Copper-Catalyzed Tethered Aziridination of Unsaturated *N*-Tosyloxy Carbamates

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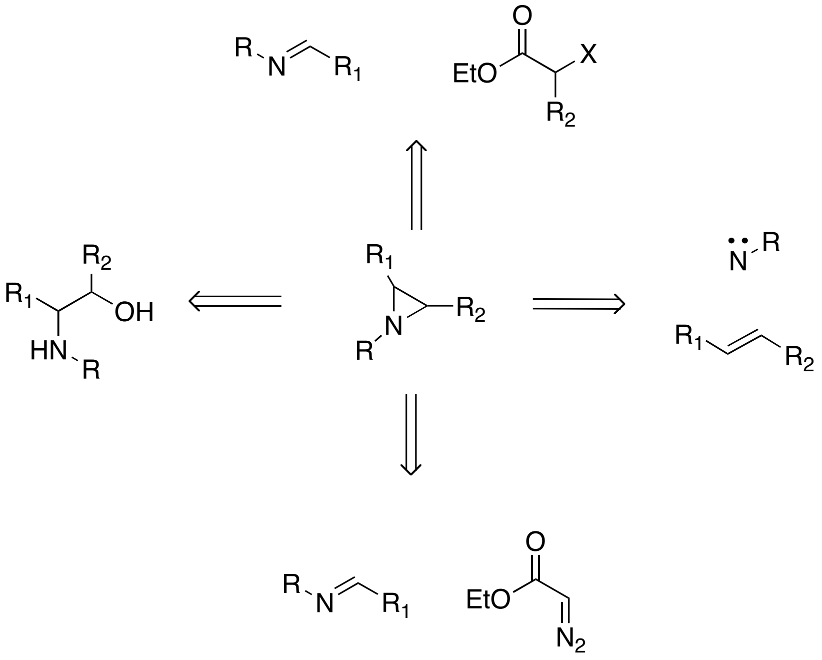
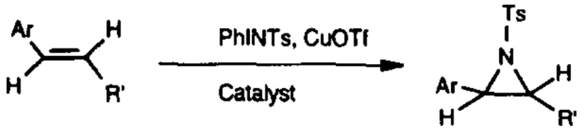
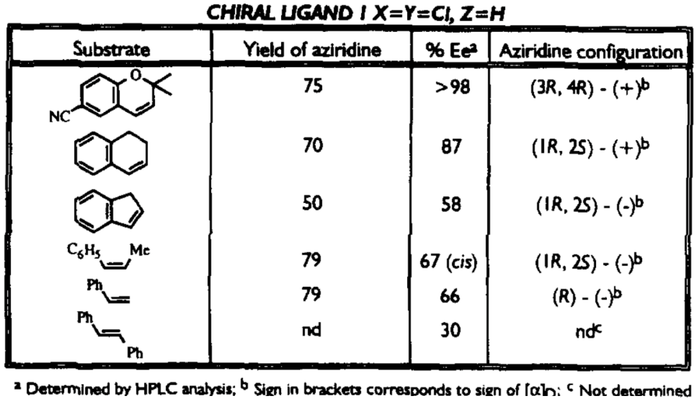
General Methods to Form Aziridines



For Review: Osborn, H. M.; Sweeney, J. *Tetrahedron: Asymmetry,* **1997**, 1693

Asymmetric Copper-Catalyzed Aziridination of Olefins

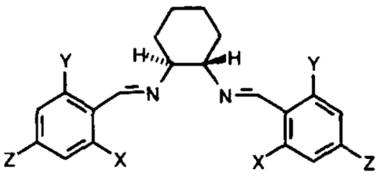




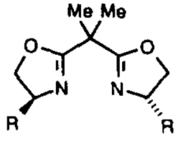
CHIRAL LIGAND 1 X=Y=Cl, Z=H

Substrate	Yield of aziridine	% Ee[a]	Aziridine configuration
NC, O	75	>98	(3*R*, 4*R*) - (+)[b]
	70	87	(1*R*, 2*S*) - (+)[b]
	50	58	(1*R*, 2*S*) - (-)[b]
C_6H_5 Me	79	67 (*cis*)	(1*R*, 2*S*) - (-)[b]
Ph	79	66	(*R*) - (-)[b]
Ph Ph	nd	30	nd[c]

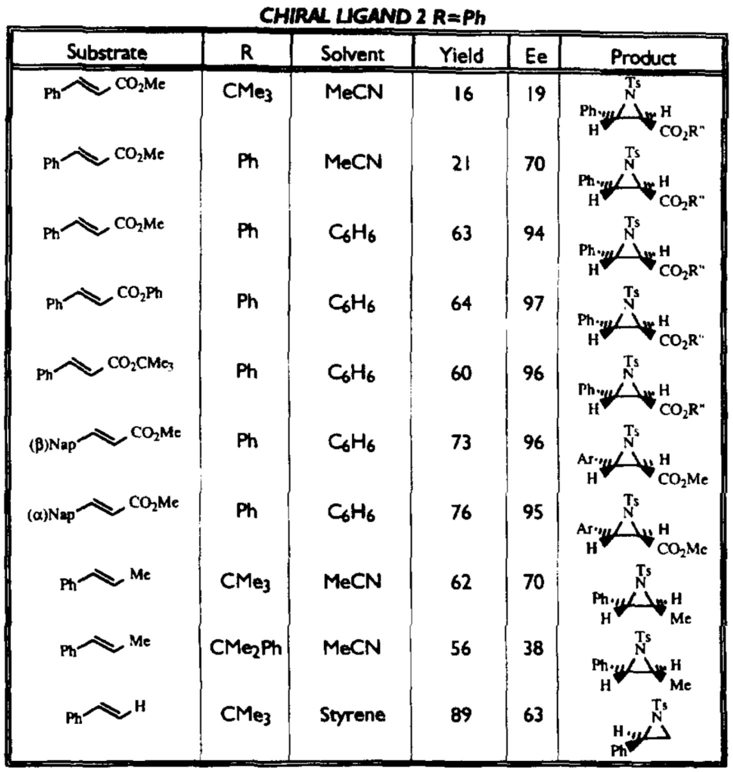
[a] Determined by HPLC analysis; [b] Sign in brackets corresponds to sign of $[\alpha]_D$; [c] Not determined



Chiral ligand 1
Optimum results when X=Y=Cl, Z=H



Chiral ligand 2
Optimum results when R=Ph



CHIRAL LIGAND 2 R=Ph

Substrate	R	Solvent	Yield	Ee	Product
Ph CO_2Me	CMe_3	MeCN	16	19	
Ph CO_2Me	Ph	MeCN	21	70	
Ph CO_2Me	Ph	C_6H_6	63	94	
Ph CO_2Ph	Ph	C_6H_6	64	97	
Ph CO_2CMe_3	Ph	C_6H_6	60	96	
(β)Nap CO_2Me	Ph	C_6H_6	73	96	
(α)Nap CO_2Me	Ph	C_6H_6	76	95	
Ph Me	CMe_3	MeCN	62	70	
Ph Me	CMe_2Ph	MeCN	56	38	
Ph H	CMe_3	Styrene	89	63	

a) D. A. Evans, M. M. Faul, M. T. Bilodeau, B. A. Anderson, D. M. Barnes, J. Am. Chem. Soc., 1993, 115, 5328; b) D. A. Evans, M. M. Faul, M. T. Bilodeau, J. Am. Chem. Soc., 1994, 116, 2742; c) Z. Li, K. R. Conser, E. N. Jacobsen, J. Am. Chem. Soc., 1993, 115, 5326.

R. W. Quan, Z. Li, E. N. Jacobsen, J. Am. Chem. Soc., 1996, 118, 8156.

Rhodium Catalyzed Aziridination with Nitrenes

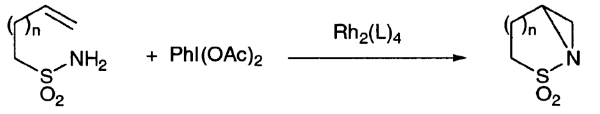
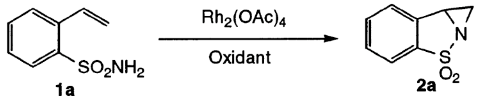
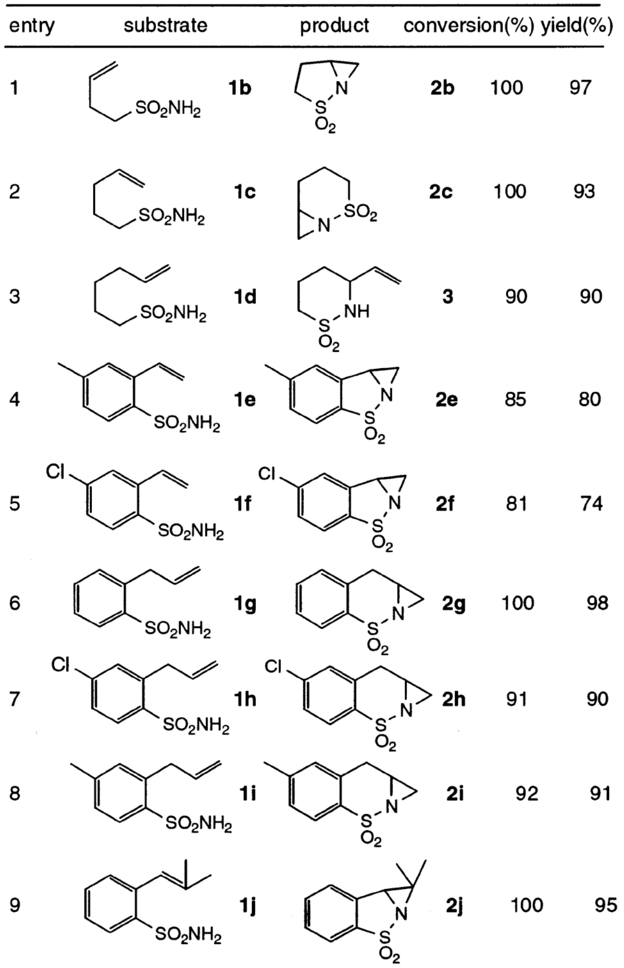


Table 1. Optimization of Reaction Conditions Catalyzed by $Rh_2(OAc)_4$[a]



entry	oxidant	solvent	conversion (%)	yield (%)
1	$PhI(OAc)_2$	CH_2Cl_2	99	83
2	$PhI(OAc)_2$	CH_3CN	63	83
3	$PhI(OAc)_2$	C_6H_6	90	71
4	$PhI(OAc)_2$	THF	85	74
5	PhIO	CH_2Cl_2	95	67
6	2,6-Cl_2pyNO	CH_2Cl_2	0	0

[a] All reactions were performed at 40 °C for 3 h with a $Rh_2(OAc)_4$/**1a**/$PhI(OAc)_2$/Al_2O_3 molar ratio of 0.02:1:1.5:2.5.



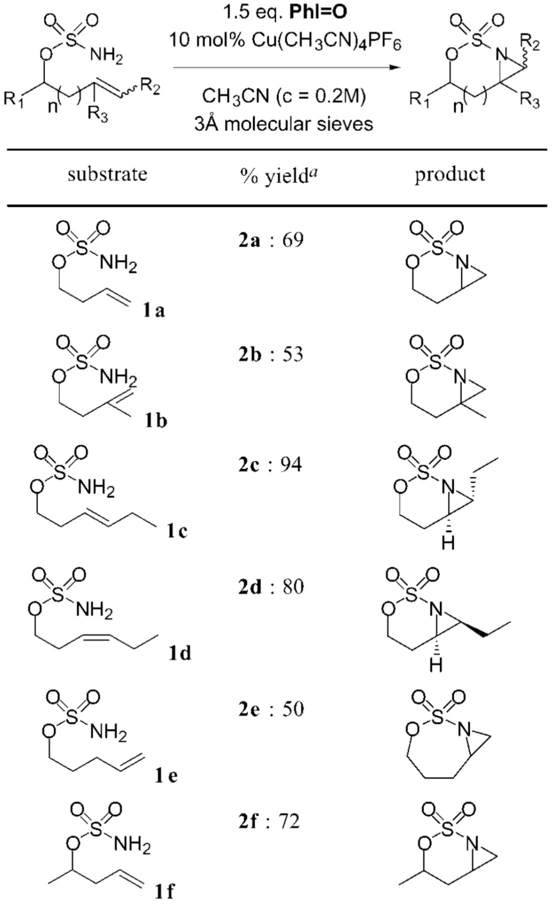
entry	substrate	product	conversion(%)	yield(%)
1	**1b**	**2b**	100	97
2	**1c**	**2c**	100	93
3	**1d**	**3**	90	90
4	**1e**	**2e**	85	80
5	**1f**	**2f**	81	74
6	**1g**	**2g**	100	98
7	**1h**	**2h**	91	90
8	**1i**	**2i**	92	91
9	**1j**	**2j**	100	95

[a] Reaction conditions: $Rh_2(OAc)_4$/substrate/$PhI(OAc)_2$/Al_2O_3 = 0.02:1:1.5:2.5; all reactions were performed in CH_2Cl_2 at 40 °C for 3 h.

Liang, J.-L.; Yuan, S.-X.; Chan, P. W. H.; Che, C.-M. *Org. Lett.* **2002**, 4507

PhI=O Mediated Copper-Catalyzed Aziridination

Table 1. Intramolecular Copper-Catalyzed Reactions



substrate	% yield[a]	product
1a	**2a** : 69	
1b	**2b** : 53	
1c	**2c** : 94	
1d	**2d** : 80	
1e	**2e** : 50	
1f	**2f** : 72	

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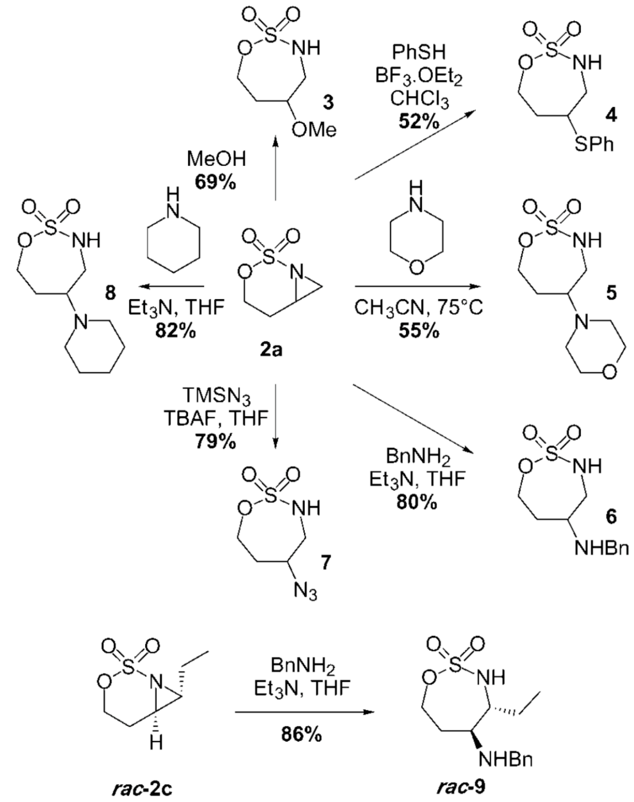
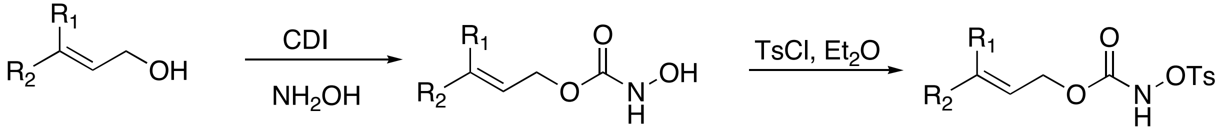
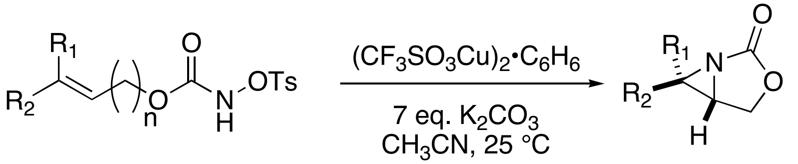
[a] Isolated yield after flash chromatography.



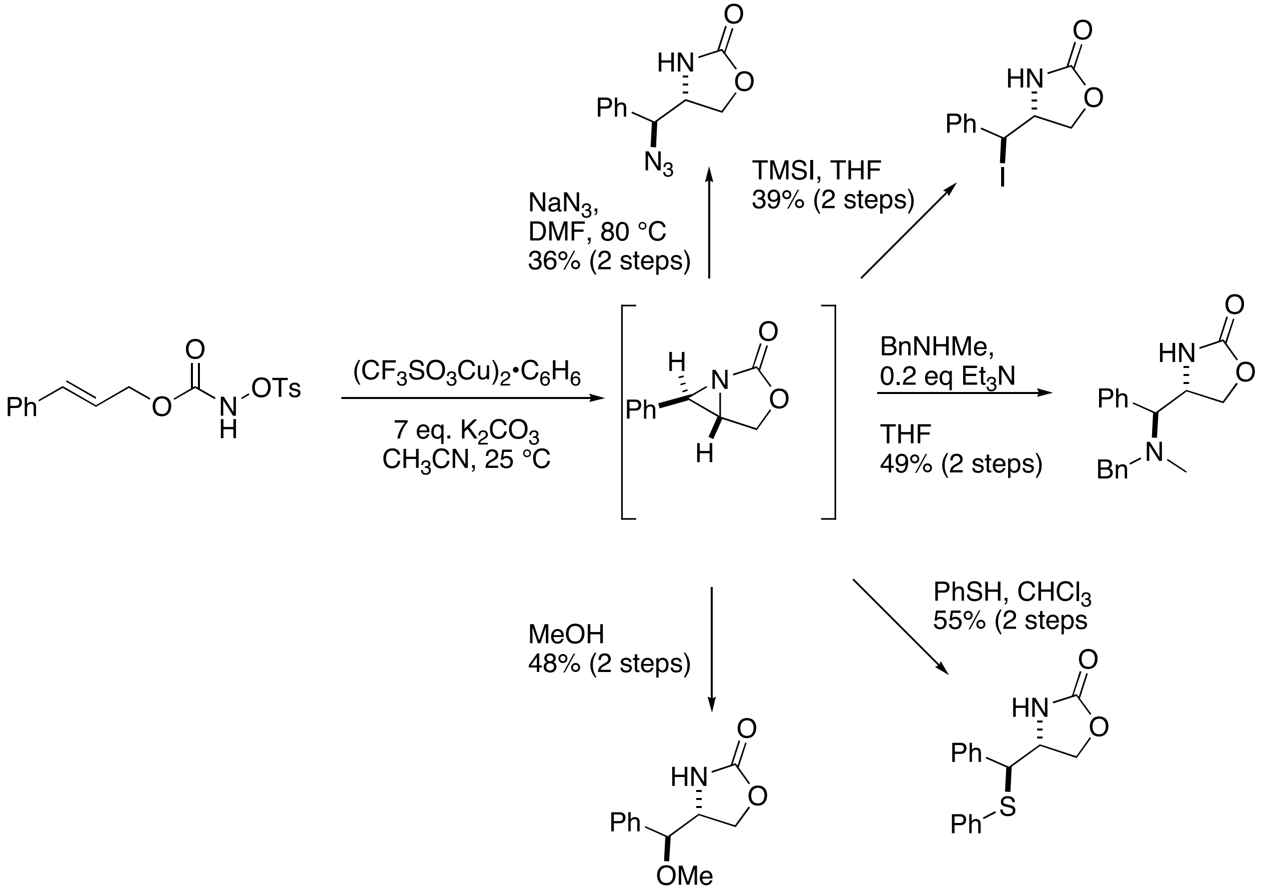
Copper-Catalyzed Aziridination of *N*-Tosyloxy Carbamates

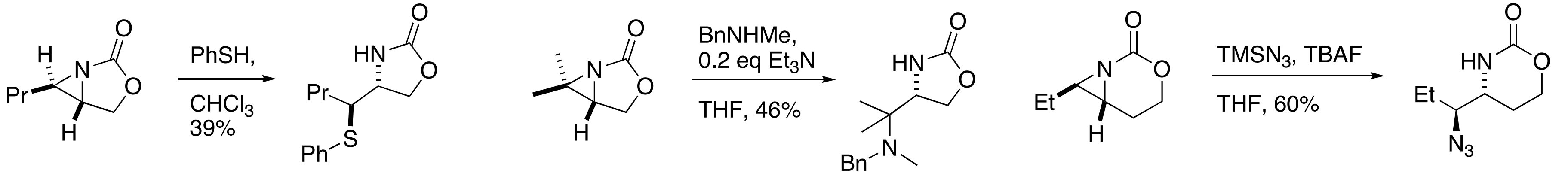




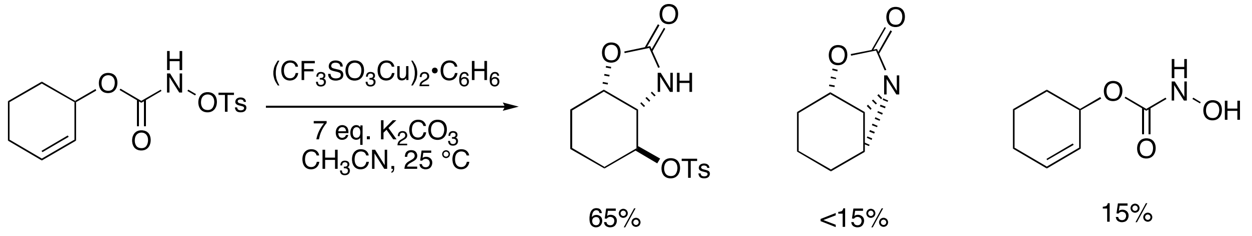
R_1=H, R_2=Pr, n=1	53%, 10:1 R_1=H, R_2=Pr : R_1=Pr R_2=H
R_1=Pr, R_2=H, n=1	42% 1.5:1 R_1=Pr, R_2=H : R_1=H, R_2=Pr
R_1=H, R_2=Ph, n=1	>90% (NMR)
R_1=R_2=Me, n=1	>90% (NMR)
R_1=H, R_2=Et, n=2	45%

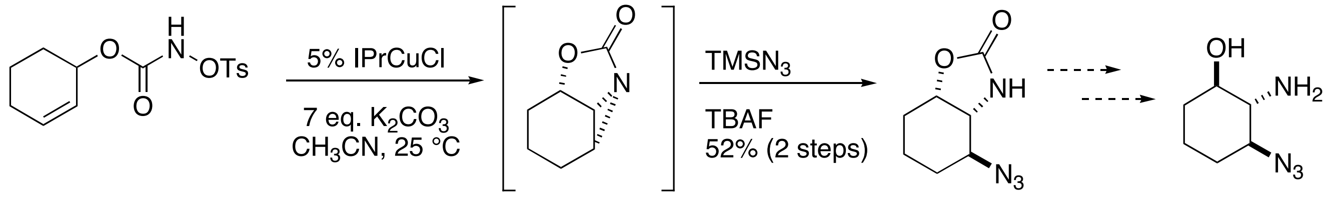
Opening of the Strained Bicycle

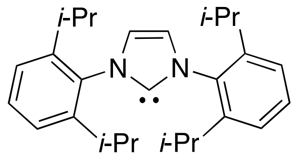




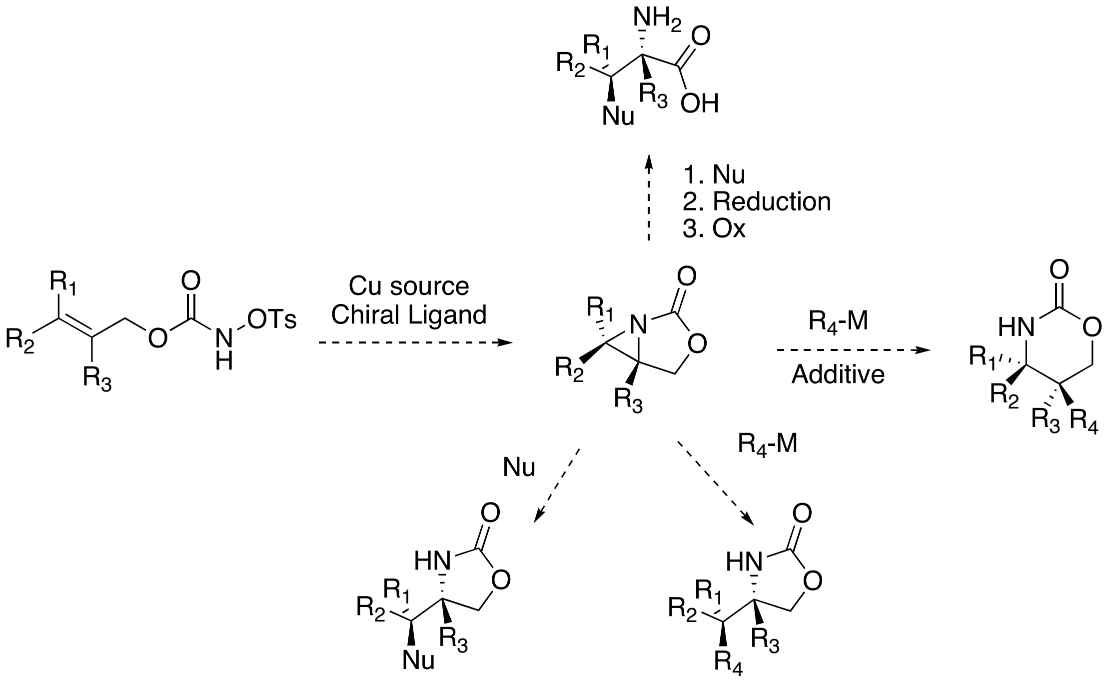
Application toward Tamiflu

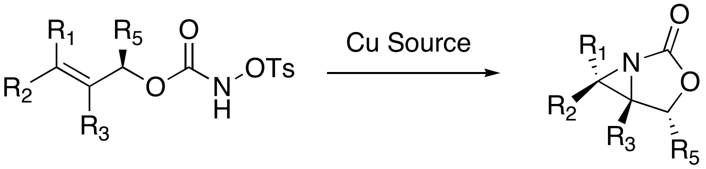






Possible Improvements and Applications





Conclusions

- Reports the synthesis strained bicyclic aziridines from hydroxamic derivatives.
- These aziridines are regio- and stereoselectively opened with nucleophiles to afford cyclic carbamates.
- This skeleton could be exploited in the development of unique molecular architecture through a number of different pathways.