Synthesis of a Novel Chelating Hemicryptophane for Stabilization of Cu(I)

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Introduction

Cryptophanes are molecules composed of two cyclotriveratrylene (CTV) units joined together to form a capsule.[1] Hemicryptophanes are derived from cryptophanes by replacing one of the CTV units with an alternative C_3-symmetric moiety.[1] The introduction of such an alternative south 'pole' to the molecule allows a more diverse array of molecules to be designed and synthesized to target particular guests.[1] Our lab has recently demonstrated the capacity of hemicryptophane **L** to bind fluoride in aqueous solution upon protonation of its tris(2-aminoethyl)amine (TREN) south pole (Fig. 1a).[2,3] We have further shown that the amines of the TREN in **L** can chelate a copper (I) center capable of binding CO (Fig. 1b). Furthermore, this complex is air-stable, resisting the oxidation of Cu(I) to Cu(II). There are currently few published examples of long-term air-stable Cu(I) small-molecule complexes.[4,5]

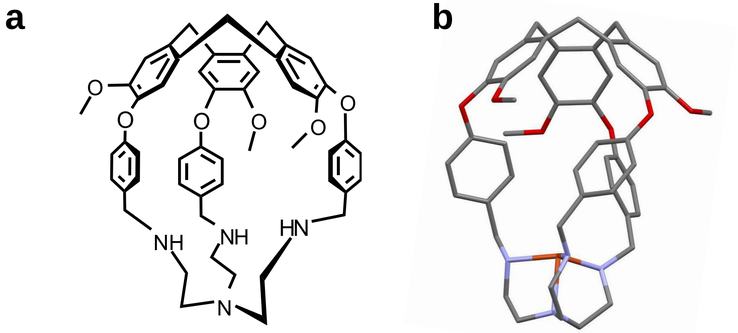


Figure 1. Molecular structure (a) and crystal structure (b) of [Cu**L**]BPh_4.

Project Motivation: *L2*

Hemicryptophane **L2** was designed to study the effect of the elimination of the methoxy groups from the CTV cap of **L** on copper binding and subsequent CO and air stability. It is hypothesized that the air-stability of this complex is attributable to the lack of access that O_2 has to the inside of the capsule. Thus, the removal of these methoxy groups would increase accessibility of the cavity to outside guests, reducing the air-stability of the complex.

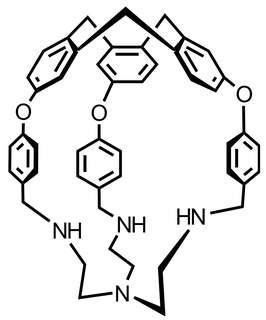
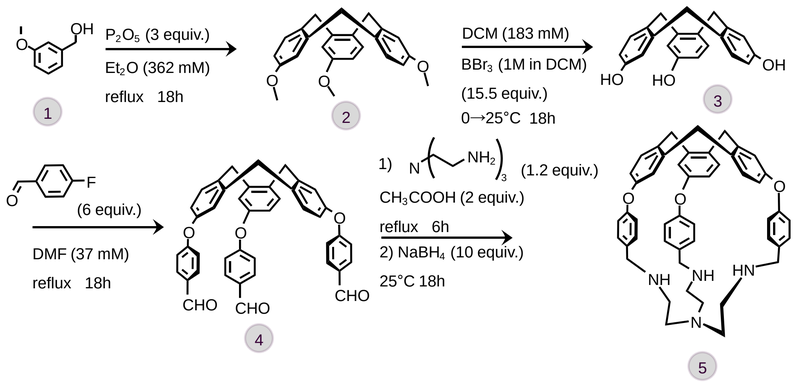


Figure 2. Structure of ***L2***.

Results



Scheme 1. Synthesis of **L2**.

Table 1. Yields of Steps in Synthesis of **L2**

Step	Attempt 1	Attempt 2	Attempt 3	Attempt 4	Attempt 5
1→2	0.9%	1.9%	1.41%	0.4%	0.6%
2→3	17%	52.9%	82.5%		
3→4	34.9%	23.6%			
4→5	4.4%				

Discussion

The production of **L2** is primarily constricted by step 1, which is prone to uncontrollably forming polymeric side products. Furthermore, this step has been optimized and is scaled down from a larger, previously reported scale.[6] Attempts to improve the yield of this step have been unsuccessful. Demethylation in step 2 sees better yields, but step 4 faces a heavy entropic tax that comes with forming such large macrocycles and the formation of polymers which unpredictably restricts the yield.

Future Work

Further work towards the synthesis of pure **L2** will include improvements of step 4→5, specifically with regard to post-reaction purification methods to reduce product loss.

With pure **L2** in hand, the first step moving forward is acquisition of an x-ray crystal structure so that comparison can be done with **L**. The x-ray crystal structure will shed some light on how the removal of the methoxy groups will impact the structure and the dominant conformation.

Secondly, a copper (I)-bound derivative of **L2** is to be synthesized and purified. With the pure copper (I) complex attained, air stability could be assessed and compared to **L**. Once pure copper (I)-bound **L2** is obtained, crystallization will be attempted in order to obtain an x-ray crystal structure and compare it to **L**.

Lastly, CO binding will be attempted with the copper(I)-bound **L2**. We hypothesize that the removal of the methoxy groups will greatly impact the dynamics of CO binding.

References

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