A Supramolecular Toolkit for Molecular Structure Determination

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Single-crystal X-ray diffraction is arguably the most definitive and reliable method for molecular structure determination. Yet it can be frustrated by the inability to grow sufficiently large single crystals for conventional X-ray diffraction analysis, the tendency of many compounds to form oils or amorphous phases, low melting points that preclude solidification at convenient temperatures, and decomposition under ambient conditions. In the case of chiral molecules, insufficient anomalous scattering due to the absence of heavy can preclude absolute configuration determination. We report herein a straightforward approach to molecular structure determination that relies on a versatile toolkit of guanidinium organosulfonate (GS) hydrogen-bonded host frameworks that encapsulate target molecules to form crystalline inclusion compounds in a single-step. This approach complements the so-called crystalline sponge method, in which the structures of target molecules trapped in metal-organic frameworks have been determined by single-crystal X-ray diffraction, while circumventing many of its limitations. The alternative approach described herein relies on the peculiar properties of the GS host frameworks to include a wide range of guest molecules in stoichiometric amounts, typically without disorder or accompanying solvent, thereby affording well-refined structures as well as reliable determination of absolute configuration of chiral target molecules owing to anomalous dispersion by the sulfur atoms in the framework. The ever-expanding library of more than 100 different organosulfonates, which has produced more than 500 host-guest combinations to date, provides a knowledge base that enables facile selection of frameworks suitable for specific target molecules based on the size and shape of the target molecules. This is demonstrated herein for a diverse set of host-guest combinations to illustrate the versatility and generality of using GS frameworks for the determination of molecular structure, include reliable assignment of relative stereochemistry and absolute configuration of stereogenic centers.

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