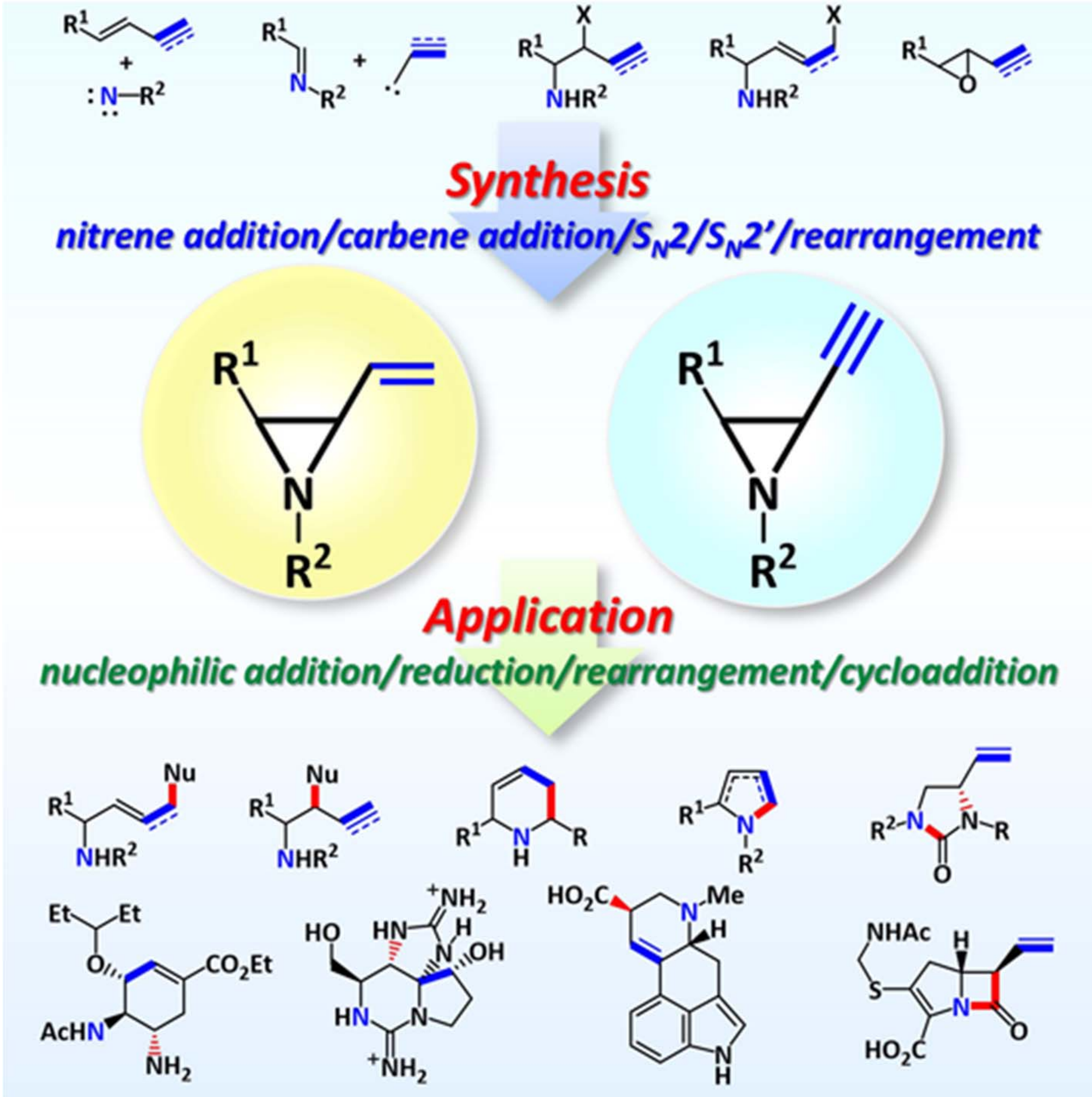
Synthesis and Application of Vinylaziridines and Ethynylaziridines

Rong Zeng

Dong Group

Jan. 7th, 2015

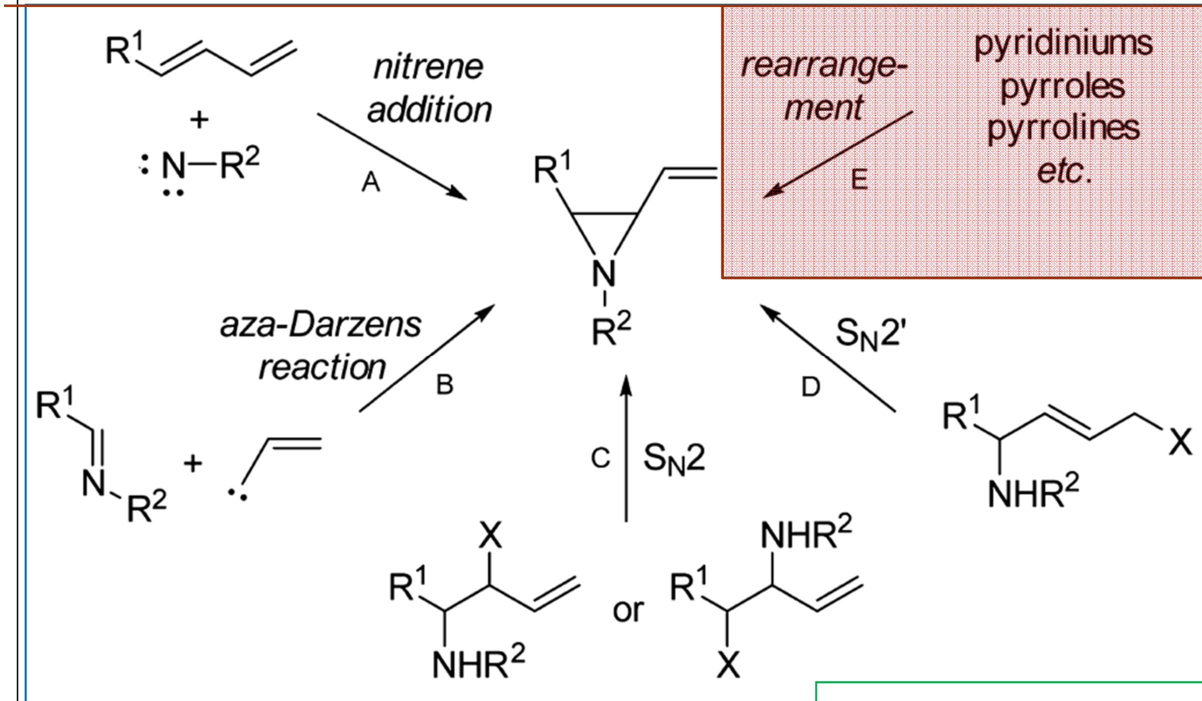


Hiroaki Ohno, *Chem. Rev.* **2014**, *114*, 7784

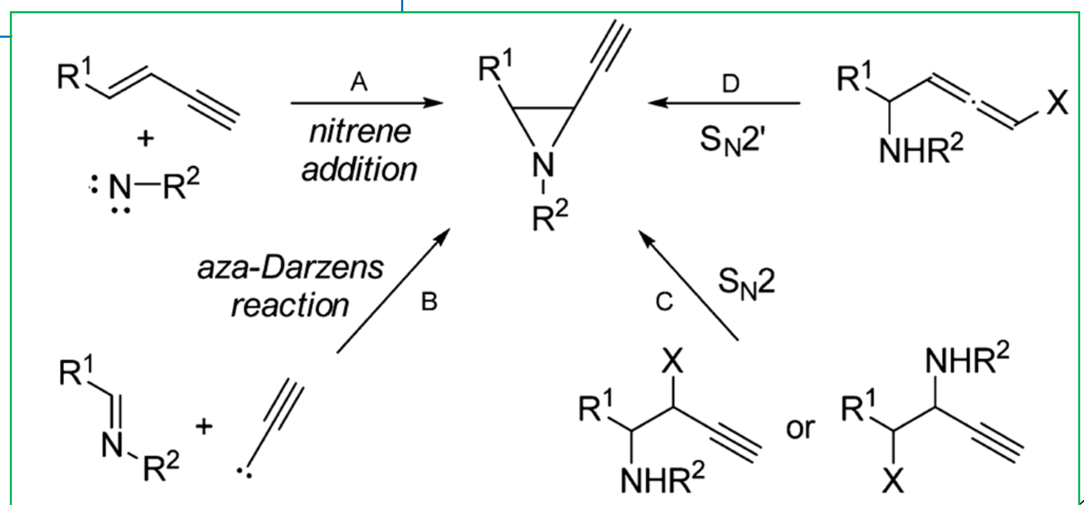
Outlines

- Synthesis of Vinyl- and Ethynylaziridine
- Ring-Opening with Nucleophiles
- Reductive Ring-Opening Reactions
- Rearrangement and Isomerization
- Cycloaddition

Synthesis of Vinyl- and Ethynylaziridines

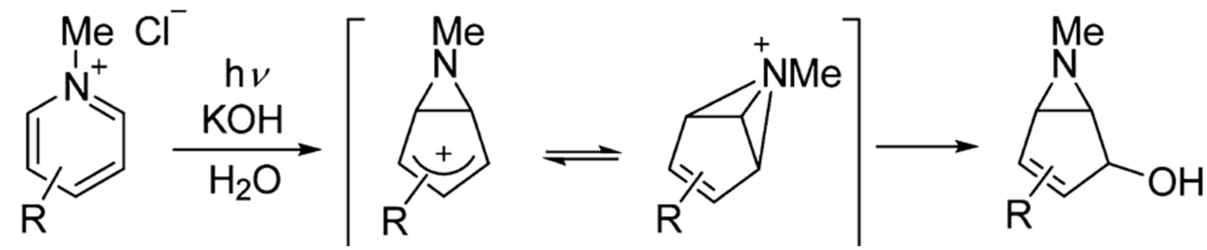


For synthesis of aziridines, see Haye Min's presentation.

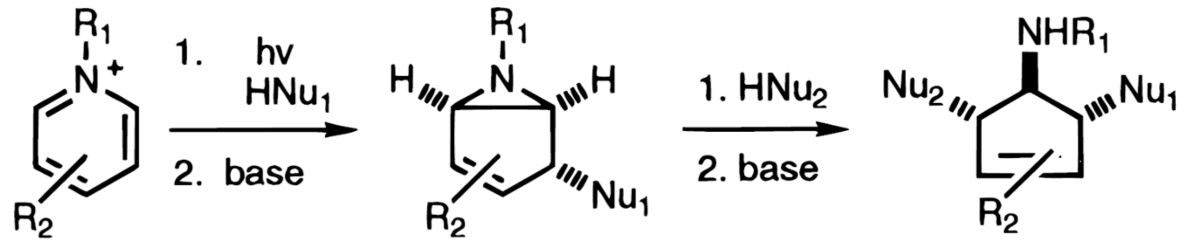


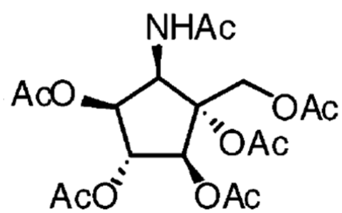
Hiroaki Ohno, *Chem. Rev.* **2014**, *114*, 7784

Synthesis of Vinylaziridines from Rearrangement



Kaplan, L.; Pavlik, J. W.; Wilzbach, K. E. *J. Am. Chem. Soc.* **1972**, *94*, 3283.
King, R. A.; **Lüthi, H. P.**; Schaefer, H. F., III; Glarner, F.; Burger, U. *Chem.-Eur. J.* **2001**, 7, 1734

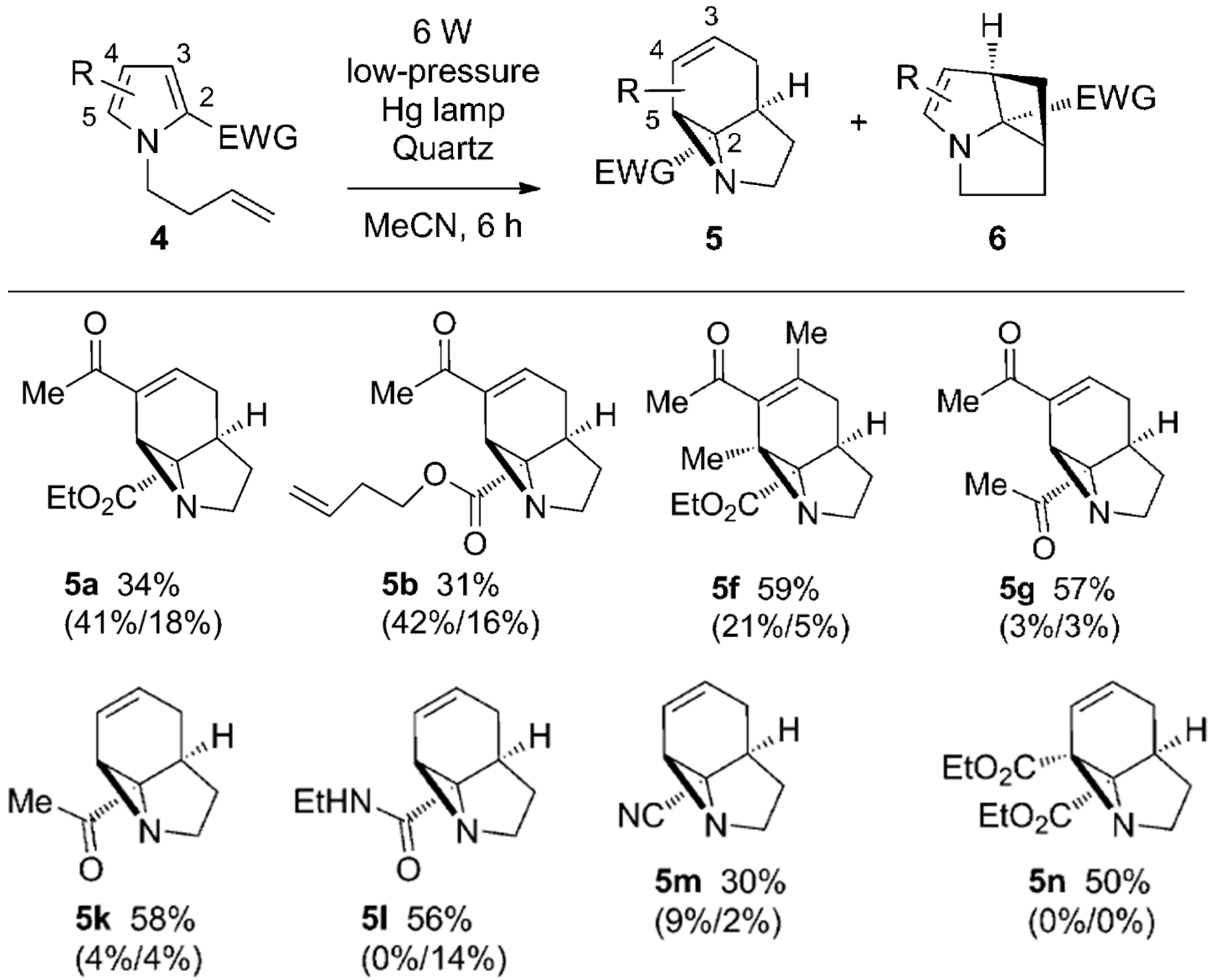




hexacetylated
(+/-)-trehazolamine

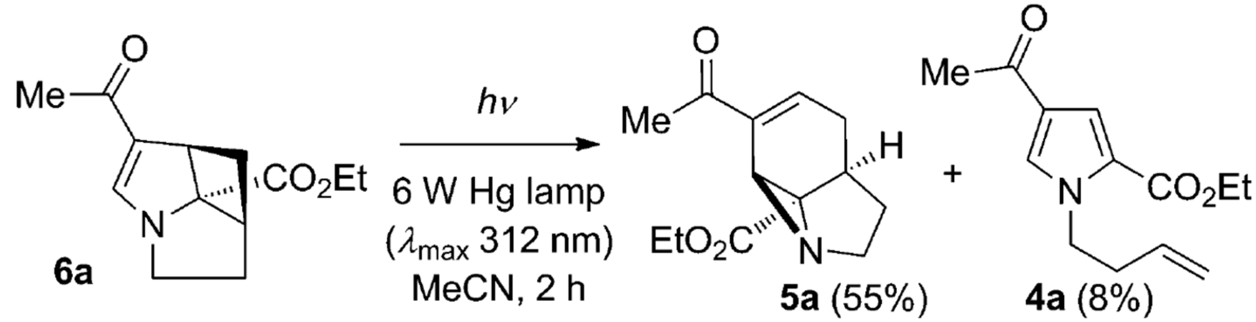
(R = H, >95 % ee
after 1 recrystall.)

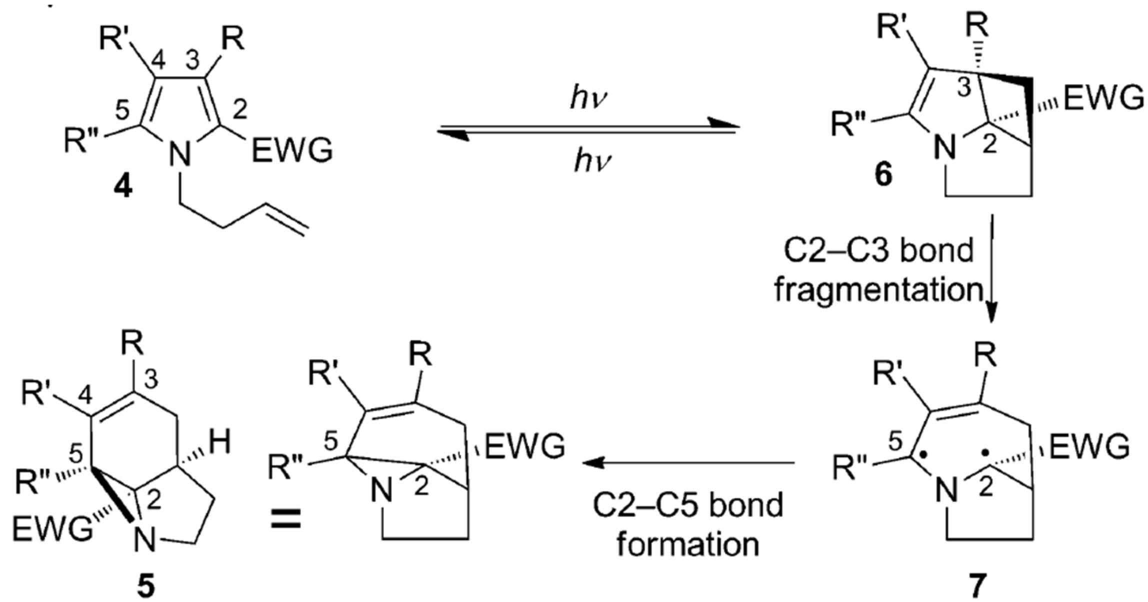
Ling, R.; Yoshida, M.; **Mariano, P. S**. *J. Org. Chem.* **1996**, *61*, 4439.
Feng, X.; Duesler, E. N.; **Mariano, P. S**. *J. Org. Chem.* **2005**, *70*, 5618.
Zhao, Z.; Duesler, E.; Wang, C.; Guo, H.; **Mariano, P. S**. *J. Org. Chem.* **2005**, *70*, 8508.



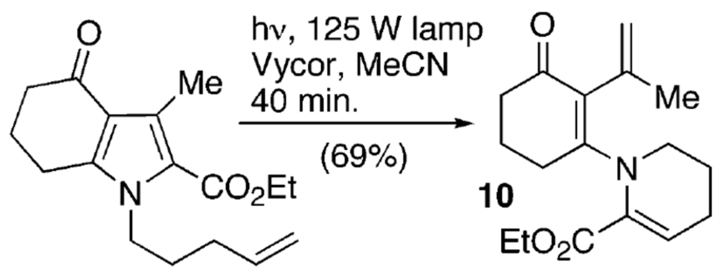
All products are racemic. Results in brackets: yield of 6/recovered 4.

Maskill, K. G.; Knowles, J. P.; Elliott, L. D.; Alder, R. W.; **Booker-Milburn, K. I.** *Angew. Chem., Int. Ed.* **2013**, *52*, 1499.



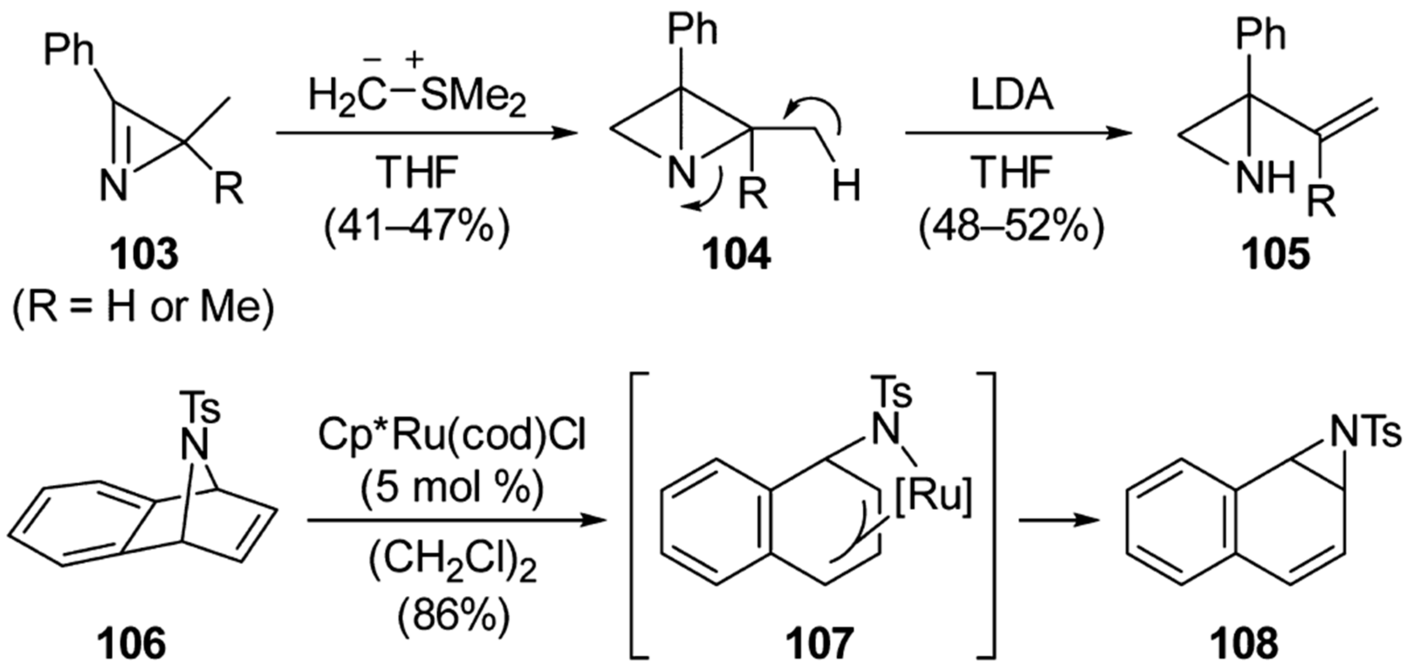


Booker-Milburn, K. I. Et. al. *Angew. Chem., Int. Ed.* **2013**, *52*, 1499.



Elliott, L. D.; Berry, M.; Orr-Ewing, A. J.; **Booker-Milburn, K. I**. *J. Am. Chem. Soc.* **2007**, *129*, 3078

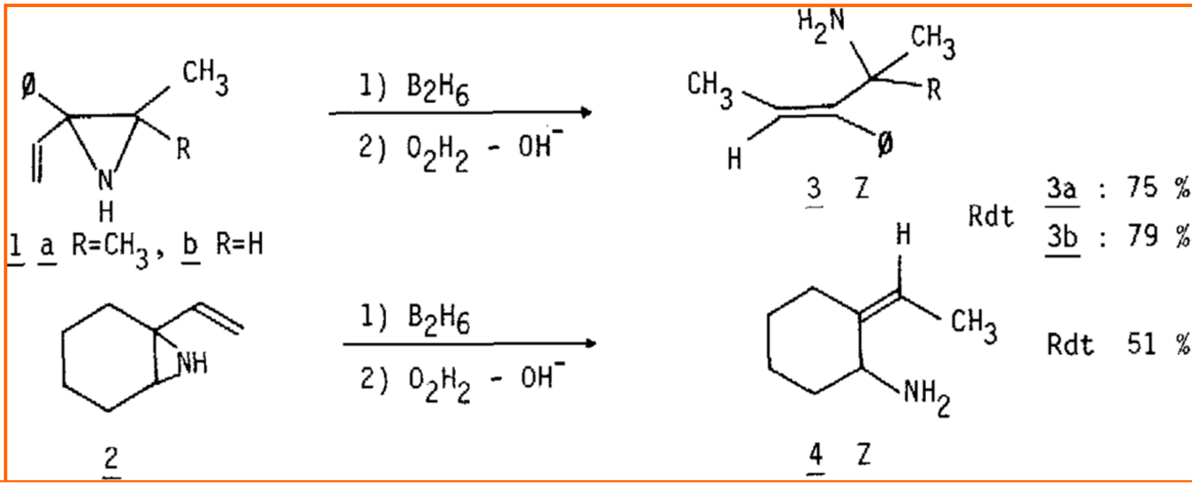
imino Corey−Chaykovsky reaction

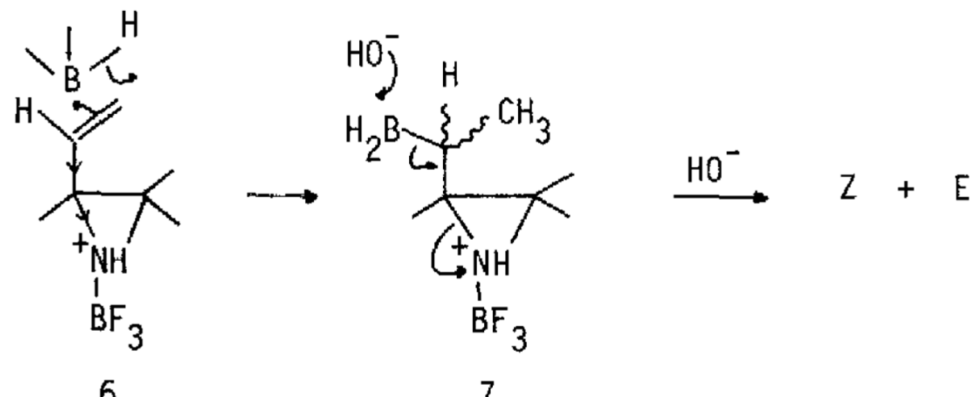


Hortmann, A. G.; Koo, J.-Y. *J. Org. Chem.* **1974**, *39*, 3781.
Hortmann, A. G.; Robertson, D. A. *J. Am. Chem. Soc.* **1972**, *94*, 2758.
Villeneuve, K.; **Tam, W.** *J. Am. Chem. Soc.* **2006**, *128*, 3514.

- Synthesis of Vinyl- and Ethynylaziridine
- **Ring-Opening with Nucleophiles**
- Reductive Ring-Opening Reactions
- Rearrangement and Isomerization
- Cycloaddition

Using Boron Hydrides as Nucleophile





	Rdt %	Z/E
3a	42	53/47
3b	58	82/18
4	32	72/28

Schéma III

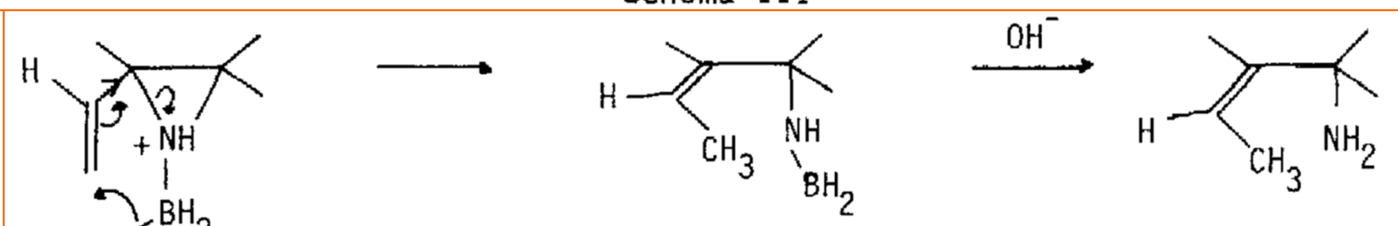
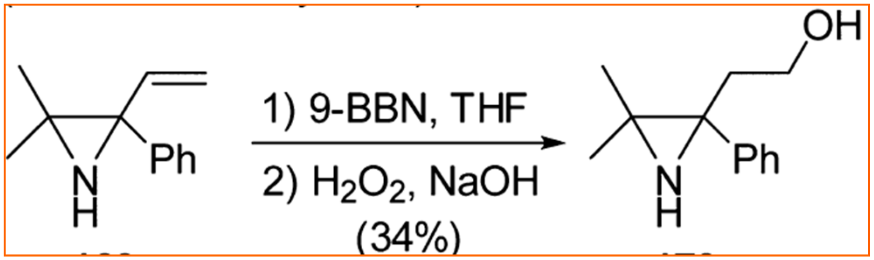
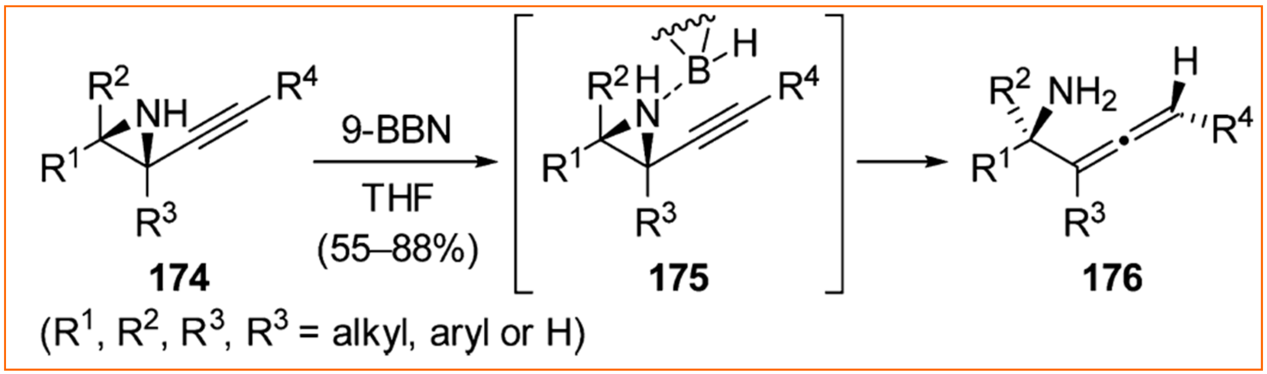


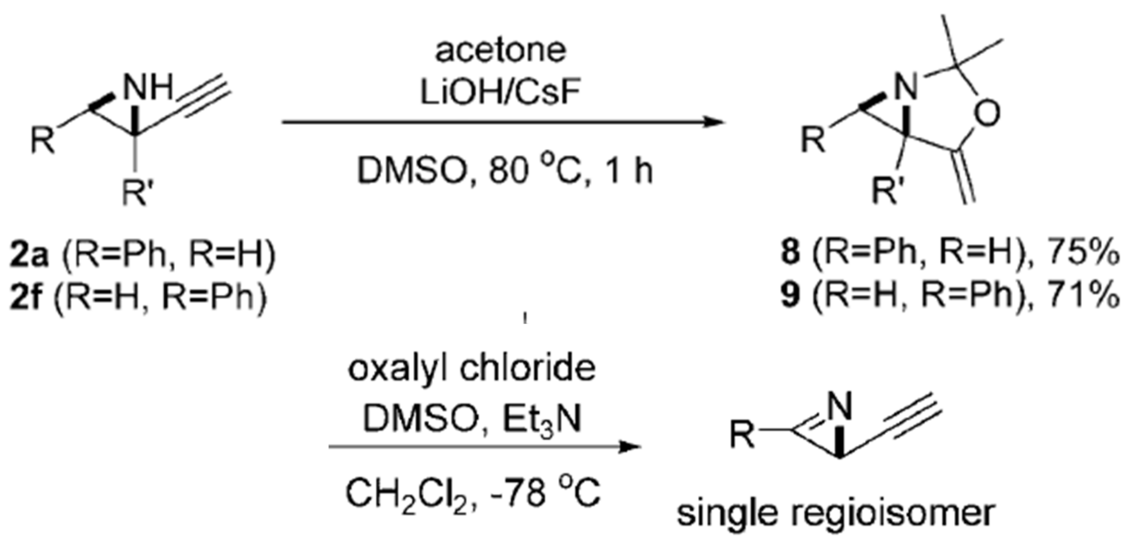
Schéma II

Chaabouni, R.; **Laurent, A.** *Tetrahedron Lett*. **1976**, *17*, 757.



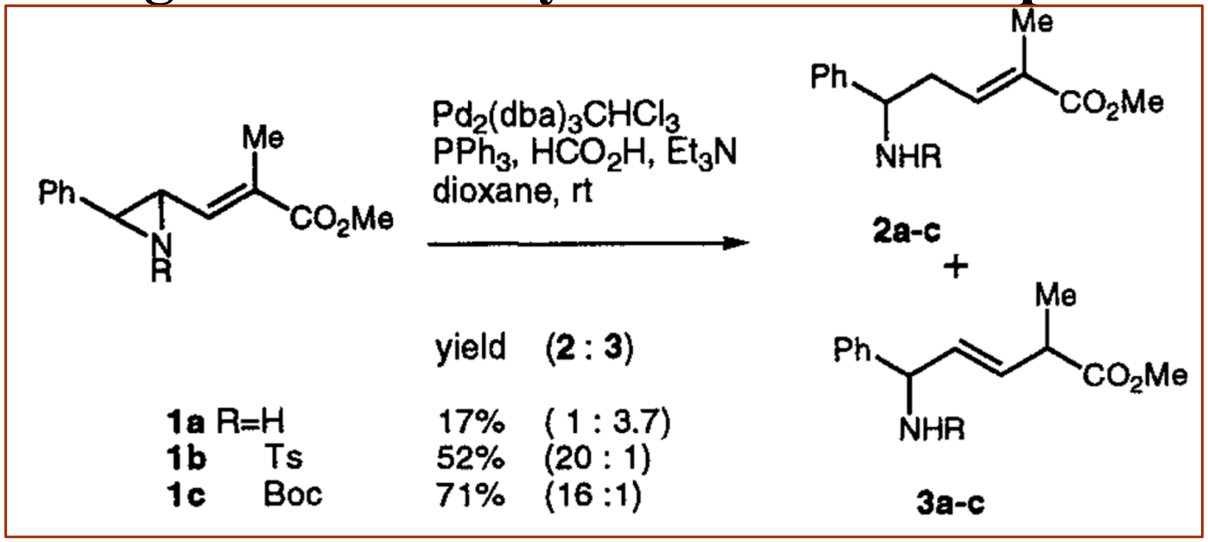
Chaabouni, R.; **Laurent, A.;** Marquet, B. *Tetrahedron* **1980**, *36*, 877.

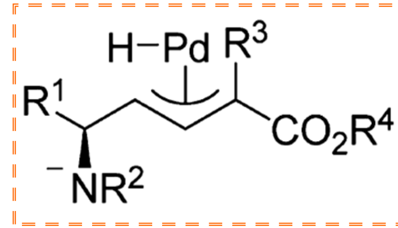




He, Z.; **Yudin, A. K**. *Angew. Chem., Int. Ed*. **2010**, *49*, 1607.

Using Palladium Hydrides as Nucleophile

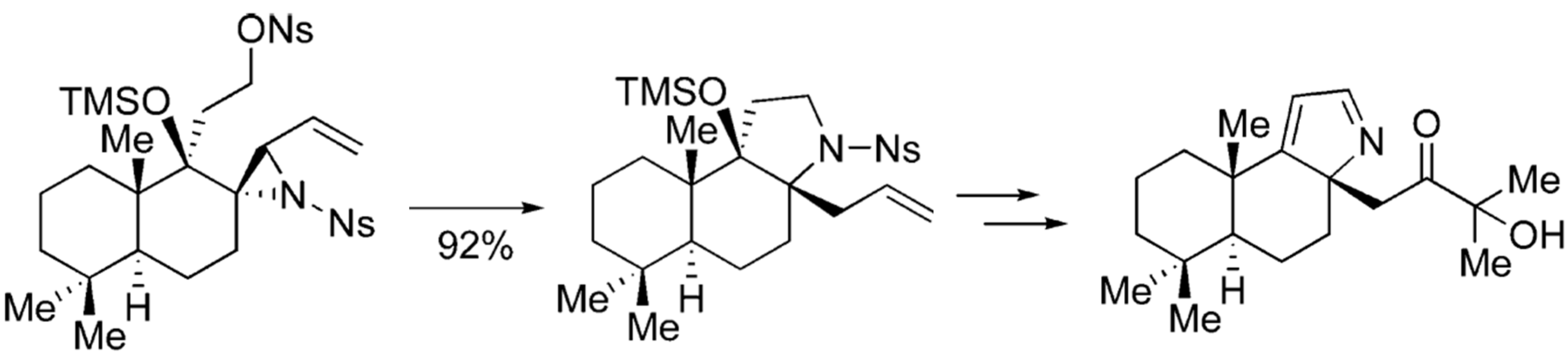




The ratios of the two products were found to be dependent on the reaction conditions (i.e., additive, solvent, and catalyst).

Satake, A.; **Shimizu, I.;** Yamamoto, A. *Synlett* **1995**, 64.

Ohno, H.; Mimura, N.; Otaka, A.; Tamamura, H.; Fujii, N.; **Ibuka, T.; Shimizu, I.;** Satake, A.; Yamamoto, Y. *Tetrahedron* **1997**, *53*, 12933



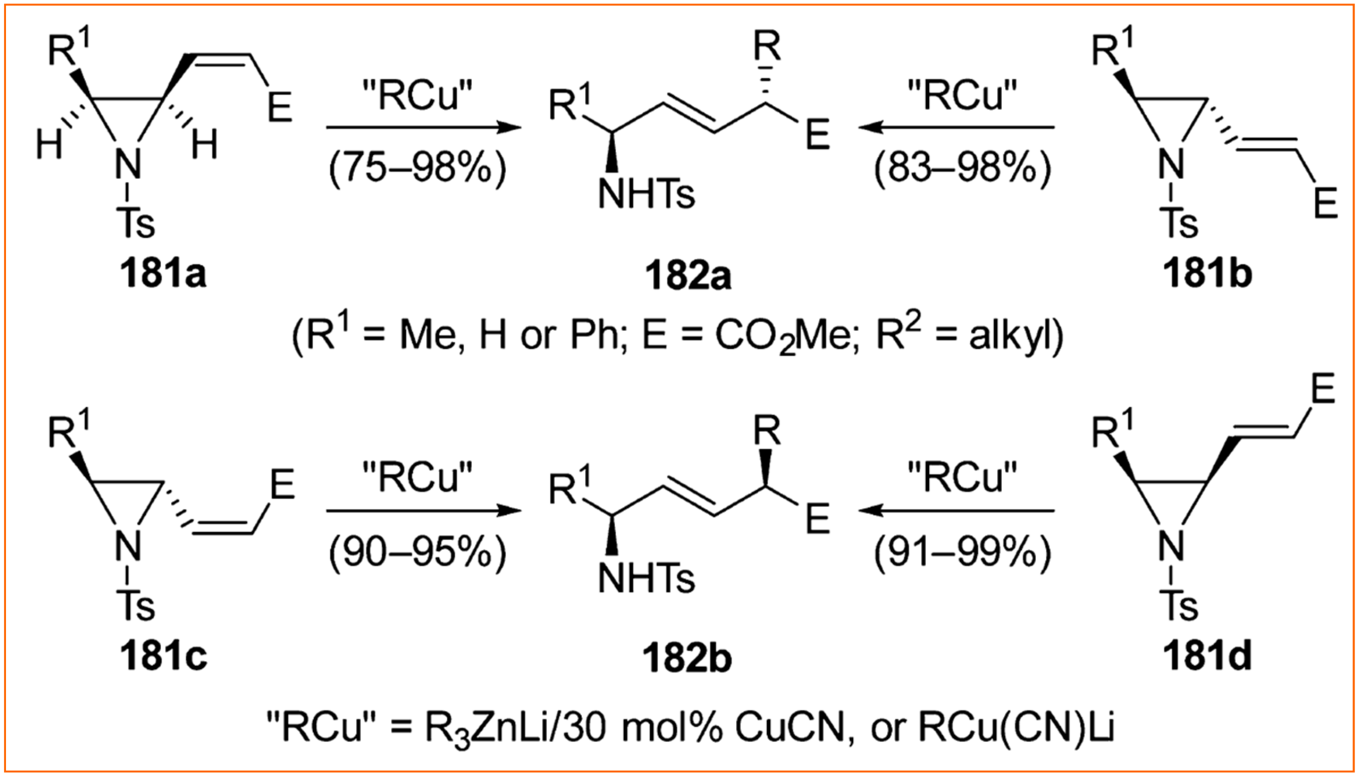
2

(–)-Chamobtusin A

Suzuki, H.; **Aoyagi, S.** *Org. Lett.* **2012**, *14*, 6374.

Carbon Nucleophiles

Using Organocopper as Nucleophile

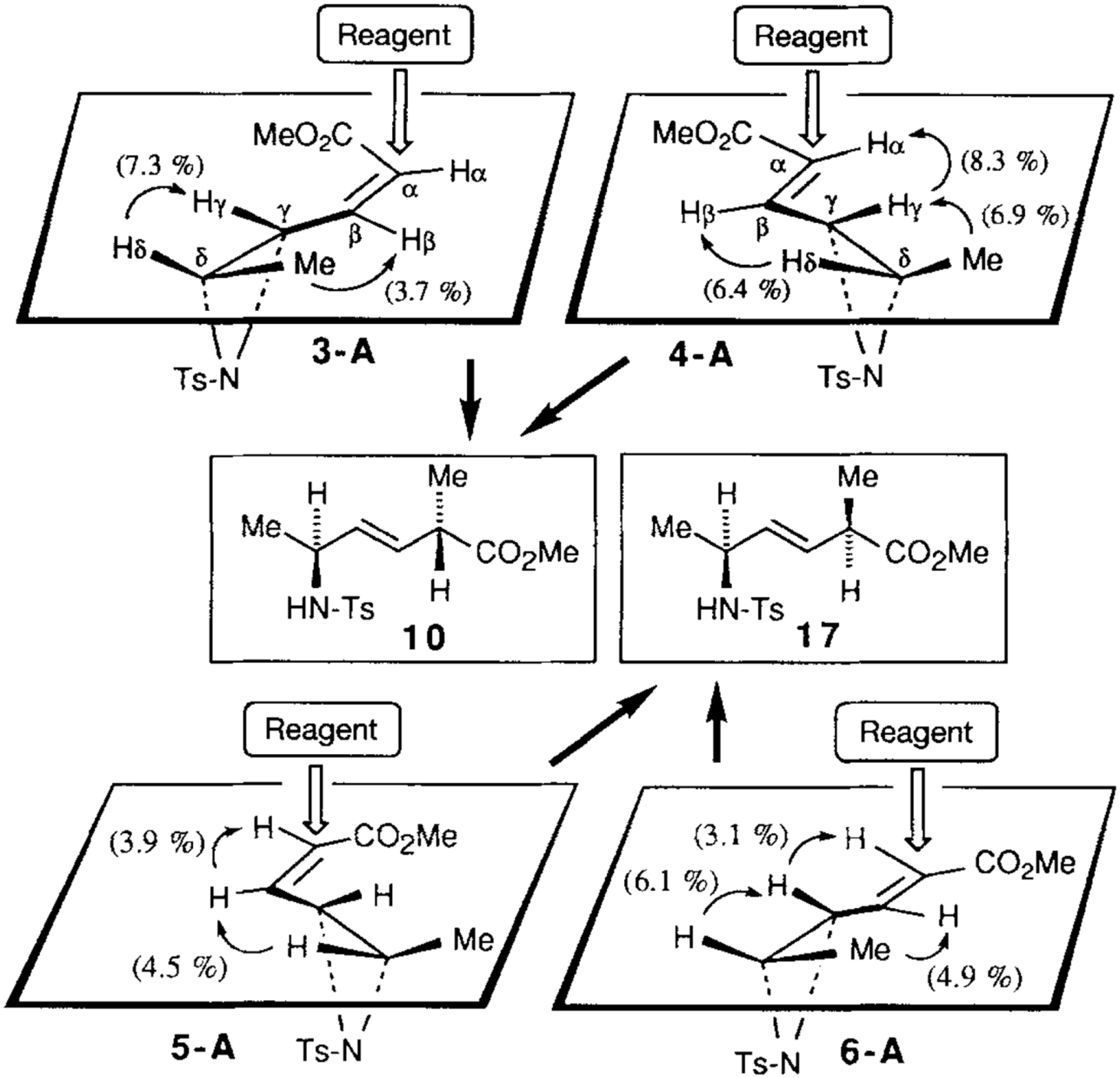


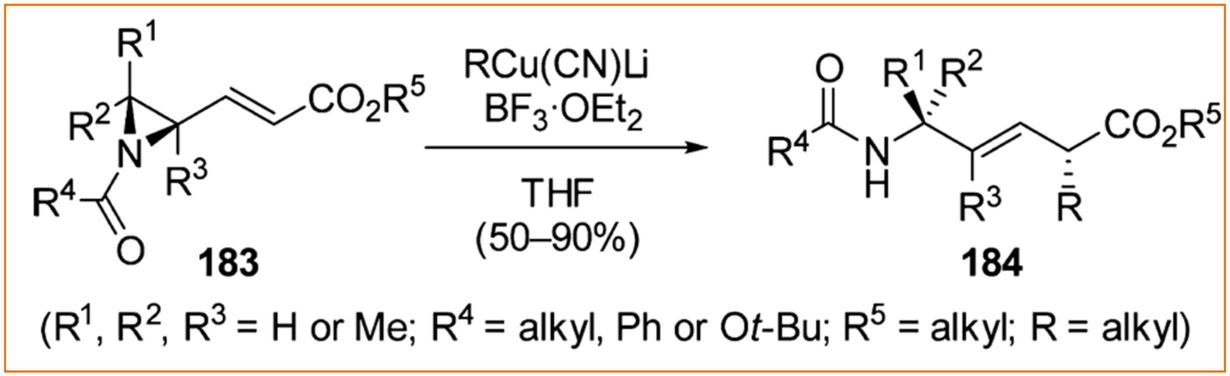
S_N2 products were less than 6%; No conjugate addition product

Ibuka, T.; Nakai, K.; Habashita, H.; Hotta, Y.; **Fujii, N**.; Mimura, N.; Miwa, Y.; **Taga, T.**; **Yamamoto, Y.** *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 652.

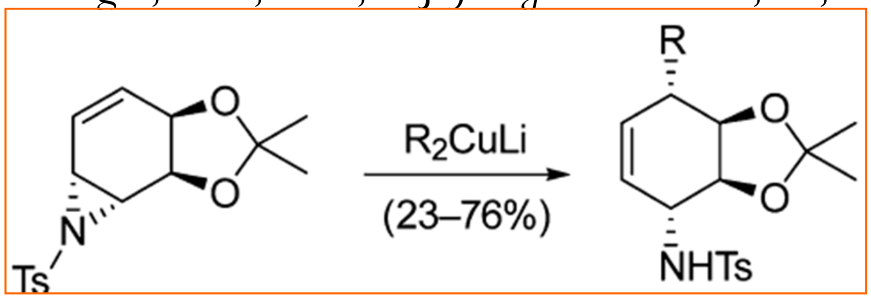
Fujii, N.; Nakai, K.; Tamamura, H.; Otaka, A.; Mimura, N.; Miwa, Y.; Taga, T.; **Yamamoto, Y**.; **Ibuka, T.** *J. Chem. Soc., Perkin Trans. 1* **1995**, 1359

The preferred conformations of the four stereoisomeric compounds **3-6** have been determined by variable-temperature 'H NMR spectroscopy in [D]-THF and X-ray analysis.

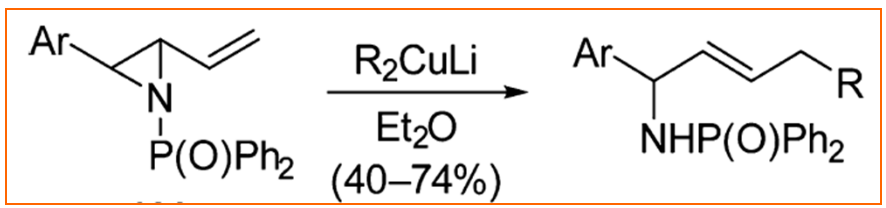




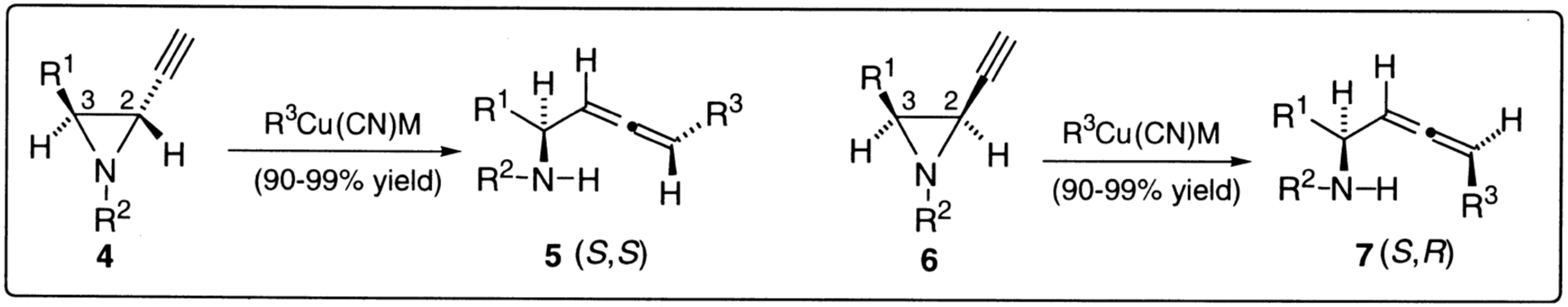
Wipf, P.; Fritch, P. C. *J. Org. Chem.* **1994**, *59*, 4875.
Wipf, P.; Henninger, T. C. *J. Org. Chem.* **1997**, *62*, 1586.
Wipf, P.; Henninger, T. C.; Geib, S. J. *J. Org. Chem.* **1998**, *63*, 6088.



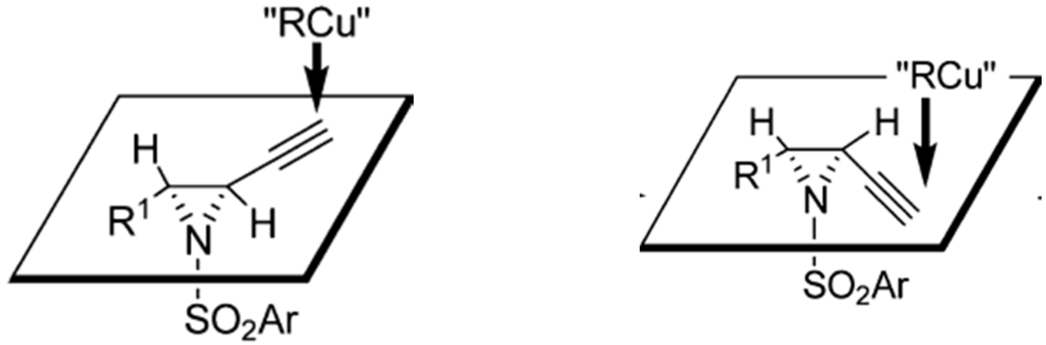
Hudlicky, T.; Tian, X.; Königsberger, K.; Rouden, J. *J. Org. Chem.* **1994**, *59*, 4037.
Hudlicky, T.; Tian, X.; Königsberger, K.; Maurya, R.; Rouden, J.; Fan, B. *J. Am. Chem. Soc.* **1996**, *118*, 10752



Cantrill, A. A.; Jarvis, A. N.; Osborn, H. M. I.; Ouadi, A.; **Sweeney, J. B**. *Synlett* **1996**, 847.
Jarvis, A. N.; McLaren, A. B.; Osborn, H. M. I.; **Sweeney, J**. *Beilstein J. Org. Chem.* **2013**, *9*, 852.

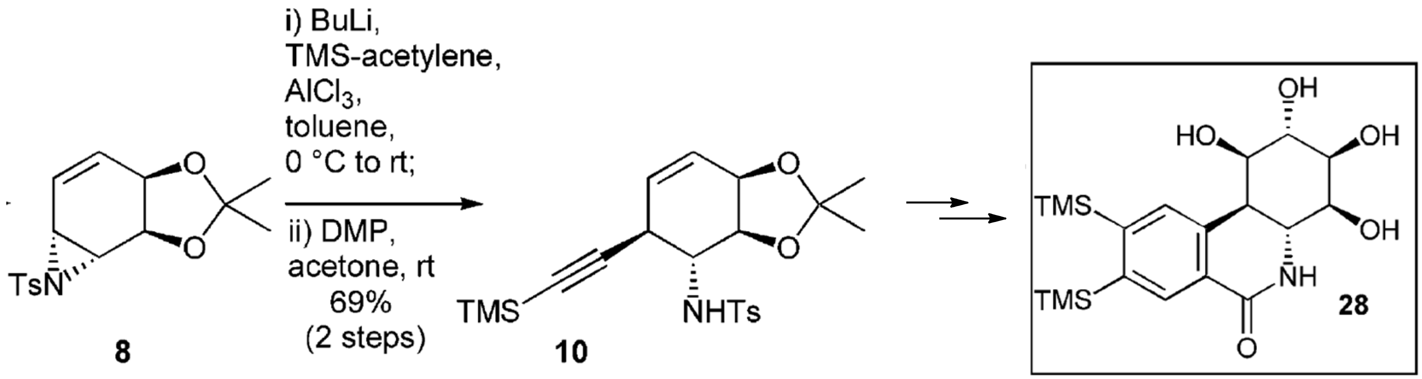


M.Li or MgBr; R^1.alkyl; R^2.arylsulfonyl; R^3.alkyl or tri-^{n}butylstannyl.



Ohno, H.; Toda, A.; Miwa, Y.; Taga, T.; Fujii, N.; **Ibuka, T.** *Tetrahedron Lett.* **1999**, *40*, 349.
Ohno, H.; Toda, A.; Fujii, N.; Takemoto, Y.; Tanaka, T.; Ibuka, T. *Tetrahedron* **2000**, *56*, 2811.

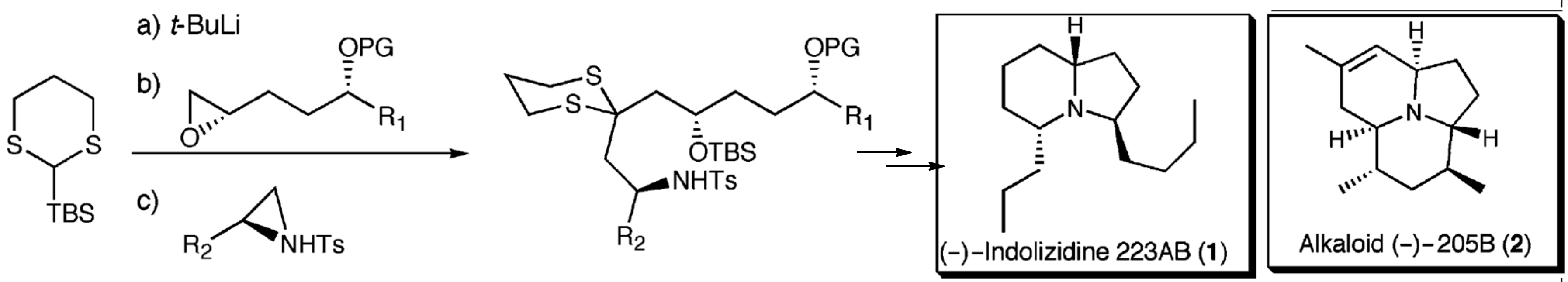
Using Organolithium as Nucleophile



Deoxygenated Pancratistatin Core

Moser, M.; Sun, X.; **Hudlicky, T.** *Org. Lett.* **2005**, 7, 5669.

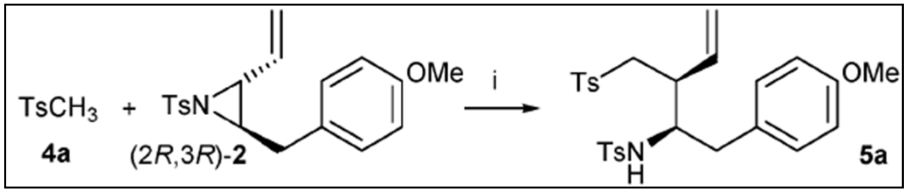
Hudlicky, T.; Moser, M.; Banfield, S. C.; Rinner, U.; Chapuis, J.-D.; Pettit, G. R. *Can. J. Chem.* **2006**, *84*, 1313



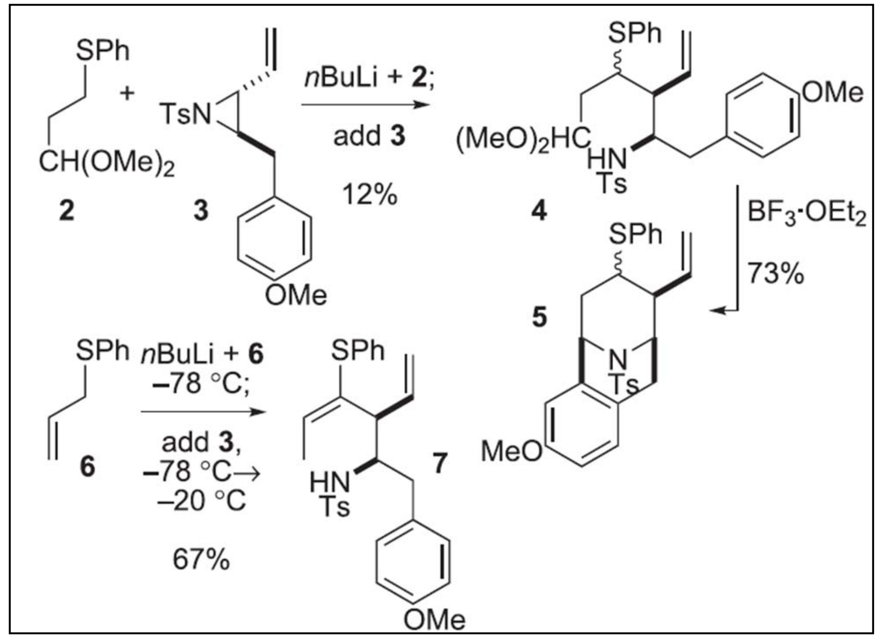
Through Brook rearrangment; 33% yield

Smith, A. B., III; Kim, D.-S. *J. Org. Chem.* **2006**, *71*, 2547.

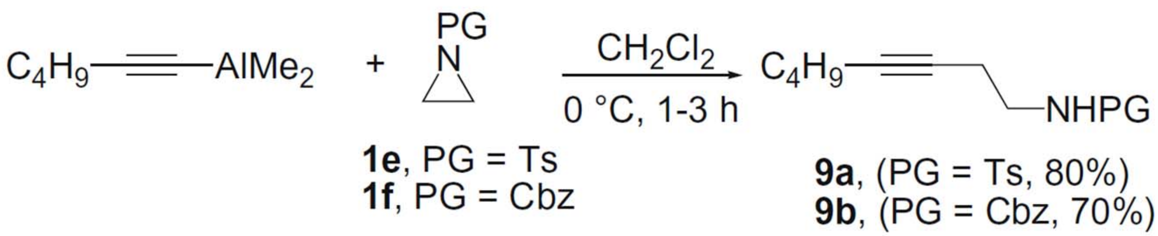
sulfur-stabilized carbanions

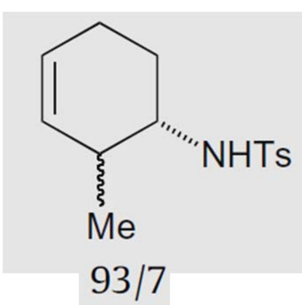


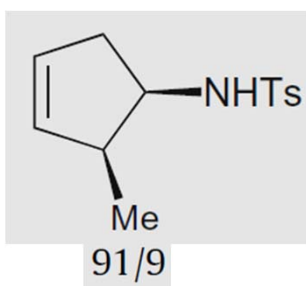
Craig, D et al. *Chem. Commun.* **2009**, 451.
Tetrahedron **2010**, *66*, 6376.

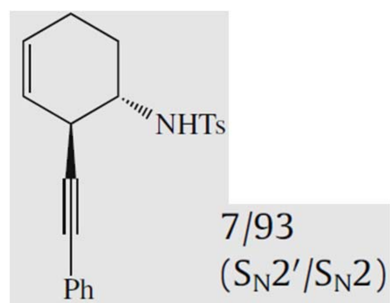


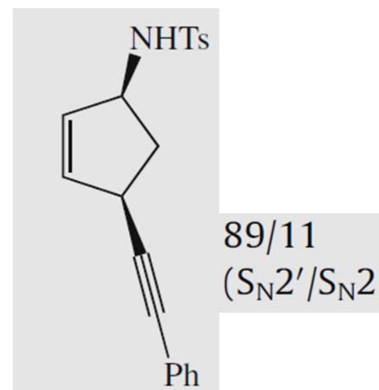
organoaluminium reagent







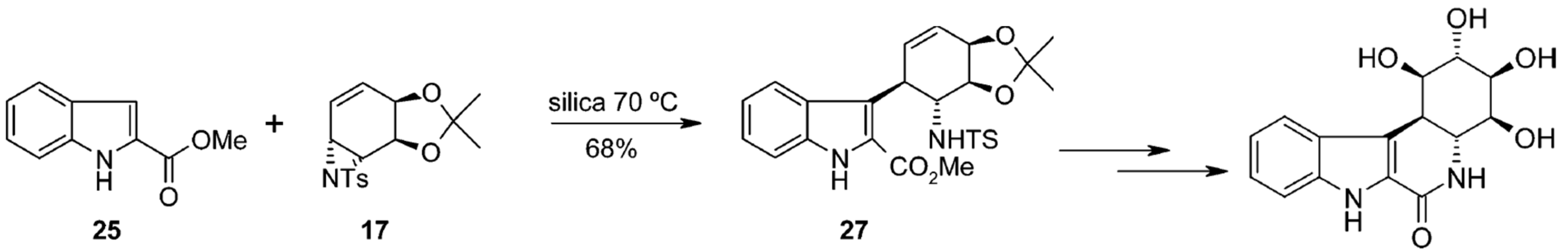




Tetrahedron Lett. **2009**, *50*, 4515.

The increased soft character of this organoaluminium reagent

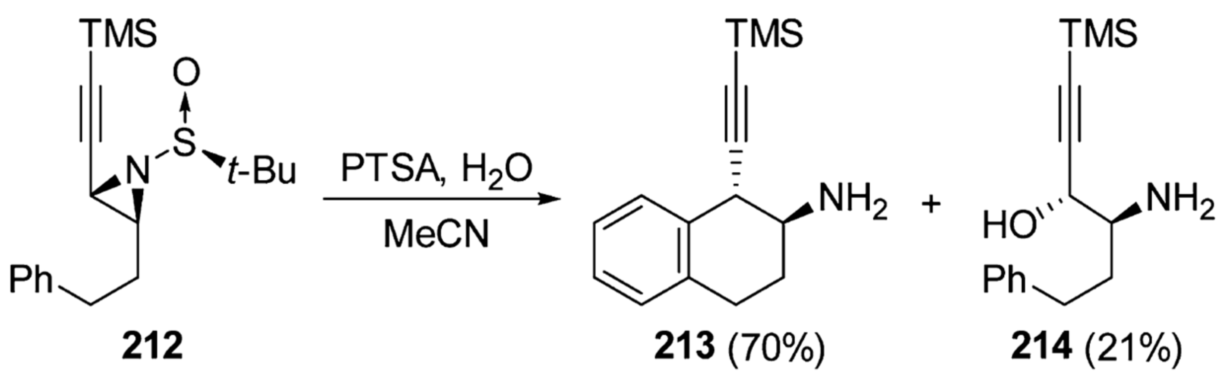
Silica promoted reaction



Hudlicky, T. et al. *Angew. Chem., Int. Ed.* **2004**, *43*, 5342.
J. Org. Chem. **2005**, *70*, 3490.

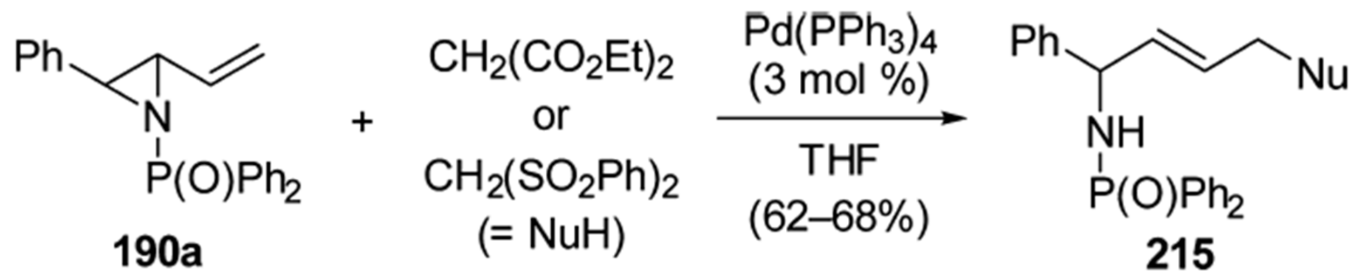
***β*-Carbolin-1-one Mimic of Pancratistatin**

Bronsted acid promoted reaction

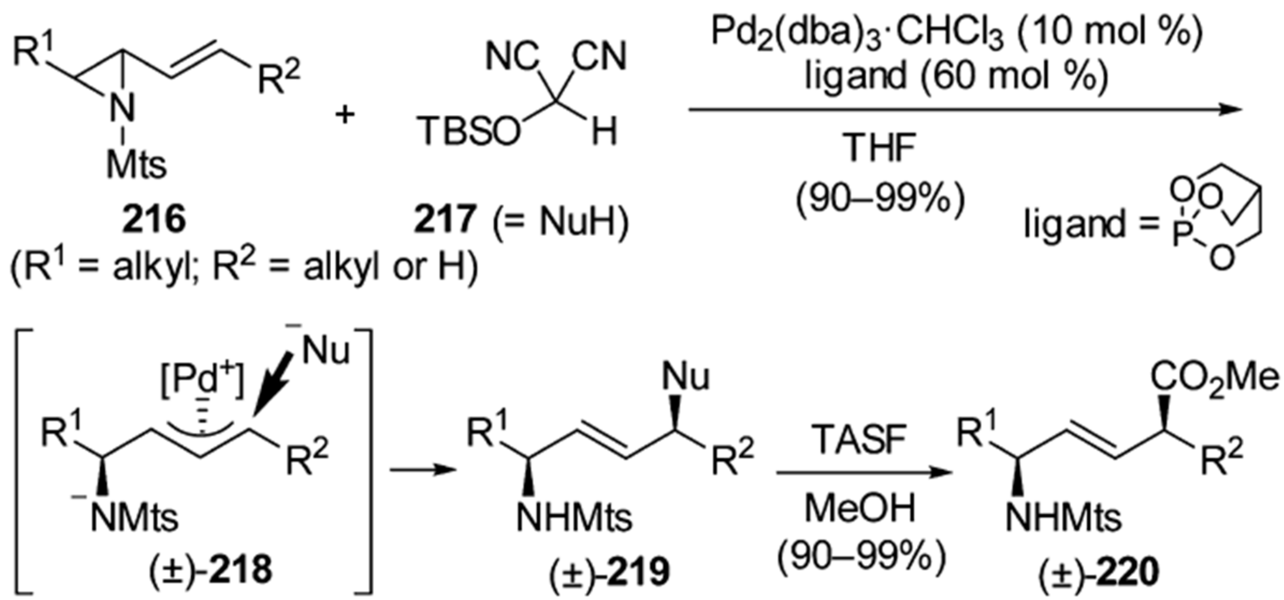


Palais, L.; Chemla, F.; **Ferreira, F**. *Synlett* **2006**, 1039.

Palladium-catalyzed reactions

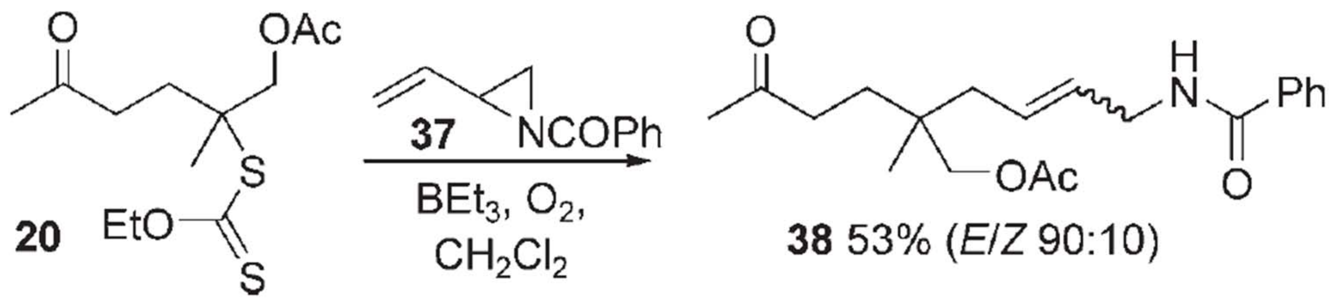


Cantrill, A. A.; Jarvis, A. N.; Osborn, H. M. I.; Ouadi, A.; **Sweeney, J. B.** *Synlett* **1996**, 847.
Jarvis, A. N.; McLaren, A. B.; Osborn, H. M. I.; **Sweeney, J**. *Beilstein J. Org. Chem.* **2013**, *9*, 852.



Kawamura, T.; Matsuo, N.; Yamauchi, D.; Tanabe, Y.; Nemoto, H. *Tetrahedron* **2013**, *69*, 5331.

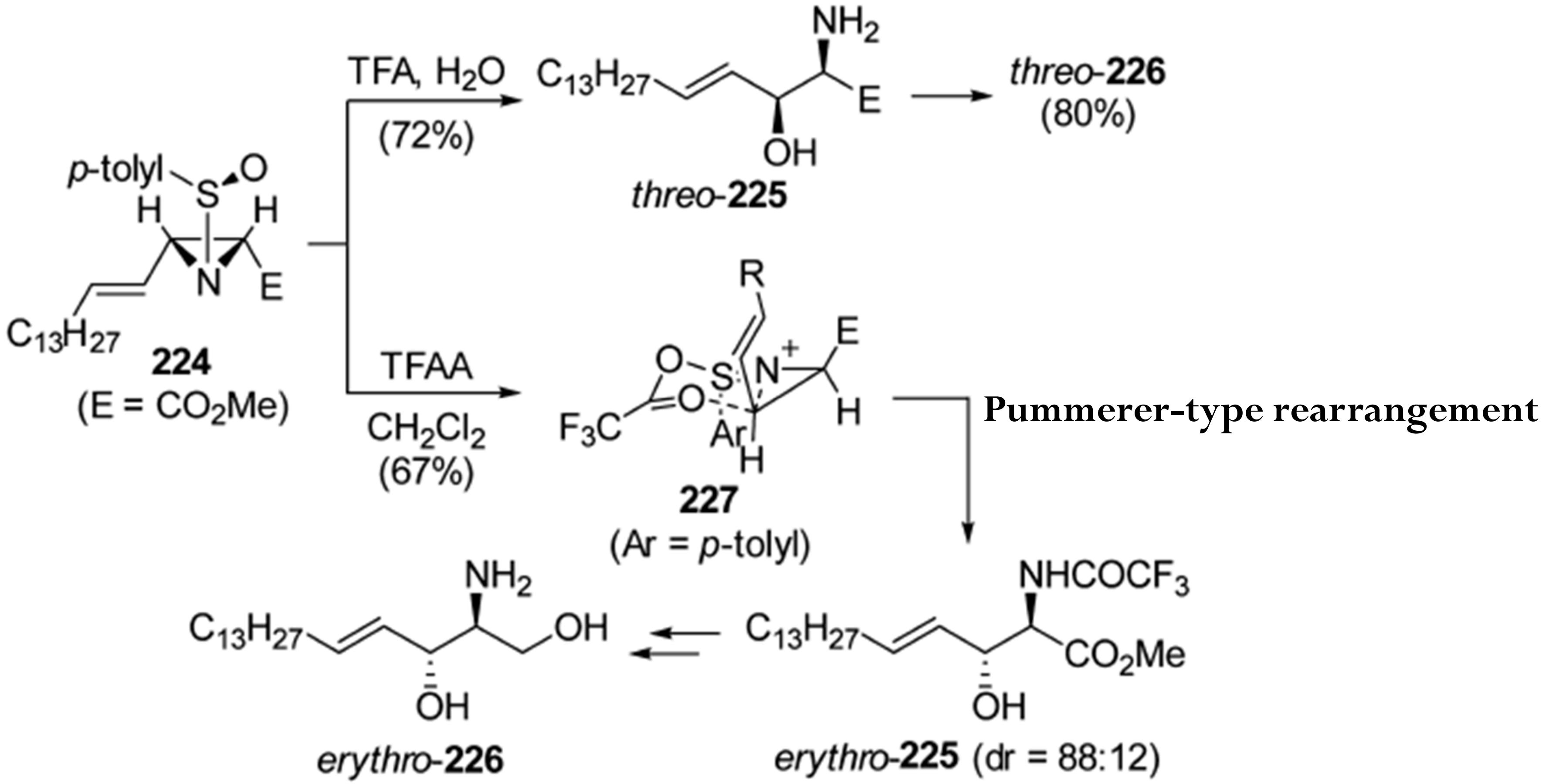
Radical reaction



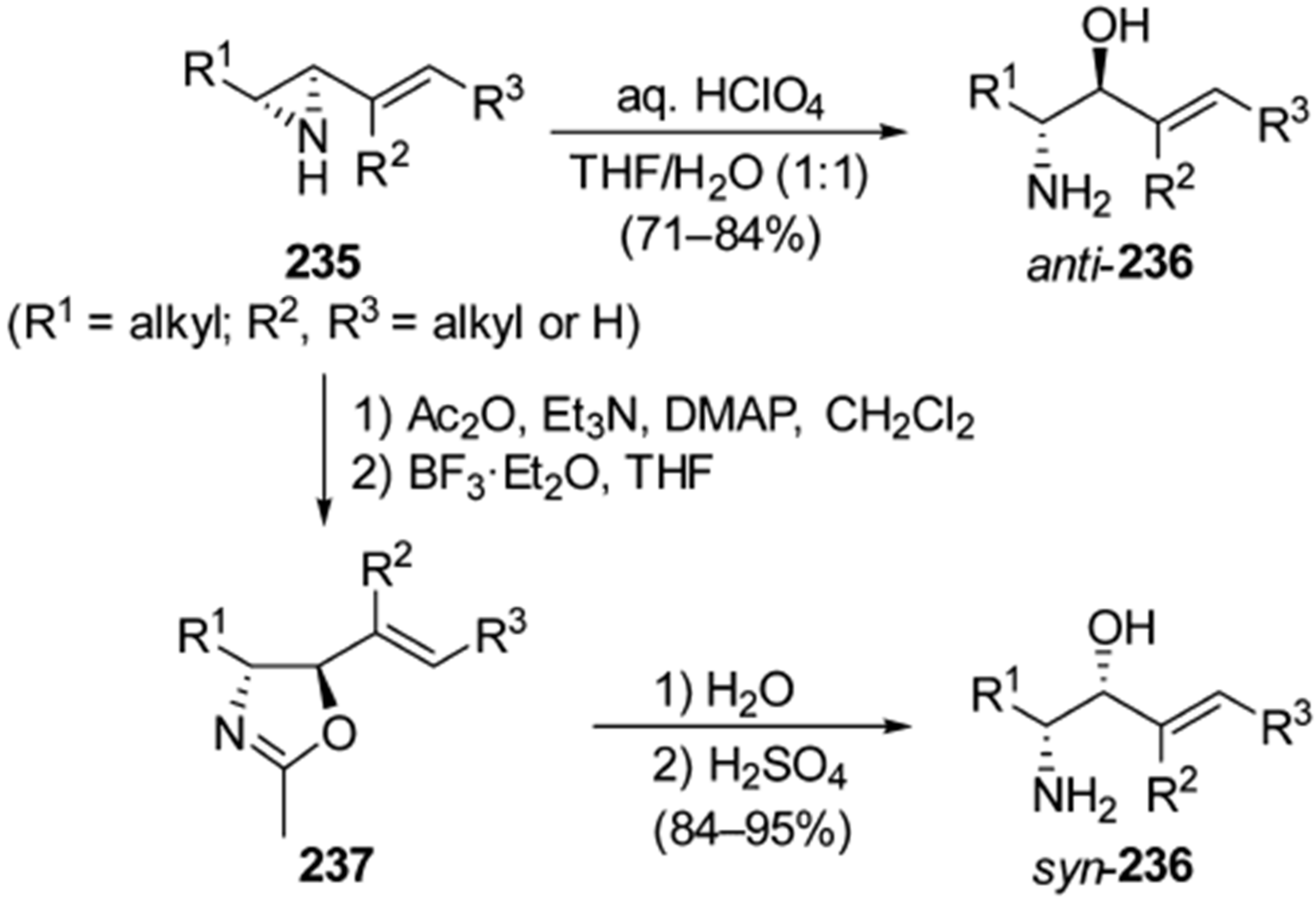
Charrier, N.; Gravestock, D.; **Zard, S. Z**. *Angew. Chem., Int. Ed.* **2006**, *45*, 6520.

Reaction with Oxygen Nucleophiles

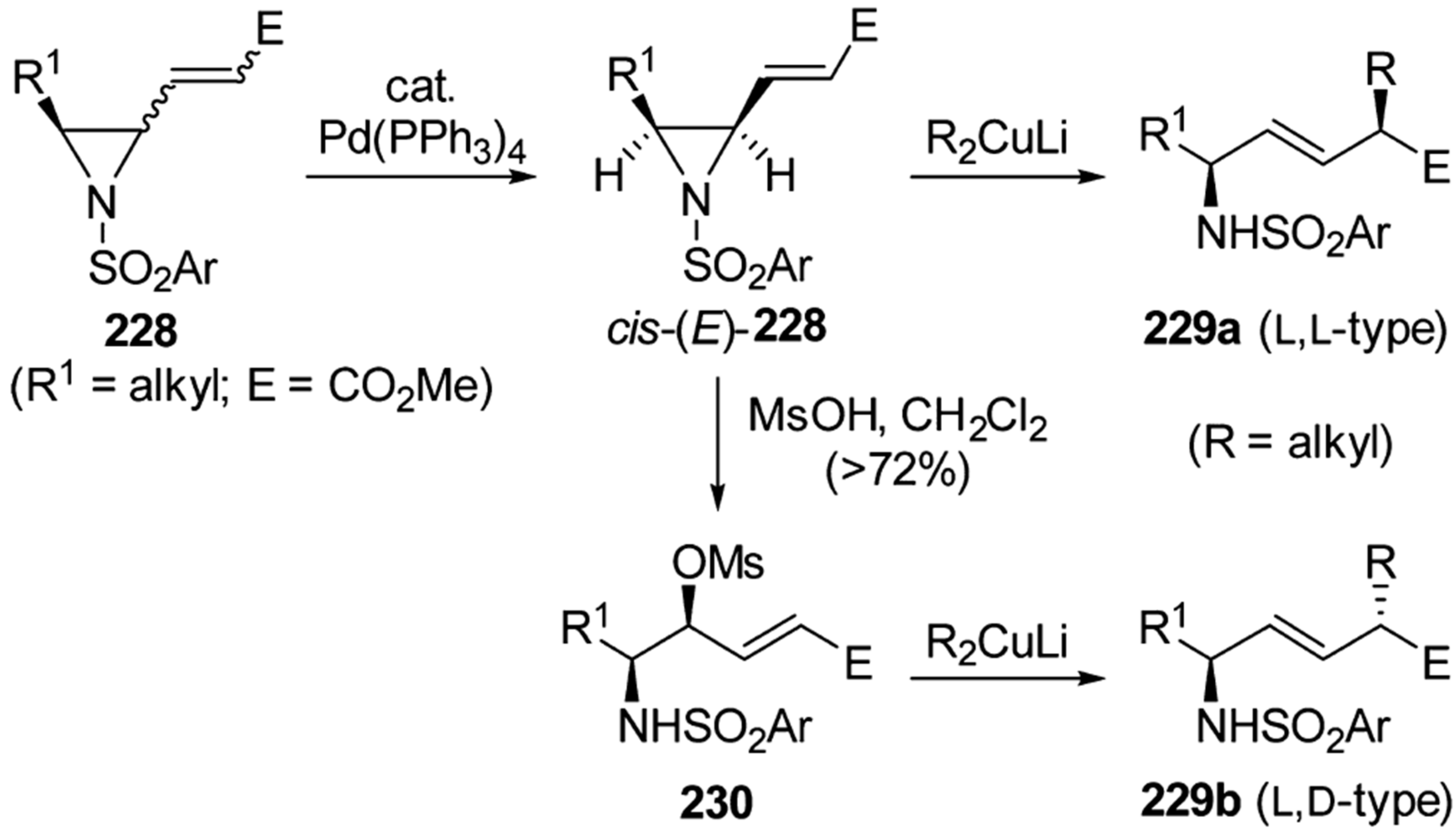
Acid promoted reactions



Davis, F. A.; Reddy, G. V. *Tetrahedron Lett*. **1996**, *37*, 4349



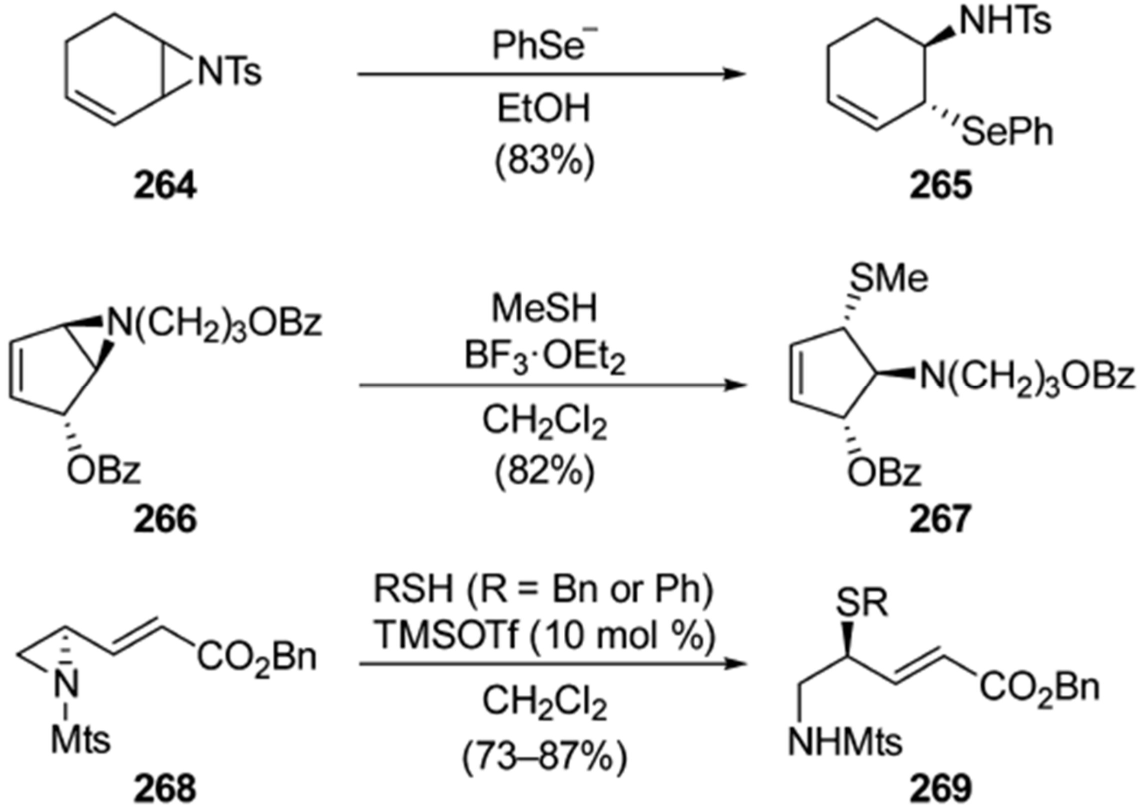
Olofsson, B.; Khamrai, U.; **Somfai, P.** *Org. Lett.* **2000**, *2*, 4087.
Olofsson, B.; **Somfai, P.** *J. Org. Chem.* **2002**, *67*, 8574.



Oishi, S.; Tamamura, H.; Yamashita, M.; Odagaki, Y.; Hamanaka, N.; Otaka, A.; Fujii, N. *J. Chem. Soc., Perkin Trans. 1* **2001**, 2445.

Tamamura, H.; Hiramatsu, K.; Ueda, S.; Wang, Z.; Kusano, S.; Terakubo, S.; Trent, J. O.; Peiper, S. C.; Yamamoto, N.; Nakashima, H.; Otaka, A.; Fujii, N. *J. Med. Chem*. **2005**, *48*, 380.

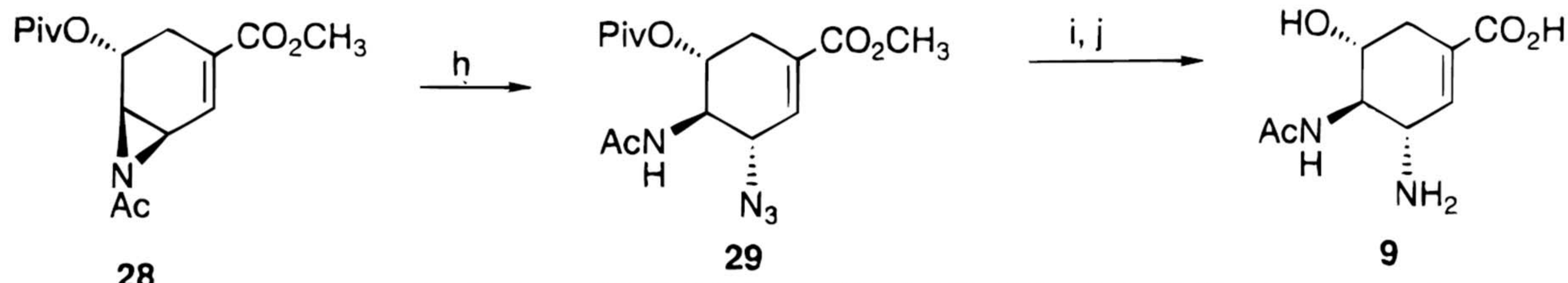
Reaction with Sulfur and Selenium Nucleophiles



Gupta, V.; Besev, M.; Engman, L. *Tetrahedron Lett.* **1998**, *39*, 2429.
Acar, E. A.; Glarner, F.; Burger, U. *Helv. Chim. Acta* **1998**, *81*, 1095.
Tamamura, H.; Tanaka, T.; Tsutsumi, H.; Nemoto, K.; Mizokami, S.; Ohashi, N.; Oishi, S.; Fujii, N. *Tetrahedron* **2007**, *63*, 9243.

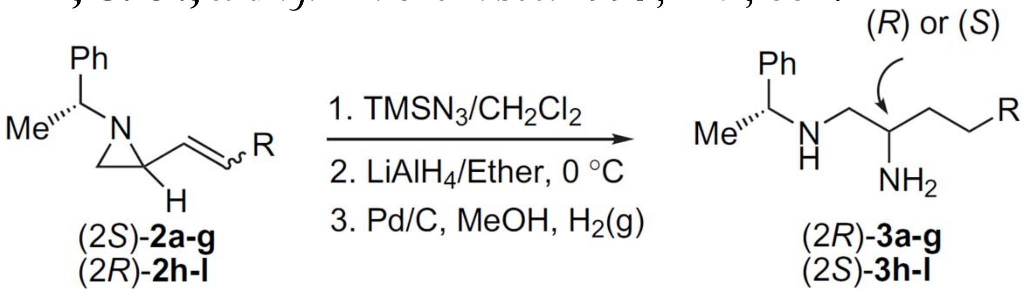
Reaction with Nitrogen Nucleophiles

Azides



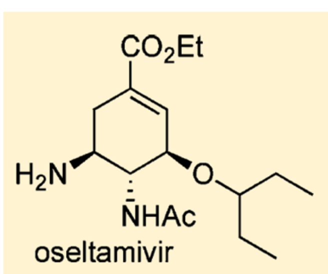
(h) NaN_3, NH_4Cl, DMF; (i) KOH, CH_3OH, H_2O; (j) H_2, Lindlar catalyst.

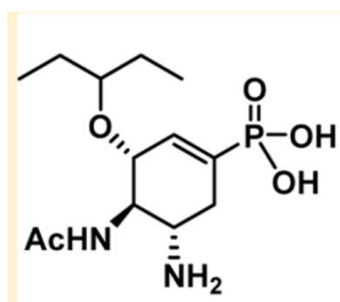
Kim, C. U.; *et al. J. Am. Chem. Soc.* **1997**, *119*, 681.

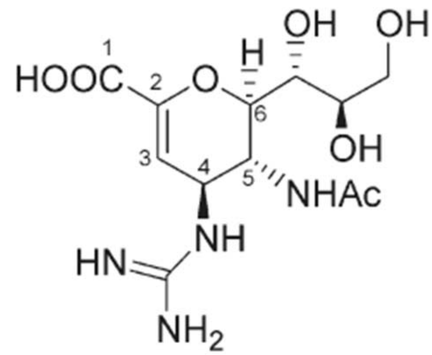


Lee, W. K.;Ha, H.-J. et al. *Tetrahedron* **2006**, *62*, 8393.

Righi, G. et al. *Synthesis* **2012**, *44*, 3202.



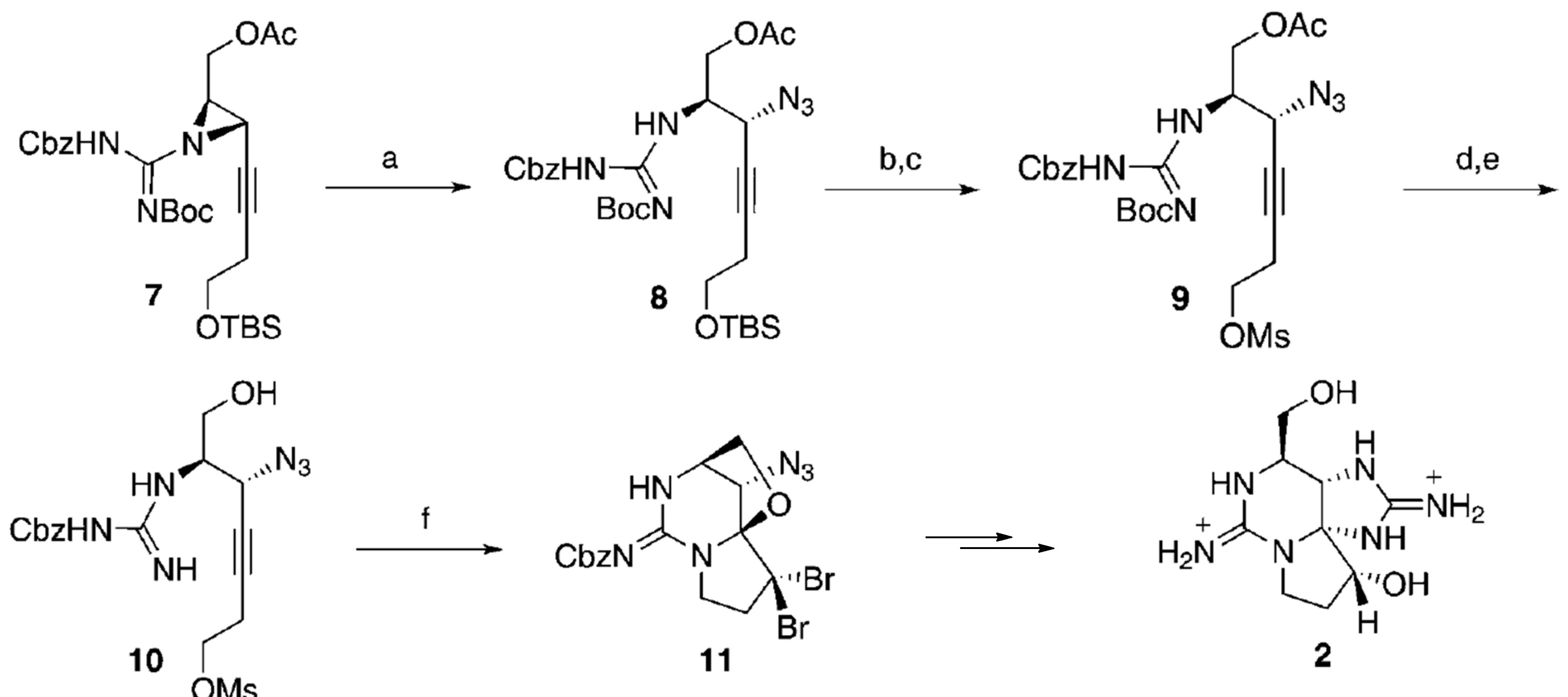




Zanamivir

Carbohydr. Res. **2001**, *332*, 23. *J. Med. Chem.* **2010**, *53*,7377. *Tetrahedron* **2011**, *67*, 2044.

J. Org. Chem. **2011**, *76*, 10050. *J. Med. Chem.* **2012**, *55*, 8657.

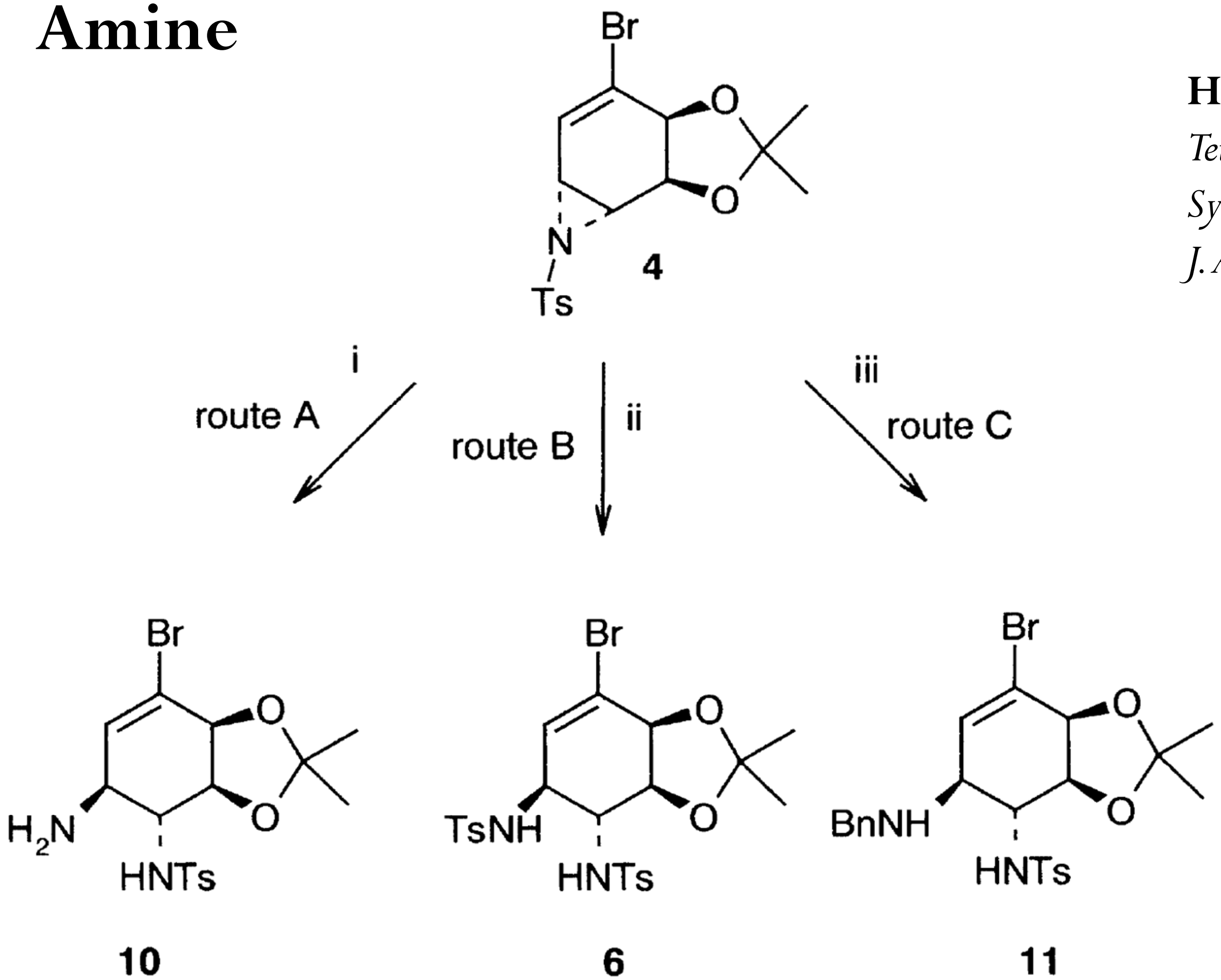


decarbamoyl α-saxitoxinol (**2**)
(*Lyngbya wollei* toxin 4)

a) NaN_3 (1.5 equiv), DMF, RT, 4.5 h; b) TBAF (1.5 equiv), THF, RT, 30 min; c) MsCl (1.05 equiv), Et_3N (3 equiv), CH_2Cl_2, 0°C to RT, 40 min; d) KCN (1.05 equiv), EtOH, RT, 12 h; e) TFA, CH_2Cl_2, RT, 2 h; f) $PyHBr_3$ (3 equiv), K_2CO_3 (10 equiv), CH_2Cl_2, H_2O, RT, 1 h, 24% for 6 steps.

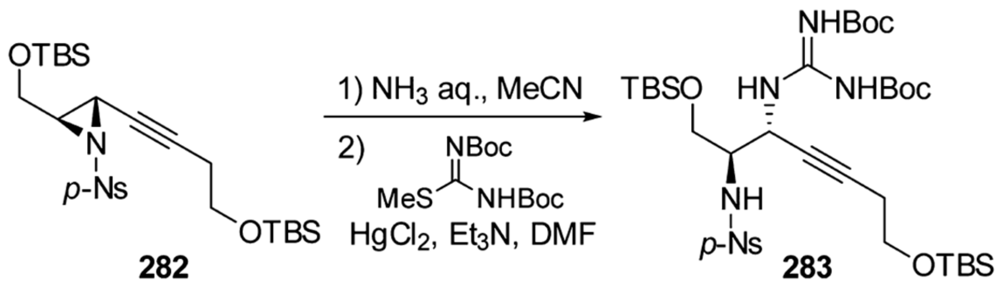
Sawayama, Y.; Nishikawa, T. *Angew. Chem., Int. Ed.* **2011**, *50*, 7176.

Amine

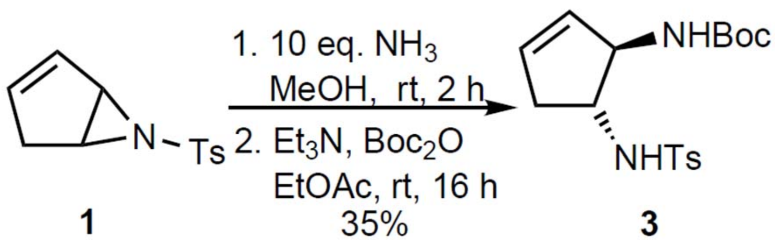


Hudlicky,T. et al.
Tetrahedron Lett. **2001**, *42*, 6433.
Synthesis **2001**, 952.
J. Am. Chem. Soc. **2002**, *124*, 10416.

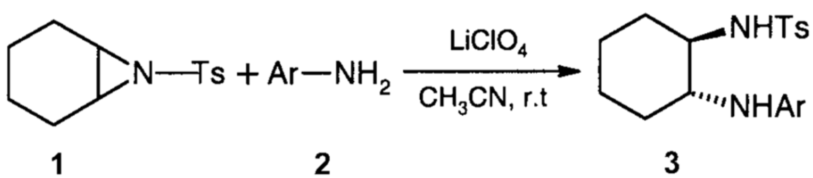
Scheme 2. Different strategies for vinyl aziridine opening; *reagents and conditions*: (i) $NH_{3(l)}$, $Yb(OTf)_3$, sealed tube; (ii) **5**, DMSO, TBAF; (iii) $Yb(OTf)_3$, 1,4-dioxane, $BnNH_2$.



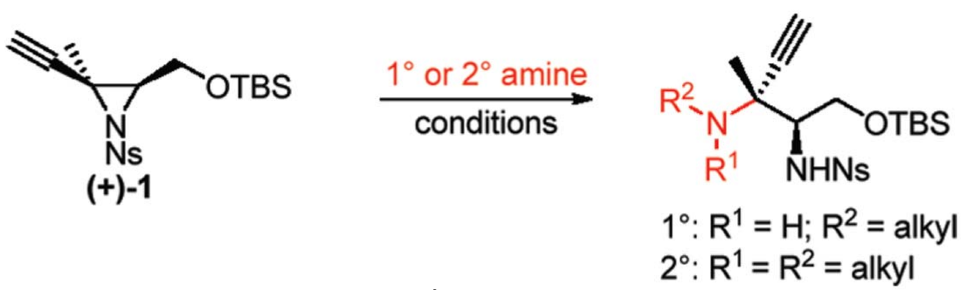
Sawayama, Y.; Nishikawa, T. *Synlett* **2011**, 6



Baron, E.; O'Brien, P.; Towers, T. D. *Tetrahedron Lett.* **2002**, *43*, 723.



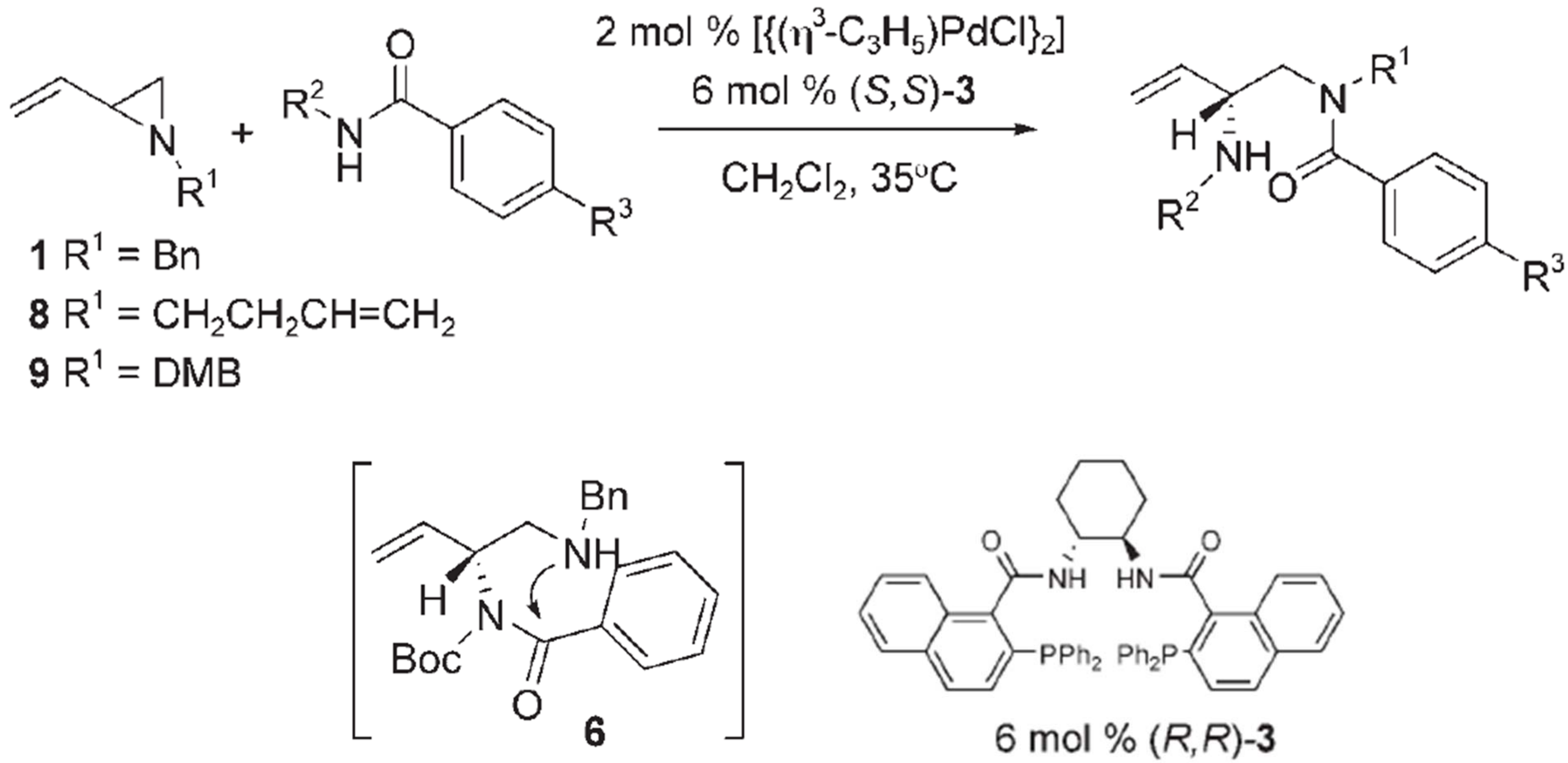
Yadav, J. S.; Reddy, B. V. S.; Jyothirmai, B.; Murty, M. S. R. *Synlett* **2002**, 53.



Kelley, B. T.; Joullié, M. M. *Org. Lett.* **2010**, *12*, 4244.

No promoting reagent

The dynamic kinetic asymmetric transformations (DYKATs)



Trost, B. M.; Fandrick, D. R.; Brodmann, T.; Stiles, D. T. *Angew. Chem., Int. Ed.* **2007**, *46*, 6123.

The dynamic kinetic asymmetric transformations (DYKATs)

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Vol. 9, No. 12
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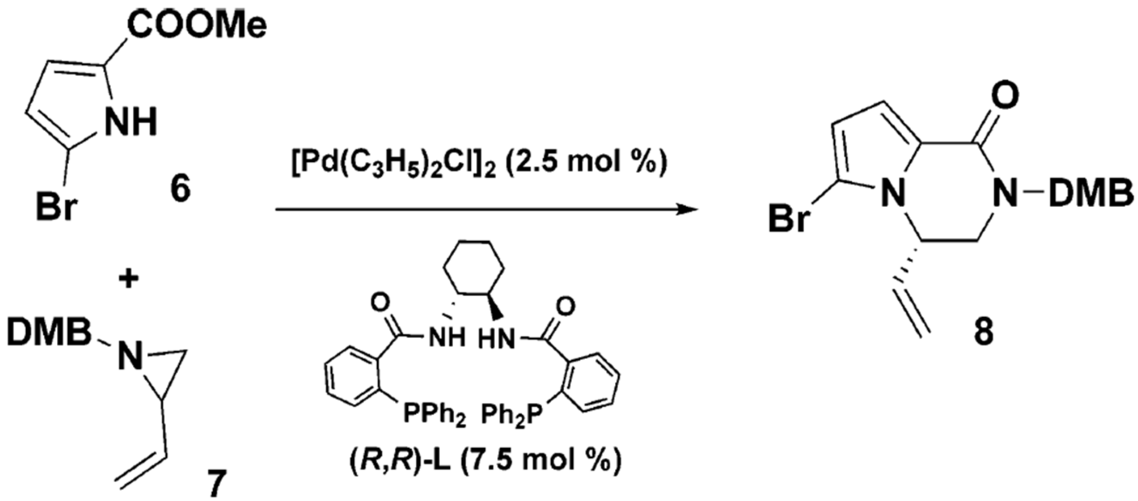
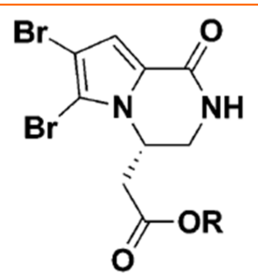
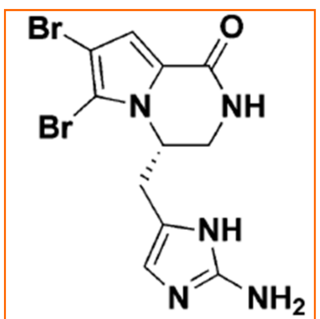


Trost, B. M.; Dong, G.

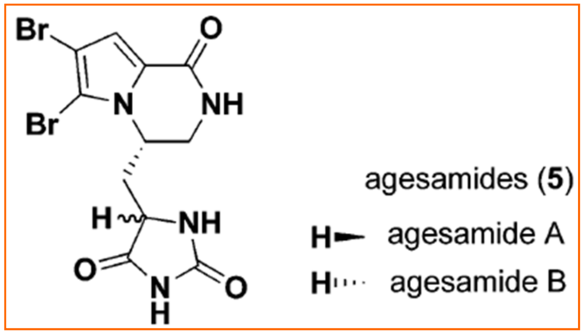
entry	additives	yield,[b] %	ee,[c] %
1	10 mol % HOAc	19 (28)[d]	71
2	50 mol % Cs_2CO_3	41	89
3	none	72	95

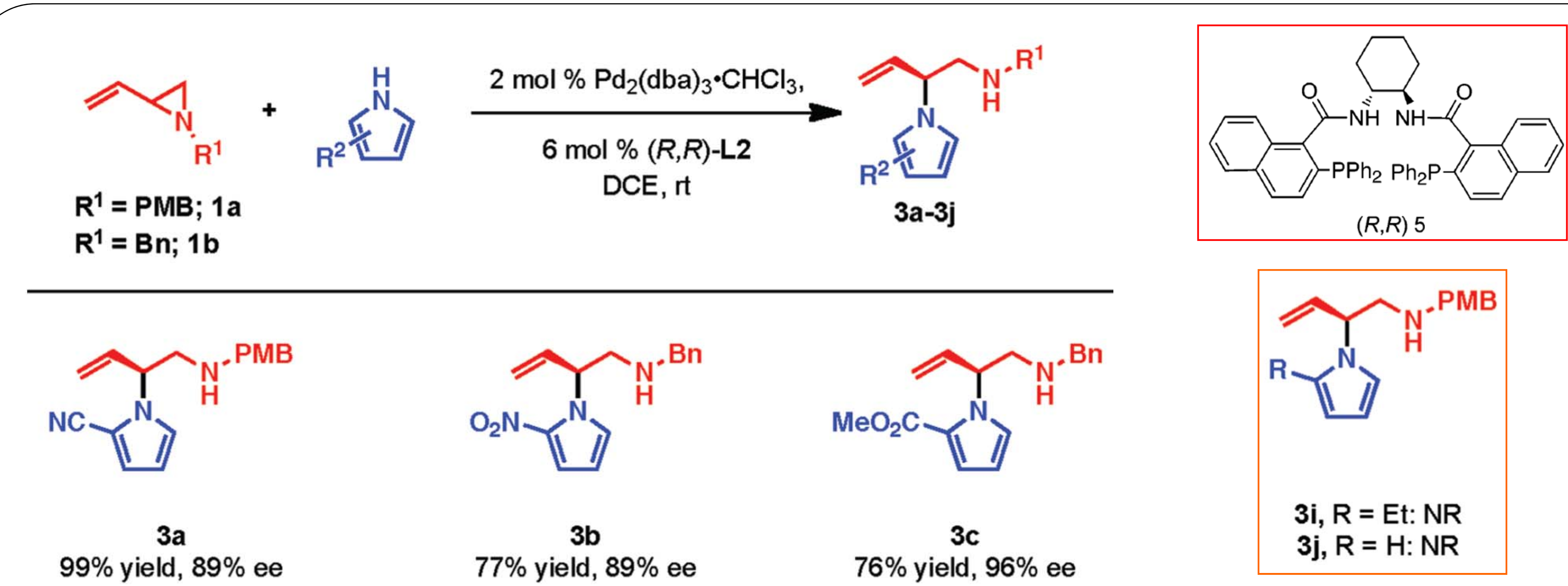


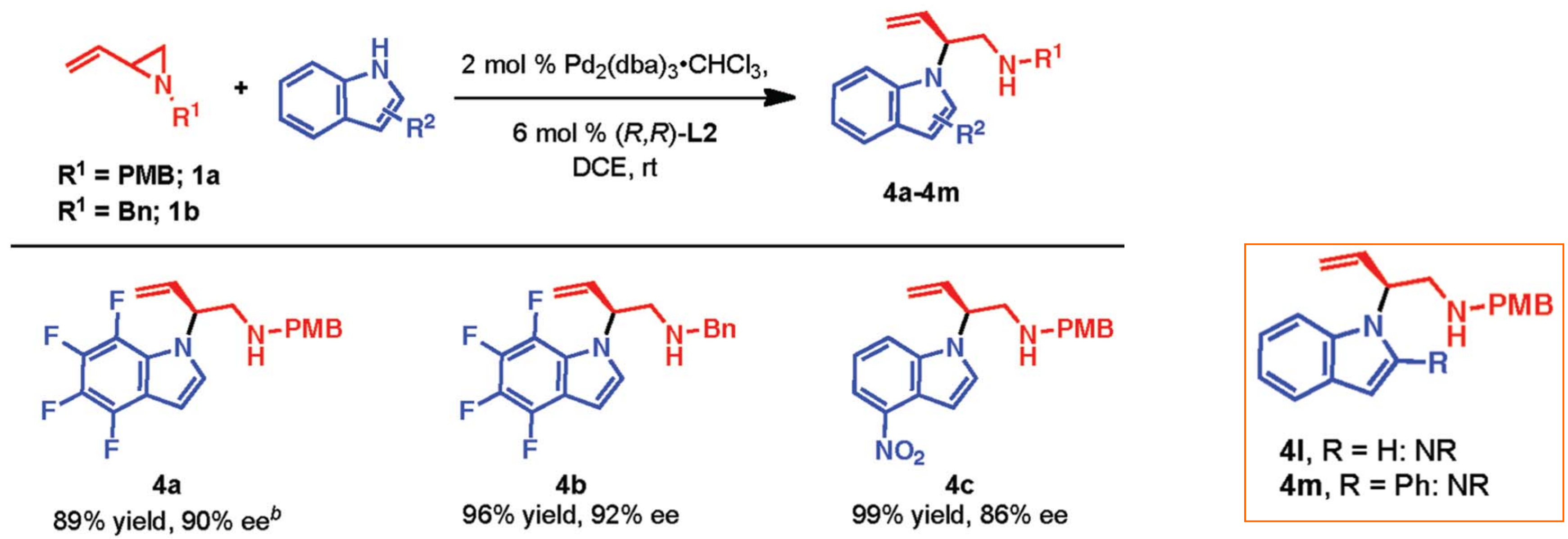
R = H; longamide B (**1**)
R = Me; longamide B methyl ester (**2**)
R = Et; hanishin (**3**)



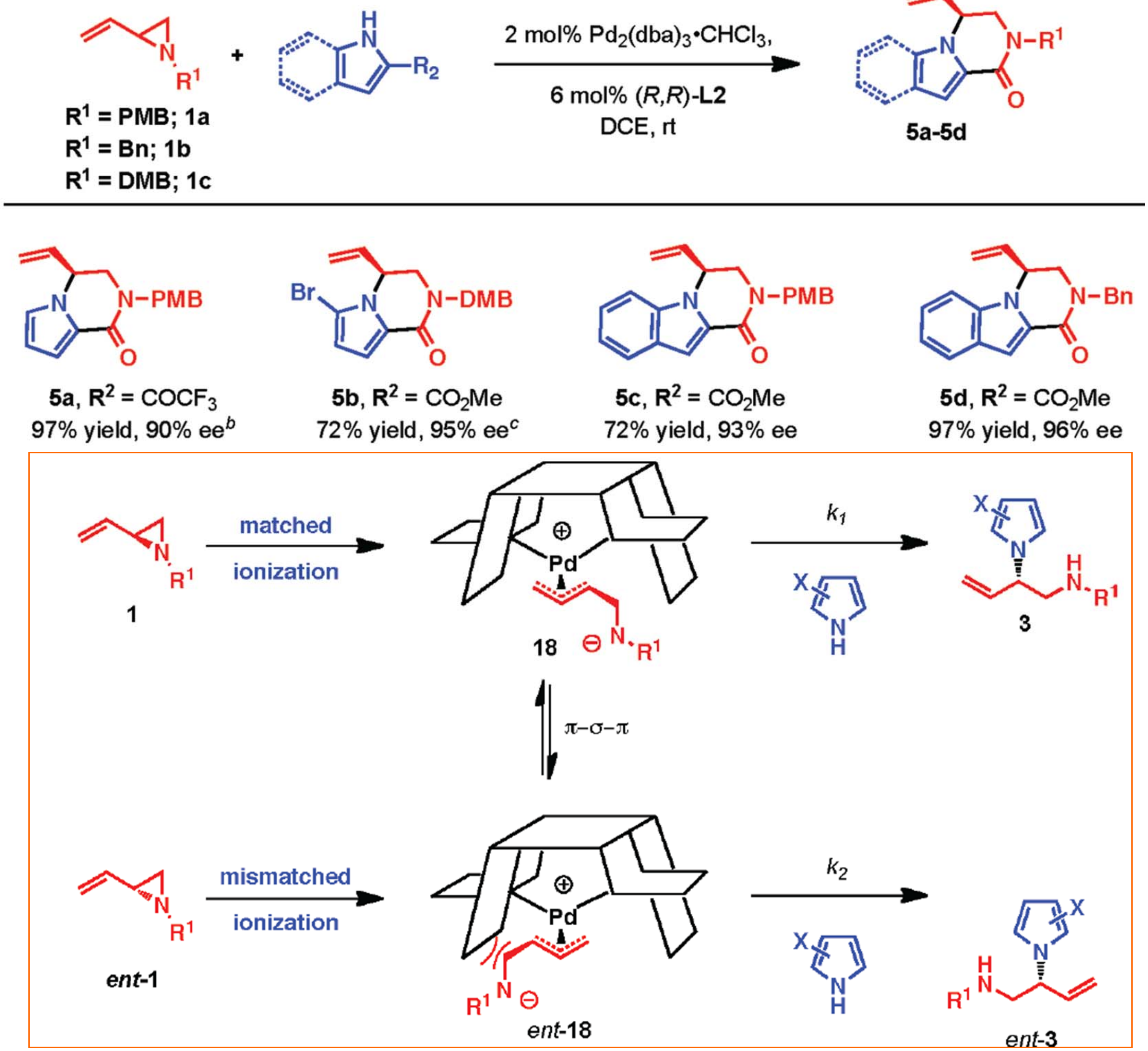
cyclooroidin (**4**)





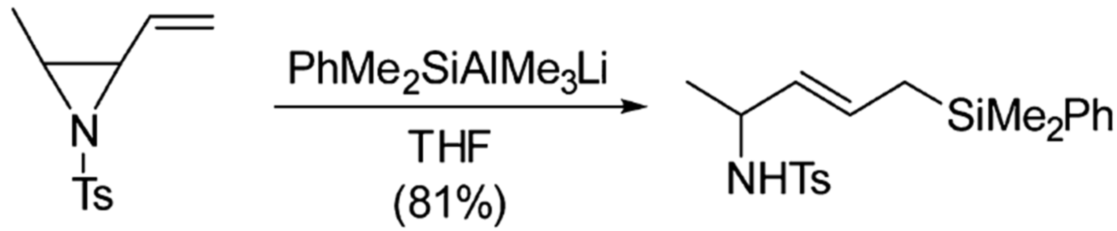


Trost, B. M.; Osipov, M.; Dong, G. *J. Am. Chem. Soc.* **2010**, *132*, 15800.

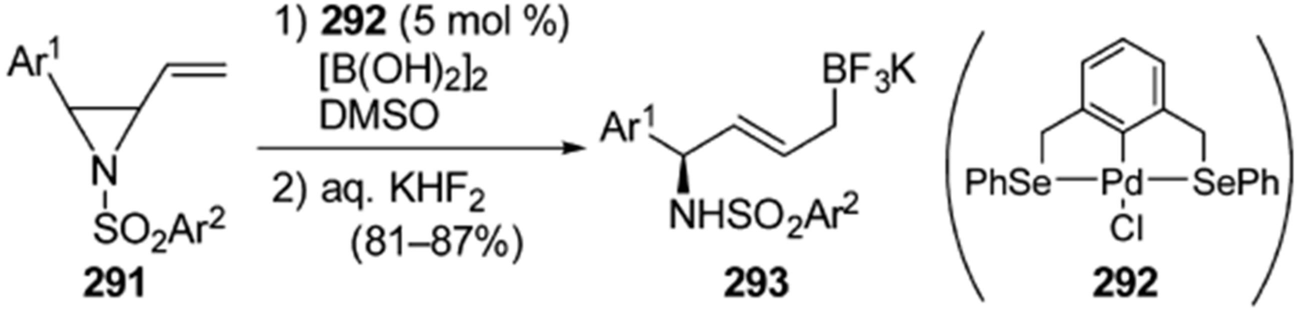


R1 = PMB; 1a
R1 = Bn; 1b
R1 = DMB; 1c
2 mol% Pd2(dba)3•CHCl3,
6 mol% (R,R)-L2
DCE, rt
5a-5d
5a, R2 = COCF3
97% yield, 90% ee b
5b, R2 = CO2Me
72% yield, 95% ee c
5c, R2 = CO2Me
72% yield, 93% ee
5d, R2 = CO2Me
97% yield, 96% ee
matched
ionization
mismatched
ionization
1
ent-1
18
ent-18
π–σ–π
k1
k2
3
ent-3

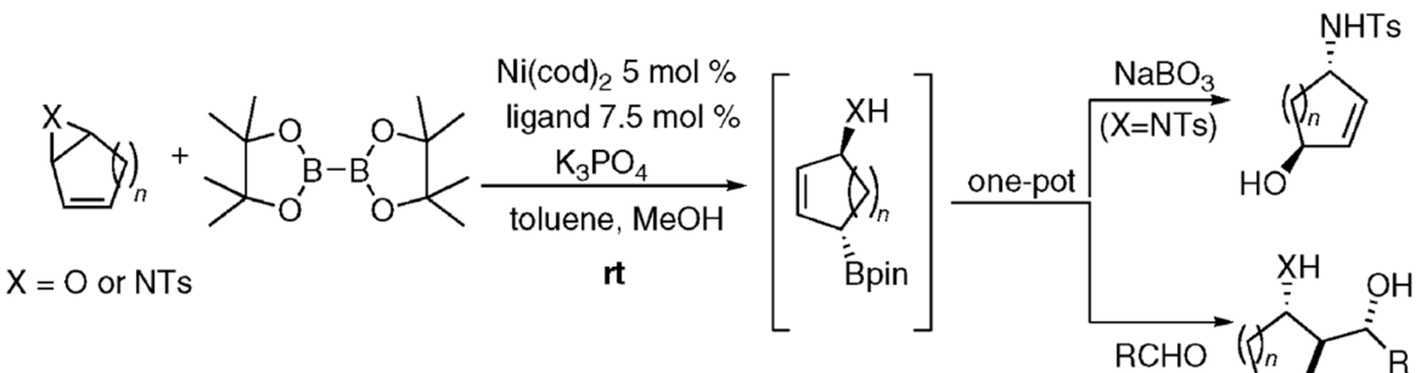
Reaction with Other Nucleophiles



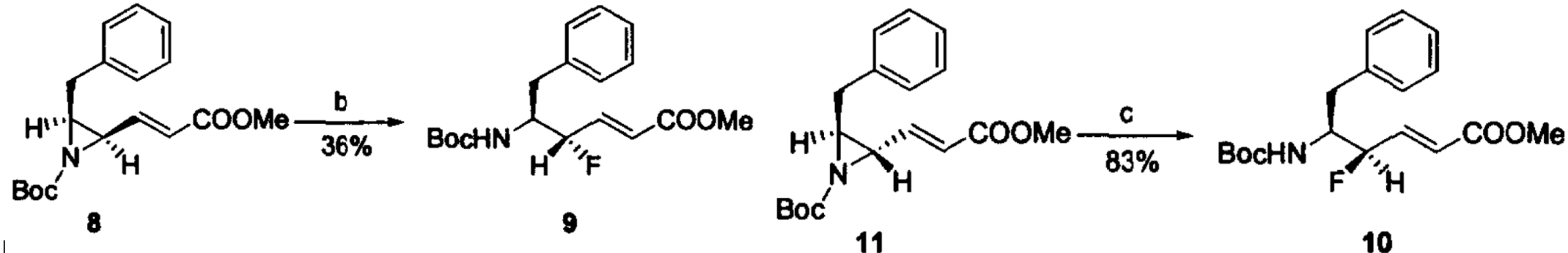
Fugami, K.; **Oshima, K.;** Utimoto, K.; Nozaki, H. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 2509.



Sebelius, S.; Olsson, V. J.; **Szabó, K. J.** *J. Am. Chem. Soc.* **2005**, *127*, 10478.

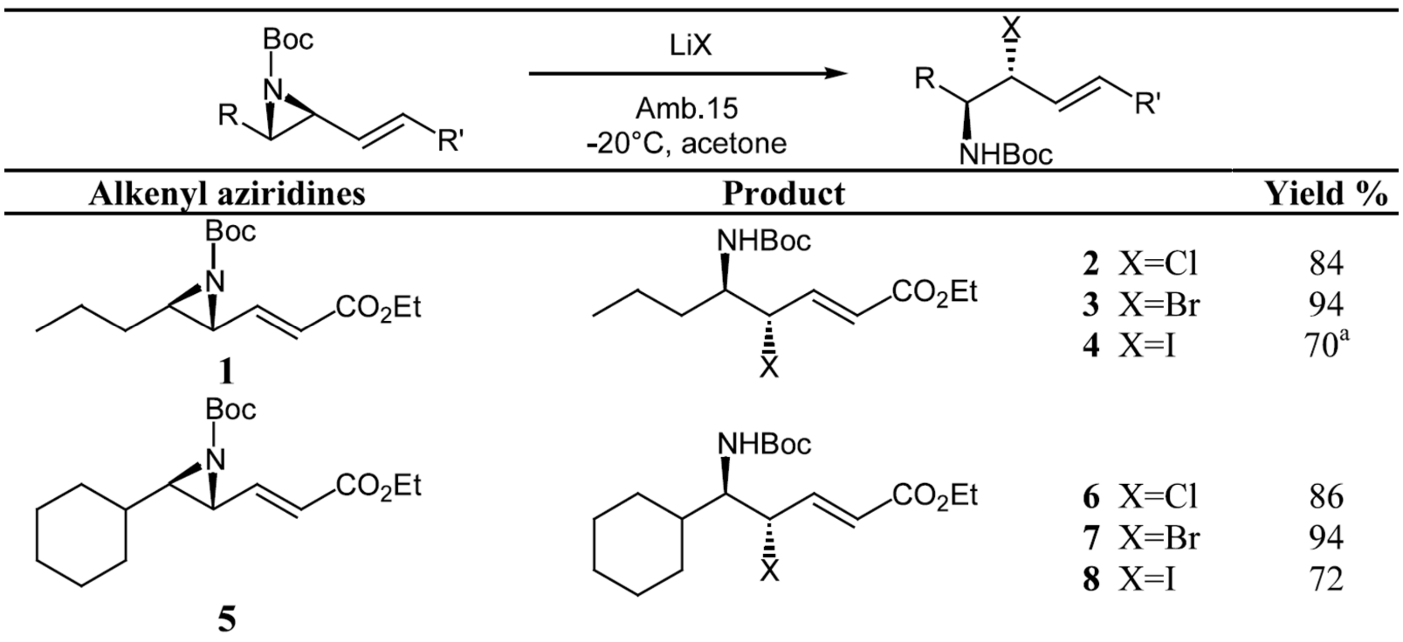


Crotti, S.; Bertolini, F.; Macchia, F.; **Pineschi, M**. *Org. Lett.* **2009**, *11*, 3762.



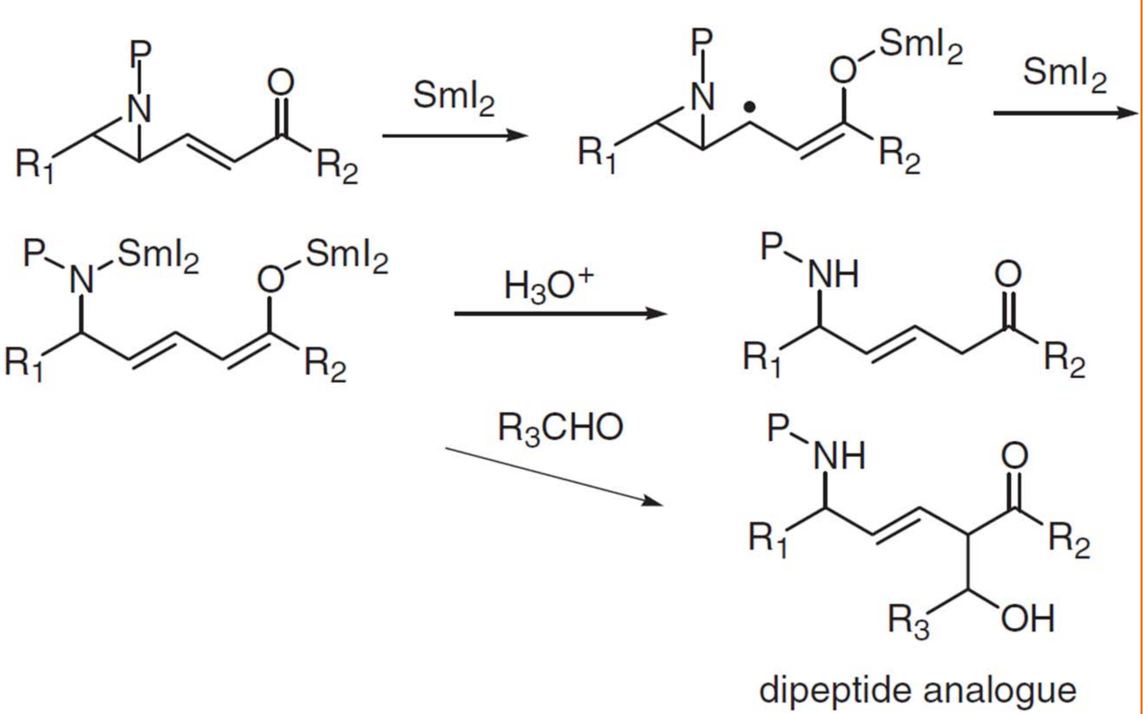
b: DAST (neat), SbCl,, rt; **c: DAST, CH_2Cl_2, molecular sieves, rt.**

Berts, W.; **Luthman, K.** *Tetrahedron* **1999**, *55*, 13819.

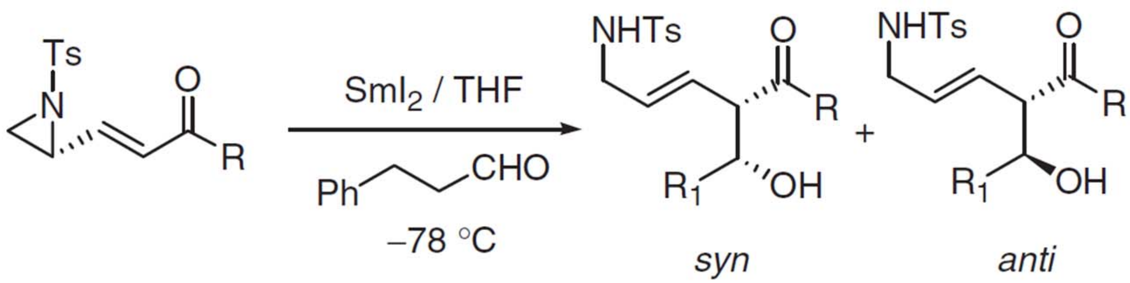


Righi, G.; Potini, C.; Bovicelli, P. *Tetrahedron Lett*. **2002**, *43*, 5867.

- Synthesis of Vinyl- and Ethynylaziridine
- Ring-Opening with Nucleophiles
- **Reductive Ring-Opening Reactions**
- Rearrangement and Isomerization
- Cycloaddition



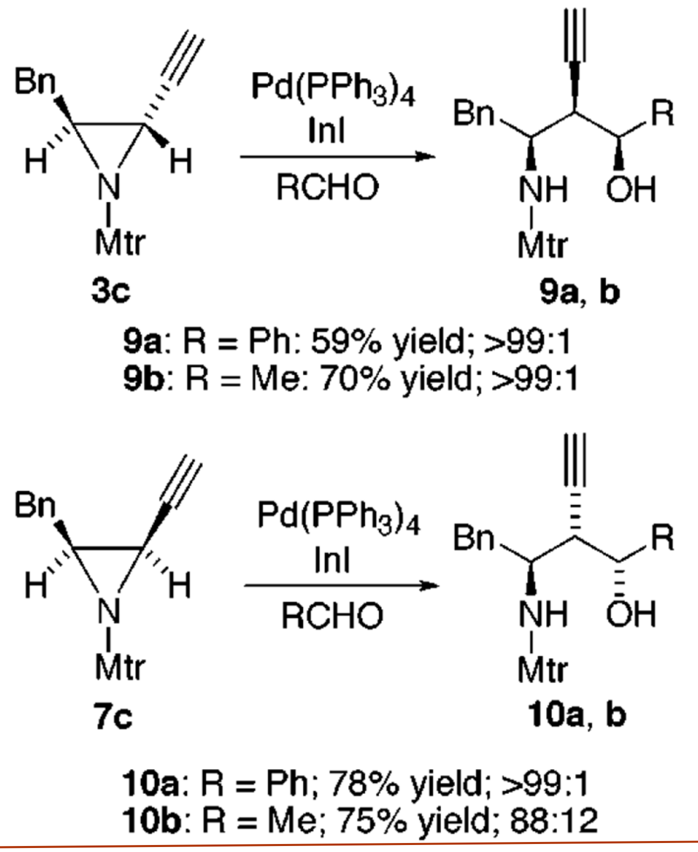
Molander, G. A.; Stengel, P. J. *Tetrahedron* **1997**, *53*, 8887.

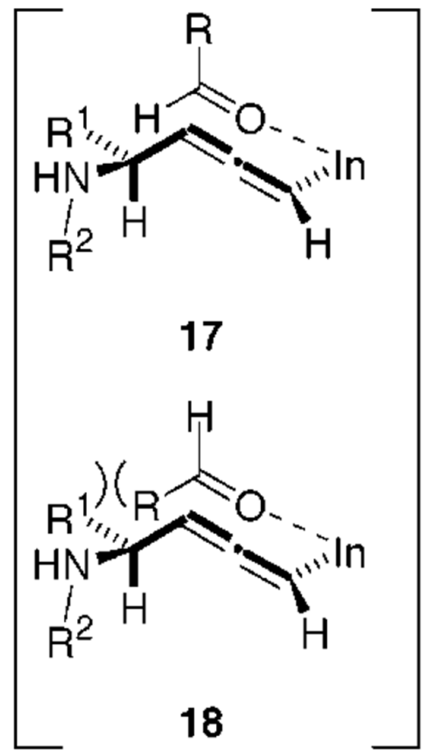


Entry	Aziridine		Product	Yield/%	
		R			(*syn*/*anti*)
1	**2**	Ph	**2a**	61	(58/42)
2	**3**	NEt_2	**3a**	83	(60/40)
3	**4**	2-oxazolidinone	**4a**	81	(>95/<5)

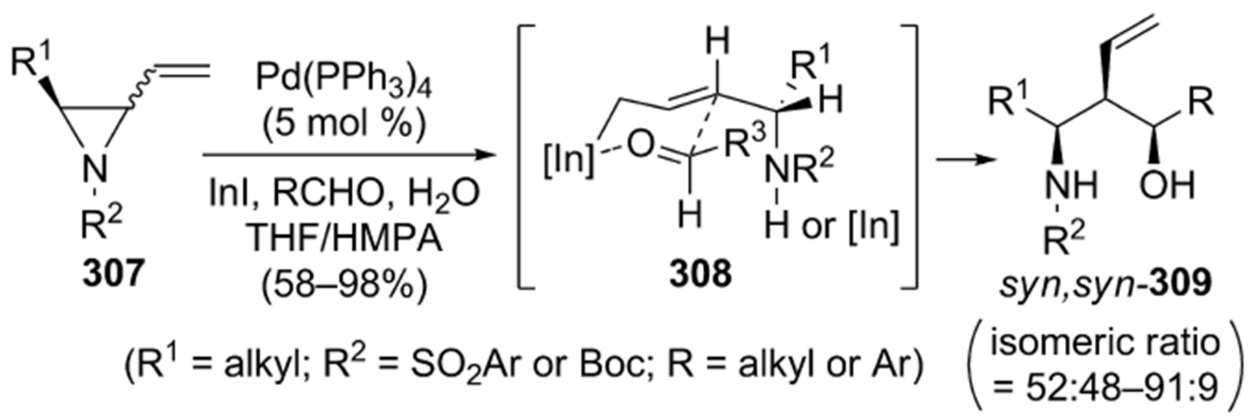
Ogawa, Y.; Kuroda, K.; Mukaiyama, T. *Chem. Lett*. **2005**, *34*, 372.

Ogawa, Y.; Kuroda, K.; **Mukaiyama,** T. *Bull. Chem. Soc. Jpn*. **2005**, *78*, 1309.

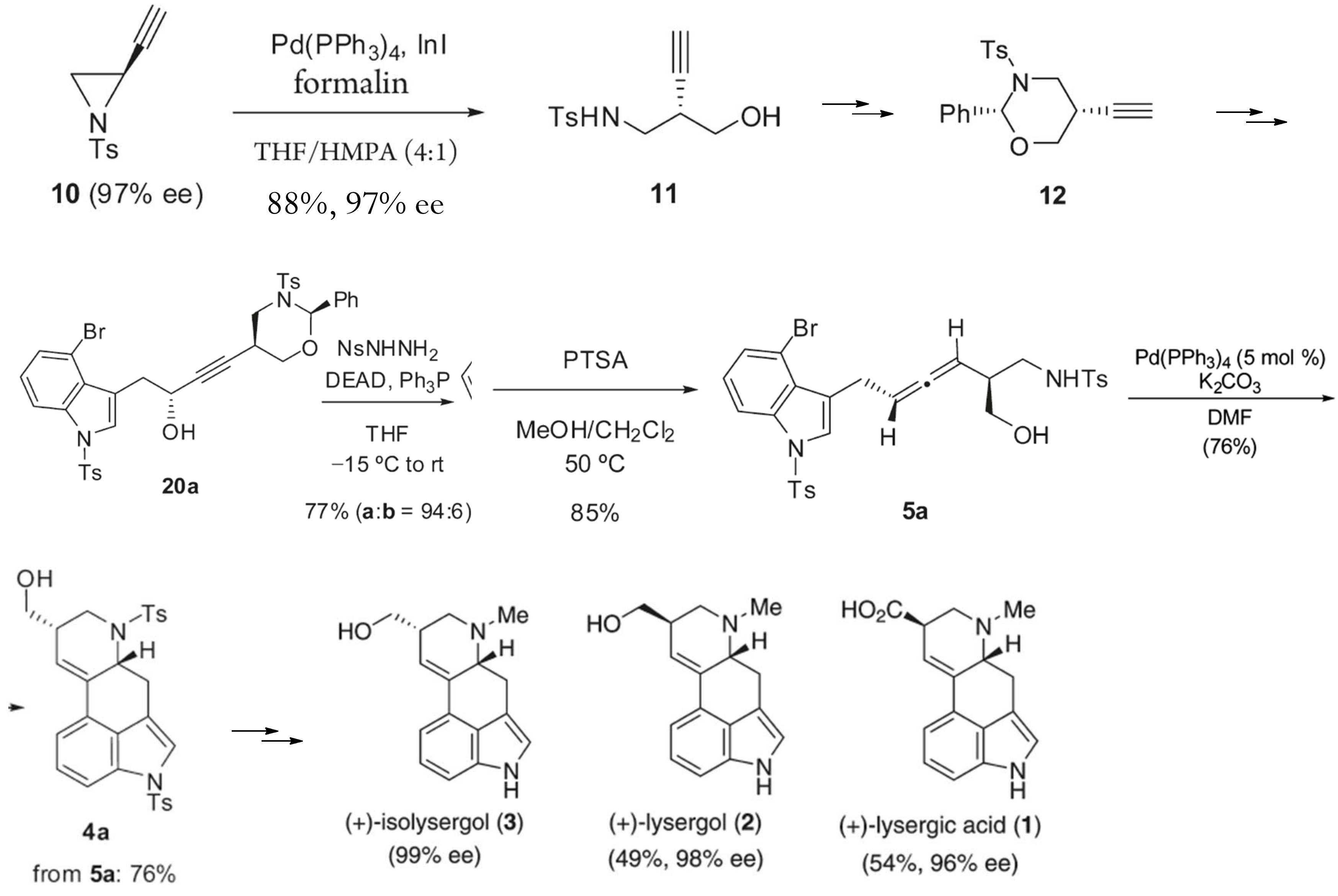




Tanaka, T. et al.
Org. Lett. **2000**, *2*, 2161.
J. Org. Chem. **2001**, *66*, 1867.



Takemoto, Y.; et al.
Tetrahedron Lett. **2001**, *42*, 1725
Tetrahedron **2002**, *58*, 5231.



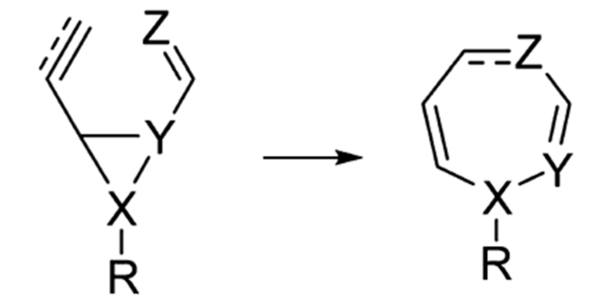
Inuki, S.; Iwata, A.; Oishi, S.; **Fujii, N.;** Ohno, H. *J. Org. Chem.* **2011**, *76*, 2072.
Inuki, S.; Oishi, S.; **Fujii, N.; Ohno, H**. *Org. Lett.* **2008**, *10*, 5239.

- Synthesis of Vinyl- and Ethynylaziridine
- Ring-Opening with Nucleophiles
- Reductive Ring-Opening Reactions
- **Rearrangement and Isomerization**
- Cycloaddition

Rearrangement

[2+3+2]

1. aza-[3,3]-Claisen

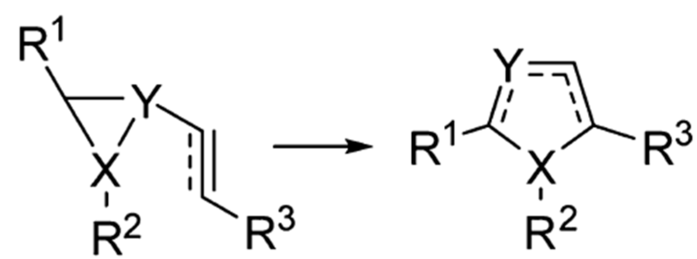


317 **318**

(X or Y = N; Z = CR_2, O, or S)

[2+3]

2. pyrroline/pyrrole formation

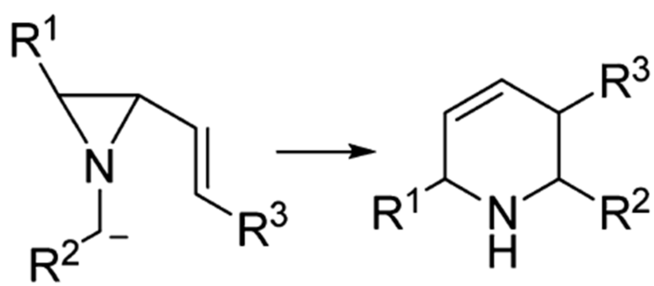


319 **320**

(X or Y = N)

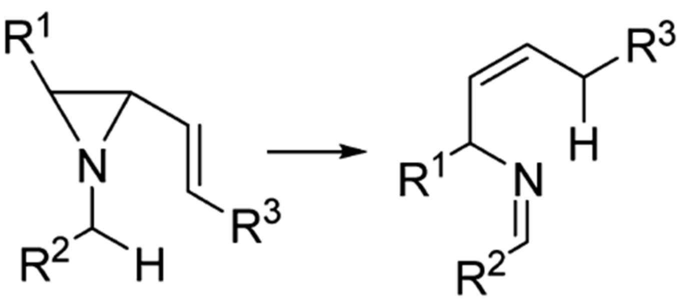
[2+3+1]

3. aza-[2,3]-Wittig



321 **322**

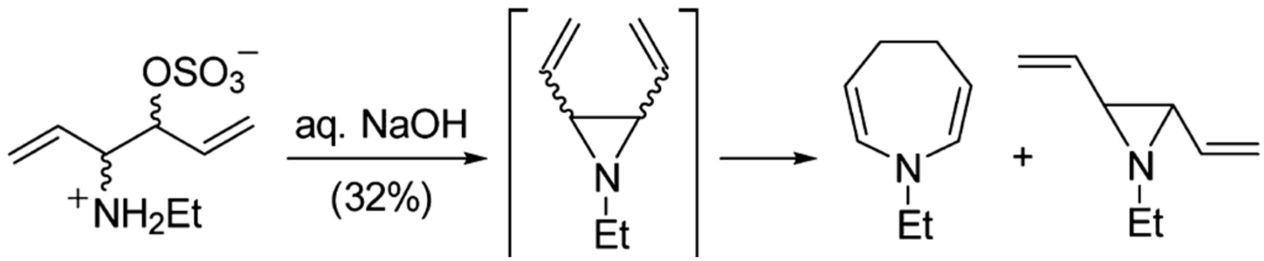
4. [1,5]-hydrogen shift



323 **324**

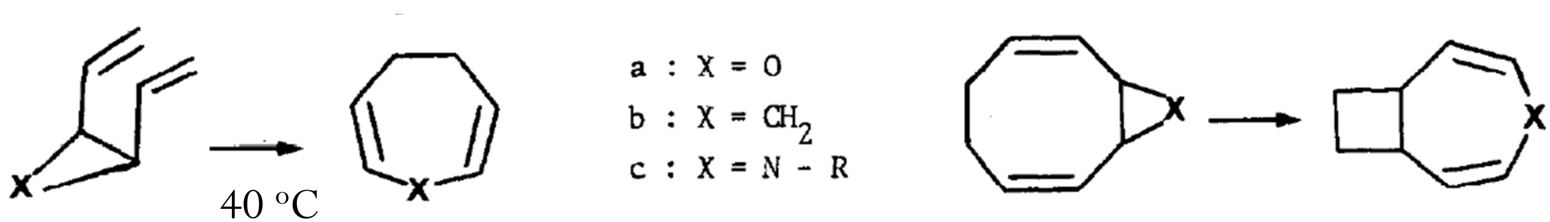
Aza-[3,3]-Claisen Rearrangement

2,3-divinylaziridine

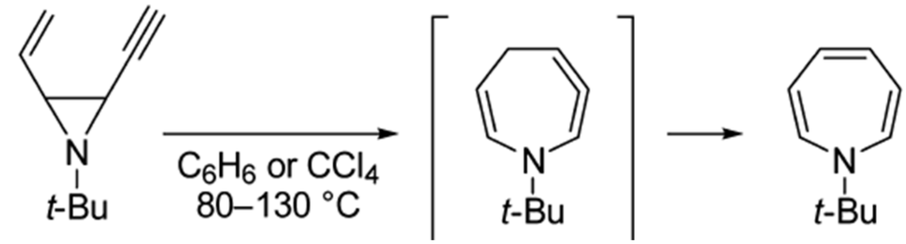


4,5-dihydro-1H-azepine

Stogryn, E. L.; Brois, S. J. *J. Org. Chem.* **1965**, *30*, 88.

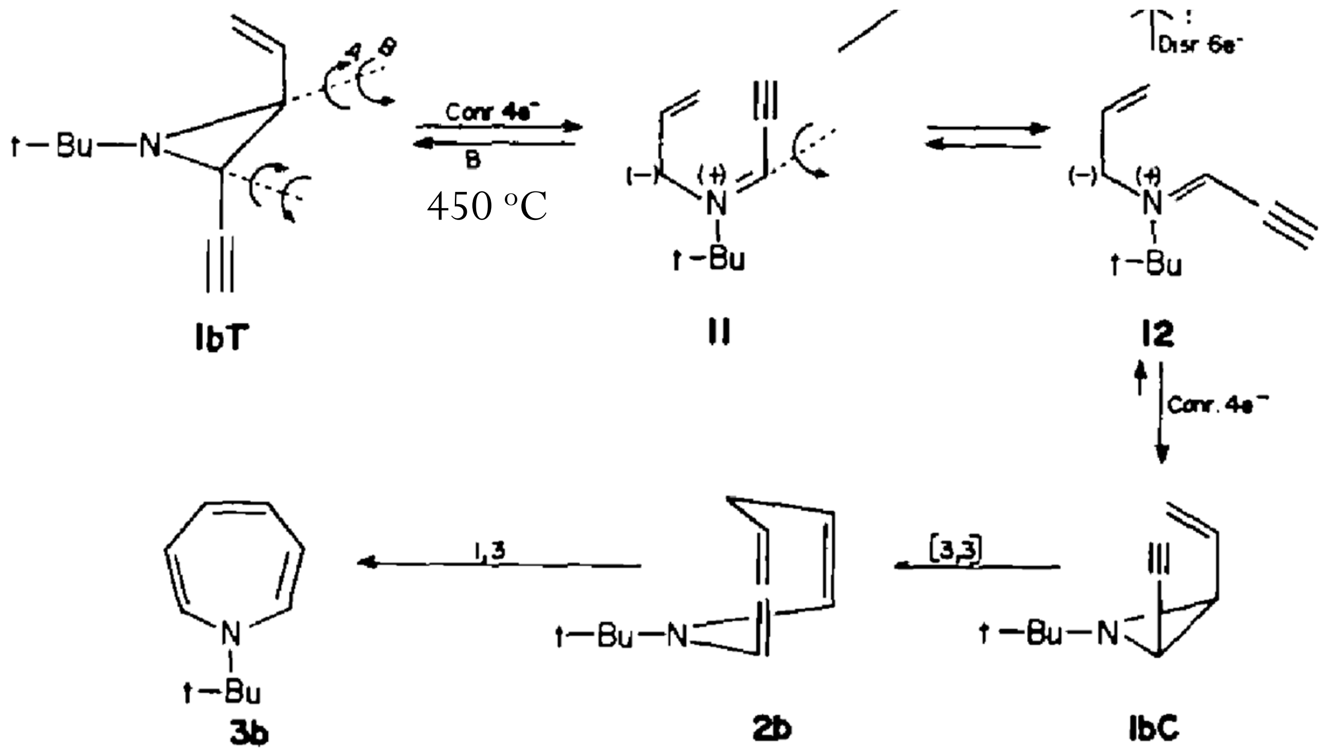


Pommelet, J. C.; **Chuche, J**. *Tetrahedron Lett*. **1974**, *44*, 3897.



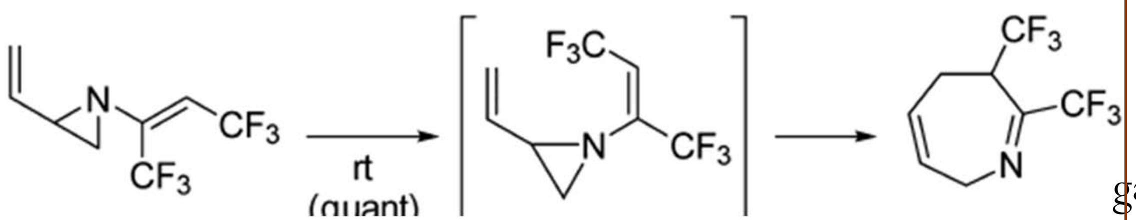
1H-azepine

Manisse, N.; **Chuche, J.** *J. Am. Chem. Soc.* **1977**, *99*, 1272.



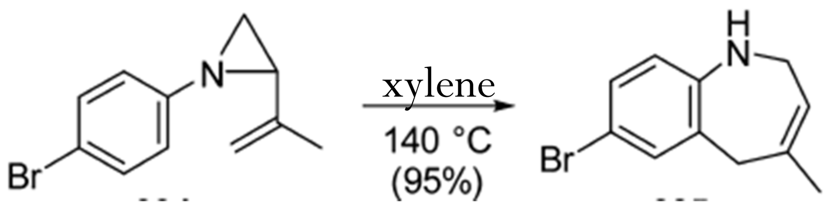
Manisse, N.; **Chuche, J.** *Tetrahedron* **1977**, *33*, 2399.

1,2-divinylaziridine



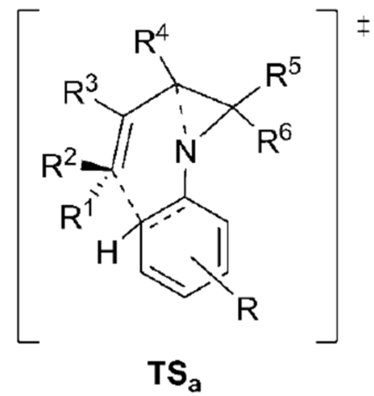
Stogryn, E. L.; Brois, S. J. *J. Am. Chem. Soc.* **1967**, *89*, 605.

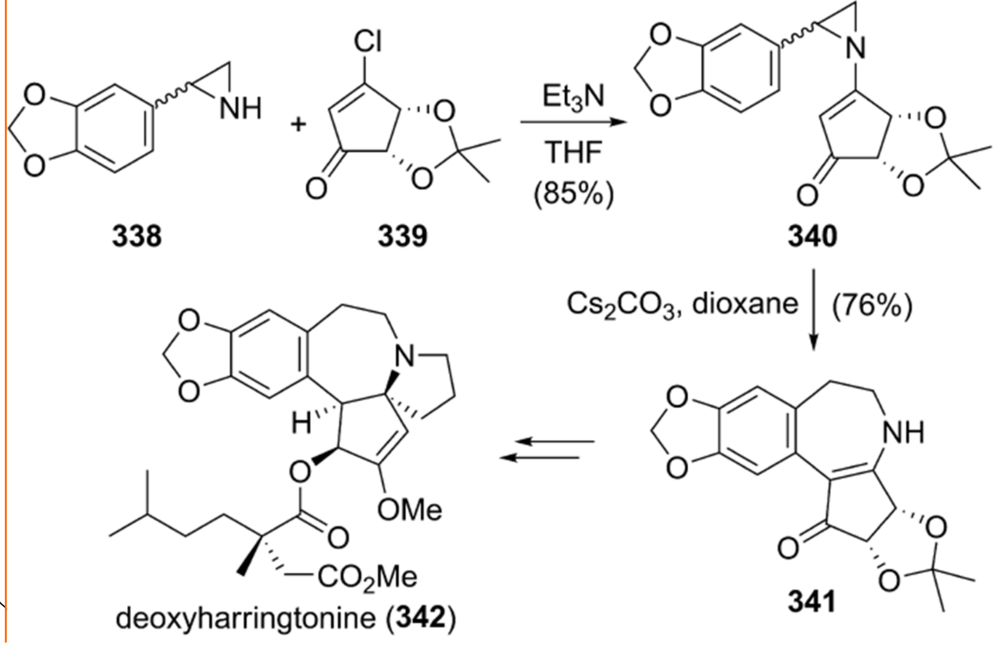
gas-liquid partition chromatography



Scheiner, P. *J. Org. Chem.* **1967**, *32*, 2628.

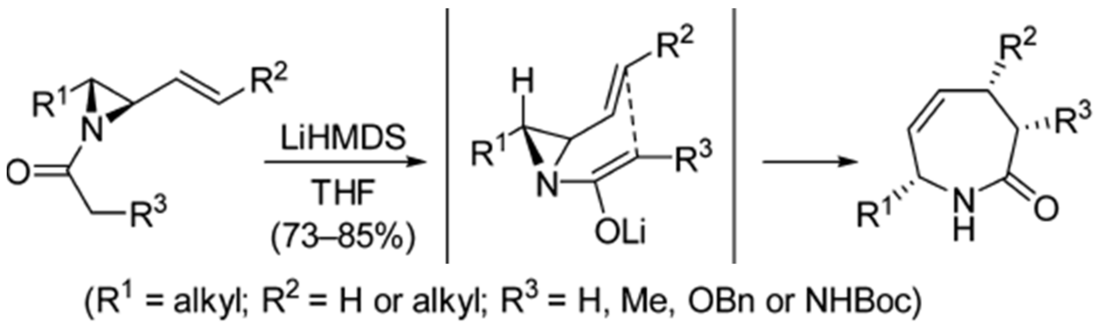
concerted [3,3]-sigmatropic rearrangemen



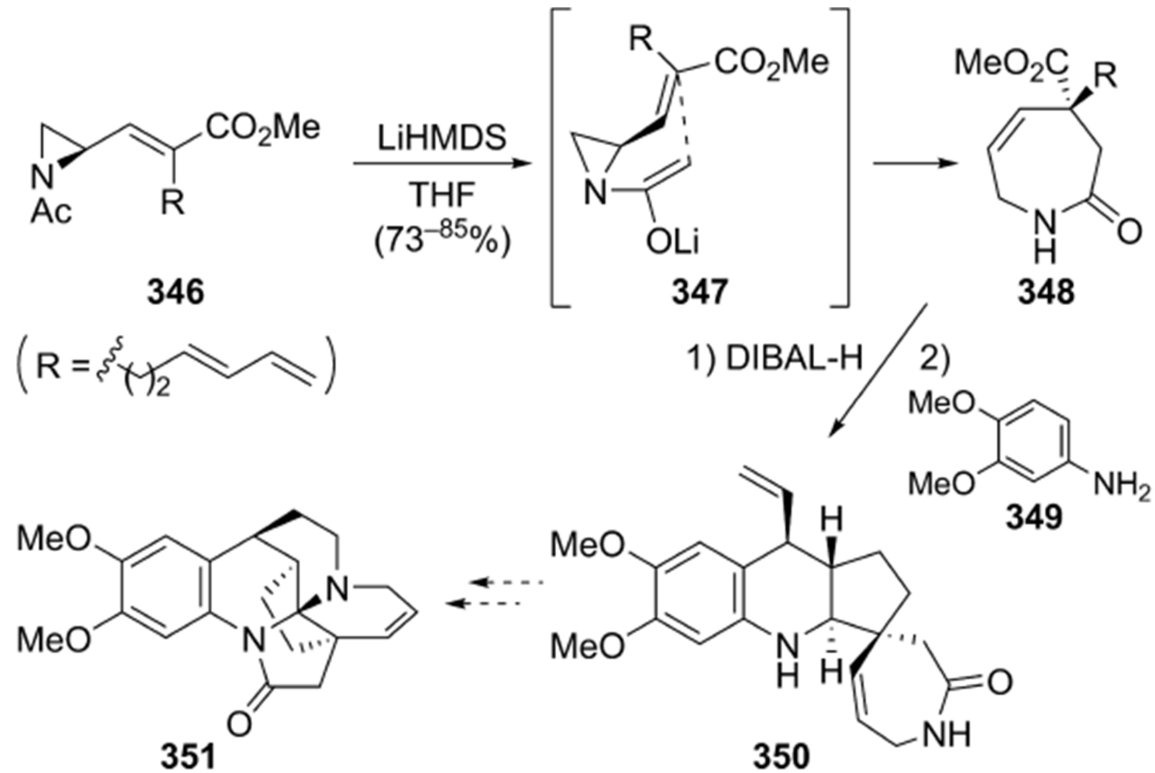


Eckelbarger, J. D.; Wilmot, J. T.; Gin, D. Y. *J. Am. Chem. Soc.* **2006**, *128*, 10370.

Enolate

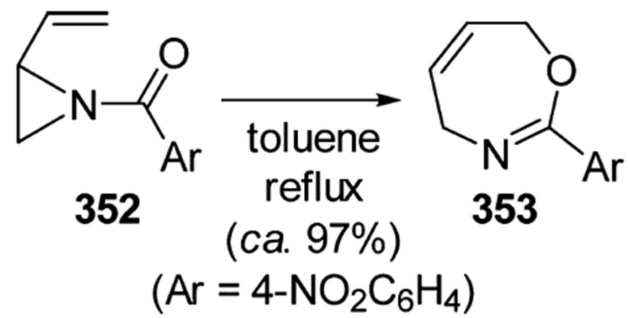


Lindström, U. M.; **Somfai, P**. *J. Am. Chem. Soc*. 1997, *119*, 8385.
Lindström, U. M.; **Somfai, P**. *Chem. Eur. J*. 2001, *7*, 94.



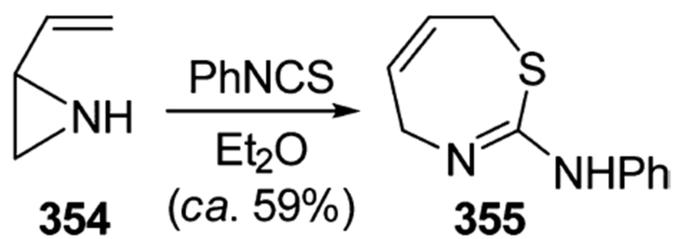
Zhou, J.; Magomedov, N. A. *J. Org. Chem*. **2007**, *72*, 3808.

Carbonyl Group



Mente, P. G.; Heine, H. W.; Scharoubim, G. R. *J. Org. Chem.* **1968**, *33*, 4547.

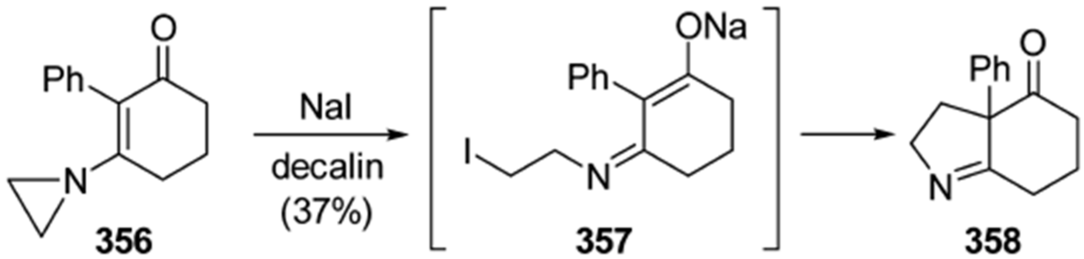
Thiocarbonyl Group



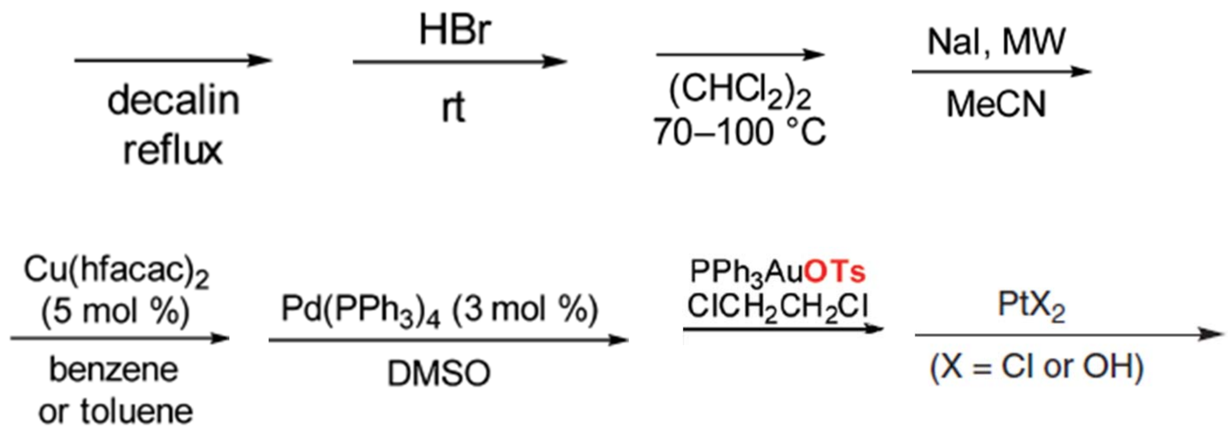
Mente, P. G.; Heine, H. W. *J. Org. Chem.* **1971**, *36*, 3076.

Pyrroline/Pyrrole Formation

Pyrroline/Pyrrole Formation



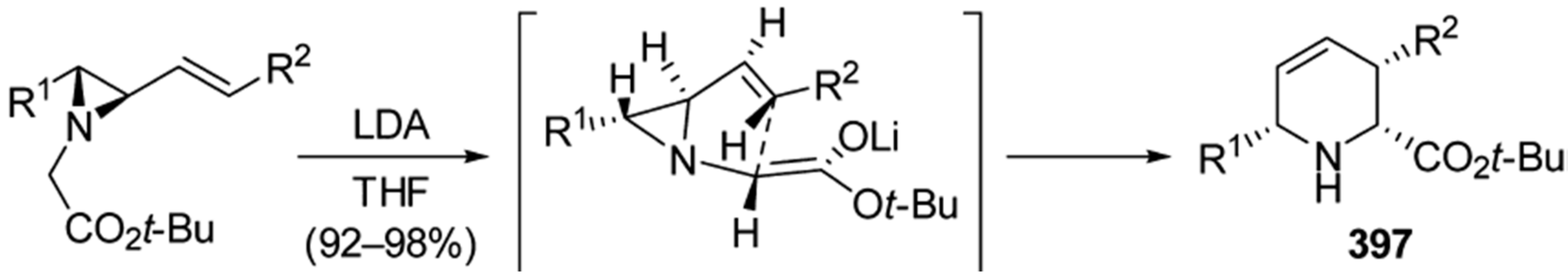
Whitlock, H. W., Jr.; Smith, G. L. *Tetrahedron Lett.* **1965**, *6*, 1389.



(a) *Chem. Commun.* **1967**, 1232. (b) *J. Chem. Soc. C* **1969**, 778. (c) *J. Org. Chem.* **1990**, *55*, 5719.
(d) *Tetrahedron Lett.* **198**5, *26*, 3527. (e) *Synth. Commun.* **1987**, *17*, 1155. (f) *Synlett* **2005**, 3099.
(g) *Synlett* **2011**, 674. (h) *Chem. Eur. J.* **2011**, *17*, 11553. (i) *Tetrahedron Lett.* **1985**, *26*, 857.
(j) *Tetrahedron* **1989**, *45*, 3089. (k) *Org. Lett.* **200**8, *10*, 5023.(l) *Org. Lett.* **2011**, *13*, 1110.
(m) *Org. Lett.* **2009**, 11, 2293. (n) *Synthesis* **2009**, 2454……

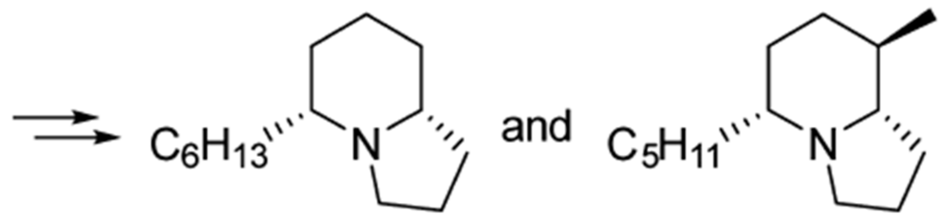
Aza-[2,3]-Wittig Rearrangement

Aza-[2,3]-Wittig Rearrangement



397
single isomer

Somfai, P. et al.
J. Am. Chem. Soc. **1994**, *116*, 9781.
J. Org. Chem. **1996**, *61*, 8148.

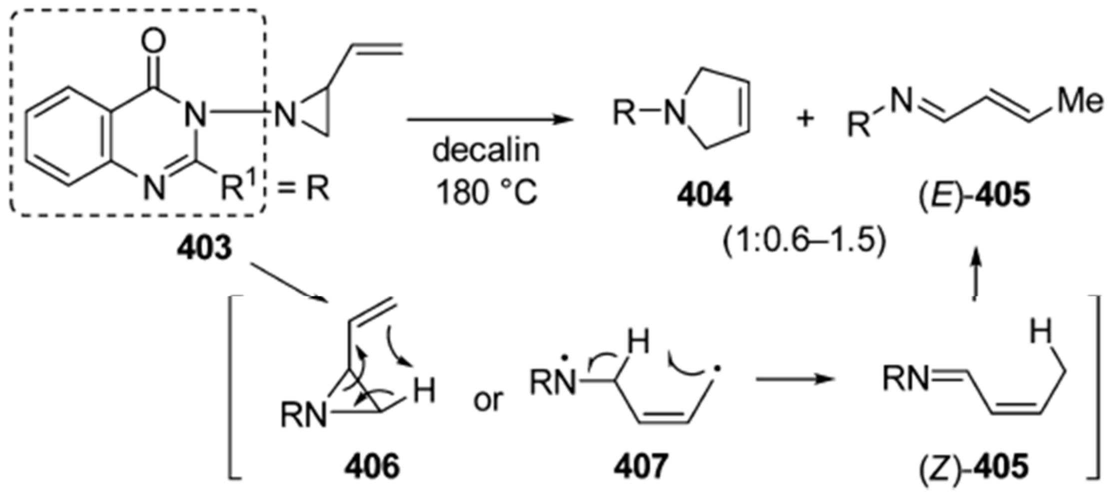


indolizidine 209D (**398**)

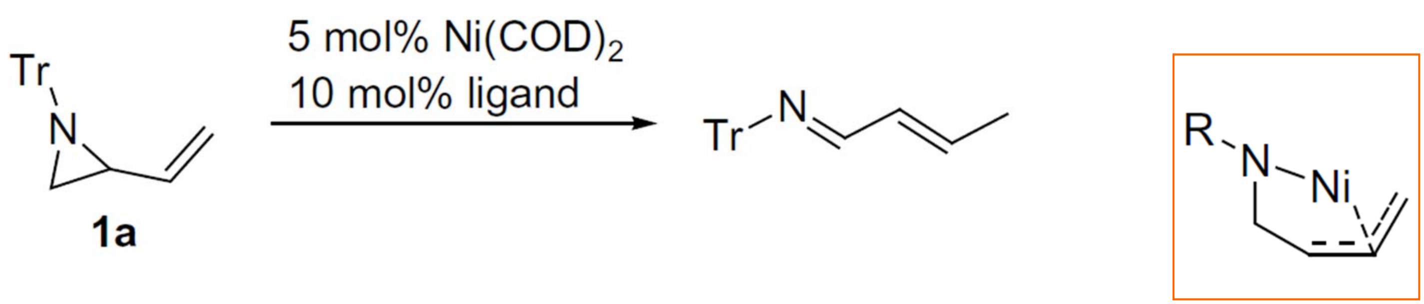
indolizidine 209B (**399**)

Åhman, J.; **Somfai, P**. *Tetrahedron Lett*. **1995**, *36*, 303.
Åhman, J.; **Somfai, P.** *Tetrahedron* **1995**, *51*, 9747.
Somfai, P.; Jarevång, T.; Lindström, U. M.; Svensson, A. *Acta Chem. Scand.* **1997**, *51*, 1024.

Hydrogen Shift: Hydrogen from Aziridine

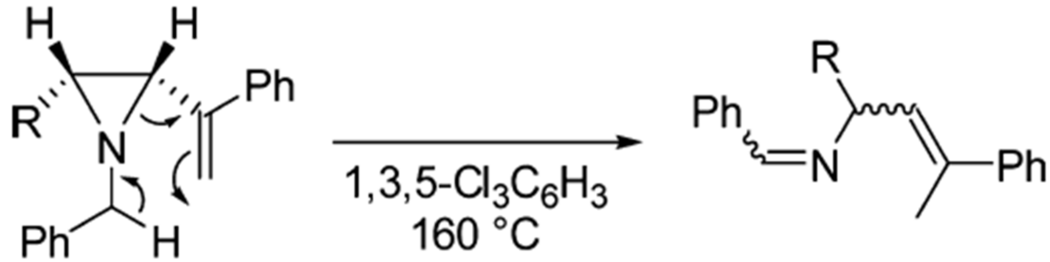


Gilchrist, T. L.; **Rees, C. W.;** Stanton, E. *J. Chem. Soc. C* **1971**, 3036.

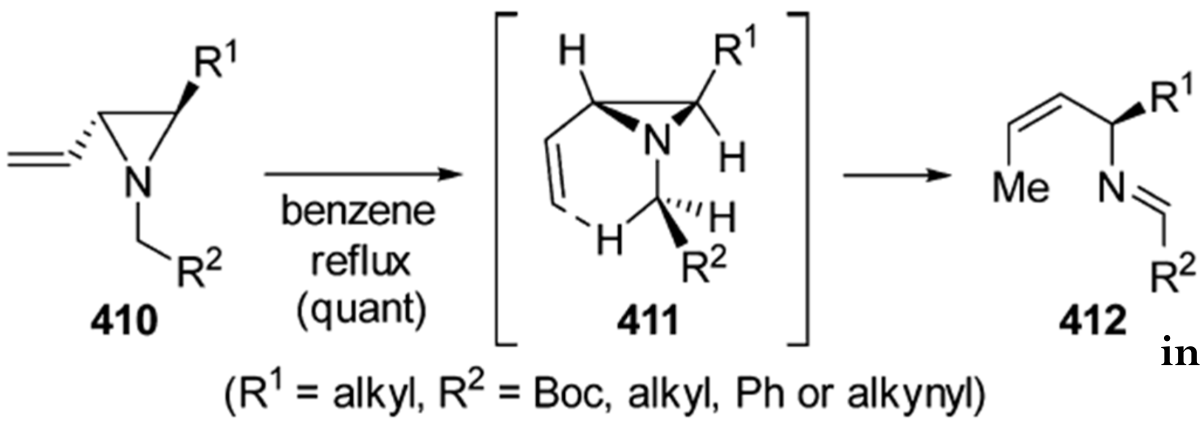


Zuo, G.; Zhang, K.; **Louie, J.** *Tetrahedron Lett.* **2008**, *49*, 6797.

Hydrogen Shift: Hydrogen from Substituent



Borel, D.; Gelas-Mialhe, Y.; Vessière, R. *Can. J. Chem.* **1976**, *54*, 1590.

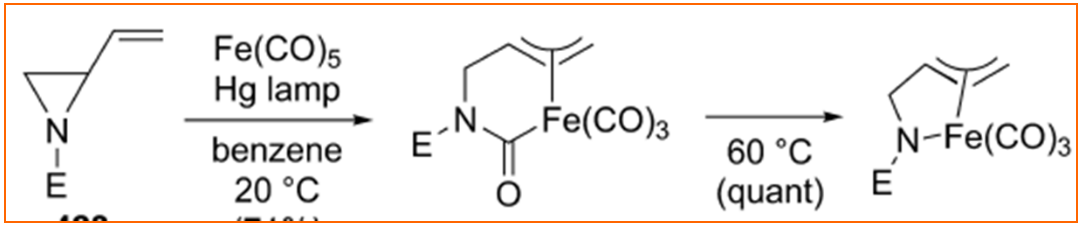


in a stereoselective manner

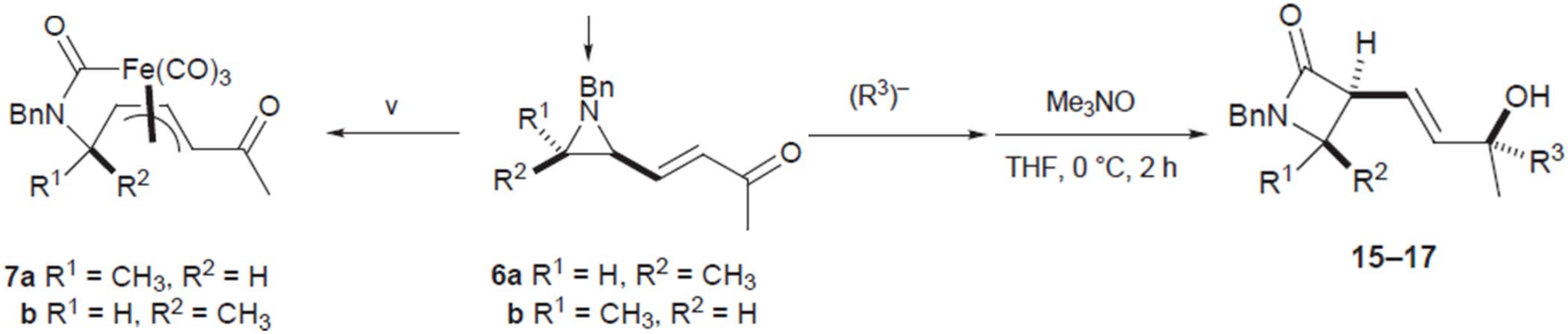
Åhman, J.; **Somfai, P.**; Tanner, D. *J. Chem. Soc., Chem. Commun.* **1994**, 2785.
Åhman, J.; **Somfai, P.** *Tetrahedron Lett.* **1995**, *36*, 1953.
Åhman, J.; **Somfai, P.** *Tetrahedron* **1999**, *55*, 11595.

- Synthesis of Vinyl- and Ethynylaziridine
- Ring-Opening with Nucleophiles
- Reductive Ring-Opening Reactions
- Rearrangement and Isomerization
- **Cycloaddition**

Carbonylative Ring Expansion to Lactams

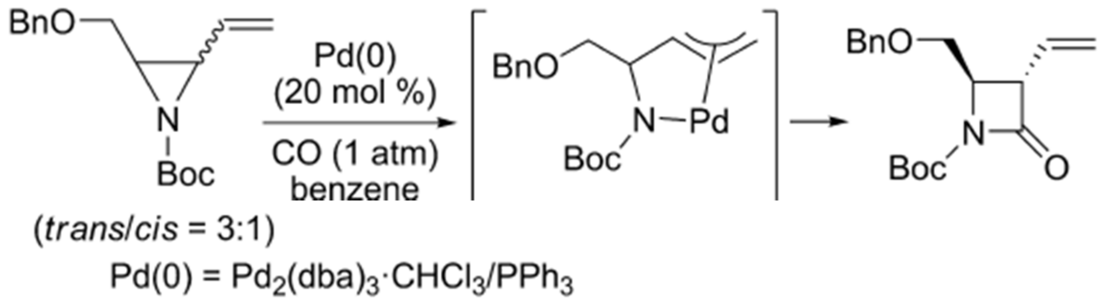


Aumann, R.; Fröhlich, K.; Ring, H. *Angew. Chem., Int. Ed*. **1974**, *13*, 275.

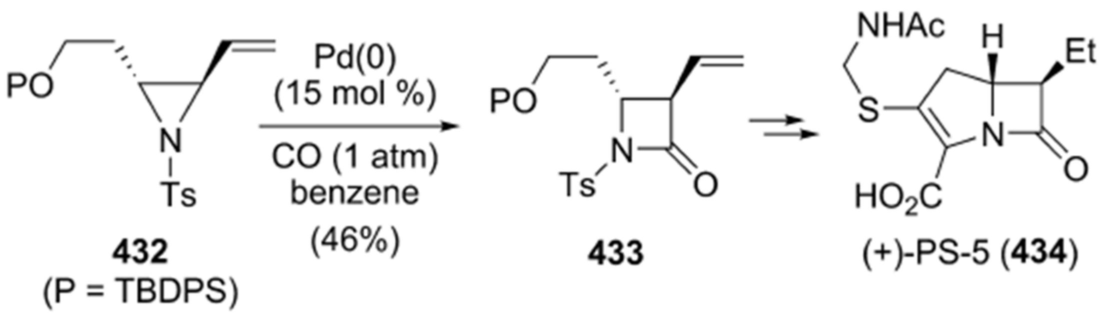


$Fe_2(CO)_9$, benzene, sonication, 30 °C, 3 h, 68% (dr 14:1) (**7a**), 77% (dr 10:1) (**7b**)

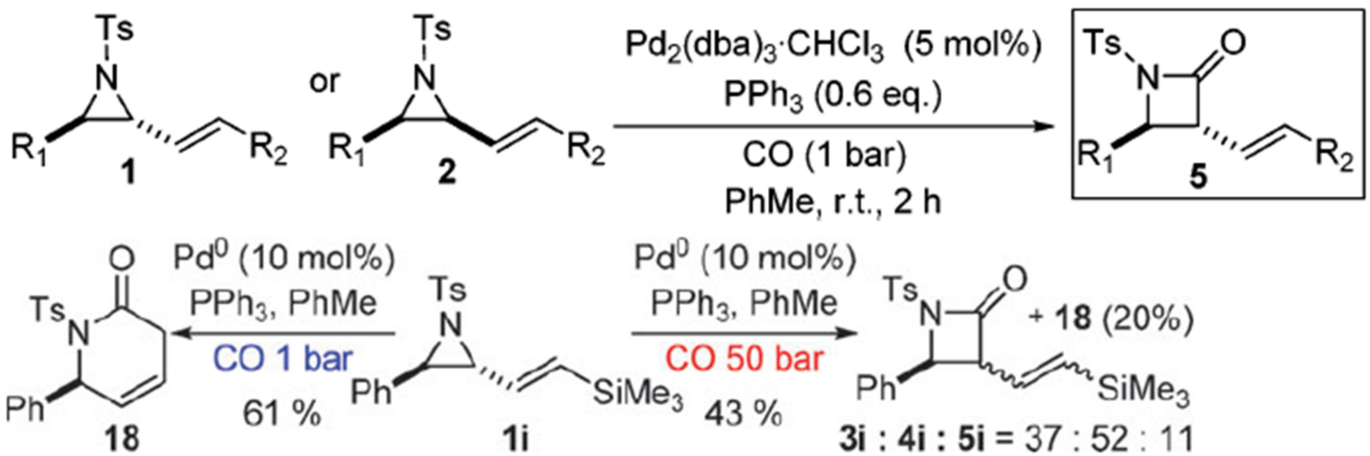
Ley, S.V.; Middleton, B. *Chem. Commun*. **1998**, 1995.



Spears, G. W.; Nakanishi, K.; **Ohfune, Y.** *Synlett* **1991**, 91.

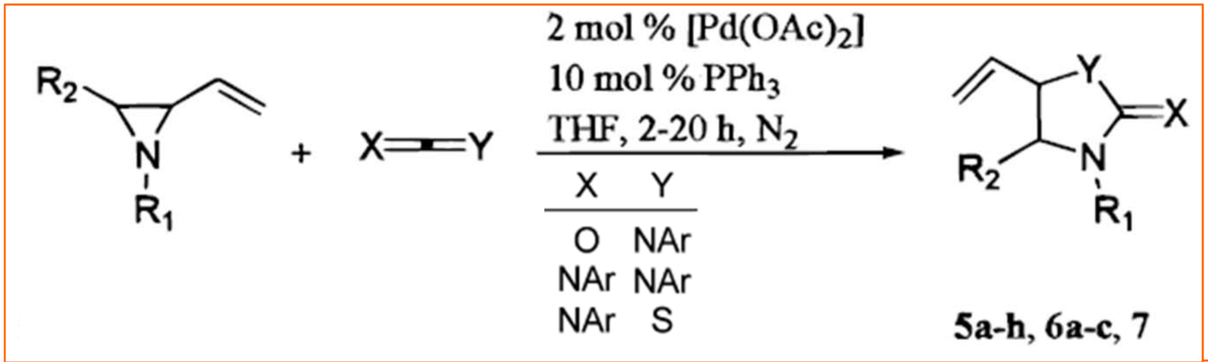


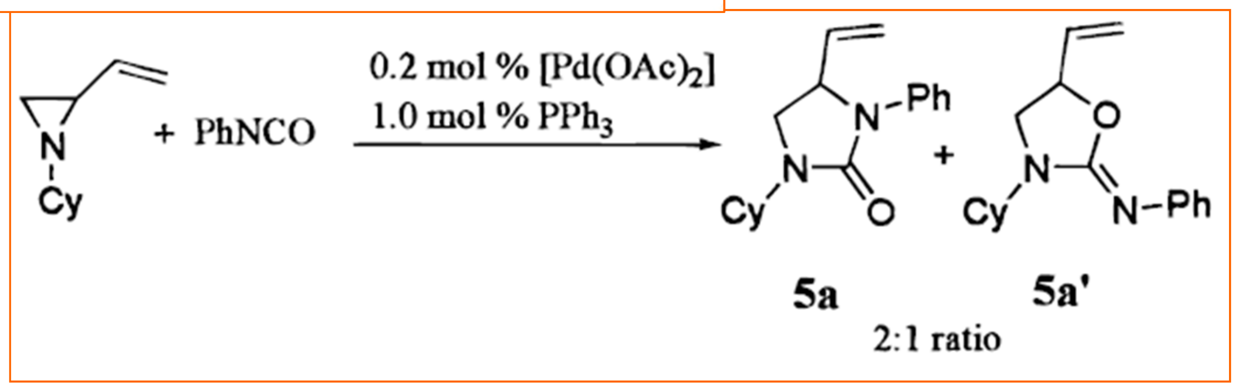
Tanner, D.; **Somfai, P.** *Bioorg. Med. Chem. Lett.* **1993**, *3*, 2415.



Aggarwal, V. K. et al. *Chem. Commun.* **2010**, *46*, 267.

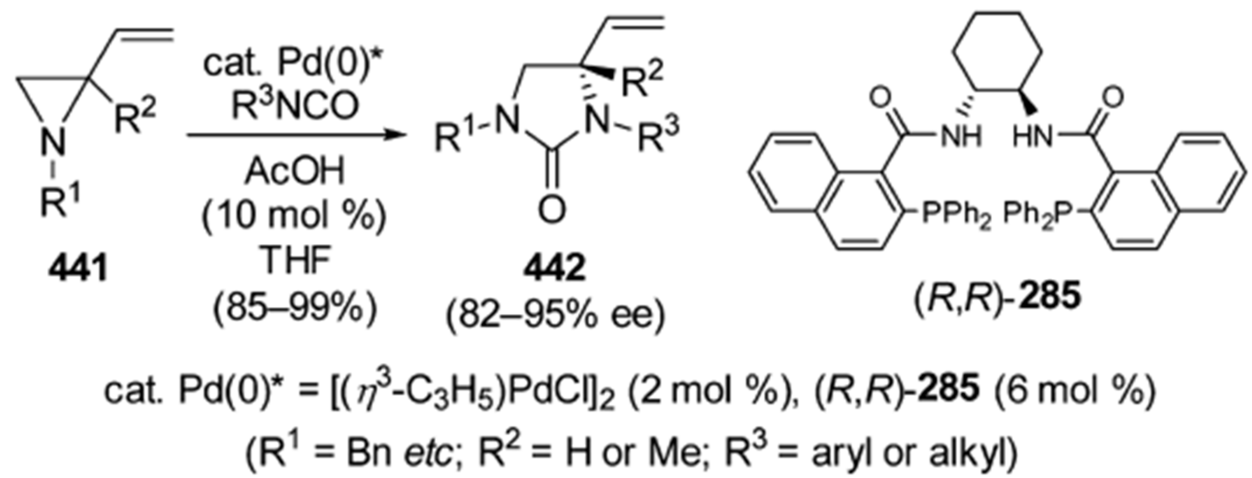
Cycloaddition with Isocyanates and Related Compounds



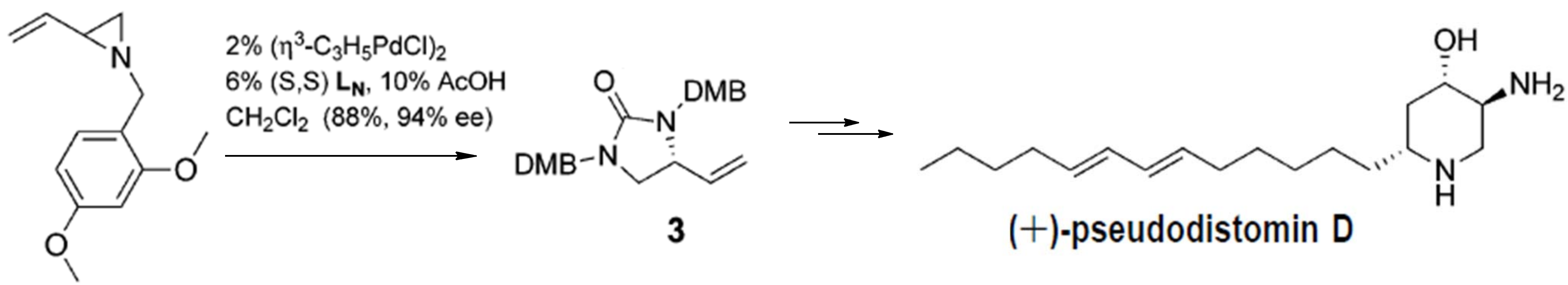


Butler, D. C. D.; Inman, G. A.; **Alper, H.** *J. Org. Chem.* **2000**, *65*, 5887.

Kanno, E.;Yamanoi, K.; Koya, S.; Azumaya, I.; Masu, H.;Yamasaki, R.; **Saito, S.**
J. Org. Chem. **2012**, 77, 2142.

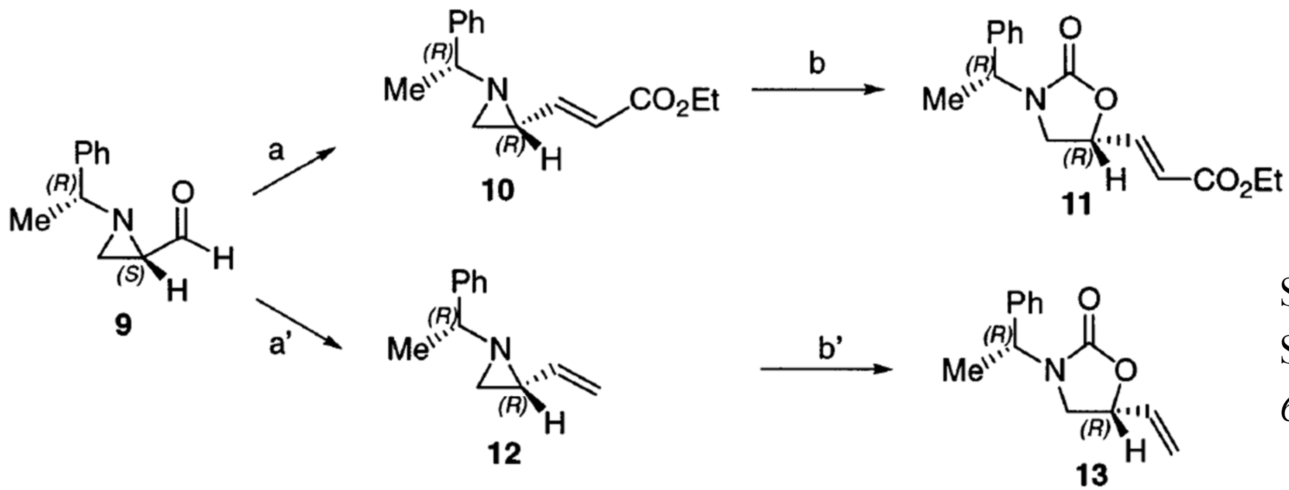


B. M. Trost, D. R. Fandrick, *J. Am. Chem. Soc.* **2003**, *125*, 11836



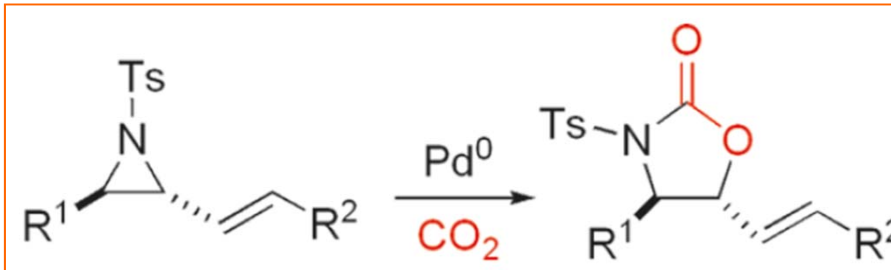
B. M. Trost, D. R. Fandrick, *Org. Lett.* **2005**, *7*, 823

Cycloaddition with CO_2



[a] Reagents and conditions: (a) 1.2 equiv of $(EtO)_2POCH_2CO_2Et$, 1.2 equiv of LiHMDS, THF, at rt, 2 h, 96%. (b) 1.5 equiv of $ClCO_2CH_3$, CH_3CN, reflux, 7 h, 97%. (a′) 2 equiv of $CH_3PPh_3{}^+I^-$, 1.5 equiv of *n*-BuLi, THF, −78 °C. (b′) 1.5 equiv of $ClCO_2CH_3$, CH_3CN, reflux, 7 h, 85%.

Sim, T. B.; Kang, S. H.; Lee, K. S.; **Lee, W. K.** *J. Org. Chem.* **2003**, *68*, 104.

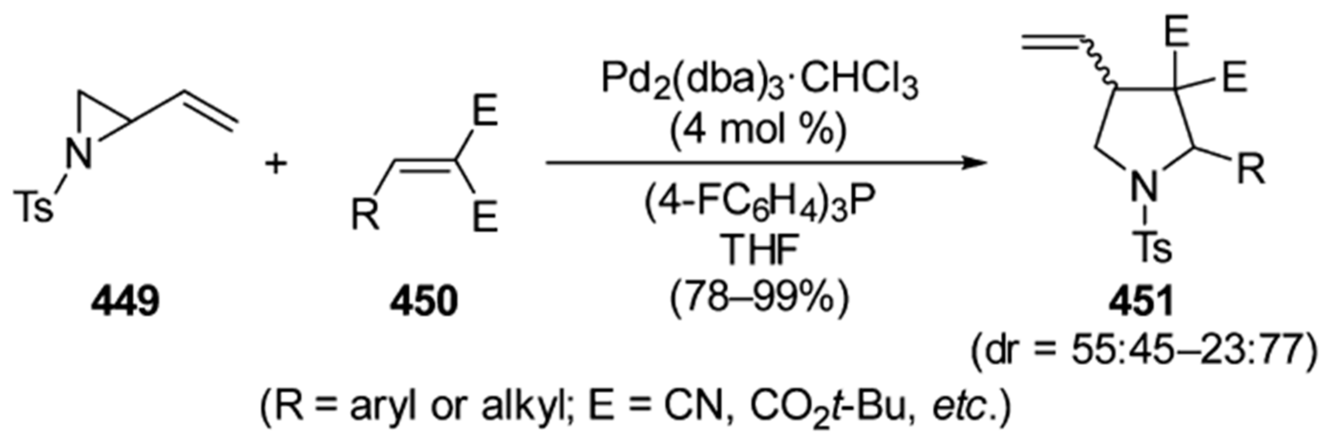


R^1 = Ar, alkyl, H
R^2 = Ar, alkyl, H

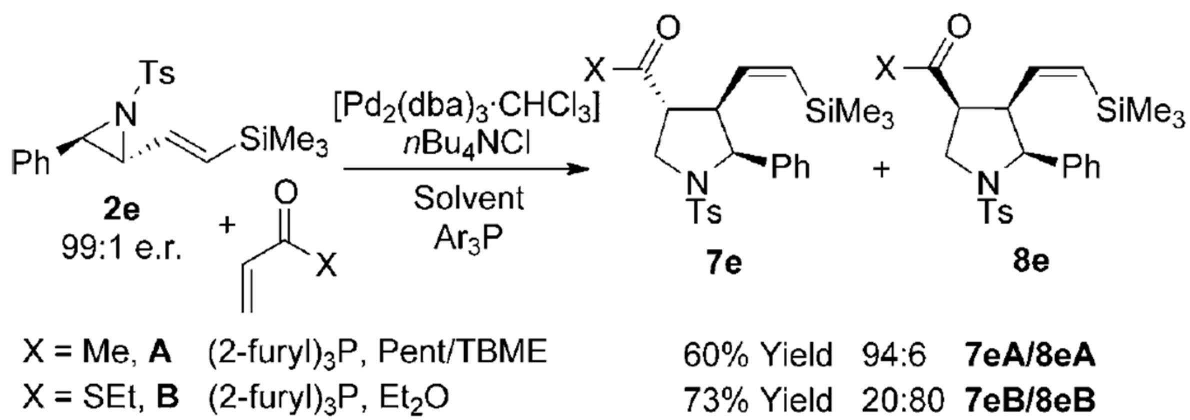
12 examples
40-92% yield

Fontana, F.; Chen, C. C.; **Aggarwal, V. K.** *Org. Lett.* **2011**, *13*, 3454.

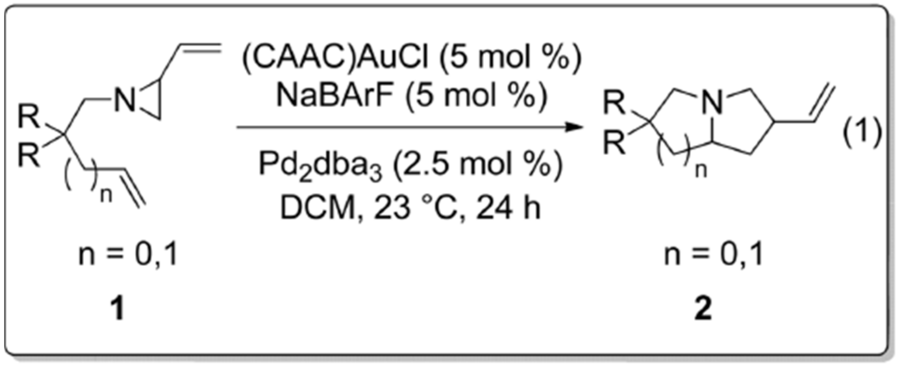
Cycloaddition with a Carbon−Carbon Multiple Bond

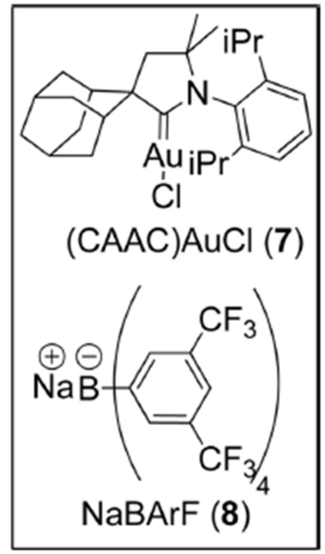


Aoyagi, K.; Nakamura, H.; **Yamamoto, Y.** *J. Org. Chem.* **2002**, *67*, 5977.



Lowe, M. A.; Ostovar, M.; Ferrini, S.; Chen, C. C.; Lawrence, P. G.; Fontana, F.; Calabrese, A. A.; **Aggarwal, V. K.** *Angew. Chem., Int. Ed.* **2011**, *50*, 6370.



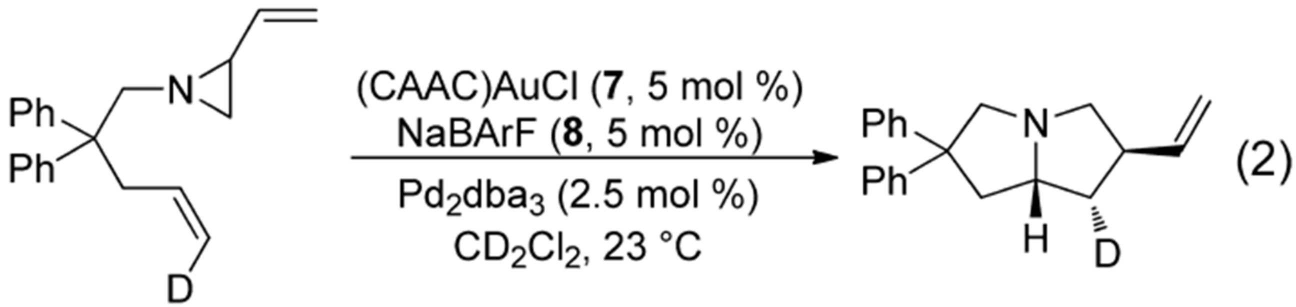


catalyst(s)	loading	time (h)	conversion[a]
(CAAC)AuCl/NaBArF (7/8)	5.0 mol %/5.0 mol %	15	No reaction
CAAC carbene/Pd_2dba_3	10. mol %/5.0 mol %	16	No reaction
$PdCl_2(PPh_3)_2/AgSbF_6$	10. mol %/20. mol %	16	Decomposition
Pd_2dba_3	5.0 mol %	15	7%
NaBArF (**8**)	5.0 mol %	16	No reaction
CAAC carbene	10. mol %	16	No reaction

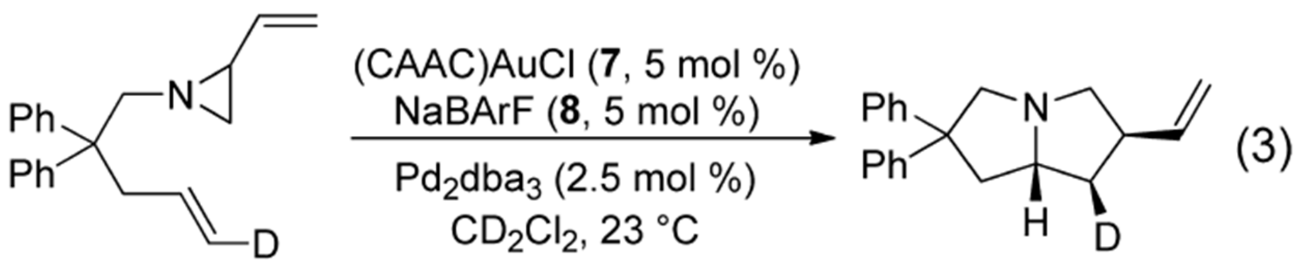
[a]By ^{1}H NMR spectroscopy using substrate **1a**.

Hirner, J. J.; Roth, K. E.; Shi, Y.; **Blum, S. A.** *Organometallics* **2012**, *31*, 6843.

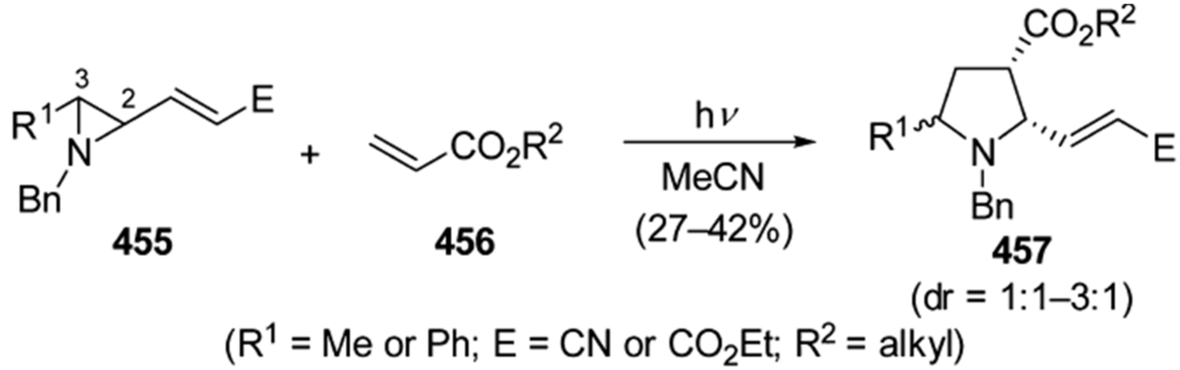
Mechanistic Studies:



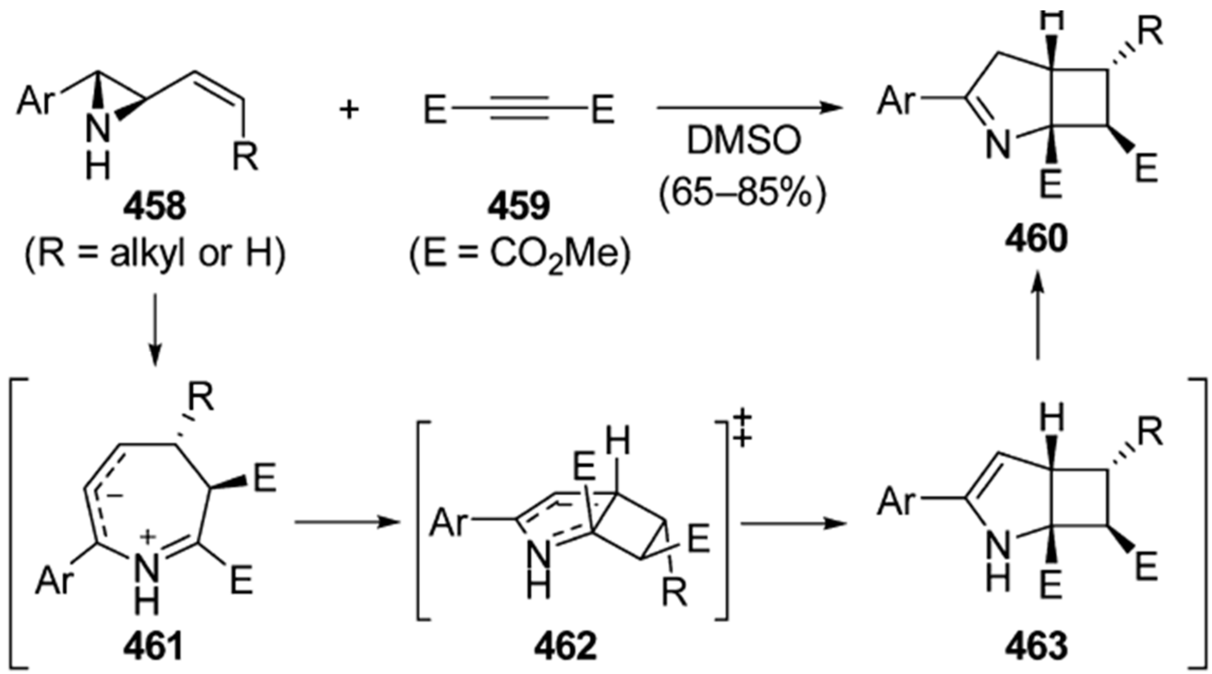
1a' **2a'**



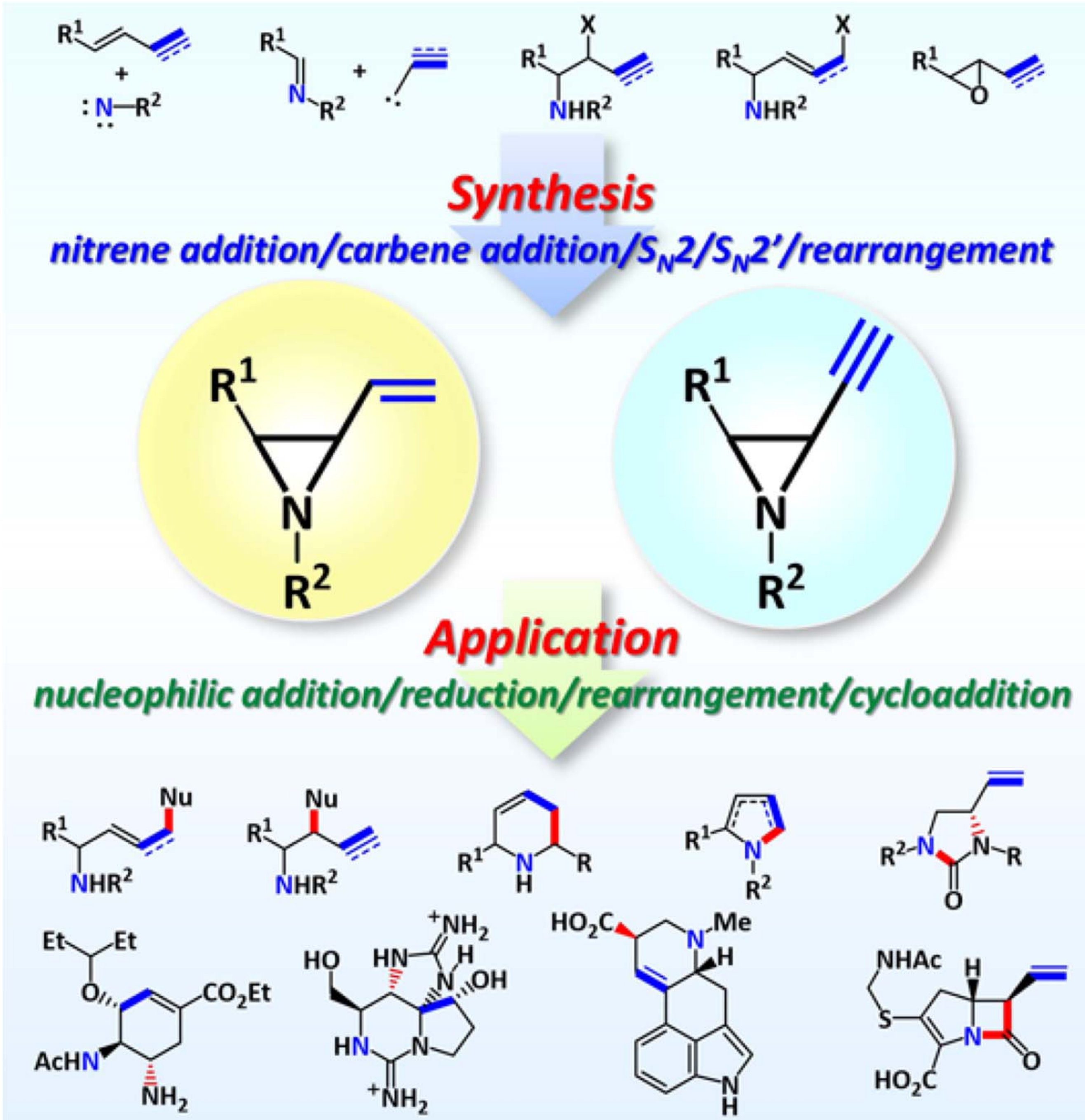
1a'' **2a''**



Ishii, K.; Sone, T.; Shigeyama, T.; Noji, M.; Sugiyama, S. *Tetrahedron* **2006**, *62*, 10865.

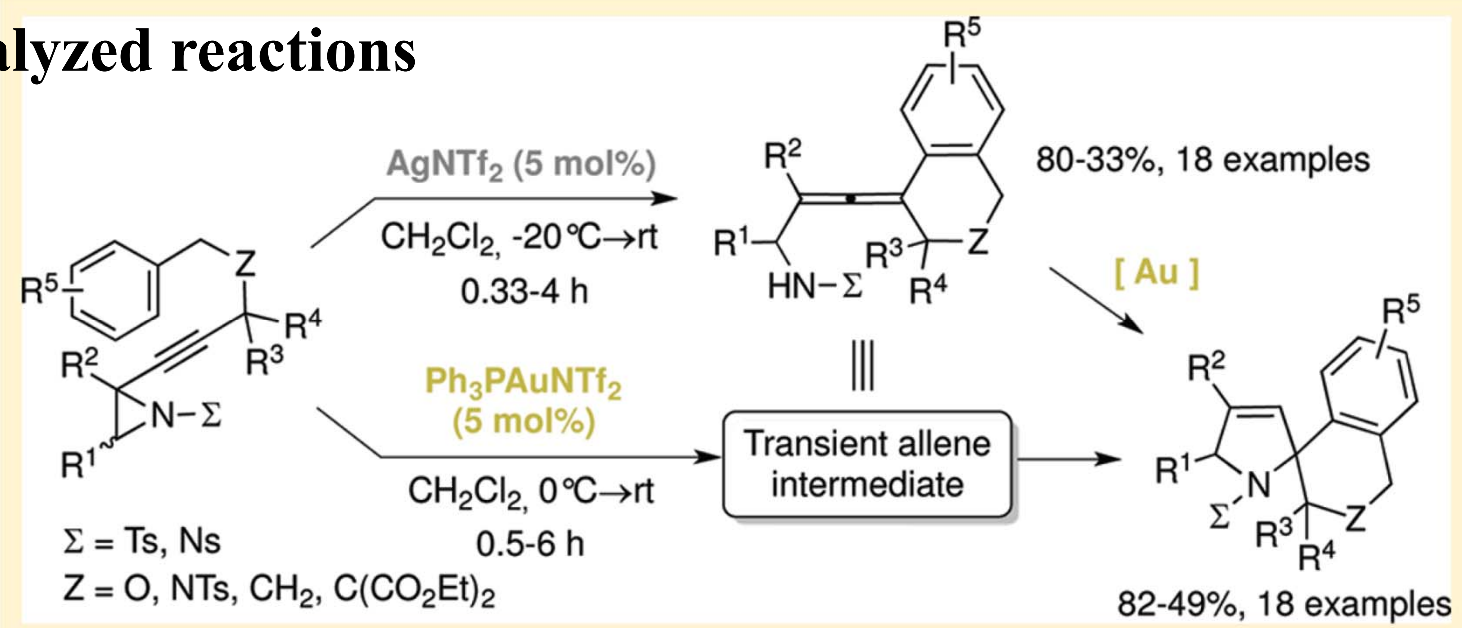


Baktharaman, S.; Afagh, N.; Vandersteen, A.; Yudin, A. K. *Org. Lett*. **2010**, *12*, 240.

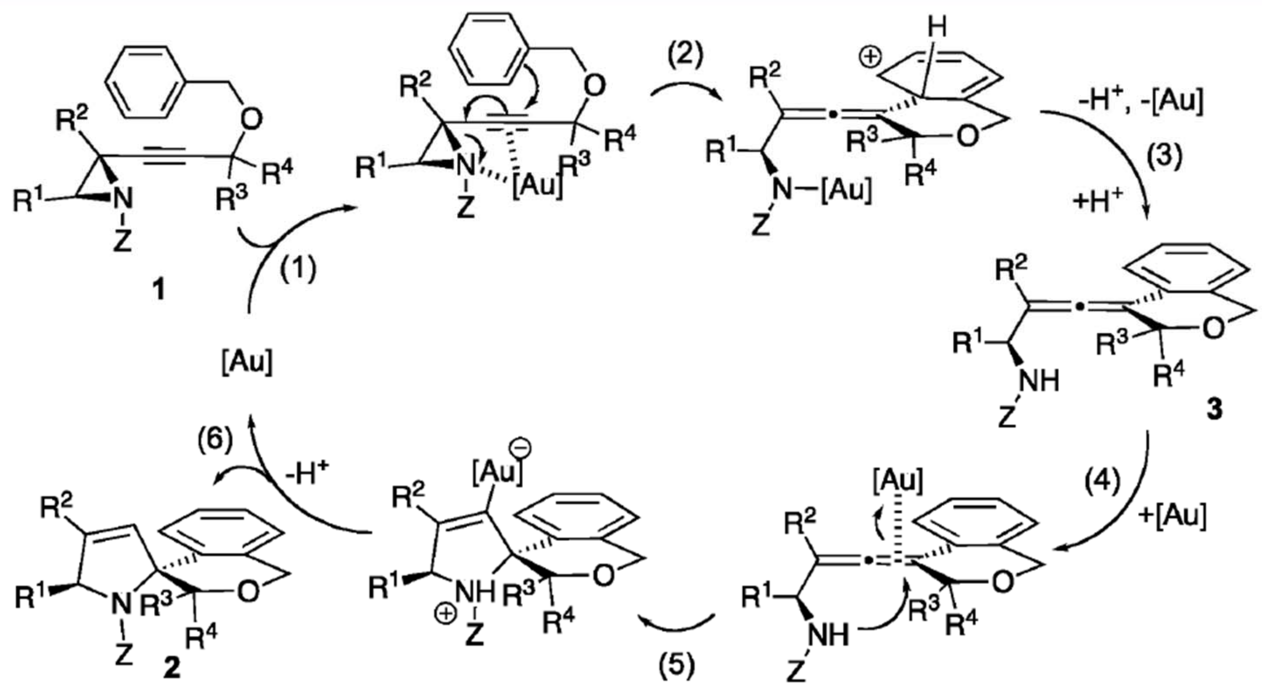

Synthesis
nitrene addition/carbene addition/SN2/SN2'/rearrangement
Application
nucleophilic addition/reduction/rearrangement/cycloaddition

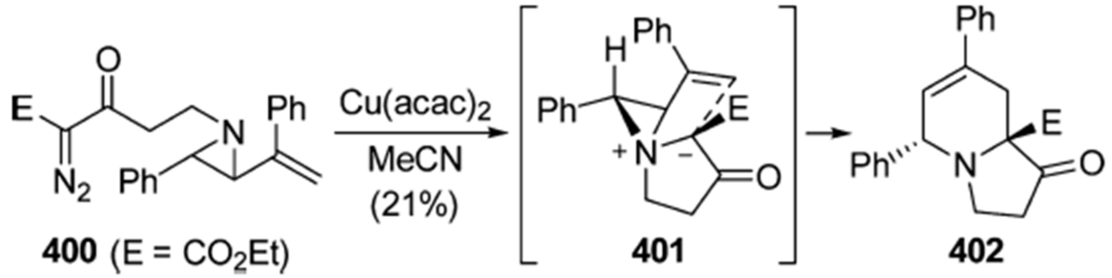
Thank you for your attentions

Au or Ag catalyzed reactions

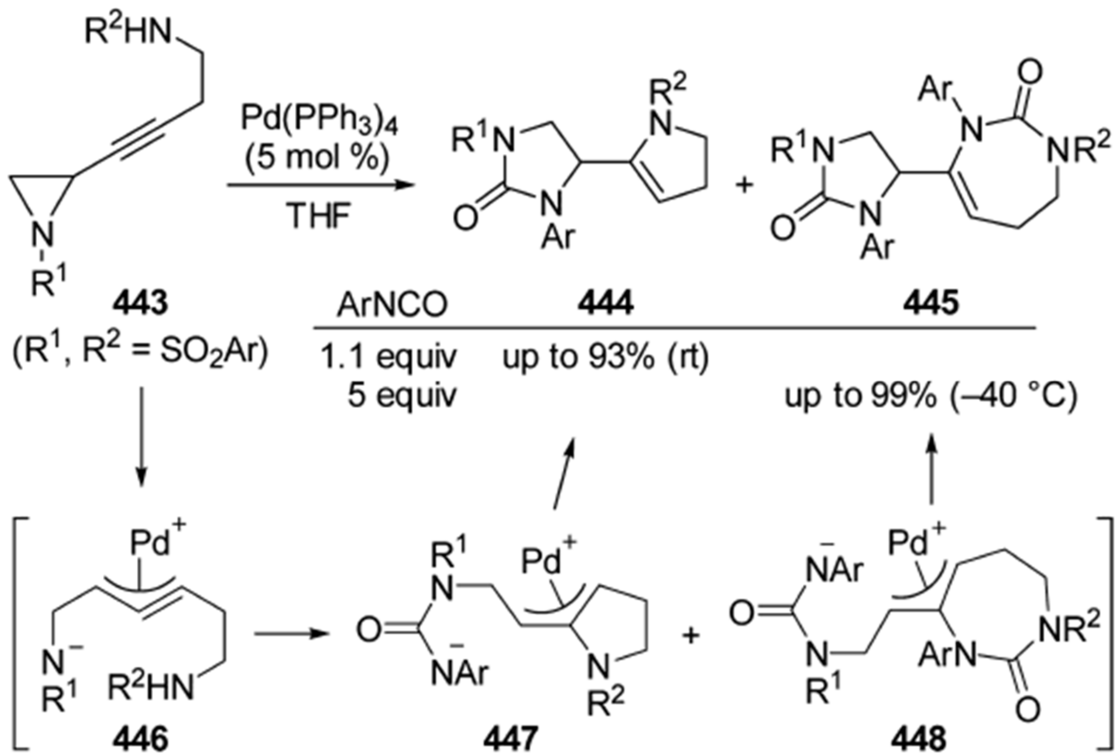


Blanc, A.; Pale, P. *et al*. *Chem. Commun*. **2011**, *47*, 6665.
J. Org. Chem. **2012**, *77*, 4323.

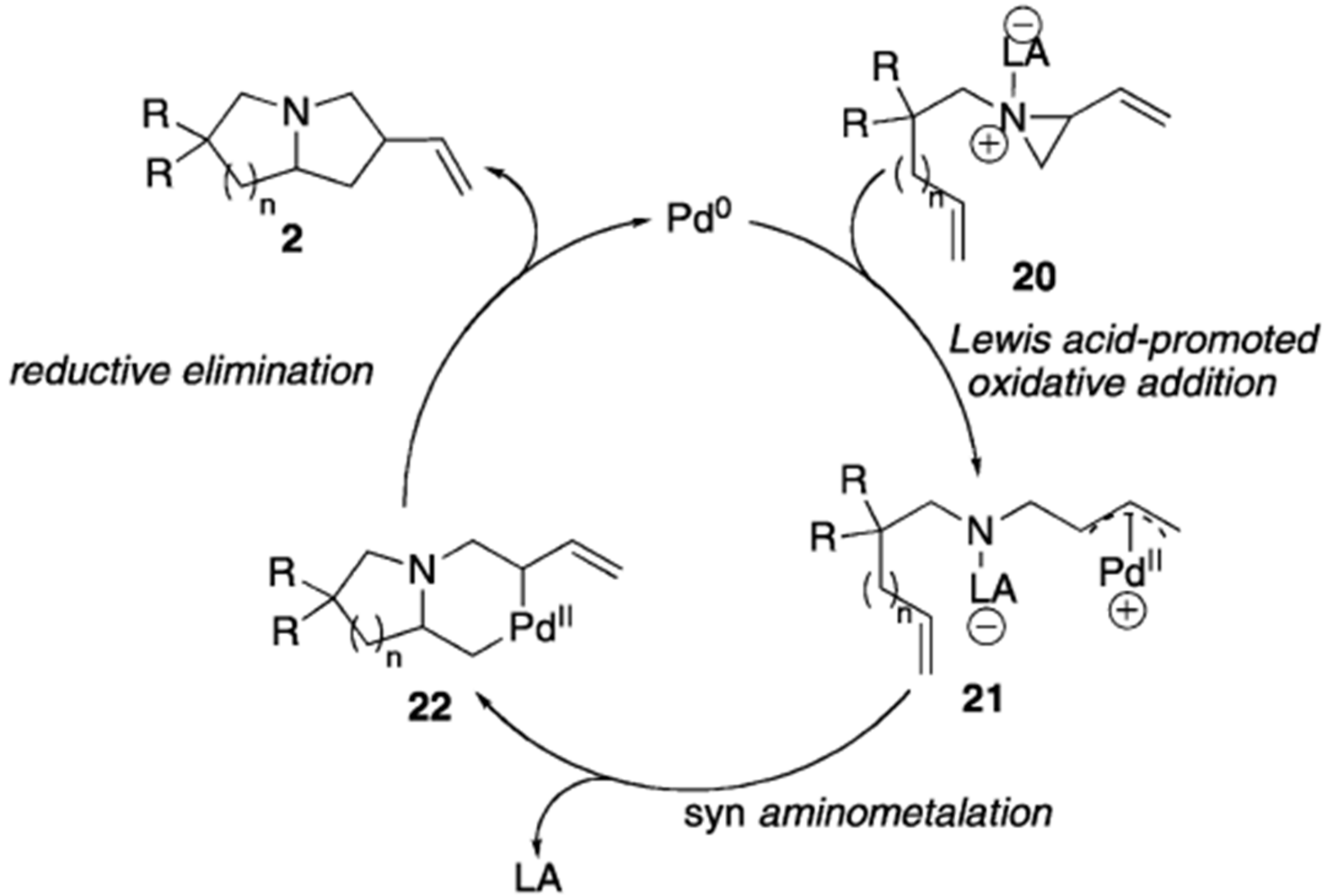




Rowlands, G. J.; Barnes, W. K. *Tetrahedron Lett.* **2004**, *45*, 5347.



Okano, A.; Oishi, S.; Tanaka, T.; Fujii, N.; **Ohno, H.** *J. Org. Chem.* **2010**, *75*, 3396.



Pd⁰
Lewis acid-promoted oxidative addition
syn aminometalation
reductive elimination
LA
Pd^II
2
20
21
22