CAFFEINE AND THEOPHYLLINE AS SUSTAINABLE, BIOSOURCED NHC LIGAND PRECURSORS FOR EFFICIENT CROSS-COUPLING REACTIONS

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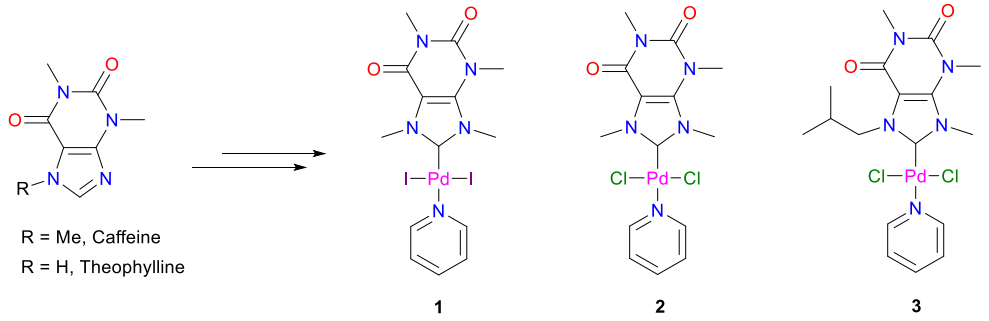
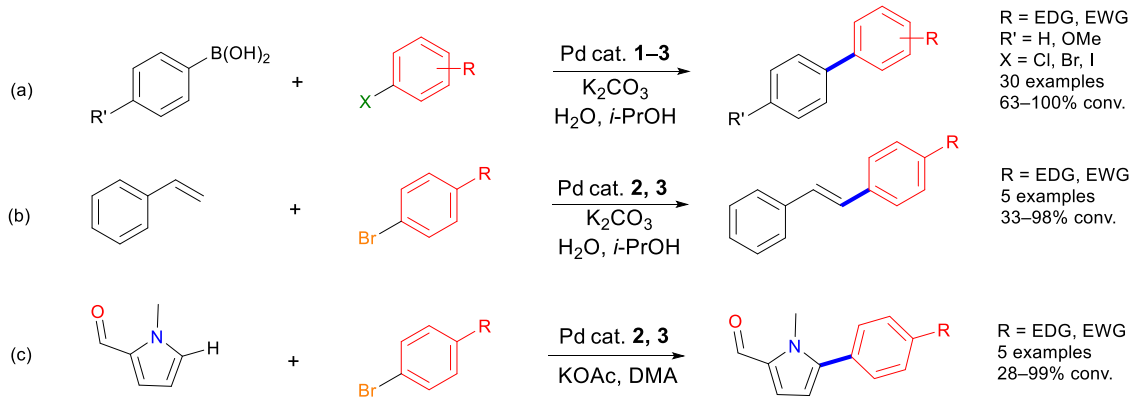
Caffeine and theophylline are two substrates of choice for generating new ligand systems, thanks to their large availability, low cost of extraction, and ability to form different types of N-heterocyclic carbenes (NHCs).[1] The alkylation of caffeine with methyl iodide afforded 1,3,7,9-tetramethylxanthinium iodide, which was further reacted with $PdCl_2$, KI, and K_2CO_3 in neat pyridine to afford the $[PdI_2(NHC)(Py)]$ complex **1**. An intermediate anion exchange led to the analogous dichloride complex **2**. Theophylline was successfully converted into a new xanthinium salt bearing an isobutyl group on its N7 atom, which was further employed to prepare the $[PdCl_2(NHC)(Py)]$ complex **3**.[2]



Complexes **1**–**3** displayed a high catalytic activity in the Suzuki–Miyaura cross-coupling of aryl halides with phenylboronic acids (a),[2] in the Mizoroki–Heck cross-coupling of styrene with aryl bromides (b), and in the C–H activation of 1-methyl-2-pyrrole-carboxaldehyde with aryl bromides (c).



References:

(1) Makhlou, A.; Frank, W.; Ganter, C. *Organometallics* **2012**, *31*, 7272–7277.

(2) Mazars, F.; Zaragoza, G.; Delaude, L. *Submitted for publication* **2022**.