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Characterization of Encapsulating Supramolecules by Using CSI-MS with Ionization-Promoting Reagents

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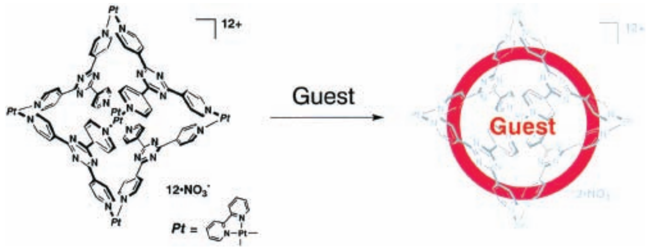
ABSTRACT



Guanidine nitrate, DMF, DMA, and DMSO are proven to be efficient ionization-promoting reagents in coldspray ionization mass spectrometry (CSI-MS) for the self-assembled cage Pt compound 1 in aqueous solution. These reagents made it possible to characterize the structures of encapsulated guest molecules in the cage. Detailed structure determinations of the cage compound encapsulating various kinds of guest molecules by using positive CSI-MS with ionization-promoting reagents are described.

The self-assembled cage Pt compound **1** (Scheme 1), constructed from ten molecular components including six Pt(2,2′-bpy)$(NO_3)_2$ **2** and four tris(4-pyridyl)-1,3,5-triazine **3**, has the ability to encapsulate various molecules (**4**−**8**) within the internal hydrophobic space in aqueous solution (Scheme 2).[1]

Characterization of these complexes including encapsulated guest molecules has generally been carried out with NMR spectroscopy. However, it is difficult to analyze the precise number and/or structures of the guest molecules by means of NMR if plural guest molecules are encapsulated within the cage **1**. Although it was expected[2] that electrospray ionization (ESI)[3] mass spectrometry (MS) would be applicable, only fragment ions [*m*/*z* 413.0 **2**−$(NO_3)^+$, 725.2 **2**·**3**−$(NO_3)^+$] were observed, because this cage compound **1** is unstable at the temperature (100 °C) of the desolvation plate (Figure 1a). Recently we reported a new ionization method, coldspray ionization (CSI),[4] a variant of electrospray

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[1] (a) Fujita, M.; Oguro, D.; Miyazawa, M.; Oka, H.; Yamaguchi, K.; Ogura, K. *Nature* **1995**, *378*, 469. (b) Kusukawa, T.; Fujita, M. *Angew. Chem., Int. Ed.* **1998**, *37*, 3142. (c) Ibukuro, F.; Kusukawa, T.; Fujita, M. *J. Am. Chem. Soc.* **1998**, *120*, 8561. (d) Kusukawa, T.; Fujita, M. *J. Am. Chem. Soc.* **1999**, *121*, 1397. (e) Yoshizawa, M.; Kusukawa, T.; Fujita, M.; Yamaguchi, K. *J. Am. Chem. Soc.* **2000**, *122*, 6311. (f) Ito, H.; Kusukawa, T.; Fujita, M. *Chem. Lett.* **2000**, 598.

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[3] (a) Yamashita, M.; Fenn, J. B. *J. Phys. Chem.* **1984**, *88*. 4451. (b) Fenn, J. B.; Mann, M.; Meng, K.; Wong, S. F.; Whitehouse, C. M. *Science* **1989**, *246*, 64. (c) Kebarle, P.; Tang, L. *Anal. Chem.* **1993**, *65*, 972A. (d) Bruins, A. P. *J. Chromatogr., A* **1998**, *794*, 345.

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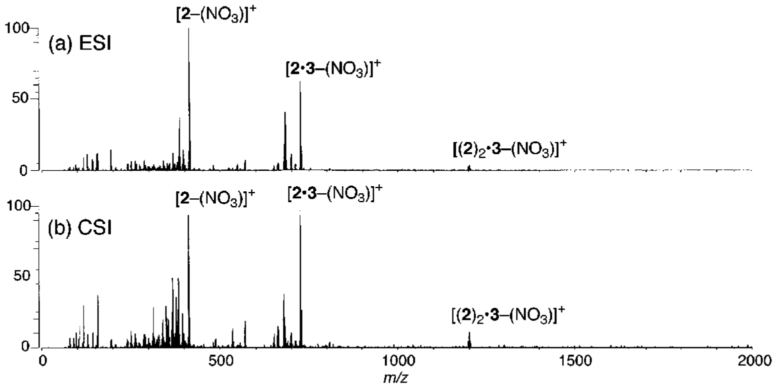
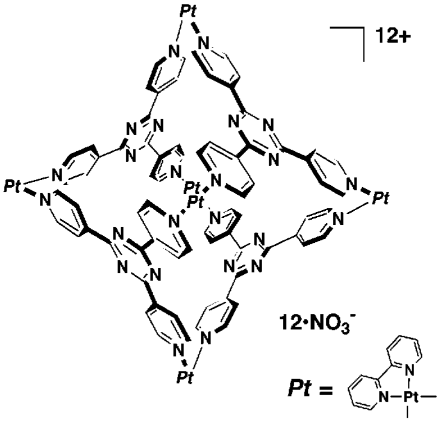


Figure 1. (a) ESI- and (b) CSI-MS spectra of **1**.

(ESI) MS operating at low temperature, which allows facile and precise characterization of labile self-assembling nanosized structures in acetonitrile solution. However, molecular ions [**1**$-x$(NO$_3$)]$^{x+}$ have never been observed even in CSI-MS in aqueous solution. It seems difficult to pull out (slip over)[3c] the molecular ions from sprayed droplets of aqueous solution at low temperature, owing to the high surface tension (Figure 1b).

Scheme 1



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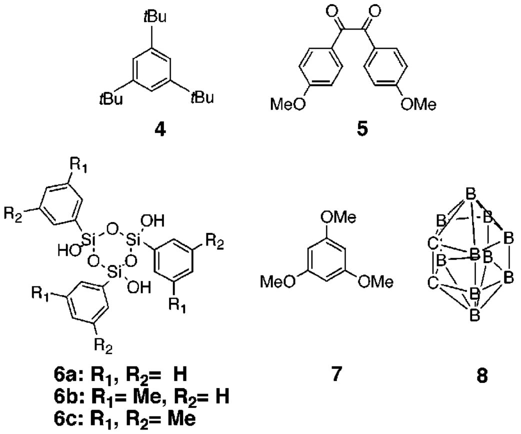
Scheme 2



We therefore examined several additives[5] expected to promote dissociation of the counteranions by decreasing the interaction of the cage compound **1** with solvating water molecules. Guanidine, recognized as a strong base, as well as some organic solvents having both carbonyl and hydrophobic groups, such as DMF, DMA, and DMSO, were found to be effective reagents, promoting ionization in an aqueous solution of **1**. These findings have made it possible to characterize the structures of guest molecules encapsulated in the cage of **1**. We report here detailed structure determination of the encapsulated guest molecules in self-assembled cage compound **1** by positive CSI-MS with the aid of ionization-promoting reagents.

CSI-MS spectra of a 1 mmol/L aqueous solution of **1** with (a) guanidine nitrate or (b) DMF as an additive were measured.[6] In case (a), multiply charged molecular ions of **1**, [**1**$-x$(NO$_3$)]$^{x+}$ (x = 3−9), were clearly observed (Figure

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(4) (a) Sakamoto, S.; Fujita, M.; Kim, K.; Yamaguchi, K. *Tetrahedron* **2000**, *56*, 955. (b) Ikeda, A.; Ayabe, M.; Shinkai, S.; Sakamoto, S.; Yamaguchi, K. *Org. Lett.* **2000**, *2*, 3707. (c) Yamanoi, Y.; Sakamoto, Y.; Kusukawa, T.; Fujita, M.; Sakamoto, S.; Yamaguchi, K. *J. Am. Chem. Soc.* **2001**, *123*, 980. (d) Zhong, Z.; Ikeda, A.; Ayabe, M.; Shinkai, S. Sakamoto, S.; Yamaguchi, K. *J. Org. Chem.* **2001**, *66*, 1002. (e) Fujita, N.; Biradha, K.; Fujita, M.; Sakamoto, S.; Yamaguchi, K. *Angew. Chem., Int. Ed.*, in press.

(5) Previously reported ionization-promoting reagents for ESI: (a) Henderson, W.; Nicholson, B. K. *J. Chem. Soc., Chem. Commun.* **1995**, 2531. (b) Henderson, W.; McIndoe, J. S.; Nicholson, B. K.; Dyson, P. J. *Chem. Commun.* **1996**, 1183. (c) Cheng, X.; Gao, Q.; Smith, R. D.; Simanek, E. E.; Mammen, M.; Whitesides, G. M. *J. Org. Chem.* **1996**, *61*, 2204. (d) Scherer, M.; Sessler, J.; Moini, M.; Gebauer, A.; Lynch, V. *Chem. Eur. J.* **1998**, *4*, 152.

(6) CSI-MS measurements were performed with a four-sector (BE/BE) tandem mass spectrometer (JMS-700T, JEOL) equipped with the CSI source. Typical measurement conditions are as follows: acceleration voltage, 5.0 kV; needle voltage, 2.0 kV; needle current, 300−700 nA; orifice voltage, 60−100 V; ion source temperature, 14−25 °C; spray temperature, −20 °C; resolution (10% valley definition), 1000 or 4000; sample flow rate, 8 μL/min; sample concentration, 1 mmol/L; (a) solvent, H_2O:acetonitrile = 99:1; guanidine nitrate concentration, 0.1 mmol/L; (b) solvent, H_2O: DMF=98:2.

(7) Complex **1**: [$(C_{132}H_{96}N_{36}Pt_6)^{12+}\cdot 12(NO_3^-)$], MW 4101.0; **1**$^{3+}$, ($m/z$) 1305.1 (9.6%); **1**$^{4+}$, 963.4 (45.2); **1**$^{5+}$, 758.3 (100); **1**$^{6+}$, 621.6 (98.4); **1**$^{7+}$, 524.0 (87.3); **1**$^{8+}$, 450.7 (76.6); **1**$^{9+}$, 393.7 (48.8).

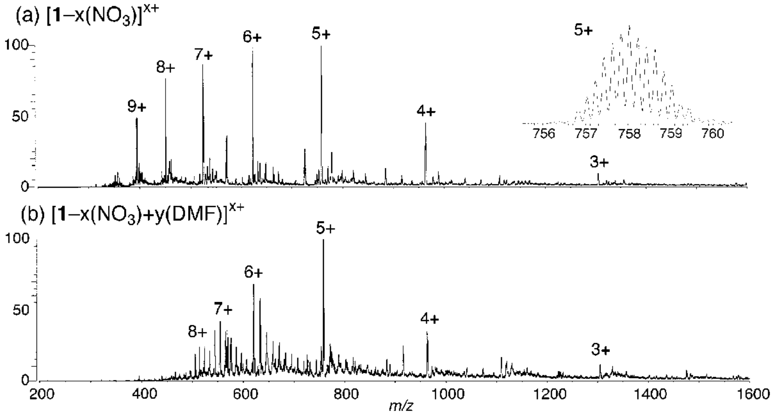
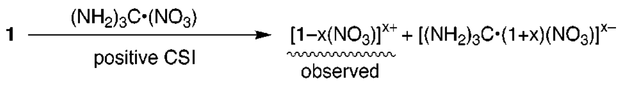


Figure 2. CSI-MS spectra of **1** with (a) guanidine nitrate and (b) DMF.

2a),[7] because the nitrate ions, the counteranions of **1**, were efficiently trapped by guanidine nitrate to form denitrated molecular cations (Scheme 3). In case (b), multiply charged molecular ions of **1** adducted with many DMF molecules, $[\mathbf{1}-x(NO_3) + y(DMF)]^{x+}$ ($x = 3-8$, $y = 0-8$), were also clearly observed (Figure 2b).[8] It is suggested that the carbonyl oxygen of DMF was coordinated to Pt ions instead of nitrate ions to form denitrated molecular cations which can easily slip over from droplets, because the cations are surrounded by the hydrophobic methyl groups of DMF. DMA and DMSO gave similar results. However, the spectrum of (b) seems to be rather complicated, compared with that of (a). We therefore selected guanidine nitrate as an ionization-promoting reagent to characterize a series of encapsulated supramolecules in this study.

Scheme 3



The multiply charged molecular ions of the complex **1** and a molecule of tri-*tert*-butylbenzene **4** (MW 246.4), $[\mathbf{1}(\mathbf{4})-x(NO_3)]^{x+}$ ($x = 4-8$) were observed in CSI-MS with guanidine nitrate, together with the multiply charged major molecular ions of the vacant cage **1**, $[\mathbf{1}-x(NO_3)]^{x+}$ ($x = 3-9$), suggesting partial encapsulation.[9]

Two molecules of diketone derivative **5** (MW 270.3) were proven to be encapsulated within the cage **1** by NMR study.[1d] In this compound, multiply charged molecular ions of $\mathbf{1}(\mathbf{5})_2$, $[\mathbf{1}(\mathbf{5})_2-x(NO_3)]^{x+}$ ($x = 3-9$) were clearly observed in the CSI-MS spectrum of $\mathbf{1}(\mathbf{5})_2$ without any ion peak due to the vacant cage **1**[10] (Figure 3).

Some of us[1e] have already reported that labile cyclic trimers of siloxanes **6a**−**c** (MW 414.6, 456.7, and 498.8, respectively) can be obtained by the condensation of trialkoxysilanes inside the cage **1**. This process is named "ship-in-a-bottle synthesis". In that paper,[1e] the structures of **6a**−**c** were determined by negative ESI-MS and ^{1}H NMR. However, negative ESI-MS did not afford precise structural information, because the intensities of the $[M + 2(NO_3)]^{2-}$ ion peaks were low and the spectrum contained many decomposed ion peaks, which could not be assigned.

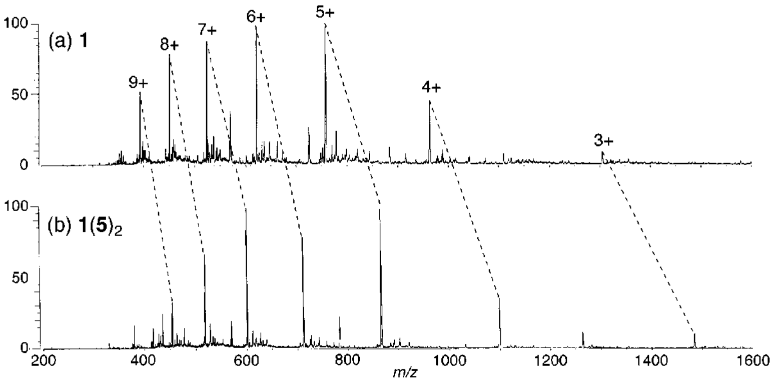


Figure 3. Comparison of CSI-MS spectra of (a) **1** and (b) $\mathbf{1}(\mathbf{5})_2$ with guanidine nitrate. Dotted lines indicate the mass shift based on encapsulation.

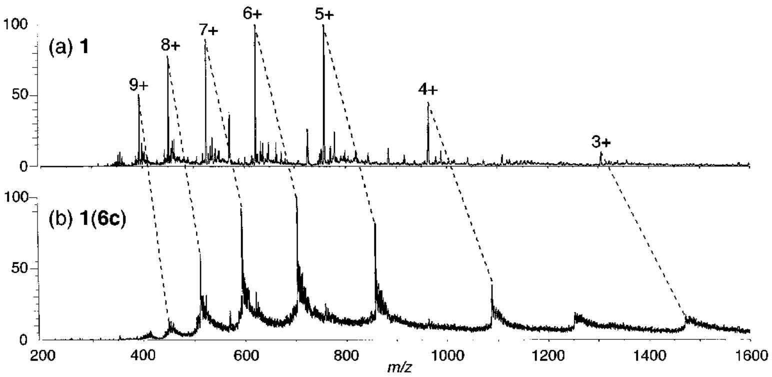


Figure 4. Comparison of CSI-MS spectra of (a) **1** and (b) **1**(**6c**) with guanidine nitrate. Dotted lines indicate the mass shift based on encapsulation.

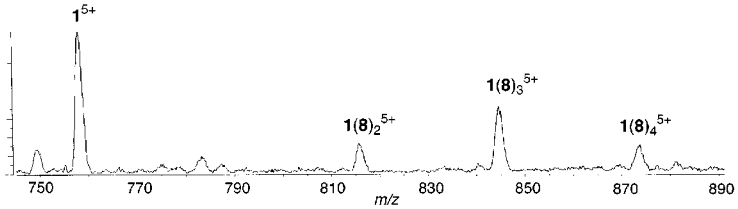


Figure 5. CSI-MS spectrum of **1**(**8**)$_4$ obtained in the presence of guanidine nitrate.

Therefore, we examined the application of CSI-MS with guanidine nitrate to these compounds. The multiply charged molecular ions of [**1**(**6a**−**c**)−x(NO$_3$)]$^{x+}$ (x = 3−9) were clearly observed[11,12] [Figure 4b]. Distinct mass shifts due to the encapsulated guest molecule, **6a**−**c**, were seen. Thus, the reported structures of the “ship-in-a-bottle synthesis” products were confirmed.

In the cases of 1,3,5-trimethoxybenzene **7** (MW 168.2) and *o*-carborane **8** (MW 144.2), the quaternary encapsulated structures in the cage **1** were suggested by ^{1}H NMR measurements.[1b] The ions of [**1**(**7**)$_n$−x(NO$_3$)]$^{x+}$ (x = 3−7, n = 1−4) and [**1**(**8**)$_n$−x(NO$_3$)]$^{x+}$ (x = 3−8, n = 1−4), for **1**(**7**)$_4$ and **1**(**8**)$_4$, respectively, were observed by using our method (Figure 5).[13,14] However, molecular ions of the vacant cage **1** were also seen in the spectra, as in the case of **1**(**4**).

In summary, we found that CSI-MS in conjunction with ionization-promoting reagents such as guanidine nitrate, DMF, DMA, and DMSO is a powerful tool to determine in detail the structures of encapsulated guest molecules inside a self-assembling cage compound. Direct observation of the molecular behavior of guest compounds as well as the precise structures of various labile inclusion compounds in a cavity should be possible by using this technique of CSI-MS with appropriate additives.

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(8) **1**$^{3+}$, (m/z) 1305.1 (11.9%); **1**$^{4+}$, 963.2 (35.7); **1**$^{5+}$, 758.2 (100); **1**$^{6+}$, 621.6 (68.2); **1**+DMF^{6+}, 633.6 (58.1); **1**+2DMF^{6+}, 645.9 (34.4); **1**+3DMF^{6+}, 657.9 (16.6); **1**+DMF^{7+}, 533.7 (21.3); **1**+2DMF^{7+}, 544.2 (35.6); **1**+3DMF^{7+}, 554.7 (42.0); **1**+4DMF^{7+}, 565.2 (34.7); **1**+5DMF^{7+}, 575.7 (30.4); **1**+6DMF^{7+}, 586.1 (24.3); **1**+7DMF^{7+}, 596.5 (19.7); **1**+6DMF^{8+}, 504.9 (19.0); **1**+7DMF^{8+}, 513.8 (23.8); **1**+8DMF^{8+}, 523.3 (23.9).

(9) Complex **1**(**4**): $[(C_{132}H_{96}N_{36}Pt_6)^{12+}\cdot(C_{18}H_{30})\cdot12(NO_3^-)]$, MW 4347.4; **1**$^{3+}$, ($m/z$) 1305.0 (13.3%); **1**(**4**)$_1^{4+}$, 1024.9 (10.3); **1**$^{4+}$, 963.1 (38.3); **1**(**4**)$_1^{5+}$, 807.3 (15.1); **1**$^{5+}$, 758.1 (88.5); **1**(**4**)$_1^{6+}$, 662.6 (17.8); **1**$^{6+}$, 621.4 (100); **1**(**4**)$_1^{7+}$, 559.1 (30.8); **1**$^{7+}$, 523.8 (90.7); **1**(**4**)$_1^{8+}$, 481.5 (31.8); **1**$^{8+}$, 450.6 (81.0); **1**(**4**)$_1^{9+}$, 421.1 (16.6); **1**$^{9+}$, 393.6 (45.6).

(10) Complex **1**(**5**)$_2$: $[(C_{132}H_{96}N_{36}Pt_6)^{12+}\cdot(C_{16}H_{14}O_4)_2\cdot12(NO_3^-)]$, MW 4641.6; **1**(**5**)$_2^{3+}$, (m/z) 1485.2 (10.4%); **1**(**5**)$_2^{4+}$, 1098.4 (34.8); **1**(**5**)$_2^{5+}$, 866.3 (100); **1**(**5**)$_2^{6+}$, 711.5 (78.3); **1**(**5**)$_2^{7+}$, 601.1 (98.5); **1**(**5**)$_2^{8+}$, 518.2 (66.5); **1**(**5**)$_2^{9+}$, 453.7 (32.4).

(11) (a) Complex **1**(**6a**): $[(C_{132}H_{96}N_{36}Pt_6)^{12+}\cdot(C_{18}H_{18}O_6Si_3)\cdot12(NO_3^-)]$, MW 4515.6; **1**(**6a**)$_1^{3+}$, (m/z) 1443.1 (17.2%); **1**(**6a**)$_1^{4+}$, 1066.8 (44.7); **1**(**6a**)$_1^{5+}$, 841.0 (100); **1**(**6a**)$_1^{6+}$, 690.6 (99.9); **1**(**6a**)$_1^{7+}$, 583.1 (47.1); **1**(**6a**)$_1^{8+}$, 502.4 (12.4); **1**(**6a**)$_1^{9+}$, 439.6 (8.6). (b) Complex **1**(**6b**): $[(C_{132}H_{96}N_{36}Pt_6)^{12+}\cdot(C_{21}H_{24}O_6Si_3)\cdot12(NO_3^-)]$, MW 4557.7; **1**(**6b**)$_1^{3+}$, (m/z) 1457.4 (25.0%); **1**(**6b**)$_1^{4+}$, 1077.6 (57.5); **1**(**6b**)$_1^{5+}$, 849.7 (90.2); **1**(**6b**)$_1^{6+}$, 697.8 (100); **1**(**6b**)$_1^{7+}$, 589.3 (97.3); **1**(**6b**)$_1^{8+}$, 507.8 (79.9); **1**(**6b**)$_1^{9+}$, 444.5 (50.4); **1**(**6b**)$_1^{10+}$, 393.7 (15.3). (c) Complex **1**(**6c**): $[(C_{132}H_{96}N_{36}Pt_6)^{12+}\cdot(C_{24}H_{30}O_6Si_3)\cdot12(NO_3^-)]$, MW 4599.8; **1**(**6c**)$_1^{4+}$, (m/z) 1088.1 (38.6%); **1**(**6c**)$_1^{5+}$, 858.2 (81.7); **1**(**6c**)$_1^{6+}$, 704.8 (100); **1**(**6c**)$_1^{7+}$, 595.2 (97.1); **1**(**6c**)$_1^{8+}$, 513.0 (60.3); **1**(**6c**)$_1^{9+}$, 449.1 (15.6).

(12) In Figure 4b, addition of several water molecules, [**1**(**6c**)+x(H$_2$O)−(NO$_3$)$_n$]$^{n+}$ was also observed, suggesting solvation of the Pt^{2+} ions by H$_2$O.

(13) Complex **1**(**7**)$_4$: $[(C_{132}H_{96}N_{36}Pt_6)^{12+}\cdot(C_9H_{12}O_3)_4\cdot12(NO_3^-)]$, MW 4773.8; **1**$^{3+}$; ($m/z$) 1304.7 (6.1%); **1**(**7**)$_3^{4+}$, 1089.5 (10.2); **1**(**7**)$_2^{4+}$, 1047.2 (12.1); **1**(**7**)$_1^{4+}$, 1005.2 (9.0); **1**$^{4+}$, 963.2 (36.7); **1**(**7**)$_4^{5+}$, 892.4 (20.4); **1**(**7**)$_3^{5+}$, 858.8 (42.9); **1**(**7**)$_2^{5+}$, 825.4 (20.0); **1**(**7**)$_1^{5+}$, 791.8 (12.3); **1**$^{5+}$, 758.0 (100); **1**(**7**)$_4^{6+}$, 733.6 (42.3); **1**(**7**)$_3^{6+}$, 705.3 (58.0); **1**(**7**)$_2^{6+}$, 677.4 (43.5); **1**(**7**)$_1^{6+}$, 649.5 (22.4); **1**$^{6+}$, 621.2 (59.2); **1**(**7**)$_3^{7+}$, 595.8 (58.1); **1**(**7**)$_2^{7+}$, 571.6 (61.2); **1**(**7**)$_1^{7+}$, 547.8 (31.8); **1**$^{7+}$, 523.6 (67.6).

(14) Complex **1**(**8**)$_4$: $[(C_{132}H_{96}N_{36}Pt_6)^{12+}\cdot(C_2H_{12}B_{10})_4\cdot12(NO_3^-)]$, MW 4677.9; **1**(**8**)$_1^{3+}$, (m/z) 1353.0 (25.1%); **1**$^{3+}$, 1304.5 (11.5); **1**(**8**)$_3^{4+}$, 1071.1 (17.7); **1**(**8**)$_2^{4+}$, 1035.5 (19.6); **1**(**8**)$_1^{4+}$, 999.3 (11.2); **1**$^{4+}$, 963.2 (50.8); **1**(**8**)$_4^{5+}$, 873.8 (15.9); **1**(**8**)$_3^{5+}$, 844.6 (36.4); **1**(**8**)$_2^{5+}$, 815.7 (16.8); **1**$^{5+}$, 758.0 (76.9); **1**(**8**)$_4^{6+}$, 718.2 (7.1); **1**(**8**)$_3^{6+}$, 693.7 (13.6); **1**(**8**)$_2^{6+}$, 669.8 (19.7); **1**(**8**)$_1^{6+}$, 645.6 (26.0); **1**$^{6+}$, 621.5 (83.1); **1**(**8**)$_4^{7+}$, 606.8 (15.7); **1**(**8**)$_3^{7+}$, 586.0 (18.5); **1**(**8**)$_2^{7+}$, 565.1 (28.5); **1**(**8**)$_1^{7+}$, 544.3 (37.8); **1**$^{7+}$, 523.8 (100); **1**(**8**)$_3^{8+}$, 505.1 (19.5); **1**(**8**)$_2^{8+}$, 487.0 (39.9); **1**(**8**)$_1^{8+}$, 468.7 (41.4); **1**$^{8+}$, 450.3 (32.1).