Poster Presentation

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Anisotropic crystal growth of carbamazepine form I and a hydroxysulfonamide

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Carbamazepine form I, CBZ, and 4-hydroxy-N-phenylbenzenesulfonamide, HPS, both exhibit highly anisotropic needle-like crystal growth. CBZ has been observed to have a corresponding anisotropy in its dissolution. Using the assumption that crystal growth and dissolution have reciprocal mechanisms[1] molecular dynamics, MD, simulations of CBZ and HPS crystal dissolution have been used to examine the mechanism of the needle growth/dissolution. MD simulations of CBZ dissolution using AMBER[2] reproduce the highly anisotropic crystal dissolution. Blocks containing between 48 and 256 molecules in 50 to 90 Å3 boxes of solvent show rapid loss of molecules from the a face. Simulation of HPS crystal dissolution also shows high anisotropy however the dissolution of HPS is much slower than that of CBZ due to the presence of hydrogen bonding chains in the structure. A two unit cell molecule centroid distance matrix analysis was used to detect molecular stacking in both structures. The direction of the hydrogen bonding in HPS is normal to the direction of growth. However the relatively rapid dissolution is in the stacking direction in both crystal structures and is attributed to the higher relative energy of surface molecules at the ends of the stacks that have a higher fraction of exposed atoms. A related analysis has been applied to flat molecule structures which are stacked. [3] If flat molecule stacks can be compared to stacks of pizza boxes then the non-flat molecules described here can be compared to stacked chairs.

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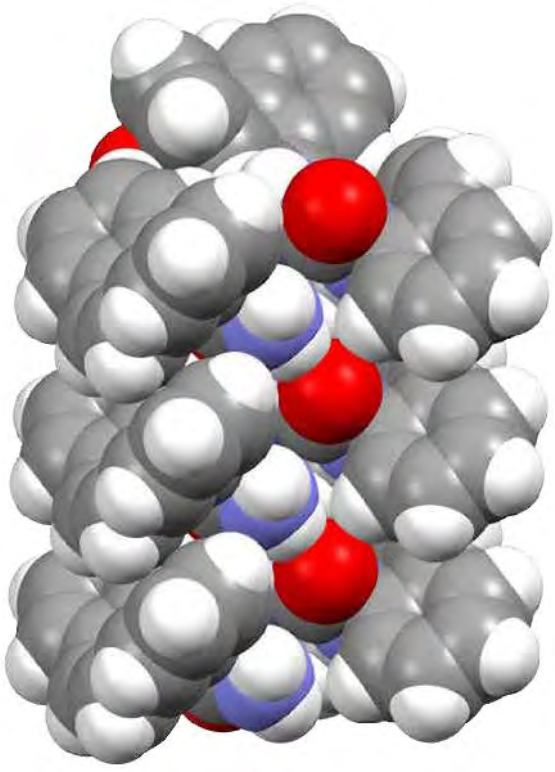

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