Structural study of dibenzoylmethane from *Hottonia palustris* L.

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Isolation

The herb *H. palustris* (Primulaceae) was dried (1160 g) in the dark at room temperature immediately after harvesting and then shredded. Next, the plant material was subjected to exhaustive extraction in a Soxhlet apparatus with petroleum. After removing the solvent under vacuum at 40℃, 75 g of crude extract was obtained. The extract separation of the extract was performed using Sephadex LH-20 (GE Healthcare, Uppsala, Sweden), by column chromatography (CC) using isocratic (CH_3Cl : CH_3OH, 3:2, v/v). The flavonoid-rich fraction was applied for further separation by CC using silica gel (0.063-0.200 mm) (Merck, Darmstadt, Germany). Elution was performed with a mobile phase composed of a mixture of n-C_6H_{14} and ethyl acetate with gradually increasing polarity. Fractions eluted with n-C_6H_{14}: ethyl acetate at the ratio 95:5 (v/v) were combined and allowed to evaporate under low pressure at 40℃.

Crystallization

The amorphous dry powder was dissolved in *n*-C_6H_{14}. Monoclinic (space group $P2_1/c$), small and pale-yellow colored crystals of the first polymorph (Fig. 1, left) were obtained by fast evaporation of the solvent at 20℃. Orthorhombic (space group *P*bca)., large, and intense-yellow colored crystals of the second polymorph (P(2), (Fig. 1, right) appeared within a few weeks as a consequence of the slow evaporation of the solvent at 20℃. The total mass of the crystalline substance was 0.425 g.

Fig. 1. Image from under the microscope presenting two polymorphic forms of crystals of the dibenzoylmethane

Studies of dibenzoylmethane structure

This study aims to describe the crystal structures of two polymorphic forms of dibenzoylmethane using modern, state-of-the-art quantum crystallographic methods and to explain the differences in molecular conformations employing an electronic structure approach. The structural analysis of both polymorphs indicated the presence of the dibenzoylometane (Fig.2.) in its keto-enol tautomeric form within both crystal lattices. However, a closer inspection of both crystal structures showed that hydroxyl proton is mutually bound by two oxygen atoms rather than is covalently attached to a particular hydroxyl oxygen atom.

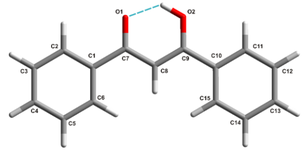

Figure 2. The molecular structure of dibenzoylmethane.

Monoclinic polymorph molecules are oriented practically parallel to each other while in orthorhombic polymorph molecules orientation is nearly perpendicular. Additionally, to the crystal packing crystal voids in the unit cells are mapped. The shortest C…C distance for both structures is similar (monoclinic 3.392Å; orthorhombic 3.387Å), and the values indicate the π-stacking interaction.

However, looking along with the C…C distance, differences in the shift are observed. In the case of an orthorhombic structure, the offset is stabilized by sigma-pi interactions between phenyl rings. In the case of monoclinic structures, the offset indicates the interaction between a phenyl ring and a malondialdehyde quasi-ring. This interaction affects the system of conjugate bonds in the latter, causing electron density delocalization. To better apprehend this interaction, the electron densities of molecular systems have been studied using the Quantum Theory of Atoms in Molecules (QTAIM). Molecular graphs for the two molecular systems are presented in Fig. 3.

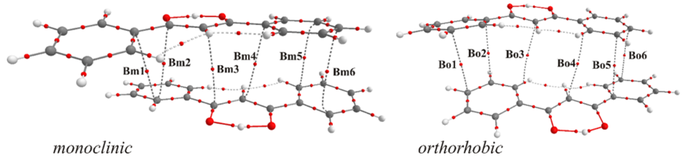

Fig. 3. Molecular graphs of two closest parallel molecules in crystal structures. showing intermolecular bond paths and bond critical points.

Additionally, diffraction data of ultra-high resolution and quality, measured at various temperatures allowed us to engage the quantum-crystallography method (Hirshfeld atom refinement, Fig.4-5.) to determine proton positions based on experimental diffraction data.

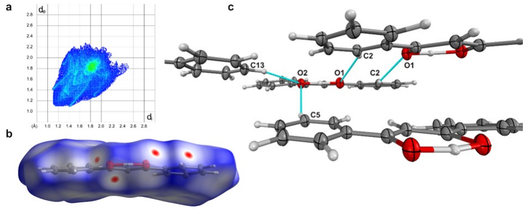

Fig. 4. The finger print plot along (a) with the molecular Hirshfeld surface (b) and hydrogen bonds pattern (c) of the monoclinic crystal structure.

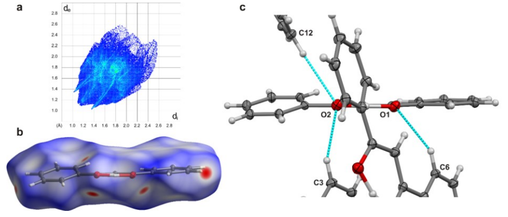

Fig. 5. The finger print plot (a) along with the molecular Hirshfeld surface (b) and hydrogen bonds pattern (c) of the orthorhombic crystal structure.

As expected, the differences in shapes of the Hirshfeld surfaces and the red spots distribution are a clear conformation of two polymorphic forms. Detailed data available after contact via e-mail.

Conclusion

We suggest that the presence of the enol form with a unified proton position results from the stabilization of the molecule by the intramolecular hydrogen bond-forming the malondialdehyde quasi-ring. In consequence, the intramolecular hydrogen bond significantly lowers the energy of the molecule. Including initial research [1], the obtained results are published the first time from this plant.

References

[1] Strawa, J.; Szoka, Ł.; Tomczyk, M. Planta Med. 2019, 85, 1544.