Notes

o.m6.o5 Polymorphs of paracetamol – theoretical investigations on an over-the-counter drug. T. Beyer, S.L. Price, *Centre of Theoretical and Computational Chemistry, University College London, 20 Gordon Street, London WC1H OAJ, U. K.*
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Paracetamol is known to crystallise in three polymorphic forms[1], two of which are stable enough for experimental investigations of their structure and physical properties.

Form I (monoclinic) and form II (orthorhombic) have been successfully reproduced using an accurate model for the intermolecular forces based on a Distributed Multipole expansion of an *ab initio* charge distribution for the dominant electrostatic contribution and an empirical atom-atom repulsion-dispersion potential.

Furthermore, a systematic search for minima in the lattice energy has successfully found both experimental structures as low energy forms, reproducing the order of thermodynamical stability.

The compression ability of a crystal form is crucial in tablet production. In contrast to the normal marketed form I, form II is suitable for direct compression. To investigate this difference in mechanical behaviour, elastic constants of the experimental structures have been calculated.

The relevance of a comparison of physical properties, like elastic constants and morphology for experimentally known polymorphs and hypothetical low energy structures generated in the systematic search is discussed.

[1] Di Martino, P., Guyot-Hermann, A-M., Conflant, P., Drache, M., Guyot, J-C. "A new pure paracetamol for direct compression: the orthorhombic form", Int. J. Pharm., (1996), 128: 1 – 8.