to give a Pt(IV) silyl–silylene intermediate.[12] Similar α-silyl shifts have been proposed by Pannell and by Ogino in photochemical reactions of polysilyl iron complexes.[13] However, an alternative route is via η^2-disilene intermediates, followed by fast back-reaction with dihydrogen. Stable platinum η^2-disilene complexes have been reported by Pham and West to undergo facile hydrogenolysis of the silicon–silicon bond to yield platinum bis(silyl)s.[14] Investigations into the nature of this process are currently in progress.

Acknowledgment. M.J.F. thanks the Tulane Center for Bioenvironmental Research and the Tulane Committee on Research for support of this work. We also thank Drs. Fred Davidson and Joseph Lazar (Du Pont) and Drs. Brian Tobias and Deborah A. Grimm (Tulane University Coordinated Instrumentation Facility) for assistance with NMR and mass spectra. The expert technical assistance of Chris Adams, Will Marshall, and John Nguyen is greatly appreciated.

Supplementary Material Available: Listings of NMR, MS, and elemental analysis data, tables of crystal data, atomic coordinates and temperature factors, hydrogen coordinates, and intramolecular bond distances and angles (12 pages); tables of calculated and observed structure factors of **3** (19 pages). Ordering information is given on any current masthead page.

---

(12) (a) Yamamato, K.; Okinoshima, H.; Kumada, K. *J. Organomet. Chem.* **1970**, *23*, C7–C8. (b) Yamamato, K.; Okinoshima, H.; Kumada, M. *J. Organomet. Chem.* **1971**, *27*, C31–C32. (c) Okinoshima, H.; Yamamato, K.; Kumada, M. *J. Organomet. Chem.* **1975**, *86*, C27–C30.

(13) For leading references: (a) Pannell, K. H.; Sharma, H. *Organometallics* **1991**, *10*, 954–959. (b) Ueno, K.; Hamashima, N.; Shimoi, M.; Ogino, H. *Organometallics* **1991**, *10*, 959–962.

(14) (a) Pham, E. K.; West, R. *J. Am. Chem. Soc.* **1989**, *111*, 7668-7670. (b) Pham, E. K.; West, R. *Organometallics* **1990**, *9*, 1517-1523.

Selective-Solvation-Induced Intramolecular Electron Transfer: Time Resolution via Pulsed Accelerated Flow Spectrophotometry

Jody A. Roberts, James C. Bebel, Michelle L. Absi, and Joseph T. Hupp*

Department of Chemistry, Northwestern University
Evanston, Illinois 60208

Received November 25, 1991
Revised Manuscript Received August 3, 1992

Despite extensive theoretical interest, relatively few experimental reports exist concerning *nonphotochemical* intramolecular electron-transfer (ET) kinetics, at least for chemically reversible (i.e., thermodynamically well-defined) redox systems.[1-3] Nevertheless, the few that do exist[1,2] have yielded important insights concerning donor–acceptor electronic coupling and solvent reorganization, especially over longer distances. We wish to report here an experiment which adds in an unusual way to the limited list of both chemical systems and chemical methodologies for inducing intramolecular ET.[4] Our approach is based on the ability of added solvent to influence redox potentials, and therefore oxidation-state distributions, in selected asymmetric mixed-valence systems.[5,6]

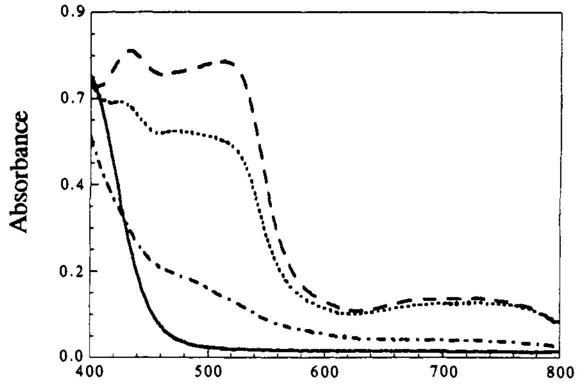
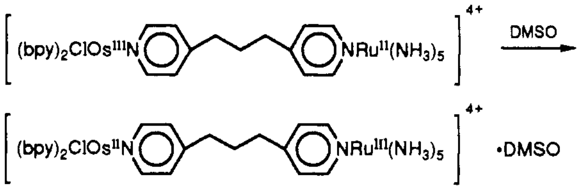


Figure 1. Visible absorption spectra for the following: $(NH_3)_5Ru^{II}$(4-methylpyridine)$^{2+}$ in NM (—); $(bpy)_2ClOs^{III}(TMB)Ru^{II}(NH_3)_5{}^{4+}$ in NM (-··-); $(bpy)_2ClOs^{II}(TMB)Ru^{III}(NH_3)_5{}^{4+}$ in 88% NM, 8% CH_3CN, and 4% DMSO (···); $(bpy)_2ClOs^{II}$(4-methylpyridine)$^+$ in 88% NM, 8% CH_3CN, and 4% DMSO (- - -). (Residual Os^{II} absorption for the nominal $Os^{III}(TMB)Ru^{II}$ probably orginates from slight redox isomerization.)

The system we have examined is a trimethylenebipyridine-bridged ruthenium/osmium complex (**1**) in nitromethane (NM) as the parent solvent:[7]



(1)

As shown by Figure 1, addition of as little as 4 vol % dimethyl sulfoxide (DMSO) is sufficient to convert the visible absorption spectrum from one largely characteristic of $(NH_3)_5Ru^{II}$(pyridine-CH_3) to one indicative of the presence of a $(bpy)_2ClOs^{II}$(pyridine-CH_3) fragment.[5a] (Note that the metal(III) fragments are nearly transparent in the green and red portions of the spectrum.) Quantitative spectral experiments show that, when 4% DMSO is present, redox trapping at Os is favored by 16-fold ($\Delta G_{Et} = -1.6$ kcal mol^{-1}) over trapping at Ru. From previous studies[5,6] the redox isomerization is known to arise from negative shifts in the Ru–ammine formal potential. The shifts are associated with preferential solvation and stabilization of the Ru(III) oxidation state via specific ammine/solvent interactions.

To time resolve the electron transfer we have employed a rapid (microsecond) mixing technique: pulsed accelerated flow (PAF) spectrophotometry. PAF is a highly efficient (in terms of time and reagent consumption) multiple-velocity variant of continuous flow spectrophotometry and has been described in detail by Margerum and co-workers.[8] In our experiments a solution of **1** in 100% NM was rapidly mixed with a solution containing 72% NM, 20% CH_3CN, and 8% DMSO. (Acetonitrile was required in order to achieve refractive index matching and eliminate Schlieren scattering effects[7] which can accompany mixing.) The

---

(1) Organic systems: (a) Closs, G. L.; Calcaterra, L. T.; Green, N. J.; Penfield, K. W.; Miller, J. R. *J. Am. Chem. Soc.* **1986**, *90*, 3673. (b) Closs, G. L.; Miller, J. R. *Science* **1988**, *240*, 440. (c) Johnson, M. D.; Miller, J. R.; Green, N. S.; Closs, G. L. *J. Phys. Chem.* **1989**, *93*, 1173. (d) Penfield, K. W.; Miller, J. R.; Paddon-Row, M. N.; Cotsaris, E.; Oliver, A. M.; Hush, N. S. *J. Am. Chem. Soc.* **1987**, *109*, 5061.

(2) Inorganic systems: Isied, S. S.; Vassilian, A.; Magnuson, R. H.; Schwartz, H. A.; *J. Am. Chem. Soc.* **1988**, *110*, 635.

(3) Representative studies of irreversible systems: (a) Lee, G. H.; Della Ciana, L.; Haim. A. *J. Am. Chem. Soc.* **1989**, *111*, 2535. (b) Isied, S. S.; Vassilian, A.; Magnuson, R. H.; Schwartz, H. A. *J. Am. Chem. Soc.* **1985**, *107*, 7432. (c) Schaffer, L. J.; Taube, H. *J. Phys. Chem.* **1986**, *90*, 3669.

(4) For an imaginative discussion of potential experimental strategies for inducing intramolecular ET, see: Richardson, D. E. *Comments Inorg. Chem.* **1985**, *3*, 367.

(5) (a) Hupp, J. T.; Neyhart, G. A.; Meyer, T. J. *J. Am. Chem. Soc.* **1986**, *108*, 5349. (b) Curtis, J. C.; Roberts, J. A.; Blackbourn, R. J.; Dong, Y.; Massum, M.; Johnson, C. S.; Hupp, J. T. *Inorg. Chem.* **1991**, *30*, 3856.

(6) See also: (a) Curtis, J. C.; Blackbourn, R. L.; Ennix, K. S.; Hu, S.; Roberts, J. A.; Hupp, J. T. *Inorg. Chem.* **1989**, *28*, 3791. (b) Ennix, K. S.; McMahon, P. T.; Curtis, J. C. *Inorg. Chem.* **1987**, *26*, 2660.

(7) $[(bpy)_2ClOs^{II}(TMB)Ru^{II}(NH_3)_5](PF_6)_3$ was prepared and purified essentially as described in ref 5a for the pyrazine-bridged analog. Anal. Calcd: C, 27.5; H, 3.15; N, 11.1. Found: C, 29.2; H, 3.34; N, 11.35. The mixed-valence form was prepared in methanol, but isolated as a solid by using Br_2 vapor as the oxidant. No differences in ET reactivity were seen with different oxidants.

(8) (a) Nemeth, M. T.; Fogelman, K. D.; Ridley, T. Y.; Margerum, D. W. *Anal. Chem.* **1987**, *59*, 283. (b) Jacobs, S. A.; Nemeth, M. T.; Kramer, G. W.; Ridley, T. Y.; Margerum, D. W. *Anal. Chem.* **1984**, *56*, 1058.

0002-7863/92/1514-7957$03.00/0

progress of the reaction was monitored at 720 nm (appearance of Os(II), see Figure 1).

In the flow experiment, the appearance kinetics can be modeled by consecutive mixing and ET processes. (Microscopic re-solvation is viewed, in this case, as faster than either.[9]) Following Margerum,[8] the appropriate transient absorbance expression is

$$M_{\text{exp}} = \left(\frac{A - A_\infty}{A_0 - A_\infty}\right) = \frac{1 - e^{-Y}}{Y} \tag{2}$$

where

$$Y = \left(\frac{1}{b}\right)\left(\frac{1}{k_{\text{mixing}}} + \frac{v}{k_{\text{ET}}}\right) \tag{3}$$

In the expression, b is the reaction path length, v is the flow velocity, and A_0, A, and A_∞ are initial, intermediate, and final absorbances. For 1.4×10^{-5} M **1**, measurements of M_{exp} at each of 250 separate velocities (per push) between 3.5 and 12.5 meter s^{-1} yielded $k_{\text{ET}} = 136 \pm 18\ s^{-1}$.[10,11] Follow-up experiments with a 9-fold variation in reactant concentration overall yielded nearly identical ET kinetics,[12] confirming the intramolecular (i.e., first-order) nature of the reaction. Finally, it should be noted that the observed ET rate falls well below the upper rate measurement limit of the current instrument (ca. $2 \times 10^5\ s^{-1}$).[8]

A detailed comparison of this rate with the predictions of contemporary theory is clearly of interest, but is necessarily beyond the scope of the current paper. It is worth noting, however, that simple computer models suggest a metal-to-metal separation distance of ca. 16 Å (fully extended bridged) and that thermal charge tranfer over a similar distance in an isoproline-linked Os/Ru complex yields much faster kinetics ($k_{\text{ET}} \approx 3 \times 10^5\ s^{-1}$).[2] For the isoproline case both the solvent and the Os coordination environment differ. The ligand environments for the ruthenium centers, however, are similar. For the two systems, driving-force effects should account for about a factor of 5 in reactivity difference. The balance may be due to a combination of (1) unique barrier effects associated with microscopic re-solvation,[6,13] and (2) enhanced nonadiabaticity effects associated with (formal) π/σ orthogonality effects along the length of the TMB bridging ligand.

In addition to the theory comparisons, current work focuses on bridge modifications and on systematic driving-force variations. Indeed, the ability to employ solvent to obtain a continuously adjustable range of driving forces (and rates) may be the most promising feature of the new method.

Acknowledgment. We thank Prof. Dale Margerum and his students at Purdue University for generous and helpful advice on construction of the pulsed accelerated flow spectrophotometer and Matt Todd at Northwestern for computational assistance. We gratefully acknowledge support from the Department of Energy, Office of Energy Research, Division of Chemical Sciences (Grant No. DE-FG02-87ER 13808). The PAF instrument was constructed with funds from an NSF equipment grant (CHE-8710014) and from a Presidential Young Investigator Award. J.A.R. acknowledges a Joseph W. Richards Fellowship from the Electrochemical Society. J.T.H. acknowledges support as an Alfred P. Sloan Fellow (1990–1992) and a Dreyfus Teacher-Scholar (1991–1996).

Supplementary Material Available: Figure S1 showing representative M_{exp} vs velocity data for a single PAF push (1 page). Ordering information is given on any current masthead page.

---

(9) This assumption was confirmed by examining the DMSO-induced solvatochromism of $Ru(NH_3)_5(4\text{-methylpyridine})^{2+}$ with the PAF instrument; microscopic re-solvation was too fast to measure. We note further that photophysical (time-resolved luminescence) studies with $(NH_3)_2Ru(bpy)_2{}^{2+}$ in mixed solvents have previously shown that charge-transfer-induced re-solvation (by DMSO) is complete in less than 5 ns (Doorn, S. K.; Kosmoski, J.; Hupp, J. T. Unpublished results).

(10) Standard deviation is based on an average of 6 runs of 3–6 pushes each. Single-push signal-to-noise was typically 10–20. In some instances, M_{exp} values greater than unity (a nonphysical result) were observed at high velocities, because of base-line drift. Consequently, M_{exp} vs velocity plots were translated slightly (0–0.1) along the M_{exp} axis to achieve optimal kinetic fits (250 points, eqs 2 and 3).

(11) k_{mixing} was measured separately as $(2.7 \pm 0.3) \times 10^3\ m^{-1}$.

(12) Five concentrations between 6.6×10^{-6} and 6.2×10^{-5} M were examined. The average rate constant was $118 \pm 30\ s^{-1}$, with no reactant concentration pattern to the variations, except that the single largest k_{ET} value ($160\ s^{-1}$) was recorded at the highest concentration. Attempted fits instead to second-order (bimolecular) kinetics yielded very low correlation coefficients and enormous variations in apparent rate constant with initial reactant concentration.

(13) (a) Hupp, J. T.; Weydert, J. *Inorg. Chem.* **1987**, *26*, 2657. (b) Blackbourn, R. L.; Hupp, J. T. *Inorg. Chem.* **1989**, *28*, 3786.

Reductively Activated Mitomycin C: An Efficient Trapping Reagent for Electrophiles

Pascal Schiltz and Harold Kohn*

Department of Chemistry
University of Houston
Houston, Texas 77204-5641

Received May 29, 1992

Mitomycin C, a clinically significant antineoplastic antibiotic, is considered to be the prototype of the bioreductive alkylating agents.[1] Studies with nucleosides, oligonucleotides, and DNA restriction fragments documented that **1** selectively bonds to the nucleophilic 2-amino site of specific guanines.[2-5] It is accepted, however, that mitomycin C undergoes both C(1)-nucleophilic and electrophilic substitution transformations under aqueous reductive conditions in the absence of external nucleophiles (Scheme I).[6] Investigations have shown that when the pH was above 7, the C(1)-nucleophilic adducts *cis*- and *trans*-1-hydroxy-2,7-diaminomitosenes[6] (**4**) were produced almost exclusively, and when conditions were moderately acidic, the electrophilic adduct 2,7-diaminomitosene[6,7] (**5**) predominated. It has been suggested that quinone methide **3**[1c] served as the central precursor to both **4** and **5**.[6a] In this communication, we provide evidence that *reductively activated mitomycin C functions primarily as a trapping agent for electrophiles in water at all operational pH values* and that this pattern is altered only when nucleophiles are added under select conditions. The origin for previous misconceptions[6] concerning the reactivity of reduced **1** has been identified.

Plots are provided in Figure 1 for the percentage of C(1)-electrophilic mitosene products generated as a function of pH using two different $Na_2S_2O_4$-mediated reductive conditions[8] (HPLC analysis,[9] protocol 1[10a]). In method A, only 0.2 equiv of $Na_2S_2O_4$ was used, thereby ensuring substantial levels (>64%) of unreacted **1**. In method B, we employed excess $Na_2S_2O_4$ (1.2–2.0 equiv). Under these conditions, **1** accounted for less than 11% of the

---

(1) (a) Szybalski, W.; Iyer, V. N. In *Antibiotics I. Mechanism of Action*; Gottlieb, D.; Shaw, P. D., Eds.; Springer: New York, 1967; pp 211–245. (b) Keyes, S. R.; Heimbrook, D. C.; Fracasso, P. M.; Rockwell, S.; Sligar, S. G.; Sartorelli, A. C. *Adv. Enzyme Regul.* **1985**, *23*, 291. (c) Moore, H. W.; Czerniak, R. *Med. Res. Rev.* **1981**, *1*, 249.

(2) (a) Tomasz, M.; Lipman, R.; Verdine, G. C.; Nakanishi, K. *Biochemistry* **1986**, *25*, 4337. (b) Tomasz, M.; Lipman, R.; Chowdary, D.; Pawlak, J.; Verdine, G. L.; Nakanishi, K. *Science* **1987**, *235*, 1204. (c) Bizanek, R.; McGuinness, B. F.; Nakanishi, K.; Tomasz, M. *Biochemistry* **1992**, *31*, 3084.

(3) Teng, S. P.; Woodson, S. A.; Crothers, D. M. *Biochemistry* **1989**, *28*, 3901.

(4) Millard, J. T.; Weidner, M. F.; Raucher, S.; Hopkins, P. B. *J. Am. Chem. Soc.* **1990**, *112*, 3637.

(5) (a) Li, V.-S.; Kohn, H. *J. Am. Chem. Soc.* **1991**, *113*, 275. (b) Kohn, H.; Li, V.-S., Tang, M.-s. *J. Am. Chem. Soc.* **1992**, *114*, 5501.

(6) (a) Tomasz, M.; Lipman, R. *Biochemistry* **1981**, *20*, 5056. (b) Pan, S.-S.; Andrews, P. A.; Glover, C. J.; Bachur, N. R. *J. Biol. Chem.* **1984**, *259*, 959. (c) Peterson, D. M.; Fisher, J. *Biochemistry* **1986**, *25*, 4077. (d) Hong, Y. P.; Kohn, H. *J. Am. Chem. Soc.* **1991**, *113*, 4634 and references therein.

(7) Han, I.; Russell, D. J.; Kohn, H. *J. Org. Chem.* **1992**, *57*, 1799.

(8) Schiltz, P.; Kohn, H. *Tetrahedron Lett.* **1992**, *33*, 4709.

(9) All products were identified by coinjection of an authentic sample with the reaction mixture in the HPLC using two different sets of HPLC conditions.[10]

(10) HPLC conditions using C_{18} μBondapak (SS) column 3.9 mm × 30 cm. (a) Protocol **1**: linear gradient from 100% A (3 mM triethylammonium phosphate, pH 4.7), 0% B (3 mM triethylamine in acetonitrile) to 50% A, 50% B in 25 min. (b) Protocol **2**: isocratic for 5 min 90% A (0.1 M triethylammonium acetate, pH 6.5), 10% B (acetonitrile) and then linear gradient from 90% A, 10% B to 50% A, 50% B in 20 min.

0002-7863/92/1514-7958$03.00/0