# Study of the attack of OH radical to the protein backbone

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## Introduction

OH attack in proteins:

a) to the aminoacid side chains

b) to the peptide backbone.

Products:

a) Addition

b) Hydrogen abstraction

Phenylalanine as example:

a) Backbone: abstraction: from N or from $C_\alpha$.

b) Aminoacid side chain:

- Abstraction from: phenyl ring (ortho, meta, para positions) or $-CH_2$.
- Addition to carbons of phenyl ring in ortho, meta or para positions.

Solvent effects:

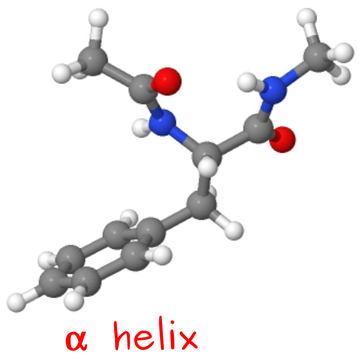
We have considered solvent effects at different dielectrics:

a) $\varepsilon$=4 for inner aminoacids (far from water)

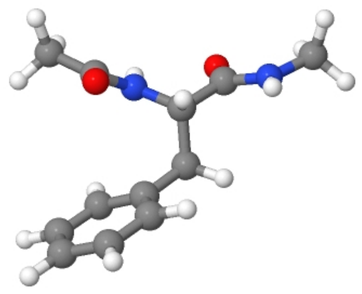
b) $\varepsilon$=78 for outter aminoacids (close to water)

## Backbone Moldels

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



α helix



β–sheet

## Methods

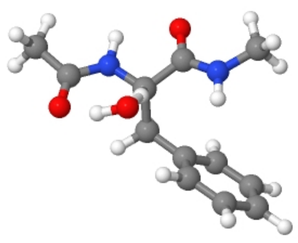
- Optimization and Frequencies in gas phase: MPWB1K/6–31+G(d,p).
- Single points at $\varepsilon$=4 and $\varepsilon$=80: MPWB1K/6–311+G(2df,p).
- $H_{sol}^{298}=E_{sol}+H(cont)_{gas}^{298}$. IRC for Transition States.

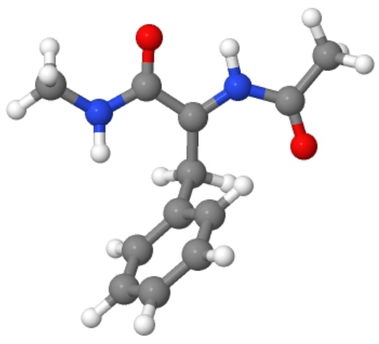
## Results

### Attack to the Backbone

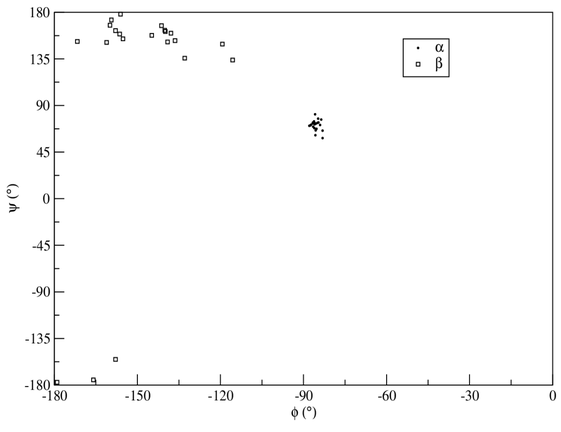
- Abstraction from N and $C_\alpha$ considered. In all cases, the latter more favorable about 15–20 kcal/mol, regardless the considered R and different solvent effects.

TS

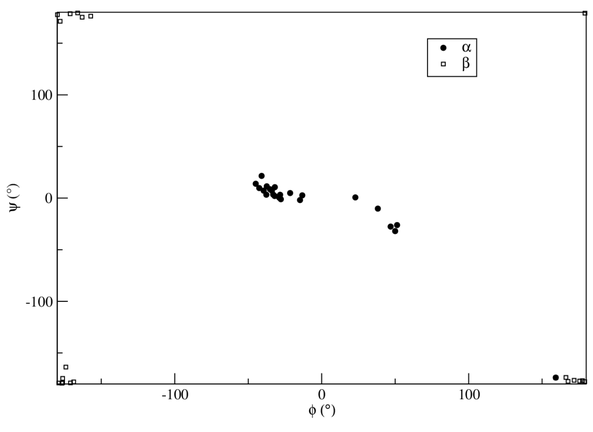




Ramachandran React.

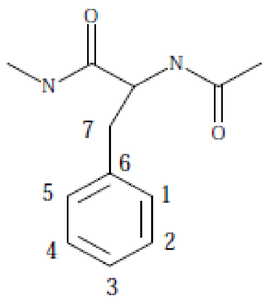



Ramachandran Prod.




- Abstraction from $C_\alpha$ favored.
- α–helix radical intermediate: ψ ≈ 0, and ϕ = −50 to 50.
- β–sheet: radical intermediate: ψ ≈ ± 180, and ϕ = ± 180.

### Attack to the Side Chain (Phenylalanine)




Addition

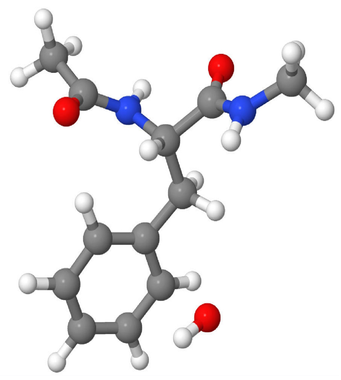
| | $r_{CO}^{TS}$ | $\Delta H_4^{TS}$ | $\Delta H_{aq}^{TS}$ | $r_{CO}^{Prod}$ | $\Delta H_4^{Prod}$ | $\Delta H_{aq}^{Prod}$ |
|---|---|---|---|---|---|---|
| Adduct | | | | | -4.8 | -1.7 |
| C1 | 1.985 | -0.4 | 1.1 | 1.425 | -18.0 | -17.2 |
| C2 | 1.969 | 1.0 | 1.7 | 1.423 | -16.3 | -16.0 |
| C3 | 1.974 | 0.4 | 1.0 | 1.423 | -18.0 | -17.0 |
| C4 | 1.965 | 1.0 | 1.7 | 1.419 | -16.5 | -15.5 |
| C5 | 2.011 | -4.5 | -1.3 | 1.434 | -17.7 | -15.1 |
| C6 | 1.999 | -0.5 | 0.6 | 1.442 | -18.6 | -14.9 |

Abstraction

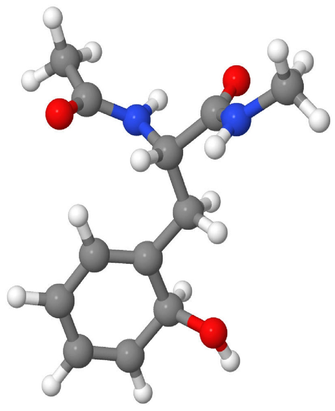
| | $r_{CH}^{TS}$ | $r_{OH}^{TS}$ | $\Delta H_4^{TS}$ | $\Delta H_{aq}^{TS}$ | $\Delta H_4^{Prod}$ | $\Delta H_{aq}^{Prod}$ |
|---|---|---|---|---|---|---|
| C1 | 1.236 | 1.240 | 4.1 | 4.9 | -4.6 | -4.9 |
| C2 | 1.241 | 1.228 | 3.7 | 4.1 | -4.7 | -5.5 |
| C3 | 1.240 | 1.229 | 4.1 | 4.7 | -4.2 | -4.9 |
| C4 | | | | | -5.4 | -6.2 |
| C5 | | | | | -4.9 | -5.4 |
| C7 | 1.149 | 1.524 | 0.1 | 3.2 | -29.7 | -29.1 |

### Addition to C1

TS



Product



- Abstraction from C7 thermodynamically favored.
- Addition to phenyl ring favored vs abstraction.
- Abstraction from $C_\alpha$ competitive. $DH_{sol}^{298}$ = −33 kcal/mol

## Acknowledgements

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