

## Modelling the structure and triplet-triplet energy transfer of the 6-4 photoproduct.

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It is well known that DNA is a target for UV-induced damage, generating two main photolesions: cyclobutane pyrimidine dimers (CPD), (6-4) photoproducts (6-4PP) and their Dewar isomers [1]. These lesions are highly cytotoxic and genotoxic if they are not repaired by enzymes. 6-4PP can be even more harmful for DNA, this lesion may act as sensitizer by its 5-methyl-2-pyrimidone (Pyo) moiety, inducing Triplet Triplet Energy Transfer (TTET) toward an adjacent thymine [2]. We studied 6-4PP structure in B-DNA along 1  $\mu$ s classical Molecular Dynamics simulation (MD) and we investigated its spectroscopic properties using hybrid quantum-mechanics/molecular-mechanics (QM/MM) techniques rooted in TD-DFT. First, investigations were performed on Pyo as an artificial nucleobase in double-stranded DNA [3]. MD simulations shown that Pyo disturbs nor the overall B-DNA helicity neither the Watson-Crick pairing, and exhibits a strong stacking with adjacent thymine, which is needed for the Dexter type TTET. Our QM/MM calculations revealed that this energy transfer is facile, with a barrier of 0.4 eV (see Figure 1).

However, these results may differ for 6-4PP, which can trigger a strong distortion strongly the double helix to accomodate the cross-link. Along our dynamics for a 16-bp duplex, we probe the rearrangement of the structure which is bent in order to restore a  $\pi$ -stacking with a proximal thymine.

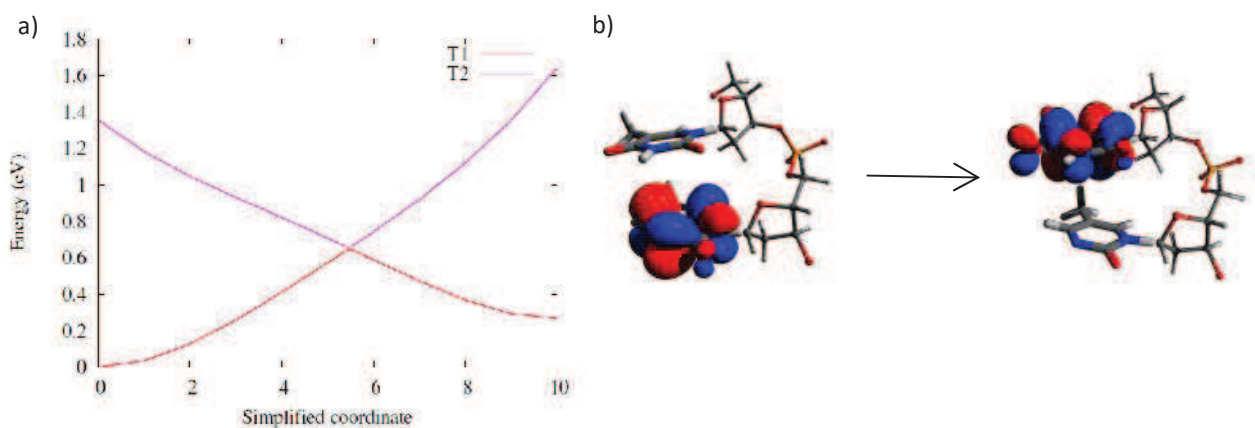


Figure 3. a) TTET energy path along the simplified coordinate. b) Natural-transition Orbitals (NTOs) show the TTET between pyo (up) and the adjacent thymine (bottom).

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3. Bignon, E; Gattuso, H.; Morell, C.; Monari, A.; Dumont, E. *Chem. Eur. J.*, **2015**, 32, 11509-11516.