Adaptable water networks inside a metal-organic framework for atomic-resolution structure elucidation of bioactive compounds

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X-ray analysis of metal-organic frameworks (MOFs) encapsulating target compounds could not only reveal important information about the target structures¹ and host-guest interactions², but also observe chemical reactions³ including metastable species.⁴ However, to date, only a handful of MOFs have been identified to be compatible for a wide range of substrates since guest capture and stabilization is typically achieved by a series of finely-balanced host-guest interactions, which are difficult to rationally design.

In this study, a MOF with azaphenalenyl based ligand was used for the encapsulation and structural characterization of 14 bioactive compounds. The single crystal analysis revealed that guests were surrounded by hydrogen-bonded water networks and clusters inside the pores, which adapted depending on the guest molecule, providing clearly defined crystallographic sites. As a result, the guest structures could be determined with high resolution, and limited number of constraints and restraints. The calculations of host-guest structures showed that the guests were primarily interacting with the MOF through weak dispersion interaction. On the other hand, the coordination and hydrogen bonds contributed less to the overall stabilization energy, however they provided highly directional point interactions, thus helping to align the guests inside the pore allowing to achieve greater crystallographic resolution.

![Image](image_url)

**Figure 1.** Artemether analysis results: a) ORTEP drawing of artemether@Co-3TPHAP (> 50% probability), b) Fo electron density map for artemether@MOF (> 2.5eÅ⁻³ level) and c) displaying hydrogen bonds between MOF, water and artemether. The water highlighted in purple is free inside pore.

References