Supramolecular Metallacycles and Their Binding of Fullerenes

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Abstract: The synthesis of a new triaminoguanidinium-based ligand with three tris-chelating \( [\text{NNO}] \)-binding pockets and \( C_3 \) symmetry is described. The reaction of tris-(2-pyridinylene-N-oxide)triaminoguanidinium salts with zinc(II) formate leads to the formation of cyclic supramolecular coordination compounds which in solution bind fullerenes in their spherical cavities. The rapid encapsulation of \( \text{C}_{60} \) can be observed by NMR spectroscopy and single-crystal X-ray diffraction and is verified using computation.

Introduction

The development of supramolecular coordination compounds and their corresponding cages has attracted wide interest in recent years.[1] They have the potential to transport chemicals from one location to another in a specific manner, for example, being used in drug delivery or as contrast agents.[2] The structural design of these containers requires precise and complementary building blocks but they are not limited to the incorporation of small organic molecules.[3] There are only a few examples of toroid coordination compounds and larger aggregates in the literature (Figure 1A).[4] Those compounds can be used as single molecular magnets or in the separation of fullerenes.[5] Stang introduced the concept of using building blocks to form cage compounds,[6] whereas the groups of Saalfrank, Fujita, and Nitschke used cages to stabilize reactive species like white phosphorous \( \text{P}_4 \) and organometallic complexes.[6b, 7]

Toroids can be useful in binding guest molecules. Covalently bonded systems are quite common, for example, cyclodextrins, cucurbiturils and cryptands which bind cations,[8] anions,[9] or hydrophobic molecules[10] by variation of their peripheral decora-

Figure 1. (a) Previously reported supramolecular metallacycles. Hydrogen atoms and solvent molecules were omitted for clarity. Different scales were applied and metal ions highlighted as spheres. (b) Synthesis of subunit \( \text{H}_3(\text{pyO})_3\text{L} \) (5-X). (c) Supramolecular metallacycle \( [\text{Zn}_2\text{Cl}_2(\text{pyO})_2\text{L}]_2 \) (\( \text{ZnCl}_2 \) in green), schematic drawing and inclusion complex \( \text{C}_{60} \).

Supporting information and the ORCID identification number(s) for the author(s) of this article can be found under:

https://doi.org/10.1002/chem.201905390.

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Chem. Eur. J. 2020, 26, 3609 – 3613

DOI: 10.1002/chem.201905390

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encapsulated supramolecular entity. We were able to compute spectroscopic properties and assign the \( C_{60} \) signals in both the free state and bound inside of the metallacycle (Figure 1C). There are a large number of studies reporting the computations of \( C_{60} \) itself. However, publications focusing on the interaction of \( C_{60} \) with other macrocycles are limited. Most studies including these interactions involve smaller, and often purely organic macrocyclic systems.\(^{[11]}\) To the best of our knowledge, this is the first study to computationally investigate such large interacting systems (>4000 electrons) using non-truncated models.

### Results and Discussion

Our group demonstrated the synthesis of supramolecular structures by self-assembly of \( C_7 \) symmetric building blocks with three \( tris \)-chelating binding pockets and suitable co-ligands (analogous to Figure 1B).\(^{[13]}\) Counter ions or solvent molecules typically serve as templates in the synthesis, so that discrete coordination cages like \( M_{12}L_4 \) (Figure 2, left), \( M_{18}L_{16} \) or \( M_{63}L_{24} \) are accessible.\(^{[13d]}\) We did not observe any activation of small molecules with these assemblies, even though a high number of potential catalytically active metal centers are located proximal to each other.

![Figure 2. \( M_{12}L_4 \) tetrahedron and \( M_{18}L_{16} \) dimer (\( M = \text{Cd, Sn, respectively} \)). Hydrogen atoms and solvent molecules were omitted for clarity.]()

The overall negative charge of these complexes might be the reason why substrates like lactide are not satisfactorily activated. It was thus necessary to increase the amount of positive charges of the resulting coordination compounds by using stronger Lewis acids, such as \( \text{Sn}^+ \) or \( \text{Zr}^5 \), instead of \( \text{Cd}^0 \) or \( \text{Pd}^0 \). The resulting complexes typically form dimers or trimers and are able to oligomerize acetone in up to 15 repeating units (Figure 2, right).\(^{[13, 14, 15]}\)

In this work we address the charge issue by increasing the number of positive charges in the ligand itself, while maintaining the isoelectronic structure of the previously reported ligands. The ligand is prepared from an condensation reaction between 2-formylpyridine-\( N \)-oxide and the corresponding triaminoguanidinium salts TAG\(_{-}\)Cl (4-Cl), TAG-NCS (4-NCS), or TAG-BF\(_{4} \) (4-BF\(_{4} \)), respectively (Figure 1B).

The synthesis of \( N \)-oxide (3) requires standard protection and deprotection procedures for the aldehyde moiety. The oxidation of the pyridine nitrogen can be realized under mild conditions by using urea hydrogen peroxide with phthalic anhydride in acetonitrile.\(^{[16]}\) Triaminoguanidinium salts (4-X) are obtained by the amination of guanidinium salts with hydrazine hydrate.\(^{[17]}\) The resulting compounds (5-X) serve as an excellent ligands for \( \text{Zn}^2 \). The reaction of \([\text{H}_2\text{(pyO)}_4]\text{Cl} \) (5-Cl) with \( \text{Zn(O}_2\text{CH})_2 \) in \( \text{N,N}-\text{dimethylformamide} \) results in the formation of a supramolecular coordination compound \( \left\{ \text{Zn}_{ij}\text{Cl}_{4}\{(pyO)}_4\text{L}_{ij}\right\} \) (6, Figure 1C) next to a coordination polymer of unknown composition. This torus-shaped metallacycle exhibits an outer diameter of 31.7 Å and \( \text{Zn}^2 \) ions are octahedrally coordinated between two alternately oriented ligands holding together the assembly (Figure 3 and Figure 4, left). The \( \text{ZnCl}_2 \) moieties occupy the remaining [NNO] binding pockets. A spherical cavity of 10.7 Å can be found inside the complex with a pore opening of 8.2 Å. Each value is corrected by the covalent radii of hydrogen or carbon atoms.

![Figure 3. Molecular dimensions of metallacycles by X-ray diffraction compared to spectroscopic data of 7. The void space is indicated by the blue sphere.]

An isostructural cyclic coordination oligomer \( \left\{ \text{Zn}_{j}\text{Br}_{6}\{(pyO)}_4\text{L}_{j}\right\} \) (7) can be crystallized from the reaction mixture containing \([\text{H}_2\text{(pyO)}_4]\text{L}_{18}u\text{ZnBr}_2\) and \( \text{NaO}_2\text{CH} \). DOSY-NMR spectroscopy ([D\(_6\)]DMSO) of 7 shows neither decomposition nor aggregation of the coordination complex in solution. Only one species is detected in addition to solvents and water. The diffusion coefficient of 7 is found to be \( D = (7.36 \pm 0.08) \times 10^{-7} \text{ cm}^2 \text{s}^{-1} \). The hydrodynamic diameter of 7 can be determined to be 29.9 ± 1.2 Å using the Stokes–Einstein equation,
which corresponds well with the observed diameter of the crystal structure (Supporting Information Figure S5 and S6).

Introduction of isothiocyanate leads to the formation of the analogous NCS-metallacycle [Zn$_{60}$(NCS)$_{16}$(O$_2$CH)$_{12}$](pyO)$_2$L$_{12}$] (8) with a 59% yield. The zinc(II) ions, which were formally occupied by the halides Cl$^-$ or Br$^-$, share those sites with isothiocyanate and formate co-ligands (Figure 4, right). The presence of this coordination compound, and the absence of smaller or larger aggregates in the DMSO solution, was confirmed by dynamic light scattering (Supporting Information). Since the co-ligands point outwards and exhibit a slightly increased steric demand, the system crystallizes in the tetragonal space group P42_1c with solvent filled channels along the crystallographic c-axis (Figure 5a).

Host-guest chemistry seems feasible since the cavities of the coordination oligomers should be accessible in the solid state. To our surprise, it was not possible to soak crystals of [Zn$_{60}$(NCS)$_{16}$(O$_2$CH)$_{12}$](pyO)$_2$L$_{12}$] (8) with a toluene solution of C$_{60}$ as there was no observed color change. From these experimental results we decided to encapsulate the fullerenes into the metallacycles in solution. A solution of empty metallacycle (8) was added to a toluene solution of C$_{60}$ or C$_{70}$. Single crystals of the respective inclusion compounds were collected after a few days (Figure 5b–d). The C$_{60}$ and C$_{70}$ are fully incorporated into the cavity of the metallacycle [Zn$_{60}$(NCS)$_{16}$(O$_2$CH)$_{12}$](pyO)$_2$L$_{12}$] (9). The lattice parameters underwent a slight change compared to 8, whereas the space group was maintained. The periphery of the metallacycle was slightly perturbed, presumably due to the change in polarity of the solvent mixture.

The incorporation of C$_{60}$ in solution is validated by NMR spectroscopy (Figure 6). Crystals of 8 and C$_{60}$C$_{9}$ were removed from the crystallization solution, washed with THF and dissolved in [D$_6$]DMSO. The $^1$H NMR spectrum shows a shift and broadening of the signals due to the molecular tumbling of C$_{60}$. The $^{13}$C NMR of C$_{60}$C$_{9}$ shows only one signal for C$_{60}$ which is in agreement with all carbon atoms being chemically and magnetically equivalent. The encapsulated C$_{60}$ can only be detected next to free C$_{60}$ in a highly diluted solvent mixture, and therefore $^{13}$C-enriched C$_{60}$ was used. The 2 ppm signal shift from 142.18 ppm (free C$_{60}$) to 140.40 ppm (C$_{60}$C$_{9}$) clearly indicates the incorporation of C$_{60}$ in the cavity of the metallacycle.

Calculations predicted the encapsulation of C$_{60}$ by the metallacycle (6) to be favorable (Figure 7c A). However, there is an additional local minimum (C) where the C$_{60}$ interacts with the periphery of the metallacycle. This has also been observed crystallographically. An analogous binding plot is observed for the C$_{70}$ case (see Supporting Information for details). The use of dispersion corrections in these calculations is critical in order to correctly model the attractive interaction. In addition to the entropy loss, there is an electronic energy barrier (B) that C$_{60}$ (and C$_{70}$) must overcome caused by steric interactions between the C$_{60}$/70 and pyridinyl groups located at the entrance of the metallacycle. Due to the nature of these calculations, stepwise single-point calculations from the fully optimized state (A) were applied. The binding energetics are only

**Figure 5.** (a) Crystal packing of 8. π-π-interactions are highlighted in turquoise. (b,c) C$_{60}$C$_{9}$. (d) C$_{70}$C$_{9}$. Disordered solvent molecules were removed by the Squeeze routine and hydrogen atoms were omitted for clarity.

**Figure 6.** (a,b) $^1$H NMR spectra in [D$_6$]DMSO of 8 and C$_{60}$C$_{9}$ respectively. (c) $^{13}$C NMR spectrum of 8 (1 equiv) and C$_{60}$C$_{9}$ (2 equiv) in [D$_6$]DMSO/1,2-dichlorobenzene-d$_4$ 1:1 (v/v). (d) $^{13}$C NMR spectrum of C$_{60}$C$_{9}$ in [D$_6$]DMSO.
The differences in electrostatic potentials for $6-8$ are shown in Figure 7b. The chloride metallacycle has the largest positive inner core while the outside ZnCl$_2$ moieties carry the negative potential. This is gradually attenuated in the series of $6 > 7 > 8$ with $8$ having the least positive inner core. These potentials might be useful in tuning the affinity and specificity for guest molecules.

In agreement with experimental data, spectroscopic assignments using computations (DFT, see Supporting Information for details) predict an approximately 2.0 ppm upfield shift for the encapsulated C$_{60}$ species versus the free C$_{60}$ (144.3 ppm vs. 142.2 ppm) (Figure 7a). The IR signatures of an empty chloride metallacycle ($6$) also match the computed IR spectrum and the fingerprint region contains several characteristic absorptions (Figure S25 in the Supporting Information).

**Summary**

We report the synthesis of a new type of tris-chelating pyridine-N-oxide based ligands [H$_3$(pyO)$_3$L]X. Coordination of zinc(II) ions leads to structurally interesting cyclic coordination oligomers which serve as hosts for fullerenes C$_{60}$ and C$_{70}$. The inclusion of fullerenes was observed by single-crystal X-ray diffraction and NMR spectroscopy, and was validated using computations. These metallacycles are robust and show no sign of decomposition. Although computations on such large systems are challenging, we were able to model the C$_{60}$/C$_{70}$ encapsulated metallacycles and even predict spectroscopic data, which are in strong agreement with the experimental results. Electrostatic potential maps reveal that the positive charges of the cavity cores can be tuned by the peripheral halide co-ligands. These computations help to provide a deeper understanding of host-guest interaction in these metallacycles. Similar computations will no doubt be useful for the rational design of host molecules with other cargo. In the future, these complexes could serve as container molecules transporting important cargo.$^{[2f, 20]}$

**Experimental Section**

Experimental methods, synthesis, computational details and results can all be found in the Supporting Information. CCDC 1830922, 1830936, 1830997, 1851696, 1831512, 1831515, 1831516 (3, 5-Cl, 6, 7, 8, C$_{60}$C$_{9}$, C$_{70}$C$_{9}$, respectively), contain the supplementary crystallographic data for this paper. These data are provided free of charge by The Cambridge Crystallographic Data Centre.

**Acknowledgements**

We gratefully acknowledge the International Research Training Group 1628 SeleCa “Selectivity in Chemo- and Bio-catalysis” (Deutsche Forschungs-gemeinschaft) for funding this work. Furthermore, we like to thank Dr. Khai Ngii Truong from the group of Prof. Dr. Ulli Engelert (RWTH Aachen University) and Manuela Winter from the group of Prof. Dr. Roland A. Fischer (Ruhr-Universität Bochum) for collection single-crystal X-ray diffraction data, Rachida Bmaharat and Dr. Gerhard Fink for NMR spectroscopic measurements. We are grateful to the Alexander von Humboldt Foundation for support of A.E. We thank Prof. Dr. John A. Gladysz (Texas A&M University) and the U.S. National Science Foundation (CHE-1566601, 1664866, 1900549) for financial support. We thank Prof. Dr. Michael B. Hall and Dr. Lisa M. Pérez (Texas A&M University) for fruitful discussions and the Laboratory for
Molecular Simulation. We thank the Texas A&M High Performance Research Computing Facility for computational resources. We thank Prof. Dr. Steven E. Wheeler (University of Georgia) for providing scripts to generate ESP plots.

Conflict of interest

The authors declare no conflict of interest.

Keywords: cage compounds · density functional calculations · fullerences · host-guest systems · self-assembly

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Manuscript received: November 28, 2019
Accepted manuscript online: December 12, 2019
Version of record online: March 5, 2020