carbonyls, but the subtle differences in their bonding properties lead to many interesting reactions. One major difference between metal carbonyls and metal thio- and selenocarbonyls is the present scarcity of complexes containing multiple CS and CSe groups. It is probable that future research may well show that these types of complexes are difficult to obtain because of the destabilizing effects resulting from the strong π-acceptor capacities of the CS and CSe ligands. Finally, since it has been demonstrated that various metal chalcocarbonyl complexes can be prepared, it is anticipated that the catalytic potential of these complexes will become an important research area. The optically active chromium complexes, $(\eta^6\text{-arene})Cr(CO)(CS)L$, are particularly promising as catalysts for asymmetric organic synthesis.

Noncovalent Interactions

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The purpose of this Account is to show the interplay between theory and experiment in studies of noncovalent interactions. We define noncovalent interactions as those in which: (1) electrons stay paired in reactants and products and (2) there is no change in the type of chemical bonding in reactants and products. $He\cdots He$, $H_2O\cdots H_2O$, $BH_3\cdots NH_3$, and $FH\cdots F^-$ are examples of such interactions. We hope to show the reader the important role that theory continues to play in studies of these noncovalent interactions, which are responsible for many of the *physical* properties of condensed phases of matter.

We feel that the theory has two roles in chemistry: first, to provide quantitative predictions of phenomena; and second, to provide a language to enable one to interpret the large body of chemical facts.[1] We feel the study of noncovalent interactions is currently very exciting because, unlike the studies of covalent bonds, theory has often led experiment in studies of noncovalent bonding. For example, the structures of water dimer, $(H_2O)_2$, and hydrogen fluoride dimer, (HF_2), were predicted rather well by the theory. In addition, the "intrinsic" structure of noncovalent bonds is much harder to characterize because these bonds are weaker and much more sensitive to environment than covalent bonds. Thus, an average chemist's insight into the nature of these bonds is still far behind his understanding of covalent bonding.

Theoretical and Experimental Methodology

To be able to treat intermolecular potentials in a reasonable way, all methods must include "quantum-mechanical" effects implicitly or explicitly, since the Pauli exchange repulsion plays a crucial role in keeping two closed-shell molecules from approaching each other too closely. An intermolecular potential can only be defined within the Born–Oppenheimer approximation, which assumes that the nuclei move in an "effective" potential which contains both the nuclear–nuclear repulsions and the electronic terms (electronic kinetic energy, electron–electron repulsion, and nuclear–electron attraction). One expects that the Born–Oppenheimer approximation[2] and the neglect of relativistic and fine structure effects[3] in treating intermolecular interactions are an excellent approximation for analyzing the energy and structure of intermolecular complexes.

Quantum mechanical studies of intermolecular interactions have predominately used the "supermolecule" approach (see, however, ref 4 and 5). This approach uses direct solutions to the Schroedinger equation (with a single or multideterminant wave function whose orbitals are usually a linear combination of atomic-based functions) for both complex and isolated fragments. This should be the method of choice for relatively "small" complexes, where quantitative predictions are of importance. Recently, Morokuma[6] and others[7] have broken down the interaction energy into components which correspond closely to the different energy components of a perturbation theory expansion. These energy components are electrostatic,

(1) These roles are eloquently described by Parr (R. G. Parr, *Proc. Natl. Acad. Sci. U.S.A.*, **72**, 763 (1976)).

(2) R. J. Cross, *Acc. Chem. Res.*, **8**, 225 (1975).

(3) For more detailed description of the calculation of such effects, see H. F. Schaefer, "The Electronic Structure of Atoms and Molecules: A Survey of Rigorous Quantum Mechanical Results", Addison-Wesley, Reading, Mass., 1972.

(4) For perturbation theory approaches to intermolecular complex formation, see J. C. G. M. van-Duijneveldt-van de Rijdt and F. B. van Duijneveldt, *J. Am. Chem. Soc.*, **93**, 5644 (1971).

(5) See, for example, Y. S. Kim and R. G. Gordon, *J. Chem. Phys.*, **61**, 1 (1974), G. A. Parker, R. L. Snow, and R. T. Pack, *ibid.*, **64**, 1668 (1976), and Quantum Chemistry Program Exchange Program No. 305 for an interesting modified Thomas–Fermi approach to studying intermolecular complexes.

(6) K. Morokuma, *J. Chem. Phys.*, **55**, 1236 (1971).

(7) See P. Kollman, "Hydrogen Bonding and Donor Acceptor Interactions", in "Modern Theoretical Chemistry", Vol. 4, H. F. Schaefer, Ed., Plenum Press, in press, for detailed descriptions of this.

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exchange repulsion, polarization, charge transfer, and dispersion. We will limit our remarks to calculations of the ab initio variety (see a recent Account by Hehre).[8] We should stress at this point that most of these studies have been carried out at the SCF (single determinant) level. Unlike potential surfaces for covalent bonds, where, for example, H_2 dissociates to partially ionic H atoms, SCF theory does not suffer such a fundamental flaw in its study of noncovalent bonding, since electron pairs are conserved in products (the complex) and reactants (the monomers). Even though there are errors associated with the limitations of single determinant theory in studying noncovalent complexes,[7] they are easier to correct for than errors in studies of covalent bonding and are of a quantitative, rather than qualitative, nature.

Empirical potential functions should be mentioned here, since they are of such utility in examining properties of large molecules and polymers. These are generally simple functions which include the electrostatic, exchange repulsion, and dispersion terms of the intermolecular potential and whose form is based on classical or quantum mechanical analysis of the expected radial and angular dependence of these terms.[9] These functions can be chosen by fit to ab initio potentials[10] or by using empirical properties of the molecules to derive simple forms of the potential. In the latter case the important role of the quantum mechanical methods is to allow comparison with the simpler potentials for small complexes. For example, Stillinger and Rahman[11] and Shipman and Sheraga[12] made use of the accurate quantum mechanically calculated surfaces for water dimer to check their empirical interaction potentials.

Because the manifestations of intermolecular forces are so ubiquitous, they have been studied by a large variety of methods. In this Account we concentrate our attention on the methods which study the complex in an inert (or relatively inert) environment, because these allow the most precise comparison between experiment and theory. The extensive application of these methods has occurred very recently and has led to an exciting interplay between theory and experiment. They include: (1) matrix isolation infrared spectroscopy, in which one examines the vibrations of the intermolecular complex at a low temperature in an inert matrix, and (2) gas-phase infrared and microwave spectroscopy (at equilibrium or using supersonic nozzle beams). We need not review the details of experimental studies of intermolecular forces further, because two recent Accounts in this journal by Ewing[13] and Cross[2] have done so.

Theoretical and Experimental Studies of Complex Formation

We will now proceed to discuss representative examples of theoretical and experimental studies of noncovalent interactions. Our purpose will be twofold.

First, we hope to demonstrate that the agreement between the theoretical and experimental studies is sufficiently good that theoretical methods can be used as a powerful and predictive tool for studing noncovalent interactions. Second, we will be laying the groundwork for drawing some "chemical" generalizations from these results.

We will first discuss very weak complexes between molecules, at least one of which has no dipole moment. This causes the long-range term in the electrostatic energy to be at most quadrupole–dipole ($1/R^4$ dependence, where R is the distance between the molecules). These complexes are typically very weakly bound (dissociation energy <1 kcal/mol). The most extensively studied are the rare gas dimers, where the sole attractive force is dispersion (the leading attractive term has a $1/R^6$ dependence). The short-range part of the potential can be calculated with direct quantum mechanical "supermolecule" methods; these calculations can be carried out with sufficiently large basis sets to predict very accurate short-range potentials. However, a "supermolecule" calculation to predict dispersion requires going beyond the single determinant approximation and is quite complicated, even for $(He)_2$.[3]

More interesting from a chemical point of view are the weak "molecular" complexes, which include Ar–H_2, Ar–N_2, Ar–HCl, Ar–FCl, H_2–H_2, O_2–O_2, N_2–N_2, F_2–F_2, Cl_2–Cl_2, and (benzene)$_2$. The interaction of Ar with N_2, FCl, and HCl has the geometry one would predict if one considers Ar an electron donor. Thus Ar—N_2 has a "T" structure[14] and Ar$\cdots$H—Cl[15] and Ar$\cdots$Cl—F[16] have the electropositive atom pointing toward the rare gas. These results are consistent with the fact that the rare gases have a filled octet and are electron rich.

H_2, N_2, F_2, and Cl_2, and O_2, and NO[17] all have nonzero quadrupole moments. A simple electrostatic model would predict that all homonuclear diatomic dimers would have

$$T(\overset{A}{\underset{A}{|}} \cdots A{-}A)$$
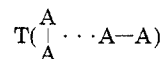
shaped structures in order to optimize their quadrupole–quadrupole interactions. This appears to be true for $(H_2)_2$[13,18,19] and $(N_2)_2$,[13] but not for $(F_2)_2$[20] and $(Cl_2)_2$.[21] Although the evidence is indirect and not all in yet, these dimers appear to have a "loose" L structure.

$$(A{-}A\cdots A{-})\overset{\overset{A}{\diagup}{\overset{\theta}{\downarrow}}}{-}\,, \theta \approx 75°$$
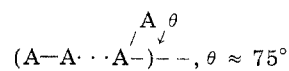
We asked ourselves why.[19] We thus evaluated the electrostatic potential around H_2, N_2, F_2, and Cl_2;[22] SCF

(8) W. H. Hehre, *Acc. Chem. Res.*, 9, 339 (1976).

(9) See A. Warshel, "The Consistent Force Field and Its Quantum Mechanical Extension", "Modern Theoretical Chemistry", Vol. 7, G. Segal, Ed., Plenum Press, in press, for a cogent review of this area.

(10) H. Kistenmacher, H. Popkie, E. Clementi, and R. O. Watts, *J. Chem. Phys.*, 60, 4455 (1974).

(11) F. Stillinger and A. Rahman, *J. Chem. Phys.*, 60, 1545 (1974).

(12) L. Shipman and H. A. Scheraga, *J. Phys. Chem.*, 78, 2055 (1974).

(13) G. Ewing, *Acc. Chem. Res.*, 8, 185 (1975).

(14) The sign of the quadrupole moment and our electrostatic potential calculations indicate that the most "positive" direction to approach N_2 is toward the center of the bond axis.

(15) S. E. Novick, P. Davies, S. H. Harris, and W. Klemperer, *J. Chem. Phys.*, 59, 2273 (1974).

(16) S. J. Harris, S. E. Novick, W. Klemperer, and W. Falconer, *J. Chem. Phys.*, 61, 193 (1974).

(17) NO and CO have very small dipole moments (0.15 and 0.11 D, respectively), so their intermolecular interactions die off more slowly than $1/R^4$.

(18) Reference 14 notes that this molecule is very floppy, but available theoretical calculations (e.g., C. F. Bender, H. F. Schaefer, and P. Kollman, *Mol. Phys.*, 24, 235 (1972), and ref 19) suggest that its lowest energy structure is the T.

(19) E. Kochanski, *J. Chem. Phys.*, 58, 5823 (1973).

(20) H. Umeyama, K. Morokuma, and S. Yamabe, *J. Am. Chem. Soc.*, 99, 330 (1977); these authors find θ only slightly greater than 0 when dispersion effects are included.

(21) S. J. Harris, S. E. Novick, J. S. Winn, and W. Klemperer, *J. Chem. Phys.*, 61, 3866 (1974).

calculations on these dimers[22] were consistent with the approach of the most positive potential of one molecule to the most negative of the other. In addition, the minimum energy could be predicted for heterodimers A_2–B_2 from the *location* of the positive and negative potentials and their relative *magnitudes*. Thus, we conclude that the structures of many of these weak complexes are consistent with a simple electrostatic model; it is the point quadrupole approximation that is inadequate.

$(O_2)_2$ and $(NO)_2$ appear to have different structures from the other diatomic dimers.[13] $(O_2)_2$ appears[13] to have a rectangular shape. The fact that it does not have a T structure can be partially rationalized by its extremely small quadrupole moment ($\theta = -0.4$ B vs. $= -1.5$ B (N_2); 6.14 B (Cl_2); -4.3 B (CO_2); B = buckinghams = 10^{-26} esu cm^2)), but the role of weak "chemical" forces involving pairing between the unpaired electrons on the O_2 molecule may also be important. The NO dimer is an intriguing case in which chemical forces are clearly important, even though the bonding is extremely weak ($D_e = 1.6$ kcal/mol). This molecule has a nearly rectangular structure

$$
\begin{array}{cc}
N \!\!-\!\!\!-\!\! N \\
| \qquad | \\
O \cdots O
\end{array}
$$

despite the relatively large quadrupole moment ($\theta = 1.8$ B) of NO monomer. Minimal basis calculations indicate that the minimum energy structure of $(NO)_2$ is rectangular-cis, with a calculated dissociation energy of the same order of magnitude as the experimental energy.[23]

At this stage, it appears that the structure of weak *closed-shell* complexes can be explained by considering that the electrostatic forces, if nonzero, dominate the directionality of the interaction. However, more precise calculations on these complexes, using energy-component analyses,[6] are needed to help show the role of the different energy terms in these complexes. Experiments which would be of great interest and would further our understanding of these interactions include studies on $(CO)_2$; CO has a quadrupole moment of similar magnitudes as NO, but no unpaired electrons. Determining the structure of some of the other "mixed" dimers involving the molecules discussed above would be of considerable interest. For example, rare gas–Cl_2 complexes would be expected to be linear rather than T shaped.[22]

In the area of hydrogen bonds, quantum mechanical "supermolecule" calculations sometimes preceded the accurate experimental determination of the structure of such complexes. Subsequent to our first studies,[24] experimental data on three of the complexes, $(H_2O)_2$, $(HF)_2$, and $H_2O\cdots HF$, became available, and these structures agreed very well with our and other calculations. The various calculations differ significantly in their predicted dissociation energy, primarily due to the differences in the multipole moments and polarizabilities predicted by the different basis sets used.

Only for $(H_2O)_2$ has the Hartree–Fock limit[8] been approached; when one adds dispersion (0.8 kcal/mol) and other correlation corrections (0.4 kcal/mol), one

predicts a D_0 for the water dimer of ~ 5 kcal/mol and a ΔH (dimerization) at 298 K of 3.4 kcal/mol,[7] somewhat below the best current experimental value of 5.2 $\pm$ 1.5 kcal/mol. It does not appear that error bounds on the theoretical calculation are as large as those bound on the experiment; it is likely that more precise experimental determinations of the dimerization enthalpy will tend toward the lower limit of the current value. We have recently analyzed[7] the H-bond energies in a number of dimers, making approximate vibrational and dispersion corrections, and have concluded that, although the general agreement between theoretical and experimental H is good, there are further studies of importance for each. Specifically, more precise theoretical calculations of the ΔH (dimerization) of $(NH_3)_2$ and more accurate experiments on the ΔH (dimerization) of $(HF)_2$ are in order.

Studies on "charge-transfer" complexes have been carried out in the groups of Morokuma[20] and Schaefer.[25] Examples of complexes studied are NH_3–F_2, dicyanocarbonyl–OR_2, and $H_3N\cdots SO_2$. It appears at this time that such complexes (when their atoms are from the first or second row of the periodic table) are held together mainly by electrostatic forces in the ground state. This is perhaps a somewhat surprising conclusion to many, but is consistent with the simple theoretical analyses by Hanna and Lefevre et al.[26] on the benzene-I_2 complex.

The example which most intrigued us was in a recent study by Lucchese et al.,[27] who found the minimum energy structure of $NH_3\cdots SO_2$ to have $\theta \sim 75°$, very different from what one would predict from considering this interaction to be dominated by dipolar forces (which would predict $\theta = 0$). We thus carried[22] out a component analysis calculation on this complex and found that the electrostatic energy had its minimum near $\theta = 75°$, confirmation that the directionality of this interaction was dominated by the electrostatic energy.
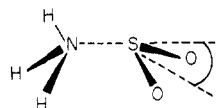
We now come to examples of "strong interactions", mainly from our own work, which illustrate that the supermolecule approach can also be useful to study noncovalent interactions having nearly the strength of normal "chemical" bonds.

Although simple empirical models are capable of rationalizing the structure and properties of alkali halide dimers, supermolecule calculations have provided a priori predictions of the structure of $(LiH)_2$, $(NaH)_2$, and $(LiF)_2$, as well as the dimerization enthalpy of the two hydrides.[28] The dimerization enthalpy of LiF was computed in reasonable agreement with experiment.

We have been very interested in the structure and energy of the water surrounding cations. Ion–water and ion–two water surfaces have been used to build up larger clusters of water surrounding Li^+, Be^{2+}, Na^+, and

(22) P. Kollman *J. Am. Chem. Soc.*, 99, in press.

(23) T. Vladimiroff, *J. Am. Chem. Soc.*, 94, 8850 (1972).

(24) P. Kollman and L. C. Allen, *J. Chem. Phys.*, 51, 3286 (1969); 52, 5085 (1970). These were the first studies to appear on $H_2O\cdots HF$ and $(HF)_2$ and the second (first was K. Morokuma and L. Pedersen, *J. Chem. Phys.*, 48, 3275 (1968)) on $(H_2O)_2$.

(25) R. Lucchese and H. F. Schaefer, *J. Am. Chem. Soc.*, 97, 7205 (1975).

(26) M. Hanna, *J. Am. Chem. Soc.*, 90, 285 (1968); R. Lefevre, D. V. Radford, and R. J. Stiles, *J. Chem. Soc. B*, 1297 (1968).

(27) R. Lucchese, K. Haber, and H. F. Schaefer, *J. Am. Chem. Soc.*, 98, 7617 (1976).

(28) C. P. Baskin, C. F. Bender, and P. A. Kollman, *J. Am. Chem. Soc.*, 95, 5868 (1973); P. Kollman, S. Rothenberg, and C. F. Bender, *ibid.*, 94, 8016 (1972).

Mg^{2+} (studies on Al^{3+}, K^+, and Ca^{2+} are in progress). Studies on Li^+ hydration[29] show clearly that one must consider *at least* three body forces explicitly or implicitly in order to derive qualitatively correct features about the structure of water surrounding cations. The hydration energies we determined were in good agreement with Kebarle's experiments.[30] The above cation–H_2O interactions have the minimum-energy structure one would predict from simple electrostatics—planar, with C_{2v} symmetry.

Our studies of the structures of $Cl^-(H_2O)$ and $F^-(H_2O)$ are in good agreement with structures found by more accurate calculations.[29] For these studies, we used a crude basis set which overestimated the interaction energies. We also carried out extremely simple electrostatic calculation, placing charges of -1.0 on the anion, $+0.46$ on H, and -0.92 on O, to "calculate", for each given anion–oxygen distance, the minimum-energy angle. The intriguing result is that the simple electrostatic model is capable of rationalizing the directionality of the $F^-\cdots H_2O$ and $Cl^-\cdots H_2O$ interactions. For anion–water interactions at short distances (R-($X^-\cdots O$) = 2.5 Å) the proton is predicted to lie very near the anion–oxygen O line; for $R = 3 - 3.5$ Å, the minimum-energy angle lies about halfway between the "H-bonded" and "dipolar" structure

These simple electrostatic calculations are in good agreement with the most precise calculations.

More recently, we have studied proton affinities of multiply substituted compounds and second-row bases and have compared proton affinities to Li^+ affinities as well.[31] As one can see from Table I,[32-40] there is qualitative agreement between the calculations and experiment. Table I has a selective comparison of theoretical and experimental studies and the results contained therein support the following conclusions:

Very precise SCF calculations can predict near-quantitative geometries for noncovalent complexes (e.g., $(H_2O)_2$, (H_2O-HF), $(HF)_2$) and for strong complexes

(29) P. Kollman and I. D. Kuntz, *J. Am. Chem. Soc.*, **98**, 6820 (1976).

(30) P. Kebarle, in "Environmental Effects on Molecular Structure and Properties", B. Pullman, Ed., D. Reidel, Holland, 1976, p 80.

(31) P. Kollman and S. Rothenberg, *J. Am. Chem. Soc.*, **99**, 1333 (1977).

(32) J. D. Dill, L. C. Allen, W. C. Topp, and J. A. Pople, *J. Am. Chem. Soc.*, **97**, 7220 (1975).

(33) See R. K. Thomas, *Proc. R. Soc. London, Ser. A*, **344**, 579 (1975), for ΔE; J. W. Bevan, A. C. Legon, D. J. Mullen, and S. C. Rogers, *J. Chem. Soc., Chem. Commun.*, 341 (1975), for R.

(34) Theoretical: E. Clementi, J. Mehl, and W. von Niessen, *J. Chem. Phys.*, **54**, 508 (1971); experimental: A. D. H. Clague and H. J. Bernstein, *Spectrochim. Acta, Part A*, **25**, 593 (1969); we have estimated ΔE_0 to be ~1 kcal/mol more exothermic than ΔH_{298}; this estimate is based on the analysis of a number of dimers in ref 7.

(35) See H. Kistenmacher, H. Popkie, and E. Clementi, *J. Chem. Phys.*, **59**, 5842 (1973), for a complete thermodynamic analysis of these ion–water interactions.

(36) Theory: W. Kraemers and G. H. F. Diecksen, *Chem. Phys. Lett.*, **5**, 463 (1970); experimental, P. Kebarle, S. K. Searle, A. Zolla, J. Scarborough, and M. Arshadi, *J. Am. Chem. Soc.*, **89** 6393 (1971) (this latter is a ΔH_{298}, and part of the reason for the 4-kcal/mol discrepancy is clearly the need to compare similar thermodynamic variables).

(37) R. L. Woodin, F. Houle, and W. A. Goddard III, "The Nature of Bonding of Li^+ to H_2O and NH_3. Ab Initio Studies", submitted for publication.

(38) See ref 31; this was a "double-zeta" level calculation; so the absolute value of the interaction energy was overestimated. In ref 27, the Li^+ affinities of NH_3 and H_2NCHO are predicted to be 49.4 and 59.8 kcal/mol; the corresponding experimental quantities (R. H. Staley and J. L. Beauchamp, *J. Am. Chem. Soc.*, **97**, 5920 (1975)) are 39 and 51 kcal/mol.

(39) P. A. Kollman and C. F. Bender, *Chem. Phys. Lett.*, **21**, 271 (1973).

(40) H. Umeyama and K. Morokuma, *J. Am. Chem. Soc.*, **98**, 4400 (1976).

Table I
Comparison of Theoretical and Experimental Binding Energies and Geometries of Non-Covalent Complexes

Complex	$-\Delta E$,kcal/mol[a]		Geometry (R in Å)[b]	
	Theor	Exptl	Theor	Exptl
$(N_2)_2$[c]	0.32		T structure ($R = 3.6$)	T structure
$(H_2O)_2$[d]	5.1	6.9 ± 1.5	Linear ($R = 3.00$)	Linear ($R = 2.98$)
$(HF)_2$[d]	5.4	7.4 ± 1.5	Linear ($R = 2.85$)	Linear ($R = 2.80$)
H_2O-HF[e]	9.2	7.2 ± 1.7	Linear ($R = 2.74$)	Linear ($R = 2.68$)
$(HCOOH)_2$[f]	16.2	15.0	2.7	2.7
K^+-H_2O[g]	16.2	17.9	2.7	
Na^+-H_2O[g]	23.3	24.0	2.2	
Li^+-H_2O[g]	34.1	34.0	1.9	
$H_3O^+-H_2O$[h]	32.2	36.0	2.4	
Li^+-NH_3[i]	40	41	1.9	
Li^+-NH_2-CHO[j]	60	51	1.8	
F^--H_2O[g]	22.2	23.3	2.5	
H^+-H_2O[h]	168	166		
H^+-NH_3[l]	222	207		
$H^+-NH_2CH_3$[l]	234	216		
$H^+-NH-(CH_3)_2$[l]	237	222		
$H^+-N(CH_3)_3$[l]	243	227		

[a] For the theoretical calculations, this is uniformly the D_0 (with no vibrational corrections); for the experimental, this varies from case to case; see footnotes. [b] See the original papers for a description of the geometrical parameters. [c] Theoretical, ref 22; experimental, ref 14. [d] See ref 6 for more detailed discussion of theory and experiment in $(H_2O)_2$ and $(HF)_2$; the experimental values have been changed from ΔH_{298} to ΔE_0 to compare with the theoretical. [e] Theoretical, ref 32; experimental, ref 33. [f] Reference 34. [g] Reference 35. [h] Reference 36. [i] Reference 37. [j] Reference 38. [k] Reference 39. [l] Reference 40.

(Li^+-H_2O, F^--H_2O, H^+-H_2O) can predict interaction energies very well. Experimental ΔE's for weak and moderate strength complexes are of questionable accuracy, and available experimental techniques do not yield geometries of *strong* complexes. In these cases, the results of very accurate theoretical studies (considering the cases where comparisons can be made) can be considered semiquantitatively reliable. In most of our work we have used mainly "double-zeta" level calculations, which predict geometries quite well but exaggerate ΔE's. Even for relatively crude ab initio calculations, the geometries of complexes are well predicted, and the trends in the ΔE's are almost always correct.

The most accurate (lowest total energy) ab initio calculations of which we are aware have been used in constructing Table I; many other studies on these molecules are in the literature.[7,41] (We have actually published calculations at the double-zeta level for all the molecules in the table except $(HCOOH)_2$).

Application of Theoretical Methods to More Complex Phenomena

Thus far we have concentrated on gas-phase dimerization, an area in which the most direct theoretical–experimental comparison can be made. It is one of the real challenges of chemical theory to make

(41) L. J. Schaad in "Hydrogen Bonding", Joesten and L. Schaad, Marcel Dekker, New York, N.Y., 1974, and P. Schuster in "The Hydrogen Bond, Recent Developments in Theory and Experiment", P. Schuster, G. Zundel, and C. Sandorfy, Ed., North-Holland Publishing, Co., Amsterdam, 1976.

Table II
Component Energies[a] (kcal/mol) for $(HF)_2$ as a
Function of θ

	$(HF)_2$[b]		F—H$\cdots$F$\overset{\displaystyle H}{\underset{\displaystyle /\theta}{\cdots}}$		
θ, deg	0	30	37.5	45	60
ΔE^c	−7.44	−7.71	−7.79	−7.82	−7.59
$\Delta E_{ES}{}^d$	−8.36	−8.67	−8.76	−8.78	−8.50
$\Delta E_{POL}{}^e$	−0.67	−0.60	−0.56	−0.52	−0.45
$\Delta E_{CT}{}^f$	−2.46	−2.79	−2.95	−3.14	−3.55
$\Delta E_{EX}{}^g$	4.04	4.35	4.48	4.63	4.90

[a] See ref 6 for a definition of these components.
[b] $R(F\cdots F) = 2.69$ Å, F—H$\cdots$F linear. [c] Total SCF dimerization energy for $(HF)_2$. [d] Electrostatic contribution to the dimerization energy of HF. [e] Polarization contribution to the dimerization energy of HF. [f] Charge-transfer contribution to the dimerization energy of HF. [g] Exchange-repulsion contribution to the dimerization energy of HF.

Table III
Comparison of Predictions of Equation 1 and
ab Initio Calculations

Complex[a]	POTA[a]	POTB[a]	$-\Delta E$ (predicted)[b]	$-\Delta E$ (calcd)[c]
$(Cl_2)_2$	0.008	−0.002	−0.1	−0.2
$O_2C\cdots OH_2$	0.020	−0.059	−4.7	−5.6
$H_3N\cdots SO_2$	0.038	−0.075	−11.5	−11.4
$F^-\cdots H_2O$	0.030	−0.250	−30.2	−39.3
$Li^+\cdots OH_2$[d]	0.265	−0.059	−62.9	−47.2
$H_4N^+\cdots F^-$	0.185	−0.250	−186	−163
$F\cdots HF(^2\pi)$	0.044	−0.005	−0.9	−1.2[e]

[a] In atomic units; considered just minimum energy geometry of complex, as discussed in text. For example, for $O_2C\cdots OH_2$, this is the approach with the water O approaching the CO_2 carbon. For $F^-\cdots H_2O$, used $\theta = 0$ geometry. [b] In kcal/mol. [c] With the exception of $F\cdots HF$, 431G calculations reported in ref 22. [d] Used reference potential at 2 Å from Li^+. [e] Estimated from tabulated results in ref 48.

semiquantitative predictions of solution phenomena and small-molecule–large-molecule interactions in solution. There has been much activity in these areas during the last few years—enough for a complete Account.

Our own interests have led us to examine the energetics of ion-pair *creation* in solution. We chose to study the energetics of the reaction $NH_3 + HF \rightarrow NH_4{}^+F^-$ as a function of water content.[29,42] We treated the first shell of waters quantum mechanically and subsequent shells with a continuum model, and we calculated a ΔH for the above reaction of -20 ± 5 kcal/mol, in surprisingly good agreement with the experimental value of -18 kcal/mol. The reaction is very endothermic in the gas phase, and we were able to delineate the relative stabilities of various solvated structures (*contact* and *solvent-separated* ion pairs) in determining the structure of NH_4F in aqueous solution.

A second area of our interest, stimulated by the great utility of the electrostatic potential in studying small-molecule—small-molecule interactions, has been to evaluate the electrostatic potential at the "active site" of enzymes and between the base pairs of polynucleotides.[43-45]

Generalizations about Noncovalent Interactions

What kind of generalizations emerge from the vast number of studies of noncovalent potential surfaces? Above, we have alluded to the fact that the electrostatic energy is the key component in many interactions. This is not to say that the other components (exchange repulsion, polarization, charge transfer, and dispersion) are not of appreciable magnitude; only that the *directionality* of the electrostatic component and its relative magnitude for different geometries and different complexes are extremely good predictors of the strength and directionality of noncovalent interactions. An interesting example is $(HF)_2$, where we had earlier argued that the reason for the nonzero θ (calculated = 40°) was the charge-transfer component.[46] Recently, we[22] and Umeyama and Morokuma[47] showed clearly

that the electrostatic component was the key (Table II) and that the angular dependence of exchange repulsion and charge transfer cancel each other. A simple dipole–dipole model fails to correctly predict this directionality, but a more "complete" electrostatic picture does correctly predict it. Below, we discuss two further issues: first, how do we derive a simple, electrostatic approach which does predict relative magnitudes and directionalities of noncovalent interactions, and, second, what are some of the exceptions to such a simple picture.

We have suggested that the *electrostatic potentials* of the monomers are good predictors of the nature of nonvalent interactions. The electrostatic potential is not the same as the electrostatic energy, and its magnitude may be a predictor of the other energy components. The reason for our focus on electrostatic potentials is that they are properties of a given monomer and not dependent on evaluating the energy components for each complex involving this monomer.

We have derived an equation[22] (eq 1) which allows

ΔE (kcal/mol)
$$= 4020 \times \text{POTA (au)} \times \text{POTB (au)} \quad (1)$$

one to predict the interaction energy of a Lewis acid and Lewis base (ΔE), given their electrostatic potentials (POTA and POTB) at reference positions. This equation was derived using the results of 431G ab initio electrostatic potentials and potential surfaces. It has qualitative predictability for noncovalent complexes ranging from $(H_2)_2$ to $NH_4{}^+F^-$ (Table III[48]).

We then asked ourselves how we can predict interaction energies involving monomers for which we have done no ab initio calculation; i.e. what is the simplest charge distribution that can qualitatively predict the strength and directionality of the many ab initio calculated noncovalent interactions?

We have found[49] that a simple localized orbital charge distribution, similar to the old Lennard-Jones–Pople model for H_2O, can explain much of the strength and directionality of these noncovalent interactions. The key question is where do we place the point charges for complex molecules? There are probably a number of satisfactory ways to make such choices, but we have chosen to use electronegativities, dipole moments, and

(42) See also J. O. Noell and K. Morokuma, *J. Phys. Chem.*, **80**, 2675 (1976), for a theoretical study of this reaction.
(43) D. M. Hayes and P. A. Kollman, *J. Am. Chem. Soc.*, **98**, 3335 (1976).
(44) D. M. Hayes and P. Kollman, *J. Am. Chem. Soc.*, **98**, 7811 (1976).
(45) M. E. Nuss and P. Kollman, *J. Am. Chem. Soc.*, to be submitted.
(46) P. Kollman, *J. Am. Chem. Soc.*, **94**, 1837 (1972).
(47) H. Umeyama and K. Morokuma, *J. Am. Chem. Soc.*, **99**, 1316 (1977).
(48) P. Noble and R. Kortzeborn, *J. Chem. Phys.*, **52**, 5375 (1970).
(49) P. A. Kollman, unpublished results.

van der Waals radii in our model to determine the location of the charges. Some examples of molecules for which we have derived the charge distribution are shown in Figure 1. For these noncovalent complexes, lone pairs need explicit representation, but bond pairs (both σ and π) can be incorporated into a partial charge representation. A partial charge (atom-centered) representation of lone pairs as well is adequate (as we have discussed above) for $X^-\cdots H_2O$, but not for $(HF)_2$, where such a distribution would predict the dimer to be linear ($\theta = 0°$). There are some ambiguities: is the nitrogen lone pair in formamide a lone pair or part of a conjugated system? Either representation correctly predicts that this nitrogen, unlike an amine N, is a rather poor Lewis base.

In summary, we feel that the prescription is a very powerful tool which can be used to derive a "first-order" description of the electronic structure of molecules. The electrostatic potential surrounding such a charge distribution is a very useful predictor of the structure and energetics of the noncovalent interactions in which such a molecule can participate. Del Bene[50] has noted that dimer surfaces of H-bonded systems often have the A–H bond pointing toward a "lone pair", but often long-range dipole–dipole effects cause deviations from this lone-pair directionality. In considering the electrostatic potentials from the simple charge representations described above, we incorporate both of these effects. Tomasi et al.[51] have developed a transferable point-charge representation of electron distributions from ab initio wave functions; this approach is similar in spirit to our approach. Allen[52] has developed a simple model for hydrogen bonding which has elements in common with our eq 1.

Some Exceptions to the Simple Electrostatic Picture

Equation 1 correctly predicts that amines are better bases toward H^+ than are ethers and fluorides but does not correctly predict the order of proton affinities upon methyl substitution in the amines: $H_3N < MeNH_2 < (Me)_2NH < Me_3N$.[31] The polarization energy (Me has a higher polarizability than H) can rationalize this trend.[31,42] The simple picture does not take into account geometry changes and "covalent bonding effects" upon complex formation; thus, $C=C$ π-bonded molecules have a significantly higher proton affinity than the electrostatic model suggests.[31]

One of the intriguing trends in proton affinities is the difference in the methyl substituent effect on N, O, and F bases. The differences between the proton affinities of MeX and HX (MeX has the greater proton affinity) are 9, 16, and 35 for X = N, O, and F. We were able to show[31] that these differences are mostly due to the difference in electrostatic properties of the monomers. For example, the lone-pair region of MeF is more negative (nucleophilic) than that of HF, whereas $MeNH_2$ has a less negative region than NH_3 (MeOH and H_2O have close to identical lone-pair electrostatic potentials).

Lithium atom interacts very strongly with polar molecules, significantly more strongly than one would

Table IV
Amine and Amide Affinities for a Number of Lewis Acids^a

Acid	Base		
	NH_3	$N(CH_3)_3$	H_2NCHO
H^+	222	243	202
HF	16.1	16.0	13.0
Li^+	49.4	49.2	59.8
LiF	30.5	29.7	30.6
ClF	8.0		5.9

^{a} Interaction energies calculated with the 431G basis set (for Li, used the 521G basis) in kcal/mol; see ref 31.
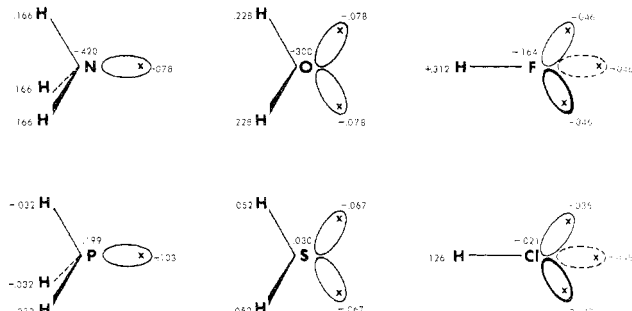

Figure 1. Charge representation of some molecules discussed in ref 22. The lone-pair locations are determined by the van der Waals radii and the hybridization.

predict from electrostatic potential considerations.[53] This is because of its unusually high polarizability relative to its small size.

The relative affinity of amines and amides for Li^+, LiF, H^+, HF, and FCl is shown in Table IV. These results find Li^+ and LiF to be unusual Lewis acids in that they interact more strongly with amides than amines. We have argued[31] that this is because amides have a more tightly held lone pair than amines and, thus, Li^+ is able to penetrate much more closely to the amide than the amine. At a given Li–B distance the amine interaction has a larger *attractive* energy (electrostatic + polarization + charge transfer) than the amide (see ref 22), but the smaller magnitude of the exchange repulsion in the amide allows the Li^+ to penetrate more closely to this species.

Above, we have pointed out that covalent (spin-pairing) effects probably make an important contribution to the stability of $(O_2)_2$ and $(NO)_2$. $2BH_3 \rightarrow B_2H_6$ is not a noncovalent interaction according to our earlier definition because the nature of the covalent bonding is different in reactants and products.

Complexes involving transition-metal atoms and heavier members of the periodic chart are likely to involve more exceptions from eq 1 than those molecules made up from the lighter elements. For example, the qualitative structures of amine–I_2 complexes are consistent with the predictions of the electrostatic potentials, but the relative interaction energies for the amines $|\Delta H(TMA-I_2)| > |\Delta H(NH_3-I_2)|$[54] indicate that charge-redistribution effects are likely to be larger than those found when F_2 or Cl_2 as the Lewis acid.[25] Completely nonpolar complexes would be held together by dispersion attraction.[22,55]

(50) J. Del Bene, *J. Chem. Phys.*, **63**, 4666 (1975), and references therein.
(51) R. Bonaccorsi, E. Scrocco, and J. Tomasi, *J. Am. Chem. Soc.*, submitted for publication.
(52) L. C. Allen, *J. Am. Chem. Soc.*, **97**, 6921 (1975).

(53) M. Trenary, H. F. Schaefer, and P. Kollman, *J. Am. Chem. Soc.*, **99**, in press.
(54) S. Nagakura, *J. Am. Chem. Soc.*, **80**, 520 (1958); note that there are solution-phase experimental studies. Whether this is the correct order in the gas phase has not been resolved.

Summary and Future Directions

As we have tried to indicate, the study of noncovalent complexes involves a fruitful interplay between theory and experiment. We have concentrated our attention mainly on the structure and binding energy of such complexes; much theoretical and experimental work has concerned itself with spectroscopic properties (NMR, UV, IR), but we have not had space here to discuss these.[7,41]

It is an important theme of our work that the "electrostatic" properties of molecules are a key to the structure and energy of their interactions, and we have tried to put all noncovalent bonding into a single picture. We do not feel there is anything intrinsically special about hydrogen bonding, van der Waals complexes, charge-transfer interactions, or ionic interactions but feel all are, to first order, electrostatic interactions. The other energy components are important, and we have tried to show specific examples of this. However, it is our opinion that the approach outlined above is the most sensible way to think about the directionality and relative energies of most noncovalent interactions.[55] Not only does it give a simple way to semiquantitatively systematize a large body of known facts but it also is consistent with more quantitative empirical potential function approaches to study intermolecular interactions.

It is also worth stressing that the directionality of electrophilicity and nucleophilicity predicted from our simple model is often the same as that predicted by a simple HOMO–LEMO picture. For example, the direction of the most positive electrostatic potential and the site of the largest LEMO coefficient in SO_2 coincide (above the molecular plane, approximately over the sulfur). Thus, it is likely that some of the features of our charge distributions can be used to rationalize chemical reactivity as well as noncovalent interactions. For the purpose of noncovalent interactions, we have stressed the electrostatic aspects, rather than the HOMO–LEMO aspects, of the charge distributions because of the many examples discussed above in which the electrostatic component has been the dominant determinant of directionality.

We have concentrated in this Account on intermolecular effects, but there have been a number of ab initio studies on intramolecular interactions. These indicate that electrostatic effects, after factoring out the intramolecular geometry constraints and the energetic contributions from eclipsed bonds and other types of "strain", can provide a qualitative prediction of strength and directionality of many intramolecular noncovalent interactions.[56]

(55) With the obvious exception of rare gas–rare gas and hydrocarbon–hydrocarbon interactions, which are likely to be mainly dispersion dominated.

(56) P. Kollman and G. L. Kenyon, *J. Am. Chem. Soc.*, **99**, 1892 (1977); S. Dietrich, P. Kollman, E. C. Jorgensen, and S. Rothenberg, *ibid.*, **98**, 8310 (1976).

Electrolyte Theory—Improvements since Debye and Hückel

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In 1923 Debye and Hückel[1] provided, in a simple theory, the correct equation for the behavior of electrolyte solutions in the limit of very low concentration. This eliminated an anomaly that had troubled physical chemists and allowed a great advance in the semiempirical, semitheoretical treatment of dilute electrolytes at finite concentrations. While the severe approximations of Debye and Hückel were found not to affect the limiting law, great uncertainty[2] remained concerning any higher order terms.

There were many intermediate advances[3] through the years, especially in the work of Mayer, Kirkwood, Poirier, and Friedman. However, a really sound and fruitful theory for electrolytes at substantial concentration has only emerged in the last decade. While these contributions have been summarized in reviews[4,5] addressed to specialists in statistical mechanics and electrolyte theory, it seemed desirable to call this advance to the attention of physical chemists and solution chemists more generally. This more recent theory may be too complex for use or for presentation in some cases, but even then it should be realized that a rigorous

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(1) P. Debye and E. Hückel, *Phys. Z.*, **24**, 185, 334 (1923); **25**, 97 (1924).
(2) H. S. Frank and P. T. Thompson, *J. Chem. Phys.*, **31**, 1086 (1959).
(3) This work is reviewed by H. L. Friedman, "Ionic Solution Theory", Wiley-Interscience, New York, N.Y., 1962.
(4) H. C. Andersen, *Mod. Aspects Electrochem.*, **No. 11**, 1 (1975).
(5) J. C. Rasaiah, *J. Solution Chem.*, **2**, 301 (1973).