

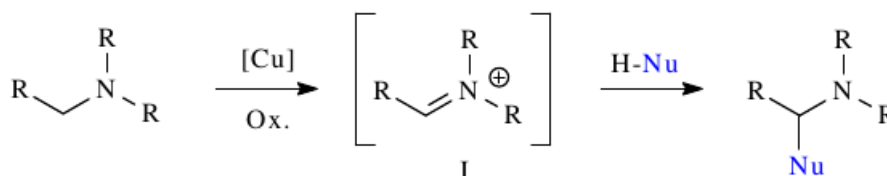
The mechanism of the aerobic Cu-catalysed oxidative cross-coupling of tertiary amines. An experimental and computational study.

Giovanni Ghigo,¹ Stefano Dughera,¹ Pierpaolo Morgante¹

¹Dipartimento di Chimica, Università di Torino, via P. Giuria 7-10125 Torino.

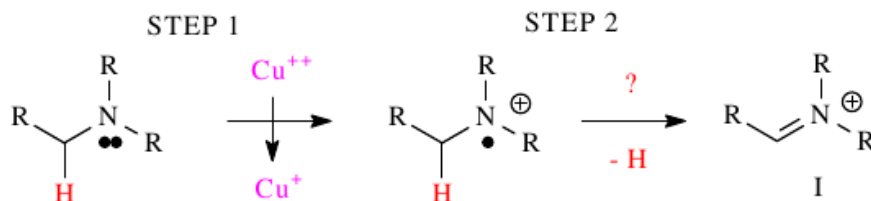
e-mail: giovanni.ghigo@unito.it

Cross-Coupling reactions catalysed by transition metals are used since several years in the synthesis of organic molecules and applied to a wide spectrum of substrates.¹ Among them, we focused our interest on the Aerobic Oxidative Cross-Coupling catalysed by copper and in particular, the reaction involving the tertiary amines.² In this poster, we presents the preliminary results of a combined experimental and computational study of the mechanism of this reaction. Although the reaction has been extensively tested from the synthetic point of view² the details of the reaction are still unknown. The mechanistic studies are still limited to a few experimental³ and computational⁴ works that have allowed only to verify the role as the oxidant of copper (Cu^{++}) in the formation of the iminium as intermediate for the reaction with some nucleophilic reactant HNu (Scheme 1).



Scheme 1

What is the real process leading to the iminium (Scheme 2), *i.e.* what is the specie that actually completes the oxidation through the hydrogen-abstraction (STEP 2 in Scheme 2) is still unknown. The ignorance of these details prevents an efficient application, extension and optimization of this reaction. For this reason we challenged to fill this gap with the combined use of computational and experimental methods. In particular, the roles of the counter-ion of $\text{Cu}^{+/++}$ and of the molecular oxygen used as oxidant (a part from the oxidation of Cu^+ to Cu^{++} regenerating the catalyser) are the subject of our study. The preliminary results indicate, in fact, that the commonly accepted mechanism is too naive and that it does not take in account a possible role for these species.



Scheme 2

- 1) Yeung C. S., Dong V. M. *Chem. Rev.* **2011**, *111*, 1215–1292.
- 2) Zhang C., Tang C., Jiao N. *Chem. Soc. Rev.* **2012**, *41*, 3464–3484; Klussmann M., Jones. K. M. *SYNLETT* **2012**, *23*, 159–162.
- 3) (a) Boess, E.; Schmits, C.; Klussmann M. *J. Am. Chem. Soc.* **2012**, *134*, 5317–5325; (b) Scott, M.; Sud, A.; Boess, E.; Klussmann, M. *J. Org. Chem.* **2014**, *79*, 12033–12040.
- 4) Cheng, G. J.; Song, L. J.; Yang, Y. F.; Zhang, X.; Wiest, W.; Wu, Y.-D. *ChemPlusChem* **2013**, *78*, 943–951.