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## Robustness of thioamide dimer synthon, carbon bonding and thioamide-thioamide stacking in ferrocene-based thiosemicarbazones

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### Abstract:

The role of thioureas in crystal engineering as robust supramolecular synthons is now recognized, but their analogs, namely thiosemicarbazones/*N*-imino thioureas, have not received the attention they deserve. A series of five structurally related ferrocene-based thiosemicarbazones **1-5** have been designed, synthesized and crystallographically characterized in order to investigate the prevalence of the thioamide dimer synthon and carbon bonding. All the compounds have shown a general preference for the adoption of the *cis*, *trans* conformation about the central thiourea moiety which is ideal for the formation of a dimeric hydrogen-bonded  $R_2^2(8) \{ \cdots H-N-C=S \}_2$  synthon as the building block. Therefore, this dimeric synthon is observed in all the compounds, with the methyl group particularly set for playing its supportive stabilization role through C-H $\cdots$ S and carbon bonding interactions. Carbon bonding has been observed in all of the compounds except compound **2**. The centrosymmetrically arranged thioamide protons present in *trans* conformation through N-H $\cdots$ H-C interactions give rise to the formation of tapes of varying topology in all the compounds except **3**, where a stair-case arrangement of dimeric molecules is observed. Another notable feature of the crystal packing of **1-5** is the presence of thioamide-thioamide stacking, which has been observed in all five compounds. The prevalence of the thioamide dimer synthon, carbon bonding, and observation of new thioamide-thioamide stacking interactions indicates a much larger role for this class of compounds as a design element in crystal engineering than anticipated so far.

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## Introduction

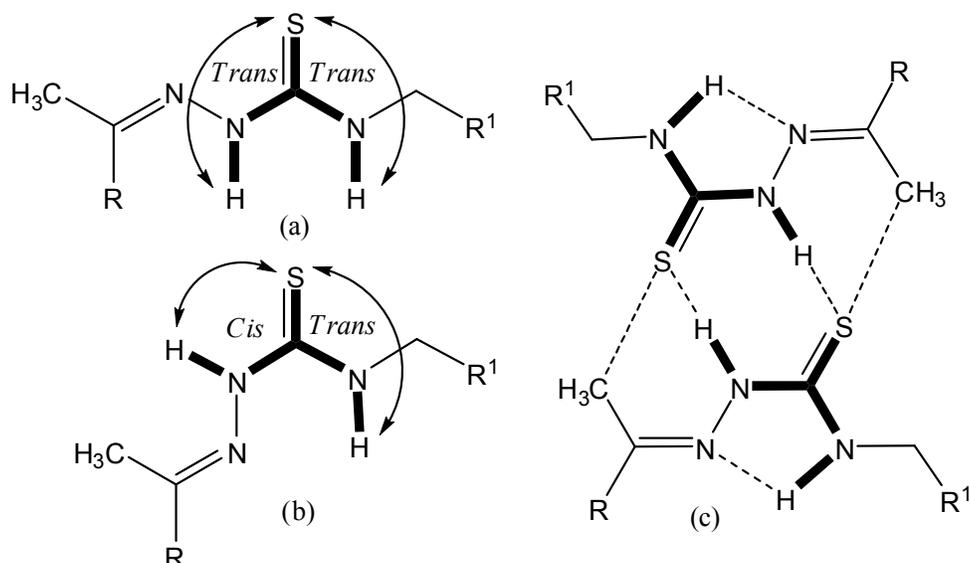
As function is always related to three-dimensional structure, the quest for supramolecular synthons in three dimensional networks is one of the main aims of crystal engineers to understand and explore the principles involved in the formation of that particular structure.<sup>1-20</sup> The acquired knowledge can then be used for the deliberate design of novel crystalline materials with desired properties.<sup>21-26</sup> For this purpose, however, highly consistent synthons with sufficiently directional intermolecular forces are required. Recently, urea and thiourea have attracted great attention as supramolecular synthons from the crystal engineering community, owing to the formation of persistent hydrogen-bonded chains in a variety of environments.<sup>27-35</sup> However, thioureas at one stage were underestimated and their potential in crystal engineering as a design element have been far less explored in comparison to ureas, perhaps due to the consideration of weaker hydrogen-bond accepting ability of the thiocarbonyl group than the carbonyl group.<sup>36-39</sup> More recently, it has been reported by Desiraju<sup>40, 41</sup> that the strength of any hydrogen bond is more dependent on donor acidity than on acceptor basicity. Consequently, being more acidic NH-donors,<sup>42</sup> thioureas also emerged as equally attractive and reliable supramolecular synthons in crystal engineering.<sup>39, 43-48</sup> In fact, a larger dimerization constant in solution has been observed for the thioureas in a comparative study of structurally similar urea and thiourea derivatives.<sup>49</sup>

Thiosemicarbazones or *N*-imino thioureas are the condensation products of thiosemicarbazides and carbonyl compounds (aldehydes, ketones) that are widely studied with diverse applications in medicinal chemistry.<sup>50-55</sup> However, being thiourea analogs and having slightly more acidic NH-protons (better H-bond donors) than thiourea due to the presence of the additional *N*-imino moiety, these are even more interesting with respect to crystal engineering applications.<sup>56-58</sup> As seen in the available crystal structures of this class of compounds, they preferentially adopt the *cis*, *trans* conformation, most probably due to intramolecular H-bond stabilization, in comparison to both *trans*, *trans* and *cis*, *trans* geometries for thioureas depending on the substituents (Figure 1). Due to this preferred *cis*, *trans* conformation (Figure 1b), the *cis*-thioamide moiety of thiosemicarbazones has the ability to form intermolecular  $R_2^2(8)$  cyclic dimers via two complementary N-H $\cdots$ S hydrogen bonds and can act as a robust supramolecular  $\{\cdots\text{H}-\text{N}-\text{C}=\text{S}\}_2$  synthon (Figure 1c). However, it is also worth mentioning that the most reliable supramolecular  $R_2^2(8)$  synthons i.e. carboxylic acid  $\{\cdots\text{H}-\text{O}-\text{C}=\text{O}\}_2$ , and amide  $\{\cdots\text{H}-\text{N}-$

C=O<sub>2</sub> dimer synthons, that has been used to good effect in the context of crystal engineering, has been observed in approximately one-third of the organic molecules containing the carboxylic acid and amide functionality, respectively.<sup>59,60</sup> This observation has largely been attributed to the competing sites for intermolecular interactions. In this context, it will be worthwhile to investigate the prevalence of the thioamide { $\cdots\text{H}-\text{N}-\text{C}=\text{S}$ }<sub>2</sub> dimer synthon in thiosemicarbazones in the presence of competing non-covalent interactions.

Carbon bonding is a new kind of non-covalent interaction, in which an sp<sup>3</sup> hybridized carbon atom as the electrophilic centre non-covalently interacts with nucleophilic atoms such as oxygen, nitrogen, sulfur and chlorine. This was first introduced theoretically by Mani and Arunan<sup>61</sup> and very recently experimentally validated by Guru Row and co-workers based on X-ray charge density analysis.<sup>62</sup> Based on their observation of a  $\sigma$ -hole on the C atom, a phenomenon first demonstrated by Politzer *et al.* for pnictogen, chalcogen and halogen bonding,<sup>63,64</sup> this interaction has been suggested to be a realistic interaction with broad implications in supramolecular chemistry.

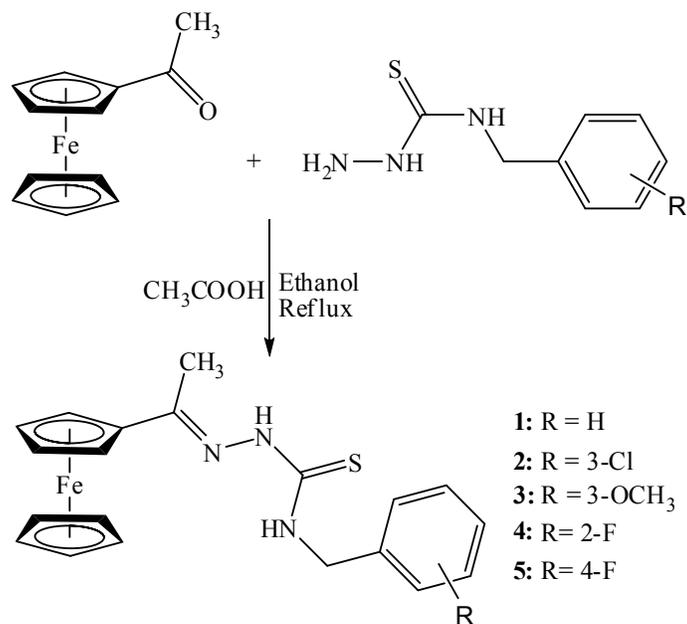
With this background and as continuation of our research interest in the study of intermolecular interactions,<sup>65-67</sup> five new ferrocene-based thiosemicarbazones have been designed and synthesized to investigate the prevalence of the thioamide { $\cdots\text{H}-\text{N}-\text{C}=\text{S}$ }<sub>2</sub> dimer synthon and carbon bonding. Keeping in view the available structural data of this class of compounds, no one has ever highlighted their potential in crystal engineering. Therefore, this study is an attempt to point out that this class of compounds is more attractive than thiourea in crystal engineering owing to its structural features. The *N*-imino functionality is not only freezing its conformational mobility through intramolecular hydrogen bonding but also increasing the acidity of the neighbouring NH, making it a better H-bond donor. As anticipated, the thioamide dimer synthon has been observed in the solid state structures of all five thiosemicarbazones, whereas four of them are found to have carbon bonding. Another intriguing feature of these crystal structures is the presence of a thioamide-thioamide stacking interaction in all five compounds which, to best of our knowledge, has not been reported to date.



**Figure 1.** Possible conformations of thiourea moiety in thiosemicarbazones: a) *trans, trans*; b) *cis, trans*; c) formation of thioamide {...H-N-C=S}<sub>2</sub> dimer synthon due to *cis, trans* conformation and possible carbon bonding

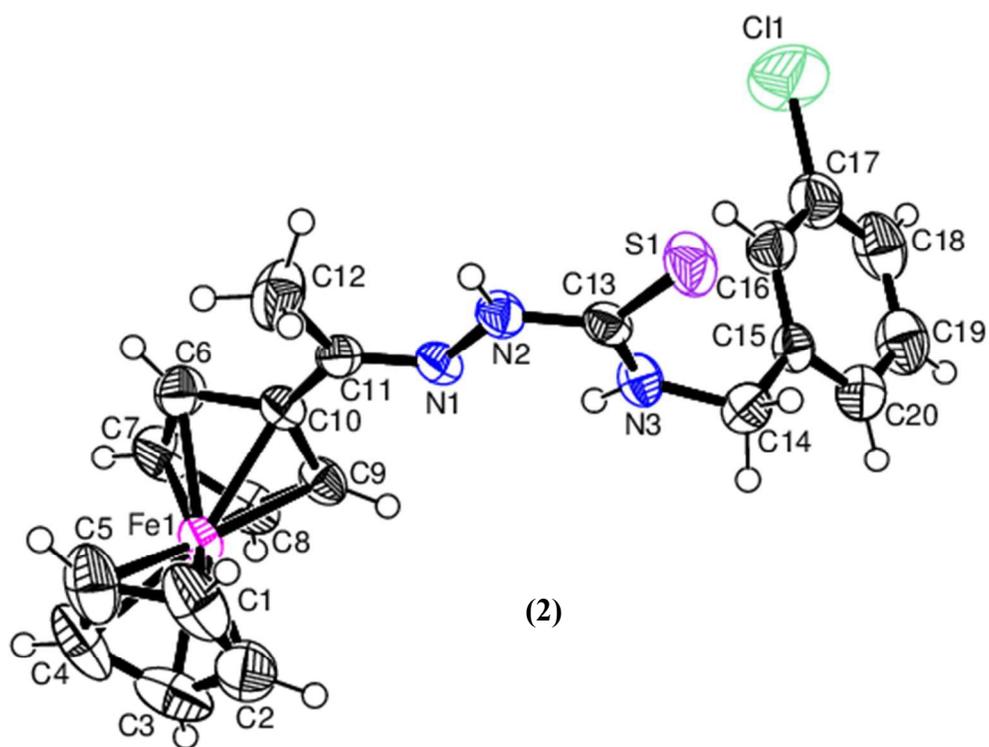
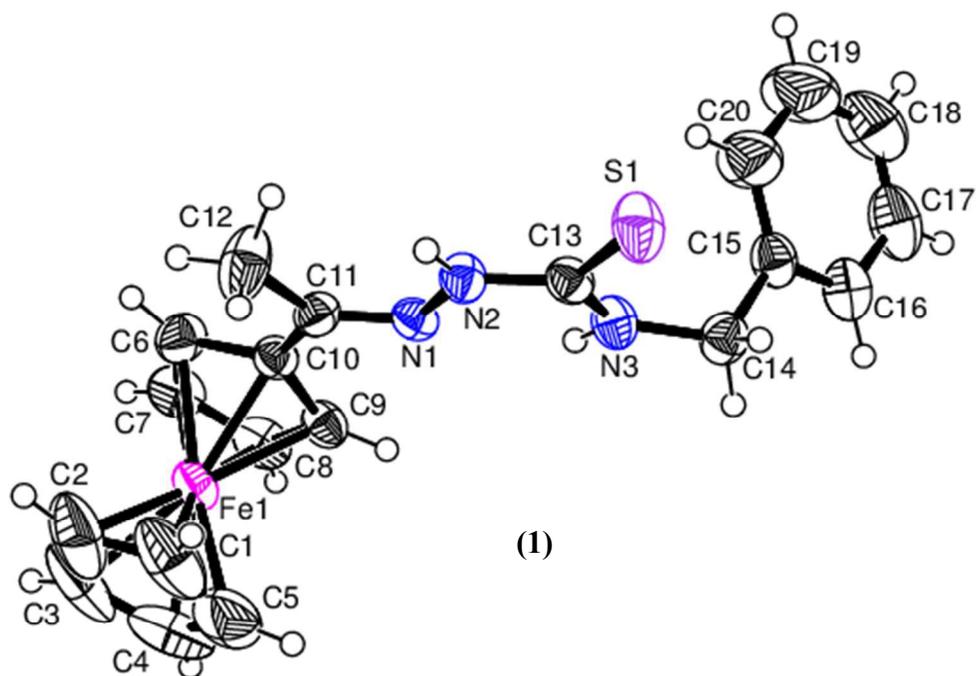
## Results and discussion

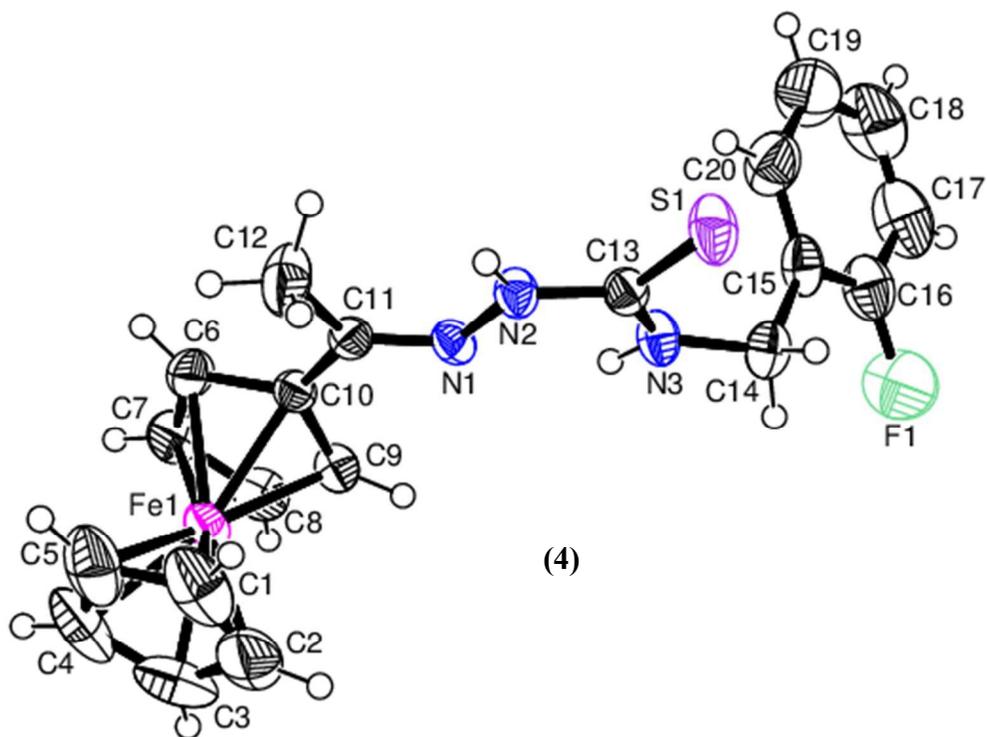
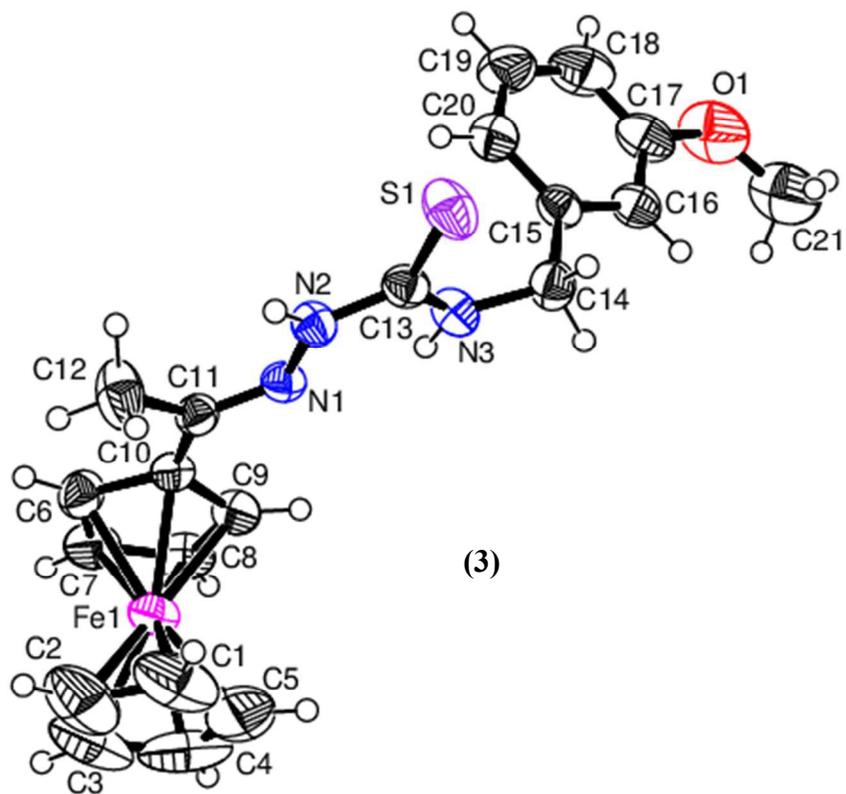
The designed ferrocene-based thiosemicarbazones **1-5** were obtained in a simple one-step condensation reaction, in which acetyl ferrocene is reacted with substituted thiosemicarbazides in ethanol solvent containing a catalytic amount of acetic acid under reflux conditions in good to excellent yields (Scheme 1).

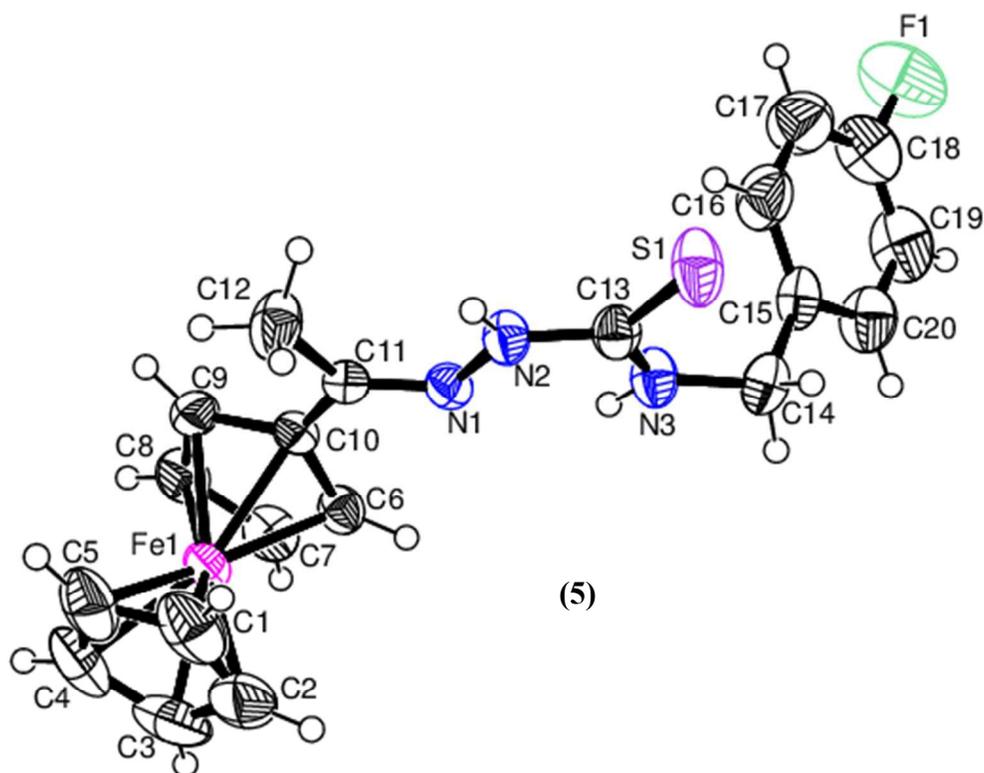


**Scheme 1.** Synthesis of ferrocene-based thiosemicarbazones **1-5**

The molecular structures of ferrocene-based thiosemicarbazones **1-5** along with crystallographic numbering schemes are illustrated in Figure 2. Selected geometric parameters for all five molecules are presented in Table 1. The magnitude of the standard uncertainty values associated with these geometric parameters prohibits explanation of any definitive trends across the series. The central core comprising the *N*-iminothiourea moiety is essentially planar in the crystal structures of all five compounds. This planarity extends further to include the benzylic carbon as well in all. This planarity can be attributed to the partial double bond character of C-N bonds of thiourea moiety due to significant delocalization of nitrogen lone pair towards thiocarbonyl group as indicated by the shorter bond lengths of N(2)-C(13)-N(3) [N(2)-C(13) 1.350-1.356 Å & C(13)-N(3) 1.330-1.335 Å] (Table 1). The slightly longer bond lengths of N(2)-C(13) indicate less delocalization towards thiocarbonyl, most probably due to the attachment of sp<sup>2</sup>-hybridized nitrogen atom. This observation, coupled with the planarity of the central core of the molecules, allows the assignment of different conformations described in the introduction (Figure 1). As shown in Figure 2, all the compounds **1-5** display the same *cis*, *trans* conformations. The adoption of only one conformation is credited to relatively strong intramolecular hydrogen bond [(N(3)-H(3A)⋯N(1) 2.169-2.195Å)]. It is important to mention here that the present observation for these thiourea analogs (thiosemicarbazones) is entirely different from thioureas where there is no such internal stabilization due to which they can adopt both *trans*, *trans* and *cis*, *trans* conformations depending on the situation.<sup>39</sup> An expected consequence of *cis*, *trans* conformation is the facile formation of a centrosymmetric thioamide R<sub>2</sub><sup>2</sup>(8) {⋯H-N-C=S}<sub>2</sub> synthon which is found in all the compounds **1-5** and shown in Figure 3; see also Table 2 for geometric parameters associated with the hydrogen-bond interactions operative in **1-5**.





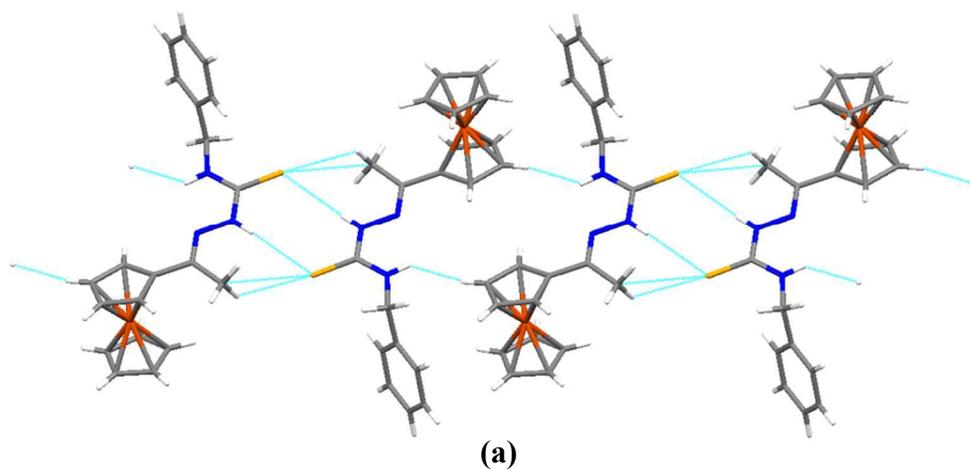


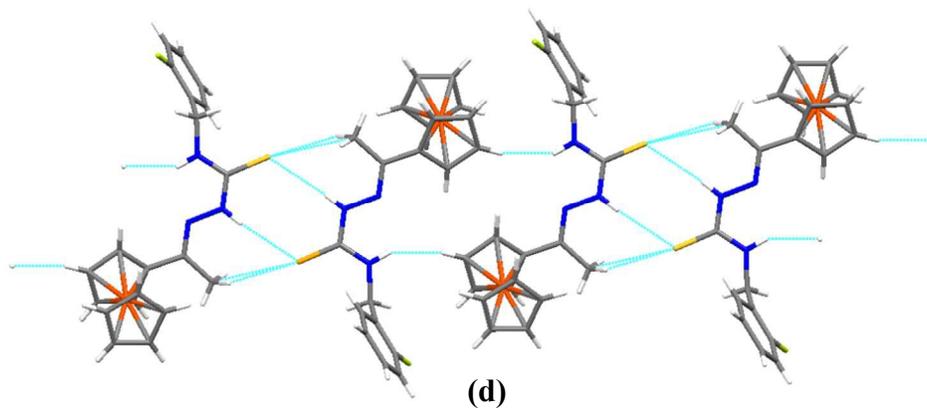
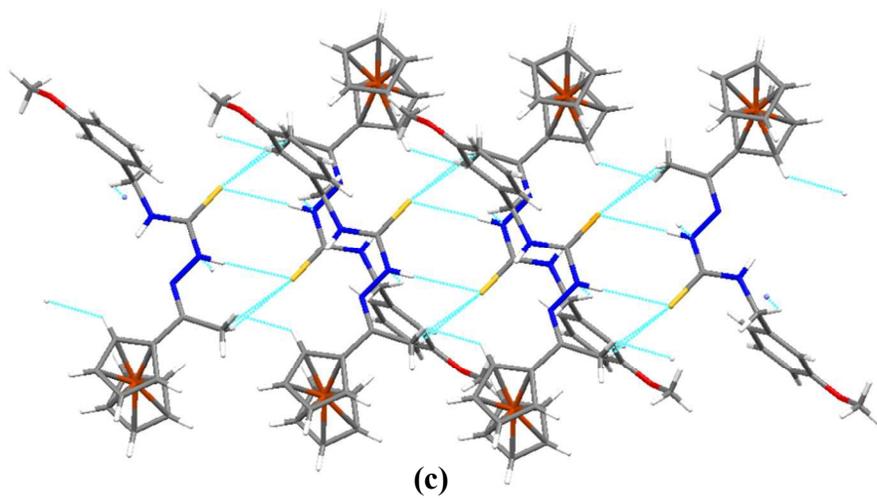
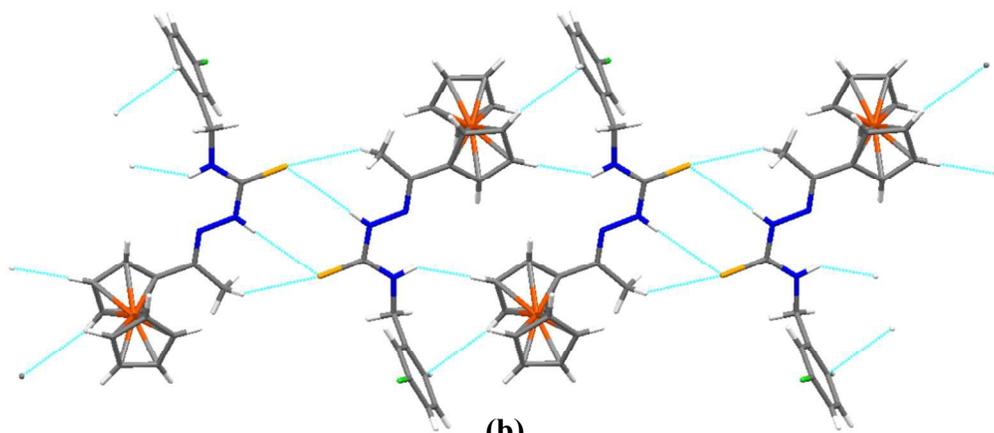
**Figure 2.** The molecular structures of ferrocene-based thiosemicarbazones **1-5**

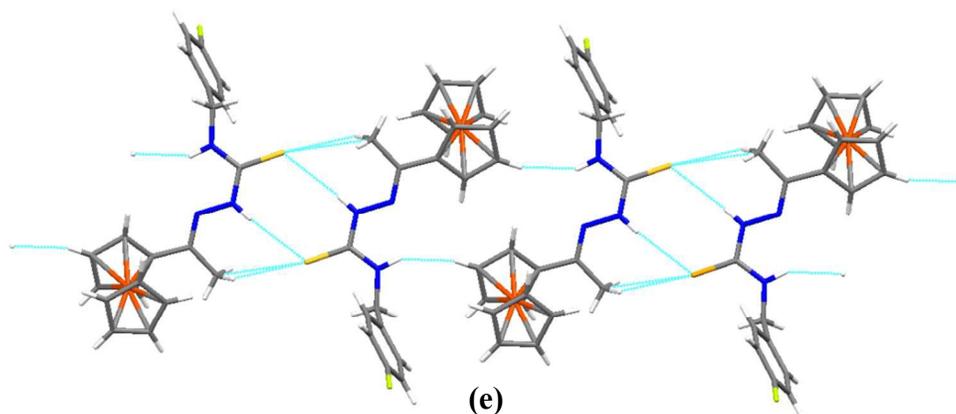
**Table 1.** Selected geometric parameters; bond lengths (Å), bond angles (°) and torsion angles (°) for **1-5** derived from the X-ray crystallographic study

Compound	1	2	3	4	5
S(1)-C(13)	1.6912(17)	1.680(2)	1.6837(19)	1.678(2)	1.680(2)
N(1)-C(11)	1.284(2)	1.280(3)	1.282(2)	1.286(3)	1.286(2)
N(1)-N(2)	1.3854(19)	1.381(3)	1.382(2)	1.383(2)	1.383(2)
N(2)-C(13)	1.356(2)	1.350(3)	1.352(2)	1.352(3)	1.353(2)
N(2)-H(2A)	0.8600	0.8600	0.8600	0.8600	0.8600
N(3)-C(13)	1.330(2)	1.332(3)	1.330(2)	1.333(3)	1.335(3)
N(3)-C(14)	1.456(2)	1.447(3)	1.452(2)	1.453(3)	1.454(3)
N(3)-H(3A)	0.8600	0.8600	0.8600	0.8600	0.8600
C(11)-C(12)	1.488(3)	1.495(3)	1.490(3)	1.491(3)	1.494(3)
C(11)-N(1)-N(2)	118.12(15)	118.2(2)	118.54(15)	118.25(18)	118.44(16)
C(13)-N(2)-N(1)	118.22(14)	119.1(2)	118.30(15)	118.44(18)	118.22(16)

C(13)-N(2)-H(2A)	120.9	120.5	120.9	120.8	120.9
N(1)-N(2)-H(2A)	120.9	120.5	120.9	120.8	120.9
C(13)-N(3)-C(14)	125.11(15)	125.6(2)	125.69(16)	124.94(19)	125.08(18)
C(13)-N(3)-H(3A)	117.4	117.2	117.2	117.5	117.5
C(14)-N(3)-H(3A)	117.4	117.2	117.2	117.5	117.5
N(3)-C(13)-N(2)	116.16(15)	115.8(2)	115.65(16)	115.58(19)	115.63(17)
N(3)-C(13)-S(1)	124.51(13)	124.60(19)	124.55(14)	124.15(17)	124.18(15)
N(2)-C(13)-S(1)	119.33(13)	119.64(19)	119.80(14)	120.27(17)	120.19(15)
N(3)-C(14)-C(15)	114.75(15)	115.2(2)	114.61(16)	113.8(2)	114.52(18)
N(1)/N(2)/C(13)/S(1)	179.89(11)	-178.74(16)	179.38(12)	-179.92(15)	178.17(13)
C(14)/N(3)/C(13)/S(1)	4.6(3)	4.9(3)	2.9(3)	3.7(3)	2.0(3)
N(1)/N(2)/C(13)/N(3)	0.2(2)	0.5(3)	-0.6(2)	0.5(3)	-1.7(3)
C(13)/N(3)/C(14)/C(15)	-100.4(2)	-104.3(3)	-100.9(2)	-96.2(3)	-95.5(2)
N(3)/C(14)/C(15)/C(20)	38.3(3)	-147.3(2)	30.1(3)	36.2(3)	-145.4(2)
C(9)/C(10)/C(11)/N(1)	18.3(3)	16.6(4)	16.7(3)	20.8(3)	-158.94(19)

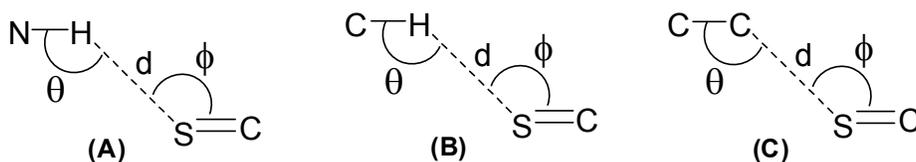






**Figure 3.** Supramolecular association in **1-5**: (a) tapes of **1**; b) tapes of **2**; c) staircase ladder-like arrangement of dimeric molecules in **3**; d) tapes of **4**; e) tapes of **5**

**Table 2.** Geometric parameters associated with the hydrogen-bonding and carbon bonding in **1-5**



Compound	(A)			(B)			(C)		
	d (Å)	Θ (°)	φ (°)	d (Å)	Θ (°)	φ (°)	d (Å)	Θ (°)	φ (°)
<b>1</b>	2.752	164.51	122.47	2.876	116.56	173.70	3.415	122.79	163.13
<b>2</b>	2.911	159.76	123.47	2.853	126.62	170.81	3.512	124.24	163.30
<b>3</b>	2.801	161.64	121.21	2.858	122.23	171.82	3.466	121.91	160.38
<b>4</b>	2.673	173.23	123.90	2.833	116.56	169.54	3.374	123.44	168.15
<b>5</b>	2.683	173.97	123.50	2.858	117.29	172.21	3.406	122.42	165.79

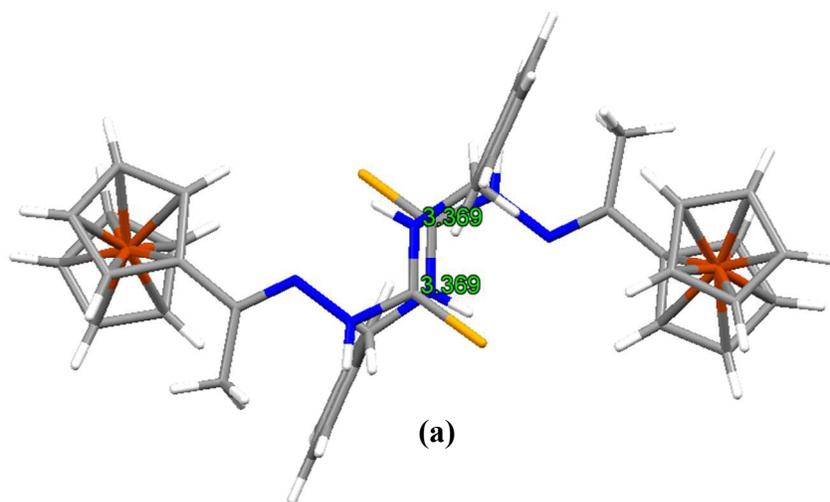
Another important feature, which we have taken into consideration during the design of compounds **1-5** to observe possible carbon bonding,<sup>62</sup> is the introduction of bulky ferrocene ring so that desired orientation of methyl group can be obtained. As expected, methyl group in all the solid state structures of **1-5** is oriented in such a way (same plane as the thiourea core) that it can participate in carbon bonding by exerting its cooperative role to the thioamide synthon (Figure 3,

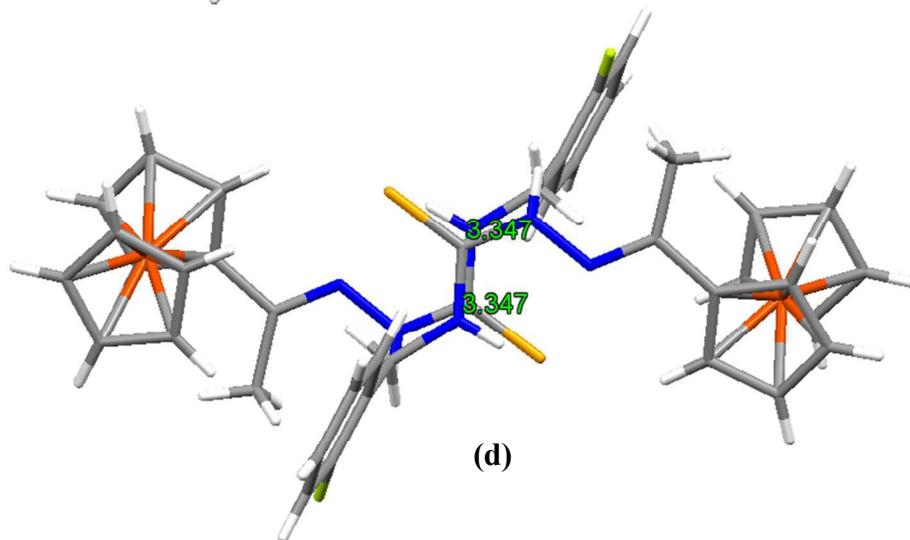
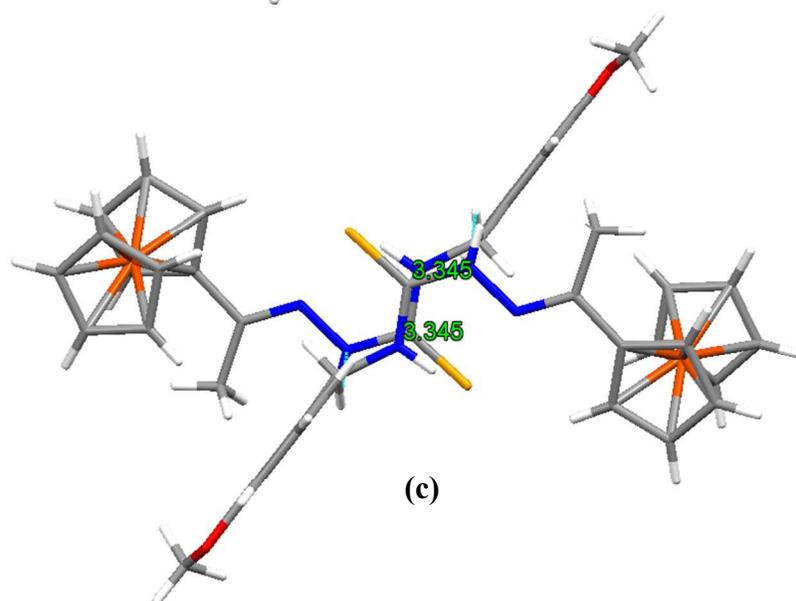
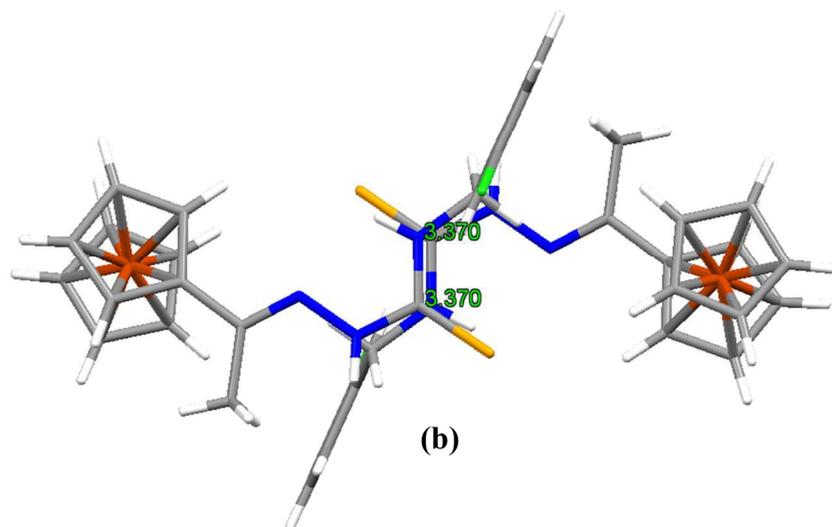
Table 2). However, as illustrated by the torsion angle data collected in Table 2, both ferrocene ring and benzylic aryl are significantly twisted from the central plane.

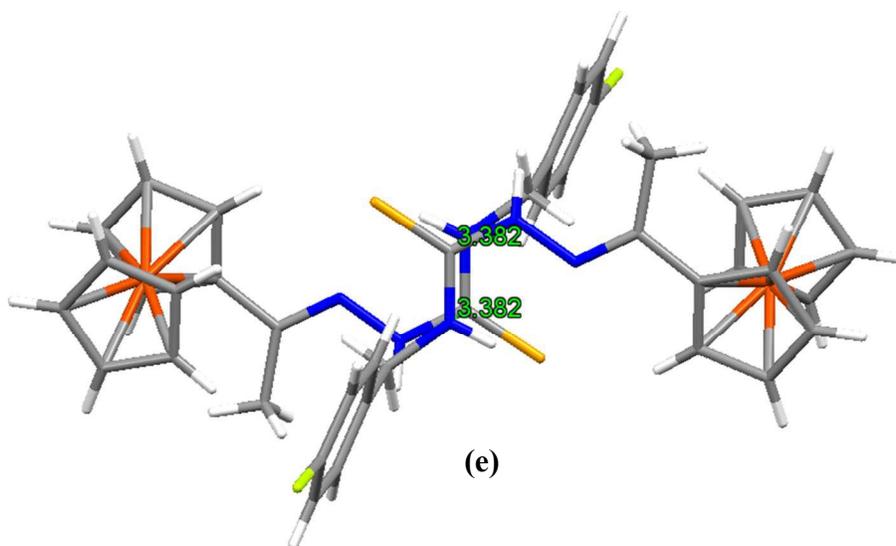
Interestingly, the compound **1** (R = H) and **3** (R = 3-OCH<sub>3</sub>) crystallize in monoclinic system, space group, space group *C2/c*, whereas compound **2** (R = 3-Cl), **4** (R = 2-F) and **5** (R = 4-F) crystallize in triclinic system, space group *P*<sup>-1</sup>, with one molecule in the asymmetric unit in all five structures. Despite having this same supramolecular synthon and the same molecular core, the structures **1-5** are not isomorphous, reflecting the influence of the substituents on the molecular packing (Table S1). As shown in Figure 3, all the five structures feature a centrosymmetric { $\cdots\text{H}-\text{N}-\text{C}=\text{S}$ }<sub>2</sub> synthon cooperated by C-H $\cdots$ S and carbon bonding (except in **2**) interactions and this clearly is the predominant supramolecular synthon operating in each of the crystal structures; geometric parameters associated with this synthon are listed in Table 2. Indeed, the sulfur atom involved in these interactions may be considered as either bifurcated (in case of **2**) or trifurcated (in case of **1,3, 4** and **5**) as it forms close interactions with NH, CH and C (Figure 3). It is worth mentioning here that the distance of sulfur to carbon for carbon bonding is well below their sum of van der Waals radii i-e  $\sim 3.50$  Å except for compound **2** i-e 3.512 Å (Table 2).

Over and beyond the thioamide synthon that has some cooperation of C-H $\cdots$ S and carbon bonding, the crystal packing of **1** (R = H) is dominated by two types of H $\cdots$ H interactions. The thioamide hydrogens, that are present in *trans* conformation to the sulfur, interact with the ferrocene hydrogens of neighbouring molecule to form a R<sub>2</sub><sup>2</sup>(20) [H(3A) $\cdots$ H(8) 2.348 Å] motif, resulting in the formation of tapes (Figure 3). These tapes are then stacked on each other by means of another H $\cdots$ H [H(9) $\cdots$ H(12B) 2.312 Å]<sup>68, 69</sup> and centrosymmetrically related thioamide-thioamide stacking (Figure 4a) [(C(13) $\cdots$ N(3) 3.396 Å] interactions, respectively, defining an overall 2D-network structure of **1** (Figure 5a). Similar tapes that have no carbon bonding [as S(1) $\cdots$ C(12) distance i.e. 3.512 Å is greater than sum of their van der Waals radii], but an additional CH $\cdots$  $\pi$  interactions [C(7)-H(7) $\cdots$ C(20) 2.850 Å] are observed in case **2** (R = Cl) (Figure 3). These tapes of **2** are stacked on each other through thioamide-thioamide stacking [(C(13) $\cdots$ N(3) 3.370 Å] (Figure 4b), H<sub>ferrocene</sub>-H<sub>methyl</sub> [H(9) $\cdots$ H(12C) 2.266 Å] and C-H $\cdots$ N [C(14)-H(14A) $\cdots$ N(2) 2.736 Å] interactions. Further, these stacked tapes are connected with each other by means of chlorine $\cdots$  $\pi$  [Cl(1) $\cdots$ C(5) 3.421 Å] and  $\pi$  $\cdots$  $\pi$  [C(4) $\cdots$ C(4) 3.312 Å] interactions, making an overall 3D-network structure (Figure 5b).

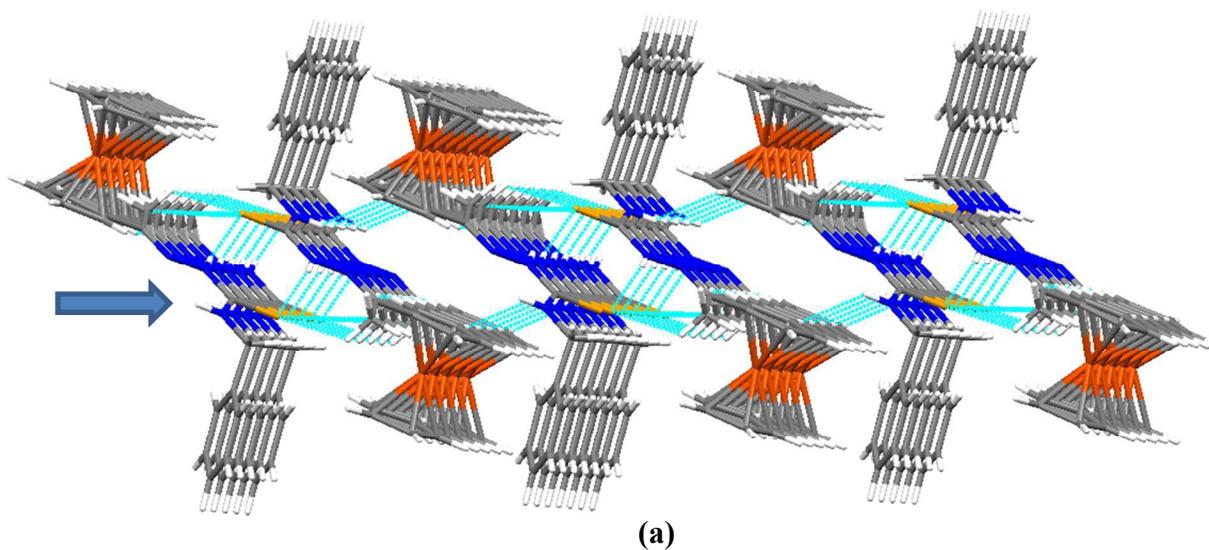
In contrast to the structures of **1** and **2**, tapes are not observed in the structure of **3** ( $R = 3\text{-OCH}_3$ ). Rather two centrosymmetric molecules connected through thioamide  $R_2^2(20)$  [H(3A)···H(8) 2.348 Å] synthon, C-H···S and carbon bonding shows 1D-staircase ladder-like arrangement (Figure 3c). Every dimer connects with the next lower dimer by means of thioamide-thioamide stacking [(C(13)···N(3) 3.345 Å] (Figure 4c),  $H_{\text{ferrocene}}\text{-}H_{\text{methyl}}$  [H(9)···H(12A) 2.398 Å] and centrosymmetrically related C-H···N [C(14)-H(14A)···N(2) 2.722 Å] interactions to form a 1D-staircase ladder. These stacked 1D-staircase ladders of **3** are sideways connected with each other by means of CH··· $\pi$  [C(18)-H(18)···C(4) 2.869 Å] interactions, providing a 2D-network structure (Figure 5c). Interestingly, methoxy substituent here is not involved in any kind of interaction.<sup>67</sup> Similar tapes, as observed in case of **1** and **2**, are detected in case of **4** ( $R = 2\text{-F}$ ) and **5** ( $R = 4\text{-F}$ ). The tapes are also stacked by means of thioamide-thioamide stacking [(C(13)···N(3) 3.347 Å in **4**, (C(13)···N(3) 3.382 Å in **5**] and  $H_{\text{ferrocene}}\text{-}H_{\text{methyl}}$  [H(9)···H(12C) 2.346 Å in **4**, H(6)···H(12C) 2.375 Å in **5**] interactions. By virtue of  $\pi\cdots\pi$  [C(4)···C(4) 3.212 Å in **4** and C(4)···C(4) 3.187 Å in **5**] interactions, the stacked tapes further extend themselves to provide 3D-network structures in both **4** and **5** (Figure 5d & 5e). Interestingly, the aryl rings carrying the fluorine substituents in both **4** and **5** are not involved in any kind of interactions.<sup>70-73</sup>

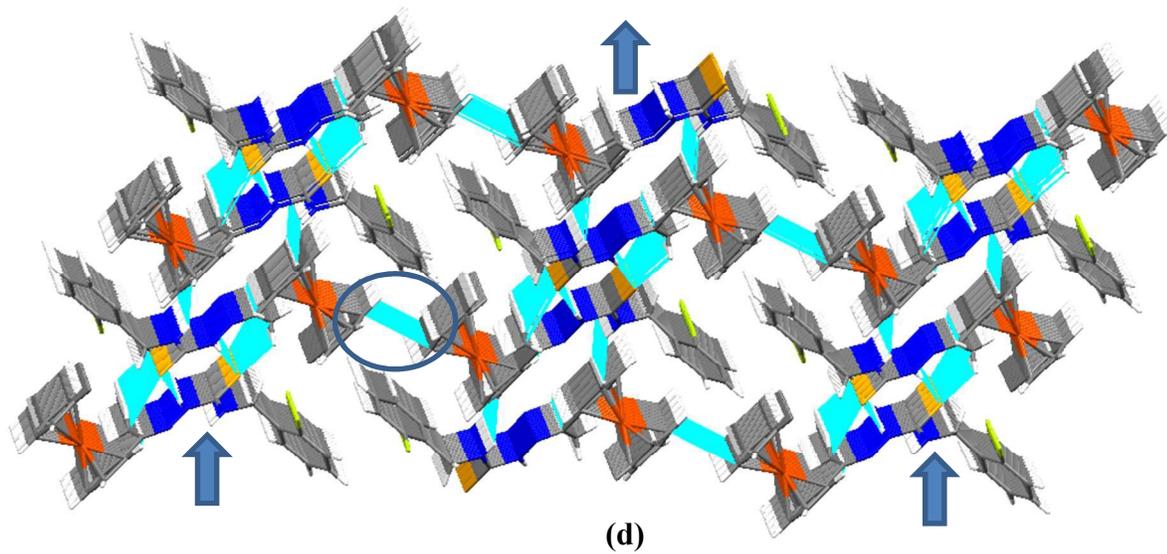
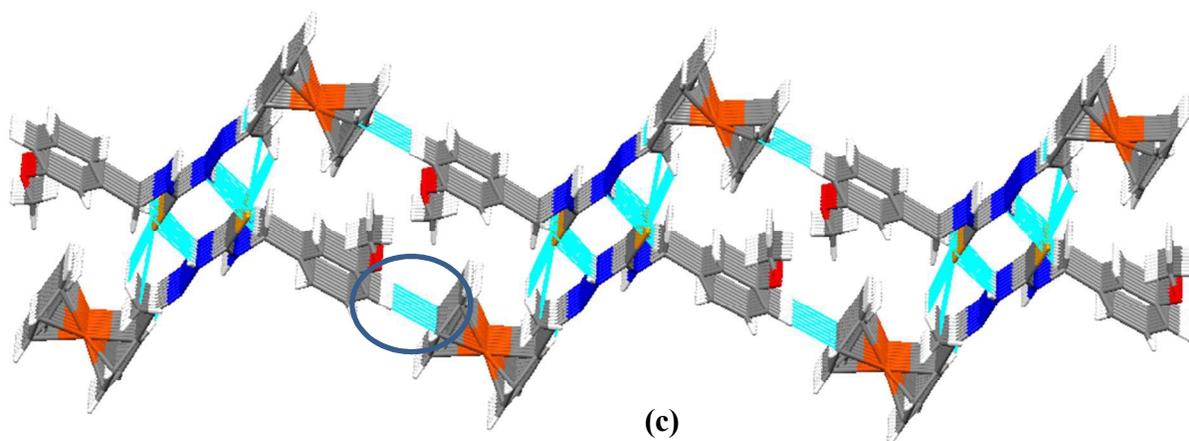
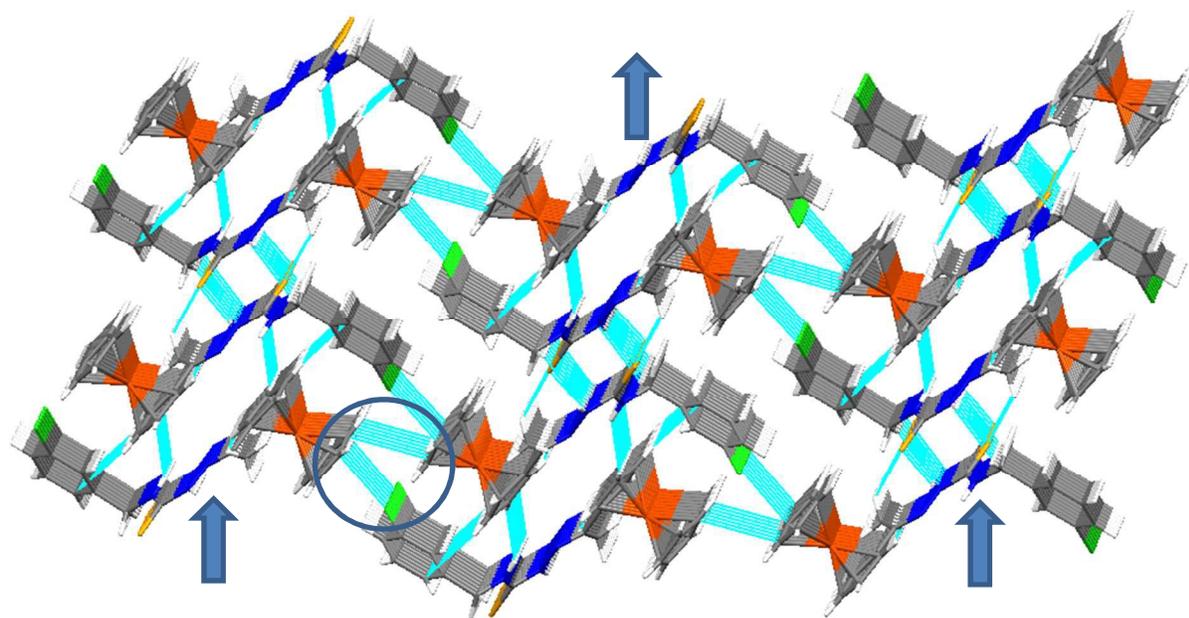


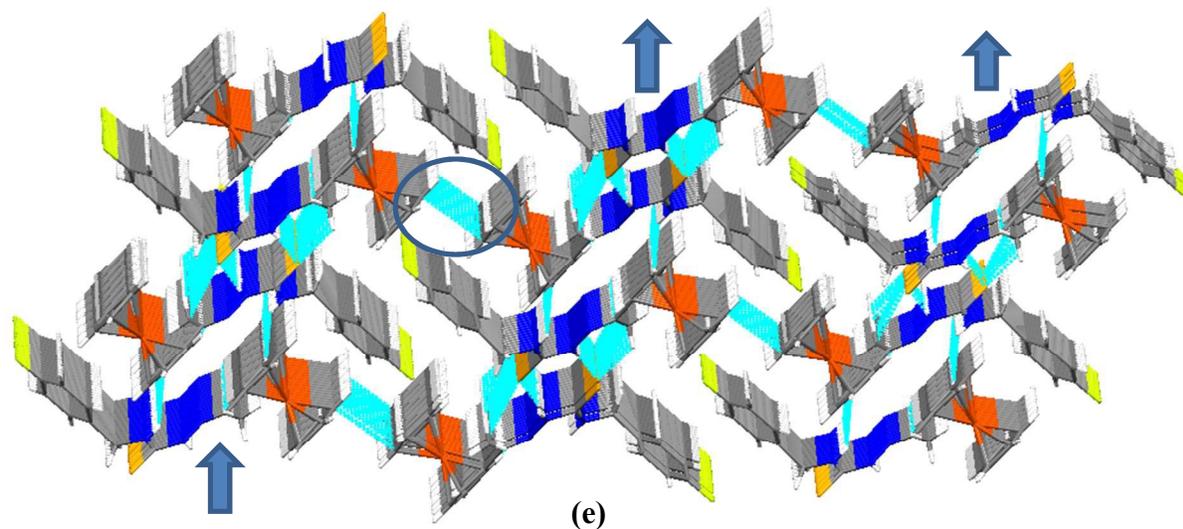




**Figure 4.** Highlighting thioamide-thioamide stacking interactions (a) **1** (R = H); **2** (R = 3-Cl);  
b) **3** (R = 3-OCH<sub>3</sub>); **4** (R = 2-F); **5** (R = 4-F);







**Figure 5.** View of the crystal packing; (a) **1** (R = H) along *a*-axis; b) **2** (R = 3-Cl) along *b*-axis, circle highlights chlorine $\cdots\pi$  and  $\pi\cdots\pi$  interactions; c) **3** (R = 3-OCH<sub>3</sub>) along *a*-axis, circle highlights CH $\cdots\pi$  interactions; d) **4** (R = 2-F) along *a*-axis, circle highlights  $\pi\cdots\pi$  interactions; **5** (R = 4-F) along *b*-axis, circle highlights  $\pi\cdots\pi$  interactions. Arrows indicates the direction of tapes.

Generally it is believed that the linear bonds ( $150^\circ < \theta < 180^\circ$ ) are structurally more significant due to the dipole-monopole and dipole-dipole contribution to the electrostatic energy which is a maximum at  $\theta = 180^\circ$  and zero at  $\theta = 90^\circ$ .<sup>41</sup> Careful analysis of the bond angles  $\theta$  in Table 2 demonstrates that the hydrogen bonds involved in the formation thioamide  $\{\cdots\text{H}-\text{N}-\text{C}=\text{S}\}_2$  dimer synthon are relatively linear and significant. However, the same angle  $\theta$  associated with C-H $\cdots$ S and carbon bonding is bent and should not have any significant role in directing the structure, it means these interactions are ‘structure guided’ not ‘structure guiding’. Furthermore, the angle  $\phi$  is usually measured to see O/S-atom lone-pair directionality. It is an established fact that the NH donors approach to the thiocarbonyl acceptor sidewise and linear to the carbonyl.<sup>74</sup> <sup>75</sup> Therefore, angle  $\phi$  for thiocarbonyls can be expected below  $130^\circ$  as it is in the range of  $120$ – $140^\circ$  for carbonyl acceptors. As shown in table 2, angle  $\phi$  is more consistent for thioamide dimer synthon as compared to the C-H $\cdots$ S and carbon bonding, which is again indicative of their dominating character. Keeping in view the ability of hydrogen bonding of chloro and methoxy substituents, it can be anticipated that thioamide  $\{\cdots\text{H}-\text{N}-\text{C}=\text{S}\}_2$  dimer synthon is robust and strong enough to play the main structure guiding role. Furthermore, thioamide-thioamide stacking observed in all the structures and in which the dipoles are anti-aligned, is an attractive

and relatively strong interaction led by dispersion and electrostatic contributions, an observation which is consistent with recently explored amide-amide stacking that was found comparable in strength to amide-amide hydrogen bond.<sup>76,77</sup>

## Conclusions

In conclusion, we have synthesized five structurally-related ferrocene-based thiosemicarbazones **1-5**, which showed a *cis*, *trans* conformation in the solid state around thiourea, providing thioamide moiety for the formation of hydrogen bonded  $R_2^2(8) \{ \dots H-N-C=S \}_2$  synthon. Methyl group also adopt such a conformation that it can play its cooperative role either through C-H $\cdots$ S interactions or through carbon bonding (a recently explored interaction). By virtue of these specific conformations, thioamide synthon is observed in all the five compounds; however, carbon bonding that is basically a structure guided interaction was noticed in four cases. The thiourea hydrogens that are not part of thioamide synthon interacts further on both sides with the neighboring dimeric molecules through centrosymmetrically related N-H $\dots$ H-C interactions to provide tapes of varying topology in all the compounds except **2**, where staircase ladder-like arrangement of dimeric molecules is observed. Furthermore, thioamide-thioamide stacking is also observed in the packing of all the compounds which, to best of our knowledge, has not been reported so far. The substituents, for example methoxy in case of **3** and fluoro in case of **4** and **5**, did not directly participate in any of the non-covalent interactions, but their electronic influence in dictating the formation 2D- and 3D-structures, respectively cannot be overlooked. On the basis of the observed solid state structural features, it can be anticipated that this particular class of compounds of general formula  $R-C=N-NH-C(=S)-NH-CH_2-R^1$ , being thiourea analogs, is more attractive in crystal engineering than thiourea and deserves more attention from crystal engineering community. The reason behind this is the presence of *N*-imino-moiety that is not only increasing the acidity of NH-protons making it better H-bond donor, but also playing a crucial role in the stabilization of *cis*, *trans* conformation around thiourea moiety by intramolecular hydrogen bonding offering robust supramolecular thioamide synthon. The prevalence of thioamide dimer synthon, carbon bonding and thioamide-thioamide stacking in this study would provide a route towards the use of this class of compounds as the design element in crystal engineering.

## Experimental

### General.

All reagents and solvents used in this study were used as obtained from the supplier or recrystallized/redistilled as required. Thin layer chromatography (TLC) was performed using aluminium sheets coated with silica gel 60 F<sub>254</sub> (Merck). Melting points of all the synthesized compounds have been determined in open capillary tubes by using Gallenkamp apparatus (MP-D) and were uncorrected. IR spectra in the range of 4000-400 cm<sup>-1</sup> were obtained on a Thermo Nicolet-6700 FT-IR Spectrophotometer. The <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded on Bruker spectrometer at 300 MHz and 75 MHz in CDCl<sub>3</sub>, respectively using residual solvent signals as a reference.

### General Procedure for the Synthesis of Ferrocene-based Thiosemicarbazones 1-5

To a stirred hot solution of acetyl ferrocene (2 mmol) in 10 mL ethanol containing catalytic amount (2-3 drops) of acetic acid was added a dropwise ethanolic solution (10 mL) of appropriate thiosemicarbazides and the reaction mixture was heated to reflux for 4-6 hours. The resultant orange precipitates were filtered by suction filtration. Thorough washing with ethanol followed by recrystallization from hot ethanol furnished the desired compounds **1-5** in pure form. The single crystals suitable for X-ray analysis were cultivated by slow evaporation of chloroform:ethanol (10:1) solution of the compounds at room temperature over a period of 10 days.

### Crystallographic data collection and structural refinement

Single crystals of **1-5** were mounted on a thin glass fiber at room temperature and the reflection data were collected on a Bruker kappa APE XII CCD diffractometer equipped with graphite mono-chromated MoK $\alpha$  radiation ( $\lambda = 0.71073 \text{ \AA}$ ). The data were also corrected for Lorentz and polarization effects. The structure was solved using SHELXS-97. Final refinement on F<sup>2</sup> was carried out by full-matrix least-squares techniques using SHELXL-97.<sup>78</sup> The crystal data of **1-5** and refinement values are summarized in Table S1.

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## GRAPHICAL ABSTRACT

**Robustness of thioamide dimer synthon, carbon bonding and thioamide-thioamide stacking in ferrocene-based thiosemicarbazones**

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