Poster

Diversity of the host-guest crystalline assemblies of *p*-sulfonatocalix[*n*]arenes with benzamidines

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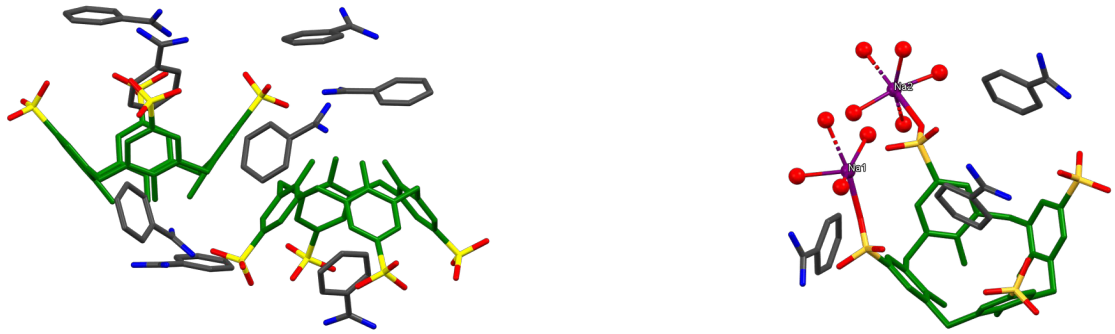
Water-soluble *p*-sulfonatocalix[*n*]arenes are extensively examined for their complexation ability with different guests both in solution and solid state. These hosts have interior surfaces and sulfonate groups that serve as binding sites for both hydrophobic and hydrophilic molecules, respectively. The three-dimensional, flexible, and electron-rich cavities of calixarenes enable them to interact with various biomolecules through non-covalent interactions, making them suitable for incorporating active agents for biomedical applications. Nevertheless, there is no information on their crystal complex formation with benzamidines.

Benzamidines are the simplest water-soluble aryl amidines that act as reversible competitive inhibitors of trypsin, trypsin-like enzymes, and serine proteases [1]. Since the benzamidine moiety is found in many pharmaceuticals it is interesting to study its binding behavior with *p*-sulfonatocalix[*n*]arenes. The cationic amidinium group of benzamidine allows it to interact with anionic *p*-sulfonatocalix[*n*]arenes via charge-assisted hydrogen bonds.

This study focuses on the cocrystallization attempts of *p*-sulfonatocalix[4]arenes and *p*-sulfonatocalix[6]arene with benzamidine to form supramolecular host-guest structures. We have explored the influence of the crystallization solvent and the nature of the benzamidine substituents on the crystallization and crystal structure of the host-guest assemblies. Moreover, we have used the water "slurry" method for the host-guest cocrystallization and compared such solid-state complexes to those obtained through classical solution crystallization. We have found that the nature of the host-guest crystal complexes is very sensitive to the crystallization conditions and a variety of crystal forms can be obtained from the same host and guest starting components. For example, at certain conditions, the crystallization of ternary complexes between *p*-sulfonatocalix[4]arene, benzamidine, and sodium cations takes place, in which benzamidine cation is included in the macrocyclic cavity while sodium cations are coordinated to both upper and lower rim of the calix[4]arene. Additional aspects to discuss are the deprotonation of one of the phenolic groups of the macrocyclic host and the trapping of oxonium cations in the host-guest crystalline assemblies.



a *b*

Figure 1. Host-guest complexes of *p*-sulfonatocalix[4]arene with benzamidine obtained from (a) H_2O ($P2_1/n$), (*b*) H_2O/EtOH ($P\bar{1}$).

[1] Tanizawa, K., Ishii, S., Hamaguchi, K., Kanaoka, Y. (1971). *The Journal of Biochemistry*, **69**, 5, 893–899.

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