reactions as involving strong coupling in the activated complex perhaps by direct attack on the ring system, but the slow ferrocyanide reaction seems to imply nonadiabaticity. The autoxidation of $[Co^{II}(sep)]^{2+}$ [36] (sep = sepulchrate) yields a value of 1.3 M^{-1} s^{-1} for the O_2/O_2^- self-exchange rate; this should be interpreted with caution because $Co(sep)^{2+/3+}$ has not yet been shown generally to obey the Marcus cross relationship.

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Registry No. Ru(III), 46372-32-1; Ru(II), 19471-53-5; OH, 3352-57-6; CO_2^-, 14485-07-5; $HC(OH)_2$, 14840-85-8; HO_2, 3170-83-0; O_2^-, 11062-77-4; H, 12385-13-6; $[Ru(NH_3)_5isn](TFMS)_2$, 74763-99-8; $[Ru(NH_3)_5H_2O](TFMS)_3$, 53195-18-9.

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Affinity of Aquopentaammineruthenium(II) and -(III) for Esters of Amino Acids

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The paper is concerned with the change in affinity for amines of $Ru(NH_3)_5H_2O^{2+}$ and $Ru(NH_3)_5H_2O^{3+}$ when hydrogen on NH_3 is progressively replaced by alkyl groups. A kinetic method was used to determine the association quotients for Ru(II), and electrochemical measurements then fix those for Ru(III). The equilibrium quotient at 25 °C for the association of Ru(II) with the ligands NH_3, ethyl glycinate, methylamine, and methyl sarcosinate are 3.5×10^4 (earlier work, corrected for the statistical factor), 3.2×10^3, 3.5×10^3, and 50 ± 10 M^{-1}, respectively, and for Ru(III) are 3.6×10^5, 5.5×10^2, 3.5×10^3, and 2.0 M^{-1}. The decrease in affinity for Ru(II) registered when H on ammonia is replaced by an alkyl group is in marked contrast to the effect of the same change when sulfur is the donor atom.

Qualitative observations made by a number of different investigators working in these and perhaps other laboratories have suggested that the affinity of an amine for $Ru(NH_3)_5^{2+}$ decreases when hydrogen in ammonia is replaced by an alkyl group, but no equilibrium quotients have been reported except for NH_3.[1,2] In view of the importance of the polar group NH_2–R in polypeptide and protein chemisty, we felt it to be worthwile to extend the studies on rates and affinities to primary and other amines.

Experimental Section

Chemicals and Reagents. Distilled water used for kinetic runs was purified by distillation from alkaline permanganate before use. Isonicotinamide (Aldrich) was purified by recrystallizing it twice from hot water. Glycine ethyl ester hydrochloride and sarcosine methyl ester hydrochloride were purchased from Aldrich Chemical Co. and United States Biochemical Corp., respectively. They were used without further purification. $[Ru(NH_3)_5Cl]Cl_2$ was prepared according to the method described by Vogt et al.[3] All other chemicals were reagent grade and were used as received.

Preparation of Pentaammineruthenium(II) Complexes. $[Ru(NH_3)_5NH_2CH_2CO_2C_2H_5](PF_6)_2$[4] and $[Ru(NH_3)_5NH_2CH_3](PF_6)_2$[5] were prepared according to the cited literature methods.

Electrochemical Measurement. Reduction potentials of the complexes were measured on a Princeton Applied Research Model 173 potentiostat and Model 175 Universal Programmer system. Platinum was used in the working and counter electrodes; the saturated calomel was used as a reference electrode. The concentration of the complexes was kept at $\sim 1 \times 10^{-3}$ M, and the ionic strength was maintained at $\mu = 0.10$ (LiCl). Reversible behavior was observed in all cases at a scan rate of 100 mV s^{-1}.

Kinetic Measurements. All the kinetic runs were followed by using a Beckman Acta MVII recording spectrophotometer. Temperatures of the experiments were controlled by a Haake FK2 temperature bath. $Ru(NH_3)_5OH_2^{2+}$ solutions were prepared by dissolving $Ru(NH_3)_5Cl^{2+}$ in water and then reducing with zinc amalgam under argon for 20 min. In measuring the rate constants for the formation of amino acid complexes, the competition method[2] was adopted, using isonicotinamide as the competitor ligand. The pH of the solution was adjusted to between 9 and 10 with 4 M NaOH and the ionic strength maintained at $\mu = 0.10$ with lithium chloride. The resulting solution was monitored at $\lambda = 478$ nm, the band maximum of isonicotinamide complex, until no further change in absorbance was observed. Isonicotinamide was chosen as scavenger also in the aquation experiments, and the rates were obtained by measuring the formation of isonicotinamide complex. Because of the slow rate of aquation, side reactions interfere toward the end of the reaction, and accordingly the calculated value of A_∞, based on the measured extinction of 11.9×10^3 M^{-1} cm^{-1} [1] at $\lambda = 478$ nm, was used in the analysis of the data on the aquation of ethyl glycinate and methylamine complexes.

Table I. Reaction of Ethyl Glycinate with $Ru(NH_3)_5OH_2^{2+}$ [a]

pH	10^2[isn], M	10^2[EG], [b] M	$10^3 k_{obsd}$, s^{-1}
9.48	0.983	0.605	1.69
9.73	1.10	0.818	1.87
9.57	1.12	1.06	2.14
9.61	1.02	1.23	2.33

[a] $[Ru(NH_3)_5OH_2^{2+}] = (1.0\text{–}1.5) \times 10^{-4}$ M, $\mu = 0.10$ (LiCl), $T = 25$ °C. [b] EG = ethyl glycinate ester.

The reactions for these systems are very sensitive to oxygen. The oxygen problem becomes even more serious in the study of kinetics of formation because of the instability of the ammineruthenium complexes in the basic solution[6] required for the formation reactions. To minimize interference by oxygen, we used the Zwickel reaction flask[7] and syringe technique[8] for transfers throughout in the reactions. Small amounts of ascorbic acid[9] were added to the reaction mixtures

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Table II. Reaction of Methyl Sarcosinate with $Ru(NH_3)_5OH_2^{2+}$ [a]

pH	10^2 [isn], M	10^2 [SM], [b] M	$10^3 k_{obsd}$, s^{-1}
9.37	1.03	1.18	1.24
9.65	0.989	2.97	1.62
9.46	1.03	3.76	1.73
9.60	0.974	5.61	2.23

[a] $[Ru(NH_3)_5OH_2^{2+}] = (1.0\text{–}1.5) \times 10^{-4}$ M, $T = 25$ °C, $\mu = 0.10$ (LiCl). [b] SM = sarcosinate methyl ester.

to take care of the oxygen which might leak in during kinetic runs. The temperature was maintained at 25 °C for all the measurements.

Results

Ethyl Glycinate Ester. Since the products $Ru(NH_3)_5L^{2+}$ (L = ethyl glycinate ester, methyl sarcosinate ester, methylamine) have absorption spectra not markedly different from that of the reactant $Ru(NH_3)_5OH_2^{2+}$, the competition method was used in the formation experiments. Under pseudo-first-order conditions with both L and isonicotinamide (isn) in large excess, k_{obsd} as measured in an experiment is equal to k_{isn}[isn] + k_L[L]. The rate constant k_{isn} was measured in the present work over the pH range 8.24–10.31 as 0.101 ± 0.003 M^{-1} s^{-1}, close to the value of 0.105 M^{-1} s^{-1} reported[2] for pH 3.5. In the measurement of k_{obsd} the isonicotinamide concentrations were kept at $\sim 1 \times 10^{-2}$ M while the concentrations of amino acid ester varied. The concentrations of $Ru(NH_3)_5OH_2^{2+}$ were maintained around 1×10^{-4} M. The results are shown in Table I. The rate constant for the reaction of ethyl glycinate, k_{EG} was obtained from the slope of the one-parameter linear least-squares fit of the $k_{obsd} - k_{isn}$[isn] vs. [EG] plot. The rate constant thus obtained was found to be $k_{EG} = 0.100 \pm 0.008$ M^{-1} s^{-1}.

Aquation of the ethyl glycinate ester complex was followed by using isonicotinamide to scavenge $Ru(NH_3)_5OH_2^{2+}$ as it is formed. The pH of the solution was maintained at 4–5. The rate constant obtained was observed to be independent of the concentration of isonicotinamide (from 0.05 to 0.2 M) and was found to be $(3.17 \pm 0.03) \times 10^{-5}$ s^{-1}.

Complications were met in the measurements of the rate of aquation above pH 6. These are due in part at least to the hydrolysis of the amino acid ester.[10]

From the measured values of specific rates of forward and reverse reactions the equilibrium quotient for reaction 1 is calculated as $(3.2 \pm 0.3) \times 10^3$ M^{-1} at $\mu = 0.10$.

$$Ru(NH_3)_5OH_2^{2+} + NH_2CH_2COOC_2H_5 \rightleftharpoons Ru(NH_3)_5NH_2CH_2COOC_2H_5^{2+} + H_2O \quad (1)$$

The reduction potential for the $Ru(NH_3)_5NH_2CH_2CO_2C_2H_5^{3+/2+}$ couple was measured in 0.10 M HCl as well as at pH 4 ($\mu = 0.10$ (LiCl)), yielding the same results, namely, $E_f = 0.145$ V (vs. NHE). The reduction potential for $Ru(NH_3)_5OH_2^{3+/2+}$ has been reported[7] as 0.100 V in 0.10 M HCl. With use of electrochemical data and the equilibrium quotient for reaction 1, K_{eq} governing the affinity of $Ru(NH_3)_5OH_2^{3+}$ for $NH_2CH_2CO_2C_2H_5$ is calculated as $\sim 5.5 \times 10^2$ M^{-1}.

Sarcosinate Methyl Ester. There is difficulty in measuring the kinetics of the formation of sarcosinate ester with $Ru(NH_3)_5OH_2^{2+}$, reaction 2, with use of the competition method

$$Ru(NH_3)_5OH_2^{2+} + N(CH_3)HCH_2CO_2CH_3 \rightleftharpoons Ru(NH_3)_5N(CH_3)HCH_2CO_2CH_3 + H_2O \quad (2)$$

because the aquation of the complex interferes and A_∞ for the forward process cannot be obtained directly. To minimize this interference we took only the data early in the reaction and used Guggenheim's[11] method for analysis. The results are shown in Table II. The linear least-squares fit of $k_{obsd} - k_{isn}$[isn] vs. [SM] gives the specific rate constant $k_{SM} = (2.1 \pm 0.4) \times 10^{-2}$ M^{-1} s^{-1} at $\mu = 0.10$.

The solutions of the complex used in the study of the kinetics of the aquation reaction were prepared either by the dissolution of the isolated complex (as PF_6^- salt) in water or by mixing $Ru(NH_3)_5OH_2^{2+}$ with the ligand. In using the latter method, $Ru(NH_3)_5OH_2^{2+}$ ($\sim 1 \times 10^{-3}$ M) was kept in contact with 0.1 M ligand at pH 9 over zinc amalgam under argon atmosphere for 1 h. The measurement of aquation rate was then followed by transferring 1 mL of the solution anaerobically, using the syringe technique, to 9 mL of 0.1 M predeaerated isonicotinamide solution which had been adjusted to pH ~ 4.5, and the resulting solution was monitored at $\lambda = 478$ nm until no further absorbance change was observed. Both methods gave the same kinetic results although the isolated complex we used was known to be impure, as shown by the elemental analysis of the solid and by the fact that the yield of $Ru(NH_3)_5isn^{2+}$ complex at the end of the kinetic runs was only 75% of the theoretical. The rate constant of aquation was found to be independent of the concentration of isonicotinamide and was determined as $(4.2 \pm 0.2) \times 10^{-4}$ s^{-1}. With this and the specific rate constant of formation, the equilibrium quotient for reaction 2 was calculated as 50 ± 10 M^{-1}. The reduction potential for $Ru(NH_3)_5N(CH_3)HCH_2CO_2Me^{3+/2+}$ solution was measured in a solution of $\mu = 0.1$ (LiCl) and pH 2. The value obtained is 0.185 V (vs. NHE); this together with the association quotient of $Ru(NH_3)_5OH_2^{2+}$ for the sarcosinate, leads to 2.0 M^{-1} as the association quotient for $Ru(NH_3)_5OH_2^{3+}$ with the same ligand.

Table III. Reaction of Methylamine with $Ru(NH_3)_5OH_2^{2+}$ [a]

pH	$10^2 \times$ [isn], M	$10^2 \times [MA]_0$, [b] M	$10^2 \times [MA]_{free}$, M	$10^3 \times k_{obsd}$, s^{-1}	$10^2 k_{MA}$, M^{-1} s^{-1}
11.18	0.972	0.569	0.459	1.15	3.66
11.66	0.901	5.69	5.27	3.01	3.98
					av 3.82 ± 0.20

[a] $[Ru(NH_3)_5OH_2^{2+}] = (1.0\text{–}1.5) \times 10^{-4}$ M, $\mu = 0.10$ (LiCl), $T = 25$ °C. [b] MA = methylamine. [c] pK_a of methylamine = 10.66.

Methylamine. The kinetics of the the formation and aquation of $Ru(NH_3)_5NH_2CH_3^{2+}$ complex for reaction 3 were

$$Ru(NH_3)_5OH_2^{2+} + CH_3NH_2 \rightleftharpoons Ru(NH_3)_5NH_2CH_3^{2+} + H_2O \quad (3)$$

measured the same way as that of ethyl glycinate ester complex. The results for the formation reaction are summarized in Table III. The rate constant of the aquation reaction was found to be $(1.08 \pm 0.05) \times 10^{-5}$ s^{-1}, on the basis of two separate experiments.

Since the aquation rate of $Ru(NH_3)_6^{2+}$ is close to that of $Ru(NH_3)_5NH_2CH_3^{2+}$, it was necessary to investigate the possibility that both ammonia and methylamine are dissociated in the aquation reaction of the latter complex, and accordingly we analyzed the content of NH_4^+ in the product solution by using Nessler's reagent. A solution 1×10^{-3} M in $Ru(NH_3)_5NH_2CH_3^{2+}$, 0.10 M in LiCl, and at pH 4.5 was allowed to aquate for 24 h. A total of 10 mL of the product solution was then passed through a cation-exchange column (Bio-Rad AG 50W X2, 200–400 mesh) and eluted with 100 mL of 0.30 M LiCl at pH 3. The eluate was concentrated and then diluted to a volume of 10.0 mL. No color indicative of NH_4^+ was observed upon addition of Nessler's reagent. It was shown[4]

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Table IV. Affinities of Various Acids for Amines[a]

base	H^+ [b]	$Ru(NH_3)_5^{2+}$	$Ru(NH_3)_5^{3+}$	Cd^{2+}	Ni^{2+}
NH_3	7.6×10^9 [c]	3.5×10^4 [g]	3.6×10^5 [g]	5.5×10^2 [h]	2.3×10^2 [i]
NH_2CH_3	1.4×10^{11} [d]	3.5×10^3 [f]	3.5×10^3 [f]	5.6×10^2 [h]	
$NH_2CH_2CO_2Et$	1.9×10^8 [e]	3.2×10^3 [f]	5.5×10^2 [f]		2.0×10^2 [j]
$NH(CH_3)CH_2CO_2Me$	1.3×10^8 [e]	50 ± 10 [f]	2.0 [f]		

[a] At 25°, $\mu = 0.10$ unless otherwise specified. [b] Statistical corrections applied (the measured values are 1.9×10^9, 4.6×10^{10}, 6.3×10^7, and 6.3×10^7). [c] Reference 12. [d] $\mu = 0.03$–1.5.[13] [e] Our values obtained in NaCl(aq), literature[14] value of 5.6×10^7 in $NaNO_3$(aq) for $NH_2CH_2CO_2Et$ (without statistical correction). [f] Present work. [g] Corrected for statistical factor.[2] [h] $\mu = 2.2$.[15] [i] $\mu = 1.0$.[15] [j] $\mu = 1.0$ at 30 °C.[16] In ref 14 it is shown that the temperature coefficient for the association of EG with Cu^{2+} is small.

that NH_4^+ at the level of 1.0×10^{-5} M would have been detectable. This indicates that less than 2% of the starting complex yielded NH_3. Using a solution of $Ru(NH_3)_6^{2+}$ under the same condition, we found that after 24 h NH_4^+ had formed corresponding to somewhat more than 1 half-life for the aquation of the first NH_3. This experiment constitutes a second blank establishing the validity of the analytical method.

The value of K_{eq} for reaction 3 was calculated from the analytical results as $(3.5 \pm 0.4) \times 10^3$ M^{-1}. The reduction potential for $Ru(NH_3)_5NH_2CH_3^{3+/2+}$ couple was measured in 0.10 M HCl medium. The value obtained is 0.100 V which is identical with the reported one[5] and is the same as that of the $Ru(NH_3)_5OH_2^{3+/2+}$ couple. The equilibrium quotient governing the association of CH_3NH_2 with $Ru(NH_3)_5OH_2^{3+}$ is therefore the same as that with $Ru(NH_3)_5NH_2CH_3^{2+}$.

Discussion

Though the relative affinity of the amine series with protons has been a topic of considerable discussion, little attention seems to have been paid to the same issue where metal ions are acting as acids. In Table IV are summarized such data as seem extensive enough to help illuminate the issue.

One item in the comparisons that merits mention is that none of the metal ions show the increase in affinity that is observed for the proton when NH_2CH_3 replaces NH_3. It is expected that steric factors are more important for the metal ions than for the protons, and they countervail against inductive effects. The shielding by alkyl groups of the metal ion from interaction with the solvent is a related factor; the large changes in affinity registered for Ru(III) compared to the other metals suggests that this becomes very important when the charge is 3+.

A point of interest in this context is that although the association quotient is quite sensitive to alkyl substitution on ammonia, the quotient decreasing in the case of Ru(II) by a factor of 700 from NH_3 to the sarcosine methyl ester, the rate of substitution decreases by a factor of only 3.2. Thus in treating the equilibrium quotient as a ratio of specific rates forward and reverse, alkyl substitution exerts by far the greater effect on the rate of the reverse or aquation reaction. A corollary of this behavior is that equilibrium is reached more rapidly, the less stable the complex. This follows because the approach to equilibrium is governed by $k_f + k_r$ (where under pseudo-first-order conditions k_f includes the concentration of the ligand as a factor), and k_r increases rapidly in the series.

The experiment on the interaction of Ru(II) with methylamine was done to highlight the observation[7] that the affinity of H_2S for Ru(II) is much less than that of $(CH_3)_2S$. This is remarkable in view of the comments just made on steric and solvation effects. It becomes even more remarkable considered in the context of the large decrease in affinity for Ru(II) registered by a secondary amine compared to ammonia. In terms of current ideas on metal ions interacting with ligands, it seems necessary to invoke back-bonding to account for the high affinity which reduced sulfur compounds show for Ru(II). The sensitivity of the affinity to the nature of the group attached to sulfur lends credence to the idea that σ^* rather than d orbitals on sulfur accept electon density from the metal.[17]

Finally, it should be noted that the decrease in affinity for Ru(II) noted for a primary amine compared to NH_3 only amounts to 1 kcal/mol or so. The difference does however affect the application of $Ru(NH_3)_5^{2+}$ to biological molecules. While 10^{-2} M Ru(II) suffices to complex free ammonia rather completely, a 10-fold greater concentration is needed when it is desired to complex NH_2 of glycine fully. There may be significant differences in the affinities even for closely related amino acids, and the extension of the studies to others seems worthwhile.

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Registry No. $Ru(NH_3)_5OH_2^{2+}$, 21393-88-4; $Ru(NH_3)_5OH_2^{3+}$, 25590-52-7; ethyl glycinate, 459-73-4; methyl sarcosinate, 5473-12-1; methylamine, 74-89-5; $Ru(NH_3)_5NH_2CH_2CO_2C_2H_5^{3+}$, 73690-16-1; $Ru(NH_3)_5N(CH_3)HCH_2CO_2Me^{3+}$, 74924-85-9; $Ru(NH_3)_5NH_2CH_3^{3+}$, 74924-86-0.

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