STRUCTURAL EDITING OF PYRIDINE VIA ZINCKE IMINE INTERMEDIATES

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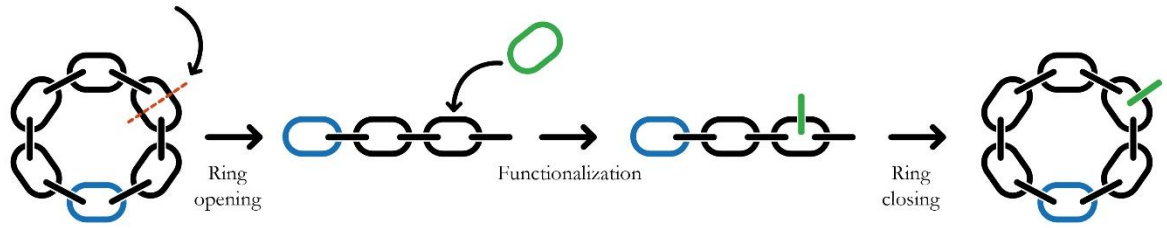
Pyridine is a simple six-membered ring containing a nitrogen atom, yet it plays an outsized role in modern chemistry. Found in more than 20% of all FDA (Food and Drug Administration) approved drugs, pyridine is a cornerstone in the development of pharmaceuticals, agrochemicals, and advanced materials. However, despite its widespread use, modifying pyridine's structure-especially at certain positions on the ring-remains a major challenge. Such transformations are critical in the development of new bioactive molecules, but current strategies are often limited, unselective, or reliant on toxic and expensive reagents.

The objective of this project is to develop methodologies for peripheral and skeletal editing of the pyridine scaffold through the Zincke Imine intermediate, harnessing high reactivity towards radicals and distinctive rearrangements into different heterocycles, **notably isoxazoles.** These unique intermediates are generated by temporarily opening the pyridine ring, allowing access to new reactive sites and enabling transformations that would otherwise be impossible. This approach opens two exciting avenues of chemical exploration:

- **Peripheral editing**, where functional groups such as aryl or azo units are selectively attached to the ring, and
- **Skeletal editing**, where the ring itself is modified or converted into entirely new structures, including those found in drug-like compounds.



The project is structured into three integrated work packages. The first will develop light-driven chemical reactions that enable selective modifications at hard-to-reach positions on the pyridine ring. The second explores ring-altering reactions that convert pyridines into new heterocycles such as isoxazoles-scaffolds with promising medicinal applications. The third will adapt these processes to **flow chemistry**, a modern, industry-friendly approach to chemical synthesis that enhances safety, efficiency, and scalability.

A key part of this work will involve understanding how these transformations occur. Using advanced techniques available at the Institute of Organic Chemistry PAS-such as NMR spectroscopy, mass spectrometry, and computational modelling-this project will probe the underlying reaction mechanisms to inform future innovations. Promising reactions will be tested on complex, drug-like molecules to assess real-world applicability.

If successful, the project will deliver a **versatile, modular platform for pyridine editing**, offering chemists new tools to design and fine-tune functional molecules. These developments are expected to significantly accelerate **drug discovery and material innovation**, while also advancing sustainable chemical practices. Ultimately, this research will broaden the chemical space available to scientists, strengthening pyridine's status as a central player in the chemistry of the future.