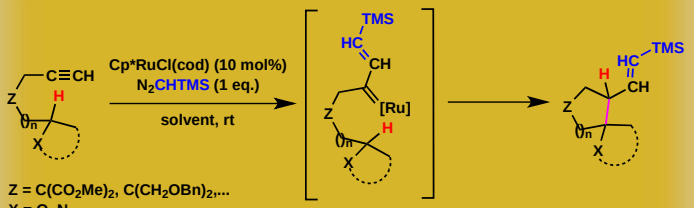
"New Cyclizations Catalyzed by Ruthenium Carbenes"

Fermín Cambeiro, Jesus A. Varela , Susana López and Carlos Saá*
Departamento de Química Orgánica y Centro Singular de Investigación en Química Biológica y Materiales Moleculares (CIQUS), Universidade de Santiago de Compostela,15782 Santiago de Compostela, SPAIN
Email: fermin.cambeiro@usc.es

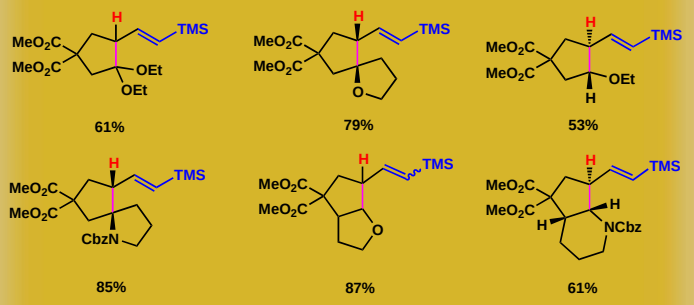
Previous Work

We have recently described a mild procedure based on a novel tandem Ru-catalyzed carbene addition to terminal alkynes/insertion into Csp^3-H bonds in alkynyl acetals, ethers and amines to form complex spiro and fused bicyclic compounds by 1,5- or 1,6-hydride shift/cyclization sequence.[1]



Z = $C(CO_2Me)_2$, $C(CH_2OBn)_2$,...
X = O, N
n = 0, 1
[Ru] = Cp*RuCl

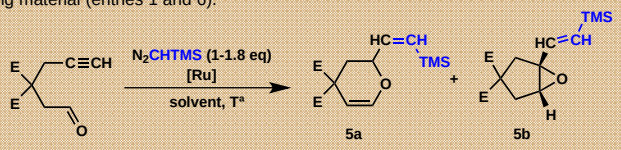
1,5-hydride shift



1,6-hydride shift

Aldehyde Cyclization via Ruthenium Carbene Intermediates

We now report similar Ru-catalyzed cyclizations of 5-alkynals to give the interesting dihydropyranes **5a** as exclusive or major products. Minor amounts of vinyloxiranes **5b** were also isolated.[2,3] Ether or isopropanol were chosen as solvents depending on the nature of the starting material (entries 1 and 6).

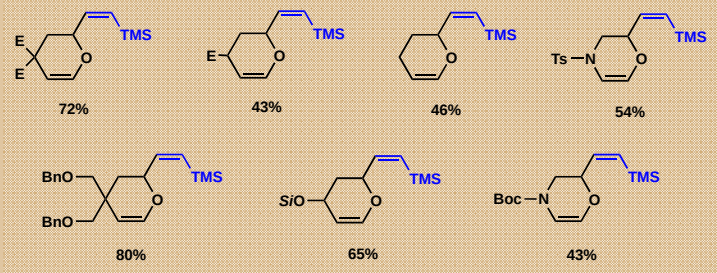


Entry	Solvent	[Ru]	5a (%)[b]	5b (%)[b]
1	Et_2O, rt	Cp*RuCl(cod)	70	---
2	Et_2O, rt	CpRuCl(cod)	70 (1:4 Z:E)	
4	Et_2O, rt	$[CpRu(CH_3CN)_3]PF_6$	Complex mixture	
5	MeOH, rt	Cp*RuCl(cod)	SM	
6	*i*PrOH, rt	Cp*RuCl(cod)	72	8
7	*t*BuOH, 70 ºC	Cp*RuCl(cod)	59	8
8	Acetone, rt	Cp*RuCl(cod)	57	10

Conditions: Cp*RuCl(cod) (10 mol%), N_2CHTMS (1 – 1.8 eq), rt, [1a] = 0.15 M.
[b] Isolated yields.

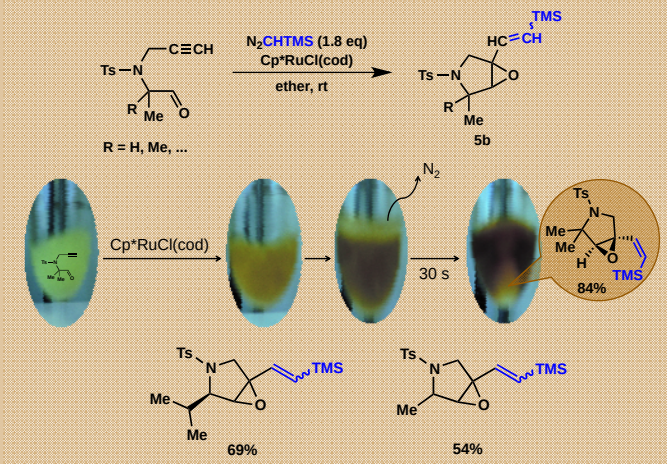
Acknowledgement: *This work was supported by MICINN [Projects: CTQ 2011-28258, Consolider Ingenio 2010 (CSD 2007-00006)] and the Xunta de Galicia (CN 2011/054). F.C. thanks to Xunta de Galicia for a predoctoral contract.*

Unsubstituted, 3- or 3,3-substituted 5-alkynals and *N*-propargyl-*N*-protected acetaldehydes were transformed into the corresponding dihydropyranes and oxazines in moderate to good yields.



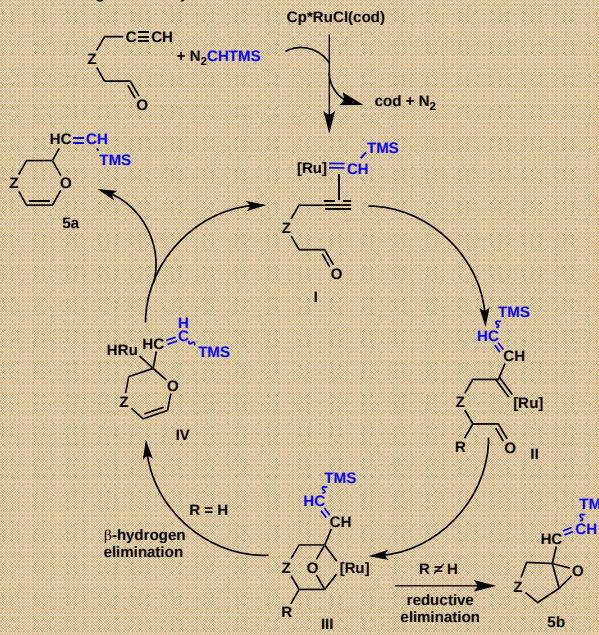
E = CO_2Me
Si = *t*-Bu(Me)$_2$Si

Interestingly, when *N*-propargyl-*N*-tosyl-2-methyl- and 2,2-dimethylacetaldehydes were used, exclusive formation of bicyclic vinyloxiranes were obtained in good yields.



Mechanistic Proposal

The catalytic transformation of alkynal derivatives with (trimethylsilyl)diazomethane in the presence of Cp*RuCl(cod) could be understood supposing the initial formation of ruthenium carbene species **I**. Oxidative coupling to give a metalacyclobutene followed by opening of this species would lead to the ruthenium vinyl carbene **II**. This intermediate could undergo a nucleophilic attack to the carbene, followed by a β-hydrogen elimination to give the ruthenium species **IV**. Reductive elimination from **IV** would lead to the observed dihydropyrane **5a**. On the other hand, vinyl ruthenium carbene **III** could undergo a reductive elimination affording to the vinyloxirane **5b**.



1) Cambeiro, F.; López, S.; Varela, J. A.; Saá, C. *Angew. Chem. Int. Ed.* **2012**, *51*, 723.
2) Monnier, F.; Castillo, D.; Dérien, S.; Toupet, L.; Dixneuf, P. H. *Angew. Chem. Int. Ed.* **2003**, *42*, 5474.
3) a) Varela, J.A.; González-Rodríguez, C.; Rubín, S. G.; Castedo, L.; Saá, C. *J. Am. Chem. Soc.* **2006**, *128*, 9576,
b) Batuecas, M.; Escalante, L.; Esteruelas, M. A.; García-Yebra, C.; Oñate, E.; Saá, C. *Angew. Chem. Int. Ed.* **2011**, *50*, 9712.