

Attack of OH radical to the OH- and S-containing amino acids

Jon M. Matxain, Jon Uranga and Jon I. Mujika

Kimika Fakultatea, Euskal Herriko Unibertsitatea (UPV/EHU), and Donostia International Physics Center (DIPC)

P.K. 1072, 20080 Donostia (Basque Country)

electronic address: jonmattin.matxain@ehu.es

Introduction

Radical Reactive Oxygen Species (ROS) are one of the cause of oxidative stress. Among others, they attack proteins, causing protein damage:

OH attack in proteins:

- to the aminoacid side chains
- to the peptide backbone.

Reactivity:

- electron transfer
- Hydrogen abstraction
- Addition

We have focused on the subsequent attack of two OH radicals towards:

- OH-containing amino acid side chains (Serine and threonine).
- S-containing amino acid side chains (Cysteine and methionine).

First radical attack: H abstraction or electron transfer (Cys and Met)

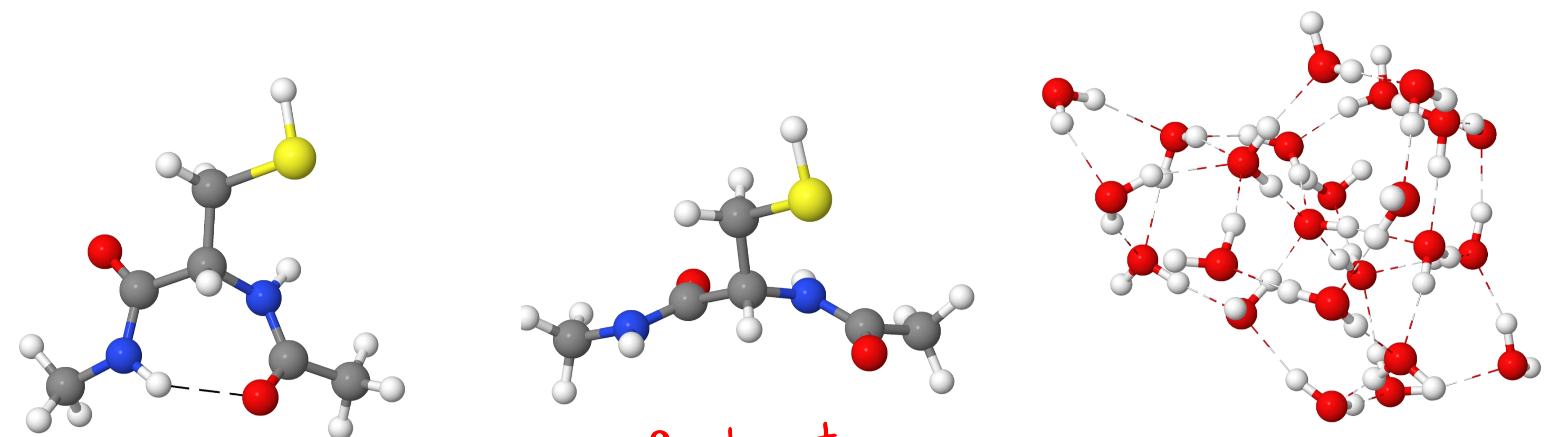
Second radical attack: H abstraction or OH addition.

solvent effects considered to simulate different environments:

- $\epsilon=4$ for inner aminoacids (far from water)
- $\epsilon=78$ for outter aminoacids (close to water)

Peptide Moldels

- Tripeptide (AA1-AA2-AA3). AA2 complete, AA1, AA3 cut at C α .
- For backbone: two types of folding: α -helix and β -sheet.



α helix

β -sheet

e^- transfer

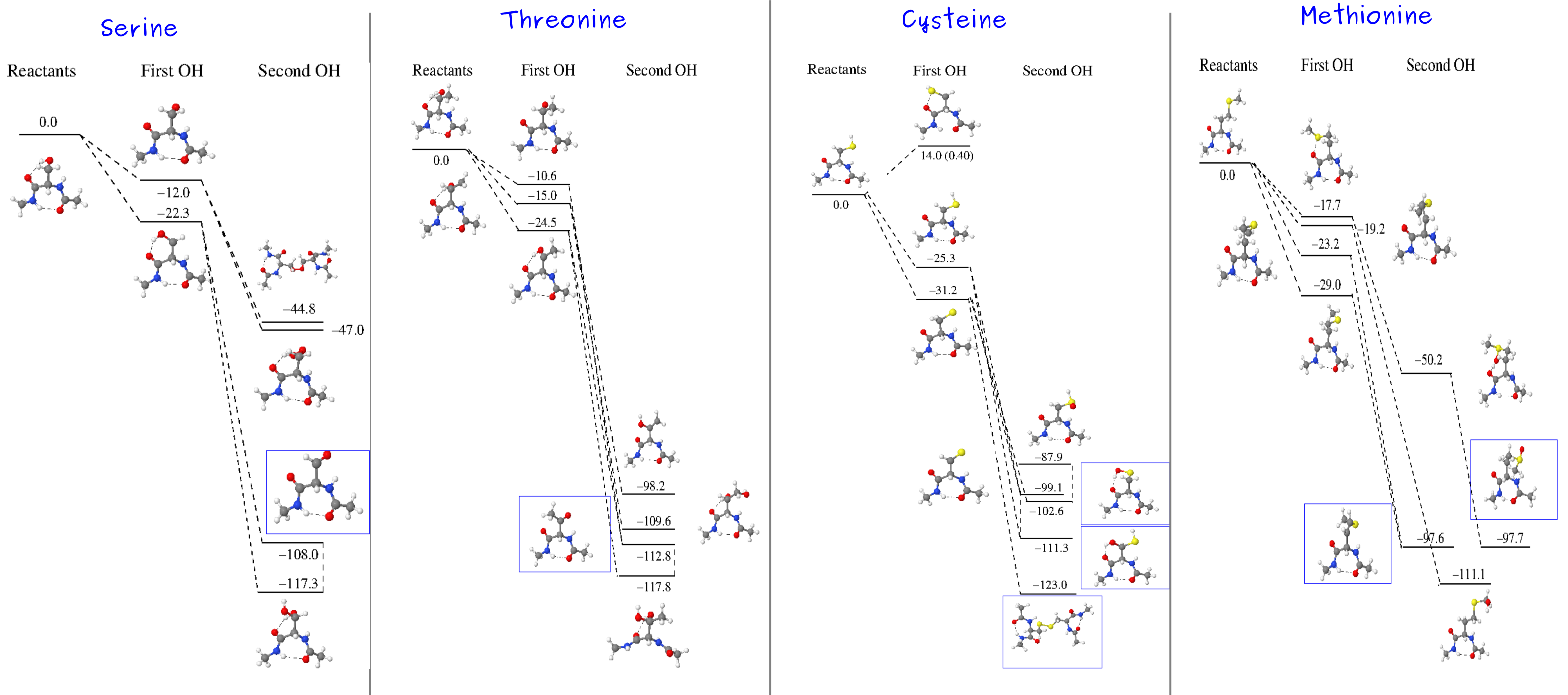
$E_{exp}^0 = 1.9$ V; $E_{theo}^0 = 1.8$ V

Methods

- Optimization and Frequencies in gas phase: MPWB1K/6-31+G(d,p).
- Single points at $\epsilon=4$ and $\epsilon=80$: MPWB1K/6-311+G(2df,p).
- $H_{sol}^{2,48} = E_{sol} + H(cont)_{gas}^{2,48}$. IRC for Transition States.

Blue lines: The most probabla reaction pathways.

Blue boxes: Main experimental products



- 2 \bullet OH attack mechanisms: H abstraction and addition.
- First \bullet OH: H abstraction from C β favored.
- Second \bullet OH: addition to C β favored: Hydration of ketones.
- Prediction of new products.

- 3 \bullet OH attack mechanisms: H abstraction, e^- transfer, addition.
- First \bullet OH: H abstraction (C γ in Met, S γ in Cys) favored.
- e^- transfer: in Met depending on the stability of \bullet S.
- Second \bullet OH: H abstraction (Met) and addition (S-S Cys) possible. Prediction of new products.

Acknowledgements

Research unded by Eusko Jaurlaritza (the Basque Government) and the Spanish Ministerio de Economia y Competitividad. The SGI/IZO-SGIker UPV/EHU (supported by Fondo Social Europeo and MCyT) is gratefully acknowledged for generous allocation of computational resources.



eman ta zabal zazu



Universidad
del País Vasco

Euskal Herriko
Unibertsitatea