Aryl C-CN Insertions

1-25-2025

Group Meeting

Jacob Grygus
Texas A&M University

Outline

Part I. Characterization of Aryl C-CN Insertion

Part II. Aryl C-CN Bond Activation in Synthesis

Historical Precedent

- **DuPont (1971)**

We find some parallel to the reactivity of $Pt[P(C_2H_5)_3]_4$ in the chemistry of $Ni[P(C_2H_5)_3]_4$.[12] This complex, an off-white crystalline compound, was formed almost quantitatively by reaction of bis(1,5-cyclooctadiene)nickel(0) with triethylphosphine. It dissolved in hydrocarbon solvents with ligand dissociation to give intensely purple solutions of $Ni[P(C_2H_5)_3]_3$. This tris complex reacted smoothly with chlorobenzene and with benzonitrile *at room temperature* to give the corresponding *trans*-$C_6H_5NiX[P(C_2H_5)_3]_2$ compounds.[13] Work is in progress to examine other aspects of reactive d^{10} complexes of Ni, Pd, and Pt.

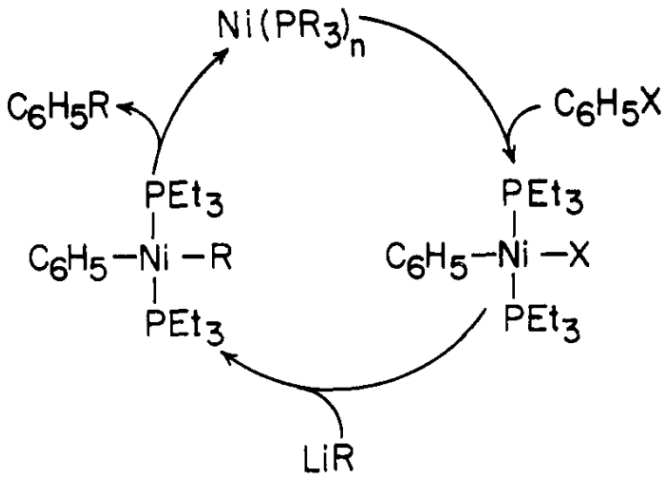
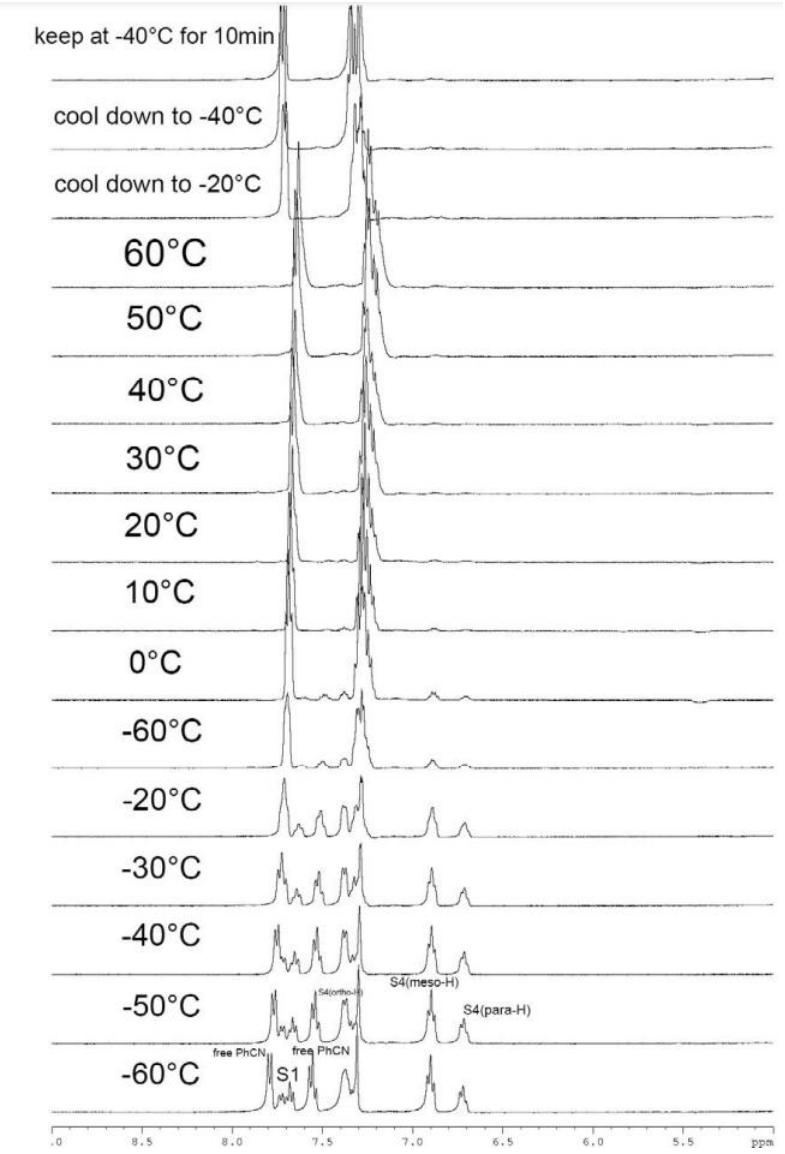


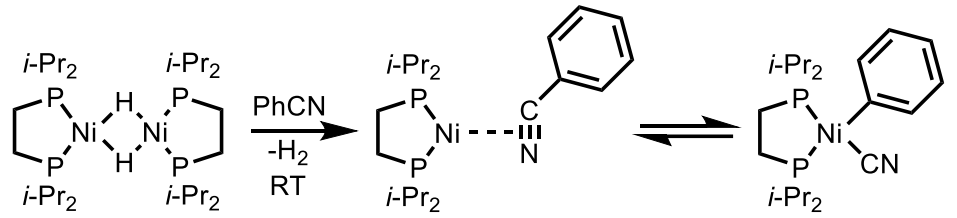
Figure 1. Cycle for alkylation, arylation, and cyanation of halobenzenes catalyzed by zerovalent nickel complexes. R = alkyl, aryl, CN.

Muetterties, E. L.; Gerlach, D. H.; Kane, A. R.; Parshall, G. W.; Jesson, J. P. *J. Am. Chem. Soc.* ***1971***, *14*, 3543-3544.

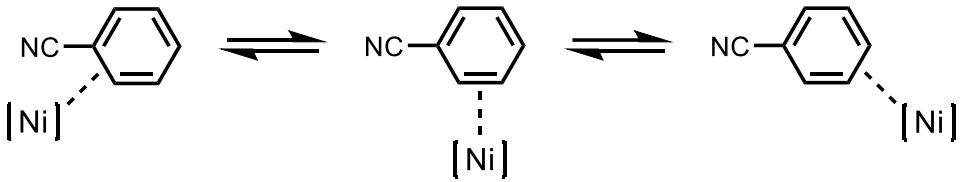
Parshall, G. W. *J. Am. Chem. Soc.* ***1974***, *8*, 2360-2366.

Characterization of Ni Insertion into Benzonitrile





S1 S5

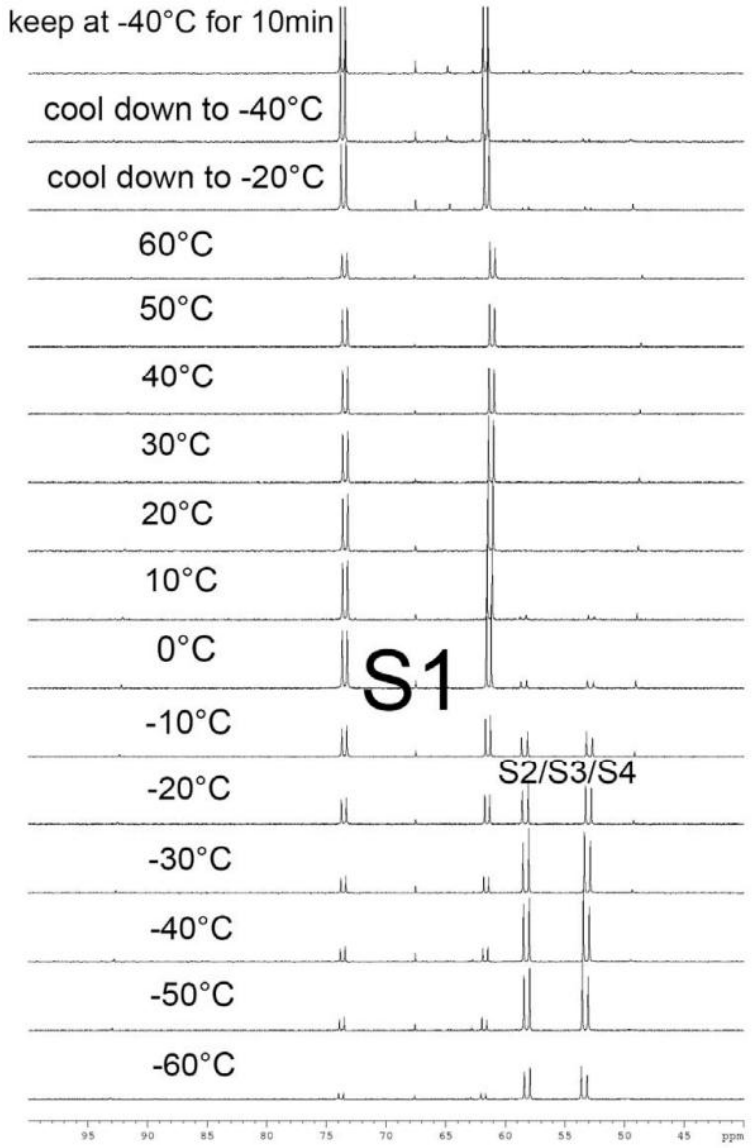


S2 S3 S4

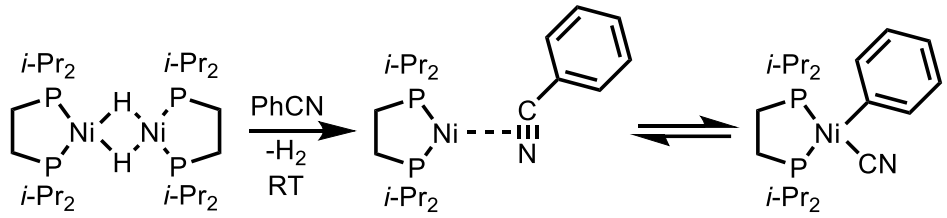
^{1H} NMR

Ateşin, T. A.; Li, T.; Lachaize, S.; García, J. J.; Jones, W. D. *Organometallics* ***2008***, *27*, 3811-3817.

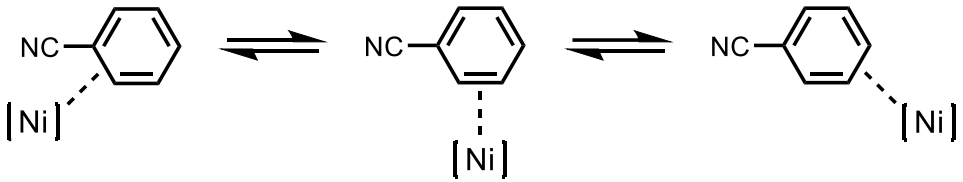
Characterization of Ni Insertion into Benzonitrile



^{31}P NMR



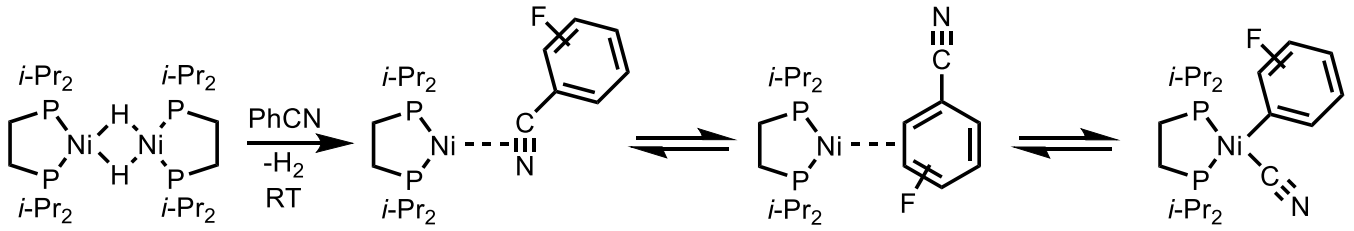
S1 S5

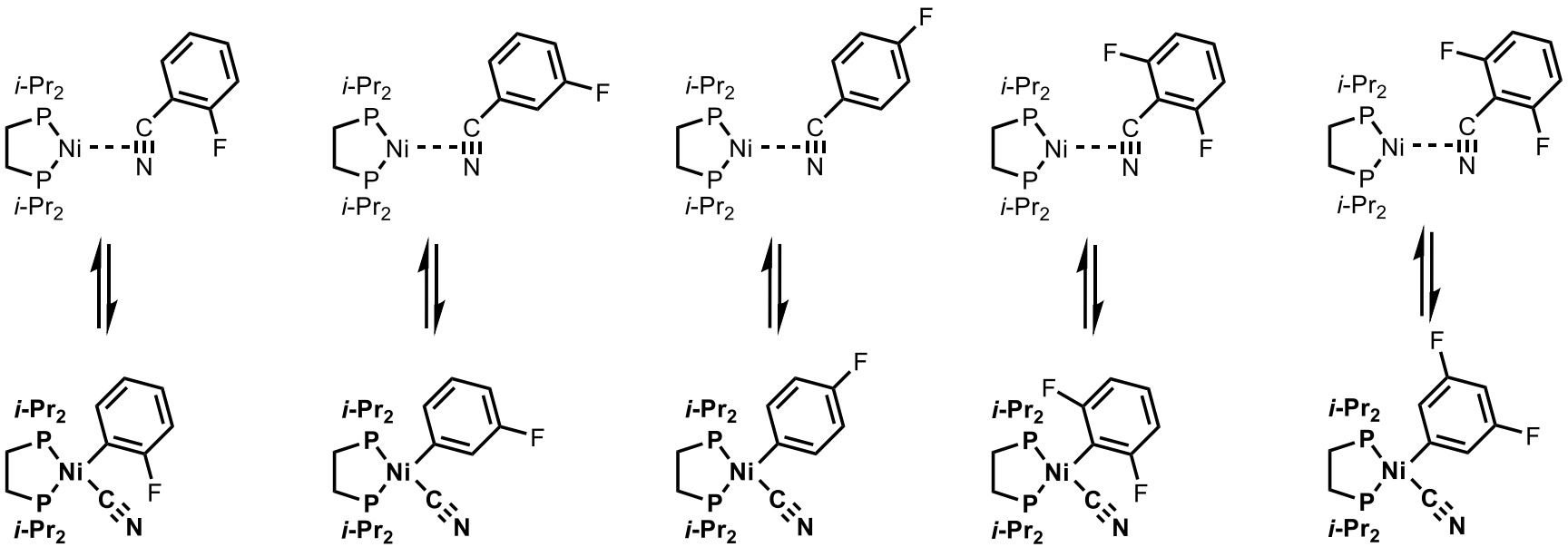


S2 S3 S4

Ateşin, T. A.; Li, T.; Lachaize, S.; García, J. J.; Jones, W. D. *Organometallics* ***2008***, *27*, 3811-3817.

Fluoro-Substituted Benzonitrile C-CN Insertion





1 day, 74 °C
99%

5 days, 43.7 °C
99%

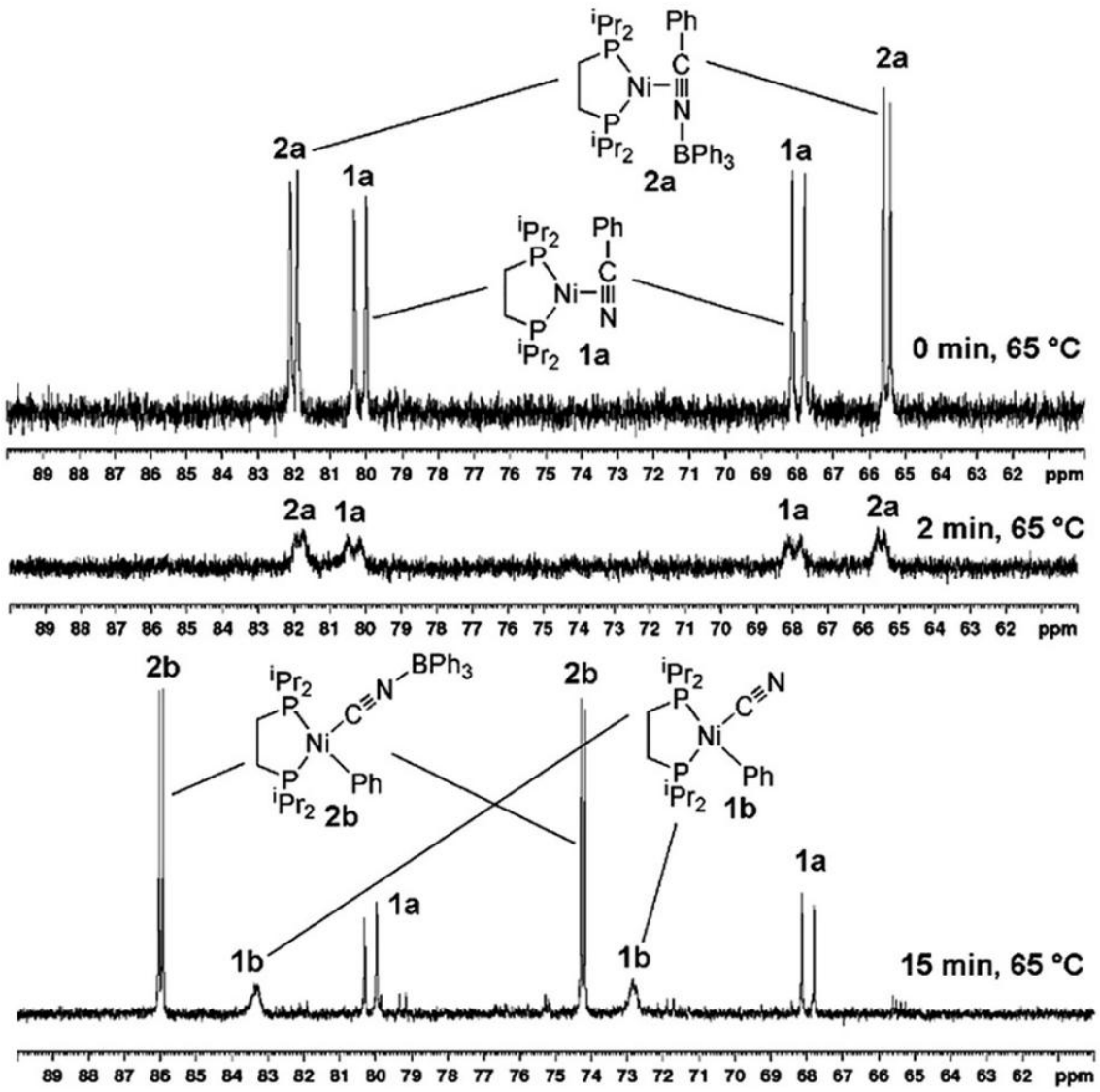
"several days", 70 °C
~85%

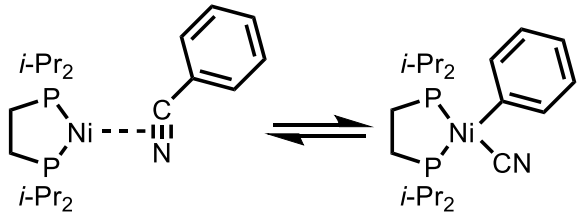
1 Month, 70 °C
100%

15 h, 70 °C
~68%

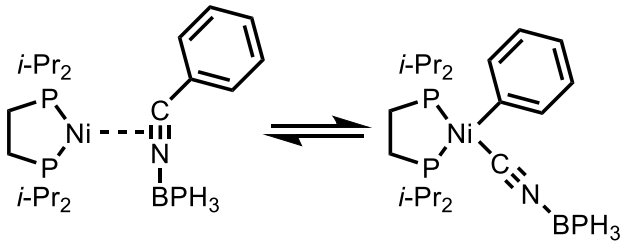
Lachaize, S.; Gallegos, C. D.; Antonio, J. J.; Atesin, A. C.; Ateşin, T. A.; Jones, W. D. *Organometallics* ***2023***, *15*, 2134-2147.

Lewis Acid Assisted Aryl C-CN Cleavage





1a 1b

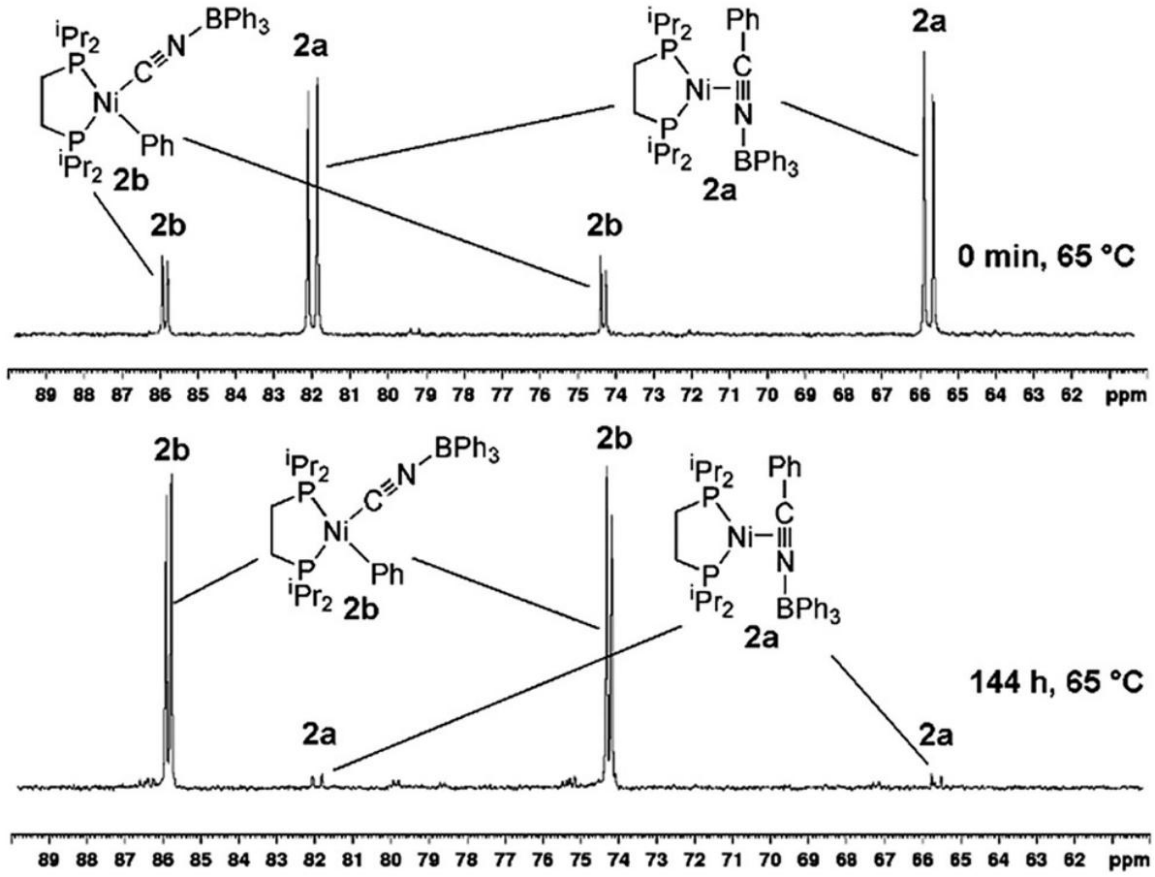


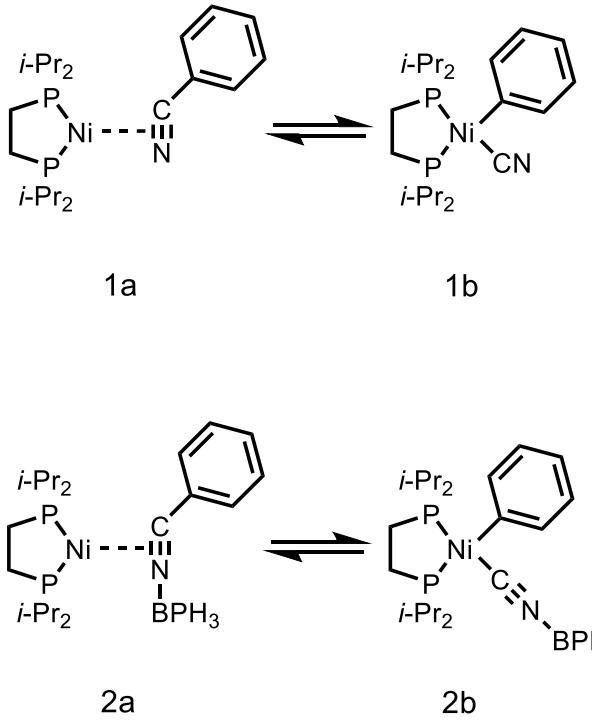
2a 2b

[(dippe)NiH]$_2$, (1.0 equiv) benzonitrile (2.0 equiv), and BPh_3 (0.5 equiv)

Swartz, B. D.; Brennessel, W. W.; Jones, W. D. *Synlett* ***2018***, *29*, 747-753.

Lewis Acid Assisted Aryl C-CN Cleavage





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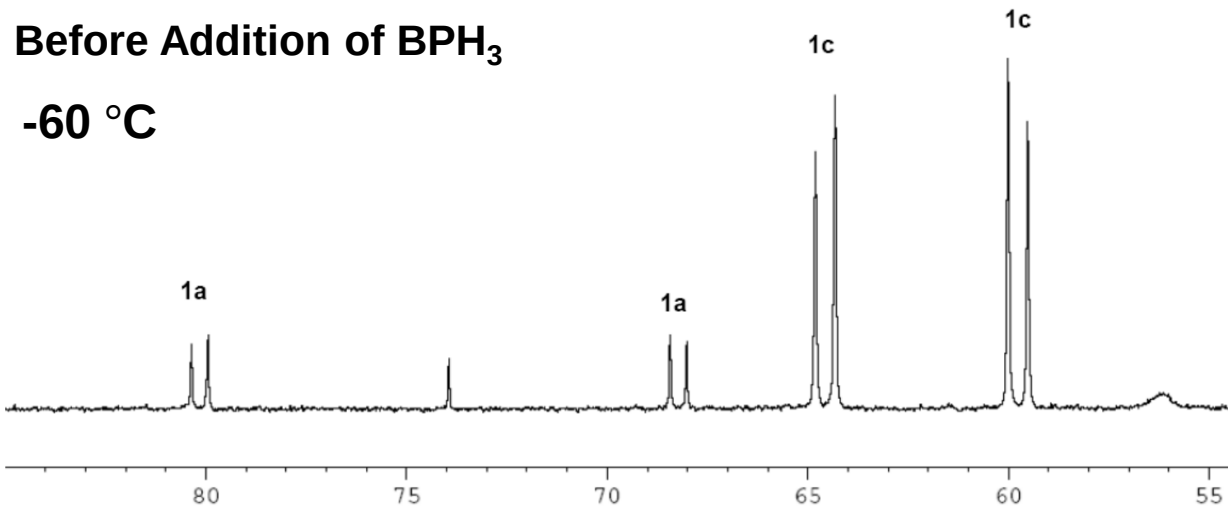

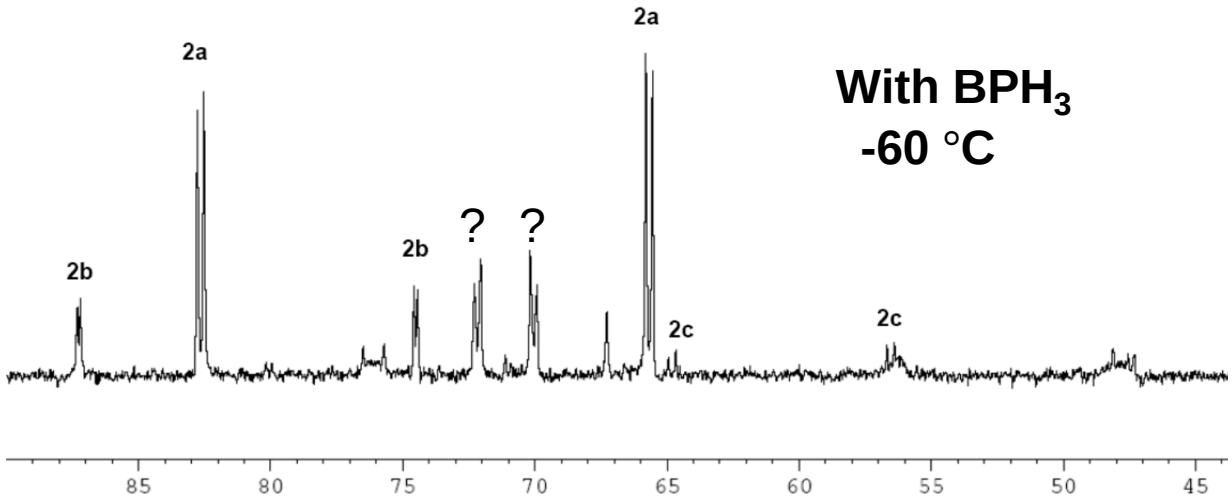

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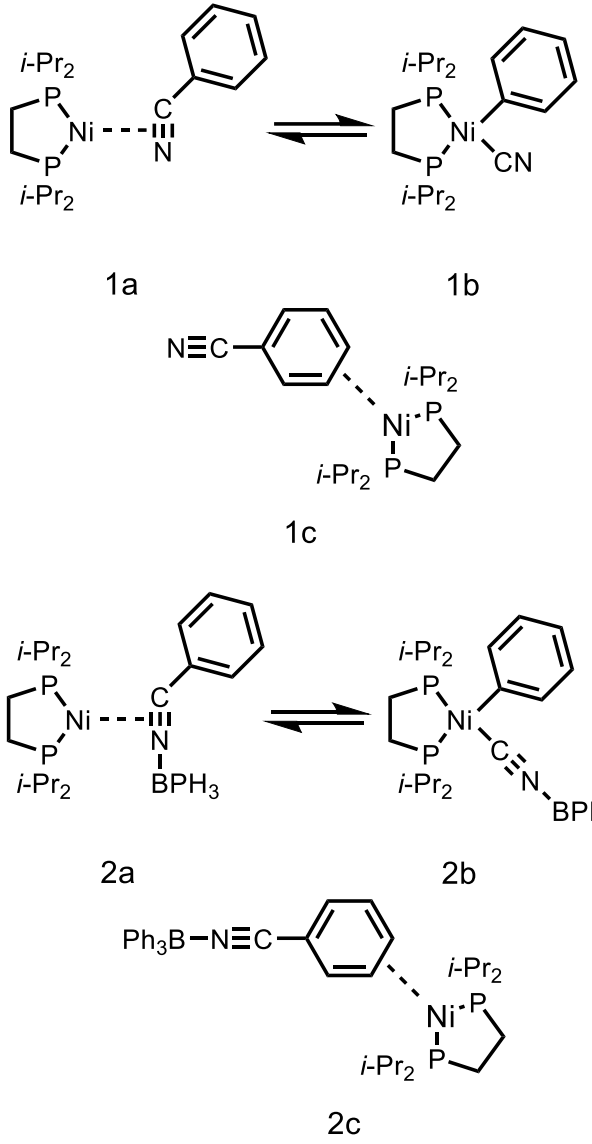

Swartz, B. D.; Brennessel, W. W.; Jones, W. D. *Synlett* ***2018***, *29*, 747-753.

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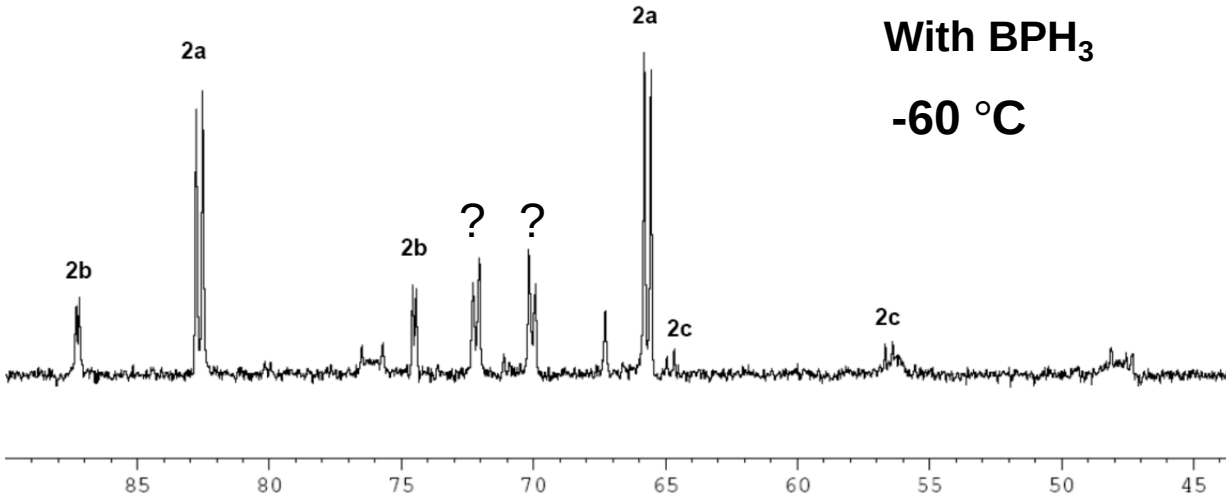
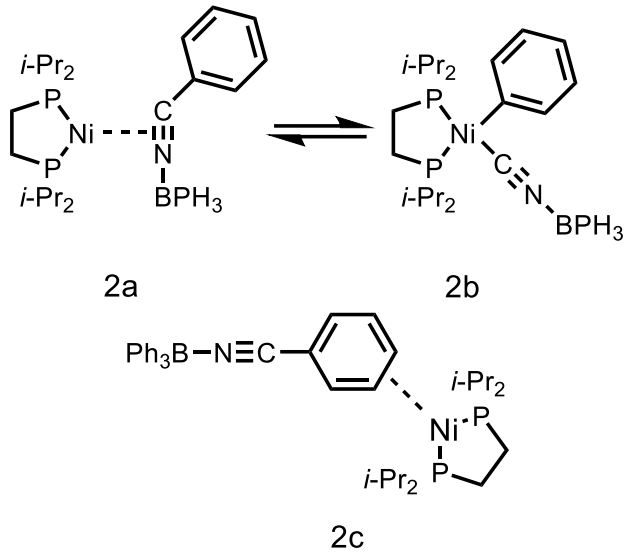
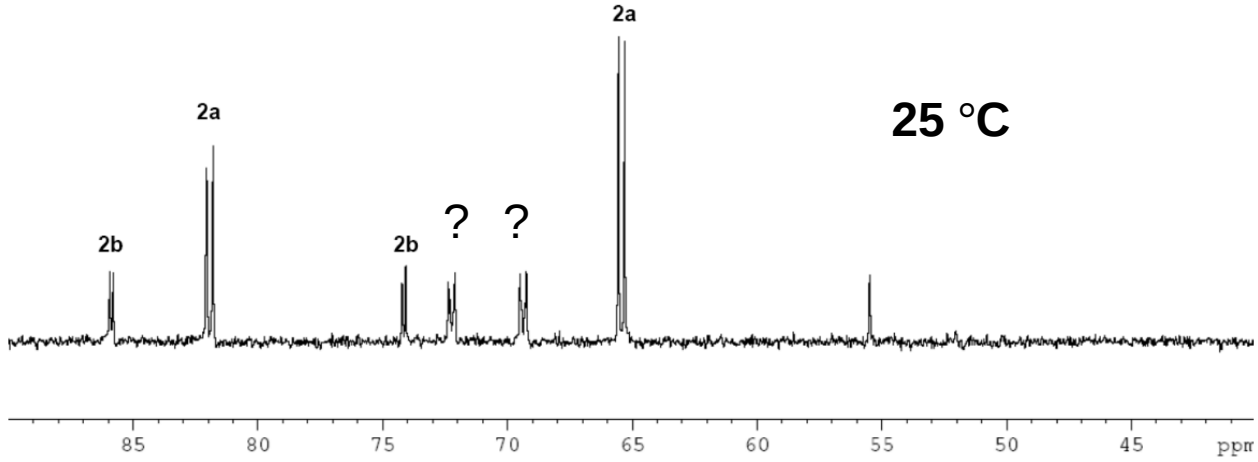




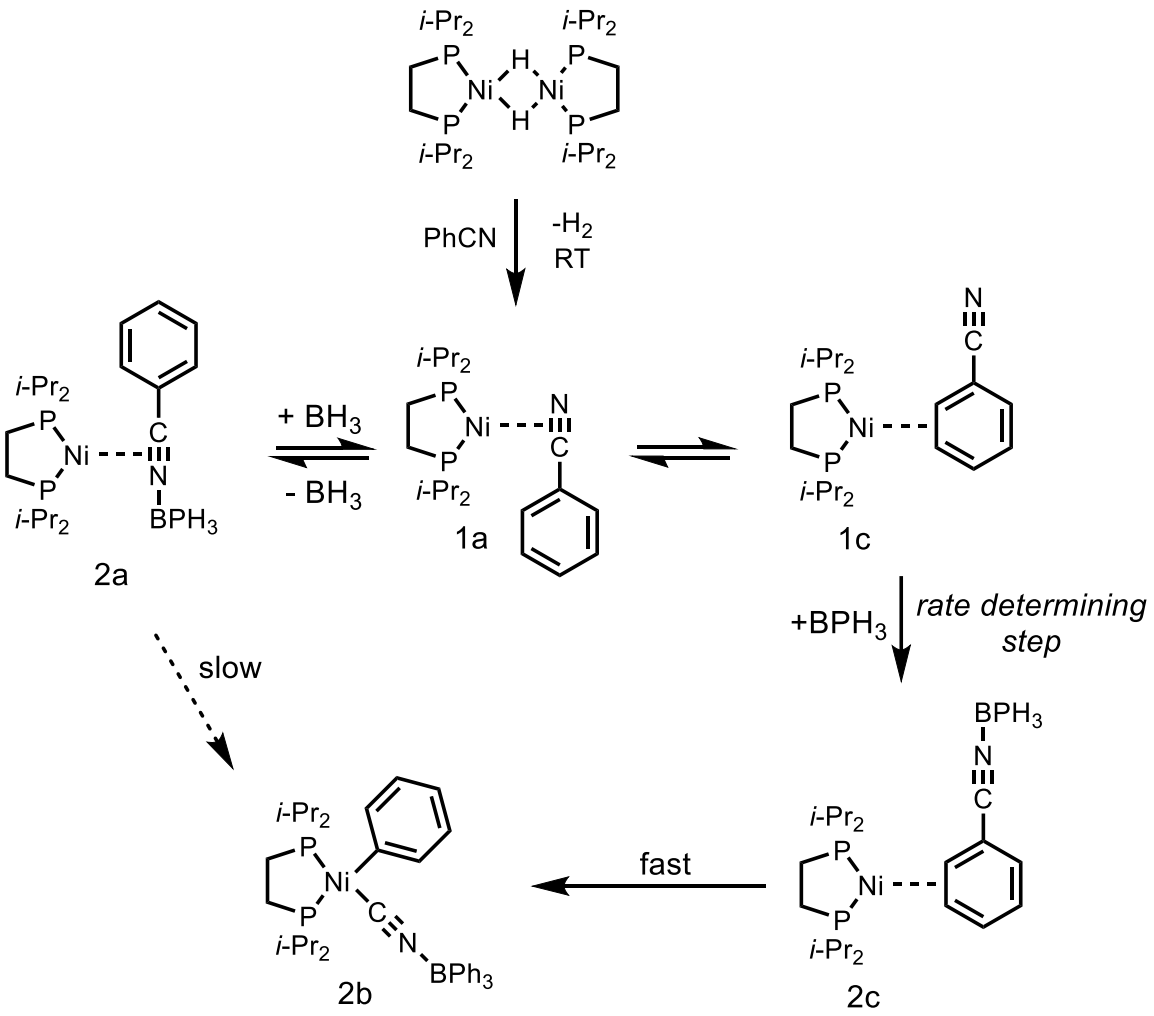


- 2b, 2c existing concurrently is significant

$[(dippe)NiH]_2$, (1.0 equiv) benzonitrile (2.0 equiv), and BPh_3 (1.0 equiv)

Swartz, B. D.; Brennessel, W. W.; Jones, W. D. *Synlett* ***2018***, *29*, 747-753.

Proposed Mechanism



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Outline

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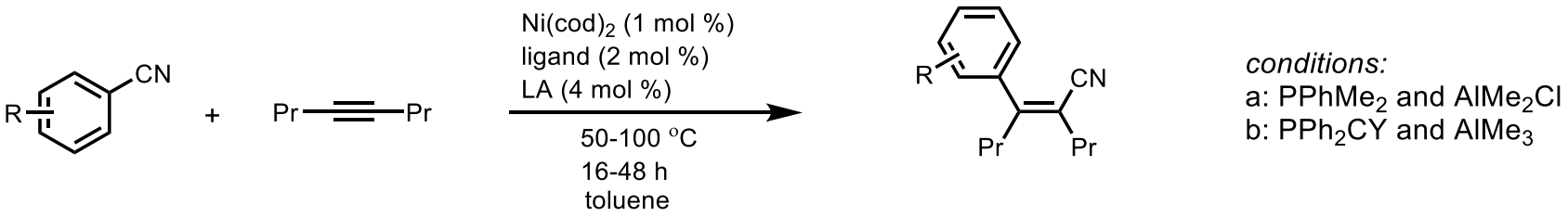
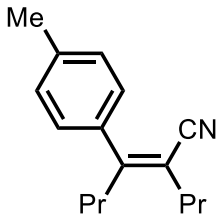
Part II. Aryl C-CN Bond Activation in Synthesis

Ni/Lewis Acid-Catalyzed Arylcyanation





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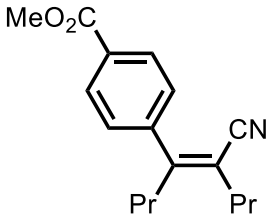
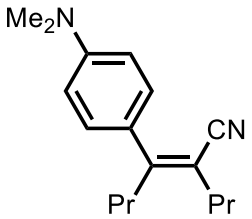


93%[a]



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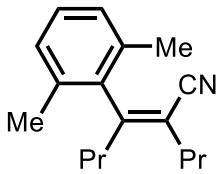

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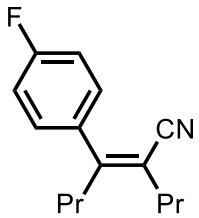

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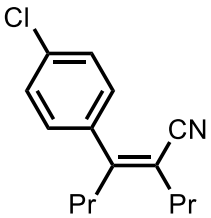

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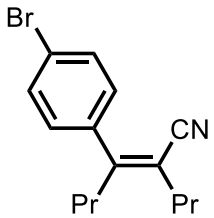
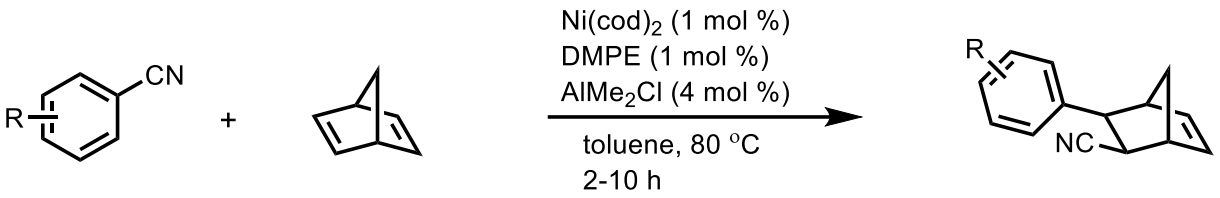
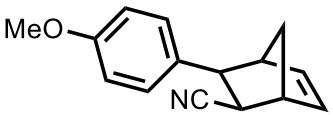


72%[a]

Yada, A.; Ebata, S.; Idei, H.; Zhang, D.; Nakao, Y.; Hiyama, T. *Bull. Chem. Soc. Jpn.* ***2010***, *10*, 1170-1184.

Ni/Lewis Acid-Catalyzed Arylcyanation





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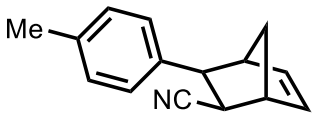

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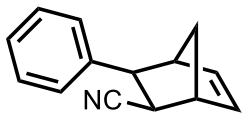

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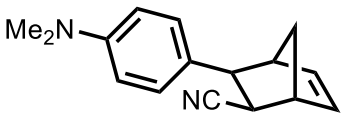

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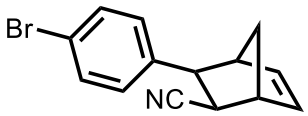

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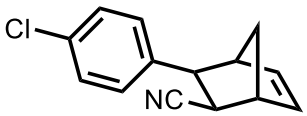

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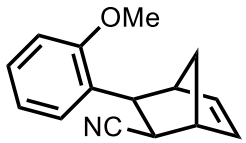

58%

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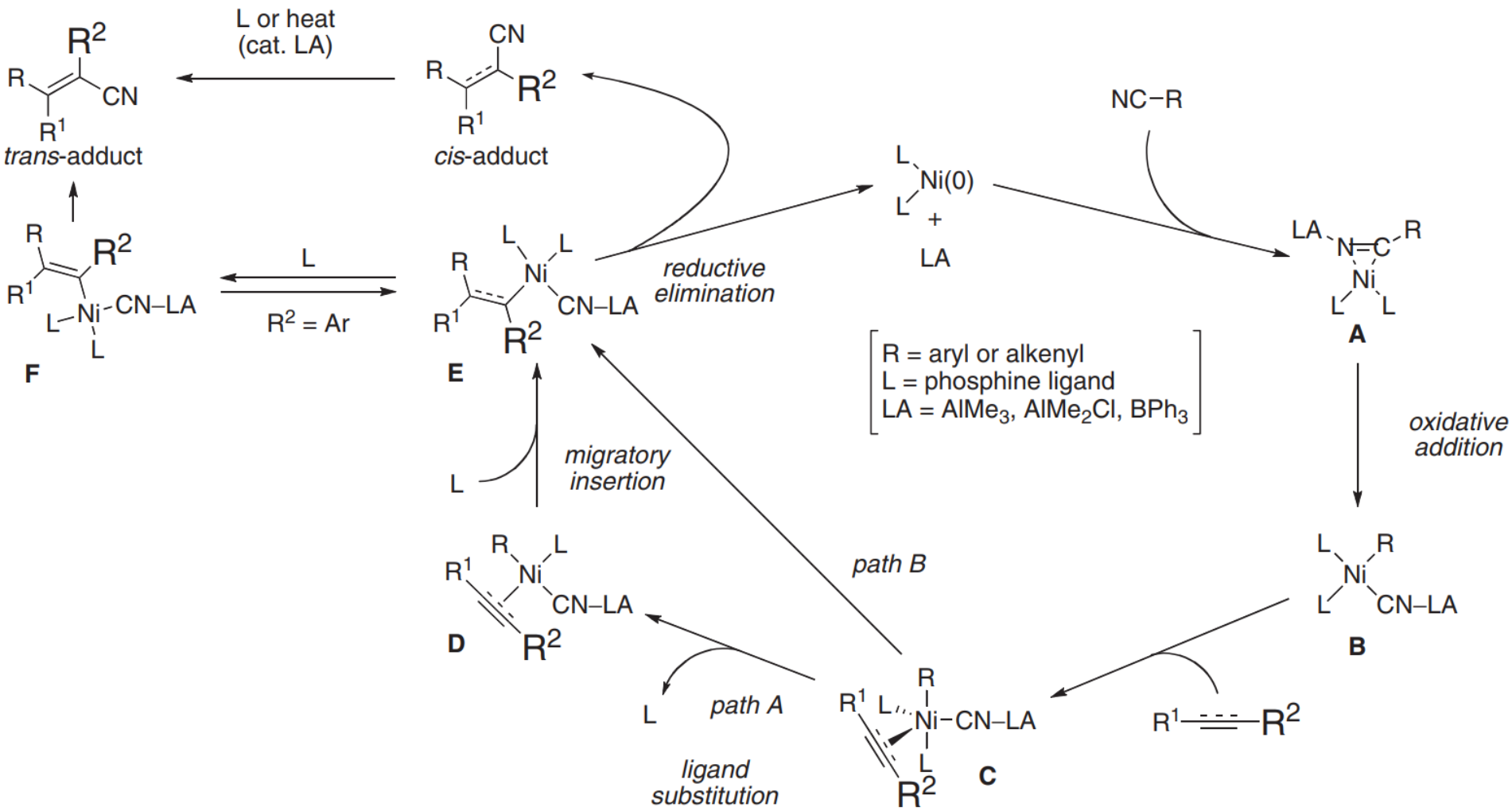
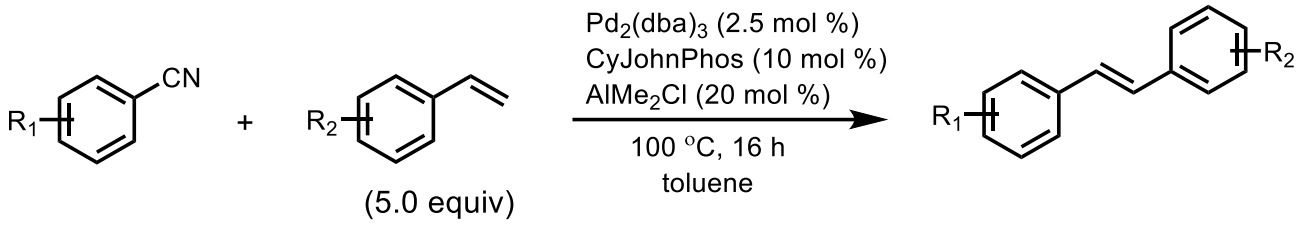
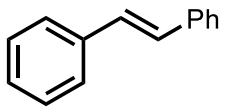
Ni/Lewis Acid-Catalyzed Arylcyanation



Yada, A.; Ebata, S.; Idei, H.; Zhang, D.; Nakao, Y.; Hiyama, T. *Bull. Chem. Soc. Jpn.* ***2010***, *10*, 1170-1184.

Mizoroki-Heck-Type Reactions of Aryl Cyanides





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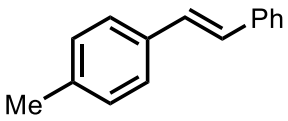

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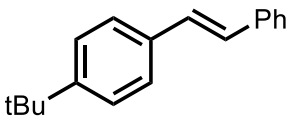

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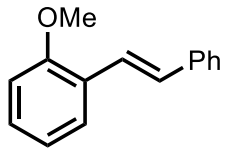

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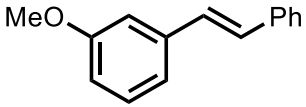

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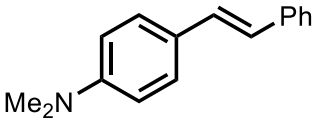

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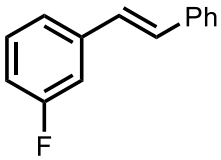

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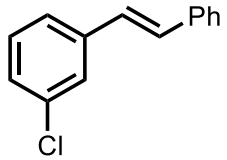
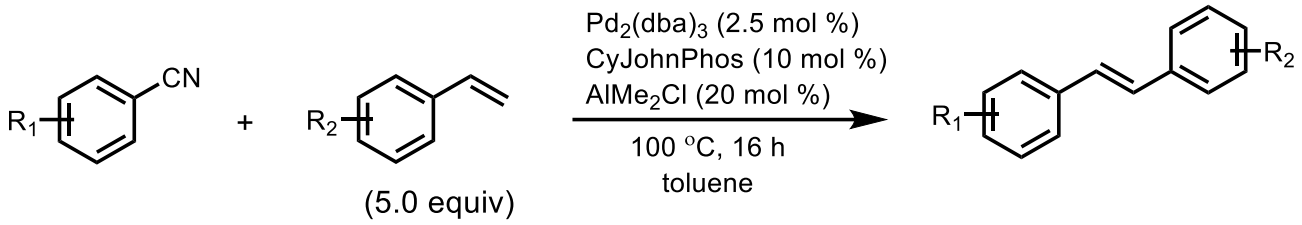
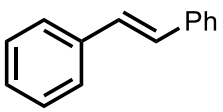


53%

Fang, X.; Yu, P.; Cerai, G. P. Morandi, B. *Chem. Eur. J.* ***2016***, *22*, 15629-15633.

Mizoroki-Heck-Type Reactions of Aryl Cyanides





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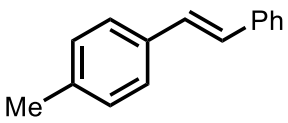

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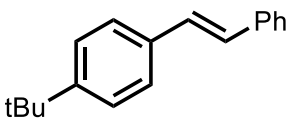

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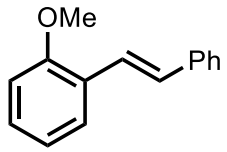

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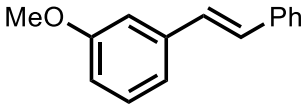

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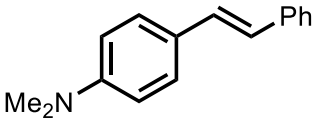

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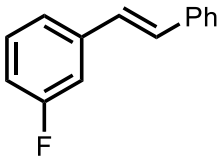

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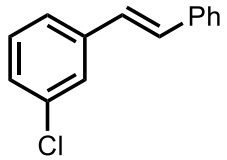

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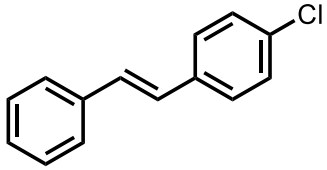

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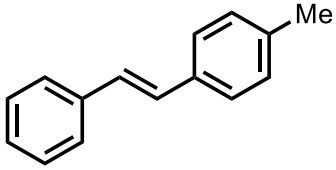

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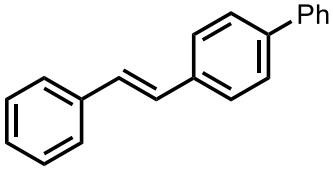

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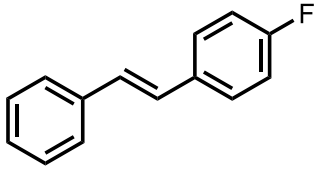

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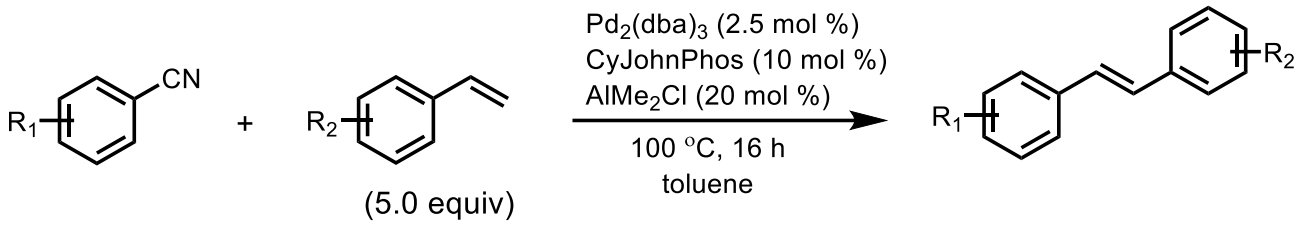
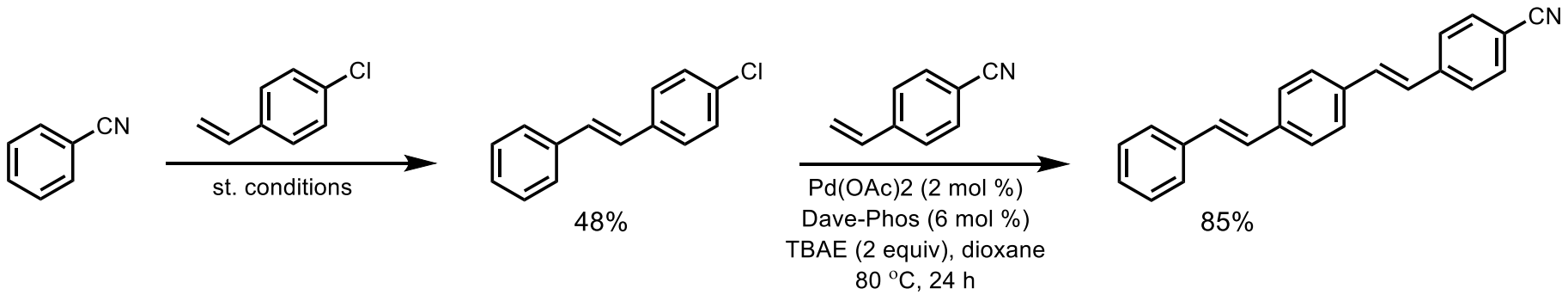
Fang, X.; Yu, P.; Cerai, G. P. Morandi, B. *Chem. Eur. J.* ***2016***, *22*, 15629-15633.

Two-Step Synthesis of Orthogonal Heck Reactions



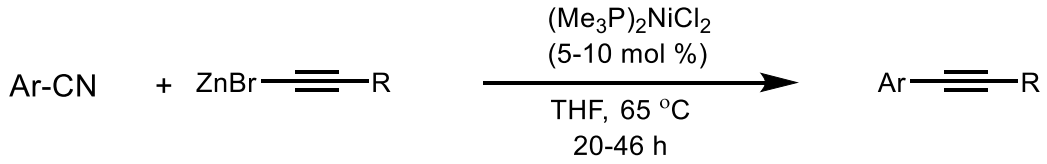


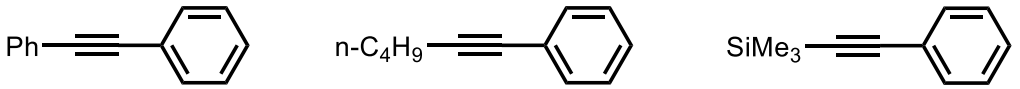
CN cleavage in the presence of Cl

Cl cleavage in the presence of CN

Fang, X.; Yu, P.; Cerai, G. P. Morandi, B. *Chem. Eur. J.* ***2016***, *22*, 15629-15633.

Ni-Catalyzed Alkynylation of Benzonitriles





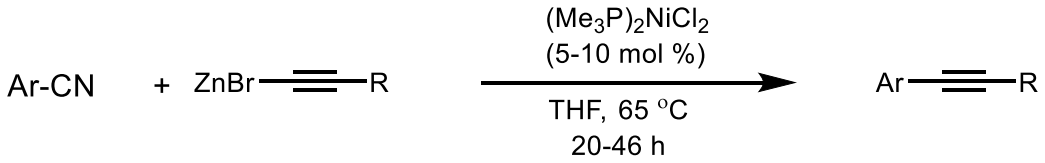
79% 95% 87%

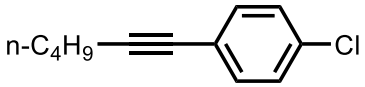
45% 75% 74% 91%

80% 65%*

Penney, J. M.; Miller, J. A. *Tetrahedron Letters* **2004**, *45*, 4989-4992.

Ni-Catalyzed Alkynylation of Benzonitriles





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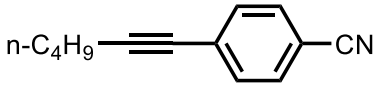

N.D.

“Remarkable”

Penney, J. M.; Miller, J. A. *Tetrahedron Letters* **2004**, *45*, 4989-4992.

Conclusions

- Low valent Ni(0) systems are very effective at aryl C-CN insertion
- Lewis Acids greatly accelerate oxidative addition into aryl C-CN bonds
- Aryl C-CN bonds can be activated, in some cases with excellent chemoselectivity!