

## Structural insight into $\pi$ -stacking interactions of non-aromatic oxazolo[5,4-*d*]pyrimidine derivatives and their neuroactivity in a *Galleria mellonella* model

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### Streszczenie

In this study, the physicochemical characteristics, quantum-chemical properties, and neurobiological activity of 6-*N*-benzyloxazolo[5,4-*d*]pyrimidin-7(6*H*)-imine derivatives **1–9** were investigated. Solid-state structural analysis using single-crystal X-ray diffraction (XRD) revealed intermolecular  $\pi$ -stacking interactions involving the formally non-aromatic oxazolo[5,4-*d*]pyrimidine scaffold. Energy decomposition analysis (EDA) showed that the tested crystallographic dimers are energetically stabilizing, with dispersion representing the largest attractive contribution throughout the series. Complementary non-covalent interaction (NCI) analysis demonstrated spatially extended regions of weak non-covalent interactions between the stacked molecular fragments. Density functional theory (DFT) calculations showed that the HOMO–LUMO gaps and related global reactivity descriptors varied only within a narrow range across derivatives **1–9**. Combined crystallographic and thermal analyses indicated that the nature and position of substituents on the *N*-6-benzyl group are associated with differences in crystal packing, melting behavior, and thermal stability. The neurobiological effects of the tested compounds were assessed *in vivo* using the *Galleria mellonella* model. Following an initial screening of oxazolo[5,4-*d*]pyrimidine derivatives **1–9**, compounds **5** and **6** were selected for more detailed locomotor analysis and showed the most pronounced changes in larval behavior. Overall, the combined crystallographic, EDA, and NCI results provide complementary structural, energetic, and real-space evidence supporting dispersion-dominated stacking interactions in the solid state, whereas their possible relationship with the observed neurobiological effects remains to be established.

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Oxazolo[5,4-d]pyrimidine,  $\pi$ -stacking interaction, Thermal stability, Quantum-chemical properties, Neuroactivity, in vivo model

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