CONTINUOUS FLOW SEQUENTIAL SYNTHESIS OF COMPLEX INTERMEDIATE COMPOUNDS

G. Sartori[1], L. Soldi[1], S. Loebbecke[2], R. Maggi[1]

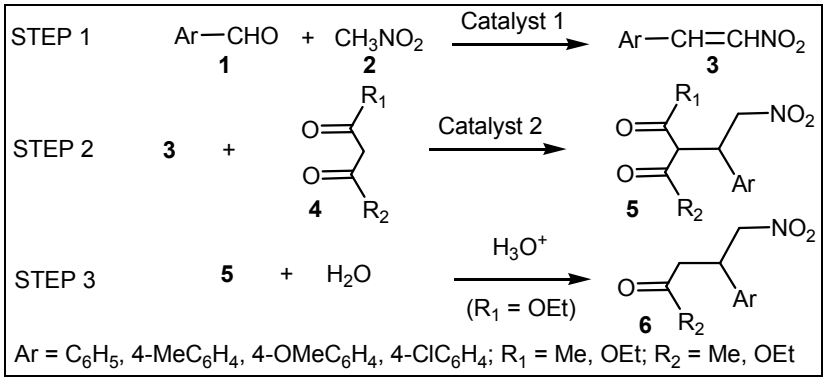
1 - Universita di Parma, Dipartimento di Chimica Organica e Industriale, Viale G.P. Usberti 17A 43100 Parma, Italy

2 - Fraunhofer Institute for Chemical Technology ICT, Joseph von Fraunhofer Str. 7, 76327 Pfinztal, Germany

giovanni.sartori@unipr.it

A great number of products for fine-, pharmaceutical- and material-chemistry with an ever increasing level of complexity has been developed over the past several decades through multistep synthetic methods. In multistep synthesis the preparative complexity increases significantly with the number of steps mainly due to extensive isolation and purification operations. These drawbacks can be overcome by exploiting a multistep-sequential synthetic methodology, without isolation of the previously formed intermediates.[1]

The continuous flow process for the production of complex intermediate compounds has been performed by a combination of two column reactors packed with different organic immobilized catalysts. The first step of the reaction, the nitroaldol condensation between aromatic aldehydes and nitromethane, is promoted by a silica gel supported primary amine; the second step, the Michael addition of β-dicarbonyl compounds to the nitrostyrenes obtained in the first stage, is catalyzed by a silica gel supported guanidine. The resulting final products are isolated in good yield and selectivity and can be easily transformed into the corresponding γ-nitrocarbonyl compounds.



[1] L. F. Tietze, V. Beifuss, Angew. Chem., Int. Ed. Engl. 1993, 32, 131-163.