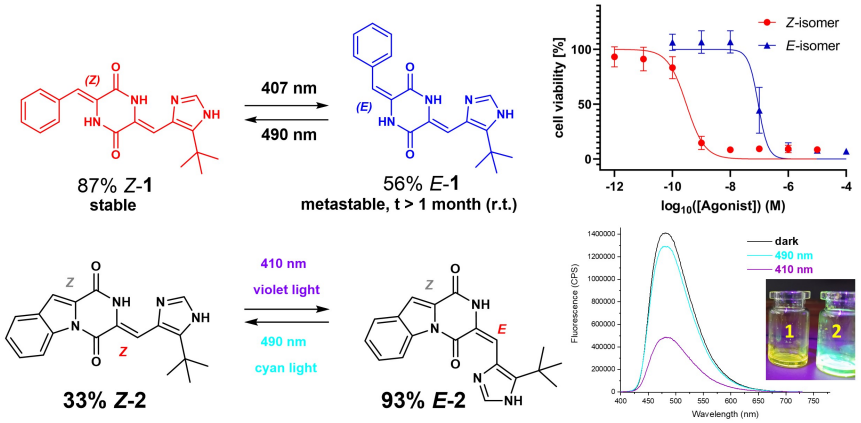
Hemipiperazines: peptide-derived photoswitches with low-nanomolar toxicity

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Cyclic dipeptides (CDP) are common structural motifs in biology, potent pharmacophores, and important constituents of numerous supramolecular systems based on hydrogen bonding.[1] Light-triggered photomodulation of their properties, e.g. upon merger with molecular photoswitches,[2,3] opens the way for photopharmacology applications, or producing smart materials.

Upon investigation of light-triggered release of CDP drugs from photochromic supramolecular hydrogels [4], we have discovered that plinabulin (*Z*-**1**) – a low-nM antimitotic agent - reversibly photoisomerizes to its thermally stable photoisomer (*E*-**1**) with significantly lower activity, which can be isolated and used as a photoactivated pro-drug.[5] Moreover, its previously unreported photochromic system – hemipiperazine – constitutes a new class of molecular photoswitches [2,3] with broad application potential, ranging from smart materials to photopharmacology. We have examined basic photophysical properties of the isolated hemipiperazine photochrome.[5,6] Finally, the "locked" plinabulin **2** exhibits enhanced fluorescence, and reversible photomodulation of the fluorescence level upon photoisomerization - which may in turn find applications e.g. in super-resolution microscopy.[5]



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