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ARTICLE

Transient photocyclization in Ruthenium (II) polypyridine Complexes of indolamines

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Ruthenium polypyridine complexes have proved to be useful caging groups for visible-light photodelivery of biomolecules. In most photoreactions, one ligand is expelled upon irradiation, yielding Ruthenium mono-aqua complexes and no other photoproduct. In this work we show that a long-lived transient photoproduct is generated when the Ruthenium complexes involve indolamines. The spatial conformation of this species is compatible with a cyclic structure that contains both the amine and the normally non-coordinating aromatic ring coordinated to the Ruthenium center.

Introduction

Caged compounds or phototriggers constitute important tools in the field of cellular physiology [1-3]. Traditionally caged compounds involve an organic caging group covalently bonded to the molecule to be delivered. A pulse of UV light is necessary to break the bond and release the biomolecule.[4-6] In the last years we have presented a new family of inorganic-based caged compounds based on Ruthenium polypyridyl complexes. In these systems, visible light induces the uncaging of several biomolecules which act as as monodentate ligands in the Ru coordination sphere. Examples include 4-aminopyridine,[7] serotonin,[8] GABA,[9,10] glutamate,[11] nicotine,[12] dopamine [13] and some analogues of these compounds.[8]

Other Ru-polypyridine phototriggers carrying bioactive molecules have been recently evaluated as agents for photodynamic therapy. The can induce cellular toxicity by photo-releasing of the caged compound[14-16] or alternatively provide groups that bind DNA or proteins.[16]

Most of these compounds are of the form *cis*-$[Ru(pp)_2(L_1)(L_2)]^{n+}$, with pp a bidentate polypyridine such as 1,10-phenanthroline (phen), 2,2'-bipyridine (bpy) or their derivatives. In aqueous solution these complexes usually deliver (only upon irradiation) one or two ligands to yield the mono-aqua or bis-aqua complexes $[Ru(pp)_2(L)(H_2O)]^{n+}$ and $[Ru(pp)_2(H_2O)_2]^{n+}$, repectively. The energy of the MLCT absorption bands is strongly dependent on the σ-donor and π-acceptor nature of the monodentate ligands,[17] providing a simple methodology to follow the conversion into products along the photoreaction by UV-Vis spectrometry. In the specific case of $[Ru(pp)_2(L)_2]^{n+}$ complexes where L is an aliphatic amine, the aqua complexes obtained upon release of one L unit are usually photostable and do not release a second L moiety.

Indolamines are among the most important molecules involved in many signaling pathways in the central nervous system (CNS). Serotonin (5-hydroxy tryptamine) is a ubiquitous neurotransmitter and several members of the family are drugs known to elicit different actions at the CNS.[18,19]

While attempting to induce the photo-detachment of indolamines from $\{Ru(bpy)_2\}^{2+}$ complexes, we noticed the development of blue shifted absorption bands immediately after irradiation which in the dark, and after persisting from seconds to minutes, reverted to the ones in the original spectra. The spectral features associated with the transient species were similar to those often reported in $\{Ru(bpy)_2\}^{2+}$ complexes bearing poor σ-donor ligands, such as pyridines or nitriles.[16,20] This behaviour proved to be reproducible and the systems could be cycled between the initial and the transient states an indefinite number of times, indicating that the photoreaction is essentially reversible and no decomposition of the reactant takes place (Figure 1).

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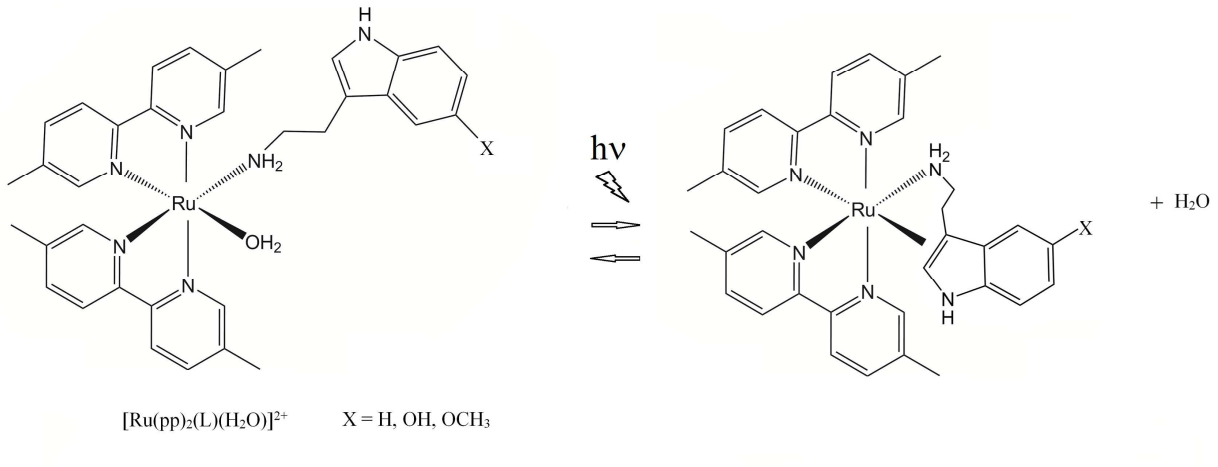

Figure 1. Structure of *cis*-$[Ru(pp)_2(L)(H_2O)]^{n+}$ (pp = 5,5'dmbpy ; L = indolamine). The irradiation of a solution of these complexes promotes photocyclization, which reverts spontaneously in the dark.

In this work, we explore the photochemical reactions that involve $[Ru(pp)_2(H_2O)(L)]^{2+}$, (L tryptamine (TRYP), serotonin (5-hidroxytryptamine, 5HT) or 5-methoxytryptamine (5MT)) and the subsequent back reaction in the dark. We focus on the nature of the transient species and provide experimental evidence supported by complementary DFT computations to propose the formation of a stable cyclic structure in which the aliphatic amine maintains its coordination, while the usually non-coordinating aromatic ring is also bound to the metal center.

Experimental Section

Materials and methods

All reagents but 5-methoxytryptamine·HCl were commercially available and used as received. $Ru(bpy)_2Cl_2$ was synthesized according to the literature[21] the same procedure was followed to synthesize $Ru(55dmb)_2Cl_2$ (55dmb = 5,5'dimethyl 2,2'bipyridine). The UV-Vis spectra were taken with a HP8452A diode-array spectrometer or in an Ocean Optics CHEM2000 diode-array spectrometer. NMR spectra were obtained using a 500 MHz Bruker AM-500. HESI mass spectrometry was performed using a Thermo Scientific QExactive with a Orbitrap detector. Visible light irradiation of samples were performed using an array of 10 Luxeon Star III Green (530 nm centered, 20 nm wide, 300mW each) high power LED. All syntheses were done degassing the solutions with either Ar or N_2 prior to heating to prevent oxidation of the Ruthenium aqua complexes and O_2-sensitive ligands as serotonin.

Computational Methodology

Density Functional Theory (DFT) computations were employed to fully optimize the in vacuo ground-state geometries of $[Ru(55dmb)_2(5MT)(H_2O)]^{2+}$ and $[Ru(55dmb)_2(5MT)]^{2+}$. The calculations were done with *Gaussian 09* [22] using Becke's three parameter hybrid functional with the correlation functional of Lee, Yang and Parr formalized as the B3LYP hybrid functional [23-26] and the effective core potential basis set LanL2DZ [27-30], which proved to be suitable for the geometry optimization and spectral computation and assignment of coordination compounds containing transition metals of the second row. Tight SCF convergence criteria and default setting were used along the geometry optimizations. In all cases vibrational analyses prove that the stationary points reached along the optimizations correspond to local minima in the potential energy surface. The analysis was complemented with (TD)DFT computations including up to 80 states of the same multiplicity as the ground state. The spectra were computed at the gas phase geometry but solvation effects in aqueous solution were taken into account employing the PCM approximation, as implemented in Gaussian 09.

Syntheses.

5-methoxytryptamine·HCl. (5MT.HCl) 420 mg of melatonin were dissolved in 4 mL of isobutanol. To this solution, 300 mg of NaOH and 30 mg of sodium dithionite were added. The mixture was heated at 100°C under N_2. After 2hs, 5mL of distilled water were added. Phases were separated and the aqueous one was washed twice with 2mL of isobutanol. Organic phases were collected and concentrated HCl was added until acid reaction to a wet pH-paper. Upon evaporation of the solution at reduced pressure, 5-methoxytryptamine precipitated abundantly. The solid was redissolved in 5 mL of

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hot 96% ethanol. Cooling this solution recrystallized 110 mg of 5-methoxytryptamine·HCl. (Yield = 25%) NMR (Methanol-d4): ^{1}H δ 3.10 (t, 2H), 3.22 (t, 2H), 3.82 (s, 3H), 6.80 (dd, 1H), 7.05 (d, 1H), 7.12 (s, 1H), 7.26 (d, 1H).

$[Ru(bpy)_2(L)_2]Cl_2$ for L = phenylpropylamine (PPA), 5-hydroxytryptamine (5HT), tryptamine (TRYP) 5-methoxytryptamine (5MT). In a typical preparation, 100 mg of $Ru(bpy)_2Cl_2$ were suspended in 10 mL of distilled water, N_2 was bubbled during 15 minutes and the suspension was heated at 80°C until total dissolution. The formation of the $[Ru(bpy)_2(H_2O)_2]^{2+}$ complex was determined by its band at 480 nm. After formation of the di-aqua complex, 5 to 10 equivalents of the ligand dissolved in a small amount of 96% ethanol were added. For the 5MT and 5HT ligands, which are presented as hydrochlorides, NaOH was added to reach pH 9. The solution was heated until no changes between the UV-Vis spectra at pH 7 and 12 were apparent. The solution was filtered to remove any insoluble particles and precipited with NH_4PF_6 saturated solution or HPF_6 60% in water after cooling. The precipitate was washed with several portions of cold water. The PF_6^- counterion was replaced for Cl^- by exchanging the product with Dowex 22 Chloride form in a 1:1 mixture of Acetone/water in order to increase its solubility in water. L = 5HT, Yield = 48%, NMR (D_2O): ^{1}H δ 1.91 (m, 2H), 2.41 (m, 2H), 2.62 (m, 4H), 2.88 (t, 2H), 3.13 (t, 2H), 6.31 (s, 2H), 6.85 (dd, 2H), 6.90 (s, 2H), 6.94 (t, 2H), 7.29 (d, 2H), 7.33 (d, 2H), 7.46 (t, 2H), 7.61 (t, 2H), 7.85 (d, 2H), 7.87 (d, 2H), 7.91 (t, 2H), 8.54 (d, 2H). L = TRYP, Yield = 79%, NMR (D_2O): ^{1}H δ 2.02 (m, 2H), 2.37 (m, 2H), 2.75 (m, 4H), 3.05 (t, 2H), 3.12 (t, 2H), 7.02 (s, 2H), 7.04 (t, 2H), 7.12 (m, 4H), 7.39 (m, 4H), 7.42 (t, 2H), 7.56 (d, 2H), 7.73 (t, 2H), 7.94 (t, 2H), 8.03 (d, 2H), 8.06 (d, 2H), 8.49 (d, 2H). L = PPA, Yield = 60%, NMR (Acetone-d_6): ^{1}H δ 1.70 (m, 4H), 1.88 (m, 2H), 2.05 (m, 2H), 3.82 (t, 2H), 4.00 (t, 2H), 6.86 (d, 4H), 7.16 (m, 6H), 7.28 (t, 2H), 7.69 (d, 2H), 7.89 (t, 2H), 7.91 (t, 2H), 8.29 (t, 2H), 8.50 (d, 2H), 8.60 (d, 2H), 9.34 (d, 2H). L = 5MT, Yield = 62%, NMR (Acetone-d_6) ^{1}H δ 2.15 (m, 2H), 2.48 (m, 2H), 2.73 (m, 4H), 3.70 (m, 4H), 3.70 (s, 6H), 6.62 (d, 2H), 6.80 (dd, 2H), 6.88 (s, 2H), 7.20 (t, 2H), 7.29 (d, 2H), 7.56 (t, 2H), 7.58 d, 2H), 7.82 (t, 2H), 8.11 (t, 2H), 8.34 (d, 2H), 8.45 (d, 2H), 8.94 (d, 2H).

$[Ru(bpy)_2(L)(H_2O)]Cl_2$ for L = phenylpropylamine (PPA), 5-hydroxytryptamine (5HT), tryptamine (TRYP) 5-methoxytryptamine (5MT). A 0.1 M solution of the corresponding complex $[Ru(bpy)_2(L)_2]Cl_2$ was photolized under a 530 nm LED until no further changes in the spectrum were shown. The solutions were left in the dark for 24 hs before the corresponding tests were performed.

$[Ru(55dmb)_2(5MT)Cl](PF_6)$. 100 mg of $Ru(bpy)_2Cl_2$ were dissolved in 70% EtOH and heated at 70°C for 45 minutes with stirring. The obtained solution was filtered to remove any remaining solid and 1.2 equivalents of 5MT plus 1 equivalent of 1M NaOH were added and left for 90 minutes. The solution was evaporated under reduced pressure at 25°C until almost dry, 5 mL of water were added and precipitation was obtained with a saturated solution of KPF_6. The precipitate was washed with several portions of cold water. (Yield = 62%). NMR (Acetone-d6): ^{1}H δ 2.07 (m, 2H), 2.43 (s, 3H), 2.47 (s, 3H), 2.75 (t, 2H), 3.26 (broad t, 1H), 3.58 (broad t, 1H), 3.76 (s, 3H), 6.67 (s, 1H), 6.81 (dd, 1H), 6.98 (s, 1H), 7.30 (d, 1H), 7.31 (s, 1H), 7.57 (d, 1H), 7.60 (d, 1H), 7.72 (s, 1H), 7.78 (d, 1H), 7.90 (d, 1H), 8.22 (d, 1H), 8.23 (d, 1H), 8.27 (d, 1H), 8.42 (d, 1H), 8.92 (s, 1H), 9.60 (s, 1H).

$[Ru(55dmb)_2(5MT)(H_2O)](Cl)_2$. A required amount of $[Ru(55dmb)_2(5MT)Cl](Cl)$ The PF_6^- counterion of the required amount of $[Ru(55dmb)_2(5MT)(Cl)](PF_6)_2$ was replaced for Cl^- by exchanging with Dowex 22 Chloride. The product was dissolved in water at 70°C and stirred during 30 minutes. The obtained aqua-complex was lyophilized. NMR (D_2O): ^{1}H δ 1.88 (s, 3H), 1.92 (s, 3H), 1.96 (m, 2H), 2.32 (s, 3H), 2.49 (s, 3H), 2.62 (m, 2H), 3.61 (s, 3H), 6.43 (d, 1H), 6.83 (dd, 1H), 6.91 (s, 1H), 7.08 (s, 1H), 7.27 (s, 1H), 7.30 (d, 1H), 7.37 (d, 1H), 7.48 (d, 1H), 7.51 (d, 1H), 7.62 (d, 1H), 7.67 (d, 1H), 7.89 (d, 1H), 8.04 (d, 1H), 8.23 (d, 1H), 8.45 (s, 1H), 8.90 (s, 1H). ε_{max}(471nm) = 6400 $M^{-1}cm^{-1}$

Results and Discussion

Most of the $[Ru(pp)_2(L)(H_2O)]^{2+}$ complexes (L=aliphatic amine ligand) display a strong MLCT absorption band near 490 nm that shifts to longer wavelengths at high pH, as depicted in Figure 2a. However, when $[Ru(55dmb)_2(5MT)(H_2O)]^{2+}$ is irradiated on its MLCT band in aqueous solution at pH 7, the spectrum obtained immediately after irradiation shows a blue-shifted absorption band around 440 nm. The band shape is somewhat broad, suggesting that more than one species could be present in the solution. Alcalinization of the solution reveals two colored species: one has the usual red-shifted spectral profile due to the hydroxo complex $[Ru(55dmb)(5MT)(OH)]^+$ while the other at higher energy remains non-sensitive to pH (Figure 2.b. The position of the band resembles the observed in the MLCT transitions of complexes bearing weakly basic ligands such as nitriles or non-donating pyridines [20,31] This unexpected product reverts to $[Ru(55dmb)_2(5MT)(H_2O)]^{2+}$ if kept protected from the light. At this point the transient species can be repeatedly obtained at will in a series of irradiation/darkness steps.

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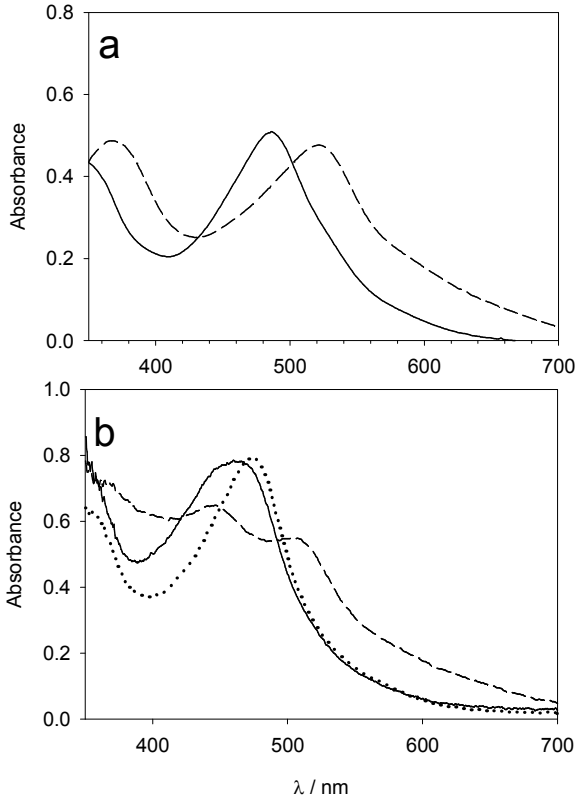

Figure 2. a) UV-Vis spectra of a solution of $[Ru(bpy)_2(PPA)(H_2O)]^{2+}$ at pH=7 (solid line) and at pH=12 (dashed line). b) UV-Vis spectra of solution of $[Ru(55dmb)_2(5MT)(H_2O)]^{2+}$ before irradiation (dotted line), immediately after irradiation (solid line) and at pH=12 (dashed line).

In our hands, all the studied indolamine complexes show the same photochemical behavior, however the complex $[Ru(55dmb)_2(5MT)(H_2O)]^{2+}$ proved to be the most suitable to perform NMR-based quantification and structural studies concerning the changes that take place during and after irradiation. The presence of methyl substituents on the bipyridine and tryptamine rings reduces the number and multiplicity of signals in the aromatic region. At the same time, the extra aliphatic proton signals are well suited for an adequate quantitative analysis of the photoconversion.

Figure 3a displays the electronic spectra of $[Ru(55dmb)_2(5MT)(H_2O)]^{2+}$ before and after 10 minutes irradiation with a high power green (530nm) LED inside an NMR tube with temperature being kept below 5°C by means of a lab-designed ice-cold water circulation system which reduces the thermal decay of the transient product. The collected ^{1}H-NMR information can be used to quantify the degree of photoconversion into the NMR tube. Under the experimental conditions employed to record Figure 3, the latter can be as high as 0.56 after irradiating for 5 minutes (see Figure S1 and S2, ESI). A chemometric analysis of the UV-Vis spectra recorded at different times over aliquots taken from the NMR tube during dark recovery (Figure 3a) allows deconvoluting the spectrum of the transient species, which has a maximum absorption at 438 nm (Figure 3b).

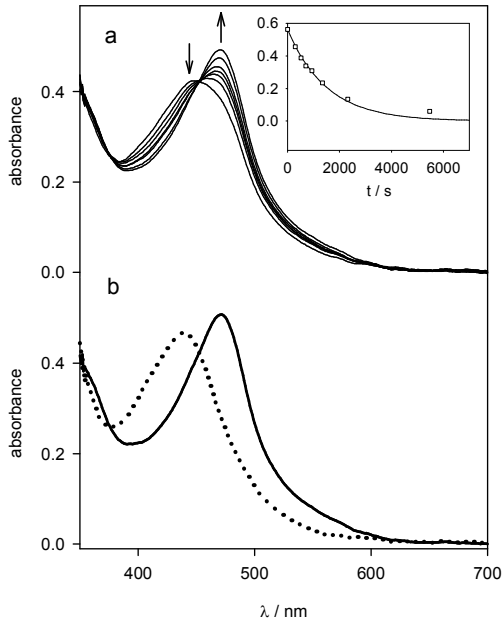

Figure 3. a) Spectra of a D_2O solution of $[Ru(55dmb)_2(5MT)(H_2O)]^{2+}$ immediately after a 5 minutes irradiation into a NMR tube (initial spectrum), and at several times during dark post-reaction. Inset: Photoconversion degree calculated from NMR quantitative analysis. Note that time intervals do not have the same duration. b) Spectrum of $[Ru(55dmb)_2(5MT)(H_2O)]^{2+}$ (solid line) and deconvoluted spectrum of the metastable species formed through irradiation (dotted line). See text for details.

Figure 4a shows the aromatic region of the ^{1}H-NMR spectrum of $[Ru(55dmb)_2(5MT)(H_2O)]^{2+}$ in D_2O. The signals of the 5MT aromatic protons are individualized as *A*, *B*, *C* and *D* and the subindex *m* denote the coordination of 5MT to the monoaqua complex. Figure 4b shows the same sample after irradiation with a 530 nm LED. The mixture still contains the original signals of the unreacted $[Ru(55dmb)_2(5MT)(H_2O)]^{2+,}$ but the transient species ones are clearly identified in this spectrum. Protons *C* and *B* show a large and medium upfield shift respectively, whereas protons *A* and *D* are strongly shifted downfield. The large shifts of the resonances corresponding to the indole protons suggest that the aromatic portion of the molecule interacts strongly with metal center, a result that is compatible with a cyclic structure in which a new coordination bond between the ligand and the metal center is established. The conversion of indole into 3H-indole upon coordination, already described for palladium indole complexes,[32] could be argued as a possible mechanism. However, the resonances of the adjacent hydrogens in the spectrum of transient species are unchanged, showing no coupling to a proton at position 3 of the indole ring, therefore precluding this option. Another possibility could involve the deprotonation of the indolic nitrogen, yielding an coordinated indolate. Two independent

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facts indicate discard this possibility: Firstly, the pH of an aqueous solution of the complex shows no changes during the formation of the transient species, as would be expected if the indole group was to release a H^+ upon coordination. Secondly, the MLCT band in the transient spectrum is shifted towards higher energies while the bands that would correspond to a negatively charged indolate anion should be red shifted.[17,33] These results indicate that deprotonation of nitrogen does not occur and that the coordination is not achieved through a negatively charged atom. The HESI mass spectrum of the complex is compatible with a structure having the formula $[Ru(55dmb)_2(5MT)]^{2+}$, bearing no coordinated water molecules. (see ESI, Figure S3). Similar mass spectra are obtained either before of after irradiation, showing that the loss of the water ligand is favoured in vacuo.

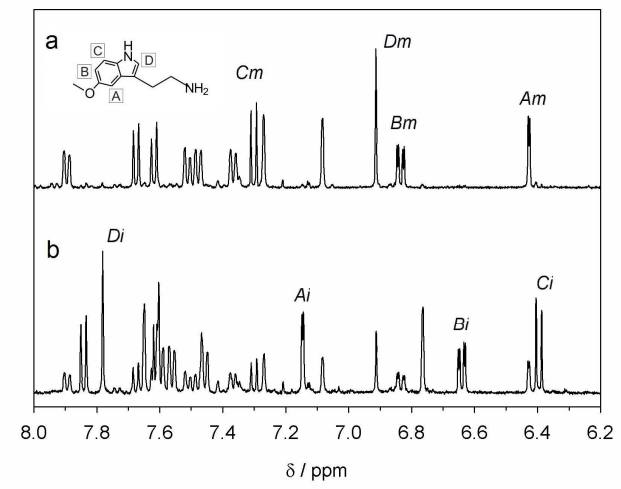

Figure 4. Portion of the aromatic region of the ^{1}H-NMR spectra of $[Ru(55dmb)_2(5MT)(H_2O)]^{2+}$ in D_2O a) before irradiation b) after irradiation. Subscript m indicates the protons of coordinated 5MT in the mono-aqua complex and subscript i indicate the coordinated 5MT in the transient species. Labelling in the indole ring: A=position 4, B=position 6, C=position 7, D=position 2.

To shed light on the nature of the new species, we performed a 2D-NOESY NMR experiment with a recently irradiated solution of $[Ru(55dmb)_2(5MT)(H_2O)]^{2+}$ (Figure 5a). The J-coupling between the ortho-hydrogens of the 55dmb become evident for the pairs *b/c, d/e, h/i and j/k*, that present negative phase. The cross peaks for the pairs *c/d* and *i/j* that correspond to hydrogens in different rings, indicate that those hydrogens must be spatially close and can be regarded as a measurement of NOE sensitivity in the experimental conditions. These correlations also help to explain the proper connectivity between the pyridine rings in each bipyridine. Apart from these correlations, there is only one other single NOE cross-peak. The latter involves proton *a* in one of the 55dmb and *Di,* the hydrogen adjacent to the indolic nitrogen. This correlation supports a cyclic structure stabilized by η^2 to the metal center. (Figure 5b). On the other hand, no NOE correlation is apparent between the corresponding protons in the aqua complex, due to the expected longer distance. NOESY and COSY spectra of the non-irradiated complex are given as supplementary information (Figures S4-S5).

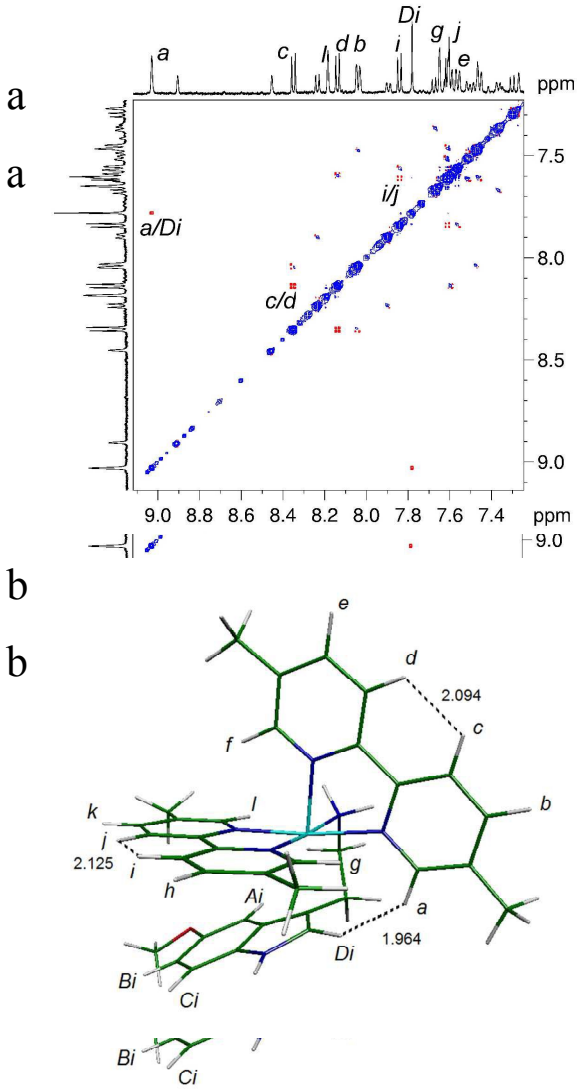

Figure 5. a) NOESY spectrum of $[Ru(55dmb)_2(5MT)]^{2+}$ immediately after irradiation of a D_2O solution of $[Ru(55dmb)_2(5MT)(H_2O)]^{2+}$. b) Proposed structure for the transient species, with the corresponding assignments.

The proposed structure is supported by DFT computations. Figure 6 depicts the optimized geometry computed for $[Ru(55dmb)_2(5MT)(H_2O)]^{2+}$ and the η^2-coordinated species, while Table S1 (supplementary information) collects the most significant structural parameters. $[Ru(55dmb)_2(5MT)(H_2O)]^{2+}$ resembles other experimental and computed structures based on the $\{Ru(bpy)_2\}^{2+}$ moiety,[34] with a Ruthenium center in a pseudo-octahedral environment comprised of five N-atoms and an O-atom. The Ru-X bondlengths (X = N, O) are slightly longer than the experimentally observed ones in available

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related compounds, as usual for this level of theory,[35-39] and deserve no further comment. Due to the relative flexibility of the aliphatic arm which connects the indole-like ring to the coordinating amino group in $[Ru(55dmb)_2(5MT)(H_2O)]^{2+}$, an elongation of the Ru-O bond followed by rotation of the indole arm of the 5MT ligand around the Ru-N-C-C dihedral angle brings the 5-member ring close to the metal center, yielding two separate $[Ru(55dmb)_2(5MT)]^{2+}$ and H_2O molecules. The optimized stationary point for the system is located 117 KJ mol^{-1} higher in energy than $[Ru(55dmb)_2(5MT)(H_2O)]^{2+}$. Two carbon atoms of the aromatic ring sit at an average distance of 2.65Å of the Ru-atom, resembling the coordination mode in η^2-coordinated unsaturated ligands. Table S1 and Figure 7 collect the most relevant metric parameters for this species, which apart from the coordination mode of the aromatic fragment has a well preserved coordination environment comprising five N-atoms. Folding of the 5MT substituent leaves the two H-atoms (labeled *a* and *Di* in Figure 5) 1.964 Å apart, in agreement with the observation of the NOESY signal (Figure 5a). The C=C bondlength at 1.412 Å in $[Ru(55dmb)_2(5MT)]^{2+}$ is slightly longer than the one in $[Ru(55dmb)_2(5MT)(H_2O)]^{2+}$ (1.391 Å) , suggesting a partial Ru-C bonding involving ligand centered orbitals of π-symmetry. The variation of the C-C Mayer bond order for both $[Ru(55dmb)_2(5MT)(H_2O)]^{2+}$ and $[Ru(55dmb)_2(5MT)]^{2+}$ and the computed Ru-C bond order (Table S1) also support the onset of a Ru-C bond. Though not unusual in organometallic Ru-based species, to our knowledge there is only one other available example of a (η^2-C=C)RuN_5 species, based on the $[Ru(NH_3)_5]^{2+}$ moiety and fumaric acid.[40] The latter shows a much shorter Ru-C bondlength at 2.172(6) Å, which in fact is comparable to other (η^2-C=C)Ru complexes, suggesting that our example actually holds a very weakly (and probably labile) coordinated "sixth" ligand. We failed to find similar stable adducts involving the heterocyclic moiety without an additional aliphatic side arm with a terminal amino group, a result that suggest that η^2-coordination of 5MT is only possible due to its additional coordination mode involving the pendant amino group.

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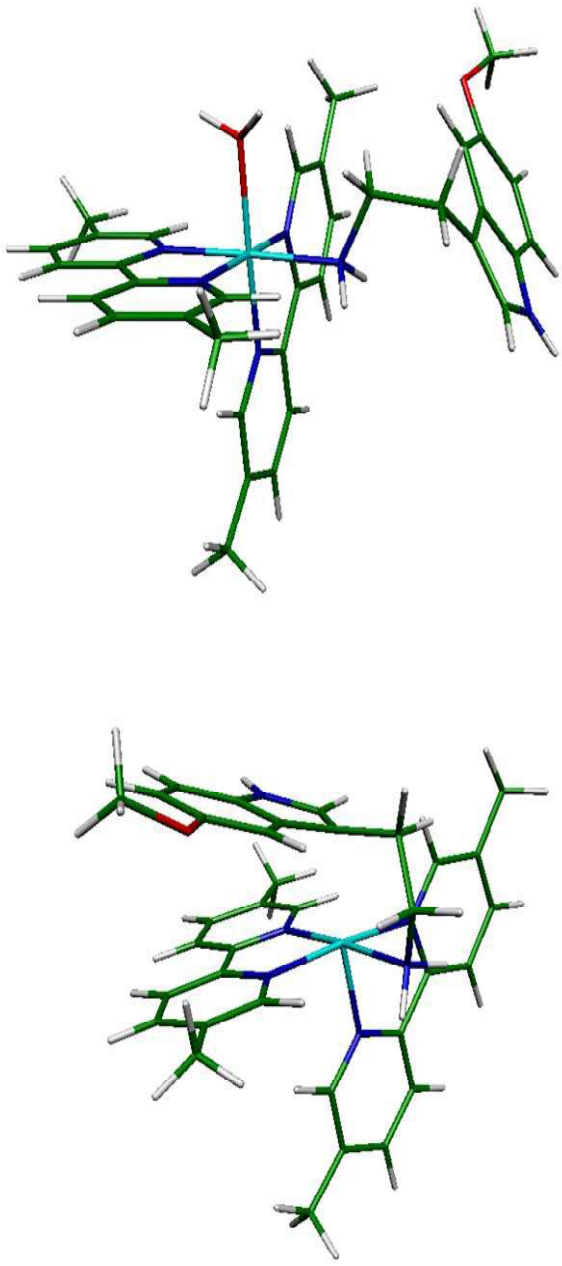

Figure 6. DFT optimized structures for (top) $[Ru(55dmb)_2(5MT)(H_2O)]^{2+}$ and (bottom) $[Ru(55dmb)_2(5MT)]^{2+}$ in vacuo.

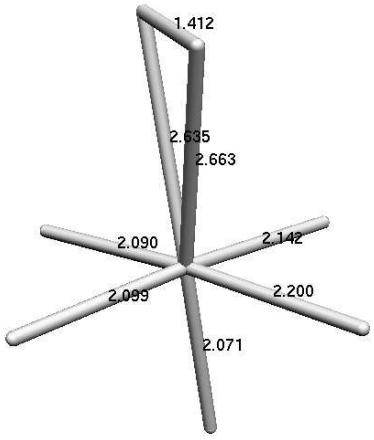

Figure 7. Coordination environment around the Ru^{II}-center in $[Ru(55dmb)_2(5MT)]^{2+}$

Figure 8 displays the experimental and DFT-computed electronic spectrum for $Ru(55dmb)_2(5MT)(H_2O)]^{2+}$. Due to specific solute-solvent interactions in $Ru(55dmb)_2(5MT)(H_2O)]^{2+}$ arising from hydrogen bonding between the coordinated and bulk water molecules the agreement between experimental and (TD)DFT predicted spectrum is not optimum. To account for this effect two additional structures adding one and two explicit H_2O molecules in the vicinity of the aqua ligand were computed without constrains at the same level of theory described above. Additional hydrogen-bridged water molecules increase the σ-donor ability of the coordinated aqua ligand, inducing slight modifications in the metric parameters of the other ligands in the first coordination sphere (DFT optimized structures in Figure S6). These changes also affect the MO energetic, destabilizing the metal center d_π set, and consequently shifting the Ru-to-bpy MLCT to lower energies. Both $Ru(55dmb)_2(5MT)(H_2O)]^{2+}$ and particularly $Ru(55dmb)_2(5MT)]^{2+}$ computed electronic spectra are in very good agreement with the experiment providing additional support for the proposed η^2-coordinated structure.

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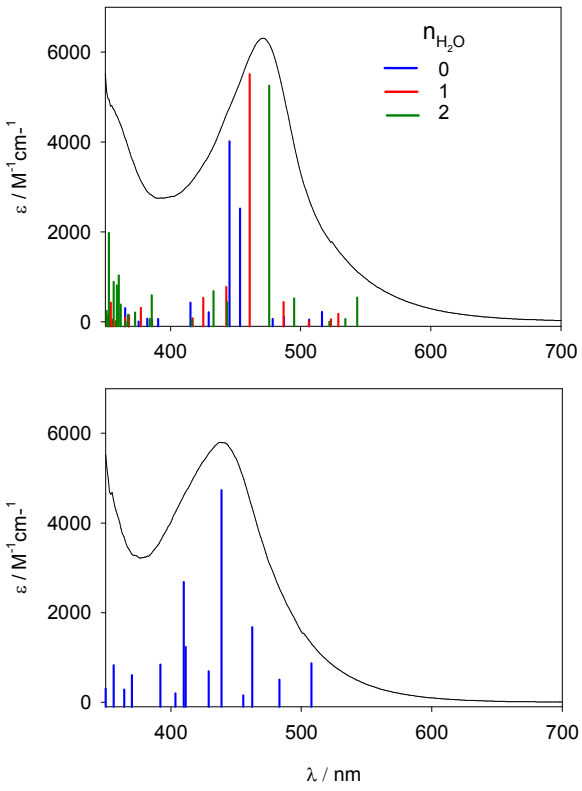

Figure 8. Experimental and computed (DFT, LanL2dz/B3LYP, PCM) spectra in water of [Ru(55dmb)2(5MT)(H2O)]2+ (top) and [Ru(55dmb)2(5MT)]2+ (bottom).

The photochemically cycled $[Ru(55dmb)_2(5MT)]^{2+}$ can revert to $[Ru(55dmb)_2(5MT)(H_2O)]^{2+}$ thermall. The usual photoreactivity of other $\{Ru(pp)_2\}^{2+}$ derived species suggests that the back-reaction can also be photo-initiated. Both pathways explain the reason why it is not possible to achieve full photoconversion to the cycled form but rather a stationary concentration which depends on the intensity and wavelength of the irradiation light. For a single wavelength irradiation the model can be written in differential form in the following way:

Eq. 1

$$\frac{d[B]}{dt} = I_{IRR}\,2.3(\varepsilon_A l[A]\varphi_{A\to B} - \varepsilon_B l[B]\varphi_{B\to A}) - k[B]$$

Where A represents the aqua complex, B the cycled metastable form, I_{IRR} is the irradiation intensity, ε_A and ε_B the respective molar absorptivities at the irradiation wavelength, l the optical path length, φ the quantum yields of the direct and inverse photoreactions and k the kinetic constant of the thermal inverse reaction. If measurements at different irradiation intensities are performed until reaching steady state (ss) and $[A]_{ss}/[B]_{ss}$ is plotted against $1/I_{IRR}$, the values of the obtained slope and ordinated are:

Eq. 2

$$m = \frac{k}{2.3\varphi_{A\to B} l \varepsilon_A} \qquad b = \frac{\varphi_{B\to A}\varepsilon_B}{\varphi_{A\to B}\varepsilon_A}$$

The irradiation was done using a 532 nm laser. By replacing the experimental values obtained under intensities between 3×10^{-6} and 3×10^{-5} einsteins/s and using the parameters ε_A=690 $M^{-1}cm^{-1}$ and ε_B=1435 $M^{-1}cm^{-1}$, we calculated the values of $\varphi_{A\to B}$ = 0.099 and $\varphi_{B\to A}$ = 0.046 at 25 °C. The detailed derivation of Eq. 2 is presented in ESI.

Similar transient products were observed in complexes bearing bpy instead of 55dmb, showing that the exact nature of the used polypiridine is not crucial. At the same time, modifications of the indolamine ligand that preserve the ring and the amine backbone also yielded the same results. This allowed us to compare the aquation of the cycled form of some other members of the family: $[Ru(bpy)_2(5MT)(H_2O)]^{2+}$, $[Ru(bpy)_2(TRYP)(H_2O)]^{2+}$ and $[Ru(bpy)_2(5HT)(H_2O)]^{2+}$. Once the complexes were irradiated until no further changes in their absorption spectra were evident (that is after achieving a stationary concentration), they were allowed to revert to the mono-aqua $[Ru(bpy)_2(L)(H_2O)]^{2+}$ species. This procedure was performed at different temperatures and repeated many times in a totally reversible way (see ESI, Figure S7). The kinetic traces for the dark back-reactions were fitted by monoexponential first-order expressions. Table 1 summarizes the rate constants and the Eyring activation parameters obtained in each case. The experimental rate constants show that 5HT and 5MT, which have groups that inject electron density to the π system of the indole ring, increase the transient's half-life compared to that of the irradiated complex bearing unsubstituted TRYP. This observation constitutes further evidence to support the η^2-coordination mode proposal. Higher electron availability within the aromatic system implies a somewhat stronger basicity and concomitant better coordination capacity of the aromatic ring. The Eyring plot depicted in Figure 9 shows that both the activation enthalpy $\Delta H^{\#}$ and the activation entropy $\Delta S^{\#}$ are independent

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of the ligand. The highly positive $\Delta S^{\#}$ value strongly suggests a dissociative mechanism for the metastable complex aquation.

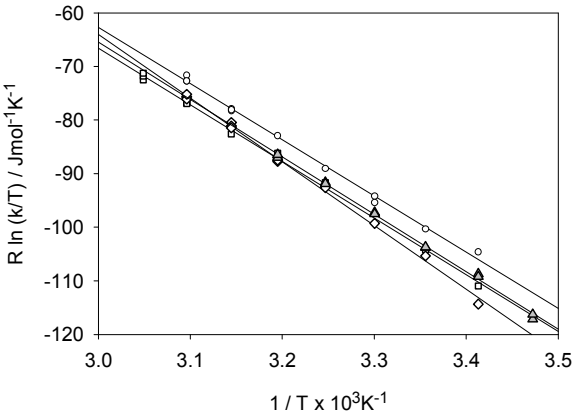

Figure 9. Eyring plot for the aquation of the bidentate complexes $[Ru(55dmbpy)_2(5MT)]^{2+}$, $[Ru(bpy)_2(5HT)]^{2+}$ (circles), $[Ru(bpy)_2(5MT)]^{2+}$ (triangles) and $[Ru(bpy)_2(TRYP)]^{2+}$ (squares) between 20 and 50 °C. Data are given in Table 1.

Table 1. Kinetics results from figure 9 and calculated Eyring parameters.

	20°C	25°C	30°C	35°C	40°C	50°C	$\Delta H^{\#}$	$\Delta S^{\#}$
	k ($10^{-4}s^{-1}$)	k ($10^{-4}s^{-1}$)	k ($10^{-4}s^{-1}$)	k ($10^{-4}s^{-1}$)	k ($10^{-4}s^{-1}$)	k ($10^{-4}s^{-1}$)	kJ / mol	J / mol.K
$[Ru(55dmb)_2(5MT)]^{2+}$	6.0	11.4	24.4	49.7	92.5		107 ±5	59 ±17
$[Ru(bpy)_2(5MT)]^{2+}$	4.7	10.7	23.7	50.3	98.9	314.0	106 ±5	53 ±16
$[Ru(bpy)_2(5HT)]^{2+}$	3.1	9.4	19.7	44.8	84.4	359.8	119 ±6	95 ±18
$[Ru(bpy)_2(TRYP)]^{2+}$	10.1	17.1	33.9	68.7	146.0	537.7	105 ±6	54 ±19

Conclusions

We have shown that the complexes of the form $[Ru(pp)_2(H_2O)(L)]^{2+}$, with pp a bidentate polypyridine and L an indolic ligand such as tryptamine, 5-hydroxytryptamine, 5-methyltryptamine or 1-methyltryptamine, which coordinate in a monodentate fashion involving an aliphatic amine nitrogen, undergo a transient isomerization when irradiated on the MLCT band. The transient species is compatible with a complex bearing a bidentate indolamine ligand in which the usually non-coordinating aromatic ring is actually coordinated to the Ru center in a η^2 fashion. This species stable enough in aqueous solutions to allow its characterization in the minutes scale before reverting to the initial aqua complex. The photoreaction can be performed many times without any signs of complex degradation. This bidentate species reverts to the monoaqua complex by means of a dissociative mechanism. This reversibility, added to the important conformational change associated to the photocyclization and the fact that several different indolamines behave in this way suggest that these structures can be used as a core for molecular switches, activatable optical probes and photoactivated molecular machines. Derivatization of the $\{Ru(pp)_2\}^{2+}$ core through the bipyridines would be an easy way to gain new functionalities as surface attachment, cell membrane anchoring and covalent bonding to other structures.

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