Registry No. Δ-(−)$_D$-[Co(L-tart)(phen)$_2$]ClO$_4$, 59532-75-1; Λ-(+)$_D$-[Co(L-tart)(phen)$_2$]ClO$_4$, 59573-75-0; Δ-(−)$_D$-[Co(L-tart)-(bpy)$_2$]ClO$_4$, 59532-77-3; Λ-(+)$_D$-[Co(L-tart)(bpy)$_2$]ClO$_4$, 59573-76-1; *cis*-[CoCl$_2$(bpy)$_2$]Cl, 14522-39-5; *cis*-[CoCl$_2$(phen)$_2$]Cl, 14267-71-1.

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The Effect of Coordination Geometry on Electrochemical Oxidation and Reduction of *N*-Methylporphyrin Complexes of Cobalt(II) and Manganese(II)

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The metal atoms in complexes of the *N*-methylporphyrins must lie significantly out of the plane of the four nitrogen atoms of the chelating ligand. In the square-pyramidal geometry of these complexes, overlap of the metal-type orbitals with the porphyrin π system appears to be significantly less than in the corresponding complexes of planar porphyrin ligands. The half-wave potentials for the reversible metal oxidations of complexes in acetonitrile occur at 0.77 V (vs. Ag|AgCl) for Co(II)–Co(III) in chloro-*N*-methyl-$\alpha,\beta,\gamma,\delta$-tetraporphinatocobalt(II), 0.72 V for Co(II)–Co(III) in chloro(*N*-methyldeuteroporphyrin IX dimethyl ester)cobalt(II), and 0.77 V for Mn(II)–Mn(III) in chloro-*N*-methyl-$\alpha,\beta,\gamma,\delta$-tetraphenylporphinatomanganese(II). The ligand oxidations for the *N*-methyltetraphenylporphyrin complexes are 1.2–1.3 and 1.4–1.6 V. The lack of a peak between 0.0 to 0.9 V in the cyclic voltammogram of chloro-*N*-methyl-$\alpha,\beta,\gamma,\delta$-tetraphenylporphinatozinc(II) and appearance of peaks at 1.1 and 1.5 V supports the oxidation potential assignments. Very similar oxidation potentials are exhibited by the cobalt(II) and manganese(II) complexes. The potential for manganese(II) oxidation is much different from the value found for the planar tetraphenylporphyrin complexes, demonstrating less stabilization of high oxidation states in the nonoctahedral geometry of the *N*-methylporphyrin complexes. Reduction of the complexes leads to two very similar half-wave potentials (at −0.77 and −0.78 V and at −1.26 and −1.23 V for Co(II) and Mn(II), respectively) which are assigned to ligand reduction. There is no evidence for reduction to Co(I) in this distorted coordination geometry which will not allow a planar environment for the d^8 species.

Introduction

Porphyrin ligands often stabilize high oxidation states of transition metal ions. Such species as Ag(II) and Mn(III) are found as common stable oxidation states in porphyrin complexes exposed to air.[1] Complexes of Cr(IV),[2] Fe(IV),[3] Ag(III),[4] Pb(IV),[5] and other high oxidation state metalloporphyrins have been generated by electrochemical means. The stability of high oxidation states of metal atoms in porphyrins has been related to the restricted size and concomitant strong σ interaction of the coordination site[6] and the ability of the porphyrin ligand to delocalize positive charge via the conjugated π system and "soften" the metal atom.[7]

In view of the pattern of stabilization of higher oxidation states, it is interesting to note that the porphyrins (and related corroles) also stabilize the 1+ oxidation state of cobalt. Early extended Hückel calculations[8] indicated that the lowest available orbital of CoTPP would be an orbital of predominantly metal character while for other first row transition metal complexes with an oxidation state of two the lowest lying orbital would be of predominantly ligand character. The reduction of Co^{II}TPP to Co^{I}TPP$^-$ has been well documented[9,10] and occurs in DMSO solution at −0.82 V. The Co(I) center is implicated in the function of vitamin B$_{12}$,[11] so that reduction of Co(II) in tetrapyrrole macrocycles takes on biological significance. Since the Co(I) complexes of tetraphenylporphyrin and the corrole ligand in vitamin B$_{12}$ are both diamagnetic, strong tetragonal distortion of the ligand field is indicated. The d^8 configuration of Co(I) would be most stabilized in a ligand field that is highly tetragonal and which could allow for some π back-bonding from the metal to the ligand. Co(I) is stabilized by such π back-bonding in carbonyl, isonitrile, and phosphine complexes.[12]

We are interested in the changes in the coordination chemistry of the porphyrins caused by N-methylation. The methylation of a pyrrolic nitrogen requires that the ligand be deformed. The bound metal atom must lie out of the plane of the four nitrogen atoms of the coordination site. The size of the region about the metal atom opposite to the porphyrin appears from molecular models to be large enough to accommodate bidentate as well as unidentate ligands although present evidence[13,14] is based only on unidentate ligands and shows single axial ligation in *N*-methylporphyrin complexes. Two recent crystal structure determinations of chlorocobalt(II) N-alkylated porphyrins[15,16] show five-coordinate geometry bonding to all four porphyrin nitrogen atoms and the chloride ligand. We propose a similar geometry for the chloromanganese(II) complex.

In this report the electrochemical properties of the cobalt(II), manganese(II), and zinc(II) complexes of *N*-methyl-$\alpha,\beta,\gamma,\delta$-tetraphenylporphyrin are compared to those of the corresponding nonmethylated porphyrin complexes. The change in coordination geometry of the metal center dramatically alters the ease of oxidation of the metal atoms.

Experimental Section

Preparation of *N*-Methylporphyrins. *N*-Methyl-$\alpha,\beta,\gamma,\delta$-tetraphenylporphine (NCH$_3$TPP) was prepared from CH$_3$SO$_3$F (Aldrich)

and tetraphenylporphine in refluxing dichloromethane, purified by column chromatography, and crystallized. Visible absorption spectra and NMR spectra match those of the analyzed sample.[13]

N-Methyldeuteroporphyrin IX dimethyl ester was obtained by the reaction of CH_3SO_3F with deuteroporphyrin IX dimethyl ester (1:1 mol ratio) in dichloromethane at 115 °C for 1 h in a glass and Teflon pressure vessel.[17] Protoporphyrin IX was obtained from horse and bovine blood (courtesy of the Colorado State University Veterinary Hospital) by the method of Yonetani[18] and was converted to deuteroporphyrin IX dimethyl ester by standard procedures.[19] The *N*-methyldeuteroporphyrin IX dimethyl ester was purified by column chromatography on alumina. Dichloromethane was used as the eluent to remove the unreacted, planar porphyrin. The second band, which appeared purple on the column, was removed with acetonitrite and dichloromethane (1:5 v/v). This second band, which eluted brown, was the monomethyl species and was rechromatographed on alumina soaked in benzene and was eluted with $CHCl_3$. NMR spectra are consistent with the proposed N-methylated product, as described previously.[20]

Preparation of the Metalloporphyrin Complexes. The cobalt(II) and zinc(II) complexes were prepared from $CoCl_2 \cdot 6H_2O$ and $ZnCl_2$ in acetonitrile. To prepare the manganese(II) complex, anhydrous $MnCl_2$[21] was dissolved in absolute ethanol. Each solution of a fivefold excess of the metal salt was dried over Linde 4 Å molecular sieves for 1 h and added to a dichloromethane solution of NCH_3TPP. An equal volume of acetonitrile and several drops of the noncoordinating base, 2,6-di-*tert*-butylpyridine (Willow Brook Laboratories), were added and crystals were obtained on slow evaporation. The crystals were washed with acetonitrile, air dried, and dissolved in dichloromethane (10 ml). Acetonitrile (40 ml) was added and crystals were obtained on slow evaporation. The crystals were analyzed (Alfred Berhardt Laboratories, Mülheim, West Germany). Anal. Calcd for $ClCoNCH_3TPP$ ($CoC_{45}N_4H_{31}Cl$): C, 74.83; H, 4.33; N, 7.76; Cl, 4.91. Found: C, 74.68; H, 4.32; N, 7.91; Cl, 4.88. Calcd for $ClZnNCH_3TPP$ ($ClZnC_{45}H_{31}N_4Cl$): C, 74.17; H, 4.29; N, 7.69. Found: C, 74.05; H, 4.39; N, 7.55. Calcd for $ClMnC_{45}H_{31}N_4Cl$: C, 75.25; N, 7.80; H, 4.35; Cl, 4.94. Found: C, 75.19; N, 7.85; H, 4.38; Cl, 4.89.

The cobalt(II) complex of *N*-methyldeuteroprophyrin IX dimethyl ester was formed in situ from the porphyrin and $CoCl_2 \cdot 2H_2O$ in acetonitrile and verified by mole ratio analysis[22] to be a 1:1 complex. Anal. Calcd: C, 61.35; H, 5.47; N, 8.67; Cl, 5.49. Found: C, 60.93; H, 5.88; N, 8.49; Cl, 5.14.

$\alpha,\beta,\gamma,\delta$-Tetraphenylporphinatocobalt(II) was prepared by the method of Adler et al.,[23] washed with ethanol, and crystallized from toluene. The visible absorption spectrum was that reported in the literature.[24] All solvents were distilled and dried by typical procedures.[25]

Chloro(deuteroporphyrin IX dimethyl ester)cobalt(II) was also prepared by the method of Adler et al. and its spectrum was the typical two-banded spectrum of metal complexes of deuteroporphyrin.

Magnetic Susceptibility Measurements. The magnetic susceptibilities of the $ClCoNCH_3TPP$ and $ClMnNCH_3TPP$ complexes were determined using the Cahn Electrobalance Model RTL permanent magnet Faraday system.

Spectral Measurements. Visible absorption spectra were recorded on a Cary 14 spectrophotometer. NMR spectra were obtained using a JEOL MH-100 spectrometer.

Electrochemical Measurements. The PAR Model 170 (Princeton Applied Research) was employed for cyclic voltammetry measurements. Acetonitrile was distilled from P_2O_5 and stored over molecular sieves. Tetraethylammonium perchlorate (Eastman) was recrystallized twice from hot anhydrous ethanol and dried for several hours at 90 °C. A platinum button electrode approximately 25 mm^2 was the working electrode, a 16 gauge platinum wire was the auxiliary electrode, and a Beckman fiber tip Ag|AgCl electrode was the reference. The electrolyte solution was 0.5 M tetraethylammonium perchlorate in acetonitrile and was deaerated with purified nitrogen for at least 30 min before measurements were taken. The tetraphenylporphyrin complexes were dissolved in 1 ml of benzonitrile before being introduced into 25 ml of electrolyte solution. Their solubility in acetonitrile is very low (about 10^{-5} M at 25 °C).

Results

Cobalt(II) and manganese(II) complexes of *N*-methyl-$\alpha,\beta,\gamma,\delta$-tetraphenylporphine ($NCH_3TPP$) are not oxidized by atmospheric oxygen even on standing in solution for weeks. Magnetic susceptibility measurements verify the assigned oxidation states. The effective magnetic moment of $ClCoNCH_3TPP$ is 4.9 ± 0.1 μ_B at 298, 229, 179, 159, and 153 °C, using the Curie Law. The spin only value for high spin Co(II) is 3.87 μ_B but typical experimental moments are in the range of 4.3 to 5.2 μ_B.[26] The effective magnetic moment for $ClMnNCH_3TPP$ is 5.7 μ_B at 297 °C. The spin only moment for Mn(II) is 5.92 while typical measured moments range from 5.7 to 6.5 μ_B.[26]

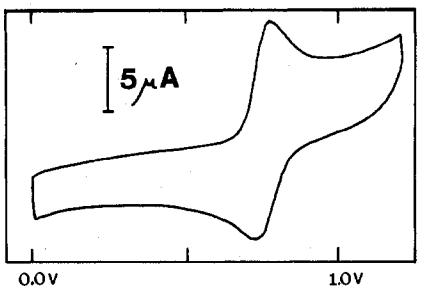

Figure 1. The cyclic voltammogram of chloro-*N*-methyl-$\alpha,\beta,\gamma,\delta$-tetraphenylporphinatocobalt(II) in acetonitrile with 0.5 M tetraethylammonium perchlorate. The reference electrode is Ag|AgCl.

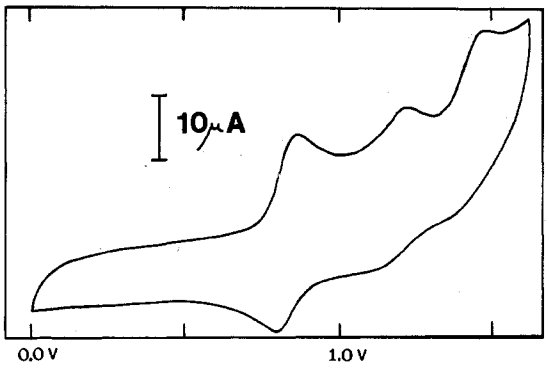

Figure 2. The cyclic voltammogram of chloro-*N*-methyl-$\alpha,\beta,\gamma,\delta$-tetraphenylporphinatomanganese(II) in acetonitrile containing 0.5 M tetraethylammonium perchlorate.

Cyclic voltammograms of chloro-*N*-methyl-$\alpha,\beta,\gamma,\delta$-tetraphenylporphinatocobalt(II) and chloro(*N*-methyldeuteroporphyrin IX dimethyl ester)cobalt(II) in acetonitrile show reversible one-electron waves with $E_{1/2}$ of 0.77 and 0.72 V, respectively. (All $E_{1/2}$ values are reported vs. Ag|AgCl.) Figure 1 shows the voltammogram for $ClCoNCH_3TPP$ in the region 0.0–1.2 V. Following the oxidation of the metal center, the porphyrin ligands are oxidized. The half-wave potentials for oxidation of the tetraphenylporphyrin ligand in $ClCoNCH_3TPP$ are 1.30 and about 1.6 V. For the *N*-methyldeuteroporphyrin IX dimethyl ester ligand the oxidation half-wave potentials are also 1.30 and 1.6 V in the cobalt(II) complex.

The cyclic voltammogram of chloro-*N*-methyl-$\alpha,\beta,\gamma,\delta$-tetraphenylporphinatomanganese(II) is very similar to that of $ClCoNCH_3TPP$. The initial measurement led to several additional preparations and magnetic susceptibility measurements to ensure that an error had not been made. The Mn(II)–Mn(III) oxidation occurs at 0.78 V and the ligand oxidations at 1.16 and 1.4 V. The voltammogram in the region 0.0–1.6 V is shown in Figure 2.

The cyclic voltammogram of the corresponding zinc(II) complex was recorded to verify the assignment of metal center and ligand oxidation. The oxidation of the $ClZnNCH_3TPP$ complex occurs at 1.05 and 1.5 V with no wave appearing in the region 0.0–0.9 V.

Cyclic voltammetry of $\alpha,\beta,\gamma,\delta$-tetraphenylporphinatocobalt(II) in benzonitrile with 0.1 M tetraethylammonium

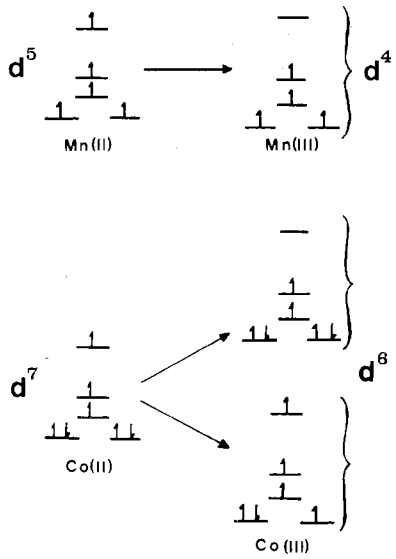

Figure 3. A simple ligand field picture of the oxidation of square based pyramidal complexes of a high spin d^5 ion (Mn(II)–Mn(III)) and a high spin d^7 ion (Co(II)–Co(III)). The d^6 product may have either two or four unpaired electrons in a square pyramidal environment.

perchlorate gave the values $E_{1/2}$ = 0.50 V (Co(II)–Co(III)), 1.19 V (ligand oxidation), and 1.6 V (ligand oxidation), agreeing reasonably with the literature values of 0.52, 1.19, and 1.4 V.[27]

Discussion

The half-wave potential for the oxidation of manganese(II) to manganese(III) is 0.78 ± 0.01 V in chloro-*N*-methyl-α,β,γ,δ-tetraphenylporphinatomanganese(II). This value is very similar to that for the Co(II) to Co(III) oxidation and is very much different from the Mn(II) to Mn(III) potential in MnTPP (−0.21V[28]). The Mn atoms in MnTPP,[29] MnTPPCl,[29] and $ClMnNCH_3TPP$ are all high spin, and presumably so is Mn(III) in a square-pyramidal environment. The Mn(II)–Mn(III) oxidation processes therefore are comparable for the N-methyl and nonmethylated complexes. The higher oxidation potential for Mn(II) in the *N*-methylporphyrin complex relative to the corresponding nonmethylated tetraphenylporphyrin complex may well arise from less stabilization of the Mn(III) oxidation state. The coordination site of the *N*-methylporphyrin ligand is less restricted in size. The strong σ interaction which has been porposed as the reason for the stability of the 3+ oxidation state[27] is thereby lessened. The ability of the distorted porphyrin to interact with metal d orbitals may be less in the case of the distorted porphyrin also, leading to poorer charge delocalization.

The half-wave oxidation potential of Co(II) in α,β,γ,δ-tetraphenylporphinatocobalt(II) is 0.52 V,[27] vs. Ag|AgCl, while the corresponding value of Co(II) in the deuteroporphyrin IX dimethyl ester complex is 0.70 V. The half-wave oxidation potential for Co(II) in chloro-*N*-methyl-α,β,γ,δ-tetraphenylporphinatocobalt(II) is 0.77 V while that of Co(II) in the *N*-methyldeuteroporphyrin IX dimethyl ester complex is 0.72 V. It is apparent that the nature of the substitutents on the *N*-methylporphyrin ligand, at least for the cases chosen, does not change the metal oxidation potential for Co(II) to as large an extent as found for the corresponding planar porphyrin complexes.

The Co(II) to Co(III) potential is not as easy to compare for the cases of the *N*-methylporphyrin and nonmethylated porphyrin complexes. The Co(II) is high spin with three unpaired electrons in the *N*-methylporphyrins and the Co(III) species are also likely to be paramagnetic in a five-coordinate environment. Both $Co^{II}TPP$ and $Co^{III}TPP^+$, however, are low

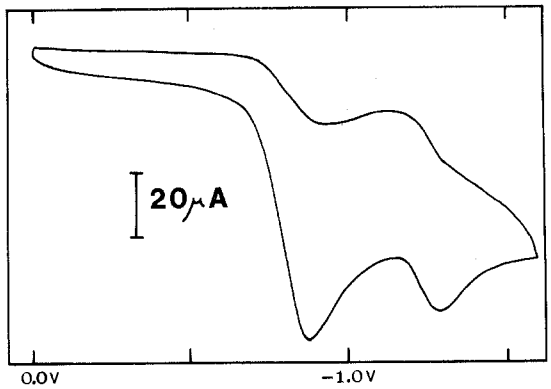

Figure 4. Cyclic voltammogram for reduction of chloro-*N*-methyl-α,β,γ,δ-tetraphenylporphinatomanganese(II) in acetonitrile with 0.5 M tetraethylammonium perchlorate.

spin.[30] The similar spin state of the *N*-methylmetalloporphyrin complexes is, in fact, the most probable reason for the striking similarity of the half-wave oxidation potentials for the Mn(II) and Co(II) *N*-methyltetraphenylporphyrin complexes. The oxidation process for square base pyramidal complexes of Mn(II) and Co(II) is depicted in Figure 3, using a conventional ligand field splitting diagram for a square-based pyramid in which one of the basal coordination sites (the *N*-CH_3 site) differs slightly from the other three basal coordination sites. There is no ambiguity concerning the expected spin state for $ClMn^{III}NCH_3TPP^{2+}$. The splitting between the d_{z^2} and d_{xy} orbitals in a square base pyramidal field is expected to be much less than that between the $d_{x^2-y^2}$ and d_{z^2} orbitals,[30] resulting in four unpaired electrons. $Co^{III}NCH_3TPP^{2+}$ could possibly have either four or two unpaired electrons in a square-pyramidal ligand field. Since the oxidations of Co(II) and Mn(II) are so similar in energy, the implication is that the electron is removed from the $d_{x^2-y^2}$ orbital in both cases, leading to $Co^{III}NCH_3TPP^{2+}$ with two unpaired electrons.

The reduction of the $ClMnNCH_3TPP$ complex gives the expected two reductions of the porphyrin ligand at approximately −0.78 and −1.23 V, as shown in Figure 4. The reduction of $ClCoNCH_3TPP$ *also* gives two similar waves at −0.77 and −1.26 V. We find no evidence for reduction to the Co(I) state. It therefore appears that the absence of the strongly tetragonal ligand field found in the nonmethylated TPP complex and/or the lower metal–ligand π interaction expected in the distorted complex are effective in preventing stabilization of Co(I). This result suggests that the distortion of the coordination geometry about the Co(I) center in its porphyrin and corrole complexes (expected because of the large size of Co(I) relative to the coordination site[32]) is not as severe as the distortion imposed by N-methylation of the coordination site.

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Registry No. $ClCo^{II}NCH_3TPP$, 51552-52-4; $ClMn^{II}NCH_3TPP$, 59765-80-9; $ClZn^{II}NCH_3TPP$, 59765-81-0; $ClCo^{II}NCH_3$ deuteroporphyrin IX dimethyl ester, 59811-75-5; $ClCo^{III}NCH_3$ deuteroporphyrin IX dimethyl ester$^+$, 59811-76-6; $ClCo^{III}NCH_3TPP^+$, 59765-82-1; $ClMn^{III}NCH_3TPP^+$, 59765-83-2.

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Complexation of Tetra-μ-carboxylato-dirhodium(II) with Imidazole

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The stepwise formation constants and the enthalpies and entropies of reactions for the formation of 1:1 and 1:2 adducts of $Rh_2(O_2CR)_4$, where R = CH_3OCH_2, CH_3, or CH_3CH_2, with imidazole have been determined by an entropy titration technique in aqueous solution at physiological pH. The thermodynamic stabilities and the negative enthalpy changes were found to be in the order propionate > acetate > methoxyacetate. This trend could be explained in terms of a desolvating effect of the R group on the bridging carboxylate ions at the axial positions of the rhodium(II) complexes. The observed variation of antitumor activity for these rhodium(II) carboxylates parallels the above order.

Introduction

In 1974 our laboratory discovered that tetra-μ-acetato-dirhodium(II) exhibited anticancer activity against Leukemia 1210 and Ehrlich ascites tumors in mice.[1] Since that time we have been investigating the anticancer activity of several rhodium(II) carboxylates and have found that the acetate, propionate, and butyrate complexes are all antineoplastic agents.[2,3] Rhodium(II) butyrate was the most potent antitumor agent followed by the propionate, acetate, and methoxyacetate complexes. All of the complexes inhibit DNA and RNA synthesis in vitro with an order of inhibition of methoxyacetate < acetate < propionate < butyrate.[2,3] These studies showed that the anticancer activity, toxicity, and enzyme inhibition increased with length of the carbon chain of the bridging acid.

In a more recent study we reported the formation constants for the complex formation reactions involving rhodium(II) methoxyacetate, acetate, and propionate and the ligands 5′-AMP, 5′-ADP, and 5′-ATP.[4] The purpose of the study was to determine if the thermodynamic stability of the rhodium(II) carboxylate adducts correlated with the disparate effects seen with respect to their biological activity. A correlation was found in that the order of stability was propionate > acetate > methoxyacetate. It was concluded that the increased stability of the rhodium(II) propionate adducts over that of the corresponding rhodium(II) acetate complex could account for at least a part of the variation in biological activity.

It is difficult to interpret the order of stability of the rhodium(II) carboxylate adducts in terms of an electronic effect. The methoxyacetate ion, being less basic than the acetate or propionate ion, should produce a lower electron density on the metal ion and thus a stronger interaction with the two axial ligands. Since rhodium(II) methoxyacetate forms weaker complexes than the rhodium(II) propionate species, some alternate interpretation seems more plausible.

In order to understand the reasons for the observed thermodynamic stabilities of the adducts we have measured the enthalpies and entropies of formation of 1:1 and 1:2 adducts of rhodium(II) methoxyacetate, acetate, and propionate with imidazole. Imidazole was chosen for the study for three reasons: (1) it is an important ligand in biologic milieu,[5] (2) it forms complexes with the rhodium(II) carboxylates at physiological pH, and (3) the system lends itself nicely to evaluation by the entropy titration technique used in this investigation.

Materials and Methods

Chemicals. Rhodium(II) acetate was obtained from Matthey Bishop, Inc., Malvern, Pa. 19355. This was further purified by recrystallization from acetone. Other carboxylates were synthesized as described previously.[6] All of the rhodium(II) carboxylates were dried before use. The purity was checked by NMR and tga and finally the molar absorptivities of the solutions were compared with the literature values: found, 224–229; lit., 230.

Imidazole was obtained from Eastman Organic Chemicals, Rochester, N.Y. It was recrystallized from an acetone–ether mixture and the purity evaluated by the standard titrimetric procedure.

Solvent. All solutions were made in a phosphate buffer prepared by dissolving potassium mono- and dihydrogen phosphates in a ratio suitable for the desired pH and ionic strength in deionized water. The concentration of total phosphate, ionic strength, and pH were 0.038 98 M, 0.1, and 7.4, respectively.

Entropy Titration. This technique allows the calculation of equilibrium constant and enthalpy and entropy of reaction from a thermometric titration curve. The procedure was popularized by Christensen et al., who successfully applied it to systems such as single-step protonation reaction[7] and multistep metal–ligand complex formation.[8] The apparatus used for continuous titration was a Tronac Model 450 calorimeter with Model 1040 temperature controller. The net heat changes Q_p's, at different points were calculated according to the standard procedure.

Correction Terms. In addition to the complexation reaction, three other factors that contribute to the measured heat and the method