Cycloisomerization of aromatic alkynols via catalytic Os-vinylidenes: formation of 3-benzoxepines

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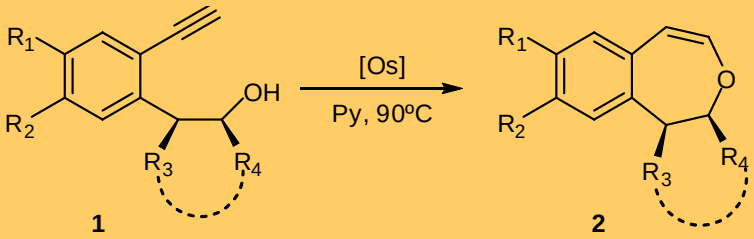
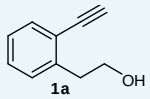
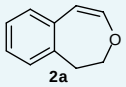
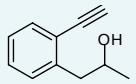
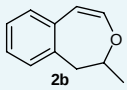
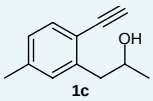
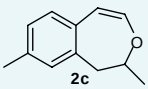
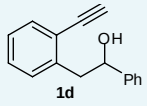
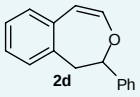
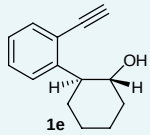
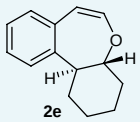
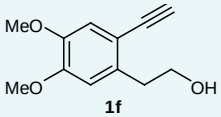
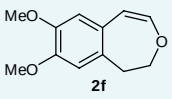
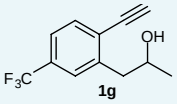
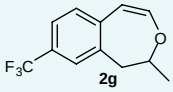
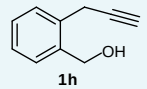
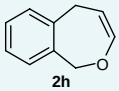
Heterocyclic compounds are widely spread in Nature. The development of new metal-catalyzed cyclizations can offer powerful means to synthesize these compounds.[1] An attractive approach to this end, under the basis of atom economy,[2] is the involvement of catalytic metal vinylidenes.[3] Herein we present a new 7-endo cyclization of aromatic alkynols 1 to give 3-benzoxepines 2 through catalytic Os-vinylidenes (Scheme 1)



$[Os] = [CpOs(Py)_3]PF_6$

Scheme 1. Os-catalyzed endo heterocyclizations of aromatic alkynols **1**

Table 1. Os-catalyzed heterocyclization of aromatic alkynols **1** into 3-benzoxepines **2**

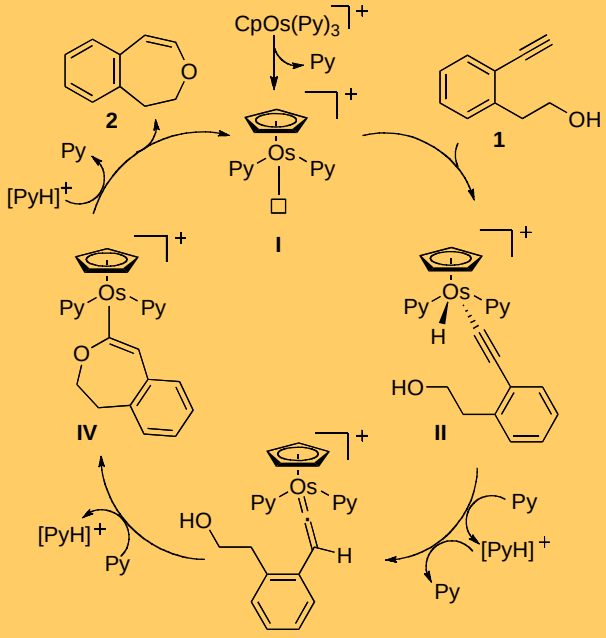
Entry	Substrate	Product	Yield (%) [a]
1	 1a	 2a	60
2	 1b	 2b	62[b]
3	 1c	 2c	67
4	 1d	 2d	58
5	 1e	 2e	56[b]
6	 1f	 2f	60
7	 1g	 2g	63
8	 1h	 2h	40

[a] 10% $[CpOs(Py)_3]PF_6$, 0.15 M, Py, 90°C. [b] 10% $[CpCH_2NHMeOs(Py)_2]PF_6$

Reaction times: 20 min – 1.5 h

Proposed catalytic cycle

After dissociation of Py from the cationic Os(II) precatalysts, cationic unsaturated 16 e- Os(II) is formed acting as the catalytic species **I**. Formation of Os vinylidenes from **I** is the key process of the catalytic cycle, which starts with coordination to the alkyne **1** followed by the easy oxidative addition to the terminal alkyne to give the cationic Os(IV) species **II**. Removal of the Os hydride by the Py followed by reprotonation on the β carbon of the alkyne gives the Os vinylidene **III**. Then, the α electrophilic center of the vinylidene undergoes an intramolecular attack by the alcohol, which after deprotonation, gives rise to the vinylic Os species **IV**. Finally, protonation of the heterocyclic ligand with the piridinium salt liberating the 3-benzoxepine **2** and regeneration of the cationic unsaturated species **I** closes the catalytic cycle



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[1] D. M. P. Mingos, R. H. Crabtree, Eds. *Comprehensive Organometallic Chemistry III*; Elsevier: Kyoto, 2007; Vol. 11.

[2] a) B. M. Trost, *Science* **1991**, *254*, 1471-1477; b) B. M. Trost, *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 259-281

[3] a) F. E. McDonald, K. S. Reddy, Y. Diaz, *J. Am. Chem. Soc.* **2000**, *122*, 4304-4309. b) B. M. Trost, Y. H. Rhee, *J. Am. Chem. Soc.* **2002**, *124*, 2528-2533. c) B. M. Trost, Y. H. Rhee, *J. Am. Chem. Soc.* **2003**, *125*, 7482-7483. d) B. M. Trost, *Angew. Chem. Int. Ed.* **2007**, *46*, 2074-2077 . e) C. Bruneau, P. H. Dixneuf. *Angew. Chem. Int. Ed. Engl.* **2006** , *45*, 2176-2203.