

Supramolecular Synthesis of Caffeine Solvates and Cocrystals

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Caffeine is a biologically active compound, widely used in food and drug industry. Besides a 0.8 hydrate, two anhydrous forms are known¹ which still defy a complete structural determination because of disorder phenomena.² We recently carried out a large number of solvent crystallizations where we obtained three new solvates. The solvates are formed with formic acid, acetic acid and methanesulfonic acid. Acetic acid and formic acid solvates lose their solvent readily. The crystal structure analysis of these solvates lead us to design two new, hitherto unknown, caffeine cocrystals in addition to the recently reported ones.³ This report describes the discovery and structural aspects of these new caffeine solvates and cocrystals. The methanesulfonic acid solvate (monoclinic, *C2/c*) has the highest calculated density (1.594 g cm⁻³) of all the solved cocrystal structures so far. The driving force for the formation of the solvates and cocrystals is presumably an additional hydrogen-bond stabilization by the introduction of an acid group as a hydrogen bond donor for the basic imidazole nitrogen of caffeine by the formation of O–H···N interactions.

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