José Barluenga

José Joaquin Barluenga Mur was born in **Tardienta** 07/27/1940

1963 BS from the University of Zaragoza
1963 - 1966 PhD with Prof. Vicente Gomez Aranda (Zaragoza)
1967 - 1970 Postdoc with Prof. Heinz Hoberg at Max-Planck-Institute für Kohlenforshung an der Rühr (Germany)
1970 - 1972 Scientific collaborator CSIC (Zaragoza)
1972 - 1975 Associate professor (Zaragoza)
1975 - 2010 Professor at the University of Oviedo. 1993 - Director of the University Institute for Organometallic Chemistry "Enrique Moles" (Oviedo)
2011 - today Emeritus Professor (Oviedo)

Numbers
632 Publications (SciFinder)
35 Reviews

Research interests
1963 - 1966 PhD in organomercury chemistry
1967 - 1970 Postdoc in organoaluminium chemistry
1970 - 1984 Addition of nitrogen nucleophiles to alkenes and alkynes (thallium, mercury)
1978 - 1988 Substituted organolithium compounds
1979 - 1992 Azabutadiene cycloadditions
1984 - 2008 Bis(pyridine)iodonium tetrafluoroborate $[IPy_2]BF_4$
1994 - 2010 Fischer carbene complexes. Recently unstabilized carbenes.
1995 - 2007 Organozirconium chemistry
2005 - 2011 Late transition metal catalysis (palladium, gold, platinum, silver, nickel...)
2009 - 2011 Metal-free reductive coupling

The Barluenga group outside the Faculty of Chemistry in 2004.

Awards
12 major awards
1989 Alexander von-Humboldt Foundation
1999 1st Gold Medal from the Spanish Royal Society of Chemisrty
2005 Rey Jaime I Research Award
2009 Silver Medal of the Principality of Asturias
2 Doctor Honoris Causa (Alcala de Henares and La Rioja)

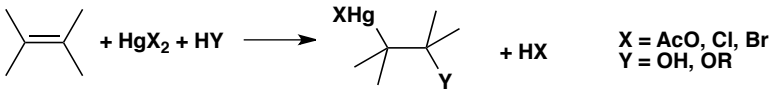
The Group
4 Full professors (Fañanás, Aznar, Tomás and González)
11 Professors
~ 19 Graduate students
~ 2 Visiting students
~ 2 Postdocs

Angewandte profile: *Angew. Chem. Int. Ed.* **2010**, *49*, 6250.

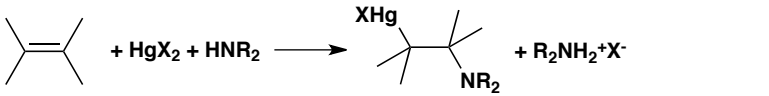
"Where there's a will there's a way"
"Draw it!! kid..."
"The straws don't let you see the forest!!"
"You must always try to undertake your daily work with passion, dedication and cope with standards of intellectual innovation and significance"
"If you continue to repeat experiments you're going to graduate in 10 years"
"For that trip no need to bring that saddlebag..."
"Is that the way you want to be scientists?!?"

Mercury and thallium: Amination reactions.

Background - Seminal Publications

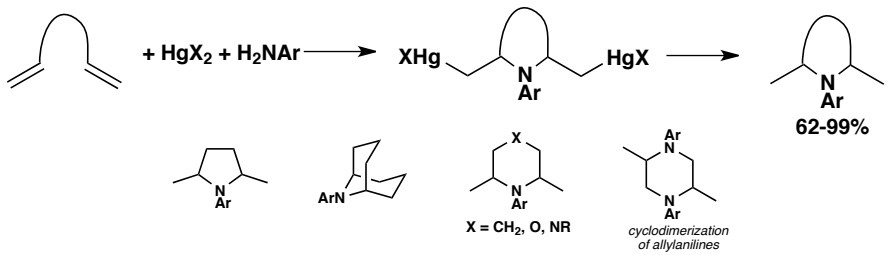


A. N. N. Deniges, *Chem. Pharm.* **1889**, *18*, 394.



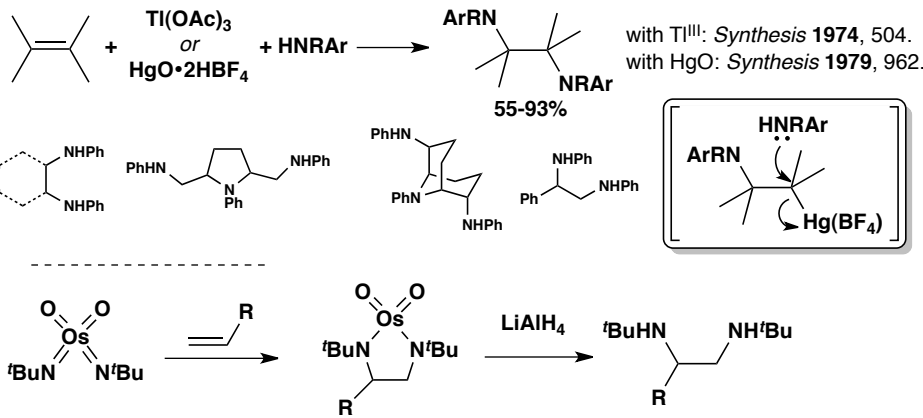
A. Lattes, J. J. Périe *Bull. Soc. Chim. Fr.* **1971**, 1378.

Aminomercuration of dienes



Anales RSEFQ **1972**, *68*, 221; *Tetrahedron Lett.* **1972**, 3621; *Synthesis* **1978**, 911; *Synthesis* **1979**, 896; *J. Heterocyclic Chem.* **1979**, *16*, 1017; *J. Heterocyclic Chem.* **1980**, *17*, 917.

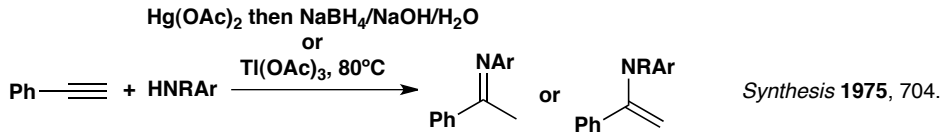
Diamination of alkenes



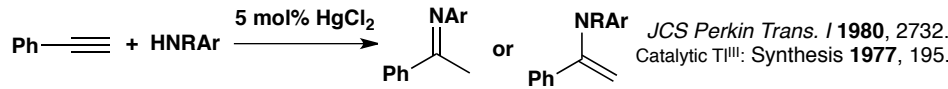
with Tl^{III}: *Synthesis* **1974**, 504.
with HgO: *Synthesis* **1979**, 962.

B. Sharpless et *al. J. Am. Chem. Soc.* **1977**, *99*, 3420. ---> only cited aminopalladation by J.E.-Backvall :)

Addition of anilines across alkynes

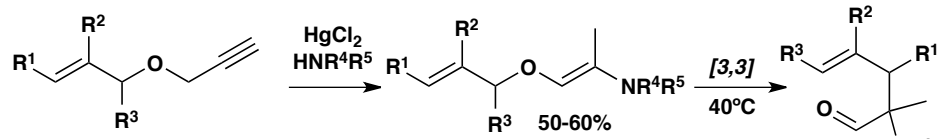


Synthesis **1975**, 704.

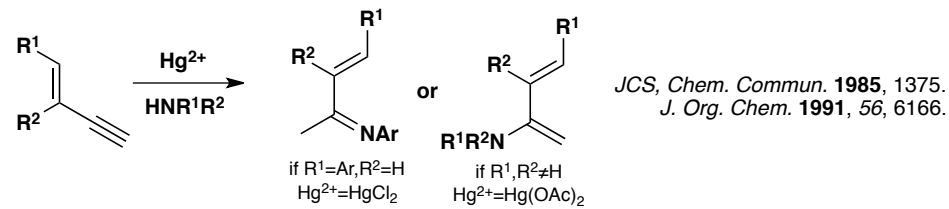


JCS Perkin Trans. I **1980**, 2732.
Catalytic Tl^{III}: Synthesis **1977**, 195.

Conjugated and deconjugated enynes

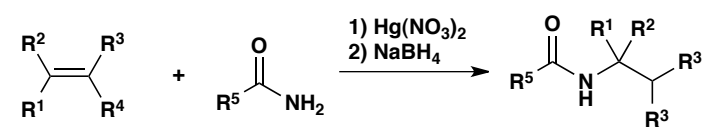


JCS, Chem. Commun. **1984**, 1427.



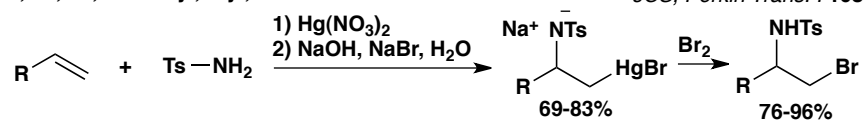
JCS, Chem. Commun. **1985**, 1375.
J. Org. Chem. **1991**, *56*, 6166.

Hydro(sulf)amidation of alkenes



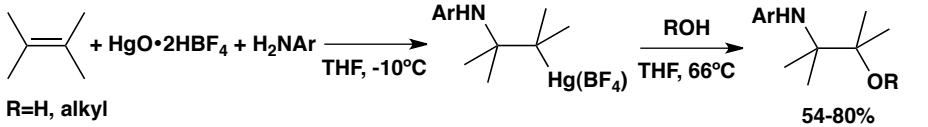
R⁵ = alkyl, aryl, H, OR, NH_2, NHR.
R^1, R^2, R^3, R^4= alkyl, aryl, H.

JCS, Chem. Commun. **1981**, 671.
JCS, Perkin Trans. I **1983**, 591.

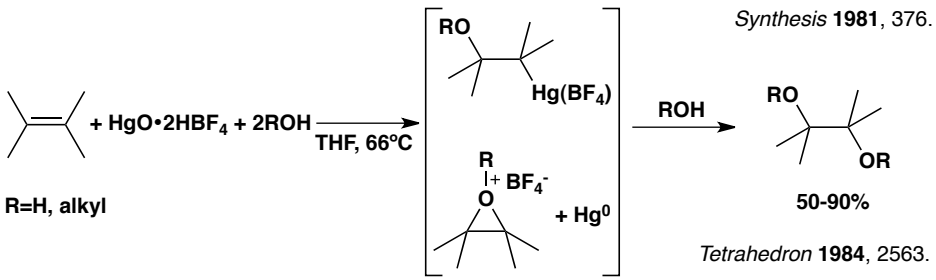


$NaBH_4$ quench: *JCS, Chem. Commun.* **1981**, 1178.
Br_2 quench: *JCS, Perkin Trans. I* **1984**, 721.

Oxygenated nucleophiles

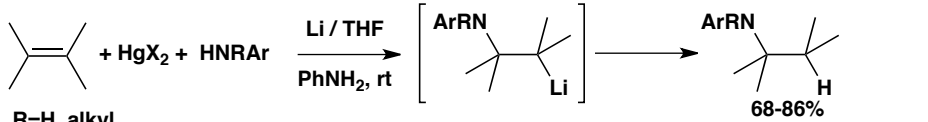


Synthesis **1981**, 376.

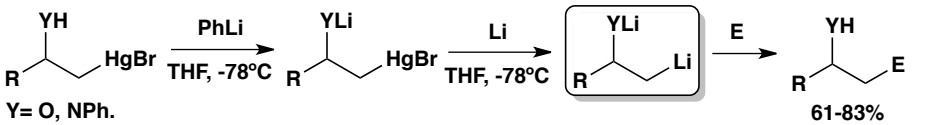


Tetrahedron **1984**, 2563.

Mercury - Lithium exchange: An entry to β-functionalized organolithiums

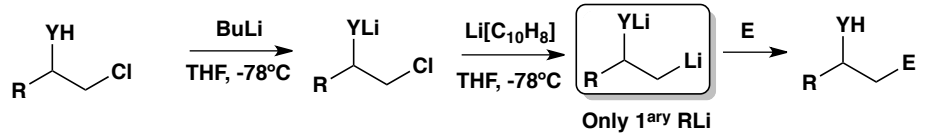


Seminal: *Synthesis* **1974**, 135; Improvement in presence of aniline: *Synthesis* **1975**, 116; same with Mg: *Synthesis* **1975**, 467.



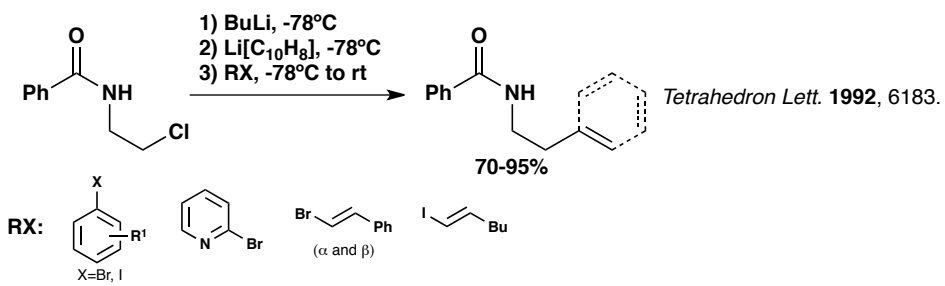
Tetrahedron Lett. **1978**, 2015; *J. Org. Chem.* **1979**, *44*, 4798.

β-Functionalized organolithiums from alkyl chlorides. Lithium naphthalenide.



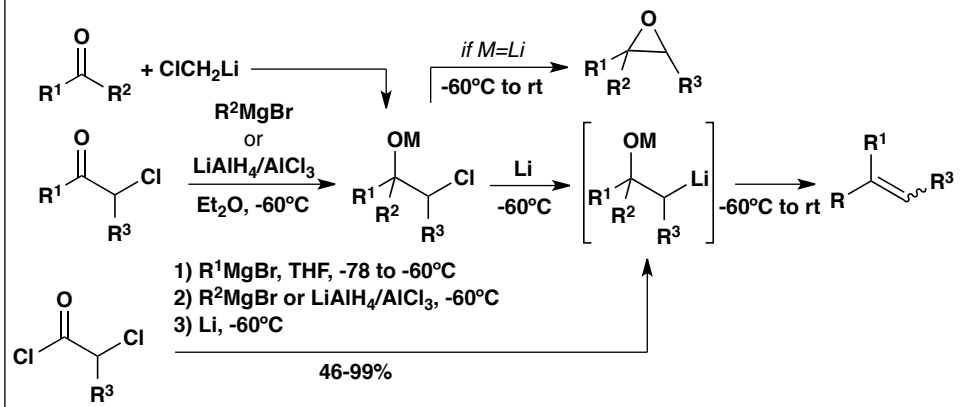
with Na and K: *J. Org. Chem.* **1981**, *46*, 1281; imines, sulphides and alkyl halides: *J. Org. Chem.* **1982**, *47*, 1560; $Li[C_{10}H_8]$ (-100ºC β-elimination): *JCS, Chem. Commun.* **1982**, 1153; *JCS Perkin Trans. I* **1983**, 3019.

Lithiation and direct coupling with aryl and vinyl bromides: The differential reactivity of dianionic intermediates.



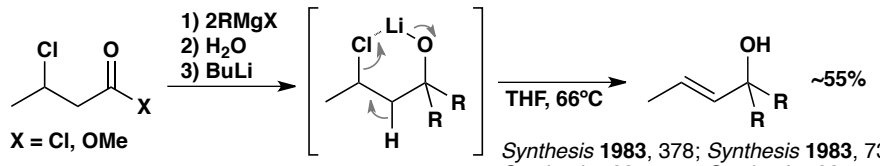
Tetrahedron Lett. **1992**, 6183.

β-Elimination of β-functionalized organolithium compounds: Synthesis of olefins.



Seminal work on β-oxide elimination: J. J. Eisch *et al. J. Am. Chem. Soc.* **1976**, *98*, 4646; From chloroketones: *J. Org. Chem.* **1981**, *46*, 2721; From chloroacyl chlorides: *J. Org. Chem.* **1983**, *48*, 609; *J. Org. Chem.* **1983**, *48*, 3116; (Chloromethyl)lithium: *JCS, Chem. Commun.* **1988**, 536; *JCS, Perkin Trans. I* **1990**, 417; *JCS, Perkin Trans. I* **1989**, 77; *J. Org. Chem.* **1999**, 2843; *J. Org. Chem.* **1997**, 5974; *Synthesis* **1988**, 234.

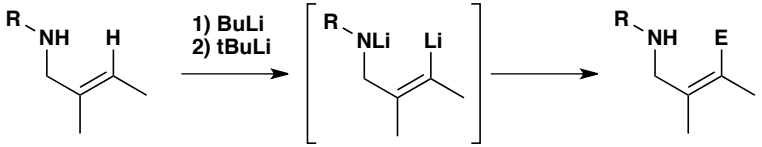
γ,δ,ε-functionalized organolithium compounds. δ,ε-functionalized compounds behave normally but the γ ones undergo a different elimination process...



Synthesis **1983**, 378; *Synthesis* **1983**, 736; *Synthesis* **1985**, 846; *Synthesis* **1987**, 819.

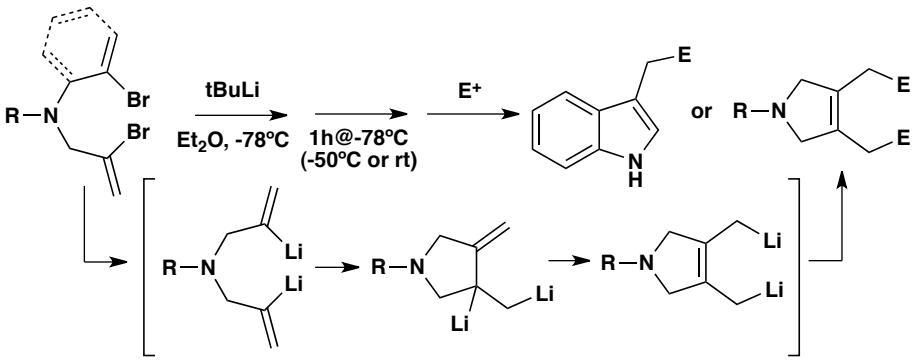
José Barluenga

Lithiation of allylamines



JCS, Chem. Commun. **1988**, 1135; *Tetrahedron Lett.* **1988**, 4859; *Tetrahedron Lett.* **1992**, 7573; *J. Org. Chem.* **1994**, *59*, 602; *J. Org. Chem.* **1994**, *59*, 1586.

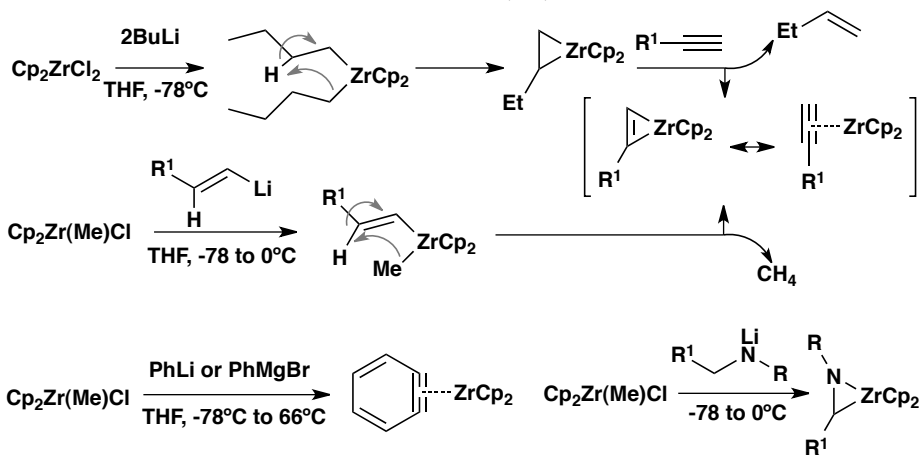
Carbolithiation of lithiated double bonds.

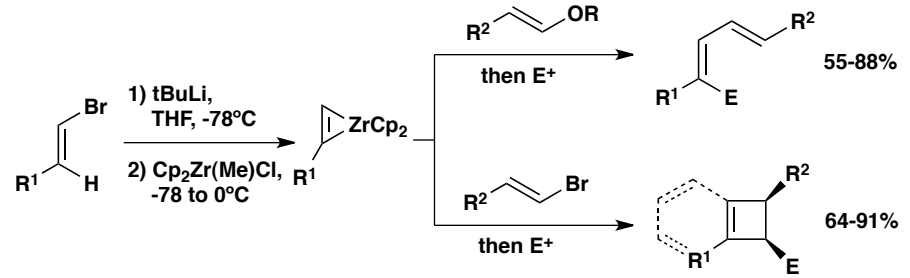


J. Am. Chem. Soc. **1998**, *120*, 4865; *Chem. Eur. J.* **2001**, *7*, 2896; *Eur. J. Org. Chem.* **2003**, 771.

Organozirconium chemistry using $Cp_2Zr(Me)Cl$
Vinyl bromides as alkyne equivalents. Enol ethers as efective cross-coupling counterparts.

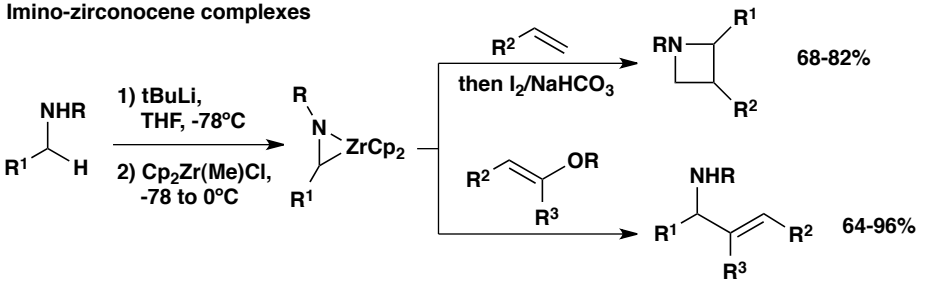
Chem. Soc. Rev. **2005**, *34*, 762.





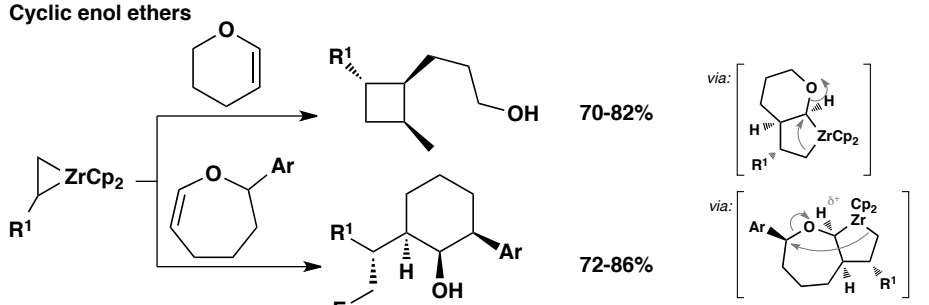
Z. Naturforsch B, **1995**, *50*, 312; *Chem. Commun.* **1995**, 1009; *Chem. Eur. J.* **1997**, *3*, 1324; *Chem. Eur. J.* **2004**, *10*, 101; *Synlett* **2005**, 2513; *Org. Lett.* **2008**, *10*, 4469.

Imino-zirconocene complexes



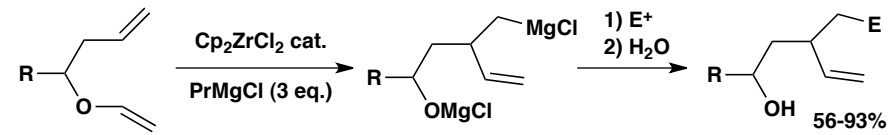
JCS, Chem. Commun. **1994**, 989; *J. Org. Chem.* **1997**, *62*, 5953; *Chem. Eur. J.* **2004**, *10*, 109.

Cyclic enol ethers



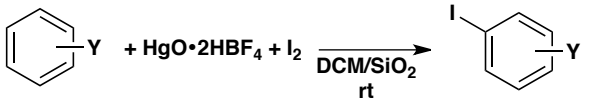
Angew. Chem. Int. Ed. **2004**, *43*, 3932; *Angew. Chem. Int. Ed.* **2007**, *46*, 2607.

Catalytic vinyl-magnesation of unactivated olefins.



Angew. Chem. Int. Ed. **2006**, *45*, 6362; *Org. Lett.* **2007**, *9*, 3081.

The serendipitous birth of $[IPy_2]BF_4$ - Barluenga's reagent



Y= H; 54%
Y=tBu; 78%
Y=OMe; 87%
Y=CO_2H; 35%
Y=NO_2; 12%

IBF_4 source? $Hg(BF_4)_2 + I_2 \longrightarrow$ "IBF_4" + $HgIBF_4$

JCS, Perkin Trans. I **1984**, 2623.

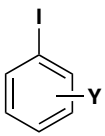
Pyridine as stabilizer of iodonium...

$HgO.2BF_4$-SiO_2 + I_2 + pyridine $\xrightarrow{DCM,\ rt}$ $[IPy_2]BF_4$ *6ppm Hg co-precipitates (ICP-MS)*

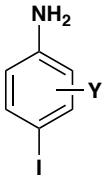
$AgBF_4$-SiO_2 + I_2 + pyridine $\xrightarrow{DCM,\ rt}$ $[IPy_2]BF_4$ Davis *et al. Org. Synth.* **2010**, *87*, 288

Electrophilic iodination of activated and unactivated arenes

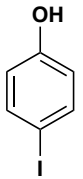
For activated arenes, the reagent is reactive enough. For non-activated ones, 1-2 eq. HBF_4 or TfOH is needed.



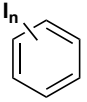
Y=H; 85%
Y=4-tBu; 99%
Y=4-OMe; 96%
Y=3-CO_2H; 86%
Y=3-NO_2; 82%



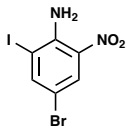
Y=H; 97%
Y=2-MeO; 97%



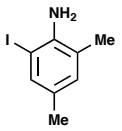
90%



n=2; 79%
n=3; 42%
n=4; 81%
n=5; 99%
n=6; 97%



99%



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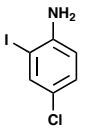
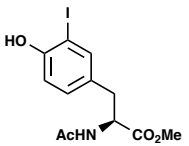
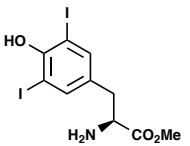


99%

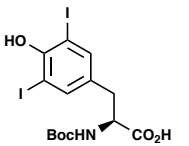
20g scale *(indole synthesis)*



93%



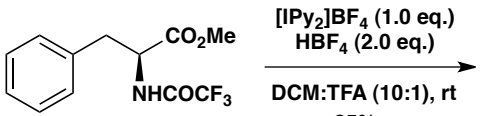
93% (in water)



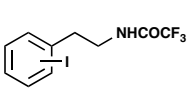
93%(in water)

JCS, Chem. Commun. **1992**, 1016; *J. Org. Chem.* **1993**, *58*, 2058; *Tetrahedron Lett.* **1993**, *34*, 3893; *J. Org. Chem.* **1996**, *61*, 5804; *JCS, Chem. Commun.* **1996**, 1505; *Chem. Commun.* **2000**, 1307.

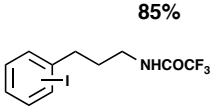
Directed aromatic iodination... *Does it remind you of something?*



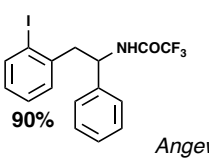
o:*p* (12.5:1)



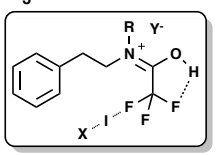
o:*p* (25:1)



o:*p* (14:1)

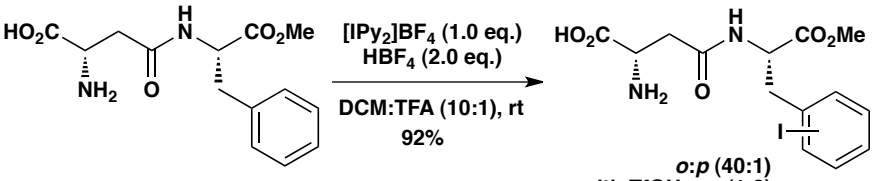


90%

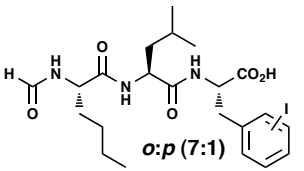


Angew. Chem. Int. Ed. **2007**, *46*, 1281.

Direct iodination of Phe residues in peptides - Iodine radiolabelling in proteins.

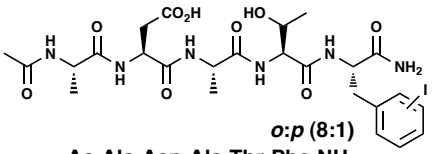


o:*p* (40:1)
with TfOH *o*:*p* (1:2)



o:*p* (7:1)

For-Nle-Leu-Phe-OH

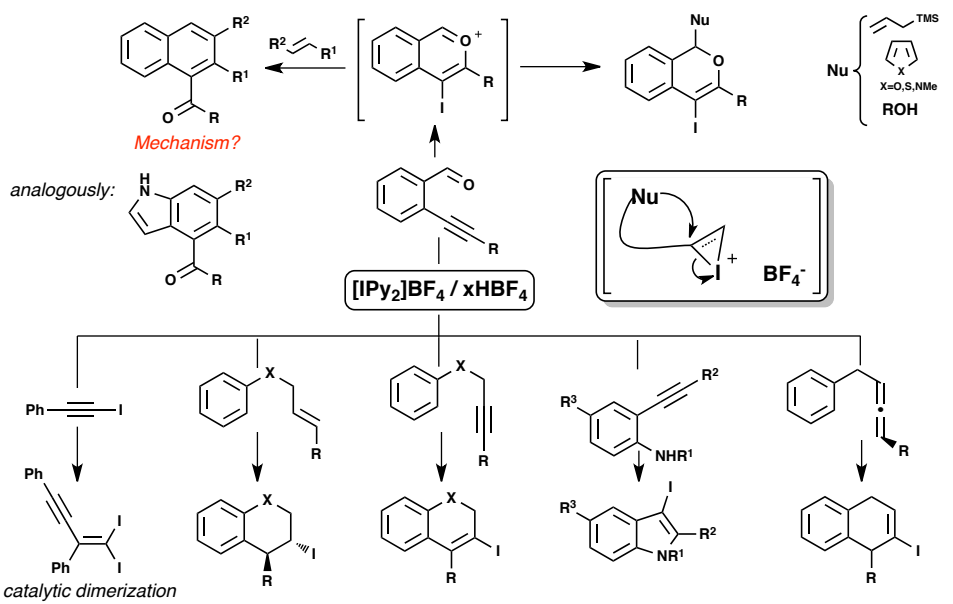


o:*p* (8:1)

Ac-Ala-Asp-Ala-Thr-Phe-NH_2

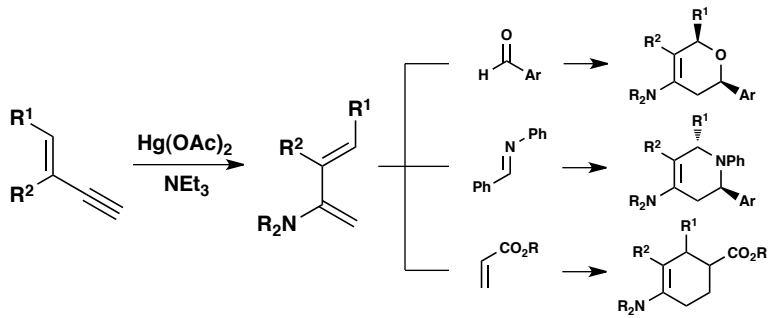
Angew. Chem. Int. Ed. **2004**, *43*, 325. Peptides in solid phase: *Tetrahedron Lett.* **1999**, 7279.

Iodonium as C-C (or C-X) bond forming promoter



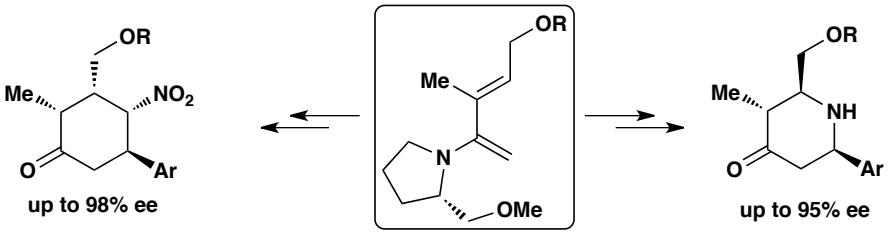
Angew. Chem. Int. Ed. **1988**, *27*, 1546; *Angew. Chem. Int. Ed.* **1993**, *32*, 893; *J. Am. Chem. Soc.* **1997**, *119*, 6933; *Angew. Chem. Int. Ed.* **1998**, *37*, 3136; *Angew. Chem. Int. Ed.* **2003**, *42*, 2406; *J. Am. Chem. Soc.* **2003**, *125*, 9028; *Org. Lett.* **2003**, *5*, 4121; *J. Am. Chem. Soc.* **2004**, *126*, 3416; *Chem. Commun.* **2005**, 2008; *Chem. Eur. J.* **2006**, *12*, 5790; *Angew. Chem. Int. Ed.* **2006**, *45*, 3140; *Chem. Eur. J.* **2009**, *15*, 8946.

Mining the gold of enyne hydroamination... 2-amino-1,3-butadienes



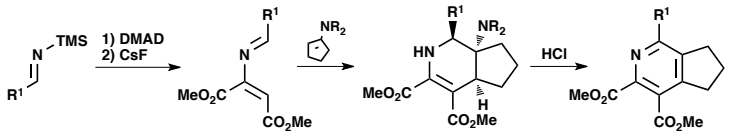
Chiral 2-amino-1,3-butadienes

Highlight: K. Krohn, *Angew. Chem. Int. Ed.* **1993**, *32*, 1582

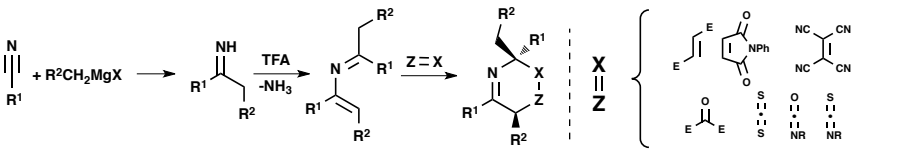


JCS, Chem. Commun. **1988**, 1247; *J. Org. Chem.* **1991**, *56*, 6166; *J. Am. Chem. Soc.* **1993**, *115*, 4403; *J. Org. Chem.* **1993**, *58*, 3391; *Chem. Eur. J.* **1996**, *2*, 805; *J. Org. Chem.* **1997**, *62*, 6746; *J. Org. Chem.* **1998**, *63*, 3918; *J. Org. Chem.* **1999**, *64*, 3736.

2-aza-1,3-butadienes - Normal and inverse demand [4+2] cycloadditions.

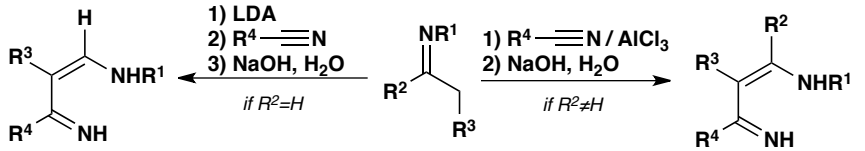


JCS, Chem. Commun. **1987**, 1195; *JCS, Chem. Commun.* **1989**, 267.



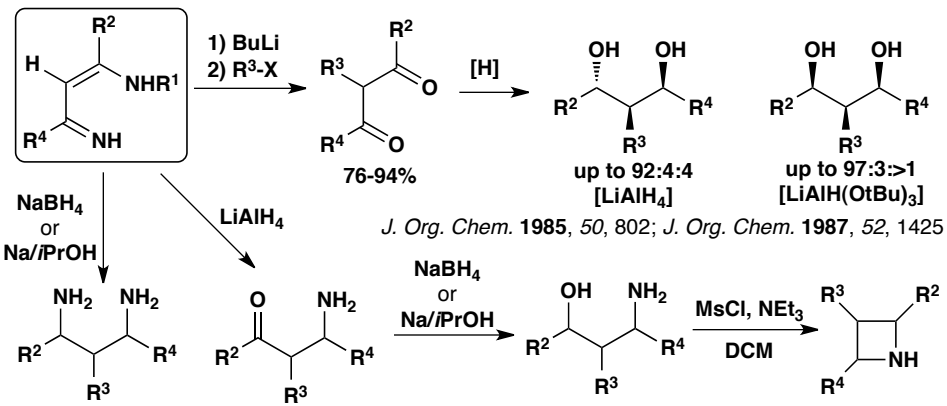
Chem. Ber. **1985**, *36*, 52; *JCS, Chem. Commun.* **1986**, 1179; *JCS, Perkin Trans. I*, **1988**, 1739; *Tetrahedron Lett.* **1989**, *30*, 2685.

4-amino-1-aza-1,3-butadienes - Synthesis.



G. Wittig et al. *Liebigs Ann. Chem.* **1973**, 1075. *Synthesis* **1970**, 142

4-amino-1-aza-1,3-butadienes - Basic reactivity.

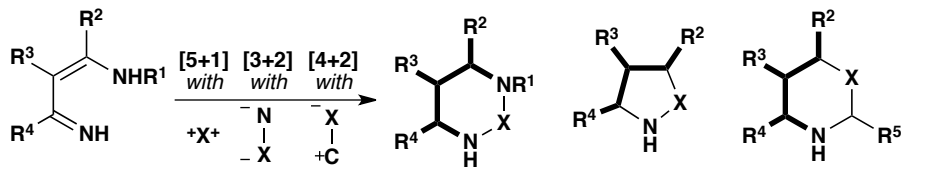


J. Org. Chem. **1985**, *50*, 802; *J. Org. Chem.* **1987**, *52*, 1425

J. Org. Chem. **1983**, *48*, 2255; *Tetrahedron Lett.* **1983**, *34*, 1981.

J. Org. Chem. **1983**, *48*, 2255; *J. Org. Chem.* **1985**, *50*, 4052; *J. Org. Chem.* **1992**, *57*, 1219; *JCS, Chem. Commun.* **1988**, 410; *J. Org. Chem.* **1993**, *58*, 5972.

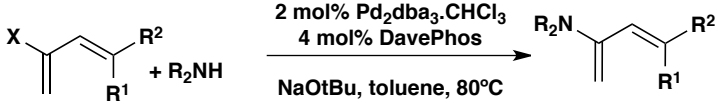
4-amino-1-aza-1,3-butadienes - cycloaddition en route to heterocycles.



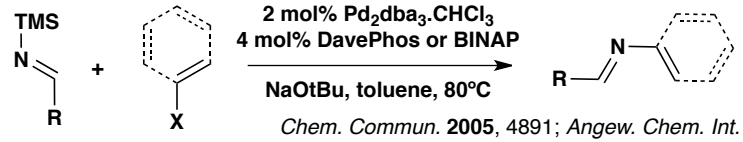
Review: *Advances in Heterocyclic Chemistry* **1993**, *57*, 1.

[5+1] - Dihydropyrimidines: *Synthesis* **1974**, 720; *Synthesis* **1979**, 346; *Synthesis* **1989**, 230; *Synlett* **1992**, 563; *JCS, Chem. Commun.* **1988**, 410. Pyrimidones: *JCS, Chem. Commun.* **1979**, 675; *J. Org. Chem.* **1980**, *45*, 2592. Thiadiazines: *JCS, Chem. Commun.* **1979**, 675; *JCS, Perkin Trans I* **1981**, 1891. Diazaphosphorines: *Synthesis* **1983**, 370; *Synthesis* **1985**, 309. Diazasilines: *Angew. Chem. Int. Ed.* **1986**, *25*, 181. Diazagermines: *Organometallics* **1992**, *11*, 2348.
[3+2] - Pyrazoles: *JCS, Chem. Commun.* **1979**, 891; *JCS, Perkin Trans I*, **1981**, 1891. Isoxazoles: *J. Org. Chem.* **1983**, *48*, 1379. Pyrroles: *J. Org. Chem.* **1982**, *47*, 1696.
[4+2] - Pyrimidines: *Synthesis* **1970**, 363. Pyridines: *Synthesis* **1975**, 191.

Palladium catalysis - new entry to amino and azadienes?

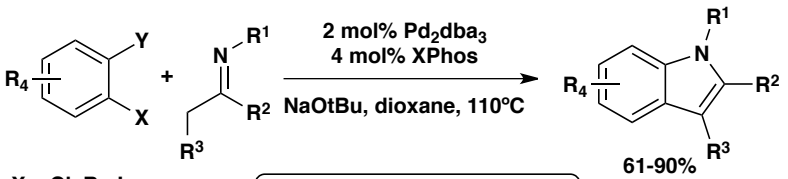


Adv. Synth. Catal. **2004**, 1697; *Chem. Commun.* **2004**, 1400.

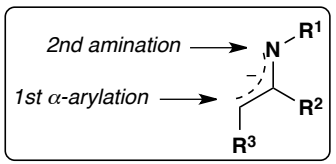


Chem. Commun. **2005**, 4891; *Angew. Chem. Int. Ed.* **2004**, *43*, 343.

A general approach to the indole ring...

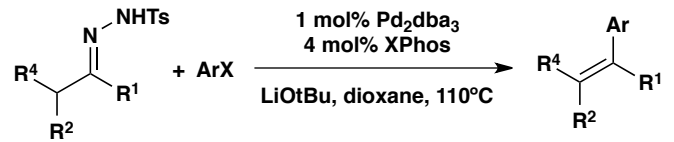


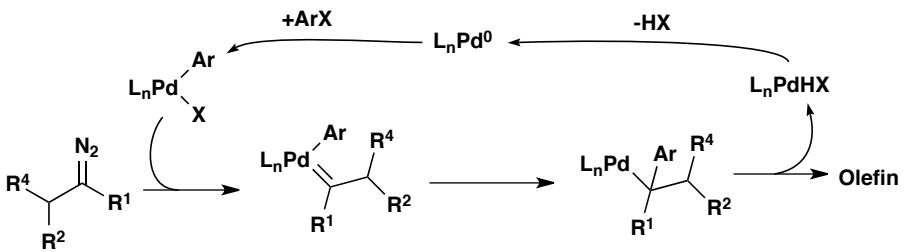
X = Cl, Br, I;
Y = ONf, Br, I.



Angew. Chem. Int. Ed. **2007**, *46*, 1529; *J. Am. Chem. Soc.* **2009**, *131*, 4031.

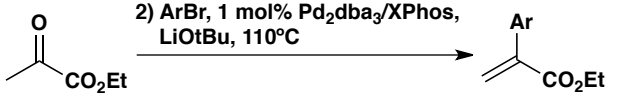
Tosylhydrazones... Efforts finds a neat reward!!



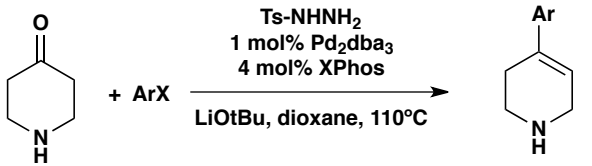


Angew. Chem. Int. Ed. **2007**, *46*, 5587; *Org. Lett.* **2011**, *13*, 510.

Application of the olefination reaction to cases of special interest...

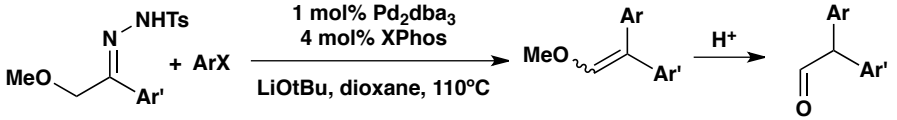


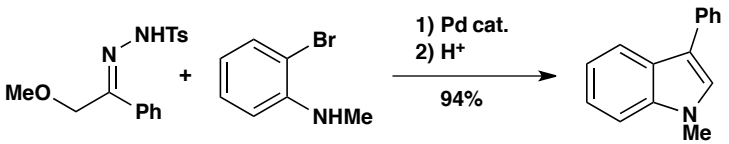
Chem. Eur. J. **2010**, *16*, 12801



Chem. Eur. J. **2008**, *14*, 4792.

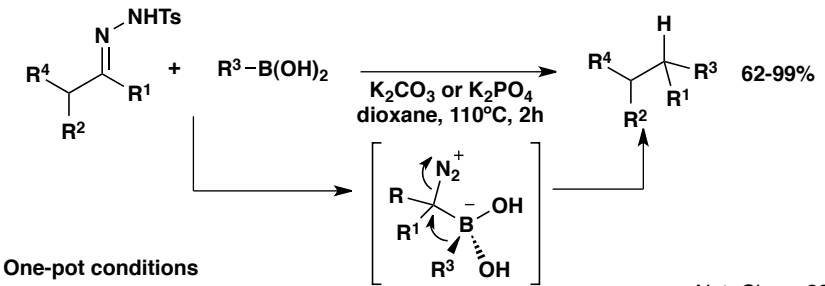
Maria Escribano's work...





Chem. Eur. J. **2009**, *15*, 13291 (VIP paper).

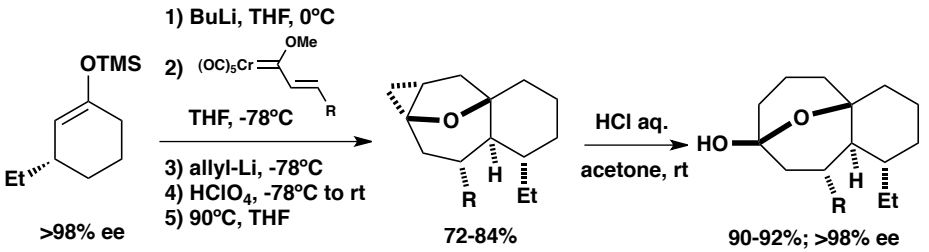
Metal-free reductive coupling of tosylhydrazones and boronic acids...



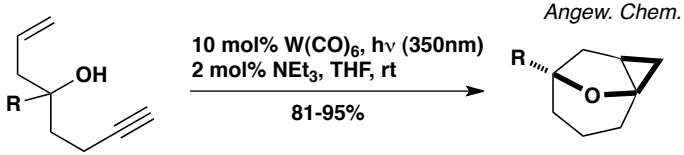
One-pot conditions
1) $TsNHNH_2$ / dioxane, 80ºC, 1.5h
2) $R^3B(OH)_2$, K_2CO_3, 110ºC, 1-5h

Nat. Chem. **2009**, *1*, 494.
Phenol insertion: *Angew. Chem. Int. Ed.* **2010**, *49*, 4993.

From Fischer carbene complexes to π-electrophilic catalysis

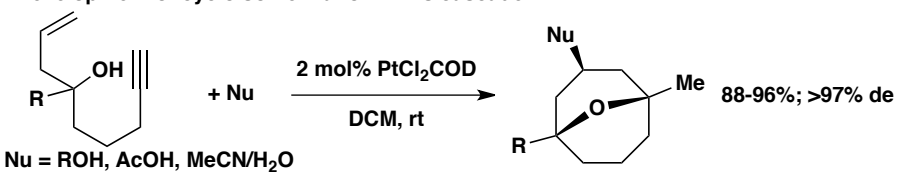


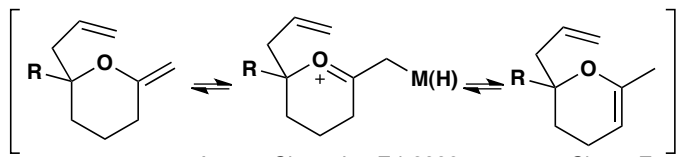
J. Am. Chem. Soc. **2002**, *124*, 9056.
Angew. Chem. Int. Ed. **2006**, *45*, 4848.



Angew. Chem. Int. Ed. **2005**, *44*, 126.

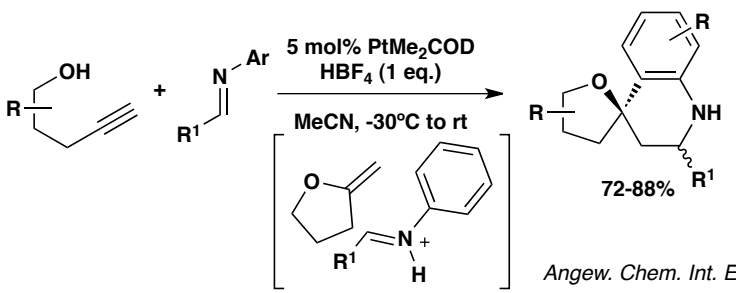
Development of cycloisomerization-Prins cascade...





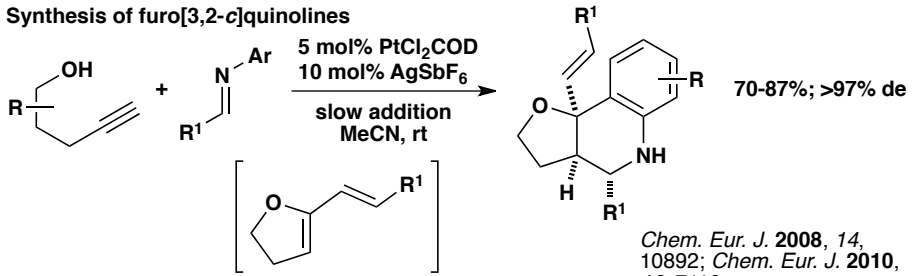
Angew. Chem. Int. Ed. **2006**, *45*, 2019; *Chem. Eur. J.* **2009**, *15*, 11660; *Chem. Eur. J.* **2009**, *15*, 8121; *Chem. Eur. J.* **2010**, *16*, 9758.

The pursuit of the catalytic generation of exocyclic enol ethers. Proof-of-concept: Povarov.



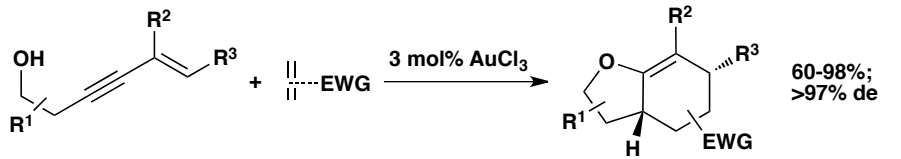
Angew. Chem. Int. Ed. **2008**, *47*, 7044.

Synthesis of furo[3,2-*c*]quinolines

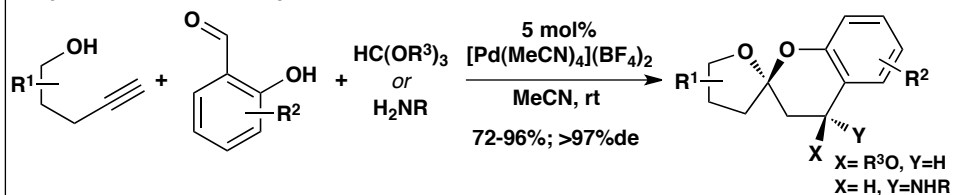


Chem. Eur. J. **2008**, *14*, 10892; *Chem. Eur. J.* **2010**, *16*, 7110.

Cycloisomerization - [4+2] cycloaddition

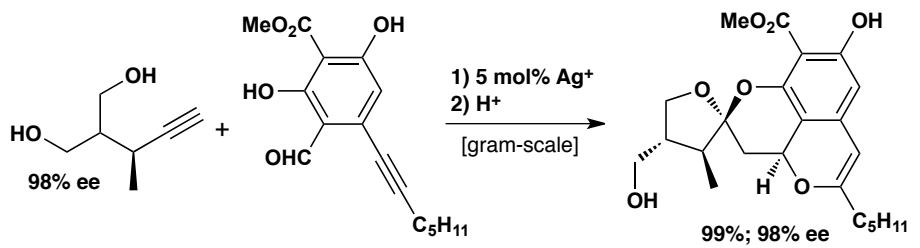


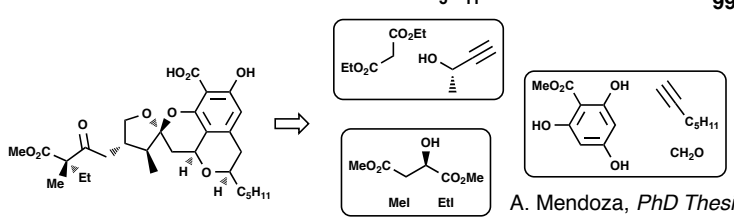
Synthesis of chroman-spiroketals



Angew. Chem. Int. Ed. **2009**, *48*, 1644.

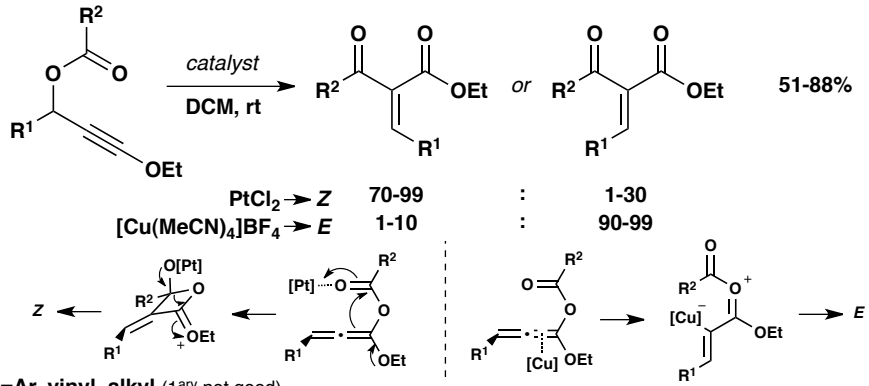
Gram-scale total synthesis of (-)-berkelic acid





A. Mendoza, *PhD Thesis*, U. Oviedo **2009**

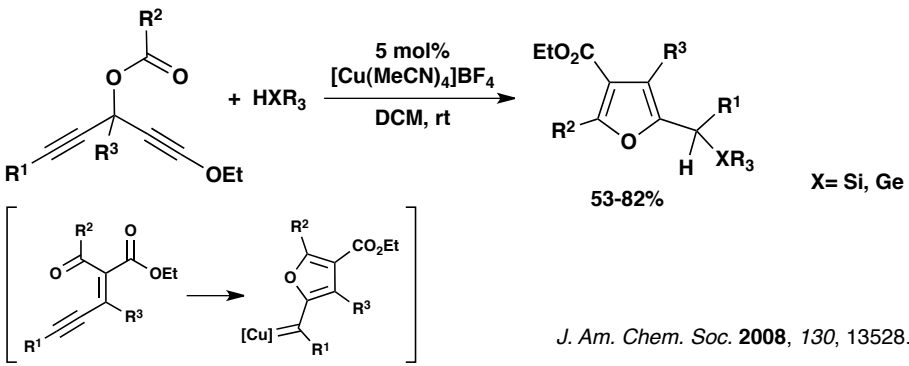
Activated propargylic esters: A new scaffold with new interesting reactivity to explore.



R¹=Ar, vinyl, alkyl (1ary not good)
R²=Ar, vinyl, alkyl, OR

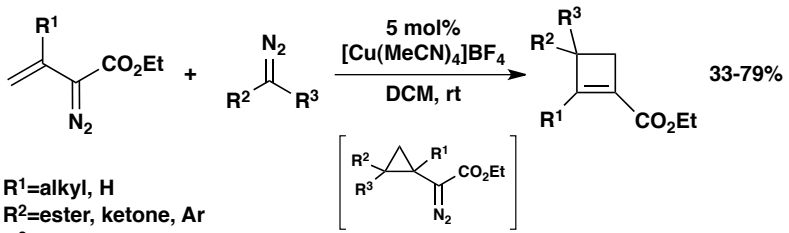
J. Am. Chem. Soc. **2007**, *129*, 7772.

New rearrangement to (2-furyl)carbenes. Hydrosilylation and hydrogermanation.



J. Am. Chem. Soc. **2008**, *130*, 13528.

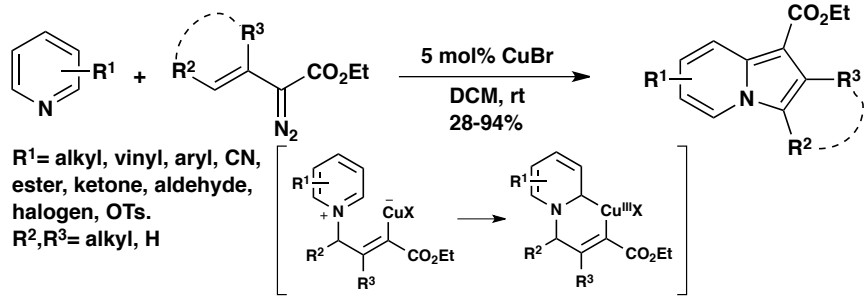
Diazo-heterocoupling



R¹=alkyl, H
R²=ester, ketone, Ar
R³=Ar, H

Angew. Chem. Int. Ed. **2009**, *48*, 7569.

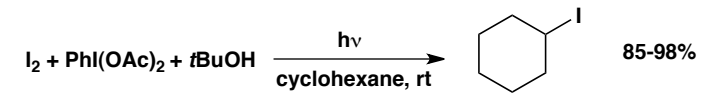
Indolizine synthesis by means of pyridine/diazocompound cross-coupling.



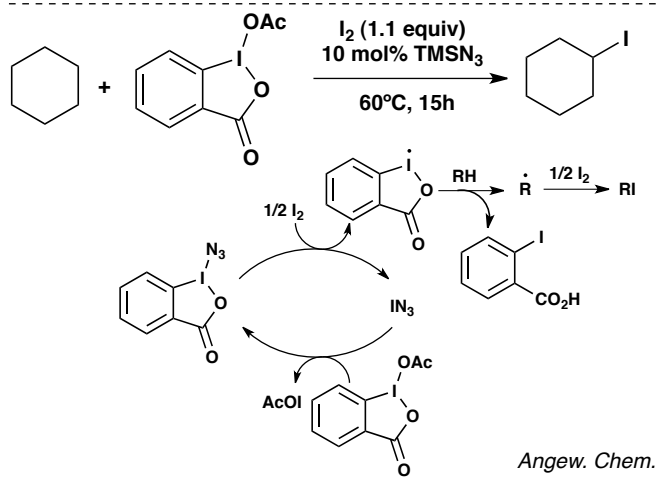
R¹= alkyl, vinyl, aryl, CN, ester, ketone, aldehyde, halogen, OTs.
R²,R³= alkyl, H

J. Am. Chem. Soc. **2010**, *132*, 13200.

Some radical iodine reactions you could be interested in...



Angew. Chem. Int. Ed. **2002**, *41*, 2556.



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