Investigating the binding of Amino-alkyl-phosphate ions in the gas phase

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1. Introduction

- Amyloid ß Protein

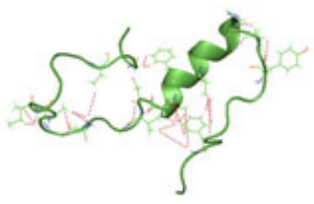

Figure 1 : Amynoloid ß Protein

https://en.wikipedia.org/wiki/Amyloid_beta#Normal_function

- The protein can bind two substrates
- Question: How is the second substrate bound?
- Hypothesis: It binds to the first substrate with a proton bond

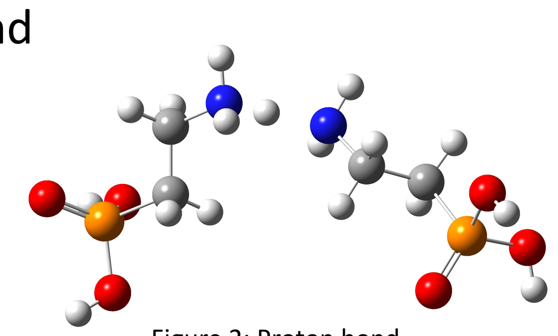

Figure 2: Proton bond

- Binding energy of the first substrate to the protein is known

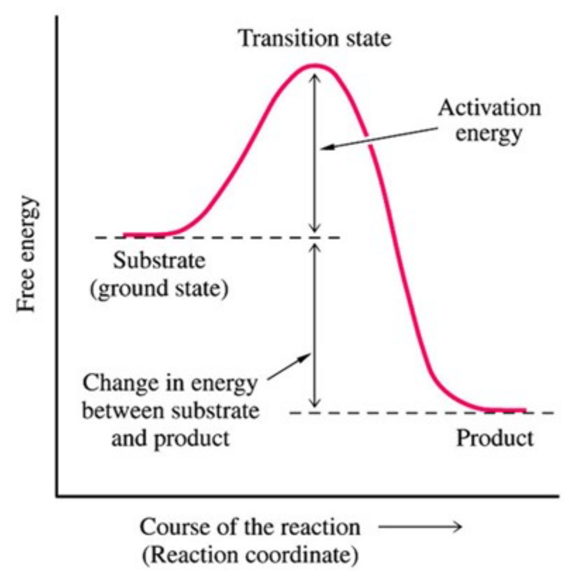

Figure 3 : Internal energy of a reaction

- Find the activation energy between similar proton-bound dimers to the substrates and compare it to the binding energy of the substrate to the protein

2. Methodology

- Generate proton-bound dimers of aminoethylphosphonic acid and aminopropylphosphonic acid by electrospray ionization.

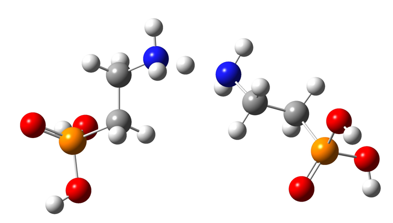

Figure 4: Aminoethyl phosphonic acid proton bound dimer

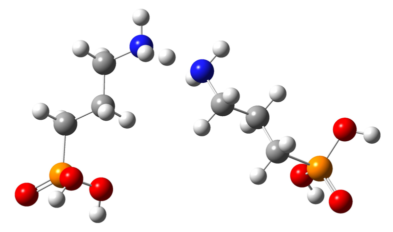

Figure 5: Aminopropyl phosphonic acid proton bound dimer

- Use triple quadrupole mass spectrometer to select the desired dimer, isolate it, and fragment it by collision-induced dissociation.

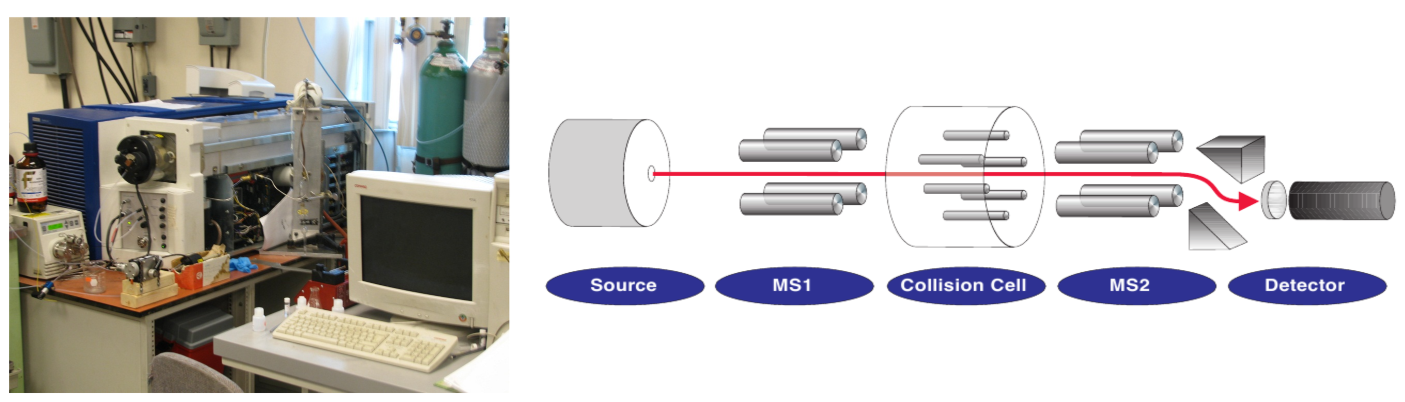

Figure 6: Triple quadrupole mass spectrometer

- Trace the graph of the relative intensity of the ions as a function of collision energy to generate a breakdown diagram

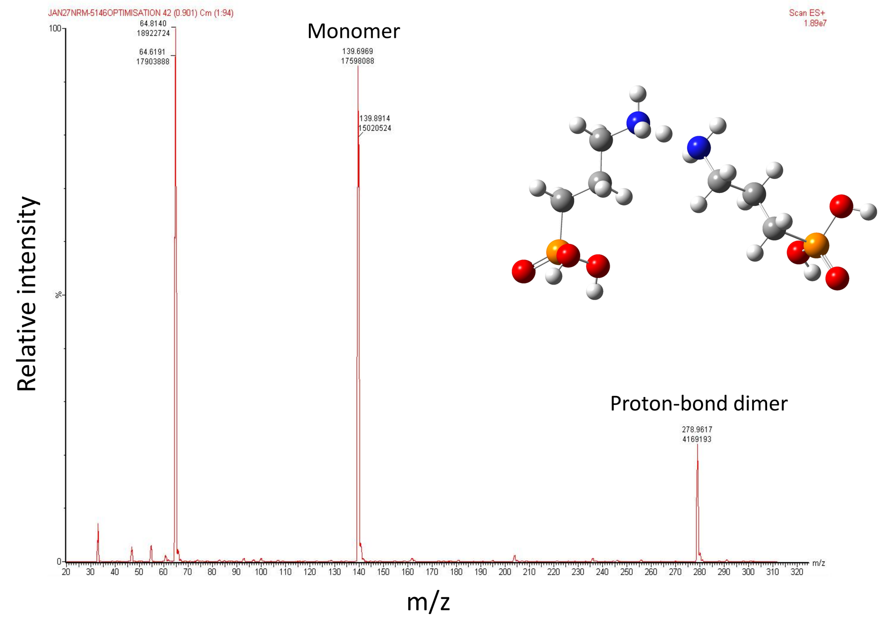

Figure 7: Scan of the mass spectrum for Aminopropyl phosphonic acid

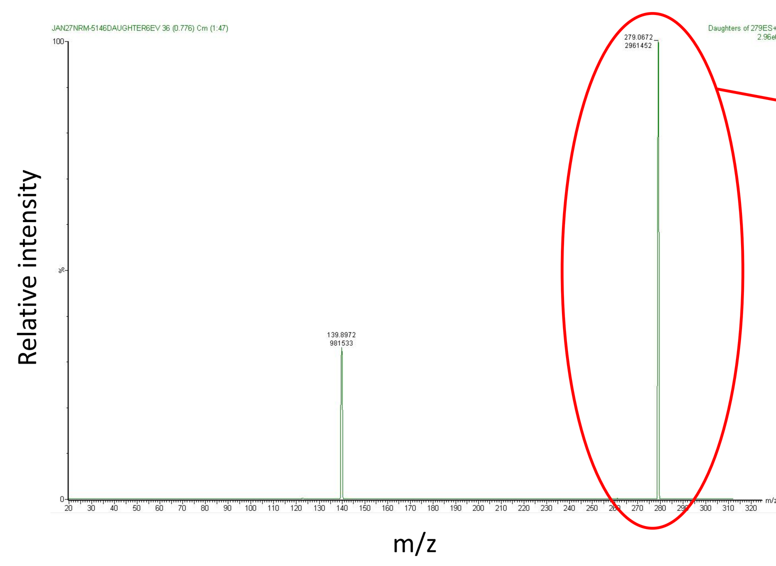

Figure 8: CID experiment of Aminopropyl phosphonic acid dimer

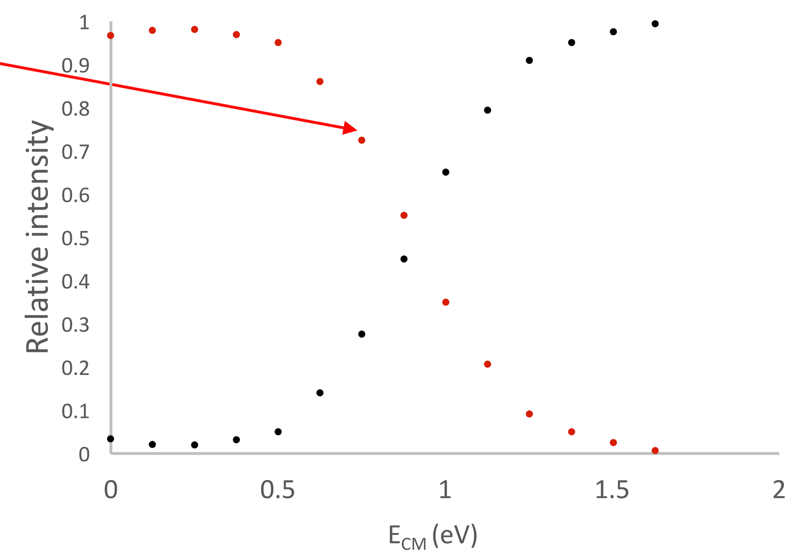

Figure 9: Breakdown curve of Aminoropyl phosphonic acid

- Calculate vibrational frequencies of the molecule and obtain its optimal structure
- Using those frequencies, model the experimental breakdown curve with a theoretical fit using the following model:

Energy of the center of mass:

$$E_{CM} = E_{LAb}\frac{M_{Ar}}{M_{Ar} + M_{ion}}$$

Temperature of the center of mass after the collision:

$$T_{CM} = T_I + \alpha E_{CM}$$

Post collision internal energy distribution:

$$P(E, E_{CM}) = \frac{\rho(E)e^{-\left(\frac{E}{RT_{CM}}\right)}}{Q(E_{CM})}$$

Rate constant:

$$k(E) = \frac{\sigma N^{\ddagger}(E - E_0)}{h\rho(E)}$$

Modeling of the breakdown curve:

$$F(E) = 1 - e^{-k(E)t}$$

The adjustable variables are E_0, $\Delta S^{\ddagger}$ and α.

The variables are adjusted through an algorithm until an acceptable breakdown curve is obtained

3. Results

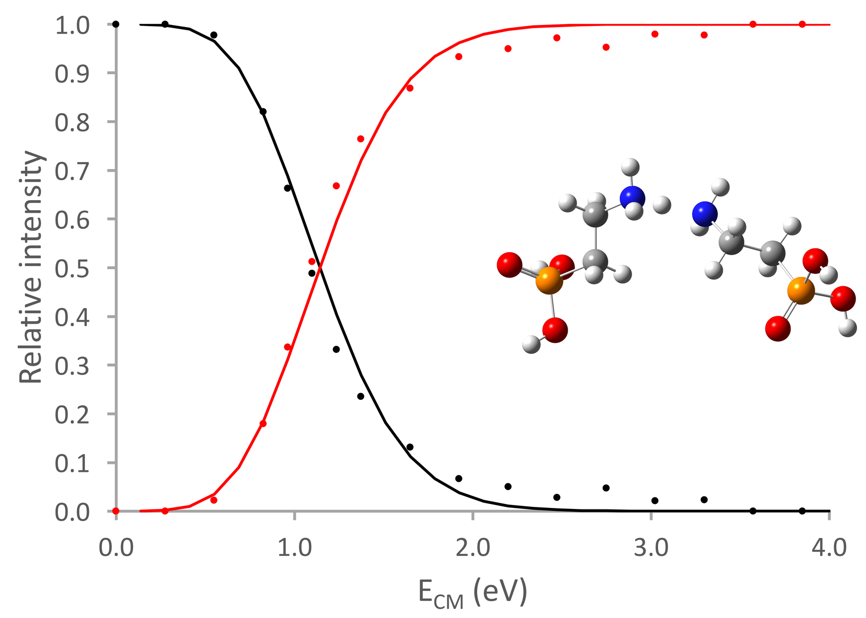

Figure 10: Fitted breakdown curve for Aminoethylphosphonic acid

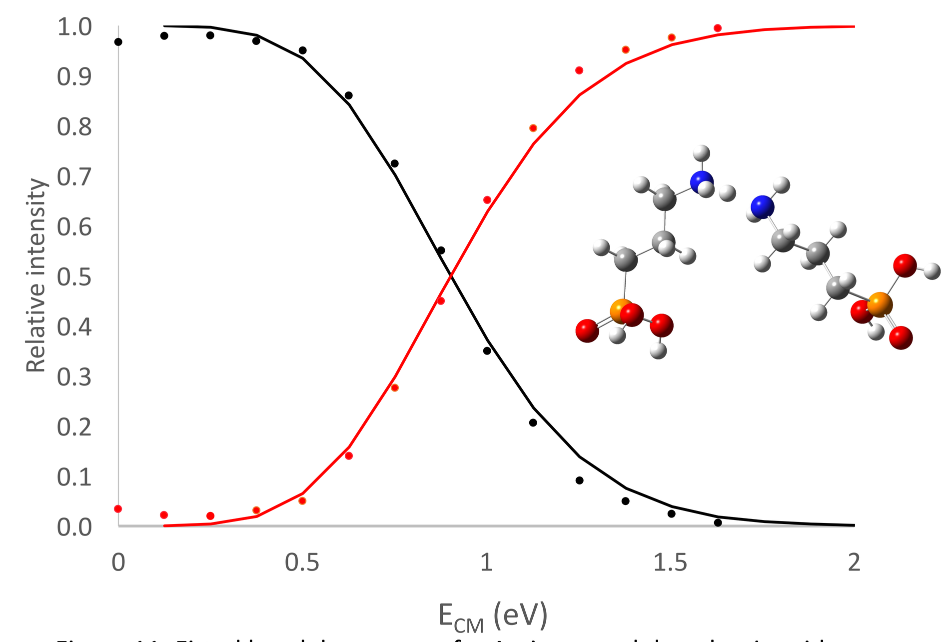

Figure 11: Fitted breakdown curve for Aminopropylphosphonic acid

Values of parameters for Amino phosphonic acids

Molecule	E_0 (eV)	$\Delta S^{\ddagger}$ (J/K/mol)	α
Ethyl	0.9	18	200
Propyl	0.89	11	230

4. Discussion

- Amyloid ß's first substrate has a binding energy to the protein of about 0.65 eV
  (Martineau and Mayer, E. a. (2011). Gas-phase binding energies for non-covalent Ab-40 peptide/small molecule complexes from CID mass spectrometry and RRKM theory. 5178-5186.
- The proton bond between the two dimers has an activation energy of 0.90 eV for ethyl and 0.89eV for propyl.
- The proton bond is stronger than the bond to the protein
- It is unlikely that the second substrate will bind to the protein itself
- It is probably bound to the other substrates
- The hypothesis appears to be correct

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