

Justyna Śniechowska

Synthesis and structural studies of modified porphyrinoids

Centre of Molecular and Macromolecular Studies, Polish Academy of Sciences

Porphyrinoids are an important class of compounds, due to their extended practical applications propensity. As a result knowledge about their chemistry, biological activity and structural complexity is strongly desired. In this dissertation, the investigations were carried out at three levels: a synthetic one, a structural one and biological one. The main aim of my research was a synthesis and structural studies of modified porphyrinoids, such as corroles, chlorins and oxospirochloins. In addition to the synthesis of model compounds, a very important part of my work was the development of methodology and the improvement of procedures applied in NMR spectroscopy for structural studies of porphyrinoids. Solid State NMR spectroscopy (SS NMR) is the most important tool, that have been used in my studies, because it does not require obtaining of a suitable high quality crystal, such as it is the case of single crystal X-ray diffraction. This is not merely a matter of convenience and shortening of experimental procedures, but also, in some cases, the only way to determine solid-state structure of these compounds, as crystallization of many porphyrinoids is very difficult. Another part of my work concerned studies on dynamic processes in solution. By employing one- and two-dimensional NMR experiments, not only a full assignment of NMR signals of the studied compounds was possible, but also dynamic processes occurring inside the macrocyclic ring and the rotation of the aryl rings in meso position were examined. The obtained experimental data were compared with the NMR shielding parameters from theoretical calculations, to ensure the correctness of the assignment.

The first part of my thesis concerns the formation of inclusion complexes of 5,10,15-tris(pentafluorophenyl)corrole with dichloromethane. My studies have shown that the formation of host-guest complexes is an efficient method for the synthesis of chiral crystals from free base corroles possessing an extremely low racemization barrier. Moreover, it has been demonstrated that Very Fast MAS SS NMR technique with a sample spinning rate of over 40 kHz can be readily used for the screening and selection of crystals of corroles, suitable for X-ray diffraction studies. Obtained chiral crystals were characterized and the chirality was confirmed employing the circular dichroism method.

The second part of this work focuses on the synthesis, the detailed structural characterization and the analysis of a molecular motion of asymmetric and fluorinated pyrrolidine-fused chlorins. The major aim of these investigations is to understand and explain the influence of chemical modifications of fluorinated pyrrolidine-fused chlorins on the dynamic processes. My investigations proved that even small modifications in the aryl rings influence their rotation. It has also been shown that the dynamics of this rotation can be controlled by temperature.

The third part of my thesis presents photochemical (spectral properties, photostability, singlet oxygen formation) and biological studies of fluorinated chlorins. Obtained chlorin derivatives were loaded into lipid vesicles and their photodynamic antibacterial potential was evaluated. The results demonstrate that chlorins exhibit high photodynamic activities against *Enterococcus faecalis*, *Staphylococcus aureus* and low activity against *Escherichia coli*. No activity was noticed against *Pseudomonas aeruginosa* and fungi: *Candida albicans* and *Trichophyton mentagrophytes*.

The last part of the dissertation presents a completely new approach for the synthesis of spirochlorin derivatives, based on the usage of imino-keto intermediate, formed in situ from 2-amino-5,10,15,20-tetraarylporphyrins, as a reagent in inverse electron demand Diels–Alder reaction. A series of new oxospirochlorins were synthesized with reasonable yields. We revealed, that yield of reaction depends on the structure of substrates, position of the substituents in the *meso* ring and their electronic characters. A plausible mechanism for the cycloaddition reaction of porphyrins and tetrazine was proposed. The obtained compounds were fully characterized by means of mass spectrometry, liquid and solid state NMR spectroscopy and X-ray crystallography.

In conclusion, synthesis and detailed studies of the obtained modified porphyrinoids can be extremely important and helpful in the design of new and effective photosensitizer, receptors, drug carriers or molecular machines.