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Molecular Interactions and Hydrogen Bond Tunneling Dynamics: Some New Perspectives

Richard J. Saykally* and Geoffrey A. Blake

The recent development of tunable far-infrared lasers and other high-resolution spectroscopic probes of weakly bound clusters is having a significant impact on our understanding of intermolecular forces and on the complex quantum tunneling dynamics that occur in hydrogen-bonded systems. Far-infrared studies of a variety of interactions are discussed, including several prototypical water-hydrophobe complexes, the water trimer, and the ammonia dimer. Particular attention is paid to the inversion of spectroscopic data to yield detailed intermolecular potential energy surfaces. Investigations of nonpairwise additivity are also described.

The widespread use of molecular modeling in modern science has lead to seminal insights into the nature of complex molecules and complicated chemical processes. As all such approaches are ultimately dependent on the "correctness" with which they represent molecular interactions, this latter subject has also received considerable recent attention. The strongest of these interactions, the hydrogen bond, is a highly revered dogma of modern science, transcending the boundaries of numerous disciplines. It is at once a structural model, an energy constraint, and an arena for an interesting kind of dynamics upon which a tremendous variety of natural phenomena depend. After many years of debate, the origin of hydrogen bonding is now generally understood to be primarily electrostatic, but with significant contributions arising from short-range charge transfer interactions. Typical hydrogen bond strengths in neutral systems fall in the range from 2 to 5 kcal/mol, whereas those involving ions are much stronger. The preponderance of modern research has shown that hydrogen bonds usually adopt a nearly linear M-H·····X: arrangement between a donor bond (M–H) and a proton acceptor (X:), typically a Lewis base. Weaker forces ("van der Waals interactions") are often assumed to be less "directional."

It is now possible to quantitatively test these long-held views. Classical routes to intermolecular potential energy surfaces (IPSs) have been augmented by powerful new spectroscopic methods that have been developed for investigating intermolecular forces and intramolecular dynamics at a vastly enhanced level of detail. The many results accumulated from these experiments have both dramatically enhanced our knowledge of molecular interactions and challenged time-honored theories and paradigms. For example, the microwave spectra of isolated clusters seem to indicate that some of our most basic notions of hydrogen bonding are not observed in several important prototypical systems (*1*).

In this article we describe one of the newest and most successful tools developed for studying molecular interactions, tunable far-infrared laser vibration-rotation-tunneling spectroscopy (FIR-VRTS) and we present some of the more interesting results that have recently been obtained with this method. By directly measuring the intermolecular vibrations of a weakly bound cluster (the term WBC is used here to denote both van der Waals and hydrogen-bonded complexes), we can resolve rotational and nuclear hyperfine structure and thus access the most sensitive measure of the IPS. These measurements have not been possible in the past simply because the necessary technology did not exist. Intermolecular vibrations typically lie in the FIR region of the electromagnetic spectrum (10 to 350 cm^{-1}), where high-performance light sources and detectors have been slow to evolve. The development of the tunable FIR laser and the emergence of improved detector materials has now revolutionized our capabilities in this spectral region.

In particular, by combining a tunable FIR laser spectrometer with a planar supersonic jet for generating WBCs, we have developed a very general tool for studying molecular interactions and hydrogen bond tunneling dynamics at an unprecedented level of detail. The origin and early development of FIR-VRTS have been reviewed previously (*2*), as have the much more advanced instruments currently in use in at least four independent laboratories (*3–5*). We present a general outline of the method in Fig. 1. Complementary results have been obtained for literally hundreds of clusters at both longer and shorter wavelengths. Interested readers may wish to consult recent reviews of these subjects (*6, 7*).

Obtaining IPSs by Inverting FIR-VRT Spectra

The weak forces between molecules lead to shallow potential surfaces with a very rich and complex topology. Intermolecular vibrational, rotational, and tunneling states can therefore become quite strongly mixed, hence our general term of FIR-VRTS. It is vital that states spanning the complete range of intermolecular coordinates be measured due to the well-known uniqueness problem associated with the inversion of spectroscopic data. The VRT transitions sample particularly large regions of the IPSs, and their use in the determination of potentials for simple binary systems has been recently reviewed by Cohen and Saykally (*8*). The general approach developed at Berkeley for the inversion of VRT data makes use of the collocation method for solving the coupled channel equations that result from expressing the Schrödinger equation in scattering coordinates. Hutson has also recently reviewed the use of the more

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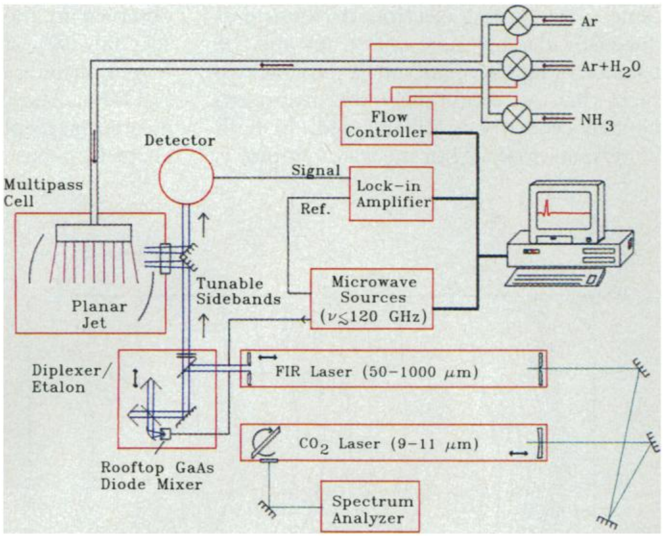
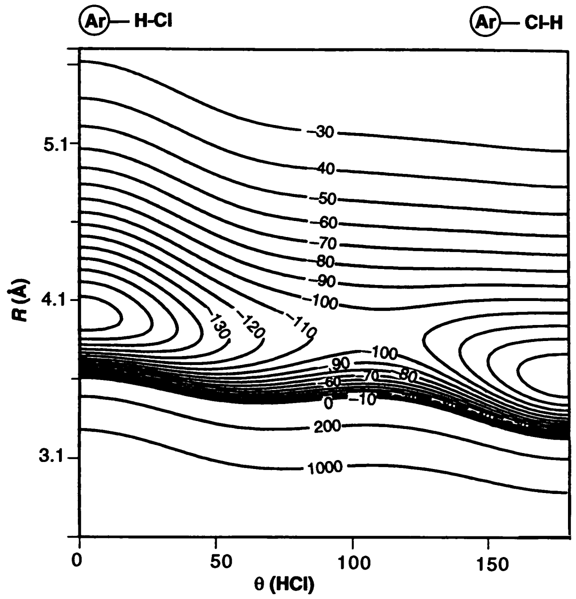


Fig. 1. Design of the Berkeley and Caltech FIR-VRT laser spectrometers. By mixing the optically pumped FIR laser with frequency agile microwave sources in a GaAs Schottky barrier diode, tunable laser sidebands at frequencies of $\nu_{\text{laser}} \pm n \cdot \nu_{\text{microwaves}}$, where n = 1,2,3,. . ., are produced. Polarizing Martin-Puplett interferometers and Fabry-Perot etalons are used to couple the laser onto the GaAs diode and to separate the laser sidebands from the more intense carrier. The sideband beams are then directed through a vacuum chamber at right angles to a planar supersonic expansion nozzle some 5 to 10 cm in length, multipassed 8 to 16 times, and detected by state-of-the-art InSb or Ga:Ge detectors. The expansion chemistry is controlled by accurately mixing several gas flows. Under routinely achieved conditions, signals as small as 1 to 10 ppm can be detected at ~1 MHz resolution. The high flux of clusters from planar expansions also enables direct absorption microwave spectra to be collected on the same apparatus (*37*). Tunability is limited only by the microwave sources available (presently ≤120 GHz). Recent improvements in millimeter-wave technology should provide nearly complete coverage up to ~150 to 200 cm^{-1}.

traditional method of close coupling for the extraction of an IPS from rare gas–hydrogen halide dimer spectra (9). Both groups use single-center multipole expansions to represent the IPS. Because of their general importance, our discussion concentrates on clusters containing water and ammonia.

Argon as a structureless probe of molecular force fields. Although their practical significance is admittedly marginal, binary systems involving a rare gas component have provided a crucial testing ground for the theories of intermolecular forces, the development of experimental methodologies, and the IPS inversion formalisms. Of these, Ar–HCl is the most thoroughly tested. Hutson's most recent IPS, determined from extensive microwave, FIR-VRT, and mid-IR spectra (*10*), is shown in Fig. 2. The global minimum occurs at the linear geometry (θ = 0°) expected if the complex were "hydrogen-bonded" (Ar is a weak Lewis base) with a secondary minimum at the linear Ar–ClH configuration. Both of the dominant long-range attractive forces, induction and dispersion, favor the hydrogen-bonded orientation, but are essentially isotropic elsewhere. The secondary minimum results from the weakening of the electron repulsion at θ = 180° due to the electron withdrawing effect of the hydrogen atom. Hence, the difference in the well depths of the primary and secondary minima in rare gas–hydrogen halide complexes decreases from the highly electronegative F to the more polarizable Cl and Br atoms. This subtle competition between attractive and repulsive forces is a critical aspect of molecular interactions that is only now becoming fully appreciated. It implies that attempts to rationalize WBC structures in terms of only the attractive forces must be viewed with suspicion.

Fig. 2. The Hutson H6(4,3,0) IPS for Ar–HCl, where *R* is the van der Waals stretching coordinate and θ describes the orientation of the HCl; θ = 0° corresponds to a linear ("hydrogen bonded") Ar–HCl geometry. Contours on all surfaces are in wave number increments (1 kcal/mol = 350 cm^{-1}).



A critical test of Hutson's H6(4,3,0) IPS has recently been carried out by Elrod *et al.* (*11*), who measured several new FIR-VRT transitions in Ar–DCl. Although the improved IPSs predicted the observed energy levels to an unprecedented level of accuracy, the new data definitively show that the secondary minimum region of the IPS is still not quantitatively well represented. As discussed below, the determination of many-body intermolecular forces (deviations from simple pairwise additivity) will depend critically on the accuracy of such pair potentials because these effects are predicted by modern quantum chemistry to be a relatively small, but critical, component of condensed-phase energetics.

The Ar–H$_2$O system has been studied in detail by several groups. Cohen and Saykally (*12*) have determined an improved IPS by inverting this large data set consisting of FIR-VRT transitions for Ar–H$_2$O, Ar–HDO, and Ar–D$_2$O. The resulting surface, denoted AW2, is shown in Fig. 3. Because three, rather than two, large amplitude coordinates must be included in the VRT Hamiltonian, the computational effort required was substantial—more than 100 cpu hours on a Cray XMP-II. Only a single minimum is evident and occurs at the "planar T-shaped" configuration in which the water symmetry axis is nearly orthogonal to the van der Waals bond axis. This result may seem surprising at first because the highly polar O–H bonds might be expected to assume a "hydrogen-bonded" orientation, as is the case with even the less polar hydrogen halides (9).

Again, however, it is the electron repulsion that dictates structure of the complex near the global minimum. Both the attractive and repulsive forces are maximized at the hydrogen-bonded orientation (θ = 52°), but the repulsive forces are sharply localized about the hydrogen atoms, which protrude some 0.3 Å beyond the oxygen van der Waals radius. The attractive forces vary much more slowly with the water orientation and yet decrease rapidly if the hydrogens are rotated out of the plane, thus forcing the minimum to occur where all four atoms are coplanar. The highly anisotropic electron exchange repulsion therefore causes the structure of the Ar–H_2O complex to be T-shaped near the IPS minimum. It is extremely interesting to note, however, that the hydrogen-bonding orientation is indeed preferred at distances greater than 3.8 Å, as is evidenced by the valley in the IPS located at $\theta = 52°$.

Another point worth emphasizing is that the repulsive wall characterizing the closest approach of the Ar atom to water is very structured. Therefore, the rapidly decaying exchange repulsion between water and an interacting partner cannot be represented by a simple exponential or inverse power law and indicates that the locations of the hydrogens, and perhaps of the unpaired electrons, should be incorporated into effective water potentials.

Schmuttenmaer *et al.* (*13*) have recently determined the Ar–NH_3 IPSs (Fig. 4) by inverting extensive FIR-VRT spectra. Again, the global minimum occurs at a T-shaped geometry, whereas a hydrogen-bonded configuration might be expected because ammonia is one of the prototypical amphoteric substances. The explanation is essentially the same as that presented above. The attractive forces from the NH_3 monomer are even more slowly varying with angle than they are for water, but so are the repulsions. Again, the repulsive terms are dominant near the van der Waals minimum and force Ar–NH_3 to adopt a T-shaped geometry that relaxes to the hydrogen-bonded orientation preferred at longer range, as in the case of Ar–H_2O. We therefore note that NH_3 is acting as a proton donor—even with argon as acceptor—in contrast with Nelson, Fraser, and Klemperer's (*1*) conclusions that NH_3 never acts as a donor. This system is indeed much more isotropic than the previous two cases, however.

Important water potentials: H_2O–N_2, H_2O–CO, H_2O–NH_3, H_2O–CH_4, H_2O–C_3H_8, H_2O–C_6H_6. Because of water's critical role in chemistry and biology, the detailed characterization of its behavior with a range of binding partners is essential. The weak interactions of water with nitrogen and carbon monoxide, for example, are of importance in many fields, including physiology, medicine, and cosmochemistry. Similarly, the water-ammonia system is a prototype for acid-base chemistry, whereas the water-methane complex provides the simplest molecular model of hydrophobicity. However, because these dimers are more complicated than those described above, the relevant IPSs are currently characterized in less detail. Considerable progress has nonetheless been achieved in understanding the molecular interactions in these systems as a result of the detailed FIR-VRTS experiments carried out at Berkeley and Caltech.

The same long-range hydrogen-bonded approach observed in the Ar–H_2O IPSs is also present in the more strongly bound H_2O–N_2 and H_2O–CO dimers. For these dimers, the leading electrostatic terms produce considerably more anisotropy and the balance of repulsive and attractive forces is such that at equilibrium the hydrogen-bonded geometry is still favored. In both dimers, an exchange of the water protons is observed in the microwave (*14*) and FIR spectra (*15*), whereas tunneling of the nitrogen nuclei is also feasible and resolved in H_2O–N_2. The observed selection rules indicate that a "planar" rotation of the water about its *c*-axis dominates the large ampli-

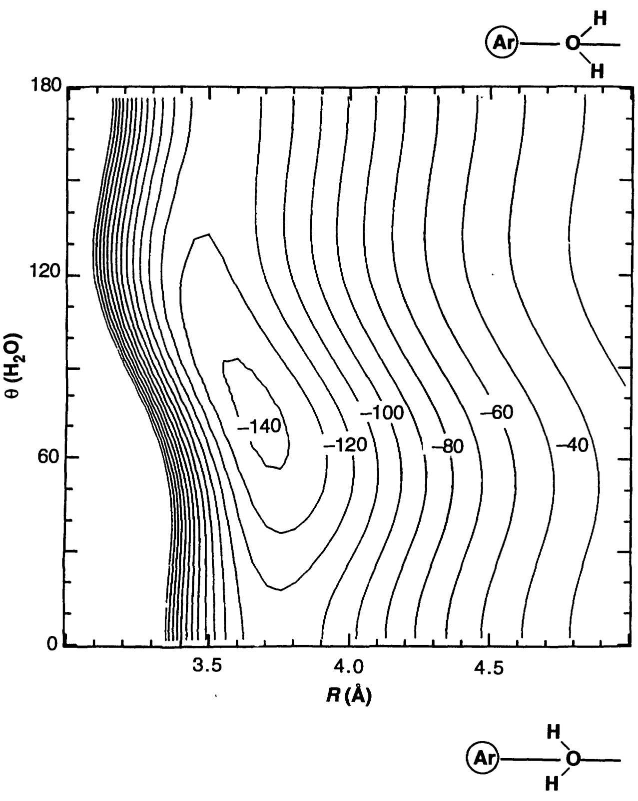


Fig. 3. The Cohen and Saykally AW2 IPS for Ar–H_2O at $\phi = 0°$. R and θ are as before, whereas ϕ denotes the rotation of water about its symmetry axis. At ($\theta = 0°$, $\phi = 0°$), the van der Waals and water axes are aligned such that the H_2O protons point toward the Ar in a planar configuration. Note the valley located at $\theta = 52°$ for $R > 3.76$ Å, which indicates a "hydrogen bonding" geometry at long range. Repulsive interactions force the "planar T-shaped" geometry ($\theta \approx 90°$) at shorter range.

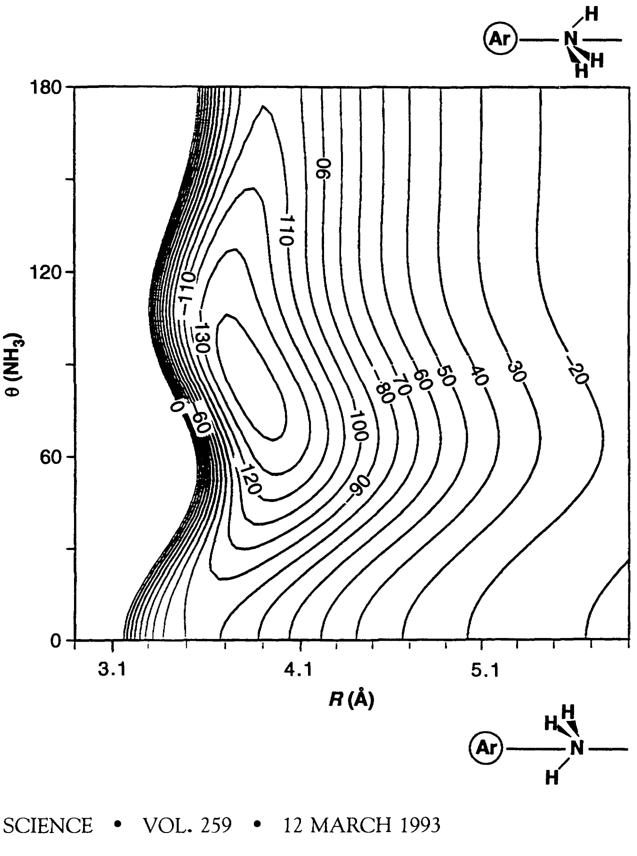


Fig. 4. The IPS of Ar–NH_3, determined by FIR-VRT spectroscopy. The coordinate system is the same as for Fig. 3. Again, note the hydrogen bonding valley at long range, as well as the T-shaped structure at the potential minimum.

tude motion in H_2O–N_2 and H_2O–CO, as might be expected from the anisotropy observed in the AW2 potential.

Indeed, ab initio calculations of the two IPSs (*16*) predict that the out-of-plane degrees of freedom are substantially "stiffer" and that the planar nitrogen tunneling motion is strongly coupled to the water moiety (see Fig. 5). Preliminary fits to the FIR tunneling splittings by Bumgarner *et al.* (*15, 16*) give barriers of ~0.4 and ~0.6 kcal/mol for the proton exchange in H_2O–N_2 and H_2O–CO. The ab initio calculations predict binding energies of ~1.4 and ~2.6 kcal/mol, respectively, and both the ab initio surfaces and the VRT data point toward a slightly nonlinear equilibrium angle for the hydrogen bond. The multiple minima, strong coupling of the angular degrees of freedom, and five-dimensional nature of the IPSs in these dimers render the inversion process described above a challenging undertaking. However, a full treatment of the hydrogen bond dynamics is clearly demanded if a true understanding of the VRT states in H_2O–N_2 and H_2O–CO is to be achieved.

The water-ammonia dimer presents a classic example of hydrogen bonding. As expected, ammonia acts as a hydrogen bond acceptor in H_2O–NH_3. By symmetry, a total of four VRT levels are expected to be populated (due to the ortho and para spin forms of H_2O and NH_3), and are observed by Stockman *et al.* (*17*), at the low temperatures characterizing molecular beams. From the recorded FIR-VRT spectra, the in-plane water proton exchange path is still lowest in energy, but the barrier has risen to ~2.0 kcal/mol out of an estimated binding energy of ~5.7 kcal/mol. The internal rotation barrier of the ammonia is estimated to be at most 0.03 to 0.04 kcal/mol, and could be substantially smaller.

From the observed free jet spectra, ab initio calculations, and matrix isolation results, a preliminary construction of the IPS is possible. Again, a slightly nonlinear equilibrium geometry is found for the hydrogen bond. Unlike the previous cases, however, the binding energy is sufficiently high that many of the VRT modes lie above the range accessible with optically pumped FIR lasers, that is, above 200 cm^{-1}. The water bending states, for example, occur near 400 and 600 cm^{-1}, but should be observable with mid-IR diode laser spectrometers.

The H_2O–CH_4 complex is the simplest water-hydrocarbon cluster and might be expected to exhibit an IPS similar to that of Ar–H_2O because the charge distribution of methane is almost spherical (the octupole is the lowest order nonvanishing multipole moment). However, because the repulsive forces depend critically on the shape of the interacting monomers—as is evidenced by the non–hydrogen-bonded equilibrium structures for Ar–H_2O and Ar–NH_3—the H_2O–CH_4 IPS might well be characterized by much higher barriers to internal rotation of the H_2O subunit than in the case of a truly spherical partner. Extensive microwave and FIR measurements of the VRT levels of H_2O–CH_4 by Dore *et al.* (*18*) have revealed a very complex spectrum that is attributed to angular momentum coupling of the two internally rotating constituents. In order to aid in the interpretation of the spectra, the VRT levels were calculated by using a variational approach. Although agreement between the experimental and theoretical VRT levels is apparently limited by the quality of the ab initio IPS, the preliminary results seem to confirm that the H_2O molecule experiences a similar force field when bound to CH_4 as it does in the presence of Ar. An empirical determination of the full six-dimensional IPS of H_2O–CH_4 will be necessary to conclusively establish the interplay of the attractive and repulsive forces in this system.

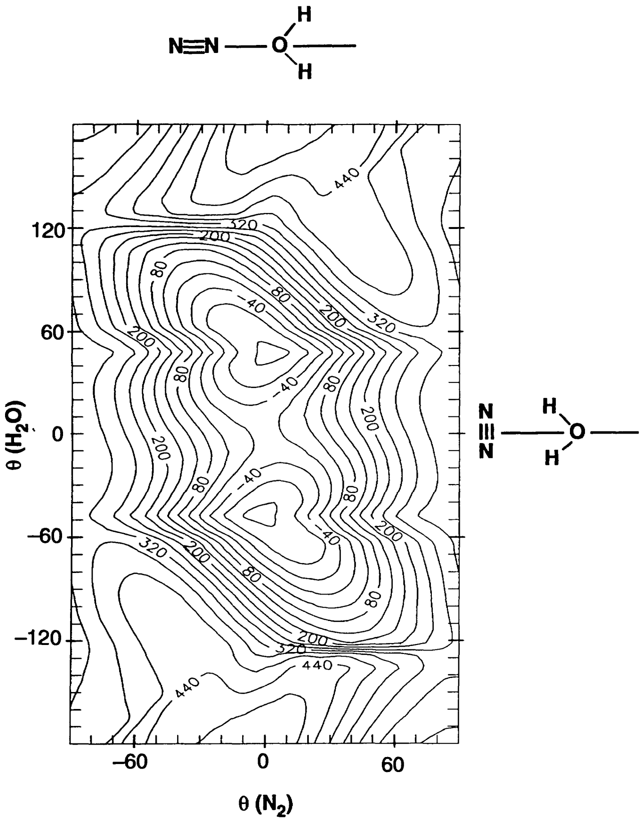


Fig. 5. A two-dimensional cut through the ab initio H_2O–N_2 IPS at R = 3.8 Å, illustrating the coplanar energetics of the dimer. As before, $\theta(H_2O)$ = 52° produces a hydrogen-bonded geometry, whereas [$\theta(N_2)$ = 0°, $\theta(H_2O)$ = 0°] defines the zero of energy and aligns the N_2 and H_2O symmetry axes with the water protons pointing toward the nitrogen. A similar path to that taken by the nitrogen nuclei in this figure leads to a secondary isocarbonyl minimum in H_2O–CO.

The H_2O–C_3H_8 complex might be expected to possess a dramatically different IPS than H_2O–CH_4 because of the existence of lower order multipoles and the distinctly nonspherical shape of propane. Preliminary results obtained by Steyert *et al.* (*19*) from microwave and FIR spectroscopy indicate a structure in which all of the heavy atoms are coplanar and the center-of-mass of the H_2O molecule lies on or near the C_2 symmetry axis of propane. The carbon backbone is curved toward the oxygen. It is proposed that one of the water protons "hydrogen bonds" to the proton-deficient region behind the methylene carbon, whereas the "free" water proton tunnels between equivalent configurations on a time scale slower than the overall rotation of the complex (<100 ps).

An interesting extension of and contrast to the Ar–H_2O and Ar–NH_3 interactions is provided by the dimers of water and ammonia with benzene. Hydrogen bond interactions with aromatic systems are interesting both from a practical and theoretical point of view. They not only provide yet another opportunity to examine the nature of hydrophobicity at the molecular level, but also present an interesting suite of test cases that probe the limits of what should or should not be considered "hydrogen bonds." For example, apparently hydrogen-bonded interactions of aromatic rings with –OH and –NH_2 groups are observed in a variety of proteins, but the intrinsic stability of such structures is difficult to estimate in vivo (*20*).

Suzuki *et al.* (*21*) and Rodham *et al.* (*22*) have obtained microwave spectra for these species with the Caltech planar jet spectrometer as a first step in the IPS characterization. Both H_2O and NH_3 reside above the benzene ring with their protons interacting with the high electron density π-cloud—even at short range. Internal rotation of the monomer frames in the sixfold potential is essentially free, and exchange of the water and ammonia protons occurs through extremely low barriers. Although the hydrogen bond donor role is a common one for water, the benzene-ammonia dimer provides an ostensibly rare example (*1*) of proton donation by gas-phase NH_3. Not surprisingly, the water interaction is the stronger of the two. The highly anharmonic IPS results in sufficiently low intermolecular vibrational frequencies, all of which may be investigated with the tunable FIR spectrometers. Unlike the Ar containing species discussed above, the nuclear quadrupole and electric dipole moments of C_6H_6–H_2O and C_6H_6–NH_3 indicate that the water and ammonia experience substantial anisotropy. The observed structures and predicted binding energies indicate that the association of proton donating groups with aromatic rings in proteins can indeed legitimately be termed hydrogen bonds (*23*).

VRT Dynamics in Hydrogen-Bonded Clusters

When WBCs contain two or more identical monomers, several effects not present in mixed dimers can occur. The pioneering microwave spectroscopy experiments of Klemperer and co-workers on $(HF)_2$, for example, revealed a rich and complex tunneling dynamics resulting from the structural degeneracy and low potential barriers in this system (*24*). In particular, the IPS for the complex exhibits a double well structure representing interchange of the identical monomers in the roles of hydrogen bond donor and acceptor, and the potential barriers impeding this motion are quite low. The rovibrational energy levels of the cluster are split into doublets as a result of these tunneling dynamics, much as those of the ammonia molecule are split by the familiar umbrella inversion tunneling. This VRT structure has since been investigated in detail by both microwave and infrared spectroscopy experiments, as well as by theoretical methods (*25*).

Subsequent microwave studies of the water dimer by Dyke and collaborators (*26*) revealed similar but considerably more complex tunneling dynamics in that cluster. Here, an eightfold structural degeneracy results from the permutation symmetry of the identical water monomers, and the potential barriers for the two most facile motions, acceptor proton tunneling and donor-acceptor interchange, are only 0.8 and 1.2 kcal/mol, respectively. As reviewed by Fraser (*27*), the combination of FIR-VRT experiments and Fourier transform microwave spectroscopy, together with results from the mid-IR, have led to a rather complete characterization of this tunneling phenomenon in the dimer ground state through the use of a high-barrier formalism.

Although the ground vibrational state of the water dimer is relatively well characterized, the effects of intermolecular vibrations on the tunneling dynamics remain essentially unexplored. Pugliano and Saykally (*28*) have recently carried out the detailed study of an intermolecular vibration in the water dimer using FIR-VRTS as a step toward obtaining a pair potential of spectroscopic accuracy for this critically important system. Both the acceptor and donor-acceptor interchange tunneling splittings were found to change drastically upon excitation of the vibrational motion and with the *K* (internal angular momentum) quantum number, indicating that, as expected, a high-barrier model is not appropriate when intermolecular vibrations are excited. A fully coupled six-dimensional dynamics treatment is likely to be required.

The water trimer: Transient chirality and nonpairwise interactions. Pugliano and Saykally (*29*) have recently measured FIR-VRT spectra of $(D_2O)_3$. The data indicate a chiral six-membered ring structure with each monomer acting both as a donor and acceptor, a result consistent with ab initio results. The intermolecular vibration observed near 89.6 cm^{-1} involves a torsional motion of the water monomers about each hydrogen bond axis. Each vibration-rotation transition is split into a quartet as a result of hydrogen bond tunneling motions occurring between left- and right-handed enantiomers. It is speculated that larger water clusters will also exhibit this transient chirality and that similar effects may occur in liquid water. Comparisons of the water trimer properties and IPSs with those of the dimer will ultimately provide a route to the quantitative assessment of nonadditive contributions to hydrogen bonding.

The ammonia dimer: A hydrogen bond paradigm resurrected. Loeser *et al.* (*30*) have recently published a detailed study of the VRT dynamics in the ammonia dimer. Analysis of extensive FIR-VRT spectra and several new microwave transitions in terms of permutation-inversion group theory, augmented by the full six-dimensional dynamics calculations of van Bladel *et al.* (*31*), has revealed several important and surprising conclusions. The umbrella inversion of the monomers is not quenched in $(NH_3)_2$, as it is in essentially all other WBCs, but instead produces pairs of slightly split VRT eigenstates. In the earliest high-resolution study of the ammonia dimer, microwave spectra in certain of these levels ("G states") measured by Klemperer and co-workers (*32*) were interpreted in terms of a model that attributed the small splittings to donor-acceptor interchange, which was thereby taken to be essentially quenched. This led to the deduction of a surprising and controversial non–hydrogen-bonded structure, which is not reproduced by high-level ab initio calculations.

Loeser *et al.* find instead that the interchange tunneling splittings are extremely large, comparable to or larger than the 15.5 cm^{-1} interchange tunneling frequency in the HCl dimer measured directly by Blake and Bumgarner (*33*) using FIR-VRTS. "Tunneling" is in some sense a misnomer for these two species in that zero-point energy from the vibration associated with the interchange coordinate places even the ground states at or above the potential energy barriers. Thus, the ammonia dimer is extremely nonrigid, which casts serious doubts on the ability of approximate methods to infer "structural" parameters from microwave data alone.

Nonpairwise Additivity in Intermolecular Forces

Experimental studies of rare gas crystal-binding energies and ab initio quantum calculations on small clusters have suggested that, although the pairwise additive approximation is accurate to within ~10%, properties that depend sensitively on the potential energy (such as preferred crystal structures) cannot be accurately predicted without the explicit inclusion of many-body terms (*34*). Unfortunately, very little is experimentally known about these effects because of the lack of data which directly probe these forces, although several researchers have been able to account for many-body effects in bulk systems by including only the leading nonadditive dispersion term, the Axilrod-Teller triple-dipole effect (*34*).

The Ar_2HCl trimer has been the recent focus of a detailed FIR-VRTS effort to understand many-body effects at a molecular level. Because the Ar–Ar and Ar–HCl pair potentials are well determined from a variety of experimental techniques, three-body forces in Ar_2HCl will be manifested by deviations in predicted properties from a pairwise additive IPS. Not only does this approach require very accurate pair potentials, but the calculation of spectroscopic observables must be as rigorous as possible in order to confidently identify discrepancies with experiment as true manifestations of three-body forces. Toward this end, FIR spectra of Ar_2HCl have been measured by Elrod *et al.* (*35*) and rigorous VRT dynamics have been performed by Cooper *et al.* (*36*). Predictions based on a pairwise additive IPS systematically deviate from the observed spectroscopic properties of Ar_2HCl, particularly for the intermolecular vibrational frequencies. The studies of Cooper *et al.* have also shown that the leading many-body dispersion and induction terms are *not* expected to be large enough to resolve these discrepancies. However, exchange repulsion between the two argon atoms results in the generation of multipole moments, which can in turn interact with the permanent moments of the HCl constituent. This particular three-body term is indeed large enough to account for the observed deviations from pairwise additivity. Future efforts are likely to yield a precise description of these exchange-induced multipole forces.

Concluding Remarks

The study of intermolecular forces has entered a new era. It is now possible to place nearly any conceivable functional group into the gas phase with supersonic jet technology. Furthermore, with the development of tunable FIR lasers, a general spectroscopic technique which probes the degrees of freedom that are most intimately related to the intermolecular potential energy surface has become available.

Theoretically, it is now possible, in principle, to directly invert high-resolution cluster spectra, although for systems of low symmetry the computational requirements are prodigious. The development of improved methods for eigenvalue generation on complicated, multidimensional potential energy surfaces can therefore be expected to have an enormous impact on not only intermolecular interactions but intramolecular dynamics as well. Nevertheless, the means to generate experimentally accurate, fully anisotropic representations of intermolecular forces, including the critical role of nonpairwise contributions, are now clearly at hand. The newly developed view of van der Waals and hydrogen bond VRT dynamics has revealed the delicate interplay between the attractive and repulsive terms in intermolecular potentials. By elucidating the true character of weak interactions, these powerful tools will enable scientists to examine the molecular details of a multitude of chemical and biological processes at unprecedented levels of accuracy and detail.

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Electronic Structure Contributions to Function in Bioinorganic Chemistry

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Many metalloenzymes exhibit distinctive spectral features that are now becoming well understood. These reflect active site electronic structures that can make significant contributions to catalysis. Copper proteins provide well-characterized examples in which the unusual electronic structures of their active sites contribute to rapid, long-range electron transfer reactivity, oxygen binding and activation, and the multielectron reduction of dioxygen to water.

Many enzymes and proteins have metal ions at their active sites that play key roles in catalysis. Metal ions can mediate facile electron transfer reactions and are capable of binding and activating small molecules, such as O_2 and N_2. The active sites of many metalloproteins exhibit distinctive spectral features as compared with small molecule inorganic complexes of the same metal ion. These features are a result of the unusual geometric and electronic structures that can be imposed on a metal ion in a protein environment. One of the major goals of research in bioinorganic chemistry has been to understand the origin of these spectral features and to use this information to generate a working model of the geometric structure of the active site in the absence of x-ray crystallographic information.

In the last decade, the crystal structures of many metalloproteins have become available at atomic resolutions. One notable example is the recently reported structure of the Fe-Mo cofactor of nitrogenase (*1*). Accurate determination of the geometric structure is, of course, a critically important goal; however, far from being the culmination of research in the bioinorganic chemistry of a class of metalloproteins, it is the starting point for fundamental studies directed toward understanding biological function at a molecular level. The focus of our research has been to combine the results of a variety of spectroscopic methods with a quantum

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