The evaluation of the role of C—H⋯F hydrogen bonds in crystal altering the packing modes in the presence of strong hydrogen bond

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ABSTRACT

Interactions involving fluorine is an area of contemporary research. To unravel the importance of weak C—H⋯F hydrogen bonds and C—H⋯π interactions in organic compounds in the presence of strong hydrogen bond, a series of N-benzylideneanilines with simultaneously hydroxyl (−OH) and fluorine substitutions were synthesized for structural analysis. These compounds have been studied through experimental single crystal X-ray diffraction analysis and computational methods (Gaussian09 and AIM2000). The hydroxyl group present in all the molecules were found to form strong O—H⋯N hydrogen bond, but the spatial arrangement of the molecules connected by this hydrogen bond have been found to be controlled by the weak C—H⋯F and C—H⋯O hydrogen bonds, weak C—H⋯π and π⋯π interactions. This manuscript illustrates the importance of several weaker interactions in altering the packing modes in the presence of strong hydrogen bonds.

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1. Introduction

Crystal engineering deals with the understanding of both strong and weak intermolecular forces to build a desired three dimensional architecture to achieve robust molecular framework for advanced applications [1]. A clear understanding of strong and weak interactions is needed for appropriate applications of crystal engineering to design different functional materials. Crystallization of molecules from different solvents and solvent mixtures or by using different crystallization techniques are known to result into different crystal structures (polymorphs) of the same compound [2]. The connection between molecular structure and its crystal structure can only be achieved through an understanding of intermolecular interactions in the solid state [3]. Various strong and weak intermolecular forces include strong and weak hydrogen bonds [3], interaction involving halogens [4], X—H⋯π (X = C, N, O) interactions [5], π⋯π interactions [6] etc. The molecules, which pack in the crystal lattice through strong hydrogen bonds are known to yield highly stable crystal structures thereby making it difficult to alter the packing features through small alteration in the parent molecule [7]. On the other hand, the crystal structures governed by only weak hydrogen bonds or by a combination of strong and a number of weak hydrogen bonds are altered easily by minor changes in the parent molecule [8]. Weaker hydrogen bonds result into lower stabilization energies while forming molecular assemblies by the formation of dimers, trimers, tetramers, chains, ladders, ribbons etc. [9] Therefore, crystal structures governed by these interactions can easily be altered by the incorporation of other functional groups. Among the weak hydrogen bonds, the interactions offered by "organic fluorine" [10] are of specific interest because of its ambiguous behaviour [11] in the solid state. In spite of the highest electronegativity of fluorine, it was considered to be weaker electron acceptor than oxygen or nitrogen and was refuted to have true hydrogen bonds by Howard et al. [11c] Thalladi et al. [12] for the first time glorified the role of C—H⋯F interactions in their structural investigations on fluoro-benzenes using newly developed techniques of in-situ crystallization [12,13]. In the last decade, a number of research groups have illustrated that organic fluorine offers various intermolecular interactions such as C—H⋯F—C, C—F⋯X—C (X = F, Cl, Br) and C—F⋯π [14]. The significance of these interactions in crystal engineering have been

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highlighted in the review by Berger et al. [15], by Chopra and Guru Row [16] in their recent highlight and further by Chopra in his perspective [17]. The polarizability of organic fluorine was earlier refuted based on the high electronegativity of F. A recent experimental charge density study first revealed the formation of sigma hole on fluorine thereby indicating that organic fluorine is also partially polarizable [18].

Since, the interactions offered by organic fluorine are generally weak in nature, their application in crystal engineering has mostly been studied in the absence of any strong hydrogen bond donor and acceptors group(s) [9a-d,14a-d]. Our recent structural investigations in a series of *N*-benzylideneaniline and azobenzene indicate that the weak interactions offered by organic fluorine are capable of offering various repetitive supramolecular synthons through C–H⋯F–C hydrogen bonds [9a-d]. In this manuscript, we intend to evaluate the structure directing/controlling ability of organic fluorine in the presence of a hydroxyl group in fluorinated *N*-benzylideneanilines. These molecules containing simultaneously –OH and C–F groups offer an opportunity for a systematic analysis of weak hydrogen bonds offered by the C–F group in the presence of strong hydrogen bonds involving the –OH group. We have structurally analysed and computationally studied these molecules to achieve an understanding of the individual roles played by organic fluorine and the hydroxyl group in crystal packing. Our earlier structural studies on *N*-benzylideneanilines contained structures of **87** compounds (**1** to **87**) [9a,c,d]. Therefore, the new compounds studied in this manuscript have been numbered from **88** to **111** so that direct comparison can be made with the previously reported structures.

2. Experimental section

2.1. Procedure for synthesis

All the starting materials were purchased from Sigma Aldrich and were used without further purification. All the compounds were synthesized using the mechano-chemical approach [19]. Corresponding benzaldehyde (0.5 mmol) and aniline (0.5 mmol) were ground using mortar and pestle with approximately 100 μl methanol. The resulting mixture slowly solidified upon grinding for 10–15 min to yield the desired product. The solid crude products were then dissolved in various solvents (methanol, ethanol, hexane, ethyl acetate, chloroform and dichloromethane) and the solutions were allowed to evaporate slowly in refrigerator (4 °C) for recrystallization and subsequent growth of single crystals suitable for structure determination.

Scheme 1 describes all the molecules studied and the method of nomenclature used in this manuscript. Based on the nature and position of the substitutions, the compounds have been sub divided into 6 groups as indicated in the Scheme 1. Out of 24 synthesized compounds, 20 compounds yielded single crystals of good quality for structural analysis. Remaining four compounds (C.N. **100**, **101**, **102** and **103**), although crystalline (PXRD pattern in ESI), have always resulted into the glassy material during the recrystallization process.

All the synthesized compounds were characterized by ^{1}H NMR (400 MHz, Bruker Biospin Advance-III NMR spectrometer) (ESI, Fig. S2: 1 to 20) and FTIR (Perkin Elmer Spectrum2) (ESI, Fig. S3: 1 to 20) spectroscopy. Powder X-ray Diffraction (PXRD) data were recorded on a Rigaku Ultima IV diffractometer using parallel beam geometry, Cu – Kα radiation, 2.5° primary and secondary solar slits, 0.5° divergence slit with 10 mm height limit slit, sample rotation stage (120 rpm) attachment and DTex

Ultra detector at 40 kV of tube voltage and 40 mA of the current. The data sets were collected over 2θ ranging from 5 to 50° with a scanning speed of 5° per minute with 0.02° step for all the compounds.

The PXRD patterns have been simulated from the crystal coordinates using Mercury [20] and compared with the observed PXRD patterns using WINPLOTR^{210} (ESI, Fig. S4: 1 to 24). The simulated PXRD patterns were found to match with the experimentally observed PXRD recorded on the bulk sample. This indicates that the bulk phase is represented by the structure determined by the single crystal X-ray diffraction technique. Melting points and the melting enthalpies of all the compounds (Table S1) were determined from the DSC (Perkin Elmer DSC 8000) traces recorded at 5° per minute heating rate under Nitrogen atmosphere (ESI, Fig. S5: 1 to 24).

3. Diffraction data collection and structure solution

Single crystal X-ray diffraction data for the crystals were recorded using Mo – Kα radiation at 100.0(1) K using Oxford cryosystem either on Bruker AXS KAPPA APEX-II CCD diffractometer or on a Rigaku XtaLAB mini diffractometer using Mercury375/M CCD detector using graphite monochromator. The data sets, which collected on Bruker diffractometer were recorded using a detector distance of 6.0 cm with varying 2θ position of the detector using the APEX-II suit [22], data reduction and integration were performed SAINT V7.685A12 [22] (Bruker AXS, 2009) and absorption corrections and scaling were done using SADABS V2008/112 [22] (Bruker AXS). The remaining data sets collected on XtaLAB mini diffractometer were recorded using a fixed detector distance of 5.0 cm and the detector kept at 2θ = 29.85° and were processed with Rigaku Crystal Clear suite 2.0 [23]. All the crystal structures were solved using SHELXS [24] and were refined using the SHELXL [24] available within Olex2 [25]. All the hydrogen atoms have been geometrically fixed and refined using the riding model except the hydrogen of the –OH group, which has been located from the difference Fourier map and was refined isotropically. Complete crystal data collection and refinement details for all the compounds are available in the Tables S1a–d (ESI). The thermal ellipsoid plots of all the molecules have been drawn at 50% probability for the non-H atoms using Mercury and are shown with the atom labels in the ESI (Fig. S6: 1 to 20). All the packing and interaction diagrams have been generated using Mercury 3.5 [20]. Geometric calculations have been done using PARST [26] and PLATON [27].

3.1. Crystallographic modelling of disorder

Among the 20 compounds reported in this manuscript, the compound **90** was found to have positional disorder due to rotation of the aniline ring around C8–N1 bond and the compounds **104** and **108** were found to exhibit positional disorder due to in-plane flipping of the molecule around C=N bond. PART command was used to analyse these positional disorders. These disorders were refined for two independent positions, namely A and B ('A' for higher occupancy). For the purpose of refinement, the position of the carbon atoms in part A and B of the phenyl rings were fixed at the same position using EXYZ command in SHELXL2013. Thermal parameters were also constrained to be equal for the atoms at the same position using EADP command in SHELXL2013. All hydrogen atoms were then positioned geometrically and refined using a riding model with U_{iso} (H) = 1.2 U_{eq} (C, N). The occupancy ratio for the two parts in **90**, **104** and **108** were