

Dual inhibition of *S. aureus* TyrRS and *S. aureus* gyrase by two 4-amino-4'-acetyldiphenyl sulfide-based Schiff bases: Structural features, DFT study, Hirshfeld surface analysis and molecular docking

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Abstract

Two 4-amino-4'-acetyldiphenyl sulfide-based Schiff bases, namely 1-[4-({4-[(E)-(2-hydroxynaphthalen-1-yl) methylideneamino]phenyl} sulfanyl)-phenyl]ethanone (I) and (E)-1-[4-({4-[(4-methoxybenzylidene)amino] phenyl}-sulfanyl)phenyl]ethan-1-one (II) were structurally studied. They crystallize respectively in the monoclinic Cc and the triclinic P1 space groups, with the respective cell parameters: [10.695(3) Å, 44.458(14) Å, 4.4437(11) Å, 99.004(9)°] and [5.7708(2) Å, 8.0867(3) Å, 19.6929(8) Å, 81.844(2)°, 86.664(3)°, 85.662(3)°]. The asymmetric units of (I) and (II) are composed of one molecule and two crystallographically independent molecules, respectively. Their molecular structures were optimized by the density functional theory and correlated correspondingly to the crystal structures. Moreover, the IR vibration modes were assigned to the calculate wavenumbers, the Mulliken atomic charges obtained and the frontier molecular orbitals evaluated. The hydrogen bonding and the non-classical intermolecular interactions within the two frameworks were investigated using Hirshfeld surface analysis which indicated the presence of C–H...H–C, C–H... π , C–H...O, C–H...N, C–H...S and π ...lp interactions as well as π ... π stacking. Additionally, in order to understand the interacting binding sites of the two molecules with the bacterial *S. aureus* protein receptors, the studied compounds were in silico evaluated by molecular docking against tyrosyl-tRNA synthetase 1JJJ and topoisomerase II DNA gyrase 2XCT enzymes. The results revealed consequently potent antimicrobial efficacy through the formed hydrogen bonds, hydrophobic contacts, π -cation interactions and π ... π stacking.