

Influence of steric hindrance on the hydrates formation. The case of 2,2,6,6-tetramethylpiperidine and 3,3,5,5-tetramethylmorpholine

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Amines can (co)crystallize with water fairly well. The crystals can be formed mostly because both components form hydrogen bonds. Depending on the stoichiometric ratios, amines can create several hydrates with different amount of water per amine molecule. An excellent example is a piperidine - an aliphatic, heterocyclic secondary amine with a six-membered ring. This system can form five different hydrates [1]: the lower ones (containing $\frac{1}{2}$ or 2 water molecules per amine) which present features characteristic for well-defined structures of cocrystals, and the higher hydrates (8.1, $9\frac{3}{4}$, 11) which have the architecture more similar to clathrate hydrates with the organic molecules embedded in the cages [2].

Steric hindrance is an interesting factor influencing the formation of hydrates. The presence of the substituent group (like a methyl group) in close proximity of the NH group can reduce an access for the other molecules and hence may lead to significant structural changes. Piperidine can be easily substituted with methyl groups in 2nd and/or in the 6th position, what maximizes the steric hindrance effect. Consequently, the number of possible 2,2,6,6-tetramethylpiperidine hydrates might be expected to be smaller than for the parent piperidine system. Another possible modification of piperidine moiety is a replacement of carbon in the 4th position with an oxygen atom giving morpholine. Interestingly, despite of similar shape and properties to piperidine, the morpholine hydrates have not been discovered up-to-date. Therefore, an intriguing problem appears whether the 3,3,5,5-tetramethylated morpholine is willing to cocrystallize with water. If so, do these hydrates reveal a similar kind of architectures to piperidine analogue or not?

Because both 2,2,6,6-tetramethylpiperidine or 3,3,5,5-tetramethylmorpholine and water are liquid at RT, amines and their hydrates were crystalized on the diffractometer, using in situ crystallization technique with IR laser [3]. As a result of throughout analyses crystals of both amines, but also of four hydrates were obtained and their structures were determined. The amines form hemihydrates and dihydrates. Interestingly, while hemihydrates of the amines have very similar, but not identical, structural motifs, dihydrates are isostructural. Despite of numerous attempts no higher hydrates (clathrate-like systems) could be obtained. This is probably due to too large size of the whole molecules to fit to the cavities observed in the clathrate hydrates.

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