



ortho-Fluorobenzanilides and *ortho*-fluorothiobenzanilides: Molecular conformations and crystal packing



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ABSTRACT

Series of 2-fluoro and 2,6-difluorobenzanilides and their thiobenzanilide analogs have been synthesized to investigate the influence of the fluorine atom on their crystal structures and self-assembly in the crystal lattice. The X-ray analysis of the single crystal revealed that the synthesized molecules adopt a geometry being deflected from planarity.

The deflection was investigated by analysis of dihedral angles between mean planes of benzoyl, amide and aniline residues. Molecular conformation depends mainly on strong N–H···O bonds, although operation of N–H···F hydrogen bonding was observed in one case. Crystal packing is controlled mainly by interactions of the C–H···O type, also by π – π stacking and in one difluorosubstituted case by operation of weak C_{Ar}–F···F–C_{Ar} halogen bonding.

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1. Introduction

Secondary amide linkage [1] RC(O)HNR₁, as a key element of polypeptide chains, is the fundamental structural unit in living organisms and one of the most important functional group in contemporary organic chemistry [2] present in many natural products, polymers, and pharmaceuticals [3]. Due to the ability to form highly directional hydrogen bonds, the amide group is also an extremely useful building block in supramolecular chemistry and crystal engineering [4].

The detailed structural parameters of the secondary amide linkage RC(O)HNR₁ such as CO and CN bonds length and orders, or planarity of the amide unit are determined by the size and electron-releasing or electron-withdrawing character of the substituents R and R₁. Restricted rotation about C–N bond in amide group results in the existence of the *cis-trans* configurational isomers. The *trans* isomer is generally more stable over the *cis* one [5] and demonstrates preferences to form intermolecular hydrogen bonding patterns (chain or polymeric structures), whereas the other one tends to create dimers.

Benzanilides with two aromatic substituents constitute a special group of amides, which due to the wide range of biological activities have been extensively studied both theoretically and

experimentally [6]. In particular, their fluorinated derivatives have gained much attention as drugs intermediates, potential drug candidates [7a–e], herbicides [7f], and useful model for observation of intra- and intermolecular interactions associated with the presence of fluorine atom and strong hydrogen bonds in crystal lattices [8].

It is known that the molecule of benzanilide having two unsubstituted phenyl rings R=R₁=Ph, in crystal lattice assumes the conformation in which the central C–C(O)–N(H)–C fragment of benzanilide molecule is essentially planar, with the phenyl rings twisted about 30° from this plane in opposite directions [9]. Additionally, the results of DFT calculations indicate that the non-planar *trans* conformer is the most stable structure for benzanilide molecule [10].

Introduction of an *ortho* substituent at either C–phenyl or N–phenyl ring in benzanilide, in close proximity to the amide bonding, should strongly affect molecular conformation of the molecule. Moreover, through interaction with the amide unit they could also affect ability of the molecule to form hydrogen bonds.

2. Results and discussion

An analysis of the Cambridge Structural Database for molecular geometry of benzanilides having *ortho* substituent on either of the C–phenyl or N–phenyl ring resulted in 316 hits. The search was restricted to the compounds neither involved in metal complexes

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