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Structural comparison of five new halogenated dihydroquinoline-4(1H)-ones

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Abstract

Compounds with dihydroquinoline-4(1H)-one nuclei have been reported in the literature for being important in the development of medicines due to their broad spectrum of activities. In this way, the structural knowledge of this class becomes relevant for obtaining new materials with desired biological properties. This study presents the structural elucidation of five halogenated dihydroquinolines, as well as the discussion about the effect on the molecular conformation of the type and position of halogen atom on aromatic rings. Compounds I and IV differ in halogen substitution on 2-phenyl ring, while compounds III and V differ in halogen substitution on the benzylidene ring. Moreover, compound H has a para-substituted 2-phenyl ring in their molecular structure. The crystal packing of all five molecules is mainly ruled by C–H···O and C–H···–halogen interactions that form dimers and chains. The shift in position and the kind of the halogen in ring C shows a starring role in the conformation of the studied compounds, and the packing of these compounds is more susceptible to variations when the halogen position changes.

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1. Introduction

Quinolines are a class of N-heterocyclic compounds, also known as benzopyridines, obtained both from natural and synthetic sources. They have attracted great attention in the scientific community being used in several industrial processes, becoming increasingly important in the development of medicines, pesticides and also due to their notable biological activities [1–3]. Among the compounds of this class, we are interested in those with the dihydroquinoline-4(1H)-one moiety; in this way, the recent studies conducted by our research group involve structural elucidation [4–6], anti-cancer properties [7,8] and their potential application as pesticides [9]. Also, other groups have explored the cytotoxic properties of this class [10–13] and as potential Middle East respiratory syndrome coronavirus (MERS-CoV) inhibitors [14].

The biological activity of a substance is dominated by its properties, which are determined by its chemical structure. Structural elucidation is essential since it allows understanding and proposing explanations for the mechanisms of action at the molecular level, helping to design and develop new materials with desirable biological properties [15,16]. A search in the CSD version 5.41 (November 2019) database showed 132 reported structures with the dihydroquinoline-4(1H)-one nucleus. Furthermore, given the biological potential of these molecules, a need to enlarge elucidated structures of this class will contribute to the applications of dihydroquinoline-4(1H)-ones.

Thus, in this paper, we investigate and report a comprehensive single-crystal analysis of five halogenated dihydroquinoline-4(1H)-ones, namely (E)-3-(2-chlorobenzylidene)-2-(2-chlorophenyl)-1-(phenylsulfanyl)-2,3-dihydroquinolin-4(1H)-one (I), (E)-3-(2-chlorobenzylidene)-2-(4-chlorophenyl)-1-(phenylsulfanyl)-2,3-...
were deposited in the Cambridge Crystallographic Data Centre diffractometer with graphite-monochromated Mo-Kα radiation on the latter two compounds. This kind of strategy allowed a careful choice. They were mounted in a Bruker APEX II CCD repositioning and re-refinement details are summarized in Table 2. The structures I to V were deposited in the Cambridge Crystallographic Data Centre (CCDC) with the code number 1994320, 1994319, 1994318, 1994317, and 1994316, respectively.

3. Results and discussion

3.1. Spectroscopy characterization

Complete assignment of the signals of 1H and 13C NMR spectra are presented in Table 1 and the infrared spectra are available in the Supporting Information. The most deshielded carbon signal, near δ 181 and assigned to carbonyl carbon (C3), was a good starting point to confirm the proposed structure and NMR signal assignments. The strong correlations with C3 in the HMBC experiment (1JCH) allowed the identification of hydrogens H8, H5, H10 and H1 (Fig. S1). Also, the correlations of these hydrogens with their respective carbons, by HSQC experiment (1JCH), enabled the assignment of the carbons C10 and C1 (Fig. S2). H10 signal is a broad singlet (Fig. S3) since it presents long-range scalar coupling with the other hydrogens of the benzylidene group. Cross peaks with C1 and H1 in the HMBC spectrum provided information for C22 and C18 assignments (Fig. S1). C9 was identified by its strong correlations with H11, H5 and H7, and weak correlation with H8 (Fig. S1). H16 (and H12 when present) was assigned based on 1JCH with C10 in HMBC.

The multiplet signal near to δ 1.71 in the 1H NMR spectrum was assigned to H24/28, since it had an integration of 2 in all the structures and presented 1JCH and 2JCH correlations only with the carbons C24/28 and C26, respectively. H25/27 was assigned by a cross peak with H24/28 signal in the COSY experiment (Fig. S4), and their HSQC correlation allowed C25/27 assignment as the carbon near to δ 2.29. H26 and C26 correlation were observed in DEPT-135 experiments, in addition to 1H and 13C analyses (Table 1).

2.2. Crystallographic characterization

Appropriate single crystals of compounds I, II, III, IV and V were carefully chosen. They were mounted in a Bruker APEX II CCD diffractometer with graphite-monochromated Mo-Kα radiation (λ = 0.71073 Å) and data were measured at 120 K. Using Olex2 [17], the structure solutions were determined by Direct Methods with SHELXS [18] and refined by full-matrix least-squares on F2 with SHELXL [19]. All the hydrogen atoms were placed in calculated positions and refined with fixed individual displacement parameters (Uiso(H) = 1.2Ueq (C) or 1.5Ueq (C)) according to the riding model (C–H bonds equal 0.93 Å for aromatic). Ring D in IIb was found to be disordered and modeled over two equal occupancy positions. Lastly, the validation of chemical parameters were made using PARST [20] and PLATON [21]. Data collection and structure refinement details are summarized in Table 2. The structures I to V were deposited in the Cambridge Crystallographic Data Centre.

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2. Experimental

2.1. Synthesis and crystallization

Compounds I to V were obtained from sulfonamide chalcones reacted with benzaldehydes in an alkaline reaction environment for 24 h (Scheme 1). The subsequent precipitates were purified by slow recrystallization from dichloromethane and ethanol (4:1), after drying at room temperature.

Nuclear magnetic resonance (NMR) spectra were acquired on a Bruker Avance III 500 spectrometer (Rheinstetten, Germany) operating at 11.75 T with a 5 mm inverse detection three-channel (1H, 2H and X-nucleus) BBI probe. The samples (ca. 10 mg) were dissolved in 600 μL of deuterated dimethylsulfoxide (DMSO-d6), containing tetramethylsilane (TMS) as the internal standard. The unambiguous signal assignment was achieved by correlation spectroscopy (COSY), heteronuclear multiple bond correlation (HMBC), heteronuclear single quantum correlation (HSQC), and DEPT-135 experiments, in addition to 1H and 13C analyses (Table 1).

Scheme 1. Synthesis of compounds I to V.
Table 1

| Compound | I | II | III | IV | V |
|----------|---|----|-----|----|---|
| | \( ^1H \) NMR spectral data assignments for the compounds I, II, III, IV and V in DMSO-\( d_6 \). |
| Atom | \( ^1H \) | \( ^1^C \) | \( ^1H \) | \( ^1^C \) | \( ^1H \) | \( ^1^C \) | \( ^1H \) | \( ^1^C \) | \( ^1H \) | \( ^1^C \) |
| C1 | 6.81 (m) | 58.4 | 6.52 (m) | 58.9 | 6.81 (s) | 60.6 | 6.79 (m) | 58.6 | 6.73 (s) | 60.7 |
| C2 | -- | 132.1 | -- | 131.3 | -- | 132.4 | -- | 132.1 | -- | 130.0 |
| C3 | -- | 181.2 | -- | 181.1 | -- | 181.2 | -- | 181.2 | -- | 181.1 |
| C4 | -- | 129.3 | -- | 127.4 | -- | 129.6 | -- | 129.3 | -- | 129.2 |
| C5 | 7.80 (ddd, 7.6; 1.6; 0.5) | 127.7 | 7.80 (ddd, 7.6; 1.6; 0.5) | 127.8 | 7.78 (ddd, 7.6; 7.2) | 127.6 | 7.82 (ddd, 7.7; 7.6; 1.0) | 127.6 | 7.80 (ddd, 7.6; 127.3) |
| C6 | 7.45 (ddd, 7.6; 7.6; 1.1) | 128.5 | 7.42 (m) | 127.8 | 7.39 (ddd, 7.6; 7.2) | 128.2 | 7.46 (m) | 128.5 | 7.45 (ddd, 7.6; 128.5) |
| C7 | 7.65 (ddd, 7.6; 7.6; 1.6) | 135.3 | 7.70 (m) | 135.4 | 7.65 (ddd, 7.6; 7.2) | 135.3 | 7.65 (m) | 135.2 | 7.65 (m) | 135.2 |
| C8 | 7.41 (m) | 128.1 | 7.65 (m) | 127.4 | 7.37 (ddd, 7.6; 127.7) | 7.39 (m) | 128.4 | 7.37 (dd, 8.2; 128.6) |

Table 2

Crystallographic and refinement details for I, II, III, IV and V.

| Chemical formula | C\(_{28}\)H\(_{19}\)Cl\(_2\)NO\(_3\)S | C\(_{28}\)H\(_{19}\)Cl\(_2\)NO\(_3\)S | C\(_{28}\)H\(_{19}\)BrCl\(_2\)NO\(_3\)S | C\(_{28}\)H\(_{19}\)Cl\(_2\)NO\(_3\)S | C\(_{28}\)H\(_{19}\)Cl\(_2\)NO\(_3\)S |
|------------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| \( M_r \) | 520.4 | 520.4 | 564.86 | 564.86 | 503.95 |
| Crystal system, space group | Triclinic, P-1 | Monoclinic, P2\(_1\)/n | Triclinic, P-1 | Triclinic, P-1 |
| Temperature (K) | 120 | 120 | 120 | 120 | 120 |
| \( a, b, c (\AA) \) | 8.0771 (2), 16.4324 (5) | 8.0771 (2), 16.4324 (5) | 8.0141 (3), 16.6545 (7) | 8.0141 (3), 16.6545 (7) | 8.0141 (3), 16.6545 (7) |
| \( \alpha, \beta, \gamma (\degree) \) | 109.114 (2), 94.537 (1), 97.435 (1) | 109.114 (2), 94.537 (1), 97.435 (1) | 108.605 (1), 95.540 (1), 97.078 (1) | 108.605 (1), 95.540 (1), 97.078 (1) | 108.605 (1), 95.540 (1), 97.078 (1) |
| \( V (\AA^3) \) | 2378.21 (12) | 2378.21 (12) | 2407.00 (17) | 2407.00 (17) | 2407.00 (17) |
| \( Z \) | 4 | 4 | 4 | 4 | 4 |
| \( \mu (\text{mm}^{-1}) \) | 0.39 | 0.39 | 1.94 | 1.94 | 1.94 |
| Crystal size (mm) | 0.17 \( \times 0.17 \times 0.09 \) | 0.37 \( \times 0.30 \times 0.27 \) | 0.19 \( \times 0.18 \times 0.14 \) | 0.19 \( \times 0.18 \times 0.14 \) | 0.19 \( \times 0.18 \times 0.14 \) |
| \( T_{min}, T_{max} \) | 0.0675, 0.745 | 0.683, 0.712 | 0.594, 0.641 | 0.594, 0.641 | 0.594, 0.641 |
| No. of measured, independent and observed \( [I > 2\sigma(I)] \) reflections | 385188, 9758, 6875 | 36094, 5954, 5242 | 54875, 11796, 9107 | 68765, 16965, 12459 | 194960, 18117, 13854 |
| \( R_{int} \) | 0.045 | 0.019 | 0.037 | 0.046 | 0.064 |
| (\( \sin \theta/\lambda_{max} \) (\AA\(^{-1}\)) | 0.627 | 0.668 | 0.668 | 0.668 | 0.668 |
| \( R(F) > 2 \sigma(F), wR(F)^2 \), S | 0.038, 0.089, 1.00 | 0.031, 0.085, 1.04 | 0.043, 0.101, 1.04 | 0.040, 0.096, 1.03 | 0.043, 0.100, 1.04 |
| No. of reflections | 975 | 5954 | 11976 | 16965 | 18117 |
| No. of parameters | 631 | 316 | 661 | 946 | 946 |
| \( \Delta \rho_{max}, \Delta \rho_{min} (\text{e} \AA^{-3}) \) | 0.36, -0.42 | 0.39, -0.38 | 1.13, -2.61 | 0.33, -0.36 | 1.90, -0.84 |
The labeling scheme for C atoms in (b) follows the same way as presented in (a). Displacement ellipsoids are drawn at the 50% probability level and H atoms have been omitted.

Table 3

| Molecule | \( \phi_1 \) (°) | \( \phi_2 \) (°) | \( \phi_3 \) (°) | \( \angle AB \) (°) |
|----------|-----------------|-----------------|-----------------|-----------------|
| Ia       | -146.9(3)       | 145.9(2)        | 87.46(16)       | 54.40(7)        |
| Ib       | -147.4(2)       | 168.88(19)      | 77.33(16)       | 62.55(7)        |
| II       | 137.5(2)        | 167.77(12)      | -84.58(13)      | 60.12(4)        |
| IIIa     | -148.9(3)       | 164.83(2)       | -104.43(2)      | 61.00(9)        |
| IIIb     | -147.7(3)       | 147.28(2)       | -87.85(4)       | 55.62(9)        |

\( \phi_1 = \text{C}_2-\text{C}_10-\text{C}_11-\text{C}_12; \phi_2 = \text{C}_2-\text{C}_1-\text{C}_17-\text{C}_22; \phi_3 = \text{N}_1-\text{S}_1-\text{C}_23-\text{C}_28. \)

The two independent molecules of I showing the atom-labeling scheme: (a) molecule Ia, (b) molecule Ib. To clarify, in (b) the labeling scheme shows only non-carbon atoms. The labeling scheme for C atoms in (b) follows the same way as presented in (a). Displacement ellipsoids are drawn at the 50% probability level and H atoms have been omitted.

Fig. 1. The two independent molecules of I showing the atom-labeling scheme: (a) molecule Ia, (b) molecule Ib. To clarify, in (b) the labeling scheme shows only non-carbon atoms. The labeling scheme for C atoms in (b) follows the same way as presented in (a). Displacement ellipsoids are drawn at the 50% probability level and H atoms have been omitted.

Fig. 2. The molecular structure of II showing the atom-labeling scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms have been omitted.

3.2. Crystallographic characterization

3.2.1. Chlorine dihydroquinolinones

Compound I belongs to the class of dihydroquinolinones having three substituents groups in its motif. A sulfonilbenzene group attached to N atom; an ortho-chlorobenzene attached to C1 atom and a chloro-2-vinylbenzene attached to C2 atom (Scheme 1). Compound I crystallizes in the triclinic system (P\( \text{T} \)) with two independent molecules in the asymmetric unit (ASU), labeled as Ia and Ib (Fig. 1). To clarify, in this paper we chose arbitrarily all the molecules within the ASU have R configuration about the stereogenic center. To understand the geometrical differences between these molecules their structures have been overlaid using the atoms C1, C3, and C5 as anchor points (Fig. S48). The primary variances noted within these structures are related to the orientations of rings B, C and D with respect to the A ring (defined on Table 3). These variances were measured using the following parameters: the torsion angles: \( \text{C}_2-\text{C}_10-\text{C}_11-\text{C}_12 (\phi_1), \text{C}_2-\text{C}_1-\text{C}_17-\text{C}_22 (\phi_2) \) and \( \text{N}_1-\text{S}_1-\text{C}_23-\text{C}_28 (\phi_3) \), and the dihedral angle between the planes formed by ring A and ring B (\( \angle AB \)) (Table 3).

The \( \angle AB \) dihedral angle is ca 8° larger in Ib than in Ia, evidencing that the rings in these two molecules have different orientation. This characteristic is also observed in other crystal structures of dihydroquinolinones derivatives [23–25]. Except for compound II, these characteristics are the same for all compounds studied here. The orientation of ring B (\( \phi_1 \)), could be considered the same in Ia and Ib, it assumes an anti-clinal orientation. Furthermore, the values of \( \phi_2 \) show that ring C assumes an anti-clinal and an anti-periplanar orientation in Ia and Ib, respectively, with a difference of 23°. Finally, \( \phi_3 \) shows a syn-clinal orientation of ring D with a difference of ca 10° between the two molecules.

Compound II, (Fig. 2), is a positional isomer of I, having a chloro-4-vinylbenzene attached to C2 atom (Scheme 1). It is the structure with \( \angle AB \) angle smaller than Ib and larger than Ia. In its molecular structure, unlike Ia, \( \phi_1 \) shows that ring B assumes an anti-clinal orientation. The change of position of the chlorine atom causes a significant geometric change concerning compounds I and III. In II the rings C and D are oppositely oriented compared with the same rings in the other compounds studied here. The values of \( \phi_2 \) indicate similarity in the molecular set and can be divided into two groups, one containing the molecules Ib, II and IIIa and the other containing the molecules Ia and IIIb. In compound II, \( \phi_2 \) and \( \phi_3 \) assume anti-periplanar and a syn-clinal orientations, respectively.

Compound III differs from I only in the presence of the bromo-2-vinylbenzene bonded to the C2 atom (Scheme 1). The two independent molecules in the ASU were labeled as IIIa and IIIb (Fig. 3). The overlay of these structures indicates a difference of 14° in \( \angle AB \) angle for IIIa and IIIb (Fig. S49). When compounds I, II and III are compared (\( \angle AB \) angle), it is possible to distinguish two sets
with similar values: first with IIIb and Ia, and second with Ib, II, and IIIa molecules. The decreasing of \( \angle AB \) angle value regarding chlorine dihydroquinolinones is Ia, IIIb, II, IIIa, and Ib (Table 3).

There is no significant difference between \( f_1 \) in the molecules of compounds I and III, but this torsion in II is, ca 10° less twisted. The values of \( f_2 \) show that ring C assumes an anti-periplanar orientation in IIIa while in IIIb it is anti-clinal with a difference of ca 17°. \( f_2 \) values are similar for Ib, II and IIIa and being ca 20° smaller for Ia and IIIb. The orientation of ring D (\( f_3 \)) in IIIa is anti-clinal while in IIIb is syn-clinal with a difference ca 17°.

The crystal structure of these chlorine dihydroquinolinones is stabilized by C\( \equiv \)H\( \cdots \)O and C\( \equiv \)H\( \cdots \)halogen hydrogen bonds listed in Table 4. Although these interactions are weak, we are interested in how they affect the packing and if the different substituents on ring C lead to different arrangements. In the molecular packing in the unit cell of compound I, two Ib molecules are involved in C27A–H27A\( \cdots \)O3A interactions leading to the formation of a \( R_2^\text{2}(12) \) dimer along the b axis. Meanwhile, one Ia molecule links to IIIa molecules. The decreasing of \( \angle AB \) angle value regarding chlorine dihydroquinolinones is Ia, IIIb, II, IIIa, and Ib (Table 3).

There is no significant difference between \( f_1 \) in the molecules of compounds I and III, but this torsion in II is, ca 10° less twisted. The values of \( f_2 \) show that ring C assumes an anti-periplanar orientation in IIIa while in IIIb it is anti-clinal with a difference of ca 17°. \( f_2 \) values are similar for Ib, II and IIIa and being ca 20° smaller for Ia and IIIb. The orientation of ring D (\( f_3 \)) in IIIa is anti-clinal while in IIIb is syn-clinal with a difference ca 17°.

The crystal structure of these chlorine dihydroquinolinones is stabilized by C\( \equiv \)H\( \cdots \)O and C\( \equiv \)H\( \cdots \)halogen hydrogen bonds listed in Table 4. Although these interactions are weak, we are interested in how they affect the packing and if the different substituents on ring C lead to different arrangements. In the molecular packing in the unit cell of compound I, two Ib molecules are involved in C27A–H27A\( \cdots \)O3A interactions leading to the formation of a \( R_2^\text{2}(12) \) dimer along the b axis. Meanwhile, one Ia molecule links to

### Table 4

| Compound | D–H–A | D–H | H–A | D–A | D–H–O |
|----------|-------|-----|-----|-----|--------|
| I        | 0.95  | 2.46| 3.374 (3) | 162 |
| II       | 0.95  | 2.36| 3.138 (3) | 138 |
| IIIa     | 0.95  | 2.38| 3.326 (3) | 175 |
| IIIb     | 0.95  | 2.50| 3.175 (3) | 128 |
| C8–H8–O2 | 0.95  | 2.44| 3.3531 (16) | 160 |
| C13–H13–O2 | 0.95 | 2.40| 3.161 (3) | 137 |
| C21–H21–O1A | 0.95 | 2.51| 3.458 (4) | 159 |
| C25–H25–O3 | 0.95 | 2.50| 3.305 (3) | 145 |
| C14–H14A–O2 | 0.95 | 2.46| 3.385 (3) | 165 |
| C19–H19–Br1 | 0.95 | 2.82| 3.626 (3) | 143 |

Symmetry codes: (1) \(-x+1, -y+1, -z+1\); (2) \(-x, -y, -z+1\); (3) \(x+1, y, z\); (4) \(-x+1, -y+2, -z+1\); (5) \(x, y, z+1\).

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**Fig. 3.** The two independent molecules of compound III, showing the atom-labeling scheme: (a) molecule IIIa, (b) molecule IIIb. To clarify, in (b) the labeling scheme shows only non-carbon atoms. The labeling scheme for C atoms in (b) follows the same way as presented in (a). Displacement ellipsoids are drawn at the 50% probability level and H atoms have been omitted.

**Fig. 4.** A partial packing view of I showing the dimer formed by C27A–H27A\( \cdots \)O3A interaction (1), and the discrete contacts C8A–H8A\( \cdots \)O3 (2), C13A–H13A\( \cdots \)O2 (3), and C14–H14–O2A (4). For clarity, H atoms not involved in the motif have been omitted.

The two independent molecules of compound III, showing the atom-labeling scheme: (a) molecule IIIa, (b) molecule IIIb. To clarify, in (b) the labeling scheme shows only non-carbon atoms. The labeling scheme for C atoms in (b) follows the same way as presented in (a). Displacement ellipsoids are drawn at the 50% probability level and H atoms have been omitted.

There is no significant difference between \( f_1 \) in the molecules of compounds I and III, but this torsion in II is, ca 10° less twisted. The values of \( f_2 \) show that ring C assumes an anti-periplanar orientation in IIIa while in IIIb it is anti-clinal with a difference of ca 17°. \( f_2 \) values are similar for Ib, II and IIIa and being ca 20° smaller for Ia and IIIb. The orientation of ring D (\( f_3 \)) in IIIa is anti-clinal while in IIIb is syn-clinal with a difference ca 17°.

The crystal structure of these chlorine dihydroquinolinones is stabilized by C\( \equiv \)H\( \cdots \)O and C\( \equiv \)H\( \cdots \)halogen hydrogen bonds listed in Table 4. Although these interactions are weak, we are interested in how they affect the packing and if the different substituents on ring C lead to different arrangements. In the molecular packing in the unit cell of compound I, two Ib molecules are involved in C27A–H27A\( \cdots \)O3A interactions leading to the formation of a \( R_2^\text{2}(12) \) dimer along the b axis. Meanwhile, one Ia molecule links to
Fig. 5. A partial packing view of II showing the chains formed by C6—H6···O2 interaction. For clarity, H atoms not involved in the motif have been omitted.

Fig. 6. A partial packing view of III, showing the dimer and the chain formed by C25—H25···O3 and C19—H19···Br1 interactions, respectively (a). The discrete contacts C13—H13···O2A (1), C14A—H14A···O2 (2), C8—H8···O3A (3), and C21—H21···O1A (4) join molecules of IIIa and IIIb in the packing (b); the motif in (a) is presented in (b) in light grey to better visualization. For clarity, H atoms not involved in interactions have been omitted.

Fig. 7. The three independent molecules of IV showing the atom-labeling scheme: (a) molecule IVa, (b) molecule IVb, and (c) molecule IVc. To clarify, in (b) and (c) the labeling scheme shows only non-carbon atoms. The labeling scheme for C atoms in (b) and (c) follow the same way as presented in (a). Displacement ellipsoids are drawn at the 50% probability level and H atoms have been omitted.

Because this is a discrete, localized contact, there is no propagation to an extended structure through this contact. The molecular packing of compound II is not as varied as that of compound I. This arrangement can be described as $C_{1}^{1}(8)$ chains that extend along the $a$ axis by molecules that are associated through a C6—H6···O2 interaction (Fig. 5). The molecular packing of compound III seems remarkably similar to compound I. The differences indicate the carbonyl groups are not related to interactions in the packing of compound I. Two molecules of IIIa are arranged by C25—H25···O3 interaction as a $R_{2}^{2}(12)$ dimer along the $b$ axis, and by C19—H19···Br1 interaction as a $C_{1}^{1}(6)$ chain along the $a$ axis. The molecules of IIIb are connected to this arrangement by discrete contacts: C13—H13···O2A, C14—H14A···O2, and C—H8···O3A along
to the \( b \) axis, while the \( C21-H21\cdots O1A \) interaction grows the packing along to the \( c \) axis. (Fig. 6).

### 3.2.2. Fluorine dihydroquinolinones

Compound **IV** has an *ortho*-chlorobenzene attached to \( C1 \) atom and a fluoro-2-vinylbenzene attached to the \( C2 \) atom (Scheme 1). The three independent molecules in ASU were labeled as **IVa**, **IVb** and **IVc** (Fig. 7). As listed in Table 5, these three structures present a variation of 10° in their \( \angle AB \) angle being the descending order equal to **IVb**, **IVa**, and **IVc** (Fig. S50). The torsion related to ring \( B (\phi_1) \) is syn-clinal oriented for **IVb** and **IVc**, and anti-clinal oriented for **IVa**, with a variation of ca 12° between them. The values for \( \phi_2 \) show that ring \( C \) has more mobility than ring \( B \), with a ca 28° of variation in this torsion. The orientation of ring \( D (\phi_3) \) varies ca 19°, in **IVa** it is almost perpendicular to \( SO2 \) group while in **IVb** and **IVc** it is almost parallel to \( O2a \) and \( O2b \) atoms, respectively.

Compound **V** is like compound **IV** but has an *ortho*-bromobenzene attached to \( C1 \) atom. The three independent molecules in the ASU were labeled as **Va**, **Vb** and **Vc** (Fig. 8). These molecules present a variation of 18° in their \( \angle AB \) angle being the descending order equal to **Vc**, **Va**, and **Vb** (Fig. S51). When \( \angle AB \) angle values for all fluorine dihydroquinolinones are compared, it is observed a decreasing order \( \text{Va} \), \( \text{IVb} \), \( \text{IVa} \), \( \text{IVc} \), and \( \text{Vb} \) (Table 5). Just like for chlorine dihydroquinolinones, it is not possible to figure out a clear correlation between the substitution of halogens and the \( AB \) ring orientation of these fluorine dihydroquinolinones. The torsion \( \phi_1 \) is anti-periplanar oriented in **Va** while in **Vb** and **Vc** it is anti-clinal. The values of \( \phi_2 \) show that ring \( C \) assumes an anti-periplanar orientation in all molecules of compound **V** with a difference of ca 14°. The torsion \( \phi_3 \) shows ring \( D \) in syn-clinal orientation in all molecules of compound **V**, with a change of ca 10°. These values, when compared with compound **IV**, shows it having more mobility in the molecule of **IVa**, being ca 9° larger than in **Vc**.

The molecular packing in the unit cell of compound **IV** and **V** is stabilized by \( C-H\cdots O \) and \( C-H\cdots \) halogen hydrogen bonds (Table 6). In compound **IV**, the contacts \( CSB-HSB\cdots O3B \), \( C18A-H18A\cdots O2A \), and \( C19A-H19A\cdots C1A \) form \( C1\cdots C2 \) chains along the \( a \) axis. Molecules of **IVa** are linked through \( C26B-H26B\cdots O3 \) and \( C15-H15\cdots O3A \) interactions, leading to crystal packing along the \( b \) axis (Fig. 9a). These motifs (molecules of **IVb** and **IVc**) are attached by the discrete contacts: \( C14A-H14A\cdots O2B \), \( C14B-H14B\cdots O2A \), \( C27A-H27A\cdots O1 \), and

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**Table 5**

Torsion angles and least-square planes of aromatic rings of **IV** and **V**.

| Molecule | \( \phi_1 \) | \( \phi_2 \) | \( \phi_3 \) | \( \angle AB \) |
|----------|-----------|-----------|-----------|-------------|
| **IVa**  | -141.7(2) | 169.45(17)| 91.06(19) | 58.77       |
| **IVb**  | -153.9(2) | 150.24(17)| 72.24(16) | 49.30       |
| **IVc**  | -150.1(2) | -178.22(16)| 75.28(16) | 59.71       |
| **Va**   | -157.7(3) | 175.3(2)  | 78.1(2)   | 44.53       |
| **Vb**   | -144.4(3) | 173.7(2)  | 72.1(2)   | 62.80       |
| **Vc**   | -149.7(3) | 161.1(2)  | 82.7(2)   | 52.79       |

\( \phi_1 = C2-C10-C11-C12; \phi_2 = C2-C1-C17-C22; \phi_3 = N1-S1-C23-C28. \)

**Table 6**

Hydrogen-bond geometry (Å, °) for compounds **IV** and **V**.

|  | \( D-H \) | \( A \) | \( D-H \) | \( A \) | \( D-H \) | \( A \) |
|---|----------|--------|----------|--------|----------|--------|
| **IV** | CSB-HSB\cdots O3B | 0.95 | 2.48 | 3.104 (2) | 123 |
|      | C14A-H14A\cdots O2B\( ^{vi} \) | 0.95 | 2.47 | 3.378 (3) | 161 |
|      | C14B-H14B\cdots O2A\( ^{vi} \) | 0.95 | 2.58 | 3.518 (3) | 168 |
|      | C15-H15\cdots O3A\( ^{iv} \) | 0.95 | 2.57 | 3.463 (3) | 156 |
|      | C18A-H18A\cdots O2A\( ^{iv} \) | 0.95 | 2.57 | 3.289 (2) | 133 |
|      | C26B-H26B\cdots O3 | 0.95 | 2.60 | 3.326 (2) | 134 |
|      | C27A-H27A\cdots O1 | 0.95 | 2.56 | 3.238 (2) | 129 |
|      | C19A-H19A\cdots C1A\( ^{iv} \) | 0.95 | 2.71 | 3.437 (3) | 155 |
| **V** | C7A-H7A\cdots O1B | 0.95 | 2.59 | 3.474 (3) | 155 |
|      | C8A-H8A\cdots F1B | 0.95 | 2.54 | 3.381 (3) | 147 |
|      | C14A-H14A\cdots O2A\( ^{vi} \) | 0.95 | 2.56 | 3.283 (3) | 133 |
|      | C18-H18\cdots O2A\( ^{vi} \) | 0.95 | 2.60 | 3.256 (2) | 131 |
|      | C26A-H26A\cdots O1A\( ^{iv} \) | 0.95 | 2.39 | 3.335 (3) | 171 |
|      | C14B-H14B\cdots O2F | 0.95 | 2.38 | 3.257 (3) | 154 |
|      | C18F-H18F\cdots O2B\( ^{iv} \) | 0.95 | 2.44 | 3.261 (2) | 145 |
|      | C24A-H24A\cdots O1A\( ^{iv} \) | 0.95 | 2.62 | 3.346 (4) | 133 |
|      | C26-H26\cdots O1 | 0.95 | 2.47 | 3.256 (4) | 140 |
|      | C27B-H27B\cdots O1A\( ^{iv} \) | 0.95 | 2.49 | 3.357 (3) | 152 |
|      | C27-H27\cdots F1A | 0.95 | 2.52 | 3.342 (3) | 144 |

Symmetry codes: (i) \( x+1, y, z \); (ii) \( x+1, y+1, z \); (iii) \( x-1, y+1, z \); (iv) \( x-1, y, z \); (v) \( x, y+1, z+1 \); (vi) \( x, y+3/2, z+1/2 \); (vii) \( x, y+z, z \); (viii) \( -x+y-z \);

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C14B-H14B\cdots O2A leading the packing to grow along to \( c \) axis (Fig. 9b).

In the crystal packing of compound **V**, two molecule of **Va** are arranged as dimers through \( C26-H26\cdots O1 \), \( R_2^{(2)} \), and \( C27-H27\cdots F1 \), \( R_2^{(2)} \), interactions. C14B-H14B\cdots O2 interaction attatches those dimers. Along to a axis there is a molecular pair formed by the following interactions: C8A\cdots H8A\cdots F1B and C7A\cdots H7A\cdots O1B (Fig. 10). The interaction C18\cdots H18\cdots O2, and
C18A—H18A···O2A (1) and C19A—H19A···C11A (2), and C5—H5B···O3B (3) interactions. In addition, the interactions C15—H15···O3A (4) and C26B—H26B···O3 (5) responsible to connect molecules of IVa to the chains. In (b) are shown the discrete contacts C14A—H14A···O2B (6), C14B—H14B···O2A (7), C27A—H27A···O1 (8), C14B—H14B···O2A (9), responsible for grow the packing along the c axis. The motif represented in (a), is presented in light grey. For clarity, H atoms not involved in the motif have been omitted.

**Fig. 9.** A partial packing view of IV showing (a) the two chains formed by C18A—H18A···O2A (1) and C19A—H19A···C11A (2), and C5—H5B···O3B (3) interactions. In addition, the interactions C15—H15···O3A (4) and C26B—H26B···O3 (5) responsible to connect molecules of IVa to the chains. In (b) are shown the discrete contacts C14A—H14A···O2B (6), C14B—H14B···O2A (7). The torsion φ2, both compounds present similar values (23° for I and 19° for IV). The torsion angle φ3 in IV is larger than I (10° and 19°, respectively). Regarding molecular packing, the chlorine compound forms C1(7) and C1(6) chains, while the fluorine compound forms C1(7) chains. All those chains grow along the a axis. Finally, discrete contacts join these chains along the b and c axis.

In contrast, compounds III and V differ in the halogen in the ortho position of ring B, chlorine, and fluorine, respectively. In terms of AB values, the decreasing order is Va, Vc, Ilib, IIIa, and Vb. The torsion φ1 in III is smaller than V (1° and 13°, respectively). Regarding the torsion φ2 both compounds present similar values (17° in III and 14° in V). Moreover, the torsion φ3 to III is larger than V (17° and 10°, respectively). These small alterations occur likely due to the change in radius of the halogen atoms. In terms of molecular packing both compounds have R2(12) dimers but in III it is related to SO2 group while in the compound V it is related to the carbonyl group. In compound III these dimers are arranged along the c axis while in compound V they are along the b axis. Also, the molecular packing in V present two C1(7) and one C1(9) chain along the c axis. All those observations show that the change in position and kind of halogen atom attached in ring C play a significant role in the conformation of the studied compounds. On the other hand, the packing of these compounds is more susceptible to variations when the substituent position changes.

**Declaration of competing interest**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

**CRedit authorship contribution statement**

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