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Telescoped CO_2-Mediated Amide Synthesis from Nitroarenes in a Continuous Flow Regime

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ABSTRACT

The amide bond is one of the most important functional groups in organic molecules, it is ubiquitous in pharmaceuticals, natural products, and crucial for biomolecules[1,2]. Herein, we describe an efficient telescoped synthesis of functionalized amides utilizing CO_2 as a mediator under continuous flow conditions. It envisions a minimal interference protocol starting from cheap and available nitroarenes undergoing electrochemical transformation to yield iminophosphoranes. Such iminophosphoranes can be reacted with carbon dioxide without the need of activating species, such as DBU, in a pressurized tube-in-tube reactor, generating isocyanates *in-situ*, followed by trapping with a variety of carboxylic acids to yield substituted amides. The initial electrochemical step is performed with quantitative yield as established by Costa e Silva[3], and the product is used in the next step without purification. So far, optimized conditions of the amidation step have been nearly established with up to four variations of carboxylic acids tested with independent yields of up to 92%, for two steps (Fig. 1).

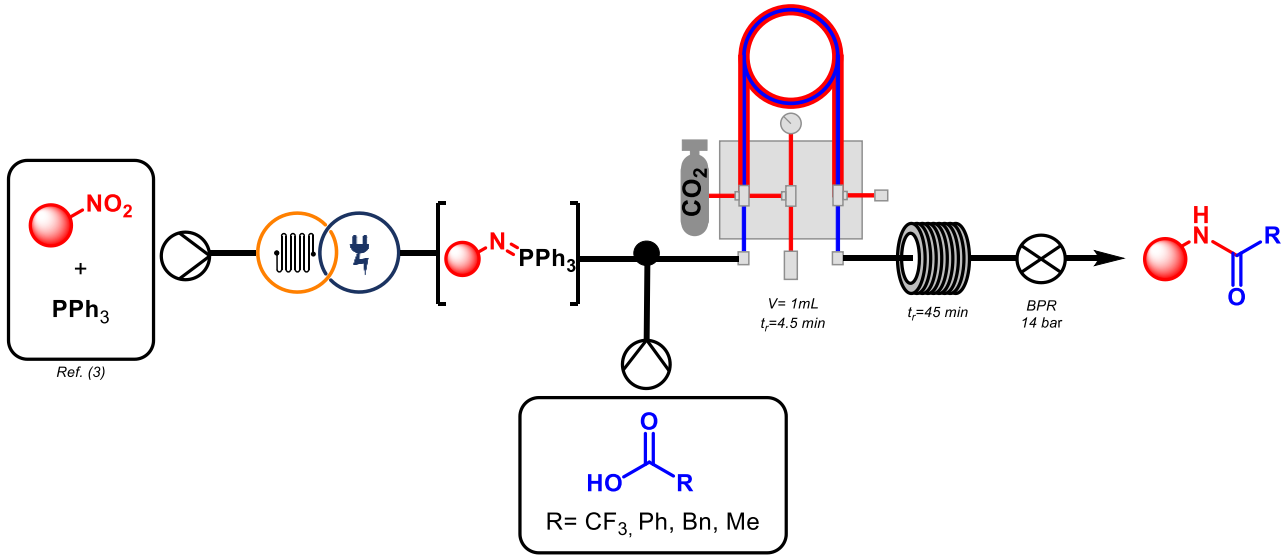

Figure 1. Telescoped CO_2-Mediated Amide Synthesis from Nitroarene in a Continuous Flow Regime.

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