

Towards Theranostic Applications of Trifluoromethyl-Substituted Iridium(III) complexes

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Among all small molecules that interfere with DNA replication, photodynamic therapeutic agents are of key interest in developing new strategies to design more specific and efficient anti-cancer treatments. Compared to classical chemotherapeutic agents, their activity can be finely controlled thanks to the light-triggering of their photoreactivity. Usually, the mechanism of photodynamic therapy relies on the generation of singlet oxygen by energy transfer from a photosensitizer. However, the activity of these type-II photosensitizers is significantly limited in hypoxic tumors. Therefore, the development of Type-I photosensitizing agents, which do not rely on the production of ROS, is highly desirable. In this context, we developed new iridium(III) complexes which are able to photoreact with biomolecules; namely, our Ir(III) complexes can oxidize guanine residues under visible light irradiation. We report the synthesis and the extensive photophysical characterization of four new Ir(III) complexes. In addition to an extensive experimental and theoretical study of the photophysics of these complexes, we characterize their photoreactivity towards model redox-active targets and the relevant biological target, the guanine base. We demonstrate that photo-induced electron transfer takes place between the excited Ir(III) complex and guanine which leads to the formation of stable photoproducts, indicating that the targeted guanine is irreversibly damaged. These results pave the way to the elaboration of new Type-I photosensitizers for targeting cancerous cells.

