An Efficient Ionization Method of Electrospray Mass Spectrometry: The Development of an Aromatic-Cored Matrix That Wraps Labile Metal Complexes through Molecular Recognition

Kazuhisa Kumazawa,[a] Michito Yoshizawa,[a] Hong-Bo Liu,[b] Yuko Kamikawa,[b] Masaya Moriyama,[b] Takashi Kato,*[b] and Makoto Fujita*[a]

Abstract: Compound **1a**, which possesses a triphenylene core and six tetraethyleneoxide side chains, shows efficient ionization of M^{II}-containing (M = Pd, Pt) complexes in electrospray ionization mass spectrometry (ESI-MS). The molecular ion peaks $[M]^+$, which are hardly detected under common ESI-MS conditions, are clearly observed as their $[M\cdot(\mathbf{1a})_n]^+$ ($n = 1$–4) adducts. UV-visible and NMR studie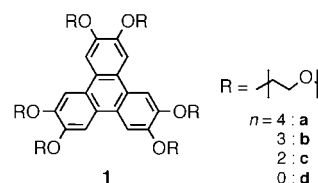s reveal that the electron-rich triphenylene core of **1a** binds to the electron-deficient frameworks of the M^{II} complexes in solution, giving rise to charge transfer (CT) complexes. We suggest that **1a** stabilizes the complexes and promotes efficient ionization through unique donor–acceptor molecular recognition.

Keywords: charge transfer · mass spectrometry · molecular recognition · palladium · pi interactions · platinum

Introduction

Electrospray ionization mass spectrometry (ESI-MS)[1] has been recently used as a useful method for determining the molecular weight of noncovalent assemblies under mild conditions.[2,3] Addition of a metal or organic salts as matrix often suppresses undesirable fragmentation and increases the stability of intended molecular ions.[4–8] They facilitate the ionization of neutral molecules or dissociation of tight ion-pairs through weak interactions with the target species. Enhancing the matrix–substrate interaction is, therefore, expected to develop a new matrix assisted ionization technique particularly suitable for labile compounds that cannot be detected by conventional ESI or other ionization methods such as fast atom bombardment (FAB) and matrix assisted laser desorption ionization (MALDI).[9]
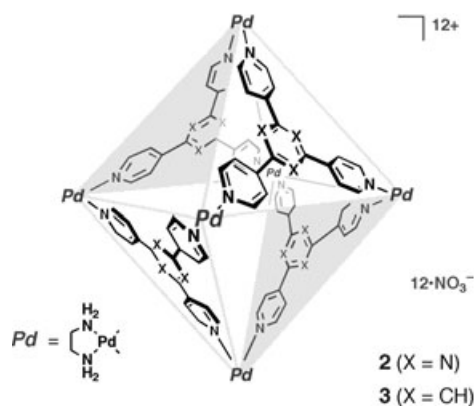
Consequently, a matrix with an aromatic core (**1**) was designed from the viewpoint of *molecular recognition* for the ESI-MS analysis of labile metal complexes. Compound **1** consists of a planar aromatic core (triphenylene) and six hydrophilic chains (oligoethyleneoxide). The core is anticipated to stack on electron-deficient aromatic systems through π–π interactions, enhancing the matrix effect of the hydrophilic chains. Therefore, ionized molecular species wrapped by **1** should be considerably stabilized and observed by ESI-MS anaylsis without significant fragmentation.

The first target compound is a cage-like Pd^{II} complex (**2**),[10] which is hardly observed by ESI-MS or coldspray ionization (CSI) mass spectrometry[3,8] under standard conditions. Complex **2** is a unique compound: it accommodates a variety of neutral organic molecules and promotes subsequent chemical transformations within its large isolated

[a] K. Kumazawa, Dr. M. Yoshizawa, Prof. M. Fujita
Department of Applied Chemistry
School of Engineering, The University of Tokyo
Hongo, Bunkyo-ku, Tokyo 113–8656 (Japan)
Fax: (+81)3-5841-7257
E-mail: mfujita@appchem.t.u-tokyo.ac.jp

[b] Dr. H.-B. Liu, Y. Kamikawa, Dr. M. Moriyama, Prof. T. Kato
Department of Chemistry and Biotechnology
School of Engineering, The University of Tokyo
Hongo, Bunkyo-ku, Tokyo 113–8656 (Japan)
Fax: (+81)3-5841-8661
E-mail: kato@chiral.t.u-tokyo.ac.jp

pocket.[11,12] It quantitatively assembles in an aqueous medium from six end-capped Pd^{II} complexes and four *exo*-tridentate panel-like ligands.[10] It is worth noting that for the Pt^{II} analogue of **2**, ionization-promoting matrices such as DMF, DMSO, or guanidine are quite effective for the observation of the molecular-ion peaks.[8] However, the noncovalent structure of **2** is not tolerant under the same MS conditions and only fragmentation peaks are observed.

We find that the addition of **1** to an aqueous solution of **2** leads to a clear observation of their inherent ions by ESI-MS.[13] Accordingly, the "molecular-recognition matrix" in ESI-MS measurements of **2** coupled with UV-visible and NMR analyses will be discussed. Finally, the importance of the formation of a charge-transfer (CT) complex through external π-stacking interactions between **1** and **2** will be emphasized.

Results and Discussion

The design of matrix 1: One of the remarkable features of coordination cage **2** is to recognize a variety of neutral organic molecules in an aqueous medium, giving rise to enclathrate compounds.[10,11] When the guests are large π-conjugated molecules (e.g., triphenylene, pyrene, and perylene), cage **2** can efficiently accommodate them in the cavity by means of π–π interactions. Since the framework of **2** is very electron deficient due to Pd^{II} coordination to the three pyridyl sites of the panel ligand, electron-rich guest molecules are strongly enclathrated within **2**, resulting in the formation of charge-transfer (CT) com-

plexes.[10,14] Such internal molecular-recognition systems as found for **2** prompted us to design a matrix **1** with an aromatic-core that is capable of *external* interaction with cage **2**. In **1**, hydrophobic triphenylene, as a planar aromatic core, is connected to six hydrophilic oligoethyleneoxide chains. For this amphiphilic matrix, it is highly expected that the core will interact with cage **2** through hydrophobic and charge-transfer interactions, whereas the side chains will stabilize cationic species and assist the molecular-ion formation under mild conditions. Presumably, cage **2** will be wrapped by a few or several molecules of **1** through external association. The side chains are also expected to help solubilization of the matrix in aqueous media.

ESI-MS measurements of complex 2 in the presence of 1: Prominent peaks derived from cagelike complex **2** were observed in ESI-MS when a mixed aqueous solution (H$_2$O/MeCN/DMF = 2:1:0.15 ratio, 1 mM) of **2** with one equivalent of **1a** was infused into the MS source at room temperature. Figure 1a shows a series of peaks corresponding to [2·-(1a)$_m$ − n NO$_3$]$^{n+}$ (m = 1–4, n = 3–8). For example, peaks at m/z 1203, 1413, and 1709 are consistent with the formulae of the 1:4 adduct ([2·(1a)$_4$ − n NO$_3$]$^{n+}$, n = 5–7), which may indicate that all of the four planar ligands of the complex are fully covered with matrices. In addition, the 1:2 and 1:3 adducts are also clearly observed at m/z 923 [2·(1a)$_2$ − 6 NO$_3$]$^{6+}$ and 992 [2·(1a)$_3$ − 7 NO$_3$]$^{7+}$. It is worth noting that almost no peaks are derived from the fragmentation of **2**. Efficient wrapping of **2** by **1a** seems to preclude solvation of **2** by
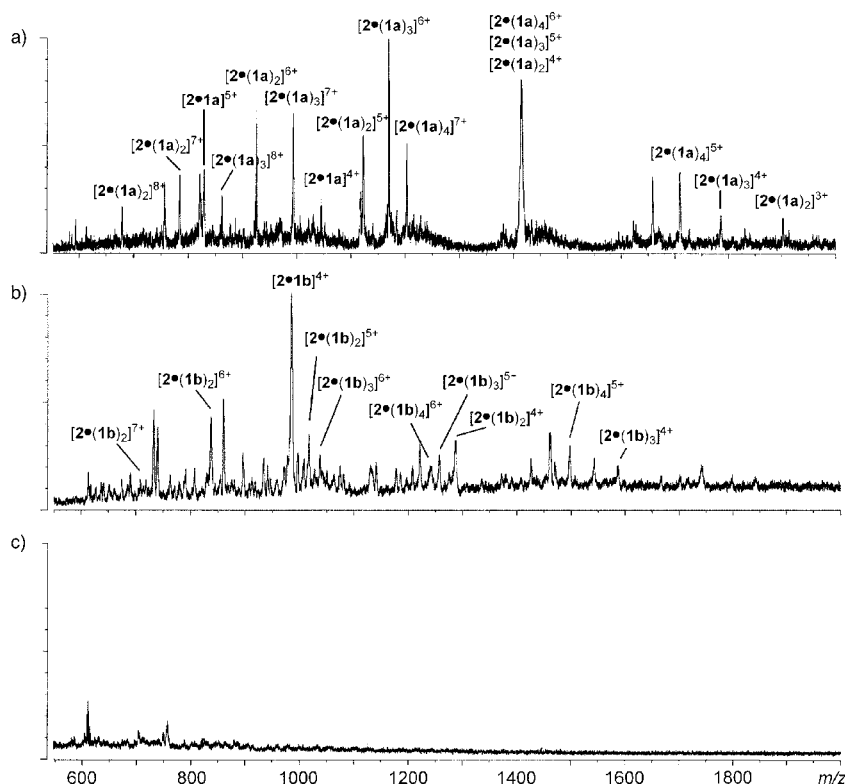

Figure 1. ESI-MS spectra of metal complex **2** with: a) matrix **1a**, b) **1b**, and c) **1c**.

DMF, as no DMF adducts are observed. However, DMF-solvated peaks are observed for the Pt^{II} analogue of **2** in the absence of the matrix. A control measurement of **2** without **1a** afforded only unassignable fragment peaks. Therefore, it is clearly demonstrated that **1a** with its aromatic core acts as a very useful matrix for the ionization of labile metal complex **2** in ESI-MS analysis.

To reveal the effect of the length of the hydrophilic chains of **1a**, we performed ESI-MS measurements of **2** with matrices **1b** and **1c**, which have six tri- and dioxyethylene chains around the periphery of the triphenylene core. In the presence of **1b**, the spectrum became less clear, though the matrix adducts of $[2 \cdot (1b)_n - m\,NO_3]^{m+}$ were still observed at, for example, m/z 837 $[2(1b)_2 - 6\,NO_3]^{6+}$, 985 $[2 \cdot 1b - 4\,NO_3]^{4+}$, and 1497 $[2 \cdot (1b)_4 - 5\,NO_3]^{5+}$ (Figure 1b). Fragmentation peaks of **2** are concomitantly observed between 600 and 1200 Da. With **1c**, peaks derived from **2** are hardly observed (Figure 1c). These results clearly reveal that the hydrophilic chains are essential for the ionization of **2**. Since tetraoxyethylene, $H(OCH_2CH_2)_4OH$, does not show any matrix effect, the aromatic core is also essential to the efficient ionization.

CT complex formation of 2 with 1a: We suggest that the matrix–analyte recognition by π–π interaction is indispensable to obtain the desirable peaks of **2** in ESI-MS analysis. In fact, when one equivalent of **1a** was added to an aqueous solution of **2**, the colorless solution quickly turned red, indicating the formation of a CT complex.[13] The UV-visible spectrum of the red solution exhibited a new absorption band around 460 nm ($\varepsilon = 800\ \mathrm{mol^{-1}dm^{-1}}$), which is derived from charge transfer between the core of **1a** and the triazine-core ligand of **2** by external π–π interactions (Figure 2a,b). The triazine core is essential for an efficient CT, since analogue **3** with a benzene core showed a weak CT band in UV-visible measurement (Figure 2c). Accordingly, ion peaks for **3** were also observed with excess **1a**, though the spectrum is considerably contaminated by their fragmentation peaks.

ESI-MS measurements of cage 2 with guest molecules: While **1a** stacks externally on cagelike complex **2**, the cavity of **2** is still capable of guest enclathration. Interestingly, the matrix preserves the accommodated guest in **2**. Charged ions of guest-enclathrated complexes were also observed in the presence of **1a**. In the presence of diketone **4**, the formation of a 2:1 inclusion complex $(4)_2 \subset 2$ was previously reported,[11] which also did not survive under standard MS conditions. However, throughout addition of **1a**, multiply
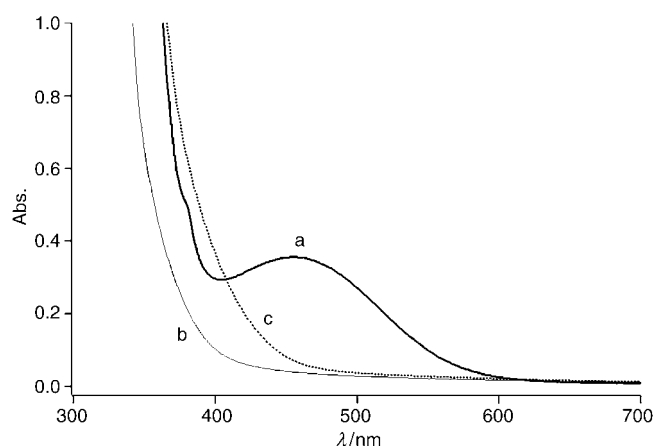

Figure 2. UV-visible spectra in H$_2$O at RT: a) complex **2** with one equivalent of **1a**, b) complex **2**, and c) complex **3** with one equivalent of **1a**.

charged molecular ions $[(4)_2 \subset 2 \cdot (1a)_m - n\,NO_3]^{n+}$ were clearly observed in ESI-MS (e.g., m/z 1015 ($m=2$, $n=6$), 1231 ($m=2$, $n=5$), and 1259 ($m=3$, $n=6$); Figure 3). There was almost no peak derived from the guest-free cage. Other guest molecules such as *o*-carborane and trimethoxybenzene within complex **2** were also detected under these conditions.
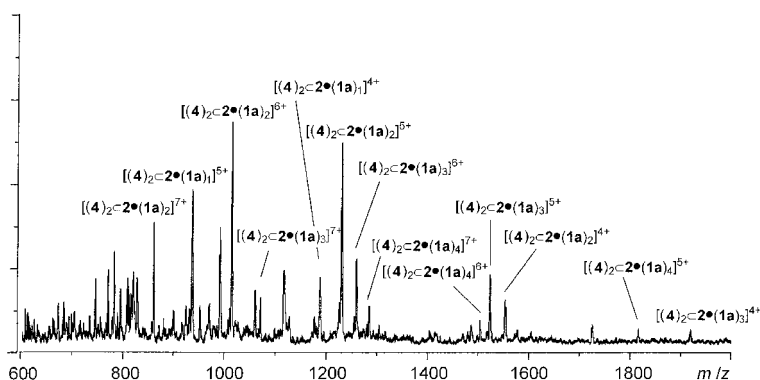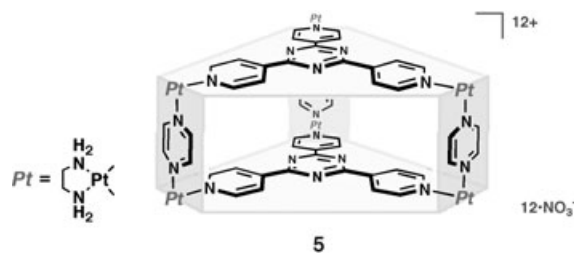

Figure 3. ESI-MS spectrum of complex $(4)_2 \subset 2$ in the presence of matrix **1a**.

ESI-MS measurements of complex 5 in the presence of 1a: The second target for the ESI-MS measurement is prismlike metal complex **5**, which assembles from eleven components: six end-capped Pt^{II} complexes, two *exo*-tridentate ligands, and three pyrazine pillars.[14] The complex contains planar

panels of a triazine core within its framework. Therefore, we expect that **1a** will assist the ionization of complex **5** in a similar manner as for complex **2**. Thus, a solution of **5** in H_2O/MeCN/DMF (2:1:0.15 ratio) with one equivalent of **1a** was analyzed by ESI-MS at room temperature. A series of simple ion peaks of **5** were observed as shown in Figure 4a. For example, prominent peaks at *m/z* 805, 950, 1152, 1456, and 1962 agreed with $[5 \cdot (1a)_2 - n NO_3]^{n+}$ ($n = 3$–7) diadducts. Mono- and triadducts of the matrix with 5^{12+} were also detected at 1000–1900 Da. However, matrix-free species were not observed.

Triphenylene derivative **1d** can be accommodated in the cavity of **5**.[14] We found that in the presence of **1a**, guest-enclathrated complex **1d⊂5** was still stable under the ESI-MS conditions leading to clear MS observation (Figure 4b). Multiply charged ion peaks of **1d⊂5** with **1a** were obtained without fragmentation (e.g., *m/z* 1018 $[1d \subset 5 \cdot (1a)_2 - 6 NO_3]^{6+}$ and 1234 $[1d \subset 5 \cdot (1a)_2 - 5 NO_3]^{5+}$). In contrast, ESI-MS of **1d⊂5** in the absence of **1a** exhibited a very complicated spectrum, which was assigned as a series of DMF adducts $[1d \subset 5 \cdot (DMF)_m - n NO_3]^{n+}$ ($m = 4$–17, $n = 3$–8) (Figure 4c). These findings clearly suggested that the wrapping effect of the matrix promotes the efficient dissociation of counterions (NO_3^-) and solvents (DMF) without fragmentation of the framework.

UV-visible and NMR studies on CT complex of 5 with 1: The colorless solution of **5** turned red when **1a** was added to an aqueous solution of complex **5**. The UV-visible spectrum of the red solution revealed a new absorption band around 455 nm ($\varepsilon = 900 \ mol^{-1} dm^{-1}$) that can be attributed to the formation of a CT complex (Figure 5a). The same color was also observed upon mixing the enclathrated complex **1d⊂5** with **1a**. Therefore, **1a** clearly recognizes both **5** and **1d⊂5**
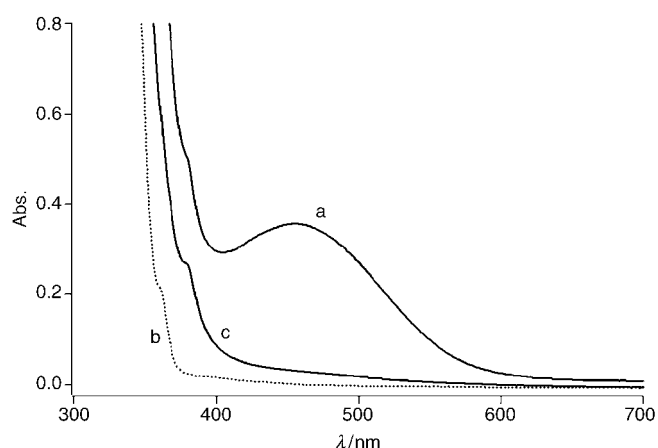

Figure 5. UV-visible spectra in H_2O at RT: a) complex **5** with one equivalent of **1a**, b) matrix **1a**, and c) complex **5**.

in solution, which is in good agreement with the clear observation of adduct species by ESI-MS.

An NMR study provided further evidence for the recognition of complex **5** by **1a**. When one equivalent of **1a** was combined with a solution of **1d⊂5** in D_2O, the ^{1}H NMR spectrum showed broad peaks for the framework of **5** in the aromatic region. In addition, the signals of **1d** and **1a** at 7.02 and 6.47 ppm were significantly shifted upfield due to internal and external π–π interactions with **5**, respectively (Figure 6a). In the aliphatic region of **1a**, the peaks of the oligoethyleneoxides chains were found without remarkable shift. These signals, which were sharp at high temperature, but split and broadened at lower temperature (Figure 6b,c). It was worth noting that the chemical shift of **1a** in the presence of **5** was apparently temperature dependent (6.47 ppm at 300 K, 7.21 ppm at 333 K). This is due to the reversible external interaction between **5** and **1a**.

Conclusion

In conclusion, we have developed a unique compound **1a** that can recognize target metal complexes by means of charge-transfer (CT) interactions. With this matrix, labile multinuclear metal complexes (**2**, **5**) were efficiently analyzed by ESI-MS, thanks to external π-stacking interactions between the aromatic core of **1a** and the aromatic framework of the complexes. A series of multiply charged molecular ions of these complexes with **1a** were clearly observed at room temperature. UV-visible
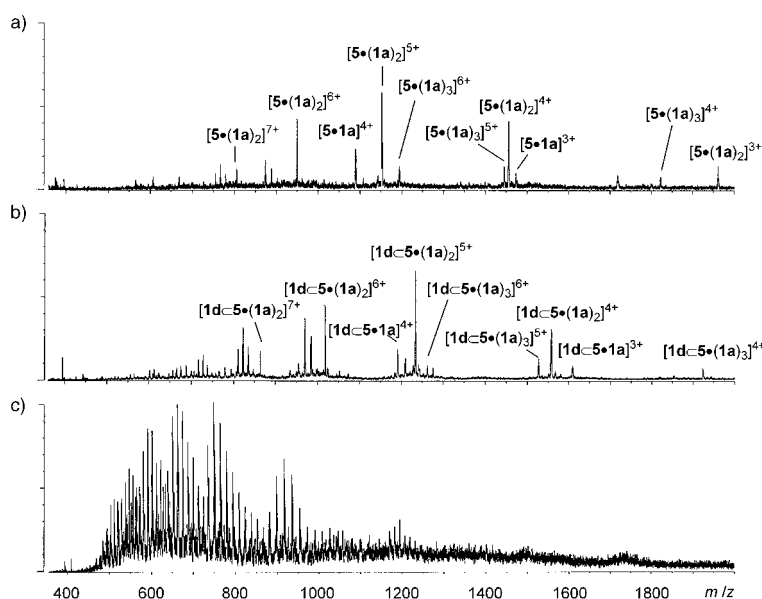

Figure 4. ESI-MS spectra: a) metal complex **5** with matrix **1a**, b) guest-enclathrated complex **1d⊂5** with matrix **1a**, and c) **1d⊂5** without matrix **1a**.
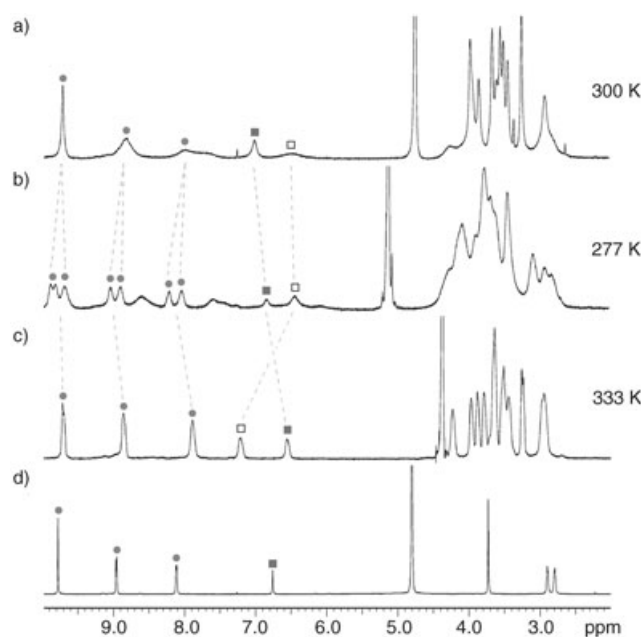
www.chemeurj.org *Chem. Eur. J.* **2005**, *11*, 2519 – 2524

Figure 6. ^{1}NMR spectra (500 MHz, D$_2$O) of complex **1d**⊂**5** with one equivalent of **1a** at: a) 300 K, b) 277 K, and c) 333 K; d) complex **1d**⊂**5** without **1a** at 300 K. Dark circles, dark squares, and squares indicate signals associated with **5**, **1d**, and **1a**, respectively.

and NMR studies revealed the CT complex formation between the complexes and **1a**, which stabilized their intrinsic structures and promoted their ionization process in ESI-MS. We believe that the present results with the use of a "molecular-recognition matrix" will open up new strategy for mass spectrometry as well as for molecular-recognition chemistry.

Experimental Section

General: All experiments were carried out on a four-sector (BE/BE) tandem mass spectrometer (JMS-700C, JEOL) equipped with a CSI source.[3,8] Typical measurement conditions are as follows: acceleration voltage 5.0 kV, needle voltage 2.0–2.5 kV, orifice voltage 10 to 100 V, ion source temperature 30–35°C, spray temperature 25°C, resolution 1000–7000 (10% valley definition), sample flow rate 0.02 mL min^{-1}.

Synthesis of 1c: Potassium carbonate (3.60 g, 26.4 mmol) was suspended in a solution of 2-(2-methoxyethoxy)ethyl *p*-tolyl sulfate (3.80 g, 13.2 mmol) in anhydrous DMF (25 mL) under Ar atmosphere. 2,3,6,7,10,11-Hexahydroxytriphenylene trihydrate (0.50 g, 1.32 mmol) was added to the mixture and the suspension was stirred for two days at room temperature. Water (50 mL) was added to the mixture and the product was extracted with CH$_2$Cl$_2$ (400 mL). The organic layer was washed with brine (200 mL) and dried over MgSO$_4$. The solution was evaporated and the residue was poured into hexane (500 mL). The resulting dark oil was separated and purified by column chromatography (CHCl$_3$/methanol=20:1) and GPC (CHCl$_3$). A pale brown oil **1c** (88 mg) was obtained in 7% yield. ^{1}H NMR (500 MHz, CDCl$_3$, TMS): δ = 7.87 (s, 6H), 4.41 (d, 12H), 3.98 (d, *J*=5 Hz, 12H), 3.79 (d, 12H), 3.61 (d, *J*=5 Hz, 12H), 3.40 ppm (s, 18H).

NMR data for 1b: ^{1}H NMR (500 MHz, D$_2$O, TMS): δ = 7.03 (s, 6H), 4.14 (br, 12H), 3.79 (br, 12H), 3.61 (d, *J*=5 Hz, 12H), 3.51 (d, *J*=5 Hz, 12H), 3.42 (d, *J*=5 Hz, 12H), 3.30 (d, *J*=5 Hz, 12H), 3.08 ppm (s, 18H).

NMR data for 1a: ^{1}H NMR (500 MHz, D$_2$O, TMS): δ = 7.41 (s, 6H), 4.35 (br, 12H), 4.03 (br, 12H), 3.82 (d, *J*=5 Hz, 12H), 3.71 (d, *J*=5 Hz, 12H), 3.61 (d, *J*=5 Hz, 12H), 3.51 (d, *J*=5 Hz, 12H), 3.46 (d, *J*=5 Hz, 12H), 3.40 (d, *J*=5 Hz, 12H), 3.22 ppm (s, 18H); ^{13}C NMR (125 MHz, D$_2$O, TMS) δ 147.2 (C_q), 122.9 (C_q), 106.0 (CH), 71.0 (CH$_2$), 70.1 (CH$_2$), 69.9 (CH$_2$), 69.7 (CH$_2$), 69.6 (CH$_2$), 69.5 (CH$_2$), 69.4 (CH$_2$), 68.2 (CH$_2$), 58.0 ppm (CH$_3$).

ESI-MS data of complex 2 in the presence of 1a: *m/z*: 1912.0 [**2**·(**1a**)$_2$−3NO$_3$]$^{3+}$, 1782 [**2**·(**1a**)$_3$−4NO$_3$]$^{4+}$, 1706 [**2**·(**1a**)$_4$−5NO$_3$]$^{5+}$, 1414 [**2**·(**1a**)$_2$−4NO$_3$]$^{4+}$/[**2**·(**1a**)$_3$−5NO$_3$]$^{5+}$/[**2**·(**1a**)$_4$−6NO$_3$]$^{6+}$, 1167 [**2**·(**1a**)$_3$−6NO$_3$]$^{6+}$, 1120 [**2**·(**1a**)$_2$−5NO$_3$]$^{5+}$, 1049 [**2**·(**1a**)$_4$−4NO$_3$]$^{4+}$, 992 [**2**·(**1a**)$_3$−7NO$_3$]$^{7+}$, 923 [**2**·(**1a**)$_2$−6NO$_3$]$^{6+}$, 860 [**2**·(**1a**)$_3$−8NO$_3$]$^{8+}$, 827 [**2**·(**1a**)$_4$−5NO$_3$]$^{5+}$, 782 [**2**·(**1a**)$_2$−7NO$_3$]$^{7+}$, 677 [**2**·(**1a**)$_2$−8NO$_3$]$^{8+}$.

ESI-MS data of complex 2 in the presence of 1b: *m/z*: 1586 [**2**·(**1b**)$_2$−4NO$_3$]$^{4+}$, 1497 [**2**·(**1b**)$_4$−5NO$_3$]$^{5+}$, 1286 [**2**·(**1b**)$_2$−4NO$_3$]$^{4+}$, 1257 [**2**·(**1b**)$_3$−5NO$_3$]$^{5+}$, 1236 [**2**·(**1b**)$_4$−6NO$_3$]$^{6+}$, 1037 [**2**·(**1b**)$_3$−6NO$_3$]$^{6+}$, 1017 [**2**·(**1b**)$_2$−5NO$_3$]$^{5+}$, 985 [**2**·**1b**−4NO$_3$]$^{4+}$, 837 [**2**·(**1b**)$_2$−6NO$_3$]$^{6+}$, 708 [**2**·(**1b**)$_2$−7NO$_3$]$^{7+}$.

ESI-MS data of complex (4)$_2$⊂2 in the presence of 1a (4 = (MeOC$_6$H$_4$CO)$_2$): *m/z*: 1920 [(**4**)$_2$⊂**2**·(**1a**)$_3$−4NO$_3$]$^{4+}$, 1817 [(**4**)$_2$⊂**2**·(**1a**)$_4$−5NO$_3$]$^{5+}$, 1554 [(**4**)$_2$⊂**2**·(**1a**)$_2$−4NO$_3$]$^{4+}$, 1524 [(**4**)$_2$⊂**2**·(**1a**)$_3$−4NO$_3$]$^{4+}$, 1504 [(**4**)$_2$⊂**2**·(**1a**)$_4$−6NO$_3$]$^{6+}$, 1259 [(**4**)$_2$⊂**2**·(**1a**)$_3$−6NO$_3$]$^{6+}$, 1231 [(**4**)$_2$⊂**2**·(**1a**)$_2$−5NO$_3$]$^{5+}$, 1187 [(**4**)$_2$⊂**2**·**1a**−4NO$_3$]$^{4+}$, 1071 [(**4**)$_2$⊂**2**·(**1a**)$_3$−7NO$_3$]$^{7+}$, 1015 [(**4**)$_2$⊂**2**·(**1a**)$_2$−6NO$_3$]$^{6+}$, 937 [(**4**)$_2$⊂**2**·**1a**-5NO$_3$]$^{5+}$, 861 [(**4**)$_2$⊂**2**·(**1a**)$_2$−7NO$_3$]$^{7+}$.

ESI-MS data of complex 5 in the presence of 1a: *m/z*: 1961 [**5**·(**1a**)$_2$−3NO$_3$]$^{3+}$, 1822 [**5**·(**1a**)$_3$−4NO$_3$]$^{4+}$, 1473 [**5**·(**1a**)$_4$−3NO$_3$]$^{3+}$, 1456 [**5**·(**1a**)$_2$−4NO$_3$]$^{4+}$, 1445 [**5**·(**1a**)$_3$−5NO$_3$]$^{5+}$, 1194 [**5**·(**1a**)$_3$−6NO$_3$]$^{6+}$, 1152 [**5**·(**1a**)$_2$−5NO$_3$]$^{5+}$, 1089 [**5**·**1a**−4NO$_3$]$^{4+}$, 1014 [**5**·(**1a**)$_3$−7NO$_3$]$^{7+}$, 950 [**5**·(**1a**)$_2$−6NO$_3$]$^{6+}$, 805 [**5**·(**1a**)$_2$−7NO$_3$]$^{7+}$.

ESI-MS data of complex 1d⊂5 in the presence of 1a: *m/z*: 2098 [**1d**⊂**5**·(**1a**)$_2$−3NO$_3$]$^{3+}$, 1924 [**1d**⊂**5**·(**1a**)$_3$−4NO$_3$]$^{4+}$, 1609 [**1d**⊂**5**·**1a**-3NO$_3$]$^{3+}$, 1558 [**1d**⊂**5**·(**1a**)$_2$−4NO$_3$]$^{4+}$, 1527 [**1d**⊂**5**·(**1a**)$_3$−5NO$_3$]$^{5+}$, 1262 [**1d**⊂**5**·(**1a**)$_3$−6NO$_3$]$^{6+}$, 1234 [**1d**⊂**5**·(**1a**)$_2$−5NO$_3$]$^{5+}$, 1191 [**1d**⊂**5**·**1a**-4NO$_3$]$^{4+}$, 1018 [**1d**⊂**5**·(**1a**)$_2$−6NO$_3$]$^{6+}$, 863 [**1d**⊂**5**·(**1a**)$_2$−7NO$_3$]$^{7+}$.

ESI-MS data of complex 1d⊂5 in the absence of 1a: *m/z*:

1218 [**1d**⊂**5**·(**DMF**)$_4$−3NO$_3$]$^{3+}$,	1194 [**1d**⊂**5**·(**DMF**)$_3$−3NO$_3$]$^{3+}$,
1169 [**1d**⊂**5**·(**DMF**)$_2$−3NO$_3$]$^{3+}$,	990 [**1d**⊂**5**·(**DMF**)$_9$−4NO$_3$]$^{4+}$,
971 [**1d**⊂**5**·(**DMF**)$_8$−4NO$_3$]$^{4+}$,	953 [**1d**⊂**5**·(**DMF**)$_7$−4NO$_3$]$^{4+}$,
934 [**1d**⊂**5**·(**DMF**)$_6$−4NO$_3$]$^{4+}$,	917 [**1d**⊂**5**·(**DMF**)$_5$−4NO$_3$]$^{4+}$,
898 [**1d**⊂**5**·(**DMF**)$_4$−4NO$_3$]$^{4+}$,	852 [**1d**⊂**5**·(**DMF**)$_{14}$−5NO$_3$]$^{5+}$,
838 [**1d**⊂**5**·(**DMF**)$_{13}$−5NO$_3$]$^{5+}$,	823 [**1d**⊂**5**·(**DMF**)$_{12}$−5NO$_3$]$^{5+}$,
809 [**1d**⊂**5**·(**DMF**)$_{11}$−5NO$_3$]$^{5+}$,	793 [**1d**⊂**5**·(**DMF**)$_{10}$−5NO$_3$]$^{5+}$,
779 [**1d**⊂**5**·(**DMF**)$_9$−5NO$_3$]$^{5+}$,	764 [**1d**⊂**5**·(**DMF**)$_8$−5NO$_3$]$^{5+}$,
750 [**1d**⊂**5**·(**DMF**)$_7$−5NO$_3$]$^{5+}$,	735 [**1d**⊂**5**·(**DMF**)$_6$−5NO$_3$]$^{5+}$,
724 [**1d**⊂**5**·(**DMF**)$_{16}$−6NO$_3$]$^{6+}$,	712 [**1d**⊂**5**·(**DMF**)$_{15}$−6NO$_3$]$^{6+}$,
700 [**1d**⊂**5**·(**DMF**)$_{14}$−6NO$_3$]$^{6+}$,	687 [**1d**⊂**5**·(**DMF**)$_{13}$−6NO$_3$]$^{6+}$,
676 [**1d**⊂**5**·(**DMF**)$_{12}$−6NO$_3$]$^{6+}$,	663 [**1d**⊂**5**·(**DMF**)$_{11}$−6NO$_3$]$^{6+}$,
651 [**1d**⊂**5**·(**DMF**)$_{10}$−6NO$_3$]$^{6+}$,	638 [**1d**⊂**5**·(**DMF**)$_9$−6NO$_3$]$^{6+}$,
622 [**1d**⊂**5**·(**DMF**)$_{17}$−7NO$_3$]$^{7+}$,	611 [**1d**⊂**5**·(**DMF**)$_{16}$−7NO$_3$]$^{7+}$,
602 [**1d**⊂**5**·(**DMF**)$_{15}$−7NO$_3$]$^{7+}$,	591 [**1d**⊂**5**·(**DMF**)$_{14}$−7NO$_3$]$^{7+}$,
581 [**1d**⊂**5**·(**DMF**)$_{13}$−7NO$_3$]$^{7+}$,	546 [**1d**⊂**5**·(**DMF**)$_{18}$−8NO$_3$]$^{8+}$,
537 [**1d**⊂**5**·(**DMF**)$_{17}$−8NO$_3$]$^{8+}$,	528 [**1d**⊂**5**·(**DMF**)$_{16}$−8NO$_3$]$^{8+}$,
518 [**1d**⊂**5**·(**DMF**)$_{15}$−8NO$_3$]$^{8+}$.	

Acknowledgement

[1] a) J. B. Fenn, M. Mann, C. K. Meng, S. F. Wong, C. M. Whitehouse, *Mass Spectrom. Rev.* **1990**, *9*, 37–70; b) P. Kebarle, L. Tang, *Anal. Chem.* **1993**, *65*, 972A–986A; c) S. J. Gaskell, *J. Mass. Spectrom.* **1997**, *32*, 677–688.

[2] C. A. Schalley, *Mass Spectrom. Rev.* **2001**, *20*, 253–309.

[3] a) S. Sakamoto, M. Fujita, K. Kim, K. Yamaguchi, *Tetrahedron* **2000**, *56*, 955–964; b) S. Sakamoto, T. Imamoto, K. Yamaguchi, *Org. Lett.* **2001**, *3*, 1793–1795; c) S. Sakamoto, K. Yamaguchi, *Angew. Chem.* **2003**, *115*, 933–936; *Angew. Chem. Int. Ed.* **2003**, *42*, 905–908; d) S. Sakamoto, K. Yamaguchi, *Tetrahedron Lett.* **2003**, *44*, 3341–3344; e) S. Sakamoto, K. Nakatani, I. Saito, K. Yamaguchi, *Chem. Commun.* **2003**, 788–789; f) K. Yamaguchi, *J. Mass Spectrom.* **2003**, *38*, 473–490.

[4] a) X. Cheng, Q. Gao, R. D. Smith, E. E. Simanek, M. Mammen, G. M. Whitesides, *J. Org. Chem.* **1996**, *61*, 2204–2206; b) K. A. Jolliffe, M. C. Calama, R. Fokkens, N. M. M. Nibbering, P. Timmerman, D. N. Reinhoudt, *Angew. Chem.* **1998**, *110*, 1294–1297; *Angew. Chem. Int. Ed.* **1998**, *37*, 1247–1251; c) C. A. Schalley, R. K. Castellano, M. S. Brody, D. M. Rudkevich, G. Siuzdak, J. Rebek, Jr., *J. Am. Chem. Soc.* **1999**, *121*, 4568–4579; d) C. A. Schalley, J. M. Rivera, T. Martín, J. Santamaría, G. Siuzdak, J. Rebek, Jr., *Eur. J. Org. Chem.* **1999**, 1325–1331.

[5] a) G. J. V. Berkel, S. A. McLuckey, G. L. Glish, *Anal. Chem.* **1991**, *63*, 2064–2068; b) J. M. E. Quirke, C. L. Adams, G. J. V. Berkel, *Anal. Chem.* **1994**, *66*, 1302–1315; c) G. J. V. Berkel, K. G. Asano, *Anal. Chem.* **1994**, *66*, 2096–2102; d) G. J. V. Berkel, J. M. E. Quirke, R. A. Tigani, A. S. Dilley, T. R. Covey, *Anal. Chem.* **1998**, *70*, 1544–1554.

[6] I. Aiello, L. D. Donna, M. Ghedini, M. L. Deda, A. Napoli, G. Sindona, *Anal. Chem.* **2004**, *76*, 5985–5989.

[7] W. E. Rudzinski, K. Zhou, X. Luo, *Energy Fuels* **2004**, *18*, 16–21.

[8] S. Sakamoto, M. Yoshizawa, T. Kusukawa, M. Fujita, K. Yamaguchi, *Org. Lett.* **2001**, *3*, 1601–1604.

[9] a) K. Tanaka, H. Waki, Y. Ido, S. Akita, Y. Yoshida, T. Yoshida, *Rapid Commun. Mass Spectrom.* **1988**, *2*, 151–156; b) M. Karas, F. Hillenkamp, *Anal. Chem.* **1988**, *60*, 2299–2301.

[10] a) M. Fujita, D. Oguro, M. Miyazawa, H. Oka, K. Yamaguchi, K. Ogura, *Nature* **1995**, *378*, 469–471; b) Coordination cage **2** is now commercially available from Wako Chemical Co. Ltd. (Pd-Nanocage®).

[11] a) T. Kusukawa, M. Fujita, *Angew. Chem. Int. Ed.* **1998**, *37*, 3142–3144; b) T. Kusukawa, M. Fujita, *J. Am. Chem. Soc.* **1999**, *121*, 1397–1898; c) T. Kusukawa, M. Fujita, *J. Am. Chem. Soc.* **2002**, *124*, 13576–13582; d) M. Yoshizawa, M. Tamura, M. Fujita, *J. Am. Chem. Soc.* **2004**, *126*, 6846–6847; e) K. Nakabayashi, M. Kawano, M. Yoshizawa, S. Ohkoshi, M. Fujita, *J. Am. Chem. Soc.* **2004**, *126*, 16694–16695; f) M. Yoshizawa, T. Kusukawa, M. Kawano, T. Ohhara, I. Tanaka, K. Kurihara, N. Niimura, M. Fujita, *J. Am. Chem. Soc.* **2005**, *127*, in press.

[12] a) H. Ito, T. Kusukawa, M. Fujita, *Chem. Lett.* **2000**, 598–599; b) M. Yoshizawa, T. Kusukawa, M. Fujita, K. Yamaguchi, *J. Am. Chem. Soc.* **2000**, *122*, 6311–6312; c) M. Yoshizawa, Y. Takeyama, T. Kusukawa, M. Fujita, *Angew. Chem.* **2002**, *114*, 1403–1405; *Angew. Chem. Int. Ed.* **2002**, *41*, 1347–1349; d) M. Yoshizawa, Y. Takeyama, T. Okano, M. Fujita, *J. Am. Chem. Soc.* **2003**, *125*, 3243–3247; e) T. Kusukawa, T. Nakai, T. Okano, M. Fujita, *Chem. Lett.* **2003**, *32*, 284–285; f) M. Yoshizawa, S. Miyagi, M. Kawano, K. Ishiguro, M. Fujita, *J. Am. Chem. Soc.* **2004**, *126*, 9172–9173.

[13] Strictly speaking, CSI-MS (a direct solution analysis method at low temperatures) was carried out in all the measurements.[3,8] Since the conditions we used are similar to ESI conditions, we believe that the present method is applicable to standard ESI-MS analysis.

[14] a) K. Kumazawa, K. Biradha, T. Kusukawa, T. Okano, M. Fujita, *Angew. Chem.* **2003**, *115*, 4039–4043; *Angew. Chem. Int. Ed.* **2003**, *42*, 3909–3913; b) M. Yoshizawa, J. Nakagawa, K. Kumazawa, M. Nagao, M. Kawano, T. Ozeki, M. Fujita, *Angew. Chem.* **2005**, *117*; *Angew. Chem. Int. Ed.* **2005**, *44*, in press.