

Quantum chemical analysis of intermolecular interactions in a muricatacin polymorph

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(+)- And (-)-muricatacin are γ -lactone-type acetogenins known for their strong antiproliferative activity against various human cancer cell lines [1]. The total synthesis of both (+)- and (-)-muricatacin has been reported [2], and their crystal structures have already been published. However, by applying a modified synthetic approach followed by recrystallization from a different solvent, a new polymorph of (+)-muricatacin was obtained. This form differs from the previously reported structure in that its asymmetric unit contains two crystallographically independent but chemically identical molecules named **A** and **B** [3]. To better understand its crystal structure, the supramolecular architecture of muricatacin polymorph was analysed through the intermolecular interaction energies. This approach allows identification of the basic structural motif (BSM) by recognizing strongly bound molecular fragments and replacing molecules with energy-vector diagrams [4] which offer a clear, topological view of crystal packing.

Calculations were performed using the ORCA program, with B97/def2-TZVP density functional method, including the atom-pairwise dispersion correction D3BJ [5]. In the crystal, the first coordination sphere of **A** contains 14 neighbouring molecules, while **B** contains 12 neighbours. The total interaction energy between the basic molecular units and all their neighbours is $-151 \text{ kcal mol}^{-1}$. Pairwise interaction energy analysis revealed that the strongest interaction, with an energy of $-20.9 \text{ kcal mol}^{-1}$, is between molecules **A** and **B** within the asymmetric unit, which are bound by an O3–H31 \cdots O6 hydrogen bond (1.80 \AA , 169°). This interaction is almost two times higher than the interaction within the other dimers, consequently designating this dimer as the dimeric building unit (DBU₀) of the structure (Fig. 1a). Each DBU₀ is surrounded by 14 neighbouring dimers, among which it forms the strongest interactions with two symmetry related dimers, each with an energy of $-30.6 \text{ kcal mol}^{-1}$. These interactions lead to the formation of a column of dimers (Fig. 1b), which can be considered the basic structural motif (BSM) in the crystal of muricatacin polymorph. The total interaction energy of DBU₀ with the neighbouring dimers within the column is $-61.2 \text{ kcal mol}^{-1}$, and dimers within column are bound by an O6–H61 \cdots O4 hydrogen bond and nonspecific interactions, with dispersion being the major component, as indicated by the dispersion correction of $-37.3 \text{ kcal mol}^{-1}$.

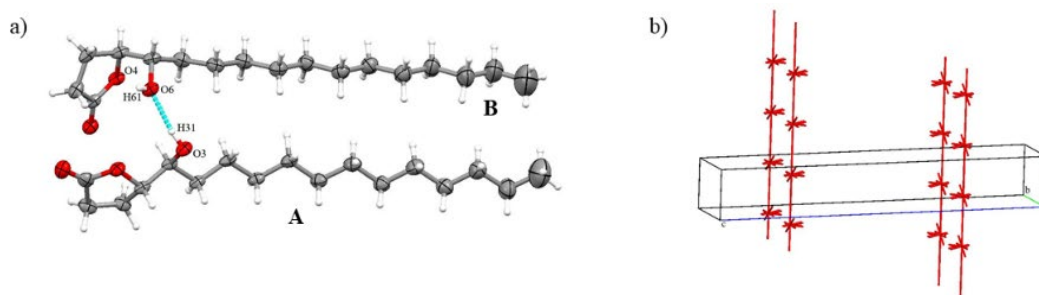


Figure 1. Dimeric building unit with the strongest interaction in the structure (a) and columnar packing of molecules in terms of energy-vector diagrams, projection along the crystallographic axis *a* (b).

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