Kinase inhibitors and microwave-assisted chemistry, a nice history.

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Protein kinases are enzymes which catalyze protein phosphorylation, a key cellular regulatory mechanism frequently deregulated in human diseases. Consequently, protein kinases represent interesting targets for the pharmaceutical industry in its search for new therapeutic agents.

Our group is mainly invested in the synthesis of C,N,S- or C,N,O-containing heterocyclic precursors of bioactive molecules able to modulate the activity of kinases. In the course of this work, the multistep synthesis of novel heterocyclic skeletons was described for the first time ten years ago. At that time, data obtained with various kinases were judged good enough for starting a synthetic program and SAR studies.

After ten years of work, more than 300 molecules were obtained and hits were identified, showing excellent affinity for DYRK family kinases which are mainly involved in the control of neurodegenerative diseases. The main part of the chemistry performed in this study was achieved under microwave irradiation as a continuation of our global strategy which consists to design adapted reactants and techniques offering operational, economic, and environmental benefits over conventional methods.

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