Gold(I)-Catalyzed endo-Selective Intramolecular α-Alkenylation of β-Yne-Furans: Synthesis of Seven-Membered-Ring-Fused Furans and DFT Calculations

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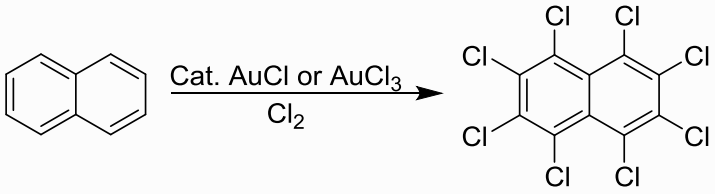
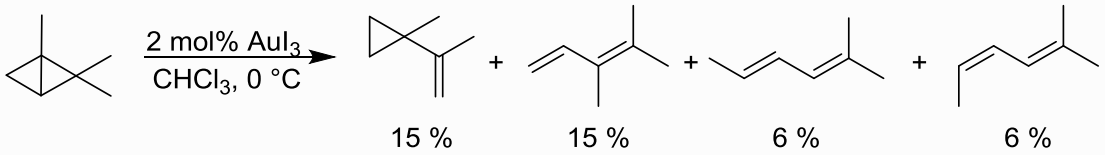
Joseph Salamoun
Wipf Group
Current Lit. 12/07/13

Earlier Examples of Gold Catalysis:
The Golden Years

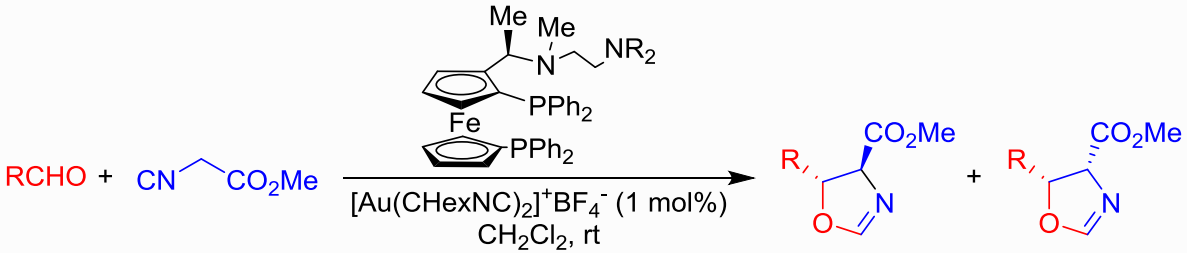
Chem. Zetralbl. **1935**, 106, 514.



JACS **1972**, 94, 7741.

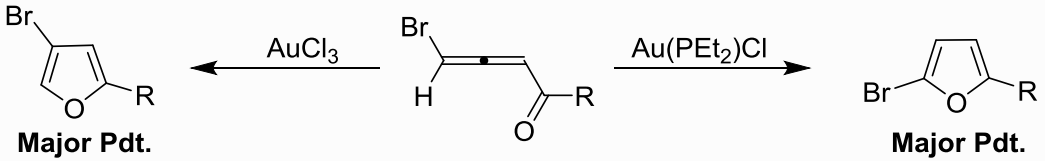


JACS **1986**, 108, 6405.



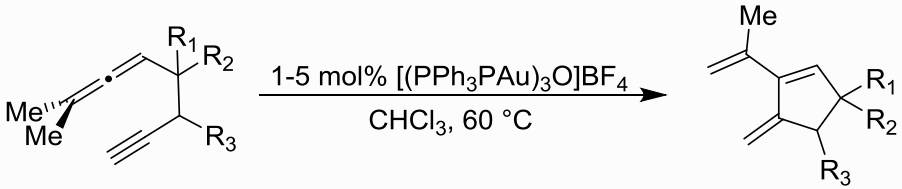
yields: 89 - 100%, **trans ratio:** 0.80 - 1 **ee% trans** 72 - 97 **cis** 0 - 52

JACS **2005**, 127, 10500.



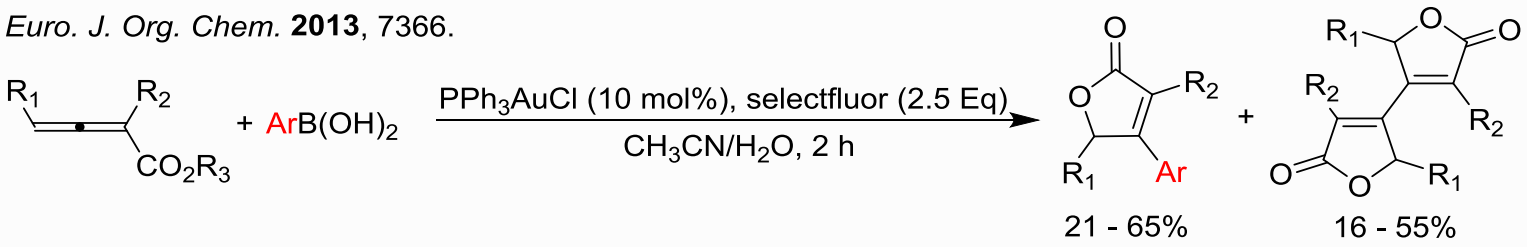
Major Pdt. **Major Pdt.**

JACS ***2008****, 130, 4517.*

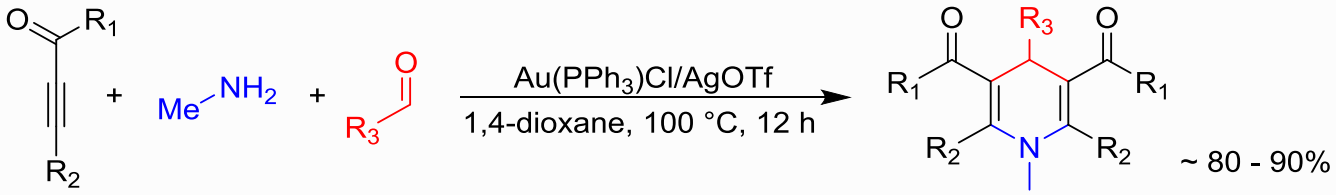


Examples of Current Surge in Gold Catalysis: The Gold Rush

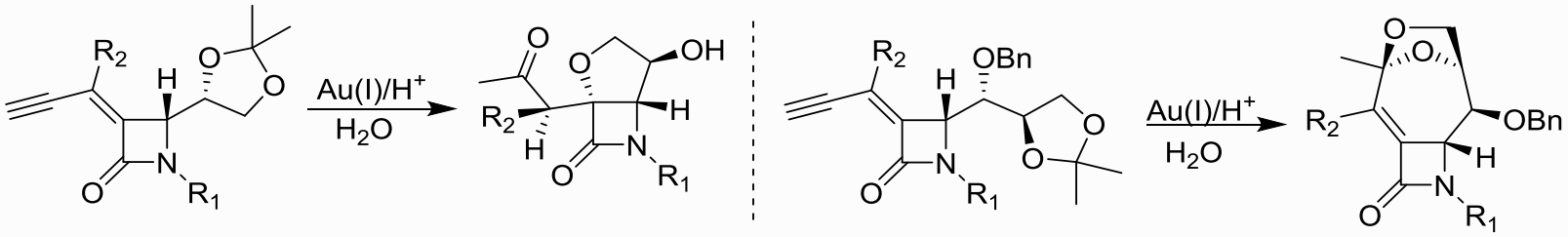
Euro. J. Org. Chem. **2013**, 7366.



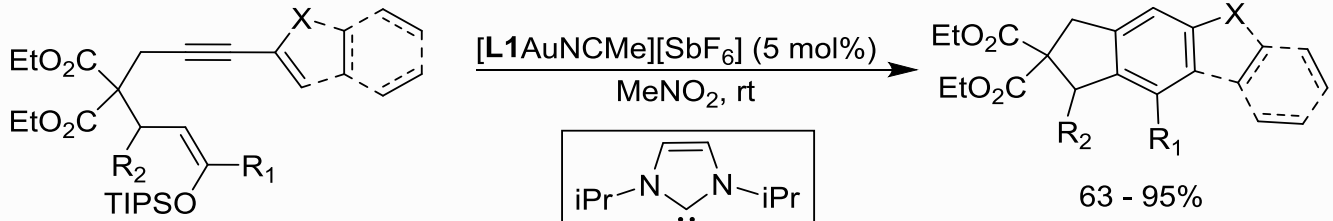
Euro. J. Org. Chem., **2013**, 7300.



J. Org. Chem. **2013**, 78, 8956.



Beilstein J. Org. Chem. **2013**, 9, 2625.

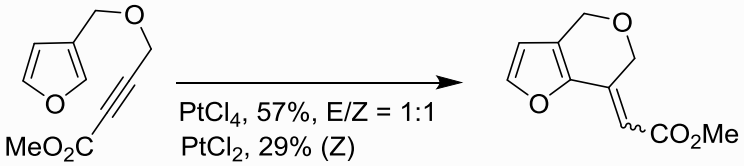


Interest in Cyclization with Yne-Furan:

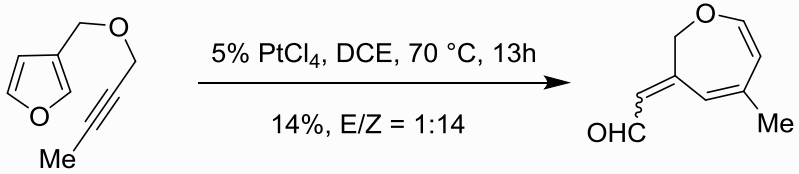
A Golden Opportunity

Literature Examples of Yne-Furan Cyclizations:

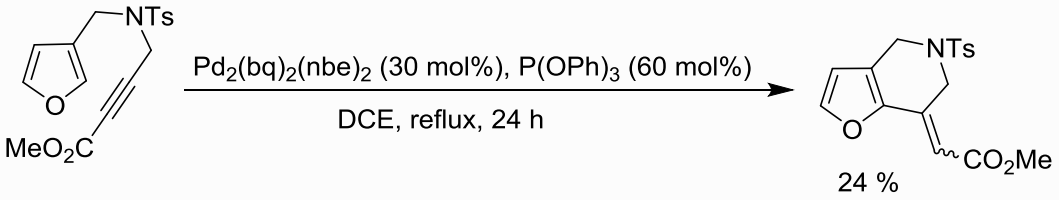
OL **2003**, 5, 1055.



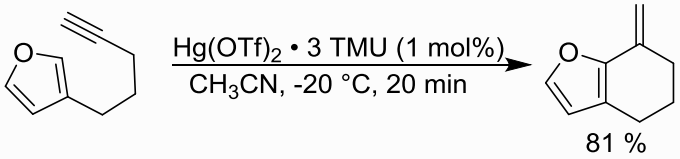
Tetrahedron **2003**, 59, 8859.

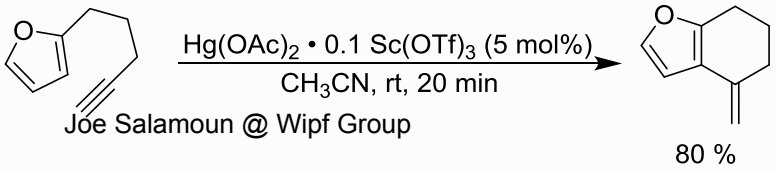


JOC **2004**, 69, 6997.

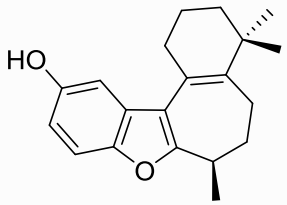


OL **2007**, 9, 1399.

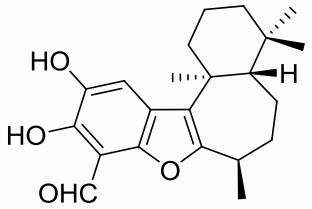




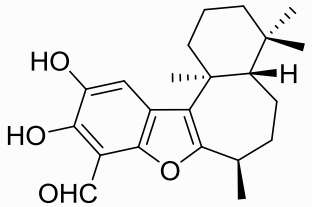
Possible application to natural product synthesis:



frondosin B



liphagal

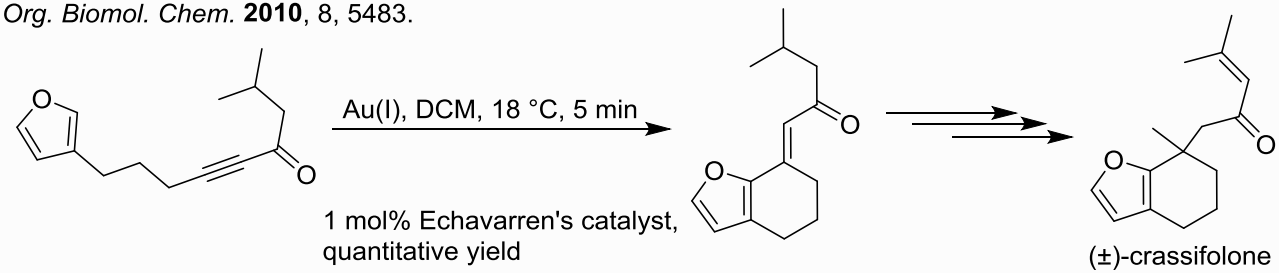


selaginoidine

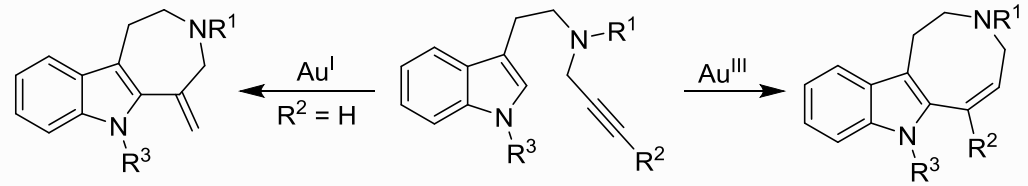
Referenced in title paper.

Precedence for Gold with Furans and Indoles: A Gold Mine

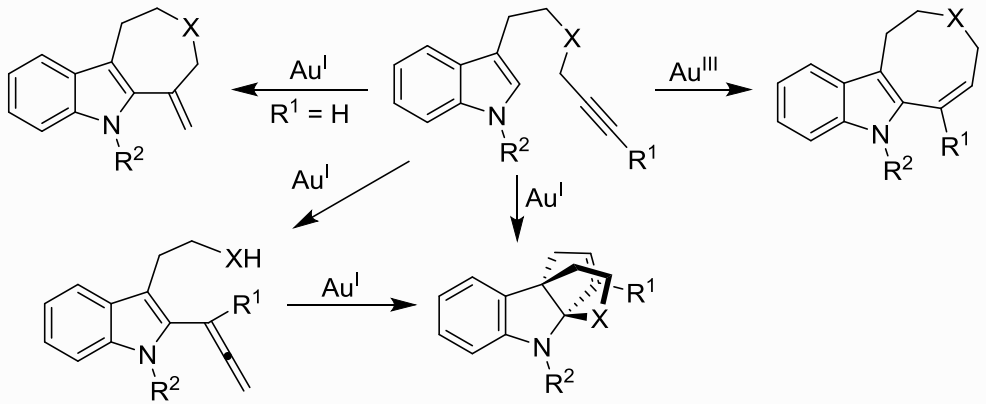
Org. Biomol. Chem. **2010**, 8, 5483.



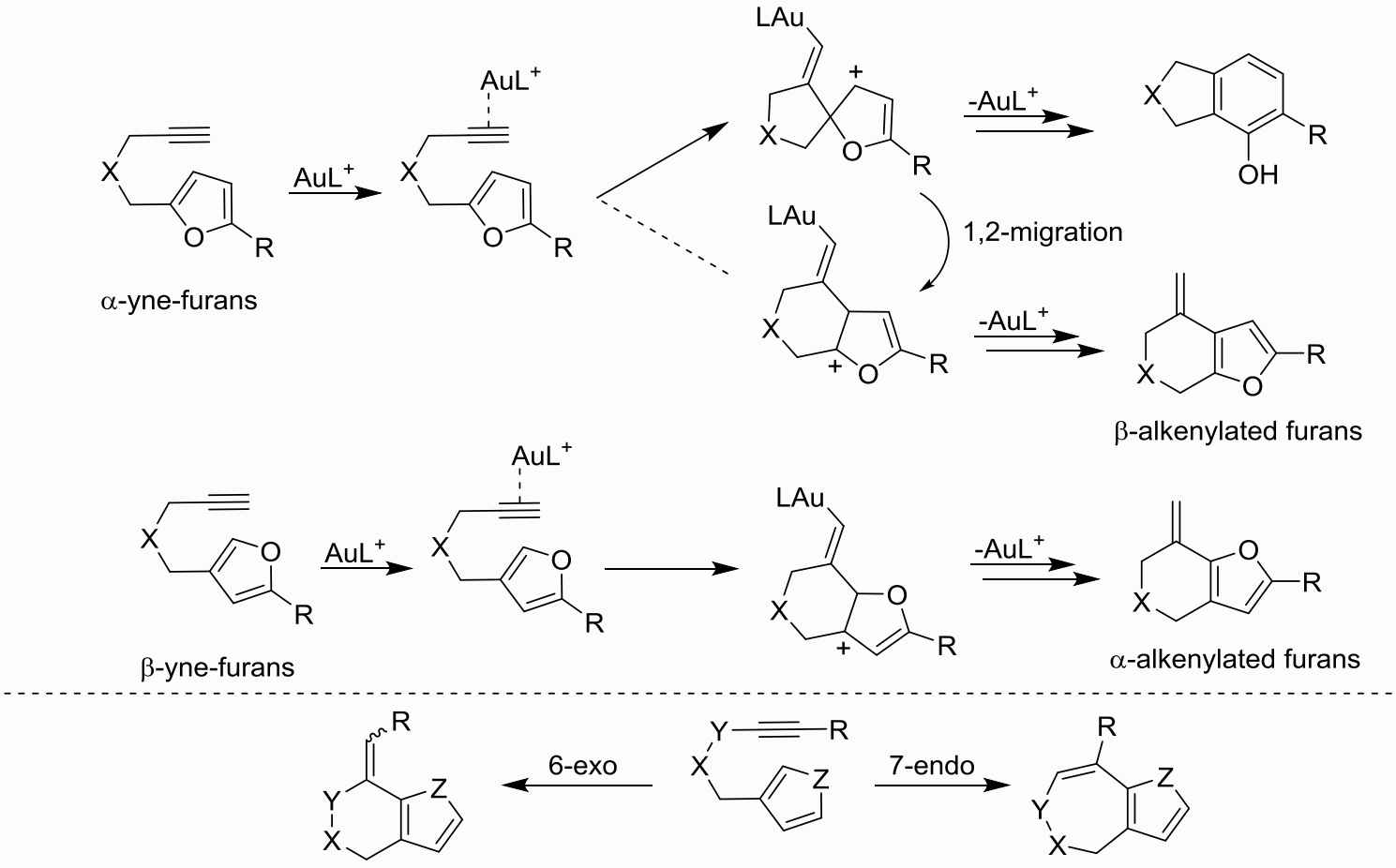
Angew. Chem. Int. Ed. **2006**, 45, 1105.



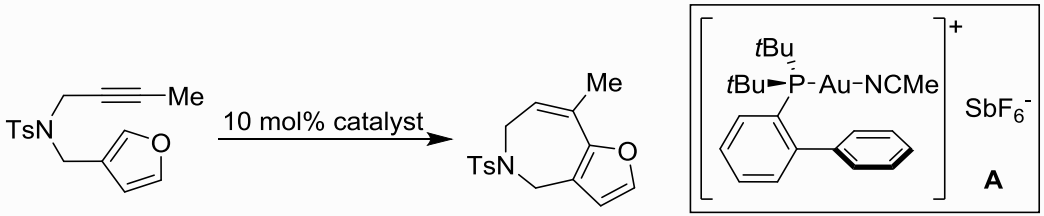
Chem. Eur. J. **2007**, 13, 1358.



Gold Catalyzed Reactions:
Going for the Gold



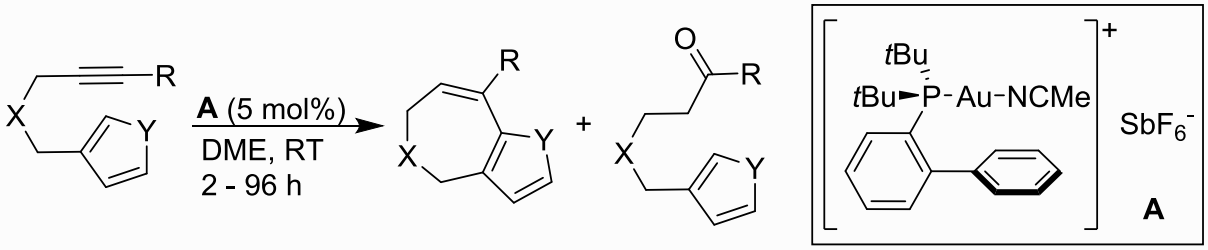
Screening of Catalysts and Success with Gold: Striking Gold

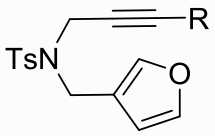


entry	solvent	catalyst	temp.	time (h)	yield
1	DCM	TfOH	rt	12	Mix
2	DCM	$AgSbF_6$	rt	24	Decomp
3	DCM	$BF_3{\cdot}Et_2O$	rt	24	Decomp
4	toluene	$PtCl_2$	70 °C	24	28%
5	DCM	$AuCl_3$	rt	10	Low convers.
6	DCM	$Au(PPh_3)Cl$ + $AgSbF_6$	rt	1	Trace
7	DCM	Au(iPr)Cl + $AgSbF_6$	rt	0.3	69%
8	DCM	$Au[P(OPh\text{-}t\text{-}Bu\text{-}2,4)_3]Cl$ + $AgSbF_6$	rt	0.5	35%
9	DCE	A	rt	0.3	74%
10	DCM	A	rt	1	60%
11	MeCN	A	70 °C	24	Trace
12	toluene	A	rt	4	87%
13	THF	A	rt	6	79%
14	DMF	A	rt	3	90%

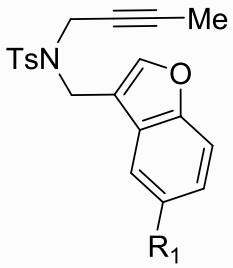
Scope of Cyclization:

Pots of Gold

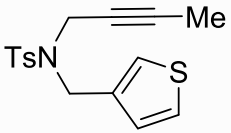


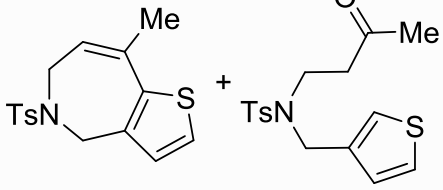


R = Me	90%	1%
R = Me + No H_2O	NR	-
R = Me + 1 drop H_2O	19%	63%
R = cyclopropyl	91%	
R = 2-propenyl	88%	
R = Ph	76%	
R = *p*-ClC_6H_4	90%	
R = *p*-$MeOC_6H_4$	98%	

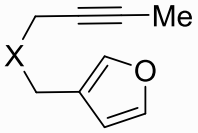


R_1 = H	71%
R_1 = OMe	74%

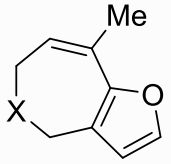




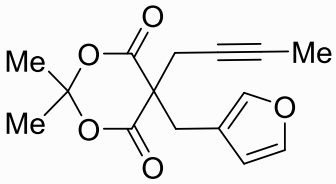
46% 39%

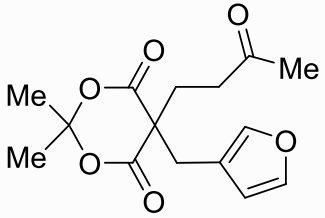


X = O
X = CH_2



60%
Decomp.

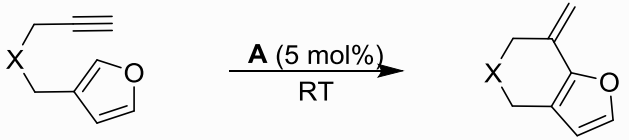




76%

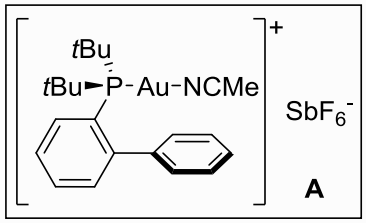
Extension of Scope:

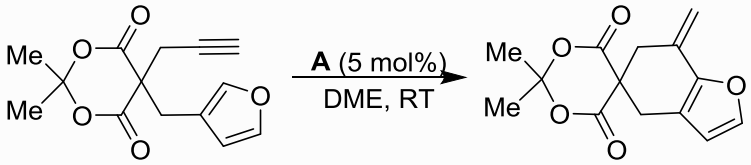
More Pots of Gold



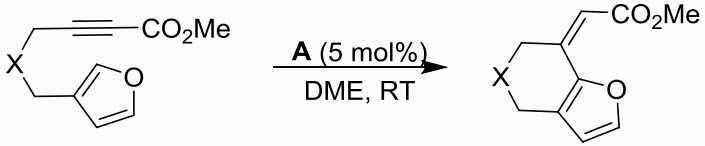
X = NTs
X = O

DME, 1 h, 50%
toluene, 20 min, 25%



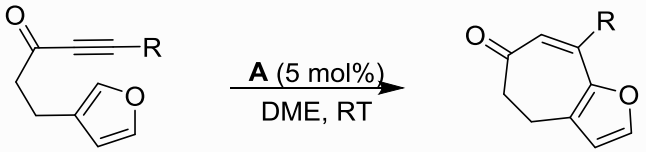


7 h, 43%



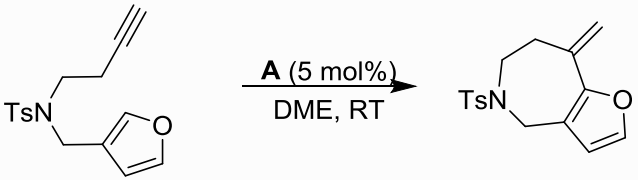
X = NTs
X = O

4 h, 92%
1 h, 76%



R = Ph
R = CH_2Bn

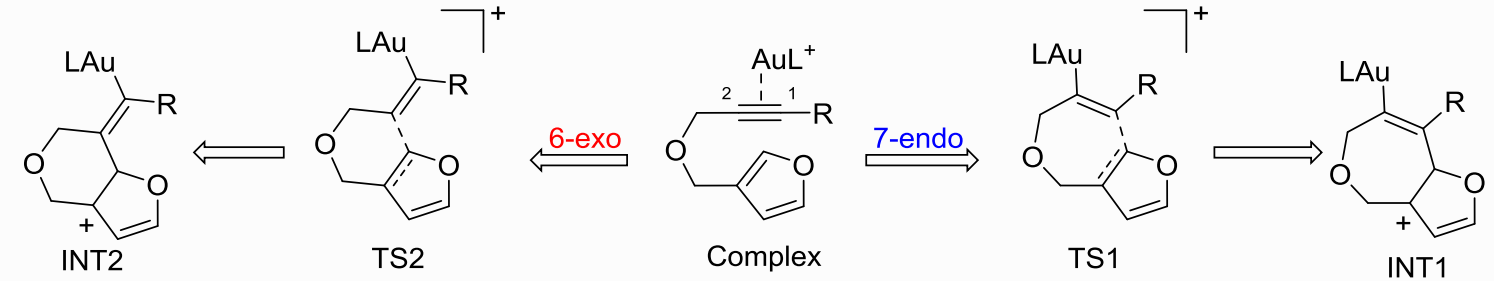
2 h , 93%
2 h, 59%



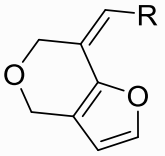
20 h, 47%

DFT and NPA Studies, Insight into Selectivity:

The Golden Path

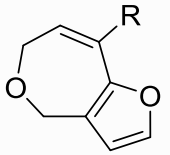


INT2	TS2	0 kcal/mol	TS1	INT1
-3.8	6.9	R = H	9.2	-6.8
7.3	16.5	R = Me	13.4	3.4
8.9	18.5	R = Ph	13.7	7.1
-3.6	9.5	R = CO_2Me	12.4	-3.0

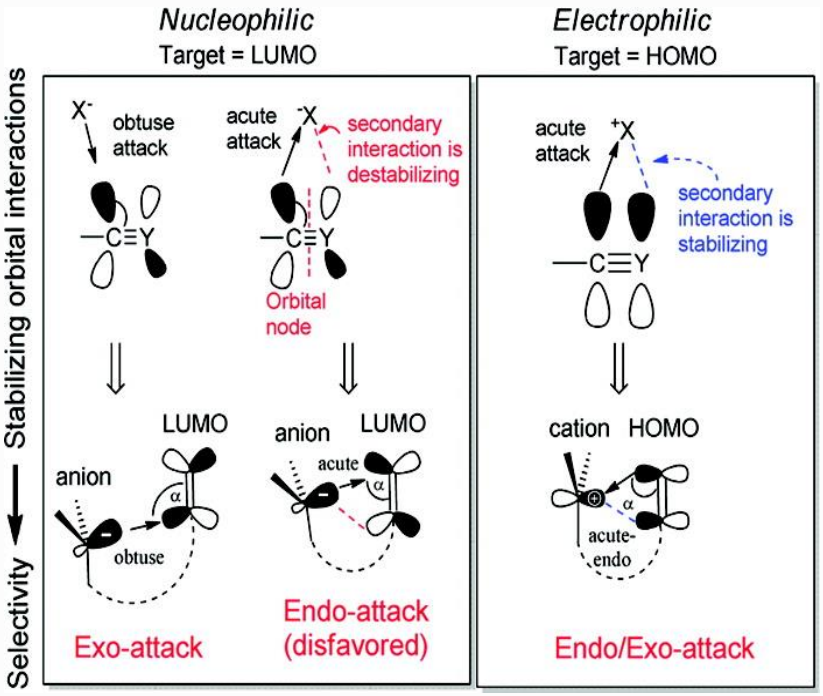


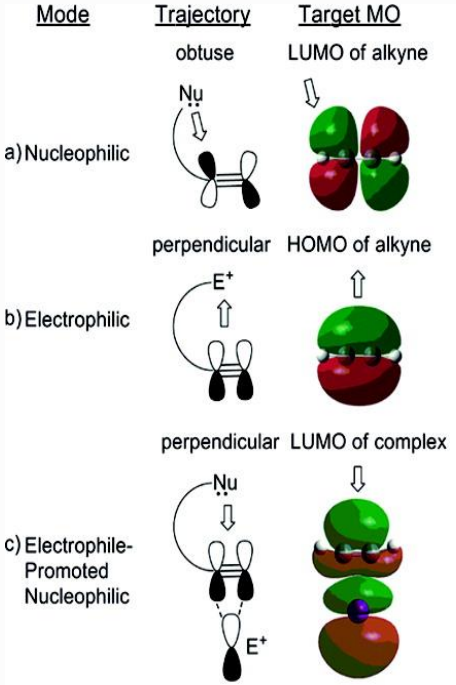
NPA Charges in Complex

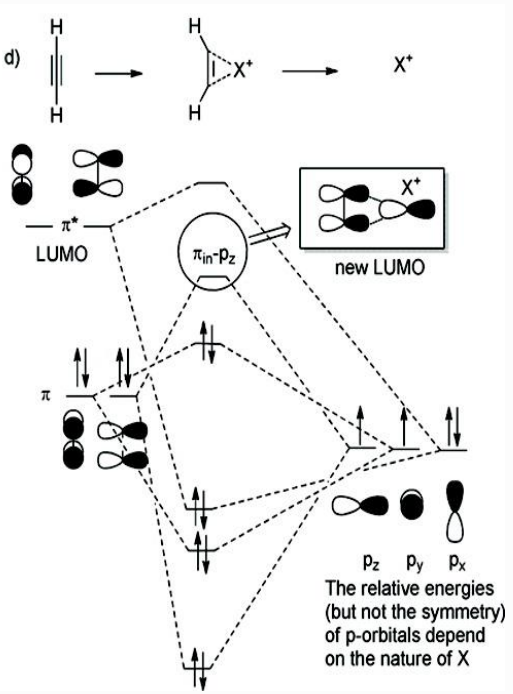
C2	R	C1
-0.008	H	-0.264
-0.094	Me	0.024
-0.168	Ph	0.091
0.014	CO_2Me	-0.122

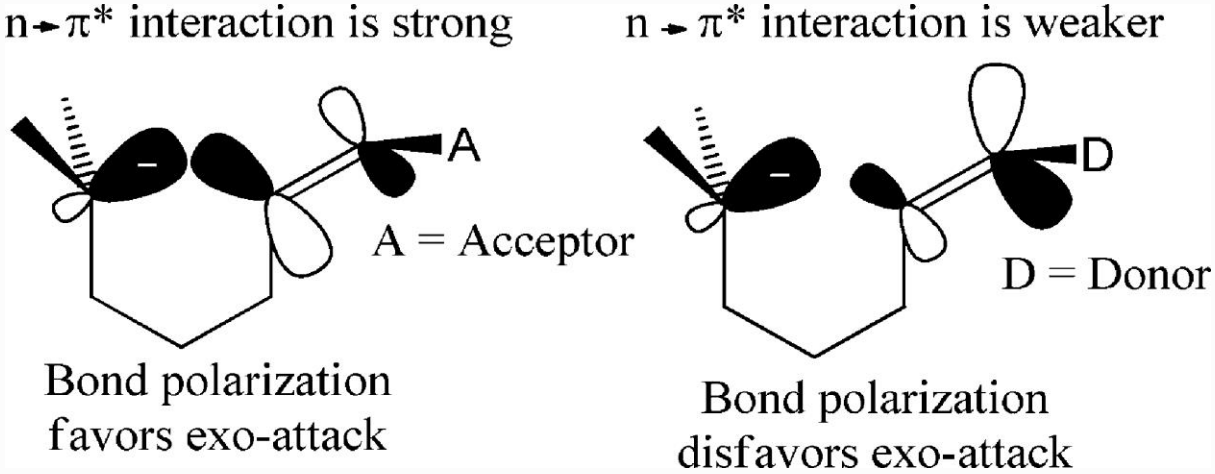


L = PMe_3









Chem. Rev. **2011,** 111, 6513.

Conclusion:
Worth its Weight in Gold?

- Transformations are interesting and potentially useful in natural product synthesis.
- The yields are good but a heteroatom is needed in the tether unless a carbonyl is placed next to alkyne.
- Tunable strategy allows for synthesis of appropriate ring size.
- DFT and NPA provide insight into the mechanism.

Commentary:
All that Glitters is not Gold?

- Even though gold was not the focus of the paper, it would be useful to get insight into why/if gold is superior to other metals. It remains unclear what gold's specific impact is (relative to other catalysts), especially since tuning the ring size is not related to the catalyst.
- It would be of great interest if they can evolve the methodology so that the catalyst can control ring size without limitation on the alkyne substitution (Au^{I} v. Au^{III}?).