PHOTOCYCLOREVERSION MECHANISM OF OXETANE DERIVATIVES AS MODELS OF (6-4) PHOTOPRODUCT DNA LESIONS

Miriam Navarrete-Miguel,[a] Angelo Giussani[a] and Daniel Roca-Sanjuán[a]
[a] *Instituto de Ciencia Molecular, Universitat de València, P.O. Box 22085, 46071 València, Spain*
miriam.navarrete@uv.es

INTRODUCTION

- **DNA** in living beings is constantly damaged by both exogenous and endogenous agents, such as UV radiation. The **direct light absorption** gives rise to **two** different **lesions**: **6-4 photoproducts**, (6-4)PP, and **cyclobutane pyrimidine dimers**, CPD.
- The photoinduced DNA lesions can be initiated by **Paternò–Büchi** photocycloaddition between two adjacent pyrimidine bases followed by rearrangement to (6-4)PP, forming an **oxetane** ring. An azetidine can be also formed by the aza-Paternò-Büchi reaction. Here we focus on oxetane ones.
- Experiments have recently found that **triplet exciplex** (^{3}EXC*) is involved in the **lesion formation**.
- The **repair mechanism** of these lesions can be represented with the **inversion of the Paternò-Büchi reaction**.
- One of the most supported hypothesis is that the (6-4)PP **repair mechanism** takes place via an **intermediate**, characterized by an **unstable oxetane ring**. Then, **oxetane derivatives** have been used experimentally as **stable models** of this intermediate.
- In this study, **BQ-ox**, **NQ-1** and **HH-1** and **HT-1**[1] are used as oxetane models.

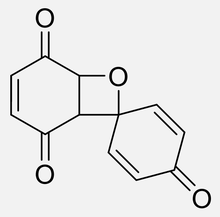


Figure 1. BQ-ox (left) and NQ-1 (right) structures

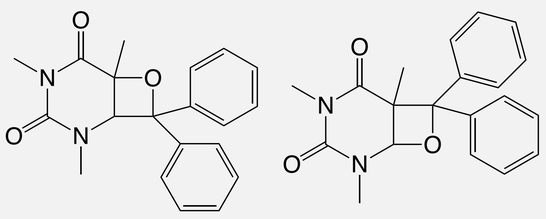


Figure 2. HH-1 (left) and HT-1 (right) structures

METHODOLOGY

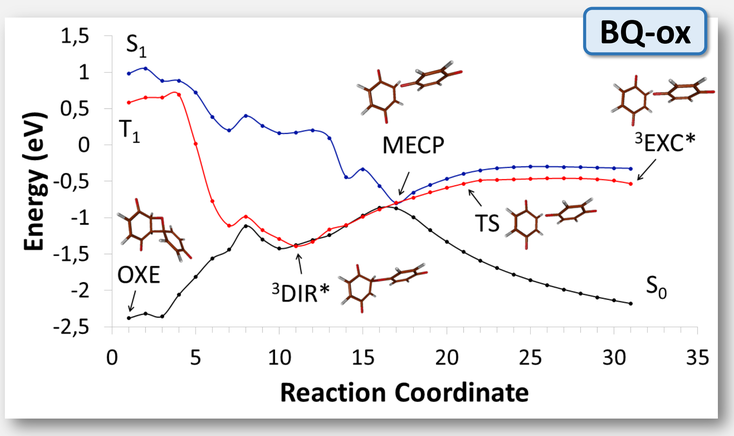
- DFT M06-2X/6-31++G** (Gaussian 09[2] package, rev. D.01)
- CASPT2//CASSCF protocol with an active space of (12,12) for NQ-1, HH-1 and HT-1 and (14,12) for BQ-ox and ANO-S-VDZP basis set (Molcas 8[3] software).
- Computational strategies: LIICs (Linear Interpolation of Internal Coordinates) and scans

OBJECTIVES

- Interpret the different photobehaviour on these systems
- Analyze if a triplet exciplex (^{3}EXC*) participates in the repair mechanism, as it happens in the lesion formation

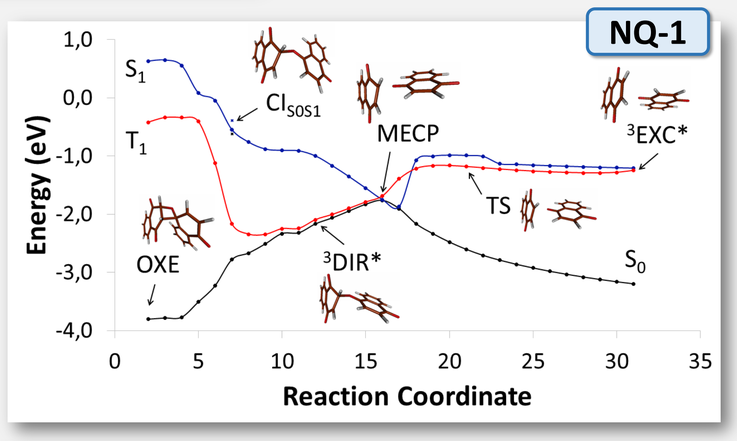
RESULTS

a) BQ-ox and NQ-1 oxetane models



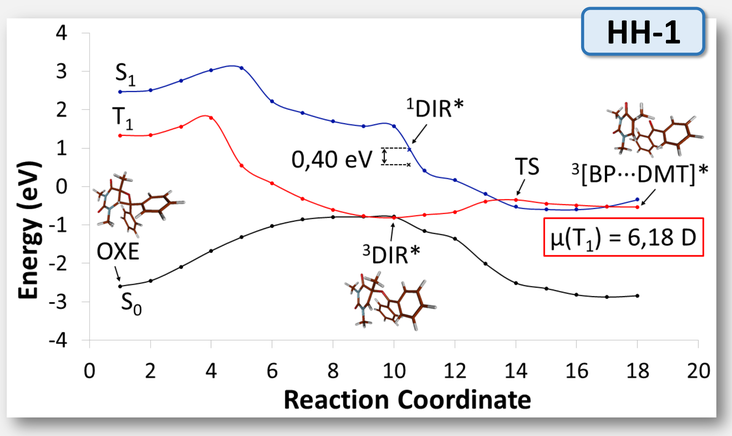
- **Decay through S_1 until MECP** between S_0, S_1 and T_1
- MECP:
  - Located before the TS and after the ^{3}DIR*
  - SOC_{S0T1}=35 cm^{-1}
  - SOC_{S1T1}=22 cm^{-1}
- Energy barrier to reach ^{3}EXC* (**ΔE=0.40 eV**)
- **Unfavorable evolution to ^{3}EXC***; decay to S_0 *via* IC

- **Decay through S_1 until MECP** between S_0, S_1 and T_1
- MECP:
  - Located before the TS and after the ^{3}DIR*
  - SOC_{S0T1}=5 cm^{-1}
  - SOC_{S1T1}=30 cm^{-1}
- Energy barrier to reach ^{3}EXC* (**ΔE=0.52 eV**)
- **Unfavorable evolution to ^{3}EXC***; decay to S_0 *via* IC



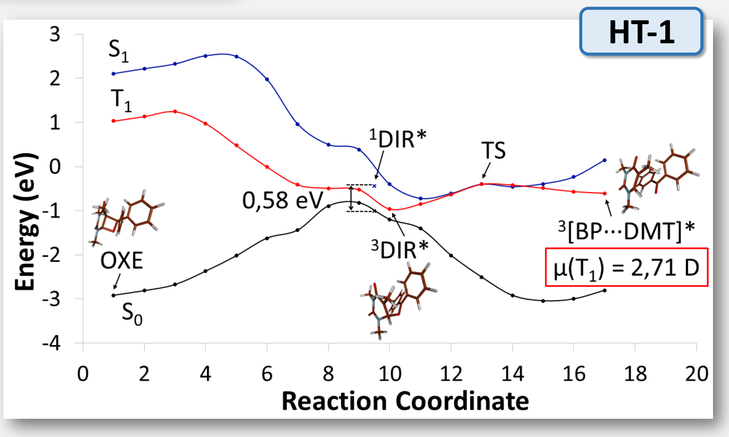
In agreement with experiments: They observed no formation of the triplet exciplex

b) HH-1 and HT-1 oxetane models



- **S_1T_1 STC**: In the TS region, related to the C-O bond breaking
- **SOC_{S0T1}** < 0.5 cm^{-1} at ^{3}DIR*
- **SOC_{S1T1}** ~4 cm^{-1} at TS
- **Favorable evolution to ^{3}EXC*** obtaining the monomers in the T_1 state

- **S_1T_1 STC**: Before the TS and after ^{3}DIR*, where only the C-C bond is broken
- It becomes trapped in the ^{3}DIR* region due to energy barrier to reach the TS
- **SOC_{S0T1}** < 0.5 cm^{-1} at ^{3}DIR*
- **SOC_{S1T1}** ~4 cm^{-1} before TS
- **Less favorable production of ^{3}EXC***, being able to decay to S_0 (despite low SOC)



In agreement with experiments: Lower intensity of the transient absorption band at 530 nm detected by LFP for HT-1

CONCLUSIONS

- **BQ-ox and NQ-1 models**
  - In both BQ-ox and NQ-1 cases, the molecule will decay to S_0 directly from S_1
  - Then, the population of the ^{3}EXC* is not favorable
  - In agreement with our experimental collaborators
- **HH-1 and HT-1 models**
  - Different photobehaviour
  - Photoinduced cycloreversion through the formation of a ^{3}EXC* occurs to a much higher extent for HH-1
  - In agreement with our experimental collaborators

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