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Partially Charged H_5O_2 as a Chemical Switch: A Bond Order and Atoms in Molecules Study of Hydrogen Bonding Determined by Surrounding Groups

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The H_5O_2 group can behave very differently in different surroundings. When partially charged, with the remainder of the charge on surrounding groups, it can have a short central hydrogen bond, with O−O distance <2.5 Å. A different arrangement of surrounding groups can produce a normal hydrogen bond, with O−O distance >2.7 Å. The transition is, for some systems, very abrupt. In the cases we discuss here, there is an example of a set of conditions in which this abrupt transition occurs. There is also a case in which intermediate values of the central hydrogen bond occur, but this behaves as though these values remain on one side of the transition point. The switch is effected by small changes in the position of the surrounding groups. To study this, several sets of four groups were used to surround the H_5O_2 group. Density functional calculations were carried out on the system, with the surrounding groups fixed in each of several positions, and the H_5O_2 group optimized. Some configurations produced short bonds, some normal bonds. The most instructive set of surrounding groups was simply four Cl^- ions, with protons added; the protons both adjusted charge and affected bonding. When the total charge on the system was −2 (including the H_5O_2 group charge), either a normal or a short bond could be produced, depending on the distance of the Cl^- ion from the H_5O_2 group. The change from normal to short occurred over a change in Cl^- position of 0.005 Å. Calculations of bond order, and with the atoms-in-molecules technique, gave consistent results. When the total charge was −3, changes in bond length, bond order, and bonding were smooth, and the system appeared to remain on one side of the transition. It appears that there exist conditions under which the H_5O_2 group can act as a chemical switch and that addition of a proton can activate the switch.

Introduction

In a previous study[18] of the gating (opening) mechanism of the KcsA ion channel, a potassium channel derived from the bacterium *S. lividans*,[7] it was shown that that the partially charged H_5O_2 group could take either of two configurations: in one, the group has a central short, strong hydrogen bond (SSHB); in the other, it has a normal hydrogen bond. In that case, the surrounding groups were acetates, in positions determined by the structure of the KcsA channel, in the region believed important for gating.[25]

The $H_5O_2^+$ ion ("Zundel ion") has been extensively studied by Zundel and others.[33,34] Extensive and detailed ab initio calculations, showing a short bond (<2.5 Å, were carried out by Xie et al.[32] However, studies of the partially charged H_5O_2 group have apparently not been reported as yet. There are many studies of the short strong hydrogen bond, both experimental and theoretical, although the subject remains slightly controversial. However, the evidence for the existence of such bonds now appears strong.[6,11,22,27−31] Many of these papers were concerned with biological systems, especially enzymes, in which catalytic rates were greatly accelerated by the existence of SSHB, or low-barrier hydrogen bonds (LBHB). The latter have a double well potential, but are more symmetric and have a lower barrier between wells than normal hydrogen bonds.

A number of theoretical studies of SSHB have been reported as well, especially using the atoms-in-molecules theory of Bader.[3,26] Grabowski[15,16] has carried out AIM studies of hydrogen bonding. NMR experimental work on SSHB has been combined with AIM studies to understand the transition between covalent and normal hydrogen bonds.[2] There have been a number of related studies.[1,9,10,13,19] It is clear that there can be a transition in hydrogen bonding between SSHB and normal hydrogen bonds and that the topological properties of the molecule and surroundings can change, depending on the environment. The normal hydrogen bond corresponds more nearly to an $H_2O + H_3O$, but they are not allowed to separate in this calculation, so we continue to refer to a "H_5O_2 group with a normal hydrogen bond". It should be understood that the separated pair of molecules is equivalent. That which has not been previously established is that the group might function as a switch that can be controlled by the neighbors of the group. Only the study we did using a model of an ion channel [17] has addressed this question up to this point. It is this that we seek to investigate here, both to show that the effect can exist and to determine, so far as is possible, the requirements for it to happen. If such a switch can exist under more general conditions, then it can be used not only by ion channels but also by other proteins to allow conformational change in response to an external stimulus. The specific stimulus for this work was an investigation of the gating of ion channels, but it appears that the same switch is likely to have more general applicability.

It should be understood that the difference of the H_5O_2 group from the $H_5O_2^+$ ion does not involve spin; the "group" is a part of the entire system, including the surrounding groups. The

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entire system, i.e., H_5O_2 with the surrounding groups, has spin 0. However, the charge is shared between the H_5O_2 and the surrounding groups so as to leave the sum of the charges on the H_5O_2 atoms less than a full charge, the remainder of the electron density being located on the surrounding groups in such a manner that the central group does not behave exactly like the ion. It is for this reason that the distinction between the "group", as defined here, and the ion, is used in this paper. The charges on the individual atoms are an output of the computation, not an input; the input consists of *total* spin (0, in all cases considered here) and *total* charge (here, -2 or -3 for the cases of primary interest). This point is crucial in understanding the nature of the calculation, and it is the reason that the H_5O_2 in this calculation is not a standard ion. We do not assume the charges on the surrounding groups nor fix them, for example, as Cl^{-1}; instead, they are part of the calculation. We have chosen the $Cl^{\delta-} + HCl$ groups (where we write $\delta-$ to indicate the shared, and thus partial, charges) as the surrounding groups. These are the simplest that we could find which had both of the following properties: (i) switching between long and short bonds with one charge but not another; (ii) a sufficiently simple structure for which extensive calculations were practical. For comparison, our earlier work on the system derived from the Doyle et al coordinates of the KcsA channel[3] showed similar switching behavior in a system of obvious biological interest, but the more extended calculation that we present here would have been extremely difficult with that system. Furthermore, it is of interest to show that there is more than one system in which switching and the accompanying charge dependence occur. This suggests that the process may have general biological relevance. Succeeding work should investigate the question of how general the behavior might be in biological systems, especially proteins, with known atomic coordinates, varying degrees of electronegativity of the surrounding groups, and the possible way in which small conformational changes might lead to much larger effects.

The H_5O_2 group is particularly important because water is always present in biological systems. The group can also form a hydrogen bond through the outer hydrogens to other groups. This appears to happen in the KcsA channel, for example; at least, the study that indicated that it was responsible for allowing the proton to gate the channel supported this interpretation. Bonding in this manner allows the H_5O_2 group to form an effective link in the structure of the protein; when the bond relaxes to a normal bond, it can allow structural relaxation of the protein. This may play a role in biological processes beyond ion channel gating.

In this study, the emphasis is on the H_5O_2 group, and its switches between the two types of bond. While a number of surrounding groups were tried, we found that the process is most clearly understandable with Cl^- ions as the surrounding groups; in particular, if the total system charge is -2, the transition can be effected by a position change in the surrounding groups actually smaller than typical vibrational amplitudes, as a displacement of 0.005 Å can switch the group between the two configurations. This does not happen if the charge is -3. We will see how the AIM calculations allow us to watch the system snap to a different topological structure.

Methods

The various configurations were set up with the Cl positions fixed, and the H_5O_2 group was then optimized, using the Gaussian98 suite of programs,[12] with the chemistry B3LYP/6-311G** (density functional theory method B3LYP,[5,21,24] and basis set 6-311G**[20,23]). Some preliminary work used the D95V or D95 basis sets of Dunning.[8] The optimized configurations provided the distances and energies used in the calculations. The bond order calculations used the NBO (Natural Bond Order) package included in the Gaussian98 suite of programs.[14] In addition, once optimized, the final positions were used to obtain a wave function file suitable for use with AIM2000 suite of programs (F. Biegler-Konig, Buro Streibel-Biegler-Konig), which was used to perform the AIM calculations. Most of these calculations were possible with default settings; however, for cases that failed to meet the Poincare-Hopf criterion, additional critical points were sought with the stepsize decremented down to 0.1× default. Thus, if a critical point is said to be missing, it is missing at that level. To check for accuracy, atomic basin integration was carried out for the central H, one of the oxygen atoms, and one chlorine, for each type of bonding found (four cases, counting two charges). The Laplacian, which should be zero when integrated over a basin, was at most 10^{-2} with kinetic energy ≈ 460, for the Cl. For the central hydrogen, it was at most 2×10^{-3}, with kinetic energy in the range 0.3 to 0.4. With the oxygen nearest the central H, the Laplacian was <0.003, energy ≈ 75. These atomic basin integration values for the various cases were examined principally to ensure accuracy of the calculation, which appears adequate.

Easyplot (v.4.00, S. Karon, published by Cherwell Scientific) was used for Figure 1.

Results

1. The results with four acetic acid groups surrounding the H_5O_2 group showed that the difference between short and normal hydrogen bonds could depend on charge.[18] In that calculation, there were also four additional water molecules optimized at the PM3 semiempirical level, and then frozen, all in positions between the outer parts (i.e., near the methyl groups) of the acetate groups. Biologically relevant coordinates from the KcsA channel were used. That is, the four glutamates (E118) of the gating region were truncated to acetate, with coordinates of carboxyl groups and the first carbon back taken from the glu coordinates. The system then showed a SSHB with -2 total charge, a normal hydrogen bond with -1 charge (also, SSHB with -3, normal with 0 charge). No attempt was made to alter acetate distances. NBO was impractical (the system included with Gaussian could not handle so large a system); no attempt was made to do AIM calculations with this system, as it had enough complexity that gaining understanding of the factors underlying bonding looked unpromising. Nevertheless, this system does show that the change from SSHB to a normal hydrogen bond can be sudden. It was reported with B3LYP/D95V calculations,[17] but has later been repeated (data not shown) for the two critical charge states, -2 and -1, with B3LYP/6-311G**, and then B3LYP/6-311+G**. The principal qualitative results did not change, although there were some quantitative changes.

2. A variety of surrounding groups were tried, all in the same manner: the central H_5O_2 group was surrounded by four of the groups, and the positions of those groups frozen while the H_5O_2 group was optimized. Groups for which this was done included NH_3, H_2S, HF (both polarities—that is, with H and with F pointed toward the central H_5O_2 group), and water, as well as HCl. Except for water and HCl/Cl^-, these gave SSHB (O−O distance <2.5 Å, generally, around 2.4 Å). The D95V basis set generally gave slightly shorter bonds than 6-311G**. For all of these, the bond order was calculated using the NBO module. There is a separation into two populations. One set had short

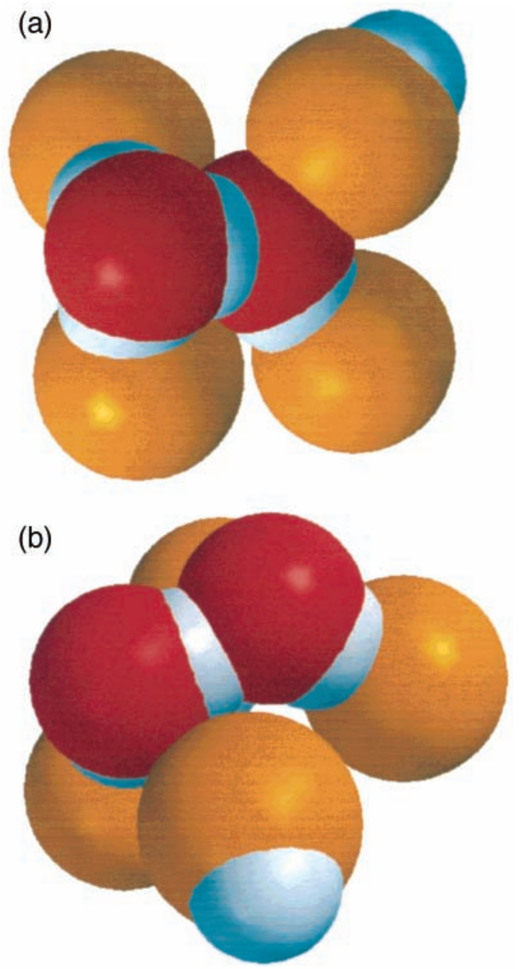

Figure 1. Space-filling models of two cases showing the positions of the atoms; oxygen is red, hydrogen white, chlorine orange: (a) short hydrogen bond, O−O distance 2.484 Å; (b) normal hydrogen bond, O−O distance 2.915 Å. In both cases, charge is −2 for the entire system. The difference in Cl atom-to-center distance is 0.05 Å for these two cases, with the longer O−O distance corresponding to the shorter Cl−center distance. (These plots were made using Spartan (Wavefunction, Inc), from the coordinates generated by Gaussian.)

TABLE 1: Short or Normal Hydrogen Bonds, as a Function of Charge

net charge (system)	O−O distance
−3	short; becomes longer as Cl moves in, but does not undergo a structural transition
−2	varied with Cl, H position
−1	normal (but: $2.6 < d < 2.7$)
0	normal
1	short

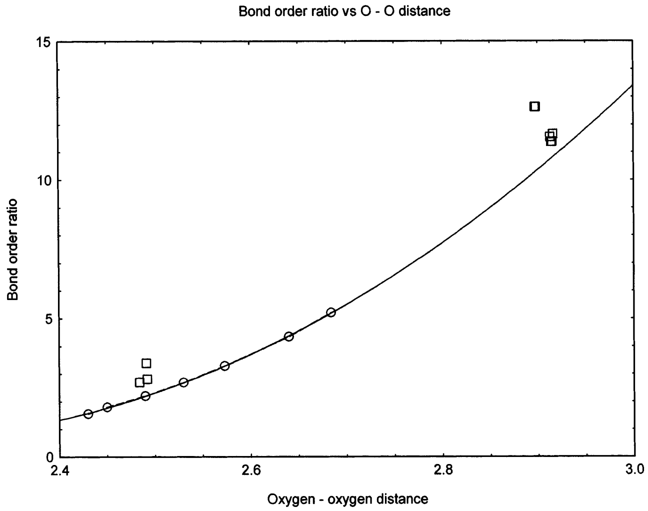

Figure 2. The ratio of the bond order of the short to the bond order of the long O−H bond in the H_5O_2 group, as a function of O−O distance in the group. Circles show the relation for −3 charge, squares for −2 charge. The parabola described by the formula on the figure corresponds to the −3 charge, and fits almost perfectly ($r^2 = 0.9997$). This suggests that the nature of the bonding is consistently partially covalent, in agreement with the AIM parameters in Table 3. The −2 charge points are entirely different, forming two clusters, with nothing between; these suggest a clear switch between two different bonding modes. The actual values of the points are either close to the −3 charge points, or near the extrapolation of the parabola, but the significance of this result is not obvious.

TABLE 2: O−O Distance in H_5O_2 as a Function of Cl^- Distance to Center, −2 Total Charge[a]

O−O distance	2.913	2.903	2.909	**2.903**	**2.484**	2.492	2.491
Cl-center	2.935	2.940	2.950	**2.955**	**2.960**	2.980	3.000

[a] The very sharp transition between short and normal distances is marked in boldface.

symmetric bonds with relatively high bond order for the longer bond (which had lower bond order than the short bond); the other set had long bonds that were appreciably longer, with lower bond order. Intermediate cases were almost nonexistent.

3. We will concentrate, however, on the four Cl^- ion cases, with protons to adjust charge. The most interesting case will turn out to be the −2 charge case, which can give long or short O−O distances. Figure 1 shows the two cases. The −3 case was also studied in detail, and provides an instructive contrast. Table 1 summarizes the results. There are two populations of bond order, one with −2 charge, the other −3. In Figure 2 we plot the ratio of the bond order of the shorter central O−H bond (from NBO calculations) to that of the longer central O−H bond, in H_5O_2, for both charges. The contrast is extreme, and instructive. With −2, we see switching behavior. All points are either on the left of the figure, short O−O distance, small ratio (nearly symmetric bonds), or on the right—normal bonds, large ratio, asymmetric. With −3, there is a continuous distribution, with the curve essentially a perfect parabola; it appears that the points are all on the left of the switching point. The conditions for the switch cannot be reached with overall charge −3, although the longest O−O distance, 2.684 Å, is nearly into the normal hydrogen bond range.

Because the −2 case showed the sharp transition with which we are concerned, Table 2 shows the O−O distance in the H_5O_2 group as a function of the Cl distance from the center with −2 charge, with the center defined as the average Cl position.

The very sharp transition between short and normal distances is marked in boldface.

There is no corresponding switch when the charge is −3. In those −2 cases with Cl−center distances equal to or larger than 2.960 Å, there is a short bond; with distances as little as 0.005 Å shorter, there is a normal bond. One would expect that there should be a structural transition at that point, which should be apparent in both the atoms-in-molecules (AIM) structures, and in bond order. We have calculated them, and the expected transition is present. The AIM theory is described in detail by its originator, Bader,[3] and in shorter form by Popelier.[26] In AIM, the virial theorem plays a central role. AIM also identifies a boundary surface between bonded atoms (hence, atoms-in-molecules), with a bond path between them. The interatomic surfaces are defined by maximum gradients of electron density

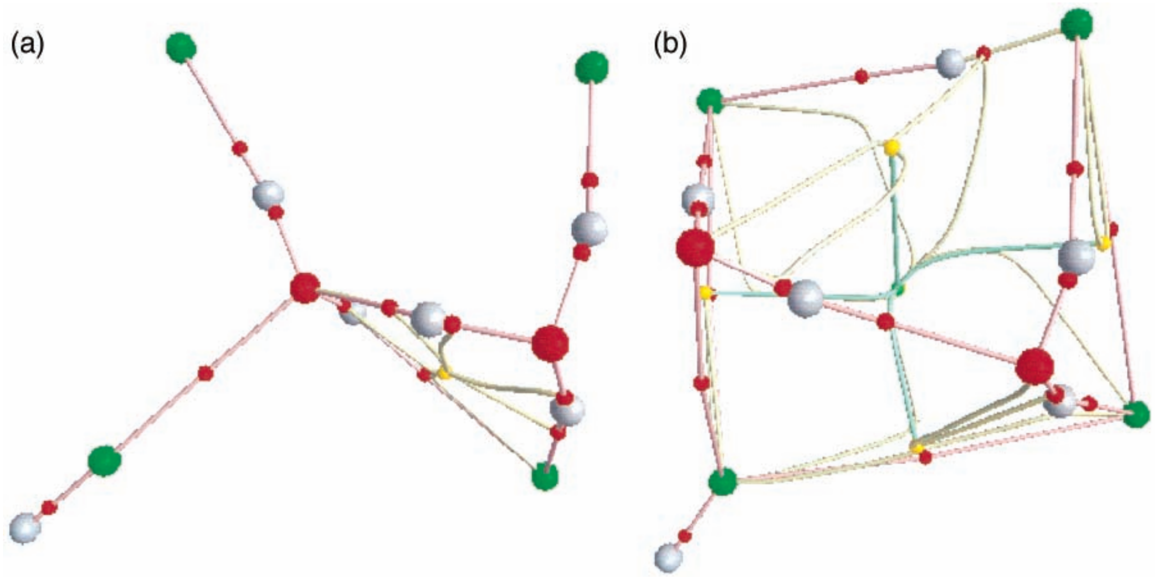

Figure 3. Two molecular graphs (from AIM) for the −2 charge case. Atomic positions are shown, with oxygen red, hydrogen white, and chlorine green, and all large spheres. Bond critical points are small red circles, ring critical points yellow, bond paths from bcp to rcp pale yellow, bond paths from near-nuclear critical points to bcp pink, and the one cage critical point (small green sphere) is in the center of B). Paths from this critical point to rcp are pale green. The figures show the two possible types of configurations of the system: (A) Short O−O distance, partially covalent bond, corresponding to line 1 of Table 3 (O−O distance = 2.49 Å). (B) Long O−O distance, noncovalent bond, O − O distance 2.91 Å. Note the difference in bonding: the short bond is accompanied by a simple molecular graph, with only one ring, which includes a single bond path between two of the Cl atoms. The long bond case has a cage structure, in which there are many twisted bond paths. There is at least one missing bcp, according to the Poincare-Hopf relation. It is apparent that switching to the "normal" hydrogen bond is accompanied by extreme shifts in the topology of the molecular bonding, with severely distorted electron density in the molecule.

through the point of the electron density minimum on the "atomic interaction line", the line connecting the atoms, and of maximum density with respect to the two dimensions orthogonal to the line. These are bond paths.

AIM follows bond paths that run from any of four types of critical points to any of the others. Here we are principally concerned with the paths from *bond critical points* (bcp) to *ring critical points* (rcp). Bond critical points are characterized by maxima in the electron density in two directions, but a minimum in density in the path between the two bonded nuclei. Rcp are characterized by a minimum in two dimensions, a maximum in one, and they exist principally in structures in which the bonding is topologically equivalent to a two-dimensional ring. The single maximum is orthogonal to the ring of bonds. A cage critical point (minimum in three directions) can occur in a nonplanar closed structure, which we do find in certain cases here. Each nucleus is very near an electron density absolute maximum, giving the fourth type of critical point, the (near) nuclear critical point. A structural change occurs as a sudden transition in the topology of the molecule as one or more atoms crosses a threshold position. The bonding changes, with a bond path appearing or disappearing as the threshold is crossed. Figure 3 and Figure 4 show the molecular graph, consisting of the bond paths joining critical points, with −2 charge and with −3 charge, each at two different distances. In Figure 3 we see a clear structural change, while in Figure 4, at −3 charge, we do not. Even with the Cl^- only 2.7 Å from the center, we get nearly the same structure (i.e., same bonds) as at longer distances, with only a quantitative difference in the positions of the atoms. There is an added bond path between Cl atoms in certain cases, but this appears to be a relatively less significant change: the rest of the system is not greatly affected, nor are the bond paths badly distorted. At 2.6 Å Cl−center distance, a third ring appears, as the Cl atoms become closer to each other.

AIM allows the description of a bcp as part of a covalent bond, or not, in another manner. If the kinetic energy density, $G(r)$ (given in J m^{-3}), is integrated over an atomic basin, defined as the region bounded by the interatomic surfaces, one gets the local kinetic energy. The local kinetic energy and potential energy obey the local virial theorem:

$$(-\hbar^2/4m)\nabla^2\rho = 2G(r) + V(r) \tag{1}$$

where $G(r)$ is the electronic kinetic energy density and $V(r)$ is the potential energy density. ρ is the electron density, N times the probability of finding a particle at some point, defined by integrating over all coordinates, and summing over all spins, of the remaining electrons.[4] Other densities are defined in like manner. The electronic energy density, defined by

$$E^{(e)} = G(r) + V(r) \tag{2}$$

integrates to the total electronic energy. This quantity is of crucial importance in determining whether a bond is covalent or not. This is also the negative of the kinetic energy density as it appears in the Schrodinger equation. $G(r) > 0$, while $V(r) < 0$; their sum can have either sign. If $E^{(e)} < 0$, the interaction between the atoms is at least partially covalent, while $E^{(e)} > 0$ is characteristic of a strictly noncovalent interaction. This has also been discussed in the context of NMR shifts by Arnold and Oldfield.[2]

We should be able to see the same thing if we calculate bond order, with an abrupt change in bond order accompanying the same transition. The bond distance, the bond order, and the AIM calculation all show a structural change. The bond order is calculated using the NBO module of Gaussian, and either the Wiberg or the NAO bond orders could be used. Table 3 shows the latter; the former follow the same trends, but show a slightly greater difference in bond order between the two central O−H bonds than latter.

There is another test of whether the results are normal or not. The Poincare-Hopf relation [26] describes the topology of

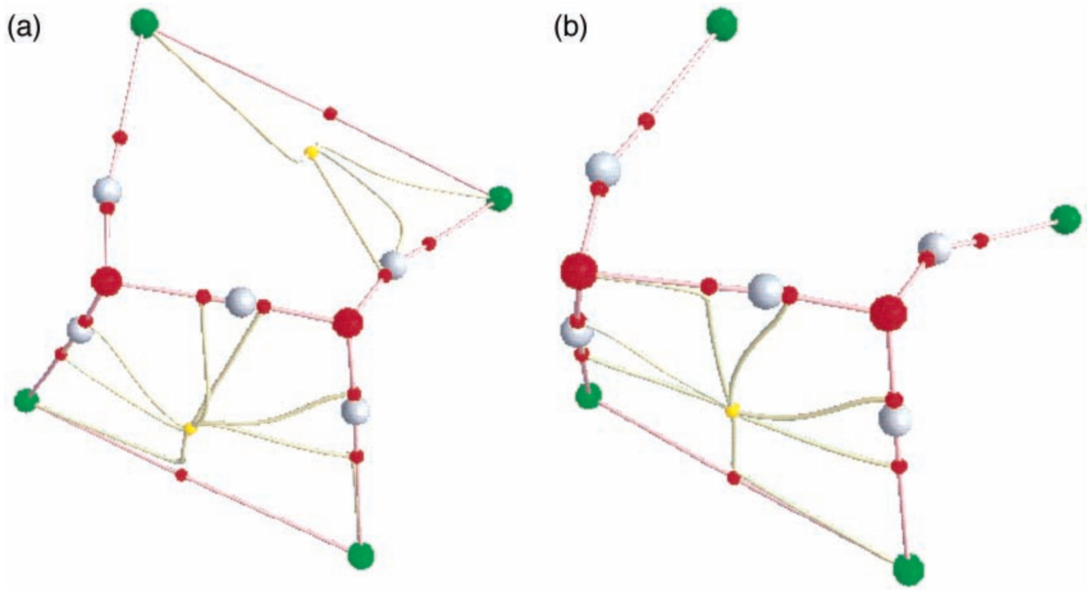

Figure 4. Two molecular graphs (from AIM) for the −3 charge case. Labeling conventions are as in Figure 3, and there are no cage critical points. The central H is in the middle of the figure, and the two oxygens are connected to it by bond paths. These show a relatively long and a relatively short O−O bond distance: (A) a short O−O distance (2.43 Å), (B) a relatively long O−O distance (2.57 Å). There is a difference in the topology of the graphs, with an additional ring formed in (B) by a bond path connecting two Cl atoms that were not connected in (A). However, this is a small difference compared to the severe twisting of the density seen in Figure 3 for the longer bond. The shorter bond, however, seems similar to its −2 charge counterpart, and gives a topology not very different from normal.

TABLE 3: Bond Orders and AIM Parameters for Total Charge −2 and −3

charge	Cl−center distance	O−O distance	short O−H bond order	long O−H bond order	local charge density, key bcp[a]	$E^{(e)}$ of key bcp* (Hartrees)
−2	3.00	2.491	.5193	.1876	.0803	−0.02486
−2	2.98	2.486	.5175	.1902	.0791	−0.02557
−2	2.96	2.484	.5168	.1915	.0816	−0.02177
−2	2.955	2.903	.6455	.0501	.0249	+0.000115
−2	2.95	2.909	.6501	.0456	.0249	+0.000125
−2	2.935	2.913	.6455	.0555	.0256	+0.000157
−2	2.91	2.914	.6412	.0564	.0255	+0.000157
−2	2.85	2.915	.6412	.0564	.0255	+0.000156
−2	2.70	2.916	.6421	.0551	.0253	+0.000152
−3	3.375	2.432	.4584	.2929	.1122	−0.0792
−3	3.20	2.453	.4772	.2564	.1099	−0.0503
−3	3.00	2.490	.4994	.2272	.0938	−0.0366
−3	2.90	2.530	.5171	.1923	.0801	−0.0255
−3	2.80	2.574	.5306	.1614	.0686	−0.0166
−3	2.70	2.640	.5443	.1274	.0556	−0.01007
−3	2.60	2.684	.5507	.1057	.0487	−0.00684

[a] key bcp = bcp in the longer O − H bond of the central O − H − O, in H_5O_2; this is the only possible “partially covalent” critical point.

the structure in terms of the four types of critical points. It states that the number of critical points of each type is related through

$$n - b + r - c = 1 \tag{3}$$

where n = number of (near) nuclear critical points, b = bond critical points, r = ring critical points, and c = cage critical points. If the relation is not obeyed, the structure is missing at least one critical point; if it is obeyed, it may be missing two critical points that compensate in the relation, but the structure is more likely correct.

All the −3 cases obey the relation, as do all the −2 cases that have short bonds. Of the −2 cases that have long (normal length) hydrogen bonds, those with the Cl^-−center distance far from the switching distance also obey the relation. However, most of those nearest the switching distance (2.910, 2.950, 2.955 Å) have the sum on the left-hand side of eq 3 equal to 2; they do not obey the Poincare-Hopf relation, and thus their molecular graphs are not complete (as noted in Methods, the step size was tested down to 0.1 of default for these cases; some others showed the last bcp at 0.5 of default, but nothing was gained in any case by going below 0.5 to 0.1; at 2.935 Å, reducing the step size to 0.5 times default produced one more bcp, satisfying the relation). Most of those cases that do obey the relation (charge −2 and −3) have relatively simple molecular graphs, with a single ring in the −2 cases, and one or two rings in the −3 cases (there is one exception, which has a three-ring structure for the shortest Cl−center distance with −3 charge, and the longest −3 oxygen−oxygen distance; the next three Cl−center distances have 1 ring, and the others, with Cl still farther out, have 2 rings). Those −2 cases that do not obey the relation have complex graphs, three with a cage critical point, demonstrating a three-dimensional structure absent in all the other cases.

The local charge density at the key bond critical point, defined as the bcp between the central H in H_5O_2 and the further oxygen atom, offers another index of the transition. With −2 charge, there are clearly two populations, with $\rho \approx 0.02$ for “normal” bonds, and with $\rho \approx 0.08$ for SSHB. With −3 charge, the change is essentially continuous, with the trend of the actual values in the same direction as the sudden change in the −2 case.

Discussion and Conclusions

The contrast between the −2 and −3 cases, with four Cl^- as surrounding groups, is instructive. Differences include (1) bonding, as shown in Figure 2, in comparison with the much smaller structural difference in Figure 3; (2) the difference in the sign of $E^{(e)}$; (3) the difference seen in Figure 1 between the bond order ratio in the −2 and −3 cases; (4) the difference in the charge trends on the key bond critical point. Taken together, they make clear that there is a qualitative difference in the behavior, especially with respect to the central bonds, of the H_5O_2 group, depending on its surroundings. The change in sign of energy density $E^{(e)}$ shows a difference in type of bonding, between closed shell interactions ($E^{(e)} > 0$) interactions, and covalent, or at least "partially covalent" ($E^{(e)} < 0$) where "partially covalent" is defined by $2G(r) > |V| > G(r)$ (see discussion under eq 2, above). The structural change shown in Figure 2 is entirely consistent with this, showing the transition in terms of a complete restructuring of the AIM molecular graph with creation of a different topology for the bond paths with the short bond, compared with the long bond. Again, the short bond accompanies the simple structure that resembles a single molecule in which there is at most one, usually zero, Cl−Cl AIM bond path between normally nonbonded atoms. The structure with the weak (or normal) hydrogen bonds looks far more complex, as the paths are severely distorted, apparently by the fact that the maxima and minima in the electron density are much smaller, and can twist in odd directions with small potential differences. The failure to satisfy the Poincare-Hopf relation confirms the oddity of the bonding in cases just past the switching point. Apparently the short bond form in H_5O_2 is the "natural" form, but the surroundings can distort and weaken this bond. The overall charge on surrounding groups affects the local bonding, so that the transition can occur only at certain charges. In this way, the addition of a proton makes possible the transition to a form that can undergo an abrupt change in bonding. While there is an abrupt change in bond length, and presumably strength, the change in the overall topology of the molecule, while abrupt, goes through further transitions as the Cl^- are withdrawn. The change in bonding is not simply a proton transfer, but involves a restructuring of the entire environment of the central group.

With −3 charge, there is a structural change, but it is limited to the formation of an extra bond path between two Cl atoms; in other respects, the topology remains that of the short bond, comparable to that of the short bond with −2 charge, and completely different from that of the "normal" bond with −2 charge.

Because of the transition, the groups to which the H_5O_2 forms hydrogen bonds through its outer hydrogens can go from being relatively weakly linked to strongly linked, or the reverse. This was seen in the carboxylic acid case that modeled an ion channel, and it appears here, with Cl^-/HCl surrounding groups. It appears that the energy change can be appreciably greater than kT, the thermal energy, which is approximately 0.001 Hartree. However, because the energy found is that for the system, it is not possible to attribute it to the central bond alone. The outer hydrogen bonds may be either strong or numerous enough for the central bond to control the overall binding of the surrounding groups. If these are protein moieties (e.g., α-helices), the strong central bond may hold the helices in proximity. A change in pH, or some other source of hydrogen ion, may allow the central bond to weaken, turning to a normal hydrogen bond. The consequence would be that the H_5O_2 group would separate, destroying the link between helices, and in turn allowing a conformational transition. That is, the H_5O_2 group can act as a conformational switch.

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