The development of photomodulatable fluorescent probes is essential for progress in the field of super-resolution fluorescence microscopy. Fluorescent photochromic diheteroarylethenes are particularly appropriate as a starting point for this development because they present reversible photoswitching between a dark and a bright isomer via a ring-closing photoreaction.[1] However, they are poorly soluble in water – a drawback when it comes to applications in cellular microscopy.

We have experimented with various strategies for the solubilization of our fluorescent diheteroarylethene derivatives,[2] including covalent and non-covalent modifications. Inclusion into hydrophobic cavities such as cyclodextrin and fatty acid binding proteins has proven effective for the conservation of the photochromic and fluorescent properties in water but fatigue resistance is reduced. Adsorption onto protein surfaces seems to inhibit photoconversion while conserving fluorescence. Covalent bonding of glucose molecules to the fluorophore favours hydrophilic interactions with the aqueous solvent, increasing significantly its solubility in water-methanol mixtures. Repeated cycles of photoswitching can be achieved with minimal photodegradation and fluorescence quantum yields, while reasonable, are expected to increase upon interaction with biological structures such as membranes. In the absence of any organic cosolvent, emission and photoconversion cease to exist, helping to reduce background fluorescence in the biological sample. Such reversibly photoswitchable, fluorescent and water-soluble probes are suitable for a wide variety of super-resolution microscopy techniques.

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