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Solvent Dependent Conformational Isomerism and Ligand Oxidation of Novel Ru(II) Cyclen Complexes

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The synthesis of *cis*-[Ru^{II}(cyclen)$(L)_x$]$^{n+}$ (cyclen = 1,4,7,10-tetraazacyclododecane and L = 2,2′-bipyridine (bpy), phenanthroline (phen) or 4-cyanopyridinium (4-$NCpyH^+$)) is reported. The freshly prepared complexes are stable in aprotic solvents and cyclen undergoes oxidative dehydrogenation reaction at high pH. These compounds also present solvent dependent conformational isomerization.

There is a strong relationship between ring size and stereochemistry in tetraazamacrocyclic ruthenium compounds, which affects the thermodynamic, kinetic, and photochemical properties of a [Ru(macrocyclic)LL′]$^{n+}$ complex.[1−6] In this context, cyclen (cyclen = 1,4,7,10-tetraazacyclododecane) complexes are exclusively cis, while with larger macrocycles they may also occur as trans. The reactivity of Co(III) cyclen complexes has been well studied,[7,8] and the occurrence of conformational isomerism and pH-dependent isomer interconversion have been reported. For *cis*-[RuCl(imcyclen)(NO)]$^{2+}$ (imcyclen = 1,4,7,10-tetrazacyclododeca-1-ene), in addition to the occurrence of two conformational isomers, the cyclen ligand undergoes oxidative dehydrogenation to imcyclen.[9,10] Cyclen complexes may also be used as interesting building blocks, since in the cis configuration there are two remaining coordination sites with cis geometry relative to each other, as illustrated by the use of a Ru cyclen complex for the construction of a supramolecular square with a cavity of well-defined size.[11] In view of those results, especially with *cis*-[RuCl(imcyclen)(NO)]$^{2+}$, we decided to investigate the occurrence of conformational isomerization and ligand oxidation in *cis*-[Ru(cyclen)$(L)_x$]$^{n+}$ (Figure 1) complexes with ligands less electron-withdrawing than nitrosyl (L = 4-cyanopyridinium (4-$NCpyH^+$), 2,2′-bipyridine (bpy), or phenanthroline (phen)), where oxidation is less likely.

All the novel[12,13] complexes are stable in aprotic solvents and in the absence of air, but they gradually decompose in

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(12) *cis*-[Ru(cyclen)(bpy)]$(BF_4)_2$: η = 65%. IR: ν_{max}/cm^{-1} (Nujol) = 3232 (NH); 2930 (CH); 750−1480 (CH); 490 (RuN). Elemental analysis, % calcd (% found) for $RuC_{18}H_{28}N_6B_2F_8$ (603 g mol^{-1}): C = 35.84 (35.10); N = 13.93 (13.80); H = 4.67 (4.30). *cis*-[Ru(cyclen)(phen)]-$(BF_4)_2$: η = 41%. IR: ν_{max}/cm^{-1} (Nujol) = 3294 (NH); 2930 (CH); 750−1480 (CH); 490 (RuN). Elemental analysis, % calcd (% found) for $RuC_{20}H_{28}N_6B_2F_8$ (627 g mol^{-1}): C = 38.30 (39.20); N = 13.40 (13.21); H = 4.50 (4.35). *cis*-[Ru(cyclen)(4-$NCpyH^+)_2$]$(BF_4)_4$: η = 70%. IR: ν_{max}/cm^{-1} (Nujol) = 3218 (NH); 2930 (CH); 2215 (NC); 750−1480 (CH); 490 (RuN). Elemental analysis, % calcd (% found) for $RuC_{20}H_{30}N_8B_4F_{16}$ (830 g mol^{-1}): C = 28.91 (28.10); N = 13.48 (13.30); H = 3.63 (3.55).
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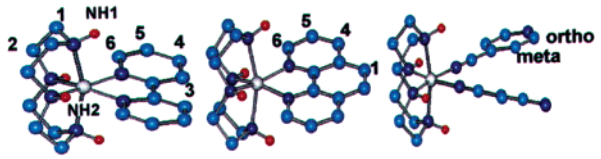

Figure 1. Structural representation of the syn,syn *cis*-[Ru(cyclen)(L)$_x$]$^{n+}$ isomers and labels for the NMR data. Structure generated in HyperChem, version 6.01.

aerobic aqueous solution, especially at pH > 6, as indicated by the ^{1}H and ^{13}C NMR spectra (DMSO-d_6 solutions) where the presence of imine proton signals (C*H*═N) (δ_H = 8.55, 8.60, and 8.37 ppm for L = bpy, phen, and 4-NCpy (obtained by dissolving the 4-NCpyH$^+$ complex in water), respectively, and imine carbon signals (*C*H═N) (δ_C = 169.7, 169.9, and 173.9 ppm for L = bpy, phen, and 4-NCpy, respectively), can be noticed. These results are consistent with a cyclen oxidative dehydrogenation reaction, forming *cis*-[Ru(imcyclen)L]$^{2+}$ and also agree with the infrared spectra of those three complexes, which all display bands at 1630 cm^{-1}, assigned to the C═N stretching ($\nu_{C=N}$), as for *cis*-[RuCl(imcyclen)(NO)](PF$_6$)$_2$.[9] The cyclen oxidative dehydrogenation occurs in the nitrosyl complex even in acidic medium (0.1 mol L^{-1} HPF$_6$), while for the present complexes, it occurs in pH > 6. This probably happens because the metal center behaves essentially as Ru(III) in the presence of NO.[10] However, without the assistance of the NO$^+$ group, such cyclen complexes require higher pH values (pH > 6) to lose an amine hydrogen. Similar observations were also reported for other substituted cyclam ruthenium(III) compounds,[13] but to the best of our knowledge, such unsaturation was not earlier reported for other hexacoordinated Ru(II) cyclen complexes, except for the nitrosyl one mentioned above.

The electronic spectral and electrochemical data of the complexes reported therein are summarized in Table 1 and refer to the complexes without separation of the conformational isomers. On the basis of energy and intensities, and by comparison with related complexes,[1d,14] the observed lower-energy bands were assigned to metal-to-ligand charge transfer (MLCT) transitions. Similarly, the bands below 300 nm were ascribed as internal ligand (IL) $\pi \rightarrow \pi^*$ transitions. *cis*-[Ru(cyclen)(4-NCpyH$^+$)$_2$]$^{4+}$ can be deprotonated to *cis*-[Ru(cyclen)(4-NCpy)$_2$]$^{2+}$; thus, their pH-dependent spectra allowed the determination of a pK_a = 2.6 for the coordinated 4-cyanopyridinium. The cyclic voltammograms of all compounds exhibit an anodic wave assigned to Ru(II) oxidation. The Ep$_a$ of the Ru(II)/(III) (Table 1) couple is more positive than that of the corresponding *cis*-[Ru(cyclam)L]$^{2+}$ species (0.65 and 0.63 V for L = bpy and phen, respectively),[15] consistent with a decrease in the macrocyclic ring size when compared to cyclam.[1d,2c]

Figure 2 shows selected regions of the ^{1}H spectra of the [Ru(cyclen)(bpy)]$^{2+}$ species in different solvents. It is known[16] that the cyclen ligand may generate three isomers when coordinated to a metal center: the syn, syn (both equatorial NH protons pointing toward the cis ligand) and anti, anti (both equatorial NH protons pointing toward the solution), as well as the less symmetric syn, anti isomer. The former two should present a pattern of two equivalent ^{1}H signals for the axial and equatorial NH groups, while the latter should present three signals, corresponding to two axial NH protons, and one syn and one anti equatorial NH proton. The following analysis for the bpy complex also holds for the phen species, for which the same spectral pattern was observed. There are indeed three NH signals observed; however, the integrals do not match the expected values for the exclusive presence of the syn, anti isomer.

Moreover, from the analysis of the aromatic region of the ^{1}H spectrum (Figure 2), one can observe that there is a mixture of two species in solution, which were labeled as isomer **a** and isomer **b**. Taking the signal integrated value, *I*, of 0.75 (DMSO-d_6 solution) for one NH proton of isomer **b** (present in the mixture as the minor component), we could assign the signal at 5.28 ppm as the anti proton of the syn, anti isomer **b** and the signals at 5.06 and 5.96 ppm as the equatorial syn protons (3H) and the axial protons (4H) of both isomers, respectively. On the basis of literature data,[16] we assume that the more symmetric isomer present in the mixture is the syn, syn (**a**). We observed a value of $I = 1$ for each NH proton of the syn, syn isomer. Thus, we could estimate a relative proportion of 57% of the syn, syn and 43% of the syn, anti isomers. NOESY experiments were performed for the phen and 4-NCpy compounds, and in the former case, the syn NH protons were easily identified, as they show an NOE correlation with proton 6 of the aromatic ligand (see Figure 1 for labels). Accordingly, we did not observe such a correlation for the amphiphilic 4-NCpy ligand complex, corroborating the coordination of this ligand to the metal center via the nitrile group instead of the nitrogen pyridine.

The ^{1}H spectrum also features a multiplet ranging from 2.5 to 3.5 ppm, $I = 28.14$; this signal could be assigned to the carbon-chain protons of the cyclen ligands of both isomers. The calculated *I* value for the mixture is 28.16, which is in very good agreement with the observed one. On the basis of the bpy protons signals intensities, we also noticed that the relative ratio of the two isomers, i.e., syn, syn and syn, anti, is solvent dependent (Figure 2) (Supporting Information). The interconversion between the syn, syn and syn, anti isomers was previously reported for Co(III) analogues in aqueous media.[8] In that case, the interconversion depends on base hydrolysis since the abstraction of an NH proton occurs prior to the inversion of the isolated electron pair of the nitrogen. There are no data available for this equilibrium in organic solvents or for ruthenium compounds. Our data show that, in the case of ruthenium, there is no necessity for base hydrolysis to assist isomer interconversion.

This is possible because the equatorial NH protons are weakly bound, i.e., the Ru(II) ion is more acidic, displaying a more pronounced inductive effect on these hydrogens.

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Table 1. Electronic Absorption and Electrochemical Data Obtained for the Compounds *cis*-[Ru(cyclen)$(L)_x]^{n+}$

compound	λ_{max}/nm (log ϵ/mol^{-1} dm^{-3} cm^{-1})[a]					Ep_a/V[b]
	MLCT[c]	MLCT	LF[d]	IL[e]	IL	$Ru^{II/III}$
cis-[Ru(cyclen)(bpy)]$^{2+}$	516(3.44)	380(3.56)	344(3.56)	292(4.29)	243(3.98)	0.91
cis-[Ru(cyclen)(phen)]$^{2+}$	513(3.63)	442(3.59)	335(3.45)	267(4.12)	223(4.08)	0.89
cis-[Ru(cyclen)(4-NCpyH$^+$)$_2$]$^{4+}$ [f]	462(4.02)			254(4.15)	216(4.29)	1.19
cis-[Ru(cyclen)(4-NCpy)$_2$]$^{2+}$ [g]	380(3.94)			254(4.12)	211(4.24)	

[a] Data collected from aqueous solutions. [b] Ep_a = anodic peak potential; the *E* values are reported vs SHE. [c] MLCT = metal to ligand charge transfer. [d] LF = ligand field. [e] IL = internal ligand. [f] pH = 1. [g] pH =6.

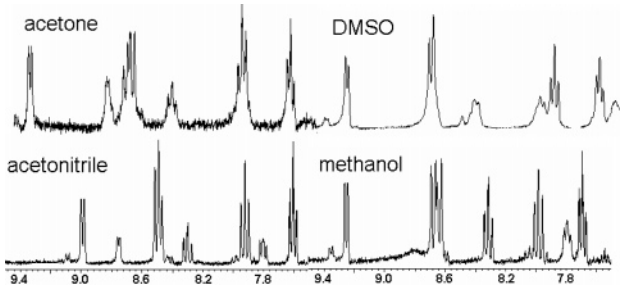

Figure 2. ^{1}H spectra of aromatic region of *cis*-[Ru(cyclen)(bpy)]$^{2+}$.

Although cyclen oxidation happens in basic media (to our knowledge, it was not observed for the Co(III) compounds), it requires the loss of one NH and one CH proton, and it might be an indirect measure of the more acidic nature of the Ru(II) ion.

Contrasting with the behavior of the bpy and phen complexes, which are isolated as a mixture of the syn, syn and syn, anti isomers, the 4-NCpyH$^+$ complex is isolated as a "pure" fraction of the syn, syn isomer, which undergoes slow isomerization in DMSO-d_6 solution, converging to an equilibrium mixture of isomers **a** and **b** after 21 days (Figure 3). The absence of isomer syn, anti (**b**) in the crude material isolated from the synthesis might mean that the isomerization is less favored in this case. Actually, it has been shown for a number of Co(III) complexes,[8] that the coordination of π-acidic ligands renders the inversion of the isolated electron pair of the nitrogen more difficult, presumably because it is less available due to the withdrawing effect of the ligand through the metal center. The absence of isomerization in the 4-NCpyH$^+$ complex species is consistent with its higher π-acceptor ability compared to that of bpy or phen, as far as reduction potentials of the complexes are concerned (Table 1). Thus, our data suggest that the Ru complexes may be behaving similarly to the Co(III) ones with respect to the influence of π-acidic ligand.

In this work, the synthesis and characterization of three novel ruthenium−cyclen complexes were described. The compounds displayed spectral and electrochemical patterns that reflect the effect of the smaller cyclen macrocycle when compared to analogous cyclam complexes. The oxidation process centered on the cyclen ligand, had only been

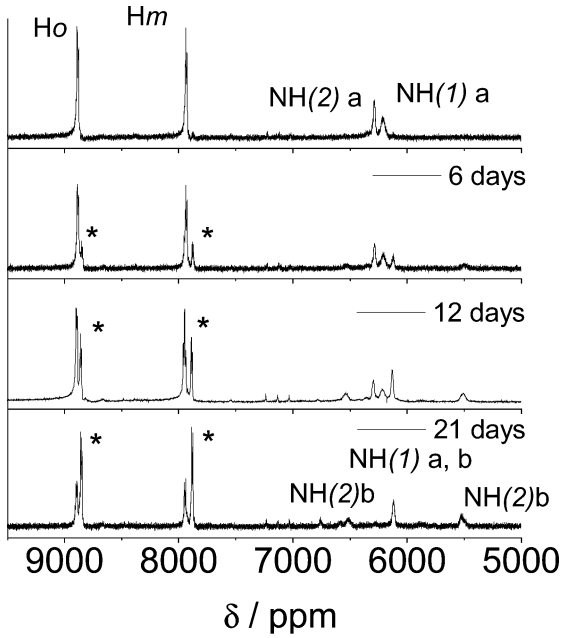

Figure 3. Evolution of the ^{1}H spectra (DMSO-d_6 solution) of *cis*-[Ru(cyclen)(4-NCpyH$^+$)$_2$]$^{4+}$ with time.

previously observed for the analogue *cis*-[RuCl(imcyclen)(NO)]$^{2+}$ even in an acidic medium (0.1 mol L^{-1} HPF_6), but it occurs only at pH > 6 in the present cases. The NMR studies showed the presence of the syn,syn and syn,anti isomers and that their relative proportion in solution is solvent dependent. Along with photochemical and chemical properties of the individual conformational isomers, a more refined NMR study of the three complexes and their solvent dependence is currently under way in our laboratories in an attempt to elucidate the isomerization mechanism of the coordinated cyclen ligand in organic media.

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Supporting Information Available: Details on synthesis, experimental conditions, and isomer ratio in different solvents. This material is available free of charge via the Internet at http://pubs.acs.org.

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