Protein backbone degradation via ·OH mediated oxidation

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Introduction

1) Reactive species e.g. ROS (·OH,·OOH,H_2O_2, etc.)

2) **Reactive species** perform essential tasks in an organism e.g. apoptosis. A careful **balance** is needed in their **concentration**.

3) **Oxidative stress** is the **excessive** production of reactive species.

4) Reactive species react with macromolecules, **proteins** are one of the main target , **oxidizing** them.

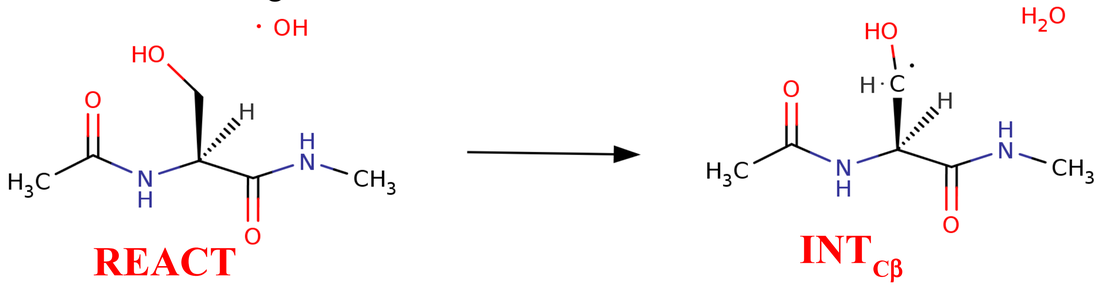
Scope of the work

- Study of the H abstraction reaction and backbone fragmentation on ALL natural amino acids.

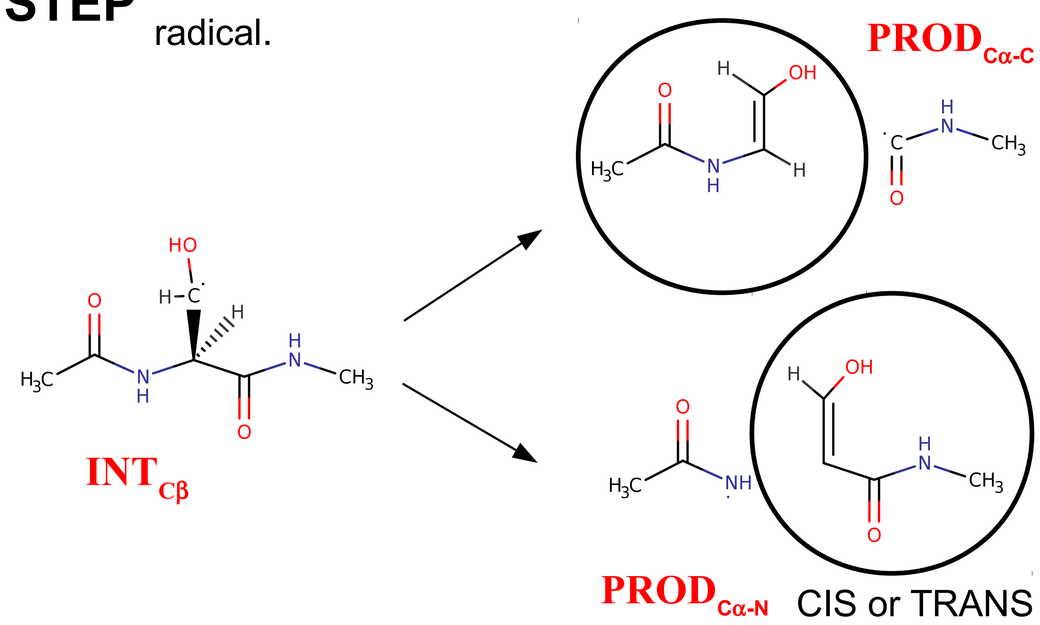
Methodology

1st STEP ·**OH attack** to the H in α ($INT_{Cα}$) and β ($INT_{Cβ}$) carbon of the amino acids.

Yielding one water molecule and a radical amino acid.

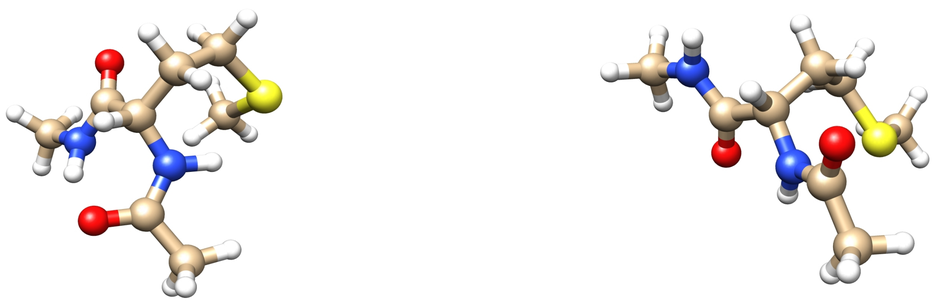


2nd STEP Protein **backbone degradation** starting from amino acid radical.



- Two amide bonds and one side chain.

- For backbone: two types of folding: α helix and β sheet.



α helix (Met)

β sheet (Met)

- Optimization and Frequencies in gas phase: MPWB1K/6-31+G(d,p).

- Single points at ε=4 and ε=78: MPWB1K/6-311++G(2df,p).

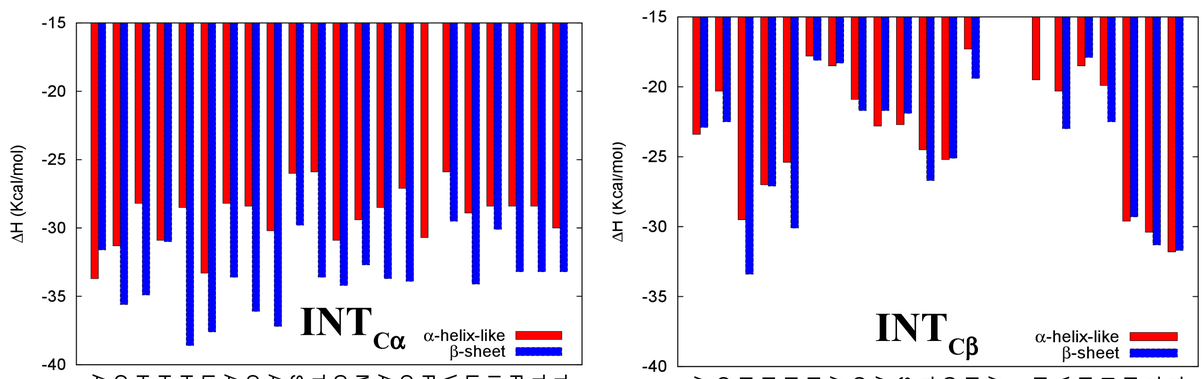
- $H_{sol} = E_{sol} + H^{corr}_{sol}$ $\quad \Delta H_{sol} = H^{i}_{sol} - H^{reactants}_{sol}$

- i = Int, Prod

- Thermodynamics is studied.

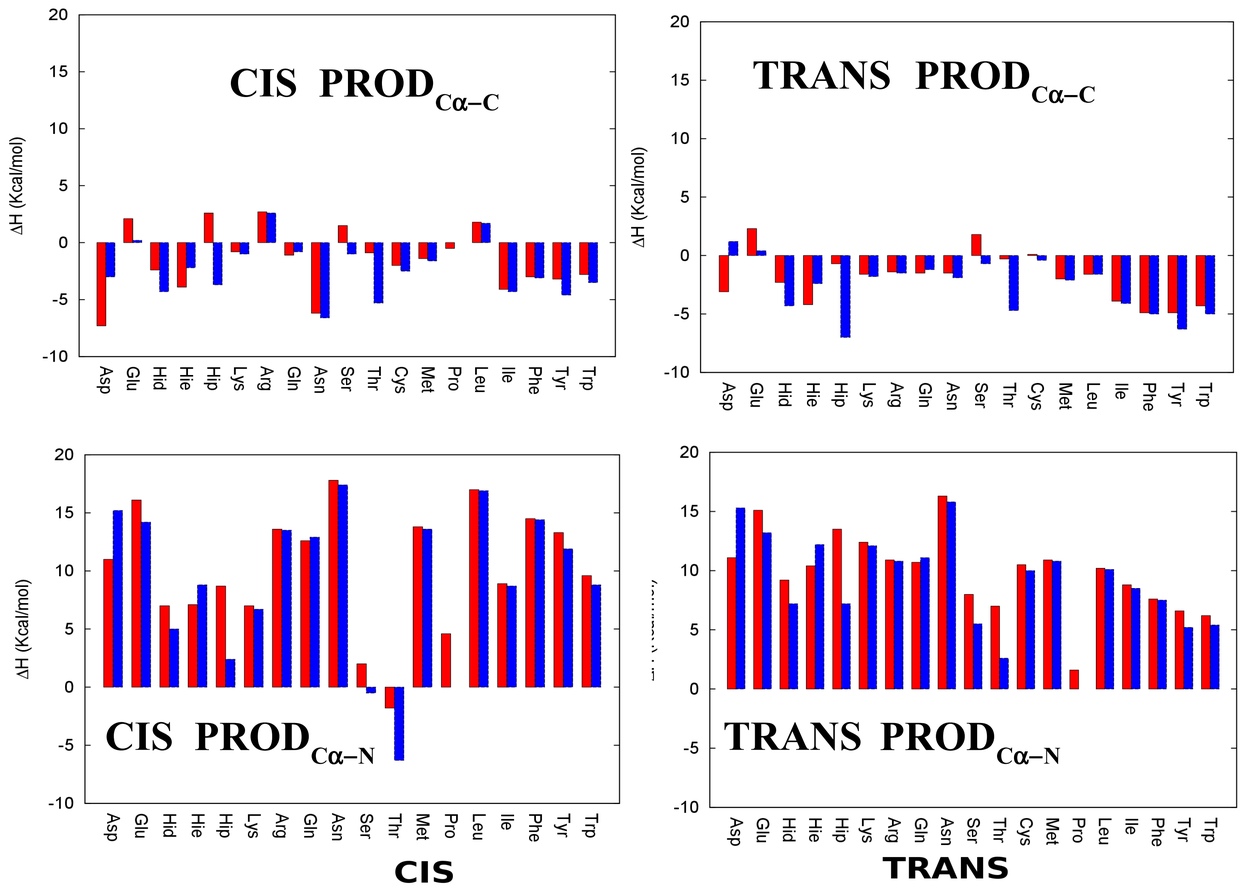
Results

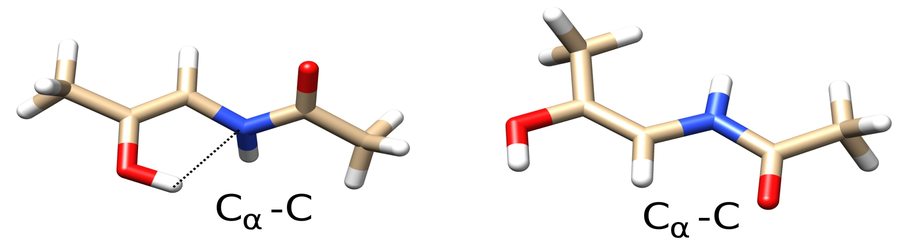
1st STEP



2nd STEP

– β abstractions followed by a backbone splitting.





Conclusions

1) Dielectric and conformation have little effect.

2) $\mathbf{C_\alpha}$ amino aci radicals more stable than $\mathbf{C_\beta}$. But they show backbone bond strengthening.

3) $\mathbf{Prod_{Cα-N}}$ backbone breaking is exothermic for **Ser and Thr**. While for the rest of amino acids $\mathbf{Prod_{Cα-C}}$ is exothermic.

4) Stabilisation of the **non-radical** product is a **key** aspect.

Acknowledgements

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