EFFECT OF MULTICOMPONENT VARIATION ON SELF-ASSEMBLED CAGES

By

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University Honors
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APPROVED

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Abstract

Self-assembled cages have great potential as biomimetic catalysts. Many types of self-assembled cage complexes are known, but most of them cannot display functional groups towards the interior cavities due to the limitation of the cage size. To solve this, we will incorporate variable coordinating groups to construct scaffolding ligands to form cavity-containing tetrahedral or cubic cages. The cages are synthesized through multicomponent self-assembly of functionalized dianiline ligands, such as 3,7-diaminosuberone, 3,7-diaminosuberol, and 3,7-diaminosuberenone, with 2-pyridinecarboxaldehyde or 2-quinolinecarboxaldehyde, and coordinating metal ions, such as Iron, Zinc or Cadmium. By tuning the flexibility of the ligand, the steric bulk of the aldehyde, and the size of the coordinating metals, we can observe how these small changes impact the overall ability of the cages to self-assemble into different geometrical shapes, with differing properties. The stoichiometry of cage assembly will be monitored using Nuclear Magnetic Resonance (NMR), Mass Spectroscopy, and X-ray crystallography.

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Introduction

Self-assembled cages have the potential to mimic biological enzyme activities. These cages contain functional cavities, which could associate with targeted substrates. In the previous papers, self-assembled M_2L_3 *meso*-helicate and tetrahedral cages, such as the fluorenol cage (See **Figure 1**) has been established with the combination of dianiline ligands, 2-pyridinecarboxyaldehyde (PCA), and iron metal.[1] However, the use of the bulky aldehyde and other metals has not been incorporated in the previous experiments. This project is interested in testing the effect of varying the aldehydes as well as the metals on the assembly of dianiline ligands because the M_2L_3 *meso*-helicate cages can potentially form larger cages with M_4L_6 or M_8L_{12} stoichiometry through the use of the more sterically demanding 2-quinolinecarboxaldehyde (QCA). When cages form with QCA, steric hindrance from the extra aromatic rings may prevent the formation of the M_2L_3 geometry, forcing the ligands to assemble into larger cages. Dianiline ligands: 3,7-diaminosuberone (DAS), 3,7-diaminosuberol (DASol), and 3,7-diaminosuberenone (DASenone) were chosen for their flexibility differences. DASol is the most flexible, followed by DAS, and DASenone being the least flexible. The procedure for synthesizing these three ligands was established in previous papers.[2-3] Aldehydes such as 2-pyridinecarboxaldehyde or 2-quinolinecarboxaldehyde, and coordinating metal ions, such as Iron, Zinc or Cadmium will be incorporated in the synthesis of the cages. The main goal of this project is to test and

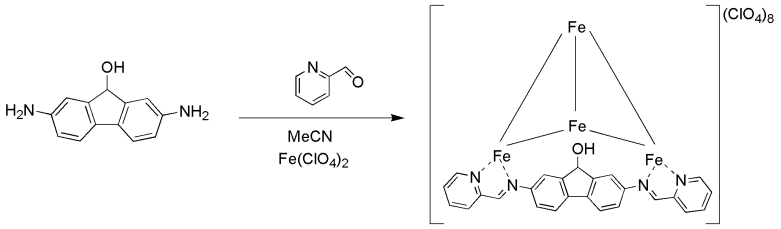


Figure 1 Synthesis of Fluorenol Iron Cage

observe the effects on the self-sorting of the self-assembled cages with variation of aldehydes and metals in order to determine a favorable condition for cage assembly.

Discussion

In this project, dianiline ligands, aldehydes, and metals are utilized as core, end, and coordinating metal to form a self-assembled cage. With alteration of the different components, experiments have been performed to optimize the conditions to make cages with functionalized cavity. A general scheme of how the ligands were synthesized is outlined in Figure 2. Three different ligands were used as core due to the differences in their flexibility. 3,7-diaminosuberol (DASol) is the most flexible out of the three because it possesses an alcohol on the middle ring, which allows it to be more bent. The next flexible ligand is 3,7-diaminosuberone (DAS) with a ketone on the middle ring. The least flexible ligand is 3,7-diaminosuberenone with a ketone and a double bond on the middle

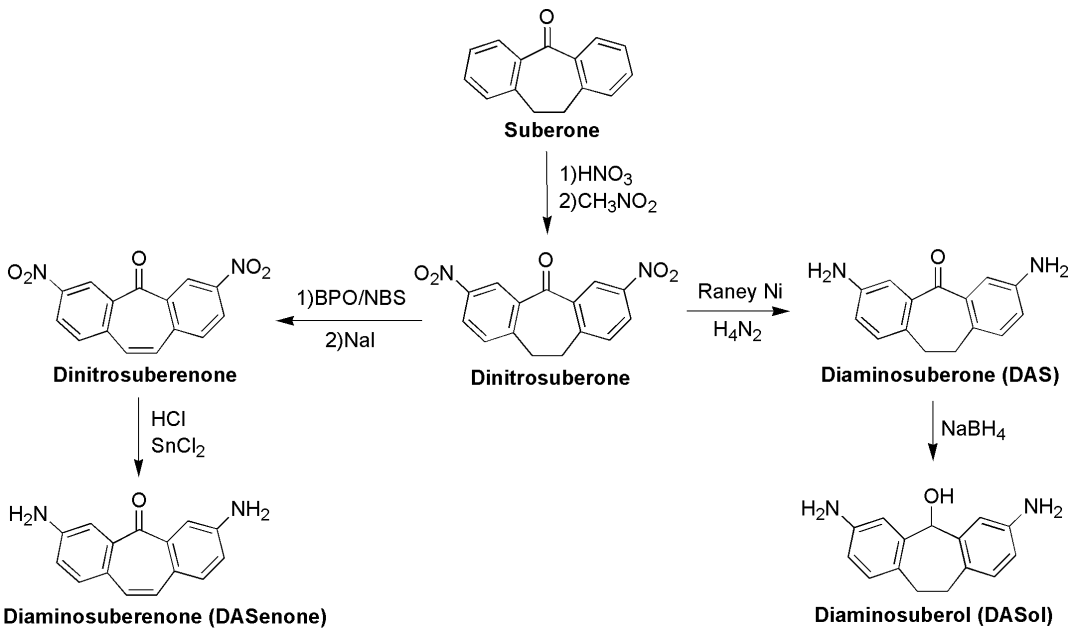


Figure 2 Ligand Synthesis from Dibenzosuberone starting material. First, Dibenzosuberone is selectively nitrated to form Dinitrosuberone, which is reduced to Diaminosuberone (DAS)[2] with Raney Ni, or brominated and eliminated to make Dinitrosuberenone.[3] Dinitrosuberenone can then be reduced to Diaminosuberenone (DASenone). Lastly, the ketone on DAS can be reduced to make Diaminosuberol (DASol).

ring, which make the ligand flat and more rigid. Because of these properties of the ligands, they were observed to accommodate different aldehydes and metals through cage synthesis. Two different aldehydes, 2-pyridinecarboxaldehyde (PCA) and 2-quinolinecarboxaldehyde (QCA) were used as ends on the ligand in cage synthesis due to their difference in size. Three different coordinating metals, $Fe(ClO_4)_2$, Zn(II)triflate, and $Cd(ClO_4)_2$ were used in cage synthesis due to their differences in radius and magnetic properties. Iron, zinc, and cadmium have atomic radius of 126pm, 139pm, and 220pm respectively. Zinc has slightly larger atomic radius than iron, and cadmium has the largest atomic radius out of the three coordinating metals chosen for the experiment. Furthermore, iron could be paramagnetic by having spin crossing over between the low spin state and the high spin state. Whereas zinc and cadmium are diamagnetic metals. The effects of the differences of the cores, ends and metals on the cage assembly will be discussed in the following paragraphs. A general cage formation is shown in Figure 3. Two types of synthesis were used: large scale cage synthesis and NMR tube cage synthesis. More details

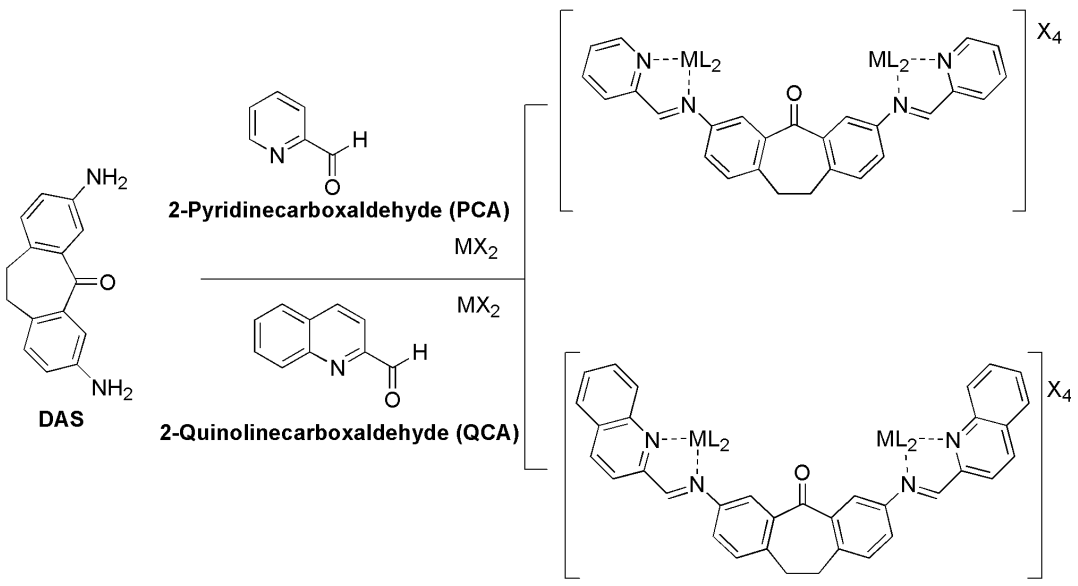


Figure 3 General Cage Synthesis. Dianiline ligands are mixed with an aldehyde and metal salt in acetonitrile to form the self-assembled cage in one pot.

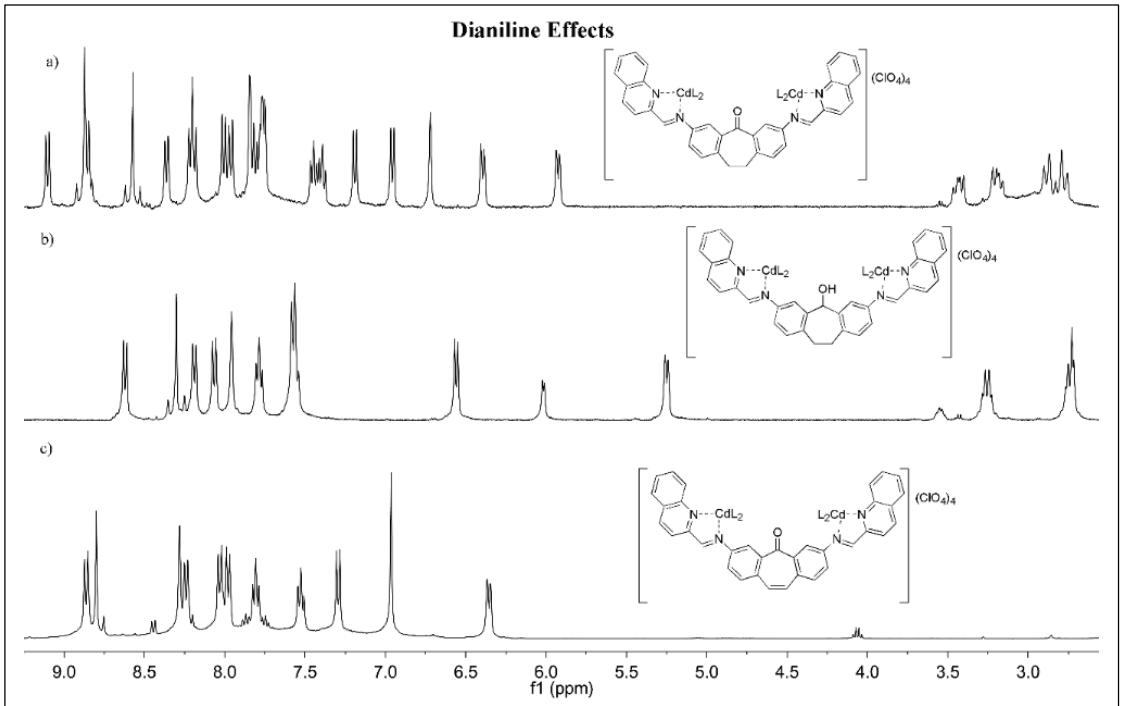


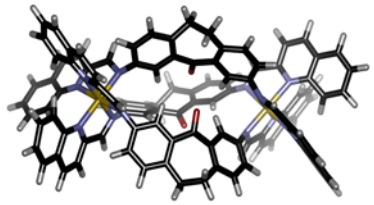
Figure 4 Dianiline Effects. a) DAS+QCA+Cd mixture of helicate and mesocate structure b) DASol+QCA+Cd c) DASenone+QCA+Cd

about the synthesis will be discussed in experimental section. Dianiline effect and paramagnetism were observed with cage formation in certain conditions. And, three types of experiments were performed to test the cage favorability and stability with various components. Metal competition and displacement, and ligand competition were the three categories for the experiments.

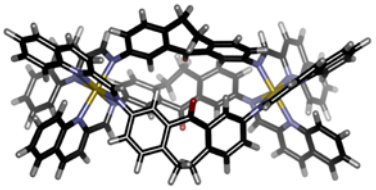
First, dianiline effect was observed when the core ligands are different, and the aldehyde and metal remain constant. When QCA and Cd were added to DASol and DASenone, symmetrical M_2L_3 *meso*-helicates were formed. However, when QCA and Cd were added to DAS, two sets of peaks were observed. One possible explanation could be the cage is a twisted M_2L_3 helicate structure, which is a diastereomer of the mesocate. Two products form in a mixture, resulting in two sets of peaks observed in ^{1}H NMR spectrum shown in Figure 4. The predicted models for DAS+QCA+Cd M_2L_3 helicate and mesocate

are shown in Figure 5. ^{1}H-DOSY NMR spectrum proved that the two products are similar in size. As well as their geometric shape to be M_2L_3 since they have a diffusion constant=2.1777x10^{-9} m^2/s, a number fall within the range of previously established M_2L_3 cages.[3]

Figure 5 Model for DAS+QCA+Cd Cage



Helicate



Mesocate

Next, paramagnetism was observed when QCA and DASol are formed into the iron cage. The DASol-QCA-Cd and DASol-PCA-Fe cages both exhibit normal diamagnetic behavior shown in Figure 6. While iron and QCA cages do not form with other rigid ligands, when QCA and iron were added to the more flexible DASol, paramagnetism is observed. The ^{1}H NMR has peaks drastically shifted from 55 to -20 ppm.

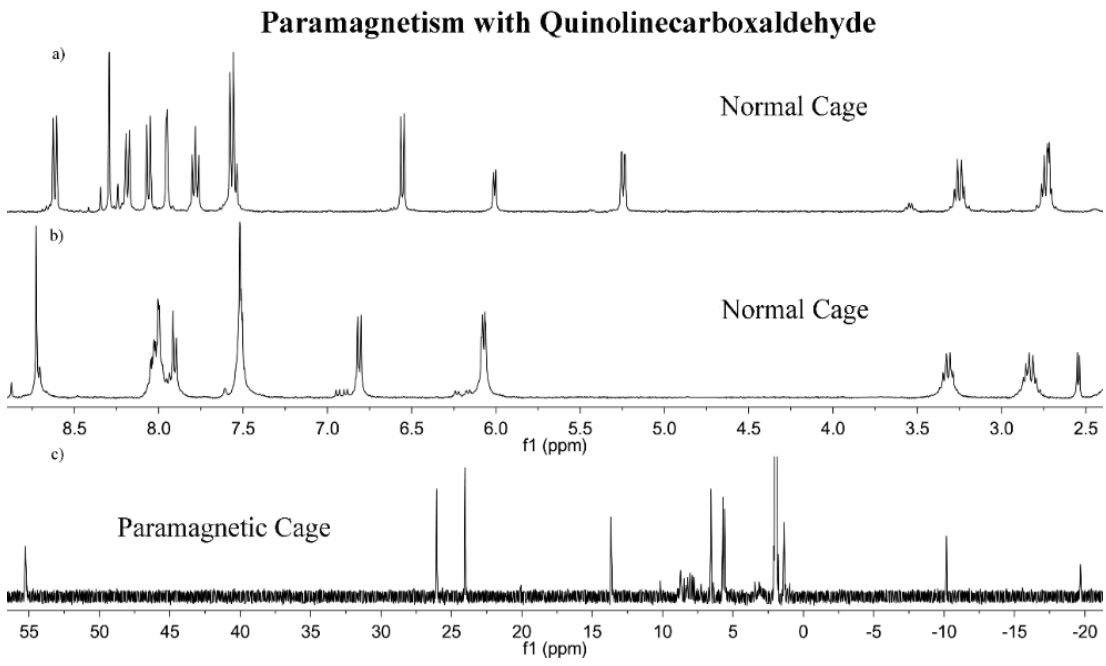
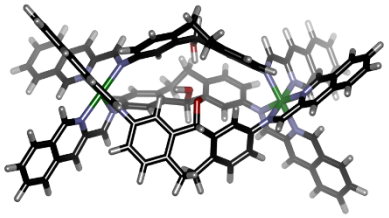


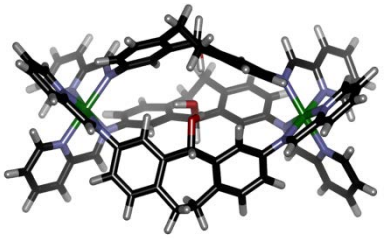
Figure 6 Paramagnetism. a) DASol+QCA+Cd b) DASol+PCA+Fe c) DASol+QCA+Fe. The paramagnetism is not observed in PCA or QCA with other metals. Hoever, when QCA and Fe are combined, paramagnetism occurs, creating large NMR shifts.

A predicted model of M_2L_3 DASol+QCA+Fe mesocate and previously established DASol+PCA+Fe mesocate are shown in Figure 7. Further investigation is needed to understand this phenomenon. One possible explanation is that Fe(II) experiences spin-cross-over from the low spin state to the high spin state when trying to coordinate the scaffolding ligands with QCA. The distance between the nitrogen on the rings coordinated to the iron may be too great for the low spin complex to form due to the strain, so the complex now favors the high spin state, which results in the observed paramagnetism.[4-5]

Figure 7 Models for DASol cages



Predicted model of M_2L_3 DASol+QCA+Fe mesocate



DASol+PCA+Fe mesocate

Moreover, after the cage formation has been established, metal competition and displacement experiments were performed to test whether the cage favors one metal more than the other. Metal selectivity experiments confirm the favorability of one metal over another (see **Figure 8**). The experiment was performed in an NMR tube, and follows the general procedure that can be found in the experimental section. When 0.33 eq. for both iron and zinc (0.66 eq. metal total is enough to form only one cage) were added to DAS+PCA, both the iron and zinc cages were observed in an almost 1:1 ratio, and there was left over aldehyde that was not fully consumed after the reaction. No heterocomplexes containing one iron and one zinc metal were observed from the ^{1}H NMR. Subsequently, when 0.66 eq. of each metal was added (i.e. excess metal is present), favorability towards the iron cage was observed, and no zinc cage was formed after the reaction was completed as shown in the ^{1}H NMR.

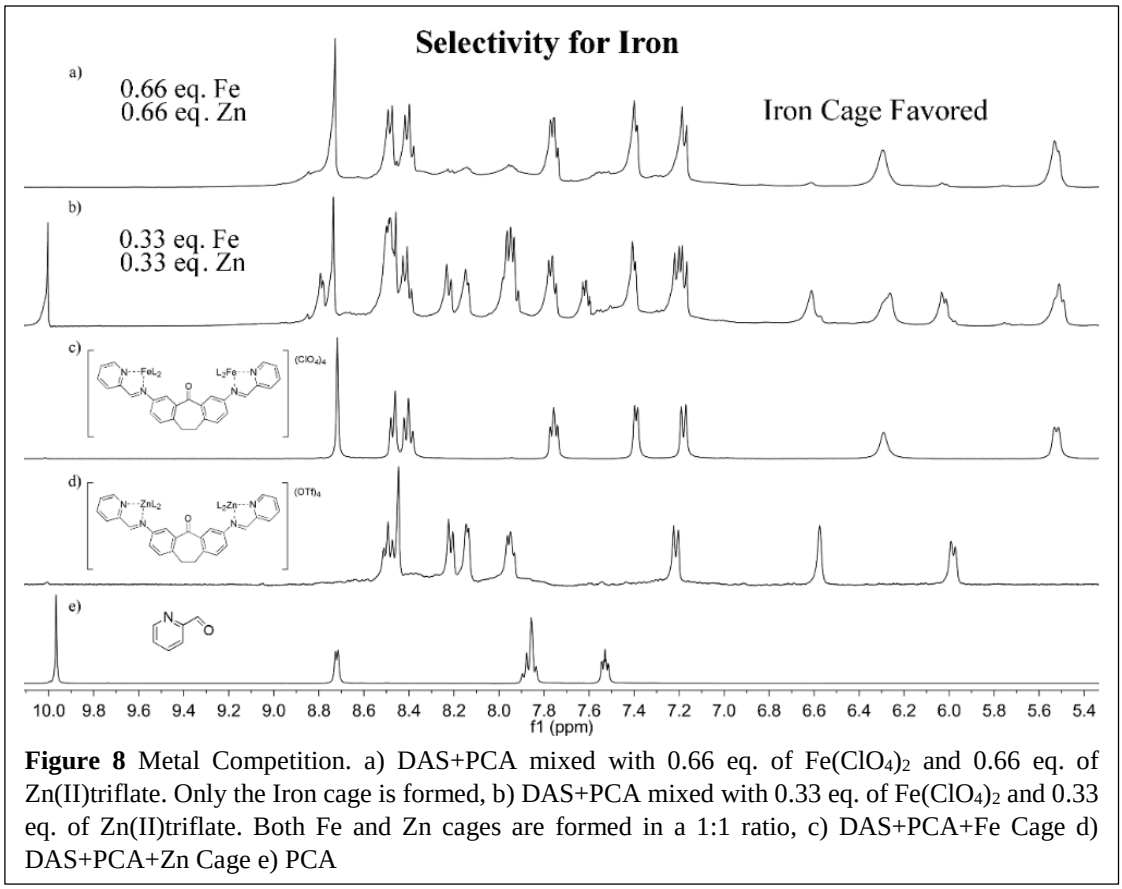


Figure 8 Metal Competition. a) DAS+PCA mixed with 0.66 eq. of $Fe(ClO_4)_2$ and 0.66 eq. of Zn(II)triflate. Only the Iron cage is formed, b) DAS+PCA mixed with 0.33 eq. of $Fe(ClO_4)_2$ and 0.33 eq. of Zn(II)triflate. Both Fe and Zn cages are formed in a 1:1 ratio, c) DAS+PCA+Fe Cage d) DAS+PCA+Zn Cage e) PCA

In addition, metal displacement experiment was performed to test whether the cage is able to freely dissociate from an existing metal and associate to a newly added metal when the a more favorable complex can be formed.[6] The experiment was performed in an NMR tube. When DASol was combined with PCA and cadmium, an unfavorable aggregate formed. However, when 2 eq. of iron was added to the aggregate, cadmium was displaced by the more favorable iron to form a stable and discrete cage (see **Figure 9**). This proves that Fe is more favorable than Cd and the cage that was preformed is not rigid and fixed, and is able to disassociate from one metal and freely associate to another metal when the condition is more favorable.

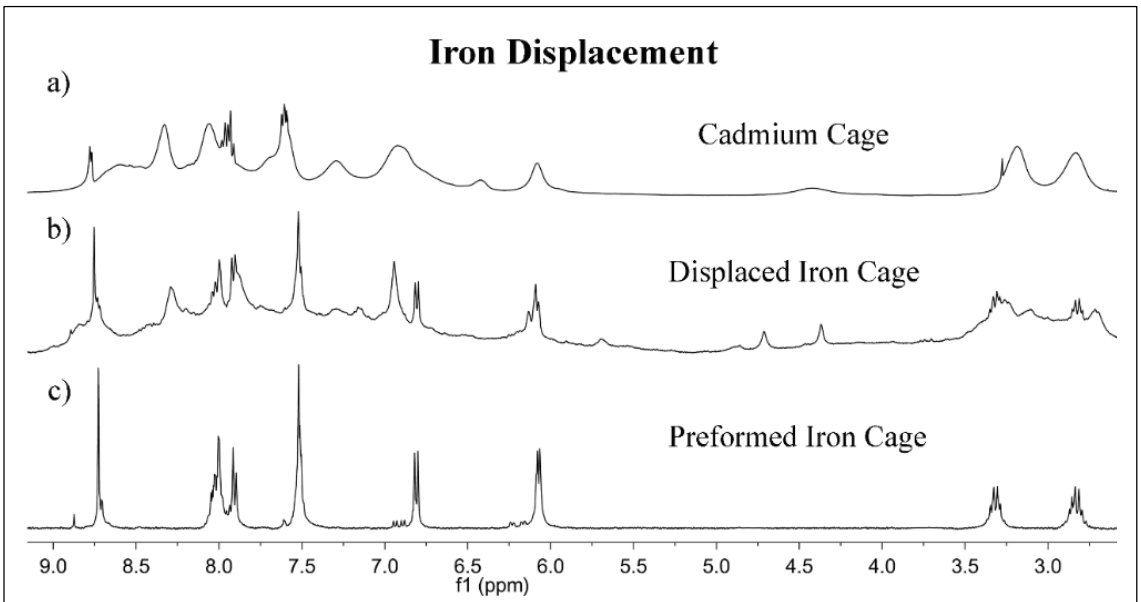


Figure 9 Metal Displacement. a) DASol+PCA+Cd Cage b) preformed DASol+PCA+Cd Cage mixed with 2 eq. Fe and heated c) DASol+PCA+Fe Cage

Conclusion

QCA was proposed to be the bulky aldehyde that might be able to form larger cages due to steric hindrance. However, after number of experiments with QCA, the three ligands and three coordinating metal, most the cages are M_2L_3 mesocate or helicate instead of the tetrahedral or cubic cages. QCA was able to form cages with all three ligands when cadmium is present. When either iron or zinc was added as coordinating metal, only DASol was able to form a cage with QCA as the end aldehyde. Because DASol is a more bent and more flexible ligand, it can accommodate the bulky QCA and the large cadmium to favor the cage assembly. On the other hand, iron has a smaller radius, which makes it an unfavorable combination with QCA. Cages can self-sort and assemble with iron coordination when PCA is present as the end aldehyde on the ligands, but not so much with QCA. Lastly, zinc as the medium radius relatively, is able to make cages with PCA with the less flexible ligands (i.e. DAS, DASenone), while makes cage with QCA with the more flexible ligand (i.e. DASol).

The synthesis of enzyme mimicking cages will help us study the interactions between enzymes and their substrates in a controlled, simplified system that is amenable to detailed mechanistic analysis. By varying the aldehyde on the existing diamines, larger cages can be synthesized with compatible cavities for target molecules. The long-term goal of this project is to create a cage with compatible substrate binding sites and to study its activity as a biomimetic catalyst. This project will contribute to the understanding on how geometric alteration affects the stoichiometry of cage assembly. Future research can be done on the exploitation of enzyme mimicking reactions, following the synthesis of the cages in this project.

Experimental Section

I. General Information

^{1}H, and ^{13}C spectra were recorded on Varian Inova 300, 400 MHz NMR spectrometers. Proton (^{1}H) chemical shifts are reported in parts per million (δ) with respect to tetramethylsilane (TMS, δ=0), and referenced internally with respect to the protio solvent impurity. Deuterated NMR solvents were obtained from Cambridge Isotope Laboratories, Inc., Andover, MA, and used without further purification. Mass spectra were recorded on an Agilent 6210 LC TOF mass spectrometer using electrospray ionization with fragmentation voltage set at 115 V and processed with an Agilent MassHunter Operating System. Predicted isotope patterns were prepared using ChemCalc. All other materials were obtained from Aldrich Chemical Company, St. Louis, MO, or TCI, Tokyo, Japan and were used as received. Solvents were dried through a commercial solvent purification system (Pure Process Technologies, Inc.). Dianiline ligand cores used in this study (3,7-diaminosuberone, 3,7-diaminosuberol, 3,7-diaminoSuberenone) were synthesized as outlined in our previous publications.[2-3] Cages were synthesized in either large scale or NMR tube scale. Two different experiments were performed to test the combination favorability of the core, ends, and metal for cage assembly.

1. Large scale general cage synthesis: 1 eq. of dianiline ligand (~25 mg) was dissolved in ~2.5 mL of acetonitrile in a 25 mL round bottomed flask. Then, 2 eq. of aldehyde were added, followed by 0.66 eq. of metal salt. The reaction mixture was allowed to stir at 70 °C for 16h. Diethyl ether was then added to the solution, and the precipitate was filtered and collected.

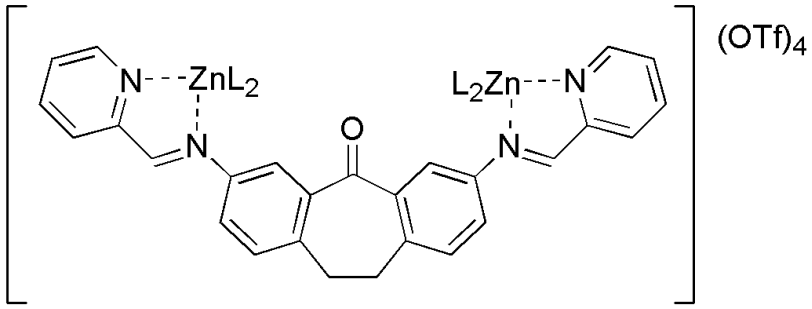
2. NMR tube general cage synthesis: 1 eq. of dianiline ligand (~10 mg) was dissolved in ~0.4 mL of CD_3CN in an NMR tube. Then, 2 eq. of aldehyde were added, followed by 0.66 eq. of metal salt. The tube was placed in an ultra-sonication bath for 5 minutes to facilitate dissolution. The sample was heated in an oil bath at 70 °C for 16h.

3. Metal displacement experiments: 1 eq. of a preformed cage is placed in an NMR tube with 0.4 mL of CD_3CN and 2 eq. of a different metal were added. The sample was sonicated followed by heating in an oil bath at 70 °C for 16 h. The purpose of this experiment is to test whether a preformed cage is able to disassociate from the existing metal and associate with the newly added metal, and whether the cage shows favorability towards one or the other.

4. Metal competition experiments: The tests were performed in an NMR tube. 1 eq. dianiline and 2 eq. aldehyde were combined with 0.33 eq. of one metal and 0.33 eq. of a second metal (0.66 eq. metal total/stoichiometric metal competition). Or 0.66 eq. of one metal and 0.66 eq. of a second metal were added to the ligand/aldehyde mixture (1.32 eq. metal total/excess metal competition). The sample was sonicated for 5 minutes to allow dissolution followed by heating in an oil bath at 70 °C for 16 h. The purpose of this experiment is to show whether heterocomplexes can be made, and the cage selectivity of the metal.

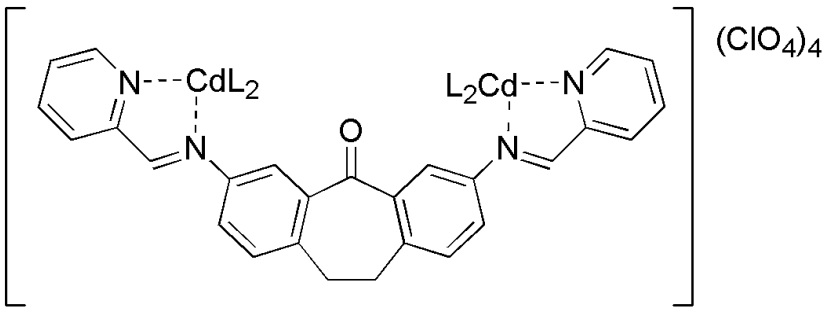
II. Synthesis of New Cage Compounds

Cage experiments were performed in an NMR tube or on a larger scale.



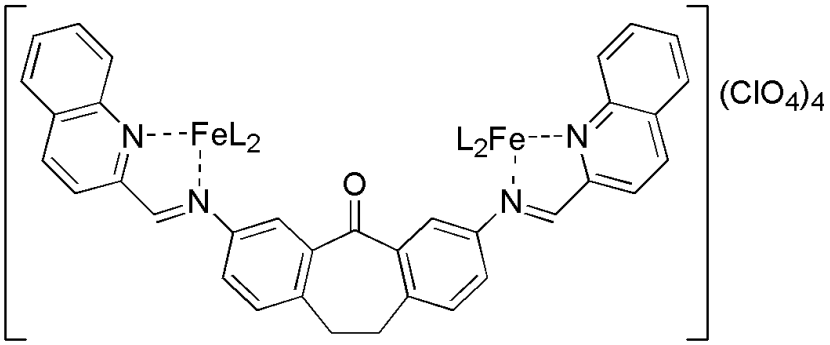
DAS+PCA+Zn Cage

Diaminosuberone (50 mg, 0.21 mmol), 2-pyridinecarboxaldehyde (40 μL, 0.42 mmol) and Zn(II)triflate•2H_2O (56 mg, 0.14 mmol) were combined in anhydrous MeCN (3 mL) in a 25 mL round-bottomed flask under a blanket of N_2 gas. The solution was then heated at 70 °C for 16 h with stirring. The orange-red solution was diluted with Et_2O (10 mL), and the resulting orange-yellow precipitate was filtered. After drying, the product was isolated as an orange-yellow solid (51 mg, 53.5 % yield). ^{1}H NMR (400 MHz, CD_3CN) δ 8.49 (td, *J* = 7.8, 1.6 Hz, 1H), 8.44 (s, 1H), 8.21 (dt, *J* = 7.9, 1.0 Hz, 1H), 8.14 (d, *J* = 4.8 Hz, 1H), 7.94 (ddd, *J* = 7.8, 5.1, 1.2 Hz, 1H), 7.21 (d, *J* = 8.1 Hz, 1H), 6.57 (s, 1H), 5.98 (dd, *J* = 7.9, 2.5 Hz, 1H), 3.22 (m, 2H).

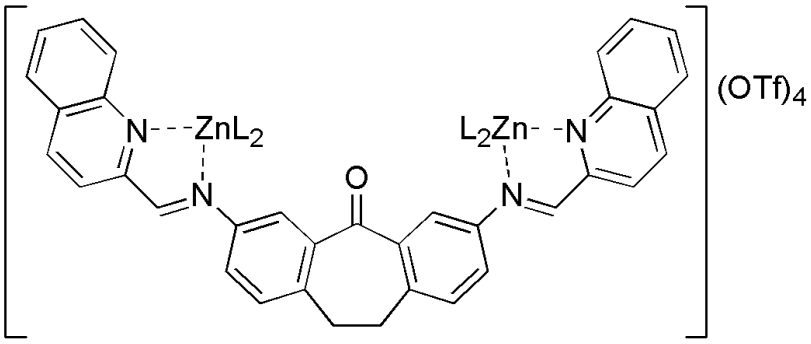


DAS+PCA+Cd Aggregate

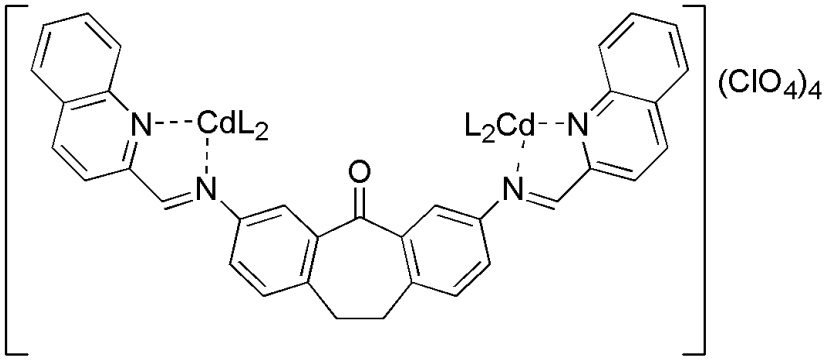
Diaminosuberone (20 mg, 0.084 mmol), 2-pyridinecarboxaldehyde (16 μL, 0.17 mmol) and $Cd(ClO_4)_2 \cdot 2H_2O$ (19 mg, 0.055 mmol) were combined in anhydrous MeCN (2.5 mL) in a 25 mL round-bottomed flask under a blanket of N_2 gas. The solution was then heated at 70 °C for 16 h with stirring. The orange solution was diluted with Et_2O (10 mL), and the resulting yellow precipitate was filtered. After drying, the product was isolated as a yellow solid (21 mg, 51.7 % yield). ^{1}H NMR (400 MHz, CD_3CN) δ 8.95 (m, 1H), 8.53 (d, *J* = 6.3 Hz, 1H), 8.36 (dd, *J* = 17.1, 9.3 Hz, 1H), 8.15 (t, *J* = 7.0 Hz, 1H), 7.85 (q, *J* = 6.4 Hz, 1H), 7.75 (t, *J* = 3.8 Hz, 1H), 7.04 (t, *J* = 7.3 Hz, 1H), 6.78 (dt, *J* = 7.7, 3.8 Hz, 1H), 2.84 (m, 2H).



DAS+QCA+Fe No Cage Formation

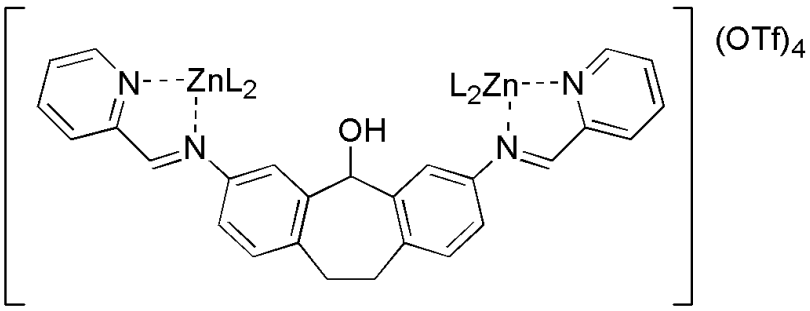


DAS+QCA+Zn No Cage Formation

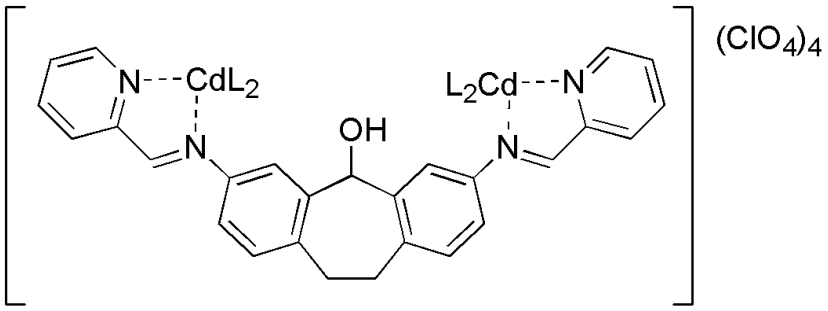


DAS+QCA+Cd Cage

Diaminosuberone (30 mg, 0.13 mmol), 2-quinolinecarboxaldehyde (40 mg, 0.25 mmol) and $Cd(ClO_4)_2 \bullet 2H_2O$ (28 mg, 0.083 mmol) were combined in anhydrous MeCN (2.5 mL) in a 25 mL round-bottomed flask under a blanket of N_2 gas. The solution was then heated at 70 °C for 16 h with stirring. The light brown-red solution was diluted with Et_2O (10 mL), and the resulting yellow precipitate was filtered. After drying, the product was isolated as a yellow solid (25 mg, 33.9 % yield). ^{1}H NMR: complex desymmetrized spectrum. See appendix figure **A3**. (400 MHz, CD_3CN) δ 9.10 (d, *J* = 8.2 Hz, 2H), 8.86 (m, 4H), 8.55 (m, 2H), 8.36 (d, *J* = 8.3 Hz, 2H), 8.20 (m, 4H), 8.01 (d, *J* = 8.4 Hz, 2H), 7.96 (d, *J* = 8.6 Hz, 2H), 7.80 (m, 8H), 7.45 (t, *J* = 7.9 Hz, 2H), 7.39 (t, *J* = 7.8 Hz, 2H), 7.19 (d, *J* = 8.0 Hz, 2H), 6.96 (d, *J* = 8.1 Hz, 2H), 6.72 (d, *J* = 2.4 Hz, 2H), 6.39 (dd, *J* = 8.1, 2.4 Hz, 2H), 5.92 (dd, *J* = 8.1, 2.5 Hz, 2H), 3.43 (dd, *J* = 15.8, 9.8 Hz, 2H), 3.19 (dd, *J* = 15.5, 9.5 Hz, 2H), 2.88 (m, 2H), 2.79 (t, *J* = 14.5 Hz, 2H).



DASol+PCA+Zn No Cage Formation



DASol+PCA+Cd Aggregate

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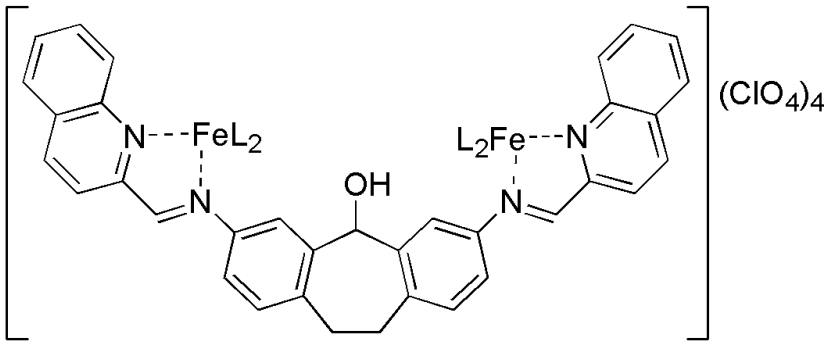
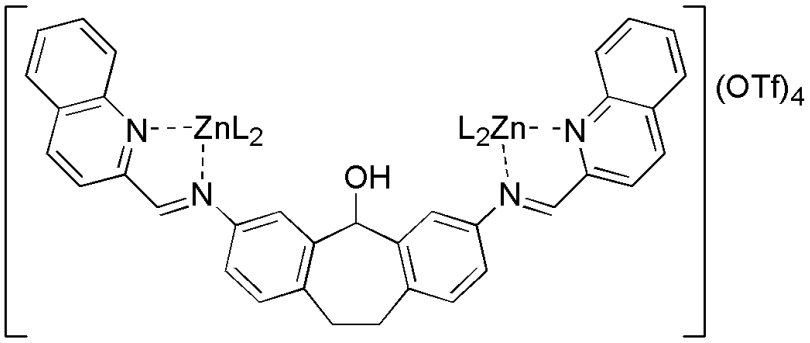


DASol+QCA+Fe Paramagnetic Cage

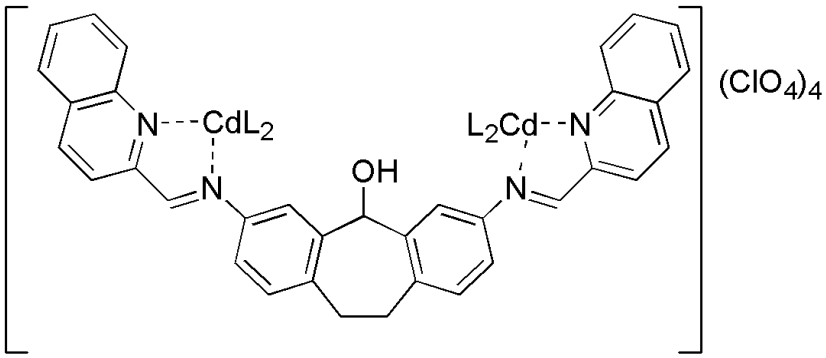
Diaminosuberol (25 mg, 0.10 mmol), 2-quinolinecarboxaldehyde (33 mg, 0.21 mmol) and $Fe(ClO_4)_2 \cdot 6H_2O$ (25 mg, 0.069 mmol) were combined in anhydrous MeCN (3 mL) in a 25 mL round-bottomed flask under a blanket of N_2 gas. The solution was then heated at 65 °C for 16 h with stirring. The brown-red solution was diluted with Et_2O (10 mL), and the resulting brown precipitate was filtered. After drying, the product was isolated as a brown solid (28 mg, 49 % yield). ^{1}H NMR (400 MHz, CD_3CN) δ 55.26 (s, 1H), 26.05 (s,

1H), 24.04 (s, 1H), 13.65 (d, *J* = 11.5 Hz, 1H), 6.56 (s, 1H), 5.72 (s, 1H), 5.58 (d, *J* = 11.5 Hz, 1H), 1.37 (s, 1H), -10.17 (s, 1H), -19.69 (s, 1H).



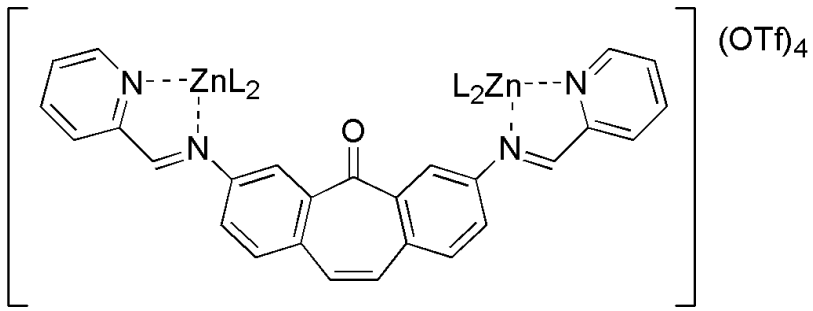
DASol+QCA+Zn Cage

Diaminosuberol (40 mg, 0.17 mmol), 2-quinolinecarboxaldehyde (53 mg, 0.34 mmol) and Zn(II)triflate•$2H_2O$ (44 mg, 0.11 mmol) were combined in anhydrous MeCN (2.5 mL) in a 25 mL round-bottomed flask under a blanket of N_2 gas. The solution was then heated at 70 °C for 16 h with stirring. The dark red solution was diluted with Et_2O (10 mL), and the resulting brown precipitate was filtered. After drying, the product was isolated as a brown solid (87 mg, 93 % yield). ^{1}H NMR (400 MHz, CD_3CN) δ 8.61 (d, *J* = 8.4 Hz, 1H), 8.17 (m, 2H), 8.02 (d, *J* = 2.6 Hz, 1H), 7.77 (t, *J* = 7.6 Hz, 1H), 7.48 (dd, *J* = 8.2, 4.0 Hz, 1H), 6.62 (d, *J* = 7.9 Hz, 1H), 6.06 (d, *J* = 5.1 Hz, 1H), 5.21 (dd, *J* = 8.1, 2.5 Hz, 1H), 3.54 (q, *J* = 7.0 Hz, 1H), 3.31 (t, *J* = 8.2 Hz, 1H), 2.78 (h, *J* = 10.6, 10.1 Hz, 1H), 2.66 (d, *J* = 5.2 Hz, 1H).



DASol+QCA+Cd Cage

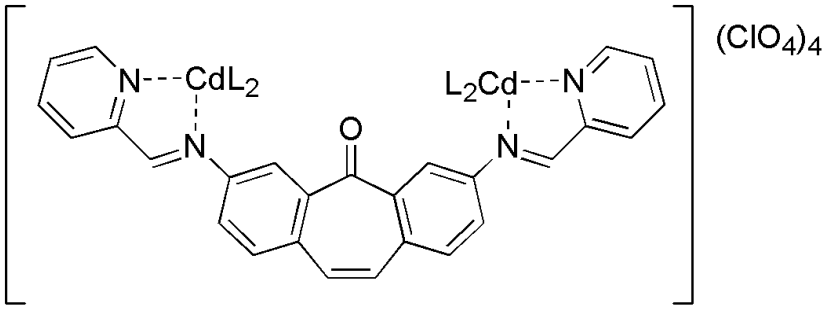
Diaminosuberol (200 mg, 0.84 mmol), 2-quinolinecarboxaldehyde (263 mg, 1.67 mmol) and $Cd(ClO_4)_2 \cdot 2H_2O$ (192 mg, 0.55 mmol) were combined in anhydrous MeCN (4 mL) in a 25 mL round-bottomed flask under a blanket of N_2 gas. The solution was then heated at 65 °C for 16 h with stirring. The orange solution was diluted with Et_2O (10 mL), and the resulting yellow precipitate was filtered. After drying, the product was isolated as a yellow solid (457 mg, 93.3 % yield). ^{1}H NMR (400 MHz, CD_3CN) δ 8.62 (d, *J* = 8.3 Hz, 1H), 8.27 (m, 1H), 8.18 (d, *J* = 8.3 Hz, 1H), 8.06 (d, *J* = 8.6 Hz, 1H), 7.95 (d, *J* = 2.4 Hz, 1H), 7.78 (dd, *J* = 8.2, 6.9 Hz, 1H), 7.56 (m, 2H), 6.55 (d, *J* = 8.0 Hz, 1H), 6.01 (d, *J* = 5.3 Hz, 1H), 5.24 (dd, *J* = 8.0, 2.4 Hz, 1H), 3.24 (m, 1H), 2.74 (m, 1H).



DASenone+PCA+Zn Cage

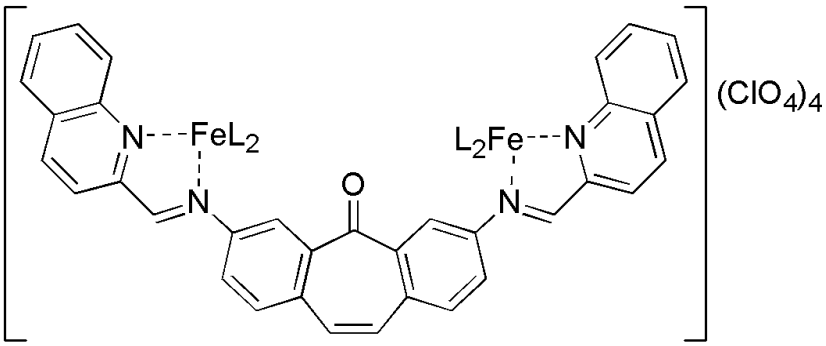
Diaminosuberenone (10 mg, 0.042 mmol), 2-pyridinecarboxaldehyde (8 μL, 0.085 mmol) and Zn(II)triflate•$2H_2O$ (10 mg, 0.028 mmol) were combined in CD_3CN (0.3 mL) in an NMR tube. The solution was sonicated for 5 minutes, then heated at 70 °C for 16 h. After

the reaction completed, the solution was orange. ^{1}H NMR (300 MHz, CD_3CN) δ 8.57 (m, 2H), 8.30 (m, 1H), 8.03 (m, 2H), 64 (m, 1H), 7.24 (d, *J* = 9.3 Hz, 1H), 6.88 (d, *J* = 2.5 Hz, 1H), 6.08 (dd, *J* = 8.3, 2.5 Hz, 1H).

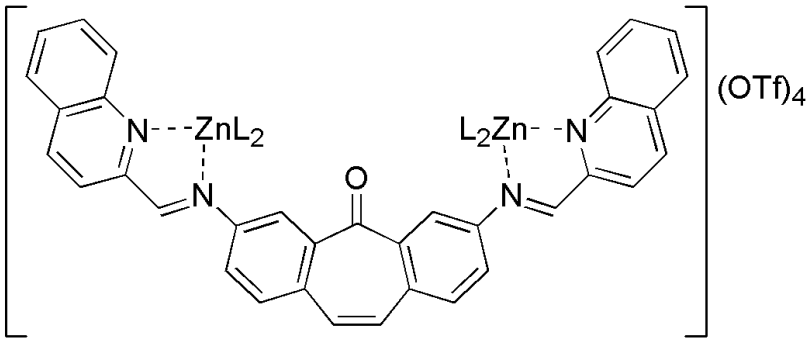


DASenone+PCA+Cd Aggregate

Diaminosuberenone (10 mg, 0.042 mmol), 2-pyridinecarboxaldehyde (8 μL, 0.085 mmol) and $Cd(ClO_4)_2$•$2H_2O$ (8 mg, 0.028 mmol) were combined in CD_3CN (0.3 mL) in an NMR tube. The solution was sonicated for 5 minutes, then heated at 70 °C for 16 h. After the reaction completed, the solution was orange. ^{1}H NMR (300 MHz, CD_3CN) δ 8.81 (m, 1H), 8.69 (m, 1H), 8.28 (dd, *J* = 16.6, 8.7 Hz, 1H), 8.06 (s, 1H), 7.99 (m, 1H), 7.86 (m, 1H), 7.37 (d, *J* = 8.5 Hz, 1H), 6.95 (s, 1H), 6.61 (d, *J* = 8.9 Hz, 1H).

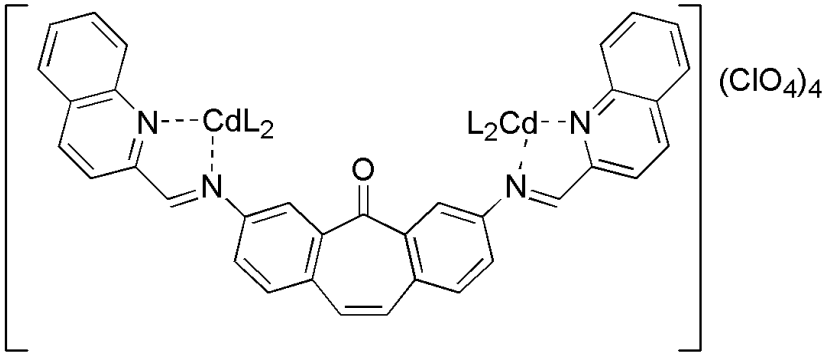


DASenone+QCA+Fe No Cage Formation



DASenone+QCA+Zn Aggregate

Diaminosuberenone (10 mg, 0.042 mmol), 2-quinolinecarboxaldehyde (13 mg, 0.085 mmol) and Zn(II)triflate•$2H_2O$ (10 mg, 0.028 mmol) were combined in CD_3CN (0.3 mL) in an NMR tube. The solution was sonicated for 5 minutes, then heated at 70 °C for 16 h. After the reaction completed, the solution was brown.

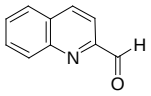
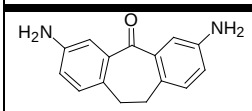
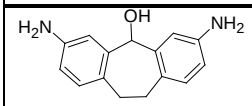
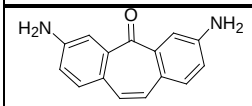


DASenone+QCA+Cd Cage

Diaminosuberenone (10 mg, 0.042 mmol), 2-quinolinecarboxaldehyde (13 mg, 0.085 mmol) and $Cd(ClO_4)_2$•$2H_2O$ (8 mg, 0.028 mmol) were combined in CD_3CN (0.3 mL) in an NMR tube. The solution was sonicated for 5 minutes, then heated at 70 °C for 16 h. After the reaction completed, the solution was red. ^{1}H NMR (400 MHz, CD_3CN) δ 8.86 (d, *J* = 8.6 Hz, 1H), 8.80 (s, 1H), 8.28 (d, *J* = 2.5 Hz, 1H), 8.24 (d, *J* = 8.4 Hz, 1H), 8.00 (m, 2H), 7.81 (t, *J* = 7.6 Hz, 1H), 7.53 (t, *J* = 7.8 Hz, 1H), 7.29 (d, *J* = 8.4 Hz, 1H), 6.96 (s, 1H), 6.36 (dd, *J* = 8.4, 2.5 Hz, 1H).

Appendix

Table 1: Summery of various combination of core, end, and metal, and whether a cage was formed.

Aniline	2-formylpyridine 	2-Qulinolinecarboxyaldehyde 	Metal
 **DAS**	Yes	No	**$Fe(ClO_4)_2$**
	Yes	No	**Zn(II)triflate**
	Yes	Yes	**$Cd(ClO_4)_2$**
 **DASol**	Yes	Yes	**$Fe(ClO_4)_2$**
	No	Yes	**Zn(II)triflate**
	Yes	Yes	**$Cd(ClO_4)_2$**
 **DASenone**	Yes	No	**$Fe(ClO_4)_2$**
	Yes	No	**Zn(II)triflate**
	Yes	Yes	**$Cd(ClO_4)_2$**

Characterization of New Cage Compounds

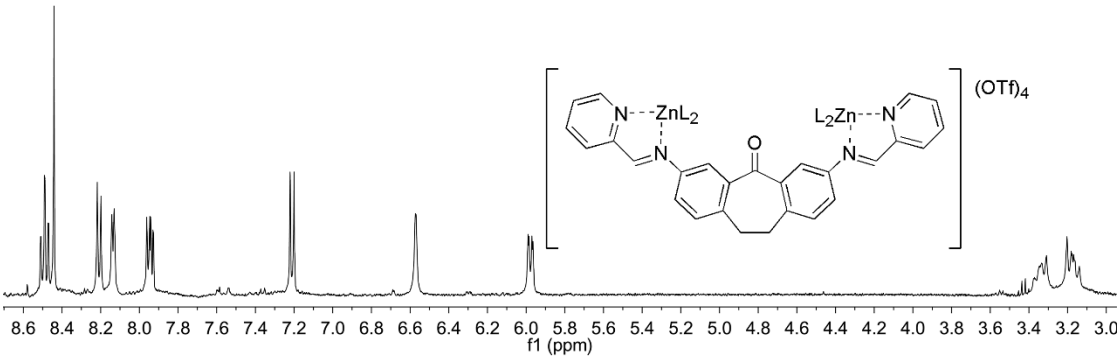


Figure A1: ^{1}H NMR spectrum of DAS+PCA+Zn (CD_3CN, 400 MHz, 298 K).

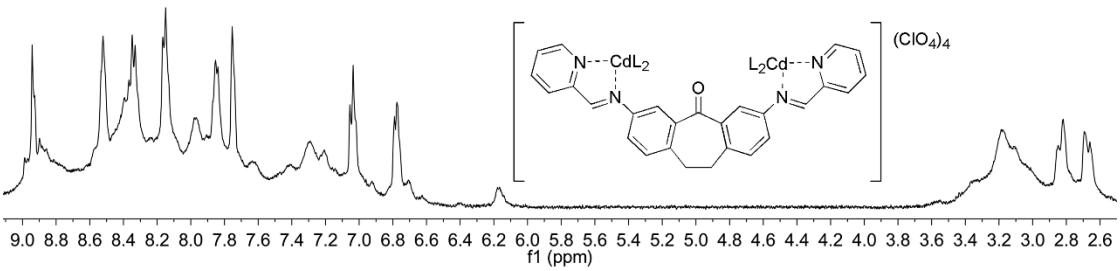


Figure A2: ^{1}H NMR spectrum of DAS+PCA+Cd (CD_3CN, 400 MHz, 298 K).

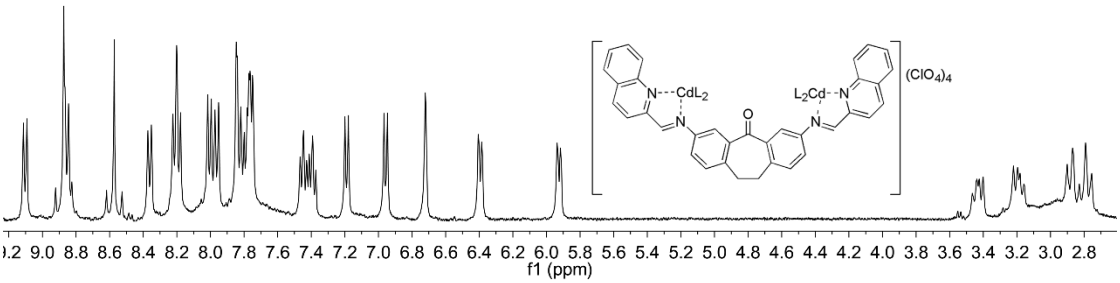


Figure A3: ^{1}H NMR spectrum of DAS+QCA+Cd (CD_3CN, 400 MHz, 298 K).

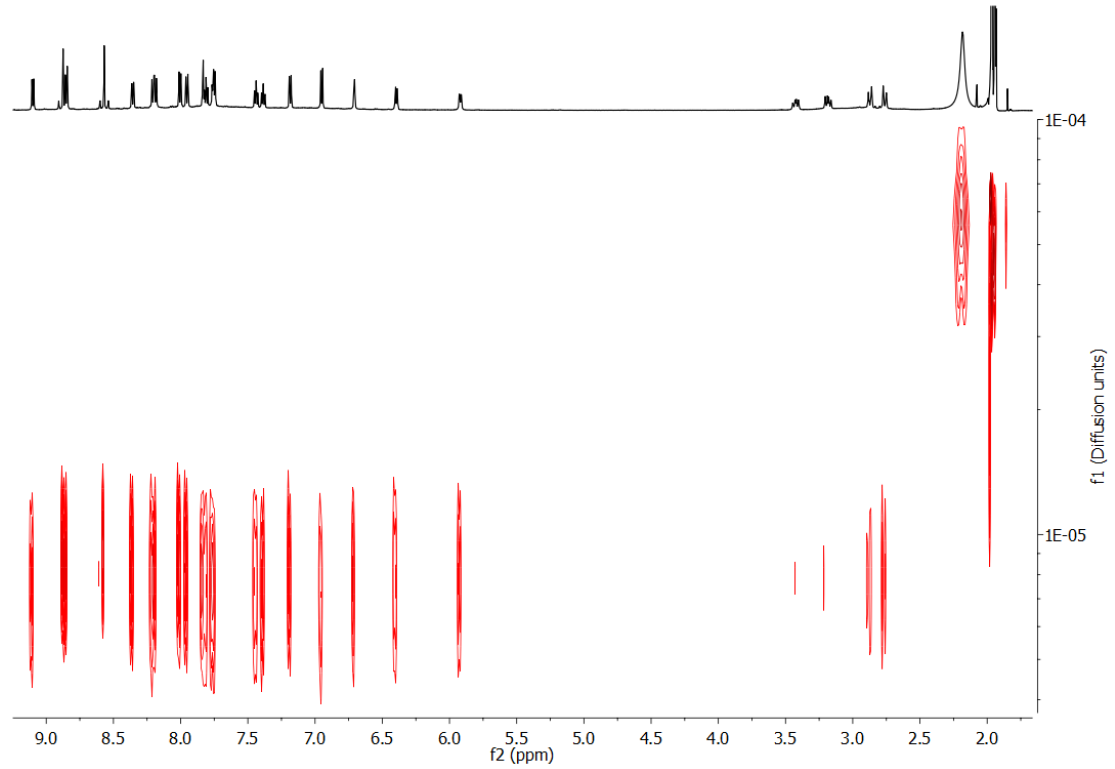


Figure A4: ^{1}H-DOSY NMR spectrum of DAS+QCA+Cd (CD_3CN, 600 MHz, 298 K, Δ = 100 ms, δ = 2.6 μs, Diffusion constant = 2.1777×10^{-9} m^2/s for DAS+QCA+Cd vs. 9.7274×10^{-9} m^2/s for the solvent).

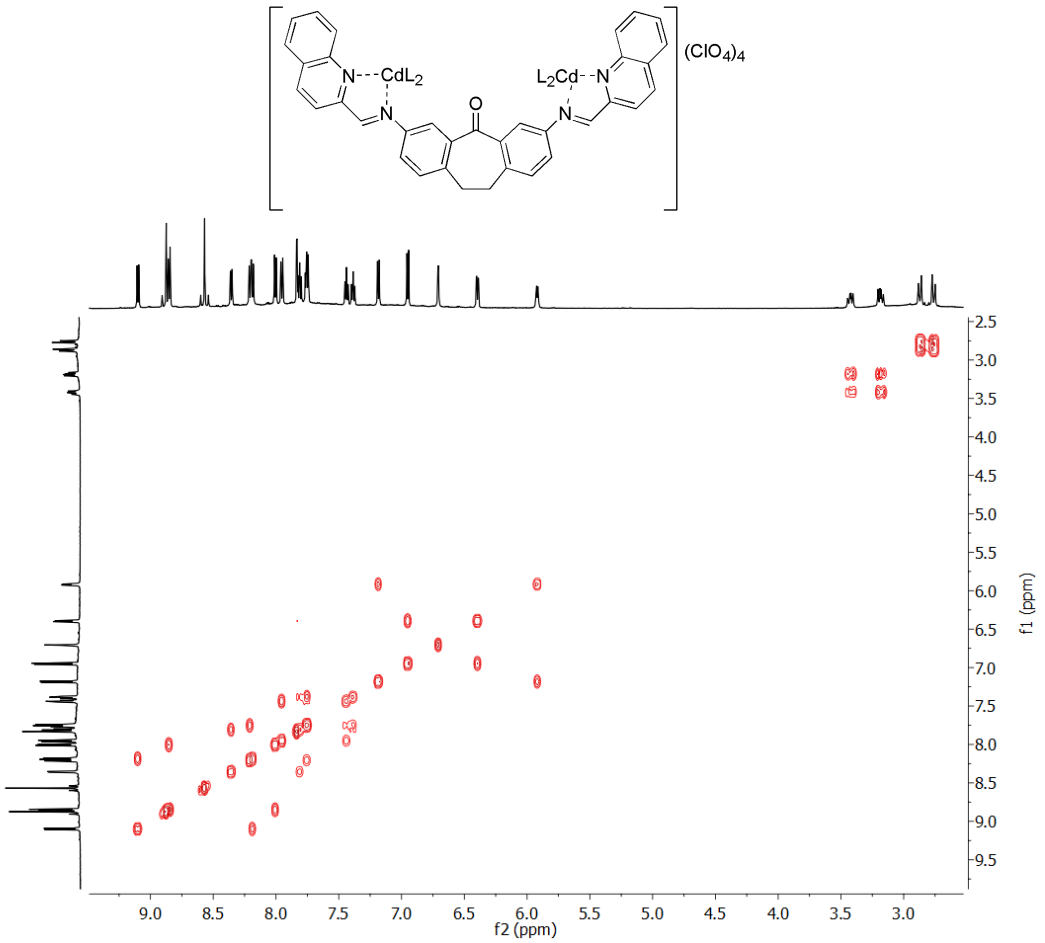


Figure A5: COSY NMR spectrum of DAS+QCA+Cd (CD_3CN, 600 MHz, 298 K).

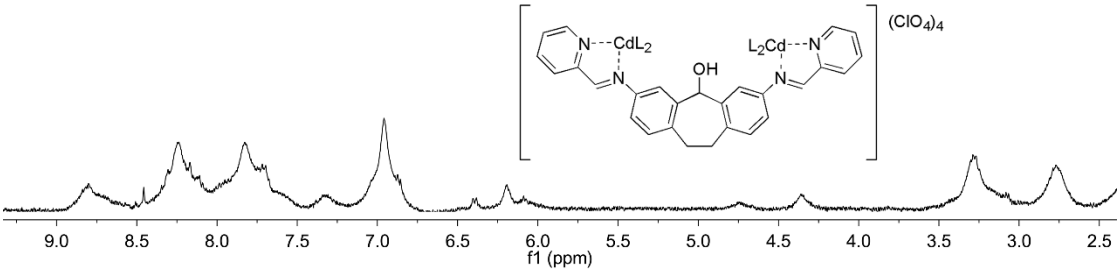


Figure A6: ^1H NMR spectrum of DASol+PCA+Cd (CD_3CN, 400 MHz, 298 K).

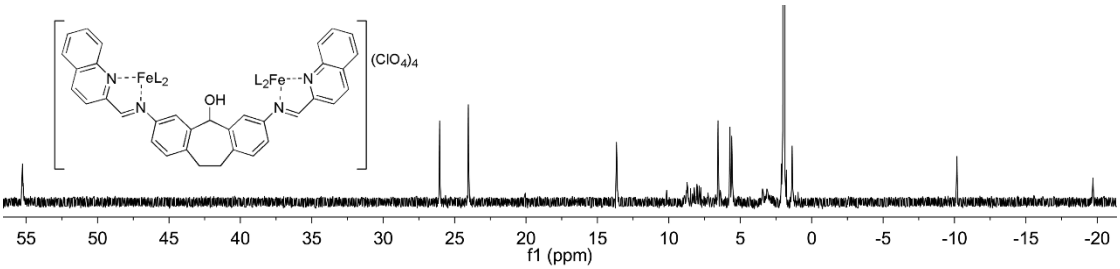


Figure A7: ^{1}H NMR spectrum of DASol+QCA+Fe (CD_3CN, 400 MHz, 298 K).

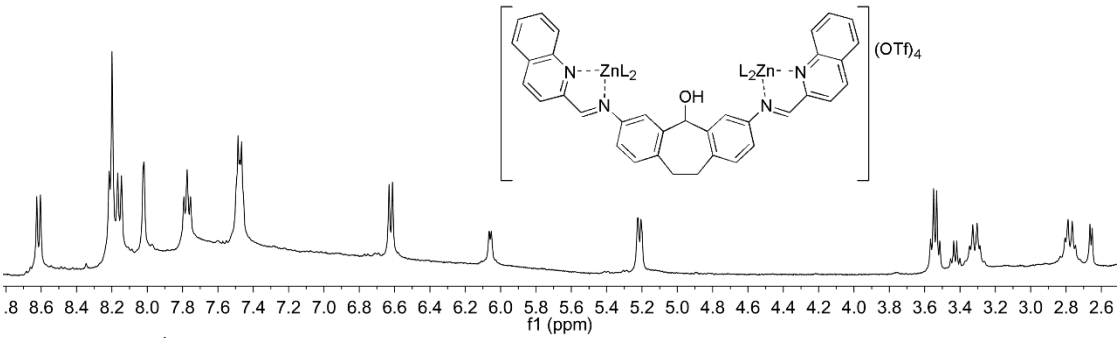


Figure A8: ^{1}H NMR spectrum of DASol+QCA+Zn (CD_3CN, 400 MHz, 298 K).

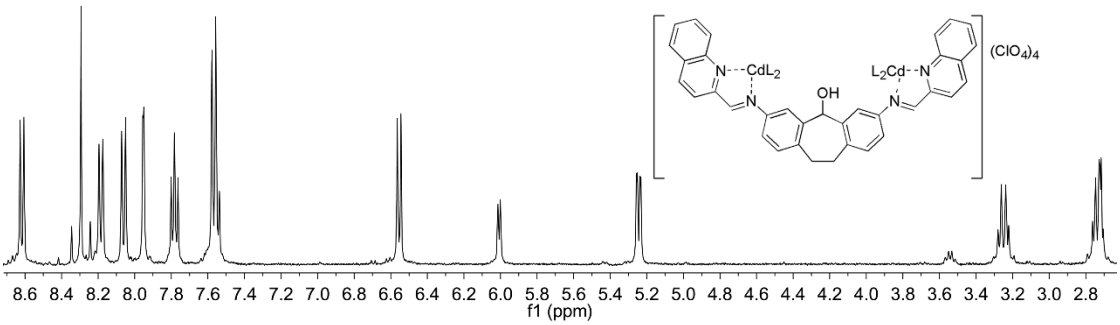


Figure A9: ^{1}H NMR spectrum of DASol+QCA+Cd (CD_3CN, 400 MHz, 298 K).

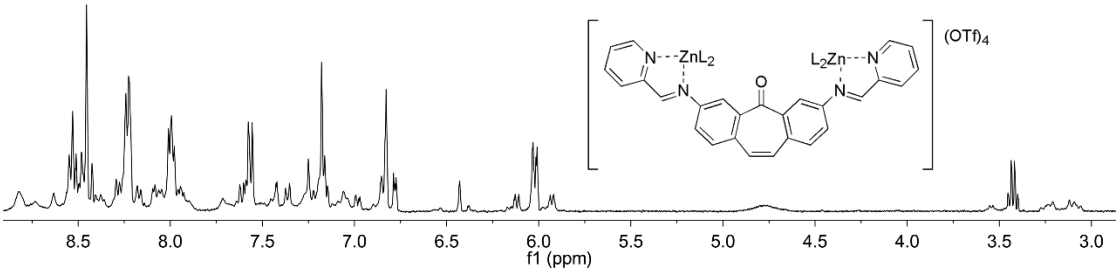


Figure A10: ^{1}H NMR spectrum of DASenone+PCA+Zn (CD_3CN, 400 MHz, 298 K).

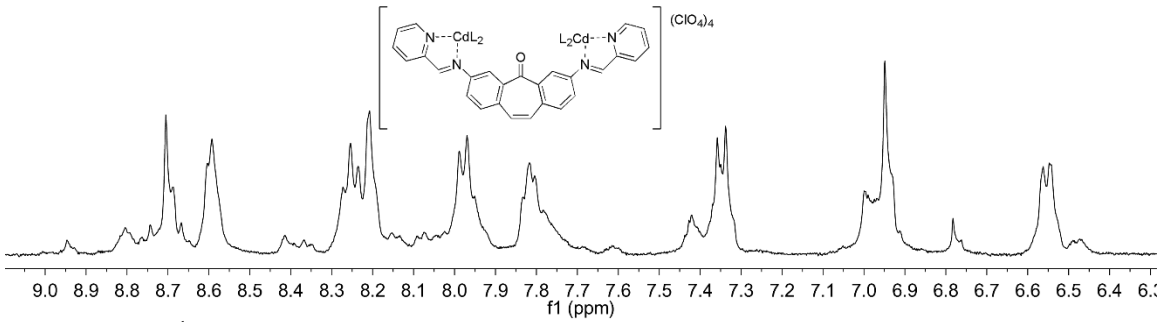


Figure A11: ^{1}H NMR spectrum of DASenone+PCA+Cd (CD_3CN, 400 MHz, 298 K).

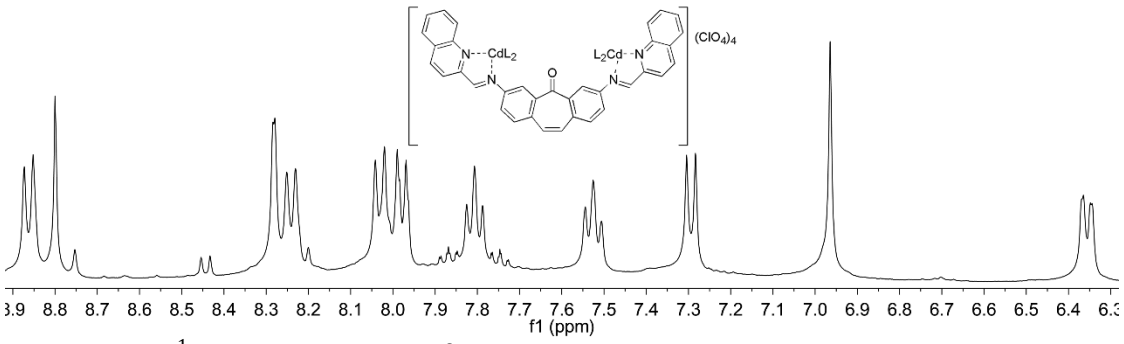


Figure A12: ^{1}H NMR spectrum of DASenone+QCA+Cd (CD_3CN, 400 MHz, 298 K).

References

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