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Contribution from the Department of Chemistry and Biochemistry,
James Cook University of North Queensland, Queensland, 4811, Australia,
and the Chemical Technology Division, Australian Atomic Energy Commission, Sydney, 2232, Australia

Cyclic Ligand Control of Kinetic Lability. Kinetics of Dissociation of Nickel(II) Complexes of a Series of O_2N_2-Donor Macrocycles in Acid

A. EKSTROM,[1a] LEONARD F. LINDOY,*[1b] and ROLAND J. SMITH[1b]

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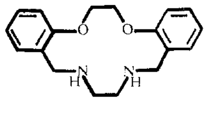
The kinetics of dissociation in acid of a range of nickel complexes of 14–17-membered macrocycles containing an O_2N_2-donor set has been studied. Macrocycle structure was found to strongly influence the observed first-order dissociation rate constants, and, for the unsubstituted macrocycles, the kinetic labilities follow the ring size sequence 14 > 15 > 16 < 17. In accord with this sequence, hole size considerations suggest that the 16-membered macrocycle provides the ring of best fit for nickel in this series of ligands. An observed enhancement of the dissociation rate in the presence of acetate ion relative to the rate in the presence of a number of other ions has also been studied.

Introduction

Reports of the interaction of transition-metal ions with macrocyclic ligands incorporating both oxygen- and nitrogen-donor atoms are becoming more frequent.[2-5] Such ligands are intermediate between the well-studied crown ether macrocycles[6] and the category of macrocycles incorporating only nitrogen-donor atoms.[7] Previously we have discussed the synthesis[2] and kinetics of formation in methanol[3] of octahedral nickel complexes of a range of O_2N_2-donor macrocycles (of which **1**–**7** are typical). X-ray structures of nickel halide complexes of **3** and **6** confirm that both have similar trans octahedral structures.[3,8]

In contrast to the labile nature of most crown complexes,[9] a feature of the complexes of nitrogen macrocycles is their considerable kinetic inertness[10,11]—one aspect of the "macrocyclic effect".[12] Discussion of the nature of the "macrocyclic effect" has centered largely (although not exclusively[13]) on studies involving N_4-donor macrocycles.[12,14-17]



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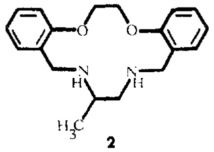

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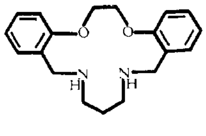

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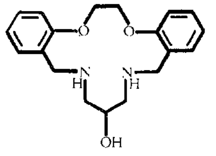

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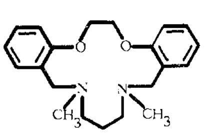

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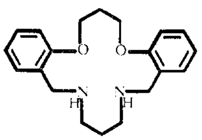

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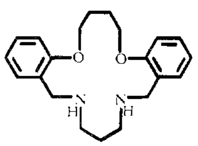

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However, in several such studies it has proved difficult to investigate the nature of this effect because of extreme kinetic inertness and associated, very high stability constants.[17] Further, comparative studies of the effects of alteration of the macrocycle ring size on the kinetics of dissociation of nickel complexes of saturated N_4-donor macrocycles (of the cyclam class) are complicated by stereochemical and spin-state changes along the series.[15,18] Thus it seemed likely that substitution of ether oxygens (weak donors) for some of the nitrogens in such N_4 macrocycles might lead to more readily

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Table I. Dissociation of $NiLCl_2$ (L = **3**) in Acid (1 M)

acid	k_{obsd}(25 °C),[a,b] s^{-1}
$HClO_4$	$(3.0 \pm 0.1) \times 10^{-3}$
CF_3SO_3H	3.2×10^{-3}
HCl	$(3.5 \pm 0.1) \times 10^{-3}$
HNO_3	$(4.2 \pm 0.1) \times 10^{-3}$
CH_3COOH (1 M CH_3COO^-)	$(2.4 \pm 0.1) \times 10^{-2}$

[a] Errors represent the average deviation from the mean. [b] Complex concentration 1.5×10^{-3} M.

studied systems. The results of an investigation of the dissociation kinetics of a system involving nickel complexes of the O_2N_2-donor macrocycles **1**–**7** are now reported.

Experimental Section

Preparation of Reagents. The preparation of ligands **1** and **3**–**7** and their nickel(II) complexes is described elsewhere;[2] because of unfavorable solubilities and/or spectral properties, not all of the compounds reported previously were suitable for the kinetic investigation. Ligand **2** was prepared by a similar procedure and was isolated as the hemihydrate of its dihydrochloride salt. Anal. Calcd for $C_{19}H_{27}Cl_2N_2O_{2.5}$: C, 57.9; H, 6.9; N, 7.1. Found: C, 58.1; H, 6.7; N, 7.1. MS: parent ion, *m/e* 312. ^1H NMR (D_2O): δ 1.53 (d, CH_3–CH), 3.32–4.05 (m, –CH and N–CH_2–C), 4.42 (s, Arom–CH_2), 4.65 (s, O–CH_2–), 7.15–7.80 (m, Arom). Ni(ligand **2**)Cl_2 was obtained as a blue solid by mixing butanol solutions of the free ligand (obtained by neutralization of the dihydrochloride salt) and nickel chloride hexahydrate. Anal. Calcd for $C_{19}H_{24}N_2O_2NiCl_2$: C, 51.6; H, 5.5; N, 6.3; Ni, 13.3. Found: C, 51.3; H, 5.8; N, 6.2; Ni, 13.2. The magnetic moment ($\mu = 3.10\ \mu_B$) together with the visible reflectance spectrum [λ_{max} = 365, 595, 760 (sh), and 1120 (w) nm] suggests that this complex has an octahedral geometry similar to that of the other complexes in the series which were reported previously.[2]

Stock solutions of the analytically pure complexes (10^{-2}–10^{-3} M) in water were prepared and the small amount of $Ni(OH)_2$ which precipitated in each case was filtered off before the respective solutions were mixed with acid. The small amount of $Ni(OH)_2$ is formed as a result of the strong basicity of the ligands which have pK_a values of 9–10. As noted elsewhere,[19] such hydrolysis has no effect on the observed kinetics except to slightly reduce the absorbance change during the reaction.

Doubly distilled water was used for all kinetic experiments. Acid solutions were prepared by using AR Volucon ampules, and metal salts were AR grade. Analyses for carbon, hydrogen, and nitrogen were determined by the Australian Microanalytical Service, Melbourne. Nickel was determined gravimetrically as the DMG complex.

Kinetic Studies. In a typical experiment, an aqueous solution of the complex was mixed with an equal volume of 2 M acid and the dissociation reaction followed by using either the stopped-flow system described elsewhere[20] or a Beckman ACTA IV spectrophotometer equipped with a thermostated cell holder. For each complex, the dissociation rate was studied at the wavelength of the $^3A_{2g} \rightarrow {}^3T_{1g}$ (F) transition—namely: **1**, 600 nm; **2**, 601 nm; **3**, 601 nm; **4**, 602 nm; **5**, 644 nm; **6**, 639 nm; **7**, 689 nm. The first-order rate constants for the dissociations in excess acid were obtained from least-squares fits of the data to the equation $\ln (A_t - A_\infty) = -k_{obsd}t$ + constant. All rate constants quoted are the average of between two and nine individual determinations.

Product Identification. In all cases the spectrum at the end of the reaction was identical with that of $NiCl_2$ in excess acid; for the reaction of Ni(ligand **3**)Cl_2 with 1 M HCl, the dihydrate of the ligand dihydrochloride salt was isolated from the solution. Anal. Calcd for $C_{19}H_{30}N_2O_4Cl_2$: C, 54.1; H, 7.2; N, 6.7. Found: C, 53.7; H, 7.3; N, 6.6.

Table II. Dissociation of $NiLCl_2$ (L = **3**) in Acetic Acid/Acetate Buffers[a]

[CH_3-COO^-], M	[CH_3-COOH], M	pH	k_{obsd}(25 °C),[b,c] s^{-1}
0.05	0.05	4.5	$(3.5 \pm 0.1) \times 10^{-3}$
0.1	0.1	4.5	$(4.7 \pm 0.1) \times 10^{-3}$
0.1	0.4	3.8	$(4.9 \pm 0.1) \times 10^{-3}$
0.2	0.2	4.5	$(7.2 \pm 0.1) \times 10^{-3}$
0.2	0.8	3.8	$(7.0 \pm 0.1) \times 10^{-3}$
0.4	0.4	4.5	$(1.2 \pm 0.1) \times 10^{-2}$
0.4	0.1	5.3	1.1×10^{-2}
0.5	0.5	4.5	$(1.4 \pm 0.1) \times 10^{-2}$
0.5[d]	0.5[d]		$(1.1 \pm 0.1) \times 10^{-2}$
1.0	1.0	4.5	$(2.4 \pm 0.1) \times 10^{-2}$

[a] Ionic strength 1.0 M ($NaClO_4$). [b] Errors represent the average deviation from the mean. [c] Complex concentration 1.5×10^{-3} M. [d] Value in 90% D_2O.

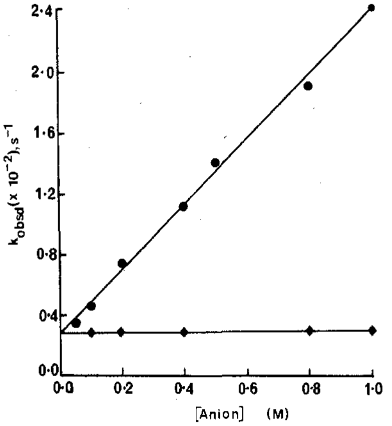

Figure 1. Variation of k_{obsd} with anion concentration for dissociation of $NiLCl_2$ (L = **3**) at 25 °C (ionic strength = 1.0, $NaClO_4$): ●, acetate, pH 4.5 (see Table II); ♦, chloride (as KCl), [H^+] = 0.05 M.

Results and Discussion

Mechanistic Details. Measurement of the dissociation rate constant for the nickel complex of ligand **3** in a series of 1 M acids showed (Table I) that the rate of dissociation is strongly catalyzed by the presence of either the acetate ion or undissociated acetic acid while no significant effect was found in the presence of chloride, perchlorate, or trifluoromethanesulfonate.[21]

The effect of acetate/acetic acid on the dissociation was examined further by first varying the concentration of undissociated acetic acid while the total acetate ion concentration was kept constant. As shown in Table II, no significant effect on the dissociation rate was observed. Similarly the rate constant in D_2O is only marginally different from that observed in H_2O. These observations suggest that it is the acetate ion which is responsible for the catalytic effect. This was confirmed by examining the effect of the acetate ion concentration (in a 1:1 acetic acid/acetate buffer at pH 4.5) on the observed rate constant at constant ionic strength. As shown in Figure 1, the results indicate a functional relationship between the observed rate constant k_{obsd} and the acetate ion (A) concentration of the form

$$k_{obsd} = k_0 + k_A[A] \qquad (1)$$

with $k_0 = 2.7 \times 10^{-3}\ s^{-1}$ and $k_A = 2.1 \times 10^{-2}\ M^{-1}\ s^{-1}$ at 25 °C. While these observations clearly show that the dissociation rate is catalyzed by the presence of the acetate ion, the precise nature of this effect is uncertain; however, the above experiments indicate that the enhancement does not reflect general-acid catalysis.[22,23] Similarly, in the absence of a larger difference between the respective rates in water and deuterium oxide (Table II), there is little evidence for the enhancement

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Table III. Kinetic Data for Dissociation of the Complexes of Type Ni(macrocycle)$^{2+}$ in HCl

macrocycle	ring size	$[H^+]$, M	k_{obsd}(25 °C),[a,b] s^{-1}
1	14	1.0	$(8.8 \pm 0.1) \times 10^{-1}$
		1.0[c]	$(6.1 \pm 0.1) \times 10^{-1}$
		0.2[d]	$(8.7 \pm 0.1) \times 10^{-1}$
2	14	1.0	1.4×10^{-1}
		1.0[c]	$(1.1 \pm 0.1) \times 10^{-1}$
		0.2[d]	1.2×10^{-1}
3	15	1.0[e]	$(3.5 \pm 0.1) \times 10^{-3}$
		1.0[c]	2.5×10^{-3}
		0.5[d]	$(3.6 \pm 0.1) \times 10^{-3}$
		0.2[d]	$(3.1 \pm 0.1) \times 10^{-3}$
		0.1[d]	$(3.1 \pm 0.1) \times 10^{-3}$
		0.05[d]	$(3.1 \pm 0.1) \times 10^{-3}$
		pH 4.5[f]	2.7×10^{-3}
4	15	1.0	1.7×10^{-2}
		1.0[c]	1.1×10^{-2}
		0.1[d]	$(1.7 \pm 0.1) \times 10^{-2}$
5	15	1.0	$(3.8 \pm 0.1) \times 10^{-4}$
		1.0[c]	$(3.2 \pm 0.1) \times 10^{-4}$
		0.1[d]	$(3.6 \pm 0.1) \times 10^{-4}$
6	16	1.0[e]	$(6.4 \pm 0.1) \times 10^{-4}$
		1.0[c]	4.7×10^{-4}
		0.1[d]	6.5×10^{-4}
7	17	1.0[g]	>0.5

[a] Errors represent the average deviation from the mean. [b] For all determinations complex concentrations were in the range 10^{-2}–10^{-3} M. [c] Value in 90% D_2O. [d] Ionic strength 1.0 (KCl). [e] Corresponding values for **3** and **6** in 90% methanol (1 M HCl) are $(6.5 \pm 0.1) \times 10^{-3}$ and $(3.6 \pm 0.1) \times 10^{-3}$ s^{-1}, respectively. [f] k_0 from data in acetic acid buffers at pH 4.5 (see text). [g] Value obtained in 90% methanol and also in 50% dimethyl sulfoxide—because of low solubility it was not possible to obtain the corresponding value in water.

Table IV. Activation Parameters for Dissociation of the Complexes of Type Ni(macrocycle)$^{2+}$ in 1 M HCl[a]

macrocycle	ring size	$\Delta H^{\ddagger}$, kJ mol^{-1}	$\Delta S^{\ddagger}$, J K^{-1} mol^{-1}
1	14	45 ± 2[b]	-95 ± 4[b]
1	14	41 ± 2[c]	-113 ± 6[c]
2	14	49 ± 2	-96 ± 6
3	15	68 ± 2	-63 ± 8
4	15	60 ± 2	-79 ± 7
5	15	81 ± 4	-6 ± 6
6	16	97 ± 2	52 ± 6

[a] Determined from least-squares fits to the Eyring equation, using data from at least six temperatures over the approximate range 10–50 °C. [b] Errors represent three standard deviations. [c] Values in 90% D_2O.

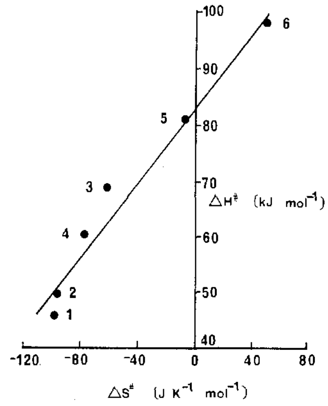

Figure 2. $\Delta H^{\ddagger}$ vs. $\Delta S^{\ddagger}$ for dissociation of $NiLCl_2$ (L = the O_2N_2-donor macrocycles **1**–**6**) in 1 M HCl.

being a consequence of general-base catalysis.[22]

Studies at different acid concentrations in the range 0.05–1.0 M indicated that, under the experimental conditions used, the reaction is zero order with respect to the acid concentration. As shown in Table III, only a marginal difference was observed for the value of k_0 obtained in acetate buffer at pH 4.5 and the values of k_{obsd} in 0.05 and 1 M HCl. Combined with the small effect of the replacement of H_2O by D_2O, these results fit the reaction mechanism (2)–(4) in which the function of

$$NiL^{2+} \xrightarrow{k_0} Ni^{2+} + L \quad \text{(rate determining)} \tag{2}$$

$$NiL^{2+} + A^- \xrightarrow{k_A} NiA^{2+} + L \quad \text{(rate determining)} \tag{3}$$

$$L + 2H^+ \rightarrow LH_2^+ \quad \text{(fast)} \tag{4}$$

the acid is to scavenge the free ligand formed in reaction 2 and in which reaction 3 is of importance only for the acetate ion.[24] Alternatively, the anion-dependent pathway could likely involve a preequilibrium of the type

$$NiL^{2+} + A^- \overset{K}{\rightleftharpoons} NiLA^+$$

followed by the rate-determining loss of L from the adduct. In such a case the observed second-order rate constant k_A would equal Kk_A' (where k_A' is the first-order rate constant for the dissociation of $NiLA^+$).

The acid independence of the dissociation rate together with studies on the related S_2N_2-donor macrocyclic complexes[25] suggests that the mechanism for removal of the macrocycle from the nickel(II) may involve cleavage of one of the Ni–O bonds in the rate-determining step. However, if such is the case, it is not clear whether it is the first or second such bond cleavage which is rate determining.

An acid-independent mechanism has also been established for the dissociation of certain alkali-metal complexes of oxygen–nitrogen cage type ligands;[19,26] however, for other complexes of this type, an acid dependence has also been observed.[19,26] A number of studies,[14,16,18] involving transition-metal complexes of macrocycles containing only nitrogen-donor atoms, have shown the existence of an acid-dependent pathway for dissociation in acid media.

Hydrochloric acid was employed for a comparative survey of the dissociation of the nickel complexes derived from ligands **1**–**7** since, for anions other than chloride, precipitation frequently occurred during the course of the reaction (especially with perchlorate or trifluoromethanesulfonate). As the anion-assisted pathway is insignificant for chloride ion, a comparison of rate constants and activation parameters for the series (Table IV) directly reflects comparison of the respective k_0 values.

Activation Parameters. In the above series the increasing rates of dissociation are accompanied by a trend to lower activation enthalpies and more negative entropies (Table IV);

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(24) In contrast to acetate, any contribution from chloride ion to the dissociation is, at the most, very small (Figure 1). For this system, $k_{Cl^-}[Cl^-] < 7\%\ k_{obsd}$ in 1 M $[Cl^-]$, whereas k_0 corresponds exactly to the value of 2.7×10^{-3} s^{-1} obtained for the acetate system. For temperatures up to 43 °C, there was still no evidence for any significant contribution of k_{Cl^-} to k_{obsd} [in 0.2 and 0.8 M chloride (ionic strength 1.0, $NaClO_4$). The observed rates of dissociation in 0.05 M acid were $(1.5 \pm 0.1) \times 10^{-2}$ s^{-1} and $(1.6 \pm 0.1) \times 10^{-2}$ s^{-1} at 43 °C].

(25) For the S_2N_2-donor analogue of ligand **3**, two consecutive first-order reactions were observed for the dissociation of its nickel complex in hydrochloric acid; the first rate constant (k_{obsd} (25 °C) = 7.2×10^{-4} s^{-1}) is about an order of magnitude greater than the second (9.4×10^{-5} s^{-1}). Both steps are acid independent and both are accelerated by acetate. For the present O_2N_2-donor systems, observed rates are greater than those for the above S_2N_2 systems (which in turn are greater than the usual rates for dissociation of N_4-donor macrocyclic nickel(II) complexes)—a further indication that the nitrogen donors are not involved in the rate-determining step.

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the range of values of $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ being well outside the experimental uncertainties in these parameters. A plot of $\Delta H^{\ddagger}$ vs. $\Delta S^{\ddagger}$ (Figure 2) reveals a reasonable isokinetic relationship,[27] with an isokinetic temperature of about 330 K. Although caution should be exercised,[28] the isokinetic correlation supports the existence of a constant mechanism throughout the series.

Macrocycle Structure and the Dissociation Rate. The rates for the nickel complexes of the unsubstituted macrocycles **1**, **3**, **6**, and **7** indicate that there is a clear dependence of the dissociation rate on macrocyclic ring size: the rate constants show a progressive decrease as the macrocyclic ring size increases from 14 to 16 membered followed by a sharp increase for the complex of the 17-membered ring. The occurrence of a minimum rate for the series at the 16-membered ring complex demonstrates dramatically the effect that macrocyclic ring size can have on kinetic lability. In addition, this sequence of kinetic stabilities follows a pattern similar to that of the thermodynamic stabilities (obtained in 95% methanol) which peak at the 16-membered macrocyclic complex.[8,29]

Previous studies involving copper complexes of S_4-donor macrocycles have also demonstrated that ring size strongly influences the dissociation rates but has a smaller effect on the rates of formation.[13] Further, limited kinetic data for two high-spin nickel(II) complexes of N_4-donor macrocycles[18] suggest that the complex of the macrocycle of best fit yields the slowest dissociation rate.

For the present series, hole size considerations suggest that the 16-ring macrocycle provides the best fit for nickel(II). A survey[8] of published data for octahedral nickel(II) indicates a mean (eight distances) nickel–ether oxygen bond distance of 2.15 Å, whereas a mean nickel–nitrogen distance of about 2.10 Å is typical of sp^3-hybridized nitrogens in high-spin macrocyclic nickel complexes.[3] Hence an optimum hole size of 4.25 Å appears reasonable for the present series. This is slightly larger than that of 4.20 Å found (sum of the mean Ni–O and Ni–N distances)[3] for the nickel chloride complex of the 15-membered macrocycle (**3**) but close to that of 4.28 Å found[8] for the nickel complex of the 16-membered analogue (**6**).[30]

Apart from ring size, macrocycle substituents also affect the dissociation rates (Table III). Compared with the case of the corresponding unsubstituted analogues, there is a decrease in the rate of dissociation for the complexes of the N-methylated (**5**) or C-methylated (**2**) derivatives. This diminution of the rate perhaps arises from the methyl groups offering a steric barrier[31] to the folding of the macrocycle which is a necessary step if ligand dissociation is to occur. Other studies[11,32] involving N_4-donor macrocycles have also shown that N-methylation can markedly affect rates of dissociation.

Preliminary studies indicate very different dissociation rates for complexes having a given macrocycle of the present type but incorporating transition-metal ions other than nickel. Such kinetic discrimination shows promise for development of efficient separation techniques for metal ions of the transition series. Further studies in this area are proceeding.

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Registry No. **2** dihydrochloride, 72228-66-1; **3** dihydrochloride, 72228-67-2; $NiCl_2$ (L = **1**), 66793-50-8; $NiCl_2$ (L = **2**), 72228-93-4; $NiCl_2$ (L = **3**), 66810-83-1; $NiCl_2$ (L = **4**), 66793-39-3; $NiCl_2$ (L = **5**), 66793-41-7; $NiCl_2$ (L = **6**), 66793-45-1; $NiCl_2$ (L = **7**), 71375-56-9.

Supplementary Material Available: A complete tabulation of all dissociation rate data (5 pages). Ordering information is given on any current masthead page.

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Contribution from the Departments of Chemistry, University of Denver, Denver, Colorado 80208, and University of Colorado at Denver, Denver, Colorado 80202

Metal–Nitroxyl Interactions. 14. Bis(hexafluoroacetylacetonato)copper(II) Adducts of Spin-Labeled Pyridines

P. M. BOYMEL, G. R. EATON,* and S. S. EATON

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Spin-labeled ligands have been prepared by condensing pyridine-4-carboxaldehyde, pyridine-3-carboxaldehyde, and pyridine-2-carboxaldehyde with 4-amino-2,2,6,6-tetramethylpiperidinyl-1-oxy. The equilibrium constants have been obtained for the coordination of these ligands to bis(hexafluoroacetylacetonato)copper(II) in CCl_4. The EPR spectra of the 1:1 complexes exhibit electron–electron coupling constants in CCl_4 at room temperature of 43.5, 94.0, and >1000 G for the 4-, 3- (two isomers of complex), and 2-substituted pyridines, respectively. Coupling constants of 71 and 150 G were observed at ca. −190 °C for the 4- and 3-substituted pyridine adducts in toluene glass.

Introduction

The widespread use of spin labels in the study of biological systems has led to considerable interest in the perturbations of the EPR spectra which may occur when a metal ion is also present.[1] We have reported several examples of copper–nitroxyl complexes in which resolved electron–electron coupling is observed in the room-temperature EPR spectra.[2-7] Values

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* To whom correspondence should be addressed at the University of Denver.

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