Supramolecular Chemistry
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713649759

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**To cite this Article** Drew, Michael G. B. , Lund, Astrid and Nicholson, David G.(1997) 'Molecular Modelling Studies on the Thiourea/ Ferrocene Clathrate', Supramolecular Chemistry, 8: 3, 197 — 212
**To link to this Article: DOI:** 10.1080/10610279708034937
**URL:** http://dx.doi.org/10.1080/10610279708034937

SUPRAMOLECULAR CHEMISTRY, 1997, Vol. 8, pp. 197–212
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# Molecular Modelling Studies on the Thiourea/Ferrocene Clathrate

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*(Received 11 July 1996)*

Computer modelling studies by means of molecular dynamics, molecular mechanics and Monte Carlo simulations have been carried out on the thiourea:ferrocene clathrate. The known crystal structure of this host:guest system was used as a model system containing four ferrocene guest molecules in a thiourea host channel of 16 Å in length. Molecular dynamics and molecular mechanics calculations indicated that the close packing of ferrocene molecules in the channel occurred despite strong steric repulsive interactions associated with neighbouring ferrocene molecules in the channel when they are positioned along the crystallographic sites. The neighbouring ferrocene molecules rotate and tilt with respect to each other in order to reduce the intermolecular repulsions. A second model containing a single ferrocene guest molecule in the thiourea host channel has also been studied. The guest adopts either a parallel alignment where the molecular five-fold axis coincides with the channel trigonal axis, or a perpendicular orientation or an intermediate orientation. Results from the molecular dynamics and molecular mechanics calculations show that the parallel positions are favoured. Monte Carlo simulations indicate a population distribution of 60%/40% for ferrocene in the parallel/perpendicular orientations. The ferrocene molecule alternates between the two orientations in the thiourea channel in order to avoid the repulsion inherent from the ideal parallel or perpendicular arrangement. Energy calculations show that only small movements off the channel trigonal axis are possible.

## INTRODUCTION

Thiourea (TU) and urea (U) host lattices form channel inclusion compounds with a wide range of guest molecules including branched-chain alkanes, cycloalkanes[1] and fatty acids. Clathrates containing molecules such as paraffins and fatty acids have been known since 1949, first reported by Schlenk.[2–7] U usually forms inclusions with straight-chain compounds such as hydrocarbons, esters and organosilanes whereas TU forms clathrates with branched-chain compounds and cycloparaffins, as reported by Redlich *et al.* in 1950.[8]

Experimental work on systems containing organic guest molecules includes crystallographic studies[2–4,9–28] on a number of U and TU compounds. X-ray studies[9] have revealed the general details of the structures of hydrocarbon-urea adducts and later X-ray diffraction and elemental analysis have been carried out on some cyclohexane derivatives in their respective thiourea adducts.[11] There have also been infrared, IR studies,[29–32] dielectric absorption studies,[33]

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wideline NMR measurements[34] on the urea systems, and thermal studies on TU compounds.[21]

Several X-ray crystallographic studies have been carried out on inclusion compounds in thiourea (Table I).[11–23] The structures of the thiourea inclusion compounds are very similar (Table I), being based on the hexagonal channel. Many of the structures are rombohedral with the channel around the three-fold axis. There is a variation in spacegroup (R3, R-3, R3c, R-3c) which are presumably due to the variations in the guest, the channel being compatible with all. Cell dimensions vary from $a$ = 15.539 to 16.40 Å and $c$ = 12.395 to 12.58 Å. This is the structure observed in our ferrocene system.[14] In many cases the guest is disordered in the channel because its shape is incompatible with spacegroup symmetry.

There are several other types of unitcell, the most popular being monoclinic $P2_1/c$ with average dimensions $a$ = 12.3, b = 15.8, $c$ = 10.2 Å, (β = 112°) which is found for cyclooctane, cyclooctanone, cyclopeptane, and tetrahydropropane guests. There is an orthorhombic $Pna2_1$ variant with similar dimensions which is observed for the cyclohexadiene-tricarbonyliron clathrate. There is one other monoclinic clathrate with 2,6-diethylnaphthalene with very different dimensions.

In the mid-1970s the list of guest molecules was extended by the addition of metallocenes, ferrocene and nickelocene by Clement, Claude and Mazieres in 1974[15] and further studies of clathrate inclusion of ferrocene and cyclopentadienyl manganese tricarbonyl (cymantrene).[35] They found that, by analogy to the behaviour of nickelocene, cymantrene does not form a thiourea clathrate in the absence of ferrocene. In 1978 one of these, the 1:3 ferrocene thiourea clathrate was structurally characterised by a X-ray diffraction study.[14] It was found that the TU molecules are aligned along trigonally intersecting twofold axes forming a honeycomb of channels with trigonal symmetry and of diameter *ca.* 10 Å. Molecules are connected via (N-H---N) links with a pitch of 120° parallel to the $c$ axis which coincided with the channel axis. Within these channels, sites of point symmetry 32 were occupied by the ion atoms of the ferrocene molecules, $Fe(C_5H_5)_2 = Fe(CP)_2$. In this structure the Fe---Fe distance in the channels is 6.197 Å. However, it proved impossible to establish the positions of the cyclopentadienyl carbon atoms because they were disordered over several sites. Two orientations of the ferrocene molecules were initially considered. First with the symmetry axis of the ferrocene molecules aligned along the channel axis (parallel orientation), and second the symmetry axis perpendicular to the channel axis (perpendicular orientation) (Figure 1). The observed electron density around the iron atoms obtained from the crystal structure proved to be inconsistent with both structures and it was concluded that the molecule axes incline at angles that vary over a range with respect to the channel axis. The orientation adopted by ferrocene in the clathrate depends on interactions with the host lattice and with other ferrocene molecules in the clathrate. Each thiourea sulphur atom is hydrogen bonded to four hydrogen atoms at distances of 2.45, 2.45, 2.50 and 2.50 Å. Each hydrogen atom is only bonded to one sulphur atom. The two independent N-H---S angles are 171.2 and 153.1°. The (C = S---H) angles range from 104.2 to 104.5°. Five crystallographic studies on the thiourea inclusion compound mentioned above are listed in Table I. As shown in Table I, the dimensions of the channel are somewhat dependent upon which inclusion compound is used.

From the end of the 1970s and up to the present time, there has been considerable interest in the TU and U clathrates. These studies include conformational spectroscopic studies of halogenated cyclohexanes in TU clathrates,[36] heat capacity and phase transitions of the thiourea-ferrocene channel inclusion compound,[37] electron spin resonance study of conformational and dynamic characteristics of molecules trapped within the channels of TU-cyclohexane

TABLE I Details of crystallographic studies of Thiourea inclusion compounds

| Clathrate | Cell Parameters (Å) | Crystal Class Spacegroup | R value[a] | Ref. |
|---|---|---|---|---|
| Cyclohexane | $a = 15.90$, $c = 12.50$ | hexagonal, b | b | 11 |
| Dioxane | $a = 9.7$, $b = 7.2$, $c = 14.2$, $\beta = 98°$ | monoclinic, P 2/m | b | 12 |
| Cyclooctadiene | $a = 12.241$, $b = 16.05$, $c = 9.630$, $\beta = 110.73°$ | monoclinic, P $2_1$/c | 0.043 | 13 |
| Ferrocene | $a = 16.36$, $c = 12.395$ | hexagonal, R-3c | 0.079 | 14 |
| Ferrocene/nickelocene | $a = 16.40$, $c = 12.50$ | hexagonal, b | b | 15 |
| Cyclooctane | $a = 12.404$, $b = 30.847$, $c = 10.346$, $\beta = 113.68°$ | monoclinic, P $2_1$/c | 0.064[c] | 16 |
| Cyclooctanone | $a = 12.099$, $b = 15.539$, $c = 10.314$, $\beta = 111.83°$ | monoclinic, P $2_1$/c | 0.032[c] | 16 |
| Carbon tetrachloride | $a = 15.539$, $c = 12.529$ | hexagonal, R-3 | 0.0430 | 17 |
| Cyclohexane | $a = 15.708$, $c = 12.431$ | hexagonal, R3 | b | 18 |
| Benzene-tricarbonylchromium | $a = 16.130$, $c = 12.569$ | hexagonal, R3c | 0.0300 | 19 |
| Cyclohexadiene-tricarbonyliron | $a = 12.562$, $b = 16.128$, $c = 9.536$ | orthorombic, Pna21 | 0.0270 | 19 |
| Cyclohexadiene-tricarbonylmanganese | $a = 16.307$, $c = 12.653$ | hexagonal, R3c | 0.0450 | 19 |
| Thrimethylenemethane-tricarbonyliron | $a = 16.234$, $c = 12.488$ | hexagonal, R3c | 0.0210 | 19 |
| 2,6-diethylnaphthalene | $a = 12.571$, $b = 9.282$, $c = 14.634$, $\beta = 92.14°$ | monoclinic, P $2_1$/c | 0.0830 | 20 |
| Cycloheptane | $a = 10.17$, $b = 15.62$, $c = 12.50$, $\beta = 114.18°$ | monoclinic, b | b | 21 |
| Tetrahydropropane | $a = 9.96$, $b = 15.70$, $c = 12.50$, $\beta = 114.73°$ | monoclinic, b | b | 21 |
| Chlorocyclohexane | $a = 10.115$, $\alpha = 104.27°$ | hexagonal, R-3c | b | 22 |
| Adamentane | $a = 16.187$, $c = 12.578$ | hexagonal, R-3c | b | 23 |

[a] The listing of an R value implies that coordinates are available from the Cambridge Crystallographic Data base unless otherwise stated.
[b] Not given.
[c] R values quoted, but coordinates not available.

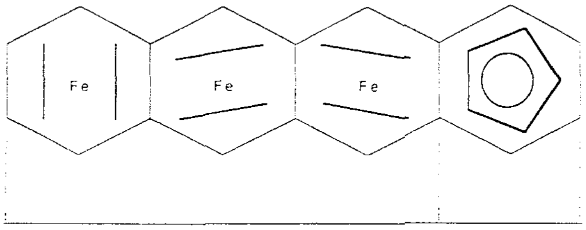

FIGURE 1 A schematic representation of possible orientations of ferrocene within the thiourea clathrate.

inclusion compounds[38] and structural aspects of U inclusion compounds and their investigation by x-ray diffraction.[39,40]

Recently, attention has been focused on studies on the TU/Fe(CP)$_2$ system using $^{57}$Fe Mössbauer and solid state $^2$H NMR spectroscopy.[41,42] Lowery *et al.*[41] studied the orientation and onset of motion of Fe(C$_5$D$_5$)$_2$ in the channels of the TU inclusion compound by using $^{57}$Fe Mössbauer and solid-state $^2$H NMR spectroscopy at different temperatures. The results are consistent with six different static ferrocene orientations at 140 K, and at this temperature *ca.* 55% of the ferrocenes were located in three positions related by the channel $C_3$ axis in which the ferrocene molecular axis coincides with the channel axis of the host TU. The other three static ferrocene positions, related to the $C_3$ axis, were located with the ferrocene molecular axis slanted *ca.* 17° off the $C_3$ axis. By increasing the temperature the ferrocene molecule started moving in the channel. At 160 K phase transitions occurred between three perpendicular orientations and three parallel orientated ferrocenes, and in the 160–225 K range the $^2$H NMR spectra collapsed from being a doublet to an ill defined peak. In the 160–225 K range the Mössbauer spectra showed that the rate of interconversion of ferrocene between perpendicular and parallel orientations was slower than *ca.* $10^5$ s$^{-1}$. At this high temperature the $^2$H NMR spectra showed only one peak. These observations are similar to those observed by us in the AlPO$_4$-5: ferrocene system.[43]

Heyes *et al.*[42] also using $^2$H NMR spectroscopy, reported that the reorientations of the ferrocene guest molecules were associated with the phase transition as the ferrocene molecules switch from parallel to perpendicular orientations with respect to the TU channel axis at (160 K.) There are four distinct orientations of the guest molecule on their lattice sites. Three equispaced orientations are defined as perpendicular, and a single orientation as parallel to the channel axis. The velocity of their switching action increases with rising temperature. At room temperature there is a population distribution of 64.3%/35.7% for the guest molecule in the perpendicular/parallel orientations. By 340 K, there is no orientational preference for the ferrocene molecules relative to the TU channel because they are rapidly tumbling, effectively spherically. For the last years more NMR studies have been carried out.[44–51]

The crystal structure of ferrocene, reported by Dunitz *et al.*[52] and the gas phase electron diffraction study[53] show that the molecular point symmetries are $D_{5d}$ and $D_{5h}$ for the crystal and the gas phases, respectively. Several theoretical studies have been carried out on ferrocene[54–59] including molecular orbital studies and *ab initio* calculations.[54–58] No theoretical work has yet been carried out on this TU: Ferrocene system, but theoretical studies on other inclusion compounds[60,61] have been reported. Thus, Rodger[60] simulated clathrate hydrates, a group of compounds in which small non-polar guest molecules such as methane are situated within the cavities formed within a crystal lattice of water. These gas hydrates are of industrial interest because of possible relevance to methane technology. By looking at ferrocenes as a non-polar guest molecules in the TU host lattice we can establish whether they show similar trends to those between the methane and the water lattice. Our interest is to model the behaviour of ferrocene as a non-polar guest molecule in the clathrate and to establish whether the weak interactions are of a similar nature.

## METHODS

*Ideal structure retrieval*—Crystallographic data were obtained from the literature.[14] In the structure determination of TU/Fe(CP)$_2$ the thiourea host lattice and the iron atoms of the metallocene are unequivocally located whilst the cyclopentadiene rings are not because of multiple disorder. The program *CRYSTAL*[62] was used to generate all the atoms in the unit cell for the given space group, build a fragment containing the required number of unit cells, and to convert the crystallographic coordinates to cartesian coordinates. The finite TU/Fe(CP)$_2$ fragment is built up from the thiourea molecules and the iron atoms of the ferrocene molecules giving a fragment that embraces 2000 atoms and 22 channels. Since the computational requirements and memory limitations dictate the size of the finite fragment chosen, we opted for one defined by ($5 \times 5 \times 5$) unit cells. These limits define a fragment of suitable size for our calculations.

In all the calculations the TU fragment was kept fixed, thus simulating an infinite host lattice. We investigated several models with differing numbers of Fe(CP)$_2$ guest molecules in different positions. In all cases however the geometry of the ferrocene was assumed staggered, a $D_{5d}$ crystal model where C–C and Fe–C distances were set at 1.37 and 2.10 Å, respectively

*Computational Techniques*—All calculations were carried out with the Biosym packages *INSIGHT* and *DISCOVER*.[63] The various possible positions of the ferrocene molecule within the channels were investigated via both molecular dynamics (MD) and Monte Carlo (MC) methods while energy minimisation was carried out with molecular mechanics (MM). Molecular mechanics and molecular dynamics calculations were carried out using the consistent valence force field, *cvff*[64] within the *DISCOVER* program with input files generated by *INSIGHT*. For each structure, the dynamics was carried out with a step size of 1.0 fs at temperatures of either 300 or 1000 K. Structures were saved every 1.0 ps and subsequently minimised by molecular mechanics. These two sets of structures are called MD and MM respectively. Molecular dynamics allows us to follow the movement of the ferrocenes within the cavity while Monte Carlo provides a random search method to investigate possible positions. We used the *DOCKER* program[65] which has previously been used to investigate the random orientations of an energy-screened structure for a guest molecules into a host channel molecule structure like aluminium phosphates and zeolites and is therefore appropriate for the thiourea: ferrocene channel complex. In this work we established 100 different positions below an energy threshold which were subsequently minimised by molecular mechanics. Electrostatic interactions were included in all classical simulations. Partial atomic charges for the TU were calculated by means of Quantum Mechanics (QM) semi-empirical calculations[66–68] using the electrostatic potential method within the *MOPAC* program[69] and were subsequently scaled to reflect 6-31G* values.[70,71] Two different sets of charges were used for values within the ferrocene molecules. For one set we used values calculated by Lüthi *et al.*[57] with *Hartree-Fock* (*HF*) methods and for the other we calculated values using the density functional (*DF*) program *DMOL*.[72] These charges are quite different (for example for the iron atom Lüthi *et al.* gave 1.38e and *DMOL* Fe: 0.21e), and so both sets were used in the majority of calculations to compare the results obtained. All values of charges used in this work are given in Table II.

Minimised structures were characterised by using the graph functions in the *DISCOVER* analysis module. From the trajectory files, we calculated geometric properties such as tilt angles (the rotations off the channel trigonal axis parallel/perpendicular), off-axis distances (the distances between the channel trigonal axis and the guest molecule 90° perpendicular to the axis) and displacement distances (translations along the channel axis). In particular in this work we have paid attention to the tilt angles and off-axis distances.

TABLE II Partial charges on atoms

| Atom types | | Charge (e) |
|---|---|---|
| *TU*[a] | | −0.37 |
| S | | |
| N | | −0.74 (−0.74)[b] |
| N | | −0.74 |
| C | | 0.55 |
| H | | 0.35 (0.32)[b] |
| H | | 0.35 |
| H | | 0.30 |
| H | | 0.30 |
| *Fe(CP)₂* | | |
| Fe | 1.38[c] | 0.21[d] |
| C | −0.27 | −0.27[d] |
| H | 0.13[c] | 0.25[d] |

[a] *MOPAC* (esp) charges used for S and C atoms.

[b] Mean average *MOPAC* (esp) charges used for N and H atoms, respectively.

[c] Charges calculated by Lüthi *et al.*[37]

[d] Charges calculated by *DMOL*.[37]

## RESULTS AND DISCUSSIONS

The total picture of channel inclusion compounds provided by a large range of studies shows the enclosed molecules being loosely held by the host lattices. These forces are not strong enough to impede molecular motions and in the case of ferrocene the molecules appear to have considerable degrees of freedom as we will see from the results below.

We investigated several models with differing numbers of $Fe(CP)_2$ guest molecules in different positions. Each model is considered in turn.

*Model 1: TU/Fe(CP)₂, (1/4)*—This starting model contained the TU host channel with four internally constrained $Fe(CP)_2$ molecules as guests, with the Fe atoms of the ferrocenes being placed in accordance with the crystal structure (Figure 2) at 6.197 Å apart. The iron atoms were constrained to site on the axis but allowed to move along it. Thus, when the ferrocenes are positioned with their molecular symmetry axis aligned with the channel trigonal axis, neighbouring ferrocenes are subjected to strong repulsive forces. The nearest intermolecular C---C dis-

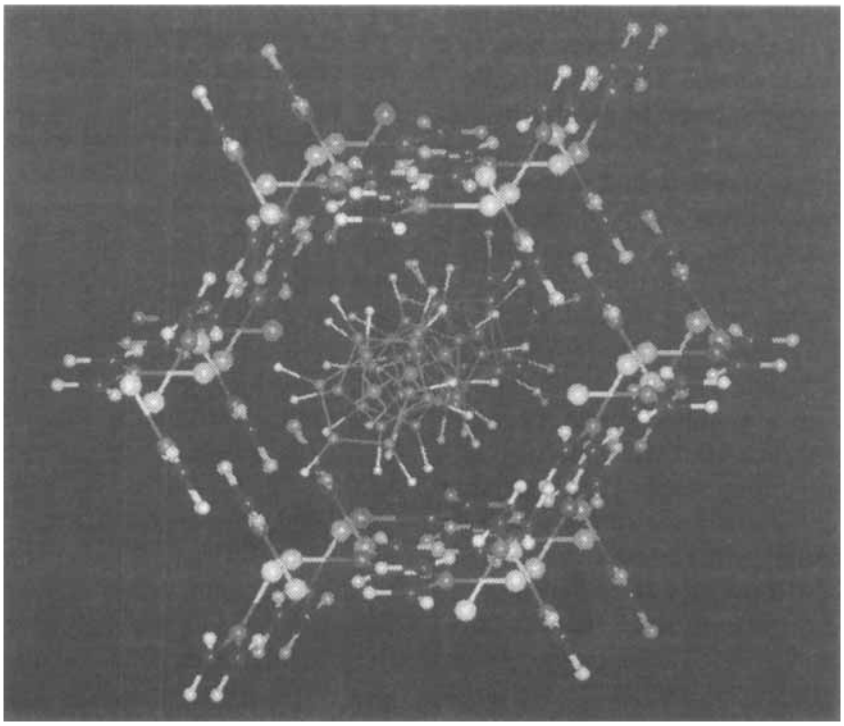

FIGURE 2 Model 1: TU/FE(CP)₂ (1/4). The S, C, N, H and Fe atoms are coloured yellow, green, blue, white and red, respectively. (See color plate II).

tances (the distance between CP rings on neighbouring $Fe(CP)_2$ molecules) are very short at 3.01 Å, a distance significantly less than the sum of van der Waals radii. MM were carried out and the repulsion between adjacent $Fe(CP)_2$ molecules lead to much larger inter-ring distances (3.60–3.82 Å) in the minimised structure. The number of guest molecules in a given channel must therefore be reduced if this parallel ferrocene orientation is to be maintained. Hence, if the actual crystallographically observed iron positions are to be maintained then a different orientation of the ferrocene molecules needs to be found. We therefore repeated the calculations using both MD (carried out at 1000 K) and MM, with the positions of the iron atoms fixed in accordance with the crystal structure but with the orientation of the ferrocenes allowed to vary. Analysis of the results (Table III) shows parallel orientated guest molecules in the host channel. The tilt angles are calculated to be in the range from 9 to 19° (mean tilt angle of 14°) and 1° for the MD and MM calculations, respectively. The minimised structures show aligned ferrocene guest molecules with tilt angles of only 1° off the channel axis.

Clearly this indicates that there is no orientation available to the ferrocene molecules within the channel that can reduce the close intermolecular contacts between them. The crystal structure and the model represent a very tight fit of ferrocene molecules within the channels. Because of the rigid structure of the channels it seems likely that these could expand significantly.

*Model 2: TU/Fe(CP)$_2$, (1/1)*—We now wished to focus on guest—host interactions by studying the ferrocene orientation within the TU channel. Therefore we constructed a model containing a single internally constrained ferrocene molecule in the same length of fixed TU channel

TABLE III Analysis of results

| Analysis | | Off-axis distance of centroid[a] (Å) | Mean tilt angle[b] of ferrocene (°) |
|---|---|---|---|
| *Model 1* | MD (1000 K) | | 14[d] |
| | MM | | 1[d] |
| *Model 2* | *Charge Set 1 (HF[57])* | | |
| | MD (1000 K) | 0.05–0.90 | 13 |
| | MM | 0.10–0.30 | 4 |
| | MC | 0.15–1.00 | 43 |
| | *Charge Set 2 (DF[72])* | | |
| | MD (1000 K) | 0.05–0.80 | 11 |
| | MM | 0.025–0.40 | 5 |
| *Model 3* | MD (1000 K) | | |
| | $Na(2)^+$ | 0.02–3.45 | |
| | $Na(3)^+$ | 0.06–3.55 | |
| | MM | | |
| | $Na(2)^+$ | 2.80–3.15 | |
| | $Na(3)^+$ | 2.75–3.20 | |
| *Model 4* | MD (1000 K) | 0.05–1.10 | 22 |
| | MM | 0.15–1.90 | 2 |
| *Model 5* | MD (1000 K) | [c] | 74 |
| | MM | [c] | 54 |

[a] Fe atom for $Fe(CP)_2$, in the center of the ring.

[b] The angle between the main axis of the guest molecule and the main channel trigonal axis. Angles of 0° and 90° refer to parallel and perpendicular orientations, respectively.

[c] Results show that the toluene guest molecule does not move off-axis.

(Figure 3). The initial position of the ferrocene molecule was compatible with the crystal structure but it was subsequently allowed to move. MD calculations were carried out at 300 and 1000 K but the molecule was relatively static at the lower temperature. Results from the 1000 K simulations are given in Table III. The displacement distances along the channel are calculated to be in the range from −10.0 to 12.5 Å thus indicating that the molecule is moving freely from one end to the other. The guest molecule stays close to the axis as indicated by small off-axis deviations ranging from 0.05 to 0.90 Å. The histogram in Figure 4a shows the distribution of off-axis distances for the iron atom and indicates that 51% of the time, it is more than 0.30 Å from the channel axis but only 10% over 0.85 Å. The simulation was repeated with both sets of charges on the ferrocene but little difference was observed (Table III, Figures 4a and b). The ferrocene guest molecule tilts with angles of 1 to 60° and 1 to 44° for the two sets of charges. The mean tilt angle is 13 or 11° and values of 0° (the parallel orientation) are occasionally adopted. No perpendicular orientations (90° angles) are found and indeed the maximum tilt angle is only 60 or 44°.

The structures from the MD run were then minimised using MM and the structures analysed. As shown in Table III, the results are not very different from those in the MD run. However the off-axis distances are significantly shorter in that now 100% (rather than 51%) of distances are less than 0.3 Å and the tilt angles are also significantly less than those from the unrefined MD results. The minimisation leads to a more regular set of positions for the ferrocene.

MC simulations on Model 2 were carried out using the *DOCKER* program[65] and 100 different random orientations of the guest below an energy threshold (10 kcal/mol) were obtained. As the results for the MD calculations were not significantly different with the two sets of charges, we decided to use just the Lüthi *et al.*[57] charges in the MC calculations. Results showed a wide range of orientations ranging from the parallel to the perpendicular. Table III summarises the results of the guest orientations achieved from the MC simulations. Off-axis distances are calculated to range from 0.15 to 1.00 Å (a mean off-axis distance of 0.50 Å) with only 20% less than 0.3 Å (Figure 4a). The off-channel tilt angle, $\theta$ is calculated to be in the range of 2 to 90°, with a mean value of 43°. We classified orientations as parallel or perpendicular according to whether the tilt angle lay in the range 0–45° or 45–90° and found a ratio of 3:2 in favour of the parallel orientation. Of the perpendicular orientated conformations 8% of these have a tilt angle of approximately 90°. Figure 5 shows a perpendicularly orientated ferrocene guest molecule in the host channel.

The energies and tilt angles from the MM calculations are given in Table IV. These results give the energy variations with different tilt angles for the different model structures. The results show that the most stable conformations correspond to the smallest tilt angles. The calculated mean tilt angles correspond to less stable conformations. We carried out MC calculations on Model 2, as described above, using a threshold energy value of 10.0 kcal/mol. For the most stable conformation with energy of (−36.0 kcal/mol) the ferrocene molecule adopts a parallel position due to a tilt angle of 2°. This energy contribution is less negative than for the MM results and the tilt angle is calculated to be just 1° larger than the one from MM, and still the ferrocene molecule is parallel orientated. The mean tilt angle that corresponds to an energy of (−10.0 kcal/mol) is even larger, a value of 43° indicates a nearly perpendicular orientation (defined as the tilt angles ranged from 45–90°). These results show that movements of the $Fe(CP)_2$ molecule are restricted due to a tight fit.

From Model 2, the MD, MM and MC calculations all show possible movements of the $Fe(CP)_2$ guest molecule in the host channel. The preferred orientation is parallel aligned with the channel axis and is obtained from MD and MM calculations, but the guest also adopts perpen-

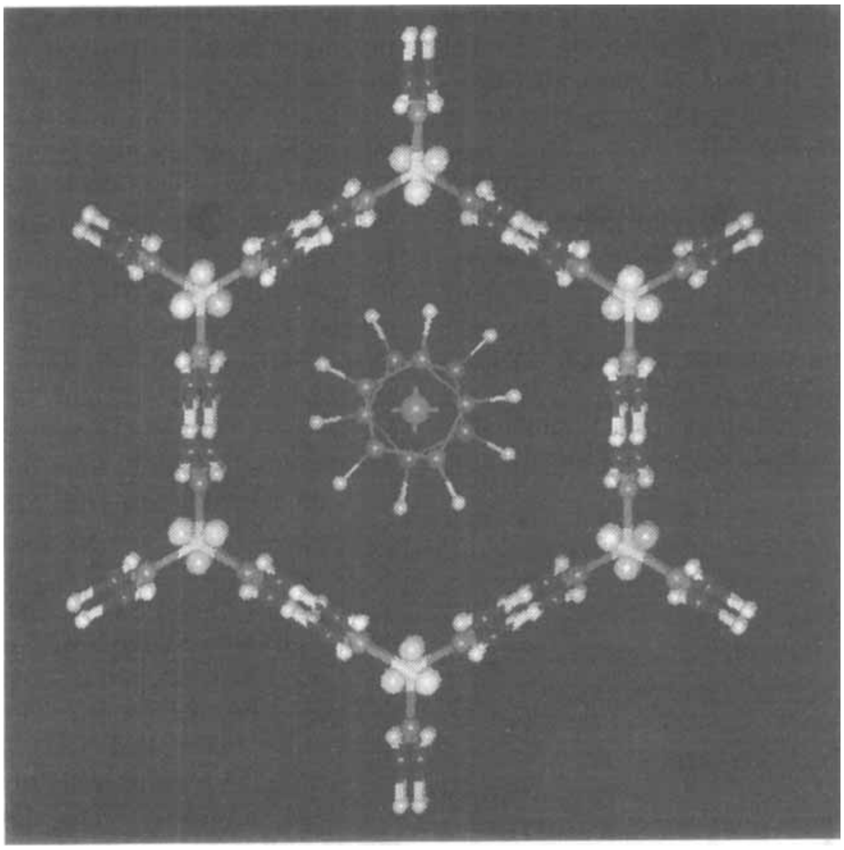

FIGURE 3 Model 2: TU/FE(CP)$_2$, (1/1). The S, C, N, H and Fe atoms are coloured yellow, green, blue, white and red, respectively. (See color plate III).

dicular orientations from MC simulation. The movement of Fe(CP)$_2$ involves tilting as well as rotational and oscillatory movements in the TU channel, but the large size of sulphur atoms in the thiourea molecules may hinder off-axis translation motions. However, the ferrocene guest adopts translation motions along the host channel trigonal axis. The small off-axis distances found show that movements of the Fe(CP)$_2$ molecule in the channel are restricted due to a tight fit. We therefore decided to model the movement of discrete cations in the channel.

*Model 3: TU/Na ions (1/4)*—As our cation we used the Na$^+$ ion for which parameters were available in the force field.[63,64] The starting model used was a fixed TU host lattice with two outer Na$^+$ (numbered 1 and 4) guest ions fixed and two inner Na$^+$ (numbered 2 and 3) guest ions allowed to move (Figure 6). MD calculations were carried out as described above. From 100 frames, we found 19 different positions of the two inner Na$^+$ ions that were allowed to move within in the channel. All the 19 positions were investigated, but the results here concentrate on the most stable form where the two inner Na$^+$ ions are located off the axis in opposite directions towards the channel sides (as in Figure 7). To characterise the movement of the Na$^+$ guest ions, we calculate the distances between the inner mobile Na$^+$ ions and the outer fixed Na$^+$ ion positions perpendicular to the TU channel trigonal axis. The distance (Å) between the two outer fixed Na$^+$ ions (Na(1)$^+$–Na(4)$^+$) is 18.73 Å. We analysed the distances (Na(1)$^+$–Na(2)$^+$) and Na(3)$^+$–Na(4)$^+$ for the mobile Na$^+$

ions number 2 and 3, respectively. The off-axis distances (the distances between the channel trigonal axis and the ions 90° perpendicular to the axis) of Na(2)$^+$ and Na(3)$^+$ perpendicular to the channel axis were also analysed and they range from 0.02 to 3.45 Å and from 0.06 to 3.55 Å for the two ions (Table III). These guest positions were all minimised by MM. Figures 7 gives a picture of the most stable conformation. The most stable frame shows the two inner Na$^+$ ions as a "staggered" form such that the Na(2)$^+$–Na(3)$^+$ vector makes an angle of 45° with the channel axis. By contrast for the least stable form the two inner Na$^+$ ions "eclipse" each other and the vector-channel axis angle is 90°, approximately, thus they are at the same coordinate along the channel axis but positioned directly opposite each other.

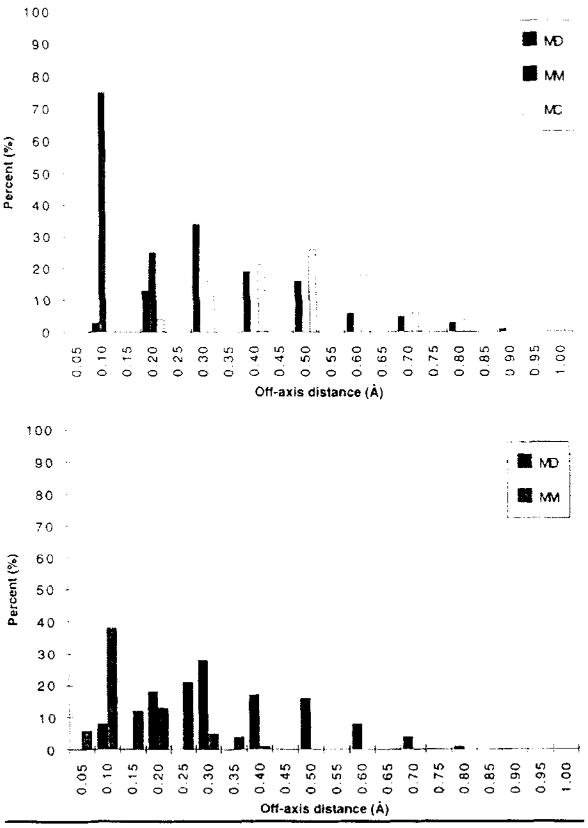

FIGURE 4 The distribution (%) of off-axis distances (Å) for the Model 2. a) Analysis of MD, MM and MC results for Model 2 with Charge Set 1 (*HF*[57]) b) Analysis of MD and MM results for Model 2 with Charge Set 2 (*DF*[72]).

It is also interesting to characterise the guest interactions with the host lattice. The inner two Na$^+$ ions interact with the H and S atoms in the TU host lattice. The results show that the guest–host or non-bonded interactions are longest in the most stable form. The most stable values reported here are calculated to be 2.29 Å (Na(2)$^+$–H) and 3.05 Å (Na(2)$^+$–S) for ion no. 2, and 2.39 Å (Na(3)$^+$–H) and 3.28 Å (Na(3)$^+$–S) for ion no. 3. The non-bonded distances between ions vary only slightly from their MD calculations on minimisation with MM. The off-axis distances of Na(2)$^+$ ion are calculated to be in the range from 2.80 to 3.15 Å and the Na(3)$^+$ ion in between 2.75 and 3.20 Å. The distribution of off-axis positions for the Na(2)$^+$ and Na(3)$^+$ ions are plotted as a function of frequency. The line diagram in Figure 8 show that the mean off-axis distance for Na(2)$^+$ and Na(3)$^+$ ions are 3.10 Å (57%) and 3.15 Å (40%), respectively.

Thus in all calculations the discrete ions have moved well away from the channel trigonal axis, and close to the framework. Because of the potential of the framework which is similar all the way down the channel, we conclude that the Na$^+$ guest ions move through the TU channel well away from the channel axis. Indeed they are attracted towards the side and this may show how the ions move through the channel.

*Model 4*: *TU/Benzene (1/1)*—We then modelled a guest molecule of a size intermediate between the Fe(CP)$_2$ molecules and the Na$^+$ ions to establish how large the guest molecules can be before they are to bulky to move or indeed fit with the channel at all. We chose benzene and toluene, because of their known mobility in the thiourea host lattice. Of particular interest was their preferred orientation whether parallel or perpendicular. While there was no direct experimental evidence that benzene could be occluded into the thiourea lattice, it was noticeable that a range of

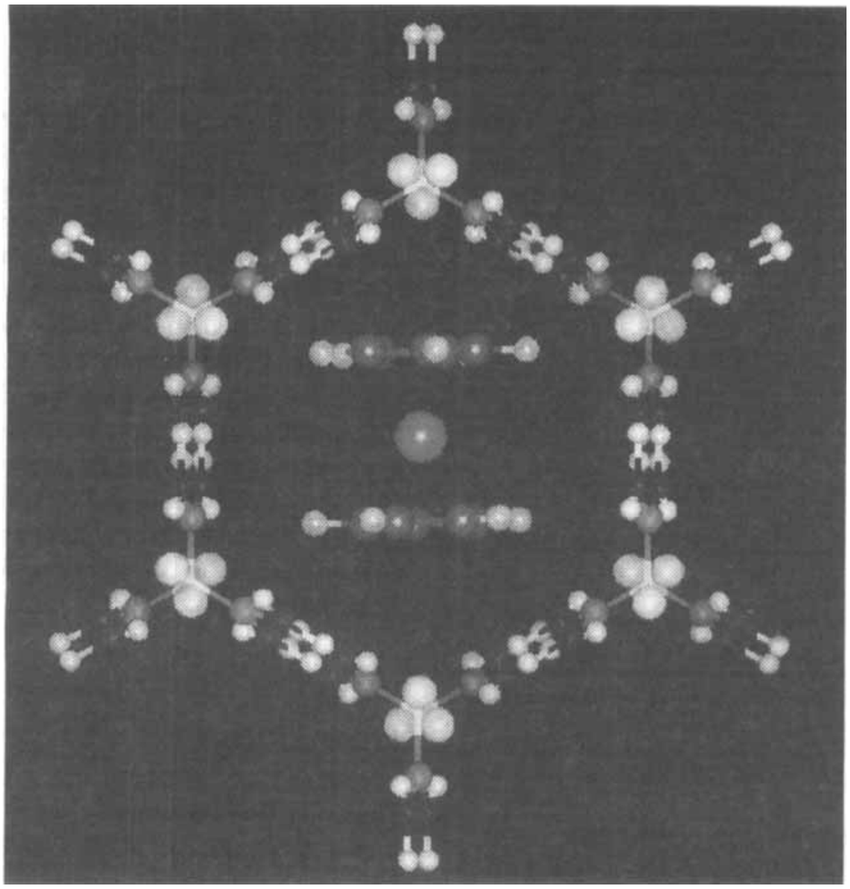

FIGURE 5 Model 2: A perpendicular orientated ferrocene molecule in the TU channel. The S, C, N, H and Fe atoms are coloured yellow, green, blue, white and red, respectively. (See color plate IV).

alkanes and cycloalkanes have been observed to form clathrates.[8,10–13,16,18,19,21,22,34,36,38,45]

The starting model used was a fixed TU host lattice with a benzene molecule as the guest, but to prevent the guest molecule in the channel from moving out, two outer fixed $Na^+$ cations were kept at either end of the channel. We included just one benzene molecule and began our simulation with the molecule in a parallel orientation with its major rotation axis coincident with the channel axis. The centre of the molecule was positioned in one of the vacant crystallographic sites with 32 symmetry. Atoms in the benzene molecule were given default *INSIGHT* charge values; (C: −0.10 and H: 0.10 e). From 100 frames from MD, we obtained a large number of different positions of the benzene molecule where the benzene molecule moves in each direction and rotates in the channel. Table III summarises the results obtained from both the MD and MM calculations and the results are presented in Figure 9. The benzene molecule is primarily aligned along the channel axis, with off-axis positions of the centroid ranging from 0.1 to 1.1 Å. 75% of the benzene positions show the centroid of the molecule at distances off the axis in the range up to 0.3 Å with only 25% above that value thus indicating that the guest molecule prefers to be located in a position close to the channel trigonal axis. The orientations of the benzene molecule cover all possible values of tilt angles (values in the range 1–90° were ob-

TABLE IV Energy values (kcal/mol) and corresponding tilt angles (°) from MM calculations on the several models

| | Model systems | Energies (kcal/mol) | Tilt angles (Mean tilt angles) (°) |
|---|---|---|---|
| *Model 1* | | | |
| | MM | −495.70 | 1<br>(1) |
| *Model 2* | Charge Set 1 (HF[57]) | | |
| | MM | −555.24 | 1<br>(4) |
| | MC | −36.0 | 2<br>(43)[a] |
| *Model 3* | | | |
| | MM | 161.66 | b |
| *Model 4* | | | |
| | MM | 6.66 | 2<br>(2) |
| *Model 5* | | | |
| | MM | 1.83 | 65<br>(54) |

[a] This value corresponds to the energy of −10.0 kcal/mol from the MC calculations.
[b] No tilt angles for Model 3 that contains of ions only.

served) although the mean tilt angle is calculated to be 22° indicating a nearly parallel orientation. The molecular dynamics results indicate a large number of different positions for the benzene molecule and among these there are some frames perpendicular orientated with tilt angles close to 90°.

The structures found from the MD simulation were then minimised with MM but very little variation was found (Table III and Figure 9). In the majority of structures the guest stays close to the channel axis in parallel orientated positions. After refinement only one perpendicular orientation was formed.

*Model 5*: *TU/Toluene (1/1)*—We then repeated the calculations with the slightly larger toluene molecule in order to see whether an extra methyl group would cause the perpendicular orientation to be more favoured. The centre of the benzene ring was positioned as for the benzene molecule. Charges on the toluene atoms were default (*INSIGHT*) values (aromatic C: −0.10, methyl (C: −0.30) and H: 0.1 e).

Results given in Table III show a mean tilt angle of 74° (tilt angles are ranged from 45 to 95°) and a mean tilt angle of 57° (tilt angles are ranged from 44 to 92°) from the MD and MM calculations, respectively. The lowest energy structure (1.83 kcal/mol) had a tilt angle of 65°, and the molecule is orientated with the methyl group directed along the channel axis (Figure 10). The guest molecule stays along the channel axis so that the off-axis distances were close to zero. The extra methyl group lengthens the molecule sufficiently to preclude the parallel orientation of the guest in the host channel and lead to a significantly larger mean tilt angle than for benzene (54, 22° respectively).

## CONCLUSIONS

There are three distinct ways in which the ferrocene molecule can align itself in the thiourea channel. Firstly, the molecular fivefold axis may coincide with the channel threefold trigonal axis. Secondly, the molecular axis lies perpendicular to the channel axis with tilt angles of 90°, and finally the molecular axis is inclined at varying tilt angles less than 90° to the channel axis. The results obtained here quantify the three possibilities of guest orientations in the host channel.

According to x-ray crystallographic studies[14] of ferrocene included in a thiourea host lattice, the first alternative would result in a distance of only 3.01 Å between intermolecular distances in the CPs. We find from the molecular mechanics results on Model 1 that distances ranged from 3.60 to 3.82 Å values which indicate significant repulsions. The rings on neighboring ferrocene guest molecules repel each other and avoid close interactions which is the driving force behind the tilting and rotating of the ferrocenes. Any tilted orientations were unfavorable as they

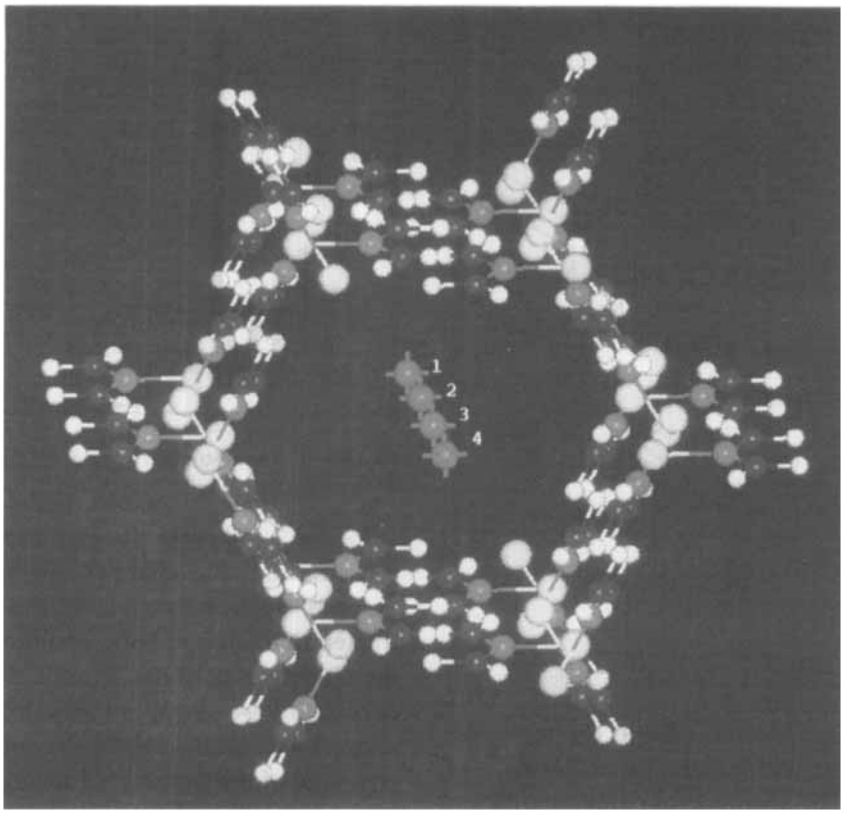

FIGURE 6 Model 3: Position of sodium ions in the TU channel. The S, C, N, H and Na ions are coloured yellow, green, blue, white and red, respectively. (See color plate V).

would increase the effective length and diameter of the molecule in the channel and the switching between the parallel and perpendicular positions were hindered for this reason, too.

Model 2 adopts both parallel orientation where the molecular fivefold axis coincides with the channel trigonal axis and tilt angles are 0 or 180°, and perpendicular orientations with tilt angle of 90°. The molecular dynamics and molecular mechanics calculations of this system with one ferrocene in the TU channel were favorable to the parallel positions of the guest molecule. Such molecules are distributed over a range of orientations close to parallel with the channel axis. Monte Carlo simulations of this model implicates a population distribution of 60%/40% for ferrocene in the parallel/perpendicular orientations. 8% of the 40% perpendicular orientations have tilt angles of exact 90°, and the Fe atom in the guest is then positioned on the channel axis. But, the ferrocene molecule probably alternates between the two orientations in the channel in order to avoid the repulsion inherent from a complete parallel or perpendicular arrangement. Small off-axis positions indicate restricted movements off the axis. However the guest adopts translation motions along the host channel axis. The simulations are consistent with results obtained from recent NMR experimental studies.[41,42] There was not enough space for the guest to move off the axis in the channel, because the channel is too tight. The large size of the sulphur atoms in the TU lattice suggested to lead to periodicity of the van der Waals forces along the length of the channel. The included molecules are trapped at potential minima and

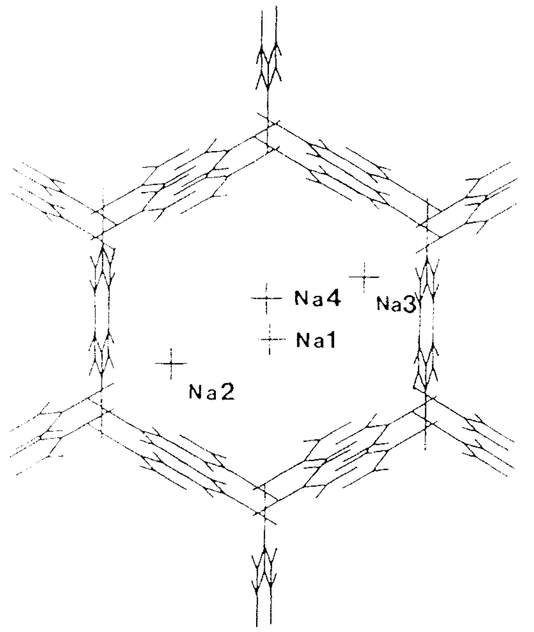

FIGURE 7 The most stable form of Model 3.

hinder translation motion off the channel axis. This is consistent with results from the work of Heyes *et al.*[42] The results from this simulation lead to a further examination of the system with cations, only in the TU channel as guests, and investigate their movements in the channel.

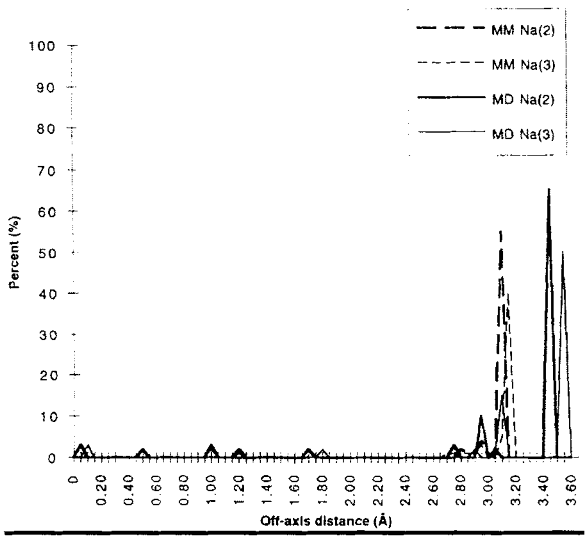

FIGURE 8 The distribution (%) of off-axis distances (Å) for Model 3.

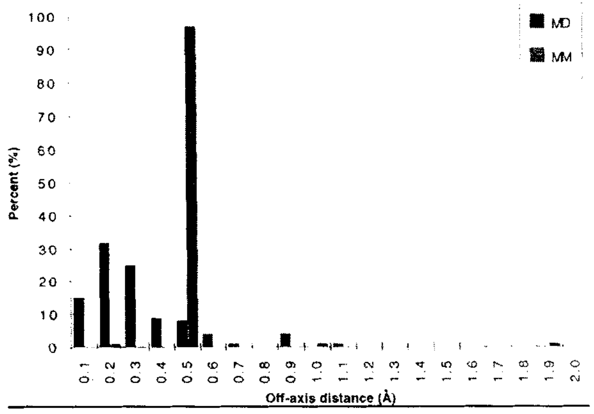

FIGURE 9 The distribution (%) of off-axis distances (Å) for Model 4.

Model 3 indicates the free movements of the ions through the channel. All structures show the ions well off the channel axis as they are attracted to the framework, and the distances from the channel axis range from 2.75 to 3.20 Å. The cations adopt staggered positions on opposite sites of the channel axis. Because of the equal potential of the framework through the channel, we assume that this is the most likely way for

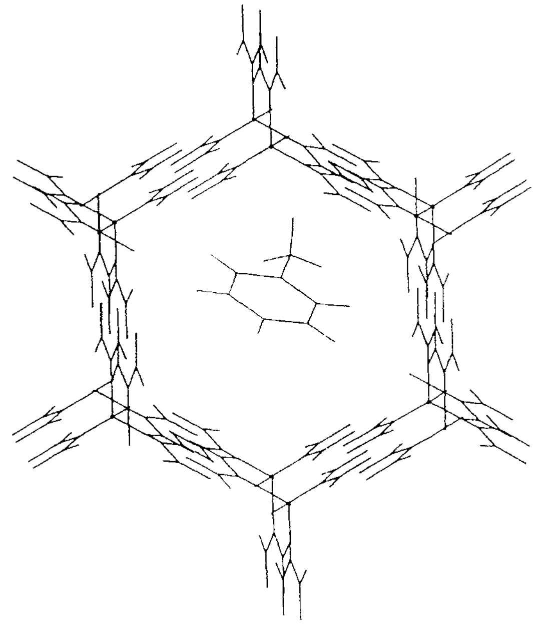

FIGURE 10 Model 5: The most stable position of the toluene in the TU channel.

the ions to move down the channel. It can be concluded from our results that our model is suitable for analysis of the TU/Fe($CP_2$) system. To conclude this work similar theoretical calculations were carried out on cycloalkenes forming clathrates.

Two systems, thiourea/benzene (Model 4) and thiourea/toluene (Model 5) were studied. According to expectations benzene is more mobile in the host channel than the ferrocene and many different orientations are observed, whereas the toluene shows more restricted movements because of the additional methyl group and gives more configurations with the methyl group coincident with the channel axis. The methyl group pointing in the channel direction precludes the parallel orientation of the guest in the host channel. The calculations show that the ferrocene can move along the channel axis but not very far if off the axis. Since there also are possibilities for perpendicular orientations in the channel, the theoretical work is consistent with experimental studies.

This molecular modelling study has considerably added to our understanding of the molecular dynamics of the ferrocene molecules in thiourea, and the study illustrates the general utility of our approach in using theoretical techniques into reorientations of guests in metallocene clathrates. These theoretical studies are useful in studying the dynamic behaviour of guest molecules in host structures, and the methods are transferable to related systems *i.e.* zeotypes.

## *Acknowledgment*

Financial support of this work by the Norwegian Research Council (NFR) by the Norwegian Research Council (NFR), and VISTA (STATOIL) and the British Council for awarding travel and subsistence grants are gratefully acknowledged.

We thank S.E.R.C. for the provision of computer modelling equipment at the University of Reading, BIOSYM Technologies Inc. for providing the *INSIGHT/DISCOVER* suite of programs and Dr. Clive Freeman for providing his *DOCKER* program.

## *References*

[1] Takemoto, K. and Sonoda, N. (1984). in *Inclusion Compounds* Atwood, J. L., Davies, J. E. D. and MacNicol, D. D. Eds., Academic Press, London, 2.
[2] Schlenk, W. (1949). *Annalen*, **565**, 204.
[3] Schlenk, W. (1949). *Annalen*, **573**, 142.
[4] Schlenk, W. (1950). *Experientia*, **6**, 292.
[5] Schlenk, W. (1959). *Fette u. Seifen*, **52**, 654.
[6] Schlenk, W. (1950). *Angew. Chem.*, **62A**, 299.
[7] Schlenk, W. (1951). *Fortschr. Chem. Forsch.*, **2**, 92.
[8] Redlich, O., Gable, C. M., Beason, L. R. and Millar, R. W. (1950). *J. Am. Chem. Soc.*, **72**, 4161.
[9] Smith, A. E. (1952). *Acta Cryst.*, **5**, 224.
[10] Lenne, H. V. (1954). *Acta. Cryst.*, **7**, 1.
[11] Clement, R., Gourdji, M. and Guibe, L. (1971). *Mol. Phys.*, **21**, 247.
[12] Chekova, G. N., Dyadin, Yu. A., Oglezneva, I. M., Aprova, T. Ya. and Gaponenko, L. A. (1987). *Ser. Khim. Nauk.*, **1**, 70.
[13] Garneau, I., Raymond, S. and Brisse, F. (1995). *Acta Crystallogr., Sect. C: Cryst. Struct. Commun.*, **C51**, 538.
[14] Hough, E. and Nicholson, D. G. (1978). *J. Chem. Soc. Dalton Trans.*, 15.
[15] Clement, R., Claude, R. and Mazieres, C. (1974). *J. Chem. Soc. Chem. Comm.*, 654.
[16] Vergelati, C. and Brisse, F. (1986). *ACA*, **14**, 52.
[17] Fait, J. F., Fitzgerald, A., Caughlan, C. N. and McCandless, F. P. (1991). *Acta Cryst., Sect. C: Cryst. Struct. Commun.*, **47**, 332.
[18] Fait, J. F., Fitzergerald, A., Caughlan, C. N. and McCandless, F. P. (1985). *ACA*, **13**, 55.
[19] Tam, W., Eaton, D. F., Calabrese, J. C., Williams, I. D., Wang, Y. and Anderson, A. G. (1989). *Chemistry of Materials*, **1**, 128.
[20] Shindo, T., Shindo, M., Ohnuma, H. and Kabuto, C. (1993). *Bull. Chem. Soc. Jpn.*, **66**, 1914.
[21] Clement, R., Jegovdez, J. and Mazieres, C. (1974). *J. Solid State Chem.*, **10**, 46.
[22] Harris, K. D. M. (1990). *J. Solid State Chem.*, **84**, 280.
[23] Gopal, R., B. E. Robertson and Rutherford, J. S. (1989). *Acta Cryst., Sect. C: Cryst. Struct. Commun.*, **45**, 257.
[24] Weber, G. (1983). *Acta Cryst., Sect. C: Cryst. Struct. Commun.*, **39**, 986.
[25] Weber, G. and Sheldrick, G. M. (1984). *Acta Cryst., Sect. A: Fnd. Cryst.*, **40**, 275.
[26] Weber, G. (1984). *J. Incl. Phenom.*, **1**, 339.
[27] Drew, M. G. B. and Nicholson, D. G. (1985). *Acta Cryst., Sect. C: Cryst. Struct. Commun.*, **41**, 1358.
[28] Anderson, A. G., Calbrese, J. C., Tam, W. and Williams, I. D. (1987). *Chem. Phys. Lett.*, **134**, 392.
[29] Stuart, A. A. V. (1956). *Rec. Trav. Chim.*, **75**, 906.
[30] Radell, J. and Hunt, P. O. (1958). *J. Am. Chem. Soc.*, **80**, 2683.
[31] Barlow, G. B. and Corish, P. J. (1959). *J. Chem. Soc.*, 1706.

[32] Fischer, P. H. H. and McDowell, C. A. (1960). *Can. J. Chem.*, **38**, 187.

[33] Meakins, R. J. (1955). *Trans. Faraday Soc.*, **51**, 953.

[34] Gilson, D. F. R. and McDowell, C. A. (1961). *Mol. Phys.*, **4**, 125.

[35] Bozak, R. E. and Barone, A. D. (1975). *Chem. Lett.*, **1**, 75.

[36] Gustavsen, J. E., Klæboe, P. and Kvila, H. (1978). *Acta Chem. Scand.*, **A32**, 25.

[37] Sorai, M., Ogasahara, K. and Suya, H. (1981). *Mol. Cryst. Liq. Cryst.*, **73**, 231.

[38] Meirovitch, E. (1983). *J. Phys. Chem.*, **87**, 3310.

[39] Harris, K. D. M. and Thomas, J. M. (1990). *J. Chem. Soc., Faraday Trans.*, **86**, 2985.

[40] Harris, K. D. M. (1990). *J. Solid State Chem.*, **84**, 280.

[41] Lowery, M. D., Wittebort, R. J., Sorai, M. and Hendrickson, D. N. (1990). *J. Am. Chem. Soc.*, **112**, 4214.

[42] Heyes, S. J., Clayden, N. J. and Dobson, C. M. (1991). *J. Phys. Chem.*, **95**, 1547.

[43] Lund, A., Nicholson, D. G., Parish, R. V. and Wright, J. (1994). *Acta Chem. Scand.*, **48**, 738.

[44] Clement, R., Gourdji, M. and Guibe, L. (1975). *Magn. Reson. Chem.*, **20**, 345.

[45] Meirowitch, E. (1984). *J. Phys. Chem.*, **88**, 6411.

[46] McKinnon, M. S. and Wasylishen, R. E. (1986). *Chem. Phys. Lett.*, **130**, 565.

[47] Mueller, K. (1992). *J. Phys. Chem.*, **96**, 5733.

[48] Mueller, K. (1992). *Magn. Reson. Chem.*, **30**, 228.

[49] Macintosh, M. R., Fraser, B., Gruwel, M. L. H., Wasylishen, R. E. and Cameron, T. S. (1992). *J. Phys. Chem.*, **96**, 8572.

[50] Aliev, A. E. and Harris, K. D. M. (1993). *J. Am. Chem. Soc.*, **115**, 6369.

[51] Mueller, K. (1995). *Magn. Reson. Chem.*, **33**, 127.

[52] Dunitz, J. D., Orgel, L. E. and Rich, A. (1956). *Acta Cryst.*, **9**, 373.

[53] Haaland, A. and Nilsson, J. E. (1968). *Acta Chem. Scand.*, **22**, 2653.

[54] Armstrong, D. R., Fortune, R. and Perkins, P. G. (1976). *J. Organomet. Chem.*, **111**, 197–213.

[55] Taylor, T. E. and Hall, M. B. (1985). *Chem. Phys. Lett.*, **114**, 338.

[56] Lüthi, H. P., Ammeter, J. H., Almlöf, J. and Korsell, K. (1980). *Chem. Phys. Lett.*, **69**, 540.

[57] Lüthi, H. P., Ammeter, J. H., Almlöf, J. and Fægri Jr, K. (1982). *J. Chem. Phys.*, **77**, 2002.

[58] Lüthi, H. P., Siegbahn, P. E. M., Almlöf, J., Fægri Jr., K. and Heiberg, A. (1984). *Chem. Phys. Lett.*, **111**, 1.

[59] Thompson, N. D., Clark, R. L. and Bosnich, B. (1993). *J. Am. Chem. Soc.*, **114**, 7264.

[60] Rodger, M. (1990). *Chemistry in Britain*, 1090.

[61] George, A. R. and Harris, K. D. M. (1994). *J. Mater. Chem.*, **4**, 1731.

[62] Drew, M. G. B., Fisher, A. and Smith, C. M. (1991). *CRYSTAL*, The University, Reading, U.K.

[63] *INSIGHT/DISCOVER*, Biosym Technologies, San Diego, California, U.S.A. *INSIGHT* version 2.1.0, *DISCOVER* version 2.8, (1992).

[64] Dauber-Osguthorpe, (1988). *DISCOVER* User Guide 1, version 2.8, (1992), 3–9, Biosym Technologies, San Diego, California, U.S.A.

[65] Freeman, C. L. (1991). *DOCKER Program*, Private Communication.

[66] Clark, T. (1985). *A Handbook of Computational Chemistry*, John Wiley and Sons, Ltd.

[67] Hehre, W. J., Radom, L., Schleyer, P. v. R. and Pople, J. A. (1986). *Ab initio molecular orbital theory*, John Wiley and Sons, Ltd.

[68] Hinchliffe, A. (1988). *Computational and Quantum Chemistry*, John Wiley and Sons, Ltd.

[69] Stewart, J. J. P. Quantum Chemistry program Exchange, Program No 455, *MOPAC*, version 5, Indiana University, Chemistry Department, Indiana, U.S.A.

[70] Merz, K. M. and Kollmann, P. A. (1990). *J. Comp. Chem.*, **11**, 431.

[71] Orozco, M. and Luque, F. J. (1990). *J. Comp. Chem.*, **11**, 909.

[72] *DMOL*, version 2.2, Biosym Technologies, San Diego, California, U.S.A., (1992).