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Molecular mechanics and cluster analysis of nickel(II) six-membered rings†

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An agglomerative, hierarchical, single-link cluster analysis was used to find all the conformational families available to nickel(II) six-membered rings. All saturated nickel(II) solid-state structures in the Cambridge Structure Database were clustered. The reasons why high-energy non-chair conformations are adopted were analysed by molecular mechanics. The high-energy structures of sixteen-membered tetraaza- and tetrathia-macrocycles can only be accounted for by assuming that they are artifacts of their metal incorporation mechanism. No correlation between the conformation and the spin state of the nickel(II) or the co-ordination geometry was found. The identity of the ligating atoms did not affect the co-ordination geometry or ring conformation.

Nickel is found in many co-ordination compounds and in the last 15 years it has been found to be an essential component of four enzymes.[1] The study of these complexes is complicated by the fact that nickel is a d^8 system, which can adopt high-spin and low-spin forms, and that these have been found in a variety of co-ordination geometries. High-spin nickel(II) can adopt six- (octahedral), five- [trigonal-bipyramidal (*TBPY*) and square-pyramidal (*SPY*)], and four-co-ordinate (tetrahedral) geometries, while low-spin complexes have been found in five- (*TBPY*, *SPY*) and four-co-ordinate (square-planar) geometries. We have previously used the cluster and molecular mechanics techniques to analyse cobalt(III)–propanediamine rings.[2] We chose cobalt because it is a 'well behaved' transition metal and easy to model using molecular mechanics. In this paper we have extended our work to nickel(II) complexes due to its importance and in order (*i*) to investigate the effect of spin state on the conformation of the six-membered rings, (*ii*) to establish the effect of having ligating atoms other than nitrogen in the six-membered ring and (*iii*) to find out how the conformations of the six-membered rings are influenced by the co-ordination geometry of the metal ion.

The aim of a cluster analysis is to place objects into groups, also called clusters, in such a way that all the objects within a cluster are very similar and that all the objects in different clusters are very dissimilar to each other. Recently three programs have been released that cluster molecules on the basis of their conformations; two were written primarily for the analysis of structures generated in molecular dynamics runs,[3,4] and one was written primarily for conceptual database analysis.[5] In this study we have used the XCLUSTER program[3] which is an agglomerative, hierarchical, single-link method. The first step, in such a cluster analysis, is to find a similarity criterion and arrange all the molecules in a generic ordering according to their similarities. Therefore structure 2 is most similar to structures 1 and 3, while 3 is most similar to structures 2 and 4, and very dissimilar to molecules much higher in the genetic ordering. In clustering level 1 all the structures are generically ordered and placed in separate clusters. In each following clustering level the two molecules that are most similar to each other are joined to form a cluster. If the two structures are in separate clusters, the clusters are joined. At the end all the structures will be joined in one large cluster. If N structures are being clustered, at clustering level 1 there will be N clusters each containing one structure, at level 2 there will be $N - 1$ clusters, and at level N there will be one cluster containing all N structures. One of the difficulties in an agglomerative, hierarchical, single-link method is to choose between all the clustering levels and find a level, or levels, at which the clusters are significantly different. We have found that the separation ratio[3] and visual inspection of both the distance maps and clustering mosaics are the best indicators of a significant clustering level. Some reservations have been expressed that single-link methods can link dissimilar clusters that contain bridging outlying members. However, this was not found to be a problem in clustering cobalt(II)–propanediamine complexes and we will show that single-link clustering is also able to separate all the six-membered nickel(II) ring conformations shown in Fig. 1.

Chair

Boat

λ Twist-boat (symmetrical)

δ Twist-boat (symmetrical)

Half-chair

Sofa

Fig. 1 Common conformations adopted by six-membered rings

Cluster analysis has effectively been used in the contraction of conformational space in the multiconformational analysis of solution nuclear Overhauser effect (NOE) data,[6] drug discovery,[7] database searching,[8] analytical chemistry[9] and biochemistry.[10] A cluster analysis of organic six-membered ring systems has been published.[11] However, to date no such analysis of any nickel complexes has been reported, and our cluster analysis of cobalt(III) was the first for a transition metal.

Inorganic molecular mechanical calculations have become increasingly popular in the last decade,[12] and molecular mechanical analyses of nickel(II) complexes have become common. Nickel has been modelled in porphyrins,[13] methyl-

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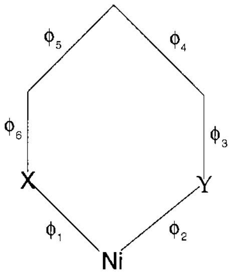
† *Non-SI unit employed*: dyn = 10^{-5} N.



Scheme 1 Six-membered nickel(II) fragment with dihedral labelling used in Table 1

coenzyme M reductase,[14] macrocycles[15] and in organometallic compounds.[16]

Cyclohexane and its organic derivatives have been extensively studied for more than 100 years.[17] Six-membered rings such as cyclohexane can adopt chair(D_{3d}), boat(C_{2v}), twist-boat(D_2), half-chair(C_2) and sofa(C_3) geometries, see Fig. 1, which can be uniquely defined by the six intraannular dihedral angles, or more efficiently by the three Cremer–Pople[18] or the three Haasnoot[19] parameters. The energy surface of cyclohexane is best described as an inverse Mexican hat potential. The chair conformation sits at the tip of the hat 26.4 kJ mol^{-1} lower in energy than the boat conformation which is located on a slight bump on the rim of the hat 2.6 kJ mol^{-1} higher in energy than the twist boat conformation that is also located on the rim.[20,21] An energy barrier of 4.6 kJ mol^{-1} has been calculated for the twist-boat interconversion, which passes through the boat form along the rim of the hat. The interconversion between the chair and the twist-boat form has to go through the sofa or half-chair form with an energy barrier 43.9 kJ mol^{-1}.[22]

Since the bond lengths between the nickel ion and the ligating atoms are much longer than the carbon–carbon bonds in cyclohexane, the potential energy surface of nickel-containing six-membered rings does not resemble a new, symmetric inverse Mexican hat, rather it resembles a rather worn and distorted Mexican hat. The chair conformation is still the lowest-energy conformation and resides at the tip of the hat, however all the boats and twist boats are no longer identical, nor are the paths from the chair to the boats or twist-boats identical.

The conformations of cyclohexane have also been represented by a spherical map.[23] The two poles of the sphere correspond to the chair conformations, while the twist-boat and boat conformations lie on the equator. Pseudo-rotational conformational changes are depicted horizontally (latitudinally) and symmetrical changes vertically (longitudinally).

Experimental

The Cambridge Structure Database (CSD)[24] V5.11 was searched for all nickel(II) six-membered rings having the substructure shown in Scheme 1. Structures having only sp^3 hybridized carbons and ligating atoms in the six-membered rings were saved. Version 5.11 of the CSD was released in April 1996 and contains 152 464 crystal structures. All the hits were stored and converted into MACROMODEL format using the CSDCONV program. All atoms that were not part of the fragment shown in Scheme 1 were removed with the draw function in MACROMODEL.[25] Atoms were renumbered so that all six-membered rings were numbered in the same way, and placed into a masterfile for cluster analysis. The XCLUSTER[3] program was used for cluster analysis. Proximity matrixes were obtained by determining the pairwise distances between six-membered rings using (*i*) the root-mean-square (r.m.s.) differences between corresponding dihedral angles and (*ii*) the r.m.s. displacement between pairs of identically numbered atoms after optimum rigid-body superimposition.[26] The rings were symmetry adapted as described previously.[2]

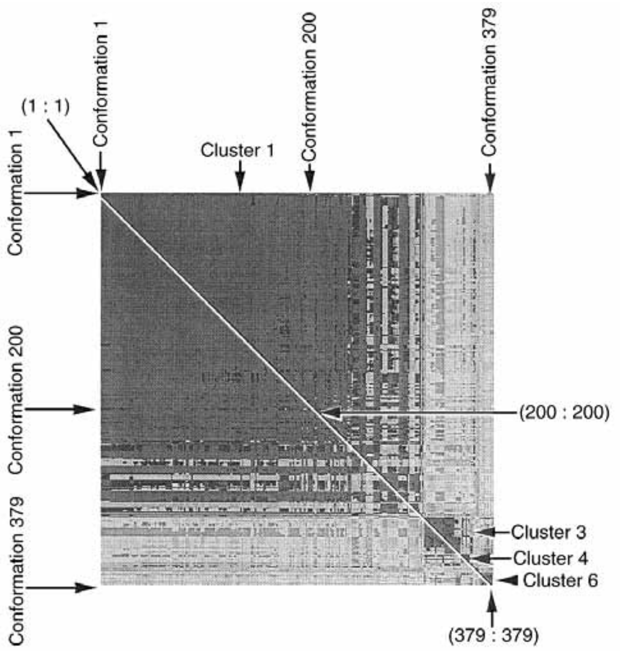


Fig. 2 Distance map of the 379 nickel(II) six-membered propanediamine rings. The cross-coordinates of conformationally similar rings are darkly coloured, while dissimilar structures are lightly coloured

The correlation/covariance spreadsheet of VISTA 2.0 in the CSD was used to establish whether any correlations between structural parameters were present.

The program MACROMODEL v5.5 was used for all the molecular mechanical analysis. The MM2* parameter set was used with some additional parameters. Hancock's[27] and Lindoy's[28] nickel and nitrogen parameters were used and the following nickel(II) and sulfur parameters were added: Ni–S ($r^0 = 2.42$ Å, $k = 0.68$ mdyn Å^{-1}), S–Ni–S ($\theta° = 90$ or 180°, $k = 0.50$ mdyn rad^2) and Ni–S–C ($\theta° = 109.5°$, $k = 0.50$ mdyn rad^2). As is usually the case in inorganic molecular mechanics the torsions around the metal ion were taken as zero.[26] Molecular dynamics runs were used to sample the conformational space around the different [16]aneN_4 and [16]aneS_4 configurations (1,5,9,13-tetraaza- and 1,5,9,13-tetrathia-cyclohexadecane respectively). One nanosecond simulations at 1000 K were sampled 100 times and the sampled structures were minimized to find low-energy conformations.

Results and Discussion

One hundred and ninety structures containing the sub-structure shown in Scheme 1, where X = Y = N, were obtained from the CSD search. Most of these complexes have one or more six-membered ring, resulting in three hundred and seventy-nine six-membered rings that were saved. The Cartesian coordinates and all the parameters associated with the rings (bond lengths, angles, dihedrals and the Cremer–Pople parameters) were saved from the CSD. No correlation was found between the Ni–N bond length or the N–Ni–N bond angles and the Cremer–Pople parameters, which define the rings conformation.

The distance map that was obtained from the cluster analysis of the 379 nickel(II)–propanediamine rings is shown in Fig. 2. It can be viewed as a matrix in which the structures are generically ordered with structure 1 in the top left-hand corner and all the other structures numerically ordered from the top to bottom, and from left to right. Therefore structure 379 is located in the top right corner and also in the bottom left corner. The map is coloured according to the similarity of the structures that define the coordinates. The (1:1), (2:2), (3:3)...(200:200) ...(379:379) coordinates are all very dark as they are comparing two identical structures, on the other hand, the (1:379)

Table 1 Average torsional angles of each cluster at clustering level 373, and of ideal and minimized six-membered ring conformations

	Torsion angle/°							
Cluster	φ_1	φ_2	φ_3	φ_4	φ_5	φ_6	Conference	Abundance (%)
1	−40.0	39.8	−56.5	68.3	−68.0	56.1	Chair	83.4
2	−10.9	20.1	−26.5	70.8	−62.3	11.1	Sofa	0.3
3	−58.5	57.1	−8.8	60.5	58.9	10.7	Boat	10.3
4	−44.0	19.6	14.6	51.2	−81.3	32.1	λ twist-boat	2.4
5	−17.4	−40.4	62.6	−49.5	−23.6	65.5	λ twist-boat	0.8
6	35.9	23.8	−67.0	45.3	26.0	−48.9	δ twist-boat	2.9
7	6.9	−6.9	−4.9	−0.1	0.6	4.4	Flat	0.3
	−60.0	60.0	−60.0	60.0	−60.0	60.0	Idealized chair	
	−60.0	60.0	0.0	60.0	−60.0	0.0	Idealized boat	
	−33.3	−33.3	70.0	−33.3	−33.3	70	Idealized twist-boat	
	0.0	0.0	−30.0	60.0	−60.0	30.0	Idealized sofa	
	−58.2	58.2	−65.2	58.2	−65.2	58.2	Minimized chair	
	−59.2	8.1	48.7	−67.7	14.1	51.0	Minimized twist-boat	

coordinate in the bottom left corner and the (379 : 1) coordinate in the top right corner are very light as structures 1 and 379 are very far apart in the genetic ordering and therefore have very different conformations. The figure shows that there is one large cluster that contains many similar structures and that there are numerous smaller less distinct clusters.

At a given clustering level, the separation ratio is the ratio of the largest conformational distance between any two structures in the same cluster at that level to the shortest conformational distance between any two structures that are not in the same cluster at that clustering level.[3] Together with the distance map we have found it to be a very useful way of finding significant clustering levels in the analysis of six-membered rings.[2] In the cluster analysis described here the minimum separation ratio for clustering level 373 is 0.275 higher than its neighbouring clustering levels. Taken together with the distance map this led us to focus our attention on clustering level 373. At this level there are seven clusters. Their average torsion angles, the torsion angles of the ideal cyclohexane conformations, and the dihedral angles obtained when minimizing the ideal conformations are displayed in Table 1. There are 316 members in cluster 1, they are all chairs and make up 83% of all the saturated nickel(II) six-membered rings in the CSD. The conformations and relative abundance of the other clusters are also given in Table 1.

An isolated nickel(II)–propanediamine ring was minimized from an ideal chair conformation. The resulting conformation has similar internal torsional angles to the average dihedral angles of cluster 1 and is clearly still a chair, see Table 1. A conformational search revealed that this conformation is located at the global minimum. Only one other minimum was located in the search, a twist-boat. The chair is 16.1 kJ mol^{-1} lower in energy than the twist-boat conformation. As is the case for cyclohexane, the boat conformation is a minimum between the two chair forms and a saddle point between the two twist-boats. Owing to the long Ni–N distances, the nickel(II)–propanediamine rings do not behave like cyclohexane, and the low-energy chair conformation is slightly different to the symmetric ideal chair in cyclohexane.

Cluster 2 contains one member which is in the sofa conformation. Although the sofa is fairly common when part of the six-membered ring is unsaturated, it is unusual in saturated rings. The complex (CSD name = PAKVUS[29]) containing the six-membered ring in the sofa conformation is shown in Fig. 3. It is a strained complex that has four six-membered rings, two of which are chairs, one a sofa and one a twist-boat. The twist-boat is located in cluster 4. Molecular mechanics calculations reveal that this is indeed the most stable conformation of the complex. The twist-boat is formed in order to accommodate chair conformations in the other two rings, while the sofa is formed because non-bonded repulsions between the hydrogens shown in Fig. 3 prevent the adoption of a chair conformation in this ring.

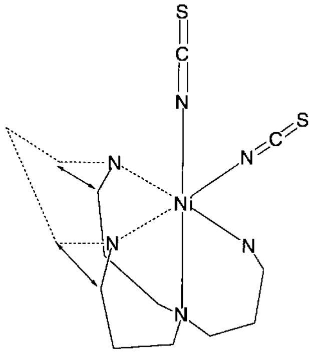


Fig. 3 The structure of PAKVUS, the sofa six-membered ring is drawn with the dotted line (------) and the non-bonded interactions preventing the adoption of a chair conformation are indicated by the ⟵⟶

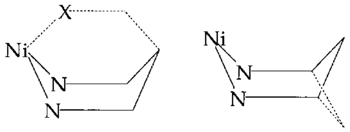


Fig. 4 Structural fragments responsible for enforcing boat conformations

Even though one cannot expect a Boltzmann distribution, one should still see a relationship between the abundance of a conformation and its potential energy. Therefore it is not surprising to see that the chair conformation, which has the lowest strain energy, is the most common conformation, however there has to be a reason for the high abundance of the boat conformation, which is a saddle point.

Investigation of the 39 boats found in cluster 3 reveals that they are all due to one of the two structural constraints shown in Fig. 4, and that the rings in these complexes cannot adopt chair conformations. The Ni–N–C angles of the boats are much closer to the expected tetrahedral angles than those of the chairs and twist-boats. Although this is energetically favourable, it is more than counterbalanced by the eclipsing of two endocyclic dihedral angles. The high-energy boat conformations are adopted because the co-ordination of a pendant arm linked to the six-membered ring structurally prevents the adoption of a chair conformation (Fig. 4, left), or because the six-membered ring is part of a bicyclic system in which one of the rings adopts a chair conformation and therefore prevents the other ring from doing so (Fig. 4, right).

The twist-boats in cluster 4 are due to the preference for equatorial methyl groups in pentane-2,4-diamine ligands and its derivatives, to structural constraints in tripod ligands, and in

Table 2 All the configurations of nickel(II) complexes of [16]aneN_4 and [16]aneS_4 with the conformations of the six-membered rings and the relative strain energy

Macrocycle	Configuration	Ring 1	Ring 2	Ring 3	Ring 4	Relative energy/kJ mol^{-1}
[16]aneN_4	$++++$	Chair	λ-t.b.	Chair	Sofa	−267.98
	$+++-$	Chair	Chair	δ-t.b.	λ-t.b.	−280.35
	$++--$	Chair	Chair	δ-t.b.	λ-t.b.	−279.86
	$+-+-$	δ-t.b.	λ-t.b.	δ-t.b.	λ-t.b.	−281.58
[16]aneS_4	$++++$	Chair	Chair	Chair	Chair	−603.00
	$+++-$	Chair	Chair	δ-t.b.	λ-t.b.	−581.27
	$++--$	Chair	λ-t.b.	Chair	δ-t.b.	−584.33
	$+-+-$	λ-t.b.	δ-t.b.	λ-t.b.	δ-t.b.	−536.08

t.b. = Twist-boat.

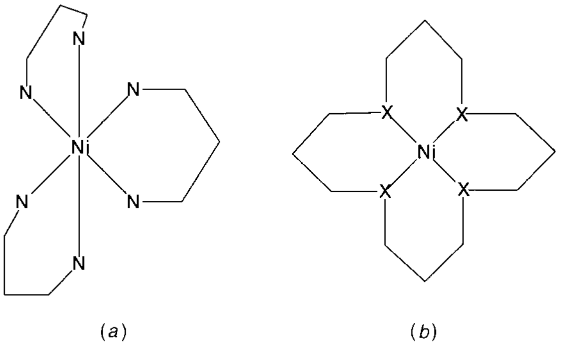


Fig. 5 The structures of (*a*) CULXOW and (*b*) DITVIL (X = N, *i.e.* [16]aneN_4) and KURLIS (X = S, *i.e.* [16]aneS_4)

the case of PAKVUS due to the interannular interactions shown in Fig. 3.

The three λ twist-boats in cluster 5 are all found in triazadodecane macrocycles. The 11 δ twist-boats in cluster 6 can all be modelled by molecular mechanics, except DITVIL[30] (see Fig. 5) which will be discussed in more detail later on in this paper, and CULXOW[31] (see Fig. 5) which has one chair, one twist-boat and one flat phenyl-like ring found in cluster 7. The most likely reason molecular mechanical calculations cannot model the crystal structures of DITVIL and CULXOW is the presence of packing interactions in the solid state that are not considered in the calculations.

Octahedral (63%), square-planar (28%), square-pyramidal (5%) and trigonal-bipyramidal (4%) nickel(II) geometries were found in the 190 nickel(II)–propanediamine complexes. There was no correlation between the geometry of the metal ion and the conformation of the six-membered rings as quantified by the cluster membership. Seventy-five percent of the CSD hits were found to be high-spin nickel(II) complexes, and there was no correlation between cluster membership and spin state. All low-spin complexes were square planar and the Ni–N distances were less than 2.00 Å.

In order to establish the effect of having ligating atoms other than nitrogen in the six-membered ring, and the consequence of having longer Ni–X distances, the CSD was searched for all nickel(II) six-membered rings with the sub-structure shown in Scheme 1, where X and Y are not both nitrogens. Thirty hits were saved with oxygen, sulfur and phosphorus ligating atoms. Eighteen of the complexes were octahedral, 10 were square planar and two were square pyramidal. Fifty-four six-membered rings were obtained upon separating the 30 complexes into six-membered rings.

Although the same clusters were obtained at high clustering levels when using atomic overlap or torsional differences as similarity criteria, at lower clustering levels there were noticeable differences. The reason for this is fairly obvious; when the dihedral angles are used as a measure of similarity, the lengths of the Ni–X and C–X bonds are not important. However, if the difference in Cartesian coordinates between identical pairs of atoms is used, then differing bond lengths will result in larger differences and therefore in different clusters. The fact that the same clusters are obtained at the more important higher clustering levels indicates that the agglomerative, hierarchical, single-link clustering method is a fairly robust technique.

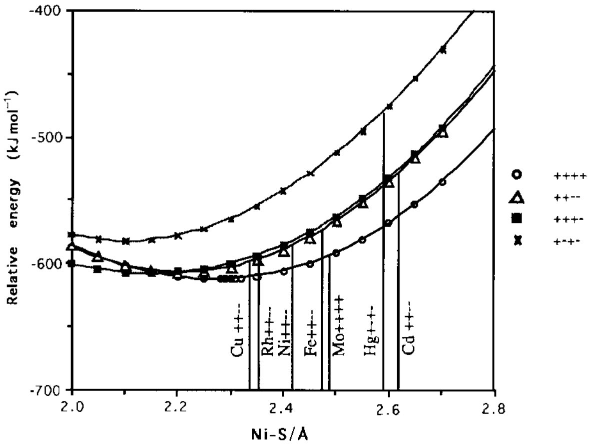


Fig. 6 Plot of the relative strain energy *vs.* the metal–sulfur distance for [16]aneS_4

At clustering level 50 both similarity measures resulted in five identical clusters containing boats (13% of the structures), two clusters of λ twist-boats (7 and 5%), chairs (66%) and δ twist boats (7%). There was no correlation between the nature of the ligating atoms and the six-membered ring conformation. The formation of all the boat conformations can be explained in the same way as shown in Fig. 4, for the nickel(II)–propanediamine structures. When the 54 six-membered rings with $X \neq N$ were added to the 379 six-membered rings with X = N the same conformational clusters were obtained at high clustering levels with both similarity measures.

Since the conformations found for the crystal structures of both the tetraaza (DITVIL) and tetrathia (KURLIS[32]) sixteen-membered macrocycles were different to those predicted by our molecular mechanics calculations we investigated them in more detail. As each nitrogen in [16]aneN_4 is bound to one hydrogen that can be located above or below the plane of the macrocyclic ligand, the nickel(II) macrocyclic complex can adopt four different configurations. The same is true for [16]aneS_4, in which the relative positions of the sulfur lone pairs determines its configuration. A common notation[33] for the different configurations is to denote the hydrogens or lone pairs above the plane by a + and those below it with a −.

A thorough conformational search revealed that the $+-+-$ configuration is the most stable square-planar Ni^{II}([16]aneN_4) configuration. This configuration has the four six-membered rings in alternating λ and δ twist-boat conformations, see Table 2. The solid-state tetraaza macrocycle structure has the $+++-$ configuration and has a chair, chair, δ twist-boat and a λ twist-boat. It is 1.23 kJ mol^{-1} higher in energy than the $+-+-$ configuration, which can easily be accounted for by packing forces.

The energies of the different configurations were obtained as a function of the metal–ligand distance using the method of Hancock.[34] Similar results were obtained when using Wiberg's method.[35] Ideally, we would have used constraints in place of restraints,[36] however we did not have access to the software. It was found that the $+-+-$ configuration is the lowest-energy configuration up to 2.1 Å and that the $++--$ configuration is the lowest at greater nickel–nitrogen distances. It is interesting that the $++--$ and $+++-$ configurations behave identically from 2.0 to 2.7 Å. A CSD search revealed that for most other transition metals [16]aneN$_4$ complexes are not square planar. This is not surprising given that Chantron and Hancock[37] have determined that the tetrahedral $+-+-$ configuration of [16]aneN$_4$ has the lowest strain energy. The only other square-planar [16]aneN$_4$ structure deposited in the CSD with all its coordinates is the chromium complex;[38] just like the nickel complex the solid-state structure is in the $+++-$ configuration and has the same six-membered ring conformations.

Plots of the strain energy *vs*. the metal–sulfur distance for [16]aneS$_4$ are shown in Fig. 6. The $++++$ configuration, which has all its six-membered rings in the chair conformation, is the lowest-energy configuration for metal–sulfur distances greater than 2.15 Å. The $++++$ configuration was also found as the global minimum structure in a conformational search of Ni^{II}([16]aneS$_4$). However, the complex does not adopt this configuration in its solid state,[29] instead it is in the $++--$ configuration which has alternating chairs and twist-boats, and is 18.67 kJ mol^{-1} higher in energy than the $++++$ configuration. A CSD search found square-planar [16]aneS$_4$ complexes with Cu,[39] Rh,[40] Ni,[29] Mo,[41] Fe,[42] Hg[43] and Cd.[42] Their solid-state configurations are shown in Fig. 6. The complexes of Cu, Rh, Ni, Fe and Cd all adopt the higher-energy $++--$ configuration, and only Mo adopts the global minimum structure. The solid-state structure of the mercury complex of [16]aneS$_4$ is in the $+-+-$ configuration, which is at 92.6 kJ mol^{-1} higher energy than the $++++$ configuration at a metal–sulfur distance of 2.60 Å. Although it is possible to explain away a 1.23 kJ mol^{-1} energy difference, in the case of Ni^{II}([16]aneN$_4$), by invoking packing forces, it is not possible that the corresponding [16]aneS$_4$ complex adopts a configuration 92.6 kJ mol^{-1} higher in energy than the lowest-energy configuration just due to crystal packing forces.

Although the [16]aneS$_4$ complexes do not always adopt the configuration with the lowest energy, in all cases they exhibit the lowest-energy conformations available to the macrocycles with their given configuration. X-Ray,[29,39] spectroscopic,[44] thermodynamic[45,46] and kinetic studies of nickel(II) and copper(II) complexes of [16]aneS$_4$ have shown that they only exist in one configuration, the $++--$. However, ^{13}C NMR studies in nitroethane have shown that nickel(II) $++++$ and $++--$ conformations exist in solution[47] and that exchange of metal ions between individual tetrathioether molecules is slow on the NMR time-scale.[48]

The only way to explain the observation that the [16]aneS$_4$ macrocycles adopt high-energy configurations upon complexation, if configurational inversion can occur after complexation, is by assuming that the kinetics of the interconversion is slower than the crystallization itself or that crystallization rates are configurationally dependent. On the other hand, if interconversion between configurations is not possible after complexation, we suggest that the configuration that is adopted is an artifact of the mechanism by which the metal ions are incorporated into the macrocyclic cavity. The macrocycle cannot incorporate the metal ion in a single step, instead the metal loses one of its ligands, binds one of the macrocyclic sulfurs and then repeats the process until it is incorporated in the macrocycle. Such a mechanism which might be responsible for the macrocycles final conformation has been proposed for Me$_6$[14]aneN$_4$ (5,5,7,12,12,14-hexamethyl-1,4,8,11-tetraazacyclotetradecane).[49] Even in cases where the kinetics of metal incorporation is rapid and reversible, it is quite possible that the macrocycle will not adopt the lowest-energy configuration because it can never be accessed from the configuration adopted by the metal incorporation mechanism. If this is true, it is an important finding in the field of ligand design. On the basis of this work it seems that in designing a sequestering agent one should not only consider the size selectivity of the lowest-energy configuration and the degree of preorganization of the ligand,[50,51] but it is also important to consider the properties of the configuration that results from the particular metal incorporation mechanism.

Conclusion

We have shown that cluster analysis is a very robust method that is able to find all the common conformations of six-membered rings. The method is even effective in clustering the conformations of complexes with Ni−X distances differing from 1.9 to 2.5 Å, especially if the difference in pairwise dihedrals is used as a similarity criterion.

In all but three cases, molecular mechanics can be used to establish why high-energy non-chair conformations are adopted. We propose that the high-energy conformations of the sixteen-membered tetraaza and tetrathia macrocycles are artifacts of the metal incorporation mechanism. We found no correlation between the conformations of six-membered rings and the spin state of the nickel ion, or the co-ordination geometry around the metal.

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