

Statistical Analysis of Noncovalent Interactions of Anion Groups in Crystal Structures. III. Metal Complexes of Thiocyanate and their Hydrogen-Donor Accepting Function

LUBA TCHERTANOV*† AND CLAUDINE PASCARD

CNRS, Institut de Chimie des Substances Naturelles, UPR 2301, Avenue de la Terrasse, 91198 Gif Sur Yvette CEDEX, France. E-mail: Luba.Tchertanov@icsn.cnrs-gif.fr

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The article is dedicated to the memory of Professor Yu. Struchkov

Abstract

The bidentate function of the thiocyanate anion was studied using the Cambridge Structural Database System. Complexing properties (metal–thiocyanate interactions) with respect to metal cations were analysed. Two main classes were distinguished: (a) alkali and alkaline earth metals, and (b) metals of Zn and Cu groups and transition metals (group VIII). Good correlations were found between the nature of the metal (radius, oxidation state and charge) and its position relative to the thiocyanate unit. Hydrogen-bond acceptor properties of discrete and complexed SCN units were compared. The extraordinarily active hydrogen-bonding behaviour allows this anion to act as a powerful bridge between different molecular fragments. In metal complexes the cation provokes a redistribution of anionic charge in SCN and the distribution of electron density, in turn, controls the hydrogen-bonding properties of the terminal acceptor atom. Binding properties of thiocyanate in biological systems were illustrated using the Brookhaven Protein Data Bank. A comparison of anion binding in small-molecule structures and in macromolecular structures shows good agreement.

1. Introduction

Coordination effects by those anions (anionic environment) which play a fundamental role in biological systems have been a subject of growing interest in recent years. Since experimental data concerning associations between macromolecules and anions are very rare and far from accurate, the best way to study anionic interactions is to investigate fine details of their hydrogen-bonding capacity through a survey of small-molecule crystal structures.

The present work concerns the *thiocyanate* anion, which has been used recently as a crystallizing agent in protein crystal growth, although its binding mode remains unclear (Ducruix & Giegé, 1992). It has been demonstrated that, for basic proteins, thiocyanate anions can form crystals at a much lower salt

concentration than other anions (Riès-Kautt & Ducruix, 1989, 1991). Three-dimensional protein structures, crystallized from a thiocyanate solution, show a bridging (cohesive) role of this anion, as in erabutoxin-b (Saludjian *et al.*, 1992) and lysozyme (Howell, 1995). Crystallographic studies of some metalloproteins have shown the thiocyanate–metal partnership: inhibitor binding sites in human carbonic anhydrase II (Eriksson, Kylsten, Jones & Liljas, 1988), coordination of thiocyanate to the haem iron in myoglobin (Conti *et al.*, 1993) and hexameric insulin stabilized by thiocyanate (Whittingham, Chauhuri, Dodson, Moody & Dodson, 1995). Analysis of interactions between thiocyanate and metals and/or organic ligands using the Cambridge Structural Database (CSD; Allen *et al.*, 1979) can provide structural evidence for the rôle of the anion.

In an earlier report we analysed the hydrogen bonding of discrete thiocyanate anions (Tchertanov & Pascard, 1996). We now extend the study of the hydrogen-bonding capability of free (SCN)[−] to that of the metal-bonded anion in order to see if the hydrogen-bond acceptor properties of (SCN)[−] are modified by coordination through one terminal atom. This research entailed the following steps: (a) a general analysis of the metal coordination features of SCN. This step was found necessary as no such systematic analysis had previously been conducted; (b) a study of the influence (if any) of N or S complexation on the acceptor properties of the S (or N) terminus; (c) a study of the general internal geometry of the SCN unit and the influence of the different binding types.

Finally, a comparative analysis with macromolecular structures is reported. Binding properties of thiocyanate in biological systems are illustrated using the Brookhaven Protein Data Bank (Bernstein *et al.*, 1977).

2. Methods

2.1. CSD

The Cambridge Crystallographic Database (CSD; Version 5.10; Allen *et al.*, 1979) was searched interactively for compounds containing thiocyanate, thiocyanato and/or isothiocyanato fragments using

† As L. Tchertanova in previously published papers.

Table 1. Number of crystal structures with various modes of SCN metal complexation

Metal/ mode	A	D	E	F	G	N_{tot}
I A						
Li	21	0	3	0	1	25
Na	18	0	1	0	1	20
K [†]	21	3	3	0	6	33
Rb [†]					0	3
Cs [†]					1	4
II A						
Mg	5	0	0	0	0	5
Ca	14	0	0	0	0	14
Sr	7	0	0	0	0	7
Ba	6	0	1	0	0	7
III A						
Al	2	0	0	0	0	2
Tl	1	2	0	0	0	3
I B						
Cu	89	8	0	3	36	118
Ag	0	6	0	3	8	13
Au	0	7	0	0	1	8
II B						
Zn	21	0	0	0	0	21
Cd	12	1	1	0	10	24
Hg	0	17	0	0	8	25
VII B						
Mn	36	0	0	0	2	38
Tc	4	0	0	0	0	4
Re	13	0	0	0	0	13
VIII						
Fe	49	1	0	0	1	51
Ru	2	0	0	0	2	4
Os	0	0	0	1	0	1
Co	94	3	0	0	1	98
Rh	0	4	0	0	0	4
Ir	0	2	0	1	0	3
Ni	188	0	1	0	8	197
Pd	16	17	0	0	5	38
Pt	1	8	0	0	0	9

The digits in bold characters represent the number of structures considered for the geometrical analysis. † Cations prefer to interact with the π -system of thiocyanate [B and C modes of coordination, (I)].

QUEST3D (CSD, 1992) for the following compounds: (a) ionic crystals containing the $(\text{SCN})^-$ anion; (b) compounds containing SCN bonded to one metal and compounds in which the SCN unit acts as a bridge between two metal atoms (number of hits for each case is included in Table 1). This gave rise to a series of smaller files for the different metals which were analysed with the CSD system programs VISTA and PLUTO. Certain fragments formed bridges when a single (or both) terminal atom of thiocyanate was bonded to two metal atoms. This gave rise to biased results and we excluded these dimer units and polymers from the statistical analysis.

We therefore analysed the geometry only for fragments in which thiocyanate acted as a unidentate ligand, binding metal ions only through S or N atoms.

Structures were accepted without any *R*-factor screening, but were required to have error-free coordinate sets in the CSD check procedures and to exhibit no crystallographic disorder. For each thiocyanate fragment we calculated $d(\text{N}-\text{C})$, $d(\text{S}-\text{C})$ and $\angle(\text{SCN})$ together with additional parameters, characteristic of each type of interaction: (i) Element...anion. The element *EE* was restricted to boron, carbon, silicon, VA, VIA and VIIA groups of elements, and for (*EE*)-N and (*EE*)-S within covalent-bond contact criteria. (ii) Metal...anion. The element *M* was restricted to groups IA, IIA, IIIA, IB, IIB, VIIIB, and VIII elements. For each group we calculated $d(\text{M}\cdots\text{A})$ and $\angle(\text{MAC})$, where *A* = S or N. Limiting contact criteria of $\text{M}\cdots\text{N} \leq 3.6$ and $\text{M}\cdots\text{S} \leq 4.0$ Å were used to establish search hits. (iii) Hydrogen donor...acceptor. The *D*-H distances (*D* = O, N) were normalized using geometrical criteria (Taylor & Kennard, 1984); non-bonded contact criteria of $\text{D}\cdots\text{N} < 3.6$, $\text{D}\cdots\text{S} < 4.0$ Å and $90 < \angle(\text{AHD}) < 180^\circ$ were used.

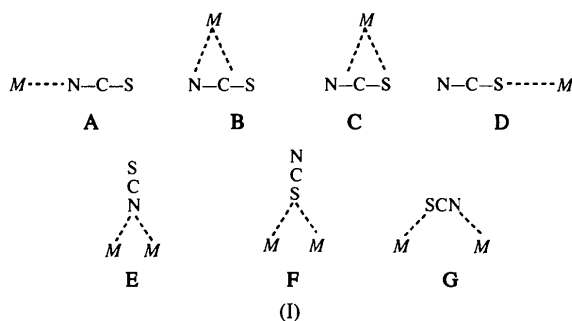
2.2. PDB

To compare the CSD results with those from macromolecular structures, the Protein Data Bank (PDB: Bernstein *et al.*, 1977) containing 3897 entries (April 1996 Version) was searched for thiocyanate...metal or/and thiocyanate...H-donor interactions, as for the small-molecule structures.

3. Structural aspects of metal-thiocyanate interactions

3.1. Empirical investigations

There are numerous experimental reports of metal coordination by thiocyanate. It is well known that this anion exhibits a wide variety of coordination geometries, partially as a result of its two modes of coordination (I): through nitrogen (mode A: $\text{M}-\text{NCS}$) or sulfur (mode D: $\text{M}-\text{SCN}$) (Mitchell & Williams, 1960; Norbury, 1965).



Such ligands are termed ambidentate (two different donor sites give rise to the possibility of linkage isomerism, *N*-thiocyanato and *S*-thiocyanato; Cotton &

Wilkinson, 1988). It has been suggested by Pearson (1963) that the S atom in SCN is soft and prefers to coordinate with soft acids (class *b* metals), whereas N in SCN is hard and coordinates with hard acids [class *a* metals (Ahrland, Chatt & Davies, 1958)]. Later it was reported that some cations preferentially bind to sulfur (Snow & Boomsma, 1972), whereas others prefer nitrogen (Jain & Lingafelter, 1967). However, the difference is sometimes not pronounced, since in some structures the thiocyanate ion coordinates through both N and S to the same cation [bridging *M*—SCN—*M*, mode *G* (Cannas, Carta, Cristini & Marongiu, 1977)].

3.2. Theoretical calculations

Ab initio calculations have been used to study Li(SCN⁻) and Cu(SCN⁻) isomerization (Musaev, Yakobson & Charkin, 1989; Musaev, Makhaev & Charkin, 1991; Parrini & Morales, 1993), *i.e.* the ability of the thiocyanate anion to form intermediate isomers between linear [terminal S or N, modes *A* and *D*, (I)] and cyclic bridging arrangements [lateral modes *B* and *C*, (I)]. It appears that two isomers correspond to energetic minima: linear structure *A* with $C_{\infty v}$ symmetry corresponding to the global minimum and cyclic *B* (C_s) to a local minimum. The energy difference (energy of isomerization) between these isomers is 67 kJ mol⁻¹ for Cu and 98 kJ mol⁻¹ for Li. However, in these isolated examples no principles emerge that permit a general empirical confirmation of this problem and the complexation function of thiocyanate is still poorly understood.

4. Results

We have not analysed all aspects and the specificity of metal–thiocyanate interactions, rather we have tried to evaluate the influence of metal–cation complexation on the hydrogen-bonding function of thiocyanate. For this we probed metal–thiocyanate interactions within several groups of elements of different size, charge and valence state. The following metals were analysed: alkali and alkaline earth metals; the Zn and Cu metal groups; transition metals; elements of group VIIA; trivalent metals. Elements with no stable isotopes are not considered here.

4.1. Observed modes of complexation

Preliminary data analysis shows that all modes of coordination are observed (Table 1), although with different occurrences. These include the ligand binding through terminal N or S atoms to a single metal centre [modes *A* and *D*, (I)] and binding with two metal centres [unidentate bridging modes *E*, *F* and bidentate bridging mode *G*, (I)]. The preferred interaction of the SCN group with a metal cation is unidentate. In a few cases (Cu, Ag, Cd, Ni and Hg) thiocyanate shows non-

negligible *G*-type bidenticity. The coexistence in the same crystal of two different modes of coordination is also observed: SAHDOU is of interest since both Cu—SCN and Cu—NCS modes of coordination exist in the same structure (Fig. 1), while the Cu complex BULTUX shows an *N*—NCS mode and *G*-bridging (Fig. 2).

4.1.1. *Classes IA and IIA.* Alkali and alkaline-earth metals bind to thiocyanate mainly through nitrogen. Whereas the lighter elements bind neatly in the *A* mode, heavier alkali metals ($M = K, Rb$ and Cs) prefer to interact with the π -system of thiocyanate (modes *B* and *C*) with no distinct acceptor S or N atoms (Fig. 3). Among the 33 K^+ complexes we observed six mixed-metal complexes [K —(SCN)— M' ($M' = Co, Ag, Hg, Cu, U$)], in which potassium is almost always coordinated with sulfur. For Rb and Cs there are few examples (three and four, respectively: one of the Cs structures is a mixed-metal complex).

4.1.2. *Class IB.* In spite of the general similarity in their electronic structures, Cu, Ag and Au differ completely in their complexing properties with thiocyanate. We found 118 coordinate entries of Cu complexes. The coexistence, in the same crystal, of two modes of coordination (*A* and *D* as in Fig. 1 or *A* and *G* as in Fig. 2) is not unusual for copper complexes. There are 89 complexes which exist with a single Cu atom bonded to nitrogen. Numerous (36) dimers and polymers exist in the *G* mode. Coordination through

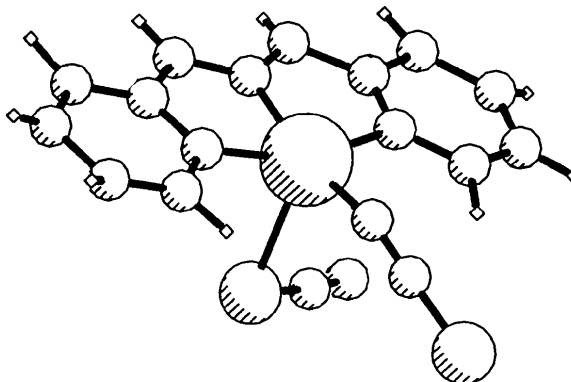
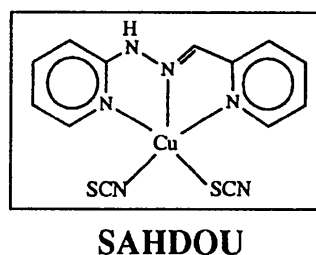


Fig. 1. *PLUTO* (Motherwell & Clegg, 1978) diagram illustrating the coexistence of two different modes of coordination (Cu—SCN and Cu—NCS) in SAHDOU.

sulfur with one or two Cu atoms is rare. For silver and gold, only sulfur binding (**D** and **F** modes) or **G** bridging were observed. Class **II B**: In all cases, Zn coordinates only through nitrogen. For Cd the most frequent coordination is Cd—NCS as well as the Cd—SCN—Cd bridge. Hg is coordinated by sulfur or participates in —SCN— bridging. Class **VII B**: Elements of the manganese group (Mn, Tc and Re) are bonded with SCN through nitrogen.

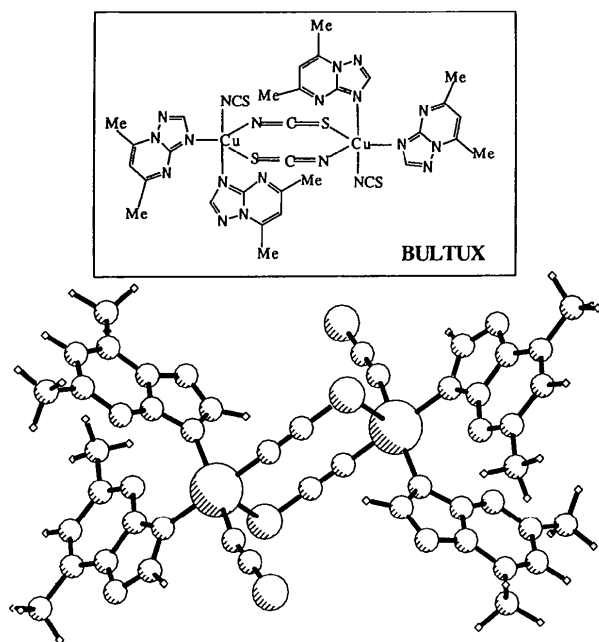


Fig. 2. *PLUTO* (Motherwell & Clegg, 1978) diagram illustrating the coexistence of two different modes of coordination, by one terminal atom and/or forming bridge-bonding in BULTUX.

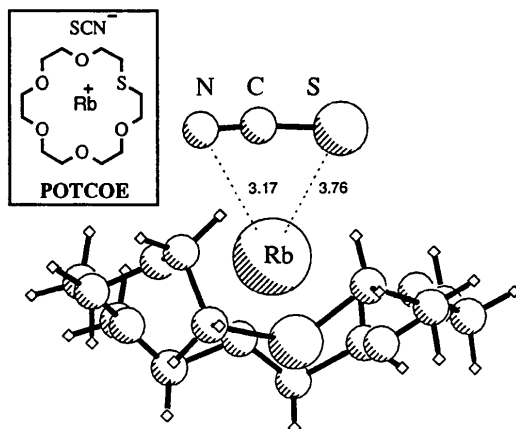


Fig. 3. *PLUTO* (Motherwell & Clegg, 1978) diagram illustrating the lateral mode of coordination in POTCOE. Bond distances: Rb...S 3.76, Rb...C 3.20, Rb...N 3.17 Å; bond angles: $\angle(\text{RbSC})$ 58, $\angle(\text{RbCS})$ 96, $\angle(\text{RbNC})$ 81°, showing **B** or **C** modes.

4.1.3. *Group VIII*. Most Fe, Co and Ni complexes retrieved from the CSD have nitrogen as their preferred coordination centre. Pd shows an equal capability for complexation through nitrogen and sulfur and Pt binds with thiocyanate only through sulfur.

Metals complexed with thiocyanate (and isothiocyanate) exhibit several coordination numbers: within our data files we observed that in complexes, Ni and Cu have a valence state of II with a coordination number from 4 to 6. Fe has valence states II and III and coordination numbers 5, 6 and 7, as well as π -complexes. Co has valence states II and III with coordination numbers 4, 5 and 6. Elements of the manganese group (Mn, Tc and Re) have varied valence states.

4.2. Geometrical parameters of the unidentate metal complexes

We selected only unidentate fragments of types **A** and **D** occurring in more than five structures in the database. We omitted all polymer and dimer complexes (bridge-mode formation). The statistics for all extracted fragments are summarized in Tables 2 and 3.

4.2.1. *Geometry of $M \cdots \text{NCS}$* . The geometry of the $M \cdots \text{NCS}$ fragment was analysed using 1004 unique and independent $M \cdots \text{N}$ interactions, extracted from 575 CSD entries. The mean values of bond distance $M \cdots A$ and valence angle $\angle(\text{MAC})$ for each metal are listed in Table 2.

IA and **IIA**: The bonds between the SCN and alkali and alkaline-earth metals are essentially ionic. As expected, there is a good correlation between the ionic radius and the average $\text{N} \cdots M$ distance (see Table 2). However, in classes **IA** and **IIA**, cations of different size may favour different positions above the delocalized thiocyanate (Fig. 4): the smaller cations (Li^+ , Na^+ and Mg^{+2}) clearly interact solely with nitrogen; the larger cations (K^+ and Ba^+ , for example) prefer to interact with a larger part of the linear anion (π -system of SCN). It appears that there is a correlation between the ionic radius and the $M\text{—NCS}$ angle (Fig. 5). It is mostly visible for class **IA**.

Other elements: **IB**, **II B**, **VII B** and **VIII**. The elements of these groups are covalently bonded to SCN, as shown in Table 2. For the distribution of copper cations binding to the N terminal, the most populated domain is a dense cluster of observations corresponding to $\text{Cu} \cdots \text{N}$ distances from 1.8 to 2.0 Å [mean 1.944(5) Å] and angles of 150–180° [mean 166.1(6)°] (see Fig. 6a). There is a long tail on the distance distribution which represents interactions with the thiocyanate C—N π -system. There is no correlation between the geometry of $\text{Cu} \cdots \text{NCS}$ and its oxidation state: in all cases, its valence state is II and the coordination number is 4 or 5. Two metals of group **II B** (Zn and Cd) show different positions above the delocalized thiocyanate (Fig. 6b).

Table 2. Mean values of the geometrical parameters, with mean SD, for $M \cdots NCS$ (nitrogen: ionic radius = 1.46 Å, covalent radius = 0.70 Å)

All values for covalent and ionic radii from Wells (1984).

Metal	N_{obs}	$M \cdots N$	$\angle(MNC)$	Sum of ionic radii	Sum of covalent radii
IA					
Li	22	1.987 (7)	168 (2)	2.06	
Na	20	2.38 (1)	150 (3)	2.41	
K	28	2.85 (2)	133 (4)	2.79	
IIA					
Mg	10	2.093 (8)	169 (1)	2.11	
Ca	31	2.437 (8)	160 (2)	2.45	
Sr	18	2.624 (5)	161 (2)	2.59	
Ba	13	2.84 (1)	152 (4)	2.81	
IB					
Cu(all)	135	2.03 (1)	162 (1)		2.05
Cu(cluster)†	104	1.944 (5)	166.1 (6)		
IIIB					
Zn	33	1.99 (1)	163 (4)		2.01
Cd	24	2.28 (2)	152 (3)		2.18
VIIIB					
Mn	55	2.04 (1)	171 (1)		2.07
Re	41	2.163 (8)	160 (1)		
VIII					
Fe	74	2.043 (7)	166 (1)		1.93
Co(all)	185	1.983 (5)	167.8 (6)		2.02
Co ^{III}	120	1.934 (3)	169.4 (6)		
Co ^{II}	65	2.074 (4)	165 (1)		
Ni(all)	301	2.043 (4)	165.8 (5)		2.09
Ni(4,5)	38	1.893 (9)	171.1 (9)		
Ni(6)	263	2.065 (2)	165.1 (5)		
Pd	15	2.027 (7)	166 (1)		2.11

† The cluster corresponds to the most populated area (Fig. 5a).

Table 3. Average value of $M \cdots SCN$ geometry, with mean SD (sulfur: ionic radius = 1.84 Å, covalent radius = 1.04 Å)

All values for covalent and ionic radii from Wells (1984).

M	N_{obs}	$M \cdots S$	$\angle(MSC)$	Ionic radii	Covalent radii
Cu	16	2.57 (7)	98 (2)	2.80	2.39
Ag	10	2.53 (8)	102 (2)	3.10	2.57
Au	12	2.54 (8)	102 (2)	3.21	2.54
Hg	77	2.507 (9)	99.0 (4)	2.94	2.52
Pd	25	2.351 (7)	106.2 (8)		2.41
Pt	13	2.36 (2)	106.4 (9)		2.43

The geometrical parameters of $Zn \cdots NCS$ [mean 1.99(1) Å and 163(4)°] differ from those for Cd [2.28(2) Å and 152(3)°]. The larger cation prefers interacting with many centres (π -system of the C—N bond), as was observed for alkali and alkaline-earth metals. The valence state of both metals is II. Mn and Re in group VIIIB show the same behaviour as Zn and Cd. The mean bond distance and angle values for $Mn \cdots NCS$ and $Re \cdots NCS$ are 2.04(1) Å, 171(1)° and

2.163(8) Å, 160(1)°, respectively (Fig. 7). In group VIII, we found only nitrogen-bonded complexes with Fe, Co and Ni and Pd. Two clusters in the cobalt complex correlation diagram (Fig. 8b) correspond to different valence states of Co: the larger Co—N distance [2.074(4) Å] indicates a six-coordinated Co^{II} complex, while the shorter Co—N distance [mean = 1.934(3) Å] exists for four- or five-coordinated Co^{II} and six-coordinated Co^{III}. The geometry of Ni complexes shows a good example of geometry *versus* coordination number correlation. The small cluster (38 observations) [1.893(9) Å, 171.1(9)°] corresponds to four- or five-coordinate Ni^{II}, whereas the second cluster (263 observations) with the longer distance [2.065(2) Å] and larger valence angle [165.1(5)°] corresponds to only six-coordinate Ni^{II} (Fig. 8c). This

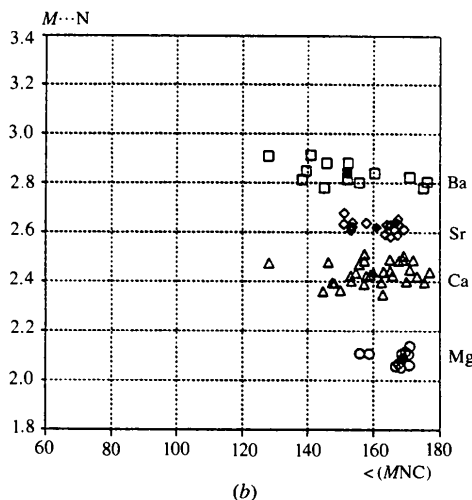
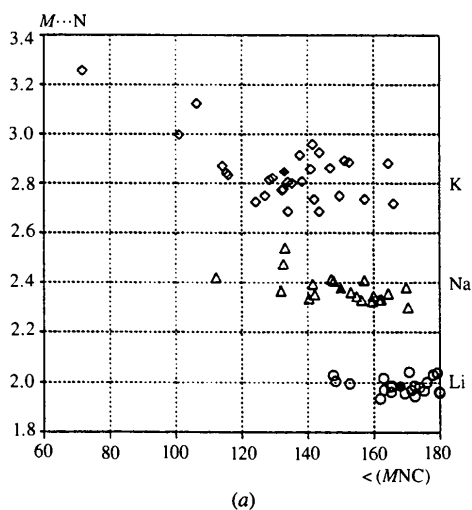


Fig. 4. Scatterplots of $M \cdots N$ distances (Å) versus $\angle(MNC)$ (°). (a) Alkali metals; (b) alkaline earth metals. The circles are Li (a) and Mg (b); triangles are Na (a) and Ca (b); rhombs are K (a) and Sr (b); squares are Ba. Black symbols correspond to the mean values for each metal.

agrees with the concept of increasing covalent radius corresponding to higher coordination number (Wells, 1984). Fe^{II} and $\text{Fe}^{\text{III}} \cdots \text{NCS}$ interactions are superimposed (Fig. 8a). A small quantity of data for Pd complexes are presented in Fig. 8(d).

4.2.2. *Geometry of $M \cdots \text{SCN}$.* The geometry of $M \cdots \text{SCN}$ fragments was analysed using 153 unique and independent $M \cdots \text{S}$ interactions extracted from 63 CSD entries. The mean $M \cdots \text{S}$ bond distance and $\angle(\text{MSC})$ valence angle for each metal are listed Table 3.

All analysed $M \cdots \text{SCN}$ fragments show average distances in the range from 2.351(7) (Pd) to 2.57(7) Å (Cu), which corresponds mainly to covalent bonds, and a very small dispersion of the $\angle(\text{MSC})$ valence angle [98(2)–106.4(9)°, Fig. 9]. We can distinguish only two different clusters belonging to Hg

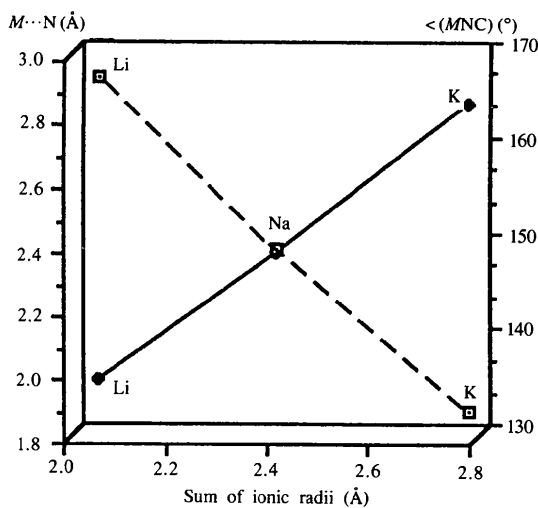
and Pd, Pt. The discrete tail above 2.6 Å corresponds to interactions with partial ionic character for some metals such as Ag, Au and Cu (Pauling, 1960).

4.3. Summary of thiocyanate–metal–bonding observations

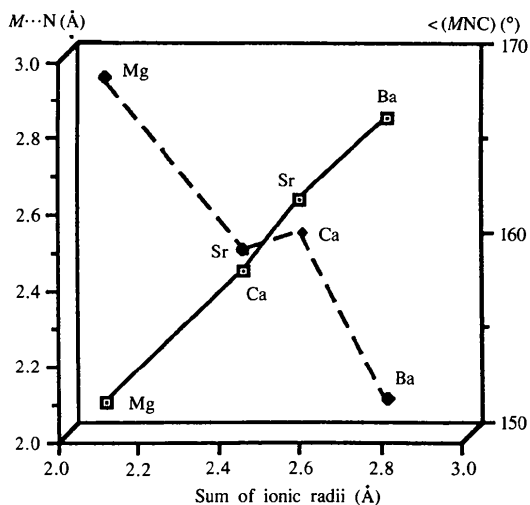
(i) The principal observed mode of binding is unidentate through nitrogen or through sulfur (A and D) or bridging (most favoured G type).

(ii) In 80% of all reported cases the metal is bound through the terminal N atom, in 9% through the S atom and in the remaining 11% the SCN group acts as a bidentate ligand, *i.e.* it is coordinated at both ends.

(iii) SCN forms strong complexes with metals: ionic with those of class (a) cations and covalent with metals of other groups. The covalent interaction with the

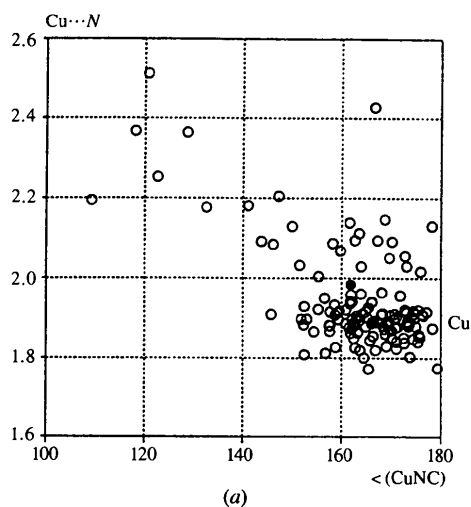


(a)

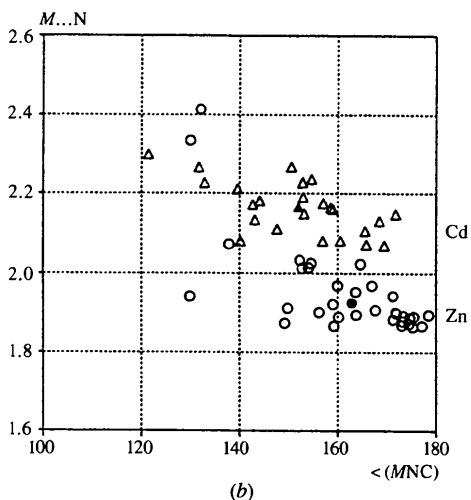


(b)

Fig. 5. Correlation of the bond distances (solid line) and angles (dashed lines) versus ionic radii: (a) alkali metals and (b) alkaline earth metals.



(a)



(b)

Fig. 6. Scatterplots of $M \cdots \text{N}$ distances (Å) versus $\angle(\text{MNC})$ (°). (a) Cu, (b) Zn and Cd. The circles are Cu (a) and Zn (b); triangles are Cd (b). Black symbols correspond to the mean values for each metal. Two mean values for the Cu complexes correspond to all data and to the most populated cluster.

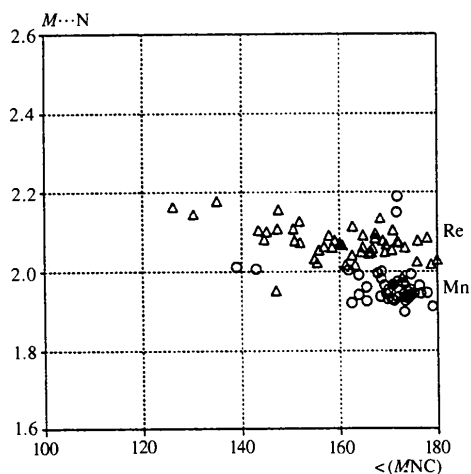


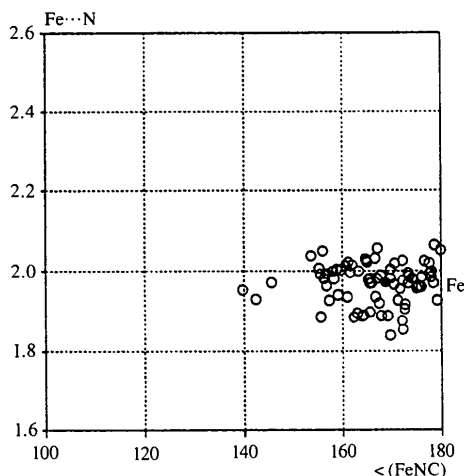
Fig. 7. Scatterplots of $M \cdots N$ distances (Å) versus $\angle(MNC)$ (°) in the metal complexes of group VII B. The circles are Mn and triangles are Re. Black symbols correspond to the mean values for each metal.

metals of the Cu subgroup (Cu, Ag and Au) has a partial ionic character.

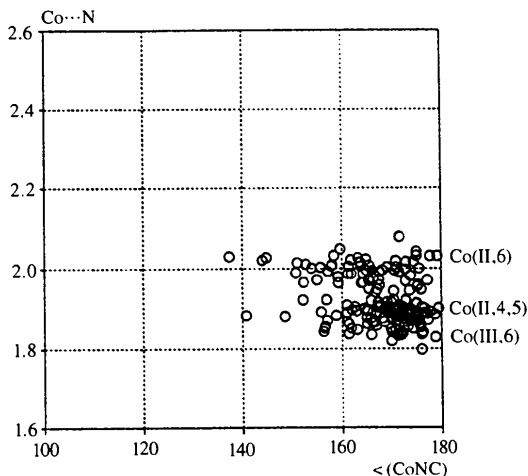
(iv) Only variations of metal bond distances corresponding to the differences in the metal covalent radii are observed in $M-SCN$ fragments, whereas the angular parameter is almost equal for all thiocyanate complexes ($\sim 100^\circ$).

(v) The $M-NCS$ fragment geometry shows larger variations in the $M \cdots N$ distance as well as significant variations in the angles at the N atom. While the bond length differences clearly reflect the differences in the cation radii (either ionic or covalent), various metal positions with respect to the linear anion are observed: the largest cations interact with the π -system of the anion. This is mostly evident for alkali metals, the class II A elements being less attracted by π -electrons.

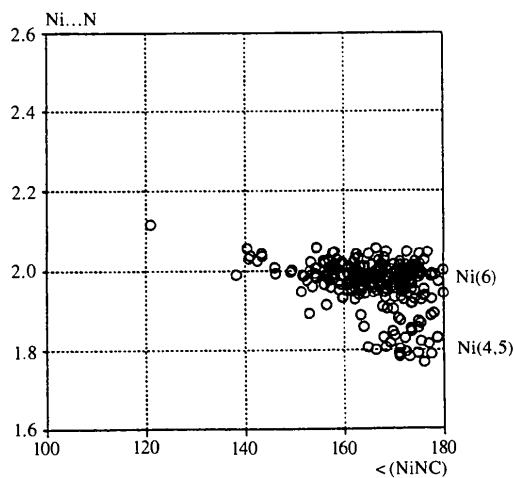
This analysis was sufficiently precise to show the correlation between coordination number and the covalent radius in the Co and Ni complexes.



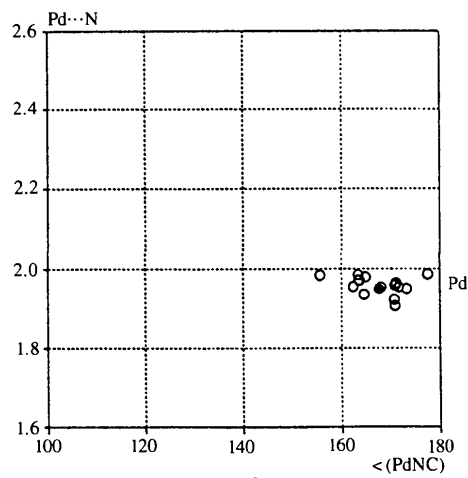
(a)



(b)



(c)



(d)

Fig. 8. Scatterplots of $M \cdots N$ distances (Å) versus $\angle(MNC)$ (°) in the metal complexes of group VIII. Black symbols correspond to the mean values for each metal.

5. Hydrogen bonding to metal-coordinated isothiocyanates and thiocyanates

The most important observations resulting from the previous analysis of hydrogen bonding of discrete thiocyanate ions (Tchertanov & Pascard, 1996) can be summarized here. Thiocyanate is able to accept all types of hydrogen donors (oxygen and nitrogen). The distribution of hydrogen donors around the discrete anion shows that sulfur, nitrogen and the π -system of the anion may act as hydrogen-bond acceptors. This accounts for the two preferred areas of the hydrogen-donor occurrences: (a) around sulfur on a torus centred at the S end, the axis of which coincides with the linear anion; (b) on a spherical cap around nitrogen. 80% of thiocyanates bind through *both* acceptor centres.

The role of the metal cation in the three-dimensional hydrogen-bond network is unclear. It may act as a template, dictating the orientation of the remote hydrogen-bonding surfaces as a consequence of the stereochemical preferences of the cation. Conversely, the metal cation may exert a specific electronic influence on the groups at the remote hydrogen bonding site, thereby providing a means of tuning the strength of the intermolecular interactions.

To be able to discuss the hydrogen-bonding capability of the metal-bonded SCN we have to compare it with that of a discrete anion. For this comparison, we used the most recent version of the CSD (April, 1996). Therefore, the numbers of retrieved fragments of discrete thiocyanate reported here differ slightly from those in our previous paper (Tchertanov & Pascard, 1996). The data reported here for the discrete anion only concern multiple hydrogen-bonding properties.

Three-dimensional (3D) searches for all discrete SCN anions revealed 88 hydrogen-bonded S acceptor centres

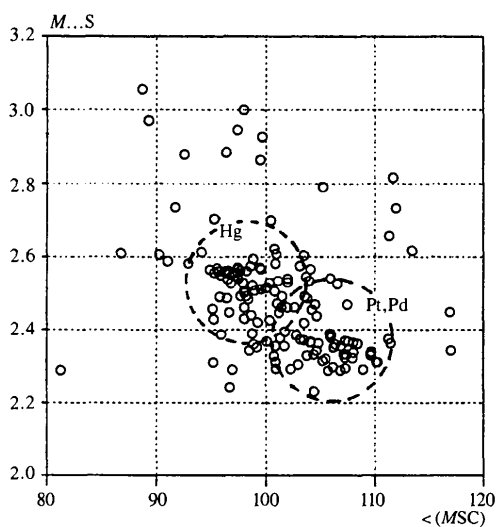


Fig. 9. Scatterplots of $M \cdots S$ distances (\AA) versus $\angle(MSC)$ ($^\circ$). The preference areas corresponding to Hg and Pt, Pd are shown.

Table 4. Multiple hydrogen bonding

Number of retrieved fragments for discrete and metal-bonded anion. For comparison we used the most recent version of the CSD (April, 1996), and therefore the number of extracted fragments of discrete thiocyanate reported here differs slightly from the values in our previous paper (Tchertanov & Pascard, 1996). The observed occurrences of metals are as follows: $M-NCS \cdots HD$: Ni 196; Co 64; Cu 35; Mn 23; Zn 20; Ca 12; Cr 11; Mo 7; Ag, Fe and Cd 4, Li, Mg, Pd, Re, Sn one case each; $M-SCN \cdots HD$: Ag 11; Cu 8; Hg 6; Bi 2 and Pd, Pb one case each.

<i>n</i> HB/Accept	Free (SCN)		Metal-bonded SCN	
	N	S	<i>M</i> -SCN	<i>M</i> -NCS
1HB	35	34	9	103
2HB	39	20	6	47
3HB	15	11	3	24
4HB	4	21		10
>4HB		2		3
Total	93	88	18	187

and 93 hydrogen-bonded N acceptor centres (Table 4). Each acceptor centre participates in a unique hydrogen bond in only 38% of cases, 62% being engaged in multiple hydrogen bonding: in most cases a nitrogen binds twice (39 occurrences), but three and four hydrogen bonds are observed in 15 and 4 cases, respectively. The occurrences of two, three and four hydrogen bonds around the sulfur are observed in 20, 11 and 21 cases, respectively. In two fragments sulfur shows five- and six-coordination with hydrogen-donor groups. Obviously, the discrete anion forms an almost equivalent number of hydrogen bonds at both ends: 202 hydrogen bonds through sulfur and 174 through nitrogen acceptors.

The observed preference for N-metal coordination results in a preponderance of data for hydrogen bonding through sulfur. For metal-bonded isothiocyanate we encountered 309 hydrogen bonds from 184 terminal sulfurs and only 30 hydrogen bonds from 18 terminal nitrogens for thiocyanate. The very small number of SCN groups bonded to a metal through sulfur is insufficient for a detailed statistical study of the accepting properties of terminal nitrogen. Consequently, we limit the discussion to the comparative statistics around sulfur as the hydrogen acceptor. However, details concerning the hydrogen bonding of nitrogen will be illustrated using selected structures.

Table 4 shows that multiple hydrogen bonding around sulfur is less frequent for $M-NCS$ than for the discrete anion. A single hydrogen bond is observed in 55% of all occurrences in $M-NCS$ compared with 38% for the discrete anion. The strength of the hydrogen bond is only slightly influenced by the metal linkage, as can be seen by the small increase in bond length (Table 5). Both of these observations imply a weaker hydrogen-accepting function. In both cases (discrete and metal-bonded SCN), there is the expected slight increase in hydrogen-bond lengths as the number of donors increases. The long hydrogen bonds represent the best

compromise between the optimum requirements of multiple and strong hydrogen bonding (Taylor & Kennard, 1984). The $D-H \cdots S$ bonds are quite directional, the angle at S being around 98° for both free and terminal coordinations. In $M-NCS \cdots HD$ 82% of the donors are nitrogen (90% in 'free' anions).

Excellent examples representing the different modes of metal complexation of thiocyanate and hydrogen bonding with the same thiourea ligand are shown in Fig. 10. The $M-SCN$ fragment only forms two hydrogen bonds in ZZZUGC01 and three in TCAGTU through the terminal N atom, while the $M-NCS$ fragment accepts, through sulfur, multiple H atoms from the five donor sites in KAPPEW and the four donor sites in ICTHFE.

Intramolecular hydrogen bonds in $M-NCS$ fragments are not typical, being observed in only five

structures. However, in structures having long chains containing a donor group, internal interaction is probable. The $S \cdots H-N$ bond in BUFHAL (Fig. 11) and $S \cdots H-O$ in JEXTAH (Fig. 12) exhibit strong intramolecular hydrogen-bond interactions [$S \cdots O$ 3.311 (5), $S \cdots H$ 2.35 (1) Å, \angle at H 147 (1) $^\circ$ in JEXTAH and $S \cdots N$ 3.447 (3), $S \cdots H$ 2.65 (1) Å, \angle at H 135 (1) $^\circ$ in BUFHAL].

6. SCN internal geometry

The geometry and electronic structure of SCN and its substituted isomers have been studied in a series of experimental and theoretical papers. Some non-metal-substituted SCN such as halogen- and hydrogen-thiocyanates and isothiocyanates (Howell, Absar & Van Waze, 1973; Leung, Suffolk & Watts, 1986),

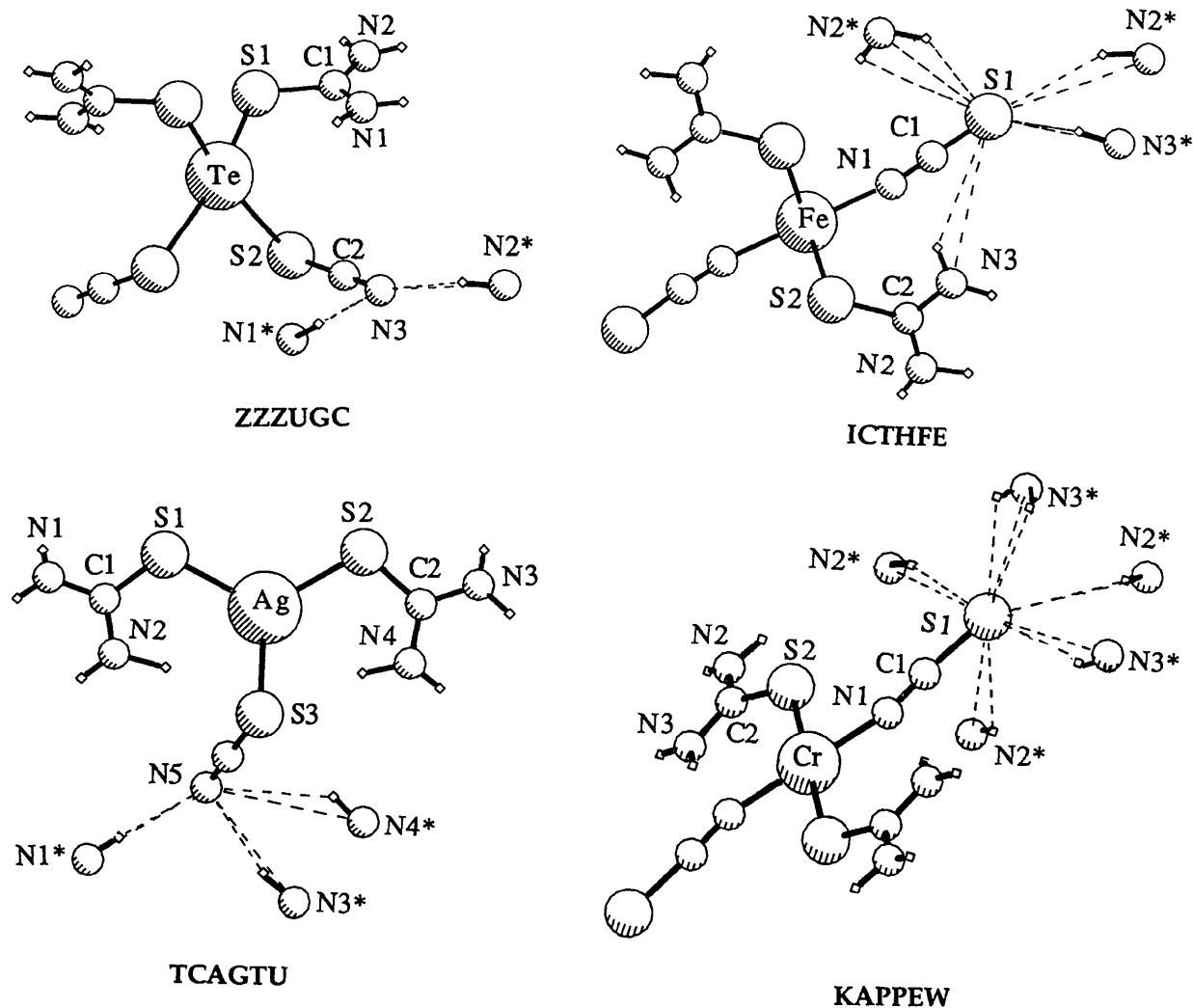


Fig. 10. Hydrogen bonding of the terminal thiocyanate atoms in the thiourea family complexes: ZZZUGC, TCAGTU, ICTHFE and KAPPEW. Hydrogen bonds are shown by dashed lines only for crystallographically independent fragments.

Table 5. Multiple hydrogen bonding around sulfur (average geometry of $D-H\cdots S$ fragment for discrete SCN and $M-NCS$)

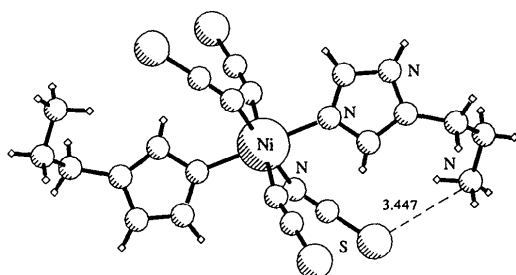
HB	(NCS) ⁻ ...HD				M-NCS...HD			
	S...D (Å)	H...D (Å)	∠H (°)	∠S (°)	S...D (Å)	H...D (Å)	∠H (°)	∠S (°)
1HB	3.44 (3)	2.62 (5)	153 (3)	94 (3)	3.46 (2)	2.70 (3)	147 (2)	97 (2)
2HB	3.53 (3)	2.78 (5)	146 (3)	97 (3)	3.55 (2)	2.78 (3)	145 (2)	100 (2)
3HB	3.60 (3)	2.86 (5)	140 (3)	97 (4)	3.60 (2)	2.93 (4)	137 (2)	97 (3)
4HB	3.57 (2)	2.89 (3)	136 (2)	100 (2)	3.62 (3)	3.01 (5)	131 (3)	101 (3)

cyclopropyl isothiocyanate (Durig, Sullivan, Berry & Cradock, 1987), methyl- and cyano- derivatives (Barone, Cristinziano, Lelj & Russo, 1982) were analysed using *ab initio* calculations. Electronic molecular properties of thiocyanate and the metal-anion pair were analysed only for Li (Musaev, Yakobson & Charkin, 1989; Parrini & Morales, 1993; Squalli, Costa, Cartier & Chabanel, 1994) and Cu (Musaev, Makhaev & Charkin, 1991).

The large number of observations we collected allows us to analyse the influence of binding on the internal geometry of SCN. We extracted all SCN fragments which are bonded to a metal or a non-metallic atom by S or by N, and all SCN units in the anionic form. The geometrical parameters of the SCN fragment are listed in Table 6.

We find practically no variation in the C—N bond length and SCN bond angle, regardless of the binding mode. However, the S—C bond is much more sensitive to both the mode of coordination (by sulfur or by nitrogen) and the nature of the partner. The extreme values [the shortest in SCN—*R* 1.574 (5) Å and the longest in *R*—SCN 1.683 (5) Å] belong to bonds with a non-metallic ligand ('pure covalent'). This result agrees with microwave measurements in CH₃—NCS and NCS—CH₃ (1.56 and 1.61 Å, Beard & Dailey, 1949).

This peculiarity may be explained by different contributions of the limiting canonic forms in both cases. Thus, bonding in the SCN—*R* system is determined primarily by the charge-smearred S=C=N—*R* and ⁺S≡C—N⁻—*R* components rather than by the ⁻S—C≡N⁺—*R* form, whereas the *R*—SCN mode of coordination, on the contrary,



BUFHAL

Fig. 11. Intramolecular hydrogen bonding in BUFHAL (S...HN).

Table 6. Comparative analysis of the internal geometry of differently substituted thiocyanates

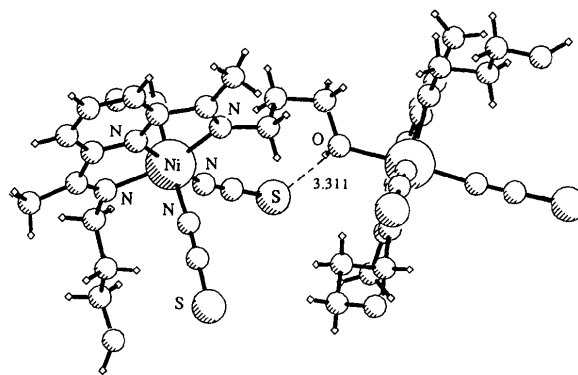
Fragment/parameter	S—C	C—N	<(SCN)	<i>N</i> _{obs}
SCN— <i>R</i> †	1.574 (5)	1.153 (5)	176.8 (3)	42
SCN— <i>M</i> (all)	1.621 (1)	1.146 (1)	177.0 (9)	1724
(covalent)‡	1.621 (1)	1.150 (1)	177.5 (1)	905
(ionic)§	1.626 (3)	1.147 (2)	177.0 (1)	155
Discrete SCN	1.624 (4)	1.137 (5)	175.7 (4)	258
<i>M</i> —SCN	1.648 (4)	1.152 (3)	176.4 (4)	227
<i>R</i> †—SCN	1.683 (5)	1.147 (4)	176.0 (4)	30

† *R* = C, B, P, Si and As in SCN—*R* and C in *R*—SCN complexes.

‡ Only covalent *M*...NCS interactions. § Only ionic *M*...NCS interactions.

features a greater contribution of the uncharged *R*—S—C≡N bonding pattern than that of the *R*—S⁺=C=N⁻ mesomer. The similar behaviour of the S—C bond length is observed in metal complexes, but the difference is less obvious [1.621 (1) Å in SCN—*M* and 1.648 (4) Å in *M*—SCN]. Here, statistical calculations do not show a considerable variation of the C—N bond values in different binding modes, which can indicate the participation of various resonance forms. Individual results for purely covalent and purely ionic SCN...*M* bonding do not show a real difference (Table 6).

Fig. 10 shows a good example of organometallic structures with the same ligands, thiourea and thiocyanate, bonded to different metals (Te, Fe, Cr and Ag). The S—C bond length is longer [1.649 (2) (ZZZUGC)



JEXTAN

Fig. 12. Intramolecular hydrogen bonding in JEXTAN (S...HO).

and 1.662(1) Å (TCAGTU)] in SCN metal-bonded through sulfur than when it is metal-bonded through nitrogen [1.631(1) (ICTHFE) and 1.622(1) Å (KAPPEW)].

Free (SCN)⁻ has intermediate dimensions which correspond well to the *ab initio* calculated geometry (Parrini & Morales, 1993) with the net charge on the sulfur and nitrogen being the same, *i.e.* both atomic centres are negative while the carbon centre is electron-deficient. This agrees with the observed identical ability by both terminal atoms to accept a donor group.

The metal cation provokes a redistribution of anionic charge in metal-bonded SCN and the particular distribution of electron density in turn controls the hydrogen-bonding properties of the terminal acceptor atom.

7. Thiocyanate binding in proteins

From a chemical point of view, all types of interactions realized in small molecules are identical to those observed in proteins. As in the case of small molecule structures, thiocyanate can be bonded to different partners (metal or hydrogen-donor group) by various modes of interaction (through sulfur or/and nitrogen). Only five proteins containing the SCN units have been deposited in the PDB (Table 7).

Two proteins, lysozyme (Howell, 1995) and erabutoxin-b (Saludjian *et al.*, 1992) were crystallized from thiocyanate and contain SCN in anionic form. In the hexagonal form of turkey egg white lysozyme, the anion plays a bridging role between two symmetry-related molecules: a pair of hydrogen bonds through the sulfur (S··NH₂ and S··H₂O) stabilizes good contact with an arginine residue of the protein molecule and with a water molecule. From the other terminal atom (nitrogen), a pair of hydrogen bonds through water molecules (N··NOH) binds the anion with a symmetry-related molecule of protein. In erabutoxin-b, a post-synaptic neurotoxin isolated from the venom of the sea-snake *Laticauda semifasciata*, the thiocyanate anion is located in a polar cleft formed by three molecules (*A* and *B*, crystallographically independent, and *A**, symmetrically related). The contacts N··OG Ser23B (2.68 Å) and N··NH Arg33A (3.26 Å) can be interpreted as hydrogen bonds with polar residues. Sulfur is at a distance of 3.31 Å to the oxygen of Cys54B and 3.43 Å to the water molecule, which bridges two crystallographically independent molecules. Thus, thiocyanate is seen to act as an anionic bridge between the different protein molecules. Its behaviour is similar to that observed in small molecule structures.

In two proteins, thiocyanate insulin (Whittingham, Chauhuri, Dodson, Moody & Dodson, 1995) and carbonic anhydrase (Eriksson, Kylsten, Jones & Liljas, 1988), SCN is bonded to zinc. In hexameric insulin the linear anion is on a threefold axis and located between

Table 7. *Protein structures, containing the SCN subunit*

Refcode	Compound	Source	Reference
1TEW	Lysozyme	Turkey EGG white	Howell (1995)
6EBX	Erabutoxin-b	Sea-snake venom	Saludjian <i>et al.</i> (1992)
2CA2	Carbonic anhydrase II	Huan	Eriksson, Kylsten, Jones & Liljas (1988)
2FAM	Myoglobin	Sea hare	Conti <i>et al.</i> (1993)
2TCI	Thiocyanate insulin	Sus scrofa, pig	Whittingham, Chauhuri, Dodson, Moody & Dodson (1995)

three symmetrically related proteins. The Zn—N bond distance of 1.69 Å and ∠(ZnNC) bond angle of 180° agree well with our small-molecule analysis. The terminal sulfur is situated in a hydrophobic region. In the carbonic anhydrase complex the SCN anion is bonded to the penta-coordinated zinc along with a water molecule and three histidine residues [Zn—N 1.91 Å, ∠(ZnNC) 173°]. The terminal sulfur sits in a hydrophobic pocket, but is at 4.1 Å from a backbone NH (Thr199). This is the site of the 'deep' water which is supposed to bind to Thr199 in the catalytic mechanism; SCN acts as an inhibitor. We observe an intramolecular bond (HOH··N) between two neighbouring zinc ligands, H₂O and NCS.

In the sea hare myoglobin (*Aplysia Limacina*, ferric) complex with SCN (Conti *et al.*, 1993), SCN is coordinated to the *haem* iron through the S atom and the terminal nitrogen forms two hydrogen bonds with an arginine residue and a water molecule. As our analysis of small molecule complexes has shown, such Fe··SCN binding has indeed a low statistical probability (1 case out of 50). In protein structural work it might be difficult, with a resolution of 1.65–2 Å, to discriminate between the two isoforms of thiocyanate.

8. Conclusions

This work represents the first systematic study of the thiocyanate metal complexes and their hydrogen-bond-accepting properties. We have previously analysed the hydrogen bonding of the discrete anions [both terminal atoms as acceptor centres (Tchertanov & Pascard, 1996)]. This study provides clear evidence of the metal-cation influence on the hydrogen-bond accepting function of SCN, and a comparison of the geometrical data and relative frequencies of unique and multiple hydrogen-bond formation around discrete and metal-bonded SCN was made. In the latter case there is evidence to suggest that the multiple hydrogen-bond function of the terminal atom appears weak.

The study also provides analysis of the metal-thiocyanate binding mode for different classes of elements; there is a clear predominance of SCN binding through the N terminal. Alkali metals clearly form ionic bonds with, for large cations, interactions with the π-

system of the anion. Binding with metals of other groups shows an essentially covalent interaction.

The average dimensions of SCN have been analysed for the different binding modes and partner type. The influence of both factors is perceivable in the S—C bond length, with a longer S—C bond when SCN is covalently bonded through sulfur, and shorter when it is bonded through nitrogen. This correlates very well with theoretical calculations and spectroscopic measurements.

The above results are in good accordance with the observations in macromolecular complexes, with the exception of the myoglobin (ferric) complex with SCN.

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