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Like Ion Pairs of Hydronium and Hydroxide in Aqueous Solution?

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The like-charge ion pairings of hydronium and hydroxide were investigated both with *ab initio* cluster calculations and QM/MM–MD aqueous simulations. While only a two-water-bridged $H_3O^+(H_2O)_2H_3O^+$ is found in hydronium cluster calculations, three clusters of $HO^-(H_2O)_2HO^-$, $HO^-(H_2O)_3HO^-$ and $HO^-(H2O)_4HO^-$ are stable dihydroxide aggregates. In addition, an interesting yet very stable parallelogram structure of $[O–H\cdots H–O]^{2-}$ without any bridging water was also discovered from QM/MM-MD simulations. According to our analysis, its unique structure reduces the electrostatic repulsion and allows stable coordination with solvents at the same time. In conclusion, hydroxide can form stronger like ion pairs than hydronium in aqueous solution mostly due to its versatile coordination ability with solvents.

The interaction of ions in solution is fundamentally important in various chemical and biological processes.[1-4] They play a vital role in determining the structure and function of proteins[4] and in ion selectivity of ion channels at biological membranes.[5,6] A virtual issue of the Journal of Physical Chemistry B of ion pairing[7] nicely presented recent advances on this subject. An interesting phenomenon of ion interactions is the possibility of like-charge ion pairing, which has been observed in a wide range of polyelectrolyte systems.[8,9] There is also accumulated structural evidence for the those species, such as anions bound to anionic protein surfaces[10,11] and arginine-arginine paring[12-15]. This indicates that they may have significant effect on the structure and association of proteins. X-ray diffraction[16] and neutron scattering experiments[17,18] provide further evidence for the existence of halide ion pairs in solution. Although the medium's dielectric constant reduces Coulombic interactions, like-charge ions in principle repel each other. Zangi[19] proposed two mechanisms of an effective attraction between like-charged monovalent ions. The stronger local electric field of paired two ions augments the favorable alignment of neighboring waters toward the ions. In addition, a counter-ion that is either bridging the two like-charged ions or paired to only one of them, increases attractions. In another theoretical study of guanidinium in aqueous solution, Inagaki *et al.*[13] showed that the stability of like-charge ions is determined by a very subtle balance between interionic interactions and ionic solvation/hydrophobic effects. With a recently developed quantum mechanics/molecular mechanics molecular dynamics (QM/MM-MD) scheme,[20] significant quantum mechanical interactions between bridging water molecules and Na^+ ions in the study of Na^+–Na^+ pairs in aqueous solution were also revealed,[21] suggesting an important role of bridged water solvents in like-charge ion pairings.

Among the most important ions in aqueous solutions are hydronium and hydroxide. There is no doubt that the possibility of their like-charge pairings can have profound effects on every aspect of chemical reactions in aqueous solutions. Despite their importance, little attention has been paid to these possibilities in solution. In solid phase, cyclic species of composition $(H_{14}O_6)^{2+}$ and $(H_{18}O_8)^{2+}$, where two hydroniums are cyclically connected by water molecules, was discovered[22-24] and theoretically proved.[25] Later, Bernal[26] also revealed that hydrated hydroxide anions can be acyclic as well as cyclic. An asymmetry of like-charge ion parings was also found in the comparative study of Na^+–Na^+ and Cl^-–Cl^- pairs in aqueous solution,[21] where the positive like-charge ions of Na^+–Na^+ have a stronger tendency of pairings than Cl^-–Cl^-. In another dynamics study on hydronium and hydroxide,[27,28] the efficiency of proton transfer for hydronium was found to be significantly higher than that for hydroxide. Therefore it is not obvious that they behave similarly in aqueous solution. As an extension to our previous studies, the like ion pairings of hydronium and hydroxide were systematically studied in this paper.

We first performed *ab initio* calculations on the model clusters of $H_3O^+(H_2O)_nH_3O^+$ and $HO^-(H_2O)_nHO^-$ (n = 0 – 4) at the CCSD(T)/aug-cc-pVTZ//MP2/aug-cc-pVTZ level. Fig. 1 shows the representative optimized structures having bridged water molecules and the predicted stabilization energies with respect to full dissociation of the cluster into its neutral and ionic molecular constituents. In the case of hydronium, only two-water-bridged $H_3O^+(H_2O)_2H_3O^+$ is found as a minimum among the model clusters of $H_3O^+(H_2O)_nH_3O^+$.

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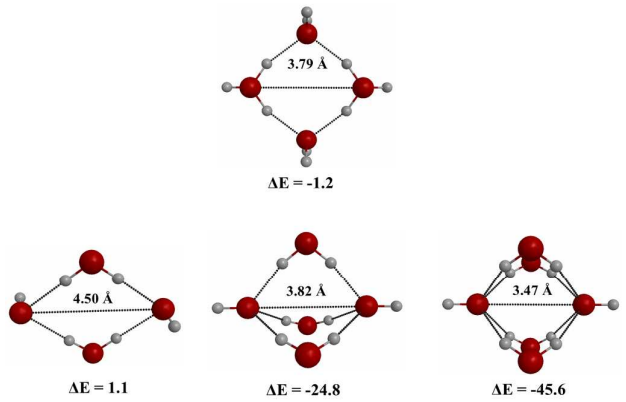

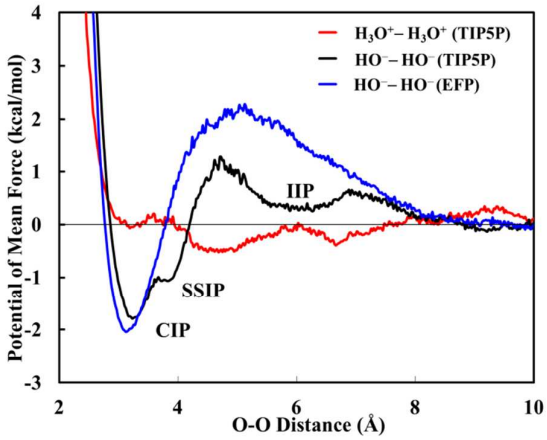

Fig. 2 The potential of mean force (PMF) along the oxygen-oxygen distance (r_{OO}) of the HO^-–HO^- (black) and H_3O^+–H_3O^+ (red) ion pairs as obtained with QM/TIP5P-MD simulations. The diagram also shows the PMF of hydroxide calculated with QM/EFP-MD simulations (blue)

As in the case of $Na^+(H_2O)_nNa^+$ like-ion pairs,[21] the *p* orbital of water oxygen is shared by two hydrogens of hydronium, indicating a strong orbital overlaps between hydronium and bridging waters. However, additional water molecules can only be outside of the bridging region, since only two hydrogens of hydronium can be utilized for the bridged water-hydronium configuration. Energetically, $H_3O^+(H_2O)_nH_3O^+$ is slightly exothermic by 1.2 kcal/mol. On the other hand, water-bridged clusters of $HO^-(H_2O)_2HO^-$, $HO^-(H_2O)_3HO^-$, and $HO^-(H_2O)_4HO^-$ are minima on the potential energy hypersurfaces of dihydroxide-water aggregates, since the hydroxide oxygen can accept up to penta-coordinations. Although $HO^-(H_2O)_2HO^-$ is slightly endothermic, the other two bridged clusters are highly exothermic. Especially, in the case of four water-bridged cluster, the relative stability become as large as -45.6 kcal/mol. As the number of bridged water increases, the inter oxygen distances of hydroxide decreases from 4.50 to 3.47 Å. In short, it appears that the versatile coordination of hydroxide as compared to hydronium increases the chances of like ion pairings. As compared to static quantum mechanical calculations, the free energy from molecular dynamics simulations involves various dynamic effects. Therefore it is not straightforward to assume that the exothermic species predicted by *ab initio* calculations can be formed in real solution. However, it was shown that the large exothermicities of $Na^+(H_2O)_nNa^+$ clusters eventually led to a strong tendency of like-ion pairings.[21]

The formations of *ab initio* predicted structures and its consequences for like ion pairings in aqueous solution were investigated with QM/MM-MD[20] simulations. The particular hybrid schemes in our QM/MM modeling are QM/EFP and QM/TIP5P.[29] The effective fragment potential (EFP) water model[30] is a quantum mechanical rigid and polarizable force field for water with fitted exchange–repulsion corrections. The applicability of our hybrid QM/MM to a long-time MD simulation of a chemical reaction in aqueous solution has been repeatedly examined.[20,31-35] Identical spherical systems of H_3O^+–H_3O^+ and HO^-–HO^- pairs with 400 explicit water molecules were prepared for the QM/MM-MD simulations with spherical boundary potential (SBP). Two ions were treated quantum mechanically at the B3LYP/6-31G(d) level, while all of the water molecules were represented by either EFP or TIP5P. We performed umbrella samplings (US) with nine windows covering ion–ion distances from 2.0 to 10.0 Å with a spacing of 1.0 Å. A force constant of 2 kcal/mol/Å^2 was used for both SBP and the US restraints. NVT simulations of QM/EFP and QM/TIP5P-MD were performed for 150 ps with initial equilibrations of 50 ps. The time step was set to 1 fs. Finally, the weighted histogram analysis method (WHAM)[36] was used to obtain the PMFs for the like-ion pairs. All calculations were performed with a recent version of GAMESS.[37]

The PMFs along the O–O distance of hydroxide and hydronium from the QM/TIP5P-MD and QM/EFP-MD simulations are compared in Fig. 2. In the case of hydroxide, a strong minimum consistently appears near 3.2 Å with a stabilizing free energy of ~2 kcal/mol in both QM/TIP5P and QM/EFP-MD simulations, which is labeled as CIP (Contact Ion Pair). After careful examination of the QM/TIP5P-MD results, additional minima at 3.9 and 6.0 Å were also identified and labeled as SSIP (Solvent Separated Ion Pair), and IIP (Intermediate Ion Pair), respectively. Since the EFP model supposedly provides a better description of the solvation structures than the TIP5P water model, the additional features from QM/TIP5P-MD may be due to the overbindings of TIP5P, which shall be further discussed in the solvent structure section. In contrast, three flat and shallow minima at 3.2, 4.8 and 6.7 Å appear in the PMF of hydronium. Other than the slightly exothermic minima at 4.8 and 6.7 Å, the close contact minimum of hydronium is relatively insignificant. The less attractive hydronium pairings are consistent with the cluster calculations, where only the two-water-bridged $H_3O^+(H_2O)_2H_3O^+$ is found to be stable. These differences in PMFs clearly indicate that the hydroxide like-ion pair is more likely to exist than that of hydronium in aqueous solution, which is consistent with our *ab initio* cluster predictions.

Considering the typical cluster O–O distances of 4.50 – 3.47 Å in Fig. 1, the CIP minimum at 3.2 Å is rather short. To characterize it, interionic hydration structures (IHSs) of hydroxide pairs as shown in

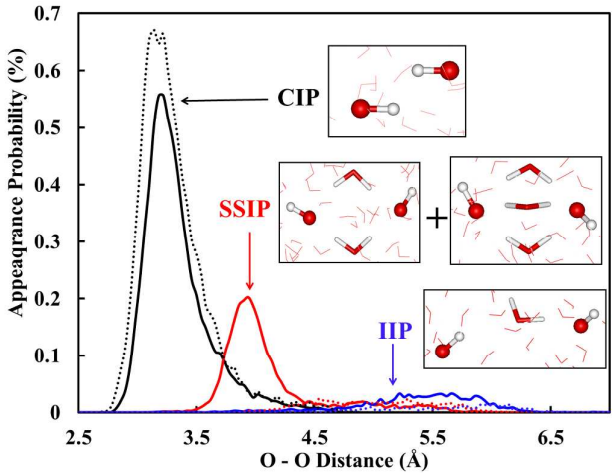

Fig. 3 Distribution of the interionic hydration structures (IHSs) found in QM/TIP5P-MD (solid lines) and QM/EFP-MD (dot lines) simulations. The numbers are presented in percentage scale. The CIP, SSIP, and IIP are presented in black, red, and blue, respectively

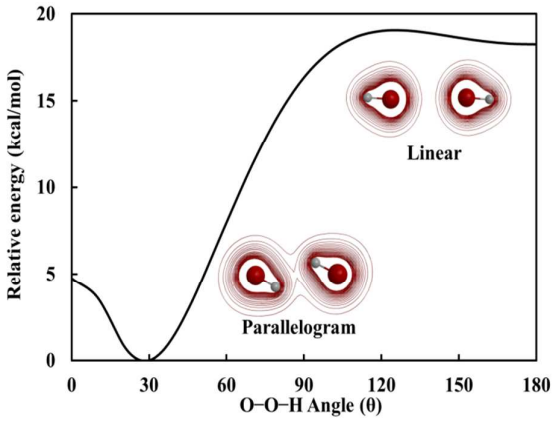

Fig. 4 Relative potential energies of ion pairs of hydroxide as a function of the rotation of O–H at the fixed O–O distance of 3.2 Å calculated with MP2/aug-cc-pVTZ level of theory. The diagram also shows the parallelogram and linear structures at ∠O–O–H = 30° and 180°, respectively, with electron density contour maps

Fig. 1 were extracted from all the snapshots of umbrella sampling windows. The recognition of IHS was entirely based on the ion–water and water–water connectivity as shown in our previous studies.[21,34] For example, bridging water is recognized, if a water molecule is close enough to both ions at the same time. It should be pointed out that IHS analysis only considers the bridging water molecules between the two ions. The quantitative distribution of IHS in QM/TIP5P-MD shows three main peaks at 3.2, 3.9 and 5.5 Å in Fig. 3. In the case of QM/EFP-MD, only one main peak at 3.2 Å appears and the other two peaks are negligible. These peak positions are well correlated with those of the three minima in the PMF, indicating a strong correlation between the minimum positions in PMF and IHS distribution. Our IHS analysis shows that CIP is mostly a hydroxide direct contact pair with two hydrogens pointing towards each other. It forms an interesting parallelogram structure, where the O–O and H–H distances are ~3.2 Å and ~2.5 Å, respectively (See the snapshot of Fig. 3). Additional analyses on CIP were performed to substantiate its existence.

The potential energy curve of $[O–H\cdots H–O]^{2-}$ at MP2/aug-cc-pVTZ level of theory was obtained as a function of both H–O–O and O–O–H angles from 0 to 180° at the fixed O–O distance of 3.2 Å and is shown in Fig. 4. The parallelogram structure with ∠O–O–H = 30° is more stable than the linear structure with ∠O–O–H = 180°, $[H–O\cdots O–H]^{2-}$ by 13.5 kcal/mol, clearly indicating a preference of the parallelogram structure.

Table 1: Results of LMO-EDA Analysis. Decomposition of ion-ion interaction energies into ES (electrostatics), EX (exchange), REP (repulsion), and POL (polarization) contributions. All calculations were done at the MP2/aug-cc-pVQZ level of theory.

	ES	EX	REP	POL
$HO^-–OH^-$	106.8	-2.5	3.2	-5.4
$OH^-–HO^-$	80.9	-16.2	23.9	-6.2

Localized molecular orbital energy decomposition analysis (LMO-EDA) was further performed on the parallelogram and linear structures and the results are listed in Table 1. As two molecules get close, they tend to repel each other to retain individual identities, which is described by exchange plus repulsion (EX+REP) term. Therefore, the slightly increased EX+REP (~7 kcal/mol) of the parallelogram structure is understandable, since the two hydrogens are point towards each other in the parallelogram structure. The main driving force for the formation of the parallelogram structure as compared to the linear structure comes from the strong reduction of electrostatic (ES) interaction by ~26 kcal/mol. By putting positively charged hydrogens in between the negatively charged oxygen atoms in "−⋯+⋯−" combination, one can expect a reduction of electrostatic repulsions between the two oxygen atoms.

In addition to these solute structures, it is helpful to explore the hydration structures of CIP. Fig. 5 represents the hydroxide radial distribution functions (RDFs), $g_{O^*–Ow}(r)$ at r_{OO} = 3, 4, 6, and 10 Å windows from QM/TIP5P-MD and QM/EFP-MD, where O* denotes the oxygen of either hydroxide. It is well known that hydroxide prefers coordination number (CN) = 4 or 5 as shown in RDF of QM/EFP-MD simulation. On the other hand, the TIP5P water model tends to slightly over-coordinate hydroxide,[38] which may be a reason of additional minima in the PMF. The coordination numbers (CNs) of $g_{O^*–Ow}(r)$ are the same for all four US windows in the first solvation shell, which indicates that the CN does not depend on the O–O distance. From the CIP's point of view, putting two hydrogen atoms in the inner part of the CIP is the only way to make the two oxygen atoms available for the additional coordinations with solvents. Therefore the parallelogram structure of CIP not only reduces electrostatic repulsions between the two hydroxides but also allows proper coordinations on the two oxygen atoms with solvents, which cooperatively makes it quite stable on the free energy surface.

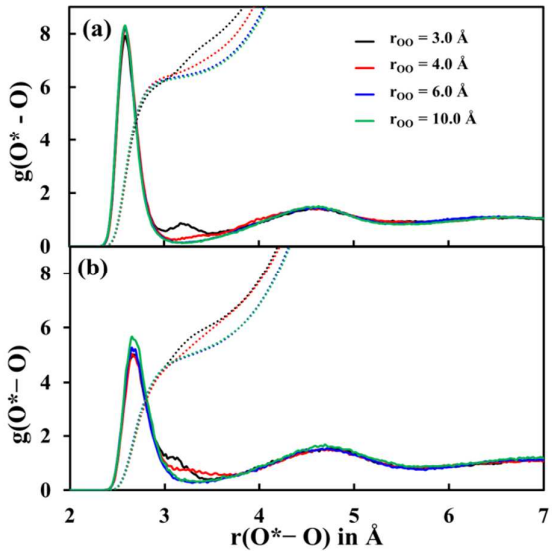

Fig. 5 The radial distribution functions (solid lines) and their coordination numbers (dot lines) at four US windows with r_{OO} = 3, 4, 6, and 10 Å calculated with (a) QM/TIP5P-MD and (b) QM/EFP-MD simulations

In summary, the like ion pairings of hydronium and hydroxide were investigated both with *ab initio* calculations on model clusters and QM/MM–MD simulations on the solvation systems. In the case of hydronium, only two-water-bridged $H_3O^+(H_2O)_2H_3O^+$ is found as a minimum, while water-bridged clusters of $HO^-(H_2O)_2HO^-$, $HO^-(H_2O)_3HO^-$, and $HO^-(H_2O)_4HO^-$ are minima in the cases of hydroxide ion. The water-bridged hydroxide pairs are energetically more stable than that of hydronium. In addition, our QM/TIP5P-MD and QM/EFP-MD simulations consistently showed that the energetically preferred hydroxide pairs also form stable like-ion pairs in aqueous solution. An interesting yet very stable parallelogram structure of $[O–H\cdots H–O]^{2–}$ was discovered from MD simulations for the first time, which is a direct contact ion pair (CIP) without any intervening solvent. Our analysis showed that the parallelogram structure of $[O–H\cdots H–O]^{2–}$ is stabilized by the cooperative effects of reduced electrostatic repulsion between oxygen atoms by inner hydrogens and a large coordination number on oxygen atoms. As compared to hydronium, the versatile coordination ability of hydroxide oxygen atoms makes hydroxide like-ion pairs much more probable in real solution.

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