Near IR Spectroscopic Studies on the Interaction between Acetamide and Ln(dpm)$_3$ in Carbon Tetrachloride

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The interactions between Ln(dpm)$_3$ [$Ln^{3+}=Eu^{3+}$, Yb^{3+}, Pr^{3+}, Sm^{3+}, Tb^{3+} and Ho^{3+}; dpm=tris 2,2,6,6-tetramethylheptane-3,5-dionate] and acetamide in CCl_4 solution were investigated using near IR absorption spectroscopy. From the measured $2\nu_{C=O}+$ amide III combination band of acetamide in the region of 2130-2180 nm (4695-4587 cm^{-1}), it was found that acetamide is coordinating through its carbonyl oxygen atom to Ln(dpm)$_3$ [$C=O\cdots Ln(dpm)_3$)] and forms only 1 : 1 stoichiometric Ln(dpm)$_3$- acetamide complex. The ΔH^o values for the formation of Ln(dpm)$_3$-acetamide obtained from the temperature studies are -39.1, -28.4, -25.5, -24.7, -21.1 and -17.7 kJ mol^{-1} for Eu(dpm)$_3$, Yb(dpm)$_3$, Pr(dpm)$_3$, Sm(dpm)$_3$, Tb(dpm)$_3$ and Ho(dpm)$_3$, respectively, which are larger than those of the hydrogen bond between amide and various hydrogen acceptors. Except Eu(dpm)$_3$ and Yb(dpm)$_3$, $-\Delta H^o$ value increases as the ionic size increases.

Introduction

Because lanthanide ions (Ln^{3+}) have a relatively long life time (100 μs-ms) of luminescence in the air, it can be applied in numerous fields such as biochemistry, analytical method, and TV monitor, etc.. The luminescence intensity of Ln^{3+} is largely dependent on the coordination of the ligands or solvents, so the quantitative data for the coordination are crucial for the enhanced luminescence intensity.[1~3] Moreover, when Ln^{3+} ions are introduced *in vivo* as a contrast agent, the field of MRI (nuclear Magnetic Resonance Imaging), the study of the interaction between amide linkage and Ln^{3+} is essential to determine the distribution of contrast agents in the human body.[4] It is therefore of fundamental importance to obtain the thermodynamic stabilities and the coordination numbers of the Ln^{3+} ion-based complexes with amide. In an attempt to provide a better understanding of the interaction between Ln^{3+} and polypeptide, lanthanide complexes with small amides have been studied by using NMR and luminescence spectroscopy.[1,4] Because of their complexities, however, there are many experimental limits. The near IR spectroscopic method has been demonstrated to be one of the most suitable methods for the hydrogen bonding studies involving amide, since the combination absorption bands in near IR region are well separated to assign and therefore provide the quantitative analysis.[5] As far as we know, however, it has never been applied for the studies of lanthanide-amide systems.

In the present work, we employed near IR absorption spectroscopic method for the study of Ln^{3+} ion-amide systems. To provide the fundamental information about the interaction between polypeptide and Ln^{3+} ion-based complex, as a model system acetamide and tris 2,2,6,6-tetramethylheptane-3,5-dionate lanthanide(III) (Ln(dpm)$_3$; $Ln^{3+}=Eu$, Yb, Pr, Sm, Tb, and Ho) in CCl_4 solution was investigated. Acetamide has strong absorption bands in near IR region at 1957 nm (5110 cm^{-1}) and 2152 nm (4647 cm^{-1}) corresponding to the combination band of antisymmetric N-H stretching ($\nu_{N\text{-}H}$) and amide II ($\nu_{N\text{-}H}+$amide II), and that of C=O overtone and amide III ($2\nu_{C=O}+$amide III), respectively.[6] Ln(dpm)$_3$ is one of the most common lanthanide shift reagent (LSR) in NMR spectroscopy and not shown any notable absorption band in the region of 1920-2180 nm. In order to obtain the fundamental information for the complex formation, such as coordination number, equilibrium constant K, ΔG^o, ΔH^o and ΔS^o, the concentration and the temperature dependence of the spectra have been measured.

Experimental

Ln(dpm)$_3$ were purchased from Aldrich (99+%) and dehydrated at 80 ℃ under reduced pressure for 24 hours. Acetamide (Aldrich, 99+%) was also dried under reduced pressure and stored over P_2O_5 in a desiccator, and CCl_4 (Merk, LC grade) was dried over 4 Å molecular sieves. To prevent hydration during sample preparations, the samples were prepared in N_2-filled glove box.

Near IR absorption spectra of acetamide were obtained with CARY 17DX spectrophotometer by using 10 cm cylindrical spherical quartz cell. The bands due to Ln(dpm)$_3$ and solvent were eliminated by placing a matching cell containing equal amounts of Ln(dpm)$_3$ and solvent in the path of reference beam. The spectra were obtained after reaching the thermal equilibrium at each temperature. The temperature controlled by a Constant-Temperature Bath (Polyscience Inc.) with an accuracy of ±0.1 ℃.

The $2\nu_{C=O}+$amide III combination band of acetamide complexed with Ln(dpm)$_3$ overlaps with that of monomeric acetamide. The observed near IR absorption bands were assumed to be Lorentzian-Gaussian product and were deconvoluted by the previously reported method.[5] A modified simplex search algorithm was used for curve fitting. The program terminates its iteration when chi square is less than 1.0×10^{-5}. The digitized data of measured spectra were obtained by scanning method with Summagraphics digitizer.

Results and Discussion

Upon addition of Ln(dpm)$_3$ to acetamide, no effects on the spectra of $2\nu_{N\text{-}H}$ (the first overtone band of N-H stretching vibration) near 1443 nm were observed through a series of this work. The $\nu_{N\text{-}H}$+amide II band at 1957 nm, which previously has been chosen for the studies involving hydrogen bond between amides and other hydrogen acceptors,[5,7] was also shifted slightly causing difficulties in quantifying the data. On the other hand, $2\nu_{C=O}$+amide III band at 2152 nm was shifted to lower energy region significantly. The results imply that AA is coordinating through its carbonyl oxygen atom to Ln(dpm)$_3$[C=O···Ln(dpm)$_3$)], which is in agreement with the results of NMR studies.[8] The $2\nu_{C}$=O+amide III combination band of acetamide at 25 ℃ with various molar ratios of Eu(dpm)$_3$ (0.5 mM-2.3 mM) to acetamide (2.5 mM) is shown in Figure 1. As the concentration of Ln(dpm)$_3$ increases, the intensity of the band at 2152 nm is decreased and that of the shoulder at 2163 nm is increased. The appearance of an isosbestic point indicates an equilibrium of only two species, monomeric and complexed acetamide. The observed spectrum was resolved into two distinct Lorentzian-Gaussian product components. The fitted spectrum of [Eu(dpm)$_3$] (1.5 mM)/[acetamide](2.5 mM)(ρ=0.6) in CCl$_4$ at 25 ℃ is shown in the inset of Figure 1. An intensive peak at 2152 nm and a shoulder at 2163 nm were assigned to the $2\nu_{C=O}$+amide III combination band of the monomeric acetamide and that of the complexed acetamide, respectively, on the basis of acetamide only spectrum in CCl$_4$ solution. The complexed acetamide should be 1 : 1 Ln(dpm)$_3$-acetamide adducts. Under the concentration range used in our experiment the formation of 1 : 2 Ln(dpm)$_3$-2(acetamide) adducts is not observed, even though 1 : 2 LSR-N,N-dimethylamide complexes have been reported when the methyl groups in dpm of Ln(dpm)$_3$ were replaced by fluorine atoms, namely 1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octanedione (fod).[9] It has been known that CCl$_4$ does not form inner-sphere complex with Ln^{3+} ion, so the coordination number of Ln^{3+} in Ln(dpm)$_3$ is 7. The result is consistent with the results of NMR studies for various LSR with dpm ligand[10] and Molecular Mechanics Calculation (MM2MX) on Eu(dpm)$_3$ with quinnuclidine.[11]

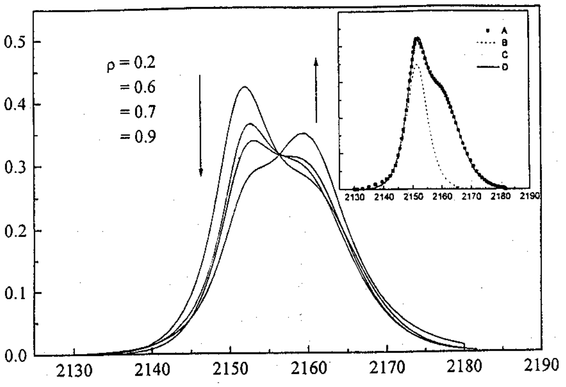

Figure 1. $2\nu_{C=O}$+amide III combination band of acetamide at 25 ℃ in CCl$_4$ as a function of molar ratios of Eu(dpm)$_3$ to acetamide (2.5 mM) (ρ=[Eu(dpm)$_3$]/[acetamide]). The inset is shown the resolved monomeric and the complexed acetamide with Eu(dpm)$_3$(1.5 mM) (ρ=0.6) in CCl$_4$. Measured absorption spectrum, fitted band of monomeric acetamide, and that of complexed acetamide with Eu(dpm)$_3$ are represented by (A), (B) and (C), respectively. The thick line (D) is the sum of (B) and (C).

To obtain the thermodynamic parameters, experiments were carried out between 15 ℃ and 45 ℃. At a fixed molar ratio, the increment of the temperature leads to decrement of the band at 2152 nm and the growth of the band at 2163 nm with an isosbestic point. Within our experimental conditions, the equilibrium for the complex formation and the equilibrium constant K can be described as follow,

$$\mathrm{Ln(dpm)_3+acetamide} \rightleftharpoons \mathrm{Ln(dpm)_3\text{-}acetamide}\ \ (1:1\ \text{complex}) \qquad (1)$$

$$K=C_{1:1}/C_{free}\,C_{mono},\quad C_{1:1}/C_{mono}=K\,C_{free} \qquad (2)$$

where $C_{1:1}$ is the concentration of the complexed acetamide, C_{free} is the concentration of the free Ln(dpm)$_3$ and C_{mono} is the concentration of monomeric acetamide. The ratio of $C_{1:1}$ to Cmono is directly obtained from the area of two resolved bands, and the linear fit for the $C_{1:1}/C_{mono}$ *vs* C_{free} plot yields the equilibrium constant *K*. Figure 2 shows a typical plot of $C_{1:1}/C_{mono}$ *vs* C_{free} at various temperatures. The thermodynamic parameters, ΔH^o and ΔS^o, can be evaluated from the following equation using the formation constant obtained as above,

$$-d(\ln K)/d(1/T)=\Delta H^o(1/R) \qquad (3)$$

assuming that these quantities are independent of the temperature. The plot of *R* ln *K* *vs* 1/*T* for the formation of Ln(dpm)$_3$-acetamide complexes is shown in Figure 3 and the obtained thermodynamic parameters are summarized in Table 1. The result shows that Eu(dpm)$_3$ forms the most stable complex with acetamide and Ho(dpm)$_3$ forms the weakest

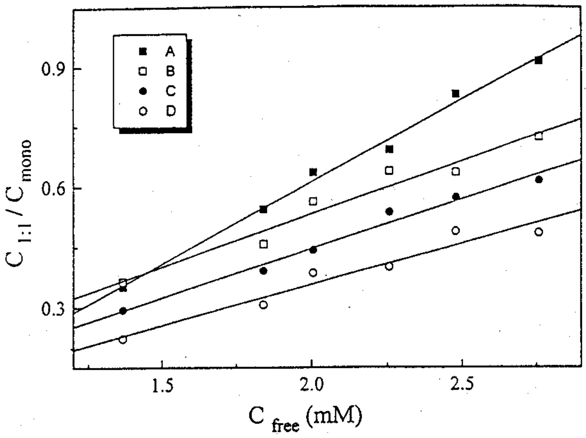

Figure 2. Plot of $C_{1:1}/C_{mono}$ *vs* C_{free} with various molar ratios of Sm(dpm)$_3$ to acetamide (2.5 mM) in CCl$_4$ solution at 15 ℃ (A), 25 ℃ (B), 35 ℃ (C) and 45 ℃ (D).

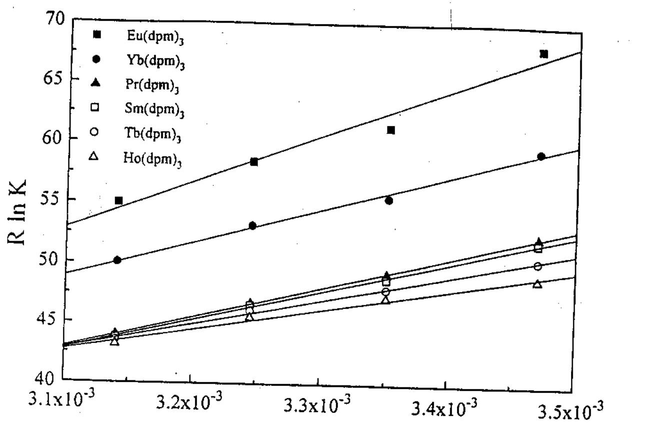

Figure 3. R ln K *vs* $1/T$ plot for the formation of Ln(dpm)$_3$-acetamide complexes. The slops and intercepts represent -ΔH^os and ΔS^os, respectively.

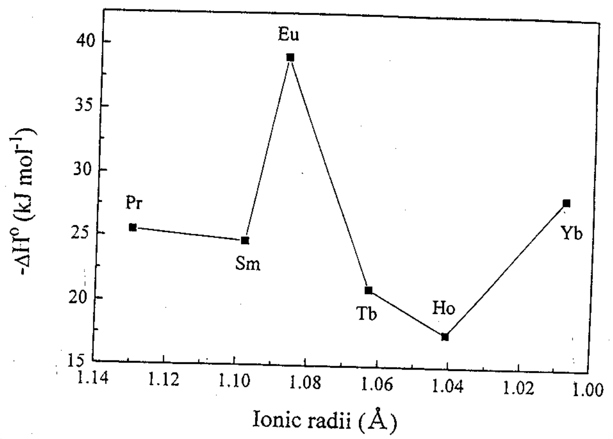

Figure 4. Plot of -ΔH^o against the 6-coordinate ionic radius of the Ln^{3+}.

one with the formation constant of 1,606 M^{-1} and 363 M^{-1} at 25 ℃, respectively, and the formation constants decrease with increasing temperature. The formation constant of Eu(dpm)$_3$ with 4,4-dimethyl-5α-cholestan-3β-one, more bulky substrate molecule than acetamide in CCl$_4$ has been reported to be 126 M^{-1} at 39 ℃ using NMR spectroscopic method and the value is even smaller than that of acetamide-Eu(dpm)$_3$ at 45 ℃.[12] The ΔH^o values for the formation of Ln(dpm)$_3$-acetamide complexes are in the range between -39.1 kJ mol^{-1} and -17.6 kJ mol^{-1}, and the values are larger than those of the hydrogen bond between amide and various hydrogen acceptors (15-20 kJ mol^{-1}, typically).[5,7,13] It has been known that the bond character in Ln^{3+} complex is ionic. The quantitative result suggests that the formation of Ln(dpm)$_3$-acetamide involves the ion-dipole interaction between Ln^{3+} in Ln(dpm)$_3$ and O=C of acetamide, Ln^{3+}···O=C. It is evident that the electrostatic interaction between Ln(dpm)$_3$ and acetamide, and steric repulsions in an 1 : 1 complex may be important factors in determining the stability of the Ln(dpm)$_3$-acetamide complex.

It is well known that the radii of the lanthanide ions decrease monotonically with increase in atomic number (lanthanide contraction). As the ionic radius decreases there would be two opposing factors. First, in the absence of steric factors both the charge density of Ln^{3+} increase and acceptor properties of Ln(dpm)$_3$ would presumably increase. Secondly, steric repulsions in the Ln(dpm)$_3$-acetamide complex would also increase, which tends to make this complex less stable. Figure 4 shows a plot of -ΔH^o values *vs* radii of Ln^{3+} ions assuming that the coordination number is 6. Because the ionic radii of 7-coordinated Ln^{3+} have not been reported in the literature and the orders of reported Ln^{3+} ionic radii in atomic number with various coordination numbers have shown same as that of 6-coordinated Ln^{3+} ion.[14] Except Eu(dpm)$_3$ and Yb(dpm)$_3$, -ΔH^o decreases as the ionic size decreases. The result implies that the steric repulsions of three bulky ligands surrounding lanthanide ion is more important than electrostatic interaction between Ln(dpm)$_3$ and acetamide. It should be noted that the obtained values of enthalpy and entropy show linear correlation as illustrates in Figure 5 eventhough that of Eu(dpm)$_3$ and Yb(dpm)$_3$ have shown the deviation from the tendency towards ionic radii. The linear correlation of -ΔH^o *vs* -ΔS^o plot suggests that each 1 : 1 adducts formed in this work involves similar mechanisms and structures.

The unusual results in Eu(dpm)$_3$ and Yb(dpm)$_3$ systems can be interpreted as follows. Eu^{3+} and Yb^{3+} have relatively low reduction potentials at -0.35 V and -1.05 V *vs* NHE in aqueous solution, respectively.[15] When C=O group in acetamide approaches to Eu(dpm)$_3$ or Yb(dpm)$_3$, Eu^{3+} or Yb^{3+} in Ln(dpm)$_3$ would have more electron affinity than other lanthanide ions. As a result, C=O group could approach closer to Eu(dpm)$_3$ or Yb(dpm)$_3$ and forms more stable acetamide-Ln(dpm)$_3$ adducts than others. Without further studies,

Table 1. Thermodynamic parameters for the formation of Ln(dpm)$_3$-acetamide complexes in CCl$_4$

Ln(dpm)$_3$ •	15 ℃		25 ℃		35 ℃		45 ℃		$-\Delta H^o$	$-\Delta S^o$
	K (M^{-1})	$-\Delta G^o$ (kJ mol^{-1})	K	$-\Delta G^o$	K	$-\Delta G^o$	K	$-\Delta G^o$	(kJ mol^{-1})	(J mol^{-1} K^{-1})
Eu(dpm)$_3$	3634	19.64	1606	18.30	1130	18.01	746	17.50	39.1± 0.2	68.3± 0.5
Yb(dpm)$_3$	1301	17.18	799	16.57	602	16.40	414	15.94	28.4± 0.2	39.2± 0.3
Pr(dpm)$_3$	551	15.11	375	14.69	277	14.40	200	14.07	25.5± 0.2	36.1± 0.3
Sm(dpm)$_3$	522	14.99	357	14.57	271	14.35	194	13.94	24.7± 0.2	33.8± 0.1
Tb(dpm)$_3$	437	14.57	323	14.33	257	14.21	188	13.85	21.1± 0.2	22.6± 0.1
*Ho(dpm)$_3$	363	14.13	294	14.09	240	14.04	180	13.73	17.6± 0.3	12.0± 0.2

<6% experimental error. *<10% experimental error

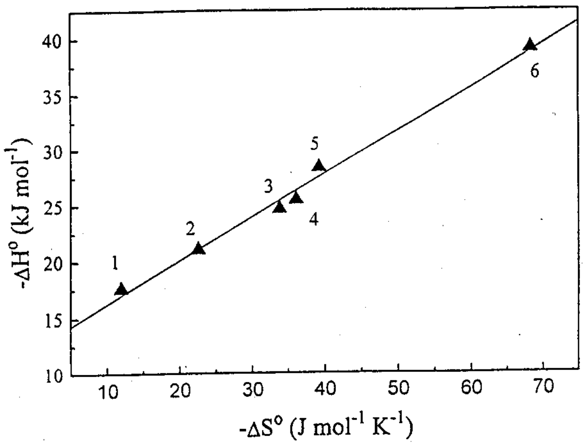

Figure 5. Correlation of $-\Delta H^o$ and $-\Delta S^o$ for the formation of 1 : 1 complexes of acetamide with (1) $Ho(dpm)_3$, (2) $Tb(dpm)_3$, (3) $Sm(dpm)_3$, (4) $Pr(dpm)_3$, (5) $Yb(dpm)_3$ and (6) $Eu(dpm)_3$.

however, it is not clear at this point.

Conclusions

The near IR absorption spectroscopic method has been applied for the study of the interactions between $Ln(dpm)_3$ and acetamide in CCl_4 solution. From the measured $2\nu_{C=O}$ + amide III combination band of acetamide in the near IR region, it was found that acetamide is coordinating through its carbonyl oxygen to $Ln(dpm)_3$[$C=O\cdots Ln(dpm)_3$)] and forms only 1 : 1 stoichiometric $Ln(dpm)_3$-acetamide complex indicating the coordination number is 7. The ΔH^o values for the formation of $Ln(dpm)_3$-acetamide complexes are in the range between -39.1 kJ mol^{-1} and -17.6 kJ mol^{-1}, and the values are larger than those of the hydrogen bond between amide and various hydrogen acceptors. Except Eu(dpm)$_3$ and $Yb(dpm)_3$, $-\Delta H^o$ value increases as the ionic size increases implying the steric repulsions of three bulky ligands surrounding lanthanide ion are more important than the charge density of Ln^{3+} ion in $Ln(dpm)_3$.

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