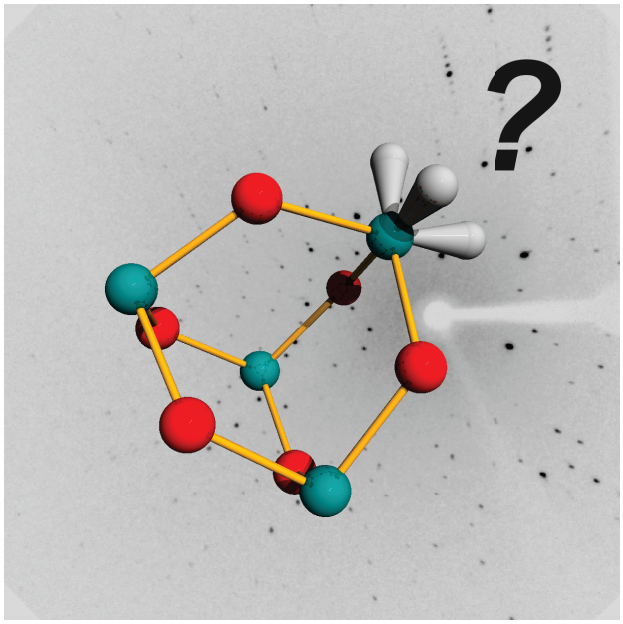

Figure 1. Dispersion of arsenic lone electron pair into three domains located *trans* with respect to the primary As–O bonds.

Keywords: charge density, arsenic(III) oxide, lone electron pair, stereoactivity

MS28-P2 Experimental charge density analysis for doxycycline

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Doxycycline is a well established wide-spectrum antibiotic, known for its antibacterial and anti-protozoal activity and included in the WHO Model List of Essential Medicines. The drug is commercially available in the hyclate (hydrochloride hemiethanolate hemihydrate) or monohydrate form. Since in the crystal structures of both doxycycline presents the same tautomeric form as that observed in the antibiotic-protein complexes, both crystal forms are interesting in terms of modeling antibiotic-protein interactions.

Presented here are the results of the experimental charge density analysis for both doxycycline monohydrate and doxycycline hydrochloride. The network of intra- and intermolecular interactions of the doxycycline in both crystal forms is analyzed and classified in terms of topological analysis, interaction energies and source function contributions. Interaction energies are also compared with the results of theoretical periodic calculations.

The additional proton bound to the O3 oxygen in the case of doxycycline hydrochloride does not change the global conformation of the antibiotic molecule, but it significantly influences the distribution of charges and the resulting electrostatic potential of the molecule. As the oxygen atom O3 is directly involved in the intermolecular interactions of doxycycline with the host proteins, availability of the electron density distribution for both protonated and deprotonated variant enables more exact prediction of the antibiotic-protein interactions at different host protein protonation states.

The conformation of the antibiotic in the crystal lattice of both forms is compared with the conformation known for the antibiotic-target protein complexes deposited in PDB. The major difference is the breaking of the intramolecular hydrogen bond network in order to form two protein-ligand contacts. The differences are also explored by means of Hirshfeld surface analysis of the doxycycline in the crystal network and doxycycline in the protein environment.

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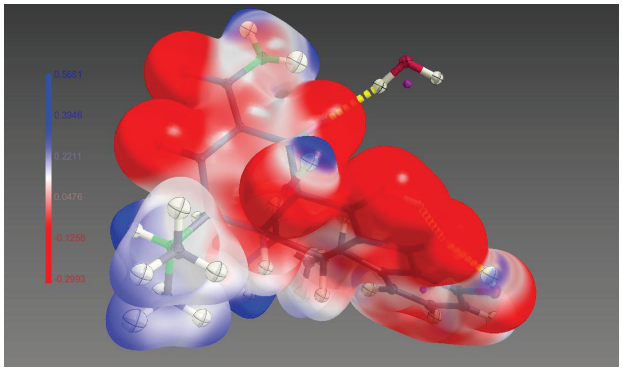

Figure 1. The electrostatic potential around doxycycline moiety in doxycycline monohydrate.

Keywords: doxycycline, antibiotic, protein-ligand interactions

MS28-P3 Dithiadiazolyl radicals - structures and charge densities of their crystals and cocrystals

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Purely organic systems can exhibit conductivity, superconductivity or magnetically ordered phases - properties usually thought as restricted only for crystals containing metallic centres (Cu, Mn, etc.). One of the most intriguing groups of such systems is a family of dithiadiazolyl radicals.[1] These radicals are chemically stable, so they can be arranged in closely packed structures. Relatively high electrostatic polarization allows for inter- and intramolecular S…N interactions. In the crystal phase, the dithiadiazolyl group often co-exists with a phenyl molecular fragment, which further stabilizes the crystal lattice by introducing an intermolecular $\pi...\pi$ aromatic interactions (e.g. phenyl…perfluorophenyl stack interaction). The spin structure of these compounds is strongly coupled to the crystal structure. One can then try to adjust the magnetic properties (e.g. FM-AFM ordering) of such systems by small changes of structural parameters (e.g. distances between molecules in stack). This and other intriguing properties suggest that the dithiadiazolyl radicals are promising candidates for the construction of molecular devices.

The scope of the work was to determine the quantitative electron density distribution and its parameters (ρ and $\Delta\rho$ in critical points, integrated charges, etc.) for the series of model crystals of radicals belonging to dithiadiazolyl family.[2] The Hansen-Coppens multipole expansion of electron density model was refined against the high resolution ($\sin\theta / \lambda > 0.7 Å^{-1}$). X-ray diffraction data to obtain the best models of the electron density distribution in given crystals. These models were then used to calculate quantitative electron density properties using the Bader's Quantum Theory of Atoms in Molecules (QTAIM) such as critical points parameters (ρ_{CP}, $\Delta\rho_{CP}$, bond paths), atomic basins or integrated electron density parameters (integrated charges, atomic multipoles and volumes, etc). The obtained results and detailed analysis of dithiadiazolyl radicals should hopefully help in a better understanding of the magnetic phenomena in organic systems.

[1] Rawson, J. M., Alberola, A., Whalley, A., J. Mater. Chem. 16, (2006), 2560-2575. [2] C. Allen, D.A. Haynes, C.M. Pask, J.M. Rawson, CrystEngComm 11, (2009), 2048-2050.

Keywords: electron charge density, radicals, cocrystals