similar situation might apply. Table V presents kinetic data at differing ionic strengths in acidic solution. The observed rate constants do show a clear trend toward smaller values at higher ionic strengths. However, when we apply the revised Davies equation for ionic strength dependence[24] to the rate data, the charge on the attacking nucleophile (assuming the cation to be +3) is calculated to be −0.41. Therefore, the data would indicate that even in 0.11 M perchloric acid, a hydroxide attack pathway is still operative. However, in order to account for the calculated charge, water must also contribute to the hydrolysis reaction. Since a similar reactivity is not present with the 4-cyanopyridine *N*-oxide complex, neighboring group participation by the *N*-oxide function adjacent to the nitrile group is indicated. To answer whether only water is being activated by the *N*-oxide group or both water and hydroxide requires further kinetic studies, which are under way at this time.

(24) Davies, C. W. *Ion Association*; Butterworths: London, 1962; p 41.

Contribution from the Department of Chemistry,
Boston College, Chestnut Hill, Massachusetts 02167

Substitution Kinetics of *trans*-$[O_2(Py)_4Tc]^+$ in Methanol, DMF, and MeOH/DMF Mixtures (Py = Pyridine, Picoline, and Lutidine)

Jun Lu and M. J. Clarke*

Received September 14, 1988

The substitution kinetics of $[O_2(Py)_4Tc]^+$, where Py = pyridine, 4-methylpyridine, and 3,5-dimethylpyridine, have been studied with 4-aminopyridine, 4-(dimethylamino)pyridine, imidazole, ethylenediamine, cyanide, and cyclam as incoming ligands in alcohol and the first four also in DMF. In alcohols, the reaction proceeds by a solvent-mediated mechanism and is independent of both the incoming and leaving ligands. For the substitution of 4-(dimethylamino)pyridine onto $[O_2(py)_4Tc]^+$ in methanol, k = (2.41 ± 0.02) × 10^2 s^{-1}, ΔH^* = 97.6 ± 3 kJ/mol, and ΔS^* = 63.5 ± 2.5 J/(mol K). In DMF the reactions proceed by a dissociative mechanism according to the rate law $d[O_2A_4Tc]/dt = k_1k_2[O_2(Py)_4Tc][A]/(k_{-1}[Py] + k_2[A])$, where A is the incoming ligand. For the substitution of 4-(dimethylamino)pyridine onto $[O_2(py)_4Tc]^+$ in DMF, k_1k_2/k_{-1} = 0.18 ± 0.03 s^{-1} and k_1 = 0.60 ± 0.04 s^{-1}. Up to X_{MeOH} = 0.1, adding alcohol to DMF increases substitution rates; however, higher concentrations result in a decrease.

As a result of its central location in the periodic table, relatively small differences in solution environment or ligands often result in fairly large changes in the chemistry of the synthetic element technetium.[1,2] It follows that technetium complexes may provide an excellent basis for systematically investigating the consequences of subtle effects on reactivity, geometry, and oxidation state of transition-metal ions. Compounds containing the oxotechnetium(V) cores $[O{=}Tc]^{3+}$ and $[O{=}Tc{=}O]^+$ are among the most common starting materials for the synthesis of new technetium compounds.[3-8] These moieties also occur in radiodiagnostic imaging agents[9,10] and are involved as intermediates in the formation of many lower valent complexes from $[TcO_4]^-$. Despite their importance in synthesis, there have been few investigations of the reaction mechanisms of these ions.[11] Quantitative studies of the substitution kinetics of *trans*-dioxotechnetium(V) ions should provide insight into the reactivity of oxo complexes in general, facilitate the development of new technetium syntheses, and aid in deciphering the metabolic fates of important technetium radiopharmaceuticals as well as in understanding their interactions with biological molecules.

An example of the effects generated by minor ligand modifications is seen in the net formation constants of mixed-valent μ-oxo technetium species, which vary by almost an order of magnitude for each methyl group added in the series py = pyridine, picoline, and lutidine, even though these groups present no appreciable steric hindrance.[12] The variation in isomerization constants (K_{iso} = [dissym]/[asym]) between the dissymmetric $[Cl(Py)_4TcOTc(Py)Cl_4]$ and asymmetric $[Cl(Py)_3ClTcOTc(Py)Cl_3(Py)]$ complexes in this series is less dramatic, increasing only by a factor of 3 in proceeding from pyridine to lutidine.[12] Complexes of the type *trans*-$[O_2(Py)_4Tc]^+$ have recently been shown to be versatile synthetic starting materials, since the pyridine ligands are fairly easily substituted.[6,13] As expected,[6-8] substitution of the pyridine ligands occurs in a stepwise fashion, which Pearlstein and Davison have used to advantage in developing a synthetic route to a variety of mixed-ligand complexes with a combination of halides, alkoxides, and aromatic amines.[13] In this study, the substitution kinetics of *trans*-$[O_2(Py)_4Tc]^+$ are investigated in alcohol and DMF solvents in order to assess the effects of minor variations in ligand and variations in mechanism as a function of the solvent.

Abbreviations: Py, generic pyridine ligand; py, pyridine; pic, 4-picoline; lut, 3,5-lutidine; Apy, 4-aminopyridine; DMApy, 4-(dimethylamino)pyridine; Im, imidazole, en, ethylenediamine; cyclam, 1,4,8,11-tetraazacyclotetradecane.

Experimental Section

Synthesis. The starting material, $[(n\text{-}Bu)_4N][TcOCl_4]$, was prepared from $(NH_4)TcO_4$ (Oak Ridge) by the method of Cotton (X = Cl).[14]

(1) Clarke, M. J.; Podbielski, L. *Coord. Chem. Rev.* **1987**, *78*, 253–331.
(2) Nicolini, M.; Bandoli, G.; Mazzi, U. *Technetium in Chemistry and Nuclear Medicine 2*; Raven Press: New York, 1987.
(3) Trop, H. S.; Jones, A. G.; Davison, A. *Inorg. Chem.* **1980**, *19*, 1993.
(4) Thomas, R. W.; Davison, A.; Trop, H. S.; Deutsch, E. *Inorg. Chem.* **1980**, *19*, 2840.
(5) Davison, A.; Jones, A. G. *Int. J. Appl. Radiat. Isot.* **1982**, *33*, 793–799.
(6) Kastner, M. E.; Fackler, P.; Deutsch, E.; Clarke, M. J. *Inorg. Chem.* **1984**, *23*, 4683–4688.
(7) Fackler, P.; Kastner, M. E.; Clarke, M. J. *Inorg. Chem.* **1984**, *23*, 3968–3972.
(8) Clarke, M. J.; Kastner, M. E.; Podbielski, L. A.; Fackler, P. H.; Schreifels, J.; Meinken, G.; Srivastava, S. C. *J. Am. Chem. Soc.* **1988**, *110*, 1818–1827.
(9) Jones, A. G.; Davison, A.; et al. *J. Nucl. Med.* **1982**, *23*, 801–809.
(10) Jurrison, S.; Aston, K.; Fair, C. K.; Schlemperer, E. O.; Sharp, P. R.; Troutner, D. E. *Inorg. Chem.* **1987**, *26*, 3576–3782.
(11) DePamphilis, B. V.; Jones, A. G.; Davison, A. *Inorg. Chem.* **1983**, *22*, 2292–2297.
(12) Lu, J.; Clarke, M. J. *Inorg. Chem.* **1988**, *27*, 4761.
(13) Pearlstein, R. M.; Lock, C. J. L.; Faggiani, R.; Costello, C. E.; Zeng, C.-H.; Jones, A. G.; Davison, A. *Inorg. Chem.* **1988**, *27*, 2409–2413.
(14) Cotton, F. A.; Davison, A.; Day, V. W.; Gage, L. D.; Trop, H. S. *Inorg. Chem.* **1979**, *18*, 3024.

0020-1669/89/1328-2315$01.50/0

Pyridine ligands were obtained from Aldrich and distilled before use. Imidazole, 4-aminopyridine, and 4-(dimethylamino)pyridine were purified by sublimation. Potassium cyanide, ethylenediamine, and cyclam were used without further purification. Compounds of the type *trans*-$[O_2(Py)_4Tc]Cl$ were prepared by previously reported methods.[7]

Caution! All syntheses were performed with ^{99}Tc, which is a β-emitting isotope with a half-life of 2.15×10^5 years. Only milligram quantities should be handled with the minimum shielding present under normal laboratory conditions. Precautions for handling this material are described elsewhere.[1,15]

trans-$[O(OCH_3)(Py)_2Cl_2Tc]$ complexes, where Py = pyridine, picoline, and lutidine, were prepared by methods similar to recently published techniques[7,12,13] in which 100 mg of *trans*-$[O_2(Py)_4Tc]Cl$ (0.2 mmol) was dissolved in 15 mL of methanol in a 30-mL beaker and concentrated HCl added dropwise until the original yellow solution turned green. Two additional drops of HCl were added, and the mixture was allowed to stand for 10 min. The resulting pale green solid was collected by filtration and washed with methanol and diethyl ether; yield 90%. Anal. Calcd for *trans*-$[O(OCH_3)Cl_2(lut)_2Tc]Cl$: H, 4.91; C, 41.78; N, 6.50; Cl, 16.44. Found: H, 4.86; C, 41.84; N, 6.47; Cl, 16.50. UV–visible (λ_{max}, nm (ϵ, M^{-1} cm^{-1})): 353 (sh), 650 (ϵ = 5980). IR: $\nu_{Tc=O}$ = 932 cm^{-1}. These compounds were also made by a similar method starting with $[n\text{-}(C_4H_9)_4N][OCl_4Tc]$ and added pyridine.

trans-$[O_2(4\text{-aminopyridine})_4Tc]Cl\cdot 2H_2O$ was prepared by dissolving 96 mg (0.18 mmol) of *trans*-$[O_2(pic)_4Tc]Cl$ in 5 mL of methanol, adding 125 mg of 4-aminopyridine (1.44 mmol), and stirring for 10 min. The initially yellow mixture gradually turned to a deep pink solution, which was rotary evaporated under vacuum to give a pink residue. This was suspended in 30 mL of benzene by scraping, filtered, and washed with benzene to remove unreacted ligand. Anal. Calcd for $[H_{28}C_{20}N_8O_4TcCl]$: H, 4.86; C, 41.50; N, 19.36. Found: H, 4.80; C, 42.07, N, 19.10.

Compound Characterization. Elemental analyses were performed by Chemical Analytical Services, Berkeley, CA. Infrared spectra were taken on a Perkin-Elmer Model 599B grating spectrophotometer in CsI pellets. UV–visible spectra were obtained on a Perkin-Elmer Model 575 instrument equipped with a digital background corrector and a thermostated sample cell. HPLC separations were done on a 15-cm Waters μC_{18} column with a Gilson UV detector and IBM isocratic pump. The eluent was 70% methanol/30% water at a flow rate of 0.7 mL/min.

Kinetic Studies. In order to verify that the fully substituted compounds were obtained, 40 mg of *trans*-$[O_2(Py)_4Tc]Cl$ (Py = py, pic, lut) was dissolved in 25 mL of the reaction solvent. In the case of DMF or water, additional Py was added to prevent decomposition of the starting material. A 3.00-mL aliquot was diluted to 10.00 mL and its electronic spectrum determined. A 20-μL aliquot of the respective ligand was then added to give an approximately 16-fold excess of the ligand and the spectrum redetermined. In all cases the final spectra were identical within experimental error with published values for the fully substituted compounds with the respective incoming ligands. Titrations of *trans*-$[O_2(pic)_4Tc]^+$ in methanol with Apy or in DMF with DMApy yielded stoichiometric ratios of 4:1 for the titrating ligand substituting onto the complex, and maximum absorbances were obtained at ratios of 8:1 at technetium concentrations (2.3 mM) approximating those in reactant solutions.

Rate constants were determined by dissolving *trans*-$[O_2(Py)_4Tc]Cl$ in 3.00 mL of the desired solvent in a UV–visible cuvette. When DMF was the solvent, additional leaving-group ligand was added to prevent decomposition. The cell was then allowed to come to thermal equilibrium in the thermostated cell compartment for about 15 min before adding 10.0–60.0 μL of the incoming ligand and mixing by rapid inversion of the cuvette. The temperature was held to within ±0.1 °C. Reactions were initially monitored by repetitive scans to determine the presence of isosbestic points. Pseudo-first-order rate constants were determined from least-squares analysis of plots of log ($A_\infty - A_t$) versus time at an absorbance characteristic of the product, in the case of 4-Apy (525 nm) and 4-DMApy (519 nm), or at the λ_{max} value of the reactants for substitution by ethylenediamine, imidazole, cyanide, and cyclam. Plots were linear over 2–3 half-lives in all cases. While the analysis of sequential reactions can be difficult close to equilibrium,[16,17] the treatment is simplified under forcing conditions. Computer simulation of the exact four-step process (the program is given in the supplementary material) was performed to verify that simple semilogarithmic plots would accurately yield the rate of the slow step under pseudo-first-order conditions where the incoming ligand concentration was at least 15 times that of Tc.

Table I. Rate Constants for Substitution of L onto *trans*-$[O_2(Py)_4Tc]^+$ in Various Alcohol Solvents at 15 °C

entering group	leaving group	$10^{-2}k$, s^{-1} methanol	ethanol	50% CH_3OH/ 50% DMF
Apy	py	2.34 ± 0.05	1.27 ± 0.05	3.94 ± 0.02
	pic	1.43 ± 0.08	0.51 ± 0.04	2.13 ± 0.02
	lut	2.74 ± 0.06	1.50 ± 0.04	5.3 ± 0.1
DMApy	py	2.41 ± 0.02	1.27 ± 0.02	
	pic	1.40 ± 0.02	0.52 ± 0.02	
	lut	2.63 ± 0.04	1.31 ± 0.04	
en	py	2.76 ± 0.07	1.80 ± 0.04	
	pic	1.70 ± 0.05	1.02 ± 0.04	
	lut	4.95 ± 0.1	3.18 ± 0.04	
Im	py	2.06 ± 0.07	1.10 ± 0.04	
	ic	1.23 ± 0.05	0.48 ± 0.01	
	lut	2.42 ± 0.02	1.13 ± 0.01	
cyanide	py	1.66 ± 0.44	*a*	
	pic	1.20 ± 0.03		
	lut	1.90 ± 0.07		
cyclam	py	2.64 ± 0.04	1.50 ± 0.06	
	pic	1.70 ± 0.05	1.79 ± 0.01	
	lut	4.71 ± 0.02	1.81 ± 0.04	

[a] Insoluble product.

Results

Reactions in Alcohol. Observed first-order rate constants for the various incoming ligands substituting onto *trans*-$[O_2(Py)_4Tc]^+$ in methanol and ethanol, where Py = py, pic, and lut, at 15 °C are listed in Table I. Results in both solvents are similar, except that in ethanol the values of k_{obs} are about half those in methanol. In order to verify complete substitution, the reaction with the weakest ligand (Apy) with regard to the leaving groups was run in methanol and the product isolated and subjected to elemental analysis, which was consistent with quantitative substitution. In all cases, the spectra of the final products were consistent with tetrasubstitution of the original pyridine ligands. Reference to this table reveals that the rates vary very little as a function of the incoming ligand and that the order of reactivity as a function of the leaving group is lut > py > pic, with the lutidine complex generally reacting about twice as fast as the picoline. With Apy as the incoming ligand and either pic or py as the leaving group, the rates were independent of the concentration of either the incoming ligand over a concentration range of 6–30 mM or the leaving group over a concentration range of 1.6–135 mM in solutions where the concentration of the technetium complex was 0.5–1 mM. As shown in Figure S1 in the supplementary material, the observed rate constants increased linearly with the mole fraction of methanol, when the reaction was run in methanol/toluene mixtures. Consequently, the overall rate law is solvent dependent and is of the form

$$\frac{d[O_2A_4Tc]}{dt} = k[ROH][O_2(Py)_4Tc]$$

A correction for changes in the activity coefficient of MeOH in toluene[18] yielded a steeper slope for the line in Figure S1a ($k = 0.053a_{MeOH}^{-1}$ s^{-1}). Addition of DMF to the solvent mixture enhances the rate as shown in Figure S1b. Activity coefficients are not available for this ternary mixture, but estimates with parameters derived from the binary mixtures[18] yielded a steeper slope ($k = 0.12a_{MeOH}^{-1}$ s^{-1}) with a slight convex curvature. Consequently, it is likely that the slight concave curvature evident in Figure S1b is due to changes in the activity of methanol as a function of its concentration in toluene/DMF.

A study was performed in water at $\mu = 0.2$ to determine the effects of pH on the reaction. For the substitution of Apy onto *trans*-$[O_2(py)_4Tc]^+$ at pH 6.5, $k_{obs} = (3.6 \pm 0.2) \times 10^{-2}$ s^{-1}, and

(15) Clarke, M. J.; Podbielski, L. In *Handbook on the Toxicity of Inorganic Compounds*; Seiler, H. G., Sigel, H., Eds.; Marcel Dekker: New York, 1988; pp 665–667, and references therein.
(16) Manes, M.; Hofer, L. J. E.; Weller, S. *J. Chem. Phys.* **1950**, *18*, 1355.
(17) Hollingsworth, C. A. *J. Chem. Phys.* **1957**, *27*, 1346–1348.
(18) Schäfer, K., Lax, E., Eds.; *Zahlenwerte und Funktionen aus Physik und Chemie*; Landolt-Börnstein II-2a; Springer-Verlag: West Berlin, 1960; pp 499, 650, 3439–3440.

Table II. Activation Parameters for Substitution of 4-Aminopyridine onto *trans*-$[O_2(Py)_4Tc]^+$ in Various Solvents

leaving group	solvent	ΔH^*, kJ/mol	ΔS^*, J/(mol K)
py	methanol	97.6 ± 3	63.5 ± 2.5
	ethanol	94.2 ± 6	46.2 ± 4
	DMF	74.0 ± 5	−10.6 ± 1
	MeOH/DMF	99.6 ± 3	74.1 ± 3
pic	methanol	94.7 ± 2	49.0 ± 1
	ethanol	98.6 ± 5	53.2 ± 3
	DMF	92.9 ± 2	51.1 ± 2
	MeOH/DMF	98.8 ± 3	66.5 ± 3
lut	methanol	88.6 ± 3	33.5 ± 1.5
	ethanol	86.0 ± 1	18.7 ± 4
	DMF	74.8 ± 3	−2.1 ± 0.1
	MeOH/DMF	96.9 ± 4	66.9 ± 4

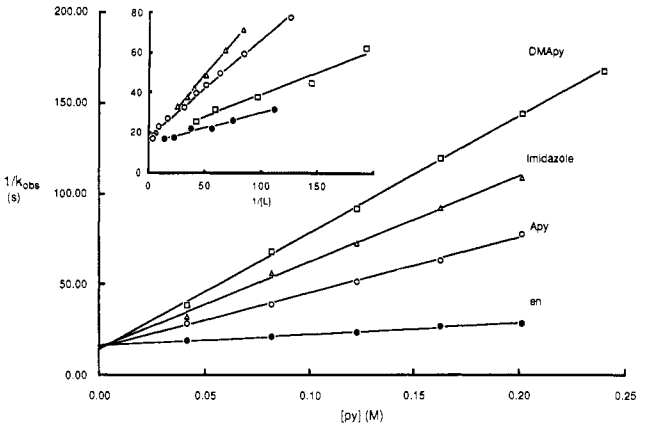

Figure 1. Plot of $1/k_{obs}$ versus [Py] for the substitution of L onto *trans*-$[O_2(py)_4Tc]^+$, where L = Apy (○), DMApy (□), Im (△), and en (●), in DMF at 15 °C. Inset: Plot of $1/k_{obs}$ versus 1/[L] for the substitution of L onto *trans*-$[O_2(py)_4Tc]^+$, where L = Apy (○), DMApy (□), Im (△), and en (●), in DMF at 15 °C.

at pH 10.4 a value of $(2.9 \pm 0.1) \times 10^{-2}$ s^{-1} was obtained. The rates were independent of [py] from 24 to 207 mM and of [APy] from 1 to 10 mM; however, a minimum concentration (~0.02 M) of pyridine was necessary to stabilize the complex.

Values of ΔH^* and ΔS^* for the substitution of Apy onto the three different complexes in all the various solvents are summarized in Table II. In general, the trend of the values of ΔH^* for rates of substitution onto the three complexes is pic > pyr > lut.

Reactions in DMF. Dissolution of *trans*-$[O_2(Py)_4Tc]^+$ in neat DMF resulted in decomposition to a darkly colored material, which was presumed to be TcO_2; however, addition of some of the pyridine ligand prevented this decomposition. Figure S2 in the supplementary material illustrates that the inverse of the observed rate constant is linearly dependent on the concentration of the leaving molecule, which is free in solution. Figure S3 in the supplementary material shows that the inverse of the observed rate constant for the substitution of Apy onto *trans*-$[O_2(Py)_4Tc]^+$, where Py = py, pic, and lut, at 15 °C in DMF is linearly dependent on the inverse of the concentration of the incoming ligand. Parts a and b of Figure 1 are analogous to Figures S2 and S3, except that pyridine is the constant leaving group and DMApy, Apy, Im, and en are the entering ligands. Consequently, the observed rate law, expressed in a double-reciprocal fashion, is

$$\frac{1}{\text{rate}} = \left(\frac{1}{k_a}\frac{[Py]}{[A]} + \frac{1}{k_b}\right)\frac{1}{[O_2(Py)_4Tc]}$$

Values of k_a and k_b listed in Table III were obtained from an overall fit to this equation with the data for a given entering and leaving group represented in Figures 1, S2, and S3.

Reactions in Methanol/DMF Mixtures. When k_{obs} for the substitution of Apy onto *trans*-$[O_2(Py)_4Tc]^+$, where Py = py, pic, and lut, was determined in a mixed methanol/DMF solvent, the rate was observed to go through a maximum when $X_{MeOH} = 0.1$, as illustrated in Figure 2. These curves were fit by assuming that the rate proceeded in pure methanol and DMF at the known rates

Table III. Kinetic Parameters for Substitution of L onto *trans*-$[O_2(Py)_4Tc]^+$ in DMF at 15 °C

entering group	leaving group	k_a (k_2K), s^{-1}	k_b (k_1), s^{-1}	k_2/k_{-1}
Apy	py	0.13 ± 0.01	0.065 ± 0.001	2.0 ± 0.1
	pic	0.046 ± 0.003	0.0430 ± 0.0006	1.13 ± 0.05
	lut	0.25 ± 0.04	0.150 ± 0.008	1.6 ± 0.2
DMApy	py	0.18 ± 0.03	0.060 ± 0.004	2.9 ± 0.4
Im	py	0.57 ± 0.1	0.068 ± 0.005	0.8 ± 0.1
en	py	0.54 ± 0.1	0.065 ± 0.002	8.2 ± 1

Table IV. Kinetic Parameters for the Substitution of 4-Aminopyridine onto *trans*-$[O_2(Py)_4Tc]^+$, Where Py = py, pic, and lut, in Methanol/DMF at 15 °C[a]

	leaving ligand		
	py	pic	lut
k_1, s^{-1}	0.084 ± 0.003	0.034 ± 0.001	0.134 ± 0.004
K_1	28 ± 5	68.5 ± 15	13 ± 2
K_2	1.6 ± 0.3	0.9 ± 0.3	1.5 ± 0.13

[a] [L] = 0.0672 M, [Tc] = 0.5–1 mM, [Apy] = 0.0238 M.

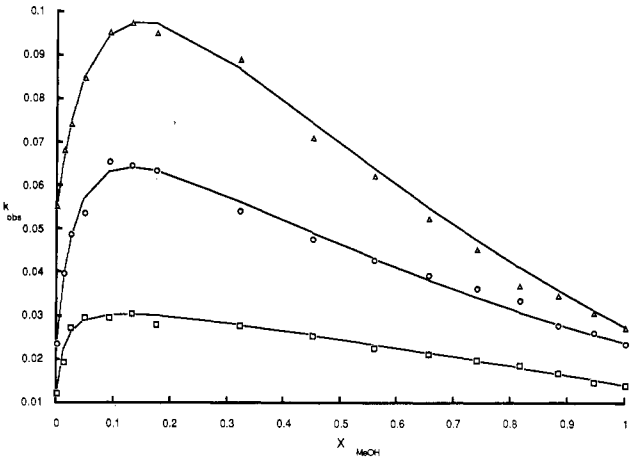

Figure 2. Variation of k_{obs} versus the mole fraction of methanol in DMF for the substitution of Apy onto *trans*-$[O_2(Py)_4Tc]^+$, Py = py, pic, and lut, at 15 °C.

and that a mixed solvated species reacted at a different rate. Consequently, the overall rate law becomes

$$\frac{d[O_2A_4Tc]}{dt} = (k_0\alpha_0 + k_1\alpha_1 + k_2\alpha_2)[O_2(Py)_4Tc]$$

where k_0 is the pseudo-first-order rate constant in the first solvent (DMF), k_1 is that for the mixed solvent system, and k_2 is the observed rate constant in the second solvent (methanol). The α values are the fractions of the reactant technetium complex, which are essentially in either the pure solvent or the mixed solvent. Assuming a minimum number of molecules (one) necessary to form the mixed-solvated species, this becomes

$$\frac{d[O_2A_4Tc]}{dt} = \frac{k_0 + k_1RK_1 + k_2R^2K_1K_2}{1 + RK_1 + R^2K_1K_2}[O_2(Py)_4Tc]$$

where $R = X_{MeOH}/X_{DMF}$ and K_1 and K_2 are the equilibrium constants for the two solvation reactions. The fitted curves in Figure 2 were obtained by a least-squares regression with this expression and the results summarized in Table IV.

Discussion

Reactions in Alcohol. While all the reactions observed resulted in the quantitative replacement of the leaving pyridine by the incoming ligand, the isolation of *trans*-$[O(OCH_3)(Py)_2Cl_2Tc]$ from acidic methanol solutions of *trans*-$[O_2(Py)_4Tc]^+$, where Py = py,[13] pic,[12] and lut, and the blurring of the isosbestic points in the substitution reactions at low temperature indicate that the pyridine molecules are sequentially substituted at least in methanol, and probably in most solvents. The substitution of the pyridine ligands

in methanol and ethanol is clearly solvent mediated, so that the rate-limiting step is very probably alcohol replacement of pyridine on the technetium. The intermediates that involve coordinated alcohol in the following proposed mechanism most likely retain the solvent as an alcoholate. However, since both methanol and ethanol are known to replace axial oxo groups as RO^- and equatorially coordinated alcoholates are also known,[7,12,13] the solvated intermediates may involve 7-coordination, or axially or equatorially 6-coordinated species. A likely sequence of reactions is outlined in Scheme I. Rate laws of the same form as that

Scheme I

$$ROH + [O_2(Py)_4Tc]^+ \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} [ROH{\cdot}O_2(Py)_4Tc]^+$$

$$[ROH{\cdot}O_2(Py)_4Tc]^+ \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} [O_2(Py)_3(RO)Tc] + HPy^+$$

$$A + [O_2(Py)_3(RO)Tc] \underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}} [O_2(Py)_3ATc]^+ + RO^-$$

$$HPy^+ + RO^- \rightleftharpoons ROH + Py$$

derived experimentally can be obtained regardless of whether steps 1, 2, and 3 are rate-limiting (see supplementary material). However, since loss of the pyridine ligand is rate-limiting in DMF (see below) and formation of the alkoxide bond must be accompanied by ligand rearrangement, step 2 might be expected to be the slowest. Assuming step 2 is slow, the following rate law is obtained:

$$\frac{d[O_2A_4Tc]}{dt} = \frac{k_1k_2[ROH][O_2(py)_4Tc]}{k_{-1} + k_2}$$

Consistent with step 2 being rate limiting is the relative ordering of the substitution rates with the leaving group, i.e. lut > py > pic. Reference to Table II reveals significant differences in ΔH^* for the three leaving pyridines. Since bonds formed to the solvent can be considered to be similar in all three complexes, differences in ΔH^* must arise from bonds severed to the leaving group. While the differences between these pyridine ligands are slight, the methyl group in the γ-position of pic makes this the most strongly electron-donating ligand and, consequently, the one with the strongest bond to the Tc. Electron donation from the two methyls in lut is weak since they are in the β-positions and some steric hindrance between adjacent lutidine ligands is expected as they rotate around their Tc–N axes. As a result lut is the most easily lost of the three leaving ligands. Subsequent substitution steps are expected to proceed more rapidly as better donor groups substitute onto the metal.

The observed rate for the substitution of Apy onto *trans*-$[O_2(py)_4Tc]^+$ in water was similar to that in methanol. Since this rate was independent of the concentrations of both the entering and leaving ligands, a solvent-dependent mechanism obtains in aqueous media as well. These rates were also nearly independent of pH in the range 6.5–10.4, so that it is likely that pH changes within several units of neutral would have no substantial effect on the substitution rates in methanol.

Reactions in DMF. A totally different mechanism holds in DMF, which is a poorly coordinating ligand relative to methoxide. In this solvent, the rate varied with the concentration of both the incoming and leaving molecules. As in methanol, the picoline complex reacts more slowly than the pyridine, consistent with bond breaking being important. Reference to the activation enthalpies listed in Table II also indicates that bond breaking plays a dominant role in this solvent. Assuming that the reaction proceeds by a largely dissociative pathway, a likely mechanism is given in Scheme II. With use of a steady-state treatment for $[O_2(Py)_3Tc]^+$

Scheme II

$$[O_2(Py)_4Tc]^+ \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} [O_2(Py)_3Tc]^+ + Py$$

$$A + [O_2(Py)_3Tc]^+ \xrightarrow{k_2} [O_2A(Py)_3Tc]^+$$

$$3A + [O_2(Py)_3Tc]^+ \xrightarrow{k_3} [O_2A_4Tc]^+ + 3Py$$

and on the assumption that step 2 is slow, the rate law is

$$\frac{d[O_2A_4Tc]}{dt} = \frac{k_1k_2[O_2(Py)_4Tc][A]}{k_{-1}[Py] + k_2[A]}$$

Written in double-reciprocal fashion, this becomes

$$\frac{1}{\text{rate}} = \left(\frac{k_{-1}[Py]}{k_1k_2[A]} + \frac{1}{k_1}\right)\frac{1}{[O_2(Py)_4Tc]}$$

which is of the same form as the experimental rate law, with $k_a = k_2K$ and $k_b = k_1$. Interpreted in these terms, the data presented in Table III reveal that k_1 varies substantially with the three different leaving groups but remains essentially constant with the same leaving group and different entering ligands, which is consistent with the first step being ligand dissociation. The values of k_2K and k_2/k_{-1} vary somewhat more, since they also depend upon the nature of the entering group. In the case of pyridine as the leaving group, k_{-1} can be considered to be constant, so that values of k_2/k_{-1} depend only on the entering group and vary over a factor of 10 between imidazole and ethylenediamine. The high value of k_2/k_{-1} for ethylenediamine causes the 5-coordinate intermediate formed in step 1 to substitute before it can back-react to the starting material. Consequently, the ethylenediamine substitution reaction is almost independent of the pyridine concentration (see Figure 1) and the rate law approaches the case where only step 1 is rate limiting. This also accounts for the high level of uncertainty in k_2/k_{-1} for this reaction. Again, substitution of the second through fourth ligands (step 3) is expected to proceed rapidly upon addition of stronger donor ligands and is consistent with the linearity of the semilogarithmic plots.

Reactions in Mixed Solvents. In methanol/DMF mixtures, three pathways were evident. Two can be attributed to those that occur in the pure solvents alone. The maximum rate obtained at $X_{MeOH} = 0.1$ (see Figure 2) was enhanced by 30–75% above the sum of the two rates in the individual solvents, so that the rate in the mixed solvent cannot be attributed solely to there being both pathways open for reaction. Moreover, the rate varies in a nonlinear fashion as a function of the solvent ratios. Also, the rate enhancement for the reaction run in toluene with both methanol and DMF added is significantly greater than with methanol alone (see Figure S1). Consequently, it is clear that some solvation phenomenon specific to MeOH/DMF is affecting the reaction.

The maxima in rates cannot be attributed to polarity differences between the two solvents, since their dielectric constants are similar. Nor does it result from changes in the activity of the two solvents as a function of mixing, since the product and reactant molecules have the same charge and the activity coefficients for MeOH/DMF mixtures are close to unity.[18,19] Indeed, replotting Figure S6 (supplementary material) as a function of a_{MeOH} yields a curve with the maximum shifted only slightly to $a_{MeOH} = 0.097$. Rather, it is likely that the protic nature of the methanol assists the dissociative reaction dominant in DMF by hydrogen-bonding or protonating an oxo group on the technetium complex.

Owing to its larger Gutmann donor number, DMF is known to preferentially coordinate simple metal cations.[19,20] However, the strong affinity of Tc(V) for anionic oxygen ligands[21] and the isolation of technetium methanolate complexes suggest coordination of methoxide, which is a substantially stronger ligand than DMF. As such, it would be expected to be slower to undergo replacement on metal complexes than DMF. Cations, especially large complexes with organic ligands, are often preferentially solvated by the more "organic" solvent in a mixed solvent.[22] On the other hand, hydrogen bonding to the oxo atoms would be expected to favor solvation by methanol. One speculative possibility that would account for the rate enhancement at $X_{MeOH} = 0.1$ is that the complex is preferentially solvated in DMF over

(19) Dickert, F. L. *Z. Phys. Chem.* **1977**, *106*, 155–166.
(20) Gomaa, E. A *Thermochim. Acta* **1984**, *80*, 355–359.
(21) Davison, A.; Jones, A. G. *Int. J. Appl. Radiat. Isot.* **1982**, *33*, 875–881.
(22) Coetzee, J. F.; Ritchie, C. D. *Solute-Solvent Interactions*; Marcel Dekker: New York, 1969; pp 77, 301–342.

methanol around the equatorial, pyridine ligands, but the reverse occurs at the axial oxo ligands. Should H-bonding at the oxo ligands facilitate equatorial ligand loss as it does oxo exchange in *trans*-$[O_2(en)_2Re]^+$,[23] then ligand replacement by DMF would be favored over a given range of X_{MeOH}.

In conclusion, (1) complexes of the type *trans*-$[O_2(Py)_4Tc]^+$ tend to undergo substitution via dissociative mechanisms, which may be strongly solvent mediated, (2) in aqueous solvents, in which these complexes rapidly form an intractable $TcO_2 \cdot nH_2O$ complex, the leaving ligand must be present to stabilize the complex, and (3) specific solvation effects can significantly alter substitution rates in mixed solvents. Finally, while the effects exerted by minor alkyl substitutions on the pyridine ring may produce only a factor of 2-3 difference in the substitution rates, synthetic technetium reactions frequently proceed through several steps with side reactions often present. Small effects in individual steps or in siphoning off product into other reactions can be multiplied through successive intermediates, resulting in the large differences in yields noted in some reactions.

Acknowledgment. This work was supported by NSF Grant CHE-8618011.

Registry No. Apy, 504-24-5; DMApy, 1122-58-3; $[(n\text{-}Bu)_4N][TcOCl_4]$, 71341-65-6; *trans*-$[O(OCH_3)(py)_2Cl_2Tc]$, 120610-32-4; *trans*-$[O(OCH_3)(pic)_2Cl_2Tc]$, 120610-33-5; *trans*-$[O(OCH_3)(lut)_2Cl_2Tc]$, 120610-34-6; *trans*-$[O_2(py)_4Tc]Cl$, 93383-85-8; *trans*-$[O_2(pic)_4Tc]Cl$, 93383-86-9; *trans*-$[O_2(lut)_4Tc]Cl$, 93383-87-0; *trans*-$[O_2(Apy)_4Tc]Cl$, 120610-35-7; ethylenediamine, 107-15-3; imidazole, 288-32-4; cyanide, 57-12-5; cyclam, 295-37-4.

Supplementary Material Available: A plot of k_{obs} versus mole fraction of methanol in toluene for the substitution reaction of Apy onto *trans*-$[O_2(Py)_4Tc]^+$ and an analogous plot but with methanol added in a 50% methanol/DMF mixture, a plot of $1/k_{obs}$ versus [Py] for the substitution of Apy onto *trans*-$[O_2(Py)_4Tc]^+$, a plot of $1/k_{obs}$ versus [Apy] for the substitution of Apy onto *trans*-$[O_2(Py)_4Tc]^+$, Eyring plots for activation parameters in Table II, listings of data for all graphs, derivations of rate equations, and the kinetic simulation program (34 pages). Ordering information is given on any current masthead page.

(23) Kriege, L. B.; Murman, K. *J. Am. Chem. Soc.* **1982**, *94*, 4557.

Contribution from the Department of Chemistry, The University of Calgary, Calgary, Alberta, Canada T2N 1N4

Kinetics of the Bis(2,9-dimethyl-1,10-phenanthroline)copper(I/II) Self-Exchange Reaction in Solution

Hideo Doine, Yoshiko Yano,† and Thomas W. Swaddle*

Received September 7, 1988

The rate of the $Cu(dmp)_2^{+/2+}$ electron-transfer reaction has been measured by ^1H NMR spectroscopy in the perdeuterated solvents water (with the chloride salts), acetonitrile, and acetone (with the $CF_3SO_3^-$ salts). The respective kinetic parameters k_{ex}^{298}/kg mol^{-1} s^{-1}, ΔH^*/kJ mol^{-1}, and ΔS^*/J K^{-1} mol^{-1}, at ionic strength I/mol kg^{-1}, are as follows: for D_2O, 2.0×10^5, 24, and −63, at 0.002; for CD_3CN, 4.9×10^3, 29.6, and −75, at 0.1; for $(CD_3)_2CO$, 3.0×10^3, 29.2, and −80, at 0.1. For acetonitrile and acetone, respectively, variable-pressure studies gave $\Delta V^* = -3.4$ and −7.8 cm^3 mol^{-1}. No significant concentration dependences of these parameters were observed. With these data, the measured rate of the oxidation of $Ru^{II}(CF_3COCHCOCF_3)_3^-$ by $Cu(dmp)_2^{2+}$ in CH_3CN can be satisfactorily accounted for, by using the Marcus cross relation. There is evidence that the Cu^{II} complex contains coordinated solvent in solution; with this qualification, the characteristics of the electron-transfer reactions conform to the Marcus outer-sphere adiabatic model.

Introduction

Copper(I/II) couples are important in many biological redox systems[1-3] and in other contexts, and their self-exchange rates have been estimated from the Marcus cross relationship for a variety of ligand environments.[4-13] Kinetic data for redox reactions of simple copper complexes are relatively sparse, partly because of limitations imposed by the poor water solubility of many copper(I) species and their tendency to disproportionate,[14] but also because the coordination numbers, bond lengths, and stereochemistry of the two oxidation states are often very different, resulting in severe retardation of outer-sphere electron transfer through the large internal rearrangement contribution ΔG_{IR}^* to the free energy of activation.[15]

The Marcus cross relationship, however, often gives discordant values of the self-exchange rate constant k_{ex} for a given pair of copper(I/II) complexes when different redox partners are used[6,8,10-13] or when k_{ex} values obtained from oxidation reactions are compared with those from the corresponding reductions.[4,9] It could be that, in these cases, the mechanism of reaction is inner sphere[14] or outer sphere but multistep.[4] Whatever the reason, there is a clear need for direct experimental determination of k_{ex} for some typical copper(I/II) couples.

To date, direct measurements of k_{ex} for copper(I/II) couples have been reported only for (i) $Cu^ICl_x/Cu^{II}Cl_y$ in concentrated aqueous HCl,[16] which probably proceeds by an inner-sphere mechanism[14] and may not be pertinent to copper(I/II) reactions generally, most of which are thought to be outer-sphere processes, (ii) $Cu(TAAB)^{+/2+}$ in methanol-d_4, where TAAB is the rather rigid quadridentate macrocycle tetrabenzotetraazacyclo-

* To whom correspondence should be addressed.
† Visiting scientist from Wayo Women's University, 2-3-1 Konodai, Ichikawa, Chiba, Japan.

(1) *Copper Coordination Chemistry: Biochemical and Inorganic Perspectives*; Karlin, K. D., Zubieta, J., Eds.; Adenine Press: Guilderland, NY, 1983.
(2) Sykes, A. G. *Chem. Soc. Rev.* **1985**, *14*, 283.
(3) McGinnis, J.; Sinclair-Day, J. D.; Sykes, A. G.; Powls, R.; Moore, J.; Wright, P. E. *Inorg. Chem.* **1988**, *27*, 2306 and references cited therein.
(4) Martin, M. J.; Endicott, J. F.; Ochrymowycz, L. A.; Rorabacher, D. B. *Inorg. Chem.* **1987**, *26*, 3012.
(5) Goodwin, J. A.; Stanbury, D. M.; Wilson, L. J.; Eigenbrot, C. W.; Scheidt, W. R. *J. Am. Chem. Soc.* **1987**, *109*, 2979.
(6) Davies, K. M.; Byers, B. *Inorg. Chem.* **1987**, *26*, 3823.
(7) Davies, K. M.; Guiliani, B. *Inorg. Chim. Acta* **1987**, *127*, 223.
(8) Davies, K. M. *Inorg. Chem.* **1983**, *22*, 615.
(9) Al-Shatti, N.; Lappin, A. G.; Sykes, A. G. *Inorg. Chem.* **1981**, *20*, 1466.
(10) Lappin, A. G.; Youngblood, M. P.; Margerum, D. M. *Inorg. Chem.* **1980**, *19*, 407.
(11) Augustin, M. A.; Yandell, J. K. *Inorg. Chem.* **1979**, *18*, 577.
(12) Clemmer, J. D.; Hogaboom, G. K.; Holwerda, R. A. *Inorg. Chem.* **1979**, *18*, 2567.
(13) Yoneda, G. S.; Blackmer, G. L.; Holwerda, R. A. *Inorg. Chem.* **1977**, *16*, 3376.
(14) Holwerda, R. A.; Wherland, S.; Gray, H. B. *Annu. Rev. Biophys. Bioeng.* **1976**, *5*, 363.
(15) Vallee, B. L.; Williams, R. J. P. *Proc. Natl. Acad. Sci. U.S.A.* **1968**, *59*, 498.
(16) McConnell, H. M.; Weaver, H. E., Jr. *J. Chem. Phys.* **1956**, *25*, 307. McConnell, H. M.; Berger, S. B. *J. Chem. Phys.* **1957**, *27*, 230.

0020-1669/89/1328-2319$01.50/0