

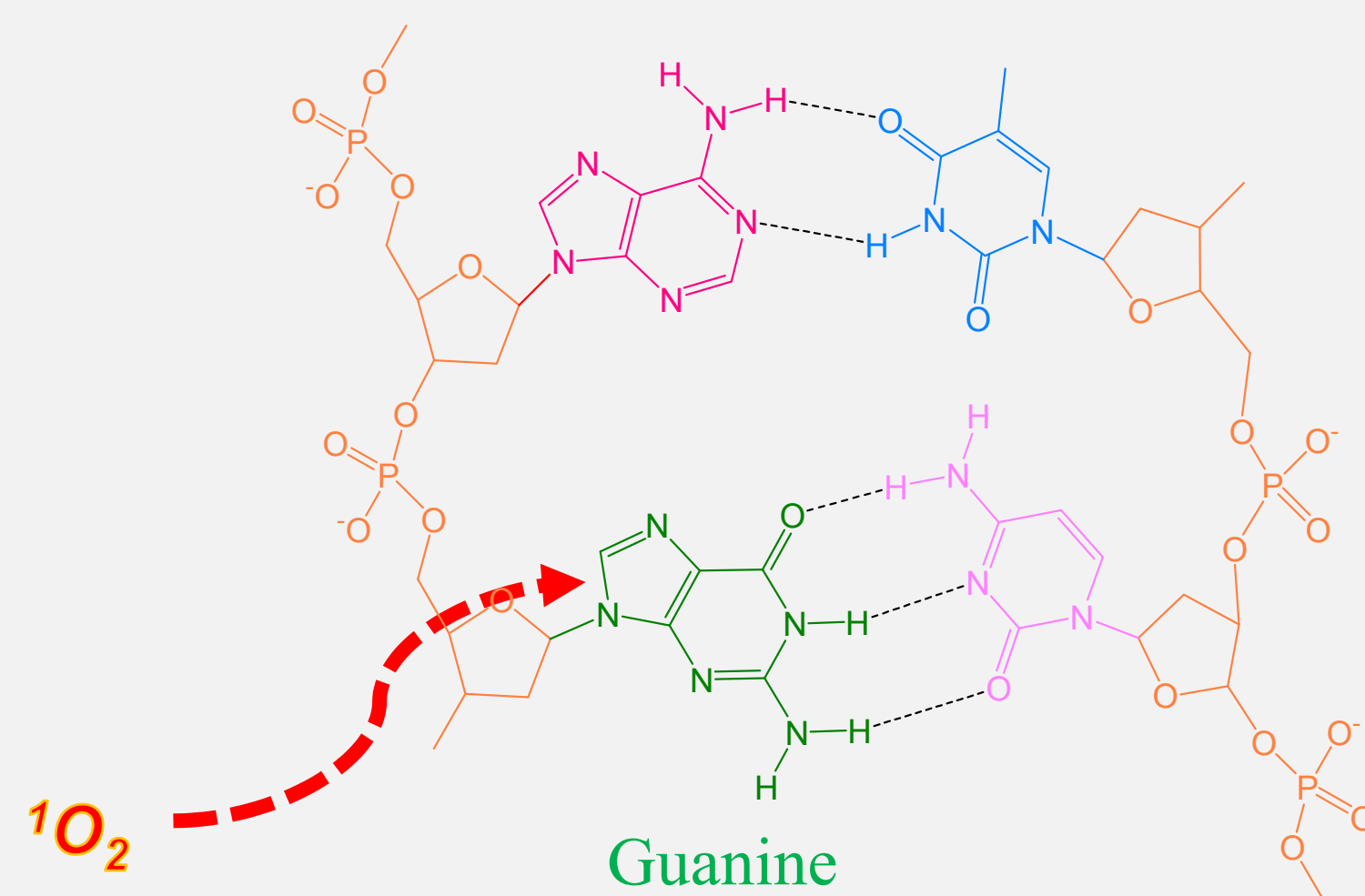
Oxidation Dynamics of 8-Oxoguanine by Singlet O₂ Using Guided-Ion Beam Scattering and Density Functional Theory

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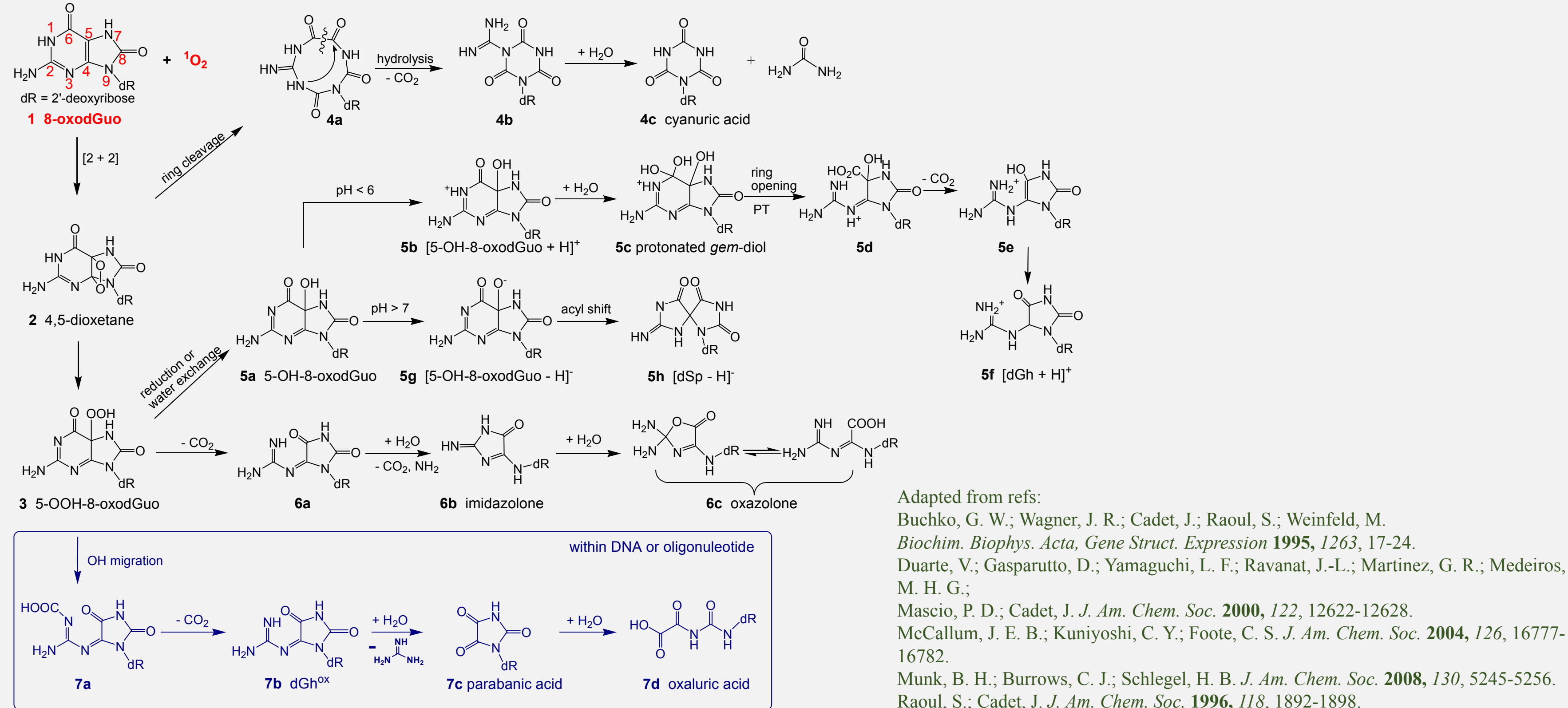


Introduction

- Singlet oxygen (¹O₂): one of the most common reactive oxygen species in live organisms, and causes mutation and cell death.
- Guanine: the exclusive DNA target toward ¹O₂ oxidation.
- 8-Oxoguanine: more reactive toward ¹O₂ than the undamaged guanine.

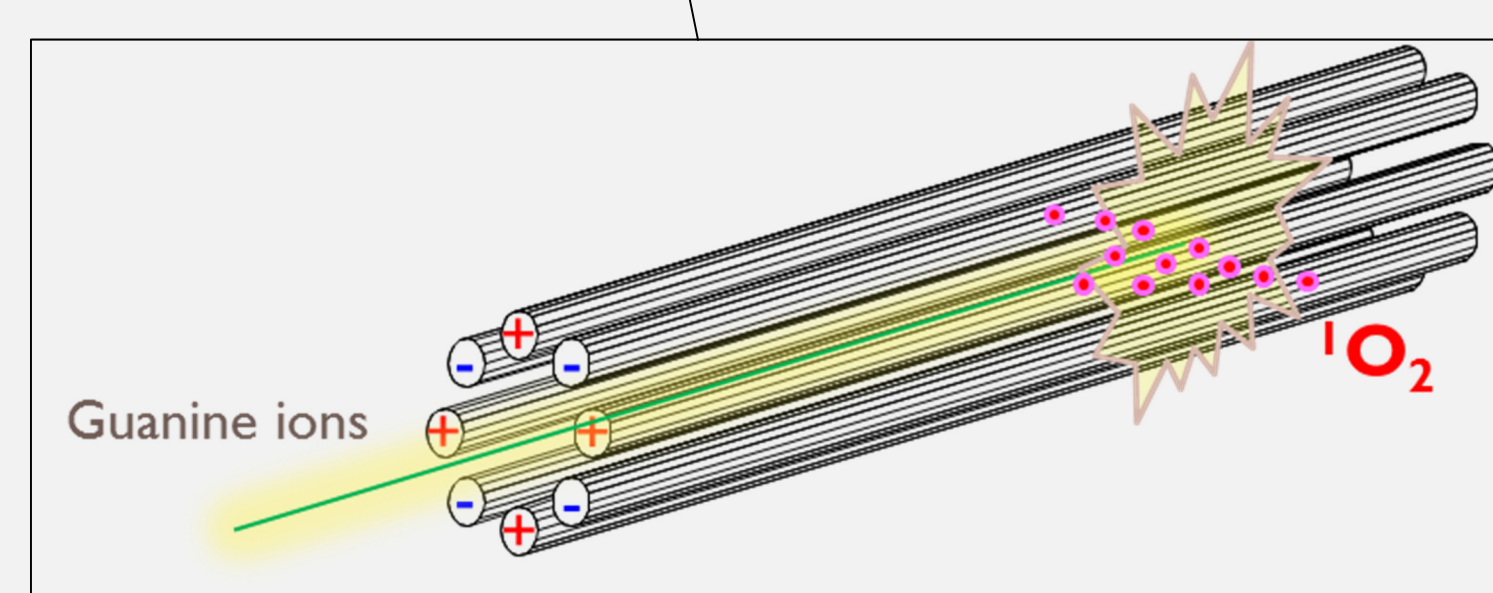
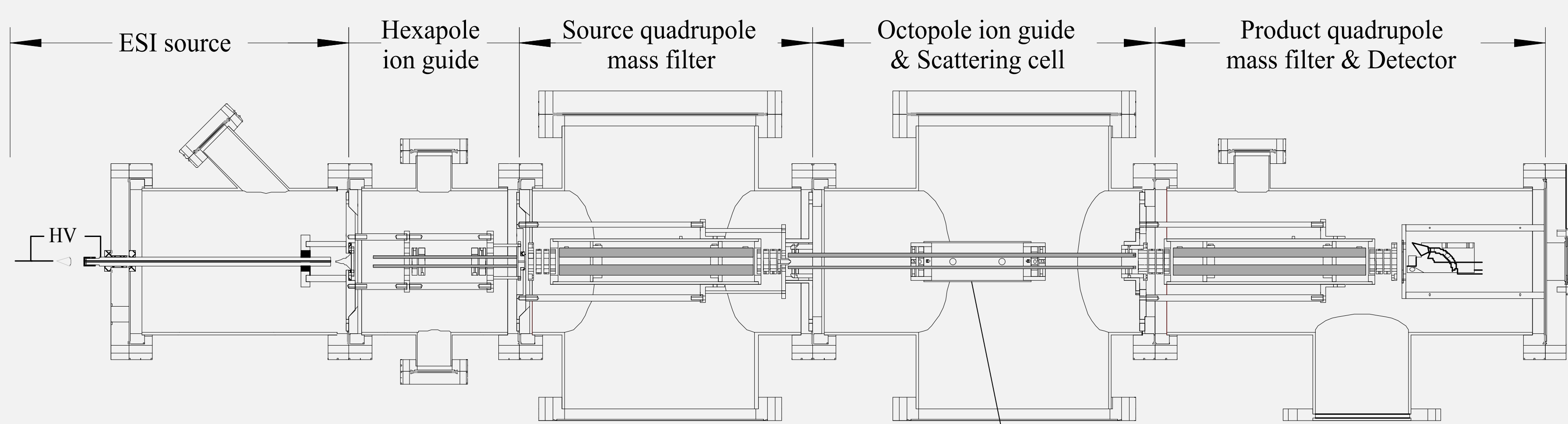


- Literature proposed mechanisms of ¹O₂-induced oxidation of 8-oxodGuo:



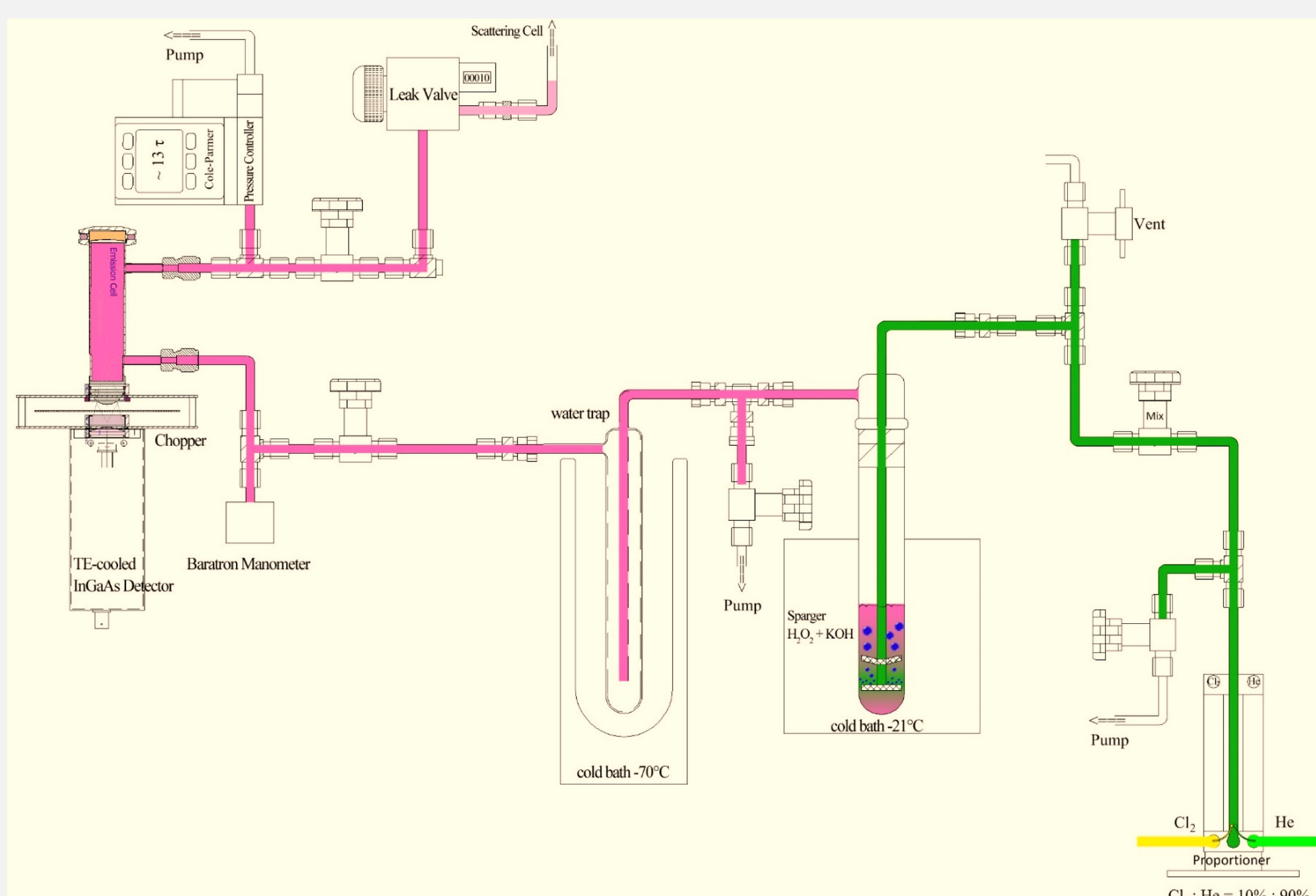
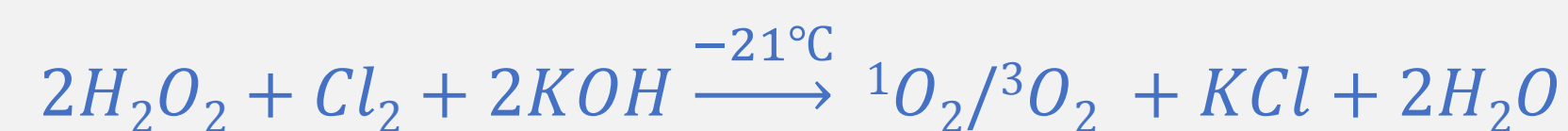
Instrumentation and Methodology

- Guided-ion-beam tandem mass spectrometer [Y. Fang and J. Liu, *J. Phys. Chem. A.* 2009, 113, 11250-11261.]

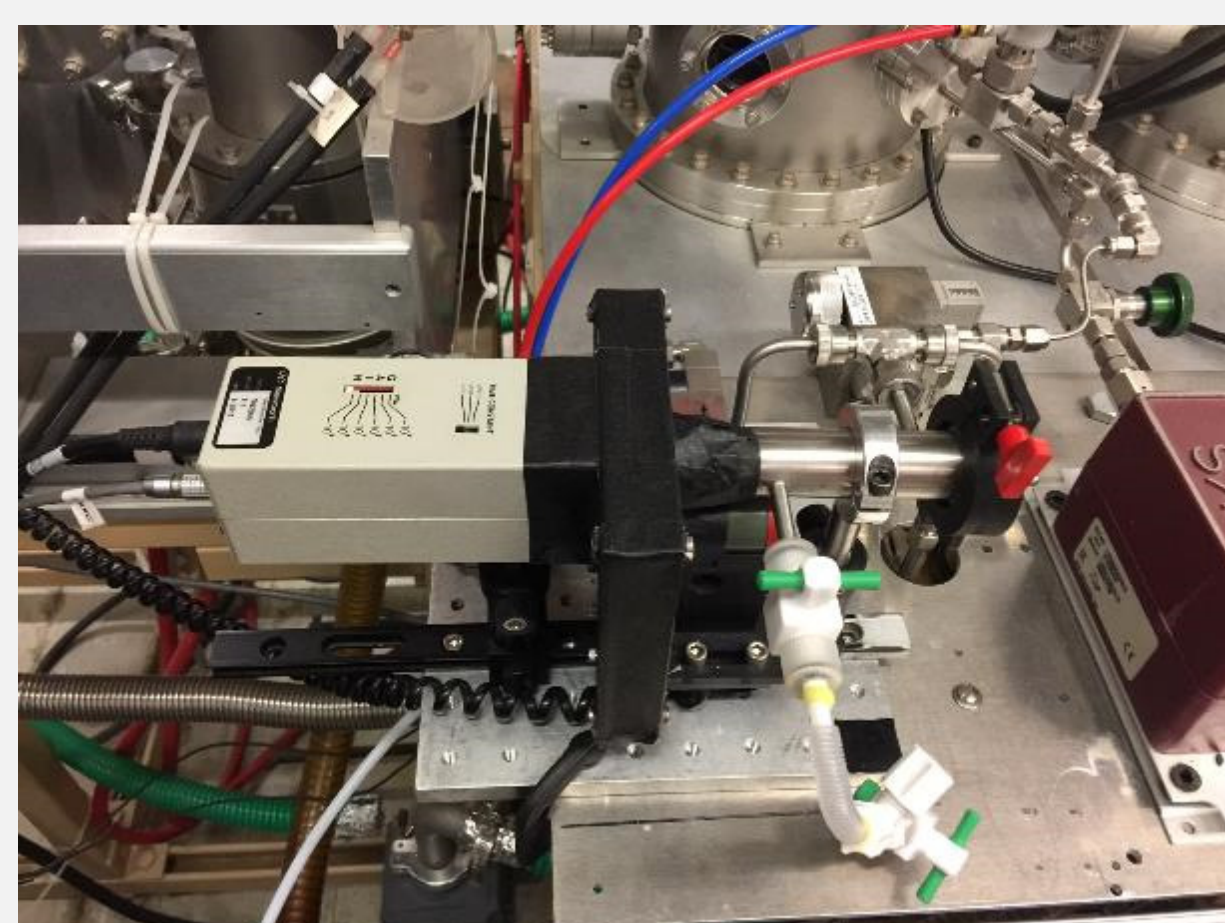
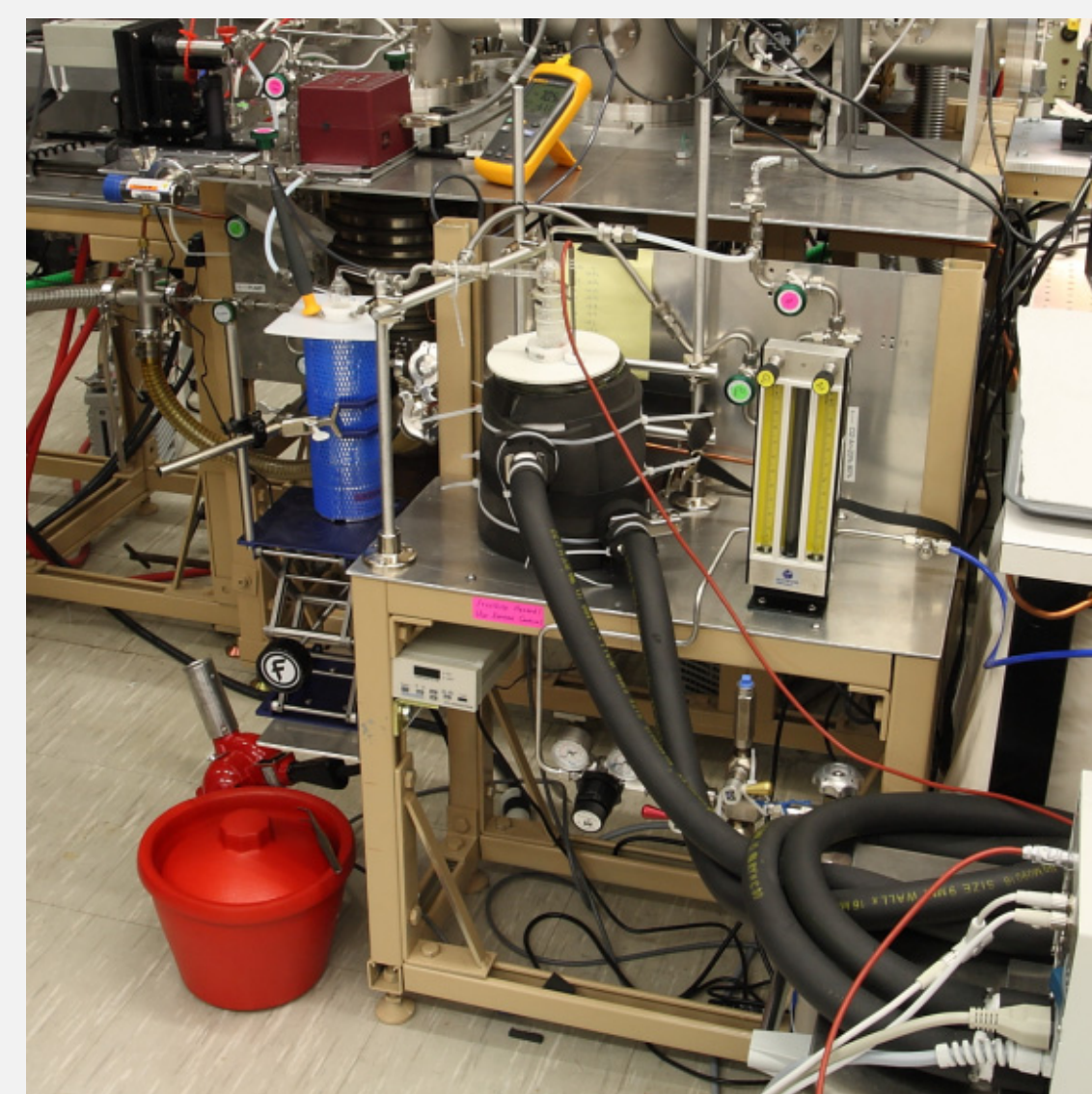
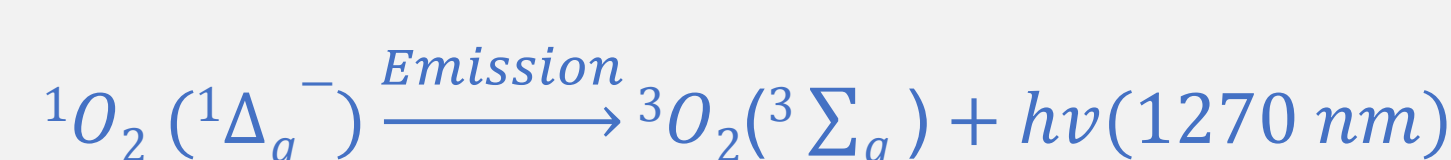


- ¹O₂ Generation and detection [Y. Fang, F. Liu, A. D. Bennett, S. Ara, and J. Liu, *J. Phys. Chem. B.* 2011, 115, 2671-2682.]

- Chemical ¹O₂ generator



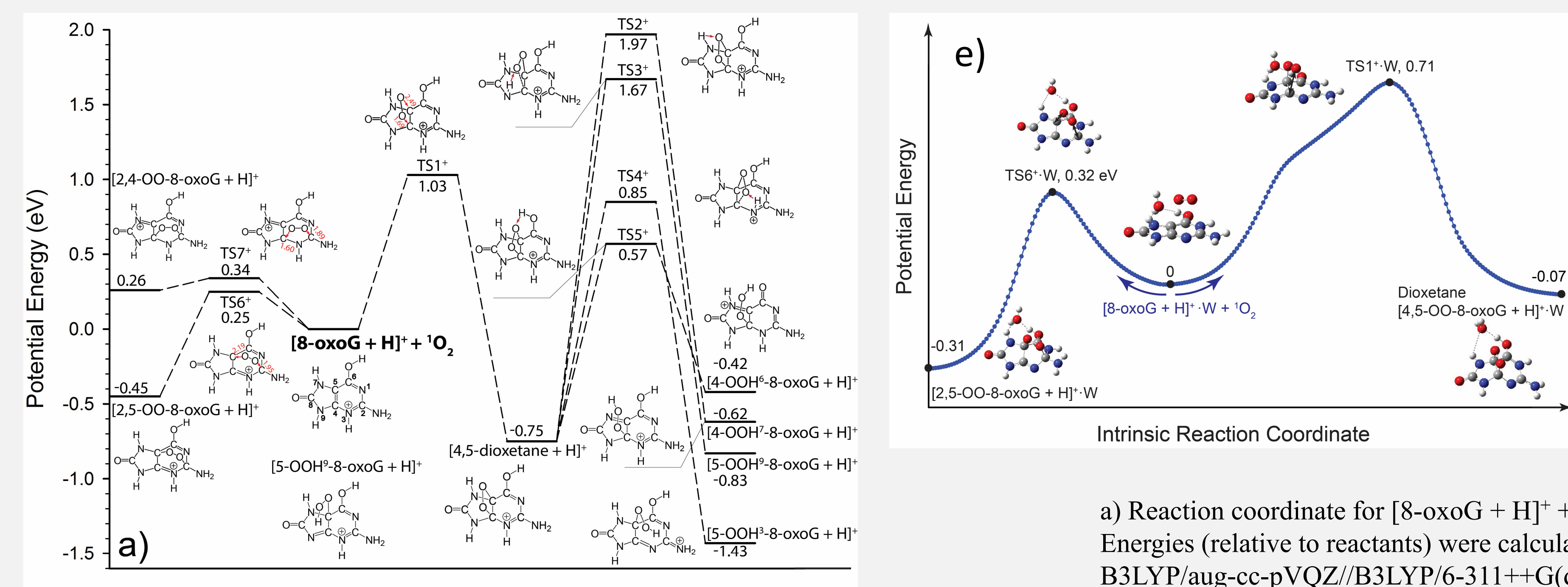
- Determination of ¹O₂ concentration



Results

[Y. Sun, W. Lu and J. Liu, *J. Phys. Chem. B.* 2017, 121, 956-966.]

- Reaction PESs of protonated [8-oxoG + H]⁺ with ¹O₂



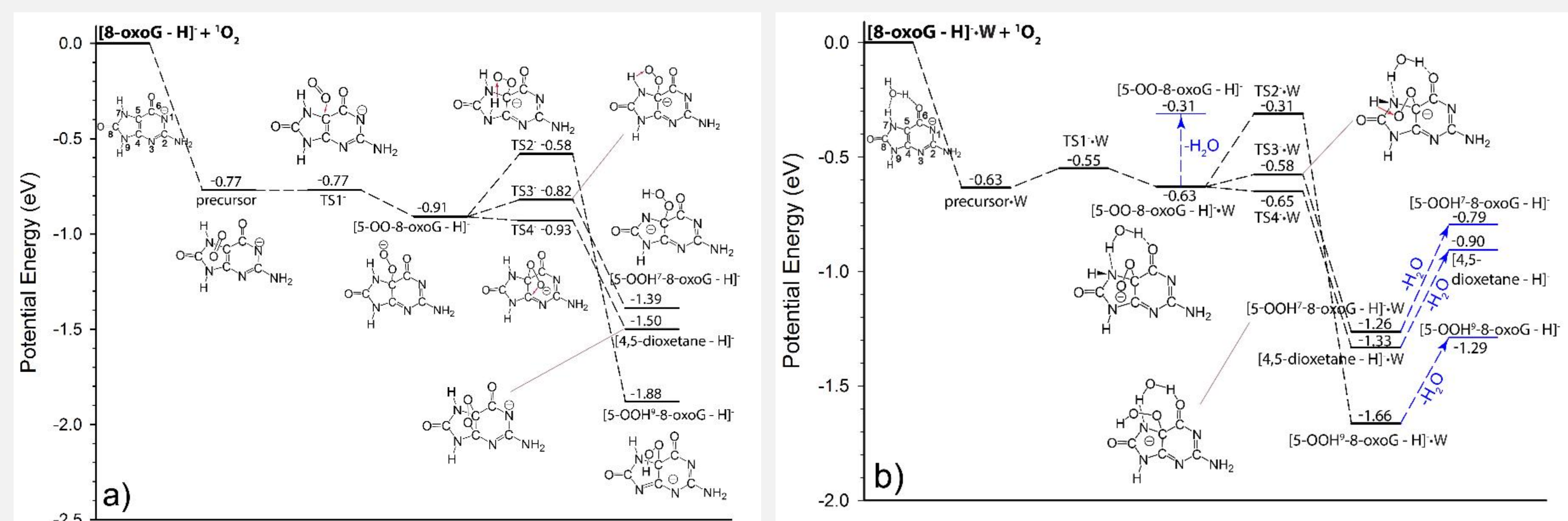
a) Reaction coordinate for [8-oxoG + H]⁺ + ¹O₂. Energies (relative to reactants) were calculated at B3LYP/aug-cc-pVQZ//B3LYP/6-311++G(d,p), including thermal corrections at 298 K.

b – d) 2D-PESs for the addition of ¹O₂ to the C4 – C5, C2 – C5 and C2 – C4 positions of [8-oxoG + H]⁺, respectively. Numbers in the contour maps are potential energies calculated at B3LYP/6-311++G(d,p). Colored lines represent IRC trajectories.

e) IRC trajectory for hydrated [8-oxoG + H]⁺-W with ¹O₂. Compared to dehydrated [8-oxoG + H]⁺, the activation barrier for 4,5-addition to [8-oxoG + H]⁺-W decreases by 0.32 eV whereas that for 2,5-addition increases by 0.07 eV.

Experimental Findings: No product was observed for the reaction of [8-oxoG + H]⁺·(H₂O)_{0,1} + ¹O₂ because insurmountable barriers block the addition of ¹O₂ to reactant ions.

- Reaction of deprotonated [8-oxoG – H]⁻ with ¹O₂



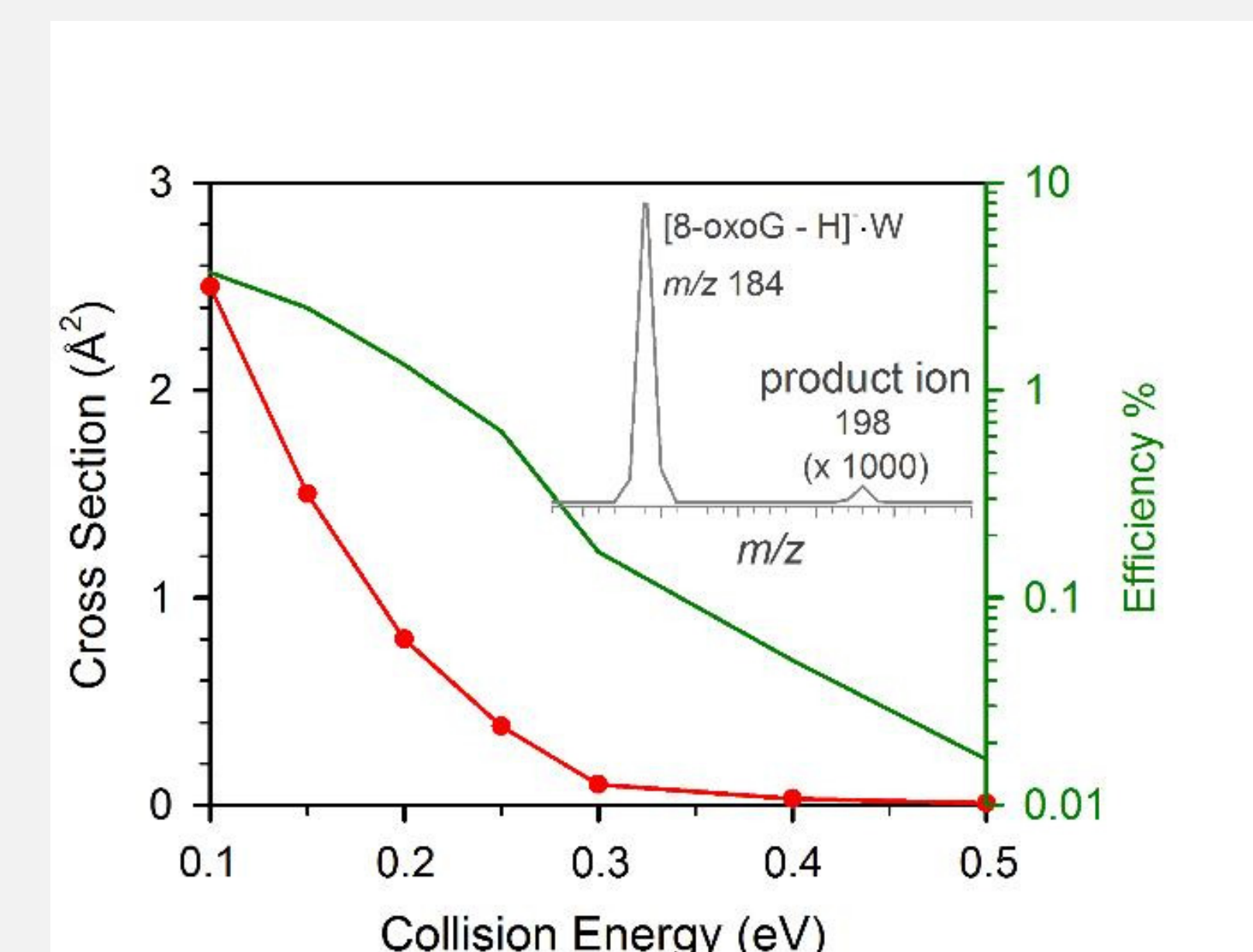
Experimental Findings: Neither is [8-oxoG – H]⁻ reactive with ¹O₂, in this case due to the rapid decay of transient intermediates to starting reactants.

However, the nonreactivity of [8-oxoG – H]⁻ toward ¹O₂ is inverted by hydration of the reactant ions; as a result, 4,5-dioxetane of [8-oxoG – H]⁻ was captured as the main oxidation product.

Reaction cross section (σ_{reaction}) for [8-oxoG – H]⁻·W + ¹O₂ over the E_{col} range of 0.1 to 0.5 eV, along with the reaction efficiency.

σ_{reaction} increases with decreasing E_{col} , indicating that this reaction is exothermic and there is no activation barrier above reactants.

The oxidation reaction enthalpy is larger than the water dissociation energy (between 0.32 and 0.47 eV) which makes it possible to kick out a H₂O ligand.



- Similarities & differences between protonated vs. deprotonated system

The oxidation of [8-oxoG + H]⁺ begins by concerted cycloaddition of ¹O₂, but all pathways are blocked by high activation barriers. On the contrary, synchronous addition does not occur to [8-oxoG – H]⁻. The latter involves a low-energy, stepwise addition starting with formation of a 5-terminal peroxide, followed by evolving into a 4,5-dioxetane and a 5-hydroperoxide.

Compared to the dehydrated systems, hydration not only changes the stabilities of protonated 8-oxoG conformations, but “cools down” the energized oxidation intermediates of deprotonated 8-oxoG, suppressing their otherwise complete decomposition back to reactants.

Acknowledgement



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