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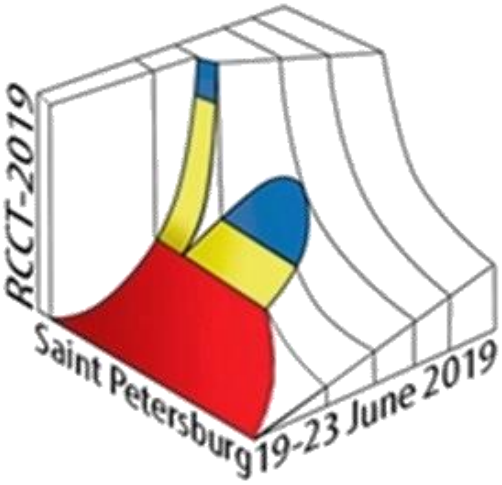

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BOOK OF ABSTRACTS

Saint Petersburg State University
Ministry of Science and Higher Education
Kurnakov Institute of General and Inorganic Chemistry of the Russian Academy of Sciences
Russian Academy of Sciences
The Mendeleev Russian Chemical Society
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PIII-51. The Conformational Equilibrium of Mefenamic Acid in DMSO: Thermodynamic or Kinetic Origin?

Belov K.V.,[1,2] Khodov I.A.[2,3], Kiselev M.G.,[1] Efimov S.V.[3], Batista de Carvalho L.A.E.[4]

[1]G.A. Krestov Institute of Solutions Chemistry, Russian Academy of Sciences, Russia
[2]Ivanovo State University, Ivanovo, Russia
[3]Kazan Federal University, Russia
[4]University of Coimbra, Coimbra, Portugal

ilya.khodov@gmail.com

This work presents main results of studies and conformational properties of the mefenamic acid molecule (2-[(2,3-dimethylphenyl)amino]benzoic acid), which is a derivative of N-phenylantranyl acid. This compound is used as medicine and belongs to the group of nonsteroidal anti-inflammatory drugs. The aim of this work is determination of the most probable conformers of mefenamic acid dissolved in dimethyl sulfoxide using the methods of NMR spectroscopy and computer simulation. The obtained information can help to determine possible nucleation mechanisms.

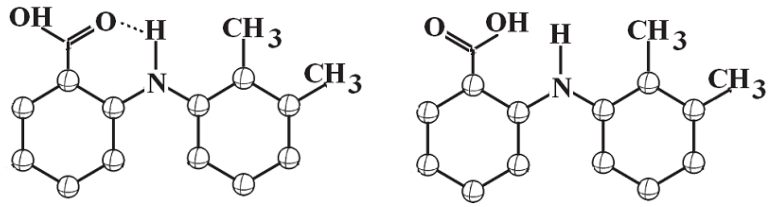

Figure 1. Structure of the mefenamic acid molecule for the polymorph MEF I (left) and MEF II (right).

Studies of mefenamic acid conducted in groups of McConnell and Lee [1], revealed that it can crystallize in two forms, called MEF I and MEF II. They are formed by different conformations of the mefenamic acid molecules (Fig.1), having different orientations of the carboxyl group. The phase transition from MEF I to MEF II in the solid state is observed in the range from 160 to 190°; the transition temperature depends on the heating rate. This transition can also be induced by mechanical compression of solid material. Our hypothesis is that the molecular conformation existing in the saturated solution defines the polymorphic type obtained by evaporation of this solution. Recently we have shown on the example of felodipine [2], that the spatial structure of the molecule changes upon increasing the concentration to the saturated state, and eventually becomes like the configuration found in the crystal. On the other hand, a possibility of complicated, multi-stage mechanism of arising of polymorphic forms is also possible, as it was found during study of ibuprofen [3]. We believe that the multi-stage mechanism is the consequence of competition between processes of solvation (or kinetic) and thermodynamic effects. In this work we try to discuss the influence of the thermodynamic effects on conformation equilibrium of mefenamic acid.

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