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The halogen C-Br···S bonding in the crystal structure of an oxazole derivative: a charge density study

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Microtubules are key components of the cytoskeleton consisting of αβ-tubulin heterodimers and are involved in a wide range of various cellular functions, such as cell division, where they are responsible for mitotic spindle formation and proper chromosomal separation. The biological importance of microtubules in mitosis and cell division makes them an interesting target for the development of anticancer agents: many of them are already in clinical use (epothilone, paclitaxel) or in clinical trials such as combretastatin A-4 (3'-hydroxy-3,4,4',5-tetramethoxy-*cis*-stilbene, CA-4), however the search of new potent agents is still continued.

Our successful investigation on novel potent inhibitors of tubulin polymerization from group of CA-4 thioderivatives [1] prompted us to prepare a new series of oxazole-bridged CA-4 analogues. They were synthesized using the Van Leusen multicomponent reaction between corresponding benzaldehydes and *p*-toluenesulfonylmethyl isocyanides (TosMICs).

In the crystal structure of one of the new derivatives, namely 4-[3-bromo-5-methoxy-4-(methylsulfanyl)phenyl[-5-(4-bromo-3-nitrophenyl)-1,3-oxazole, a very short and directional C-Br···S halogen bonding was found (Br···S 3.264Å, C-Br···S 168.8°). In fact, it is the shortest such distance in all organic structures found in the CSD. As we were able to prepare the crystals of very good quality, high resolution diffraction data were collected, up to $\sin\theta/\lambda=1.10 Å^{-1}$, and the electron density was modelled using Hansen-Coppens pseudoatom multipolar model [3]. The deformation density maps, together with the Atom-In-Molecules topological analysis of interactions will be presented in the communication. Also the comparison with the quantum chemistry calculations results show the importance of halogen bonding for the crystal structure.

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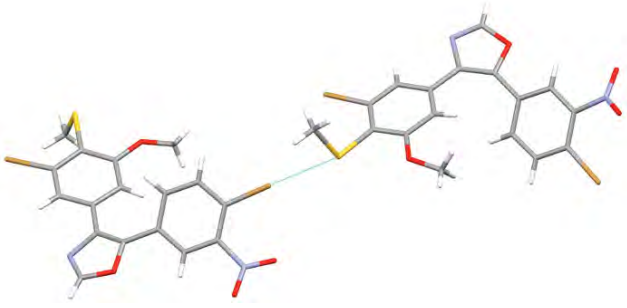

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