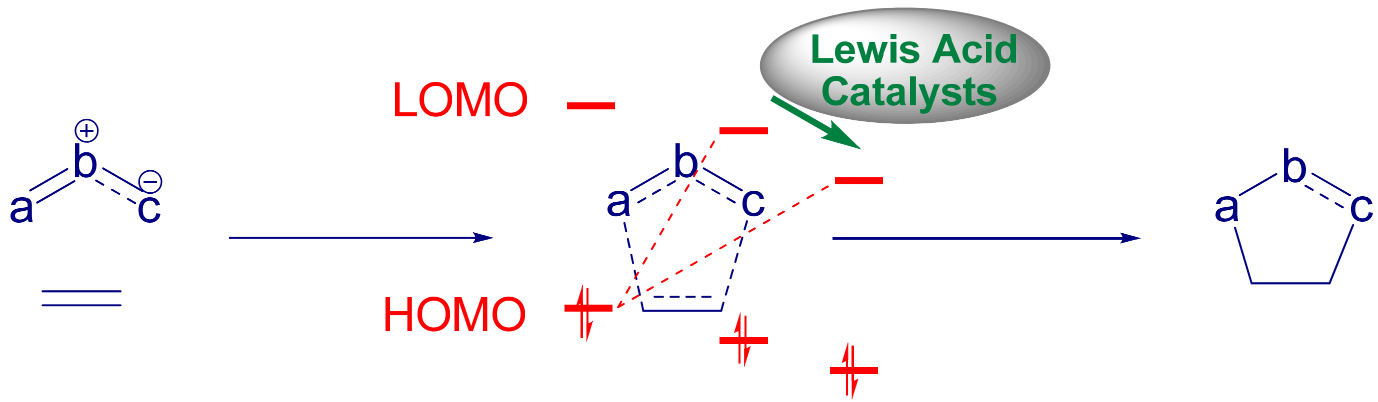
Asymmetric Catalytic 1,3-Dipolar Cycloaddition

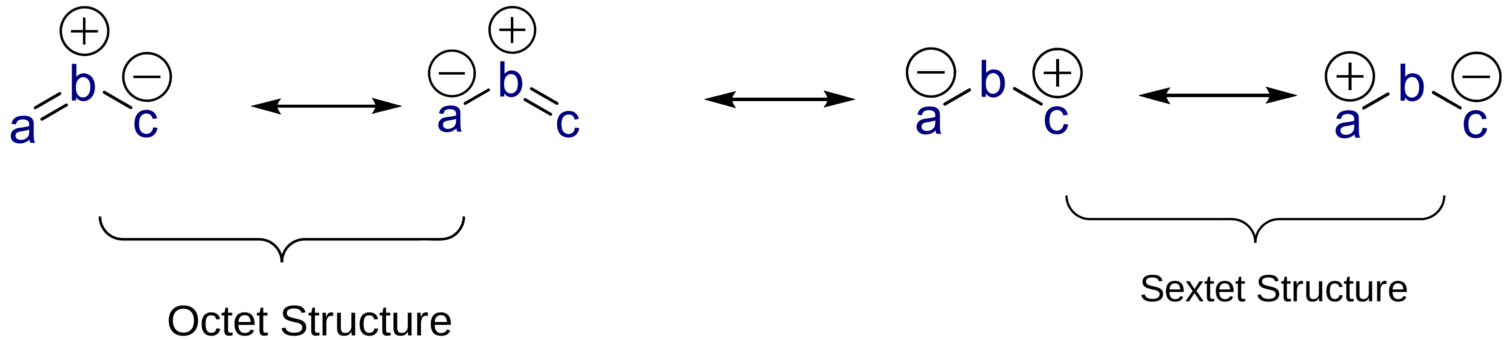


Reporter: Yang, Guoqiang

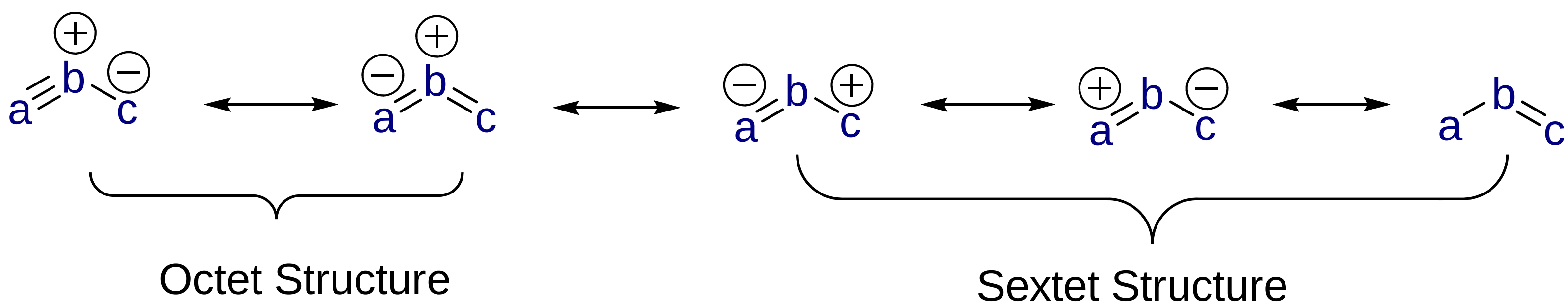
2010. 09. 11

Wanbin Group Literature Seminar

A: Allyl Anion Type

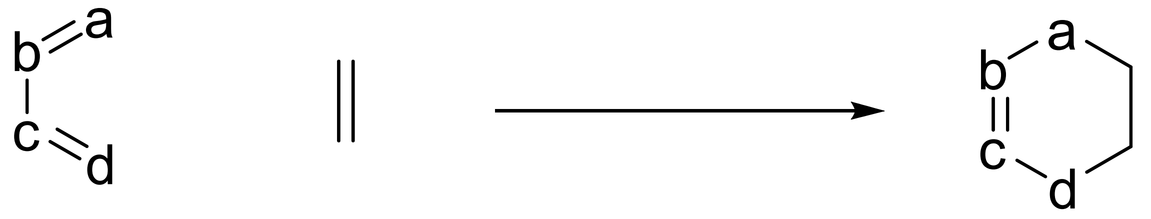


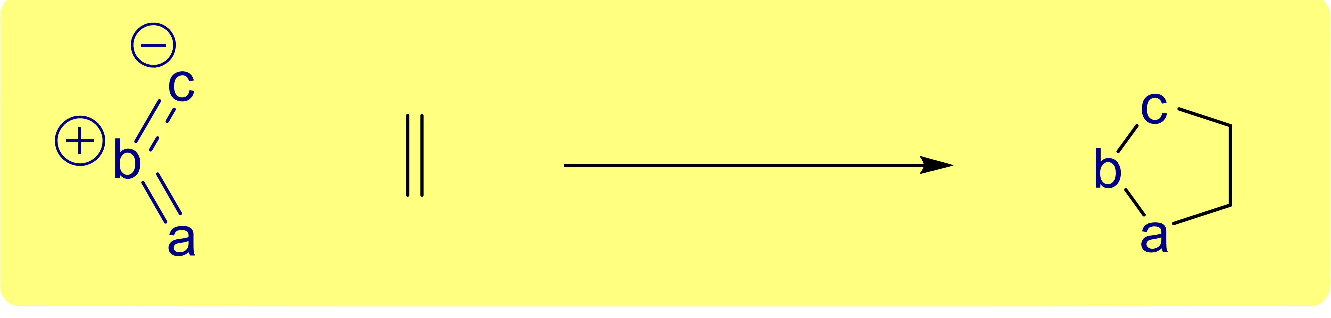
B: Propargyl or Allenyl Anion Type



C: Hypervalent Type

$a=b=c$ $\quad$ $a\equiv b=c$

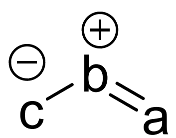

b
a
c
d
b
a
c
d

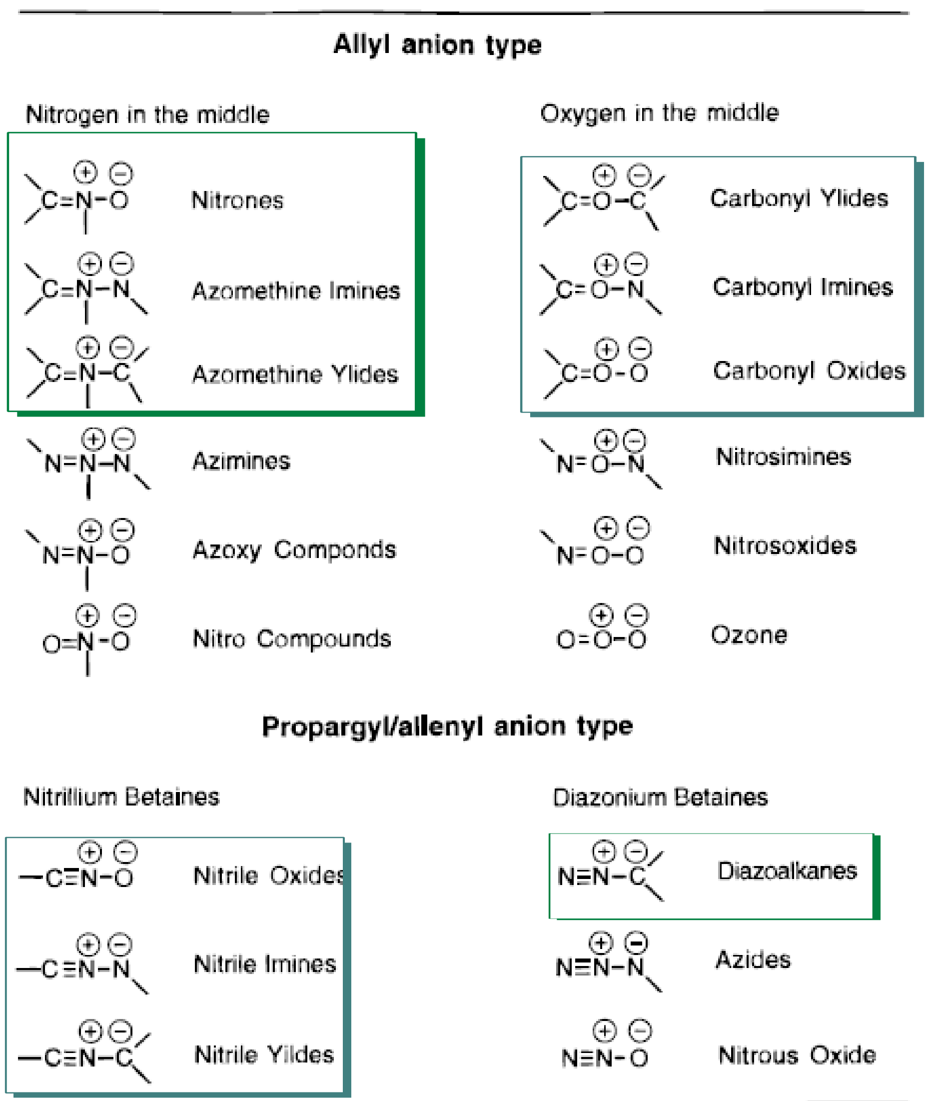

c
b
a
c
b
a

Content

- 1. Introduction (basic aspects)
- 2. EC Nitrone Cycloadditions
- 3. EC Azomethine Ylide Cycloadditions
- 4. EC Azomethine Imine Cycloadditions
- 5. Conclusion and Prospect

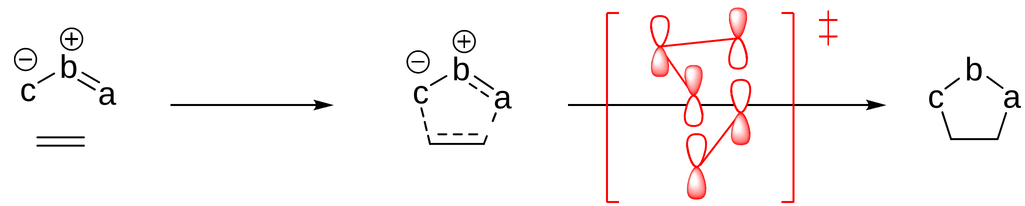
1.1 Basic Aspects – Classic 1,3-Dipoles



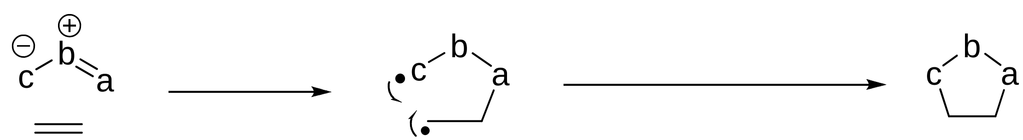


1.2 *Basic Aspects* – Mechanism

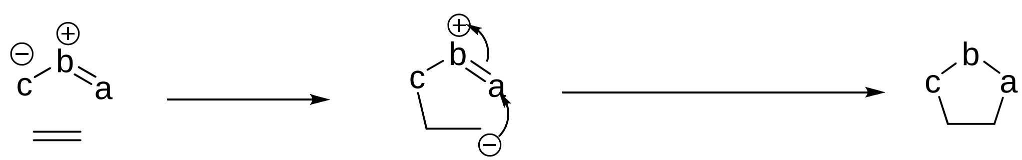
Concerted Mechanism

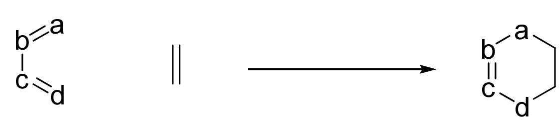


Diradical Mechanism

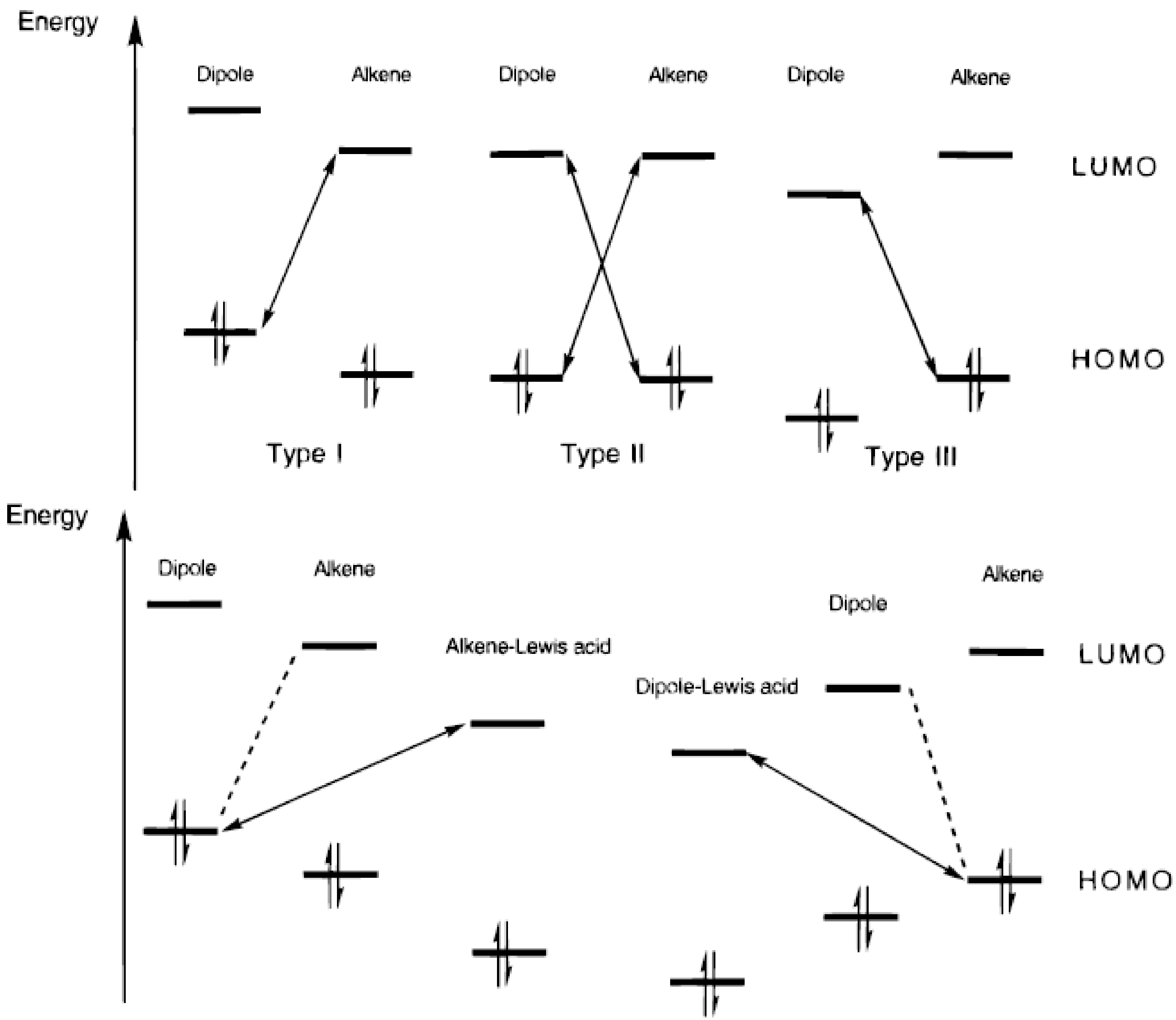


Anion Mechanism



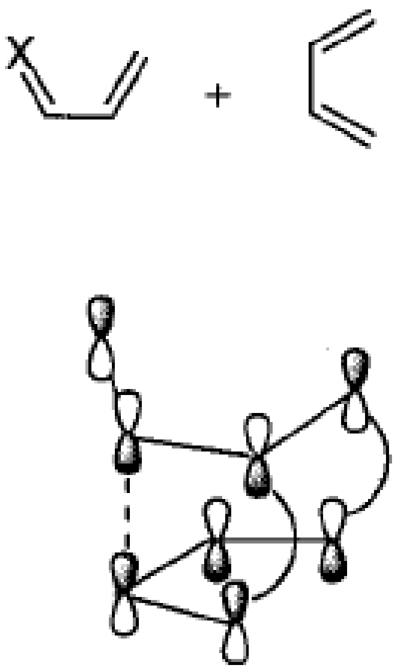


1.3 Basic Aspects – **Lewis Acid Activation**

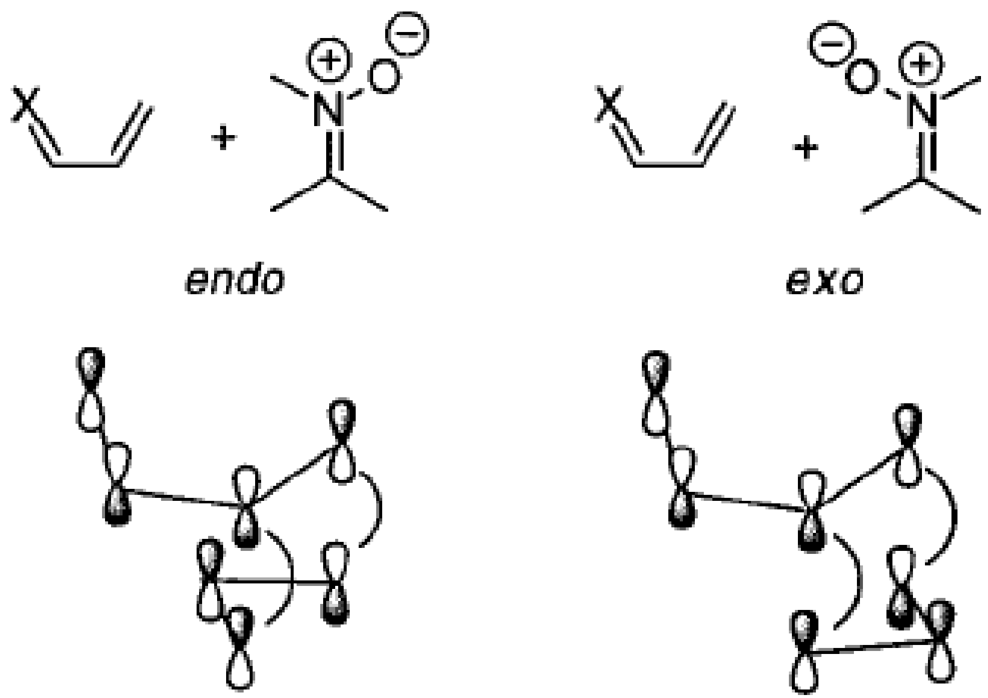


1.4 Basic Aspects – Selectivity

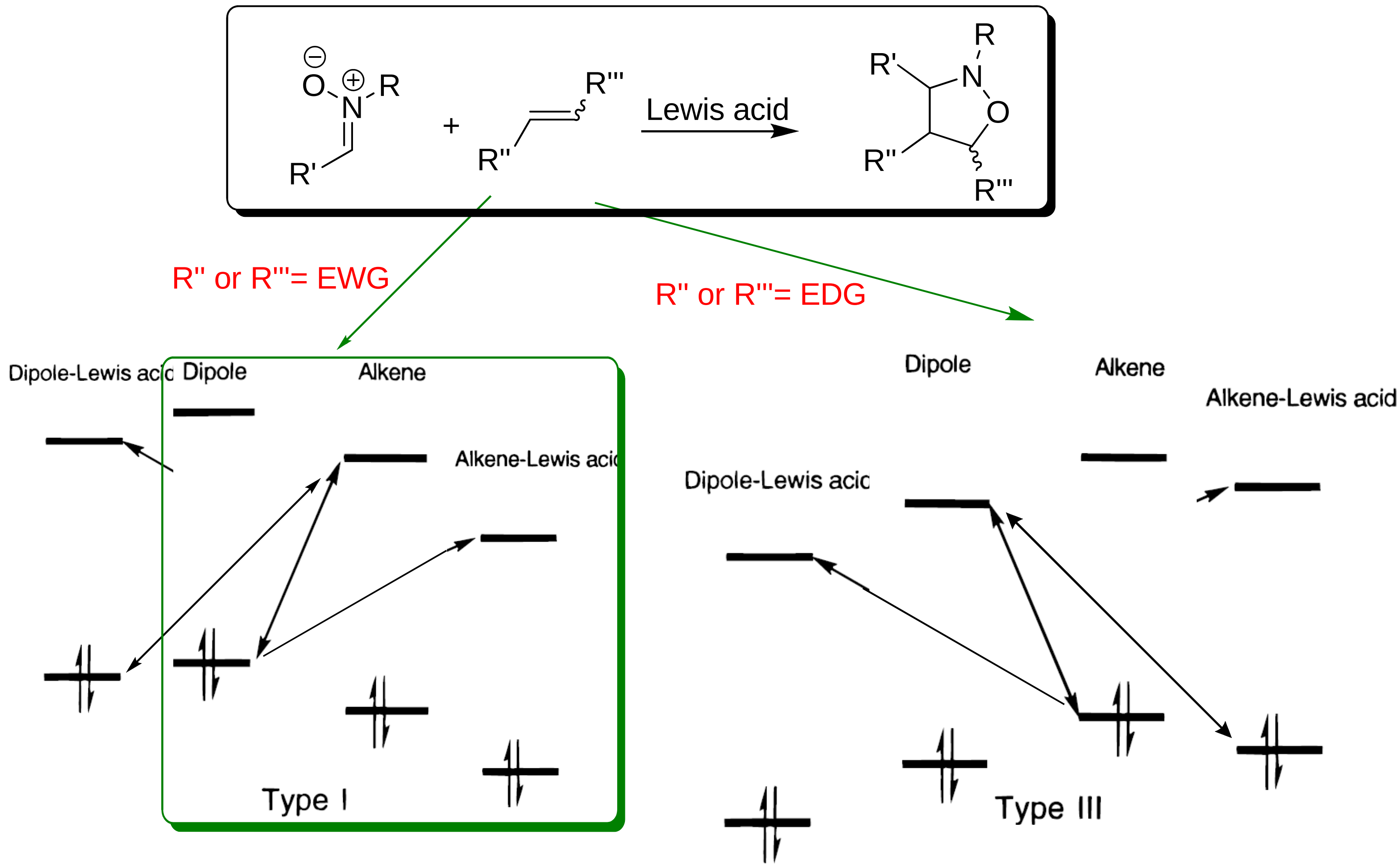
Endo-transition state for the Diels-Alder reaction

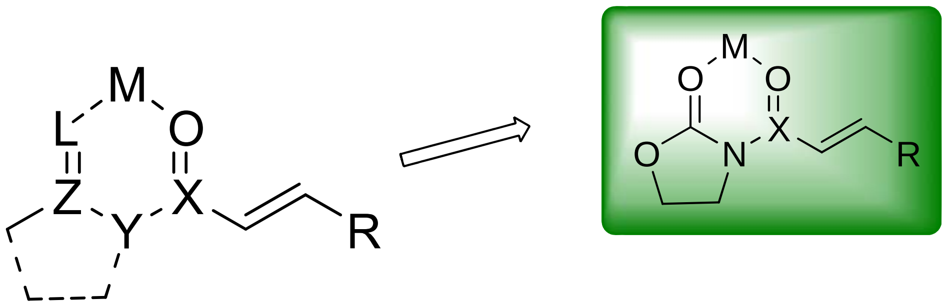


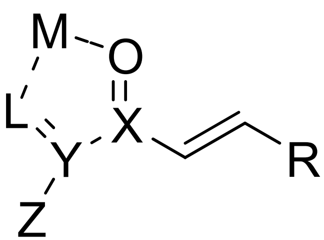
Transition state for 1,3-dipolar cycloaddition

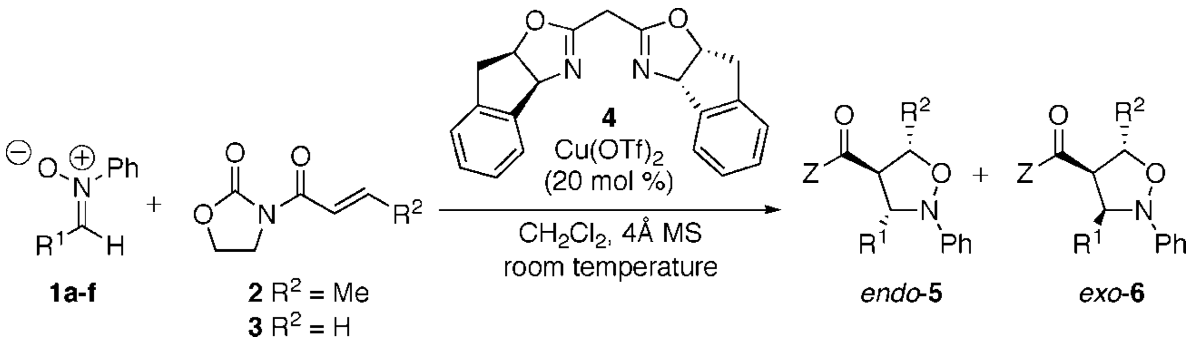


2.1 EC Nitrone Cycloadditions with alkene

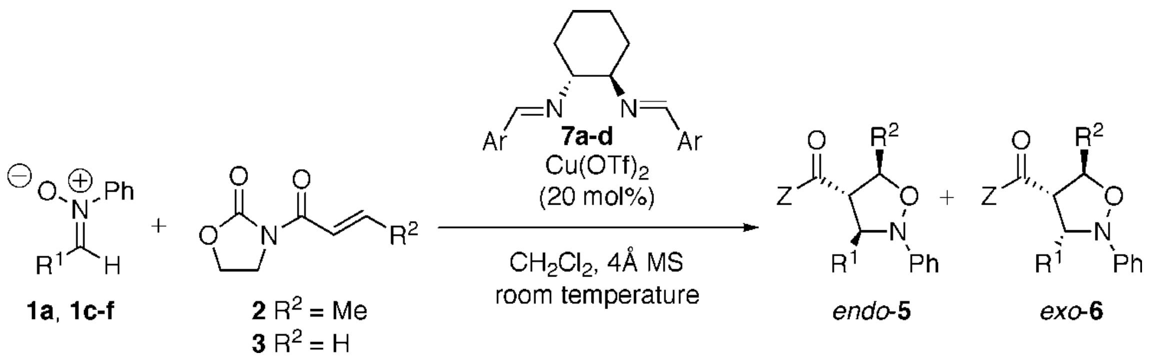






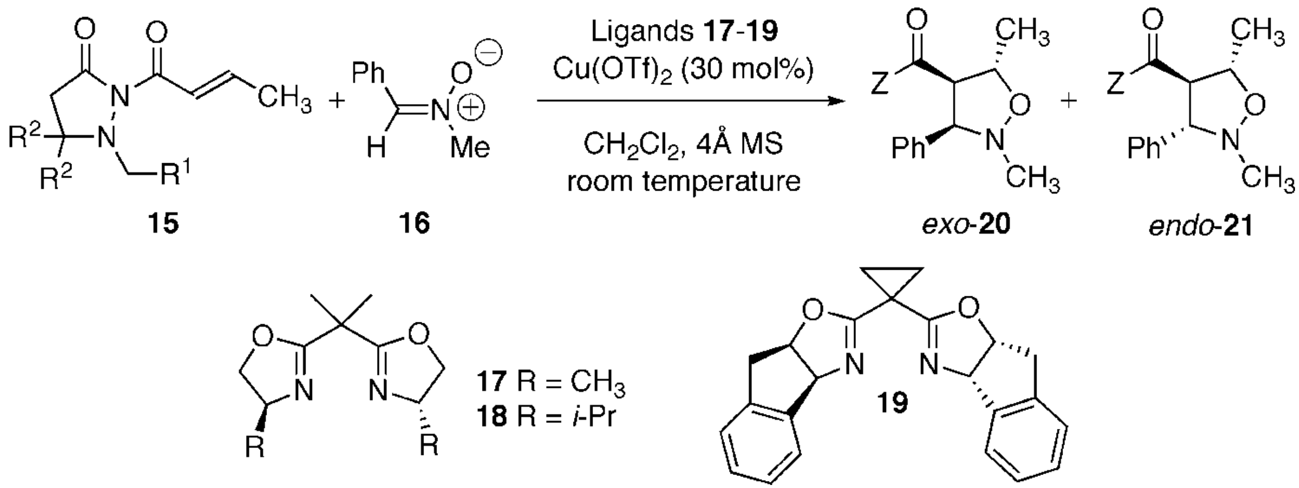


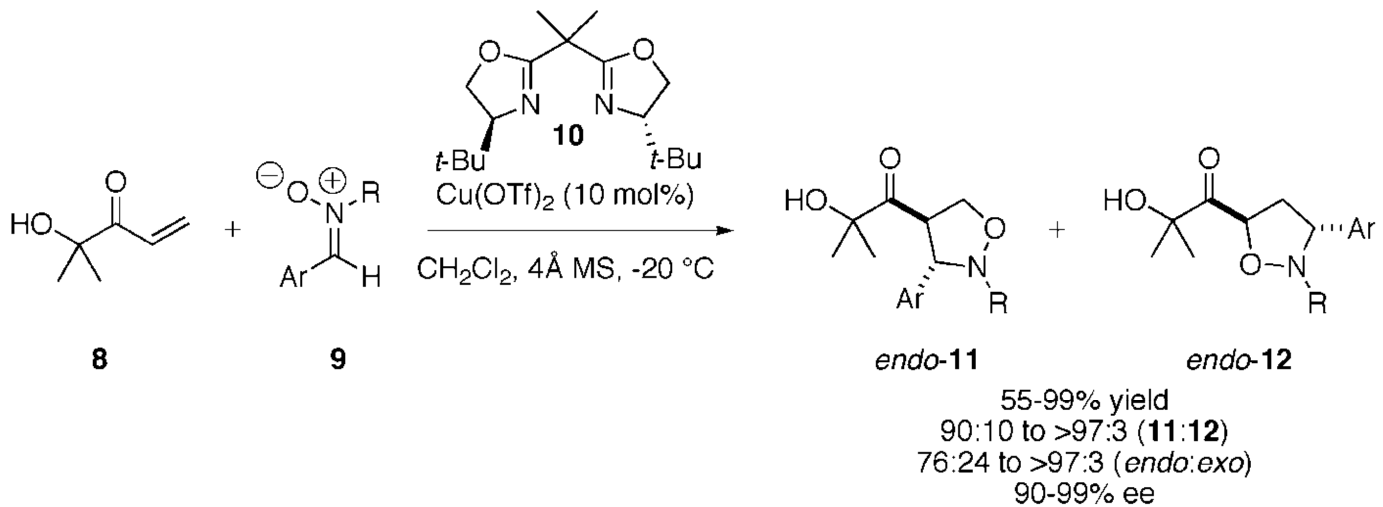
entry	R^1	R^2	yield (%)	*endo*/*exo*	*endo* ee (%)	*exo* ee (%)
1	Ph (**1a**)	Me	99	70:30	99	99
2	4-$CH_3OC_6H_4$ (**1b**)	Me	71	50:50	99	99
3	4- $CH_3C_6H_4$ (**1c**)	Me	97	70:30	99	99
4	4- $CF_3C_6H_4$ (**1d**)	Me	99	86:14	95	94
5	2-Naphthyl (**1e**)	Me	94	60:40	95	98
6	2-Furyl (**1f**)	Me	90	91:09	96	99
7	Ph (**1a**)	H	93	22:78	52	96



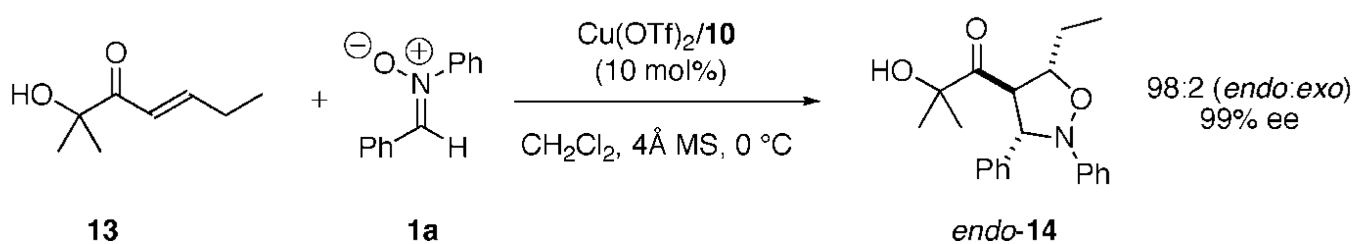
endo/exo: up to 95/5

Saito, T.; Yamada, T.; Miyazaki, S.; Otani, T. *Tetrahedron Lett.* **2004**, *45*, 9581.
Saito, T.; Yamada, T.; Miyazaki, S.; Otani, T. *Tetrahedron Lett.* **2004**, *45*, 9585.


Ligands 17-19
Cu(OTf)2 (30 mol%)
CH2Cl2, 4Å MS
room temperature
15
16
exo-20
endo-21
17 R = CH3
18 R = i-Pr
19

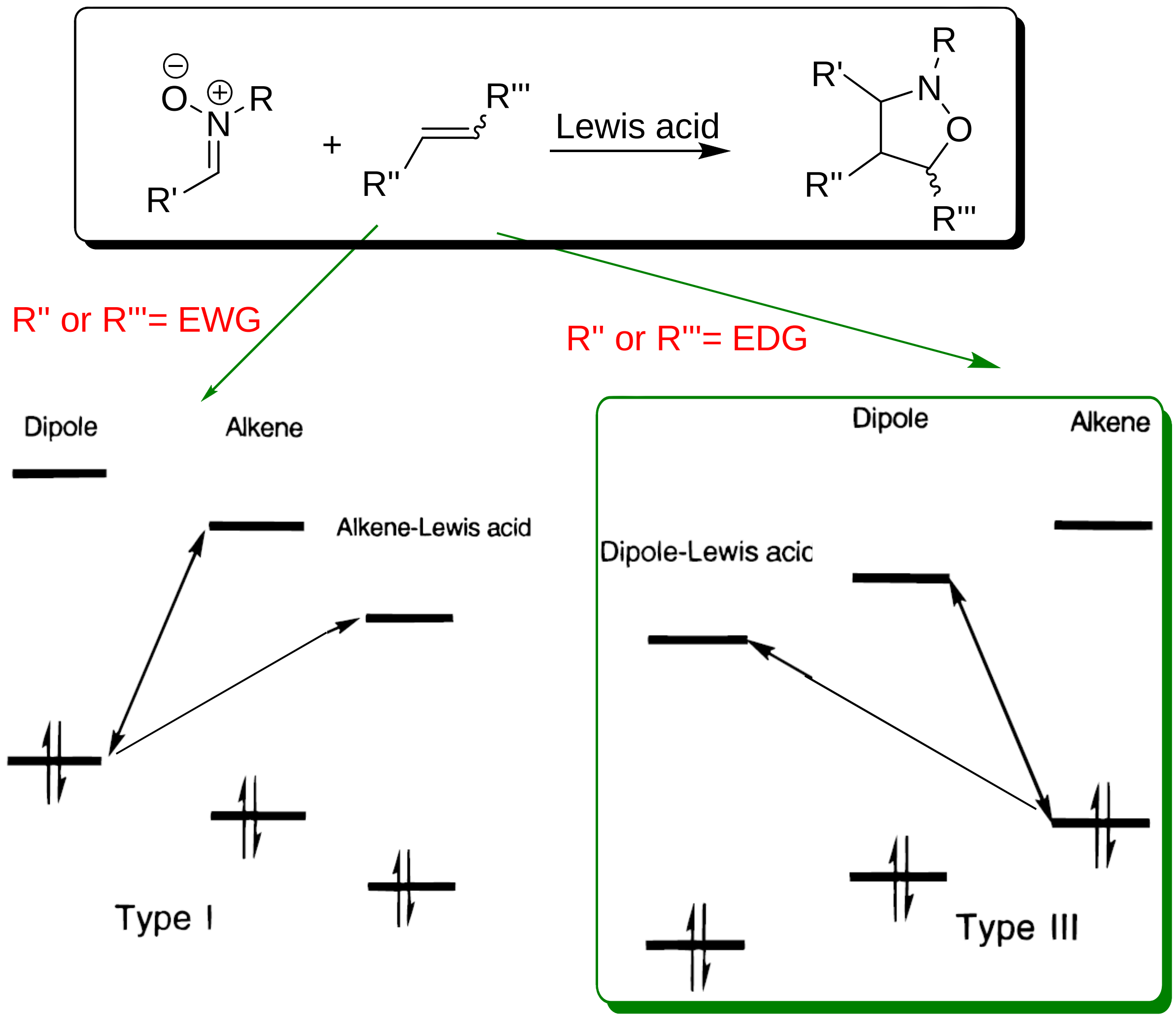

10
t-Bu
t-Bu
Cu(OTf)2 (10 mol%)
CH2Cl2, 4Å MS, -20 °C
8
9
endo-11
endo-12
55-99% yield
90:10 to >97:3 (11:12)
76:24 to >97:3 (endo:exo)
90-99% ee

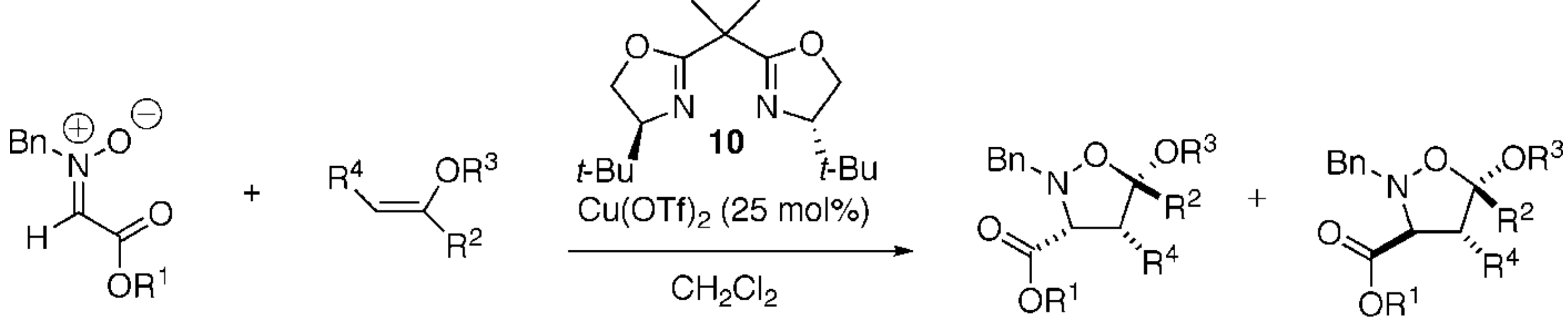
(1)


Cu(OTf)2/10
(10 mol%)
CH2Cl2, 4Å MS, 0 °C
13
1a
endo-14
98:2 (endo:exo)
99% ee

(2)

2.1 EC Nitrone Cycloadditions





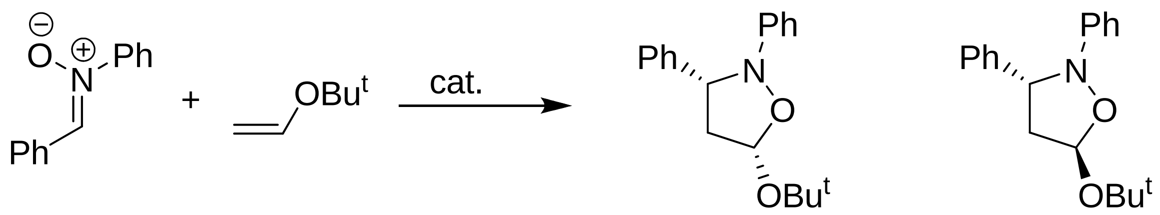
29 R^1 = Et
30 R^1 = t-Bu

31

exo-**32**

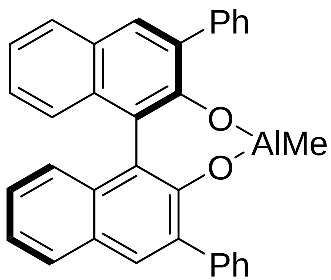
endo-**33**

entry	R^1	R^2	R^3	R^4	yield (%)	*exo/ endo*	ee (*exo*/*endo* %)
1	Et	H	Et	H	83	77:23	89/16
2	Et	Me	Me	H	83	31:69	90/94
3	Et	H	$-(CH_2)_2-$		43	50:50	12/0
4	*t*-Bu	H	Et	H	52	50:50	0/0



exo

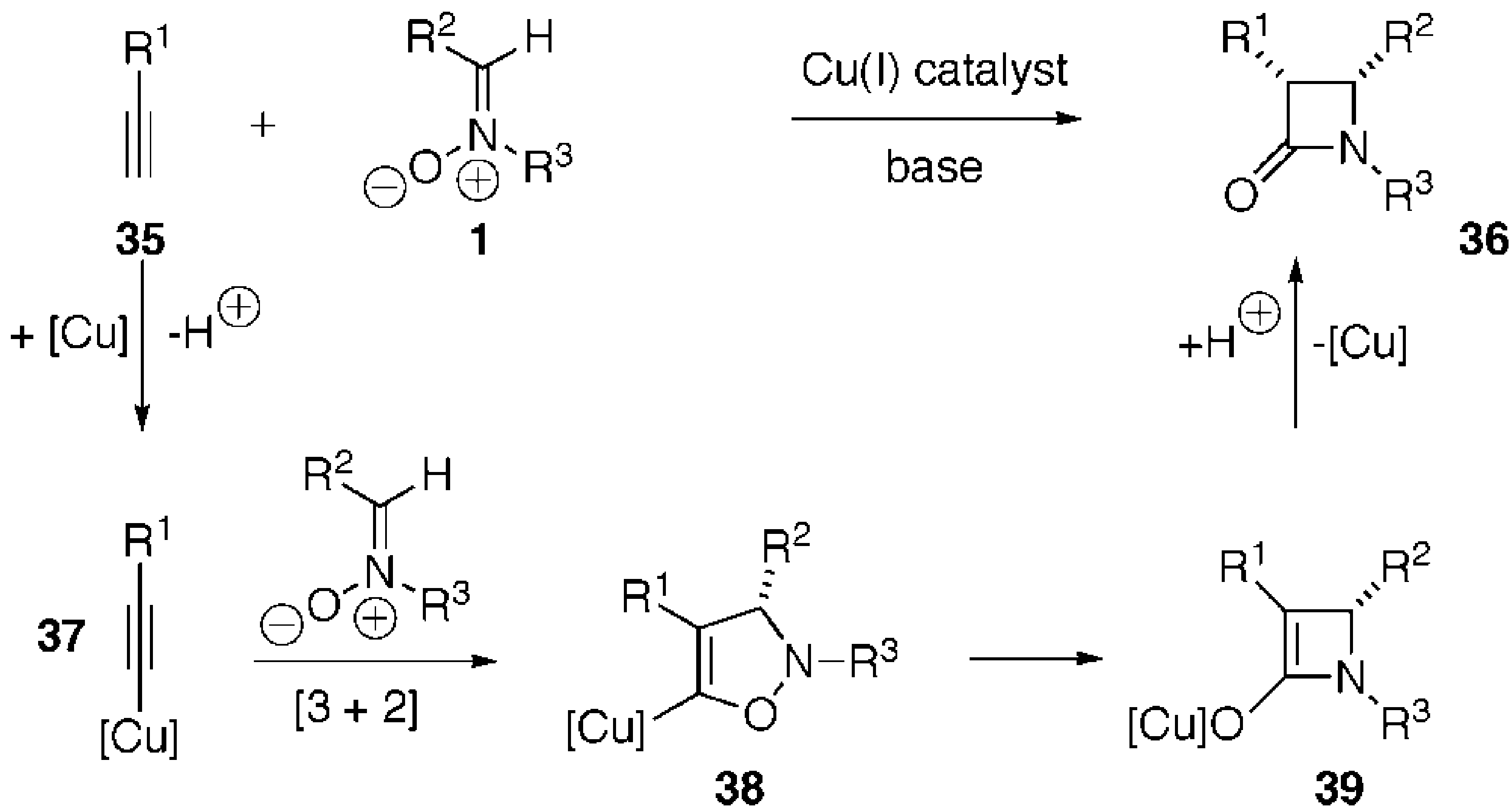
endo

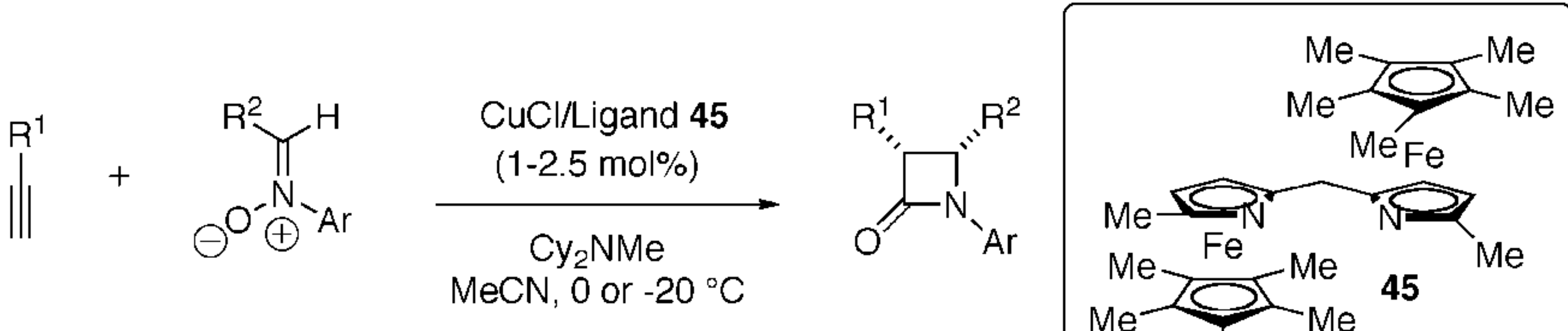


			yield		ee
20	toluene/	>95/45 min	74	<5:>95	93

Jensen, K. B.; Hazell, R. G.; Jørgensen, K. A. *J. Org. Chem.* **1999**, *64*, 2353.
Simonsen, K. B.; Bayo´n, P.; Hazell, R. G.; Gothelf, K. V.; Jørgensen, K. A. *J. Am. Chem. Soc.* **1999**, *121*, 3845.
Jensen, K. B.; Roberson, M.; Jørgensen, K. A. *J. Org. Chem.* **2000**, *65*, 9080.

2.2 EC Nitrone Cycloadditions with alkyne
----Kinugasa reaction

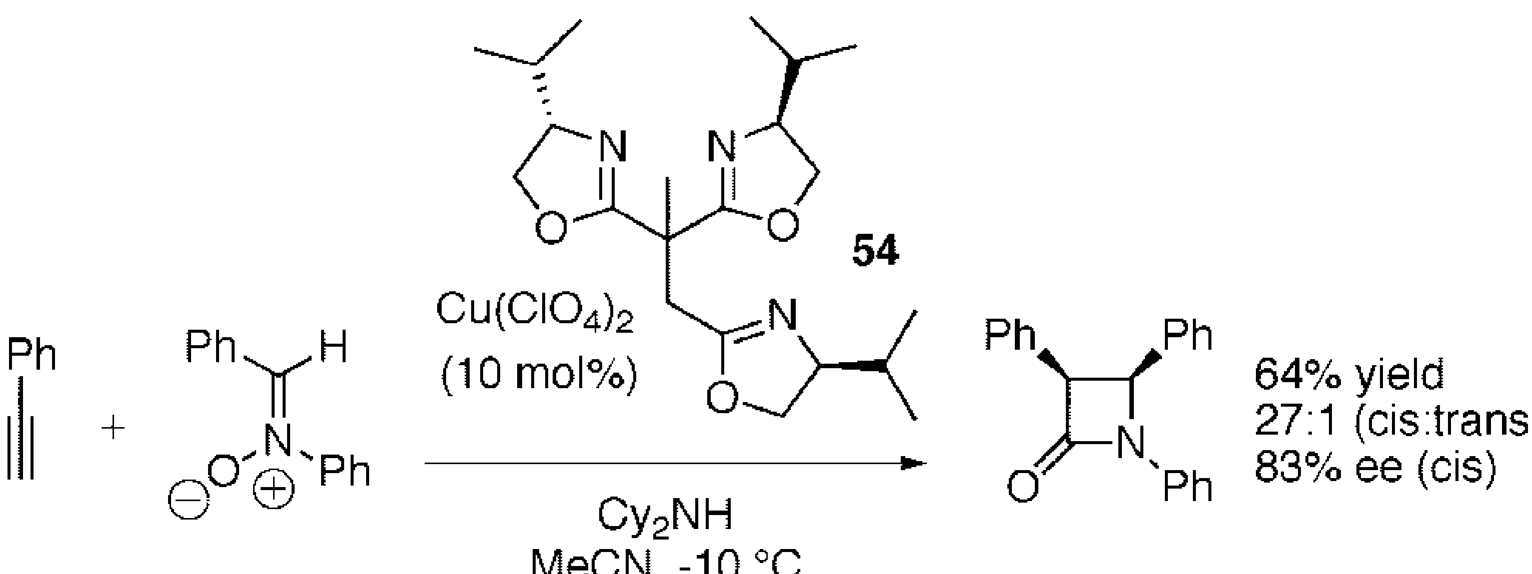




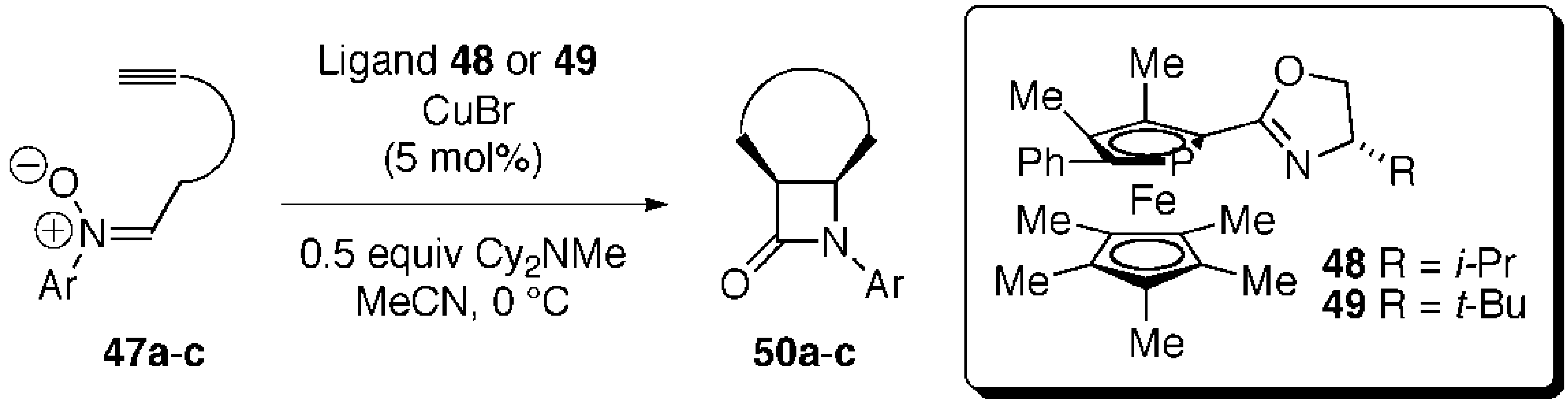
36 **1a**, **41-44** **46**

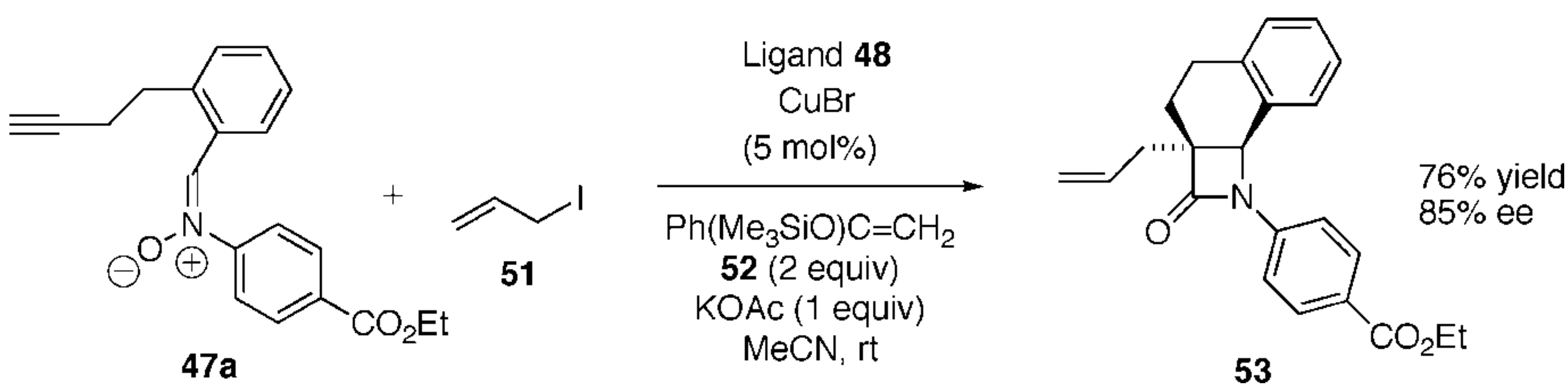
1a R^2 = Ph, Ar = Ph
41 R^2 = Ph, Ar = 4-(MeO)C_6H_4
42 R^2 = Ph, Ar = (EtO_2C)C_6H_4
43 R^2 = 4-(F_3C)C_6H_4, Ar = 4-(MeO)C_6H_4
44 R^2 = Cyclohexyl, Ar = 4-(MeO)C_6H_4

Up to 93% ee

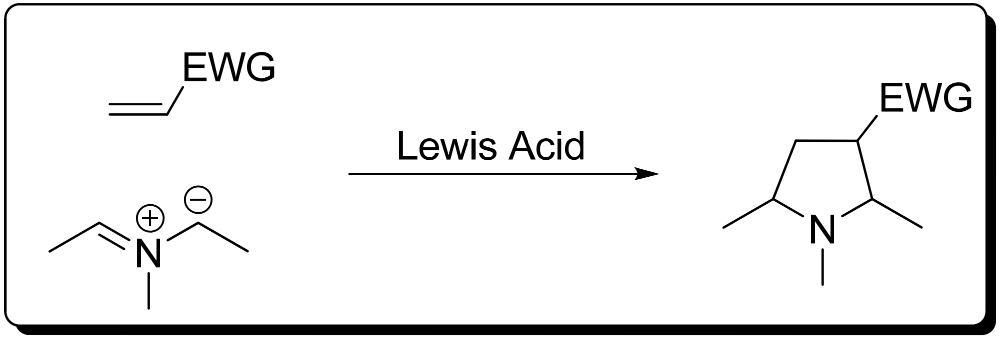


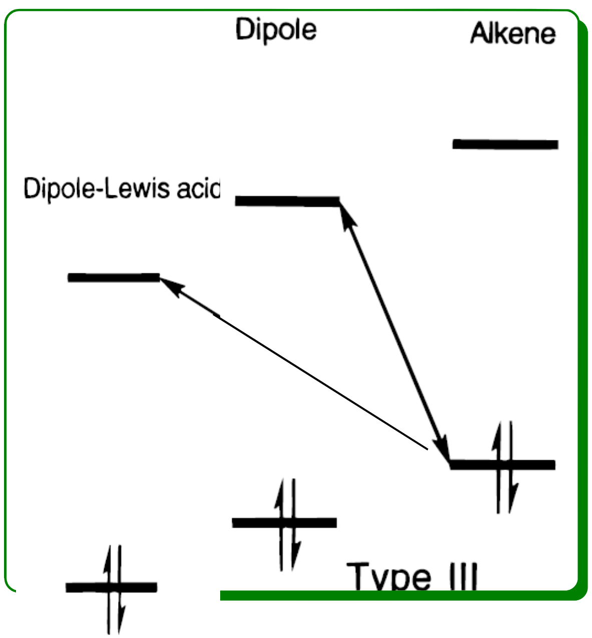
35a **1a** **40**

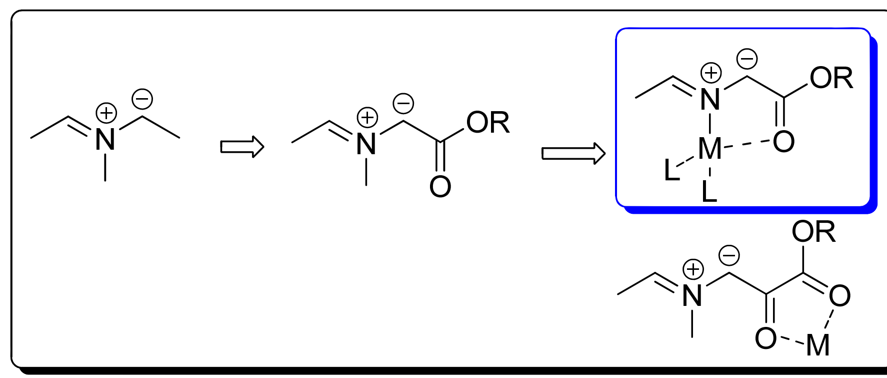

Ligand 48 or 49
CuBr
(5 mol%)
0.5 equiv Cy2NMe
MeCN, 0 °C
O
N
Ar
47a-c
O
N
Ar
50a-c
Me
Me
Ph
P
Fe
Me
Me
Me
Me
Me
O
N
R
48 R = i-Pr
49 R = t-Bu

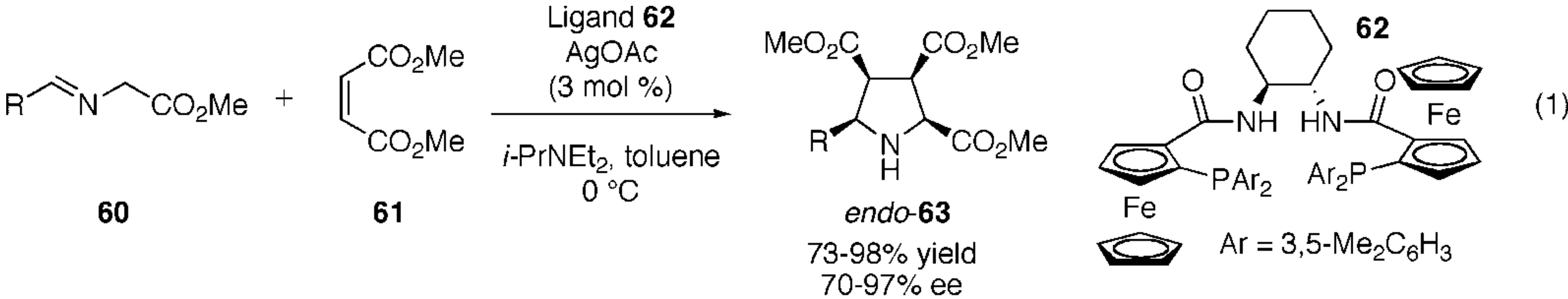

N
O
CO2Et
47a
+
I
51
Ligand 48
CuBr
(5 mol%)
Ph(Me3SiO)C=CH2
52 (2 equiv)
KOAc (1 equiv)
MeCN, rt
O
N
CO2Et
53
76% yield
85% ee

3. EC Azomethine Ylide Cycloadditions







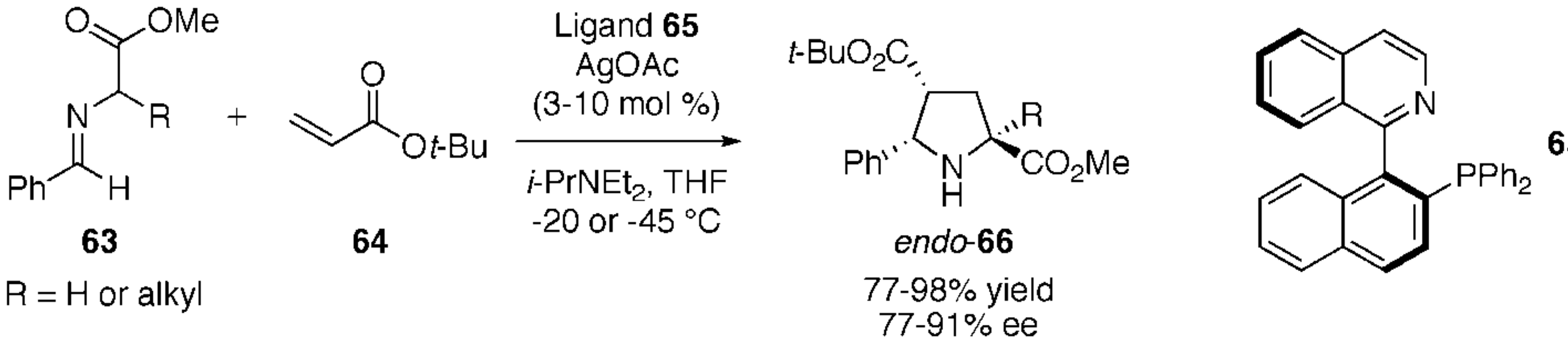


60 **61** *endo*-**63** **62**

73-98% yield
70-97% ee

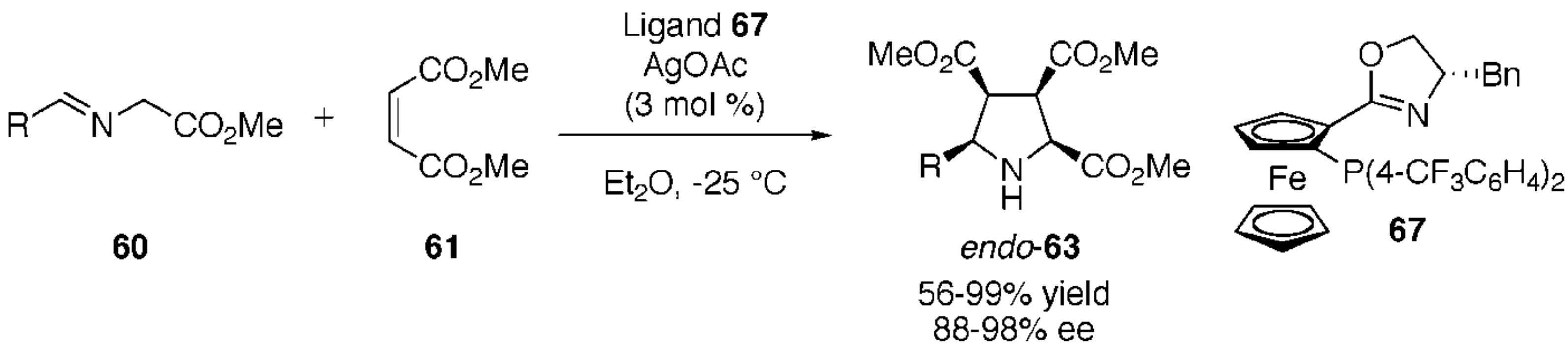
(1)

Longmire, J. M.; Wang, B.; Zhang, X. *J. Am. Chem. Soc.* **2002**, *124*, 13400.



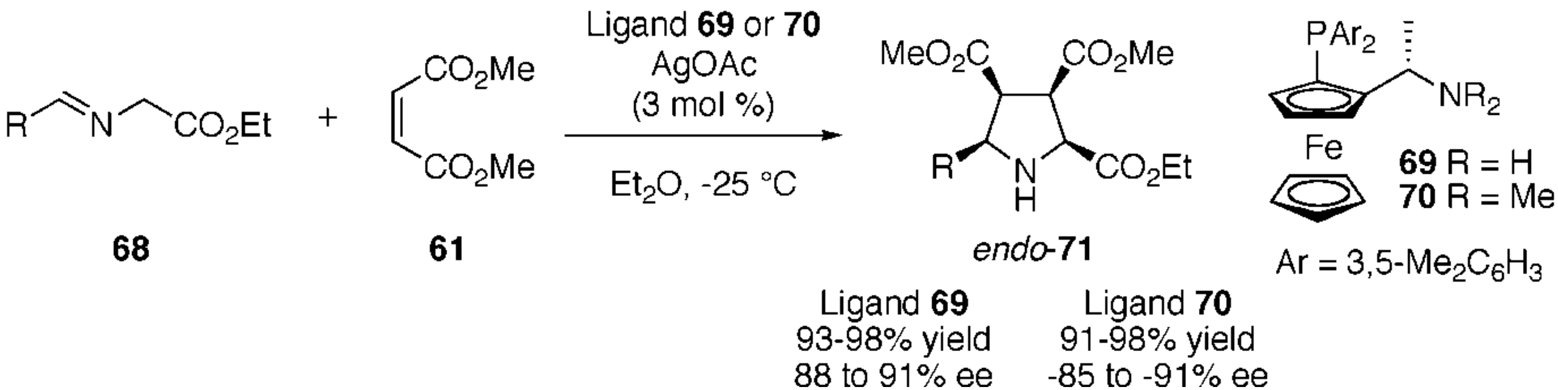
Ligand **65**
AgOAc
(3-10 mol %)
i-PrNEt2, THF
-20 or -45 °C
63
R = H or alkyl
64
endo-**66**
77-98% yield
77-91% ee
65

(2)



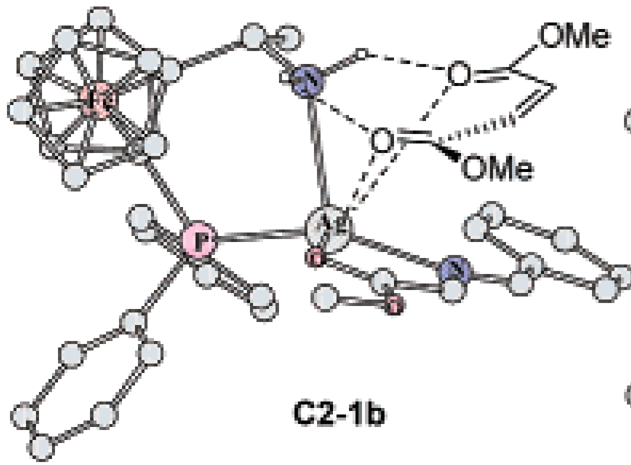
Ligand **67**
AgOAc
(3 mol %)
Et2O, -25 °C
60
61
endo-**63**
56-99% yield
88-98% ee
67

(3)

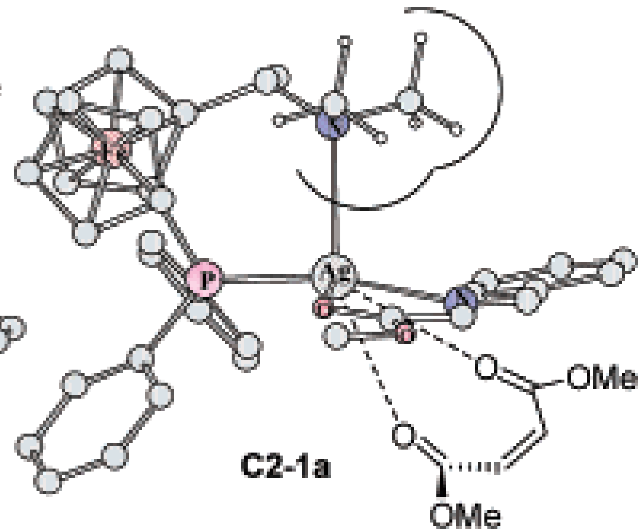


Ligand **69** or **70**
AgOAc
(3 mol %)
Et2O, -25 °C
68
61
endo-**71**
Ligand **69**
93-98% yield
88 to 91% ee
Ligand **70**
91-98% yield
-85 to -91% ee
69 R = H
70 R = Me
Ar = 3,5-Me2C6H3

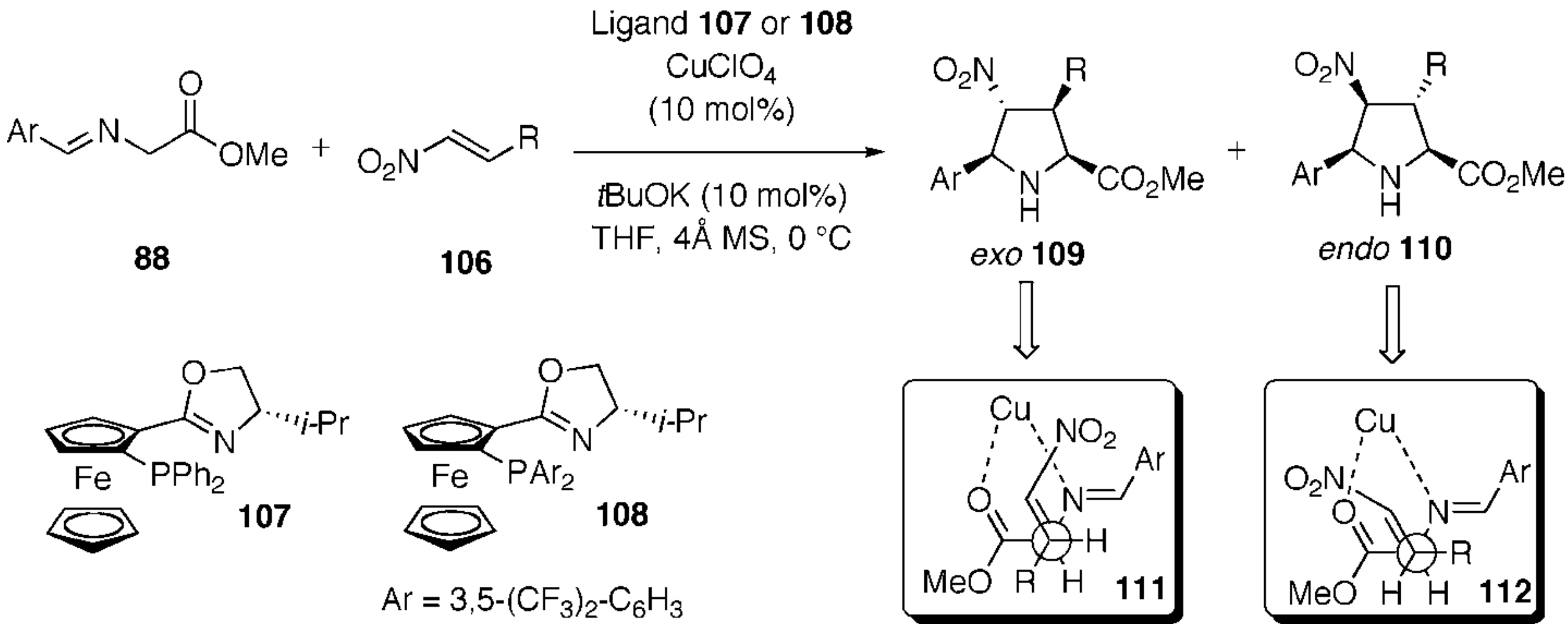
(4)



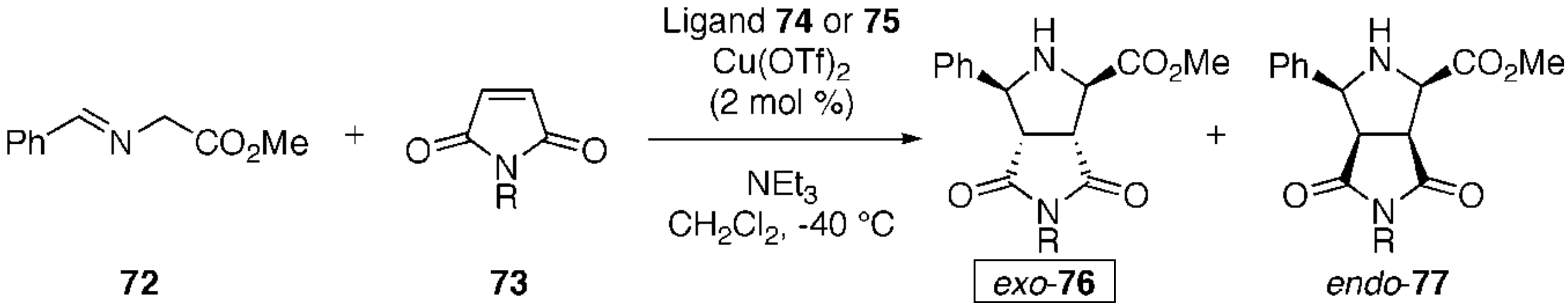
C2-1b

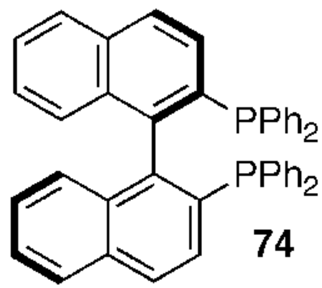


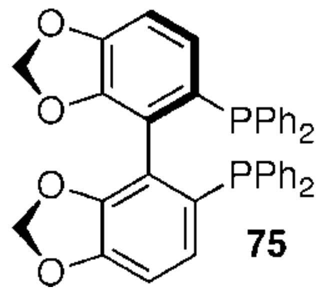
C2-1a



entry	Ar	R	ligand	*exo*/*endo*	yield (%)	*exo* ee (%)	*endo* ee (%)
1	Ph	Ph	**107**	only *exo*	87	95	
2	Ph	4-NO_2–C_6H_4	**107**	only *exo*	70	96	
3	Ph	4-MeO-C_6H_4	**107**	only *exo*	77	96	
4	Ph	*i*-Pr	**107**	only *exo*	74	98	
5	4-MeO-C_6H_4	Ph	**107**	89:11	96	97	
6	2-naphthyl	Ph	> **107**	92:08	92	92	
7	Ph	Ph	**108**	14:86	85		98
8	Ph	4-MeO-C_6H_4	**108**	30:70	79		95
9	Ph	*i*-Pr	**108**	06:94	88		97
10	4-MeO-C_6H_4	Ph	**108**	18:82	79		96
11	2-naphthyl	Ph	**108**	19:81	98		97

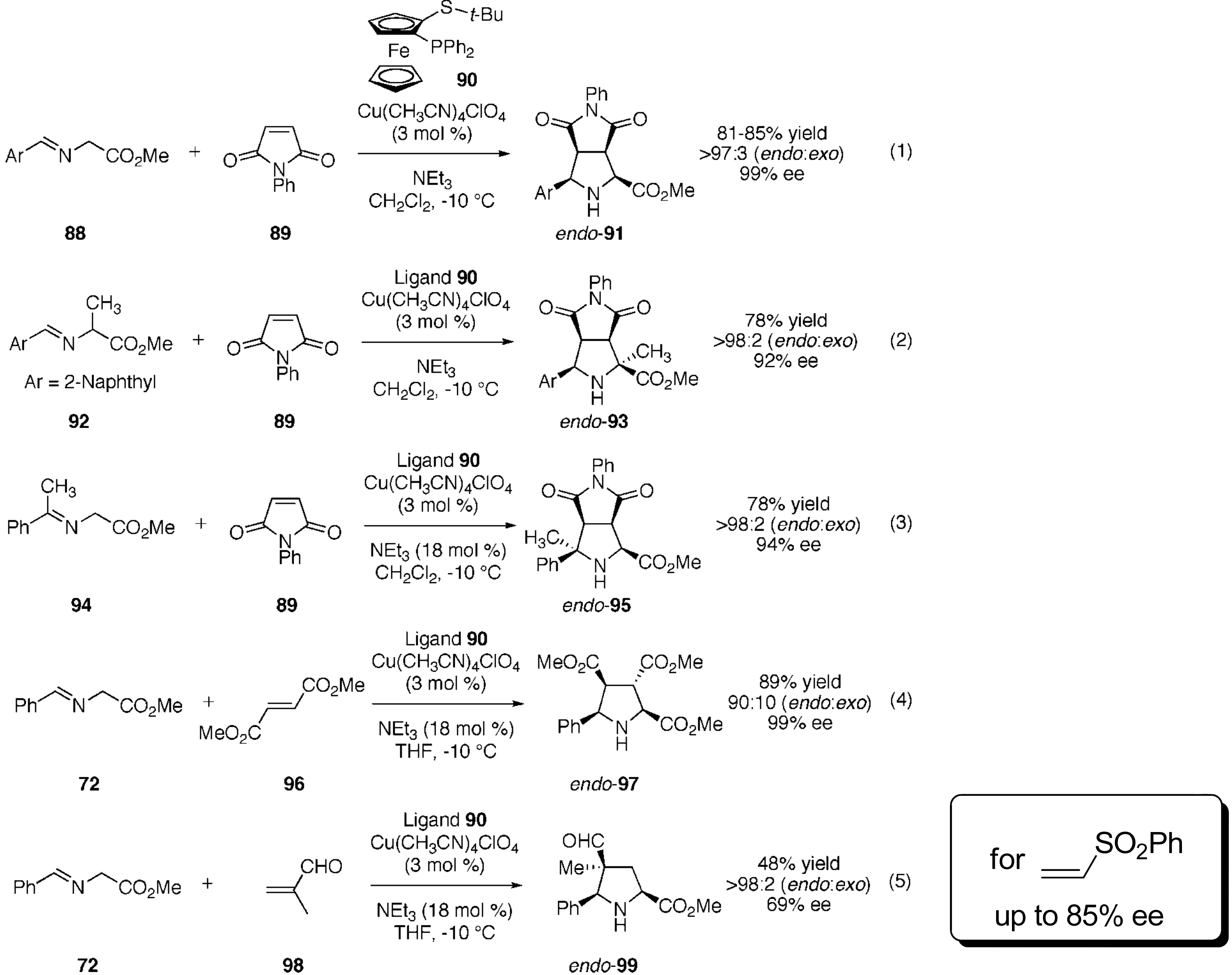






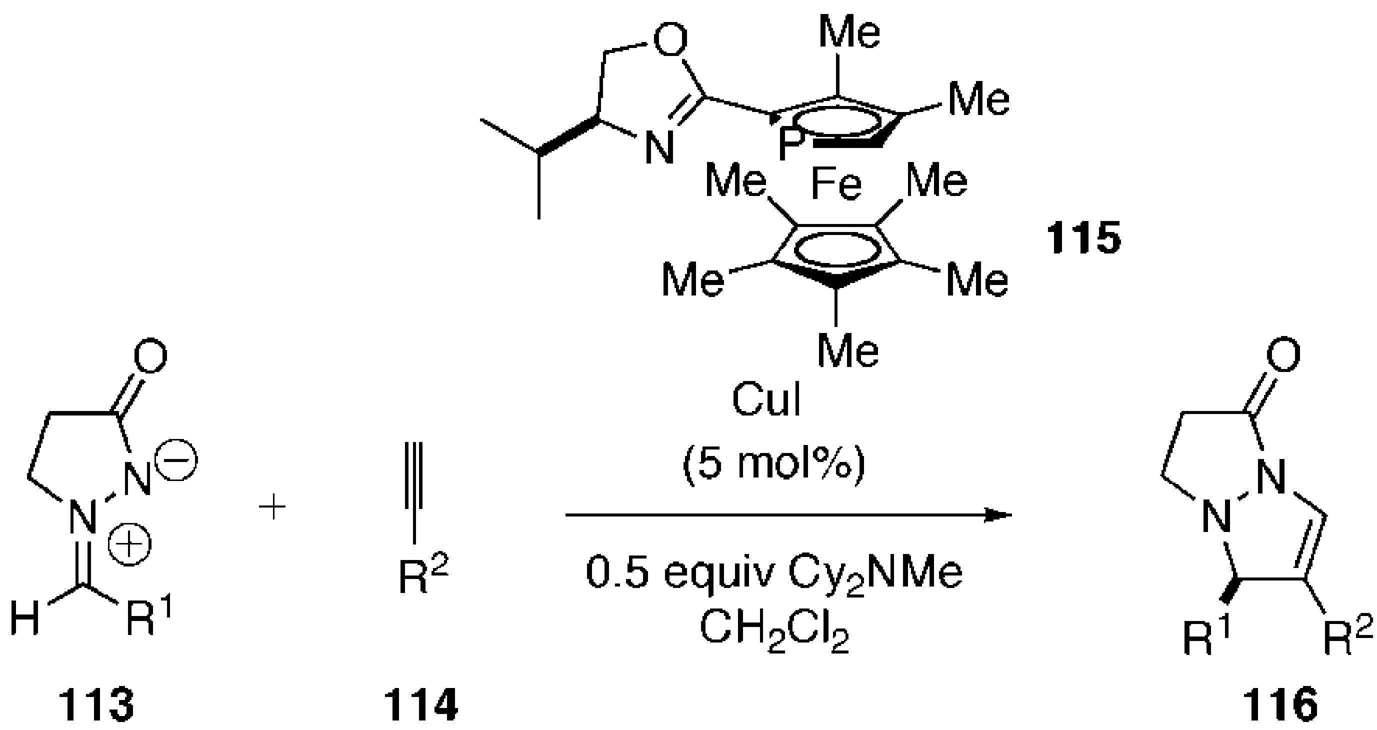
entry	ligand	R	yield (%)	*exo*:*endo*	*exo* ee (%)
1	**74**	Ph	71	>95:05	64
2	**75**	Ph	78	89:11	72
3	**74**	Me	64	72:28	55
4	**75**	Me	64	86:14	62

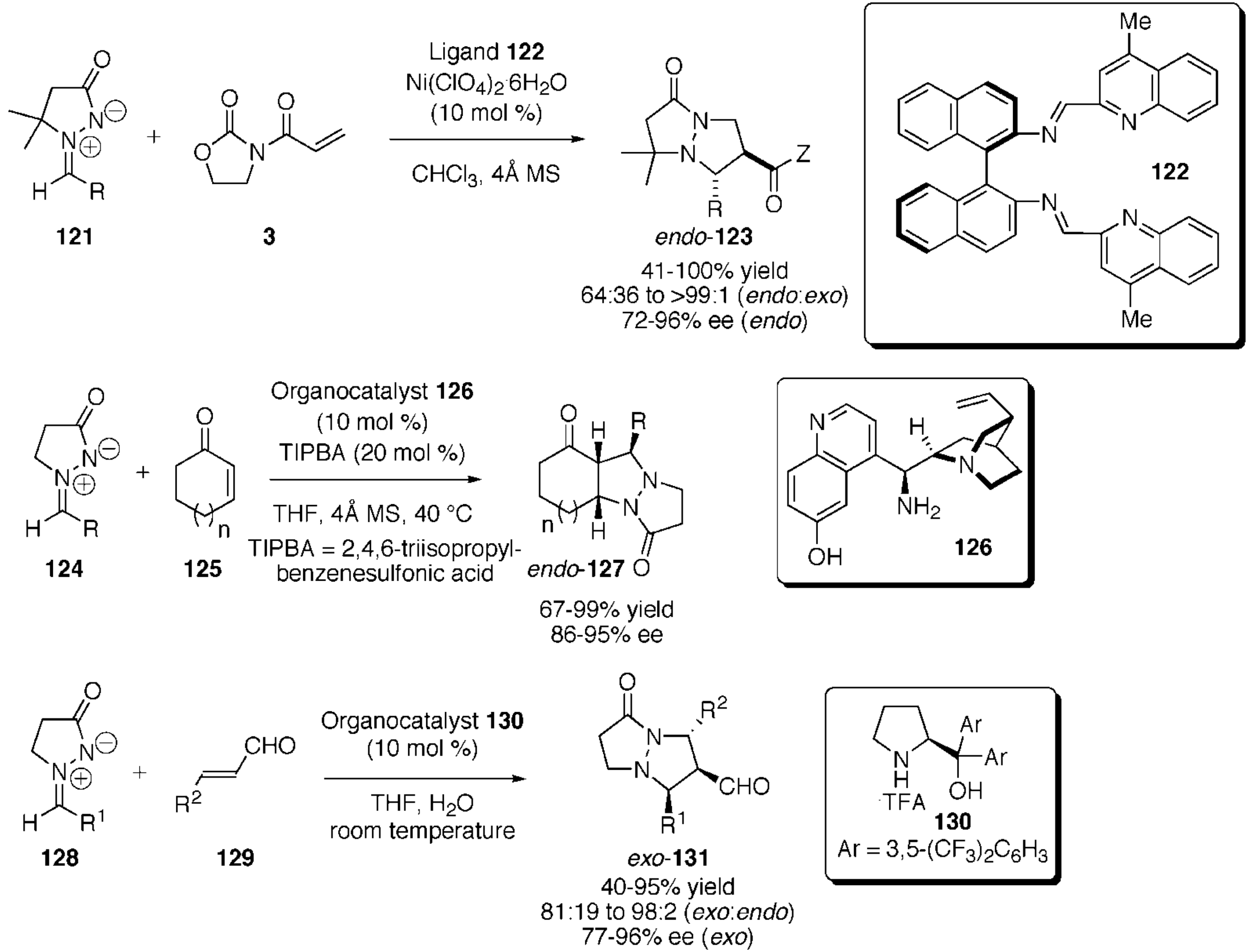
Oderaotoshi, Y.; Cheng, W.; Fujitomi, S.; Kasano, Y.; Minakata, S.; Komatsu, M.
Org. Lett. **2003**, *5*, 5043



(a) Cabrera, S.; Arrayás, R. G.; Carretero, J. C. *J. Am. Chem. Soc.* **2005**, *127*, 16394.
(b) Cabrera, S.; Arrayás, R. G.; Martín-Matute, B.; Cossío, F. P.; Carretero, J. C. *Tetrahedron* **2007**, *63*, 6587.

4. EC Azomethine Imine Cycloadditions




Ligand **122**
Ni(ClO4)2·6H2O
(10 mol %)
CHCl3, 4Å MS
121
3
endo-123
41-100% yield
64:36 to >99:1 (endo:exo)
72-96% ee (endo)
Me
122
Organocatalyst **126**
(10 mol %)
TIPBA (20 mol %)
THF, 4Å MS, 40 °C
TIPBA = 2,4,6-triisopropyl-benzenesulfonic acid
124
125
endo-127
67-99% yield
86-95% ee
126
Organocatalyst **130**
(10 mol %)
THF, H2O
room temperature
128
129
exo-131
40-95% yield
81:19 to 98:2 (exo:endo)
77-96% ee (exo)
·TFA
130
Ar = 3,5-(CF3)2C6H3

(1)

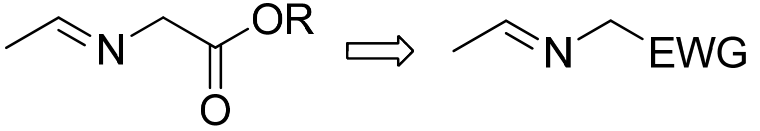
(2)

(3)

5. Conclusion

底物拓展，

催化剂效率



- $-SO_2R$
- $-PO(OR)_2$
- $-CN$
- $-NO_2$
- --------