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Self-assembly of a cavitand-based heteronuclear coordination cage

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ABSTRACT

A new self-assembly protocol leading to the formation of heteronuclear coordination cage **10** is reported. Reaction of tetradentate cavitand ligand **1**, bearing one ethynylpyridine and three benzonitriles at the apical positions, with Pt(dppp)OTf_2 and Pd(dppp)OTf_2 in a 1:3 ratio yields **10** as the thermodynamic product. Under the same conditions, the self-assembly of **1** with either Pt or Pd metal precursors gives a mixture of isomeric homonuclear cages **8a–c** or **9a–c**, respectively.

1. Introduction

The self-assembly of coordination cages has reached a high level of sophistication with regard to ligand design and selection of metal precursors.[1] As a result, the shape, dimensions, and polarity of the internal cavity can be engineered, allowing for inclusion of diverse neutral[2] and charged guests[3] in different solvents. The compartmentalization of these guests imparts a wide spectrum of useful properties, including catalysis,[4,5] storage,[6] and the stabilization of labile chemical species.[7]

A missing feature in these self-assembly protocols is the differentiation in metal/ligand reactivity necessary for the generation of heteronuclear coordination cages. As a first step in this direction, Kobayashi and co-workers reported the preparation of heterocages, coordination cages featuring two different ligands.[8,9] Two complementary tetradentate cavitand ligands were prepared, each bearing four identical coordination groups at the apical positions, either nitriles[10] or pyridines.[8] By utilizing the two cavitand's different coordination ability, they devised self-assembly conditions leading to the formation of either homonuclear Pd or Pt heterocages as the dominant product under kinetic control.

The formation of heteronuclear cages introduces a further level of complexity, where at least two metal/ligand couples must undergo self-sorting during the assembly procedure. For instance, the choice of coordinating ligands and metal precursors must be well-defined to differentiate their cross-reactivity. At the same time, the different coordinating groups must be inserted at a single macrocyclic ligand site and organized in a precise relative spatial orientation.

In this paper we report a thermodynamically controlled self-assembly protocol leading to the exclusive formation of a Pd/Pt heteronuclear cage. The protocol is based on a tetradentate cavitand ligand functionalized with three nitriles and one pyridine at the upper rim.

2. Result and discussion

2.1. Synthesis of cavitand 1

The tetradentate cavitand ligand **1**, designed for the self-assembly of heteronuclear coordination cages, presents three benzonitrile and one ethynylpyridine ligands, all of which inserted at the apical positions of a methylene-bridged cavitand (Fig. 1). The choice of these different ligands at the upper rim of the cavitand was dictated by two factors: (i) their different coordination ability toward transition metals like Pt or Pd and (ii) their almost identical distance and orientation with respect to the cavitand scaffold, in order to avoid mismatch during self-assembly.[11]

The four-step synthesis of cavitand **1** is presented in Scheme 1. Resorcinarene **2**, equipped with hexyl feet to assure solubility in organic solvents, was synthesized according to published procedure.[12] Tetraiodo-resorcinarene **3** was obtained from the reaction of resorcinarene **2** with iodine in the presence of sodium hydrogencarbonate.[13] The reaction was carried out at room temperature in a 1:1 mixture of water and diethyl ether. The desired product

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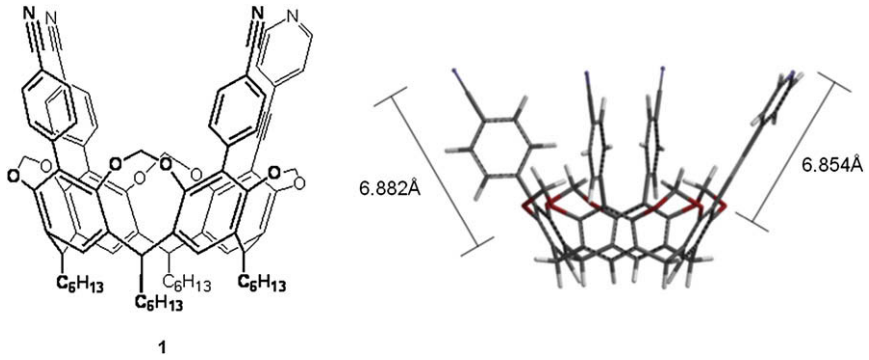


Figure 1. Structure of cavitand **1** and Spartan modeling showing the distance and orientation of the two ligands with respect to the cavitand scaffold.

precipitated in pure form at the water–organic interface (36% yield). Reaction of **3** with CH_2ClBr in a Schlenk apparatus[14] afforded methylene-bridged tetraiodo-cavitand **4** in very high yield (88%). Sonogashira coupling on **4** gave monoethynylpyridine derivative **5**, which underwent a multiple Suzuki coupling to give the desired cavitand **1**.

2.2. Self-assembly of cage 8

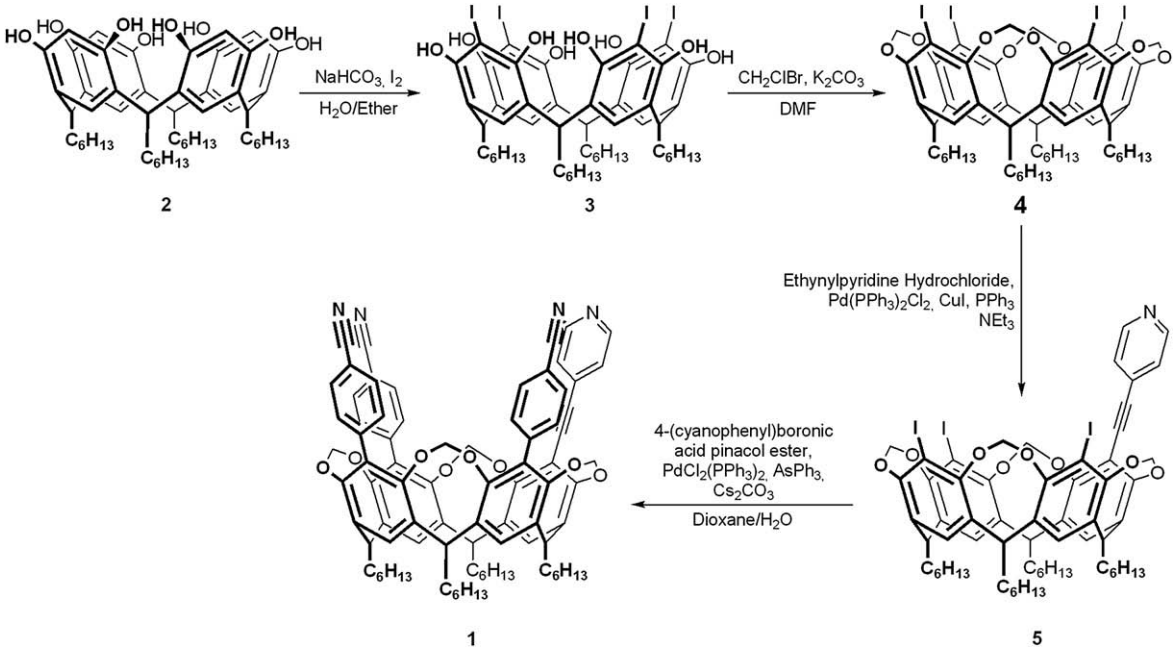
We first explored the complexation behavior of tetradentate ligand **1** against a single metal precursor of general structure $M(dppp)OTf_2$, where dppp is 1,3-bis(diphenylphosphino)propane. A stepwise protocol, depicted in Scheme 2, was devised for both $Pt(dppp)OTf_2$ and $Pd(dppp)OTf_2$.

Metal complex (0.5 equiv) was added to a 5 mM solution of cavitand **1** in a mixture of CD_2Cl_2 (400 μL) and CD_3NO_2 (100 μL). CD_3NO_2 was added to accelerate the ligand exchange[15] in order to reach the thermodynamic equilibrium in reasonable time. Subsequently, the remaining 1.5 equiv of metal precursor was added to the solution. ^1H and ^{31}P NMR spectra were used to track the self-assembly process. The cages were identified by ESI mass spectrometry.

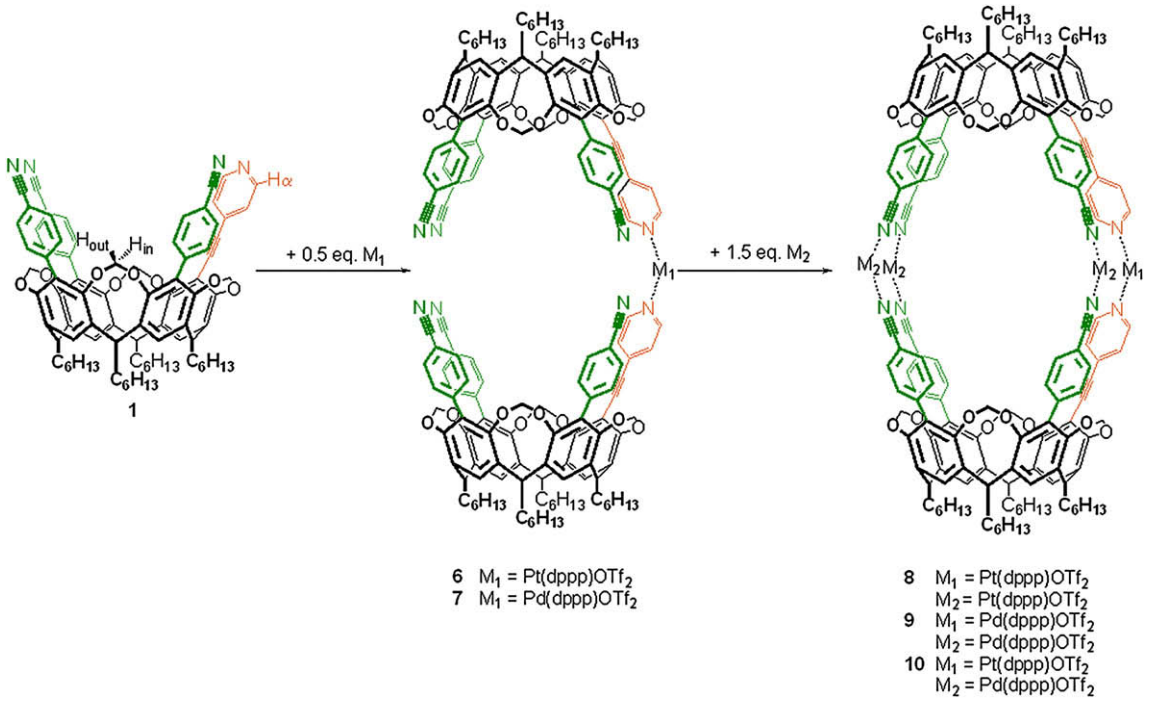
The addition of further 1.5 equiv of $Pt(dppp)OTf_2$ led to complete closure of the cage, as confirmed by ESI MS. The mass spectrum evidenced a prominent signal at 2938.2 *m*/*z*, corresponding to the doubly charged cage ion. However, as shown in Figure 2c and d, two NMR signals corresponding to the ethynylpyridine α-H were present at 8.81 and 8.61 ppm. The intensity ratio of the two peaks was 1:1 immediately after the addition of the metal complex, but became 1:3 after 48 h and remained stable thereafter. Moreover, a splitting of the signals corresponding to H_{in} and H_{out} of the methylene bridges was observed. After completion of the reaction, the ^{31}P NMR spectrum presented a second signal at −10.02 ppm, in addition to −15.60 ppm peak in a 3:1 ratio.

Taken together these observations indicate the presence of more than one isomeric cage in solution. As shown in Figure 3, in addition to the structure in which the two ethynylpyridines are coordinated to the same metal center (**8a**), the formation of two other isomers is conceivable. In such isomers (**8b** and **8c**), one $Pt(dppp)OTf_2$ complex is coordinated to an ethynylpyridine and a benzonitrile ligand. In the case of **8b**, 2 equiv structures are possible, obtained by rotating one cavitand ligand in **8a** by ±90°.

As reported by Kobayashi and co-workers,[8] the ^1H NMR signal corresponding to the α-H protons of the ethynylpyridine ligand is



Scheme 1. Synthesis of tetradentate cavitand ligand **1**.



Scheme 2. Stepwise self-assembly protocol.

slightly upfield shifted for the EtPy–Pt–NCPh system compared to the EtPy–Pt–EtPy system. Therefore, the new signal detected at 8.61 ppm is consistent with cages **8b** and **8c**, which cannot be differentiated by NMR.

Kobayashi and co-workers demonstrated that heterocages can be formed as kinetic products, whereas the thermodynamic products were always the homocages of ethynylpyridine and benzonitrile.[8] The driving force of the self-assembly was the higher coordination ability of the ethynylpyridine ligand. The homocage composed by two identical tetraethynylpyridine cavitand was the thermodynamically favored product.

However, in our system all isomeric cages require the formation of the same set of coordinative bonds, namely two EtPy–Pt and six PhCN–Pt bonds. There is no energy gain in binding two ethynylpyridines to the same metal center, as opposed to binding them to two different Pt complexes. Therefore, the three possible structures are energetically equivalent, as demonstrated by the 3:1 observed **8b**,**c**/**8a** ratio.

2.3. Self-assembly of cage 9

The same protocol was utilized for the formation of Pd cages **9a–c** starting from Pd(dppp)OTf_2. Just as with the Pt cages, when 0.5 equiv of Pd(dppp)OTf_2 was added to a 5 mM solution of cavitand **1** in CD_2Cl_2/CD_3NO_2, hemicage **7** was formed. Due to its higher coordination ability, ethynylpyridine sequestrated the whole amount of metal complex added and led to the exclusive formation of **7**. The ^1H NMR spectrum showed the characteristic downfield

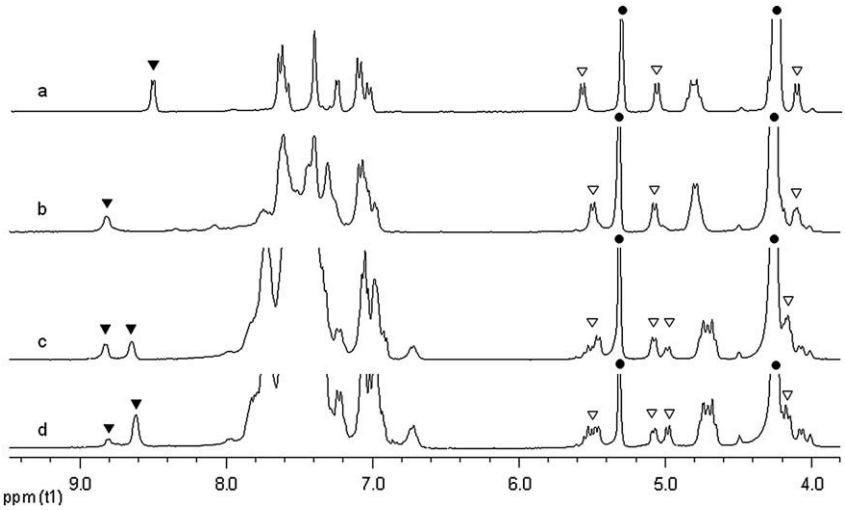


Figure 2. ^1H NMR (300 MHz, 400 μL CD_2Cl_2 and 100 μL CD_3NO_2) spectra of (a) 5 mM cavitand **1**, (b) 5 mM cavitand **1** and 0.5 equiv Pt(dppp)OTf_2, (c) 5 mM cavitand **1** and 2 equiv Pt(dppp)OTf_2, (d) 5 mM cavitand **1** and 2 equiv Pt(dppp)OTf_2 after 48 h. ▼ ethynylpyridine α-H protons, ▽ H_{in} and H_{out} methylene bridges protons, ● residual solvent peaks.

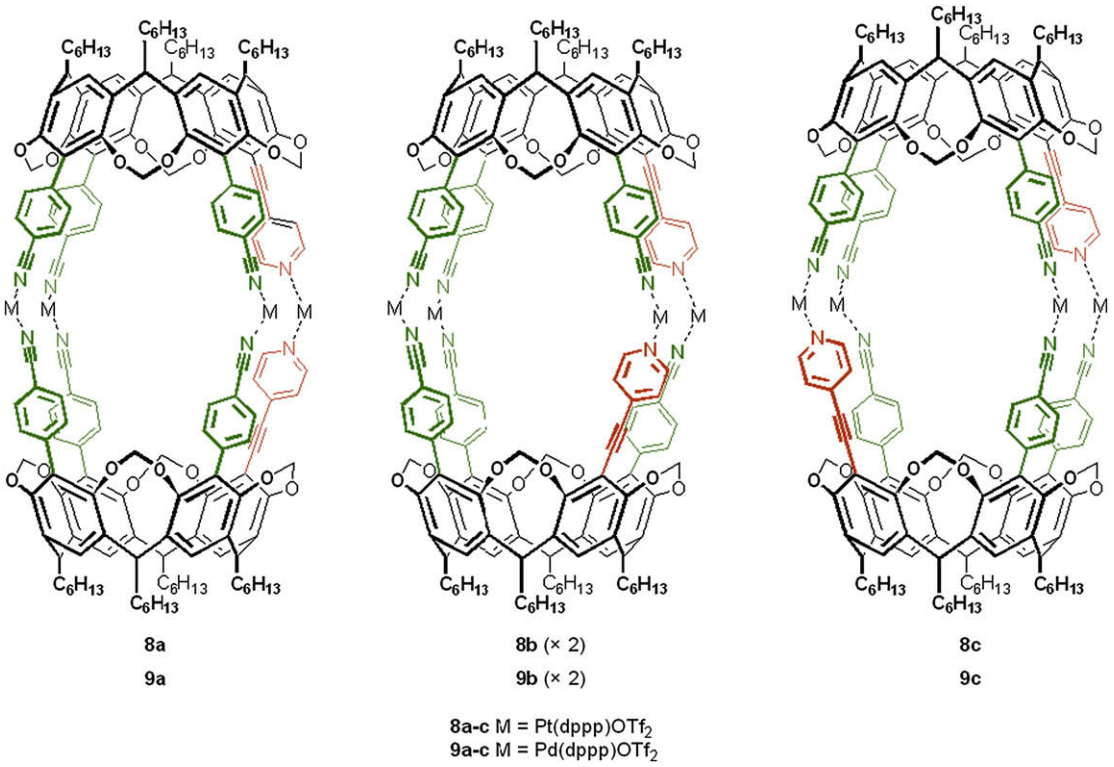


Figure 3. Isomeric coordination cages **8a–c** and **9a–c**.

shift of the peak corresponding to the α-H of the ethynylpyridine ($\Delta\delta=\delta_{\text{hemicage}}-\delta_{\text{free cavitand}}=0.26$ ppm, from 8.51 to 8.77 ppm). In addition, the H_{out} and H_{in} signals of the methylene bridges adjacent to the ethynylpyridine shifted upfield from 5.60 to 5.49 ppm and from 4.12 to 4.08 ppm (Fig. 4). The ^{31}P NMR signal shifted upfield from 17.26 to 6.14 ppm ($\Delta\delta=\delta_{\text{hemicage}}-\delta_{\text{free Pd metal complex}}=$ 11.12 ppm).

After the addition of 1.5 further equivalents of metal complex, two signals for the α-H of the ethynylpyridine were observed at 8.81 and 8.59 ppm, as was the splitting of the H_{in} and H_{out} signals of the methylene bridges. The intensity of the two signals reached a ratio of 1:3 after ca. 48 h (Fig. 4c). Two of the six ^{31}P signals showed the $^{2}J_{P-P}=25$ Hz, which is characteristic for the desymmetrization of the dppp signal in EtPy–CNPh systems.[8] The diagnostic M^{2+} ion of coordination cages was observed via ESI MS at 2760.1 *m/z* (Fig. 5). Those data confirmed the formation of three isomeric cages, as previously reported for the Pt experiment.

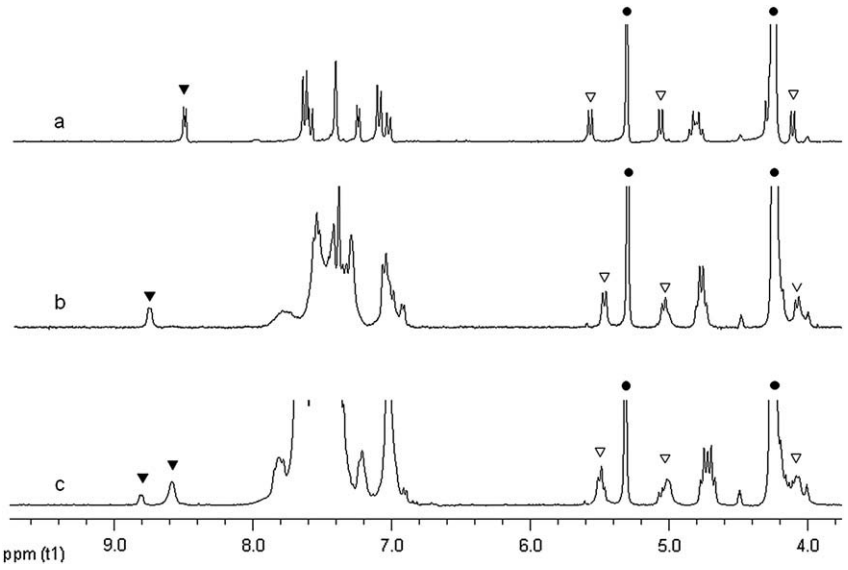


Figure 4. ^{1}H NMR (300 MHz, 400 μL CD_2Cl_2 and 100 μL CD_3NO_2) spectra of (a) 5 mM cavitand **1**, (b) 5 mM cavitand **1** and 0.5 equiv Pd(dppp)OTf_2, (c) 5 mM cavitand **1** and 2 equiv Pt(dppp)OTf_2 after 48 h. ▼ ethynylpyridine α-H protons, ▽ H_{in} and H_{out} methylene bridges protons, ● residual solvent peaks.

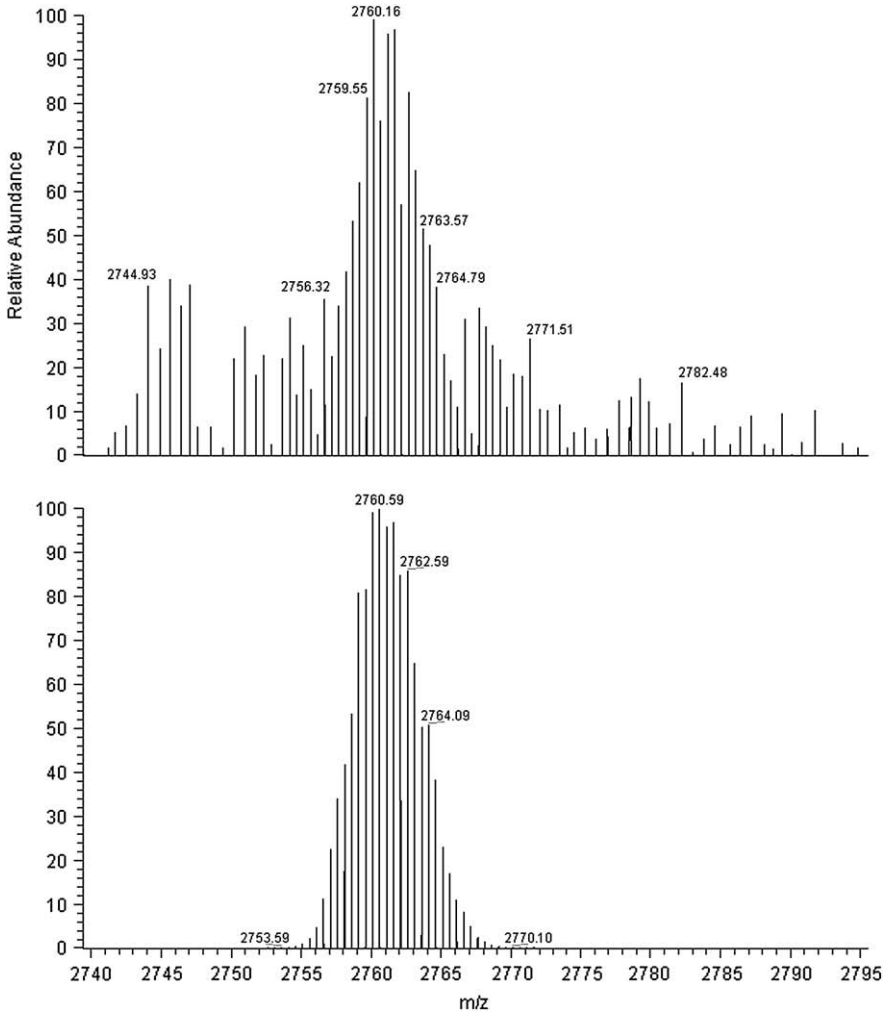


Figure 5. Selected region of the experimental (top) and calculated (bottom) ESI MS spectrum of CD_2Cl_2/CD_3NO_2 solution of cage **9** showing $[M-2CF_3SO_3]^{2+}$ signal at *m*/*z* 2760.1.

The different coordination ability of the ligands in **1** could only be exploited for the first step of the self-assembly protocol, leading to homocages **6** and **7**. Further addition of the same metal led to ligand scrambling during subsequent cage closure, regardless of the metal used. We can conclude that, in itself, the presence of different ligands at the upper rim of the cavitand is not sufficient to drive self-assembly toward the formation of a single molecular cage. Therefore, an additional strategy was

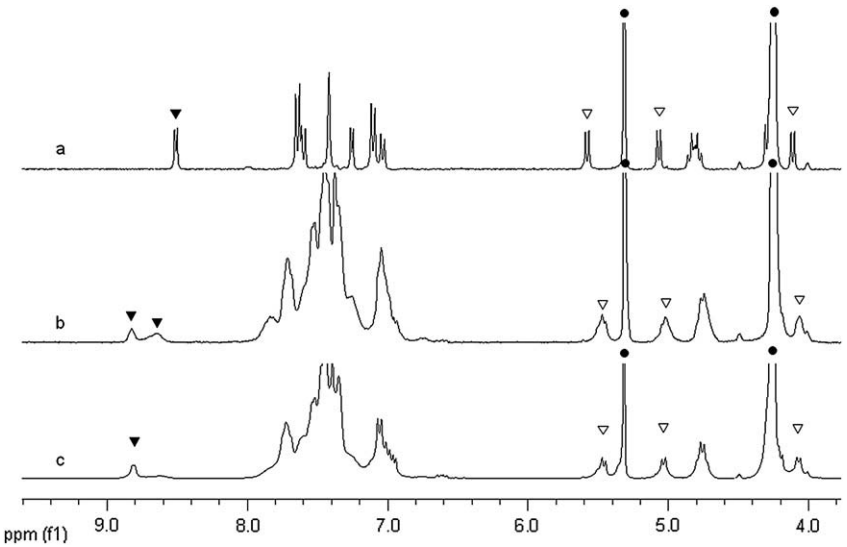


Figure 6. ^1H NMR (300 MHz, 400 μL CD_2Cl_2 and 100 μL CD_3NO_2) spectra of (a) 5 mM cavitand **1**, (b) 5 mM cavitand **1**, 0.5 equiv Pt(dppp)OTf_2, and 1.5 equiv Pd(dppp)OTf_2, (c) 5 mM cavitand **1**, 0.5 equiv Pt(dppp)OTf_2, and 1.5 equiv Pd(dppp)OTf_2 after one week. ▼ ethynylpyridine α-H protons, ▽ H_{in} and H_{out} methylene bridges protons, ● residual solvent peaks.

devised, involving two different metal centers, to obtain selectively a single cage.

2.4. Self-assembly of heteronuclear cage 10

Addition of 1.5 equiv of Pd(dppp)OTf_2 to a solution of Pt-hemicage **6** led to the exclusive formation of the heterocage **10**. Only one signal for the α-H protons of ethynylpyridine groups and two signals for H_{in} and H_{out}, respectively, were observed in the ^{1}H NMR spectrum.

Moreover, α-H protons of the ethynylpyridine and H_{in} signals were shifted slightly upfield with respect to hemicage **6** due to the complete closure of the cage ($\Delta\delta=\delta_{cage}-\delta_{hemicage}=0.06$ ppm for ethynypyridine group and $\Delta\delta=\delta_{cage}-\delta_{emicage}=0.05$ppm for H_{in}). ^{31}P NMR exhibited three peaks at −15.48 (EtPy–Pt–PyEt), 11.82 (PhCN–Pd–CNPh), and 15.36 ppm (PhCN–Pd–CNPh) in a 1:2:1 ratio, consistent with the structure of **10**. The presence of the M^{2+} ion in the ESI MS at m/z=2803.5 confirmed the formation of the heteronuclear cage. The absence of the M^{2+} ions corresponding to **8** and **9** excluded their presence in solution.

The thermodynamic versus kinetic stability of cage **10** was determined by using a one-pot procedure. Cavitand **1** was reacted with a mixture of Pd(dppp)OTf_2 and Pt(dppp)OTf_2 in a 3:1 ratio in the standard CD_2Cl_2/CD_3NO_2 solution. Initially, two peaks corresponding to the α-H protons of the ethynylpyridine appeared at 8.82 and 8.64 ppm, as did broad signals corresponding to H_{in} and H_{out}, suggesting the formation of a mixture of different cages (Fig. 6b). Within several hours, however, the 8.64 ppm signal disappeared, and the broad H_{in} and H_{out} signals evolved into four doublets at 5.47, 5.05, 4.22 (partially obscured by residual nitromethane solvent signal), and 4.08 ppm. The ^{1}H NMR spectrum remained unchanged after one week (Fig. 6c). These results indicate the initial formation of several isomeric cages (kinetic products), which interconvert into cage **10** (the thermodynamic product) over time. ^{1}H and ^{31}P NMR confirmed a complete transformation of the isomeric cages into structure **10**.

3. Conclusion

The exclusive formation of heteronuclear coordination cage **10** demonstrates the versatility of this type of self-assembly procedure. The design of the appropriate tetradentate cavitand ligand is the key element in driving the self-assembly toward the formation of the desired product. In the specific case of the heteronuclear coordination cages reported here, it is crucial to differentiate the type, number, and position of the ligands, to reach the correct metal/ligand cross-reactivity. A single ligand substitution with respect to the parent tetrabenzonitrile cavitand[10] is sufficient to shift completely the outcome of the self-assembly protocol from homonuclear to heteronuclear cages. For the same reason, cavitand **1** is unfit for homocage self-assembly, as it leads to the formation of a set of isomeric cages. Efforts to extend this strategy to the self-assembly of large cage networks[16] are underway.

4. Experimental

4.1. General

Reagents and solvents were purchased as reagent grade and used without further purification. Analytical TLC was performed on Merck silica gel 60 F_{254} precoated plates. Column chromatography was performed using silica gel (Merck 70–230 mesh). ^{1}H NMR spectra were recorded at 300 MHz on a Bruker AC 300 Avance spectrometer with solvent peaks as reference. ^{31}P NMR spectra were recorded at 162 MHz, on a Bruker 400 spectrometer. Mass spectra were measured either on a Helwett–Packard 3395 Waters 74 spectrometer or on a LTQ-linear ion trap mass spectrometer (Thermo Fisher Corp.) equipped with an electrospray source.

4.2. Tetraiodo-resorcinarene (3)

To a solution of 0.496 g of resorcinarene **1** (6.02×10^{-4} mol) in a 1:1 mixture of water and diethyl ether (16 mL), 0.202 g of $NaHCO_3$ (2.41×10^{-4} mol), and 0.614 g of I_2 (2.41×10^{-4} mol) were added. The solution was stirred overnight at room temperature. Following Buchner filtration, the precipitate was washed with cold ethanol. The pure product was collected as white solid (Yield 36%). ^{1}H NMR (acetone-d_6, 300 MHz) δ=8.16 (s, 8H, ArO*H*), 7.65 (s, 4H, Ar*H*), 4.43 (t, 4H, ArC*H*, J=8.6 Hz), 2.29 (m, 8H, ArCHCH_2), 1.24 (m, 32H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 0.85 (t, 12H, CH_2CH_3, J=7.4 Hz); ESI MS (m/z): 1327 $[M]^-$ [M=$C_{52}H_{68}I_4O_8$].

4.3. Tetraiodo-cavitand (4)

Compound **1** (0.593 g, 4.46×10^{-4} mol) was dissolved in dry DMF (8 mL) in a dry Schlenk tube. To the solution were added 1.208 mL of CH_2ClBr (1.78×10^{-2} mol) and 0.493 g of K_2CO_3 (3.57×10^{-3} mol). The mixture was stirred at 85 °C for 3 h. After neutralization with HCl 2%, a precipitate formed; following Buchner filtration, the resulting solid was the pure product (Yield 88%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ=7.05 (s, 4H, Ar*H*), 5.96 (d, 4H, $OCH_{in}H_{out}O$, J_2=8.2 Hz), 4.84 (t, 4H, ArC*H*, J=9.0 Hz), 4.30 (d, 4H, $OCH_{in}H_{out}O$, J_2=8.2 Hz), 2.18 (m, 8H, ArCHCH_2), 1.31 (m, 32H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 0.89 (t, 12H, CH_2CH_3, J=7.4 Hz); ESI MS (m/z): 1399 $[M+Na]^+$ [M=$C_{56}H_{68}I_4O_8$].

4.4. Monoethynylpyridine-cavitand (5)

Dry Et_3N (10 mL) was degassed in a dry flask for 30 min; 0.5 g of **2** (3.63×10^{-4} mol), 0.084 g of ethynylpyridinehydrochloride (6.25×10^{-4} mol), 0.0102 g of Pd(PPh_3)$_2Cl_2$ (1.45×10^{-5} mol), 0.0051 g of CuI (3.5×10^{-5} mol), and 0.0057 g of PPh_3 (2.2×10^{-5} mol) were added and the mixture was stirred for 1 h at 60 °C and for 48 h at 90 °C. After cooling to room temperature, $CHCl_3$ was added and the crude product was washed with water and extracted with $CHCl_3$. The pure product was obtained by purification with silica gel flash chromatography with CH_2Cl_2/AcOEt (95:5) as eluent (Yield 35%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ=8.60 (d, 2H, PyH_o, J=6.0 Hz), 7.30 (d, 2H, PyH_m, J=6.0 Hz), 7.11 (s, 1H, Ar*H*), 7.08 (s, 1H, Ar*H*), 7.06 (s, 1H, Ar*H*), 5.95 (m, 4H, $OCH_{in}H_{out}O$), 4.84 (m, 4H, ArC*H*), 4.48 (d, 2H, $OCH_{in}H_{out}O$, J_2=8.1 Hz), 4.29 (d, 2H, $OCH_{in}H_{out}O$, J_2=8.2 Hz), 2.21 (m, 8H, ArCHCH_2), 1.28 (m, 40H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 0.88 (t, 12H, CH_2CH_3, J=7.2 Hz); ESI MS (m/z): 1352.7 $[MH]^+$ [M=$C_{63}H_{72}I_3NO_8$].

4.5. Monoethynylpyridine-tribenzonitrile cavitand (1)

To a solution of 0.1088 g of **5** (7.45×10^{-5} mol) in 10 mL of dioxane 0.0157 g of Pd(PPh_3)$_2Cl_2$ (2.24×10^{-5} mol), 0.208 g of 4-(cyanophenyl)boronic acid pinacol ester, (9.07×10^{-4} mol), 0.057 of $AsPh_3$ (1.86×10^{-4} mol), and 0.4748 g of Cs_2CO_3 previously dissolved in 0.25 mL of water were added. The mixture was stirred under Argon for 40 h at 110 °C. The solution was cooled at room temperature and concentrated under vacuum. Cavitand **1** was obtained as white solid by precipitation with diethylether in 36% yield. ^{1}H NMR ($CDCl_3$, 300 MHz) δ=8.51 (d, 2H, PyH_o, J=6.0 Hz), 7.65 (d, 4H, NCArH_o, J=9.1 Hz), 7.59 (d, 2H, NCArH_o, J=9.1 Hz), 7.29 (s, 4H, Ar*H*), 7.21 (d, 2H, PyH_m, J=6.0 Hz), 7.15 (d, 4H, NCArH_m, J=9.1 Hz), 7.09 (d, 2H, NCArH_m, J=9.1 Hz), 5.60 (d, 2H, $OCH_{in}H_{out}O$, J_2=7.8 Hz), 5.17 (d, 2H, $OCH_{in}H_{out}O$, J_2=7.7 Hz), 4.80 (m, 4H, ArC*H*), 4.38 (d, 2H, $OCH_{in}H_{out}O$, J_2=7.8 Hz), 4.12 (d, 2H, $OCH_{in}H_{out}O$, J_2=7.7 Hz), 2.30 (m,

8H, ArCHCH_2), 1.22 (m, 32H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 0.90 (t, 12H, CH_2CH_3, J=7.3 Hz); ESI MS (m/z): 1278.6 $[MH]^+$, [M=$C_{84}H_{84}N_4O_8$].

4.6. Stepwise self-assembly of Pt-hemicage (6) and Pt cage (8)

To a solution of 3.2 mg of **1** (5.0×10^{-3} M) in CD_2Cl_2 (0.4 mL) and CD_3NO_2 (0.1 mL) in the NMR tube 1.1 mg of Pt(dppp)OTf_2 was added to give hemicage **6** and ^{1}H NMR and ^{31}P NMR spectra were recorded. ^{1}H NMR (CD_2Cl_2+CD_3NO_2, 300 MHz): δ=8.82 (d, 4H, Py*Ho*), 7.76–6.98 (m, 48H, P*Ph*$_2$+NCAr*H*$_o$+Py*H*$_m$+NCAr*H*$_m$), 5.49 (d, 4H, $OCH_{in}H_{out}O$), 5.07 (d, 4H, $OCH_{in}H_{out}O$), 4.80–4.78 (m, 8H, ArC*H*), 4.20 (d, 4H, O*CH*$_{in}$$H_{out}O$ partially under residual solvent peak), 4.10 (d, 4H, O*CH*$_{in}$$H_{out}O$), 2.29 (m, 16H, ArCHC$H_2$), 1.29 (m, 64H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 0.90 (br t, 24H, CH_2CH_3); ^{31}P NMR (CD_2Cl_2+CD_3NO_2, 162 MHz): −15.60 ppm (J_{P-Pt}=3033 Hz).

An additional 3.4 mg of Pt(dppp)OTf_2 was added to same solution and ^{1}H NMR and ^{31}P NMR spectra were recorded again. ^{1}H NMR (CD_2Cl_2+CD_3NO_2, 300 MHz): δ=8.81 (d, 4H, Py*Ho*), 8.61 (d, 12H, Py*Ho*), 7.82–6.98 (m, 416H, P*Ph*$_2$+NCAr*H*$_m$+NCAr*H*$_o$), 6.92 (d, 4H, Py*H*$_m$), 6.72 (d, 12H, Py*H*$_m$), 5.55–5.42 (m, 16H, $OCH_{in}H_{out}O$), 5.08 (d, 8H, $OCH_{in}H_{out}O$), 4.98 (d, 8H, $OCH_{in}H_{out}O$), 4.75–4.65 (m, 32H, ArC*H*), 4.26–4.22 (m, 16H, O*CH*$_{in}$$H_{out}O$), 4.23 (d, 8H, O*CH*$_{in}$$H_{out}O$ partially under residual solvent peak), 4.18 (d, 16H, O*CH*$_{in}$$H_{out}O$), 2.90 (m, 64H, dppp), 2.75 (m, 32H, dppp), 2.29 (m, 64H, ArCHCH_2), 1.29 (m, 256H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 0.90 (br t, 96H, CH_2CH_3); ^{31}P NMR (CD_2Cl_2+CD_3NO_2, 162 MHz): −15.60, −10.02 (J_{P-Pt}=3444 Hz).

ESI MS (m/z): 2938.2 $[(M-2OTf)]^{2+}$, [M=$C_{284}H_{272}F_{24}N_8O_{40}P_8Pt_4S_8$].

4.7. Stepwise self-assembly of Pd hemicage (7) and Pd cage (9)

To a solution of 3.1 mg of **1** (4.85×10^{-3} M) in CD_2Cl_2 (0.4 mL) and CD_3NO_2 (0.1 mL) in the NMR tube 1 mg of Pd(dppp)OTf_2 was added to give hemicage **7** and ^{1}H NMR and ^{31}P NMR spectra were recorded. ^{1}H NMR (CD_2Cl_2+CD_3NO_2, 300 MHz): δ=8.77 (d, 4H, Py*Ho*), 7.67–7.30 (m, 32H, P*Ph*$_2$+NCAr*H*$_o$), 7.06 (d, 12H, NCAr*H*$_m$), 6.94 (d, 4H, Py*H*$_m$), 5.49 (d, 4H, $OCH_{in}H_{out}O$), 5.05 (d, 4H, $OCH_{in}H_{out}O$), 4.81–4.75 (m, 8H, ArC*H*), 4.22–4.19 (m, 4H, O*CH*$_{in}$$H_{out}O$, partially under residual solvent peak), 4.08 (d, 4H, O*CH*$_{in}$$H_{out}O$), 3.12–2.91 (dppp signals), 2.32 (m, 16H, ArCHCH_2), 1.29 (m, 64H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 0.87 (br t, 24H, CH_2CH_3); ^{31}P NMR: (CD_2Cl_2+CD_3NO_2, 162 MHz): δ=6.14 ppm.

An additional 2.9 mg of Pd(dppp)OTf_2 was added to same solution and ^{1}H NMR and ^{31}P NMR spectra were recorded again. ^{1}H NMR (CD_2Cl_2+CD_3NO_2, 300 MHz): δ=8.81 (d, 4H, Py*Ho*), 8.59 (d, 12H, Py*Ho*), 7.84–6.89 (m, P*Ph*$_2$+NCAr*H*$_m$+NCAr*H*$_o$+Py*H*$_m$), 5.51–5.46 (m, 16H, $OCH_{in}H_{out}O$), 5.07–4.99 (m, 16H, $OCH_{in}H_{out}O$), 4.77–4.66 (m, 32H, ArC*H*), 4.19–4.07 (m, 32H, O*CH*$_{in}$$H_{out}O$ partially under residual solvent peak), 2.90–2.75 (m, three signals of dppp), 2.29 (m, 64H, ArCHCH_2), 1.40–1.29 (m, 256H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 0.87 (br t, 96H, CH_2CH_3); ^{31}P NMR (CD_2Cl_2+CD_3NO_2, 162 MHz): δ=15.77, 12.41, 11.50 (d, $^2J_{P-P}$=25 Hz), 10.90 (d, $^2J_{P-P}$=25 Hz), 6.14, 4.91 ppm.

ESI MS (m/z): 2760.16 $[(M-2OTf)]^{2+}$, [M=$C_{284}H_{272}F_{24}N_8O_{40}P_8Pd_4S_8$].

4.8. Self-assembly of heteronuclear cage (10)

4.8.1. Stepwise procedure

To a solution of 3.2 mg of **1** (5×10^{-3} M) in CD_2Cl_2 (0.5 mL) in the NMR tube 1.1 mg of Pt(dppp)OTf_2 was added to form Pt-hemicage **6**. Pd(dppp)OTf_2 (3 mg) was added to same solution and ^{1}H NMR and ^{31}P NMR spectra were recorded. ^{1}H NMR (CD_2Cl_2, 300 MHz): δ=8.89 (d, 4H, Py*Ho*), 7.73–7.30 (m, 92H, P*Ph*$_2$+NCAr*H*$_o$), 7.13–7.07 (m, 12H, NCAr*H*$_m$), 6.98 (d, 4H, Py*H*$_m$), 5.47 (d, 4H, $OCH_{in}H_{out}O$), 5.05 (d, 4H, $OCH_{in}H_{out}O$), 4.80–4.72 (m, 8H, ArC*H*), 4.28–4.26 (m, 4H, O*CH*$_{in}$$H_{out}O$), 4.08 (d, 4H, O*CH*$_{in}$$H_{out}O$), 3.24 (m, 8H, dppp), 2.90 (m, 8H, dppp), 2.30 (m, 24H, dppp+ArCHCH_2), 1.42–1.34 (m, 64H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 0.93 (br t, 24H, CH_2CH_3); ^{31}P NMR (CD_2Cl_2, 162 MHz): δ=15.36, 11.82, −15.48 (J_{P-Pt}=3189 Hz).

4.8.2. One-pot procedure

To a solution of 3.5 mg of **1** (5.4×10^{-3} M) in CD_2Cl_2 (0.4 mL) and CD_3NO_2 (0.1 mL) in the NMR tube 1.25 mg of Pt(dppp)OTf_2, and 3.3 mg of Pd(dppp)OTf_2 were added. ^{1}H NMR and ^{31}P NMR spectra were recorded. ^{1}H NMR (CD_2Cl_2+CD_3NO_2, 300 MHz): δ=8.82 (d, 4H, Py*Ho*), 7.72–7.25 (m, 92H, P*Ph*$_2$+NCAr*H*$_o$), 7.07–6.94 (m, 16H, Py*H*$_m$+NCAr*H*$_m$), 5.46 (d, 4H, $OCH_{in}H_{out}O$), 5.03 (d, 4H, $OCH_{in}H_{out}O$), 4.79–4.74 (m, 8H, ArC*H*), 4.20 (d, 4H, O*CH*$_{in}$$H_{out}O$ partially under residual solvent peak), 4.07 (d, 4H, O*CH*$_{in}$$H_{out}O$), 3.23–2.83 (m, dppp), 2.30 (m, 16H, ArCHCH_2), 1.40–1.29 (m, 64H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 0.87 (br t, 24H, CH_2CH_3); ^{31}P NMR (CD_2Cl_2+CD_3NO_2, 162 MHz): δ=15.84, 12.35, −15.07 (J_{P-Pt}=3075 Hz).

ESI MS (m/z): 2803.51 $[(M-2OTf)]^{2+}$, [M=$C_{284}H_{272}F_{24}N_8O_{40}Pd_3P_8PtS_8$].

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