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FROM DYNAMIC STRUCTURES TO FUNCTIONAL MATERIALS

Resolving the Hierarchy of Non-Covalent Interactions in Squaramide Bola-Amphiphile Self-Assembly, with an Odd Preference for Hydrophobicity

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Supramolecular self-assembly in aqueous media is fundamental to the formation of functional biomaterials; however, it remains difficult to predict because multiple non-covalent interactions act simultaneously, and hydrophobic effects often dominate, masking the contributions of other forces. Using a series of squaramide-based bola-amphiphiles with a systematically increasing number of squaramide units and a fixed internal alkyl spacer, we used water-miscible organic solvents as reference points to isolate the roles of hydrogen bonding and π-π stacking before returning to water as the system of interest. Isopropanol, a polar protic solvent, favours extended intermolecular hydrogen bonding, driving all analogues alike toward large, ordered, head-to-tail assemblies with a characteristic absorption feature at 330 nm. Acetonitrile, a polar aprotic solvent, does not solvate via hydrogen bonding to the same extent, and instead favours π-π stacking over hydrogen bonding. The series here first shows a deviation from linearity along the parity line of squaramide units. Even-numbered analogues continue to form head-to-tail assemblies, while for odd-numbered analogues, π-stacking completely overpowers extended hydrogen bonding, resulting in the loss of the 330 nm band. In water, both packing modes remain accessible, but which one will dominate depends on hydrophobicity, which strongly adds a further driving force on top of hydrogen bonding and π-π stacking, and it favours π-stacked, turn-stack-turn-like packing over the extended head-to-tail arrangement. But this hydrophobic effect does not vary evenly across the series: it is most pronounced for the odd-numbered analogues, and especially for the three-squaramide analogue, which predominantly forms short, turn-stack-turn-like fibers; at higher concentration, it can also access the head-to-tail state, but the turn-stack-turn packing remains dominant. This effect does not simply scale up with squaramide number; for the four-squaramide analogue, the trend loses its edge, as the increasing number of hydrogen-bonding units and the increasing hydrophobicity that come with each added squaramide unit in the molecular design counterbalance one another, leaving its behaviour intermediate and probably having a mixture of aggregates using both the two packing modes. The three-squaramide analogue thus stands out as the clearest case where hydrophobicity, rather than hydrogen bonding, dictates the assembly outcome, establishing squaramide unit parity as a key design parameter for directing self-assembled architecture in water.

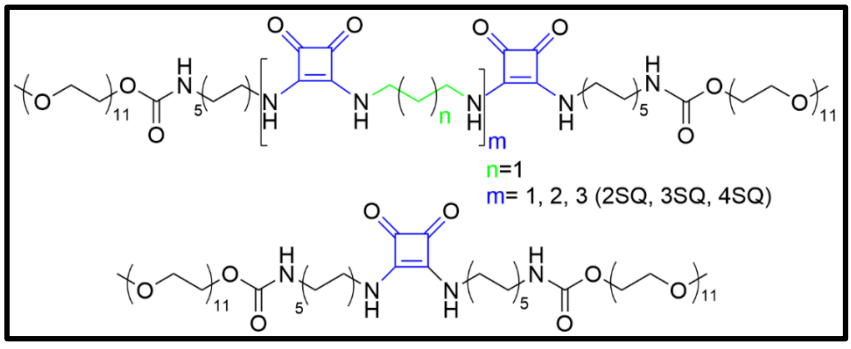

Figure1: Structures of the multi-SQ series (Top) and control molecule, 1SQ (bottom)