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Intercalation Reaction of Carbonate MgAl-layered Double Hydroxide Using Alcohol as Solvent

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We succeeded in the first direct intercalation of an organic compound into carbonate layered double hydroxide (LDH) by using alcohol as the solvent at 50 °C. Furthermore, carbonate ion in carbonate LDH was easily exchanged with chloride or nitrate ion in methanol.

Layered double hydroxide (LDH) is a double hydroxide with a structure consisting of a positively charged brucite-like octahedral layer and interlayer anions.[1] The interlayer anions can be exchanged with other anions. In general, anions with larger negative charge are preferentially intercalated, and the affinity of anions in the interlayer space of LDH has been reported by Miyata as $I^- < NO_3^- < Br^- < Cl^- < F^- < OH^- < SO_4^{2-} \ll CO_3^{2-}$.[2] It is known that carbonate ion is the most stable in the interlayer space. Therefore, for intercalation reactions, nitrate or chloride LDH usually has been employed as the starting material. Carbonate LDH has been used as calcined-LDH by heating in an oven at 500 °C.[3] It has been utilized as a host for reconstruction reactions,[4,5] but the crystallinity of the obtained intercalation compound is poor. Hydrotalcite (carbonate LDH) is a biocompatible material that has been approved for use in antacids.[6] Its complexes with drugs efficiently stabilize the drugs and are applied as matrices for drug delivery systems (DDS). Furthermore, it is easy to synthesize carbonate LDH with high crystallinity. If carbonate ions in carbonate LDH can be exchanged with other inorganic and organic anions, other anion LDHs with high crystallinity may be formed, creating more applications for the intercalation chemistry of LDH. However, decarbonation of carbonate LDH has long been thought to be difficult, as mentioned above. Recently, Iyi et al. reported that decarbonation did occur in a mixed solution of hydrochloric acid and sodium chloride or in acetate buffer and sodium chloride with pH control.[7–9] An improved method using acetate buffer under N_2 flow made it possible to form chloride, perchloride, and nitrate LDHs at low salt concentration.[10] In this work, it was found for the first time that carbonate ions in carbonate LDH could be easily exchanged with organic and inorganic anions by using alcohol as the solvent.

Carbonate MgAl-LDH (LDH3-CO_3) [$Mg_{0.75}Al_{0.25}(OH)_2(CO_3)_{0.125}\cdot 0.52H_2O$, Mg/Al = 3.0] and chloride MgAl-LDH (LDH2-Cl) [$Mg_{0.69}Al_{0.31}(OH)_{2.03}Cl_{0.26}(CO_3)_{0.01}\cdot 0.48H_2O$, Mg/Al = 2.0] were obtained from Kyowa Kagaku Kogyo Co., Ltd. and Tomita Chemical Co., Ltd., respectively. Nitrate MgAl-LDH (LDH2-NO_3) [$Mg_{0.66}Al_{0.33}(OH)_2(NO_3)_{0.27}(CO_3)_{0.02}\cdot 0.20H_2O$, Mg/Al = 2.0] was synthesized by coprecipitation.[11] Carbonate LDH is abbreviated as LDH*x*-CO_3, where *x* is the ratio of Mg to Al, and CO_3 is the anion in the interlayer region. The same abbreviation applies to LDH*x*-Cl and LDH*x*-NO_3. The intercalation reaction was performed by stirring LDH and 50 mL of aqueous or alcohol [methanol (MeOH), ethanol (EtOH), and propanol (PrOH)] solution in a closed flask under air atmosphere. Alcohols were used without further purification, and the aqueous solution was decarbonated by N_2 in advance. The suspension was centrifuged, and the obtained solid was washed with the solvent used in the reaction and dried under vacuum for 3 h at room temperature. The compounds were characterized by powder X-ray diffraction (XRD), ATR-IR spectroscopy, and elemental analysis.

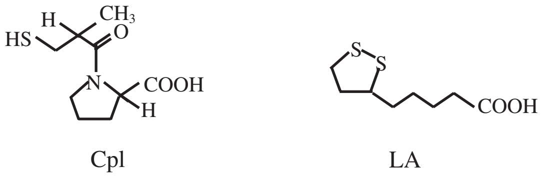

Figure 1. Structures of captopril (Cpl) and lipoic acid (LA).

Table 1. Interlayer distance (*d*) of LDHs before and after the reaction with Cpl or LA in H_2O or EtOH for 3 h at 60 °C

	d/nm				
	Before	Cpl		LA	
		H_2O	EtOH	H_2O	EtOH
LDH2-NO_3	0.89	1.85	0.89	1.95	0.89
LDH2-Cl	0.78	1.83	0.78	1.95	0.78
LDH3-CO_3	0.77	0.77	1.73	0.77	1.86

Captopril (Cpl) and lipoic acid (LA) shown in Figure 1 were used as organic anions for the intercalation reaction. It has been reported that captopril, an antihypertensive drug, was intercalated into MgAl-LDH by coprecipitation.[12] In this work, intercalation was conducted by ion exchange. Thus, suspensions of LDHs (0.1–0.25 g) in 50 mL of alcohol or H_2O with 1–70 mM Cpl or LA were stirred for 10–180 min at 30–60 °C. Table 1 shows the interlayer distances of the LDHs before and after the reaction with Cpl or LA by stirring in aqueous or ethanol solution using 0.25 g of LDHs and 50 mM Cpl or 30 mM LA solutions. After the reaction in aqueous solution, the interlayer distance of LDH2-NO_3 and LDH2-Cl expanded to about 1.8 nm for Cpl and 2.0 nm for LA, suggesting the intercalation of Cpl and LA. These results support the affinity of the interlayer anion in LDHs, as mentioned above.[2] There were no expansions for LDH2-NO_3 and LDH2-Cl in ethanol (Table 1, Figure S1[19]). For LDH3-CO_3, the interlayer distance clearly expanded after treatment in ethanol solution of Cpl or LA, whereas there was no change in aqueous solution. This indicates that Cpl and LA were easily intercalated in LDH3-CO_3 by using ethanol as the solvent. The uptake amounts were calculated by elemental analysis (Figure S2A[19]). The amounts increased above 40 °C, although the reaction did not proceed at 30 °C. Furthermore, the uptake depended on the concentration and reaction time (Figures S2B and S2C[19]). The maximum uptake amounts were

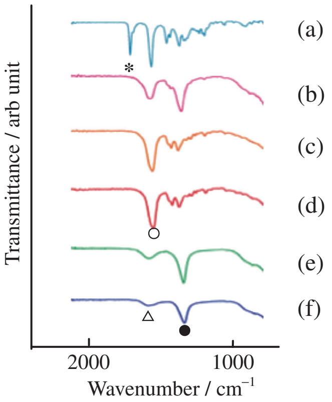

Figure 2. ATR-IR spectra of Cpl (a), LDH3-CO_3 (f), and products obtained after the reaction with 30 mM Cpl in various solvents for 3 h at 60 °C except for MeOH (50 °C): (b) PrOH, (c) EtOH, (d) MeOH, (e) H_2O. $*$: 1746, △: 1643, ○: 1589, ●: 1370 cm^{-1}.

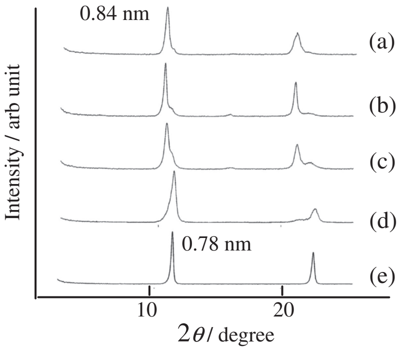

Figure 3. XRD patterns (λ (Cu Kα) = 0.1542 nm) of LDH3-CO_3 after the reaction with $NaNO_3$ in H_2O (e) or MeOH (a–d) solution for 3 h at 50 °C. The amount of added $NaNO_3$ is (a, e) 240, (b) 30, (c) 15, and (d) 6 mmol per gram of LDH3-CO_3. The numerical values in the figure are the interlayer distances (d).

3.4 mmol g^{-1} for Cpl or 3.0 mmol g^{-1} for LA at 60 °C for 3 h in 70 mM solution, which are close to the theoretical ion-exchange capacity (IEC) of LDH3-CO_3 (3.0 mmol g^{-1}).

The intercalation reactions of Cpl and LA (each 30 mM) into LDH2-NO_3 and LDH3-CO_3 (each 0.25 g) were examined in more detail by using various alcohols (50 °C for MeOH, 60 °C for EtOH and PrOH) as solvent. From the XRD patterns (Figures S3 and S4[19]), the intercalation by LDH3-CO_3 proceeded in any alcohol, in contrast to LDH2-NO_3 for which intercalation proceeded only in aqueous solution. It can be seen from the peak intensities of unreacted LDH3-CO_3 and the intercalation compound that the reactivity was different in various alcohols. The optimum alcohol as solvent was MeOH for Cpl and PrOH for LA. ATR-IR spectra of the obtained samples were measured in order to investigate the intercalation mechanism of Cpl into LDH3-CO_3 (Figure 2). In the spectrum of LDH3-CO_3 before the reaction (Figure 2f), the bands due to hydroxy group and carbonate ion were observed at 1643 and 1370 cm^{-1}, respectively. No change of spectrum was observed after the reaction in aqueous solution (Figure 2e), suggesting no intercalation. This fact supports no change of the interlayer distance (Table 1 and Figure S3[19]). However, in the spectra of LDH3-CO_3 after the reaction in alcohols (Figures 2b–2d), the band from carbonate ion (1370 cm^{-1}) disappeared completely in MeOH and EtOH. In PrOH, carbonate ion remains in the interlayer space, in accord with the XRD pattern in which the peak of the original LDH3-CO_3 was clearly observed. A band at 1746 cm^{-1} corresponding to the carboxyl group in Cpl shifted to 1589 cm^{-1}, which arose from the carboxylate ion. This confirmed that carbonate ion in LDH3-CO_3 was exchanged with anionic Cpl, that is, the ion-exchange reaction for LDH3-CO_3 occurred in alcohol. Also in the reaction with LA, it was confirmed that anionic LA exchanged with carbonate ion in LDH3-CO_3 (Figure S5[19]). Thus, this observation was the first case of a large organic anion easily intercalating into LDH3-CO_3 through direct ion exchange using alcohol as solvent.

We next investigated whether the ion exchange of LDH3-CO_3 with inorganic anions in alcohol is possible. The experiment was carried out by suspending 0.05–0.25 g of LDHs and 50 mL of 30–240 mM of $NaNO_3$ or NaCl in aqueous or methanol solution for 10 min to 1 d at 30–50 °C. Figure 3 shows XRD patterns of LDH3-CO_3 after the reaction with $NaNO_3$ in aqueous or MeOH solution for 3 h at 50 °C. The XRD pattern after the reaction in aqueous solution of $NaNO_3$ was similar to that of original LDH3-CO_3 (Figure 3e). Contrary to this, for samples reacted in MeOH, the interlayer distance shifted gradually to 0.84 nm with increasing concentrations of $NaNO_3$ (Figures 3a–3d). The pH of the solution increased by 4 after the reaction, likely because of the release of carbonate ion from LDH3-CO_3 without the destruction of the brucite-like structure in LDH.

ATR-IR spectra were measured in order to clarify the reason for the expansion of the interlayer distance (Figure 4A). The band at 1370 cm^{-1} from carbonate ion shifted to 1361 cm^{-1} with a shoulder around 1419 cm^{-1} with increasing concentration of $NaNO_3$ in MeOH (Figures 4A(c)–4A(g)). When the amount of added $NaNO_3$ was 240 mmol per gram of LDH3-CO_3, the spectrum of product obtained in MeOH was similar to that of LDH2-NO_3 (Figures 4A(g) and 4A(h)), and these bands (1361 and 1419 cm^{-1}) were attributed to nitrate ion. The composition of carbonate ion calculated by elemental analysis decreased to 0.015 from 0.125 in starting LDH3-CO_3 [$Mg_{0.75}Al_{0.25}(OH)_2(CO_3)_{0.125}\cdot 0.52H_2O$] with increasing the amount of added $NaNO_3$ (Figure S6A[19]). And the content of nitrate ion increased. This is further evidence that the carbonate ion in the interlayer space of LDH3-CO_3 exchanged with nitrate ion in MeOH. In fact, the interlayer distance of 0.84 nm in Figure 3a was identical to that of LDH3-NO_3.[13] This is the first case in which LDH3-CO_3 was converted to high crystalline LDH3-NO_3 simply by stirring in MeOH. Furthermore, this exchange reaction with nitrate ion proceeded even at 30 °C, and was complete within 30 min at 50 °C (Figure S7[19]).

The reaction of LDH3-CO_3 and NaCl was also examined in a similar manner (Figure 4B). When the amount of added NaCl was 150 mmol per gram of LDH3-CO_3, the band (1370 cm^{-1}) from the carbonate ion in the ATR-IR spectrum mostly disappeared (Figure 4B(n)), and the composition of carbonate ion also decreased to 0.015 from 0.125 (Figure S6B[19]). Therefore, it was confirmed that the ion-exchange reaction of LDH3-CO_3 with NaCl proceeded by stirring in MeOH, which resulted

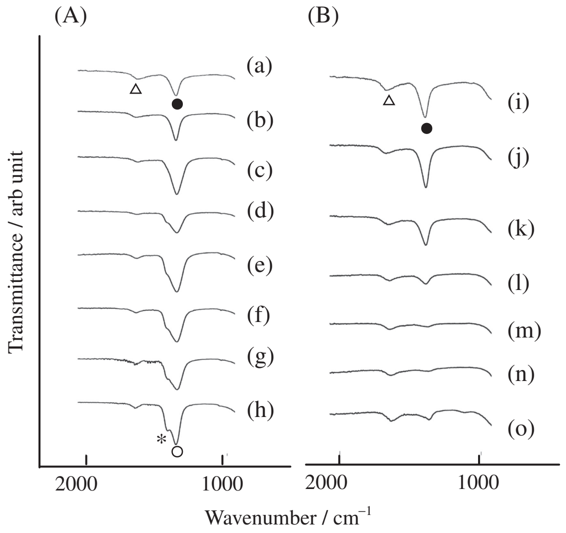

Figure 4. ATR-IR spectra of starting materials [(a, i) LDH3-CO_3] and products obtained after the reaction with $NaNO_3$ (A) and NaCl (B) solution for 3 h at 50 °C. The solvents used are H_2O (b, j) or MeOH (c–g, k–n). The spectra of (h) is LDH2-NO_3 only, (o) is LDH2-Cl only. The amount of added $NaNO_3$ or NaCl is (b, g) 240, (c, k) 6, (d, l) 15, (e) 30, (j, f, n) 150, and (m) 60 mmol per gram of LDH3-CO_3. △: 1643, ∗: 1419, ●: 1370, ○: 1361 cm^{-1}.

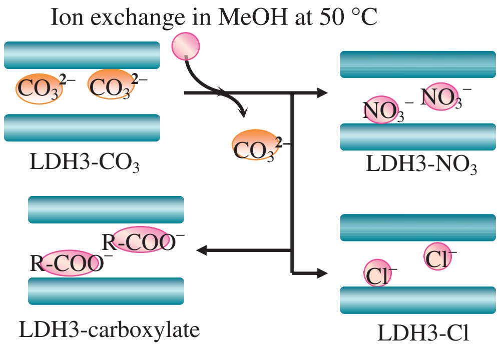

Figure 5. Scheme of ion-exchange reaction of LDH3-CO_3 in MeOH.

in LDH3-Cl. In addition, the interlayer distances in the samples changed slightly from 0.78 to 0.80 nm, supporting this conclusion (Figure S8[19]).[13]

In summary, without using calcination, LHD3-CO_3 could be used as the starting material for the one-step intercalation of some anionic organic guests by conducting the intercalation reaction in alcohol (Figure 5). To date, decarbonation in heated glycerol, reaction of molten acids by thermal reaction, and incorporation of carboxylates in alcohol under solvothermal conditions have been examined.[14–16] Compared to these conditions, the reaction temperature we used in this study is much lower. We have also shown for the first time that by the use of MeOH as solvent, carbonate ions in the LDH interlayer space were readily deintercalated and exchanged with nitrate and chloride ions (Figure 5). The mechanism of these reactions is not clear yet but is under investigation. Swelling of LDH in alcohol, solvation of guest anion by alcohol, or extraction of carbonate ion by protonic solvent are possibilities.[17,18] Whatever the mechanism, the ion-exchange reaction of LDH3-CO_3 reported in this letter is a simple and easy process to prepare high-quality LDH compounds. This finding challenges the common view that use of LDH3-CO_3 as a starting material for intercalation is impossible. We believe that this process will expand the possibilities for the intercalation chemistry of LDH, for example, the intercalation of insoluble compounds in aqueous solution.

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