Metal-Catalyzed Carbocyclization by Intramolecular Reaction of Allylsilanes and Allylstannanes with Alkynes

Carolina Fernández-Rivas, María Méndez, and Antonio M. Echavarren*

Departamento de Química Orgánica
Universidad Autónoma de Madrid
Cantoblanco, 28049 Madrid, Spain
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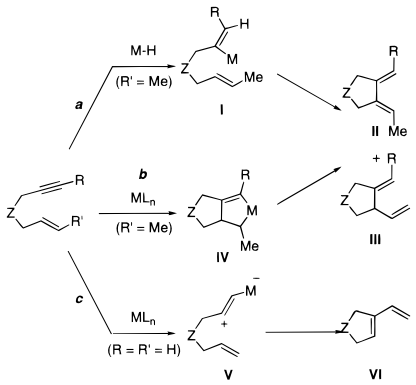
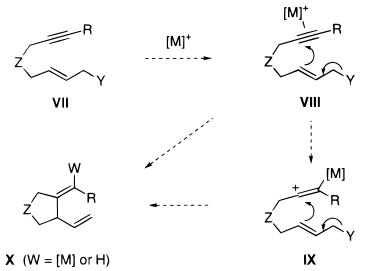
Transition-metal-catalyzed carbocyclizations of α,ω-enynes can proceed by three major pathways (Scheme 1). Thus, insertion of a metal hydride species M−H into the alkyne gives **I**, which may evolve by insertion and elimination to give the regioisomeric dienes **II** and **III** resulting in an overall cycloisomerization of the enyne (Scheme 1, pathway *a*).[1] Alternatively, an oxidative metallacycloaddition to form metalacycle **IV** followed by β-hydride elimination[1,2] may give rise to a mixture of **II** and **III** (pathway *b*). A more complex pathway has recently been uncovered in the reaction of enynes with electrophilic metal complexes that involves a rearrangement initiated by a complex of type **V** to afford metathesis-type products **VI** (pathway *c*).[3,4]

However, transition-metal-catalyzed carbocyclizations by intramolecular attack of mild nucleophilic reagents such as allylsilanes or allylstannanes (**VII**, M = SiR_3, SnR_3) onto alkynes to form dienes **III** are unknown,[5] although a stoichiometric process using $HgCl_2$ as an electrophile in the presence of a base has recently been developed.[6,7] Interestingly, strong Lewis acids such as $HfCl_4$ promote the endo-dig cyclization of allylsilanes **VII** (M = SiR_3).[8] Here we report that allylsilanes[9,10] and allylstannanes[11] cyclize readily upon treatment with several electrophilic Pt(II), Pd(II), Ru(II), and Ag(I) metal salts as catalysts.

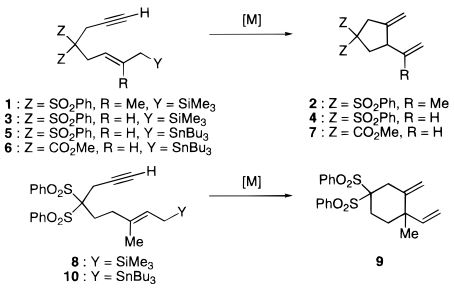
Scheme 1



Scheme 2



Scheme 3



Certain Ru(II) complexes react with terminal alkynes to form vinylidenes.[12] In this process, it has been proposed that the Ru(II) coordinates with the alkyne to form a η^2-alkyne complex.[13] Thus, we hypothesized that reaction of the alkyne with a Ru(II) complex could promote the nucleophilic attack of the allylsilane or stannane (Scheme 2). Alternatively, intermediate **VIII** could give rise to vinyl cation **IX**. An anti attack of the allyl nucleophile onto the η^2-alkyne metal complex or the metal-stabilized vinyl cation would then give cycle **X**. We have found that this process could be carried out catalytically with a variety of electrophilic metal complexes.

Heating a solution of allylsilane **1** in the presence of CpRuCl-$(PPh_3)_2$ (5 mol %) and $NaPF_6$ (10 mol %) in MeOH, conditions known to readily form vinylidene ruthenium complexes with terminal akynes,[13] gave cleanly carbocycle **2** in high yield (Scheme 3 and Table 1, entry 1). This transformation was also carried out with $RuCl_3$ under the same conditions (entry 2). Interestingly, Pd(II), Pt(II), and Ag(I) salts also triggered the carbocyclization reaction (entries 3−9). The best results were

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(3) Reaction catalyzed by palladacyclopentadiene complexes: (a) Trost, B. M.; Tanoury, G. J. *J. Am. Chem. Soc.* **1988**, *110*, 1636. (b) Trost, B. M.; Trost, M. K. *J. Am. Chem. Soc.* **1991**, *113*, 1850. (c) Trost, B. M.; Trost, M. K. *Tetrahedron Lett.* **1991**, *32*, 3647. (d) Trost, B. M.; Yanai, M.; Hoogsteen, K. A. *J. Am. Chem. Soc.* **1993**, *115*, 5294. (e) Trost, B. M.; Hashmi, A. S. K. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1085. (f) Trost, B. M.; Hashmi, A. S. K. *J. Am. Chem. Soc.* **1994**, *116*, 2183. (g) See also: Fürstner, A.; Szillat, H.; Gabor, B.; Mynott, R. *J. Am. Chem. Soc.* **1998**, *120*, 8305.

(4) Reaction catalyzed by Ru complexes or Pt salts: (a) Chatani, N.; Morimoto, T.; Muto, T.; Murai, S. *J. Am. Chem. Soc.* **1994**, *116*, 6049. (b) Blum, J.; Berr-Kraft, H.; Badrieh, Y. *J. Org. Chem.* **1995**, *60*, 5567. (c) Chatani, N.; Furukawa, N.; Sakurai, H.; Murai, S. *Organometallics* **1996**, *15*, 901. (d) Chatani, N.; Kataoka, K.; Sakurai, H.; Murai, S.; Furukawa, N.; Seki, Y. *J. Am. Chem. Soc.* **1998**, *120*, 9104.

(5) Palladium-catalyzed intramolecular reaction of allylsilanes with dienes: (a) Castaño, A. M.; Bäckvall, J.-E. *J. Am. Chem. Soc.* **1995**, *117*, 560. (b) Castaño, A. M.; Persson, B. A.; Bäckvall, J.-E. *Chem. Eur. J.* **1997**, *3*, 482.

(6) Huang, H.; Forsyth, C. J. *J. Am. Chem. Soc.* **1997**, *62*, 88595.

(7) Reviews of organoallylmetalation of alkynes: (a) Knochel, P. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 4, Chapter 4.4. (b) Yamamoto, Y.; Naoki, A. *Chem. Rev.* **1993**, *93*, 2007. (c) Normat, J. F.; Alexakis, A. *Synthesis* **1981**, 841.

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(10) Synthesis of allylsilanes from allyl carboxylates: (a) Tsuji, Y.; Funato, M.; Ozawa, M.; Ogiyama, H.; Kajita, S.; Kawamura, T. *J. Org. Chem.* **1996**, *61*, 5779. (b) Tsuji, Y.; Kajita, S.; Isobe, S.; Funato, M. *J. Org. Chem.* **1993**, *58*, 3607.

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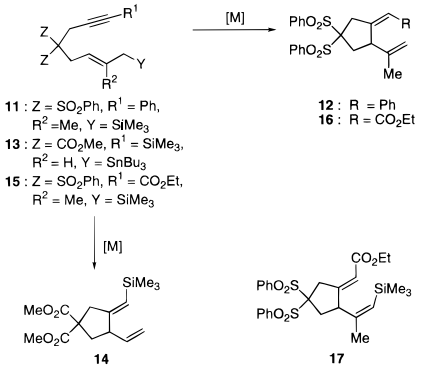
Table 1. Metal-Catalyzed Cyclization of Enynes **VII** (Schemes 3 and 4)[a]

entry	enyne	catalyst (mol %)	solvent	product	yield (%)
1	**1**	$CpRuCl(PPh_3)_2$ (5)[b]	MeOH	**2**	92
2	**1**	$RuCl_3$ (5)	MeOH	**2**	53
3	**1**	$PdCl_2$ (5)	MeOH	**2**	47
4	**1**	$Pd(MeCN)_2Cl_2$ (5)	MeOH	**2**	65
5	**1**	$Pd(MeCN)_4(BF_4)_2$ (5)	MeOH	**2**	82
6	**1**	$PtCl_2$ (5)	acetone	**2**	94
7	**1**	$PtCl_2$ (5)	acetone[c]	**2**	83
8	**1**	$Pt(MeCN)_2Cl_2$ (5)	MeOH	**2**	95
9	**1**	AgOTf (5)	dioxane	**2**	54
10	**3**	$CpRuCl(PPh_3)_2$ (20)[b]	MeOH	**4**	50
11	**3**	$PtCl_2$ (5)	MeOH	**4**	82
12	**3**	$PtCl_2$ (5)	acetone[c]	**4**	81
13	**5**	$PtCl_2$ (5)	MeOH	**4**	62
14	**6**	$CpRuCl(PPh_3)_2$ (20)[b]	MeOH	**7**	81
15	**6**	$PtCl_2$ (5)	MeOH[d]	**7**	43
16	**8**	$PtCl_2$ (2)	MeOH	**9**	48
17	**10**	$PtCl_2$ (2)	MeOH	**9**	79
18	**10**	AgOTf (28)	dioxane	**9**	32
19	**10**	$Pd(MeCN)_4(BF_4)_2$ (20)	dioxane	**9**	31
20	**11**	$PtCl_2$ (5)	MeOH	**12**	87
21	**13**	$CpRuCl(PPh_3)_2$ (50)	MeOH	**14**	79
22	**15**	$PtCl_2$ (5)	MeOH	**16** (+**17**)	50 (+43)

[a] Unless otherwise stated, all reactions were carried out under refluxing conditions for 17 h. [b] 2 equiv (based on Ru) of $NaPF_6$ were also added. [c] Reaction temperature = 23 °C. [d] Reaction time = 48 h.

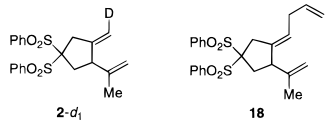
Scheme 4



obtained by using $PtCl_2$ or $Pt(MeCN)_2Cl_2$ as the catalysts in acetone or MeOH as the solvents (entries 6−8). The cyclization could not be promoted by proton or Lewis acids.[14] Similarly, silane **3** reacts in the presence of $CpRuCl(PPh_3)_2$ (entry 10) or $PtCl_2$ (entries 11 and 12) to give **4**. Allylstanannes **5** and **6** also react under these conditions to furnish **4** and **7**, respectively (entries 13−15). Cyclization of allylsilane **8** with $PtCl_2$ catalyst in refluxing MeOH proceeded rather sluggishly to give six-membered-ring carbocycle **9** (entry 16). The corresponding allylstannane **10** was more reactive, furnishing **9** in good yield with $PtCl_2$ as the catalyst (entry 17).

Substituted alkynes also react with electrophilic metal catalysts to give the corresponding carbocycles (Scheme 4). Thus, phenyl-substituted alkyne **11** reacted uneventfully in the presence of $PtCl_2$ to give selectively *Z*-**12** (Table 1, entry 20).[15] The cyclization of trimethylsilyl-substituted alkynes proceeded more slowly and had to be carried out with the more reactive allylstannane in the presence of $CpRuCl(PPh_3)_2$ (50 mol %). Under these conditions, **13** gave exclusively **14** with an E configuration on the trimethylsilyl-substituted alkene (entry 21).[15] Substrate **15**, bearing an alkyne activated with an electron-withdrawing group, reacted in the presence of $PtCl_2$ to give a 1:1 mixture of **16**, with the exocyclic alkene with a Z-configuration,[15] and **17**,[15] the product of a formal metal-catalyzed ene-cyclization.[3]

To ascertain the mechanism of the metal-catalyzed cyclization, the reaction of allylsilane **1** was carried out using methanol-d_4 as the solvent. Under the conditions of entry 8, **1** gave exclusively **2**-d_1.[16] This result indicates that the metal probably coordinates the alkyne as shown in **VIII**, thus triggering an anti attack of the allyl nucleophile. Cleavage of the carbon−metal bond of **X** (W = PtCl) by methanol-d_4 accounts for the formation of **2**-d_1. The



isolation of Z-configured **12** and **16** is also consistent with an anti attack of the allyl nucleophile to the η^2-coordinated complex **VIII** or a vinyl cation **IX**. On the other hand, the formation of **14** in the cyclization of **13** can be explained by an attack of the allylstannane anti to the more sterically hindered trimethylsilyl substituent of the vinyl cation, in agreement with that proposed for a similar cyclization mediated by $HgCl_2$.[6]

Trapping of intermediate alkeny−metal complex **X** (W = [M]) could lead to the formation of an additional C−C bond. Thus, it could be conceived that insertion of allyl chloride into the alkenyl−Pd bond followed by elimination of $PdCl_2$ could give an allylated derivative.[17] In the event, performing the cyclization of **1** with $Pd(MeCN)_2Cl_2$ as the catalyst (5 mol %) in THF in the presence of excess allyl chloride and 4 Å molecular sieves led stereoselectively to **18** (43%),[15] along with **2** (19%).[18]

In summary, we have found that the cyclization of allylsilanes and allylstannanes with alkynes proceeds catalytically in the presence of a variety of electrophilic metal salts. The use of $PtCl_2$ in methanol or acetone gives rise to the best results in most cases. This reaction is regio-complementary to that promoted by Lewis acids.[8] Metathesis-type products, which are the major products in the cyclization of enynes with electrophilic metal salts,[4,5] are not formed in this metal-catalyzed cyclization.[19] Since allylsilanes and allylstannanes are readily available from allyl carboxylates,[10,11b] this new carbocyclization offers a synthetically useful alternative to the cyclization−carbonylation of allyl halides or carboxylates with alkynes catalyzed by nickel or palladium.[20] The stereoselective formation of ene-type product **17** in the cyclization of **15** is also of interest and suggests that further optimization of the catalysts by the use of appropriate ligands[2] could lead to a general synthesis of functionalized carbocycles.

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Supporting Information Available: Experimental details, characterization data, and copies of the ^1H and ^{13}C NMR spectra for new carbocycles (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(14) No cyclization was observed with: (a) $NaPF_6$, MeOH, reflux; (b) BF_3·OEt_2, reflux. The reaction in the presence of TsOH led to decomposition.

(15) The configuration of this compound has been determined by NOEDIFF or NOESY experiments. See the Supporting Information for details.

(16) The configuration of **2**-d_1 was determined by the absence of the signal corresponding to the methylidene E-hydrogen (4.96 ppm) of **2**. See the Supporting Information for details.

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(18) When the reaction was carried out in MeOH, **18** was obtained in only 9% yield, along with **2** (84%).

(19) (a) Interestingly, the simple enyne dimethyl (propargyl)(allyl)malonate, which gives methathesis products with other metal catalysts,[4a,c] reacted with $CpRuCl(PPh_3)_2$ (20 mol %) and $NaPF_6$ (20 mol %) in MeOH (reflux, 17 h) reacts by a different pathway to give known dimethyl 3-formyl-4-methyl-3-cyclopenten-1,1-dicarboxylate (54%).[19b] (b) Parsons, W. H.; Kuehne, M. E. *J. Org. Chem.* **1977**, *42*, 3408.

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