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EXECUTIVE SUMMARY OF THE THESIS

Exploring the solid-state synthesis and host-guest chemistry of $M_{12}L_8$ poly- $[n]$ -catenanes using tris-pyridyl benzene ligand

TESI MAGISTRALE IN CHEMICAL ENGINEERING – INGEGNERIA CHIMICA

AUTHOR: **Stefano Elli**

ADVISOR: **Prof. Javier Martí-Rujas**

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1. Introduction

Catenanes are defined by IUPAC as: “Hydrocarbons having two or more rings connected in the manner of links of a chain, without a covalent bond. More generally, the class catena compounds embraces functional derivatives and hetero analogues”.^[1] For compounds having a large number of interpenetrated rings the wording poly- $[n]$ -catenane is used. As the definition suggests, these are supramolecular materials showing properties similar to those of real chains, both from a structural and mechanical point of view. The synthesis of catenanes can be performed both by means of a statistical approach or a template-directed approach. The first one is a stochastic method based on the probability of cyclization of a linear molecule around a pre-formed ring, which is highly inefficient and only produces small quantities. In the second method, non-covalent interactions are exploited to pre-organize the molecules and to promote their cyclization in the desired manner. This represents a much more controlled approach and allows for higher yields. In addition, the synthesis can proceed along a kinetic path, favoured by irreversible reactions and short times, or a thermodynamic one, favoured by

reversible reactions but longer reaction times. In the latter case, an error-checking process intervenes to generate the most stable form of the product. In light of the above, it is easy to imagine that the synthesis of these compounds represents a challenging task. Nevertheless, in recent years, the number of scientific publications on poly- $[n]$ -catenanes has grown considerably. Indeed, their topology is characterised by a high void fraction, guaranteeing a broad spectrum of applications for these materials.^[2] These include applications in the biomedical field as well as in catalysis, gas storage, separation, drug delivery and water harvesting. The work described in the present thesis represents a continuation of a previous study,^[3] and concerns the implementation of the synthesis and the applications of the poly- $[n]$ -catenane $[(ZnX_2)_{12}(TPB)_8]$ (Figure 1.1).

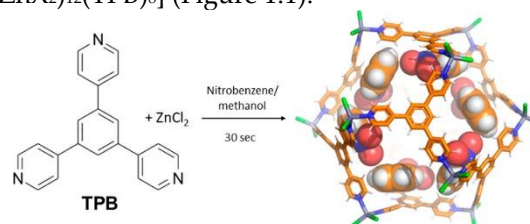


Figure 1.1: Instant synthesis of $[(ZnCl_2)_{12}(TPB)_8]$ poly- $[n]$ -catenanes^[3]

In the previous study, the slow crystallization and fast synthesis approaches were used to produce an interlocked chain of icosahedral cages made up of 1,3,5-Tri(pyridin-4-yl)benzene ligand and zinc chloride as secondary building unit, by means of Nitrobenzene as solvent.

In the light of today's ecological standards, the possibility to synthesize the poly-[*n*]-catenane [(ZnX₂)₁₂(TPB)₈] under eco-friendly, solvent-free conditions was explored. Solvents are undoubtedly a problem in the chemical industry and, in accordance with the 12 principles of green chemistry, their use should be minimized and avoided wherever possible. In this respect, a mechano-chemical route based on a grinding process to access the [(ZnX₂)₁₂(TPB)₈] structure was investigated.

Finally, the focus was moved on the synthesis of a small library of differently functionalized 1,3,5-Tri(pyridin-4-yl)benzene derivatives to be used as ligands for the synthesis of the corresponding poly-[*n*]-catenanes. The goal was to investigate the relationship between the stereoelectronic properties of the ligand employed and the topology of the corresponding supramolecular structure. To this end, two different synthetic pathways were explored to access mono- or tri-substituted 1,3,5-Tri(pyridin-4-yl)benzene derivatives.

2. Mechanochemical synthesis

Mechanochemical experiments were carried out in the form of Liquid Assisted Grinding (LAG) and Neat Grinding (NG) (Figure 2.1), then the sample analysed with PXRD, IR, solid-state NMR and elemental analysis.^[4]



Figure 2.1: Mechanochemical synthesis of [(ZnBr₂)₁₂(TPB)₈] poly-[*n*]-catenanes^[4]

First, Liquid Assisted Grinding (LAG) experiments were performed. 30 mg of TPB ligand were

grinded with a stoichiometric amount of ZnBr₂ (34 mg) in the presence of 0.05 mL of methanol. After 15 minutes of grinding, the obtained powder was analysed by X-ray powder diffraction. The pattern showed peaks attributable to those of the TPB ligand suggesting an incomplete conversion of the reaction. To solve this problem, an excess of metal was added, and the mixture was subjected to further grinding. Interestingly, XRPD on the thus formed sample showed a crystalline material which became amorphous during the analysis.

To obtain a stable crystalline phase, useful for determining the structure, the sample was immersed in a solution of 1,2-dichlorobenzene and methanol (Figure 2.2).

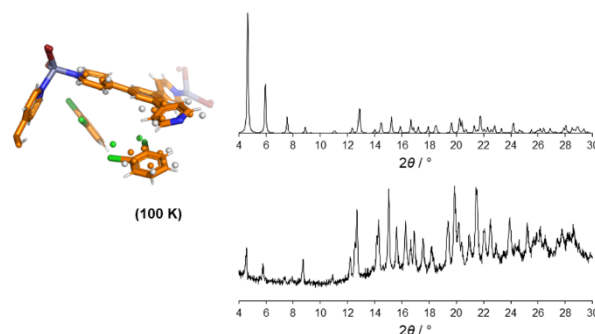


Figure 2.2: Top: simulated PXRD of a single crystal containing 1,2-dCB. Bottom: PXRD pattern of the amorphous to crystalline transformation.^[4]

Thermogravimetric analysis showed that the treated sample contained a fair amount (approx. 24 %w/w) of the solvent used. 1,2-dichlorobenzene enters the cages and settles both in an orderly manner, stacking to the walls through non-covalent interactions (π - π interactions and hydrogen bonds), and in a disorderly manner in the centre of the cage where the interactions are weaker.^[3] Methanol was found to play a key role in enabling this type of transformation from an amorphous to a crystalline phase, as it is a small molecule that fits into the cages and opens the entrance to the larger 1,2-dichlorobenzene molecules, which are then able to enter and exert their templating effect. The solvent that gets in succeeds in swelling the chains, which are then able to stack, generating a crystalline phase. Consequently, Neat Grinding (NG) experiments were carried out, in the absence of any solvent, confirming previous results. With these tests yields of [(ZnX₂)₁₂(TPB)₈] greater than 80% were achieved. The samples were subjected to Elemental Analysis,

IR, and solid-state NMR, confirming both the formula and the topology of the poly- $[n]$ -catenane. To further prove the green character of the material, recyclability tests were performed.

Interestingly, it was found that the poly- $[n]$ -catenane could be break by simply immersing it in deionized water. The result is an aqueous solution of the metal where the ligand remains as a fine dispersion. After filtration and drying, the ligand was analysed through NMR and found to be highly pure, confirming its potential reuse.

3. Applications

As mentioned above, there are several applications in which poly- $[n]$ -catenanes play a prominent role. In this thesis the focus was put on two of them: molecular storage and isomer recognition.

Trials on the instant synthesis and adsorption experiments with different solvents has been made. Knowing that nitrobenzene and 1,2-dichlorobenzene allowed the amorphous to crystalline transformation, other aromatic molecules were chosen as the starting point. Toluene and *p*-chlorotoluene confirmed the previously obtained results, due to the π - π interactions between the solvent and ligand molecules. Alcohols with increasing chain lengths, from methanol to *n*-butanol, showed some templating effect but this lasted for a short time due to their volatility. Small molecules, such as chloroform, unable to take part in strong interactions did not show a templating effect leading to amorphous materials.

The role of the SBUs counterions was also investigated, by using zinc chloride, iodide, and bromide salts for the synthesis of the poly- $[n]$ -catenane. The resulting materials showed increasing crystallinity with the following trend: Cl > Br > I. Therefore, a linear correlation between the radius of the metal salt's counteranion and the crystallinity of the corresponding catenane was found. A thermal analysis was used to study the material behaviour up to 270 °C. The crystallinity of three samples obtained by instant synthesis, each with a different counterion, was measured by *ex-situ* PXRD, increasing the temperature by 10 °C after each measurement. Upon thermal heating all the samples showed a crystalline-to-amorphous transition ascribable to the complete solvent evacuation from the voids of the catenanes.

Interestingly, at temperatures depending on the counteranion employed, a second crystalline phase was observed for each sample. Exposing the samples to higher temperatures resulted in the degradation of the materials which showed the formation of an amorphous phase.

With respect to the use of poly- $[n]$ -catenanes for isomer recognition, the lead experiments were done on the structural isomers of dichlorobenzene. The synthesis of the catenane in the presence of 1,3-dichlorobenzene resulted in the formation of a crystalline phase. By using the solid 1,4 isomer, the formation of an amorphous phase was initially found. This result would have given access to the possibility of separating the different dichlorobenzene isomers. However, by repeating the experiments with different amounts of 1,4-dichlorobenzene, samples revealed to be crystalline. We attributed this phenomenon to the amount of 1,4-dichlorobenzene employed, which must be in sufficient quantity to exert its templating effect. Further studies are required to investigate this behaviour.

4. Diversification

Simultaneously to the above discussed studies, the synthesis of TPB derivatives bearing different substituents was explored to investigate their effect on the structure of the final poly- $[n]$ -catenane. To this end, among all possible synthetic strategies, the Suzuki-Miyaura cross-coupling reaction was selected.^[5] This is a well-known palladium-catalysed reaction between an aryl halide species and an aryl boron reagent (*e.g.* aryl boronic acids or esters), widely used both in academia and in industry. Firstly, the optimization of the reaction conditions was carried out by reacting 1,3,5-tribromobenzene with an excess of 4-pyridineboronic acid pinacol ester (Figure 4.1a) to obtain the unsubstituted TPB ligand. Then, the same protocol was successfully extended to the synthesis of compound **6** bearing 6 chlorine atoms in the α positions of each pyridine ring. The purification conditions of this latter compound are currently under optimization.

Later, the stoichiometric control of the reaction to obtain the disubstituted 4,4'-(5-bromo-1,3-phenylene)dipyridine was investigated. The ultimate goal was the introduction of only one substituted pyridine out of three. However, also in

this case TPB was detected as the sole reaction product indicating the poor control on the reaction (Figure 4.1b).

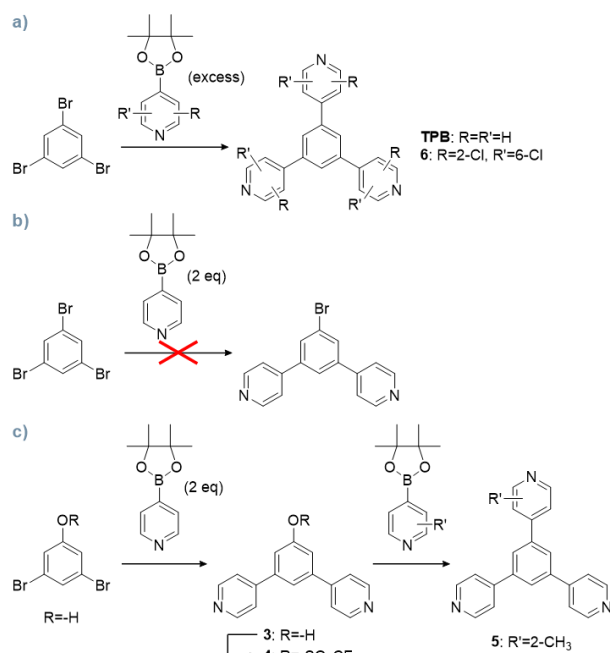


Figure 4.1: Synthesis of 1,3,5-tri(pyridin-4-yl)benzene

To achieve our goal, a different synthetic approach was investigated (Figure 4.1c). We started from 3,5-dibromophenol to selectively introduce two unsubstituted pyridine moieties obtaining compound **3**. This was then converted to compound **4** using triflic anhydride. Finally, the thus introduced functionality was employed as the leaving group for the subsequent Suzuki-Miyaura cross-coupling reaction which yielded compound **5**.

Initial efforts were made for the purification of both compounds **5** and **6** through flash column chromatography. However, it should be underlined that the high polar character of these tripyridyl derivatives make their purification a challenging task. Current studies are focused on their purification through crystallization.

Once purified, and characterised, these products can be used as organic ligands for the synthesis of new poly- $[n]$ -catenanes.

5. Conclusions and further works

In the present work the possibility to synthesize the [(ZnX₂)₁₂(TPB)₈] poly- $[n]$ -catenane as an amorphous phase under eco-friendly solvent-free conditions was demonstrated. In particular, the poly- $[n]$ -catenane can be prepared in good yield by simple grinding of ligand powder and metal salts within about 15 minutes.

The focus on the applications of the material based on the host-guest interactions gave promising results. Tests on the adsorption of several different guest molecules confirmed the templating effect covered by aromatic solvents. The study of the topological properties of the materials was further investigated with a thermal analysis. Moreover, working on the isomer recognition field, trials on the separation of the structural isomers of dichlorobenzene showed that some further work is necessary.

Remarkably, the possibility of recycling the material, by simple immersion in water was confirmed. The recovered ligand showed a purity grade comparable to that of the commercially available TPB.

Possible further applications of the catenane comprise gas adsorption, drug delivery and catalysis. The pursuit in the separation topic with different molecules will be one of the main themes, with the aim of using the catenane as stationary phase for column chromatography. Finally, two different pathways for the synthesis of mono- or trisubstituted TPB derivatives was established and employed for the obtainment of compounds **5** and **6**.

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