Title: Self-assembled palladium and platinum coordination cages: Photophysical studies and anticancer activity

Authors: Felix Kaiser; Andrea Schmidt; Wolfgang Heydenreuter; Philipp Johannes Altmann; Angela Casini; Stephan A. Sieber; Fritz Elmar Kühn

This manuscript has been accepted after peer review and the authors have elected to post their Accepted Article online prior to editing, proofing, and formal publication of the final Version of Record (VoR). This work is currently citable by using the Digital Object Identifier (DOI) given below. The VoR will be published online in Early View as soon as possible and may be different to this Accepted Article as a result of editing. Readers should obtain the VoR from the journal website shown below when it is published to ensure accuracy of information. The authors are responsible for the content of this Accepted Article.

To be cited as: Eur. J. Inorg. Chem. 10.1002/ ejic.201600811

Link to VoR: http://dx.doi.org/10.1002/ ejic.201600811
Self-assembled palladium and platinum coordination cages: Photophysical studies and anticancer activity


Abstract: Self-assembled coordination cages are interesting as drug delivery systems. Therefore, the synthesis of new $\text{M}_2\text{L}_4$ (M = Pd, Pt) molecular cages, derived from highly fluorescent, rigid polyaromatic ligands is reported and the first $\text{Pd}_2\text{L}_4$ cage with a ligand and a second ligand and a second ligand as simply mixing bidentate ligands and metal precursors. The assemblies rely largely on coordinative interactions of Pd$^{2+}$ and pyridine moieties,[2] although some examples with different metal ions, such as Pt$^{2+}$,[3] Cu$^{2+}$,[4] and Zn$^{2+}$ are known.[3a, 4a] So far only a few fluorescent $\text{M}_2\text{L}_4$ cages were obtained using ligands with extensive π-systems or attached fluorophores,[3a, 4] although highly fluorescent metallocages would be very interesting for biological imaging in cells by fluorescence microscopy. Aside from fluorescence, the encapsulation of (counter)ions has been reported.[4a-d, 5a, 7] Moreover, supramolecular coordination complexes are also capable to encapsulate metal compounds[2b, 6b, 8] (e.g. cisplatin) and some of them have been tested concerning most widely applied anticancer agent against ovarian, bladder and testicular cancer to name just a few.[10] However, its effectiveness is accompanied by severe side effects, thus limiting the applicable dose.[10b] The necessity to reduce side effects and toxicity of cisplatin and its derivatives has gained growing appreciation in current research. One possibility is to utilize the so called EPR (= enhanced permeability and retention) effect, which was discovered in 1986 by Maeda and Matsamura.[11] Until now a plethora of vectors for cisplatin has been examined, e. g. liposomes,[12] nanoparticles,[13] macrocycles,[14] and as already mentioned above, also metallocages.[8c, 9] Recently, our group evaluated palladium cage compounds as drug delivery systems for cisplatin in vitro in cancer cells and ex vivo in healthy rat liver tissue.[8b, 8a] Goal of this research is to ensure a safe transport of the active molecules selectively to the target entity. Solubility, toxicity and size of the transporter are of high importance in this context. Based on recent results, in this work the synthesis and characterization of new $\text{M}_2\text{L}_4$ molecular cages with enhanced solubility are described. The photophysical properties of the metallocages were investigated, in order to examine the possibility of uptake studies in cells. The incorporation of electron-donating methoxy groups in the ligand framework could potentially increase the photoluminescence of the ligands, thus enhancing the emissive properties of the metallocages. Moreover, the host-guest relationship with cisplatin is examined for the palladium cages and the cytotoxicity of the cages and their cisplatin inclusion compounds towards human cancer cells is examined in vitro.

Introduction

Almost two decades have passed, since McMorrn and Steel reported the first $\text{Pd}_2\text{L}_4$ molecular cage, capable of enclosing a hexafluorophosphate counterion.[11] Since then increasing interest on $\text{M}_2\text{L}_4$ complexes with inner cavities has emerged, as they are readily accessible through self-assembly by simply mixing bidentate ligands and metal precursors. The assemblies rely largely on coordinative interactions of Pd$^{2+}$ and pyridine moieties,[2] although some examples with different metal ions, such as Pt$^{2+}$,[3] Cu$^{2+}$,[4] and Zn$^{2+}$ are known.[3a, 4a] So far only a few fluorescent $\text{M}_2\text{L}_4$ cages were obtained using ligands with extensive π-systems or attached fluorophores,[3a, 4] although highly fluorescent metallocages would be very interesting for biological imaging in cells by fluorescence microscopy. Aside from fluorescence, the encapsulation of (counter)ions has been reported.[4a-d, 5a, 7] Moreover, supramolecular coordination complexes are also capable to encapsulate metal compounds[2b, 6b, 8] (e.g. cisplatin) and some of them have been tested concerning their cytotoxicity for cancer cells.[8a-e, 9] Cisplatin is one of the...
Isostructural M$_2$L$_4$ (M = Pd, Pt) cages 2$^{Pd}$, 3$^{Pd}$ and 3$^{Pt}$ were obtained through self-assembly of the ligands 2 and 3 with [Pd(NCCH$_3$)$_4$(BF$_4$)$_2$] or [Pt(NCCH$_3$)$_2$Cl$_2$] and AgClO$_4$, respectively (Scheme 2).

The cages were prepared from a suspension of stoichiometric amounts of the starting materials in acetonitrile by heating to reflux for one hour (Pd) or two days (Pt). For the platinum cage 3$^{Pt}$ a purification step via column chromatography was necessary.

Cage formation was validated by $^1$H NMR, DOSY NMR, ESI HRMS, and X-ray structure analysis. In $^1$H NMR spectra, significant shifts are observed, when comparing the cages and the corresponding free ligands (Figure 1 and Figure 2).

All proton signals of both ligands 2 and 3, and of the complexes 2$^{Pd}$, 3$^{Pd}$, and 3$^{Pt}$ show the same diffusion coefficient ($D$). The ratio $D_{ligand}$ to $D_{complex}$ is approximately 2:1, which is due to the presence of larger cage molecules in solution. Using the Einstein-Stokes correlation, the Stokes radii $r_0$ were calculated for each cage compound. The values are given in Table 1.

Electrospray ionization high-resolution mass spectra (ESI HRMS) provide additional support for the formation of the cage complexes. For every cage the signals for the tetra-cationic unit [M$_2$L$_4$]$^{4+}$ (M$^{2+}$ = Pd$^{2+}$, Pt$^{2+}$; L = 2, 3) and its association with one or two counterions, [M$_2$L$_4$](X)$_{n-}$ ($X^{-}$ = BF$_4^-$, ClO$_4^-$) are clearly observable (Figure 3, SI). The isotopic distributions fit calculated values, which are exemplarily depicted in Figure 4 for the fragment [Pt$_3$L$_3$](X)$_{n-}$ in 3$^{Pt}$.
X-ray single crystal structure analysis reveals the formation of paddle wheel shaped coordination cages. Single crystals suitable for single crystal X-ray diffraction were grown by vapor diffusion of diethyl ether into an acetonitrile solution of 2\textsuperscript{Pd} and likewise a solution of 3\textsuperscript{Pd} in acetone over several days. Cage compound 2\textsuperscript{Pd} crystallizes in the triclinic space group \(\overline{P}\) with the inversion center located centrally inside the cavity (Figure 5).

Each Pd\textsuperscript{II} ion is coordinated in a square-planar fashion by pyridyl moieties of four molecules 2 (angles N–Pd–N between 88.6(1)° and 90.8(2)°), resulting in a lantern-shaped cage with a central cavity. The latter is stocked with disordered solvent molecules, not with counterions. The anions are disordered and located outside the cage, half of them at the apical position of Pd. These observations are in accordance to previously reported results,\[8g\] although numerous examples of M\textsubscript{2}L\textsubscript{4} cage compounds with encapsulated counterions exist in literature as well.\[1, 6a, 7a, 17\] The cage diameter, calculated between two opposing methoxy-moieties is \(\approx 22.6\ \text{Å}\) (averaged distances between outer hydrogen atoms). This fits the value calculated from diffusion coefficients (\(\approx 22.9\ \text{Å}\)) well (Table 1). The Pd–Pd distance is 12.0 Å, diagonally opposing central carbon atoms display an averaged distance of 10.5 Å.

Cage 3\textsuperscript{Pd} also crystallizes in the triclinic space group \(\overline{P}\) with an inversion center located centrally inside the cage (Figure 6). The Pd\textsuperscript{II} ions are again coordinated in a square-planar fashion to one pyridyl moiety of four ligand molecules 3. The resulting lantern-shaped cage compound exhibits a central cavity that is occupied by two non-disordered acetone molecules. The respective carbonyl oxygen atoms are pointing to the metal ions with a distance of Pd–O of 3.3 Å. The methyl groups are orientated towards the ligands’ central pyridine N-atoms with an averaged distance C–N of 3.6 Å. As in 2\textsuperscript{Pd}, the BF\textsubscript{4}\textsuperscript{−} counterions are located outside the cage, half of them at the apical position of
Pd\textsuperscript{II}. The cage diameter calculated between two opposing methoxy-moieties is ≈22.4 Å (averaged distances between outer hydrogen atoms), which correlates well with the value calculated from diffusion coefficients (≈21.9 Å, Table 1). The distance between the two Pd atoms is 11.6 Å, diagonally opposing central pyridine N display an averaged distance of 10.9 Å.

**Figure 6.** Molecular structure of 3\textsuperscript{Pd}. Thermal ellipsoids are shown at a 50% probability level. Side view, drawn with two encapsulated acetone molecules (spacefilling representation at 100% of van-der-Waals radii, visualizing the steric demand inside the cage); H and counter ions omitted for clarity. Element colors: C – grey, N – blue, O – red, Pd – turquoise.

Complexes 2\textsuperscript{Pd}, 3\textsuperscript{Pd} and 3\textsuperscript{Pt} are soluble in polar solvents like DMSO, DMF, acetonitrile and acetone but insoluble in chloroform, dichloromethane, pentanes or diethyl ether. They are stable in solid state and in solution for weeks. Compound 3\textsuperscript{Pt} is slightly sensitive to oxygen and thus has to be stored under an argon atmosphere.

The ligands’ and cages’ photophysical properties show a striking dependence on the coordination of metal ions, especially concerning photoluminescence. The absorption spectra of ligand 2 and its corresponding cage are depicted in Figure 7. Ligand 2 displays its strongest absorption bands between 210 and 320 nm and a weaker band is located between 330 and 370 nm. The absorption maximum is observed at 232 nm, with an extinction coefficient \(\varepsilon_{232} (2) = 47700 \text{ l} \cdot \text{mol}^{-1} \cdot \text{cm}^{-1}\). Upon coordination to Pd\textsuperscript{II} a bathochromic shift of 9 nm is observed and absorption increases by 3.78 (\(\varepsilon_{232} (2\textsuperscript{Pd}) = 180500 \text{ l} \cdot \text{mol}^{-1} \cdot \text{cm}^{-1}\)), only differing by 5% from the estimated quadrupling with respect to the four molecules 2 per complex 2\textsuperscript{Pd}.

**Figure 7.** UV/Vis-spectra of 2 (c = 2 \cdot 10^{-5} M, black) and 2\textsuperscript{Pd} (c = 5 \cdot 10^{-5} M, red) in MeCN, width of cuvette: 10 mm.

As shown in Figure 8, ligand 3 shows strong absorptions between 200 and 330 nm with a local absorption maximum at 321 nm. It displays an extinction coefficient \(\varepsilon_{321} (3) = 32500 \text{ l} \cdot \text{mol}^{-1} \cdot \text{cm}^{-1}\). Through coordination to Pd\textsuperscript{II} or Pt\textsuperscript{II} the band shapes alter, resulting in formal hypsochromic shifts of the maxima (313 nm for Pd\textsuperscript{II} and 314 nm for Pt\textsuperscript{II}). The extinction coefficients rise by factors 4.51 and 3.36, respectively to \(\varepsilon_{313} (3\textsuperscript{Pd}) = 146600 \text{ l} \cdot \text{mol}^{-1} \cdot \text{cm}^{-1}\) and \(\varepsilon_{314} (3\textsuperscript{Pt}) = 109300 \text{ l} \cdot \text{mol}^{-1} \cdot \text{cm}^{-1}\), differing +13% and -16% from the expected quadrupling due to the presence of four ligand molecules per cage. Furthermore, upon coordination each a new maximum is observed at 230 nm and 229 nm with extinction coefficients of \(\varepsilon_{230} (3\textsuperscript{Pd}) = 171400 \text{ l} \cdot \text{mol}^{-1} \cdot \text{cm}^{-1}\) and \(\varepsilon_{229} (3\textsuperscript{Pt}) = 142200 \text{ l} \cdot \text{mol}^{-1} \cdot \text{cm}^{-1}\).

**Figure 8.** UV/Vis-spectra of 3 (c = 2 \cdot 10^{-5} M, black), 3\textsuperscript{Pd} (c = 5 \cdot 10^{-5} M, red) and 3\textsuperscript{Pt} (c = 5 \cdot 10^{-5} M, blue) in MeCN, width of cuvette: 10 mm.

While absorption properties of 2 and 3 show a minor influence of metal coordination, luminescence is strongly dependent on the metal. Excitation of a solution of 2 in acetonitrile with UV light leads to a strong emission (\(\varphi_{290 \text{ nm}} (2) = 42\%\)), with a maximum at \(\lambda_{\text{em,max}} (2) = 412 \text{ nm}\). However, coordination to Pd\textsuperscript{II} lowers significantly the quantum yield (\(\varphi_{290 \text{ nm}} (2\textsuperscript{Pd}) = 7\%\)), while the emission maximum remains almost unaffected \(\lambda_{\text{em,max}} (2\textsuperscript{Pd}) = 413 \text{ nm}\), \(\Delta \lambda_{\text{em,max}} = 1 \text{ nm}\), as depicted in Figure 9.

The ligands’ and cages’ photophysical properties show a striking dependence on the coordination of metal ions, especially concerning photoluminescence. The absorption spectra of ligand 2 and its corresponding cage are depicted in Figure 7. Ligand 2 displays its strongest absorption bands between 210 and 320 nm and a weaker band is located between 330 and 370 nm. The absorption maximum is observed at 232 nm, with an extinction coefficient \(\varepsilon_{232} (2) = 47700 \text{ l} \cdot \text{mol}^{-1} \cdot \text{cm}^{-1}\). Upon coordination to Pd\textsuperscript{II} a bathochromic shift of 9 nm is observed and absorption increases by 3.78 (\(\varepsilon_{232} (2\textsuperscript{Pd}) = 180500 \text{ l} \cdot \text{mol}^{-1} \cdot \text{cm}^{-1}\), only differing by 5% from the estimated quadrupling with respect to the four molecules 2 per complex 2\textsuperscript{Pd}.

**Figure 7.** UV/Vis-spectra of 2 (c = 2 \cdot 10^{-5} M, black) and 2\textsuperscript{Pd} (c = 5 \cdot 10^{-5} M, red) in MeCN, width of cuvette: 10 mm.
Ligand 3 shows an even higher quantum yield ($\Phi_{300\text{nm}}$ (3) = 48%), and as intended, the methoxy-functionalization leads to a significantly increased fluorescence compared to the unsubstituted ligand (48% vs. 1.1% $\Phi$).[8a]

Analogous to 2, upon coordination of PdII, the quantum yield is lowered significantly to $\Phi_{300\text{nm}}$ (3rd) = 3%, and the emission maximum is bathochromically shifted from $\lambda_{\text{em,max}}$ (3) = 345 nm to $\lambda_{\text{em,max}}$ (3rd) = 352 nm. Platinum cage 3rd is hardly emissive with a quantum yield of less than 0.2%. The emission maximum is almost the same as for 3rd ($\lambda_{\text{em,max}}$ (3rd) = 349 nm). The emission spectra of all three compounds are shown in Figure 10. Unfortunately, uptake studies of the cages in cells by fluorescence microscopy could not be performed due to low photoluminescence.

To examine the encapsulation properties of the palladium cages, solutions of 2rd and 3rd were treated with distinct amounts of cisplatin and analyzed by NMR spectroscopy. Convincing evidence for cisplatin encapsulation, both in 2rd and 3rd was received. Successive addition of 2 and 10 equivalents of cisplatin in DMF-d6 to a DMF-d6 solution of 2rd results in a significant broadening of the H2 signals. These hydrogen atoms are pointing directly into the cages inner cavity and thus apparently interact with encapsulated cisplatin guest molecules (Figure 11). The other signals remain unaffected. This behavior is consistent with a similar example reported earlier and was described as an indication for the encapsulation of cisplatin.[8a]

Figure 11. $^1$H NMR spectrum cutouts (400 MHz, CD$_2$CN, 296 K) of: a) 3rd, b) 2rd with 2 equiv. cisplatin, and c) 3rd with 10 equiv. cisplatin.

Addition of 2 equivalents of cisplatin to a CD$_2$CN solution of cage 3rd, heating to 60°C for 10 min and finally ultrasonic treatment for 2 min leads to a distinct, macroscopically visible dissolution of cisplatin. The $^1$H NMR spectrum gives also evidence for the encapsulation. Primarily the signal from H4 is broadened noticeably and furthermore shifted downfield, thus indicating an interaction with encapsulated guest molecules (Figure 12). This is consistent with similar literature results.[8a, c, g] Alkene experiments with 3rd resulted in decomposition products.

![Normalized intensity vs. wavelength for 2 and 2rd in acetonitrile upon excitation with UV light, intensities normalized.](image)

**Figure 9.** Luminescence spectra of 2 (2 $\cdot$ 10$^{-5}$ M, $\lambda_{\text{ex}}$ = 290 nm) and 2rd (5 $\cdot$ 10$^{-5}$ M, $\lambda_{\text{ex}}$ = 310 nm) in acetonitrile upon excitation with UV light, intensities normalized.

![Normalized intensity vs. wavelength for ligand 3, 3rd, and 3th in acetonitrile upon excitation with UV light, intensities normalized.](image)

**Figure 10.** Luminescence spectra in acetonitrile of 3 (2 $\cdot$ 10$^{-5}$ M, $\lambda_{\text{ex}}$ = 300 nm), 3rd (5 $\cdot$ 10$^{-5}$ M, $\lambda_{\text{ex}}$ = 310 nm) and 3th (5 $\cdot$ 10$^{-5}$ M, $\lambda_{\text{ex}}$ = 310 nm) in acetonitrile upon excitation with UV light, intensities normalized.

Table 2. IC$_{50}$ values of the compounds [µM] in A549 and HepG2, [(cisplatin)$_2$ $\rightarrow$ 2rd] and [(cisplatin)$_2$ $\rightarrow$ 3rd], normalized to the concentration of cisplatin.

<table>
<thead>
<tr>
<th>Compound</th>
<th>IC$_{50}$ [µM] (A549)</th>
<th>IC$_{50}$ [µM] (HepG2)</th>
</tr>
</thead>
<tbody>
<tr>
<td><a href="BF$_4$">Pd(NCCH$_3$)$_2$</a>$_2$</td>
<td>$&gt;$ 100</td>
<td>$&gt;$ 100</td>
</tr>
<tr>
<td>2$^a$</td>
<td>&gt; 100</td>
<td>&gt; 100</td>
</tr>
<tr>
<td>3$^a$</td>
<td>&gt; 100</td>
<td>&gt; 100</td>
</tr>
<tr>
<td>2rd$^a$</td>
<td>&gt; 100</td>
<td>&gt; 100</td>
</tr>
<tr>
<td>3rd$^a$</td>
<td>71.8 ± 9.1</td>
<td>44 ± 11</td>
</tr>
<tr>
<td>cisplatin</td>
<td>16.8 ± 0.7</td>
<td>6.7 ± 0.9</td>
</tr>
<tr>
<td>[(cisplatin)$_2$ $\rightarrow$ 2rd]</td>
<td>11.0 ± 1.3</td>
<td>5.2 ± 0.3</td>
</tr>
</tbody>
</table>

Copyright. All rights reserved.
As previously reported, this type of metallocages can potentially function as drug delivery systems due to their ability to encapsulate two molecules cisplatin. 1H NMR studies provide evidence of the encapsulation of cisplatin within cage 2Pd and 3Pd (see Figure 11 and Figure 12). The antiproliferative effects of the host-guest complexes [{cisplatin}2 = 2Pd] and [{cisplatin}2 = 3Pd] were studied against human carcinoma A549 and HepG2 (Figure 13). Notably, both host-guest systems show an increased cytotoxic effect in A549 compared to cisplatin and the cage by itself, while in HepG2 these systems are similar effective or even less potent than cisplatin. The low cytotoxicity of the cage compounds and the enhanced cytotoxic effect of the host-guest systems compared to cisplatin make these metallocages attractive candidates as drug delivery systems.

Conclusion

The synthesis and characterization of new M2L4 (M = Pd, Pt) molecular cages 2Pd, 3Pd and 3Pd, starting from rigid, highly fluorescent, ligands 2 and 3 is described. The first Pd2L4 cage with a rigid tris-pyridine ligand (3) is presented. Additionally, absorption and photoluminescence studies of both ligands and cages have been performed, showing a lower fluorescence of the metalloccages in comparison to the highly fluorescent free ligands. It could be demonstrated that both 2Pd and 3Pd are capable of encapsulating the anticancer drug cisplatin. Notably, the palladium precursor and the ligands are non-toxic and the palladium cages possess only a low cytotoxicity in cancer cells. However, the cage compounds encapsulating cisplatin show an increased cytotoxic effect towards human lung cancer cells (A549). Thus, the methoxy-functionalized coordination cages are promising drug delivery vectors for the anticancer agent cisplatin.

Further ligand modifications are currently performed in our laboratories to increase cage fluorescence.

Experimental section

General remarks

All chemicals were purchased from commercial sources and used without further purification, solvents were distilled prior to use. NMR-spectra were recorded on a Bruker AV 400 or a Bruker AV 400 HD spectrometer. IR spectra were collected on a Varian 670 spectrometer. ESI HRMS measurements were conducted on a Thermo LTQ FT Ultra. UV/Vis spectra were recorded on an Agilent Cary 60. Emission spectra and absolute quantum yields were obtained on a Hamamatsu Absolute PL QY spectrometer (C1547). Compound 1 was synthesized according to literature procedures.10

3.5-Bis((5-methoxy-pyridin-3-yl)-ethynyl)-aniline (2)

A mixture of 2 (32.0 mg, 90.0 µmol, 4.00 eq) and [Pd(NCCH2Ph)2] (20.0 mg, 45.0 µmol, 2.00 eq) in 9 ml acetonitrile is heated to reflux for 1 h. After cooling to room temperature, the product is precipitated by addition of diethyl ether (80 ml). The solid is filtered off, washed with diethyl ether and dried under reduced pressure. 2Pd is obtained as an off-white solid (30.0 mg, 18.2 µmol, 81%). 1H NMR (400 MHz, CD3CN, 297 K): δ (ppm) = 8.90 (d, J = 1.4 Hz, 8H, H2, 3′′′), 8.79 (d, J = 2.6 Hz, 8H, H2, 2′′′), 7.24 (dd, J = 2.6, 1.4 Hz, 8H, H1), 7.18 (t, J = 1.4 Hz, 4H, H4), 6.88 (d, J = 1.4 Hz, 8H, H2, 3′′′), 4.57 (s, 8H, NH2, 4′′′), 3.95 (s, 24H, H2, 4′′′), 3.02 (s, 12H, H1, 4′′′), 3.01 (s, 24H, H1, 4′′′). 13C NMR (101 MHz, CD3CN, 293 K): δ (ppm) = 158.4, 148.9, 145.8, 139.0, 128.0, 124.6, 124.0, 123.5, 119.2, 95.3, 84.0, 57.7. DOSY NMR (CD3CN, 400 MHz, 298 K): D (m s−1) = 5.33 – 1013. HRMS (ESI, MeCN): m/z = 356.14 [2H2] (calcd. for C24H24N6O2 356.14), 176.57 [2H2] (calcd. for C12H12N4O2 176.57). FTIR (KBr): δ (cm−1) = 3323 (br), 3190 (br), 2934 (w), 2833 (w), 2211 (w), 1820 (w), 1592 (s), 1454 (m), 1426 (s), 1371 (m), 1314 (m), 1288 (m), 1243 (m), 1123 (s), 1150 (m), 1108 (w), 1055 (s), 1006 (w), 912 (m), 858 (s), 699 (m), 581 (m), 534 (s).
143.4, 138.6, 136.9, 126.9, 122.7, 119.5, 90.9, 86.4, 55.8. DOSY NMR (CD$_3$CN, 400 MHz, 298 K): D (m$^2$-s$^{-1}$) = 1.22 - 10$^3$. HRMS (ESI, MeCN): m/z = 342.12 [M+$H^+]$ (calcd. for C$_{16}$H$_8$N$_4$O$_4$: 342.12), 171.57 [M+2$H^+]$ (calcd. for C$_{16}$H$_{16}$N$_4$O$_4$: 171.57). FTIR (KBr): $\Gamma$ (cm$^{-1}$) = 3438 (br), 3046 (w), 2983 (w), 2946 (w), 2219 (w), 1582 (s), 1454 (s), 1417 (s), 1313 (w), 532 (w), 419 (w).

Pd$^\text{cage}$ [Pd$_2$(3)(2)Br$_4$(4)]$^{3\text{Pd}}$

A mixture of (w), 2983 (w), 2946 (w), 2219 (w), 1582 (s), 1454 (s), 1417 (s), 1313 (w), 532 (w), 419 (w).

Acknowledgement

Supported by Deutsche Forschungsgemeinschaft (DFG) through the TUM International Graduate School of Science and Engineering (IGSSE). The authors are grateful for the financial support of the TUM Graduate School of Chemistry. EU COST action CM1105 is gratefully acknowledged for funding and fruitful discussion. Dr. Alexander Pöthig is acknowledged for crystallographic advice and assistance with the photoluminescence measurements.

Keywords

Drug delivery, antitumor agents, cisplatin, coordination cages, self-assembly

References and notes


[18] as mentioned before, 3rd was not examined due to the instability towards oxygen and possible instability in the presence of cisplatin.
New non-toxic, self-assembled $M_2L_4$ coordination cages are synthesized from highly fluorescent ligands. The cages are able to encapsulate the anticancer drug cisplatin and enhance its cytotoxicity towards cancer cells.

Key topic: coordination cages