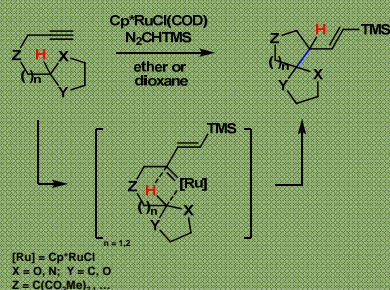


"Synthesis of Spiro and Fused Bicyclic Compounds via Catalytic Ruthenium Carbene Insertion into sp^3 C-H Bonds"

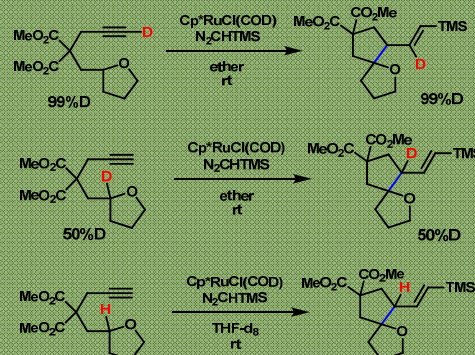
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Objective

We have recently developed a new procedure to promote cyclizations based on the easy formation of catalytic Ru carbenes from alkynes and (trimethylsilyl)diazomethane. The ruthenium carbene intermediate undergoes a tandem 1,5- and 1,6-hydride shift/cyclization sequence under mild conditions to afford complex spiro and fused bicyclic compounds.



Labelling Studies



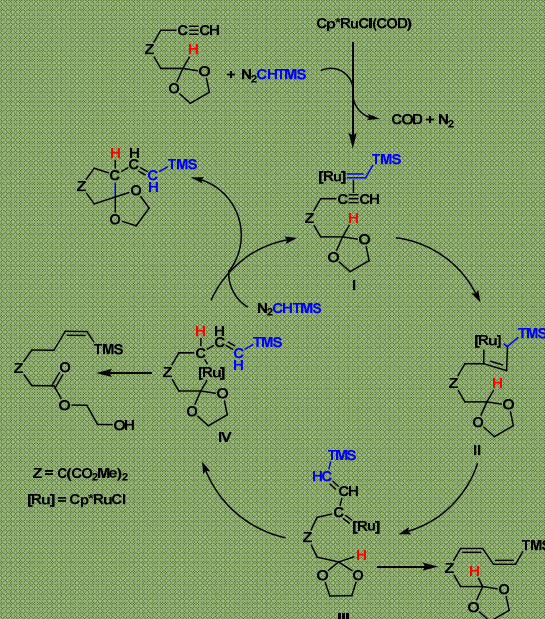
Ru-catalyzed 1,5 and 1,6-Hydride Shift/Cyclization

Entry	Substrate	Product	Yield(%) ^a
1,5-Hydride Shift			
1			80
2			65 ^b
3			25
4			61
5			61
6			79
7			90
8			52 ^c
9			85
1,6-Hydride Shift			
10			90
11			61
12			60
1,5-Fused Bicycles			
13			87 ^c
14			61

CONDITIONS: a) ether, rt; b) dioxane, rt; c) dioxane, 60°C

Mechanism

The catalytic transformation of alkyne derivatives with (trimethylsilyl)diazomethane in the presence of Cp*RuCl(COD) could be understood supposing the initial formation of Cp*RuCl(=CHTMS) as the catalytic active species, which once coordinated to the alkyne and formed the ruthenacyclobutene II evolves to the crucial vinylcarbene III. Subsequent hydride transfer to the electrophilic Ru-carbene (**Csp³-H activation**) gives rise to the ruthenacycle IV that, after reductive elimination, would lead to the bicyclic products. β -hydride elimination from III or opening of ruthenacycle IV by acetal assistance could explain the formation of the linear products found.



Conclusion

In summary, we have shown that a series of readily available alkyne acetals, ethers and amines could react with an electrophilic Ru vinyl carbene catalyst (from Cp*RuCl(COD) and N₂CHSiMe₃) to produce a range of structurally complex spiro or fused bicyclic structures. These cyclizations, which could be applied mainly to terminal alkynes, allow the efficient conversion of secondary or tertiary sp^3 C-H bonds into new C-C bonds under practical conditions.

Acknowledgement: This work was supported by the MEC (CTQ2008-06557), Consolider Ingenio 2010 (CSD2007-00006), and the Xunta de Galicia (2007/XA084 and INCITE08PXIB209024PR). F.C. thanks Xunta de Galicia for a predoctoral contract.