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**AB INITIO PREDICTION OF PLAUSIBLE CONFORMERS OF A FLEXIBLE
N-(3-CHLORO-4-FLUOROPHENYL)THIOUREA (CFT) MOLECULE:
A VALIDATION STUDY****A.D. Stephen¹, P.V. Nidhin¹, P. Srinivasan²**¹*Department of Physics, Sri Shakthi Institute of Engineering and Technology, Coimbatore, India*
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The current aim of the *ab initio* crystal structure prediction is to find the possible conformers of the flexible N-(3-chloro-4-fluorophenyl)thiourea (CFT) molecule using gas phase optimisation with an MP2/6-31G(*d,p*) basis set, and the lattice energy minimization in the presence of a repulsion-dispersion electrostatic potential. If the molecule deviates from the gas phase conformation, suitable intermolecular interactions are added, and the molecule favours stable packing. The crystal structure is said to be feasible if the intermolecular lattice energy compensates the intermolecular energy penalty associated with the suboptimal gas phase conformers. The idea of the current research is to find the least energy hydrogen bonded crystal structure from a set of rigid conformers in a conformation region, with a significant similarity of packing, which may lead to the prediction of polymorphs associated with the considered CFT molecule.

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Keywords: *ab initio* crystal structure prediction, lattice energy minimisation, polymorphism.**INTRODUCTION**

The key importance of the *ab initio* crystal structure prediction method lies in the application area where a successful prediction method can give a good understanding of the crystallisation process [1], and also the prediction of highly energetic molecules might decrease the level of experimental risks. It also got much importance in the field of pharmaceuticals where the prediction of organic drug molecules with a specific action may create a revolution. Organic drug molecules are flexible compared to CHNO-based energetic crystals. Such flexible molecule have the tendency to show high degrees of polymorphism. The presence of a polymorph of an organic molecule in a crystal structure can differently affect the action of the organic molecule or alter the molecular geometry [2], which may lead to the development of a new drug or to opt out the negative effect of the concerned drug system. The crystal structure prediction method allows the theorists to discover new polymorphs of such molecules. In a different way, some polymorphs can have good application values. Recently, in the report on the fifth blind test, Price et al. have analyzed the polymorphic hydrate of gallic acid mono hydrate [3] by reducing the search space to a more manageable level and by identifying possible ranges of values for flexible torsions. Therefore, it is highly important to predict stable polymorphs that are very difficult to observe in experiments. Since some polymorphs are in transition states, the *ab initio* crystal structure prediction method with an accurate potential energy function [4] proves to be successful in predicting polymorphs.

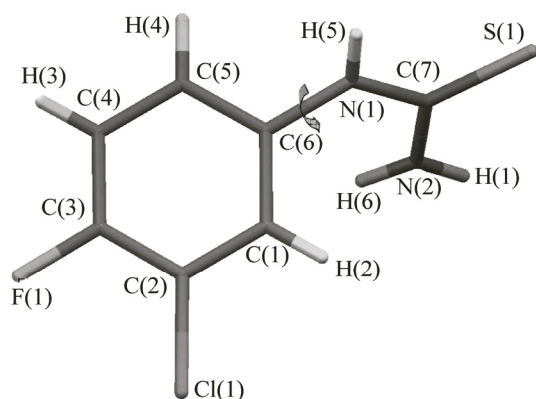


Fig. 1. Molecular structure of an N-(3-chloro-4-fluorophenyl)thiourea (CFT) molecule showing the relaxed torsion angle

The important challenge faced in the *ab initio* prediction of stable conformers closest to the global minimum is to find the flexible torsion creating the search space. The conformers produced in the crude space need an analysis and a calculation of the minimised lattice energy and the intermolecular lattice energy penalty which satisfies the relation

$$E_{\text{tot}} = U_{\text{lattice}} + \Delta E_{\text{intra}} \quad (1)$$

The relation can be used to find the thermodynamic stability of the conformers [5].

Thiourea derivatives are mostly used as steel corrosion inhibitors and as antioxidants. The introduction of a thiourea system into a polymer has many applications [6]. In the current studies the attempts were made to find the lowest energy conformer of the thiourea system N-(3-chloro-4-fluorophenyl)thiourea (CFT) (Fig. 1) from the structures generated in a potential energy scan, identifying the ranges of occurring plausible conformers. The potential energy surface scan is made after the selection of the key torsion angle of the molecule. The conformational space region can be identified using these sets of torsion angles. Each conformation generated in the estimated conformational space is taken as a single rigid molecule and optimized by minimizing the lattice energies using an intermolecular potential. The evaluation of E_{tot} , U_{lattice} , and ΔE_{intra} can be used to find the stable conformers having almost reasonable cell parameters and lattice energies with respect to the experimentally generated crystal structures. The search for the low energy structures can be expanded over more space groups within which an exact result can be reproduced.

METHODOLOGY

An *ab initio* calculation of a flexible N-(3-chloro-4-fluorophenyl)thiourea (CFT) molecule was carried out at the MP2 level of theory and the conformational optimizations were performed using Gaussian 03 [7] with a 6-31G(*d,p*) basis set to find out the stable structure. A distributed multipole analysis was made for each conformer from the charge density description using the GDMA program [8]. The present study mainly deals with a set of constrained conformers in which the key torsion angle [9] is relaxed while the rest of the molecule was kept frozen (cons), along with experimental conformers (expminexp) with hydrogen atoms restricted to neutron diffraction values.

The global search for space groups ($P2_1/c$, $P\bar{1}$, $C2/c$, $Pbcn$, $P2_12_12_1$, $P2_1$, etc.) of the low energy structures were performed using MOLPAK [10] to find the close-packed structures within the energy range. The structures with the least energy and their space groups, mostly $P2_1/c$, $P\bar{1}$, $C2/c$, were selected based on ΔE_{intra} and the lattice energy minimized using the DMACRYS algorithm [11]. The Ewald summed [12] energies in terms of charge-charge, charge-dipole, and dipole-dipole terms were also calculated together with the volume and density of the selected structures using the repulsion-dispersion potential

$$U = \sum_{i \in 1} \sum_{k \in 2} \sqrt{(A_{ik} A_{kk})} \exp[-(B_{ii} + B_{ik})R_{ik} / 2] - \sqrt{(C_{ii} C_{kk})} / R_{ik}^6, \quad (2)$$

where i and k are the atoms in molecules 1 and 2 of different types.

All the lattice energy minimized conformers are thoroughly analyzed and compared with the experimental molecule (within a range of few kJ/mol), to determine the exactness of the lattice minimized molecules. The conformers that did not reach the true minimum usually can be revealed to be in transition states and were discarded from the scenario. The analyzed stable molecular structures which were found to exactly correspond to the experimental molecule were visualized using Mercury [13] to determine the packing similarity of the conformers. From all the above analytical studies, the con-

Table 1

Constrained conformers (expmincon) with the corresponding torsion angles and the energy deviation from the local minima

| Torsion angle (θ) | Energy difference, kJ/mol | Torsion angle (θ) | Energy difference, kJ/mol | Torsion angle (θ) | Energy difference, kJ/mol |
|----------------------------|---------------------------|----------------------------|---------------------------|----------------------------|---------------------------|
| -180 | 6.05684 | -40 | 0.64067 | 80 | 3.21254 |
| -160 | 11.63098 | -20 | 3.0444 | 100 | 3.39978 |
| -140 | 16.59135 | 0 | 7.39151 | 120 | 0.81864 |
| -120 | 0.78803 | 20 | 12.76693 | 140 | 0 |
| -100 | 3.30596 | 40 | 18.06644 | 160 | 1.78733 |
| -80 | 3.43305 | 60 | 0.54231 | 180 | 6.05676 |
| -60 | 0.84676 | | | | |

formers with space groups compared to the experimental CFT molecule can be taken as polymorphs of the corresponding structure.

RESULTS

Searching for the conformational space (Scan for the potential energy surface). The scan for the potential energy surface was carried out by relaxing the C(1)—C(6)—N(1)—C(7) torsion angle and rest of the molecule were fixed to the experimental geometry [14]. Each scan is considered as a series of the partial gas phase optimization with the relaxed torsion angle and rest of the molecule was under the freezing condition. One of the challenges with the *ab initio* studies of flexible molecules is the existence of a conformational barrier that may allow the molecule to change the confirmations. From the PES scan studies the location of local minima can be clearly identified, hence the selection of possible stable conformers can be more specific.

The PES scan plot calculated the minimum energy for each angle and the local minima were found for the conformer with a torsion angle of 140°. The energy peaks visible at the plot between the energy difference (compared to the local minima, Table 1) and the angle (Fig. 2) show the unstable conformers of the considered CFT molecule.

The structures formed in the trough region were expected to be more stable conformers, with the least energy difference corresponding to the global minima. The conformer generated in the potential energy surface scan with a torsion angle of 140° is found to be the least energy conformer in which N(2) approaches the π density region of the C(5) atom and comes out of the central ring plane. The highest peak at a torsion angle of 40° indicates a conformer with less stability in which the N(2) atom goes away from the π density region of the C(5) atom and the corresponding nitrogen atom is fully eclipsed by the central aromatic ring. The search space was selected from the troughs of the PES scan plot. The selection of the expected stable constrained conformers was made within the energy difference <0.9 kJ/mol.

Reproduction of the crystal structures. The intermolecular potential used here was validated from the reproduction of the CFT crystal structure by the lattice energy minimization, using the experimental (expminexp) and constrained (expmincon) confor-

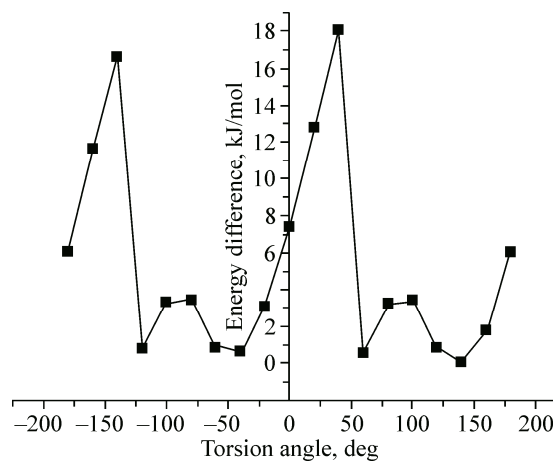


Fig. 2. PES plot between the energy difference (kJ/mol) compared to the local minima and the torsion angle (θ) for the CFT molecule

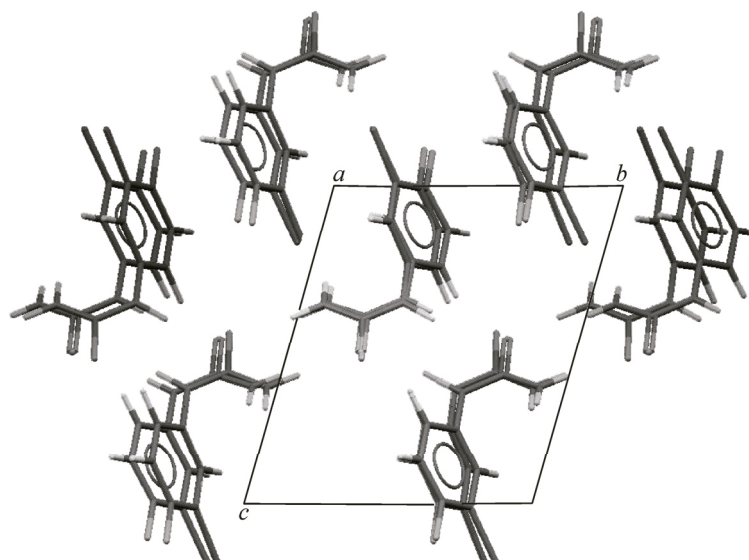


Fig. 3. Packing similarity of the conformer (expminexp) and the experimental CFT molecule, with an rmsd value of 0.448 and 20 % tolerance

mers of CFT structures in which the selected torsion angle C(1)—C(6)—N(1)—C(7) was allowed to be free and rest of the molecule are fixed at the experimental values. The resulting rigid conformers were selected, compared, and overlaid with the experimental structure to find the root mean square deviation in the packing similarity with 20 % and 10 % tolerance Fig. 3. The conformer generated at the torsion angle of 60° shows a deviation percentage of 0.5, 1.2, and 3.4 to the α , β , and γ values from the experimental CFT structures respectively. The reproduced conformer with the torsion angle of -60° had a deviation of 1.2, 3.5, and 5.8 % with the a , b , and c values of the experimental structure. The deviation from the experimental structure indicates the importance of considering other flexible torsion angles to determine the crystal packing. The remaining reproduced conformers showed a comparatively less deviation of the cell parameters from the experimental crystal structure, which indicates the torsion angle considered here to be more vital in determining the packing and stability.

Relatively least energy conformers are reproduced at -120° and 120° angle steps, with a comparatively higher deviation of $\sim 1.2\%$ in the packing similarity with the cell density lower than that of the experimental (expminexp) conformer by $\sim 0.032 \text{ g/cm}^3$, while all other reproduced conformers had the density almost coinciding with that of the experimental (expminexp) conformer. It was found that for the above described conformers the b values were highly reduced or contracted with respect to the reference structure. This may be due to the effect of pressure in the concerned direction of the experimental structure. The minimized lattice energies U_{lattice} of the conformers listed in Table 2 indicate the stability of the conformers. The crystal conformer with the angle of 60° shows the lattice energy close to the experimental value, which demonstrates that the molecule is much more thermodynamically stable when compared with the rest of the generated conformers. The discrepancies in the minimized lattice energies may be due to the sensitivity of the lattice energy to molecular conformations [15].

Search for the low-energy conformers. The most stable conformer was expected to be formed in the deep trough of the PES scan plot, where the condition $E_{\text{tot}} = U_{\text{lattice}}$ satisfied [16]. The gas optimized conformer was subjected to the lattice minimisation using DMAREL package and the lowest energy structure which expected to be more stable compared to rest of the structure has the minimised U_{lattice} energy value of -152.15 kJ/mol .

The PES scan was executed by making the C(1)—C(6)—N(1)—C(7) torsion angle relaxed and fixing the rest of the molecule fixed as in the experimental data. The angles were constrained at 20° intervals from -180° to 180° . The most expected stable conformers of the CFT molecule are in the energy range near to the global minima, (i.e.) the structures with ΔE_{intra} below 0.9 kJ/mol . All such

Table 2

Comparison of the cell parameters with the experimental structure, experimental conformers (expminexp) and constrained conformers (expmincon). The first row shows the conformers with the same space group with 20 % tolerance and the second row shows the lowest energy conformer at each step of the PES scan

| Angle, deg. | <i>a</i> | <i>b</i> | <i>c</i> | α | β | γ | Cell volume, Å ³ | U_{lattice} , kJ/mol | Packing rmsd |
|--------------|----------|----------|----------|----------|---------|----------|-----------------------------|-------------------------------|--------------|
| Experimental | 5.4642 | 8.3919 | 9.6469 | 105.228 | 94.455 | 95.321 | 422.584 | | |
| Expminexp | 5.6149 | 7.7408 | 9.5834 | 104.9591 | 91.1407 | 92.1946 | 401.930 | -176.42 | 0.448 |
| Expmincon | | | | | | | | | |
| 60 | 6.031 | 7.795 | 8.948 | 104.373 | 93.335 | 92.075 | 406.259 | -154.740 | 0.663 |
| | 6.395 | 7.751 | 16.281 | 90.000 | 83.465 | 90.000 | 801.770 | -157.735 | 0.862 |
| -40 | 5.317 | 7.967 | 11.310 | 119.412 | 89.363 | 90.825 | 417.292 | -143.624 | 0.606 |
| | 5.412 | 7.862 | 19.595 | 90.000 | 89.931 | 90.000 | 833.774 | -145.542 | 0.544 |
| -120 | 5.724 | 9.262 | 8.314 | 102.884 | 97.665 | 90.585 | 425.462 | -104.155 | 0.775 |
| | 6.811 | 4.026 | 15.220 | 75.951 | 97.056 | 92.533 | 409.713 | -149.551 | 1.126 |
| 120 | 5.617 | 9.273 | 8.545 | 94.492 | 101.847 | 92.149 | 433.574 | -104.960 | 0.790 |
| | 6.859 | 3.999 | 15.464 | 103.257 | 97.544 | 87.045 | 409.225 | -149.684 | 1.193 |
| -60 | 5.398 | 8.102 | 10.243 | 105.845 | 82.144 | 100.689 | 421.730 | -130.031 | 0.452 |
| | 6.414 | 7.754 | 16.798 | 90.000 | 105.842 | 90.000 | 803.674 | -156.871 | 0.836 |

Table 3

Selected crystal structures with the lowest energies (E_{tot}) and considerable packing rmsd values (15-molecule coordination sphere) in the conformational region of the computational search

| Conformers label | Space group | E_{tot} , kJ/mol | Volume, Å ³ | Packing rmsd |
|------------------|-------------|---------------------------|------------------------|--------------|
| AM | $P2_1/c$ | -157.198 | 801.770 | 0.862 |
| CA | $P\bar{1}$ | -154.202 | 406.259 | 0.663 |
| FA | $P2_1/c$ | -152.149 | 832.495 | 0.619 |
| CA* | $P\bar{1}$ | -149.582 | 406.058 | 0.801 |
| AB | $P\bar{1}$ | -149.582 | 406.076 | 0.801 |
| FC | $P2_1/c$ | -147.670 | 795.406 | 0.619 |
| AK | $P2_1/c$ | -145.933 | 800.509 | 0.619 |
| DE | $C2/c$ | -144.895 | 1663.733 | 0.877 |
| DD | $C2/c$ | -143.798 | 1746.208 | 0.619 |
| DC | $C2/c$ | -143.805 | 1746.222 | 0.619 |
| AI | $P2_1/c$ | -143.688 | 821.831 | 0.619 |
| CC | $Pbca$ | -143.187 | 1784.206 | 0.619 |

CA* — the conformer reproduced at torsion angle of 140° with space group $P\bar{1}$.

conformers have been analyzed in detail and tabulated (Table 3). The lowest energy conformer calculated from the PES scan of the gas phase optimization was used to find the set of stable space groups compared to the local minima using the MOLPAK-DMAREL package. From all these calculations, 20 conformers were refined.

The comparison of the plot (Fig. 4, *a* and *b*) of U_{lattice} and E_{tot} with the steps of torsion angles at each search gives the idea about the crude regions of the conformational space where the presence of

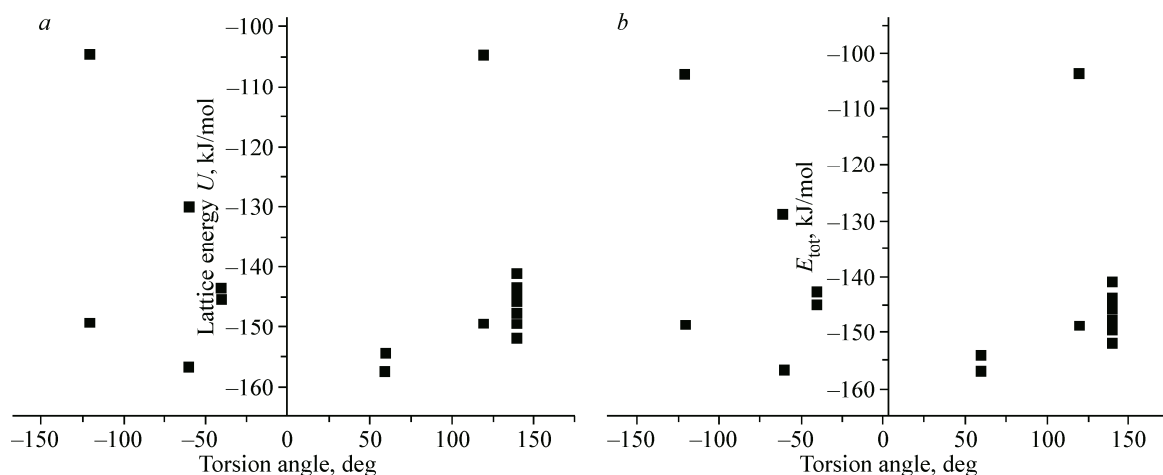


Fig. 4. Plot of U_{lattice} (a) and E_{tot} (b) with steps of the torsion angle

stabilizing conformers can be more expected, and it is clear from the plot that some of stable CFT conformers from the gas phase optimization do not make stable crystal structures.

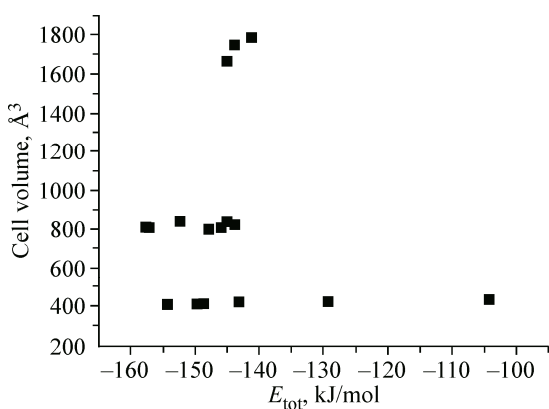
The plot (Fig. 5) of E_{tot} and the cell volume (\AA^3) clearly shows that the majority of the conformers are reproduced in the energy region ranges from -140 to -160 kJ/mol, which increases the chance of expecting a much more stable conformer in that crude region. From the comparison of all the plots and the energy values, it can be estimated that the most stable conformers can be produced in the above energy region.

Analysis of low energy structures. From all the comparisons made, structures are selected according to E_{tot} and the packing rmsd values. The list of the lowest energy conformers generated from the *ab initio* prediction studies are detailed in Table 3.

Table 4 shows that the conformers which are likely to be stable and reproduced within a short range of the global minima correspond to the experimental structure. It is clear from Fig. 5 that very similar structures are generated in the conformational region of $\Delta E_{\text{intra}} < 0.9$ kJ/mol. A detailed analysis of the lowest energy structures is made by considering the formation of H bonds within the crystal structure: the more the number of H bonds, the higher the stability.

From a comparison the H bond motif of all the conformers it is seen that certain hydrogen bond motifs frequently appeared in all crystal structures, mainly showing the interaction between nitrogen and sulfur atoms which plays the key role in the stability of the crystal structure.

Certainly, the possibilities of the occurrence of many H bonds within the conformation space can result in conformational polymorphism which is thermodynamically feasible. The detailed analysis of possible hydrogen bond motifs for the experimental structure of CFT molecules shows that the crystal structure is mainly stabilized by the N—H \cdots S hydrogen bond having N(1) and N(2) as donors and



S(1) as the acceptor. There are two ring motifs ($R_2^2(8)$ and three chain motifs ($C_2^1(6)$, $C_2^2(8)$ and $C_4^3(14)$). It is found that both ring and chain motifs rise from the N(1)—H(5) \cdots S(1) and N(2)—H(1) \cdots S(1) hydrogen bonds and also exhibit a zigzag manner of packing in the crystal structure of the molecule.

The comparative study of the experimental conformer (expminexp) with the experimental molecules

Fig. 5. Plot of E_{tot} and U_{lattice} of the crystal conformers selected within 0.9 kJ/mol ΔE_{intra}

Table 4

Mechanical stiffness analysis of the predicted conformers and the experimental conformer

| Predicted conformer | Diagonal elements of the elastic stiffness tensor matrix C_{ij} , GPa | | | | | | Young's modulus, GPa |
|---------------------|---|---------|--------|--------|--------|--------|----------------------|
| | C11 | C22 | C33 | C44 | C55 | C66 | |
| Expminexp | 35.334 | 59.011 | 57.338 | 45.06 | 28.806 | 24.726 | 46.2 |
| AM | 32.514 | 54.505 | 51.541 | 35.837 | 25.206 | 21.426 | 42.7 |
| CA | 34.272 | 50.2471 | 44.862 | 30.605 | 27.107 | 24.169 | 39.4 |

shows the exact similarity in the case of hydrogen bond motifs, proves that these common motifs $R_2^2(8)$, $C_2^1(6)$, $C_2^2(8)$ and $C_4^3(14)$ play a key role in the stability of the molecule.

Similar studies were extended to analyze the constrained conformers (expmincon), which show that almost all conformers have the similar hydrogen motifs, except some extra motifs observed for AM, AE, DE, and CA conformers where an N(2)—H(6)···Cl(1) hydrogen link was observed for CA conformers. The presence of this bond means that the concerned conformer is more stabilized than the rest of the reproduced conformers. The presence of additional 17 hydrogen bond motifs for DE and AI conformers, where most of the interaction is between N(2) and S(1), shows that these two conformers might be in a transition state which soon transits to much more stable space groups.

Stability of the lowest energy conformers. Most CSP techniques assume that the most stable polymorphs appear in the lowest energy region of the lattice energy surface, as stated by G.M. Day [17]. The same selection was made in this current scenario where the most stable geometrical conformers were assumed to be in the lowest lattice energy region of the energy surface. As explained in the Eq. (1), within $\Delta E_{\text{intra}} < 0.9$ kJ/mol of the global minimum the geometric conformers can be assumed to be stable and overcome the energy penalty to reach the global minimum. Thus, the least energy conformers within the region generated via the *ab initio* CSP methodology were selected and their stable nature was studied through the analysis of hydrogen bond motifs, as in the previous section. The studies revealed the almost exact similarity with the experimental CFT molecule and justified the reasonable stability of the predicted structures. Furthermore, the studies were carried out to analyze the properties of the second derivative of the predicted conformers from the Hessian matrix. They show that the structures achieved the Born criteria of stability, which reflects the thermodynamically stable nature of the theoretical structures. Table 4 shows the comparison of the mechanical properties via the diagonal elements of the C_{ij} matrix [18].

The most stable conformer reproduced was found to be AM with the space group $P2_1/c$ at $E_{\text{tot}} = -157.19$ kJ/mol, with a packing rmsd value of 0.862 in 20 % tolerance. A better computer-generated stable conformer was found in the conformational region with E_{tot} of ~ -154.2 kJ/mol with a packing similarity of 0.663 (CA) in a 15-molecule coordination sphere at 20 % tolerance. This reproduction was found to be triclinic with the space group $P\bar{1}$. From the hydrogen bond analysis, the CA conformer can be taken as a better result because of the presence of the key hydrogen motifs such as $R_2^2(8)$, $C_2^1(6)$, $C_2^2(8)$ and $C_4^3(14)$ which play a vital role in stability. The lowest energy AM conformer lacks $C_2^2(8)$ and $C_4^3(14)$, which shows that the $P2_1/c$ space group can shift to the $P\bar{1}$ space group to acquire more stability.

Hirshfeld surface and vibrational analysis of the stable conformers. The studies to find short inter- and intramolecular contacts of the crystal structure have been carried out by analyzing the finger print plots of the experimental and predicted conformers. The comparative studies with the experimental structure revealed almost exact short contact regions for the predicted conformers, except the absence of F···H/H···F interactions with a contribution of 14.3 % to the Hirshfeld surface area [19] of the crystal structure using the Crystal Explorer package [20]. Figs. 6, 7 represent the 2D finger print plots for the experimental CFT molecule and the predicted conformers.

The analysis of the 2D finger print plot revealed the donor—acceptor interaction between the CFT sulfur and hydrogen atoms. The two spike portions in the low d_i and d_e region indicate the inter-

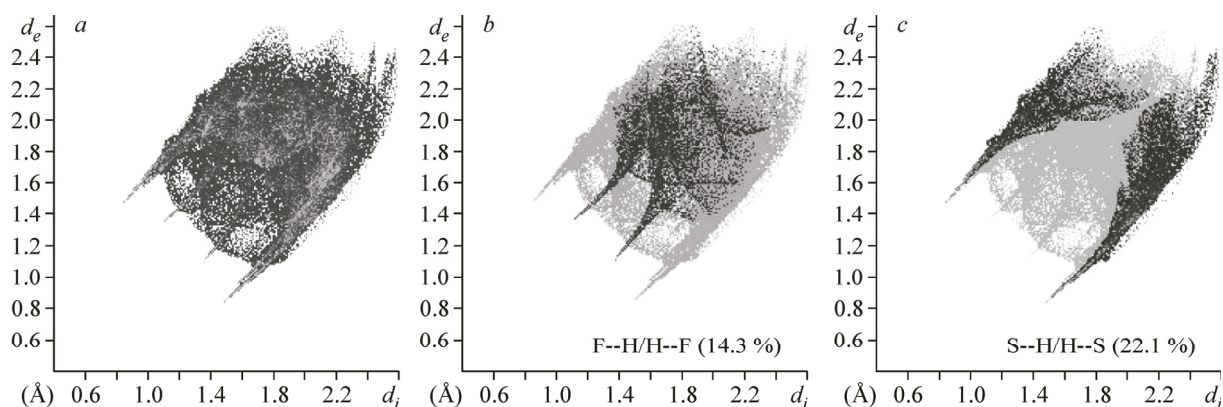


Fig. 6. 2D finger print plot for the experimental CFT molecule (a), full resolved $F\cdots H/H\cdots F$ interaction (b), resolved $S\cdots H/H\cdots S$ interaction (c), with the percentage of contributions to the Hirshfeld surface

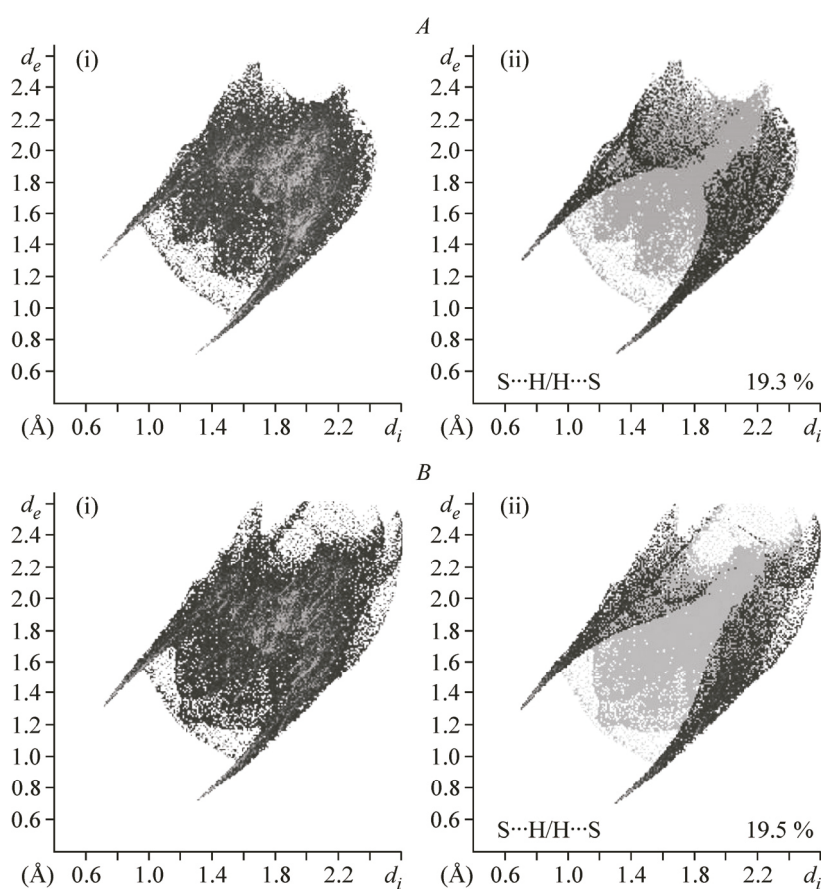


Fig. 7. 2D finger print plots for the predicted AM (A) and CA (B) conformers of the (i) full and (ii) resolved $S\cdots H/H\cdots S$ interaction and its percentage of contributions to the Hirshfeld surface area of CFT

actions. As it can be identified, for the experimental CFT molecule the $F\cdots H/H\cdots F$ interaction, which is found to be in a larger d_i , d_e region, can be considered as a weak interaction. Apart from this variation, the plot showed an approximate similarity with each other, which in turn justifies the stability.

The vibrational analysis of the lowest energy conformers to find the IR activity of the concerned rigid molecule was carried out using the Gaussian G09 package. The resulting spectrum analyzed with the GaussSum software indicated the absence of imaginary IR frequencies and a higher IR activity

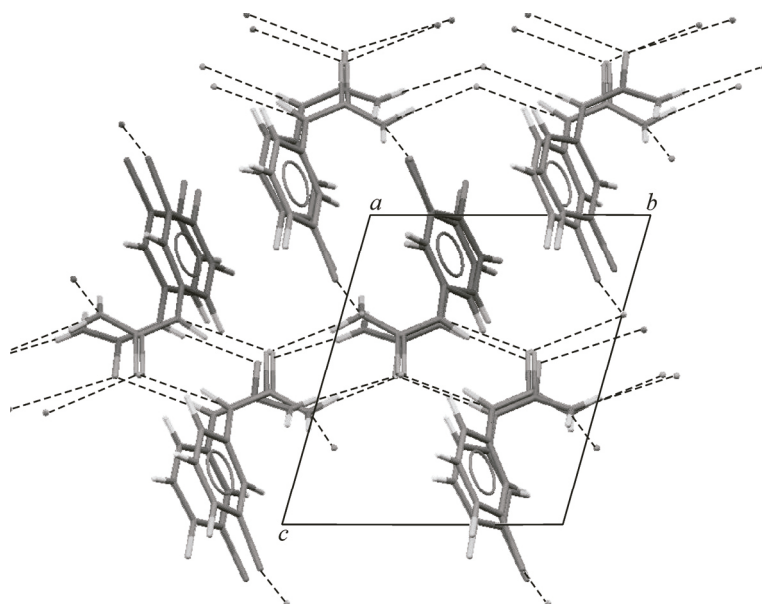


Fig. 8. Comparison of the experimental CFT structure with the stable least energy conformer generated by the MOLPAK-DMAREL energy minimization

were exhibited at a frequency of $\sim 4496 \times 10^{10}$ Hz almost as in the experimental CFT molecule (a higher IR deviation was found at $\sim 4400 \times 10^{10}$ Hz), giving evidence of the stable nature of the predicted geometric conformers. Fig. 8 represents the overlay between the experimental CFT molecule and the predicted least energy conformer with considerable accuracy.

DISCUSSION

The present approach to the crystal structure prediction involves the search for a conformational crude region within an energy penalty limit for stable conformers of the CFT molecule, which are separated by an energy barrier and closest to the global minima. Since the search area is considerably vast, selections were made to refine the generated results. Each structure in the conformational region was taken as a rigid molecule and subjected to the gas phase optimization and the lattice minimization to find the more accurate stable crystal structure. The search method using the MOLPAK algorithm is also aimed at the understanding of the space group of stable conformers, which gives a closer packing, and also at the analysis of hydrogen bond motifs in each rigid structures. Thus, this approach can be used to study the molecules capable of forming hydrogen bonds in their polymorphs.

CONCLUSIONS

The current methodology used for the *ab initio* prediction of possible hypothetical geometrical conformers of CFT in the lowest energy region by means of the global search mechanism of the MOLPAK algorithm and the lattice energy minimization of the hypothetical closest structures with distributed multipole analysis using DMACRYS package was found to be successful. The PES scan analyzed the plausible conformers within a flexible terminal torsion angle range from -180° to 180° . The global search using MOLPAK with only a repulsion potential, analyzes the structures within a energy penalty region less than 0.9 kJ/mol to find the closest hypothetical conformers using its unique orientation method. The selected closest hypothetical conformers generated from MOLPAK were subjected to the lattice energy minimization via the distributed multipole analysis implemented in the DMACRYS package within a dispersion repulsion potential field. Thus, the MOLPAK-DMACRYS optimized conformers were selected and compared with the parent molecule to analyze the stable nature. The properties of the second derivative of the molecule were also analyzed by the C_{ij} matrix and the vibrational spectrum analysis for IR radiations carried out to justify the structural sta-

bility of CFT. The nature of the shortest molecular contacts was studied using the 2D finger print plots of the molecule implemented in the Hirshfeld surface, showing the possible thermodynamic stability of the concerned CFT conformers. Thus, the conformers listed in Table 4 can be considered as possible polymorphs of CFT yet to be discovered.

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