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Continuous Flow Telescoped Synthesis of Levetiracetam

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Levetiracetam is one of the best sold antiepileptic drugs, and many efforts are done for the development of sustainable synthesis providing it. To develop innovative synthetic strategies, photocatalysis and flow chemistry emerges as victorious strategies.

In this work, we report the development of the first continuous flow telescoped process for the synthesis of Levetiracetam. The telescoped process is divided in three different stages, that are all merged in a single continuous process (Figure 1).

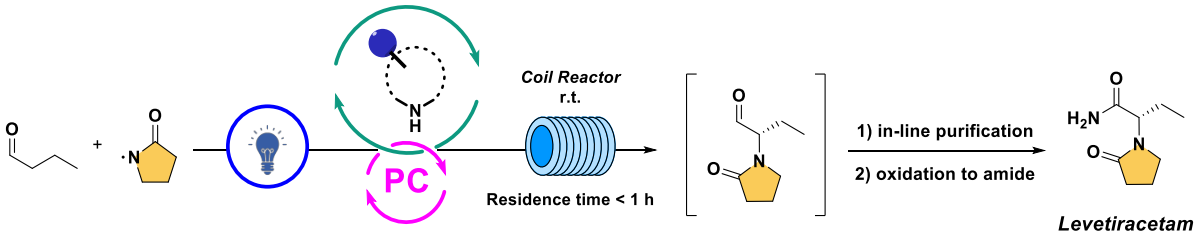

Figure 1: Continuous Flow Telescoped Process for the Synthesis of Levetiracetam

In the first step the γ-lactam moiety is added to a cheap starting aldehyde through a photocatalytic strategy that enables the direct stereoselective introduction of the lactam ring, via nitrogen radicals.[1] The innovative strategy proposed in this work, that combines photocatalysis and organocatalysis, was developed in our research group by taking inspiration from a work of MacMillan and coworkers.[2] The desired aldehyde is obtained in a good yield and excellent enantiomeric excess.

In the second stage, the continuous stream resulting from the first reaction stage is purified, using an extraction solvent and an in-line separator.

Finally, in the third stage, the obtained aldehyde is oxidized to the corresponding amide, that represents the target compound itself.[3]

Levetiracetam is achieved in a continuous flow telescoped process, with productivities and space-time yields improved respect to the corresponding conventional batch procedure, exploiting an innovative synthetic methodology not known in literature.

References:

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