New Diethylenetriaminepentaacetic Acid-Derived Lanthanide Tags for NMR Screening in Drug Discovery

Boym, Mikhail (School: Moscow South-Eastern School Named After V.I. Chuikov)
Miturich, Vasily (School: Moscow South-Eastern School Named After V. I. Chuikov)

Our work is aimed at the synthesis of new lanthanide labels based on derivatives of DTPA (diethylenetriaminepentaacetic acid) for NMR screening. The introduction of a spin label into a protein changes the magnetic properties of atoms that are in vicinity of the lanthanide ion, which alters their peaks in NMR spectra. This way, compounds that interact with the protein can be found, and new drugs could be developed on their basis. More than 40% of the drugs that are in use nowadays were found by NMR screening. Therefore, our work primarily focuses on the study of promising DTPA-derived labels which have not previously been studied in detail. New labels have been proposed, in which, firstly, an effective DTPA fragment is used, and secondly, simple functionalization is achieved using a click reaction of the spin moiety with different fragments which selectively connect to the amino acid residues of a protein, allowing to produce a wide range of useful spin labels easily and with high yields. The synthesis of the proposed compounds was planned and successfully implemented. The new compounds were isolated and characterized by 1H and 13C NMR spectroscopy. The ability for complexation of the obtained spin labels with lanthanide ions was studied and their effectiveness for NMR screening was shown on the model system. The spin labels are planned to be used in experiments on NMR screening of pharmacologically significant biomacromolecules. Furthermore, the labels can be used in the structural studies of proteins.

Awards Won: