

THE 67TH INTERNATIONAL



OPEN READINGS

CONFERENCE FOR STUDENTS OF PHYSICS AND NATURAL SCIENCES

**BOOK OF
ABSTRACTS** | **2024**



Vilnius
University

VILNIUS UNIVERSITY PRESS

Editors:

Martynas Keršys
Rimantas Naina
Vincentas Adomaitis
Emilijus Maskvytis

Cover and Interior Design:

Goda Grybauskaitė

Vilnius University Press
9 Saulėtekio Av., III Building, LT-10222 Vilnius
info@leidykla.vu.lt, www.leidykla.vu.lt/en/
www.knygynas.vu.lt, www.journals.vu.lt

Bibliographic information is available
on the Lithuanian Integral Library Information System (LIBIS) portal www.ibiblioteka.lt
ISBN 978-609-07-1051-7 (PDF)

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STRUCTURAL AND NMR PROPERTIES OF SUPRAMOLECULAR COMPLEXES OF DRUG MOLECULES

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Cavitands are molecules found within the field of supramolecular chemistry that are capable of forming host-guest complexes acting as containers for smaller molecules. The formation of such complexes is determined by non-covalent interactions, bearing a resemblance to biological structures such as enzymes. The similarity between enzymes and cavitands is also apparent for their ability to confine and orient molecules for unusual reactions [1]. The container-like structures of cavitands allow for the separation of solvent and guest molecule - resorcinarene cavitands form such structures and the resulting non-polar cavity may prove useful in the solvation of water-insoluble reagents [2, 3]. The aforementioned qualities of cavitands make them relevant in drug delivery systems, chemical synthesis, etc.

The cavitand introduced by de Mendoza is a cup-shaped molecule that contains four 2-benzimidazolone (cyclic carbamide) bridges, enabling the cavitand to form dimers via hydrogen bonds (Fig. 1) [4]. The base portion of the molecule is a resorcinarene ring, which has four groups of pyridine “feet” attached to it [5]. This particular cavitand containing pyridine groups demonstrates good solubility in water making it useful for manipulating hydrophobic compounds in water solutions. NMR spectra measured by Zhang et. al., indicate the formation of cavitand-ibuprofen and cavitand-albendazole complexes in aqueous solutions (Fig. 2 & 3). The nonsteroidal anti-inflammatory ibuprofen and anti-parasitic albendazole are drugs that are poorly soluble in water, making them useful for evaluating the cavitand complex.

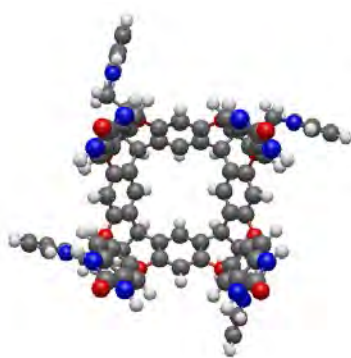


Fig. 1. Resorcinarene Cavitand

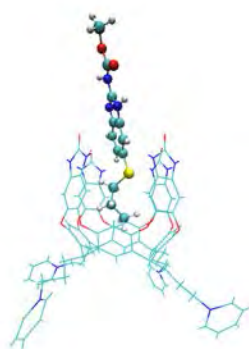


Fig. 2. Cavitand-albendazole complex

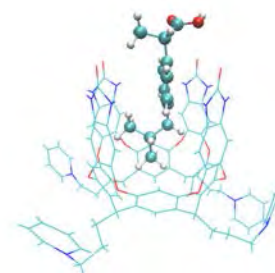


Fig. 3. Cavitand-ibuprofen complex

In this work, classical MD simulations and QM/MM calculations of the ibuprofen and albendazole molecules confined within the supramolecular cavitand were performed aiming to evaluate the intermolecular structure of the complex in aqueous solution. The initial geometries were constructed using Gaussian, utilizing the HF/6-31+G* basis set. MD simulations were performed using AMBER. Our MD simulations show the formation of a stable complex between the drug molecules and the cavitand. The registered trajectories provide insight into the formation and stability of the complex. Furthermore, QM/MM calculations of NMR spectra provide further insights into the structural properties of the complex.

Acknowledgement. Computations have been performed on the resources provided by the high-performance computing center “HPC Saulėtekis” of Vilnius University.

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- [1] Moran et. al., Cavitands: Synthetic Molecular Vessels, *Journal of the American Chemical Society* 104 (21), 5826-5828 (1982)
 - [2] Ajami et. al., Social Isomers of Picolines in a Small Space, *Chemistry* vol. 19,50 (2013).
 - [3] Tzeli et. al., Theoretical Study of Hydrogen Bonding in Homodimers and Heterodimers of Amide, Boronic Acid, and Carboxylic Acid, Free and in Encapsulation Complexes, *Journal of the American Chemical Society* vol. 133, no 42, pp. 16977-16985 (2011).
 - [4] Ebbing et. al., Resorcinarenes with 2-Benzimidazolone Bridges: Self-aggregation, Self-Assembled Dimeric Capsules, and Guest Encapsulation, *Proceedings of the National Academy of Sciences*, vol. 99, no. 8, pp. 4962-4966 (2002).
 - [5] Zhang et al., Complexation of Alkyl Groups and Ghrelin in a Deep, Water-Soluble Cavitand, *Chem. Commun.*, vol. 50, no. 38, pp. 4895-4897 (2014)