

Intermolecular Interaction Energies in Molecular Crystals of 4-Formylcoumarin Derivatives

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Abstract: Most of the crystallographic analysis that follows from structure determination involves interpretation of the molecular geometry and a working knowledge of a variety of intra- and intermolecular interactions based purely on geometrical considerations (distance and angle cut off criteria). The missing link is to explore the energetics associated with these interactions, particularly intermolecular ones, which provide a platform for the molecules to associate with each other. In this regard, PIXEL calculations have been performed on a series of six molecules of 4-formylcoumarin derivatives. PIXEL calculations suggest the presence of different structural motifs that play significant role in the stabilization of the structure. Analysis of these motifs shows that bifurcated C-H...O and $\pi \dots \pi$ stacking are the major contributors towards the stabilization of the structure. However, it is found that molecular pairs interacting via dimeric C=O...C=O interaction also make significant contribution of almost -5 kcal mol⁻¹. In addition to these motifs, the role of weak C-H...X (F, Cl or Br) has also been explored in the stabilization of molecular packing.

Keywords: Coumarin, PIXEL, Hydrogen bonding, Intermolecular interactions, Lattice energy

Introduction

Coumarins form an important group of naturally occurring compounds possessing a 2H-1-benzopyran-2-one nucleus. The derivatives of coumarins usually occur as secondary metabolites present in seeds, roots and leaves of many plant species¹. Coumarins derivatives are widely recognized in the pharmaceutical industry for their broad structural diversity as well as their wide range of pharmacological activities. Coumarins have been reported to possess numerous medicinal activities which include enzymatic inhibition, anticoagulant, anticonvulsant, antioxidant and anti-inflammatory activities *etc.*^{2,3}. The diversity of biological effects of these molecules is due to the nature of different ring substituents⁴.

Hydrogen bonds play a vital role in crystal engineering because of their three peculiar features *i.e.* strength, directionality and flexibility⁵. Strong hydrogen bonds such as O-H...O and N-H...O are well documented^{6,7}, but weak interactions such as C-H...O, C-H... π , C-H...X (X-halogen atom) and C-H...N have also attracted considerable interest because of their frequent occurrence in organic crystal structures⁸⁻¹². The recent focus is to investigate

the role of weak intermolecular interactions and its influence on crystal packing. In addition to the description of the crystal packing in terms of the presence of different intermolecular interactions, based purely on the concept of geometry (distance–angle criteria), it is also very important to analyze the intermolecular interaction energies of different non-covalent interactions in the solid state in order to obtain more detailed insight into the crystal packing¹³⁻¹⁶.

In this regard, a series of six molecules of 4-formylcoumarin derivatives have been taken into account and calculated theoretically their lattice energies by using PIXEL approach. The chemical name, molecular code, chemical structure for each structure is presented in Table 1. The X-ray crystallographic structures of these molecules are already reported¹⁷ and their precise crystallographic description is presented in Table 2. We have performed energy calculations by obtaining CIF files of these molecules from CCDC. All the molecular pairs involved in the crystal packing were extracted from crystal packing after PIXEL calculation and the nature and energies associated with the intermolecular interactions associated with these molecular pairs were analyzed to explore the role of these interactions in the stabilization of the crystal lattice. A representative illustration of the coumarin moiety indicating the atomic numbering scheme used for the present work is shown in Figure 1.

Table 1. Chemical name, coding scheme and chemical structure of the compounds

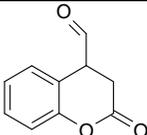
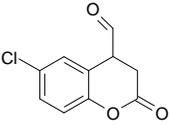
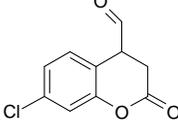
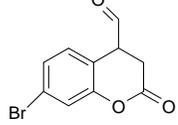
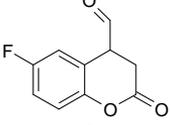
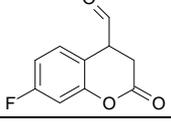
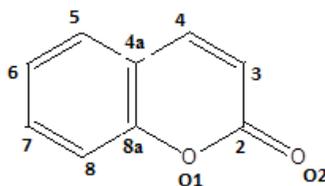
| Code | Chemical Name | Structure |
|------------|---------------------------|--|
| M-1 | 4-formylcoumarin |  |
| M-2 | 6-Chloro-4-formylcoumarin |  |
| M-3 | 7-Chloro-4-formylcoumarin |  |
| M-4 | 7-Bromo-4-formylcoumarin |  |
| M-5 | 6-Fluoro-4-formylcoumarin |  |
| M-6 | 7-Fluoro-4-formylcoumarin |  |

Table 2. Precise crystallographic details of 4-formylcoumarin derivatives

| Data | M-1 | M-2 | M-3 | M-4 | M-5 | M-6 |
|----------------|---|---|---|---|-----------------------------------|----------------------------------|
| Formula | C ₁₀ H ₆ O ₃ | C ₁₀ H ₅ ClO ₃ | C ₁₀ H ₅ ClO ₃ | C ₁₀ H ₅ BrO ₃ | C ₁₀ H ₅ FO | C ₁₀ H ₅ F |
| Mol. Weight | 174.15 | 208.59 | 208.59 | 253.05 | 192.14 | 192.14 |
| Crystal system | Monoclinic | Monoclinic | Monoclinic | Monoclinic | Monoclinic | Triclinic |
| Space group | P21/c | P21/n | P21/n | P21/c | P21/n | P $\bar{1}$ |
| a(Å) | 3.824(1) | 7.0980(1) | 7.984(2) | 8.122(1) | 6.115(1) | 5.746(1) |
| b(Å) | 9.108(1) | 8.5800(1) | 5.939(1) | 10.216(1) | 8.082(1) | 8.552(1) |
| c(Å) | 22.252(2) | 14.328(2) | 18.452(2) | 10.709(2) | 16.330(5) | 9.212(2) |
| α (°) | 90 | 90 | 90 | 90 | 90 | 113.792(3) |
| β (°) | 91.263(5) | 97.913(5) | 101.333(5) | 92.753(5) | 94.23(1) | 102.163(3) |
| γ (°) | 90 | 90 | 90 | 90 | 90 | 93.126(3) |
| Z | 4 | 4 | 4 | 4 | 4 | 2 |
| R | 0.0592 | 0.0281 | 0.0582 | 0.0417 | 0.0597 | 0.0585 |

**Figure 1.** Coumarin moiety indicating the atomic numbering Scheme used

Theoretical calculations

PIXELC module embedded in Coulomb-London-Pauli (CLP) computer program package (version 13.2.2012) has been used for performing interaction energy calculations in the undertaken structures¹⁸⁻²⁰. Intermolecular energy is calculated as a numerical integral over a large number of electron density pixels, obtained from a standard molecular orbital calculation (20K pixels for a typical medium-size organic molecule). One of the advantages of this method is that it allows the total energy to be partitioned into coulombic, polarization, dispersion and repulsion contributions, which enable us to have better understanding of the nature and role of these interactions in the stabilization of the crystal packing²¹⁻²³. The total lattice energy partitioned into such components for the compounds M1-M6 is presented in Table 3. All the stabilizing molecular pairs involved in crystal packing were selected from the mlc output file (generated after PIXEL energy calculations) and were analyzed with their interaction energies. The symmetry operator and centroid-centroid distance along with coulombic, polarization, dispersion, repulsion and total interaction energies between the molecular pairs are presented in Table 4. Mercury software²⁴ is employed to generate these molecular motifs and packing diagrams. The geometrical restrictions placed on the intermolecular *H*-bonds present in the selected molecular pairs are the sum of the van der Waals radii + 0.4Å and the directionality is greater than 110°.

Table 3. Lattice energy from CLP (in kcal mol⁻¹)

| Molecule | E _{Coul} | E _{Pol} | E _{Disp} | E _{Rep} | E _{Tot} |
|----------|-------------------|------------------|-------------------|------------------|------------------|
| M-1 | -9.53 | -2.91 | -22.9 | 13.95 | -21.41 |
| M-2 | -10.58 | -3.44 | -26.45 | 16.87 | -23.63 |
| M-3 | -11.49 | -3.72 | -26.74 | 17.3 | -24.66 |
| M-4 | -13.4 | -3.58 | -26.67 | 20.07 | -23.58 |
| M-5 | -10.37 | -3.01 | -21.84 | 14.19 | -21.05 |
| M-6 | -12.33 | -3.53 | -22.46 | 16.53 | -21.77 |

Table 4. PIXEL interaction energies (I.E.) (kcal mol⁻¹) between molecular pairs related by a symmetry operation and the associated intermolecular interactions in the crystal

| Motif | Centroid Distance (Å) | E _{Coul} | E _{Pol} | E _{Disp} | E _{Rep} | E _{Tot} | Symmetry | Important interactions |
|------------|-----------------------|-------------------|------------------|-------------------|------------------|------------------|--------------------------|---|
| M-1 | | | | | | | | |
| 1 | 7.414 | -5.57 | -1.48 | -3.20 | 3.37 | -6.86 | 1-x,-1/2+y, 1/2-z | C3-H3...O1, C3-H3...O2, C9-H9...O2, C8-H8...O2 |
| 2 | 3.824 | -0.88 | -0.97 | -9.39 | 6.57 | -4.71 | -1+x,y,z | Molecular stacking, C=O...C=O |
| 3 | 6.585 | -1.38 | -0.62 | -2.94 | 1.17 | -3.80 | 2-x,- 1/2+y,1/2-z | C8-H8...O2, C3-H3...O1, C9-H9...O2 |
| 4 | 7.961 | -2.15 | -0.57 | -2.60 | 1.82 | -3.51 | 3-x,1-y,1-z | C6-H6...O3 |
| 5 | 6.900 | -0.64 | -0.14 | -2.58 | 0.62 | -1.46 | 2-x,1-y,1-z | C=O...C(sp ³) |
| 6 | 9.108 | -0.21 | -0.34 | -1.48 | 0.83 | -1.19 | x,-1+y,z | C7-H7...O3 |
| 7 | 9.935 | -0.50 | -0.33 | -1.94 | 1.00 | -0.76 | 3-x,2-y,1-z | C(sp ³)-H...H- C(sp ²) |
| M-2 | | | | | | | | |
| 1 | 3.488 | -1.72 | -1.55 | -12.09 | 8.46 | -6.93 | 1-x,-y,1-z | Molecular stacking |
| 2 | 3.661 | -1.17 | -1.15 | -11.35 | 7.17 | -6.50 | -x,-y,1-z | Molecular stacking |
| 3 | 8.088 | -4.80 | -1.29 | -3.70 | 3.51 | -6.26 | 1/2-x,- 1/2+y,1.5-z | C3-H3...O1, C3-H3...O2, C9-H9...O2, C8-H8...O2 |
| 4 | 8.820 | -1.69 | -0.53 | -2.15 | 1.43 | -2.94 | -1/2+x,-1/2- y,-1/2+z | C7-H7...O2 |
| 5 | 9.000 | -2.10 | -0.38 | -1.57 | 1.24 | -2.82 | 1-x,1-y,1-z | C9-H9...O3 |
| 6 | 8.544 | -0.47 | -0.41 | -2.1 | 0.84 | -2.15 | 1/2+x,1/2- y,1/2+z | C9-H9...Cl1 |
| 7 | 8.617 | -0.86 | -0.31 | -2.67 | 1.81 | -2.03 | 1/2- x,1/2+y,1/2-z | C(sp ³)- Cl...O=C |

| | | | | | | | | |
|------------|--------|-------|-------|--------|------|-------|-------------------------|--|
| 8 | 8.580 | -0.41 | -0.31 | -1.69 | 0.83 | -1.57 | $x, -1+y, z$ | C7-H7...O3 C8-H8...O3 |
| M-3 | | | | | | | | |
| 1 | 3.725 | -1.84 | -1.17 | -10.49 | 6.05 | -7.45 | $1-x, -y, 1-z$ | Molecular stacking |
| 2 | 4.327 | -1.41 | -0.86 | -8.84 | 4.94 | -6.16 | $2-x, -y, 1-z$ | Molecular stacking |
| 3 | 6.594 | -3.51 | -1.43 | -4.42 | 4.04 | -5.32 | $1-x, -1-y, 1-z$ | C8-H8...O2 C8-H8...O1 |
| 4 | 5.939 | -2.34 | -0.52 | -4.18 | 2.08 | -4.97 | $x, -1+y, z$ | C=O...C=O |
| 5 | 7.724 | -2.84 | -0.78 | -3.48 | 2.7 | -4.39 | $2-x, 1-y, 1-z$ | C5-H5...O3, C6-H6...O3 |
| 6 | 9.444 | -2.92 | -1.00 | -2.17 | 2.72 | -3.37 | $1.5-x, -1/2+y, 1.5-z$ | C3-H3...O2 |
| 7 | 9.923 | -1.17 | -0.64 | -2.17 | 2.41 | -1.57 | $-1/2+x, 1/2-y, -1/2+z$ | C9-H9...C11 |
| 8 | 9.947 | -0.02 | -0.16 | -1.79 | 0.76 | -1.24 | $1.5-x, 1/2+y, 1/2-z$ | C6-H6...C11 |
| M-4 | | | | | | | | |
| 1 | 8.418 | -6.14 | -1.77 | -3.73 | 5.06 | -6.59 | $-x, -1/2+y, -1/2-z$ | C3-H3...O1, C9-H9...O2, C8-H8...O2 |
| 2 | 4.049 | -1.53 | -1.19 | -10.54 | 7.03 | -6.21 | $-x, -y, -z$ | Stacking |
| 3 | 4.086 | -2.01 | -0.67 | -9.03 | 5.62 | -6.07 | $1-x, -y, -z$ | Stacking |
| 4 | 7.509 | -2.27 | -0.74 | -4.42 | 2.72 | -4.71 | $x, 1/2-y, -1/2+z$ | C=O...C=O |
| 5 | 8.217 | -1.82 | -0.54 | -3.15 | 2.46 | -3.06 | $1-x, 1/2+y, 1/2-z$ | C6-H6...O3 C5-H5...Br1 |
| 6 | 10.216 | -1.62 | -0.38 | -2.03 | 2.98 | -1.07 | $x, -1+y, z$ | C(sp ²)-Br1...O3 |
| M-5 | | | | | | | | |
| 1 | 7.517 | -4.87 | -1.31 | -2.82 | 2.92 | -6.09 | $-1-x, -y, 1-z$ | C8-H8...O2 |
| 2 | 6.115 | -2.7 | -0.57 | -3.68 | 1.96 | -4.97 | $-1+x, y, z$ | C=O...C=O |
| 3 | 4.109 | -0.16 | -1.07 | -8.91 | 6.26 | -3.89 | $-x, -y, 1-z$ | Stacking |
| 4 | 5.224 | -0.88 | -0.35 | -5.68 | 3.08 | -3.82 | $-x, 1-y, 1-z$ | Stacking |
| 5 | 7.575 | -2.25 | -0.69 | -1.79 | 1.91 | -2.82 | $-1/2-x, -1/2+y, 1/2-z$ | C=O...C=O |
| 6 | 8.529 | -1.33 | -0.41 | -1.96 | 0.95 | -2.74 | $1/2+x, 1/2-y, 1/2+z$ | C3-H3...F1 |
| 7 | 7.907 | -1.26 | -0.38 | -1.65 | 1.15 | -2.15 | $1/2-x, -1/2+y, 1/2-z$ | C3-H3...O3 |
| 8 | 7.903 | -0.38 | -0.24 | -2.22 | 1.34 | -1.50 | $1-x, 1-y, 1-z$ | C5-H5...F1 |
| M-6 | | | | | | | | |
| 1 | 8.490 | -8.15 | -2.17 | -3.8 | 5.76 | -8.36 | $-x, -y, -z$ | C3-H3...O2 |
| 2 | 6.899 | -5.99 | -1.84 | -3.44 | 4.95 | -6.33 | $-x, 1-y, 1-z$ | C8-H8...O2 |
| 3 | 4.092 | -1.26 | -0.86 | -8.15 | 5.13 | -5.13 | $1-x, 1-y, 1-z$ | Molecular stacking |

| | | | | | | | | |
|---|-------|-------|-------|-------|-------|-------|-------------|--------------------|
| 4 | 5.746 | -2.25 | -0.67 | -4.44 | 2.48 | -4.89 | -1+x,y,z | C=O...C=O |
| 5 | 4.519 | -1.31 | -0.86 | -7.91 | 5.54 | -4.52 | 1-x,-y,1-z | Molecular stacking |
| 6 | 7.809 | -3.23 | -1.00 | -3.35 | 3.51 | -4.04 | 2-x,-y,1-z | C5-H5...O3 |
| 7 | 9.344 | -1.17 | -0.33 | -1.88 | 1.26 | -2.13 | 2-x,1-y,2-z | C6-H6...F1 |
| 8 | 9.718 | -0.07 | -0.17 | -1.00 | -0.72 | -0.55 | x,1+y,1+z | C9-H9...F1 |

Results and Discussion

4-Formylcoumarin (*M-1*)

Molecular pairs (1-7) providing significant contribution towards the stabilization along with their interaction energies are shown in Figure 2. The molecular pair with maximum energy stabilization (motif 1) shows the presence of bifurcated C-H...O hydrogen bonds in which donor atom H3 (interacting with O1 and O2) and acceptor atom O2 (interacting with H3 and H9) are bifurcated. Along with these interactions, this pair also shows C8-H8...O2 interaction and hence results in a total interaction energy of $-6.86 \text{ kcal mol}^{-1}$ with 55% contribution from coulombic component. This molecular pair along with pairs 4 (dimeric C6-H6...O3, I.E. = $-3.51 \text{ kcal mol}^{-1}$), 6 (C7-H7...O3, I.E. = $-1.19 \text{ kcal mol}^{-1}$) and 7 (dimeric C-H...H-C, I.E. = $-0.76 \text{ kcal mol}^{-1}$) participate in the formation of a two dimensional molecular sheet in the bc plane as shown in Figure 3a. The packing in the crystal also involves the stacking of the molecules along a-axis via motif 2, contributing $-4.71 \text{ kcal mol}^{-1}$ (80% dispersion contribution) towards stabilization. Adjacent stacks are then interlinked via motif 6 (C7-H7...O3) forming layers in the ab plane (Figure 3b).

6-Chloro-4-formylcoumarin (*M-2*)

The molecular pairs (1-8) extracted from the crystal packing along with their respective interaction energies are shown in Figure 4. The maximum stabilization to the structure comes from molecular stacking. Molecules are stacked along the crystallographic a-axis via motif 1 and 2, both having similar interaction energies (-6.93 and $-6.5 \text{ kcal mol}^{-1}$) with major dispersion component (Table 4). The stacked dimers are then connected via dimeric C9-H9...O3 (motif 5, I.E. = $-2.82 \text{ kcal mol}^{-1}$) and bifurcated acceptor C-H...O (H7 and H8 with O3, motif 8, I.E. = $-1.57 \text{ kcal mol}^{-1}$) intermolecular interactions as shown in Figure 5a. The packing in the crystal also displays the formation of molecular chains via motif 3 ($-6.26 \text{ kcal mol}^{-1}$) and 8 ($-1.57 \text{ kcal mol}^{-1}$). The chains thus formed are interconnected with C(sp²)-Cl1...O3=C (motif 7) dipolar interaction (Figure 5b) having a contribution of $-2.03 \text{ kcal mol}^{-1}$ towards stabilization, the dispersion component (70%) imparting the maximum stabilization.

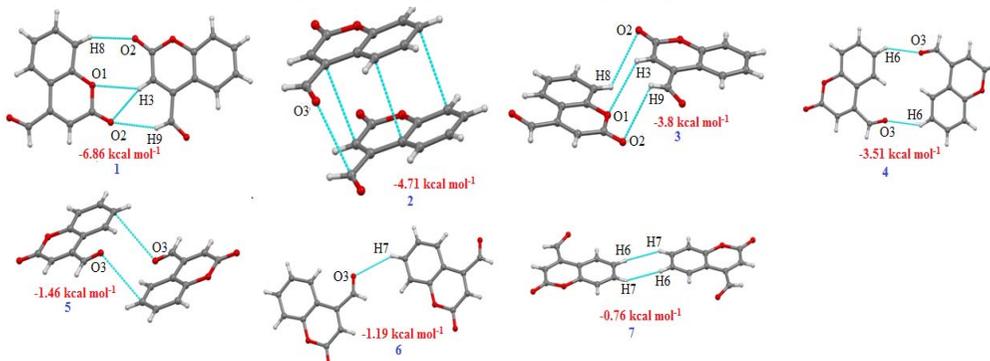


Figure 2. Molecular pairs (1-7) along with their interaction energies in C-1

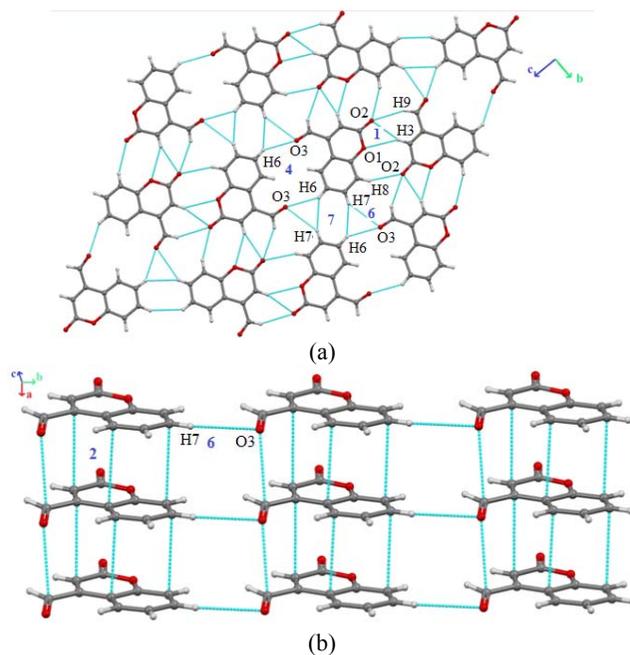


Figure 3. Packing of the molecules in C-1 showing (a) formation of sheets in the bc plane (b) stacking of the molecular down the ab plane

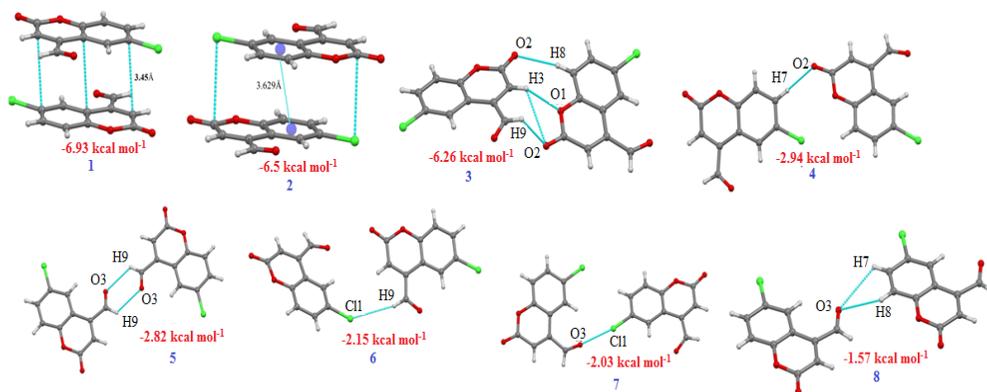
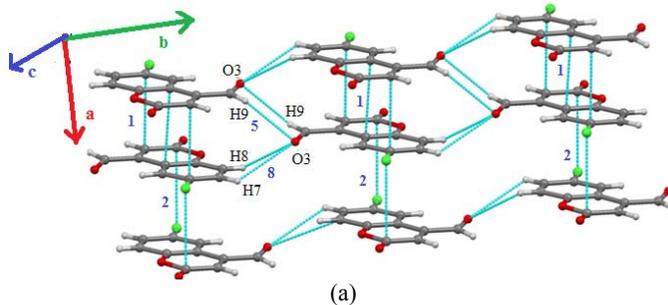


Figure 4. Molecular pairs (1-8) along with their interaction energies in C-2



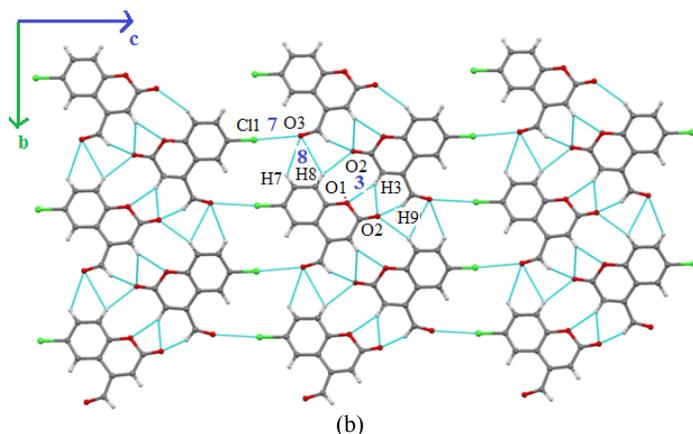


Figure 5. Packing of the molecules in C-2 showing (a) stacking of the down the ab plane (b) molecular chains interconnected via Cl...O interaction

7-Chloro-4-formylcoumarin (M-3)

The principal stabilizing molecular pairs (1-8) imparting maximum stabilization to the crystal are presented in Figure 6. The packing of the molecules in M-3 involves the stacking of the molecules along crystallographic a axis via pairs 1 and 2, contributing -7.45 and -6.16 kcal mol⁻¹ respectively towards stabilization. Molecular stacks so formed are then interlinked via dimeric bifurcated C-H...O hydrogen bonds exhibited by motifs 3 and 5, forming layers in the ab plane as shown in Figure 7. Motif 3 (I.E.= -5.32 kcal mol⁻¹) involves the interaction of bifurcated donor atom H8 with O1 and O2 whereas motif 5 involves the interaction of H5 and H6 with bifurcated acceptor atom O3. Motif 4 involves carbonyl carbonyl interaction (C=O...C=O) and makes a contribution of -4.97 kcal mol⁻¹ towards the stabilization, with the maximum contribution coming from dispersion energy (60%). Motif 6 contributing -3.37 kcal mol⁻¹, shows the presence of weak C-H...O hydrogen bond involving H3 with O2. Motif 7 and 8, both showing the presence of hydrogen bonds with halogens, were also found to make almost equal contributions of -1.57 and -1.24 kcal mol⁻¹ respectively towards crystal stability. Dispersion energy makes maximum contribution towards the stabilization of these motifs (Table 4), thereby indicating the dispersive nature of the halogen bonded interactions.

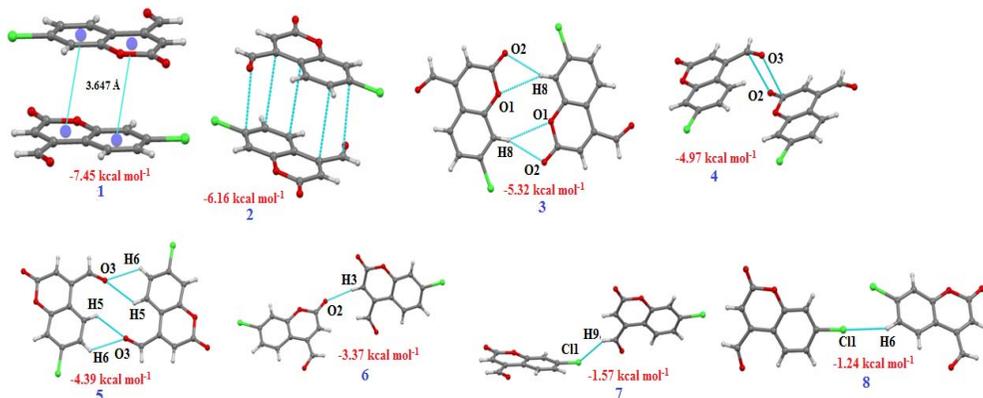


Figure 6. Molecular pairs (1-8) along with their interaction energies in C-3

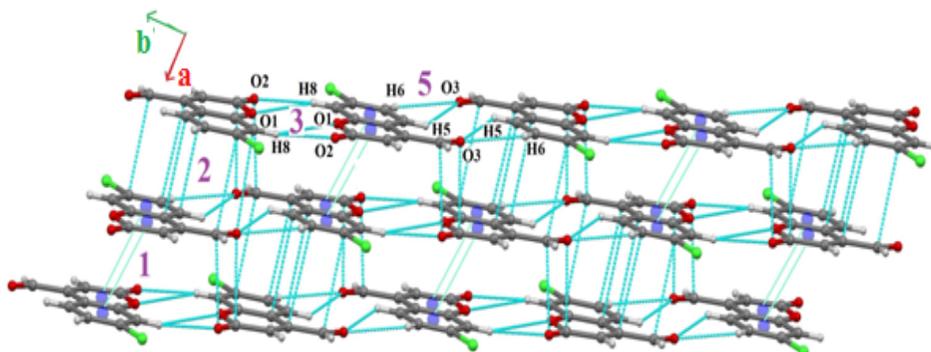


Figure 7. Packing of the molecules in C-3 down the ab plane

7-Bromo-4-formylcoumarin (M-4)

The principal stabilizing molecular pairs (1-6) extracted from the crystal packing after PIXEL calculation are shown in Figure 8 along with their respective stabilizing energies. The crystal structure involves the formation of molecular chains along the crystallographic *c*-axis, utilizing motif 1 and motif 5. Motif 1 having the highest energy stabilization of $-6.59 \text{ kcal mol}^{-1}$ (50% contribution from coulombic component), shows the presence of $\text{C}(\text{sp}^2)\text{-H}\dots\text{O}$ hydrogen bonds, whereas another $\text{C}(\text{sp}^2)\text{-H6}\dots\text{O3}$ hydrogen bond along with $\text{C}(\text{sp}^2)\text{-H5}\dots\text{Br1}$ binds the molecules in motif 5 ($-3.06 \text{ kcal mol}^{-1}$). The molecular chains so formed, are then stacked along *a*-axis via motif 2 ($-6.21 \text{ kcal mol}^{-1}$), 3 ($-6.07 \text{ kcal mol}^{-1}$) and 4 ($-4.71 \text{ kcal mol}^{-1}$), forming layers down the *ac* plane as shown in Figure 9a. Motif 4 involving $\text{C}=\text{O}\dots\text{C}=\text{O}$ interaction is similar to motif 4 of M-3, energy contributions are also almost same (-4.97 and $-4.71 \text{ kcal mol}^{-1}$). The packing in the crystal also displays the formation of zig-zag chains along *b*-axis via motif 1 and 6 ($\text{C}=\text{O}\dots\text{Br}-\text{C}(\text{sp}^2)$, $-1.07 \text{ kcal mol}^{-1}$). The zig-zag chains are then interconnected via motif 5 ($-3.06 \text{ kcal mol}^{-1}$) generating molecular sheets in the *bc* plane (Figure 9b).

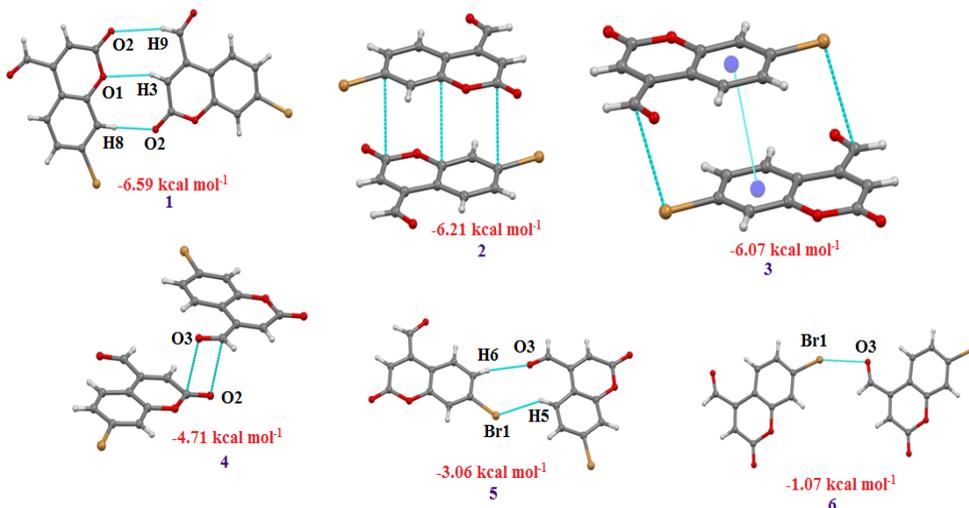


Figure 8. Molecular pairs (1-6) along with their interaction energies in C-4

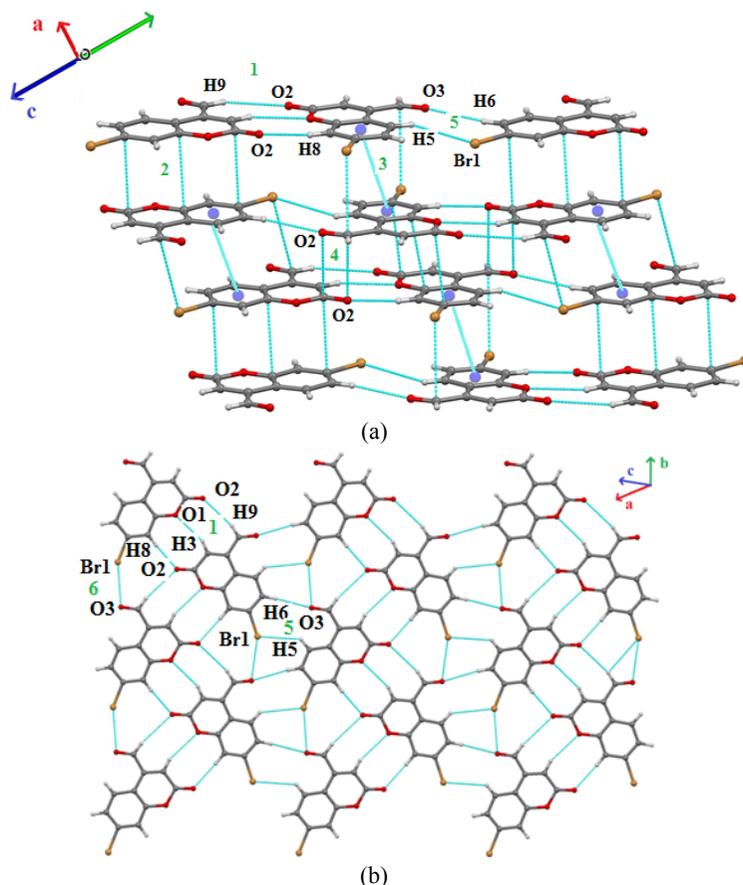


Figure 9. Packing of the molecules in C-4 showing (a) stacking of the molecules along a-axis (b) zig- zag chains formed by C-H..... O hydrogen bonds

6-Fluoro-4-formylcoumarin (M-5)

The important structural motifs (1-8) having significant energy contribution towards stabilization are shown in Figure 10 along with their stabilization energies. The maximum stabilization to the structure comes from weak but directional C-H...O=C hydrogen bond involving H8 with O2 (motif 1, Figure 10), forming dimers across the centre of symmetry with an interaction energy of $-6.09 \text{ kcal mol}^{-1}$ (with 54% coulombic component). These dimers are then connected via weak dimeric C-H...F hydrogen bonds involving H5 with F1 (motif 8, I.E = $-1.5 \text{ kcal mol}^{-1}$) forming chains along a axis. The chains so formed are interlinked via stacking interactions (motif 3 and 4, both having similar interaction energies of -3.89 and $-3.82 \text{ kcal mol}^{-1}$ resp., with maximum dispersion contribution) along with C=O...C=O interaction (motif 2, identical to motif 4 of M-3 and M-4) having stabilization energy of $-4.97 \text{ kcal mol}^{-1}$ (Figure 11a). The packing in the crystal also involves the formation of molecular chains via C(sp²)-H3...F1 (motif 6), contributing $-2.74 \text{ kcal mol}^{-1}$ (with significant coulombic and dispersion component) towards stabilization of the crystal structure. The molecular chains are then interconnected with more stabilized motif 2 (I.E. = $-4.97 \text{ kcal mol}^{-1}$) as shown in Figure 11b.

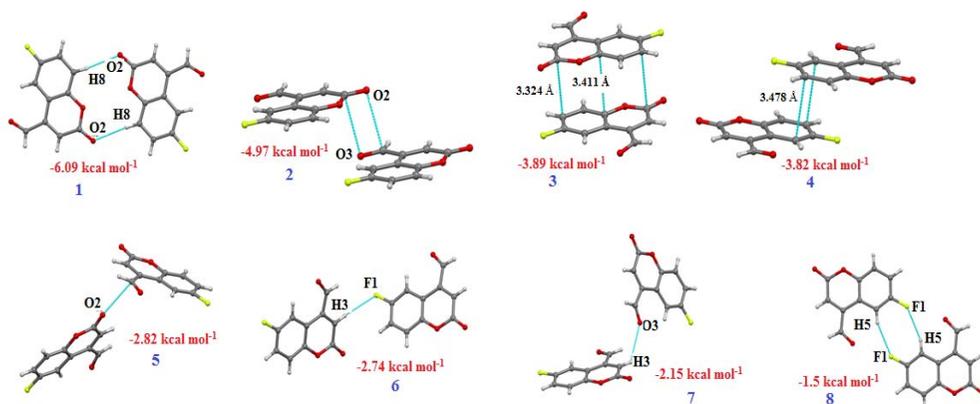


Figure 10. Molecular pairs (1-8) along with their interaction energies in C-5

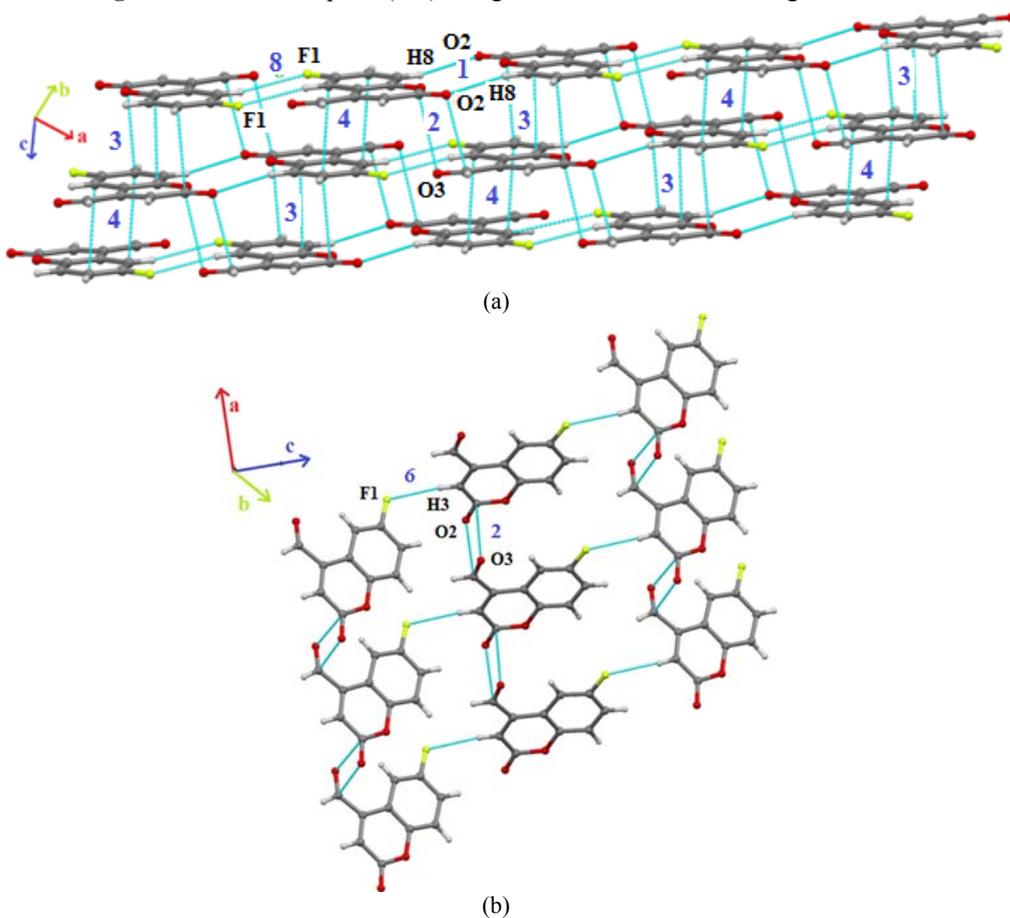


Figure 11. Packing of the molecules in C-4 depicting (a) stacking of molecules chains formed via C-H...F and C-H...O hydrogen bonds (b) formations of chains via C-H...F hydrogen bonds

7-Fluoro-4-formylcoumarin (*M-6*)

Molecular pairs (1-8) imparting maximum contribution to the crystal structure are presented in Figure 12 along with their interaction energies. The packing in the crystal structure displays the formation of molecular chains along the crystallographic *a*-axis via dimeric C(sp²)-H8...O2 hydrogen bonds as exhibited by molecular pairs 2 (-6.33 kcal mol⁻¹, with mostly coulombic contribution) and 6 involving dimeric C(sp²)-H5...O3 (-4.04 kcal mol⁻¹, with almost equal contribution from coulombic and dispersion energies). The molecular chains so formed are then linked via motifs 1, 7 and 8 (Figure 13a). Motif 1, the most stabilized pair in the structure, shows the presence of dimeric C(sp²)-H3...O2 hydrogen bonds and contributes -8.36 kcal mol⁻¹ towards steric stabilization of the structure. Motif 7 (-2.13 kcal mol⁻¹) involves the presence of dimeric C(sp²)-H6...F1 while another C9-H9...F1 hydrogen bond links the molecules in motif 8 (-0.55 kcal mol⁻¹). The third and fifth molecular pairs, stacked alternatively along the crystallographic *b*-axis, have contribution of -5.13 and -4.52 kcal mol⁻¹ to the stabilization of the crystal packing. Adjacent stacks are then connected via dimeric C(sp²)-H3...O2 (motif 1) and dimeric C(sp²)-H6...F1 (motif 7) intermolecular hydrogen bonds (Figure 13b).

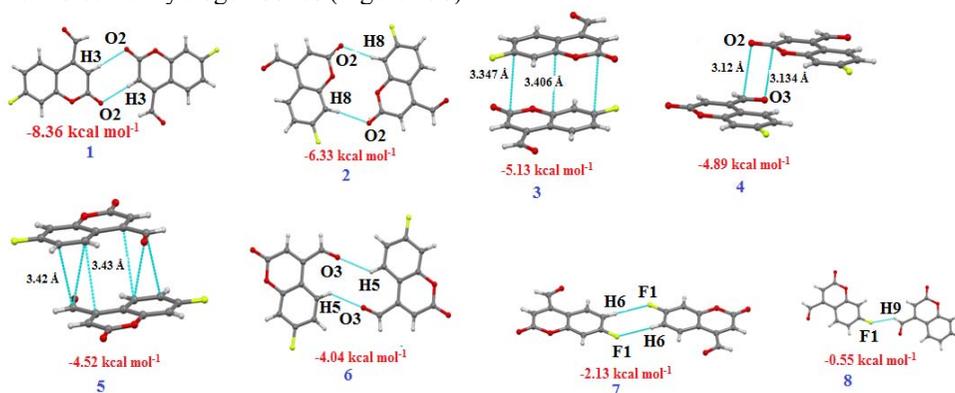
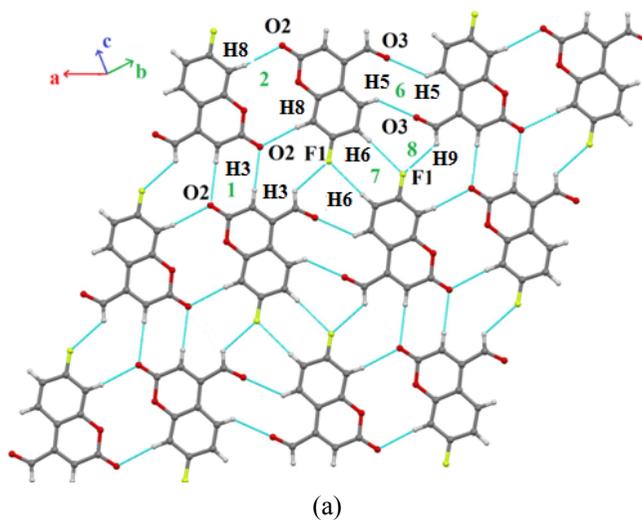


Figure 12. Molecular pairs (1-8) along with their interaction energies in C-6



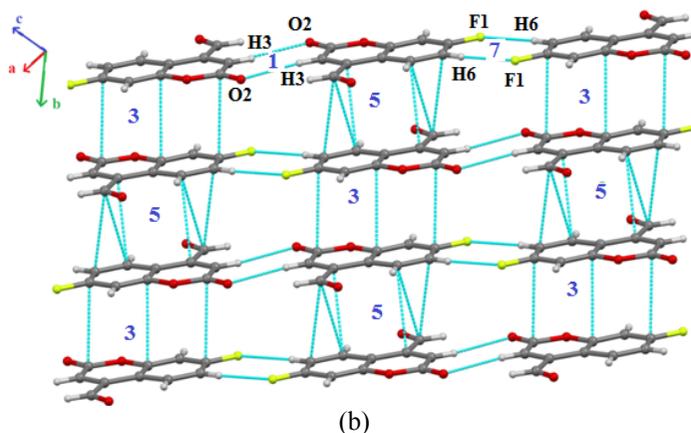


Figure 13. Packing of the molecules in C6 depicting (a) molecules chains formed via C-H...O hydrogen bonds (b) stacking of the molecules down the b-axis

A careful analysis of some key supramolecular motifs as obtained in these compounds leads to the following relevant observations:

1. The lattice energy of the structures lies in the range -21 to -25 kcal mol⁻¹ with maximum contribution from dispersion component.
2. The maximum stabilization to the crystal structure is imparted by molecular motifs interacting via C-H...O or π ... π stacking interaction.
3. The energy of molecular pairs interacting via π ... π lies in the range -6 to -7.5 kcal mol⁻¹ with almost 70-90 % contribution from dispersion component.
4. Dimeric C-H...O hydrogen bonds are also found to have significant role in the stabilization of the packing and makes an essential contribution of -3 to -8 kcal mol⁻¹ towards stabilization.
5. Motifs interacting via dimeric C=O...C=O interaction contributes almost -5 kcal mol⁻¹ towards stabilization and the principal stabilization of around 55-60% corresponds to dispersion component.
6. Weak intermolecular interactions involving halogen atom C-H...X (Cl, Br, F) is also found to make small but significant contribution towards the stabilization of the packing.

Conclusion

The present work describes the nature and energetics of weak intermolecular interactions that operate between organic molecules and cause them to condense to form ordered crystalline solids. A better understanding of these interactions operating between the atoms that help molecules to associate with each other will play an important role in the field of Crystal Structure prediction, where one tries to predict the structure of unknown crystals. PIXEL calculations enable us to distinguish several kinds of interaction that seems to play more or less important roles in the stabilization of the crystal structure.

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