Conformational Analysis of a *Trans*-fused Model for the FGH Ether Rings in Brevetoxin A

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Brevetoxin A, a potent polycyclic marine ether and neurotoxin produced by the "red tide" dinoplagellate, can cause severe respiratory problems in higher organisms such as humans by binding to a receptor on sodium ion channels. Important to the ligand-protein binding are the flexible *trans*-fused ether rings. Therefore, in this project, the conformational behavior and flexibility of a model for the *trans*-fused ether rings are studied using molecular mechanics. Previously, Shida et al. reported only two *trans*-fused conformations within 50 kJ/mol; the "crown" and "boat-chair," and reported that all MacroModel force fields/solvent models favored the boat-chair by 2 – 12 kJ/mol while their NMR results indicated that the crown should be 3.6 kJ/mol more stable. In our hands, each of the MacroModel force fields identifies significantly more unique low energy structures within the 50 kJ/mol ensemble on the same surfaces, including alternative crown and pure boat conformations. These results will be presented, along with energetic quantum comparisons and effects of solvation.