The Possible Covalent Nature of N−H···O Hydrogen Bonds in Formamide Dimer and Related Systems: An Ab Initio Study

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The N−H···O hydrogen bonds are analyzed for formamide dimer and its simple fluorine derivatives representing a wide spectrum of more or less covalent interactions. The calculations were performed at the MP2/6-311++G(d,p) level of approximation. To explain the nature of such interactions, the Bader theory was also applied, and the characteristics of the bond critical points (BCPs) were analyzed: the electron density at BCP and its Laplacian, the electron energy density at BCP and its components, the potential electron energy density, and the kinetic electron energy density. These parameters are used to justify the statement that some of the interactions analyzed are partly covalent in nature. An analysis of the interaction energy components for the systems considered indicates that the covalent character of the hydrogen bond is manifested by a markedly increased contribution of the delocalization term relative to the electrostatic interaction energy. Moreover, the ratio of stabilizing the delocalization/electrostatic contributions grows linearly with the decreasing lengths of the hydrogen bond.

Introduction

The hydrogen bond is a common phenomenon in crystals, liquids, and often in the gas phase.[1,2] That interaction is often the driving force influencing the arrangement of molecules in crystals and is important in many chemical, physical, and biochemical processes.[3] The studies on hydrogen bonding are not only devoted to particular types of systems and the specific kinds of environments involved in processes but are also of more general, exploring the physical nature of hydrogen-bond interactions. There are even problems connected with the definition of hydrogen bonding. Pauling's early definition states that "under certain conditions an atom of hydrogen is attracted by rather strong forces to two atoms, instead of only one, so that it may be considered to be acting as a bond between them. This is called the hydrogen bond."[4] Pauling also claimed that the hydrogen bond "is formed only between the most electronegative atoms."[4] Pauling (and later others) also indicated that the hydrogen bond is mostly electrostatic in nature and that the acceptor of the proton within the X−H···Y hydrogen-bonded bridge (X designates the proton donor whereas Y is an acceptor of proton) should contain at least one free electron pair that is responsible for the electrostatic attraction of proton.[4,5]

The situation is not so clear because in the last century, numerous types of hydrogen bonds were investigated, such as C−H···Y,[6] X−H···π (or C) and even C−H···C, that were not in line with Pauling's classical definition.[4] One can also mention the dihydrogen bonds[7] and other "unconventional" interactions that hardly may be classified as hydrogen bonds.[8] The problem was mainly connected with the "border" between the hydrogen bonds and weaker van der Waals interactions, and for some of the interactions, it was difficult to classify them to any kind.[9]

However, the other problem is mentioned in the literature from time to time as is the borderline between hydrogen bonds and covalent bonds. Recently, there have been heated disputes regarding the hypothesis that nearly all enzymes covalently speed reactions,[10] and hence, more precise criteria are needed to measure the covalent character of hydrogen bonds.

The covalent nature of some of hydrogen bonds was analyzed early by Pauling [4] who stated that "the bond was for some time thought to result from the formation of two covalent bonds by the hydrogen atom, the hydrogen fluoride ion $[HF_2]^-$ being assigned the structure

$$[:\underset{..}{\ddot{F}}:H:\underset{..}{\ddot{F}}:]^{-}_{.}\text{''}$$

There are also the other early studies on the covalent nature of hydrogen bonding.[11] However, this problem has appeared more often in the past decade because the number of hydrogen-bonded systems analyzed by experimental as well as theoretical techniques has increased rapidly, and among them are those containing very short proton···acceptor distances and those characterized by binding energies close to the values of dissociation energies of covalent bonds.

Analyses of O−H···O interactions in dimers of carboxylic acids have been performed very recently,[12] and it was found that, according to the AIM (atoms in molecules theory)[13] topological parameters, they may be classified as partly covalent in nature. There are also experimental evidences concerning the partly covalent nature of strong hydrogen bonds. For example, a low-temperature study of intramolecular hydrogen bonding in benzoylacetone was carried out with X-ray (8.4 K) and neutron diffraction data (20 K).[14] The charge density obtained from X-ray and neutron data has been analyzed by using

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multipolar functions and topological methods, which provided evidence of π-electron delocalization in the keto−enol group. It is shown that the hydrogen position is stabilized by both electrostatic and covalent bonding contributions at each side of the hydrogen atom. Other important studies on the covalency of hydrogen bonds may be mentioned.[15]

The Bader theory based on the analysis of electron density of the systems investigated[13] is a powerful technique to explore the nature of interactions. This theory was often applied to analyze hydrogen bonds and the other interactions, among them covalent bonds.[16] For a pair of interacting atoms, the characteristics of the bond critical point (BCP) such as the electron density at BCP (ρ_C), its Laplacian ($\nabla^2\rho_C$), the electron energy density at BCP (H_C), the kinetic electron energy density (G_C), and the potential electron energy density (V_C) are important and useful as descriptors of the considered interaction. For share interactions, the negative value of Laplacian designates the concentration of the electron density, whereas if the Laplacian is positive, then there is a depletion of electron charge. The previous interactions correspond to covalent bonds and the latter to van der Waals interactions, to ionic interactions as well as to hydrogen bonds.[16] Hence, the Bader theory is often applied to classify and characterize interactions, among them hydrogen bonding. If the Laplacian value for the proton···acceptor BCP is negative, then the hydrogen bond is covalent in nature. The following equation relates the energetic properties of BCP and its Laplacian (all values of eq 1 in au).

$$(1/4)\ \nabla^2\rho(r_C) = 2G_C + V_C \qquad (1)$$

Hence, some authors claim that if the H_C value ($H_C = G_C + V_C$) is negative, then the interaction is partially covalent in nature.[17]

The aim of this study is to analyze hydrogen-bond interactions for formamide dimer and its simple fluoro derivatives. It was pointed out that the delocalization energy term is an important attractive term for stabilizing the structures of carboxylic acids.[12] Hence, in this study, we analyze the broader sample of dimers related to formamide to assess the dependencies between geometrical, topological, and energetic parameters and to compare the stronger homonuclear O−H···O hydrogen bonds with the weaker heteronuclear N−H···O ones.

Computational Details

The calculations have been performed with Gaussian 98[18] and Gaussian 03[19] sets of codes using the second-order Møller−Plesset perturbation method (MP2).[20] The 6-311++G(d,p) basis set [21] was used, and full optimizations have been performed for the considered dimers of formamide and its fluorine derivatives. The optimizations were performed with symmetry constraints fixing the inversion centers between the interacting monomers; hence, within the dimers, there are two equivalent NH···O hydrogen bonds, and both monomers are of equivalent geometry. For all mentioned dimers, the corresponding tautomeric forms obtained as a result of the double proton-transfer reaction, N−H···O ⇔ N···H−O, were taken into account. Additionally the transition states (TSs) for such reaction were considered. Figure 1 shows the molecular graphs of dimers of two tautomeric forms of formamide as well as of the corresponding transition state. It should be mentioned that for the formamide dimer, there are two hydrogen atoms belonging to each monomer that do not participate in the hydrogen-bond interactions. Hence, three cases of F-substitution of formamide are possible. For each case, the corresponding dimer, the corresponding dimeric tautomeric form, and TS were considered. For all dimers, the symmetry constraints mentioned above were applied during optimization.

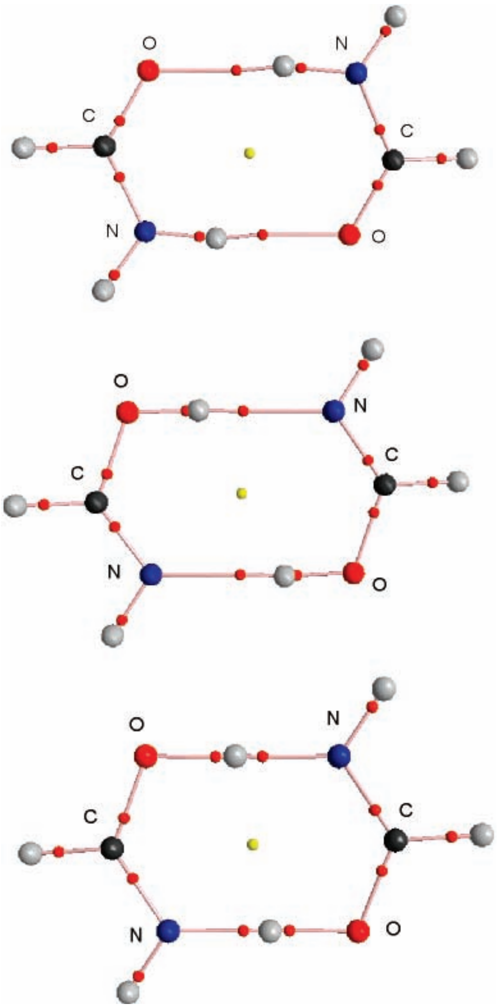

Figure 1. Molecular graphs of the formamide dimer, the corresponding tautomeric form, and transition state; big circles correspond to attractors and the small ones to the bond and ring critical points.

Deeper insight into the physical nature of interactions of the molecular complexes analyzed here could be obtained by analysis of the interaction energy components. Hence, the variation−perturbation approach[22] was applied. The starting wave functions of the subsystems are obtained in this approach in the dimer-centered basis set (DCBS).[23]

The following interaction energy components free of BSSE can be obtained in the dimer basis set if the following decomposition scheme is applied

$$\Delta E = E_{EL}{}^{(1)} + E_{EX}{}^{(1)} + E_{DEL}{}^{(R)} + E_{CORR}{}^{(2)} \qquad (2)$$

where $E_{EL}{}^{(1)}$ is the first-order electrostatic term describing the Coulomb interaction of the static charge distributions of both molecules; $E_{EX}{}^{(1)}$ is the repulsive first-order exchange component resulting from the Pauli exclusion principle and is defined as the difference of the Heitler−London energy and the electrostatic term; and $E_{DEL}{}^{(R)}$ and $E_{CORR}{}^{(2)}$ correspond to higher order delocalization and correlation terms, respectively. These contributions define on the same time scale gradually simplified theory levels starting from MP2, SCF, and Heitler−London down to electrostatic models able to reproduce well the structural characteristics of classical hydrogen-bonded systems.[24] The

TABLE 1: Geometrical Parameters of the Analyzed Dimers (in Å, in Degrees)

system	ΔNH(OH)	ΔCO	ΔCN	d(NH/OH)	H···N/O	∠NHO
NH•O	0.016	0.013	−0.019	1.023	1.903	172.6
N(F)H•O	0.010	0.014	−0.033	1.027	1.870	164.2
NH•O(C−F)	0.009	0.012	−0.016	1.016	1.938	165.8
N(F)H•O(C−F)	0.005	0.010	−0.022	1.021	1.946	158.7
OH•N	0.043	−0.031	0.015	1.011	1.673	176.9
OH•N(F)	0.025	−0.023	0.007	0.993	1.772	172.4
OH•N(C−F)	0.070	−0.042	0.021	1.036	1.556	179.8
OH•N(F)(C−F)	0.039	−0.029	0.011	1.006	1.683	175.2
NH•O(TS)[a]	0.330	0.067	−0.063	1.337	1.152	179.2
N(F)H•O(TS)[a]	0.216	0.060	−0.088	1.233	1.243	175.1
NH•O(C−F)(TS)[a]	0.411	0.081	−0.068	1.418	1.094	178.8
N(F)H•O(C−F)(TS)[a]	0.289	0.070	−0.086	1.305	1.168	176.6
OH•N(TS)[b]	0.184	−0.063	0.032	1.152	1.337	179.2
OH•N(F) (TS)[b]	0.275	−0.070	0.029	1.243	1.233	175.1
OH•N(C−F)(TS)[b]	0.128	−0.357	0.029	1.094	1.418	178.8
OH•N(F)(C−F)(TS)[b]	0.201	−0.065	0.026	1.168	1.305	176.6

[a] Transition states related to formamide tautomers. [b] Transition states related to imide tautomers.

TABLE 2: Energy Difference Between the O−H···N Tautomeric Form or the Transition State (TS) and the Corresponding (Most Energetically Favorable) N−H···O Tautomeric Form (in kcal/mol)

system	energy difference
OH•N	19.61
OH•N(F)	1.27
OH•N(C−F)	27.63
OH•N(F)(C−F)	15.78
NH•O(TS)[a]	20.51
N(F)H•O(TS)[a]	8.81
NH•O(C−F)(TS)[a]	27.81
N(F)H•O(C−F)(TS)[a]	18.08

[a] Transition state.

interaction energy decomposition scheme was implemented [25] in the GAMESS quantum chemistry package.[26] The supermolecular approach was applied here to calculate the binding energies. This indicates that the interaction energy of the two systems A and B is calculated as the difference between the energy of the dimer, E_{AB}, and the energies of the monomers, E_A and E_B, each calculated for a given nuclear configuration.[27]

Moreover, to analyze the hydrogen-bond interactions, especially in terms of their covalent nature, the AIM theory[13] mentioned in the Introduction was applied, and the characteristics of the BCPs corresponding to hydrogen bonds were determined. The AIM2000 program[28] was used to find and analyze the BCPs.

Results and discussion

Geometries and Energies. Table 1 presents some geometrical parameters of the investigated systems. As was mentioned in the previous section, the dimer of formamide as well as its fluorine derivatives are analyzed. The following designations are applied in Table 1 and also in the other tables. NH•O designates the formamide dimer; N(F)H•O means that the hydrogen atom of the amine group that does not participate in hydrogen bonding is replaced by a fluorine atom; NH•O(C−F) designates the dimer where to the carbon atoms fluorine atoms are attached instead of hydrogen atoms; N(F)H•O(C−F) represents the case where all hydrogen atoms that do not participate in hydrogen bonds are replaced by fluorine atoms. The corresponding tautomeric forms with O−H···N hydrogen bonds are considered and are designated in a similar way (Table 1). The transition states between all pairs of tautomeric forms and corresponding to the double proton-transfer reaction, N−H···O ⇔ N···H−O, are also taken into account. The first column of Table 1 shows the designations of the systems considered; the next three columns present the changes of some of the geometrical parameters due to complexation. There are differences between the NH/OH proton donating bond, the CN and CO bond lengths on one hand and the corresponding bond lengths of monomers not involved in any interactions on the other hand. In the case of N−H···O tautomers, there are C═O double and C−N single bonds. The C═O bonds are elongated due to complexation, whereas the C−N bonds are shortened. In the case of O−H···N tautomers, the C═N double bonds are elongated, and the C−O single bonds are shortened because the imide forms are connected through hydrogen bonds. Hence, the Δ-values (Table 1) suggest these changes, which are partly related to the process of π-electron delocalization; the positive values indicate the elongation of bonds as a result of complexation, and the negative values indicate their shortening. The transition forms are also included in Table 1, each of them twice because the TSs are related to the amide as well as to the imide forms.

One can observe the following changes as being the result of complexation; there are greater changes for the OH···N forms than for the corresponding NH···O forms. The greatest changes (Δ-values) are observed for transition states. There are also the following tendencies (Table 1): hydrogen bonds for transition states are closer to linearity than OH···N systems. Mostly bent hydrogen bridges are observed for N−H···O dimers. Similarly, for TSs, the proton···acceptor (H···Y) distances are the shortest; the longest H···Y distances are observed for NH···O dimers. This is in line with the Leffler−Hammond postulate[29] because for systems closer to the transition state, the corresponding hydrogen bonds are stronger, and the geometries are also closer to those found for TSs; OH···N systems are closer to TSs than the NH···O systems. Such analyses were performed for the intramolecular N−H···O hydrogen bonds, and results that are in line with this postulate were found.[30]

The statements presented above are based on the assumption that for stronger hydrogen bonds, the proton···acceptor distances are shorter. However, these observations based on geometrical parameters are also supported by the energetic results. Table 2 presents the energy differences between the transition state forms and the OH···N forms on one hand and the corresponding NH···O forms on the other hand. The NH···O dimers are the most stable (are characterized by the lowest energies). One can observe (Table 2) that the OH···N forms are sometimes very close to the corresponding transition states. For example, the OH···N system with the fluorine atom connected with carbon is only 0.18 kcal/mol lower in energy than the corresponding

TABLE 3: Decomposition of the Interaction Energy for Dimers of Formamide and Its Tautomeric Form as Well as Their Fluoro Derivatives, All Energies in kcal/mol at the MP2/6-311++G(d,p) Level

energy component[a]	NH·O	N(F)H·O	NH·O (C−F)	N(F)H·O (C−F)	OH·N	OH·N(F)	OH·N (C−F)	OH·N(F) (C−F)
$\Delta E^{(1)}$	−3.62	−2.48	−4.95	−3.51	8.76	3.58	13.95	6.45
$E_{EL}^{(1)}$	−23.31	−22.55	−20.02	−17.32	−45.42	−31.99	−57.05	−37.67
$E_{EX}^{(1)}$	19.68	20.08	15.07	13.81	54.18	35.57	71.00	44.12
$E_{DEL}^{(R)}$	−8.47	−8.98	−6.48	−6.12	−26.55	−17.38	−40.11	−23.81
ΔE_{SCF}	−12.09	−11.46	−11.43	−9.63	−17.80	−13.81	−26.16	−17.36
E_{CORR}	−0.01	0.14	0.11	0.26	−2.67	−1.85	−3.59	−2.91
ΔE_{MP2}	−12.10	−11.32	−11.33	−9.37	−20.47	−15.65	−29.76	−20.27

[a] $\Delta E_{MP2} = \Delta E_{SCF} + E_{CORR}$, $\Delta E^{(1)} = E_{EL}^{(1)} + E_{EX}^{(1)}$.

transition state. This is in line with the Hammond postulate[29b] as well as with findings of Gilli et al.[30] that systems lower in energy possess weaker hydrogen bonds. For the systems investigated here, the NH···O dimers are of lower energy than the corresponding OH···N dimers; the former possess weaker hydrogen bonds than the latter, and the OH···N forms are closer to TSs than NH···O systems.

Components of Intermolecular Interaction Energy. Table 3 presents the interaction energies of the systems investigated; the results of the energy partitioning are also included. One can observe that the strongest hydrogen bond is for the OH···N(C−F) system because E_{MP2} is lowest. It may be explained that the fluorine substituent, the electronegative one, causes a decrease in the proton affinity of the O−H bond, and hence, the system is the stronger Lewis acid than the unsubstituted formamide species. However, other factors can also play a significant role, and such an explanation is a rough simplification. Another example is the dimer with fluorine atoms attached to the amino groups. The fluorine atom causes the decrease in the proton affinity of nitrogen. Hence, the remaining N−H bonds in the dimer should be classified as stronger Lewis acids than the corresponding bonds in formamide. The geometrical results collected in Table 1 confirm this because H···O distances for formamide are greater than such distances for fluorine derivative: 1.903 Å for formamide and 1.870 Å for the fluorine derivative. Similarly, there are greater changes for CO and CN bonds for fluorine derivatives, which are connected with the greater π-electron delocalization. However, Table 3 shows that hydrogen bonds of formamide are slightly stronger than those for fluorine derivatives because the binding energies are equal to −12.1 and −11.3 kcal/mol, respectively. These results show that the hydrogen-bond strength vs H···Y distance relationship is not always fulfilled. Similarly, the substituent effect may be discussed for dimers of the corresponding tautomeric forms where OH···N hydrogen bonds exist. For the O−H···N system not substituted by fluorine atoms, the H···N distance amounts to 1.673 Å, whereas for fluorine, the corresponding form (fluorine attached to the nitrogen atom) is equal to 1.772 Å. For the latter complex, there are smaller changes in the CO and CN bonds due to complexation than for the previous dimer. This may be explained in the following way: the fluorine substituent causes a decrease in the proton affinity of the nitrogen atom, and hence, the nitrogen center is the weaker Lewis base. Correspondingly, the hydrogen bond should be weaker than that for the unsubstituted species. The energy results of Table 3 confirm the geometrical results because the binding energies for these unsubstituted and substituted dimers are equal to −20.5 and −15.7 kcal/mol, respectively.

Table 3 also shows that the Heitler−London first-order interaction energy term $\Delta E^{(1)}$ is negative for NH···O systems, whereas it is positive for OH···N systems. The latter is connected with the fact that the exchange energy term $E_{EX}^{(1)}$ outweighs the electrostatic term $E_{EL}^{(1)}$ for OH···N systems. One can also observe that the attractive delocalization interaction energy term $E_{DEL}^{(R)}$ is one that causes OH···N systems to be stable. Figure 2 shows the dependence between the H···Y distance and the energy terms. There are two regions: the first one with OH···N species and shorter H···Y distances, with more important exchange, electrostatic, and delocalization interaction energy terms, and the second region with greater H···Y distances and less important energy terms mentioned above. The correlation term is meaningless for NH···O systems; it is slightly positive, whereas for OH···N systems, it is negative and in the range between −1.9 and −3.6 kcal/mol. Because the dispersion interaction energy term is the most important attractive term as a component of the correlation energy, one could also state that, for stronger hydrogen bonds (those of shorter H···Y distances and hence greater covalency), the dispersion energy is more important. However, the most important and driving energy components are the delocalization term and the electrostatic term. Figure 3 presents the dependence between the H···Y distance and the ratio of delocalization and electrostatic energy terms. One can observe that, if such a ratio is relatively low (lower than ca. 0.45), then it stands for NH···O weaker hydrogen bonds where H···Y distances are greater; for higher values of that ratio (more than about 0.45), there is a region of OH···N bonds with shorter H···Y distances. Hence, in weaker hydrogen-bond systems, electrostatic effects are dominant; covalent effects could be represented mainly by the delocalization term for stronger hydrogen bonds. These findings are confirmed by recent

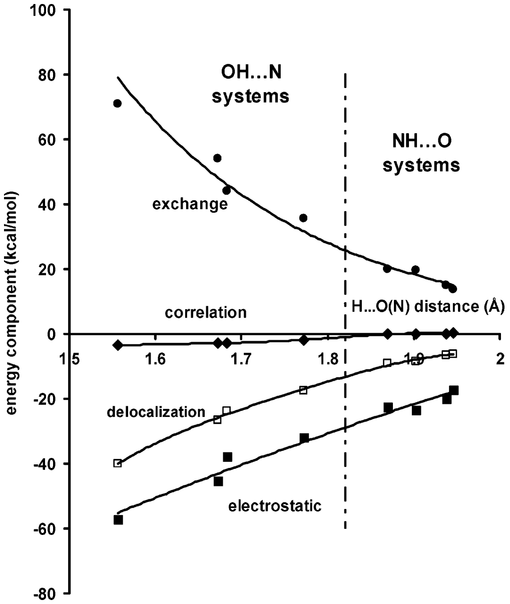

Figure 2. Relationship between the proton···acceptor distance (in Å) and the components of the interaction energy: ● exchange, ◆ correlation, □ delocalization, ■ electrostatic.

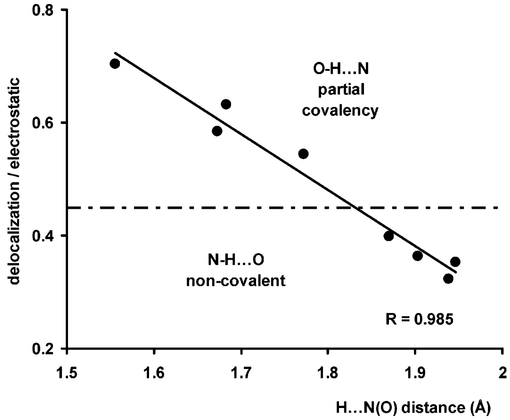

Figure 3. Relationship between the proton···acceptor distance (in Å) and the ratio: delocalization to electrostatic interaction energy components.

TABLE 4: NH Bond Lengths and H···N Distances (both in Å) and Their Topological Parameters, Electron Density at BCP, Its Laplacian, the Potential Electron Energy Density, and the Kinetic Electron Energy Density (all in au) at the MP2/6-311++G(d,p) Level

system	NH(H···N)	ρ_C	$\nabla^2\rho_C$	G_C	V_C
NH·O	1.023	0.3209	−1.7653	0.0525	−0.5464
N(F)H·O	1.027	0.3224	−1.8561	0.0491	−0.5623
NH·O(C−F)	1.016	0.3262	−1.8193	0.0528	−0.5604
N(F)H·O(C−F)	1.021	0.3301	−1.9067	0.0495	−0.5756
OH·N	1.673	0.0559	0.1052	0.0404	−0.0545
OH·N(F)	1.772	0.043	0.1066	0.0324	−0.0386
OH·N(C−F)	1.556	0.0742	0.0962	0.0515	−0.0789
OH·N(F)(C−F)	1.683	0.0531	0.1108	0.0398	−0.0519
NH·O[a]	1.337	0.1327	−0.0895	0.0693	−0.1609
N(F)H·O[a]	1.233	0.1742	−0.3985	0.0706	−0.2408
NH·O(C−F)[a]	1.418	0.1061	0.0272	0.0645	−0.1221
N(F)H·O(C-F)[a]	1.305	0.1426	−0.1529	0.0716	−0.1815

[a] Transition state.

results on very strong dihydrogen bonds [31] and also on the broader spectrum of hydrogen-bond interactions.[32] For homonuclear intermolecular O−H···O, existing in formic and acetic acid centrosymmetric dimers, the ratio mentioned here amounts to 0.48 and 0.47, respectively.[12] In both dimers, the H_C values for H···O BCPs are negative, indicating the partly covalent character of the interactions. These findings on carboxylic acid dimers are related to the MP2/6-311++G(d,p) level of approximation. Figure 3 also shows the region of OH···N systems named as those that are partly covalent. The latter statement is discussed in detail in the next section where the AIM theory is applied.

Figure 4 illustrates simultaneously the interaction energies at different theory levels (horizontal lines) and various physical components (vertical arrows) for complexes arranged according to the growing lengths of the shortest intermolecular contact. From the inspection of this plot, it is evident that with decreasing distance, the importance of the delocalization term becomes gradually more significant, whereas the largest electrostatic term is partially canceled by the exchange term. This supports the conclusions derived from Figure 3 that the ratio of the delocalization/electrostatic energies could constitute a quantitative measure of covalent/noncovalent interactions.

The Results of AIM Theory. The Bader theory[13] is applied to explore the nature of hydrogen bonds of the systems investigated here. Figure 1 shows the molecular graphs of three systems analyzed; nonsubstituted species are presented: formamide, the corresponding tautomer, and the transition state. For the H···O and H···N contacts of the hydrogen bonds, the characteristics of the corresponding H···Y BCPs are very important because they provide information concerning the interaction types.[16,33,34] This was explained briefly in the Introduction. In this study, the BCPs of covalent bonds as well as of intermolecular contacts are analyzed. The following characteristics of BCPs are taken into account: the electron density at BCP (ρ_C), its Laplacian ($\nabla^2\rho_C$), the total electron energy density at BCP (H_C), and the components of the latter (the kinetic electron energy density (G_C) and the potential electron energy density (V_C)). Tables 4 and 5 collect these appropriate values. Table 4 presents the characteristics of the H···N pair of interacting atoms; these are N−H covalent bonds in NH···O hydrogen bridges, H···N contacts in O−H···N hydrogen bonds as well as H···N contacts of transition states. Similarly, the O···H pairs of atoms are collected in Table 5. One can see from Table 4 that short NH distances slightly greater than 1 Å correspond to covalent bonds with negative values of Laplacians. There are relatively high values of electron densities at the corresponding BCPs (0.32−0.33 au). The next cases in Table 4 concern H···N interactions of O−H···N hydrogen bonds; H···N distances are between 1.56 Å and 1.77

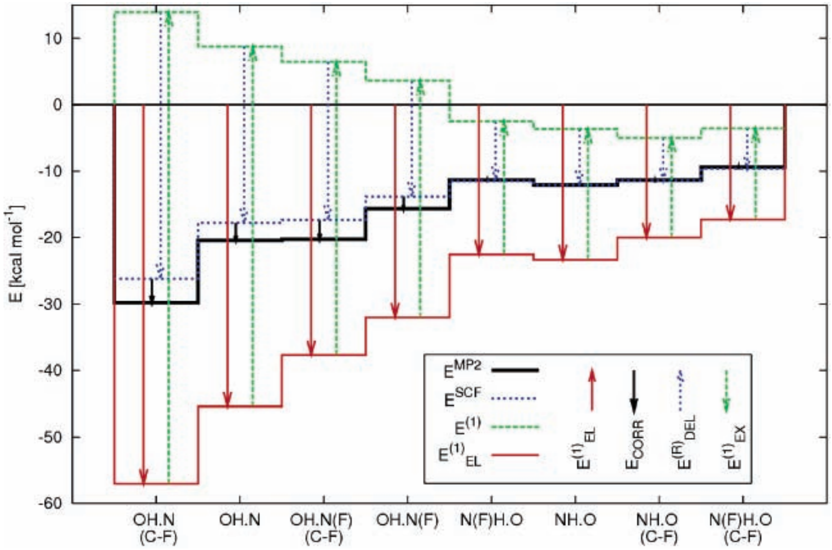

Figure 4. Interaction energies at different theory levels (horizontal lines) and various physical components (vertical arrows) for complexes arranged according to the increasing hydrogen-bond lengths. Down arrows represent the attractive energy components, whereas up arrows show the repulsive exchange energy term.

TABLE 5: H···O Distances and OH Bond Lengths (both in Å) and Their Topological Parameters, Electron Density at BCP, Its Laplacian, the Potential Electron Energy Density, and the Kinetic Electron Energy Density (all in au) at the MP2/6-311++G(d,p) Level

system	H···O(OH)	ρ_C	$\nabla^2\rho_C$	G_C	V_C
NH·O	1.903	0.0273	0.0961	0.0227	−0.0214
N(F)H·O	1.87	0.0289	0.1031	0.0246	−0.0235
NH·O(C−F)	1.938	0.0239	0.0919	0.0207	−0.0184
N(F)H·O(C−F)	1.946	0.0231	0.0911	0.0203	−0.0179
OH·N	1.011	0.3028	−2.0661	0.0711	−0.6586
OH·N(F)	0.993	0.3218	−2.2704	0.0689	−0.7059
OH·N(C−F)	1.036	0.2769	−1.782	0.0749	−0.5953
OH·N(F)(C−F)	1.006	0.3054	−2.1221	0.0689	−0.6683
NH·O[a]	1.152	0.1977	−0.6496	0.0912	−0.3447
N(F)H·O[a]	1.243	0.1534	−0.1661	0.0912	−0.2239
NH·O(C−F)[a]	1.094	0.2316	−1.1694	0.0849	−0.4622
N(F)H·O(C−F)[a]	1.168	0.1861	−0.5298	0.0919	−0.3163

[a] Transition state.

Å. Positive values of Laplacians indicate noncovalent interactions. However, for all latter cases, H_C is negative because $|V_C| > G_C$. This indicates partial covalency. This may be easily explained because OH···N hydrogen bonds as those existing within systems close to the corresponding transition states and are much stronger than NH···O hydrogen bonds (see Table 3). This was also mentioned in the previous section that for OH···N dimers, there is greater π-electron delocalization than for complexes connected through NH···O hydrogen bonds. The values of H_C's for H···O BCPs of NH···O connections (see Table 5) are positive, indicating that NH···O hydrogen bonds are weaker than OH···N bonds and are not covalent in nature.

For TSs (Table 5), the H···O distances are in the range 1.094−1.243 Å, relatively close to such bonds within O−H···N tautomers, 0.993−1.036 Å. The $\nabla^2\rho_C$ values for H···O contacts of TSs are negative. On the other hand, H···N contacts of TSs are in the range 1.233−1.418 Å, and $\nabla^2\rho_C$'s for the corresponding critical points are negative, except for one case, the TS of the system with fluorine atoms substituted for carbon atoms. The last case represents a situation where the OH···N tautomeric form is very close to TS. For example, the OH bonds are equal to 1.036 and 1.094 Å for OH···N system and TS, respectively. Hence, the corresponding H···N contact of TS is only partly covalent in nature ($\nabla^2\rho_C > 0$ and $H_C < 0$).

Figures 5 and 6 present the energetic properties of BCP (H_C, G_C, and V_C values) for H···N and H···O pairs of interacting atoms, respectively. For both figures, there are three regions of interactions starting from the shortest distances: covalent bonds, contacts within the TSs, and the hydrogen-bond intermolecular distances. One can see (Figure 5) that for all H···N pairs, H_C values are negative. Such interactions are at least partly covalent in nature. There is the region of the longest H···O distances (Figure 6), corresponding to N−H···O hydrogen bonds for which H_C values are positive. Figure 6 also shows how close the OH bond lengths of the OH..N systems and the H..O contacts of TSs are, that is, how close the OH···N tautomeric forms are to the corresponding transition states.

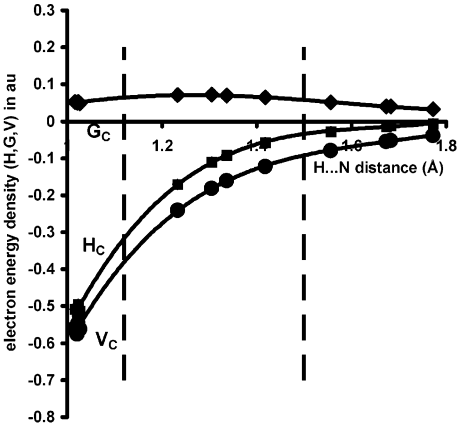

Figure 5. Dependence between the H···N distance (in Å) and the energy properties of BCP: H_C, G_C, and V_C (in au). There are three regions designated by broken lines: shortest distances, covalent bonds; medium distances, contacts of TSs; longest distances, intermolecular contacts of O−H···N dimers.

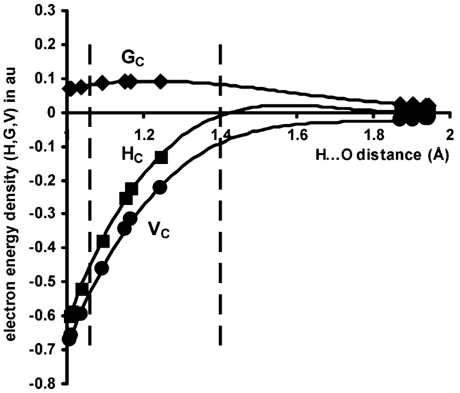

Figure 6. Dependence between the H···O distance (in Å) and the energy properties of BCP: H_C, G_C, and V_C (in au). There are three regions designated by broken lines: shortest distances, covalent bonds; medium distances, contacts of TSs; longest distances, intermolecular contacts of N−H···O dimers.

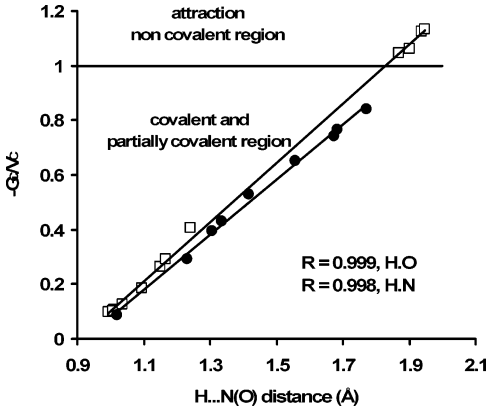

Figure 7. Relationship between H···Y distance (☐ for Y=O, ● for Y=N) and the $-G_C/V_C$ ratio. Two regions are designated: for $-G_C/V_C > 1$, there are attractive, noncovalent interactions; for $-G_C/V_C < 1$, there are covalent and partially covalent interactions.

Figure 7 presents the relationship between the H···N/O distance and the $-G_C/V_C$ ratio. If such a ratio is greater than unity, it corresponds to positive H_C values—noncovalent interactions, even partly. Again, this is observed for H···O contacts within NH···O systems. For all other interactions, covalent bonds, contacts of TSs, and H···N contacts of OH···N tautomers, this ratio is smaller than unity; all such interactions are at least partly covalent. If the $-G_C/V_C$ ratio is smaller than 0.5, thus not only the H_C is negative but also is the corresponding Laplacian indicating covalent bond or any covalent interaction. A similar relationship between distance and reverse ratio ($-V_C/G_C$) was analyzed by Molins and co-workers.[34]

Conclusions

Heteronuclear intermolecular N−H···O hydrogen bonds were investigated here in the dimer of formamide and the related fluorine systems. It was found that covalency increases for these species if the binding energies are greater and the proton··· acceptor distances are shorter. The covalency is connected with the delocalization interaction energy term because such a term is more important for shorter H···Y distances. It is known that typical hydrogen bonds that are in line with the Pauling definition of hydrogen bonding are mostly electrostatic in nature. Here, we found the correlation between the H···Y distance and the delocalization/electrostatic ratio. The latter increases for shorter H···Y distances. In other words, for stronger hydrogen bonds that are more covalent in nature, the delocalization attractive interaction energy term becomes more important than the electrostatic term.

On the other hand, the topological parameters derived from the Bader theory have shown that the $-G_C/V_C$ ratio increases with increasing H···Y distance. The statement that for the negative H_C values the interactions are partly covalent in nature is in line with the findings based on the interaction energy components. The $-G_C/V_C$ ratio mentioned above correlates well with the H···Y distance. This is in line with the findings connected with the decomposition of the interaction energy. Indeed, the linear relationship observed in Figure 3 is paralleled by a corresponding linear relationship shown in Figure 7. Of course, such excellent linear relationships may not always be observed as is the case here due to the close structural relationship of the considered systems. Nevertheless, the similar character of Figures 3 and 7 may indicate the validity of both quantitative measures of covalent/noncovalent character, i.e., $E_{DEL}^{(R)}/E_{EL}^{(1)}$ and $-G_C/V_C$. Such measures could be very useful for determining and classifying the covalent nature of transition state interactions with some enzyme active centers, which is currently a subject of hot dispute in the literature.[10] The other findings of this study are in line with the topics concerning the character of enzyme centers' interactions. We have found that almost all H···N and H···O contacts of the TSs are covalent in nature because $\nabla^2\rho_C$'s are negative; in only one case the Laplacian is positive, but H_C is negative, indicating that the interaction is partly covalent in nature. For all OH···N tautomeric forms, H_C values are negative for BCPs of H···N interactions. Hence, these interactions are partly covalent. Additionally, OH···N systems are closer to the corresponding TSs than are the NH···O systems.

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