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Strength of the N—H···O═C and C—H···O═C Bonds in Formamide and *N*-Methylacetamide Dimers

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The structures of the dimers of formamide and *N*-methylacetamide have been calculated at the ab initio electronic structure theory level, second-order Møller−Plesset perturbation theory (MP2) with augmented correlation consistent basis sets. Five unique structures were optimized for the formamide dimers at the MP2/aug-cc-pVDZ and MP2/aug-cc-pVTZ levels. At the optimized geometries obtained with the aug-cc-pVTZ basis set, MP2 energies were evaluated with the aug-cc-pVQZ basis set, allowing an extrapolation of the energies to the complete basis set limit. Four structures were found for the *N*-methylacetamide dimer at the MP2/aug-cc-pVDZ level, and single-point energies were calculated at the MP2/aug-cc-pVTZ level. In both systems, the basis set superposition error was estimated with the counterpoise method. The strength of the N—H···O═C bond has a mean value of 7.1 kcal/mol in the formamide dimers and a mean value of 8.6 kcal/mol in the *N*-methylacetamide dimers. The difference in hydrogen bond strengths is attributed to differences in basicity at the carbonyl oxygen receptor site. In several dimers C—H···O═C hydrogen bonds play an important role in stabilizing these intermolecular complexes, increasing the interaction energy by 1.1−2.6 kcal/mol per interaction.

Introduction

It is well established that N—H···O═C hydrogen bonds play a critical role in the structure and properties of proteins and nucleic acids as well as in the behavior of many solvent systems.[1] It is important to include the effects of hydrogen bonding in molecular simulations based on classical force fields if one hopes to reproduce and explain a wide range of chemical phenomena. Because there is a paucity of experimental data with respect to hydrogen bond strengths and structures of isolated systems, quantum chemical calculations have been used to aid in parametrizing the molecular mechanics force fields. Until recently, the main source of these parameters has been low-level electronic structure calculations (Hartree−Fock with small basis sets) that are simply not good enough for a reliable prediction of the hydrogen bond strength.[2] However, it has been established that if high-quality basis sets are used with treatment of the electron correlation at the second-order Møller−Plesset (MP2)[3] level, then one can predict reliable hydrogen bond strengths for molecular systems with modest to strong hydrogen bonds.[4−9] Here we report the results of high-level calculations on the dimers of formamide and *N*-methylacetamide (NMA) to better determine the structures and relative stabilities of the intramolecular hydrogen-bonding interactions that occur between simple amides.

Formamide is the simplest amide structure, and many calculations on the formamide dimer have been made to study N—H···O═C hydrogen bonds.[9−29] The most stable structure reported for the formamide dimer, both theoretically and experimentally,[30] has two hydrogen bonds corresponding to the head-to-tail cyclic structure, **1** (see Chart 1). The total electronic association energy for **1** has been calculated with the MP2 method, yielding values of −11.4 to −14.0 kcal/mol depending on the basis set used.[9,23,29] The highest level of basis set, cc-pV5Z, provides the highest interaction energy. Density functional theory has also been used to study the dimerization energy of **1**, and the best agreement with the MP2 calculations was obtained with the BLYP exchange-correlation functional.[25] The majority of the prior theoretical studies have considered only dimer **1**, and only a few have examined the possibility of different orientations between the two amides. Formamide dimerization energies have not been experimentally determined in the gas phase.

Dimers of NMA are the simplest model for studying the N—H···O═C hydrogen bonds that occur in proteins. Like formamide, most prior computations of hydrogen bond strengths for NMA dimers have been limited to coplanar arrangements.[11,14,19,26,31−35] Because of the high barrier to rotation about the amide bond, NMA exhibits cis (methyl groups on the same side) and trans (methyl groups on opposite sides) geometric isomers (see Chart 2). The most recent theoretical study[35] reports one structure for a *cis*-NMA dimer and one structure for a *trans*-NMA dimer with HF/DZP optimized geometries and MP2 single-point energies with the aug-cc-pVDZ basis set at these geometries. The *cis*-NMA formed the most stable dimer with a cyclic structure very similar to that in **1** with a total association energy of 14.0 kcal/mol. Like formamide, NMA dimerization energies have not been experimentally determined in the gas phase.

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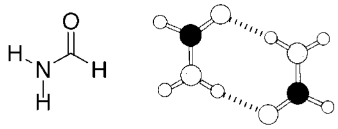
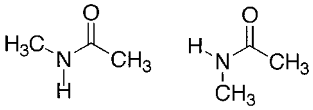
CHART 1



formamide **1**

CHART 2



trans-NMA *cis* -NMA

Herein we report the results of calculations on five formamide dimers at the MP2 level of theory with high-quality basis sets. Three of them are in agreement with previous results, and the other two have not been reported. We also report calculations on four NMA dimers. We find the same cyclic structure previously reported for the most stable *cis*-NMA dimer, but the previously reported *trans*-NMA dimer is not stable at the higher level of theory used in our study. Complete structural parameters and energies are reported for all structures. Energies for individual N—H···O=C and C—H···O=C hydrogen bonds are estimated and discussed.

Theoretical Details

Starting geometries of the formamide and NMA dimers were obtained at the Hartree−Fock (HF) level (HF/6-31G*) with the program system JAGUAR.[36] All possible formamide dimers found at the HF level were reoptimized at the MP2 level with the augmented correlated-consistent basis sets[37] aug-cc-pVDZ and aug-cc-pVTZ. Since MP2/aug-cc-pVQZ geometry optimizations would be extremely computationally expensive, we used the geometry obtained at the MP2/aug-cc-pVTZ level for the MP2/aug-cc-pVQZ calculations. We extrapolated the MP2/aug-cc-pVXZ for $X = D$, T, and Q total energies to the complete basis set (CBS) limit using the mixed exponential Gaussian extrapolation.[38] For NMA dimers, the geometry optimizations were done at the MP2/aug-cc-pVDZ level and single-point MP2/aug-cc-pVTZ calculations were performed at these geometries. Electronic association energies, D_e, were obtained by subtracting the energy of two fully optimized monomers from the energy of the dimer. Basis set superposition error (BSSE) was estimated by the counterpoise method[39] for all dimers with each basis set. In this method the energy of the monomer in the geometry of each dimer was evaluated with "ghost" orbitals and without these additional orbitals. Total energies and Cartesian coordinates are provided as Supporting Information.

All MP2 optimizations and single-point energy calculations were performed by using the NWChem program[40] on the massively parallel IBM computer in the Molecular Science Computing Facility in the William R. Wiley Environmental Molecular Sciences Laboratory at Pacific Northwest National Laboratory.

Results and Discussion

Formamide Dimers. The optimized geometries found for the formamide dimers **1**−**5** are shown in Figure 1, and structural parameters for the hydrogen bonds are given in Table 1. As expected, cyclic conformer **1** (Figure 1) is the most stable in agreement with previous studies. This structure has two N—H···O=C hydrogen bonds, with both monomers lying in the plane. Dimer **2** has one N—H···O=C hydrogen bond and one C—H···O=C hydrogen bond. Dimers **3** and **4** have been not reported previously. In these structures, there is one N—H···O=C hydrogen bond and the monomers lie in different planes. A previously reported structure for a formamide dimer with only one N—H···O bond in which both monomers lie in the same plane[23,27] is not stable at the MP2 level with the augmented correlation-consistent basis sets used in this study. The least stable dimer, **5**, exhibits two C—H···O=C hydrogen bonds.

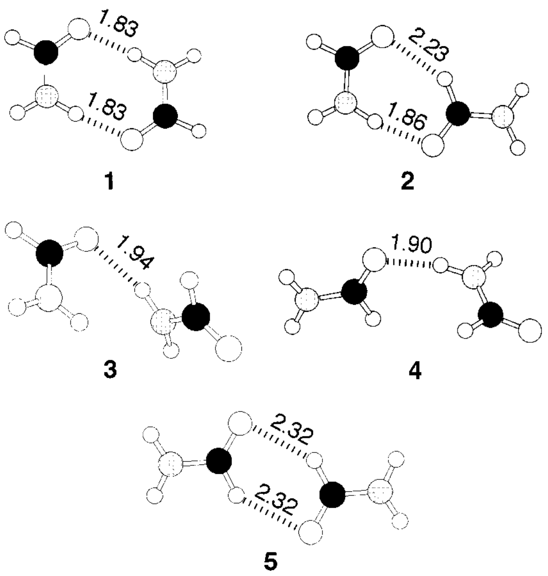


Figure 1. Formamide dimers **1**−**5** optimized at MP2/aug-cc-pVTZ. Hydrogen bonds and distances (Å) are shown.

As shown in Table 1, the structural parameters for the hydrogen bonds obtained at the MP2/aug-cc-pVDZ and MP2/aug-cc-pVTZ levels are very similar for all dimers. The mean difference between the two basis sets for H···O distances is 0.03 Å in the N—H···O hydrogen bonds and 0.04 Å in the C—H···O hydrogen bonds. The aug-cc-pVTZ basis set always yields slightly shorter distances and more linear hydrogen bonds. The remaining geometry parameters show even less dependence on the basis set. As shown in Table 1, the shortest hydrogen bond distances for H···O and N···O interactions are for dimer **1**, and these are also the most linear hydrogen bonds.

Comparison of our high-level calculations with previous lower level calculations (Table 1) for dimers **1**, **2**, and **5** shows that, in all cases, the smaller DZP basis set yields larger H···O and N···O distances, with the largest difference being ~0.15 Å. A similar trend is found for the hydrogen bond angles where a small basis set yields less linear hydrogen bonds.

Electronic association energies, D_e, for **1**−**5** were obtained with several basis sets at the aug-cc-pVDZ optimized geometry. The results are given in Table 2, with and without BSSE correction, and the extrapolated D_e values are also included. The various energies for the different dimers as a function of the basis set are shown in Figure 2. Comparison to previous calculations is also given where possible.

The extrapolated D_e value for **1** is −14.4 kcal/mol, 2.6 kcal/mol more stable than a previous MP2/DZP calculation without BSSE correction[23] and 0.3 kcal/mol more stable than the most recent MP2 calculation,[29] although we note that it is not possible to obtain an accurate D_e in the latter case. For this dimer, a previous calculation at the CCSD(T) level with an aug-cc-pVDZ basis set for hydrogens gives −13.4 kcal/mol.[9] We note that the BSSE-corrected value for the aug-cc-pVQZ basis set is within 0.1 kcal/mol of the CBS value. Dividing by 2, we find that $D_e = -7.2$ kcal/mol per N—H···O=C hydrogen bond in **1**.

TABLE 1: Structural Parameters for Hydrogen Bonds in Dimers 1−5[a]

	N—H···O=C bond				C—H···O=C bond			
	H···O	N—H···O	C=O···H	N···O	H···O	C—H···O	C=O···H	C···O
1								
aug-cc-pVDZ[b]	1.836	174.2	120.2	2.863				
aug-cc-pVTZ[b]	1.825	174.2	120.1	2.842				
ref 23[c]	1.99	169.7		2.99				
2								
aug-cc-pVDZ	1.876	168.8	106.4	2.891	2.274	143.6	113.8	3.231
aug-cc-pVTZ	1.857	168.9	105.7	2.863	2.234	144.9	113.1	3.190
ref 23[c]	2.00	164.3		2.99	2.38	138.7		3.28
3								
aug-cc-pVDZ	1.976	156.0	111.0	2.939				
aug-cc-pVTZ	1.935	158.4	110.3	2.902				
4								
aug-cc-pVDZ	1.940	162.7	108.1	2.929				
aug-cc-pVTZ	1.904	165.8	108.9	2.894				
5								
aug-cc-pVDZ[b]					2.355	142.3	95.3	3.301
aug-cc-pVTZ[b]					2.320	144.4	93.2	3.271
ref 23[c]					2.46	134.0		3.32

[a] Angles in degrees and distances in angstroms. [b] Both hydrogen bonds are identical. [c] Geometries optimized at the MP2/DZP level.

TABLE 2: Electronic Association Energies (D_e, kcal/mol) for the Formation of Dimers 1−5 as a Function of Basis Set

	aug-cc-pVDZ[a]		aug-cc-pVTZ[b]		aug-cc-pVQZ[b]		est CBS value
	w/o BSSE	w/BSSE	w/o BSSE	w/BSSE	w/o BSSE	w/BSSE	
1	−15.80	−14.68	−16.83	−13.98	−15.37	−14.49	−14.35
	−17.0[c1]	−11.4[c1]					
	−17.4[d1]	−12.4[d1]					
	−17.3[d2]	−12.5[d2]					
		−12.36[e]		−13.52[e]		−14.02[e]	
2	−10.81	−9.01	−11.59	−9.39	−10.48	−9.77	−9.70
	−11.7[c1]	−7.2[c1]					
3	−8.63	−6.22	−9.15	−7.21	−8.08	−7.43	−7.34
4	−7.66	−5.77	−8.16	−6.58	−7.33	−6.80	−6.76
5	−5.97	−4.61	−6.24	−4.79	−5.52	−5.02	−5.02
	−6.3[c1]	−2.8[c1]					
	−6.4[c2]	−4.9[c2]					

[a] Geometries optimized at the MP2/aug-cc-pVDZ level. [b] Geometries optimized at the MP2/aug-cc-pVTZ level. [c] Reference 23: (1) MP2/DZP, (2) MP2/TZ2P. [d] Reference 25: (1) MP2/6-31G(d,p), (2) BLYP/6-31G(d,p). [e] Reference 29, single-point energies at MP2/DZ(d,p) geometries. At the aug-cc-pV5Z level, $D_e = -14.04$ kcal/mol. See the discussion of how association energies were calculated in the footnote.

The D_e values shown in Table 2 for dimers **3** and **4** correspond directly to the hydrogen bond strength since only one N—H···O hydrogen bond is present in each structure. Thus, taking the three D_e values of −7.2 (**1**), −7.3 (**3**), and −6.8 (**4**) kcal/mol, we obtain an average of −7.1 ± 0.3 kcal/mol for the strength of the N—H···O=C hydrogen bond. Again, the BSSE-corrected aug-cc-pVQZ basis set results are within 0.1 kcal/mol of the CBS value.

The second most stable dimer, **2**, has a D_e value of −9.7 kcal/mol. Taking the mean D_e value for a N—H···O=C hydrogen bond to be −7.1 kcal/mol, the association energy for dimer **2** shows that there is an extra interaction stabilizing this structure. This extra stabilization can be attributed to a C—H···O=C hydrogen bond that contributes an additional −2.6 kcal/mol. Similarly, **5** has two C—H···O=C hydrogen bonds, and by dividing the D_e value by 2, we obtain a C—H···O=C hydrogen bond strength of −2.5 kcal/mol. The best previous calculation,[23] shown in Table 2, for this dimer predicts a C—H···O=C hydrogen bond with a $D_e = -3.2$ kcal/mol without BSSE correction. However, if the BSSE correction is included, the strength of this hydrogen bond is closer to our estimate, now differing by only 0.2 kcal/mol. Analogous hydrogen-bonding motifs involving formyl hydrogen donors have been computed at comparable levels of theory for acetal[7] and *N*,*N*-dimethylformamide (DMF) dimers.[41] The calculated D_e values for individual C—H···O=C bonds in these systems, after BSSE correction, are −2.8 and −2.7 kcal/mol, respectively.

Examination of Table 2 reveals that the BSSE corrections are more uniform and, in general, smaller for the biggest basis set. At the MP2/aug-cc-pVDZ level, the BSSE correction ranges from 7% in dimer **1** to 28% in dimer **3**, whereas, at the MP2/aug-cc-pVQZ level, the BSSE correction varies between 6% and 9%. The BSSE-corrected aug-cc-pVQZ results are in excellent agreement with the values extrapolated to the CBS limit.

The BSSE corrections show some interesting behavior with respect to geometry at the smaller aug-cc-pVDZ basis set level, as shown in Table 3. We calculated the energies at the MP2/aug-cc-pVDZ level with geometries optimized at this level and at the MP2/aug-cc-pVTZ level. Prior to the BSSE correction, the D_e values at both geometries are very similar. However, the BSSE corrections result in significant changes in energy. For example, with dimer **1**, the difference in D_e without the BSSE corrections is 0.02 kcal/mol and with the BSSE correction this difference is 1.3 kcal/mol. These results suggest that one must be careful with BSSE corrections at basis sets of the size of aug-cc-pVDZ.

For systems the size of the formamide dimer, it is computationally prohibitive to calculate vibrational frequencies at the levels of theory that we used for the geometry optimization. To estimate the zero-point energy (ZPE) and thermal correction for this system, we carried out density functional calculations with the BLYP[42] gradient-corrected exchange-correlation functional. These calculations were performed using the DGauss program[43] and the TZVP(A2) basis set[44] for all dimers. The results of these corrections are shown in Table 4.[45] We found that the total corrections (ZPE and thermal at 298 K) are in the range from 2.1 kcal/mol for **5** to 2.4 kcal/mol for **2**. This means that the enthalpy of binding at 298 K for these dimers would be an average of 1.7 kcal/mol less negative than D_e values given in Table 2 after the enthalpy correction term of $-RT$ ($T = 298$ K) is included.

NMA Dimers. The cis isomer of NMA is less stable than the trans isomer of NMA.[46] An experimental NMR measurement estimates the energy difference to be 2.8 kcal/mol.[47] We find

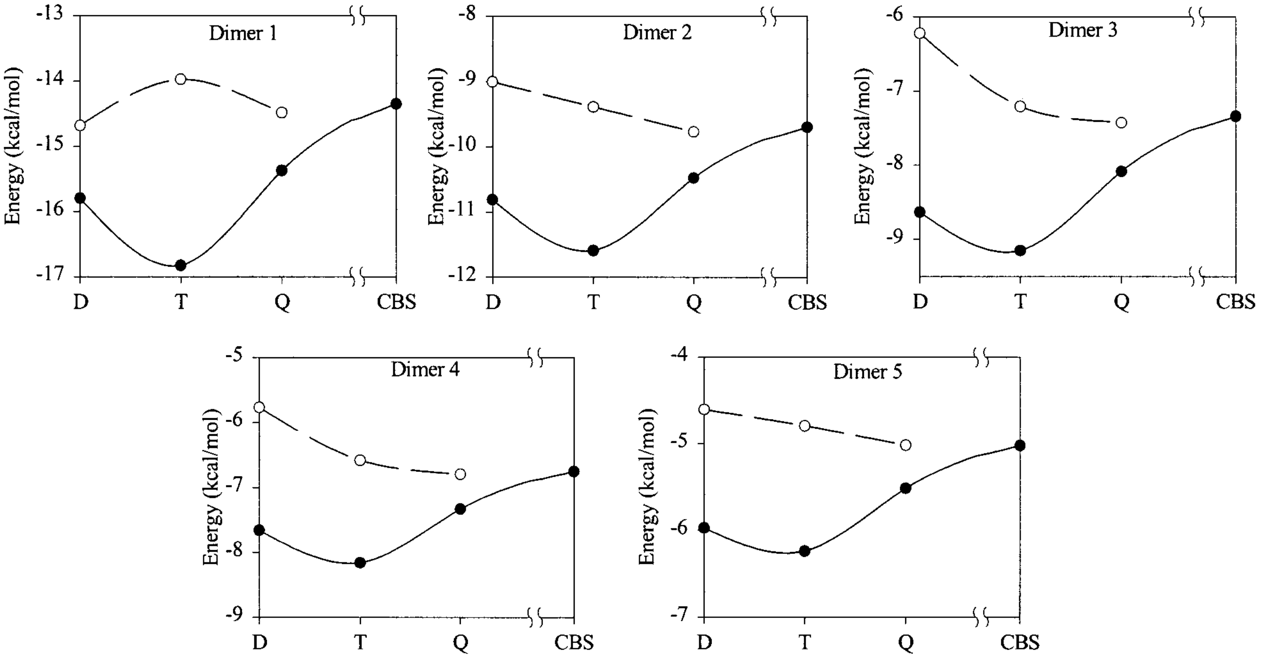


Figure 2. Behavior of the electronic association energies (D_e) for formamide dimers as a function of the basis set. *D* is for aug-cc-pVDZ, *T* for aug-cc-pVTZ, *Q* for aug-cc-pVQZ, and CBS is the extrapolated value. The solid line is for the D_e without BSSE corrections, and the dashed line includes the BSSE correction.

TABLE 3: Comparison of Electronic Association Energies (D_e, kcal/mol) for the Formation of Dimers 1−5 at the MP2/aug-cc-pVDZ Level with Different Optimized Geometries

	aug-cc-pVDZ optimized geometry		aug-cc-pVTZ optimized geometry	
	w/o BSSE	w/BSSE	w/o BSSE	w/BSSE
1	−15.80	−14.68	−15.82	−13.34
2	−10.81	−9.01	−10.81	−8.92
3	−8.63	−6.22	−8.61	−6.77
4	−7.66	−5.77	−7.65	−6.21
5	−5.97	−4.61	−5.94	−4.50

TABLE 4: Electronic Association Energies and Dimerization Enthalpies for the Formation of Dimers 1−5[a]

	D_e	ΔE^0	ΔE^{298}	ΔH^{298}
1	−14.35	−12.10	−12.06	−12.65
2	−9.70	−7.62	−7.26	−7.86
3	−7.34	−5.53	−5.04	−5.63
4	−6.76	−5.34	−4.52	−5.11
5	−5.02	−4.00	−2.90	−3.49

[a] D_e values are the CBS limit electronic association energies without basis set superposition energy corrections. ΔE^0 values are the binding energies plus the zero-point energies. ΔE^{298} values are the binding energies plus zero-point energies and thermal corrections. $\Delta H^{298} = \Delta E^{298} + \Delta nRT$. All the quantities are in kilocalories per mole.

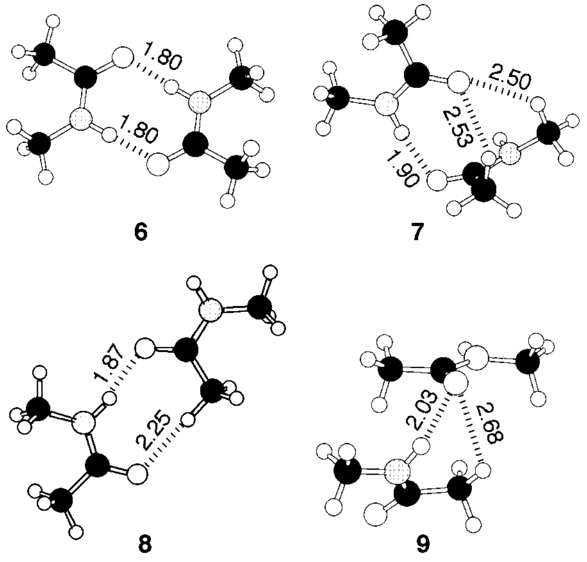


Figure 3. NMA dimers **6**−**9** optimized at MP2/aug-cc-pVDZ. Hydrogen bonds and distances (Å) are shown.

the *cis*-NMA monomer to be less stable than the *trans*-NMA monomer by 2.3 kcal/mol at the MP2/aug-cc-pVTZ level calculated at the MP2/aug-cc-pVDZ geometry. In the current study we report dimers formed between two *cis*-NMA monomers and between two *trans*-NMA monomers, but do not consider mixed dimers composed of *cis*-NMA and *trans*-NMA. Examination of possible structures yielded three *cis*-NMA dimers, **6**−**8**, and one *trans*-NMA dimer, **9**. The optimized geometries found are shown in Figure 3, and structural parameters for the hydrogen bonds are given in Table 5. Electronic association energies, D_e, for these dimers are reported in Table 6. To allow a direct comparison of hydrogen bond strengths, we have taken the *cis*-NMA monomer as a reference for computing D_e values of **6**−**8** and the *trans*-NMA monomer as a reference for computing the D_e value of **9**.

The *cis*-NMA dimer **6**, with two N−H···O=C hydrogen bonds, is the most stable structure. After BSSE correction, our best level of theory (MP2/aug-cc-pVTZ) predicts that a single N−H···O=C hydrogen bond in this molecule has $D_e = -8.6$ kcal/mol. This is 1.5 kcal/mol stronger than the average for the same type of hydrogen bond in the formamide dimer. The difference cannot be rationalized in terms of the acidity of the N−H donor. Examination of the gas-phase proton affinities of the conjugate anions of formamide (360 kcal/mol)[48] and NMA (362 kcal/mol)[49] reveals the N−H proton of NMA to be a slightly weaker acid than that of formamide. However, the stronger N−H···O=C hydrogen bond found for NMA can be explained by the enhancement in the basicity of the C=O acceptor that results from methyl substitution. The gas-phase

TABLE 5: Structural Parameters for Hydrogen Bonds in Dimers 6−9[a]

	N—H···O ═C bond				C—H···O ═C bond			
	H···O	N—H···O	C═O···H	N···O	H···O	C—H···O	C═O··· H	C···O
6	1.799[b] 2.00[c]	177.7	118.6	2.832				
7	1.904	171.1	101.0	2.919	2.527	119.2	120.9	3.211
					2.496	126.5	163.6	3.273
8	1.867	169.0	122.2	2.881	2.249	177.4	117.4	3.346
9	2.035	148.1	106.3	2.949	2.685	118.3	91.4	3.347

[a] Angles in degrees and distances in angstroms. [b] Both hydrogen bonds are identical. [c] Reference 35.

TABLE 6: Electronic Association Energies (D_e, kcal/mol) for the Formation of Dimers 6−9 as a Function of Basis Set at MP2/aug-cc-pVDZ Geometries

	aug-cc-pVDZ		aug-cc-pVTZ	
	w/o BSSE	w/ BSSE	w/o BSSE	w/ BSSE
6	−17.90 −16.4[a]	−16.23 −14.0[a]	−19.06	−17.18
7	−13.35	−11.83	−14.18	−12.37
8	−11.49	−10.20	−12.24	−10.76
9	−12.77	−10.53	−11.44	−9.67

[a] Reference 35, MP2/aug-cc-pVDZ single- point energy on HF/DZP optimized geometry.

proton affinity of formamide (196.5 kcal/mol) is significantly lower than that of NMA (212.4 kcal/mol).[50]

The *cis*-NMA dimers **7** and **8** each have one N—H···O═C hydrogen bond. The more stable dimer, **7**, has two C—H···O═C hydrogen bonds, whereas the less stable dimer, **8**, has only one. Taking −8.6 kcal/mol as the strength of a N—H···O═C hydrogen bond in NMA, we estimate each C—H···O hydrogen bond in **7** to contribute 1.9 kcal/mol to the observed D_e and in **8** to contribute −2.2 kcal/mol to the observed D_e. These estimates are consistent with prior observations of C—H···O═C bond strengths ranging from 2 to 3 kcal/mol for aliphatic hydrogen donors in cases where the conjugate carbanion is stabilized by electron-withdrawing substituents or delocalization.[41] In **7** and **8**, where the methyl hydrogen donor is attached to a carbonyl carbon, the conjugate carbanion is stabilized by the presence of an enolate resonance form.

The previously reported geometry of *trans*-NMA[35] is not stable at the higher level of theory used here and relaxed to the new structure **9**. Dimer **9** has one N—H···O═C hydrogen bond and one C—H···O═C hydrogen bond. Dimer **9** exhibits a D_e value most similar to that of **8**, consistent with the number and type of hydrogen bonds. Again taking −8.6 kcal/mol as the D_e value for the N—H···O═C hydrogen bond, we obtain our lowest estimate, $D_e = -1.1$ kcal/mol for a C—H···O═C interaction. In a prior study of DMF dimers, we found that analogous C—H···O═C hydrogen bonds, involving *N*-methyl hydrogen donors, gave an average $D_e = -2.1$ kcal/mol.[41]

Conclusions

We have reported the most accurate structures and energetics available for formamide dimers and NMA dimers. In several cases, previously reported geometries could not be located at the higher levels of theory. In addition, several new geometries have been identified. For both sets of dimers, the most stable geometry is a cyclic structure with two N—H···O═C hydrogen bonds. However, the strength of this hydrogen bond in the NMA dimer, **6**, is 1.5 kcal/mol stronger than in the formamide dimer, **1**. We attribute the difference in N—H···O═C hydrogen bond strengths to the differences in oxygen basicity. We find that C—H···O═C hydrogen bonds also play an important role in stabilizing these intermolecular complexes, adding stabilization ranging from 1.1 to 2.6 kcal/mol.

Computation of accurate structures and hydrogen-bonding energies for dimers of this sort is critical to the development of accurate molecular mechanics force fields.[51] In particular, if the force field contains an explicit representation of electronic polarizability, it becomes feasible to fit force field parameters directly to gas-phase dimers and expect that correct results will be obtained in the condensed phase. Preliminary results indicate that employment of the dimer data presented above to develop polarizable force field models for formamide and acetamide yields excellent agreement with experiment for condensed-phase properties obtained from liquid-phase simulations (heat of vaporization, volume, radial distribution function). In contrast, use of binding energies and structures obtained from lower levels of theory results in significant errors in these properties if the same force field development protocol (in which direct fitting of parameters to condensed-phase experimental data is minimized) is applied. The ability to produce benchmark hydrogen-bonded structures and energies over a wide range of chemistry will allow such polarizable force fields with broad coverage of chemical space to be developed. In a subsequent paper, we will demonstrate that the high-quality results described here can be reproduced at a significantly lower computational cost via the use of pseudospectral local MP2 methods.[52]

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Supporting Information Available: Total energies and Cartesian coordinates of optimized structures in angstroms. This material is available free of charge via the Internet at http://pubs.acs.org**.**

References and Notes

(1) (a) Baker, E. N.; Hubbard, R. E. *Prog. Biophys. Mol. Biol.* **1984**, *44*, 97. (b) Dill, K. A. *Biochemistry* **1990**, *29*, 7133. (c) Popot, J.-L.; Engelman, D. M. *Biochemistry* **1990**, *29*, 4031. (d) Jeffrey, G. A.; Saenger, W. *Hydrogen bonding in biological structures*; Springer-Verlag: Berlin, 1991. (e) Stickle, D. F.; Presta, L. G.; Dill, K. A.; Rose, G. D. *J. Mol. Biol.* **1992**, *226*, 1143.

(2) (a) Halgren, A. T. *J. Comput. Chem.* **1996**, *17*, 520. (b) Kong, J.; Yan., J.-M *Int. J. Quantum Chem.* **1993**, *46*, 239. (c) Merz, K. M. *J. Comput. Chem.* **1992**, *13*, 749. (d) Faerman, C. H.; Price, S. L. *J. Am. Chem. Soc.* **1990**, *112*, 4915. (e) Spackman, M. A. *J. Phys. Chem.* **1987**, *91*, 3179. (f) Sokalski, W. A.; Lowrey, A. H.; Roszack, S.; Levchenco, V.; Blaisdell, H.; Hariharan, P. C.; Kauffman, J. J. *J. Comput. Chem.* **1986**, *7*, 693. (g) Weiner, S. J.; Kollman, P. A.; Nguyen, D. T.; Case, D. A. *J. Comput. Chem.*

1986, *7*, 230. (h) Hurst, G. J. B.; Fowler, P. W.; Stone, A. J.; Buckingham, A. D. *Int. J. Quantum Chem.* **1986**, *29*, 1986. (i) Dykstra, C. E. *Chem. Rev.* **1993**, *93*, 2339. (j) McDonald, D. Q.; Still, W. C. *Tetrahedron Lett.* **1992**, *33*, 7747.

(3) (a) Møller, C.; Plesset, M. S. *Phys. Rev.* **1934**, *46*, 618. (b) Pople, J. A.; Binkley, J.; Seeger, R. *Int. J. Quantum Chem., Symp.* **1976**, *10*, 1.

(4) (a) Xantheas, S. S. *J. Chem. Phys.* **1995**, *102*, 4505. (b) Xantheas, S. S. *J. Chem. Phys.* **1994**, *100*, 7523.

(5) Sponer, J.; Leszczynski J.; Hobza, P. *J. Phys. Chem.* **1996**, *100*, 1995.

(6) Feyereisen, M. W.; Feller, D.; Dixon, D. A. *J. Phys. Chem.* **1996**, *100*, 2993.

(7) Kim, K.; Friesner, R. A. *J. Am. Chem. Soc.* **1997**, *119*, 12952.

(8) Lii, H.-L.; Allinger, N. L. *J. Comput. Chem.* **1998**, *19*, 1001.

(9) Hobza, P.; Sponer, J. *J. Mol. Struct.: THEOCHEM* **1996**, *388*, 115.

(10) Dreyfus, M.; Maigret, B.; Pullman, A. *Theor. Chim. Acta* **1970**, *17*, 109.

(11) Johansson, A.; Kollman, P.; Rothenberg, S.; McKelvey, J. *J. Am. Chem. Soc.* **1974**, *96*, 3794.

(12) Ottersen, T. J. *J. Mol. Struct.* **1975**, *26*, 365.

(13) Ottersen, T. J.; Jensen, H. H. *J. Mol. Struct.* **1975**, *26*, 335.

(14) Kolaskar, A. S.; Lakshminarayanan, A. V.; Sarathy, K. P.; Sasisekharan, V. *Biopolymers* **1975**, *14*, 1081.

(15) Yamabe, S.; Kitaura, K.; Nishimoto, K. *Theor. Chim. Acta* **1978**, *47*, 11.

(16) Peters, D.; Peters, J. *J. Mol. Struct.* **1980**, *68*, 255.

(17) Jeffrey, G. A.; Rubble, J. R. McMullan, R. K.; DeFrees, J. D. Pople, J. A. *Acta Crystallogr.* **1981**, *B37*, 1885.

(18) Pullman, A.; Berthord, H. *Theor. Chim. Acta* **1968**, *10*, 641.

(19) Sapse, A. M.; Fugler, M.; Cowborn, D. *Int. J. Quantum Chem.* **1986**, *29*, 1241.

(20) Dory, M.; Delhalle, J.; Fripiat, J. G.; Andre, J.-M. *Int. J. Quantum Chem., Quantum Biol. Symp.* **1987**, *14*, 85.

(21) Wojcik, M. J.; Hirakawa, A. Y.; Tsuboi, M.; Kato, S.; Morokuma, K. *Chem. Phys. Lett.* **1988**, *143*, 450.

(22) Novoa, J. J.; Whangbo, M.-H. *J. Am. Chem. Soc.* **1991**, *113*, 9017.

(23) Neuheuser, T.; Hess, B. A.; Reutel, C.; Weber, R. *J. Phys. Chem.* **1994**, *98*, 6459.

(24) Florian, J.; Leszcynski, J.; Johnson, B. *J. Mol. Struct.* **1995**, *349*, 421.

(25) Florian, J.; Johnson, B. G. *J. Phys. Chem.* **1995**, *99*, 5899.

(26) Adalsteinsson, H.; Maulitz, A. H.; Bruice, T. C. *J. Am. Chem. Soc.* **1996**, *118*, 7689.

(27) Suhai, S. *J. Phys. Chem.* **1996**, *100*, 3950.

(28) Bleckmann, P.; Breitenbach, P.; Dickhut, K. U., Keller, D.; Schwittek, C. *Fresenius' J. Anal. Chem.* **1997**, *359*, 115.

(29) (a) Sponer, J.; Hobza, P. *J. Phys. Chem. A* **2000**, *104*, 4592. (b) These authors report interaction energies based on the energy of the dimer and the energy of the monomers in the dimer geometry. To obtain the electronic association energies, D_e, defined by us and most others, one needs to subtract a deformation energy, ΔE^{DEF}, due to relaxation of the two monomers. However, only a single ΔE^{DEF} of 1.73 kcal/mol is reported at the MP2/DZ(d,p) level. To estimate values of D_e for comparison with our results, we subtracted 1.73 kcal/mol from each of the reported interaction energies.

(30) Desfrancois, C.; Periquet, V.; Carles, S.; Schermann, J. P.; Andamowicz, L. *Chem. Phys.* **1998**, *239*, 475.

(31) Ramachandran, G. N.; Lakshminarayanan, A. V.; Kolaskar, A. S. *Biochim. Biophys. Acta* **1973**, *303*, 8.

(32) Renugopalakrishnan, V.; Rein, R. *Biochim. Biophys. Acta* **1976**, *434*, 164.

(33) Cheam, T. C.; Krimm, S. *J. Mol. Struct.* **1986**, *146*, 175.

(34) Guo, H.; Karplus, M. *J. Phys. Chem.* **1992**, *96*, 7273.

(35) Dixon, D. A.; Dobbs, K. D.; Valentini, J. J. *J. Phys. Chem.* **1994**, *98*, 13435.

(36) JAGUAR V3.0, Schrörindinger, Inc., Portland, OR, 1997.

(37) (a) Dunning, T. H., Jr. *J. Chem. Phys.* **1989**, *90*, 1007. (b) Kendall, R. A.; Dunning, T. H., Jr.; Harrison, R. J. *J. Chem. Phys.* **1992**, *96*, 6796.

(38) (a) Woon, D. E.; Dunning, T. H., Jr. *J. Chem. Phys.* **1994**, *101*, 8877. (b) Peterson, K. A.; Woon, D. E.; Dunning, T. H., Jr. *J. Chem. Phys.* **1994**, *100*, 7410.

(39) Boys, S. F.; Bernardi, F. *Mol. Phys.* **1990**, *19*, 553.

(40) Bernholdt, D. E.; Apra, E.; Fruchtl, H. A.; Guest, M. F.; Harrison, R. J.; Kendall, R. A.; Dutteh, R. A.; Long, X.; Nicholas, J. B.; Nichols, J. A.; Taylor, H. L.; Wong, A. T.; Fann, G. I.; Littlefield, R. J.; Nieplocha, J. *Int. J. Quantum Chem., Symp.* **1995**, *29*, 475.

(41) Vargas, R.; Garza, J.; Dixon, D. A.; Hay, B. P. *J. Am. Chem. Soc.* **2000**, *122*, 4750.

(42) (a) Becke, A. D. *Phys. Rev. A* **1988**, *38*, 3098. (b) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785.

(43) Dgauss is a program that is part of UniChem and is available from Oxford Molecular: (a) Andzelm, J.; Wimmer, E.; Salahub, D. R. In *The Challenge of d and f Electrons: Theory and Computations*; Salahub, D. R., Zerner, M. C., Eds.; ACS Symposium Series, No. 394; American Chemical Society: Washington, DC, 1989; p 228. (b) Andzelm, J. In *Density Functional Methods in Chemistry*; Labanowski, J., Andzelm, J., Eds.; Springer-Verlag: New York, 1991; p. 155. (c) Andzelm, J.; Wimmer, E. *J. Chem. Phys.* **1992**, *96*, 1280.

(44) Godbout, N.; Salahub, D. R.; Andzelm, J.; Wimmer, E. *Can. J. Chem.* **1992**, *70*, 560.

(45) The D_e values (kcal/mol) for dimers **1**−**5** at the BLYP/TZVP(A2) level of theory are (**1**) −13.22, (**2**) −8.40, (**3**) −5.70, (**4**) −5.95, and (**5**) −3.40. These association energies are 0.8−1.6 kcal/mol weaker than the estimated MP2/CBS values given in Table 2.

(46) Clement, O.; Rapko, B. M.; Hay, B. P. *Coord. Chem. Rev.* **1998**, *170*, 203.

(47) Drakenberg, T.; Forsen, S. *J. Chem. Soc., Chem. Commun.* **1971**, 1404.

(48) Taft, R. W. *Prog. Phys. Org. Chem.* **1987**, *16*, 1.

(49) Decouzon, M.; Exner, O.; Gal, J.-F.; Maria, P. C. *J. Org. Chem.* **1990**, *55*, 3980.

(50) Hunter, E. P. L.; Lias, S. G. *J. Phys. Chem. Ref. Data* **1998**, *27*, 413.

(51) Stern, H. A.; Kaminski, G. A.; Banks, J. L.; Zhou, R. H.; Berne, B. J.; Friesner, R. A. *J. Phys. Chem. B* **1999**, *103*, 4730. Banks, J. L.; Kaminski, G. A.; Zhou, R. H.; Mainz, D. T.; Berne, B. J.; Friesner, R. A. *J. Chem. Phys.* **1999**, *110*, 741. Liu, Y. P.; Kim, K.; Berne, B. J.; Friesner, R. A.; Rick, S. W. *J. Chem. Phys.* **1998**, *108*, 4739.

(52) Murphy, R. B.; Beachy, M. D.; Friesner, R. A.; Ringnalda, M. N. *J. Chem. Phys.* **1995**, *103*, 1481.