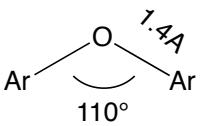
Cu-Catalyzed Synthesis of Diaryl Thioethers and S-Cycles by reaction of Aryl Iodides with Carbon Disulfide in the Presence of DBU.

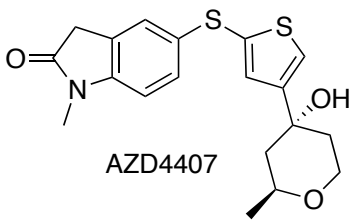
Peng Zhao, Hang Yin, Hongxin, Gao, Chanjuan Xi.; *J. Org. Chem.* Article ASAP
DOI: 10.1021/jo400709s

James Johnson
Current Literature
5/11/2013

Diarylthioethers

- Diarylthioethers have shown activity against cancer, HIV, Alzheimer's disease, inflammation, and asthma.
- Electronegativity and Bonding
  - Oxygen 3.44





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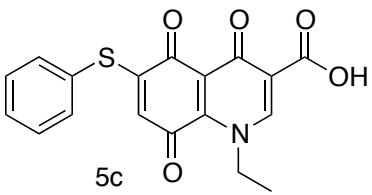
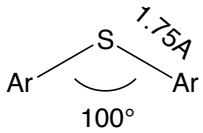


5c

  Sulfur 2.58



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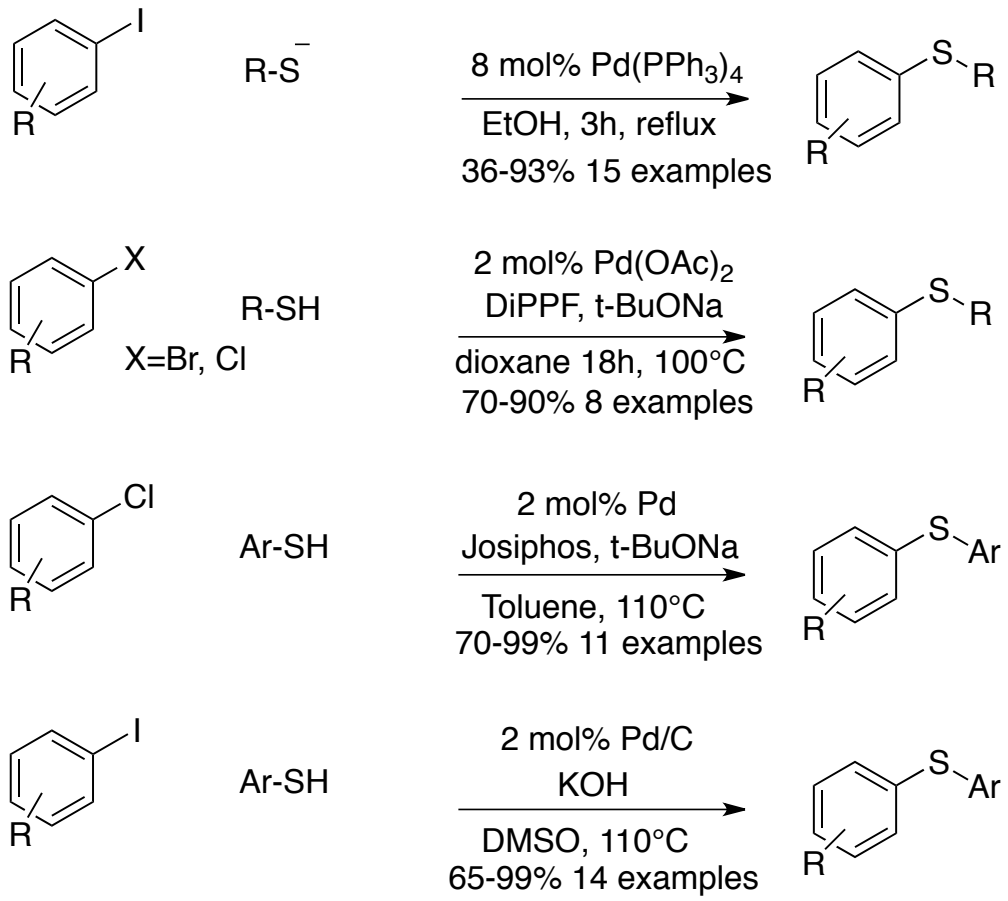
Molecules **2011**, *16*, 590-608
Top Organomet Chem (2010) 31: 39–64
Tetrahedron **1984**, *40*, 1433.

Palladium Catalyzed S-Arylation



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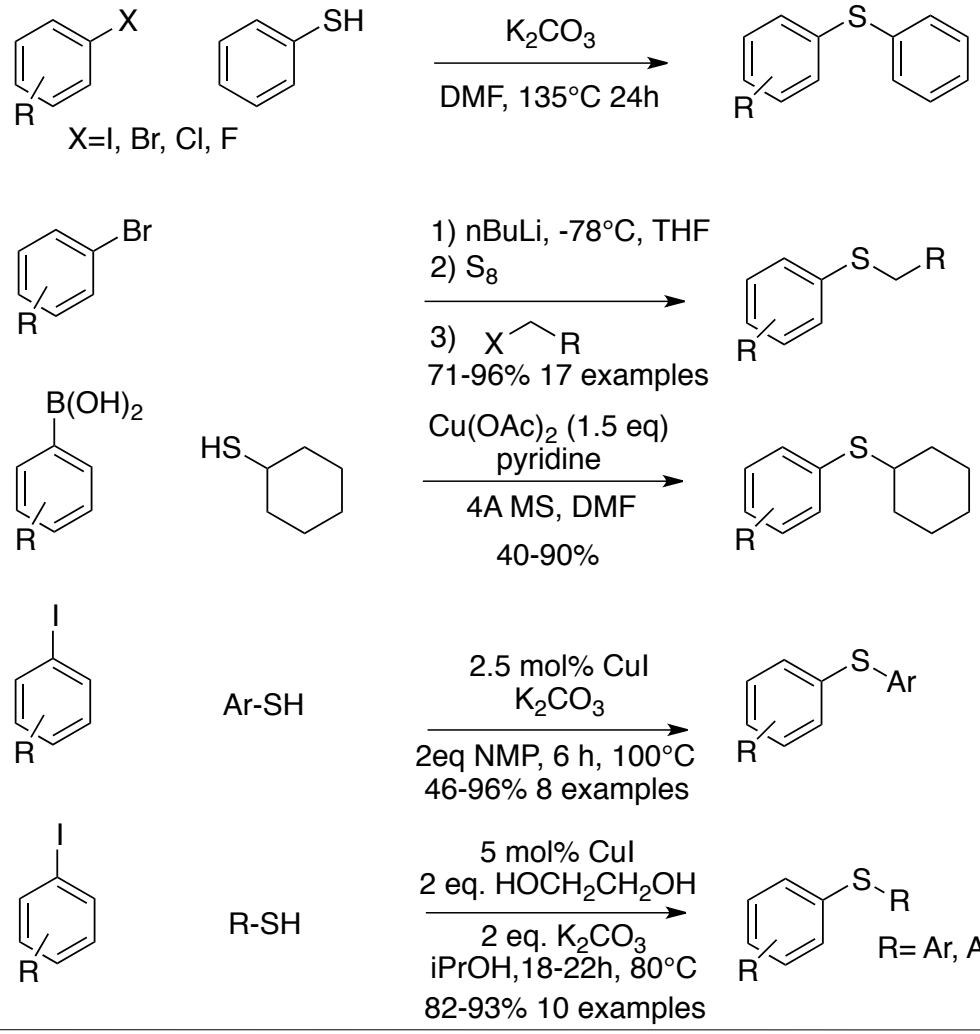
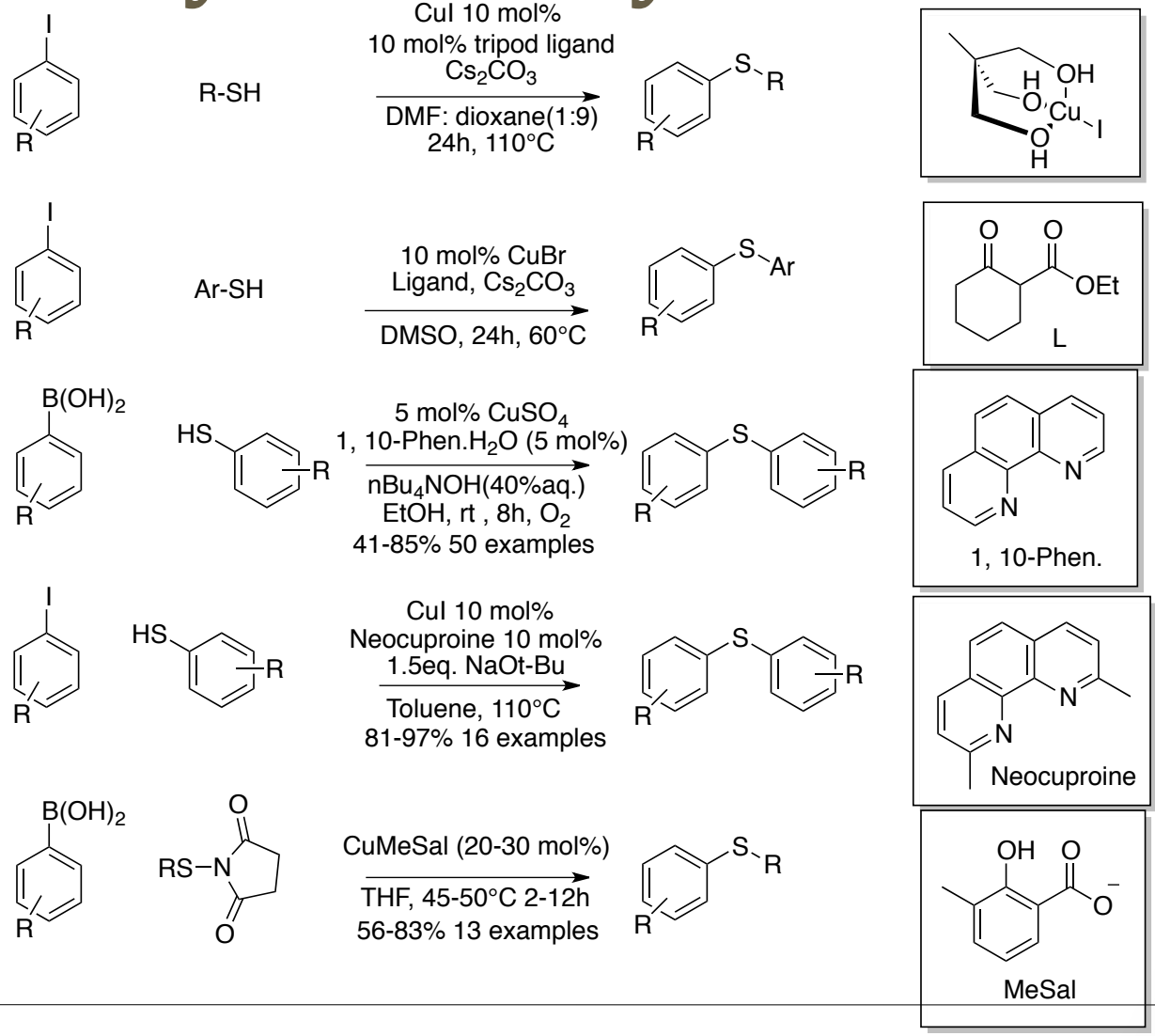
JOC. 2004, 69, 3236-3239
Chem. Eur. J. 2006, 12, 7782 – 7796
Adv. Synth. Catal. 2009, 351, 2558 – 2562

Cu Catalyzed S-Arylation



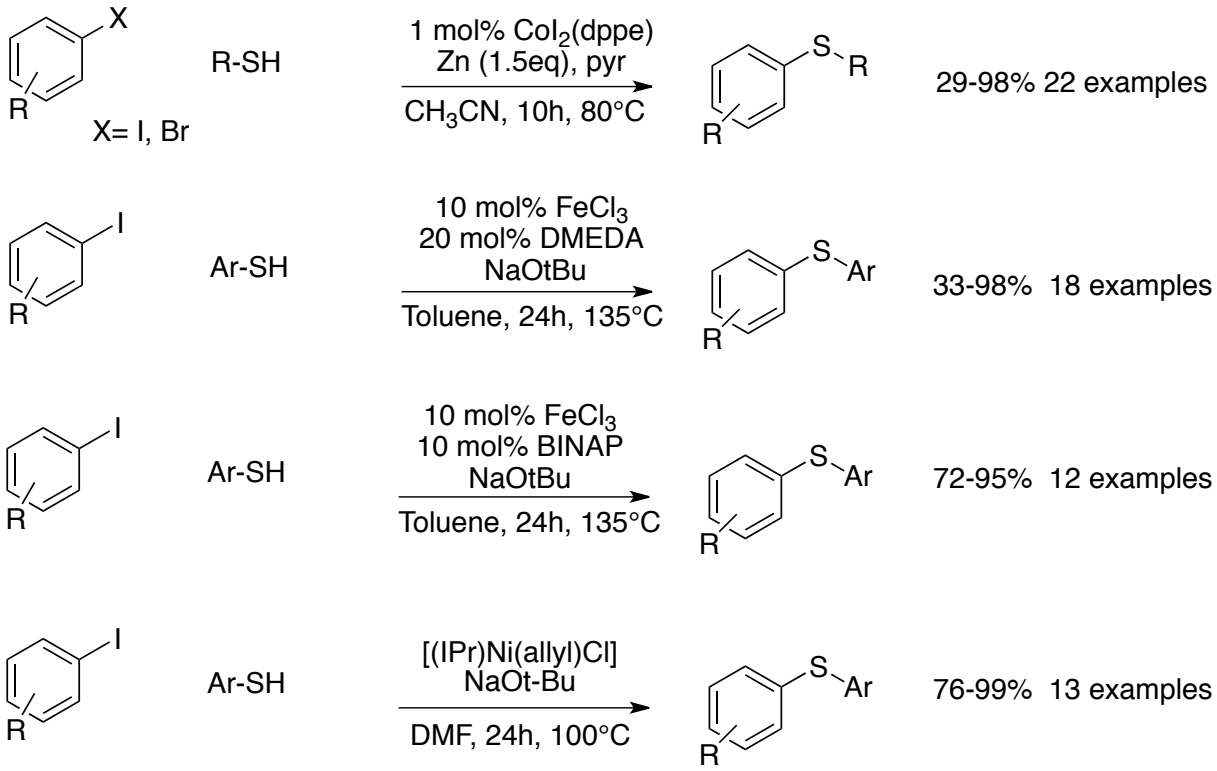
Tet Lett 39 (1998) 6283-6286
J. Org. Chem. 2004, 69, 3236-3239
J. Org. Chem. 2012, 77, 2878−2884
J. Org. Chem. **2008**, *73*, 5625–5628

Cu Catalyzed S-Arylation



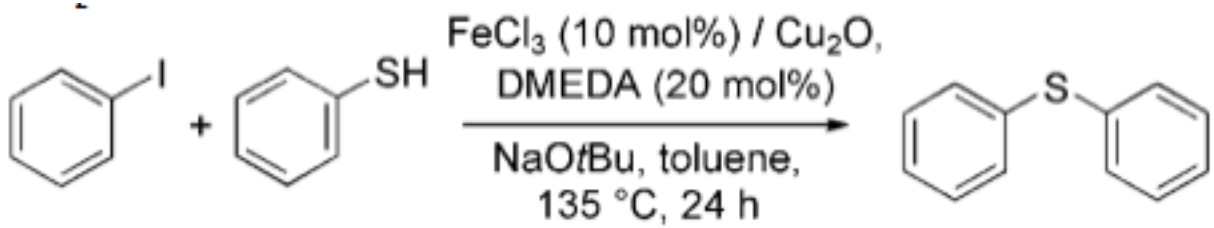
Org. Lett., 2002, 4,. 20, 3517
Org. Lett., 2002l. 4,. 16, 2803-2806

Other Metal Catalyzed S-arylation



Org. Lett., Vol. 8, No. 24, **2006**
Chem. Commun., 2009, 4450–4452
Angew. Chem. Int. Ed. 2008, 47, 2880 –2883
Org. Lett. **2007,** *9*, 3495-3498

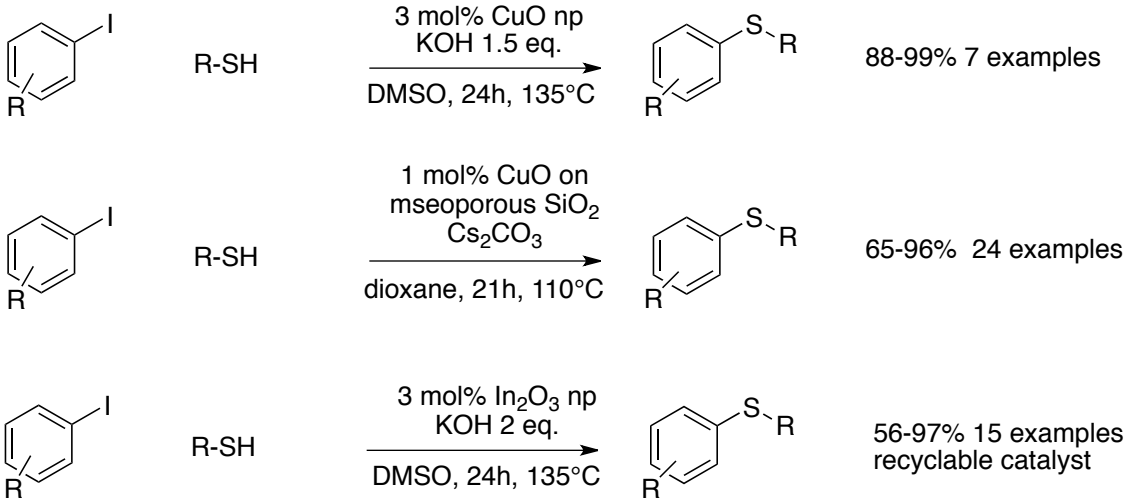
Is it Fe or Cu?



$FeCl_3/Cu_2O$	Yield [%] (GC)
>98% (Merck)	91 (ref. [3f])
>98% (Aldrich)	4
>99.99 (Aldrich)	2
>99.99% + 10 ppm Cu_2O	42
>99.99% + 100 ppm Cu_2O	99
>99.99% + 1000 ppm Cu_2O	93

Angew. Chem. Int. Ed. **2009,** *48*, 5586-5587.

Nanoparticles



Angew. Chem., Int. Ed. 2007, 46, 5583.
Chem. Commun. 2010, 46, 282.
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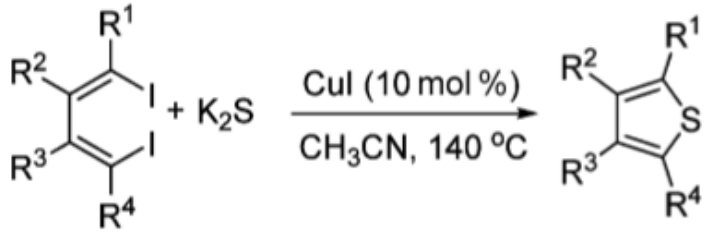
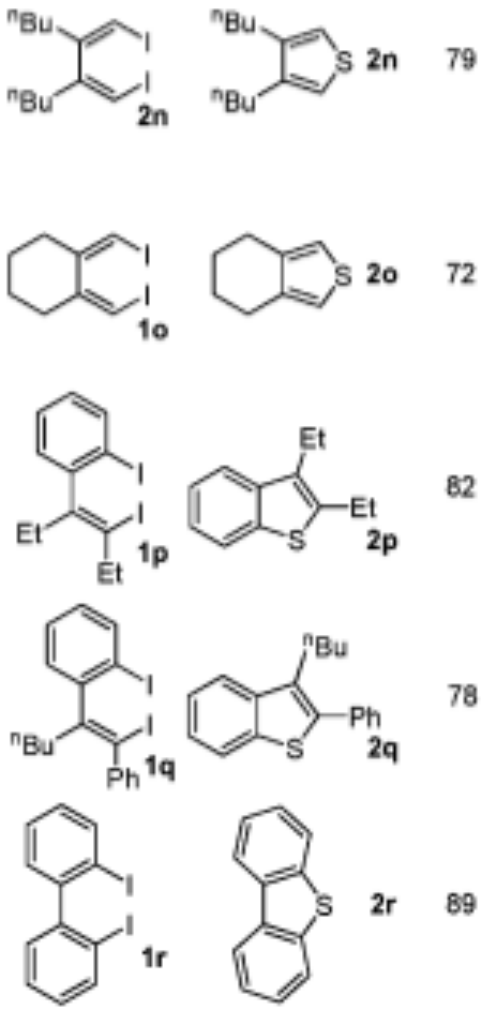
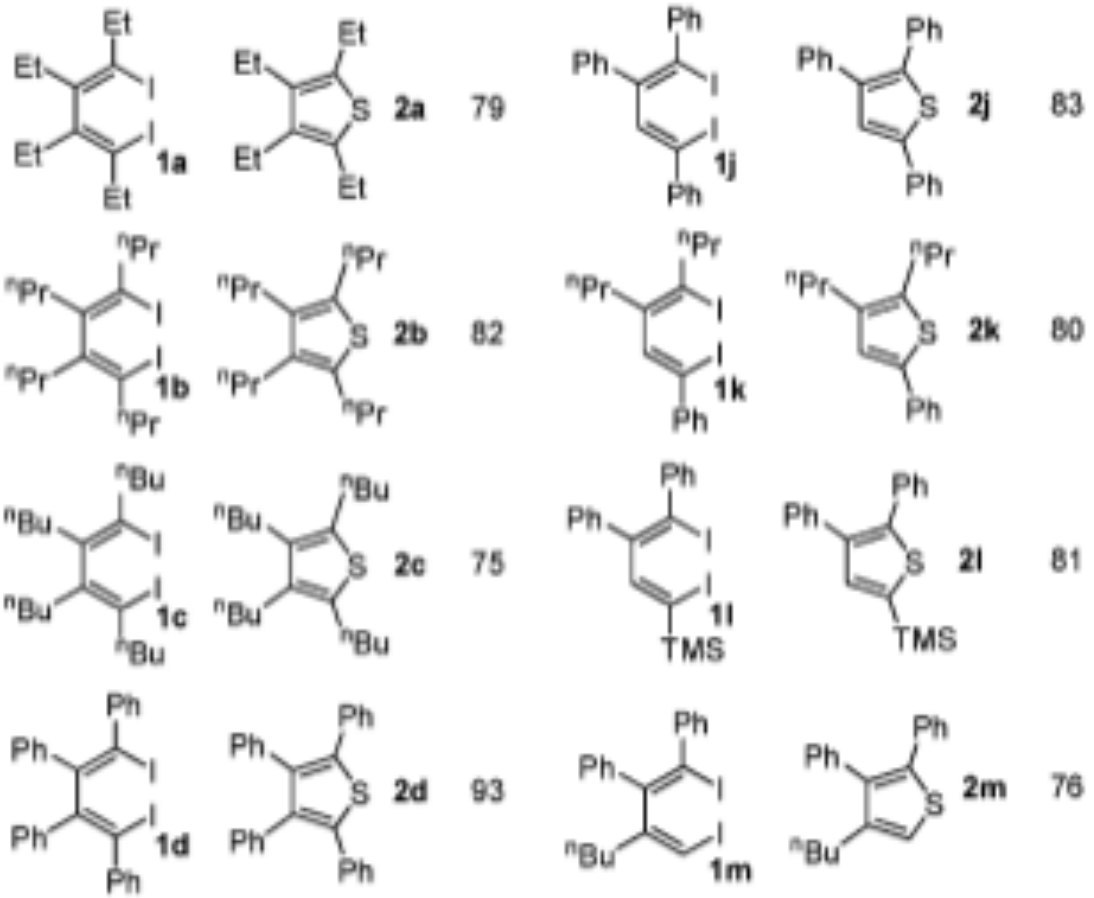
Previous work

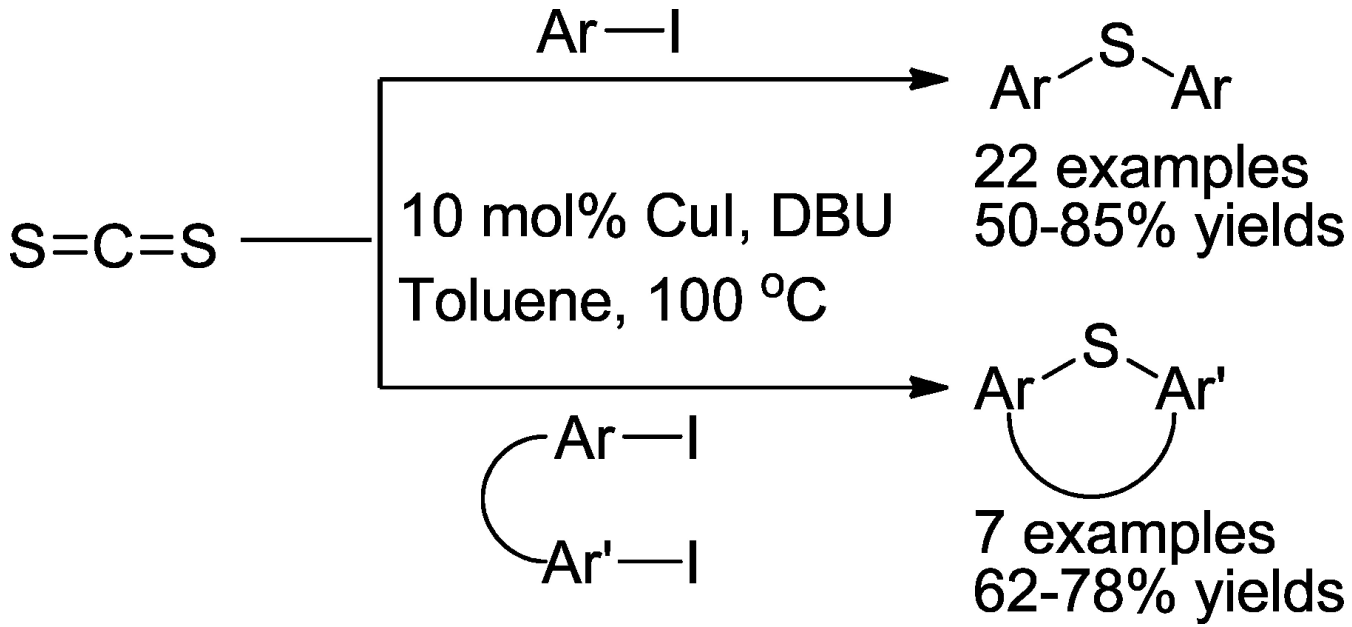






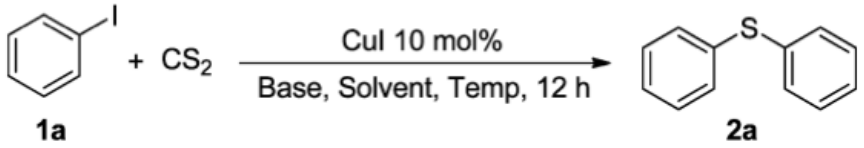
Org. Lett., 2010, 12, 17, **3930**

Title Paper



DOI: 10.1021/jo400709s

Optimization

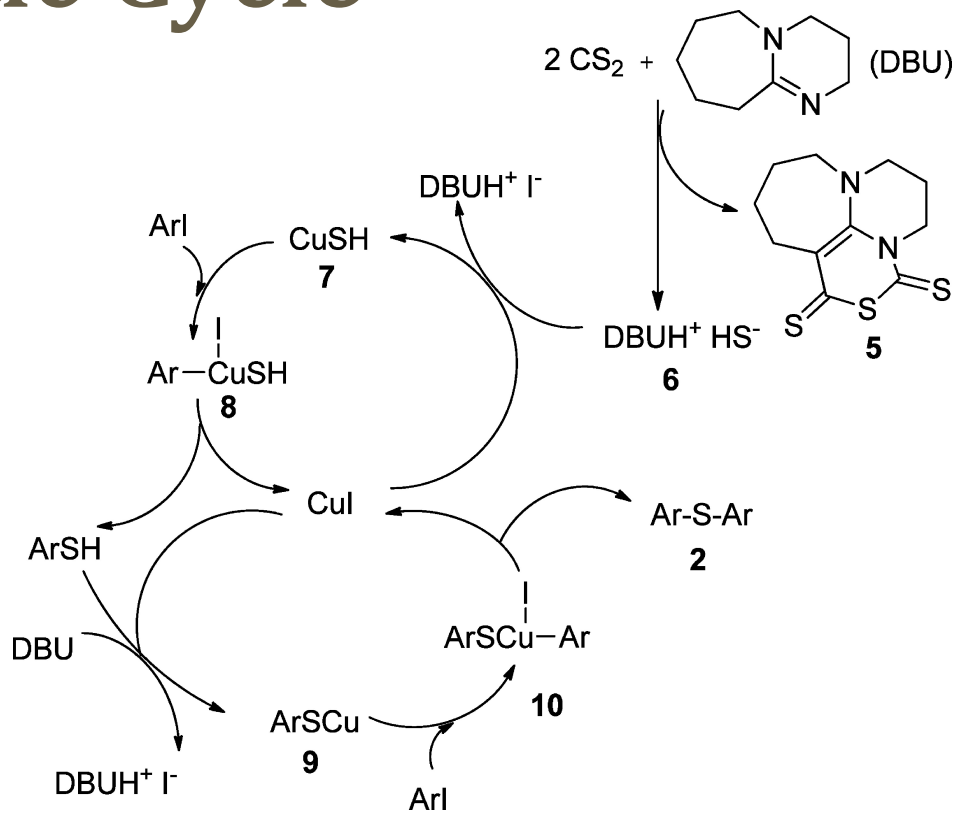


1a **2a**

entry	base	solvent	temp (°C)	yield (%)[b]
1	Cs_2CO_3	toluene	100	NR
2	K_3PO_4	toluene	100	NR
3	KOH	toluene	100	NR
4	^tBuONa	toluene	100	NR
5	Et_3N	toluene	100	NR
6	DABCO	toluene	100	NR
7	DBU	toluene	100	91 (85)
8	DBU	dioxane	100	89 (81)
9	DBU	THF	100	16
10	DBU	CH_3CN	100	68
11	DBU	DMF	100	3
12	DBU	toluene	80	21
13	DBU	toluene	100	NR[c]
14	DBU	toluene	100	65[d]
15	DBU	toluene	100	49[e]
16	DBU	toluene	100	27[f]
17	DBU	toluene	100	61[g]

DOI: 10.1021/jo400709s

Catalytic Cycle



J. Acta Crystallogr. 1986, C42, 487.
Published in: Peng Zhao; Hang Yin; Hongxin Gao; Chanjuan Xi; *J. Org. Chem.* Article ASAP
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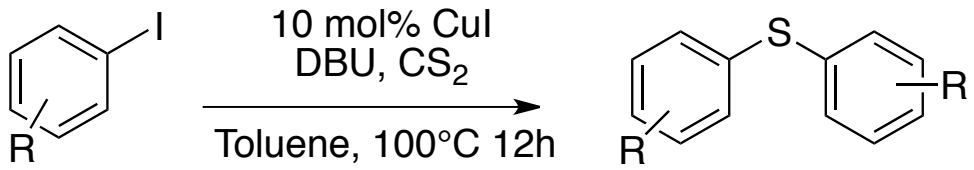
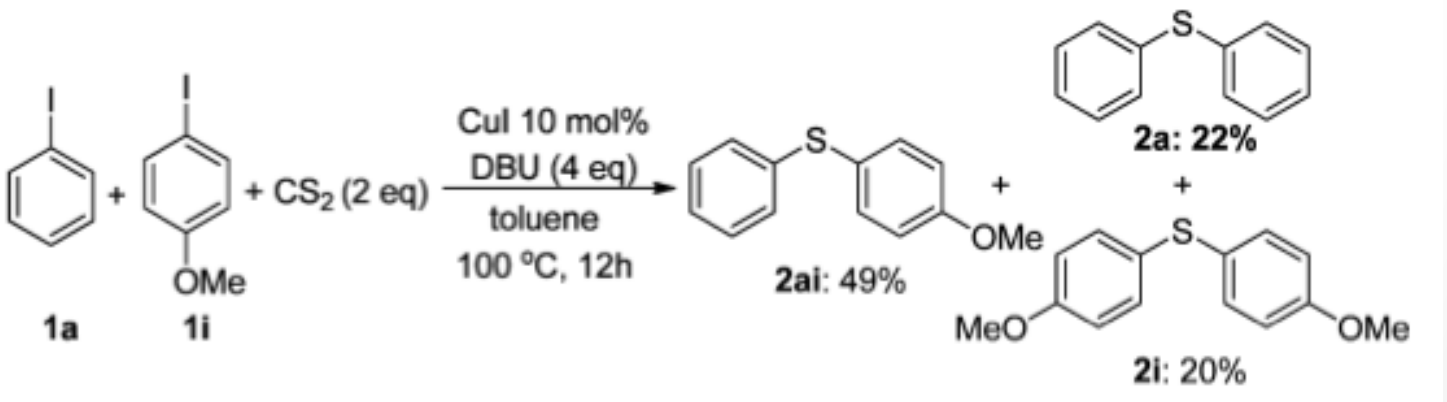
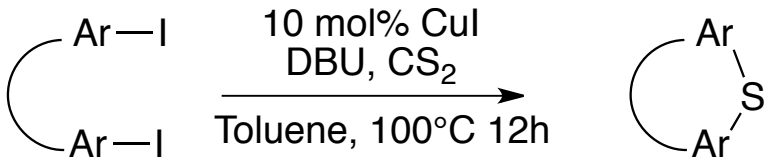
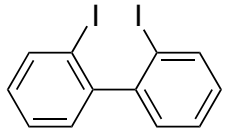


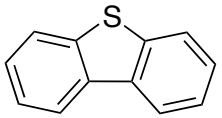
R	Yield	R	Yield	R	Yield	R	Yield
H	85%	2-NMe_2	78%	2-OMe	83%	4-Ph	56%
4-OMe	80%	2-OH	81%	2-Me	75%	2,4-Me	70%
3-Me	65%	4-Me	68%	2-Br	65%	2,5-Me	68%
4-Br	74%	3-CO_2Me	65%	4-CO_2Me	65%	2,4,6-Me	50%
4-Cl	70%	4-CF_3	78%	1-Nap	84%	4-Pyr	75%
2-Pyr	66%	2-Thiophene	70%				



Intramolecular C-S-C formation







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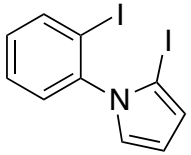

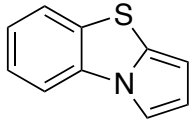

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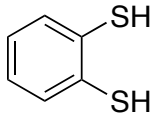

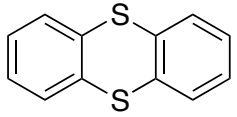

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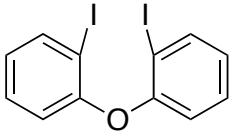

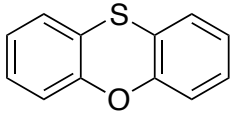

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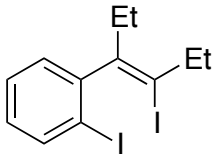

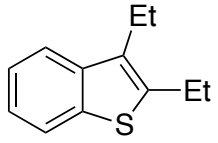

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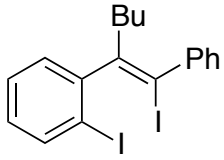

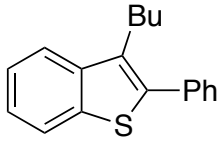

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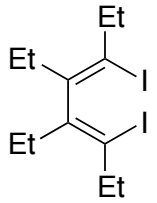
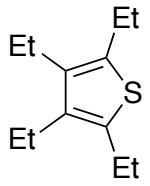




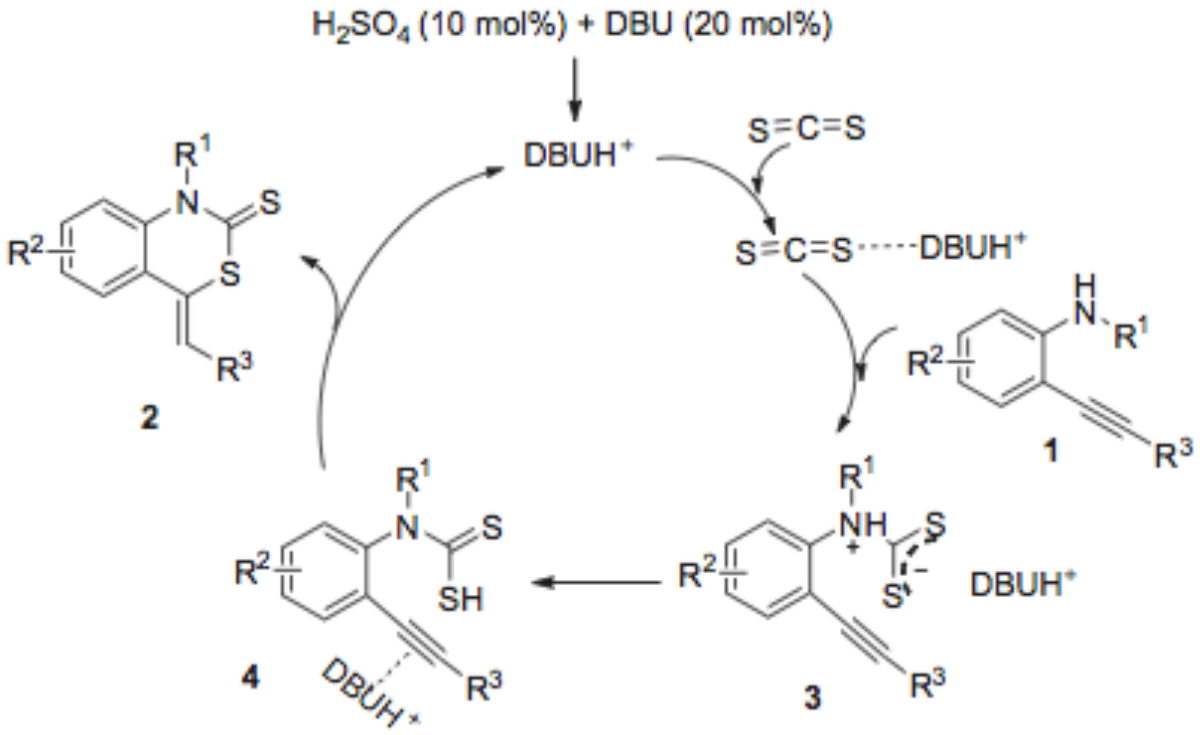
78%

Conclusions

- Intramolecular coupling of two aryl iodides to form a diaryl thioether.
- Functional group tolerant.
- CuI \$.23/g, $Pd(OAc)_2$ \$94/g, $FeCl_3$ \$.26/g
- Homocoupling application
- CS_2 inexpensive and easy to use

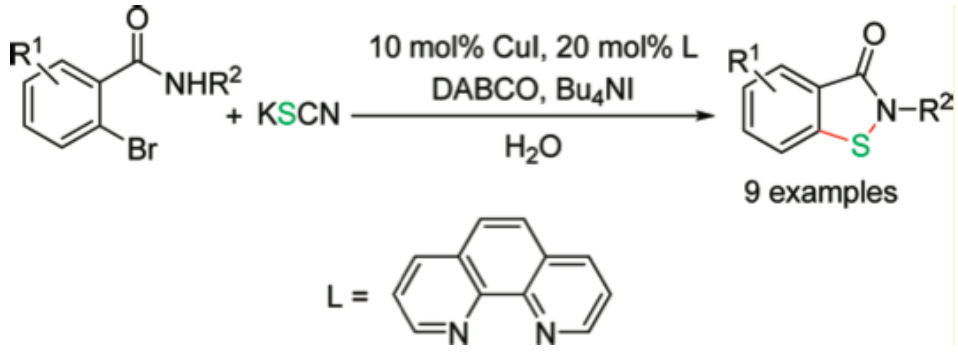
Alfa Aesear
Top Organomet Chem (2010) 31: 39–64
Tetrahedron **1984**, *40*, 1433.

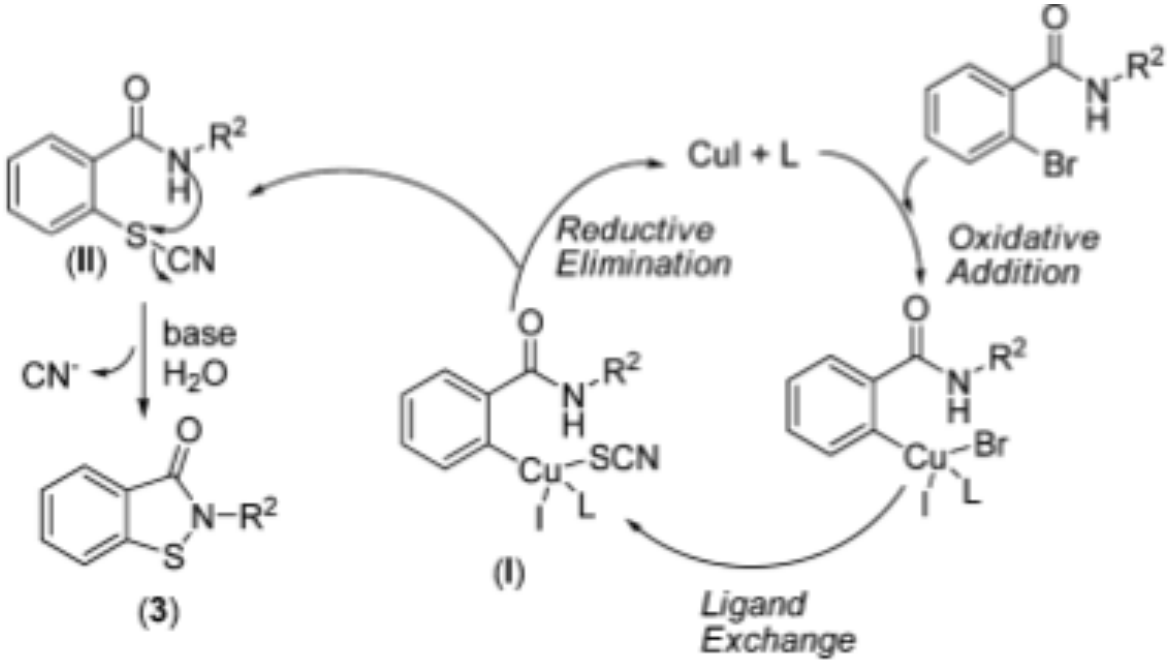
Previous work:



JOC. 2012, 77, 4148−4151
Org. Lett., 2010, 12, 17, **3930**
Tet Lett 54 (2013) 2357–2361

Previous work:





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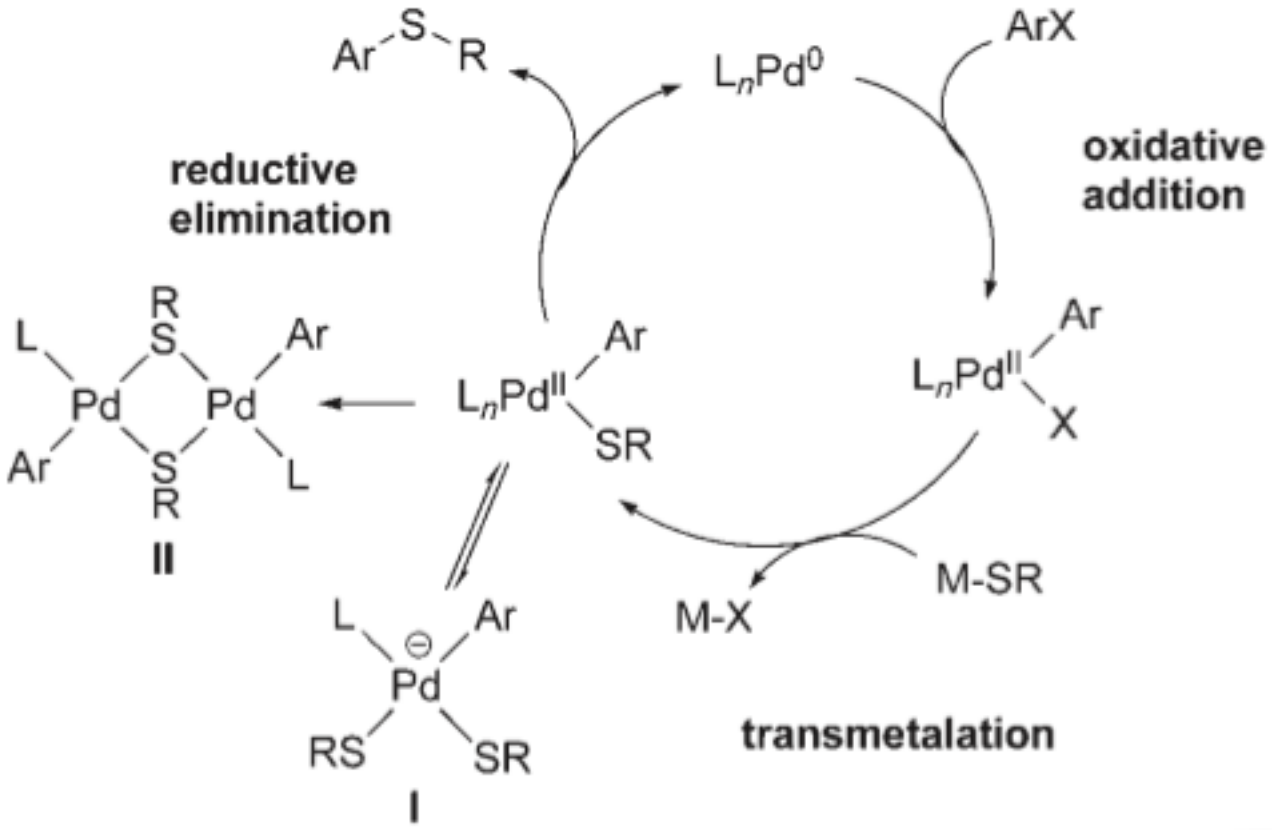
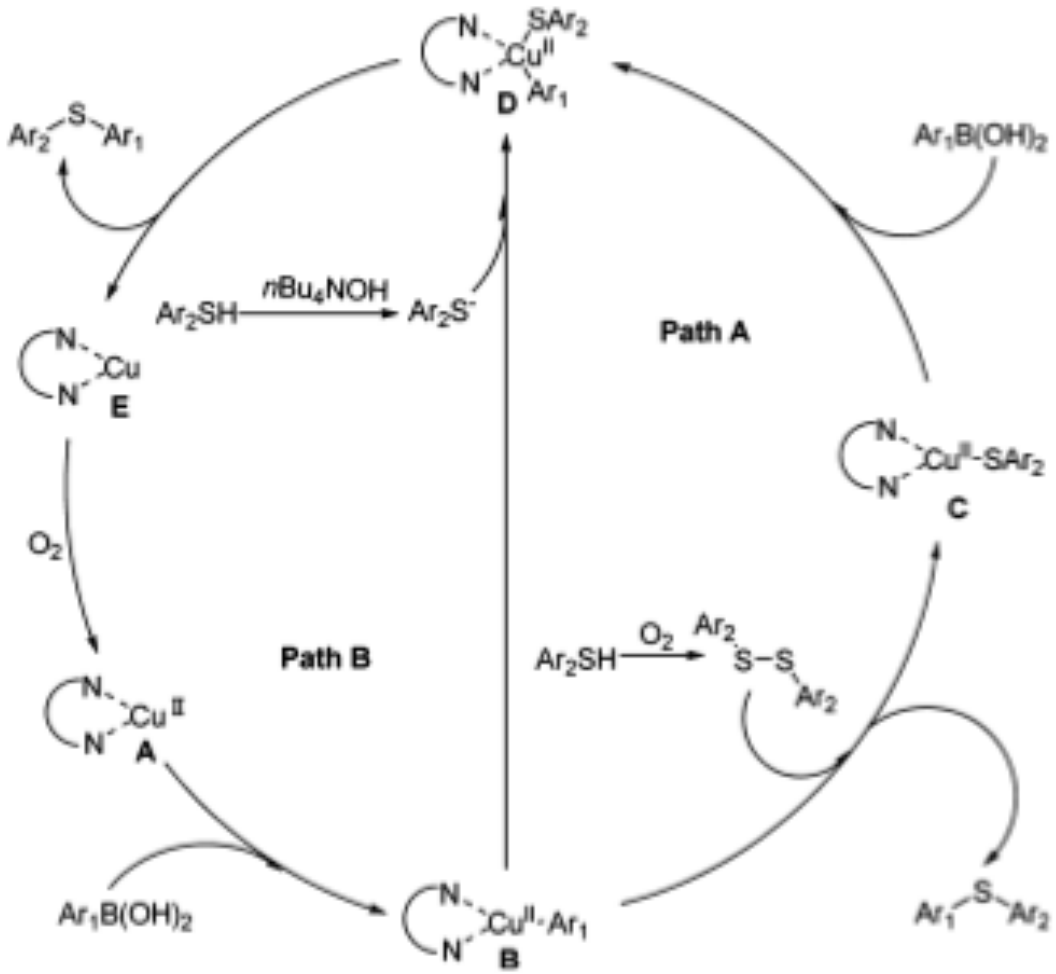
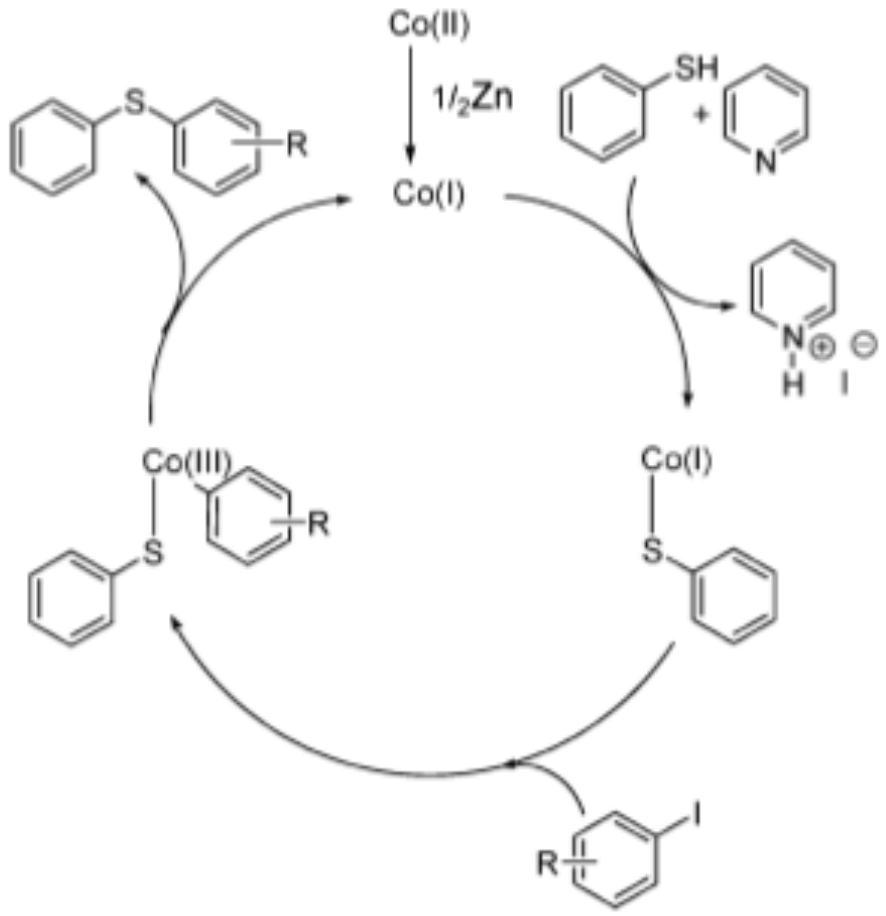
Palladium catalytic cycle

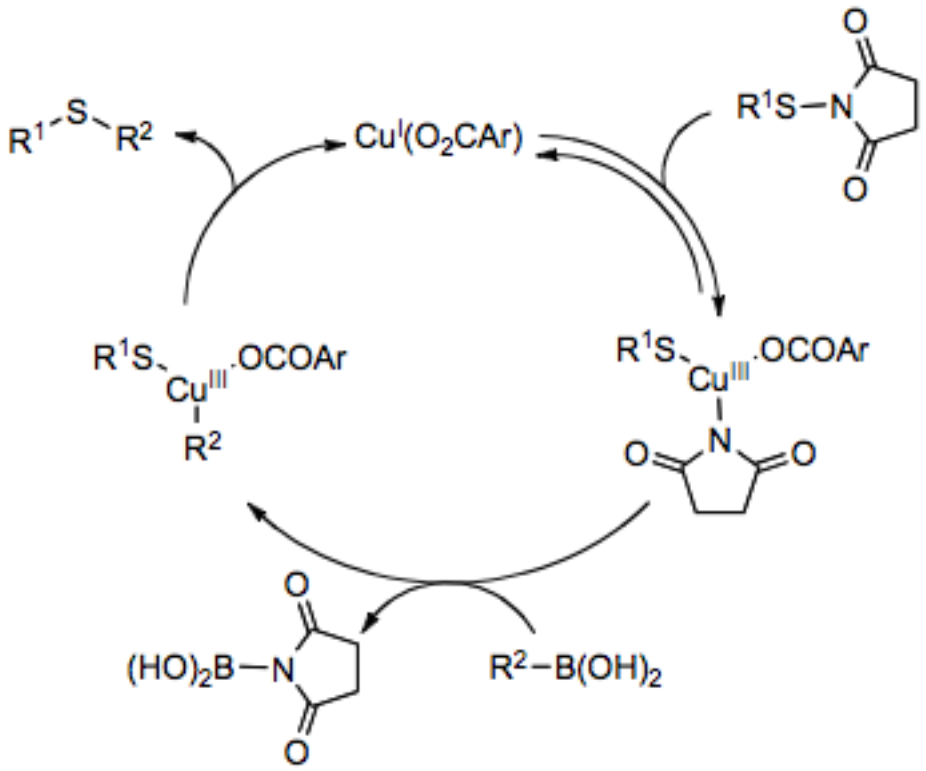


Chan Lam Catalytic cycle



Cobalt Catalyzed





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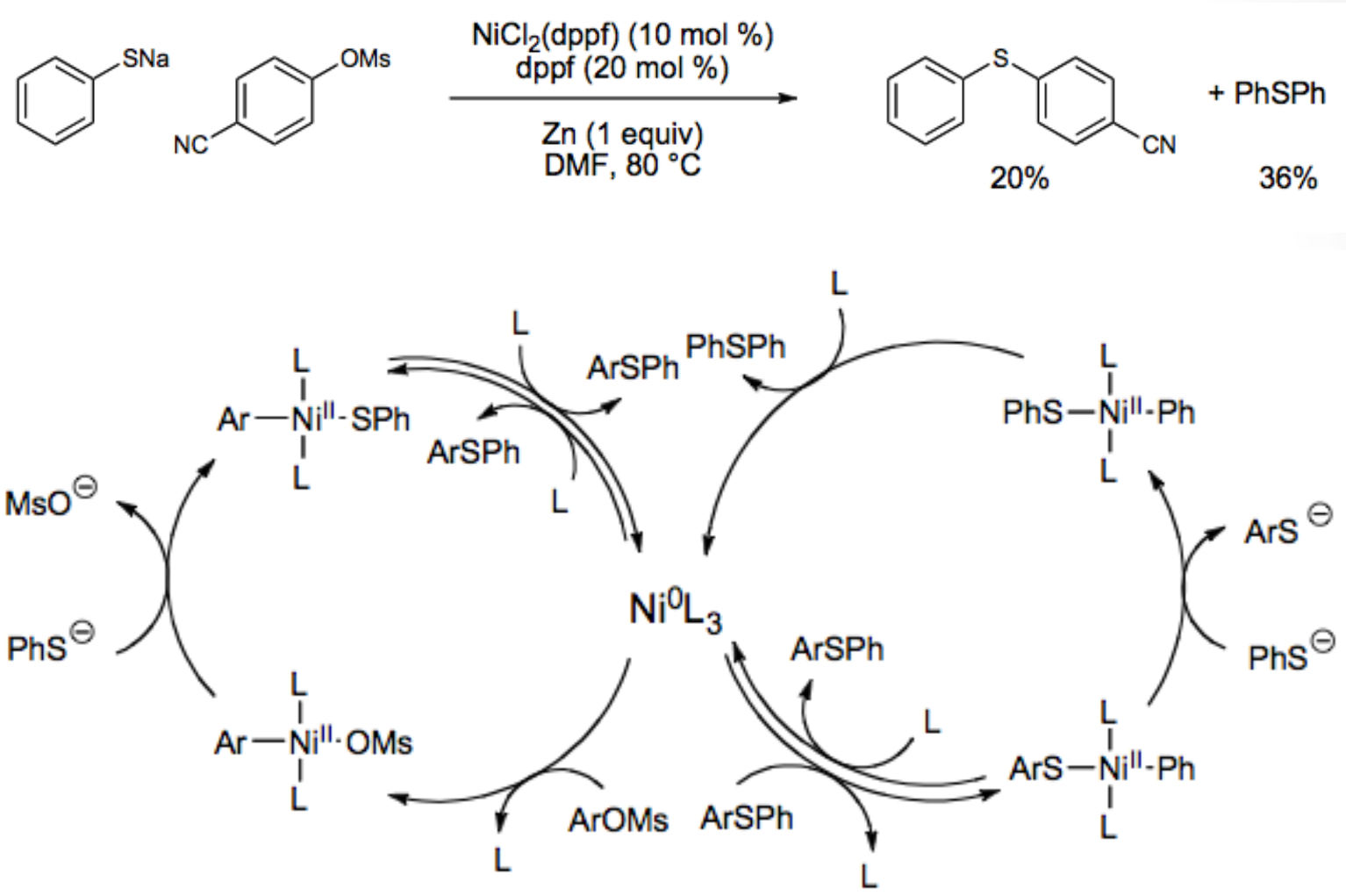

J. Med. Chem. **2005,** *48*, 2892-2905