

Aminium Radicals for Discovering Novel Antiparasite Endoperoxides

Research project for a Master2 internship. Duration 6 months, starting from February 2023.

Keywords: leishmaniasis, malaria, peroxides, electrochemical methods, radical chemistry.

Context: Leishmaniasis are neglected diseases of human and veterinary importance causing thousands of human and canine deaths per year.^[1] Among all the leishmaniasis, visceral leishmaniasis caused by *L. infantum* is present in tropical regions, as well as in all the Mediterranean areas, including the South of France, whereas *L. major* is responsible for cutaneous leishmaniasis. There is a high need to develop novel therapies because of the absence of human vaccines, the poor efficacy of canine vaccine, the toxicity of current antileishmanial drugs and drug resistance that is well-documented or at risk.^[2] In this context, endoperoxides constitute a singularly interesting class of molecules, offering promising perspectives in the fight against *Leishmania* parasites. Indeed, derivatives of the iconic antimalarial natural product artemisinin (2015 Nobel Prize in Physiology/Medicine awarded to Tu Youyou) and a range of other endoperoxide compounds have been shown to be active against pathogenic organisms beyond the sole *Plasmodium* species^[3], including *Leishmania* parasites as confirmed by a recent study.^[4]

Project: In this project, we wish to develop new synthetic methods for the synthesis of original polycyclic endoperoxides, that can then be evaluated in assays carried out by our partners biologists. Our strategy involves the generation of aminium radical intermediates, from well-chosen amine precursors. It is based on earlier work carried out by our research group.^[5-7] The key oxidation steps will be performed at ENS Paris, in collaboration with the group of Dr Olivier Buriez.

Profile: We are looking for a student with excellent academic records. The candidate should like experimental work and have a precise, rigorous approach towards science. Ability to work in a team is also important. A strong background in Synthetic Organic Chemistry is preferred.

Funding: This internship can be funded by the ANR (as part of the programme ARDIROX that was selected for funding in the years 2023-2026).

Contact: To apply, please contact Dr Yvan Six (yvan.six@polytechnique.edu), with a detailed CV, transcripts of records and the names of potential referees.

Address: Laboratoire LSO, Ecole Polytechnique, route de Saclay, 91128 Palaiseau Cedex, France.
Telephone: +33 (0)1 6933 5979.

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