DEVELOPMENT OF VISIBLE LIGHT-SENSITIVE TOOLS TO IMPROVE THE PHARMACOKINETICS OF PHOSPHORUS MOLECULES AS PART OF A PRODRUG STRATEGY

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Phosphorus drugs often exhibit unfavorable pharmacokinetic properties due to their hydrophilicity and negative charge at physiological pH, resulting in poor cellular internalization and rapid elimination. The prodrug approach makes it possible to temporarily mask these characteristics to improve their bioavailability. The ChemPhosBio team in the CB3S laboratory has recently developed photosensitive prodrugs that can be activated by near-UV radiation, validating their efficacy in vitro on tumor cells[1]. However, their in vivo activation requires an implantable medical device, due to the low penetration of UV through biological tissues. To overcome this limitation, we propose the design of sensitive prodrugs to visible irradiation, incorporating a fluorophore motif derived from Xanthenium[2]. This fluorophore will enable us not only to monitor their cellular localization prior to irradiation, but also to confirm drug release after photoactivation via fluorescence and HPLC analysis[3]. Finally, evaluation of their cytotoxicity in vitro on various cancer cell lines will enable us to optimize their therapeutic efficacy. We will present here the synthesis of these new photosensitive prodrugs.

References:

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