Cycloadditions of allenes and the application in natural product syntheses

Dong group at UT Austin

Xuan Zhou

Nov 12, 2014

Cycloadditions of allenes

Content

- [2+2] Cycloadditions of allenes
- [3+2] Cycloadditions of allenes
- [M+N] Cycloadditions of allenes
- [4+2] and [4+3] Cycloadditions of allenes

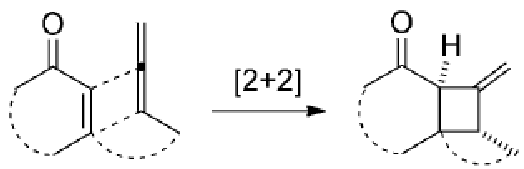
Reviews about cycloaddition of allenes:

S. Ma, *Chem. Rev.*, **2005**, *105*, 2829–2871.

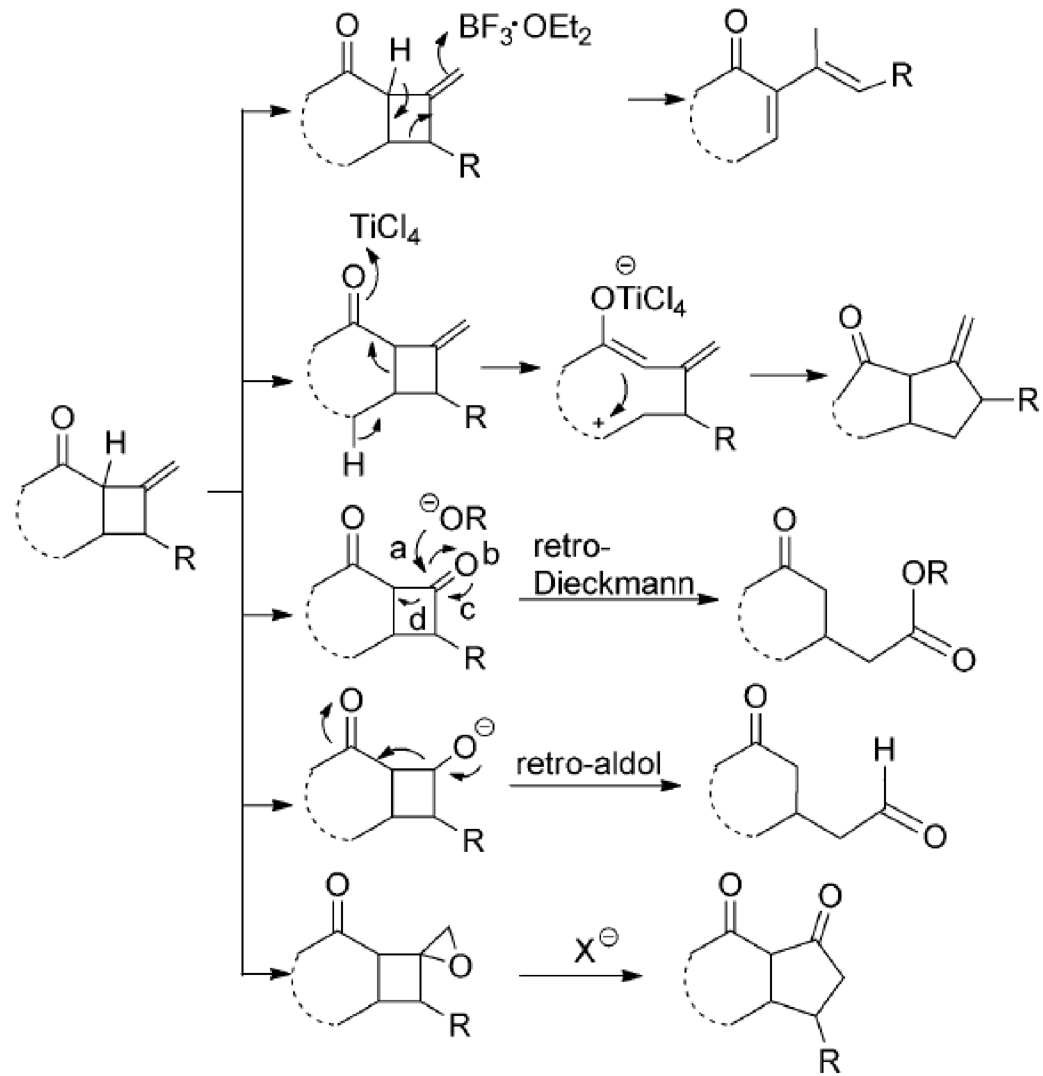
S. Yu and S. Ma, *Angew. Chem., Int. Ed.*, **2012**, *51*, 3074–3112.

F. Lopez and J. L. Mascarenas, *Chem. Soc. Rev.*, **2014**, *43, 2904--2915*

[2+2] Cycloadditions of allenes

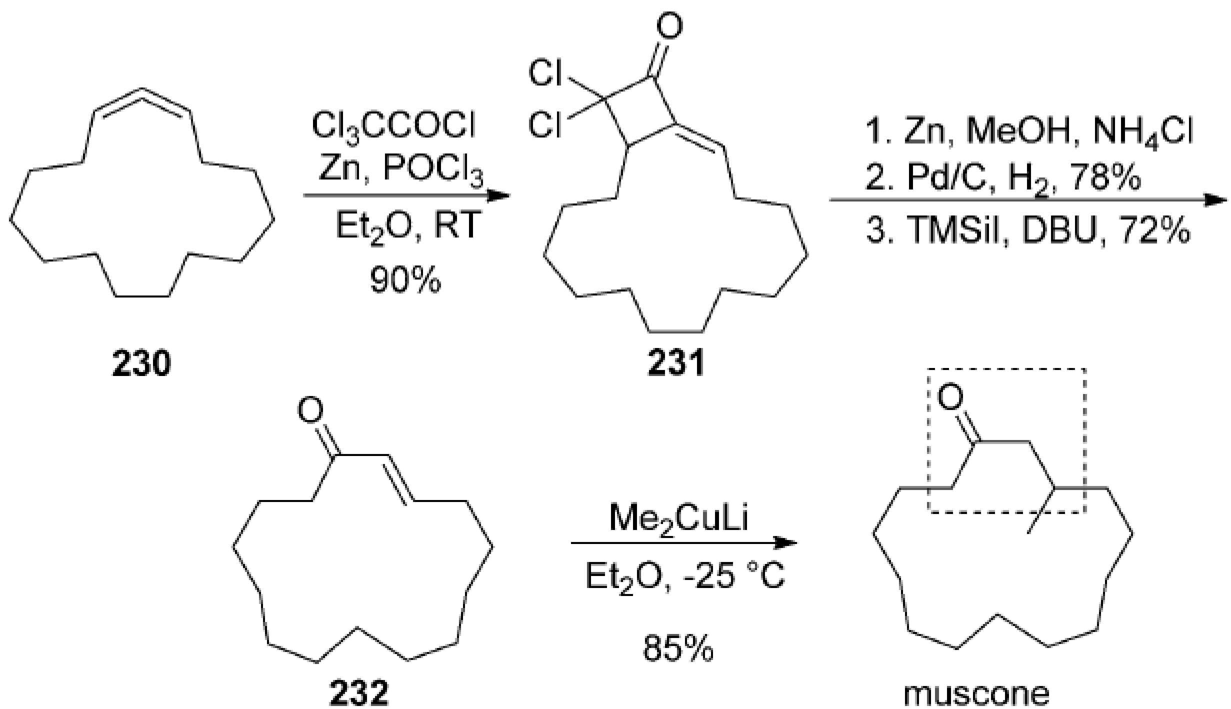


[2+2] Cycloaddition of allenes with enones.



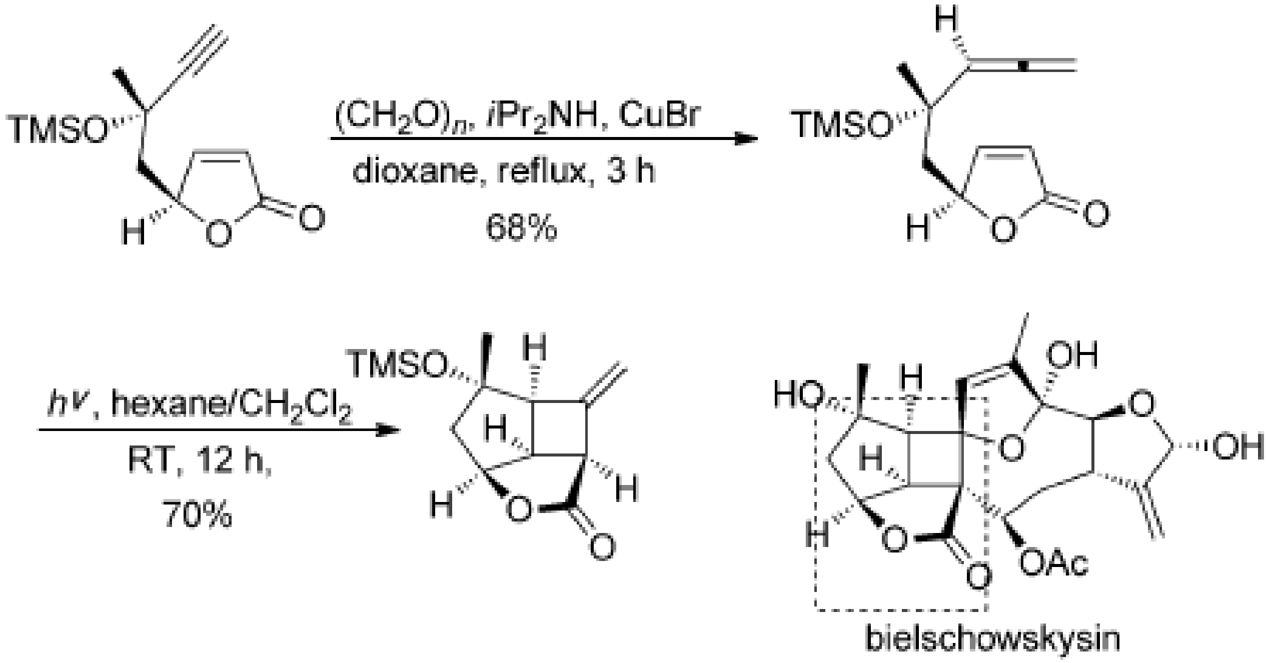
Fragmentation and ring expansion of alkylidine cyclobutanes

Total synthesis of Muscone by a intermolecular [2+2] cycloaddition



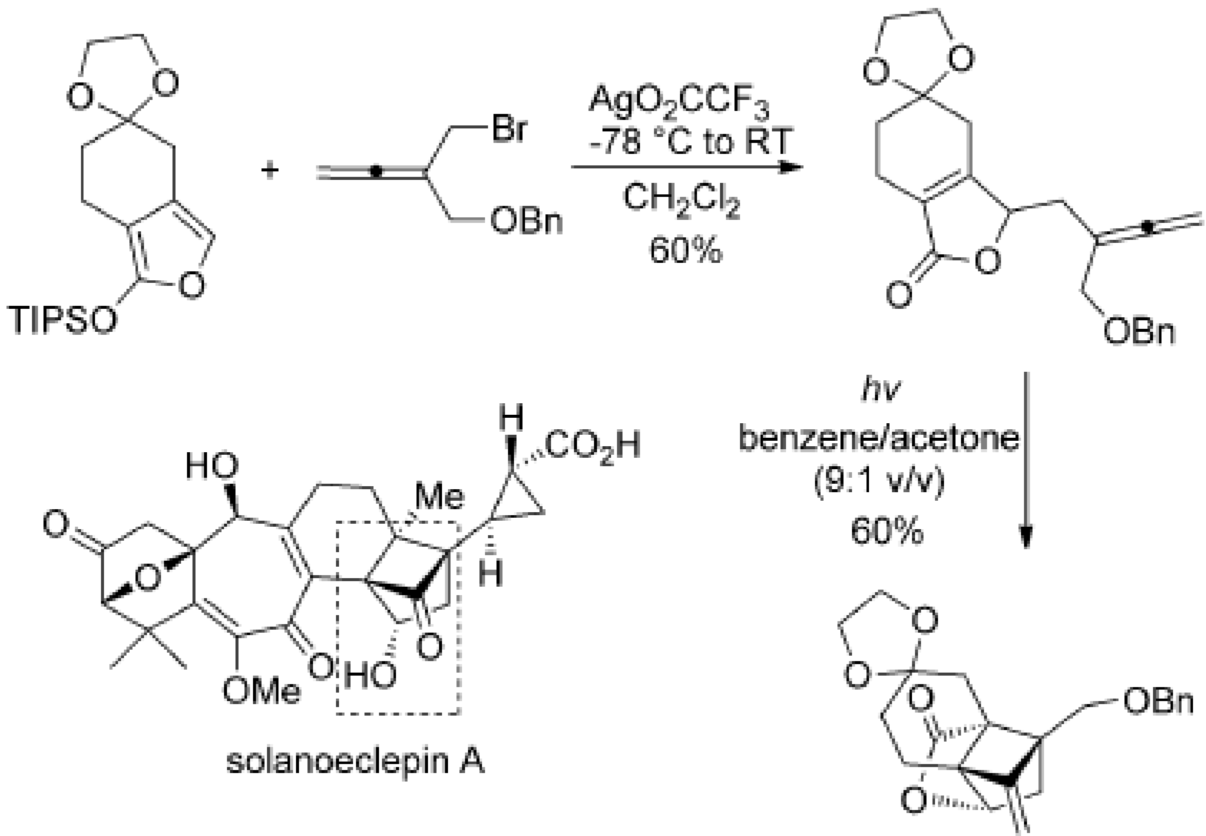
Ihsan Erden etc*, Tetrahedron*, **2008**, *64*, 5497-5501

Synthesis key structure of Bielschowskysin by a intarmolecular [2+2] cycloaddition



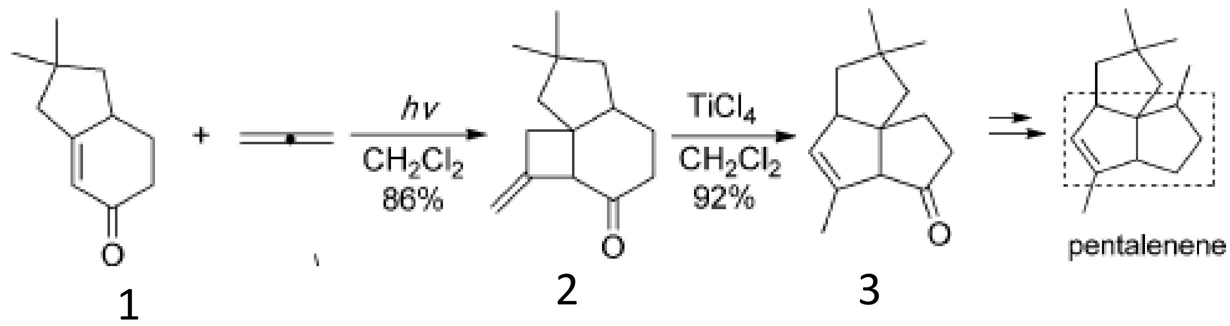
Martin J. Lear etc*, Tetrahedron Lett*, **2009**, *50*, 1731-1733

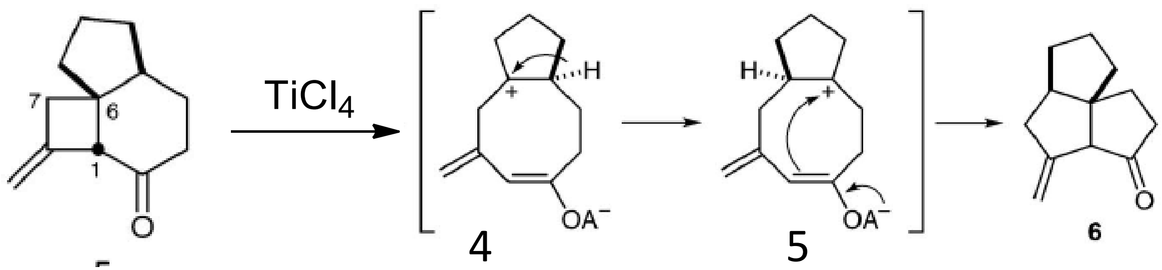
Synthesis of the bicyclo[2.1.1] hexane substructure of Solanoeclepin A

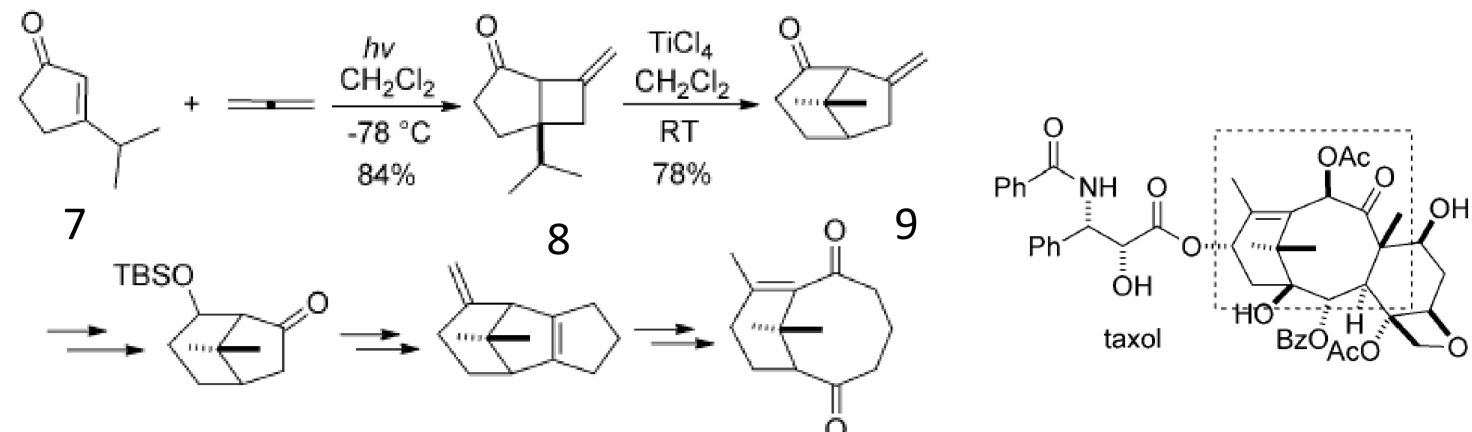


K.K. Larson etc, *Org. Biomol. Chem*. **2003**, *1*, 4364-4366

Formal synthesis of (±)-pentalenene





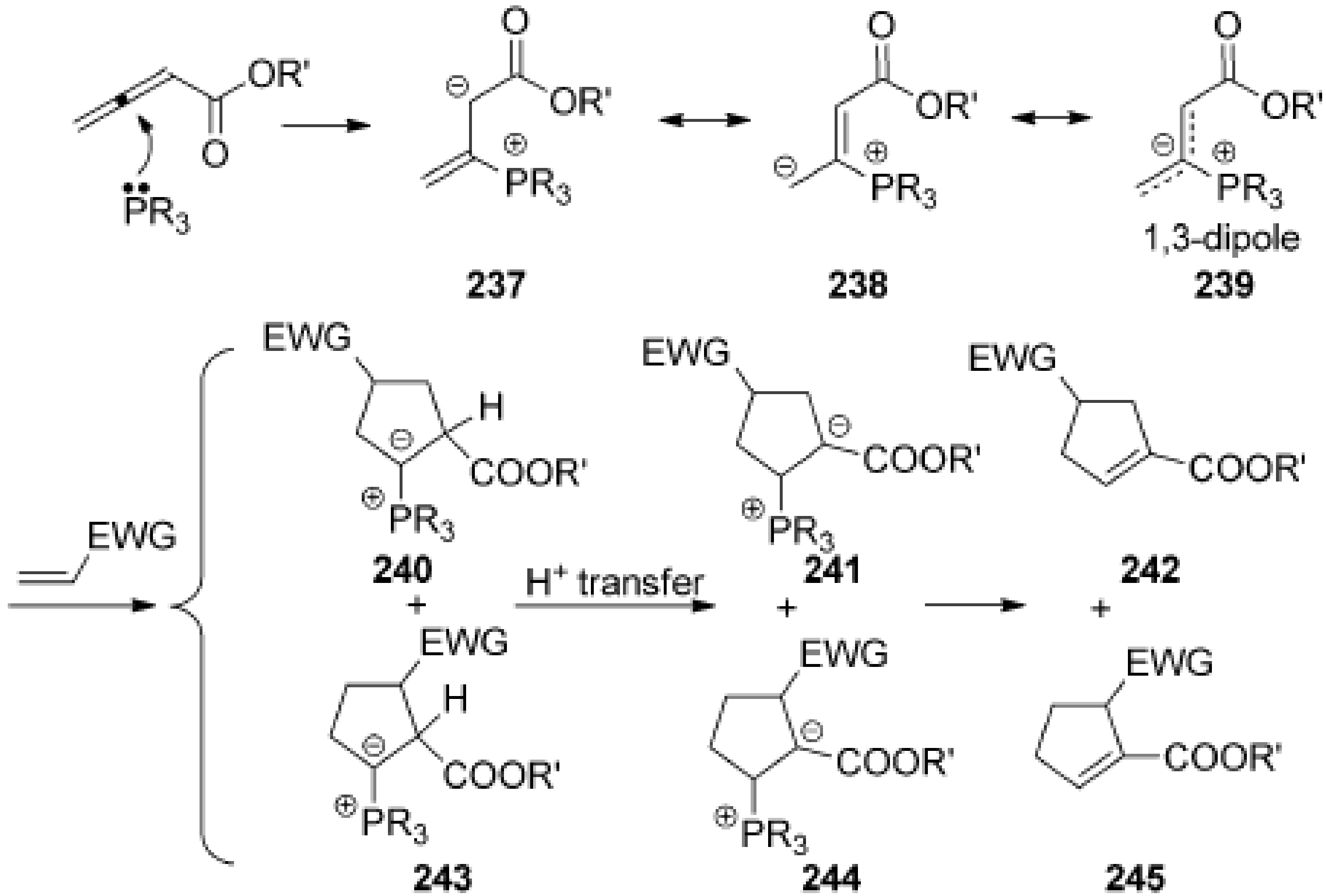


Construction of the AB ring of Taxol

K. LKakiuchi etc, *Synthesis*. **2004**, *5*, 753-756

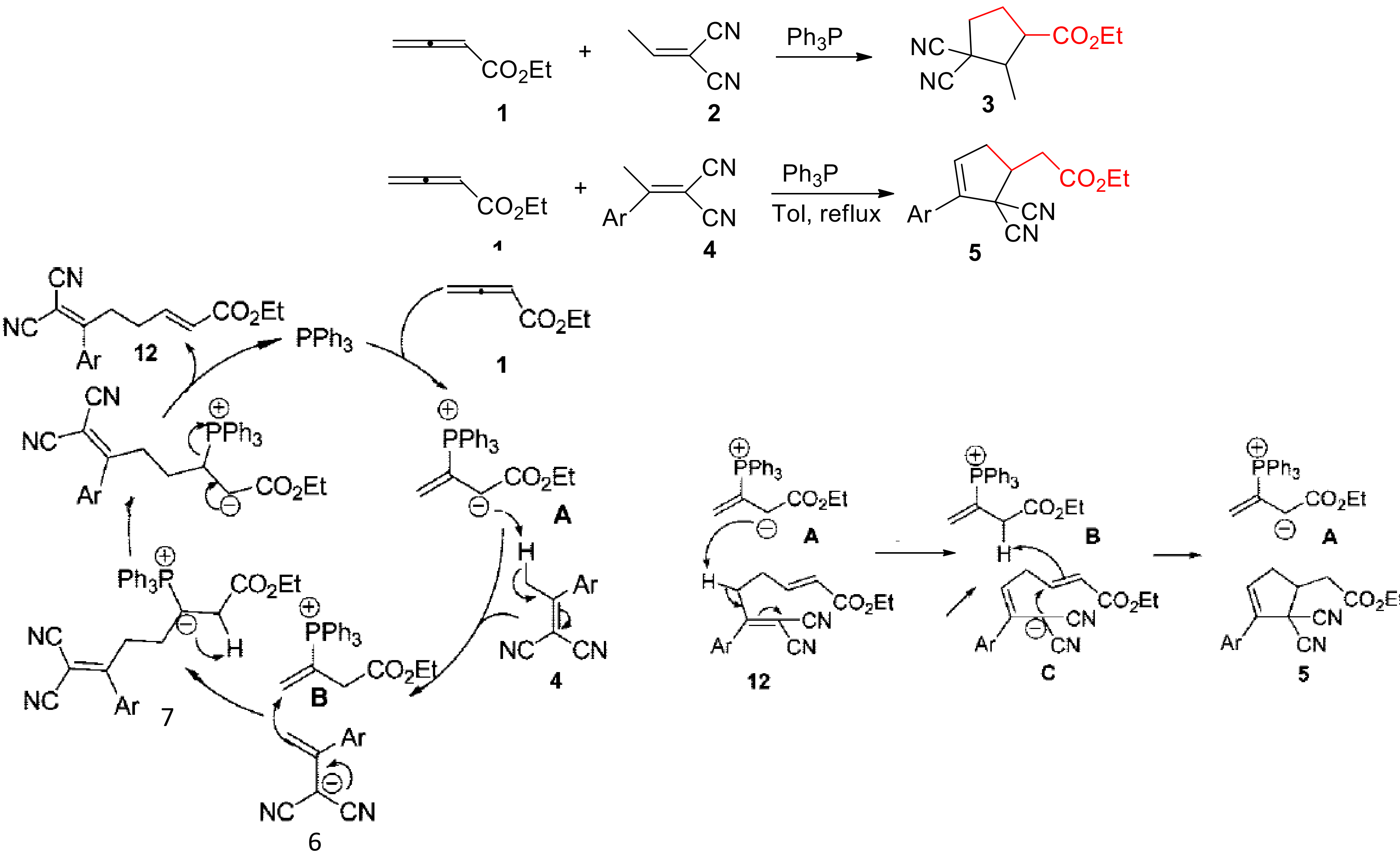
K. LKakiuchi etc, *Tetrahedron Lett*. **2003**, *44*, 1401-1403

Phosphine-catalyzed [3+2] cycloadditions



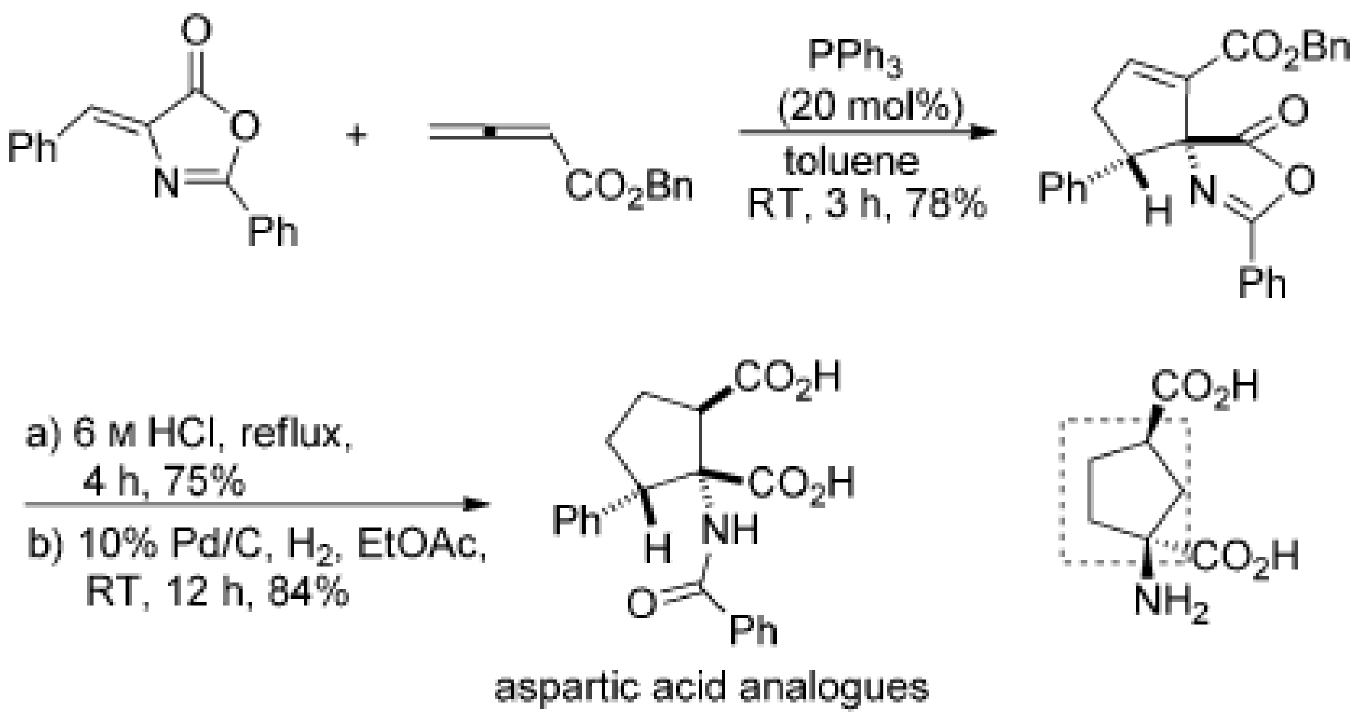
Xiyan Lu etc, *J. Org. Chem*.**, 1995**, *60*, 2906-2908

Phosphine-catalyzed [3+2] cycloadditions



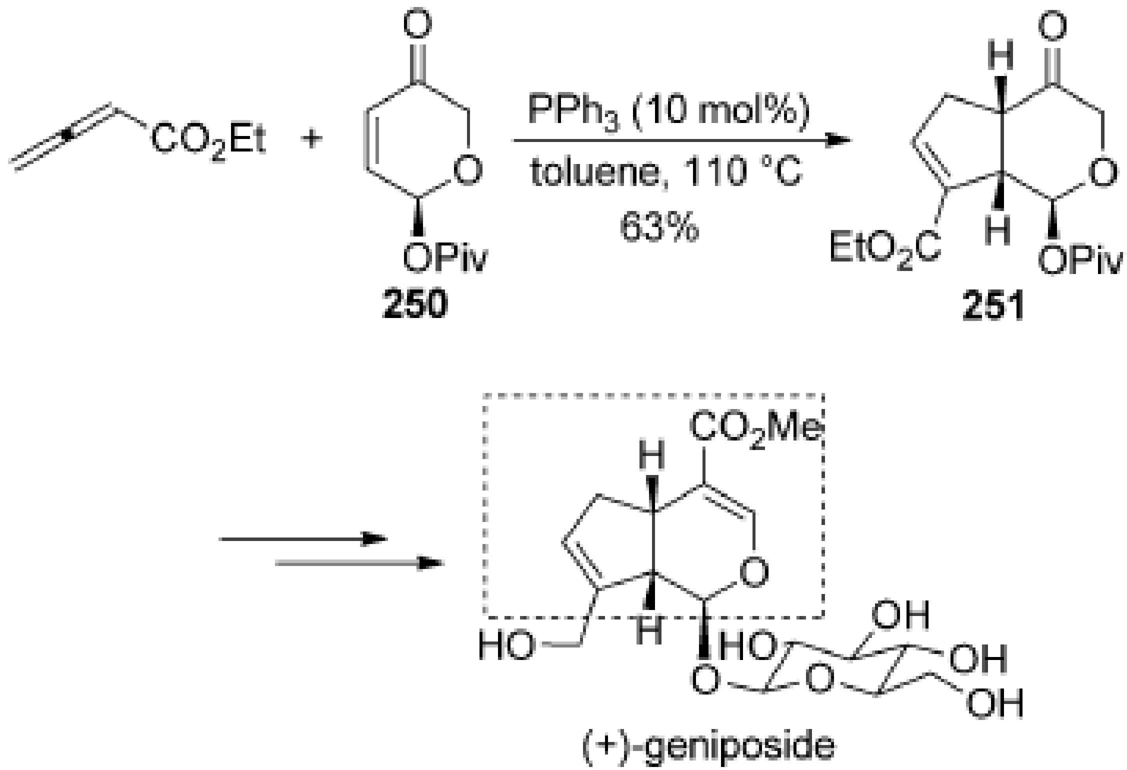
Xiyan Lu etc, *Org. lett*., **2008**, *15*, 3267-3270

Synthesis of Aspartic acid analogues through [3+2] Cycloadditions



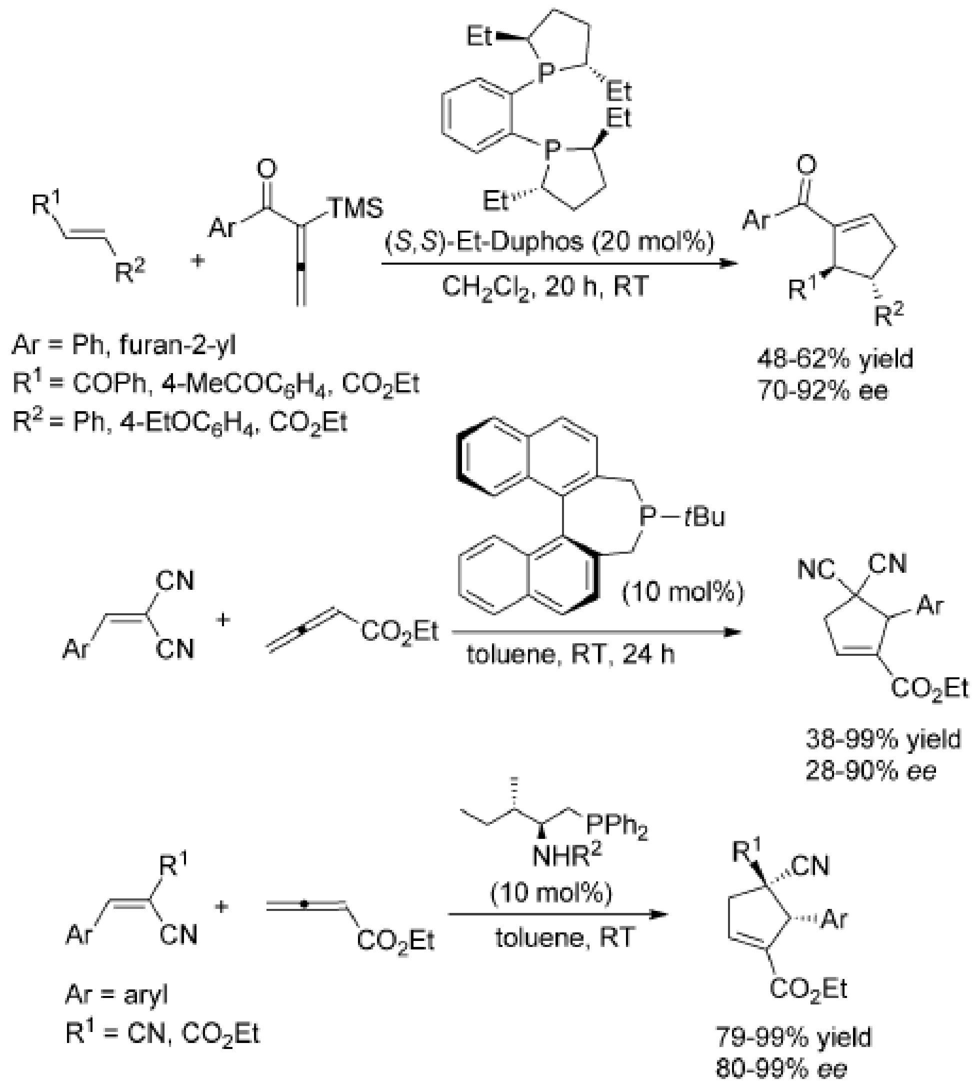
Wenjing Xiao ect., *Synlett*, **2011**, *7*, 1000-1004

Synthesis of (+)-geniposide through [3+2] Cycloadditions



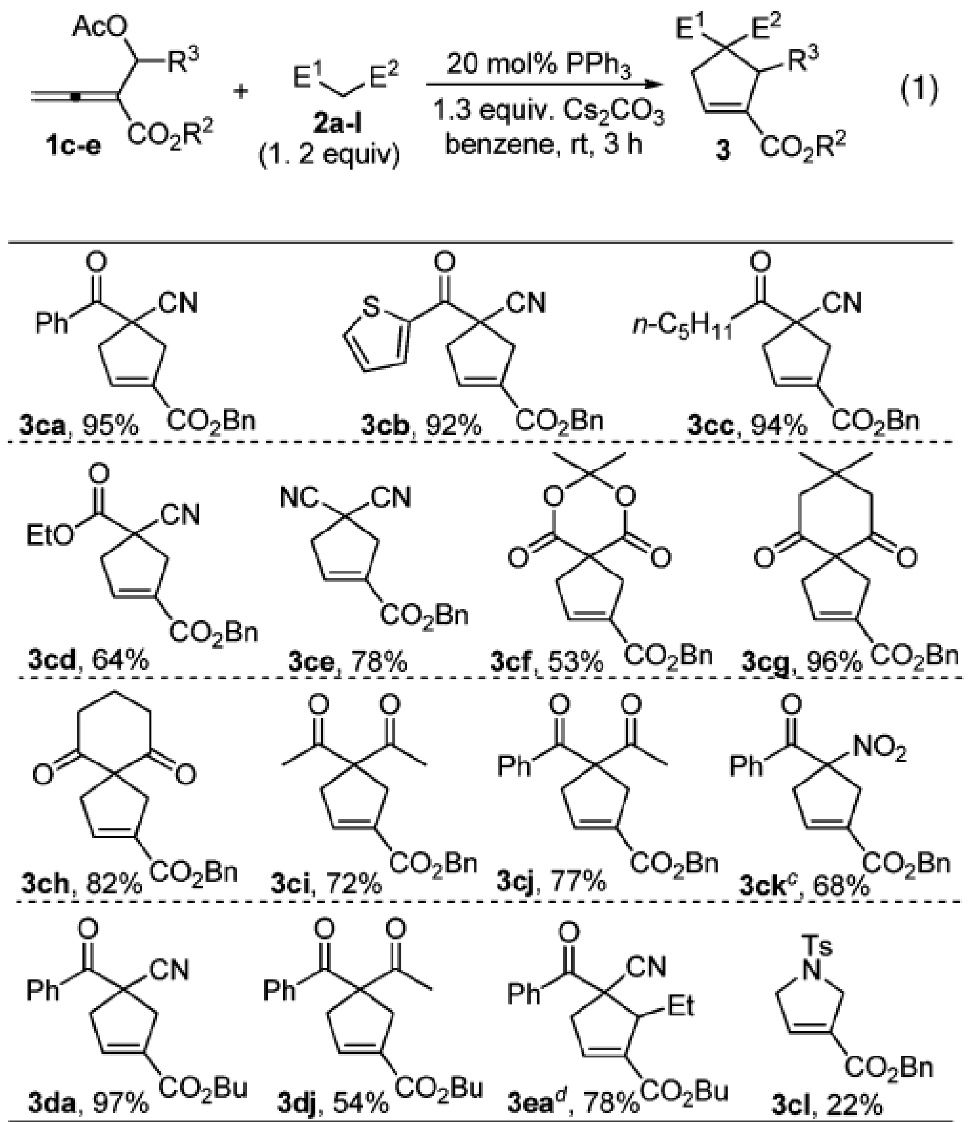
Michael J. Krische etc, *Org. lett*.**,** **2009**, *8*, 1849-1851

Enantioselective [3+2] cycloadditions



S. Yu and S. Ma, Angew. Chem., Int. Ed., **2012**, *51*, 3074–3112.

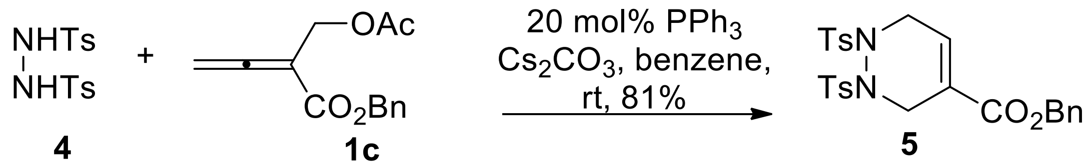
Phosphine catalyzed [4+1] Annulation

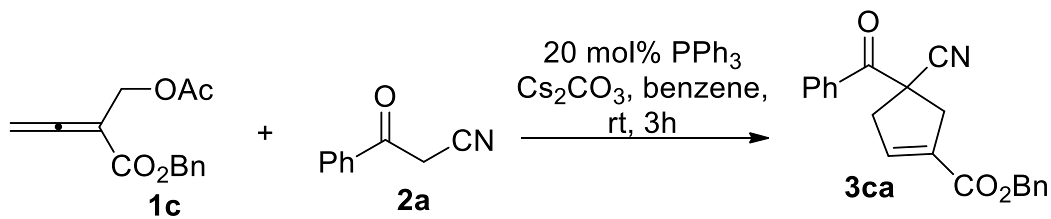


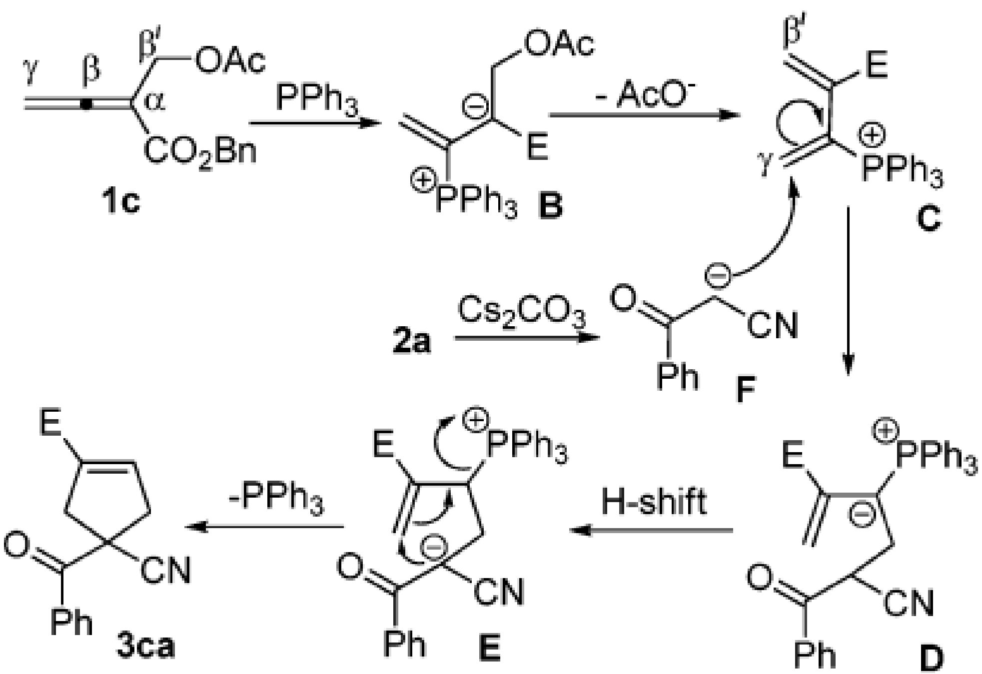
Xiaofeng Tong etc, *J. Am. Chem. Soc*, **2010**, *132*, 2550-2551

Plausible mechanism of [4+1] annulation

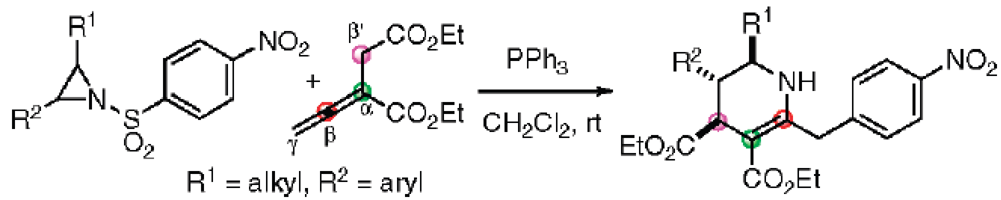
[4+2] annulation

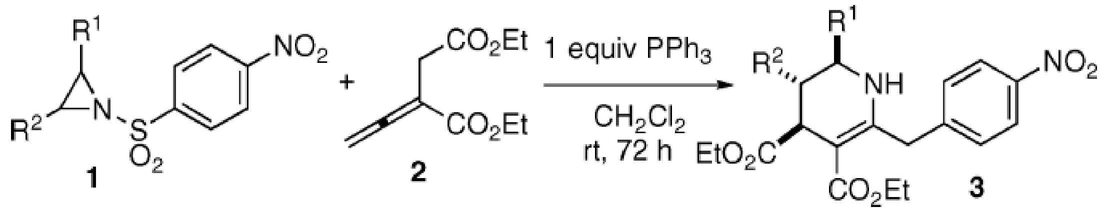






Phosphine-promoted [3+3] annulations of aziridines with allenoates

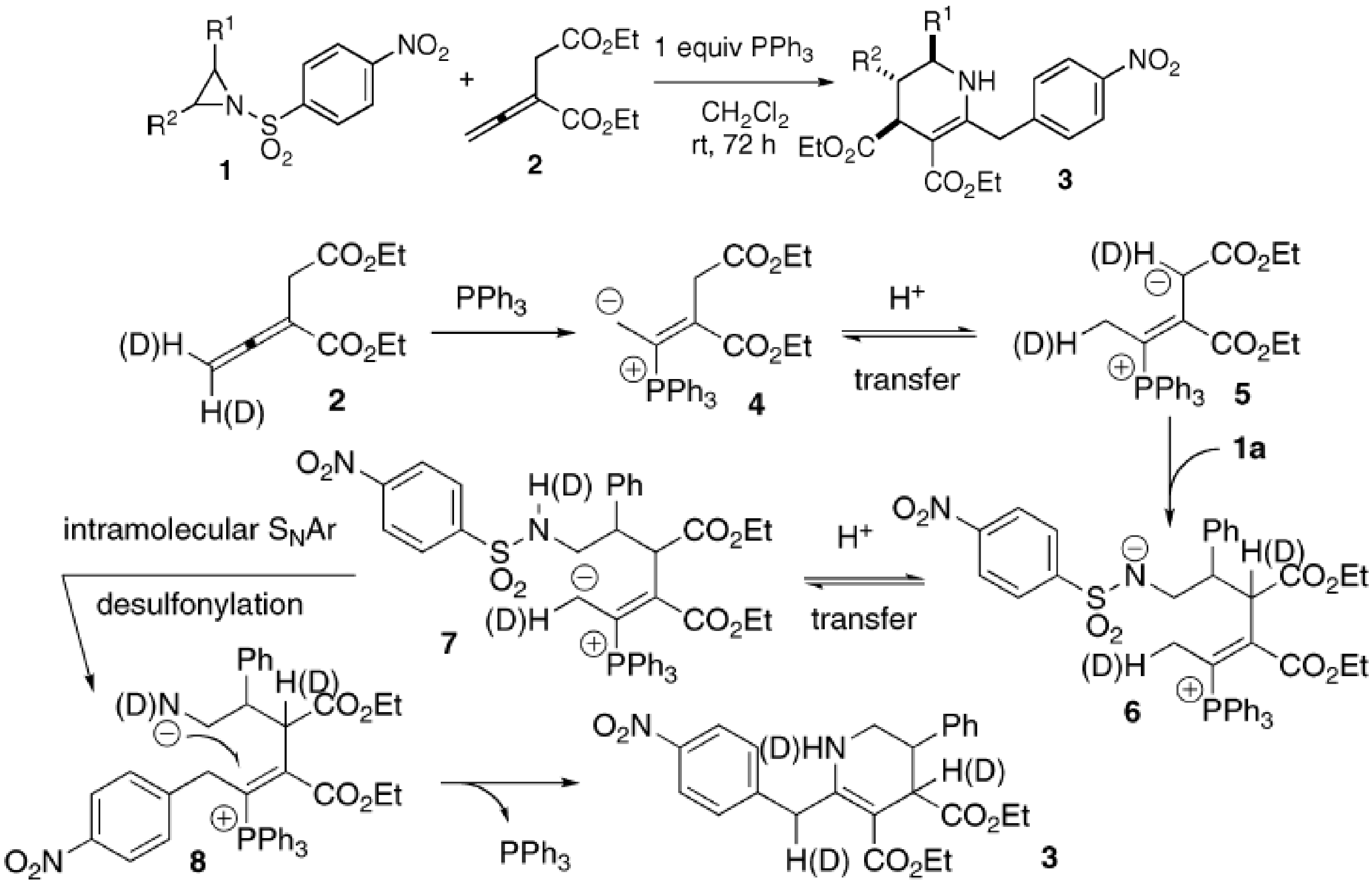




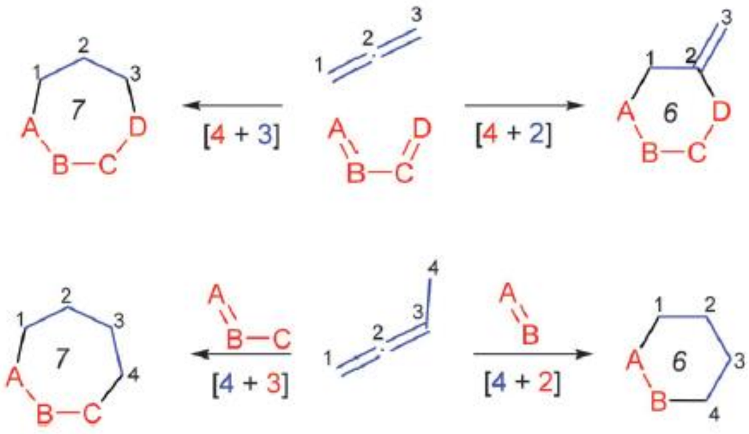
entry	R^1	R^2	product	yield (%)[b]	dr (trans/cis)[c]
1	H (**1b**)	2-MeC_6H_4	**3b**	88	90:10
2	H (**1c**)	3-MeC_6H_4	**3c**	82	86:14
3	H (**1d**)	4-MeC_6H_4	**3d**	64	89:11
4	H (**1e**)	2,4-$Me_2C_6H_3$	**3e**	82	81:19
5	H (**1f**)	2,5-$Me_2C_6H_3$	**3f**	98	92:8
6	H (**1g**)	4-FC_6H_4	**3g**	76	88:12
7	H (**1h**)	2-ClC_6H_4	**3h**	46	97:3
8	H (**1i**)	3-ClC_6H_4	**3i**	86	83:17
9	H (**1j**)	4-ClC_6H_4	**3j**	84	90:10
10	H (**1k**)	3-BrC_6H_4	**3k**	58	85:15
11	H (**1l**)	4-BrC_6H_4	**3l**	75	88:12
12	H (**1m**)	2-naphthyl	**3m**	58	85:15

Ohyun Kwon etc, *J. Am. Chem. Soc*, **2009**, *131*, 6318-6319

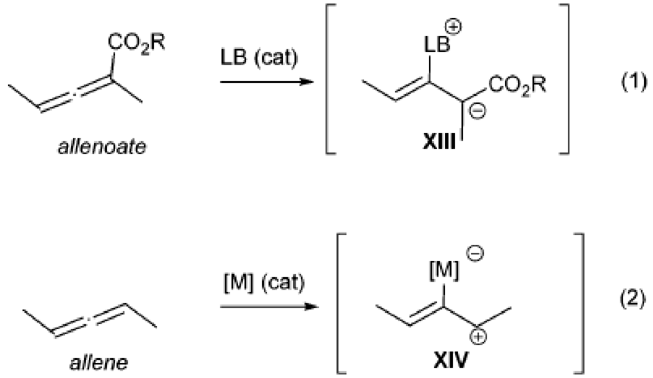
Suggested mechanism of [3+3] annulation



[4+2] and [4+3] Cycloadditions of allenes

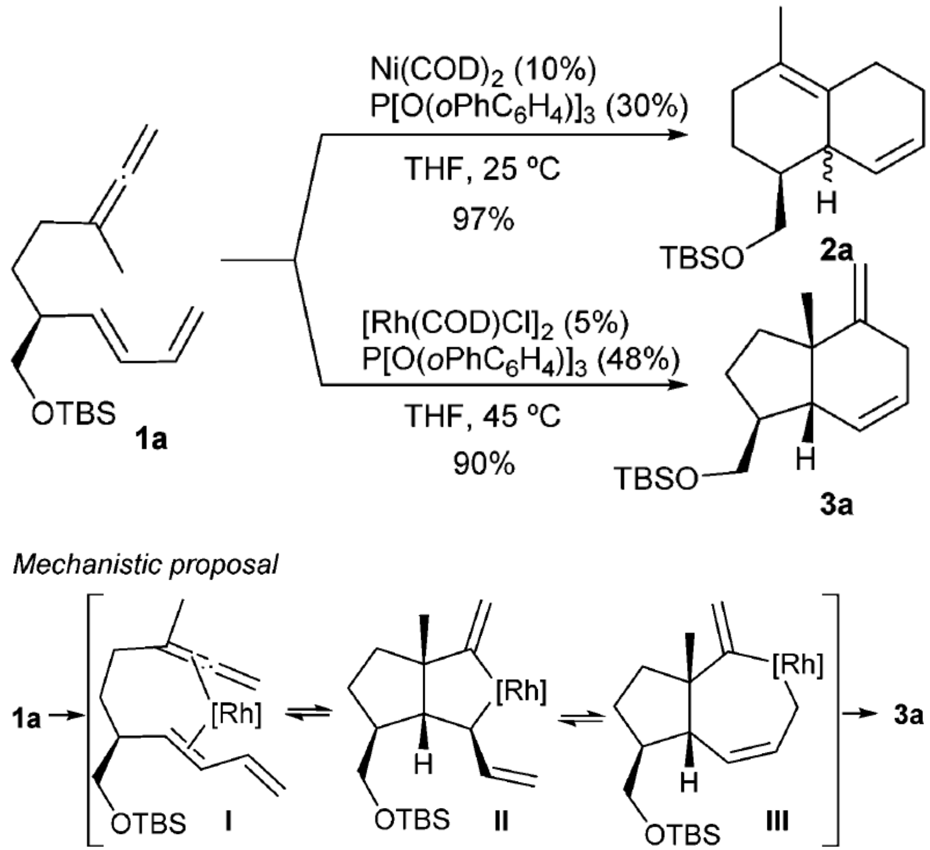


- ➢ catalytic cycloadditions through metallacyclic intermediates
- ➢ catalytic cycloadditions through zwitterionic intermediates
- • reactions promoted by lewis-base catalysts
- • reactions promoted by transition metal catalyst



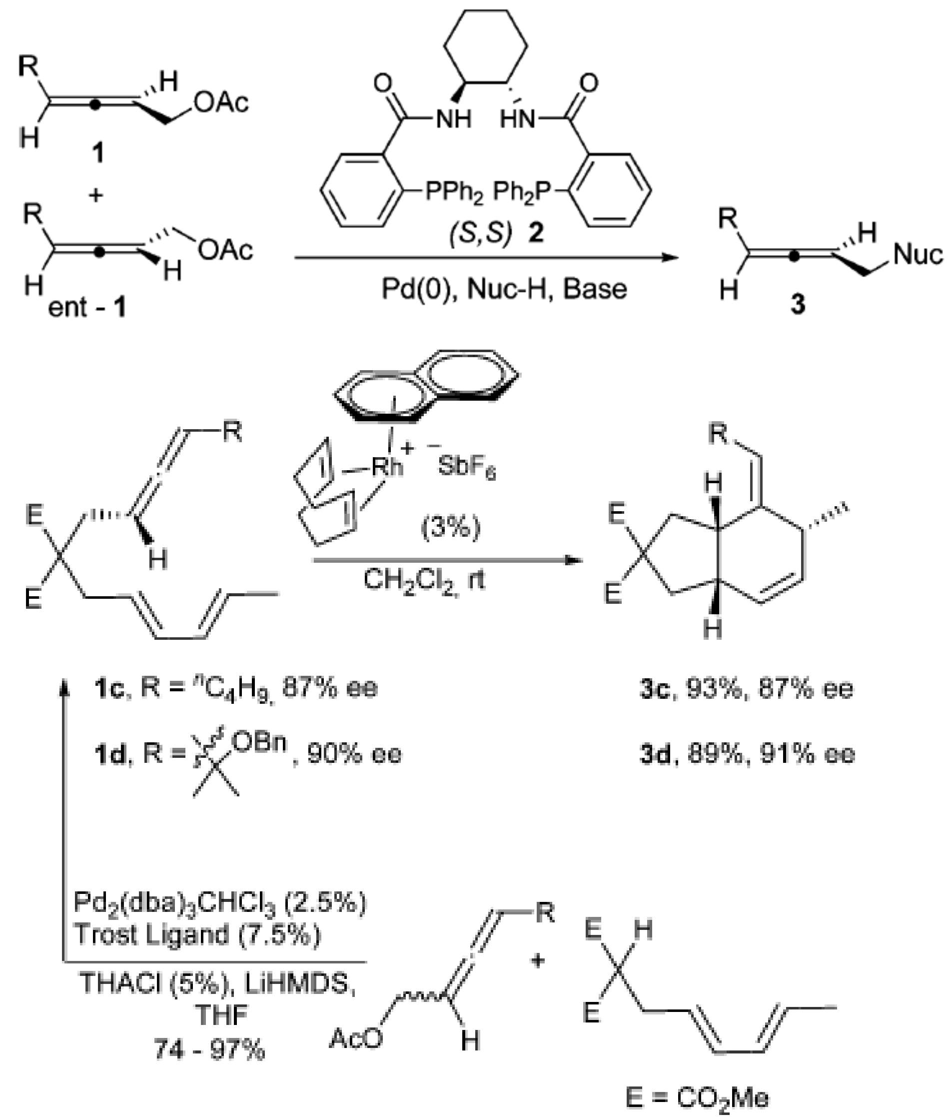
F. Lopez and J. L. Mascarenas, *Chem. Soc. Rev.*, **2014**, *43*, *2904--2915*

Transition metal catalyzed [4+2] cycloadditions



Paul A. Wender etc, *J. Am. Chem. Soc*, **1995**, *117*, 1843-1844

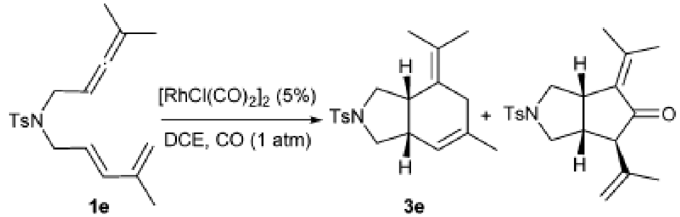
Enantiospecific Rh-catalyzed [4+2] allene-diene cycloadditions



Asymmetric [4+2] processes through metallacyclic intermediates using allenes as substrates have not been reported

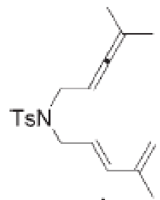
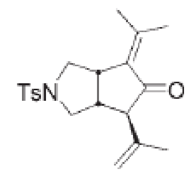
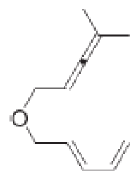
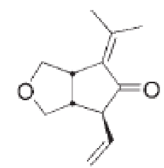
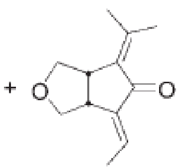
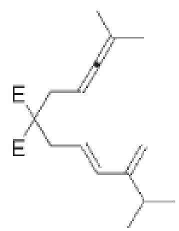
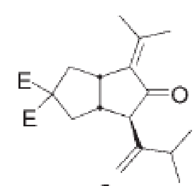
Barry M. Trost etc, *J. Am. Chem. Soc*, **2005**, *127*, 14186-14187

Metal catalyzed [2+2+1] cycloadditions of allene-diene cycloadditions



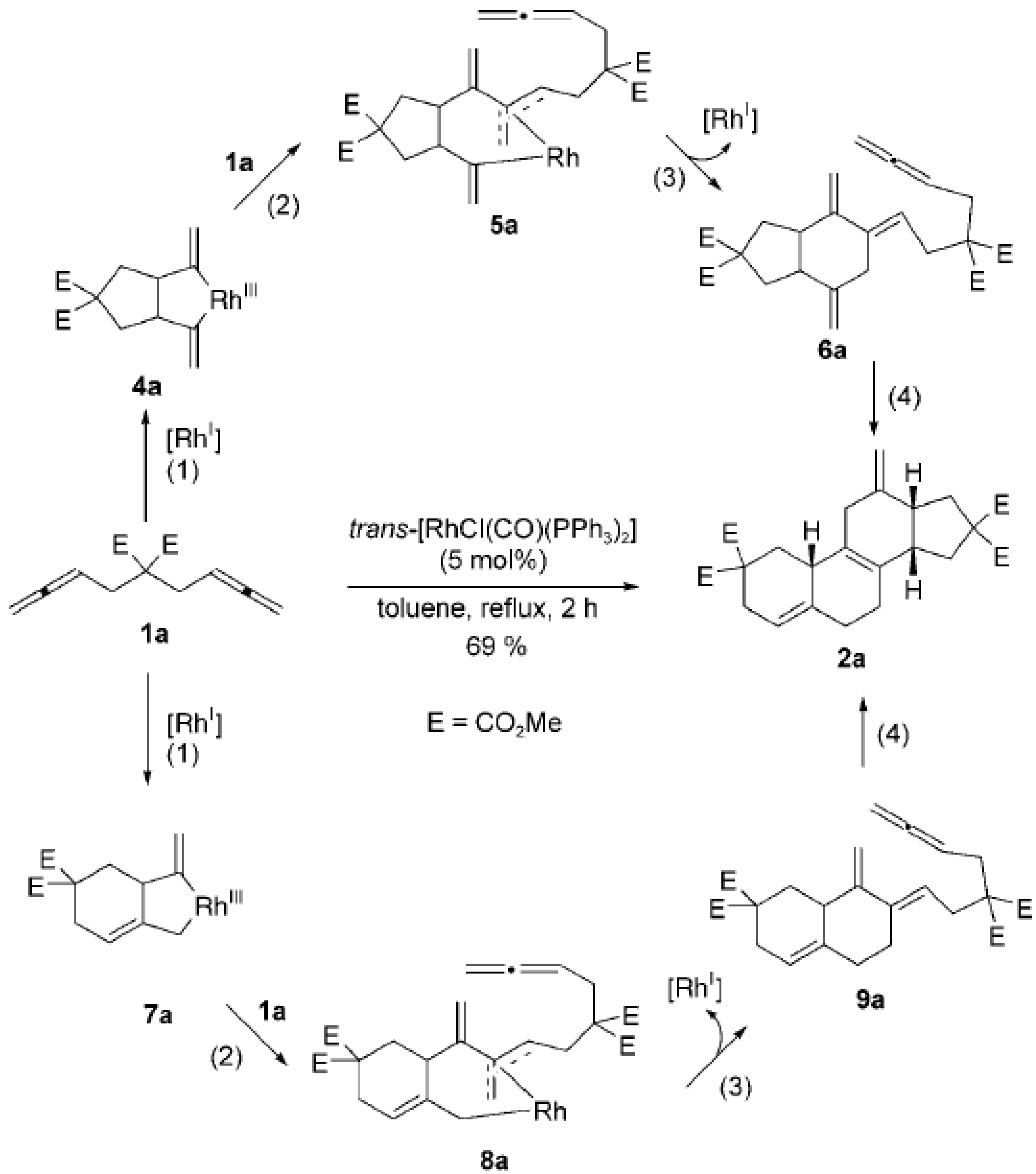
1e 3e

		3e	
80ºC, 1h		52%	43%
rt, 7h		0%	99%

Entry	Diene–allene	Conditions[a]	t [h]	Product	Yield
1	 1	A	8	 2	97
2	 4	B	1.5	 5 +  6	97 (2.9:1)
3	 7	C	0.3	 8	92

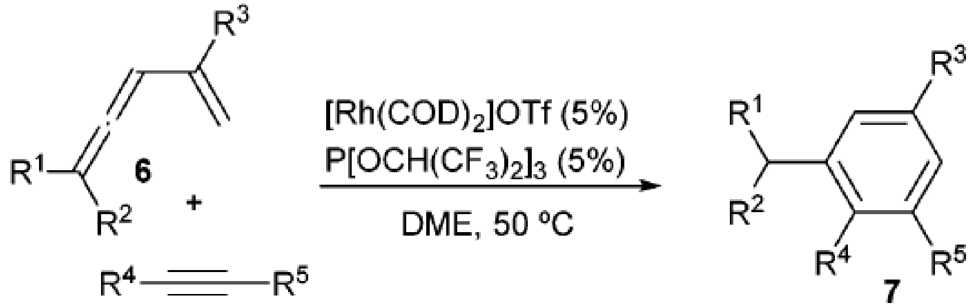
Paul A. Wender etc, *Angew. Chem., Int. Ed.*, **2006**, *45*, 2459–2462.

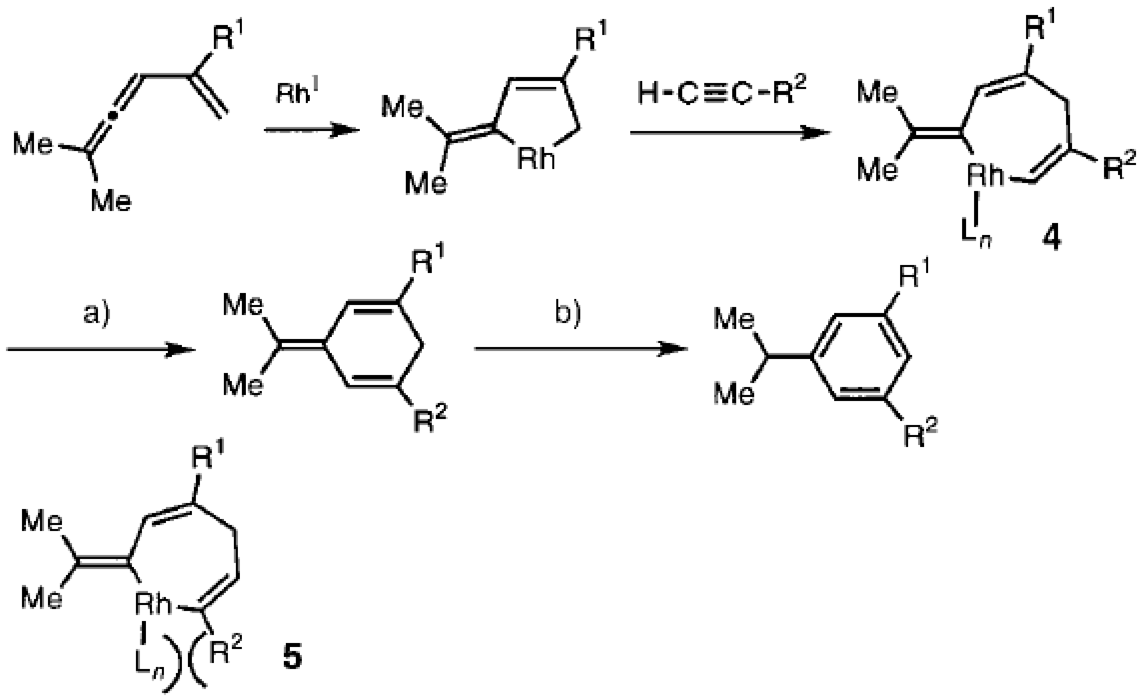
Rh-catalyzed cascade cycloadditions of bisallenes



Shengmin Ma etc, *Angew. Chem.*, *Int. Ed.*, **2005**, *44*, 5275–5278.

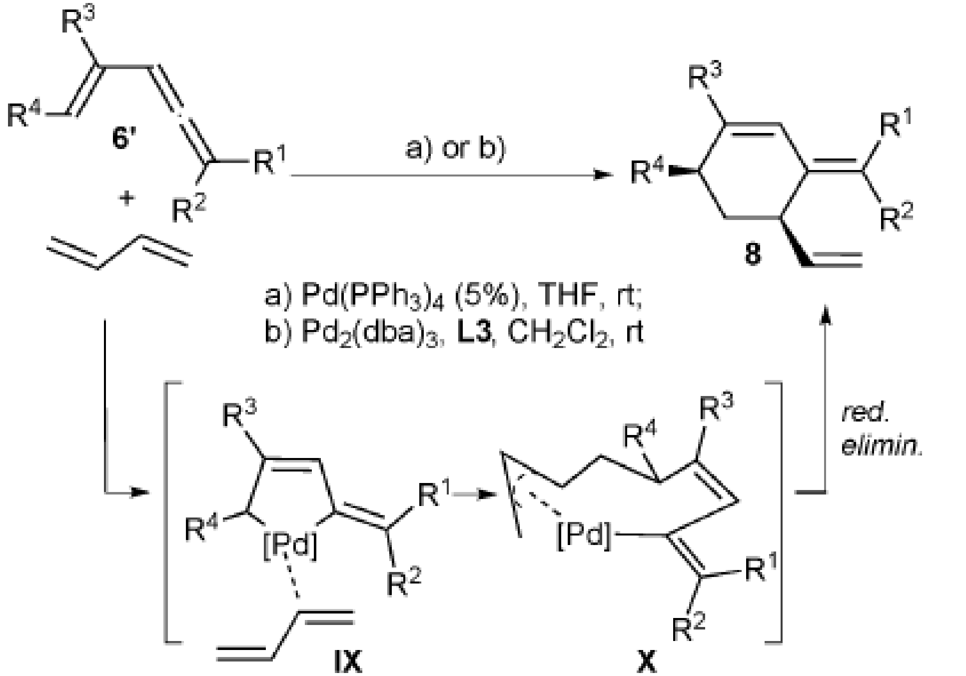
[4+2] cycloadditions of vinyl allenes and alkynes

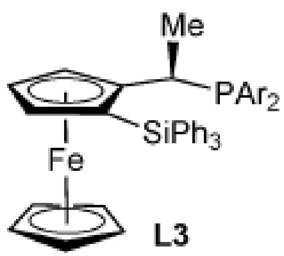




Masahiro Murakami etc, *Angew. Chem., Int. Ed.*, **1998**, *37*, 2248–2249.

[4+2] cycloaddition of vinylallenes and 1,3-diene



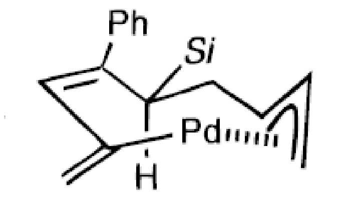


L3

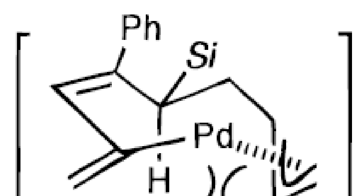
Ar = 3,5-$(CF_3)_2C_6H_3$

R^1	R^2	R^3	R^4	yield (%)[a]	ee (%)[a]
Me	Me	Ph	H	89	77
Me	Me	CO_2Et	Ph	85	83
Me	Me	^{n}Pr	^{n}Pr	76	52

[a] Values obtained under conditions *b*.[16]



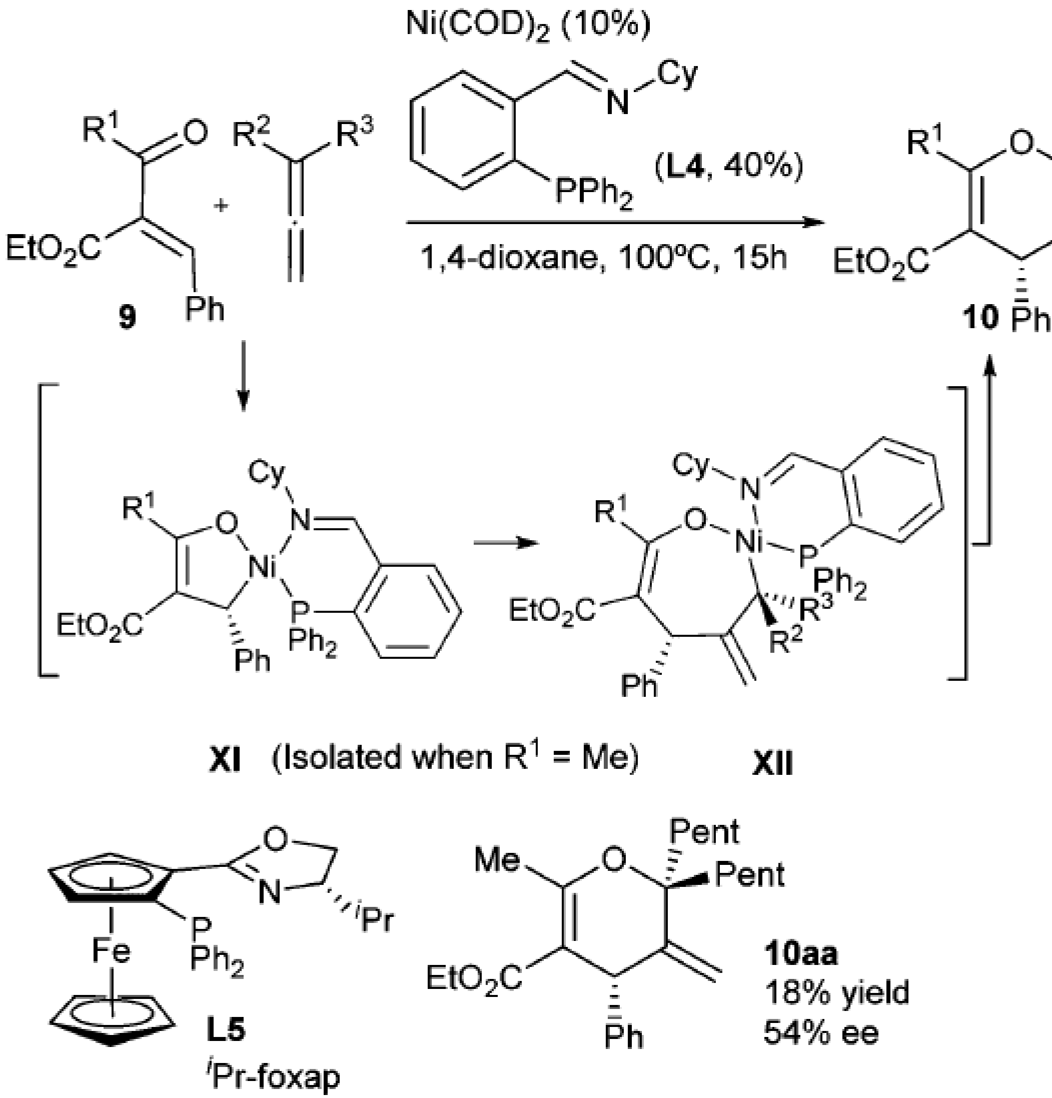
4 π-allyl complex



5 disfavored

Masahiro Murakami etc, *J. Am. Chem. Soc*, **1997**, *119*, 7163-7164

Hetero [4+2] cycloaddition between allenes and enones

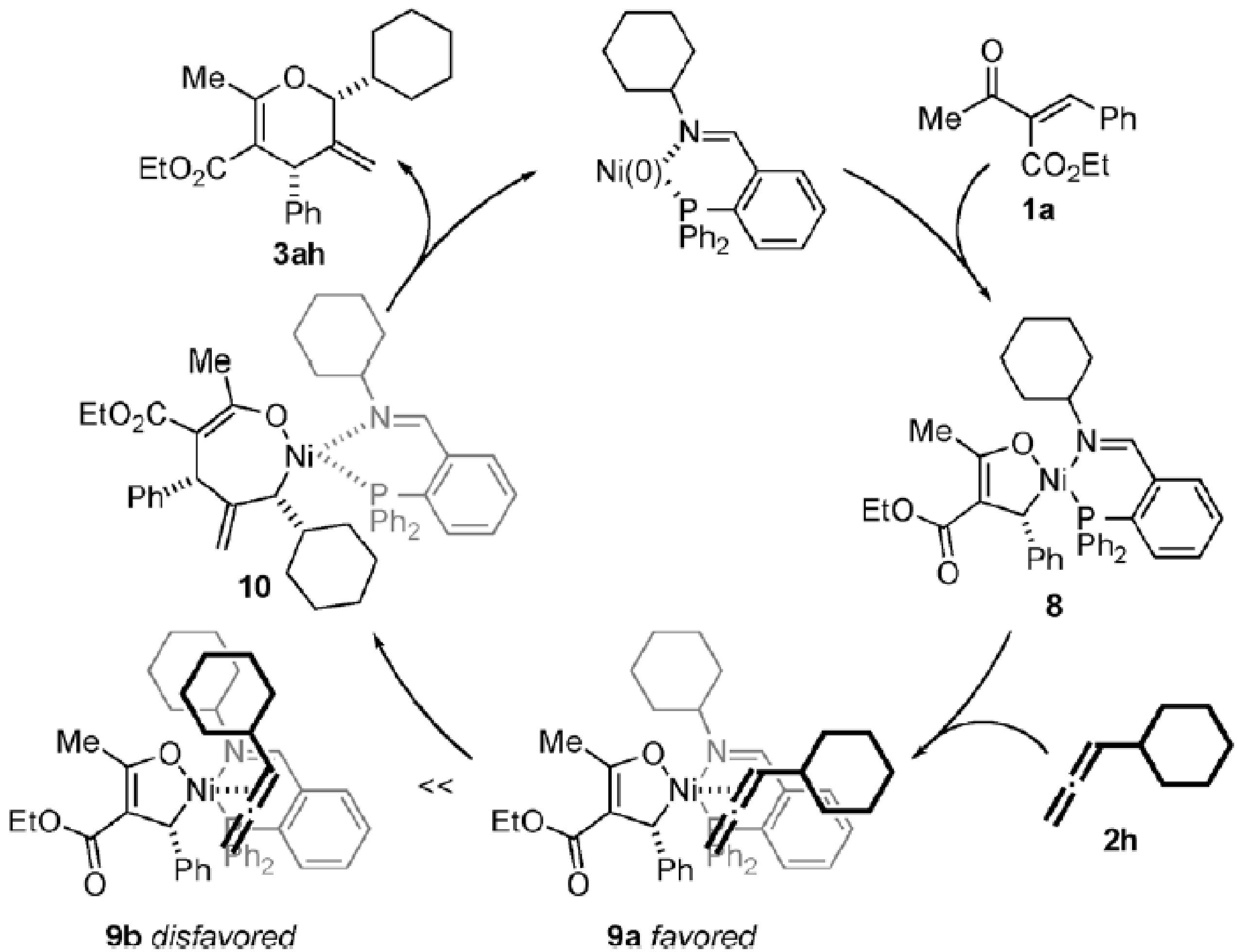


R^1	R^2	R^3	Yield(%)
Me	pent	pent	98
Ph	pent	pent	18
Me	Me	Me	40
Me	H	Cy	94[a]

[a] *dr* = 9: 1

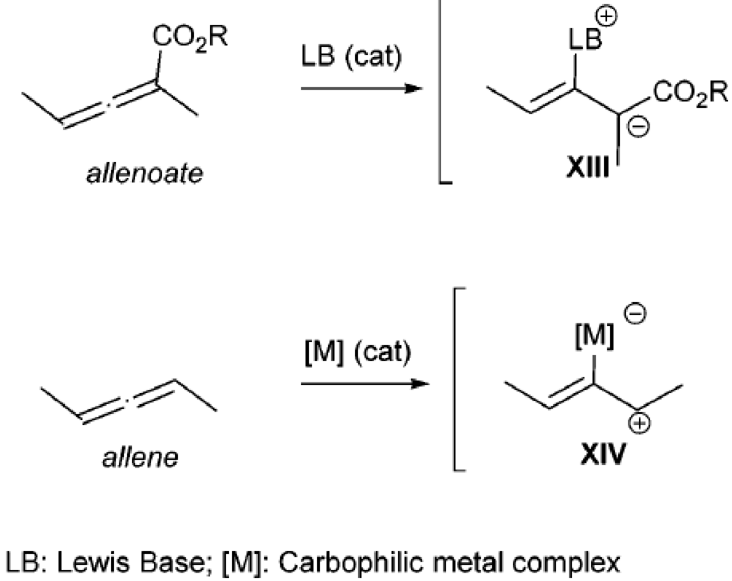
Takuya kurahashi etc, *Chem. Commun.*, **2011**, *47*, 6150-6152

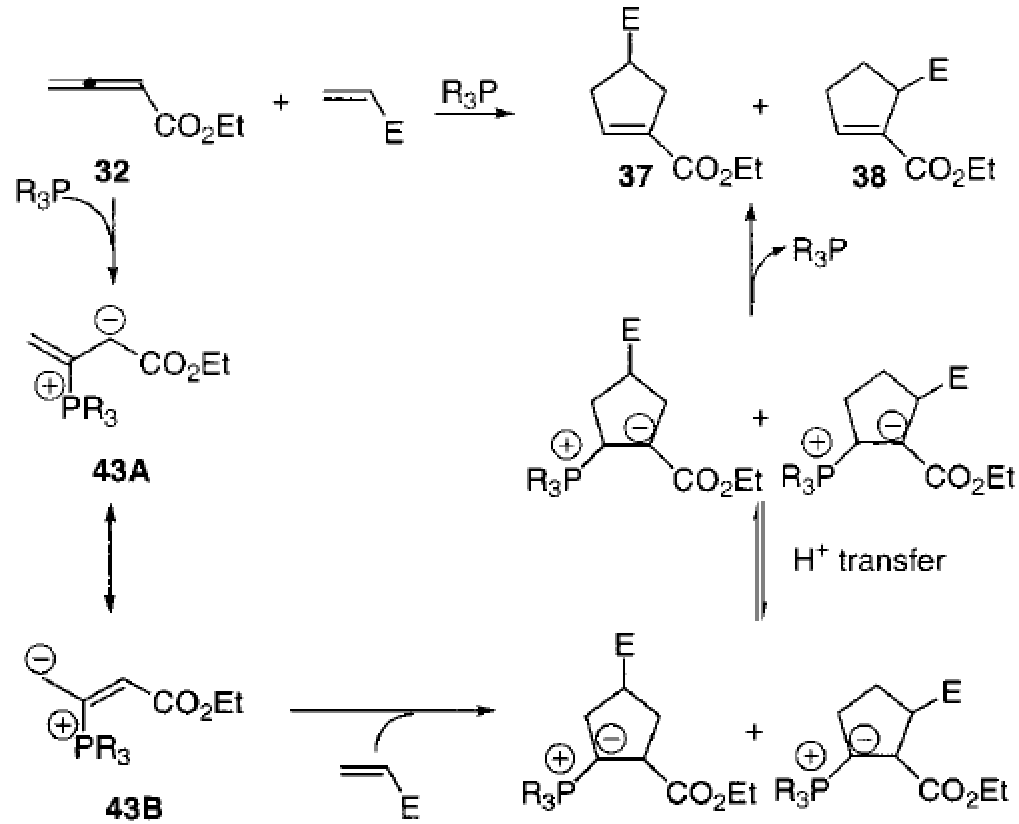
Hetero [4+2] cycloaddition between allenes and enones



catalytic cycloadditions through zwitterionic intermediates

Reactions promoted by Lewis-base catalyst

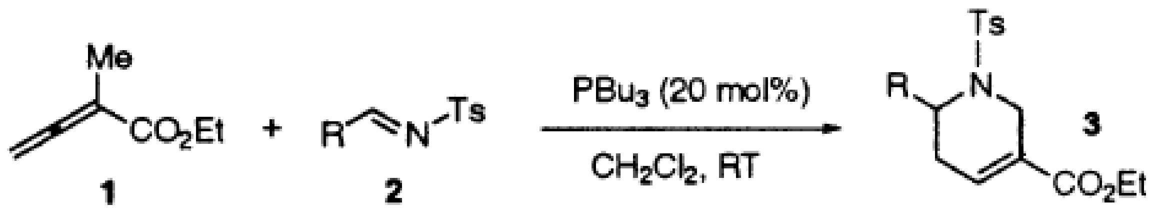




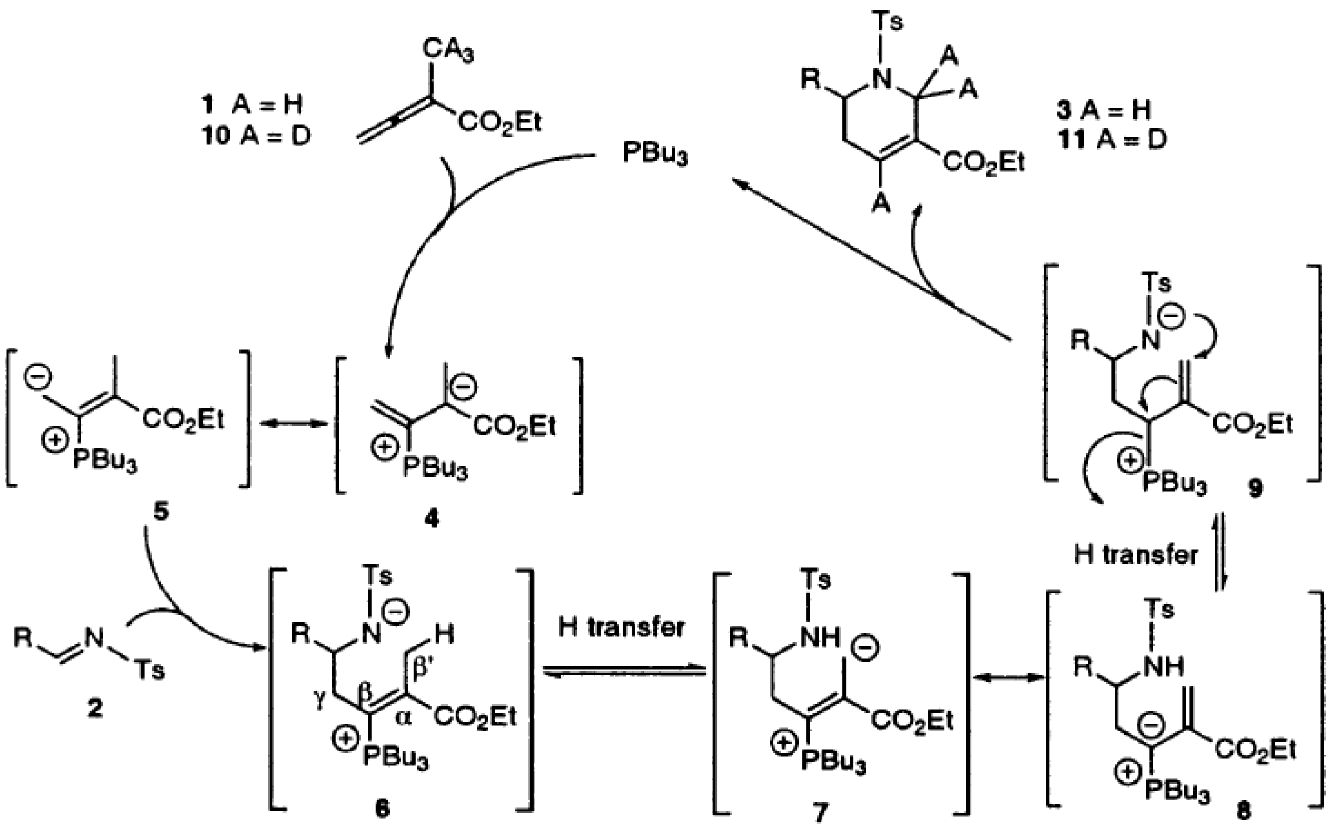
[3+2] cycloadditions

F. Lopez and J. L. Mascarenas, *Chem. Soc. Rev.*, **2014**, *43*, *2904--2915*

Lewis-base catalyst [4+2] cycloadditions

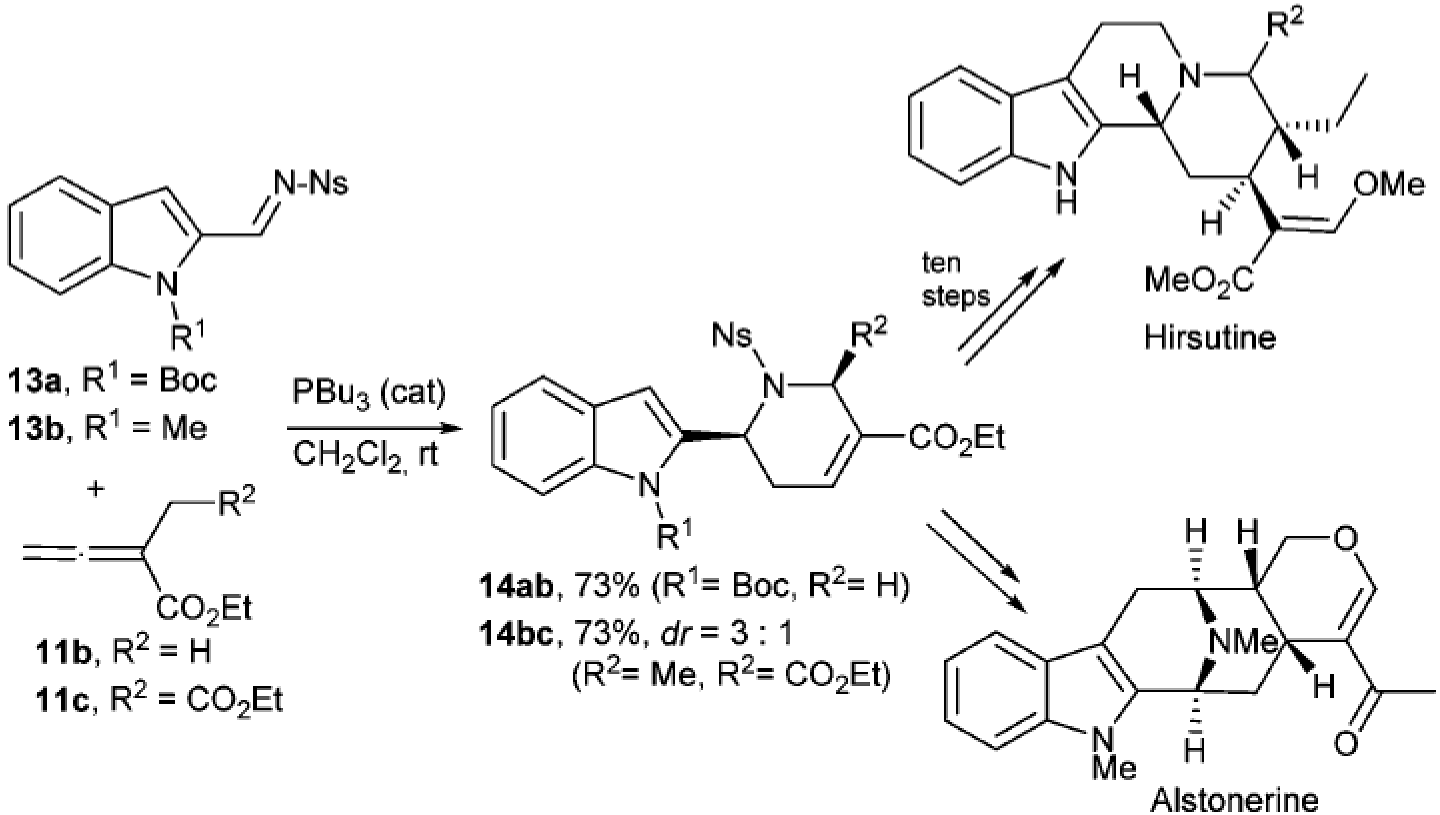


92-99% yield



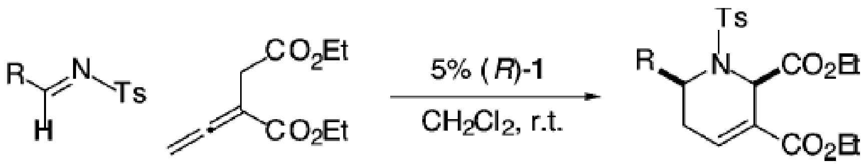
Ohyun Kwon etc, *J. Am. Chem. Soc*, **2003**, *125*, 4716-4717

Synthesis of (±)-Hirsutine through Imine-Allene [4+2] annulation

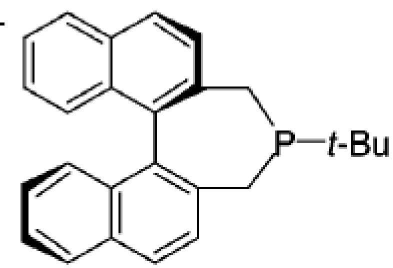


Ohyun Kwon etc, *Org. lett*., **2012**, *14*, 4634-4637

Asymmetric [4+2] cycloadditions between allenonates and imines



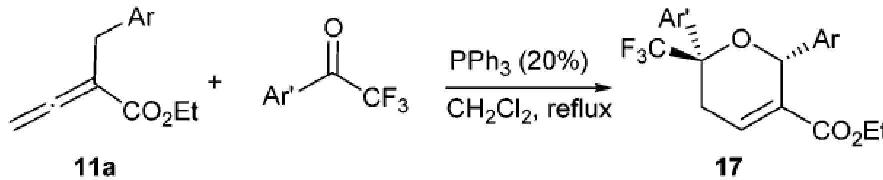
entry	R	ee (%)[b]	cis:trans	isolated yield (%)
1	Ph	98	91:9	93
2	3-MeC_6H_4	98	93:7	98
3	3,4,5-$(MeO)_3C_6H_2$	96	96:4	86
4	4-$(MeO)C_6H_4$	98	93:7	42
5	4-ClC_6H_4	96	91:9	99
6	3-BrC_6H_4	99	89:11	98
7	2-$(NO_2)C_6H_4$	68	96:4	98
8	2-ClC_6H_4	60	79:21	75
9	2-naphthyl	99	93:7	96
10	2-furyl	97	87:13	98
11	3-pyridyl	97	91:9	76



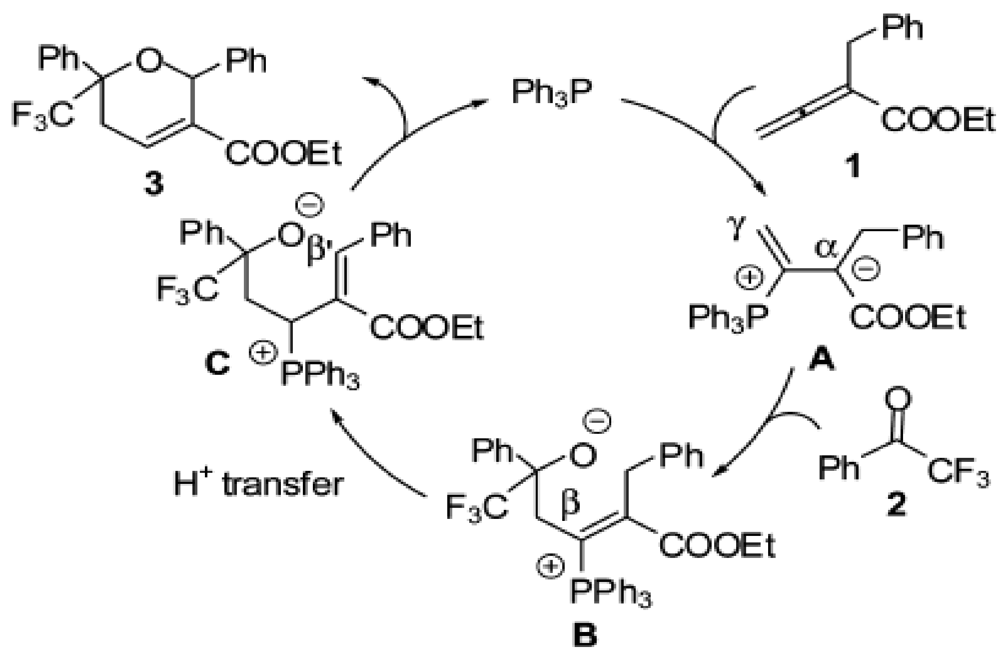
(R)-1

Gregory C. Fu etc, *J. Am. Chem. Soc*, **2005**, *127*, 12234-12235

[4+2] cycloadditions of allenoates and ketones

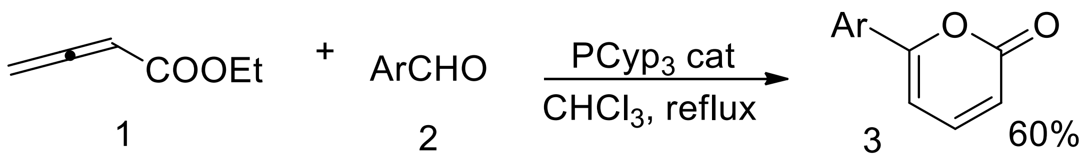


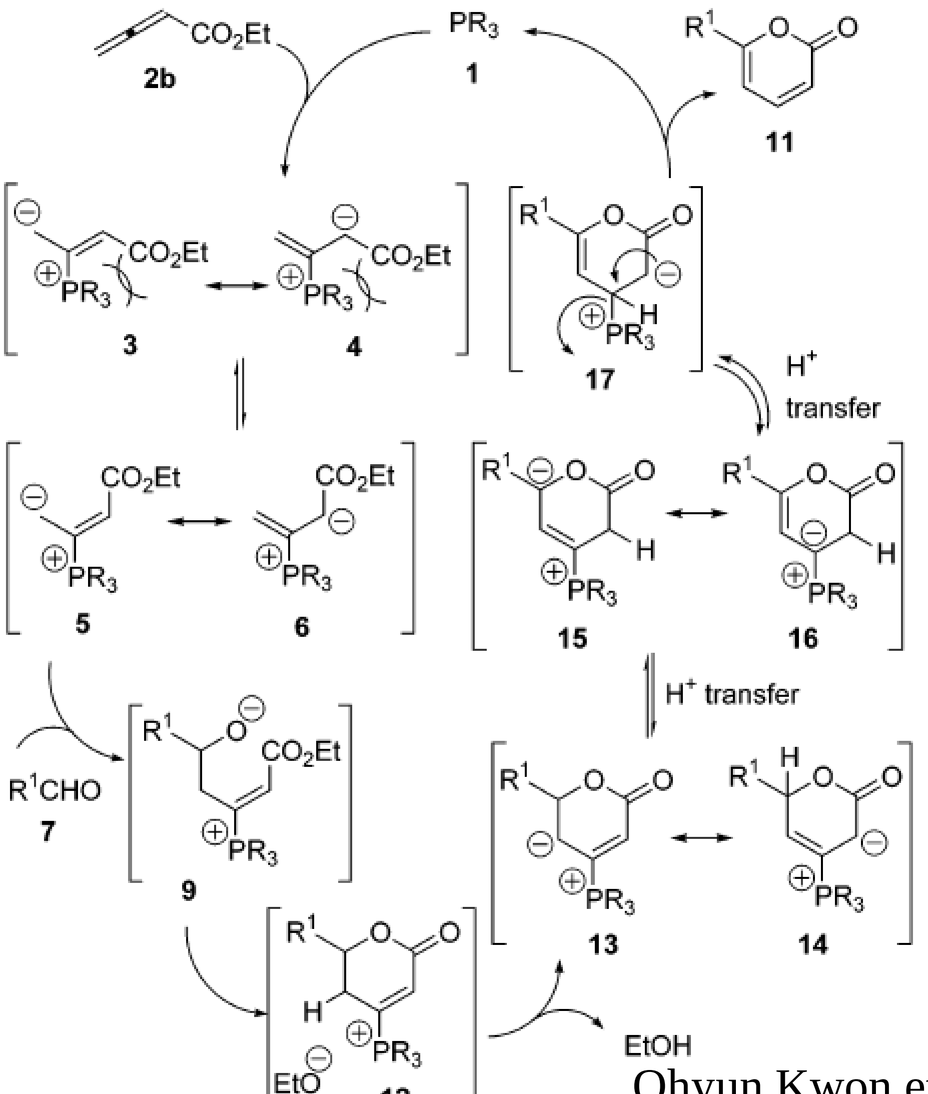
Ar	Ar'	*dr*	**17**, yield
Ph	Ph	14:1	76%
p-MePh	Ph	15:1	75%
o-BrPh	Ph	14:1	85%
Ph	*p*-MePh	11 : 1	66%
Ph	*p*-ClPh	25 : 1	85%
Ph	*p*-MeOPh	10 : 1	53%



Song Ye etc, *Org. lett*.**, 2010**, *12*, 4168-4171

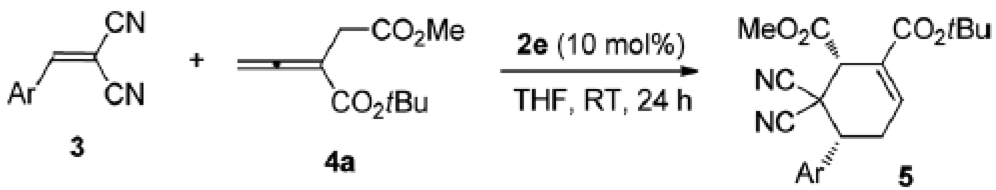
[4+2] cycloadditions of butadienoates with aldehydes



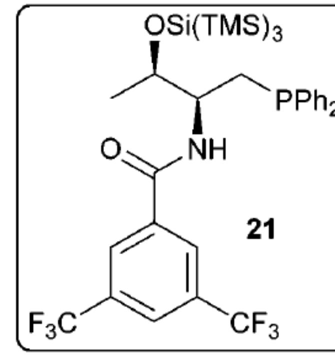


Ohyun Kwon etc, *Org. lett*.**, 2008**, *10*, 429-432

All carbon [4+2] cycloadditions of allenoates



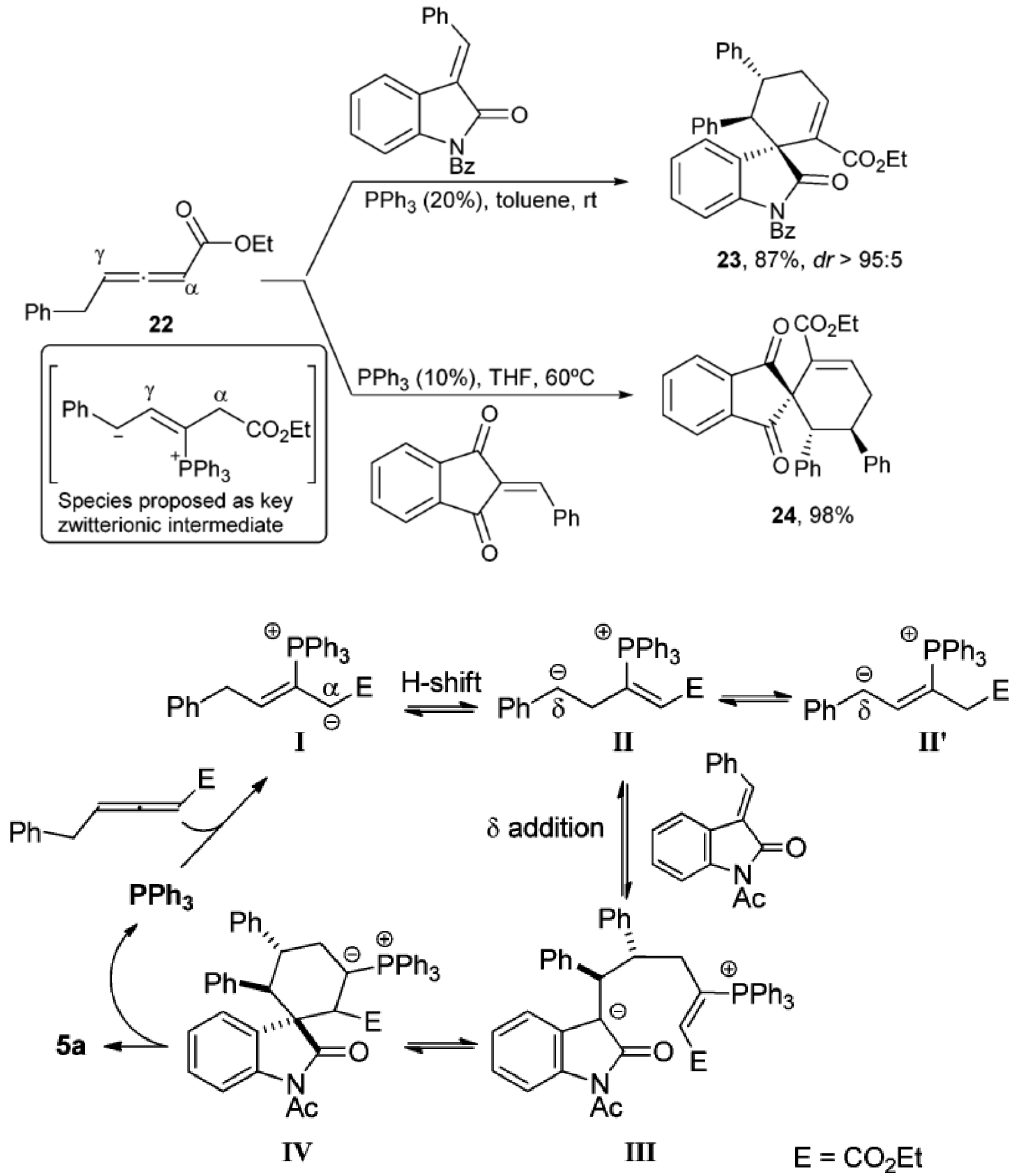
Entry	Ar (5)	*cis*/*trans*[b]	Yield (%)[c]	*ee* (%)[d]
1	C_6H_5 (**5a**)	86 : 14	92	98
2	4–CF_3–C_6H_4 (**5b**)	84 : 16	89	93
3	4–Et–C_6H_4 (**5c**)	82 : 18	91	98
4	4–OMe–C_6H_4 (**5d**)	83 : 17	89	95
5	4–F–C_6H_4 (**5e**)	82 : 18	92	95
6	4–Br–C_6H_4 (**5f**)	78 : 22	88	95
7	3–Cl–C_6H_4 (**5g**)	85 : 15	96	99
8	3–Br–C_6H_4 (**5h**)	85 : 15	94	99
9[e]	3–Me–C_6H_4 (**5i**)	81 : 19	93	98
10	2–F–C_6H_4 (**5j**)	71 : 29	89	95
11	2–Me–C_6H_4 (**5k**)	76 : 24	90	99
12	2-Ethynyl-C_6H_4 (**5l**)	77 : 23	85	91
13	2–Cl–C_6H_4 (**5m**)	75 : 25	95	98
14	3,4–Cl–C_6H_3 (**5n**)	82 : 18	92	98
15	2-Furyl (**5o**)	60 : 40	86	93
16	2-Thiophenyl (**5p**)	79 : 21	93	97
17	2-Naphthyl (**5q**)	87 : 13	94	97



2e

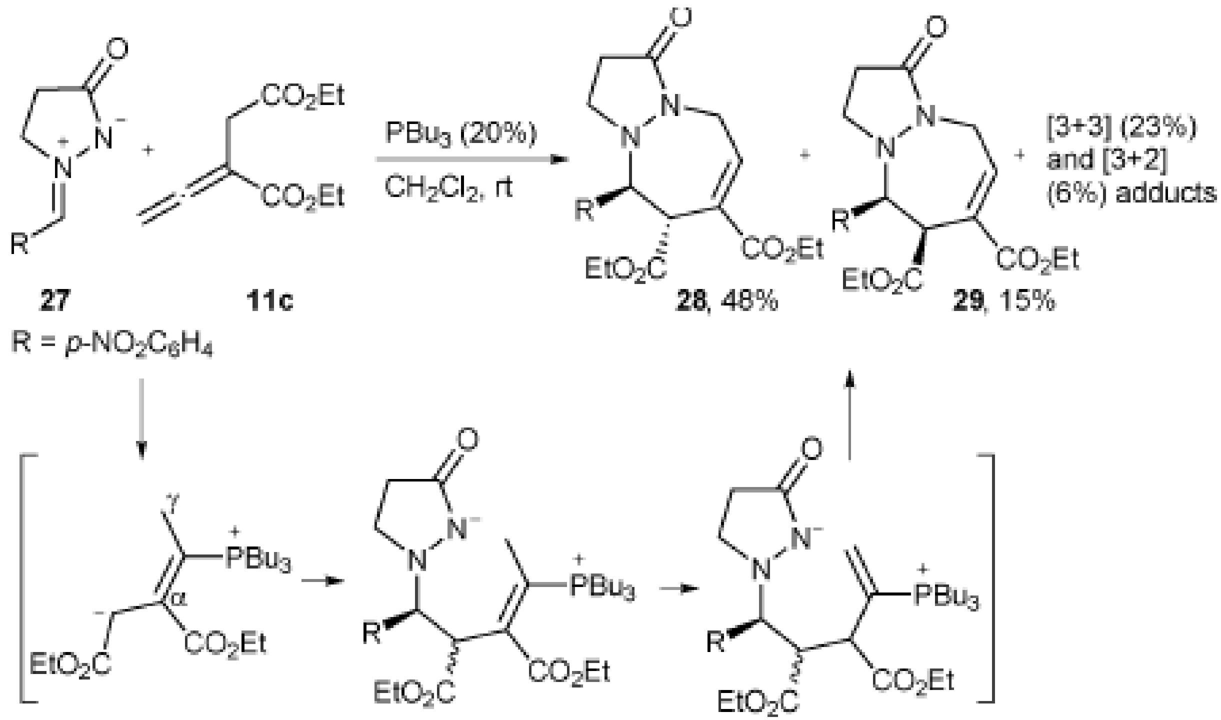
Yixin Lu etc, *Chem. Sci*., **2012**, 3, 1231-1234

γ-substituted allenoate [4+2] cycloaddition



Arnaud Voituriez etc, *Org. lett*., **2013**, *15*, 4002-4005

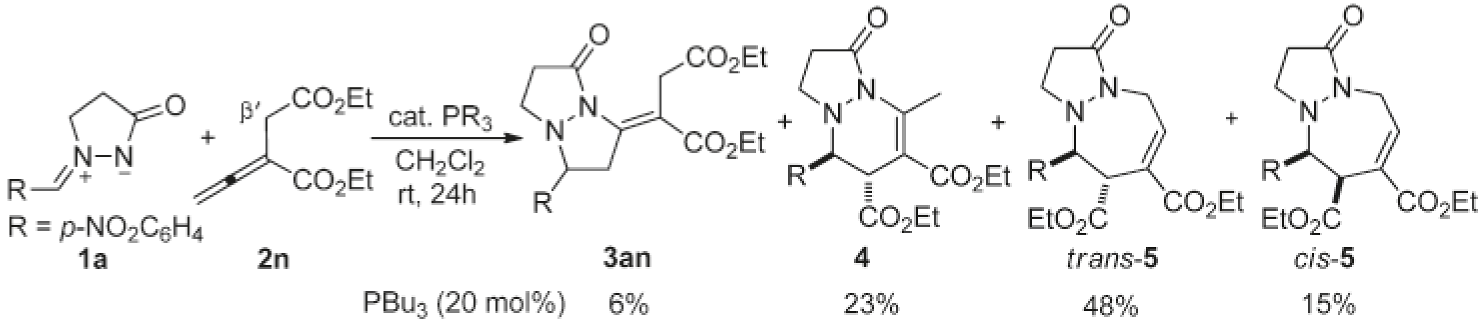
Allene as 4C-atom component in [4+3] cycloadditions

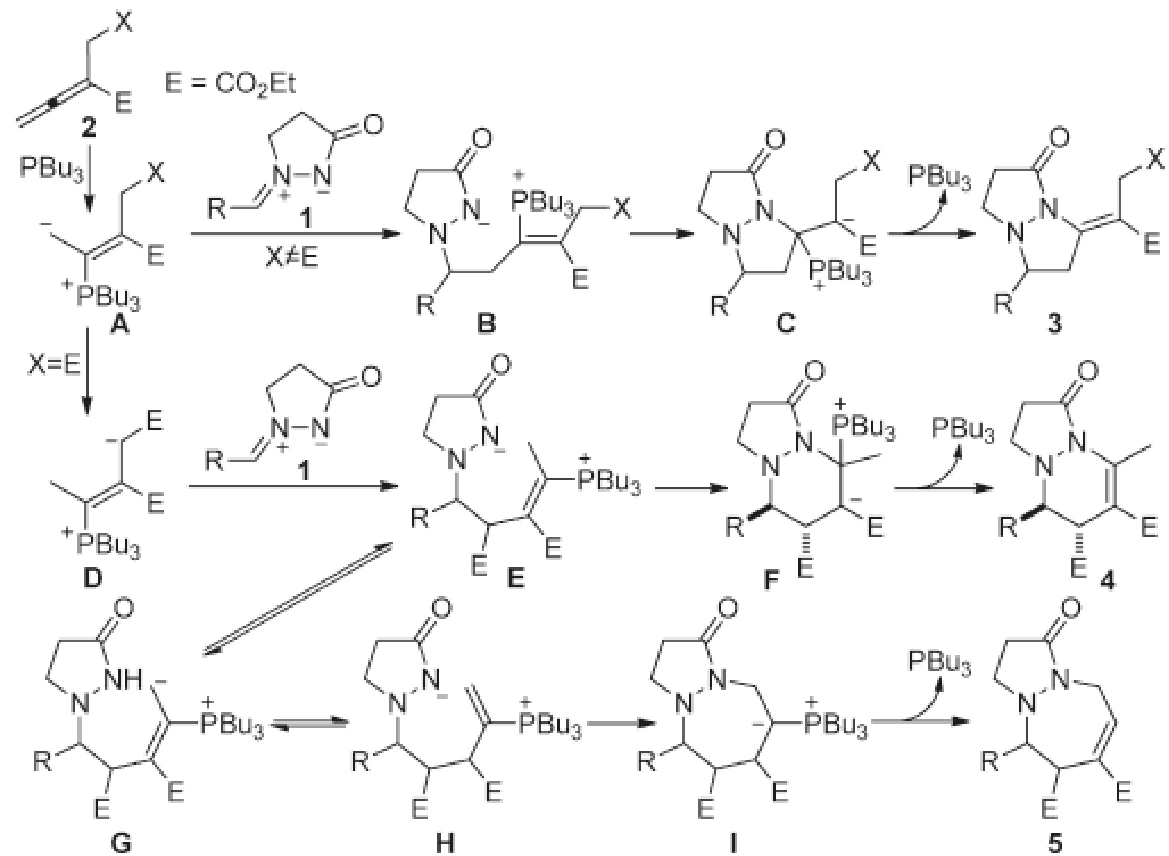


a b c

Ohyun Kwon etc, *J. Am. Chem. Soc*, **2011**, *133*, 13337-13348

Allene as 4C-atom component in [4+3] cycloadditions

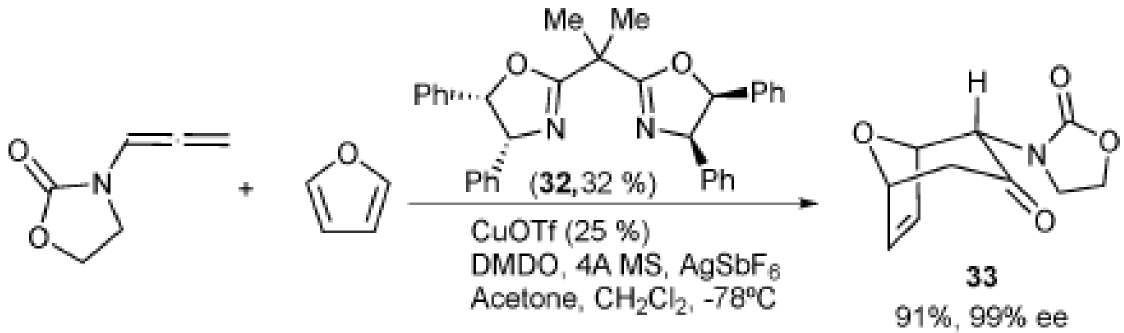


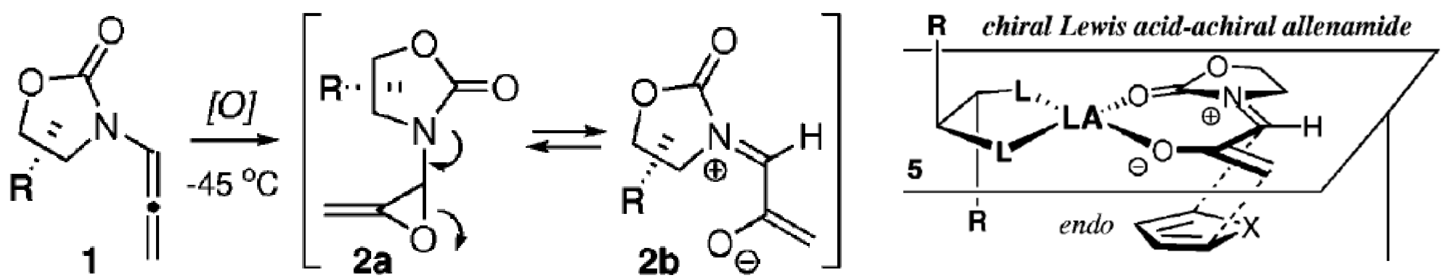


catalytic cycloadditions through zwitterionic intermediates

Reactions promoted by transition metal catalysts

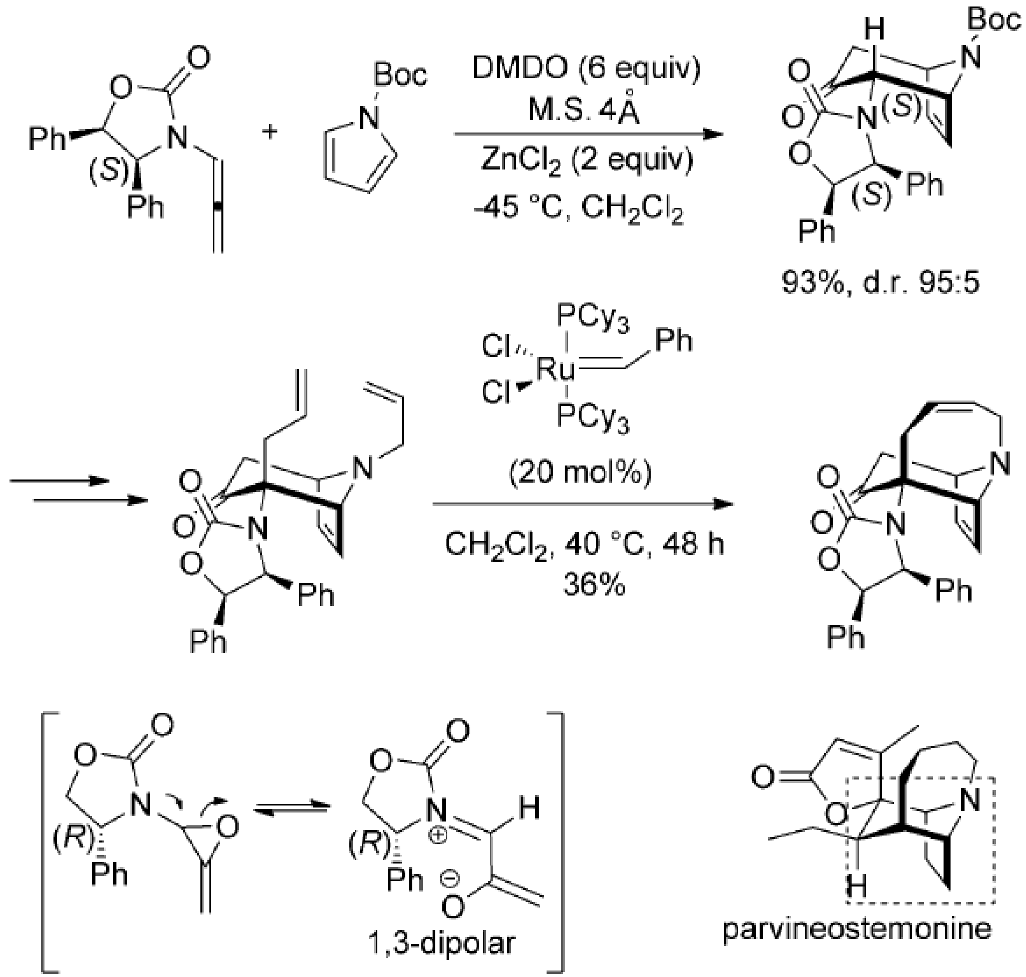
Intermolecular [4+3]





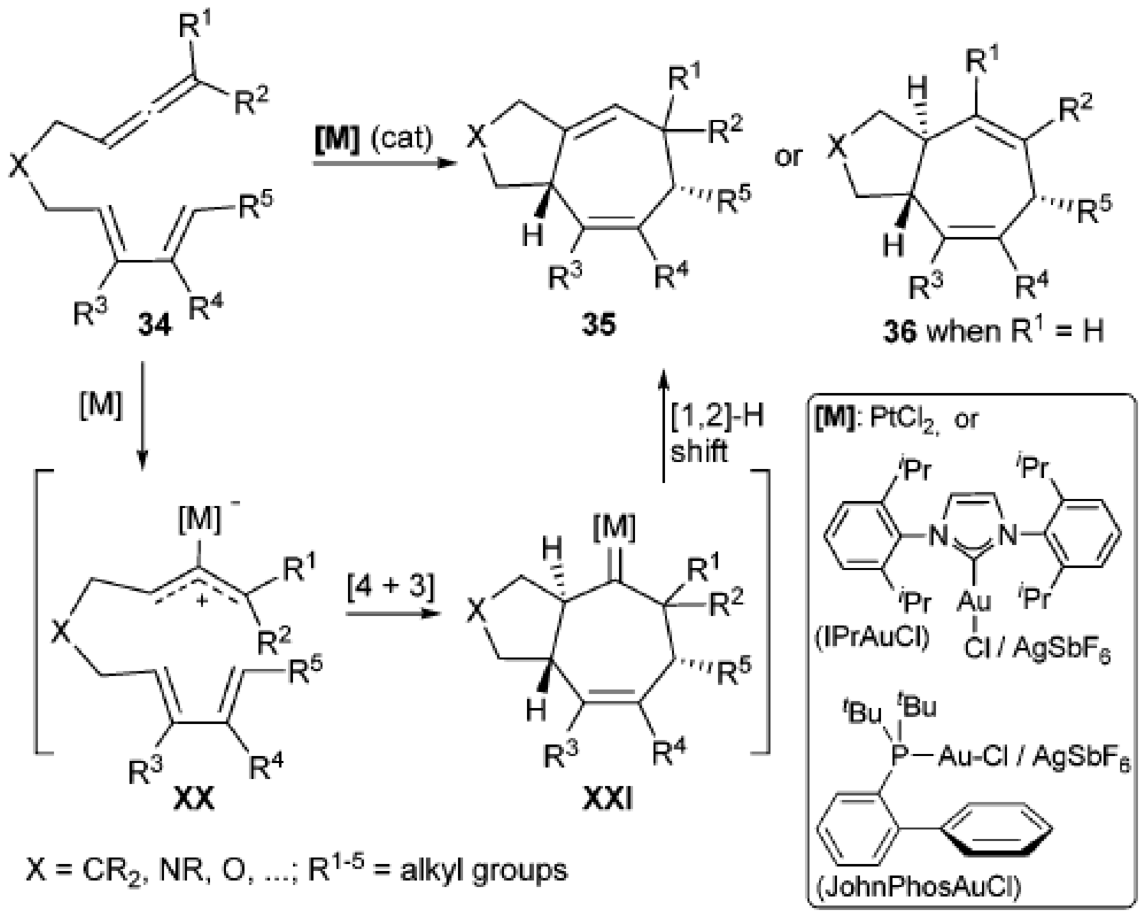
Richard P. Hsungetc, *J. Am. Chem. Soc*, **2005**, *127*, 50-51

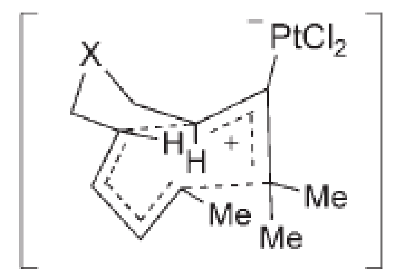
Synthesis of the azatricycle core of parvineostemonine through [4+3] cycloaddition



Richard P. Hsung, *Org. lett*.**, 2007**, *9*, 1275-1278

Au and Pt-catalyzed intramolecular [4+3] cycloadditions of allene-dienes



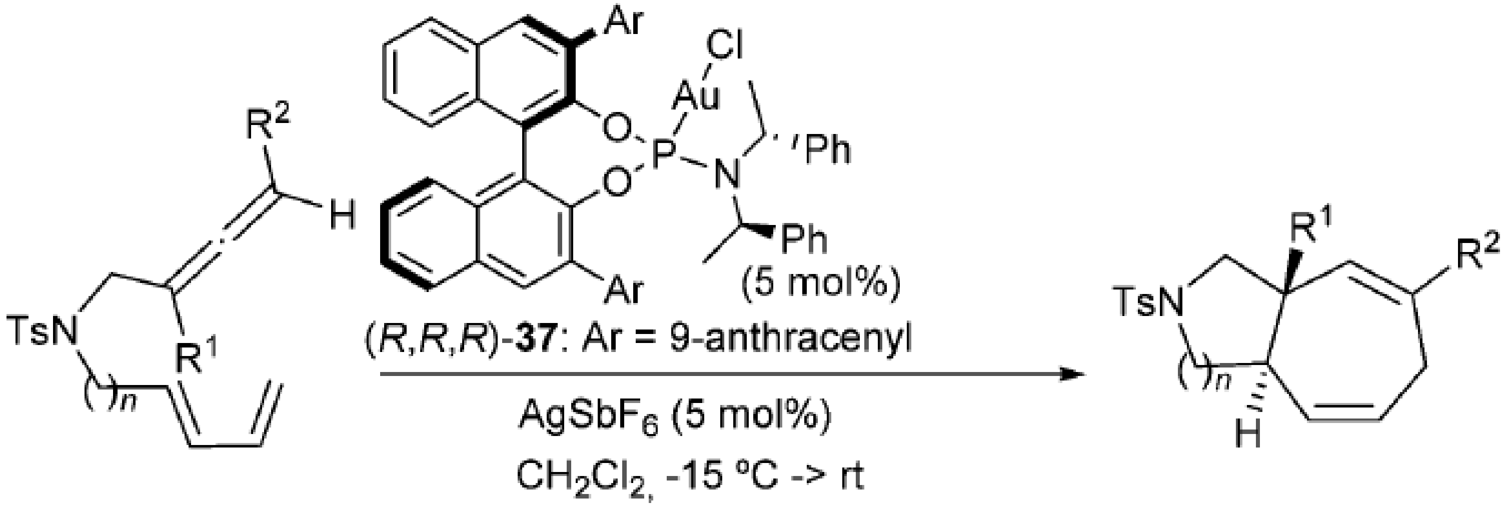


TS for 34

R_1, R_2, R_5 = Me

Fernando lopez etc, *Angew. Chem. Int. Ed*, **2008**, *47*, 951-954

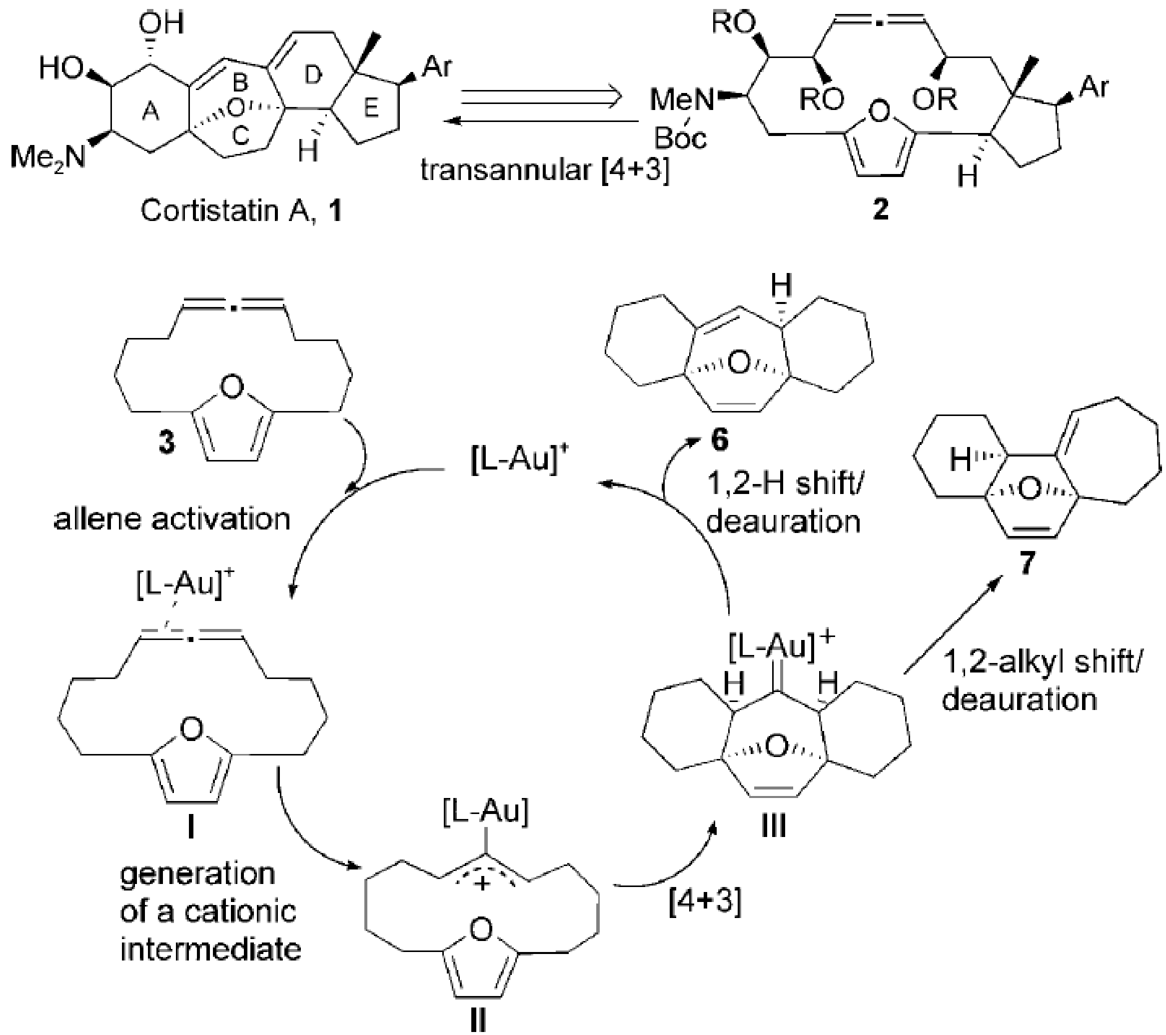
Au catalyzed enatioselective intramolecular [4+3] cycloadditions of allene-dienes



n	R^1	R^2	yield	ee
1	H	Ph	74%	95%
1	Me	Me	78%	95%
1	Me	^{i}Pr	76%	95%
2	Me	Me	95%	98%

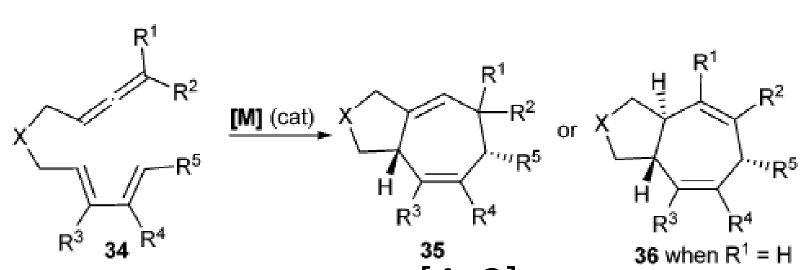
Fernando lopez etc, *Angew. Chem. Int. Ed*, **2011**, *50*, 11496-11500

Au catalyzed [4+3] cycloadditions in natural product synthesis

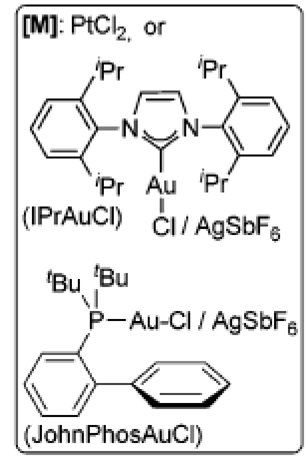


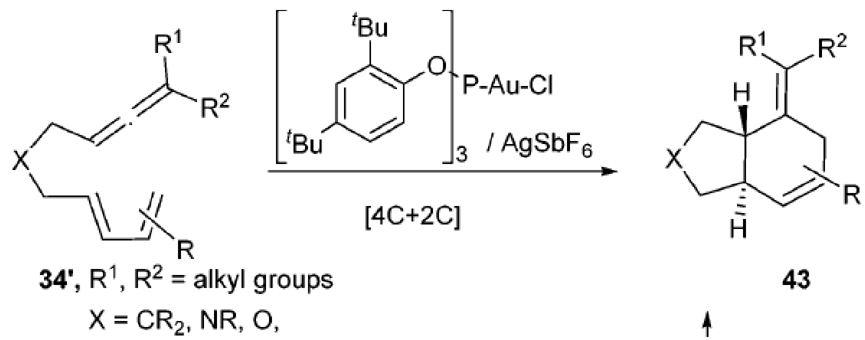
Benjamin W. Gung etc, *chem. Eur. J.* **2010**, *16*, 639-644

Au catalyzed intramolecular [4+2] cycloadditions

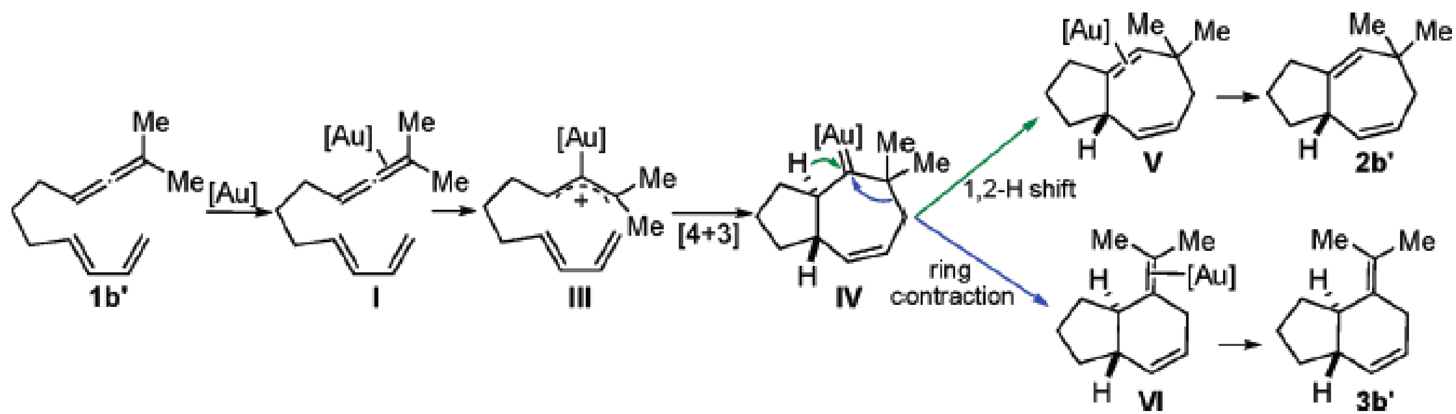


[4+3]



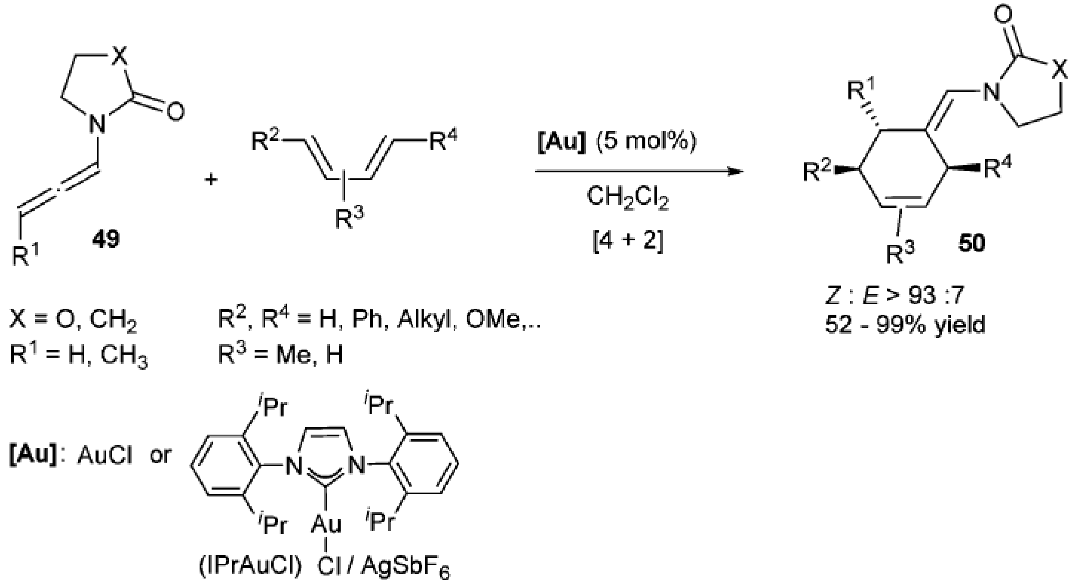


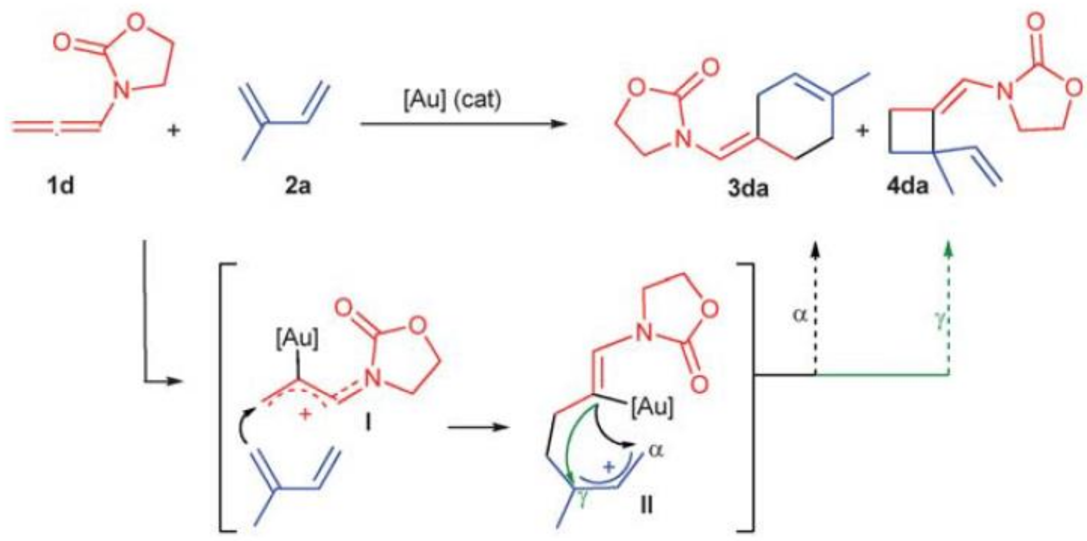
[4+2]



Fernando lopez etc, *J. Am. Chem. Soc*, **2009**, *131*, 13020-13030

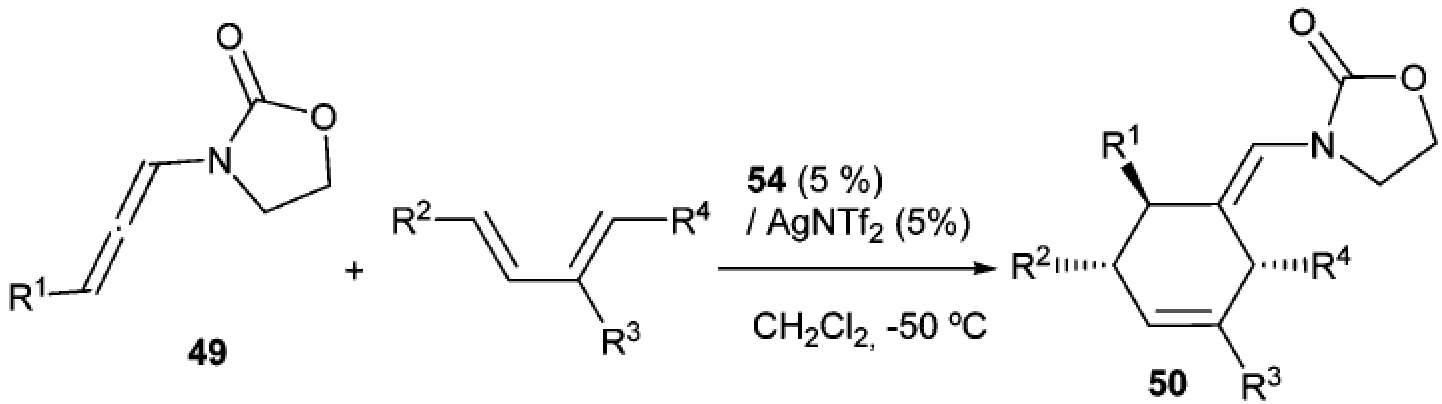
Au catalyzed intermolecular [4+2] cycloadditions

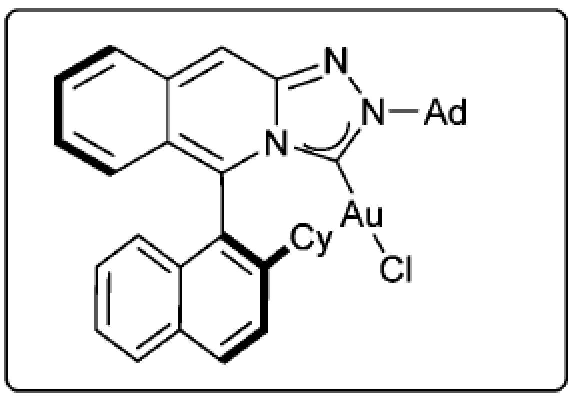




Fernando lopez etc, *chem. Sci.*, **2011**, *2*, 633-637

Au catalyzed enantioselective [4+2] cycloadditions





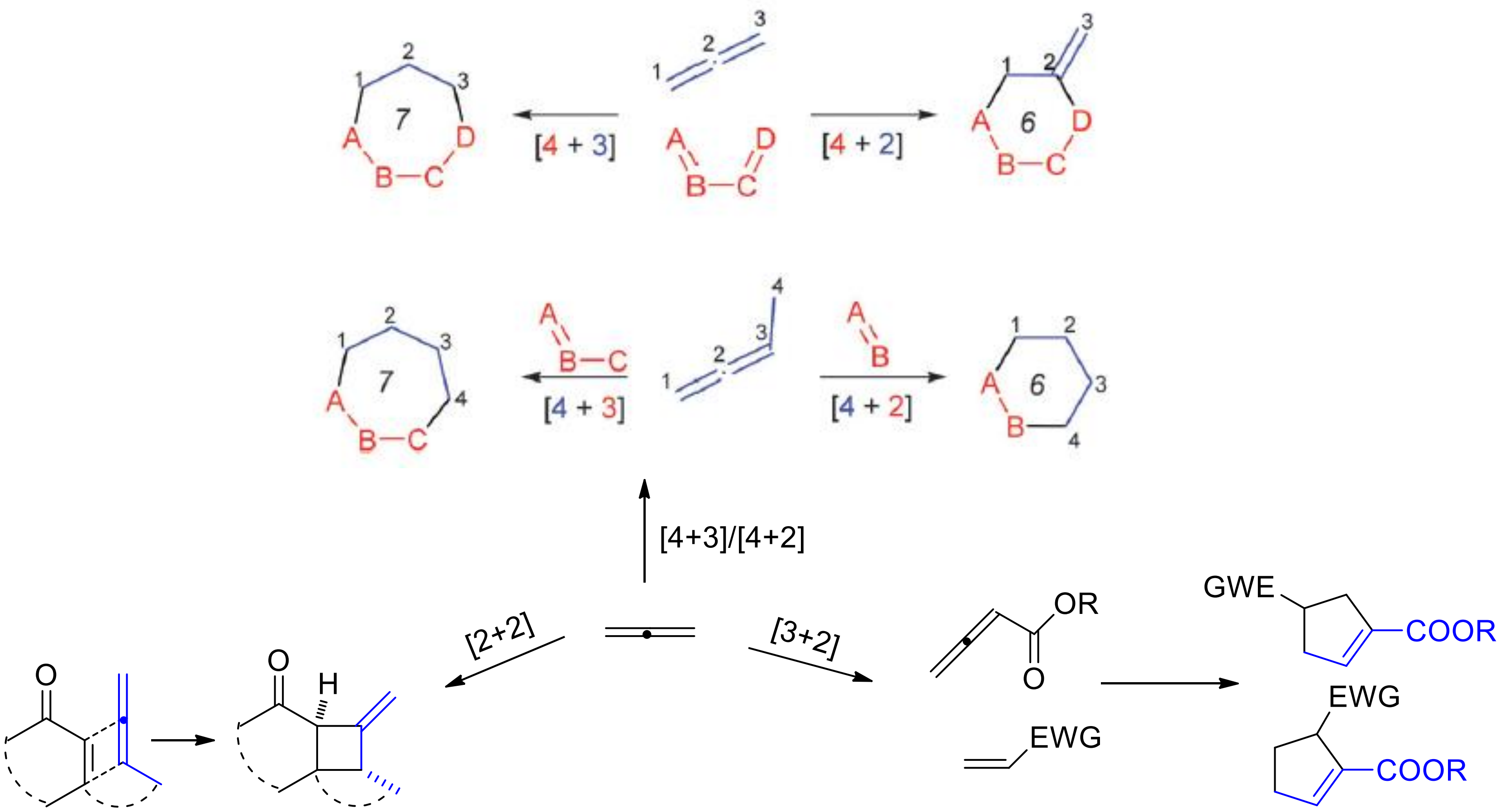
54, Ad: 1-Adamantyl

R^1	R^2	R^3	R^4	yield	ee
H	H	H	Ph	88%	99%[a]
H	H	Me	Ph	88%	95%
H	Me	H	Ph	85%	94%
H	H	H	Me	71%	91%
H	Me	H	Me	56%	87%
Me	Me	H	Ph	51%	91%[b]

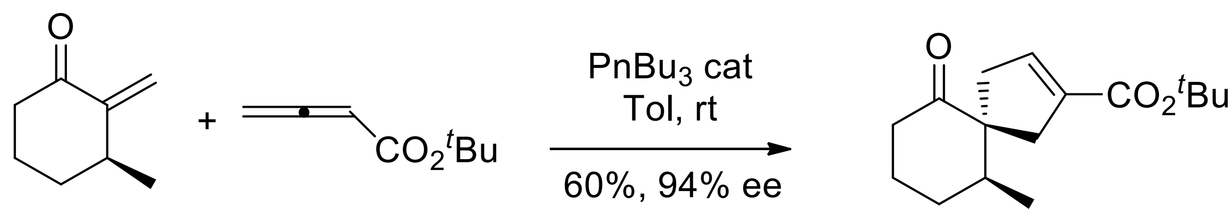
[a] Carried out at -78ºC; [b] Carried out at 10 ºC

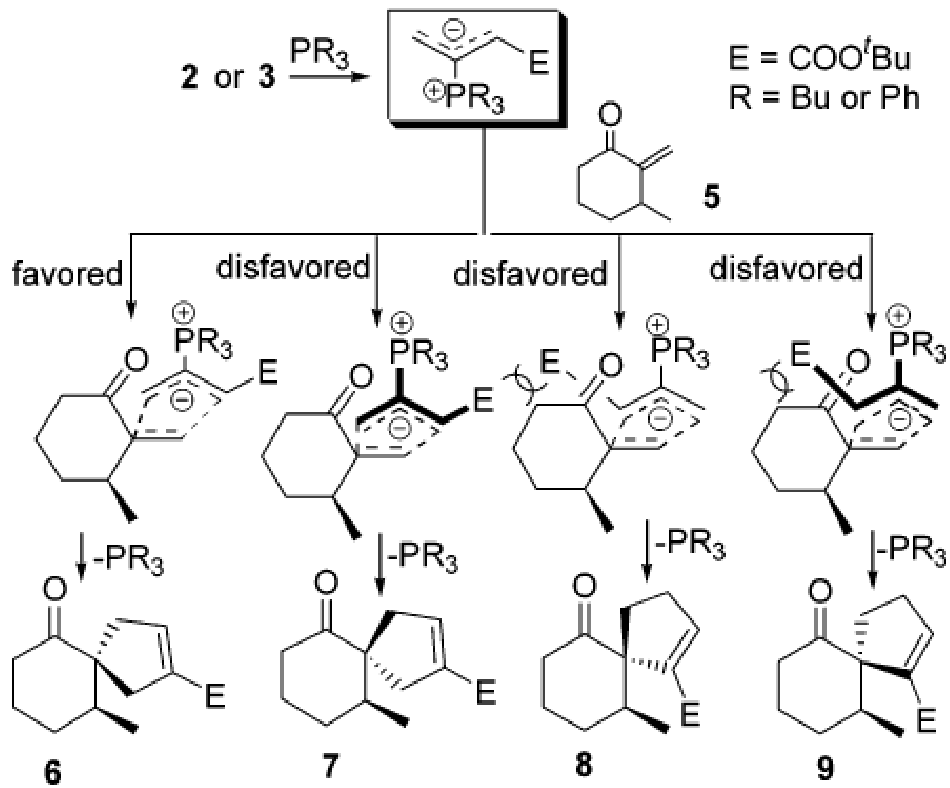
Fernando lopez etc, *J. Am. Chem. Soc*, **2012**, *134*, 14322-14325

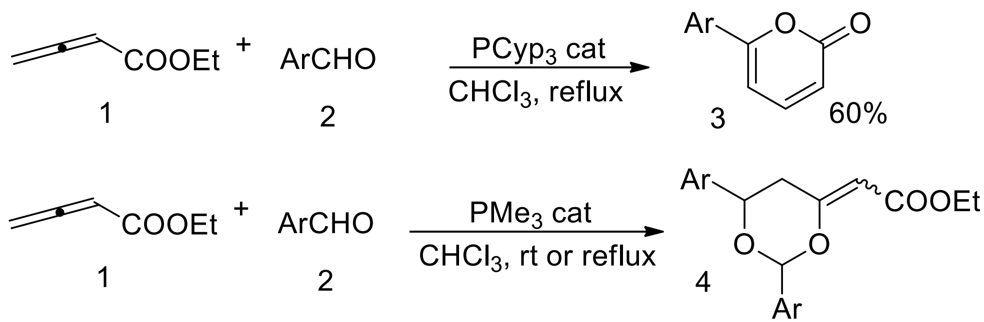
conclution

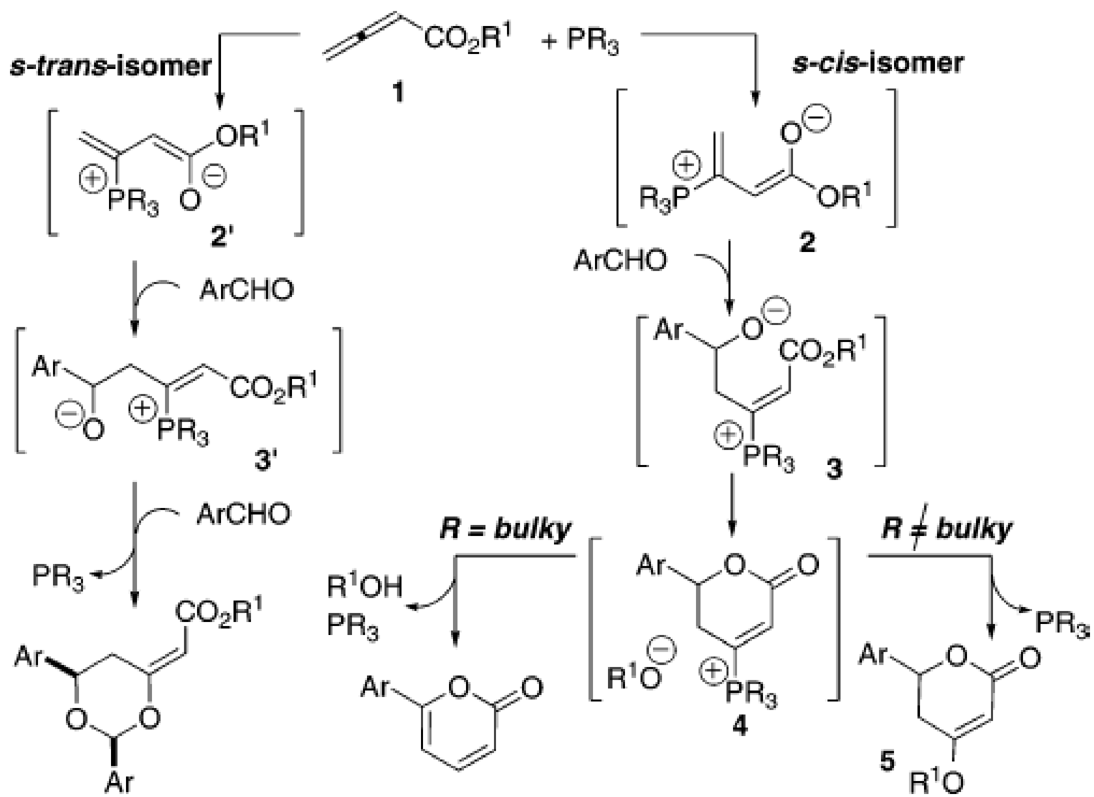


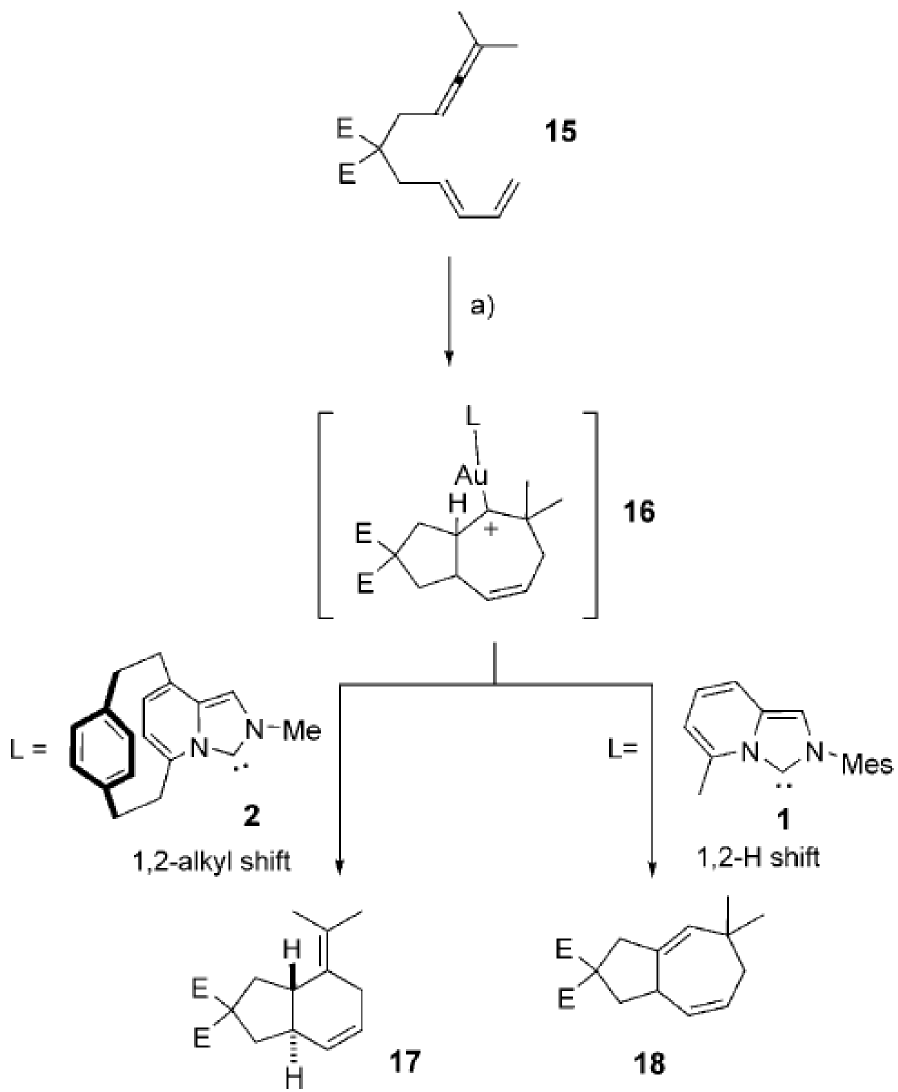
Thanks!


O
CO2tBu
PnBu3 cat
Tol, rt
60%, 94% ee
CO2tBu


2 or 3
PR3
E
PR3
E = COOtBu
R = Bu or Ph
5
favored
disfavored
disfavored
disfavored
-PR3
-PR3
-PR3
-PR3
6
7
8
9


COOEt
+
ArCHO
PCyp3 cat
CHCl3, reflux
Ar
O
O
1
2
3
60%
COOEt
+
ArCHO
PMe3 cat
CHCl3, rt or reflux
Ar
COOEt
O
O
Ar
1
2
4


CO2R1
+ PR3
1
s-trans-isomer
s-cis-isomer
OR1
PR3
O
2'
O
R3P
OR1
2
ArCHO
ArCHO
Ar
O
CO2R1
PR3
3'
Ar
O
CO2R1
PR3
3
ArCHO
PR3
R = bulky
R ≠ bulky
R1OH
PR3
Ar
O
O
R1O
PR3
4
PR3
CO2R1
Ar
O
O
Ar
Ar
O
O
Ar
O
O
5
R1O


15
a)
16
L =
2
1,2-alkyl shift
L=
1
1,2-H shift
17
18