Electrochemical Carbonylation of Primary Amines to Symmetrical N,N'-Disubstituted Ureas Using Palladium (II) Catalyst in Combination with Its Anodic Recycling

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Subtituted ureas have been of recent interest due to appearance of this functionality in drug candidates such as HIV protease inhibitors; in addition, ureas have found widespread use as agricultural chemicals, resin precursors, dyes and additives to petroleum compounds and polymers. N,N'-Disubstituted ureas are usually obtained by reaction of primary amines with isocyanates, phosgene or phosgene derivatives. Although the yields are generally high for these reactions, other aspects can be problematic, such as the reagents toxicity and the use of drastic reaction conditions. The possibility of performing efficient electrochemical transformation with catalysts, avoiding toxic reagents, represents a fondamental target of the modern organic chemistry.

We are developing new, selective and enviromental friendly methodologies based on the use of electrochemistry for fine chemicals preparation, and recently reported the synthesis of oxazolidin-2-ones from of 2-amino-1-alkanols using a palladium(II) complex as catalyst in combination with its anodic recycling at a graphite electrode.¹ In this study, we want to extend this new procedure for an efficient synthesis of N,N'-disubstituted ureas. Aromatic and aliphatic primary amines undergo oxidative carbonylation under atmospheric pressure of carbon monoxide at room temperature using Pd(II) catalyst in combination with its anodic recycling at a graphite electrode. (Eq. 1).

 $2RNH_2 + CO \xrightarrow{Pd cat} RNHCNHR + 2H^+ + 2e^- (1)$

The following general procedure was used: in a cell with three separated compartments, kept at 50 \pm 0.1°C, the electrolysis was carried out on a solution of amine (0.5 mmol) in 30 dm³ of CH₃CN containing n-Bu₄NBF₄ (0.2 mol dm⁻³) as supporting electrolyte, in the presence of Pd(OAc)₂, (0.05 mmol) and NaOAc (2 mmol), under 1 atm of CO at +0.4 V vs SCE. An AMEL potentiostat model 552 equipped with an integrator was used in controlled potential electrolyses. A graphite electrode, of apparent area 3 cm², was used as working electrode. The counter-electrode was a Pt wire and the reference was a saturated calomel electrode (SCE). After the end of electrolysis, the anodic solution was analyzed by HPLC, (CH₃CN/H₂O, 9/1). The preliminary results show that the reaction efficiently proceeded under atmospheric pressure of carbon monoxide with the catalyst systems taken into account (62-80% yields). The use of a base is necessary to avoid the

formation of HPd(II)(PPh₃) $_2^+$ or of HPd(II) $^{+2}$, that do not react in this reaction.²

To sum up, we have development a new electrochemical method for the reoxidation of Pd(0) to Pd(II), which can be used for a large variety of organic synthesis.

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References

1. Chiarotto, I.; Feroci M. Tetrahedron Letters 2001, 42, 3451-3453

2. Amatore, C.; Jutand, A.; Meyer, G.; Carelli, I.; Chiarotto, I. *Eur. J. Inorg. Chem.* **2000**, *8*, 1855-1859.