Electronic Supplementary Material (ESI) for New Journal of Chemistry.

Electronic Supplementary Information for manuscript:

X-Ray characterization, Hirshfeld surface analysis, DFT calculations, *in vitro* and *in silico* lipoxygenase inhibition (LOX) studies of dichlorophenyl substituted 3-hydroxy-chromenones

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Table of contents:

Description of the X-ray packing of compound 1

In **1** (Fig. S1), 3-hydroxychroman-4-one moiety A (C1-C9/O1-O3) and 1,3-dichlorobenzene ring B (C10-C15/C6CL1/CL2) are roughly planar with root mean square (r.m.s) deviation of 0.0207 and 0.0271 Å, respectively. Dihedral angle among mean plane of moiety A and ring B is 59.92 (3)°. Selected bond lengths and bond angles are specified in Table S1. The molecular configuration of **1** is stabilized by intramolecular O-H…O bonding to form S (5) as displayed in Fig. S2. The molecules are interlinked in the form of dimers by strong O-H…O bonding to form $R_2^2(10)$ loop in which carbonyl O-atom acts as H-bond acceptor. The dimers are connected with each other through weak non-covalent interaction of type C-O…π with O…π distance ranges from 3.405 Å to 3.962 Å, carbonyl O-atom is involved in this interaction. The molecules are further interlinked by off-set π…π stacking interaction between aromatic rings with inter-centroid separation rages from 3.993 Å to 4.192 Å with ring off-set range from 1.918 Å to 2.410 Å. A zigzag chain of molecules is formed along [001] due to this interaction as displayed in Fig. S3. The crystal packing is further stabilized by weak C-H…π interaction with H…π distance ranges from 2.80 Å to 2.88 Å that connect the molecules along [100] direction to form infinite chain as displayed in Fig. S4.

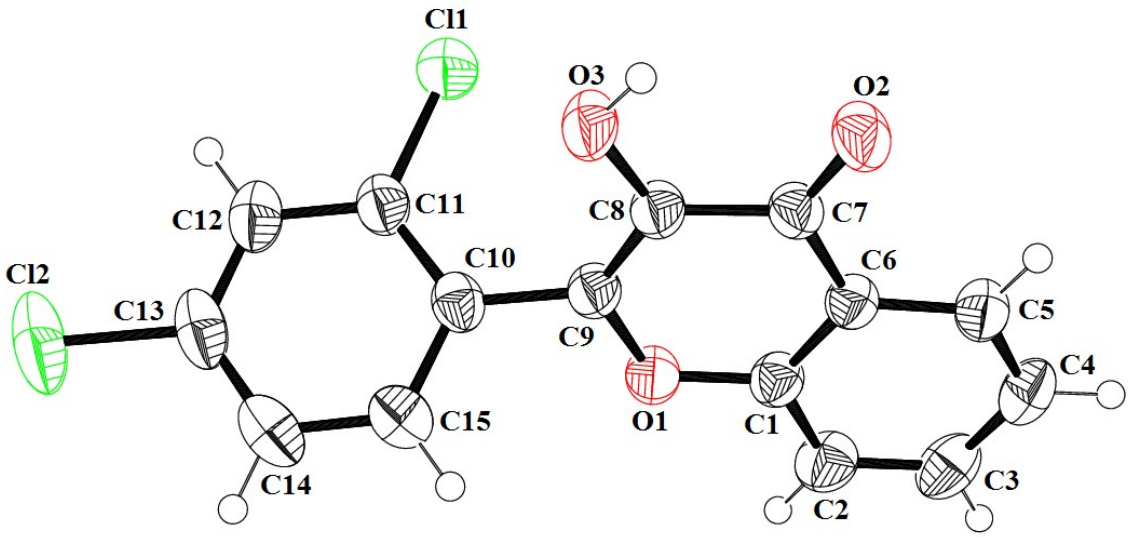

Fig. S1 ORTEP diagram of **OF5** drawn at probability level of 50%. H-atoms are shown by small circle of arbitrary radii.

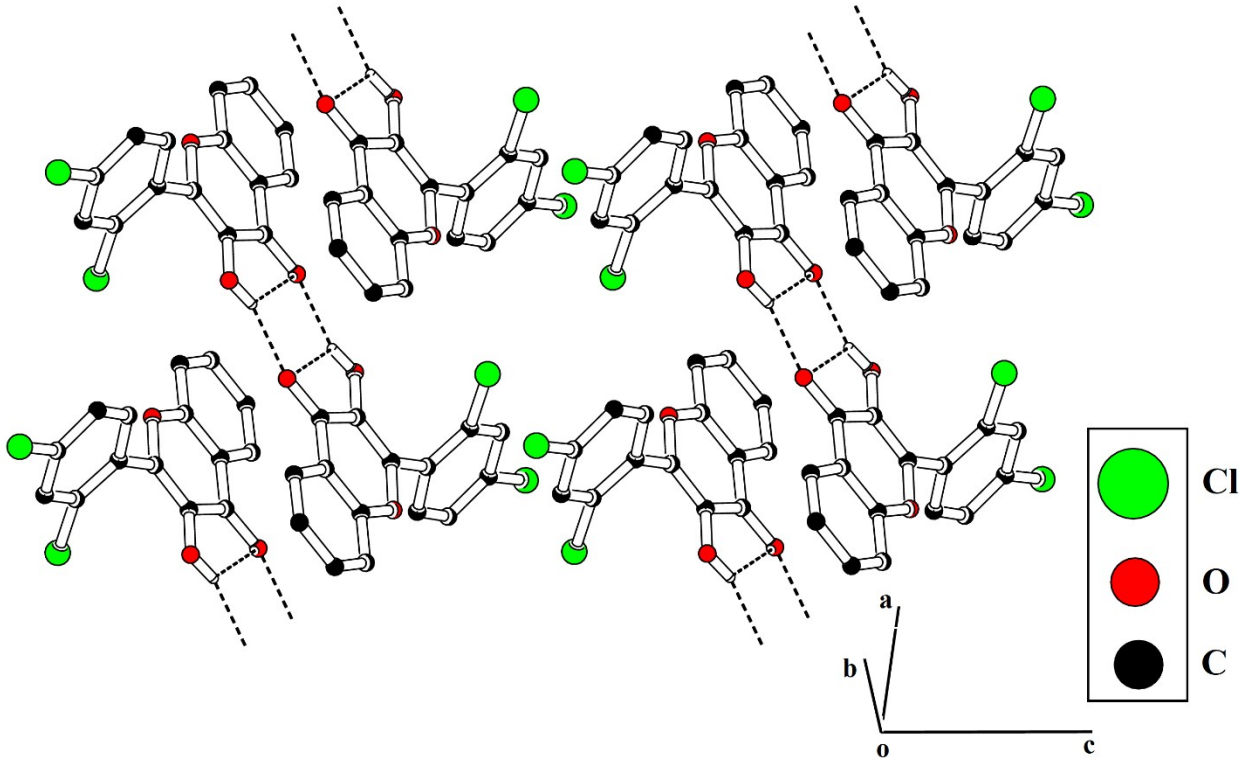

Fig. S2 Packing diagram of **1** showing dimerization of molecules through O-H…O bonding. Selected H-atoms are shown for clarity.

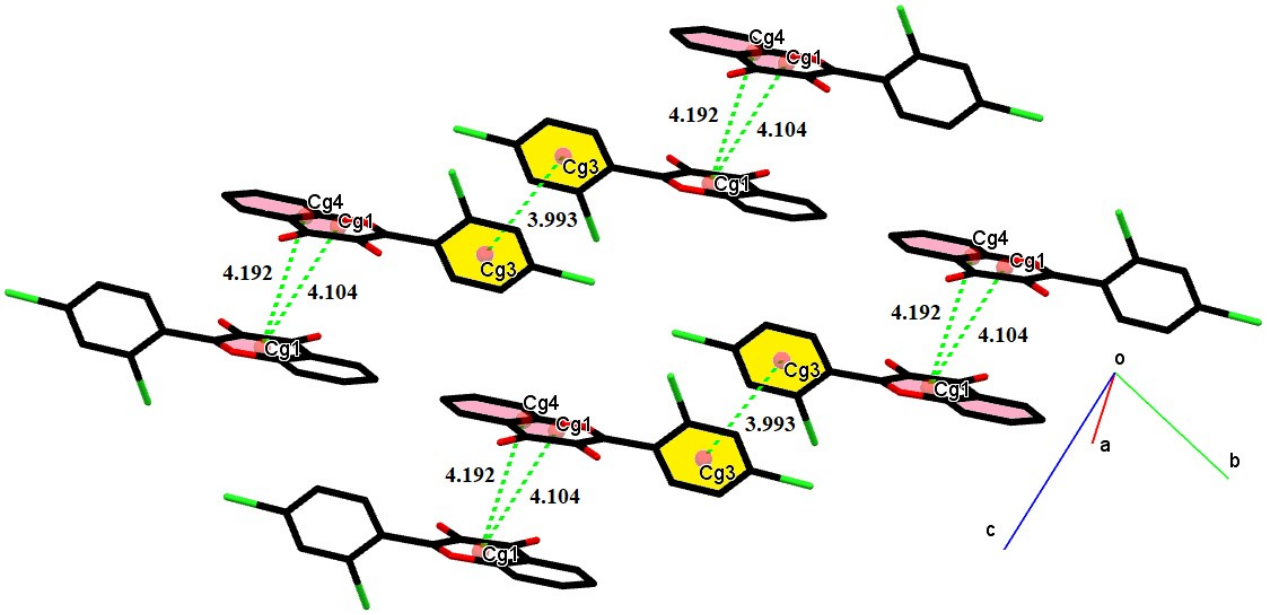

Fig. S3 Graphical representation of off-set π…π stacking interaction in **1** that links the molecules along [001] direction. H-atoms are not shown for clarity. Distances are measured in Å.

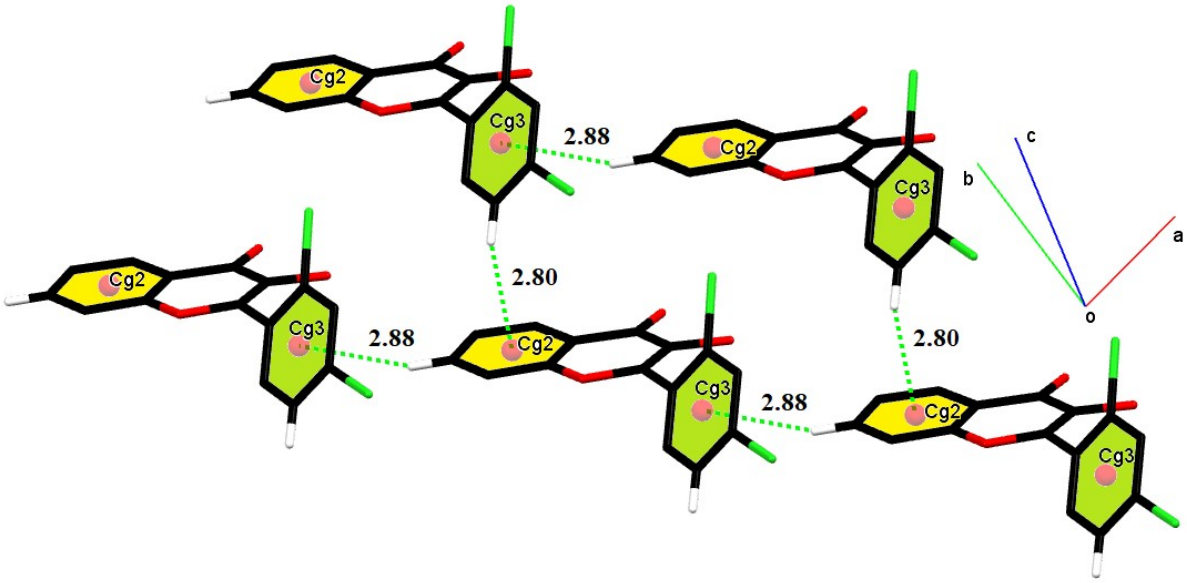

Fig.: S4 Graphical representation of C-H…π interaction for **1**. Selected H-atoms are shown for clarity. Distances are measured in Å.

Description of the X-ray packing in compound 2

In **2** (Fig. S5), 3-hydroxychroman-4-one moiety A (C1-C9/O1-O3) and 1,2-dichlorobenzene ring B (C10-C15/CL1/CL2) are roughly planar with root mean square (r.m.s) deviation of 0.0164 and 0.0048 Å, respectively. Dihedral angle among mean plane of moiety A and ring B is 69.64 (3)°. Selected bond lengths and bond angles are specified in Table S2. The molecular configuration of **2** is stabilized by intra-molecular O-H…O bonding to form S (5) loop. The molecules are interlinked in the form of dimers by strong O-H…O bonding to form $R_2^2(10)$ loop in which carbonyl O-atom acts as H-bond acceptor. The dimers are interlinked through comparatively weak C-H…O bonding to form $R_2^2(16)$ loop in which O-atom of hydroxyl group acts as H-bond acceptor as displayed in Fig. S6 and specified in Table S2. C11 zigzag chain is formed by the combination of O-H…O and C-H…O bonding that runs along a crystallographic axis as displayed in Fig. S7. The molecules related by inversion symmetry (-x, 1-y, -z) are involved in C-O…π interaction in which carbonyl group of one molecule is connected with phenyl ring (C11-C16) of other molecule with O…π distance of 3.83 Å as displayed in Fig.s S8 and S9. The crystal packing is further stabilized by another non-covalent interaction of type off-set π…π interaction. For this

interaction, centroid to centroid separation ranges from 3.56 Å to 4.11 Å and ring off-set ranges from 0.97 Å to 2.26 Å. Overall 2D network is formed by the molecules through O-H…O bonding C-O…π and off-set π…π stacking interaction in the plane (100) with base vectors [001] and [010].

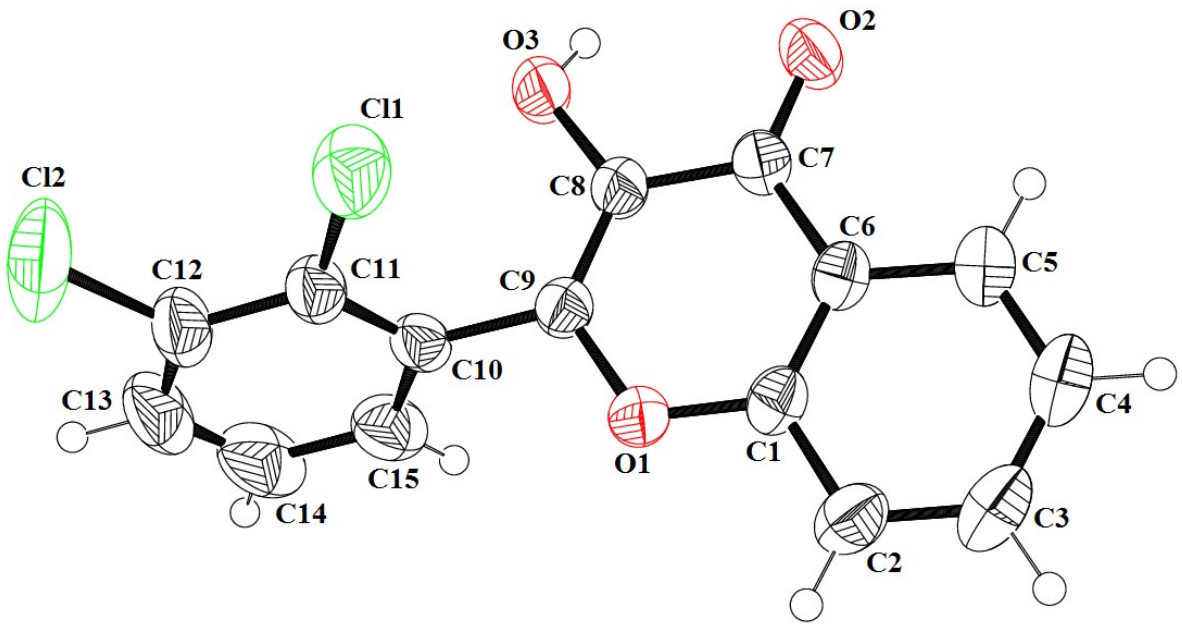

Fig. S5 ORTEP diagram of **2** drawn at probability level of 50%. H-atoms are shown by small circle of arbitrary radii.

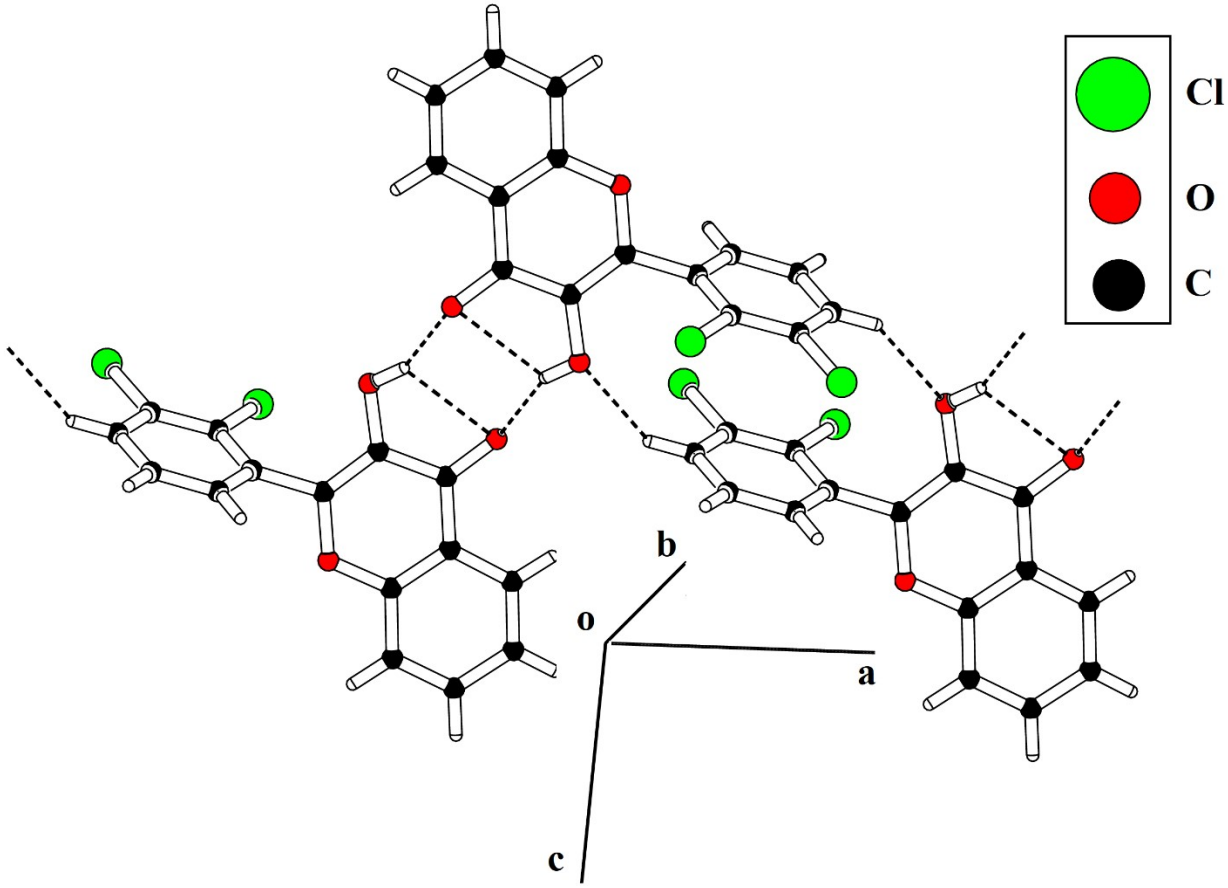

Fig. S6 First view of packing diagram of **2** indicating dimerization of molecules through H-bonding.

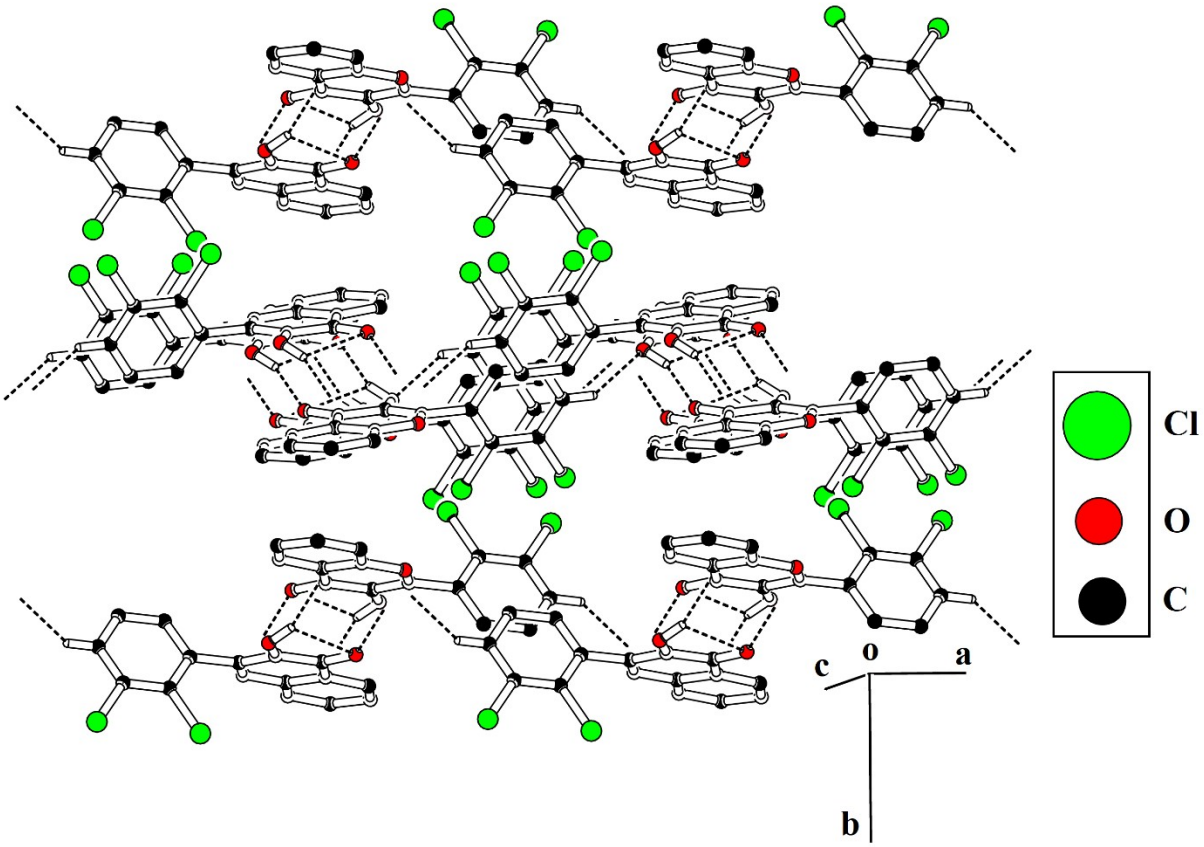

Fig. S7 Second view of packing diagram of **2**, selected H-atoms are shown for clarity.

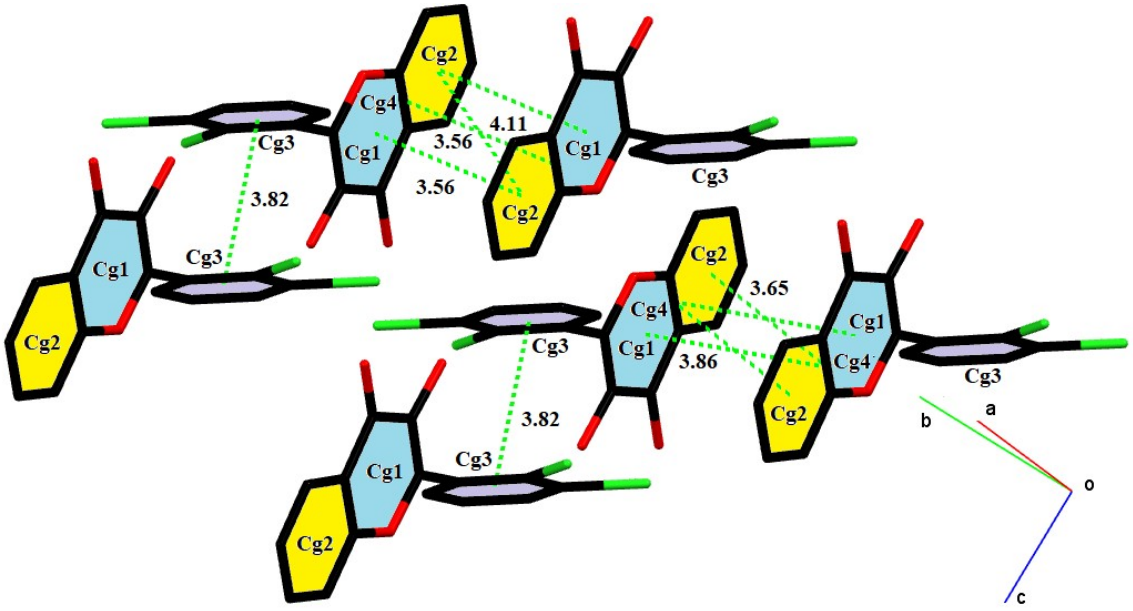

Fig. S8 Graphical representation of off-set π…π stacking interaction in **2**. H-atoms are not shown for clarity. Distances are measured in Å.

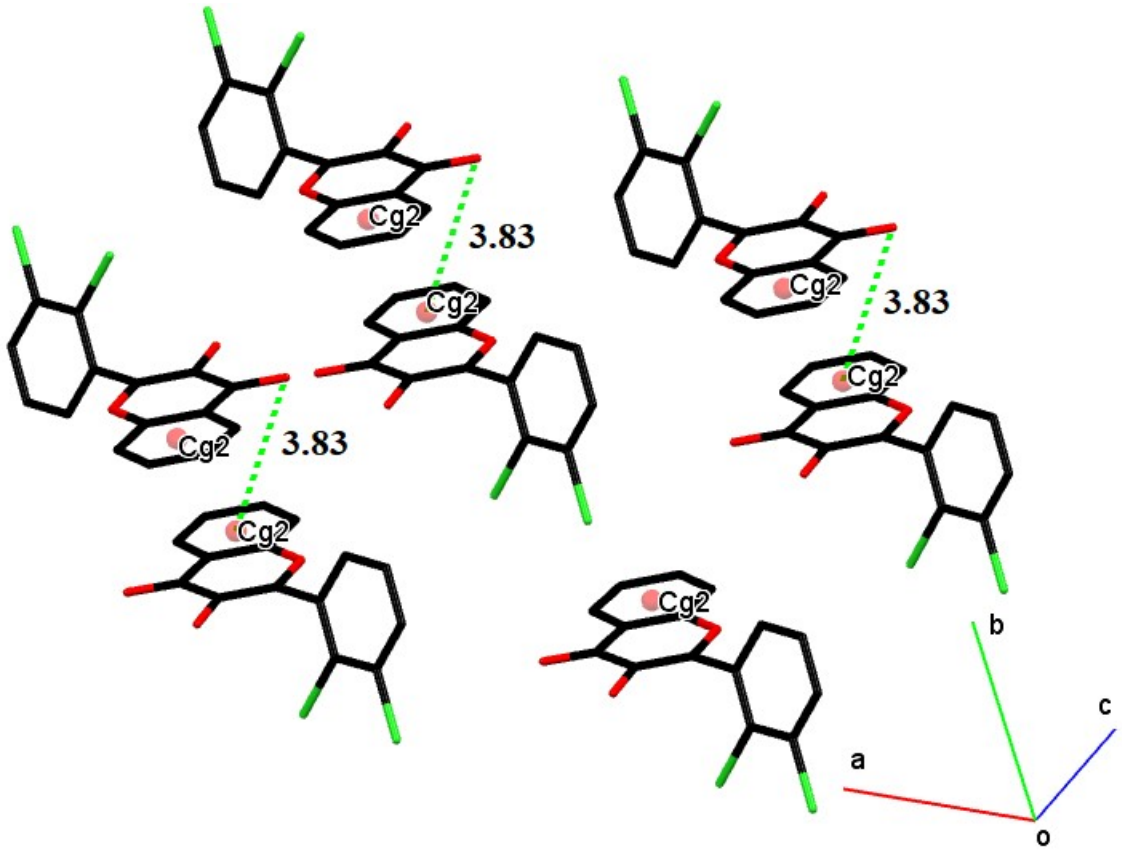

Fig. S9 Graphical representation of C-O…π interaction in **OF6**. H-atoms are not shown for clarity. Distances are measured in Å.

Description of the X-ray packing in compound 3

In **3** (Fig. S10), 3-hydroxychroman-4-one moiety A (C1-C9/O1-O3) and 1,5-dichlorobenzene ring B (C10-C15/CL1/CL2) are roughly planar with root mean square (r.m.s) deviation of 0.0061 and 0.0143 Å, respectively. Dihedral angle among mean plane of moiety A and ring B is 84.95 (3)° indicating that moiety A and ring B are almost perpendicular to each other. Selected bond lengths and bond angles are specified in Table S1. The molecular configuration of **3** is stabilized by intra-molecular O-H…O bonding to form S (5) loop. The molecules are interlinked in the form of dimers

by strong O-H…O bonding to form $R_2^2(10)$ loop in which carbonyl O-atom acts as H-bond acceptor. The dimers are interlinked through comparatively weak C-H…O bonding to form $R_2^2(16)$ loop in which O-atom of hydroxyl group acts as H-bond acceptor as displayed in Fig. S11 and specified in Table S2. C11 zigzag chain is formed by the combination of O-H…O and C-H…O bonding that runs along b crystallographic axis. Crystal packing is further stabilized by off-set π…π stacking interaction between aromatic rings of molecules with inter-centroid separation ranges from 3.81 Å to 4.36 Å that result in the formation of zigzag infinite chain along b crystallographic axis as displayed in Fig. S12. Ring off-set for this interaction ranges from 1.670 Å to 2.851 Å. Non-covalent interactions of type C-Cl…π and C-O…π is also found that helps in further stabilization of crystal packing.

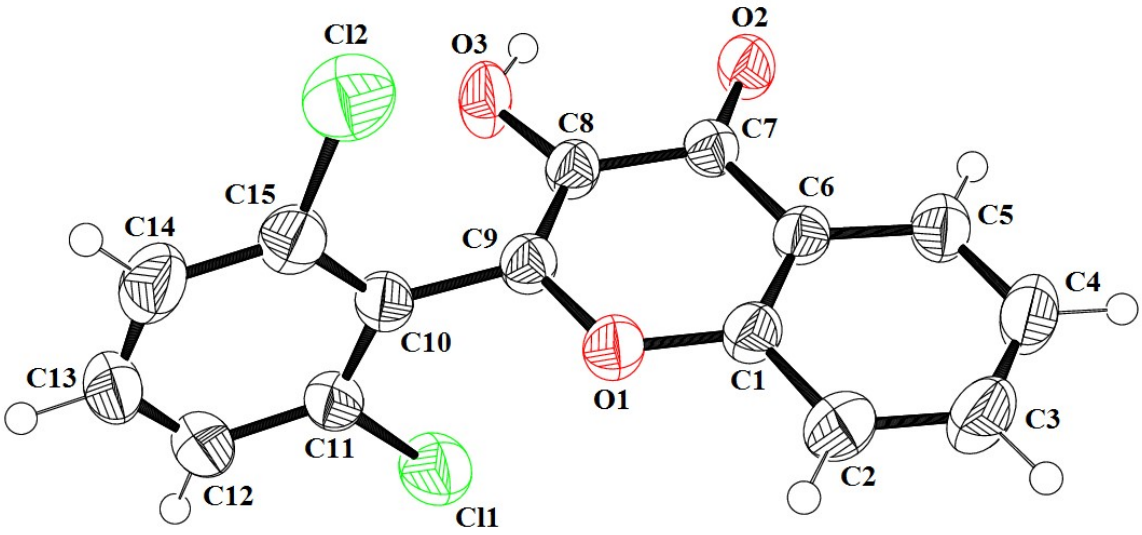

Fig. S10 ORTEP diagram of **3** drawn at probability level of 50%. H-atoms are shown by small circle of arbitrary radii.

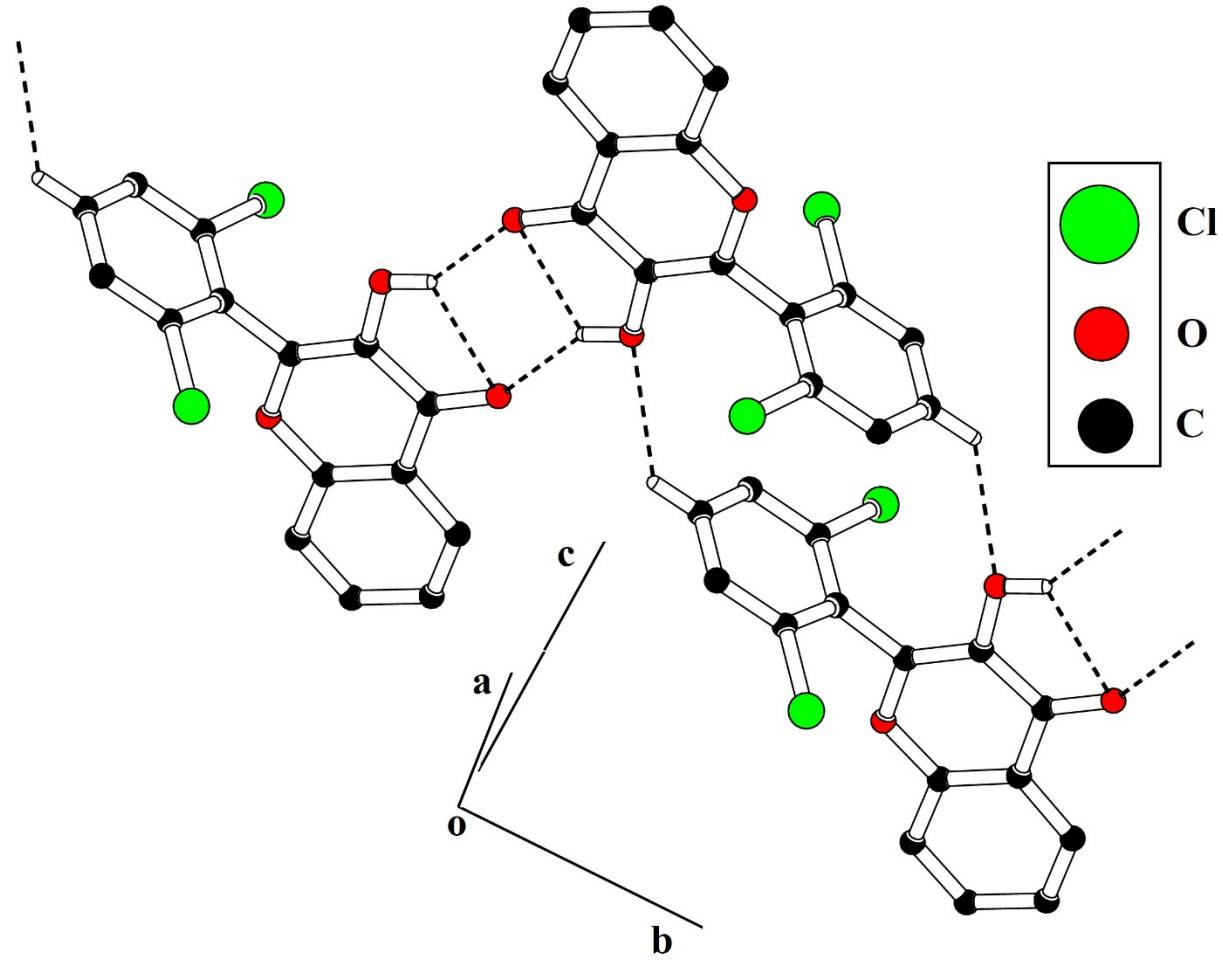

Fig. S11 packing diagram of **3** showing dimerization of molecules through H-bonding. Selected H-atoms are shown for clarity.

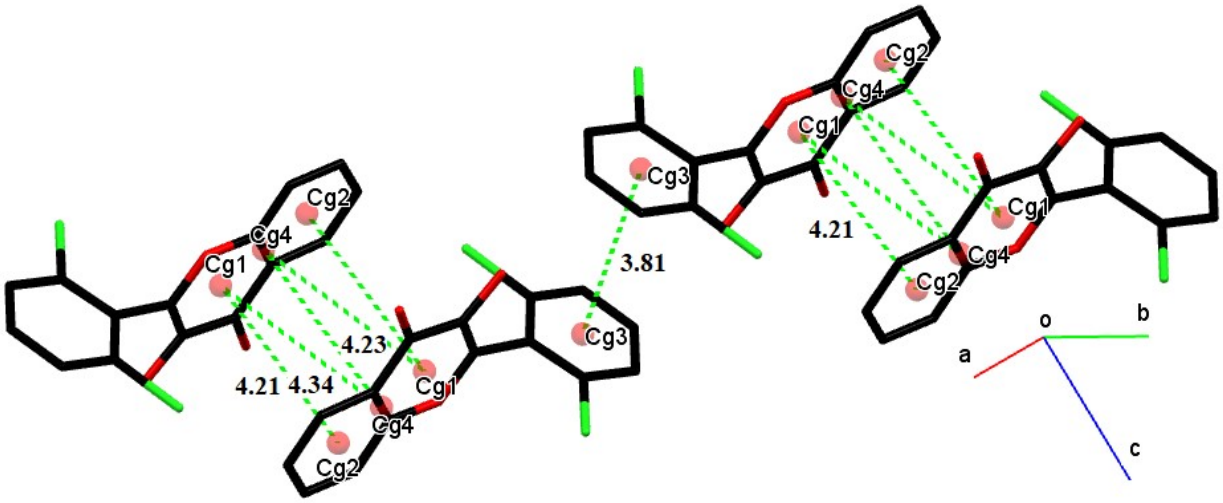

Fig. S12 Graphical representation of off-set π…π stacking interaction in **3**. H-atoms are not shown for clarity. Distances are measured in Å.

Table S1 Selected bond lengths (Å) and bond angles (°) in **1**, **2**, **3**

Bond lengths	**1**	**2**	**3**
O1-C1	1.361 (2)	1.368 (2)	1.370 (2)
O1-C9	1.368 (2)	1.366 (2)	1.362 (2)
O2-C7	1.235 (2)	1.236 (2)	1.235 (2)
O3-C8	1.352 (2)	1.352 (2)	1.345 (2)
Cl1-C11	1.733 (2)	1.719 (2)	1.734 (2)
Cl2-C12	-	1.729 (2)	-
Cl2-C13	1.735 (2)	-	-
Cl2-C15	-	-	1.731 (2)
Bond angles	**1**	**2**	**3**
C1-O1-C9	119.3 (1)	119.3 (1)	118.8 (1)
O1-C9-C8	122.7 (1)	122.3 (1)	123.0 (1)
C9-C8-O3	119.1 (1)	118.9 (2)	118.5 (1)
C8-C7-O2	122.0 (1)	121.5 (2)	121.3 (1)
O2-C7-C6	122.9 (2)	123.6 (2)	123.9 (1)
C10-C11-Cl1	120.5 (1)	120.1 (1)	119.0 (1)
C12-C13-Cl2	118.5 (1)	-	-
C12-C11-Cl2	-	120.3 (2)	-
C10-C15-Cl2	-	-	119.6 (1)

Table S2: Hydrogen-bond geometric features with symmetry codes for compounds 1, 2 and 3

Compound	***D*—H···*A***	***D*—H**	**H···*A***	***D*···*A***	***D*—H···*A***
1	O3—H3*A*···O2	0.82	2.36	2.7715 (15)	112
	O3—H3*A*···O2^{i}(i) −*x*+3, −*y*+1, −*z*	0.82	1.94	2.6820 (14)	150
2	O3—H3*A*···O2^{ii}(ii) −*x*, −*y*+1, −*z*+1	0.82	1.94	2.6973 (18)	154
	C13—H13···O3^{iii}(iii) −*x*+1, −*y*+1, −*z*+1	0.93	2.47	3.247 (2)	141
3	O3—H3*A*···O2	0.82	2.35	2.7690 (17)	112
	O3—H3*A*···O2^{iv}(iv)−*x*, −*y*, −*z*	0.82	1.98	2.6846 (16)	144
	C13—H13···O3^{v} (v) −x, −y+1, −z	0.93	2.48	3.181 (2)	132