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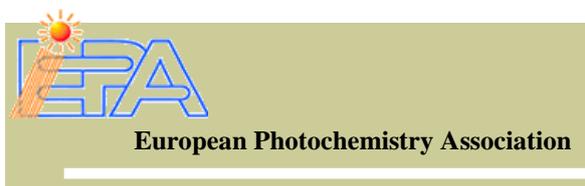
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Imine Photochemistry: Photoinduced Radical Reactions of Imines (IMPHOCHEM)

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Context

Photochemical reactions are an important tool of organic synthesis. Electronic excitation by light absorption considerably changes the chemical reactivity of chemical compounds.¹ Thus, new compounds or compound families becomes available which are hardly or not obtained by more classical methods of organic synthesis. Especially, in the field biologically active compounds, photochemical reactions have now become highly interesting.² Research activities in synthetic organic photochemistry have been intensified in both the academic and industrial domain. It should be pointed out that the application of photochemical reaction to organic synthesis is part of sustainable (green) chemistry. Photons can be thus used by chemists as "traceless" reagent.³⁻⁵

Heterocyclic compounds play a key role in the pharmaceutical as well as well as the agrochemical domain and photochemical reactions for the preparation of such compounds are very attractive.⁶⁻⁸ In this context, imine photochemistry became particularly interesting.⁹ The organic photochemistry of imines combines aspects of photochemistry of carbonyl compounds and alkenes.¹⁰ Typical photochemical reactions such E/Z-isomerization, cycloaddition, photoreductions and related reactions

or rearrangements are also observed with imines. In the context of the IMPHOCHEM project, we are particularly interested in photochemically induced hydrogen atom transfer (HAT) and its application to organic synthesis.

Continuous-flow microstructured technologies, which involve channels or tubes from tens of micrometres to a few millimetres in diameter are now recognized as alternatives to batch processing. Their benefits for organic photochemistry have been highlighted recently.¹¹⁻¹⁴ While reducing irradiation time, higher conversions and selectivities can be achieved because of (i) extensive penetration of light, even for concentrated chromophore solutions, (ii) minimization of side reactions or decompositions by flow-operation, (iii) easy control of the irradiation time and (iv) safer conditions (for example when involving heat-sensitive oxygenated intermediates). The integration of LEDs (Light-Emitting Diodes) as light sources in these technologies provides also additional opportunities. They present high electrical yields, long lifetimes, and spatial compactness, with the possibility of selecting the emission spectral domain and modulating the emitted radiant power.

Implementing flow photochemistry emerges thus as a relevant strategy to study imine photochemistry in terms of reaction pathways but also for rapid reaction screening and optimization

The project

IMPHOCHEM (<https://youtu.be/O4XrOmJeBsI>) is a comprehensive research project on photochemical reactions of imines (Figure 1). The project is funded by the French Research Agency (ANR-18-CE07-0026). Theoretical and physicochemical aspects, stereoselectivity and scope of the reaction will be investigated as important parameters for organic synthesis. For that, in addition to conventional batch reactors, LED-driven microreactors will be implemented, in an original way and from the beginning of the study, as a tool (i) to perfectly control the operating parameters (irradiation, temperature) that could influence selectivity and yield, (ii) to understand and model their influence of the reaction's output, and (iii) to access the feasibility of the transfer into meso-scale continuous flow-equipment.

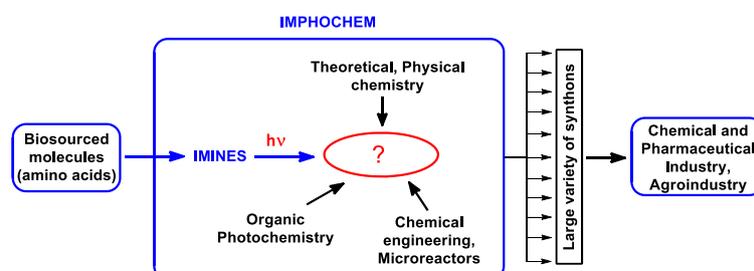


Figure 1. IMPHOCHEM as a comprehensive and multidisciplinary research project.

The consortium

The consortium is composed of three partners from France and Japan.

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The **scientific objectives** are to

- Acquire profound knowledge of the basic photochemistry of cyclic imines.
- Control the selectivity of the reaction.
- Identify scope and limitations
- Implement continuous-flow chemistry all along the stages of the proposal

These objectives will be achieved by the following tasks:

Task 1 will take over the comprehensive study of the photochemical reaction of imines and the optimisation of the operating conditions for a large substrate scope.

Task 2 will take over the computational calculations for the characterisation of diradical species involved in the reaction to identify the key structural parameters that influence selectivity.

Task 3 will develop the reaction under flow conditions in microreactors irradiated by a purpose-built UV-LED array. This process allowed accurate control of irradiation (emission spectrum and intensity), temperature and reaction time. A modelling approach will be also implemented.

Impact and benefits of the project

IMPHOCHEM deals with a comprehensive study of the **photochemical transformation of imines**. The global objective is to have access to a large structural variety of molecules useful as synthons, mainly **nitrogen containing heterocycles**, for chemical and pharmaceutical companies, from bio sourced substrates. The methodology is based on an original combination of **organic photochemistry, theoretical physical chemistry, chemical engineering and flow photochemistry** expertises. The use of LED-driven microreactors from the first steps will offer undeniable advantages for understanding how operating conditions control selectivity, but also for acquiring information (kinetic data) to transpose these photochemical routes to an **industrial scale using continuous-flow technologies**. Thus, this proposal will contribute to the development of **continuous, integrated processes for a safe and sustainable production of fine chemicals and pharmaceuticals**.

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