Tandem Rh-Catalyzed C-H Allylation / Oxidative Cyclization of Acetanilides: A New Entry to Indoles

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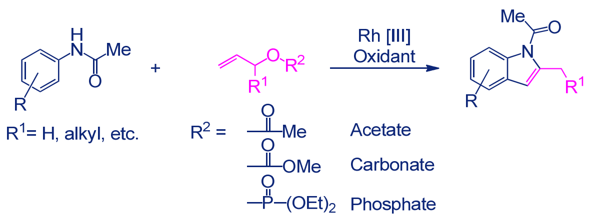
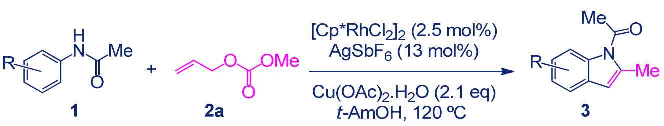
Objective

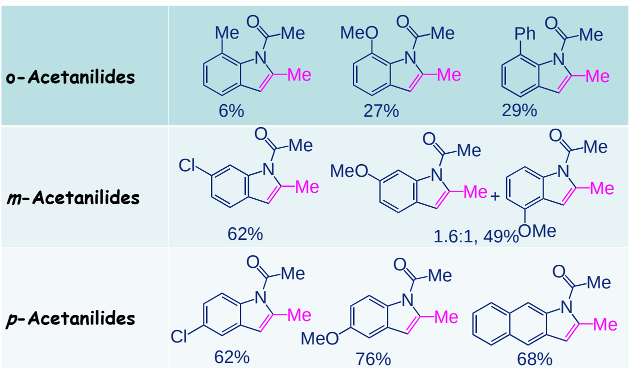
Direct C-H bond functionalization of organic compounds by transition metal catalysis represents an effective economy-step method for the synthesis of a variety of heterocycles.[1] The synthesis of 2,3-disubstituted indoles by Pd-, Ru- and Rh-catalyzed cyclization of aniline derivatives with *internal* alkynes has been deeply studied over the last few years.[2]

Herein, we report a new synthesis of 2-substituted indoles by tandem Rh-catalyzed cyclization of acetanilides with allylic derivatives, thus showing the equivalency of these coupling partners with *terminal* alkynes.

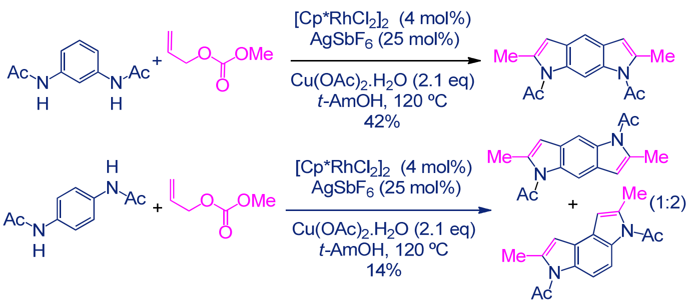


2-Methylindoles 3 by Tandem Rh-Catalyzed Cyclization of Substituted Acetanilides

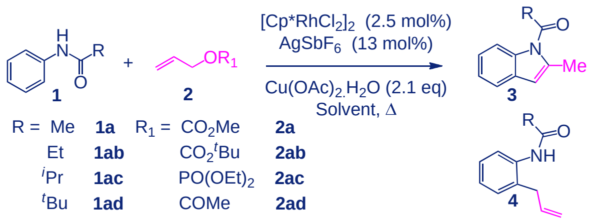




Bis-indoles by Tandem Rh-Catalyzed Cyclization of *Bis*-acetanilides



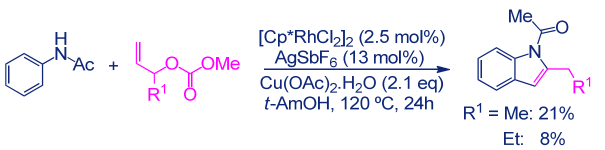
Optimization



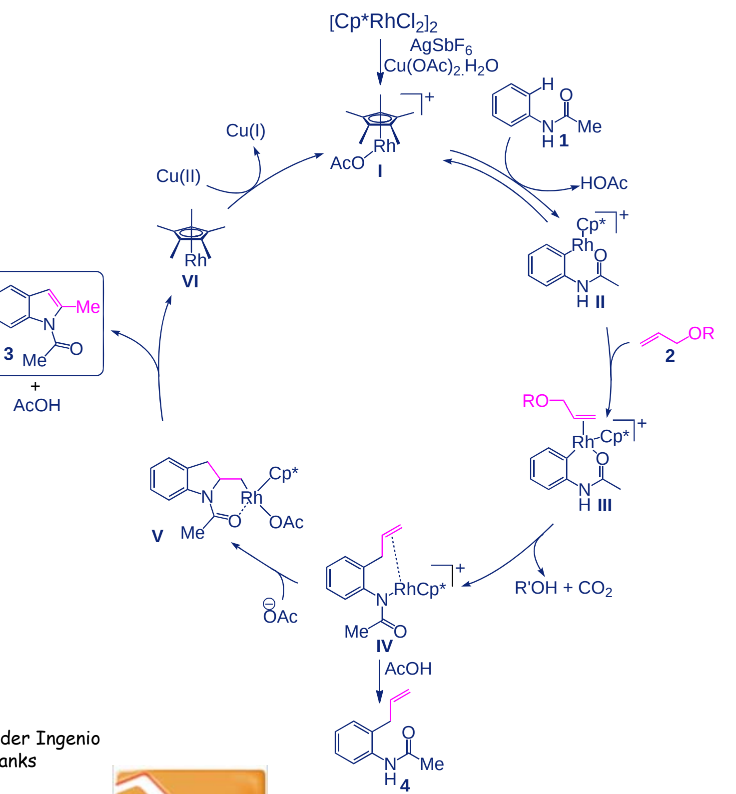
Entry	Substrate	Allylic derivative	Solvent	T/°C	Time	Yield (%)[a]
1	1a	2a	DCE	120	20 h	66
7	1a	2a	*t*-BuOH	130	24 h	75
8	1a	2a	*t*-AmOH	120	24 h	82
9[b]	1a	2a	*t*-AmOH	120	15 h	75
12	1a	2ab	*t*-AmOH	120	24 h	47
13	1a	2ac	*t*-AmOH	120	24 h	49
14	1a	2ad	*t*-AmOH	120	24 h	68
15	1a	2ae	*t*-AmOH	120	24 h	32
16	1ab	2a	*t*-AmOH	120	24 h	63
17	1ac	2a	*t*-AmOH	120	24 h	38
18	1ad	2a	*t*-AmOH	120	24 h	(59)[c]

[a] *Conditions*: **1a** (0.37 mmol), **2a** (0.41 mmol), [**1a**] = 0.074 M. Isolated yields of **3**. [b] *Conditions*: $[Cp^*Rh(CH_3CN)_3]SbF_6$ (5 mol%). [c] *o*-allylacetanilide **4** was obtained.

2-Alkyl Indoles by Tandem Rh-Catalyzed Cyclization of Acetanilide with Allylic Derivatives



Proposed Mechanism



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References:

[1] (a) Yamaguchi, J.; Yamaguchi, A. D.; Itami, K. *Angew. Chem. Int. Ed.* **2012**, *51*, 8960-9009. (b) Kuhl, N.; Hopkinson. M. N.; Wencel-Delord J.; Glorius, F. *Angew. Chem. Int. Ed.* **2012**, *51*,, 10236-10254.

[2] [Pd]: (a) Wurtz, S.; Rakshit, S.; Neumann, J. J.; Droge, T.; Glorius, F. *Angew. Chem. Int. Ed.* **2008**, *47*, 7230-7233. [Ru]: (b) Ackermann, L.; Lygin, A. V. *Org. Lett.* **2012**, *14*, 764-767. [Rh]: (c) Stuart, D. R.; Alsabeh, P.; Kuhn, M.; Fagnou, K. *J. Am. Chem. Soc.* **2010**, *132*, 18326-18339.