

## Reactivity of Metal Chelates of Sulphur-Containing Ligands towards Lewis Bases. Part I. Reaction of Chloro-, Bromo-, Iodo- and Thiocyanato(S-methyl-N-(2-pyridyl)- methylenediazinecarbodithioate)nickel(II) Chelates with Pyridines

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The reaction of chloro-, bromo-, iodo- and thiocyanato(S-methyl-N-(2-pyridyl)methylenediazinecarbodithioate)nickel(II),  $NiLX$ , chelates with pyridine and 4-methylpyridine were studied spectrophotometrically. The stability constants as well as the thermodynamic parameters ( $\Delta G^\circ$ ,  $\Delta H^\circ$  and  $\Delta S^\circ$ ) for bis-adduct,  $NiLXB_2$ , formation were measured. The stability of the formed bis-adducts decreases in the order  $NCS > Cl > Br > I$  and is correlated with  $pK_w$ , electronegativity, polarizability, nephelauxetic effect and field strength of the in-plane unidentate ligand ( $X$ ). The variation of both  $\Delta H^\circ$  and  $\Delta S^\circ$  with  $X$  is explained in terms of a competitive effect between the in-plane  $Ni-X$  and axial  $Ni$ -heterocyclic nitrogen  $\pi$ -bonding.

### Introduction

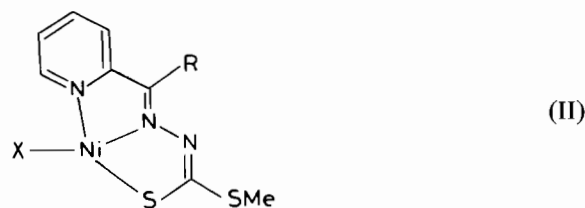
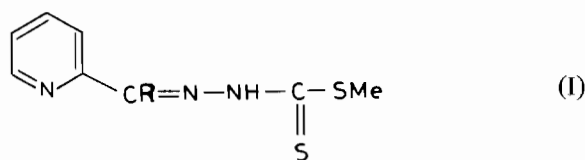
Terdentate Schiff bases with NNS set of donor atoms have been reported to possess marked antitumour activity [1–3]. Most of these Schiff bases are derived from the condensation of  $\alpha$ -(N)-aromatic heterocyclic aldehydes and ketones with either thiosemicarbazide or S-methylhydrazinecarbodithioate. A large number of bivalent and trivalent metal chelates with this type of ligand have been synthesized and characterized [4–8]. The antitumour activity of some transition metal chelates with the terdentate Schiff base ligands (I,  $R = H$  and  $CH_3$ ), derived from S-methylhydrazinecarbodithioate, has been also reported [9, 10]. The nickel(II) chelate (II,  $R = CH_3$ ,  $X = Cl$ ) was found to be the most active against P 388 lymphocytic leukaemia in mice [10].

The cytotoxic activity of this class of chelates was attributed to the presence of a labile uni-negative ligand ( $X$ ) trans to the nitrogen donor [10]. Furthermore, the square planar arrangement around nickel(II) [8] makes these chelates good Lewis acids and their antitumour activity may also be due to their

interaction with nucleophilic sites in DNA or other similar targets to form a wide variety of adducts within cells. This paper reports a detailed study on the interaction of the nickel(II) chelates (II,  $R = H$ ,  $X = Cl, Br, I$  and  $NCS$ ), hereafter abbreviated as  $NiLX$ , with pyridine type bases in benzene. The effects of uni-negative ligand ( $X$ ) on the stability and thermodynamic parameters of the formed adducts will be discussed.

### Results and Discussion

The solution electronic spectra of  $NiLX$  (II,  $R = H$ ,  $X = Cl, Br, I$  and  $NCS$ ) in benzene show gradual spectral changes on the addition of pyridine or 4-methylpyridine. Typical spectral variations of  $NiLCl$

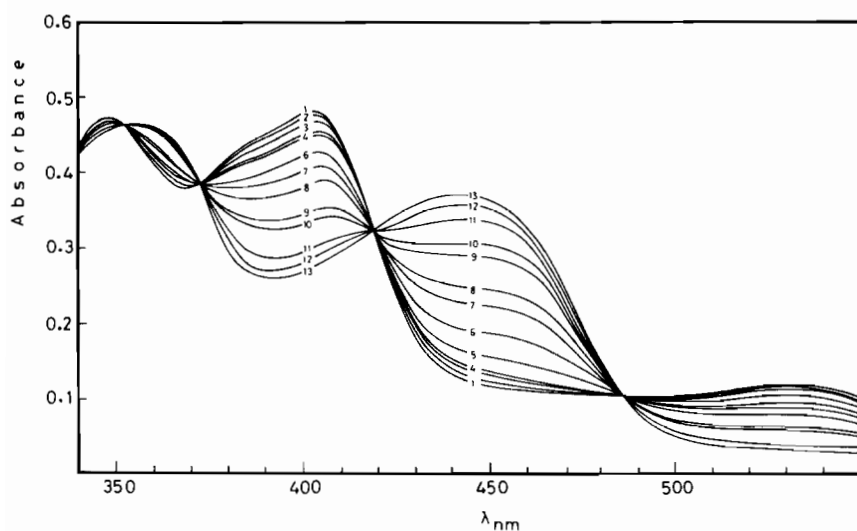


at a given concentration ( $C_{NiLCl} = 5 \times 10^{-5}$  mol  $dm^{-3}$ ) with increasing concentration of pyridine ( $C_{Py} = 0.025$ – $0.400$  mol  $dm^{-3}$ ) are shown in Fig. 1. Similar spectral variations were also observed for other systems. It is apparent that the successive absorption curves pass through three sharp fixed isosbestic points at 375, 420 and 487 nm, implying the existence of two light-absorbing species in equilibrium, namely the square planar chelate  $NiLX$  ( $X = Cl, Br, I$  and  $NCS$ ) and the formed adduct  $NiLXB_n$

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TABLE I. Stability Constants and Thermodynamic Parameters for Bis-adducts of NiLX (II) with Pyridine and 4-Methylpyridine in Benzene at 25 °C.

X	n	Log K	$-\Delta G^\circ$ kJ mol <sup>-1</sup>	$-\Delta H^\circ$ kJ mol <sup>-1</sup>	$-\Delta S^\circ$ J K <sup>-1</sup> mol <sup>-1</sup>
<i>Pyridine adducts</i>					
Cl	1.98	2.20 ± 0.02	12.6	69.7 ± 4.7	192 ± 16
Br	2.01	1.99 ± 0.01	11.4	64.5 ± 3.8	178 ± 14
I	2.00	1.59 ± 0.01	9.1	60.8 ± 3.8	174 ± 14
NCS	1.96	2.90 ± 0.02	16.6	42.3 ± 2.6	87 ± 10
<i>4-Methylpyridine adducts</i>					
Cl	2.00	2.85 ± 0.02	16.3	68.3 ± 5.0	183 ± 15
Br	1.95	2.56 ± 0.03	14.6	64.9 ± 5.0	172 ± 15
I	2.02	2.23 ± 0.01	12.7	63.3 ± 4.4	170 ± 14
NCS	2.02	3.38 ± 0.02	19.3	64.0 ± 4.6	150 ± 14

Fig. 1. Spectrophotometric titration of NiLCl ( $5 \times 10^{-5}$  mol dm<sup>-3</sup>) with pyridine in benzene at 30 °C.  $C_{Py} \times 10^2$  mol dm<sup>-3</sup>. 1) 0.00, 2) 2.50, 3) 5.00, 4) 7.50, 5) 10.00, 6) 15.00, 7) 20.00, 8) 25.00, 9) 35.00, 10) 40.00, 11) 60.00, 12) 80.00 and 13) 100.00.

(B = pyridine and 4-methylpyridine). This was confirmed by the analysis of the spectrophotometric data using the Coleman, Varga and Mastin method [11]. Such equilibria can be represented by eqn. 1, and the formation constant K is defined by eqn. 2:



$$K = [\text{NiLXB}_n] / [\text{NiLX}] [\text{B}]^n \quad (2)$$

In all systems studied, a large excess of the base B was used as compared to the initial concentration of NiLX ( $C_B/C_{\text{NiLX}}$  varies from 100 to 1200), thus the analytical concentration of the base  $C_B$  will be taken as the equilibrium concentration [8].

From the variation of absorbance measured at 460 nm with base concentration, the formation cons-

tant K of the formed adduct can be determined using the logarithmic eqn. 3:

$$\log (A_0 - A) / (A - A_\infty) = \log K + n \log C_B \quad (3)$$

where  $A_0$ , A,  $A_\infty$ , n and log K have their usual significance [12]. The values of both log K and n were obtained respectively from the intercept and gradient of the least squares line plots of  $\log (A_0 - A) / (A - A_\infty)$  versus  $\log C_B$ . Both enthalpy ( $-\Delta H^\circ$ ) and entropy ( $-\Delta S^\circ$ ) changes of the adduct formation reaction were calculated from the variation of log K with temperature (20–40 °C). The calculated values of log K together with the thermodynamic functions  $\Delta G^\circ$ ,  $\Delta H^\circ$  and  $\Delta S^\circ$  for all systems studied are collected in Table I.

The data given in Table I show that in all systems studied  $n = 2$ . This suggests that the reaction of

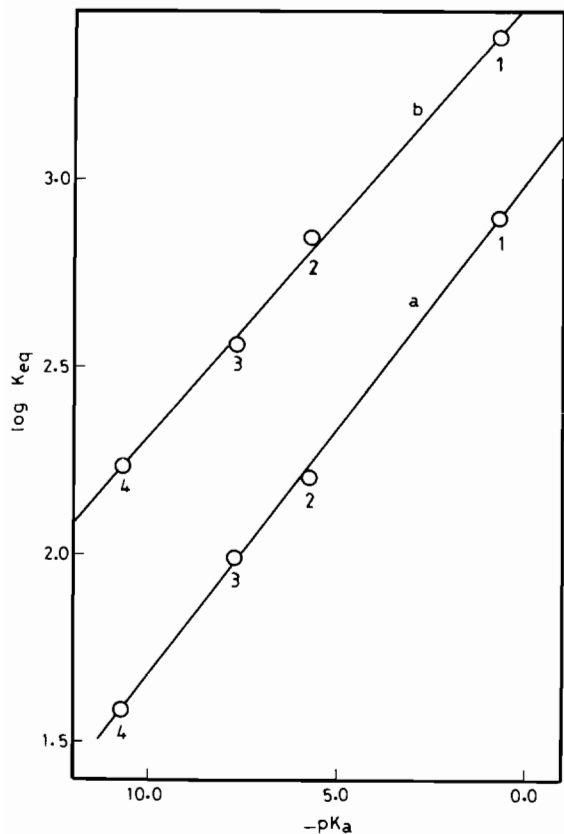
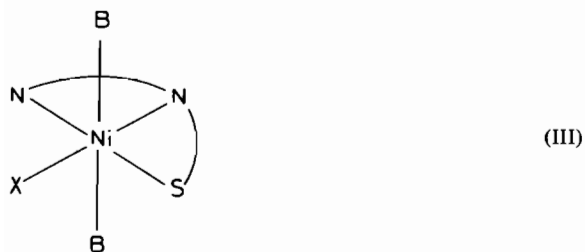


Fig. 2. Variation of  $\log K$  measured for a) bispyridine and b) 4-methylpyridine adducts of  $\text{NiLX}$ ; X, 1) NCS, 2) Cl, 3) Br and 4) I chelates as a function of  $\text{pK}_a$  (acidity constant of HX acids).

pyridine or 4-methylpyridine with  $\text{NiLX}$  chelates proceeds with the formation of octahedral bis-Lewis base adducts (III). It is also evident that the stability,



as measured by  $\log K$ , as well as the thermodynamics of bis-adduct formation are greatly influenced by the nature of the in-plane ligand X in the square planar nickel(II) chelates.

A linear free energy relationship (LFER) between  $\log K$  measured for pyridine and 4-methylpyridine adducts and the estimated  $\text{pK}_a$  values [13] of the corresponding hydrogen acids of the in-plane ligands is observed. The best fitting lines for pyridine and 4-methylpyridine adducts, Fig. 2, can be expressed respectively by

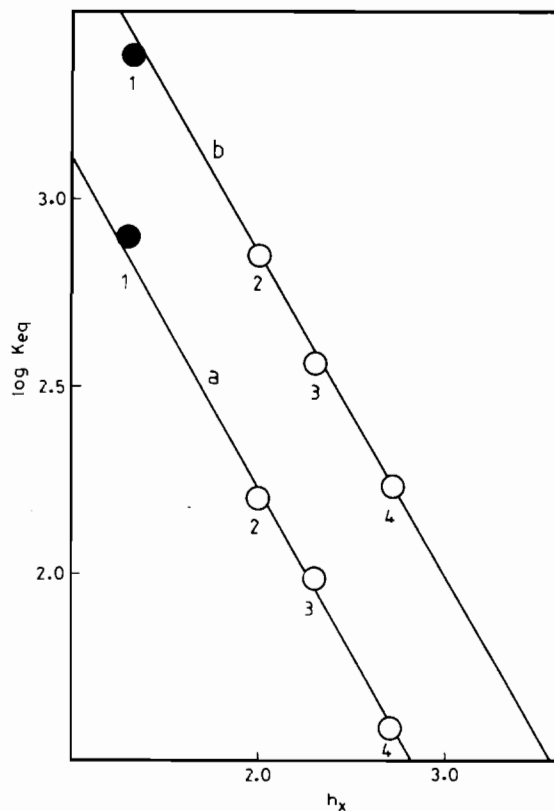


Fig. 3. Plots of  $\log K$  for a) bispyridine and b) 4-methylpyridine adducts versus the nephelauxetic parameter of the anionic ligands X; 1) NCS (estimated), 2) Cl, 3) Br and 4) I.

$$(\log K)_{\text{Py}} = 2.98 + 0.13 \text{ pK}_a$$

$$(\log K)_{4\text{MePy}} = 3.47 + 0.12 \text{ pK}_a$$

As expected, these LFER's reveal that the intrinsic acidity of  $\text{NiLX}$  chelates increases as the  $\text{pK}_a$  of the in-plane ligand X increases.

As the anionic in-plane ligands (X) do not impose any appreciable steric effects on the stability of the formed bis-adducts, the observed stability sequence,  $\text{NCS} > \text{Cl} > \text{Br} > \text{I}$ , can be related to the electronic effects of X that can be transmitted to the nickel(II)-Lewis base bond by means of metal orbitals. Both the electronegativity ( $\chi$ ) and polarizability ( $\alpha$ ) of the in-plane ligand X can be used as a quantitative measure for the electronic effects, mainly inductive, transmitted to the nickel(II) ion. Apart from the thiocyanate group for which neither  $\chi$  nor  $\alpha$  values have been estimated, the stability of the formed bis-adducts increases linearly as the electronegativity of X increases due to increase in the formal positive charge on Ni(II).

Increasing the polarizability of X results in a linear decrease in the stability. Jørgensen [14, 15] has summarized arguments which indicate that both electronegativity and polarizability values of a ligand

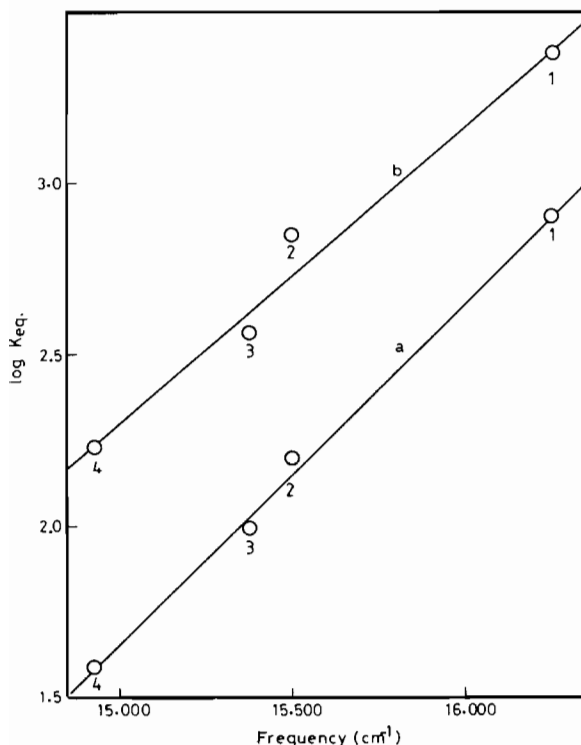


Fig. 4. Plots of  $\log K$  for a) bispyridine and b) 4-methylpyridine adducts versus the frequency of the lowest energy charge transfer band of the square planar NiLX chelates; X, 1) NCS, 2) Cl, 3) Br and 4) I.

are related to its nephelauxetic effect and can be quantitized by the ligand nephelauxetic parameter  $h_x$ . As depicted in Fig. 3, both  $(\log K)_{Py}$  and  $(\log K)_{4MePy}$  are linearly correlated to  $h_x$  of the ligands Cl, Br and I. Least squares treatment of the data available gives

$$(\log K)_{Py} = 3.98 - 0.88 h_x$$

$$(\log K)_{4MePy} = 4.61 - 0.88 h_x$$

from which  $h_x$  for NCS group can be estimated as  $1.32 \pm 0.12$ .

Furthermore, it was reported [8] that the position of the charge transfer bands in the mull and solution electronic spectra in benzene of NiLX chelates depends on the nature of the in-plane ligand X. A shift to lower frequencies occurs in the order  $NCS > Cl > Br > I$  in agreement with the field strength of these ligands in the spectrochemical series, as well as the stability order of the bis-base adducts. A straight line relationship between  $\log K$  and the frequency of the lowest energy transition of NiLX chelates in benzene, Fig. 4, is observed. Jørgenson [14, 15] has also attempted to quantify the spectrochemical series relative to water as standard ligand with a field factor  $f_x = 1.0$ . A plot of  $\log K$

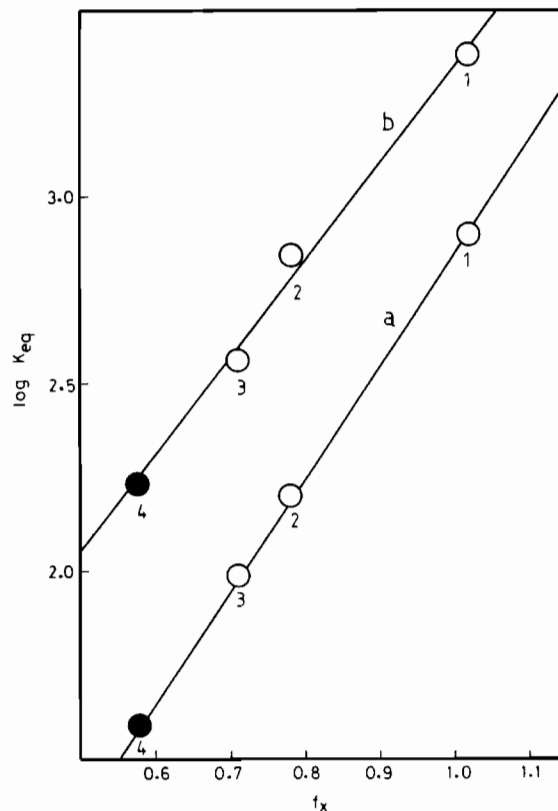


Fig. 5. Plots of  $\log K$  for a) bispyridine and b) 4-methylpyridine adducts versus the field factor of the anionic ligands; X, 1) NCS, 2) Cl, 3) Br and 4) I (estimated).

for both pyridine and 4-methylpyridine bis-adducts against  $f_x$  of Cl, Br and NCS ligands gives a straight line, Fig. 5, and  $\log K$  can be correlated to  $f_x$  by

$$(\log K)_{Py} = -0.156 + 3.00 f_x$$

$$(\log K)_{4MePy} = 0.760 + 2.58 f_x$$

It is worthwhile noting that there is no reported value of  $f_x$  for the iodide ligand. However, the linear relationship between  $\log K$ ,  $h_x$  and  $pK_a$  as well as  $\nu$  suggests a similar linear relationship between  $\log K$  and  $f_x$  for Cl, Br and I. Thus the  $f_x$  value for the iodide ligand can be adequately estimated to have the value  $0.58 \pm 0.01$ . These results reveal that the stability of the formed bis-adducts increases as the field strength of the in-plane ligand X increases. Also, the higher stability of the thiocyanate adducts relative to the corresponding chloro adducts indicates that the thiocyanate ligand is coordinated to the Ni(II) *via* nitrogen (M-NCS) rather than sulphur (M-SCN).

Inspection of the data given in Table I reveals that the enthalpy change ( $-\Delta H^\circ$ ) for pyridine adduct formation reactions decreases in the order  $Cl > Br >$

I > SCN, while for 4-methylpyridine adducts the values of  $-\Delta H^\circ$ , within experimental error, ( $\pm 4$  KJ mol $^{-1}$ ) remain almost constant and do not show much dependence on the nature of X. If the observed variation of  $-\Delta H^\circ$ , in the case of pyridine adducts, as a function of X is mainly due to electronic effects transmitted to nickel(II) via  $\sigma$  bond (purely inductive),  $-\Delta H^\circ$  should fall in the sequence NCS > Cl > Br > I while the entropy term remains relatively unaffected. However, the data cited in Table I indicate that the entropy change ( $-\Delta S^\circ$ ) for adduct formation reactions shows dependence on X and decreases in the order Cl > Br > I > NCS. No doubt solvation accounts in part for the observed variation of  $-\Delta S^\circ$ , but this is thought of as being relatively unimportant since no charged species are presented and benzene is a fairly non-coordinating solvent.

The dependence of  $-\Delta S^\circ$  on the nature of X can be attributed to  $\pi$ -bond formation between non-bonding nickel(II) d-electrons and antibonding pyridine  $\pi$ -orbitals ( $d\pi-p\pi$ ) in the formed bis-adducts. The formation of such  $\pi$ -bonding will restrict rotation around the Ni-N bond and results in a remarkable increase in  $-\Delta S^\circ$ . The extent of axial Ni-N bonding is greatly influenced by the  $\pi$ -acceptor character of the in-plane ligand X in such a way that increasing the  $\pi$ -acceptor power of X in the order Cl < Br < I < NCS results in a decrease in axial Ni-X bond order. This of course, will reflect on the values of  $-\Delta S^\circ$  and explains the gradual decreasing order Cl > Br > I > NCS. Accordingly, the extra stability of both pyridine and 4-methylpyridine bis-adducts with NiLNCS as compared to NiLI is mainly due to entropy effects.

The formation of strong  $\pi$ -bonding between nickel(II) and thiocyanate ligand results in the stabilization of the parent square chelate (II, R = H, X = NCS), while the formed pyridine bis-adduct (III, R = H, X = NCS and B = Py) is destabilized. This is in agreement with the observed low value of  $-\Delta H^\circ$  for thiocyanate pyridine bis-adducts relative to other halogen analogues. Also, the strong dependence of both  $-\Delta H^\circ$  and  $-\Delta S^\circ$  on X in the case of pyridine as compared to 4-methylpyridine bis-adducts can be related to the lower  $\pi$ -acceptor ability of 4-methylpyridine.

The competitive effect between the in-plane Ni-X and the axial Ni-N  $\pi$ -bonding was previously proposed by King, Koros and Nelson [16] to explain the variation of the thermodynamic parameters for the addition of two pyridine molecules to tetrahedral CoPy $_2$ X $_2$  with the anionic ligands X.

## Experimental

### Materials

Chloro-, bromo-, iodo- and thiocyanato(S-methyl-N-(2-pyridyl)methylenehydrazinecarbodithioate)-nickel(II) chelates were prepared as previously described [8] and crystallized from chloroform. Pyridine and 4-methylpyridine were of AR grade and were distilled over KOH before use. The solvent was analytical grade benzene which was dried and distilled over sodium.

### Physical Measurements

The electronic spectra were recorded on a Pye Unicam SP 1801 spectrophotometer equipped with a thermostatted cell holder. The actual temperature of the solution was measured by a calibrated thermocouple.

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