text for details of calculations). When the calculations are repeated for disc-shaped molecules (modeled by fused benzenoid aromatics) or globular molecules (modeled by a diamond lattice), the values of $\Delta G_{(trans+rot)}$ are smaller at all ligand masses by approximately 2 and 4 kJ mol^{-1}, respectively. Since these differences are smaller than the uncertainties in the semiquantitative values of $\Delta G_{(trans+rot)}$, we produce only the data for the molecular cylinder, which should be of general applicability. Uncertainties in $\Delta G_{(trans+rot)}$ arise not only from the semiempirical correction for gas-phase to solution entropies but also from the lack of detailed knowledge of residual molecular motions in the ligand/receptor complexes. Nevertheless, the plot serves as a useful guide, for use in conjunction with eqs 1 and 2 (see text), as to whether a hypothetical association is likely to be productive. The adverse effect on binding constant (10^x) is given by $x = \Delta G_{(trans+rot)}/5.7$.

Registry No. 1, 19436-52-3; 2, 64-19-7; D-Ala, 338-69-2; L-Ala, 56-41-7; *N*-Ac-D-Ala-D-Ala, 19993-26-1; vancomycin, 1404-90-6; ristocetin A, 11021-66-2; D-lactic acid, 10326-41-7; L-lactic acid, 79-33-4; D-thiolactic acid, 33178-96-0; L-thiolactic acid, 57965-30-7; α-hydroxyisobutyric acid, 594-61-6; α-aminoisobutyric acid, 62-57-7.

Communications to the Editor

Efficient Electrocatalytic and Stoichiometric Oxidative Cleavage of DNA by Oxoruthenium(IV)

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The oxidative cleavage of DNA by metal complexes is important in drug applications,[1] the development of synthetic restriction enzymes,[2] and studies of tertiary DNA structure.[3] Polypyridyl complexes are extraordinarily attractive in studies of both DNA binding and oxidative cleavage.[4] The complex $Ru^{IV}(tpy)(bipy)O^{2+}$ (bipy = 2,2′-bipyridine, tpy = 2,2′2″-terpyridine) oxidizes organic hydrocarbons and alcohols via hydride transfer (eq 1).[5,6] We have found that this complex also oxidizes

(1)

DNA efficiently under anaerobic conditions. This oxidation can be performed either chemically by addition of $Ru^{IV}(tpy)(bipy)O^{2+}$ or electrocatalytically by controlled potential electrolysis of $Ru^{II}(tpy)(bipy)OH_2^{2+}$ at 0.8 V (Ag/AgCl).

The changes in the optical absorption spectrum of $Ru^{IV}(tpy)(bipy)O^{2+}$ that occur during the oxidation of isopropyl alcohol to acetone have been characterized in detail,[6,7] and we observe analogous changes during the oxidation of DNA.[8] Oxidation by the $Ru^{IV}O^{2+}$ form dominates the early stage of the reaction, and spectra taken during this stage are characterized by an isosbestic point at 363 nm (Figure 1A). The later stage is dominated by oxidation of the DNA by $Ru^{III}(tpy)(bipy)OH^{2+}$, which is generated by comproportionation of the Ru(IV) and Ru(II) species. Accordingly, a new isosbestic point at 406 nm is observed, as is an increase in absorption at 477 nm due to the quantitative formation of the $Ru^{II}(tpy)(bipy)OH_2^{2+}$ (Figure 1B). In solutions containing a 1:1 molar ratio of calf thymus DNA (nucleotide phosphate) to $Ru^{IV}(tpy)(bipy)O^{2+}$, the isosbestic behavior at 406 nm is reached in approximately 1 h. Under the conditions shown in Figure 1B ([DNA-nucleotide phosphate] = 2 mM, $[Ru^{IV}(tpy)(bipy)O^{2+}]$ = 0.1 mM), the later stage of the reaction is reached before a spectrum can be acquired; *i.e., all of the $Ru^{IV}(tpy)(bipy)O^{2+}$ is consumed immediately upon mixing with the DNA.* The kinetics are strongly dependent on the extent of binding of the Ru complex to the DNA; a detailed kinetic study is underway.

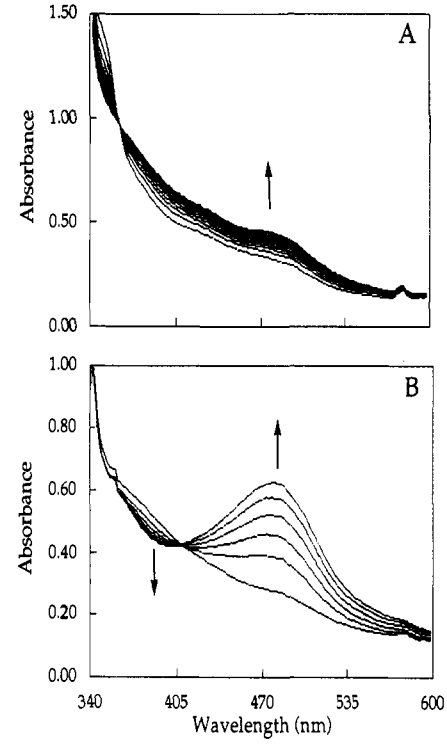

Figure 1. (A) UV-vis spectra taken at 2-min intervals during the oxidation of calf thymus DNA (0.5 mM nucleotide phosphate) by $[Ru^{IV}(tpy)(bipy)O](ClO_4)_2$ (0.5 mM) under N_2. (B) UV-vis spectra taken at 5-min intervals during the oxidation of calf thymus DNA (2 mM) by $[Ru^{IV}(tpy)(bipy)O](ClO_4)_2$ (0.1 mM) under N_2.

The cyclic voltammogram of $Ru^{II}(tpy)(bipy)OH_2^{2+}$ shows two waves corresponding to the $Ru^{III}(tpy)(bipy)OH^{2+}/Ru^{II}(tpy)(bipy)OH_2^{2+}$ ($E_{1/2}$ = 0.49 V) and $Ru^{IV}(tpy)(bipy)O^{2+}/Ru^{III}(tpy)(bipy)OH^{2+}$ ($E_{1/2}$ = 0.62 V) redox couples (cyclic voltam-

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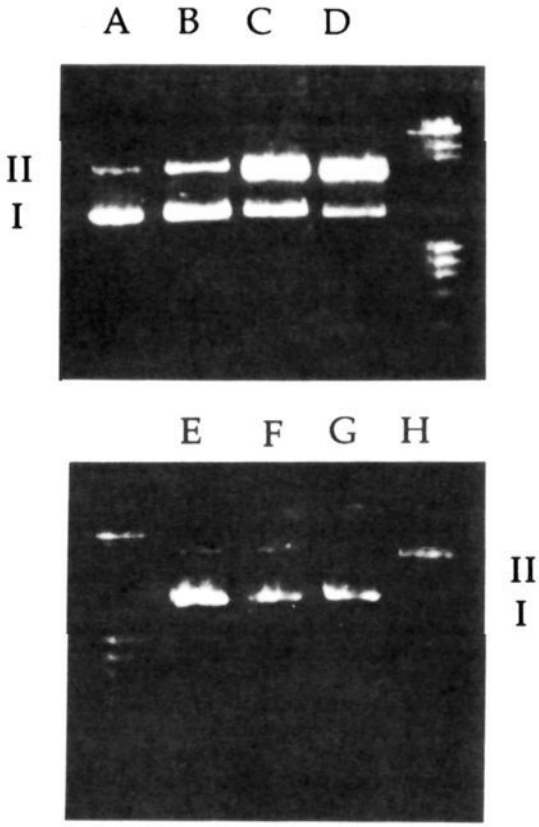

Figure 2. The 1% agarose ethidium bromide gels showing the electrophoresis of solutions containing 60 μM pSport1 DNA with (A) no ruthenium and with 20 μM $[Ru^{II}(tpy)(bipy)OH_2](ClO_4)_2$ electrolyzed at 0.8 V for (B) 15 min, (C) 30 min, and (D) 1.5 h, (E) shows 60 μM pSport1 with no ruthenium, and (F) shows 60 μM pSport1 that has been electrolyzed at 0.8 V in the absence of metal complex for 2 h, (G) shows 60 μM pSport1 incubated at 25 °C with 0.2 mM $[Ru^{II}(tpy)(bipy)OH_2](ClO_4)_2$ for 1 h, and (H) shows 60 μM pSport1 incubated with 0.2 mM $[Ru^{IV}(tpy)(bipy)O](ClO_4)_2$ for 1 h. Molecular weight markers are from DRIgest III (λ DNA-Hind III/*φX174*-Hae III digest) purchased from Pharmacia.

mograms with and without DNA are given in the supplementary material).[9,10] In oxidations of small molecules, controlled potential electrolysis at 0.8 V of $Ru^{II}(tpy)(bipy)OH_2^{2+}$ leads to electrocatalytic conversions mediated by the Ru(IV) form.[7] Similarly, controlled potential electrolysis at 0.8 V of solutions containing DNA and $Ru^{II}(tpy)(bipy)OH_2^{2+}$ leads to nearly complete conversion of the supercoiled DNA to the nicked circular form in 1.5 h (Figure 2, lane D).[11,12] Addition of $Ru^{IV}(tpy)(bipy)O^{2+}$ directly to the DNA effects conversion to form II (lane H). In control experiments, incubation of the DNA with $Ru^{II}(tpy)(bipy)OH_2^{2+}$ (lane G) or electrolysis of DNA alone for 2 h (lane F) causes no change in the supercoiled/nicked ratio.

The system is ideal for probing the redox pathways of DNA cleavage. Rate constants for cleavage of DNA can ultimately be obtained from electrochemistry and optical measurements. The *quantitative* conversion of $Ru^{IV}(tpy)(bipy)O^{2+}$ to $Ru^{II}(tpy)(bipy)OH_2^{2+}$ and the characteristic optical properties of these species present an attractive opportunity for studying concurrently the fate of both the metal complex and the nucleic acid during oxidative DNA cleavage.

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Registry No. $Ru^{IV}(tpy)(bpy)O^{2+}$, 73836-44-9.

Supplementary Material Available: Cyclic voltammograms of $Ru^{II}(tpy)(bipy)OH_2^{2+}$ with and without calf thymus DNA and a discussion of the effects of DNA on the electrochemistry (4 pages). Ordering information is given on any current masthead page.

(9) Cyclic voltammetry was performed at 0.32 cm^2 tin-doped indium oxide working electrodes as previously described (Thorp, H. H.; Brudvig, G. W.; Bowden, E. F. *J. Electroanal. Chem.* **1990**, *290*, 293) with a PAR 273A potentiostat and PAR Model 270 software.

(10) The addition of DNA to solutions of $Ru^{II}(tpy)(bipy)OH_2^{2+}$ causes decreases in peak currents in the cyclic voltammogram indicative of binding of the complex to the DNA. Importantly, peak currents in the cyclic voltammograms taken with and without DNA exhibit a linear dependence on the square root of the sweep rate, showing that adsorption of the complex or the DNA on the electrode does not occur. For detailed discussions of the effects of DNA binding on the cyclic voltammetry of metal complexes, see: (a) Carter, M. T.; Rodriguez, M.; Bard, A. J. *J. Am. Chem. Soc.* **1989**, *111*, 8901. (b) Carter, M. T.; Bard, A. J. *J. Am. Chem. Soc.* **1987**, *109*, 7528. (c) Carter, M. T.; Bard, A. J. *Bioconjugate Chem.* **1990**, *1*, 257.

(11) Solutions were electrolyzed in the same cell used for cyclic voltammetry and stirred by bubbling buffer-saturated N_2 through the solution. Fractions were loaded onto 1% agarose gels containing ethidium bromide and electrophoresced for 30 min at 44 V and photographed under UV light. pSport1 plasmid DNA was purchased from Bethesda Research Laboratories and used as received.

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Relative Oxygen Donor Potential of Dioxirane and Carbonyl Oxide. A Theoretical Study

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Although a dioxirane has only recently been isolated and characterized by Murray,[1a] earlier experimental work by Edwards and Curci[1b] stimulated the theoretical community[2] to calculate the chemical and physical properties of the parent dioxirane **1** and its more elusive tautomer, carbonyl oxide **2** (Figure 1). In the relatively short history[3] of this class of oxidant, dimethyldioxirane and several related peroxo species have proven to be powerful oxygen atom transfer reagents of unusual synthetic utility. It is now well established that dioxirane **1** is more stable than its dioxygen ylide **2** and that the respective barriers for their interconversion are sufficiently high that each exhibits its own chemical behavior when independently generated. Calculated[2] energy differences between these isomeric peroxy compounds range from 29.7 to 54.1 kcal/mol while the theoretical estimates of the barrier for ring closure of **2** and **1** range from 20 to 33.6 kcal/mol.[2a,3b] On the basis of a cleverly designed mechanistic probe involving competitive oxidation of sulfides and sulfoxides, Adam[4a] has

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