Experimental and computational analysis of supramolecular motifs involving $C_{sp^2$(aromatic$)-F$ and $\text{CF}_3$ groups in organic solids†

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A detailed experimental (SCXRD) and theoretical (PIXEL and QTAIM) investigation of the evolution of different supramolecular motifs formed via the presence of both $C(sp^2)/(sp^3)–F$ groups in the crystal packing has been performed in a series of newly synthesized substituted benzanilides (containing "both" the fluorine and the trifluoromethyl group in the same molecule) along with previously reported similarly related crystal structures [CrystEngComm, 2008, 10, 54–67; CrystEngComm, 2012, 14, 1972–1989, CrystEngComm, 2013, 15, 3711–3733]. It was observed that the highest stabilized molecular motifs primarily consist of $C(sp^2)–H\cdots F–C(sp^2)$ $H$-bonds in preference to $C(sp^2)–H\cdots F–C(sp^3)$ $H$-bonds in the crystal. The motifs involving $C(sp^2)–H\cdots F–C(sp^2)/(sp^3)$ $H$-bonds were observed to be present over the entire distance range between 2.2 and 2.7 Å, albeit the difference in energies of stabilization involving fluorine atoms attached to $sp^2$ and $sp^3$ carbon is not significant in molecular crystals. From QTAIM analysis, the $C(sp^2)/(sp^3)–F\cdots H$ interactions were observed to be a closed shell in nature and provide local stabilization, indicating the formation of bonds, similar to weak hydrogen bonds observed in crystals.

Introduction

The introduction of a fluorine atom to the carbon atom (termed as “Organic Fluorine”) can lead to the formation of many weak interactions like $C–H \cdots F–C$ hydrogen bonds, $C–F \cdots F–C$, and $C–F \cdots \pi^\perp$ interactions and the study of these interactions involving organic fluorine is still an expanding area of research amongst the scientific community. However, there has been an enduring discussion regarding the ability of organic fluorine to act as a hydrogen bond acceptor because of its low polarizability. However, the crystal structure analysis of fluoro-benzenes and ribonucleic acids unfasten the area of research regarding the study of interactions involving organic fluorine. Further, such interactions with the protein active site through $C–F \cdots C≡O$ and $C–F \cdots H\cdots C_a$ interactions have been reviewed by Diederich et al. Since then many studies via inputs from crystallography, spectroscopy and theoretical calculations have established the fact that the interactions involving fluorine are ubiquitous and can play an important role in the stabilization of the crystal packing and influence the phenomenon and properties in the solid state, one such example is polymorphism. The extensive literature on compounds related to the presence of organic fluorine has been excellently combined in reviews and a book chapter. It was initially postulated that the weak interactions involving fluorine like $C–H \cdots F–C$ hydrogen bonds are only significant in the absence of any other strong intermolecular forces. The analysis of the nature of fluorine interactions on many molecules has been performed, wherein the possibility of the formation of strong hydrogen bonds was eliminated. Amongst these, benzene, naphthalene, anthracene and phenanthrene, isoquinolines, trifluoroacetophenones, N-phenylmaleimides and corresponding phthalimides, benzonitriles, pyridines, azobenzenes, N-benzylidenanilines, toluene, and N-methyl-N-phenylbenzamides are a few examples to be mentioned. There is no sufficient literature on the study of these intermolecular interactions in molecules wherein strong intermolecular forces are present. However, fluorinated N-(2-chloropyridin-4-yl)-N’-phenylureas, fluoro-N-(pyridyl)-benzamides, fluoro-substituted benzoic acid, and fluorine-substituted benzimidazoles are a few examples wherein the evaluation of interactions involving fluorine was realized in the presence of a strong hydrogen bond. Keeping in mind the above-mentioned points, improvements aimed towards understanding the nature, capability and energetics of interactions...
Involving organic fluorine (in particular C–H···F and C–F···F–C interactions) in the presence of a strong hydrogen bond have been undertaken by our research in the past few years.\textsuperscript{17,39–41}

Our main goal was (i) a systematic exploration of the participation of the fluorine atom in different intramolecular interactions, (ii) robustness of the interaction (i.e., how often they are present) in the formation of different supramolecular motifs, (iii) the role of hybridization of the C-atom to which fluorine is attached and finally (iv) the calculation of stabilization energy and topological parameters such as the electron densities (\(\rho\)), Laplacian (\(\nabla^2 \rho\)), local potential energy (\(V_\rho\)), and kinetic potential energy (\(G_h\)) at the bond critical point by quantum theory of atoms in molecules (QTAIM).\textsuperscript{42} In this regard, a large library of molecules containing the organic fluorine group have been synthesized, crystallized and investigated for different intermolecular interactions involving organic fluorine. The systems were designed such that they have only one strong donor and acceptor (the amide group \(\text{–NH–C} = \text{O}\) in our studies) atom, which connects at least one phenyl ring wherein the position of the fluorine (connected to the C-atom) of different hybridization, [C(sp\(^3\)]–F and –C(sp\(^3\)]–F\(_3\) groups] may vary, keeping the main molecular connectivity invariant. Hence, different molecules, namely fluorine substituted benzanilides,\textsuperscript{17} fluorine and –CF\(_3\) substituted \(N\)-phenylacetamides and \(N\)-methylbenzamides,\textsuperscript{19} and –CF\(_3\) substituted benzanilides have been studied.\textsuperscript{40} The purpose of selecting the CF\(_3\) group is as follows: (i) the –CF\(_3\) group being strongly electron-withdrawing in nature increases the acidity of hydrogen atoms in its vicinity, (ii) better H-bond acceptor abilities of C(sp\(^3\)]–F can be exploited, (iii) in addition to C–H···F–C hydrogen bonds, the propensity of the formation of other interactions namely C–F···F–C and C–F···π is now increased and (iv) in addition to all the above-mentioned points, a comparative study of the role of hybridization of the C-atom to which fluorine is attached can be achieved in the crystal.

Therefore, we have synthesized a library of substituted benzanilides (eighteen in number) containing both the fluorine and trifluoromethyl group on the same molecule (Scheme 1).

Experimental section

All the compounds were synthesized by the procedure that is already reported in the literature.\textsuperscript{40} Scheme 1 describes the general route for the synthesis of all the 18 compounds and their corresponding nomenclature code used in this paper. All the synthesized compounds were characterized by FTIR [Fig. S1(a–p)], and \(^1\)H NMR [Fig. S2(a–p)] (Section S1, ESI†). Melting points were recorded using a DSC [Fig. S3(a–p), ESI†] on the pure powder compounds. Powder X-ray diffraction (PXRD) data were recorded for all the solid compounds and then compared with their calculated PXRD patterns [Fig. S4(a–p), ESI†]. In order to ensure the phase purity, a profile fitting refinement (Section S2, ESI†) was performed using a JANA2000.\textsuperscript{49}

![Scheme 1](image-url)
In the case of 1F2T, 2F3T, 2T1F and 3T1F, high values of the profile fitting parameters \( (R_p, R_{wp}) \) were observed, which may indicate the possibility of the presence of more than one phase in the bulk powder.

The details of all the crystallization experiments of all the solid compounds from different solvents and solvent mixtures are presented in the ESI† (Table S1).

Data collection, structure solution and refinement

Single crystal X-ray diffraction data were collected on a Bruker AXS SMART APEX II CCD diffractometer at 100 K. All the data were collected at 100(2) K. All the crystal structures were solved by direct methods using SIR92 \(^{50} \) and refined using the full matrix-least-squares method using SHELXL2013 \(^{51} \) present in the program suite WinGX. \(^{52} \) The non-hydrogen atoms were refined anisotropically and the hydrogen atoms bonded to C and N atoms were positioned geometrically and refined using a riding model with \( U_{iso}(H) = 1.2 U_{eq} \) \( [C(sp^2)] \). The disorder associated with the CF3 group (in the case of compounds 2F2T and 2T1F, w) and the positional disorder of the F-atom (in the case of compounds 1F1T, 2F1T, 2F2T, 2T1F, 2T1F, w and 2T2F) were modeled with PART command in SHELXL 2013 at two independent orientations (the major component was labeled ‘A’) \( [\text{Fig. S5, ESI}^{†}] \). Molecular and packing diagrams were generated using Mercury software. \(^{53} \) Table S2 (ESI†) lists all the crystallographic and refinement data. ORTEPs of all compounds are presented in Fig. S5(a–m) in the ESI†.

Computational tools and theoretical calculations

The PIXEL method \([\text{in the CLP computer program package (version 10.2.2012)}\] has been used for the interaction energy of the selected molecular pairs, extracted from the crystal packing and related by the corresponding symmetry element as mentioned in our previous work. \(^{31} \) In the method, the total interaction energy is partitioned into their Coulombic \( (E_{coul}) \), polarization \( (E_{pol}) \), dispersion \( (E_{disp}) \) and repulsion \( (E_{rep}) \) contributions. In the case of disordered molecules, the molecular conformation with the maximum population was considered for the calculations. The PIXEL method was observed to provide better and useful insights into the nature of different types of intermolecular interactions present in the different molecular pairs/motifs. \(^{54,55} \) The PIXEL interaction energy was further compared with the interaction energies obtained from theoretical calculations at the DFT+Disp/B97D \(^{58,59} \) level at the higher aug-cc-pVTZ basis set using TURBOMOLE. \(^{60} \) The hydrogen atoms were moved to neutron values \( (1.083 \text{ Å for C–H}) \) before the calculations. The basis set superposition error (BSSE) for the interaction energies was corrected by using the counterpoise method. \(^{61} \) Table S3 (ESI†) \( [\text{divided into two parts: S3a and b, separately for C–F}_p\cdot\cdot\cdot\text{F–C in Table S3b, ESI}^{†}] \) lists the selected intermolecular interactions \( \text{(in the decreasing order of their stabilization energy)} \) in different motifs along with their interaction energies \( \text{(I.E.) of the motifs. In the case of highly disordered compounds 2T1F, w} \) [having the rotational disorder associated with the CF3 group and the positional disorder of the fluorine atom at the phenyl ring along with the presence of half molecule of water in the asymmetric unit, Fig. S5(h), ESI†], PIXEL calculations have not been performed. Instead, BSSE corrected interaction energies for the selected dimers were calculated at the DFT+Disp/B97D level using the aug-cc-pVTZ basis set \( [\text{Table S5, ESI}^{†}] \).

Analysis of topological parameters (QTAIM calculations)

Topological parameters on the selected dimers at the crystal geometry were performed using the same procedure as mentioned previously \(^{41} \) using AIMALL (version 13.05.06). \(^{62} \) The selected topological parameters like electron densities \( (\rho_b) \), Laplacian \( (\nabla^2 \rho_b) \), local potential energy \( (V_b) \), and kinetic energy density \( (G_b) \) at the bond critical points \( (\text{BCPs}) \) were calculated. The dissociation energies for different intermolecular interactions were also estimated through the following two empirical approaches: (i) \( \text{D.E.}^\text{b}(\text{int}) = -0.5V_b \) \( \text{(in atomic units)
The presence of weak C–H···F–C hydrogen bonds in the motifs III, IV and V was characterized topologically by using the QTAIM approach. There was the presence of (3, 1) bond critical points (BCPs) recognized for these interactions (Table S4b, ESI†) along with other related interactions present in the respective motifs [Fig. 1(d)].

(2) N-(3-Fluorophenyl)-2-(trifluoromethyl)benzamide (2F1T)

Compound 2F1T crystallizes in the monoclinic centrosymmetric space group P2₁/c with three molecules in the asymmetric unit (Z′ = 3) (Fig. 2). Two (molecule 2 and 3) out of three molecules in the asymmetric unit observed in the formation of the most stabilized molecular motif I (−13.3 kcal mol⁻¹) involved strong N–H···O=C, weak C–H···π and C–H···F–C(sp³) hydrogen bonds along with π···π interactions. Selected molecular pairs, which contribute towards the stabilization of the crystal packing in 2F1T, are presented in Fig. 2(c) along with their interaction energies (I.E.). The three most stabilized molecule motifs I, II (−13.1 kcal mol⁻¹) and III (−12.2 kcal mol⁻¹), consisting of strong N–H···O=C hydrogen bonds along with other weak interactions (Table S3a, ESI†) were observed to be involved in the formation of a molecular chain along the crystallographic a-axis in the crystal packing [Fig. 2(a) and (b)]. Such chains were observed to be connected with the utilization of motifs IV,
V and VII in the crystal packing [Fig. 2(a)]. The motif IV (I.E. = −5.3 kcal mol⁻¹) consists of short C–H⋯O=C (2.39 Å/149°) and C–H⋯π (2.68 Å/141°) hydrogen bonds while the motif V (−4.7 kcal mol⁻¹) involves the presence of weak C–H⋯F–Csp³ hydrogen bonds [Fig. 2(a)] along with π⋯π interactions. A short C–H⋯F–Csp³ (2.39 Å/127°) and a weak C–H⋯π (2.86 Å/155°) hydrogen bond were recognized to connect the molecules in motif VII. Moreover, the packing of molecules in 2F1T are also stabilized by the presence of weak C–H⋯F–Csp² hydrogen bonds in the motifs VIII, IX and XI with the stabilization energy ranging from −1.3 to −2.6 kcal mol⁻¹ [Table S3, ESI† and Fig. 2(c)]. It is to be noted that the motif X, involves the presence of bifurcated Csp²−F⋯F–Csp³ interactions [type I (2.88 Å, 110°, 94°) and other a “near” type II (3.133 Å, 152°, 83°) contact], provides stabilization towards the crystal packing with an interaction energy of 1.7 kcal mol⁻¹, the nature being primarily of dispersive origin. A very recent charge density analysis has revealed the polarization of the electron density on the fluorine atoms on the trifluoromethyl group, which facilitate the formation of type II C–F⋯F–C contacts in the crystal.⁶⁷ Furthermore, a very short type I Csp²−F⋯F–Csp³ interaction [2.736 Å, 146°, 149°, motif XII] was observed in the crystal packing, providing almost negligible stabilization [0.1 kcal mol⁻¹] [Fig. 2(c)]. This stabilization energy is similar to the value reported in a recent analysis by ab initio calculations on all the unique dimers, extracted from the crystal structure of CF₄, C₂F₄ and C₆F₆ by Osuna et al.⁶⁸

(3) N-(2-Fluorophenyl)-3-(trifluoromethyl)benzamide (1F2T)

Compound 1F2T crystallizes in the monoclinic centrosymmetric space group with Z = 4. Fig. 3(a) depicts the packing of molecules in 1F2T in all the three directions with the utilization of different molecular motifs I to VIII (Table S2, ESI†). The highest stabilized molecular motif I (I.E. = −11.8 kcal mol⁻¹) consists of strong N–H⋯O=C, a short and directional C–H⋯F–Csp³ (2.47 Å, 168°) and a short C–H⋯π (2.66 Å, 158°) hydrogen bond along with C–F⋯π interactions. The motif I along with motif III [I.E. = −4.8 kcal mol⁻¹; consists of a short

Fig. 2 (a) Packing of molecules in 2F1T via the network of strong N–H⋯O=C, weak C–H⋯π and C–H⋯F–Csp³ hydrogen bonds. (b) Clear depiction of the molecular chain along the crystallographic a-axis. Different color codes of carbon atoms indicate the presence of three molecules in the asymmetric unit. Grey: molecule 1, purple: molecule 2 and green: molecule 3. (c) Selected molecular pairs extracted from the crystal packing of 2F1T along with their interaction energies (Table S3, ESI†).
Fig. 3  (a) Packing of the molecules down the bc crystallographic plane in 1F2T via the network of strong N–H⋯O=C, weak C–H⋯π, C–H⋯F–Csp2 and C–H⋯F–Csp3 hydrogen bonds along with π⋯π, Csp2–F⋯π and Csp2–F⋯F–Csp3 interactions. (b) Part of the crystal packing in 1F2T down the ab plane, displaying the presence of weak C–H⋯F–Csp2 and C–H⋯F–Csp3 hydrogen bonds along with π⋯π (off set) and Csp2–F⋯F–Csp3 interactions. (c) Selected molecular motifs (denoted with Roman numbers from Table S4, ESI†) in 1F2T, showing different intermolecular interactions. The small brown spheres represent bond critical points (BCPs) on the bond path. Only the interacting part of the motifs is shown in case of IV, VI–VIII.
C–H⋯π (2.61 Å, 159°) and C–H⋯O=C hydrogen bond] and motif V [I.E. = −1.9 kcal mol⁻¹; involves a bifurcated C–H⋯F–Csp³ along with the presence of C–F⋯π interactions] were observed to pack the molecules along the c-axis with the utilization of c-gliding perpendicular to b-axis. A short and directional C–H⋯F–Csp³ (2.45 Å, 168°) hydrogen bond along with the two π⋯π interactions in the motif II (−6.4 kcal mol⁻¹) was observed to connect the molecules along the crystallographic a-axis.

Fig. 4  (a) Packing of molecules in 2F2T via the network of strong N–H⋯O=C, and weak C–H⋯O, C–H⋯π hydrogen bonds. (b) Packing of molecules in 2F2T, displaying the network of strong N–H⋯O=C, weak C–H⋯O, C–H⋯F–Csp² and C–H⋯F–Csp³ hydrogen bonds along with Csp³⋯F⋯F–Csp³ interactions. (c) Part of crystal packing in 2F2T, depicting the presence of different motifs involving fluorine interactions.
The molecular chains, formed along the a-axis, with the utilization of motif II [Fig. 3(b)], were observed to be connected via motifs IV, VI to VIII in the generation of a molecular layer down the ab plane. Amongst these, motif VI (−1.5 kcal mol⁻¹) and VII (−1.1 kcal mol⁻¹) were found to consist of a short C–H···F–Csp³ (2.47 Å, 161°; 2.57 Å, 139°) hydrogen bond while the motif IV (I.E. = −2.0 kcal mol⁻¹) involves dimeric Csp³–F···F–Csp³ interaction and a weakly stabilized (−0.2 kcal mol⁻¹) motif VIII consists of type I Csp³–F···F–Csp³ (2.942 Å, 158°, 158°) interactions. Further, QTAIM calculations reveal the presence of a (3, 1) BCP for all C–H···F and C–F···F–C interactions [Fig. 3(c)].

(4) N-(3-Fluorophenyl)-3-(trifluoromethyl)benzamide (2F2T)

Compound 2F2T crystallizes in the orthorhombic centrosymmetric space group Pbcn with Z = 8. The most stabilized molecular motif I (I.E. = −12.1 kcal mol⁻¹) consists of strong N–H···O=C hydrogen bonds supported by weak C–H···O and C–H···π hydrogen bonds. A molecular chain, formed via motif I utilizing c-glide, was observed to connect via the weak C–H···π hydrogen bonds recognized in the motif II (−4.2 kcal mol⁻¹), VI (−2.1 kcal mol⁻¹), VIII (−1.6 kcal mol⁻¹) [Fig. 4(a)]. Furthermore, the packing of molecules in 2F2T was stabilized by the formation of motifs III (−3.0 kcal mol⁻¹) and IV (−2.4 kcal mol⁻¹) comprising of dimeric weak C–H···F–Csp³ hydrogen bonds.

Fig. 5  (a) Formation of a molecular layer down the bc crystallographic plane with the utilization of strong N–H···O=C, weak C–H···π hydrogen bonds and π···π interactions in 2F3T. (b) Packing of molecules down the ab plane via the networks of strong N–H···O=C and weak C–H···F–Csp³ hydrogen bonds in 2F3T. (c) Part of the crystal packing in 2F3T, displaying the formation of bifurcated weak C–H···O=C and dimeric Csp³–F···F–Csp³ interactions. (d) Part of the crystal packing 2F3T showing the presence of Csp³–F···F–Csp³ hydrogen bonds and dimeric Csp³–F···F–Csp³ interactions forming a chain motif along with a strong N–H···O=C hydrogen bond. (e) Selected molecular motifs (Table S4, ESI†) in 2F3T, showing different intermolecular interactions. The small brown spheres represent bond critical points (BCPs) on the bond path. Only the interacting part of the motif was shown in the case of VI–IX.
It is of interest to note that a short and directional C<sub>sp3</sub>–F/C/C/C/Cp [3.134 Å, 150°, Table S3, ESI†] interaction, utilizing 2-fold rotation parallel to the b-axis, provided (motif V) stabilization to the crystal packing [2.3 kcal mol<sup>−1</sup>] with dispersion being a major contributor. Moreover, bifurcated weak C–H···F–C<sub>sp2</sub> hydrogen bonds (motif VII, −1.7 kcal mol<sup>−1</sup>) were realized in the formation of a molecular chain, utilizing a c-glide plane perpendicular to the b-axis. Such chains were connected with the presence of motif IX (−0.2 kcal mol<sup>−1</sup>), possessing a pair of weak type I C<sub>sp3</sub>–F/C/C/C/Cp interactions including the one at a short distance (2.873 Å, 122°, 122°) [Fig. 4(b)]. It was also noticed that the two sides of the phenyl ring, substituted with the fluorine and –CF<sub>3</sub> group, were observed in the formation of different supramolecular motifs in the crystal packing [Fig. 4(c)].

(5) N-(3-Fluorophenyl)-4-(trifluoromethyl)benzamide (2F3T)

Compound 2F3T was found to crystallize in the monoclinic centrosymmetric space group C2/c with Z = 8. The strong N–H···O=C hydrogen bond along with the weak C–H···O=C hydrogen bond and π···π interactions (motif I, −12.3 kcal mol<sup>−1</sup>) were observed to engage in the formation of molecular chains along the crystallographic b-axis. Such a chain is connected by the utilization of weak C–H···π hydrogen bonds and π···π interactions in the formation of a molecular layer down the

Fig. 6  (a) Packing of molecules in 3F3T down the ab crystallographic plane with the utilization of strong N–H···O=C, weak C–H···O=C, C–H···F–C<sub>sp2</sub>, C–H···F–C<sub>sp3</sub> and π···π interactions. (b) Packing of molecules in 3F3T down the bc crystallographic plane via weak C–H···F–C<sub>sp2</sub>, C–H···F–C<sub>sp3</sub> and C–H···π hydrogen bonds along with C<sub>sp2</sub>–F···C<sub>sp2</sub>, C<sub>sp3</sub>–F···C<sub>sp3</sub>, C<sub>sp3</sub>–F···C<sub>sp3</sub> and π···π interactions. (c) Selected molecular motifs (Table S4, ESI†) in 3F3T, showing different intermolecular interactions. The small brown spheres represent bond critical points (BCPs) on the bond path. Only the interacting part of the motif is shown in the case of III, V–VII, IX and X.
bc plane [Fig. 5(a)], involved in the next three stabilized motifs II
(−7.6 kcal mol⁻¹), III (−7.4 kcal mol⁻¹) and IV (−6.1 kcal mol⁻¹).
The packing of molecules down the bc plane [Fig. 5(b)] was
detected as the formation of a molecular sheet with the utiliza-
tion of bifurcated weak and short C–H···F–C₃sp² hydrogen bonds
[2.55 Å, 145° (motif VIII, −1.3 kcal mol⁻¹); 2.55 Å, 125° (motif IX,
−1.1 kcal mol⁻¹)], along the b-axis. Furthermore, the crystal
packing of 2F3T was also observed to be stabilized by the formation
of similarly stabilized molecular motifs V (−2.2 kcal mol⁻¹) and VI
(−2.1 kcal mol⁻¹) [Fig. 5(c)]. The motif V consists of bifurcated weak C–H···F–C₃sp² hydrogen bonds while the motif
VI involves in the formation of dimeric C₃sp³–F···F–C₃sp³ inter-
actions. In addition, a type II C₃sp³–F···F–C₃sp³ interaction (motif
VII, −1.9 kcal mol⁻¹) was also observed to form a chain,
utilizing the 2₁ screw axis along the crystallographic b-axis in the
crystal packing [Fig. 5(d)]. The selected motifs, containing weak
C–H···F and Csp²–F···F–Csp³ interactions, were characterized by the QTAIM theory and the presence of (3, −1) BCPs was observed on the bond path of these interactions [Fig. 5(e) and Table S5, ESI†].

(6) N-(4-Fluorophenyl)-4-( trifluoromethyl)benzamide (3F3T)

Compound 3F3T crystallizes in the triclinic centrosymmetric space group P1 with Z = 2. As expected, the most stabilized molecular motif I (−11.7 kcal mol⁻¹) was noticed to involve strong N–H···O=C hydrogen bonds along with weak C–H···O=C hydrogen bonds and π···π interactions. The motif I was found to be involved in the formation of a molecular chain along the crystallographic a-axis. Such chains were interconnected via dimeric weak C–H···F–Csp² hydrogen bonds [motif VII (−1.4 kcal mol⁻¹) and VIII (−1.1 kcal mol⁻¹)] and dimeric weak Csp²–F···F–Csp³ interactions [motif IX (−0.7 kcal mol⁻¹)] in the formation of a molecular layer down the ab plane. Further, in the molecular packing of 3F3T, the molecular chains formed with the utilization of motifs VIII and IX were observed to be connected by the molecular motifs II to VI which consist of other weak interactions in the crystal packing [Fig. 6(b)]. The motif II involves the presence of a weak C–H···π hydrogen bond and a short Csp²–F···O=C (3.118 Å, 120°) interaction, the interaction energy being −6.1 kcal mol⁻¹. The motifs III and IV were noticed to provide similar stabilization towards the crystal packing (−4.7 kcal mol⁻¹ and −4.0 kcal mol⁻¹ respectively) but observed to involve different interactions. The motif III consists of weak C–H···F–Csp³ and C–H···π hydrogen bonds while the weak π···π interaction was observed in motif IV. Moreover, a dimeric short C–H···F–Csp³ (2.45 Å, 157°) contact was observed to stabilize (motif V, −2.8 kcal mol⁻¹) the crystal packing in 3F3T. In addition, dimeric weak Csp²–F···π interactions [motif VI, −2.2 kcal mol⁻¹] were also observed to provide stabilization to the crystal packing in 3F3T. The weak interactions involving fluorine in 3F3T were studied with QTAIM theory and the presence of (3, −1) BCP was observed for these interactions in their corresponding molecular motifs [Fig. 6(c)].

(7) 2-Fluoro-N-(3-(trifluoromethyl)phenyl)benzamide (2T1F)

Compound 2T1F crystallizes in the centrosymmetric orthorhombic space group Pbcn with Z = 8. A strong N–H···O=C hydrogen bond along with π···π interactions (motif I, −11.6 kcal mol⁻¹) was observed in the generation of a zig-zag chain with the utilization of b glide perpendicular to the a-axis. The chains are interconnected utilizing motif VII which consists of the weak near type II Csp²–F···F–Csp³ (2.990 Å, 108°, 154°) interactions (I.E. being −1.0 kcal mol⁻¹). The next most stabilized motif II (−4.5 kcal mol⁻¹), consisting of weak π···π interaction, was found to connect the molecular chain [Fig. 7(b)] generated via a 2v screw along the b-axis utilizing weak C–H···π hydrogen bonds (motif V, −2.8 kcal mol⁻¹). Furthermore, there was the formation of a herringbone pattern down the ac plane [Fig. 7(c)] observed in the crystal packing of 2T1F, exploiting motifs III, IV and VI. The motif III (−3.0 kcal mol⁻¹) was noticed to involve weak C–H···O and C–H···F–Csp³ hydrogen bonds while it was short bifurcated C–H···F–Csp³ hydrogen bonds which were observed in the motif IV, the stabilization energy being 2.8 kcal mol⁻¹. Moreover, a weak C–H···F–Csp³ hydrogen bond was recognized in the motif VI (−1.4 kcal mol⁻¹).

(8) 2-Fluoro-N-(3-(trifluoromethyl)phenyl)benzamide hydrate (2T1F_w)

Hydrate of the compound 2-fluoro-N-(3-(trifluoromethyl)phenyl)benzamide (2T1F_w) crystallizes in the orthorhombic centrosymmetric space group Pbcn with half molecule of water in the asymmetric unit (Table S2, ESI†). It has been characterized using differential scanning calorimetry (DSC), thermal gravimetry analysis (TGA) and hot stage microscopy (HSM) (Section S3 in the ESI†). The packing of the molecules in 2T1F_w was observed to be stabilized by the solvent molecule with the formation of strong hydrogen bonds like N–H···Owater and O_water–H···O=C, noticed in motifs I and II with I.E. being −5.04 kcal mol⁻¹ and −5.63 kcal mol⁻¹ respectively [Table S3c, ESI† and Fig. 8(a)]. A stacked motif III along the a-axis (utilizing a 2v screw), consisting of two weak C–H···F–Csp³ hydrogen bonds along with π···π interactions, is a highly stabilized (−14.2 kcal mol⁻¹) molecular pair in the crystal packing [Fig. 8(a) and Table S3c, ESI†]. The packing of the molecules down the bc plane shows the formation of a molecular layer utilizing motifs I, II, IV and V [Fig. 8(b)]. The molecular chain

![Fig. 8](https://example.com/fig8.png)
with alternate interactions of the compound and solvent was observed to be connected with weak C–H⋯F–C\textsubscript{sp3} hydrogen bonds (motif VI, -1.64 kcal mol\(^{-1}\)) utilizing \(c\)-glide perpendicular to the \(b\)-axis [Fig. 8(b)]. Moreover, the presence of highly short type I C\textsubscript{sp3}–F⋯F–C\textsubscript{sp3} interactions was recognized in the weakly stabilized molecular motif VII (+1.29 kcal mol\(^{-1}\)) using \(c\)-glide perpendicular to the \(b\)-axis [Fig. 8(b)].

(9) 2-Fluoro-N-(4-(trifluoromethyl)phenyl)benzamide (3T1F)

Compound 3T1F crystallizes in the non-centrosymmetric orthorhombic space group \(P\textsubscript{2}_1cn\) with \(Z = 4\). The packing of molecules in 3T1F involves the formation of a molecular chain along the \(b\)-axis with the utilization of strong N–H⋯O═C along with weak C–H⋯O═C hydrogen bonds and \(\pi\cdots\pi\) interactions (motif I, -9.7 kcal mol\(^{-1}\), Table S3, ESI†). Such chains are interconnected by the utilization of next two similarly stabilized motifs II (-6.5 kcal mol\(^{-1}\)) and III (-6.3 kcal mol\(^{-1}\)) in the formation of a molecular layer down the (101) plane [Fig. 9(a)]. The motif II involved a pair of weak C–H⋯C\textsubscript{sp3} hydrogen bonds along with short C\textsubscript{sp3}–F⋯F–C\textsubscript{sp3} (2.663 Å, 132°, 132°) and short C\textsubscript{sp2}–F⋯C=O (3.134 Å, 146°) interactions (Table S3, ESI†) whereas a short and directional C–H⋯\(\pi\) (2.65 Å, 156°) and C–H⋯F–C\textsubscript{sp3}, C–H⋯F–C\textsubscript{sp3}, C–H⋯C\textsubscript{sp3} interactions were present in motif III. Furthermore, a molecular chain formed by the utilization of bifurcated C–H⋯F–C\textsubscript{sp3} hydrogen bonds (motif IV, -1.9 kcal mol\(^{-1}\), the \(2_1\) screw parallel to the \(a\)-axis) was observed to be interconnected via motifs II, III and V in the packing of

![Fig. 9](https://example.com/fig9.png)

(a) Packing of molecules in 3T1F via the network of strong N–H⋯O═C, weak C–H⋯\(\pi\), and C–H⋯F–C\textsubscript{sp3} hydrogen bonds along with C\textsubscript{sp2}–F⋯F–C\textsubscript{sp3}, C\textsubscript{sp3}–F⋯F–C\textsubscript{sp3} and \(\pi\cdots\pi\) interactions. (b) Packing view down the \(ac\) plane in 3T1F via the network of weak C–H⋯\(\pi\) and C–H⋯F–C\textsubscript{sp3} hydrogen bonds along with C\textsubscript{sp3}–F⋯F–C\textsubscript{sp3}, C\textsubscript{sp3}–F⋯C=O interactions. (c) Selected molecular motifs (Table S4, ESI†) in 3T1F, showing different intermolecular interactions. Only the interacting part of the motif is shown in the case of IV–V.
molecules down the ac plane in 3T1F. The motif V (−1.6 kcal mol$^{-1}$) was found to consist of weak C–H···F–Csp$^3$ hydrogen bonds. These were the presence of (3, −1) BCPs identified in the case of weak C–H···F and C–F···F–C interactions [Fig. 9(c) and Table S4, ESI$^\ddagger$].

### (10) 3-Fluoro-N-(2-(trifluoromethyl)phenyl)benzamide (1T2F)

Compound 1T2F crystallizes in the centrosymmetric monoclinic space group $P2_1/c$ with two molecules in the asymmetric unit ($Z = 8$). The two most and similarly stabilized molecular motifs I (−12.9 kcal mol$^{-1}$) and II (−12.4 kcal mol$^{-1}$) were observed to consist of strong N–H···O–C hydrogen bonds along with short Csp$^3$–F···C=O (3.090 Å, 141°; 3.011 Å, 141° respectively, Table S3, ESI$^\ddagger$) and π···π interactions. These motifs would appear to be involved in the formation of a $\ldots$1212$\ldots$ type molecular chain along the crystallographic a-axis. Such chains are recognized to interlink with the exploitation of next four stabilized molecular motifs III, IV, V and VI. In the similarly stabilized motifs III (−4.6 kcal mol$^{-1}$) and IV (−4.4 kcal mol$^{-1}$), there were short and directional C–H···O–C (2.33 Å, 149°; 2.23 Å, 168°) hydrogen bonds recognized with the contribution from electrostatic (Coulombic + polarization) being significant (46% and 54% respectively). Further, motifs V (involving a bifurcated weak C–H···F–Csp$^3$ and C–H···π hydrogen bonds) and VI (involving a bifurcated weak C–H···F–Csp$^3$ hydrogen bond) were observed to provide similar stabilization (−3.5 and −3.2 kcal mol$^{-1}$ respectively) to the crystal packing. Moreover, intermolecular interactions involving organic fluoride of type C–H···F, C–F···F–C were noticed to stabilize the crystal packing in 1T2F and participate in the generation of different supramolecular motifs VII to XII (Table S3, ESI$^\ddagger$) in the crystal packing [Fig. 10(b) and (c)]. The motif VII (−2.8 kcal mol$^{-1}$) was observed to be composed of dimeric weak C–H···F–Csp$^3$ hydrogen bonds along with dimeric Csp$^3$–F···F–Csp$^3$ interactions while a dimeric weak C–H···F–Csp$^3$ hydrogen bond, interacting side wise, was recognized in the equally stabilized motif VIII. Further, a bifurcated weak C–H···F–Csp$^3$ hydrogen bond was observed in motif IX (−1.8 kcal mol$^{-1}$) whereas in the similarly stabilized motif X (−1.7 kcal mol$^{-1}$), a short C–H···F–Csp$^2$ hydrogen bond (2.48 Å, 137°) was recognized. In the last two weakly stabilized motifs XI (−1.1 kcal mol$^{-1}$) and XII (−0.6 kcal mol$^{-1}$), a weak C–H···C–Csp$^3$ hydrogen bond and weak type I Csp$^3$–F···F–Csp$^3$ interactions were observed respectively. All the molecular pairs consisting of weak C–H···F and C–F···F–C interactions were analyzed by the theory of QTAIM and the topological parameters were obtained (Table S4, ESI$^\ddagger$). There was presence of (3, −1) BCPs noticed for these interactions along with other related contacts in the respective motifs [Fig. 10(d)].

### (11) 3-Fluoro-N-(3-(trifluoromethyl)phenyl)benzamide (2T2F)

Compound 2T2F crystallizes in the non-centrosymmetric monoclinic space group $Cc$ with four molecules in the unit cell.
A strong N–H···O=C hydrogen bond along with π···π interactions (motif I, −11.3 kcal mol\(^{-1}\)) steer the molecules along [110] in the formation of a molecular chain. Such chains are interlinked with the involvement of next two stabilized motifs II (−5.5 kcal mol\(^{-1}\)) and III (−4.8 kcal mol\(^{-1}\)) in the crystal packing. The motif II was recognized to involve weak π···π interactions with substantial contribution from dispersion energy towards the total stabilization whereas a weak C–H···O=C along with two short C–H···F–C\(_{sp2}\)/C\(_{sp3}\) (2.45 Å, 133°; 2.53 Å, 136° respectively) hydrogen bonds were observed in motif III. Further the molecular ladder formed via the motif III was observed to be connected by the utilization of motifs IV, V and VI in the crystal packing [Fig. 11(b) and (c)]. The motif IV (−2.2 kcal mol\(^{-1}\)) consists of bifurcated weak C–H···F–C\(_{sp3}\) hydrogen bonds while a short C–H···F–C\(_{sp2}\) (2.50 Å, 146°) hydrogen bond was observed in motif V (−1.5 kcal mol\(^{-1}\)). Moreover, a weak type I C\(_{sp2}\)–F···F–C\(_{sp3}\) interaction (motif VI, −1.2 kcal mol\(^{-1}\)) was also recognized to stabilize the packing of the molecules in 2T2F (Table S3, ESI†). The presence of (3, −1) BCPs were observed for the weak C–H···F and C–F···F–C interactions in the respective motifs [Fig. 11(d)].

(12) 4-Fluoro-N-(2-(trifluoromethyl)phenyl)benzamide (1T3F)

Compound 1T3F crystallizes in the centrosymmetric monoclinic space group P2\(_{1}\)/n with two molecules in the asymmetric unit (Z = 8). The two most stabilized motifs I (−12.8 kcal mol\(^{-1}\)) and II (−12.7 kcal mol\(^{-1}\)), involving similar interactions (strong N–H···O=C hydrogen bonds along with π···π interactions), were observed in the formation of a molecular chain of molecules 1 and 2 in the asymmetric unit, respectively, utilizing π-glide along the b-axis [Fig. 12(a)]. Such chains are interconnected alternatively with the utilizations of motifs III, IV, V and VII. The motifs III and IV provide similar stabilization (−4.4 kcal mol\(^{-1}\) and −4.1 kcal mol\(^{-1}\) respectively) and both are involved in the formation of highly short and directional C–H···O=C (2.29 Å, 152°; 2.22 Å, 167° respectively, Table S3, ESI†) hydrogen bonds. A short C–H···F–C\(_{sp2}\) (2.56 Å, 132°) along with a weak C–H···π hydrogen bond were noticed to connect the molecules in motif V whereas a near type II along with a near type I C\(_{sp2}\)–F···F–C\(_{sp3}\) interactions (2.983 Å, 110°, 165°; 3.128 Å, 90°, 117°) were recognized to stabilize (I.E. being −2.7 kcal mol\(^{-1}\)) the crystal packing, existing as motif VII (Table S2, ESI†). Further, the packing of molecules in 1T3F stabilized the formation of two dimeric motifs VI (−3.3 kcal mol\(^{-1}\)) and VIII (−2.1 kcal mol\(^{-1}\)) [Fig. 12(b)]. The motif VI involved two C–H···F–C\(_{sp3}\) hydrogen bonds along with weak C\(_{sp3}\)–F···F–C\(_{sp3}\) interactions (Table S3, ESI†). And the dimeric motif VIII was observed to possess short C–H···F–C\(_{sp2}\) (2.48 Å, 131°) hydrogen bonds in the crystal packing in 1T3F. Moreover, there were three equally stabilized (1.5 kcal mol\(^{-1}\)) molecular motifs IX, X and XI observed in the crystal packing and all were noticed to involve weak C–H···F–C hydrogen bonds (Table S2, ESI†). Further a motif [XII, −1.3 kcal mol\(^{-1}\)], consisting of weak C\(_{sp3}\)–F···F–C\(_{sp3}\) interactions and connecting molecules ‘1’ of
Fig. 12  (a) Packing of molecules in 1T3F via the network of strong N–H⋯O=C, weak C–H⋯O, C–H⋯π, and C–H⋯F–C\textsubscript{sp}–\textsubscript{sp}\textsubscript{2} hydrogen bonds along with C\textsubscript{sp}–F⋯C=O and C\textsubscript{sp}–F⋯F–C\textsubscript{sp}\textsubscript{2} interactions. C-atoms in purple are shown for the second molecule in the asymmetric unit. (b) Formation of the molecular layer down the ac plane with the utilization of weak C–H⋯O=C, C–H⋯π, C–H⋯F–C\textsubscript{sp}–\textsubscript{sp}\textsubscript{2} hydrogen bonds along with C\textsubscript{sp}–F⋯F–C\textsubscript{sp}\textsubscript{2} interactions in 1T3F. (c) Part of crystal packing in 1T3F showing the presence of weak C–H⋯F–C\textsubscript{sp}–\textsubscript{sp}\textsubscript{2} hydrogen bonds along with C⋯F–C\textsubscript{sp}\textsubscript{2} interactions. (d) Selected molecular motifs (Table S4, ESI) in 1T3F showing different intermolecular interactions. Only the interacting part of the motif is shown in the case of V–XII.
the asymmetric unit, was observed to stabilize the crystal packing in 3T3F [Fig. 12(c)]. The weak C–H⋯F–C hydrogen bonds and C–F⋯F–C interactions present in the motifs V to XII in 3T3F were characterized by the theory of AIM. The presence of (3, –1) BCPs was observed for these interactions [Fig. 12(d)].

(13) 4-Fluoro-N-(4-(trifluoromethyl)phenyl)benzamide (3T3F)
Compound 3T3F crystallizes in the centrosymmetric monoclinic space group $P2_1/c$ with $Z = 4$. A strong N–H⋯O=C hydro bond, supported by weak C–H⋯O=C and C–H⋯π hydrogen bonds (motif I, 11.6 kcal mol$^{-1}$), was observed in the formation of a molecular chain utilizing c-glide perpendicular to the $b$-axis in 3T3F [Fig. 13(a) and (b)]. Such chains are interconnected via the motifs II, III, V and VIII. The weak π⋯π interactions were observed to connect molecules in the dimeric motifs II ($-5.9$ kcal mol$^{-1}$) and III ($-4.6$ kcal mol$^{-1}$). In the motif V ($-2.6$ kcal mol$^{-1}$), weak C–H⋯F–C(sp$^2$) hydrogen bonds along with C–H⋯C=O interactions were recognized whereas a short C–H⋯F–C(sp$^3$) hydrogen bond was observed in motif VIII ($-1.4$ kcal mol$^{-1}$). The packing of the molecules in 3T3F involved the formation of a herringbone pattern down the crystallographic $ab$ plane with the utilization of motifs IV [$-2.7$ kcal mol$^{-1}$; involving short C–H⋯π hydrogen bonds (2.79 Å, 133°; Table S2, ESI†)], V and VIII [Fig. 13(c)]. Moreover, a bifurcated C–H⋯F–C(sp$^2$) hydrogen bond (motif VII, $-2.2$ kcal mol$^{-1}$), utilizing c-glide, was noticed in the formation of a molecular chain [Fig. 13(d)]. The chain was interlinked via the presence of motifs VI, VIII and IX. The motif VI ($-2.6$ kcal mol$^{-1}$) was found to involve the weak C–H⋯F–C(sp$^3$) hydrogen bond in the formation of a molecular chain utilizing c-glide [Fig. 13(d)]. Dimeric and weakly stabilized (−0.4 kcal mol$^{-1}$) short C(sp$^3$)–F⋯F–C(sp$^3$) interactions were identified in the motif IX. The molecular motifs V–VIII and IX, consisting of weak interactions involving fluorine, were studied topologically using the approach of QTAIM. Bond critical points at the bond path for these interactions were observed [Fig. 13(e)].

Therefore, the detailed analysis of all crystal structures revealed that the C(sp$^3$)/(sp$^3$)–F group was observed in the formation of different robust structural motifs in the presence of a strong N–H⋯O=C hydrogen bond and other related weak interactions like C–H⋯O=C, C–H⋯π, and π⋯π. Moreover, in many cases, different supramolecular motifs (Table S3, ESI†) by C(sp$^3$)/(sp$^3$)–F from both sides of the molecules can combine co-operatively in the formation of bigger structural motifs in the crystal structures.

**Insights from atoms in molecules calculations**
It is of interest to conduct topological characterization of H⋯F and F⋯F interactions, observed in this class of compounds (including the previously reported crystal structures$^{37,38–40}$) and the analysis of the nature of these interactions along with the relationship of different topological parameters at BCP with bond path length. For this purpose, the selected dimers involving H⋯F or F⋯F interactions were identified and QTAIM calculations have been performed at their crystal geometry in accordance with the procedure reported in our earlier work.$^{41}$ The results of

![Fig. 13](image-url) (a) Packing of molecules in 3T3F via the network of strong N–H⋯O=C, weak C–H⋯O=C, C–H⋯π, C–H⋯F–C hydrogen bonds along with π⋯π interactions. (b) Depiction of a molecular chain via the motif I in 3T3F. (c) Formation of a layer down the $ab$ plane, utilizing weak C–H⋯F–C hydrogen bonds and C–H⋯C=O interactions in 3T3F. (d) Formation of a weak bifurcated C–H⋯F–C hydrogen bonds along with C(sp$^3$)–F⋯F–C(sp$^3$) interactions down the $bc$ plane in 3T3F. (e) Selected molecular motifs (Table S4, ESI†) in 3T3F, showing different intermolecular interactions. Only the interacting part of the motif is shown in the case of V–VII and IX.
the calculations are presented in Tables S4 and S5 of Section S4 in the ESI. Topological parameters of the selected C–H···F and C–F···F–C interactions are given in Table S4b (ESI†).

It is to be noted here that some of the important criteria for an interaction to be called a hydrogen bond or a closed shell type are:69,70 (i) ρ value at BCP lies within the range [0.013, 0.270] e Å⁻³, (ii) positive value of the Laplacian of the electron density [$\nabla^2\rho > 0$] indicates closed shell interactions, (iii) the range of Laplacian values [0.578 < $\nabla^2\rho$ (e Å⁻³) < 3.350] indicates the presence of a “H-bond” and (iv) the value of $|V_b|/G_b$ were also observed to be less than one (criteria for hydrogen bonds71,72) for the entire range of the bond path.

Further, it was of interest to study the role of hybridization of the C-atoms to which fluorine is attached in the C–H···F interactions. Hence the variation of dissociation energy (D.E.) (kcal mol⁻¹) and electron density (e Å⁻³) at the BCP and with H···F bond path length (Å) for C–H···F–C(sp²) hydrogen bonds in preference to C(sp²)–H···F–C(sp³) hydrogen bonds in the crystal with the difference in energies of stabilization involving fluorine atoms attached to sp² and sp³ carbon is not significant in the molecular crystal.

Analysis of H···F bonding interactions

H···F interactions were observed to lie in the range of 2.2–3.0 Å for all structures in the current work. As observed earlier,41 the dependency of electron density ($\rho_b$) shows exponential dependence with the bond path length ($r_{\text{B}}$) [Fig. 14(a)] with the values in the range of 0.085 > $\rho_b$ > 0.015 e Å⁻³. Hence these fulfill the criterion for the interactions to be called a hydrogen bond. The dissociation energy of these interactions [vary exponentially with $r_{\text{B}}$, Fig. 14(b)] were observed between ~3.0 to ~0.4 kcal mol⁻¹. The value of Laplacian observed to be positive [$|\nabla^2\rho| > 0$], Fig. 14(c) for the entire bond path length ($r_{\text{B}}$) suggesting the closed shell nature of these H···F interactions. It is to be noted that for a short C–H···F bond path length ($r_{\text{B}}$) at less than the sum of van der Waals radii [H and F, 2.67 Å], the values of the Laplacian are in accordance with the Koch and Popelier criteria for the existence of hydrogen bonds.74 Moreover, the values of $|V_b|/G_b$ were also observed to be less than one (criteria for hydrogen bonds71,72) for the entire range of the bond path [Fig. 14(d)].

Analysis of F···F bonding interactions

There are numerous C–F···F–C interactions observed in the crystal packing of this series of compounds (Tables S4 and S5, ESI†). Hence, it was also of interest to do the topological characterization of F···F interactions. The nature and role of C–F···F–C
interactions were recently studied both experimentally and theoretically by many researchers.\textsuperscript{75,76} The previous report by the QTAIM analysis of intramolecular C–F⋯C interactions on a rigid isolated molecular system showed that these are closed shell interactions and can impart as much as 14 kcal mol\(^{-1}\) of local stabilization.\textsuperscript{77} In the present work, QTAIM analysis of intermolecular C–F⋯C interactions has been performed and the results show the exponential dependence of electron density at the BCP (\(\rho_{\text{BCP}}\)), dissociation energy (D.E.) and Laplacian (\(\nabla^2 \rho\)) of the electron density at the BCP with the F⋯F bond path length \(r_{ij}\) (Fig. 16). Values of electron density and dissociation energy (local stabilization) were observed between \(\sim 0.060 \leq \rho_{\text{BCP}} (e \text{ Å}^{-3}) \leq \sim 0.010\) and \(\sim 2.8 < \text{D.E. (kcal mol}^{-1}) < \sim 0.5\) for the \(\sim 2.8 > r_{ij} (\text{Å}) > 3.45\). These values are slightly less or comparable with weak C–H⋯F interactions in the present work and observed to be similar to the previously observed values.\textsuperscript{67,77–80} Furthermore, for the entire range of the F⋯F bond path length, Laplacian values (\(\nabla^2 \rho\)) > 1 and |\(V_{\text{BCP}}/G_{\text{BCP}}\) | < 1 were observed. Hence it can be concluded that the intermolecular F⋯F interactions in the present work are of closed shell in nature. Furthermore, the nature

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**Fig. 15** Comparison of variation of (a) dissociation energy (D.E) (kcal mol\(^{-1}\)) and (b) electron density (e Å\(^{-3}\)) at the BCP and with the H⋯F bond path length (Å) for C–H⋯F–C(sp\(^2\)) [red curve] and C–H⋯F–C(sp\(^3\)) [blue curve] [total 153 data points (98 for the red curve and 55 for the blue curve)].

**Fig. 16** Variation of (a) electron density (e Å\(^{-3}\)), (b) dissociation energy (D.E) (kcal mol\(^{-1}\)) with the F⋯F bond path length (Å) [42 data points], (c) Laplacian (\(\nabla^2 \rho\)) at the BCP and (d) |\(V_{\text{BCP}}/G_{\text{BCP}}\) | with the F⋯F bond path length (Å).
of C(sp\textsuperscript{3})/C(sp\textsuperscript{2})–F/C(sp\textsuperscript{3})/C(sp\textsuperscript{2}) interactions from current and previous studies along with reports from experimental charge density analysis (Table 1) have been compared in Fig. 17. The results show the small differences in the \( \rho_b \) (e Å\textsuperscript{-3}) at the BCP for different types of C–F/C(sp\textsuperscript{3})/C(sp\textsuperscript{2})–F interactions involving fluorine atoms attached to sp\textsuperscript{2} and sp\textsuperscript{3} carbon atoms. The shorter C–F/C(sp\textsuperscript{3}) bonds in the molecule in the crystal. It is also of interest to notice variations in \( \rho_b \), dissociation energy (D.E.) and Laplacian (\( \nabla^2 \rho \)) of the electron density at the BCP for a given value of \( r_{ij} \). Different values of electron density at the BCP for C(sp\textsuperscript{3})/C(sp\textsuperscript{2})–F/C(sp\textsuperscript{3})/C(sp\textsuperscript{2}) interactions for the nearly same \( r_{ij} \) (Å) of the F–F bond path (near to the sum of van der Waals radii of the F-atom, 2.94 Å) in the case of 3, 5, 6, 7, 8, 10 have been observed [Fig. 18]. This feature may be explained due to the cooperative interplay amongst the different possible intermolecular bond paths present in the motifs 3, 5, 6, 7 and 8 whereas in the case of 10 (having the least value of \( \rho_b \) among these), only one C(sp\textsuperscript{3})–F/C(sp\textsuperscript{2}) is present.

Table 1: Topological parameters from previous reports on C–F...F–C interactions by charge density analysis of high resolution X-ray data

| Nature of interactions | \( R_{ij} \) (Å) | \( \rho \) (e Å\textsuperscript{-3}) | \( \nabla^2 \rho \) (e Å\textsuperscript{3}) | Ref. |
|------------------------|-----------------|-----------------|-----------------|-----|
| C(sp\textsuperscript{3})–F–C(sp\textsuperscript{3}); type I | 2.8091 | 0.049 | 1.030 | 78 |
| C(sp\textsuperscript{3})–F–C(sp\textsuperscript{3}); type II | 2.8187 | 0.040 | 0.820 | 79 |
| C(sp\textsuperscript{3})–F–C(sp\textsuperscript{3}); type II | 2.8240 | 0.040 | 0.900 | 80 |
| C(sp\textsuperscript{3})–F–C(sp\textsuperscript{3}); type II | 2.9255 | 0.030 | 0.633 | 67 |

Fig. 17 Comparison of the variation of the electron density (e Å\textsuperscript{-3}) at the BCP and with the F–F bond path length (Å) for C(sp\textsuperscript{3})/C(sp\textsuperscript{2})–F/C(sp\textsuperscript{3})/C(sp\textsuperscript{2}) interactions from current and previous studies [total 64 data points].

Fig. 18 Showing first ten more stabilized motifs in Fig. 17, having C(sp\textsuperscript{3})/C(sp\textsuperscript{2})–F/C(sp\textsuperscript{3})/C(sp\textsuperscript{2}) interactions near or below the sum of van der Waals radii of two F-atoms, 2.94 Å.

Conclusion

Following the analysis of the 15 crystal structures (including one hydrate) from the 18 newly synthesized compounds along with the inputs from previously reported structures, the role of organic fluorine in the crystal packing has been analyzed in the presence of strong hydrogen bonds. The formation of many “reoccurring” structural motifs by the C(sp\textsuperscript{2})–F and CF\textsubscript{3} group has been identified and investigated in terms of their nature, energetics and topological properties, which were quantified by the PIXEL method and the QTAIM approach. It was observed that the highest stabilized molecular motifs primarily consist of C(sp\textsuperscript{3})–H...F–C(sp\textsuperscript{3}) hydrogen bonds in preference to C(sp\textsuperscript{3})–H...F–C(sp\textsuperscript{3}) H bonds in the crystal. Moreover, the formation of hydrogen bonds by the C(sp\textsuperscript{3})/C(sp\textsuperscript{3})–F group was observed to be present over the entire distance range between 2.2 and 2.7 Å (from the QTAIM approach), albeit the difference in energies of stabilization involving fluorine atoms attached to sp\textsuperscript{2} and sp\textsuperscript{3} carbon atoms.
sp³ and sp³ carbon is not of significance in molecular crystals. Following the analysis of C(sp²)/(sp³)-F···F-C(sp²)/(sp³) interactions from the QTAIM approach, it was observed that these fulfill the criteria of these being of the closed shell type for the entire F···F bond path length and provide local stabilization (indicates the formation of bonds) similar to the case of weak hydrogen bonds in crystals. For future study, it would be of interest to extend this study to donor atoms in different hybridization environments with the F-C(sp²)/(sp³) group in different chemical environments. Furthermore, it is also of interest to investigate the effect of increasing fluorination on the molecule and the impact on the stabilization energies for the different supramolecular motifs involving organic fluorine present in the crystal.

Acknowledgements

PP thanks UGC-India for research scholarship. D. C. thanks IISER Bhopal for research facilities and infrastructure and DST-SERB for research funding.

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