

Two mefenamic acid derivatives: Structural characterization from PXRD and MEP

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Mefenamic acid (MA), 2- [(2, 3- (dimethylphenyl) amino] benzoic acid, is a well-known non-steroidal anti-inflammatory drug (NSAID) used for the relief of postoperative and traumatic inflammation, treatment of rheumatoid arthritis and acute respiratory tract infection. Since the free carboxylic acid moiety of MA is thought to be responsible for its increased risk of stomach ulcers and gastrointestinal disorder new compounds are designed by modifying the acid functionality of MA to ester, amide or NO releasing groups. Crystal structures of two MA derivatives, prop-2-ynyl 2-(2,3-dimethylphenylamino)benzoate (2) and N'-(dihydro-2H-pyran-4(3H)-ylidene)-2-((2,3-dimethylphenyl)amino)benzohydrazide (3) have been determined using X-ray powder diffraction. The diffraction data were recorded at room temperature (293 K) using a Bruker D8 Advance diffractometer utilizing CuK α radiation (1.5418 Å). The indexing of X-ray powder patterns with EXPO-2014 [1] resulted in monoclinic unit cells with space group P21/n for 2 and P21/c for 3. Crystal structures were solved by the direct space structure solution program FOX [2]. The Rietveld refinement carried out using the software GSAS [3] converged to $R_p = 0.0558$, $wR_p = 0.0759$ for 2 and $R_p = 0.0404$, $wR_p = 0.0559$ for 3. The DFT optimized molecular geometry in 2 and 3 agrees closely to that obtained from the crystallographic study. The nature of intermolecular interactions in 2 and 3 has been analyzed through Hirshfeld surfaces and two-dimensional fingerprint plots, and compared with that in the mefenamic acid polymorphs. Intermolecular N-H \cdots N, C-H \cdots O/N and C-H \cdots π (arene) interactions in 2 and 3 assemble molecules into two and three-dimensional supramolecular frameworks. Hydrogen-bond based interactions in 2 and 3 have been complimented by calculating molecular electrostatic potential surfaces. Hirshfeld surface analyses of 2, 3, three mefenamic acid polymorphs and a few related mefenamic acid derivatives retrieved from the Cambridge Structural Database (CSD) indicate that about 80% of the Hirshfeld surface areas in these compounds are due to H \cdots H and C \cdots H/H \cdots C contacts.

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[2] Favre-Nicoli. V. and Cerny. R. (2002) J. Appl. Cryst. 35(6), 734-743.

[3] Larson. A. C. and Von Dreele. R. B. (2000) General Structure Analysis System (GSAS), Los Alamos Laboratory Report (LAUR), pp 86-748.

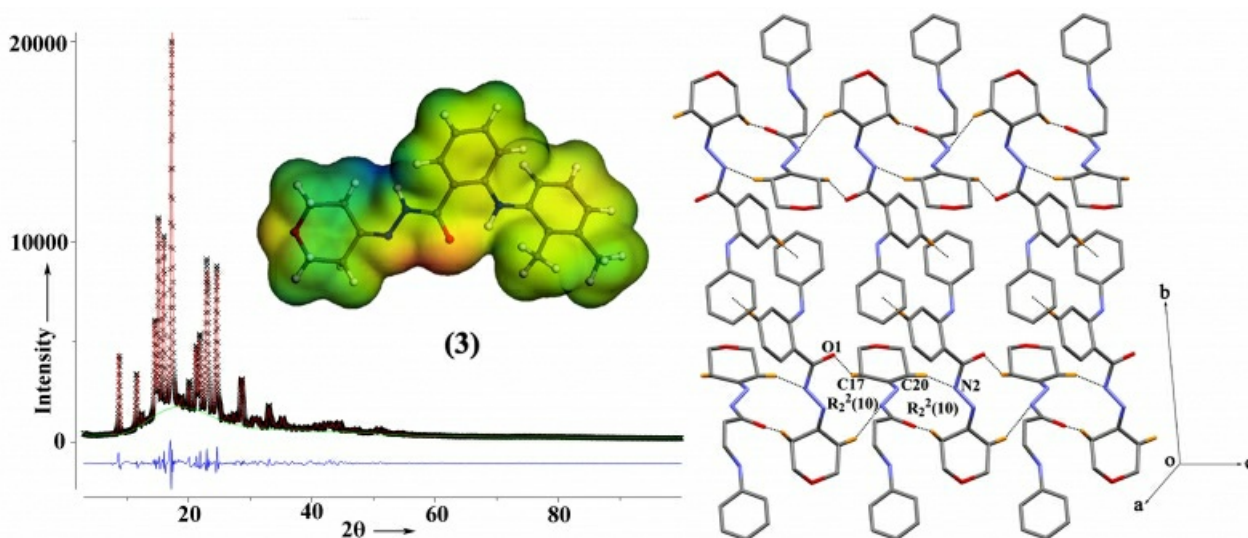


Fig. 1: Final Rietveld plot and MEP surface of 3 along with the two dimensional architecture formed by it

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