# Syntheses, Structural Characterization and Catalytic Applications of *N*-Heterocyclic Carbene Copper(I) Complexes

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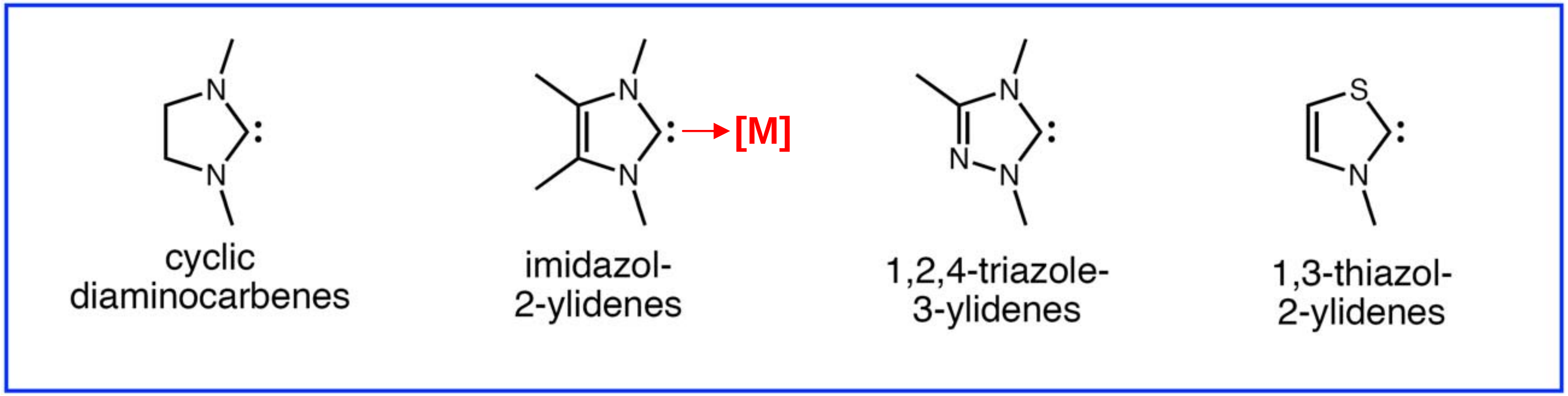
# *N*-Heterocyclic Carbenes



- NHCs are stronger σ-donors than the most electron rich phosphine, weak π-acceptor
  - less likely to dissociate from the metal during the reaction

- NHCs have come to replace phosphines in many organometallic and organic reactions

- NHCs can be useful spectator ligands, tunable electronically and sterically

- NHCs are most frequently prepared via deprotonation of the corresponding azolium salts

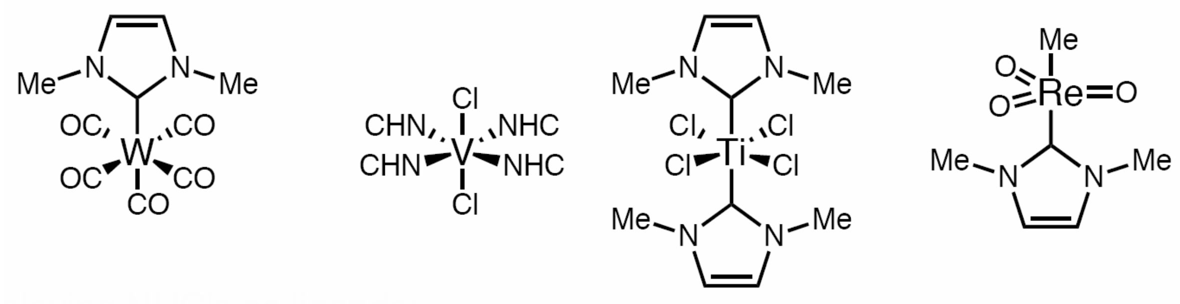
# *N*-Heterocyclic Carbenes as Ligands

- In the early 90's NHC were found to have bonding properties similar to trialklyphosphanes and alkylphosphinates.

Herrmann, W. A.; Öfele, K; Elison, M.; Kühn, F. E.; Roesky, P. W. *J. Organomet. Chem.* **1994**, *480*, C7-C9.

- compatible with both high and low oxidation state metals

- examples:



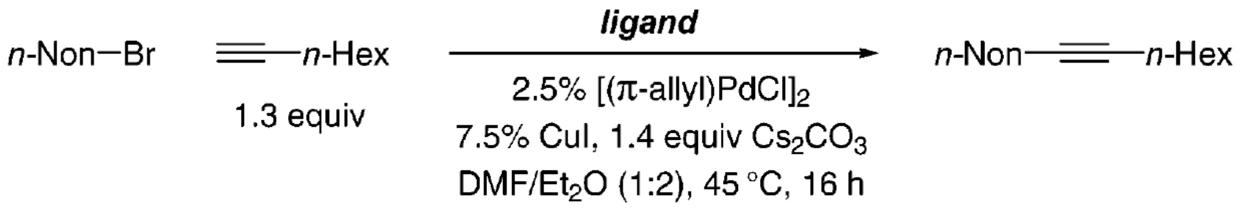
- reaction employing NHC's as ligands:

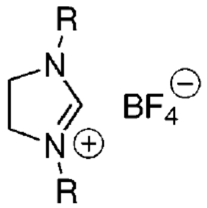
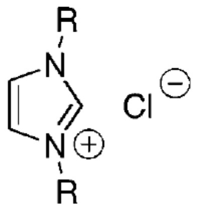
Heck and Suzuki Couplings
Aryl Amination
Amide α-Arylation
Hydrosiylation
Olefin Metathesis
Metathesis Cross-Coupling
Sonogashira Coupling
Ethylene/Carbon Monoxide Copolymerization

Kumada Coupling
Stille Coupling
C-H Activation
Hydrogenation, Hydroformylation
Furan Syntheis and Alkyne Coupling
Olefin Cyclopropanation
Arylation and Alkenylation of Aldehydes
Reduction of Aryl Halides
Atom-Transfer Radical Polymerization
Asymmetric Catalysis

Herrmann, W. *Angew. Chem. Int. Ed.* **2002**, *41*, 1290-1309.

# The First Example of Carbene Ligands in Sonogashira Cross-Coupling Reactions

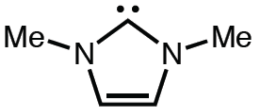
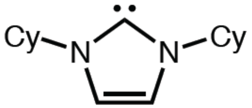
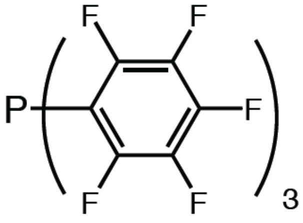


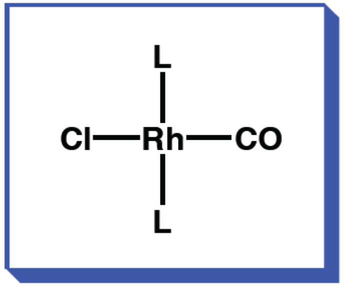
| entry | ligand | yield (%)[a] |
|---|---|---|
| 1 | 10% $PPh_3$ | <5 |
| 2 | 10% $PCy_3$ | <5 |
| 3 | 10% $P(t\text{-}Bu)_2Me$ | <5 |
| 4 | 10% $PCy(1\text{-pyrrolidinyl})_2$ | <5 |
| 5 | <br>R = mesityl (5%) | <5 |
| 6 | R = 2,6-($i$-Pr)$_2$Ph (5%) | 58 |
| 7 | <br>R = 2,6-($i$-Pr)$_2$Ph (5%) | 67 |
| 8 | R = $t$-Bu (5%) | 81 |
| 9 | R = 1-adamantyl (5%) | 80 |
| 10 | R = 1-adamantyl (5%)[b] | <5 |
| 11 | R = 1-adamantyl (5%)[c] | <5 |

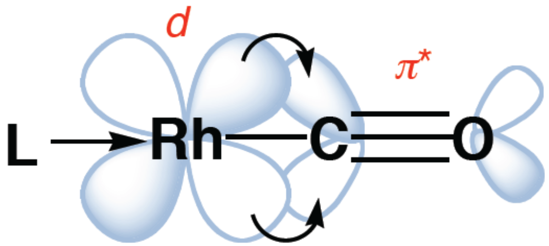
[a] Determined by GC versus a calibrated internal standard (average of at least two runs). [b] Reaction was conducted without [(π-allyl)PdCl]$_2$. [c] Reaction was conducted without CuI.

Eckhardt, M.; Fu, G. C. *J. Am. Chem. Soc.* **2003**, *125*, 13642-13643.

# Carbonyl Stretching Frequencies of Complexs of the Type *trans*-RhL$_2$(CO)Cl

| L | $\nu$ (cm$^{-1}$) |
|---|---|
|  | 1924 |
|  | 1929 |
| $PCy_3$ | 1939 |
| $PMe_3$ | 1957 |
| $PPh_3$ | 1983 |
|  | 2003 |
| $P(OPh)_3$ | 2018 |





more electron density on the metal

↓

more pi-backbonding on CO

↓

longer CO bond

↓

shorter CO stretching frequency

Kocher, C.; Herrmann, W. A. *J. Organomet. Chem.* **1997**, *532*, 261-265.

# The Catalytic Applications of Cu(I)

- ***Sonogashira Reaction***
- ***O-arylation of Phenols***
- ***Kharasch-Sosnovsky Reaction (Allylic Oxidations of Olefins)***
- ***S-arylation of Thiols***
- ***N-arylation of Amines (Buchwald-Hartwig Reaction)***
- ***Hydrosilylation of Ketones***
- ***Heck reaction***
- ***Oxidation of Alcohols***
- ***Substitution Reaction***
- ***Epoxidation Reaction***
- ***Reductive Aldol Reaction***

# Drawback of Traditional Copper-mediated Reactions

- insoluble in organic solvents
  - heterogeneous

- harsh reaction conditions
  - high temperatures around 200 °C
  - strong bases
  - toxic solvent such as HMPA
  - sensitive to functional groups on aryl halides
  - long reaction times
  - the yields are often irreproducible

- in comparison with palladium, copper-based catalysts are quite attractive from an economic standpoint
  - $PdCl_2$ **\$4005.00(150g)** ReagentPlus® (Aldrich)
  - CuCl **\$96.10(2kg)** reagent grade (Sigma-Aldrich)

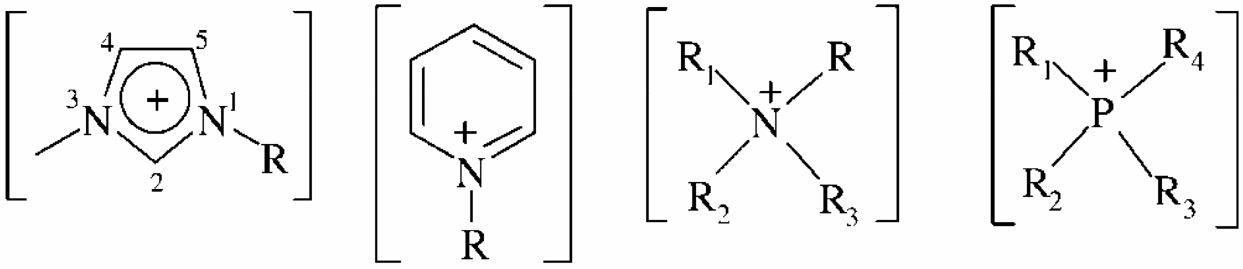
# Green Chemistry

01. Prevention
02. Less Hazardous Chemical Syntheses
03. Design for Degradation
04. Design Safer Chemicals
05. Safer Solvents and Auxiliaries
06. Atom Economy
07. Design for Energy Efficiency
08. Use Renewable Feedstocks
09. Reduce Derivatives
10. Catalysis
11. Real-Time Analysis for Pollution Prevention
12. Inherently Safer Chemistry for Accident Prevention

Anastas, P. T.; Warner, J. C. *Green Chemistry: Theory and Practice*, Oxford University Press, oxford, 1998.

# “Green” Solvent Alternatives -Ionic Liquids

Most commonly used cations:



1-alkyl-3-methyl-imidazolium

*N*-alkyl-pyridinium

Tetraalkyl-ammonium

Tetraalkyl-phosphonium

($R_{1,2,3,4}$ = alkyl)

Some possible anions:

water-insoluble → water-soluble

| water-insoluble | | water-soluble |
|---|---|---|
| $[PF_6]^-$ | $[BF_4]^-$ | $[CH_3CO_2]^-$ |
| $[(CF_3SO_2)_2N]^-$ | $[CF_3SO_3]^-$ | $[CF_3CO_2]^-$, $[NO_3]^-$ |
| $[BR_1R_2R_3R_4]^-$ | | $Br^-$, $Cl^-$, $I^-$ |
| | | $[Al_2Cl_7]^-$, $[AlCl_4]^-$ (decomp.) |

Most commonly used alkyl chains:

ethyl
butyl
hexyl
octyl
decyl

Seddon, K. R.; Stark A., Torres M. J. *Pure Appl. Chem.* **2000**, *72*, 2275-2287.

# Motivation

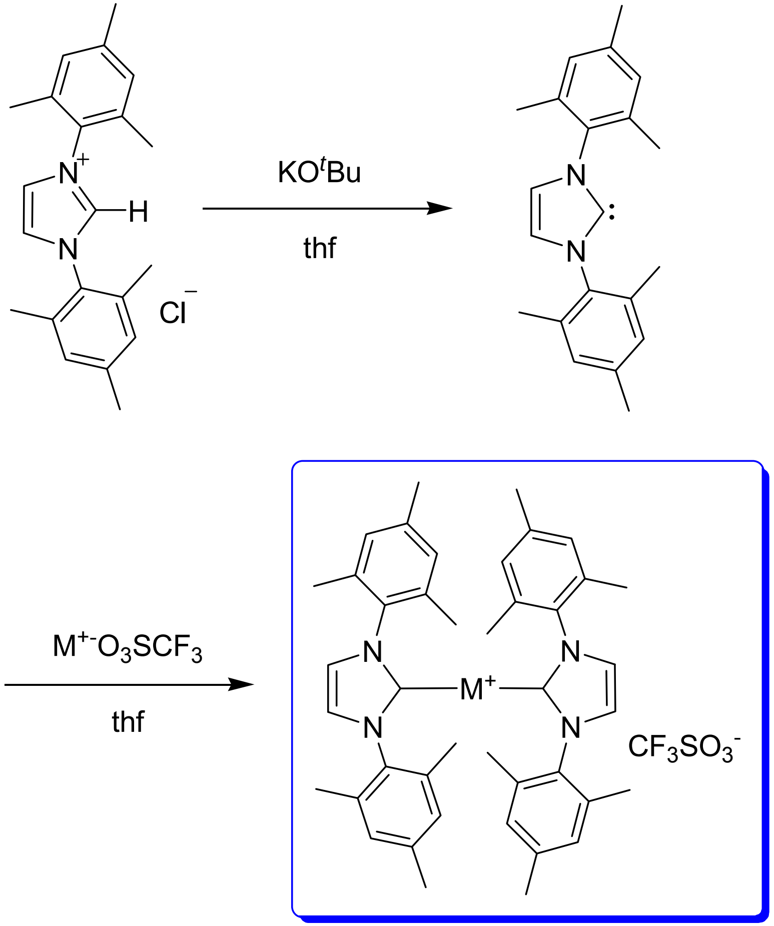
- ***Inexpensive Cu to replace Pd as catalyst for various C–X coupling reactions (X = C, N, O, S)***

- ***Increase solubility of Cu(I) complex through incorporation of special design ligand***

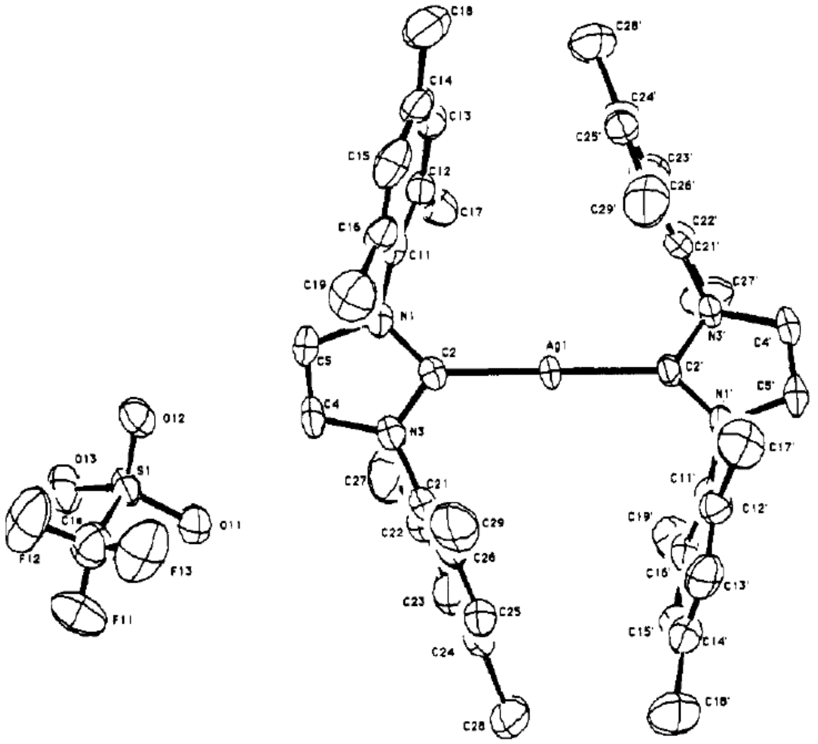
- ***Greener solvents***
  ***R.T. ionic liquids, (hmim)HBr, (hmim)HPF*** $_6$

- ***Energy saving***
  ***Catalysis under efficient microwave flash heating to replace conventional thermal heating***

# The First Isolable Carbene-Silver(I) and Carbene-Copper(I) Complexes

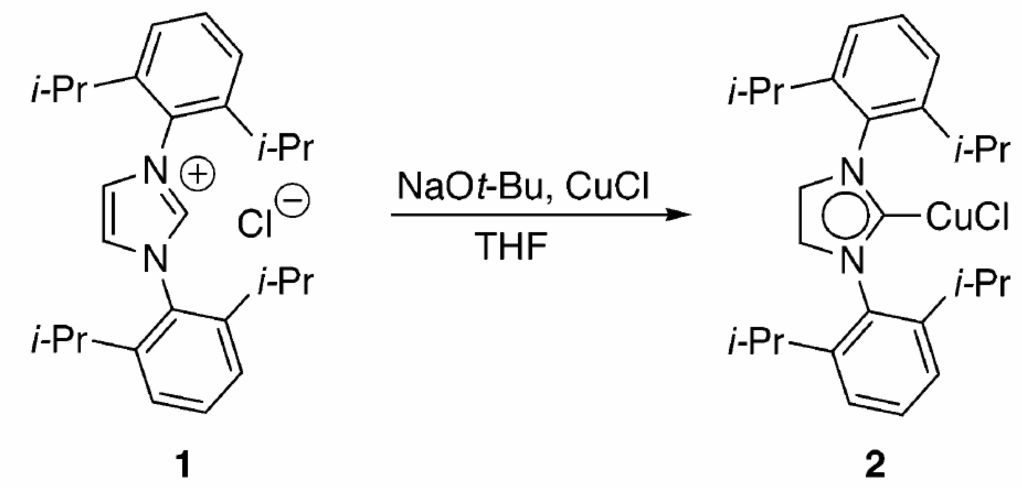


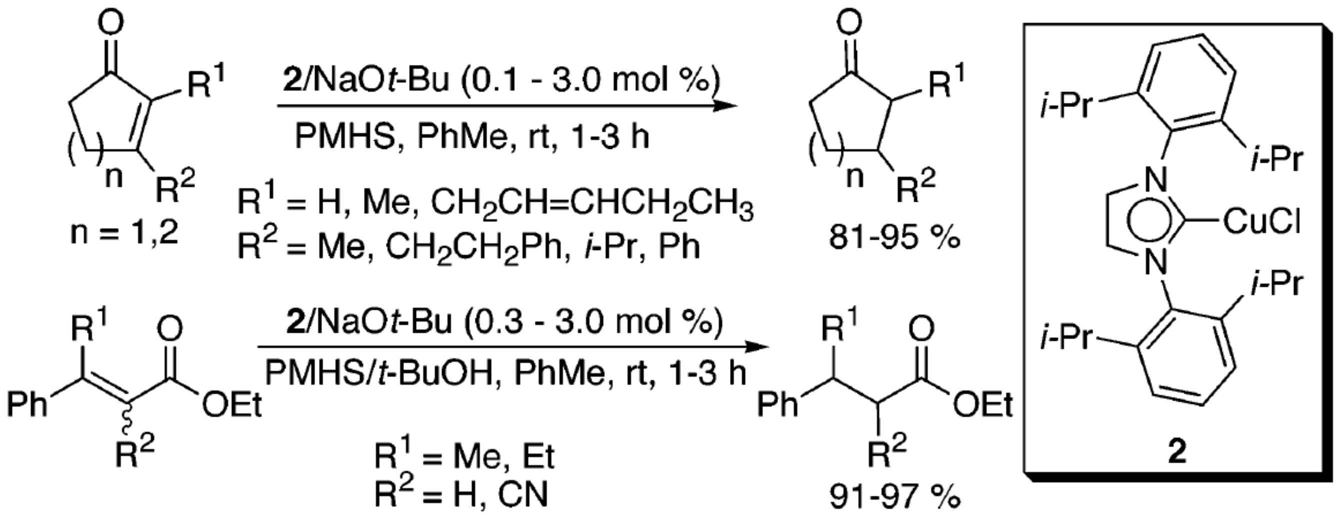
M = Cu, Ag



Arduengo, A. J., III; Dias, H. V. R.; Calabrese, J. C.; Davidson, F. *Organometallics* **1993**, *12*, 3405-3409.

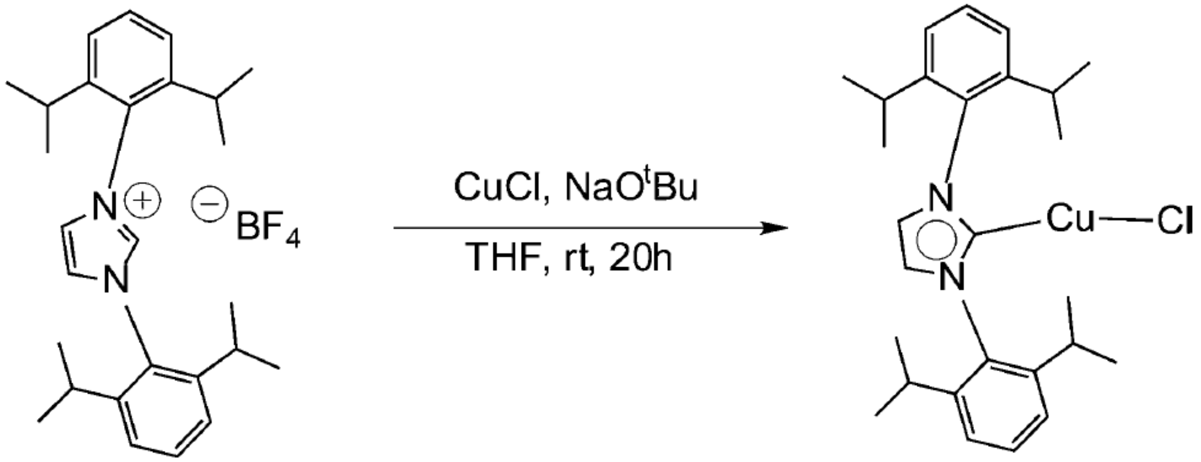
# Conjugate Reduction of α, β-Unsaturated Carbonyl Compounds Catalyzed by a Copper Carbene Complex

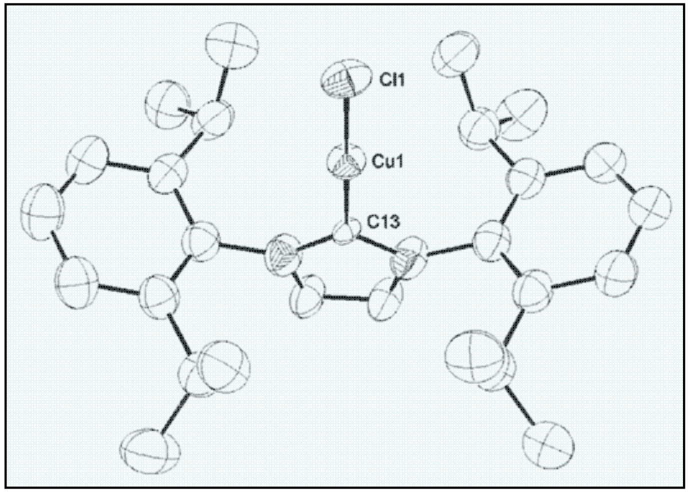




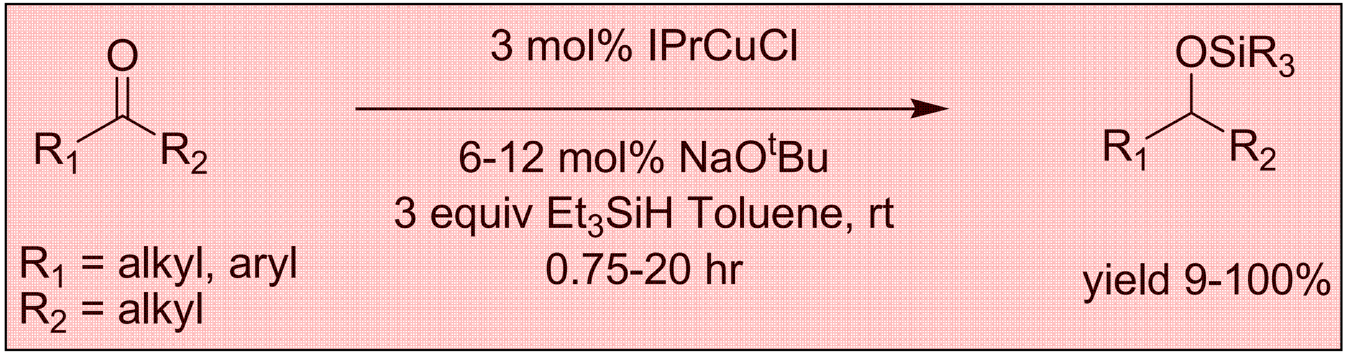
Jurkauskas, V.; Sadighi, J. P.; Buchwald, S. L. *Org. Lett.* **2003**, *5*, 2417-2420.

# Catalytic Reduction of Ketones Using a Well-Defined (NHC)Cu$^I$ Complex





| | |
|---|---|
| Cu(1)-C(13) | 1.953(8) Å |
| C(1)-Cu(1)-I(1) | 180° |



3 mol% IPrCuCl

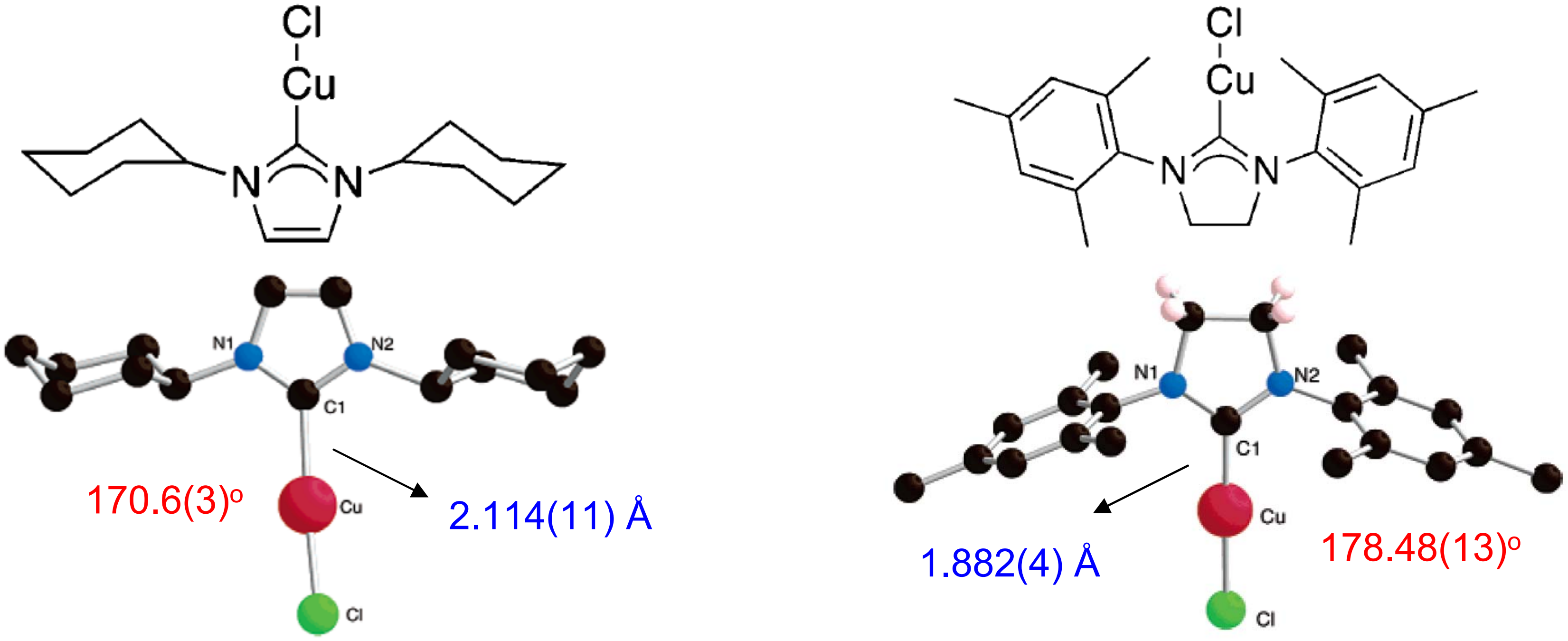
6-12 mol% NaO$^t$Bu
3 equiv $Et_3SiH$ Toluene, rt
0.75-20 hr

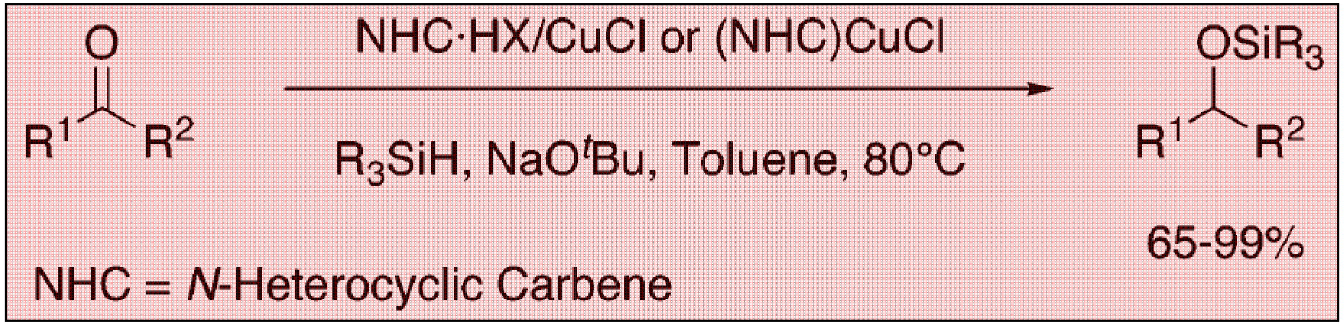
$R_1$ = alkyl, aryl
$R_2$ = alkyl

yield 9-100%

Kaur, H.; Zinn, F. K.; Stevens, E. D. Nolan, S. P. *Organometallics* **2004**, *23*, 1157-1160.

# A Simple and Efficient Copper-Catalyzed Procedure for the Hydrosilylation of Hindered and Functionalized Ketones





NHC·HX/CuCl or (NHC)CuCl

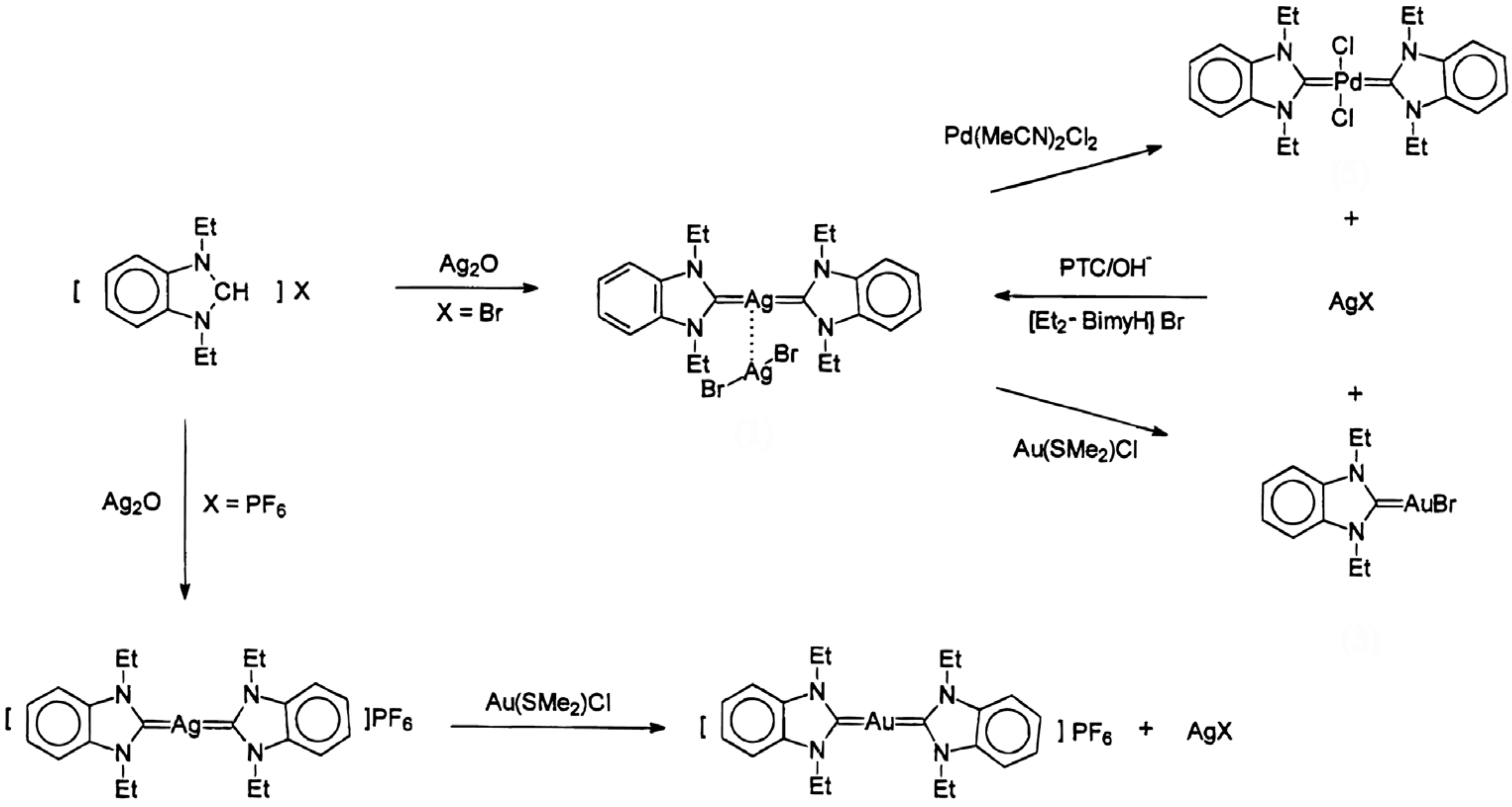
$R_3SiH$, NaO$^t$Bu, Toluene, 80°C

65-99%

NHC = *N*-Heterocyclic Carbene

Díez-González, S.; Kaur, H.; Zinn, F. K.; Stevens, E. D.; Nolan, S. P. *J. Org. Chem.* **2005**, *70*, 4784-4796.

# Facile Synthesis of Silver(I)-Carbene Complexes. Useful Carbene Transfer Agents



Wang, H. M. J.; Lin, I. J. B. *Organometallics* **1998**, *17*, 972-975.

# Quantum Chemical Calculations for the *N*-Heterocyclic Carbene Complexes of MCl (M = Cu, Ag, Au)

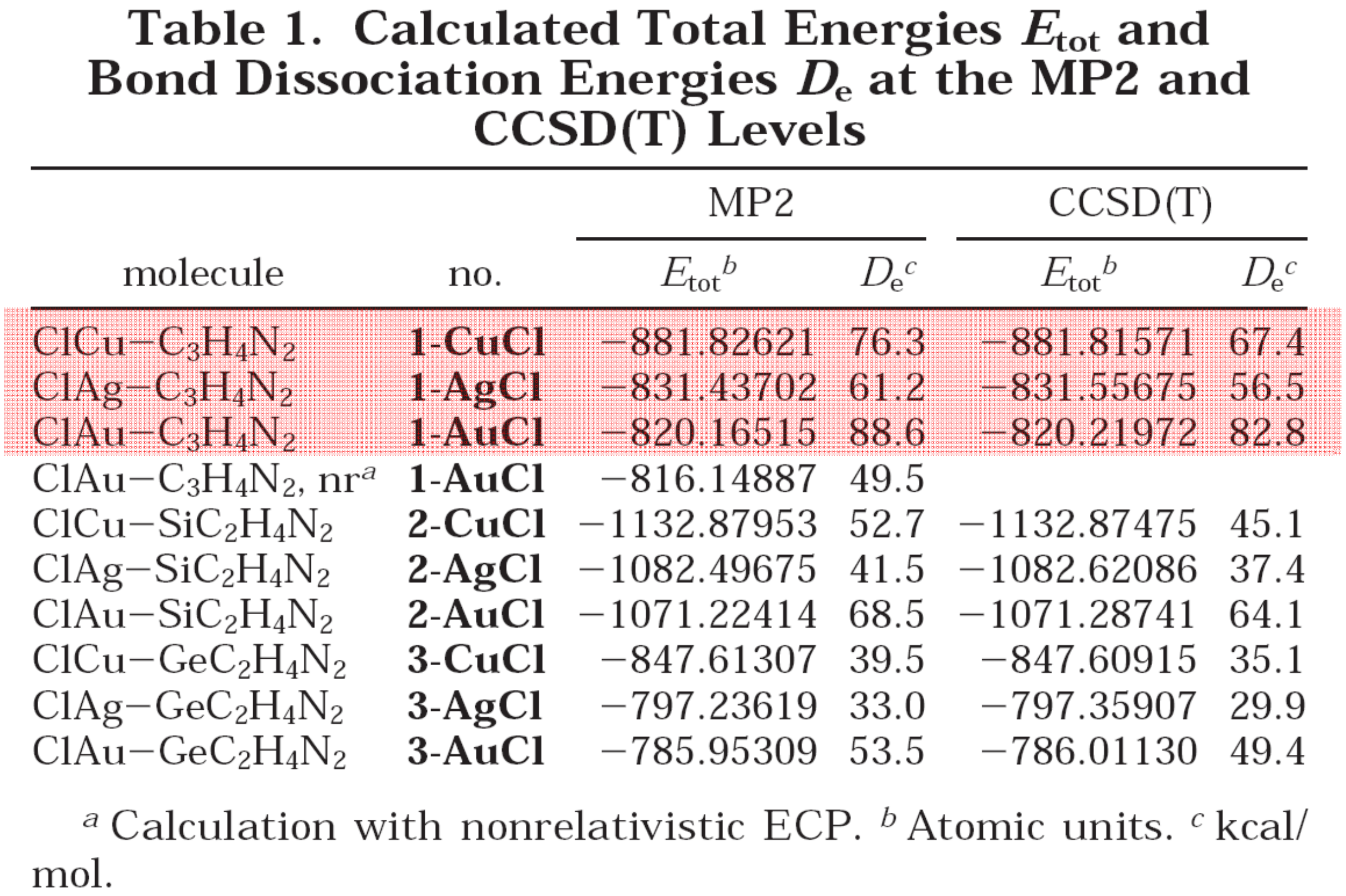
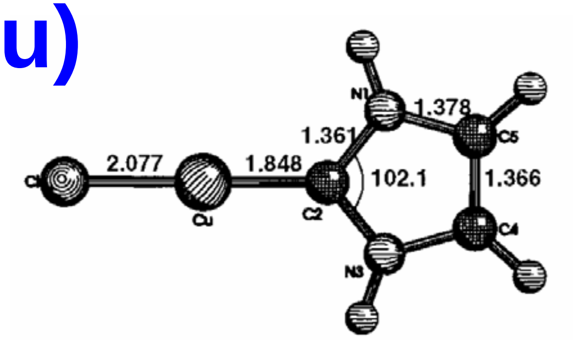


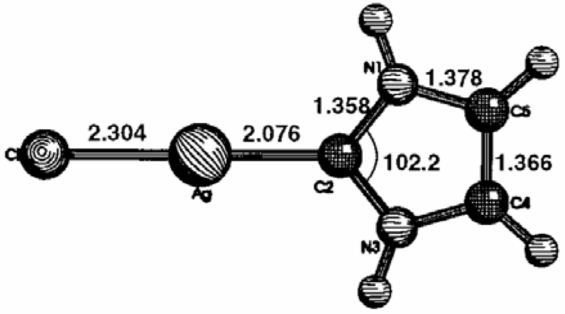
**Table 1. Calculated Total Energies $E_{tot}$ and Bond Dissociation Energies $D_e$ at the MP2 and CCSD(T) Levels**

| molecule | no. | MP2 $E_{tot}$[b] | MP2 $D_e$[c] | CCSD(T) $E_{tot}$[b] | CCSD(T) $D_e$[c] |
|---|---|---|---|---|---|
| $ClCu{-}C_3H_4N_2$ | **1-CuCl** | −881.82621 | 76.3 | −881.81571 | 67.4 |
| $ClAg{-}C_3H_4N_2$ | **1-AgCl** | −831.43702 | 61.2 | −831.55675 | 56.5 |
| $ClAu{-}C_3H_4N_2$ | **1-AuCl** | −820.16515 | 88.6 | −820.21972 | 82.8 |
| $ClAu{-}C_3H_4N_2$, nr[a] | **1-AuCl** | −816.14887 | 49.5 | | |
| $ClCu{-}SiC_2H_4N_2$ | **2-CuCl** | −1132.87953 | 52.7 | −1132.87475 | 45.1 |
| $ClAg{-}SiC_2H_4N_2$ | **2-AgCl** | −1082.49675 | 41.5 | −1082.62086 | 37.4 |
| $ClAu{-}SiC_2H_4N_2$ | **2-AuCl** | −1071.22414 | 68.5 | −1071.28741 | 64.1 |
| $ClCu{-}GeC_2H_4N_2$ | **3-CuCl** | −847.61307 | 39.5 | −847.60915 | 35.1 |
| $ClAg{-}GeC_2H_4N_2$ | **3-AgCl** | −797.23619 | 33.0 | −797.35907 | 29.9 |
| $ClAu{-}GeC_2H_4N_2$ | **3-AuCl** | −785.95309 | 53.5 | −786.01130 | 49.4 |

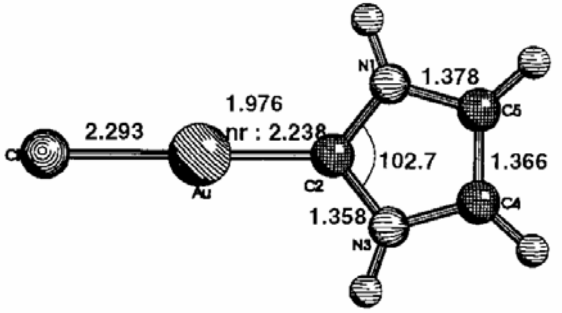
[a] Calculation with nonrelativistic ECP. [b] Atomic units. [c] kcal/mol.



**1-CuCl**



**1-AgCl**

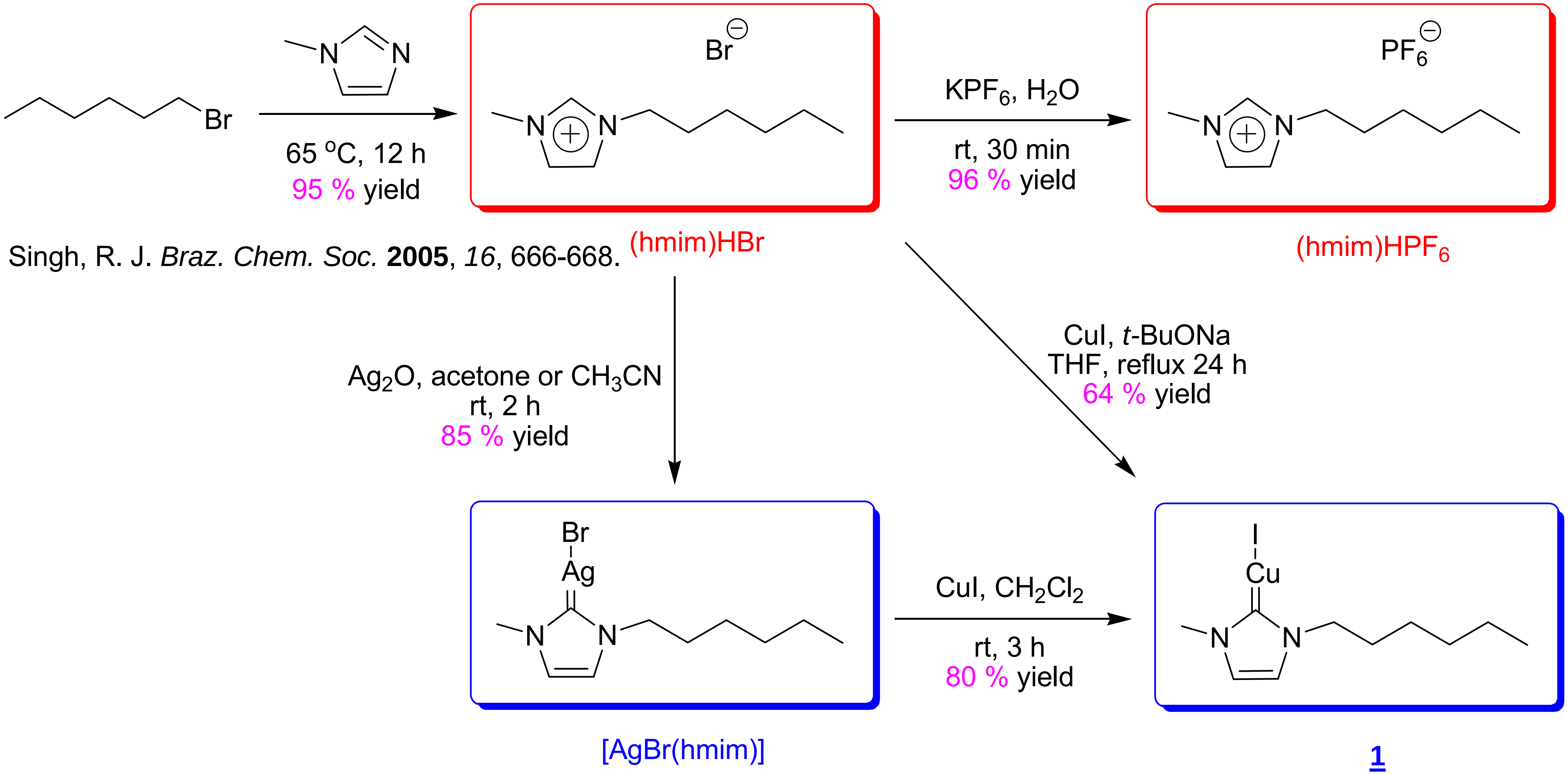


**1-AuCl**

The trend of the bond energies for the metal fragments is AuCl > CuCl > AgCl

Boehme, C. and Frenking, G. *Organometallics* **1998**, *17*, 5801-5809.

# Preparation of Copper(I) Complex Catalyst



65 °C, 12 h
95 % yield

(hmim)HBr

Singh, R. J. *Braz. Chem. Soc.* **2005**, *16*, 666-668.

$KPF_6$, $H_2O$
rt, 30 min
96 % yield

(hmim)$HPF_6$

$Ag_2O$, acetone or $CH_3CN$
rt, 2 h
85 % yield

CuI, *t*-BuONa
THF, reflux 24 h
64 % yield

[AgBr(hmim)]

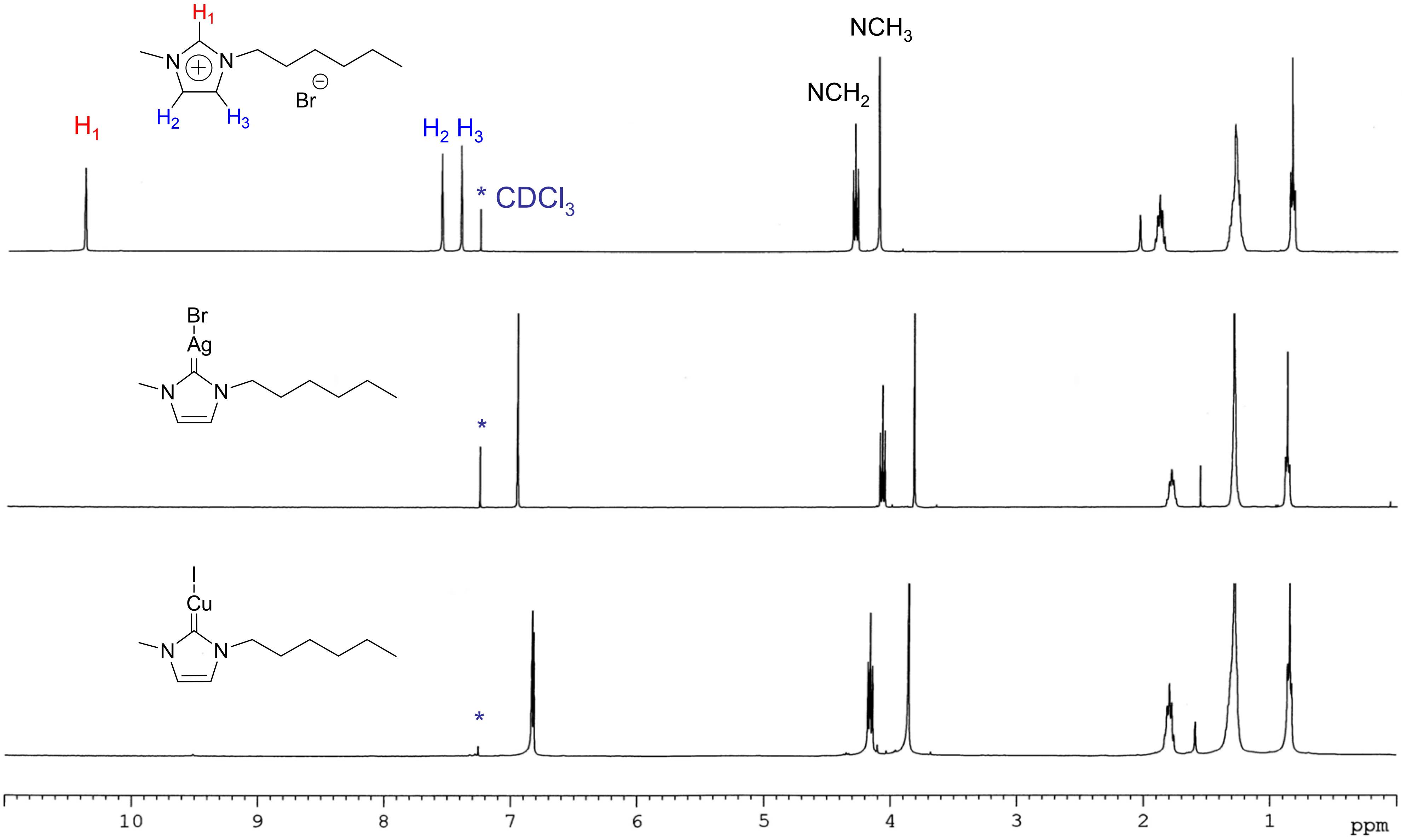
CuI, $CH_2Cl_2$
rt, 3 h
80 % yield

**1**

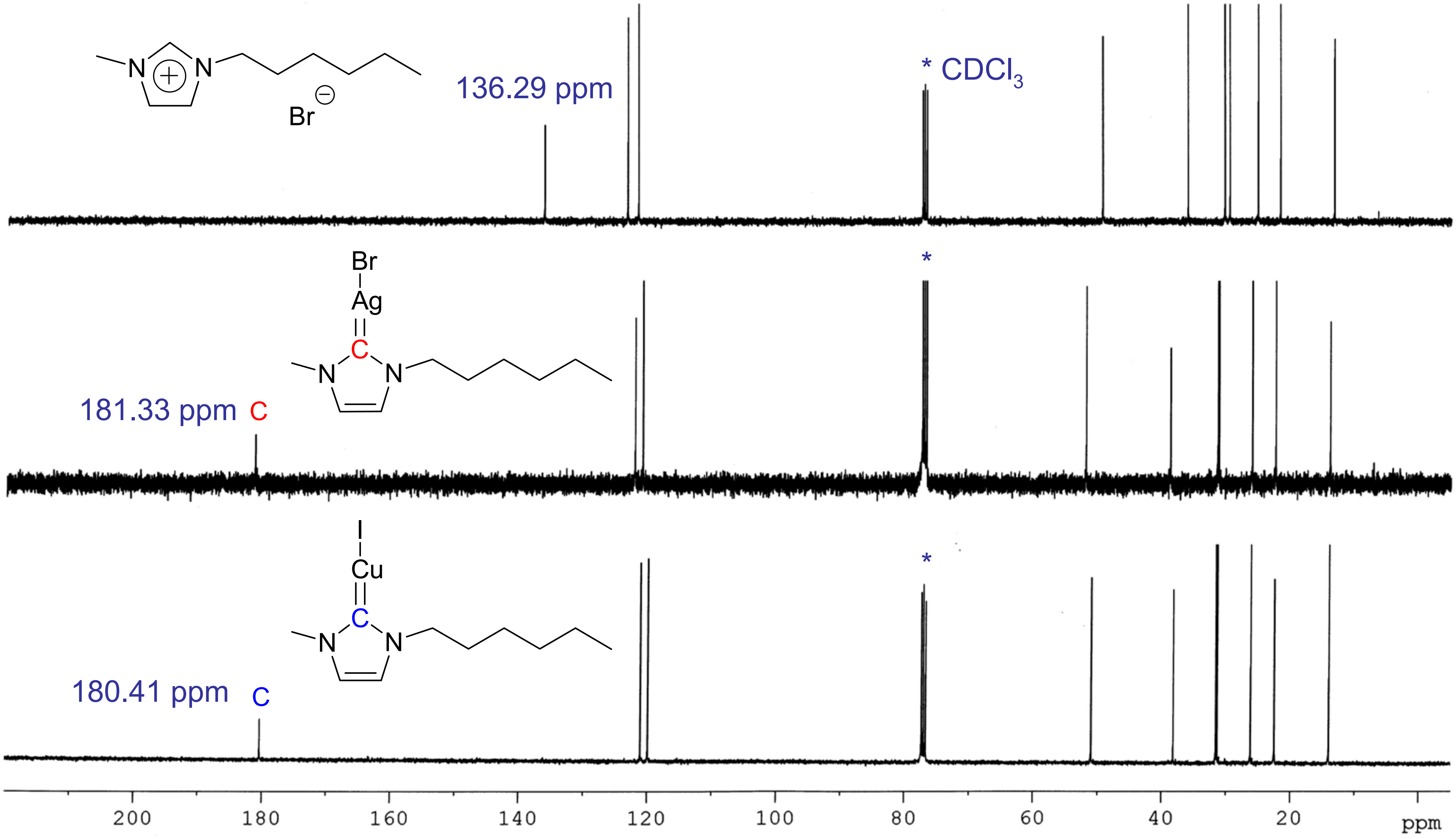
(hmim)HBr = 1-hexyl-3-methylimidazolium bromide

Calcd: C, 33.67; H, 5.09; N, 7.85
Found: C, 33.55; H, 5.18; N, 7.66

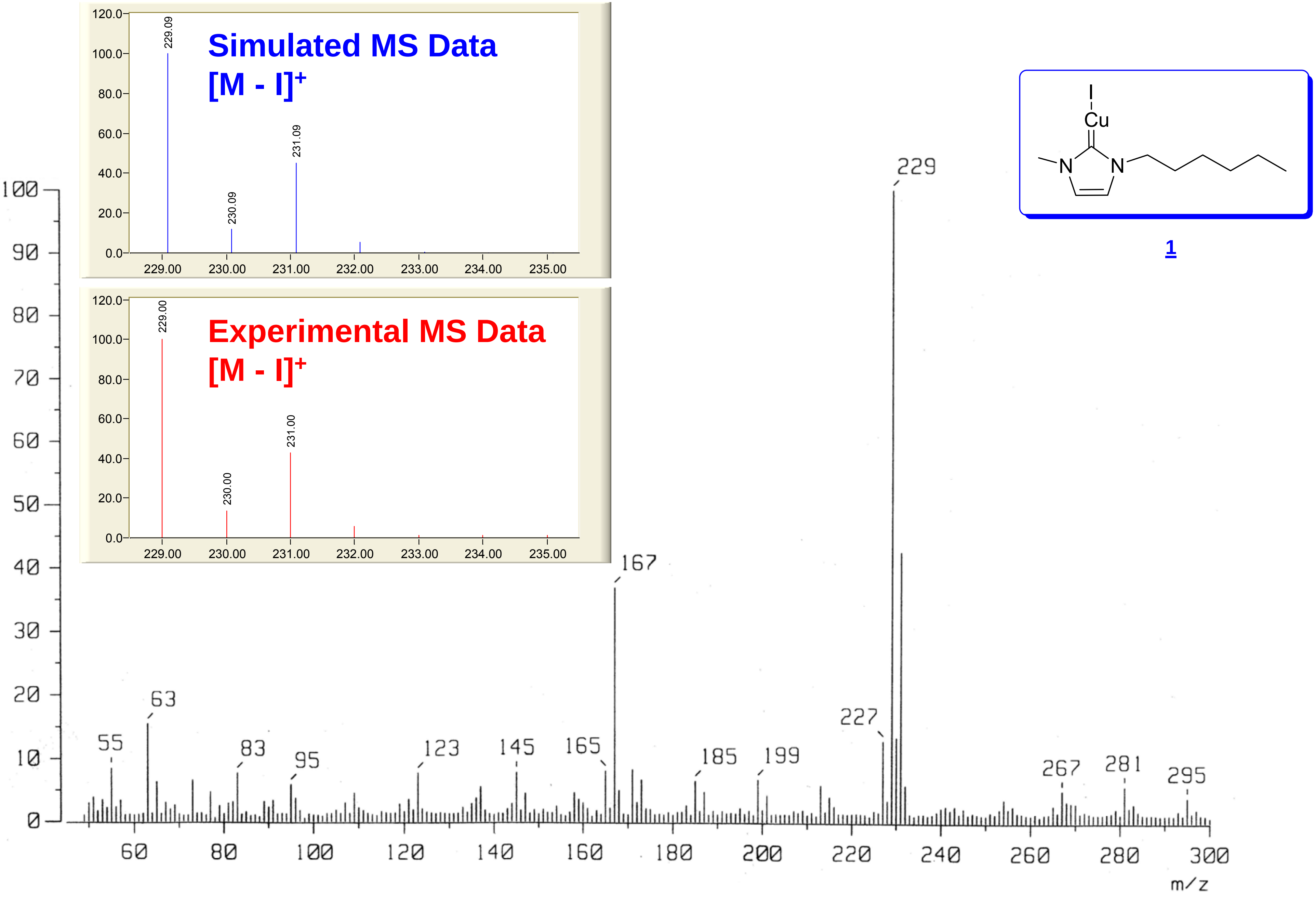
# $^1$H NMR Spectra of (hmim)HBr, [AgBr(hmim)] and Complex 1



# $^{13}$C NMR Spectra of (hmim)HBr, [AgBr(hmim)] and Complex 1

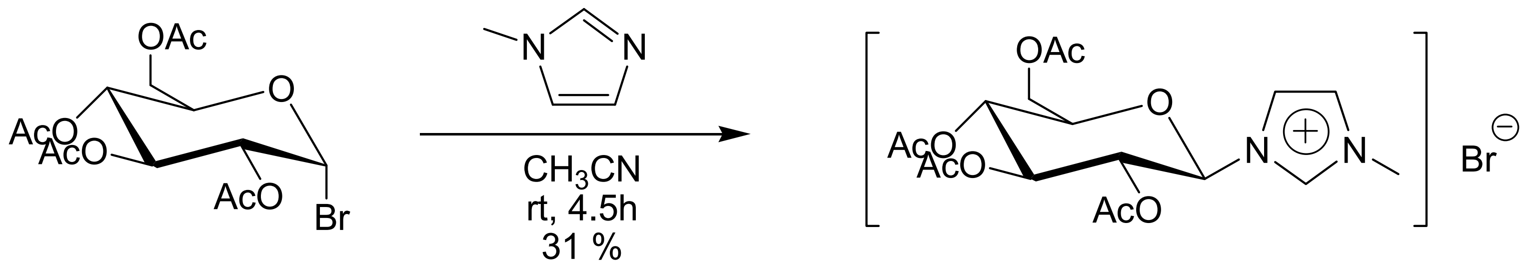


# FAB-MS Spectrum of Complex 1

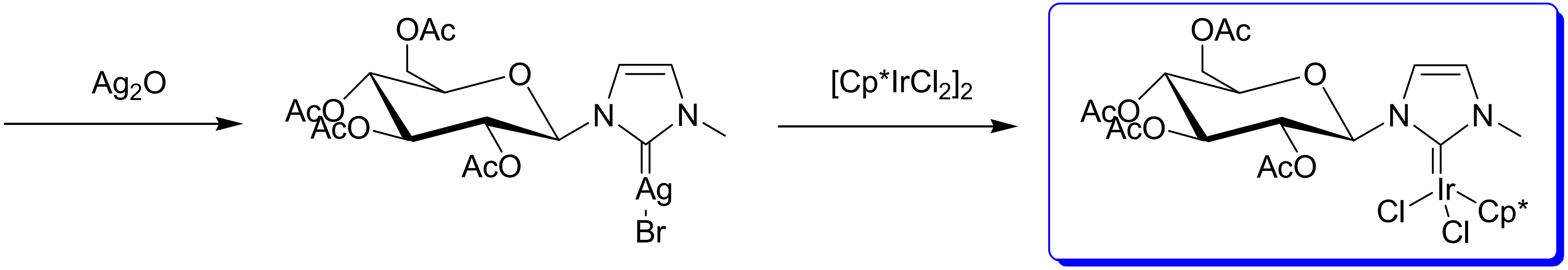


**1**

# Sugar-Incorporated *N*-Heterocyclic Carbene Complexes

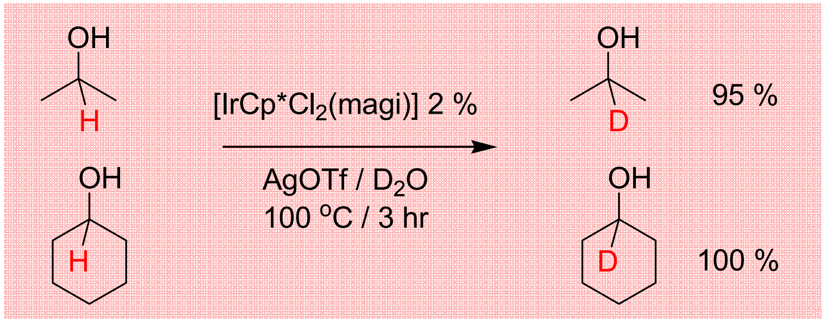


(magi)HBr



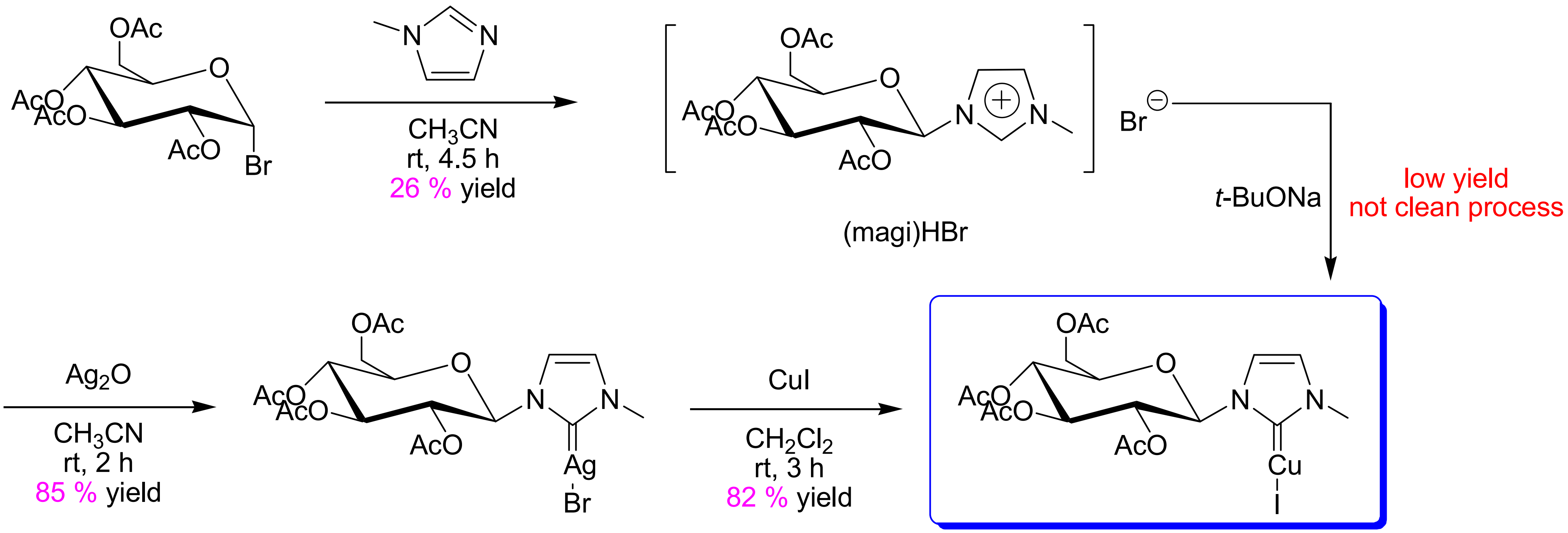
$[AgBr(magi)]$

$[IrCp^*Cl_2(magi)]$



Nishioka, T.; Shibata, T.; Kinoshita, I. *Organometallics* **2007**, *26*, 1126-1128.

# Preparation of Copper(I) Complex Catalyst



low yield
not clean process

(magi)HBr

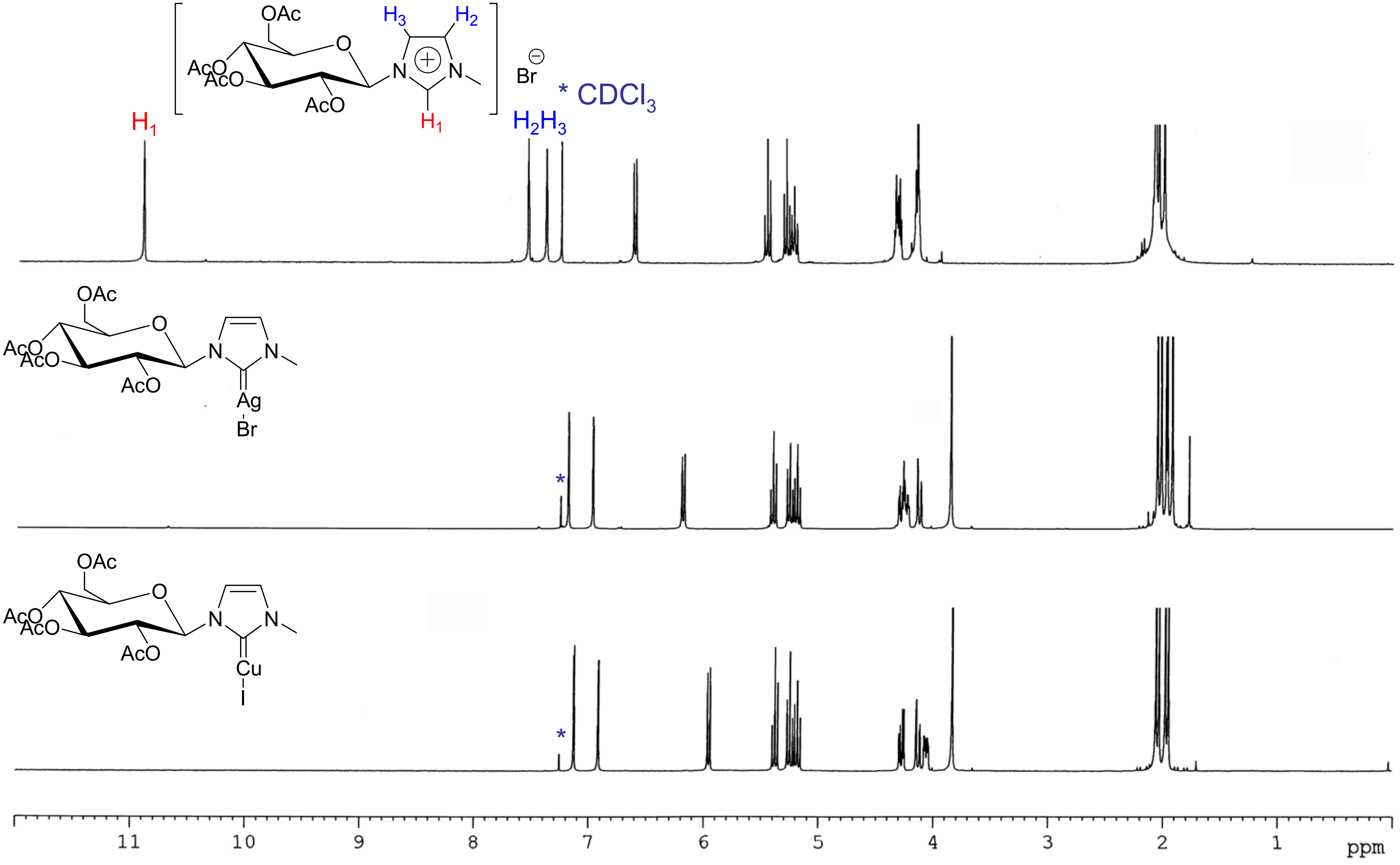
[AgBr(magi)]

**2**

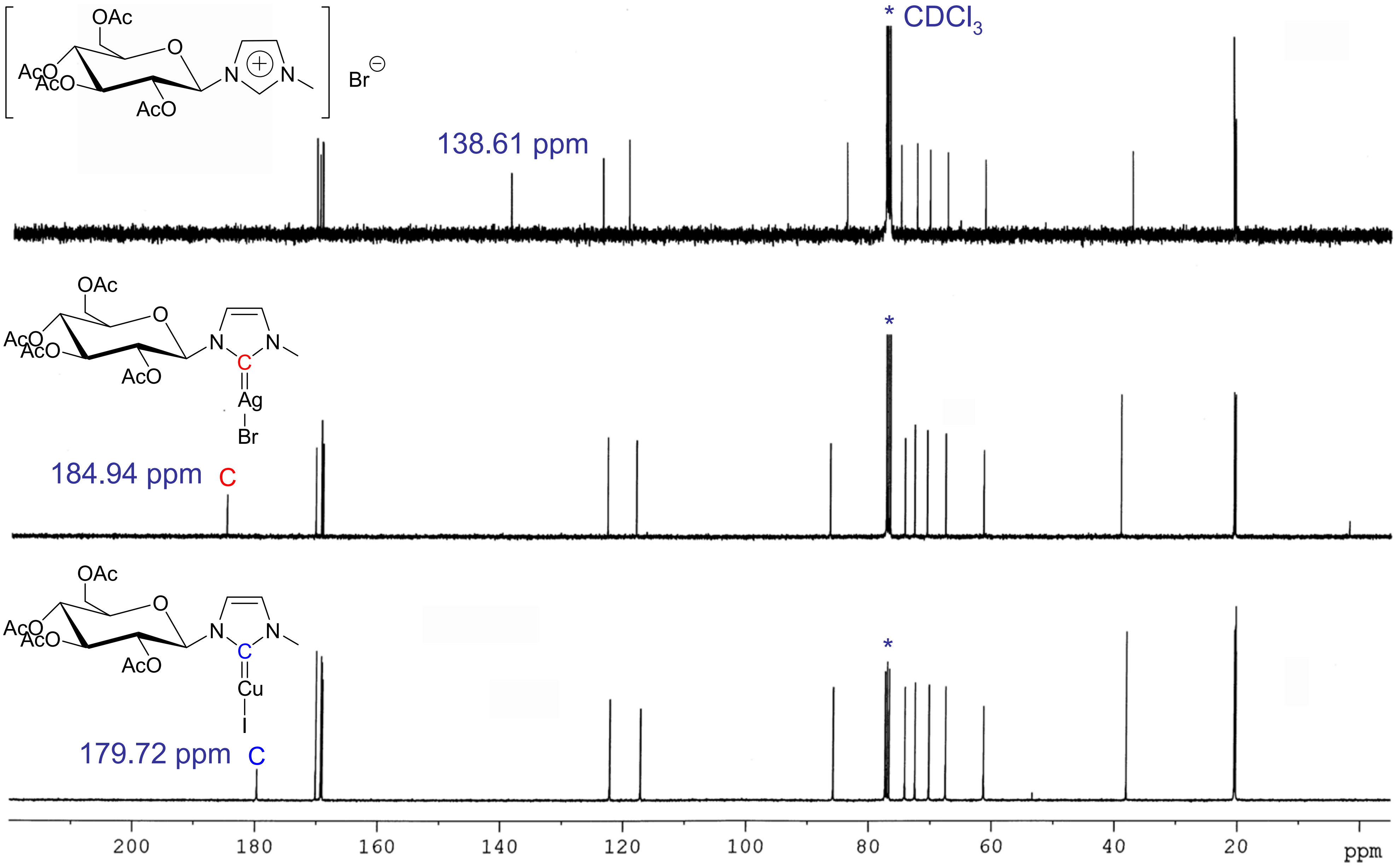
(magi)HBr = 1-methyl-3-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)imidazolium bromide

Calcd: C, 35.86; H, 4.01; N, 4.65
Found: C, 36.14; H, 4.11; N, 4.33

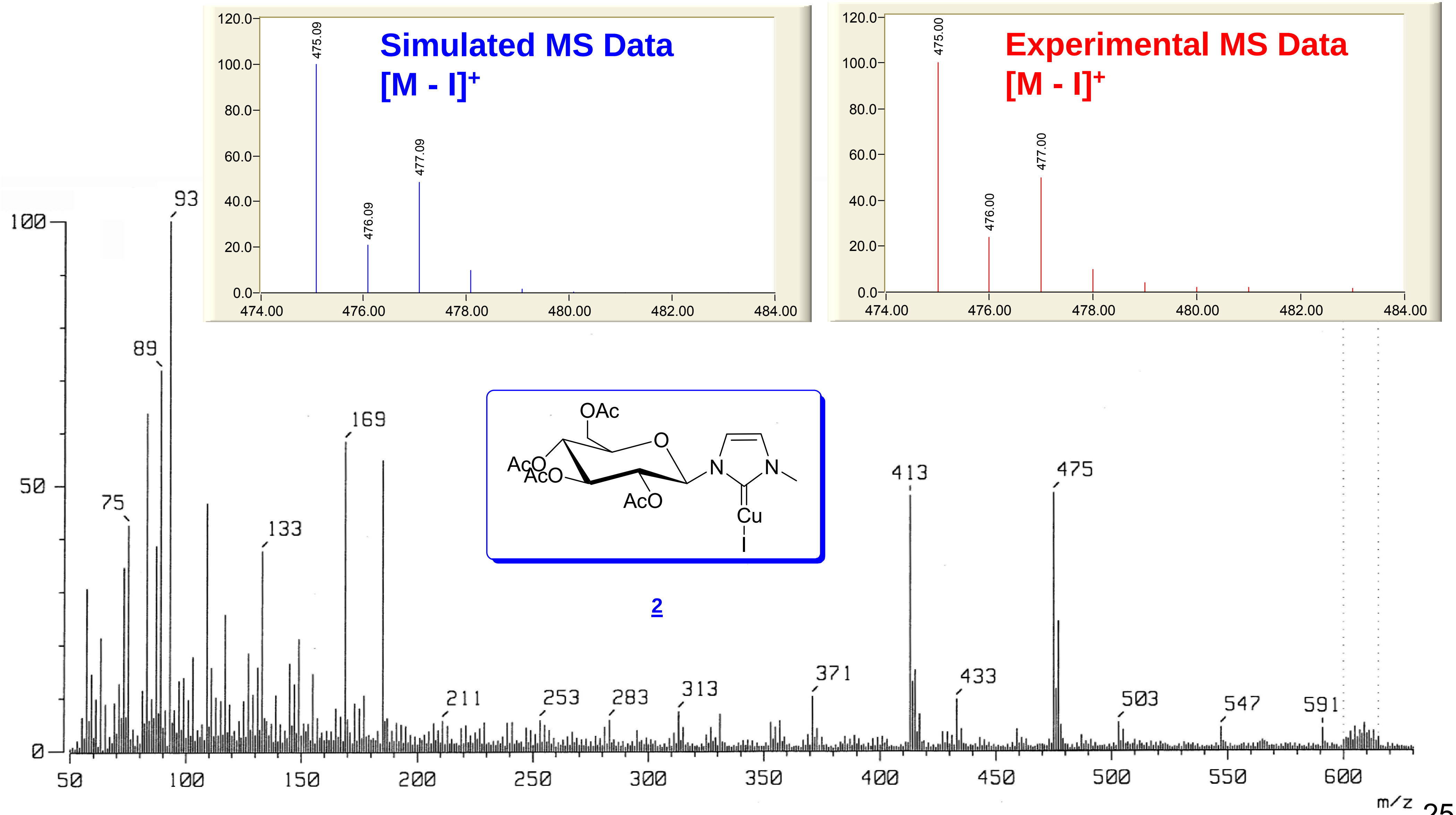
# $^1H$ NMR Spectra of (magi)HBr, [AgBr(magi)] and Complex 2



# $^{13}$C NMR Spectra of (magi)HBr, [AgBr(magi)] and Complex 2



# FAB-MS Spectrum of Complex 2



Simulated MS Data

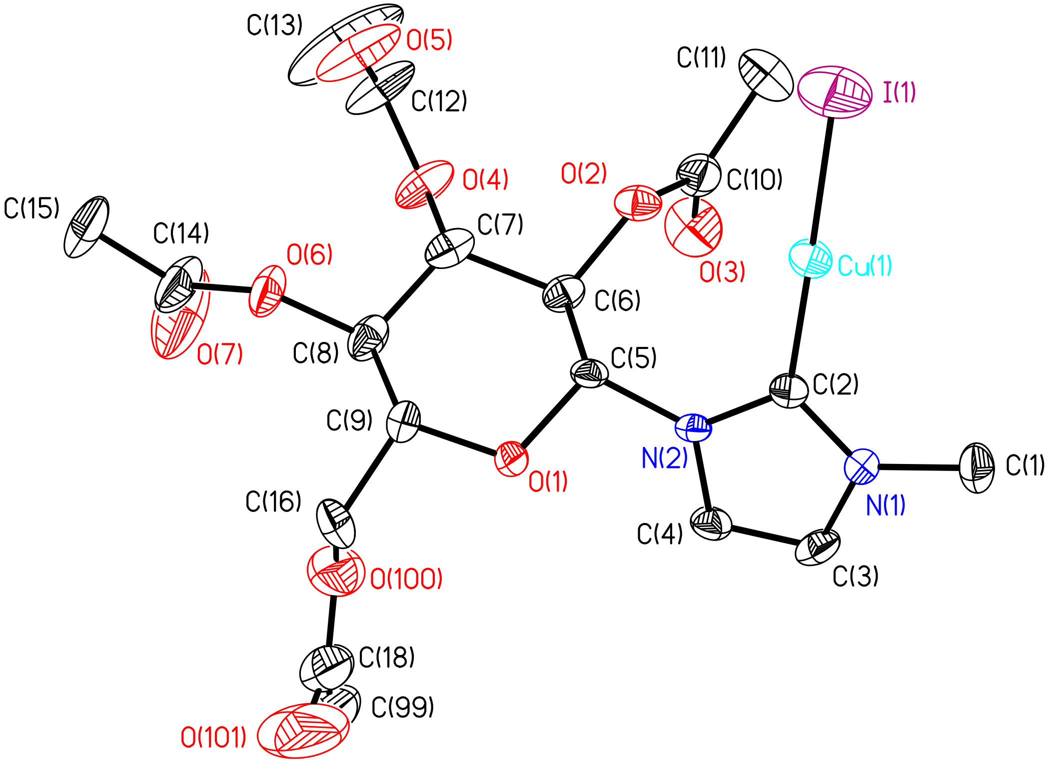
[M - I]$^+$

Experimental MS Data

[M - I]$^+$

**2**

# Single-Crystal X-ray Structure of Complex 2



| Empirical formula | C18 H24 Cu I N2 O9 |
|---|---|
| Temperature | 298(2) K |
| Space group | P 21 |

Unit cell dimensions

| | |
|---|---|
| a = 9.8766(14) Å | α = 90° |
| b = 7.0101(10) Å | β = 94.389(5)° |
| c = 17.321(2) Å | γ = 90° |

Volume 1195.7(3) Å$^3$

Final R indices [I>2sigma(I)]

R1 = 0.0846, wR2 = 0.2651

| bond lengths [Å] | | angles [deg] | |
|---|---|---|---|
| Cu(1)-C(1) | 1.874(8) | C(1)-Cu(1)-I(1) | 174.3(3) |

# The Catalytic Applications of Cu(I) Compounds

1. ***Sonogashira(C-C Coupling) Reactions***

2. ***Carbon-Surfur Coupling Reactions***

3. ***Kharasch-Sosnovsky(C-O Coupling) Reactions (Allylic Oxidations of Olefins)***

4. ***Buchwald-Hartwig(C-N Coupling) Reactions***

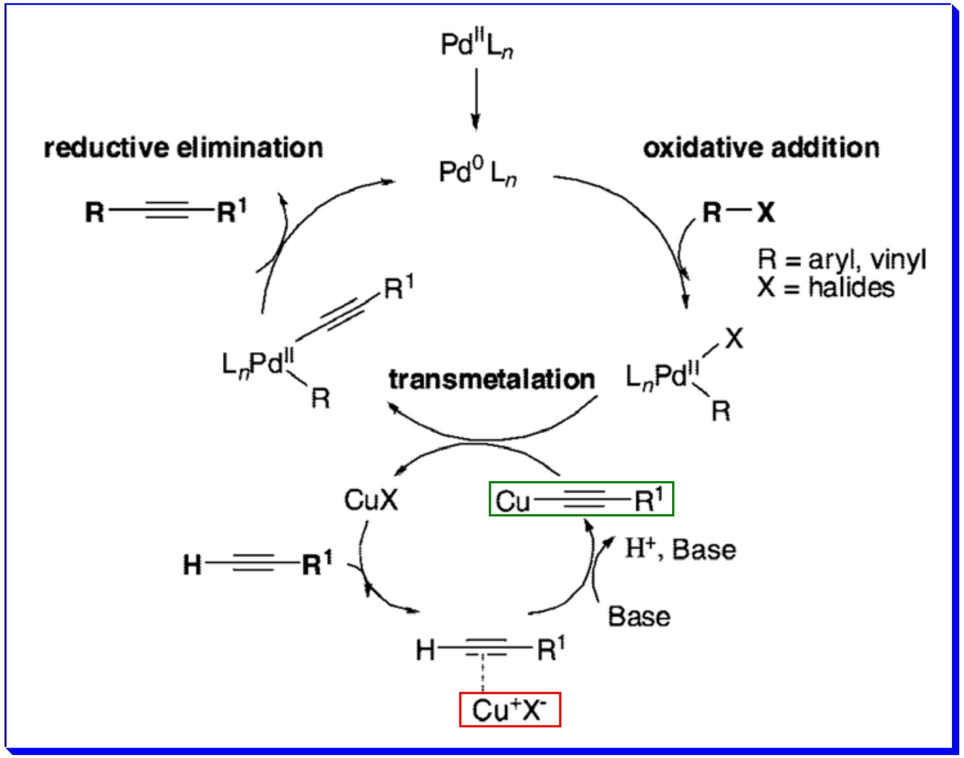
# Sonogashira Coupling Reactions

$$\mathrm{RX} + \equiv\!\!-\mathrm{R'} \xrightarrow[\mathrm{Et_2NH,\ N_2,\ rt,\ 3\text{-}6\ h}]{\mathrm{10\ mol\%\ (PPh_3)_2PdCl_2,\ 5\ mol\%\ CuI}} \mathrm{R}\!-\!\equiv\!-\mathrm{R'}$$

27-99 %

RX = iodoarenes, bromoalkenes,
bromopyridines

R' = H, Ph, $CH_2OH$



Sonogashira, K.; Tohda, Y.; Hagihara. N. *Tetrahedron Lett*. **1975**, *16*, 4467-4470.

# The First Example of Copper(I) Catalyzed Sonogashira Reactions

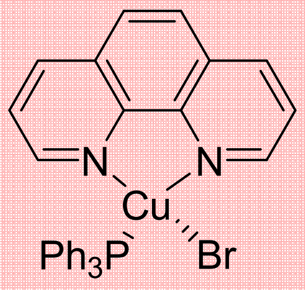
$$R^1X + HC\equiv CR^2 \xrightarrow[\text{DMF or DMSO, 80-120 }^{o}\text{C, 10-40 h}]{\text{5 mol\% CuI, 10 mol\% PPh}_3\text{, K}_2\text{CO}_3} R^1C\equiv CR^2$$

8-98 %

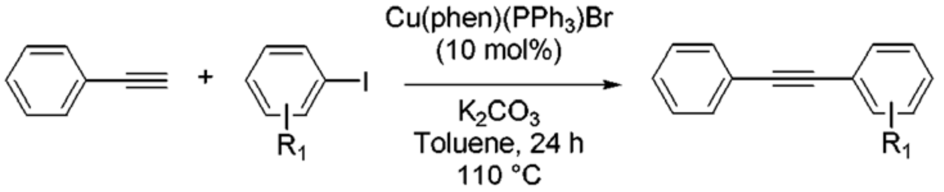
$R^1$ = aryl, vinyl; X= Br, I; $R^2$ = Ph, n-pentyl

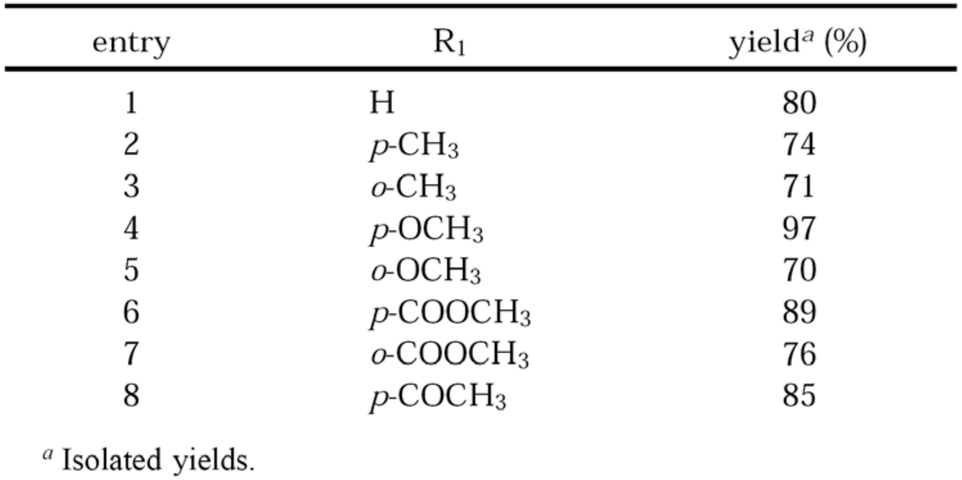
Okuro, K.; Furuune, M.; Miura, M.; Nomura, M. *Tetrahedron Lett*. **1992**, *33*, 5363-5364.

# Cu(phen)($PPh_3$)Br Catalyzed Sonogashira Reactions



Cu(phen)($PPh_3$)Br



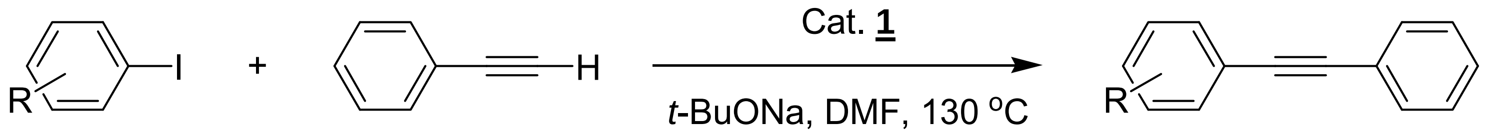


| entry | $R_1$ | yield[a] (%) |
|---|---|---|
| 1 | H | 80 |
| 2 | *p*-$CH_3$ | 74 |
| 3 | *o*-$CH_3$ | 71 |
| 4 | *p*-$OCH_3$ | 97 |
| 5 | *o*-$OCH_3$ | 70 |
| 6 | *p*-$COOCH_3$ | 89 |
| 7 | *o*-$COOCH_3$ | 76 |
| 8 | *p*-$COCH_3$ | 85 |

[a] Isolated yields.

Gujadhur, R. K.; Bates, C. G.; Venkataraman, D. *Org. Lett.* **2001**, *3*, 4315-4317.

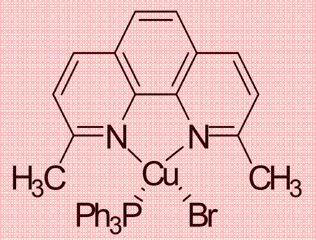
# Cu(I)-Catalyzed Sonogashira Reactions



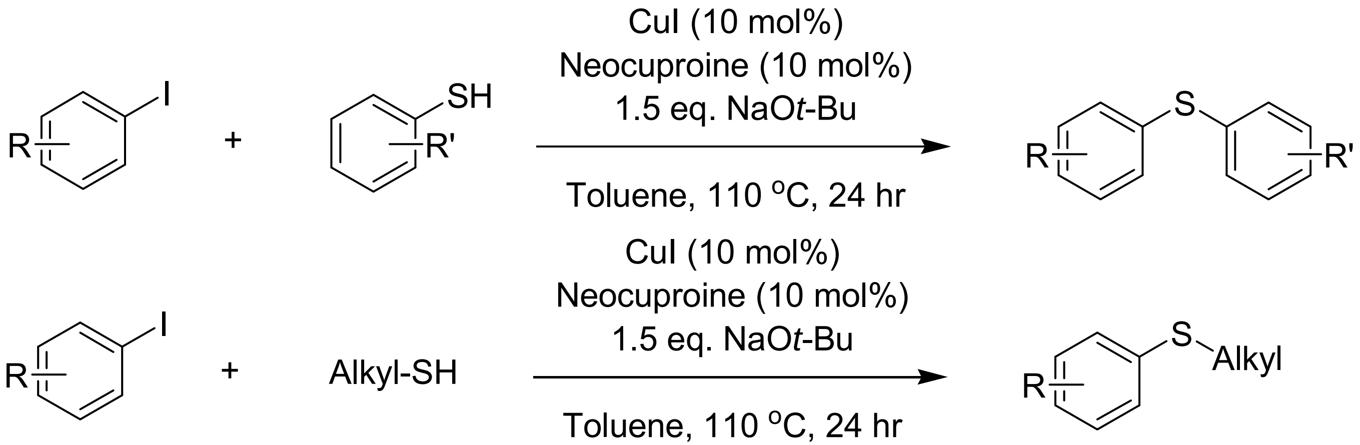
| Entry | R | Time (hr) | Conversion (%) |
|---|---|---|---|
| 1 | H | 12 | 80 |
| 2 | *p*-$CH_3$ | 24 | 66 |
| 3 | *p*-$OCH_3$ | 24 | 51 |
| 4 | *p*-$COCH_3$ | 10 | 86 |

Reaction conditions: catalyst loading = 10 mol%; aryl iodide = 1.00 mmol; phenylacetylene = 1.27 mmol; *t*-BuONa = 1.20 mmol; DMF = 1.0 mL

# Cu(I) Catalyzed C-S Coupling Reactions



Cu(neocup)($PPh_3$)Br



Yield =77%-98%

Bates, C. G.; Gujadhur, R. K.; Venkataraman, D. *Org. Lett.* **2002**, *4*, 2803-2806.

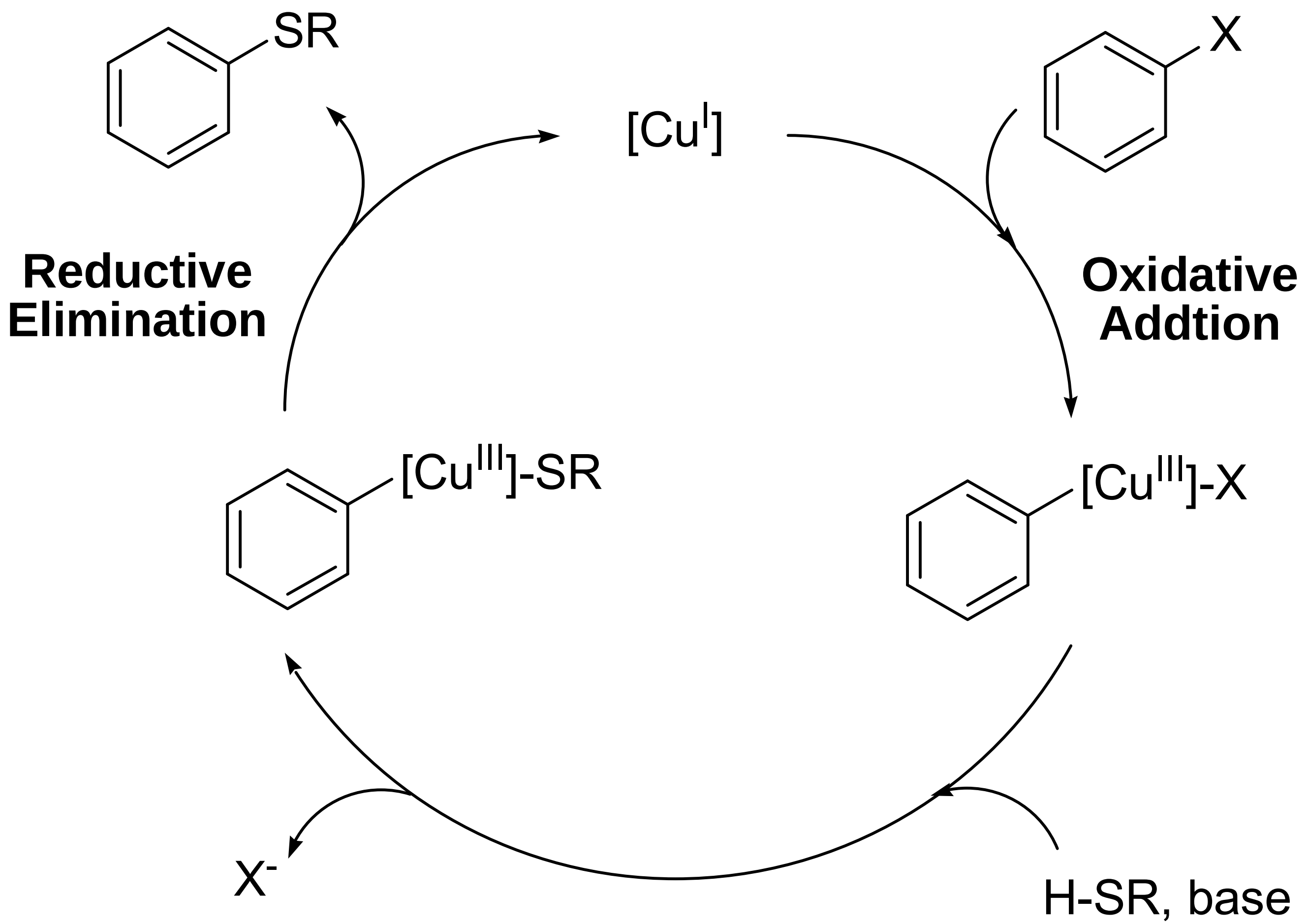
# Copper-Catalyzed C-S Coupling Reactions Using Microwave Heating

$$\text{R-SH} \quad + \quad \text{Ar-X} \quad \xrightarrow[\text{microwave, 2-6h}]{\text{CuI (10 mol\%)}\\ Cs_2CO_3\text{ (2 equiv.)}} \quad \text{R-S-Ar}$$

67-89 %

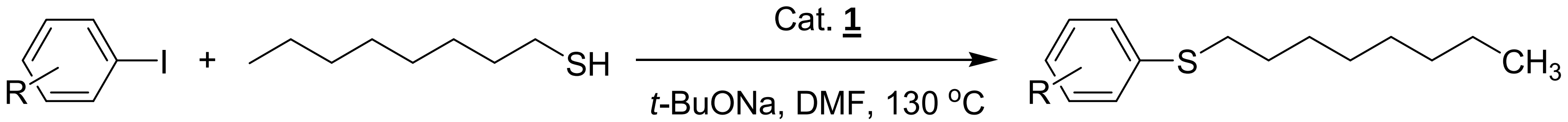
Wu, Y.-J.; He, H. *Synlett* **2003**, *14*, 1789-1790.

# Proposed Mechanism for C-S Coupling



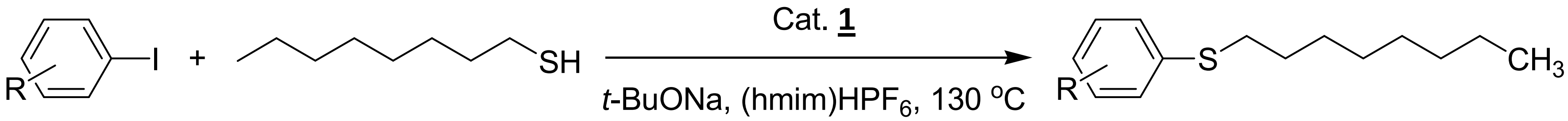
Bates, C. G.; Gujadhur, R. K.; Venkataraman, D. *Org. Lett.* **2002**, *4*, 2803 -2806.

# Cu(I)-Catalyzed C-S Coupling Reactions



| Entry | R | Time (hr) | Conversion (%) |
|---|---|---|---|
| 1 | H | 1.0 | 96 |
| 2 | *p*-$CH_3$ | 1.0 | 91 |
| 3 | *p*-$OCH_3$ | 1.5 | 80 |
| 4 | *p*-$COCH_3$ | 1.0 | 99 |
| 5 | *o*-$COCH_3$ | 1.0 | 92 |

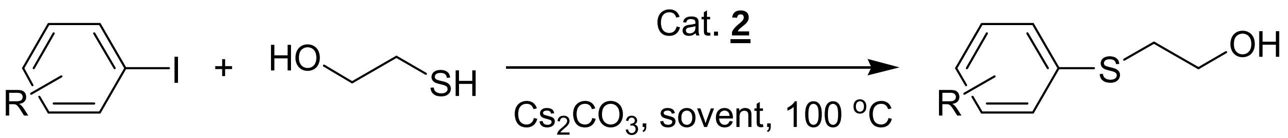
Reaction conditions: catalyst loading = 10 mol%; aryl iodide = 1.00 mmol; 1-octanethiol = 1.20 mmol; *t*-BuONa = 1.50 mmol; DMF = 1.0 mL



| Entry | R | Time (hr) | Conversion (%) |
|---|---|---|---|
| 1 | H | 1.0 | 93 |
| 2 | *p*-$CH_3$ | 1.0 | 88 |
| 3 | *p*-$OCH_3$ | 1.5 | 83 |
| 4 | *p*-$COCH_3$ | 1.0 | 99 |
| 5 | *o*-$COCH_3$ | 1.0 | 91 |

Reaction conditions: catalyst loading = 10 mol%; aryl iodide = 1.00 mmol; 1-octanethiol = 1.20 mmol; *t*-BuONa = 1.50 mmol; (hmim)$HPF_6$ = 1.0 mL

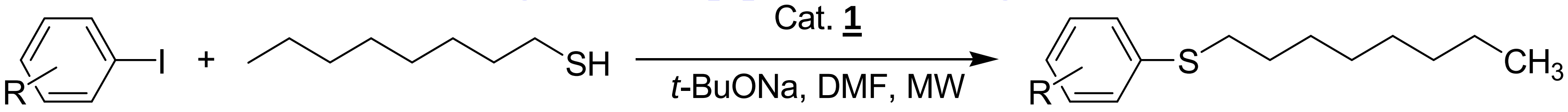
# Cu(I)-Catalyzed C-S Coupling Reactions



| Entry | R | sovent | Time (hr) | Conversion (%) |
|---|---|---|---|---|
| 1 | H | (hmim)HBr + $H_2O$ | 1.0 | 86 |
| 2 | *p*-$CH_3$ | (hmim)HBr + $H_2O$ | 1.5 | 85 |
| 3 | *p*-$OCH_3$ | (hmim)HBr + $H_2O$ | 1.5 | 81 |
|  |  |  | 2.5 | 99 |
| 4 | *p*-$COCH_3$ | (hmim)HBr + $H_2O$ | 1.0 | 95 |
| 5 | *o*-$COCH_3$ | (hmim)HBr + $H_2O$ | 1.0 | 89 |

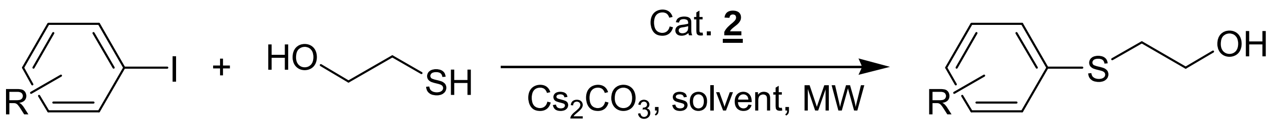
Reaction conditions: catalyst loading = 10 mol%; aryl iodide = 1.0 mmol; 2-mercaptoethanol = 1.42 mmol; $Cs_2CO_3$ = 1.5 mmol; solvent = 1.0 mL ((hmim)HBr : $H_2O$ = 1 : 1)

# Microwave Assisted C-S Coupling Reactions by Cu(I) Catalyst



| Entry | R | Time (sec) | Conversion (%) |
|---|---|---|---|
| 1 | H | 50 | 92 |
| 2 | *p*-$CH_3$ | 60 | 88 |
| 3 | *p*-$OCH_3$ | 60 | 82 |
| 4 | *p*-$COCH_3$ | 10 | 99 |
| 5 | *o*-$COCH_3$ | 10 | 92 |

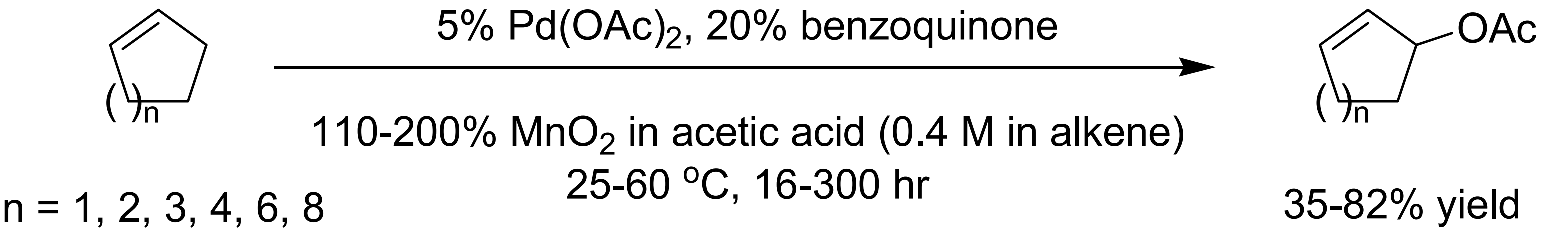
Reaction conditions: catalyst loading = 10 mol%; aryl iodide = 1.00 mmol; 1-octanethiol = 1.20 mmol; *t*-BuONa = 1.50 mmol; DMF = 1.0 mL(add 3 drops of (hmim)HBr); power = 600 W



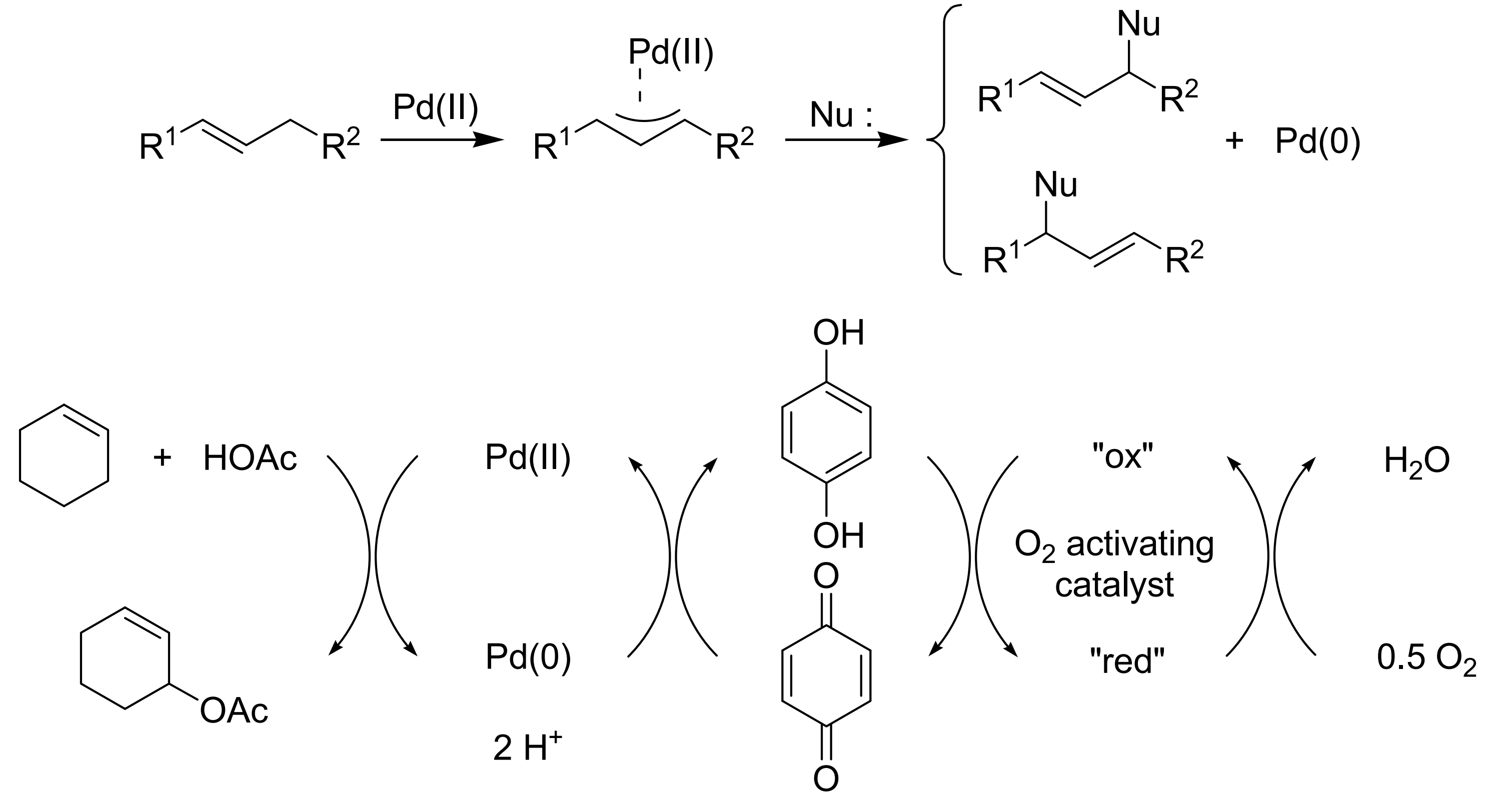
| Entry | R | sovent | Time (sec) | Conversion (%) |
|---|---|---|---|---|
| 1 | H | (hmim)HBr + $H_2O$ | 50 | 84 |
| 2 | *p*-$CH_3$ | (hmim)HBr + $H_2O$ | 50 | 88 |
| 3 | *p*-$OCH_3$ | (hmim)HBr + $H_2O$ | 60 | 79 |
| 4 | *p*-$COCH_3$ | (hmim)HBr + $H_2O$ | 25 | 98 |
| 5 | *o*-$COCH_3$ | (hmim)HBr + $H_2O$ | 25 | 91 |

Reaction conditions: catalyst loading = 10 mol%; aryl iodide = 1.0 mmol; 2-mercaptoethanol = 1.42 mmol; $Cs_2CO_3$ = 1.50 mmol; solvent = 1.0 mL ((hmim)HBr : $H_2O$ = 1 : 1); power = 600 W

# Pd(II)-Catalyzed Allylic Oxidation of Olefin

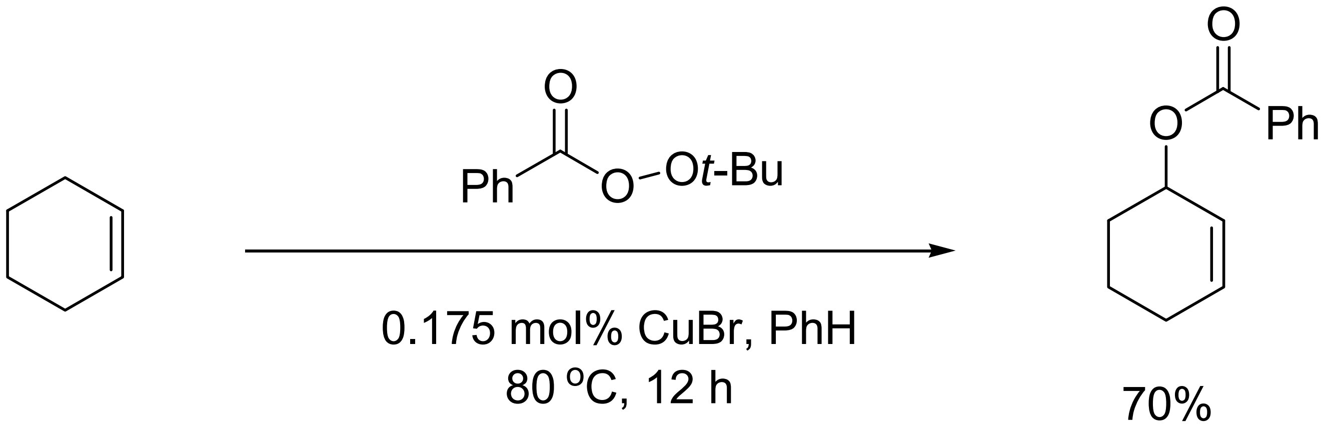


## *Mechanism*



Hansson, S.; Heumann, A.; Rein, T.; Aakermark, B. *J. Org. Chem.* **1990**, *55*, 975-984.

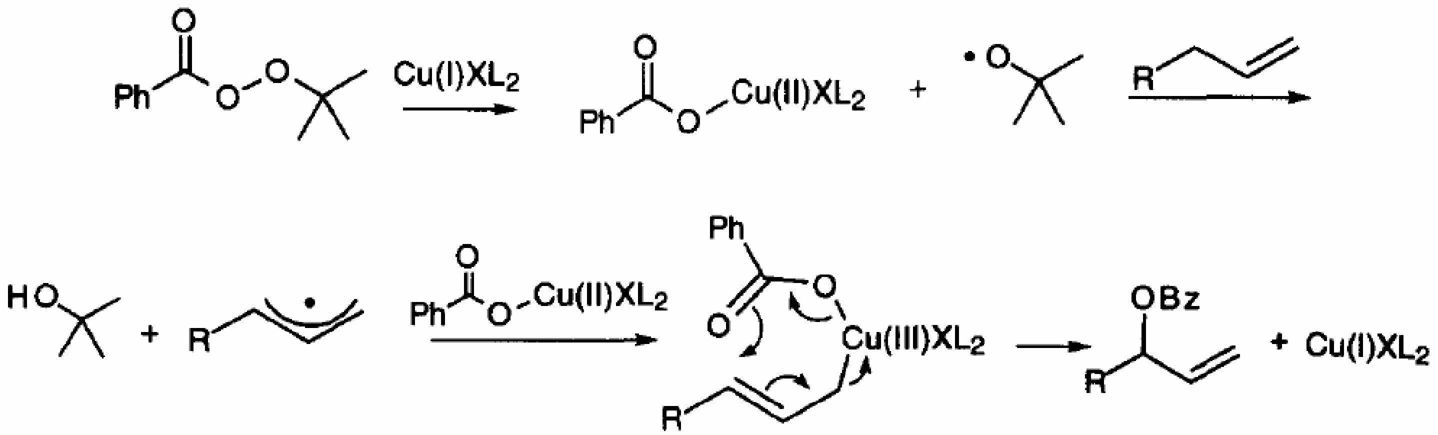
# Allylic Oxidation of Olefin (*Kharasch-Sosnovsky Reaction*)



0.175 mol% CuBr, PhH
80 °C, 12 h

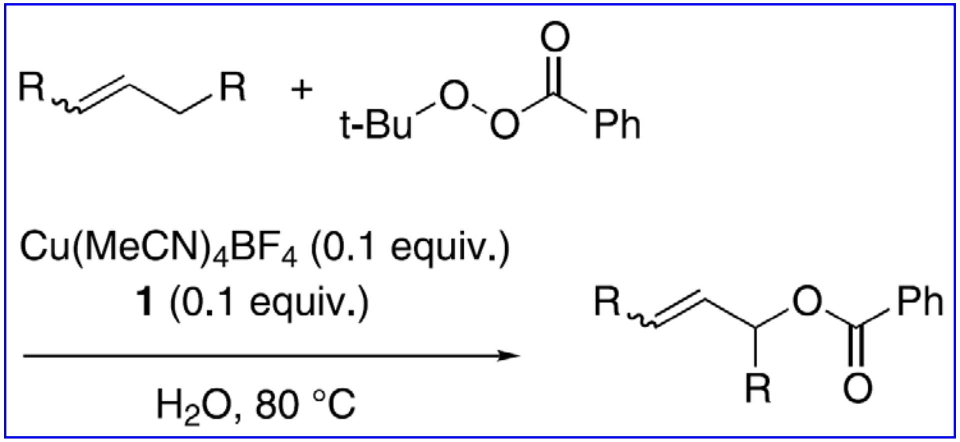
70%

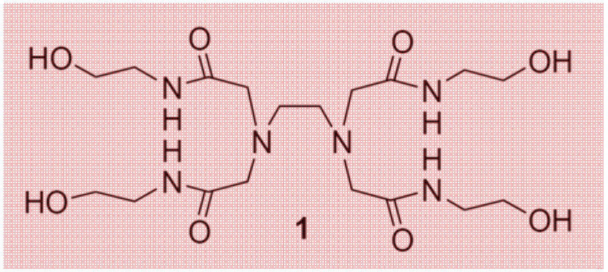
***Mechanism***



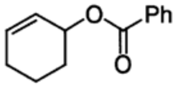
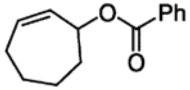
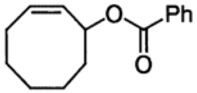
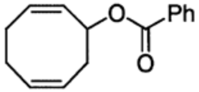
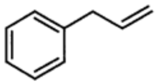
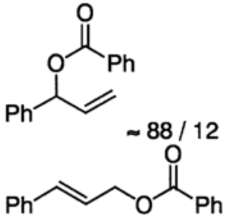
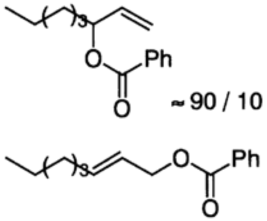
Kharasch, M. S.; Sosnovsky, G.; Yang, N. C. *J. Am. Soc. Chem*. **1959**, *81*, 5819-5824.

# Cu(I)-Catalyzed
# Allylic Oxidation of Olefin Reactions





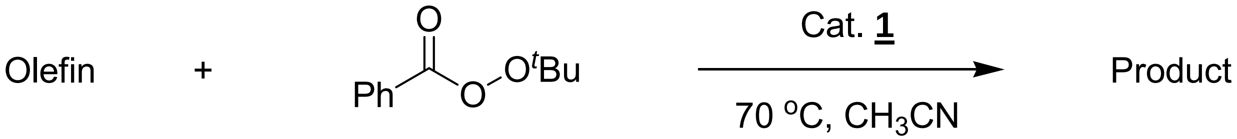
**1**

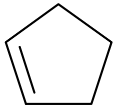
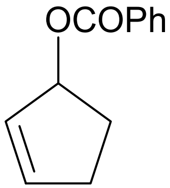
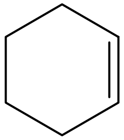
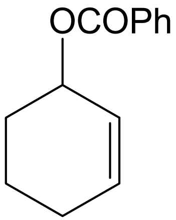
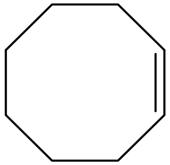
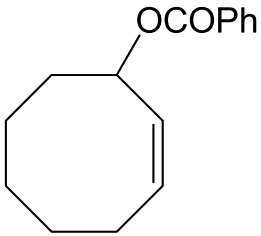
| Entry | Olefin **2** | Time (h) | Product **3** | Yield (%)[a] |
|---|---|---|---|---|
| *a* |  | 48 |  | 67 |
| *b* |  | 48 |  | 64 |
| *c* |  | 120 |  | 42 |
| *d* |  | 48 |  | 75 |
| *e* |  | 72 |  ~88 / 12 | 47 |
| *f* |  | 240 |  ~90 / 10 | 13 |

[a] Isolated yield calculated on the amount of $PhCO_3t$-Bu introduced.

Bras, J. L.; Muzart, J. *Tetrahedron Lett.* **2002**, *43*, 431-433.

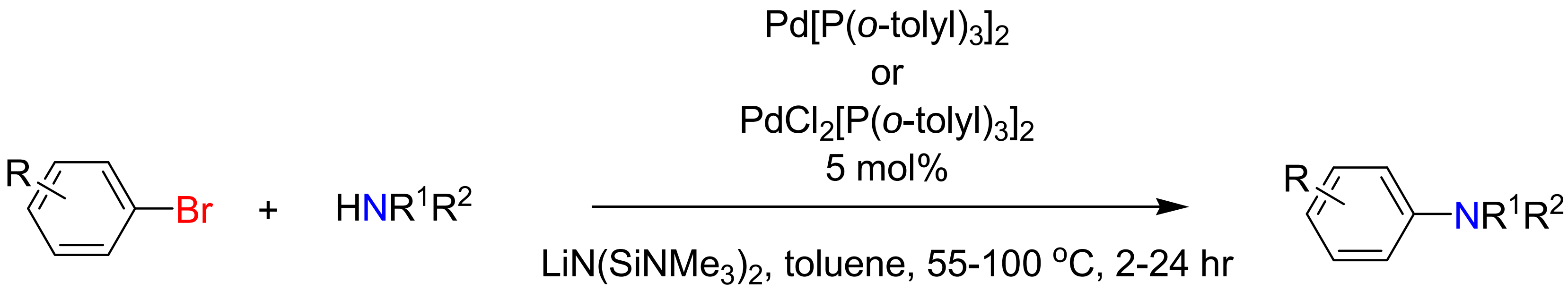
# Cu(I)-Catalyzed
# Allylic Oxidation of Olefin Reactions



| Entry | Olefin | Product | Time (hr) | Conversion (%) |
|---|---|---|---|---|
| 1 |  |  | 8 | 92 |
| 2 |  |  | 10 | 90 |
| 3 |  |  | 10 | 64 |

Reaction conditions: catalyst loading = 5 mol%; olefin = 5.00 mmol; *t*-butyl peroxybenzoate = 1.00 mmol; $CH_3CN$ = 1.0 mL

# Aryl-N Coupling Reactions (Buchwald-Hartwig Cross Coupling)

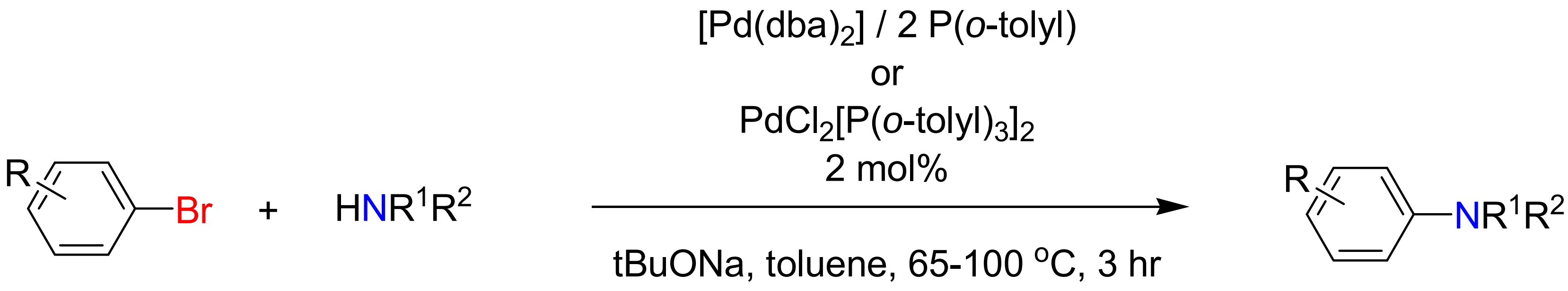


$Pd[P(o\text{-tolyl})_3]_2$
or
$PdCl_2[P(o\text{-tolyl})_3]_2$
5 mol%

$LiN(SiNMe_3)_2$, toluene, 55-100 °C, 2-24 hr

28-94 %

Louie, J.; Hartwig, J. F. *Tetrahedron Lett.* **1995**, *36*, 3609-3612.



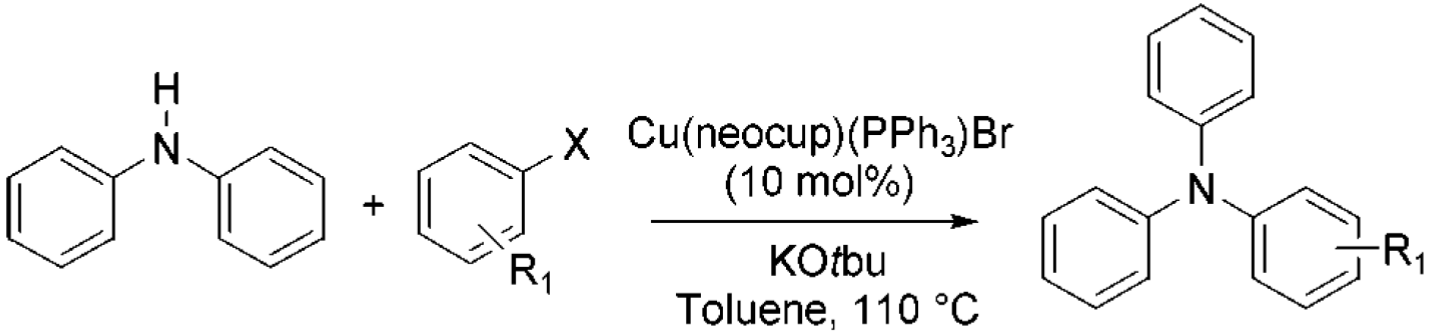
$[Pd(dba)_2]$ / 2 P(*o*-tolyl)
or
$PdCl_2[P(o\text{-tolyl})_3]_2$
2 mol%

tBuONa, toluene, 65-100 °C, 3 hr

67-89 %

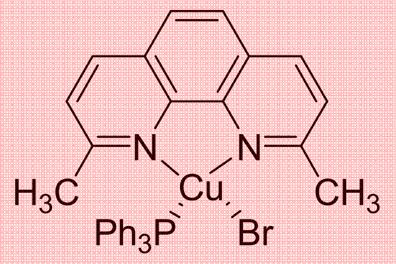
Guram, A. S.; Rennels, R. A.; Buchwald, S. L. *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1348-1350.

# $Cu(neocup)(PPh_3)Br$ Catalyzed Aryl-N Coupling Reactions



| entry | $R_1$ | X | time (h) | yield (%) |
|---|---|---|---|---|
| 1 | H | I | 6 | 78 |
| 2 | H | Br | 36 | 73 |
| 3 | H | Cl | 36 | 49[a] |
| 4 | o-$CH_3$ | I | 6 | 88 |
| 5 | p-$CH_3$ | I | 6 | 70 |
| 6 | o-$CH_3$ | Br | 36 | 50[a] |

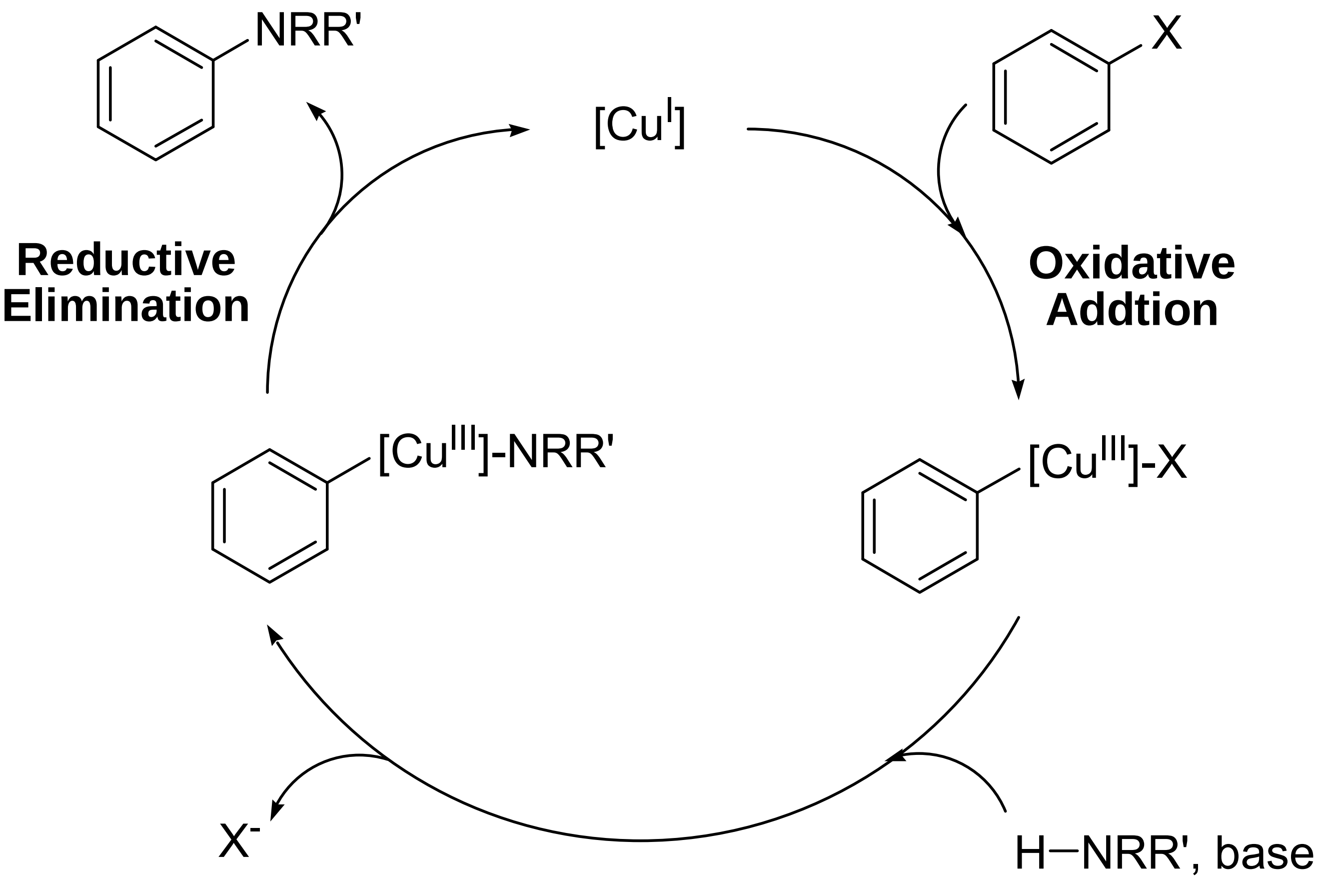
[a] GC yields.



$Cu(neocup)(PPh_3)Br$

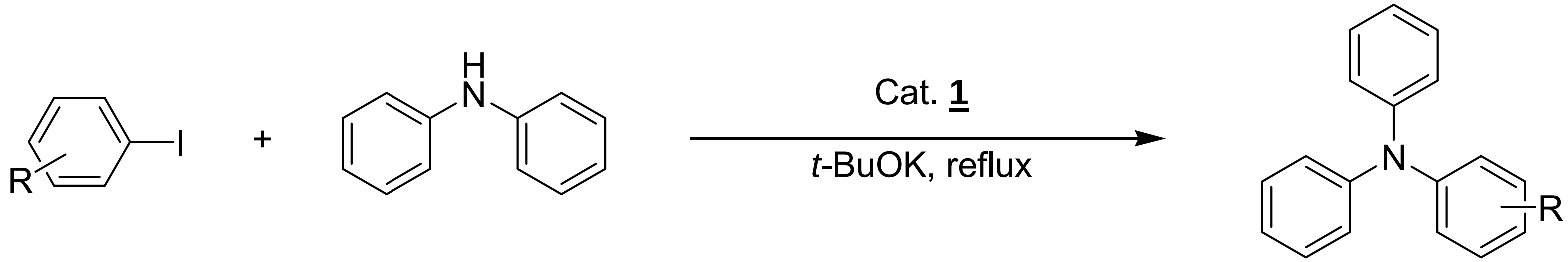
Gujadhur, R. K.; Bates, C. G.; Venkataraman, D. *Org. Lett.* **2001**, *3*, 4315-4317.

# Proposed Mechanism for Aryl-N Coupling



Gujadhur, R.; Venkataraman, D.; Kintigh, J. T. *Tetrahedron Lett.* **2001**, *42*, 4791-4793.

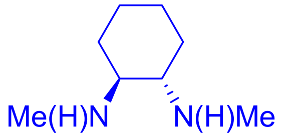
# Cu(I)-Catalyzed Aryl-N Coupling Reactions



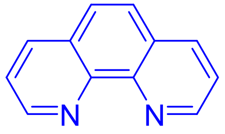
| Entry | R | sovent | Time (hr) | Conversion (%) |
|---|---|---|---|---|
| 1 | *p*-$CH_3$ | toluene | 8 | 95 |
| | | *p*-xylene | 2.5 | 92 |
| 2 | *o*-$CH_3$ | toluene | 10 | 87 |
| 3 | *p*-$OCH_3$ | toluene | 8 | 91 |
| | | *p*-xylene | 3 | 91 |
| 4 | *m*-$OCH_3$ | toluene | 8 | 99 |

Reaction conditions: catalyst loading = 10 mol%; aryl iodide = 1.00 mmol; diphenylamine = 1.10 mmol; *t*-BuOK = 2.00 mmol; solvent = 1.5 mL

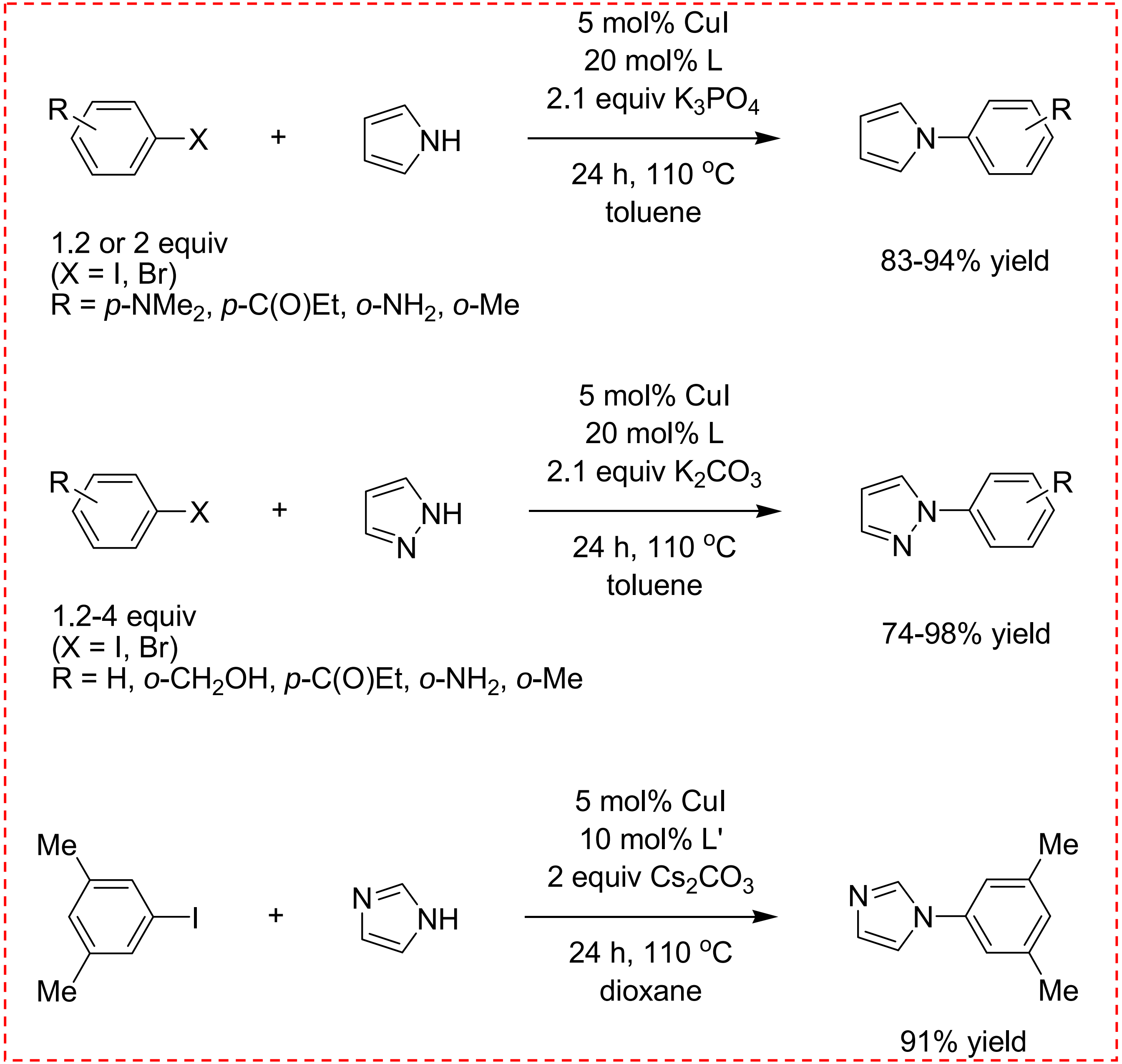
# Copper-Catalyzed *N*-Arylation of Nitrogen Heterocycles



**L**



**L'**



5 mol% CuI
20 mol% L
2.1 equiv $K_3PO_4$

24 h, 110 °C
toluene

1.2 or 2 equiv
(X = I, Br)
R = *p*-$NMe_2$, *p*-C(O)Et, *o*-$NH_2$, *o*-Me

83-94% yield

5 mol% CuI
20 mol% L
2.1 equiv $K_2CO_3$

24 h, 110 °C
toluene

1.2-4 equiv
(X = I, Br)
R = H, *o*-$CH_2OH$, *p*-C(O)Et, *o*-$NH_2$, *o*-Me

74-98% yield

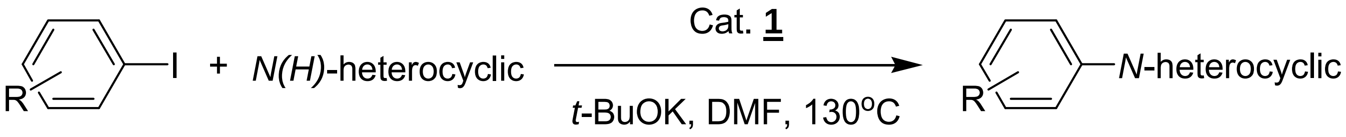
5 mol% CuI
10 mol% L'
2 equiv $Cs_2CO_3$

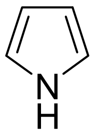
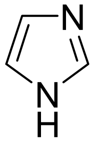
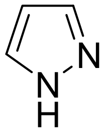
24 h, 110 °C
dioxane

91% yield

Antilla, J. C.; Baskin, J. M.; Barder, T. E.; Buchwald. S. L. *J. Org. Chem.* **2004**, *69*, 5578-5587.

# Cu(I)-Catalyzed Aryl-N Coupling Reactions



| Entry | R | *N*(*H*)-heterocyclic | Time (hr) | Conversion (%) |
|---|---|---|---|---|
| 1 | *p*-$CH_3$ |  | 1.5 | 93 |
| 2 | *o*-$CH_3$ |  | 2.0 | 91 |
| 3 | *p*-$OCH_3$ |  | 2.0 | 92 |
| 4 | *m*-$OCH_3$ |  | 1.0 | 90 |
| 5 | *p*-$CH_3$ |  | 2.5 | 87 |
| 6 | *o*-$CH_3$ |  | 2.0 | 62 |
| 7 | *p*-$OCH_3$ |  | 2.5 | 84 |
| 8 | *m*-$OCH_3$ |  | 1.5 | 92 |
| 9 | *p*-$CH_3$ |  | 1.5 | 90 |
| 10 | *o*-$CH_3$ |  | 2.0 | 91 |
| 11 | *p*-$OCH_3$ |  | 2.5 | 92 |
| 12 | *m*-$OCH_3$ |  | 1.0 | 92 |

Reaction conditions: catalyst loading = 10 mol%; aryl iodide = 1.00 mmol; amine = 1.10 mmol; *t*-BuOK = 1.50 mmol; DMF = 1.5 mL

# Conclusions

1. *Complex* ***<u>1</u>*** *was characterized by* $^{1}$*H- and* $^{13}$*C-NMR, FAB-MS, EA.*

2. *Complex* ***<u>2</u>*** *was characterized by* $^{1}$*H- and* $^{13}$*C-NMR, FAB-MS, EA as well as X-ray crystallography.*

3. *We have successfully demonstrated the catalytic activity of the Cu(I) complex* ***<u>1</u>*** *for Sonogashira、C–N coupling、Allylic Oxidations of olefins and C–S coupling reactions.*

4. *The saccharide-incorporated NHC ligand makes the target copper complex catalyst* ***<u>2</u>*** *highly soluble in polar solvents. The same C–S coupling reactions in a greener medium of mixed water/(hmim)HBr can be performed with a loading of 10 mol% of [CuI(magi)] (****<u>2</u>****) under either thermal or microwave irradiation conditions.*

5. *The successful use of microwave irradiation for C–S coupling to further accelerate reaction rates and increase conversions.*