

**Università degli Studi di Salerno**  
**Dipartimento di Chimica e Biologia “A. Zambelli”**



**Corso di Dottorato di Ricerca in Chimica**  
**XIV CICLO NUOVA SERIE**

**Tesi di dottorato in:**

***“Synthesis of calixarene derivatives active towards  
proteic targets involved in tumor pathologies”***

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## Abstract

Over the last 30 years a growing interest has been directed toward the biomolecular recognition of calixarene derivatives and more in particular to the interaction with druggable target(s).<sup>1,2</sup>

The aim of this PhD thesis was the synthesis and the study of calixarenes that were able to interact with biomolecules involved in tumor pathologies.

One of the main topic of this work was the synthesis of calix[4]arene conjugates bearing pyrenylisoxazolidine moieties at the exo rim which could act as potential DNA intercalators. The in vitro cytotoxic activity against different human tumor cell lines was also tested.

Moreover, the biomolecular recognition abilities of designed calixarenes was studied through a chemical proteomics approach.

As calix[*n*]arene scaffolds are particularly suitable for the synthesis of multivalent ligands,<sup>3</sup> the attention was also focused on the synthesis of multivalent iminosugar-calix[8]arene conjugates for the inhibition of glycosidases.

The synthesis, characterization and all the biomolecular recognition studies were herein described.

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<sup>1</sup> (a) de Fátima, A.; Fernandes, S. A.; Sabino, A. A. *Curr. Drug. Discov. Technol.* **2009**, *6*, 151-170. (b) Giuliani, M.; Morbioli, I.; Sansone, F.; Casnati, A. *Chem. Commun.* **2015**, *51*, 14140-14159; (c) Park, H. S.; Lin, Q.; Hamilton, A. D. *Proc. Natl. Acad. Sci. USA* **2002**, *99*, 5105-5109; (d) Baldini, L.; Casnati, A.; Sansone, F.; Ungaro, R. *Chem. Soc. Rev.* **2007**, *36*, 254-266; (e) Schrader, T. *Nat. Chem.* **2012**, *4*, 41529-41542.

<sup>2</sup> Da Silva, E.; Lazar, A. N.; Coleman, A. W. *J. Drug. Del. Sci. Tech.* **2004**, *14*, 3-20.

<sup>3</sup> Consoli, G.; Cunsolo, F.; Geraci, C.; Mecca, T.; Neri, P. *Tetrahedron Lett.* **2003**, *44*, 7467-7470. Brissonnet, Y.; Ortiz Mellet, C.; Morandat, S.; Garcia-Moreno, M.I.; Deniaud, D.; Matthews, S. E.; Vidal, S.; Sestak, S.; El Kirat, K.; Gouin, S. *G. J. Am. Chem. Soc.* **2013**, *135*, 18427-18435.