Project 2.3. Synthesis of small fluorophores possessing aromatic imide scaffold for virus proteases' detection

Supervisor: prof. Daniel T. Gryko

Institute: Institute of Organic Chemistry, Polish Academy of Sciences

WWW: https://www.icho.edu.pl/, https://ww2.icho.edu.pl/DTG_group/

Background:

One of the key elements to be improved versus currently available fluorescent probes is their brightness, which is defined as a product of fluorescence quantum yield (Φfl) and molar absorption coefficient (ε). In other words, in order to increase this critical parameter one has not only improve the fluorescence efficiency but also to increase the strength of absorption. In principle, this challenge does not have to be difficult in general since there are chromophores possessing ε ≈ 400,000 such as porphyrins. These dyes however are simply too large, hence they interfere with protease-peptide recognition process as it was proven by preliminary studies. The task of increasing ε becomes problematic if it has to be combined with maintaining a small size of the fluorophore.

Aim:

The overall research objective of this project is to design and synthesize advanced, emissive dyes and to apply them as fluorescent reporters in activity-based probes for SARS-CoV-2 proteases imaging. This new generation of fluorescent platforms will possess the following properties: (a) large brightness (product of fluorescence quantum yield and molar absorption coefficient); (b) good photostability; (c) narrow emission. The major challenge in this project is that one has to optimize in parallel all above-described properties but at the same time to maintain small size of fluorophores so that: (a) they do not induce precipitation of the final small peptide; (b) they do not interfere with protease-peptide recognition process.
Thus the goal of this project would be to reach the brightness ca. 50,000 compared with 10,000 for the coumarin-based fluorophores currently used. This would translate into 5 times higher sensitivity which is of critical importance because both SARS-CoV-2 viral proteases have relatively low enzyme activity and for their detection in biological samples really very sensitive detection tag is critically needed.

Requirements:

- MSc in chemistry, specialization – organic chemistry,
- good knowledge of English.