Rhodium(III)-Catalyzed Azidation and Nitration of Arenes by C-H Activation

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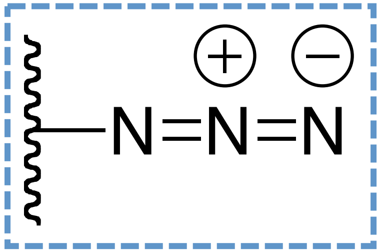
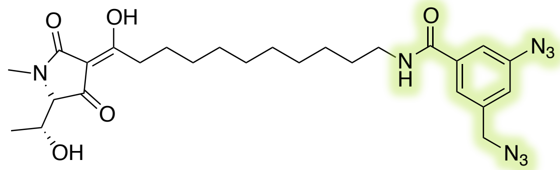
Angew. Chem. Int. Ed., **2013**, *52*, 11862 –11866

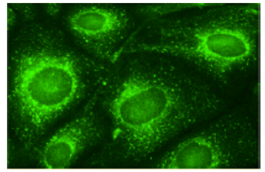
Eakkaphon Rattanangkool
Wipf Group-Current Literature

Azide compounds : Utilization



✧ Labeled target molecule[1]

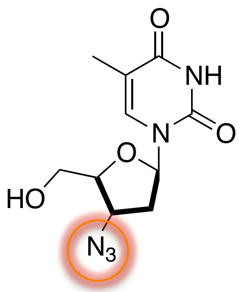


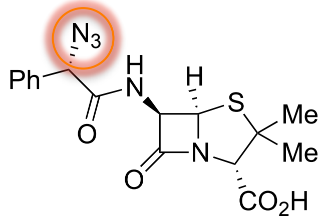


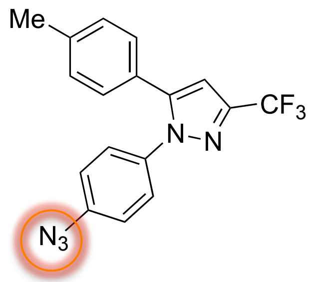
PTK2 cell

✧ Used as intermediates and building blocks[2]

✧ Anti HIV drug (Azidothymidine, Retrovir®)
✧ Antibiotic drug (Azidocillin, Longatren®)
✧ COX-2 inhibitor (derivartive of Celecoxib)



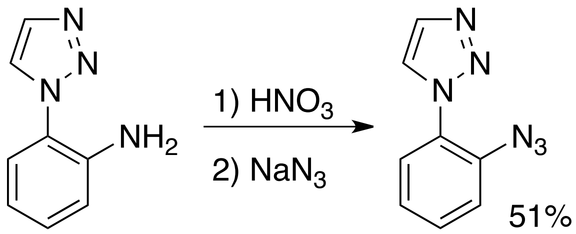




[1]Kempf, K. et. al., *J. Org. Chem.* **2013***, 78,* 2455.
[2](a)Brase, S.; Banert, K. *Organic Azides: Syntheses and Applications;* Wiley: Chichester, U.K., 2009. (b) Scriven, E. F. V. *Azides and Nitrenes: Reactivity and Utility*; Academic Press: Orlando, FL, 1984. (c) Brase, S.; Gil, C.; Knepper, K.; Zimmermann, V. *Angew. Chem.Int. Ed.,* **2005**, *44*, 5188.

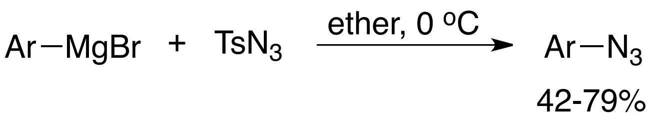
Synthesis of azide groups: Classical methods

1.) Sandmeyer reaction



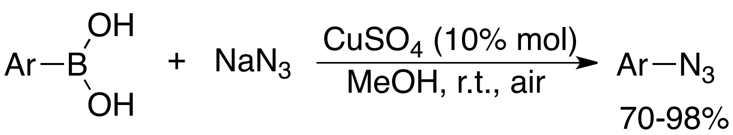
Kauer, J.C. and Caboni, R.A., *J. Am. Chem. Soc***. 1967**, *89*, 2633.

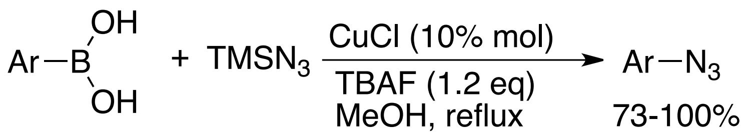
2.) Coupling of organometalic reagents



Smith, P.A.S. et. al., *J. Org. Chem.* ***1968****, 34, 3430.*

3.) Copper-catalyzed coupling



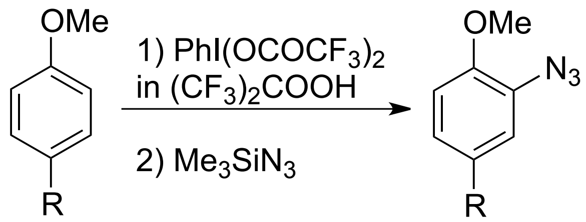


Tao, C.Z. et. al., *Tetrahedron Lett.* **2007***, 48,* 3525.

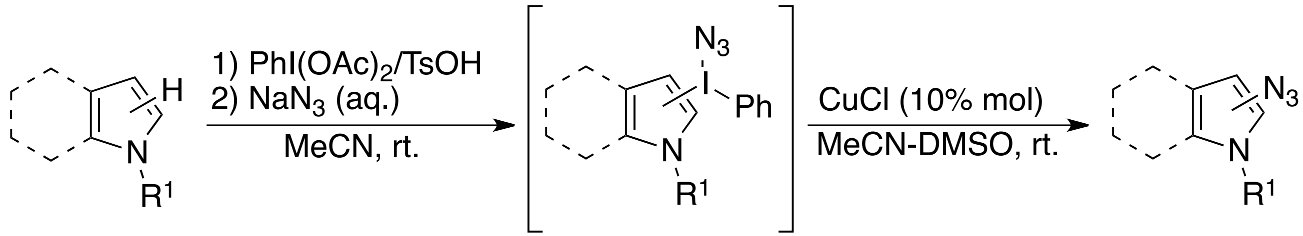
Li, Y. et. al., *Chem. Eur. J.* **2010***, 16,* 7969.

Synthesis of azide groups: Classical methods

4.) Hypervalent iodine(III) reagents



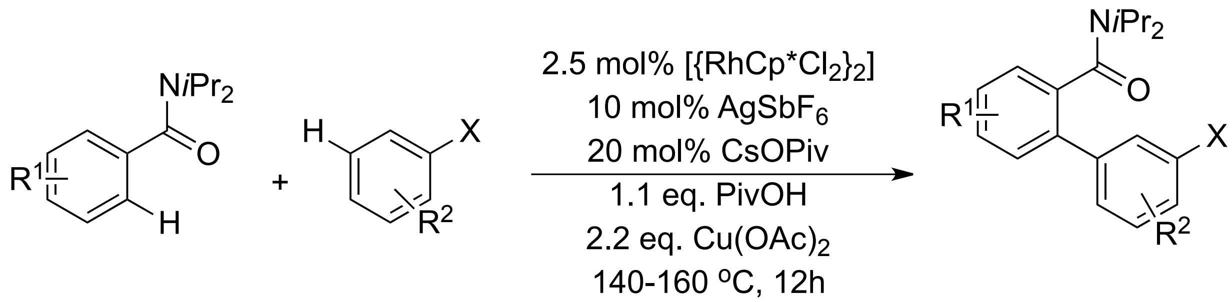
Kita, Y. et. al., *Tetrahedron Lett*. **1991**, *32*, 4321.



Lubriks, D. et. al., *J. Am. Chem. Soc*. **2012**, *134*, 15436.

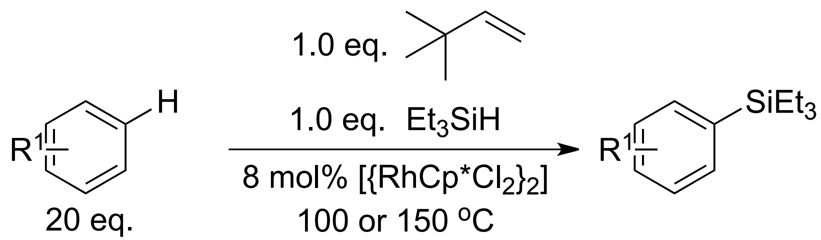
Rhodium(III)-catalyzed C-H activation

1.) Arylation of benzamides with bromoarenes



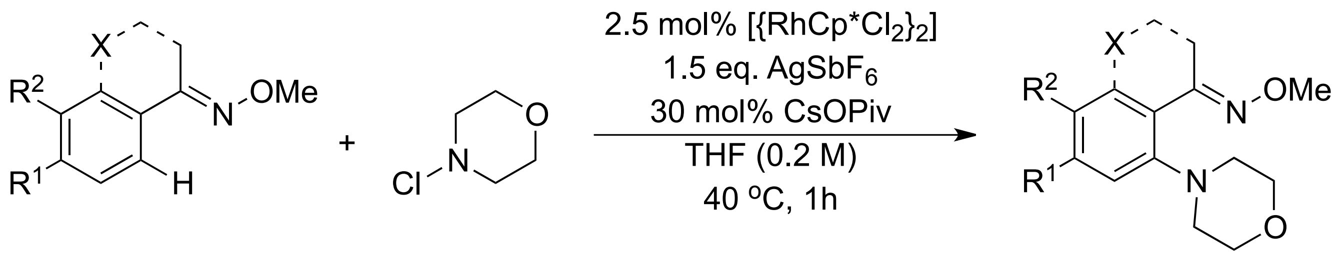
Delord, J.W. et. al., *Angew. Chem. Int. Ed.* **2012**, *51*, 2247.

2.) Silylation of arenes with triethylsilane



Ezbiansky, K. et. al., *Organometallics* **1998**, *17*, 1455.

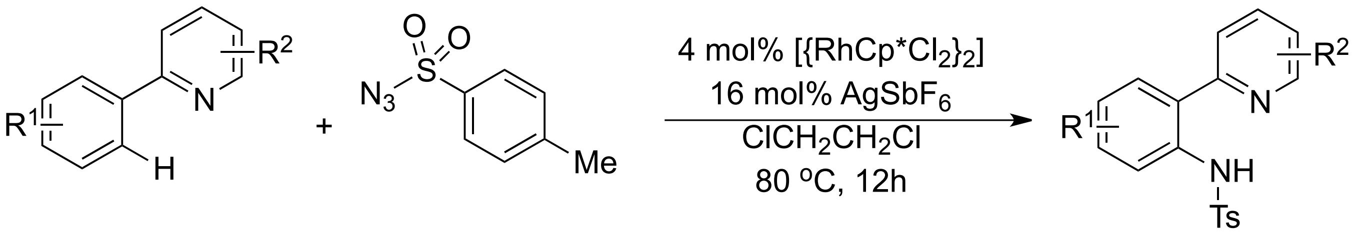
3.) Amination of aromatic C-H bonds with *N*-chloroamines



Ng, K.H.. et. al., *Org. Lett.* , **2012**, *14*, 272.

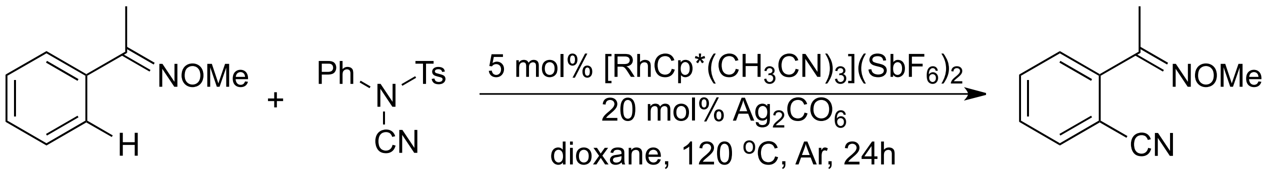
Rhodium(III)-catalyzed C-H activation

4.) Amidation of arenes with sulfonyl azides



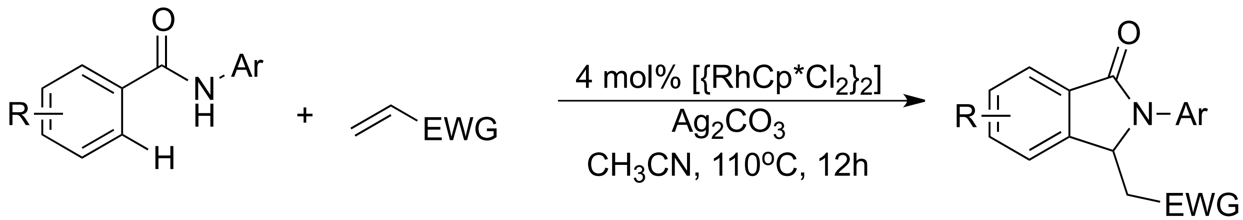
Kim, J.Y. et. al., *J. Am. Chem. Soc*. **2012**, *134*, 9110.

5.) Cyanation of arenes with *N*-cyano-*N*-phenyl-*p*-toluenesulfonamide



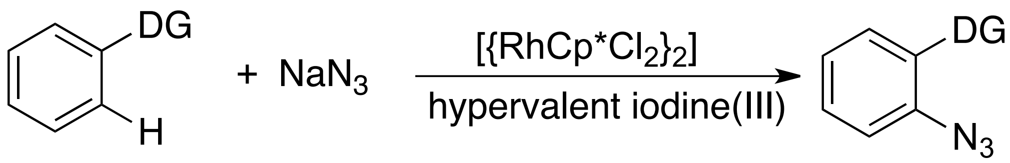
Gong, T.J. et. al., *J. Am. Chem. Soc*. **2012**, *135*, 10630.

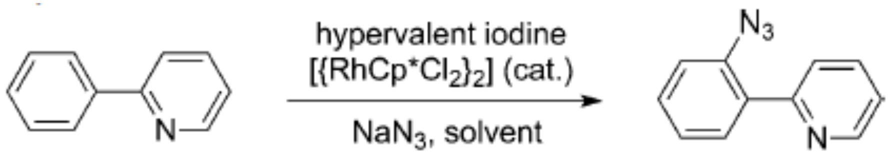
6.) Olefination-Michael reaction



Wang, F.. et. al., *Org. Lett.* , **2010**, *12*, 5430.

Aim and Optimization for azidation

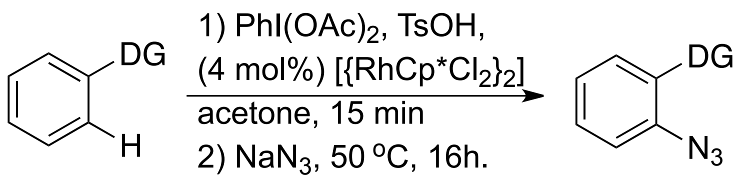


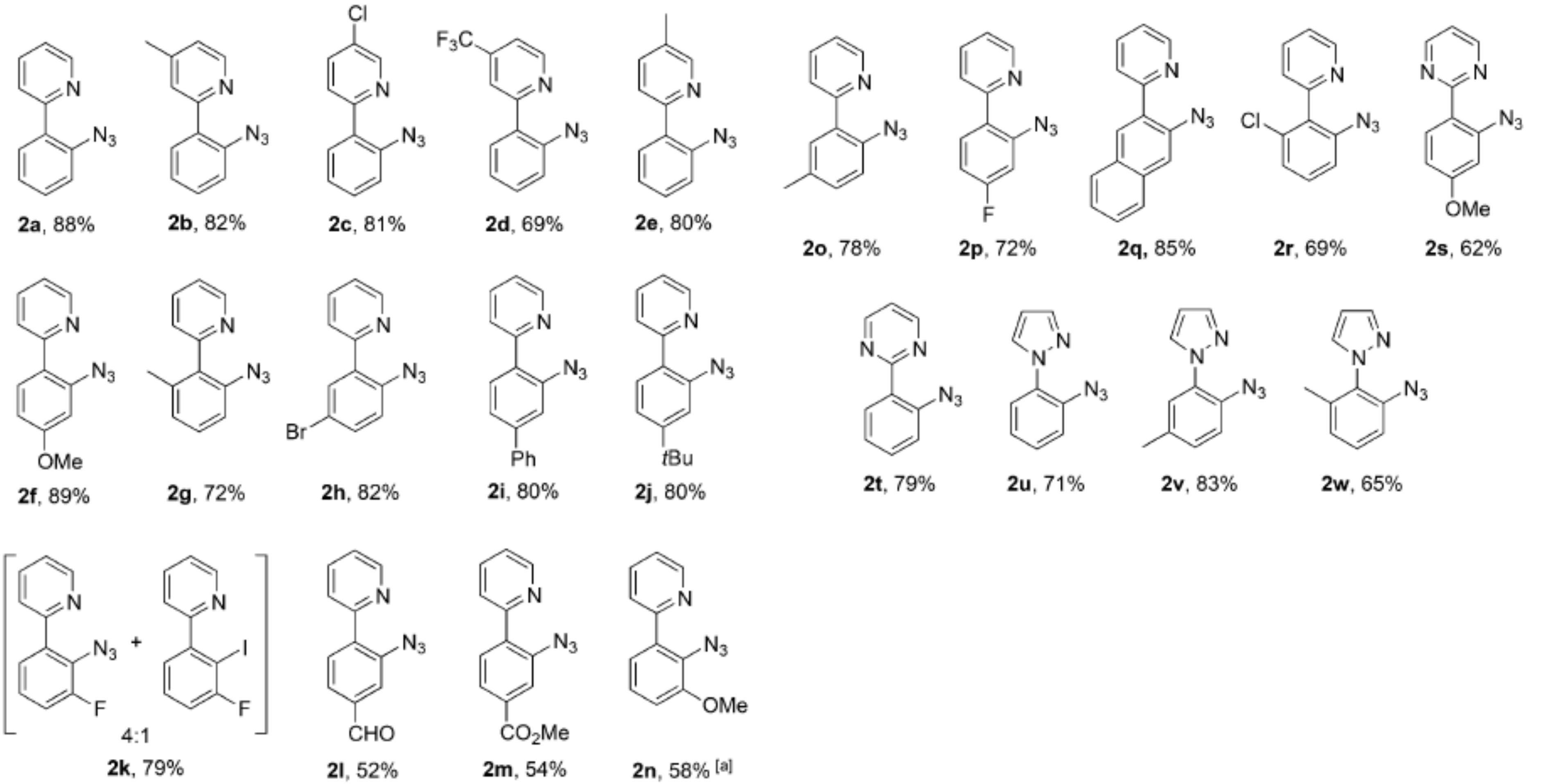


2a

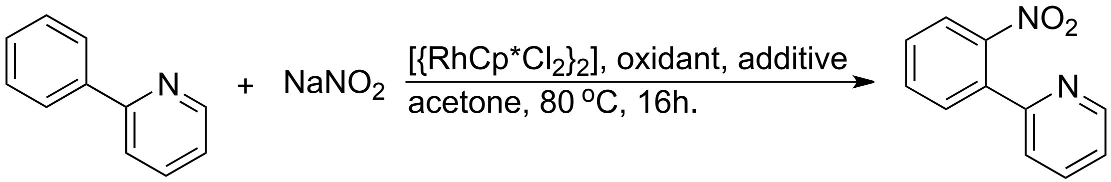
Entry	Oxidant	Additive	Solvent	T [°C]	Yield [%][b]
1	PIDA	–	MeCN	70	< 3
2	PIDA	$TsOH \cdot H_2O$	MeCN	70	20
3	PIDA	$TsOH \cdot H_2O$	MeCN	90	34
4	PIDA	$TsOH \cdot H_2O$	CH_2Cl_2	70	28
5[c]	PIDA	$TsOH \cdot H_2O$	CH_2Cl_2	70	15
6	PIDA	$TsOH \cdot H_2O$	dioxane	90	< 3
7	PIDA	$TsOH \cdot H_2O$	DMF	90	< 3
8	PIDA	$TsOH \cdot H_2O$	TFE	60	40
9	PIDA	$TsOH \cdot H_2O$	acetone	50	88
10	PIDA	$TsOH \cdot H_2O$	acetone	30	68
11[d]	PIDA	$TsOH \cdot H_2O$	acetone	50	56
12	PhI(OH)OTs	AcOH	acetone	50	83
13[e]	PIDA	$TsOH \cdot H_2O$	acetone	50	86

C-H azidation of arenes



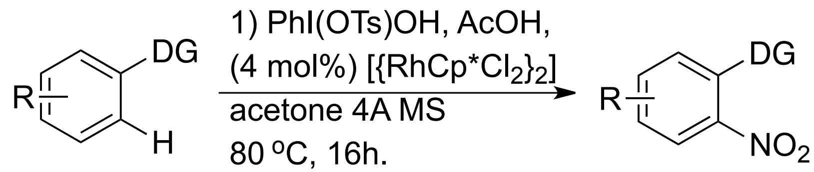


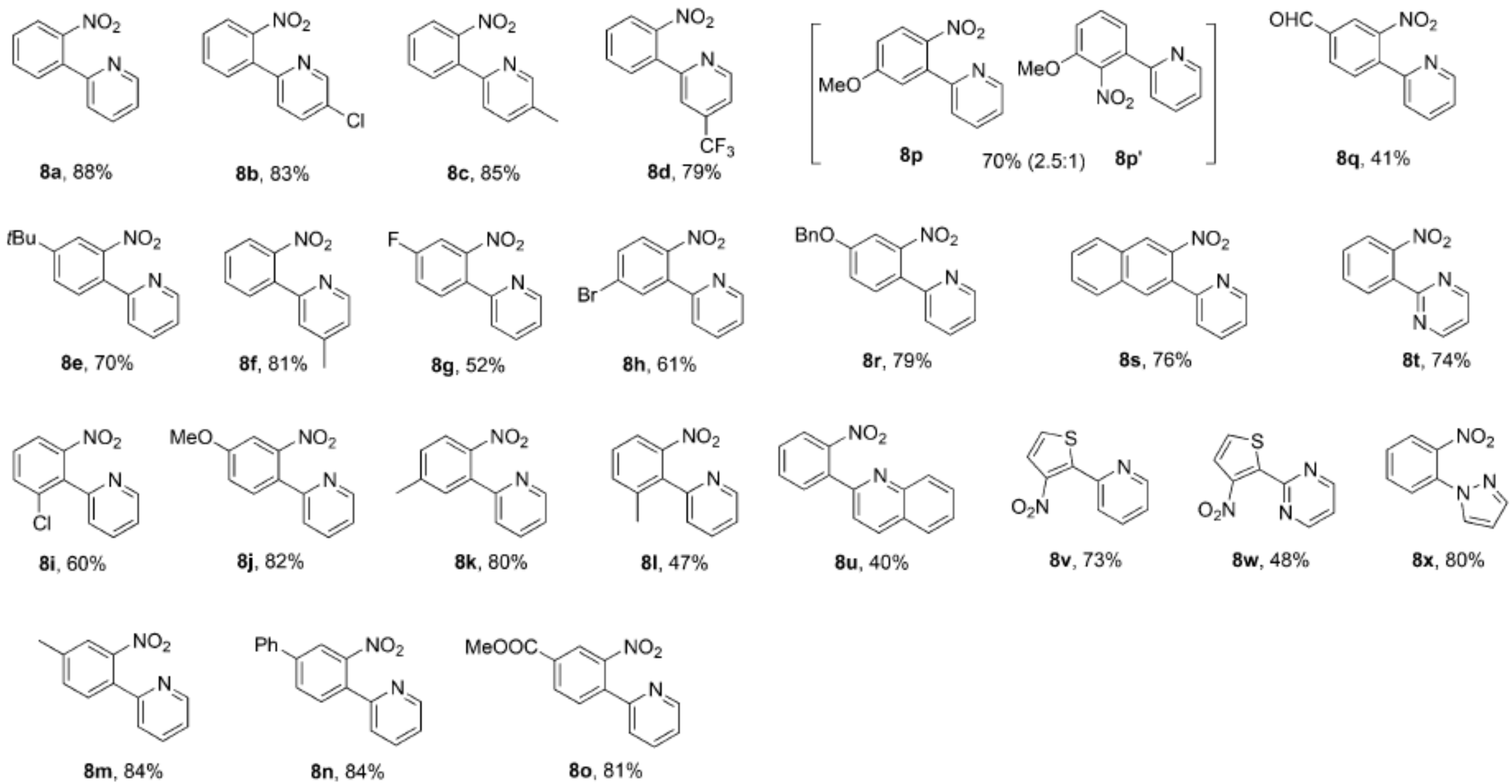
Optimization for nitration



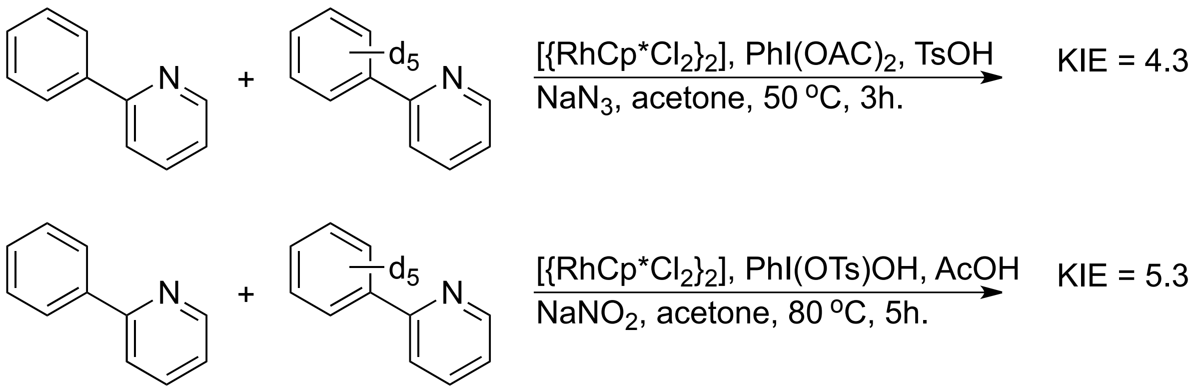
Entry	Catalyst	Oxidant	Additive	Yield / %
1	$[RhCp^*Cl_2]_2$	$PhI(OAc)_2$	TsOH	40
2	$[RhCp^*Cl_2]_2$	$PhI(OAc)_2$	TFA	nd
3	$[RhCp^*Cl_2]_2$	PhI(OTs)OH	TFA	nd
4	$[RhCp^*Cl_2]_2$	PhI(OTs)OH	AcOH	59
5	$[RhCp^*Cl_2]_2$	PhI(OTs)OH	PivOH	61
6[b]	$[RhCp^*Cl_2]_2$	PhI(OTs)OH	PivOH	50
7[c]	$[RhCp^*Cl_2]_2$	PhI(OTs)OH	PivOH	85
8[c]	$[RhCp^*Cl_2]_2$	PhI(OTs)OH	AcOH	88
9[d]	$[RhCp^*Cl_2]_2$	PhI(OTs)OH	AcOH	72
10	-	PhI(OTs)OH	-	0
11	$[RhCp^*Cl_2]_2$	PhI(OTs)OH	-	67

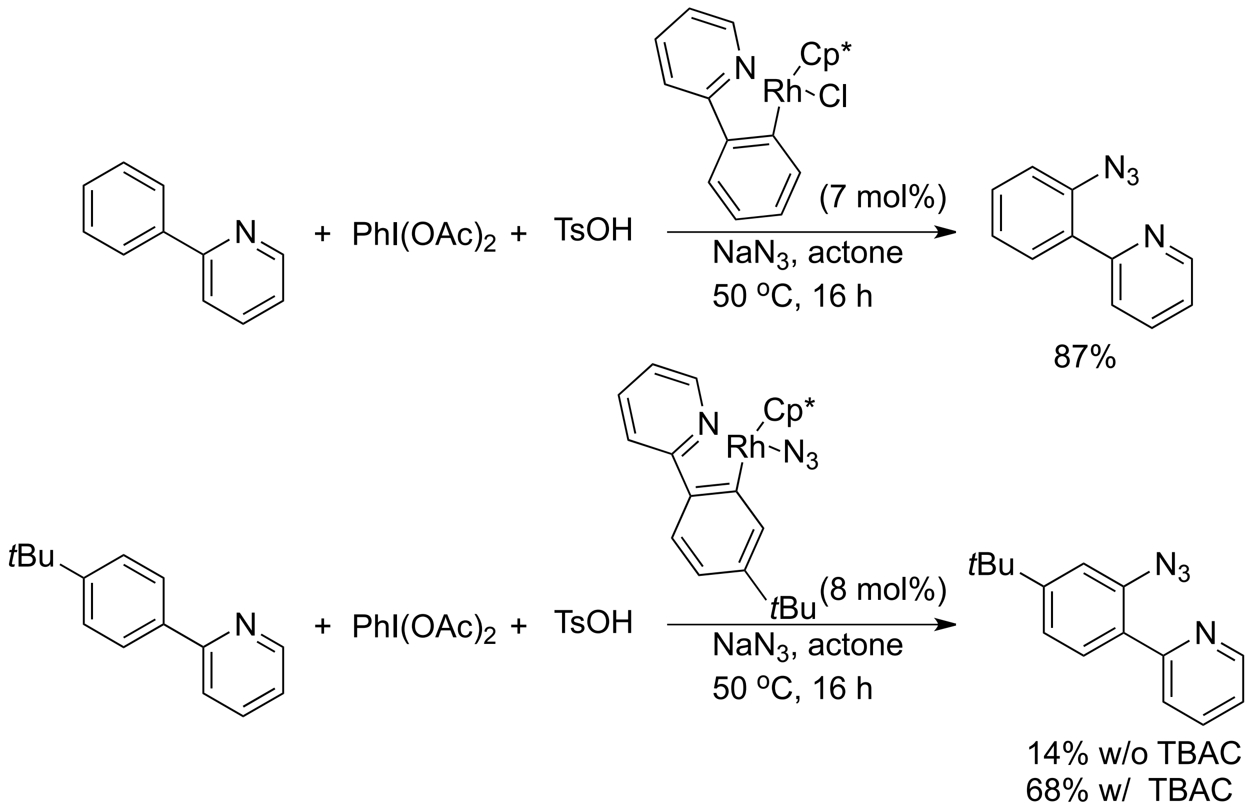
C-H nitration of arenes



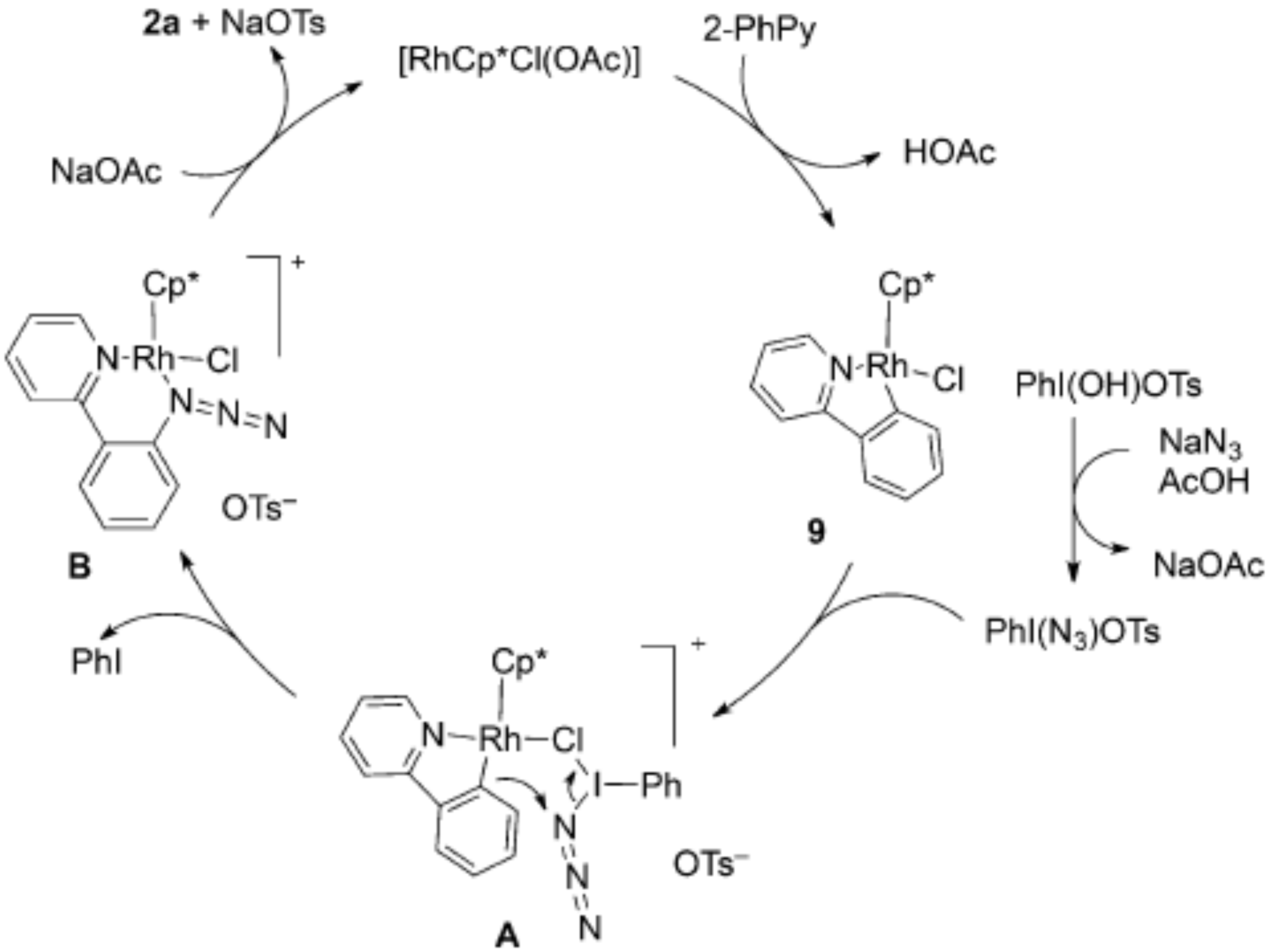


Mechanistic studies





A Plausible Mechanism



Conclusions

- The azide and nitrite compounds were first successfully synthesized from arenes using a rhodium(III)-catalyzed C-H activation
- The C-H activation is the rate-limiting step from the preliminary mechanistic studies
- The cyclometalated Rh^{III} chloride complex is a likely reaction intermediate.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Natick
Grazie
Danke
Ευχαριστίες
Dalu
Obrigado
Thank You
Köszönöm
Tack
Спасибо
Dank
Gracias
谢谢
Merci
Seé
ありがとう

ขอบคุณครับ