THE IMPACT OF ELECTRON-DONATING/-WITHDRAWING GROUPS ON RED-FLUORESCENT BODIPY MOLECULAR ROTOR

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Fluorescent molecular probes are very useful for studying live cells and various organelles because they can indicate changes in environmental properties [1]. One of these properties—microviscosity—can be detected with viscosity–sensitive fluorophores called 'molecular rotors'. The mechanism of these derivatives is based on the competition between intramolecular rotation and fluorescence, which can be registered by time-resolved fluorescence spectroscopy. Molecular rotation alters the electronically excited state and causes a faster non-radiative relaxation, which consequently determines a longer fluorescence lifetime in a highly viscous medium [2].

Many microviscosity probes are based on dipyrromethene boron difluoride, commonly known as BODIPY. One of such molecular rotors is BODIPY-C_{10}, an excellent lifetime-based microviscosity sensor exceptional for data-simplifying monoexponential fluorescence decay. However, green absorbance and fluorescence spectra make BODIPY-C_{10} imperfect to use for microviscosity imaging in biological samples where light scattering is an issue. The extension of molecular conjugation length is a simple solution to red–shift absorbance and emission spectra. It should also be considered that a single BODIPY conjugate can be sensitive to all three environmental parameters: microviscosity, temperature and polarity. Recently, we investigated BODIPYs with extended molecular conjugation [3] and decided to explore how the sensory properties of these derivatives can be tuned by introducing different moieties.

To find out how electron-donating/withdrawing groups (EDG/EWG) can affect molecular rotor's properties of sensing viscosity, temperature and polarity, we compare the most popular green-fluorescent BODIPY-C_{10} and four *β*–phenyl–substituted BODIPYs (Fig. 1A): BP-PH as a red-emitting reference, methyl-substituted BP-PH-8M with suppressed rotation, as well as trifluoromethyl-substituted BP-PH-CF_3 and methoxy-substituted BP-PH-OMe to evaluate the effects of EWG and EDG, respectively. All *β*–phenyl–substituted conjugates, except BP-PH-8M, have an increased conjugation of the molecule, which helps to achieve the red spectral region required for the biological samples.

In this work [4], we present investigation of quantum chemical calculations, absorbance and fluorescence spectra, time-resolved fluorescence measurements and sensitivity to viscosity, temperature and polarity. DFT calculations showed that BP-PH-8M has the highest activation energy barrier (almost 0.3 eV) because the methyl groups prevent molecular rotation. In contrast, the other conjugates have twice as low barrier, resulting in faster non-radiative relaxation. Steady-state fluorescence measurements revealed that EWG blue-shifts the fluorescence spectrum, while EDG shifts it to the longer wavelengths (Fig. 1B). Finally, fluorescence decay kinetics demonstrated that BP-PH-CF_3 is a moderate temperature sensor, while BP-PH-OMe could be used as a lifetime–based polarity probe (Fig. 1C).

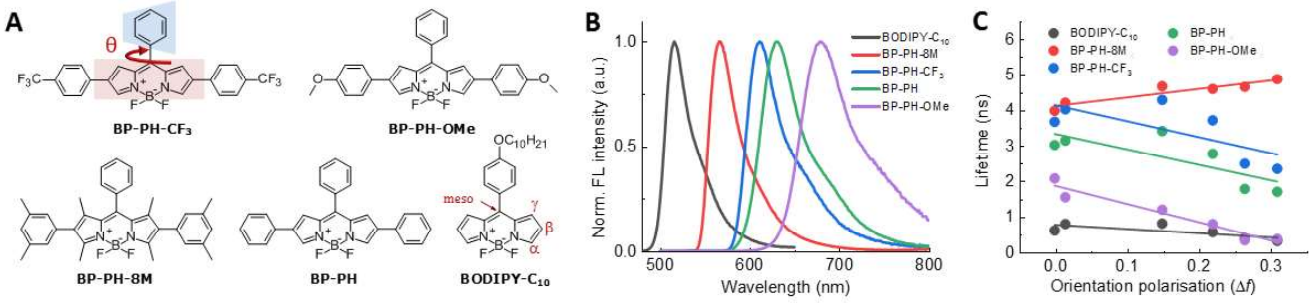

Fig. 1. (A) The structures of the molecular rotors used in this work, and the rotor mechanism showed on BP-PH-CF_3. Fluorescence spectra (B) and polarity-dependent fluorescence lifetimes (C) of BODIPY-C_{10} (grey), BP-PH-8M (red), BP-PH-CF_3 (blue), BP-PH (green) and BP-PH-OMe (purple).

[1] P. Sarder, D. Maji, and S. Achilefu, "Molecular probes for fluorescence lifetime imaging," Bioconjug. Chem., vol. 26, no. 6, pp. 963–974, 2015.
[2] M. K. Kuimova, "Mapping viscosity in cells using molecular rotors," Phys. Chem. Chem. Phys., vol. 14, no. 37, pp. 12671–12686, 2012.
[3] K. Maleckaitė et al., "Designing a red-emitting viscosity-sensitive BODIPY fluorophore for intracellular viscosity imaging," Chem. Eur. J., vol. 27, no. 67, pp. 16768–16775, 2021.
[4] K. Maleckaitė et al., "Give or take: Effects of electron-accepting/-withdrawing groups in red-fluorescent BODIPY molecular rotors," Molecules, vol. 27, no. 1, art. no. 23, 2021.