Electrospray Mass Spectrometry Study on Polynuclear Pd(II) and Ni(II) Complexes of 3,6,9,16,19,22-Hexaazatricyclo[22.2.2.2^{11,14}]triaconta-11,13,24,26(1),27,29-Hexaene

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Polynuclear Pd(II) and Ni(II) complexes of macrocyclic polyamine 3,6,9,16,19,22-hexaazatricyclo[22.2.2.2^{11,14}]-triaconta 11,13,24,26(1),27,29-hexaene (L) in solution were investigated by electrospray ionization mass spectrometry (ESIMS). For methanol solution of complexes M_2LX_4 (M = Pd(II) and Ni(II), X = Cl$^-$ and I$^-$), two main clusters of peaks were observed which can be assigned to $[M_2LX_3]^+$ and $[M_2LX_2]^{2+}$. When Pd_2LCl_4 was treated with 2 or 4 mol of $AgNO_3$, it gave rise formation of $Pd_2LCl_2(NO_3)_2 \cdot H_2O$ and $[Pd_2L(H_2O)_m(NO_3)_n]^{(4-n)+}$, respectively. ESMS spectra show that the dissociation of the former in the ionization process gave peaks of $[Pd_2LCl_2]^{2+}$ and $[(Pd_2LCl_2)NO_3]^+$, while dissociaqtion of the later gave the peaks of $[Pd_2L(CH_3CO_2)_2]^{2+}$ and $\{[Pd_2L(CH_3CO_2)_2] \cdot (NO_3)\}^+$ in the presence of acetic acid. Similar species were observed for Pd_2LI_4 when treated with 4 mol of $AgNO_3$. When $[Pd_2L \cdot (H_2O)_m(NO_3)_n]^{(4-n)+}$ reacted with 2 mol of oxalate anions at 40℃, $[Pd_4L_2(C_2O_4)_2(NO_3)_2]^{2+}$ and $[Pd_4L_2(C_2O_4)_2 \cdot (NO_3)]^{3+}$ were detected. This implies the formation of square-planar molecular box $Pd_4L_2(C_2O_4)_2(NO_3)_4$ in which $C_2O_4^{2-}$ may act as bridging ligands as confirmed by crystal structure analysis. The dissociation form and the stability of complex cations in gaseous state are also discussed. This work provides an excellent example of the usefulness of ESIMS in the identification of metal complexes in solution.

Keywords   Electrospray mass spectrometry, macrocyclic polyamine, metal complex, ionization, dissociation, palladium complex

Introduction

Transition metal polynuclear complexes of macro-cyclic polyamines are attracting much attention in the field of the mimetic of metalloenzymes since these ligands can give a high degree of preorganization on metal complex formation.[1-4] The title macrocyclic polyamine 3,6,9,16,19,22-hexaazatricyclo[22.2.2.2^{11,14}]-triconta-11,13,24,26(1),27,29-hexaene (Ligand L, Fig. 1) can form polynuclear metal complexes readily. Moreover, its binuclear Eu(III), Pr(III) complexes and Zn(II) complexes were found to activate the hydrolysis of bi(p-nitrophenyl)phosphate (BNP).[5,6] The binuclear Cu(I) complexes of an analogous ligand are excellent model of tyrosinase,[7] and imidazato-bridged binuclear Cu(II) complexes can mimic the active site of Cu-Zn SOD.[8] Macrocyclic polyamine metal complexes can also associate with anions such as amino acids, inorganic phosphates and RNA.[8-11] The activity of these compounds is related to their structures especially the coordination environment of the metal centers.

Electrospray ionization mass spectrometry (ESIMS), a powerful technique to analyze large biomolecules,[12] has now been applied in the investigation of coordination and organometallic compounds,[13-15] studies on the interaction of metal ions with peptides and proteins that have just begun.[16,17] The composition and structural information of metal complexes obtained by precise determination of their molecular masses and charges via ESIMS technology may facilitate the understanding of the structure of the complexes. In this paper, we report the ESIMS investigation of polynuclear Pd(II) and Ni(II)

complexes of macrocyclic polyamine in solution. The ESIMS results are discussed on the basis of counter anion dissociation in ionization process, and compared with the crystallographic data.
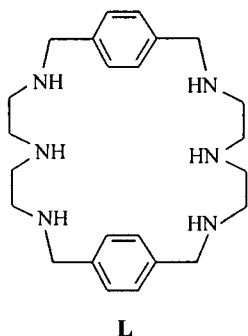

Fig. 1   Structure of Ligand **L**.

Experimental

All common chemicals are of analytical grade reagents. The synthesis, characterization and structure description of complexes $[M_2LX_2X_2']$ (M = Pd(II) and Ni(II), X = Cl⁻, I⁻ and $CH_3CO_2^-$, X' = X and NO_3^-) and $Pd_4L_2(C_2O_4)_2(NO_3)_4 \cdot 6H_2O$ will be reported elsewhere.[18]

ESIMS *measurement*

An electrospray mass spectrometer (LCQ, Finnigen) was employed to determine molecular mass of polynuclear Pd(II) or Ni(II) complexes of macrocyclic polyamine in positive ion mode. Samples dissolved in methanol were diluted to 100 $\mu mol \cdot L^{-1}$. 1.0 μL or 2.0 μL such solutions were loaded into the injection valve of the LCQ unit and then injected into the mobile phase solution (CH_3OH), and carried through the electrospray interface into the mass analyzer at a rate of 200 $\mu L/min$. The working voltage at the electrospray needle was 5 kV and the capilliary was heated to 200 ℃. A maximum ion injection time of 200 ms along with 10 scans was used in these experiments. The predicted isotope distribution patterns for complex cations were calculated using the IsoPro 3.0 program.[19]

Dehalogenation *of* $Pd_2LX_4(X = Cl, I)$

Partial dehalogenation of Pd_2LCl_4 *and synthesis of* $Pd_2LCl_2(NO_3)_2 \cdot H_2O$

The complex was obtained by treating Pd_2LCl_4 with 2 mol of aqueous $AgNO_3$ solution in dark at 30 ℃ for 5 h. After removing the precipitate (most of them were formed at once when the $AgNO_3$ was added) by centrifugation, the clear solution obtained was slowly evaporated at room temperature and pale-yellow crystals were formed.

Complete dehalogenation of $Pd_2LX_4(X = Cl, I)$ *and synthesis of* $Pd_2L(NO_3)_4([Pd_2L(H_2O)_m(NO_3)_n]^{(4-n)+})$

Pd_2LX_4 (X = Cl, I) was mixed with 4 mol of aqueous $AgNO_3$ solution and stirred at 35 ℃ for 5 h in dark. Aqua complex solution (40 $mmol \cdot L^{-1}$) was obtained after centrifugation. The solution (10 μL) was diluted with 200 μL of water, then acidified with acetic acid (2 μL) and determined by ESIMS.

Results and discussion

Dissociation *of* M_2LX_4 (M = Pd, Ni; X = Cl, I) *in ionization process*

Pd_2LI_4 Fig. 2 shows the ESIMS spectrum of Pd_2LI_4. There are only two main clusters of peaks with $m/z = \sim 1004$ and ~ 439, and the peaks in the former are separated by 1.0 m/z, and the later separated by 0.5 m/z. Based on the molecular mass and charges, the experimental isotopic distribution patterns (IDPs) are very similar to IDPs of $[Pd_2LI_3]^+$ and $[Pd_2-LI_2]^{2+}$ calculated by IsoPro program.[19] This result suggests that only two I⁻ directly coordinate to the metal centers and the other two I⁻ are counter anions and can be losed during the electrospray ionization process.

Pd_2LCl_4 Similar to Pd_2LI_4, in the ESIMS spectrum of Pd_2LCl_4, there are two main clusters of peaks at $m/z = \sim 731$ and ~ 346, whose IDPs are almost identical with the predicted IDPs for $[Pd_2LCl_3]^+$ and $[Pd_2LCl_2]^{2+}$ (Fig. 3). This suggests that Pd_2LCl_4 has the same coordination mode as Pd_2LI_4.

Ni_2LCl_4 The ESIMS spectrum of the complex is shown in Fig. 4. Similarly, the two clusters of peaks can be assigned as $[Ni_2LCl_3]^+$ and $[Ni_2LCl_2]^{2+}$ accordingly.

Based on the positive species detected by ESIMS, the dissociation procedure of the three complexes during

the soft-ionization process can be summarized as follows:

$$M_2LX_4 \longrightarrow [M_2LX_3]^+ \longrightarrow [M_2LX_2]^{2+}$$
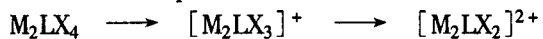
This suggests that the metal centers may be quadruplely coordinated by one halogen X atom and three N atoms from the same diethyl triamine moiety of **L**, based

on the knowledge of coordination chemistry (Scheme 1). Therefore, the two X⁻ coordinate to the metal enter is difficult to dissociate, on the contrary, the two X⁻ as counter anoins can be dissociated readily.[18]
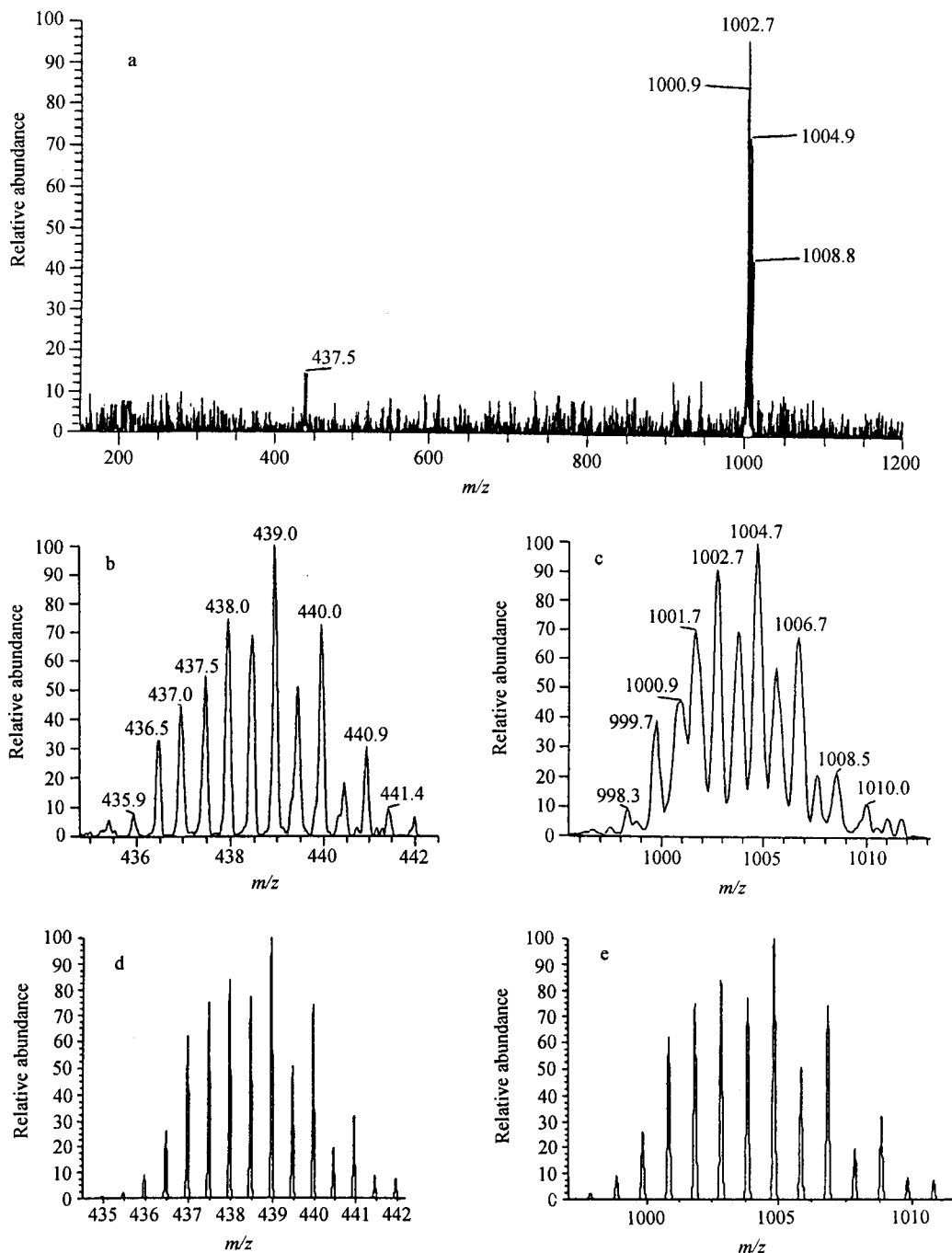

Fig. 2   ESIMS spectrum of Pd_2LI_4 (a), (b) and (c) show the isotopic distribution patterns of $[Pd_2LI_2]^{2+}$ (m/z ~ 439) and $[Pd_2LI_3]^+$ (m/z ~ 1004) observed; (d) and (e) are the predicted isotopic distribution patterns of $[Pd_2LI_2]^{2+}$ (m/z ~ 439) and $[Pd_2LI_3]^+$ (m/z ~ 1004) given by IsoPro. 3.0 program.
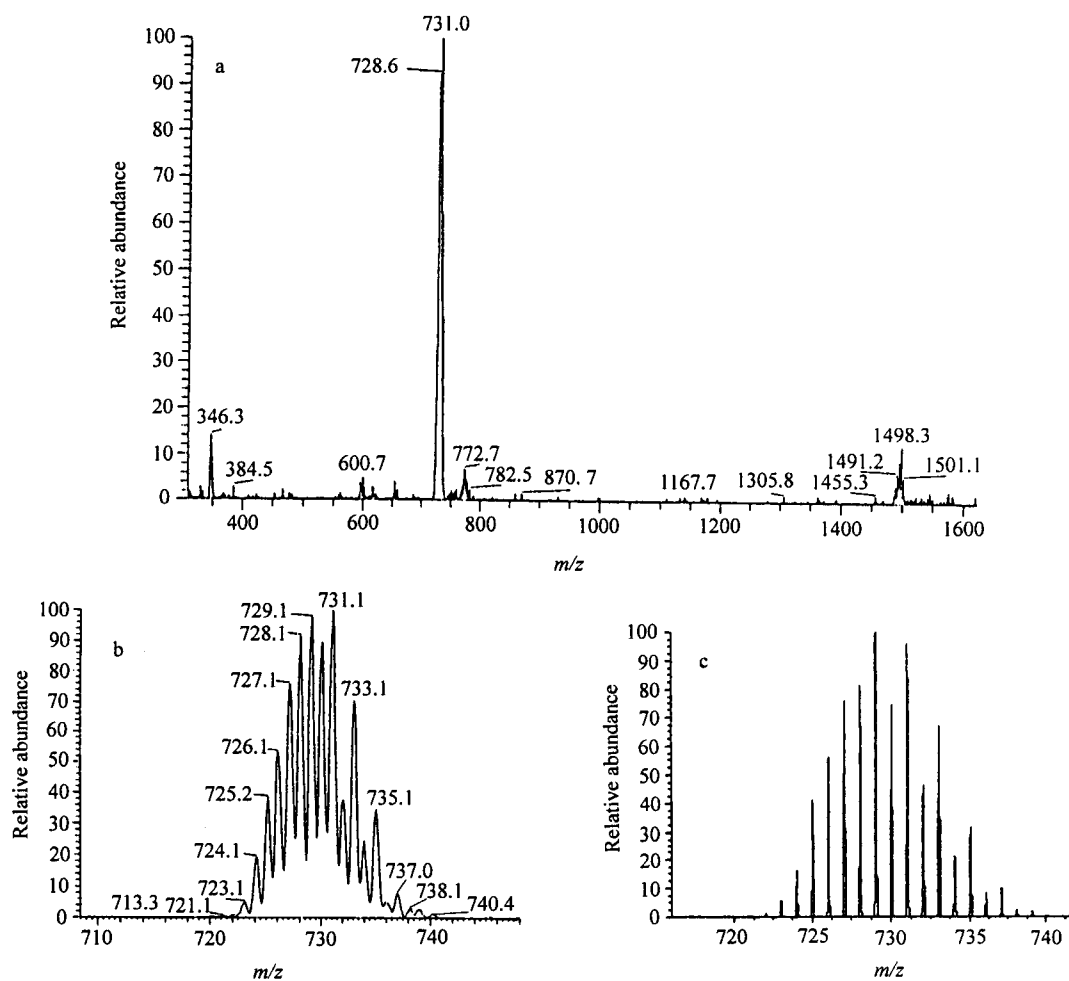
Fig. 3   ESIMS spectrum of Pd_2LCl_4 (a), (b) shows the isotopic distribution patterns of $[Pd_2LCl_3]^+$ ($m/z \sim 731$) observed;   (c) is the predicted isotopic distribution patterns of $[Pd_2LCl_3]^+$ ($m/z \sim 731$) given by IsoPro. 3.0 program.

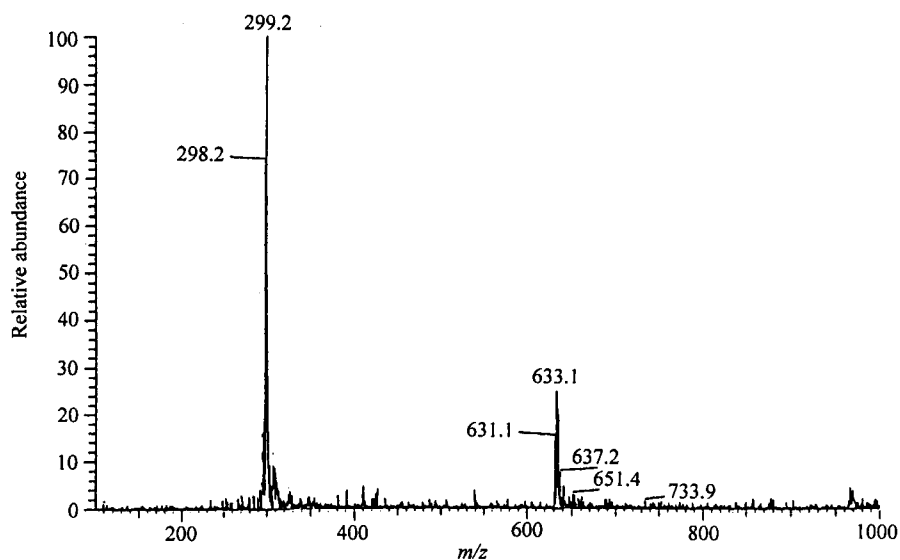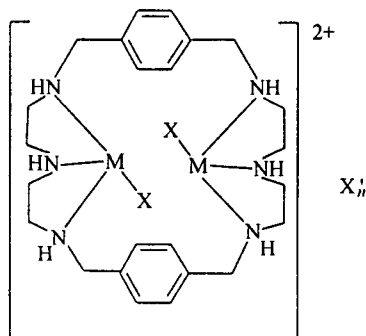Fig. 4   ESIMS spectrum of Ni_2LCl_4.

Scheme 1

$M = Pd(II)$ or $Ni(II)$; $X = Cl^-$, I^- or $CH_3CO_2^-$;

$X' = X$ or NO_3^-; $n = 0, 1$

For Pd_2LX_4 ($X = Cl$ and I), the intensity of the peak of $[Pd_2LX_3]^+$ is relatively much stronger than that of $[Pd_2LX_2]^{2+}$, especially in the case of Pd_2LI_4, suggesting that $[Pd_2LX_3]^+$ is more stable than $[Pd_2LX_2]^{2+}$ during the ionization process. In contrast with Pd_2LX_4 ($X = Cl$ and I), the peaks for $[Ni_2LCl_2]^{2+}$ at $m/z \sim 299$ in Ni_2LCl_4 is stronger than that of $[Ni_2LCl_3]^+$ at $m/z \sim 633$, indicating the complex is dissociated readily and mainly exists in the form of $[Ni_2LCl_2]^{2+}$.

Dehalogenation of complexes

Partial dehalogenation of Pd_2LCl_4

According to the dissociation procedure of complexes M_2LX_4 ($M = Pd(II)$ or $Ni(II)$, $X = Cl$ or I) in ionization process and the crystal structure of Pd_2LI_4, two halogen atoms in the out sphere of $Pd(II)$ can be readily removed. Thus the reactions of Pd_2LCl_4 with 2 or 4 equivalent $AgNO_3$ are carried out to study its dissociation in solution.

The ESIMS spectra of the solution obtained from partial dehalogenation of Pd_2LCl_4 shows only two main groups of peaks at $m/z \sim 347$ and ~ 755. Their IDPs are identical with those of $[Pd_2LCl_2]^{2+}$ and $[(Pd_2LCl_2) \cdot NO_3]^+$ calculated by IsoPro program (Fig. 5), implying the formation of $Pd_2LCl_2(NO_3)_2$ in which each $Pd(II)$ is coordinated by three N atoms of diethyl triamine and Cl^-. The ESIMS spectra of $Pd_2LCl_2(NO_3)_2 \cdot H_2O$ for structure analysis is identical with that of the

solution. The X-ray crystal analysis confirmed that the structure of $Pd_2LCl_2(NO_3)_2 \cdot H_2O$ and each $Pd(II)$ is indeed coordinated by three N atoms of diethyl triamine and Cl^-, with the counter anions being NO_3^- instead of Cl^-. All these suggests that Pd_2LCl_4 may exist in the form of $[Pd_2LCl_2]^{2+}$ and $[(Pd_2LCl_2)Cl]^+$ in solution, and two counter anions Cl^- which can be dissociated are readily precipitated by $AgNO_3$.

Complete dehalogenation Pd_2LX_4 ($X = Cl, I$)

The coordinated X^- can be removed from Pd_2LX_4 when stirred with 4 mol of $AgNO_3$ to give bi-$Pd(II)$ aqua complex cation $[Pd_2L(H_2O)_m(NO_3)_n]^{(4-n)+}$. As shown in Fig. 6, there are only two main cluster of peaks at $m/z = \sim 371$ and ~ 806, when determined in the presence of acetic acid. Comparing the zoom scan spectra for main clusters of peak with the corresponding calculated IDPs of $[Pd_2L(CH_3CO_2)_2]^{2+}$ and $\{[Pd_2L \cdot (CH_3CO_2)_2](NO_3)\}^+$, it can be noted that the observed peaks with $m/z = 368.4$—374.9 separated by 0.5 m/z fit quite well with those calculated for $[Pd_2L \cdot (CH_3CO_2)_2]^{2+}$, and the peaks at $m/z = \sim 806$ can be attributed to $\{[Pd_2L(CH_3CO_2)_2](NO_3)\}^+$. The added acetic acid coordinate to $[Pd_2L(H_2O)_m \cdot (NO_3)_n]^{(4-n)+}$, giving rise to the two species observed. As expected, ESIMS spectra of the aqua complexes obtained from Pd_2LI_4 and Pd_2LCl_4 are identical. If the sample is directly determined without acetic acid, its ESIMS spectrum will be complicated. The weak ligands such as NO_3^-, H_2O or CH_3OH are able to coordinate competitively to $Pd(II)$, and these ligands may be partly or completely dissociated in the ionization process. The presence of many cationic species makes the ESIMS spectrum complicated.

ESIMS spectra of square-planar molecular box $Pd_4L_2(C_2O_4)_2(NO_3)_4 \cdot 6H_2O$

$Pd_4L_2(C_2O_4)_2(NO_3)_4 \cdot 6H_2O$ was obtained by reacting $[Pd_2L(H_2O)_m(NO_3)_n]^{(4-n)+}$ with oxalate anions. Its crystals were dissolved in DMSO, and then diluted with 100 times of methanol. Fig. 7 shows the ESIMS spectrum of the complex with inserted zoom scan spectra of the main clusters of peak at $m/z = \sim 773$ and ~ 495. These two cluster peaks are almost identical

to IDPs of $[Pd_4L_2(C_2O_4)_2(NO_3)_2]^{2+}$ (**I**) and $[Pd_4L_2$-$(C_2O_4)_2(NO_3)]^{3+}$ (**II**) (the separation of peaks and relative abundance). The dissociation from **I** to **II** indicates NO_3^- may act as counter anions, since the ionization in ESIMS is soft-ionization in which covalent bonds

are difficult to break. Because the complex cation $[Pd_4L_2(C_2O_4)_2]^{4+}$ has high positive charge, NO_3^- acts as counter anion can associated with them to decrease its high positive charge and stabilize it. Therefore, the complex species detected in ionization process evidently
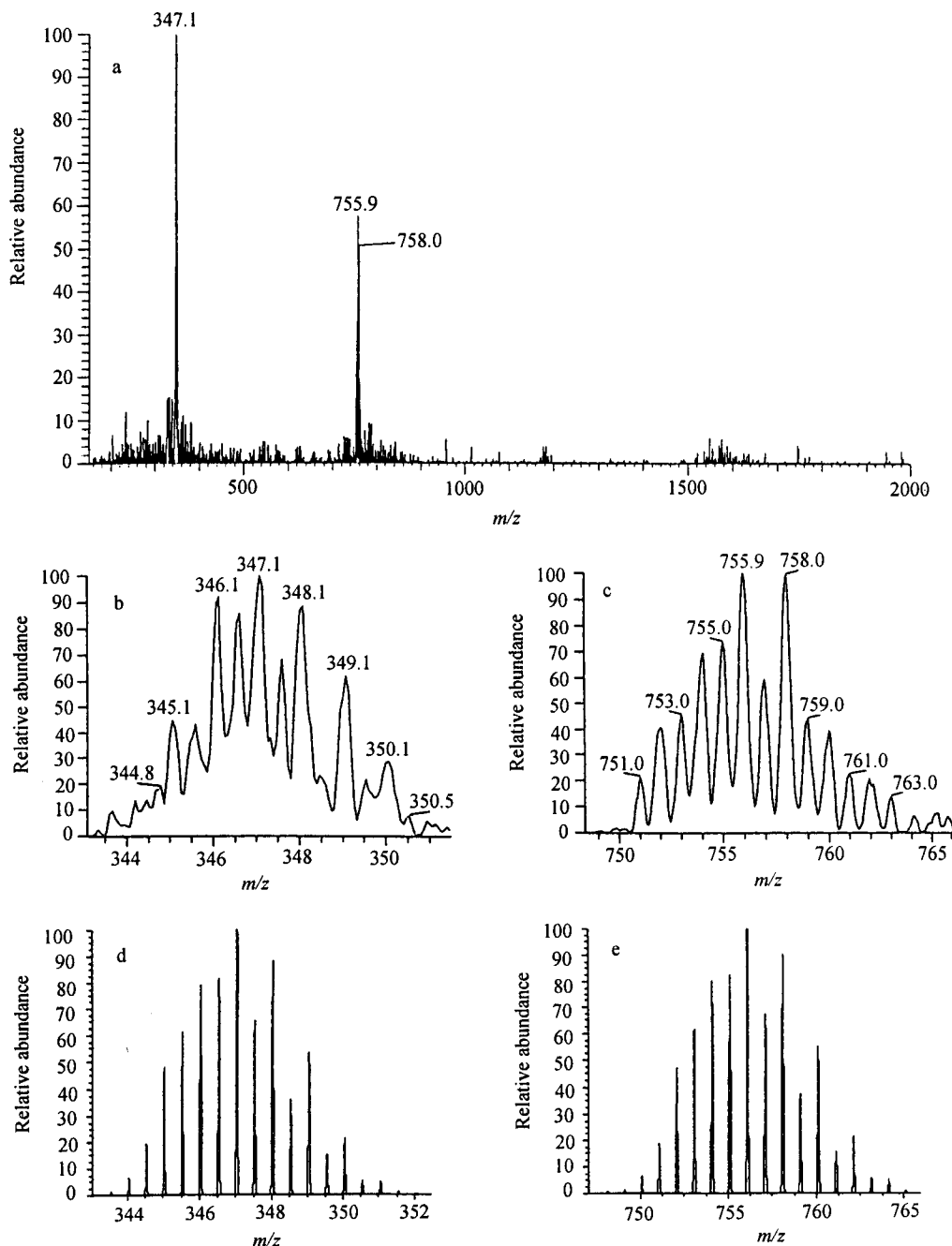
Fig. 5 ESIMS spectrum of $Pd_2LCl_2(NO_3)_2 \cdot H_2O$ (a), (b) and (c) show the isotopic distribution patterns of $[Pd_2LCl_2]^{2+}$ (m/z ~347) and $[(Pd_2LCl_2)NO_3]^+$ (m/z ~755) observed;   (d) and (e) are the predicted isotopic distribution patterns of $[Pd_2LCl_2]^{2+}$ (m/z ~347) and $[(Pd_2LCl_2)NO_3]^+$ (m/z ~755) given by IsoPro. 3.0 program.

indicates that the dissociation is closely related to the dissociation form in solution. There are no peaks for $[Pd_4L_2(C_2O_4)_2(NO_3)_3]^+$, suggesting that it is unstable and readily converts into **I** and **II**. Because the coor-

dination ability of carboxylic anion to Pd(II) is stronger than NO_3^-, the two species strongly suggests the formation of $Pd_4L_2(C_2O_4)_2(NO_3)_4$ in which $C_2O_4^{2-}$ may act as bridging ligands to connect the two {Pd_2L} moieties.
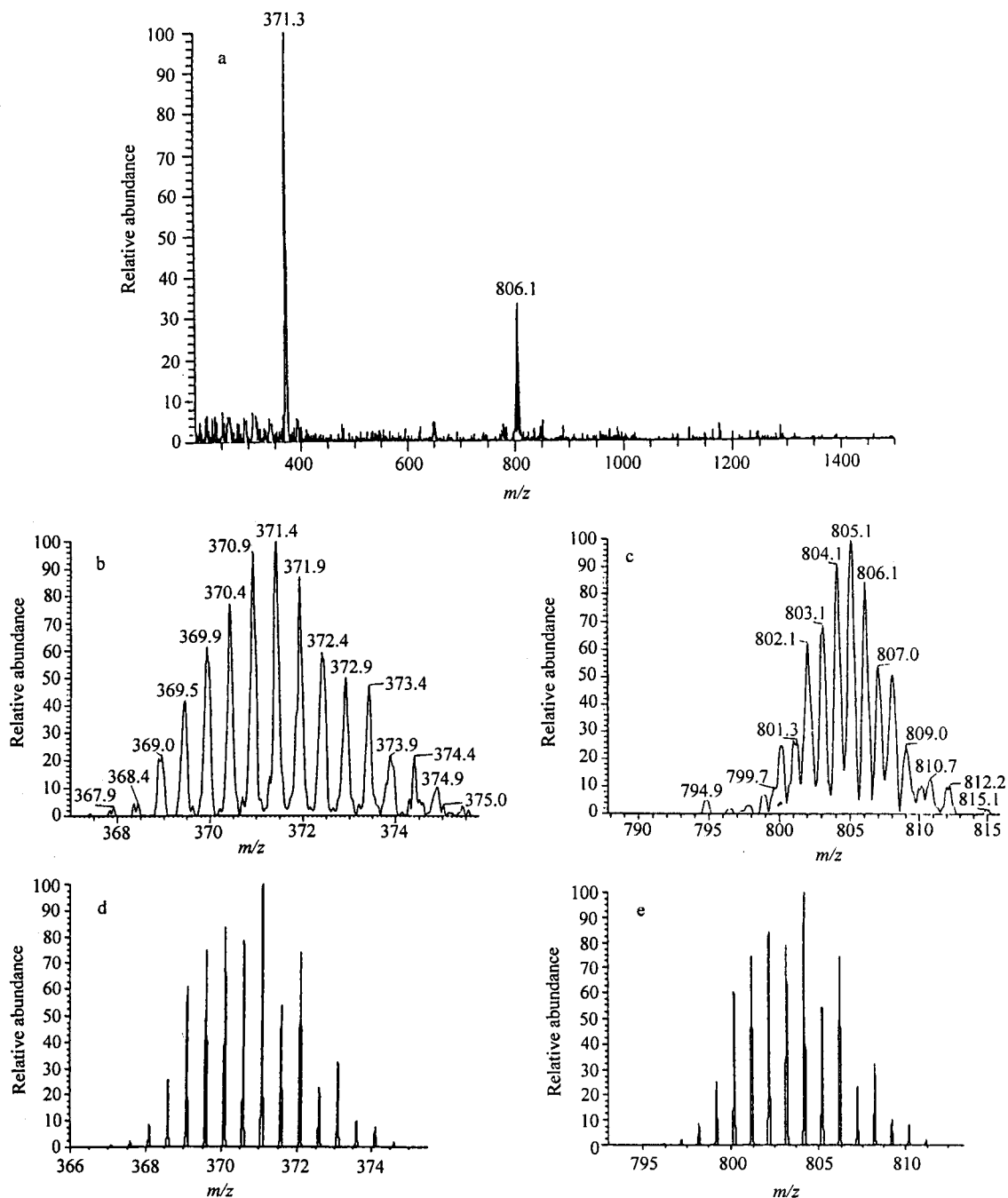
Fig. 6 ESIMS spectrum of $[Pd_2L(H_2O)_m(NO_3)_n]^{(4-n)+}$ (a), (b) and (c) show the isotopic distribution patterns of $[Pd_2L(CH_3CO_2)_2]^{2+}$ ($m/z \sim 371$) and $\{[Pd_2L(CH_3CO_2)_2](NO_3)\}^+$ ($m/z \sim 806$) observed; (d) and (e) are the predicted isotopic distribution patterns of $[Pd_2L(CH_3CO_2)_2]^{2+}$ ($m/z \sim 371$) and $\{[Pd_2L(CH_3CO_2)_2](NO_3)\}^+$ ($m/z \sim 806$) given by IsoPro. 3.0 program.
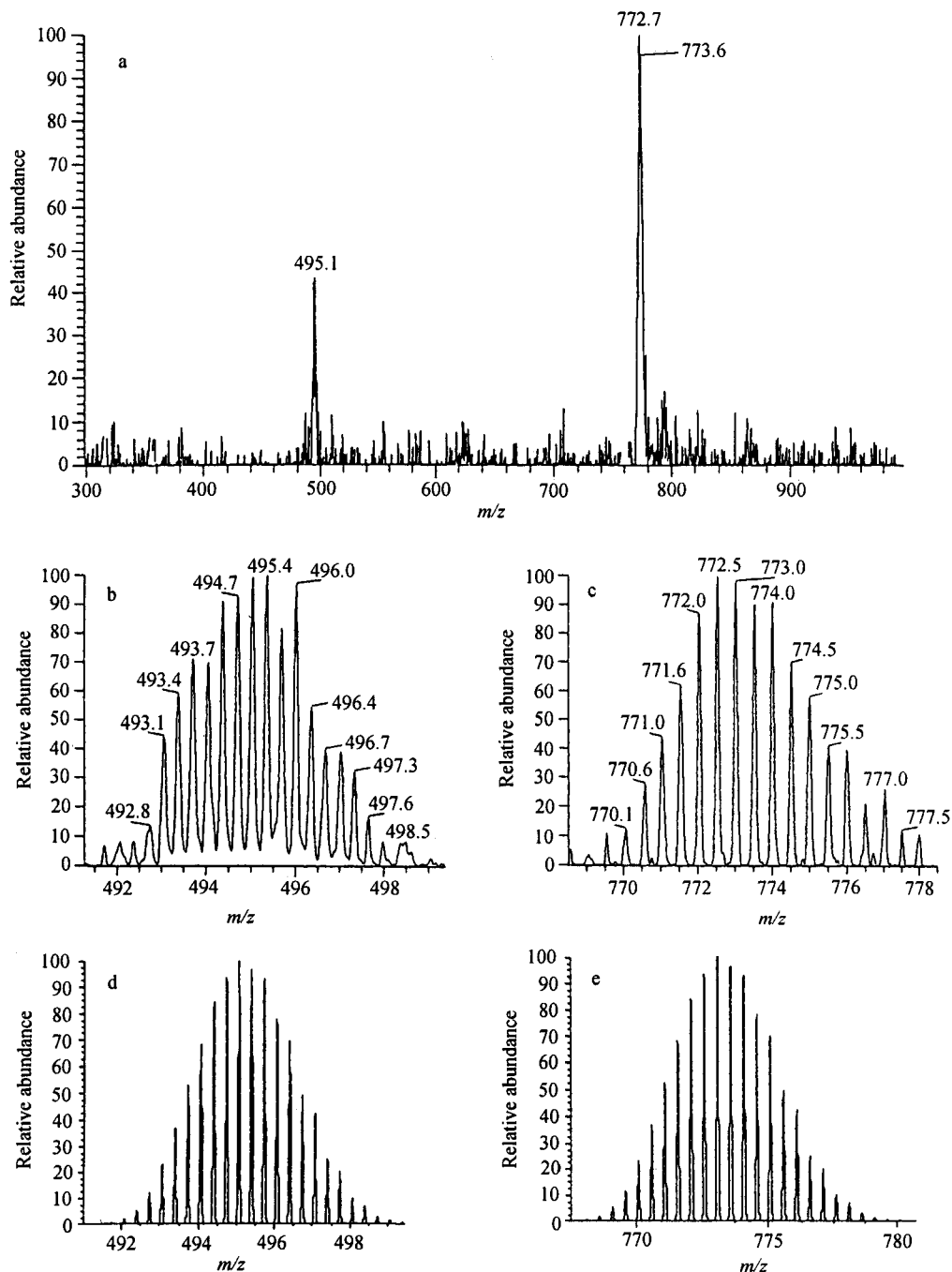
Fig. 7 ESIMS spectrum of $Pd_4L_2(C_2O_4)_2(NO_3)_4 \cdot 6H_2O$ (a), (b) and (c) show the isotopic distribution patterns of $[Pd_4L_2(C_2O_4)_2-(NO_3)]^{3+}$ (m/z ~495) and $[Pd_4L_2(C_2O_4)_2(NO_3)_2]^{2+}$ (m/z ~773) observed; (d) and (e) are the predicted isotopic distribution patterns of $[Pd_4L_2(C_2O_4)_2(NO_3)]^{3+}$ (m/z ~495) and $[Pd_4L_2(C_2O_4)_2(NO_3)_2]^{2+}$ (m/z ~773) given by IsoPro. 3.0 program.

Structure analysis confirmed that it is a square-planar molecular box in which two Pd_2L are bridged by two oxalate anions ([2 + 2] form, Fig. 8).[18]

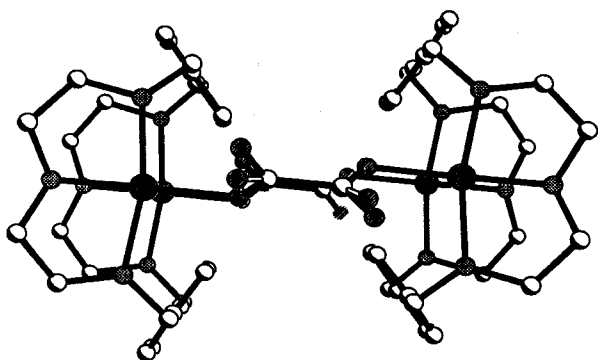**Conclusion**

ESIMS results reveal that the coordinated X^- (Cl^-

Fig. 8 A square-planar molecular box formed in the crystal of $Pd_4L_2(C_2O_4)_2(NO_3)_4 \cdot 6H_2O$.

and I^-) and $CH_3CO_2^-$ anion in complexes $M_2LX_2X_2'$ [M = Pd(II) and Ni(II), X = Cl$^-$, I$^-$ and $CH_3CO_2^-$, X' = X and NO_3^-] or $Pd_4L_2(C_2O_4)_2(NO_3)_4 \cdot 6H_2O$ are intact during the electrospray ionization process, while the counter anions are readily dissociated to form the complex cations in gas phase. Therefore, the complex cations, such as $[M_2LX_2]^{2+}$ (M = Pd(II) and Ni(II), X = Cl$^-$, I$^-$ and $CH_3CO_2^-$) and $[M_2LX_2X']^+$ [M = Pd(II) and Ni(II), X = Cl$^-$, I$^-$ and $CH_3CO_2^-$, X' = X and NO_3^-] are observed. To stabilize the cation in gas phase, the counter anions usually associate with $[M_2LX_2]^{2+}$ to decrease its positive charge, therefore the intensity of $[M_2LX_3]^+$ is often relatively higher than that of $[M_2LX_2]^{2+}$. However, if the complex cations themselves in soft-ionization process are more stable than cations with low positive charge number, the complex cations with higher positive charge number may also observed with higher abundance suggesting the dissociation during ionization process is similar to that in the solution. But in most case, the small charge number is beneficial for its stability in the process. This work demonstrates that the ESIMS is a powerful technique for compositional and structural analysis of these kinds of metal complexes. The results are in accordance with the X-ray crystal analysis data.

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