Crystal structure, Hirshfeld surface analysis and contact enrichment ratios of 5,5-dimethyl-2-(2,4,6-tris(trifluoromethyl)phenyl)-1,3,2-dioxaborinane

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ABSTRACT
The title compound C_{14}H_{12}BF_{9}O_{2} (1) was obtained as the sole product during a failed attempt to make a new organoboron compound. Characterization of the title compound by NMR (1H, 13C, 19F) spectroscopy and single crystal X-ray diffraction confirmed the formation of 1. Compound 1 crystallizes in the triclinic space group P-1, with a = 8.275(5) Å, b = 8.611(5) Å, c = 10.910(5) Å, α = 89.634(5)°, β = 89.637(5)°, γ = 87.403(5)°, V = 776.6(7) Å³, and Z = 2. The intermolecular interactions in 1 were analyzed using the Hirshfeld surface method including 2D fingerprint plots and enrichment ratios (E), which shows that the most favorable intermolecular contacts are the C_p/C/H–C and C–H–F–C interactions. The interaction energies between molecular pairs revealed the importance of these weak non-covalent interactions in stabilizing the molecular structure of 1. The title compound was also studied by DFT calculations and UV-Vis spectroscopy.

KEYWORDS
Fluorinated boronate esters; solid state structure; Hirshfeld surface analysis; contact enrichment ratios; DFT calculations

1. Introduction
Non-covalent interactions involving halogens play an important role in medicinal chemistry [1–6], crystal engineering [7–12], supramolecular chemistry [8, 13, 14], functional materials [15–18], and catalysis [19]; among these are fluorine-based interactions, where fluorine substituents e.g. –CF_{3} can form different weak intermolecular C–F⋯F–C, C⋯F–C and C–H⋯F–C interactions that can stabilize the crystal structure [20]. Unlike other halogens, the dominant interactions in organic fluorine compounds are C–H⋯F interactions rather than C–F⋯F–C contacts. These non-covalent interactions are most widely discussed in the context of the σ-hole model [21], where electrostatic attraction takes place between a partially negative charge on a nucleophile and a partially positive charge on the hydrogen atom of the second halogen atom known as σ-hole. Generally, fluorine can’t form σ-holes due to its low polarizability, therefore C–F⋯F–C contacts are not very common. The C–H⋯F–C

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interactions can play an important role in stabilizing crystal structures [22–24] and has been classified as a weak hydrogen bond according to the latest IUPAC definition [25]. On the other hand, the C···F–C interactions has been a debated subject [26–28]. Nonetheless, it has been reported that, when the aromatic ring is substituted with electron-withdrawing groups e.g. CF₃, the F–C groups tend to point toward the center of the electron-poor rings [29].

Herein, we report on the solid-state structure of a new fluorinated arylboronic ester, where the involved non-covalent interactions are studied using Hirshfeld surface analysis. In addition, the new compound was analyzed using different spectroscopic techniques and DFT calculations.

2. Experimental section

2.1. General considerations

All air-sensitive experiments were carried out under an atmosphere of dry nitrogen using standard Schlenk techniques. 1,3,5-Tris(trifluoromethyl)benzene, BCl₃, n-BuLi, and 2,2-dimethyl-1,3-propanediol were purchased from Sigma-Aldrich and used without further purification. Solvents were purchased from Sigma-Aldrich and were dried using activated alumina columns. Thin-layer chromatography (TLC) and flash chromatography were performed on silica gel. ¹H-, ¹³C-, ¹⁹F-, ¹¹B- NMR spectra were recorded on Bruker Avance III-HD 500 MHz spectrometer (¹H: 500.10 MHz, ¹³C: 125.7 MHz, ¹⁹F: 470.6 MHz, ¹¹B: 160.5 MHz) spectrometer at room temperature. They are reported with chemical shifts in δ (ppm) units downfield from tetramethylsilane with the solvent as the reference signal (chloroform-d₅: ¹H at 7.26 ppm) or by the ²H solvent lock signal [30]. UV-Vis spectrum was recorded on a LABOMED UVD-3000 spectrophotometer.

2.2. Synthesis of 1

The title compound 1 was obtained as the sole product of a sequence of reactions, which were designed to make a new organoboron compound. The targeted compound decomposed and was not further investigated Scheme 1, instead compound 1 was the sole product.

Reaction steps that led to the formation of the title compound: A solution of n-BuLi (1.6 M in hexane, 5.6 mL, 9.0 mmol) was added slowly to a dry Et₂O (30 mL) solution of 1,3,5-Tris(trifluoromethyl)-benzene (2.5 g, 1.7 mL, 8.8 mmol) at −78°C and mixed for 3 h at −78°C and left to mix over night at room temperature. The resulting orange solution was added via a cannula to a solution of BCl₃ (1.0 M in heptane, 3.0 mL, 3.0 mmol) at −78°C and stirred at the same temperature for 1 h and for another 2 h at room temperature. The resulting yellow suspension was filtered over celite under nitrogen and then a solution of lithiated 2-(4-bromophenyl)-5,5-dimethyl-1,3-dioxane (0.8 g, 3.0 mmol) in dry Et₂O (50 mL) was added slowly at −78°C and mixed for 3 h at −78°C and left to mix over night at room temperature.

Solvents were evaporated under reduced pressure and the resulting residue was redissolved in CHCl₃ then washed with H₂O and dried over anhydrous Na₂SO₄. Then CHCl₃ was evaporated under reduced pressure and the crude product was sonicated
hexanes, filtered, and kept in the freezer at −18°C to give (0.1) g of the title compound 1 as colorless needle-shaped crystals (Yield: 5.0% based on BCl3)

1H NMR (CDCl3, δ, ppm): 8.05 (2H, s), 3.79 (4H, s), 1.10 (6H, s). 13C NMR (CDCl3, δ, ppm): 135.12 (q, 2JC- F = 32.7 Hz, ortho-C6H2), 131.83 (q, 2JC- F = 35.2 Hz, para-C6H2), 125.50 (meta-C6H2), 123.42 (q, 1JC- F = 274.2 Hz, ortho-CF3), 122.69 (q, 1JC- F = 272.9 Hz, para-CF3), ipso-C6H2 not observed, 72.88 (s, aliphatic CH2), 31.90 (s, aliphatic q C), 22.37 (s, aliphatic CH3). 19F NMR (CDCl3, δ, ppm): −60.03 (6 F, s, ortho), −63.31 (3 F, s, para). 11B NMR (CDCl3, δ, ppm): 27.38

2.3. Theoretical calculations

All computations were performed using ORCA code version 4.2.0 [31, 32]. Full geometry optimizations at the DFT level of compound 1 were carried out using the perturbatively corrected double-hybrid functional B2PLYP [33] and the Ahlrichs def2-TZVPP [34] basis set, which is a triple-zeta basis with “enhanced” polarization functions. The effect of the dichloromethane solvent was considered in the geometry optimization for 1 using the conductor-like polarizable continuum model (CPCM) [35]. The lowest 20 singlet-singlet vertical electronic excitations based on B2PLYP optimized geometries were computed using the Time-Dependent Density Functional Theory (TD-DFT) formalism [36] in dichloromethane applying the conductor-like polarizable continuum model (CPCM) using the same level of theory as that used for the geometry optimizations, i.e., [B2PLYP/def2-TZVPP/CPCM(DCM)]. Gabedit program [37] was used to compute and draw the isosurface densities of the molecular orbitals. CrystalExplorer 17.5 package [38] was used to compute and visualize Hirshfeld surfaces and their associated 2-D fingerprint plots, enrichment ratios (E), and interaction energies (at the CEB3LYP/6-13G(d,p) energy level).
2.4. X-ray crystallographic analysis

Colorless needle-shaped crystals of 1 were obtained by cooling a hexanes solution containing the compound at $-18^\circ$C. Crystals were mounted on a glass fiber and data collection was done on a Rigaku Xcalibur Ruby Gemini Ultra single-crystal X-ray diffractometer, with graphite-monochromated MoK$_\alpha$ radiation. Data were processed using the CrysAlisPro software package and corrected for absorption effects. The molecular structures were solved by direct methods using SHELXS-18 [39] and refined by full-matrix least-squares procedures on $F^2$ using SHELXL-18 [40, 41]. The dataset of the chosen crystal contained two major domains that were integrated independently and merged into a hklf5 file (BASF = 0.49). All non-hydrogen atoms were refined anisotropically and a riding model was employed in the treatment of the hydrogen atom positions, except otherwise noted. Crystallographic data of 1 are summarized in Table 1. The reported crystallographic data for 1 have been deposited with the Cambridge Crystallographic Data Center (Deposition No. CCDC 2120318. The data can be obtained free of charge via https://www.ccdc.cam.ac.uk/structures/, or by emailing: data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Center, 12 Union Road, Cambridge CB21EZ, UK; fax: +44 1223 336033.

| Table 1. Crystallographic data and refinement details for 1. |
|------------------------------------------------------------|
| Empirical formula                                          | C$_{14}$H$_{12}$BF$_9$O$_2$ |
| Formula weight (g/mol)                                     | 394.05                        |
| Temperature (K)                                            | 99.9(2)                        |
| Wavelength (Å)                                             | 0.71073                      |
| Crystal system                                             | Triclinic                     |
| Space group                                                | P-1                           |
| Unit cell dimensions                                       |                               |
| $a$ (Å)                                                    | 8.275(5)                      |
| $b$ (Å)                                                    | 8.611(5)                      |
| $c$ (Å)                                                    | 10.910(5)                     |
| $\alpha$ (°)                                               | 89.634(5)                     |
| $\beta$ (°)                                                | 89.637(5)                     |
| $\gamma$ (°)                                              | 87.403(5)                     |
| Volume (Å$^3$)                                             | 776.6(7)                      |
| $Z$                                                        | 2                             |
| Density (calculate) Mg/m$^3$                               | 1.685                         |
| Absorption coefficient mm$^{-1}$                           | 0.181                         |
| $F(000)$                                                   | 396                           |
| Crystal size mm$^3$                                        | 0.4 x 0.4 x 0.4               |
| $\Theta$ range (°)                                        | 3.340 to 25.997               |
| Index ranges                                              |                               |
| $-10 < h < 109$, $-10 < k < 10$, $-13 < l < 13$            |                               |
| Reflections collected                                      | 5311                          |
| Independent reflections                                    | $R_{int} = 0.0327$            |
| Data Completeness                                          | 99.2%                         |
| Data/ restraints/ parameters                               | 5311 / 0 / 264                |
| Goodness-of-fit on $F^2$                                   | 0.956                         |
| Final $R$ indices ($I > 2\sigma(I)$)                       | $R_1 = 0.0412$, $wR_2 = 0.0777$ |
| $R$ indices (all data)                                     | $R_1 = 0.0546$, $wR_2 = 0.1101$ |
| Largest diff. peak and hole (e.Å$^{-3}$)                   | 0.283 and $-0.251$            |

$R_1 = \Sigma |F_o| - |F_c|/\Sigma |F_o|$, $wR_2 = \{\Sigma w(F_o^2 - F_c^2)^2\}/\Sigma [w(F_o^2)^2])^{1/2}$. 
3. Results and discussion

Scheme 1 shows the synthetic steps that lead to the formation of the title compound while Scheme 2 shows the proposed reaction that led to the formation of the title compound 1. We expect that the acetal used in this reaction may have contained some diol, which reacted with dichloroborane to form compound 1. It’s worth mentioning that all steps were done in situ, that is no attempts were made to isolate intermediate products.

The title compound is stable at ambient conditions in the solid state and in solution. Also, it is soluble in polar organic solvents like tetrahydrofuran, chloroform, and dichloromethane, but hardly soluble in hexanes.

Compound 1 was identified by single crystal X-ray crystallography, and NMR (1H, 13C{1H}, 19F, and 11B) spectroscopies in CDCl3. The 1H NMR spectra of 1, Fig. S1, is consistent with the molecular structure, showing resonances with the expected patterns for the CH3, CH2 and CH moieties. The two CH protons of the phenyl ring are observed at 8.05 ppm as a singlet, while the aliphatic CH2 protons appear as a singlet at 3.79 ppm. A singlet at 1.10 ppm is found for the CH3 protons. The most pronounced signals in the 13C NMR spectrum, Fig. S2, beside the aliphatic carbons, are the two quartets resulting from the 2JC-F coupling of the ortho- and para-C6H2 are at 135.1 and 131.8 ppm, respectively; in addition to the two quartets resulting from the 1JC-F coupling of the ortho- and para-CF3 are at 123.4 and 122.7 ppm, respectively. The 19F NMR spectroscopy (Fig. S3) shows the characteristic signals of the trifluoromethyl aryl ligand: a resonance peak at around −60.04 ppm for the ortho-CF3 groups, and a singlet at about −63.32 ppm corresponding to the para-CF3 groups [42–44]. The 11B NMR spectrum, Fig. S4, of 1 displays a singlet at 27.4 ppm, which appears in the region of literature reported C–B(OR)2 connection pattern [44].

The crystallographic and refinement data of 1 are summarized in Table 1 and the molecular structure of 1 is shown in Fig. 1. Selected bond distances (Å), bond angles (°), and torsion angles (°) are given in the caption of Fig. 1. Compound 1 crystallizes in the triclinic space group P-1 with one molecule in the asymmetric unit. Rotational disorder was found for one of the ortho-CF3 groups, which is usually observed in compounds containing this group [45, 46, 47, 48, 49]. The six-membered boronate ester ring adopts a half chair type conformation with the CMe2 entity pointing out of the BO2C2 plane by 45° (Fig. 1). The BO2 motif and the benzene ring are rotated by 86.7(2)° against each other to avoid repulsive interaction with the CF3 substituents on both ortho positions, which in turn provide kinetic stability by effectively shielding the empty p-orbital on boron against attack by nucleophiles [50]. The B-Cph bond length of 1.598(3) Å is significantly longer than the B–O bonds (1.350(3) and 1.347(3) Å), due
to the partial orbital overlap. Together with C1–B1–O angles of 117.61(17) and 117.59(16)° they are in accordance with those reported for similar compounds [44, 51–53].

The solid-state crystal packing of 1 is stabilized by lone pair F···π and F···H–C intermolecular interactions that form a band-type structure along the crystallographic a-axis. The former exists between the ortho C7-labeled CF3 entity and the arene (Fig. 2). The C9-labeled pendant instead, is not involved in intermolecular interactions. The shortest
F⋯π contact is F2⋯C5 (at 3.085(5) Å), which is less than the sum of the corresponding vdW radii \((C = 1.70 \text{ Å}, F = 1.47 \text{ Å}, \Sigma_{C,F} = 3.17 \text{ Å})\). The disordered part the CF₃ group (34\% occupancy) is rotated by 27°, resulting in a F3′⋯C5 distance of 3.130(17) Å. Both fluorine atoms are positioned almost perpendicularly above the C5 atom, represented by the corresponding F⋯C5–H5 angles of 100°. The interactions result in a dimeric structure, of which the major component is shown in Fig. 2 (green). The shortest distance between the fluorine atoms and the centroids of the phenyl rings is 3.1353(19) Å between F2 and Cg2 in an angle of 143°, indicating a lone pair F⋯π interaction toward the centroid [54].

Weaker F⋯C interactions of 3.161(3) Å (C10) and 3.134(3) Å (C12) are observed between the para CF₃ substituent and both CH₂ entities of the boronic ester fragment (Fig. 2, blue). Thus, each molecule is stabilized by four contacts toward an adjacent molecule of 1 positioned along the crystallographic \(a\)-axis, resulting in a band-type structure. Therein, arene and boronate entities, as well as the ortho-CF₃ groups appear with alternating orientations, with the C9-labeled entity consequently facing the outside, while the C7-based group directs inwards.

The geometrical parameters of 1, i.e. bond angles and bond lengths, determined using DFT calculations, are in good agreement with the experimental values (Table S1). For example, the calculated C1–B1 bond length is 1.595 Å while the X-ray value is 1.598(3) Å. DFT calculations at the triple zeta double hybrid level shows that the electron density of the HOMO, LUMO, HOMO –1, and LUMO +1 is mainly delocalized over the benzene ring. The isosurface density of the frontier molecular orbitals of 1 are shown in Fig. S6. A DFT analysis of the calculated excited states of 1 reveals that the UV-Vis absorption band, with \(\lambda_{\text{max}}\) value found at 261 nm (see Fig. S5), is assigned to a HOMO → LUMO, HOMO –1 → LUMO, HOMO → LUMO +1, and HOMO –1 → LUMO +1, all of which corresponding to a typical π–π* transition.

The Hirshfeld surfaces and their associated 2D fingerprint plots were generated with the CrystalExplorer17.5 program using the crystallographic information file (.cif) and were analyzed to identify the important intermolecular interactions and to better understand the overall crystal packing of 1. The Hirshfeld surfaces were mapped over the normalized contact distance \((d_{\text{norm}})\), which is defined in terms of \(d_e\), \(d_i\) and the vdW radii of the atoms, where \(d_e\) and \(d_i\) are the distances from a point on the surface to the nearest atom outside (external) and inside (internal), respectively. The Hirshfeld surface colors are used to visualize the inter-atomic contacts as: longer than vdW contacts (blue), equal to vdW (white), and shorter than vdW (red).

The colors of the points on the 2-D fingerprint plots correspond to the frequency of the \(d_e\) and \(d_i\) combinations on the Hirshfeld surface, where red represents a larger fraction or contribution and green to blue represent moderate to small contributions, respectively.

The Hirshfeld surfaces of 1, mapped over \(d_{\text{norm}}\), are shown in Fig. 3, the red spots in Fig. 3a are associated with C⋯F interaction, while the red spots in Fig. 3b are associated with H⋯F interactions; both types of interactions are also observed in the corresponding 2-D fingerprint plots (Fig. 4) as a pair of symmetrical spikes at \((d_e + d_i) \approx 3.1\text{ Å}\) for the C⋯F/F⋯C contacts (10.1\% of the total Hirshfeld surface) and \(\approx 2.7\text{ Å}\) for the F⋯H/H⋯F contacts (49.3\% of the total Hirshfeld surface), which equals the
The sum of vdW radii of C/F and H/F, respectively. The full 2-D fingerprint plot for 1 and the decomposed contacts representing H···H (16.1%), F···F (14.5%), and O···H (6.0%) interactions are shown in Fig. S7. In addition, the Hirshfeld surface was mapped with the shape-index property, where the blue bump shape represents the donor atom(s) and the red hollow shape represents the acceptor atom(s) of the intermolecular interaction. Fig. 5 shows the F···π intermolecular interaction in the crystal packing, where the red hollow shape represents the electron poor aromatic surface and the blue bump shape represent the fluorine atoms.

The enrichment ratios \(E\), the ratio between the actual contacts proportion in the crystal and random contacts, were computed using the surface contact data derived from the Hirshfeld surface analysis [55]. Values of \(E > 1\) indicate that the pair of elements involved have a high propensity to form contacts in the crystal structure, while an \(E < 1\) value indicates that the propensity would be low. The contributions to the surfaces in 1 and the corresponding enrichment ratios are presented in Table 2.
enrichment ratios of 1 show that the C···F contacts ($E_{CF} = 1.69$) is the most favored contact in the crystal packing followed by the O···H contacts ($E_{OH} = 1.57$), and H···F contacts ($E_{FH} = 1.25$), respectively. While H···F contacts cover almost half the total Hirshfeld surface of 1 (49.3%), the surface contacts of C···F and O···H cover only 10.1% and 6.0%, respectively, which illustrates the importance of the C···F contacts in stabilizing the molecular packing of 1. Also, the high enrichment values of the C···F contacts correlate very well with the interaction energies calculations, vide infra.

Intermolecular interaction energies were assessed with the CE-B3LYP model embedded in Crystal Explorer 17.5 to evaluate their role in stabilizing the molecular packing of 1 [56]. The interaction energies between molecular pairs were computed for a cluster of 3.8 Å around a reference molecule. The molecular pairs interaction energies

![Hirshfeld surface of 1 mapped with shape-index property. Blue bump shape represents donor atom(s) and red hollow shape represents acceptor atom(s).](image)

**Figure 5.** Hirshfeld surface of 1 mapped with shape-index property. Blue bump shape represents donor atom(s) and red hollow shape represents acceptor atom(s).
are expressed in terms of total energy (E_tot), electrostatic energy (E_ele), polarization energy (E_pol), dispersion energy (E_dis), and repulsion energy (E_rep). The values of these energies for 1 are listed in Table S2. The highest stabilized molecular pair in 1 (E_tot = -49.9 kJ/mol) is related to the pair of molecules (Fig. S8) linked by the C···F short contacts (all within the sum of vdW radii), where the main stabilizing energy is due to E_dis contribution followed by E_ele. Similarly, the second highest stabilized molecular pairs in 1 (E_tot = -45.5 kJ/mol) is related to the pair of molecules linked by the C···F short contacts (all within the sum of vdW radii), with the main stabilizing energy being E_dis followed by E_ele. In addition, the third highest stabilized molecular pairs in 1 (E_tot = -29.0 kJ/mol) is related to the pair of molecules linked by the H···F short contacts (all within the sum of vdW radii), with the main stabilizing energy being E_dis followed by E_ele. These results support earlier studies which indicate that fluorine atoms can form stabilizing contacts with electron-deficient aromatic surfaces [57].

4. Conclusion

Single crystal X-ray analysis shows that the solid-state crystal packing of 1 maybe stabilized by C–H···F and lone pair (F)···π. The large enrichment ratios of C···F and H···F contacts and their major participation in the stabilization energy of the molecular pairs, indicate that these intermolecular interactions are the most favored and play an important role in the crystal packing formation. Hirshfeld surface analysis of 1 has confirmed the ability of -CF₃ groups to form stabilizing interactions with electron-poor aromatic surfaces. Comparison of calculated and experimental values of bond lengths and bond angles showed very good agreement. The main UV-Vis absorption band is assigned to local π → π* excitations, which mainly involves the conjugated benzene ring.

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