Alkynal cyclizations and cycloisomerizations

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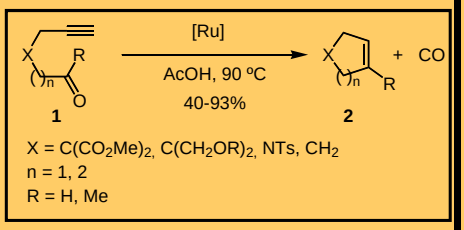
•Ru-vinylidene catalyze cyclizations

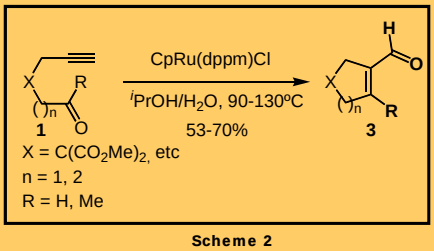
We have recently described the Ru-catalyzed decarbonylative cyclization of terminal 5-and 6-alkynals and 5-alkynones 1 to cycloalkenes 2 in moderate to excellent yields (Scheme 1).[1]



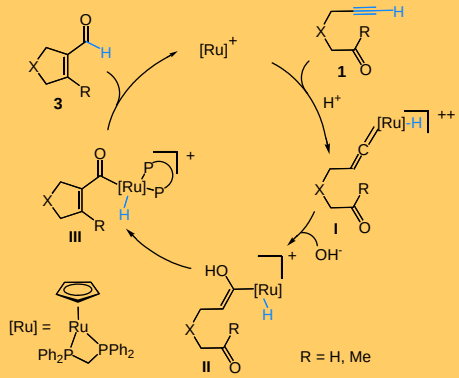
Scheme 1

•Ru-vinylidene catalyze cycloisomerizations

Cycloisomerization of alkynals and alkynones 1 to α,β-unsaturated aldehydes 3 was achieved using CpRu(dppm)Cl as catalyst (Scheme 3).
In this case no decarbonylation takes place due to the bidentate nature of dppm ligand, being favored the reductive elimination of III.



Scheme 2

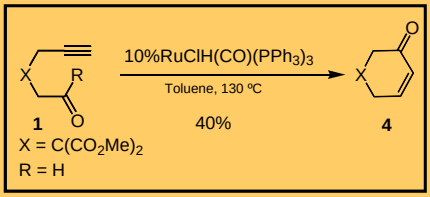


Scheme 3

The proposed mechanism starts with the formation of ruthenium vinylidene species I[2] which upon nucleophilic addition of the H_2O affords the vinyl Ru species II. Next, an aldol-type condensation gives the acyl Ru-hydride III, which after reductive elimination affords the observed exo cycloalkenones 3 (Scheme 3).

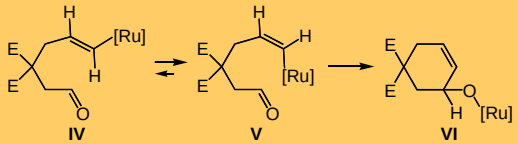
•Vinyl-Ru catalyze cycloisomerization

Other ruthenium alkynal cycloisomerization is possible in presence of a catalytic amount of $RuClH(CO)(PPh_3)_3$. Endocyclic α,β-unsaturated ketones was obtained as reaction products with moderate yields (scheme 4).



Scheme 4

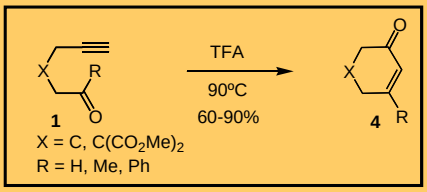
The mechanism could begins with the formation of an vinyl-Ru species IV witch undergoes isomerisation to a new vinyl-Ru V, witch thought the carbonyl insertion leads the alkoxy-Ru VI. A final β-elimination affords the observed conjugated ketone.



Scheme 4

•Brønsted acid- promoted endo-cyclizations

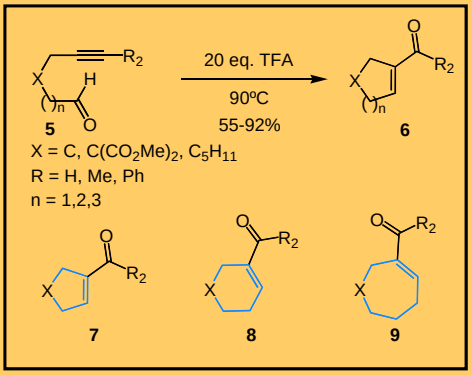
When terminal 5-alkynals and alkynones were subjected under trifluoroacetic acid conditions, endo-cyclohexenones derivatives 4 were obtained in good to excellent yields.[3]



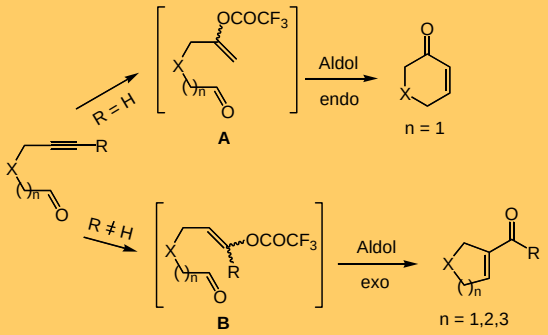
Scheme 6

•Brønsted acid- promoted exo-cyclizations

In addition we have described here the first cycloisomerization of non-terminal alkynals promoted by Brönsted acids (mainly trifluoroacetic acid) to give seven-membered exo cycloalkenones 9, an important core in several biologically important natural products,[5] as well as new cycloisomerizations of alkynals to give exo and endo five- and six-membered cycloalkenones 7 and 8 (Scheme 7).



Scheme 7



Scheme 8

A plausible mechanism for the cycloisomerizations is show in Scheme 8, although alternative oxete intermediates – as reported previously[4] – cannot be ruled out. Addition of TFA to the terminal and non-terminal alkynes could lead to the formation of vinyl trifluoroacetates A or B, respectively. These intermediates can undergo aldol-type condensations to give the observed endo or exo cyclic enones, respectively. These products could be considered as being derived from a controlled tandem alkyne hydration/aldol condensation process.

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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.
[3] González-Rodríguez, C.; Escalante L.; Varela, J. A.; Castedo, L.; Saá, C. *Org. Lett.* **2009**, *11*, 1531.
[4] a) Harding, C. E.; King, S. L. *J. Org. Chem.* **1992**, *57*, 883; Rhee, J. U.; Krische, M. J. *Org. Lett.* **2005**, *7*, 2493.