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METAL COMPLEXES OF SULPHUR–NITROGEN CHELATING AGENTS

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A. INTRODUCTION

Metal complexes of ligands containing sulphur, selenium, or tellurium as donor atoms were reviewed[1] in 1965. More recently there have appeared reviews on reactions involving metal complexes of sulphur ligands[2], on certain types of sulphur–sulphur and sulphur–oxygen chelates, viz. 1,1- and 1,2-dithiolate and dithioacid complexes[3–5], and monothio-β-diketones[6,7]. A recent review[8] deals with complexes of pyridine thiols, which are ambidentate ligands capable of coordinating via either sulphur or nitrogen but not both; hence they are not chelating agents. However, there seems to be no review devoted exclusively to metal chelates of sulphur–nitrogen ligands.

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B. PROPERTIES ASSOCIATED WITH SULPHUR DONORS

The particular features of sulphur as a donor atom have been discussed in some detail in an earlier review[1]. Since they are very relevant, they are summarized here as follows.

(*i*) Whereas the permanent dipole moment and the coordinating ability decrease in the order: $H_2O > ROH > R_2O$, the reverse order holds for sulphur, viz. $H_2S < RSH < R_2S$.

(*ii*) From a consideration of both electrostatic and covalent models the strength of bonding to a metal ion is in the order: $RO^- > RS^-$ and $R_2O > R_2S$. However, sulphur has vacant *d* orbitals which can be used for $d_\pi - d_\pi$ bonding such as can occur with the later transition metals and with the early transition metals in unusually low oxidation states. Consequently, if π-bonding occurs, it can cause a reversal of the order to $RS^- > RO^-$ and $R_2S > R_2O$.

(*iii*) The polarizabilities of sulphur donors decrease in the order $S^{2-} > RS^- > R_2S$; furthermore, the number of lone pairs decreases in the same order. Consequently, thiolo ligands are more polarizable but not as effective d_π electron acceptors as thioethers.

(*iv*) Sulphur donors bind more strongly to (b) class metals than do oxygen donors. Class (b) metals form a triangular area in the centre of the Periodic Table. The oxidation state of the metal affects the degree of (b) character, which is strongest for transition metals in low oxidation states; i.e. metals having non-bonding *d* electrons and thus capable of forming $d_\pi - d_\pi$ bonds by donating a pair of electrons to the ligand.

(*v*) The spectrochemical series of ligands is arranged according to the spectroscopic splitting parameter Δ or $10Dq$. Although some sulphur donors, including S-bonded SCN^-, $(RO)_2PS_2^-$, and S^{2-}, have a low position in the series near Cl^-, R_2S falls in the middle of the series, probably between H_2O and N-bonded SCN^-, while S-bonded SO_3^{2-} has a late position near NO_2^-. The position of RS^- has not been established.

(*vi*) Sulphur ligands occupy a late position in the nephelauxetic series, which is, in effect, a measure of the degree of covalent bonding between metal and ligand. The series of donor atoms (arranged according to decreasing values of $1-\beta$) is roughly: $F < O < N < Cl < Br < S \simeq I < Se$.

(*vii*) The low-spin d^8 ions palladium(II), platinum(II) and gold(III), and the d^{10} ions copper(I), silver(I), gold(I) and mercury(II), have high stability constants when complexed with sulphur ligands. Being typically (b) class, they form strong σ-bonds with soft ligands and also $d_\pi - d_\pi$ bonds by donation of a pair of electrons to the ligand.

(*viii*) Thiols but not thioethers cause spin-pairing in complexes of cobalt(II) and nickel(II).

Some additional general observations can be made.

Sulphur atoms in heterocyclic rings have very poor coordinating ability due to the pseudo-aromatic nature of the ring, which has the twofold effect of causing the lone pairs on the sulphur atom to be less available for donation and the π-orbitals to be less capable of accepting electrons from the metal. Towards (b) class and borderline metals the coordinating ability of the various types of sulphur donors is: $RS^- > R_2S > RC{=}S \gg$ ring sulphur.

All ligands except the "hardest" base, fluoride ion, cause spin-pairing of cobalt(III). Thiols, monothio-β-diketones, and other charged sulphur ligands such as diethyl dithiophosphate, but not thioethers or thiones, cause spin-pairing of nickel(II). However, only the "softest" bases such as cyanide ion, diarsine, and certain charged sulphur ligands cause spin-pairing of iron(III). A series denoting the decreasing ability to cause spin-pairing is[9]: $CN^- > RCS_2^- \simeq ROCS_2^- \simeq R_2NCS_2^- > RNHCS_2^- \simeq (EtO)_2PS_2^- \simeq RCS{=}CHCOR' > R_2S$.

Some data are available on the nucleophilic reactivity of sulphur ligands[9a]. The methylmercury cation CH_3Hg^+ has been used as a reference for bases L, since it acts as a Lewis acid as follows:

$$CH_3Hg^+ + L \rightleftharpoons [CH_3HgL]^+$$

The values for $pK(CH_3Hg^+)$, as given by the dissociation constant for $[CH_3HgL]^+ \rightarrow CH_3Hg^+ + L$, can be determined for a number of Lewis bases. Sulphur ligands have very high values for $pK(CH_3Hg^+)$: S^{2-}, 21.3; RS^- in cysteine, 15.9; $S_2O_3^{2-}$, 10.95; SO_3^{2-}, 8.16. For comparison, the values of some other ligands are: CN^-, 14.0; I^-, 8.66; NH_3, 7.65; Br^-, 6.7; Cl^-, 5.3; F^-, 1.55. These data can be used to predict the effect of the changing of the nature of the leaving group on the rate of either an S_N2 or an S_N1 reaction[9a].

It appears that polarizability is the most important factor in determining the reactivity of a nucleophile. Nevertheless, it should be emphasised that there is no one scale of nucleophilic reactivities. A scale has been devised to give nucleophilic reactivity constants n^0_{Pt} with reference to *trans*-$Pt(py)_2Cl_2$ as the standard. The values for n^0_{Pt} for sulphur ligands vary considerably: from 3.29 for $(PhCH_2)_2S$ to 7.34 for $S_2O_3^{2-}$. It is noteworthy that the mercaptide ligand PhS^- has the high value of 7.17. Ligands with low values for n^0_{Pt} are Cl^- (3.04), NH_3 (3.06), pyridine (3.13) and Br^- (4.18). Ligands with highest values for n^0_{Pt} are tertiary arsines and phosphines, which have values in the range 7.54 – 8.85. These ligands are capable of dative π-bonding to platinum(II) in the transition state[9a].

Metal–sulphur stretching frequencies lie within the range 480 – 210 cm^{-1}. In chelate complexes coupling can occur; this can be attributed to ν(M–S) + ring deformation[10]. In many instances two bands are observed: one of medium to strong intensity and a weaker band at a frequency 10 – 40 cm^{-1} lower than the stronger band. The frequencies ν(Pd–S) and ν(Pt–S) for a large number of complexes[11] lie within the range 400 – 280 cm^{-1}. However, the frequency of ν(M–S) is not very sensitive to the atomic mass of M. Monothio-β-diketone complexes of a wide range of bi- and trivalent metals[7] display ν(M–S) within the range 399 – 376 cm^{-1}. Furthermore, there is no marked difference between thiolo complexes and thioether complexes in regard to the frequency of ν(M–S).

C. PROPERTIES PECULIAR TO SULPHUR–NITROGEN LIGANDS

What has been stated about complexes of sulphur ligands applies also to complexes of sulphur–nitrogen chelating agents. However, the nitrogen atom tends to lower the solubility of the complexes in non-aqueous solvents so that complexes of sulphur–nitrogen ligands are, in general, either sparingly soluble or insoluble in non-polar solvents.

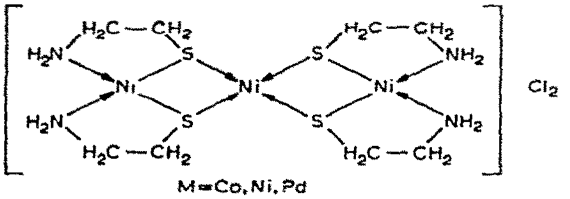
From the sparse data available, sulphur–nitrogen ligands appear to give rise to a smaller reduction in the interelectronic repulsion energy than sulphur–sulphur ligands. This presumably is due to nitrogen having a low position compared to sulphur in the nephelauxetic series. Consequently, sulphur–nitrogen donors would be expected to give rise to higher values of β than sulphur donors alone.

Metal–nitrogen stretching frequencies can occur over a wide range, viz. from 600 to below 200 cm^{-1}. For unidentate amines ν(M–N) occurs usually within the range 500 – 370 cm^{-1}, while for pyridine complexes[10] it occurs in the range 287 down to below 200 cm^{-1}. For a range of tetragonal diamine complexes of cobalt(II) and nickel(II) ν(M–N) occurs[12] in the range 400 – 338. Consequently, in a chelate complex it is often impossible to identify ν(M–N) with any certainty. However, in some nickel(II) complexes of an NSN tridentate, ν(M–N) and ν(M–S) were reported to occur at 415 – 412 and 328 – 326 cm^{-1}, respectively[13].

D. SULPHUR–NITROGEN CHELATES HAVING A THIOLO GROUP

2-Aminoethanethiol is the simplest representative of this class of ligand. Jensen[14] first observed the formation of two nickel complexes of 2-aminoethanethiol in solution. The stability constants for the complexes with cobalt(II), nickel(II), zinc(II), cadmium(II) and lead(II) have been determined[15]; the value of log β_2 for the nickel complex is 19.8 at 30°C, showing that the complex has relatively high thermodynamic stability.

Jicha and Busch[16,17] have made a detailed study of the complexes of 2-aminoethanethiol. Two types of complex are formed with transition metal ions, viz. the monomeric bis-ligand complexes $M(H_2NCH_2CH_2S)_2$ (M = Ni, Pd) and the trinuclear cationic complexes I; the structure I has been confirmed for the nickel complex by X-ray diffraction[18]. The cobalt complex has a magnetic moment of 2.49 B.M. per metal atom[16].



I

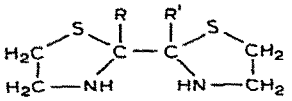
Busch et al.[19–21] have investigated the S-alkylation of the nickel and palladium complexes of 2-aminoethanethiol. The nickel complex reacts with alkyl halides in dimethylformamide solution to give a complex of the S-alkylated ligand. A typical reaction is

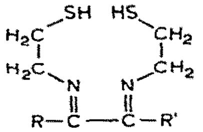
$$\mathrm{Ni(SCH_2CH_2NH_2)_2} + 2\,\mathrm{MeI} \longrightarrow \mathrm{Ni(MeSCH_2CH_2NH_2)_2I_2}$$

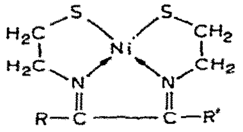
square-planar
diamagnetic

octahedral
paramagnetic

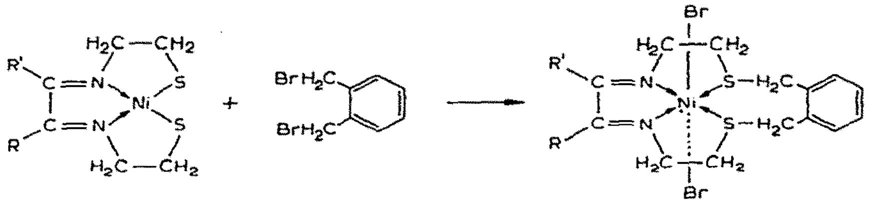
2-Aminoethanethiol reacts with α-diketones to yield a thiazolidinyl, II, as the main product, although a small amount of the tautomeric Schiff base III is also formed. If the reaction is carried out in the presence of nickel ions, the nickel complex IV is formed in high yield. It has been concluded that the metal ion acts as a template which favours the formation of the Schiff base[22].


II

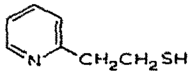

III

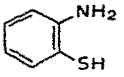

IV

Kinetic studies have shown that the sulphur atom remains coordinated during the S-alkylation reaction[19]. α, α′-Dibromo-o-xylene reacts with square-planar nickel complexes of Schiff bases derived from α-diketones and 2-aminoethanethiol, V, to yield paramagnetic octahedral nickel complexes VI[19,23,24]. In these reactions the nickel atom serves as a template for closure of the macrocyclic ring. These and other template reactions involving sulphur ligands have been discussed by Lindoy and Busch[2,25].

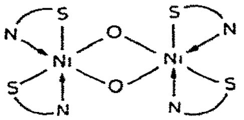

V VI

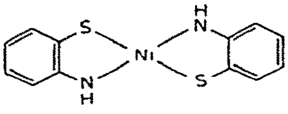
2-(2-Mercaptoethyl)pyridine (VII; N-SH) forms the complexes $\mathrm{M(N\text{-}S)_2}$ (M = Co, Ni, Pd, Pt). Trinuclear complexes $\mathrm{[M_3(N\text{-}S)_4]X_2}$, similar to those obtained with 2-aminoethanethiol, are known; however, these trinuclear complexes can only be isolated if the anion X is of low coordinating power – in the presence of halide ions, thiolo-bridged neutral, binuclear complexes $\mathrm{M_2(N\text{-}S)_2X_2}$ are obtained[22,26].


VII

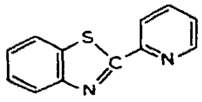

VIII

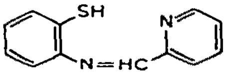
2-Aminobenzenethiol, VIII, forms inner complexes with cobalt(II), cobalt(III), nickel(II) and palladium(II)[27,28]. The buff-coloured nickel(II) complex can be oxidized in strongly alkaline solution to a dark blue compound which was considered to be the μ-dioxo-nickel(IV) complex IX[27]. Subsequent work has shown that this dark blue oxidation product does not contain oxygen and has the structure X. The compound shows two reversible polarographic reduction waves. The polarographic and ESR data obtained for this complex have been interpreted as indicating that the compound contains nickel(II) with the ligand in an oxidized state[29–32]. Larkworthy et al.[32] reported the preparation of 2-aminobenzenethiolo complexes of vanadyl(IV), chromium(III), manganese(II), iron(II), cobalt(II), nickel(II), nickel(IV), copper(I) and zinc(II) complexes under anaerobic conditions. The complexes $M(SC_6H_4NH_2)_2$ (M = Mn, Fe, Co) exhibit antiferromagnetism[32].


IX

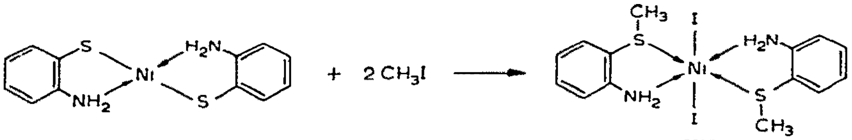

X

2-Aminobenzenethiol reacts with pyridine-2-aldehyde to yield the pale yellow 2-(2-pyridyl)benzothiazoline, XI, which, when treated with alkali, forms a deep red solution of the tautomeric Schiff base, *N*-2-mercaptophenylene-2′-pyridylmethyleneimine (XII; N-N-SH). In the presence of molybdenum(III), nickel(II), copper(II), zinc(II) or cadmium(II) the benzothiazoline XI rearranges to give deeply coloured metal chelates of the Schiff base XII[33]. The complexes $Mo_2(N\text{-}N\text{-}S)_2X_4(H_2O)_3$ (X = Cl, Br) to which thiolo-bridged structures have been assigned, have anomalously low magnetic moments (ca. 1 B.M.) for the d^3 configuration, presumably due to metal–metal interaction either directly or via the thiolo bridges[34].


XI

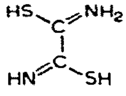

XII

Methyl iodide reacts with a suspension of bis(2-aminobenzenethiolo)nickel(II), XIII, in acetone to yield the six-coordinate complex diiodobis(2-methylthioaniline)-nickel(II), XIV, which can also be prepared from 2-methylthioaniline and nickel iodide[35]. The reactions and interconversions of XIII and its derivatives have been extensively investigated by Lindoy and Livingstone[35].

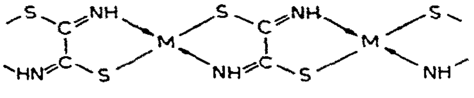

XIII
square-planar diamagnetic

XIV
octahedral paramagnetic

Dithiooxamide (XV; rubeanic acid) has long been used for the detection and determination of many metals[36–39]; with nickel(II) and copper(II) it forms insoluble chelates[40], which are polymeric and probably possess the structure XVI. The structures of these complexes and those of *N*, *N*′-disubstituted thiooxamides have been discussed by Hurd et al.[41,42]. Dimethyldithiooxamidenickel(II) has a magnetic moment of 2.4 B.M. The magnetic properties of the nickel complexes of dithiooxamide and three of its derivatives have been investigated by Kanekar and Casey[43], who explained the magnetic behaviour by postulating that the polymeric structure consists of both planar and octahedral nickel atoms.

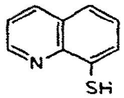


XV

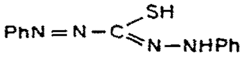


XVI

8-Mercaptoquinoline, XVII, forms very stable chelates with (b) class metal ions[44–48]. The chelates of the platinum metals with 5-chloro- and 5-bromo-8-mercaptoquinoline are more stable than those of 8-mercaptoquinoline itself. The stabilities of the complexes of 5-chloro-8-mercaptoquinoline are in the order[49,50]: Pd > Pt > Rh > Ir > Ru > Os.



XVII

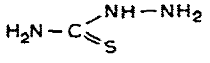


$PhN{=}N{-}C(SH){=}N{-}NHPh$

XVIII

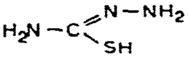
3-Mercapto-1,5-diphenylformazan (dithizone; XVIII, Hdz) forms neutral complexes with (b) class metals and several borderline metals[51,52]. In the mercury complex $Hg(dz)_2(py)_2$ the dithizone ions are bound by the sulphur atom, while the nitrogen atom of the azo group is situated at a distance 0.5 Å greater than that expected for an Hg–N covalent bond so that the mercury atom has a distorted tetrahedral arrangement[53]. However, in the copper complex $Cu(dz)_2$ the ligand is bidentate, being coordinated by nitrogen and sulphur in a square-planar configuration[54].

Thiosemicarbazide (tscH) can exist in the tautomeric forms XIX and XX and can act as a neutral or (by loss of a proton) as a charged bidentate ligand. Metal complexes containing the ligand in the uncharged form have been more extensively investigated than those containing the deprotonated form of the ligand. Metal complexes of neutral thiosemicarbazide are discussed in Section F of this review.



$H_2N{-}C({=}S){-}NH{-}NH_2$

XIX

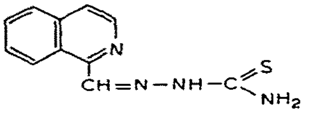


$H_2N{-}C(SH){=}N{-}NH_2$

XX

The complexes $M(tsc)_2$ (M = Ni, Pd, Pt) have been obtained in two forms which were assumed to be *cis–trans* isomers[55,56]. A crystal structure determination showed that the red form of $Ni(tsc)_2$ has a *trans* configuration[57]. Haines and Sun[58] found that the red and grey forms of $Ni(tsc)_2$ have identical spectra and concluded that the two forms are different crystal modifications of the *trans* isomer. The cobalt complex Co(tsc)$_3$ has been obtained in two forms which were assumed to be *cis–trans* isomers[59].

Neutral complexes of nickel(II), copper(II), and zinc(II) with anthranilaldehyde thiosemicarbazone are known; the nickel complex is paramagnetic and six-coordinate[60]. Metal complexes of isoquinoline-l-carboxaldehyde thiosemicarbazone, XXI, have been reported[61]. The crystal structure of bis(isoquinoline-l-carboxaldehyde thiosemicarbazono)nickel(II) monohydrate has been determined[62]. The nickel atom is octahedrally coordinated by two approximately planar SNN ligands but the water molecule is not coordinated. The Ni–S bond lengths of 2.425 and 2.412 Å are at the low end of the range (2.4 – 2.6 Å) generally found in six-coordinate nickel(II) complexes[63,64].

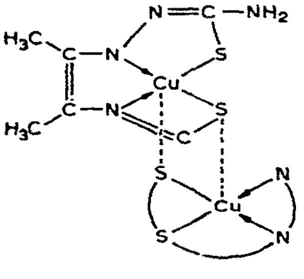


XXI

A number of thiosemicarbazones of aliphatic and aromatic aldehydes and ketones have been studied by Gingras et al.[65]. The copper(I) complexes of some N- and S-substituted thiosemicarbazones are polymeric, the metal ion being bonded through the nitrogen and sulphur of the thiosemicarbazone moiety[66]. Reactions of some diketones with thiosemicarbazide yield mono- and bis-thiosemicarbazone Schiff bases and some cyclization products[75]. The monothiosemicarbazone Schiff bases, which readily form complexes with copper(II) in alkaline or neutral media, were found not to react with silver(I), mercury(II), nickel(II), manganese(II), zinc(II), cobalt(II), iron(II) and iron(III)[67], which seems surprising. Copper(I) complexes of *o*-fluoro- and *m*-fluorobenzaldehyde thiosemicarbazone are associated in benzene solution but are apparently dimers at infinite dilution[68].

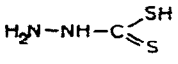
The thiosemicarbazone of benzoylformic acid behaves as a monobasic acid under acid conditions and as a dibasic acid in alkaline solution. The iron(II), cobalt(II), nickel(II), cadmium(II) and lead(II) complexes of the dibasic form have been reported[69].

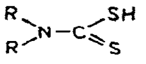
The structure of the copper(II) complex of diacetylbis(thiosemicarbazone) consists of two planar units within the unit cell related by an inversion centre, XXII. The axial Cu–S distance within the unit cell is 3.102 Å. The sixth coordination position of the copper ion is occupied by a sulphur atom from a molecule in an adjacent unit cell. At low temperatures there is magnetic interaction between the copper atoms[70].

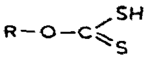


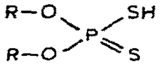
XXII

Until recently dithiocarbazic acid, XXIII, and its derivatives had been less thoroughly investigated than other dithioacids such as dithiocarbamates, XXIV, xanthates, XXV and dialkyl dithiophosphates, XXVI[71–73].


XXIII


XXIV


XXV

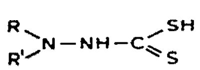

XXVI

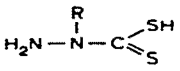
Free dithiocarbazic acid has been isolated only recently[74], although its ammonium and hydrazinium salts have long been known[75]. A crystal structure determination of $[N_2H_5][H_2NNHCS_2]$ has shown that the NCS_2 group closely resembles that in *N*,*N*-dialkyl dithiocarbamates[76].

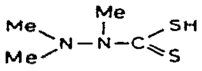
Jensen[77] was probably the first to prepare the nickel complex of dithiocarbazic acid, and he considered the ligand to be coordinated to the metal ion by the thiolo sulphur and the β-nitrogen atoms. Complex formation by dithiocarbazic acid with platinum(II) was studied by Mashentsev and Chernyaev[78] who reported that the platinum complex exhibited "hydrazo reaction" due to the reversible migration of a proton into the complex. They also reported the isolation of *cis* and *trans* forms of $Pt(H_2NNHCS_2)_2$, although no supporting physical measurements were made. The *cis* isomer was prepared from *cis*-$Pt(NH_3)_2Cl_2$ and the *trans* isomer was obtained from K_2PtCl_4. Later work was unable to confirm the occurrence of *cis–trans* isomerism for this complex, since the samples obtained from both preparative methods had identical infrared spectra and X-ray powder diffraction patterns[79]. The ammonia and ethylenediamine adducts of $Ni(H_2NNHCS_2)_2$ have been reported[80]. Cambi et al.[81] have reported complexes of dithiocarbazic acid with rhodium(III), nickel(II), zinc(II), cadmium(II) and lead(II). However, the reported compositions of some of these complexes, e.g. $Ni_2(H_2NNHCS_2)(H_2NNCS_2)_2.N_2H_4.5H_2O$, are open to question. The complexes $M(H_2NNHCS_2)_2$ (M = Ni, Pd, Pt, Zn, Cd, Pb) and $Cr(H_2NNHCS_2)_3.2H_2O$ were prepared from hydrazinium dithiocarbazate; their infrared spectra display ν(M–S) within the range 350 – 375 cm^{-1}. The red nickel complex is diamagnetic[79]. The electronic spectrum of the chromium complex is significantly different from the spectra of chromium(III) complexes of disulphur chelates such as dithiocarbamates and xanthate. The values of the Racah parameter B and the nephelauxetic coefficient β for $Cr(H_2NNHCS_2)_3.2H_2O$ are 630 cm^{-1} and 0.7 (ref. 79). The values of β for chromium(III) complexes of disulphur chelates[82] are ca. 0.45. The much higher value of β for the dithiocarbazate complex illustrates the difference between this compound and the SS bonded complexes and suggests the occurrence of NS coordination[79]. This is further substantiated by Anthoni's infrared studies[83] on the nickel(II) complexes of several N-substituted dithiocarbazic acids. The infrared data are interpreted as indicating NS coordination.

Battistoni et al.[84] have prepared the nickel(II) and zinc(II) chelates of a range of N-substituted dithiocarbazic acids XXVII (R = H, R′ = Ph; R = R′ = Me; R = R′ = Ph; R = Me, R′ = Ph), XXVIII (R = Me, Et, *n*-Pr, *n*-Bu) and XXIX. The bis-ligand nickel complexes are diamagnetic and square-planar but a high-spin tris-ligand complex $[N(n\text{-}Bu)_4][Ni(Me_2NNHCS_2)_3]$ was also isolated. The substituents on the nitrogen atoms were found to affect the mode of coordination (either NS or SS) of the ligand.

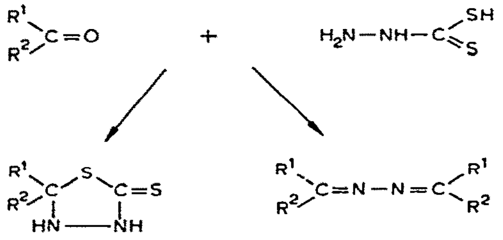
From electronic spectral data the authors concluded that the low-spin nickel complexes fall into two groups: those with NiS_2N_2 and those with NiS_4 chromophores. The ligands XXVII have SS coordination to nickel, whereas the ligands of types XXVIII and XXIX have NS coordination.


XXVII


XXVIII


XXIX

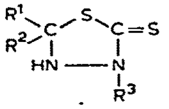
The reaction between dithiocarbazic acid and aldehydes and ketones has been investigated by Heugebaert and Willems[85], who reported that aliphatic and π-deficient aldehydes and ketones form 1, 3, 4-thiadiazolidine-2-thiones, XXX, whereas aromatic and π-rich heterocyclic aldehydes and ketones form azines XXXI.

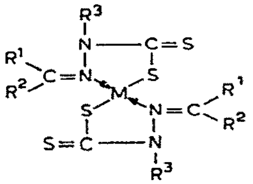

XXX

XXXI

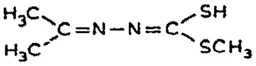
The preparation of a number of S-esters of dithiocarbazic acid and their reactions with aliphatic and aromatic aldehydes and ketones have been reported[86,87].

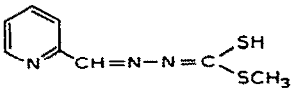
In the presence of certain metal ions, such as nickel(II), palladium(II) and copper(II), 1,3,4-thiadiazolidine-2-thiones (XXXII; $R^1 = H$, Me; $R^2 = o\text{-}C_5H_4N$,Me; $R^3 = H$, Me) undergo rearrangement to yield neutral chelates XXXIII of the tautomeric Schiff base[88].


XXXII


XXXIII

The acetone Schiff base *S*-methyl-*N*-isopropylidendithiocarbazate (XXXIV; N-SH) forms the stable complexes $M(N\text{-}S)_2$ (M = Co, Ni, Pd, Pt, Cu). The nickel, palladium, platinum and copper complexes are square-planar but magnetic and spectral evidence indicates that the cobalt complex is tetrahedral[89].


XXXIV


XXXV

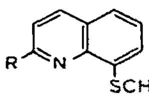
The pyridine-2-aldehyde Schiff base *S*-methyl-*N*-(2-pyridyl)-methylendithiocarbazate (XXXV; N-N-SH) forms the square-planar 1 : 1 complexes [M(N-N-S)X] (M = Ni, Pd, Pt, Cu; X = Cl, Br, I, NCS or NO_3) and $[Cu(N\text{-}N\text{-}S)H_2O]ClO_4$ and the octahedral 2 : 1 complexes $[M(N\text{-}N\text{-}S)_2]$ (M = Fe, Ni). The manganese(III) complex is probably octahedral and polymeric. With iron(III) the complexes $[Fe(N\text{-}N\text{-}S)_2]ClO_4$ and $[Fe(N\text{-}N\text{-}S)_2][FeCl_4]$ were obtained. Both the iron(II) complex and the iron(III) complex cation $[Fe(N\text{-}N\text{-}S)_2]^+$ are spin-paired. The Mössbauer spectrum of $[Fe(N\text{-}N\text{-}S)_2][FeCL_4]$ confirms the presence of the low-spin cation and the high-spin tetrahedral anion. The values for the isomer shift and quadrupole splitting of the low-spin iron(III) cation are 0.34 and 2.38 $mm.sec^{-1}$, respectively, at 293°K, in close agreement with the values found for $[Fe(N\text{-}N\text{-}S)_2]ClO_4$. The isomer shift for the high-spin $[FeCl_4]^-$ anion is 0.49 $mm.sec^{-1}$ at 293°K; the small quadrupole splitting (0.22 $mm.sec^{-1}$) indicates only slight distortion from tetrahedral symmetry. Bivalent cobalt is oxidized to yield the cobalt(III) complex ion $[Co(N\text{-}N\text{-}S)_2]^+$, which was isolated as $[Co(N\text{-}N\text{-}S)_2]NO_3\ H_2O$ and $[Co(N\text{-}N\text{-}S)_2]_2[CoX_4]$ (X = Cl, Br, NCS)[89].

Metal chelates of *S*-alkyl derivatives of dithiocarbazic acid are discussed in Section E, while chelates of thiols having ONS donor atoms are discussed in Section G.

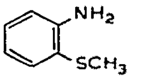
E. CHELATES WITH NITROGEN AND THIOETHER SULPHUR AS DONORS

(i) Bidentate chelates

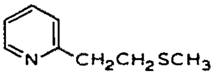
8-Methylthioquinoline (XXXVI, R = H; N-SMe) forms complexes with (b) class metal ions. Nickel gives only high-spin six-coordinate complexes of the type $[NiX_2(N\text{-}SMe)_2]$ (X = Cl, Br, I, NCS). Attempts to prepare a gold(III) complex led to S-demethylation of the ligand[90] and the isolation of $AuCl_2(N\text{-}S)$. S-Demethylation of the palladium(II) and platinum(II) complexes can be effected by the heating of the complexes in dimethylformamide[91].



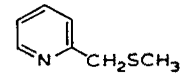
XXXVI



XXXVII



XXXVIII



XXXIX

2-Methyl-8-methylthioquinoline (XXXVI, R = Me; mmtq) is a poorer chelating agent than 8-methylthioquinoline. It does not form nickel(II) and cobalt(II) complexes readily and its gold(III) and palladium(II) complexes do not undergo S-dealkylation. However, complexes of cobalt(II) and nickel(II) can be isolated from 2,2′-dimethoxypropane solution. The 2-methyl group causes severe steric hindrance to other ligands in the square plane. The complex $AuCl_3$mmtq contains five-coordinate gold(III). Spectral evidence suggests that the compounds MX_2mmtq (M = Co, Ni, Cu; X = Cl, Br) have a pseudo-tetrahedral configuration[92].

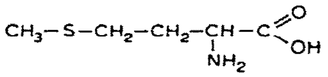
o-Methylthioaniline (XXXVII; N-SMe) forms high-spin complexes with nickel of the type $NiX_2(N\text{-}SMe)_2$. The copper complexes $CuX_2(N\text{-}SMe)$ (X = Cl, Br) can be obtained from alcohol solution at 0°C but are not very stable. The compounds

$PdCl_2$(N-SMe) and $[Pt(N\text{-}SMe)_2][PtCl_4]$, on being heated in dimethylformamide, undergo S-demethylation[91,93] to yield the thiolo-bridged complexes $M_2Cl_2(N\text{-}S)_2$.

2-(2-Methylthioethyl)pyridine (XXVIII; N-SMe) gives the complexes MX_2(N-SMe) and $[M(N\text{-}SMe)_2](ClO_4)_2$ (M = Pd, Pt, Cu, Hg) but attempts to isolate complexes of cobalt and nickel were, surprisingly, unsuccessful[94]. With 2-methylthiomethylpyridine (XXXIX; N-SMe) the following complexes were isolated[95]: $MX_2(N\text{-}SMe)_2$ (M = Co, Ni), MX_2(N-SMe) (M = Pd, Pt, Cu), $[M(N\text{-}SMe)_2]$-$(ClO_4)_2$ (M = Pd, Pt, Hg), $[Cu(N\text{-}SMe)_2]ClO_4$ and $[Ag_2(N\text{-}SMe)_2](ClO_4)_2$.

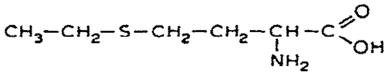
Formation constants have been determined for complexes of nickel(II) and copper(II) with methyl 2-aminoethyl sulphide, $CH_3SCH_2CH_2NH_2$, of cobalt(II) and nickel(II) with bis(2-aminoethyl) sulphide, $S(CH_2CH_2NH_2)_2$, and of cobalt(II), nickel(II) and copper(II) with 1,8-diamino-3,6-dithiaoctane, $H_2NCH_2CH_2SCH_2CH_2SCH_2CH_2NH_2$. In all cases the sulphur–nitrogen ligands gave much less stable complexes than the analogous polyamines containing no sulphur[96]. Metal complexes of methyl 2-aminoethyl sulphide (N-SMe) with *3d* metal ions have been isolated, viz. $M(N\text{-}SMe)_2X_2$ (M = Co, Ni, Cu, Zn; X = Cl, Br, I, NO_3, ½SO_4), $[Ni(N\text{-}SMe)_3]X_2$ (X = I, ClO_4), and $Cu(N\text{-}SMe)_4Cl_2$. In the complexes $Co(N\text{-}SMe)_2Cl_2$, $Zn(N\text{-}SMe)_2Cl_2$ and $Cu(N\text{-}SMe)_4Cl_2$ the ligand is bound by nitrogen only[97].

DL-Methionine (XL; mthH) acts as a bidentate ligand with bivalent and trivalent metal ions. From infrared spectral data it has been concluded that in the complexes $M(mth)_3$ (M = Al, Cr, Fe, Rh, Bi) the ligand is coordinated through the nitrogen and carboxyl oxygen atoms. The complexes $M(mth)_2$ (M = Mn, Co, Ni, Cu, Zn, Cd, Hg, Pb) are octahedral and polymeric with carboxylato bridges so that the ligand coordinates to one metal ion via the nitrogen atom and one oxygen atom of the carboxyl group and to a neighbouring metal ion via the other oxygen atom of the carboxyl group[98]. The infrared spectra of $M(mthH)Cl_2$ (M = Pd, Pt) were interpreted as indicating that the methionine was coordinated via the nitrogen and sulphur atoms and that the compounds had a polymeric structure due to intermolecular hydrogen bonding between the carboxylic acid residues[99]. An X-ray structural determination of $Pd(mthH)Cl_2$ showed that the methionine ligand is coordinated via the nitrogen and sulphur atoms with Pd–S and Pd–N distances of 2.265 and 2.061 Å, respectively. The methionine moiety does not have the zwitterion structure that it possesses in the free state. The un-ionized carboxyl group is hydrogen-bonded to the carboxyl group of an adjacent molecule so that the $Pd(mthH)Cl_2$ molecules pack together as dimers[100,101].



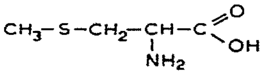
$CH_3{-}S{-}CH_2{-}CH_2{-}\underset{NH_2}{\underset{|}{C}H}{-}C\begin{smallmatrix}\nearrow O\\ \searrow OH\end{smallmatrix}$

XL



$CH_3{-}CH_2{-}S{-}CH_2{-}CH_2{-}\underset{NH_2}{\underset{|}{C}H}{-}C\begin{smallmatrix}\nearrow O\\ \searrow OH\end{smallmatrix}$

XLI

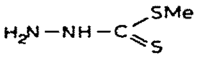


$CH_3{-}S{-}CH_2{-}\underset{NH_2}{\underset{|}{C}H}{-}C\begin{smallmatrix}\nearrow O\\ \searrow OH\end{smallmatrix}$

XLII

Complexes of DL-ethionine (XLI; ethH) and *S*-methyl-L-cysteine (XLII; SmcH) have been investigated[102]. Spectral and magnetic data indicate that the complexes are of four types, as follows: (*a*) the complexes ML_2 (L = eth, Smc; M = Mn, Co, Ni, Cu, Zn, Cd) which are polymeric in the solid state with carboxyl bridges; the metal atom is six-coordinate and the amino acid is bound to one metal atom via the nitrogen and one oxygen and to another metal atom via the second oxygen; (*b*) the complexes $M(LH)X_2$ (M = Pd, Pt; X = Cl, Br) in which the amino acid is bound to the four-coordinate metal via the nitrogen and sulphur only; the M–S stretching frequency occurs in the range 385 – 378 cm^{-1}; (*c*) the compound $[Hg(ethH)_2](ClO_4)_2.H_2O$, in which the ethionine is bound via the nitrogen atom only; (*d*) the mixed-metal complex $[AgCu(Smc)_2]NO_3$ in which the amino acid residue is coordinated to the copper ion via nitrogen and oxygen and to the silver ion via the sulphur atom[102].

S-Methyldithiocarbazate, XLIII, yields the tris-ligand complexes $[Ni(H_2NNHCSSCH_3)_3]X_2$ (X = Cl, Br, NO_3) and the bis-ligand complexes $[Ni(H_2NNHCSSCH_3)_2X_2]$ (X = Cl, NCS); both types are high-spin and spectral evidence indicates NS coordination. The complexes $M(H_2NN{=}CSSCH_3)_2$ (M = Ni, Pd, Pt) containing deprotonated *S*-methyldithiocarbazate have also been isolated; the nickel complex is diamagnetic[79].



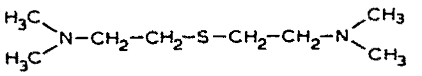
$H_2N{-}NH{-}C(SMe){=}S$

XLIII

(ii) Tridentate chelates

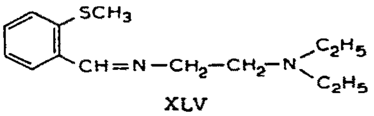
The formation constants of metal complexes of the two tridentates 1,8-diamino-3,6-dithiaoctane and bis(2-aminoethyl) sulphide have been mentioned in Section E (*i*) above.

Bis(2-dimethylaminoethyl) sulphide (XLIV; NSN) forms the complexes $M(NSN)X_2$ (M = Co, Ni; X = Cl, Br, NCS) which are five-coordinate in the solid state but in solution they give rise to an equilibrium between monomeric five-coordinate and associated species. The magnetic moments of the cobalt complexes range from 4.44 to 4.55 B.M. at room temperature, while the moments of the nickel complexes[103] fall within the range 3.24 – 3.32 B.M.



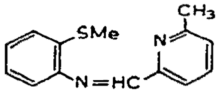
$(H_3C)_2N{-}CH_2{-}CH_2{-}S{-}CH_2{-}CH_2{-}N(CH_3)_2$

XLIV

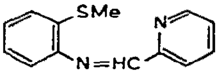


XLV

The Schiff base XLV formed by *o*-methylthiobenzaldehyde and *N*, *N*-diethylethylenediamine forms high-spin complexes $M(N\text{-}N\text{-}SMe)X_2$ (M = Co, Ni; X = Cl, Br, I, NCS). The nickel halide complexes are five-coordinate in the solid state, whereas in solution in inert solvents they give rise to temperature-dependent equilibria between tetrahedral and five-coordinate species. The cobalt halide complexes are pseudo-tetrahedral both in the solid state and in solution; in the cobalt complexes the Schiff base is coordinated by the two nitrogen atoms only, the sulphur not being coordinated. In boiling *n*-butanol the nickel iodide complex is S-demethylated[104] to the brown, diamagnetic complex Ni(N-N-S)I.



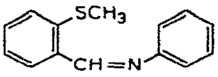
XLVI



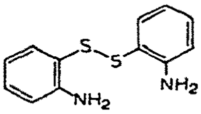
XLVII

6-Methylpyrid-2-yl-*N*-(2′-methylthiophenyl)methyleneimine (XLVI; SNNMe) forms the mono-ligand complexes $M(SNNMe)X_2$ (M = Mn, Fe, Co, Ni, Cu; X = Cl, Br, I, NCS). Spectral evidence indicates that in the solid state the manganese, iron and cobalt complexes are five-coordinate, whereas the nickel and copper complexes are six-coordinate and polymeric. The bis-ligand complexes $[M(SNNMe)_2]X_2$ (M = Fe, Ni, Cu; X = ClO_4, BF_4) have also been isolated. The iron(II) complex is low-spin but the magnetic moment of the nickel complex is normal[105] for high-spin octahedral nickel(II).

The bis-ligand cobalt(II) complexes of XLVI, viz. $[Co(SNNMe)_2]X_2$ (X = I, ClO_4, BF_4), are spin-free, whereas the corresponding complexes of 2-pyridyl-*N*-(2′-methylthiophenyl)methyleneimine, XLVII, are spin-paired. This difference in magnetic behaviour arises from the lower effective ligand-field strength of XLVI presumably due to the steric inter-ligand interference introduced by the methyl group in the 6-position. The moments of the cobalt complexes are temperature-dependent because of a thermal equilibrium between the nearly equi-energetic spin-paired and spin-free states of the cobalt(II) ion in these complexes[106].



XLVIII

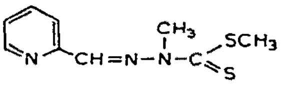


XLIX

N-(2-Methylthiophenyl)-2′-methylthiophenylmethyleneimine (XLVIII; SNS) forms the complexes $M(SNS)X_2$ (M = Co, Ni; X = Cl, Br, I, NCS). The electronic spectra indicate that the cobalt halide complexes are five-coordinate, whereas the complex $Co(SNS)(NCS)_2$ and the nickel complexes are six-coordinate and polymeric. The copper complexes $Cu(SNS)X_2$ (X = Cl, Br) are possibly five-coordinate. The bis-ligand complexes of nickel, $[Ni(SNS)_2]X_2$ (X = ClO_4, BF_4) are high-spin but the complex $[Co(SNS)_2](ClO_4)_2$ is low-spin with a moment of 1.97 B.M. at room temperature[107].

2,2′-Dithiodianiline (XLIX; dta) forms the nickel complexes $NidtaX_2$ (X = Cl, Br) but with cobalt(II) and copper(II), products of indefinite composition were obtained. The infrared and electronic spectra of $NidtaX_2$ indicate that the ligand coordinates via the two amino groups and one sulphur atom. The electronic spectra and magnetic moments are typical of six-coordinate nickel(II). The metal atom probably achieves six-coordination by means of a polymeric structure involving halogen bridges[13].

The dithiocarbazic acid derivative, α-*N*-methyl-*S*-methyl-β-*N*-(2-pyridyl)methylendithiocarbazate (L; N-NMe-S) acts as a neutral NNS tridentate ligand forming stable complexes with transition metal ions but shows little tendency to form five-coordinate neutral complexes with bivalent metal ions. The complexes $M(N\text{-}NMe\text{-}S)X_2$ (M = Mn, Ni; X = Cl, Br, I or NCS) are probably halogen-bridged, six-coordinate, and polymeric. The structures of the analogous copper complexes are uncertain. The bis-ligand complexes $[M(N\text{-}NMe\text{-}S)_2](ClO_4)_2$ (M = Fe, Co, Ni) and $[M(N\text{-}NMe\text{-}S)_2][MX_4]$ (M = Fe, Co; X = Cl, Br, I, NCS) have been reported. In the complexes of the latter type the iron(II) cation is diamagnetic (low-spin) but the cobalt(II) cation is high-spin[108].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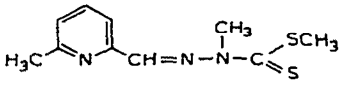
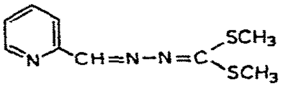

LI

α-*N*-Methyl-*S*-methyl-β-*N*-(6-methylpyrid-2-yl)methylendithiocarbazate (LI; MeN-NMe-S) also acts as a neutral NNS tridentate and forms stable complexes with iron(II), cobalt(II), nickel(II), and copper(II). However, the methyl group in the 6-position of the pyridine moiety increases the tendency of LI, relative to L, to form five-coordinate metal complexes. Spectral evidence indicates that the halogeno complexes $M(MeN\text{-}NMe\text{-}S)X_2$ (M = Fe, Ni, Cu; X = Cl, Br) are five-coordinate, probably with a distorted trigonal-bipyramidal structure. On the other hand, the thiocyanato complexes $M(MeN\text{-}NMe\text{-}S)(NCS)_2$ (M = Fe, Ni) are six-coordinate and probably polymeric with thiocyanato bridges. Bis-ligand complexes of the type $[M(MeN\text{-}NMe\text{-}S)_2](ClO_4)_2$ are formed by iron, cobalt and nickel but not by copper. The complexes $[Co(MeN\text{-}NMe\text{-}S)_2][CoX_4]$ (X = Cl, Br, NCS) and $[Fe(MeN\text{-}NMe\text{-}S)_2][FeI_4]$ were also obtained. The iron(II) cation $[Fe(MeN\text{-}NMe\text{-}S)_2]^{2+}$ is low-spin[109].

The bis(S-methylated) derivative, 2-(2,3-diaza-4-methylthio-5-thiahexa-1,3-dienyl)-pyridine (LII; N-N-SMe) forms stable complexes with manganese(II), cobalt(II), nickel(II) and copper(II). The ligand acts as an NNS tridentate in the complexes $[Ni(N\text{-}N\text{-}SMe)_2](ClO_4)_2$ and $Ni(N\text{-}N\text{-}SMe)X_2$ (X = Cl, Br, I, NCS); the latter complexes are six-coordinate and anion-bridged. The complexes $Co(N\text{-}N\text{-}SMe)X_2$ (X = Cl, Br, I) are tetrahedral with the ligand acting as an NN bidentate, while the nitrato complex $[Co(N\text{-}N\text{-}SMe)NO_3]NO_3$ is probably five-coordinate in the solid state and in solution. In the complexes $[M(N\text{-}N\text{-}SMe)_2]X_2$ (M = Co, Cu; X = ClO_4, BF_4) the ligand behaves as NN bidentate; the cobalt complexes are low-spin. The complex $[Cu(N\text{-}N\text{-}SMe)_2I]BF_4$ was also isolated[110].


LII

(iii) Quadridentate chelates

Open-chain quadridentate ligands (i.e. not closed-ring quadridentates such as porphyrins) can be divided into four stereochemical types[111,112]:

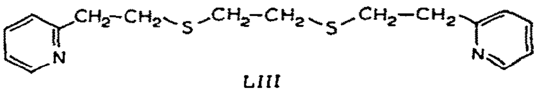
(*a*) Those which, because of structural constraints, can coordinate so that all four donor atoms are in the one plane.

(*b*) Those which can coordinate only in a tetrahedral arrangement.

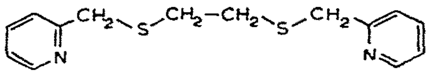
(*c*) Tripod-type ligands which apply a constraint to the metal ion, often causing it to adopt a non-typical configuration, e.g. trigonal bipyramidal.

(*d*) Those which are flexible and can coordinate in either a planar or non-planar arrangement (facultative quadridentates).

The facultative quadridentate 1,8-bis(2-pyridyl)-3,6-dithiaoctane (LIII; NSSN) can present its four donor atoms in either a planar or non-planar arrangement. It forms the planar complexes $[M(NSSN)](ClO_4)_2$ (M = Pd, Pt, Cu), the tetrahedral complex $[Cu(NSSN)]ClO_4$, and the octahedral complex $[Ru(NSSN)bipy](ClO_4)_2$, in which the quadridentate must coordinate to two equatorial and two apical sites of the octahedron[113].

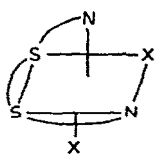


LIII

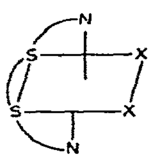


LIV

A similar ligand, 1,6-bis(2-pyridyl)-2,5-dithiahexane (LIV; NSSN), forms three five-membered chelate rings, involving the sulphur atoms and the pyridine nitrogen atoms, in contrast to LIII, which forms two six-membered rings and a five-membered ring. The ligand LIV might be considered to be a facultative quadridentate; however, models indicate that steric requirements prevent coordination to a metal ion in a planar arrangement. The two sulphur atoms, separated by only two carbon atoms, interact sterically and there is also interaction between the protons attached to the α-carbon atoms of the pyridyl rings. The ligand cannot take up a tetrahedral configuration but it could coordinate around octahedral sites in either of the configurations LV or LVI. The compounds $M(NSSN)X_2$ (M = Fe, Co, Ni; X = Cl, Br, I, NCS) have been isolated; they are high-spin, six-coordinate complexes which have appreciable conductivities in nitromethane due to replacement of X by a molecule of solvent[114].

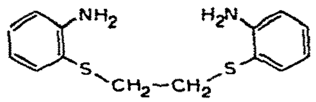


LV



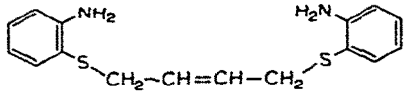
LVI

1,2-Di(*o*-aminothiophenoxy)ethane (LVII; NSSN) forms the high-spin six-coordinate nickel(II) complexes $[Ni(NSSN)X_2]$ (X = Cl, Br, I, NCS, NO_3, ClO_4); the nitrato and perchlorato groups are coordinated in the solid state. The cobalt(III) complex $[Co(NSSN)Cl_2]Cl$ and the palladium(II) complexes $Pd(NSSN)X_2$ (X = Cl, Br, I) were also obtained. The palladium complexes are non-electrolytes and in these complexes the ligand is coordinated via the two sulphur atoms only[115].

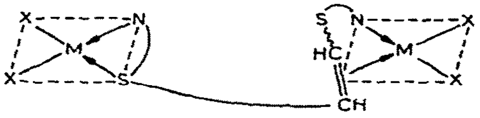


LVII

1,4-Di-(*o*-aminothiophenoxy)but-*trans*-2-ene (LVIII; datb) forms the complexes M_2X_4(datb) (M = Pd, Pt; X = Cl, Br, I, SCN). No complexes were obtained with the first-row transition metals, cobalt, nickel, copper or zinc. In the complexes each of the two metals appears to exist in a different environment. The structure LIX has been suggested for these complexes[116].



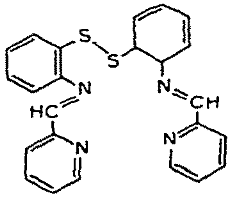
LVIII



LIX

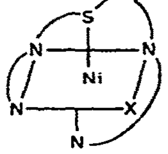
(iv) Quinquedentate chelates

To the authors' knowledge there is only one reported case of a quinquedentate ligand containing exclusively sulphur and nitrogen atoms as donors. This is the ligand recently reported by Livingstone and Nolan, viz. α,α'-[dithiobis-(*o*-phenylenenitrilo)]-di-2-picoline (LX; dtpp)[13].



LX

Surprisingly, few studies have been made of ligands which contain the disulphide linkage. Molecular models show that LX can act as a quinquedentate with the four nitrogens and one of the sulphur atoms acting as donors as in structure LXI. The complexes which were isolated are [MdtppX] X (M = Mn, Ni; X = Cl, Br), [NidtppCl] ClO_4, [NidtppX] BF_4 (X = Cl, Br) and [Mndtppl] ClO_4. The nickel complexes are high-spin and the magnetic, conductivity, and spectral data are consistent with six-coordinate nickel(II), indicating that the ligand is acting as a quinquedentate[13].

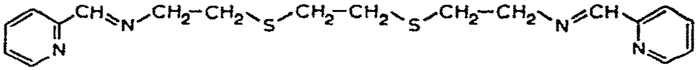


LXI

(v) Sexadentate chelates

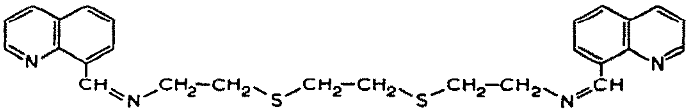
A considerable number of sexadentate chelating agents containing sulphur, nitrogen, and oxygen as donors have been prepared by Dwyer, Lions, and co-workers; the metal complexes of these ligands are discussed in Section G of this review.

1,8-Bis-(α-pyridylmethyleneamino)-3,6-dithiaoctane* (LXII; NNSSNN) forms the violet complexes $[Fe(NNSSNN)](ClO_4)_2$ and $[Fe(NNSSNN)]I_2.2H_2O$. The iodide was resolved into optical antimers with $[M]_D^{20} \pm 18,300°$; the high rotation arises from the asymmetry of the sexadentate chelate. Since the low-spin cobalt(II) complex $[Co(NNSSNN)](ClO_4)_2$ (μ_{eff}, 1.85 B.M.) is not easily oxidized, the authors suggested that the ligand may behave towards cobalt(II) as a planar NSSN quadridentate. The perchlorate can be oxidized with ceric nitrate to the unstable cobalt(III) complex $[Co(NNSSNN)](ClO_4)_3$. The copper complex $[Cu(NNSSNN)](ClO_4)_2$ was also reported[117].



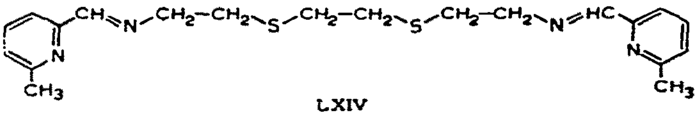
LXII

1,8-Bis-(8-quinolylmethyleneamino)-3,6-dithiaoctane (LXIII; NNSSNN) forms the complexes $[M(NNSSNN)]I_2.2H_2O$ (M = Fe, Co, Ni) and $[M(NNSSNN)]$-$(ClO_4)_2.H_2O$ (M = Cu, Zn)[118].



LXIII

1,8-Bis-(6′-methyl-2′-pyridylmethyleneamino)-3,6-dithiaoctane (LXIV; NNSSNN) gives the spin-paired complexes $[M(NNSSNN)]X_2$ (M = Fe, Co; X = I, ClO_4)[113].



LXIV

1,5-Bis-[2-(2-pyridylmethyleneimino)phenyl]-1,5-dithiapentane (LXV; NNSSNN) also gives spin-paired complexes with iron(II) and cobalt(II) but the nickel(II) complexes are high-spin, as expected for six-coordinate nickel(II). The high degree of conjugation in this ligand requires that each NNS sequence must be planar. Therefore, if the ligand occupies all six octahedral positions about a metal ion, it can do this in but two ways represented by the enantiomorphic configurations LXVI and LXVII[119].

The complex cations $[M(NNSSNN)]^{2+}$ (M = Fe, Co, Ni) were isolated with various

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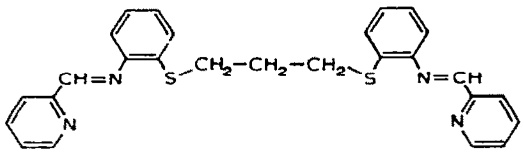
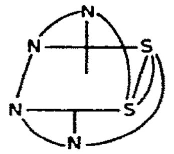
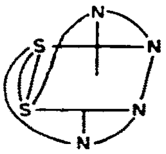
* *Authors' note.* In this review, so as to avoid confusion, we have tended to use the names given by the authors to the various ligands, even though, in many cases, these are not the systematic names.

anions. Many of these complexes crystallize with solvent of crystallization (water, acetone, ethyl alcohol, or dimethylformamide) which is difficult to remove; for example a thermogravimetric study showed that the acetone in [Fe(NNSSNN)]-$[FeCl_4]_2.(CH_3)_2CO$ is lost sharply at 260°C. The infrared spectra indicate that the solvent molecules are not coordinated. X-ray diffraction data show that this compound has a host framework of four molecules per unit cell; the structure contains cavities into which the acetone molecules fit. These guest molecules determine the type of structure adopted by the clathrate compound. The ligand LXV was found to give indefinite products with the square-planar ions palladium(II), platinum(II) and gold(III). The failure to isolate pure compounds of these (b) class metals was ascribed to their reluctance to adopt six-coordination[119].


LXV


LXVI


LXVII

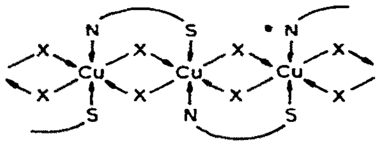
F. CHELATES WITH NITROGEN AND THIONE SULPHUR AS DONORS

Thiosemicarbazide in the tautomeric form XIX is one of the simplest representatives of this type of ligand. Reactions of thiosemicarbazide with various metal ions in solution have been studied by a number of workers[120–124]. The stability constants for some metal chelates of thiosemicarbazide have been determined[125–127].

The nickel(II) complexes of thiosemicarbazide have been studied in considerable detail. The complexes $Ni(tscH)_2X_2$ (X = Cl, Br, I) are spin-paired, whereas $Ni(tscH)_2(SCN)_2$ and $Ni(tscH)_2(ClO_4)_2$ are high-spin[128]. An X-ray structural determination of the blue complex $[Ni(tscH)_2(H_2O)_2](NO_3)_2$ has shown that the nickel atom is *trans*-octahedrally coordinated by the two sulphur atoms, the two terminal hydrazine nitrogen atoms, and the two water molecules[129]; the Ni–S distance is 2.41 Å. Jensen and Raneke-Madsen[55] reported two forms of $Ni(tsc)_2SO_4$, one reddish-brown and the other greenish-grey, and suggested that they were *cis-trans* isomers. The α-form was later found to be a trihydrate and has a *trans* square-planar configuration; the water molecules are not coordinated but occupy spaces between the complex ion and the sulphate ions[130]. The structure of the β-form has also been determined. The most remarkable feature of the structure is the presence of both *cis*- and *trans*-isomers in the one crystal. In both forms the bond angles about the nickel atom are close to 90° but the Ni–S distance in the *cis* form (2.145 Å) is significantly shorter than that in the *trans* form (2.165 Å). This is attributed to the stronger *trans* effect of sulphur compared to nitrogen[131]. The thiocyanato complex is *trans*-octahedral[132] with Ni–S distances of 2.40 Å.

Complex formation between thiosemicarbazide and various cobalt(II) salts in aqueous solution has been studied[133], and it was found that the complex formed is $[Co(tscH)_3]^{3+}$. *Cis–trans* isomerism was recognized to occur in these complexes[134, 135] and the kinetics of isomerization have been investigated by paper chromatography[136]. The *cis* and *trans* forms of $[Co(tscH)_3]Cl_3$ have been isolated; the *cis* isomer has the greater stability. Both isomers were resolved and absolute configurations have been assigned on the basis of optical rotatory dispersion and circular dichroism measurements. The interconversion of these optically active complexes in aqueous solution was studied and a bond-rupture mechanism has been proposed to account for the observed inversion and isomerization[137].

Two series of copper(II) complexes with thiosemicarbazone have been reported[55, 138,139]. The complexes $Cu(tscH)_2X_2$ (X = Cl, Br, NO_3, ClO_4, ½SO_4) have distorted octahedral structures. It has been proposed that the complexes $Cu(tscH)X_2$ (X = Cl, Br) have a structure in which the halide ions are coordinated in a square-planar arrangement about the copper ion, giving infinite polymeric chains, and the thiosemicarbazide moieties link different copper ions as in LXVIII[139].



LXVIII

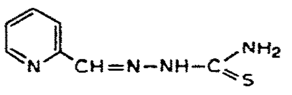
In the zinc complex $Zn(tscH)Cl_2$ the metal atom is tetrahedrally coordinated[140]. There are at least two instances where thiosemicarbazide acts as a neutral unidentate ligand. The complexes Ag(tscH)Cl and Ag(tscH)SCN have structures which consist of polymeric chains with the thiosemicarbazide moiety coordinated by the sulphur atom only. In the chloro complex there are two types of silver atom in the unit cell, both with tetrahedral coordination. One silver atom is coordinated by two chlorines (at 2.65 and 2.75 Å) and two sulphurs (at 2.50 Å), while the other silver atom is bound to one chlorine (at 2.66 Å) and three sulphurs (at 2.48, 2.51 and 2.77 Å)[141]. In the thiocyanato complex the silver atom has a distorted trigonal bipyramidal arrangement involving two sulphur atoms from two thiosemicarbazide moieties and one nitrogen and one sulphur from two different thiocyanato groups. The thiocyanato groups bridge the silver atoms and link the coordination polyhedra in zig-zag chains. The two sulphur atoms of the thiosemicarbazide are located[142] at 2.43 and 2.48 Å, while the sulphur of the thiocyanato group is further away at 2.99 Å.

The Mössbauer spectra of some high-spin thiosemicarbazate complexes of iron(II) have been reported[143].

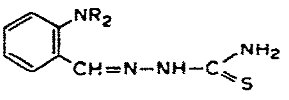
Ablov and Gerbeleu have investigated the complexes formed by cobalt, nickel, copper and zinc with thiosemicarbazones of a number of aldehydes and ketones[144].

They proposed octahedral structures for M$\{Me_2C{=}NNHC({=}S)NH_2\}_2Cl_2 . H_2O$- (M = Co, Ni) but an X-ray structural determination of the nickel complex showed that the complex has a trigonal bipyramidal structure[145].

Pyridine-2-aldehyde thiosemicarbazone (LXIX; NNSH) forms with iron(II) and nickel(II) stable complexes in which it behaves as a neutral tridentate ligand. The iron complexes $[Fe(NNSH)_2]X_2$ (X = Cl, Br) are spin-paired, whereas the nickel complexes $[Ni(NNSH)_2]X_2$ (X = Cl, NO_3) are spin-free. The ligand can be deprotonated[146] to yield the complexes $[M(NNS)_2]$ (M = Fe, Ni) and $[Co(NNS)_2]Cl.3H_2O$.



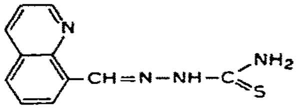
LXIX



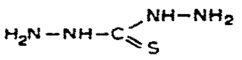
LXX

o-Aminobenzaldehyde thiosemicarbazone (LXX; R = H) and *o*-(*N*-dimethylamino)-benzaldehyde thiosemicarbazone (LXX; R = Me)[147] give octahedral nickel complexes $[Ni(NNSH)_2]Cl_2$.

Copper(II) complexes of quinoline-8-aldehyde thiosemicarbazone (LXXI; NNSH) have been reported[61], viz. $Cu(NNSH)X_2$ (X = Cl, NO_3), Cu(NNS)X (X = Cl, Br, NCS), and Cu(NNS)bipyCl.



LXXI



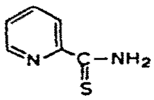
LXXII

Thiocarbohydrazide (LXXII; tch), the next higher homologue of thiosemicarbazide, acts as a neutral bidentate ligand coordinating through the thione sulphur and one of the terminal nitrogen atoms. The complexes reported are $[M(tch)_2]Cl_2$ (M = Zn, Cd, Hg, Pd), $[Fe(tch)_2(NCS)_2]$, $[Co(tch)_2Cl_2]$ and $[M(tch)_3]Cl_2$ (M = Ni, Cu). Spectral data indicate that the iron, cobalt, nickel, and copper complexes have distorted octahedral stereochemistry[148].

Complexes of N-substituted thiocarbazide, $RNHNHC(S)NHNH_2$ (R = acetyl, benzoyl, nicotinyl, 2-chlorobenzoyl, 2-hydroxvbenzoyl) with cobalt(II) and nickel(II) have been investigated. The complexes $Ni(tcH)_2Cl_2$ (tcH = N-substituted thiocarbazide) have magnetic moments within the range 3.78 – 3.87 B.M. and are considered to be pseudo-tetrahedral with the thiocarbazide being coordinated via the sulphur atom only. The complexes $Ni(tcH)Cl_2.4H_2O$ have moments of 3.30 – 3.31 B.M. and are considered to be distorted octahedral with the thiocarbazide coordinating through the sulphur and terminal nitrogen and to possess polymeric structures involving chloro bridges. The complexes $Ni(tc)_2$, which have moments in the range 3.09 – 3.18 B.M., are polymeric with sulphur bridges[149].

The cobalt(II) complexes $Co(tcH)_2Cl_2$, $[Co(tcH)_2NO_3]NO_3$, $Co(tcH)_2Cl_2$.2dioxane, and $Co(tc)_2$ are spin-free with moments lying between 4.86 and 5.16 B.M. The spectra indicate octahedral stereochemistry. The complexes $Co(tc)_2$ are polymeric with sulphur bridges and are isomorphous with the corresponding nickel complexes, whereas the complexes $Co(tcH)_2Cl_2$ are not isomorphous with their nickel analogues[150].

2-Thioamidopyridine, LXXIII, acts as a neutral bidentate ligand forming complexes with a wide range of metal ions[151–155]. This ligand can coordinate via the pyridine nitrogen and either the amido nitrogen or the thione sulphur. Bonding via the pyridine nitrogen and the thione sulphur occurs with ruthenium(III), osmium(III), cobalt(II), nickel(II), palladium(II), silver(I), gold(I), gold(III) and mercury(II)[156].

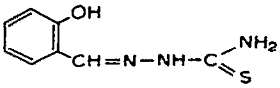


LXXIII

G. CHELATES WITH SULPHUR, NITROGEN AND OXYGEN AS DONORS

(i) Tridentate chelates

Ablov and Gerbeleu have studied the metal complexes formed by salicylaldehyde thiosemicarbazone (LXXIV; $ONSH_2$). This ligand readily loses a proton from the phenolic group and acts as a singly charged tridentate coordinating through the oxygen, the imino nitrogen, and the thione sulphur atoms. It also can act as a doubly negatively charged tridentate by losing a proton from the mercapto group of the tautomeric form analogous to XX. The cobalt(III) complexes $[Co(ONSH)_2]Cl$ and $[Co(ONSH)(ONS)].H_2O$, the chromium(III) and iron(III) complexes $[Cr(ONSH)_2]Cl$, $[Cr(ONSH)(ONS)].H_2O$, and $NH_4[M(ONS)_2]$ (M = Cr, Fe) have been reported[157, 158].



LXXIV

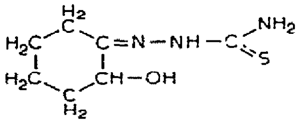
With nickel(II) the ligand LXXIV forms the green, paramagnetic complex $Ni(ONSH_2)_2(NO_3)_2$ and the reddish-brown, diamagnetic complexes [Ni(ONS)B] ($B = H_2O, NH_3$, pyridine, aniline). The mode of coordination of the neutral ligand in $Ni(ONSH_2)_2(NO_3)_2$ is in doubt, although the authors assume that the ligand is tridentate and formulate the compound as $[Ni(ONSH_2)_2](NO_3)_2$ without any supporting evidence. With copper(II) and zinc(II) the complexes $CuX(ONSH).H_2O$ ($X = Cl, HCO_2$) and $Zn(ONSH_2)_2X_2$ ($X = Cl, NO_3$) are formed[159].

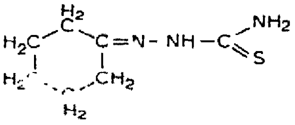
The Mössbauer spectra of the iron(III) complexes of LXXIV and of the 5-chloro and 5-bromo analogues of LXXIV indicate a temperature-dependent transition between high- and low-spin states[160].

Mössbauer spectral data have been obtained for the iron(II) and iron(III) complexes of the thiosemicarbazones of salicylaldehyde and biacetyl monoxime at 80 and 300°K. In the iron(III) complexes the greater proportion of the iron atoms are in the low-spin state even at 323°K. The iron(II) complex of salicylaldehyde thiosemicarbazone is high-spin but the iron(II) complex of biacetyl monoxime thiosemicarbazone is low-spin[161].

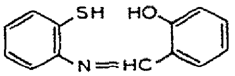
Nickel(II) and copper(II) complexes of N-substituted derivatives of salicylaldehyde thiosemicarbazone, $OH.C_6H_4.CH{=}NNRC(S)NH_2$ (R = Ph, *o*-tolyl, styryl) have been reported. The complexes $Ni(ONSH_2)_2(NO_3)_2$ are six-coordinate, while the complexes Ni(ONS)B (B = H_2O, amine) and CuX(ONSH) are square-planar[162].

Adipoin thiosemicarbazone (LXXV; ONSH) forms the complexes $M(ONSH)_2X_2.nH_2O$ (M = Co, Ni; X = Cl, Br, NCS or NO_3) and $[Co(ONS)_2].CH_3CO_2$. The involvement of the oxygen atom in coordination is indicated by the fact[163] that cyclohexanone thiosemicarbazone, LXXVI, does not form complexes with cobalt(III).

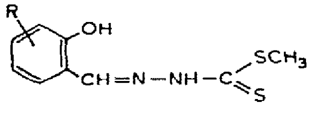

LXXV

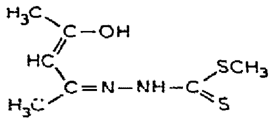

LXXVI

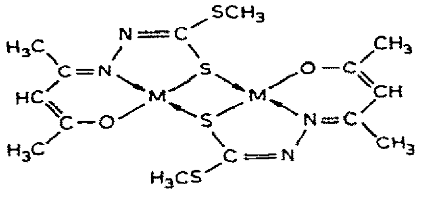
The copper complex of 2-(salicylideneamino)benzenethiol (LXXVII; $ONSH_2$), viz. Cu(ONS) exhibits very weak magnetic exchange interactions. It has been suggested that this compound has a polymeric chain structure in which the copper atoms are trigonal bipyramidal and are linked by alternate oxygen and sulphur atoms[164].


LXXVII

S-Methyl-β-*N*-(2-hydroxyphenyl)methylendithiocarbazate (LXXVIII, R = H)-($ONSH_2$), its substituted derivatives (LXXVIII; R = 5-chloro, 5-bromo, 5-nitro and 3-methoxy), and the acetylacetone Schiff base, 2-hydroxy-4-methyl-5,6-diaza-7-thiono-8-thianona-2,4-diene (LXXIX; $acacONSH_2$), by the loss of two protons act as doubly negatively charged ONS tridentates. The square-planar complexes M(ONS)B (M = Ni, Cu; B = H_2O, py) and the octahedral cobalt(III) complex have been isolated. The complexes M(acacONS) (M = Ni, Pd, Pt) are considered to possess the square-planar, dimeric thiolo-bridged structure LXXX[165].

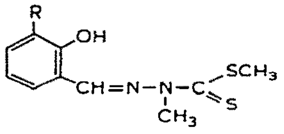

LXXVIII


LXXIX

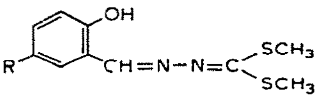

LXXX

The copper complexes Cu(ONS) of the 5-chloro-, 5-bromo- and 3-methoxy-salicylaldehyde Schiff bases are red and have anomalously low magnetic moments which decrease with decrease in temperature. This behaviour is attributed to antiferromagnetic interaction due to an oxygen-bridged dimeric structure. The moment of the green copper complex of the 5-nitrosalicylaldehyde Schiff base increases with decrease in temperature, rising to 2.43 B.M. at 83°K. The magnetic data fit an expression for a tetrahedral cluster of four ferromagnetically interacting copper atoms. The green complex Cu(acacONS) is also ferromagnetic[165,166].

The Schiff bases, α-*N*-methyl-*S*-methyl-β-*N*-(2-hydroxyphenyl)-methylenedithiocarbazate (LXXXI; R = H) (HONMeS), its 3-methoxy derivative (LXXXI; R = OMe), 1-(2-hydroxyphenyl)-2,3-diaza-4-methylthio-5-thiahexa-1, 3-diene (LXXXII; R = H), and its 5-chloro and 5-bromo derivatives (LXXXII; R = Cl, Br) (HONSMe) by loss of a proton act as uni-negatively charged ONS tridentate ligands. The complexes Ni(ONMeS)X (X = Cl, Br, NCS) are diamagnetic and square-planar, while $Ni(ONMeS)_2$ is paramagnetic and octahedral. The copper complexes $Cu(ONMeS)NO_3$, $Cu(ONSMe)NO_3$ $Cu(ONSMe)NO_3$, Cu(5ClONSMe)Cl, and Cu(5BrONSMe)Cl display normal magnetic behaviour. The complex $Cu_2(3MeOONMeS)Cl_3$ displays antiferromagnetic interaction between the copper atoms in the dimer. The magnetic data for $Cu_3(ONMeS)_2Cl_4$ and $Cu_3(ONSMe)_2Cl_4$ indicate a linear trimeric arrangement with three antiferromagnetic interacting copper atoms[167].



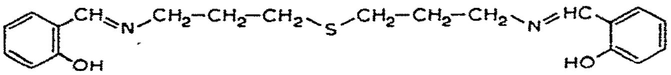
LXXXI



LXXXII

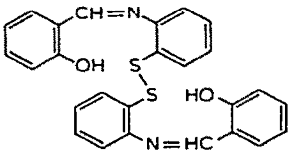
(ii) Quinquedentate chelates

1,7-Bis-(salicylideneamino)-4-thiaheptane, LXXXIII, has been reported to be capable of acting as a quinquedentate[111].



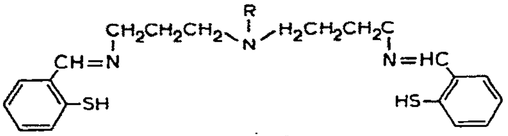
LXXXIII

The nickel complex of bis[2-(salicylideneamino)phenyl]disulphide, LXXXIV, has been reported but no physical data were given[168].



LXXXIV

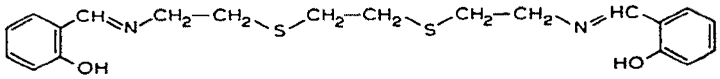
The *o*-mercaptobenzaldehyde Schiff bases (LXXXV; R = H, Me) give rise to the five-coordinate complexes $M(SNNNS)_2$ (M = Co, Ni). The nickel complexes have moments of 3.25 B.M., while the moments of the cobalt complexes[169] are in the range 4.10 – 4.17 B.M.


LXXXV

(iii) Sexadentate chelates

In a series of papers Dwyer et al. reported a considerable number of sexadentates, most of which had the ONSSNO donor sequence. They succeeded in resolving several of the cobalt(III) complexes into their optical enantiomers.

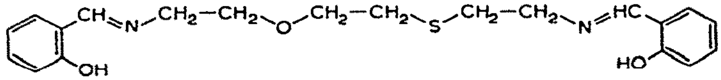
1,8-Bis(salicylideneamino)-3,6-dithiaoctane (LXXXVI; HONSSNOH) yields the complexes M(ONSSNO) (M = Fe, Co, Ni, Cu, Zn) and the cobalt(III) complexes [Co(ONSSNO)] X (X = Cl, I, NO_3, ClO_4). The iodide was resolved and found to have a molecular rotation[170], $[M]^{20}_{5461}$, of ± 50,160°. The magnetic moment of the iron(II) complex was reported[171] as having the rather surprising value of 3.32 B.M.; it needs reinvestigating. The analogous ligand 1,8-bis-(β-hydroxy-α-naphthylideneamino)-3,6-dithiaoctane (HONSSNOH) gave a cobalt(III) complex [Co(ONSSNO)] Br with a molecular rotation[170] of 73,370°.


LXXXVI

A series of sulphur-containing α, ω-diamines, $H_2N(CH_2)_x S(CH_2)_y S(CH_2)_z NH_2$ (x, y and z = 2 or 3) were condensed with salicylaldehyde or 2-hydroxy-1-naphthaldehyde to give ligands, analogous to LXXXVI, which behave as sexadentates. Most of the cobalt(III) complexes of these ligands were resolved. The highest value for $[M]^{20}_{D}$ – viz. 87,000° – was obtained for 1,10-bis-(2'-hydroxo-1'-naphthylmethyleneamino)-4,7-dithiadecanecobalt(III) bromide trihydrate[172].

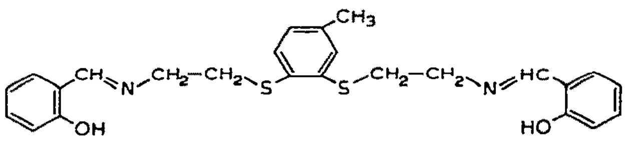
Cobalt(III) complexes were isolated with another series of sexadentates obtained by the condensation of 1,8-diamino-3,6-dithiaoctane with several *o*-hydroxylated aromatic aldehydes[173].

Dwyer et al. prepared 1,8-bis-(salicylidene-amino)-3-oxa-6-thiaoctane, LXXXVII, in order to ascertain if the replacement of one sulphur of the ligand LXXXVI by oxygen would still allow the compound to function as a sexadentate. Cobalt(III) complexes of LXXXVII and of the di-oxygen analogue of LXXXVI were obtained, indicating that both ligands were acting as sexadentates[174].

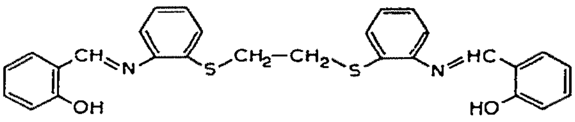

LXXXVII

Cobalt(III) complexes were also obtained with bis(salicylidene) derivatives of 1,9-diamino-3,6-dithianonane and 1,10-diamino-3,7-dithiadecane[175].

Several ligands similar to LXXXVI have been prepared with one or more of the polymethylene bridges replaced by one side of a benzene ring. Atoms attached to a benzene ring are constrained to lie in the plane of that ring. In such a ligand the flexing of the chelate moiety to encompass the metal atom must occur at the nitrogen and sulphur atoms. One such ligand is 3,4-bis-(γ-salicylideneamino-α-thiapropyl)-toluene, LXXXVIII. This and other similar ligands were found to act as sexadentates[176] and to give complexes of the type [Co(ONSSNO)] X.



LXXXVIII

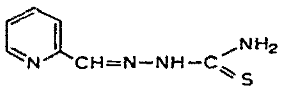


LXXXIX

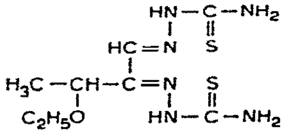
1,2-Di-(*o*-salicylaldiminophenylthio)ethane, LXXXIX, also gives a cobalt(III) complex [Co(ONSSNO)] X (X = Cl, I)[115,176].

H. CARCINOSTATIC AND ANTIVIRAL ACTIVITY OF SULPHUR-NITROGEN LIGANDS AND THEIR COMPLEXES

Although in 1956 it was reported that pyridine-2-carboxaldehyde thiosemicarbazone, XC, displays carcinostatic (anti-cancer) activity in the lymphoid leukaemia-1210 test, no mechanism of action was proposed[177]. French and co-workers[178–180] studied the carcinostatic activity of a number of thiosemicarbazones containing nitrogen heterocycles and they suggested that these compounds, by loss of a proton from their tautomeric thiol form, act as tridentate chelating agents, sequestering metal ions which are involved in carcinogenesis. The involvement of metal ions in some types of cancer has been discussed by a number of authors[181–183].



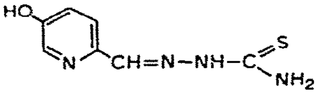
XC



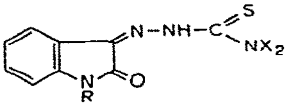
XCI

Kethoxal bis(thiosemicarbazone) (XCI; KTS) has marked carcinostatic action[184]. The cytotoxicity of KTS is enhanced by the presence of copper and zinc ions and it has been shown[185] that the copper(II) chelate of KTS is involved in the cytotoxic action of KTS. A crystal structure determination of the copper(II) complex shows that KTS behaves as an SNNS quadridentate and that the coordination about the copper ion is a very distorted square[186]. The two Cu(KTS) molecules in the unit cell interact magnetically[187].

Isoquinoline-1-carboxaldehyde thiosemicarbazone, XXI, has a broad range of carcinostatic activity and a low toxicity[179]. The most active anti-leukaemia reagent[188] among all the thiosemicarbazide derivatives investigated is 5-hydroxypyridine-2-carboxaldehyde thiosemicarbazone, XCII.


XCII

Among the few anti-viral drugs known are the isatin thiosemicarbazones, XCIII, which probably act by binding strongly to copper. The 1-methyl derivative ("Marboran") is a specific preventive of smallpox. It can ward off an attack in patients, exposed to an epidemic, whom it would be too late to vaccinate. As the lipophilicity of the molecule is increased the action against variola and some other DNA-containing viruses is replaced by one against the RNA-containing organisms such as polio virus[189].

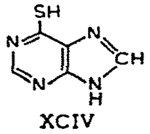

XCIII

(a) R = H, X = H – active against variola virus
(b) R = Me, X = Me – active against ectromelia virus
(c) R = Me, X = Bu – active against poliomyelitis virus

The preparation of some metal complexes of dithiocarbazic acid, H_2NNHCS_2H, and their biological applications have been the subject of some patents[190,191].

A considerable number of metal complexes of ligands derived from dithiocarbazic acid have been tested for carcinostatic activity. The complexes $Pd(H_2NN{=}CSSMe)_2$, $Cr(C_5H_4NCH{=}NNMeCSSMe)Cl_3$, and $Cu(C_5H_4NCH{=}NN{=}CSSMe)Cl$ show anti-tumour activity. The ligand XXXV and the complexes $Pd(Me_2C{=}NN{=}CSSMe)_2$ and $CuCl(o\text{-}C_5H_4N{-}CH{=}NN{=}CSSMe)$ have shown confirmed cytostatic activity in the 9KB test system – which is an in vitro test system giving a better indication of the carcinostatic activity of a compound over a wider range of cancers than other test systems. These compounds are undergoing further in vivo tests in leukaemia L-1210, Lewis lung, and B-16 melanoma systems[192].

The palladium and platinum complexes of 6-mercaptopurine, XCIV, are known to destroy some adenocarcinomas[193].


XCIV

Many cancers are known to have viruses associated with them and a few cancers are believed to be actually caused by viruses. Consequently an anticancer drug may actually be an antiviral agent[183]. Kirschner et al.[193] have observed that the protein and nucleic acid portions of viruses are effective chelating agents and the aim of the metallotherapeutic designer is to alter the virus by metal chelation so that the viral activity is diminished. He has pointed out that moderately stable metal chelates are necessary, since the metal ion must not be so weakly bound as to be free enough to be complexed by non-viral chelating agents such as amino acids and enzymes present in the body; secondly, the chelating agent should be able to be displaced by the virus; and thirdly, the metal ion has to be selective in regard to benign and malignant viruses.

It is apparent that the thermodynamic stability of the metal chelates is of less importance than kinetic considerations. Cancer growth is dependent on the reproduction of malignant cells having a kinetic advantage over the body's defence mechanisms. Therefore the metal complex, to be effective, has to be sufficiently labile to outpace the cancer growth[183]. From a recent study of the anti-tumour activity of some neutral complexes of the type PtA_2X_2 (A = amine; X = halogen), it has been suggested that kinetic factors are of importance in determining the effective dose of metal complex[194].

From the limited data available it seems to us that the following criteria are of importance in determining whether a metal complex will have carcinostatic activity:

(*i*) The metal chelate should have reasonably high thermodynamic stability.

(*ii*) The metal should be a (b) class metal, in particular palladium and platinum.

(*iii*) The complex should be reasonably labile; hence iridium complexes are unlikely to be effective.

(*iv*) Ligands with sulphur donors are likely to be the most effective, since they usually confer lipid solubility on the metal complex and they form stable complexes with (b) class and borderline metals.

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