Supramolecular effects as driving force of dipyrrin based functional materials engineering

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Abstract. Dipyrrin based luminophores are of major interest in different areas of chemistry, material science and molecular biology. Vast variety of the structures with dipyrrin motif were synthesized and investigated up to date. Modern trend in the dipyrrin chemistry is the aimed functionalization of the ligand or complex structure allowing to gain the mechanism based on supramolecular interactions for controlling spectral and photophysical characteristics of compounds for tuning practically valuable properties for specific tasks. Presented paper summarize the results of our research group, working in the field of dipyrrin complexes with p-elements: synthesis, spectral characteristics evaluation and possibilities of practical application investigation. Discussion is focused on the opportunities of molecules preorganization for achieving the supramolecular interactions causing the tuning of fluorescence of the compounds in solutions, polymeric matrices and thin films.

1. Introduction

A brief review of existing data and some applications of dipyrrin coordination compounds – chemically stable compounds with intense chromophore and fluorescent properties, would be presented in the following paper. Dipyrrin core – the basic "building" motif of blood heme, chlorophyll, bilirubin and related compounds. The undoubted success of dipyrrhin complexes is primarily caused by the synthetic possibilities of modifying its structure (Figure 1), which allows to "adjust" the spectral-luminescent characteristics, reactivity and physicochemical properties of molecules for specific tasks. To date, more than 30 groups around the world are using this tool for obtainment the new dipyrrin based structures and its using as components of the functional materials of different fields.
The wide possibilities of directional control of light-gathering and light-transmitting properties due to the variation of "internal", mainly structural factors, and "external" conditions (the nature of the environment) make it possible to predict the high prospects of dipyrrin complexes and materials on their basis as the electron-optical molecular converters for needs molecular sensorics, optical conversion, and modern photovoltaics.

2. Supramolecular effects in the chemistry of Bodipy dyes
Among the variety of complexes with dipyrrin ligands Bodipy are the most interest. Boron dipyrrins (Bodipy) are unique complexes occupying an "intermediate" position between classical coordination and organometallic compounds. The enormous interest of researchers from all over the world to the compounds of this class has by now provided an endless stream of publications that requires generalization.

Bodipy is proved to be a compound of unique kinetic stability in acids, due to covalent binding of Boron atom with Nitrogen heteroatoms and increasing the stability of coordination unit. Bodipy is very resistant to hazardous chemicals including acids and alkali, allowing to expand the range of pH of Bodipy applications including molecular sensorics and hybrid materials synthesis. Stability ranges of different Bodipy dyes could be found in literature as well as the mechanisms of Bodipy dissociation in aqueous and non-aqueous solutions \[1\]. This results demonstrate the great advantages of Bodipy over other dyes of organic and organometallic nature due to their high chemical resistance to acids and alkalis. The other advantage of Bodipy complexes are they photo- and thermal stability in solutions, which can be further increased via immobilization in the polymeric matrices of organic, or inorganic nature \[2\]. The listed features of Bodipy dyes determine the breadth of their use as optical converters in laser technologies. However, the use of Bodipy as components of smart materials for molecular sensing requires further modification of the structure of dipyrrins.

For the last several years our team was focused on Bodipy complexes with meso-substitution by bulky organic moieties or alkyl chains (Figure 2). This allowed us to investigate the influence of supramolecular organization of Bodipy molecules in solutions, polymeric matrices and thin films via π-π staking causing the formation of aggregates and tuning the photophysical characteristics.
Figure 2: Structures of the Bodipy complexes with bulky substituents.

In dilute solutions the compounds demonstrate intensive fluorescence with the peak at around 540 nm, small Stokes shift and the substituent nature does not affect strongly the spectral properties of the dyes. Spectral and photophysical properties of the discussed Bodipy dyes were evaluated in a range of organic solvents and polymeric matrices. Immobilization does not affect the character of the absorption and fluorescence spectra of the dye. The highest quantum yields changes under the solvent variation was observed for 7, where the changing of the solvent from carbon tetrachloride to ethanol cause fluorescence quenching from 0.633 to 0.028. At the same time, fluorescence intensity is increasing in case of solvent polarity growth for compounds 2-4 with extended aromatic moiety at meso-position, it is not typical for Bodipy, where polar solvents are usually regarded as fluorescence quenchers. That fact could be explained by the high hydrophobicity of compounds under investigation. Taking that into account the Bodipy with bulky substituents could be used as the fluorescent media polarity indicators in analytical chemistry and biochemistry [3].

For compound 1 the effect of the substituent interaction with phenyl moiety of the phenyl-modified silica matrix was observed. This effect is caused by π-π interactions of the dye molecule with matrix. This effect could be used for fine control of the matrix formation process and leads to increase of the dye emission in the final material for further practical applications [4].

There is an increased interest in compounds that contain two or three Bodipy domains. Combining two or three dipyrrin moieties with a phenyl fragment through some spacer could lead to an increase in photophysical characteristics with respect to the individual Bodipy. Our assumption is based on the fact that individual domains still have to influence each other, showing either a positive or negative synergistic effect. Several poly-dipyrrin Bodipy bridged by the di- and triphenylamine spacers were synthesized and characterized. Such compounds showed increased absorption characteristics and intense fluorescence. Peaks positions are the same as mono-Bodipy analogies. Obtained compounds demonstrate enhanced aggregation stability, caused by the intramolecular interactions of the separate domains.

8-phenyl and 8-biphenyl substituted Bodipy (compounds 1 and 5) were found to be the fluorescent molecular rotor (Figure 3). The term "molecular rotors" refers to compounds whose molecules consist of two or more fragments that can rotate relative to each other. The major part is called the stator, and the smaller rotator or rotor. The effect of the fluorescent molecular rotor should not be understood purely mechanically, as the rotation of the parts of the molecule relative to each other. The molecule first goes into a twisted state, while the system becomes coplanar and there is a dissipation of energy in the excited state. These molecules exhibit two types of de-excitation pathways once they are in the excited state: a fluorescence radiative pathway and a non-radiative de-excitation pathway. This intermolecular mechanism allowed to use investigated Bodipy as molecular sensors demonstrating the
fluorescence changes under the temperature variations unlike the Bodipy with larger substituents [5, 6].

![Graph showing fluorescence quantum yield vs dynamic viscosity](image)

**Figure 3**: the dependence of the fluorescence quantum yield of 1 on the dynamic viscosity of the binary (2-propanol – glycerol) solvent: 1 - $\chi_{\text{glycerol}} = 0$; 2 - $\chi_{\text{glycerol}} = 0.3$; 3 - $\chi_{\text{glycerol}} = 0.5$; 4 - $\chi_{\text{glycerol}} = 0.7$. Reprinted form [6].

At medium and high concentrations, the extension of the substituent π-conjugation enhances molecular association caused presumably by π-π interaction between the substituents of the neighboring molecules. Aggregation leads to bathochromic shifts in absorption and fluorescence spectra displaying the ability of the investigated dyes to show aggregation induced emission enhancement. Displacement of the monomer-associate equilibrium in the hybrid materials with polymethyl methacrylate and polyvinylcarbazole was exploited for directional tuning their emission. The fabricated OLED devices were found to demonstrate moderate electroluminescence efficiency. Both self-absorption and aggregation induced emission effects cause desirable emission color changes but decrease efficiency of the active layer (Figure 4) [7].
Next we examined investigated Bodipy in Langmuir-Schaefer thin films [8]. It was proved that the substituent’s nature greatly affects the photophysical properties of the studied dyes via the shift of a monomer – excimer equilibrium in the obtained films. In particular, compound 7 can form only monomers in the films, while the other dyes demonstrate the different degree of aggregation.

It was shown that the film surface reliefs are uniform and without typical for macroheterocyclic compounds aggregation centers. The results of the XRD analysis showed a single-layer arrangement of the BODIPY molecules located parallel to the substrate surface. The microcrystals observed by the fluorescence microscopy were found to form the same structure as thin films but with a higher crystallinity. Intermolecular hydrogen bond formation and π-π staking of the Bodipy cores were found.
to be the structure forming forces during the films manufacturing. Bodipy 7 is the first example of the solid state monomeric Bodipy with strong fluorescence, making it promising for solid state optoelectronics.

3. Oxophosphoryl complexes of dipyrrins (Podipy) as the evolution of Bodipy ideas to biological applications

Supramolecular mechanisms could be applied for Bodipy usage as fluorescent molecular sensors on biomolecules. Thus, we observed the pronounced changes of dyes fluorescence in presence of the proteins and biofluids. 8-aryl Bodipy derivatives were found to have high fluorescent respond upon the protein addition. The results of fluorescence spectroscopy indicated that the fluorescence of hydrophobic Bodipy dyes substantially increases in the presence of bovine serum albumin (BSA). The prospected reason is binding of the dye to the BSA hydrophobic cavities in the subdomain IIA. π-cation stacking between BODIPY and arginine amino acid residue of the protein was detected. It is also shown that far phenyl moiety of compound 5 can undergo parallel π-π stacking interaction with aromatic fragment of TRP213, being possible way for the energy transfer. Namely, such geometry causes strong influence of the ligand on the protein fluorescence. Aromatic moiety size increase causes shifting of the interaction driving force from mostly non-specific to the π-stacking. Among all probes, the 8-phenyl substituted dye showed the highest sensitivity and the quantitative fluorescent response for BSA in aqueous solution [9].

Figure 6: π-π stacking interaction between compound 5 and tryptophan. Reprinted from [9].

Photophysical properties of several Bodipy based fluorescent dyes were investigated in systems containing blood plasma biomolecules. The interaction between the investigated dyes and protein plasma components changes spectral characteristics of the dyes and leads to bathochromic and hypochromic absorption spectra shifts accompanied by changing of fluorescence intensity. It was shown that the static factor of molecular dye-biopolymers complex formation prevails at plasma protein concentration up to 1 g/l, while the higher viscosity range is characterized mainly by nonspecific fluorophore interactions. The increase of fluorescent characteristics of phenyl-substituted Bodipy in the presence of proteins caused by resonance energy transfer and change of physicochemical properties of the molecular environment of the fluorophore was shown for the first time [10].

The development of new methods and the improvement of existing techniques for studying physicochemical processes in living cells is an urgent task of modern biomedicine, the solution of which opens up new opportunities for studying pathologies and controlling the effectiveness of disease therapy. Among the variety of existing solutions in the field of biochemical processes and medical diagnostics, fluorescent technologies - fluorescence spectroscopy and fluorescence microscopy in steady-state and time-resolved modes deserve special attention. These methods require the use of fluorophores as imaging agents, as labels of biomolecules or systems, process and state sensors. In this regard, the development of new luminophores with the required characteristics for specific applications and their approbation is a complex task of synthetic, physical and biological chemistry.

Among the variety of factors reflecting the state of the cell, the local viscosity of the cytosol, the pH gradients, and the polarity of the biopreparation sites are among the most significant. The difficulty of accurately mapping these parameters in the cell in norm and pathology is a key problem, the
solution of which is directed at this project. The use of existing organic luminophores for determining the indicated parameters is largely limited by the solubility of the sensor molecules in water. The use of co-solvents for the solubilization of fluorophores makes interpretation of the results difficult, due to the influence of the solvent on the characteristics of the investigated systems. In this connection, the most promising solution will be the use of water-soluble fluorophores with the necessary spectral properties and possibilities for spectral response to changes in the parameters under study.

The proposed fundamentally new solution of the preparation of fluorophores for cell diagnostics based on oxiphosphoryl dipyrrin complexes has a number of competitive advantages, the most important of which are the presence in the structure of the compound of the oxophosphoryl groups, which determines compound’s water solubility without additional modifications, and the resistance to quenching of fluorescence in the aquatic environment. From the one hand, such compounds could be used with no additional cosolvent simplifying the interpretation of experimental results. From the other hand, combination in one molecule of the polar oxophosphoryl group with high hydrophilicity with hydrophobic meso-phenyl substituent could farther increase the discussed supramolecular effects for such compounds rising the fluorescent response.

At the time of writing, only three articles on the synthesis of PODIPY [11], quantum-chemical study of properties [12], as well as the use of mercury (II) cations as sensors [13] can be found in the literature. It should be noted that examples of the use of Podipy complexes as markers or sensors of biological molecules are currently not available in the scientific literature. At the same time, that the synthesis of PODIPY is currently not worked out, the general approaches to obtaining compounds of this class coincide with those for the widely studied BODIPY complexes.

We used standard synthetic routes for obtaining dipyrrin ligands, then the Podipy was obtained according to [11] (Figure 7). Synthesized dyes were tested in the range of solvents under the variation of solvent polarity, acidity and abilities for the specific interactions with the dye (Figure 8). Spectral properties of Podipy generally the same as for Bodipy dyes: narrow absorption and fluorescence peaks at about 510-520 nm and 530-550 nm respectively. We should mention hypsochromic shifts of the peaks comparing to Bodipy in the same solvents, indicating the lower polarization of ligand electronic system and, thus, lower stability of the complexes. General spectral changes were observed under the solvent variation, reversible character of the band shifts indicate the solvatochromic or aggregation induced mechanism of the process.

![Figure 7: Structure of the Podipy complex.](image-url)
Figure 8: Electron absorption and fluorescence spectra of Podipy complex in the range of solvents: 1 – CH₂Cl₂; 2 – C₆H₆; 3 – C₂H₆OS; 4 – C₂H₅OH; 5 – C₃H₇NO; 6 – CCl₄; 7 – CHCl₃; 8 – H₂O; 9 – C₆H₁₂; 10 – C₆H₁₄.

It should be noted, that investigated Podipy demonstrate the moderate water solubility preserving the intensive fluorescent respond unlike Bodipy 1 with the same structure of the ligand. The presence of hydrophilic oxophosphoryl site and hydrophobic phenyl moiety lead to the interesting supramolecular effect, thus, even at small concentrations aggregates formation were detected with the batochromic shifts of fluorescence band. Further research is required for synthesis of the Podipy structures with enhanced amphiphilic properties for address adjustment of spectral characteristics by controlling the supramolecular organization.

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