



# University of Salerno

Department of Chemistry and Biology  
"Adolfo Zambelli"

## PhD Course in Chemistry

XXXIV Cycle

Thesis on

# *Synthesis of New Naphthol-Based Macrocycles for Supramolecular Applications*

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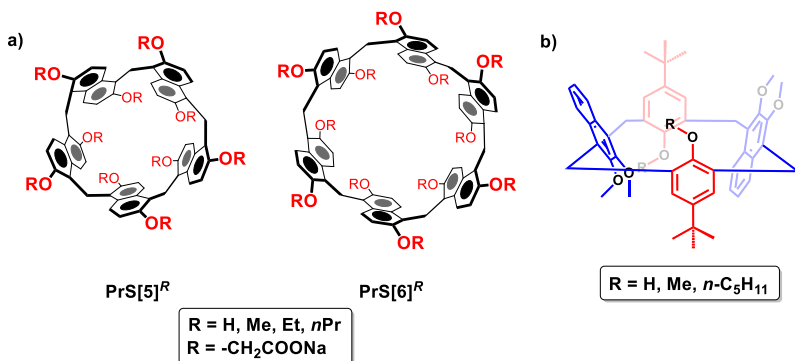
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# Abstract

*Nature* has always inspired supramolecular chemists who, with the aim to mimic the structural features of the natural receptors, have designed artificial systems with amazing functions and properties. Therefore, in the last two decades, macrocyclic compounds based on naphthalene or anthracene units have been reported, with the aim of obtaining new supramolecular hosts embedding deep  $\pi$ -electron-rich aromatic cavity.<sup>1</sup>

Prompted by these considerations, during this PhD project, I focused my efforts on the synthesis of novel naphthol-based macrocycles. Thus, prismarenes<sup>b</sup> (a in **Figure**) and the calix[2]naphtha[2]arene<sup>c</sup> (b in **Figure**) have been obtained and their supramolecular properties were investigated.



**Figure.** (a) Chemical drawing of prism[n]arenes; (b) Chemical drawing of the calix[2]naphtha[2]arene.

<sup>1</sup> Yao, H.; Jiang, W. *Naphthol-Based Macrocycles*, in Handbook of Macrocyclic Supramolecular Assembly, Springer, Singapore, 2019.

Methoxy-based prism[n]arenes ( $n = 5$  and  $6$ ),<sup>b</sup> were formed by exploiting thermodynamic intermolecular templating effects with alkylammonium-guests.<sup>2</sup> Differently, the formation of prismarenes bearing longer alkyl chains,<sup>d</sup> such as ethyl or propyl groups, was obtained by a thermodynamic intramolecular self-templating effect due to the alkyl chains, which drive the macrocyclization toward the formation of the hexameric derivatives.<sup>d</sup> Prismarenes were found to be interesting for their molecular recognition properties: in fact, their  $\pi$ -electron rich deep cavities can host ammonium guests by cation $\cdots\pi$  and  $^+NC-H\cdots\pi$  interactions.<sup>b,d</sup> We have also investigated a procedure for the synthesis of *per*-hydroxylated prism[n]arenes **PrS[n]<sup>OH</sup>** ( $n = 5$  and  $6$ ).<sup>e</sup> In details, **PrS[5]<sup>Me</sup>** can be efficiently demethylated by a supramolecularly assisted reaction in the presence of tetramethylammonium iodide. **PrS[n]<sup>OH</sup>** can be considered as useful synthetic precursors to obtain novel hosts with intriguing supramolecular properties. In fact, starting by *per*-hydroxylated prism[n]arenes **PrS[n]<sup>OH</sup>** ( $n$

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<sup>2</sup> Della Sala, P.; Del Regno, R.; Talotta, C.; Capobianco, A.; Hickey, N.; Geremia, S.; De Rosa, M.; Spinella, A.; Soriente, A.; Neri, P.; Gaeta, C. *J. Am. Chem. Soc.* **2020**, *142*, 1752-1756. Highlighted in: Yang, L.-P.; Jiang, W. *Angew. Chem. Int. Ed.* **2020**, *59*, 15794-15796.

<sup>c</sup> Del Regno, R.; Della Sala, P.; Spinella, A.; Talotta, C.; Iannone, D.; Geremia, S.; Hickey, N.; Neri, P.; Gaeta, C. *Org. Lett.* **2020**, *22*, 6166–6170.

<sup>d</sup> Della Sala, P.; Del Regno, R.; Di Marino, L.; Calabrese, C.; Palo, C.; Talotta, C.; Geremia, S.; Hickey, N.; Capobianco, A.; Neri, P.; Gaeta, C. *Chem. Sci.* **2021**, *12*, 9952-9961.

<sup>e</sup> Del Regno, R.; Della Sala, P.; Picariello, D.; Talotta, C.; Spinella, A.; Neri, P.; Gaeta, C. *Org. Lett.* **2021**, *23*, 8143–8146.

= 5 and 6), water-soluble prism[n]arenes ( $n = 5$  and  $6$ ) bearing carboxylato anionic groups were obtained.<sup>f</sup> Carboxylato-prism[n]arenes ( $n = 5$  and  $6$ ), **PrS[5]<sup>COONa</sup>** and **PrS[6]<sup>COONa</sup>** were able to form complexes with organic ammonium cations **G<sup>n+</sup>@PrS[n]<sup>COO-</sup>** ( $n = 5$  and  $6$ ) in water as confirmed by NMR titration experiments. ITC studies showed that the complexation processes, are driven by different thermodynamic factors depending on prismarene size and cation charge. Finally, we obtained a new class of phenol–naphthalene hybrid macrocycles, named calix[2]naphth[2]arenes.<sup>c</sup> X-ray studies show that calix[2]naphth[2]arene adopts a rare 1,2-alternate conformation (**b** in **Figure**). Moreover, this conformation is also observed when alkali metal cations are added to the solution of host.

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<sup>f</sup> Del Regno, R.; Santonoceta, G. D. G.; Della Sala, P.; De Rosa, M.; Soriente, A.; Talotta, C.; Spinella, A.; Neri, P.; Sgarlata, C.; Gaeta, C. *Org. Lett.* **2022**, *24*, 2711-2715.