ABSTRACT

This thesis presents a multi-faceted investigation of noncovalent interactions, focusing on three key problems: sulfur-centered hydrogen bonding involving disulfide bridges, the use of hydrogen bonding as a probe for aromaticity in five-membered heterocycles, and the inductive effects of alkyl substituents. Studying these systems in isolated conditions, without the interference of solvent molecules and larger molecular complexes, necessitated the development of custom-built equipment. The thesis work is divided into two principal parts:

I. Establishing Gas-Phase LASER Spectroscopy Laboratory: A major, foundational contribution of this work is the design, construction, and optimization of a custom-built gas-phase spectroscopy laboratory and supersonic jet-cooled molecular beam machine. This high-vacuum apparatus enables the recording of high-resolution, mass-selective UV and IR spectra of monomers and dimers under jet-cooled conditions. This capability provides the necessary access for isolating and interrogating weakly-bound molecular complexes. This advanced instrumentation was essential for obtaining the high-quality, cold-molecule spectroscopic data used for benchmarking theoretical methods. Furthermore, home-built software written in LabView was developed and used to control the LASERs, pulsed-valve, HV-power supply, and oscilloscope for data acquisition and analysis.

II. Quantitative Benchmarks for Noncovalent Interactions: Experimental results, supported by quantum mechanical calculations, provide new quantitative insights: 1. Sulfur-Centered Hydrogen Bonding: Gas-phase spectroscopic measurements of model systems, supported by Protein Data Bank (PDB) analysis, demonstrate that disulfide bridges engage in O–H···S and N–H···S hydrogen bonding. These weak yet directional interactions contribute to protein stability and intermolecular recognition. Conformational searches further revealed the structural landscapes of the O–H···S and N–H···S hydrogen-bonded dimers, allowing for direct comparison with experimental benchmarks. 2. Aromaticity Assessment: Systematically probing furan, thiophene, and selenophene using O–H···π hydrogen bonding and high-resolution spectroscopy resolved long-standing inconsistencies, establishing the definitive aromaticity order as selenophene > thiophene > furan. The study also identified the Gauge-Including Magnetically Induced Current (GIMIC) index as a particularly reliable descriptor. 3. Alkyl Inductive Effect: Using H-bonding as a sensitive experimental probe, spectroscopic measurements unambiguously confirmed the traditional +I effect of alkyl groups, challenging recent computational predictions of a –I effect. Benchmarking of atomic charge schemes revealed systematic biases arising from electronegativity-driven partitioning, which can be corrected to align theoretical predictions with experimental evidence.

By successfully establishing a state-of-the-art gas-phase spectroscopy lab and applying its unique capabilities, this thesis provides the vibrational signature of sulfur-centered hydrogen bonding with disulfide groups, resolves ambiguities in aromaticity assessments, and redefines the reliability of atomic charge-based inductive predictions. These findings not only deepen the understanding of noncovalent interactions but also establish experimental data for validating computational models in physical and theoretical chemistry.