Ru-Catalyzed Cycloisomerization of Aromatic Homo- and Bis-homopropargyl Amines/Amides

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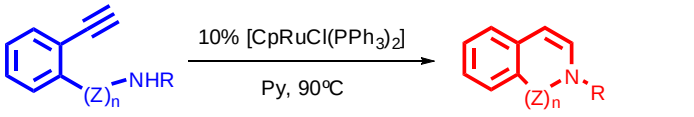
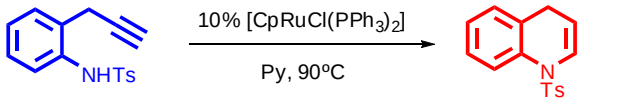
The development of new metal-catalyzed cyclizations can offer powerful means to synthesize bioactive heterocyclic compounds. An attractive approach to this end involves the nucleophilic trapping of electrophilic metal vinylidenes. As part of our ongoing program devoted to the synthesis of heteroaromatic compounds using commercial or easily available metal catalysts,[1] herein we present new Ru-catalyzed 5-*endo* and regioselective 6-*endo* heterocyclizations or **aromatic homo- and bis-homopropargyl amines/amides** to give **indoles 2**, **dihydroisoquinolines 4** and **dihydroquinolines 6** in good-to-excellent isolated yields.[2]



1, n = 0
3, n = 1

Z = CO, SO_2, CH_2
R = H, alkyl, COR, SO_2Ar

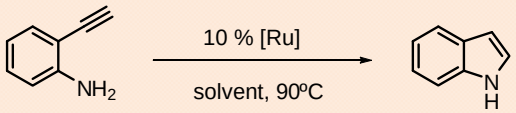
2, n = 0, Indoles
4, n = 1, Dihydroisoquinolines



5

6, Dihydroquinoline

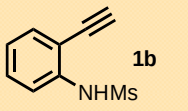
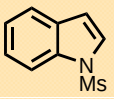
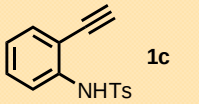
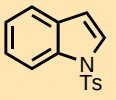
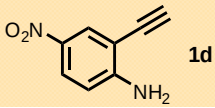
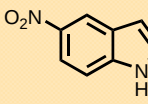
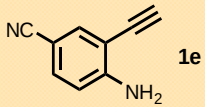
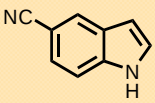
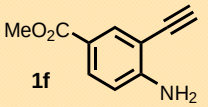
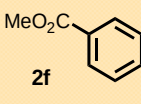
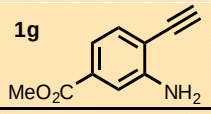
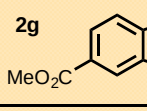
Optimization



1a **2a**

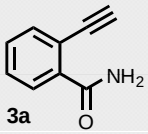
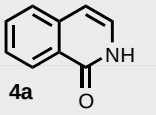
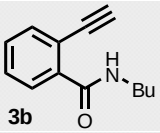
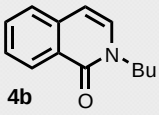
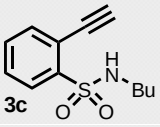
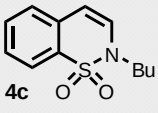
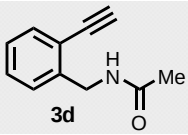
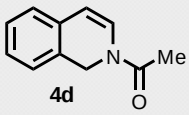
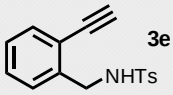
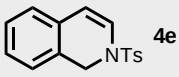
Entry	Catalyst	Solvent	t	(%)
1	[CpRuCl(PPh$_3$)$_2$]	*n*-BuNH$_2$	25 min	61
2	[CpRuCl(PPh$_3$)$_2$]	Py	25 min	84
3	[CpRuCl(PPh$_3$)$_2$]	DCE	12 h	50
4	5% [CpRuCl(PPh$_3$)$_2$]	Py	50 min	54
5	[Cp*RuCl(PPh$_3$)$_2$]	Py	35 min	48
6	[CpRu(CH$_3$CN)$_3$]PF$_6$	Py	1 h	67
7	---	Py	48 h	---

Formation of indoles

Entry	Substrate	Product	t (min)	(%)
1	 **1b**	 **2b**	40	73
2	 **1c**	 **2c**	40	80
3	 **1d**	 **2d**	20	72
4	 **1e**	 **2e**	30	98
5	 **1f**	 **2f**	30	98
6	 **1g**	 **2g**	90	92

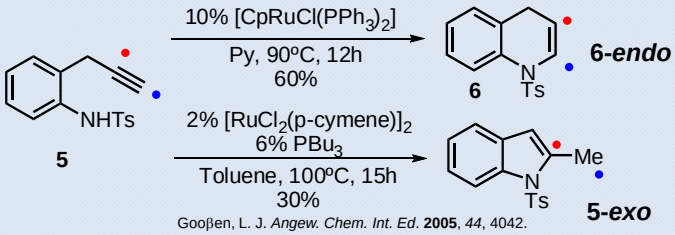
10% [CpRuCl(PPh$_3$)$_2$], Py, 90ºC

Formation of dihydroisoquinolines

Entry	Substrate	Product	t (h)	(%)
1	 **3a**	 **4a**	1	80
2	 **3b**	 **4b**	6	74
3	 **3c**	 **4c**	6	61
4	 **3d**	 **4d**	5	56
5	 **3e**	 **4e**	4	82

10% [CpRuCl(PPh$_3$)$_2$], Py, 90ºC

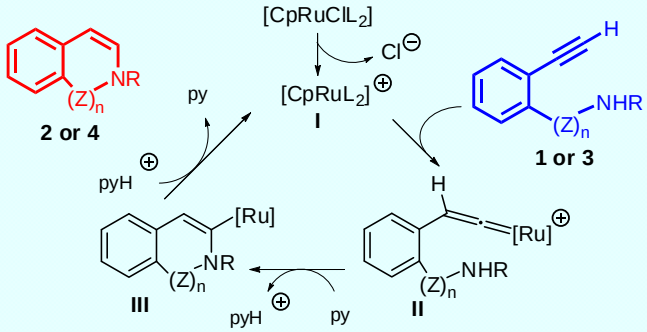
Formation of dihydroquinolines: a comparative



5 **6**

Gooβen, L. J. *Angew. Chem. Int. Ed.* **2005**, *44*, 4042.

Mechanism



[Ru] = $CpRuL_2$
L = PPh_3

Z = CO, SO_2, CH_2
R = H, alkyl, COR, SO_2Ar

[1] a) Varela-Fernández, A.; González-Rodríguez, C.; Varela, J. A.; Castedo, L.; Saá, C. *Org. Lett.* **2009**, *11*, 5350. b) Varela-Fernández, A.; García-Yebra, C.; Varela, J. A.; Esteruelas, M. A.; Saá, C. *Angew. Chem. Int. Ed.* **2010**, *49*, 4278.
[2] Varela-Fernández, A.; Varela, J. A.; Saá, C. *Adv. Synth. Catal.* **2011**. In press.

We thank the MICINN (Spain) (CTQ2008-06557), Consolider Ingenio 2010 (CSD2007-00006), Xunta de Galicia and European Regional Development Fund (2007/XA084 and INCITE08PXIB209024PR) for financial support. A. V.-F. thanks XUGA and USC for a predoctoral grant.