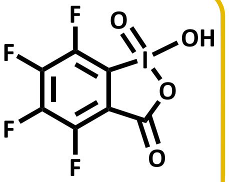
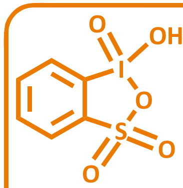


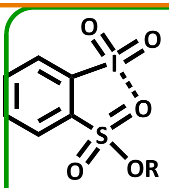
FIBX
(2007)

IBS analogs

Pseudocyclic



IBS
(2006)



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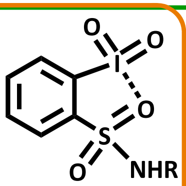

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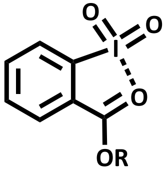
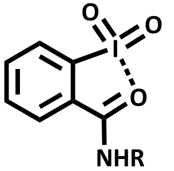
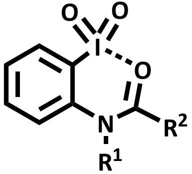


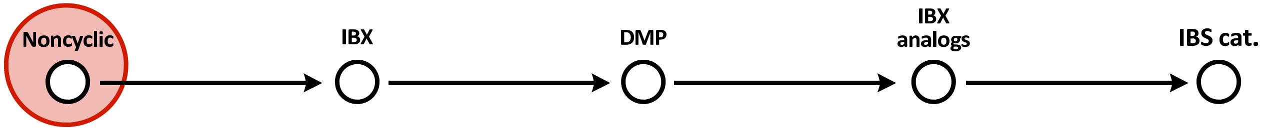
IBX-esters
(2004)



IBX-amides
(2003)



NIPA
(2005)



Noncyclic iodylarene

- Iodylbenzene ($PhIO_2$) = simplest iodyl arene reagent
- No functional group for intramolecular interactions with I(V)

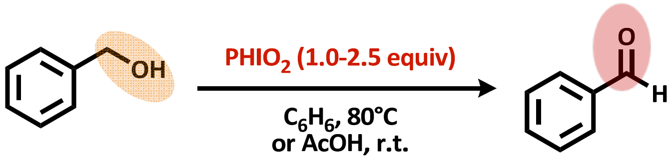
- Preparation:

New method[7] Classical method[8]

$$\text{ArI + AcOOH/AcOH} \xrightarrow[\text{64-94\%}]{\text{RuCl}_3\text{ (0.08 mol\%), 40°C, 16 h}} \text{ArIO}_2 \xleftarrow[\text{30-91\%}]{\text{30\% aq. AcOH, reflux, 3-6 h}} \text{ArI + NaIO}_4$$

Common oxidizing reagents: $NaIO_4$, NaOCl, DMDO, oxone.

- Appl.: $PhIO_2$-mediated oxidation of benzyl alcohols to the corresponding aldehydes[9].

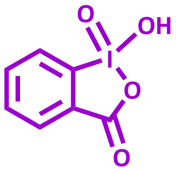


$PHIO_2$ (1.0-2.5 equiv)

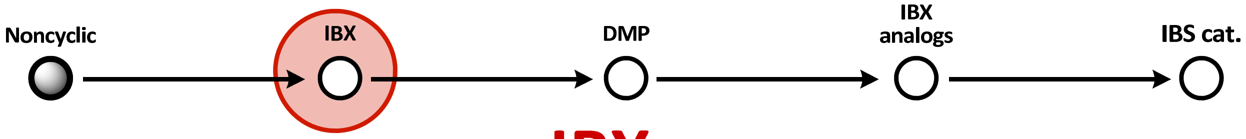
C_6H_6, 80°C
or AcOH, r.t.

- Rate accelerated in protic solvent such as acetic acid.

(7) Kraszkiewicz, L.; Skulski, L. *ARKIVOC* **2003**, *vi*, 120
(8) Koposov, A. Y.; Zhdankin, V. V. *J. Org. Chem.* **2006**, *71*, 9912
(9) Barton, D. H. R.; Godfrey, C. R. A.; Morzycki, J. W.; Motherwell, W. B.; Stobie, A. *Tetrahedron Lett.* **1982**, *23*, 957

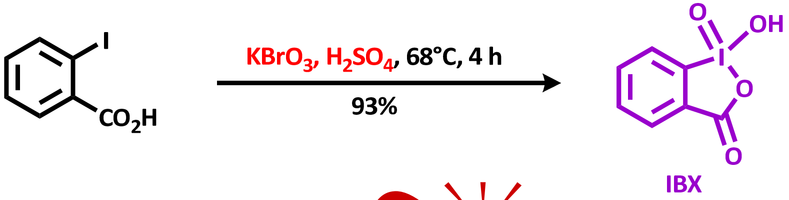


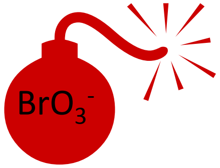
IBX



IBX

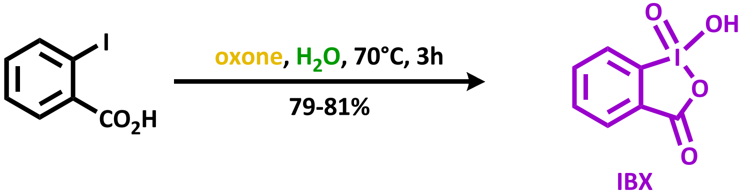
- The most important representative of pentavalent iodine heterocycles
- Cyclic benziodoxole oxide
- First prepared in 1893 by Hartman and Meyer[13]
- Formerly most commonly used preparation[14]:





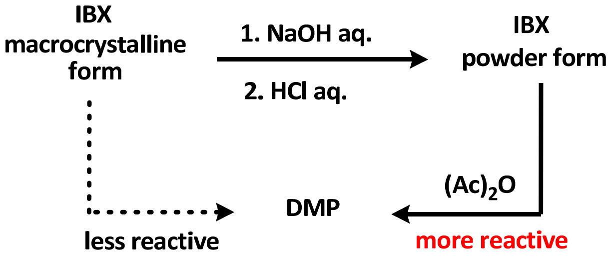
- Bromate impurities ➡ explosive under excessive heating or impact

- **Convenient procedure[15] reducing explosive impurities:**



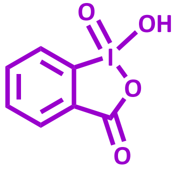
Oxone® = $2KHSO_5H \bullet KHSO_4 \bullet K_2SO_4$, a trademark of DuPont

- Powder and macrocrystalline IBX forms:



- **pK_a(IBX) = 2.40** (in H_2O)[16]

(13) Hartman, C.; Meyer, V. *Chem. Ber.* **1893**, *26*, 1727
(14) Boeckman, R. K.; Shao, P.; Mullins, J. J. *Org. Synth.* **2000**, *77*, 141
(15) Frigerio, M.; Santagostino, M.; Sputore, S. *J. Org. Chem.* **1999**, *64*, 4537
(16) Gallen, M. J.; Goumont, R.; Clark, T.; Terrier, F.; Williams, C. M. *Angew. Chem. Int. Ed.* **2006**, *45, 2929*

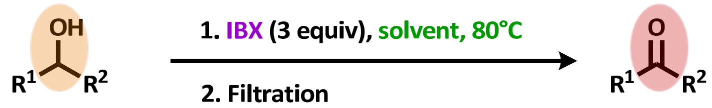


IBX

IBX Synthetic Applications

IBX in common organic solvents

- Synthetic usefulness of IBX in general is significantly restricted by its **low solubility in most organic solvents...** However[18]:



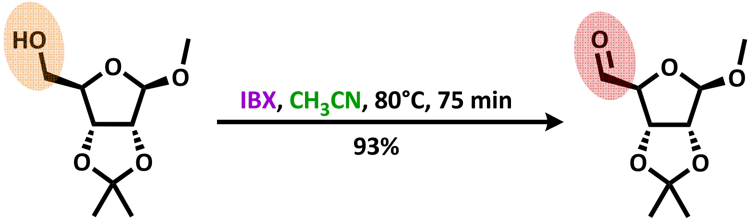
1. IBX (3 equiv), solvent, 80°C

2. Filtration

✓EtOAc, $CHCl_3$, DCE, acetone, PhH, CH_3CN

~~THF, PhCH$_3$~~ → oxidation of the solvent observed

- In CH_3CN:



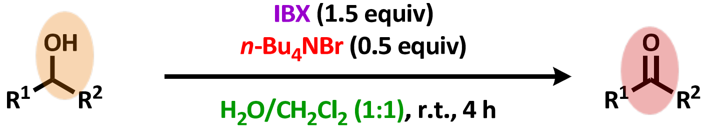
IBX, CH_3CN, 80°C, 75 min

93%

ribosyl aldehyde

- ↳ stereoselective synthesis of the core structure of the of the **polyoxin** and **nikkomycin** antibiotics[19]

- In H_2O/CH_2Cl_2[20]:



IBX (1.5 equiv)
***n*-Bu$_4$NBr (0.5 equiv)**

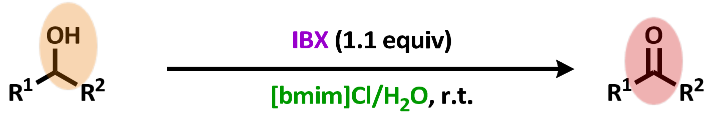
H_2O/CH_2Cl_2 (1:1), r.t., 4 h

R^1 = alkyl, alkenyl, aryl
R^2 = H, alkyl

12-94%

- Advantages:
  - TBAB = simple & inexpensive phase-transfer catalyst
  - ↘ organic solvent

- In ionic liquid[21]:



IBX (1.1 equiv)

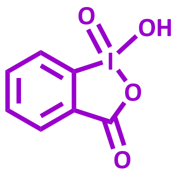
[bmim]Cl/H_2O, r.t.

R^1 = alkyl, alkenyl, aryl
R^2 = H, alkyl

88-99%

- Advantage: recycling &reuse of the solvent ➡ eco-friendly procedure

(18) More, J.; Finney, N. *Org. Lett.* **2002**, *4*, 3001
(19) More, J.; Finney, N. *Synlett* **2003**, 1307
(20) Kuhacarn, C.; Kittigowittana, K.; Ghabkham, P.; Pohmakotr; M. Reutrakul, V. *Synth. Commun.* **2006**, *36*, 2887
(21) Liu, Z.; Chen, Z.C.; Zheng, Q.G. Org. Lett. **2003**, *5*, 3321

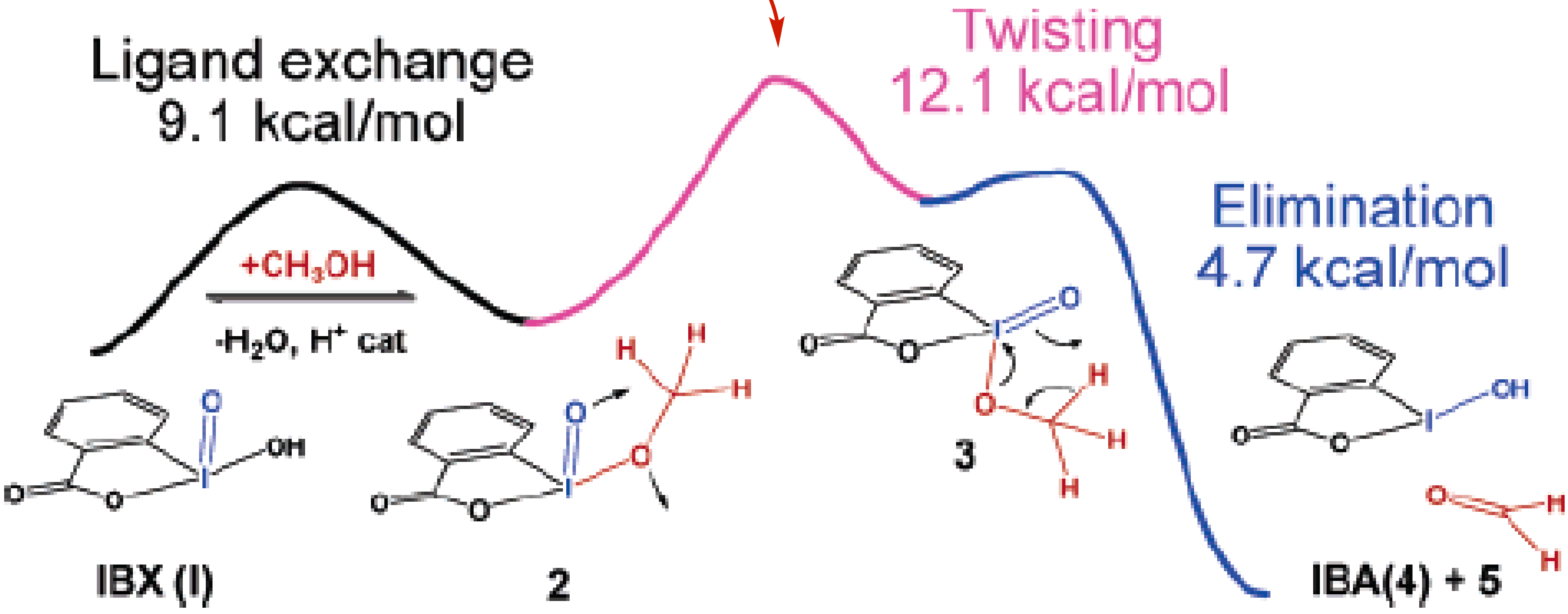


IBX

Mechanistic Study[17]

Let's Twist a bit !

TWIST = RATE-LIMITING STEP



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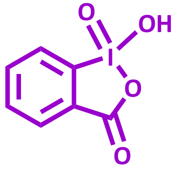
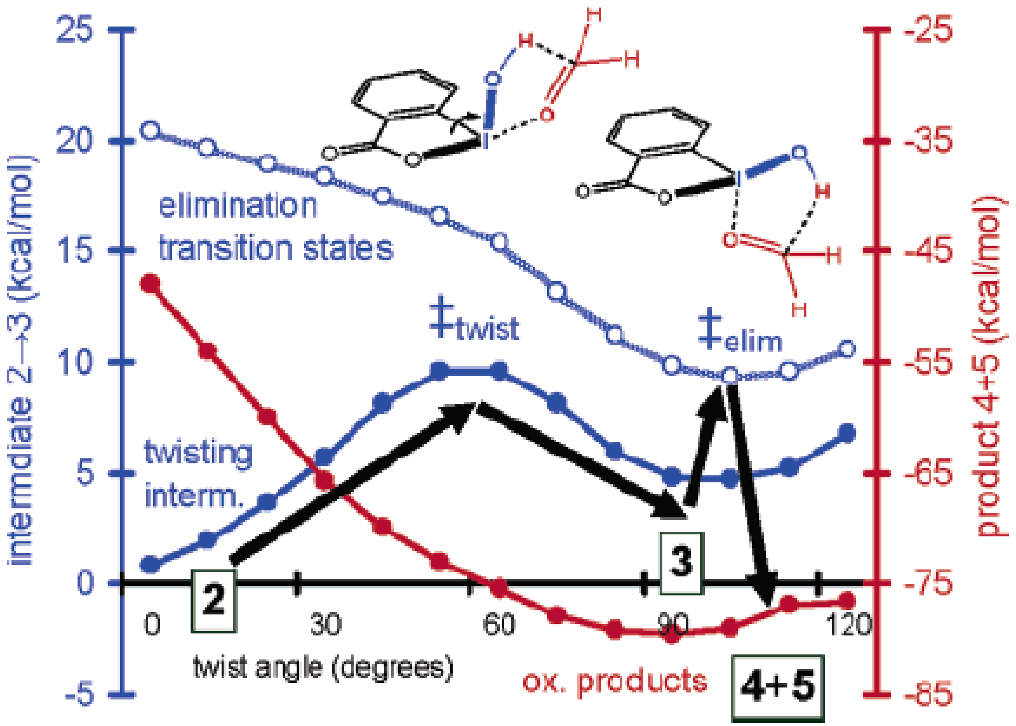
(17) Su J. T.; Goddard W. A. *J. Am. Chem. Soc.* **2005**, *127*, 14146



IBX

Mechanistic Study

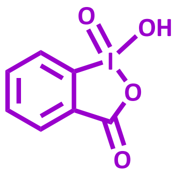
Let's Twist a bit !



- H. T. is a coordinated motion of ligands driven by the necessity of generating a **stable planar form** of the byproduct IBA from an IBX-alcohol intermediate.
- IBA stable in a **planar form (-48 kcal/mol relatively to other form)**.
- Intermediate 2 prefers to **twist first (12 kcal/mol)**, then **eliminate IBA (5 kcal/mol)**, rather than eliminate IBA directly without twisting (20 kcal/mol).

- The H. T. mechanism explains the **propensity of IBX to oxidize large alcohols faster than small ones**.

(17) Su J. T.; Goddard W. A. *J. Am. Chem. Soc.* **2005**, *127*, 14146

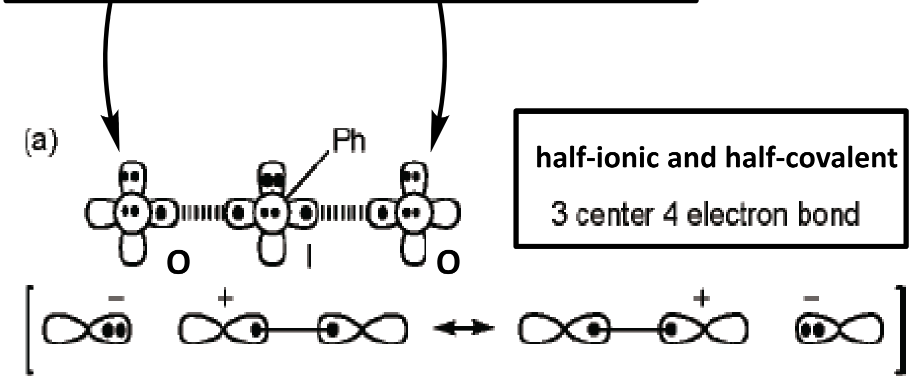


IBX

Mechanistic Study

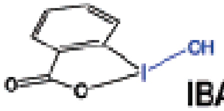
An orbitalar approach

The 2 anionic ligands must be opposite to each other to gain full stability from resonance.



half-ionic and half-covalent

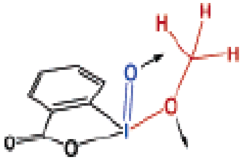
3 center 4 electron bond



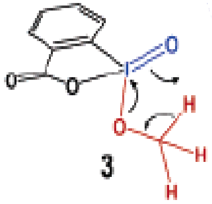
IBA(4)

- Iodine makes a normal covalent bond to the phenyl covalent carbon, **leaving 2 doubly occupied 5p orbitals** tperpendicular to this bond.

(17) Su J. T.; Goddard W. A. *J. Am. Chem. Soc.* **2005**, *127*, 14146

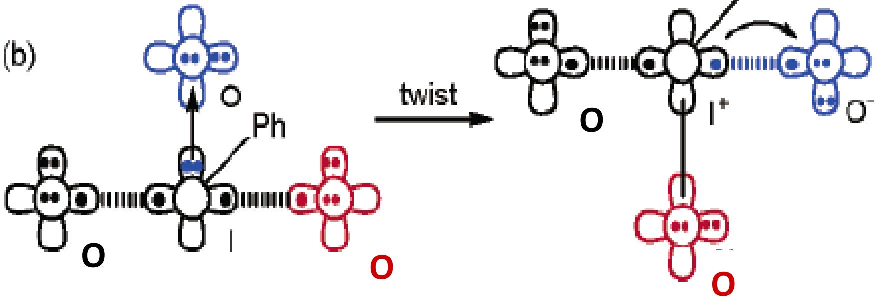


2

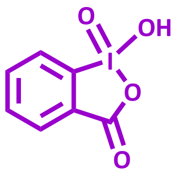


3

ΔG~3kcal/mol



- Upon twisting, the **alkoxy ligand** loses resonance with the **acid ligand**, making it less strongly bound, but the ***oxo* group** picks up the resonance with that ligand to compensate.
- The ***oxo* bond** becomes more covalent as the iodine transfers an electron to the oxygen **to avoid placing 3 electrons in one p orbital**.

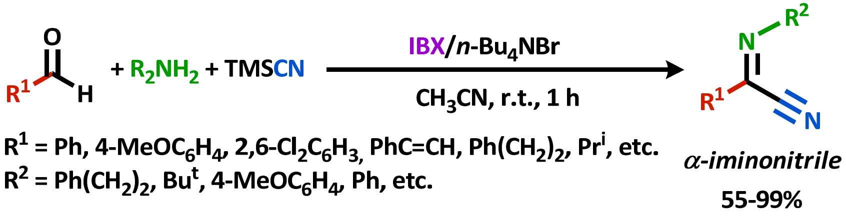


IBX

IBX Synthetic Applications

Here are the MCR !!!

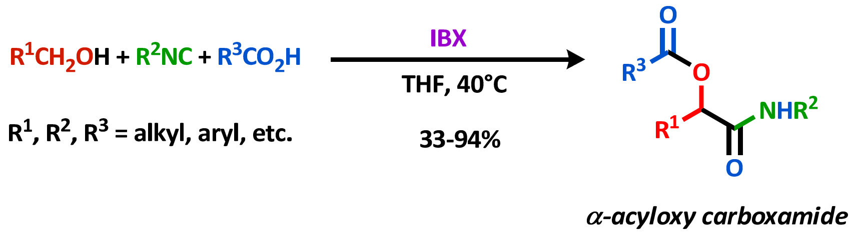
- **Oxidative Strecker** reaction[22]:



R^1 = Ph, 4-$MeOC_6H_4$, 2,6-$Cl_2C_6H_3$, PhC=CH, $Ph(CH_2)_2$, Pr^i, etc.
R^2 = $Ph(CH_2)_2$, Bu^t, 4-$MeOC_6H_4$, Ph, etc.

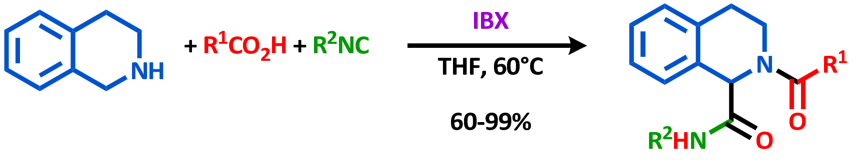
↳ 2-step synthesis of **indolizidine** via a **microwave-assisted** intramolecular cycloaddition of α-iminonitrile

- **Passerini** reaction[23]:

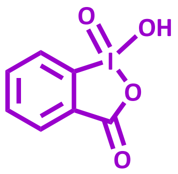


- Works with **alcohol** instead of **carbonyl compound**

- **Oxidative Ugi-type** reaction[24] applicated to tetraisoquinolines:



(22) Fontaine, P.; Chiaroni, A.; Masson, G.; Zhu, J.; *Org. Lett.* **2008**, *10*, 1509
(23) Ngouansavanh, T.; Zhu, J. *Angew. Chem. Int. Ed.* **2006**, *45*, 3495
(24) Ngouansavanh, T.; Zhu, J. *Angew. Chem. Int. Ed.* **2007**, *46*, 5775



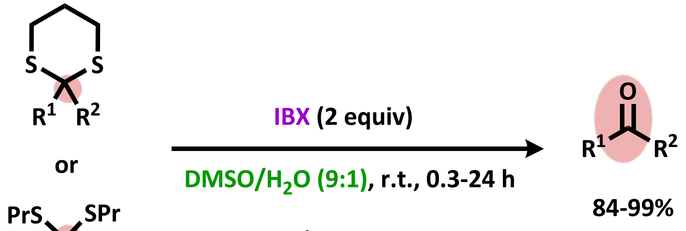
IBX

IBX Synthetic Applications

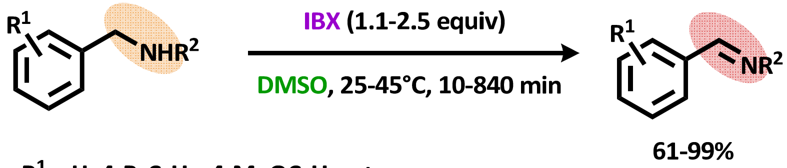
And what about DMSO ?!

- Remember some slides ago: « Synthetic usefulness of IBX in general is significantly restricted by its **low solubility in most organic solvents... with the exception of DMSO !** »

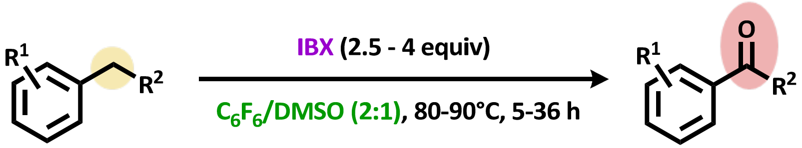
- **IBX in DMSO:**
  - dithianes deprotection[25]
  - amines → imines[25]
  - benzylic oxidation[26]
  - phenols → *o*-quinones[27]
  - alcohols → α,β-unsaturated carbonyl compound[26]
  - 1,2-diols → α-ketones or α-ketols[28]
  - N-heterocyclization[29]



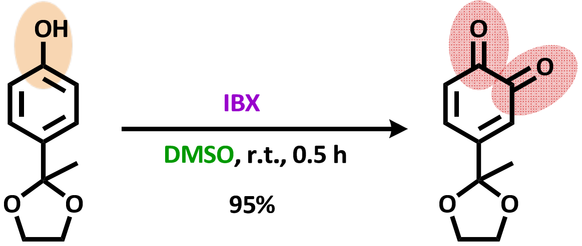
R^1 = H, alkyl
R^2 = alkenyl, aryl



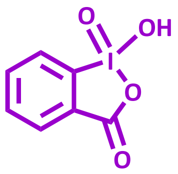
R^1 = H, 4-BrC_6H_4, 4-MeOC_6H_4, etc.
R^2 = 4-BrC_6H_4, 4-MeOC_6H_4, CH_3, OH, OBn, etc.



R^1 = H, 4-Bu^tC_6H_4, 2-MeC_6H_4, 3-IC_6H_4, 4-BrC_6H_4, 3,4-$(MeO)_2C_6H_3$, 2-PhC_6H_4, 4-(pyridyl)C_6H_4, etc.
R^2 = H, C_3H_7, etc.



(25) Nicolaou, K. C.; Mathison, C. J. N.; Montagnon, T. *J. Am. Chem. Soc.* **2004**, *126*, 5192
(26) Nicolaou, K. C.; Baran, P. S.; Zhong, Y.-L. *J. Am. Chem. Soc.* **2001**,*123*, 3183.
(27) Magdziak, D.; Rodriguez, A. A.; Van De Water, R. W.; Pettus, T. R. R. *Org. Lett.* **2002**, *4*, 285.
(28) Moorthy, J. N.; Singhal, N.; Senapati, K. *Org. Biomol. Chem.* **2007**, *5*, 767.
(29) Nicolaou, K. C.; Baran, P. S.; Zhong, Y.-L.; Barluenga, S.; Hunt, K. W.; Kranich, R.; Vega, J. A. *J. Am. Chem. Soc.* **2002**,*124,* 2233.

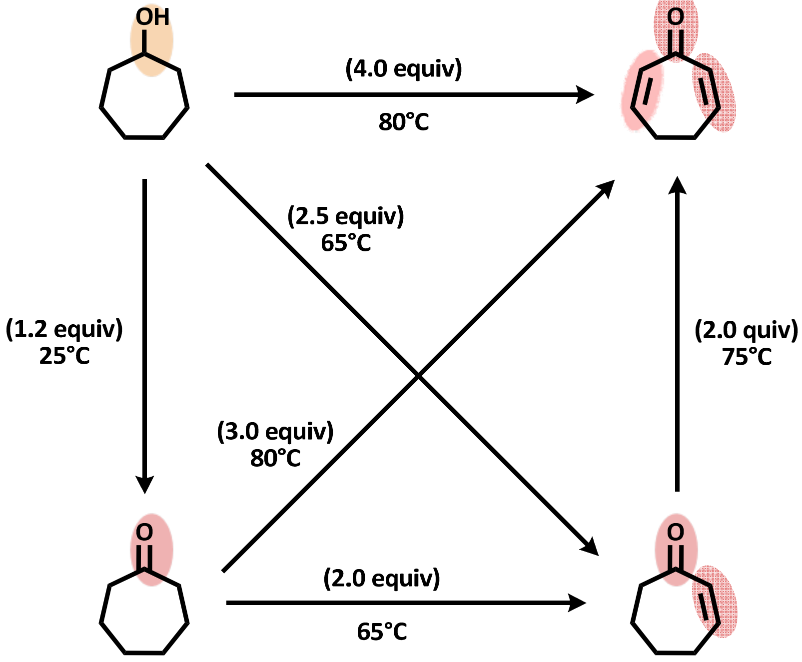


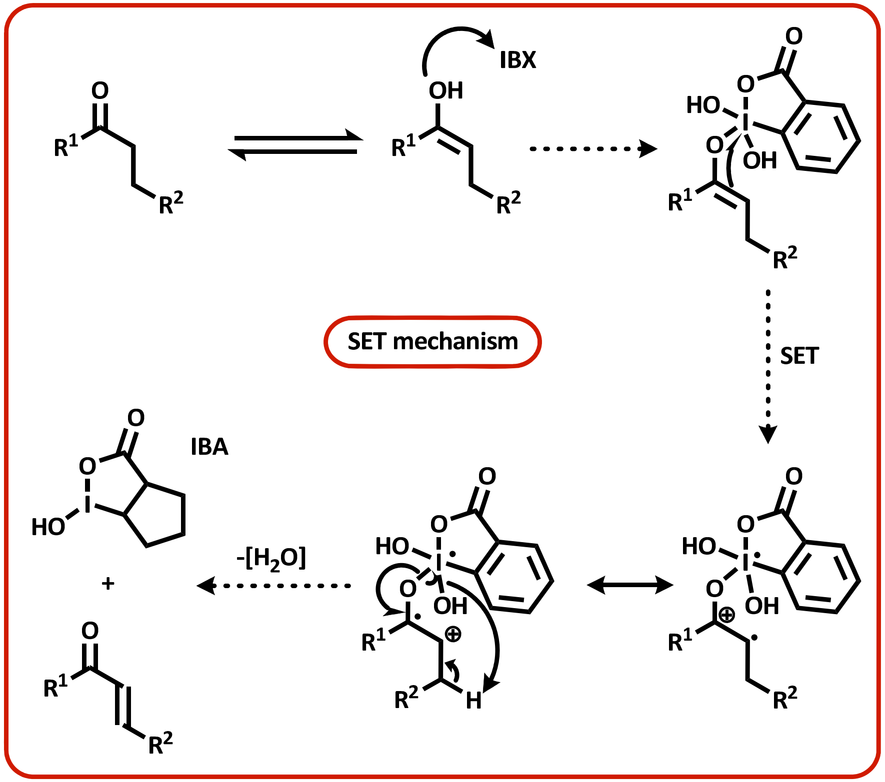
IBX

IBX Synthetic Applications

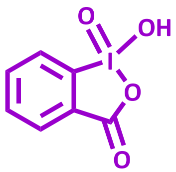
α,β-unsaturated

IBX in **DMSO**



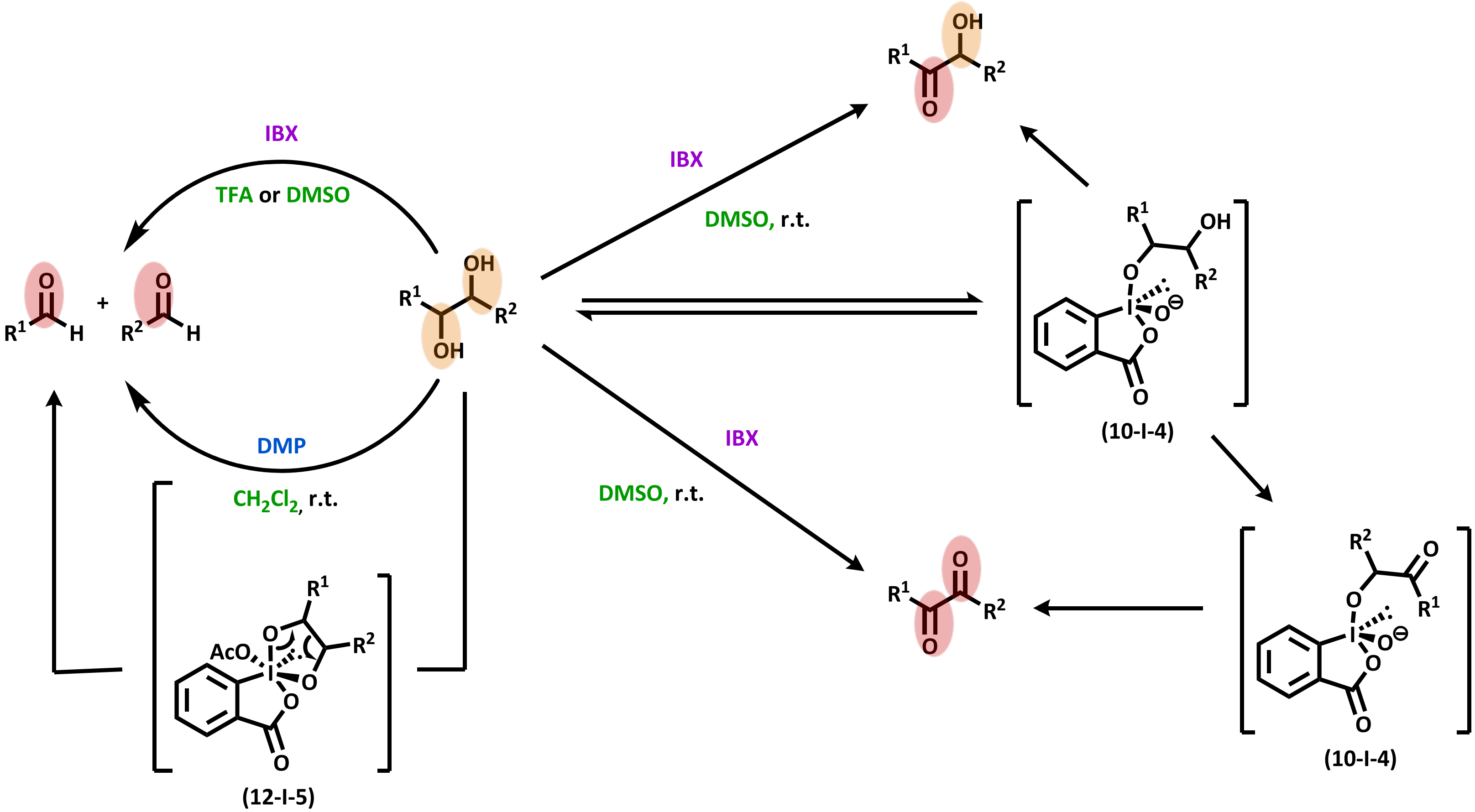


(26) Nicolaou, K. C.; Baran, P. S.; Zhong, Y.-L. *J. Am. Chem. Soc.* **2001**,*123*, 3183.

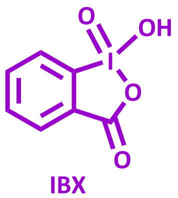

IBX

IBX Synthetic Applications

1,2-diols



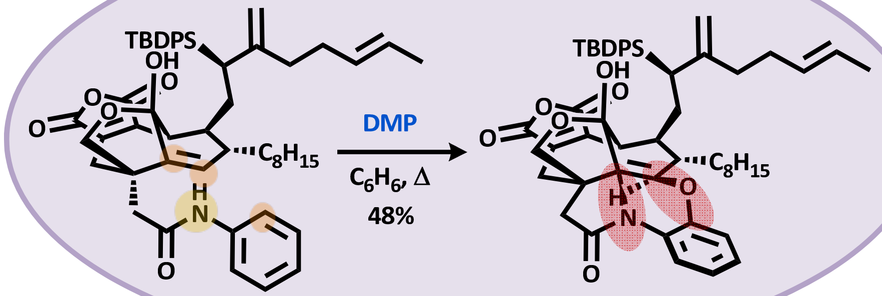
(28) Moorthy, J. N.; Singhal, N.; Senapati, K. *Org. Biomol. Chem.* **2007**, *5*, 767.

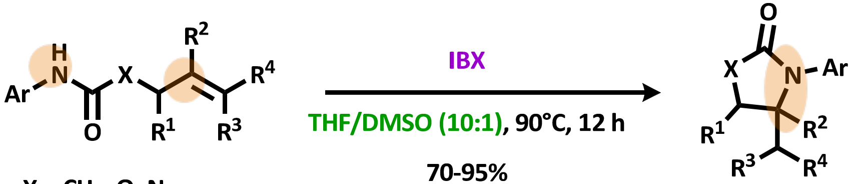


IBX Synthetic Applications

SET N-heterocyclization: a new way to heterocycles

- On the way to the synthesis of CP-molecules, tremendous discovery was made with iodine oxidants[25-27]:

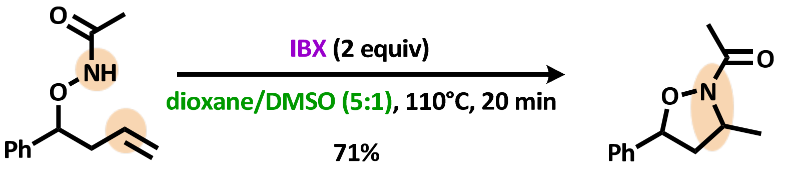




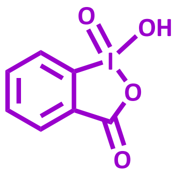
X = CH_2, O, N
Ar = Ph, 3-Et-C_6H_4, 3-BrC_6H_4, 3-FC_6H_4, 4-EtC_6H_4, etc.
R^1 - R^4 = H, alkyl, cycloalkyl, etc.

- **Mechanism steps** of IBX-mediated cyclization of anilides in THF:
  - **SET**
  - **deprotonation**
  - **radical cyclization**
  - **hydrogen abstraction from THF**

- In the same way[28]:

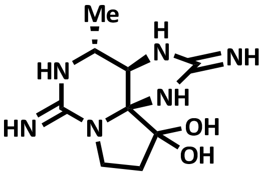


(25) Nicolaou, K. C.; Zhong, Y.-L.; Baran P. *Angew. Chem. Int. Ed.* **2000**, *39*, 622
(26) Nicolaou, K. C.; Baran P. S.; Zhong, Y.-L. *Angew. Chem. Int. Ed.* **2001**, *40*, 202
(27) Nicolaou, K. C.; Baran P. S. ; Zhong, Y.-L.; Barluenga, S.; Hunt, K. W.; Kranich, R.; Vega, J. *Angew. Chem. Int. Ed.* **2002**, *39*, 622
(28) Janza, B.; Studer, A. *J. Org. Chem.* **2005**, *70*, 6991



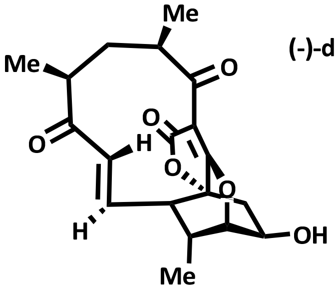
IBX

Some Total Syntheses…



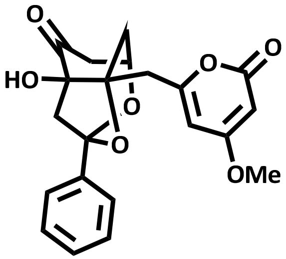
(-)-decarbamoyloxysaxitoxin, Nagasawa K., 2007

IBX used 2 times

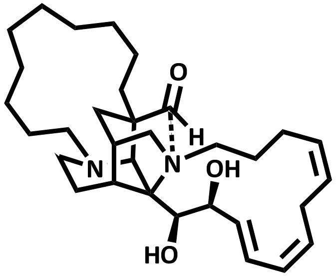


abyssomicin C, Nicolaou K., 2006

IBX used 2 times

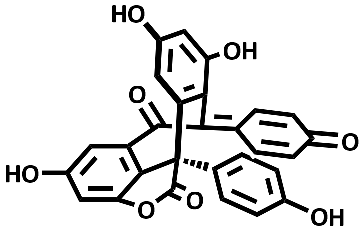


wailupemycin B, Bach T., 2003

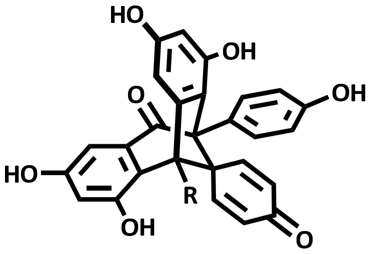


(-)-sarain A, Overman L., 2006

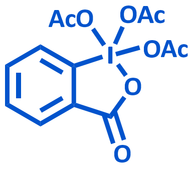
IBX used 2 times
DMP once



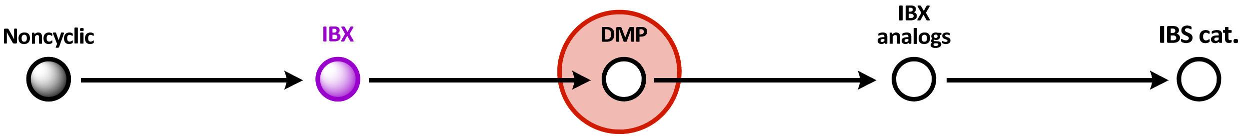
hopehainol A, Nicolaou K., 2009



hopeanol, Nicolaou K., 2009

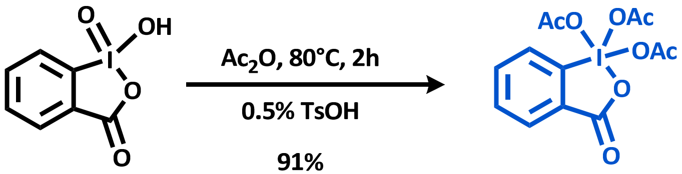


DMP



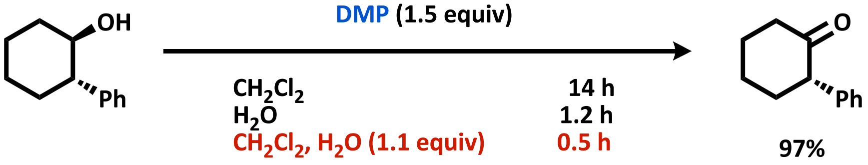
Dess Martin Periodinane

- Introduced by D. Dess and J. Martin in 1983[40]



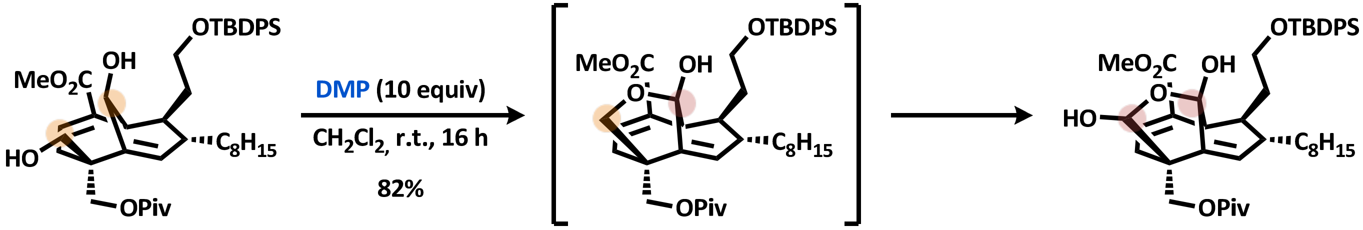
IBX **DMP**

- Water accelerated oxidation in 1994[41]



- Water is added before or during the reaction.

- CP Molecules[25-27]:



primary and secondary alcohols

intermediate *hemiketal*

γ-hydroxylactol

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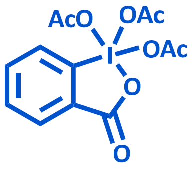
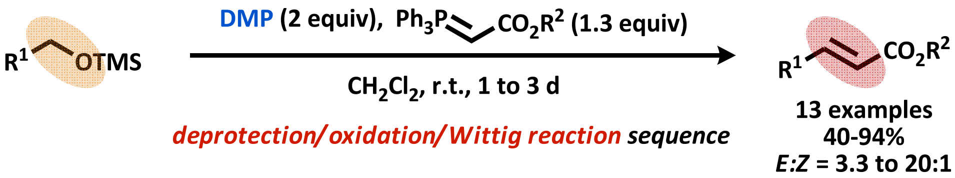
(40) Dess, D. B.; Martin, J. C. *J. Org. Chem.* **1983**, *48*, 4155
(41) Meyer, S. D.; Schreiber S. L. *J. Org. Chem.* **1994**, *59*, 7549



DMP

DMP Synthetic Applications

- In the case of epimerization sensitive substrate, DMP allows clean oxidation with virtually no loss of *ee*[42]
- Silyl ethers can be effectively used instead of alcohols[43]



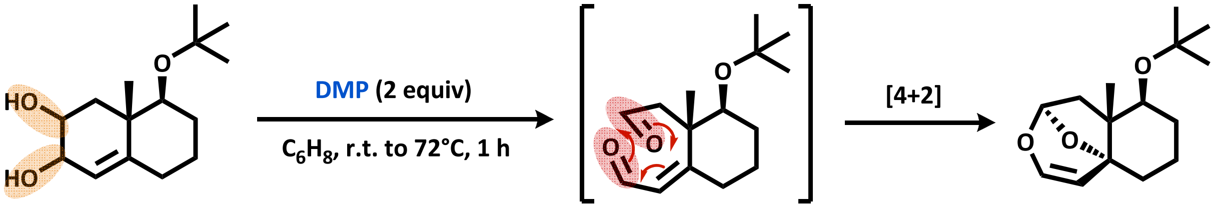
DMP (2 equiv), Ph_3P=CHCO_2R^2 (1.3 equiv)

CH_2Cl_2, r.t., 1 to 3 d

deprotection/oxidation/Wittig reaction sequence

13 examples
40-94%
***E:Z* = 3.3 to 20:1**

- DMP generally cleaves the glycol C-C bond of 1,2-diols[44]



DMP (2 equiv)

C_6H_8, r.t. to 72°C, 1 h

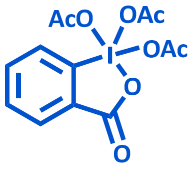
[4+2]

1,2-diol cleavage/intramolecular cycloaddition sequence

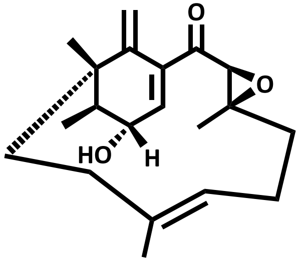
- Other synthetically useful oxidative transformations:
  - oxidative aromatization of 1,4-dihydropyridines[45]
  - oxidative cyclization of thioformanilides[46]
  - synthesis of thioesters from corresponding aldehydes and thiols[47]
  - etc…

(42) Myers, A. G.; Zhong, B.; Movassaghi, M.; Kung, D. W.; Lanman, B. A.; Kwon, S. *Tetrahedron Lett.* **2000**, *41*, 1359.
(43) Deng, G.; Xu, B.; Liu, C. *Tetrahedron* **2005**, *61*, 5818.
(44) Candela Lena, J. I.; Martin Hernando J. I.; Rico Ferreira, M. d. R.; Altinel, E.; Arseniyadis, S. *Synlett* **2001**, 597.
(45) Karade, N. N.; Gampawar, S. V.; Kondre, J. M.; Shinde, S. V. *ARKIVOC* **2008**, *xii*, 9.
(46) Bose, D. S.; Idrees, M. J. Org. Chem. **2006**, *71*, 8261.
(47) Bandgar, S. B.; Bandgar, B. P.; Korbad, B. L.; Sawant, S. S. *Tetrahedron Lett.* **2007**, *48*, 1287.

More Total Syntheses !

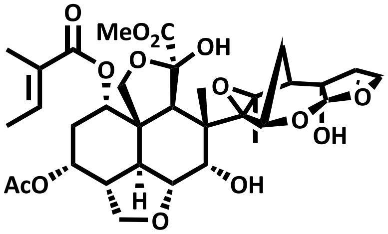


DMP

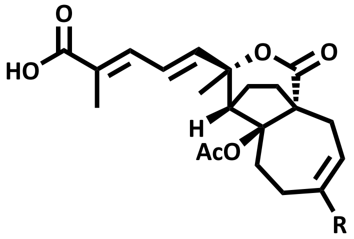


(+/-)-phomactin B2, Wulff W., 2007

DMP used 3 times

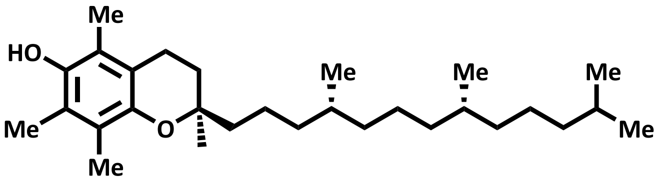


azadirachtin, Ley S., 2007

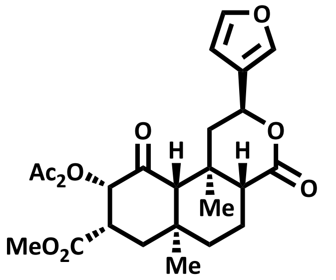


pseudolaric acid A(R = Me) and B(R = CO_2Me),
Chiu P., 2006 and Trost B., 2007

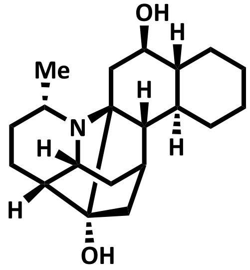
DMP used 3 times



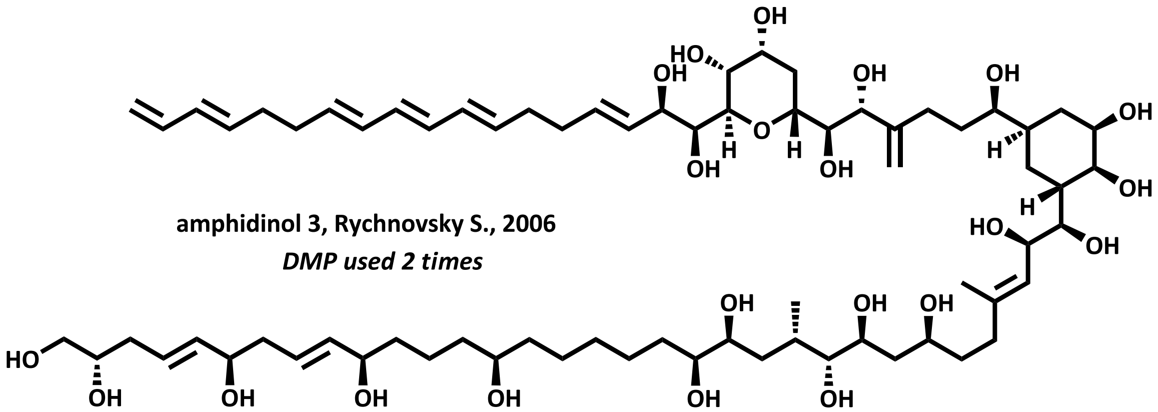
(R,R,R)-α-tocopherol, Breit B., 2007



salvinorin A, Evans D., 2007

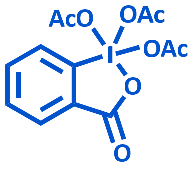


(-)-himgaline, Chackalamannil S., 2006

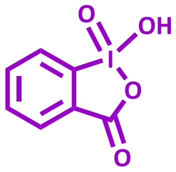


amphidinol 3, Rychnovsky S., 2006

DMP used 2 times



DMP



IBX

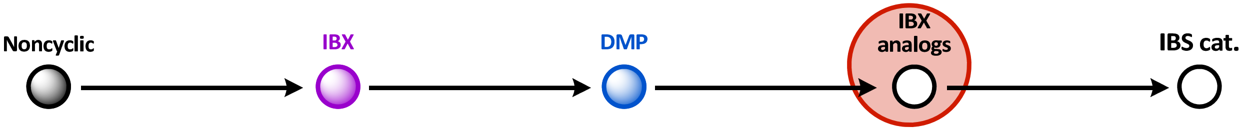
Where to go ?

☹

- IBX potentially explosive
  & insoluble in common organic solvents
- DMP highly sensitive to moisture

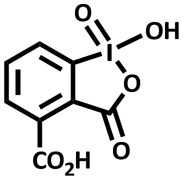
☺

- Improvements…
  - highly soluble and nonexplosive pseudocyclic derivatives of IBX
  - polymer supported recyclable analogues



Noncyclic → IBX → DMP → IBX analogs → IBS cat.

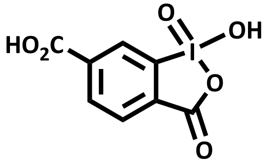
Arene-modified IBX Analogs



mIBX[54]
(2002)

- Called « water-soluble »
- Difficult to prepare

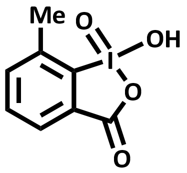
- Selective oxidation of benzyl alcohols in H_2O



(2008)[55]

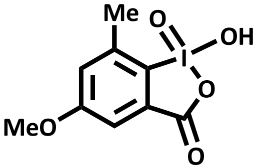
- 2 step synthesis
- Soluble in both H_2O and DMF

- Oxidation of alcohols via SET mechanism



(2005)[56]

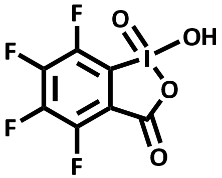
- Me enhances the *hypervalent twwisting*



MeIBX[57]
(2008)

- Soluble in common organic solvents

- Oxidation of alcohols and sulfides at r.t. with short reaction time



FIBX[58]
(2007)

- More reactive than IBX

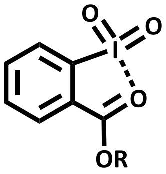
- Can cleave 1,2-diols in CH_3CN at r.t.

Relevance

Application

(54) Thottumkara, A. P.; Vinod, T. K. *Tetrahedron Lett.* **2002**, *43*, 569.
(55) Kommreddy, A.; Bowsher, M. S.; Gunna, M. R.; Botha, K.; Vinod, T. K. *Tetrahedron Lett.* **2008**, *49*, 4378.
(56) Su, J. T.; Goddard III, W. A. *J. Am. Chem. Soc.* **2005**, *127*, 14146.
(57) Moorthy, J. N.; Singhal, N.; Senapati, K. *Tetrahedron Lett.* **2008**, *49*, 80.
(58) Richardson, R. D.; Zayed, J. M.; Altermann, S.; Smith, D.; Wirth, T. *Angew. Chem. Int. Ed.* **2007**, *46*, 6529.

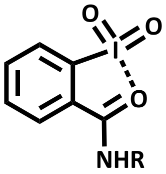
Ortho-group-modified IBX Analogs



IBX-esters[59]
(2004)

- Pseudo-benziodoxole structure
- Stable and soluble
- Intramolecular I···O
➡ better solubility

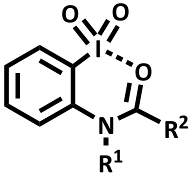
- Sulfides → sulfoxides (without overoxidation to sulfones)
- Alcohols → carbonyl compounds
with TFAA or $BF_3.Et_2O$



IBX-amides[60]
(2003)

- Pseudo-benziodoxole structure
- Planar geometry

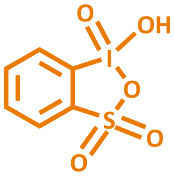
- Alcohols → carbonyl compounds
CH_2Cl_2, mild conditions, excellent yields without acid additives



NIPA[61]
(2005)

- Unique pseudobenziodoxazine structure
- 1st reported example of a 6-membered pseudocyclic scafold for I(V)
promising structure for further elaboration of chiral iodine(V) oxidants

- Selectively oxidize alcohols or sulfides

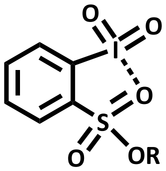


IBS[62]
(2006)

- Thia-analogue of IBX
- Unstable in organic solvent such as CH_3CN, DMSO, MeOH

(59) (a) Zhdankin, V. V.; Litvinov, D. N.; Koposov, A. Y.; Luu, T.; Ferguson, M. J.; McDonald, R.; Tykwinski, R. R. *Chem. Commun.* **2004**, 106
(b) Zhdankin, V. V.; Koposov, A. Y.; Litvinov, D. N.; Ferguson, M. J.; McDonald, R.; Luu, T.; Tykwinski, R. R. *J. Org. Chem.* **2005**, *70*, 6484
(60) Zhdankin, V. V.; Koposov, A. Y.; Netzel, B. C.; Yashin, N. V.; Rempel, B. P.Ferguson, M. J.; Tykwinski, R. R. *Angew. Chem. Int. Ed.* **2003**, *42*, 2194
(61) (a) U. Ladziata, A. Y. Koposov, K. Y. Lo, J. Willging, V. N. Nemykin; V. V. Zhdankin, Angew. Chem., Int. Ed., 2005, 44, 7127.
(b) Koposov, A.; Zhdankin, V. V. *J. Org. Chem.* **2006**, *71*, 9912
(62) A. Y. Koposov, D. N. Litvinov, V. V. Zhdankin, M. J. Ferguson, R. McDonald and R. R. Tykwinski, Eur. J. Org. Chem., 2006, 4791.

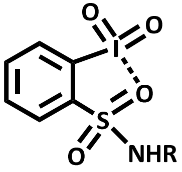
Ortho-group-modified IBX Analogs



IBS-esters[63]
(2005)

- Low solubility in non-polar organic solvents such as $CHCl_3$ and CH_2Cl_2

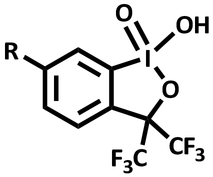
- Oxidizes alcohols with acid additives



IBS-sulfonamides[64]
(2004)

- Low solubility in non-polar organic solvents such as $CHCl_3$ and CH_2Cl_2
- Combination of intra- and intermolecular I···O
➡ unique heptacoordinated iodine(V) center

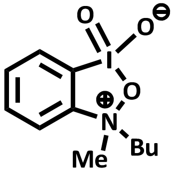
- Alcohols, sulfures, secondary amines in CH_3CN, reflux



(1991)[65]

- 1st non-aromatic I(V) reagent

- Oxidizes alcohols, good yields, mild conditions



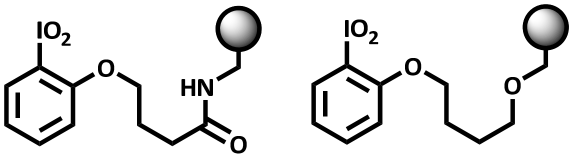
(2008)[66]

- 1st 2-iodyl-N,N-dialkylaniline

- Selectively oxidizes alcohols, mild conditions, in presence of TFAA

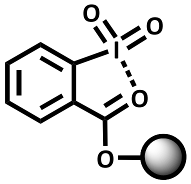
(63) (a) Kraszkiewicz, L.; Skulski, L. *ARKIVOC* **2003**, *vi*, 120
(b) Koposov, A. Y.; Litvinov, D. N.; Zhdankin, V. V. *Tetrahedron Lett.* **2004**, *45*, 2719
(c) Zhdankin, V. V.; Goncharenko, R. N.; Litvinov, D. N.; Koposov, A. Y. *ARKIVOC* **2005**, *iv*, 8.
(64) Koposov, A.; Zhdankin, V. V. *J. Org. Chem.* **2006**, *71*, 9912
(65) Kano, N.; Ohashi, M.; Hoshiba, K.; Kawashima, T. *Tetrahedron Lett.* **2004**, *45*, 8173.
(66) Zhdankin, V. V.; Nemykin, V. N.; Karimov, R. R.; Kazhkenov, Z.-G. *Chem. Commun.* **2008**, 6131.

Polymer Supported Analogs

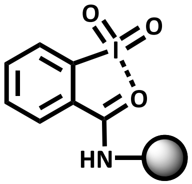


(2007)[68]

- New recyclable polymer-supported iodylphenol ethers
- Selectively oxidizes a wide range of alcohols



PS IBX-esters

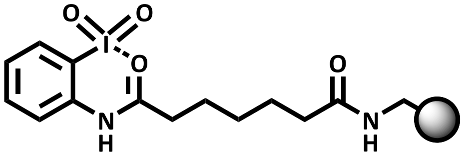


PS IBX-amides

(2003)[67]

- Easily prepared from polystyrene or Merrfield resins
- Recycling of the resin is possible with minmal loss of activity

- Excellent oxidative activity toward benzylic alcohols

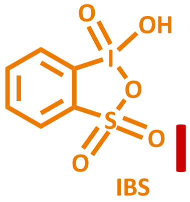


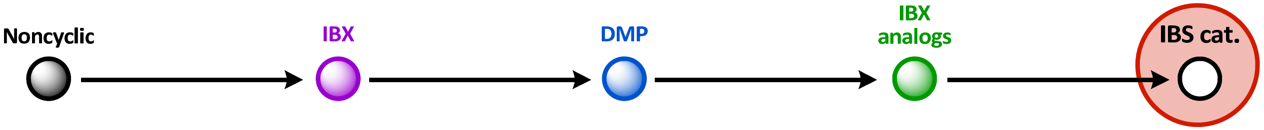
NIPA resin[69]
(2008)

- NIPA resin = recyclable polymer supported N-(2-iodylphenyl)acylamides

- Rapidly oxidizes a wide range of alcohols

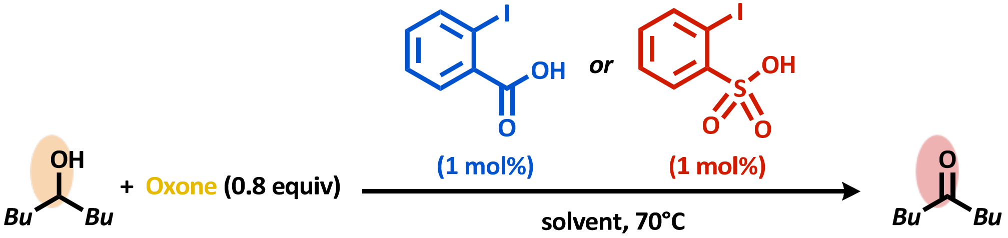
(67) (a) Chung, W.-J.; Kim, D.-K.; Lee, Y.-S. *Tetrahedron Lett.* **2003**, *44*, 9251
(b) Chung, W.-J.; Kim, D.-K.; Lee, Y.-S. *Synlett* **2005**, 2175
(c) Jang, H.-S.; Chung, W.-J.; Lee, Y.-S. *Tetrahedron Lett.* **2007**, *48*, 3731.
(68) Karimov, R. R.; Kazhkenov, Z.-G. M.; Modjewski, M. J.; Peterson, E. M.; Zhdankin, V. V. *J. Org. Chem.* **2007**, *72*, 8149.
(69) Ladziata, U.; Willging, J.; Zhdankin, V. V. *Org. Lett.* **2006**, *8*, 167.

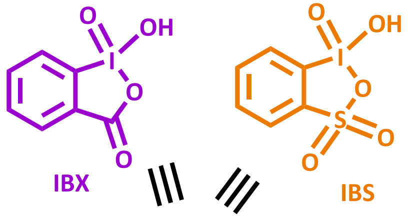


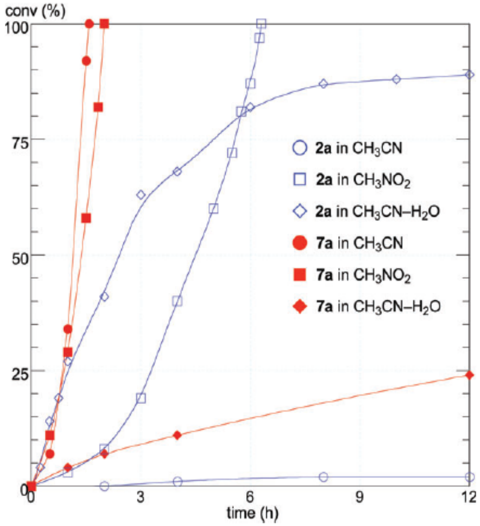


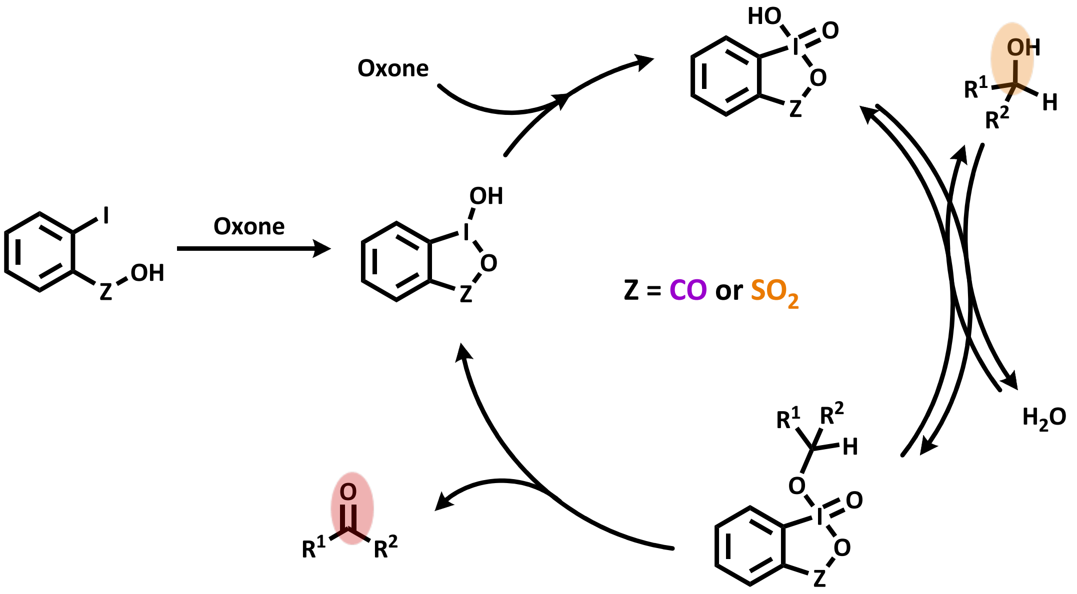
IBS-catalyzed oxidation of alcohols with Oxone®

- Investigation of catalytic efficiencies of **in-situ generated IBX and IBS**[70]**:**



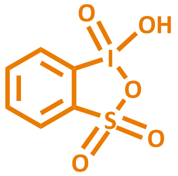






- In CH$_3$NO: **TOF = 50 h^{-1} vs. 16 h^{-1}**
- In Ch$_3$CN: **TOF = 63 h^{-1}** & **TON > 2000**
- With powdered Oxone: **TOF = 120 h^{-1}**

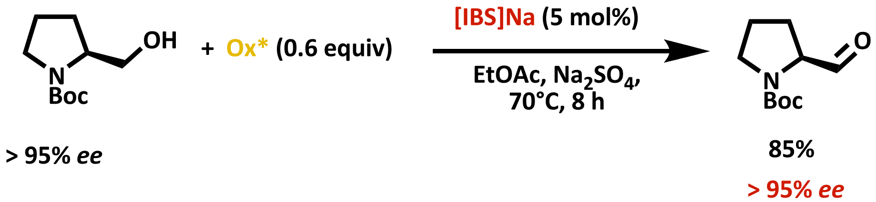
(70) Uyanik, M.; Akakura, M.; Ishihara, K. J. Am. Chem. Soc. **2009**, *131*, 251.

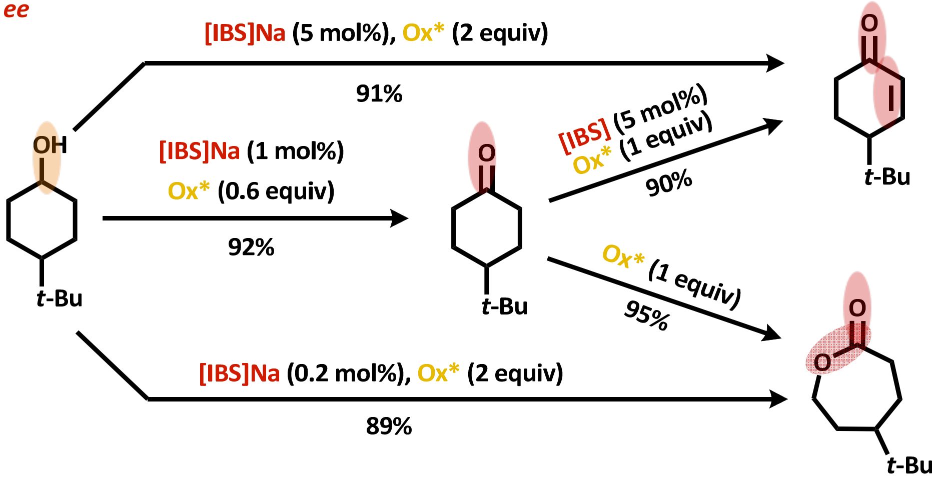


IBS

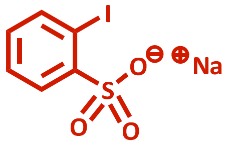
IBS goes catalytic

- No *ee* loss





Ox*: *powdered* Oxone



[IBS]Na

Oxone® = $2KHSO_5H \bullet KHSO_4 \bullet K_2SO_4$, a trademark of DuPont

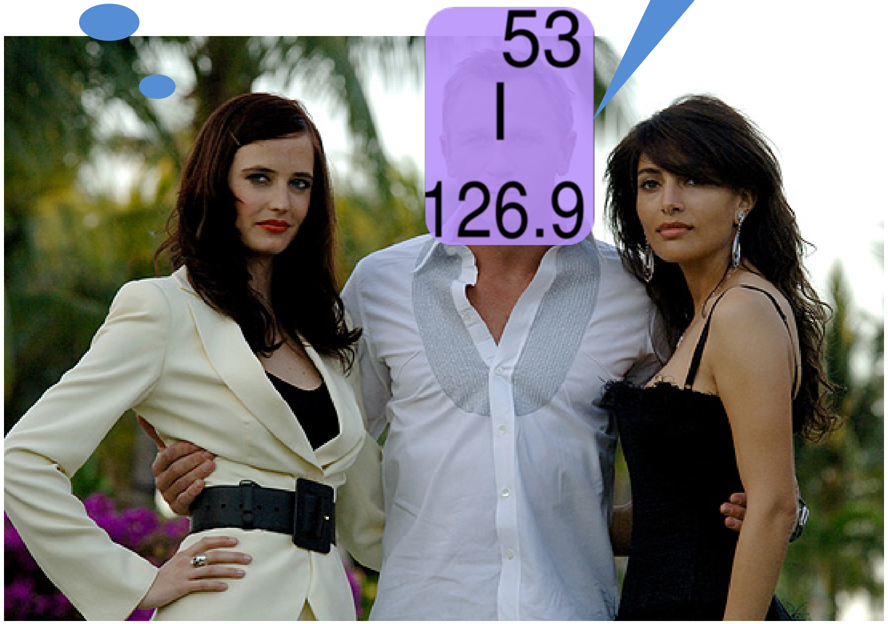
- Oxone offers several great advantages, including **stability, ease of transport, simple handling, controllable addition, non toxic nature, etc…** although aqueous H_2O_2 and gaseous O_2 are more atom economically begnin than Oxone.

(70) Uyanik, M.; Akakura, M.; Ishihara, K. J. Am. Chem. Soc. **2009**, *131*, 251.

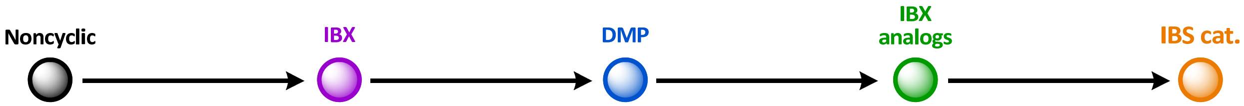
Conclusion

- Future Goals:
  - Searching for newer reagents that will lead to new reaction transformations.
  - Recyclable polymer-supported reagents
  - Broadening the scope of reactivity by studying transition metal-mediated reactions

- The chemistry of hypervalent iodine reagents is cool because:
  - Fundamental reactions with versatility have been developed
  - Mild reactivity with good yields
  - Readily available reagents easy to work with
  - Non-toxic, enviromentally-friendly reagents



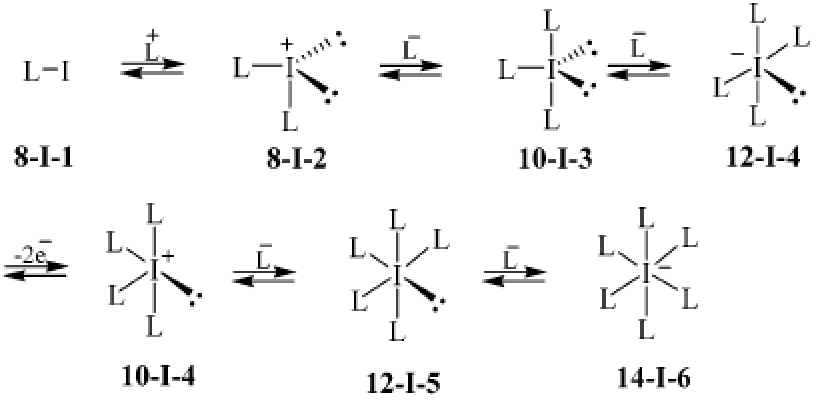
(71) Lee, S. *The Chemistry of Hypervalent Iodine* **2003**.



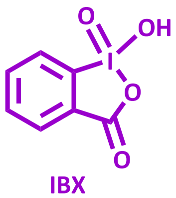
Thank you so much STéRéO !

To go farther…

- *Although it is rare in the solar system and Earth's crust, the iodides are very soluble in water, and the element is concentrated in seawater. This mechanism helps to explain how the element came to be required in trace amounts by all animals and some plants, being by far the heaviest element known to be necessary to living organisms.*

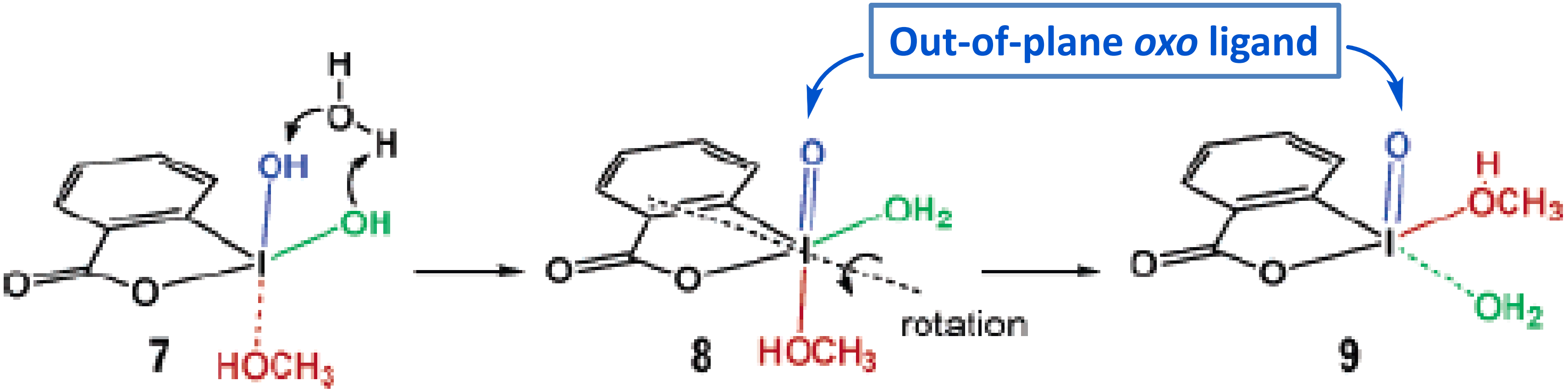


N-I-L
N= number of valence electrons
L= number of ligands



Mechanistic Study[17]

Alcohol/Water Exchange



- Alcohols /water exchange occurs via 2 steps:
  - a **fast proton transfer**
  - a **slower coordinated ligand motion**

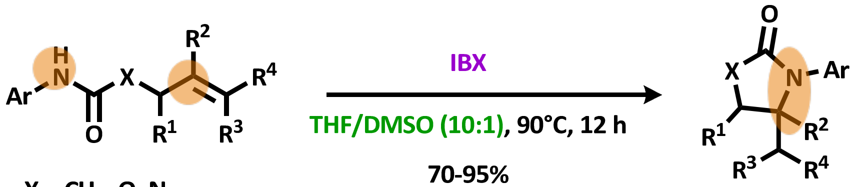
- Lacking an anionic ligand to twist with, the **dative oxo ligand (I^+-O^-)** stays out of the plane to **maximize charge transfer**.

(17) Su J. T.; Goddard W. A. *J. Am. Chem. Soc.* **2005**, *127*, 14146

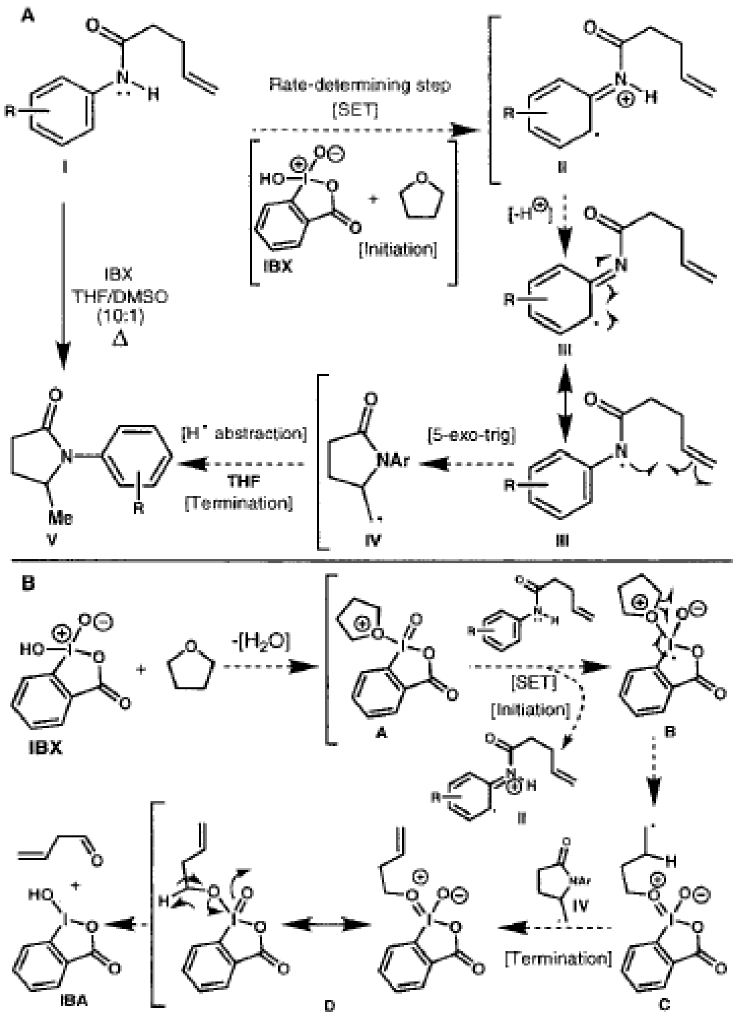
To go farther…

IBX insoluble in common organic solvents due to the strong intermolecular secondary bonding creating a 3D polymeric structure.

(A) Mechanistic Rationale for the SET-Based
IBX-Mediated Cyclization of Anilides and Related Compounds
(B) Plausible Role of the Solvent in These Reactions



X = CH_2, O, N
Ar = Ph, 3-Et-C_6H_4, 3-BrC_6H_4, 3-FC_6H_4, 4-EtC_6H_4, etc.
R^1 - R^4 = H, alkyl, cycloalkyl, etc.



To go farther…

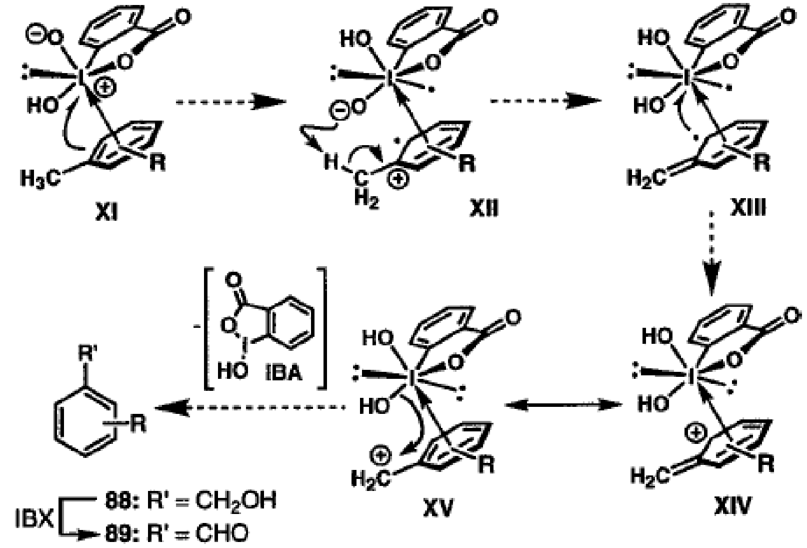


Figure 6. Concerted mechanism for the IBX-mediated benzylic oxidation.

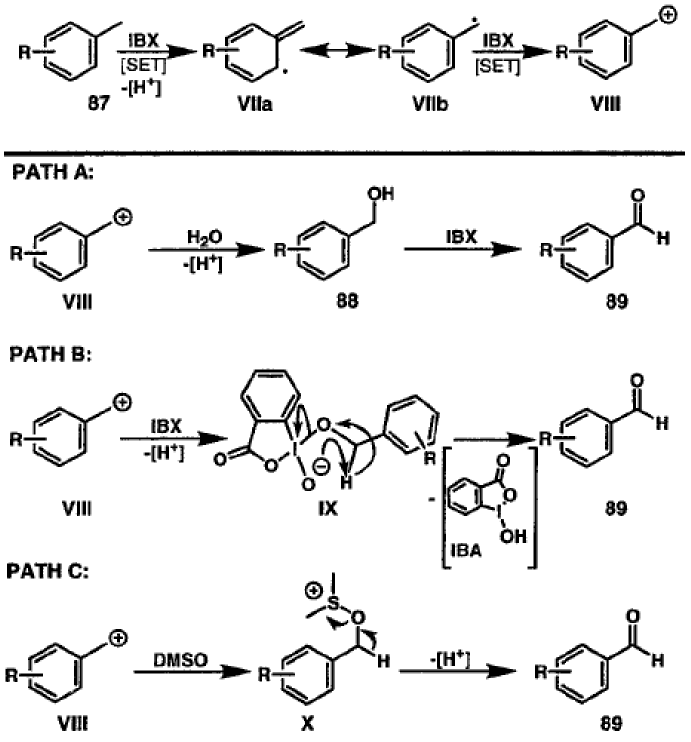


Figure 5. Postulated mechanistic pathways for benzylic oxidation using IBX.

To go farther…

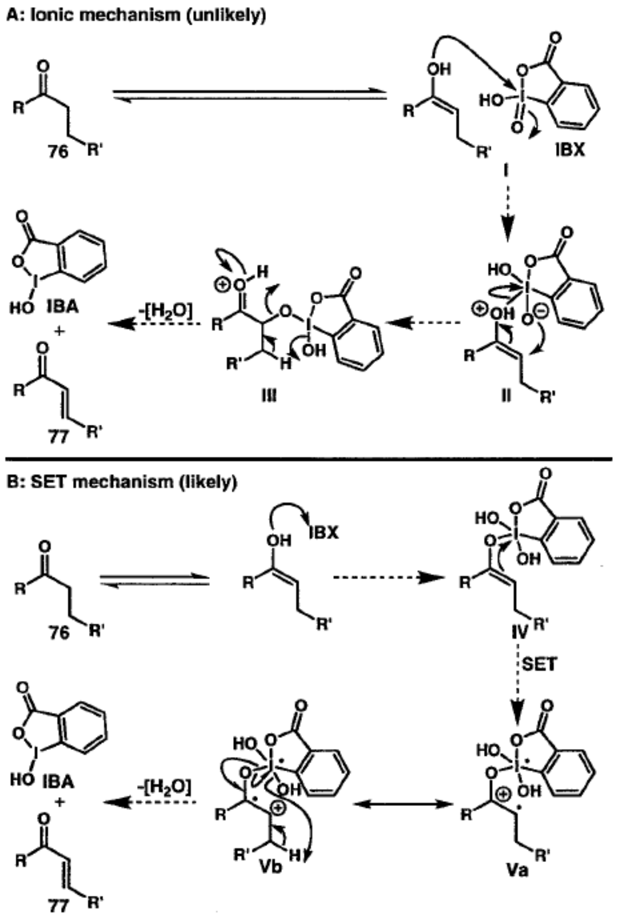
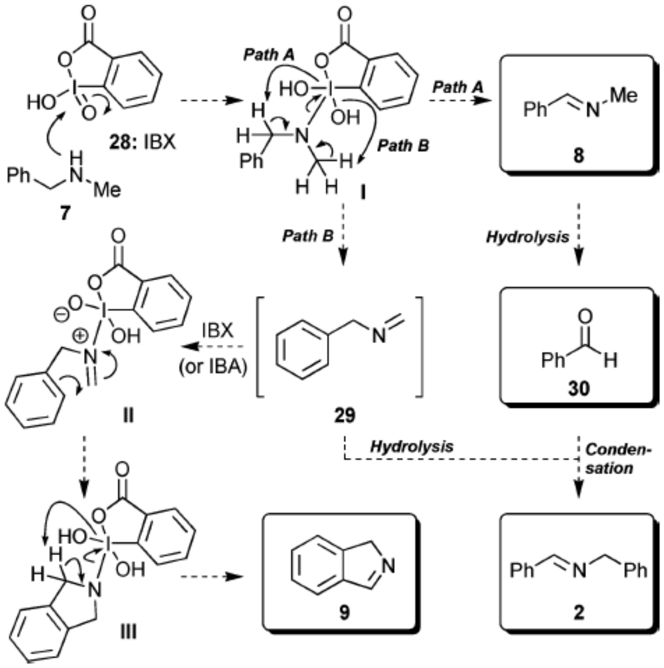


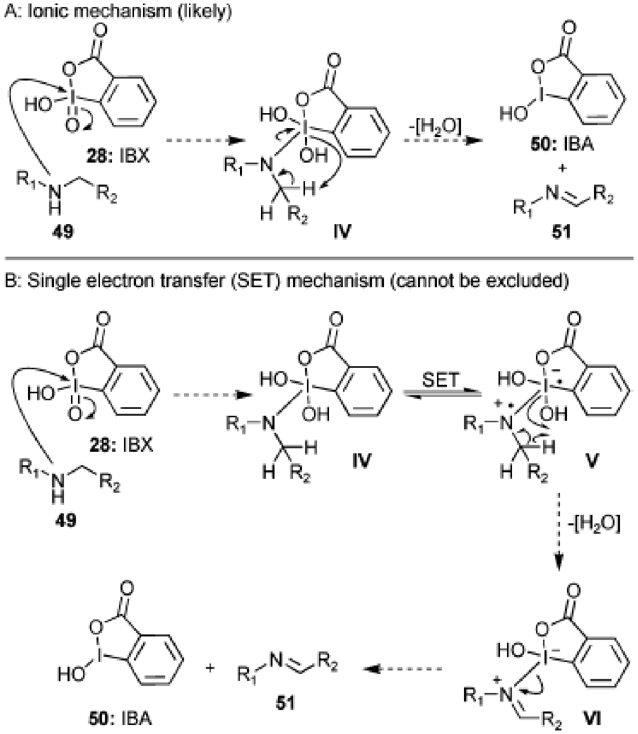
Figure 3. Possible ionic- (A) and SET-based (B) mechanisms for the dehydrogenation of carbonyl compounds by IBX. Alternatively IBX may also be considered to effect the initial enolization of the carbonyl compound to yield **IV** directly.

Scheme 1. Proposed Mechanism Leading to the Formation of **2**, **8**, and **9** from Precursor Secondary Amine **7**



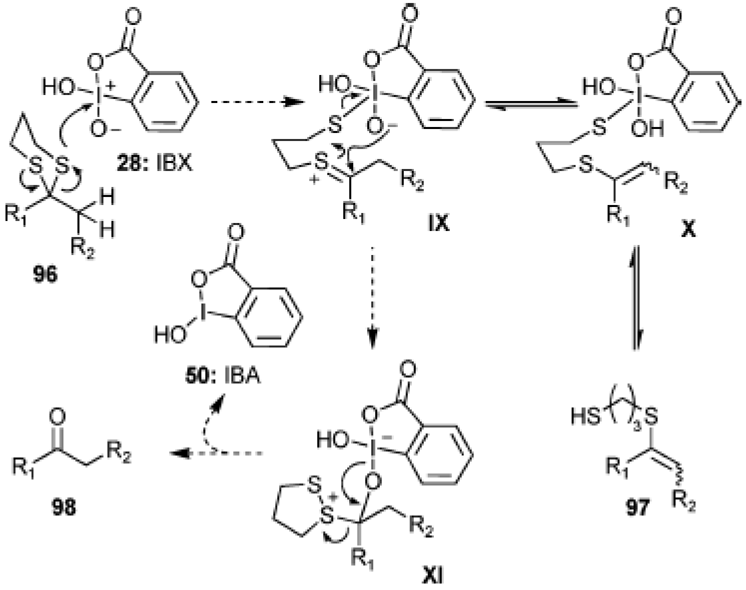
To go farther…

Scheme 3. Proposed (A) Ionic and (B) Single Electron Transfer (SET) Mechanisms for the Oxidation of Amines Mediated by IBX

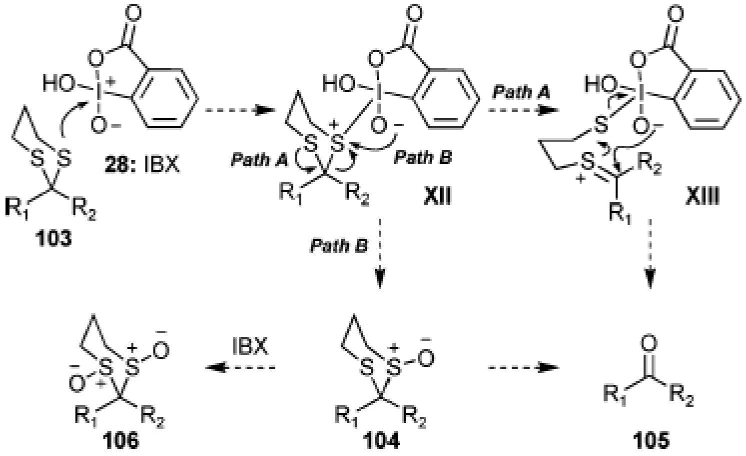


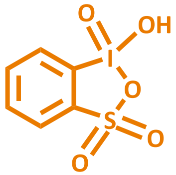
To go farther…

Scheme 7. Postulated Mechanistic Rationale for the Deprotection of Dithianes by IBX under Neutral Conditions



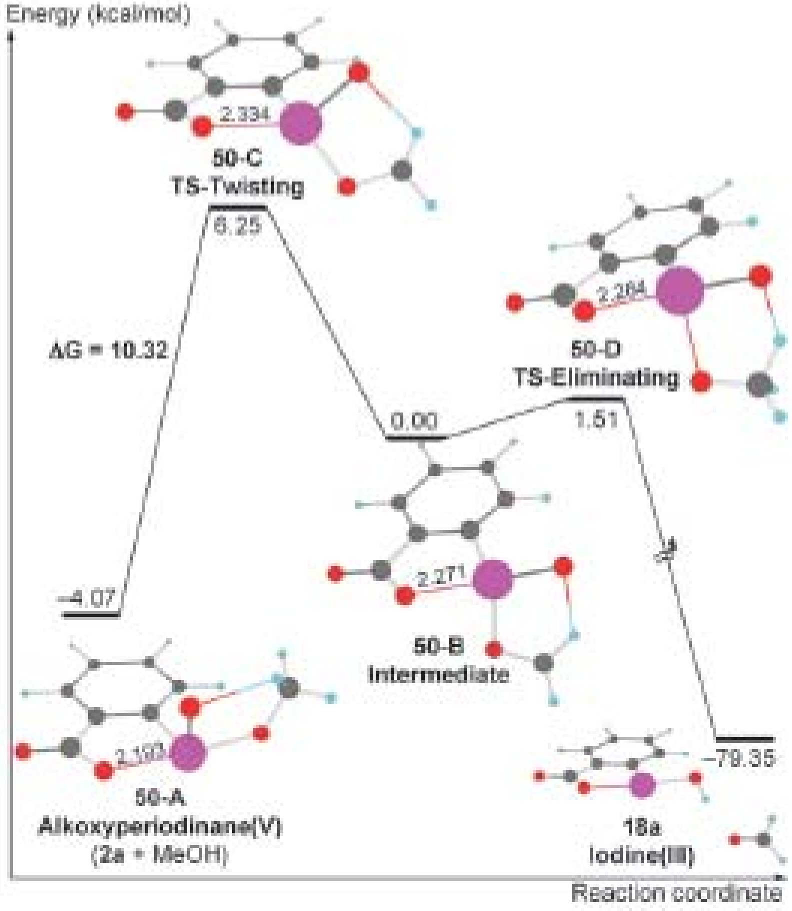
Scheme 9. Postulated Mechanistic Rationale for the Deprotection of Sterically Hindered Dithianes, Lacking α-Hydrogens, by IBX

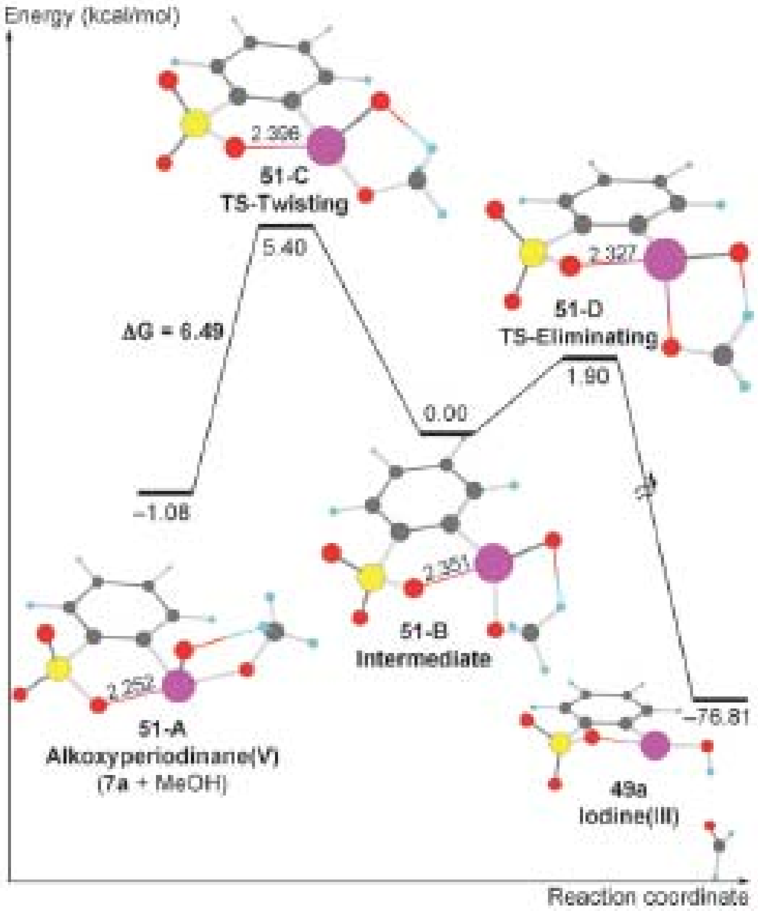




IBS

IBS goes catalytic





(70) Uyanik, M.; Akakura, M.; Ishihara, K. J. Am. Chem. Soc. **2009**, *131*, 251.

About the painting…

Claude GELLÉE dit Claude LORRAIN[50]
Chamagne (Vosges), vers 1602 - Rome, 1682

Port de mer, effet de brume (L'Embarquement d'Ulysse, ou d'Énée, Iule et Achate ?)[51]
1646
H. : 1,19 m. ; L. : 1,5 m.
Musée du Louvre, Paris
Richelieu
2 e étage
Claude Gellée, dit Le Lorrain
Salle 15

L'identité du destinataire de ce tableau peint "pour Paris'' n'est pas précisée dans le *Liber Veritatis* ("Livre de vérité") que Claude Gellée tenait à jour.
Collection de Louis XIV (acquis en 1695).
Département des Peintures.

- Claude LORRAIN pour qui ***" La lumière est moins le moyen de faire voir les choses que le sujet même du tableau"***. (Ozenfant – Mémoires)

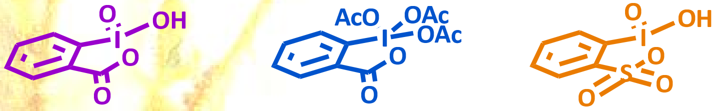
(50) http://fr.wikipedia.org/wiki/Claude_Lorrain
(51) http://cartelen.louvre.fr/cartelen/visite?srv=car_not_frame&idNotice=1150

Alternative First Page

William Turner Painting

Hypervalent Iodine(V) compounds: an oxidative journey

From IBX to DMP and IBS



Damien Mailhol, 1st year Ph.D.