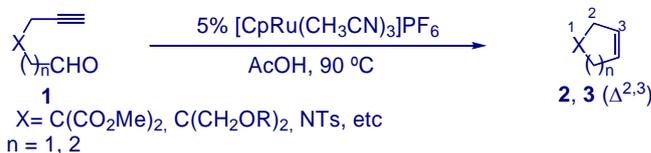


Jesús A. Varela, Carlos González-Rodríguez, Silvia G. Rubín, Luis Castedo and Carlos Saá*

Departamento de Química Orgánica y Unidad Asociada al CSIC, Facultad de Química, Universidad de Santiago de Compostela
15782 Santiago de Compostela, Spain
qocsa@usc.es

Ru(II)-Catalyzed Cyclization of Terminal Alkynals

We recently described a new, efficient Ru(II)-catalyzed cyclization of terminal alkynals **1** to cycloalkenes **2**.¹ Heating the 5-alkynal **1a** ($n=1$, $X=C(CO_2Me)_2$) in a 5% solution of the catalyst in AcOH afforded, after 24 h at 90 °C, the cyclopentene **2a** in excellent yield. Heating at higher temperatures led to faster reactions, but with increasing amounts of isomer **3a**. Use of the more electron-rich and sterically demanding catalyst $[Cp^*Ru(CH_3CN)_3]PF_6$ gave similar results. Interestingly, addition of 5% of dppf to the reaction mixture led exclusively to **2a**.



entry	catalyst ^a	t ^o C	time	yield (%) ^b	2a : 3a
1	$[CpRuL_3]PF_6$	90	24 h	95	95 : 5
2	"	130	1.5 h	96 ^c	60 : 40
3	"	150	50 min	93 ^c	50 : 50
4	$[Cp^*RuL_3]PF_6$	90	5.5 h	95 ^c	80 : 20
5	"	150	50 min	92 ^c	50 : 50
6	$[Cp^*RuL_3]PF_6$ + 5% dppf	90	8 h	85	100 : 0

^a L = CH₃CN, dppf = diphenylphosphinoferrocene. ^b Isolated yields. ^c GC yields.

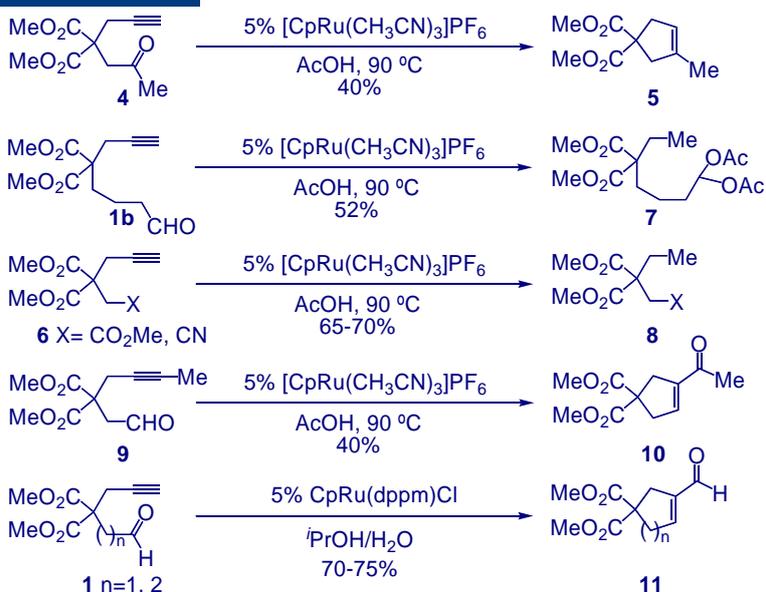
Mechanistic Considerations

- Alkynone **4** afforded the corresponding cyclopentene **5**, indicating that an oxidative addition of the ruthenium to the aldehyde C-H bond is unlikely.

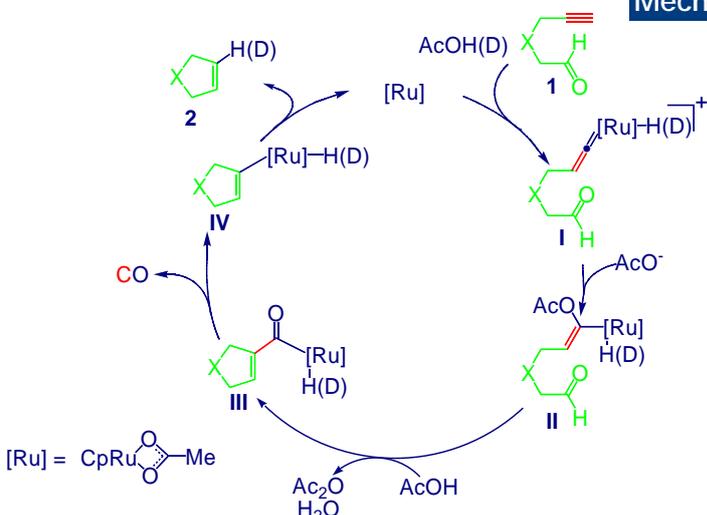
- Either enlarged alkynals **1b** ($n=3$), or alkynes without the aldehyde group **6**, gave rise to non cyclized compounds, **7** and **8**, respectively, with loss of one carbon, which suggested that the terminal carbon of the alkyne is the one lost during the reaction.

- When non-terminal alkynal **9** was used, the conjugated ketone **10**, keeping all the carbons, was isolated.

- Interestingly, terminal alkynals were able to cycloisomerize to conjugated aldehydes (all the carbons of the starting material remained) by just using $CpRu(dppm)Cl$ as catalyst in *i*PrOH/H₂O as solvent.



Mechanistic Proposal



The likely mechanism² would involve the formation of Ru(II) vinylidene species **I**, which upon nucleophilic addition of the acetic acid, would afford the vinyl Ru species **II**. Next, an aldol-type condensation would give the acyl Ru hydride **III**. Then, decarbonylation (*being the terminal carbon of the alkyne the one lost as CO*) followed by reductive elimination would afford the observed cycloalkenes **2**. When $CpRu(dppm)Cl$ was used as catalyst, the conjugated aldehydes **11** were obtained by reductive elimination from **III** (no decarbonylation takes place in this case due to the bidentate nature of dppm ligand).

Acknowledgement: This work was supported by the M.E.C. (Project CTQ2005-08613) and the Xunta de Galicia (Project PGIDT03PXIC20909PN). J.A.V. and C.G. also thank the M.E.C. for a research contract under the Ramón y Cajal program and one F.P.I. fellowship (BES-2003-0839) respectively. S.G.R. thank the Segundo Gil Dávila Foundation for a predoctoral fellowship.

References: ¹ Varela, J. A.; González-Rodríguez, C.; Rubín, S. G.; Castedo, L.; Saá, C. *J. Am. Chem. Soc.* **2006**, *128*, 9576.

² Tokunaga, M.; Suzuki, T.; Koga, N.; Fukushima, T.; Horiuchi, A.; Wakatsuki, Y. *J. Am. Chem. Soc.* **2001**, *123*, 11917.