Poster Presentation

MS35.P08

Charge density analysis of paracetamol, acetotoluidine and methacetin

D. Druzhbin[1,2], T. Drebushchak[1,2], E. Boldyreva[1,2]

[1]*Institute of SolidState Chemistry and Mechanochemistry, Novosibirsk, Russia,* [2]*Novosibirsk State University, Novosibirsk, Russia*

Paracetamol (p-hydroxyacetanilide, Pbca), acetotoluidine (p-methylacetanilide, P21/c) and methacetin (p-methoxyacetanilide, Pbca) contain acetamide group included in molecular fragments, which play an important role in many drugs and proteins. As all of them are derivatives of acetanilide used in medicine, and due to the presence of the amide bond, their charge density analysis is important for better understanding amide infinite peptide chains. Thus, comparing the data obtained for paracetamol with acetotoluidine and with methacetin charge density data can provide deeper insight into NH···O bonding. Another point of interest is the possibility of methyl group rotation that remains to be ambiguous in these acetanilide molecule based compounds. In the present study we have attempted to elucidate these problems using precise X-ray diffraction at 100K with subsequent charge density topological analysis. All charge density refinements were based on the Hansen and Coppens multipolar atom model. The topologies of the inter- and intramolecular interactions are carefully analyzed for compounds. The atomic charges, bond orders, and the electrostatic energy in molecules are discussed. The topological characteristics in the critical point of the NH···O bond of paracetamol, acetotoluidine and methacetin are shown in the table below. In contrast to similarity in NH···O bonds for all studied compounds, intermolecular interactions between the double bonded oxygen atom and the hydrogen of dimer's methyl group are different. In acetotoluidine and methacetin the (3, –1) critical points with the same topological characteristics were detected between these atoms. In comparison to them, paracetamol with disordered methyl group [1, 2] has no such point. That can be related to the absence of the methyl group disorder in acetotoluidine and methacetin.

[1] *B. Kolesov, M. Mikhailenko, E. Boldyreva, Phys. Chem. Chem. Phys., 2011, 13, 14243-14253,* ***[2]*** *C. Wilson, Z. Kristallogr., 2000, 215, 693–701*

	ρ, eÅ^{-3}	$\Delta\rho$, eÅ^{-5}	R (O···H), Å	Bond order	Energy (a. u.)
paracetamol	0.133	2.20	1.97	0.046	0.0035
acetotoluidine	0.185	1.85	1.89	0.083	–0.0007
methacetin	0.195	2.58	1.84	0.063	0.0011

Keywords: paracetamol, acetotoluidine, methacetin