Charged vs. neutral hydrogen bonded complexes:

Is there any difference between the nature of their hydrogen bonds?

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Abstract

A theoretical study on some carboxylic acid dimers formed by positively or negatively charged molecules has been carried out using DFT methods. The resulting dimers possess either +2 or -2 charge. In addition, the corresponding neutral complexes have been also considered. The electron density distribution described by the Atoms in Molecules (AIM) and the Natural Bond Orbital (NBO) methods, as well as the electric field maps of the systems, have been analyzed and compared without finding significant differences between the neutral and ionic complexes. The interaction energy along the dissociation path of the charged dimers shows both a local minimum and a local maximum, defining a stability region between them. When this energetic profile is corrected by the repulsion between the charged groups, it resembles to those of the neutral molecules. Hence, the characteristics of the charged dimers are similar to those of the neutral ones: the addition of a repulsion term for the charged groups permits to retrieve the energetic profiles dependence with the distance in the charged system. The Interacting Quantum Atom (IQA) method has been used to calculate the interaction energy terms, including the classic coulombic term between the whole molecules and the corresponding of the carboxylic acid groups. The IQA results show repulsive electrostatic interactions when the whole molecules are considered in the ionic complexes, but attractive ones between the carboxylic groups in both neutral and ionic complexes.

Keywords: Hydrogen bonds, neutral vs. charged, electric field, Interacting Quantum Atoms.

Introduction

Aggregates of ions of the same sign are not expected to be found in gas phase due to the Coulombic repulsive interactions, although such aggregates are frequently observed in condensed media.^[1] Theoretical calculations show however the possibility to form stable hydrogen bonded aggregates in gas phase between charged molecules with the same sign, even though they show positive binding energies. First theoretical results on small complexes formed by monodeprotonated oxalic and malonic acid with the conjugate base of glycine^[2] were confirmed by electrospray ionization-mass spectroscopy (ESI-MS) experiments that succeed in the detection of similar complexes formed by small peptides^[3] or betaine.^[4] More complex aggregates, formed by two deprotonated sulfamic acid molecules and a variable number of neutral ones have been also detected by ESI-MS, and their stability demonstrated by theoretical calculations.^[5]

The stability of such aggregates with large Coulombic repulsion seems contradictory, in spite of the common view of the hydrogen bond (HB) as an attractive electrostatic interaction. For this reason, the existence of an anti-electrostatic HB has been recently postulated based on natural bonding orbital (NBO) analysis,^[6] although the need of such re-interpretation of the HB has been discarded on the basis of the energy decomposition analysis.^[7] The analysis of the electric field lines in complexes formed by two hydrogen bonded phosphates demonstrate that, in spite of the overall Coulombic repulsion, local electrostatic forces can be attractive in the HB region,^[8] and they are able maintain the formation of these aggregates. Besides the aforementioned studies in gas phase, the effect of the environment (solvent or counterions) has been also explored in anion-anion^[9] and cation-cation^[10], suggesting the results of this last study that such aggregates could be common in biological systems.

In the present article, a total of 20 complexes formed by two neutral or charged carboxylic acids have been considered. The complexes are composed of two identical molecules formed by a carboxylic acid group and a terminal group separated by a variable number of methylene groups (Scheme 1). The geometry of the complexes at the equilibrium geometry and along the dissociation profiles has been determined by DFT methods. Electron density, electrostatic potential and energy decomposition analyses allow an estimation of the separate contributions of Coulombic repulsion and hydrogen bonding interactions, demonstrating that there is no difference between hydrogen bonds in ionic or neutral complexes.

Scheme 1. Complexes considered in the present article.

Computational Methods

The complexes can be grouped in four sets according to the terminal group, which can be amino or alcohol in their neutral or ionic forms. The only difference between complexes in the same set is the number of methylene groups (n), which vary from $n = 0$ to $n = 4$. While the two sets are composed of neutral molecules, the complexes in the set with the protonated amino present charge +2 and those with the deprotonated alcohol have charge -2. Henceforth, the complexes will be identified by $[X, n]$, where X is the terminal group and n the number of methylene groups.

The geometry of the systems has been fully optimized with the M06-2X/aug-cc-pVTZ computational level^[11] and its gathered in Table S1 of the Supplementary Material. Frequencies calculations have been carried out at the same computational level to confirm that the geometries obtained correspond to energetic minima. Binding energies have been calculated as the difference between the energy of the complex minus the sum of the isolated monomers in their energetic minima configuration. Thus, negative values of the binding energy are associated to stabilization processes while positive ones to destabilizing ones. Dissociation paths for all complexes were obtained by varying the distance between the carbon atoms of the acid groups. Starting at the equilibrium geometry, this distance was increased in steps of 0.1 Å and the geometry was fully optimized at each step up to a maximum of 3.0 Å. In addition, steps of 0.5 Å were considered for another 5 Å. To visualize the energy minimum, the C...C distance was decreased by 0.3 Å in three steps of 0.1 Å. All these calculations have been carried out with the Gaussian-09 package.^[12]

The electron density of the complexes was analyzed within the atoms in molecules (AIM) methodology^[13] using the AIMPAC and the AIMAll programs.^[14] The electric field maps have been calculated from the electrostatic potential, as calculated from AIMAll and represented with the Matplotlib library.^[15] The Natural Bond Orbital (NBO) method^[16] has been used to analyze the intermolecular charge transfer

between the occupied and empty orbitals. The NBO6 program^[17] connected to the Gaussian-09 package has been used for these calculations.

The different terms of the interaction energy for all complexes have been calculated with the interacting quantum atoms (IQA) and Localized Molecular Orbital Energy Decomposition Analysis (LMOEDA) methodologies.

Within the IQA framework,^[18] the total electronic energy of a system can be obtained as the sum of the intra-atomic energies associated to each atom, $E_{intra}^A(i)$, and all the possible inter-atomic pairwise energies, $V_{inter}^A(i, j)$ (Eq. 1). The interaction energy (Eq. 2) between two molecules (A and B), is the sum of the deformation energies of the two molecules (Eq. 3) plus the sum of the inter-atomic energies of all the atoms of molecule A with those of molecule B. This last term can be divided in a classic Coulombic contribution, $V_{cl}^{A:B}(i, j)$, and an Exchange correlation term that account for the covalent character of the interaction, $V_{xc}^{A:B}(i, j)$ (Eq. 4).

$$E^A = \sum_{i \in A} E_{intra}^A(i) + \sum_{i \in A} \sum_{j \in A > i} V_{inter}^A(i, j) \quad \text{Eq. 1}$$

$$E_{int}^{A:B} = E_{def}^A + E_{def}^B + \sum_{i \in A} \sum_{j \in B} V_{inter}^{A:B}(i, j) \quad \text{Eq. 2}$$

$$E_{def}^A = [\sum_{i \in A} E_{intra}^{A:B}(i) + \sum_{i \in A} \sum_{j \in A > i} V_{inter}^{A:B}(i, j)] - [\sum_{i \in A} E_{intra}^A(i) + \sum_{i \in A} \sum_{j \in A > i} V_{inter}^A(i, j)] \quad \text{Eq. 3}$$

$$\sum_{i \in A} \sum_{j \in B} V_{inter}^{A:B}(i, j) = \sum_{i \in A} \sum_{j \in B} V_{cl}^{A:B}(i, j) + \sum_{i \in A} \sum_{j \in B} V_{xc}^{A:B}(i, j) \quad \text{Eq. 4}$$

In the same way that the IQA methodology can be used to analyze the interaction energy of two molecules, it can be also applied to a set of atoms being associated to A and another set being associated to B. In the present case, the four atoms that form the carboxylic acid group of the each of the two molecules of the dimers have been considered as A and B. These calculations have been carried out with the AIMAll program.

The LMOEDA method^[19] at the M06-2X/aug-cc-pVTZ computational level has been used to obtained the interaction energy terms (Eq. 5).

$$E_{int} = E_{elec} + E_{exc} + E_{rep} + E_{pol} + E_{disp} \quad \text{Eq. 5}$$

where E_{elec} is the electrostatic term describing the classical Coulombic interaction of the occupied orbitals of one monomer with those of the other, E_{exc} and E_{rep} are the exchange and repulsive components

associated with the Pauli exclusion principle, and E_{pol} and E_{disp} correspond to the polarization and dispersion terms, respectively. These calculations have been carried out with the Gamess program.^[20]

Results and Discussion

The dimers at the equilibrium configuration

Equilibrium configurations are found for the neutral and ionic complexes with the shared geometrical characteristics showing indistinguishable molecular graphs (see Table S1 of the Supplementary Material). All neutral complexes exhibit negative values of the binding energy (E_b), magnitude becoming positive in their ionic counterparts (Figure 1 and Table S2). These trends indicate that the neutral complexes are more stable than the isolated monomers, while the opposite happens in the ionic ones. As previously stated,^[4] the positive value implies the presence of an energetic barrier that should be overcome for forming or breaking the complex. The $\text{O}\cdots\text{H}$ distance in the HBs ($d_{\text{O}\cdots\text{H}}$) is also larger in the ionic complexes than in the neutral ones (Figure 2), presumably for the effect of the Coulombic repulsion between the charged terminal groups.

Fig. 1. Binding energy (E_b) and distance $\text{O}\cdots\text{H}$ ($d_{\text{O}\cdots\text{H}}$) for all the complexes in the equilibrium configuration.

In all cases, the existence of attractive electrostatic forces in the hydrogen bonding can be observed by the combined analysis of the topologies of the electron density ($\rho(\mathbf{r})$)^[8-9, 13a] and of the electrostatic potential ($\phi(\mathbf{r})$).^[21] The electric field in the plane defined by the carboxylic groups for the neutral and protonated

glycine dimer ($[\text{NH}_2, 1]$ and $[\text{NH}_3^+, 1]$, respectively) and the neutral and deprotonated glycolic acid ($[\text{OH}, 1]$ and $[\text{O}^-, 1]$, respectively) is shown in Figure 2. The analogous figures for the rest of the dimers have been gathered in the Supplementary Material.

Fig. 2. Electric field maps of all the complexes with $n = 1$. The volume of one of the molecules, as defined by the AIM methodology,^[22] has been indicated in dark grey.

The atomic volume of one of the monomers, defined within the AIM methodology, has been indicated with a shaded region. By looking at the electric field lines, calculated from the negative derivative of $\phi(\mathbf{r})$, it is possible to visualize the direction of the electrostatic forces acting on a region.^[23] From this analysis, it has been shown that, in the $\text{O}\cdots\text{H}$ HB, there is an intermediate region where the electric field lines start in the H-atom while the electron density belongs to the O-atom.^[24] This region, henceforth the electrostatic attraction region (EAR) is indicative of the electrostatic attractive forces in the HB region. The EAR is observed in the neutral and ionic complexes, indicating the existence of local attractive forces of electrostatic nature.

Indeed, as can be observed in Figure 2, while the ionization induce important changes in the conformation of the electric field lines around the molecule,^[23] the behavior of the electric field in the HB region is very similar in ionic complexes and their neutral counterparts. In addition, the comparison of anionic and cationic complexes does not reveal any significant difference between positive or negative charges within the HB region. Moreover, in spite of the qualitatively different effect of protonation or deprotonation in the electric field lines (compare $[\text{NH}_3^+, 1]$ and $[\text{O}^-, 1]$ in Figure 2), the effect of Coulombic repulsion in the properties of the complexes is the same regardless of the sign of the ionic charge.

Effect of the chain length

As can be observed in Figure 1, the dependence of E_b and $d_{\text{O}\cdots\text{H}}$ with the increase of n is qualitatively different for neutral or ionic complexes. While in the neutral complexes the lowest E_b is observed for $n = 0$, this property decreases with n for the ionic complexes, following a tendency that could eventually result, for n larger than those considered here, in ionic complexes with negative E_b . The HB distance $d_{\text{O}\cdots\text{H}}$ also decreases with n in the ionic complexes, a behavior that is not observed in the neutral cases.

Taking into account that the charge in the ionic complexes is located around the terminal groups, the observed behaviors are consistent with a weakening of the Coulombic repulsion as the chain is larger. Thus, it is expected that the influence of the terminal group in the HB became less significant as the chain lengthens, and that the properties dependent of the intermolecular interaction, such as the E_b or $d_{\text{O}\cdots\text{H}}$, converge toward a hypothetical infinite chain limit. This convergence is observed in Figure 1, although it's far from being achieved with the short chains considered here because of the slow decay of the Coulombic repulsion with the distance. Indeed, the difference in E_b decreases from 6.4 kJ/mol between $[\text{NH}_2, 0]$ and $[\text{OH}, 0]$ to 1.5 kJ/mol for $[\text{NH}_2, 4]$ and $[\text{OH}, 4]$, while for $d_{\text{O}\cdots\text{H}}$ the largest difference is 0.215 Å between $[\text{NH}_2, 0]$ and $[\text{O}^-, 0]$, and this difference reduces to 0.048 Å for $[\text{NH}_2, 4]$ and $[\text{O}^-, 4]$.

Energetic profile along the dissociation path.

The representation of the dissociation paths, calculated by increasing $d_{\text{O}\cdots\text{H}}$ in small steps reveals the profile of the energetic barrier that should be overcome for breaking the complex (Figure 3). Thus, starting on the energy minimum, the energy increases until a maximum is reached, and then decreases asymptotically to zero from positive values. It must be noticed that what is represented is one trajectory in the complex potential energy surface (PES) of the complex. While it cannot be excluded that other possible dissociation paths on the same PES could present a lower energetic barrier, larger variations in the height of this barrier are not expected because of the effect of the Coulombic and hydrogen bonding forces on the PES.^[9b]

The difference between the maximum of the energetic barrier and E_b has been taken as the dissociation energy (D_i) for the ionic complexes (Figure 4 and Table S3) while for the neutral ones $D_i = -E_b$ because there

is no energetic barrier and the interaction energy approaches to zero from negative values. As for E_b and $d_{O\cdots H}$, the values of D_i for neutral and ionic complexes converge as the chain lengthens and the Coulombic repulsion weakens. In the same sense, the energetic profiles of the charged complexes in Figure 4 progressively approach to what is expected in a neutral system, that is, the positive value of the local maximum lowers, while the local minimum E_b decreases. With this behavior, E_b decreases faster than the maximum of the energetic barrier, explaining the increase in D_i with n , expected for the ionic complexes in order to converge with the neutral ones.

Fig. 3. Dissociation profile of a) $[\text{NH}_3^+, n]$ vs. the N...N intermolecular distance (Å) and b) $[\text{O}^-, n]$ vs. the C...C intermolecular distance, being C the carbon attached to the O^- atom. The red line represents the repulsion of two point unit charges located at the same distance that the N and C-atoms, respectively.

Fig. 4. Dissociation energy (D_i) in the complexes studied.

The energy profiles of the ionic complexes (Figure 3) correspond roughly to the sum of two main contributions, one for the HB and the other for the Coulombic repulsion. As the latter force dominates at

long distances, the tails of these energy profiles superposes to the interaction energy of two point charges with one unit value and the same sign situated in the position of the charged group, namely at the N-atom for NH_3^+ and at the C-atom bonded to O^- , which corresponds to the approximate location of the center of charge in the molecules. The only exception to this behavior is $[\text{O}^-, 0]$, where the assumption of a center of negative charge close to this C-atom is not valid as the carbon belongs to the carboxylate group involved in the HB.

Fig. 5. Dissociation profile with Coulombic repulsion removed for the ionic complexes and some of the neutral ones ($n=0-3$). N...N and C...C intermolecular distances are defined as in Figure 4. The removed Coulombic repulsion corresponds to the red lines in Figure 4. The curve for $[\text{O}^-, 0]$ in b) presents a minimum at -173 kJ mol^{-1} not shown in the graphic.

In order to explore the relationship between the energetic profiles for the ionic and the neutral complexes, the profiles of the former have been plotted in Figure 5 after removing the point charge contribution represented in Figure 3. These dissociation profiles with the removed Coulombic repulsion resembles nicely the energetic profile of neutral complexes with the only exception of $n=0$, where the closeness of the terminal group to the carboxylate group makes the point charge assumption to fail. Using the values of the local minima in the corrected profiles, the binding energy of these complexes can be estimated without the significant influence of the charged groups (Figure 6). The values obtained using this simple procedure are closer to those of the neutral complexes than without removing the Coulombic contribution, converging ionic and neutral complexes to very similar values as the number of methylene groups increases and the influence of the terminal group in the electron density of the carboxylate weakens. This convergence is much faster for $\text{NH}_2/\text{NH}_3^+$ than for OH/O^- , being the difference between $[\text{NH}_3^+, 4]$ and $[\text{NH}_2, 4]$ of only 0.6 kJ/mol .

Fig. 6: E_b corrected of Coulombic repulsion (local minima values in Figure 5) for the $[\text{NH}_3^+, n]$ and $[\text{O}^-, n]$ complexes, compared with E_b (Figure 2) for $[\text{NH}_2, n]$ and $[\text{O}, n]$.

According to this analysis, if the Coulombic repulsion can be corrected, even in a rough way, what remains is qualitatively similar to a neutral complex, a result strongly suggesting that HBs between ions or neutral molecules are not significantly different. This is in agreement with the topological analysis of the electron density,^[25] where it is observed that the dependence of the topological properties at the HB critical points with $d_{\text{H}\cdots\text{O}}$ in ionic complexes are just as in neutral complexes,^[26] a behavior previously observed in similar comparisons between ionic and neutral complexes.^[9a] In the same sense, the NBO analysis shows that the energy stabilization, $E(2)$, due to the charge transfer from the lone pair of the carbonyl group towards the σ^* O-H orbital follows the same trend in the neutral and in the charged dimers (see Fig. S2 of the Supplementary Material)

IQA analysis and comparison with EDA methods.

The contribution of the electrostatic interaction can be separated from other energy contributions by means of energy decomposition methods. Different contributions to the interaction energy obtained according to the IQA and LMOEDA methods are given in Figures 7 and 8, respectively.

Fig. 7: Components of the energy decomposition and total interaction energy ($E_{int,IQA}$) according to the IQA method for the complexes in the equilibrium conformation vs the chain length. TS lines correspond to the maximum in the energy profile of the ionic complexes.

Fig. 8: Components of the energy decomposition and total interaction energy ($E_{int,LM}$) according to the LMOEDA method for the complexes in the equilibrium conformation vs the chain length. TS lines correspond to the maximum in the energy profile of the ionic complexes.

According to the IQA method, all complexes present a large and positive deformation contribution (E_{def}) that is compensated by a negative exchange-correlation term (V_{xc}). Both terms account for the electron density reorganization that takes place in the hydrogen bonding region when the closed shells of the interacting molecules are in contact. These effects include the repulsion of the closed shells and the concomitant removal of electron density from the bonding region, represented by E_{def} , and the early stages of the transition from a closed shell to a shared interaction, which is associated to the covalent character of the HB and is represented by V_{xc} . In all the complexes the destabilizing contribution of E_{def} is cancelled in a 79-91% by the stabilizing contribution of V_{xc} .

The variation of both E_{def} and V_{xc} is small in the neutral complexes, presenting all of them very similar values of both contributions independently of the chain length or the terminal group. For the ionic complexes, the values of E_{def} and V_{xc} become lower in absolute value as the length of the chain is reduced. Thus, both energy contributions in $[\text{NH}_3^+, 0]$ are about one third of the values for the neutral complexes or the ionic complexes with $n = 4$. This behavior can be attributed to the effect of the charged groups, which can modify the electron population of the carboxylate groups, hence affecting the decomposition energy terms. In spite of the numerical variations induced by this effect of the terminal group on the HB, the qualitative behavior is the same for ionic and neutral complexes.

Given the almost complete cancellation of E_{def} and V_{xc} , the total interaction energy ($E_{\text{int,IQA}}$) is dominated by the electrostatic contribution V_{cl} , hence the similarity found between this contribution and $E_{\text{int,IQA}}$ in Figure 7. V_{cl} is qualitatively different between neutral and ionic complexes because it includes the Coulombic repulsion of the terminal groups in the latter case. For the neutral complexes, this contribution is negative and independent on the terminal group or the chain length. In the ionic complexes with $n=0$ V_{cl} is positive, progressively decreasing toward the value of the neutral case as the length of the chain increases and the distance between terminal groups is larger.

The same energy decomposition analysis applied to the transition state corresponding to the highest point of the dissociation barrier for the ionic complexes exhibits also an interaction dominated by V_{cl} . E_{def} and V_{xc} present very low values because of the long distance between the interacting molecules, which prevents significant electron density reorganization in the HB region. In spite of a larger separation between the terminal groups, V_{cl} is larger in the transition state than in the equilibrium configuration. This behavior, which has been already observed in other complexes by using other energy decomposition schemes,^[7] can be rationalized on the basis that, although this contribution is dominated by the Coulombic repulsion of the terminal groups, it also includes the contribution of electrostatic attractive forces involving the carboxylate groups. Given their non-monopolar nature, the stabilizing contribution of these attractive forces decay faster with the intermolecular distance than the destabilizing contribution of the terminal groups repulsion,

hence the overall increase in V_{cl} when moving from the equilibrium configuration to the maximum of the energetic barrier.

In spite of the different theoretical framework, results from LMOEDA (Figure 8) are in line with those obtained with the IQA method. Thus, the interaction is dominated by the electrostatic contribution (E_{elec}), whose behavior mimics the total interaction energy ($E_{int,LM}$), while stabilizing contributions that can be attributed to the HB interaction, represented by the sum $E_{exc}+E_{pol}+E_{disp}$, are cancelled by a destabilizing contribution when the closed shells of the interacting molecules are in contact (E_{rep}). Here, the electrostatic contribution E_{elec} behaves as V_{cl} in the IQA method, with the same qualitative differences between neutral and ionic systems and the increase in its positive value when moving from the equilibrium configuration to the transition state in the ionic case. Thus, the same conclusions, which confirm the most important electrostatic contribution to the HB in ionic complexes, can be drawn from both energy decomposition schemes.

An important feature of the IQA method is that it allows the decomposition of the interaction energy of two molecular fragments. Thus, the decomposition of the interaction energy of the two carboxylic groups defined by the four atoms (CO_2H) can be calculated for neutral and ionic complexes and compared between them (Figure 9). It can be assumed that the contribution of the HB to the energy components is contained in the interaction between these groups. Indeed, E_{def} and V_{xc} are numerically very similar for either the interaction between carboxylic groups or complete molecules, as these quantities are related to the electron density reorganization in the HB region. The only exception is $[NH_3^+, O]$, for which the ratio of E_{def} for the interaction between carboxylic groups and complete molecules is only 0.30, outside the range 0.79 – 1.04 where the rest of the complexes lay, indicating that the electron density redistribution induced by the formation of the hydrogen bond extends beyond the carboxylate group.

The electrostatic component V_{cl} in Figure 9 is dominated by the contribution of the HB, leaving apart the electrostatic repulsion of the terminal groups in the case of the ionic complexes. Hence, V_{cl} for the interaction between carboxylic groups is stabilizing both in ionic and neutral complexes, with the numerical differences arising from the influence of the terminal groups in the carboxylate group. As a consequence of the negative value of V_{cl} , the total interaction energy between carboxylates (E_{int} in Figure 9) is always stabilizing, allowing the formation of the complex in spite of the repulsion of the terminal groups when charged.

The energy components in Figure 9 present the expected behavior for a hydrogen bonded complex with the only exception of $[NH_3^+, O]$, which presents a slightly positive V_{cl} and a value of V_{xc} much larger than E_{def} . The fact that the negative value of E_{int} in this case is due to V_{xc} does not mean that the stabilizing force in this complex arises from the covalent character of HB instead of an electrostatic interaction. As stated

before, this is the only case where the contribution of the HB to the energy components is not confined to the carboxylic group. Topological analysis of the electron density according to the Atoms In Molecules (AIM) theory ^[13a] does not exhibit any evidence of covalent character for this complex. Even more, this analysis (see Fig. S3 of the Supplementary Material) indicates that the HB in $[\text{NH}_3^+, \text{O}]$ should be classified as a pure closed shell interaction while in the other complexes it presents a significant shared character ^[27]. The NBO analysis supports the results of the topological analysis, as $[\text{NH}_3^+, \text{O}]$ presents by far the lowest value of the E(2) term related to the charge transfer between the carbonyl lone pair and the σ^* O-H orbital (see Supplementary Material). Also, $d_{\text{O}\cdots\text{H}}$ is significantly longer for $[\text{NH}_3^+, \text{O}]$ than for the other complexes (Figure 2). The large $d_{\text{O}\cdots\text{H}}$ can be explained from the atomic charges, as obtained from the integration of the electron density in the atomic volumes as defined in the AIM theory ^[13a]. Thus, according to this integration, the carboxylic group in the complexes with $n = 0$ is positively charged, with charges in the range 0.35 – 0.47 e; while for $n > 0$ the expected behavior of a negatively charged or neutral group is observed, being the charge in the range -0.31 – 0.00 e. The electronegative atom in the terminal group steals charge from the carboxylic group for $n = 0$, while for $n > 0$ this charge transfer is blocked by the interposing carbonyl groups. Coulombic interactions involving the carboxylic group are superposed to the HB contribution to V_{cl} given in Figure 9. To the case of $[\text{NH}_3^+, \text{O}]$, they become the main contribution, giving rise to the positive value of V_{cl} observed in this complex. In addition, the case $[\text{NH}_3^+, \text{O}]$ is also particular because, besides the interaction between carboxylic groups, there is a Coulombic repulsion between them and the terminal groups, which could explain the long $d_{\text{O}\cdots\text{H}}$ for this complex (Figure 2).

Fig. 9: Components of the energy decomposition and total interaction energy according to the IQA method of the carboxylate groups in the complexes at equilibrium conformation vs the chain length.

Conclusions

All the carboxylic acid dimers studied present equilibrium conformations regardless of their electrical charge. While the neutral complexes present negative binding energies, the ionic ones present positive binding energy and an energetic barrier that must be overcome before dissociation of the complex. As the chain of methylene separating the carboxylic group from the charged terminal group is longer, the properties of the ionic and neutral complexes progressively converge. This convergence is fast for properties directly related to HBs, such as the HB distance, as in these cases the differences arise from the influence of the terminal group on the carboxylate group. In the case of properties depending on the Coulombic repulsion of the terminal groups, such as the binding energy, this convergence is slow and far from being achieved with the short chains considered in this work. In the case of the dissociation profiles, the dissociation energy of the ionic complexes progressively converge with the binding energy of the neutral ones as the chain lengthens. The convergence is slow enough as to prevent a negative binding energy and the disappearing of the energetic barrier in the charged studied complexes, both features being expected to be observed for longer chains.

The progressive convergence of neutral and ionic complexes as the charged terminal groups are farther from the HB region suggests that there is no formal difference between HBs in neutral and ionic complexes. Indeed, the analysis of the electric field lines reveals the same attractive electrostatic forces in the HB region in neutral and ionic complexes, and the application of energy decomposition methods demonstrates that, in spite that the electrostatic interaction is dominated by the Coulombic repulsion of the charged groups, there is a stabilizing electrostatic interaction involving the carboxylate groups. Moreover, the energetic contributions coming from hydrogen bonding and Coulombic repulsion can be roughly separated by representing the latter with a simple model of point charges close to the charged groups. Accordingly, the contribution of the HB to the dissociation profile calculated in this way resembles that of the neutral complexes. All these results are indicative that the ionic character of the molecules has no influence on the nature of the HB.

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References

- [1] a) S. Camiolo, P. A. Gale, M. B. Hursthouse, M. E. Light and A. J. Shi, *Chem. Commun.* **2002**, 758-759; b) Z. Wang, Y. Cheng, C. Liao and C. Yan, *CrystEngComm* **2001**, 3, 237-242; c) D. Braga, F. Grepioni and J. J. Novoa, *Chemical Communications* **1998**, 1959-1960; d) E. Espinosa, C. Lecomte, E. Molins, S. Veintemillas, A. Cousson and W. Paulus, *Acta Crystallogr., Sect. B* **1996**, 52, 519.
- [2] S. R. Kass, *J. Am. Chem. Soc.* **2005**, 127, 13098-13099.
- [3] S.-W. Lee and J. L. Beauchamp, *J. Am. Soc. Mass. Spectrom.* **1999**, 10, 347-351.
- [4] L. Feketeova and R. A. J. O'Hair, *Chem. Commun.* **2008**, 4942-4944.
- [5] M. Pszona, K. Haupa, A. Bil, K. Mierzwicki, Z. Szewczuk and Z. Mielke, *J. Mass Spectrom.* **2015**, 50, 127-135.
- [6] F. Weinhold and R. A. Klein, *Angewandte Chemie International Edition* **2014**, 53, 11214-11217.
- [7] G. Frenking and G. F. Caramori, *Angew. Chem. Int. Ed.* **2015**, 54, 2596-2599.
- [8] I. Mata, I. Alkorta, E. Molins and E. Espinosa, *Chemphyschem* **2012**, 13, 1421-1424.
- [9] a) I. Mata, I. Alkorta, E. Molins and E. Espinosa, *Chem. Phys. Lett.* **2013**, 555, 106-109; b) I. Mata, E. Molins, I. Alkorta and E. Espinosa, *J. Phys. Chem. A* **2015**, 119, 183-194.
- [10] A. Shokri, M. Ramezani, A. Fattahi and S. R. Kass, *J. Phys. Chem. A* **2013**, 117, 9252-9258.
- [11] a) Y. Zhao and D. Truhlar, *Theor. Chem. Acc.* **2008**, 120, 215-241; b) T. H. Dunning, *J. Chem. Phys.* **1989**, 90, 1007-1023.
- [12] M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery Jr., J. E. Peralta, F. Ogliaro, M. J. Bearpark, J. Heyd, E. N. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. P. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, N. J. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, Ö. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski and D. J. Fox in *Gaussian 09, Vol.* Gaussian, Inc., Wallingford, CT, USA, **2009**.
- [13] a) R. F. W. Bader, *Atoms in Molecules: A Quantum Theory*, Clarendon Press, Oxford, **1990**, p; b) P. L. A. Popelier, *Atoms In Molecules. An introduction*, Prentice Hall, Harlow, England, **2000**, p.
- [14] a) T. A. Keith in *AIMAll, Vol.* TK Gristmill Software, Overland Park KS, USA, **2011 Version** p. (aim.tkgristmill.com); b) F. W. Biegler-König, R. F. W. Bader and T. H. Tang, *J. Comput. Chem.* **1982**, 3, 317-328.
- [15] J. D. Hunter, *Computing in Science & Engineering* **2007**, 9, 90-95.
- [16] A. E. Reed, L. A. Curtiss and F. Weinhold, *Chem. Rev.* **1988**, 88, 899-926.
- [17] E. D. Glendening, J. K. Badenhoop, A. E. Reed, J. E. Carpenter, J. A. Bohmann, C. M. Morales, C. R. Landis and F. Weinhold in *NBO 6.0, Vol.* Theoretical Chemistry Institute, University of Wisconsin, Madison, WI, **2013**.
- [18] M. A. Blanco, A. Martín Pendás and E. Francisco, *Journal of Chemical Theory and Computation* **2005**, 1, 1096-1109.
- [19] P. Su and H. Li, *J. Chem. Phys.* **2009**, 131, 014102.
- [20] M. W. Schmidt, K. K. Baldridge, J. A. Boatz, S. T. Elbert, M. S. Gordon, J. H. Jensen, S. Koseki, N. Matsunaga, K. A. Nguyen, S. J. Su, T. L. Windus, M. Dupuis and J. A. Montgomery in *Gamess*, , Vol. Iowa State University, **2013**.
- [21] S. R. Gadre, S. A. Kulkarni and I. H. Shrivastava, *J. Chem. Phys.* **1992**, 96, 5253-5260.
- [22] R. F. W. Bader, M. T. Carroll, J. R. Cheeseman and C. Chang, *J. Am. Chem. Soc.* **1987**, 109, 7968-7979.
- [23] I. Mata, E. Molins and E. Espinosa, *J. Phys. Chem. A* **2007**, 111, 9859-9870.
- [24] I. Mata, E. Molins, I. Alkorta and E. Espinosa, *J. Phys. Chem. A* **2007**, 111, 6425-6433.
- [25] R. F. W. Bader and H. Essén, *The Journal of Chemical Physics* **1983**, 80, 1943-1960.
- [26] I. Mata, I. Alkorta, E. Molins and E. Espinosa, *Chemistry - A European Journal* **2010**, 16, 2442-2452.

[27] E. Espinosa, I. Alkorta, J. Elguero and E. Molins, *Journal of Chemical Physics* **2002**, *117*, 5529-5542.