In our opinion, these points are not convincing support for the contention[4-6,8] that photoredox behavior can be excluded. First, and perhaps most importantly, the belief of Younes, Pilz, and Weser[8] that the Cu 2p binding energies they observed for Cu(en)$_2$(SCN)$_2$ are typical of Cu(II) is incorrect. While satellite structure due to Cu(II) is apparently present,[8] the energies of the primary Cu 2p photolines which they report in their paper (Cu 2p$_{1/2}$ at 952.0 eV and Cu 2p$_{3/2}$ at 932.0 eV)[8] are in fact characteristic of Cu(I). The binding energies of unreduced Cu(en)$_2$(SCN)$_2$ had been reported earlier by Best and Walton;[16] the resulting Cu 2p spectrum is shown in Figure 1a. The Cu 2p$_{1/2}$ and Cu 2p$_{3/2}$ primary photolines are located at 955.3 and 935.3 eV, and their associated satellite structure is at ~+8 eV relative to the 2p$_{1/2,3/2}$ peaks. A small amount of Cu(I) is clearly present (peaks at ~952.5 and ~932.5 eV), and this must arise from a trace of photoreduction. In the case of the study by Younes, Pilz, and Weser,[8] it is apparent that almost complete reduction to Cu(I) had occurred during the XPS measurements.

The fact that some residual Cu(II) satellite structure can still be observed in the Cu 2p XPS even when most of the Cu(II) originally present has been photoreduced to Cu(I) is a factor which was not apparently taken into account in the interpretations by Younes, Pilz, and Weser.[8] This possiblity is illustrated in Figure 1b in the case of the Cu 2p spectrum of [Cu(py)$_2$(SCN)$_2$]$_n$. This complex is subject to a rapid X-ray-induced reduction within the spectrometer.[16] While the Cu 2p$_{1/2,3/2}$ peaks of Cu(I) (at 952.5 and 932.5 eV) dominate the spectrum, a small amount of Cu(II) is still present. The latter is characterized by weak Cu 2p$_{1/2}$ and Cu 2p$_{3/2}$ primary photolines (see Figure 1b) and clearly defined (but weak) Cu 2p$_{3/2}$ satellite structure at ~944 eV. Since reduction of Cu(en)$_2$(SCN)$_2$ occurs under the experimental conditions used by Younes, Pilz, and Weser,[8] it seems likely that this has also occurred with other copper complexes they studied.[4-6,8]

We turn now to the second piece of evidence which was cited (vide supra) in support of the proposal that X-ray-induced reduction of copper had not occurred.[8] Since treatment of the copper–penicillamine complex with H$_2$O$_2$ would be expected to destroy the Cu–thiol bonding, and this is indeed what happens, there is no reason to expect that the resulting material will be as photoredox active as the untreated complex. Accordingly, this experimental observation[8] does not bear on the question of whether the untreated samples of the copper–penicillamine complex will be X-ray sensitive or not.

Finally, the third observation can similarly be explained in terms of photoreduction. Thus an alternative interpretation to the one advanced by Younes, Pilz, and Weser[8] is that the excess Cu(II) which is present in the product obtained by mixing Cu(II) with penicillamine in a 3:1 mole ratio[8] is not reduced, while that smaller portion of the Cu(II) which is complexed to the thiol group of penicillamine is converted to Cu(I) upon irradiation.

An additional observation which supports photoreduction of the copper as the most likely explanation of the XPS results is that the S 2p binding energies (163.0–163.9 eV[4-8]) can then be assigned to disulfide sulfur (RSSR) rather than unstable ·SR radical species.[17,18] In this event, the photoredox behavior of these copper(II)–thiol complexes can be represented formally as the internal redox reaction $2\mathrm{Cu^{II}(SR)} \rightarrow \mathrm{Cu^{I}_{2}(RSSR)}$.[19]

Registry No. Cu(en)$_2$(SCN)$_2$, 15489-50-6; [Cu(py)$_2$(SCN)$_2$]$_n$, 26445-55-6.

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[15] The presence of Cu(I) can be seen from the asymmetric shape of the Cu 2p$_{3/2}$ photoline shown in the figure presented in ref 5.

[16] Best, S. A.; Walton, R. A. *Isr. J. Chem.* **1976**, *15*, 160.

[17] The range of S 2p binding energies of these copper–thiol complexes is typical of disulfide sulfur rather than thiol sulfur,[18] further supporting the notion that reduction of the copper and concomitant oxidation of the sulfur-containing moiety has occurred.

[18] Walton, R. A., accepted for publication in *Coord. Chem. Rev.*

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Geometry of Nickel(II) Complexes Containing a 12-Membered Ring in Solution

Sir:

Martin, DeHayes, Zompa, and Busch[1] have illustrated by means of calculations a relationship between the ring size of a macrocyclic ligand and the amount of strain such ligands would impose on a metal complex on the assumption that the cyclic ligand is bonded in a coplanar manner with the metal ion. If the ring size of the ligand is too small to coordinate with a given metal ion in a coplanar manner without imposing large strain energies, distortion from square-planar coordination will occur. The most common type of distortion involves the macrocyclic ligand folding so as to form either a cis-octahedral[1-5] or a trigonal-bipyramidal structure.[3,5] A square pyramid with the metal ion extruded from the basal plane is another type of distortion from a square-planar geometry which has been observed.[6,7] Calculations of strain energies by Martin et al. suggested that a 12-membered ring, [12]aneN$_4$, would have difficulty in forming square-planar or trans-octahedral complexes with either cobalt(III) or nickel(II).[1] Although they did not take into account that the nickel–nitrogen bond is smaller in a low-spin complex than in a high-spin complex and as a result [12]aneN$_4$ might be able to assume planar chelation with a metal ion, no such complexes have yet been isolated.

Fabbrizzi[8] recently reported that in an aqueous solution of [Ni([12]aneN$_4$)]$^{2+}$ at 88 °C (or [Ni([12]aneN$_4$)]$^{2+}$ dissolved in 6 M NaClO$_4$) there coexisted in equilibrium a square-planar nickel(II) species and a six-coordinate nickel(II) species. An aqueous solution of [Ni([12]aneN$_4$)]$^{2+}$ at room temperature is purple, a color typically indicative of six-coordinate nickel(II); however, at higher temperatures (or in 6 M NaClO$_4$) the solution was yellow, a color commonly observed for square-planar NiN$_4$ systems. The lower temperature spectra were typical of six-coordinate nickel(II) complexes, but at higher temperatures the spectra appeared to contain bands associated with both a six-coordinate nickel(II) complex and a square-planar nickel(II) complex.[8]

We have observed that the green [Ni(tb[12]aneN$_4$)Cl]Cl (tb[12]aneN$_4$ = 1,4,7,10-tetrabenzyl-1,4,7,10-tetraazacyclododecane) is a five-coordinate complex (believed to be a

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trigonal bipyramid) both in nonaqueous solution and in the solid state.[3] The magnetic moment of this complex is 3.7 μ_B in the solid state. However, the blue solid $[Ni(tb[12]aneN_4)(NO_3)]NO_3$ has a coordination number of 6 and has a magnetic moment of 3.2 μ_B.[3] When dissolved in water at room temperature, both complexes resulted in yellow solutions having nearly identical electronic spectra. These spectra were interpreted on the assumption that there existed a trigonal-bipyramidal structure around the nickel(II).[3] We believed that the yellow nickel(II) species in water was the five-coordinate $[Ni(tb[12]aneN_4)(H_2O)]^{2+}$ cation.[3] However, on the basis of Fabbrizzi's research, it is possible that the yellow species we observed in aqueous solution is the square-planar $[Ni(tb[12]aneN_4)]^{2+}$ and not the five-coordinate $[Ni(tb[12]aneN_4)(H_2O)]^{2+}$.

The magnetic moment of $[Ni([12]aneN_4)(NO_3)]NO_3$ in the solid state is 3.15 μ_B,[2] and in aqueous solution it is 3.25 μ_B. The magnetic moment of $Ni([12]aneN_4)Cl_2$ at room temperature (300 K) in the solid state is 3.1 μ_B, and in aqueous solution it is 3.1 μ_B. Such data suggest that the nickel(II) ions in these complexes at room temperature are six-coordinate both in water and in the solid state. However, if the six-coordinate species were in equilibrium with a diamagnetic square-planar compound, the magnetic moment should be less than 3 μ_B. For example, the magnetic moment of $[Ni(1,4,8,11\text{-}[14]aneN_4)]Cl_2$ (cyclam) in water is 1.73 μ_B and that of $[Ni(1,4,7,11\text{-}[14]aneN_4)]Cl_2$ ($1,4,7,11\text{-}[14]aneN_4$ = 1,4,7,11-tetraazacyclotetradecane) in water is 2.41 μ_B. Both magnetic moments indicate that there is a diamagnetic square-planar complex in equilibrium with the six-coordinate species. In a 6 N $NaClO_4$ solution, both $[Ni(1,4,8,11\text{-}[14]aneN_4)]Cl_2$ and $[Ni(1,4,7,11\text{-}[14]aneN_4)]Cl_2$ are diamagnetic, indicating that the equilibrium has been shifted to favor the square-planar compound. Such magnetic data are consistent with the observed spectral data.

The effective magnetic moments of $[Ni([12]aneN_4)(NO_3)]NO_3$ and for $[Ni([12]aneN_4)Cl_2]$ at room temperature in 6 N $NaClO_4$ were determined to be 2.97 and 3.06 μ_B, respectively. However, at 330 K and 6 N $NaClO_4$ the effective magnetic moment for $[Ni([12]aneN_4)Cl_2]$ was reduced to 2.64 μ_B. In contrast, the magnetic moment we observed in the solid state for the high-spin trigonal-bipyramidal $[Ni(tb[12]aneN_4)Cl]Cl$ was 3.70 μ_B. The above results are consistent with Fabbrizzi's interpretation, i.e., that the yellow species observed in a $[Ni([12]aneN_4)]X_2\text{–}H_2O\text{–}NaClO_4$ solution is a low-spin square-planar complex.

A 6 N $NaClO_4$–dioxane–H_2O mixture containing $[Ni([12]aneN_4)(NO_3)]NO_3$ had a slightly higher magnetic moment, 3.14 μ_B, than the same mixture without dioxane, 2.97 μ_B. (A limiting magnetic moment could not be obtained at higher dioxane concentrations because of precipitation of solute and $NaClO_4$.) Increasing the quantity of standard, *tert*-butyl alcohol, had a similar effect. (A minimum quantity of standard was employed in order to obtain easily measured changes in the chemical shifts of the methyl group.)[9]

A possible explanation for the shifts in the paramagnetic–diamagnetic equilibria can be made if these metal complexes are considered to be slightly hydrophobic species. Hydrophobic materials dissolved in water will result in the water molecules forming stronger and more hydrogen bonds to each other. Therefore, $Ni^{II}([12]aneN_4)$ should have some resistance to forming the diaquo six-coordinate species $[Ni([12]aneN_4)(H_2O)_2]^{2+}$. However, dioxane and alcohols are hydrophilic substances and as a result will decrease the hydrogen bonding in the bulk solvent, H_2O, and thereby increase the nucleophilic activity of the water. The more nucleophilic water should shift the equilibrium to the diaquo species, $[Ni([12]aneN_4)(H_2O)_2]^{2+}$. The observed magnetic moments in solution are consistent with these results. The $tb[12]aneN_4$ ligand should be considerably more hydrophobic than the $[12]aneN_4$. The $Ni(tb[12]aneN_4)X_2$ complexes are yellow (suggestive of more diamagnetic species in solution) in H_2O while the $[Ni([12]aneN_4)]X_2$ complexes are purple (more paramagnetic) in H_2O. Unfortunately, attempts to obtain magnetic moments of $[Ni(tb[12]aneN_4)](NO_3)_2$ or $[Ni(tb[12]aneN_4)]Cl_2$ in water were unsuccessful because of the limited solubility of these compounds in water. However, in an 80% acetone–water mixture, the magnetic moment of $[Ni(tb[12]aneN_4)](NO_3)_2$ was almost the same as that of the solid, 3.2 μ_B, suggesting the nickel ion is in a six-coordinated environment. Both the electronic spectrum and the blue color of the solution are also consistent with a six-coordinate nickel(II) species.[3] Acetone should decrease the amount of hydrogen bonding in water, and therefore it should function to make water less polymeric. The effect of acetone and the dioxane is to promote the six-coordinate nickel(II) species.

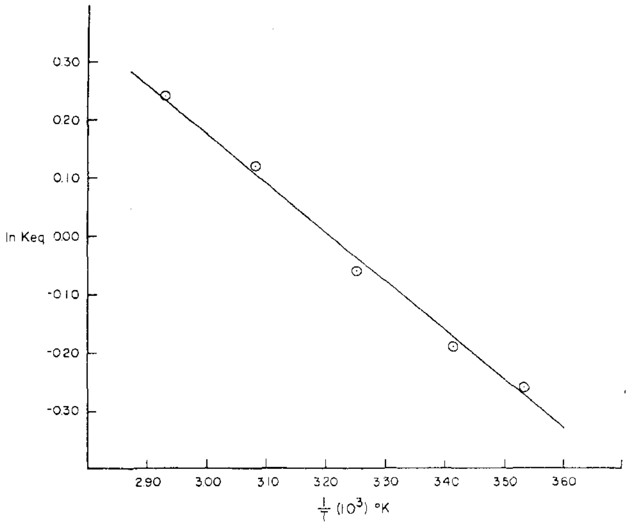

Figure 1. Plot of ln K_{eq} vs. $1/T$ for $[Ni([12]aneN_4)(NO_3)]NO_3$ in water.

An estimation of the equilibrium constant between the six-coordinate species and the diamagnetic species can be made in 6 N $NaClO_4$. When the temperature of an aqueous solution of $[Ni([12]aneN_4)]^{2+}$ is increased, the band at 23 000 cm^{-1} increases in intensity (believed to be due to four- or five-coordinate species) while the bands at 18 182 and 11 360 cm^{-1} decrease in intensity (these bands are believed to be due to the six-coordinate species). The K_{eq} for this equilibrium can be measured at 11 360 cm^{-1} by using the measured optical density at this wavelength. At 10 °C in pure H_2O it is assumed that only the six-coordinate species exists. (This assumption is justified on the basis of our magnetic data.) It is also assumed that the extinction coefficient of the reduced coordinate species at 11 360 cm^{-1} is negligible. The method of calculating K_{eq} from the spectral data at 11 360 cm^{-1} is the same as that employed by Fabbrizzi.[10] A plot of ln K_{eq} against $1/T$ yielded a ΔH of 1.7 kcal/mol and a ΔS of 5.5 cal/mol (Figure 1).

The relatively low equilibrium constant for the above reaction as compared to similar reactions is due to the entropy term. The ΔS values for six-coordinate nickel(II) complexes going to a square-planar complex, $NiL(H_2O)_2^{2+} \rightleftharpoons NiL^{2+} + 2H_2O$ where L is $[14]aneN_4$ or 3,2,3-tet, are 20.4 and 15

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(9) We employed 2% *tert*-butyl alcohol as our standard in D_2O. We assume that if no *tert*-butyl alcohol was employed, the solutions would be slightly more diamagnetic.

(10) Fabbrizzi, L. *Inorg. Chim. Acta* **1977**, *24*, L21.

cal/(mol K), respectively, in only 0.1 N $NaClO_4$[10] as compared to the 6 N $NaClO_4$ employed in our experiment. (As the concentration of salt increases, so does K_{eq} and ΔS.) A plausible explanation for the relatively low entropy term for the reaction involving the Ni[12]aneN_4 complex is that a five-coordinate complex is formed rather than the four-coordinate species. As a consequence of forming a five-coordinate species, fewer water molecules are lost. It is also possible that the small ΔS value is somehow related to the ligand's rearrangement from cis octahedral to square planar. A lower endothermicity of the blue to yellow conversion for [Ni([12]aneN_4)]X_2 complexes compared with the nickel(II) species containing 14-membered tetraaza macrocyclic ligand in 0.1 N $NaClO_4$ can be rationalized if the former complexes are converted from a cis-octahedral nickel(II) compound to a five-coordinate compound while the latter complexes involve a trans-octahedral to square-planar conversion. The conversion of a six-coordinate metal complex to a square-planar complex involves the contraction of all the in-plane metal to donor bonds. However, a conversion from a cis-octahedral species to either a trigonal bipyramid or a square pyramid with the metal extruded out of the plane of the donor atoms should involve only minor bond and angle alterations.

It has been shown that the stronger the ligand-field strength of a given ligand, the more it will stabilize the square-planar nickel(II) species over the octahedral species.[11] The smaller the size of the N_4 macrocycle coordinating to a metal ion in a planar fashion the higher its ligand-field strength.[1,12] Consequently, a 12-membered N_4 ring should exert an abnormally high ligand-field effect on the nickel(II), thereby stabilizing the square-planar geometry. This high ligand-field strength would be due to a mechanical constrictive effect which would result in shortening the nickel–nitrogen bond distance.[1] Assuming this mechanical constrictive effect to be the only operational factor determining the magnitude of K_{eq} and that the [12]aneN_4 could and did bond in a coplanar manner with the nickel(II), we would therefore expect higher K_{eq} values for the Ni([12]aneN_4) systems compared to those of nickel(II) complexes containing larger macrocyclic ligands. Since the K_{eq} is smaller for the [12]aneN_4 compared to larger size macrocycles, we believe that the [12]aneN_4 does not chelate in a planar fashion with the nickel(II) ion. It is also possible that the relatively low K_{eq} value found for the $[Ni([12]aneN_4)]^{2+}$ system may be due to a large increase in the strain energy of square-planar $[Ni([12]aneN_4)]^{2+}$ compared to that in nickel(II) complexes with larger macrocyclic ligands. However, [13]aneN_4 should impose a larger mechanical constrictive effect (thereby stabilizing the square-planar geometry) and also more strain energy (thereby stabilizing the six-coordinate species) than the [14]aneN_4 ligand.[1] The fact that the square-planar nickel(II) complex containing [13]aneN_4 was isolated from water and not the trans six-coordinate complex[13] suggests that the mechanical constrictive effect is a more important parameter in determining the position for the above paramagnetic–diamagnetic equilibrium than the strain energy. Also the more favorable ΔH values (less endothermic) for Ni([12]aneN_4)X_2 compounds compared to those of similar reactions in which larger macrocycles were employed suggest that it is not likely that a highly strained square-planar $[Ni([12]aneN_4)]^{2+}$ complex is formed. It is more likely that the complex is five-coordinate.

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Mutagenicity and Modes of Metal Binding to Nucleic Acids

Sir:

Recent work in this laboratory has shown that adenine and cytosine are capable of forming stable bonds to transition metals through their exocyclic nitrogens.[1,2] Unequivocal verification of this has now been made by Graves and Hodgson[3] utilizing crystals of $[(1\text{-MeCyt}^-)(NH_3)_5Ru](PF_6)_2$ prepared here. Metal coordination in this fashion makes available stable modes of metal–nucleic acid interaction, including cross-linking possibilities which have not hitherto been considered in the design of transition-metal anticancer drugs.[4] Moreover, it suggests alternative mechanisms to account for the mutagenicity of ammineruthenium(III) complexes[2,5] and perhaps that of other metal ions as well.[6,7]

Attack by ruthenium on adenosine (Ado) or cytidine (Cyd) is greatly facilitated by reduction of the metal to the more labile dipositive oxidation state.[2] Initial binding on Ado and possibly Cyd appears to occur on the pyrimidine-ring nitrogen adjacent to the exocyclic amine,[1] but some interaction may also occur at the N(7) site of Ado. Subsequent oxidation of the metal to the tripositive state probably facilitates deprotonation of the nearby exocyclic amine and so converts this nitrogen from a poor to an excellent coordination site.[1] Linkage isomerization can then take place from the ring to the exocyclic nitrogen. Abundant evidence exists for the relatively rapid linkage isomerization of $(NH_3)_5Ru^{II}$ and -Ru^{III} complexes upon changing either the oxidation state of the metal or the protonation state of the ligand.[2,8] Furthermore, it should be noted that this mechanism is applicable to other metal complexes initially binding at a ring nitrogen proximal to an exocyclic amine, providing these can also significantly increase the acidity of this group and will firmly coordinate the resulting amide.

Contrary to the interpretation of Graves and Hodgson,[3] it is likely that the thermodynamic stability of complexes involving Ru(III) coordinated to the deprotonated exocyclic nitrogen of nucleosides is in good part due to π interactions. Evidence of the π-acceptor ability of Ru(III) was first indicated by Brown, Sutton, and Taube,[9] and thermodynamic

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