principle, the binding modes of other stereochemically related classes of complexes may also be able to be estimated from the unwinding angles. The potential applicability of the method to other metal and nonmetal compounds will be interesting to examine.

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Stereoselective Covalent Binding of Aquaruthenium(II) Complexes to DNA

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Abstract: A group of seven mono- and diaquapolypyridyl complexes of Ru(II) have been shown to bind covalently to DNA by ultrafiltration, extensive dialysis, and ethanol precipitation. Incubation of the metal complex with calf thymus DNA in 50 mM phosphate buffer produces solutions of DNA exhibiting visible absorptions clearly due to the metal complex. These absorptions remain unchanged upon prolonged ultrafiltration or dialysis, demonstrating covalent binding of the metal complex to the DNA. Determination of the amount of bound metal complex either from the spectrum of the labeled DNA or from quantitation of the free metal complex in the filtrate obtained following ultrafiltration gives r_b = [Ru]$_b$/[DNA-nucleotide phosphate] = 0.01–0.02 for all of the complexes. Circular dichroism (CD) spectroscopy of the filtrate obtained following the reaction of DNA with racemic Ru(phen)$_2$(py)OH$_2^{2+}$ shows an enrichment of the solution in the Δ isomer by comparison with the known CD spectrum of the complex. Careful quantitation of the degree of enrichment in the filtrate shows that 90 ± 2% of the complexes bound to DNA are the Λ isomer, giving an enantiomeric excess for binding of the Λ isomer of 80 ± 4%. Other chiral complexes give lower selectivities, although the Λ isomer is preferred in all of the tested cases.

In studies of the interactions of metal complexes with DNA, ruthenium(II) centers can serve either as a substitution-inert template for intercalating ligands[1] or as a carrier of labile ligands that can be replaced by covalent binding to nitrogenous bases of the DNA.[2] In the latter case, early studies centered on aquapolyammine complexes,[3] and one more recent report discussed the polypyridyl complex *cis*-Ru(phen)$_2$Cl$_2$ (phen = 1,10-phenanthroline).[4] In the covalent binding of *cis*-Ru(phen)$_2$Cl$_2$, Barton and Lolis have reported a chiral selectivity that favors covalent binding of the Λ isomer to DNA. This observation is particularly striking when considered in light of the known chiral selectivity for noncovalent (intercalative) binding, which shows a preference for the opposite (Δ) isomer.

We have studied the covalent binding of an extensive series of L$_5$Ru(OH$_2$)$^{2+}$ and L$_4$Ru(OH$_2$)$_2^{2+}$ complexes in our laboratory and have obtained results consistent with the earlier findings on *cis*-Ru(phen)$_2$Cl$_2$. It has been commented[1] that the chiral selectivity for covalent binding is quite high, significantly larger than that for intercalation. To date, however, the degree of chiral selectivity for these reactions has not been carefully quantitated due to the difficulty in obtaining authentic samples of the resolved Λ and Δ isomers of the complexes studied thus far. Fortunately, a member of the series of complexes under investigation in our laboratory, *cis*-Ru(phen)$_2$(py)OH$_2^{2+}$ (Figure 1), has been resolved previously by Bosnich.[5] We report here that the covalent binding of this complex to DNA proceeds with a suprisingly high stereoselectivity.

Experimental Section

Metal Complexes. [Ru(tpy)(bpy)OH$_2$](ClO$_4$)$_2$,[6] [Ru(tpy)(phen)OH$_2$](ClO$_4$)$_2$,[7] [Ru(tpy)(tmen)OH$_2$](ClO$_4$)$_2$,[7] [Ru(bpy)$_2$(py)OH$_2$](ClO$_4$)$_2$,[8] Ru(bpy)$_2$Cl$_2$,[9] Ru(phen)$_2$Cl$_2$,[4] and Ru(bpy)$_2$CO$_3$[9] were prepared by literature procedures (bpy = 2,2′-bipyridine, tmen = *N*,*N*,*N*′,*N*′-tetramethylethylenediamine). Racemic [Ru(phen)$_2$(py)OH$_2$](PF$_6$)$_2$ was prepared by a method analogous to that for Ru(bpy)$_2$(py)OH$_2^{2+}$.[10] Anal. Calcd. for [Ru(phen)$_2$(py)OH$_2$](PF$_6$)$_2$·2H$_2$O: C, 39.43; H, 3.04; N, 7.91. Found: C, 39.44; H, 3.10; N, 8.09. UV–vis, λ, nm (ε, M^{-1} cm^{-1}): 466 (10100), 422 sh (10600), 318 sh (6800), 266 (85000). Preparation of Δ-Ru(phen)$_2$(py)OH$_2^{2+}$ by the method of Bosnich[5] gave the reported CD spectrum.

Binding Measurements. Calf thymus DNA was purchased from Sigma and used as described.[11] All experiments were performed in 50 mM phosphate buffer, pH 7. Water was obtained from a Millipore filtration system. Ethanol precipitation experiments were performed as described by Barton and Lolis.[4] Ultrafiltration was carried out in either a 3-mL or a 180-mL cell from Amicon with a 3000 molecular-weight-cutoff membrane. The results were identical using either cell. Buffer was added to the DNA compartment until no free ruthenium could be detected by optical spectroscopy in filtrate fractions. Quantitation of bound ruthenium from either the spectrum of the DNA or the spectrum of the filtrate gave identical values of r_b. Extensive dialysis was performed in a bag of 3000 molecular weight cutoff tubing (3–4 mL) against 4 L of phosphate buffer. Dialysis was continued for at least 72 h, during which time the buffer was changed 3 times. Continued dialysis showed no change in the ruthenium concentration inside the dialysis bag.

Absorption spectra were obtained by using an HP8452 diode array spectrophotometer. CD spectra were acquired on a JASCO J-600 spectrophotometer. During experiments involving chiral complexes, the acquisition of reproducible CD spectra was strongly dependent on careful protection of the samples from light. When light was not carefully excluded, lower enantiomeric excesses were obtained. Circular dichroism (CD) spectra of filtrates obtained following ultrafiltration of Ru(phen)$_2$(py)OH$_2^{2+}$ in the absence of DNA showed no signal, ruling out resolution of the complexes by the membrane itself.

(1) Pyle, A. M.; Barton, J. K. *Prog. Inorg. Chem.* **1990**, *38*, 413
(2) Clarke, M. J. *Met. Ions Biol. Syst.* **1980**, *11*, 231
(3) Clarke, M. J.; Taube, H. *J. Am. Chem. Soc.* **1974**, *96*, 5413. Clarke, M. J. *Inorg. Chem.* **1977**, *16*, 738. Clarke, M. J. *Inorg. Chem.* **1980**, *19*, 1103.
(4) Barton, J. K.; Lolis, E. *J. Am. Chem. Soc.* **1985**, *107*, 708.
(5) Bosnich, B. *Inorg. Chem.* **1968**, *7*, 178.
(6) Takeuchi, K. J.; Thompson, M. S.; Pipes, D. W.; Meyer, T. J. *Inorg. Chem.* **1984**, *23*, 1845.
(7) Grover, N.; Gupta, N.; Singh, P.; Thorp, H. H. *Inorg. Chem.*, in press.
(8) Moyer, B. A.; Meyer, T. J. *Inorg. Chem.* **1981**, *20*, 436.
(9) Sullivan, B. P.; Salmon, D. J.; Meyer, T. J. *Inorg. Chem.* **1978**, *17*, 3334.
(10) Moyer, B. A.; Thompson, M. S.; Meyer, T. J. *J Am. Chem. Soc.* **1980**, *102*, 2310.
(11) Carter, M. T.; Rodriguez, M.; Bard, A. J. *J. Am. Chem. Soc.* **1989**, *111*, 8901.

0002-7863/92/1514-3390$03.00/0

Table I. Covalent Binding Properties of Aquapolypyridyl Complexes

complex	$\lambda_{max,f}$,[a] nm	$\lambda_{max,b}$,[b] nm	r_b dialysis[c]	r_b ultrafiltration[c]	r_b EtOH precip[c]	$t_{1/2}$[d]
$Ru(tpy)(bpy)OH_2^{2+}$	476	476	0.010	0.014	0.020	30
$Ru(tpy)(phen)OH_2^{2+}$	476	476	0.012	0.020	0.026	40
$Ru(tpy)(tmen)OH_2^{2+}$	520	518	0.012	0.018	0.024	30
$Ru(bpy)_2(OH_2)_2^{2+}$	484	482	0.022	0.027	0.022	30
$Ru(bpy)_2(py)OH_2^{2+}$	470	474	0.011	0.009	0.017	35
$Ru(phen)_2(OH_2)_2^{2+}$	464	472	0.013	0.012	0.020	30
$Ru(phen)_2(ph)OH_2^{2+}$	452	456	0.008	0.014	0.008	30

[a] Free complex in aqueous solution. [b] Complex covalently bound to calf thymus DNA. [c] Values of r_b = $[Ru]_b$/[DNA-nucleotide phosphate]. [d] Estimated from r_b versus time plots (Figure 2) obtained from ethanol precipitation experiments.

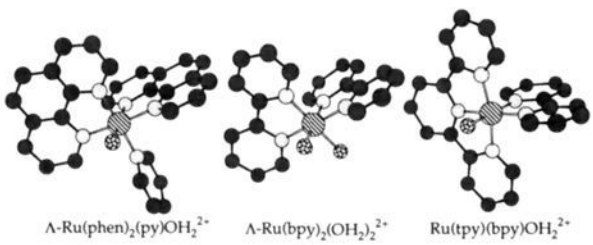

Figure 1. Structures of representative complexes.

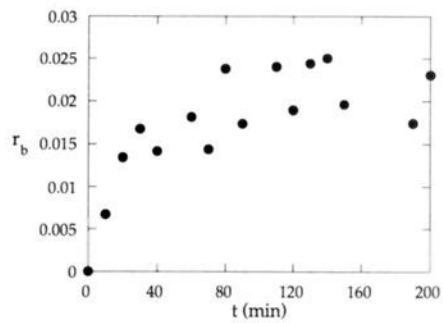

Figure 2. Values of r_b as a function of time for the covalent binding of $Ru(tpy)(bpy)OH_2^{2+}$ to calf thymus DNA. Ethanol precipitation was performed as in ref 4.

Results and Discussion

Solutions of DNA were incubated with metal complex for 12 h and subjected to ultrafiltration, which was continued until no ruthenium could be detected in the filtrate. The spectra of the resulting DNA solutions exhibit visible absorptions that can be attributed to MLCT transitions of the bound ruthenium complexes. In all cases, the absorption was unchanged upon repeated dilution and ultrafiltration, demonstrating covalent binding of the ruthenium to the DNA. The absorption maxima for all seven complexes both free in solution and covalently bound to DNA are given in Table I.

The ratio of bound ruthenium to DNA, r_b = $[Ru]_b$/[DNA-nucleotide phosphate], can be calculated from the absorption spectrum of the ruthenium-labeled DNA. These values are based on the extinction coefficients of the free metal complexes and therefore rely on the assumption that replacement of the aqua ligand does not significantly alter the extinction coefficient of the MLCT band. We have confirmed the validity of this assumption by collecting the filtrate from the ultrafiltration of the DNA–ruthenium reaction mixtures. The concentration of ruthenium in the filtrate can be determined accurately, since these complexes remain as the unsubstituted aqua form, for which we know the exact extinction coefficient. The concentration of ruthenium on the DNA can then be determined by subtraction of the concentration in the filtrate from the initial concentration of ruthenium. Importantly, values of r_b determined from the absorption spectrum of the DNA are identical to those determined from the absorption spectrum of the filtrate.

Extensive dialysis of solutions of DNA incubated with the complexes also provides spectra identical to those obtained from ultrafiltration. Dialysis was continued for 72 h to obtain spectra that remained unchanged upon further dialysis. Values of r_b could be determined from the spectra of the covalently labeled DNA, and the r_b values thereby obtained are in satisfactory agreement with those determined from ultrafiltration (Table I).

Ethanol precipitation experiments similar to those performed by Barton and Lolis[4] were also carried out. Solutions of calf thymus DNA were reacted with the metal complex and aliquots were removed at 5-min intervals. The DNA was precipitated, and values of r_b were determined at each time point from the concentration of metal complex remaining in the supernatant. A plot of r_b versus time for $Ru(tpy)(bpy)OH_2^{2+}$ is shown in Figure 2. The data level off at a value of r_b = (0.02 ± 0.005); r_b values for the other complexes are given in Table I. Clearly, this experiment leads to appreciable scatter in the data; however, an advantage of this experiment is that the time scale for the reaction is evident. A $t_{1/2}$ of ~30 min for the covalent binding reaction can be estimated from Figure 2. Other $t_{1/2}$ values are given in Table I.

An important question is whether covalent binding induces cleavage of the DNA. We have previously reported electrophoresis results on plasmid DNA incubated with $Ru(tpy)(bpy)OH_2^{2+}$ and $Ru^{II}(tpy)(tmen)OH_2^{2+}$.[7,12] In these experiments, there is no evidence for conversion of supercoiled plasmid DNA to nicked circular DNA. We have similarly tested all of the complexes in Table I and find no conversion of supercoiled to nicked DNA. Thus, even with supercoiled plasmids, where cleavage is relatively facile, there is no evidence for metal-promoted nicking by aquaruthenium(II) complexes. Of course, oxidation of the metal complex to oxoruthenium(IV) leads to efficient cleavage, as we have discussed in detail elsewhere.[7,12]

In addition to monofunctional complexes based on $Ru(tpy)(bpy)OH_2^{2+}$ and $Ru(bpy)_2(py)OH_2^{2+}$, studies were also performed on the difunctional complexes $Ru(phen)_2(OH_2)_2^{2+}$ and $Ru(bpy)_2(OH_2)_2^{2+}$. In the earlier $Ru(phen)_2Cl_2$ experiments, it was *assumed that hydrolysis of the chloro ligands was efficient and* that formation of a diadduct was feasible. We have confirmed this assumption by preparing the complex $Ru(bpy)_2CO_3$, which is known to form the authentic $Ru(bpy)_2(OH_2)_2^{2+}$ complex immediately upon dissolution in water.[9] The results obtained with this complex are indistinguishable from those obtained with $Ru(bpy)_2Cl_2$, suggesting that the nature of the adduct is the same in both cases.

The values in Table I show a level of binding at saturation of r_b = 0.01–0.02 that is relatively low. These values reflect the maximum r_b that can be obtained; the initial concentration of metal complex in each case was at least 10 times that which ultimately bound to the DNA. For comparison, *cis*-$Pt(NH_3)_2Cl_2$ can reach a value of r_b = 0.20.[13] The lower values for the ruthenium complexes are probably a result of the higher steric constraints of the octahedral metal geometry and the polypyridyl ligands. In addition, there is essentially no apparent difference in r_b for monofunctional and difunctional complexes. The $Ru(bpy)_2(OH_2)_2^{2+}$ complex does show consistently higher r_b values than the other complexes, and this complex is certainly the smallest

(12) Grover, N.; Thorp, H. H. *J. Am. Chem. Soc.* **1991**, *113*, 7030.
(13) Macquet, J. P.; Butour, J. L.; Johnson, N. P. *ACS Symp. Ser.* **1983**, *No. 209*, 75.

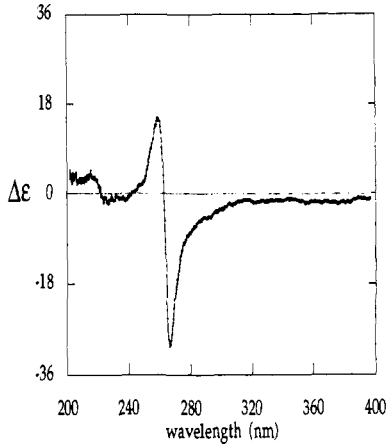

Figure 3. CD spectrum of the filtrate following ultrafiltration of an 50 mM phosphate buffer (pH 7) solution of 0.23 mM *cis*-$Ru(phen)_2(py)OH_2^{2+}$ (racemic) incubated with calf thymus DNA (3.2 mM) for 12 h.

in size and therefore probably forms the least sterically demanding adduct. Thus, the increased r_b value for $Ru(bpy)_2(OH_2)_2^{2+}$ may be a result simply of steric effects and not the distinction between mono- and difunctional complexes. The ability of mono- and difunctional complexes to bind at the same level is apparent in Pt chemistry; *cis*-$Pt(NH_3)_2Cl_2$, *trans*-$Pt(NH_3)_2Cl_2$, and $Pt(dien)Cl^+$ all exhibit the same r_b in the presence of excess metal complex (dien = diethylenetriamine).[13]

Chiral Complexes. An important feature of complexes based on *cis*-$Ru(bpy)_2$ is that they are chiral. We have acquired CD spectra on the filtrates obtained following ultrafiltration of DNA that had been reacted with racemic mixtures of all of the chiral metal complexes: $Ru(phen)_2(OH_2)_2^{2+}$, $Ru(phen)_2(py)OH_2^{2+}$, $Ru(bpy)_2(py)OH_2^{2+}$, $Ru(bpy)_2(OH_2)_2^{2+}$. The spectrum obtained by using $Ru(phen)_2(py)OH_2^{2+}$ is shown in Figure 3. In all four cases, we make the same observation as Barton and Lolis:[4] the filtrates are enriched in the Δ isomer, demonstrating a preference of the Λ isomer for covalent binding. The chiral selectivity is observed for the monofunctional as well as the difunctional complexes, showing that the formation of a diadduct is not the source of the selectivity.

The cyclic voltammetry of $Ru(L)_2(py)OH_2^{2+}$ is quite different from that of $Ru(L)_2(OH_2)_2^{2+}$, because Ru(V) and Ru(VI) are accessible in the diaqua complexes.[14] Thus, it is straightforward to determine whether the pyridine ligand stays bound to the metal over prolonged periods in aqueous solution. We and others[8,14] have found no evidence for pyridine dissociation from $Ru(phen)_2(py)OH_2^{2+}$ or $Ru(bpy)_2(py)OH_2^{2+}$ in aqueous solution. Thus, it seems certain that the initial step in the covalent binding of these complexes to DNA is the formation of a monoadduct by replacement of the aqua ligand. It is therefore likely that the chiral selectivity arises from recognition of the monofunctional complex.

For the complex $Ru(phen)_2(py)OH_2^{2+}$, the absolute configuration is known, as are the Δε values for pure samples of the two isomers. In the filtrate obtained after ultrafiltration of a DNA–$Ru(phen)_2(py)OH_2^{2+}$ reaction mixture, the observed Δε at 260 nm is +15.7, compared to an expected value of +50 for a pure sample, which was obtained by Bosnich[5] and has been reproduced in our laboratory. The concentrations of the two isomers in the filtrate can be determined as

$$([\Delta]_f - [\Lambda]_f)/C_f = \Delta\epsilon(\text{obsd})/\Delta\epsilon(\text{expected}) \quad (1)$$

where $[\Delta]_f$ and $[\Lambda]_f$ are the concentrations of the Δ and Λ isomers free in solution, C_f is the total concentration of Ru free in solution, Δε(obsd) is the measured Δε, and Δε(expected) is the known Δε for a pure sample. We can obtain C_f from the absorption spectrum of the filtrate to determine $([\Delta]_f-[\Lambda]_f)$. We can then write expressions that permit the determination of the bound concentrations of each isomer

$$[\Delta]_f + [\Lambda]_f = C_f \quad (2)$$

$$[\Delta]_b + [\Delta]_f = [\Lambda]_b + [\Lambda]_f = 0.5C_t \quad (3)$$

where $[\Delta]_b$ and $[\Lambda]_b$ are the concentrations of the bound Δ and Λ isomers and C_t is the total concentration of metal complex. From eqs 2 and 3 we can determine $[\Lambda]_b$ and $[\Delta]_b$. *Repeated determinations give a percentage of bound* Λ *isomer of 90 ± 2%.* Thus, we obtain an enantiomeric excess (% Λ − % Δ) of 80 ± 4% for the covalent binding of $Ru(phen)_2(py)OH_2^{2+}$ to DNA.

Table II. Stereoselectivities of Chiral Complexes

complex	C_f, mM	$\Delta\epsilon_{obsd}$[a]	$\Delta\epsilon_{expected}$[a]	% Λ(bound)[b]	ee, %
$Ru(phen)_2(py)OH_2^{2+}$	0.19	+15.7	+50[c]	90 ± 2	80 ± 4
$Ru(phen)_2(OH_2)_2^{2+}$	0.19	+4.0		70[d]	40
$Ru(bpy)_2(py)OH_2^{2+}$	0.20	+1.7		54[e]	8
$Ru(bpy)_2(OH_2)_2^{2+}$	0.14	+3.6	+150[f]	52	4

[a] All Δε values are at 260 nm. [b] Calculated from eqs 1–3. Calf thymus DNA concentration was 3.2 mM, concentration of racemic metal complex was 0.23 mM. [c] Reference 5. [d] Based on the known Δε value for $Ru(phen)_2(py)OH_2^{2+}$. [e] Based on the known Δε value for $Ru(bpy)_2(OH_2)_2^{2+}$. [f] Reference 16.

The results for all of the chiral complexes are shown in Table II. The expected Δε's are known only for $Ru(phen)_2(py)OH_2^{2+}$ and $Ru(bpy)_2(OH_2)_2^{2+}$.[5,15] The selectivity for $Ru(phen)_2(OH_2)_2^{2+}$ is based on the expected Δε for $Ru(phen)_2(py)OH_2^{2+}$; i.e., we have assumed that the expected Δε is the same for both complexes. Bosnich has shown that the CD spectra for all of the complexes $Ru(phen)_2(py)_2^{2+}$ and $Ru(phen)_2(py)X^{n+}$ (X = H_2O, Cl^-, etc.) are identical.[5] It therefore seems reasonable to assume that $Ru(phen)_2(OH_2)_2^{2+}$ would also have a very similar CD spectrum. Likewise, the calculated selectivity for $Ru(bpy)_2(py)OH_2^{2+}$ is based on the known Δε for $Ru(bpy)_2(OH_2)_2^{2+}$.[15] It is perhaps worth pointing out that although the λ_{max} values for the CD spectra of $Ru(phen)_2(py)OH_2^{2+}$ and $Ru(bpy)_2(OH_2)_2^{2+}$ are identical, the Δε value for the bpy complex is larger by a factor of 3.

The magnitudes of the enantiomeric excesses follow the order $Ru(phen)_2(py)OH_2^{2+} > Ru(phen)_2(OH_2)_2^{2+} \gg Ru(bpy)_2(py)OH_2^{2+} > Ru(bpy)_2(OH_2)_2^{2+}$. Since the expected Δε's are known exactly for $Ru(phen)_2(py)OH_2^{2+}$ and $Ru(bpy)_2(OH_2)_2^{2+}$, it is unambiguous that the chiral selectivity is much higher for $Ru(phen)_2(py)OH_2^{2+}$. Thus, it appears that the larger phen complexes are more sterically demanding and have a more easily recognized chirality. The selectivities for the $Ru(L)_2(py)OH_2^{2+}$ complexes are approximately twice those for the $Ru(L)_2(OH_2)_2^{2+}$ complexes when L is either bpy or phen. The higher selectivity for the py–aqua complexes than the diaqua complexes also follows the trend of size of the complexes, with the pyridine complexes being somewhat larger than the diaqua complexes.

Conclusions

We have shown that mono- and diaqua complexes of ruthenium(II) bind covalently to calf thymus DNA by ethanol precipitation, extensive dialysis, and ultrafiltration. Our results on an extensive family of complexes are consistent with the earlier work of Barton and Lolis on $Ru(phen)_2Cl_2$.[4] We observe a relatively low level (r_b = 0.01–0.02) of binding under conditions where the ruthenium complexes are in excess. The ruthenium-labeled DNA is stable to prolonged dialysis or ultrafiltration. The magnitude of r_b does not appear to be a function of the ability of the complex to form a mono- or diadduct.

The reactions proceed with a stereoselectivity that favors covalent binding of the Λ isomer. The selectivity is surprisingly high for $Ru(phen)_2(py)OH_2^{2+}$, which shows an enantiomeric excess of 80%. The degree of selectivity is much higher for bis(phen) complexes than for bis(bpy) complexes, and a factor of 2 higher for $Ru(L)_2(py)OH_2^{2+}$ complexes compared to $Ru(L)_2(OH_2)_2^{2+}$

(14) Takeuchi, K. J.; Samuels, G. J.; Gersten, S. W.; Gilbert, J. A.; Meyer, T. J. *Inorg. Chem.* **1983**, *22*, 1409.

(15) Arce Saguês, J. A.; Gillard, R. D.; Smalley, D. H.; Williams, P. A. *Inorg. Chim. Acta* **1980**, *43*, 211.

complexes. These results suggest that the oxidized $Ru^{IV}O^{2+}$ complexes based on these Ru(II) precursors may show striking chiral selectivities not only in their known DNA cleavage reactions[7,12] but also in oxidations of numerous small molecules.[16]

Acknowledgment. The experimental assistance of Dr. Gregory A. Neyhart and Professor C. C. Hardin is gratefully acknowledged. H.H.T. thanks the Camille and Henry Dreyfus Foundation for a New Faculty Award, the National Science Foundation for a Presidential Young Investigator Award, the David and Lucile Packard Foundation for a Fellowship in Science and Engineering, and the North Carolina Biotechnology Center for an Academic Research Initiation Grant.

(16) Meyer, T. J. *J. Electrochem. Soc.* **1984**, *131*, 221C. Thompson, M. S.; Meyer, T. J. *J. Am. Chem. Soc.* **1982**, *104*, 4106. Binstead, R. A.; Meyer, T. J. *J. Am. Chem. Soc.* **1987**, *109*, 3287.

Registry No. $Ru(tpy)(bpy)OH_2^{2+}$, 20154-63-6; $Ru(tpy)(phen)OH_2^{2+}$, 101241-02-5; $Ru(tpy)(tmen)OH_2^{2+}$, 127714-17-4; $Ru(bpy)_2(OH_2)_2^{2+}$, 72174-09-5; $Ru(bpy)_2(py)OH_2^{2+}$, 67202-42-0; $Ru(phen)_2(OH_2)_2^{2+}$, 47668-18-8; $Ru(phen)_2(py)OH_2^{2+}$, 47768-50-3.

Formation and Reactions of Mono- and Bis(peralkylcyclopentadienyl) Complexes of Calcium and Barium. The X-ray Crystal Structure of $[(Me_4EtC_5)Ca(\mu\text{-}NSiMe_2CH_2CH_2SiMe_2)]_2$

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Abstract: The reaction of $K(Me_4EtC_5)$ and CaI_2 in THF forms the colorless metallocene $(Me_4EtC_5)_2Ca(THF)$ in high yield. Both it and $Cp^*_2Ca(THF)_2$ ($Cp^* = Me_5C_5$) can be used in a variety of reactions to form mono(peralkylcyclopentadienyl) complexes of calcium, in which disproportionation via Schlenk equilibrium plays a smaller than expected role. Thus, $(Me_4EtC_5)CaI(THF)_2$ reacts with K[Otamp] (Otamp = 2,4,6-tris[(dimethylamino)methyl]phenoxide) or $KNSiMe_2CH_2CH_2SiMe_2$ to produce $(Me_4EtC_5)Ca(OC_6H_2\text{-}t\text{-}Bu_2\text{-}2,6\text{-}Me\text{-}4)$, $(Me_4EtC_5)Ca(Otamp)$, and $[(Me_4EtC_5)Ca(\mu\text{-}NSiMe_2CH_2CH_2SiMe_2)]_2$. These compounds represent the first mixed cyclopentadienyl amide or aryl oxide complexes of the heavy alkaline-earth metals to be described. Crystals of $[(Me_4EtC_5)Ca(\mu\text{-}NSiMe_2CH_2CH_2SiMe_2)]_2$ grown from toluene are monoclinic, space group $P2_1/a$, with $a = 17.846$ (4) Å, $b = 12.405$ (2) Å, $c = 18.140$ (3) Å, $\beta = 97.32$ (1)° and D(calcd) = 1.160 g cm^{-3} for $Z = 4$. Least-squares refinement on the basis of 2200 observed reflections measured at −172 °C led to a final R value of 0.057. The compound crystallizes in the form of a dimer containing a planar $[Ca\text{-}N\text{-}]_2$ ring. The two shorter Ca–N distances average 2.41 (1) Å, and the two longer Ca–N′ distances average 2.48 (1) Å. The average Ca–C(ring) distance is 2.70 (3) Å. $Cp^*_2Ca(THF)_2$ ($Cp^* = Me_5C_5$) reacts with $LiN(SiMe_3)_2$ and $LiCH(SiMe_3)_2$ in THF to form a precipitate of LiCp* and generate the hydrocarbon-soluble mono(pentamethylcyclopentadienyl) complexes $Cp^*CaE(THF)_3$ ($E = N(SiMe_3)_2$, $CH(SiMe_3)_2$). Mixing THF solutions of $Cp^*_2Ba(THF)_2$ with $LiN(SiMe_3)_2$ or $LiCH(SiMe_3)_2$ does not form LiCp*, and the hydrocarbon-insoluble organobarates $Li[Cp^*_2BaE](THF)_2$ ($E = N(SiMe_3)_2$, $CH(SiMe_3)_2$) can be isolated from the reaction mixtures in near quantitative yield.

Introduction

Increasing interest in the organometallic chemistry of the calcium subgroup metals (Ca, Sr, and Ba) has strikingly revealed how comparatively little is known about the stoichiometry, structure, and reactivity of these compounds.[1] The large metal radii, polar metal–ligand bonding, and high kinetic lability associated with the alkaline earths (Ae) should create opportunities for developing unusual stoichiometric and catalytic chemistry. These same attributes, however, can lead to insoluble, nonvolatile compounds with high air and moisture sensitivity and a propensity for ligand loss and decomposition.

Monocyclopentadienyl complexes (Cp′AeX) offer attractive possibilities for exploiting the potential chemistry offered by the Ae elements while avoiding some of the difficulties.[2] The use of a variety of Cp rings and the addition or removal of neutral donor ligands provide considerable flexibility in adjusting the metal coordination environments. In addition, the relatively exposed metal center in a monocyclopentadienyl complex should simplify the construction of poly- and heterometallic complexes.

Two general methods have been described in the literature for preparing monoring compounds of the calcium subgroup metals, lanthanides, and actinides. The first of these involves the addition of a ring to a metal, metal halide, or metal aryl oxide; this can be achieved by oxidizing a metal with a cyclopentadienyl iodide,[3] but is usually done by reacting an alkali metal or thallium cyclopentadienide with a metal halide or aryl oxide.[4-8] The second general method selectively removes a cyclopentadienyl ring from

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(1) Hanusa, T. P. *Polyhedron* **1990**, *9*, 1345-1362.
(2) McCormick, M. J.; Sockwell, S. C.; Davies, C. E. H.; Hanusa, T. P.; Huffman, J. C. *Organometallics* **1989**, *8*, 2044-2049.
(3) Watson, P. L.; Whitney, J. F.; Harlow, R. L. *Inorg. Chem.* **1981**, *20*, 3271-3278.
(4) Tilley, T. D.; Andersen, R. A. *Inorg. Chem.* **1981**, *20*, 3267-3270.
(5) Evans, W. J.; Grate, J. W.; Choi, H. W.; Bloom, I.; Hunter, W. E.; Atwood, J. L. *J. Am. Chem. Soc.* **1985**, *107*, 941-946.
(6) Hazin, P. N.; Huffman, J. C.; Bruno, J. W. *Organometallics* **1987**, *6*, 23-27.
(7) Heeres, H. J.; Meetsma, A.; Teuben, J. H. *J. Chem. Soc., Chem. Commun.* **1988**, 962-963.
(8) Ernst, R. D.; Kennelly, W. J.; Day, C. S.; Day, V. W.; Marks, T. J. *J. Am. Chem. Soc.* **1979**, *101*, 2656-2664.

0002-7863/92/1514-3393$03.00/0