Resorcinarene Nanocapsule Library for Metal Extractions

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ABSTRACT Resorcinarene Tetraalkene Tetrathiol 'RTATT' polymeric nanocapsules were prepared in the absence of sacrificial template, surfactants or self-assembly. A series of functionalized 'RTATT' nanocapsules were prepared in a one-pot light mediated thiol-ene click reaction using various ligands. The metal extraction ability of several as prepared nanocapsule solutions were tested for their ability to extract metal cations (Ni²⁺, Cu²⁺, Co²⁺, Au³⁺, Pt²⁺, and Pt⁴⁺) in small scale liquid-liquid extraction studies. The extraction abilities of representative nanocapsules are promising, revealing the impact of functionalization on their metal extraction capabilities.

Introduction

Calixarenes, resorcinarenes and similar supramolecular units have been of interest in applications involving molecular recognition and the coordination of metals.¹ Moreover, derivative molecules bearing the calix[n]arene template have been known to interact with metals forming molecular scaffolds,² serving as metal chelators (with dependence on attached chelation groups),³ selectively binding to ions,⁴ heavy metals⁵ and in the extraction and removal of various metals.^{6,7} The properties of metal extractants in general, can be attributed to associated functional groups.⁸ Many well-known extractants contain functional groups such as carboxylic acids, amines, amides, ketones, oximes and phosphorus bearing acids.⁸ Appropriate conditions for metal binding are often associated with pH dependent chelation between ionized forms of the ligand, and the metal of interest, which will result in adjustable metal affinities depending on pH and kinetic conditions. In hydrometallurgical extraction processes, metal extraction and extractant recovery are often achieved through reversible metal coordination complexes which can bind and release specific metal cations.⁸ However, as opposed to common extractants which might typically be used commercially, the properties of extractants derived from calixarene attain additional favorable features towards metal binding, which enable their enhanced affinities.⁹ Such enhancements depend on the possible conformations of the general tetrameric structure, multiple functionalization locations, metal docking sites, all of which allow for the extended usefulness of such extractants. Likewise, the supramolecular molecules derived from calixarene may be further incorporated into structural frameworks, while retaining their desired attributes. In a recent review¹⁰, such modifications as incorporating calixarenes in polymer supports, absorbents, or self-polymerized structures were discussed, and can be complementary by retaining their metal binding characteristics under an array of frameworks. The resorcinarene structure 1-2, is a subset of calixarenes widely known through hostguest chemistry, and can be readily synthesized through condensation of resorcinol with an aldehyde, forming an octol, resorcinarene, which holds various conformations.¹¹ Resorcinarene based cavitands (example **3** and **4**), which maintain a characteristically more rigid conformation and stable cavity, can be easily synthesized through bridging the phenolic groups of resorcinarene.¹² Likewise, this cavitand structure maintains many properties of the calixarene family, having many advantages towards the binding of guests including (metal cations), since these cavitand variants retain rigid pockets with fixed dimensions capable of fitting guests of appropriate size.¹² In this work, Resorcinarene Tetraalkene Tetra Thiol 'RTATT' was utilized for the goal of metal extraction, due to its qualification with respect to the discussed parameters of the calix[4]arenes mentioned. Prior studies involving the RTATT 4 (Scheme 1) have shown efficient self-polymerization

into organized nanocapsules and subsequent functionalization via thiol-ene photopolymerization under one pot conditions (Scheme 2).^{13, 14} Moreover, thiol-ene photopolymerization, under the functionalization may be carried out through the addition of thiol containing ligands and re-irradiation, to а variety of possible ligand leading functionalization. Towards this overall goal, new, functionalized RTATT nanocapsules (NCs 1 - 5) were generated, possessing ligands containing carboxylic acid and amine moieties, which are constituents of many notable extractants^{8,15}. Such nanocapsules were tested for their ability to extract various metal chlorides such as: NiCl₂, CuCl₂, CoCl₂, HAuCl₄, K₂PtCl₄, and H₂PtCl₆.

Experimental

Metal Chlorides. All metal chlorides and hydrates were obtained from commercial suppliers and used as such. The following metal chlorides: NiCl₂·6(H₂O), CuCl₂·2(H₂O), CoCl₂·6(H₂O), HAuCl₄·3(H₂O), K₂PtCl₄, and H₂PtCl₆·6(H₂O), were used as sources for the respective metal cations (Ni²⁺, Cu²⁺, Co²⁺, Au³⁺, Pt²⁺, and Pt⁴⁺). Stock solutions of each respective metal were initially prepared at 0.2mM [M⁺] in 0.01M HCl and were subsequently diluted accordingly prior to use in FAAS calibration and for extraction assessments.

General Procedure for Nanocapsule Synthesis and Functionalization. Photoirradiation experiments were all performed in a Srinivasan-Griffin Rayonet photochemical reactor equipped with four 254 nm and 300 nm lamps.^{13, 14} The photopolymerization of nanocapsules (1-4) were each conducted in 50 mg (~1.5 mM RTATT in CHCl₃) scales in a 40 ml quartz photoreaction vessel. Prior to photoirradiation, all solutions were degassed with argon for 30 s. Following min of photopolymerization, the first 15 functionalization agents were added in (4 - 5) molar equivalents, degassed again before further photoirradiation (30 min). After the photopolymerization, the subsequent reaction mixtures were diluted with CHCl₃ to roughly equate 1 mM concentrations with respect to the initial concentration of RTATT. Functionalized nanocapsules were washed with nanopure water and brine.

General Extraction Procedure and Quantification. In a 20 mL scintillation vial, an aqueous solution (5 mL) Longazel containing 0.1 mM of metal ion (prepared by diluting stock solutions of 0.2 mM [M⁺] / 0.01 M HCl with an equal amount of acetate buffer (pH = 4.5) or 0.01 M HCl) was stirred with 5 mL of nanocapsules in CHCl₃ (containing 1 mM of RTATT monomer prior to photopolymerization) at 300 rpm, for a 12-hour period. Subsequently, the layers were allowed to separate, and 3.5 ml of aqueous phase was collected for analysis by Flame Atomic Absorption Spectroscopy.

Instrumentation. Flame atomic absorption spectroscopy was performed using a Shimadzu AA-7000 Atomic Absorption Spectrophotometer, operating in flame continuous mode with BGC-D2 lamp mode enabled. The repetition sequence SM-M-M with a 5 second integration time was employed for all measurements. Prior to assessment, calibration plot linearity was ensured within the anticipated analytical range.

Extraction Percent Calculation. Extraction percent was calculated using **Equation 1.** adapted from use in the study¹⁶. Wherein, C_i is the initial concentration 0.100mM for each [M⁺], and C_e is concentration extracted from solution, and quantified by Flame Atomic Absorption Spectroscopy.

Equation 1. Calculation of extraction percent E (%).

$$E(\%) = \frac{C_i - C_e}{C_i} \times 100\%$$

Results and Discussion

Preparation of RTATT Monomer. The following compounds (1 - 4) were synthesized as shown in **Scheme 1.**¹⁷ Slight modifications to the reported procedure were tested. In the bromination of resorcinarene **1**, the reaction duration and equivalents of N-bromosuccinamide (NBS) were varied. When the reaction duration was extended beyond what was reported,¹⁷ increased amounts of alkyl brominated bromoresorcinarene **2** were observed, resulting in decreased yields. Likewise, when the equivalents of NBS were lowered (from 6 eq. to ~ 4.5 eq.), incomplete aryl bromination was observed, even when reaction duration was prolonged.

Scheme 1. Synthesis of RTATT.



Synthesis and functionalization of Nanocapsules. Scheme 2 shows the one pot synthesis and functionalization of RTATT nanocapsules. The thiolene photopolymerization is typically advantageous, as it allows polymerization control through UV irradiation and tolerates the presence of multiple functional groups.¹⁸

Scheme 2. One pot synthesis and functionalization for RTATT nanocapsules.



Capsules containing carboxylic acid ligands were made by following the general procedure for functionalized nanocapsules reported previously.¹⁴ The synthesis of **NC 1 – 4** was carried out on a larger scale when compared to what was done previously.¹⁴ As prepared mixtures of functionalized nanocapsules were subjected to an aqueous work-up, primarily for the removal of unfunctionalized ligand. The success of which varied depending on the hydrophobicity of the

ligand employed. While 3-mercaptopropionic acid and N-acetyl L cysteine could be removed after 3 washes, 11-mercaptoundecanoic acid could not be removed due to its limited solubility in water. NC 4 was not used in the extraction experiments as unbound ligands could not be removed even after 7 washings. For each tested nanocapsules, the absence of functionalization agent was confirmed with ¹H NMR prior to their use in the extraction studies. Given the utility of amino calixarenes in metal chelation and extraction,¹⁹ RTATT nanocapsules were functionalized with amine ligands to expand their potential targets. Based on literature reports²⁰, 1 - 2 molar equivalents (with respect to each functionalization agent) of 2,2dimethoxy-2-phenylacetophenone (DMPA) were added during the functionalization of N-acetyl-L-Cysteine and Cysteamine HCl for NC 3 and NC 5. In the case of ligands such as **3** and **5** with limited solubility in chloroform, MeOH was introduced in minimal quantities $\sim 0 - 5$ %wt. during the functionalization stage after the initial photopolymerization and formation of the template nanocapsule structure. Wherever applicable, solutions containing methanol were evaporated under reduced pressure and redissolved in CHCl₃ prior to aqueous workup. The presence of oligomeric species along with the polymeric nanocapsules is known.^{13, 21} The ¹H-NMR of the as-prepared functionalized nanocapsules showed both regular and broader peaks perhaps originating from the presence of oligomeric and polymeric species. The addition of excess hexanes to a concentrated solution of NC 3 in chloroform, however, led to the immediate precipitation of the polymeric nanocapsules, shown in Figure 1 as NC 2.



Figure 1. NMR Spectra of RTATT 4 and purified NC-2.

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For Cysteamine functionalized nanocapsules **NC 5**, the standard workup involving water washing had resulted in the formation of an emulsion demonstrating that these nanocapsules were not suitable for extraction in their current form.



Figure 2. Photographs of metal extractions with NC-2, after 12 h.



Figure 3. Graphical representation of extraction percent among tested nanocapsules.

Table 1. Summary of extraction of various metals with **NC 1-3**.

| NCs | Ni ²⁺ | Cu ²⁺ | Co²+ | Au ³⁺ | Pt ²⁺ | Pt⁴+ |
|-----|------------------|------------------|------|------------------|------------------|------|
| 1 | 0 | 0 | 0 | 37 | 45 | 34 |
| 2 | 0 | 47 | 0 | 78 | 31 | 38 |
| 3 | 95 | 85 | 0 | 96 | 39 | 35 |

Extraction Results. Liquid-liquid solvent extraction experiments were carried out to test the metal extraction capabilities for various nanocapsules (**Figure 2**). Briefly, 1 mM solutions of various **NC (1 – 3)** in chloroform were stirred in the presence of 0.1 mM of metal ion for a period of 12 hours at ambient

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temperature. Figure 3 and Table 1 summarize the results of the amount of metal extracted by various nanocapsules. Substantial differences in extraction were observed with differing functionalization. The unfunctionalized nanocapsules NC 1, polymerized in the absence of any functionalization agent for 45 min, possessing only thiol and sulfide groups after polymerization, didn't lead to any extraction of Ni²⁺, Cu²⁺, and Co²⁺. This is not surprising, as thiols and sulfides are regarded as soft Lewis bases, while Ni²⁺, Cu²⁺, and Co²⁺ are all considered to be intermediate Lewis acids. The binding between soft Lewis bases and hard Lewis acids is not preferred according to HSAB theory.²² It is expected that Ni²⁺, Cu²⁺, and Co²⁺ will each remain in their metal chloride form, preferentially binding to the much harder Lewis bases present in solution, like Cl⁻. Conversely, when softer Lewis acids Au³⁺, Pt²⁺, and Pt⁴⁺ are introduced, NC 1 was able to extract these metal cations with 37%, 45% and 34% respectively. This is not surprising, as RTATT nanocapsules have been known to act as a template for synthesis of gold nanoshells and nanoparticle aggregates.²³ The affinity of **4** (monomer) to gold has also been previously reported, where 4 was known to bind to and extract gold colloids,¹⁷ and readily form assemblies on gold surfaces. Functionalized nanocapsules showed significantly higher extraction of Au³⁺. Soft Lewis bases Pt²⁺ and Pt⁴⁺ didn't show any significant difference between NC 1 – 3, indicating the lack of effect of functionalization in extracting these metal cations. Extractions with NC 2 and NC 3 were performed in acid buffered solutions (pH 4.5), which is close to the pKa of a typical carboxylic acid. In this range the carboxylate species present can chelate where applicable in a reversible fashion. Ni²⁺ was extracted only bv the N-acetyl-L-Cysteine functionalized nanocapsules. Notably, the extraction results of Cu²⁺ showed significant differences when extracted with NC 1 - 3. Unfunctionalized nanocapsules (NC-1) had failed to extract Cu²⁺, however after functionalization, with either ligands 2 or **3** an increase in extraction percentage was observed. As shown in literature,²⁴ various chelating agents with multiple COOH moieties like EDTA and NTA were compared with respect to their chelation abilities towards and extraction of various heavy metals including Cu²⁺ under variable conditions, which showed that copper recovery was dependent on pH. Moreover, the pKa of the R-COOH group of N-acetyl-L -cysteine is lower (~3.14)²⁵ than that of a generic carboxylic acid (~4.7), meaning more carboxylate species would have been present during the extraction by **NC 3**, allowing more effective chelation ability towards the Cu^{2+} cation.

Conclusions

Various RTATT nanocapsules were synthesized and functionalized with a variety of ligands 1 - 5 through the thiol-ene photopolymerization reaction. The extraction studies revealed some characteristics about the nature of functionalization and binding affinities of the tested nanocapsules towards the extraction of specific metals. Results were promising, revealing how some of the prepared capsules had varying extraction percentages based on the hardness of moieties or chelation abilities towards certain metal cations. Currently, efforts are on to expand the scope of functionalization and metal extraction studies.

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