From Macrocycles to Molecular Shuttles: Exploring the Supramolecular Assembly of Resorc[4]arenes.

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Many biologically active compounds feature low solubility in aqueous media and, thus, poor bioavailability. The formation of host-guest complex by using calixarene-based macrocycles (i.e., resorcinol-derived cycloligomers) with a good solubility profile can improve solubilization of hydrophobic drugs.[1,2] Herein, we explore the ability of resorc[4]arenes (**BSK**, **R1**, **R2** and **R3**) (Figure 1) to self-assembly in polar solutions and to act as molecular shuttles of a poorly water-soluble isoflavone endowed with anticancer activity, namely Glabrescione B (GlaB).[3] Accordingly, we synthesized several architectures featuring different pattern of substitution on the upper rim including functional groups able to undergo acid dissociation (i.e., carboxyl and hydroxyl groups). The aggregation phenomenon of the amphiphilic resorc[4]arenes has been investigated in THF/water solution by UV–visible spectroscopy, at different pH values. Based on their ionization properties, we demonstrated that the supramolecular assembly of resorc[4]arene-based systems can be modulated at given pH values, and thus promoting the solubility of GlaB.

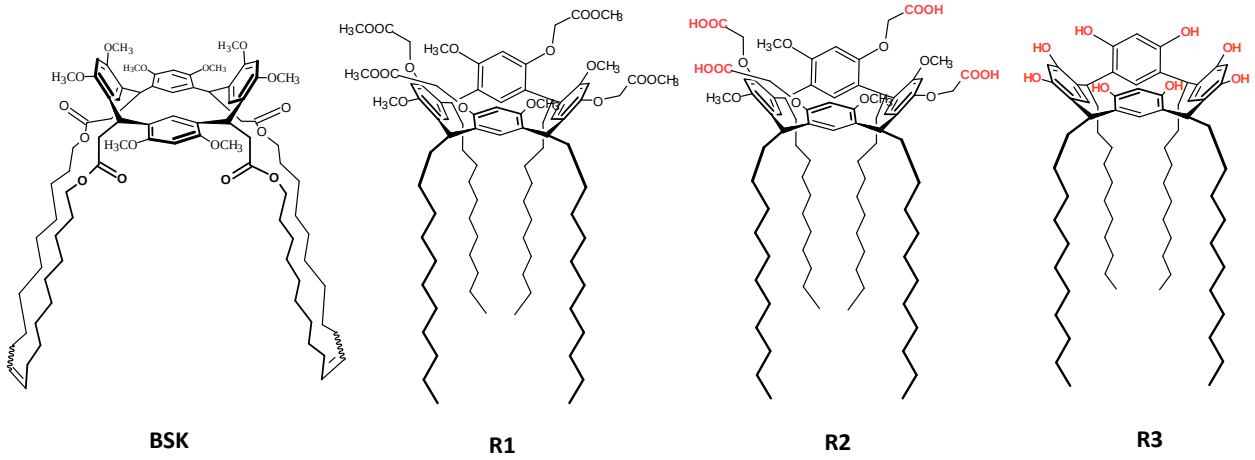

Figure 1. 3D chemical structures of **BSK**, **R1**, **R2** and **R3**.

References

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