Development of Novel Fluorescent Dyes and Their Application as Probes to Study Biological Processes

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Used as probes for the detection, visualization and characterization of biological molecules, synthetic fluorescent compounds have become indispensable tools in chemical biology. [1] Over the last years, a wide range of fluorescent compounds has been synthesized and employed in the field, such as coumarins, BODIPYs and rhodamins.[1,2] Efforts have been constantly put into research to improve the fluorophores, in order to increase the quantum yield,[3] to make the compounds more stable and to increase the Stokes shift.[4]

Our group has investigated the keteniminium species derived from electrophilic amide activation and engaged them in a variety of useful transformations.[5] In 2016, azides were utilized with a ketenimium species to afford the α-aminated amides.[6] Interestingly, an unexpected reactivity from azides with benzylic amide led to the serendipitous discovery of a highly fluorescent pyridinium moiety (**1**, Figure 1b). Herein, we present the use of a modular synthetic method from commercially available or easily accessible feedstocks (Figure 1a) to access a library of analogues in which their structure-activity relationship has been established (Figure 1b). Moreover, the emitting wavelength of these molecules can also be easily tuned (Figure 1c,d). Finally, we successfully conjugated our PyrAte core with bio-active compounds like citalopram (Figure 1c), which allowed successful labeling of living cells expressing serotonin transporters (Figure 1d).

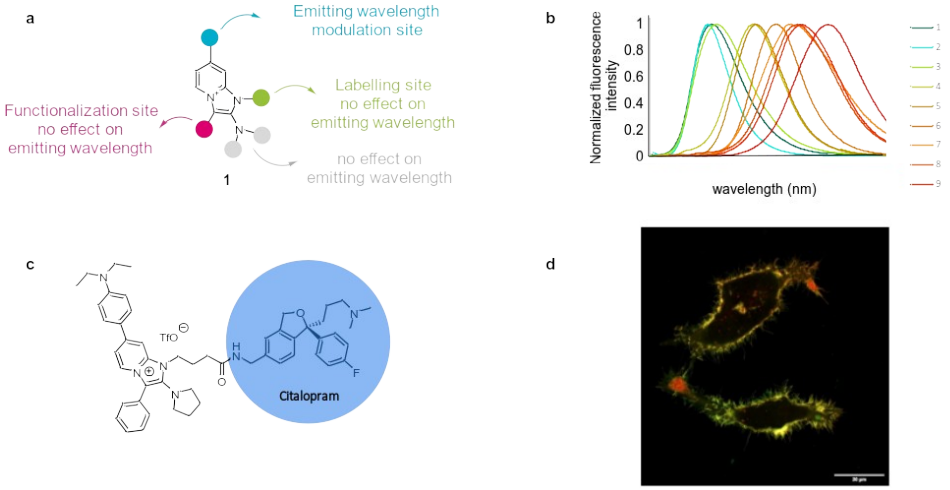

Figure 1. Facile modular synthesis of fluorescent dyes **1**, the absorbance-emission curves of some of the scope examples, and the PyrAte-citalopram conjugate and the successful labelling of a living SERT-expressing cell with such conjugate.

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