

# SPIN-ORBIT COUPLING INDUCED INTERSYSTEM CROSSING IN PEROXYNITRITE

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## INTRODUCTION

Spin-orbit coupling (SOC) is a relativistic effect with significant implications in the fields of chemistry, physics, and biology. Peroxynitrite (PNT) is an extremely reactive oxidant that plays a vital role in the destruction of pathogenic particles by immune cells. Nevertheless, when its production within the cell is disrupted, it results in the oxidation of lipids and mitochondrial respiration inhibition, as well as the inactivation of enzymes and the modulation of the protein profile of cancer cells. Scientists have noted [1] that it is important to take into account intratumoral PNT activity when developing anticancer therapies. Our research concentrates on investigating the internal magnetic interactions within peroxynitrite that define the chemical activity of the molecule.

## METHODS

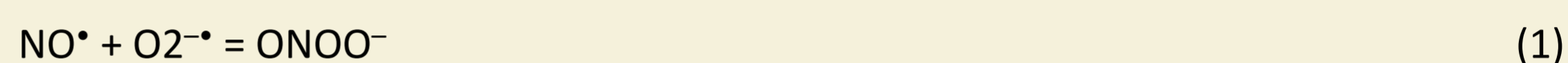
In this research study, we employed a range of quantum chemical methods, including DFT, TD-DFT, CASSCF, and the software package Orca 5.0.4.

The ground state of peroxynitrite was optimised using the DFT method. The potential energy surface (PES) was constructed using the TD-DFT method based on the ground state term with a frozen N-O bond. The spin-orbit coupling (SOC) was evaluated at the level of CASSCF and TD-DFT theory.

The possibility of the intersystem crossing was estimated by analyzing the PES and the results of the spin-orbit coupling matrix element (SOC ME).

## RESULTS

The SOC has the ability to alter the chemistry of the molecule's ground state during its generation through recombination of two radicals, which we will consider in our study using peroxynitrite as an example:



According to scientists' data [2-4], it has been reported that oxidase and oxygenase enzymes activate oxygen through the high spin-orbit coupling in  $\text{O}_2^{\bullet-}$ . It is worth noting that in PNT, which is formed by the interaction between the radical superoxide anion and radical nitric(II) oxide (1), the PNT's SOC does not have a direct relationship with the superoxide anion, since  $\text{ONOO}^-$  is not a radical. Nevertheless, this observation suggests the existence of a similar phenomenon for PNT.

**Table 1.** Calculated geometric parameters of the *cis* and *trans* isomers of the singlet ground state peroxynitrite  $^1\text{ONOO}^-$  ion

Parameter	<i>cis</i> -isomer	<i>trans</i> -isomer
N1=O2, Å	1.21315	1.22793
N1-O3, Å	1.36745	1.33856
O3-O4, Å	1.38851	1.40838
O2-N1-O3, °	116.336	111.18
N1-O3-O4, °	118.334	114.12
Total energy, au	-280.25147	-280.24624

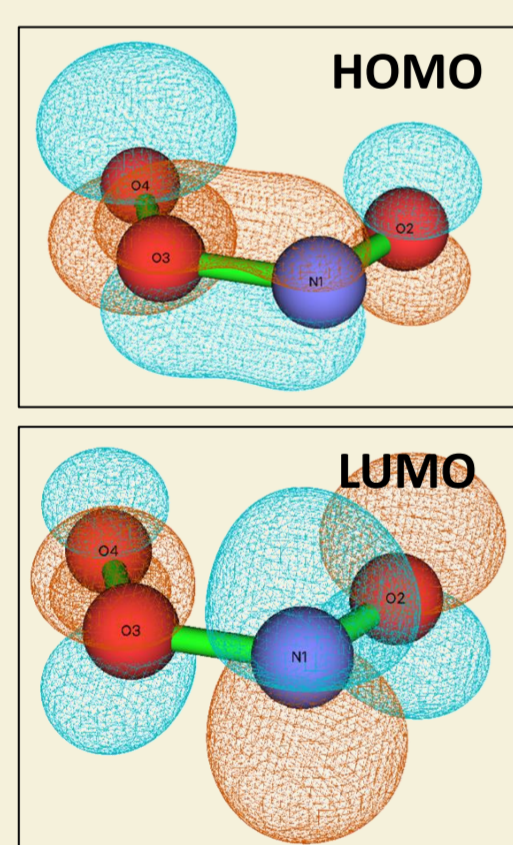
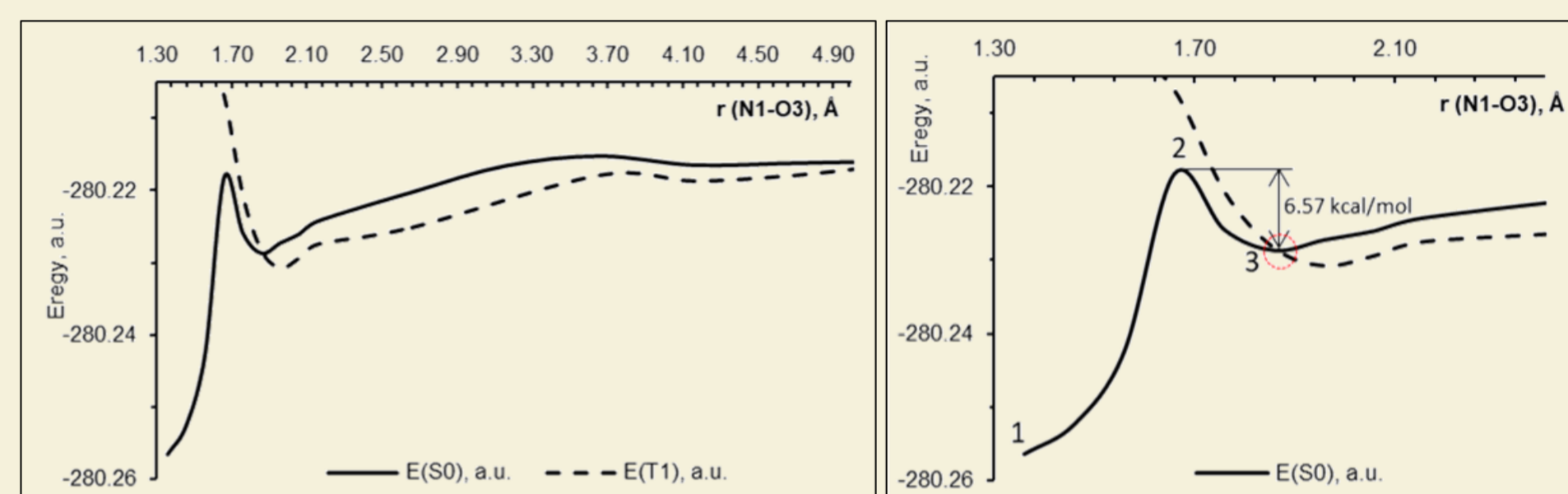


Figure illustrates the highest occupied and lowest unoccupied molecular orbitals (HOMO and LUMO) of the peroxynitrite anion. Notably, the HOMO is mainly localised on the oxygen and O-O-N peroxynitrite's fragment. In contrast, the LUMO is mainly localised on the nitric oxide fragment and is similar to the  $\pi^*$ -orbitals of nitric oxide NO. The distribution of charges on the atoms supports the assumptions made: N1 has a charge of -0.332, O2 has a charge of 0.006, and O3 and O4 have charges of -0.226 and -0.447 respectively. According to these data, it can be seen that most of the negative charge is localised on the superoxide fragment O3-O4, which is consistent with the spatial distribution of the peroxynitrite's HOMO.



**Fig. 1.** PES cross sections of the ground singlet state of the PNT and the first excited triplet state (left); in more detailed (right)

The figure depicts the interaction between the superoxide anion  $\text{O}_2^{\bullet-}$  and the nitric oxide  $\text{NO}^{\bullet}$ . As shown in Fig. 1, PNT has two local minimums (point 1 and point 3) in its ground state. The first local minimum of the  $\text{O}_2^{\bullet-}\text{-NO}^{\bullet}$  system in the singlet state corresponds to the *cis*-isomer of PNT, which is the ground state of the molecule. It has been observed that a low energy barrier exists (point 2) between the (1) and (3) local minima, equivalent to 6.57 kcal/mol (0.28 eV).

It is worth mentioning that the PES curves of the singlet and first triplet states are intersected near the local minimum of the singlet state (point 3). This point is noteworthy because it suggests a possible intersystem crossing (ISC) in this system. In order to further examine this issue, we have carried out a SOC calculation. According to the results, a non-zero spin-orbit coupling matrix element (SOCME) between S0 and T1 states was found, which is equal to  $\langle T_1 | H_{so} | S_0 \rangle = 42.12 \text{ cm}^{-1}$  at the CASSCF (16,12) level.

The probability of the T1→S0 transition, which is caused by the SOC, may be characterised by the zero-field splitting that occurs as a result of the magnetic interaction of electrons. Since the energy gap between T1 and S0 is 0.73 eV, according to the TD-DFT method, the possible ISC can be predicted by recombination between  $\text{O}_2^{\bullet-}$  and  $\text{NO}^{\bullet}$  radicals.

## CONCLUSION

In the entrance channel of reaction (1) we have six triplets and two singlets because the ground state of superoxide  $\text{O}_2^{\bullet-}(\chi^2\Pi)$  is doubly degenerate in orbital space. If we neglect SOC in reaction (1), all triplet states would not produce products, since the T states have large activation barriers. The T→S transition in the local minima regions makes all entrance channels in reaction (1) reactive. This is attributed to the strong spin-orbit coupling (SOC) interaction inducing intersystem crossing (ISC), which turns the formed triplet molecules into the singlet. This discovery indicates that peroxynitrite is produced in biological systems at a higher rate than previously assumed. Thus, the rate constant of the total recombination reaction (1) increases. This, in turn, leads to a greater pathological impact of peroxynitrite in case of its excessive content in living cells.

## REFERENCES

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