In line with the proposal, we started to work on conjugating tris(2-pyridylmethyl)amine (TPA) ligand 2 to concave scaffold 3 (Figure 1). The reaction conditions were optimized for obtaining capsule 1 in satisfactory 65% yield. $^1$H NMR spectroscopic measurements along with molecular mechanics and density functional theory calculations showed that $C_3$ symmetric 1 is poorly preorganized with three pyridines at the rim adopting a propeller-like orientation and undergoing a rapid $P$-to-$M$ (or vice versa) stereoisomerization ($\Delta G^\ddagger < 8 \text{ kcal/mol}$). Moreover, the tertiary nitrogen group undergoes a low barrier inversion of configuration ($E_a \approx 10 \text{ kcal/mol}$). As a result of such poor preorganization, capsule 1 was found to be a poor host for trapping CH$_4$, CH$_3$Cl, CH$_2$Cl$_2$, CHCl$_3$ and CCl$_4$ guests ($K_a < 7 \text{ M}^{-1}$; Figure 1). Note that trapping small hydrocarbons in the cavities of molecular capsules is essential for their activation. Accordingly, protonation of 1 with HCl gave

\[ [1\cdot\text{H}]\text{-Cl}, \text{ with the solid-state structure showing the TPA lid being “flattened” at the top of the host and } ^1\text{N-H---Cl hydrogen bonded group residing outside (Figure 2). Importantly, the } P\text{-to-}M \text{ stereoisomerization for } [1\cdot\text{H}]\text{-Cl was found to be slower (} \Delta G^\ddagger = 11 \text{ kcal/mol, VT } ^1\text{H NMR}), \text{ with the quaternary center unable to invert its configuration. More preorganized } [1\cdot\text{H}]\text{-Cl acted as a good host of CH}_4 \text{ but could also complex CH}_3\text{Cl, CH}_2\text{Cl}_2, \text{ CHCl}_3 \text{ and CCl}_4 \text{ guests (} K_a = 100\text{-}400 \text{ M}^{-1}, ^1\text{H NMR spectroscopy). The results of both theory (DFT) and experiments (} ^1\text{H/}^{13}\text{C NMR spectroscopy) suggested that the complexation of increasingly larger guests took place in an induced-fit fashion, with the TPA (a) elongating along its vertical axis by moving the TPA “lid” by 1Å and concurrently (b) twisting pyridines from } P \text{ into } M \text{ (or vice versa) chiral orientation. Capsule 1 is an allosteric host that, after being prompted with a chemical input, changes the conformational dynamics of its TPA lid, while predominantly preserving the shape of its cavity, to affect the encapsulation thermodynamics. Moreover, the entrapment of differently sized achiral guests switches the capsule’s helical chirality. These results were published as an article in } J. \text{ Am. Chem. Soc. } 2018, 140, 11091-11100 \text{ and we have acknowledged the financial support from ACS PRF. Three students working on the projected (supported by PRF) benefited from this work by learning about (a) synthetic methodologies for the preparation of complex molecules, (b) physical organic methods for characterizing encapsulation complexes and (c) computational methods for guiding design and characterization of molecules.} \]
To examine the activation of methane with capsule 1, we added CuOTf to its solution in acetone and obtained desired $1 \cdot Cu(I)$ complex. This coordination compound was, however, labile with interesting dynamic characteristics. With $^1$H NMR spectroscopy, we observed the coordination of acetonitrile to Cu(I) with this ligand occupying the capsule’s inner space.

In an attempt to obtain a more stable Cu(I) containing capsule, we worked on conjugating TPA 4 to basket scaffold 2 (Figure 3). The synthesis was optimized with, importantly, 5 being able to coordinate Cu(I) and give stable $5 \cdot Cu(I)$ complex (fully characterized with NMR spectroscopy and mass spectrometry). Indeed, x-ray structure of 5 (Figure 4) showed its preorganization with four nitrogen atoms poised to complex Cu(I) and position it on top of the cavity (where the oxidation should take place). Following, we used UV-Vis spectroscopy to examine the complexation of oxygen to $5 \cdot Cu(I)$. To our surprise $O_2$ could not form a complex (even at a higher pressure and lower temperatures) from which we hypothesized that this molecule is a poor ligand unable to shed solvents away from the cavity of $5 \cdot Cu(I)$. Next, we turned to study the complexation of better NO ligand using variable temperature UV-Vis spectroscopy. To our delight, we found that NO would bind to $5-Cu(I)$ and then change into another molecule (Figure 5).

The formation of $5-Cu(I)CN=O$ was found to be transient with the complex turning into $5-Cu(II)CN=O$. We hypothesize, that the transformation occurs by a mechanism shown in Figure 5 in which the elusive Cu(III)O forms! At present, we are completing VT-IR and EPR measurements to test our mechanistic hypothesis. If the formation of Cu(III)O indeed precedes the product formation (Figure 5), we should be able to intercept it with CH4 or another more reactive molecule (ethylene, isopropane, ethane etc.) and have the insertion of oxygen into C–H taking place. This work will be published in the second year of the project. Students are learning a variety of spectroscopic methods for characterizing coordination complexes and completing catalytic reactions in confined environments. We are also collaborating with Prof. Shiyu (OSU) on spectroscopic measurements in which students correspond with researchers from other (inorganic chemistry) areas of science. Finally, students presented this work at several local symposia and tremendously benefited from discussing their progress with other scientists. We believe that the progress we have made, in the first year of the project, is exceptional and should help us develop important knowledge pertaining the activation of hydrocarbons in confined spaces.

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**Figure 3.** Preparation of molecular capsule 5, holding a Cu(I) at top of its cavity.

**Figure 4.** X-Ray structure of molecular capsule 5, holding a molecule of acetone in its cavity.

**Figure 5.** Coordination complex $5 \cdot Cu(I)$ is able to activate NO (excess) in CH4Cl2 and turn it into $5 \cdot Cu(II)CN=O$. 

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