KINETIC ASPECTS OF POLYMORPHISM IN RESPECT TO DRUG SUBSTANCES

Elena Boldyreva

REC-008 Novosibirsk State University, Institute of Solid State Chemistry Russian Academy of Sciences, Kutateladze, 18, Novosibirsk, 128, Russia, boldyrev@nsu.ru

The problem of controlling polymorphism is one of the "hot topics". It is important for pharmaceuticals and materials, and it is also a challenge as an illustration of our ability (or, disability) to control the 3D organization of chemical species. Many attempts of "polymorph prediction" are based on a comparison of the energies / enthalpies (but very rarely – of free energies, if at all) of several packing arrangements, and on the selection of optimum candidates with the lowest energies. As was noted in many publications, this approach, being very useful, in principle, cannot provide any information on the conditions, under which a particular polymorph can be obtained. Due to the role of ***kinetic factors***, the polymorphs that are really obtained under given conditions, are quite often not the ones that are thermodynamically the most stable under these conditions. At the same time, a polymorph can be preserved indefinitely long under the conditions, at which it is not stable thermodynamically.

In the present contribution we shall illustrate this at several examples, which are of importance for pharmaceutical industry. In particular, we shall consider the effect of traces of liquids and gasses on the polymorphic transitions in solid drugs and in slurries, the complicated effects of mechanical action (grinding, hydrostatic loading of single crystals vs powders, crystallization from solution at high pressure) and of cooling / heating rates on the polymorphs of drugs, the effects of the sample pre-histrory and of the choice of the starting forms on the polymorphic transitions.

The study was supported by Humboldt Foundation, a grant from BRHE (NO-008-XI), and a grant from RFBR (05-03-32468)