

Halogen bonds as promoters of isostructurality in crystal structures of novel aminoflavone derivatives

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One way to develop new drug molecules is by chemically modifying compounds of natural origin possessing biological activities. Flavones, a subgroup of flavonoids, are known for their anti-inflammatory, antioxidant or anticancer properties [1-3]. As a part of our ongoing project focused on the synthesis and structural characterization of new, potentially active molecules based on a flavone scaffold, we have obtained six pyrrole-substituted compounds bearing halogen atoms (Cl, Br, I), as illustrated in Figure 1.

Among 6-substituted derivatives, those with bromine and iodine atoms are isostructural, whereas the chloro-substituted analogue adopts different structural arrangements. In the latter case, the structural motifs and the overall crystal packing are governed solely by hydrogen bonding. In turn, in the structures of **6-Br** and **6-I** compounds, the primary building blocks, chains and planes are also formed by hydrogen bonding, while the crystal packing is based on halogen bonding.

Crystals of **7-Cl** and **7-Br** are isostructural, both crystallizing in the triclinic space group, *P*-1, with the unit cell parameters of about: *a*=7.756 Å, *b*=8.348 Å, *c*=15.801 Å, α =94.91°, β =99.14° and γ =116.94°. In contrast, compound **7-I** crystallizes in a monoclinic space group *P*2₁/*c*, with unit cell parameters that are comparable to those of chloro- and bromo-derivatives; *a*=8.1705 (3) Å, *b*=32.4225 (8) Å, *c*=8.0102 (3), β =117.333°. As the unit cell parameters indicate, one (chains) and two-dimensional (planes) structural motifs are alike in all three structures. Thus, these structures have 2D conformity. However, the overall crystal packing is different in **7-I**. In crystals **7-Cl** and **7-Br**, the relative orientation of adjacent layers aligns the pyrrole rings against each other, thereby facilitating the formation of hydrogen and halogen bonds. In contrast, in crystal **7-I**, planes are shifted, and there are no interplanar interactions (Figure 1).

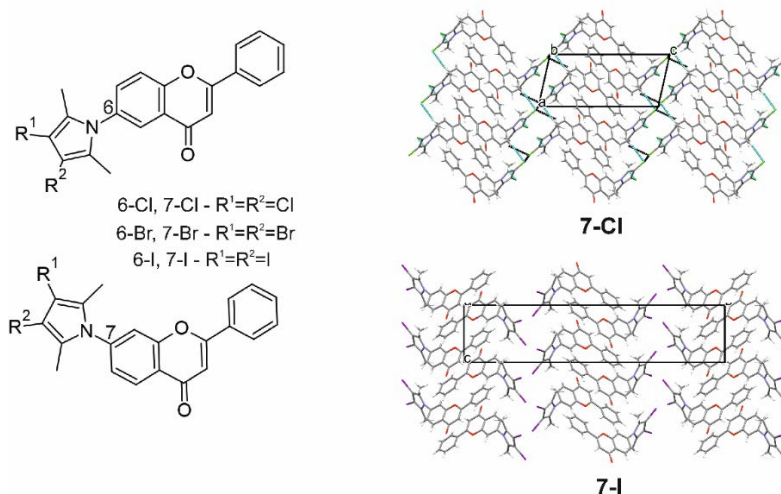


Figure 1. Scheme of the synthesized compounds and crystal packing observed in crystals **7-Cl** and **7-I**. Interplanar interactions in **7-Cl** are shown as black lines.

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[3] Khan, A. U., Dagur, H.S., Khan, M., Malik, N., Alam, M. & Mushtaque, M. (2021). *EJMCR*, **3**, 100010. [4] Balzar, D. & Popa, N. C. (2004).