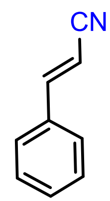
Content

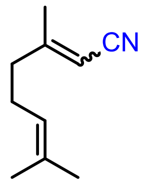
- Introduction of nitriles
- Shuttle catalysis
- Transfer hydrocyanation

The application of nitriles

香料



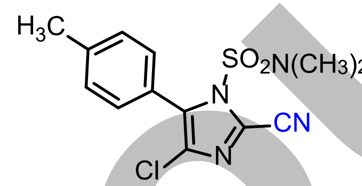
肉桂腈



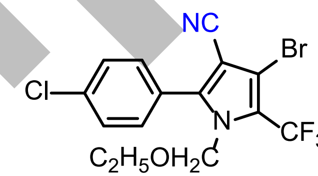
柠檬腈

Keller, W. et al. *Ber. Dtsch. Chem. Ges* **1932**, *65*, 1677.

农药



氯霜唑

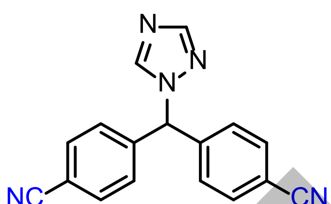


AC30360

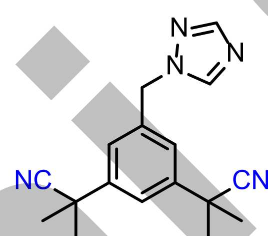
Froberger, C. F. et al. *J. Org. Chem*. **1957**, *22*, 1050.

Djandjighian, L. et al. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 6213.

医药



来曲唑

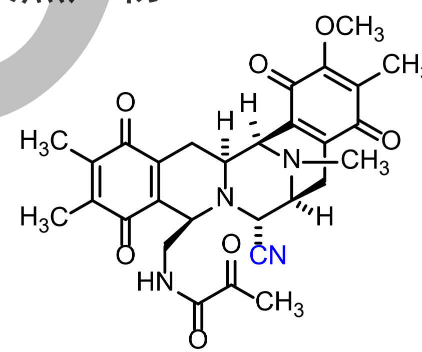


阿那曲唑

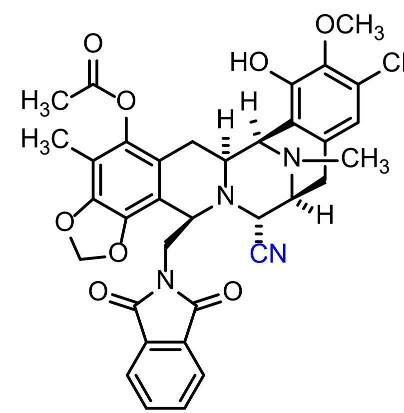
Bleasdale, J. E. et al. *J. Med. Chem*. **2002**, *45*, 1785.

Sanno, Y. et al. *J. Med. Chem*. **1977**, *20*, 141.

天然产物



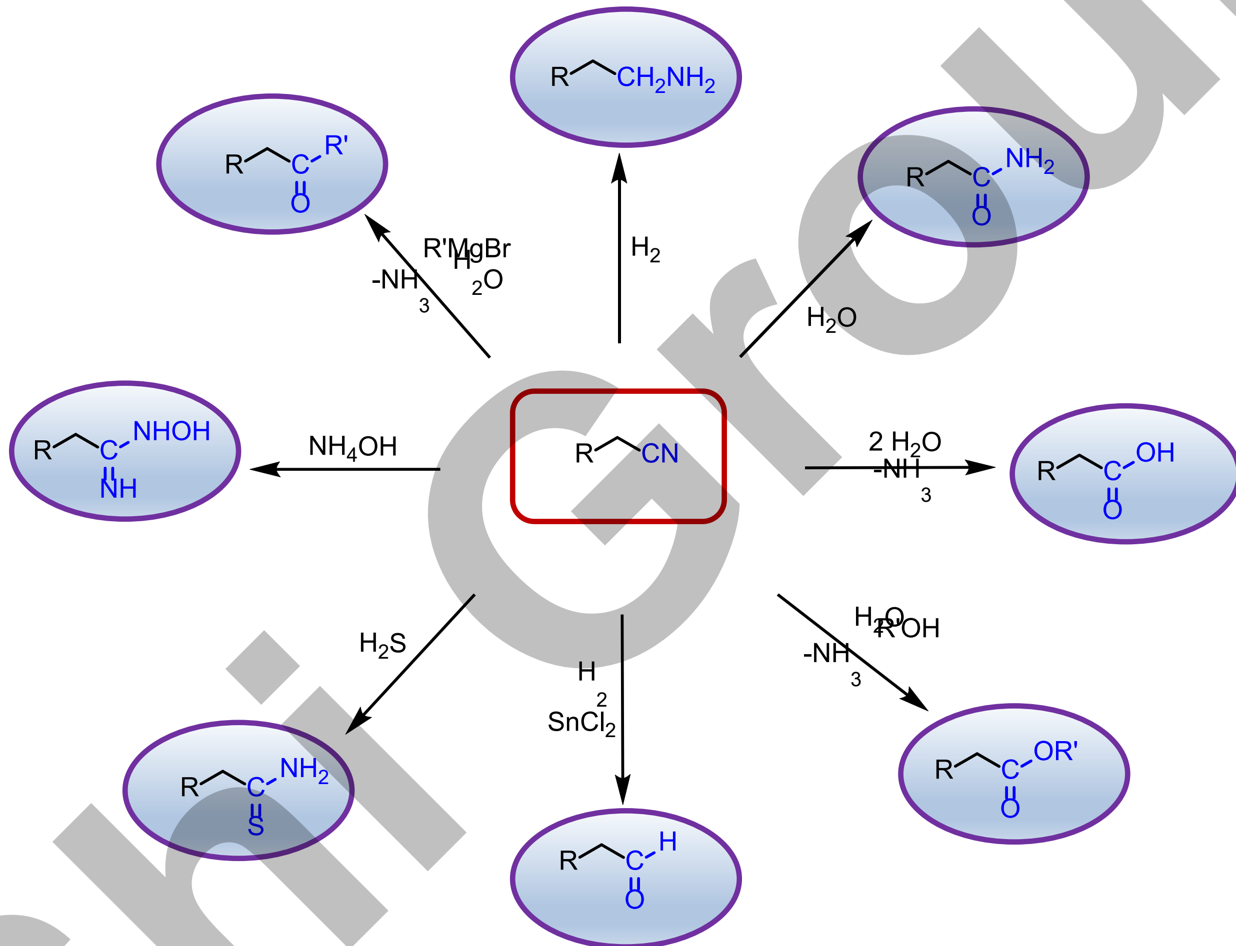
番红霉素A



Et-743

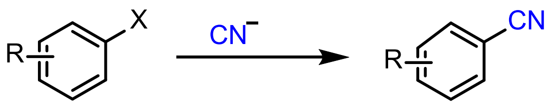
Corey, E. J. et al. *Org. Lett*. **1999**, 1, 75.

The derivatives of nitriles



Vogt, D. et al. *ChemCatChem* **2010**, *2*, 590.

The synthesis of nitriles

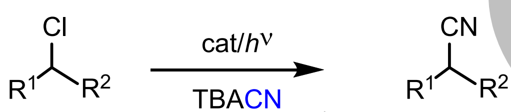


X = I, Br, Cl, OMs, OTs

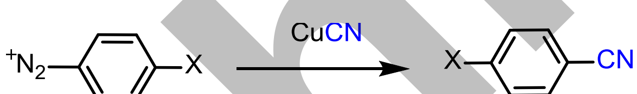
Lee, J. B. et al. *J. Org. Chem.* **1967**, *32*, 855.

Chatani, T. et al. *J. Org. Chem.* **1986**, *51*, 4714.

Rice, K. C. et al. *Tetrahedron. Lett.* **1998**, *39*, 2907.

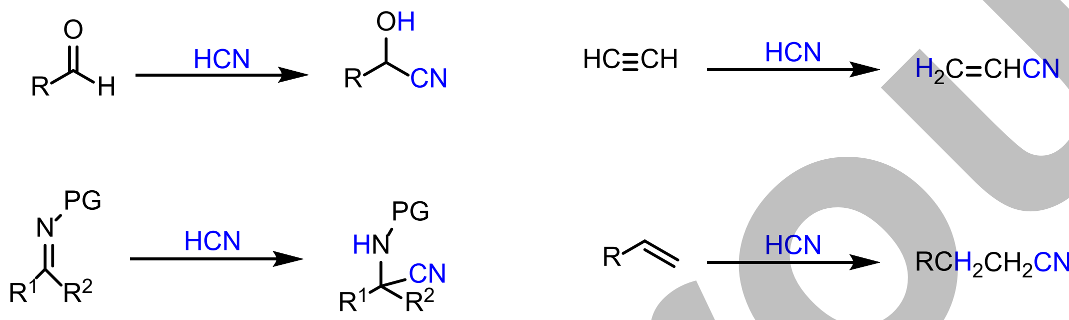


Peters, J. C. et al. *J. Am. Chem. Soc.* **2015**, *137*, 13902.



Petrovskii, P. V. et al. *J. Organomet. Chem.* **2004**, *689*, 3810.

The synthesis of nitriles

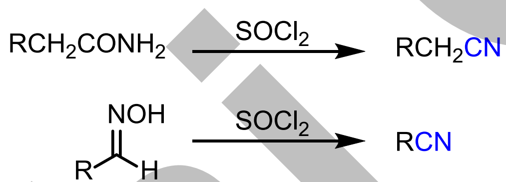


Choudary, B. M. et al. *Tetrahedron*. **2008**, *64*, 3351.

Otaka, K. et al. *J. Org. Chem*. **1991**, *56*, 6740.

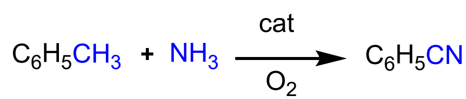
Inoue, S. et al. *J. Am. Chem. Soc*. **1992**, *114*, 7965.

Liu, Y. H. et al. *J. Am. Chem. Soc*. **2018**, *140*, 7385.



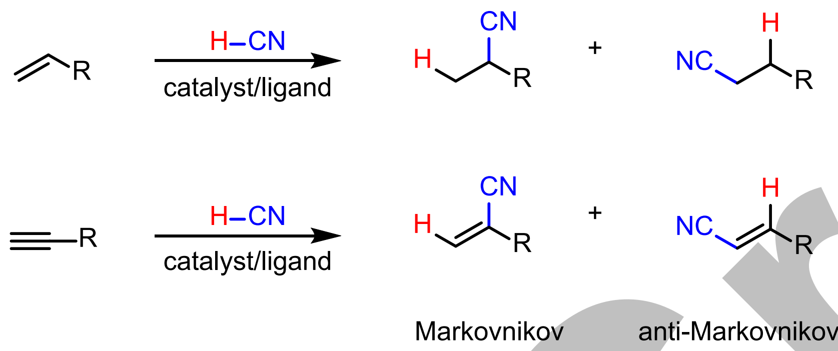
Akamanchi, K. G. et al. *J. Org. Chem*. **2007**, *72*, 662.

Mizuno, N. et al. *Angew. Chem. Int. Ed*. **2007**, *46*, 3922.



Mowry, D. F. et al. *Chem. Rev*. **1948**, *42*, 189.

Traditional hydrocyanation of alkenes and alkynes



Vogt, D. et al. *Chem. Commun.* **2010**, *46*, 8325.
Jacobsen, E. J. et al. *J. Am. Chem. Soc.* **2008**, *130*, 12594.

HCN: Toxicity!

Corrosive!

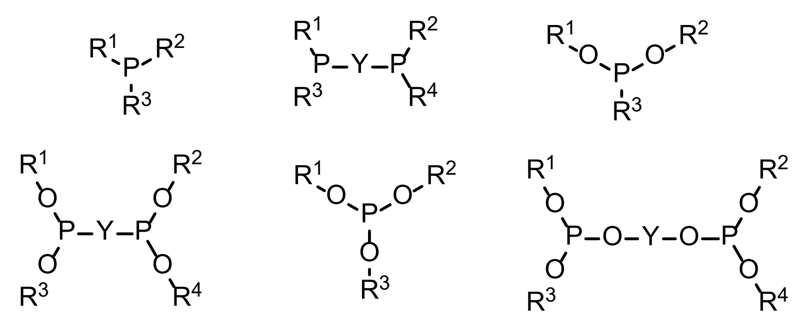
Explosive!

Poor selectivity!

Metal

钴 Co	镍 Ni	铜 Cu
铑 Rh	钯 Pd	汞 Hg

Ligand



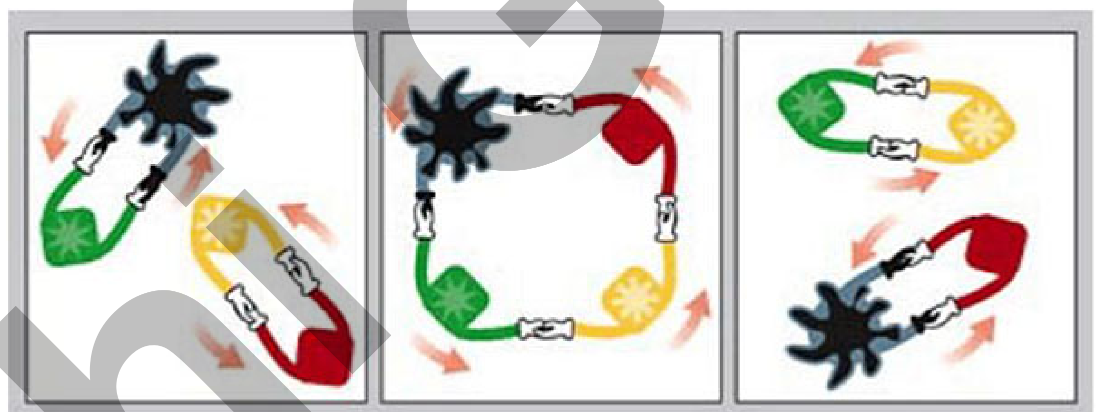
New strategy for hydrocyanation of alkenes and alkynes

Alkene metathesis

Richard Schrock

Robert H. Grubbs

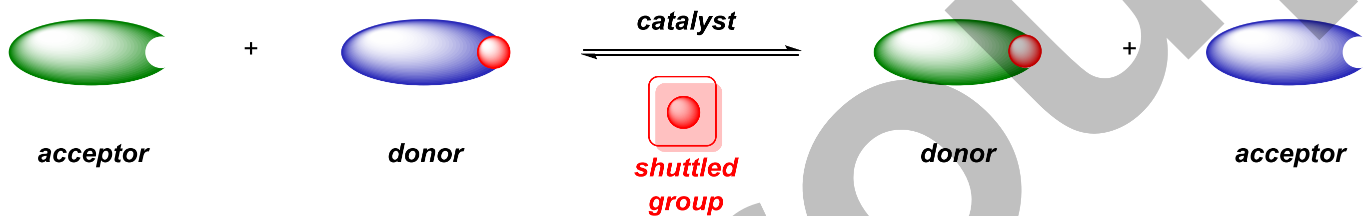
Yves Chauvin



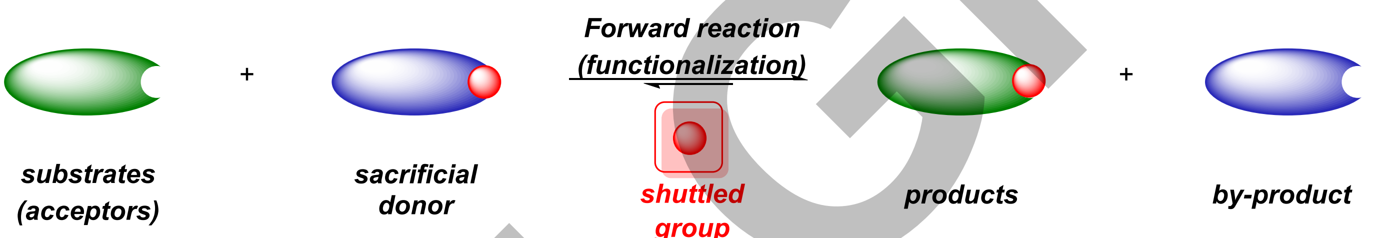
Chauvin, Y. et al. *Makromol Chem*, **1971**, *141*, 161.
Schrock, R. et al. *J. Am. Chem. Soc.* **1981**, *103*, 1440.
Grubbs, R. H. et al. *J. Am. Chem. Soc. 1992, 114,* 3974.

New strategy for hydrocyanation of alkenes and alkynes

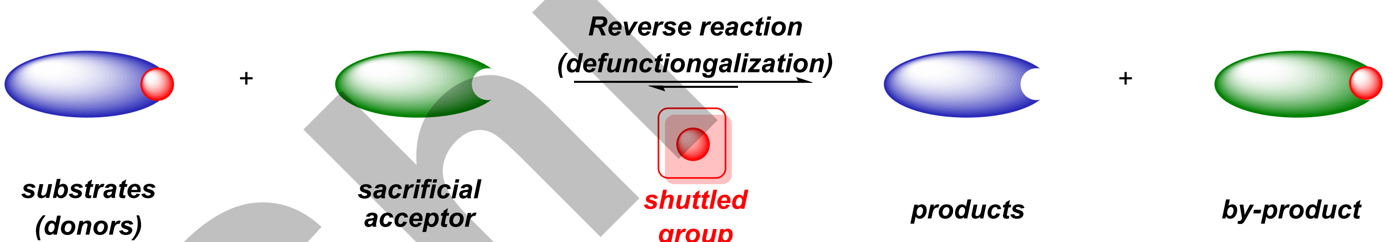
Shuttle Catalysis



Morandi, B. et al. *ACS Catal*. **2016**, *6*, 7528.



Driving forces
-gas release
-aromatization
-formation of conjugated system

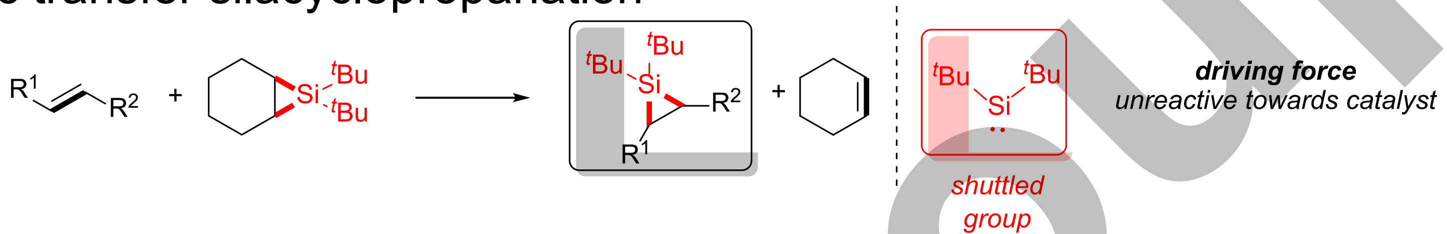


Driving forces
-strain release
-chemical trapping

Morandi, B. et al. *ACS Catal*. **2016**, *6*, 7528.

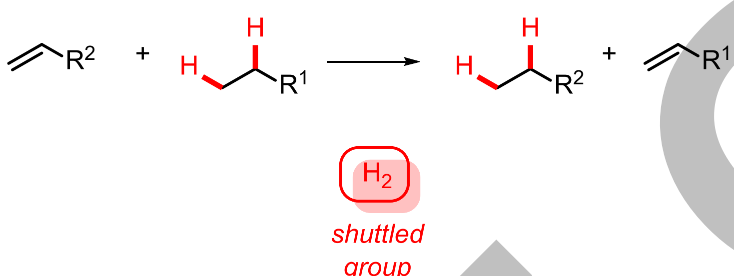
The examples of shuttle catalysis

Catalytic transfer silacyclopropanation



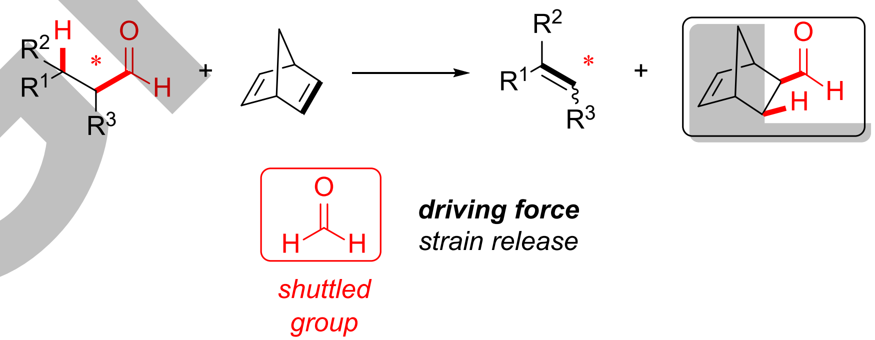
Driver, T. G. et al. *J. Am. Chem. Soc.* **2003**, *125*, 10659.

Catalytic transfer hydrogenation



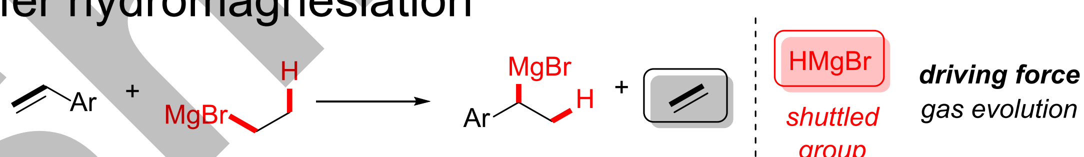
Wang, D. et al. *Chem. Rev.* **2015**, *115*, 6621.

Catalytic transfer hydroacylation



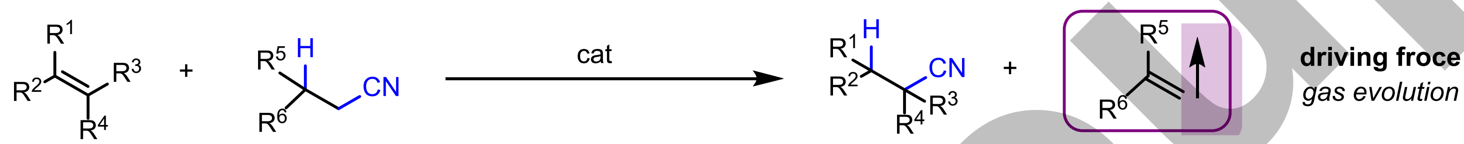
Murphy, S. K. et al. Science **2015**, *347*, 56.

Catalytic transfer hydromagnesiation

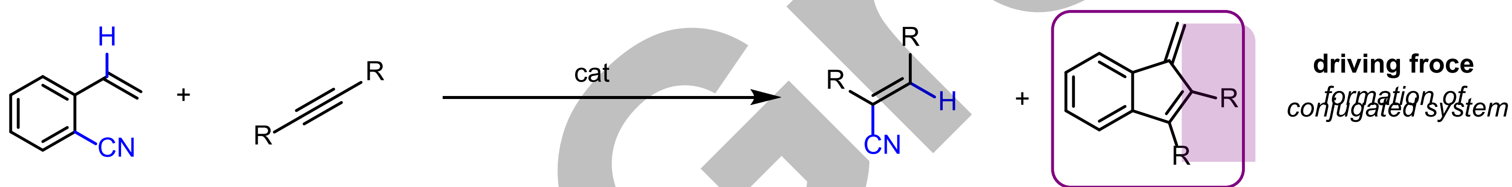


Greenhalgh, M. D. et al. *J. Am. Chem. Soc.* **2012**, *134*, 11900.

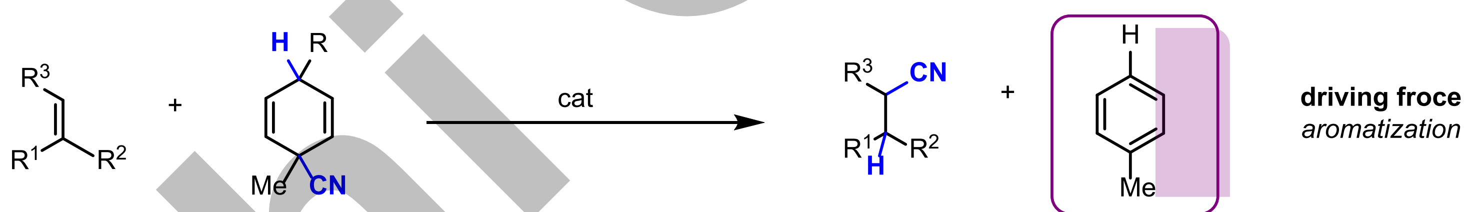
Hydrogen cyanide as shuttle catalysis



Morandi, B. et al. *Science* **2016**, *351*, 832.



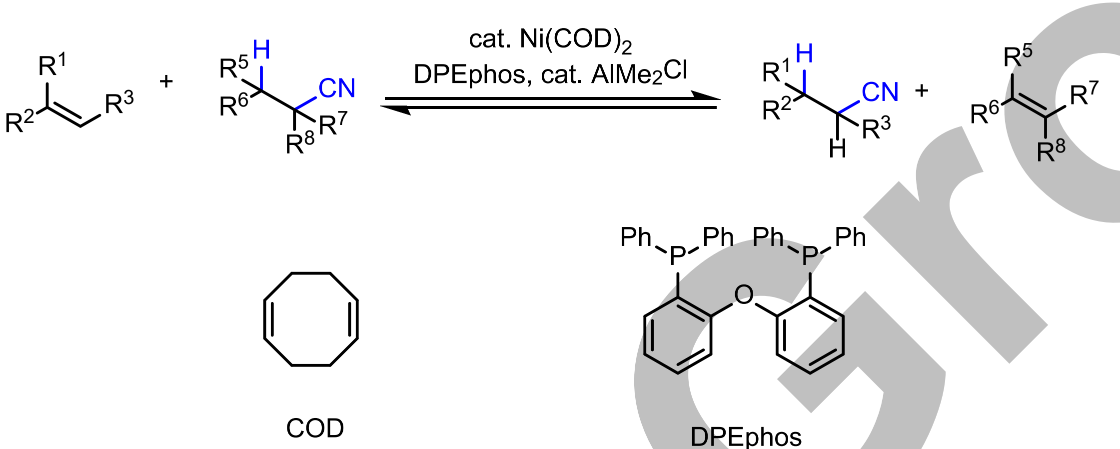
Morandi, B. et al. *Chem. Eur. J.* **2016**, *22*, 15629.



Studer, A. et al. *J. Am. Chem. Soc.* **2018**, *140*, 16353.

Oestreich, M. et al. *Angew. Chem. Int. Ed.* **2019**, *58*, 3579.

Catalytic reversible alkene-nitrile interconversion through controllable transfer hydrocyanation

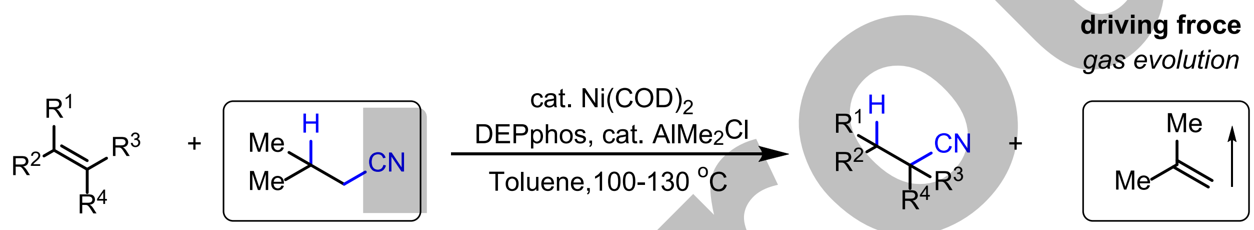


No HCN!
Reversible!
Anti-Markovnikov selectivity!
Broad subtrate scope (60 examples)!

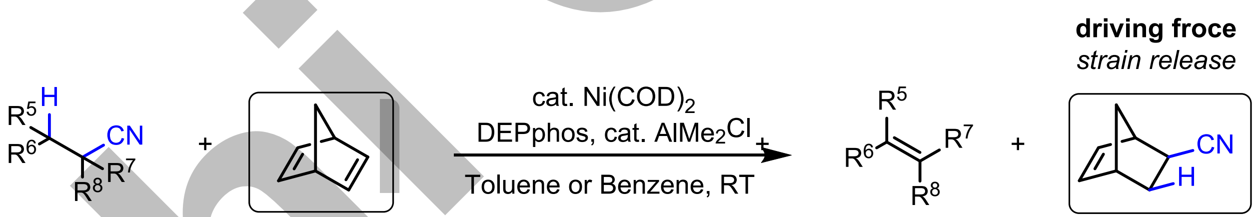
Morandi, B. et al. *Science* **2016**, *351*, 832.

Reversible transfer hydrocyanation of nitriles and alkenes

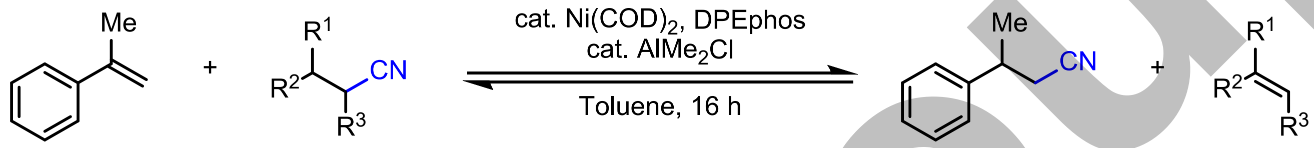
Catalytic Transfer Hydrocyanation (forward reaction)



Catalytic Retro-Hydrocyanation (reverse reaction)

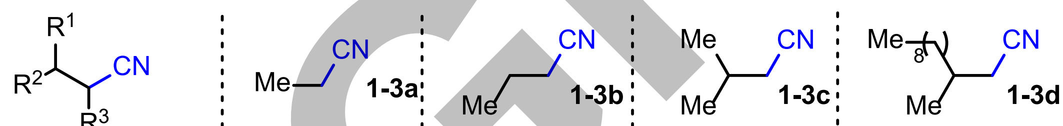


Selective manipulation of the alkene/nitrile equilibrium



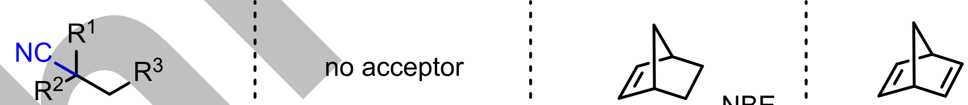
1-1 1-2 1-3 1-4

Hydrocyanation



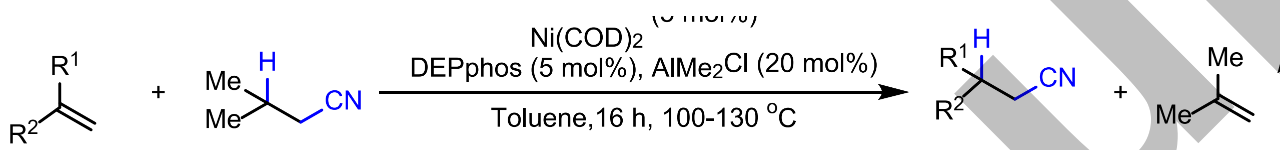
	1-3a	1-3b	1-3c	1-3d
yield (100 °C)	3%	26%	69%	60%
open system	—	41%	86%	67%

Retro-Hydrocyanation



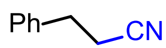
	no acceptor	NBE	NBD
yield (28 °C)	<5%	46%	99%

Exploration of hydrocyanation substrate scope

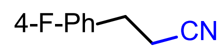


1-1 **1-2c** **1-3** **1-4c**

Aromatics

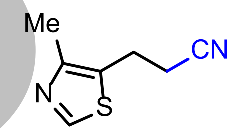


1-3e 86% (81:19)



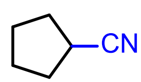
1-3f 91% (83:17)

1-3g 93% (79:21)

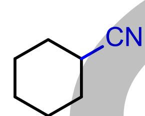


1-3h 71% (88:12)

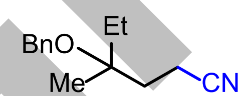
Aliphatics



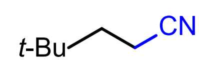
1-3i 83%



1-3j 91%

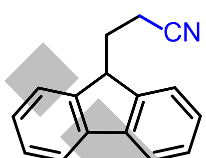


1-3k 79% (>95:5)

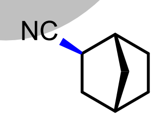


1-3l 69% (>95:5)

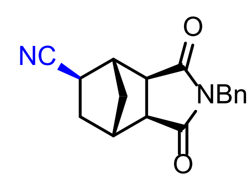
Activated



1-3m 65%



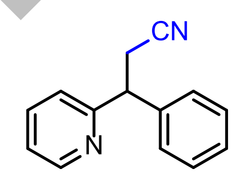
1-3n 85%



1-3o 92%

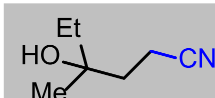
Drug Precursors

1-3p 96% (80:20)

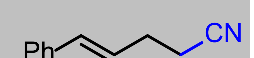


1-3q 47% (>95:5)

Unsuccessful Examples



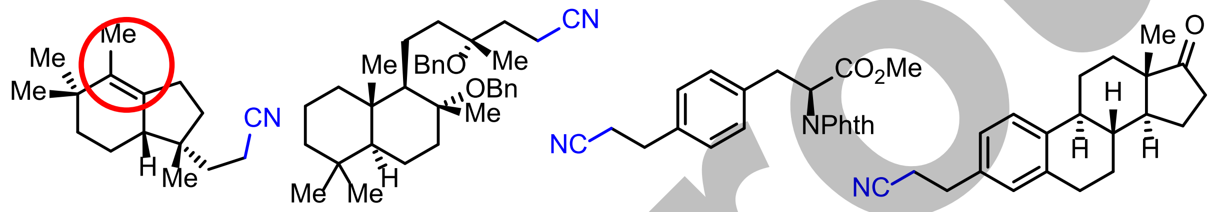
1-3r 0%



1-3s 0%

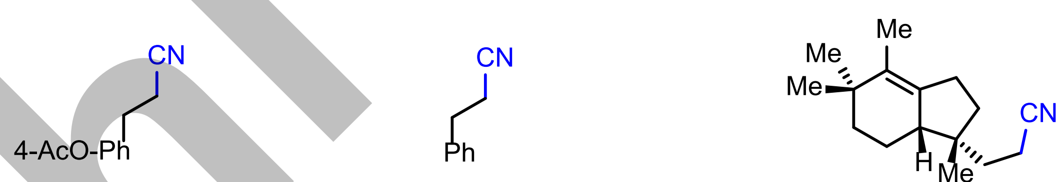
Exploration of hydrocyanation substrate scope

Late-stage Transfer Hydrocyanation



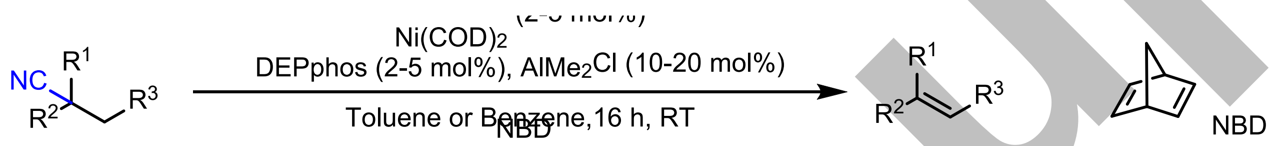
1-3t 95% (>95:5) **1-3u** 62% (>95:5) **1-3v** 88% (87:13) **1-3w** 81% (79:21)

Scale-up Using an Inexpensive Reagent



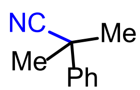
1-3x **3.5 g**, 93% (85:15) **1-3e** **4.95 g**, 94% (82:18) **1-3t** **4.3 g**, 93% (>95:5)

Exploration of retro-hydrocyanation substrate scope

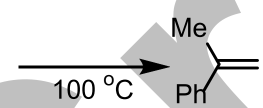


1-5 **1-6**

Styrene Synthesis

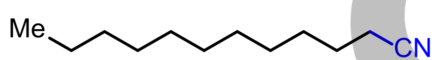


1-5a



1-6a 94%

Aliphatics

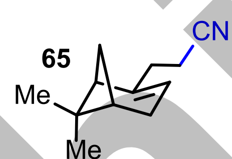


1-5b

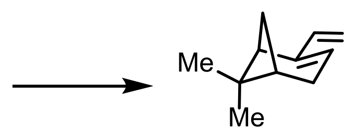
1-6b 93%

Terpene Derivatives

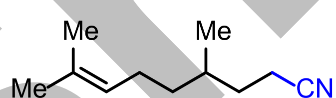
65



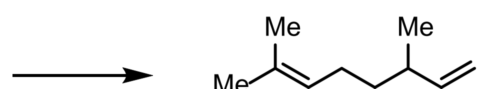
1-5c



1-6c 73%



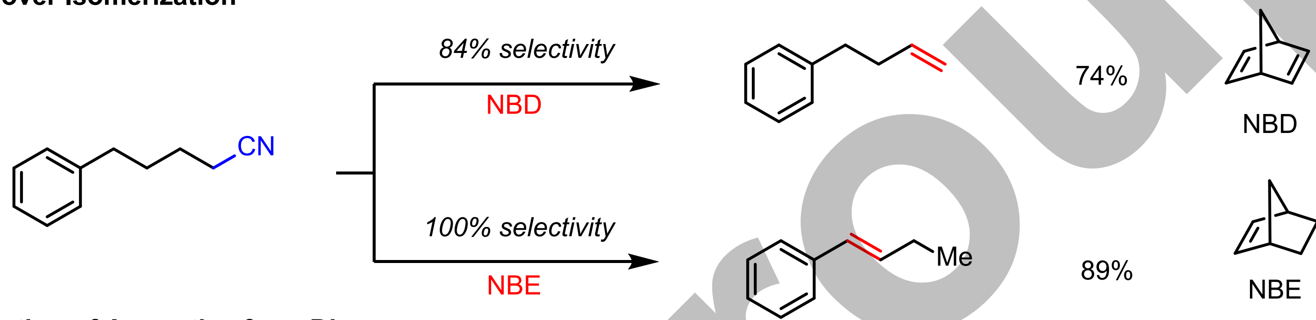
1-5d



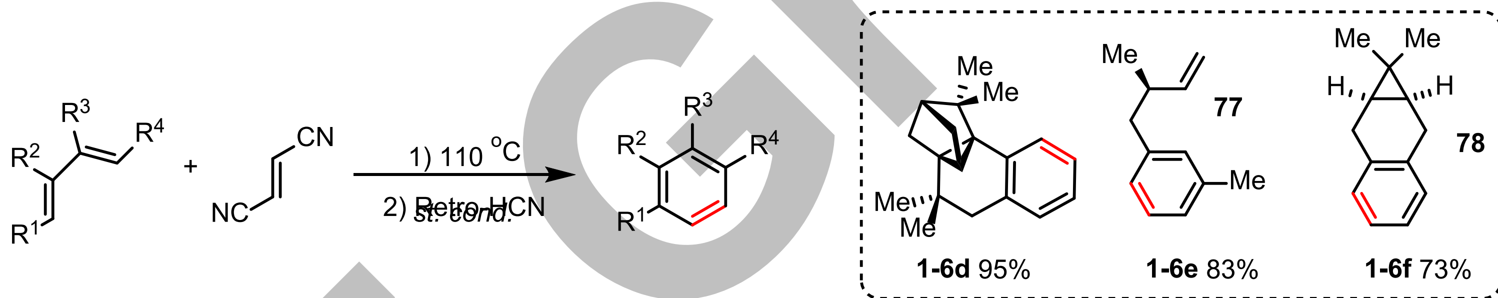
1-6c 71%

Exploration of retro-hydrocyanation substrate scope

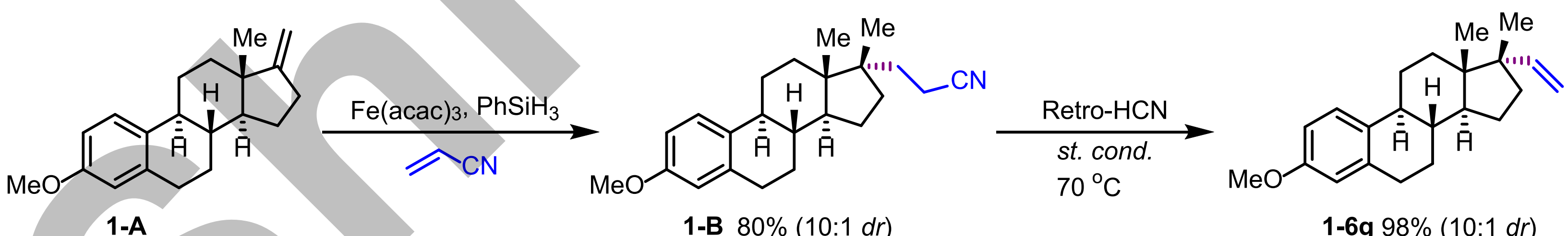
Control over isomerization



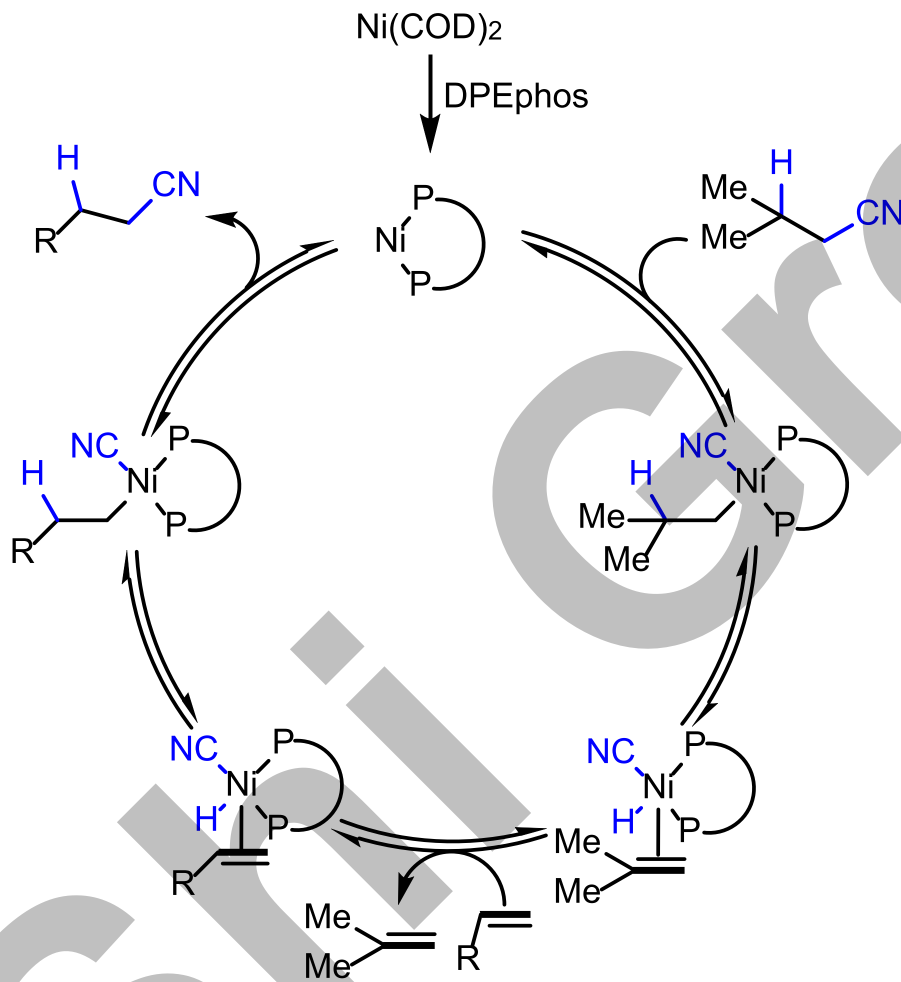
Construction of Aromatics from Dienes

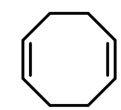


Stereoselective Installation of a Chiral Quaternary Vinyl Group

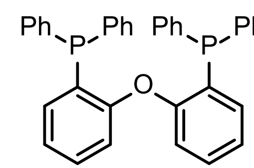


Mechanism of the Transfer Hydrocyanation



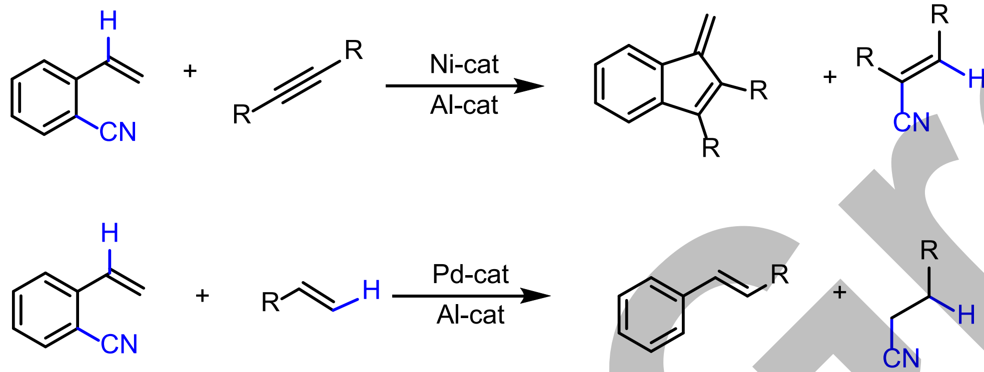


COD



DPEphos

Unlocking Mizoroki–Heck-type reactions of aryl cyanides using transfer hydrocyanation as a turnover-enabling step

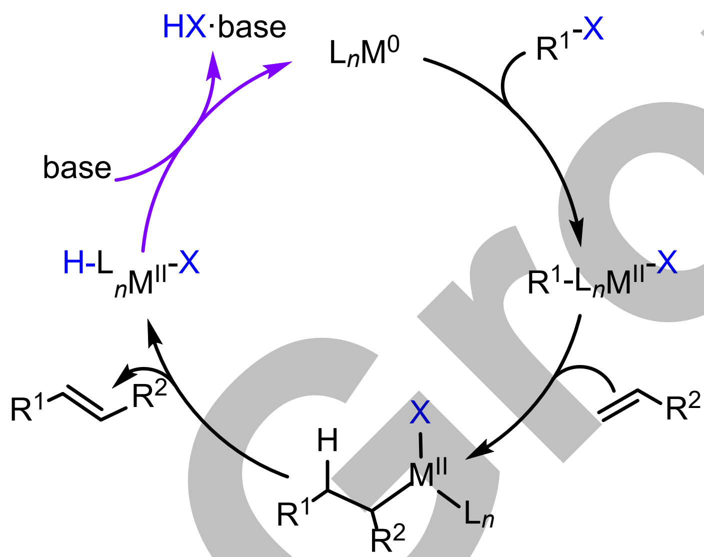


No HCN!
Irreversible!
Mizoroki–Heck-type!

Morandi, B. et al. *Chem. Eur. J.* **2016**, *22*, 15629.

Traditional Mizoroki–Heck reaction

Mechanism



$$\text{H-L}_n\text{M}^{II}\text{-X} + \text{base} \longrightarrow \text{L}_n\text{M}^0 + \text{HX}\bullet\text{base}$$

Heck, R. F. et al. *Org. React*. **1982**, *27*, 345.

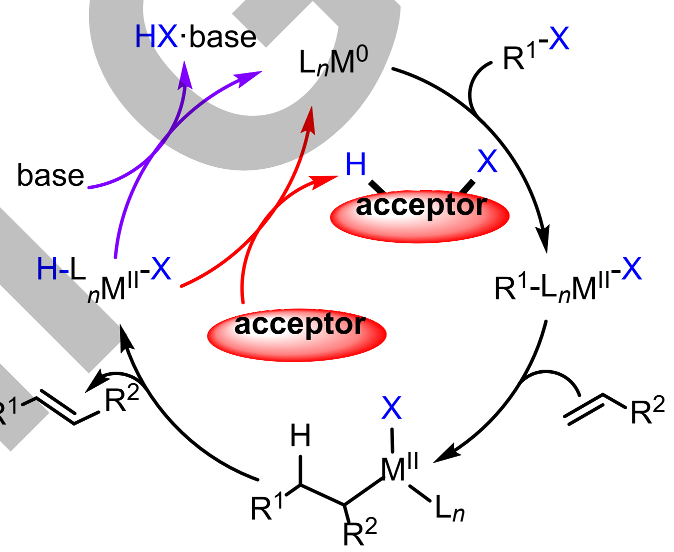
New approach for Mizoroki–Heck

Jacobsen, E. N. et al. *J. Am. Chem. Soc*. **2008**, *130*, 12594.

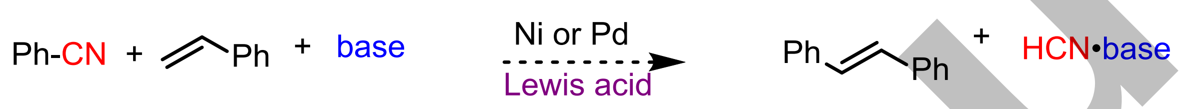
Shi, Z. J. et al. *Org. Lett*. **2009** ,*11*, 3374.

Jiao, N. et al. *Chem. Rev*. **2014**, *114*, 8613.

Mechanism

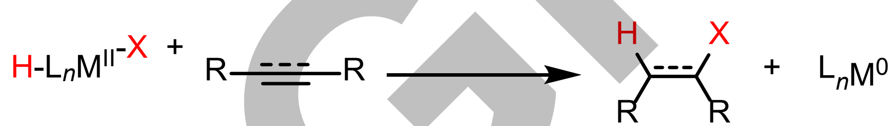


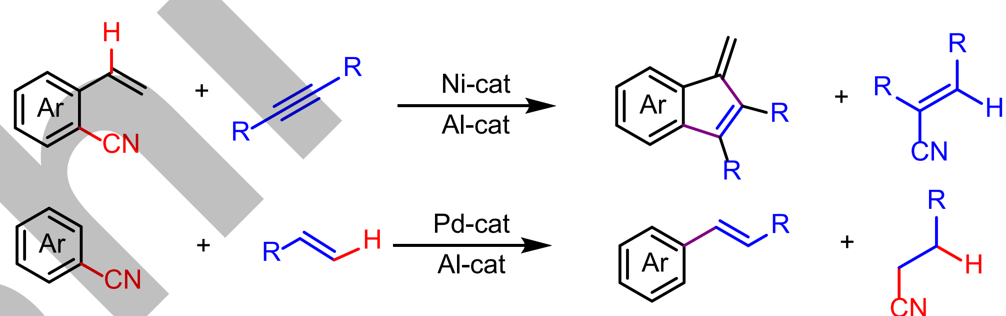
Transfer hydrocyanation for aryl cyanides



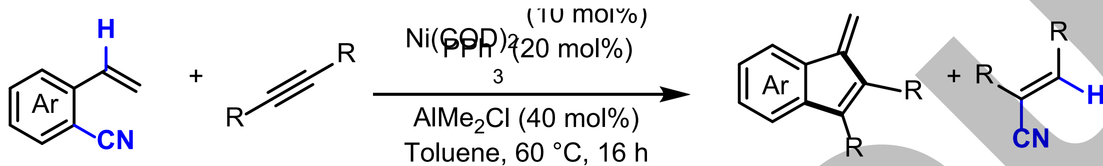
Results: ***no conversion*** using base only
low yield using base and Lewis acid

⇨ **needs** Lewis acid but only **low reactivity** in the presence of base

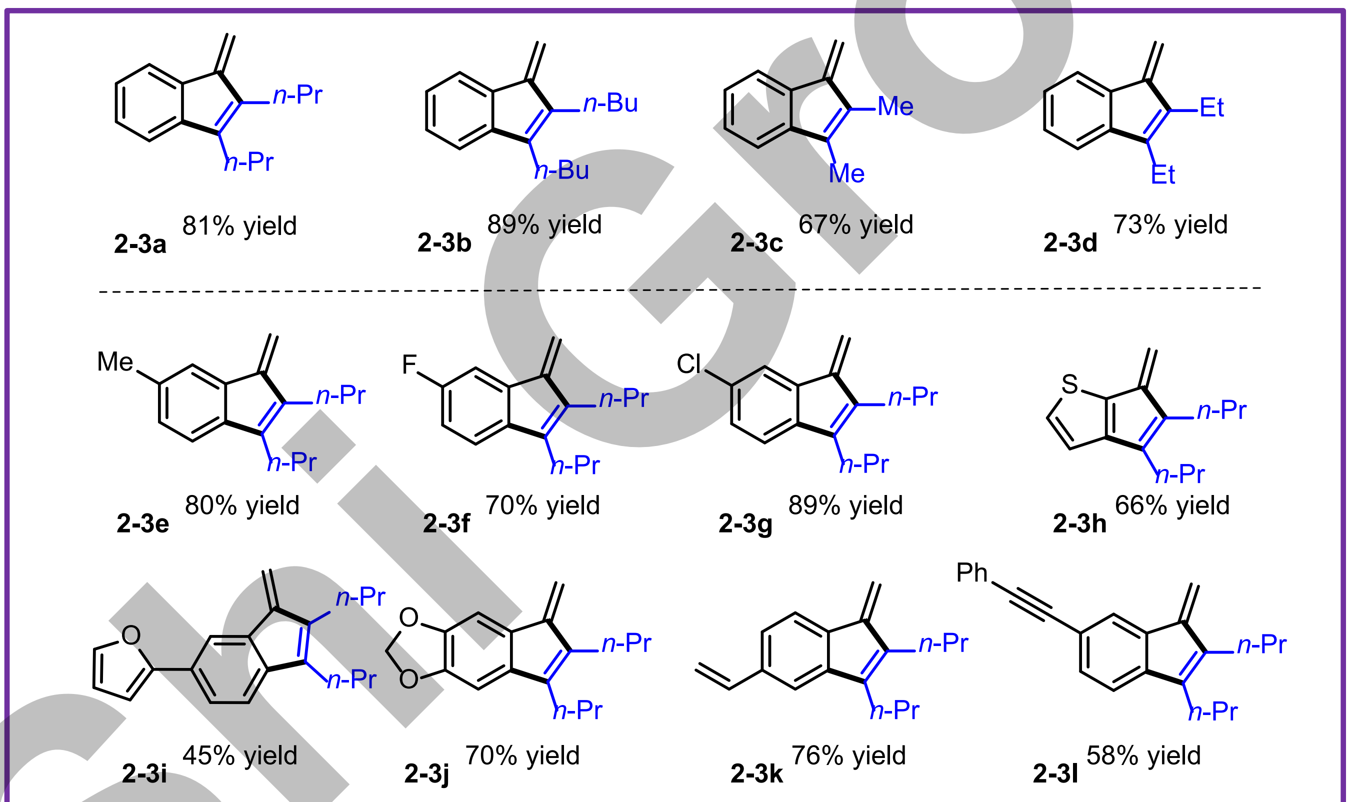




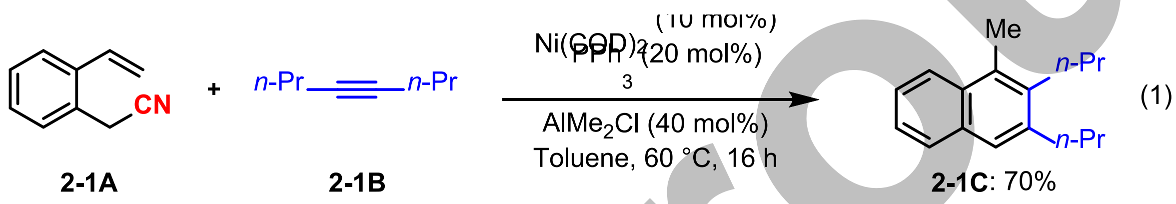
Scope of the intramolecular MH-type reaction

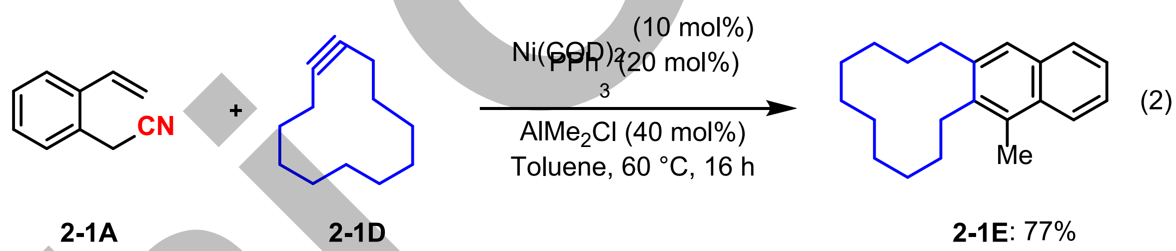


2-1 2-2 2-3 2-4

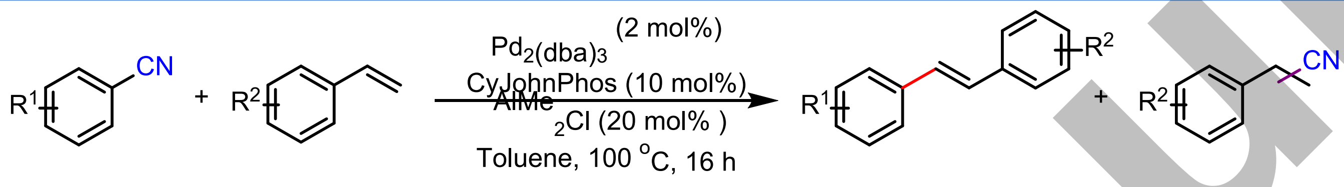


Synthesis of polysubstituted naphthalene compounds

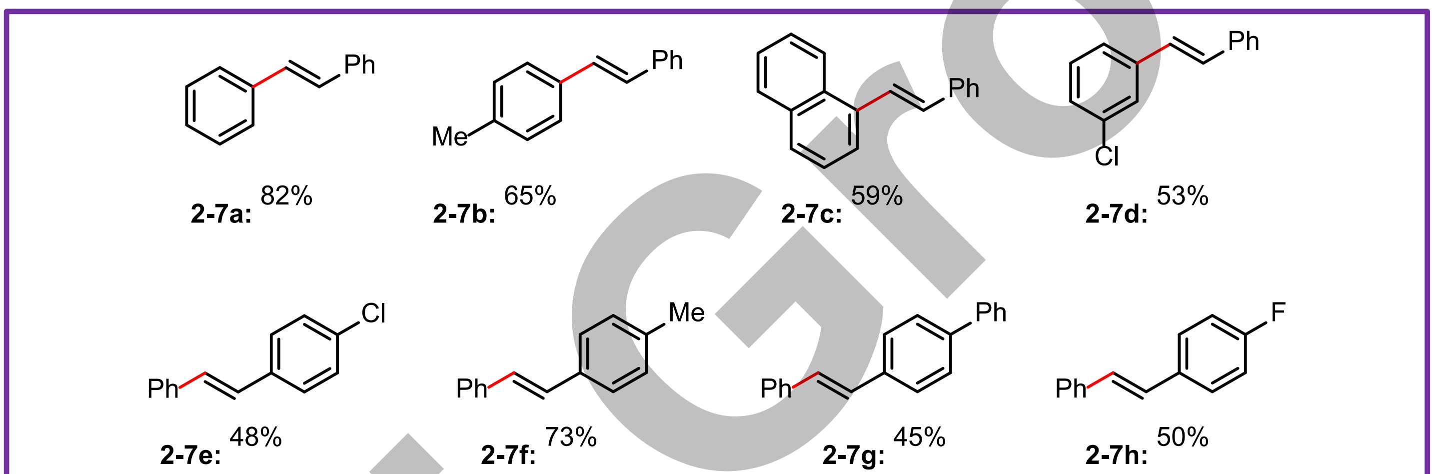




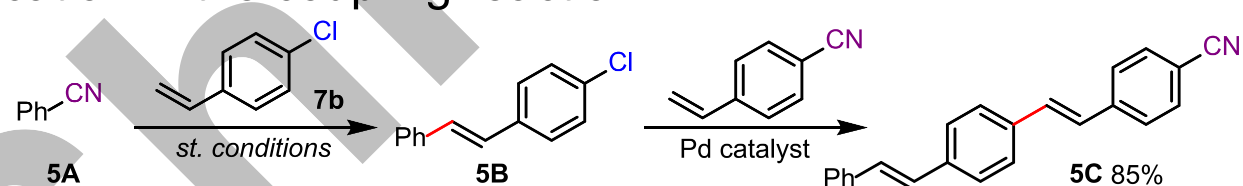
Scope of the intermolecular Heck-type reaction



2-5 **2-6** **2-7** **2-8**



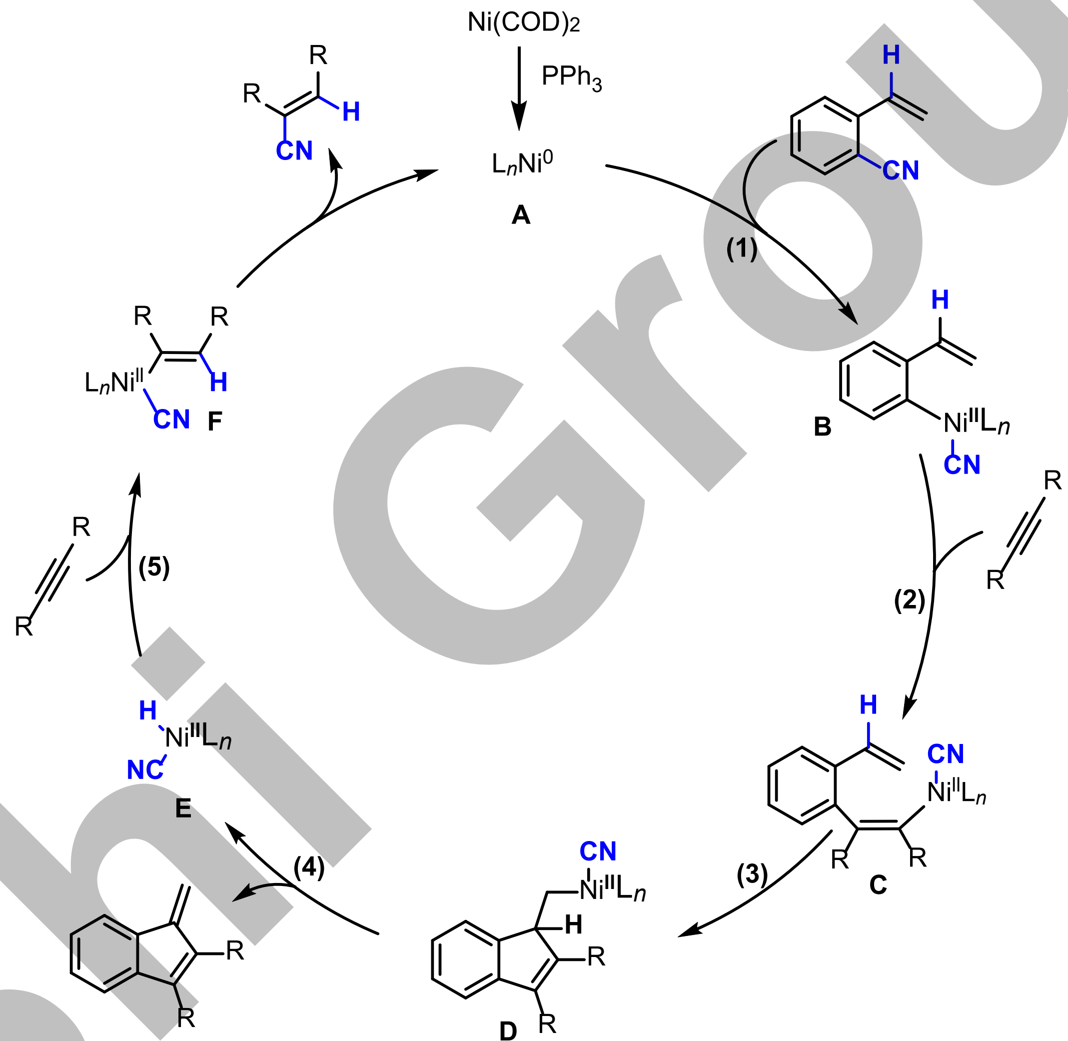
The application in the coupling reaction



CN cleavage in the presence of Cl

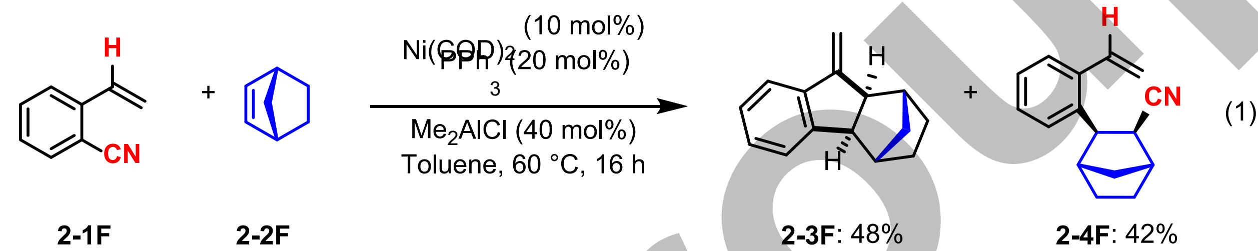
Cl cleavage in the presence of CN

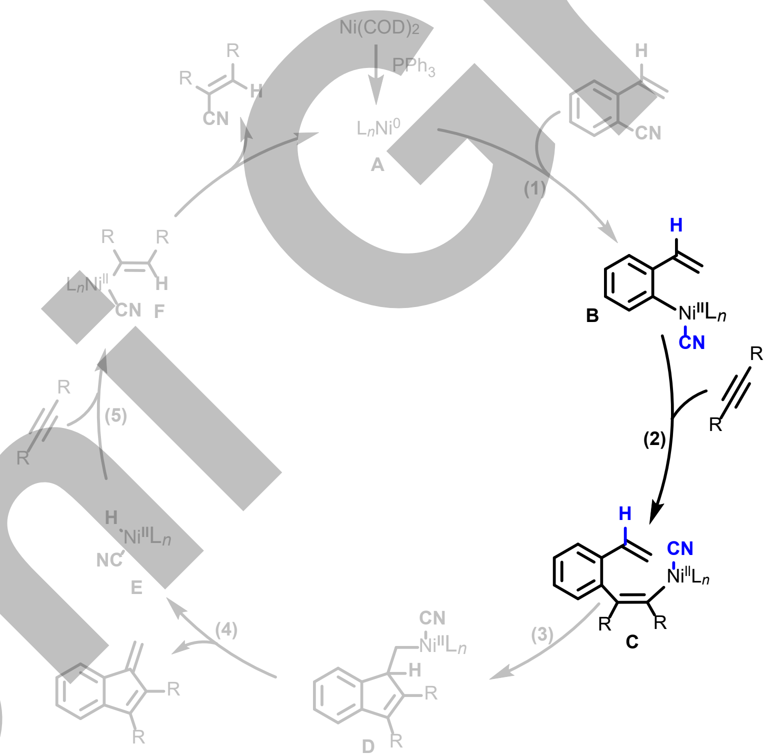
Proposed mechanism



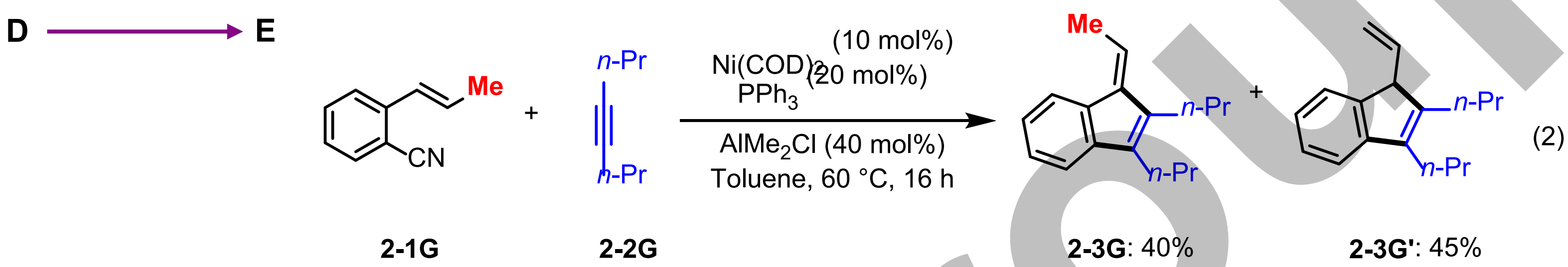
Mechanistic experiments

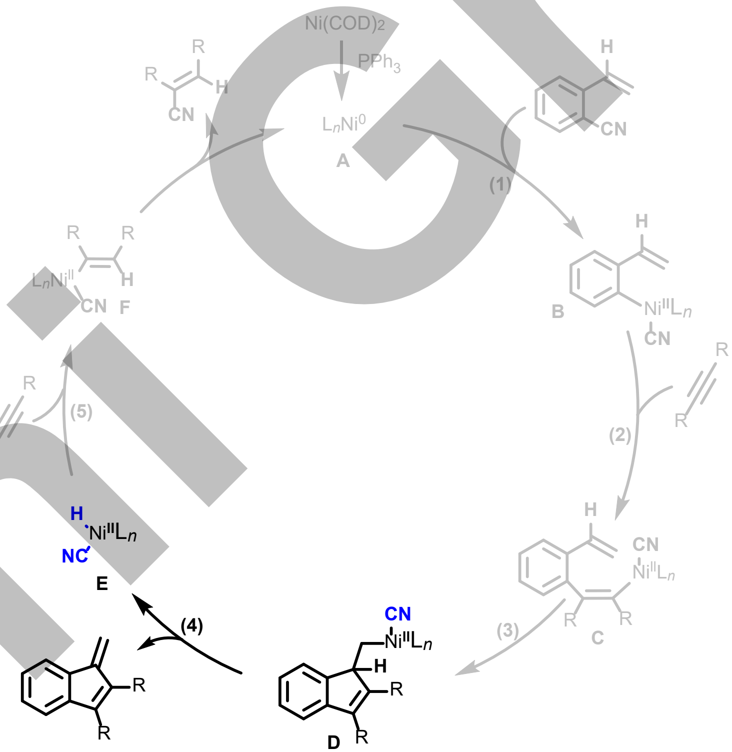
B → C



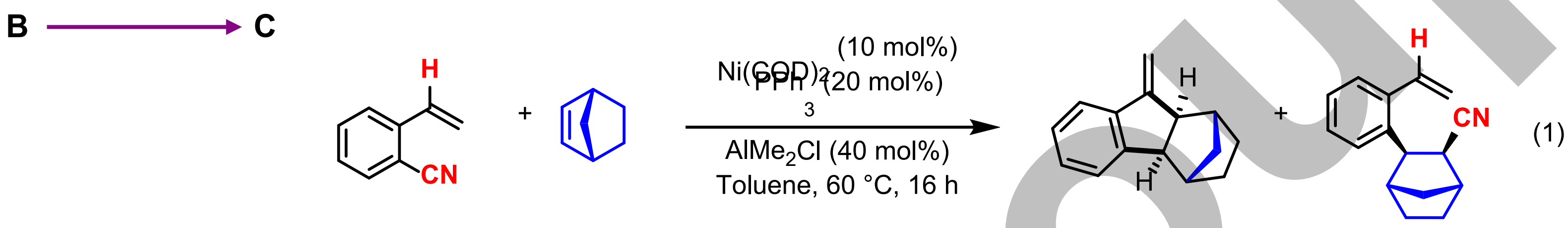


Mechanistic experiments

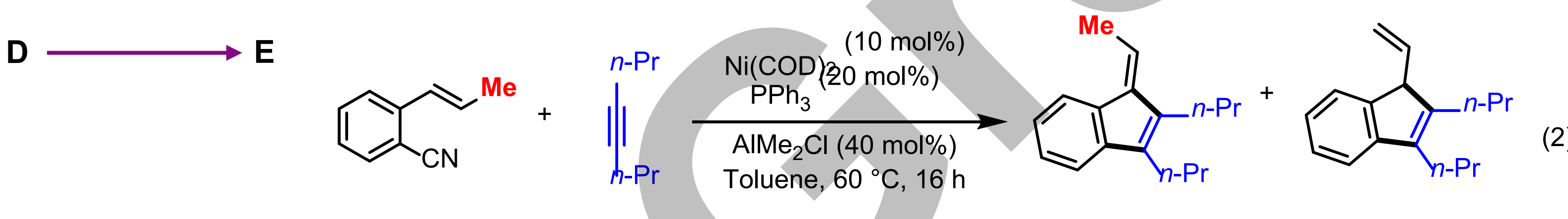




Mechanistic experiments

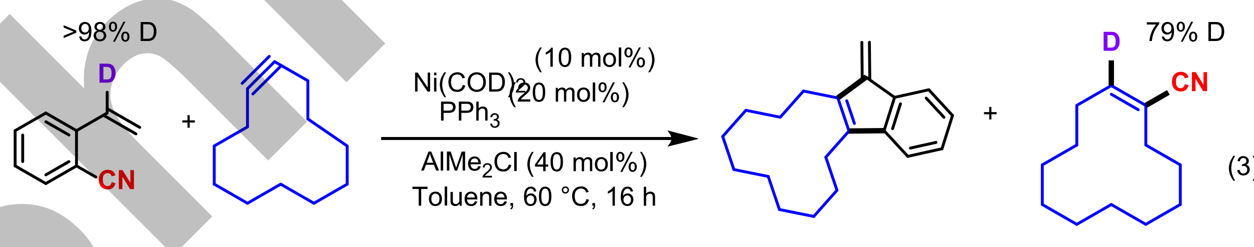


2-1F **2-2F** **2-3F**: 48% **2-4F**: 42%



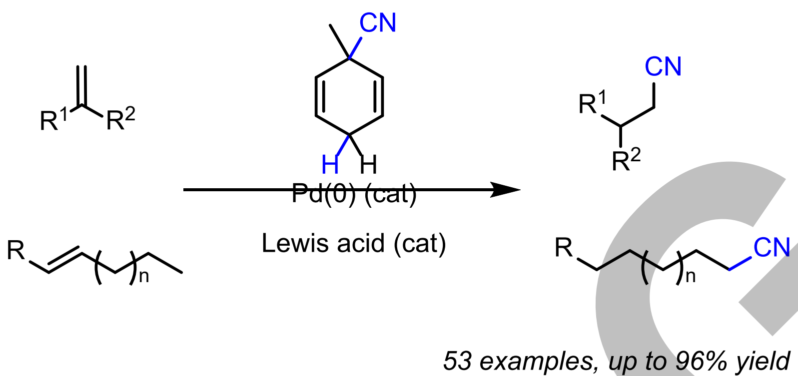
2-1G **2-2G** **2-3G**: 40% **2-3G'**: 45%

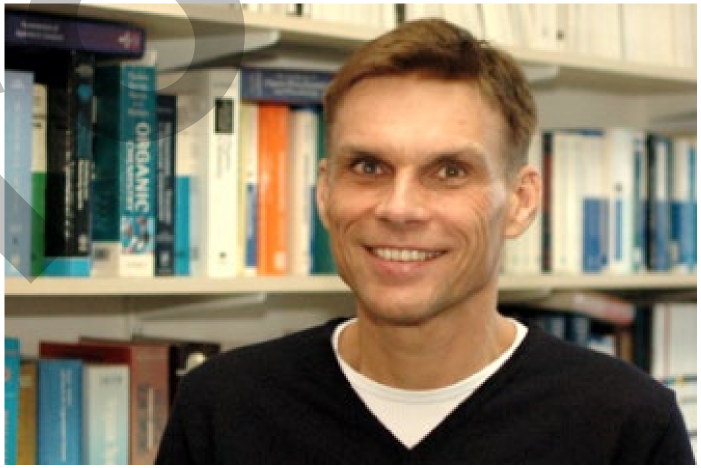
Deuterated experiment



2-1H **2-2H** **2-3H**: 96% **2-4H**: 90%

Cooperative palladium/lewis acid-catalyzed transfer hydrocyanation of alkenes and alkynes

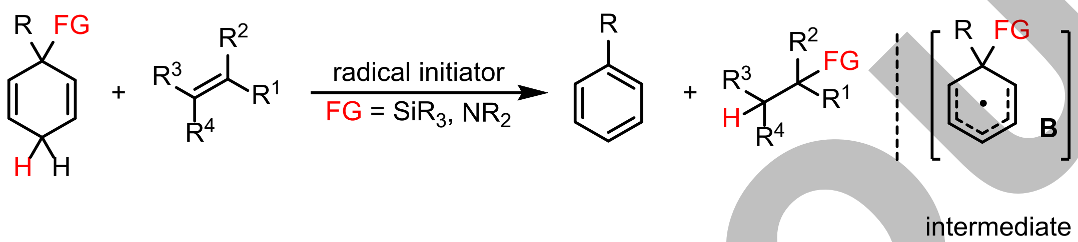




No HCN!
Anti-Markovnikov selectivity!
Broad scope!
Chain walking!

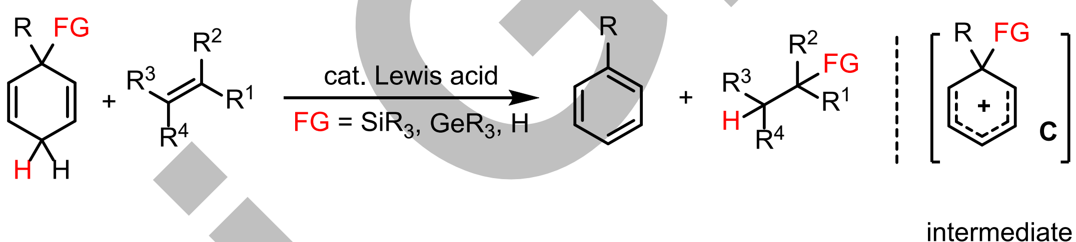
Studer, A. et al. *J. Am. Chem. Soc.* **2018**, *140*, 16353.

CHD core as reagents for functional group transfer reactions



Studer, A. et al. *Org. Lett.* **2001**, *3*, 2357.

Studer, A. et al. *Chem. Commun*. **2002**, 1592.



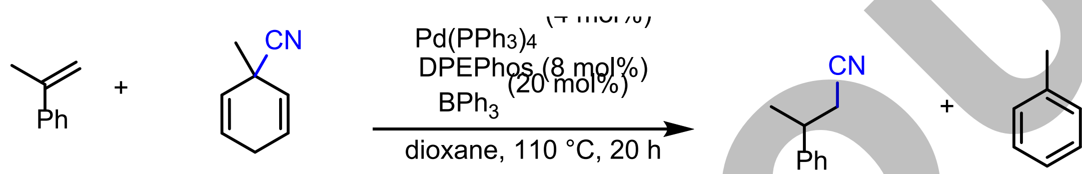
Oestreich, M. et al. *Angew. Chem. Int. Ed.* **2013**, *52*, 11905.

Oestreich, M. et al. *Org. Lett.* **2017**, *19*, 1898.

Oestreich, M. et al. *Angew . Chem. Int. Ed.* **2015**, *54*, 12158.

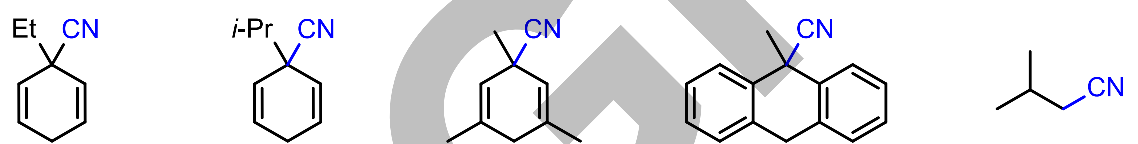
Oestreich, M. et al. *Angew. Chem. Int. Ed.* **2015**, *54*, 1965.

Palladium/lewis acid-cocatalyzed transfer hydrocyanation

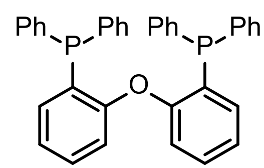


(1.0 equiv) (1.5 equiv)

3-1a **3-2a** **3-3a** 89%



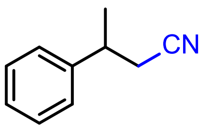
3-2b (53%) **3-2c** (39%) **3-2d** (22%) **3-2e** (0%) **3-2f** (15%)



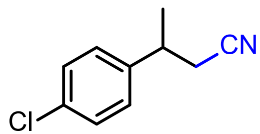
DPEphos

Transfer hydrocyanation of various alkenes and alkynes

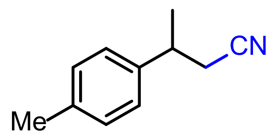
α-Substituted alkenes



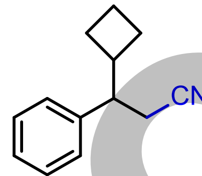
3-1b 89%



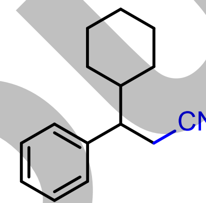
3-1c 80%



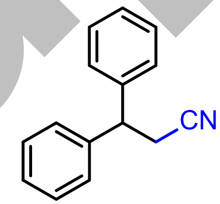
3-1d 86%



3-1e 87%

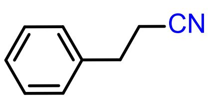


3-1f 78%

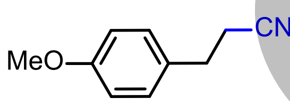


3-1g 59%

Styrenes

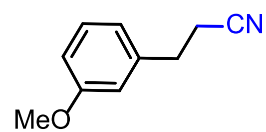


3-1h 90% (90:10)

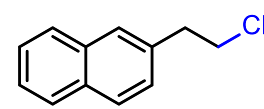


3-1i 87% (91:9)

3-1j 94% (90:10)

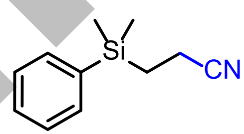


3-1k 82% (89:11)

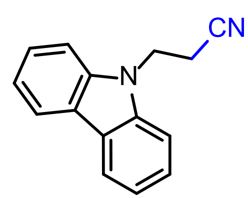


3-1l 95% (90:10)

Activated alkenes

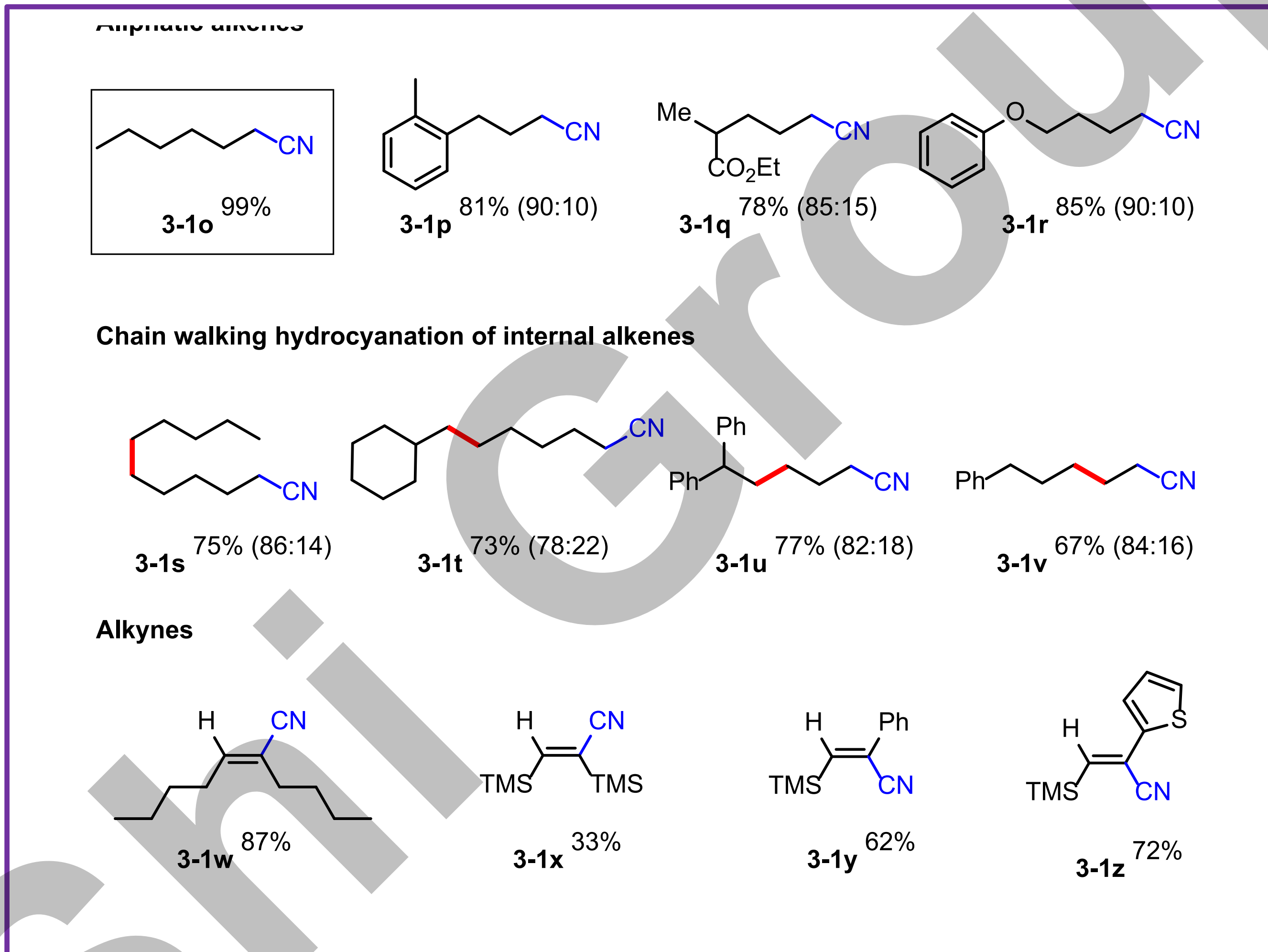


3-1m 96%



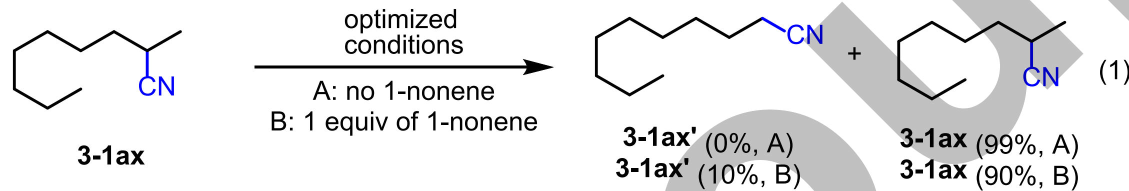
3-1n 83%

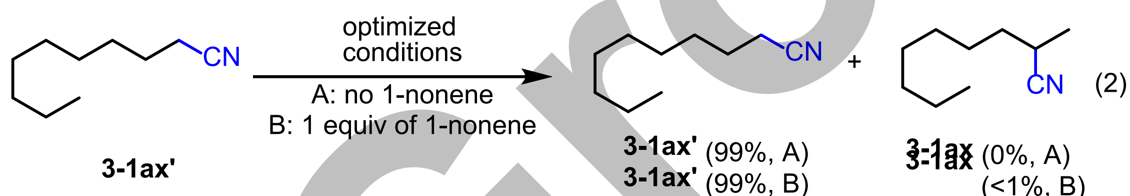
Transfer hydrocyanation of various alkenes and alkynes



Mechanistic studies

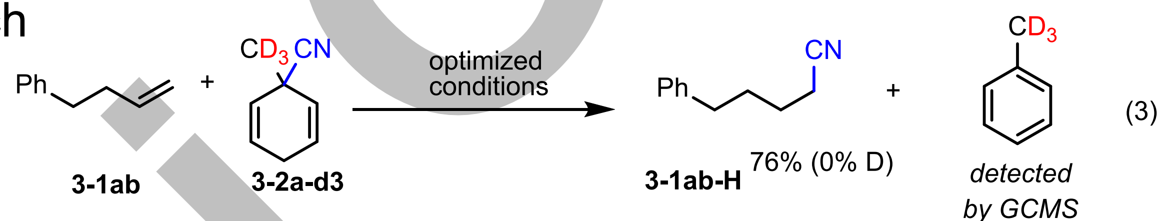
Isomerization research

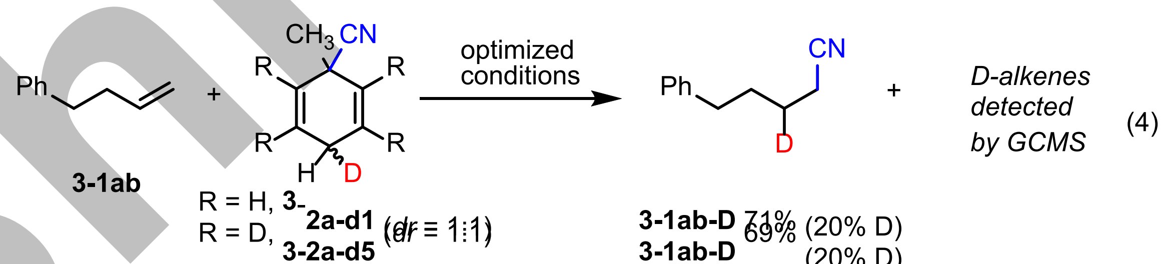




These results show that the branched nitrile can be transferred to the linear nitrile

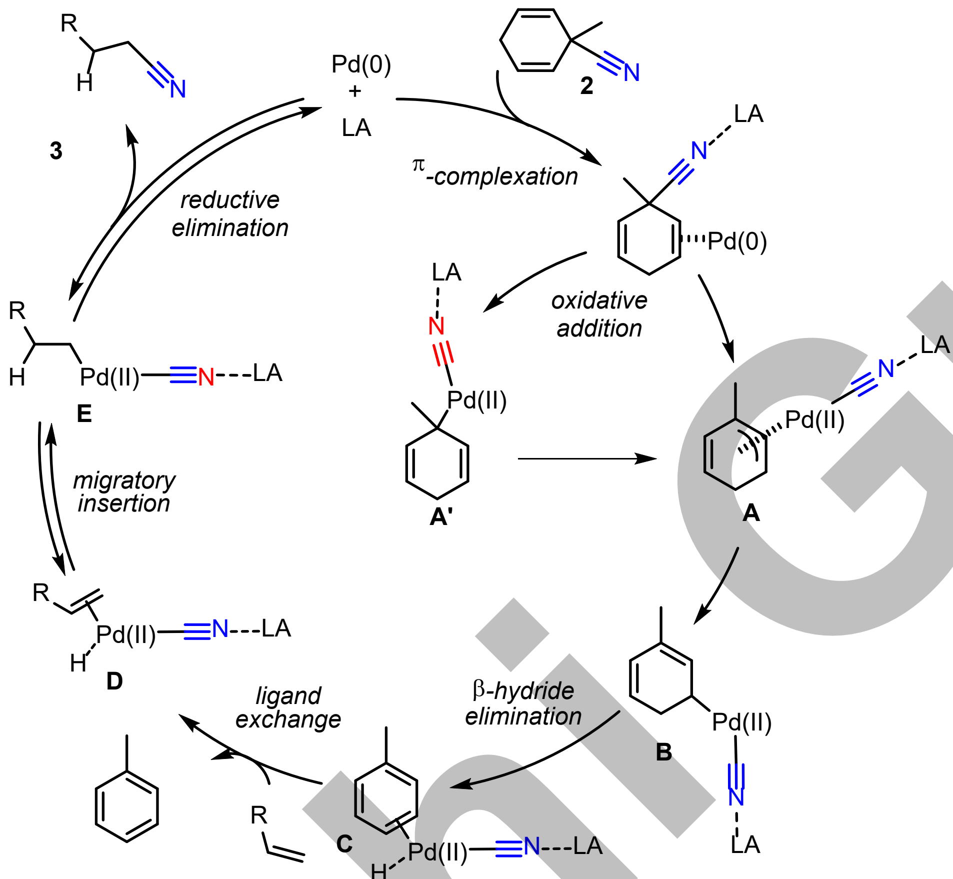
Deuterated research

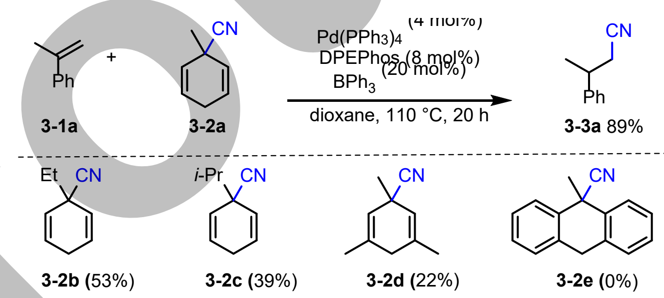


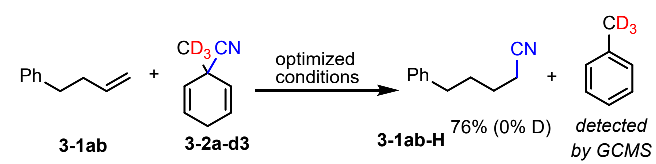


These results show that the H atom is derived from the methylene group

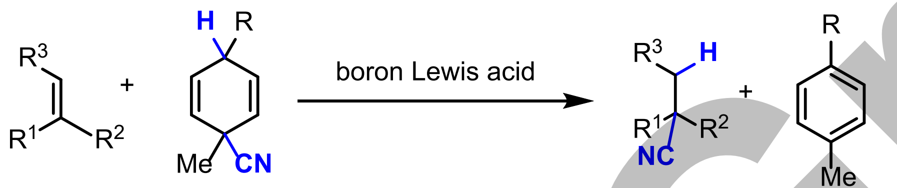
Proposed mechanism







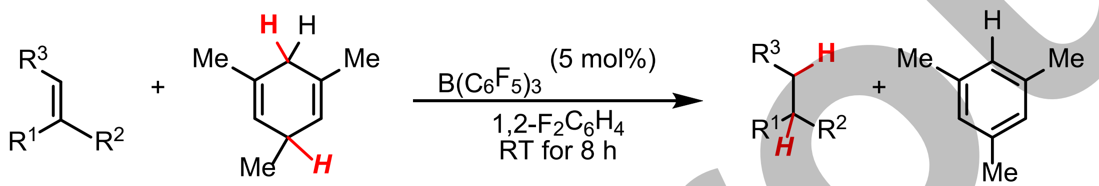
Transfer hydrocyanation of α- and α,β -substituted styrenes catalyzed by boron lewis acids



No HCN!
Markovnikov selectivity!

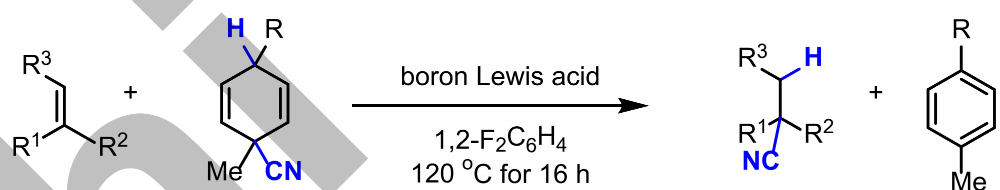
Oestreich, M. et al. *Angew. Chem. Int. Ed.* **2019**, *58*, 3579.

CHD core as reagents for functional group transfer reactions



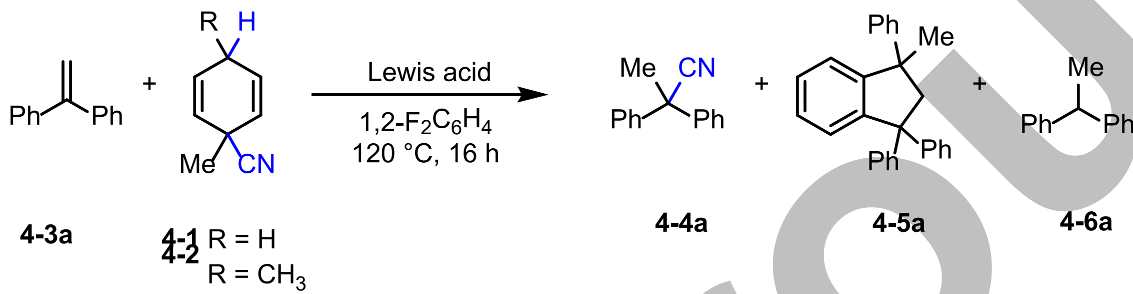
Oestreich, M. et al. *Chem. Sci*. **2017**, *8*, 4688.

Oestreich, M. et al. *Org. Lett*. **2016**, *18*, 2463.



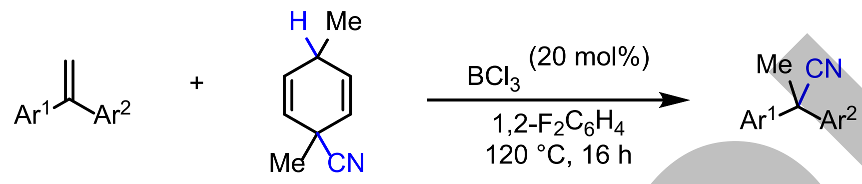
R = H or Me

Transfer hydrocyanation catalyzed by boron lewis acids

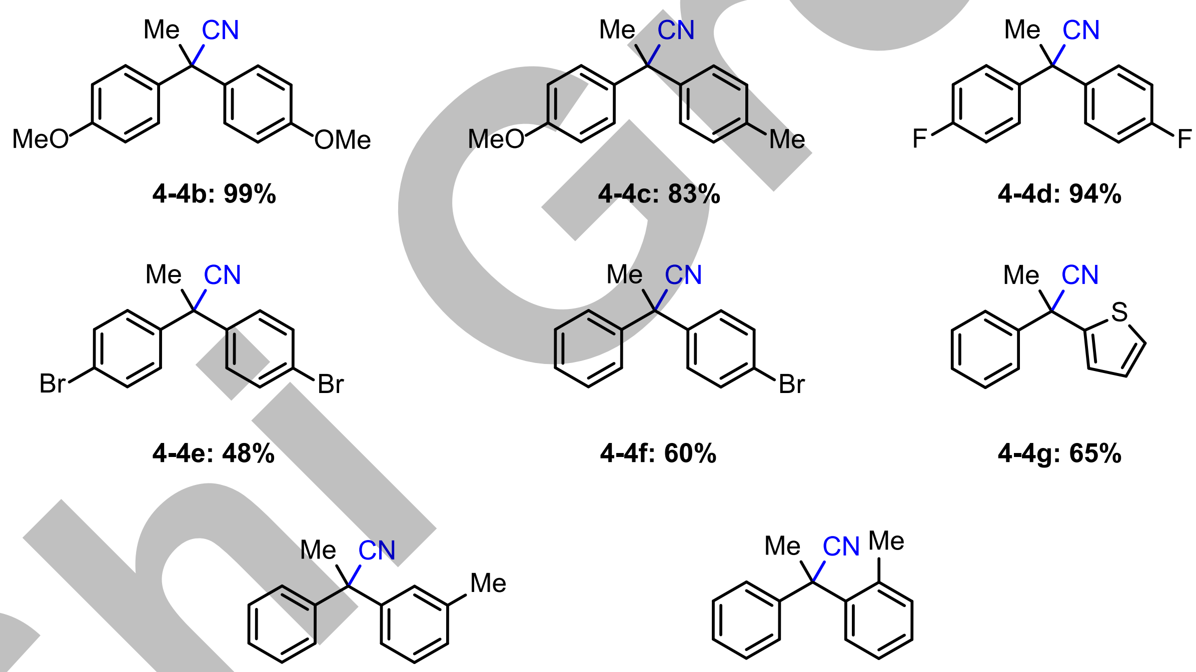


Entry	Lewis acid (mol%)	Surrogate	**4-4a/4-5a/4-6a**	Conv. [%]
1	$B(C_6F_5)_3$ (20)	4-1	42:14:44	> 99
2	$B(C_6F_5)_3$ (100)	4-1	20:70:10	> 99
3	$B(C_6F_5)_3$ (100)	4-2	18:79:3	> 99
4	BCl_3 (20)	4-2	99:1:0	> 99
5	BCl_3 (20)	4-1	94:3:3	> 99
6	BCl_3 (10)	4-2	93:7:0	> 99
7	BBr_3 (20)	4-2	88:11:1	> 99
8	$BF_3·OEt_2$ (20)	4-2	38:62:0	85
9	$B(OMe)_3$ (20)	4-2	-	0
10	$AlCl_3$ (20)	4-1	40:49:11	> 99
11	$AlCl_3$ (20)	4-2	47:52:1	99

Transfer hydrocyanation of various 1,1-diarylethylenes with BCl_3



4-3 **4-2** **4-4**

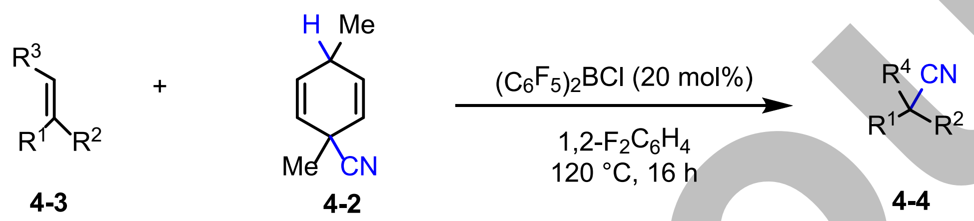


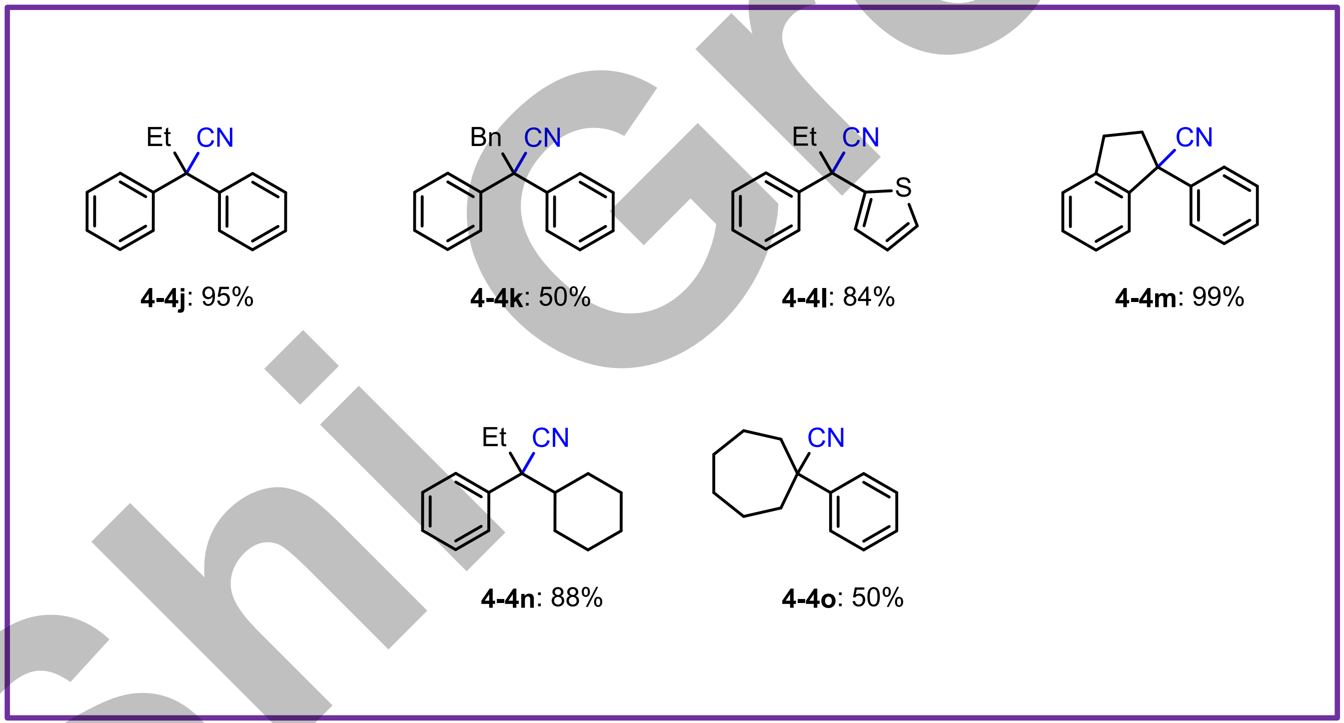
4-4b: 99% **4-4c: 83%** **4-4d: 94%**

4-4e: 48% **4-4f: 60%** **4-4g: 65%**

4-4h: 50% **4-4i: 45%**

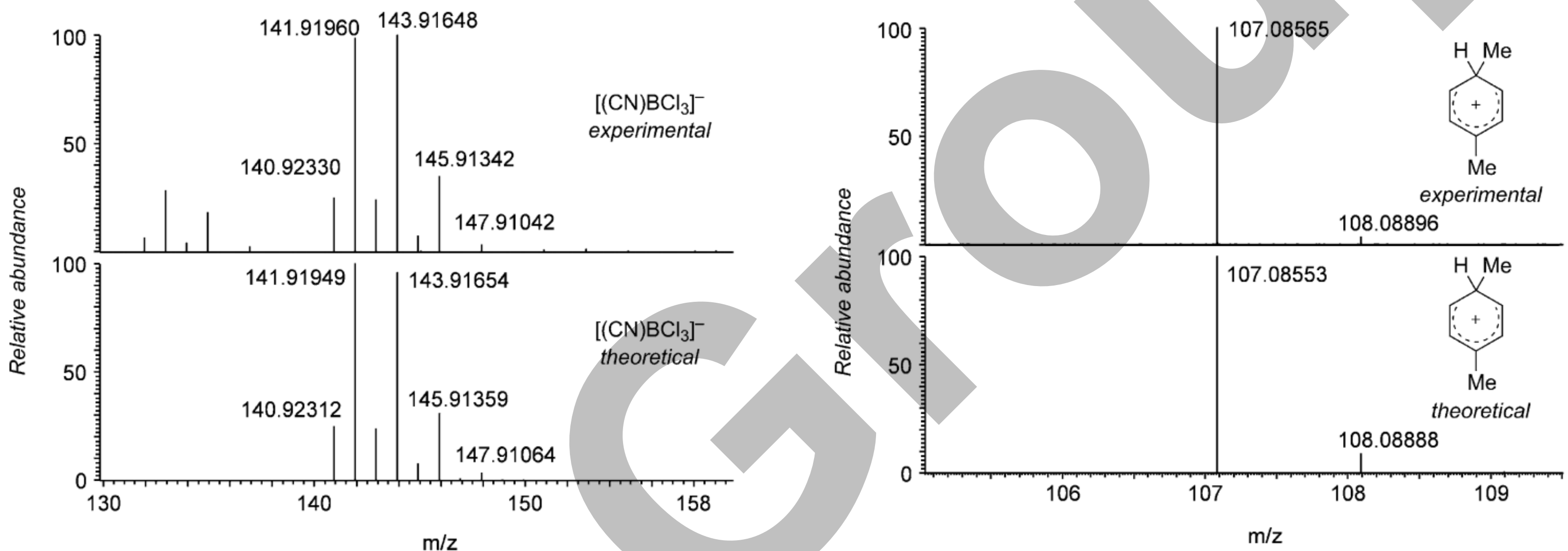
Transfer hydrocyanation of trisubstituted alkenes with $(C_6F_5)_2BCl$



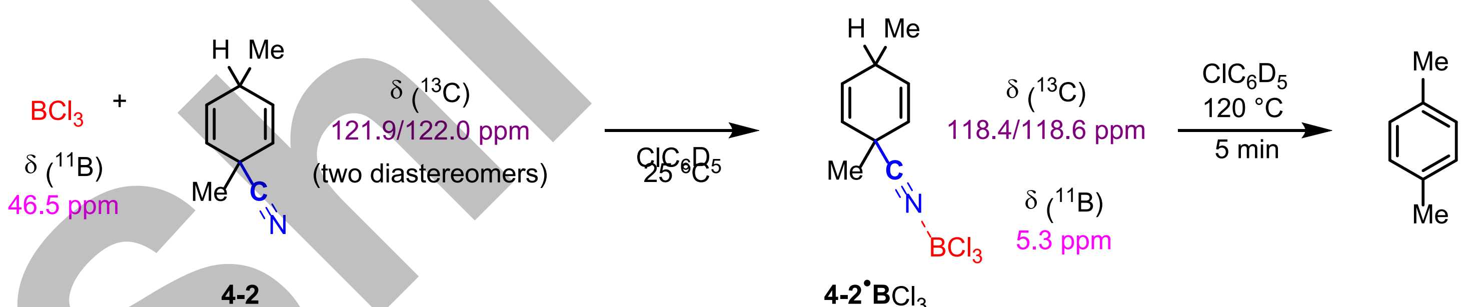


Mechanism studies

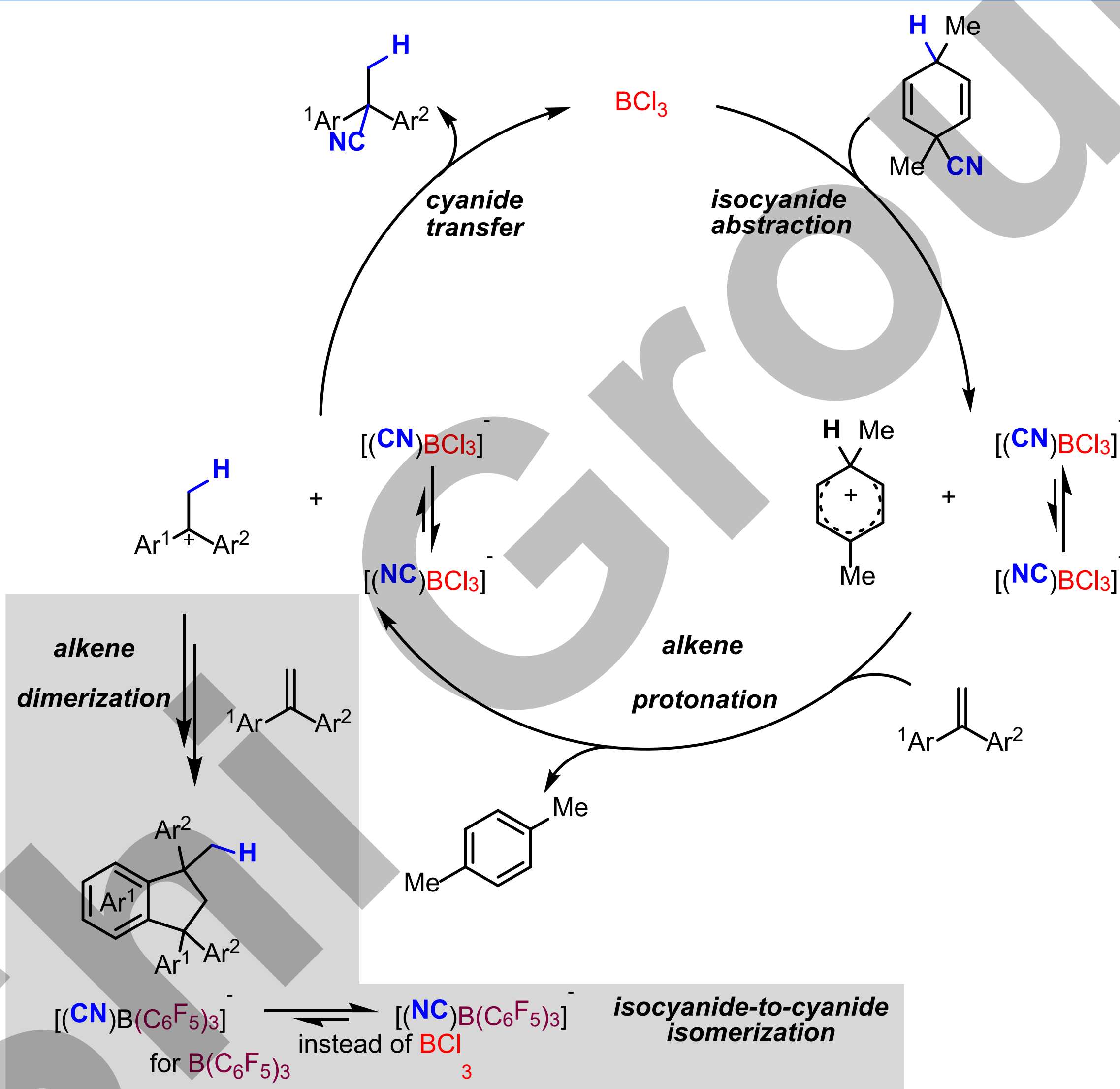
In-situ ESI-MS spectra



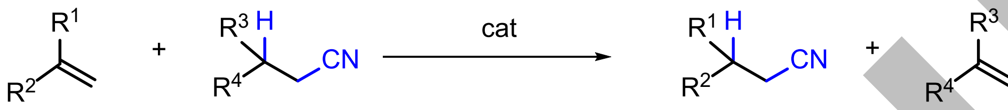
Stoichiometric NMR experiment



Proposed mechanism



Summary



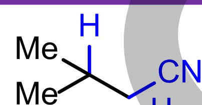
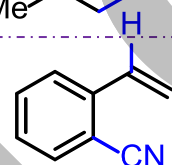
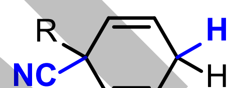
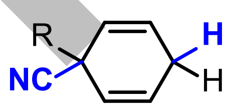
No HCN !

1 Morandi, B. et al. *Science* **2016**, *351*, 832.

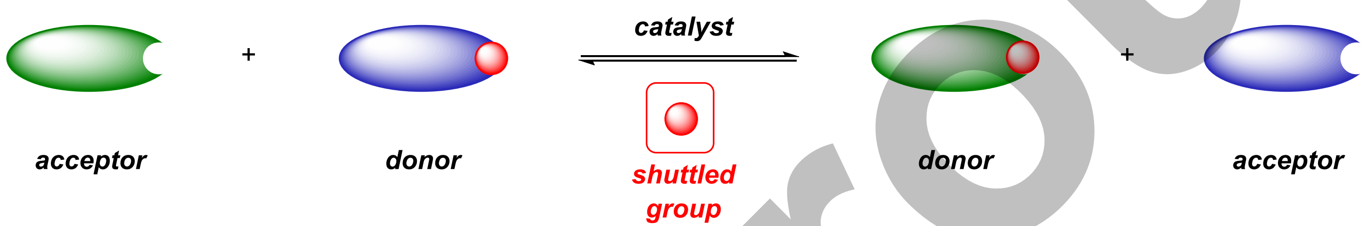
2 Morandi, B. et al. *Chem. Eur. J.* **2016**, *22*, 15629.

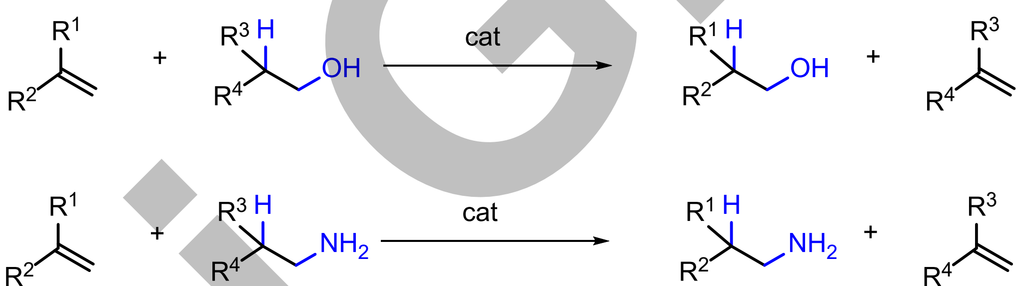
3 Studer, A. et al. *J. Am. Chem. Soc.* **2018**, *140*, 16353.

4 Oestreich, M. et al. *Angew. Chem. Int. Ed.* **2019**, *58*, 3579

Entry	Catalyst	Surrogate	Driving forces	Selectivity
1	Ni/LA		gas release	Anti-Markovnikov
2	Ni/LA or Pd/LA		conjugated system	
3	Pd/LA		aromatization	Anti-Markovnikov
4	LA		aromatization	Markovnikov

Prospect


catalyst
acceptor
donor
shuttled group
donor
acceptor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I am very grateful to everyone for listening, and I sincerely look forward to your comments and suggestions!