

Palladium-Catalyzed Perfluoroalkylative Carbonylation of Alkynes

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Despite the wide application of carbon monoxide in numerous organic chemistry reactions, its application on the laboratory scale is often problematic due to toxic, flammable and odorless nature of CO. The issue is not only limited to the safety aspects, but is also related to the increase in the cost of syntheses, owing to the requirement for purchase of the necessary equipment needed to conduct the reaction (incl. CO cylinder, pressure regulator, CO detector). The above outlined requirements impose the development of new methodologies, excluding direct application of carbon monoxide. Since the 1960s, new CO surrogates have been developed as possible sources of CO, generated both *in situ* and *ex situ*, which have been successfully implemented in a number of carbonylation reactions. To date only few reports on the application of CO surrogates in multicomponent reactions have been reported, hence there is a great necessity to develop this type of methodology, particularly in the case of reactions leading to valuable fluorinated compounds.

The aim of the research was to develop a convenient method for the direct formation of α,β -unsaturated esters bearing fluoroalkyl group in the β position by perfluoroalkylation of alkynes with subsequent carbonylation reaction, catalyzed by Pd-complexes. In developed method carbon monoxide should be generated, at best *in situ*, from an inexpensive and easy to handle carbon monoxide source. In addition, due to the ambiguities and controversies appearing in the literature related to the nature of generated vinyl radicals and the mechanism of the developed method, an important issue was a multilateral mechanistic studies, including both numerous experiments and the interpretation of a DFT calculations data.

As the result of broad optimization experiments the appropriate reaction satisfactory conditions enabling generation *in situ* of carbon monoxide through a decomposition of formates were developed. The scope of the transformation was explored, covering a variety of aromatic and aliphatic acetylenes, various formates, perfluoroalkyl iodides, as well as isotopically labeled compounds. In general, the reaction proceeded with moderate to very good yields (40-81%), excellent regio- and stereoselectivity (mainly >95:5, *E:Z*). The structures of the obtained products were confirmed by X-ray structural analysis.

Detailed mechanistic study revealed a picture of the developed multicomponent reaction composed of three independent reactions:

- base-induced decomposition of aryl formate with simultaneous formation of CO and phenoxide anion;
- radical iodoperfluoroalkylation of acetylene leading to vinyl iodide in which radical is generated by Pd(0) complex
- aryloxy carbonylation reaction with products of formate decay, proceeding through a Pd(0)/Pd(II) cycle.

Kinetic investigations were conducted for both independent steps and the multicomponent reaction as a whole. Experiments revealed that the carbonylation reaction is a rate-determining step for this transformation, whereas both formate decomposition and iodoperfluoroalkylation reactions are fast

processes. Moreover, vinyl iodide was confirmed as an intermediate in this reaction. The decay of formates caused by Cs_2CO_3 under reaction condition was proved. To complete the mechanistic picture of the transformation, the experimental study was supported by DFT calculations. Among others thing, it was proved that there is possible to produce catalytic inactive Pd-complex with CO under reaction condition.