

ABSTRACT

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Title of Thesis: Preparation and photophysical evaluation of tetra-3,4-pyridoporphyrazines suitable for the photodynamic therapy

Tetra-3,4-pyridoporphyrazines (TPyPz) are aza-analogues of phthalocyanines. Their large system of conjugated bonds enables them to absorb light in the red part of the absorption spectrum. Due to their ability to produce singlet oxygen, they can be potentially used as photosensitizers in photodynamic therapy (PDT). Its mechanism is based on co-functioning of three elements - photosensitizer, light and oxygen. Photosensitizer excited by light absorption transfers its energy into tissue oxygen, thus, creating cytotoxic singlet oxygen. This method is beneficial for its high selectivity, low toxicity, minimal invasion and fast effect.

The aim of this work was to synthesize and study water-soluble TPyPz suitable for PDT. Water solubility was achieved by quarternized amines, forming of salts or using suitable delivery systems (hydrophilic emulsion). Hydrophilicity was also increased by introduction of hydrophilic non-charged substituents (OH). At first, appropriate precursors for TPyPz (i.e., 2-substituted-5,6-dimethylpyridine-3,4-dicarbonitriles) were prepared by nucleophilic substitution according to the scheme below. Then, cyclotetramerization of **2 a, b, d** with butoxide as an initiator of the reaction gave required macrocycles. Obtained TPyPz were transferred into metal free derivatives under acidic condition and zinc was then coordinated into the center. At the end water soluble derivatives were prepared. All obtained TPyPz were characterized by physico-chemical properties and biological activity. One of the molecules (**d**) reached excellent effectivity-profile.

