

Hydration, Swelling, Interlayer Structure, and Hydrogen Bonding in Organolayered Double Hydroxides: Insights from Molecular Dynamics Simulation of Citrate-Intercalated Hydrotalcite

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Molecular dynamics (MD) simulation of the Mg/Al (3:1) layered double hydroxide (LDH), hydrotalcite (HT), containing citrate, $\text{C}_6\text{H}_5\text{O}_7^{3-}$, as the charge balancing interlayer anion provides new molecular scale insight into the interlayer structure, hydrogen bonding, and energetics of the hydration and consequent swelling of LDH compounds containing organic and biomolecules. Citrate-HT exhibits affinity for water up to very high hydration levels, in contrast to the preferred low hydration states of most LDHs intercalated with small, inorganic anions. This result is consistent with the recent experimental observation of the delamination of lactate-HT. The high water affinity is rationalized in terms of the preference of citrate ion for hydrogen bonds (H-bonds) donated from water molecules rather than from the hydroxyl groups of the metal hydroxide layer and the need to develop an integrated interlayer H-bond network among the citrate ions, water, and $-\text{OH}$ groups of the hydroxide layers. The changes in the orientation of citrate molecules with progressive hydration are also intimately related to its preference to accept hydrogen bonds from water.

I. Introduction

Layered double hydroxides (LDHs), also known as hydro-talcite-like compounds, form an important class of readily synthesized, clay-like minerals. LDHs have brucite ($\text{Mg}(\text{OH})_2$)-like lamellar structures but with positive structural charge on the metal hydroxide layers.^{1,2} The interactions between the metal hydroxide layers are much weaker than the intralayer bonding, leading to swelling of the unit cell c -parameter (perpendicular to the layers) with adsorption of energetically favorable species. LDH interlayers thus serve as excellent hosts for a broad range of organic and inorganic charge-balancing anions and a variety of neutral chemical species, making these materials useful in a wide range of applications in such diverse fields as catalysis, electrochemistry, medicine, environmental remediation, and molecular separation.^{2–4}

Incorporation of bio- and organic species into LDH interlayers has gained significant attention in recent years due to such potential applications as controlled release of drug molecules.^{5–7} One of the major challenges is, however, the very insertion of large molecules into the LDH interlayers. Recent experimental studies by Hibino and co-workers^{8,9} and Adachi-Pagano et al.¹⁰ has shown that enhanced swelling leading to exfoliation (delamination) of the LDH layers can be achieved in a solution environment if the LDH is loaded with suitable organic intercalates. The exfoliation of the LDH layers offers a gentle way of opening up the interlayer space, allowing insertion of large bio- or organic molecules.

This letter presents results from detailed MD simulations that provide fresh insight into the microscopic origin of the

swelling behavior upon hydration of bio- and organolayered double hydroxides, taking the citrate intercalated hydrotalcite, $\text{Mg}_3\text{Al}(\text{OH})_8(1/3\text{citrate})\cdot n\text{H}_2\text{O}$, as a representative case. Citrate, $\text{C}_6\text{H}_5\text{O}_7^{3-}$, has one hydroxyl group ($-\text{OH}$) and three carboxylate groups ($-\text{COO}^-$), two on terminal carbons and one on the central carbon atom. It is, thus, an effective model for moderately complex organic anionic species interacting with the hydroxide layers of hydrotalcite.

II. Methods

The simulation supercells consist of $6 \times 6 \times 1$ rhombohedral ($R\bar{3}m$) unit cells of citrate intercalated hydrotalcite (HT),¹¹ containing three metal-hydroxide layers, nine citrate ions (three per each interlayer), and a variable number ($27 \times n$) of water molecules. All three carboxylic groups of the citric acid are considered to be deprotonated, since all of their $\text{p}K_a$ values are less than 6.5.¹² The $-\text{OH}$ group is considered to remain protonated, since its $\text{p}K_a$ is about 11.¹³

The interatomic potentials employed here are based on the CLAYFF force field of Cygan et al.¹⁴ to describe the LDH layers, the SPC water model of Berendsen et al.,¹⁵ and the CVFF force field,¹⁶ which is broadly applicable to organic molecules, to describe the citrate ion. Starting from energy and stress minimized structures, NPT-ensemble MD simulations of 50 ps duration were carried out at 300 K and 1 bar pressure for different hydration states, n , of the system. After an initial 30 ps period of equilibration, the average unit cell parameters and hydration energy were calculated over the remaining 20 ps. The hydration energy, defined as

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$$\Delta U_{\text{H}}(N) = \frac{\langle U(N) \rangle - \langle U(0) \rangle}{N} \quad (1)$$

where N is the total number of water molecules and $U(N)$ the total potential energy of the system, is a simple and effective measure of the affinity of water for the interlayer.¹⁷

For selected hydration values of $n = 0, 1, 2, 3, 6, 12$, and 32, longer NVE-MD simulations of 200 ps duration, including an initial 50 ps for equilibration, were then performed at 300 K, starting from the final atomic configurations and average interlayer spacings obtained from the NPT-MD simulations. All MD simulations were performed with a time step of 0.5 fs. Periodic boundary conditions and Ewald summation techniques were employed.

III. Results and Discussion

Citrate-HT Swelling. The average a - and b - unit cell dimensions computed from NPT-ensemble MD simulations are all within 1.5% of the literature values¹¹ of $a = b = 3.1$ Å, whereas the c -axis increases with water content as shown in Figure 1. For water contents $n > 3$ this variation is linear in n , but from $n = 0$ to 3 the rate of change is slower (Figure 1) due to water molecules filling the empty interlayer space between the citrate ions.

The computed hydration energies (eq 1) show the most negative values at low water contents, relatively small changes at $n < 3$, more rapid changes over the range $3 \leq n \leq 12$, and a slower, gradual approach to the potential energy for bulk SPC water for $n > 12$ (Figure 1). Remarkably, these hydration energies remain lower than that of the bulk water (~ 10 kcal/mol for the SPC water model) to very high water contents, and there are no local minima in the energy over the entire hydration range explored. This behavior is in sharp contrast to the computed swelling energetics of chloride-HT found in previous MD studies¹⁷ and the experimentally known restricted ranges of hydration of HT containing small, inorganic anions.¹⁸ The present MD results thus suggest the absence of specifically preferred hydration states and a tendency for the system to adsorb water continuously in water-rich environments such as high relative humidity (RH) conditions or in aqueous solution. The practical outcome of this enhanced swelling is delamination of the layers, similar to that observed in the recent experimental observations of lactate-HT in water.⁹

Hydrogen Bonding. To understand the microscopic origin of the enhanced swelling behavior of the system, detailed analyses of the hydrogen bond¹⁹ (H-bond) statistics between the different donor–acceptor pairs are carried out. We use here a common H-bond definition in which an H-bond is considered to exist if the donor–acceptor distance is less than 3.5 Å and simultaneously the hydrogen–donor–acceptor angle is less than 30°. The citrate anion functions as a pure H-bond acceptor, because the hydrogens of the backbone carbons are hydrophobic and that of the –OH group forms an intramolecular H-bond with one of the oxygens of the carboxylate groups and plays no active role in intermolecular H-bonding. The M–OH groups of metal hydroxide layers act as pure H-bond donors, consistent with previous MD studies.^{17,21}

The statistics of H-bonding between the relevant donor/acceptor pairs in citrate-HT, under progressive hydration, show patterns of systematic reduction in the number of H-bonds between citrate and M–OH groups, while the number of citrate–water and M–OH–water H-bonds increases to reach their respective characteristic saturation values (Figure 2a and b). Starting from an average value of 14.2 in the dry system (n

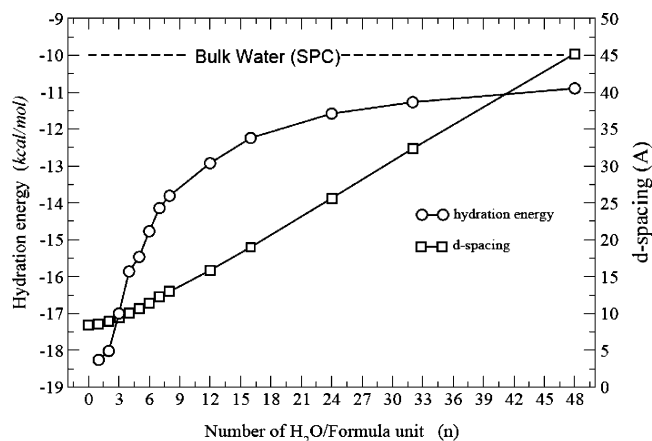


Figure 1. Variation of interlayer spacing (d -spacing) and hydration energy as a function of the number of water molecules per formula unit, n , from NPT-MD simulation at 300 K and 1 atm pressure.

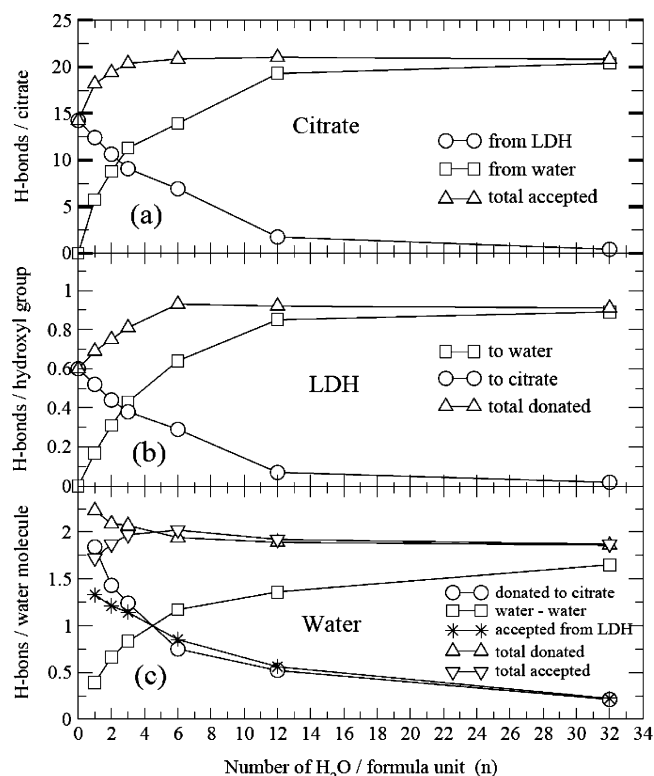


Figure 2. Hydrogen bond statistics for the different species as a function of the number of water molecules per formula unit: (a) the average number of H-bonds accepted by citrate anions from LDH and water; (b) the average number of H-bonds donated by the LDH to citrate and water; (c) the average number of H-bonds accepted/donated by water molecules from/to other species as well as among themselves.

$= 0$), the number of H-bonds accepted by the citrate molecules reaches its saturation value of about 21 by $n = 3$. Similarly, the total number of H-bonds donated by the M–OH groups (Figure 2b) is 0.6 per hydroxyl at $n = 0$, and at a little above $n = 3$ it reaches a saturation value of 0.9 per hydroxyl, a bit lower than the ideal value of one. Thus, the slow initial variation in hydration energy for $n < 3$ (Figure 1) can be readily attributed to undersaturation of the H-bond environment of citrate and metal hydroxides, wherein the additional water molecules enjoy nearly as much welcome as their predecessors. Interestingly, in this low- n regime, the total number of H-bonds donated by a water molecule (Figure 2c) significantly exceeds the number of H-bonds it accepts, reflecting the strong preference of water molecules to hydrate the citrate anions by donating H-bonds to

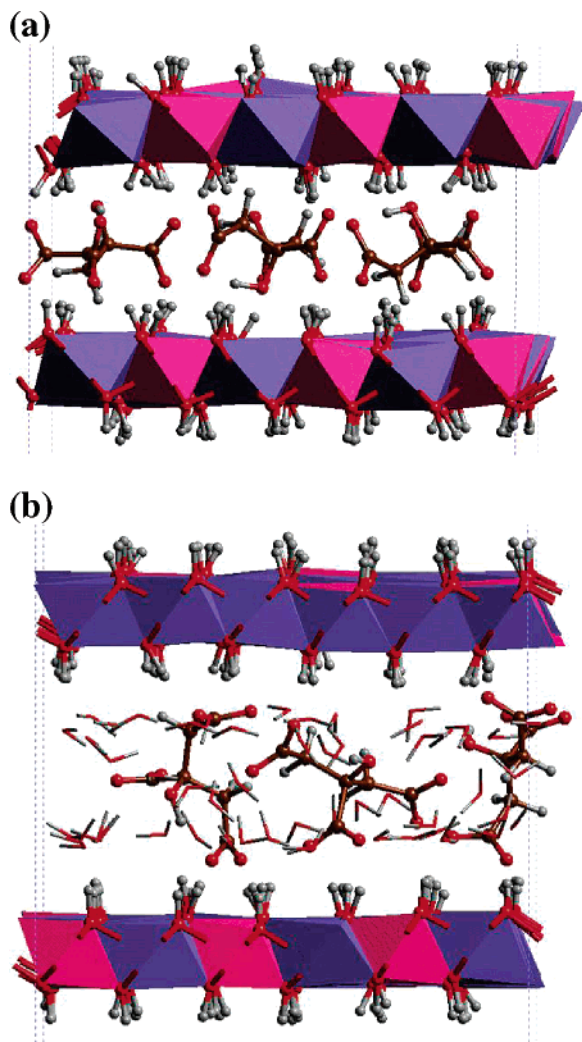


Figure 3. Snapshots from MD trajectory illustrating the changes in interlayer citrate orientation with hydration. The citrate molecules orienting (a) predominantly parallel to the layer in the dry system ($n = 0$) and (b) predominantly perpendicular to the layer at intermediate hydration values ($n = 6$).

them rather than to “wet” the LDH surface accepting H-bonds from the M–OH groups. This behavior also explains the slightly slower approach to saturation in the number of H-bonds donated by LDH (Figure 2b), in comparison to the total H-bonds accepted by the citrate (Figure 2a). It is important to note that the preference of citrate for H_2O over M–OH groups occurs despite the fact that the hydrogens of H_2O carry lower effective charges ($+0.41 |e|$) than those of M–OH ($+0.425 |e|$) in the model employed. This suggests that the smaller size and greater mobility of H_2O allow for more efficient solvation of the functional groups of citrate.

The saturation in the number H-bonds accepted by citrate and donated by the M–OH groups above $n = 3$ has a direct impact on the variation of the hydration energy (Figure 1). Over the range of $3 < n < 12$, the additional water molecules not only replace H-bonds accepted by citrate from the M–OH groups but they also contribute to an increasingly bulk-water-like behavior that causes a sharp increase in the hydration energy toward the bulk value up to about $n = 12$. Above $n = 12$, the majority of the H-bond requirements of citrate and M–OH groups are satisfied by water molecules and a well connected, bulk-water-like, H-bond network sets in among the different species. Thus, the flattening hydration energy trend in Figure 1 reflects

the addition of water molecules into an interlayer that is progressively more like bulk water.

Interlayer Orientation of the Citrates. Understanding of the orientation and organization of the intercalated bio- and organic species in LDH interlayers is important to many practical applications of these materials, but there are few detailed studies. Our results show significant changes in citrate orientation with the hydration state, as shown by the representative snapshots in Figure 3. In the dry system, $n = 0$, the citrate molecules are aligned parallel to the metal hydroxide layers so as to maximize the number of H-bonds they accept from the M–OH groups. At moderate hydration levels ($n \sim 6$), the citrate molecules tend to orient perpendicular to the layers, accepting a larger fraction of their H-bonds from water (Figure 3b). At large hydration levels ($n > 12$), the majority of the citrate molecules are oriented at high angles to the metal hydroxide layer and occupy outer-sphere sites that are separated from the M–OH groups by one monolayer of water molecules. These changes in the orientation of citrate molecules with water content further support their strong preference for water molecules relative to metal hydroxyls that plays a pivotal role in the enhanced swelling behavior of citrate-hydrotalcite.

IV. Conclusions

The hydration energies for citrate-hydrotalcite computed for a wide range of water contents suggests high water affinity of the system and a tendency for enhanced swelling with the intake of water. In contrast to HT intercalated with most inorganic anions, the citrate-HT shows no minima in the hydration energy at any investigated water content, suggesting the absence of any structurally well-defined hydration state. The results are consistent with the recent observation of the delamination of lactate-LDH⁹ and the X-ray and NMR studies for the citrate²² and glutamate²³ intercalated hydrotalcite performed to complement the present study. On the molecular scale, this swelling behavior is due to the preference of citrate molecules to accept H-bonds from H_2O rather than from the hydroxyl groups of HT, and to the need to develop an integrated H-bond network among the active functional groups in the interlayer. Significant changes in the orientation of the citrate molecules in the interlayer occur with progressive hydration, which is also intimately related to its preference to accept hydrogen bonds from water.

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