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INDIRECT ELECTROCHEMICAL CARBONYLATION OF AROMATIC AMINES WITH A PALLADIUM CATALYST

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Summary: *Aromatic amines are converted to carbamates under very mild conditions, using carbon monoxide, palladium (II) acetate and copper (II) acetate in combination with anodic reoxidation.*

Isocyanates, which are important industrial intermediates in the synthesis of polyurethanes and pesticides are commonly produced via reaction of phosgene and amines (Figure 1). Considerable research has been devoted to developing new routes to isocyanates, avoiding the use of corrosive and highly toxic phosgene.[1] One promising alternative method involves oxidative carbonylation of amines to carbamates followed by thermal decomposition to isocyanates (Figure 1).

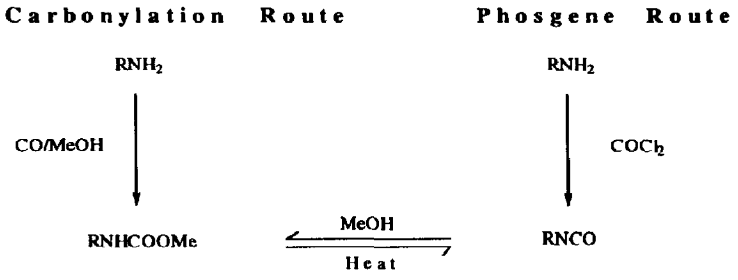

Figure 1

The literature on oxidative carbonylation of amines is relatively sparse, however interest has grown in recent years. Much of the literature in this area requires fairly drastic conditions. For example, one typical method uses Pd deposited on carbon black together with NaI promoter at 170°C and 86 bar pressure to convert amines to carbamates in high yields.[2] Some low pressure methods are also known. One example uses $PdCl_2$, $CuCl_2$, HCl, alcohol, CO and O_2 to convert amines to carbamates in excellent yields under exceptionally mild conditions (1 atm., room temperature).[3] This method, however, suffers from the drawback of using a dangerous CO/O_2 gas mixture. Another process, utilizes $PdCl_2$, $CuCl_2$, HCl, CO, alcohol plus an organic peroxide to convert amines to carbamates.[4] (The peroxide functions to reoxidize palladium). This method also afforded excellent yields of carbamate under very mild conditions (1 atm., room temperature).

Recently, our group has published reports describing the electrochemical regeneration of palladium(II) catalysts in a Wacker-like oxidative carbonylation of olefins[5] (eq. 1) and alkynes.[6]

$$\mathrm{RCH{=}CH_2 + PdCl_2 + CO + MeOH \xrightarrow[0.6\ V\ vs\ SCE]{LiCl} RCH(COOMe)CH_3} \qquad \underline{1}$$

This technique proved very convenient for regenerating spent catalyst *in situ*. As well, it enabled us to conduct carbonylations under very mild conditions (1 atm., ≤50°C). Furthermore at reaction's end, we were able to separate the catalyst from the products by reversing the voltage and electroplating palladium out onto the electrode.

We now wish to report that this technique can be applied to carbonylate aromatic amines, affording carbamates in excellent yields under mild conditions (eq. 2).

$$\mathrm{RNH_2 + CO + MeOH + Pd(OAc)_2 + Cu(OAc)_2 \xrightarrow[\substack{50^{0}C,\ 1atm \\ 0.35V\ vs\ SCE}]{NaOAc} RNHCOOMe} \qquad \underline{2}$$

Thus, treatment of p-toluidine with carbon monoxide, methanol, palladium(II) acetate as catalyst, copper (II) acetate as an electron transfer agent, sodium acetate as electrolyte, at 50°C, 1 atmosphere of CO pressure and 0.35 V vs SCE afforded methyl-N-p-tolylcarbamate in 85% yield. In contrast to our previously published work on indirect electrochemical carbonylations,[5,6] however, this process required the presence of an electron transfer agent ($Cu(OAc)_2$). This proved to be necessary, since the voltage normally required to regenerate palladium(II) directly at an electrode (~0.7 V vs SCE) is sufficient to decompose aromatic amines.[7] This problem was circumvented by employing a copper-based electron transfer agent which has a lower reoxidation voltage (~0.35 V).

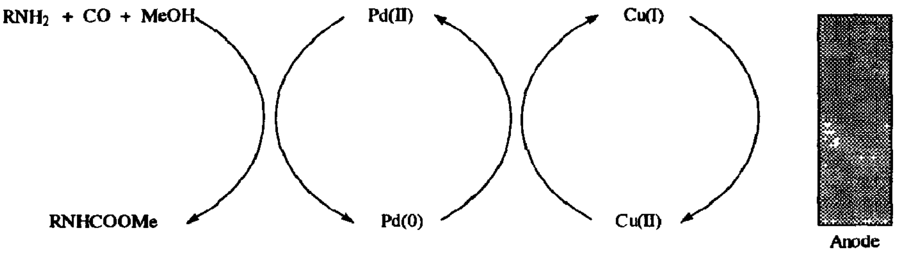

Figure 2

This system has been used to convert a variety of aromatic amines cleanly into carbamates in excellent yields. The results are given in Table 1. All optimization experiments were conducted with p-toluidine. Halide and phenol functionalities on the aromatic ring remained unaffected by this reaction. Higher alcohols such as ethanol also served as solvent, affording excellent yields of product. Palladium chloride, copper chloride and lithium chloride could be substituted for the corresponding acetates, however, yields were lower.

Table 1 **$Pd(OAc)_2$ Catalyzed Carbonylation of Aromatic Amines**

Substrates	Alcohol	% Yield Carbamate[a,b]
$p\text{-}MeC_6H_4NH_2$	MeOH	85
$C_6H_5NH_2$	MeOH	99
$o\text{-}MeC_6H_4NH_2$	MeOH	84
$p\text{-}ClC_6H_4NH_2$	MeOH	96
$HOC_6H_4NH_2$	MeOH	78
$2,6\text{-}Me_2C_6H_3NH_2$	MeOH	95
$2,5\text{-}Me_2C_6H_3NH_2$	MeOH	93
$2,4\text{-}Me_2C_6H_3NH_2$	MeOH	55
$2,3\text{-}Me_2C_6H_3NH_2$	MeOH	90
$3,5\text{-}Me_2C_6H_3NH_2$	MeOH	67
$p\text{-}MeC_6H_4NH_2$	MeOH	61[c]
$p\text{-}MeC_6H_4NH_2$	EtOH	98

[a] NMR yields.

[b] Where less than quantitative yields are shown, they are due mostly to the presence of unreacted starting materials. These reactions can be pushed to completion by the input of more electricity. The exception to this was the aminophenol reaction, which afforded a small quantity of unidentified side product.

[c] Reaction with $PdCl_2$, $CuCl_2$ and LiCl.

Ortho-substituted toluidine converted to carbamate in 84% yield - virtually the same as that from para-substituted toluidine, implying that steric crowding around the phenyl-nitrogen bond has no effect on product yield. Disubstituted anilines converted to carbamates in variable yield.

Typical reaction conditions: 0.1 M NaOAc in 150 ml MeOH was placed into a divided H cell reactor. Graphite felt electrodes (Electrosynthesis Co. type GFS6) ca. 5 x 2 x 0.5 cm were inserted into the cell. The apparatus was warmed to 50°C, and CO was bubbled through at a rate of 1 bubble/sec. Then in sequence were added $Pd(OAc)_2$ (0.5 mmol), $Cu(OAc)_2$ (1.0 mmol) and substrate (5.0 mmol). Upon addition of the substrate, the solution was electrolyzed at 0.35 V vs SCE until 2 equivalents of electricity had been consumed. Reaction time was typically $\leq$ 1 day. At the end of the reaction, electrode polarity was reversed causing catalyst to separate from the solution and plate out onto the electrode. The mixture was then filtered, evaporated, treated with acetone, filtered and concentrated to give carbamate. Further purification if necessary, was effected by column chromatography on alumina. Analyses were conducted by IR, NMR, GC and GC/MS.

This homogeneous carbonylation offers a clear advantage over heterogeneous amine carbonylations in that it does not require drastic reaction conditions to produce high yields. This method also offers advantages over other homogeneous amine carbonylations in having an efficient and safe catalyst regeneration system, coupled with facile catalyst/product separation.

In conclusion, this indirect electrochemical system converts aromatic amines to carbamates in high yields under mild reaction conditions.

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