Transition metal catalysis in confined spaces

Leenders, S.H.A.M.

Citation for published version (APA):
Chapter 2:

Characterization of Molecular Spheres through Diffusion NMR and Mass Spectroscopy

Abstract:
This chapter discusses two techniques that are further used in this thesis: Diffusion ordered NMR spectroscopy (DOSY) and Cold Spray Ionization Mass Spectrometry (CSI-MS). It is demonstrated that based on diffusion coefficients, NMR signals of different spheres can be separated with DOSY. Furthermore, the size of spheres can be determined on the basis of their diffusion coefficient. In order to be able to separate signals, non-overlapping peaks are required. The exact metal to ligand ratio of spheres can be determined with nanospray- or CSI-Mass Spectrometry. When a high resolution is obtained even the elemental composition can be determined. Also spheres based on a mixture of different building blocks can be characterized with CSI-MS.
2.1 Introduction

The analysis of supramolecular assemblies is not always straightforward, especially as the weak interactions holding the system together can sometimes easily be broken under the conditions required for the technique of the analysis. Many of these techniques require high temperatures, vacuum or high energy radiation, which could destroy the supramolecular assembly. It is therefore important that gentle or non-invasive techniques are applied to keep the structures intact and to prevent disassembly. While many different techniques can be used, for example X-ray techniques (absorption or diffraction), the equipment for these measurements is not always in house and single crystalline material is difficult to obtain. This chapter discusses two techniques to characterize assemblies with a high molecular weight.

First, Diffusion Ordered NMR Spectroscopy (DOSY) is explained and discussed. Characterization with nuclear magnetic resonance (NMR) techniques can sometimes prove to be cumbersome. This is because: 1) Many different sets of signals can be observed in an assembly of low symmetry; 2) Only one set of signals can be observed in a system with high symmetry and many different structures can be proposed that are in line with this symmetry. In order to make sure that multiple building blocks have together formed a well-defined system, DOSY can be used to measure the diffusion coefficient of the assembly. This value can be compared to the free building block and correlated to a hydrodynamic radius. In this chapter, we will look into the use of DOSY to separate NMR signals of different assemblies that have different sizes.

The second technique that is investigated in this chapter is mass spectrometry. While this technique requires more harsh conditions to measure the assemblies, it can be used to exactly determine the molecular weight of the formed assemblies, providing their ligand to metal ratio. When signals are obtained with high resolution, mass spectrometry can be used to determine the exact elemental composition. We will discuss nanospray and cold spray ionization methods.

This chapter only discusses the analysis of these compounds by the designated techniques to confirm the formation of the supramolecular assembly, and the limits of these techniques are discussed. The chemistry or applications of these type of systems are demonstrated in later chapters.
2.2.1 Basic principles of Diffusion Ordered NMR Spectroscopy (DOSY)

Diffusion Ordered NMR Spectroscopy is a technique that allows to correlate the diffusion rate to a set of signals in the nuclear magnetic resonance (NMR) spectrum.\textsuperscript{1,2} From the DOSY experiment, a translational diffusion coefficient, termed $D$, can be obtained. This coefficient relates to the size of the particle and can be used as an approximation for the radius of a compound. Furthermore, the coefficient can be used to calculate association constants in host-guest systems.\textsuperscript{3-5} Various contributions in literature have already extensively discussed the possibilities,\textsuperscript{6,7} different pulse sequences\textsuperscript{8} or even various processing methods\textsuperscript{9} for DOSY. Therefore, only a short and basic introduction is given on DOSY in this chapter.

The most important aspect of DOSY is that a gradient in the strength of the magnetic field is applied. This field gradient allows the labelling of the position of the nuclei with NMR. One of the most basic pulse sequences to demonstrate the diffusion of the nuclei is the pulsed gradient spin echo (PGSE), shown in Figure 1a. The first 90° pulse rotates the spin in the xy plane after which the first gradient pulse is applied for a duration of $\delta$ giving all the spin a different phase shift. Then, after a 180° pulse to inverse the spins, a new gradient pulse is applied after which the spin echo of the system can be measured. The effect of the diffusion that the nuclei undergo is apparent when Figure 1b is compared to Figure 1c: when no diffusion would occur full refocusing should be observed, thus giving a full spin echo intensity. However, when the nuclei do diffuse, a loss of spin echo signal is observed, thus giving less intensity of the signal.
Figure 1: Simplified visual presentation of DOSY. a) The pulsed gradient spin echo (PGSE) pulse program. Effects of the gradient pulse program are visualized in b) and c). In the absence of diffusion (b) full signal intensity is obtained while in the presence of diffusion (c) a decrease in signal is expected. Parts of this figure are adapted from reference [1].

According to the Stejskal-Tanner equation (1), the lower intensity \( I \) of the resulting signal is depending on the applied gradient \( G \). Also the duration of the pulses \( \delta \) and the delay time \( \Delta \), both parameters that can be fine-tuned with the NMR, play a role. Finally, the gyromagnetic ratio is included in the equation \( \gamma \).

\[
I(G) = I_0 e^{-\gamma^2 \delta^2 G^2 \Delta} \tag{1}
\]

It can be seen from equation (1) that, when \( \Delta \) and \( \delta \) are kept constant, the signal decay is related exponentially to the gradient field that is applied. A DOSY experiment consists of a number of 1D experiments in which the gradient \( G \) is gradually increased. The increase in gradient thus decreases the signal intensity as depicted in Figure 2a for a series of stacked \(^1\)H NMR spectra. The decrease in intensity \( (I/I_0) \) can be plotted against the gradient of the magnetic field giving a plot like Figure 2b. As apparent from equation (1) a linear line is obtained when \( G^2 \) is plotted against \( \ln(I/I_0) \) which is depicted in Figure 2c. The slope of this line can be used to deduce the diffusion coefficient \( D \).
Figure 2: After a standard DOSY experiment an array of $^1$H NMR spectra with different intensity decays are obtained (a). The decrease in intensity can be plotted against the gradient of the magnetic field (b). A straight line, plotted in (c), is obtained for the signals if the ln of the intensity decrease is plotted against the squared gradient. Finally the diffusion coefficient can be obtained from the slope and plotted against a projection of the spectra. Shown in d) is an example of the experiment processed with the Topspin software of Bruker (Spectra are those of a $\text{Pd}_{12}\text{OMe}_{24}$ sphere, depicted in Scheme 1).

In the final processing the DOSY is visualized by a projection of the signal, like a $^1$H NMR on the x-axis and the D or log D on the y-axis. An example of such a plot, obtained with Bruker’s Topspin software, is shown in Figure 2d. Note that in this plot a negative value of the log D is used. Due to this negative value, the larger species (those with a smaller D) appear higher in the plot. The diffusion coefficients obtained can be used for various purposes. It can even be used to calculate a hydrodynamic radius of the species using the Stokes-Einstein equation (equation (2)).

$$D = \frac{k_B T}{6 \pi \eta r}$$

(2)

Herein $k_B$ is the Boltzmann constant, $T$ is the temperature (in K), $\eta$ is the viscosity of the solvent and $r$ is the radius of the particle. When applying the Stokes-Einstein equation one must keep in mind that the viscosity is greatly dependent on the temperature. Therefore DOSY experiments in this thesis are kept at 25 °C, for this
temperature the viscosity and log D values of deuterated solvents are reported in literature.10

### 2.2.2 Molecular Spheres in Diffusion Ordered NMR Spectroscopy (DOSY)

DOSY is a well-established technique to determine the rate of diffusion and thus size of the species. Generally, supramolecular assemblies that are in their pure form are measured. However, sometimes mixtures can be formed and it is unclear if exchange between these mixtures occur on the NMR time scale. For this reason we set out to investigate if different diffusion bands can be observed for different species in DOSY and what the limitations are to separate spheres with DOSY. In order to see if separation of different spheres is possible, DOSY experiments were investigated with the known Pd$_{12}$OMe$_{24}$ and Pt$_6$OMe$_{12}$ spheres.11

![Scheme 1: Synthesis of the large Pd$_{12}$OMe$_{24}$ spheres (PM3-modeled structure on the right).](image)

The different diffusion coefficients of these spheres have previously been established in DMSO (Pd$_{12}$OMe$_{24}$; log D = -10.5 m$^2$/s) and DMSO/trifluoroethanol (Pt$_6$OMe$_{12}$; log D = -10.2 m$^2$/s). Because the solvent and hence viscosity is different, these numbers are not really comparable. Our investigations of the different spheres were done in acetonitrile (see Scheme 1) and first the diffusion coefficient of the palladium and platinum spheres were determined separately. The DOSY experiment on the palladium spheres resulted in a log D of -9.5 m$^2$/s. This value matches with the expected radius and reported diffusion constants in acetonitrile (Figure 3).12 The corresponding platinum analogue, although expected to give a more positive log D, diffuses slower than the palladium sphere. Considering that the diffusion band is small and the $^1$H NMR spectrum resembles the formed sphere in DMSO,11 it is expected that no oligomers are present and that a larger spherical species is formed. However, the exact species (M$_6$L$_{12}$ or M$_{12}$L$_{24}$) cannot be determined. Another reason for the smaller diffusion constant could be that due to the broader peaks on NMR for
the platinum spheres, the integration of the proton signals for DOSY becomes more difficult and less reliable.

In order to investigate if the platinum spheres have a different size from the palladium spheres, the spheres are prepared separately and then mixed and measured with DOSY. From the 'H NMR spectrum it was observed that the pyridine peaks overlap and this resulted in an diffusion band with a diffusion coefficient that is an average of the separately measured Pd and Pt spheres. This indicates that the processing of the spectrum occurs with the expectation that only one species is present and only one species is observed in the spectrum. With two species being expected this directly shows the weakness of DOSY: when peaks overlap in the spectrum, their intensities are considered to be from one species and are therefore integrated as one when using the standard software (Bruker's Topspin).

![Figure 3: Overlapping DOSY spectra of a platinum sphere (-9.81), Pd$_{12}$OMe$_{24}$ sphere(-9.45) and a mixture of pre-assembled Pd$_{12}$OMe$_{24}$+platinum spheres (-9.57). The solvent is depicted with the band at -8.36.](image)

Having established that overlapping peaks of these two systems are not separable with DOSY we switched to a system in which we have spheres of different sizes that have separated peaks in the 'H NMR spectra. Therefore building block F with a fluorine tail on the 5 position of the backbone was synthesized via a Mitsonobu reaction with 3,5-dibromophenol (1). After a Sonogashira coupling of the resulting compound 2 the desired building block was obtained (Scheme 2).
This bipyridine moiety was assembled into nanosphere $\text{Pd}_{12}\text{F}_{24}$ by addition of 0.5 equivalent of $[\text{Pd(CH}_3\text{CN})_4]_2\text{BF}_4$ in a CD$_3$CN solution of $\text{F}$. The exohedrally functionalized sphere was expected to be significantly larger than the endohedrally functionalized methoxy sphere. DOSY showed that with a log D of -9.49 m$^2$/s for the $\text{Pd}_{12}\text{F}_{24}$ spheres, their size is not much larger than that of the $\text{Pd}_{12}\text{OMe}_{24}$ spheres. With a small difference in log D of 0.06 m$^2$/s, we measured the DOSY spectrum when these two samples are mixed. As depicted in Figure 4 the DOSY yields two species with log D values expected for the individual spheres. However, looking more closely at the DOSY it can be observed that only the non-overlapping, or isolated peaks (CH$_2$ peaks of $\text{Pd}_{12}\text{F}_{24}$ and OCH$_3$ of $\text{Pd}_{12}\text{OMe}_{24}$) give nice separation with DOSY. Again the overlapping pyridine and aromatic peaks give average diffusion values in-between the values that are expected. Having established that the spheres can be separated with DOSY, we used this technique to study ligand exchange. Based on literature, no ligand exchange is expected at room temperature over a couple of days.$^{13}$ Therefore we heated the sample with the mixture of spheres overnight at 70 °C to facilitate the exchange. The DOSY showed only one diffusion band indicating that exchange has occurred. After exchange of building blocks, all the peaks have the same diffusion coefficient corresponding to a log D of the fluorous sphere. This suggests that a statistical mixture has formed of which $\text{Pd}_{12}\text{F}_{12}\text{OMe}_{12}$ is the average species. The formation of this mixture was also established by mass spectrometry, confirming that DOSY can be used in this case to demonstrate the ligand exchange. We were also interested if the same separation could be obtained with the platinum analogues of the spheres. However the broadness of the peaks hampered the possibility to obtain accurate log D values and separation of the spheres.
As a final case study we looked into the separation of the larger M_{24}L_{24} type spheres (see Scheme 3) from the Pd_{12}OMe_{24} sphere. Based on the known log D values in literature measured in DMSO the radii of the spheres are almost similar with both spheres showing a log D of -10.5 in DMSO (note that the Pyr building block is smaller than OMe). To see if they really have the same diffusion coefficient, bispyridyl-pyrrole building block Pyr was synthesized via a Stetter and subsequent Paal-Knorr reaction. The resulting building block was assembled into a large sphere (Pd_{24}Pyr_{48}) using a standard palladium precursor, and the formation was confirmed by mass spectrometry. To investigate if the M_{24}L_{48} is really of the same size as the M_{12}L_{24} sphere, they were measured individually with DOSY. Fortunately, the DOSY spectra of the pure solutions of the spheres showed that they have significantly different log D values (-9.49 m²/s for Pd_{24}Pyr_{48} vs. -9.45 m²/s for Pd_{12}OMe_{24}), indicating that these signals should be separable with DOSY.
Mixing the pre-assembled spheres in the same ratio and measuring DOSY with the same settings yields the spectrum displayed in Figure 5.

![DOSY spectrum of a mixture of Pd12OMe24 and Pd24Pyr48 in acetonitrile. While the overlapping peaks again give one average species, clearly two different species can be observed from the non-overlapping peaks. The spectrum slightly changes after heating to 70 °C for 8 hours. However, still different species of different sizes are seen.](image)

**Figure 5**: DOSY spectrum of a mixture of Pd12OMe24 and Pd24Pyr48 in acetonitrile. While the overlapping peaks again give one average species, clearly two different species can be observed from the non-overlapping peaks. The spectrum slightly changes after heating to 70 °C for 8 hours. However, still different species of different sizes are seen.

From this figure it can be observed that the peaks corresponding to the different spheres have other diffusion values. The overlapping peaks however, show a log D value which seems to be an average of the individual species, once more showing that overlapping peaks cannot be separated with DOSY using the standard software. To investigate if exchange is possible between the ligands, the solution with the mixture of spheres was heated at 70 °C for 8 hours. The resulting DOSY after heating (Figure 5, right) shows only a slight change and it still seems that two distinct spheres are present. This spectrum suggests that no exchange occurred, however, analysis by mass spectrometry shows that no more Pd24Pyr48 species are present (see section 2.3.2). While there are still Pd12OMe24 species in the solution, all pyrrole spheres have been accommodated in the Pd12 sphere, giving a mixture of [Pd12OMe24-xPyrx] (x = 1-6) spheres. This corresponds with published work from the Fujita group on the formation of Pd12 or Pd24 spheres, that depends on the average bent angle of the bispyridine building block used. The bands hence observed in Figure 5 are that of the Pd12 spheres. Presumably, the larger species (at -9.58 m²/s) is that of a distorted sphere, which contains pyrrole building blocks. Hence, this case study shows that, although DOSY can be used to give an approximation for the size of the species, the exact species cannot be determined.
Summarizing, these experiments show that based on DOSY, different species can be separated if they have peaks that do not overlap in NMR. While the non-overlapping peaks clearly show two distinct species, overlapping peaks give an average of the diffusion constants as the integration of the peaks cannot distinguish between the two different species. It could be that more elaborate fitting would make it possible to distinguish between overlapping peaks. While methods are known to process the spectra in a different way like the DOSY Toolbox as reported by Nilsson and co-workers, applying these methods yielded no desirable results. Finally we would like to state the log D obtained for platinum sphere should be taken carefully. This is because the broader peaks give less accurate diffusion determinations. This was also observed by measuring the same sample consecutive times, yielding various log D values.

2.3.1 Introduction to Cold Spray Ionization Mass Spectrometry (CSI-MS)

While NMR methods are a good in situ way for measuring the spheres in solution, it does not allow the determination of the exact molecular weight of the species that are present. For the exact molecular weight of the supramolecular assemblies, mass spectrometry can give more detail. Unfortunately, mass spectrometry in general is more destructive and the difficulty lies in keeping the spheres intact during ionization and their flight towards the detector. When using mass spectrometry, different parameters can be changed. For instance, the ionization method can be varied and many different ionization techniques are currently at a researcher’s disposal. Unfortunately, methods like Matrix Assisted Laser Desorption Ionization (MALDI) and Field Desorption (FD) are still too destructive for most supramolecular systems. ElectroSpray Ionization (ESI) is a more mild ionization technique that can be used to analyze assemblies. For the analysis of supramolecular systems also variations of ESI can be employed like nanospray ionization, sonic spray ionization and cold spray ionization (CSI). Especially for the systems discussed here, those based on palladium-pyridine interactions, CSI-MS is commonly used. In this method the ion spray and desolvating chamber are cooled so that measurements can be done between -50 to +15 °C. This low temperature compared to ESI (which can go up to 200 °C) keeps the assemblies intact and makes the dissociation of the counter ions easier. The easier dissociation is obtained due to the increase in polarizability caused by the higher dielectric constant at lower temperatures. The group of Fujita has shown that the CSI-MS methods can be used to measure a variety of palladium-pyridine systems. With different building blocks used, assemblies of the type Pd₆L₁₂, Pd₁₂L₂₄ and Pd₂₄L₄₈ have been characterized by CSI-MS.
platinum assemblies are less reported (by using CSI-MS)\textsuperscript{11}, Stang \textit{et al.} have characterized multiple platinum-pyridine assemblies with ESI-MS.\textsuperscript{24,25} In this part of the chapter we will show different mass spectra of different molecular spheres and host-guest interactions. Different techniques will be demonstrated to work with these spheres and the effect of solvent and additives on the mass spectra are discussed.

\subsection*{2.3.2 Structure determination of assemblies by mass spectrometry}

While the M\textsubscript{6}L\textsubscript{4} octahedral sphere, as reported by Fujita \textit{et al.}, has been frequently characterized by MS techniques\textsuperscript{20,21} it should be noted that measuring these systems in water is quite challenging. Due to the high surface tension of water it is more difficult to form a good spray and ionization is more challenging. Yamaguchi and coworkers needed to add additional salts to weaken the coordination of the strongly bound nitrate anion in order to detect any charged species of the cage.\textsuperscript{26} Changing the anion to PF\textsubscript{6} made the containers soluble in acetonitrile and thus easier to detect by MS. However, due to the change of solvent, the hydrophobic interactions and thus the driving force for encapsulation is lost. Therefore encapsulated species can only be measured in water, unless they are contained via a ship-in-a-bottle approach. In order to investigate whether these octahedral molecular containers can be measured with MS, we investigated both the palladium and platinum octahedral cages (displayed in Figure 6). Using different ESI/CSI-MS spectrometers no cage species could be observed, even when additives were used. Interestingly, when changing from a time-of-flight (ToF) machine to an Orbitrap (FT-ICR)\textsuperscript{27,28}, the platinum octahedral cage could be observed (see Figure 6). This was obtained via a modified set-up in which a CSI source was mounted directly for the inlet of the Orbitrap. Unfortunately the palladium analogue only showed fragmentation with this method. Figure 6 shows that different charged species can be observed for the Pt\textsubscript{6}L\textsubscript{4} species, ranging from 6+ to 4+. Although some fragmentation peaks are also observed, the major peak that is detected corresponds to the 5+ Pt\textsubscript{6}L\textsubscript{4} species. Worthy to note is that no additive was used to weaken the coordination of the nitrate counter-ion, something that was earlier reported to be necessary for the measurements of this system in water.\textsuperscript{21}
With the possibility to characterize these compounds with MS the next step was to investigate if capsules with encapsulated guests can also be observed. Co-encapsulating (Cp)Rh(cod) (4, Cp = cyclopentadiene, cod = 1,5-cyclooctadiene) together with pyrene (5) in the void of the capsule was demonstrated by NMR and will be elaborately discussed in chapter 6. When this species was subjected to the CSI-FT-ICR spectrometer many different highly charged species were observed as is clear from the spectrum, depicted in Figure 7. Importantly, the peak that belongs the $[3\cdot4\cdot5]^{4+}$ species was clearly observed. Next to this peak the mono-encapsulated species $3\cdot4$ and $3\cdot5$ were also observed. As these species are not observed in the solution (based on encapsulation studies, see chapter 6), they are likely formed during the MS experiment from $3\cdot4\cdot5$. Also, the empty container 3 was still detected (6+ to 4+), but this is expected as based on the $^1$H NMR spectrum, 74% of the spheres is filled with the guests.
Figure 7: Co-encapsulated species of (Cp)Rh(cod) 4 and pyrene (5) in a Pt octahedral cage (3). Measured in water with a CSI-FT-ICR mass spectrometer. Numbers above the m/z values annotate the charge of the peak.

The many different species present in the spectrum shows the difficulty of measuring these type of systems in water. Still, this is the first time a co-encapsulation in this container is observed and therefore cold spray FT-ICR is a promising technique to measure these type of compounds in the future.

Switching the solvent from water to acetonitrile makes mass analysis by spraying techniques easier due to the lower surface tension of most organic solvents. Hence, the previously discussed Pd_{12}OMe_{24} spheres (see Scheme 1) were investigated with CSI and nanospray MS²⁹ in acetonitrile. Measurements of these spheres in acetonitrile at –40 °C with a JEOL machine, equipped with a CSI source resulted in the spectrum displayed in Figure 8. Herein, it is observed that peaks with a m/z of lower than 1200 are species formed by fragmentation during the ionization. More
interesting are the peaks at higher \( m/z \), these peaks are expected to be from the 8+ to 5+ species (based on simulated spectra). However, the resolution that is obtained with the JEOL machine is not sufficient to determine the exact charge and elemental composition of these species.

Figure 8: \( \text{Pd}_{12}\text{OMe}_{24}(\text{BF}_4)_{24} \) spheres in acetonitrile measured with a cold-spray (–40 °C) AccuToF mass spectrometer designed by JEOL. Numbers above the \( m/z \) values annotate the expected charge of the peak when compared to figures 9 to 11.

In order to obtain the exact charge and mass of the spheres, we turned to a machine that can obtain much higher resolution, a tripleToF machine designed by Sciex. This was equipped with a nanospray ionization method which yielded the expected peaks corresponding to the 13+ to 6+ species by loss of the BF\(_4\) counterion, as depicted in Figure 9. Although still some fragmentation is observed, it can be clearly seen that the majority of the peaks correspond to the intact sphere, demonstrating that nanospray techniques are able to characterize these spheres. Changing the temperature of the nanospray from 50 to 150 °C proved to have no effect on the amount of fragmentation. Looking more closely at the detected sphere species a small peak of lower intensity was observed at lower \( m/z \) regions for each charged species, however no structure could be annotated to these peaks. A slightly different spectrum is obtained when the experiment is performed in methanol (Figure 10). A similar peak pattern can be observed with the addition of a 5+ species at 2074 \( m/z \). Interestingly, less fragmentation peaks are observed at lower \( m/z \) and the major peak now appears to be the \([\text{Pd}_{12}\text{OMe}_{24}(\text{BF}_4)_{14}]^{10+}\) species, which is different from the main peak of \([\text{Pd}_{12}\text{OMe}_{24}(\text{BF}_4)_{12}]^{12+}\) in acetonitrile.
Chapter 2

Figure 9: Pd_{12}OMe_{24}(BF_4)_{24} spheres in acetonitrile measured with a nanospray tripleToF mass spectrometer. Numbers above the m/z values annotate the charge of the peak.

Figure 10: Pd_{12}OMe_{24}(BF_4)_{24} spheres in methanol measured with a nanospray tripleToF mass spectrometer. Numbers above the m/z values annotate the charge of the peak.
The results obtained via nanospray ionization are satisfactory for the structure and elemental composition determination of these spheres. The \( \text{Pd}_{12}\text{OMe}_{24} \) sample was also studied in acetonitrile on a UHR-ToF BRUKER Daltonik maXis, equipped with cryospray. The spectrum obtained with this machine is displayed in Figure 11.

![Figure 11: \( \text{Pd}_{12}\text{OMe}_{24}(\text{BF}_4)_{24} \) spheres measured in acetonitrile with a Cryospray UHRToF mass spectrometer. On the top right the 7+ species is displayed with (top) with its simulated spectrum (bottom). Measurements were performed with a spraying temperature of \(-40^\circ\text{C}\).](image)

The measurements were performed at \(-40^\circ\text{C}\) and the benefits of the low temperature typical for cold spray ionization and high resolution of the machine are evident. Hardly any fragmentation is seen and only the expected species with charges between 14+ to 5+ are detected. This indicates that the sphere is the only species in solution and the fragmentation peaks in Figure 9 and Figure 10 are formed during the nanospray experiment. Also the major peak now resides in the 7+ species of the spheres, which is again different when compared to Figure 9 and Figure 10. The good results obtained for the palladium spheres encouraged us to also study the more difficult to measure platinum spheres in acetonitrile. Unfortunately the ionization of these spheres was rather challenging and only fragmentation or no signal was observed. We expect that the ionization is now the difficult part as platinum binds the anions stronger than palladium. Therefore spheres were prepared that have different anions (BF\(_4\), PF\(_6\), SbF\(_6\) and OTf) and these were studied in MS analysis in the presence of various additives to weaken the coordinated anion (DMSO and DMF).
However, none of these samples yielded the desired highly charged species corresponding to the platinum spheres. Also measuring the samples in methanol was not beneficial and still only fragmentation species are seen. MS spectra of the $\text{Pt}_6\text{OMe}_{12}$ species with the SbF$_6$ anion in acetonitrile have been reported,$^{11}$ however these were diluted from a solution made in DMSO/TFE (trifluoroethanol). Measuring an undiluted sample (PF$_6$ anion), formed in DMSO/TFE with cryospray resulted in the 9+ to 5+ species of the $\text{Pt}_6\text{OMe}_{12}$ sphere. In order to investigate if the TFE can act as a source to make anion more labile, and hence ionization easier, the spheres were assembled in acetonitrile and, before MS measurements, TFE was added as additive. However this didn’t result in the detection of any highly charge species.

Next to the analysis of pure sphere solutions, also solutions of mixtures were investigated with CSI-MS. As described in the previous section, if two pure assemblies based on different building blocks are combined and heated at high temperature, an exchange of the building blocks is observed. Hence a mixture of different spheres with different ratios of the separate building blocks is formed. When a solution of $\text{Pd}_{12}\text{F}_{24}$ spheres was mixed with a solution of $\text{Pd}_{12}\text{OMe}_{24}$ spheres in a 1:1 ratio and heated to 70 °C for overnight, exchange of the building blocks was observed indicated by DOSY (see Figure 4). The resulting mixture of spheres was analyzed with CSI-MS and a complex spectrum, indicative for the presence of many different species, was obtained. Various species in which a number of OMe building blocks were exchanged with F (and *vice versa*) were present in the spectrum. Peaks with high resolution ranging from $\text{Pd}_{12}\text{F}_{9}\text{OMe}_{15}$ to $\text{Pd}_{12}\text{F}_{17}\text{OMe}_{7}$, all with different charges (13+ to 9+), could be identified. Currently, these mixtures of spheres cannot be quantified with MS, as different spheres may have a different response in MS, but the exchange of building blocks under these conditions is clearly confirmed.

When the previously discussed $\text{Pd}_{24}\text{Pyr}_{48}$ and $\text{Pd}_{12}\text{OMe}_{24}$ spheres (see Figure 5) are mixed and heated at high temperature, they converge into a mixture of differently sized species, according to DOSY NMR. The CSI-MS spectrum of this exchange is depicted in Figure 12, and confirms the formation of a mixture.
Figure 12: Mass spectrum in which exchange between \( \text{Pd}_{12}\text{OMe}_{24} \) and \( \text{Pd}_{24}\text{Pyr}_{48} \) resulted in a mixture of \( \text{Pd}_{12}\text{OMe}_{24-x}\text{Pyr}_{x} \) (\( x = 0-6 \)).

In this spectrum the differently charged species do not overlap with each other and clear \( m/z \) regions can be observed for species bearing a charge between 12+ and 6+. All of these peaks correspond to \( \text{M}_{12}\text{L}_{24} \) species. It is known for these type of spheres that, based on the average bent angles between the pyridine, either a \( \text{M}_{12}\text{L}_{24} \) or a \( \text{M}_{24}\text{L}_{48} \) system is formed. A switch from \( \text{M}_{12} \) to \( \text{M}_{24} \) is somewhere expected between 131° and 134°. With the known bent angle of pyrrole of 135°, and that of the \( \text{OMe} \) building block being 120°, the average angle of less than 131° and results in the formation of \( \text{M}_{12}\text{L}_{24} \) species. From the mass spectrum, HRMS data for species up to \( \text{Pd}_{12}\text{OMe}_{18}\text{Pyr}_{6} \) are identified, and \( \text{Pd}_{12}\text{OMe}_{16}\text{Pyr}_{8} \) can still be observed with low intensity. Interestingly, while \( \text{Pd}_{12}\text{OMe}_{24} \) spheres can still be observed, no more \( \text{Pd}_{24}\text{Pyr}_{48} \) is present in the mass spectrum. This indicates that the \( \text{M}_{24}\text{L}_{48} \) spheres are fully converted into \( \text{Pd}_{12}\text{L}_{24} \) species. These observations are in line with previous reports from the Fujita group.
2.4 Conclusions

Diffusion NMR is a straightforward technique to determine the diffusion constant of a species and thus to analyze the size of assemblies. When different sizes of spheres are formed and non-overlapping peaks of the individual spheres can be observed, separation of the different species via DOSY is possible. However, if peaks of different species are overlapping, the standard software will treat the obtained signal as one species. DOSY thus gives no separation of overlapping peaks. Also when the peaks broaden, like in the case of the platinum spheres, separation turns out to be troublesome. Although diffusion values can still be obtained for the platinum spheres, one must keep in mind that they are less accurate.

For the determination of the exact species, mass spectrometry can be used to analyze the formation of the spheres. The spectrum that is obtained is dependent on the machine that is used and different ionization methods like cold spray or nanospray can be used to detect the discussed spheres. The solvent in which the sample is measured has a small influence on which charged species can be observed. Although the temperature didn’t show any influence on the measurements with nanospray (50–150 °C), measuring the large spheres with cryospray at –40 °C resulted in clear spectra and no fragmentation of the spheres was observed. Complex mass spectra are obtained when mixtures of spheres are measured with MS, which gives the possibility to determine most of the species present in such a mixture.

2.5 Acknowledgements

Arnout Hartendorp is kindly acknowledged for the synthesis and DOSY experiments with the fluorous building block. Ludwig Grobe is kindly acknowledged for the synthesis of the pyrrole building block. Jan-Meine Ernsting is acknowledged for his help with the DOSY experiments. Marc Duursma is acknowledged for helping with the CSI-FT-ICR measurements. Petra Jansen is acknowledged for the help with the nanospray measurements. Ed Zuidinga is thanked for his help with the mass measurements and helpful discussions. Maximilian Dürr is acknowledged for his help with the Cryospray measurements (CSI-MS).
2.6 Experimental Section

General Experimental
All reactions were carried out under an nitrogen atmosphere using standard Schlenk techniques when noted. Solvents were distilled prior to utilization by conventional methods. NMR spectra were measured on a Bruker AMX 400, DRX 500 and DRX 300 spectrometer. $^1$H NMR spectral data were referenced to solvent residual signal [7.26 ppm for CDCl$_3$, 4.79 ppm for D$_2$O, 1.94 ppm for CD$_3$CN, 5.32 for CD$_2$Cl$_2$]. $^{13}$C NMR chemical shifts are reported relative to deuterated solvents [77.1 ppm for CD$_3$CN, 53.8 for CD$_2$Cl$_2$, 118.26 for CD$_3$CN]. 2D $^1$H-DOSY were performed on a DRX 300 with the temperature and gradient calibration prior to the measurements, and the temperature was controlled at 298 K during the measurements. The log D value of the solvent (CD$_3$CN) was consistent each time and in line with the literature. Mass spectra were collected on an AccuToF LC, JMS-T100LP Mass spectrometer (JEOL, Japan) (for ESI) and AccuToF GC v 4g, JMS-T100GCV Mass spectrometer (JEOL, Japan) (for FD). Elemental analysis was performed by Microanalytisches Laboratorium Kolbe (Mülheim an der Ruhr, Germany). CSI-MS measurements were recorded on a UHR-ToF Bruker Daltonik (Bremen, Germany) maXis, an ESI-ToF MS capable of resolution of at least 40,000 FWHM, which was coupled to a Bruker cryospray unit. Detection was in positive-ion mode and the source voltage was between 5 kV and 6 kV. The flow rates were 280 µL/hour. The drying gas (N$_2$) was held at –35 °C and the spray gas was held at –40 °C. The machine was calibrated prior to every experiment via direct infusion of the Agilent ESI-ToF low concentration tuning mixture, which provided an $m/z$ range of singly charged peaks up to 2700 Da in both ion modes. All reagents were purchased from commercial suppliers and used without further purification.

Diffusion Ordered NMR Spectroscopy:
DOSY was measured on a Bruker DRX 300 with temperature and gradient calibration. The temperature was controlled at 298 K during the measurements. The log D value of the solvent (CD$_3$CN) was consistent each time and in line with the literature value of Log D = -8.36. Parameters used for DOSY are: $\delta$=1200 µs (p30), $\Delta$=0.2 s (d20) with an applied gradient from 2% to 98% divided over 240 steps. The amount of scans per spectrum is 32. Concentration of the sample for the measurement is based on 10 µmol building block in 0.5 mL CD$_3$CN. For the mixed sphere systems 0.25 mL of pure sphere solutions were combined and measured.

Mass spectrometry:
Orbitrap measurements were done on a LTQ-FT hybrid mass spectrometer (Thermo Fisher 15 Scientific, Bremen, Germany) with a self-modified cryospray setup. The machine designed by JEOL for CSI measurements was an AccuToF LC, JMS-T100LP Mass spectrometer (JEOL, Japan). For the measurement at –40 °C the needle voltage was kept at 2600 V, orifice 1 at 81 V, orifice 2 at 1 V and the ring lens at 1 V. Nanospray measurements were done on a TripleToF 5600 from Sciex configured with nanospray source. Sample flow rate was kept at 0.5 ìL/min, ionspray voltage floating current: 2400 V, ion source flow rate: 12, temperate: 150 °C. CSI-MS measurements were recorded on a UHR-ToF Bruker Daltonik (Bremen, Germany) maXis, an ESI-ToF MS capable of resolution of at least 40,000 FWHM, which was coupled to a Bruker cryospray unit. Detection was in positive-ion mode and the source voltage was between 5 kV and 6 kV. The flow rates were 280 µL/hour. The drying gas (N$_2$) was held at –35 °C and the spray gas was held at –40 °C. The machine was calibrated prior to every experiment via direct infusion of the Agilent ESI-ToF low concentration tuning mixture, which provided an $m/z$ range of singly charged peaks up to 2700 Da in both ion modes. All the reported HRMS data with CSI were measured with the BrukerUHR-ToF.

Synthesis of compounds and building blocks:
Pyrrole (Pyr)$^{30}$ and methoxy (OMe)$^{11}$ building blocks were synthesized according to literature.
1,3-dibromo-benzene functionalized with fluorine tail (2)

A flame dried Schlenk was charged with 3,5-dibromophenol (3.0 g, 11.91 mmol, 1 equiv.) and triphenylphosphine (3.12 g, 11.91 mmol, 1 equiv.). The solids were dissolved in 30 mL of THF to obtain an orange solution, which, after the addition of DIAD (2.43 g, 12.0 mmol, 1 equiv.) turned into a dark red solution. After stirring the mixture for 30 minutes, 1H,1H,2H,2H-perfluoro-1-decanol (5.57 g, 12.0 mmol, 1 equiv.) was added and the resulting mixture was stirred at room temperature for overnight. Then, the reaction was concentrated to a brown oil and purified using column chromatography (SiO2) with 100% hexane to obtain a white powder in 17% yield (1.4 g, 2.0 mmol).

1H NMR (400 MHz, CDCl3) δ 7.32 (t, J = 1.6 Hz, 1H), 7.03 (d, J = 1.6 Hz, 2H), 4.26 (t, J = 6.6 Hz, 2H), 2.65 (tt, J = 18.3, 6.7 Hz, 2H).

13C NMR (101 MHz, CDCl3) δ 159.02, 127.17, 123.15, 116.82, 60.47, 31.25, 31.03, 30.81.

19F NMR (376 MHz, CDCl3) δ -80.75 (t, J = 10.1 Hz), -113.26 (m), -121.39 – -121.75 (m), -121.75 – -122.19 (m), -122.52 – -122.90 (m), -123.34 – -123.58 (m), -125.90 – -126.34 (m).

Building Block F

A flame dried Schlenk was charged with (PhCN)2PdCl2 (46 mg, 0.12 mmol, 0.06 equiv.), 0.070 g [HP(t-Bu)3]BF4 (0.24 mmol, 0.12 equiv.) and NEt3 (2.93 ml, 21.02 mmol, 10.5 equiv.). A separate flame dried Schlenk was charged with 4-ethynlypyridine hydrochloride (0.0726 g, 5.2 mmol, 2.6 equiv.), copper iodide (0.015 g, 0.08 mmol, 0.04 equiv.) and a solution of (1396 mg, 2 mmol, 1 equiv.) in dioxane (12 mL) was added. This solution was added to the first solution and placed in a preheated oil bath of 45 °C and stirred for 16 hours. The resulting suspension was diluted with 36 mL ethyl acetate and 36 mL H2O and 1 mL ethylene diamine were added. After extraction with ethyl acetate (3x36 mL), the combined organic layers were dried over NaSO4. Filtration and concentrated in vacuo yielded a brown powder which was purified with column chromatography (SiO2), CHCl3 : methanol (100:1) to obtain 0.56 g of a white powder (0.8 mmol, 40%).

1H NMR (400 MHz, CD3CN) δ 8.69 – 8.57 (m, 4H), 7.53 – 7.46 (m, 4H), 7.44 (t, J = 1.3 Hz, 1H), 7.26 (d, J = 1.4 Hz, 2H), 4.41 (t, J = 6.1 Hz, 2H), 2.84 – 2.67 (m, 2H).

13C NMR (75 MHz, CD3CN, NOTE: one C peak is missing and expected underneath solvent peak at 120 ppm) δ 159.29, 152.06, 136.23, 129.91, 123.82, 97.84, 86.52, 62.05 – 61.69 (m), 31.49 (t, J = 22.3 Hz).

19F NMR (282 MHz, CD3CN) δ -81.59 (t, J = 10.6 Hz), -112.68 – -114.12 (m), -121.44 – -122.76 (m), -123.18 , -123.99 , -126.62 , -150.74.


Pd12F24(BF4)24

A vial was charged with F (7.4 mg, 10 µmol, 1 equiv.) and dissolved in CD3CN (0.8 mL). A solution of [Pd(MeCN)4](BF4)2 (2.2 mg, 5 µmol, 0.5 equiv.) in CD3CN (0.2 mL) was added and the resulting clear solution was heated at 70 °C for 3 hours. 1H NMR (300 MHz, CD3CN) δ 8.91 (d, J = 6.3 Hz, 4H), 7.64 (d, J = 6.0 Hz, 4H), 7.45 (s, 1H), 7.26 (d, J = 1.5 Hz, 2H), 4.34 (bs, 2H), 2.93 – 2.57 (m, 2H).

13C NMR (75 MHz, CD3CN, NOTE: one C peak is missing and expected underneath solvent peak at 120 ppm) δ 159.29 , 152.06 , 136.23 , 129.91 , 123.82 , 121.18 , 97.84 , 86.52 , 62.05 – 61.69 (m), 31.49 (t, J = 22.3 Hz).

19F NMR (282 MHz, CD3CN) δ -81.59 (t, J = 10.6 Hz), -112.68 – -114.12 (m), -121.44 – -122.76 (m), -123.18 , -123.99 , -126.62 , -150.74. HRMS (EI+): calc. for C30H15F17N2O: 742.0913 [M]+ found 742.0936.
Characterization of Molecular Spheres through Diffusion NMR and Mass Spectroscopy

**Pd$_{12}$OMe$_{24}$(BF$_4$)$_{24}$**
A vial was charged with OMe (3.1 mg, 10 µmol, 1 equiv.) and dissolved in CD$_3$CN (0.8 mL). A solution of [Pd(MeCN)$_4$(BF$_4$)$_2$] (2.2 mg, 5 µmol, 0.5 equiv.) in CD$_3$CN (0.2 mL) was added and the resulting pale yellow solution was heated at 70 °C for 1 hour. **H NMR** (300 MHz, CD$_3$CN) δ 9.03 – 8.84 (m, 4H), 7.82 – 7.49 (m, 6H), 7.20 (t, $J = 8.7$ Hz, 1H), 4.11 (s, 3H). **13C NMR** (75 MHz, CD$_3$CN) δ 164.39 (Ar-C), 151.91 (Py-CH), 137.23 (Ar-C), 136.37 (Ar-CH), 129.68 (Py-CH), 125.34 (Py-C), 116.29 (Ar-CH), 95.15 (C≡C), 90.37 (C≡C), 62.94 (OCH$_3$). **DOSY** (CD$_3$CN, 25 °C): log D = -9.45 m$^2$/s. **19F NMR** (282 MHz, CD$_3$CN) δ -150.27. **HRMS** (CSI+): Species Charge Found [m/z] Calculated [m/z] Pd$_{12}$OMe$_{24}$(BF$_4$)$_{10}$ 14+ 685.2533 685.2537 Pd$_{12}$OMe$_{24}$(BF$_4$)$_{11}$ 13+ 744.5808 744.5812 Pd$_{12}$OMe$_{24}$(BF$_4$)$_{12}$ 12+ 813.8800 Pd$_{12}$OMe$_{24}$(BF$_4$)$_{13}$ 11+ 895.7786 Pd$_{12}$OMe$_{24}$(BF$_4$)$_{14}$ 10+ 944.0568 Pd$_{12}$OMe$_{24}$(BF$_4$)$_{15}$ 9+ 1114.1747 Pd$_{12}$OMe$_{24}$(BF$_4$)$_{16}$ 8+ 1264.1971 Pd$_{12}$OMe$_{24}$(BF$_4$)$_{17}$ 7+ 1457.2259 Pd$_{12}$OMe$_{24}$(BF$_4$)$_{18}$ 6+ 1714.5975

**Pt$_6$OMe$_{12}$(PF$_6$)$_{12}$**
A vial was charged with OMe (3.1 mg, 10 µmol, 1 equiv.) and dissolved in DMSO:TFE (3:7 ratio, 0.8 mL). A solution of [Pt(MeCN)$_4$(PF$_6$)$_2$] (3.3 mg, 5 µmol, 0.5 equiv.) in DMSO:TFE (3:7 ratio, 0.2 mL) was added and the resulting solution was heated at 70 °C for 24 hours. Due to the use of non-deuterated TFE not all **H NMR** peaks could be observed. However are clear pyridine peak at δ = 9 ppm was observed, indicating sphere formation. The resulting solution was injected without dilution in the CSI-MS. **HRMS** (CSI+): Species Charge Found [m/z] Calculated [m/z] Pt$_6$OMe$_{12}$(PF$_6$)$_3$ 9+ 592.1121 592.1121 Pt$_6$OMe$_{12}$(PF$_6$)$_4$ 8+ 684.2467 Pt$_6$OMe$_{12}$(PF$_6$)$_5$ 7+ 802.7055 Pt$_6$OMe$_{12}$(PF$_6$)$_6$ 6+ 960.6505 Pt$_6$OMe$_{12}$(PF$_6$)$_7$ 5+ 1181.7736

**Statistical mixture of Pd$_{12}$F$_{12}$OMe$_{12}$(BF$_4$)$_{24}$**
A mixture of Pd$_{12}$OMe$_{24}$ (5/24 µmol) and Pd$_{12}$F$_{24}$ (5/24 µmol) was heated in a NMR tube at 70 °C for overnight. **H NMR** showed no change in chemical shift but DOSY and HRMS confirmed the statistical mixture. **H NMR** (300 MHz, CD$_3$CN) δ 8.92 (s br, 8H, ‘F+OMe’), 7.82 – 7.53 (m, 10H, ‘F+OMe’), 7.45 (s, 1H, ‘F’), 7.26 (s, 2H, ‘F’), 7.21 (t, $J = 7.3$ Hz, 1H, ‘OMe’), 4.34 (s, 2H, ‘F’), 4.11 (s, 3H, ‘OMe’), 2.70 (t, $J = 20.0$ Hz, 2H, ‘F’). **DOSY** (CD$_3$CN, 25 °C): log D = -9.49 m$^2$/s. **HRMS** (CSI+), a selection of peaks was made as, due to the statistical mixture, many species were observed:

<table>
<thead>
<tr>
<th>Species</th>
<th>Charge</th>
<th>Found [m/z]</th>
<th>Calculated [m/z]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pd$<em>{12}$OMe$</em>{13}$F$_{11}$(BF$<em>4$)$</em>{11}$</td>
<td>13+</td>
<td>1110.1823</td>
<td>1110.1805</td>
</tr>
<tr>
<td>Pd$<em>{12}$OMe$</em>{12}$F$_{12}$(BF$<em>4$)$</em>{11}$</td>
<td>13+</td>
<td>1143.4113</td>
<td>1143.4098</td>
</tr>
<tr>
<td>Pd$<em>{12}$OMe$</em>{11}$F$_{13}$(BF$<em>4$)$</em>{11}$</td>
<td>13+</td>
<td>1176.7167</td>
<td>1176.7161</td>
</tr>
<tr>
<td>Pd$<em>{12}$OMe$</em>{13}$F$_{11}$(BF$<em>4$)$</em>{12}$</td>
<td>12+</td>
<td>1209.9455</td>
<td>1209.9459</td>
</tr>
<tr>
<td>Pd$<em>{12}$OMe$</em>{12}$F$_{12}$(BF$<em>4$)$</em>{12}$</td>
<td>12+</td>
<td>1245.9443</td>
<td>1245.9443</td>
</tr>
<tr>
<td>Pd$<em>{12}$OMe$</em>{11}$F$_{13}$(BF$<em>4$)$</em>{12}$</td>
<td>12+</td>
<td>1281.9427</td>
<td>1281.9427</td>
</tr>
<tr>
<td>Pd$<em>{12}$OMe$</em>{13}$F$_{11}$(BF$<em>4$)$</em>{13}$</td>
<td>11+</td>
<td>1327.8505</td>
<td>1327.8505</td>
</tr>
<tr>
<td>Pd$<em>{12}$OMe$</em>{12}$F$_{12}$(BF$<em>4$)$</em>{13}$</td>
<td>11+</td>
<td>1376.1215</td>
<td>1376.1215</td>
</tr>
<tr>
<td>Pd$<em>{12}$OMe$</em>{11}$F$_{13}$(BF$<em>4$)$</em>{13}$</td>
<td>11+</td>
<td>1406.3925</td>
<td>1406.3925</td>
</tr>
<tr>
<td>Pd$<em>{12}$OMe$</em>{13}$F$_{11}$(BF$<em>4$)$</em>{14}$</td>
<td>10+</td>
<td>1469.3360</td>
<td>1469.3360</td>
</tr>
</tbody>
</table>
A vial was charged with pyrrole Pyr (20 µmol, 4.4 mg, 1 equiv.) and dissolved in 0.8 mL of CD$_3$CN. The solution of 4.4 mg of [Pd(MeCN)$_4$](BF$_4$)$_2$ (10 µmol, 0.5 equiv.) in 0.2 mL CD$_3$CN was added and the resulting yellow solution was stirred at 70 °C for 3 hours. $^1$H NMR (300 MHz, CD$_3$CN) δ 10.38 (d, $J = 35.0$ Hz, 1H), 9.20 – 8.65 (m, 4H), 7.98 – 7.55 (m, 4H), 6.95 (d, $J = 33.8$ Hz, 2H). $^{13}$C NMR (75 MHz, CD$_3$CN) δ 150.80, 141.53, 132.00, 121.23, 114.59. $^{19}$F NMR (282 MHz, CD$_3$CN) δ -150.48. DOSY (CD$_3$CN, 25 °C): log D = -9.49 m$^2$/s. HRMS (CSI+):

<table>
<thead>
<tr>
<th>Species</th>
<th>Charge</th>
<th>Found [m/z]</th>
<th>Calculated [m/z]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pd$<em>{24}$Pyr$</em>{48}$(BF$<em>4$)$</em>{30}$</td>
<td>18+</td>
<td>876.7461</td>
<td>876.5576</td>
</tr>
<tr>
<td>Pd$<em>{24}$Pyr$</em>{48}$(BF$<em>4$)$</em>{31}$</td>
<td>17+</td>
<td>933.2611</td>
<td>933.2589</td>
</tr>
<tr>
<td>Pd$<em>{24}$Pyr$</em>{48}$(BF$<em>4$)$</em>{32}$</td>
<td>16+</td>
<td>997.2148</td>
<td>996.9629</td>
</tr>
<tr>
<td>Pd$<em>{24}$Pyr$</em>{48}$(BF$<em>4$)$</em>{33}$</td>
<td>15+</td>
<td>1069.2296</td>
<td>1069.2273</td>
</tr>
<tr>
<td>Pd$<em>{24}$Pyr$</em>{48}$(BF$<em>4$)$</em>{34}$</td>
<td>14+</td>
<td>1152.4741</td>
<td>1151.8153</td>
</tr>
<tr>
<td>Pd$<em>{24}$Pyr$</em>{48}$(BF$<em>4$)$</em>{35}$</td>
<td>13+</td>
<td>1247.1123</td>
<td>1247.1091</td>
</tr>
<tr>
<td>Pd$<em>{24}$Pyr$</em>{48}$(BF$<em>4$)$</em>{36}$</td>
<td>12+</td>
<td>1358.2903</td>
<td>1358.2852</td>
</tr>
<tr>
<td>Pd$<em>{24}$Pyr$</em>{48}$(BF$<em>4$)$</em>{37}$</td>
<td>11+</td>
<td>1490.0431</td>
<td>1489.5843</td>
</tr>
<tr>
<td>Pd$<em>{24}$Pyr$</em>{48}$(BF$<em>4$)$</em>{38}$</td>
<td>10+</td>
<td>1647.4489</td>
<td>1647.2431</td>
</tr>
</tbody>
</table>

Mixture of Pd$_{12}$Pyr$_x$OMe$_{24-x}$(BF$_4$)$_{24}$ (x=1-6)

In a NMR tube a solution of Pd$_{12}$Pyr$_{48}$ (5/24 µmol) and Pd$_{12}$OMe$_{24}$ (5/24 µmol) were mixed and at 70 °C for 8 hours. HRMS (CSI+), only the 12+,10+ and 6+ species are given, due to the statistical mixture, many species were observed:

<table>
<thead>
<tr>
<th>Species</th>
<th>Charge</th>
<th>Found [m/z]</th>
<th>Calculated [m/z]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pd$<em>{12}$OMe$</em>{20}$Pyr$_4$(BF$<em>4$)$</em>{12}$</td>
<td>12+</td>
<td>784.2110</td>
<td>784.2081</td>
</tr>
<tr>
<td>Pd$<em>{12}$OMe$</em>{22}$Pyr$_3$(BF$<em>4$)$</em>{12}$</td>
<td>12+</td>
<td>799.0460</td>
<td>799.0441</td>
</tr>
<tr>
<td>Pd$<em>{12}$OMe$</em>{23}$Pyr$_2$(BF$<em>4$)$</em>{12}$</td>
<td>12+</td>
<td>806.4639</td>
<td>806.4620</td>
</tr>
<tr>
<td>Pd$<em>{12}$OMe$</em>{24}$Pyr$_1$(BF$<em>4$)$</em>{12}$</td>
<td>12+</td>
<td>813.8817</td>
<td>813.8800</td>
</tr>
<tr>
<td>Pd$<em>{12}$OMe$</em>{25}$Pyr$_0$(BF$<em>4$)$</em>{12}$</td>
<td>10+</td>
<td>940.5490</td>
<td>940.5475</td>
</tr>
<tr>
<td>Pd$<em>{12}$OMe$</em>{26}$Pyr$_0$(BF$<em>4$)$</em>{12}$</td>
<td>10+</td>
<td>949.4511</td>
<td>949.4490</td>
</tr>
<tr>
<td>Pd$<em>{12}$OMe$</em>{27}$Pyr$_0$(BF$<em>4$)$</em>{12}$</td>
<td>10+</td>
<td>958.3526</td>
<td>958.3506</td>
</tr>
<tr>
<td>Pd$<em>{12}$OMe$</em>{28}$Pyr$_0$(BF$<em>4$)$</em>{12}$</td>
<td>10+</td>
<td>967.2540</td>
<td>967.2522</td>
</tr>
<tr>
<td>Pd$<em>{12}$OMe$</em>{29}$Pyr$_0$(BF$<em>4$)$</em>{12}$</td>
<td>10+</td>
<td>976.2559</td>
<td>976.2537</td>
</tr>
<tr>
<td>Pd$<em>{12}$OMe$</em>{30}$Pyr$_0$(BF$<em>4$)$</em>{12}$</td>
<td>10+</td>
<td>985.1574</td>
<td>985.1553</td>
</tr>
<tr>
<td>Pd$<em>{12}$OMe$</em>{31}$Pyr$_0$(BF$<em>4$)$</em>{12}$</td>
<td>10+</td>
<td>994.0590</td>
<td>994.0568</td>
</tr>
<tr>
<td>Pd$<em>{12}$OMe$</em>{18}$Pyr$_6$(BF$<em>4$)$</em>{12}$</td>
<td>6+</td>
<td>1625.5848</td>
<td>1625.5820</td>
</tr>
<tr>
<td>Pd$<em>{12}$OMe$</em>{19}$Pyr$_5$(BF$<em>4$)$</em>{12}$</td>
<td>6+</td>
<td>1640.5869</td>
<td>1640.5846</td>
</tr>
<tr>
<td>Pd$<em>{12}$OMe$</em>{20}$Pyr$_4$(BF$<em>4$)$</em>{12}$</td>
<td>6+</td>
<td>1655.2565</td>
<td>1655.2538</td>
</tr>
<tr>
<td>Pd$<em>{12}$OMe$</em>{21}$Pyr$_4$(BF$<em>4$)$</em>{12}$</td>
<td>6+</td>
<td>1670.0919</td>
<td>1670.0897</td>
</tr>
<tr>
<td>Pd$<em>{12}$OMe$</em>{22}$Pyr$_4$(BF$<em>4$)$</em>{12}$</td>
<td>6+</td>
<td>1684.9294</td>
<td>1684.9257</td>
</tr>
<tr>
<td>Pd$<em>{12}$OMe$</em>{23}$Pyr$_4$(BF$<em>4$)$</em>{12}$</td>
<td>6+</td>
<td>1699.7646</td>
<td>1699.7616</td>
</tr>
<tr>
<td>Pd$<em>{12}$OMe$</em>{24}$(BF$<em>4$)$</em>{12}$</td>
<td>6+</td>
<td>1714.6601</td>
<td>1714.5975</td>
</tr>
</tbody>
</table>
2.7 References