

Original Investigations

Electrostatic Molecular Potentials in Hydrogen-Bonded Systems

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A study is made of the modifications of the electrostatic molecular potential brought about by hydrogen bonding both in the hydrogen-bond region itself and in the external regions of the proton-acceptor and proton-donor molecules. Systems up to four successive units in a chain of donor-acceptors are considered. The possibility of obtaining a satisfactory picture of the global potential by a simple superposition of the potentials of the individual units is evaluated.

Key words: Molecular electrostatic potential – Hydrogen-bonded systems

1. Introduction

Electrostatic molecular potentials appear to be an extremely useful tool for the study of protonation of biomolecules and play also a significant role in the elucidation of the affinity of such systems towards more complex cations in particular alkyl and metal cations. They have been applied for this sake in the investigation of different components of the nucleic acids: purine and pyrimidine bases [1, 2], the phosphodiester linkage [3, 4], the sugar ring [5], and also of the peptide bond [6].

Because of the particular importance in molecular biology of hydrogen-bonded systems it seems useful to investigate some aspects of the electrostatic molecular potentials in such systems. Among these aspects the most significant seem to be related to: a) the shape and value of the potential in the region of the hydrogen bond itself, b) the modifications produced in the potentials of the hydrogen-bonded units by this bonding, outside the hydrogen-bonded region; c) in case of the existence of a significant such modification, the extent to which it is transmitted along a chain of hydrogen-bonded units.

A partial answer to some of these questions, in particular to question b), has been given in our study on the interactions in a phosphate-water-cation system [7]. The present paper is an attempt at a more complete investigation of the three problems cited above. Moreover, we shall examine in the light of the results of the complete computations, the possibility of utilizing a simple superposition of the individual potentials to obtain the potential of the hydrogen-bonded system.

2. Method

The molecular electrostatic potential at a point P is defined from the electron density distribution function $\rho(i)$ and the nuclear charges z_α of the system considered by the expression [8]:

$$V(P) = \sum_{\alpha} \frac{z_{\alpha}}{r_{\alpha P}} - \int \frac{\rho(i) d\tau_i}{r_{iP}}$$

The electron density ρ used in the present paper results from *ab initio* SCF computations of the molecular wave function at the STO 3G [9] level. It is well known that the STO 3G basis exaggerates the apparent charge transfer in hydrogen bonding and at the same time underestimates the polarization and electrostatic components of the binding energies [10, 11, 12]; although this will affect the numerical values of the results, the general conclusions concerning the evolution of the potential upon hydrogen bonding are not likely to be affected as will be clear from the discussion.

3. Results and Discussion

As a starting point for our investigation, Fig. 1 presents the electrostatic molecular potential maps: a) in the vicinity of the nitrogen atom in pyridine, in the plane of the ring (a very similar map is obtained in the vicinity of the nitrogen atom of ammonia in the symmetry plane of the NH_3 pyramid); b) in the vicinity of the oxygen atom of water, in the plane of the molecule (a very similar map is obtained in the vicinity of the oxygen atom of water in the plane bisecting the HOH angle).

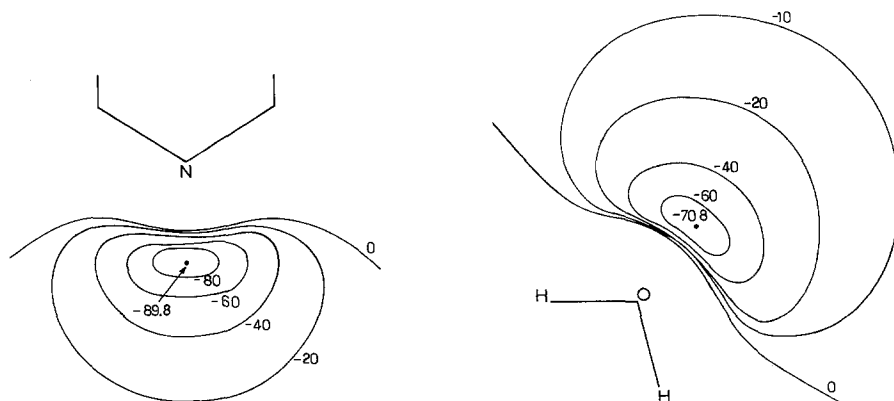


Fig. 1. Molecular potentials. a) pyridine in the molecular plane; b) water in the plane of the molecule

The four maps are thus similar in their general shape, indicating a large affinity of the lone pairs of nitrogen and oxygen for a unit positive charge with, however, noticeable differences in the value of the potential minimum: the greatest one is associated with NH_3 (-107.3 kcal/mole at a distance of 1.03 Å from N), the next one with pyridine (-89.8 kcal/mole at a distance of 1.06 Å from N) and the smallest with H_2O (-70.8 kcal/mole at a distance of 1.02 Å from O). A similar result is preserved on the potential map in the vicinity of the N atom for a trihydrate of NH_3 in which the three water molecules are fixed along the N–H bonds ($(\text{H}_2\text{O})_3\text{H}_3\text{N}$). We shall discuss in the next section the significance of the variation in the value of the maximum of the potential between free NH_3 and this hydrate. Here we wish simply to note the value of this maximum in the trihydrate: -130.2 kcal/mole at an unchanged distance of 1.03 Å from N.

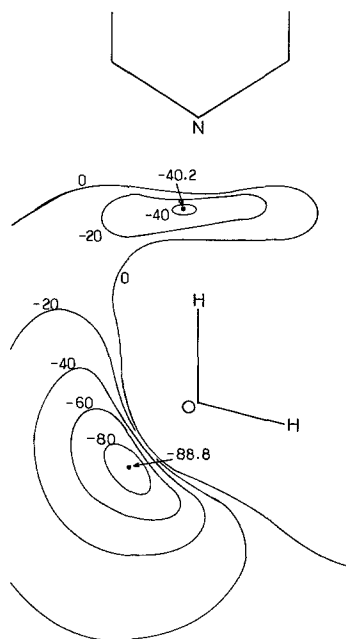


Fig. 2. Molecular potential of the system pyridine-water in the plane of pyridine (water coplanar with pyridine); a very similar result is obtained for pyridine-water in the perpendicular plane (water perpendicular to pyridine)

Figure 2 presents the potential in the plane of a water molecule bound to pyridine (whether water is in the pyridine plane or perpendicular to it, the two maps differ very little from each other). In this system, the optimal association corresponds to the perpendicular orientation of the water molecule ($\Delta E = -4.7$ kcal/mole, $\text{N}\cdots\text{H}$ distance = 1.98 Å) with the OH bond bisecting the CNC angle at the pyridine ring and thus pointing in the direction of the lone pair on N. Figure 3a gives the results for the optimal configuration of a water dimer: distance $\text{O}_1\text{--}\text{O}_2 = 2.75$ Å; bisectrix of the second water molecule in the plane of the first one and rotated by $\theta = 54^\circ 77'$ away from the O_1O_2 direction ($\Delta E = -6.4$ kcal/mole). Figure 3b corresponds to $\theta = 0$ ($\Delta E = -5.6$ kcal/mole).

Let us now consider the three above-mentioned problems in succession.

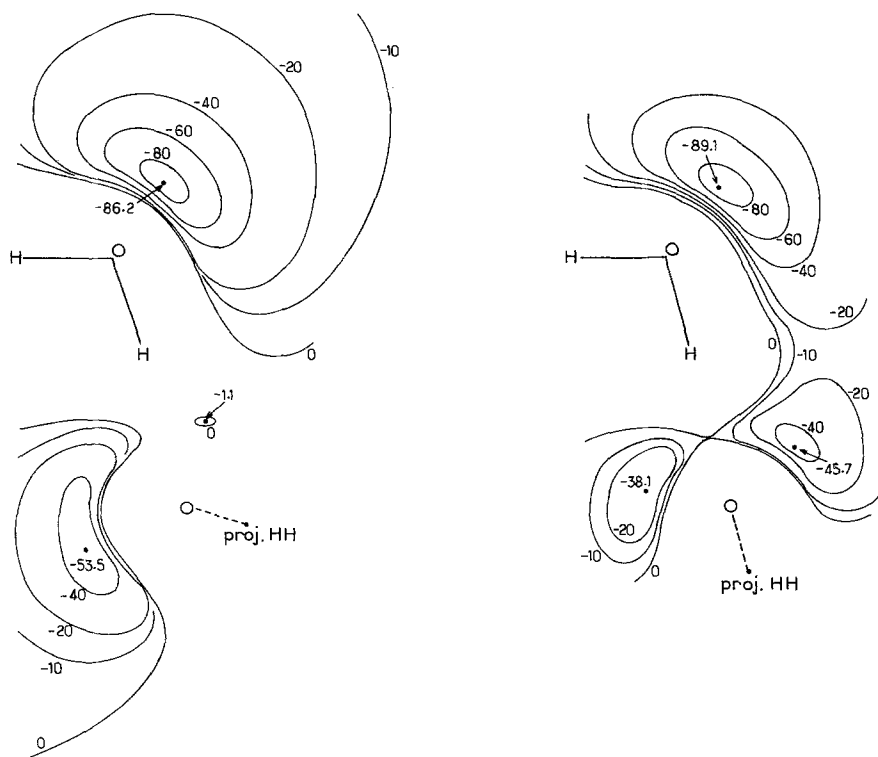


Fig. 3. Molecular potential of a) the water dimer in its optimal configuration ($\theta = 54^\circ 77'$); b) same for $\theta = 0$

3.1. The Region of the Hydrogen-Bond Itself

The results obtained are quite different according to the system considered. Thus in both the pyridine-water and the $\text{NH}_3\text{-H}_2\text{O}$ systems the region of the $\text{N}\cdots\text{H-O}$ hydrogen bond, facing the nitrogen atom, although corresponding to a more restricted zone of negative potential than in free pyridine or NH_3 , still presents a relatively pronounced minimum: ≈ -40 kcal/mole in pyridine $\text{-H}_2\text{O}$, -59.7 kcal/mole in $\text{NH}_3\cdots 4\text{H}_2\text{O}$. These minima are located in close vicinity to the $\text{N}\cdots\text{H-O}$ axis and result obviously from the partial (but not total) neutralization of the attractive potential of the free nitrogenous compounds (translating primarily the proton affinity of the lone pair on their N atom) by the repulsive potential on the proton side of the proton-donor molecule. The situation is different in the water dimer in which there is practically no zone of negative potential along the $\text{O}\cdots\text{H-O}$ hydrogen bond axis. This situation may be explained in terms of the relative values of the potentials on the donor and acceptor sites: the negative potentials in pyridine and in $(\text{H}_2\text{O})_3\text{H}_3\text{N}$ being appreciably larger than that of water are not completely cancelled by the repulsive potential of the proton donor water molecule. In the water dimer the value of the repulsive potential of the proton

donor is clearly just about sufficient for a complete cancellation of the attractive potential on the O...H line.

As another example of the situation existing in O...H-O hydrogen bonded complexes we may recall the results pertaining to the electrostatic molecular potential in the O_1PO_3 plane (involving the two anionic oxygens) of the dimethylphosphate anion (DMP^-) representing the phosphodiester linkage, and the same potential in the corresponding hexahydrate of DMP^- where each of the anionic oxygens carries three water molecules acting as proton-donors and symmetrically disposed around the PO axis. (For details see Ref. [7].) It is found that the regions of the phosphate-water hydrogen bonds are devoid of negative potential. Here the complete cancellation of the strong negative potential of the phosphate oxygens requires, however, the binding of three water molecules to each of them. When only one water molecule is bound to the phosphate group an appreciable attractive zone remains along the O...HO line.

Aside from the relative values of the attractive and repulsive character of the two partners, their mutual orientation in the hydrogen-bonded system has a strong influence on the resulting potential. This is illustrated on the case of the water dimer for the two orientations corresponding to Figs. 3a and 3b respectively. In the first case, one attractive zone remains in the neighbourhood of the proton-acceptor oxygen with a minimum of -53.5 kcal/mole. When the proton-acceptor molecule is rotated to $\theta=0$, the initial attractive zone of the isolated water molecule is partially neutralized by the repulsive potential of the proton-donor molecule bound to it, but, here the remaining attractive zone is split between two regions of smaller attraction. These variations of the attractive characteristics in the neighbourhood of the proton-accepting water according to its orientation explain that up to three ligands (one axial and two perpendicular) may be coordinated to the oxygen of water in crystals [13]. The *in situ* lability [14] of water-water binding is large enough to permit different angular situations to occur in a dimer: in the angular orientation of Fig. 3a, the proton-acceptor oxygen may attract one other proton-donor, this situation corresponding to the classical image of two binding lone-pairs; in the linear orientation of Fig. 3b, however, one may conceive the formation of two weaker bonds on each side of the HOH plane.

An analogous situation exists in the formamide dimer when the proton acceptor C=O group and the HN bond of the proton donor are collinear: it was shown that in this case two attractive regions remain on each side of the oxygen atom to which a water molecule can approach [15]. This does not necessarily mean that both positions will always be occupied.

Worth noting is the fact that this orientation-dependent effect on the remaining aptitude of a proton-acceptor to further attract proton donors (or positive charges) cannot be detected at the level of a population analysis (the net negative charge on the proton-acceptor oxygen are -0.368 and -0.366 in the linear and angular water dimers, respectively). The examination of the isodensity difference contours shows a very slight difference but only the potential maps are really unequivocal.

3.2. *Perturbations Produced in the Potentials of the Hydrogen-Bonded Units outside the Hydrogen Bond Region*

Figures 1–3 contain also an answer to this question. In the examples of Figs. 1 and 2 the attention centers on the water molecules. The maximum value of the potential in the vicinity of a free water molecule equals -70.8 kcal/mole (Fig. 1b). Figure 2 indicates that this value increases for a water molecule fixed as a proton donor on the pyridine nitrogen. The situation results from three underlying features: 1) a pure additive phenomenon due to the fact that, in the complex, the region of the potential minimum of water is located in a zone of small attractive potential for the pyridine molecule itself; 2) the fact that a hydrogen-bonded molecule acquires a small overall excess of electronic charge with respect to free water by global charge transfer from the nitrogenous ligand, and 3) the internal electron displacements on the proton donor due to the polarization by the proton acceptor (for the details of the populations of these complexes see for instance Ref. [11]). This activation of the potential associated with a water molecule functioning as a proton donor is appreciably stronger when the water is bound in this way to the anionic system of DMP^- . This is due to a much greater charge transfer effect and a stronger polarization (see Ref. [16]), but also, and in fact essentially, to the fact that the water molecule resides in a zone where the potential of the proton acceptor itself (here an anion) is appreciably stronger than that of the neutral proton acceptor.

The strong increase of the potential in the vicinity of the N atom in the trihydrate of NH_3 with respect to NH_3 itself is another example of a distant modification of the potential of a proton-donor molecule by hydrogen bonding. One observes there the accumulation of the aforementioned effects by bonding of three water molecules as proton acceptors to the other side of the NH_3 molecule.

When a molecule functions as a proton-acceptor, its attractive potential undergoes the inverse effect, as already observed in the water dimer and in the hexahydrate of dimethylphosphate [7]. The underlying reasons of this decrease are here again, the charge transfer (from the phosphate to water), the polarization of the phosphate group (see Ref. [16] for details on the electron displacements), and the simple superposition effect of the individual potentials which acts here so as to decrease the attractive character in the central zone (the proton-donor water molecule is oriented so as to contribute a positive potential in this region).

3.3. *The Transmission of the Perturbation of the Potential along a Chain of Hydrogen-Bonded Units*

The results of the previous section, which indicate that significant perturbations are produced in the electrostatic molecular potential of hydrogen-bonded systems even outside the region of the hydrogen bond itself raise the question of the possible transmission of the effect along a chain of hydrogen-bonded entities. As an example of such a transmission, we have considered first the trihydrate, tetrahydrate and pentahydrate of NH_3 in which the first three water molecules are fixed

along the N–H bonds and the 4th and 5th water molecules are bound to the N atom. We have already reported the enhancement of the attractive character of the trihydrate with respect to isolated ammonia (the potential minimum going from 107 to 130 kcal/mole). In the tetrahydrate the water molecule which is the third unit in the chain of proton-donors sees its potential minimum increase from 70 to 102 kcal/mole, but when a further proton-donor water is added, its potential does not increase further with respect to that of the previous one (=98 kcal/mole), indicating that the tendency to attract a further proton-donor water molecule has reached a plateau. This effect is equally seen in the evolution of the net electron populations on the oxygen atom of the end water molecule (-0.439 in the tetrahydrate and -0.438 in the pentahydrate) and also in the global net charge carried by this molecule ($-0.068 e$ and $-0.067 e$ respectively). More details on the transmission of the effect along a chain will be given in a forthcoming paper [17].

3.4. The Potential of H-Bonded Units Obtained by Simple Superposition of the Individual Potentials

In the preceding discussion, we have underlined that one of the important components of the effects observed on the molecular potential upon H-bonding is due to the superposition of the potentials of the individual units, the others being due to the electron displacement which take place in the system. In order to delineate in more detail the relative weight and role of these effects, we examine in this section, on the example of the water dimer, the molecular potential obtained by a simple superposition of the potentials of two isolated water molecules put in the appropriate relative geometry. Figures 4a and 4b give the results for the two

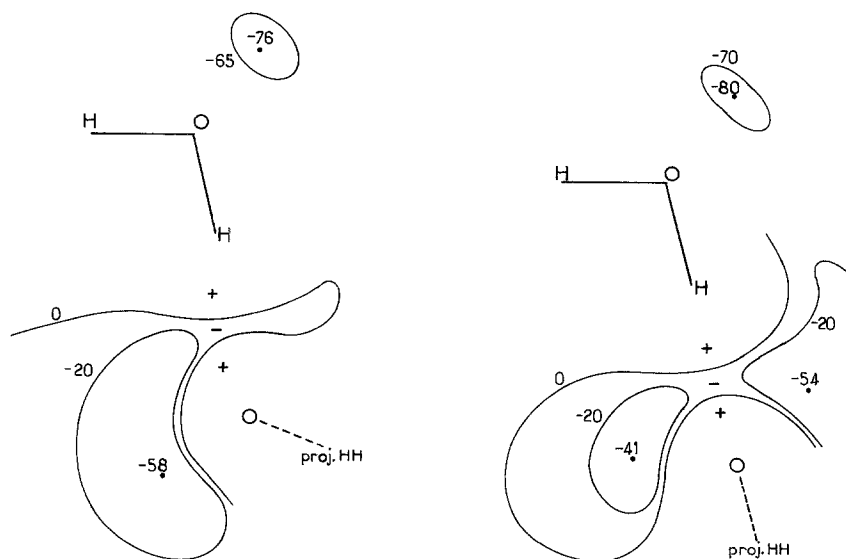


Fig. 4. Molecular potential of the water dimer obtained by superposition of the potentials of the isolated components a) angular dimer ($\theta = 54^\circ 77'$); b) linear dimer ($\theta = 0$). Only the lines essential to the discussion are represented

orientations of the proton acceptor examined previously, the exact potentials of which are given in Figs. 3a and 3b.

Comparison of the maps of Fig. 4 and 3 indicate immediately a global overall similarity in the results including: 1) an enhancement of the attractive character of the proton-donor water molecule, 2) a decrease of the attractive character of the proton-acceptor molecule; 3) a near disappearance of the attractive potential along the H-bond line. The overall shape of the various zones is similar in the exact and approximate representation and even the relative order of the minima is reproduced: compare for instance those of the two attractive regions flanking the proton-acceptor oxygen in Figs. 4b and 3b.

Nevertheless, there are also differences between the exact and superposition diagrams which essentially consist of 1) the existence of a residual small attractive potential along the H-bond line; 2) the slightly larger width of the attractive regions remaining in the vicinity of the proton-acceptor oxygen atoms accompanied by larger values of the potential minima in these zones; 3) on the contrary a smaller attractive zone than in the exact map in the vicinity of the oxygen of the proton donor, accompanied by a smaller value of the potential minimum. These differences are clearly due to the neglect, in the superposition approach, of the electron displacements which accompany the formation of the hydrogen bond (see for instance Refs. [18, 19, 20]). Both the polarization and charge-transfer effects contribute to increase the population of the oxygen of the proton donor, thus increasing its potential with respect to that obtained by pure superposition. In the hydrogen-bond region, along the OHO line and in the vicinity of the proton-acceptor oxygen, the exact potential is on the contrary decreased by the fact that hydrogen bonding produces a departure of the electrons from the central region (exchange effect [19]) and a denuding of the proton by polarization.

On the whole, however, it appears that the general image of the modifications of the molecular potential upon hydrogen bonding is approximated quite satisfactorily by superposing the potentials of the two separate entities and that this approach may be a valuable tool for the exploration of the modifications of the properties of larger hydrogen-bonded systems, provided that one keeps in mind the above-described corrections that would be brought about by the electronic perturbations.

An application of this approximation to the hydrogen-bonded base-pairs of the nucleic acids has been made [21].

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