Hydrogen Bonds: First Quantitative Agreement between Electrostatic Potential Calculations from Experimental X−(X + N) and Theoretical *ab Initio* SCF Models

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We have recently shown that quantitative agreement on the static electron density deformation $\Delta\rho(r)$ (i.e., the difference between $\rho(r)$ and the density generated by a superposition of isolated, spherical, noninteracting atoms) between *ab initio* SCF calculations and experimental X−X models[1] is obtained on medium-sized molecular systems of up to 50 non-hydrogen atoms if extended basis sets of good quality (triple-ζ for the valence shell, plus polarization functions) are utilized. Now, for large nonsymmetric systems, the evaluation of nonbonded interactions is too expensive in time and size to account for polarization effects in theoretical calculations; their study with convenient basis sets is, however, feasible if they appear inside the molecular unit, like in L-arginine phosphate monohydrate[2] (LAP), where hydrogen bonding (HB) exists in the asymmetric unit of the crystal. Features of structural and chemical interest such as bonding interactions are usually visualized by means of the static electron density deformation function, but the electrostatic potential $V(r)$ provides more information on reactivity than $\Delta\rho(r)$. Thus, a very informative electrostatic potential distribution could be derived from a good model of $\rho(r)$, in order to get a better knowledge of the chemical behavior of molecules. Furthermore, as hydrogen bonding is essentially an electrostatic interaction, it appears that $V(r)$ is the observable really worth being considered and checked in regions where HBs occur. This point was raised in the late 1970s, and theoretical investigations on the distribution of $V(r)$ in various hydrogen-bonded systems, including the water dimer[3] and phosphate−water−cation systems,[4] have been reported. Even though those early studies pointed out the basic pattern of $V(r)$ in the vicinity of a H bond, they were carried out with poor, typically STO-3G basis sets and were clearly missing a precise reference to experiment.[4] We have carried out both experimental X−(X + N) and *ab initio* SCF calculations on LAP (Figure 1), in order to test the theoretical prediction of the electrostatic potential $V(r)$ in the intermolecular and HB regions. The analysis shows a quantitative agreement between both calculations within 0.05 e Å^{-1} in the H···O region.

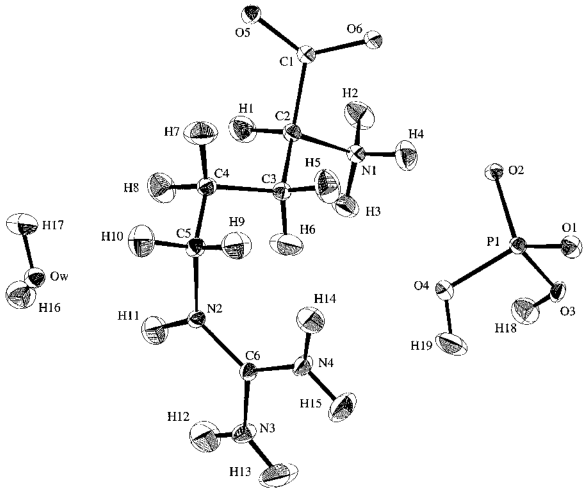

Figure 1. ORTEP view of the asymmetric unit of LAP. Thermal motion is represented by ellipsoids at 50% probability.

The experimental electron density of LAP, its related electrostatic properties inside the asymmetric unit have been derived from X-ray and neutron data at $T = 130$ K by means of an X−(X + N) model of $\rho(r)$ [multipolar refinement,[5] 6805 unique reflections, $I > 3\sigma(I)$, $\sin\theta/\lambda < 1.20$ Å^{-1}, $R_w(F) = 0.014$]. *Ab initio* SCF theoretical models of $\rho(r)$ and $V(r)$ were calculated for the asymmetric unit of LAP with basis sets of triple zeta quality for the valence shells including both diffuse and polarization functions. Atomic positions were taken from the X−(X + N) experimental model, and no geometry optimization was done.

Figure 2 displays the static electron density deformation $\Delta\rho^{X-(X+N)}(r)$ in the plane of the N1−H4···O2 hydrogen bonding and the *ab initio* SCF map $\Delta\rho^{\mathrm{theor}}(r)$ in the same plane. The corresponding cuts of the electrostatic potential distributions $V^{X-(X+N)}(r)$ and $V^{\mathrm{theor}}(r)$ are reproduced in Figures 3, along with the difference map $\Delta V(r)$. The X−(X + N) electrostatic potential calculations were performed with the pseudoisolated asymmetric unit, i.e., all information on the molecular groups was obtained from the crystal, but the $V^{X-(X+N)}(r)$ function was calculated in the molecular unit only (defined in Figure 1).

The deformation density agrees within 0.05 e Å^{-3} for all bond peaks except for N1−H3, O2−P, and lone pairs regions. The disagreement noticed in those regions could be enhanced by the location of the corresponding maxima of electron deformation density out of the reported plane. Therefore, slight changes in the gradient of $\Delta\rho(r)$ and/or in the shape of the peaks may significantly affect the value of the electron density in the plane of Figure 2. This assumption is supported by the near quantitative agreement obtained on the O−P−O(H) plane (see supporting information). We also note that the zero contour has the same shape in both cases, and that the depletion zone corresponding to the HB region is slightly more negative (0.06 e Å^{-3}) on the theoretical map. These observations concerning the deformation electron density are purely local and have little influence on the electrostatic potential function.

The models of $V(r)$ obtained from both experimental and theoretical data around the molecular unit agree quantitatively (see supporting information): a negative potential develops around the phosphate group, with an absolute minimum −0.42 e Å^{-1} (−0.22 e bohr^{-1}) located at 1.06 Å from O1 (respectively 1.11 and −0.38 e Å^{-1} (−0.20 e bohr^{-1}) for the theoretical model). A similar modeling made from the experimental data only on the isolated arginine cation moiety (i.e., without HB) shows a very extended region of positive potential around the NH_3^+ group, where the 0.15 e Å^{-1} contour extends up to 4.67 Å (along the HB direction) from the H4 atom (see supporting

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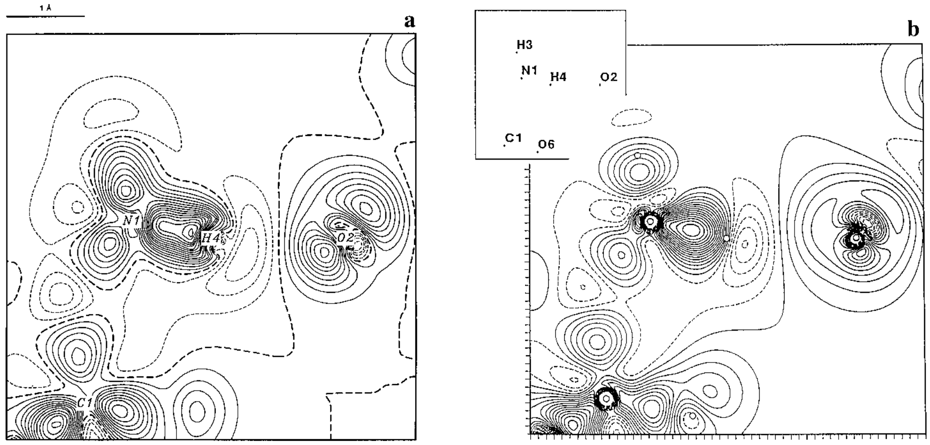

Figure 2. Static electron density deformation in the HB section N1—H4···O2: (a) $\Delta\rho^{X-(X+N)}(r)$ and (b) $\Delta\rho^{theor}(r)$. Contours interval: 0.05 e Å^{-3}; solid lines positive, dotted lines negative. The zero contour is the first solid line in the theoretical case.

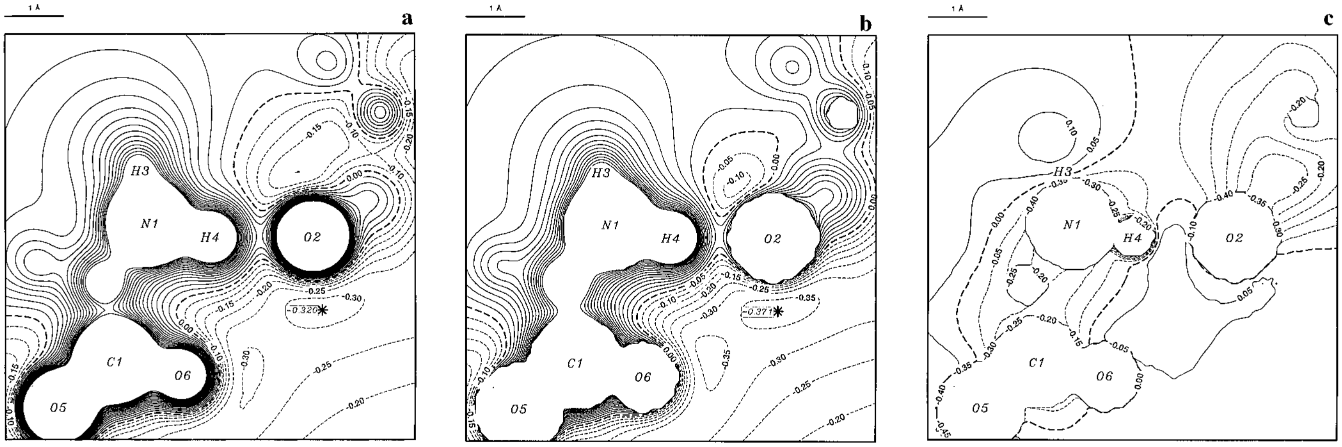

Figure 3. Electrostatic potential in the HB section N1—H4···O2; (a) $V^{X-(X+N)}(r)$, (b) $V^{theor}(r)$, and (c) $\Delta V(r) = V^{X-(X+N)}(r) - V^{theor}(r)$. Contours intervals: 0.05 e Å^{-1}; solid lines positive, dotted lines negative, and zero contour broken.

information). When arginine and phosphate groups interact to lead to the neutral molecular unit via the N1—H4···O2 HB (see Figure 3), the region of negative potential around the phosphate group splits into two negative zones separated by the H4···O2 line. In both experimental and theoretical models, a region with slightly positive $V(r)$ (between +0.10 and +0.15 e Å^{-1}), characterized by a topological saddle point (at ~0.8 Å from H4), appears close to the center of the H4···O2 line. As noticed from early *ab initio* investigations on the electrostatic potential of small molecules,[3,4,7] this saddle point represents the signature of the HB. The $\Delta V(r)$ map (Figure 3c) shows that, in the HB region, the potential in the experimental model is slightly larger by 0.05 e Å^{-1} (0.03 e bohr^{-1}) than in the theoretical one. This difference represents the order of magnitude of the experimental estimated esd of $V(r)$ outside the van der Waals surface and therefore is not significant.

The agreement between *ab initio* SCF and experimental X−(X + N) models can, therefore, be considered as quantitative in the region of the HB. The present work settles the conditions necessary to obtain such an agreement concerning the quality of the measurements as well as the extension of the basis sets. As far as theory is concerned, systematic studies have already been carried out to investigate the dependence of electrostatic potentials on the basis set quality[8] and on the treatment of electron correlation.[9] Such a systematic investigation should now be extended to the conditions of the X-ray diffraction measurements, to the influence of the multipole model, and to the effect of extending the considered system to the neighbor units, and then to the whole crystal. Beyond the mutual confirmation of X-ray diffraction and quantum chemical results, which remains necessary anyway, a field of joint theoretical and experimental investigations arises from the present results with the perspective of correlating the strength of the hydrogen bond to the topology of the electrostatic potential between the interacting fragments.

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Supporting Information Available: Experimental, theoretical, and $\Delta V(r)$ electrostatic potentials calculated from the asymmetric unit in the O1−P−O3 plane; experimental electrostatic potential of the pseudoisolated arginine cation in the same plane as Figure 3; experimental and theoretical static $\Delta\rho$ in the O1−P−O3 plane (7 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

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