Hexafluoroisopropanol as a highly versatile solvent

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Supervisor: Prof. Yong Huang
Date: Dec. 11th, 2017

Ignacio, C. *Nat. Rev. Chem.* **2017**, *1*, 0088.

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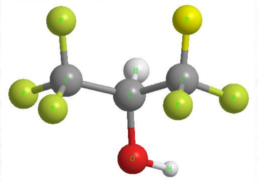
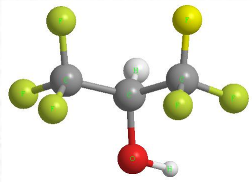


Part 1

Physical and chemical properties of HFIP

- *Physical properties*
- *Enhanced acidity*
- *Reduced nucleophilicity*
- *Hydrogen-bond donating ability*
- *Redox stability*
- *Cation stabilization*

Physical and chemical properties of HFIP

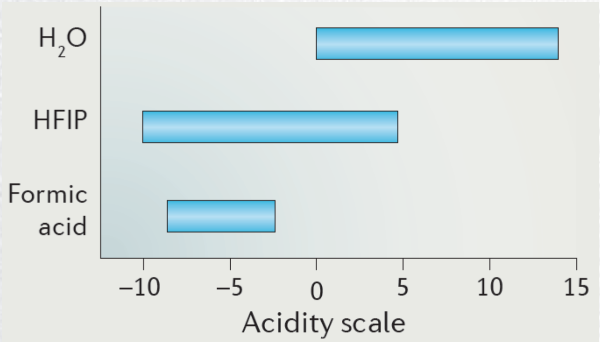


Physical properties

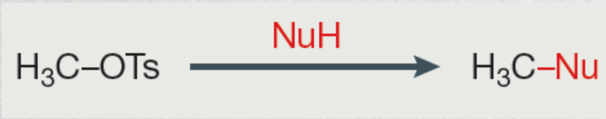
HFIP does not absorb UV light, is thermally stable and is miscible with both water and most common polar organic solvents. The low boiling point (bp = 59 ° C; for comparison, the bp of *i*PrOH is 82.2 ° C).

Enhanced acidity

HFIP in aqueous solution (p*K*a = 9.3) compared with *i*PrOH (p*K*a = 17.1)



Reduced nucleophilicity



$N_{OTs}(\text{HFIP}) = -4.23$

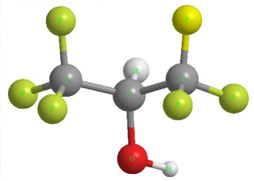
$N_{OTs}(^{i}\text{PrOH}) = 0.2$

$\log k = s_N (E + N)$

Mayr Equation

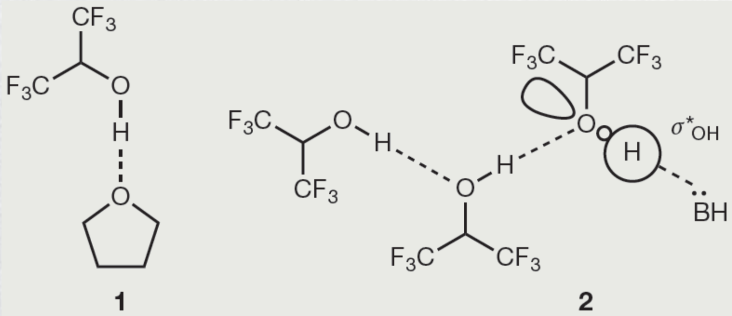
Persson, O. *J. Chem. Soc., Perkin Trans.* **1995**, *2*, 1735.
Carter, G. E. *J. Org. Chem.* **1983**, *48*, 579.

Physical and chemical properties of HFIP

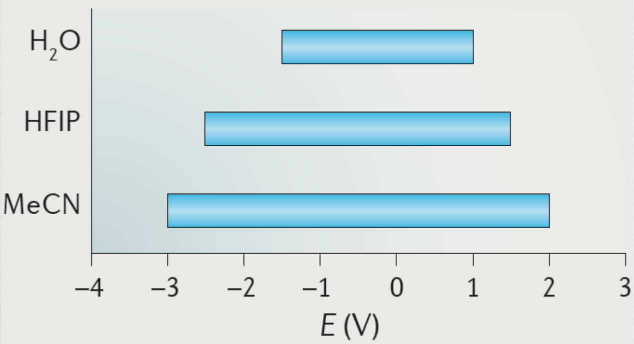


Hydrogen-bond donating ability

THF: bp = 66° C



Redox stability



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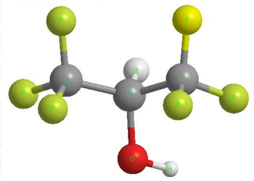
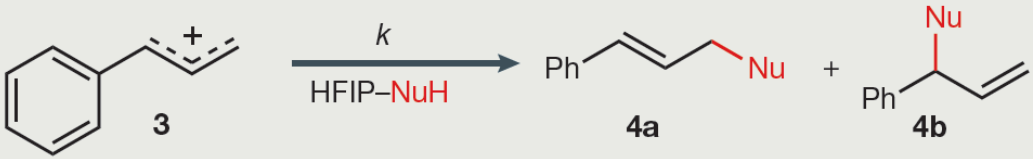
Neudorfl, J. M. *J. Am. Chem. Soc.* **2006**, *128*, 8421.
Baltruschat, H. *J. Electroanal. Chem.* **2013**, *701*, 1.

Physical and chemical properties of HFIP



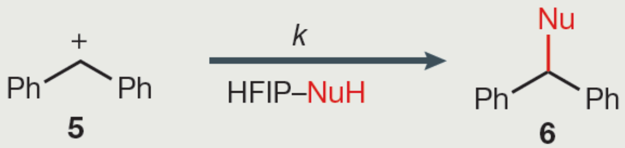
Cation stabilization

$\varepsilon = 15.7$



HFIP	$k\ (s^{-1}) = 2.2 \times 10^4$
HFIP–H_2O	$k\ (M^{-1}\ s^{-1}) = 9.5 \times 10^4$
HFIP–MeOH	$k\ (M^{-1}\ s^{-1}) = 1.8 \times 10^6$
HFIP–Br^-	$k\ (M^{-1}\ s^{-1}) = 1.5 \times 10^{10}$

$mol^{1-n} \cdot L^{n-1} \cdot s^{-1}$



HFIP–H_2O (98:2)	$k\ (s^{-1}) = 2.0 \times 10^4$
HFIP–H_2O (95:5)	$k\ (s^{-1}) = 1.7 \times 10^5$
HFIP–H_2O (90:10)	$k\ (s^{-1}) = 1.0 \times 10^6$
HFIP–H_2O (70:30)	$k\ (s^{-1}) = 7.5 \times 10^6$

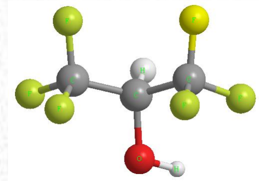
Schepp, N. P. *J. Phys. Org. Chem.* **2009**, *22*, 343.
Mayr, H. *J. Phys. Org. Chem.* **2013**, *26*, 59.

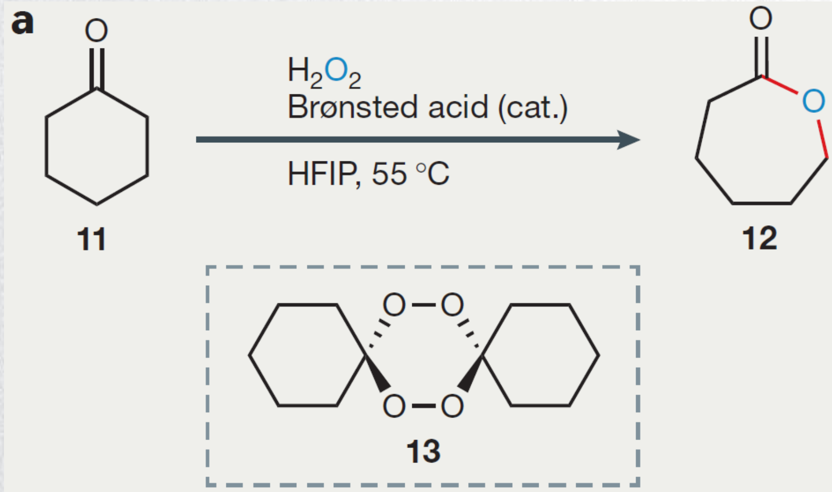
Part 2

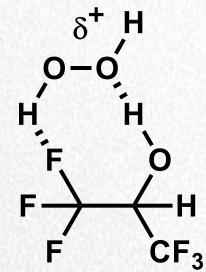
HFIP in organic chemistry

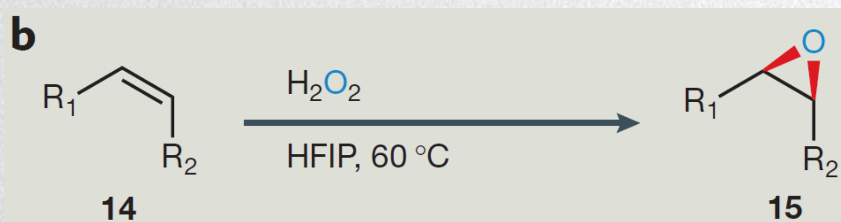
- *Activation of hydrogen peroxide*
- *Activation of organic functionalities*
- *Activation of hypervalent iodine reagents*
- *Metal-free C–H activation*

Activation of hydrogen peroxide



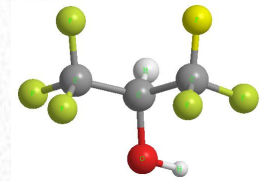






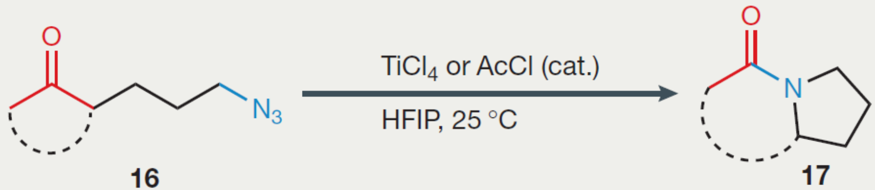
Neumann, R. *Org. Lett.*, **2000**, *2*, 2861.
Andreae, M. R. M. *Tetrahedron Lett.* **2001**, *42*, 2293.
Berkessel, A. *Angew. Chem. Int. Ed.* **2002**, *41*, 4481.

Activation of organic functionalities

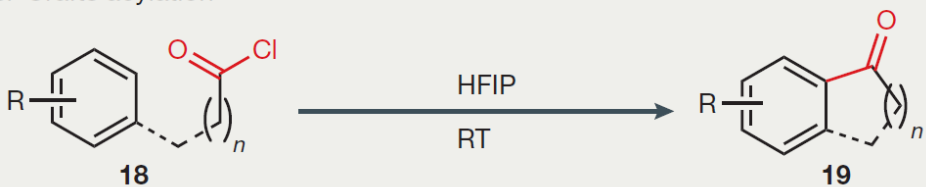


Carbonyl or acetal activation

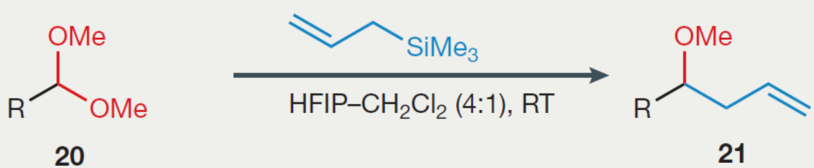
Schmidt reaction



Friedel–Crafts acylation

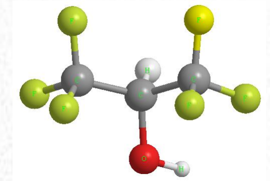


Hosomi–Sakurai reaction

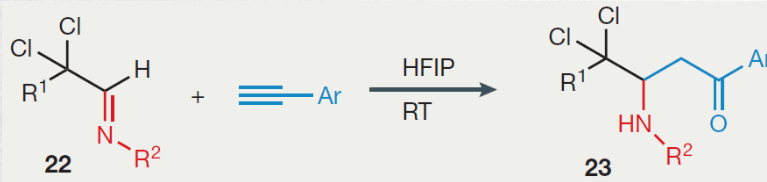


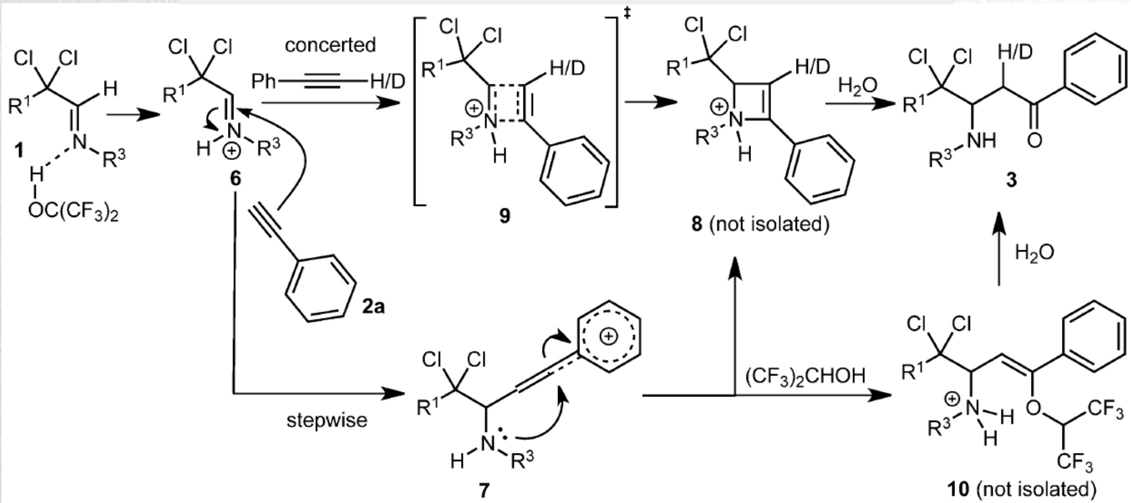
Aube, J. *Org. Lett.* **2015**, *17*, 5484.
Smit, W. A. *Angew. Chem. Int. Ed.* **2008**, *47*, 9739.

Activation of organic functionalities



Imine

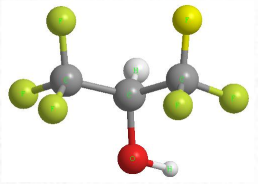




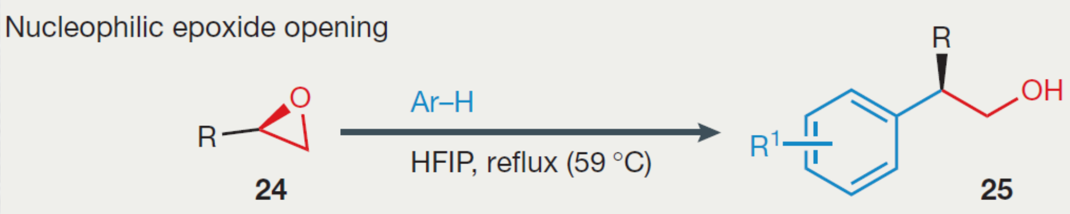
Plausible mechanisms for the formation of β-amino ketones in the presence of HFIP

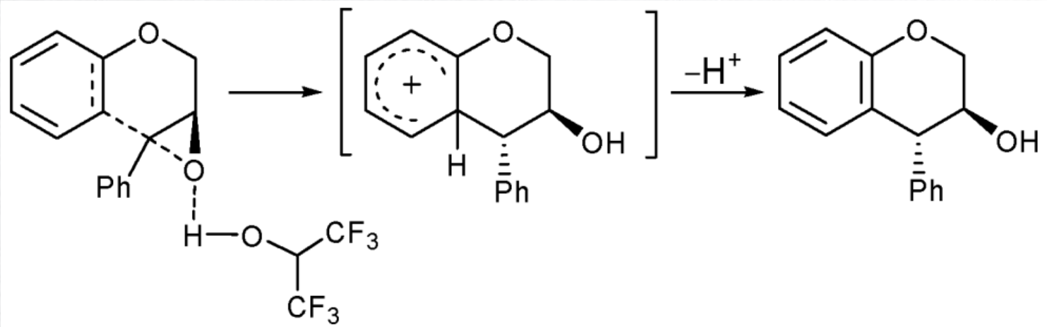
Tehrani, K. A. *Adv. Synth. Catal.* **2016**, *358*, 41.

Activation of organic functionalities



Epoxide

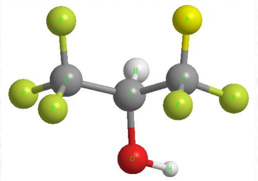




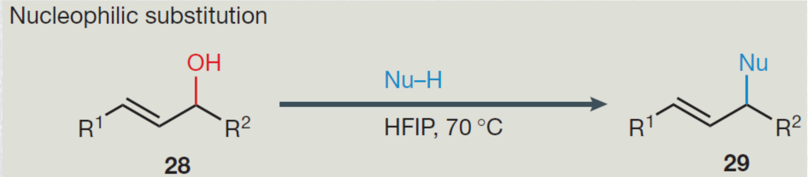
Concerted addition of arene to the proton activated oxirane

Qu, J. *Chem. Commun.* **2010**, *46*, 2653.

Activation of organic functionalities

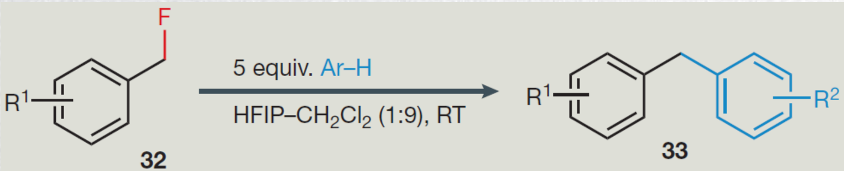


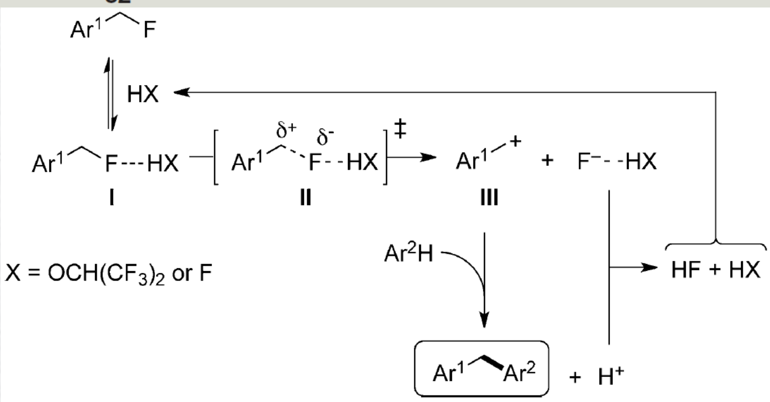
Alcohol



amines, sulfonamides, carbamates;
allyl silanes and 1,3-dicarbonyl compounds.

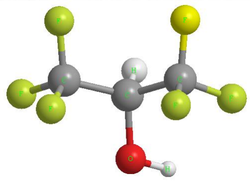
Halide



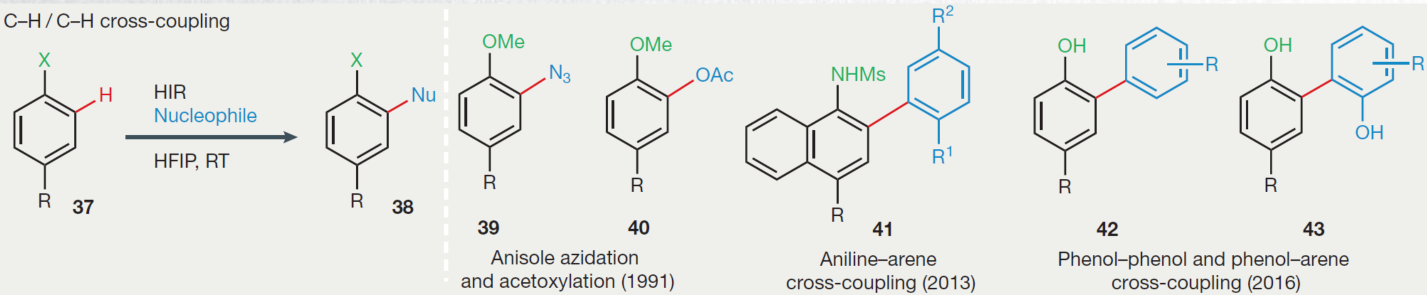


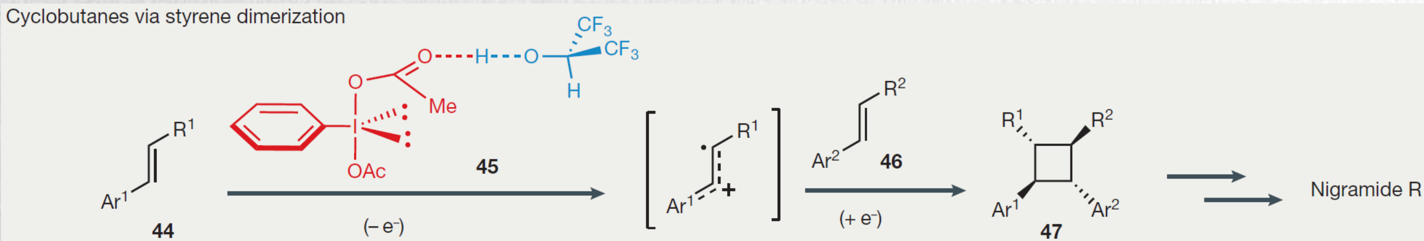
Najera, C. *J. Org. Chem.* **2012**, *77*, 7344.
Paquin, J. F. *Angew. Chem. Int. Ed.* **2014**, *53*, 13835..

Activation of hypervalent iodine reagents



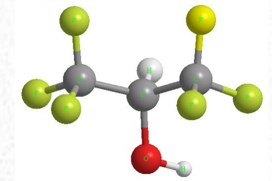
Hypervalent iodine reagents

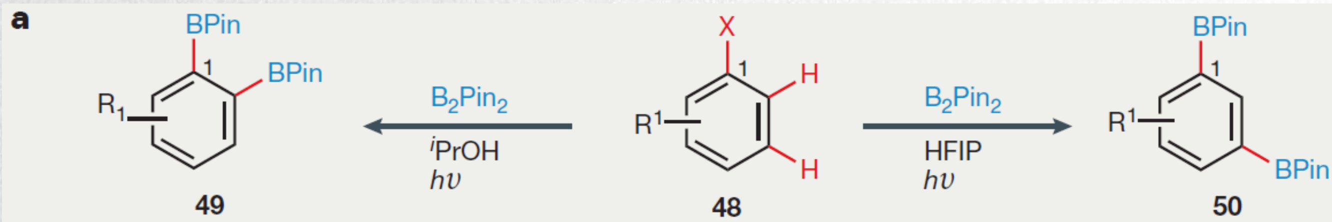


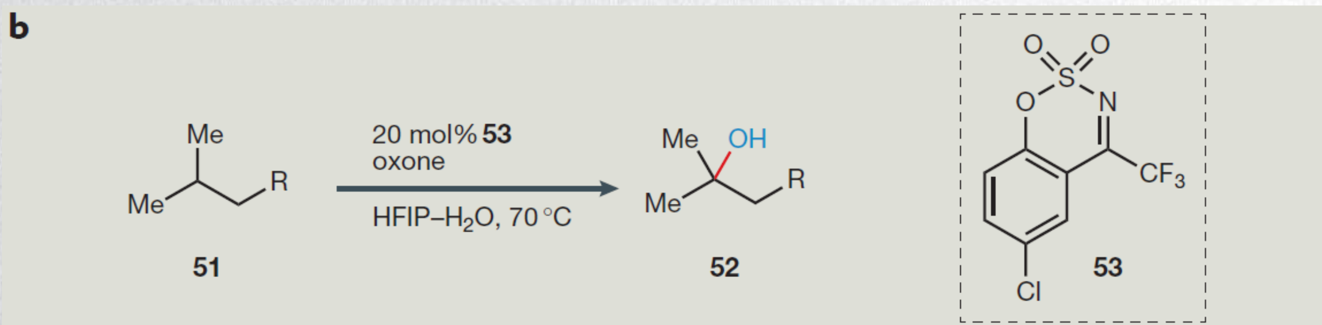


Yakura, T. *Tetrahedron Lett.* **1991**, *32*, 4321.
Ito, M. *J. Am. Chem. Soc.* **2013**, *135*, 14078.
Morimoto, K. *Angew. Chem. Int. Ed.* **2016**, *55*, 3652.
Donohoe, T. J. *Angew. Chem. Int. Ed.* **2016**, *55*, 4748.

Metal-free C–H activation







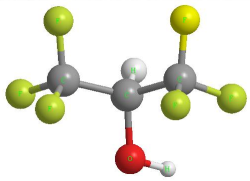
Larionov, O. V. *J. Am. Chem. Soc.* **2016**, *138*, 8408.
Du, B. J. *Chem. Sci.* **2014**, *5*, 656.

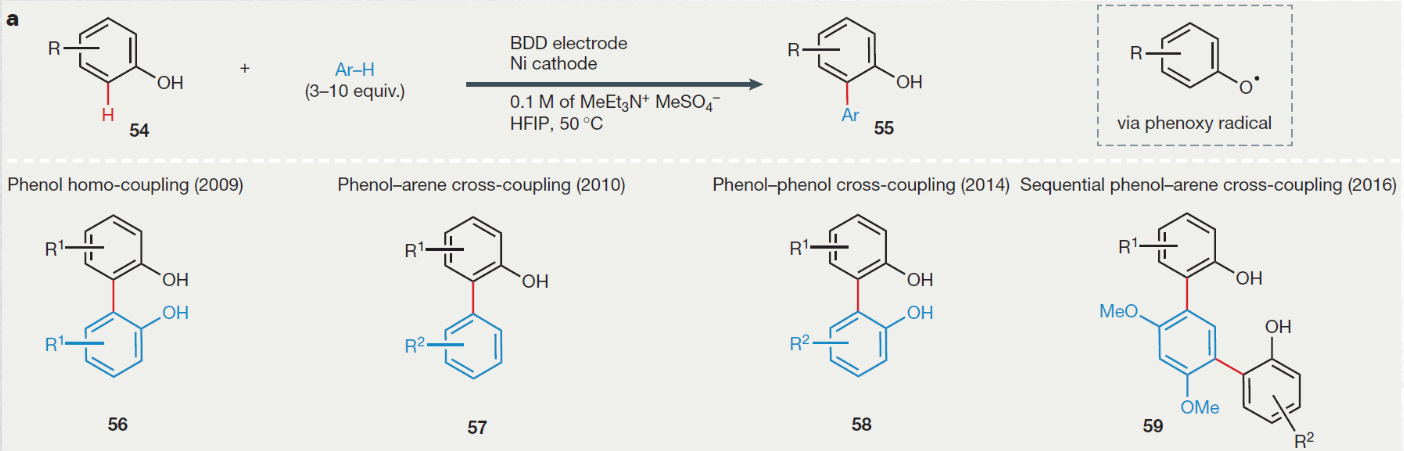
Part 3

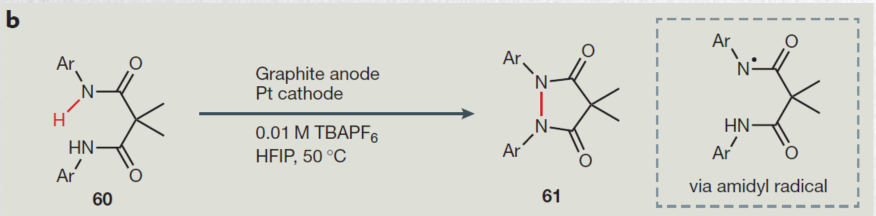
Electrochemical methods

C–H and N–H electrochemical oxidative coupling

C–H and N–H electrochemical oxidative coupling







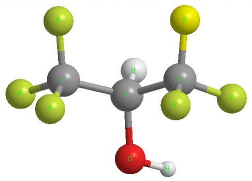
Waldvogel, S. R. *Chem. Eur. J.* **2009**, *15*, 2273.
Waldvogel, S. R. *Angew. Chem. Int. Ed.* **2010**, *49*, 971.
Waldvogel, S. R. *Angew. Chem. Int. Ed.* **2014**, *53*, 5210.
Lips, S. *Angew. Chem. Int. Ed.* **2016**, *55*, 10872.
Waldvogel, S. R. *Angew. Chem. Int. Ed.* **2016**, *55*, 9437.

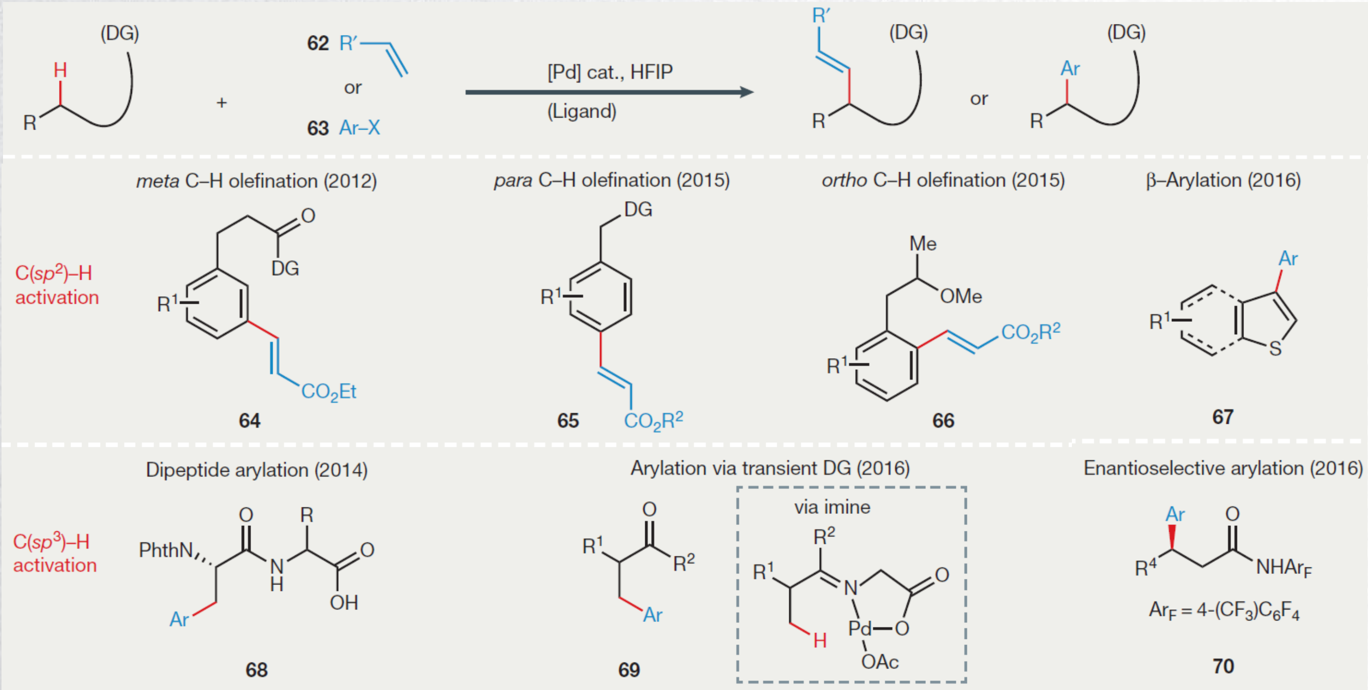
Part 4

Organometallic and inorganic chemistry

- *Metal-catalysed C–H activation*
- *Non-classical hydrogen bonding between HFIP and transition metal complexes*

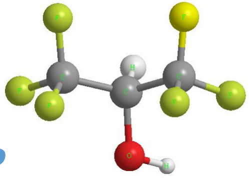
Metal-catalysed C–H activation



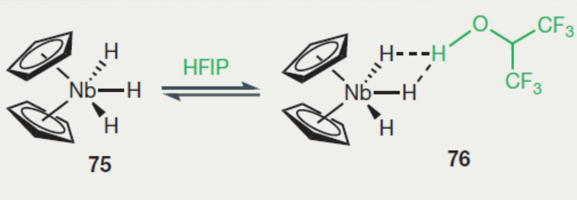


Yu, J. Q. *Nature* **2012**, *486*, 518.
Yu, J. Q. *J. Am. Chem. Soc.* **2015**, *137*, 11888.
Colletto, C. *J. Am. Chem. Soc.* **2016**, *138*, 1677.
Yu, J. Q. *J. Am. Chem. Soc.* **2014**, *136*, 16940.
Yu, J. Q. *Science* **2016**, *351*, 252.
Chen, G. *Science* **2016**, *353*, 1023.

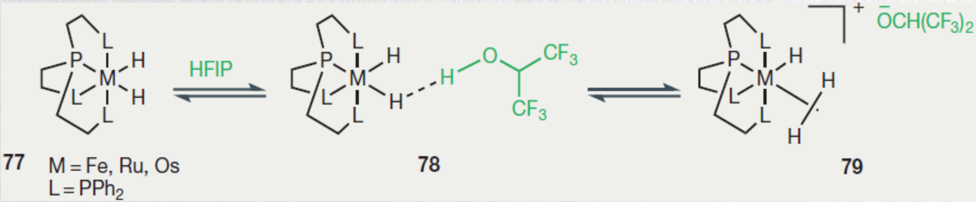
Non-classical hydrogen bonding between HFIP and transition metal complexes



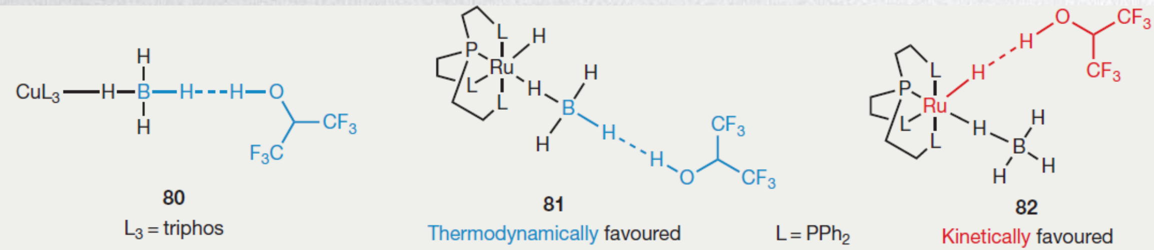
Formation of a dihydrogen bond between [NbCp2H3] and HFIP



Proton transfer through dihydrogen bonding



Protonation at B–H vs M–H



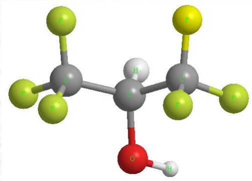
Shubina, E. S. *Chem. Eur. J.* **2004**, *10*, 661.
Belkova, N. V. *Inorg. Chem.* **2014**, *53*, 1080.
Shubina, E. S. *Can. J. Chem.* **2001**, *79*, 479.
Golub, I. E. *Dalton Trans.* **2016**, *45*, 9127.

Part 5

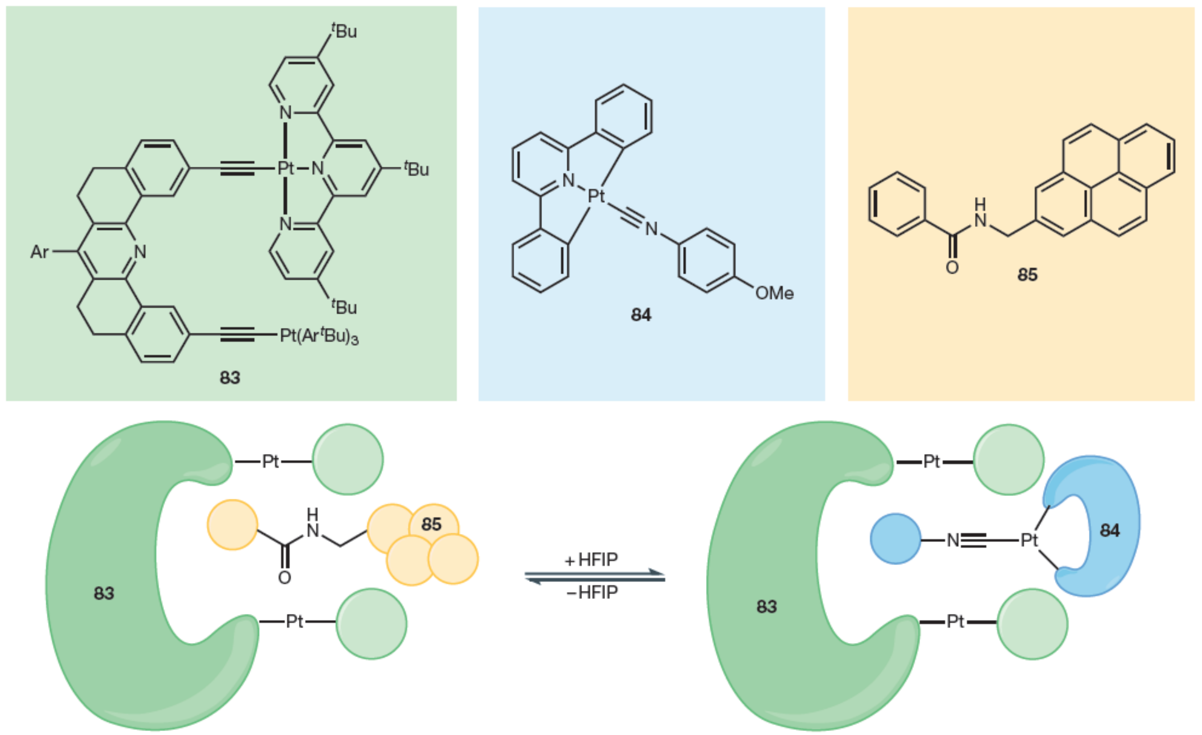
Supramolecular and polymer science

- *HFIP in polymerization reactions*
- *Electrospinning and electrocasting*

Supramolecular and polymer science

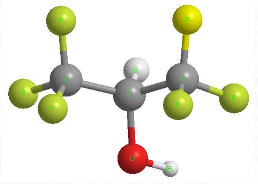


Molecular tweezers

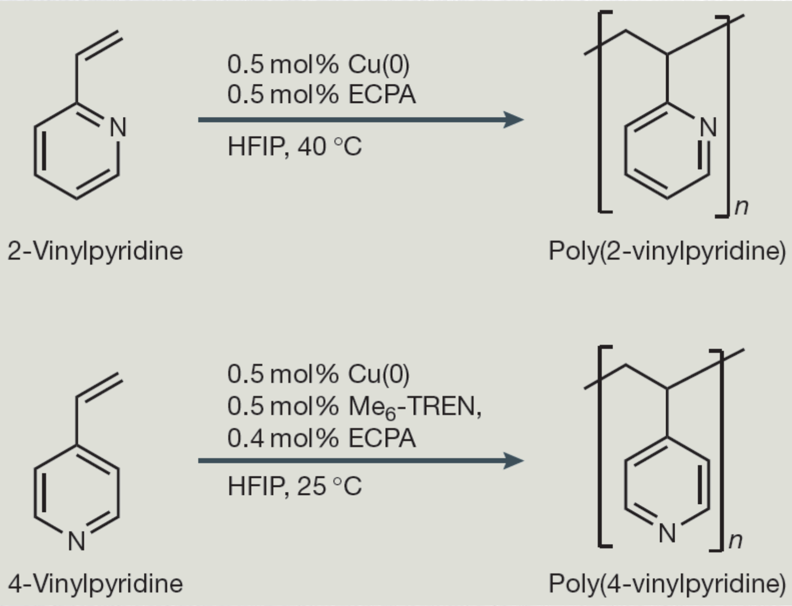


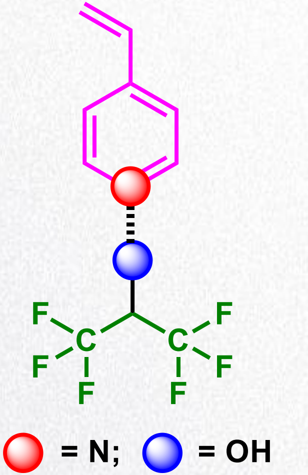
Li, Z. *Dalton Trans.* **2016**, *45*, 17290.

HFIP in polymerization reactions



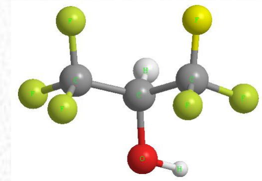
Radical polymerization reactions



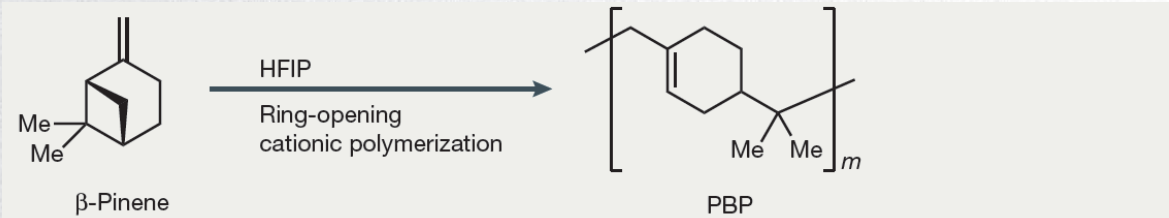


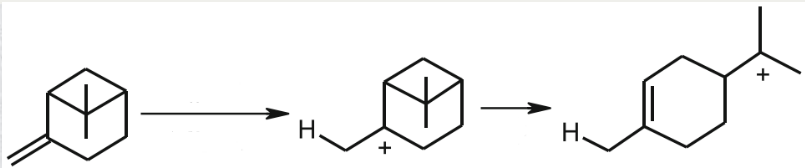
Zhu, X. L. *Polymer* **2013**, *54*, 3248.
Zhu, X. L. *Polym. Chem.* **2015**, *6*, 2620.

HFIP in polymerization reactions

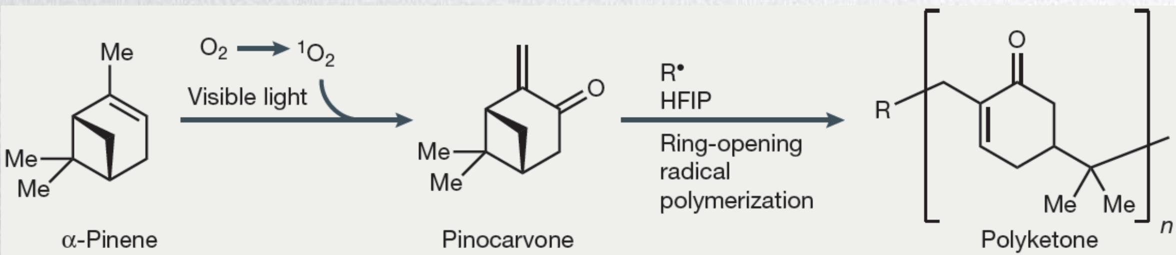


Cationic polymerization



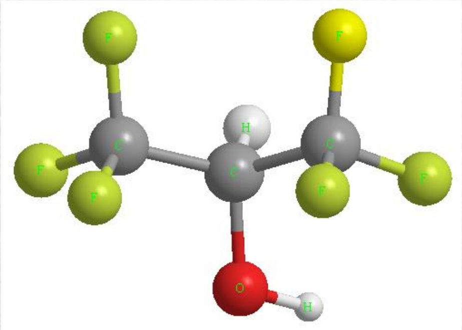


Polymerization of pinene



Smit, W. A. *J. Polym. Res.* **2012**, *19*, 9884.
Kamigaito, M. *Angew. Chem. Int. Ed.* **2016**, *55*, 1372.

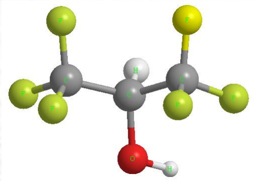
Summary



HFIP has recently become a very popular solvent or additive with applications across the spectrum of chemistry. It possesses a wide range of interesting and unique properties.

Uncovering the interactions of HFIP with functional groups within organic molecules or with metal complexes may reveal new modes of activation that will lead to new modes of reactivity.

Acknowledgement

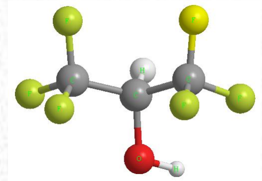


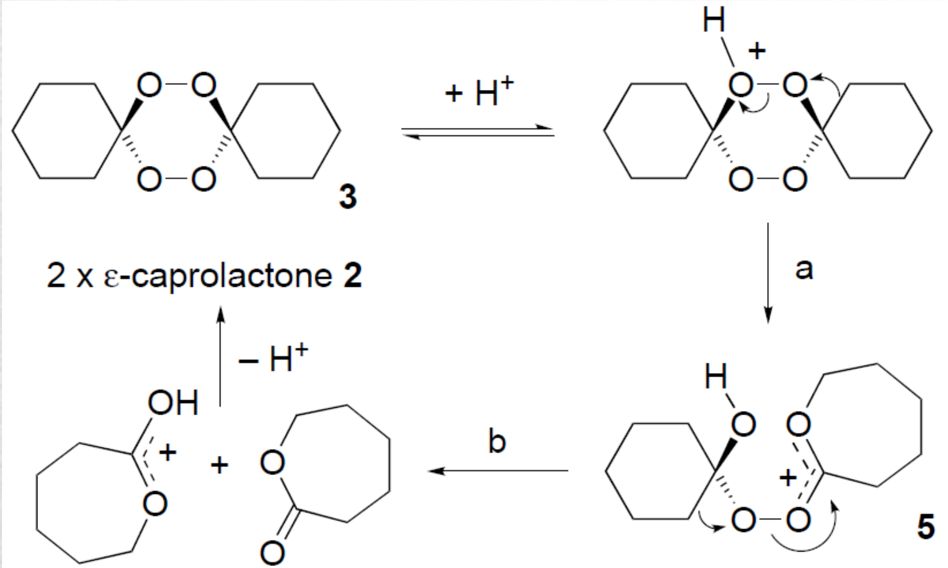
- ***Prof. Huang***
- ***Dr. Chen***
- ***All members in E201***

Thanks for your attention!

Ignacio, C. *Nat. Rev. Chem.* **2017**, *1*, 0088.

Activation of hydrogen peroxide





Postulated mechanism for the rearrangement of 3 to 2

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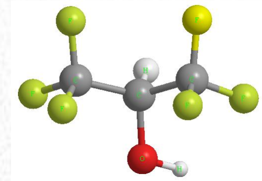
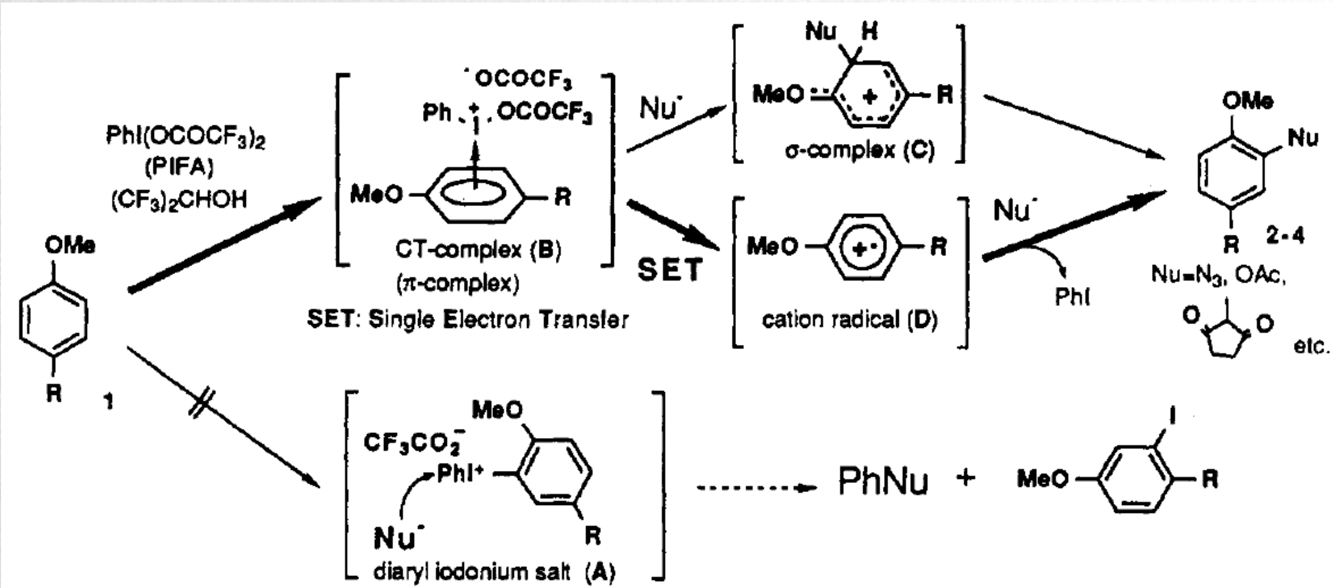
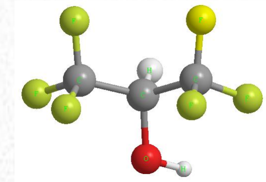
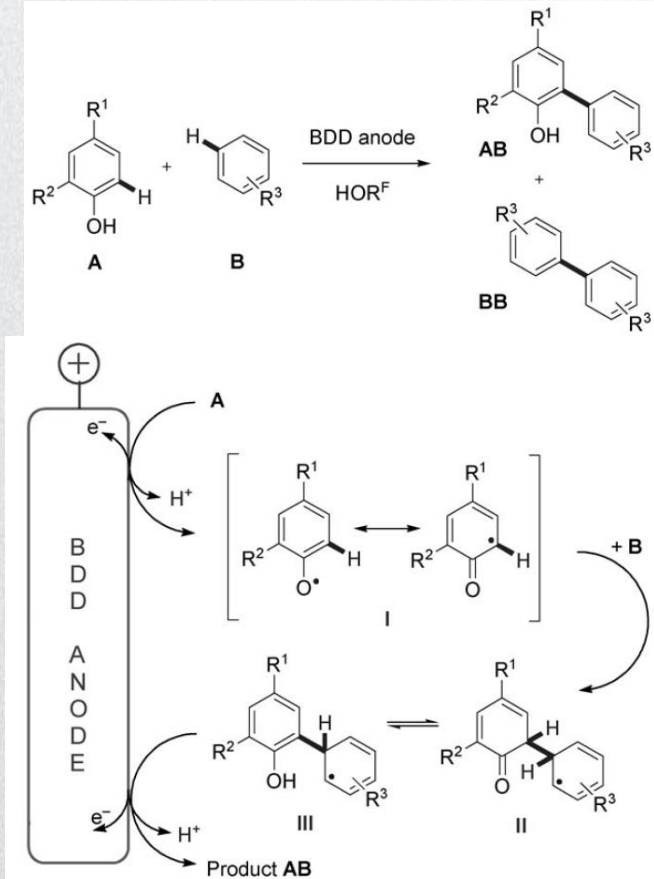
Activation of hypervalent iodine reagents





C–H and N–H electrochemical oxidative coupling





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