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Synthesis, structural analysis, DFT and molecular docking studies of N-(6-(((E)-4-methoxybenzylidene)amino)hexyl)-1-(4-methoxyphenyl) methanimine and its hydrate as a possible 2019-nCoV protease inhibitor

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Highlights

- A convenient and facile synthesis N-(6-(((E)-4-methoxybenzylidene) amino) hexyl)-1-(4-methoxyphenyl) methanimine (1) and its dihydrate (2) are accomplished.
- Single crystal analysis depicted that compound 1and 2 crystallizes in a monoclinic crystal system with *P 21* and *C 2/c* space group having trans-geometry at the C=N bond.
- The structural and electronic properties of both compounds have been calculated using DFT/B3LYP/6-311G (d,p) level of theory.

Abstract

N-(6-(((E)-4-methoxybenzylidene) amino) hexyl)-1-(4-methoxyphenyl) methanimine (1) and its hydrate (2) were synthesized by refluxing hexamethylene diamine and anisaldehyde in presence of catalytic amount of H-Beta zeolite in solvent methanol. Resulting imines were characterized by spectroscopic analysis augmented by Single crystal X-ray diffraction. Both compounds crystalize in monoclinic crystal systems with different point groups P 21 and C 2/c. Pair wise aromatic π-CH and CH- π interactions with distance 2.887 and 2.786 A^0 and iminic CH- π interactions with the distance of 2.73 A^0 are mainly responsible for extending the structure along 3 dimensions. However, hydrated structure exhibited an addition hydrogen bonding with H of water molecules with the distance of 2.030 A^0 , also methoxy O is involved in hydrogen bonding interaction with CH with the distance of 2.641 A^0. Probable contact points and most important crystal packing contributions were determined by employing Hirshfeld surface analysis. H…H and C…H contacts are the most important contributors in the Hirshfeld Surface. Electronic and structural characteristics of both compounds has been calculated using B3LYP/6-311G (d,p) theory. In addition, FMO and MEPS analyses were also accomplished for optimized structures. Molecular Docking studies of compound 1 and 2 were carried out with protease enzyme of 2019-nCoV (PDB-ID 7BRO), monohydrate(2) was involved in more favourable interactions hence accounting for greater binding energy (-7.98 kcal/mol) and inhibition constant (12.96 mM) than compound 1 exhibiting inhibition constant of 39.25 mM and binding energy of -6.23 kcal/mol.

Graphical abstract