(17) F. J. Bullock and O. Jardetzky, *J. Org. Chem.*, **30**, 2056 (1965). Note that these authors use a different numbering system.
(18) J. Salach, W. H. Walker, T. P. Singer, A. Ehrenberg, P. Hemmerich, S. Ghisla, and U. Hartmann, *Eur. J. Biochem.*, **26**, 267 (1972).
(19) G. Schöllnhammer and P. Hemmerich, *Eur. J. Biochem.*, **44**, 561 (1974).
(20) R. H. Sarma, P. Dannies, and N. O. Kaplan, *Biochemistry*, 7, 4359 (1968).
(21) B. Pullman and A. Pullman, *Proc. Natl. Acad. Sci. U.S.A.*, **45**, 136 (1959).
(22) G. Kotowycz, N. Teng, M. P. Klein, and M. Calvin, *J. Biol. Chem.*, **244**, 5656 (1969).
(23) C. Giessner-Prettre and B. Pullman, *J. Theor. Biol.*, **27**, 87 (1970).
(24) S. M. Wang and N. C. Li, *J. Am. Chem. Soc.*, **88**, 4592 (1966).
(25) M. T. Beck, "Chemistry of Complex Equilibria", Van Nostrand-Reinhold, London, 1970, p 90.
(26) C. J. Ballhausen, "Ligand Field Theory", McGraw-Hill, New York, N.Y., 1932.
(27) I. Solomon, *Phys. Rev.*, **99**, 559 (1955).
(28) H. Irving and R. J. P. Williams, *J. Chem. Soc.*, 3192 (1953).
(29) G. N. La Mar and G. R. von Hecke, *Inorg. Chem.*, **9**, 1546 (1970).
(30) R. Norrestam and B. Stensland, *Acta Crystallogr., Sect. B*, **28**, 440 (1972).

Contribution from the Fachbereich Biologie Universität Konstanz, Konstanz, West Germany,
and the Fondation Curie-Institut du Radium, Section de Biologie, Orsay, France

Flavoquinone–Metal Complexes. II. Paramagnetic Interactions

J. LAUTERWEIN, P. HEMMERICH, and J.-M. LHOSTE*

Received November 19, 1974 AIC407945

Proton magnetic resonance studies were carried out on flavoquinone complexes using divalent paramagnetic ions of the 3d series: Mn^{II}, Fe^{II}, Co^{II}, Ni^{II}, Cu^{II}. Magnetic susceptibility and electron spin resonance measurements provided complementary information about the magnetic state of these complexes. The paramagnetic contribution to the line width of the ligand resonances was analyzed as a function of metal to flavine concentration and of temperature in order to estimate the value of the correlation times involved in the relaxation processes. The isotropic shifts were analyzed in terms of contact and pseudocontact interactions using the relaxation data and structural information derived earlier, together with the g-tensor anisotropy measured by electron spin resonance. The relative importance of the two kinds of interactions compares favorably with that derived from the usual factorization procedure. Pseudocontact shifts appear noticeable in Co^{II} and Cu^{II} complexes and negligible in Ni^{II} and Fe^{II} complexes. The contact shifts exhibit a distribution pattern for the various ligand resonances very similar among the stable bidendate chelates, which could be attributed to a π-electron spin negatively polarized in the ligand orbitals. The spin-transfer mechanism appears to result from indirect σ–π spin polarization at the coordination site combined with a delocalization of negatively polarized spin in the ligand π-bonding orbitals. This mechanism for contact interaction indicates that the stability of the flavoquinone–metal complexes in aprotic solvents arises from σ-type bonding, with little, if any, π bonding.

Introduction

The stability, stoichiometry, and geometry of flavoquinone–metal chelates $M(RFl_{ox})_n{}^{m+}$ [1] have been outlined in the preceding paper.[2] In this paper we present the results of a proton magnetic resonance (PMR) study of such chelates containing paramagnetic ions of the first transition series: Mn^{II}, Fe^{II}, Co^{II}, Ni^{II}, Cu^{II}. The isotropic shifts and line broadening observed in the PMR spectrum of RFl_{ox} in solution upon addition of paramagnetic ions arise from contact Fermi and from pseudocontact through-space interaction of the electron and nuclear spin.[3] The analysis of the contact interactions can provide a direct insight into the nature of the organometallic bond if a quantitative estimation of the pseudocontact interactions can be carried out.[4] Such an estimation is facilitated for the flavoquinone chelates since their geometry has been derived from analysis of the diamagnetic interactions[2] and since the anisotropy of the magnetic susceptibility can be measured by electron spin resonance (ESR) spectroscopy. PMR of paramagnetic complexes in solution further depends upon the dynamic conditions of relaxation which should first be investigated by line width analysis.

Table I. Magnetic Data of Flavoquinone–Metal Complexes

Compd	S^a	$\mu_{eff}{}^b$	$10^6\chi_M{}^c$	$\mu_{eff}{}^d$
$Fe(TARF)_3(ClO_4)_2$	2	4.90	10,600	5.17
$Fe(H_2O)_6(ClO_4)_2$			10,980	5.25
$Co(TARF)_3(ClO_4)_2$	$^3/_2$	3.87	8,250	4.57
$Co(H_2O)_6(ClO_4)_2$			9,850	5.00
$Ni(TARF)_3(ClO_4)_2$	1	2.83	3,800	3.16
$Ni(H_2O)_6(ClO_4)_2$			4,340	3.30

[a] Spin quantum number of the ground state. [b] Effective magnetic moments (BM) as calculated from $2[S(S+1)]^{1/2}$. [c] Molar susceptibilities (cgs units) as determined by PMR at 38° in acetone-d_6. [d] Effective magnetic moments (BM) calculated from the measured χ_M values assuming that the Curie law is obeyed.

Experimental Section

The PMR spectra were recorded at 60 MHz using a Varian A-60A spectrometer equipped with the variable-temperature accessory V-6040. The faster nuclear relaxation in the paramagnetic complexes permitted use of intense radiofrequency fields without saturation effects in conditions of slow passage. All spectra were referenced to internal TMS. Magnetic susceptibility measurements were carried out by PMR methods in axial double-walled tubes following the method reported by Evans.[5] The applicability of the method was checked by measuring the susceptibility of the hexaaquo complexes of the corresponding metal ions. A Varian Model V-4500 X-band spectrometer operating at temperatures down to 4°K was used for the ESR measurements.

The solvents and the solutes used throughout this investigation as well as the sampling procedures have been described previously.[2]

3-Benzyllumiflavine, 3-benzyl-8-norlumiflavine, and 3-benzyl-7,8-norlumiflavine were synthesized according to known procedures.[6]

A crystalline Cu^{II} complex with N^3-ethyltetraacetylriboflavine was obtained in the same manner as described earlier for the Co^{II}, Ni^{II}, and Zn^{II} complexes.[2]

Anal. Calcd for $(C_{27}H_{32}N_4O_{10}ClO_4H_2O)_2Cu$: C, 45.0; H, 4.8; N, 7.8. Found: C, 45.3; H, 4.8; N, 7.9.

Results and Discussion

Magnetic Susceptibility and Electron Spin Resonance. The molar magnetic susceptibilities of dilute solutions of tetraacetylriboflavine (TARF, I) in acetone-d_6, measured as a function of the metal to flavine ratio, are reported in Figure 1 for the Fe^{II}, Co^{II}, and Ni^{II} complexes. The susceptibility

---

* To whom correspondence should be addressed at the Fondation Curie-Institut du Radium.

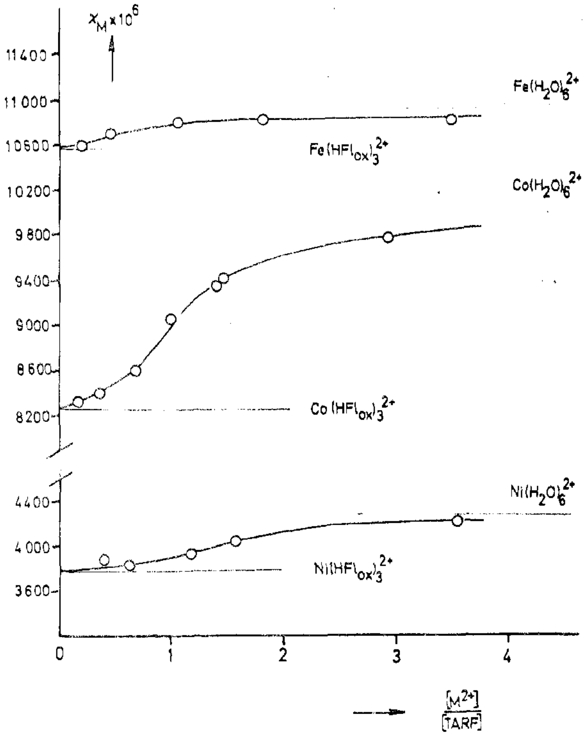
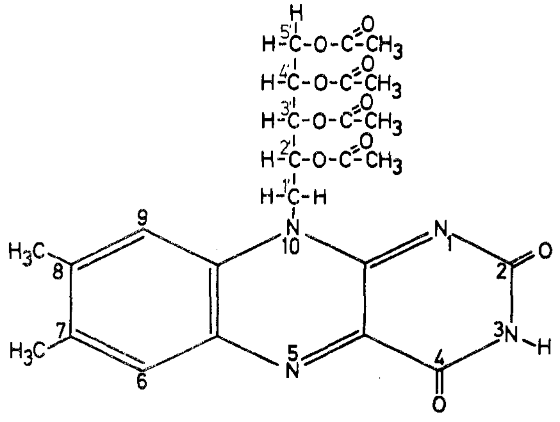


Figure 1. Molar susceptibility of flavoquinone-metal complexes in acetone-d_6. The susceptibility was measured by PMR at 38° using a 3×10^{-2} *M* TARF solution in the presence of metal perchlorates. No diamagnetic correction was applied. The susceptibility values of the tris complexes result from extrapolation of the curves to zero metal ion concentration; those of the hexaaquo complexes, which were measured independently in aqueous solution, are indicated as asymptotes to the experimental curves at high metal ion concentration.



I

values in the presence of an excess of metal ions correspond to those for the hexaaquo complexes in water, thus indicating that these complexes remain hydrated even in "dry" acetone. The effective magnetic moments derived from the susceptibility values at low metal concentration (Table I) and the smooth shape of the titration curves indicate the formation of octahedral tris complexes $M(HFl_{ox})_3^{2+}$. The effective moment values are not far away from the spin-only values for a high-spin electronic configuration. As a matter of fact, the ligand field strength in the flavine complexes, as estimated from the relative decrease in effective moment upon substitution of water molecules by flavines, appears in the same order as the complex stability constants derived earlier.[2]

The magnetic properties of the Cu^{II} complexes were easily established by ESR as compared to a rather imprecise direct measurement of the static susceptibility in dilute solution. An isotropic ESR spectrum could be recorded at room temperature and a square-planar complex of axial symmetry ($g_\| = 2.39$, $g_\perp = 2.08$) appeared in rigid solution at 77°K in agreement with the centrosymmetric bis structure derived earlier.[2] A small rhombic distortion due to the nonequivalence of the coordination sites O(4α) and N(5) appeared in the better resolved powder spectrum of the solid complex obtained with N^3-Et-TARF ($g_1 = 2.38$, $g_2 = 2.05$, and $g_3 = 2.12$). The Ni^{II} complexes exhibited a broad single resonance line with an approximately isotropic *g* value around 2.2. The ESR spectrum of the complex $Co(TARF)_3^{2+}$ broadened rapidly at temperatures higher than 20°K but revealed an axial structure ($g_\| = 3.1$ and $g_\perp = 5.45$) at 4.2°K. The isotropic spectrum of $Mn(H_2O)_6^{2+}$ observed at room temperature in acetone broadened very rapidly upon addition of TARF allowing a direct measurement of the complex formation constant.[2]

Thus, the electronic structure of the paramagnetic transition metal complexes $M(HFl_{ox})_n^{2+}$ appears in good agreement with the thermodynamic and stereochemical data previously derived and corresponds to a magnetic anisotropy which varies to a large extent from one metal to the other.

Pmr Line Width Analysis in the Paramagnetic Complexes. The paramagnetic contribution to the relaxation broadening of the PMR lines in the 3d ion complexes, $1/T_{2p}$, can be taken as the difference between the relaxation rates measured from the line width in the paramagnetic complexes, $1/T_2$, and that in the corresponding diamagnetic Zn^{II} complex, $1/T_{2d}$, namely, $1/T_{2p} = 1/T_2 - 1/T_{2d}$. In conditions where chemical exchange may occur, T_{2p} is a function of the relaxation time T_{2m} of a proton within the coordination sphere of the ion given[7] by the Bloembergen–Solomon equation

$$\frac{1}{T_{2m}} = \frac{1}{15}S(S+1)g^2\beta^2\gamma_H^2\frac{1}{R^6}\left[7\tau_c + \frac{13\tau_c}{1+\omega_s^2\tau_c^2}\right] + \frac{1}{3}S(S+1)\frac{A^2}{\hbar^2}\left[\tau_e + \frac{\tau_e}{1+\omega_s^2\tau_e^2}\right] \qquad (1)$$

in which the correlation times τ_c and τ_e are functions of the electron spin relaxation time τ_s, of the tumbling time of the complex τ_r, and of the average residence time of the proton in the coordination sphere of the metal ion, τ_h, ($1/\tau_c = 1/\tau_s + 1/\tau_r$; $1/\tau_e = 1/\tau_s + 1/\tau_h$). In a dilute solution of metal ions the paramagnetic broadening is a function of the difference in precession frequency $\Delta\omega_m$ between the coordinated and uncoordinated protons, following the equation of Swift and Connick[8]

$$\frac{1}{T_{2p}} = P_m\frac{\dfrac{1}{T_{2m}}\left(\dfrac{1}{T_{2m}} + \dfrac{1}{\tau_h}\right) + \Delta\omega_m^2}{\tau_h\left(\dfrac{1}{T_{2m}} + \dfrac{1}{\tau_h}\right)^2 + \tau_h\Delta\omega_m^2} \qquad (2)$$

in which P_m is the mole fraction of protons bound to the metal ion.

Cobalt(II) Complex. ESR of the complex $Co(HFl_{ox})_3^{2+}$ as a function of temperature indicates that τ_s is very short as usually observed in related complexes ($\tau_s \approx 10^{-12}$ sec).[9] The chemical exchange rate is comparatively slow even at ambient probe temperature (38°) since separate PMR lines for complexed and uncomplexed flavines could be observed in acetone up to −30° (Figure 2; cf. also Figure 6 reported earlier[2]). Under conditions of slow exchange, $\Delta\omega_m >> 1/\tau_h$, the line width of the complexed flavine resonances, $1/T_{2p}$, is governed by $1/T_{2m}$, i.e., by the correlation times involved in eq 1. The tumbling time τ_r, as estimated from the Debye formula $\tau_r = 4\pi\eta r^3/3kT$, using a viscosity η of 1.28 cP for acetone at 38° and a complex radius of 10 Å, is of the order

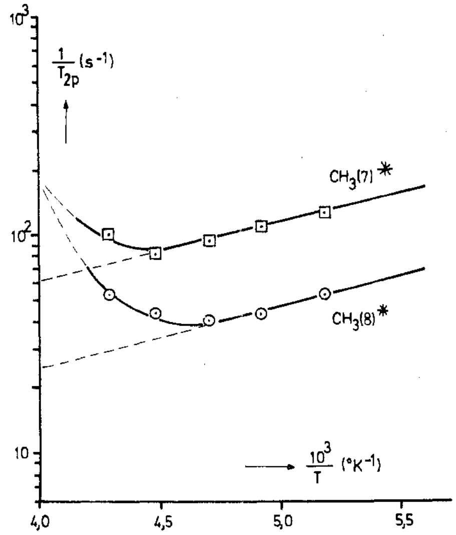


Figure 2. Paramagnetic contribution to the transverse relaxation time of the methyl protons in flavines bound within the complex $Co(HFl_{ox})_3{}^{2+}$ (N^3-Et-TARF (9×10^{-2} *M*) and $Co(ClO_4)_2 \cdot 6H_2O$ (10^{-2} *M*) in acetone-d_6) as a function of reciprocal temperature. $1/T_{2p}$ is measured from the line width at half-height by comparison with the diamagnetic Zn^{II} complex.

of 10^{-9} sec, i.e., much longer than τ_s even at the highest temperature. Thus, $\tau_c \simeq \tau_e \simeq \tau_s$, and eq 1 can be simplified to

$$\frac{1}{T_{2m}} = \frac{2}{3}S(S+1)\left[2g^2\beta^2{\gamma_H}^2\frac{1}{R^6} + \frac{A^2}{\hbar^2}\right]\tau_s \tag{3}$$

since at the magnetic field used $\omega_s{}^2\tau_s{}^2 << 1$.

τ_s may be estimated from eq 3 using the measured values of $1/T_{2m}$ for the methyl protons at C(7) and C(8) (Figure 2), the distances *R* (Table V), and the hyperfine coupling constants *A* (Table VI) derived in the following section. The contact interactions do not contribute significantly to the line widths and the τ_s value of $(1.5 \pm 0.5) \times 10^{-12}$ sec obtained at −60° compares favorably with that of 5×10^{-13} sec measured by Luz and Meiboom[10] for the $Co(CH_3OH)_6{}^{2+}$ complex at the same temperature. Using the linear relationship in the slow exchange $10^3/T > 4.5$ (Figure 2), this value may be extrapolated up to the ambient temperature: $\tau_s(38°) = (6 \pm 2) \times 10^{-13}$ sec averaged for the different protons.

When the conditions of slow chemical exchange are no longer fulfilled, the lines for both the complexed (Figure 2) and uncomplexed (Figure 3) molecules broaden rapidly with the increase in temperature. Then eq 2 simplifies to $1/T_{2p} = P_m/\tau_h$, providing a direct measurement of the chemical exchange rate $k_1 = 1/\tau_h$. k_1 was found equal to 1.0×10^{-3} sec^{-1} at 25°, and its temperature dependence in the corresponding range of temperature, $3.4 \leq 10^3/T \leq 4.3$ (Figure 3), provided a direct measurement of the enthalpy and entropy of activation for the exchange process: $\Delta H^\ddagger = +8.8 \pm 0.5$ kcal mol^{-1} and $\Delta S^\ddagger = -15.3 \pm 2$ cal deg^{-1} mol^{-1}.

At still higher temperature the range of fast exchange is reached in which the lines for complexed and uncomplexed molecules coalesce. The line width variation is reversed (Figure 3) and governed by the change in precessional frequency upon exchange, $1/T_{2p} = P_m\tau_h\Delta\omega_m{}^2$. This is indicated by the difference in line widths for the various protons.

Other Metal Complexes. The correlation times involved in the relaxation processes for the other 3d ion complexes will not appear necessary for the analysis of the paramagnetic shifts. However, they could be estimated following the same procedures.

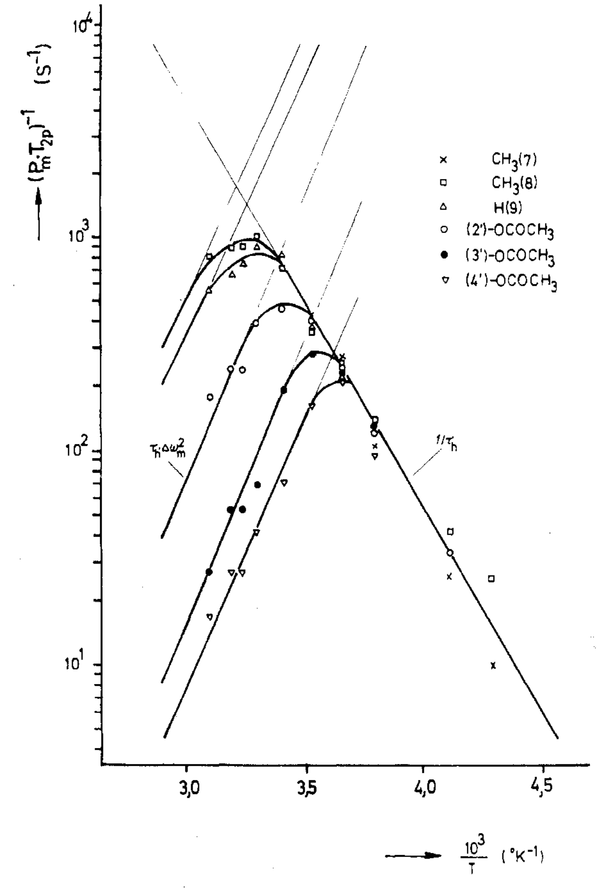


Figure 3. Paramagnetic contribution to the transverse relaxation time of the protons in flavines undergoing chemical exchange with the complex $Co(HFl_{ox})_3{}^{2+}$ in acetone-d_6 (N^3-Et-TARF (3×10^{-2} *M*), $Co(ClO_4)_2 \cdot 6H_2O$ (9×10^{-5} or 3.9×10^{-4} *M*)) as a function of reciprocal temperature. P_m is the molar fraction of protons bound within the complex (all data are normalized to $P_m = 1$).

Table II. Paramagnetic Shifts (ppm)[a] of Flavoquinone–Metal Complexes[b]

Signal	Mn^{II}	Fe^{II}	Co^{II}	Ni^{II}	Cu^{II}
2'-$OCOCH_3$	−0.4*	−0.5	+1.9	0.0	−0.1*
5'-$OCOCH_3$			+0.1	0.0	
3'-$OCOCH_3$	−1.7*	−0.5	+1.1	0.0	−0.1*
4'-$OCOCH_3$	−4.3*	−0.5	−0.4	+0.1	−0.1*
$CH_3(7)$	−1.9*	+2.1	+15.6, +12.4*	+1.7	+0.1*
$CH_3(8)$	−0.5*	−0.1	+7.4, +4.7*	−0.4	−0.5
1'-CH_2		+1.5 −0.1	+6.3	+1.6	
H(9)	−3.3*	−11.2	−7.1, −5.1*	−17.8	−6.2*
H(6)		+7.6*	+	+	
NH(3)		+3.2*	−16.9, −14.3*	+1.1	+2.8*

[a] Shift values correspond to the plateau of the titration curves or were calculated (as shown by asterisks) from the initial slope in the range of excess of flavine using the formation constants derived in ref 2. [b] TARF, 3×10^{-2} *M*, in acetone-d_6 at 38°.

The temperature dependence of the line widths was found parallel to the stability constants with the faster exchange rates in the more labile complexes: $1/\tau_h$($Ni^{II} < Co^{II} < Cu^{II} < Fe^{II} << Mn^{II}$). An electron spin relaxation time $\tau_s = (5 \pm 3) \times 10^{-12}$ sec was estimated for the Fe^{II} complex at 38° which explains the absence of an observable ESR spectrum at 77°K.

A direct evaluation of the contact contribution to the line widths in the Mn^{II} complex, using hyperfine interaction constants calculated from the observed paramagnetic shifts of the complexed flavines (Table II) and a τ_s value of 10^{-18} sec, shows that the line widths are governed by the dipolar interaction. The correlation time for this interaction τ_c must be dominated by the tumbling rate ($1/\tau_r \lesssim 10^9$ sec^{-1} for the mono complex). Then

$$\frac{1}{T_{2\mathrm{p}}P_{\mathrm{m}}} = \frac{1}{T_{2\mathrm{m}}} \simeq \frac{7}{15}S(S+1)g^2\beta^2{\gamma_{\mathrm{H}}}^2\tau_{\mathrm{r}}\frac{1}{R^6} \tag{4}$$

allowing us to estimate the distance of the manganese ion from the $CH_3(7)$, $CH_3(8)$, and H(9) protons. Together with the crystallographic data of 3-methyllumiflavine,[11] this mapping leads to the conclusion that the manganese ion is coordinated at O(4α). The relatively short distances (5–6 Å) found for the *O*-acetyl protons further suggest that the side chain is folded back over the isoalloxazine ring as already indicated by ring current induced shifts in the diamagnetic complexes.[2]

Isotropic PMR Chemical Shifts in the Paramagnetic Complexes. McConnell equations[12,13] assuming point dipoles for the electron and nuclei spins and a nondegenerate electronic ground state of spin *S* have been extensively used to describe the contact and pseudocontact contributions to the isotropic shifts in paramagnetic complexes having axial symmetry

$$\left(\frac{\Delta\nu}{\nu}\right)_{\text{contact}} = -\left(\frac{\gamma_{\mathrm{e}}}{\gamma_{\mathrm{H}}}\right)\frac{\bar{g}\beta S(S+1)}{3kT}A \tag{5}$$

$$\left(\frac{\Delta\nu}{\nu}\right)_{\text{pseudocontact}} = -\frac{\beta^2 S(S+1)}{3kT}\,\frac{(3\cos^2\Omega - 1)}{R^3}F(g) \tag{6}$$

where all notations are standard. F(*g*) in eq 6 is a function of the averaging conditions of the anisotropic electron susceptibility[14] depending upon the relative value of the Zeeman anisotropy and of τ_{r} and τ_{s}. Refined equations have been derived to take into account[14,15] the presence of low-lying excited states often revealed by deviations of the Curie law reciprocal temperature relationship due to nondegenerate Kramers doublets in $^4T_1$ or $^5T_2$ states or to take into account[16] the nonaxiality of the **g** tensor of the complex.

The pseudocontact contribution can be calculated directly if the geometry of the complex and the function F(*g*) to be used in eq 6 are known. However, the indirect factorization method has been extensively used[17,18] in order to separate the dipolar and contact contributions to the observed shifts although its validity has been reopened to discussion[4] and requires careful examination. Assuming identical modes of spin delocalization, the ratio of the contact shifts for two complexes differing only in the central metal ion should be identical for every ligand proton. Then, the pseudocontact contribution can be estimated if one of the complexes is magnetically isotropic.

The paramagnetic contribution to the large positive or negative shifts observed upon titration of flavine solutions with paramagnetic 3d metal ions (Figure 4) was obtained by subtraction of the shifts observed in the Zn^{II} complexes since the diamagnetic interactions within this series appeared very constant.[2] Representative spectra and assignments have been presented and discussed in the preceding paper[2] where equilibrium constants for complex formation have been derived. This permits the estimation of the shift values for the saturated bis or tris complexes by extrapolation of the initial slopes of the titration curves. As already noted for diamagnetic interactions[2] these shifts appeared equal, within experimental precision, to those measured directly for the mono complexes at the titration plateau which could be observed only when the resonances were not too much broadened (Table II). Only the Co^{II} complexes behave differently. It can be already noted for these complexes (Figure 4) that the intercepts of the plateau and of the initial slopes of the titration curves do not fit into the 3:1 stoichiometric ratio. This point will be discussed more quantitatively with the analysis of the paramagnetic shifts. The low solubility of some unusual model compounds (Table III) did not permit a measurement of the equilibrium constants and only relative shifts for the various protons could be estimated from the initial slope of the titration curves. The shift of the H(6) resonance could not be measured in most cases due to very rapid broadening.

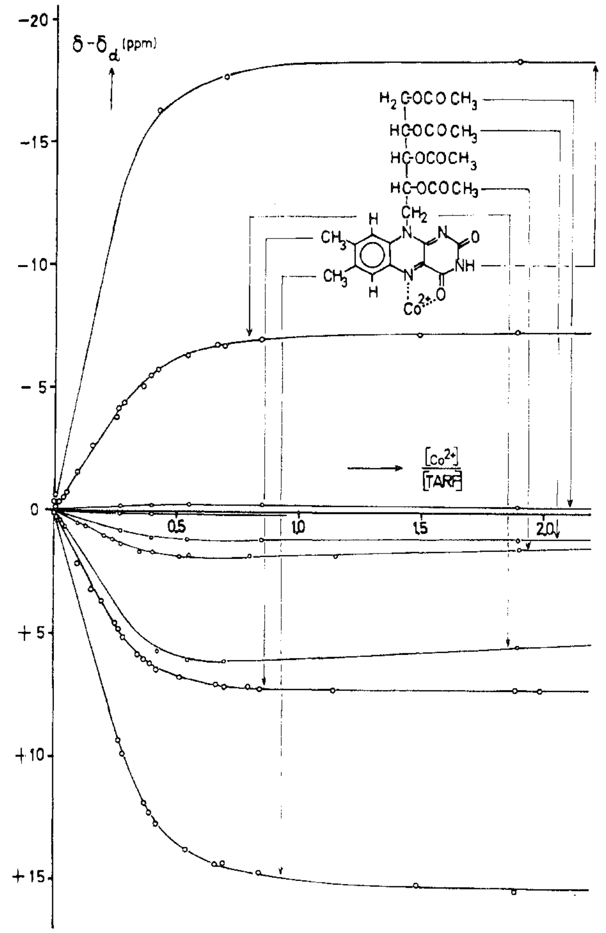


Figure 4. PMR titration curves of TARF (3×10^{-2} *M* in acetone-d_6 at 38°) by cobaltous ions. The paramagnetic shifts are taken as the difference between the observed shifts, δ, and those in the related diamagnetic Zn^{II} complex, δ_d.

Table III. Relative Paramagnetic Shifts (with the Shift of H(9) Taken Arbitrarily as −10.0 ppm) of Fe^{II} and Co^{II} Complexes[a–c] at 38° in Acetonitrile-d_3

	Fe^{II}			Co^{II}		
Signal	*a*	*b*	*c*	*a*	*b*	*c*
$CH_3(7)$	+3.0	+2.5		+18	+14	
H(7)			−2.8			+15
$CH_3(8)$	−0.7			+10		
H(8)		+0.9	+1.3		+12	+9
N(10)–CH_3	+3.0	+3.3	+2.8	+12	+6	+3
N(3)–CH_2	−1.5	−0.4	−0.1	−33	−27	−24
N(3)–C–C_5H_5	+0.7	+0.8	+0.7	−13	−8	−5
				0	+0.4	+0.8
H(6)	+5.9	+	+	+113	+	+
H(9)	−10.0	−10.0	−10.0	−10.0	−10.0	−10.0

[a] With 3-benzyllumiflavine. [b] With 3-benzyl-8-norlumiflavine. [c] With 3-benzyl-7,8-norlumiflavine.

Copper(II) Complexes. The pseudocontact contribution to the isotropic shifts in $Cu(HFl_{ox})_2^{2+}$ can be directly calculated using eq 6 since both the structure and the magnetic anisotropy of the complex are known. A tumbling correlation time of the order of 10^{-9} sec, an electron spin relaxation time of 10^{-8} sec,[8] and a measured Zeeman anisotropy corresponding to 1.8 × 10^{10} sec^{-1} result in conditions under which an average spin population is maintained upon tumbling, $\Delta\omega_g > 1/\tau_r > 1/\tau_s$. Jesson[14] calculated a lengthy expression for F(*g*) under these conditions corresponding to a value of 0.35 for the *g* anisotropy derived by ESR. The geometrical factor in eq 6 for a centrosymmetrical square-planar complex (cf. ref 2) depends only

Table IV. Separation of Pseudocontact and Contact Shifts in the Cu^{II} complex

Proton	R, Å	$1/R^3$, $cm^{-3} \times 10^{-22}$	Calcd pseudo-contact shifts, ppm	Obsd paramagnetic shifts, ppm	Resulting contact shifts, ppm
$CH_3(8)$	8.0	0.19	+0.33	−0.5	−0.8
$CH_3(7)$	6.2	0.42	+0.74	+0.1	−0.6
H(9)	6.5	0.36	+0.63	−6.2	−6.8
NH(3)	4.4	1.18	+1.19	+2.8	+1.6
H(6)	3.2	3.04	+5.32		
$1'\text{-}CH_2$	7.2	0.27	+0.47		

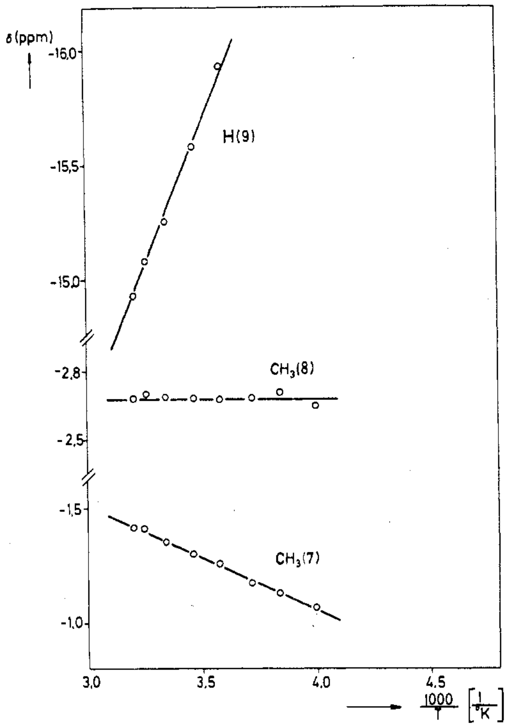


Figure 5. Curie-law dependence of the chemical shifts in the ferrous-flavine complex (TARF (3×10^{-2} *M*) and $Fe(ClO_4)_2 \cdot 6H_2O$ (1.5×10^{-2} *M*) in acetone-d_6). Extrapolation of the shifts to infinite temperature results in values within 0.5 ppm of those of the diamagnetic Zn^{II} complex.

upon the distance R, since $\Omega = 90°$ for all protons assuming that the methyl protons are positioned in the molecular plane due to their fast rotation. The distances R were estimated from the crystallographic data obtained for 3-methyllumiflavine[11] using Cu–N(5) and Cu–O(4α) distances equal to 2.0 Å although some steric repulsion may elongate the former one. The contact shifts were then estimated by difference of the calculated pseudocontact shifts from the observed paramagnetic shifts (Table IV).

Nickel(II) and Iron(II) Complexes. The nondegenerate $^3A_2$ electronic ground state of octahedral Ni^{II} complexes is not expected to exhibit large magnetic anisotropy[17,19,20] as confirmed by the apparently isotropic ESR spectrum of $Ni(HFl_{ox})_3^{2+}$. No ESR spectrum was observed at 77°K in the iron(II)–flavine complexes but the orbital degeneracy predicted[21] for the $^5T_2$ ground state could result in some anisotropy and pseudocontact interaction. However, most related octahedral complexes of Ni^{II} and Fe^{II} so far investigated by PMR[22–24] revealed a nearly complete magnetic isotropy for both kinds of complexes.

Indeed, the paramagnetic shifts observed in the nickel(II)- and iron(II)–flavine complexes exhibit also a very similar pattern for their distribution in sign and intensity around the isoalloxazine ring with no regular attenuation with the number of bonds from the chelation site (Table II). Furthermore, the direction of the shifts is reversed upon replacement of a methyl group at positions C(7) and C(8) by a hydrogen atom or for the methylene protons of a benzyl group substituted at N(3) as compared to NH (Table III). This reflects pure contact interaction arising from π-electron spin delocalization in the flavine ligand. The absence of noticeable pseudocontact is further indicated by the perfect Curie law dependence of the chemical shifts (Figure 5) which can be linearly extrapolated at infinite temperature to the diamagnetic values observed for the Zn^{II} complex, thus reflecting the absence of low-lying excited states characteristic of magnetically asymmetric complexes. Hyperfine interaction at N(10) is better understood looking at lumiflavine (10-methylisoalloxazine) as a ligand in which free rotation of the methyl group is observed (Table III).

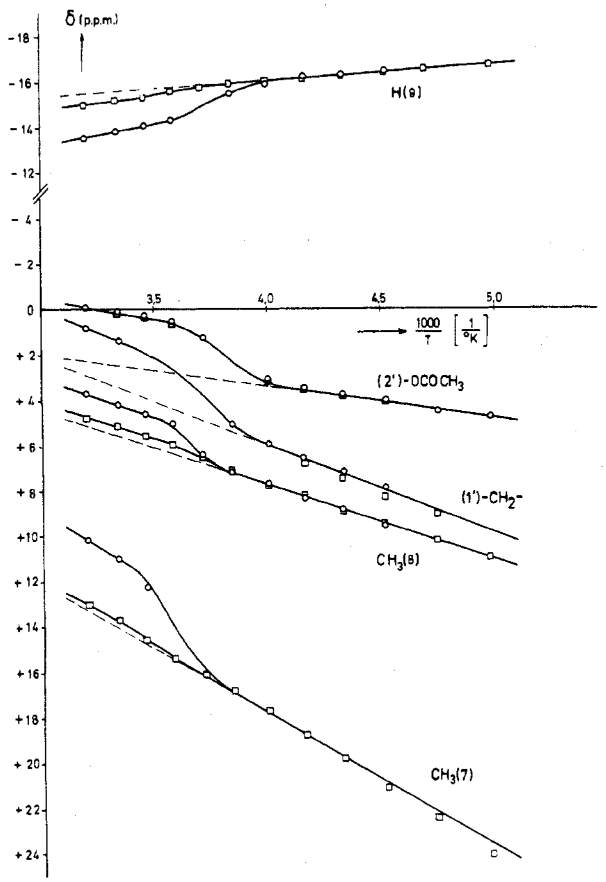


Figure 6. Temperature dependence of the chemical shifts of the flavine protons (TARF, 9×10^{-2} *M*) in an acetone-d_6 solution 3.7×10^{-2} *M* (dots) and 7.2×10^{-2} *M* (squares) in $Co(ClO_4)_2 \cdot 6H_2O$. At the lower metal concentration a transition centered at 0° corresponds to a change in the stoichiometry of the complex. The extrapolation of the linear sections of the curves to infinite temperature results in large negative values far apart from those in diamagnetic complexes.

Cobalt(II) Complexes. The large dipolar contributions expected for the paramagnetic shifts in the Co^{II} complex cannot be estimated confidently from the geometry of the complex and values of the **g** tensor since strong deviation from the Curie type temperature dependence of the shifts (Figure 6) appears from the extrapolation to infinite temperature revealing thermally populated Kramers doublets. Thus it was preferable to estimate the contribution of the contact and pseudocontact interactions at ambient temperature by comparison with the Ni^{II} complex assuming the same mechanism of spin polarization and using the factorization method.[4]

In octahedral $Co(HFl_{ox})_3^{2+}$ complexes we are faced with the problem of stereochemical isomers, one cis isomer and three trans isomers being possible (cf. Figure 10 in ref 2). The

Table V. Calculation of Pseudocontact Shifts in the Co^{II} Complex

Proton	R, Å	Ψ, deg	$(2 \cos^2 \Psi - 1)/R^3$, $cm^{-3} \times 10^{-22}$	Calcd pseudocontact shifts,[a] ppm				Obsd paramagnetic shifts, ppm	Calcd contact shifts,[b] ppm
				Ref CH_3(8)	CH_3(7)	H(9)	NH(3)		
CH_3(8)	8.0	11	+0.18		+5.2*	+4.9*	(−5.6*)	+4.7*	−0.3
					+7.5	+7.7	(−13.8)	+7.4	−0.2
CH_3(7)	6.2	14	+0.36	+10.4*		+11.5*	+11.8*	+12.4*	+1.2
				+15.1		+14.3	+14.2	+15.6	+1.2
H(9)	6.5	34	+0.15	+4.8*	+4.8*		+5.0*	−5.1*	−9.9
				+6.4	+6.0		+5.9	−7.1	−13.2
NH(3)	4.4	124	−0.45	−14.0*	−14.7*	−14.9*		−14.3	+0.2
				(−34.7)	−17.8	−17.7		−16.9	+0.8
H(6)	3.2	14	+2.66	+110.4	106.4			+	
1′-CH_2	7.2	58	−0.11	−6.2	−2.1	+6.4	−6.5	+6.3	

[a] The calculation was carried out for the mono and the tris (as shown by asterisks) complexes by comparison with the Ni^{II} complexes (Table II) using the factorization method for corresponding pairs of protons with the geometric factors of column 3. [b] Taken as the difference between the observed paramagnetic shifts and the averaged values of the calculated pseudocontact shifts (some values, within parentheses, involving the NH(3) shift have been discarded, see text).

magnetic anisotropy experienced by each flavine within these different complexes may be quite variable. The single axial spectrum observed by ESR as well as steric hindrance observed in molecular models suggests that only the more symmetrical cis isomer is stable in solution. The three flavines in this isomer correspond to each other by a threefold rotation axis and are in identical magnetic environments. Pseudocontact contributions in the trans isomer, in which the flavines experience different anisotropic magnetic interactions, should be averaged to zero at 38° by the fast chemical exchange among the three nonequivalent isomers. However, at temperatures low enough so that the chemical exchange would not average the differences in magnetic environment, a single line was observed for each proton, indicating the absence of trans isomers (cf. Figure 6 in ref 2).

The calculation of the geometrical factors in the cis isomer was carried out using a model built with three planar flavines at right angles to each other and having their O(4α) and N(5) atoms at the corners of a regular octahedron 2.0 Å from the metal ion. Hence, the symmetry axis ($g_\parallel$) of the complex is 35° out of the plane of each flavine (Figure 7) and the geometrical factor in eq 6 is $(2 \cos^2 \Psi - 1)/R^3$, Ψ being the angle of the direction vector of the proton at distance R from the metal ion with the projection of the symmetry axis in the flavine plane. With $F(g)$ negative, as indicated by the ESR data, one expects a positive contribution to the shifts for $-45° < \Psi < +45°$, viz., for the protons of the benzenoid ring, and a negative one at other positions.

The pseudocontact contributions in the Co^{II} complex were then estimated by factorization[4] of the observed shifts from the Ni^{II} and Co^{II} complexes using the ratio of the geometrical factors for the various pairs of protons (Table V). The calculations have been performed using the shifts observed in the 3:1 (extrapolated from the initial slope of the titration curves) and 1:1 (plateau values) Co^{II} complexes. It was assumed that isotropic interactions were similar in both Ni^{II} complexes since, even at the highest temperature used, slow exchange is observed at low nickel concentrations corresponding to the 3:1 complex. In both cases the calculation was carried out cyclically within the shift values for the H(9), CH_3(7), CH_3(8), and NH(3) protons providing a good check of the validity of the method.[4] All values of factorized pseudocontact shifts appeared self-consistent within 0.2–0.5 ppm (Table V) except for the values derived from some pairs of resonances including that of the NH(3) proton, suggesting that the spin delocalization onto this proton does not correspond to the same mechanism, at least quantitatively, for the Ni^{II} and Co^{II} complexes.

The factorization procedure shows that most if not all of the paramagnetic shifts in the Co^{II} complex result from pseudocontact interaction except for that of the H(9) proton which is the only proton which exhibits a large contact shift in the Ni^{II}, Fe^{II}, and Cu^{II} complexes. Finally, the pseudocontact contribution for the 3:1 and 1:1 complexes appears somewhat different as expected from the different symmetry of the complexes, even if they are both octahedral due to substitution with water molecules.[2]

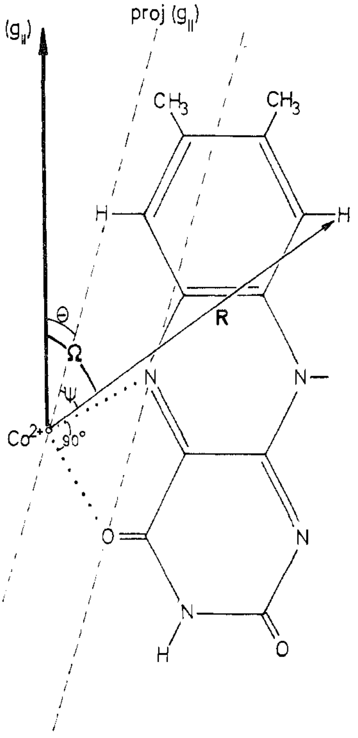


Figure 7. Geometric parameters involved in the calculation of the pseudocontact contribution to the paramagnetic shifts in the cis isomers of the flavine tris complex. $g_\parallel$ corresponds to a threefold symmetry axis 35° (Θ) out of the flavine plane.

Taking the +7.6-ppm dipolar shift of the CH_3(8) resonance as a reference, since it is the most precisely measured value due to a nearly complete lack of contact contribution, yields an $F(g)$ value of −1.73. In conditions of slow tumbling even at 38° ($1/\tau_s >> \Delta\omega_g >> 1/\tau_r$) observed from the relaxation and ESR investigations, the g-value anisotropy may be estimated[14] from $F(g) = (g_\parallel^2 - g_\perp^2)/3$, using an average g value expected for the lowest Kramers doublet of the $^4T_1$ ground state of an octahedral Co^{II} complex with pure trigonal distortion ($\bar{g}$ = 4.0–4.3).[21] Although this value is not far from that measured by ESR at 4.2°K ($\bar{g}$ = 4.66), the g anisotropy

Table VI. Hyperfine Coupling Constants[a] and Spin Densities[b] in the Flavoquinone and in the Flavosemiquinone Radical Chelates

	$M(HFl_{ox})_n{}^{2+}$				$MH\dot{F}l^+$
	Fe^{II}	Co^{II}	Ni^{II}	Cu^{II}	Zn^{II}, Cd^{II} [d]
$\bar{g}^c$	2.11	4.67	2.2	2.18	
$S(S + 1)$	6	$^{15}/_4$	2	$^3/_4$	
$A_5{}^N$					7700
$A_6{}^H$	−13.1 (+0.58)				3500
$A_7{}^H(CCH_3)$	−3.6 (−0.13)	−1.7 (−0.08)	−8.0 (−0.30)	+9.1	"Small"
$A_8{}^H(CCH_3)$	+0.2 (+0.01)	+0.3 (+0.01)	+1.9 (+0.07)	+11.7 (+0.56)	3900
$A_9{}^H$	+19.2 (−0.85)	+18.5 (−0.82)	+83.9 (−3.72)	+89.7 (−3.98)	"Small"
$A_{10}{}^N$					3100
$A_{10}{}^H(NCH_2)$	−2.6				3100
	+0.2		−7.5		
$A_3{}^H(NH)$	−5.3	−1.1	−5.2	−18.3	"Small"

[a] A (mG) calculated from the contact shifts at 38° using eq 5. [b] In parentheses ($\rho \times 10^3$); calculated with $Q^H{}_{CCH_3} = +21$ G and $Q^H{}_{CH} = -22.5$ G. [c] From ESR measurements, except for the Fe^{II} complex for which $\bar{g}$ was calculated from the effective magnetic susceptibility. [d] From ref 25 (mG).

estimated following this procedure ($\Delta g = 0.6$) is much smaller than that measured by ESR ($\Delta g = 2.5$). Thus thermal mixing of higher Kramers doublets with the ground state in the temperature range of the PMR experiments should reduce significantly the g anisotropy. However, in the whole temperature range the g values derived for the tris complex from ESR or PMR experiments correspond to an octahedral ligand field with negative trigonal distortion ($g_\parallel < g_\perp$). This symmetry of the ligand field is preserved as water molecules replace the flavines at higher metal to flavine concentrations.

Labile Monodentate Complexes. The Fe^{III}-induced shifts are parallel and about twice those observed with diamagnetic Mg^{2+} and indicate monodentate binding preferentially at $O(2\alpha)$.[2] The lack of line broadening suggests that the difference in magnitude is due to the difference of the electric charge with no paramagnetic contribution.

The larger shifts estimated for the Mn^{II} complexes from the initial slopes of the titration curves (Table II) were considered to arise from pure contact interactions. However they are negligible in terms of hyperfine coupling for their contribution to the line broadening which led to the mapping procedure described above.

Mechanism of Contact Interactions. Isotropic hyperfine interaction constants can be derived from the observed or calculated contact contributions to the paramagnetic shifts using eq 5 in which $\bar{g}\beta S(S + 1)$ is related to the magnetic susceptibility of the complexes (Table VI). The hyperfine interaction constants measured for the flavosemiquinone radical chelates[25] which exhibit a spin distribution pattern similar to that of the uncomplexed semiquinone radical[26] have been included in Table VI.

The various metal complexes exhibit a rather similar pattern of distribution of the hyperfine interaction constants at the different protons of the isoalloxazine ring with no attenuation with the distance from the chelation site and reversal of spin polarization by substitution of methyl groups by hydrogen atoms. Thus, it can be assumed that the observed interactions arise principally from the π-electron spin delocalization in the ligand orbitals.

Spin polarization through the σ electrons[27] should be responsible, at least in part, for the large shift observed for the NH(3) and H(6) protons. The odd number of bonds between these protons and $O(4\alpha)$ and N(5), respectively, is in accordance with the positive shifts measured. Such a mechanism is further indicated by the strong attenuation of the shifts observed for the methylene protons of a benzyl group substituted at N(3) as compared to unsubstituted NH(3) and by the failure of the factorization procedure for protons referred to the NH(3) proton, suggesting different spin polarization mechanisms for this proton in the Co^{II} and Ni^{II} complexes.

The copper complex exhibits contact shifts rather different from those in the Ni^{II} and Co^{II} complexes, both in magnitude and in distribution pattern. However, the magnetic susceptibility arises only from a spin $S = 1/2$ and similar delocalization mechanisms should result in shifts lower by a factor of 2.8 as compared to the Ni^{II} complex. Once this normalization procedure is taken into account, it appears that the differences in spin distribution are not very large and that the direct σ interactions which propagate as far as to the methyl group at C(7) dominate the effect of π-electron spin delocalization in the Cu^{II} complex.

Once the direct σ-delocalization mechanism at H(6) and at $CH_3(7)$ in the Cu^{II} complex is taken into account, the distribution of the hyperfine coupling constants attributed to the π-electron spin delocalization around the isoalloxazine ring appears very similar in the four paramagnetic complexes of Fe^{II}, Ni^{II}, Co^{II}, and Cu^{II}, being maximum and negative for H(9) and negative for $CH_3(7)$. They can be related to the $2p\pi$ spin density at the different carbon and nitrogen atoms of the ring using McConnell relations $A_i = Q\rho^{\pi}{}_i$. The negative Q_H and positive Q_{CH_3} values of the McConnell coefficient, e.g., $Q^H{}_{CH} = -22.5$ G[29] and $Q^H{}_{CCH_3} = +21$ G,[30,31] agree with the reversal of the shift upon methyl substitution and lead to the conclusion that negative spin density, or β spin polarized antiparallel to that of the metal ion, is present in the π orbitals of the flavine, especially at the positions of maximum spin density C(7) and C(9). Using $Q^H{}_{NCH_3} = +26$ G[31] for lumiflavine (10-methylisoalloxazine) indicates also a large and negative spin density at N(10).

These $2p\pi$ spin densities are 2 orders of magnitude lower and opposite in sign to those in the flavosemiquinone radical chelates and exhibit a very different distribution pattern. They are also much smaller than those found for many paramagnetic complexes in which the transfer of unpaired spin into the ligand orbitals was interpreted as arising from direct π–$d\pi$ delocalization to or from the metal ion.[32,33] Such a direct π-electron spin delocalization in the flavoquinone chelates should result in a positive density at most ring atoms since no inversion of the spin polarity is expected for the delocalization of a metal ion α spin to the ligand or for the inverse process. In the former case, the distribution pattern of the spin density should be qualitatively similar to that in the semiquinone, corresponding to the characteristics of the lowest empty antibonding π orbital of the flavoquinone. In the latter case, all of the 3d metal ion orbitals having at least one electron with α spin, the delocalized electron should be β polarized leaving a neat α spin in the ligand π-bonding orbitals. We may therefore conclude that the β spin delocalized on the flavine arises from an indirect polarization mechanism including spin reversal. A σ–π exchange interaction at the coordination site appears to be the most probable process for such a mechanism.[19,23,34] Indeed, unpaired electrons are always present in the e_g orbitals of the metal ions of the octahedral complexes. On the other hand, there is no unpaired electron in the t_{2g} orbitals of high-spin octahedral Cu^{II} and Ni^{II} complexes and direct π-electron spin delocalization could not be as important in these complexes as in the Fe^{II} and Co^{II} complexes.

Bond lengths in the metal complexes as well as the diamagnetic interactions have already suggested[2] that the stability of the complexes results mainly from strong interactions at O(4α), resulting in direct σ interactions propagated to the NH(3) proton. However, a σ–π spin polarization should occur mainly at N(5) since the pyrimidine moiety is very poorly conjugated to the rest of the isoalloxazine ring. The mechanisms of spin delocalization in paramagnetic complexes do not reflect directly the nature of the organometallic binding but it can be noted that the amount of delocalized π spin is directly related to the stability of the complexes.

A precise knowledge of the mechanism of spin polarization would require extended molecular orbital calculations for the whole complexes. However, PPP SCF molecular orbital calculations[35] for the isolated isoalloxazine ligand suggest that the highest filled π orbital, which should be energetically favored for a polarization process, is a poor candidate because of its very small atomic coefficient at N(5) ($c_N{}^2 = 0.002$).

The indirect mechanism and the weakness of the spin delocalization within the flavoquinone–metal complexes represent a potential barrier for partial or total electron transfer, presumably due to the long distance between N(5) and the metal ion, which may have some implications in biological oxidoreduction processes.

Acknowledgment. This work was supported by grants from the Deutsche Forschungsgemeinschaft (to J.L. and P.H.) and by the Institut National de la Santé et de la Recherche Medicale (to J.-M.L.). We are indebted to Professor A. Ehrenberg for ESR measurements at liquid helium temperature and to Dr. P. S. Song for a communication of his molecular orbital calculations of flavines.

Registry No. $Fe(TARF)_3(ClO_4)_2$, 55648-61-8; $Fe(H_2O)_6(ClO_4)_2$, 15305-57-4; $Co(TARF)_3(ClO_4)_2$, 55648-63-0; $Co(H_2O)_6(ClO_4)_2$, 15305-50-7; $Ni(TARF)_3(ClO_4)_2$, 55648-65-2; $Ni(H_2O)_6(ClO_4)_2$, 10171-10-5; $(C_{27}H_{32}N_4O_{10}ClO_4H_2O)_2Cu$, 55638-31-8; $Cu(TARF)_2{}^{2+}$, 55648-66-3; $Mn(TARF)^{2+}(H_3CC(O)CH_3)_5$, 55638-28-3; $Co(N^3\text{-Et-TARF})_3{}^{2+}$, 55648-67-4; 3-benzyllumiflavine, 14684-43-6; 3-benzyl-8-norlumiflavine, 55637-99-5; 3-benzyl-7,8-norlumiflavine, 55638-00-1; iron, 7439-89-6; cobalt, 7440-48-4.

References and Notes

(1) M stands for metal and RFl_{ox} is the flavine (isoalloxazine) ligand with R = H or alkyl substituent at N(3).

(2) J. Lauterwein, P. Hemmerich, and J.-M. Lhoste, preceding paper in this issue.

(3) For a review see G. N. La Mar, W. D. Horrocks, Jr., and R. H. Holm, Ed., "NMR of Paramagnetic Molecules: Principles and Applications," Academic Press, New York, N.Y., 1973.

(4) W. D. Horrocks, Jr., *Inorg. Chem.*, **9**, 690 (1970).

(5) D. F. Evans, *J. Chem. Soc.*, 2003 (1959).

(6) D. B. McCormick, *J. Hetereocycl. Chem.*, **7**, 447 (1970).

(7) For a review see R. A. Dwek, *Adv. Mol. Relaxation Processes*, **4**, 1 (1972).

(8) T. J. Swift and R. E. Connick, *J. Chem. Phys.*, **37**, 307 (1962).

(9) (a) N. Bloembergen and L. Morgan, *J. Chem. Phys.*, **34**, 842 (1961); (b) H. Sternlicht, R. G. Shulman, and E. W. Anderson, *ibid.*, **43**, 3123 (1965).

(10) Z. Luz and J. Meiboom, *J. Chem. Phys.*, **40**, 1058 (1964).

(11) R. Norrestam and B. Stensland, *Acta Crystallogr., Sect. B*, **28**, 440 (1972).

(12) H. M. McConnell and R. E. Robertson, *J. Chem. Phys.*, **29**, 1361 (1958).

(13) H. M. McConnell and D. B. Chesnut, *J. Chem. Phys.*, **28**, 107 (1958).

(14) J. P. Jesson, *J. Chem. Phys.*, **47**, 579 (1967).

(15) R. J. Kurland and B. R. McGarvey, *J. Magn. Reson.*, **2**, 286 (1970).

(16) G. N. La Mar, W. D. Horrocks, Jr., and L. C. Allen, *J. Chem. Phys.*, **41**, 2126 (1964).

(17) W. D. Horrocks, Jr., R. C. Taylor, and G. N. La Mar, *J. Am. Chem. Soc.*, **86**, 3031 (1964).

(18) M. L. Wicholas and R. S. Drago, *J. Am. Chem. Soc.*, **90**, 2196 (1968).

(19) J. A. Happe and R. L. Ward, *J. Chem. Phys.*, **39**, 1211 (1963).

(20) G. R. Van Hecke and W. D. Horrocks, Jr., *Inorg. Chem.*, **5**, 1968 (1966).

(21) J. S. Griffith in "The Theory of Transition-Metal Ions", Cambridge University Press, Cambridge, 1964, p 362.

(22) J. P. Jesson, S. Trofimenko, and D. R. Eaton, *J. Am. Chem. Soc.*, **89**, 3158 (1967).

(23) M. Wicholas, *J. Inorg. Nucl. Chem.*, **32**, 873 (1970).

(24) M. Wicholas and R. S. Drago, *J. Am. Chem. Soc.*, **91**, 5963 (1969).

(25) F. Müller, L. E. G. Eriksson, and A. Ehrenberg, *Eur. J. Biochem.*, **12**, 93 (1970).

(26) W. H. Walker, A. Ehrenberg, and J.-M. Lhoste, *Biochim. Biophys. Acta*, **215**, 166 (1970).

(27) R. S. Milner and L. Pratt, *Discuss. Faraday Soc.*, **34**, 88 (1962).

(28) H. M. McConnell, *J. Chem. Phys.*, **28**, 1188 (1958).

(29) I. Bernal, P. H. Rieger, and G. K. Fraenkel, *J. Chem. Phys.*, **37**, 1489 (1962).

(30) R. E. Moss, N. A. Ashford, R. G. Lawler, and G. K. Fraenkel, *J. Chem. Phys.*, **51**, 1765 (1969).

(31) L. E. G. Eriksson and W. H. Walker, *Acta Chem. Scand.*, **24**, 3779 (1970).

(32) D. R. Eaton, *J. Am. Chem. Soc.*, **87**, 3097 (1965).

(33) D. R. Eaton, A. D. Josey, W. D. Phillips, and R. E. Benson, *J. Chem. Phys.*, **37**, 347 (1962).

(34) R. J. Fitzgerald and R. S. Drago, *J. Am. Chem. Soc.*, **89**, 2879 (1967).

(35) P. S. Song, private communication.

Contribution from the Department of Chemistry,
University of Nebraska, Lincoln, Nebraska 68508

Kinetics of Tetraethylenepentamine Ligand Exchange Reactions of Copper(II)–Polyamine Complex Ions[1]

JAMES D. CARR* and VIRGIL K. OLSON

Received September 16, 1974 AIC40654V

The rates of the ligand-exchange reactions of tetren with Cu(trien), Cu(dien), and $Cu(dien)_2$ are measured using stopped-flow spectrophotometry and the pH dependence of the reaction rates analyzed. The rate constants for the attack of unprotonated tetren on CuL are 7.47×10^4 and 1.02×10^8 M^{-1} sec^{-1} for L = trien and dien, respectively, at 25° and 0.1 *M* ionic strength. For the reaction of tetren with Cu(trien), a mechanism is proposed wherein one nitrogen on the incoming ligand is bonded prior to the rate-determining step. For the reaction of tetren with Cu(dien), the rate-determining step is the rate of water loss from the Cu(dien) complex. Comparisons of structural effects are made between this work and studies for the exchange of Cu(tren) with tetren previously conducted in this laboratory.

Introduction

In this work the all-polyamine ligand-exchange reactions of Cu(trien), Cu(dien), and $Cu(dien)_2$ with tetren have been investigated by stopped-flow spectrophotometry (reactions 1–3) and the results contrasted with those of a previous study of the all-polyamine ligand-exchange reactions of Cu(tren) with

$$\mathrm{Cu(trien)^{2+} + tetren \rightarrow Cu(tetren)^{2+} + trien} \tag{1}$$

$$\mathrm{Cu(dien)^{2+} + tetren \rightarrow Cu(tetren)^{2+} + dien} \tag{2}$$

$$\mathrm{Cu(dien)_2{}^{2+} + tetren \rightarrow Cu(tetren)^{2+} + 2dien} \tag{3}$$

dien, trien, and tetren conducted in this laboratory[9] (reactions 4–6).