

# Literature Report

**Ying Chen**  
**2013-6-17**

# Rh<sup>III</sup>/Cu<sup>II</sup>-Cocatalyzed Synthesis of 1H-Indazoles through C–H Amidation and N–N Bond Formation

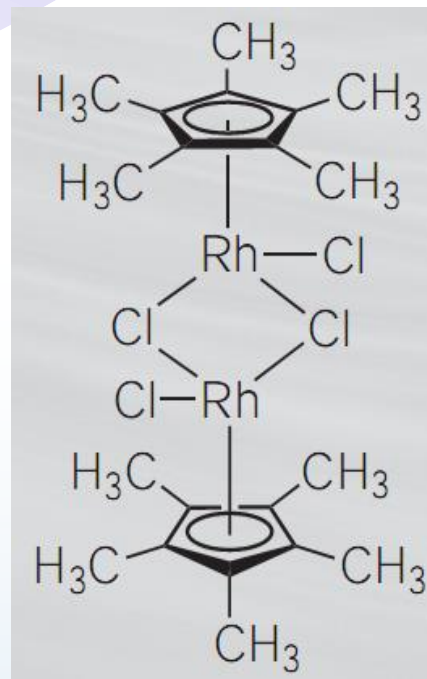
Da-Gang Yu, Mamta Suri, and Frank Glorius\*



Prof. Frank Glorius

*E-mail* : [glorius@uni-muenster.de](mailto:glorius@uni-muenster.de)

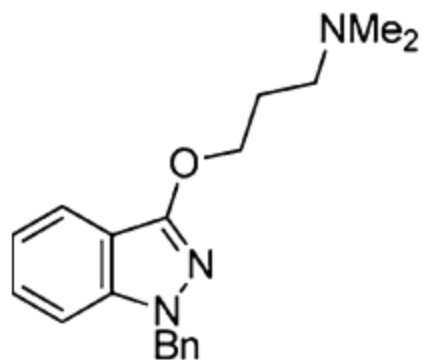
*Homepage* : <http://www.unimuenster.de/Chemie.oc/glorius/index.html>



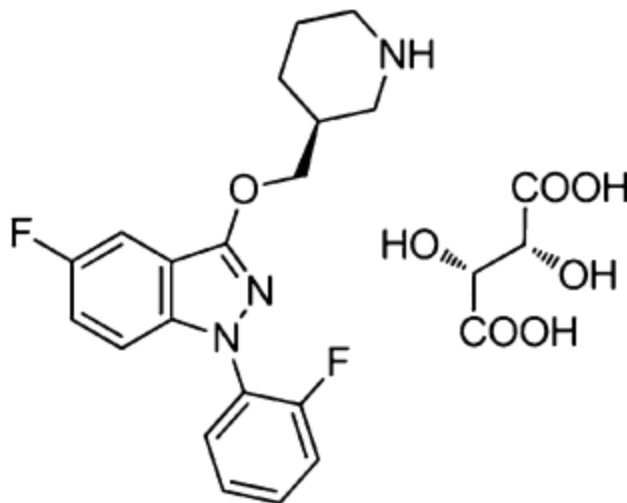
**[Cp\*RhCl<sub>2</sub>]<sub>2</sub>**

# The use of 1H-indazoles

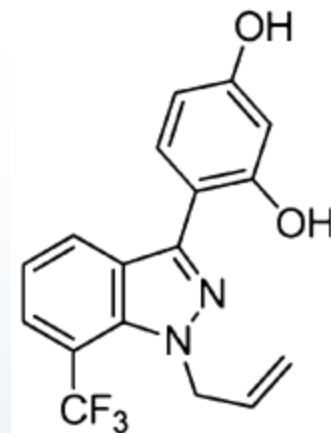
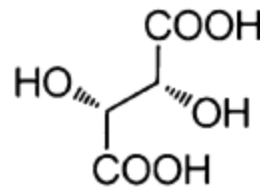
**1H-indazoles** are widely used as anti-cancer, anti-inflammatory, anti-HIV, and anti-microbial drugs



Benzydamine



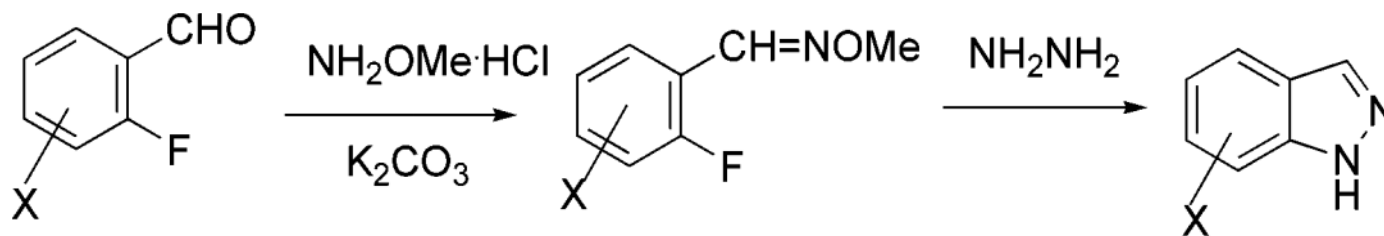
NSRI



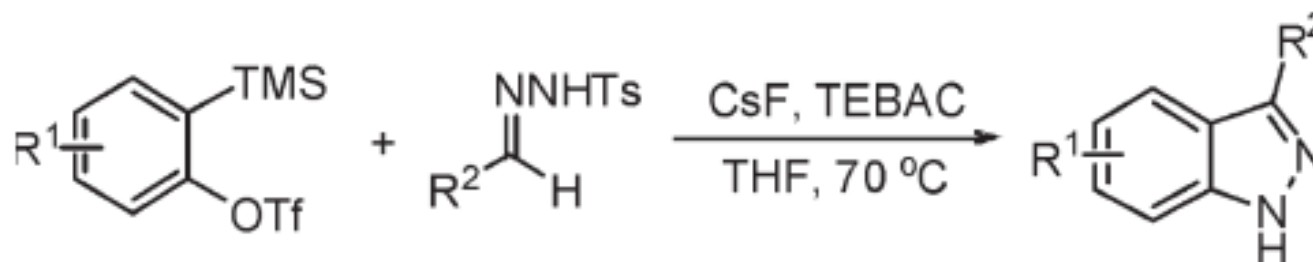
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# The methods of synthesis 1H-indazoles

## 1 Transition-metal-free processes

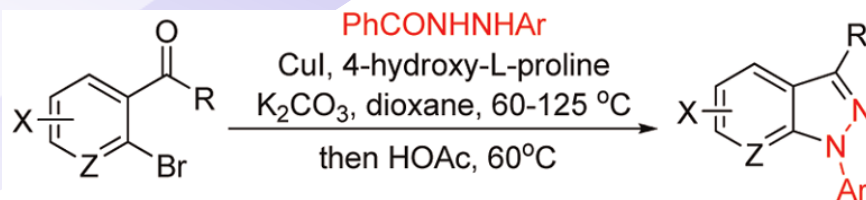
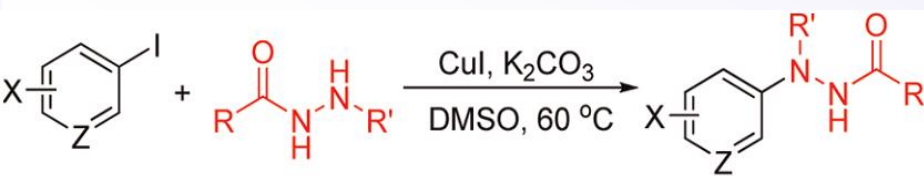


Jukin, K.; Hsu, M. C.; Fernando, D.; Leanna, M. R. *J. Org. Chem.* **2006**, 71, 8166

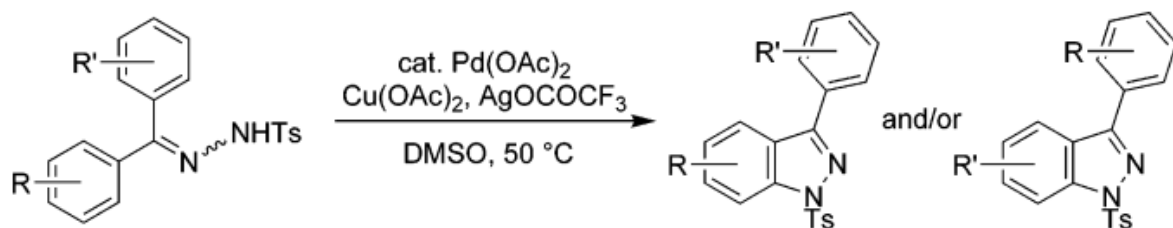


Li, P.; Zhao, J.; Wu, C.; Larock, R. C.; Shi, F. *Org. Lett.* 2011, 13,3340

## 2 Transition-metal catalyzed the synthesis of 1H-indazoles

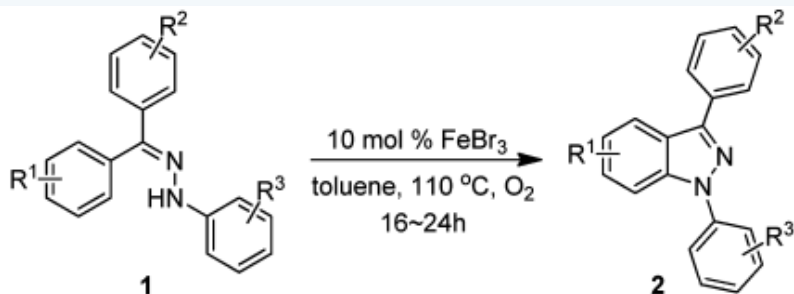


Xiong, X.; Jiang, Y.; Ma, D. *Org. Lett.* 2012, 14, 2552

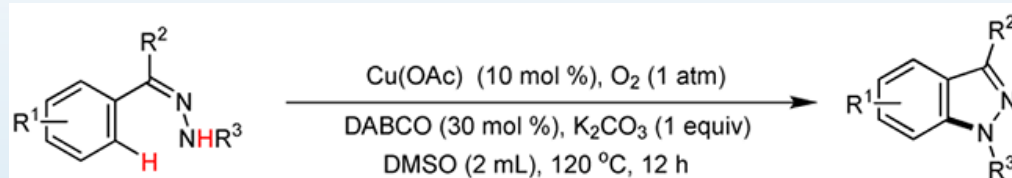


R, R' = H, OMe, NO<sub>2</sub>, CN, CO<sub>2</sub>Et, OH, NH<sub>2</sub>, Br, etc.

Inamoto, K.; Saito, T.; Katsuno, M.; Sakamoto, T.; Hiroya, K. *Org. Lett.* 2007, 9, 2931

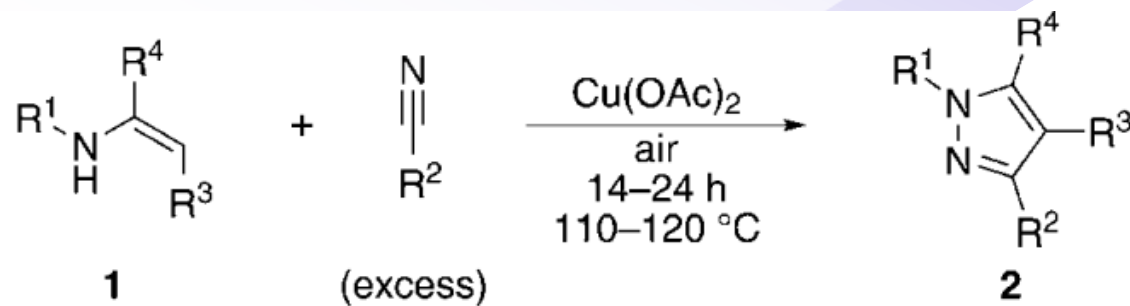


Zhang, T.; Bao, W. *J. Org. Chem.* 2013, 78, 1317

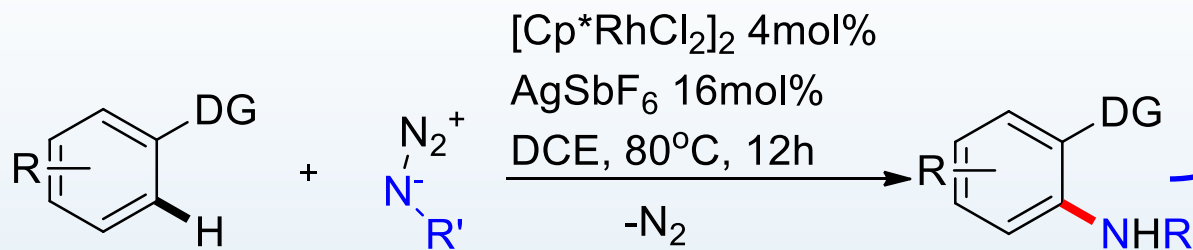


Li, X.; He, L.; Chen, H.; Wu, W.; Jiang, H. *J. Org. Chem.* 2013, 78, 3636

# New idea comes from previous work

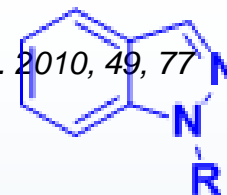


Neumann, J. J.; Suri, M.; Glorius, F. *Angew. Chem., Int. Ed.* 2010, 49, 77



Kim, J. Y.; Park, S. H.; Ryu, J.; Cho, S. H.; Kim, S. H.; Chang, S. J. *Am. Chem. Soc.* 2012, 134, 9110

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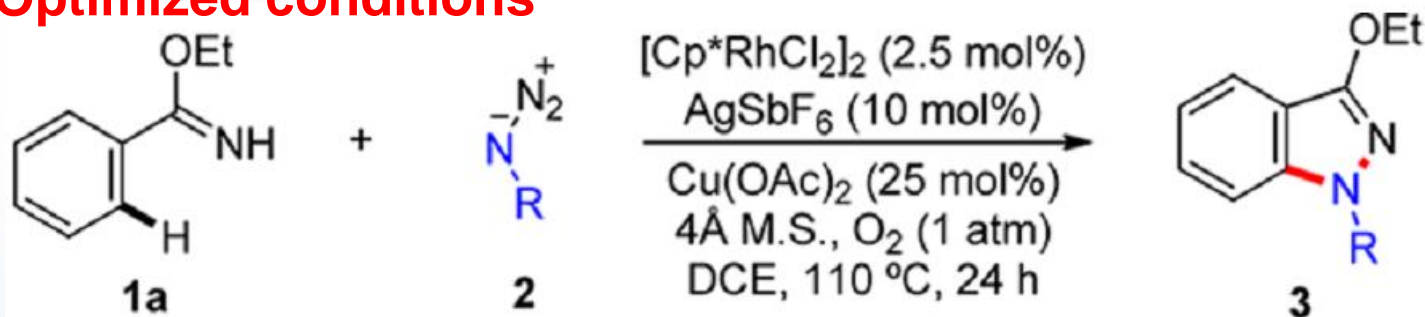


# Conquer the challenges

1).The compatibility of C–N and N–N bond formation.

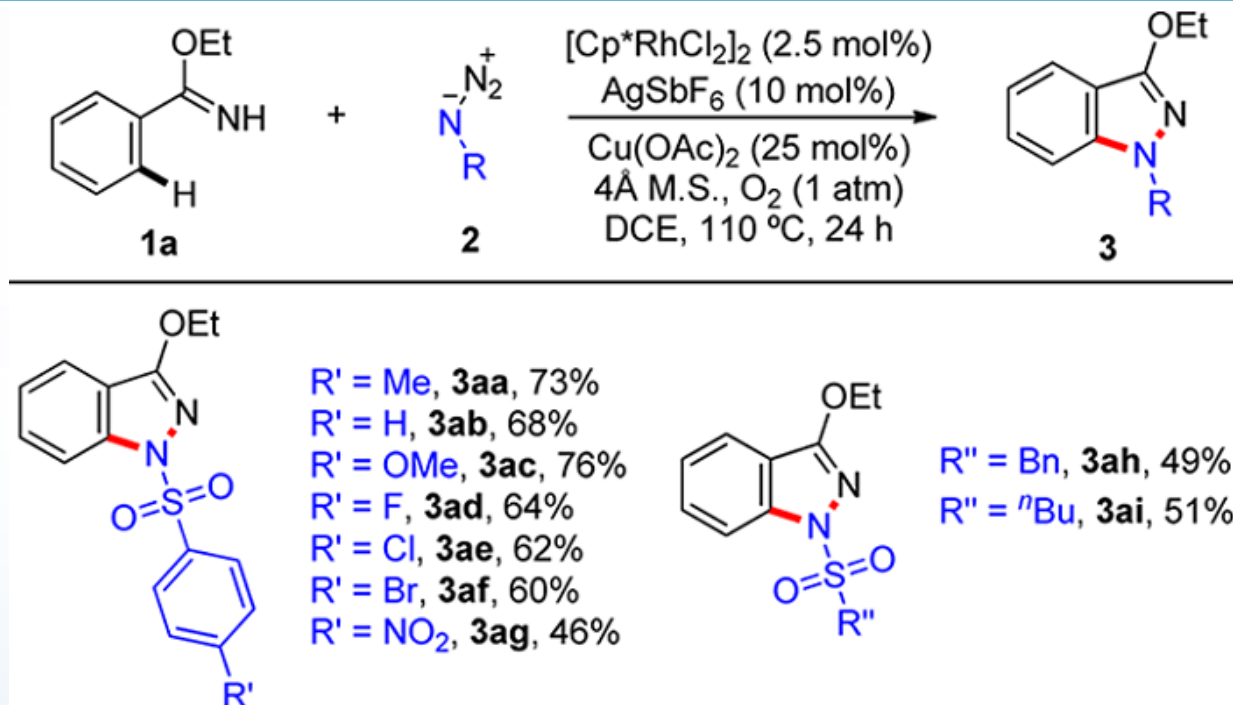
2).How to find the proper and stable N–H-containing directing groups?

## Optimized conditions



**This is the first example of the use of N-H-imidates as substrates in transition-metal-catalyzed C–H activation and also in a cascade with N–N bond formation.**

# Scope of different azides



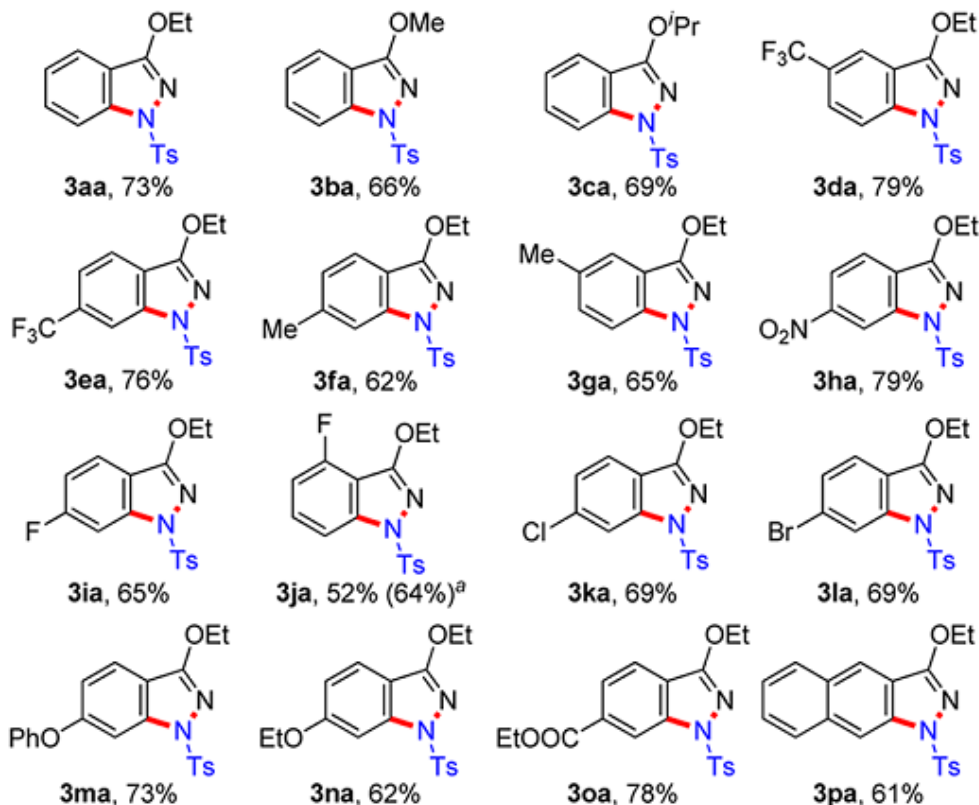
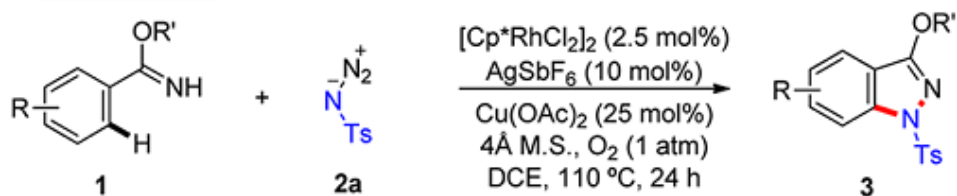
The azides with electron-donating groups showed better reactivity than those with electron-withdrawing groups.

Various kinds of functional groups, such as OMe, NO<sub>2</sub>, C-F, C-Cl, and even C-Br, were well tolerated.

Besides arylsulfonyl azides, alkylsulfonyl azides (**2h**, **2i**) also showed reactivity in this transformation



# Scope of different arylimidates



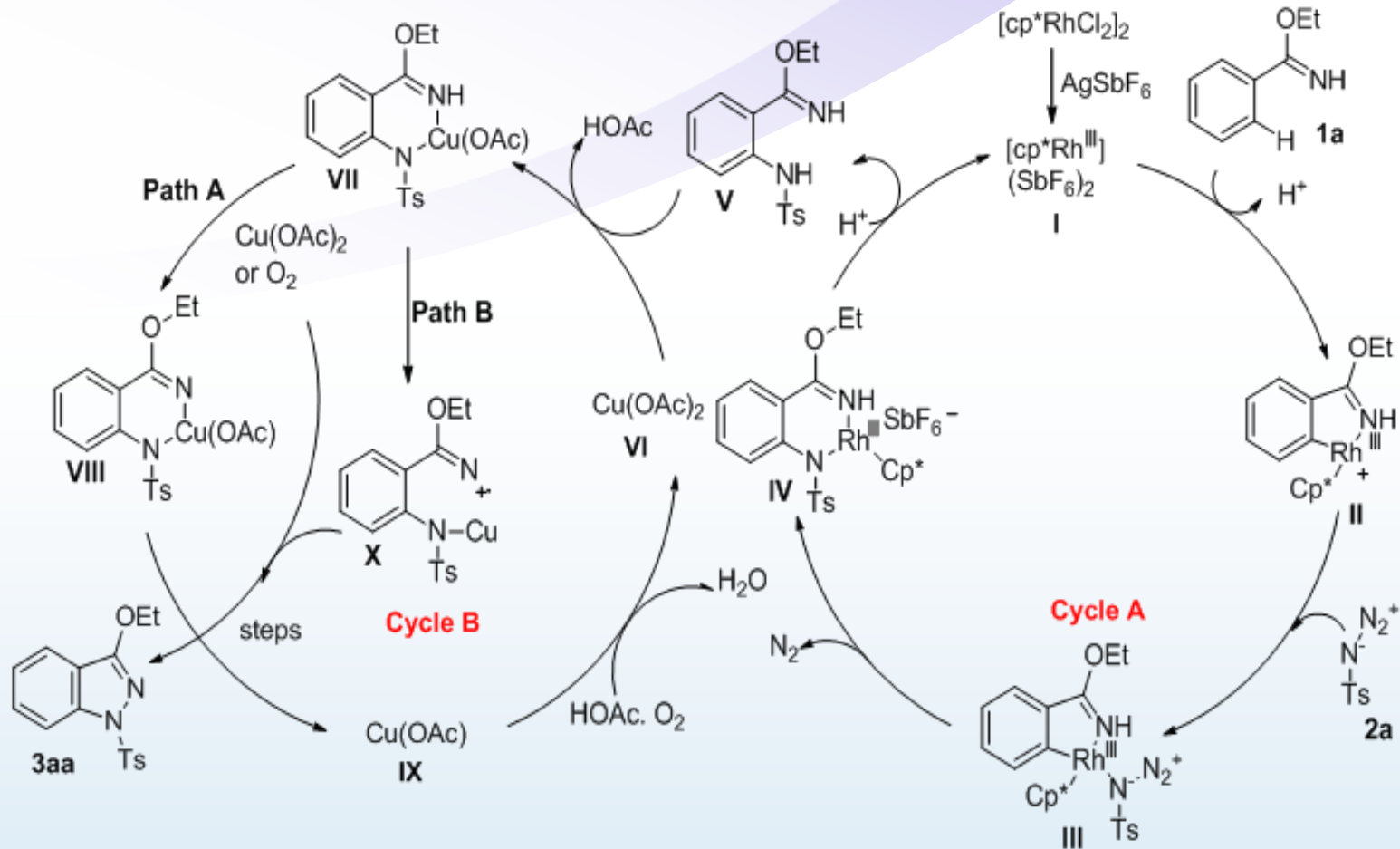
The ethylimidate (**1a**) showed better reactivity than methyl (**1b**) and isopropyl (**1c**) derivatives.

Both 3- $\text{CF}_3$  (**1d**) and 3-Me (**1g**) derivatives showed excellent selectivity to the C–H bond with less steric hindrance.

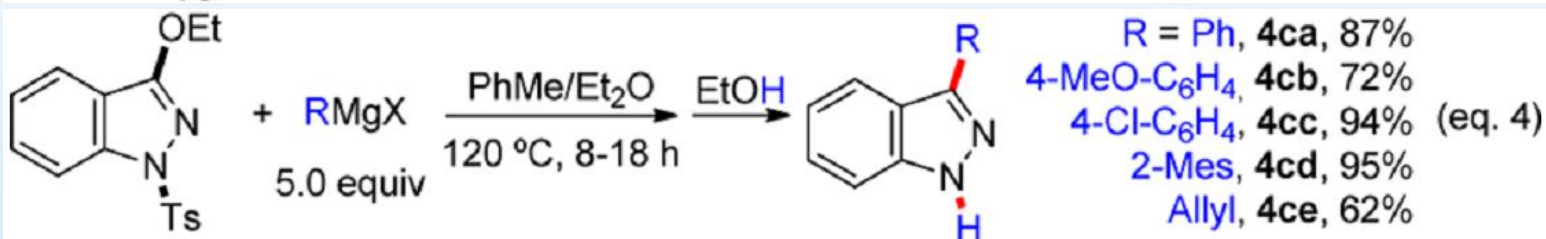
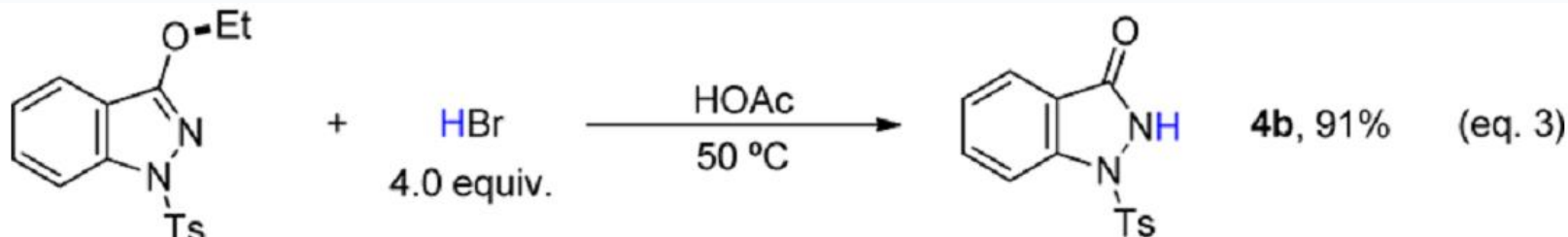
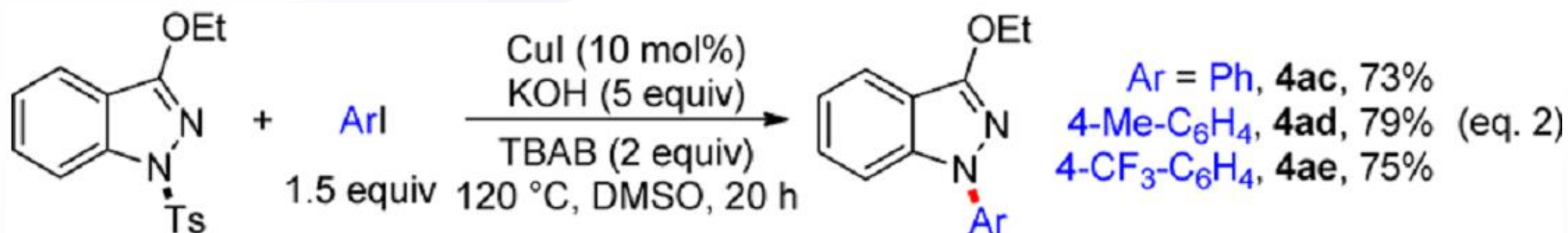
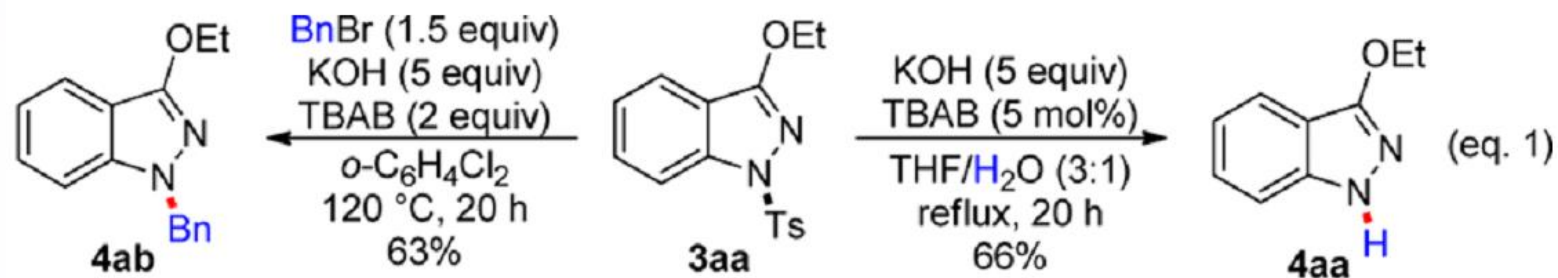
In contrast with electron-rich arylimidates, the electron-poor imidates showed better reactivities

Besides the phenyl ring, naphthylimidate also showed good reactivity in this reaction to give the product (**3pa**) in good yield and excellent regioselectivity.

# Plausible mechanism

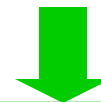
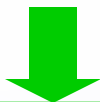


# Utility of the products



# Summary

**A novel synthesis of substituted 1H-indazoles from easily available arylimidates and organo azides via Rh<sup>III</sup>-catalyzed C–H activation/C–N bond formation and Cu-catalyzed N–N bond formation was developed.**



**N-H-Imidates** were applied as directing groups in Rh<sup>III</sup>-catalyzed C–H activation, delivering substrates that undergo intramolecular N–N bond formation.

The process is scalable and green, with O<sub>2</sub> being used as the terminal oxidant and only N<sub>2</sub> and H<sub>2</sub>O formed as the byproducts.

The corresponding 1H-indazoles were obtained in moderate to high yields with good functional group tolerance.

The products could also be further transformed to diverse important derivatives.



*END* !!!