Platinum-Catalyzed Alkoxy- and Hydroxycyclization of Enynes

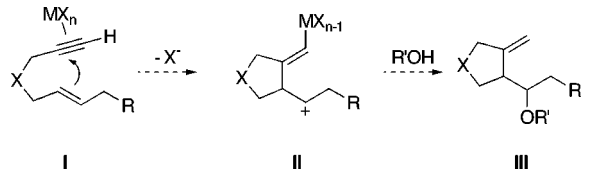
María Méndez, M. Paz Muñoz, and Antonio M. Echavarren*

Departamento de Química Orgánica
Universidad Autónoma de Madrid
Cantoblanco, 28049 Madrid, Spain

Received July 14, 2000

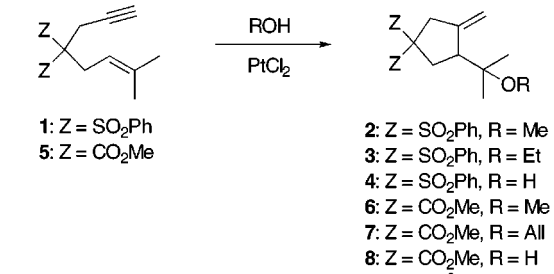
Electrophilic transition metal complexes or halides MX_n catalyze the cyclizations of α,ω-enynes.[1] Thus, Pd(II),[2] Ru(II),[3] and Rh(I)[4] complexes catalyze the cycloisomerization of enynes under mild conditions.[5] However, palladacyclopentadienes were found to catalyze a novel transformation that yields rearranged metathesis-type products.[6] Certain electrophilic Ru(II) complexes as well as Pt(II) derivatives also catalyze this process.[7,8]

We have recently reported a new cyclization that proceeds by the intramolecular reaction of allylsilanes and allylstannanes with alkynes to afford dienes.[9] This reaction was proposed to take place by coordination of the metal to the alkyne, followed by the anti attack of the allyl nucleophile. We conceived that simple enynes could react analogously by the anti-attack of the alkene onto the (η^2-alkyne)metal complex **I**. It was expected that the transient carbocation **II** resulting from this in the cyclization would be trapped by the nucleophile R′OH to give **III**. Here we report the realization of this concept by using $PtCl_2$ as the catalyst.



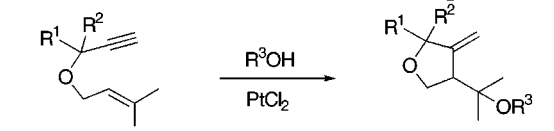
I **II** **III**

The best results on the cyclization of enynes were obtained by using $PtCl_2$ as the catalyst, which is also a catalyst for the formation of metathesis-type products from enynes.[7c,e] Thus, heating **1** with $PtCl_2$ (5 mol %) in MeOH led to **2** in high yield (Table 1, entry 1).[10] The cyclization is not a proton-catalyzed process since no reaction took place in the presence of HCl, HI, or *p*-TsOH in MeOH.[11] Reaction of **1** in EtOH led to **3** (entry 2), while reaction in aqueous acetone afforded alcohol **4** (entry 3). Malonate **5** reacted in MeOH, allyl alcohol, or water to give ethers **6** and **7** and alcohol **8** (entries 4−6), respectively. Cycloisomerization product **9** was also obtained as a minor product in the reactions of entries 4 and 6.[12]



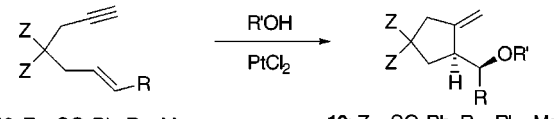
1: Z = SO_2Ph
5: Z = CO_2Me

2: Z = SO_2Ph, R = Me
3: Z = SO_2Ph, R = Et
4: Z = SO_2Ph, R = H
6: Z = CO_2Me, R = Me
7: Z = CO_2Me, R = All
8: Z = CO_2Me, R = H



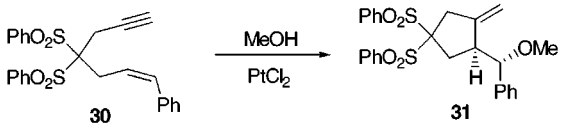
10: $R^1 = R^2 = H$
14: R^1 = Ph, R^2 = H
15: $R^1 = R^2$ = Me

11: $R^1 = R^2$ = H, R^3 = Me
12: $R^1 = R^2$ = H, R^3 = H
13: $R^1 = R^2$ = H, R^3 = Ac
16: R^1 = Ph, R^2 = H, R^3 = Me
17: $R^1 = R^2$ = Me, R^3 = Me

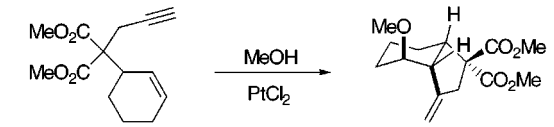


18: Z = SO_2Ph, R = Me
21: Z = CO_2Me, R = Me
23: Z = SO_2Ph, R = Ph
27: Z = CO_2Me, R = Ph

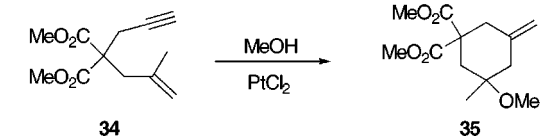
19: Z = SO_2Ph, R = R′ = Me
22: Z = CO_2Me, R = R′ = Me
24: Z = SO_2Ph, R = Ph, R′ = Me
25: Z = SO_2Ph, R = Ph, R′ = H
28: Z = CO_2Me, R = Ph, R′ = Me
29: Z = CO_2Me, R = Ph, R′ = H



30 **31**



32 **33**



34 **35**

Cyclization in MeOH or water also proceeds with propargyl prenyl ether (**10**) to give **11** and **12** (entries 7 and 8). Use of acetic acid as the solvent led to acetate **13** (entry 9). Reaction of **14** and **15** in MeOH shows that the reaction tolerates steric hindrance at the propargylic position (entries 10 and 11).

(1) Trost, B. M.; Krische, M. J. *Synlett* **1998**, 1.
(2) (a) Trost, B. M.; Lautens, M.; Chan, C.; Jebaratnam, D. J.; Mueller, T. *J. Am. Chem. Soc.* **1991**, *113*, 636 and references therein. (b) Trost, B. M.; Haffner, C. D.; Jebaratnam, D. J.; Krische, M. J.; Thomas, A. P. *J. Am. Chem. Soc.* **1999**, *121*, 6183. (c) Trost, B. M.; Krische, M. J. *J. Am. Chem. Soc.* **1999**, *121*, 6131.
(3) (a) Trost, B. M.; Toste, F. D. *J. Am. Chem. Soc.* **2000**, *122*, 714. (b) For an alternative pathway see: Trost, B. M.; Toste, F. D. *J. Am. Chem. Soc.* **1999**, *121*, 9728.
(4) Cao, P.; Wang, B.; Zhang, X. *J. Am. Chem. Soc.* **2000**, *122*, 6490.
(5) Early transition metal complexes such as $Cp_2Ti(CO)_2$ also give rise to enyne cycloisomerization: Sturla, S. J.; Kabalaeiu, N. M.; Buchwald, S. L. *J. Am. Chem. Soc.* **1999**, *121*, 1976.
(6) (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.
(7) (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. (e) Fürstner, A.; Szillat, H.; Stelzer, F. *J. Am. Chem. Soc.* **2000**, *122*, 6785.
(8) Trost, B. M.; Doherty, G. A. *J. Am. Chem. Soc.* **2000**, *122*, 3801.
(9) Fernández-Rivas, C.; Méndez, M.; Echavarren, A. M. *J. Am. Chem. Soc.* **2000**, *122*, 1221.
(10) This reaction proceeded in 98% yield with 5 mol % $Pt(MeCN)_4(BF_4)_2$. However, this complex was not active as a catalyst with other substrates.
(11) Alkynes have been used as the terminators in cationic polyenyne cyclizations. For a review, see: Sutherland, J. K. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 3, Chapter 1.9.
(12) (a) Diene **9** was recovered unchanged after being heated in MeOH with $PtCl_2$ which demonstrates that dienes are not intermediates in the formation of products **III**. (b) Reaction of enynes with $PtCl_2$ in polar, nonnucleophilic solvents led to cycloisomerization. Work to determine the generality of this reaction is in progress.

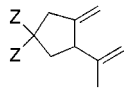
10.1021/ja002577m CCC: $19.00
Published on Web 11/03/2000

Table 1. $PtCl_2$-Catalyzed Cyclization of Enynes[a]

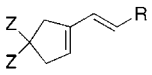
entry	enyne	nucleophile	time (h)	product	yield (%)
1	1	MeOH	14	**2**	88
2	1	EtOH	15	**3**	86
3	1	H_2O	16	**4**	70
4	5	MeOH	17	**6**	65[b]
5	5	AllOH	17	**7**	57
6	5	H_2O	17	**8**	57[c]
7	10	MeOH	14	**11**	59 (76)[d]
8	10	H_2O	15	**12**	73 (94)[d]
9	10	AcOH[e]	16	**13**	55
10	14	MeOH	15	**16**	64
11	15	MeOH	13	**17**[f]	68
12	18	MeOH	17	**19**[g]	66[h]
13	21	MeOH	16	**22**[i]	59
14	23	MeOH	16	**24**	77
15	23	H_2O	34	**25**	74[j]
16	27	MeOH	72	**28**	60
17	27	H_2O	120	**29**	86
18	30	MeOH	48	**31**	72
19	32	MeOH	17	**33**	67
20	34	MeOH	20	**35**	80[k]

[a] Unless otherwise stated, all reactions were carried out under reflux with 5 mol % catalyst. Reactions with water were carried out in aqueous acetone at 40 °C. [b] Cycle **9** was also obtained (10%). [c] 10 mol % $PtCl_2$. **9** was also obtained (17%). [d] Based on converted starting enyne. [e] Reaction at 70 °C. [f] 1.5:1 stereoisomeric mixture. [g] 5:1 stereoisomeric mixture. [h] **20** was also obtained (17%). [i] 1.5:1 stereoisomeric mixture. [j] **26** was also obtained (11%). [k] **37** was also obtained (14%).

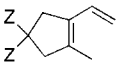
Disubstituted alkenes also undergo cyclization reaction. Thus, **18** (5:1 trans/cis) reacted with MeOH to give **19** as a 5:1 mixture of stereoisomers, along with rearranged derivative **20** as a minor product (entry 12). In contrast, cyclization of the analogous malonate **21** (5:1 trans/cis) proceeded with lower stereoselectivity to give **22** as a 1.5:1 mixture of stereoisomers (entry 13). On the other hand, **23** gave exclusively **24** and **25**, respectively (entries 14 and 15). In this last reaction, rearranged **26** was obtained as a minor product. Malonate **27** gave **28** and **29** as single isomers (entries 16 and 17). Interestingly, cis derivative **30** reacted with MeOH to give **31**, the stereoisomer of **24**[13] (entry 18). The cyclization of **32** in MeOH afforded **33** as a single isomer (entry 19), which is in accord with an anti addition of the alkyne and nucleophile across the double bond.



9: Z = CO_2Me

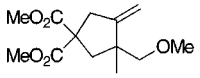


20: Z = SO_2Ph, R = Me
26: Z = SO_2Ph, R = Ph

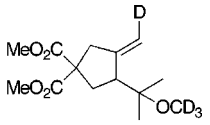


37: Z = CO_2Me

Substrate **34** reacts with MeOH in a 6-endo-trig process to give **35** as a result of the attack of the nucleophile on the more substituted carbon of the double bond. None of the alternative 5-exo-trig product **36** was formed in this reaction (entry 20). Enynes with monosubstituted alkenes do not react with $PtCl_2$.



36



6-d_4

The cyclization of **5** in methanol-d_4 led stereoselectively to **6**-d_4.[14] This result is similar to that found in the cyclization of allylsilanes and allylstannanes with alkynes,[9] which indicates that the metal coordinates as shown in **I**.[15] The overall result corresponds to a trans-attack of the alkene to the (η^2-alkyne)-platinum complex **I** (M = $PtCl_2$) or a slipped (η^1-alkyne)platinum species[16] to form homoallyl cation **II**.[17,18] Indeed, the metal-stabilized homoallyl−methylcyclopropyl−cyclobutyl cation may be the common intermediate in this new reaction as well as the metathesis-type cyclization.[19,20] However, the stereoselective cyclizations of **18**, **21**, **23**, **27**, and **30** point to a concerted trans formation of the C−C and C−O bonds.

In contrast with current methodologies for the synthesis of carbocycles based on the intramolecular attack of silyl enol ethers to alkynes promoted by $Pd(OAc)_2$ or $HgCl_2$,[21] this cyclization reaction proceeds with a maximum atom-economy by the simultaneous formation of a C−C and a C−O bond from enynes. Additionally, in most cases the reaction proceeds with high stereoselectivity. Further synthetic applications as well as mechanistic studies on this new alkyne-initiated cyclization are underway.

Acknowledgment. This paper is dedicated to Prof. José Barluenga on the occasion of his 60th birthday. We are grateful to the DGES (Project PB97-0002-C2-02) for support and to the MEC for predoctoral fellowships to M.M. and M.P.M. We also thank Johnson Matthey PLC for a generous loan of $PtCl_2$.

Supporting Information Available: Experimental details and characterization data for new carbocycles (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

JA002577M

(13) The configurations of **19**, **24**, **25**, **28**, **29**, and **31** were assigned on the basis of that of **33**.

(14) The configuration of **6**-d_4 was determined by the absence of the signal corresponding to the methylidene *E*-hydrogen.

(15) Cyclization of a terminally substituted alkyne gave a carbocycle with a *Z* alkene. See the Supporting Information for details.

(16) (a) Chisholm, M. H.; Clark, H. C. *Acc. Chem. Res.* **1973**, *6*, 202. (b) For the proposal of a related (η^1-alkyne)ruthenium complex see: Pilette, D.; Moreau, S.; Le Bozec, H.; Dixneuf, P. H.; Corrigan, J. F.; Carty, A. J. *J. Chem. Soc., Chem. Commun.* **1994**, 409.

(17) Pt(II) and Ru(II) catalyze the cycloisomerization of ω-aryl-1-alkynes via (η^1-alkyne)metal intermediates: Chatani, N.; Inoue, H.; Ikeda, T.; Murai, S. *J. Org. Chem.* **2000**, *65*, 4913.

(18) A different mechanism has been demonstrated for the cyclization of 3-arylallyl propargy ethers initiated by the insertion of a H-PdL_2OH species (L = *m*-sulfonated triphenylphosphine) on the alkyne: Galland, J.-C.; Savignac, M.; Genêt, J.-P. *Tetrahedron Lett.* **1997**, *38*, 8695.

(19) An alternative mechanism proceeding by a metallacyclopentene has been favored by Trost.[1,6,8]

(20) See also: Fürstner, A.; Szillat, H.; Gabor, B.; Mynott, R. *J. Am. Chem. Soc.* **1998**, *120*, 8305.

(21) See: Frontier, A. J.; Raghavan, S.; Danishefsky, S. J. *J. Am. Chem. Soc.* **2000**, *122*, 6151 and references therein.