Theoretical study of DNA photosensitized by an artifical nucleobase: a model toward the 6-4 photoproduct.

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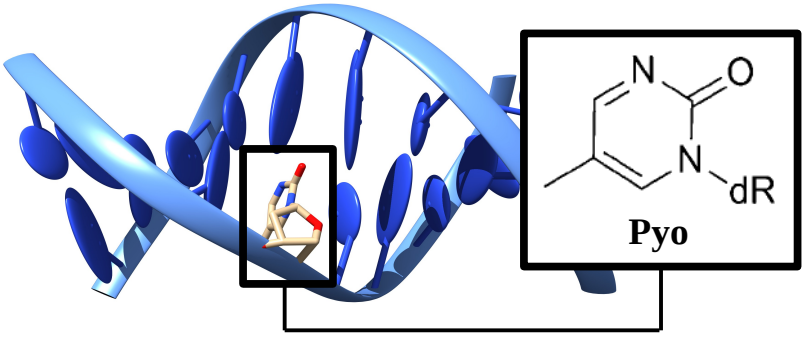
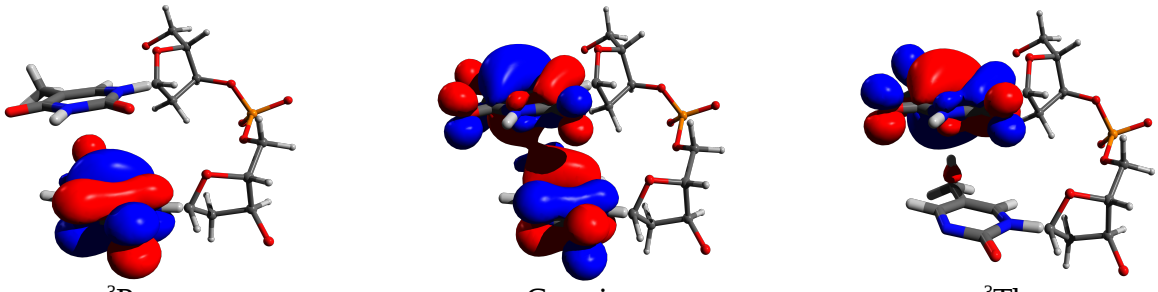
The photosensibility of DNA may cause structural modifications of its nucleobases structure under the irradiation of ultraviolet light (UV). This phenomenon can lead to mutations of DNA genes resulting by example in some cases to skin cancer. One famous lesion is the formation of thymidine dimers 6-4 photoproduct (6-4PP) which has been deeply studied to understand the mechanistic details of its formation. From experimental researches [1], it as been described that the main active chromophore of the 6-4PP is the 1-(β-D-2'-deoxyribosyl)-5-methyl-2-pyrimidone (Pyo).

According to this, we decided to investigate, in the DNA environment, the photoactivity of Pyo as a model toward a further study of 6-4PP [2]. This chromophore thus represents an artificial nucleobase directly integrated in the DNA helix.

The system we choose for this work is a crystallographic structure from the PDB databank of a double stranded B-DNA dodecamer (the sequence is CGCATPyoACGC). Then, several properties were obtained by using molecular modeling:

- The stability and the structural global induced distortion of the Pyo-containing double helix from **molecular dynamic simulations** (MD).
- Using a **QMMM** formalism, the **absorption**, **emission** and **circular dichroim** of the system.
- Finally the **triplet energy transfer** of Pyo to the close-by thymine (Thy) was characterized by obtaining adiabatic energy profiles for the phenomenon.





^{3}Pyo Crossing ^{3}Thy

[1] V. Victoria-Criado et al., *Angew. Chem. Int. Ed.*, **2013**, 52, 6476-6479.
[2] H. Gattuso et al. In preparation.