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Nanostructured bismuth SPCEs for non-enzymatic paracetamol sensing: development, testing, and computational approach

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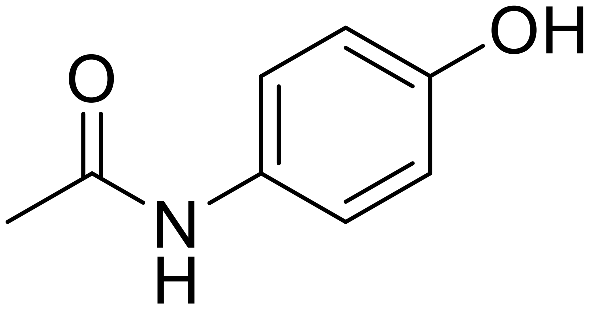
Summary

1. **Paracetamol and bismuth sensors: a brief introduction**
2. **Bismuth sub-nitrate sinthesis**
3. **Electrochemical studies**
4. **Computational studies**
5. **Conclusions**

1.Paracetamol sensing: a brief introduction

- Paracetamol is one of the most studied emerging pollutants.
- Paracetamol detection could be performed in several ways ranging from chromatographic methods to electrochemical ones.
- Electrochemical approaches represent a solid choice of all available systems.



Paracetamol

Why should choose an electrochemical sensor over other systems?

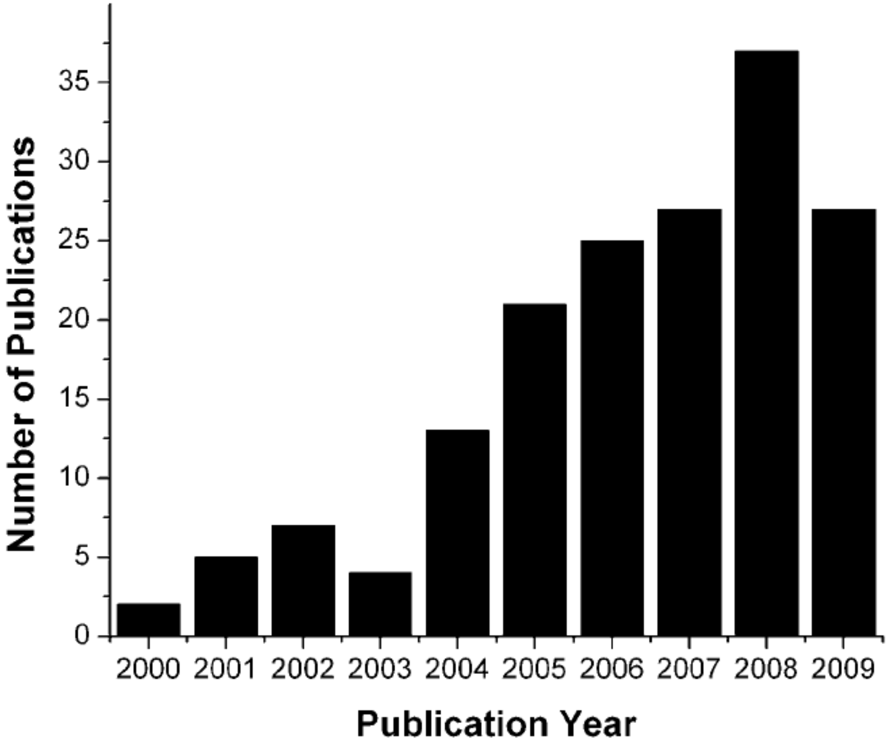
- ✓ High sensitivity
- ✓ Low limit of detection (LOD)
- ✓ Good precision and accuracy
- ✓ Fast and easy detection process

- Tasić, Žaklina Z., et al. "Review of applied surface modifications of pencil graphite electrodes for paracetamol sensing." *Results in Physics* 22 (2021): 103911.
- Chatterjee, Abhik. "Different Electrodes for Paracetamol Estimation using Cyclic Voltammetry Technique: A Review." *Research Journal of Pharmacology and Pharmacodynamics* 9.2 (2017): 88-92.

1.Paracetamol and bismuth sensors: a brief introduction

Bismuth based materials for electrosensing applications

- Bismuth is a non toxic metalloid produced as a side product of lead and from bismite.
- Bismuth could be converted in several different nitrates and subnitrates by simple solid phase reactions.
- Bismuthoxide and nitrates are quite stable under various conditions.
- Good electrochemical performances both as a sensor and in electrochemical storage.



- *Number of papers about the use of bismuth for biosensing*

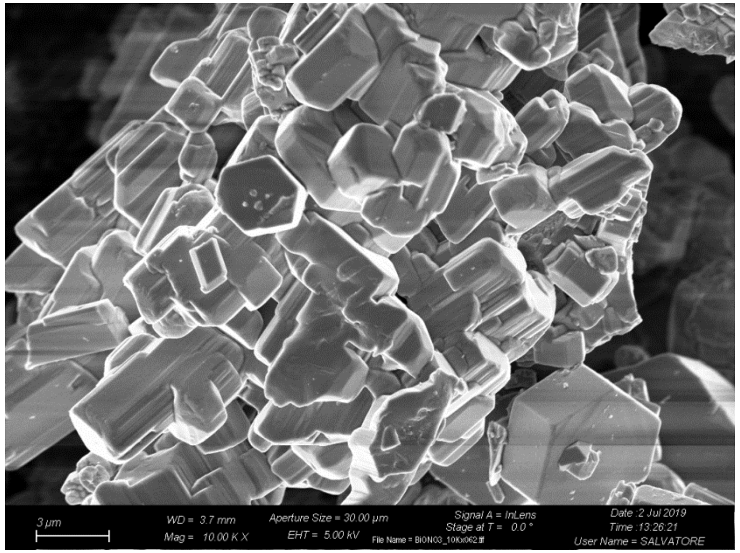
- Švancara, Ivan, et al. "A decade with bismuth-based electrodes in electroanalysis." *Electroanalysis* 22.13 (2010): 1405-1420.

2.Bismuth sub-nitrate sinthesis

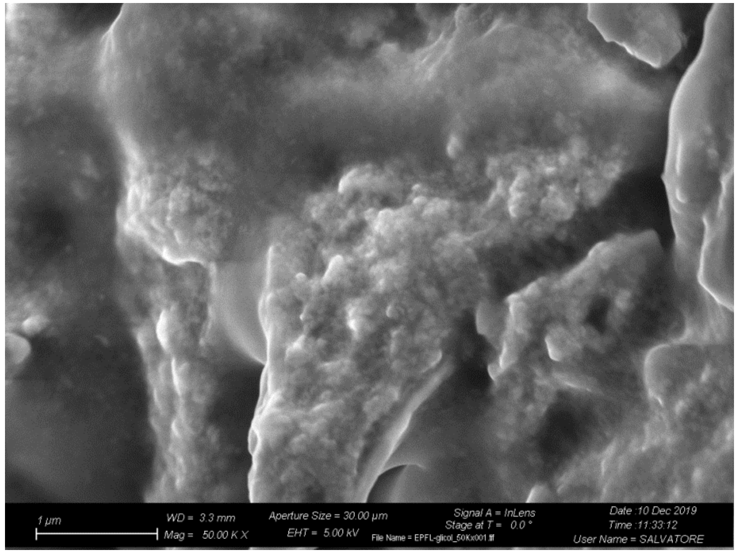
$$\begin{tikzcd}
\mathrm{Bi(NO_3)_3{\bullet}5(H_2O)} \arrow[r, "55\text{-}66°\mathrm{C}"] \arrow[d, "\begin{array}{l}\text{1)1- Butanol, 1h, sonication}\\ \text{2) Dry at 140°C}\end{array}"] & \mathrm{[Bi_6O_6]_2(NO_3)_{11}(OH){\bullet}6(H_2O)} \arrow[r, "77\text{-}130°\mathrm{C}"] & \mathrm{[Bi_6O_6](NO_3)_6{\bullet}3(H_2O)} \\
\mathrm{HO\text{-}BiONO_3} & &
\end{tikzcd}$$

- The addition of a non-ionic surfactant allowed to reduce the particle size down to sub-micrometric scale.

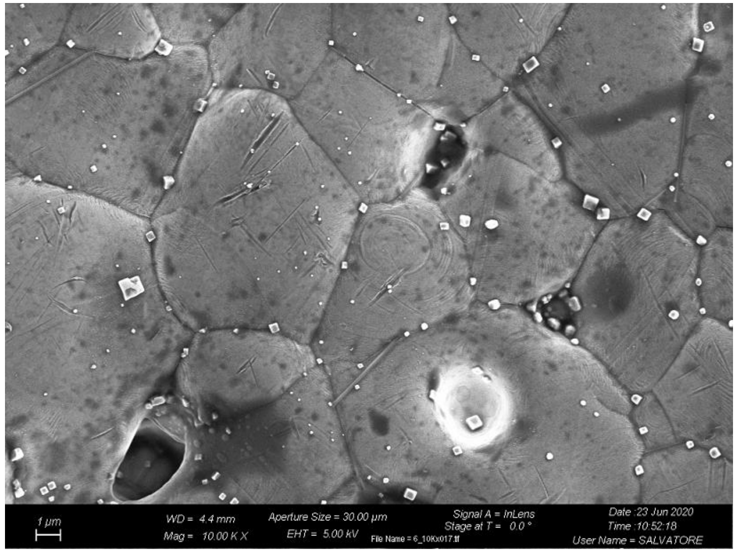
$HO-BiONO_3$



$PEG-HO-BiONO_3$



$PEG-HO-BiONO_3$ after deposition on the electrode

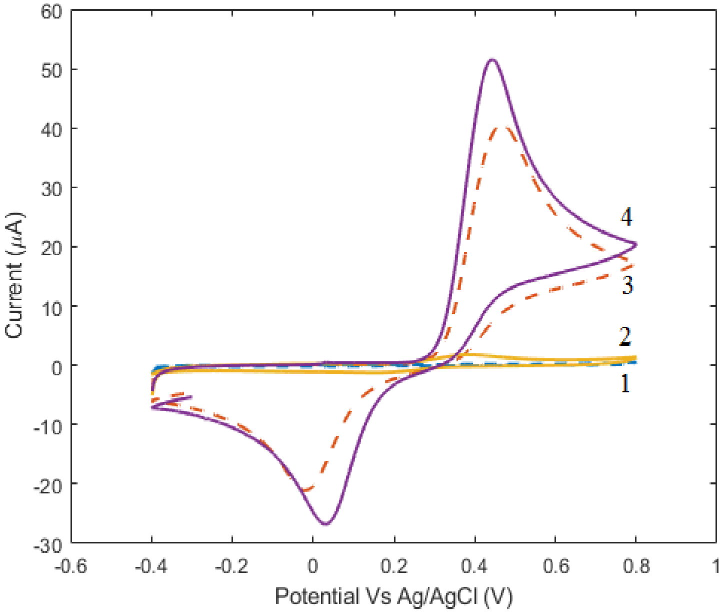


- Liu, Gen-qing, et al. "Research on nonenzymatic electrochemical sensor using HO-BiONO3 nanocomposites for glucose detection." Sensors and Actuators B: Chemical 242 (2017): 484-491.

3.Electrochemical studies

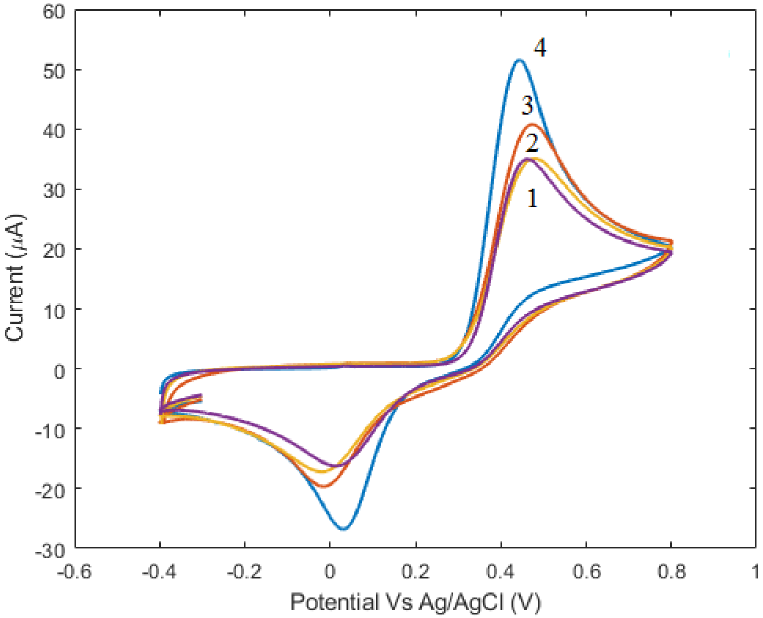
- Peak current increased by decorating a bare SPCE with HO-BiONO$_3$.

- Peak current increased by increasing the amount of HO-BiONO$_3$ used for tailoring the electrode surface.



Cyclic voltammograms of 1mM Paracetamol in 0.1M PBS at pH 7 with bare (dotted lines) and HO-BiONO$_3$ (solid lines) sensors where 1,2 without analyte and 3,4 with paracetamol in buffer solution.

Working electrode	Peak position (mV)	Peak current (μA)
SPCE	459.9 ± 1.0	33.1 ± 1.5
HO-BiONO$_3$	433.6 ± 6.1	42.0 ± 1.5
PEG HO-BiONO$_3$	385 ± 30	52.1 ± 3.0

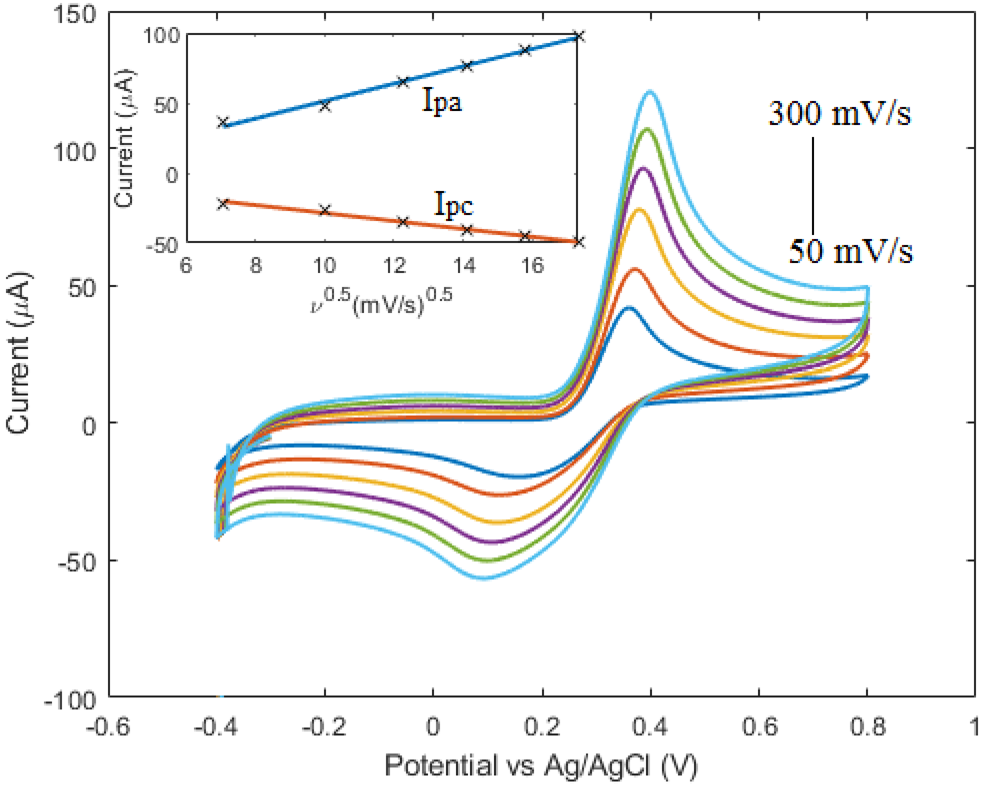


Different amounts of HO-BiONO$_3$ deposition on the surface of working electrode: from solution drops with volumes of 1) 50 μL, 2) 25 μL, 3) 10 μL, and 4) 5 μL.

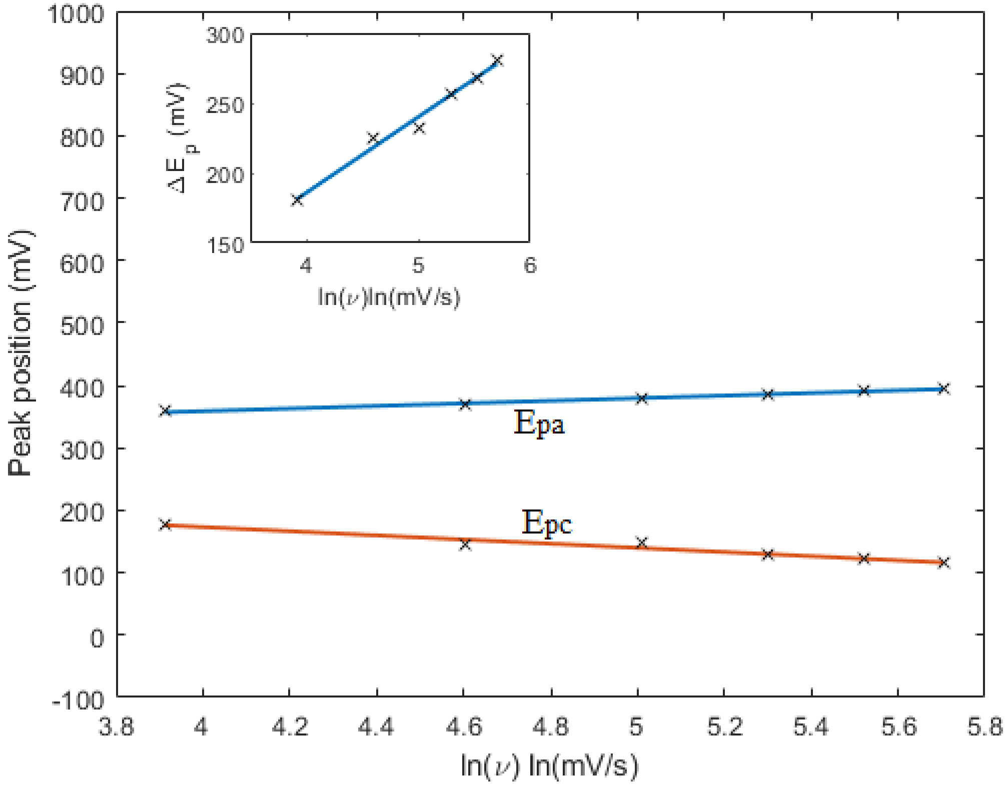
- Madagalam, Mallikarjun, et al. "Bismuth-Nanocomposites Modified SPCEs for Non-Enzymatic Electrochemical Sensors." IEEE Sensors Journal 21.9 (2021): 11155-11162.

3.Electrochemical studies

- The HO-BiONO$_3$ electrochemical system is a **freely diffusing quasi-reversible system**.



Cyclic voltammograms of 1mM paracetamol in 0.1M PBS at pH 7 with the scan rate (50 mV/s, 100 mV/s, 150 mV/s, 200 mV/s, 250 mV/s, and 300 mV/s) for PEG-coated HO-BiONO$_3$ sensor.



Plots of E_{pa} and E_{pc} with ln(v) for PEG-coated HO-BiONO$_3$ sensor. Insets: plots of ΔE_p as a funtion of ln(v).

- Madagalam, Mallikarjun, et al. "Bismuth-Nanocomposites Modified SPCEs for Non-Enzymatic Electrochemical Sensors." IEEE Sensors Journal 21.9 (2021): 11155-11162.

3.Electrochemical studies

- Laviron approach

$$E_{pc} = E^0 - \left(\frac{RT}{\alpha nF}\right) ln\left[\frac{\alpha}{|m|}\right]$$

- Cathodic potential

$$E_{pa} = E^0 + \left(\frac{RT}{(1-\alpha)nF}\right) ln\left[\frac{(1-\alpha)}{|m|}\right]$$

- Anodic potential

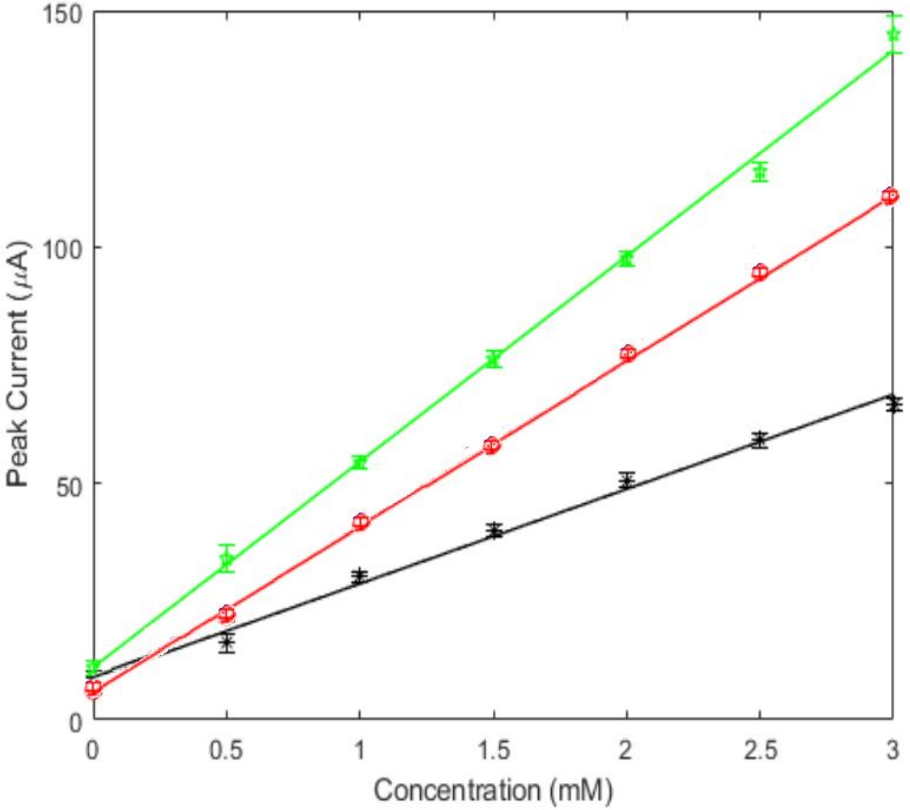
$$lnk = \alpha\, ln(1-\alpha) + (1-\alpha)ln\alpha - ln\left(\frac{RT}{nF\nu}\right) - \alpha(1-\alpha)\frac{nF\Delta E_p}{RT}$$

Working electrode	**α**	**ΔE_p (mV)**	**k(ms^{-1})**
SPCE	0.44±0.10	477±45	0.60±0.33
HO-BiONO$_3$	0.45±0.04	392±19	2.20±0.82
PEG HO-BiONO$_3$	0.40±0.04	243±10	42.0±9.8

- **n** is close to 2 supporting a 2 electron transfer process.
- Higher k for HO-BiONO$_3$ for tailored electrodes.

- Madagalam, Mallikarjun, et al. "Bismuth-Nanocomposites Modified SPCEs for Non-Enzymatic Electrochemical Sensors." IEEE Sensors Journal 21.9 (2021): 11155-11162.
- Laviron, E.. "General expression of the linear potential sweep voltammogram in the case of diffusionless electrochemical systems." *Journal of Electroanalytical Chemistry and Interfacial Electrochemistry* 101.1 (1979): 19-28.

3.Electrochemical studies



Calibration curves obtained by taking the oxidation peak currents of CVs for bare SPCE (black), HO-BiONO$_3$ (red) and PEG HO-BiONO$_3$ (green) sensors.

Working electrode	Sensitivity (µA/mM)	Detection limit (µM)	R.S.D.
SPCE	20.0 ± 0.2	2.32 ± 0.03	1.2%
HO-BiONO$_3$	34.9 ± 0.2	2.79 ± 0.01	0.48%
PEG HO-BiONO$_3$	43.5 ± 0.5	2.24 ± 0.03	1.2%

- Increment of sensitivity with surface tailoring of bare SPCE.
- The use of PEG coated HO-BiONO$_3$ led to a further improvement of sensitivity.

- Madagalam, Mallikarjun, et al. "Bismuth-Nanocomposites Modified SPCEs for Non-Enzymatic Electrochemical Sensors." IEEE Sensors Journal 21.9 (2021): 11155-11162.

4.Computational studies

How could it be possible evaluate the Electron transfer rate (k)?

Generalization of Marcus theory

$$\boxed{k = \frac{2\pi}{\hbar} J^2 (4\pi k_B T \lambda)^{-\frac{1}{2}} e^{-\frac{(\Delta G + \Delta g_s^o)^2}{4 k_B T \lambda}}} \qquad [k] = [s^{-1}]$$

where the free energy variation ΔG is:

$$\Delta G = -\Delta V^* - \Delta g_s^o$$

and the reorganization energy is:

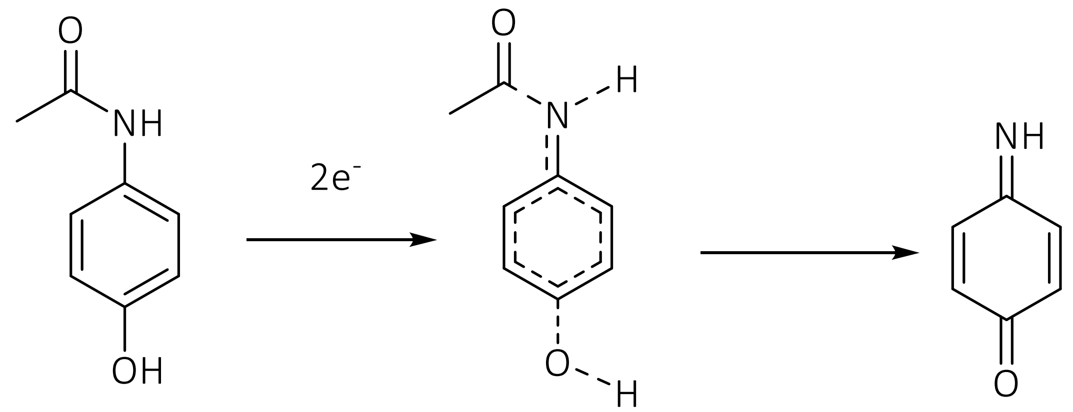
$$\lambda = \frac{e^2}{2}(\epsilon_{op}^{-1} - \epsilon_s^{-1}) \boxed{\left(\frac{1}{a} + \frac{1}{b} + \frac{1}{R}\right)}$$

- E_{int}^{solv} interaction energy between permanent dipole solvent
- IP ionization potential
- EA electron affinity
- Δg_s^e solvation energy of the ion pair due to solvent electronic polarization
- Δg_s^o solvation energy of the ion pair due to solvent orientational polarization
- e^2/R ion pair Coulomb interaction

- Tachiya, M. (1993). Generalization of the Marcus equation for the electron-transfer rate. *The Journal of Physical Chemistry*, *97*(22), 5911-5916.
- Cave, Robert J., and Marshall D. Newton. "Generalization of the Mulliken-Hush treatment for the calculation of electron transfer matrix elements." *Chemical physics letters* 249.1-2 (1996): 15-19.

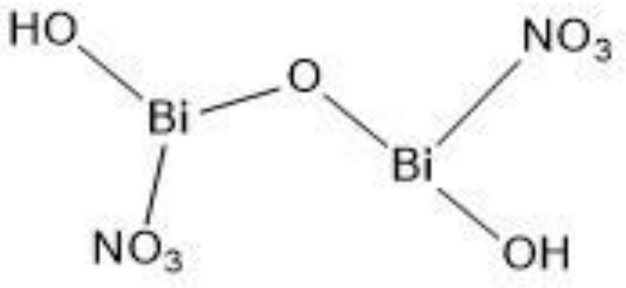
4.Computational studies

Oxidative pathway of paracetamol

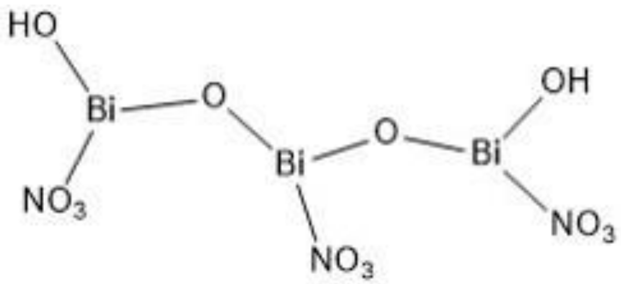


- We modelled the oxidative pathway of paracetamol considering a simultaneous 2 electron transfer.
- We selected as representative species for HO-BiONO$_3$ a dimeric and a trimeric compounds
- We implemetented a simulation of transitional state using a mixed approach based on **molecular mechanics** (MM+ method) and a **Hartree-Fock based semi-empirical method** (base PM3).

HO-BiONO$_3$ dimer



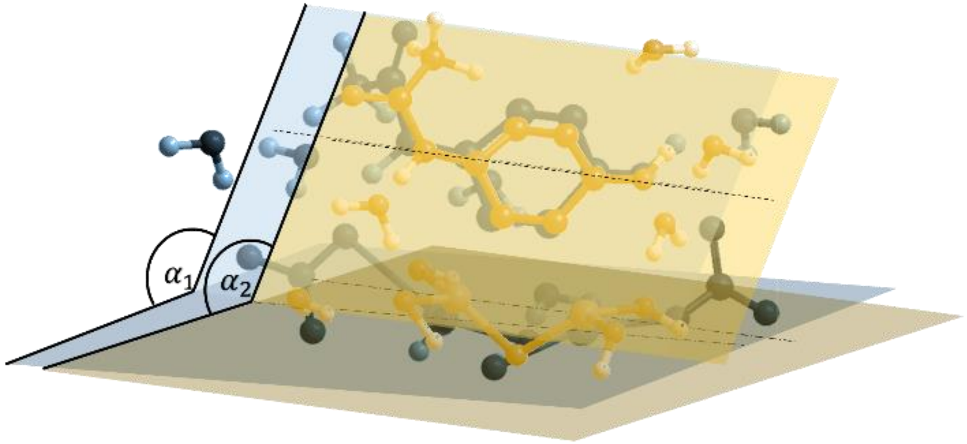
HO-BiONO$_3$ trimer

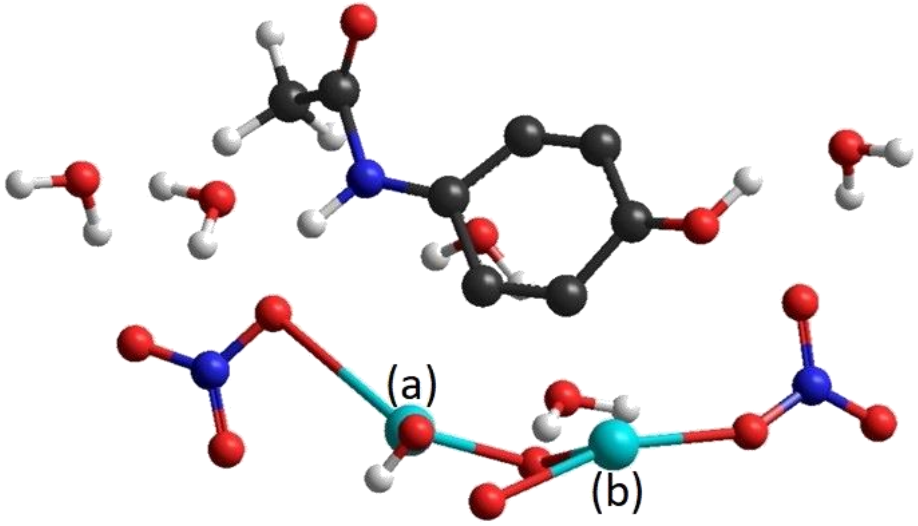


4.Computational studies

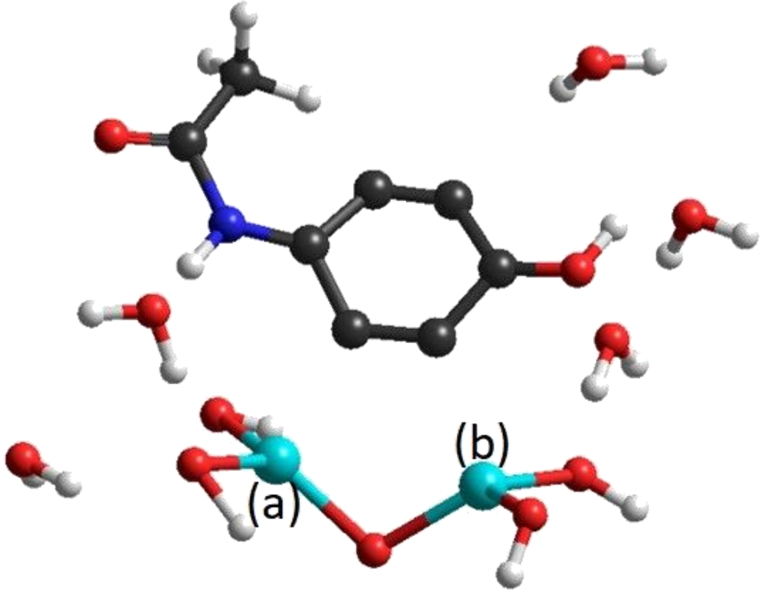
- We firstly evaluated **symmetric dimers** with two nitric or hydroxylic groups

- We added a several molecules of water. Here are reported the studies realized by using 5 water molecules.





$NO_3 - NO_3$
$k = 1.2 \cdot 10^{-3}\ s^{-1}$



$OH - OH$
$k = 2.6 \cdot 10^{-3}\ s^{-1}$

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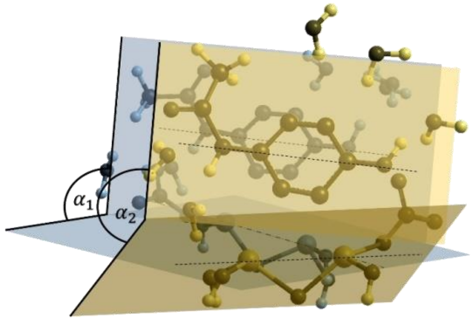
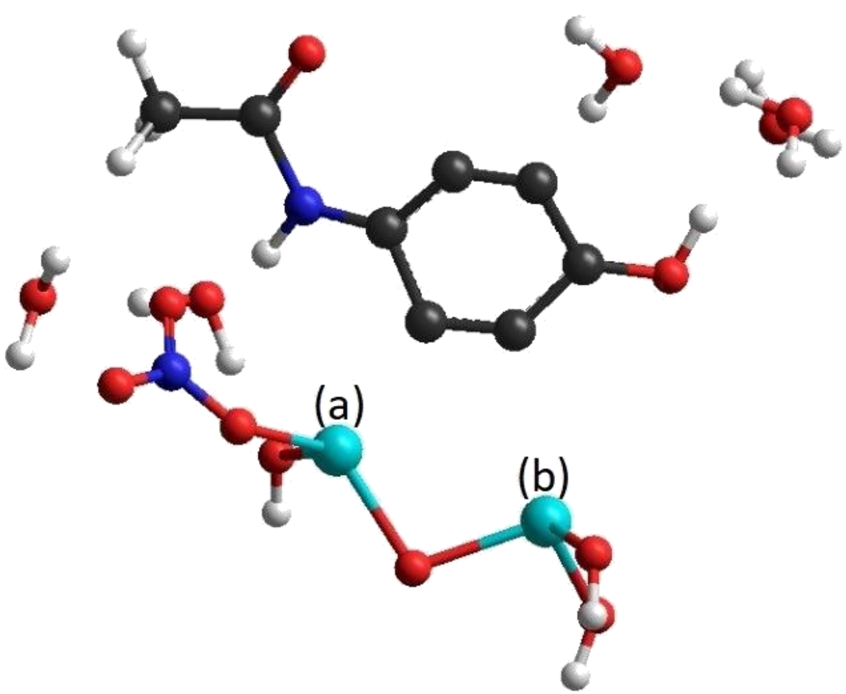
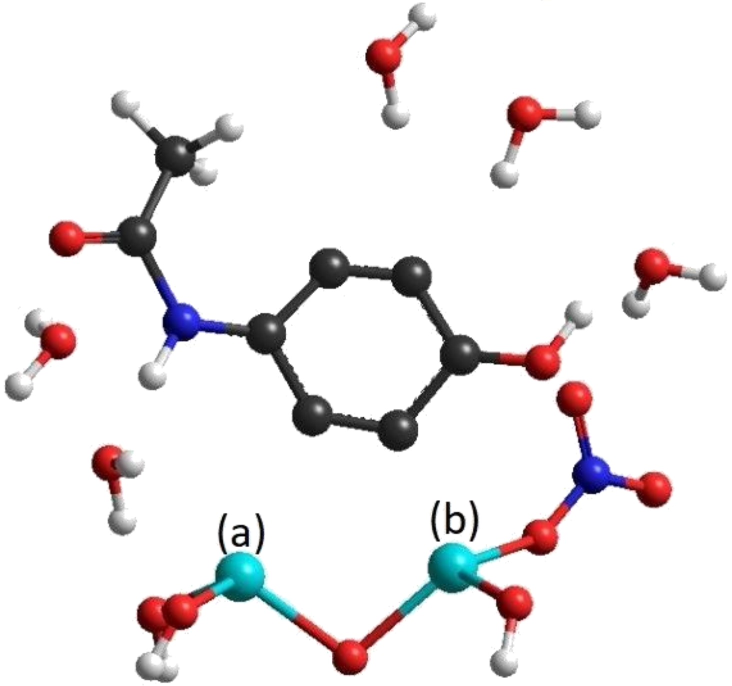
4.Computational studies

- The asymmetric dimer showed a higher k
- Misalignment of paracetamol and Bi-Bi plane.



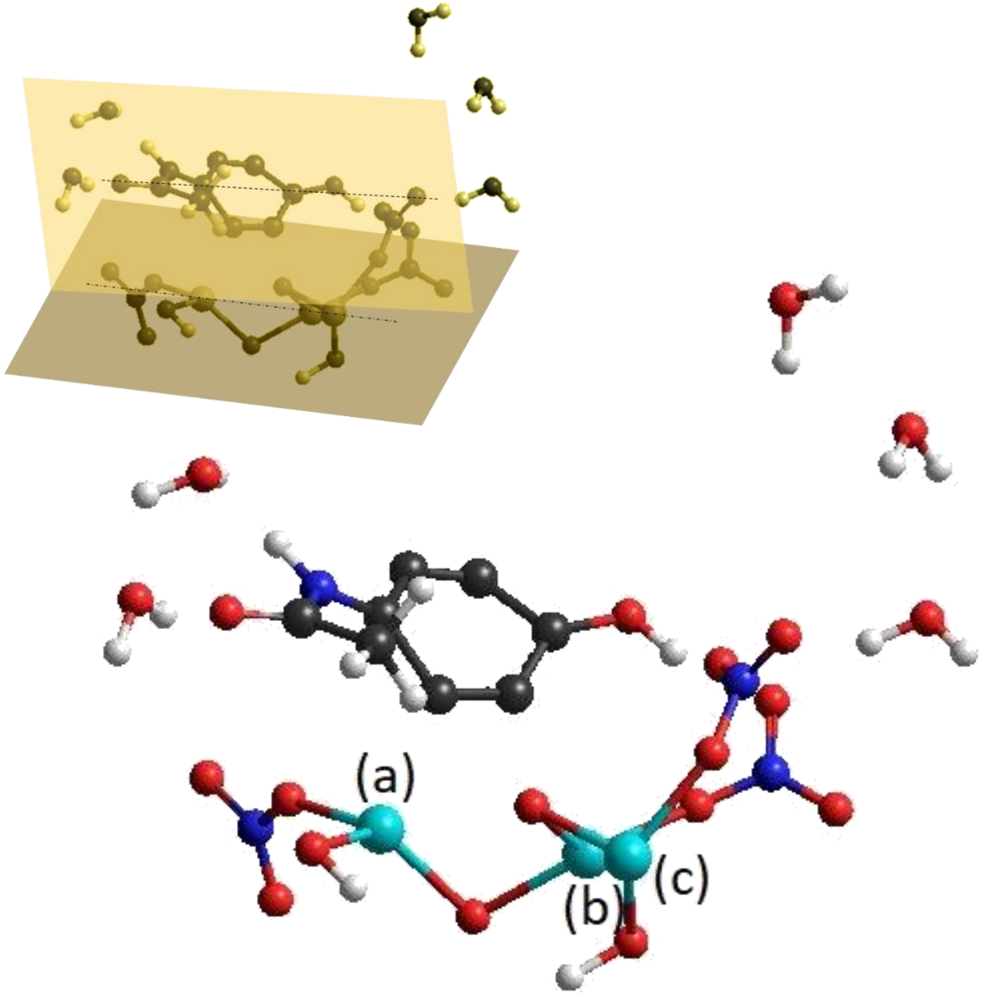


$NO_3 - OH$
$k = 2.78 \cdot 10^{-2}\ s^{-1}$

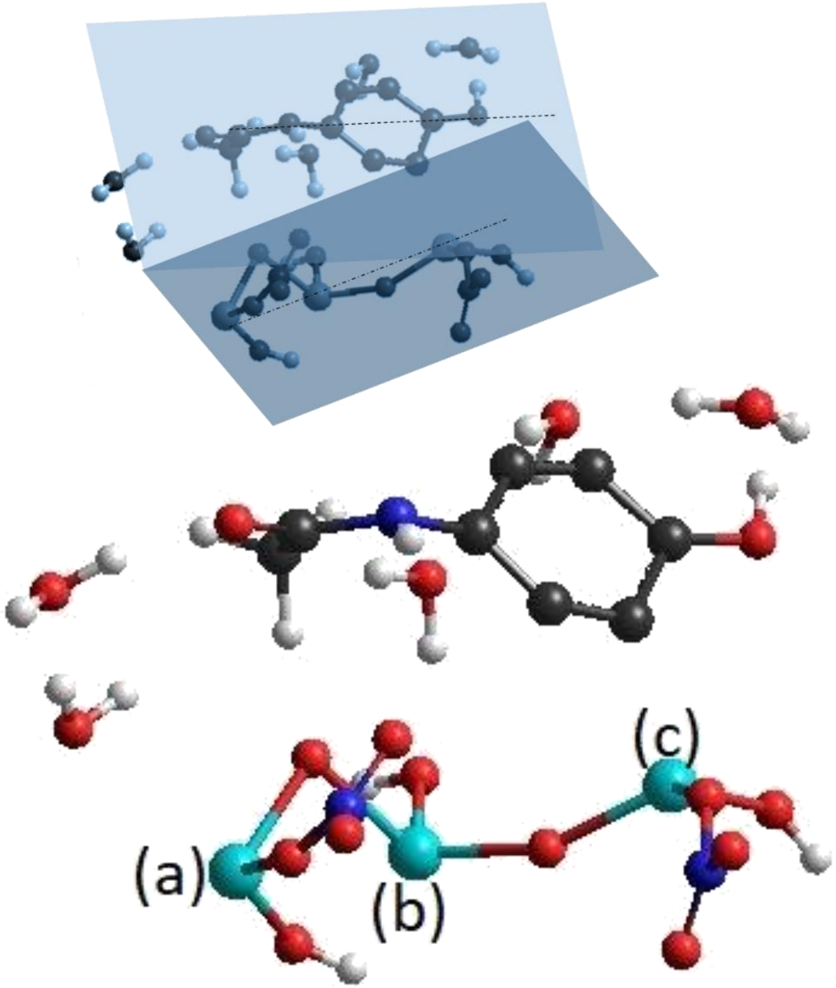


$OH - NO_3$
$k = 6.9 \cdot 10^{-3}\ s^{-1}$

4.Computational studies



$NO_3 - NO_3 - NO_3$
$k = 7.08 \cdot 10^{-5} s^{-1}$

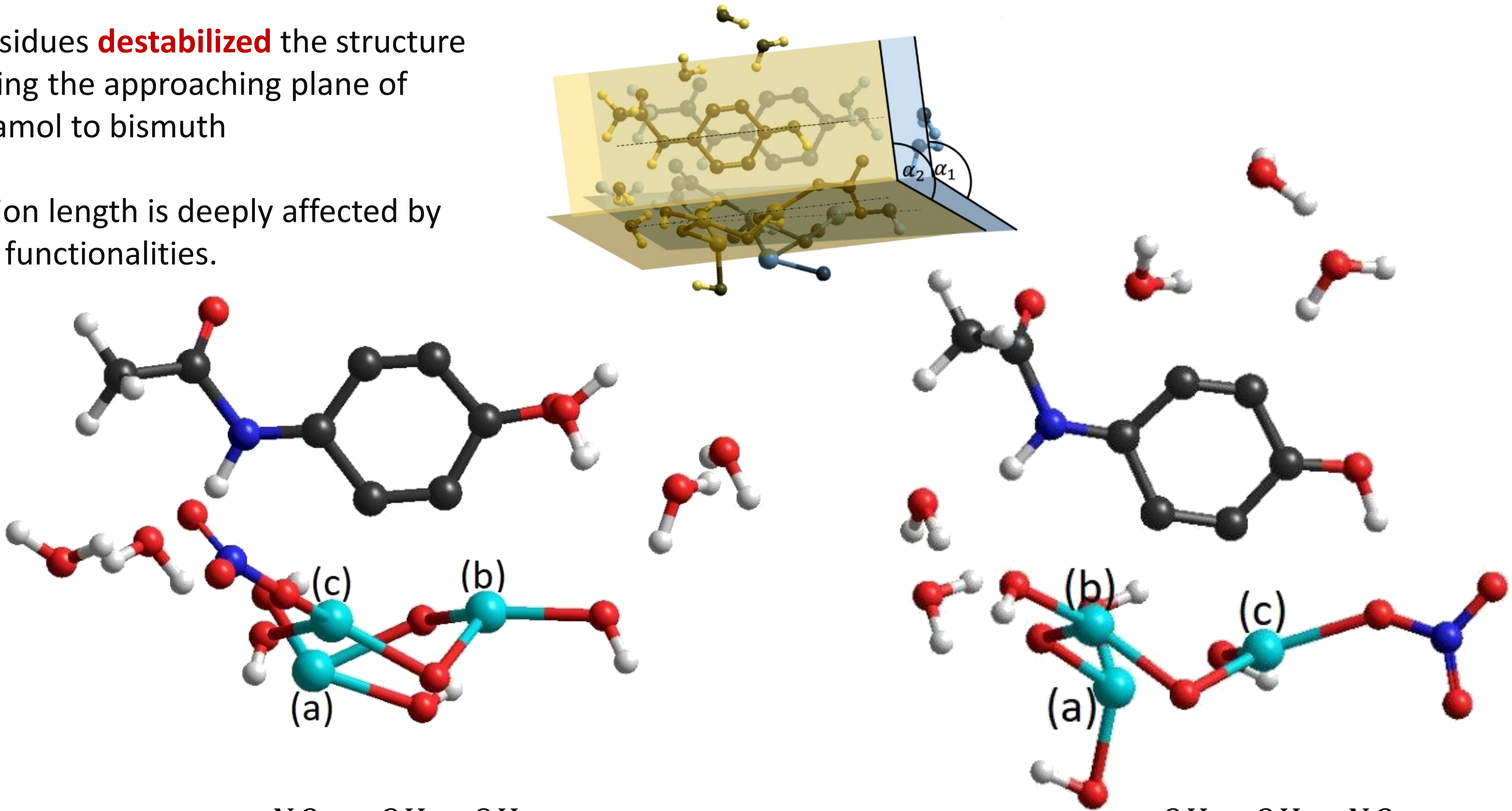


$NO_3 - OH - NO_3$
$k = 5.86 \cdot 10^{-2} s^{-1}$

4.Computational studies

- Nitric residues **destabilized** the structure by twisting the approaching plane of paracetamol to bismuth

- Interaction length is deeply affected by residual functionalities.



$NO_3 - OH - OH$
$k = 8.46 \cdot 10^{-2} s^{-1}$

$OH - OH - NO_3$
$k = 8.3 \cdot 10^{-2} s^{-1}$

4.Computational studies

- Computed k suggest that the area rich in hydroxylic functions are responsible for the electrochemical sensing according to experimental data
- Activation energy trend is not linear and is affected by both geometrical and chemical parameters

Dimer	$k[s^{-1}]$	**Activation energy** $[eV]$
NO_3-NO_3	$1.2 \cdot 10^{-3}$	9.3
OH-OH	$2.6 \cdot 10^{-3}$	10.89
OH-NO_3	$6.9 \cdot 10^{-3}$	7.74
NO_3-OH	$2.78 \cdot 10^{-2}$	7.46
Trimer	$k[s^{-1}]$	**Activation energy** $[\mathrm{eV}]$
NO_3-NO_3-NO_3	$7.08 \cdot 10^{-5}$	7.34
NO_3-OH-NO_3	$5.9 \cdot 10^{-2}$	5.75
NO_3-OH-OH	$8.46 \cdot 10^{-2}$	9.16
OH-OH-NO_3	$8.3 \cdot 10^{-2}$	9.87

5. Conclusions

- Sinthesis of different subnitrate specie by using an in solution approach
- Tailoring of bare SPCE with bismuth subnitrate species
- Observed an improvement in paracetamol detection by using tailored electrode
- Modelling the electron transfer process

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