

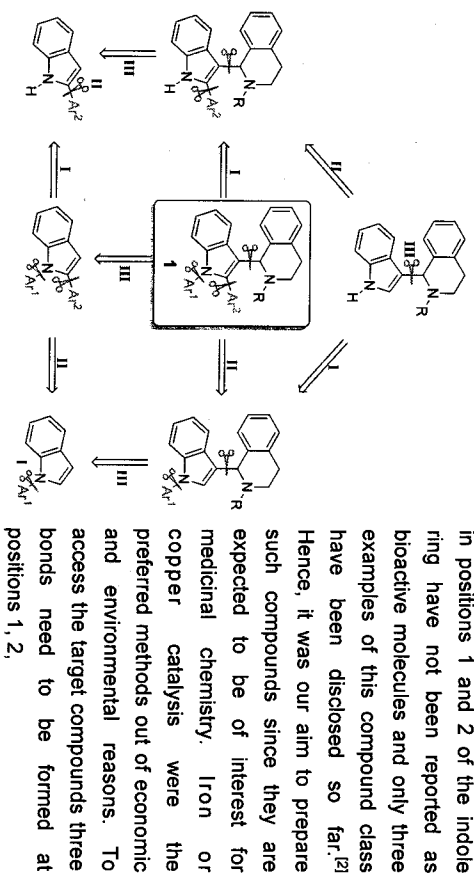
## Comprehensive investigation of the direct functionalization of indole in positions 1, 2, and 3

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1,2,3,4-Tetrahydroisoquinolines (THIQs) are common substructures in natural products and the structural motif of 1-(Indol-3-yl)-THIQ is also found in compounds with biological activity.<sup>[1]</sup> Interestingly 1-(Indol-3-yl)-THIQs carrying additional aryl substituents



in positions 1 and 2 of the indole ring have not been reported as bioactive molecules and only three examples of this compound class have been disclosed so far.<sup>[2]</sup> Hence, it was our aim to prepare such compounds since they are expected to be of interest for medicinal chemistry. Iron or copper catalysis were the preferred methods out of economic and environmental reasons. To access the target compounds three bonds need to be formed at positions 1, 2,

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2 a) M.-Z. Wang, C.-Y. Zhou, M.-K. Wong, C.-M. Che, *Chem. - Eur. J.* **2010**, *16*, 5723; b) H. Okada, (Kyocera Milia Industrial Co., Ltd., Japan), *Application: JP 2009080233*, **2009**, p. 10pp.

## Anti-Markovnikov Hydroarylation of Unactivated Terminal, Internal, and Cyclic Olefins with Electron-poor Arenes

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We report a series of hydroarylation of unactivated olefins with electron-poor arenes that occur with high selectivity for the linear product without directing groups. In addition, we show that analogous hydroarylations occur with internal, acyclic olefins to yield linear alkylarene products. Experimental and computational (DFT) mechanistic studies provide evidence for reversible C-H bond cleavage by transfer of the aryl C-H bond to a coordinated alkene, followed by trans-to-cis isomerisation and turnover-limiting reductive elimination. The formation of terminal alkenes from internal alkenes occurs by initial establishment of an equilibrium mixture of alkene isomers, followed by addition of the arene to the terminal alkene. The computed Gibbs free energy catalytic cycle for hydroarylation of propene catalyzed by Ni(IPr)<sub>2</sub> is shown below.

