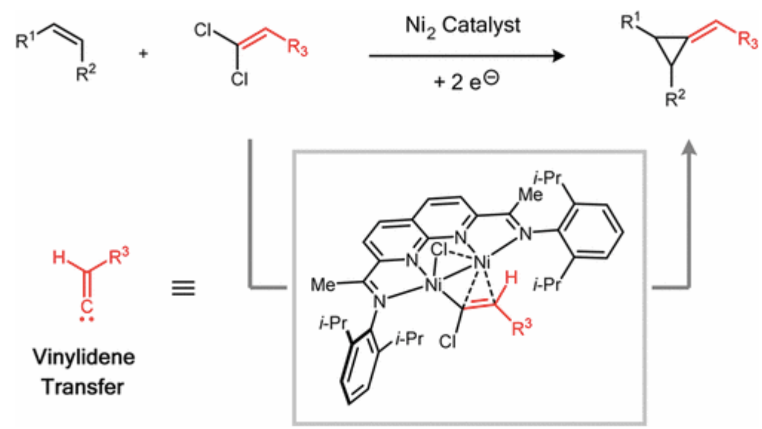
Catalytic Reductive Vinylidene Transfer Reactions

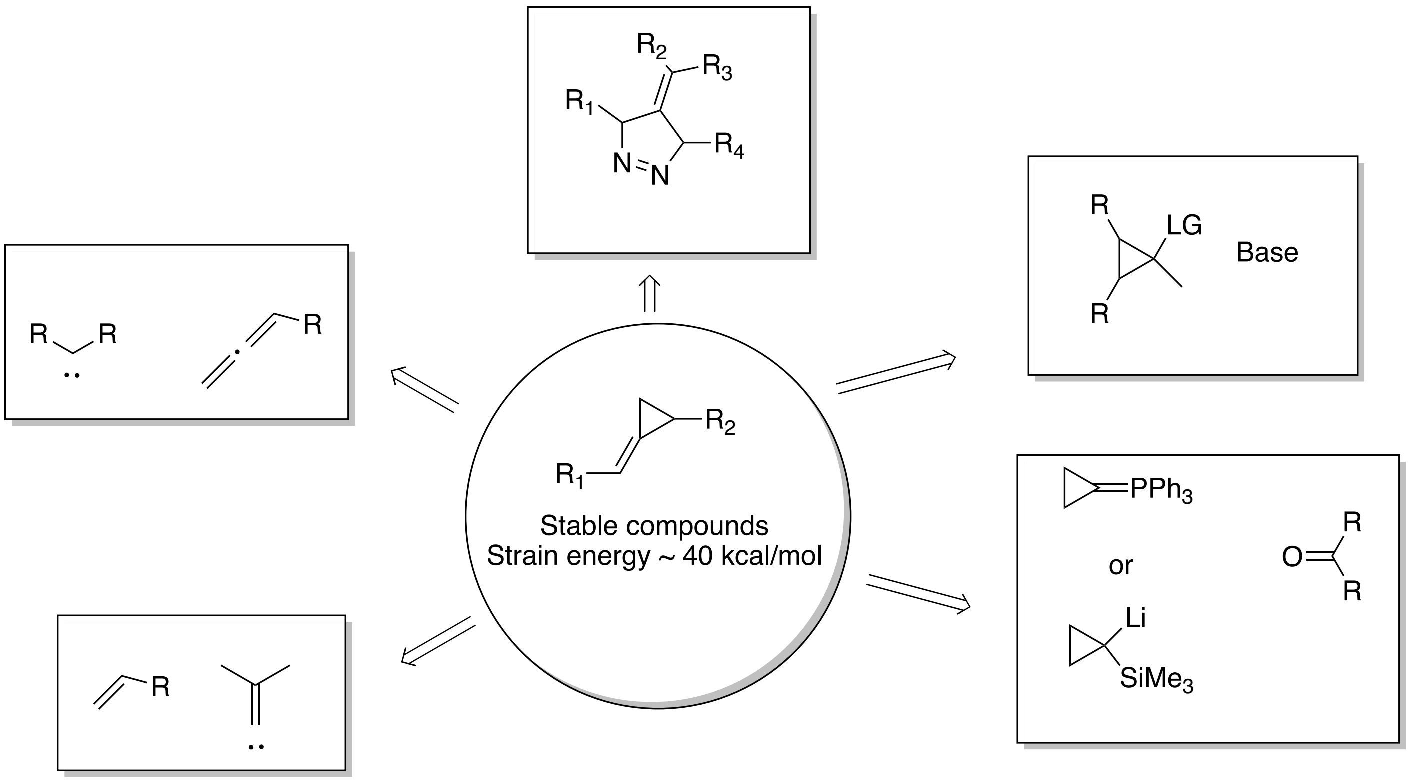


Sudipta Pal, You-Yun-Zhou and Christopher Uyeda

J. Am. Chem Soc. 2017, **139**, 11686-11689

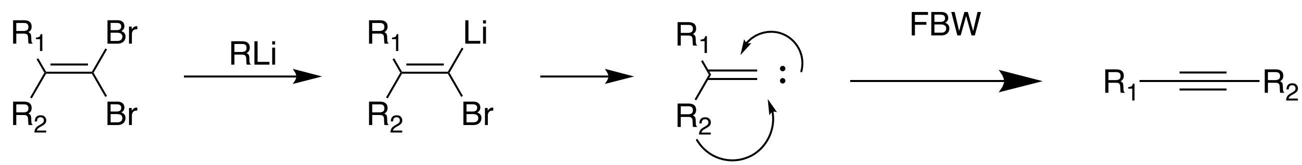
1

Common vinylidene cyclopropane disconnections

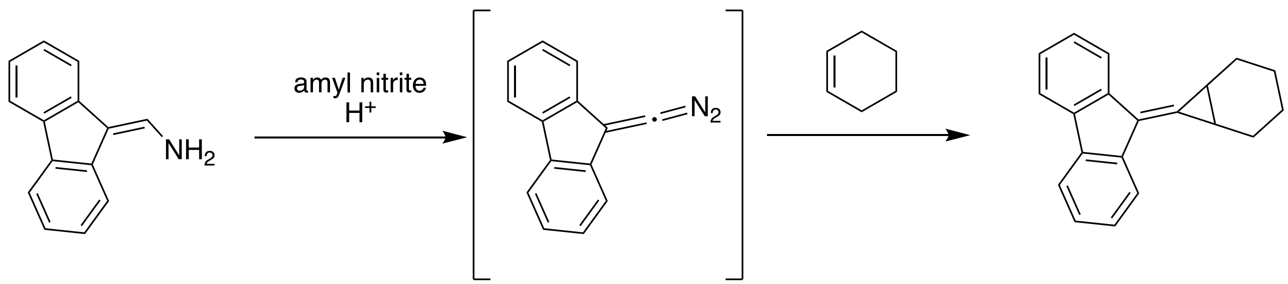


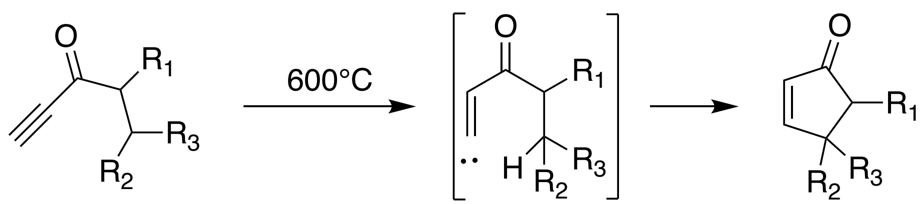
2

General methods for the generation of alkylidene carbenes



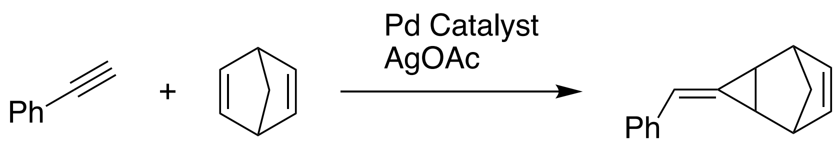
Fritsch Buttenberg Wiechell rearrangement

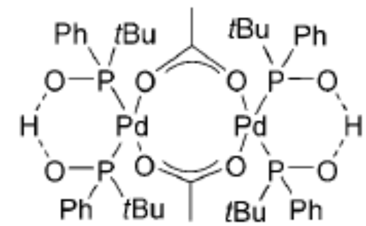




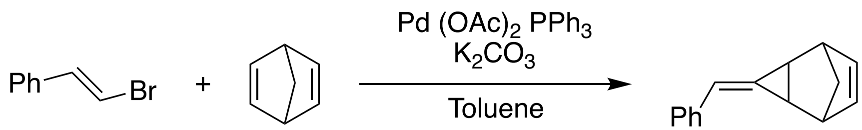
3

Pd catalysed [2+1] cycloadditon



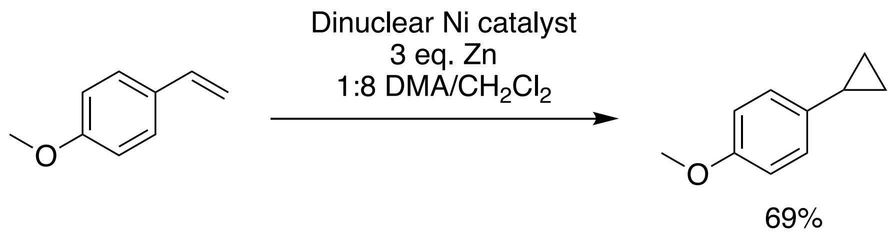


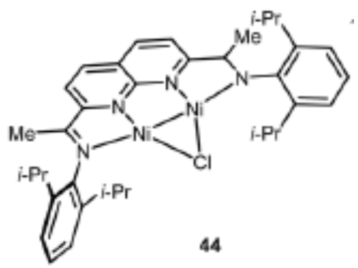
Angew. Chem. Int. Ed. 2005, **44**, 4753 –4757



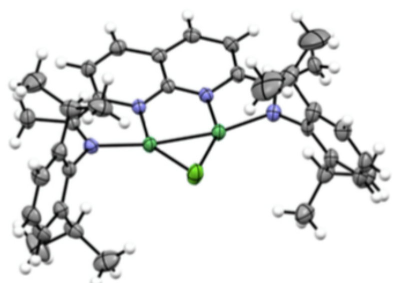
Org. Lett. 2014, **16**, 2646−2649

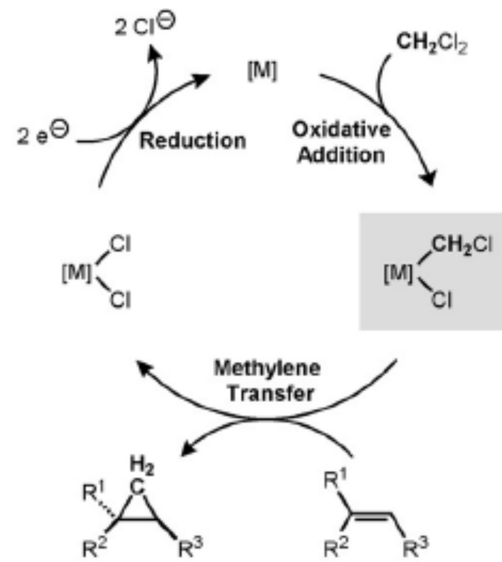
Catalytic reductive Carbene transfer





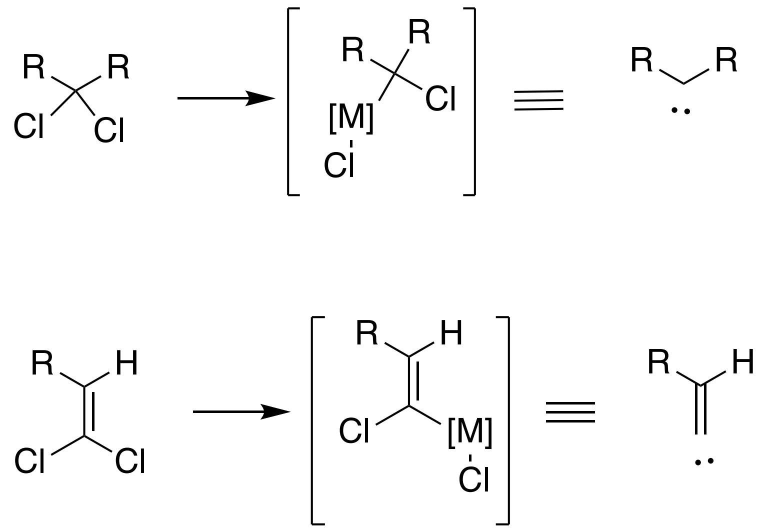
44



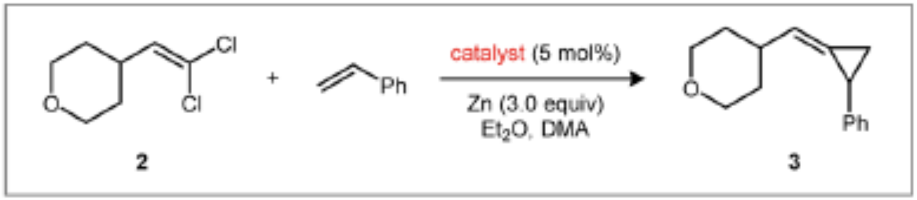


Angew. Chem. Int. Ed. 2016, **55**, 3171 –3175

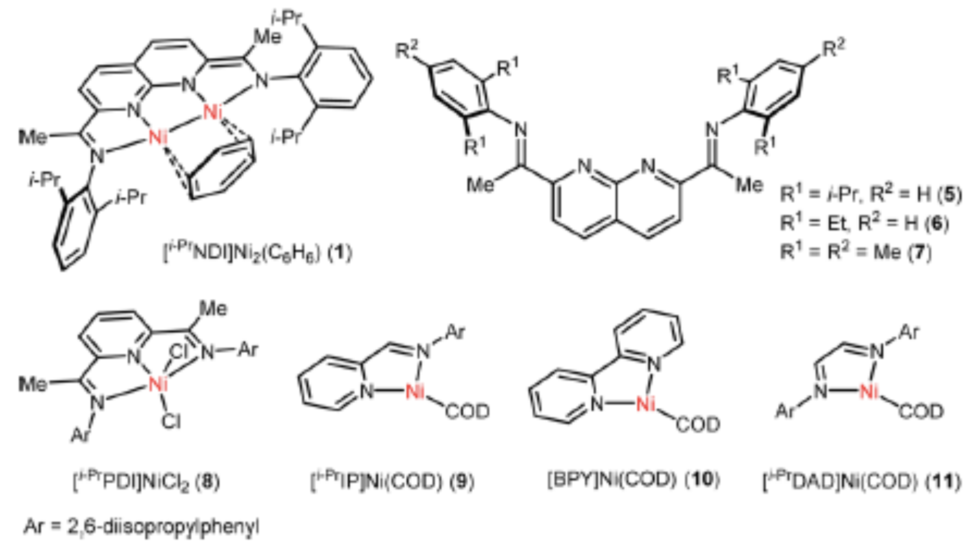
Catalytic reductive Vinylidine transfer



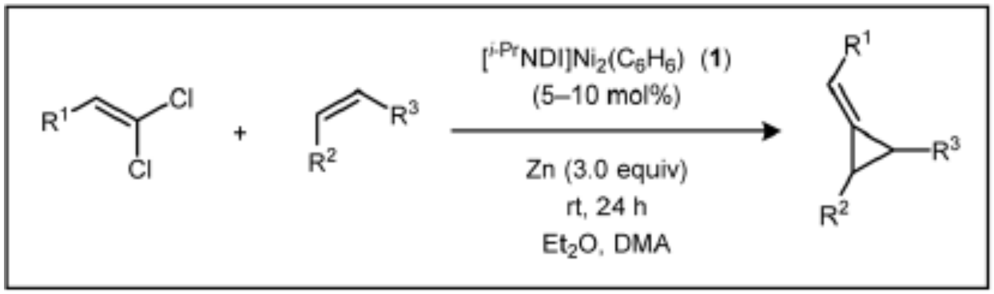
6

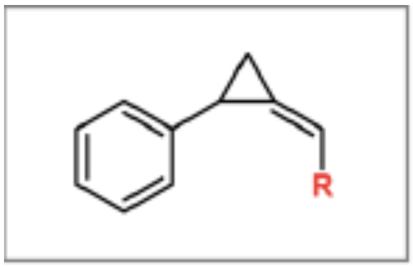


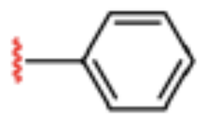
entry	catalyst	yield	E/Z ratio
1	[$^{i\text{-Pr}}$NDI]$Ni_2(C_6H_6)$ (**1**)	94%	1:5
2	[$^{i\text{-Pr}}$NDI]Ni_2Cl_2 (**4**)	87%	1:5
3[b]	$^{i\text{-Pr}}$NDI (**5**) + Ni(DME)Cl_2	92%	1:5
4[b]	^{Et}NDI (**6**) + Ni(DME)Cl_2	50%	1:1
5[b]	^{Me}NDI (**7**) + Ni(DME)Cl_2	<2%	–
6	[$^{i\text{-Pr}}$PDI]$NiCl_2$ (**8**)	<2%	–
7	[$^{i\text{-Pr}}$IP]Ni(COD) (**9**)	<2%	–
8	[BPY]Ni(COD) (**10**)	<2%	–
9	[$^{i\text{-Pr}}$DAD]Ni(COD) (**11**)	<2%	–



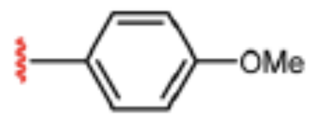
7



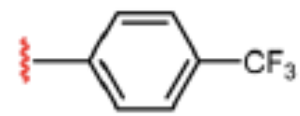




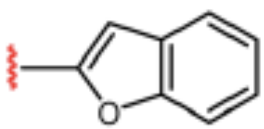
12 87% Yield (E/Z = 1:3)



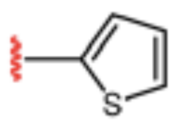
13 93% Yield (E/Z = 1:4)



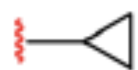
14 71% Yield (E/Z = 1:4)



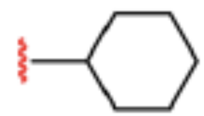
15 53% Yield (E/Z = 1:4)



16 62% Yield (E/Z = 1:3)

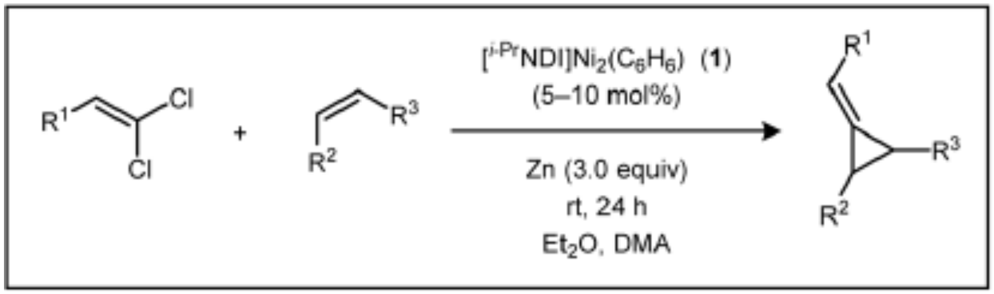


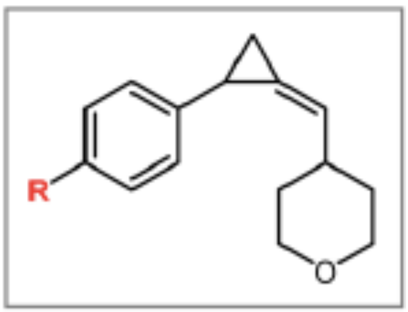
17 67% Yield (E/Z = 1:2)



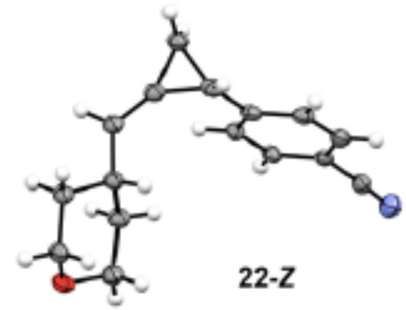
18 95% Yield (E/Z = 1:6)

8



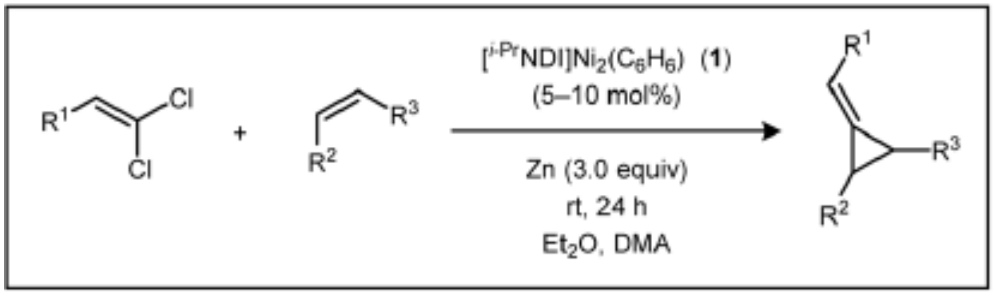


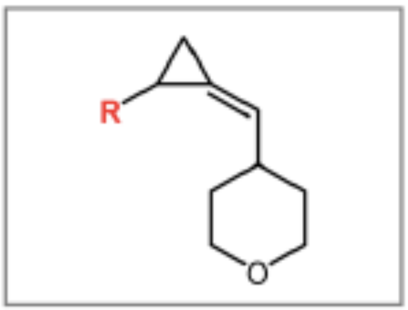
19	R = –CF_3	99% Yield, E/Z = 1:8
20	R = –CO_2Me	81% Yield, E/Z = 1:7
21	R = –OMe	89% Yield, E/Z = 1:3
22	R = –CN	74% Yield, E/Z = 1:8
23	R = –BPin	78% Yield, E/Z = 1:6
24	R = –Cl	83% Yield, E/Z = 1:6

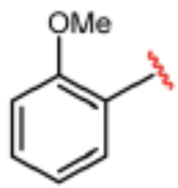


22-Z

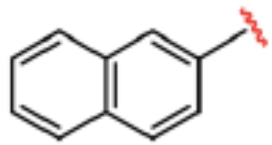
9



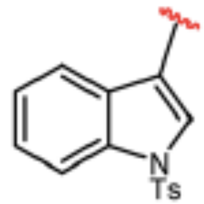




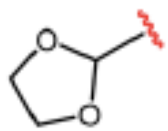
25 72% Yield (E/Z = 1:4)



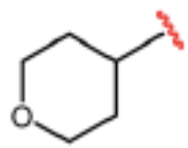
26 98% Yield (E/Z = 1:5)



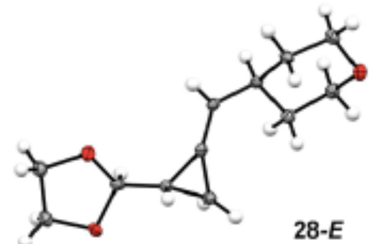
27 66% Yield (E/Z = 1:3)



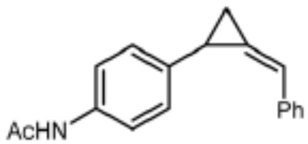
28 50% Yield (E/Z = 8:1)



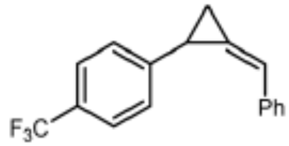
29 56% Yield (E/Z = 13:1)



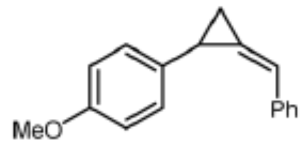
28-*E*



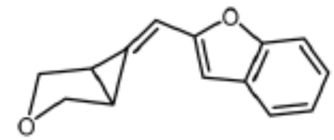
30 97% Yield
(E/Z = 1:9)



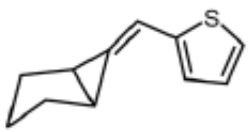
31 81% Yield
(E/Z = 1:4)



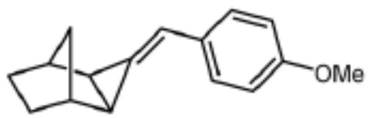
32 79% Yield
(E/Z = 1:3)



33[b] 77% Yield

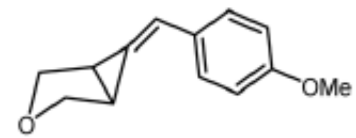


36[b] 99% Yield

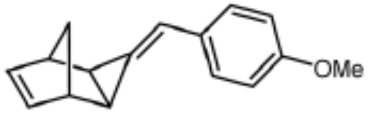


37[b] 86% Yield

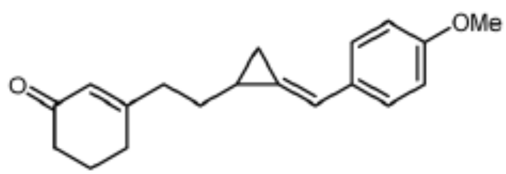
34[b] 75% Yield



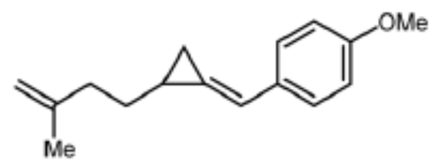
35[b] 79% Yield



38[b] 54% Yield

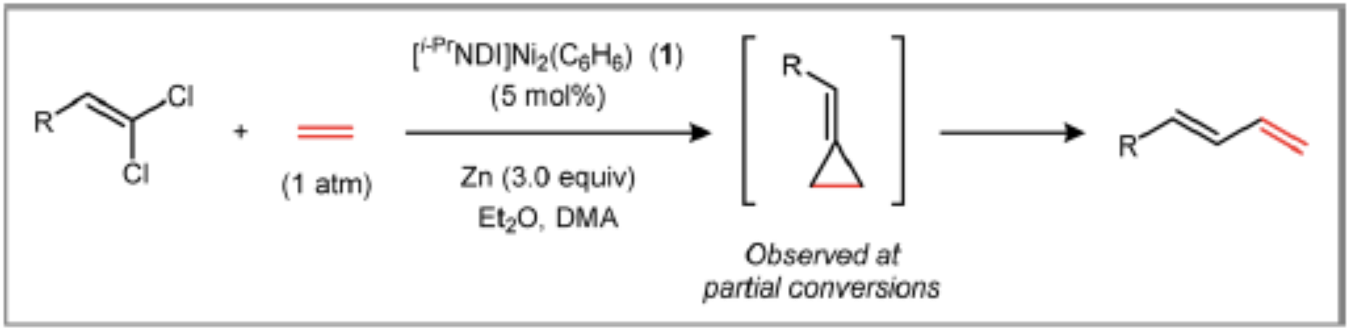


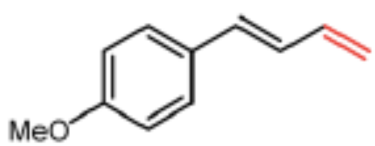
39 67% Yield
(E/Z = 1:1)



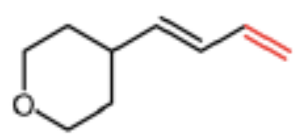
40 95% Yield
(E/Z = 1:1)

11





41 78% Yield
(E/Z = >20:**1**)

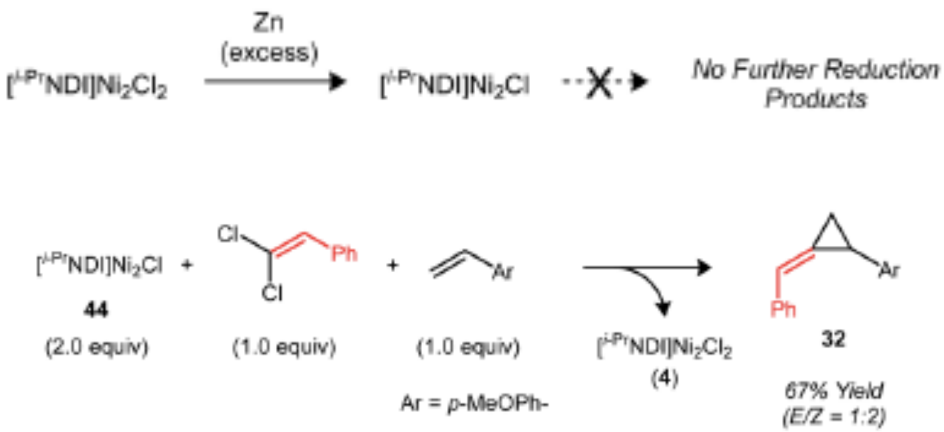


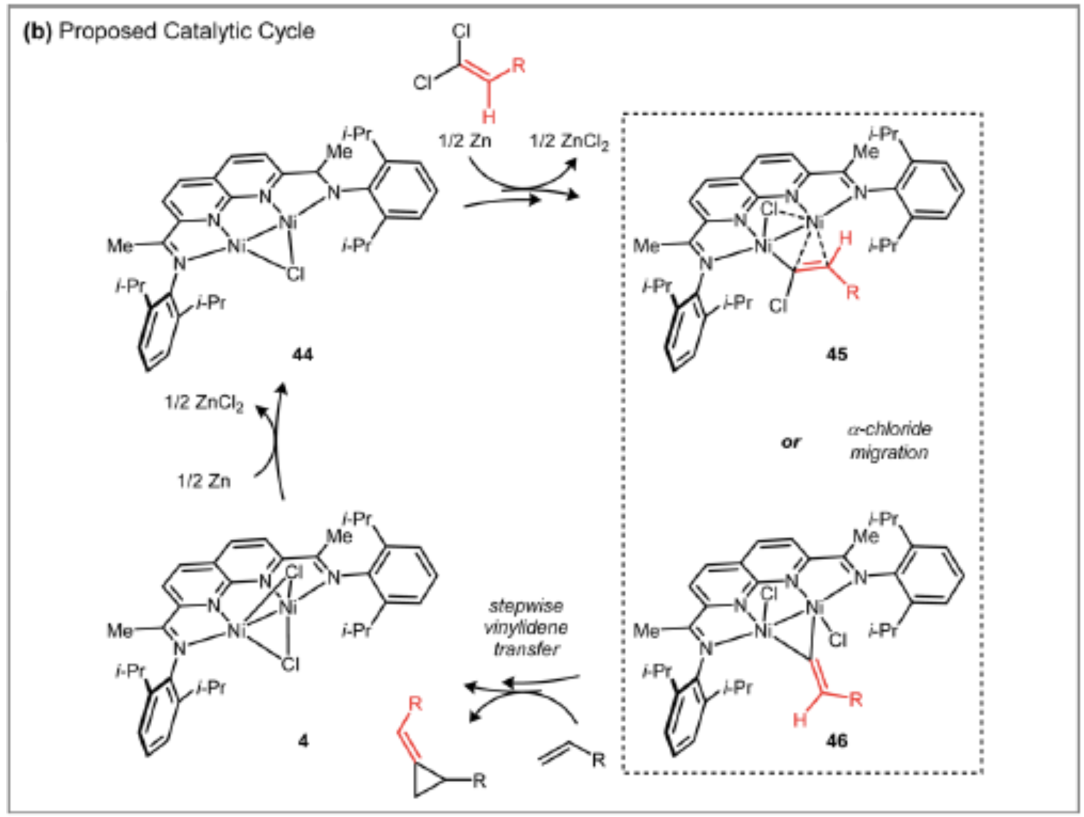
42 78% Yield
(E/Z = >20:1)

43 74% Yield
(E/Z = 8:1)

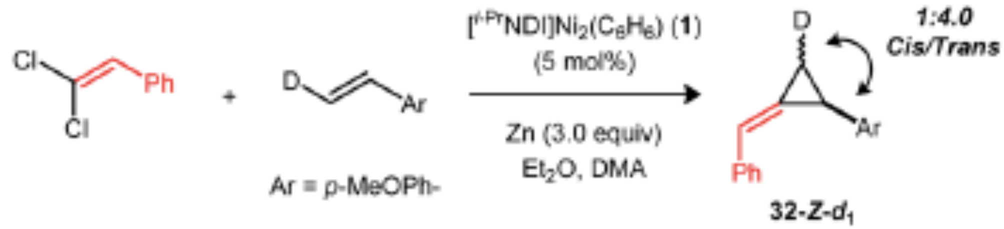
12

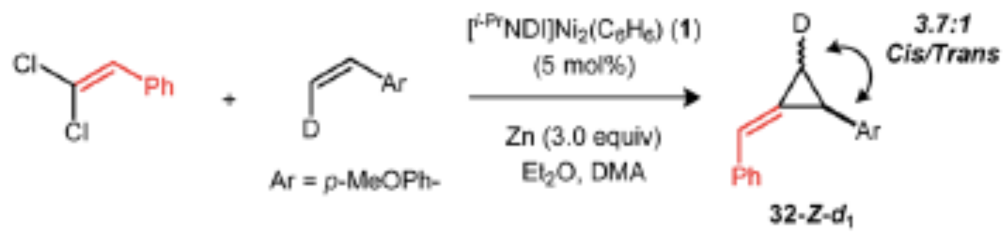
Mechanistic Studies

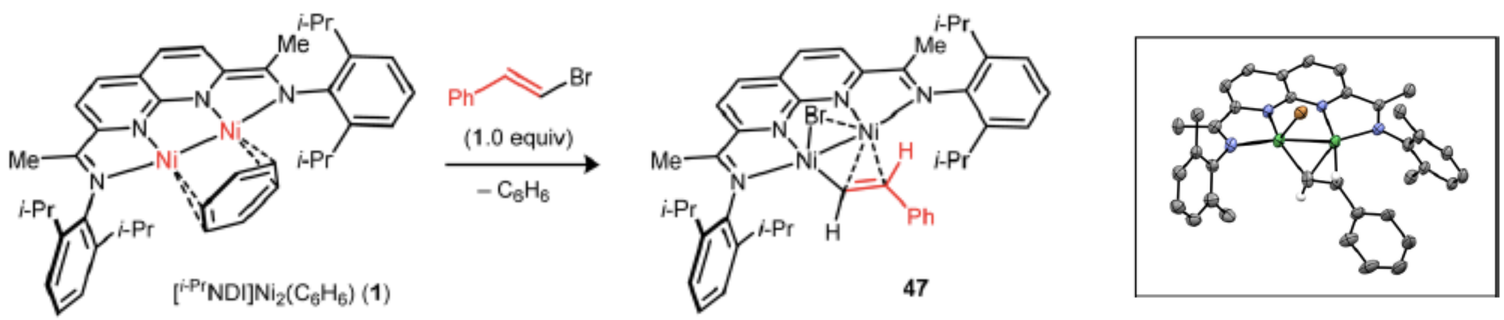




13


Cl
Cl
Ph
D
Ar
Ar = p-MeOPh-
[i-PrNDI]Ni2(C6H6) (1)
(5 mol%)
Zn (3.0 equiv)
Et2O, DMA
D
Ar
Ph
32-Z-d1
1:4.0
Cis/Trans


Cl
Cl
Ph
Ar
D
Ar = p-MeOPh-
[i-PrNDI]Ni2(C6H6) (1)
(5 mol%)
Zn (3.0 equiv)
Et2O, DMA
D
Ar
Ph
32-Z-d1
3.7:1
Cis/Trans

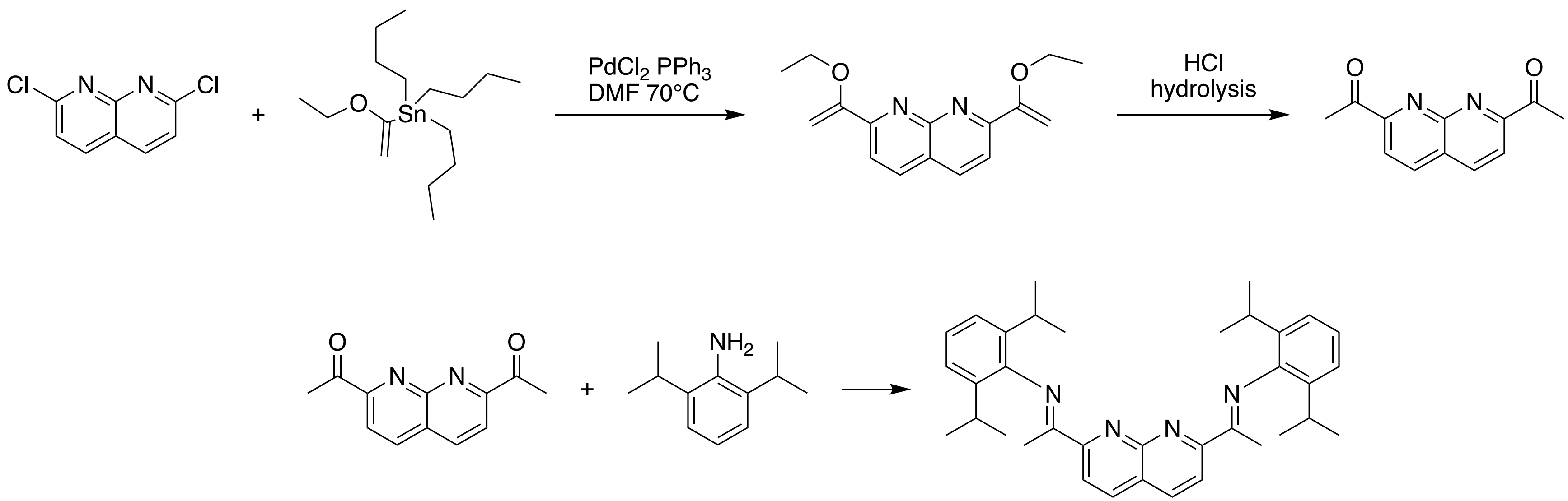

i-Pr
Me
N
N
Ni
Ni
Me
i-Pr
[i-PrNDI]Ni2(C6H6) (1)
Ph
Br
(1.0 equiv)
– C6H6
Br
H
Ph
47

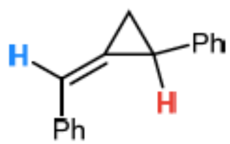
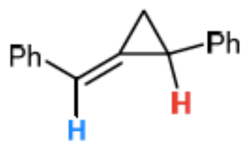
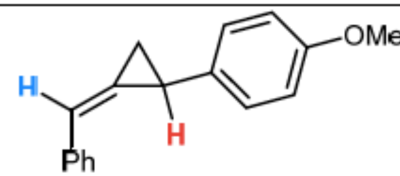
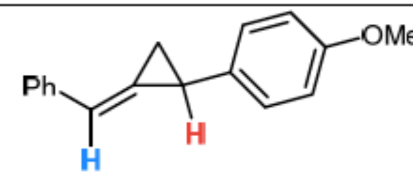
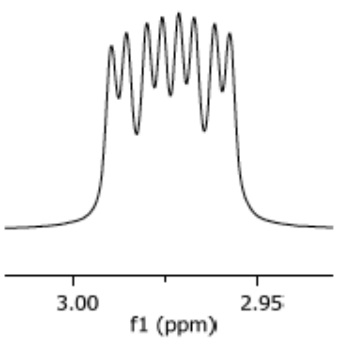
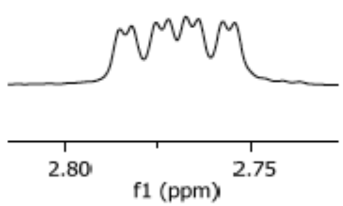
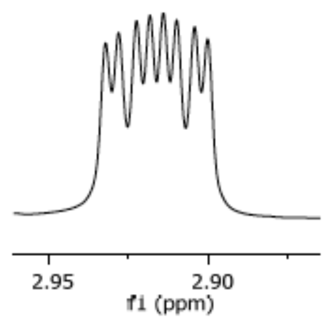
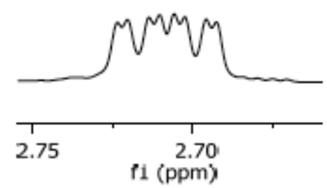
Conclusion

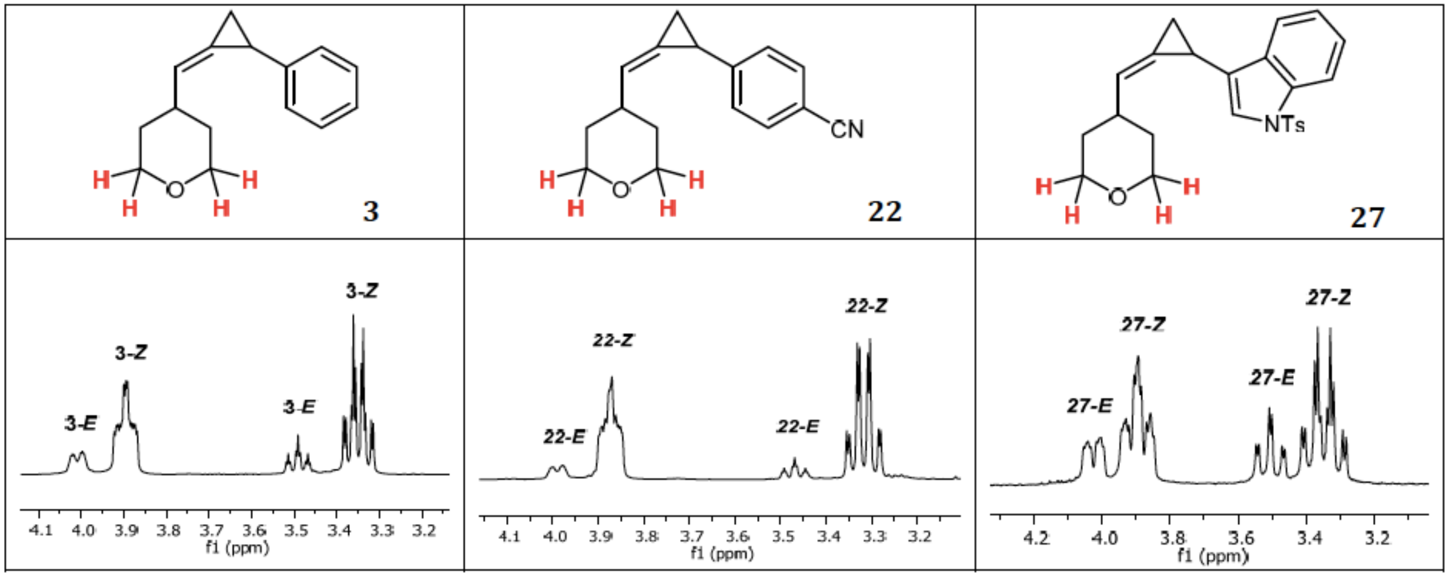
1) Developed a method for catalytic vinylidene transfer for the synthesis of MCPs in moderate to good yields.

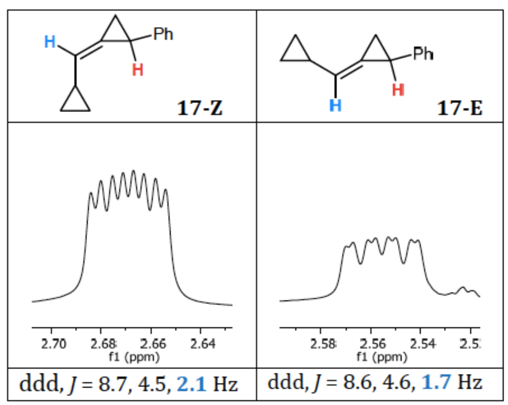
2) Utilize stable 1,1-dichloroalkenes as vinylidene precursors.

3) Substrate scope limited to sterically accessible alkenes.

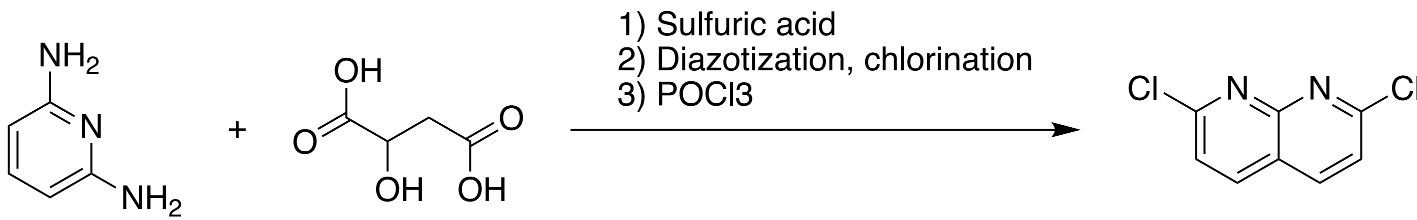

Cl
N
N
Cl
+
O
Sn
PdCl2 PPh3
DMF 70°C
O
N
N
O
HCl
hydrolysis
O
N
N
O
O
N
N
O
+
NH2
N
N
N
N

 **12-Z**	 **12-E**	 **32-Z**	 **32-Z**
			
ddd, J = 9.2, 4.9, 2.1 Hz	ddd, J = 9.1, 4.9, 1.8 Hz	ddd, J = 9.1, 4.9, 2.1 Hz	ddd, J = 9.0, 5.0, 1.8 Hz


3
22
CN
27
NTs
3-E
3-Z
3-E
3-Z
f1 (ppm)
22-E
22-Z
22-E
22-Z
f1 (ppm)
27-E
27-Z
27-E
27-Z
f1 (ppm)


Ph
17-Z
Ph
17-E
f1 (ppm)
f1 (ppm)
ddd, J = 8.7, 4.5, 2.1 Hz
ddd, J = 8.6, 4.6, 1.7 Hz

19



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