

Intramolecular Aminocyanation of Alkenes by Cooperative Palladium/Boron Catalysis

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Checker: Xiang Gao

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Nakao, Y. J. *et al.*
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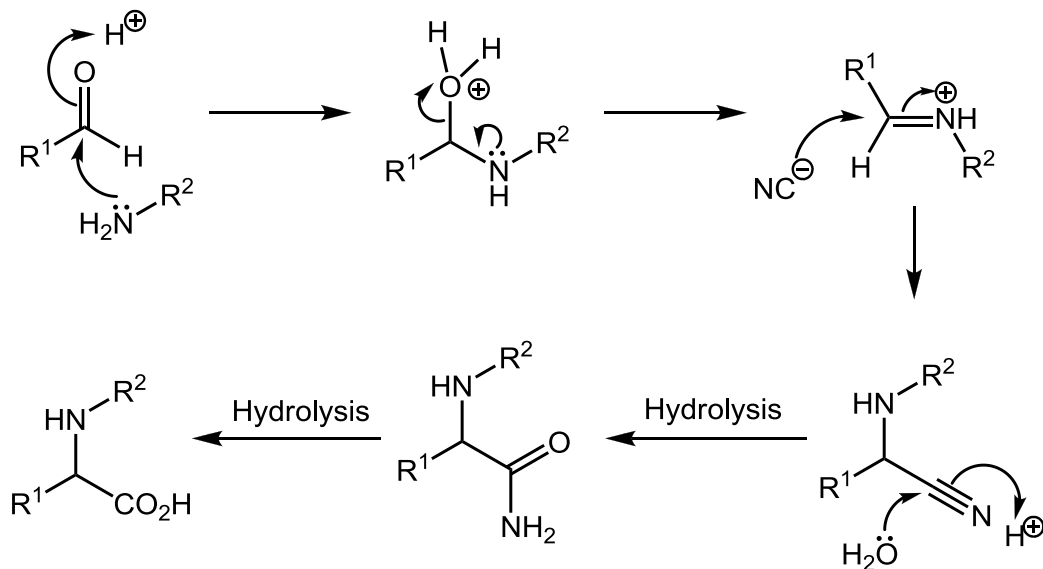
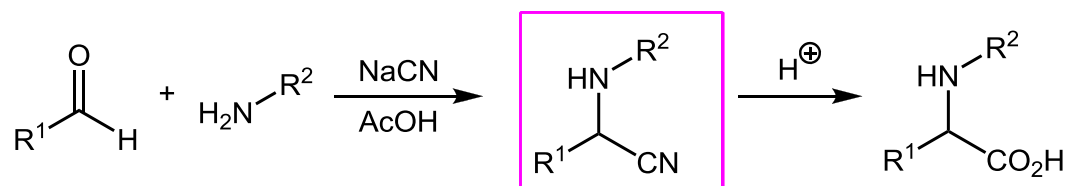
Yoshiaki Nakao (中尾佳亮)
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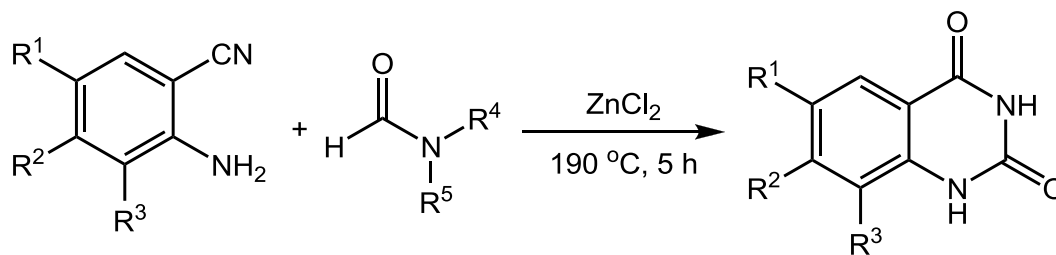
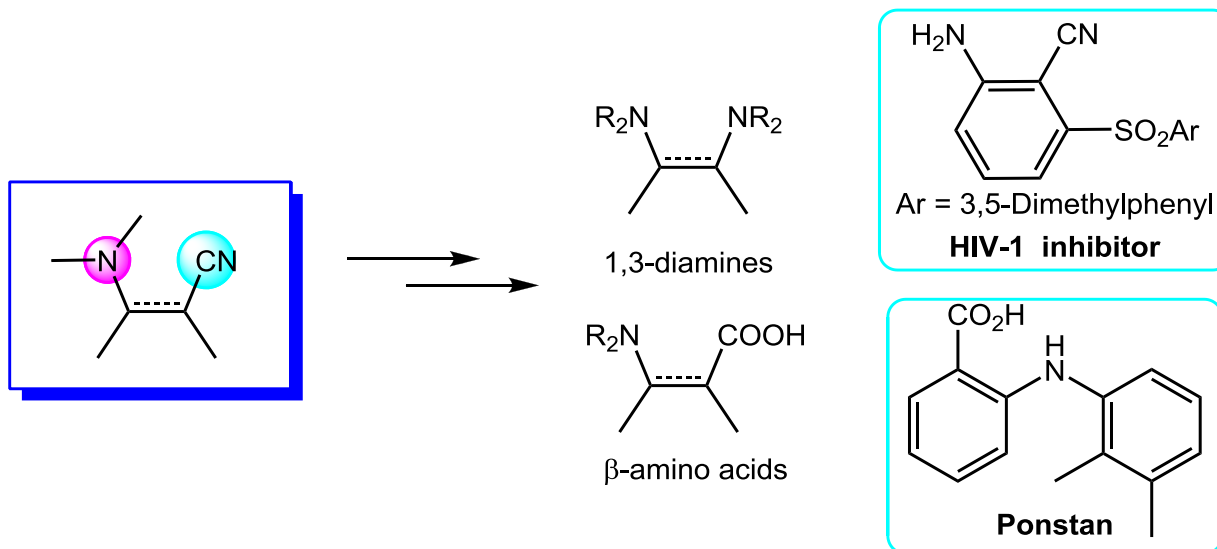
Introduction

Strecker Aminocyanation Reaction



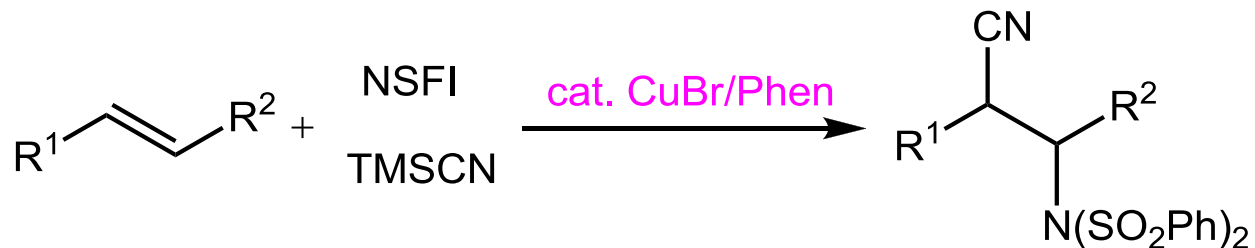
Strecker, A. *Justus Liebigs Ann. Chem.* **1850**, 75, 27.

Introduction

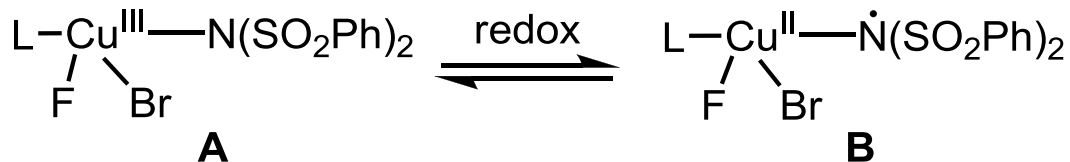
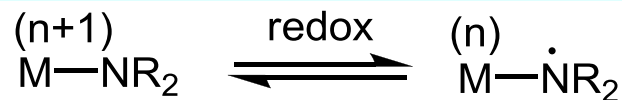


Li, *J. Org. Lett.* **2009**, *11*, 1193.

Intermolecular Aminocyanation

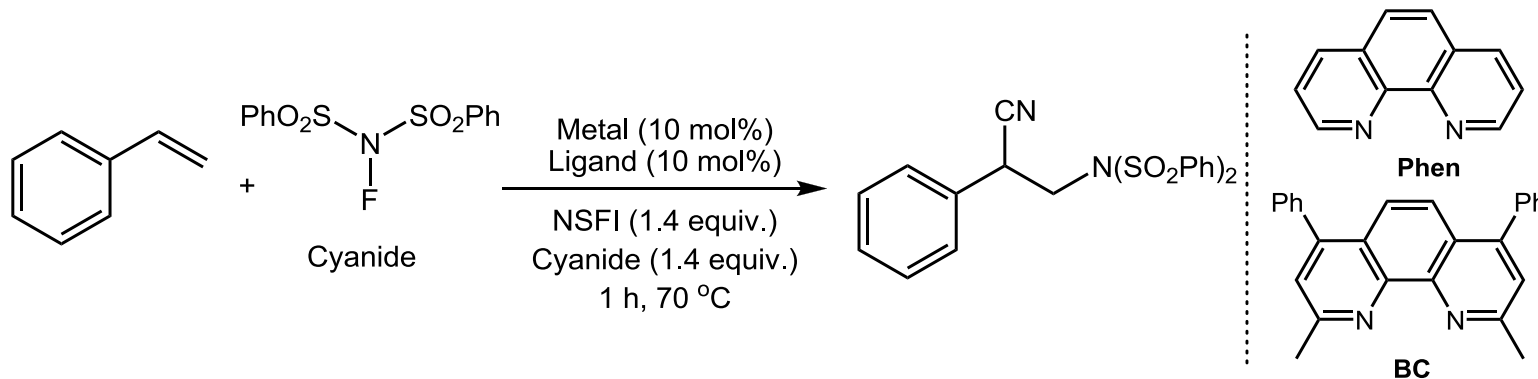


- Nitrogen-Centred Radical Initiated
- Si-F Interaction Play an Important Role



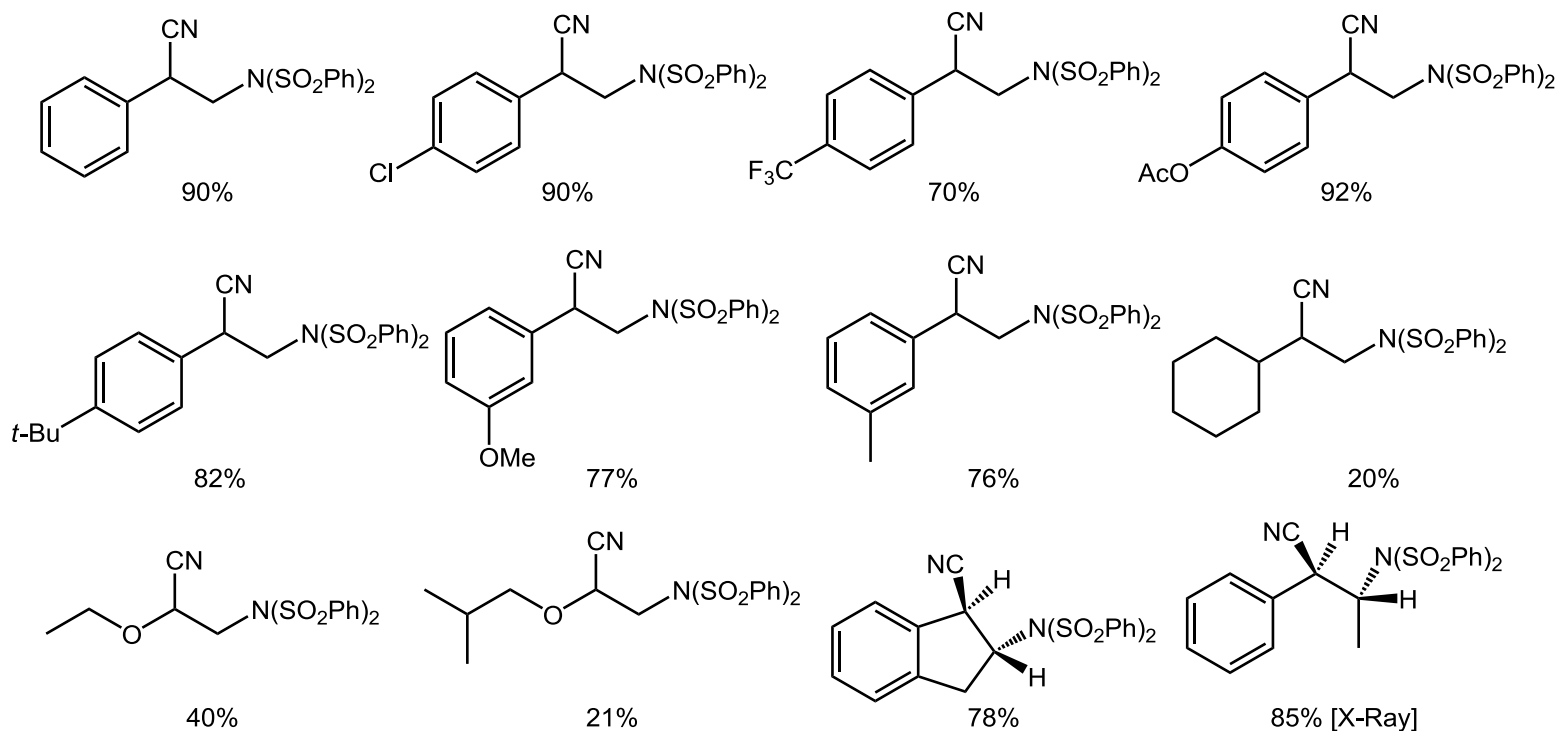
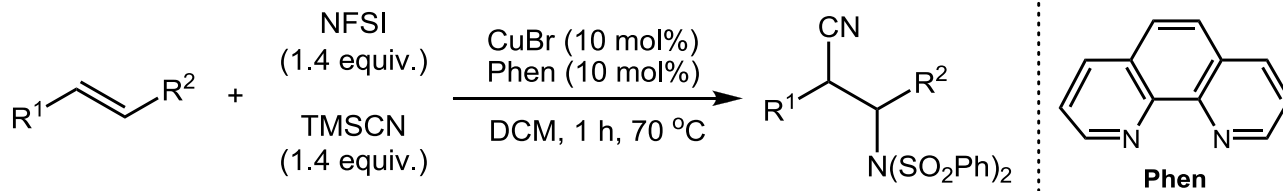
Grutzmacher, H. *Science* **2005**, 307, 235.
Zhang, Q. *Angew. Chem. Int. Ed.* **2013**, 52, 2529.

Intermolecular Aminocyanation

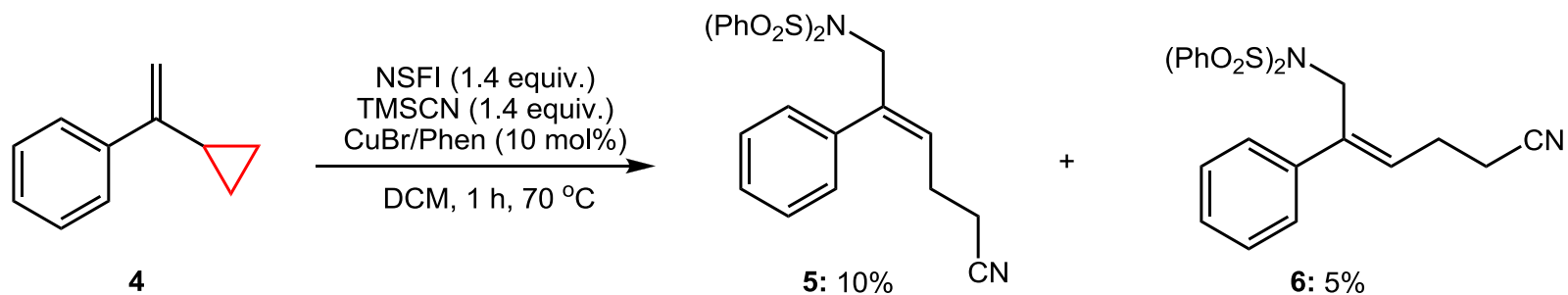
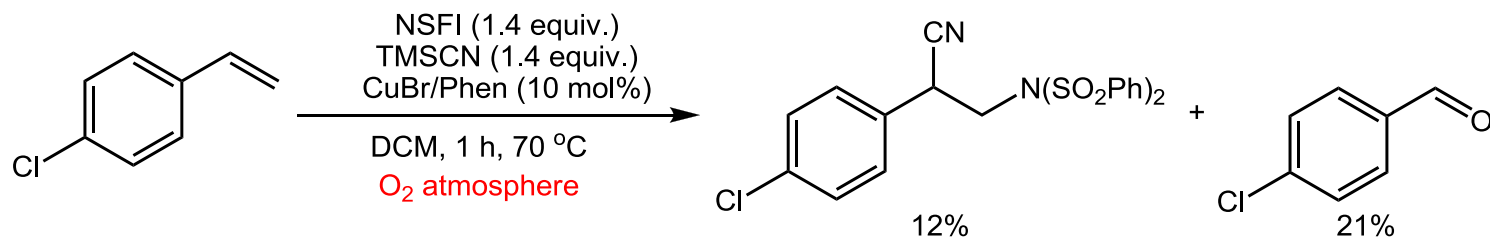


Entry	Metal	Cyanide	Ligand	Solvent	Yield [%]
1	CuBr	TMSCN	Pyridine	DCE	60
2	CuBr	TMSCN	BC	DCE	52
3	CuBr	TMSCN	Phen	DCE	85
4	CuCl	TMSCN	Phen	DCE	70
5	CuI	TMSCN	Phen	DCE	82
6	CuBr	TMSCN	Phen	MeCN	72
7	CuBr	CuCN	Phen	MeCN	23
8	CuBr	K ₃ FeCN ₆	Phen	MeCN	0
9	CuBr	TMSCN	Phen	DCE	60
10	CuBr	TMSCN	Phen	DCM	90

Intermolecular Aminocyanation

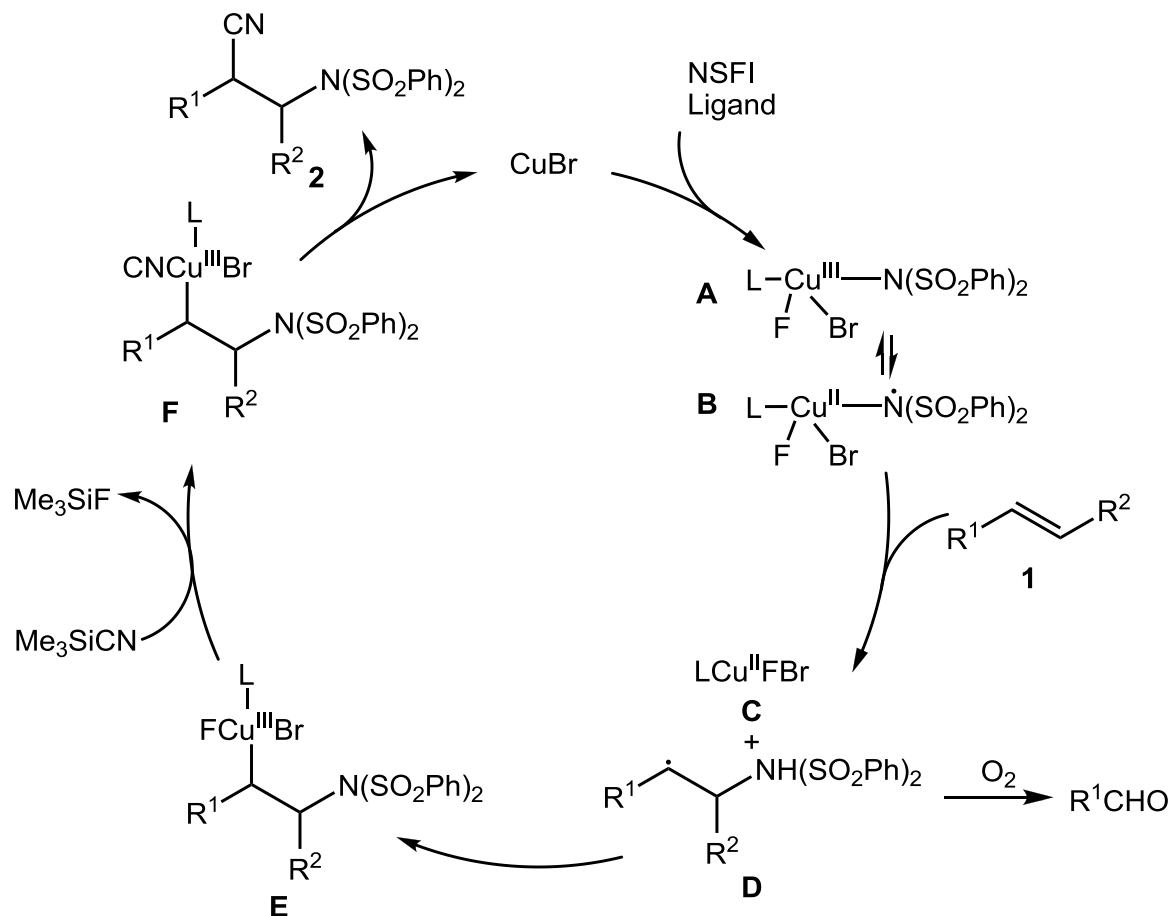


Intermolecular Aminocyanation

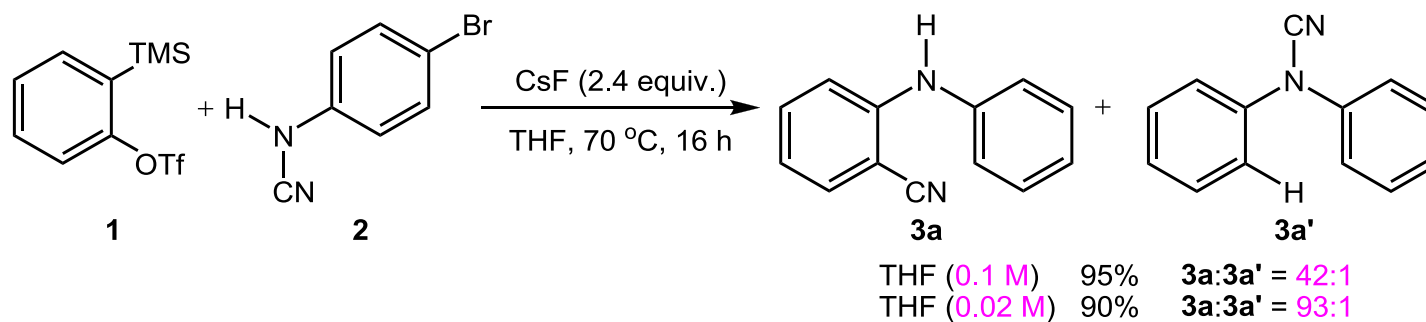
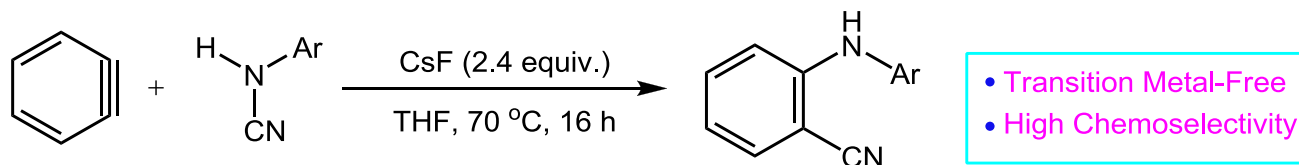


Intermolecular Aminocyanation

Proposed Mechanism

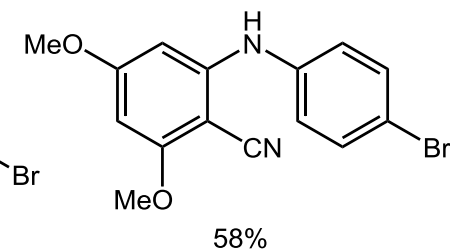
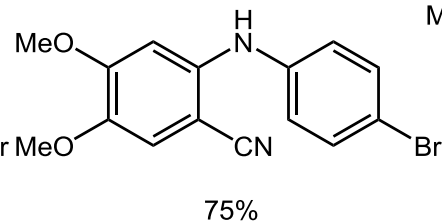
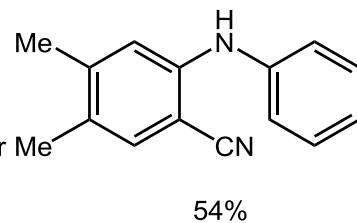
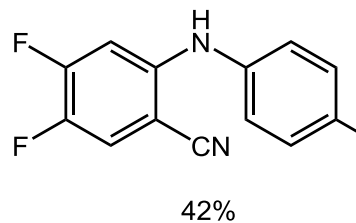
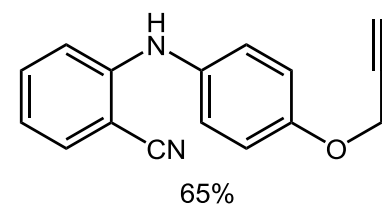
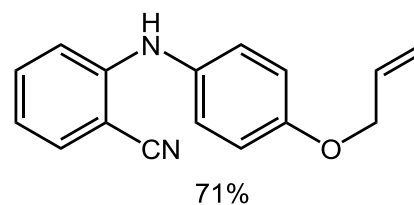
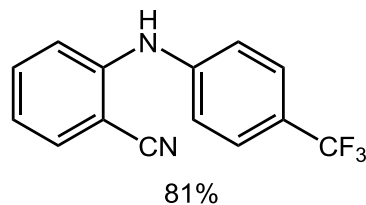
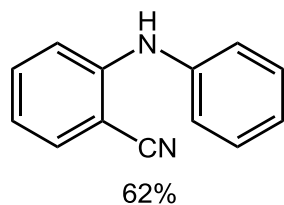
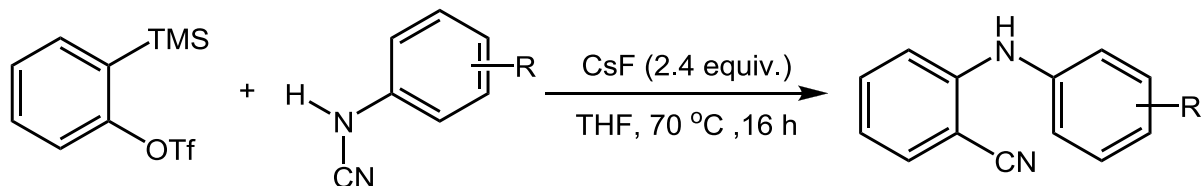


Intermolecular Aminocyanation



Zeng, X. *Org. Lett.* **2014**, 16, 314.

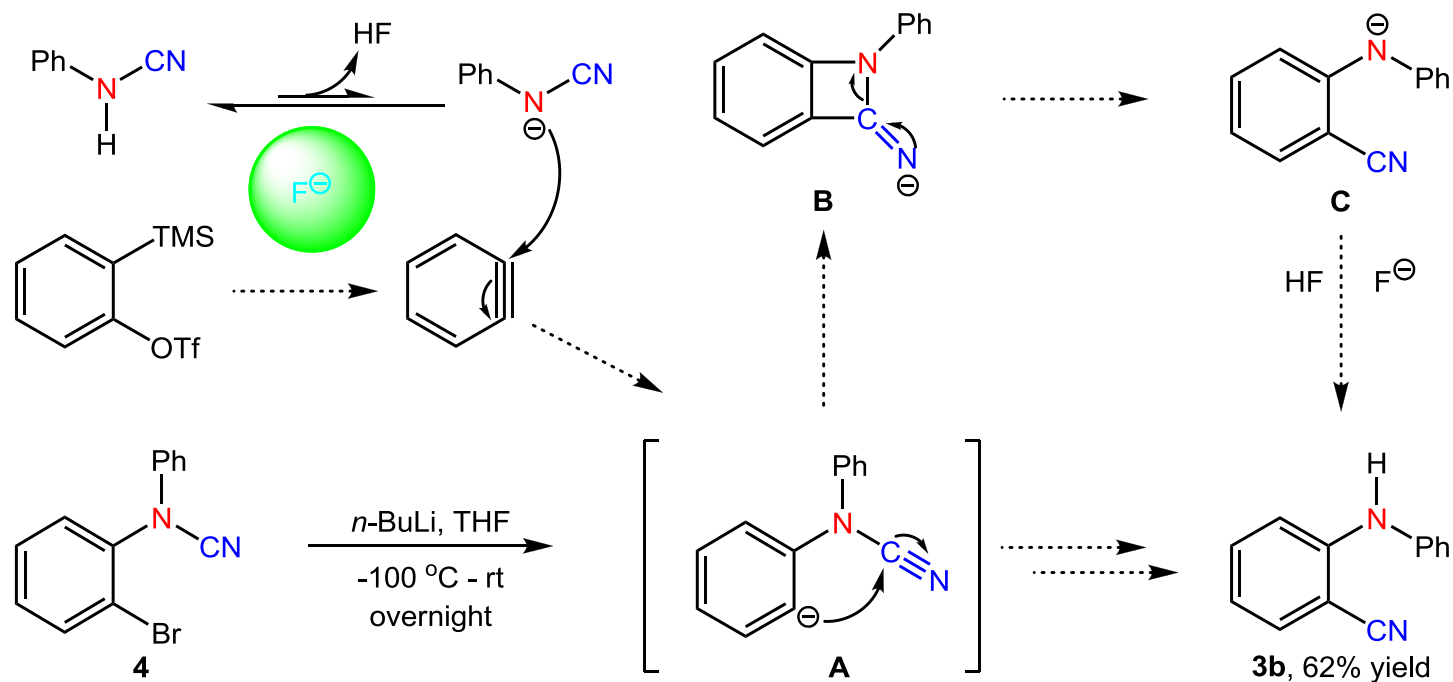
Intermolecular Aminocyanation



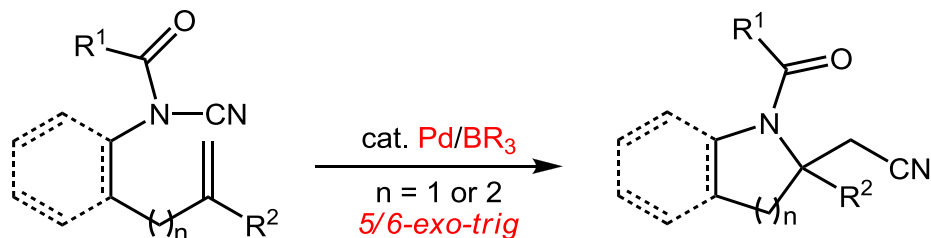
Zeng, X. *Org. Lett.* **2014**, *16*, 314.

Intermolecular Aminocyanation

Proposed Mechanism



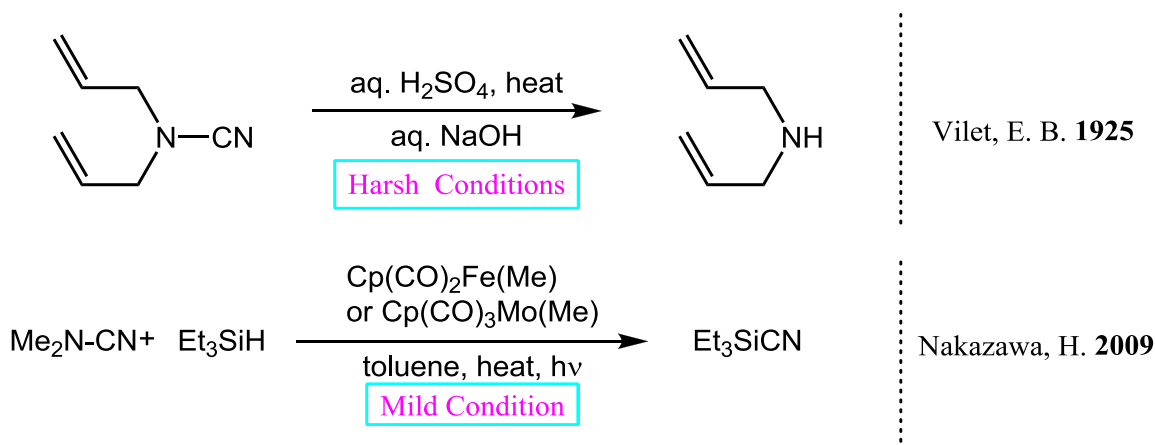
Intramolecular Aminocyanation



- Cooperative Palladium/Boron Catalysis
- Activation of N-CN Bond
- High Chemo- and Regioselectivity.

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N-C (1.47 Å) > Me(*p*-ClC₆H₄)N-CN (1.331 Å) > N=C (1.27 Å)

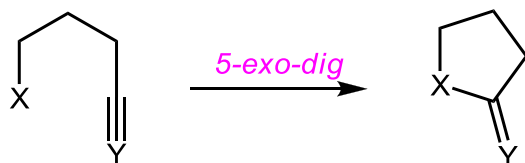
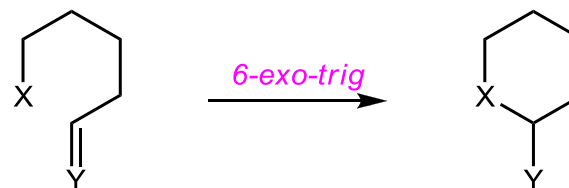
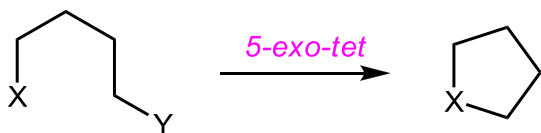
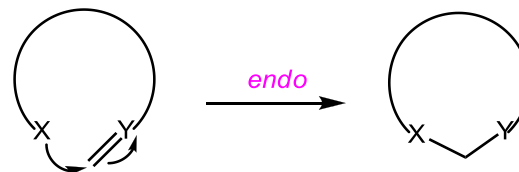
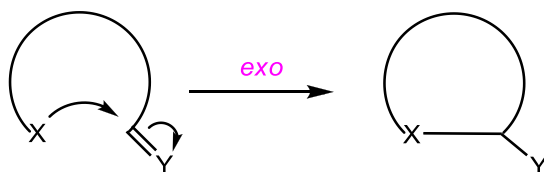


Vilet, E. B. *Org. Synth.* **1925**, 5, 43.

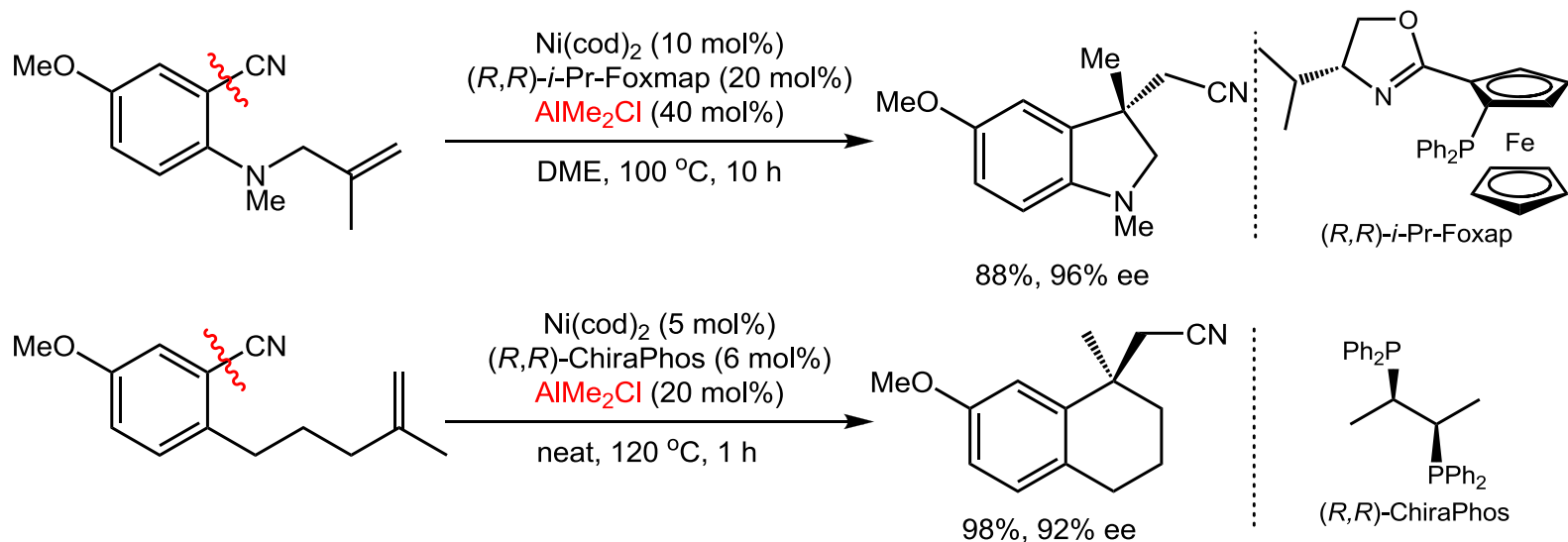
Nakazawa, H. *J. Am. Chem. Soc.* **2009**, 131, 38.

Intramolecular Aminocyanation

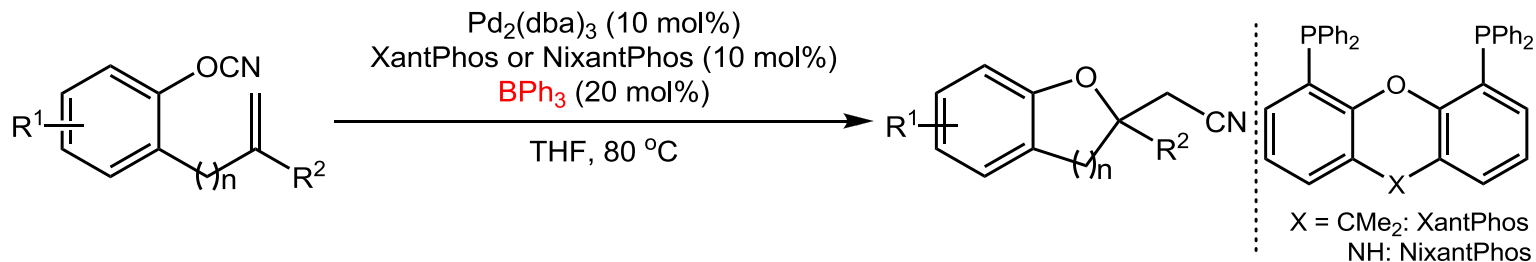
Classes of Ring Closing Processes



Intramolecular Aminocyanation

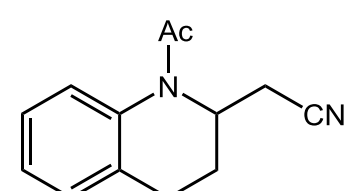
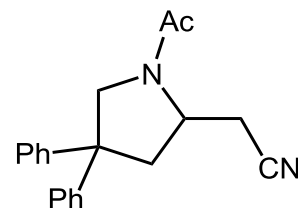
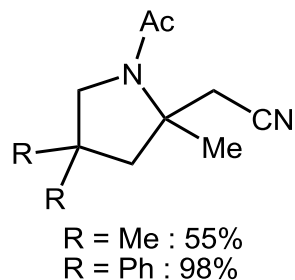
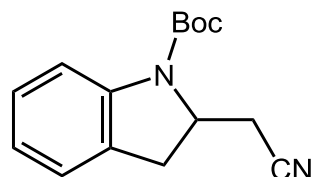
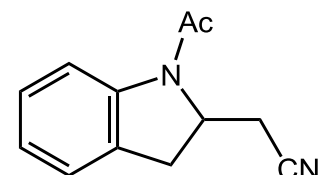
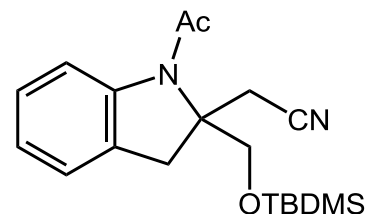
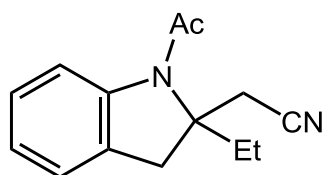
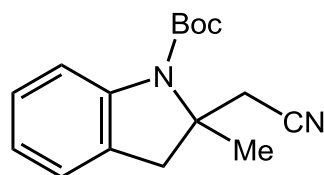
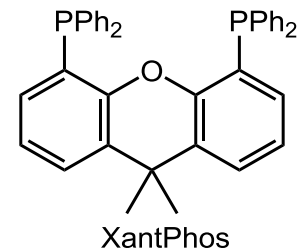
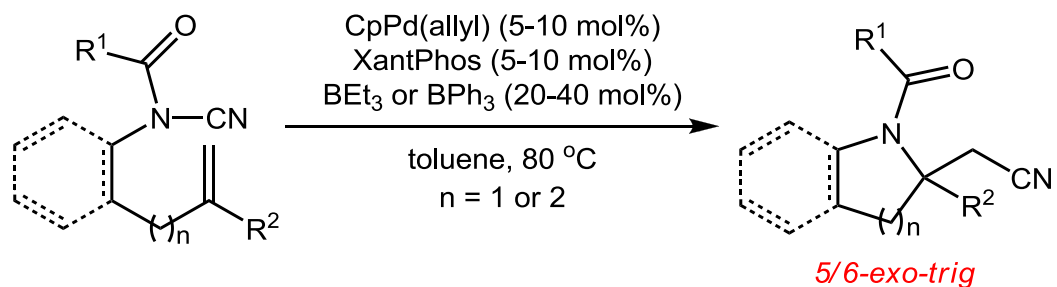


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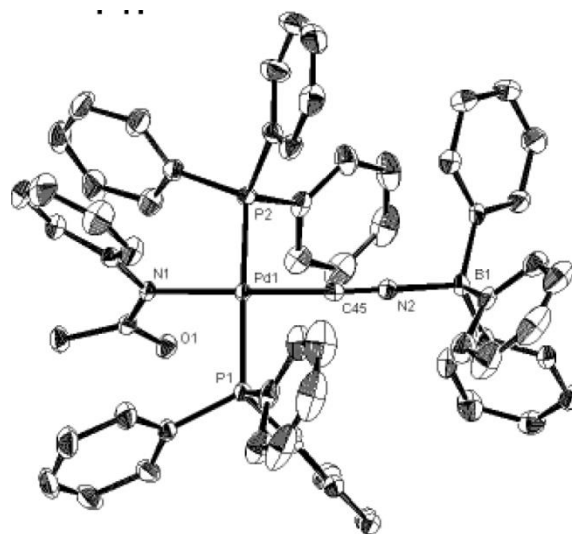
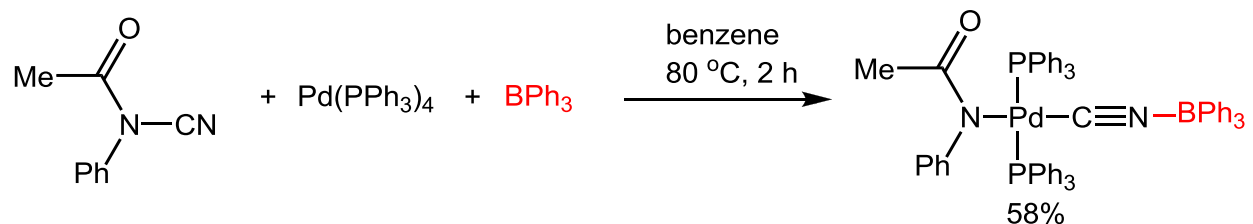


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Intramolecular Aminocyanation

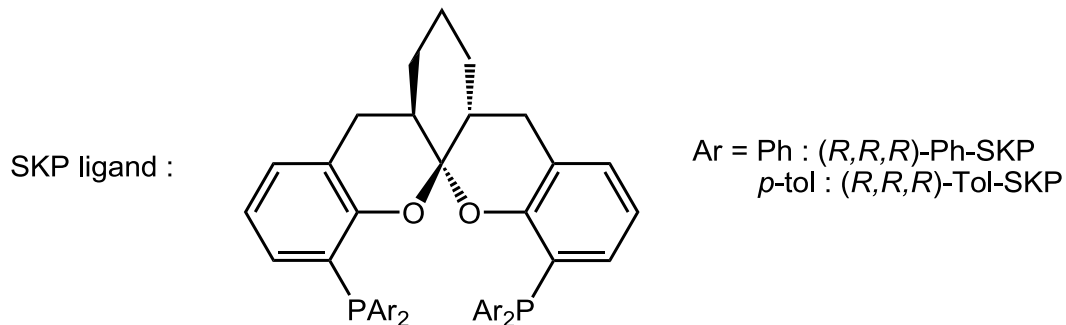
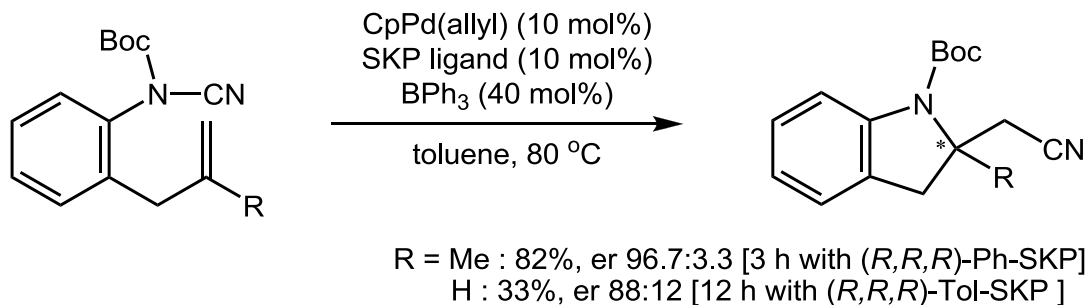


Intramolecular Aminocyanation



Nakao, Y. *J. Am. Chem. Soc.* **2014**, *136*, 3732.

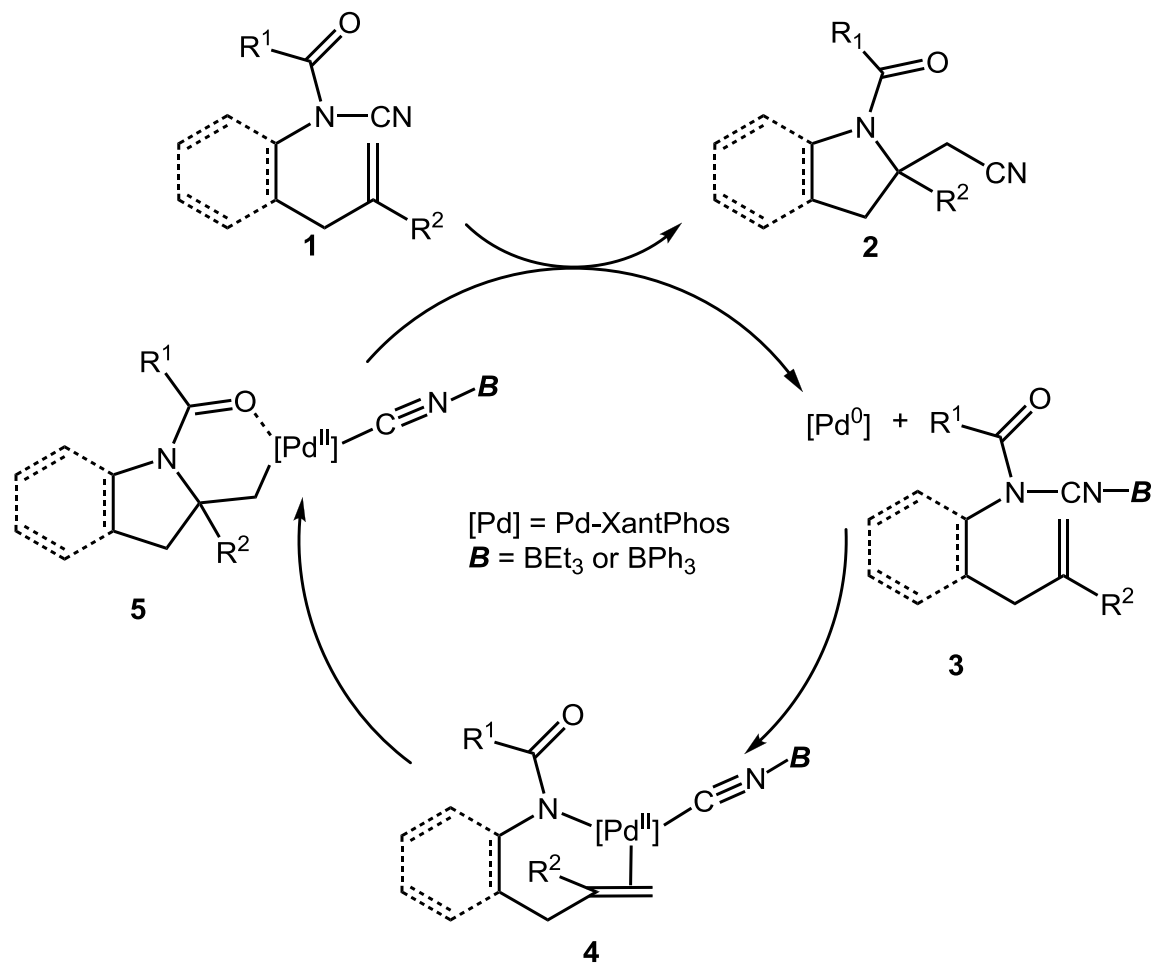
Intramolecular Aminocyanation



Nakao, Y. J. *J. Am. Chem. Soc.* **2014**, *136*, 3732.

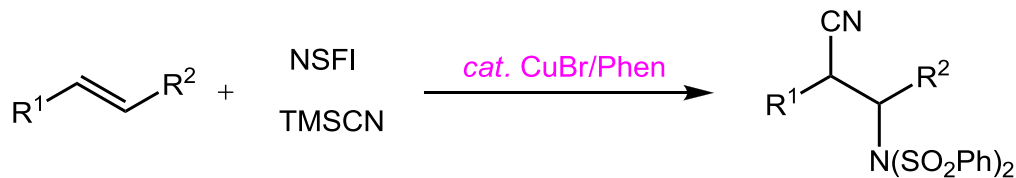
Plausible Catalytic Cycle

Plausiable Catalytic Cycle

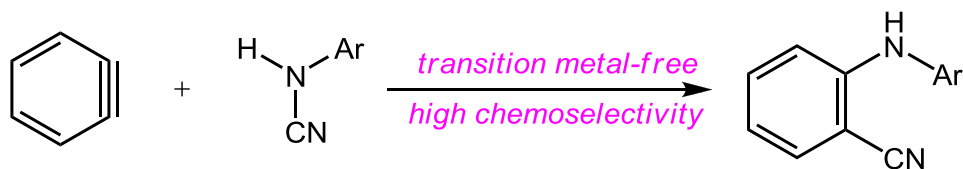


Summary

Intermolecular Aminocyanation

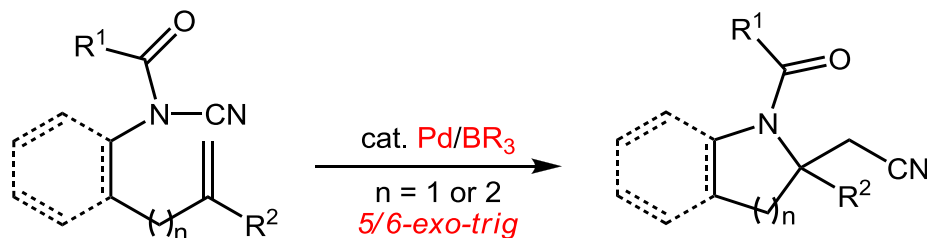


Zhang, Q



Zeng, X

Intramolecular Aminocyanation



Nakao, Y. J

Cyanofunctionalization reactions across unsaturated carbon-carbon bonds have been studied extensively because of their utility in accessing highly functionalized nitriles, which are found in a number of pharmaceutical drugs, agrochemicals, and optoelectronic materials as well as synthetic intermediates for carboxylic acids, esters, amides, and amines. Starting from simple and readily available substrate sets, silylcyanation, germylcyanation, stannylcyanation, borylcyanation, carbocyanation, thiocyanation, bromocyanation, and most recently oxycyanation of alkynes and/or alkenes have been realized by metal catalysis to give nitriles having a functional group at the position β to the cyano group.

We report herein the intramolecular aminocyanation of alkenes through N–CN bond activation by cooperative palladium/boron catalysis. **We also demonstrate the first catalytic enantioselective aminocyanation reaction.** Aminocyanation had never been achieved until the very recent report on the three-component coupling of alkenes, *N*-fluorobenzenesulfonimide, and Me₃SiCN by copper catalysis to achieve net aminocyanation. **The transformation serves as an ideal protocol to directly give β-aminonitriles, which function as synthetic precursors for highly important building blocks such as β-amino acids and 1,3-diamines .**

In summary, we have developed an intramolecular aminocyanation of alkenes by palladium/boron catalysis. The transformation allows for simultaneous installation of a tetra- or trisubstituted carbon and a cyano group through N–CN bond activation to afford variously substituted indolines and pyrrolidines, including optically active examples, which can be of interest as synthetic building blocks. Synthetically, the aminocyanation demonstrated herein can be a CO- and/or oxidant-free alternative to alkene aminocarbonylation and other aminofunctionalization reactions catalyzed by palladium. Current efforts are directed toward further development of the enantioselective aminocyanation and more detailed mechanistic studies.