

Photochemical rearrangement of lactams: A ring-expansion approach towards structurally diverse heterocycles.

This project consists of a collection of innovative approaches aiming to reveal the underrated potential of the photo-induced rearrangement of *N*-substituted lactams. Several different research directions will be pursued, with the common purpose to demonstrate the attractiveness and usefulness of the proposed reactivity in the synthesis of structurally diverse heterocycles. An undeniable advantage of the proposed transformation is that it proceeds under mild conditions and does not require any transition metal catalyst.

Nitrogen-based heterocycles belong to a highly important class of compounds which are found in various natural products, biologically active structures, and medically relevant compounds. The importance of these compounds is exemplified by their use in pharmacological structures: 84% of the pharmaceutical drugs approved by the FDA contained at least one nitrogen atom. Of these compounds, 59% contained at least one nitrogen heterocycle. In light of the importance of nitrogen-based heterocycles, the development of new and more efficient methods for their preparation is of critical importance.

In the current grant application we propose the photo-induced rearrangement of lactams as a general and convenient method for the formation of structurally diverse heterocycles. The proposed research project will consist of four main tasks.

The first will focus on the development of a fully automated process for the synthesis of six-membered enamines; versatile building blocks in natural product synthesis. The proposed synthetic strategy is based on a photo-induced cascade reaction realized under continuous flow conditions.

The second task will concern the novel, metal-free, synthesis of functionalized quinolones, benzoazepines and related analogues. These scaffolds are present in a vast number of natural compounds and pharmacologically active substances. The proposed strategy is based on the photo-induced rearrangement of *N*-aryllactams. The power and utility of this transformation will be demonstrated through the synthesis of an important precursor to *Tolvaptan*, an aquaretic drug used to treat hyponatremia.

The next goal of this proposal is to apply the photochemical rearrangement of *N*-alkenyllactams to the synthesis of polycyclic nitrogen-based heterocycles. These common structural subunits are present in numerous alkaloid natural products and serve as important scaffolds in biologically active and pharmaceutically significant compounds.

The last task of current proposal will be devoted to studies on the photochemical insertion of alkenes and alkynes into lactams, lactones or thiolactones. The utility of this reactivity will be demonstrated by the synthesis of higher gliflozin drug analogues. Gliflozin drugs are a newly developed class of oral hypoglycaemic agents used for the treatment of type-II diabetes mellitus.

We are of the opinion that, the innovative solutions presented above will significantly broaden the current field of complex nitrogen-based heterocycle synthesis and will provide very useful routes for the synthesis of complex organic molecules from simple starting materials to the greater synthetic research community. We expect the results obtained from the realization of this project to substantially enrich the chemistry of photo-induced ring-expansion of lactams and to show its immense potential as a tool for the preparation of chemically, biologically, and medically important organic compounds.