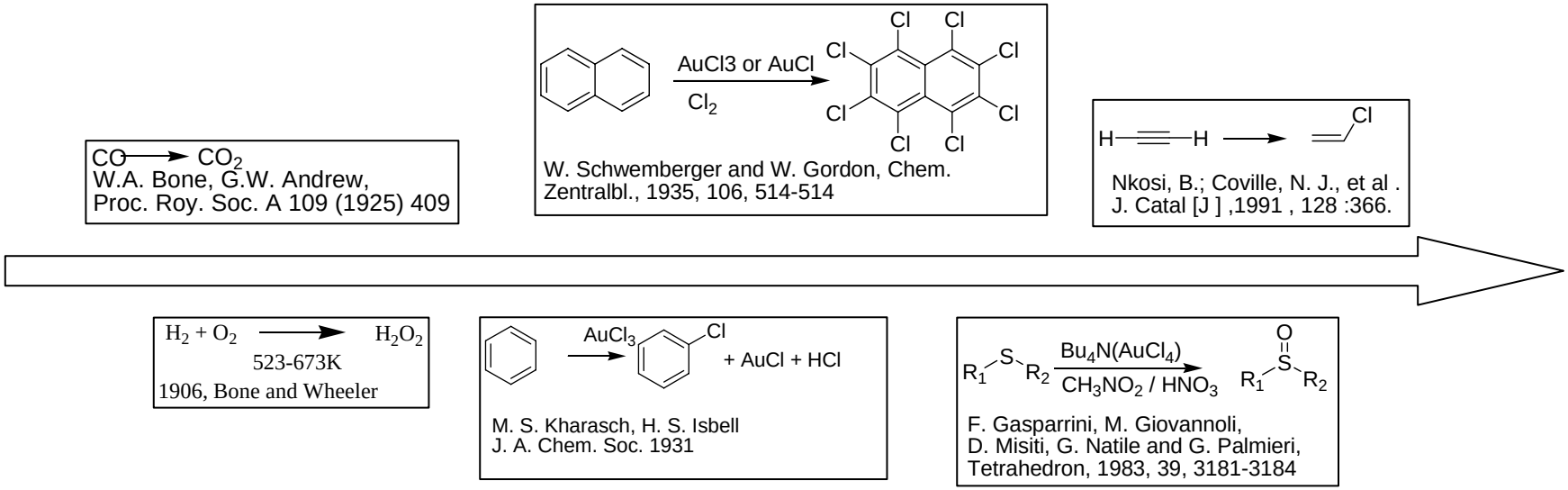
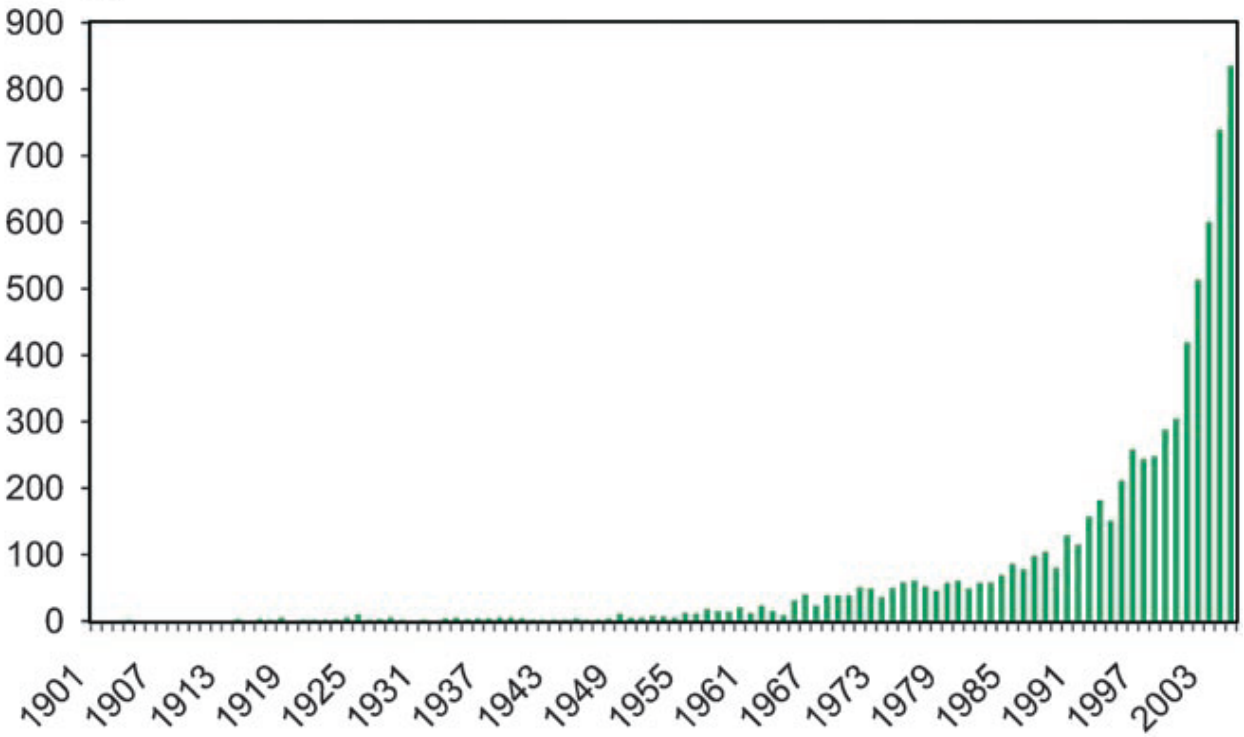
Classical Reactions in Homogenous Gold Catalysis

Rahmani Raphaël
18/10/07

Gold in Chemist history



An increasing interest

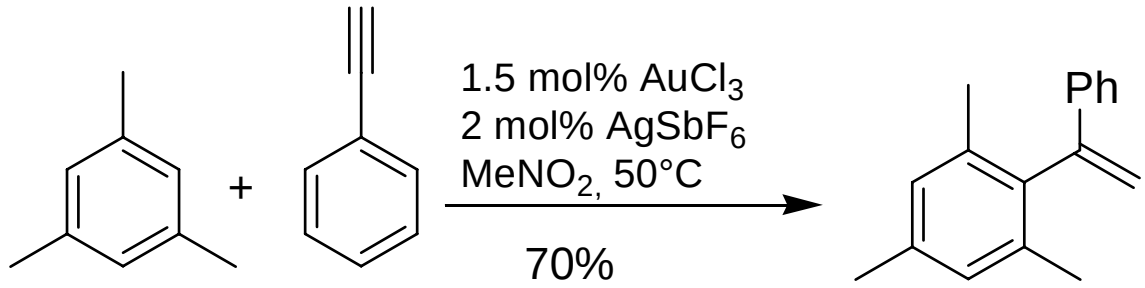


Number of publications on “gold catalysis” from 1900 to May 2006

A. Stephen K. Hashmi and Graham J. Hutchings, *Angew. Chem. Int. Ed.* **2006**, 45, 7896

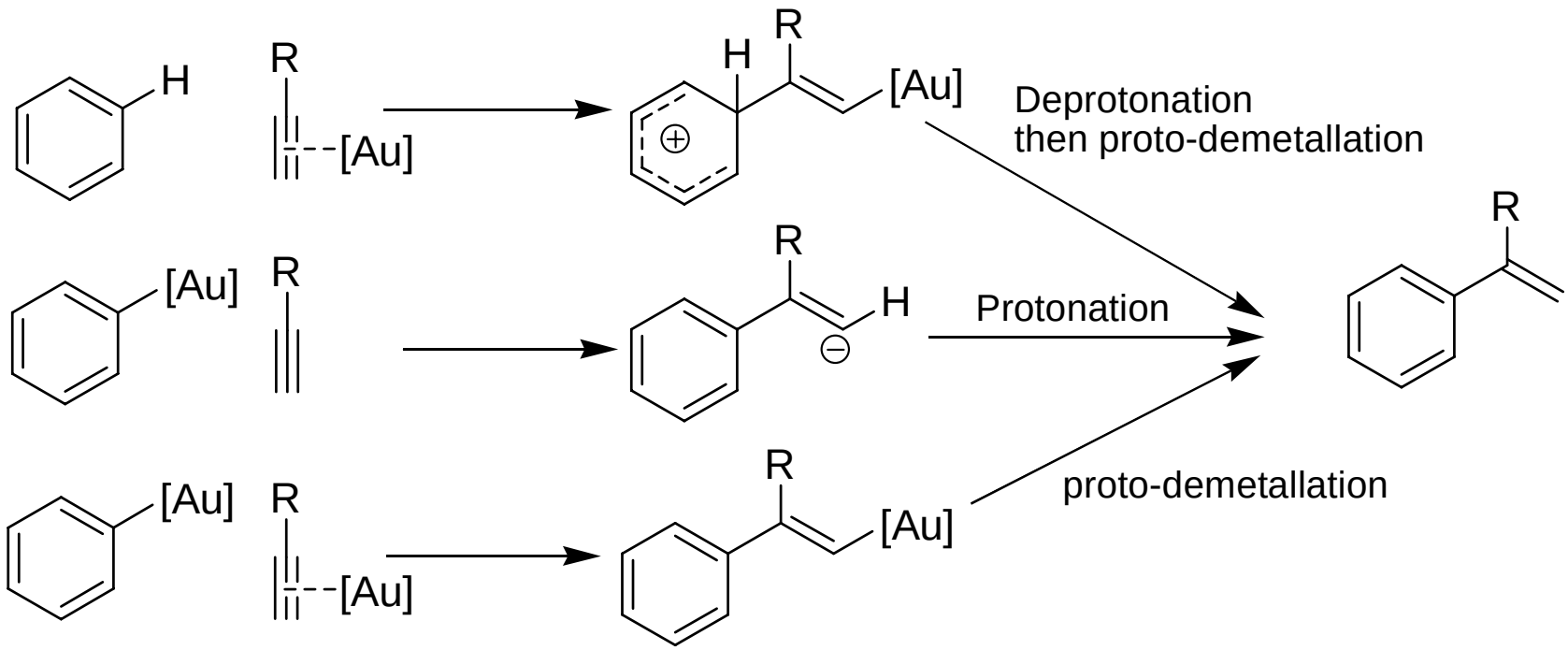
Gold and Hydroarylations

Hydroarylation



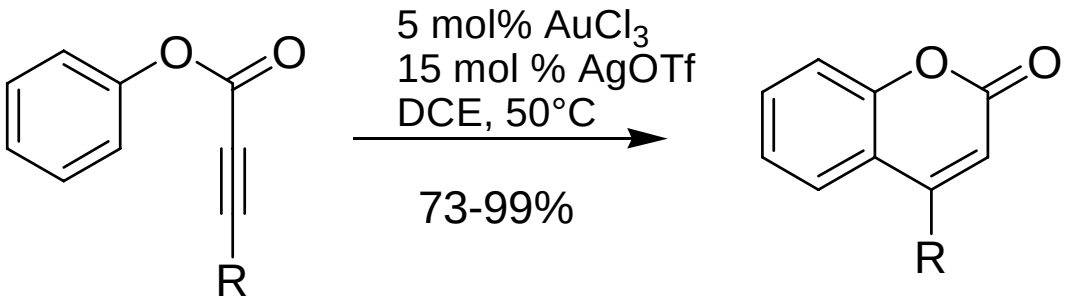
Reetz, M.T.; Sommer, K. *Eur. J. Org.Chem.* **2003,** 68, 3385

Hydroarylation : Mechanism



Reetz, M.T.; Sommer, K. *Eur. J. Org.Chem.* **2003**, 68, 3385

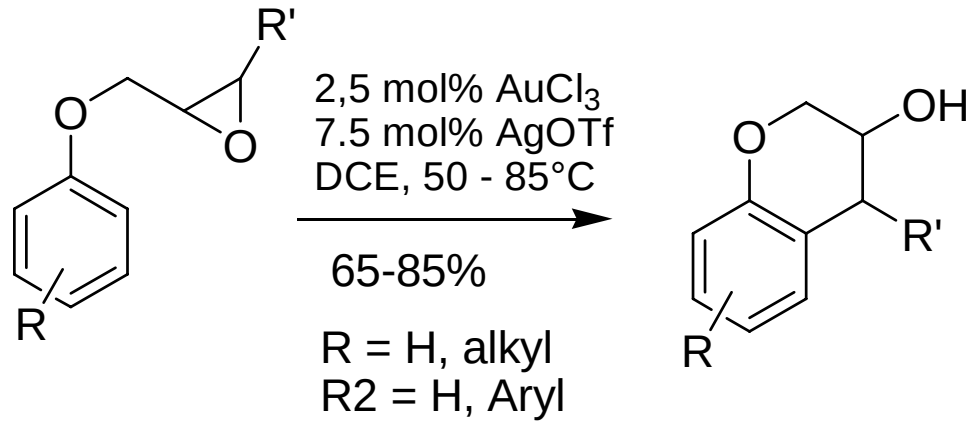
Application : Synthesis of Coumarines

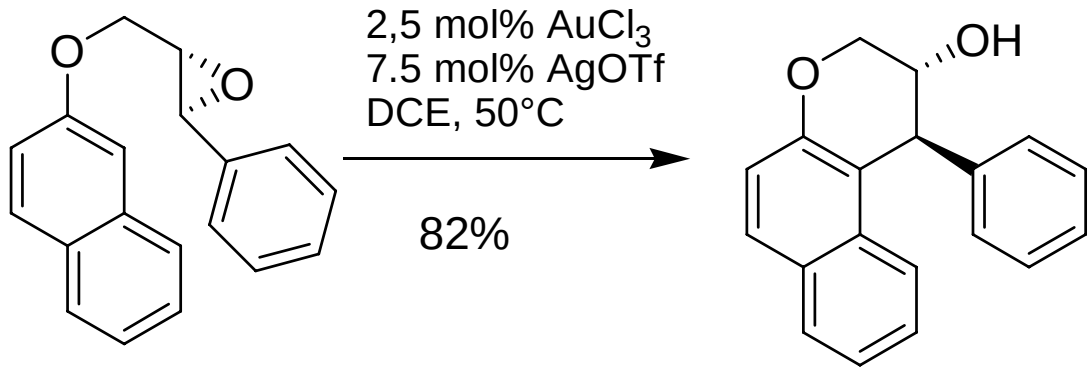


R = H, Me, Ph

Shi, Z.; He, C. *J. Org.Chem.* **2004**, 69, 3669

Hydroarylation : Reactivity with Epoxides

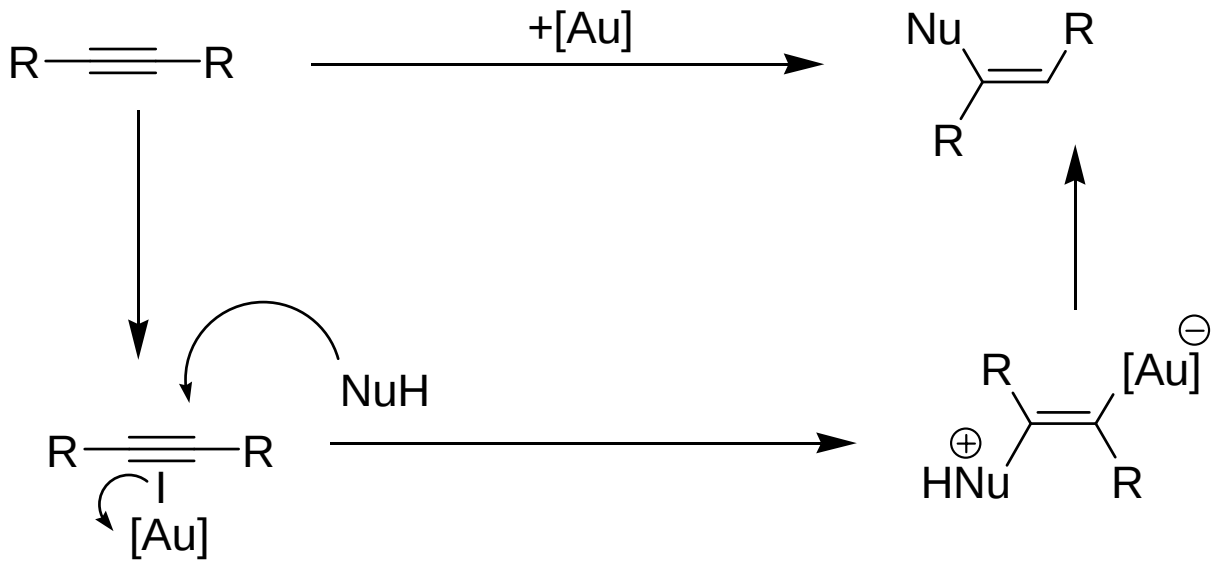




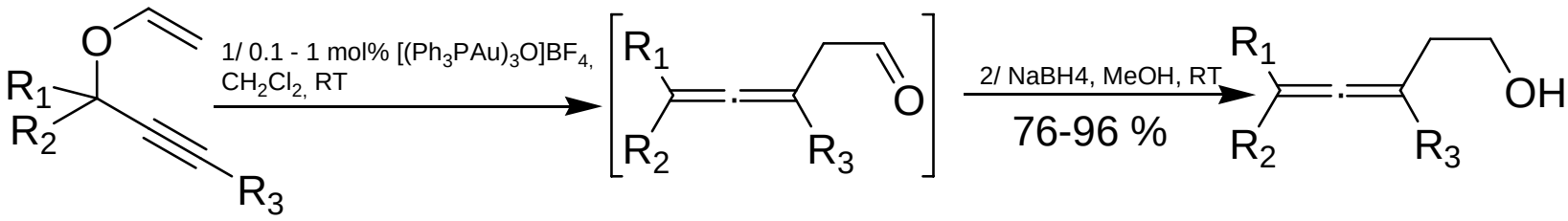
Shi, Z.; He, C. *J. Org.Chem.* **2004**, 69, 3669

Nucleophilic addition to C-C multiple bond

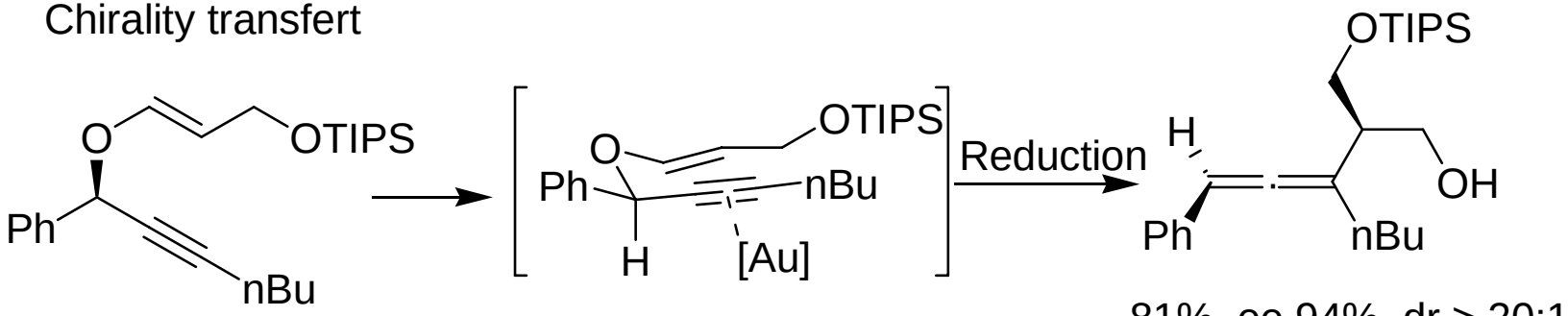
General mechanism for nucleophilic addition



Claisen Rearrangement

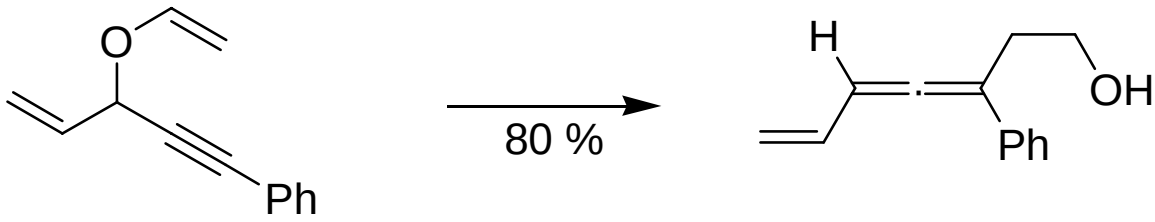


Chirality transfert



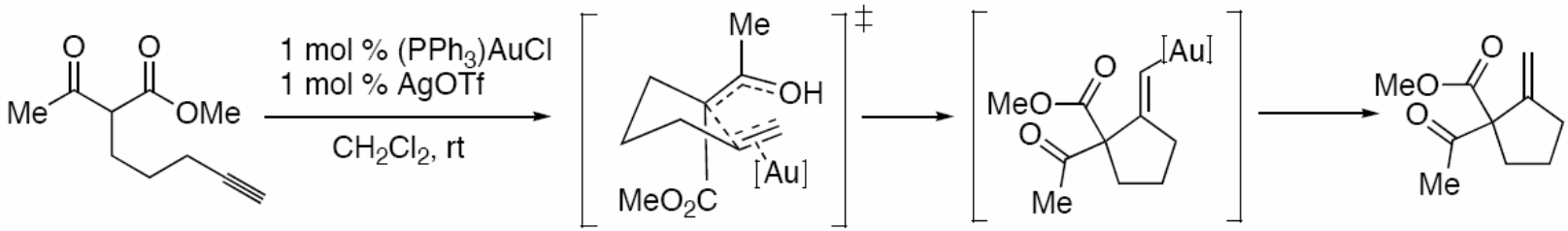
81%, ee 94%, dr > 20:1

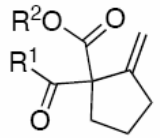
Selectivity for propargylic



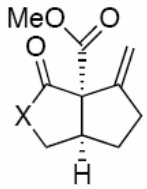
Sherry, B.D.; Toste, F.D., *J. Am. Chem. Soc.* **2004**, 126, 15978

Conia-Ene Reaction of β-Ketoesters

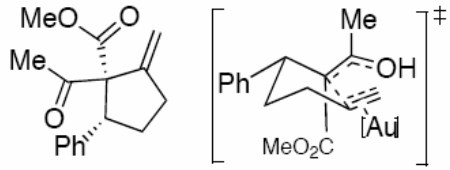




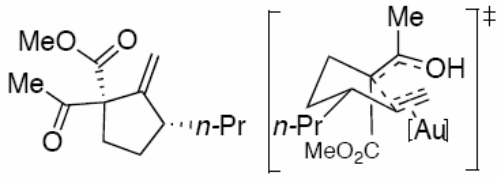
R^1	R^2	Yield (%)
Me	Me	94
Ph	Et	93
Me	*t*-Bu	81
Me	CH_2CCH	79



90%



95%, 4.2:1 dr

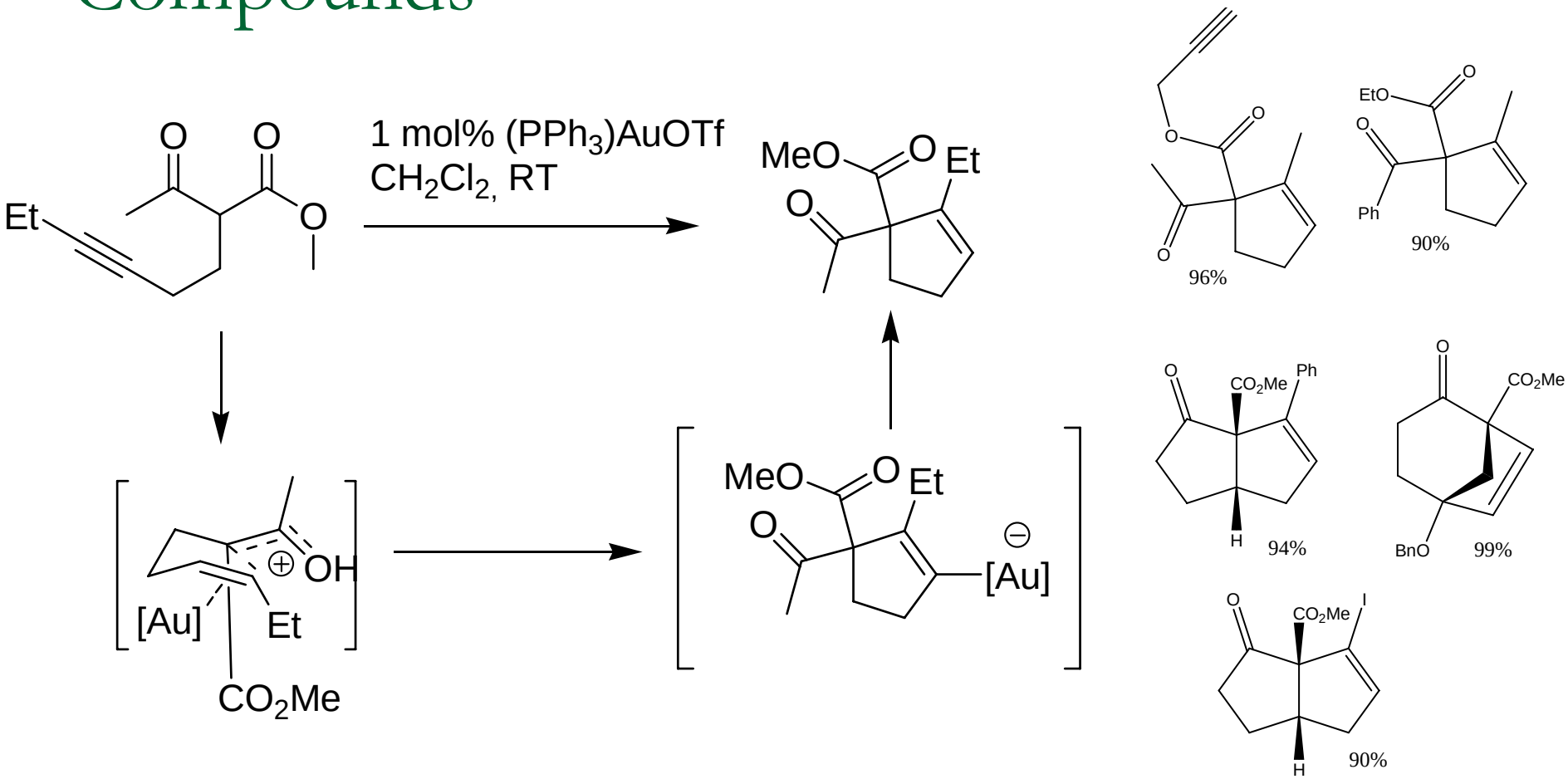


97%, 2.9:1 dr

Mechanism confirm with a deuterium study
Works with terminal alkyne only

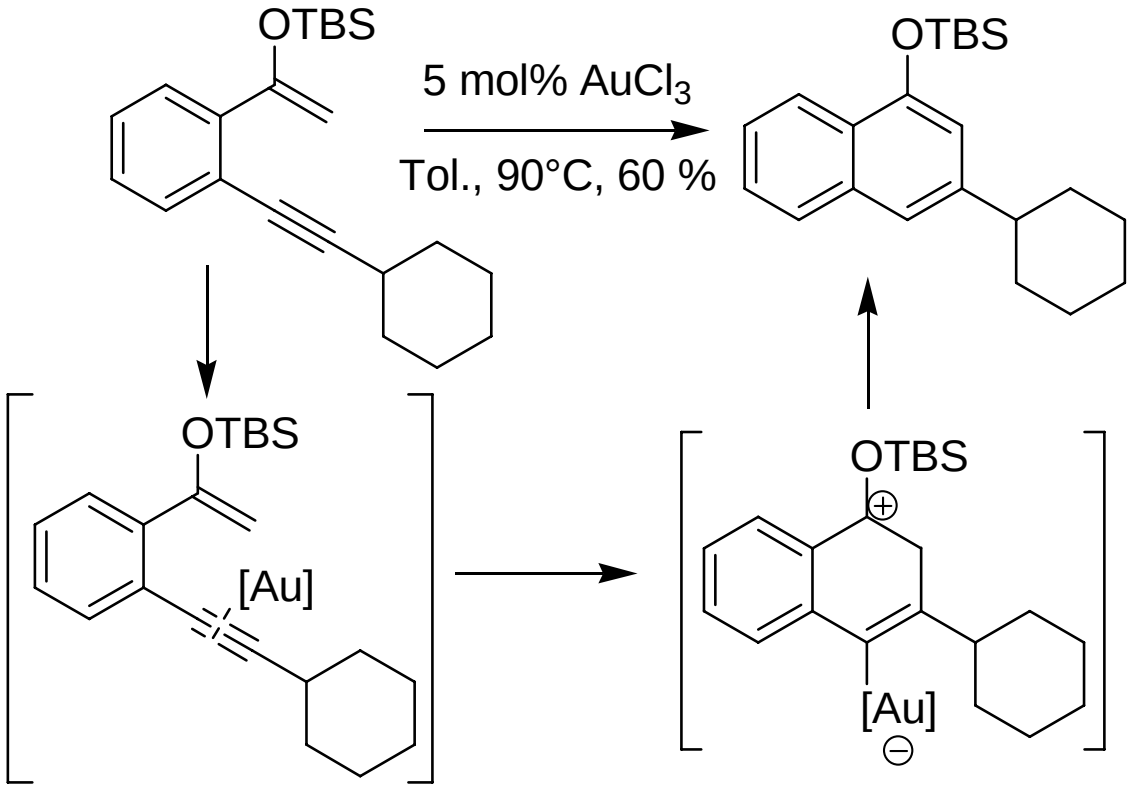
Kenedy-Smith, J.J.; Staben, S.T., Toste, F.D. *J. Am. Chem. Soc.* **2004**, 126, 4526

Carbocyclization of Acetylenic Dicarbonyl Compounds



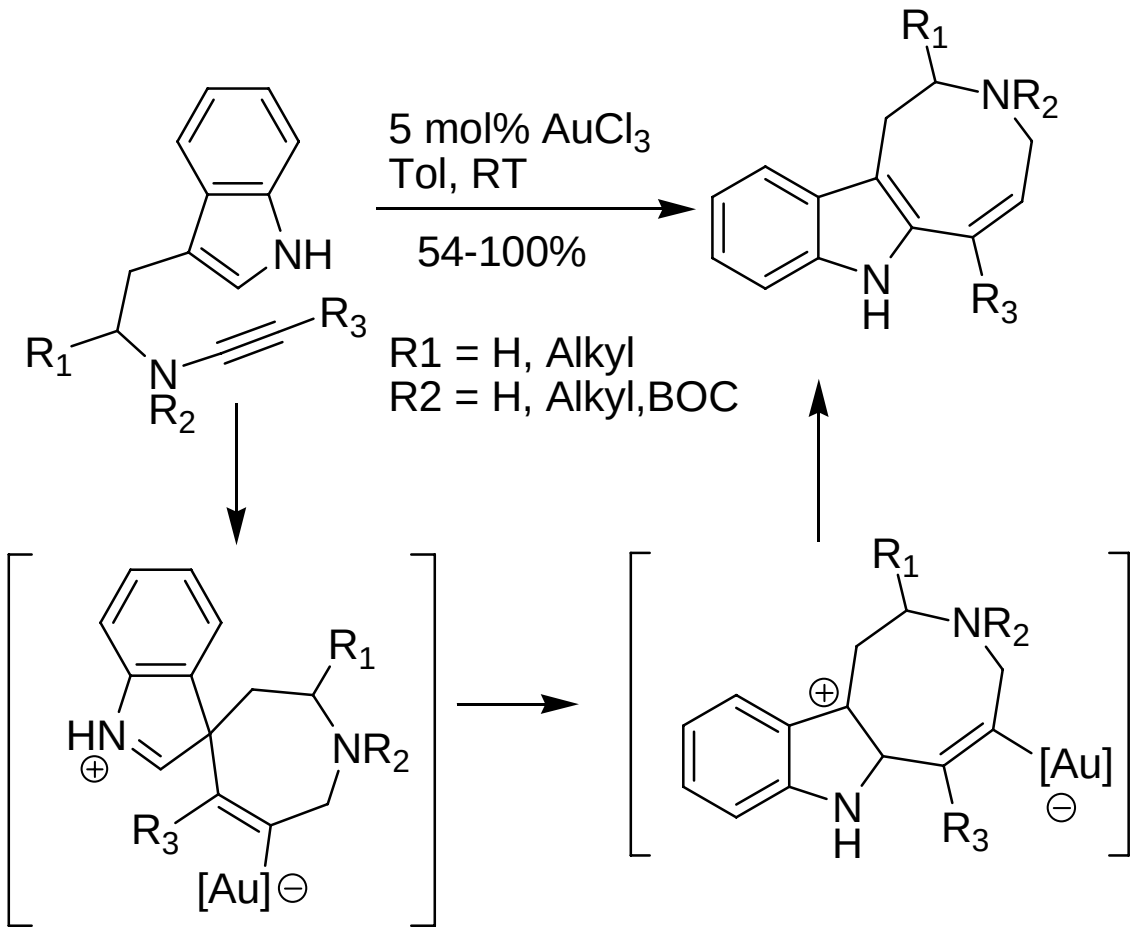
Staben, S.T., Kenedy-Smith, J.J.; Toste, F.D. *J. Am. Chem. Soc.* **2004**, 126, 5350

Cyclization of silyl enol



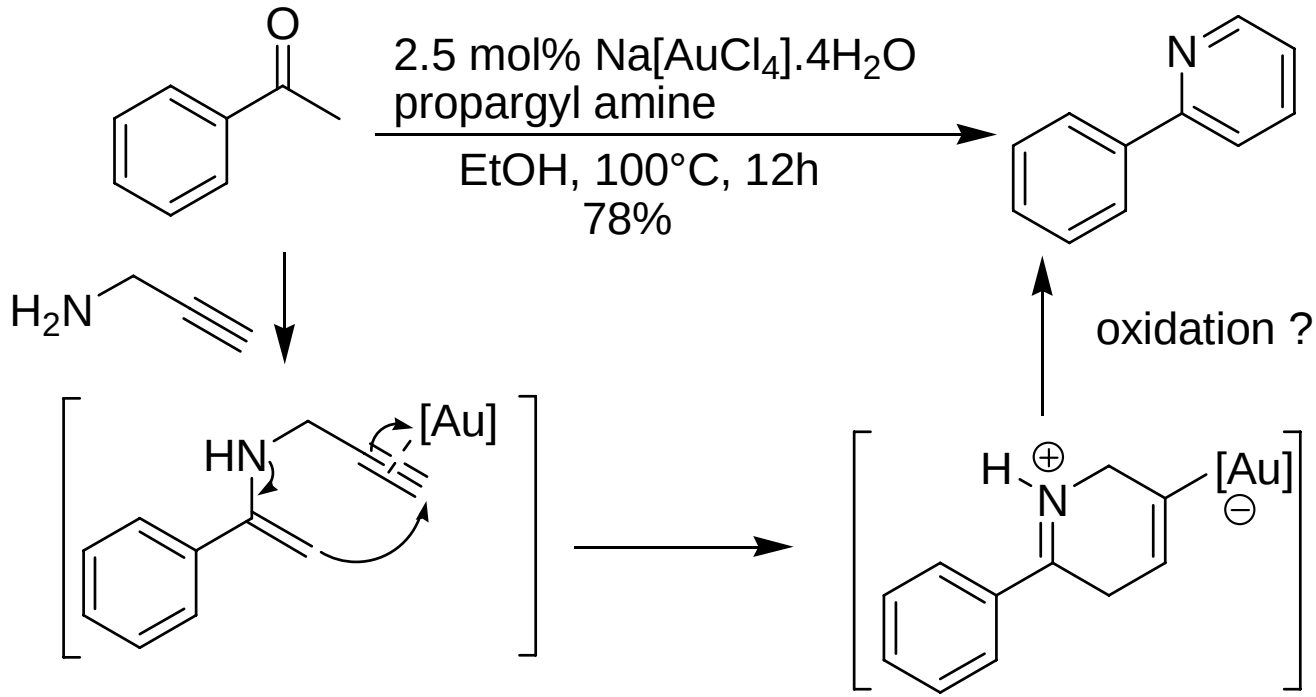
Dankwardt, J.W. *Tetrahedron Lett.* **2001**, 42, 5809

Cyclization of Enamines



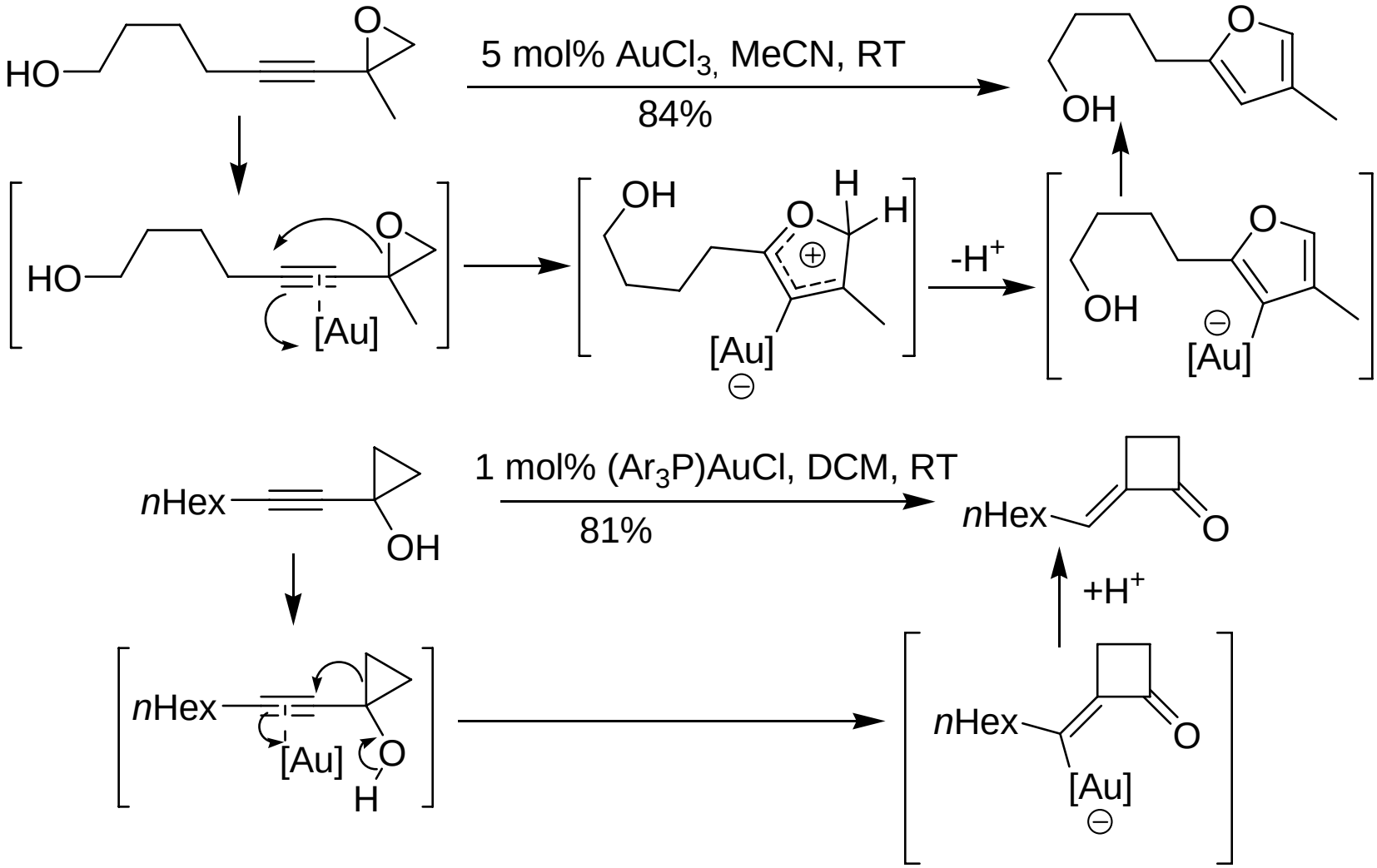
Ferrer, C.; Echavarren, A.M. *Angew. Chem. Int. Ed.* **2006**, 45, 1105

Synthesis of Pyridines



Abbiati, G. *et al J. Org. Chem.* **2003**, 68, 6959

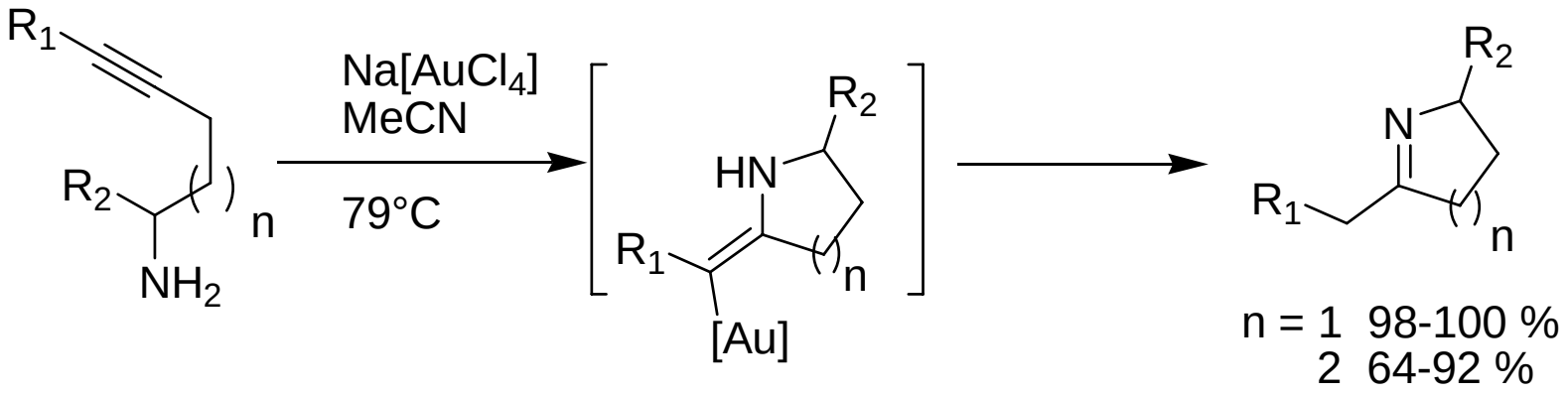
Ring Enlargement Reactions



Hasmi, A.S.K; Sinha, P. *Adv. Synth. Cat.* **2004**, 346, 432

Markham, J.P.; Staben, S.T., Toste, F.D. *J. Am. Chem. Soc.* **2005**, 127, 9708

Intramolecular hydroamination

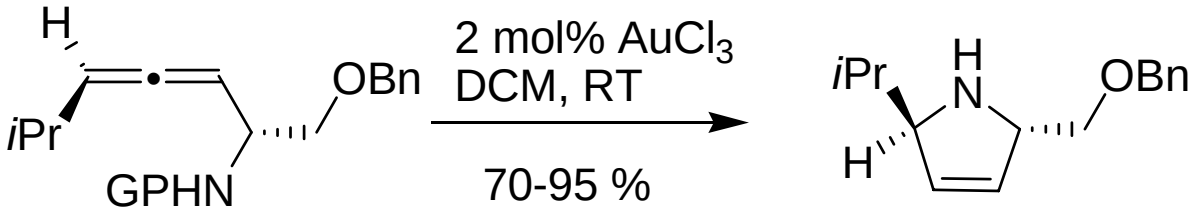


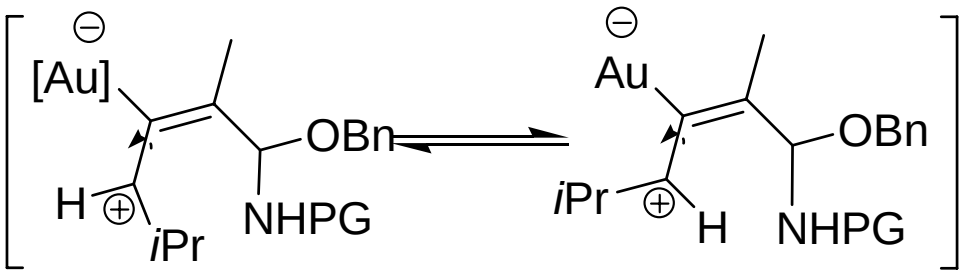
n = 1	
R1	R2
hept	H
hex	Me
hept	Me
oct	H

n = 2	
R1	R2
hex	H
et	H
pent	H
ph	H
H	Hex
H	Undec

Fukuda, Y.; Utimoto, K.; Nozaki, H. *Heterocycles* **1987**, *25*, 297
Fukuda, Y.; Utimoto, K. *Synthesis* **1991**, 975

Cyclization of allenyl amines

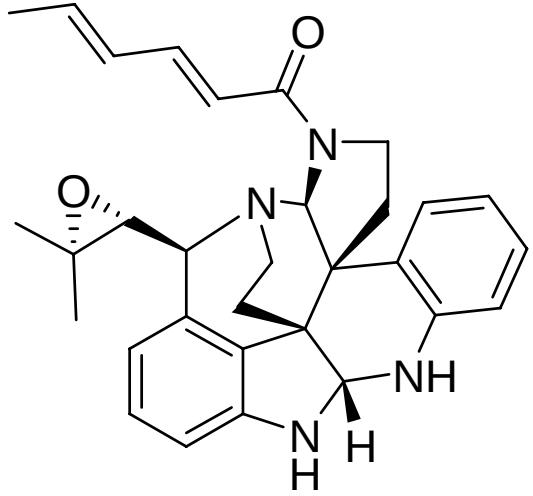




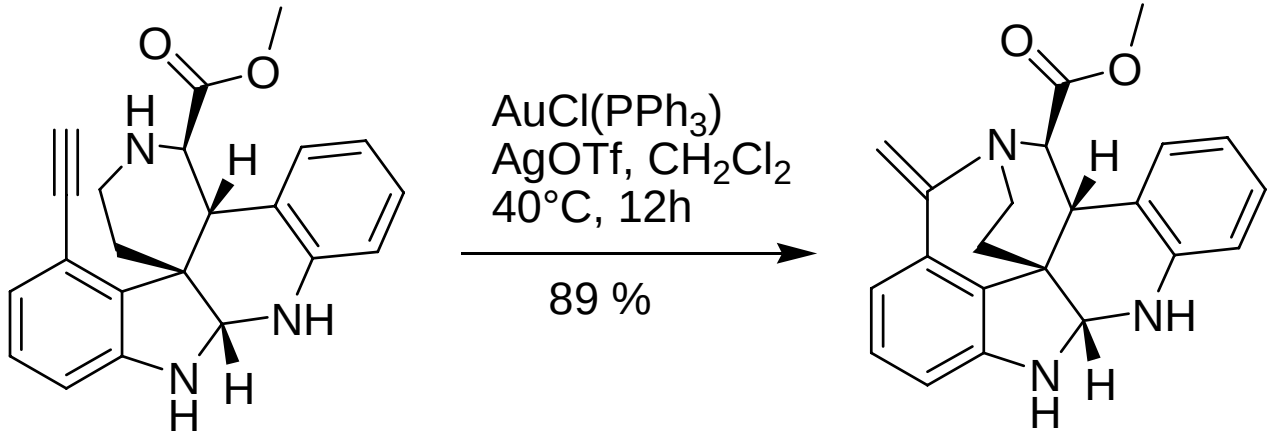
PG	time	dr
H	5 days	>99:1
Ms	30 min	94:6
Ts	-	95:5
Ac	-	70:30
Boc	-	46:54

Morita, N.; Krause, N. *Org Lett* **2004**, 6, 4121

Application : Communesin B Total Synthesis

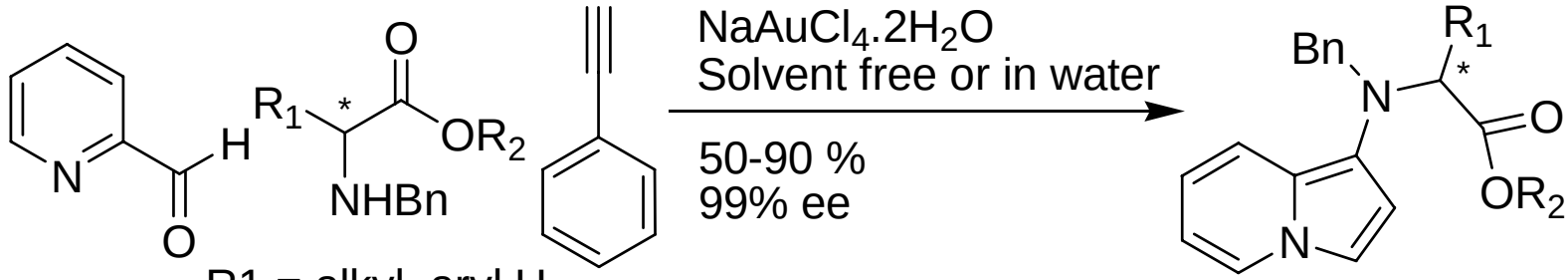


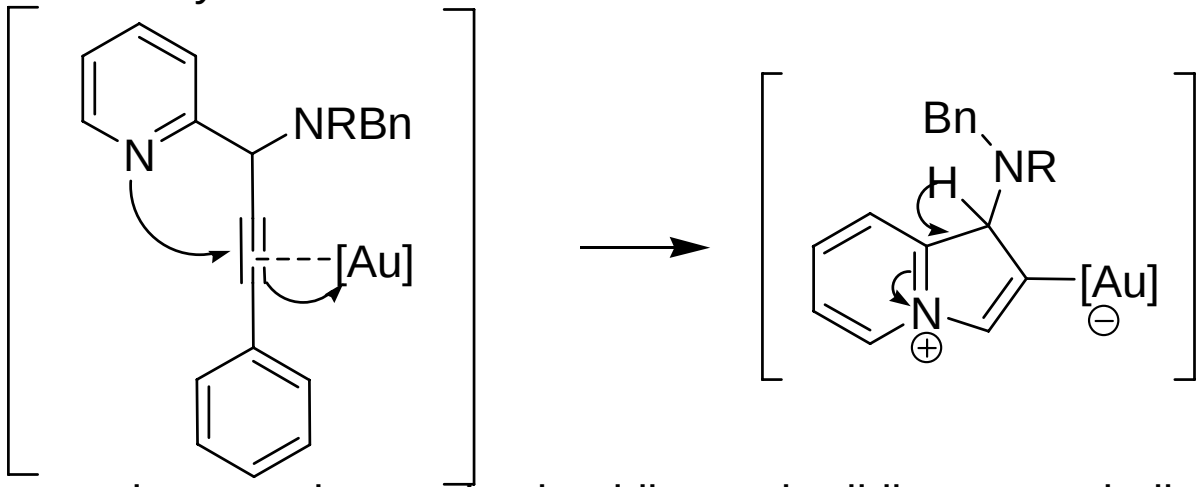
Communesin B



Seth L. Crawley & Raymond L. Funk, *Org. Lett.* **2006**, 18, 3995

Multicomponent Synthesis of aminoindolines



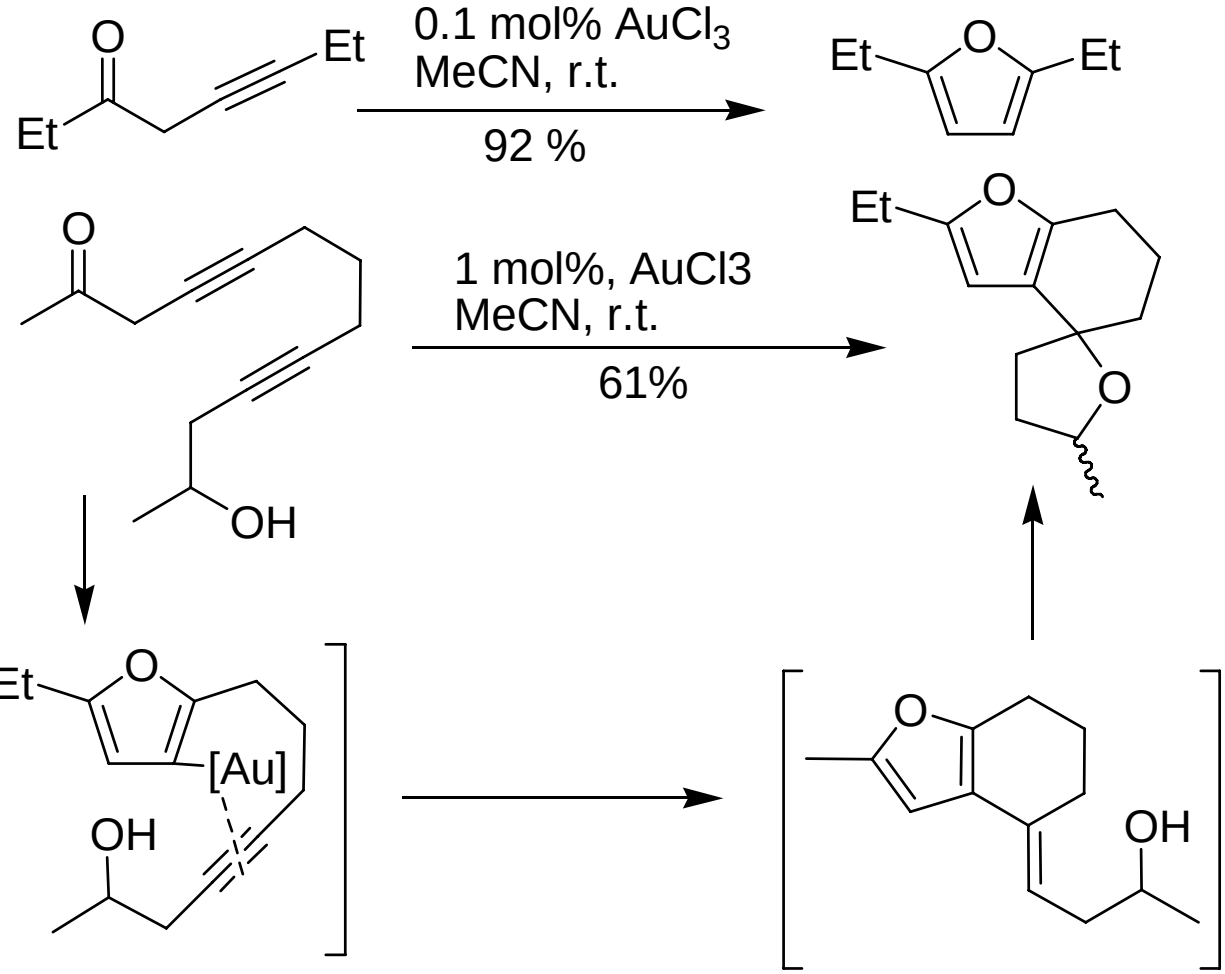


Other amines can be used : piperidines, pirrolidines, morpholine...

Bin Yan & Yuanhong Liu *Org. Lett.* **2007**, 9, 4323

Synthesis of Furane

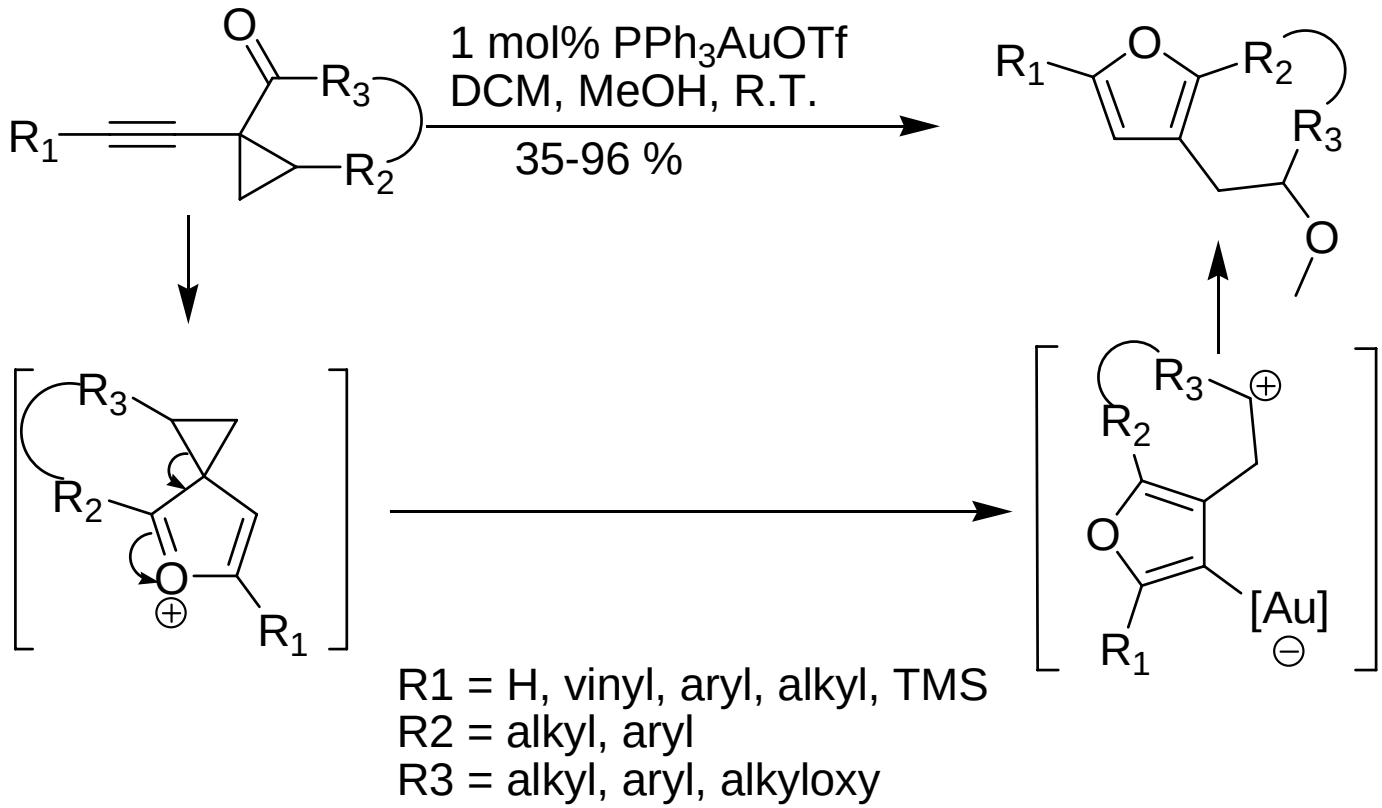
Rearrangement of alkynones



Hashmi, A.S.K. *et al Angew. Chem. Int. Ed.* **2000**, 39, 2285

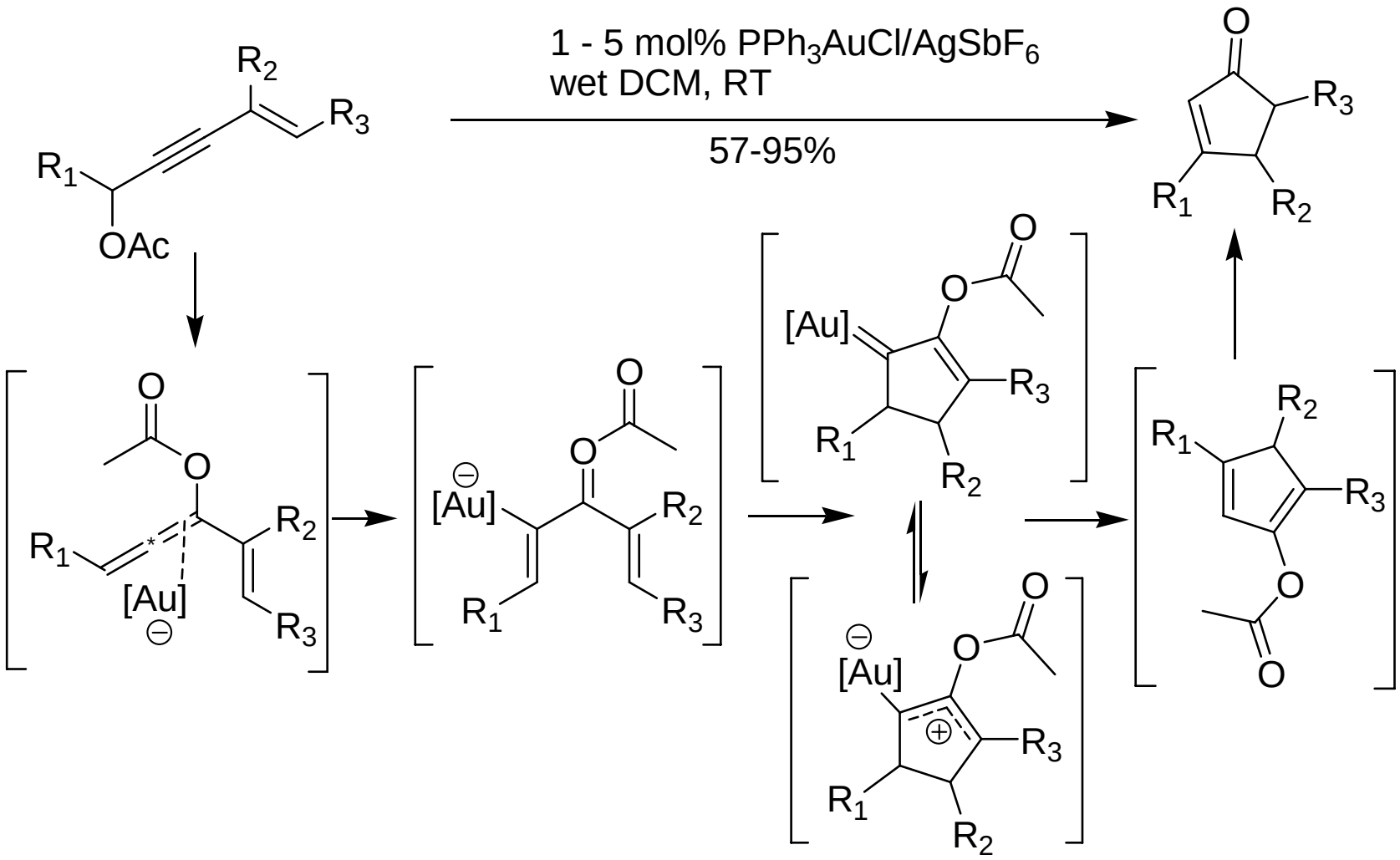
Synthesis of Furane

Rearrangement of alkynones cyclopropanes



Zhang *et al Angew. Chem. Int. Ed.* **2006**, 45, 6704

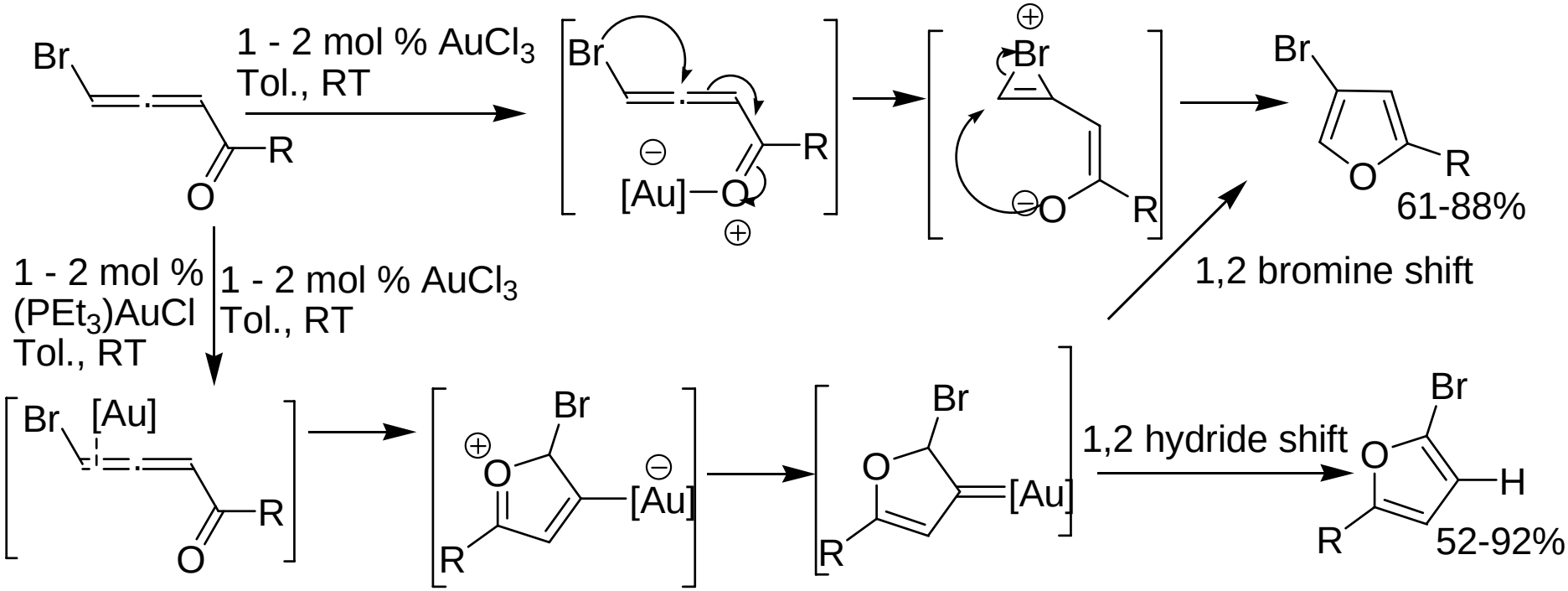
Nazarov-like Reaction



Zhang, L.; Wang, S. *J. Am. Chem. Soc.* **2006**, 128, 1442

Synthesis of 1-bromo-Furane

Rearrangement of allenyl ketones

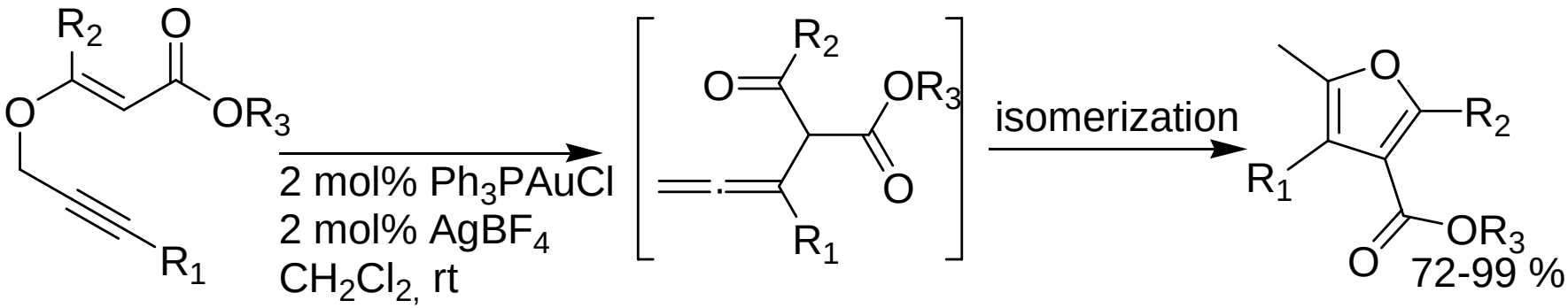


Oxidation state of Au is important for the reaction pathway

Possible with I or Cl

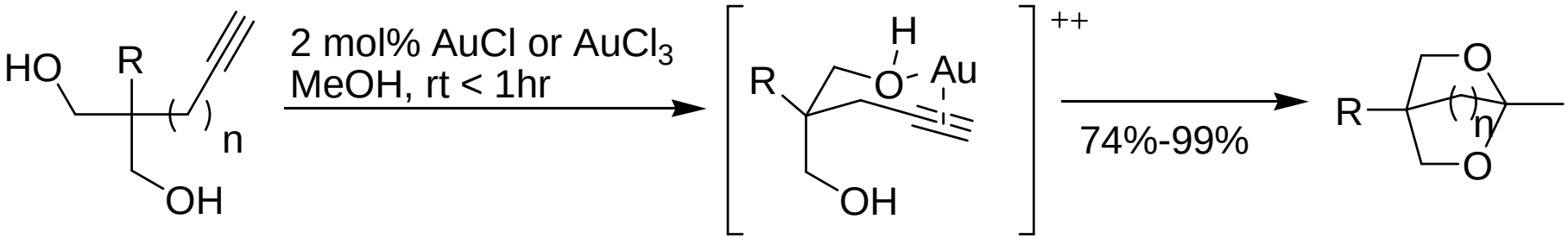
Sromed, A.W.; Rubina, M.; Gevorgyan, V. *J. Am. Chem. Soc.* **2005**, 127, 10500

Domino Claisen/ Allene Cyclisation



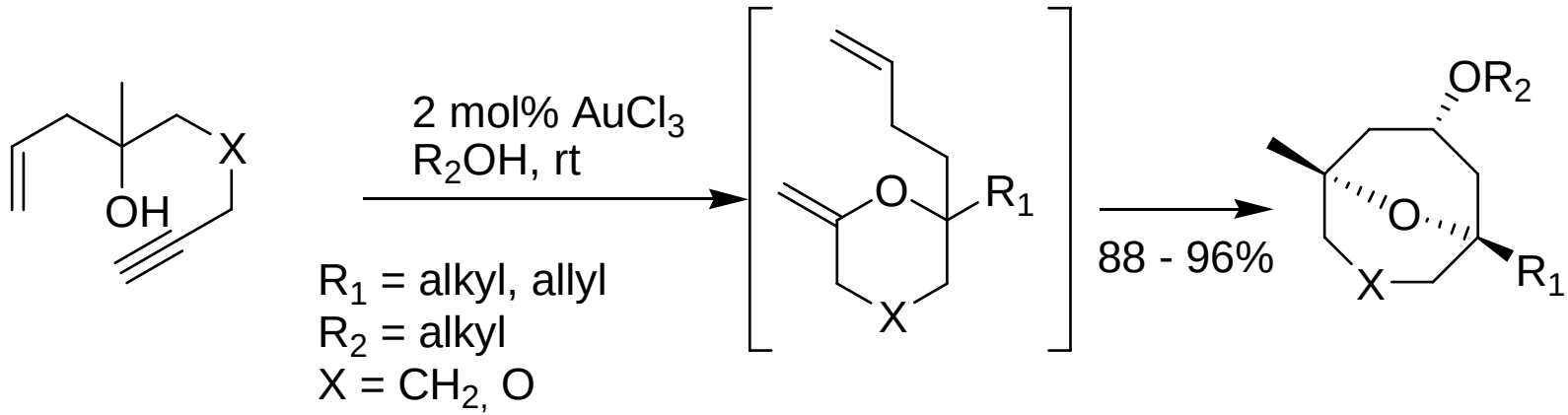
Suhre, M.H.; Reif, M.; Kirsch, S.F. *Org. Lett.* **2005**, 7, 3925

Cycloisomerization of Bis-homopropargylic Diols[1]



R = Bn, Ph, But, Cinnamyl, allyl

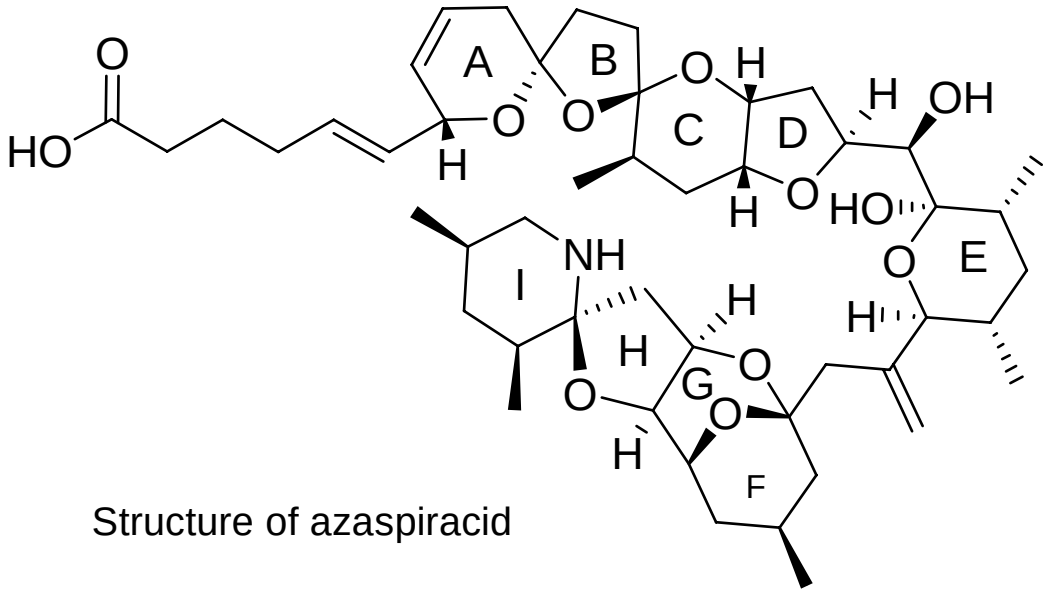
Formation of bicyclo[3.3.1]octane[2]



R_1 = alkyl, allyl
R_2 = alkyl
X = CH_2, O

[1] Antoniotti, S.; Genin, E.; Michelet, V.; Genet, J. *J. Am. Chem. Soc.* **2005**, 127, 9976
[2] Barluenga, J. *et al Angew. Chem., Int. Ed.* **2006**, *45*, 2091

Application, Synthesis of A-D rings of Azaspiracid



Structure of azaspiracid

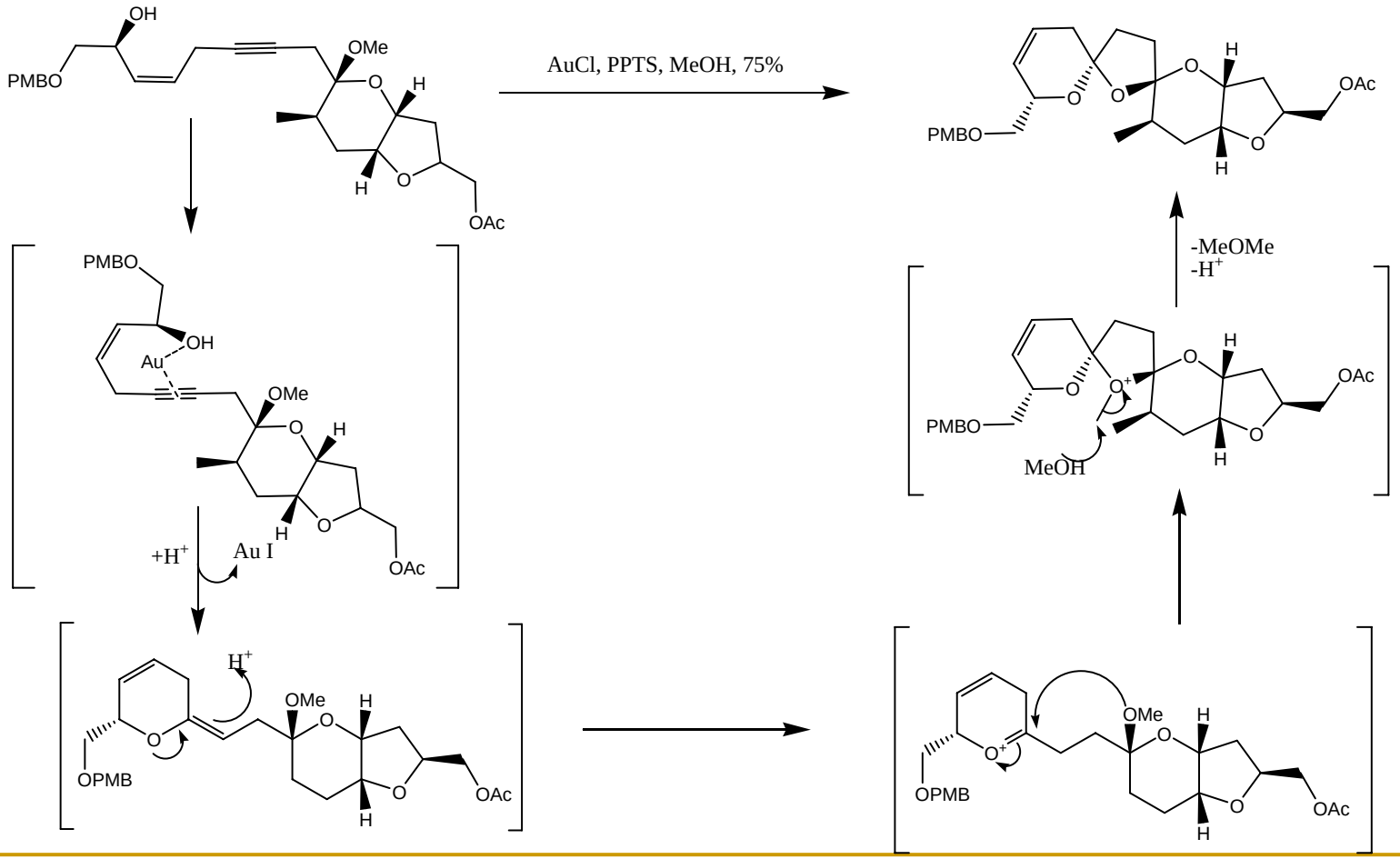
Toxin responsible for human poisonings in the Nederlands in 1995

Neurotoxic and tumor-promoting potential

Two total synthesis (Nicolaou K.C., Evans D.A.)

Neurotoxic and tumor-promoting potential

Application, Synthesis of A-D rings of Azaspiracid

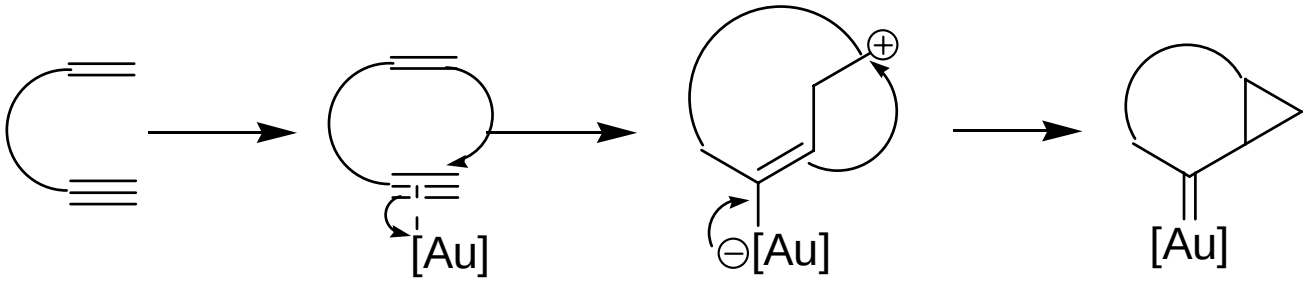


Forsyth *et al. Angew. Chem. Int. Ed.* **2007**, 46, 279

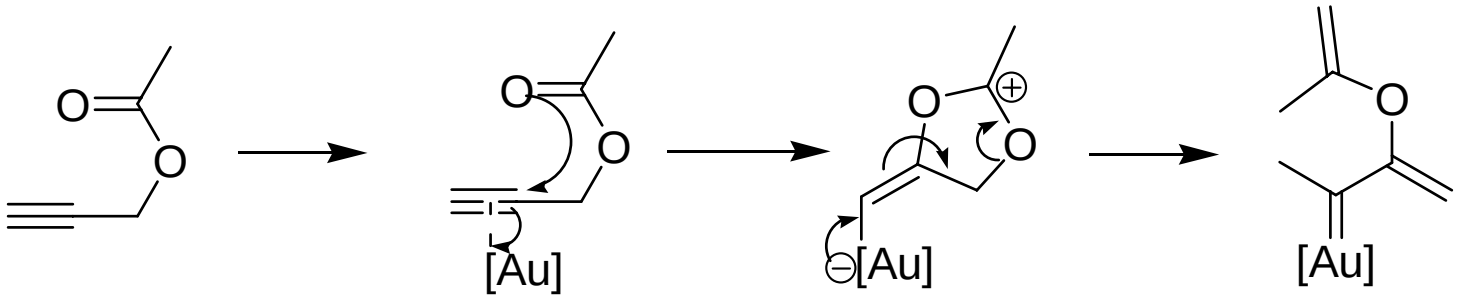
Gold Carbene Chemistry

Generation of Gold Carbenes

From alkynes and alkenes

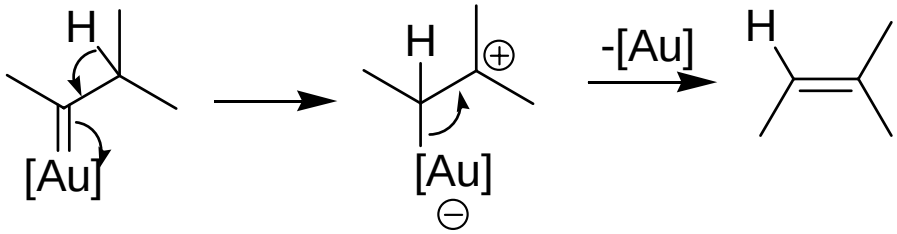


From propargyl carboxylates

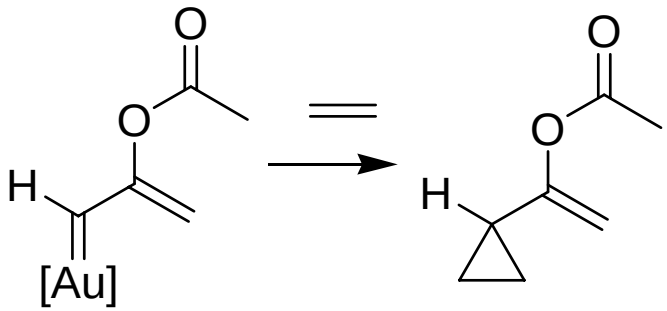


Elimination of Gold-Carbene

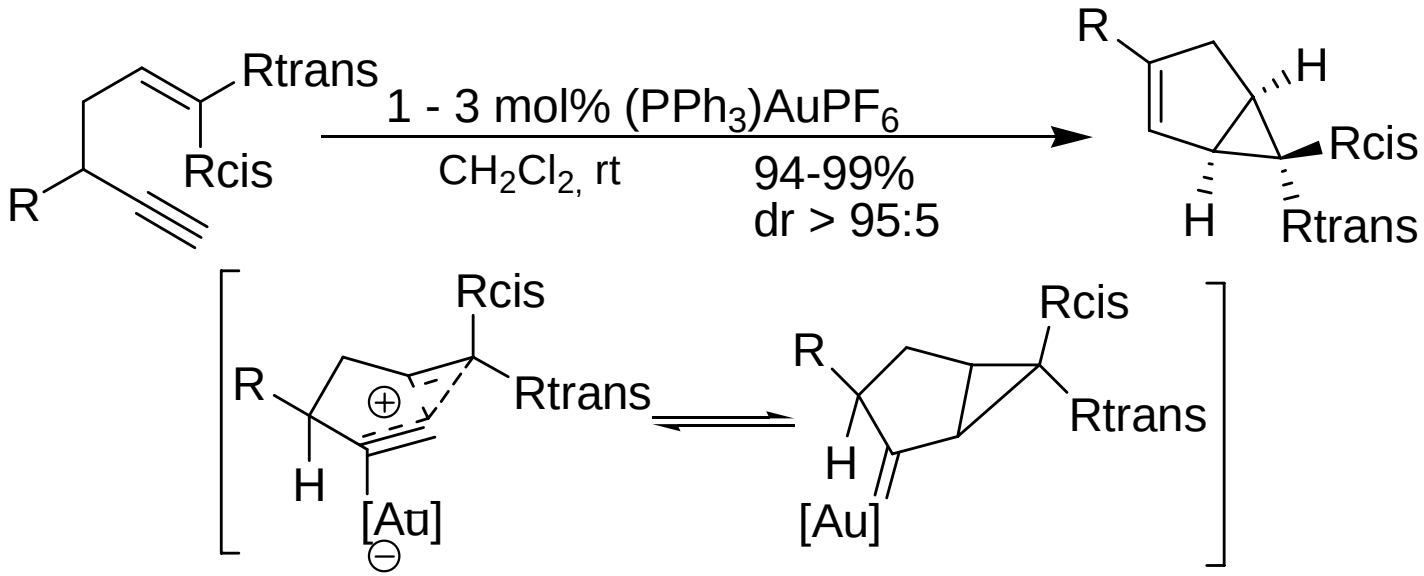
1,2 hydride shift

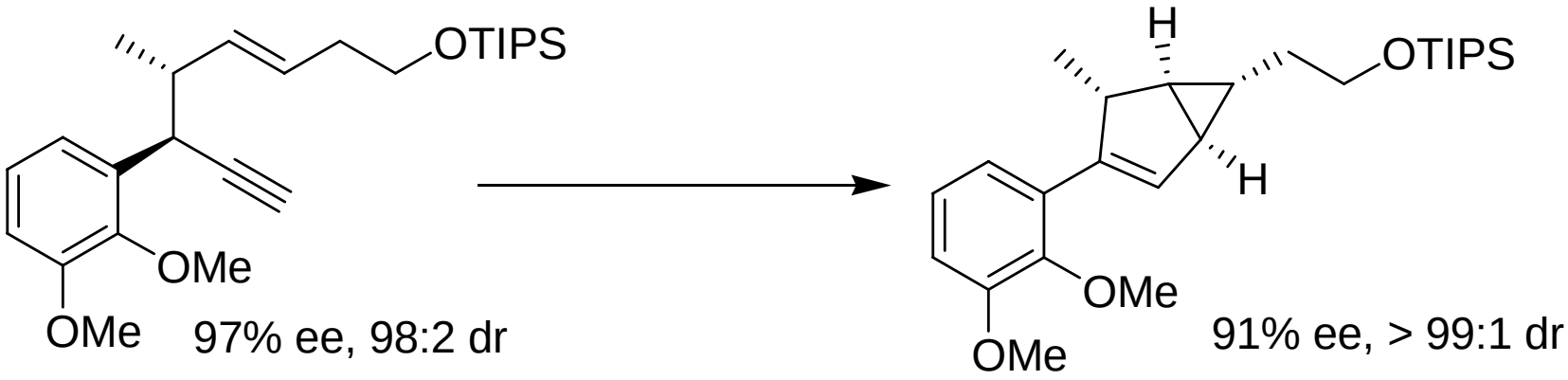


Cyclopropanation of alkene



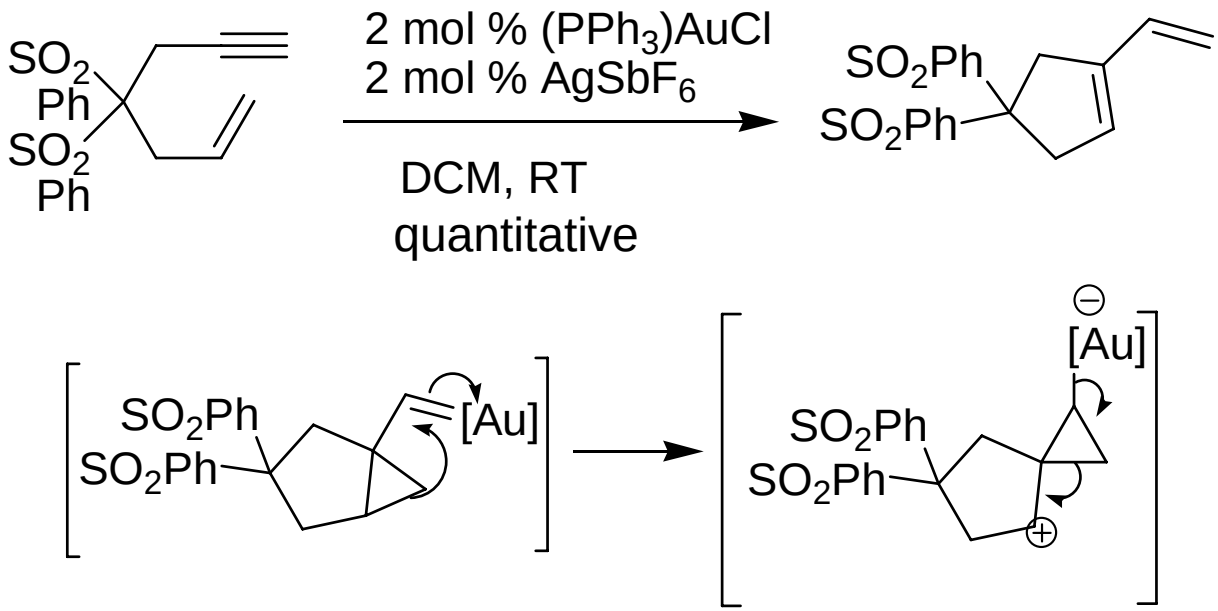
Enynes Cycloismerization





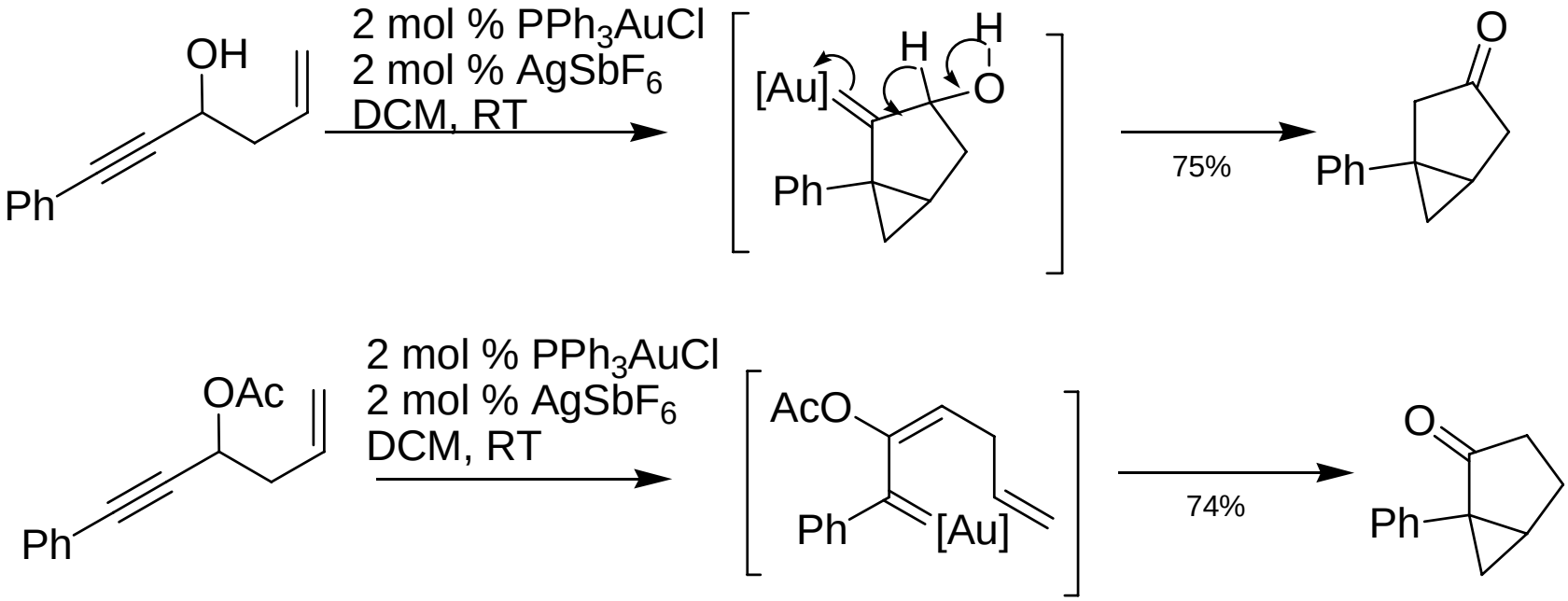
Luzung, M.R.; Markham, J.; Toste, F.D. *J. Am. Chem. Soc.,* **2004**, 126, 10858

Electron poor Enynes Cycloisomerization



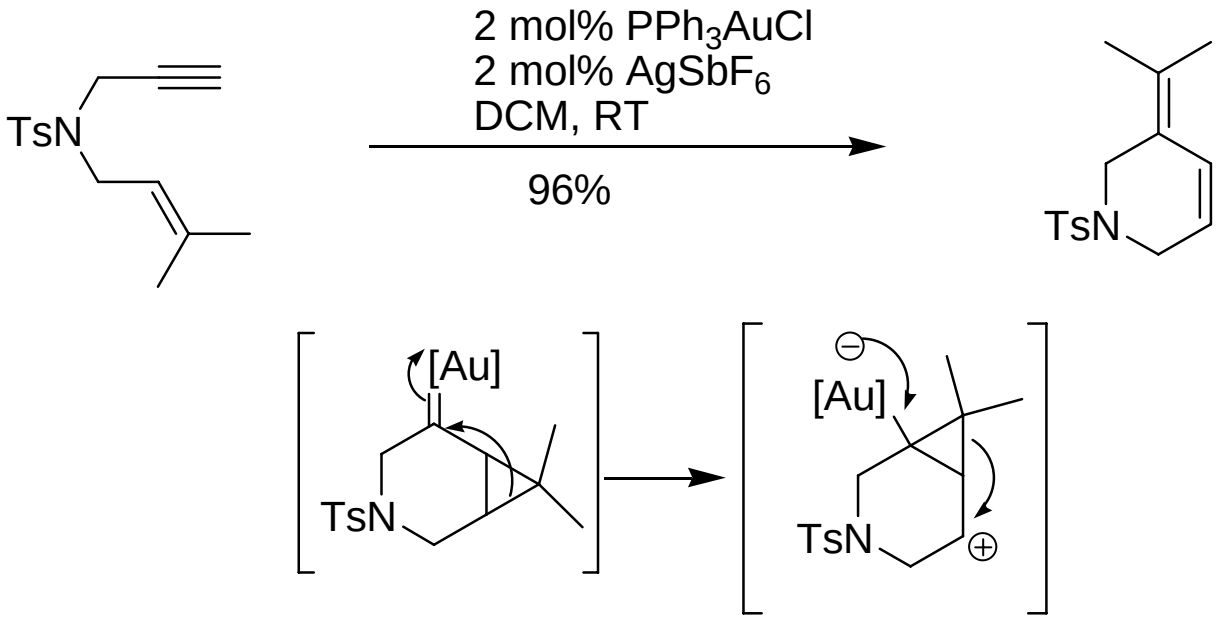
Echavarren, A.M. *et al Angew. Chem. Int. Ed.*, **2004**, 43, 2402

Another pathway for Cycloisomerizations



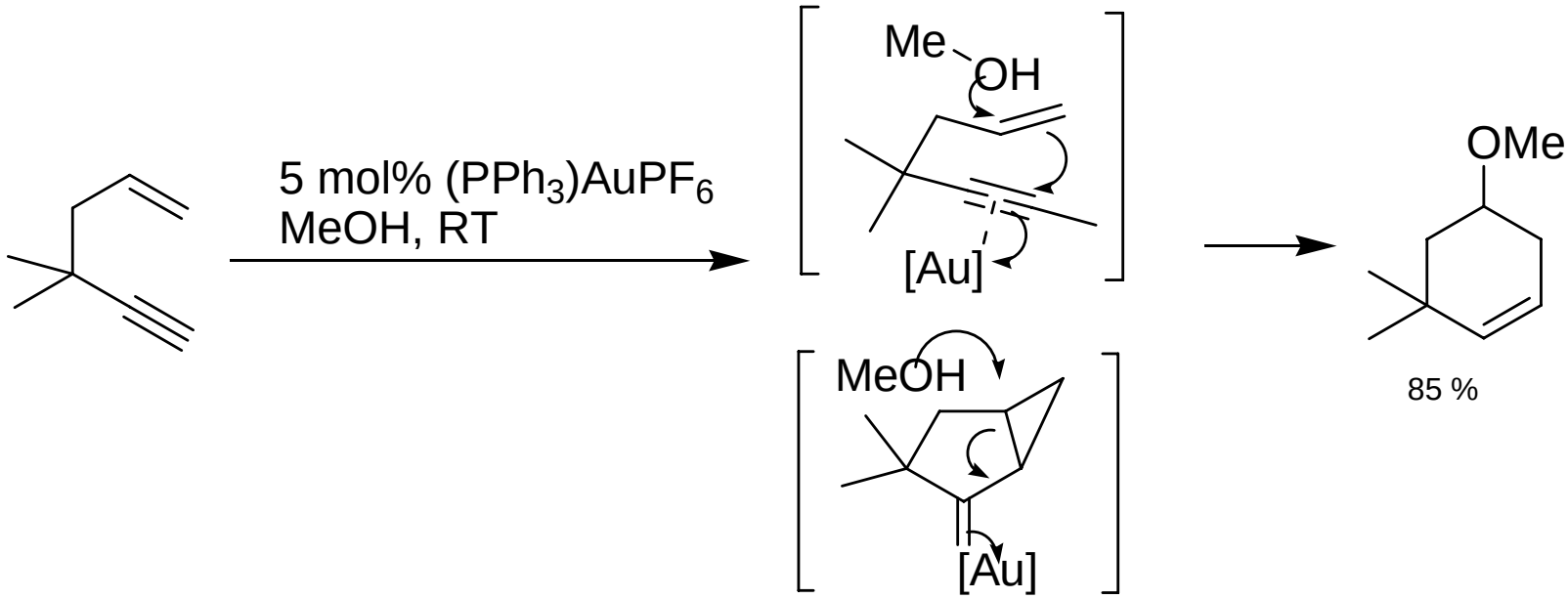
Mamane, V.; Gress, T.; Krause, H., Fürstner, A. *J. Am. Chem. Soc.,* **2004**, 126, 8054

Cyclization of Nitrogen Tethered Enynes



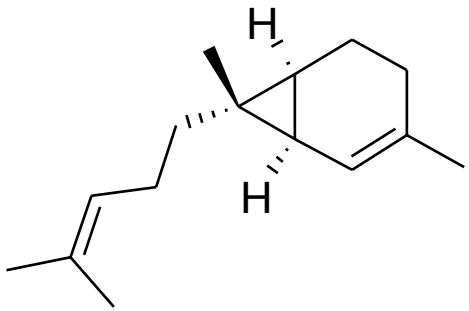
Nieto-Oberhuber, C. et al *Angew. Chem. Int. Ed.*, **2004**, 43, 2402

Nucleophilic Trapping of Gold Carbene

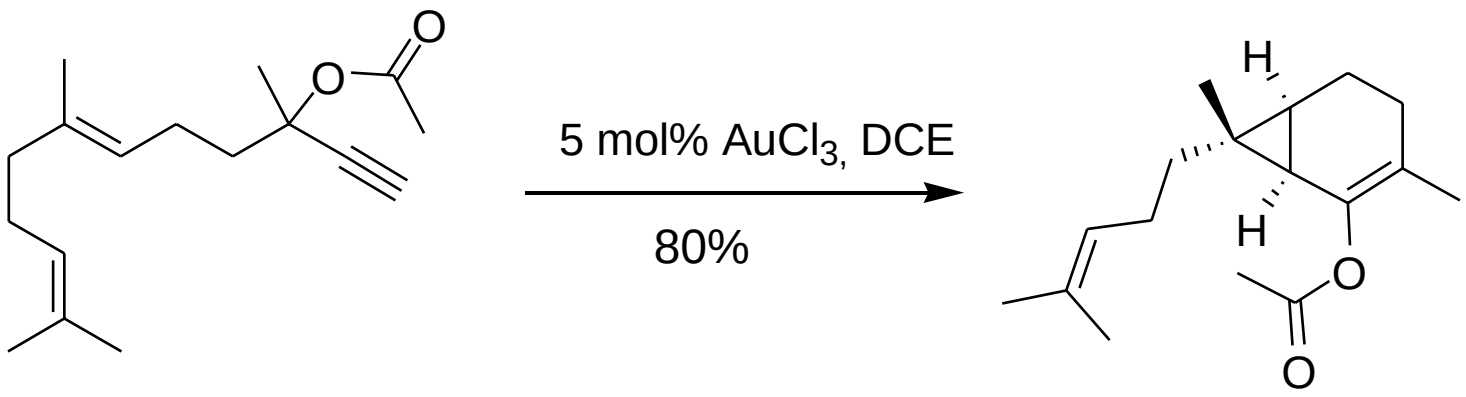


Luzung, M.R.; Markham, J.; Toste, F.D. *J. Am. Chem. Soc.,* **2004**, 126, 10858
Zhang, L.; Kozmin, S. *J. Am. Chem. Soc.,* **2005**, 127, 6962

Application : Synthesis of (-)-Sesquicarene

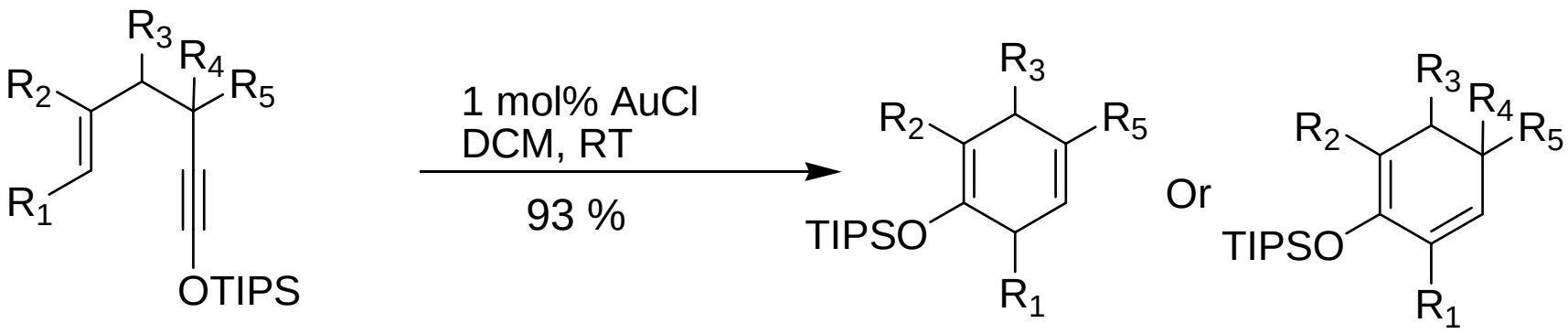


(-)-Sesquicarene



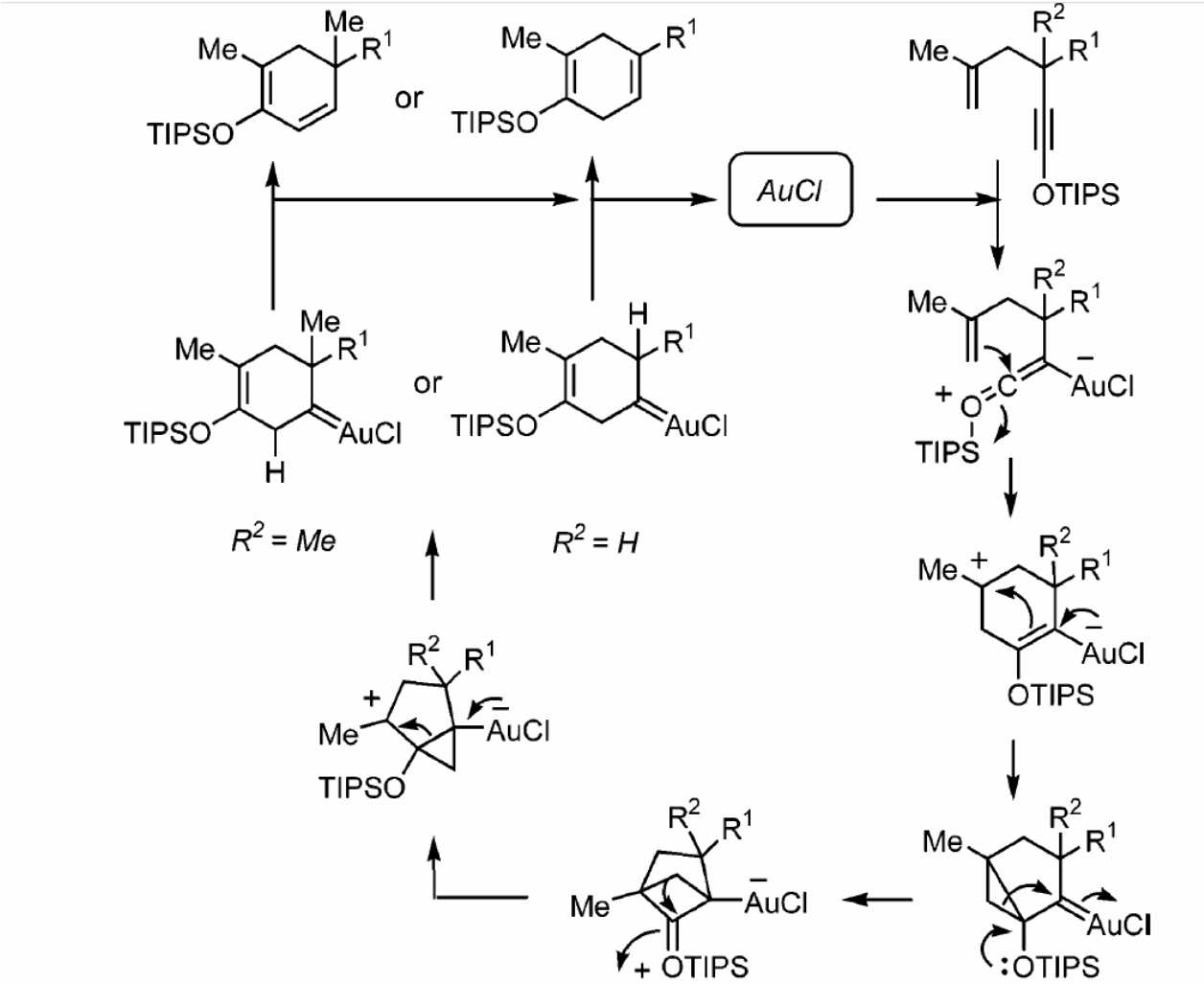
Fürstner, A.; Hannen, P. *Chem. Commun.* **2004**, 2546

Formation of 1,4/1,3-Cyclohexadienes



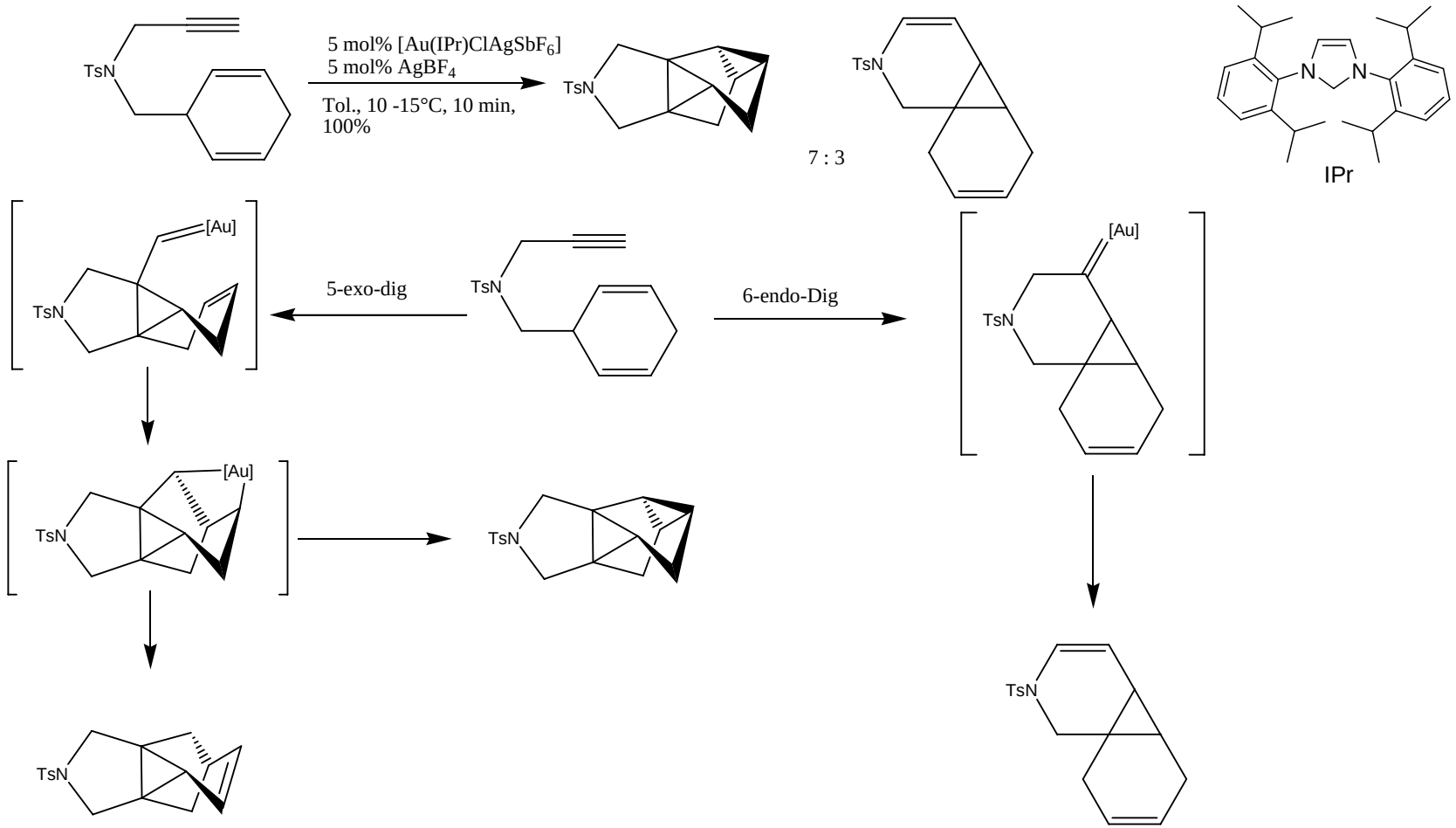
Zhang, L.; Kozmin, S. *J. Am. Chem. Soc.,* **2004**, 126, 11806

Formation of 1,4/1,3 Cyclohexadienes



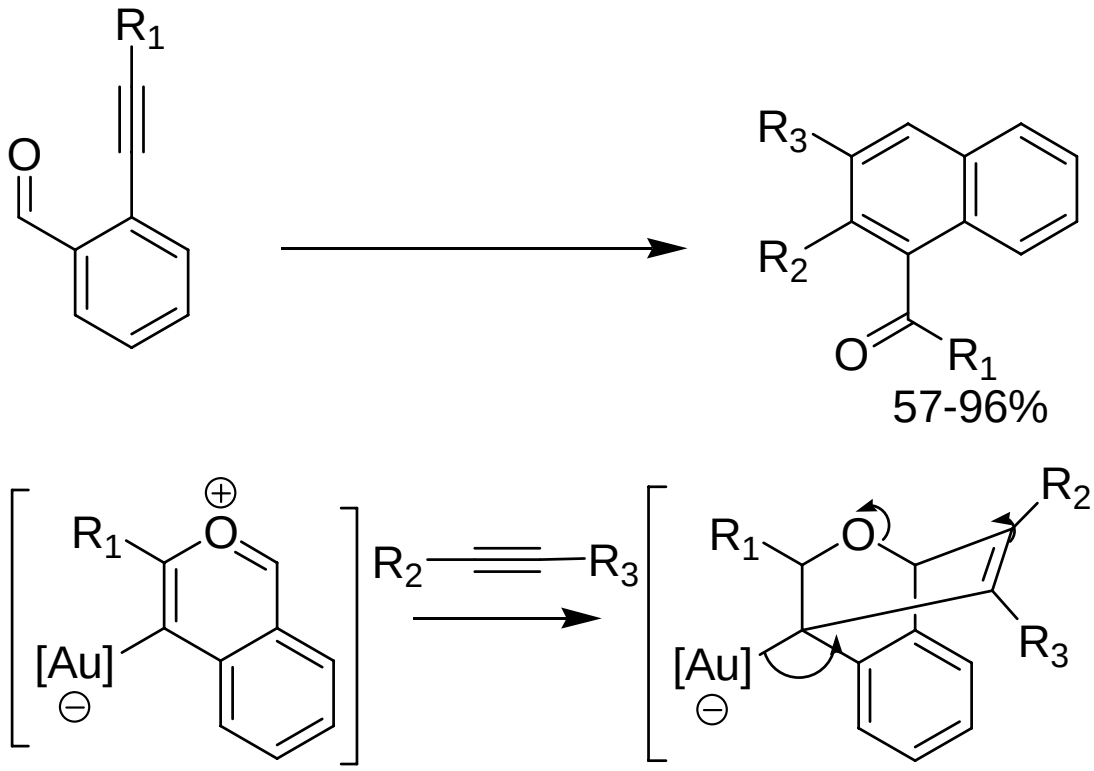
Zhang, L.; Kozmin, S. *J. Am. Chem. Soc.*, **2004**, 126, 11806

Synthesis of Tetracyclo[3.3.0.0]octanes

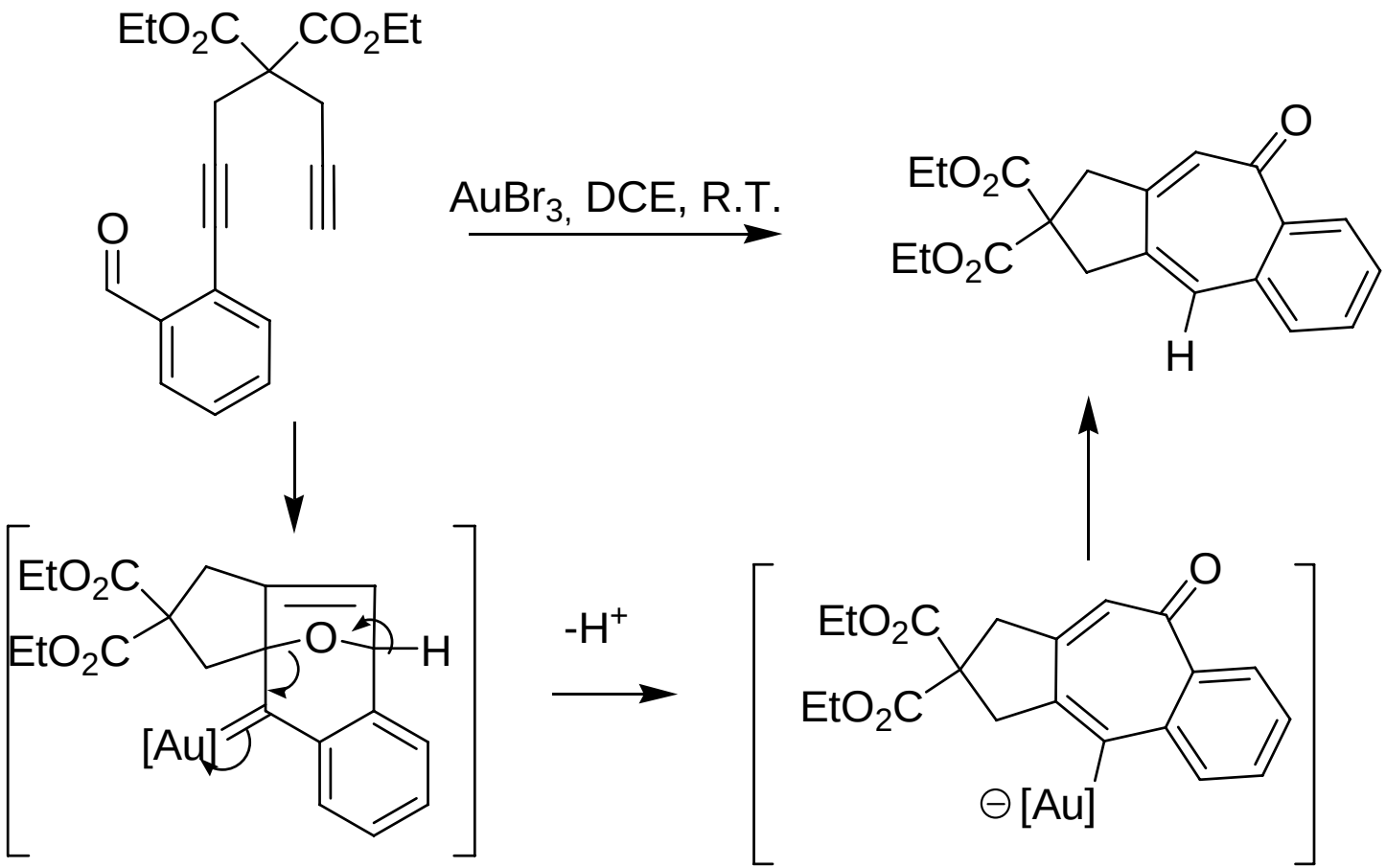


Kim, S.M.; Park, J.H.; Choi, S.Y.; Chung, Y.K. *Angew. Chem. Int. Ed.* **2007**, 46, 6172

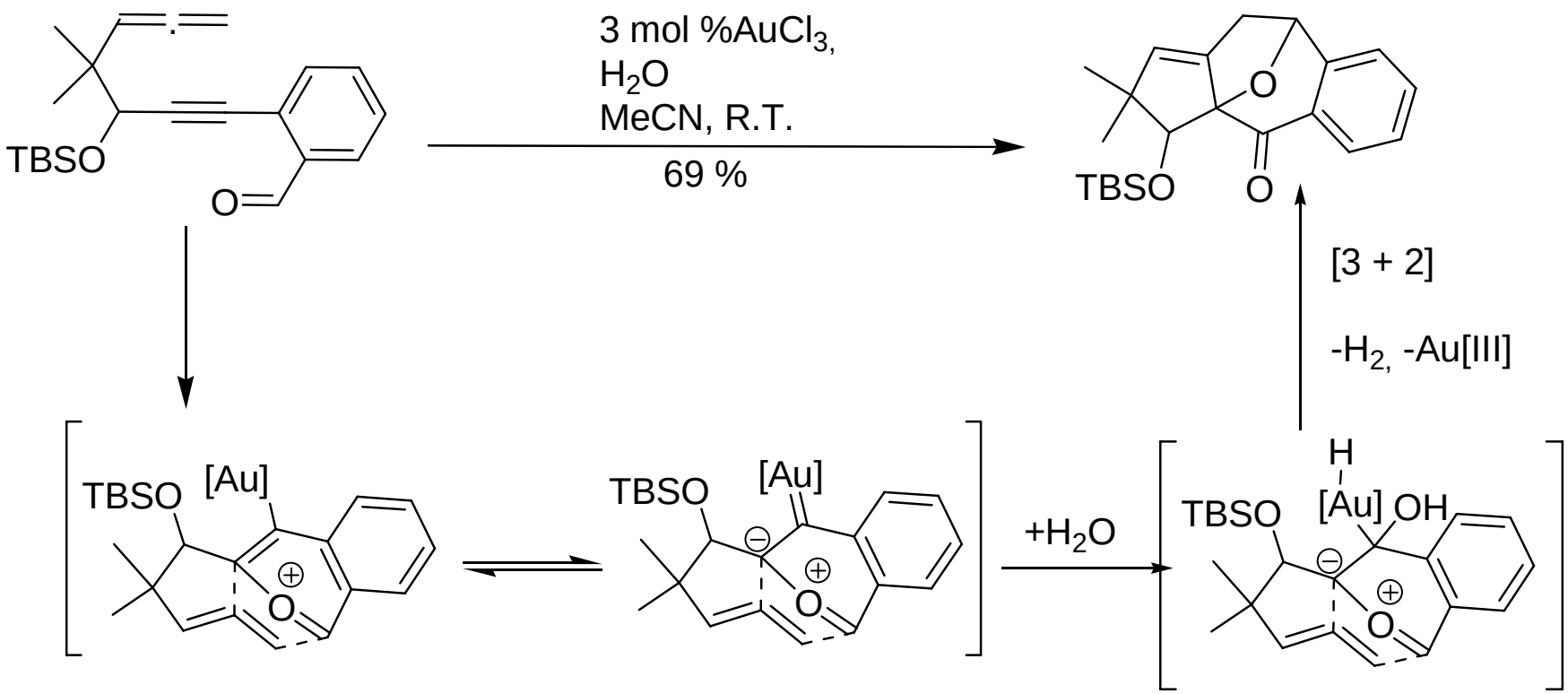
Synthesis of Naphtalenes



R1 = alkyl, aryl
R2 = alkyl, aryl, silyl, acyl, CO2alkyl
R3 = H, alkyl, silyl

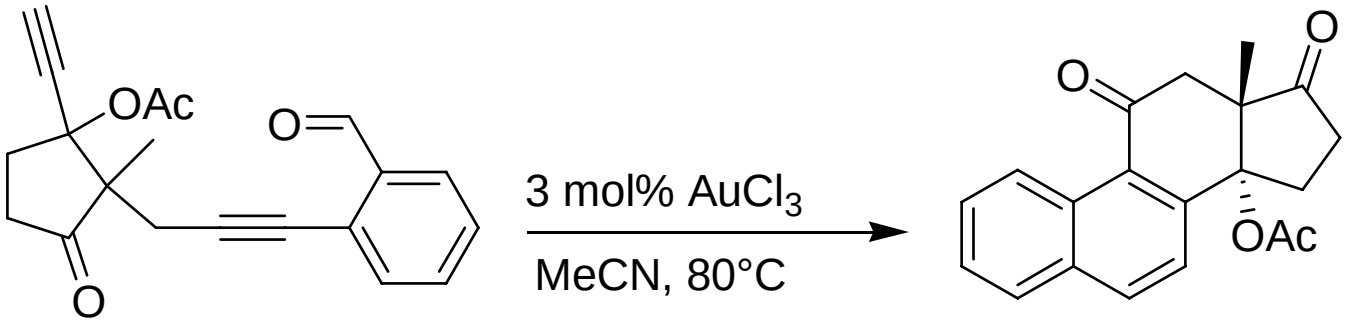


Kim, N. *et al Org. Lett*, **2005**, 7,5289
Gupta A.K. et al Green Chem., 2006, 8, 25



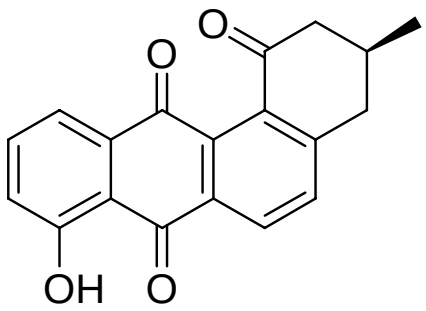
Gupta A.K. et al Green Chem., 2006, 8, 25

Application : Synthesis of the steroïd skeleton

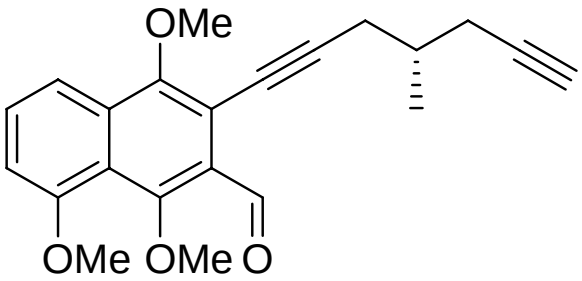


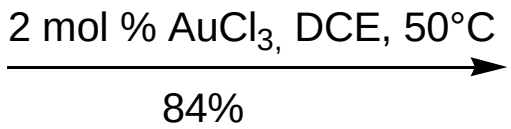
Hildebrandt, D.; Dyker, G. *J. Org. Chem* **2006**, 71, 6728

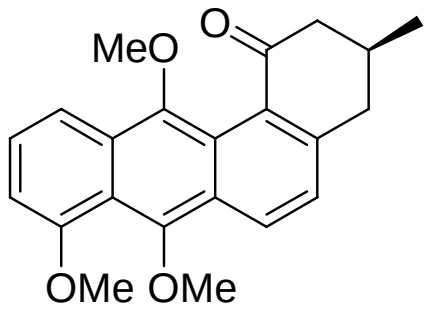
Application : Syntyhesis of (+)-Ochromycinone



(+) - Ochromycinone

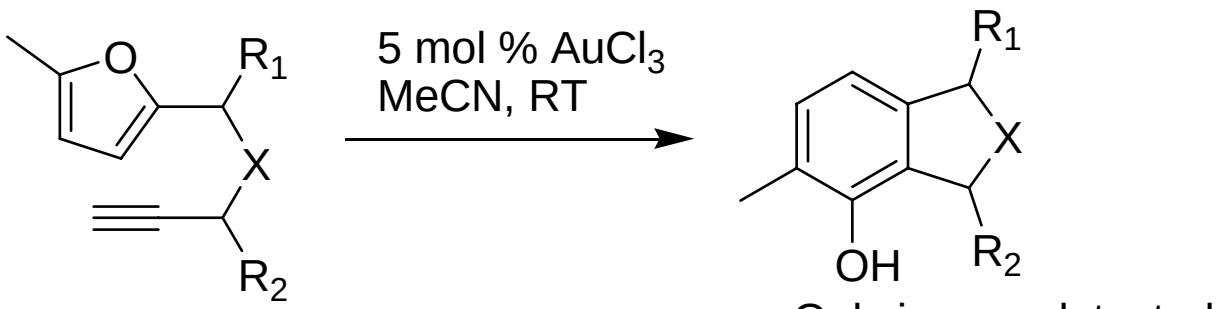






Sato, K.; Asao, N.; Yamamoto, Y. *J. Org. Chem.* **2005**, 70, 8977

Phenol Synthesis

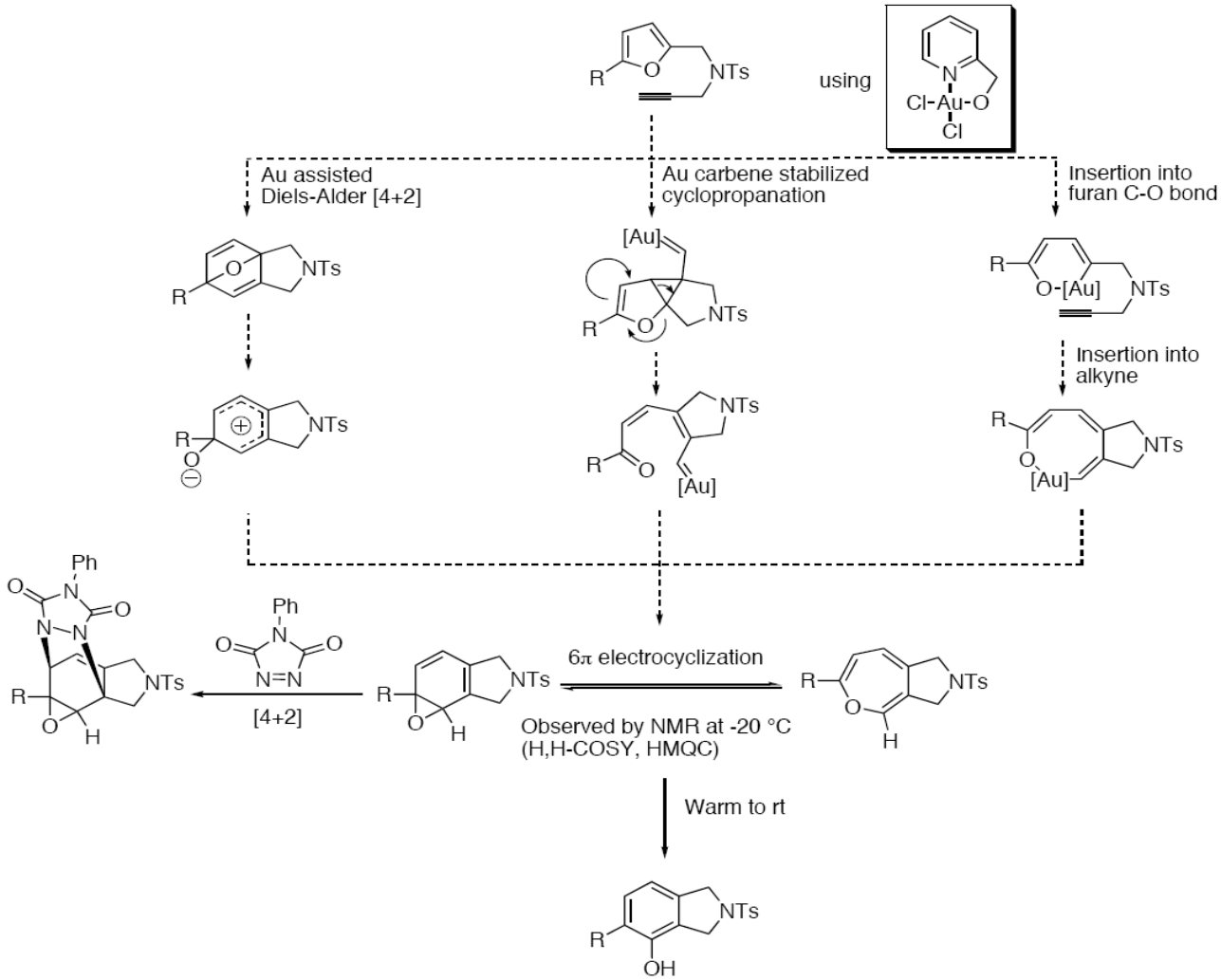


Only isomer detected

X	R1	R2	Yield (%)
CH_2	H	H	65
O	H	H	69
NTs	H	H	97
NTs	Me	H	94
NTs	H	Me	93
$C(CO_2Me)_2$	H	H	88
NTsCH2	H	H	81

Hasmi et al. *Angew. Chem. Int. Ed.* **2004**, 43, 6545

Mechanism of Phenol Synthesis



Hasmi et al. *Angew. Chem. Int. Ed.* **2005**, 44, 2798

Conclusion

- Activation of aryl CH bonds, mechanism not clear
- Activation of alkynes, allenes and alkenes (nucleophilic additions to CC multiple bond)
- Carbene reactivity (good selectivity, good yield)

Selected Reviews

- Recent reviews on gold homogenous catalysis :

Hashmi, S.K. *Chem. Rev.* **2007**, 107, 3180 - 3211
Fürstner, A.; Davies, P.W. *Angew. Chem. Int. Ed.* **2007**, 46, 3410 - 3449
Marion, N., Nolan, S.P. *Angew. Chem. Int. Ed.* **2007**, 46, 2750 - 2752
Jiménez-Núñez, E.; Echavarren, A.M. *Chem. Commun.* **2007**, 333 - 346
Nolan, S.P. *Nature* **2007**, 496 - 497
Gorin, D.J.; Toste, F.D. *Nature* **2007**, 395 - 403
Hashmi, S.K.; Graham, J.H. *Angew. Chem. Int. Ed.* **2006**, 45, 7896 - 7936
Zhang, L.; Sun, J.; Kozmin, S.A. *Adv. Synth. Cat.* **2006**, 348, 2271 - 2296
Hoffmann-Röder, A.; Krause, N. *Org. Biomol. Chem.* **2005**, 387 - 391
Hashmi, S.K. *Gold Bull.* **2004**, 37, 51 - 65
Hashmi, S.K. *Gold Bull.* **2003**, 36, 3 - 9