IC980584U

Kinetics of 2-Halopyridine Substitution at Pentaammineruthenium (II)

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Supplementary Material

Supplementary Experimental Section

Kinetic Experiments. $Ru(NH_3)_5Cl_3$ and $Ru(NH_3)_5(CF_3SO_3)_3$ were synthesized from $Ru(NH_3)_6Cl_3$ according to previously published methods.[1,2] Solutions of $[Ru(NH_3)_5H_2O]^{2+}$ were prepared by dissolving $Ru(NH_3)_5Cl_3$ in 0.1 M NaCl and sparging the solution with Ar by needle in a sealed flask. After 15-20 minutes, Zn/Hg amalgam was added to reduce the ruthenium species to $[Ru(NH_3)_5Cl]^+$, which spontaneously aquated to form $[Ru(NH_3)_5(H_2O)]^{2+}$.

Kinetic experiments were performed in a fused quartz cuvette capped by a rubber septum. The flask was purged with Ar, and Ar-sparged solutions of $[Ru(NH_3)_5H_2O]^{2+}$ and the halopyridines in the 0.10 M NaCl solution were introduced by syringe. Typical final solution concentrations were 0.5-1.5 x 10^{-4} M ruthenium and 0.008-0.20 M ligand. After mixing by repeated inversion, the solutions were monitored by either repetitive scans or single wavelength time-course measurements on a Shimadzu 2101-PC spectrophotometer. At least three different determinations of the rate constant at 25° C were made over a range of ligand concentrations; for the activation energy determinations with 2-Fpyr, at least 2 determinations each were made at temperatures of 5, 15, 25 and 35° C.

All Ar used for purging and sparging was deoxygenated by sparging through a Cr(II) solution or by passing through a heated copper catalyst column. All Ar was presaturated with water vapor by sparging through deionized water. Because halopyridines are quite volatile, Ar used to sparge solutions containing these ligands were presaturated with ligand by sparging through a halopyridine solution of similar

concentration. The concentration of the deoxygenated halopyridine stock solutions were assayed by UV spectroscopy at the time each kinetic experiment was begun, so that any change in the concentration of the ligand due to sparging could be detected.

2-Fluoropyridine did not remain in aqueous solution with sparging despite attempts at presaturation. Therefore, measured aliquots of the ligand freshly distilled from BaO under Ar were added directly to the $[Ru(NH_3)_5(H_2O)]^{2+}$ solutions using a 10µl syringe.

Solutions used in analyzing the decomposition of the putative 2-pyridine oxide (2-Opyr$^-$) complex, $[Ru(NH_3)_5(2\text{-}Opyr)]^+$, at different pHs were buffered using 42 mM N-(2-hydroxyethyl)piperazine-N'-(2-ethanesulfonic acid) (HEPES), 3-[(1,1-dimethyl-2-hydroxyethyl)amino]-2-hydroxypropanesulfonic acid (AMPSO), and (cyclohexylamino)-1-propanesulfonic acid (CAPS). Ultraviolet spectra taken of solutions containing $[Ru(NH_3)_5(H_2O)]^{2+}$ and 150 mM of the above buffers showed no evidence of the formation of Ru complexes with these buffering agents.

Data Analysis. For reactions of 2-fluoropyridine and 3-chloropyridine with $[Ru(NH_3)_5H_2O]^{2+}$, absorption at the wavelength maximum for the metal-to-ligand charge transfer transition was monitored as a function of time. Pseudo-first-order rate constants were obtained by plotting $\ln(A_\infty - A_t)$ vs. time, and bimolecular rate constants were calculated by dividing by the ligand concentration.

Activation enthalpies and entropies were obtained from the bimolecular rate constants as a function of temperature. At least two runs at each temperature of 5, 15, 25 and 35° C were used. A least-squares fit of $\ln k_1$ as a function of $1/RT$ was used in determining to determine E_a, from which $\Delta H^\ddagger$ and $\Delta S^\ddagger$ were calculated.

For reactions of 2-chloropyridine with $[Ru(NH_3)_5H_2O]^{2+}$, repetitive scans within the region between 600 nm to 350 nm were made at intervals of 70-180 seconds. In early determinations, the absorption at the apparent isosbestic point for the $[Ru(NH_3)_5(2\text{-}$

Clpyr)]$^{2+}$ and [Ru(NH$_3$)$_5$(2-Opyr)]$^+$ spectra was used to perform pseudo-first-order analysis as described above.

After the discovery of subsequent reactions of [Ru(NH$_3$)$_5$(2-Opyr)]$^+$, a more comprehensive approach was taken. Spectra from 350 to 600 nm were deconvoluted as linear combinations of a spectrum representing [Ru(NH$_3$)$_5$(2-Clpyr)]$^+$ and a spectrum representing [Ru(NH$_3$)$_5$(2-Opyr)]$^+$.

The spectrum used in deconvolutions to represent 2-Clpyr was obtained by adding an aliquot of degassed and distilled 2-Clpyr to a solution of [Ru(NH$_3$)$_5$H$_2$O]$^{2+}$ in a cuvette to obtain a nearly saturated 2-Clpyr solution. Because of the high concentration of 2-Clpyr, the substitution proceeded quickly and the absorbance at l=428 nm reached a maximum within a few minutes. A spectrum was taken at this point, before substantial amounts of the 2-Opyr complex could form. Nevertheless, the contribution of [Ru(NH$_3$)$_5$(2-Opyr)]$^+$ to this spectrum was not ignored in subsequent data analysis (see below). The spectrum used in the deconvolutions to represent [Ru(NH$_3$)$_5$(2-Opyr)]$^+$ was obtained from the reaction of 2-hydroxypyridine (2-pyridone in aqueous solution; 2-OHpyr hereafter) with [Ru(NH$_3$)$_5$(H$_2$O)]$^{2+}$ at pH 10.

The coefficients obtained from deconvolution of the spectra were then fit by computer to kinetic model for the reaction scheme reported below in Results. The model was constructed using numerical fourth-order Runge-Kutta solution[3] of the following differential equations. In these equations, Ru(II) represents [Ru(NH$_3$)$_5$(H$_2$O)]$^{2+}$, Ru(II)(2-Clpyr) represents [Ru(NH$_3$)$_5$(2-Clpyr)]$^{2+}$, and Ru(II)(2-Opyr) represents [Ru(NH$_3$)$_5$(2-Opyr)]$^+$; k$_1$ and k$_{-1}$ represent the forward and reverse 2-Clpyr substitution reactions, k$_2$ represents the hydrolysis of the Ru-bound 2-Clpyr to form 2-Opyr, and k$_3$ represents the dissociation of the 2-Opyr complex.

$$d[Ru(II)]/dt = -k_1[2\text{-Clpyr}][Ru(II)] + k_1[Ru(II)(2\text{-Clpyr})] + k_3[Ru(II)(2\text{-Opyr})] \quad (1)$$

$$d[Ru(II)2\text{-Clpyr}]/dt = -k_{-1}[Ru(II)(2\text{-Clpyr})] - k_2[Ru(II)(2\text{-Clpyr})] \quad (2)$$

$$d[Ru(II)Opyr]/dt = -k_3[Ru(II)(2\text{-Opyr})] \quad (3)$$

Using a simplex-based method,[4] deconvolutions of the experimental spectra could be fit to this model using the rates of the three reactions, molar absorptivities, the elapsed time between mixing and the initial spectrum, and mixing of the $[Ru(NH_3)_5(2\text{-}Clpyr)]^{2+}$ and $[Ru(NH_3)_5(2\text{-}Opyr)]^+$ species in the $[Ru(NH_3)_5(2\text{-}Clpyr)]^{2+}$ basis spectrum as adjustable parameters. The square of the difference between the data and the fit was minimized, with weighting functions used to emphasize data at the beginning of the experiment, where the data was most sensitive to differences in k_1.

The model was constrained by the specifying the initial concentration of $[Ru(NH_3)_5H_2O]^{2+}$ present in solution. This was estimated by mixing a measured aliquot of the reduced $[Ru(NH_3)_5H_2O]^{2+}$ solution with 0.20 M isonicotinamide at the time the 2-Clpyr kinetic run was formulated. This mixture was kept protected from light to prevent photochemical reactions[5] and assayed for $[Ru(NH_3)_5(\text{isonicotinamide})]^{2+}$ using visible spectrophotometry and the published extinction coefficient for this complex.[6] Because of the high concentration of isonicotinamide used and the high equilibrium binding constant for this complex, the concentration of the $[Ru(NH_3)_5(\text{isonicotinamide})]^{2+}$ present could be used to calculate the concentration of the reduced $[Ru(NH_3)_5H_2O]^{2+}$ in the stock solution. Multiple determinations with the same $[Ru(NH_3)_5H_2O]^{2+}$ solution indicated a reproducibility to within 3%.

The model was further constrained by specifying the total concentration of both $[Ru(NH_3)_5(2\text{-}Clpyr)]^{2+}$ and $[Ru(NH_3)_5(2\text{-}Opyr)]^+$) in the first basis spectrum used for deconvolution. This was estimated by performing an isonicotinamide assay, as described in the previous paragraph, for the $[Ru(NH_3)_5H_2O]^{2+}$ solution used in the preparation of the sample from which the basis spectrum was obtained. The use of this constraint effectively limited the range of extinction coefficients allowed in the model fits.

To assess the uncertainty in the k_1 , k_{-1}, k_2 and k_3 values obtained from the basic fitting routine, programs were developed in which a given rate constant was systematically fixed over a range of values while allowing other parameters to vary. The

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uncertainties in the fits reported in results represent the range of values over which the

sum of squares error was within a factor of two of the best fit value.

Because of the low basicity of the 2-halopyridines and the possibility of

substantial steric hindrance, formation constants for the pentaammineruthenium

complexes of these ligands may be relatively small, introducing error into the

determinations of rate constants. The maximum absorbance at 414 nm for reactions of

$[Ru(NH_3)_5(H_2O)]^{2+}$ with 2-fluoropyridine was found to vary no more than 4% over the

range of fluoropyridine concentrations from 0.183-0.019 M. These data were not

sufficient to determine an equilibrium constant, but suggest that incomplete reaction is

not a significant source of error in the pseudo-first order rate constant determinations with

this ligand.

For the reactions with 2-chloropyridine, a reverse rate constant, k_{-1}, was

incorporated into the kinetic model used for fitting the data in order to account for

possible effects of a low formation constant. The two constraints placed on the fit, those

of the total ruthenium concentration in the sample and the total bound ruthenium in the 2-

chloropyridine basis spectrum, served to fairly rigidly determine the reverse rate constant

in the fits. The mean and sample standard deviations of three determinations of k_{-1} was

$5.8 \pm 0.9 \times 10^{-4}$ s^{-1}. From the forward and reverse rates an equilibrium constant for

formation of the complex of 270 ± 60 M was obtained.

This rate constants obtained from these fits can be used to confirm the assumption

used in the fits that all Ru(II) is bound in the first basis spectrum used for deconvolution.

By putting the fitted rate constants into the model for the catalytic cycle, it was found that

the total bound ruthenium in the first basis spectrum is in error by less than 2%.

Repeating the fitted procedure with the an adjusted total ruthenium concentration for the

basis spectrum did not yield significant differences in the rate constants.

Analysis for 2-OHpyr. Products of the reactions of 2-Clpyr with

$[Ru(NH_3)_5H_2O]^{2+}$ were subjected to ion-exchange chromatography on Dowex 50W ion

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exchange resin in the Na$^+$ form. Elution with 0.1 M NaCl yielded substituted pyridine species while the cationic Ru species present remained on the resin. This eluate was showed ultraviolet absorption identical to that of a genuine sample of 2-OHpyr. Continuous extraction with dichloromethane yielded a s solution which could be assayed by gas chromatography/mass spectrometry using an HP 5890/5972A GC/MS. The resulting chromatogram and ion spectrum was nearly identical to commercial samples of 2OH-pyr run on the same system, and the ion spectrum nearly identical to that found in the stored instrument library.[7]

Synthesis of [Ru(NH$_3$)$_5$(2-Opyr)]$^+$. Attempts to isolate the [Ru(NH$_3$)$_5$(2-Opyr)]$^+$ or its protonated form as a tetrafluoroborate or hexafluorophosphate salt were fraught with difficulty. Several attempts at synthesis were made using standard methods,[2,6] using an excess of 2-OHpyr or the tetrabutylammonium or sodium salts of the conjugate base. These generally resulted in a yellowish-green product which had some of the features of the UV-visible spectrum obtained by reaction of 2-OHpyr with [Ru(NH$_3$)$_5$(H$_2$O)]$^{2+}$ in dilute solution, but was a mixture of products. Attempts to recrystallize this material generally resulted in loss of the characteristic UV-visible peak at 400 nm, due to the rapid loss of the 2-Opyr$^-$ ligand in aqueous solution in which there was no excess 2-OHpyr.

Evidence for the further substitution of ammonia ligands by 2-Opyr recommended a stoichiometric reaction between [Ru(NH$_3$)$_5$(H$_2$O)]$^{2+}$ and the sodium 2-pyridine oxide. The resulting complex was precipitated with ammonium hexafluorophosphate to yield an orange-yellow product whose UV-visible spectrum more closely resembled that of the complex formed in dilute solution. Nevertheless, its instability in aqueous solution prevented further purification and analysis.

References to Supplementary Material

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