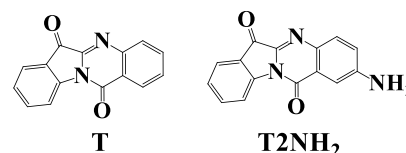


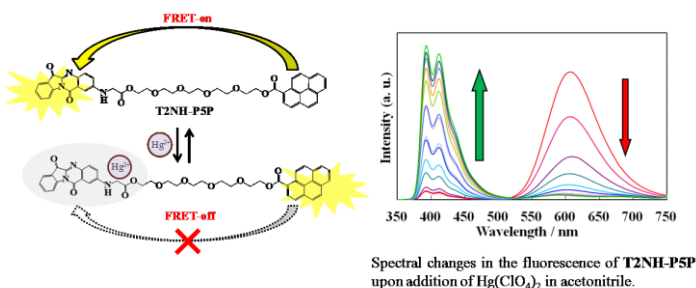
Synthesis and application of fluorescent tryptanthrin derivatives

(Graduate School of Science and Technology, Hirosaki Univ.) ○Jun Kawakami

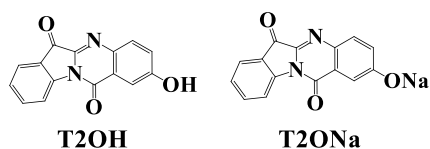
Tryptanthrin (T) is a weakly basic alkaloid found in a number of plant species that exhibits antimicrobial activity against various pathogenic bacteria and fungi. Some tryptanthrin derivatives were found to exhibit fluorescence on being synthesized as antimicrobial agents. We found that 2-aminotryptanthrin (**T2NH₂**) had especially excellent photophysical properties such as wide-wavelength absorption and emission in the visible region and a high fluorescence quantum yield [1, 2]. The fluorescence spectra of **T2NH₂** in solvents with different polarities demonstrated large positive fluorescent solvatochromism. The emission maxima ($\lambda_{f, \max}$) were red-shifted with increasing polarity in both protic and aprotic solvents, but the shift was more pronounced in the samples dissolved in protic alcohols. The emitted colors changed from green to red with increasing solvent polarity. **T2NH₂** possesses a planar, polar structure with effective intramolecular charge transfer (ICT) between the carbonyl group of the five-membered ring and the amino group. The large fluorescent solvatochromism is attributable to the influence of the ICT, although stabilization by hydrogen bonding would also contribute in the case of protic solvents. **T2NH₂** and its derivatives have widespread potential applications in highly diverse fields, such as labeling reagents, chemosensors, laser dyes, photosensitizers, and fluorescent organic devices.



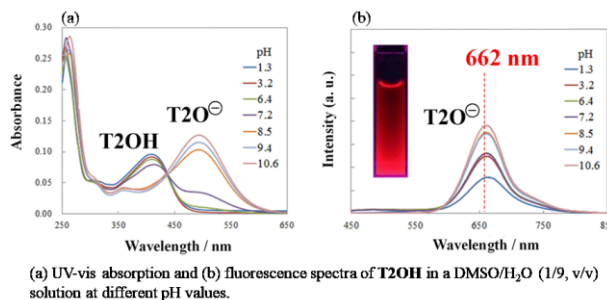
To obtain fluorescence resonance energy transfer (FRET)-based metal-cation sensors, we synthesized a 2-aminotryptanthrin derivative with pyrene (**T2NH-P5P**) in which the pyrene group, as an energy donor, and the 2-aminotryptanthrin unit, as an energy acceptor, are anchored with pentaethyleneglycol. When using excitation at 325 nm, which corresponds to the absorption of the pyrene unit of **T2NH-P5P**, emission at 600 nm, from the 2-aminotryptanthrin unit, was observed, indicating that intramolecular FRET occurs in **T2NH-P5P** (FRET-on). However, when Fe^{2+} , Fe^{3+} , Cu^{2+} , Hg^{2+} , and Al^{3+} were added to an acetonitrile solution of **T2NH-P5P**, the behavior changed from FRET-on to FRET-off remarkably, which means that the fluorescence of 2-aminotryptanthrin was quenched, whereas that of the pyrene group was revived (FRET-off) [3].



The near-infrared (NIR) region (650–900 nm) is referred to as the “optical window” of cells and tissues because of the lack of efficient endogenous absorbers in this spectral range and the subsequent high penetration depth (of the order of a few millimeters) in most tissues. Organic fluorescent dyes that emit NIR fluorescence are preferable for applications in biological systems because they can reduce auto-fluorescence and photodamage to living cells. The absorption maxima ($\lambda_{a, \max}$) of **T2NH₂** are at 447 nm in toluene and 464 nm in methanol, whereas the $\lambda_{f, \max}$ are at 516 nm in toluene and 632 nm in methanol. Therefore, we plan to shift the $\lambda_{a, \max}$ and $\lambda_{f, \max}$ of **T2NH₂** to longer wavelengths by accelerating the ICT. We synthesized



2-hydroxytryptanthrin (**T2OH**) and its sodium salt (sodium tryptanthrin-2-olate, **T2ONa**) as NIR fluorescent dyes for fluorescent imaging. The $\lambda_{a, \max}$ of **T2OH** under a pH range from 1.3 to 7.2 and from 8.5 to 10.6 were *ca.* 410 nm and *ca.* 495 nm, respectively. Moreover, the $\lambda_{f, \max}$ were *ca.* 660 nm regardless of the pH range. **T2ONa** was water soluble and the $\lambda_{f, \max}$ were *ca.* 660 nm in both aprotic and protic solvents [4].



- [1] J. Kawakami, Tryptanthrin Derivatives, Patent No. 5448046, Japan. [2] J. Kawakami *et al.*, *Trans. Mater. Res. Soc. Japan*, **2013**, *38*, 123-125. [3] J. Kawakami *et al.*, *Anal. Sci.*, **2014**, *30*, 949-954. [4] J. Kawakami *et al.*, *Anal. Sci.*, **2016**, *32*, 251-253.