

Theoretical Analysis of the Collision Induced Dissociation of the Negatively Charged Dipeptide Glycine-Serine

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Mass spectrometry (MS) is a useful tool for determining the identity and structure of molecules based on their interaction with electromagnetic fields. However, MS can only provide the charge-to-mass ratio of the fragments produced, which may not be enough information to determine the mechanism of the collision induced dissociation (CID) of the molecule. In this case, theoretical calculations provide a useful companion for MS data and yield clues about the energetics of the dissociation. In this study, negative ion electrospray tandem MS was used to study the CID of the deprotonated dipeptide glycine-serine (GLY-SER). Though negative ion MS is not as popular a choice as positive ion MS, studies by Bowie et al.¹ show that it yields unique clues about molecular structure which complement positive ion spectroscopy, such as characteristic fragmentations like the loss of formaldehyde from the serine residue. The increase in the internal energy of the mass spectrometer alters the flexibility of the dipeptide backbone, enabling different dissociations to take place depending on the internal energy.

The mechanism of the CID of GLY-SER was studied using two computational methods, B3LYP/6-311+G(2d,p) and M06-2X/6-311++G**. We analyzed two distinct pathways for molecular dissociation in 5 conformers an attempt to verify the mechanism proposed by Dr. Swan after examination of the MS data. Our results suggest that the loss of formaldehyde from serine, which Bowie et al. indicates is a characteristic of the presence of serine in a protein residue, is an endothermic reaction which is made possible by the internal energy of the mass spectrometer. We have also determined that the M06-2X functional's improved description of medium and long-range correlation makes it more effective than the B3LYP functional at finding elusive transition states, which are often difficult to complete with the B3LYP functional, and that M06-2X more accurately predicts the energy of those transition states than does B3LYP.²

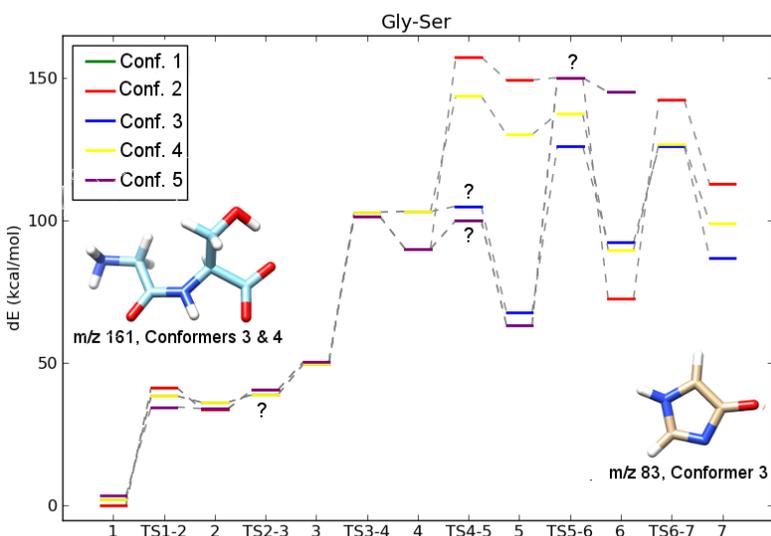


Figure 1: The energy diagram of the proposed mechanism for the CID of GLY-SER, as calculated with B3LYP/6-311+G(2d,p) for five conformers.

¹ Bowie, J. H.; Brinkworth, C. S.; Dua, S. *Mass Spectrom. Rev.* 2002, 21, 87-107.

² Complimentary results found in Zhao, Yan and Donald G. Truhlar. *Acc. Chem. Res.* 2008, 41 (2), 157-67.