# The synthesis and use of rotaxane molecules as transfer agents for ions

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## Background and Introduction

Rotaxane molecules are interlocked molecules consisting of a wheel component, axle, and blocking group component (Figure 1). Specifically, crown ether rotaxanes (Figure 2) are novel synthetic devices that can bind specific particles like cations and then transfer these cations into cells. The rotaxane-18-crown-6 molecule (R18C6) was synthesized using a multi-step synthesis that included the individual synthesis and purification of the wheel, axle, and blocking group components.

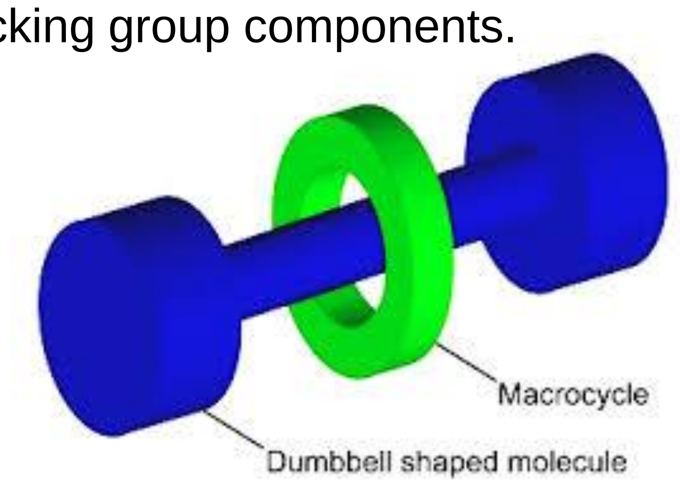


Figure 1. The general shape of a rotaxane system. The green ring represents the wheel and the blue dumbbell showing the axle.

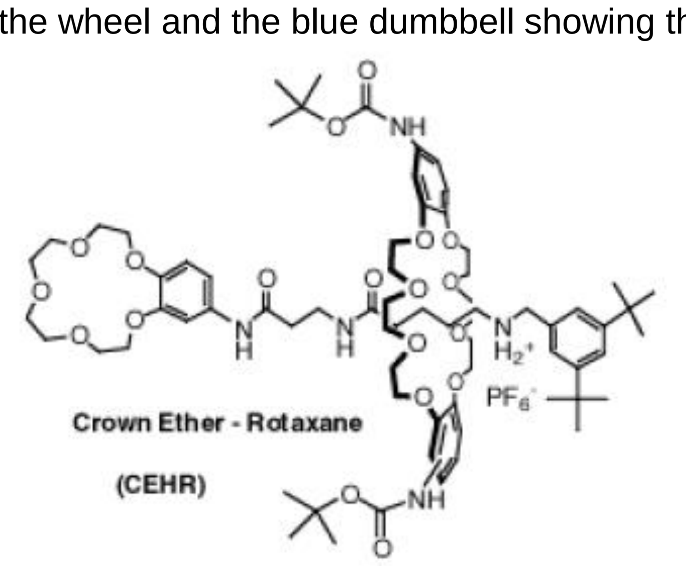


Figure 2. Specific structure of a crown ether host rotaxane.

Determining which ions transfer to the R18C6 molecule most efficiently was done by analyzing salt samples in the ICP-MS. The ICP-MS is a highly sensitive instrument that is able to detect trace levels of ions in solution, uses small amounts of product, and is relatively nondestructive to the product. It determines concentrations by ionizing small amounts of the samples into atomic particles (ions) and then determining the counts and concentrations (ppb) of those particles. The salts we used in this project were $CaCl_2$, NaCl, and KCl. Specifically, we observed the cation concentrations of these salts when in an environment with and without R18C6.

## Methods

We performed several steps to synthesize and purify the rotaxane. I primarily worked with the wheel portion of the molecule. First, we nitrated dibenzo-24-crown-8 (Figure 3). Then, we reduced the $NO_2$ molecules to $NH_2$ via a palladium/barium sulfate reaction (Rosenmund reaction) done under high pressure $H_2$ gas (Figure 4). Next, we performed a BOC reaction under argon gas and heat, using 2.2 eq. of BOC reagent and 4.1 eq. of $Na_2CO_3$ (Figure 5). This reaction was done to add the BOC protecting group to the molecule. We used column chromatography with the appropriate solvents to purify the wheel and then verified that the desired product was present using TLC of the reaction products against standards.

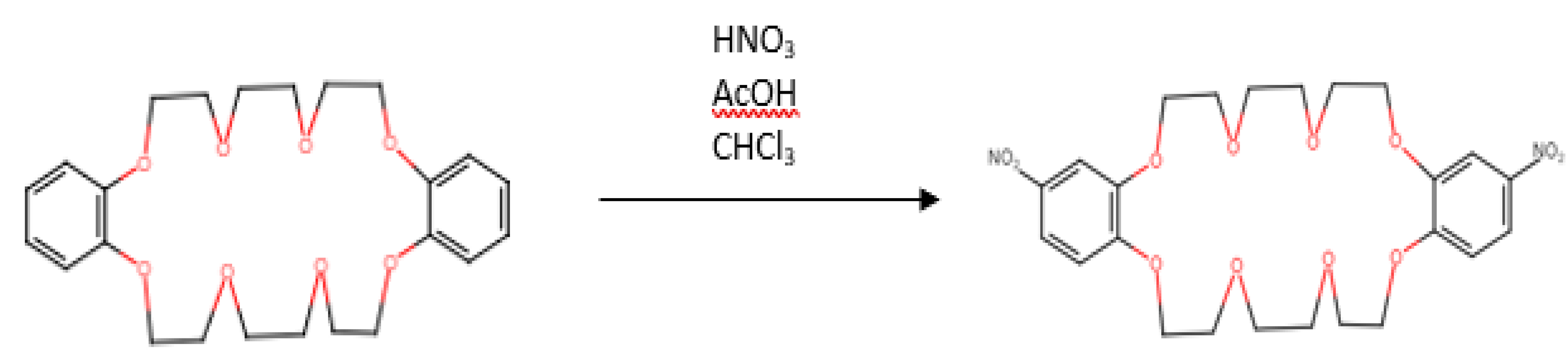


Figure 3. The nitration of the dibenzo-24-crown-8 using nitric acid, acetic acid, and chloroform.

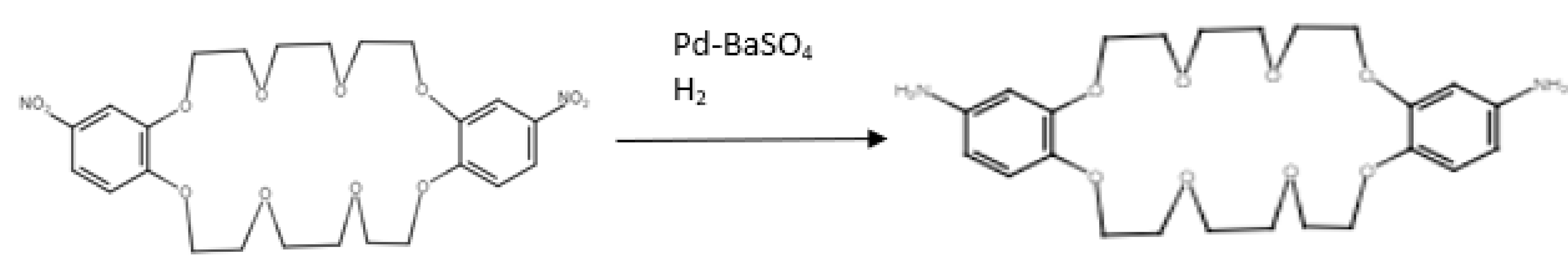


Figure 4. Reduction of the oxygen atoms to hydrogen atoms via a palladium- barium sulfate reaction.

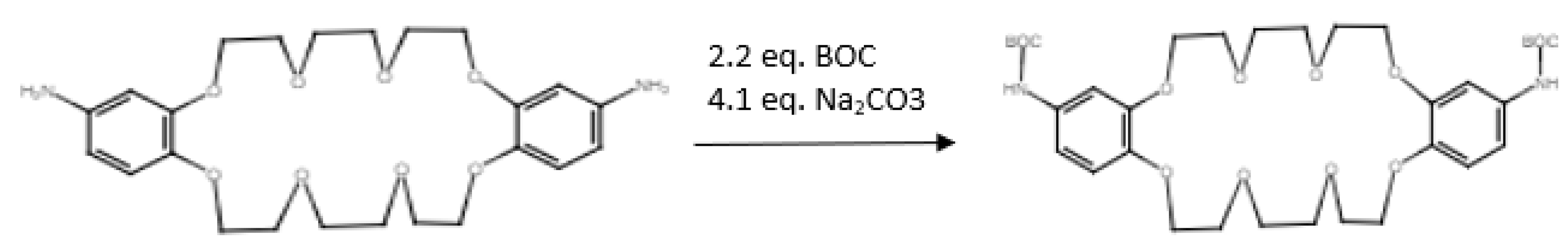


Figure 5. Reaction to add the BOC protecting group to the wheel molecule.

For each salt run in the ICP-MS, we ran seven samples: a DI water blank, a 2% $HNO_3$ blank, a calibration curve (100 ppb, 500 ppb, and 1000 ppb) made with a 100 ppm salt standard, a sample without rotaxane, and a sample with rotaxane. The samples with and without the rotaxane were made with 2M solutions of the respective salt.

For the blank sample (no R18C6), we added 250 uL of 2M salt solution to 250 uL of $CHCl_3$ and let it stir for 1 hour to ensure mixing. Following stirring,~200 uL of $CHCl_3$ layer was extracted and injected into 5 mL of $CHCl_3$. Then, we performed 3 extractions on this mixture using 2% $HNO_3$. The top layer from these extractions was used in the assay.

The sample containing rotaxane was made in the same way as the blank except the 2M salt solution was mixed with 250 uL of 0.13M R18C6/$CHCl_3$ solution. We also did a second round of extractions with 3 mL of ultra pure water after the nitric acid extractions to get the rotaxane away from the nitric acid and any ions in the solution. The rotaxane used in this assay was made prior to me joining the project.

We ran the samples under helium gas and under no gas. During analysis, we were mainly interested in the concentration (ppb) when analyzed under helium gas, which were the values we used to determine which salt the rotaxane transfers most efficiently.

## Results

The following two tables show the relevant data we used to draw conclusions about the rotaxanes abilities to transfer certain cations. Table 1 shows the concentrations (ppb) of the cations recorded when no rotaxane was present. Table 2 shows the concentrations when rotaxane was present. The cation Na+ had the lowest concentration with rotaxane and the cation Ca2+ had the highest concentration with rotaxane.

| | Helium gas | | No gas | |
|---|---|---|---|---|
| Salt | Conc. (ppb) | CPS | Conc. (ppb) | CPS |
| $Na^+$ | 111.731 | 43838708.29 | 2361.212 | -264404.30 |
| $Ca^{2+}$ | 956824.670 | 171157783.04 | 338325.164 | 811915865.73 |
| $K^+$ | 471.208 | 11712215.16 | 397.776 | 91982585.75 |

Table 1. Results of the ICP-MS run on the blank sample without the rotaxane with helium gas and without helium gas. Shown are the concentrations in ppb and the counts per second of the ion of interest.

| | Helium gas | | No gas | |
|---|---|---|---|---|
| Salt | Conc. (ppb) | CPS | Conc. (ppb) | CPS |
| $Na^+$ | 328.880 | 126982659.89 | <0.000 | -110984.43 |
| $Ca^{2+}$ | 14573.199 | 2630457.20 | 5322.879 | 12920384.54 |
| $K^+$ | 3297.864 | 82521920.39 | 2659.709 | 619619675.09 |

Table 2. Results of the ICP-MS run on the sample containing the rotaxane with helium gas and without helium gas. Shown are the concentrations in ppb and the counts per second of the ion of interest.

## Conclusions

The crown ether host rotaxane R18C6 transfers the calcium ions at higher concentrations than the other cations analyzed during this project (Table 2). Even without the rotaxane, the calcium cation was detected at the highest concentrations (Table 1).

This difference in the rotaxanes ability to transfer the cations can be explained by looking at the ions molar mass/size. The sodium ion (molar mass= 22.99 g/mol) showed the lowest concentrations and the calcium ion (molar mass=40.078 g/mol) showed at the highest concentrations (Table 2).

We also noticed that data collected using helium as a carrier gas produced better data with more consistently logical results. This is consistent with the conclusion of a previous study showing that helium gas as a carrier improves detection abilities of the ICP-MS (Castro et al., 2008).

As a continuation of this study, we could analyze more salts and their cations, such as $MgCl_2$ and LiCl. Doing so will allow us to have a more comprehensive understanding of which cations rotaxane transfers most efficiently and the shared properties of these cations.

## Acknowledgements

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## References

Castro W, Trejos T, Naes B, Almirall JR. 2008. Comparison of high-resolution and dynamic reaction cell ICP-MS capabilities for forensic analysis of iron in glass. *Analytical and Bioanalytical Chemistry.* 392: 663-672.