UTILIZING FORCE FIELD METHODS TO EXPLORE POTENTIAL ENERGY LANDSCAPES OF FLEXIBLE BIOMOLECULES

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Spectroscopic studies of single conformations of flexible biomolecules are providing considerable new physical insight to their conformational preferences. Such studies are done against a backdrop of a full potential energy surface (PES) that has great complexity, often containing thousands of minima and an even greater number of transition states separating them. Often the relationship between experiment and the full PES is unclear. In this context, it would be extremely helpful to have predictions and summaries of the PES that enable comparisons from one molecule to the next, and of one molecule under different conditions. By utilizing the speed of force field calculations, the potential energy surface may be thoroughly explored, including both minima and transition states, in a computationally inexpensive manner. As minima and transition states are found, they are added to a disconnectivity graph, a summary of the entire potential energy surface in which the different minima are connected to one another by one or more transition states, which are grouped by energy. Disconnectivity graphs have been prepared for the flexible hexamide Z-$(Gly)_5$-NHMe (where the Z-cap is a benzocarboxy substituent), which has been studied experimentally in isolated form using single-conformation spectroscopy. Disconnectivity graphs of both the isolated and solvated molecule provide insight to the solvent-induced conformational differences. In addition, the peptide Ac-Phe-Ala-NHMe has been modeled using all α-amino acids, all β-amino acids, and all γ-amino acids. As the flexibility and complexity of the triamide increases, the disconnectivity graphs illuminate changes in the relationships between different conformational families as well as any changes in the height of the barriers between those families. These results will be compared to previous results from single-conformation spectroscopy on this series.