I. Guanine oxidation mechanism and the questions we want to address

Guanine nucleus is the exclusive DNA target for $^{18}$O$_2$.

- Genomic mutation
- DNA-protein cross-linking
- Lethality

The only evidence was from photooxidation of an 8-methyl substituted guanosine compound at 78°C.

Capture transient oxidation intermediate in the gas phase using hydrated guanine ions as a target for $^{18}$O$_2$.

How we run reactions

1. Generation of guanine ions by ESI
2. Ions are passed into a quadrupole for mass selection
3. Mass-selected ions are guided into an orifice (surrounded by a collision cell) and scattered from $^{18}$O$_2$ contained within: Generation of $^{18}$O$_2$ $^{18}$O$_2$ intensity was determined by its emission before leaking into scattering cell


II. Intra-pair proton transfer and non-statistical kinetics of deprotonated [Guanine-Cytosine – H$^+$] pair

- Deprotonation of base pairs is one consequence of ionizing radiation interacting with cells, occurring after dissociative electron attachment.
- Deprotonation of a nucleobase prompts intra-pair proton transfer $\Rightarrow$ Shift of actual deprotonation site & Structural perturbation

F 1. PT equilibrium constants ($K_{PT}$), ratio of dissociation rate constants ($k_d/k_p$), and RRKM vs. Exp product branching

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<th>$K_{PT}$</th>
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Origin for non-statistical base-pair dissociation (7)

1) TS re-crossing for intra-pair PT was observed in trajectories
TS geometries are twisted that bring about a dynamic bottleneck along the constrained configuration.

2) Location of a critical configuration that separates base pair and dissociation products
Base pair dissociation has no reverse barrier and the location of the dividing surface depends on energy.
We are trying a rigorous way to locate the critical configuration in reaction.

3) RRKM assumes that IVR renders the distribution of energy a random one. But CID may produce short time non-statistical fragmentation.

On-going Work
Trajectories are being propagated starting from both activated G[C–H$^+$] and its proton-transferred tautomer, and at the proton-transfer activation barrier.

W. Lu and J. Liu, PCCP, 2016, 18, 32222.

Q2 Concerted [4+2] cycloaddition across 4,8-bond OR stepwise addition initialized by 8-peroxide?

Q3 An endo-thermic activation barrier for oxidation?

E. $^{18}$O$_2$ oxidation of guanine nucleoside (A model study)

Oxidation of protonated [9MG + H$^+$] is similar to free guanine: reaction is mediated by a [4 + 2] cycloaddition leading to formation of 5,8-endoperoxide.

Oxidation of deprotonated [9MG – H$^+$] is different and proceeds stepwise, starting with a terminal peroxide that subsequently evolves to a 4,8-endoperoxide.

2D-PES calculated at CASSCF(10,8)/6-31+G*$^*$

Implications for oxidation of guanosine
Acidic and basic media may lead to different oxidation chemistries of guanosine, starting from initial stage.

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