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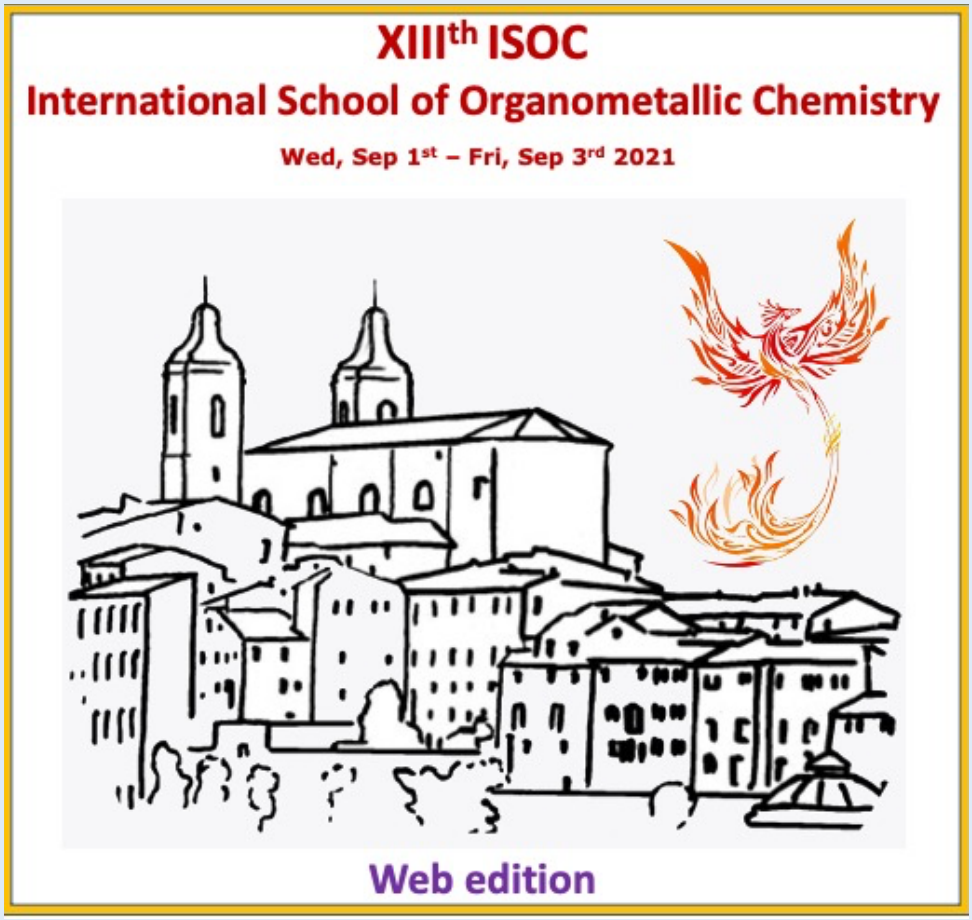

Interdivisional Group of Organometallic Chemistry

New Directions and Perspectives on Organometallic Chemistry

Abstract 10

Formate Esters as Efficient CO Surrogates in the Synthesis of Indoles by Reductive Cyclization of Nitro Styrenes

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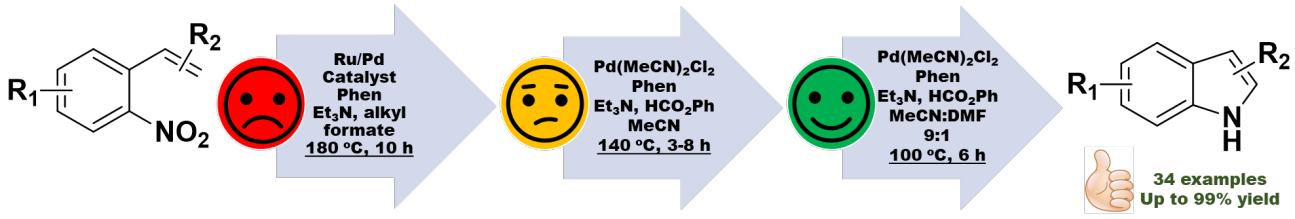
More than thirty years ago, Cenini and co-workers reported the first reductive cyclization reaction of *o*-nitroarenes to indoles using carbon monoxide as the reductant, using different transition metals as catalysts under harsh conditions (220°C, 80 bar CO).[1] Despite of the high efficiency of this kind of reactions, they have not become of widespread use. This may be due to the need to use pressurized CO, requiring safety measures that are not accessible in most synthetic organic laboratories. Alkyl and aryl formate esters were employed by our group as effective, low-toxicicy and cheap *in-situ* CO sources in the Pd- and Pd/Ru-catalyzed reductive cyclization of *o*-nitroarenes to afford indoles. Since the cost of alkyl formates is minimal, the first investigations have been made by using them as CO sources. A bimetallic Ru/Pd catalytic system was required to achieve satisfactory yields for both the decomposition of formate and the reductive cyclization of *o*-nitrostyrenes. However, the results obtained were only achieved under forcing conditions (180 °C, up to 10 h). In contrast, when phenyl formate was used, complete conversion and good selectivity was achieved at a lower temperature (140 °C) and using a Pd/phenanthroline complex alone as a catalyst.[2] However, the moderately high temperature used leaded to a low selectivity in the cyclization of certain substrates. Here we report the results of further optimizations that can improve both the yield and selectivity. A lower reaction temperature and a mixed CH_3CN/DMF solvent system allowed to get improved yield for several substrates including some for which previous conditions failed to afford the indole. The same strategy was also applicable on a 2 gram-scale reaction, which verifies the reproducibility at a large scale. The reactions can be performed in a single cheap glass pressure tube, making this kind of reaction a "General Tool" for the synthetic chemist.[3]



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[2] Formenti, D.; Ferretti, F.; Ragaini, F. *ChemCatChem* **2018**, *10*, 148-152.
[3] Fouad, M. A.; Ferretti, F; Formenti; D.; Milani, F.; Ragaini, F. *Eur. J. Org. Chem*. in press. https://doi.org/10.1002/ejoc.202100789